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Global Breast Cancer Conference 2023

"Go Beyond Cure of Breast Cancer"

Abstract Book

27Thu-29Sat April, 2023

Grand Walkerhill Seoul, Korea

한국유방암학회
Korean Breast Cancer Society

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*Exhibition: Vista Hall Lobby (B2F), Grand 1+2+3 (BIF)

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*ePoster Zone: Grand 1+2+3 (BIF)
*Exhibition: Vista Hall Lobby (B2F), Grand 1+2+3 (BIF)

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12:30-13:30	Break				
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15:00-16:15					Session for Breast Cancer Survivors 2 For Better Life of Breast Cancer Survivors KOR-ENG-VIET

*ePoster Zone: Grand 1+2+3 (BIF)
*Exhibition: Vista Hall Lobby (B2F), Grand 1+2+3 (BIF)

한국어 통역이 제공되는 세션입니다.
Sessions marked with a video icon will be broadcast live in RM 2 (Vista 3).

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Sessions marked with a video icon will be broadcast live in RM 2 (Vista 3).
KOR Korean Session (발표언어: 한국어)

한국어 통역이 제공되는 세션입니다.
KOR Korean Session (발표언어: 한국어)
KOR-ENG-VIET Korean Session-English, Vietnamese Simultaneous Interpretation to be Provided. (발표언어: 한국어 | 영어, 베트남어 동시통역 제공)

Day 1 April 27 (Thu)

09:00-10:15 Symposium 1 RM 1 (Vista 1+2)

Recent Strategies for ER+/HER2- Breast Cancer

Moderator **Young Jin Suh**
The Catholic Univ. of Korea, St. Vincent's Hospital, Korea

Moderator **Polly Suk Yee Cheung**
Hong Kong Sanatorium and Hospital, Hong Kong

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Hirslanden Klinik St. Anna, Switzerland

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National Cancer Center, Korea

Moderator **Jee Hyun Kim**
Seoul National Univ. Bundang Hospital, Korea

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ASAN Medical Center, Korea

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The Catholic Univ. of Korea, Seoul St. Mary's Hospital, Korea

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National Cancer Center, Korea

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Massachusetts General Hospital, U.S.A.

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Korea Univ. Anam Hospital, Korea

Moderator **Naoto Ueno**
Univ. of Hawai'i Cancer Center, U.S.A.

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Yale School of Medicine, U.S.A.

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Jeonbuk National Univ. Hospital, Korea

Moderator **Kevin Kalinsky**
Winship Cancer Institute of Emory Univ., U.S.A.

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Panelist **Fumikata Hara**
Cancer Institute Hospital of JFCR, Japan

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Moderator **Seock-Ah Im**
Seoul National Univ. Hospital, Korea

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Yale School of Medicine, U.S.A.

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Panelist **Fang-Ming Chen**
Kaohsiung Municipal Ta-Tung Hospital, Taiwan

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Moderator **Caroline Drukker**
Antoni van Leeuwenhoek Hospital - Netherlands Cancer Institute, Netherlands

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Presenter **Jong-Ho Cheun** *221*
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SMG-SNU Boramae Medical Center, Korea

Presenter **Dabin Kim** *222*
THE IMPACT OF CAVITARY MARGIN SHAVING OF BREAST CONSERVING SURGERY: THE ONCOLOGICAL OUTCOME
Soonchunhyang Univ. Hospital Bucheon, Korea

Presenter **Lorraine Ma** *223*
FUNCTIONALITY BETWEEN BREAST CONSERVATION SURGERY VS MASTECTOMY: SHORT TERM OUTCOME FROM A SINGLE INSTITUTION
Pamela Youde Nethersole Eastern Hospital, Hong Kong

Presenter **Jieon Go** *224*
POST-OPERATIVE OUTCOMES OF ROBOT-ASSISTED NIPPLE-SPARING MASTECTOMY WITH IMMEDIATE BREAST RECONSTRUCTION REGARDING TO ROBOT SURGICAL SYSTEMS
Severance Hospital, Korea

Presenter **Jijung Jung** *225*
COMPARISON OF LONG-TERM ONCOLOGICAL OUTCOMES OF CENTRAL LUMPECTOMY AND CONVENTIONAL BREAST-CONSERVING SURGERY FOR INVASIVE BREAST CANCE
Seoul National Univ., Korea

Presenter **Ruoh Yun Gau** *226*
RISK FACTOR OF SKIN AND NIPPLE-AREOLAR COMPLICATION AND ONCOLOGIC SAFETY IN DIFFERENT APPROACH NIPPLE SPARING MASTECTOMY: A LONG-TERM FOLLOW-UP IN A SINGLE MEDICAL CENTER
Kyungpook National Univ. Chilgok Hospital, Korea

Day 1 April 27 (Thu)

Presenter **Byeongju Kang** *227*
LONG-TERM ONCOLOGICAL OUTCOMES OF ONCOPLASTIC BREAST-CONSERVING SURGERY AFTER A 10-YEAR FOLLOW-UP: A SINGLE CENTER EXPERIENCE AND SYSTEMATIC LITERATURE REVIEW
Kyungpook National Univ. Chilgok Hospital, Korea

Presenter **Si Ying Tan** *228*
OCCULT LYMPH NODE METASTASES IN CLINICALLY NODE-NEGATIVE (CN0) BREAST CANCER PATIENTS REFERRED FOR NEOADJUVANT THERAPY (NAT)
Singapore General Hospital, Singapore

16:30-17:45 **GBCC-CACA Joint Session** **RM 5 (Art Hall)**

Programs for Breast Cancer Screening and Prevention

Moderator **Il Yong Chung**
ASAN Medical Center, Korea

Moderator **Peng Yuan**
Chinese Academy of Medical Sciences, Cancer Hospital, China

Speaker **Young-Joon Kang** *136*
KBCS GUIDELINES OF SCREENING AND CURRENT STATUS
The Catholic Univ. of Korea, Incheon St. Mary's Hospital, Korea

Speaker **Yongsheng Wang** *138*
CACA GUIDELINES OF SCREENING AND CURRENT STATUS
Shandong Cancer Hospital & Institute, China

Speaker **Yoo Seok Kim** *139*
KOREAN RECOMMENDATIONS FOR PREVENTION AND RISK MANAGEMENTS
Chosun Univ. Hospital, Korea

Speaker **Junjie Li** *140*
CHINESE RECOMMENDATIONS FOR PREVENTION AND RISK MANAGEMENTS
Fudan Univ. Shanghai Cancer Center, China

Panelist **Kyung-Hun Lee**
Seoul National Univ. Hospital, Korea

Panelist **Sung Eun Song**
Korea Univ. Anam Hospital, Korea

Panelist **Yanxia Shi**
Sun Yat-Sen Univ. Cancer Center, China

Panelist **Yu Ren**
The First Affiliated Hospital of Xi'an Jiaotong Univ., China

Day 2 April 28 (Fri)

08:30-09:15 **Satellite Symposium 2** **RM 1 (Vista 1+2)**

Moderator **Yee Soo Chae**
Kyungpook National Univ. Chilgok Hospital, Korea

Speaker **Kyung-Hun Lee** 175
PALBOCICLIB: ADDED VALUE OF LONG-TERM EFFICACY, SAFETY AND REAL-WORLD DATA
Seoul National Univ. Hospital, Korea

09:30-10:15 **Plenary Lecture 3** **RM 1 (Vista 1+2)**

Moderator **Gyungyub Gong**
ASAN Medical Center, Korea

Speaker **Edison Liu** 6
GENOMIC BIOLOGY OF TRIPLE NEGATIVE BREAST CANCER
The Jackson Laboratory, U.S.A.

10:30-11:45 **Symposium 5** **RM 1 (Vista 1+2)**

Single Cell Proteogenomic and Translational Research in Breast Cancer

Moderator **Eugene C. Yi**
Seoul National Univ., Korea

Moderator **Andi Cani**
Univ. of Michigan, U.S.A.

Speaker **Amos Lee** 23
SINGLE CELL GENOMICS IN BREAST CANCER
Seoul National Univ., Korea

Speaker **Junho Park** 24
SINGLE CELL PROTEOMIC TECHNOLOGY AND FUTURE
CHA Univ. College of Medicine, Korea

Speaker **Andi Cani** 25
SINGLE CELL GENOMICS OF CIRCULATING TUMOR CELLS IN BREAST CANCER
Univ. of Michigan, U.S.A.

10:30-11:45 **Panel Discussion 4** **RM 2 (Vista 3)**

Treatment Dilemma in the Management of Breast Cancer

Moderator **Sung Gwe Ahn**
Gangnam Severance Hospital, Korea

Moderator **Mehra Golshan**
Yale School of Medicine, U.S.A.

Speaker **Han-Byoel Lee** 55
CLINICAL STAGING IN BREAST CANCER PATIENTS UNDERGOING NEOADJUVANT TREATMENT
Seoul National Univ. Hospital, Korea

Speaker **Mehra Golshan** 56
CAN CT3/4 BREAST CANCER BE SAFELY TREATED WITH BREAST CONSERVING SURGERY AFTER NEOADJUVANT TREATMENT?
Yale School of Medicine, U.S.A.

Speaker **Jean-Francois Boileau** 57
IS SENTINEL LN BIOPSY FEASIBLE IN CLINICAL N2-3 PATIENTS AFTER NEOADJUVANT TREATMENT?
Jewish General Hospital, McGill Univ., Canada

Day 2 April 28 (Fri)

10:30-11:45 Education Session 4 RM 3 (Walker Hall 1)

Update of HER2+ Breast Cancer Treatment

Moderator **Kyung Hae Jung**
ASAN Medical Center, Korea

Moderator **Makiko Ono**
The Cancer Institute Hospital of JFCR, Japan

Speaker **Jee Hung Kim** 80
SYSTEMIC TREATMENT FOR HER2-POSITIVE EARLY BREAST CANCER
Yonsei Univ. College of Medicine, Korea

Speaker **Soo Chin Lee** 81
SYSTEMIC TREATMENT FOR HER2-POSITIVE METASTATIC BREAST CANCER
National Univ. Cancer Institute, Singapore

Speaker **Makiko Ono** 82
OVERVIEW AND MANAGEMENT OF ADVERSE EVENTS OF ANTI-HER2 ADCS
The Cancer Institute Hospital of JFCR, Japan

10:30-11:45 Oral Presentation 5 RM 4 (Walker Hall 2)

Moderator **Jai Min Ryu**
Samsung Medical Center, Korea

Moderator **Taeryool Koo**
Hallym Univ. Sacred Heart Hospital, Korea

Presenter **Tae Hyun Park** 229
COMPARATIVE MICROBIOME ANALYSIS OF THE CONTRACTED BREAST CAPSULE USING NEXT GENERATION SEQUENCING
Kyungpook National Univ. School of Medicine, Korea

Presenter **Young-Jin Lee** 230
FACTORS RELATED TO PREGNANCY RATE AND TIMING AFTER BREAST CANCER TREATMENT IN YOUNG PATIENTS
ASAN Medical Center, Korea

Presenter **Sum Lung Jeffrey Wong** 231
PRELIMINARY EFFICACY OF NEOADJUVANT NAB-PACLITAXEL AND PEMBROLIZUMAB-CONTAINING REGIMENS IN EARLY STAGED TRIPLE NEGATIVE BREAST CANCER (ETNBC) THERAPY
Queen Mary Hospital, Hong Kong

Presenter **Alan Prem Kumar** 232
DP103-REGULATED P53-SUMO/ACETYLATION SWITCH DETERMINES RESPONSE TO DOCETAXEL IN ERA-POSITIVE BREAST CANCER
National Univ. of Singapore, Singapore

Presenter **Sakshi Shukla** 233
KEY REGULATORS OF CHOLESTEROL AND LIPID METABOLISM AGGRAVATE BREAST CANCER
All India Institute of Medical Sciences, India

Presenter **Hyejo Ryu** 234
PATTERN AND COMPLICATION OF RECONSTRUCTED BREAST CANCER PATIENTS WHO RECEIVED POSTMASTECTOMY RADIOTHERAPY IN THE NATIONAL HEALTH INSURANCE SERVICE COHORT
Seoul National Univ. College of Medicine, Korea

Day 2 April 28 (Fri)

Presenter **Nalee Kim** 235
MULTIDIMENSIONAL LONGITUDINAL ASSESSMENT OF TOXICITY AND COSMESIS AFTER HYPOFRACTIONATED WHOLE-BREAST RADIOTHERAPY FOR BREAST CANCER AMONG A PROSPECTIVE COHORT OF KOREAN WOMEN: A PRELIMINARY RESULT
Samsung Medical Center, Korea

Presenter **Shraddha Kenekar** 236
IMPACT OF SURGICAL FACTORS ON AESTHETIC OUTCOME AFTER BREAST CONSERVATION THERAPY: A PROSPECTIVE COHORT STUDY
Tata Memorial Center, India

Presenter **Qingjian Li** 237
BIODEGRADEBLE AND REDOX-RESPONSIVE NANOPARTICLE PLATFORM WITH TROP2 ANTIBODY LINKAGE FOR RNA INTERFERENCE TARGETING LNCRNA MNX1-AS1 TO REDUCE RADIO-RESISTANCE IN TRIPLE NEGATIVE BREAST CANCER
Sun Yat-sen Memorial Hospital, China

10:30-11:45 Nursing Session 1 (Kor.) RM 5 (Art Hall)

The Managements for Cognitive Impairment Related to Breast Cancer

Moderator **Eun-Young Jun**
Daejeon Univ., Korea

Moderator **Nayeon Kim**
Samsung Medical Center, Korea

Speaker **Hee-Ju Kim** 151
THE IMPACT OF CHEMOTHERAPY ON COGNITIVE IMPAIRMENTS: EVIDENCE AND IMPLICATIONS
The Catholic Univ. of Korea, Korea

Speaker **Hyejin Cho** 153
THE COGNITIVE IMPAIRMENT IN BREAST CANCER PATIENTS UNDERGOING THERAPY
Ewha Womans Univ. Seoul Hospital, Korea

Speaker **Seung-Soo Baek** 155
BENEFICIAL EFFECTS OF EXERCISE ON CANCER-RELATED COGNITIVE IMPAIRMENT WITH BREAST CANCER PATIENTS
Sangmyung Univ., Korea

12:00-12:45 Plenary Lecture 4 RM 1 (Vista 1+2)

Moderator **In Ah Kim**
Seoul National Univ. Bundang Hospital, Korea

Speaker **Alphonse Taghian** 7
BREAST-CANCER RELATED LYMPHEDEMA: MYTHS, FACTS, RISK FACTORS AND NEW APPROACH
Massachusetts General Hospital, U.S.A.

13:00-13:45 Satellite Symposium 3 RM 1 (Vista 1+2)

Lilly Korea

Moderator **Jin Seok Ahn**
Samsung Medical Center, Korea

Speaker **Nadia Harbeck** 177
TAKE HOPE FURTHER FOR HR+HER2-HIGH-RISK EARLY BREAST CANCER PATIENTS WITH ABEMACICLIB
LMU Univ. Hospital, Germany

Day 2 April 28 (Fri)

14:00-14:45 **Plenary Lecture 5** **RM 1 (Vista 1+2)**

Moderator **Joon Jeong**
Gangnam Severance Hospital, Korea

Speaker **Michael Gnant** 8
ESCALATION AND DE-ESCALATION OF BREAST CANCER TREATMENT
Medical Univ. of Vienna, Austria

15:00-16:15 **Symposium 6** **RM 1 (Vista 1+2)**

The Role of Imaging in the Personalized Treatment

Moderator **Woo Kyung Moon**
Seoul National Univ. Hospital, Korea

Moderator **Bo Kyoung Seo**
Korea Univ. Ansan Hospital, Korea

Speaker **Mami Iima** 27
THE ROLE OF IMAGING FOR THE MANAGEMENT OF DCIS
Kyoto Univ. Hospital, Japan

Speaker **Savannah Partridge** 28
THE ROLE OF DW-MRI IN THE PERSONALIZED SCREENING AND DIAGNOSIS
Univ. of Washington, U.S.A.

Speaker **Vivian Youngjean Park** 30
QUANTITATIVE IMAGING IN OUTCOME PREDICTION OF BREAST CANCER
Yonsei Univ. College of Medicine, Korea

15:00-16:15 **Panel Discussion 5** **RM 2 (Vista 3)**

Locoregional Treatment for Advanced/Recurrent Breast Cancer

Moderator **Seung Ki Kim**
CHA Bundang Medical Center, Korea

Moderator **Andreas Karakatsanis**
Uppsala Univ. Hospital, Sweden

Speaker **Geok Hoon Lim** 59
SURGICAL EXTENT AFTER NEOADJUVANT CHEMOTHERAPY
KK Women's and Children's Hospital, Singapore

Speaker **Andreas Karakatsanis** 60
ROLE OF REPEAT BREAST-CONSERVING SURGERY FOR THE MANAGEMENT OF IPSILATERAL BREAST CANCER RECURRENCE
Uppsala Univ. Hospital, Sweden

Speaker **Sung-Ja Ahn** 62
RADIATION THERAPY ACCORDING TO RESIDUAL TUMOR VOLUME AFTER NEOADJUVANT CHEMOTHERAPY IN LOCALLY ADVANCED BREAST CANCER
Chonnam National Univ. Medical School, Korea

15:00-16:15 **Education Session 5** **RM 3 (Walker Hall 1)**

Liquid Biopsy: New Era of Cancer Management

Moderator **Keun Seok Lee**
National Cancer Center, Korea

Day 2 April 28 (Fri)

Moderator **Kan Yonemori**
National Cancer Center Hospital, Japan

Speaker **Eunhae Cho** 83
BASIC TECHNOLOGY OF LIQUID BIOPSY
GC Genome, Korea

Speaker **Kan Yonemori** 84
CLINICAL UTILITY OF DETECTION OF EARLY RECURRENCE OR MINIMAL RESIDUAL DISEASE USING LIQUID BIOPSY IN EARLY BREAST CANCER
National Cancer Center Hospital, Japan

Speaker **Jisun Kim** 85
CURRENT ADVANCES OF LIQUID BIOPSY IN TUMOR BURDEN DYNAMICS, RESPONSE MONITORING AND PROGNOSTIC MARKER IN METASTATIC BREAST CANCER
ASAN Medical Center, Korea

15:00-16:40 Endoscopic and Robotic Breast Surgery Session — RM 4 (Walker Hall 2)

Moderator **Hyukjai Shin**
Myongji Hospital, Korea

Moderator **Jesse Selber**
Corewell Health, U.S.A.

Speaker **Moo Hyun Lee** 104
CHALLENGES OF ROBOT BREAST SURGERY: IS THERE A ROLE FOR ROBOT BREAST SURGERY OUTSIDE OF CLINICAL TRIAL?
Keimyung Univ. School of Medicine, Korea

Speaker **Chi Wei Mok** 105
CHALLENGES OF ENDOSCOPIC BREAST SURGERY: IS IT JUST A BRIDGE FOR ROBOT BREAST SURGERY?
Changi General Hospital, Singhealth Duke NUS Breast Centre, Singapore

Speaker **Wen-Ling Kuo** 106
CURRENT STATUS OF ROBOT BREAST SURGERY
Chang Gung Memorial Hospital, Taiwan

Speaker **Jesse Selber** 107
ROBOT SURGERY FOR BREAST RECONSTRUCTION
Corewell Health, U.S.A.

15:00-16:15 Nursing Session 2 (Kor.) — RM 5 (Art Hall)

Living and Care as Women with Hereditary Breast Cancer

Moderator **Mi Young Kang**
Daerim St. Mary's Hospital, Korea

Moderator **Insook Lee**
Changwon National Univ., Korea

Speaker **Bom-Yi Lee** 156
AN OVERVIEW OF GENETIC COUNSELING FOR HEREDITARY BREAST AND OVARIAN CANCER SYNDROME
Daerim St. Mary's Hospital, Korea

Speaker **Ji Hye Yang** 158
GENETIC COUNSELING FOR HEREDITARY BREAST CANCER PATIENTS
ASAN Medical Center, Korea

Day 2 April 28 (Fri)

Speaker **Sun-Young Park** *160*
THE PROCESS OF CHOOSING CANCER RISK-REDUCING OPTIONS IN WOMEN WITH HEREDITARY BREAST CANCER: A GROUNDED THEORY STUDY
Daegu Catholic Univ., Korea

16:30-17:45 Symposium 7 RM 1 (Vista 1+2)

PMRT/RNI in the Modern Era

Moderator **Chang-Ok Suh**
CHA Bundang Medical Center, Korea

Moderator **Kyubo Kim**
Ewha Womans Univ. Mokdong Hospital, Korea

Speaker **Meena S. Moran** *32*
PERSONALIZATION OF PMRT IN THE MODERN ERA
Yale School of Medicine, U.S.A.

Speaker **Kyung Hwan Shin** *33*
THE BENEFIT OF PMRT FOR LOW NODAL BURDEN BREAST CANCER IN THE MODERN TREATMENT ERA
Seoul National Univ. Hospital, Korea

Speaker **Alice Ho** *35*
INCORPORATION OF NEW SYSTEMIC AGENTS IN PATIENTS TREATED WITH PMRT
Duke Univ., U.S.A.

16:30-17:45 Debate Session RM 2 (Vista 3)

Moderator **Jae Ho Jeong**
ASAN Medical Center, Korea

Panelist **Yeon Hee Park**
Samsung Medical Center, Korea

Panelist **Ian Krop**
Yale School of Medicine, U.S.A.

Panelist **Soo Chin Lee**
National Univ. Cancer Institute, Singapore

Speaker **Jieun Lee** *92*
ROLE OF PLATINUM AGENT IN EARLY TRIPLE NEGATIVE BREAST CANCER - PROS.
The Catholic Univ. of Korea, Seoul St. Mary's Hospital, Korea

Speaker **Min Hwan Kim** *93*
ROLE OF PLATINUM AGENT IN EARLY TRIPLE NEGATIVE BREAST CANCER - CONS.
Yonsei Univ. College of Medicine, Korea

Speaker **Dae-Won Lee** *94*
GENOMIC RISK VS. CLINICAL RISK IN EARLY-STAGE, HR+ BREAST CANCER - GENOMIC RISK
Seoul National Univ. Hospital, Korea

Speaker **Tae-Kyung Robyn Yoo** *96*
GENOMIC RISK VS. CLINICAL RISK IN EARLY-STAGE, HR+ BREAST CANCER - CLINICAL RISK
ASAN Medical Center, Korea

Day 2 April 28 (Fri)

16:30-17:45 Education Session 6 RM 3 (Walker Hall 1)

Post-operative Management and Surveillance Strategies for Breast Cancer Patients

Moderator **Tae Hyun Kim**
Inje Univ. Busan Paik Hospital, Korea

Moderator **An-Chieh Feng**
Tri-Service General Hospital, Taiwan

Speaker **Hyeong-Gon Moon** 87
SURVEILLANCE STRATEGY OVERVIEW IN KOREA
Seoul National Univ. Hospital, Korea

Speaker **An-Chieh Feng** 88
POST-OPERATIVE SURVEILLANCE AND MANAGEMENT FOR BREAST CANCER PATIENTS IN TAIWAN
Tri-Service General Hospital, Taiwan

Speaker **Jingmei Li** 89
THE STATE-OF-THE-ART RISK PREDICTION TOOLS AND HOW THEY APPLY TO ASIAN BREAST CANCER SCREENING PROGRAMS
Genome Institute of Singapore, Singapore

16:50-17:50 OPBS Session RM 4 (Walker Hall 2)

Moderator **Eun-Kyu Kim**
Seoul National Univ. Bundang Hospital, Korea

Moderator **Visnu Lohsiriwat**
Siriraj Hospital, Mahidol Univ., Thailand

Speaker **Ho Yong Park** 99
ONCOPLASTIC BREAST SURGERY: WHERE ARE WE?
Kyungpook National Univ. Chilgok Hospital, Korea

Speaker **Visnu Lohsiriwat** 101
ADVANCED SURGICAL TECHNIC FOR SUCCESSFUL OPBS IN BREAST CANCER
Siriraj Hospital, Mahidol Univ., Thailand

Speaker **Jung Ho Lee** 102
EVALUATION OF BREAST SYMMETRY AND COSMESIS FOR DENSE BREAST
The Catholic Univ. of Korea Bucheon St. Mary's Hospital, Korea

16:30-18:00 ABCN Business Meeting & Networking RM 5 (Art Hall)

Moderator **Sung-Bae Kim**
ASAN Medical Center, Korea

Speaker **Sung-Bae Kim**
OPENING REMARKS & INTRODUCTION
ASAN Medical Center, Korea

Speaker **Sibylle Loibl**
MENTORING FOR MENTORS SESSION: KEYNOTE LECTURE
GBG Forschungs GmbH, Germany

Hee Kyung Ahn
[PART 1] EXPERT PANEL DISCUSSION: NAVIGATING CHALLENGES AND BUILDING SYNERGIES IN BREAST CANCER RESEARCH: INSIGHTS FROM EXPERIENCED EXPERTS
Gachon Univ. Gil Medical Center, Korea

Day 2 April 28 (Fri)

Speaker **Kyung-Hun Lee**
TOPIC 1: THE ART OF MENTORSHIP: NURTURING A SUCCESSFUL CAREER AND STRATEGIES FOR EFFECTIVE COLLABORATION
Seoul National Univ. Hospital, Korea

Speaker **Yoo Seok Kim**
TOPIC2: BEYOND BORDERS: LEVERAGING INTERNATIONAL NETWORKS AND OVERCOMING PRACTICAL OBSTACLES
Chosun Univ. Hospital, Korea

Sung-Bae Kim
[PART 2] PROPOSAL & GENERAL DISCUSSION
ASAN Medical Center, Korea

Speaker **Sung Gwe Ahn**
PROPOSAL: NEOADJUVANT CHEMOTHERAPY OR UPFRONT SURGERY IN CLINICALLY NODE-POSITIVE, ER+HER2- BREAST CANCER: A MULTI-NATIONAL SURVEY STUDY
Gangnam Severance Hospital, Korea

Speaker **Hee Jeong Kim**
PRODUCT: KNOWLEDGE, ATTITUDES, AND BEHAVIORS TOWARD FERTILITY PRESERVATION IN PATIENTS WITH BREAST CANCER: A CROSS-SECTIONAL SURVEY OF PHYSICIANS
ASAN Medical Center, Korea

Speaker **Sung-Bae Kim**
GENERAL DISCUSSION (FEEDBACK) & WRAP-UP
ASAN Medical Center, Korea

18:00-18:45 **Satellite Symposium 4** **RM 1 (Vista 1+2)**

Novartis

Moderator **Woochul Noh**
Konkuk Univ. Medical Center, Korea

Speaker **Keun Seok Lee** *179*
OPTIMAL AND SEQUENTIAL TREATMENT STRATEGY FOR HR+ HER2- ABC PATIENTS FOR LONGER AND BETTER LIFE
National Cancer Center, Korea

Day 3 April 29 (Sat)

08:00-08:45 **Satellite Symposium 5** **RM 1 (Vista 1+2)**

AstraZeneca

Moderator **Kweon Cheon Kim**
Chosun Univ. Hospital, Korea

Speaker **Min Hwan Kim** *181*
ENHERTU, THE GAME CHANGER IN HER2+ MBC TREATMENT: FROM CLINICAL TRIAL TO CLINICAL PRACTICE
Yonsei Univ. College of Medicine, Korea

09:00-10:15 **Symposium 8** **RM 1 (Vista 1+2)**

Autologous Breast Reconstruction After Total Mastectomy

Moderator **Dong Won Lee**
Yonsei Univ. College of Medicine, Korea

Moderator **Toshihiko Satake**
Toyama Univ. Hospital, Japan

Speaker **Kyong-Je Woo** *36*
IS THE AUTOLOGOUS RECONSTRUCTION BETTER THAN THE IMPLANT OPTION?
Ewha Womans Univ. Mokdong Hospital, Korea

Speaker **Toshihiko Satake** *38*
AUTOLOGOUS BREAST RECONSTRUCTION: DIEP FLAP
Toyama Univ. Hospital, Japan

Speaker **Jung-Ju Huang** *39*
AUTOLOGOUS BREAST RECONSTRUCTION: PAP FLAP
Chang Gung Memorial Hospital, Taiwan

09:00-09:50 **Junior Doctors Forum** **RM 2 (Vista 3)**

Moderator **Ku Sang Kim**
Kosin Univ. Gospel Hospital, Korea

Speaker **Peter C. Dubsky** *148*
HOW TO BE A HAPPY SURGICAL ONCOLOGIST
Hirslanden Klinik St. Anna, Switzerland

Speaker **Jeong Eon Lee** *149*
GLOBAL MINDSET OF A BREAST CANCER SURGEON
Samsung Medical Center, Korea

09:00-10:15 **Panel Discussion 6** **RM 3 (Walker Hall 1)**

The Cost of Newly Approved Drugs: Can We Afford Them?

Moderator **Airi Han**
Yonsei Univ. Wonju College of Medicine, Korea

Moderator **Janice Tsang**
The Univ. of Hong Kong, Hong Kong

Speaker **Airi Han** *64*
THE VALUE OF THERAPEUTICS FOR BREAST CANCER
Yonsei Univ. Wonju College of Medicine, Korea

Day 3 April 29 (Sat)

Speaker **Thitiya Dejthevaporn** 65
ACCESS TO BREAST CANCER THERAPEUTICS IN ASIAN COUNTRIES
Ramathibodi Hospital, Mahidol Univ., Thailand

Speaker **Sung-Bae Kim** 66
ACCESS TO BREAST CANCER THERAPEUTICS IN KOREA
ASAN Medical Center, Korea

09:00-10:15 Survivorship Session 1 RM 4 (Walker Hall 2)

Cohort Study in Breast Cancer Survivor

Moderator **Min-Ho Park**
Chonnam National Univ. Hwasun Hospital, Korea

Moderator **Jihyoun Lee**
Soonchunhyang Univ. Hospital Seoul, Korea

Speaker **Rolf Stahel** 116
BUILDING ESMO CANCER REGISTRIES IN ASIA
ETOP IBCSG Partners Foundation, Switzerland

Speaker **Wei Zheng** 118
GENETIC RISK FACTORS OF BREAST CANCER IN ASIAN WOMEN
Vanderbilt Univ. School of Medicine, U.S.A.

Speaker **Susanna H. Hutajulu** 119
COLLABORATIONS OF COHORT STUDY IN SOUTHEAST ASIAN COUNTRIES
Universitas Gadja Mada, Indonesia

09:00-10:15 Practicing Breast Surgeons Session 1 (Kor.) RM 5 (Art Hall)

Benign Breast Condition

Moderator **Tae Ik Eom**
Hiu Breast & Thyroid Clinic, Korea

Moderator **Eun Jeong Jo**
Say-You Clinic, Korea

Speaker **Young San Jeon**
PATHOPHYSIOLOGY FOR MICROCALCIFIED BREAST LESION. BENIGN TO MALIGNANCY
Goo Hospital, Korea

Speaker **Eun Young Kim**
TIPS FOR DIFFERENTIATING BETWEEN MALIGNANT AND BENIGN MICROCALCIFICATIONS AFTER NEOADJUVANT CHEMOTHERAPY
Kangbuk Samsung Hospital, Korea

Speaker **Vivian Youngjean Park**
HOW TO MAKE THE MICROCALCIFICATIONS MORE VISIBLE WITH ULTRASOUND
Yonsei Univ. College of Medicine, Korea

Speaker **Dong-Seok Lee**
BIOPSY OF BREAST MICROCALCIFICATION - TOMOSYNTHESIS GUIDED, US GUIDED
Bunhongbitzro Hospital, Korea

Day 3 April 29 (Sat)

10:30-11:45 **Symposium 9** **RM 1 (Vista 1+2)**

Immunotherapy: Exploiting the Immune System for Breast Cancer Treatment

Moderator **Yeon Hee Park**
Samsung Medical Center, Korea

Moderator **Pamela Munster**
Univ. of California, San Francisco, U.S.A.

Speaker **Tira Tan** 40
INTEGRATING IMMUNOTHERAPY INTO THE TREATMENT STRATEGIES OF METASTATIC BREAST CANCER
National Cancer Centre Singapore, Singapore

Speaker **Pamela Munster** 41
ROLE OF IMMUNOTHERAPY FOR EARLY BREAST CANCER: TO WHOM, WHEN AND HOW
Univ. of California, San Francisco, U.S.A.

Speaker **Shigehira Saji** 42
EMERGING TARGETS OF IMMUNOTHERAPY IN BREAST CANCER
Fukushima Medical Univ., Japan

10:05-11:45 **Junior Doctors Debate** **RM 2 (Vista 3)**

Moderator **Han-Byoel Lee**
Seoul National Univ. Hospital, Korea

Moderator **Tristen Park**
Yale School of Medicine, U.S.A.

[Part 1: Voting]
UPFRONT SURGERY VS. NEOADJUVANT SYSTEMIC THERAPY WITH DUAL HER2 BLOCKADE FOR CT1CN0 HER2+ BREAST CANCE

Team 1 vs. Team 2
[Part 2: Debate on Topic #1]
CAN WE AVOID SENTINEL LYMPH NODE BIOPSY IN THE ELDERLY (AGE > 70)?

Team 3 vs. Team 4
[Part 3: Debate on Topic #2]
IS POST-MASTECTOMY RADIATION THERAPY (PMRT) NECESSARY FOR ONE POSITIVE LYMPH NODE?

10:30-11:45 **HBOC Session** **RM 3 (Walker Hall 1)**

Moderator **Sung-Won Kim**
Daerim St. Mary's Hospital, Korea

Moderator **Steven Narod**
Women's College Hospital, Canada

Speaker **Steven Narod** 109
MRI SCREENING AND BREAST CANCER MORTALITY IN BRCA1/2 CARRIERS
Women's College Hospital, Canada

Speaker **Ava Kwong** 111
GENETIC COUNSELING AND TESTING FOR BREAST AND OVARIAN CANCER IN ASIA
The Univ. of Hong Kong, Hong Kong

Day 3 April 29 (Sat)

Speaker **Jae Hoon Chung** *113*
HEREDITARY PROSTATE CANCER
Samsung Medical Center, Korea

10:30-11:45 **Survivorship Session 2** **RM 4 (Walker Hall 2)**

Management of Long-term/Late Complication After Breast Cancer Treatment

Moderator **Ilkyun Lee**
Catholic Kwandong Univ. College of Medicine, Korea

Moderator **Ho Hur**
National Health Insurance Service Ilsan Hospital, Korea

Speaker **Seung Hyun Chung** *121*
MANAGEMENT OF LYMPHEDEMA AND SHOULDER PAIN
National Cancer Center, Korea

Speaker **Eun-Jung Shim** *123*
MANAGEMENT OF COGNITIVE FUNCTION
Pusan National Univ., Korea

Speaker **Yoon-Sim Yap** *124*
MANAGEMENT OF ADVERSE EFFECTS FROM RECENTLY APPROVED BREAST CANCER DRUGS
National Cancer Centre Singapore, Singapore

10:30-11:45 **Practicing Breast Surgeons Session 2 (Kor.)** **RM 5 (Art Hall)**

Basic Skill for Breast Reconstruction

Moderator **Dong-Seok Lee**
Bunhongbitzro Hospital, Korea

Moderator **Jeong Kyeung Kim**
Maria Breast Clinic, Korea

Speaker **Sangdal Lee**
TRANSAXILLARY AUGMENTATION MAMMOPLASTY – ENDOSCOPIC BLOODLESS POCKET DISSECTION
MD Clinic, Korea

Speaker **Jae Hong Kim**
UNDERSTANDING OF BREAST IMPLANT AND ASSOCIATED COMPLICATION
The W Clinic, Korea

Speaker **Yong Suk Cho**
REPAIR OF SOFT TISSUE AND SKIN DEFECT USING ARTIFICIAL DERMIS
Hallym Univ. Hangang Sacred Heart Hospital, Korea

Speaker **Sung Hoon Kim**
MINIMAL INVASIVE TREATMENT OF INVERTED NIPPLE, AND PROSTHETIC NIPPLE FOR BREAST CANCER PATIENT: MODIFIED PURSE-STRING INVERTED NIPPLE CORRECTION
Chungdam The U Breast Surgery Center, Korea

13:30-14:45 **Session for Breast Cancer Survivors 1 (KOR-ENG)** **RM 5 (Art Hall)**

For Optimal Care After Breast Cancer Treatment

Moderator **Byung Ho Son**
ASAN Medical Center, Korea

Day 3 April 29 (Sat)

Moderator **Hyun-Ah Kim**
Korea Cancer Center Hospital, Korea

Speaker **Hwa Kyung Byun** *163*
MANAGEMENT AFTER RADIATION THERAPY (방사선치료 후 관리)
Yongin Severance Hospital, Korea

Speaker **Hyehyun Jeong** *164*
MANAGEMENT AFTER CHEMOTHERAPY (항암치료 후 관리)
ASAN Medical Center, Korea

Speaker **Hyeong-Gon Moon** *166*
SURVEILLANCE AFTER TREATMENT AND SCREENING OF FAMILY MEMBERS
(유방암 환자의 추적 검사 및 가족 검진)
Seoul National Univ. Hospital, Korea

15:00-16:15 Session for Breast Cancer Survivors 2 (KOR-ENG) RM 5 (Art Hall)

For Better Life of Breast Cancer Survivors

Moderator **Jong Han Yu**
Samsung Medical Center, Korea

Moderator **Seung Ah Lee**
CHA Bundang Medical Center, Korea

Speaker **Seockhoon Chung** *167*
BETTER SLEEP FOR BREAST CANCER SURVIVORS (유방암 생존자의 건강한 수면)
ASAN Medical Center, Korea

Speaker **Hee Jeong Kim** *168*
FERTILITY PRESERVATION FOR BREAST CANCER SURVIVORS (유방암 생존자를 위한 가임력 보존)
ASAN Medical Center, Korea

Speaker **Jung Eun Lee** *170*
HEALTH SUPPLEMENTS FOR BREAST CANCER SURVIVORS (방암 생존자의 건강보충제)
Seoul National Univ., Korea

Oral Presentation

Oral Presentation

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Plenary Lecture

"Go Beyond Cure of Breast Cancer"

A REVOLUTION IN THE MAKING: HOW ANTIBODY-DRUG CONJUGATES ARE TRANSFORMING BREAST CANCER TREATMENT

Ian Krop

Yale School of Medicine, Department of Medical Oncology, U.S.A.

The creation of a "magic bullet", a drug that specifically targets cancer cells without damaging normal tissues has been a long-time goal of oncology research. The development of antibody-drug conjugates (ADC) has been a significant step closer to this goal and is revolutionizing the treatment of breast cancer. ADC's consist of a monoclonal antibody targeting a cancer cell surface antigen coupled to a cytotoxic payload via a covalent linker. Trastuzumab emtansine (T-DM1), an ADC using a HER2-targeted antibody and an anti-microtubule payload, was the first ADC successfully developed in breast cancer. In two large, randomized trials of patients with pretreated HER2+ metastatic breast cancer (MBC), T-DM1 substantially improved overall survival and had less toxicity compared to chemotherapy and HER-2 therapy. T-DM1 thus fulfilled the promise of ADCs; demonstrating improved efficacy with decreased toxicity compared to conventional therapy. The success of T-DM1 led to the development of many 2nd generation ADC's.

Trastuzumab deruxtecan (T-DXd), a 2nd generation HER2-targeted ADC differs from T-DM1 in that it utilizes a potent topoisomerase I inhibitor payload and has a linker that allows for bystander killing, which may be important in tumors with heterogenous expression of HER2. In the Phase 3 Destiny Breast03 trial, T-DXd led to markedly improved overall survival compared to T-DM1 in HER2+ MBC and unprecedented durability of response (median Duration of Response 36.6 months). These data established T-DXd as the 2nd line standard of care. T-DXd does have higher levels of nausea, vomiting and fatigue compared to T-DM1 and is associated with a risk of interstitial lung disease (ILD) in 10-15% of patients, a potentially serious toxicity that requires monitoring.

An important complication of HER2+ MBC is the development of brain metastases, which can eventually occur in up to 50% of patients. While previous data suggested that large biologic agents such as antibodies and ADC's did not have substantial activity in the brain because of the blood brain barrier (BBB), recent results suggest that ADCs can actually have significant efficacy against brain metastases. In the Destiny Breast03 trial, T-DXD had a 63.9% intracranial response rate in patients with stable brain metastases and in several recent small studies in patients with progressive HER2+ brain metastases, T-DXd was associated with up to a 73% response rate. These data suggest that ADCs can have

meaningful activity in the CNS, perhaps because of breakdown in the BBB in the presence of metastatic lesions.

The high level of efficacy of T-DXd and other 2nd generation ADCs in HER2+ MBC led to interest in assessing their activity against cancers with lower levels of HER2 expression. The Destiny Breast04 trial assessed the efficacy of T-DXd compared to chemotherapy of physician's choice in patients with HER2 low cancers (IHC 1-2+, non-amplified cancers) who had received 1-2 prior chemotherapy agents for MBC. T-DXd improved both PFS (Hazard Ratio 0.50) and OS (Hazard Ratio 0.64) compared to chemotherapy, establishing T-DXd as the first standard of care agent for HER2-low breast cancer. The efficacy of T-DXd in HER2-low breast cancer, a population that is very common (55% of all breast cancers) and in which other HER2 agents such as trastuzumab had no activity, likely reflects the increased potency and bystander effect of T-DXd.

ADCs against other targets beyond HER2 have also proven clinically useful. Sacituzumab Govitecan is an ADC with a topoisomerase I inhibitor payload and an antibody targeting Trop-2, an epithelial antigen expressed on all subtypes of breast cancer. In both triple-negative and hormone receptor positive/HER2-negative MBC, Sacituzumab Govitecan demonstrated improved PFS and OS compared to chemotherapy in randomized phase 3 trials and is FDA approved in patients with both subtypes of MBC. Datopotamab deruxtecan, another ADC targeting Trop-2 and patritumab deruxtecan, targeting HER3, have both demonstrated promising levels of clinical activity in patients with pretreated MBC. Additional clinical trials of these agents are underway.

While multiple ADCs are now in clinical use, answers to a number of important questions are needed to optimize the use and further development of this class of agents. These include understanding the mechanisms by which cancers develop resistance to ADCs, what makes a good target antigen and does the level of this antigen matter, how best to sequence ADCs, and lastly, how to monitor, prevent and treat ILD?

With the approval of 3 ADCs for breast cancer and more in development, and substantial benefit across all subtypes and in both early and late stage disease, ADCs have revolutionized the treatment of breast cancer and their impact will increase in the years to come.

FERTILITY ISSUES IN YOUNG BREAST CANCER PATIENTS

Sibylle Loibl

GBG Forschungs GmbH, Scientific Director, Germany

All young or very young breast cancer patients should be counseled for fertility issues. Also women who have completed family planning should be informed about the risk of early menopause and loss of ovarian function induced by either chemotherapy and/or endocrine treatment.

Standard adjuvant/neoadjuvant anthracycline/taxane containing chemotherapy induce a transient or permanent loss of ovarian function. The younger the patient the more likely it is and that the ovarian function will be overcome and the patient regain premenopausal status. The median time to restoration of menstruation is about 7months. The majority of women will eventually restart menstruation especially those who are younger than 35 years. The probability to suffer from premature ovarian failure depends on age as well as on the given treatment. Higher amount of cyclophosphamide and longer chemotherapy regimen 24 vs 12 weeks are associated with a higher probability of POF. In general dose-dense regimen induce a higher rate of OFS. Tamoxifen in addition results in a higher rate of amenorrhea. Currently we do not know anything about the additional effect of checkpoint inhibitor therapy. The GeparDOUZE/B59 study did collect serum to investigate whether atezolizumab has an additional effect of POF and to generate more data on carboplatinum containing treatment. Patients with a COF loss seem to have a better outcome. If this effect is limited to patients with hormone receptor positive breast cancer is not clear.

Preservation of ovarian function should be differentiated from fertility preservation. While the first can be achieved when especially those under 40 receive an LHRH analogue starting at least two weeks prior to start of chemotherapy, the later needs referral to a specialist in reproductive medicine as the standard is cryoconservation of fertilized eggs/embryos.

Patients who wish to become pregnant after breast cancer should not be prohibited from doing so. The prognosis of a subsequent pregnancy does not seem to be decreased compared to women who did not become pregnant after breast cancer. This seems to be independent from the hormone receptor status. But we need to acknowledge that the data are limited. It is recommended to continue the endocrine therapy after pregnancy/lactation in order to complete at least 5 years of endocrine therapy.

The recently published POSITIVE trial investigated whether an early interruption of the endocrine therapy in order to become pregnant would influence the outcome, demonstrated that those who were enrolled into the study and tried to become pregnant did not have a worse outcome. The St. Gallen

panel in 2023 voted positive for interrupting the endocrine therapy in patients who want to become pregnant. There is a risk benefit analysis and patients need to be informed about their risk in order to make a well informed decision.

GENOMIC BIOLOGY OF TRIPLE NEGATIVE BREAST CANCER

Edison Liu

The Jackson Laboratory, Department of Research, U.S.A.

Systems genomics is the analysis of how all genes contribute to a specific phenotype or biological process. In cancer, combinations of key oncogenic drivers are required for the induction and sustenance of the malignant phenotype. We will describe how the genome structure is an oncogenic organizer that bundles oncogenes and tumor suppressors. Specifically, we have found a genomic configuration called the tandem duplicator phenotype (TDP) induced by specific drivers of genomic instability that generates combinations of oncogenic mutations. One form, the type 1 TDP is caused specifically by BRCA1 deficiency and mutations in TP53. We then dissected the role of type 1 TDP in chemotherapeutic resistance and found that the three key determinants of chemoresponsiveness are BRCA1 disruptive mutations, BRCA1 promoter methylation, and the expression of an immune signature. While BRCA1 mutant cancers are sensitive the cisplatin therapy, BRCA1 promoter methylated cancers quickly become demethylated restore BRCA1 expression and become platinum resistant. We call this process of chemoinsensitivity, adaptive resistance.

BREAST-CANCER RELATED LYMPHEDEMA: MYTHS, FACTS, RISK FACTORS AND NEW APPROACH

Alphonse Taghian

Massachusetts General Hospital, Department of Radiation Oncology, U.S.A.

Breast Cancer-Related Lymphedema (BCRL) is a devastating complication of axillary surgery and radiation. BCRL has a significant impact on patient's quality of life. There are several methods of measuring BCRL, as well as different definitions. The main risk factors for developing BCRL include axillary lymph node dissection (ALND), regional lymph node radiation (RLNR), BMI and other factors All risk factors will be presented. There have been precautionary measures being used to instruct patients (like avoid infusion, blood pressure, vaccines etc.. in ipsilateral arm and others) that have not been based on scientific facts; the myths and the facts about these measures will be covered. Also, means to reduce BCRL as well as future directions will be discussed.

ESCALATION AND DE-ESCALATION OF BREAST CANCER TREATMENT

Michael Gnant

Medical Univ. of Vienna, Comprehensive Cancer Center, Austria

To find the "right treatment for the right person" is the challenge of modern breast cancer treatment. With so many therapeutic options available, but also with our increasing understanding of the different molecular subtypes of the disease, we sometimes struggle to identify the optimal personalized approach. In terms of locoregional treatment, breast surgery has constantly been de-escalated over the last decades: From mastectomy to breast conservation, from axillary dissection to sentinel node biopsy major advantages for patients. There remain, however controversially discussed details e.g. how to deal with a single positive node after neoadjuvant systemic therapy? Also, in many instances, radiotherapy has been escalated after surgical de-escalation one may question whether that's eventually a good final result in terms of long-term side effects and morbidity. Furthermore, some of the pivotal trials are discussed by many, without the detailed knowledge of the limitations and scope this is true for ACOSOZ-Z011, AMAROS, but also for the most recent SOUND trial results. In general, radiotherapy has been de-escalated in terms of duration almost every indication can now be done in moderate hypofractionation. For systemic therapy, we are observing a constant decline of the use of "classical" cytotoxic chemotherapy in luminal breast cancer only few high-risk early breast cancer patients will need that if receptor-positive. For premenopausal patients at intermediate risk, however, controversy exists as to how to correctly interpret the results of trials such as RxPonder what is the actual contribution of the endocrine "side effect" of cytostatic therapy, i.e. ovarian function suppression? For endocrine therapy duration, the recent St.Gallen International Consensus Conference clearly defined that individual risk should be the determinant: Low risk = 5 years, intermediate to high risk 7 years, only patients at highest risk might benefit from an extension to 10 years treatment duration. For specific molecular subtypes, contemporary clinical trials have brought beneficial escalation: Adjuvant Olaparib for BRCA-germline-mutated disease, neoadjuvant pembrolizumab for triple-negative breast cancer of a certain size, adjuvant abemaciclib for high-risk luminal breast cancer. In summary, the "fine-tuning" of individualized breast cancer treatment strategies means de-escalation wherever possible, and escalation where indicated eventually further improving outcomes for our patients.

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OPTIMAL DURATION OF ENDOCRINE THERAPY

Polly Suk Yee Cheung

Hong Kong Sanatorium and Hospital, Department of Surgery, Hong Kong

Oestrogen receptor positive cancer is the most prevalent biological subtype of breast cancer. Adjuvant endocrine therapy after cancer surgery has substantially improve the outcome and contributed to their long term survival. While 5 years of endocrine therapy has been the standard recommendation for decades, the optimal duration of adjuvant endocrine therapy is a subject of debate.

The use of adjuvant endocrine therapy has substantially reduced breast cancer mortality by about a third throughout the first 15 years. However, more than half of the recurrences occurred beyond 5 years of treatment.

Anatomic stage remains the major determinant of late recurrences. The risk is around 10% for stage I cancers, but it increases to more than 30% in more advanced cancers with extensive nodal involvement. Biologic factors such as high grade and high Ki67 index are factors contributing to late recurrences.

Cancer cells from the primary breast cancer may disseminate into the blood stream early on and remained dormant. With change in the body microenvironment, immune surveillance and acquired resistance to endocrine therapy, late recurrences can occur from reactivation of these dormant cells. For these reasons, extended endocrine therapy is attempted in order to improve the long term outcome.

Various trials on extending the duration of adjuvant endocrine therapy has been conducted to address this question.

Extending adjuvant therapy of tamoxifen from 5 to 10 years or adding aromatase inhibitors for 5 years after tamoxifen for 5 years, both were shown to have a further reduction in recurrence and mortality particularly after year 10, thus reducing breast cancer mortality by about half throughout the second decade.

The added benefit of aromatase inhibitor by early switch from tamoxifen has shown to improve outcome. Studies addressing the prolonged use of aromatase inhibitor from 5 to 7 years was found to be beneficial, but not necessarily up to 10 years. However, prolonged endocrine therapy could also lead to increased side effects.

A tailored approach should be undertaken to weigh the anatomic and biologic risk of recurrence against the side effects of prolonged treatment. Individual patient should be well informed of the considerations to help reach an informed share-decision on the most appropriate course of therapy.

THE ROLE OF CDK4/6 INHIBITORS IN ER+/HER2- EARLY BREAST CANCER

Tadahiko Shien

Okayama Univ. Hospital, Department of Breast and Endcrone Surgery, Japan

Recently, adjuvant systemic therapy for ER+/HER2- early breast cancer has been improving exciting. A prospective randomized trial confirmed the prognostic efficacy of an additional CDK 4/6 inhibitor (abemaciclib) to adjuvant hormone therapy. Patients with high recurrence risk factors (>pN2 or pN1 with >pT3 or HG3) should receive two years of additional abemaciclib. Abemaciclib has relatively strong adverse events affecting daily life. Diarrhea should be carefully controlled by supportive care, and the cost of drugs is a significant social problem. However, no similar data exists for the other two CDK 4/6 inhibitors, and the reasons are discussing.

On the other hand, systemic chemotherapy will omit for postmenopausal patients with low recurrence scores (RS) Oncotype DX, regardless of the nodal status. Postmenopausal patients with lymph node metastasis should receive systemic chemotherapy if the RS is low. But it is under debate that the main reason for the efficacy of chemotherapy is suppressing ovarian function, and ovarian suppression by LH-RH agonists has a similar effect to chemotherapy. Adjuvant PARP inhibitors for one year after adjuvant chemotherapy should recommend for HBOC patients. The ER-positive BC patients with lymph node metastases (>pN2) should receive them. Moreover, POTENT trial confirmed the prognostic efficacy of additional adjuvant oral FU drugs for ER+/HER2- early breast cancer patients.

However, the inclusion criteria of these trials were different. The optimal adjuvant systemic therapy for these patients is very confusing. There is no data about additional abemaciclib or PARP inhibitor for RS score low and node-positive patients without adjuvant systemic therapy. We don 't know which is effective for HBOC patients, whether abamaciclib or PARP inhibitor. Which is better treatment for ER+/HER2- early BC, whether abamaciclib or oral-Fu? CDK 4/6 inhibitor, abemaciclib, prolonged survival of ER+/HER2- BC patients, but some critical questions must be solved.

ER+/HER2 NEGATIVE PREMENOPAUSAL BREAST CANCER- THE BIOMARKER WAY FORWARD

Peter C. Dubsky

Hirslanden Klinik St. Anna, Department of Surgery, Switzerland

ER+ breast cancer arising in women with intact menstrual cycles has been shown to have both quantitatively but also qualitatively distinct features to similar tumor biologies diagnosed in postmenopausal women. It is perhaps therefore not surprising that prospective validation of gene expression tests has largely failed in young women.

This lecture will briefly review data from large, prospective, randomized clinical trials with a focus on finding the right endocrine treatment and review some of the available data on adjuvant chemotherapy; keeping in mind that these treatments may have important interactions with each other.

In addition, risk assessment to identify women at high and low risk of recurrence will be reviewed and set into context with current adjuvant treatment regiments including the use of abemaciclib in this population.

IS HER2-LOW BREAST CANCER AN INDEPENDENT/ DISTINCTIVE SUBTYPE?

Naoto Ueno

Univ. of Hawai'i Cancer Center, Department of Medical Oncology, U.S.A.

Breast cancer is a heterogeneous disease with various subtypes that differ in terms of molecular and clinical characteristics. One such subtype is HER2-low breast cancer, which is characterized by low levels of human epidermal growth factor receptor 2 (HER2) expression. We define low HER2 as 1+ or 2+ with immunohistochemical staining and HER2 ISH being negative. This category of molecular subtype, low HER2, was labeled previously as "HER2-negative breast cancer." However, with the DESTINY Breat04 study, trastuzumab deruxtecan (T-DXd) showed a clinically significant benefit for patients with low HER2 metastatic breast cancer.

However, the clinical significance and independent nature of HER2-low breast cancer remain unclear from the biological perspective. This talk aims to evaluate the existing evidence regarding the distinctiveness of HER2-low breast cancer and its potential clinical implications. It provides an overview of the current understanding of HER2-low breast cancer, including its prevalence, molecular characteristics, and clinical behavior.

The talk also discusses the challenges associated with diagnosing and treating HER2-low breast cancer and the need for further research to elucidate its clinical significance.

Overall, the talk will conclude that HER2-low breast cancer represents a unique clinical subtype of breast cancer, for the time being, with unclear molecular features that require further investigation to optimize treatment strategies and improve patient outcomes.

HOW TO IDENTIFY HER2-LOW BREAST CANCER

Hee Jin Lee

ASAN Medical Center, Department of Pathology, Korea

HER2 expression in breast cancer can be heterogeneous and various guidelines for assessment of HER2 expression in breast cancer are exist. For several decades, identification of HER2 overexpressing or amplified cases was priority of HER2 assessment. However, significance of HER2-low breast cancer has been emphasized recently, and it has become important to discriminate HER2 IHC 0 from 1+. Discordance between pathologies is substantial especially for HER2 0 vs 1+ using current assessment system. We also need to pay attention to antibodies and specimen type (biopsy vs. surgery). Revised scoring systems and novel methods to identify HER2-low breast cancer are suggested.

TARGETING HER2-LOW AND THE TREATMENT SEQUENCE

Wei-Pang Chung

National Cheng Kung Univ. Hospital, Department of Medical Oncology, Taiwan

Patients diagnosed with HER2-positive breast cancer have shown a significant improvement in their overall survival rates as a result of HER2-directed therapy. HER2-positive early-stage and metastatic breast cancer patients who are treated with anti-HER2 monoclonal antibodies (trastuzumab and pertuzumab), tyrosine kinase inhibitors (lapatinib, neratinib, and tucatinib), or antibody-drug conjugates (trastuzumab emtansine and trastuzumab deruxtecan) have better survival outcomes. Owing to the fact that HER2 expression can be found in HER2 IHC 1+ and HER2 IHC 2+ breast cancer with a negative FISH result, numerous efforts have been made to investigate the effectiveness of HER2-directed therapies in the HER2-low disease. The joint analysis of the H0648g, H0649g, and H0650g studies revealed that the advantage of trastuzumab remained for metastatic breast cancer patients with HER2-FISH-positive disease. Moreover, according to the results of NSABP-B47, the addition of trastuzumab for one year in the adjuvant setting did not improve the outcomes of patients with HER2-low disease. Not only trastuzumab but also trastuzumab emtansine fails to prove its efficacy in patients with HER2-low metastatic breast cancer.

In the DESTINY-Breast03 clinical trial, the new antibody-drug conjugate trastuzumab deruxtecan established its superiority over trastuzumab emtansine in patients with HER2-positive metastatic breast cancer. Moreover, trastuzumab deruxtecan demonstrated, through the bystander effect, that it might be beneficial to patients with HER2-low metastatic breast cancer after the evaluation of early-phase clinical trials. Indeed, the DESTINY-Breast04 phase III trial demonstrated that trastuzumab deruxtecan is superior to the physician's choice of chemotherapy for patients with HER2-low metastatic breast cancer, encompassing hormone receptor-positive and -negative subgroups. In the hormone receptor-positive cohort, median progression-free survival was 10.1 months in the trastuzumab deruxtecan group and 5.4 months in the physician's choice group (hazard ratio for disease progression or death, 0.51; $P < 0.001$). In the hormone receptor-negative cohort, median progression-free survival was 8.5 months in the trastuzumab deruxtecan group and 2.9 months in the physician's choice group (hazard ratio, 0.46; 95% confidence interval, 0.24 to 0.89). After a long journey, the HER2-directed therapy with trastuzumab deruxtecan finally crosses the boundary set for other anti-HER2 agents and establishes its efficacy in HER2-low breast cancer. In the near future, we may anticipate the development of strategies or drugs for patients with HER2-low breast cancer.

NOVEL ORAL SERD AND ITS IMPLICATION IN CLINICAL PRACTICE

Yen-Shen Lu

National Taiwan Univ. Hospital, Department of Medical Oncology, Taiwan

Several endocrine therapies are currently available for the treatment of estrogen receptor (ER) positive breast cancer, but eventually the endocrine therapy drug resistance will occur. One of the important mechanism of endocrine therapy resistance is ESR1 mutations. Fulvestrant is the first-generation selective estrogen receptor degrader (SERD) has activity against ESR1 mutant tumors but has poor bioavailability therefore requires intramuscular injection and precludes optimal drug dosing. Currently, several second-generation SERDs are under developed. They are more potent and have improved oral bioavailability and pharmacokinetics. This talk will summarize the background of oral SERD development, the current status and results of clinical trials, and future perspectives.

TREATMENT STRATEGY AFTER PROGRESSION ON CDK4/6 INHIBITOR

Nadia Harbeck

LMU Univ. Hospital, Department of Breast Center, Germany

In HR+ HER2- metastatic breast cancer (MBC), CDK 4/6 inhibitors have become standard of care for the first line setting. After progression on CDK 4/6 inhibitors, optimal standard therapy is not well defined. In general, an endocrine-based approach is preferred unless there is life threatening disease. Several endocrine-based options are available depending for example on additional biomarkers, duration of response to the prior CDK 4/6 inhibitor therapy, patient comorbidities, performance status, and preferences. Additional biomarkers that are important for decision making at this point include ESR1, PIK3CA and gBRCA mutation status. In 2nd line after CDK 4/6i, treatment with CDK 4/6i beyond progression is effective as demonstrated by the MAINTAIN trial. Based on the available evidence, efficacy of this approach may be best if endocrine therapy and CDK 4/6i are changed. Another therapy option is the mTOR inhibitor everolimus which may be combined with exemestane, but also with fulvestrant or tamoxifen. For tumors haboring a PIK3CA mutation, alpelisib in combination with fulvestrant was approved based on the SOLAR-1 results. Recently, the first oral SERD, elacestrant, has been approved by FDA for treatment of tumors with an ESR-1 mutation based on the results of the EMERALD trial.

If there is life-threatening disease progression or after exhaustion of endocrine-based therapy options, chemotherapy is indicated. For patients with a gBRCA mutation, a PARP inhibitor is an evidence-based alternative to mono-chemotherapy with superiority regarding PFS. Moreover, novel ADCs have been shown beyond 1st line chemotherapy to be superior to monochemotherapy regarding OS, such as T-DXd in HER2-low and sacituzumab govitecan in HR+ HER2- MBC.

Next to all these evidence-based treatment options, participation a clinicial trial is preferred as it may give access to promising novel therapies even before approval.

NEW TARGETS BEYOND CDK4/6 INHIBITOR: DEVELOPMENT IN PROGRESS

Yong Wha Moon

CHA Bundang Medical Center, Department of Hematology and Oncology, Korea

Dysregulation of cyclin-dependent kinases (CDKs) mainly CDK4/6 and retinoblastoma protein (RB) pathway leads to sustained cellular proliferation and has been associated with the pathogenesis of hormone receptor (HR)-positive breast cancer. CDK4/6 inhibitor combined with endocrine therapy has emerged as a main treatment strategy for HR-positive/HER2-negative breast cancer as a first-line or subsequent line of therapy. Despite promising clinical outcomes, intrinsic or acquired resistance to CDK4/6 inhibitors has limited the success of these treatments.

I categorize the various mechanisms that are directly or indirectly responsible for CDK4/6 inhibitors resistance into two broad groups; cell cycle-specific mechanisms and cell cycle-nonspecific mechanisms. Cell cycle-specific resistance mechanisms include the loss of RB, activation of CDK2-cyclin E pathway, p16 amplification, amplification of CDK6, CDK4 or CDK7, and MDM2 overexpression, etc., whereas, cell cycle-nonspecific resistance mechanisms include activation of growth factor pathways such as FGFR or PI3K/AKT/mTOR, loss of FAT1, and activation of EMT pathway, etc. To overcome CDK4/6 inhibitor resistance, lots of efforts have been made by targeting these resistance pathways. Currently, CDK2/4/6 inhibitor and CDK7 inhibitor are under clinical trial and taking the lead.

In the meeting, I will present various resistance mechanisms and overcoming strategies in development in more detail.

INDIVIDUALIZED SURGICAL EXTENT AND LUMPECTOMY MARGIN IN EARLY-STAGE BREAST CANCER: DOES TUMOR HISTOLOGY AND SUBTYPE MATTER?

Naoki Hayashi

Showa Univ. School of Medicine, Department of Breast Surgical Oncology, Japan

Surgical margin-positive is known as one of risk factor of local recurrence. Even for ductal carcinoma in situ (DCIS), once local recurrence occurred, a half of the recurrent tumor will be upgraded to invasive carcinoma. Therefore, appropriate surgical procedure and accurate pathological assessment are fundamental.

A Meta-analysis of 33 studies by Houssami et al has reported that margin-positive of invasive carcinoma had double the risk of local recurrence. In addition, margin width (0 mm, 1 mm, 2 mm, 5 mmwas not associated with local recurrence rate.

Recent advance of radiological assessment and systemic therapy improved local recurrence rate and patients' prognosis. Based on these facts, Society of Surgical OncologySSOand American Society for Radiation OncologyASTRO defined margin-positive after breast-conserving surgery for Stage - invasive carcinoma as the presence of invasive or non-invasive cancer cells on surgical margin. On the other hand, they defined a 2-mm margin as the standard for an adequate margin in DCIS. However, there is no clear evidence to define a 2-mm margin for DCIS.

Horattas I. et al has reported that molecular subtype did not predict margin status. They concluded molecular subtype should not consider for surgical decision-making. The SSO and ASTRO guideline has recommended that margins wider than no ink on tumor are not indicated based on biologic subtype from the results of multiple retrospective studies.

For patients who have received preoperative chemotherapy, the chance to undergo breast-conserving surgery will be increased. However, accurate assessment of residual tumor spread become more difficult for patients who received preoperative chemotherapy than those who did not received chemotherapy. The EBCTCG meta-analysis involving 4756 women in ten trials has shown that local recurrence risk after preoperative chemotherapy was higher and the local recurrence was a prognostic factor. A large population of estrogen receptor-positive or HER2-positive breast cancer had residual in situ component after preoperative chemotherapy. Radiological findings before treatment should be considered to decide surgical procedure. Our multicenter prospective study has reported that many patients with any subtype

who were assessed by MRI and ultrasounds as ycT0/is after preoperative chemotherapy had residual tumors: negative predictive value was 65.5% for TNBC, 84.6% for ER-negative/HER2-positive, and 70.0% for ER-positive/HER2-positive (N Hayashi et al, Spotlight session San Antonio Breast Cancer Symposium 2021). About a half of these residual tumor was in situ lesion for all subtype.

Our pooled-analysis also has showed that ER-negative, node-positive preoperatively, absence of pN0, and > 3 positive nodes were independent predictive fators of local recurrence rather than margin status for patients who did not achieved pathologic complete response (A Valachis, E Mamounas, E Mittendorf, N Hayashi et al, Cancer Aug 2018).

In terms of histological type for margin status, invasive lobular carcinoma has a trend of wider tumor spread than that of radiological assessment. However, Wider negative margins than no ink on tumor are not indicated for invasive lobular cancer if margin-negative was confirmed on breast-conserving surgery based on retrospective studies. The Guideline based on retrospective studies recommended that margin width should not be altered for invasive lobular histology.

In contrast to DCIS, the presence of lobular carcinoma in situ (LCIS) at the margin does not impact ipsilateral breast tumor recurrence (IBTR). Therefore, additional resection for LCIS is not routinely recommended. Although there is concern that the pleomorphic LCIS with high grade features may have an increased risk of recurrence when at the margin. Compared to classical LCIS, there is an only limited data of small retrospective studies to address this question. Further studies are warranted.

In conclusion, regardless of molecular subtype, histological type of breast cancer, or receiving preoperative chemotherapy, accurate preoperative assessment of tumor spread and performance of surgical procedure are important.

THE ROLE OF AXILLARY SURGERY FOR DCIS AND EARLY-STAGE BREAST CANCER

Wonshik Han

Seoul National Univ. Hospital, Department of Surgery, Korea

Following sentinel lymph node biopsy (SLNB), the axillary recurrence rate is very low although SLNB has a false-negative rate of 5-10%. In the ACOSOG Z0011 trial, non-sentinel positive-lymph nodes were found in more than 20% of the axillary dissection group; the SLNB only group did not have a higher axillary recurrence rate. These findings raised questions about the direct therapeutic effect of the SLNB. SLNB has post-surgical complications including lymphedema. Considering advances in imaging modalities and adjuvant therapies, the role of SLNB in early breast cancer needs to be re-evaluated.

The NAUTILUS trial is a prospective multicenter randomized controlled trial involving clinical stage T1-2 and N0 breast cancer patients receiving breast-conserving surgery (BCS). Axillary ultrasound was mandatory before surgery with predefined imaging criteria for inclusion. Ultrasound-guided core needle biopsy or needle aspiration of a suspicious node was allowed. Patients were randomized (1:1) into the no-SLNB (test) and SLNB (control) groups. A total of 1734 patients were needed, considering a 5% non-inferiority margin, 5% significance level, 80% statistical power, and 10% dropout rate. All patients in the two groups received ipsilateral whole-breast radiation according to a predefined protocol. The primary endpoint of this trial is the 5-year invasive disease-free survival. The secondary endpoints are overall survival, distant metastasis-free survival, axillary recurrence rate, and quality of life of the patients. October 2022, 1734 patient enrollment was finished and follow-up is ongoing.

De-escalation of breast and axilla surgery is a big trend world-wide. At least four trials omitting axilla surgery in non-neoadjuvant early breast cancer patients receiving BCS are ongoing worldwide including our NATUTILUS trial. Meta-analysis and in-depth subgroup analysis must be needed in the future. On the other hand, trials omitting SLNB after NCT patients are ongoing including Korean studies, ASLAN and OPTIMIST. We expect that these studies would change current practice in the near future.

PRE-OPERATIVE GENOMIC ASSAY FOR BREAST SURGERY GUIDANCE IN HR+/HER2- BREAST CANCER

Caroline Drukker

Antoni van Leeuwenhoek Hospital - Netherlands Cancer Institute, Department of Surgical Oncology, Netherlands

The past decades gene expression profiles were developed and implemented in daily clinical practice to guide adjuvant systemic treatment decisions in women with early stage breast cancer. In the Netherlands the 70-gene signature (Mammaprint) is one of the most commonly used gene assays in breast cancer.

The prognostic value of the 70-gene signature was evaluated in the MINDACT trial. The results of this trial have shown that for post-menopausal women with HR+/HER2- breast cancer with a low risk 70-gene signature result chemotherapy can safely be omitted. In this trial chemotherapy was administered in the adjuvant setting. When it became possible to run the gene assay on FFPE samples, the possibility to use the 70-gene signature in the neo-adjuvant setting emerged. Therefore nowadays gene expression profiles can also help guide neo-adjuvant treatment decisions in HR+, HER2- breast cancer patients and therefore have an impact on the type of surgery that is required.

SINGLE CELL GENOMICS IN BREAST CANCER

Amos Lee[1], Sumin Lee[2], Sunghoon Kwon[1,2]

[1]*Seoul National Univ., Bio-max Institute, Korea,*
[2]*Meteor Biotech, Co. Ltd., Department of Research and Development, Korea*

Recent advances in single-cell omics technologies have revolutionized our understanding of the complexity and heterogeneity of cancer cells, leading to new insights into the molecular mechanisms of cancer initiation and progression. In breast cancer research, the development of spatially-resolved Laser Activated Cell Sorting (SLACS) has enabled the isolation and analysis of rare and heterogeneous populations of cancer cells within the tumor microenvironment, providing unprecedented opportunities to explore the spatial and temporal dynamics of cancer cells at the single-cell level.

In this presentation, we will discuss the latest advancements in spatial and single-cell omics technologies in breast cancer research, with a particular focus on the applications of SLACS. We will present data demonstrating the power of SLACS in identifying subpopulations of cancer cells with distinct molecular features and spatial localization within the tumor microenvironment. Furthermore, we will highlight the potential of SLACS in drug target discovery and biomarker identification for personalized cancer therapies.

We will also discuss the challenges and opportunities in translating these technologies into clinical applications, including the development of diagnostic and therapeutic tools. Overall, our presentation aims to showcase the promise of spatial and single-cell omics technologies in breast cancer research and their potential to unleash new hope for cancer patients.

SINGLE CELL PROTEOMIC TECHNOLOGY AND FUTURE

Junho Park

CHA Univ. College of Medicine, Department of Pharmacology, Korea

Single-cell proteomics (ScProteomics) using cutting-edge LC-MS system is a powerful technique that enables the analysis of proteome at single-cell level. ScProteomics allows for the identification and quantification of thousands of proteins in individual cells, providing unprecedented insights into cellular heterogeneity and cellular signaling pathways. By allowing the analysis of proteins at a single-cell resolution, this technique overcomes the limitations of traditional bulk proteomics, which average the signals from many cells and mask the complexity of individual cell states. Importantly, ScProteomics using LC-MS has the potential to greatly advance our understanding of cancer. One crucial application of this technology is the identification of new biomarkers for cancer diagnosis and prognosis. By analyzing the proteome of individual cancer cells, researchers can identify specific protein signatures of rare cell population, e.g. cancer stem cell. This information can then be used to develop more accurate and personalized cancer diagnostics, which can help guide treatment decisions and improve patient outcomes. Another important application of ScProteomics in cancer research is the identification of novel therapeutic targets. By analyzing the single-cell proteome, proteins that are overexpressed or altered in cancer cells compared to adjacent normal cells can be specified. These proteins may represent potential targets for novel therapies, which can be developed to specifically target the molecular mechanisms driving cancer exacerbation and survival. Recently, ScProteomics were significantly improved with the aid of great advance of mass spectrometer and microfluidic devices. In this talk, I would like to introduce state-of-the-art technologies in ScProteomics using LC-MS as a powerful tool for understanding the molecular mechanisms of cancer and for developing new strategies for cancer diagnosis and treatment.

SINGLE CELL GENOMICS OF CIRCULATING TUMOR CELLS IN BREAST CANCER

Andi Cani[1], Emily M. Dolce[1], Kevin Hu[3], Chia-Jen Liu[2], Elizabeth P. Darga[1], Dan Robinson[2], Yi-Mi Wu[2], Dafydd G. Thomas[2], Costanza Paoletti[1], Scott A. Tomlins[2], James M. Rae[1], Aaron M. Udager[2], Arul M. Chinnaiyan[2], Erin F. Cobain[1], Daniel F. Hayes[1]

[1]Univ. of Michigan, Division of Hematology and Oncology, Department of Internal Medicine, U.S.A., [2]Univ. of Michigan, Department of Pathology, U.S.A., [3]Univ. of Michigan, Department of Computational Medicine and Bioinformatics, U.S.A.

Clinical decisions on precision and immuno-oncology therapies are based on predictive biomarkers commonly obtained from a single metastatic biopsy or archived primary tumor tissue. This approach largely misses intratumor heterogeneity and cancer evolution. Circulating genomic biomarkers offer a minimally invasive approach to detect that heterogeneity and monitor in real-time the clinically-relevant evolving clonal architecture. We hypothesize that single-cell DNA next generation sequencing (scNGS) of circulating tumor cells (CTC) is a particularly well-suited method to complement biomarker information obtained from tissue and cell-free circulating tumor DNA (ctDNA) especially in lobular breast cancer, which is characterized by high CTC production. We analyzed 126 individual CTC, 2 ctDNA, 24 fresh/FFPE tissue, and 15 white blood cells (WBC) samples, from 15 CTC-positive lobular breast cancer patients, four of whom had CTC available at both metastatic baseline and after progression on a variety of therapies chosen at their physician's discretion. CTC were enriched with the CellSearch® system and isolated as single cells with the DEPArray™ system. Whole genome amplified CTC and WBC, as well as ctDNA underwent scNGS with the Oncomine Comprehensive Assay covering ~500 genes and 1.1Mb of genomic space to detect mutations, copy number alterations, tumor mutation burden (TMB) and microsatellite instability (MSI).

99.1% of single cells, 95.2% of ctDNA, and 92% of tissue samples were informative, with a mean sequencing depth of 664x, 802x, and 721x, respectively. Using our previously developed, CTC-based precision medicine reporting platform, MI-CTCSeq, CTC in 9 of 15 patients (60%) had mutations that were actionable by FDA-approved targeted therapies including in the oncogenes PIK3CA, FGFR2 and ERBB2. 3 of these 9 patients (33%) harbored actionable alterations not shared between all 3 analyte types (tissue, CTC and ctDNA). These included 3 found in CTC and ctDNA only, 1 in tissue and ctDNA only, and 1 in ctDNA only. However, 2 of those ctDNA mutations were identified near the limit of detection and with a priori knowledge of their presence from tissue or CTC. Further, 1 patient with plentiful CTC had no detectable ctDNA and one patient's tissue biopsy was inadequate for sequencing while both liquid biopsy analytes were abundant.

13 patients (87%) displayed intra-patient, inter-CTC genomic heterogeneity of putative driver mutations. 1 of 4 (25%) patients with CTC available in >1 timepoint displayed fluctuations in their CTC subclonal makeup between our timepoints. Data from this patient's 6 tissue samples, 5 ctDNA samples, and 32 individual CTC over 7 timepoints combined to reveal in unprecedented detail inter-metastatic lesion and inter-CTC heterogeneity and tumor evolution in response to endocrine and immunotherapy selective pressures. ScNGS of CTC helped provide an additional level of detail not appreciated by sequencing of the other two analyte types. In another patient, CTC were composed of 2 subclones which were indistinguishable by ctDNA, 1 of which appears to have not been sampled by the tissue biopsy. One of this patient's subclonal populations was abundantly represented among CTC, but at an extremely low fraction in ctDNA compared to the other clone.

Using a novel method, we enabled detection of single-cell CTC TMB and MSI. CTC TMB scores (dichotomized as above/below 10 mutations/Mb) were 100% concordant with those measured in the corresponding tissue biopsies. Further, in a novel observation, we detected intra patient, inter-CTC heterogeneity of TMB and MSI, as well as fluctuations of subclones of different TMB in response to checkpoint inhibitor immunotherapy.

Taken together, these data support the non-invasive biomarker interrogation and monitoring by liquid biopsy that incorporates CTC scNGS and complements tissue in informing precision and immuno-oncology approaches. This method may have important implications for appropriate treatment selection and identification of therapeutic resistance mechanisms.

THE ROLE OF IMAGING FOR THE MANAGEMENT OF DCIS

Mami Iima

Kyoto Univ. Hospital, Kyoto Univ. Graduate School of Medicine, Department of Diagnostic Imaging and Nuclear Medicine, Japan

Imaging plays an important role in the management of ductal carcinoma in situ (DCIS) of the breast. Mammography, ultrasound, and magnetic resonance imaging (MRI) are mainly used to diagnose and evaluate DCIS. The sensitivity of MRI in detecting DCIS is superior to that of mammography and ultrasound, MRI sensitivity being particularly high in women with high-grade DCIS. However, the optimal means of identifying, diagnosing, and managing DCIS, a nonobligate precursor of invasive breast cancer, remain controversial. The incidence of DCIS increased with the widespread implementation of screening mammography programs in the 1980-90s, which was considered to contribute significantly to overdiagnosis and overtreatment. The progression of DCIS to invasive cancer is not well understood, and various models to explain its initiation and progression have been proposed.

Imaging features have been shown to reflect the biological heterogeneity of DCIS lesions, with recent studies indicating that MRI may be capable of identifying more or less aggressive DCIS lesions.

There is a growing interest in nonsurgical management, including active surveillance, to minimize overtreatment and provide patients with more personalized options. Imaging could make a useful contribution to personalized medicine.

Trials regarding active surveillance, an alternative management strategy for DCIS that aims to reduce overtreatment, are currently underway and are expected to improve the identification of patients with low-risk DCIS and thus minimize unnecessary surgical intervention.

THE ROLE OF DW-MRI IN THE PERSONALIZED SCREENING AND DIAGNOSIS

Savannah Partridge

Univ. of Washington, Department of Radiology, U.S.A.

Diffusion-weighted MRI (DW-MRI) shows promise to address shortcomings of routine clinical breast MRI and to aid in personalized screening and diagnosis. DW-MRI measures the mobility of water molecules diffusing in tissues, revealing tissue organization at the microscopic level. Breast cancers typically exhibit hindered water diffusion, with higher DW-MRI signal intensity and lower apparent diffusion coefficient (ADC) values than normal breast fibroglandular tissue, attributed to their increased cellularity and decreased extracellular space. DW-MRI is a short scan available on most commercial MR scanners and does not require any exogenous contrast. As such, a growing number of imaging centers are incorporating DW-MRI into clinical breast MR protocols. Potential applications include improving diagnostic accuracy, guiding treatment decisions, and non-contrast screening.

A primary potential role of DW-MRI in breast imaging is reducing false positives of conventional dynamic contrast-enhanced (DCE) breast MRI. DCE-MRI has very high sensitivity but relatively modest specificity (70%-80%), leading to unnecessary biopsies. Whereas DCE-MRI reflects alterations in tissue vascularity, DW-MRI provides complementary information on tissue microstructure and cell density. Numerous retrospective studies demonstrated that ADC values can help to differentiate benign and malignant breast lesions. A prospective multi-center trial (ACRIN6702; ClinicalTrials.gov NCT02022579) further confirmed the diagnostic value of DW-MRI for MRI-detected breast lesions, identifying an optimal ADC threshold to reduce benign biopsies without lowering sensitivity.

Breast DW-MRI may also serve as a noninvasive prognostic tool. In general, ADC negatively correlates with cancer aggressiveness, lower for invasive than in situ disease, and with prognostic factors such as tumor grade, Ki-67, and Oncotype Dx score. However, results in the literature are mixed and more investigation is needed to validate the association of ADC with prognostic and molecular tumor markers. Evidence also suggests that ADC may be helpful in predicting pathological upgrade of lesions diagnosed by core-needle biopsy, from high risk to malignancy or in situ to invasive cancer. Together, the ability to use DW-MRI to characterize disease biology and aggressiveness may aid in personalizing treatments and management decisions.

For breast cancer screening, there is much interest in DW-MRI as an alternative non-contrast screening tool given the high cost of DCE-MRI examinations and uncertain long-term impact of gadolinium

deposition. Moreover, there a critical need for new cost-effective supplemental screening options for women with dense breasts where mammography sensitivity is reduced. Preliminary studies suggest DW-MRI may provide higher sensitivity than screening mammography and ultrasound for detection of breast malignancies, without the costs and toxicity of DCE-MRI. Prospective trials are currently investigating the relative screening performance of DW-MRI in various risk groups (e.g., NCT03835897, NCT03607552), which will provide more valuable insights on the potential role of DW-MRI in personalized screening strategies.

In summary, DW-MRI holds clear potential value for breast cancer screening and diagnosis. Results of multi-center trials and recent standardization efforts are helping to establish clinical guidelines. Technical advancements in DW-MRI are also helping to improve image quality and extract more biologic information from breast DW-MRI scans, which may further extend its role in breast imaging.

QUANTITATIVE IMAGING IN OUTCOME PREDICTION OF BREAST CANCER

Vivian Youngjean Park

Yonsei Univ. College of Medicine, Department of Radiology, Korea

Radiomics, involving the extraction of quantitative mineable data from digital medical images, has been an active area of research during the last decade. Numerous studies have applied radiomics to various imaging modalities in breast imaging for various indications. As breast MRI allows for both multiparametric imaging and volumetric analysis, it has been by far the most investigated imaging modality for which quantitative feature analysis has been applied. Hence, due to the large amount of published literature and restricted amount of time, this talk will focus on research regarding breast MRI.

The main anticipated advantage of applying quantitative imaging is that it can facilitate precision medicine by providing additional information to visual assessment and enabling classification/stratification of clinically meaningful subgroups. The main clinical applications of quantitative imaging that have been recently investigated include predicting pathological response following neoadjuvant chemotherapy, molecular breast cancer subtypes, prognostic factors such as Ki67 or lymphovascular invasion, and survival outcomes such as disease-free survival or systemic recurrence. Although all of these applications are indirectly or directly associated with outcome prediction, this talk will primarily review research investigating outcomes directly related to survival. Similarities and differences between published studies and trends/future directions will be reviewed.

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PERSONALIZATION OF PMRT IN THE MODERN ERA

Meena S. Moran

Yale School of Medicine, Department of Therapeutic Radiology, U.S.A.

Post-mastectomy radiation (PMRT) has seen significant evolution in its indications and delivery techniques over the last several decades. With the use of more contemporary radiation delivery methods, several pivotal randomized trials have elucidated the extended benefits of PMRT beyond improvements in local-regional relapse for high-risk patients. The Danish 82b/82c and British Columbia PMRT trials were the first PMRT trials to demonstrate the expected local-regional relapse benefits in addition to improvements in distant disease-free and overall survival with radiation delivery for patients with 1 or more positive lymph nodes. More recent trials assessing the benefits of regional nodal irradiation (RNI), such as MA-20 and EORTC 22922, re-enforce the concept that radiation may play an important role in eradicating undetected microscopic disease in lymph nodes and diminish subsequent distant disease events in high-risk patients. While many consensus recommendations have expanded their PMRT indications from routine use in patients with > 4 positive nodes, to variations of 'considering' PMRT in patients with 1-3 positive nodes (in addition to other potentially high-risk, lymph node-negative subgroups), there remains international controversy as to whether all patients in the 1-3+ nodal cohort (such as those with T1/T2 primaries with low disease burden in one node), warrant routine PMRT when no other high-risk features are present. As such, uncertainties continue to prevail about the effectiveness of PMRT for patients with 1-3 positive nodes, T3N0 tumors, and patients with clinically node-positive disease who achieve complete pathologic response after NAT, particularly in light of the marked improvements in systemic therapies in recent years that have directly impacted improvements in local control. While recent progress in genomic analysis and evaluating underlying tumor biology opens new possibilities to improve local-regional risk stratification that could eventually lead to more personalized prognostication for PMRT, the current data are conflicting, and to date, no PMRT recommendations are based on tumor biology or genomic assays alone. In this session, we will review the evolution of PMRT consensus recommendations over the last several decades and the data supporting these recommendations. We will examine clinical-pathologic features, surgical considerations, tumor biology, and genomic factors that may affect local-regional relapse. We will review the data for PMRT in the upfront surgery and neoadjuvant therapy (NAT) settings, and explore whether these recommendations should be modified based on the above factors. Surgical considerations (i.e. whether axillary dissection is performed for a node + patient), biologic subtypes, and commercially available genomic assays will be discussed. An array of published clinical nomograms estimating risk of LRR after mastectomy may be useful to re-enforce/confirm clinical decisions for personalizing recommendations for PMRT. Lastly, recent changes to the NCCN Breast 2023 Guideline for PMRT and important ongoing PMRT trials addressing relevant questions will be reviewed.

THE BENEFIT OF PMRT FOR LOW NODAL BURDEN BREAST CANCER IN THE MODERN TREATMENT ERA

Kyung Hwan Shin, Bum-Sup Jang, Ji Hyun Chang, Tae Hoon Lee

Seoul National Univ. Hospital, Department of Radiation Oncology, Korea

Although surgery is the mainstay of definitive breast cancer treatment, postoperative radiotherapy (PORT) also plays an essential role. The two main types of radical surgery for breast cancer are breast-conserving surgery (BCS) and mastectomy. PORT is crucial in most patients who have undergone BCS: several randomized trials and meta-analyses showed that PORT reduces breast cancer recurrence and death. However, PORT is not always the best option for patients who received a mastectomy. Post-mastectomy radiotherapy (PMRT) is recommended when the tumor is large (>5cm) or regional metastasis is confirmed during axillary surgery. These principles have informed breast cancer treatment for many years.

Systemic therapy is another essential component of breast cancer treatment, and has advanced greatly in recent years. Long-term hormonal therapy and ovarian suppression have been applied in patients with positive hormonal receptors to further decrease the risk of breast cancer recurrence. Trastuzumab is widely used in human epidermal growth factor receptor 2 (HER2)-positive breast cancer patients and significantly improves the prognosis. High-risk HER2-positive breast cancer patients can also benefit from pertuzumab. The addition of taxane to adjuvant chemotherapy has increased patient survival rates. However, as the major clinical trials supporting PORT did not consider these advancements, it remains uncertain whether modern systemic therapy impacts the effectiveness of radiotherapy. With the increased application of systemic therapy, de-escalation of certain aspects of PORT may be feasible in selected patients, such as field size reduction or the omission of radiotherapy.

The current indications for PMRT have been criticized. Although the Early Breast Cancer Trialists' Collaborative Group meta-analysis confirmed a benefit of PMRT for pN1 patients, this conclusion was based primarily on the results of two Danish trials criticized for their high rates of inadequate axillary surgery. In addition, more than two decades have passed since these results were reported, and the benefit of PORT may have lessened due to advances in breast cancer treatment. Secondary analysis of the prospective data of pT1-2N1 patients enrolled in the BIG 02-98 randomized trial of adjuvant chemotherapy revealed that PMRT slightly improved locoregional control, but not survival rates. Thus, the role of PMRT must be reevaluated based on more recent evidence. Although several non-randomized series have provided insight into "PORT de-escalation", oncologic safety has not been

confirmed. If the oncologic safety of PORT de-escalation can be established, breast cancer patients may benefit from reduced toxicity and lower time and medical costs.

Accordingly, the Korean Radiation Oncology Group (KROG) designed a multicenter clinical trial of PORT for patients with pN1 breast cancer: the Postoperative Radiotherapy in N1 Breast Cancer Patients (PORT-N1) trial. This trial aims to evaluate the feasibility of PORT de-escalation in pN1 breast cancer patients by establishing indications for regional nodal irradiation in patients receiving BCS, and for PMRT in patients receiving mastectomy.

INCORPORATION OF NEW SYSTEMIC AGENTS IN PATIENTS TREATED WITH PMRT

Alice Ho

Duke Univ., Department of Radiation Oncology, U.S.A.

The incorporation of systemic therapy, including biologics, targeted therapies and immunotherapy has been increasingly performed in the setting of locally advanced and metastatic breast cancer. The safety and optimal sequencing of therapies in patients receiving radiotherapy (RT) is a topic that must be informed by high quality data and robust clinical experience. Balancing the advantages of integrating these therapies without interfering with the delivery RT has always been a challenging issue in the clinic. Recently, the concept of leveraging radiation to augment the efficacy of some of these agents, such as immunotherapy and DNA damage repair-based therapies, has been an emerging topic of interest. Several phase I and II trials in Europe and the U.S. have tested combinatorial therapies of RT with immune checkpoint blockade, DNA repair based therapies and CDK 4/6 inhibitors. This presentation will review data from completed trials as well as newer, on-going clinical trials demonstrating the potential of RT to biologically harness the full potential of systemic therapies when combined, by breast cancer subtype.

IS THE AUTOLOGOUS RECONSTRUCTION BETTER THAN THE IMPLANT OPTION?

Kyong-Je Woo

Ewha Womans Univ. Mokdong Hospital, Department of Plastic Surgery, Korea

Is the Autologous Reconstruction Better than the Implant Option?:

Serial Comparison of Patient-Reported Outcomes of Immediate Breast Reconstruction: Direct-to-Implant versus Deep Inferior Epigastric Artery Perforator (DIEP) Flap

Introduction: Patient-reported outcomes (PRO) after breast reconstruction are paramount surgical outcome indicators, considering the private and intimate nature of breast reconstruction. As the frequencies of nipple-sparing mastectomy and prophylactic mastectomy have increased, single-stage direct-to-implant (DTI) breast reconstruction has become more popular than two-stage tissue expander implantation, becoming the most common method among implant-based reconstructions. The advent of autologous reconstruction has led to a dramatic shift toward microsurgical reconstruction using free tissue transfer, especially with deep inferior epigastric artery perforator (DIEP) flaps. DIEP flap has been a preferred option among autologous reconstruction because of low donor site morbidity and sufficient tissue for breast reconstruction.

Methods: The data of patients who underwent immediate breast reconstruction using DTI or DIEP flaps between July 2017 and October 2021 were retrospectively reviewed. Patient-reported outcomes were captured using the BREAST-Q reconstruction module at 6 months and >12 months after reconstruction. The outcome scores were compared between DTI and DIEP groups, and serial comparisons were performed.

Results: Of the 375 patients, 146 patients with BMI of 22.56 ± 3.11 kg/m2, and age of 48.27 ± 7.53 years completed questionnaires over 1 year follow up (20.79 ± 8.55 months). Those with DTI was in 102 patients (69.9 %) and DIEP was in 44 patients (30.1 %). There were no differences of scores in all domains between DTI and DIEP groups at postoperative 6 months. At the mean follow-up of 20.8 ± 8.6 month, patients who underwent DIEP had greater satisfaction with breast ($P < 0.001$) and satisfaction with outcome ($P < 0.001$). In DTI group, satisfaction scores did not change over time in all domains. In the DIEP group, however, the satisfaction with breast ($P = 0.001$), outcome ($P = 0.045$), psychosocial well-being (0.015), and sexual well-being (0.042) significantly increased in long term follow-up, compared to 6 months.

Conclusions: Both DTI and DIEP-flap breast reconstructions had comparable patient satisfaction in the short term. However, PRO improved over time in association with DIEP-flap reconstructions, resulting in higher satisfaction levels over long-term follow-up relative to the satisfaction associated with DTI reconstruction. The findings of this study are relevant to patient-centered decision-making, as they provide information regarding how patient satisfaction changes over time after DTI and DIEP-flap breast reconstruction.

Important points

1. Patient satisfaction associated with direct-to-implant breast reconstruction was comparable to that associated with DIEP-flap reconstruction over the short term (6 postoperative months).
2. After direct-to-implant reconstructions, BREAST-Q scores did not change between 6 months and > 1 year of follow-up.
3. After DIEP-flap breast reconstructions, BREAST-Q scores reflecting satisfaction with reconstructed breasts, overall outcomes, psychosocial well-being, and sexual well-being significantly increased after long-term follow-up, compared with the 6-month scores.
4. After long-term follow-up, the DIEP group had higher mean scores than the DTI group reflecting satisfaction with reconstructed breasts and overall outcomes.

AUTOLOGOUS BREAST RECONSTRUCTION: DIEP FLAP

Toshihiko Satake

Toyama Univ. Hospital, Department of Plastic, Reconstructive and Aesthetic Surgery, Japan

The DIEP flap allows for harvesting large volume of adipose tissue and skin from the lower abdomen and wound closure at the same time as the mastectomy or preparation of recipient site. Because of the wide range of indications for breast reconstruction using the DIEP flap, it accounts for approximately 75% of all autologous tissue reconstructions in our department.

To ensure the safety and cosmetic appearance of both the reconstructed breast and the abdominal donor site, several modifications were made and are reported here.

Preoperative MDCT, color Doppler and intraoperative ICG fluorescence angiography are used for entire flap perfusion. To avoid flattening of the abdomen after the DIEP is harvested and to express the waistline and the midline of the abdominal wall, a high-lateral tension lipo-abdominoplasty design was used, with a straight line just above the pubic bone and both ends of the skin valve aligned with the superior anterior iliac spine. Liposuction is also used at the white line, lateral border of the rectus abdominis, and lumbar region.

For the vascular pattern of the DIEP flap, a medial row perforator is selected for unilateral reconstruction and a lateral row perforator for bilateral reconstruction. SIEV and SCIV at the inferior margin of the flap are included and backed up to prevent venous congestion. Anastomosis is performed using a rib cartilage-sparing intercostal approach, and two inferior abdominal wall veins are anastomosed with the internal mammary vein, anastomosing in an antegrade and retrograde fashion.

Breast reshaping with abdominal tissue requires consideration of the location and shape of the cleavage, the inframammary line, the top, the concavity of the axillary tail, and the gentle slope of the upper pole. Fat injections are also an option for the creation of a gentle dcollet line.

Reconstruction of the sensory nerves is also considered in cases of replacement breast with abdominal skin or postmastectomy pain syndrome (PMPS). For reconstruction after nipple-sparing mastectomy, sentinel skin monitoring should always be placed at the areola margins, at the inframammary line, and on the chest incision line. In cases complicated by lymphedema of the upper extremities, the axillary scar should be removed and then the vascularized lymph nodes should be transplanted.

The main prerequisite for breast reconstruction with DIEP flap is safe transplantation. Second, the aesthetic appearance of both the reconstructed breast and abdomen should be improved. If necessary, functional reconstruction, such as sensory nerve restoration and lymph node transplantation, can be performed, allowing for wide range of applications.

AUTOLOGOUS BREAST RECONSTRUCTION: PAP FLAP

Jung-Ju Huang

Chang Gung Memorial Hospital, Department of Plastic and Reconstructive Surgery, Taiwan

Free DIEP flap has long been the standard of care in autologous breast reconstruction. However, DIEP flap can be unavailable due to previous surgery or simply inadequate in flap volume. Free PAP flap is not the second workhorse flap in the senior author's experience.

A total of 32 PAP flaps in 31 patients were performed in autologous breast reconstruction. 27 of the patients were immediate reconstruction and 3 were delay-immediate reconstruction. The rest one was delay reconstruction. 17 of them received nipple-sparing mastectomy and 13 of them received skin-sparing mastectomy and one with modified radical mastectomy. Their average age was 39.5 ± 7.1 years old, and the BMI was 21.3 ± 2.4. The available pre-operative CTA revealed that 5.3 ± 1.2 perforators can be identified in each donor site.

The average flap was 7.8 ± 0.9 cm wide and 21.3 ± 3.9 cm long, and weighed 259.6(± 73.2) grams. The average pedicle length was 5.9 (± 1.4) cm. One flap failed, resulting in a successful rate of 96.9%. Most commonly encountered complications were donor site complications. There were 7 cases (21.9%) of acute complications and 3 cases (9.4%) of late complications. Amongst the acute complications, 6 cases were from wound break-down and 1 case had a hematoma. In 3 the 3 cases of late complications, they were all related to wound break-down. In terms of revision procedures to the chest, there were a total of 12 cases of revision to the breast, of which 8 cases were fat grafting, 2 cases were flap reduction, 2 cases of mastopexy and 1 case of scar revision. With regards to the donor site, there were 6 cases of scar revision performed for the thigh.

In general, patients were happy with their aesthetic results of breast reconstruction using free PAP flap. However, a strategic flap deign and donor site management are required to achieve satisfactory outcomes.

INTEGRATING IMMUNOTHERAPY INTO THE TREATMENT STRATEGIES OF METASTATIC BREAST CANCER

Tira Tan

National Cancer Centre Singapore, Department of Medical Oncology, Singapore

Over the past decade, immune check point inhibition has changed the course of management for several solid tumors including melanoma, non-small cell lung cancers and renal cell carcinoma; tumors that were traditionally known to be resistant to treatment with chemotherapeutics. Early phase data in metastatic breast cancers demonstrated sustained and durable responses in a small and highly selected group of patients, specifically those whose tumors are triple negative (TNBC), relatively treatment nave, PD-L1 expressing, and/or associated with high tumor infiltrating lymphocytes (TIL). Despite initial enthusiasms and high expectations generated through successes in other solid tumors, patients with metastatic breast cancer have derived limited benefit from immunotherapy. Today, immunotherapy is incorporated into the treatment paradigm of only a minority of metastatic breast cancers i.e., in combination with chemotherapy in the 40% of metastatic TNBC which express PD-L1 and in the rare occurrence of microsatellite instability or high tumor mutation burden. One of the challenges in developing immunotherapeutic strategies is differential patterns of responses as compared to chemotherapeutics as measured by the Response Evaluation Criteria in Solid Tumors (RECIST) and the question of appropriateness of surrogate endpoints as a readout to measure effectiveness of an immunotherapy strategy. Improved understanding and availability of technologies to interrogate non-responsive tumors may inform on the most appropriate immunotherapy combinations and provide insights on overcoming treatment resistance. In this space, considerable efforts are ongoing to develop combinatory strategies in hope that targeting the immunosuppressive tumor microenvironment may convert a "cold" tumor to that which is "hot". A somewhat understudied area in metastatic breast cancer is the used of maintenance therapies or low-intensity therapies to suppress the disease over prolonged periods of time following maximal response to induction therapy. Finally, novel immune therapeutics currently in development include adoptive cell therapies such as TIL-based therapies, T cell receptor therapy, chimeric antigen receptor T cell therapy and engineered bispecific antibodies.

ROLE OF IMMUNOTHERAPY FOR EARLY BREAST CANCER: TO WHOM, WHEN AND HOW

Pamela Munster

Univ. of California, San Francisco, Department of Medicine, Division of Hematology/Oncology, U.S.A.

Globally over 2 million women are diagnosed with breast cancer each year despite major advances in detection and treatment of the disease. While early-stage breast cancer incidence is higher in high income countries, deaths are more common in lower income countries. Age and stage at presentation show considerable geographic variation. Breast cancer is comprised of several distinct subtypes and understanding the heterogeneity of the disease has become crucial for treatment planning in early-stage breast cancer. Therapeutic strategies span from a hormone therapy-based focus for women with estrogen receptor positive breast cancer to targeting HER2 by small molecules, antibody-drug-conjugates (ADC) and monoclonal antibodies in those with HER2 overexpression. Recent additions for select subgroups of patients include the cyclin-dependent kinase 4/6 (CDK4/6) inhibitors for women with estrogen receptor positive tumors and the poly ADP ribose polymerase (PARP) inhibitors for those with BRCA mutations.

In contrast, the treatment for women with triple negative breast cancer has until recently been solely limited to chemotherapy. Like in many other tumors, the introduction of immunotherapy has had a profound impact on the treatment options for women with early-stage triple negative breast cancer. Therefore, with the exception of women with very small, node-negative triple negative tumors, pre-operative chemotherapy with an immune check point inhibitor added to a carboplatin/taxane and anthracycline regimen should be considered followed by adjuvant immune checkpoint inhibitor therapy for the completion of a year. The addition of immune check point inhibitors not only increased the pathological complete response rate but also improved event free survival. Recent data from multiple trials suggest high PD-(L)1 expression in the majority of women with early-stage triple negative breast cancer, thus negating the need for PD-(L)1 testing in early-stage breast cancer for treatment decisions. To date, based on large prospective, double-blind randomized trials with long term follow up, only pembrolizumab has been approved by the FDA and EMA in early-stage triple negative breast cancer.

EMERGING TARGETS OF IMMUNOTHERAPY IN BREAST CANCER

Shigehira Saji

Fukushima Medical Univ., Department of Medical Oncology, Japan

The development of immune checkpoint inhibitors has continued to evolve for breast cancer treatment, especially for advanced/metastatic and early-stage TNBC.

At present, PD-L1 and PD-1 are target of drugs used in breast cancer, however, development for other immune-related factors is also warranted. Combination therapy with various molecular-targeted therapies such as angiogenesis inhibitor and signal transduction inhibitor, which is expected to alter immune responsiveness by modifying the tumor environment, is another important direction for the future, especially for hormone receptor positive breast cancer. Two challenging approaches involve chimeric antigen receptor-T cells (CAR-T) and bispecific antibodies. These forms of immunotherapy can highly select for the tumor target of interest to generate specific tumor damage. The oncolytic virus therapy approaches currently developed in brain tumor could be also interesting modality. This session will try to provide an overview of these topics.

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Panel Discussion

"Go Beyond Cure of Breast Cancer"

SCREENING AND ASSESSMENT OF BREAST CANCER IN OLDER WOMEN

Chee Hao Lester Leong

Singapore General Hospital, Department of Radiology, Singapore

There has been a surge in breast cancer diagnosis in elderly women world-wide as life expectancy increases. Hence, there is now a greater need to consider breast cancer screening in older women past the conventional upper age limit of population-based breast screening programmes. The evidence for screening and the imaging strategy of breast cancer loco-regional staging in the elderly are discussed.

SYSTEMIC THERAPY FOR OLDER BREAST CANCER PATIENTS

Jee Hyun Kim[1,2]

[1]*Seoul National Univ. Bundang Hospital, Deparment of Internal Medicine, Korea,*
[2]*Seoul National Univ. College of Medicine, Korea*

The number of older breast cancer patients are increasing with increasing incidence of breast cancer and longer life expectancy. There are limited evidence on the efficacy and safety of systemic therapy in older patients with breast cancer, due to underrepresentation of older patients in clinical trials, and older patients are less frequently offered guideline recommended standard treatment. Older patients have highly heterogenous comorbidities, life expectancy, functional status and tolerance to systemic therapy therefore treatment should be highly individualized according to patient's geriatric assessment results and preferences.

Chemotherapy is the mainstay of treatment for ER negative early breast cancer (EBC) and fit older patients can derive similar benefit from neaoadjuvant/adjuvant chemotherapy as younger patients. Careful patient selection and toxicity prediction, preferably by using tools such as CARG or CRASH score, are recommended followed by proactive management of chemotherapy related adverse events. Anti-HER2 targeted agents offer benefits in older patients with EBC and should be recommended with adequate cardiac monitoring and proactive management of complications. Endocrine therapy including aromatase inhibitors is the standard of care for HR positive EBC, and chemotherapy benefit is less certain. Gene expression profiling results may aid in the decision to use chemotherapy in this population. In the meeting, we will cover recent advances in adjuvant systemic therapy of EBC and will review efficacy and safety of systemic therapy in older patients.

SURGICAL THERAPY FOR OLDER BREAST CANCER PATIENT

Tristen Park

Yale School of Medicine, Department of Surgery, U.S.A.

In line with recent trends towards decreasing surgical intervention of the axilla for breast cancer treatment, the American Society for Surgical Oncology (SSO) and the Choosing Wisely Foundation have created guidelines recommend against routine use of sentinel lymph node biopsy (SLNB) in clinically node-negative patients 70 years of age with hormone receptor positive invasive breast cancer.

Although the morbidity associated with SLNB is minimal, there is still a small but present risk of lymphedema, paresthesia as well as wound complications. We will review in this talk the ongoing debate regarding SLNB contrasting the argument that axillary staging can help guide adjuvant radiation and systemic therapy recommendations vs the competing argument is that treatment of breast cancer is primarily guided by tumor biology making the role of SLNB questionable as it would not change management otherwise.

THE OPTIMAL ENDOCRINE COMBINATION WITH OFS

Hee Jeong Kim

ASAN Medical Center, Department of Surgery, Korea

Adjuvant endocrine therapy plays a critical role in the management of estrogen receptor-positive early breast cancer in premenopausal women. The use of ovarian function suppression (OFS) is considered standard of care for most premenopausal women, and the choice of the optimal endocrine partner is based on the risk of disease recurrence.

Tamoxifen alone is still an excellent treatment option for low-risk patients. For patients at higher risk of recurrence, the benefits of OFS and an aromatase inhibitor (AI) combination outweigh the benefits of OFS and tamoxifen. However, many questions remain unanswered regarding the optimal endocrine therapy.

Long-term follow-up studies are necessary to understand the magnitude of the benefits associated with the use of OFS, to guide the choice between an AI and tamoxifen as the best adjuvant endocrine partner. The best timing for initiating OFS in patients receiving (neo)adjuvant chemotherapy before starting adjuvant endocrine therapy remains controversial.

The best endocrine agent to combine with OFS in premenopausal women with estrogen receptor-positive/HER2-positive early breast cancer is still unknown. Moreover, the risk of suboptimal ovarian function suppression exists in patients who receive an AI as the partner of OFS, particularly in patients who are very young, overweight, and not exposed to prior chemotherapy.

Choosing the best type of extended adjuvant endocrine therapy remains challenging, particularly in women exposed to 5 years of ovarian function suppression, and particularly in those who also received an AI. The duration of ovarian function suppression and the age group of premenopausal women also need to be taken into account when deciding on the optimal adjuvant endocrine therapy.

Following the recent announcement of the efficacy of adding two years of ovarian suppression injections after cancer treatment, limited duration ovarian suppression injections can be considered in some breast cancer patients when considering the toxicity of ovarian suppression injection therapy.

In terms of the age group of premenopausal women, it is important to note that younger patients are more likely to experience premature ovarian failure and infertility linked with the use of systemic cytotoxic therapy. Therefore, the best timing and duration of ovarian function suppression should be

carefully considered in these patients to minimize the risk of these adverse effects. Additionally, the choice of the optimal endocrine therapy in premenopausal women should be carefully discussed with patients and the pros and cons should be taken into account for each strategy, based on the individual patient's age, preferences, and clinical characteristics.

In conclusion, the optimal endocrine therapy for premenopausal women with estrogen receptor-positive early breast cancer should be carefully discussed with patients, and pros and cons should be taken into account for each strategy. The choice of the best treatment partner should be based on the patient's risk of recurrence, age, and other clinical-pathological factors. Furthermore, the best timing and duration of ovarian function suppression should be considered in young patients to minimize the risk of adverse effects.

TARGETED THERAPY FOR HIGH-RISK PATIENTS AND GBRCA MUTATION PATIENTS

Hee Kyung Ahn

Gachon Univ. Gil Medical Center, Department of Hematology-Oncology, Korea

PROPHYLACTIC MASTECTOMY

Eric Schneider

Yale School of Medicine, Department of Surgery and Epidemiology, U.S.A.

Background: Patients having certain genetic mutations and/or a family history of breast cancer may choose to undergo prophylactic mastectomy (PM) to reduce their risk of breast cancer. The number of PM procedures performed each year continues to increase across the globe; however, patient-level factors associated with decision-making, including individual-specific benefits of PM in reducing breast cancer risk, and potential short and long-term harms associated with PM are fully understood.

Methods: We sought to develop a better understanding of the benefits and risks of PM by conducting a state-of-the-art review of literature. Studies reporting the incidence of PM and its effectiveness in reducing breast cancer risk were identified using a pre-determined search strategy applied across multiple databases including Medline, Scopus, Web of Science, etc. Manuscripts identified through the search were reviewed by study team personnel and selected for inclusion using predetermined criteria.

Results: Based upon this review, the incidence of prophylactic mastectomy varies widely across different regions of the world and was most common in North America and Europe. Across the majority of studies, both unilateral and bilateral PM were most commonly performed on women with known BRCA1 and BRCA2 mutations and/or a significant family history of breast cancer. Where reported, the number needed to treat (NNT) with PM to prevent development of breast cancer demonstrated considerable variability based upon individual-level risk factors, including patient age, underlying genetic susceptibility and family history. Reported estimates of NNT ranged across an order of magnitude, from ~3 to ~30 patients. Variability in factors identified as representing patient harm across studies limited our understanding of the number needed to harm (NNH). Many studies reporting harm focused on short-term post-operative complications such as hematoma, bleeding, infection, wound healing, and reconstruction failure while fewer provided information on possible longer-term patient difficulties such as psychosocial distress.

Discussion: The numbers of patients undergoing PM procedures continues to increase across the globe; however, substantial differences in within- and between-region findings suggest variability in access to this to this procedure. Current and future research will likely provide additional evidence, including better understandings of factors associated with potential harm, that will enable further optimization of patient care.

AVOIDING BREAST SURGERY IN PATIENTS WITH RADIOLOGIC COMPLETE RESPONSE

Christoph Tausch

Breast-Center Zurich, Department of Breast Surgery, Switzerland

Neoadjuvant chemotherapy (NACT) is a increasingly used to treat breast cancer patients. Not only large tumors even tumors with aggressive biology e.g. triple negative and Her2-positive carcinoma receive NACT in order to downstage the disease in the breast and the axilla.

By using modern chemo- and immunotherapy regimens in the neoadjuvant setting, a pathological complete response (pCR) could be achieved in more than 50 % of patients. In these patients, breast surgery seems to be an overtreatment and therefore we evaluate whether representative minimal invasive biopsies of the tumor bed may safely replace the role of surgery after NACT.

To date, only one small series from the MD Anderson Cancer Center demonstrated an acceptable low false negative rate (FNR) of 5% using vacuum assisted biopsy (VAB) of the tumor bed in patients with complete radiological response after NACT. All other trials in a single center or multicenter setting failed to predict pCR accurately using core needle biopsy or VAB with FNRs between 17.8% to 50.0%.

Using a machine learning algorithm which was developed by the German group in Heidelberg, the FNR could be reduced to nearly 1.2% in the German data. This algorithm was further validated in a combined analysis from trial in Germany, Korea, and the USA resulting in a FNR of 0%.

The VISION-trial is a multicenter study with a similar approach, recruiting patients in Switzerland, Germany, Austria, and the Emirates from August 2022. The machine learning algorithm is therefore applied prospectively. To date, 41 patients out of the targeted 420 patients have been enrolled in the study.

Kuerer et al. recently published data from a multicenter trial where 31 out of 50 patients were subsequently only observed if no tumor cells were detected by VAB. After a median follow-up of 26.4 months no local recurrences were detected.

The KBCSG-24-OPTIMIST-Trial recently commenced recruitment with a target number of 533 patients. In these patients, surgery will be omitted if VAB does not show tumor cells or atypia following a negative MRI. Sentinel node biopsy will also be omitted for patients who were initially cN0 and had no radiological signs of tumor involvement in the MRI and ultrasound.

Replacing surgery with VAB as a diagnostic tool in exceptional responders to neoadjuvant therapy is still under further investigation.

DE-ESCALATION OF SENTINEL LYMPH NODE BIOPSY IN PATIENTS WITH RADIOLOGIC COMPLETE RESPONSE

Shih-Che Shen, Chi-Chang Yu, Shin-Cheh Chen

Chang Gung Memorial Hospital, Department of Surgery, Taiwan

In recent years, de-escalation has become the trend in surgical management for breast cancer. As a therapeutic strategy in breast cancer management, neoadjuvant systemic therapy (NST) was initially applied to inoperable breast cancer. NST as an initial treatment helps downstage the tumor leading to de-escalate surgical treatment, and could also effectively screen out high-risk patients who do not achieve pathologic complete response (pCR). Currently, increasing studies have reported the plausibility of escalating adjuvant treatment to further lower the risk of recurrence for non-pCR patients.

With the advancement in medical treament such as target therapy and immunotherapy, the pCR rate was significantly increased in recent decades. Recently, NST is also widely applied to operable early breast cancer, and patients without clinical evidence of lymph node (LN) metastasis. In certain high-risk subtypes, the rate of pCR is even higher. To further de-escalate surgery, (for both residual breast lesion and sentinel LN (SLN)), a good predictor for pCR is urged. Recent researches have found some predictors correlate to pCR in SLN, a prospective randomized trial to de-escalate SLN biopsy is ongoing and will be discussed.

DE-ESCALATION OF RADIOTHERAPY IN PATIENTS ACHIEVED PATHOLOGICALLY COMPLETE RESPONSE

Yeon-Joo Kim

National Cancer Center, Department of Radiation Oncology, Korea

In 2012, a combined analysis of the NSABP B-18 and B-27 studies showed that regional recurrence is rare, even without regional nodal irradiation, in cT1-3N1 breast cancer patients who achieved ypN0 after neoadjuvant chemotherapy and breast-conserving surgery. In two Korean retrospective studies, KROG 12-05 and KROG 16-16, regional recurrence rates were less than 3% in patients who achieved ypN0 after neoadjuvant chemotherapy not receiving regional nodal irradiation. However, no definitive data yet support the omission of regional nodal irradiation in patients who achieve ypN0 after neoadjuvant chemotherapy.

NSABP B-51 is an ongoing trial that was initiated in June 2013 of cT1-3N1 patients who are ypN0 after neoadjuvant chemotherapy, with an estimated enrollment of 1636. Patients are randomized to either whole-breast/chest wall irradiation or whole-breast/chest wall irradiation and regional nodal irradiation. The primary outcome is invasive breast cancer recurrence-free interval. In Korea, KROG 19-09 was initiated in 2019. This is a prospective cohort study in which the patient and doctor engage in shared decision making on whether the patient receives breast irradiation or breast and regional nodal irradiation after discussing historical recurrence rates and toxicity associated with regional nodal irradiation. Like NSABP B-51, patients with cT1-3N1 disease and who are ypN0 after neoadjuvant chemotherapy are the target population, but patients who have undergone mastectomy or axillary lymph node dissection are excluded, and KROG- 19-09 aims to enroll 844 patients. The primary outcome is 5-year regional recurrence rate.

For patients who are cN1 at diagnosis and achieve ypN0 after neoadjuvant chemotherapy, the omission of regional nodal irradiation may be safe. However, we need to await the outcomes of the ongoing trials for concrete evidence.

In 2020, Borm et al. published an insightful article in Radiotherapy and Oncology. They evaluated the radiation dose to regional lymph node areas in the landmark Z0011, AMAROS, EORTC, and MA-20 breast cancer studies. Even in these landmark trials, dose distributions at axillary levels I, II and III, as well as the supraclavicular and internal mammary regions varied. These variations were the result of differences in radiotherapy techniques and field designs. Therefore, care must be taken when interpreting the results of studies on regional nodal irradiation.

In KROG 19-09, radiotherapy is delivered according to institutional protocol. We found that participating institutions used varied radiotherapy techniques and field designs, so we performed a dummy-run quality assurance study to assess inter-institutional dosimetric variation. Two sets of anonymized "dummy" CT images were provided to participating institutions: one of a patient with large breast size and one of a patient with medium breast size. Each institution created a whole breast irradiation treatment plan and a breast and regional node irradiation treatment plan for each case. Dose-volume histograms were analyzed using reference target volumes and organs at risk contoured by the host institution. We found inter-institutional and inter-case variations in radiation dose delivered to target volumes and organs at risk. As KROG 19-09 is a prospective cohort study, we accepted that there would be dosimetric variation among the different institutions. Actual patient radiotherapy plan data should be collected to achieve reliable results in KROG 19-09.

In summary, there is data that suggests regional nodal irradiation may be safely omitted in cN1 patients who achieve ypN0 after neoadjuvant chemotherapy. As this data is derived from studies that did not explicitly investigate this issue, studies are ongoing, including KROG 19-09 in Korea, which are doing so. It is important to note that analyses of other studies as well as a quality assurance study of KROG 19-09 show that differences in protocols lead to variations in regional nodal dose distributions, which must be considered when interpreting the results of these studies.

CLINICAL STAGING IN BREAST CANCER PATIENTS UNDERGOING NEOADJUVANT TREATMENT

Han-Byoel Lee

Seoul National Univ. Hospital, Department of Surgery, Korea

In patients who receive surgery for primary treatment of breast cancer, adjuvant therapy is determined according to the pathologic staging while considering the molecular subtype. With the recent increase in the proportion of patients receiving neoadjuvant systemic therapy (NST), initial clinical staging at presentation has become the critical factor in making treatment decisions.

When making decisions between upfront surgery versus NST, the clinical tumor size and the extent of nodal involvement are considered. For a hormone receptor-negative or HER2-positive cancer, most tumors > 2cm are offered neoadjuvant systemic therapy regardless of nodal involvement. In contrast, the clinical nodal stage as well as the number of lymph nodes involved is used to decide whether to proceed with upfront surgery or not.

The clinical staging is also essential to assess the response to NST and decide on the type of surgery for the breast and axillary lymph nodes. The initial involvement of the skin or chest wall may affect decisions to offer breast-conserving surgery even in the case of excellent response. It is now considered safe to perform sentinel lymph node biopsy for patients who were initially lymph node-positive but with no suspicious lymph nodes after NST, but there are conflicting evidence and opinions to whether sentinel lymph node biopsy could be offered to patients who had a cN2/3 disease. In the ongoing trials where surgery for the breast and/or the axilla is omitted in excellent responders, the clinical staging is an essential inclusion/exclusion criterion for enrollment.

Finally, in addition to the pathologic staging after surgery, the initial clinical staging is considered when making decisions for adjuvant treatment. While the residual cancer burden is more important for the administration of additional systemic treatment, the initial nodal involvement is crucial for offering radiation therapy and to what extent.

This strategy of determining the treatment plan with the clinical stage in patients with NST presupposes that the concept or the prognostic impact of the clinical and pathological stages is consistent. However, the criteria for clinical and pathological nodal staging are different in the American Joint Committee on Cancer breast cancer staging, and various suggestions for clinical staging are made in the guidelines and implanted in the real-world practice. I will discuss the disparities in the clinical staging determined by physicians in different specialties and how it could impact treatment decisions as well as clinical outcomes.

CAN CT3/4 BREAST CANCER BE SAFELY TREATED WITH BREAST CONSERVING SURGERY AFTER NEOADJUVANT TREATMENT?

Mehra Golshan

Yale School of Medicine, Department of Surgery, U.S.A.

Neoadjuvant systemic therapy (NST) has traditionally been used to convert patients with unresectable, locally advanced breast cancer to candidates for surgery. More recently, the role of NST has expanded to facilitate breast-conserving therapy (BCT) in patients with large, operable breast cancer who would otherwise require mastectomy.1-5 A meta-analysis of 10 studies including 4756 women reported an increase in BCT from 49% to 65% in patients randomized to neoadjuvant as opposed to adjuvant chemotherapy.6 However, few prospective clinical trials to date have incorporated standardized patient assessments to estimate the success of NST in converting BCT-ineligible patients to BCT eligibility. The boundary of BCT is being pushed where initial clinical T3/T4 lesions are being considered for BCT. We will discuss criteria for BCT in this group.

IS SENTINEL LN BIOPSY FEASIBLE IN CLINICAL N2-3 PATIENTS AFTER NEOADJUVANT TREATMENT?

Jean-Francois Boileau

Jewish General Hospital, McGill Univ., Department of Surgery and Oncology, Canada

It is currently widely accepted that sentinel lymph node biopsy (SLNB) can be used to re-stage the axilla of patients with biopsy proven node positive breast cancer following neoadjuvant chemotherapy. Prospective trials have shown that with optimization of surgical technique SLNB can achieve acceptable accuracy in patients that have no residual palpable disease after neoadjuvant chemotherapy. This includes clipping or marking the suspicious node(s) at the time of pre-treatment biopsy and retrieving the selected node(s) at surgery, using dual dye injection, obtaining at least two or three sentinel nodes and/or using immunohistochemistry (IHC) during pathological evaluation and considering ypN0(i+) as positive nodes.

Although cN2 was an acceptable inclusion criteria in all these prospective trials, either the technical success and false negative rates specific to this subgroup were not reported (SENTINA[1] and GANEA 2[2] studies) or were described in a very small accrued subset of patients (approx. 6%; ACOSOG Z1071[3] and SN FNAC[4] studies), with no observed false negative cases. cN3 breast cancer patients were not included in these prospective trials.

Longer term follow-up (up to 10 years) from retrospective cohort studies have shown that axillary recurrences are rare events in cN+ patients without palpable nodal disease after neoadjuvant chemotherapy (ycN0) operated with SLNB alone in the absence of identifiable residual disease (ypN0(sn)), with rates ranging from 0 to 1.6%[5][6]. These low rates of axillary recurrence were achieved whether a marked node was removed (targeted axillary dissection (TAD)) or not (SLNB alone). At present, it is unclear if the axillary recurrence rate is higher when these patients present with either cN2 or cN3 disease.

In recent years, one of the major advances in the treatment of patients with high-risk breast cancer is the demonstration that additional adjuvant therapy can improve long term outcomes when residual disease is identified after optimal neoadjuvant therapy (capecitabine for triple negative, trastuzumab emtansine for HER2+, olaparib for BRCA1/2+, etc.). Accurate evaluation of nodal response is integral to the proper assessment of pathological response. This remains the strongest argument to promote using the most accurate method available to re-stage the axilla after neoadjuvant therapy in patients with biopsy proven node positive disease, which includes planned targeting and removal of the marked node.

Evidence suggests that in the presence of heavy burden of axillary disease at presentation (4 or more suspicious nodes on axillary ultrasound), the clipped node has a higher risk of not being removed as a sentinel node (more than 3-fold when compared to patients with 3 or less suspicious nodes on axillary ultrasound)[7].

Although some guidelines remain conservative regarding targeted re-staging of the axilla following neoadjuvant therapy in patients that present with biopsy proven cN2 breast cancer[8], limited available evidence could be used to support such an approach if optimal surgical technique, including the removal of the marked node, and adjuvant regional nodal irradiation is used. For patients that present with cN3 disease, until further data becomes available, axillary node dissection and irradiation remains the standard of care following neoadjuvant therapy.

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SURGICAL EXTENT AFTER NEOADJUVANT CHEMOTHERAPY

Geok Hoon Lim

KK Women's and Children's Hospital, Department of Surgery, Singapore

Neoadjuvant chemotherapy could result in downstaging of breast cancer. This then raises the controversy on the extent of surgery needed, in cases with pathological response, in order to achieve an oncologically safe outcome. In this lecture, the extent of surgery after neoadjuvant chemotherapy for breast cancer in the breast and axilla will be discussed.

ROLE OF REPEAT BREAST-CONSERVING SURGERY FOR THE MANAGEMENT OF IPSILATERAL BREAST CANCER RECURRENCE

Andreas Karakatsanis

Uppsala Univ. Hospital, Department of Surgical Sciences and Section for Breast Surgery, Sweden

Introduction: The standard surgical management of ipsilateral breast cancer recurrence (IBCR) in patients previously treated with breast conserving surgery (BCS) and radiotherapy has traditionally been mastectomy. However, practice patterns vary and repeat BCS (r-BCS) with or without re-irradiation has been described in observational studies with varying outcomes. Recent international guidelines, as well as the 2023 St Gallen expert panel provide conflicting recommendations, suggesting that there may be a role for r-BCS in the management of these patients.

Methods: A systematic review of the literature without chronological limitations was conducted, using the search terms "ipsilateral breast tumour recurrence"," ipsilateral breast cancer recurrence", "ipsilateral breast tumor recurrence", "ipsilateral recurrent breast cancer", "IBTR", "local recurrence + breast cancer + breast conserving surgery + mastectomy".

In the absence of dedicated randomized controlled trials, prospective and retrospective comparative and non-comparative cohort studies, cross-sectional studies reporting on second local recurrence (LR) and / or survival after rBCS were considered eligible.

Studies that did not clearly specify whether the reference population had initially been treated for only DCIS, or both DCIS and invasive breast cancer (IBC), were included in the primary analysis.

Input variables included patient characteristics, type of in-breast recurrence (IBC or DCIS), type of second surgical procedure, adjuvant radiotherapy and outcomes included 5-yr local recurrence rates (LR) and overall survival (OS). The studies were assessed with the Newcastle-Ottawa Scale (NOS) and the GRADE approach was utilised to define the strength of recommendations.

Results: In total, 42 studies were included. Of these, 25 examined outcomes after a primary IBC, 16 reported on both IBC and DCIS and one on DCIS only. Twenty-seven studies examined outcomes on both LR and OS, 9 on OS only and 6 on LR only. Of the studies reporting on LR, 17 were comparative; for OS, 19 comparative studies were available.

Source studies reporting on a second LR had a median follow-up ranging from 24.5 to 165.6 months [median of medians 70 months, interquartile range (IQR): 52–73]. The overall pooled incidence of a

second LR after r-BCS was 15.7% (95% CI: 12.1–19.7) and after salvage mastectomy was 10.3% (95% CI: 6.9–14.3). Overall, among patients treated with r-BCS, those who received rRT had the lowest pooled second LR rate compared to the other subgroups (9.6%, 95% CI: 5.0–15.3). In comparative studies, median follow-up ranged from 30 to 165.5 months (median of medians 72months, IQR: 52–79). The pooled second LR rate was higher after r-BCS (19.6%, 95% CI: 15.5–24.0) versus salvage mastectomy (9.6%, 95% CI: 6.3–13.5) [Risk Ratio (RR) = 2.103; 95% CI: 1.535–2.883, $p < 0.001$, I2 = 55.1%), Only concomitant radiotherapy retained a protective effect in meta-regression analysis (coefficient: -0.317; 95% CI: -0.596, -0.038, $p = 0.026$, I2 = 40.4%). No publication bias or small-studies effect was detected (Egger's test beta1: 1.540, $p = 0.103$).

Studies on OS had a median follow-up ranging from 30 to 165.5 months (median of medians 65 months, IQR: 55–73). The pooled 5-year OS rate was 86.4% (95% CI: 82.9–89.6) after rBCS and 79.4% (95% CI: 74.1–84.1) after salvage mastectomy. Subgroup analyses did not demonstrate any factor that correlated with difference in outcomes. In comparative studies (n = 19), the median follow-up ranged from 42 to 165.5 months (median of medians 71.3 months, IQR: 59 123.5). Meta-analysis showed a small OS benefit in favour of r-BCS (82.9%; 95%CI: 77.8, 87.5) compared to salvage mastectomy (77.8%; 96%CI: 72.0, 83.1), resulting RR = 1.046 (95% CI: 1.005–1.089, $p = 0.027$, I2 = 72.3%). Radiotherapy did not affect the outcome on meta-regression analysis (coefficient: -0.0047; 95% CI: -0.0394, 0.0300, $p = 0.791$, I2 = 72.1%). With regards to primary tumor, studies reporting on both DCIS and IBC reported survival benefit for rBCS (RR: 1.153; 95% CI: 1.050 1.267, $p = 0.003$) an effect retained on meta-regression analysis (coefficient: 0.0953; 95% CI: 0.0032 0.1873, $p = 0.042$). The Egger's test detected a small-studies effect (Egger's test beta-1 0.93; $p = 0.041$).

The overall strength of recommendations was very low, due to study and reporting quality and selection bias.

Discussion: Despite the low certainty of evidence, r-BCS could be considered an option for the management of IBCR in patients previously treated with BCS and radiotherapy. Shared-decision making, appropriate patient selection and individualized approach are important for optimal outcomes.

RADIATION THERAPY ACCORDING TO RESIDUAL TUMOR VOLUME AFTER NEOADJUVANT CHEMOTHERAPY IN LOCALLY ADVANCED BREAST CANCER

Sung-Ja Ahn

Chonnam National Univ. Medical School, Department of Radiation Oncology, Korea

Introduction

Interest in the use of preoperative systemic treatment has increased because such neoadjuvant therapy could reduce the surgical extent in the management of breast cancer and primary systemic treatment has been accepted as the standard of care in women with locally advanced breast cancer (LABC). Efforts to minimize toxicity and burden of treatment are even more increasingly important in an era of personalized medicine focusing toward an improved QOL. Postoperative radiotherapy has been adopted incorporating the clinical stage before the neoadjuvant chemotherapy (NAC) as well as according to the extent of the surgery and residual tumor volume presumed to be resided in remnant breast and regional lymphatics.

Whole Breast Irradiation (WBI) in Breast Conserving Surgery after NAC

All women with breast conservation have indications for adjuvant RT to at least the conserved breast, even if no residual cancer is found at surgical pathology. Partial breast irradiation is not permitted in NAC settings. Additional boost dose to the primary tumor bed after the WBI follows the policy similarly to the up-front surgery.

Management of Axilla

In the interpretation of the results showing WBI without cALND were equally efficacious for axillary control, incidentally irradiated dose to the axilla during WBI was focused.The majority of the studies performed before era of IMRT planning used standard parallel-opposite tangential fields for WBI. Traditionally, the standard WBI covers the lower level of axillary lymph nodes and even further level I & II axillary lymph nodes using high tangents fields, which could replace ALND in patients with low burden of axillary disease. In the era of omission of ALND, radiation oncologist should be cautious on the field design of WBI. The incidental dose delivered to the axilla was significantly lower for IMRT compared to 3D-CRT. Therefore IMRT, which only includes the breast parenchyma, should be cautiously used in patients with limited positive sentinel lymph nodes and who do not undergo cALND.

Comprehensive Regional Nodal Irradiation (cRNI) after NAC

Radiation plans that targeted the supraclavicular LNs with or without internal mammary LNs were classified as comprehensive fields. Positive lymph nodes irrespective of the number of positivity or dissected nodes after NAC warrant cRNI because of the greater risk of locoregional recurrence (LRR) than that of up-front surgery. The 5-year rates of LRR according to any pathologic extent of primary and lymph node disease were higher for patients treated with NAC compared with those treated with an initial surgery and postoperative chemotherapy. Even if they have undergone mastectomy, postmastectomy radiotherapy (PMRT) is strongly supported and mandatory in patients with clinical T3 tumors or stage III disease and four or more positive nodes after NAC.

Nowadays, there is great interest in avoiding cRNI in patients with initial clinical N1 disease who convert to ypN0 following NAC. The omission of cRNI should be more debatable, especially after sentinel node biopsy only due to concerns regarding residual axillary disease. Failure to identify residual nodal disease after NAC might also have important implications regarding RT. Regardless of pathological down-staging, axillary irradiation incorporated in the field of WBI is accepted as standard adjuvant treatment in LA-BC. With regard to more cRNI, deceleration of the radiation target volume has been eagerly investigated. Unfortunately, to date, there are no prospective trials to guide clinical decision making regarding the use of RNI in cN+, ypN0 patients. Maturation of NSABP B-51 will take many years, and in the interim, there is currently no consensus among clinicians regarding appropriate RT volumes for ypN0 patients after NAC who undergo SLNB without ALND.

Furthermore, there is still controversy in internal mammary node irradiation (IMNI). A phase III clinical trial testing the disease free survival benefit from IMNI did not reach the statistical significance in patients with node-positive breast cancer from up-front surgery. Meaningfully, the subgroup analysis showed the survival benefit from the IMNI in patients with medially or centrally located tumors.

Based on the experiences from the PORT in the up-front surgery, although there has been no highly qualified evidence, NCCN guidelines strongly support the cRNI irrespective of number of the metastatic axillary lymph nodes in ypN+.

Conclusion

Currently, the consensus is usually guided based on the clinical experiences from the up-front surgery. Significant predictors of LRR after NAC were age, clinical tumor size, clinical nodal status, and nodal/breast pathologic status. Therefore, it is mandatory to evaluate carefully the initial extent of disease and to assign a clinical stage before any treatment is begun. Suboptimal and imprecise clinical extent of disease can translate in a consequent under- or over-treatment.

THE VALUE OF THERAPEUTICS FOR BREAST CANCER

Airi Han

Yonsei Univ. Wonju College of Medicine, Department of Surgery, Korea

It's undeniable that the environment is much different now than when the Health Insurance Review and Assessment Agency (HIRA), South Korea's universal payer organization and policymaker, first started. Policy can and/or should change alongside with its environment. Value-based healthcare is a big part of this change and is already having a big impact on healthcare worldwide including Korea [1-3]. However, value-based health care does not necessarily mean the best interest of patients, nor physician [4-5]. In this session, an overview of value-based care will be presented. How we as oncologists can understand and address value-based care will also be discussed.

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ACCESS TO BREAST CANCER THERAPEUTICS IN ASIAN COUNTRIES

Thitiya Dejthevaporn

Ramathibodi Hospital, Mahidol Univ., Department of Medical Oncology, Thailand

Breast cancer is the most common cancer in Asian women with an increasing incidence over time. Significant advances in medical treatment of breast cancer have been made with a shift from chemotherapy to more innovative therapies. Overall essential cytotoxic chemotherapy and hormonal agents are generally accessible. On the contrary, access to innovative cancer care is limited in many countries in Asia-Pacific, more evidently in the middle-income countries. Despite the availability of the drugs in most countries, affordability is the main limitation and creating barriers to access the life-saving treatments. The prices of innovative drugs have also increased, whereas uncertainty of their clinical benefits raised concerns over the financial sustainability of each countries' health systems. Multiple strategies have been proposed to overcome the problems such as value-based pricing, managed entry agreement, health technology assessment, etc. This has to be done under the context of each individual country in hope to improve treatment outcomes and reduce the financial hardship of the patients.

ACCESS TO BREAST CANCER THERAPEUTICS IN KOREA

Sung-Bae Kim

ASAN Medical Center, Department of Oncology, Korea

The cost of newly approved drugs is a complex issue with no easy answers. On the one hand, these drugs can offer significant benefits to patients, potentially saving lives and improving quality of life. On the other hand, the high cost of these drugs can make them inaccessible to many patients who need them, and can put a strain on healthcare systems and insurance companies.

There are a number of factors that contribute to the high cost of newly approved drugs. Developing a new drug is a lengthy and expensive process, often taking many years and requiring significant investment. In addition, pharmaceutical companies must recoup their research and development costs, as well as make a profit, in order to continue developing new drugs. Another factor is the role of patent protection. When a new drug is approved, the company that developed it is granted a patent that gives them exclusive rights to produce and sell the drug for a certain period of time (usually around 20 years). During this time, the company can charge a high price for the drug without competition from generic alternatives.

So, can we afford these drugs? It depends on how you define affordability. From a patient's perspective, the cost of a life-saving drug may be priceless, and they may be willing to pay whatever it takes to access it. From a healthcare system or insurance company's perspective, however, the cost of these drugs can be a significant burden.

One potential solution is to negotiate lower prices with pharmaceutical companies. This is something that many countries do, but it can be difficult for individual healthcare systems to negotiate effectively. Another approach is to encourage the development of generic alternatives, which can drive down the cost of drugs once the patent protection expires. Ultimately, the high cost of newly approved drugs is a complex issue that requires a multifaceted approach.

The national health insurance utilizes three methods for improving patient access to costly drugs: risk-sharing agreements, designation of essential drugs, and a waiver of cost-effectiveness analysis. Policies currently being implemented for improving patient access to novel drugs by including new breast cancer drugs under the health insurance system in Republic of Korea will be reviewed along with relevant issues as well as future policy prospects.

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CAUSES OF OVER- AND UNDERESTIMATION OF TUMOR AND AXILLARY LN AFTER NEOADJUVANT SYSTEM THERAPY

Beatriu Reig

NYU Langone Health, Department of Radiology, U.S.A

The goals of imaging after neoadjuvant therapy for breast cancer are to monitor the response to therapy and facilitate surgical planning. MRI has been found to be more accurate than mammography, ultrasound, or clinical exam in evaluating treatment response. However, MRI may both overestimate and underestimate residual disease. Accuracy of MRI is dependent on tumor morphology, histology, shrinkage pattern, and molecular subtype. We will review some of the causes of over- and under-estimation of residual disease on breast MRI.

EVALUATION OF RESPONSE TO NEOADJUVANT SYSTEMIC THERAPY: MULTIPARAMETRIC APPROACH FOR ACCURATE EVALUATION OF RESIDUAL TUMOR

Masako Kataoka

Kyoto Univ., Department of Diagnostic Imaging and Nuclear Medicine, Japan

In managing breast cancer, imaging as a tool to evaluate therapy response is becoming more important. Achievement of pathological complete response (pCR) in specific subtypes can be used as a surrogate marker of long-term outcomes. pCR or good response after neoadjuvant systemic therapy allows the de-escalation of surgical procedures. Magnetic resonance imaging (MRI) can provide morphological and quantitative information to monitor treatment response. Dynamic contrast-enhanced MRI (DCE-MRI) is the main sequence used for treatment response. RECIST criteria depend on lesion diameter, which does not always reflect tumor burden. Factors affecting the diagnostic performance of treatment response include lesion morphology (mass or non-mass enhancement), shrinkage pattern (concentric or dendritic), subtype, or specific histology.

The size and extent of the residual tumor estimated on MRI demonstrate good agreement with the residual tumor measured on histopathology. Under or overestimation, however, may be observed. Residual tumors were measured more accurately in triple-negative and HER2-positive tumors while less accurately in the luminal type. Fibrosis, reactive inflammation, and resorptive inflammation can result in overestimation, while tiny foci, non-mass enhancement, and lobular features in histology are often associated with underestimation.

Several approaches have been investigated for the more accurate evaluation of residual tumors after neoadjuvant systemic treatment. To overcome the drawbacks of conventional RECIST size criteria, three-dimensional volumetry can be used as a method less influenced by tumor morphology. The dedicated viewing software is used to measure tumor volume. For selecting only viable residual tumors and avoiding fibrosis, kinetic information from contrast enhancement may be added to the volumetry, called as a functional tumor volume. Computer-aided tumor volume with kinetic information achieved higher inter-observer agreement than conventional RECIST evaluation.

MRI-based parameters other than kinetic can be used to evaluate treatment response. The most widely-used one is the apparent diffusion coefficient (ADC) from diffusion-weighted images (DWI). ADC can be used as a marker of cellularity that can capture residual tumors from aspects different from

vascularity. T2-weighted image of the peri-tumoral area reflects reactions around the tumor reflecting inflammation. Using high-resolution DWI, tumor volume on DWI might be estimated, which can be used as a diffusion-based volumetry. Ultrafast DCE-MRI provides vascular information of the lesion that is more selective for viable and vascular-rich tumors than conventional DCE-MRI. Our preliminary results showed that the enhanced area on Ultrafast DCE-MRI is more specific to the viable tumor cells and therefore closer in lesion size on pathology than conventional DCE-MRI that may over-estimate the enhancing inflammation or scar. Combining these parameters increase the accuracy of estimating residual tumor. Radiomics and machine-learning algorisms are also introduced to further improve the accuracy.

This talk covers the basics and the recent advancement in evaluating the treatment response of neoadjuvant systemic treatment in breast cancer, focusing on a multiparametric approach.

HOW TO MANAGE RESIDUAL MICROCALCIFICATIONS AFTER NEOADJUVANT CHEMOTHERAPY

Sung Hun Kim

The Catholic Univ. of Korea, Seoul St. Mary's Hospital, Department of Radiology, Korea

Neoadjuvant chemotherapy is currently the standard of care for locally advanced and inflammatory breast cancers. Pathologic complete response is defined as no residual invasive disease in the breast and in the axilla or as no residual invasive and in situ disease after neoadjuvant chemotherapy and is a strong and favorable prognostic factor, particularly in patients with HER2+ or triple-negative breast cancers.

Assessment of response to neoadjuvant chemotherapy in vivo is important for the prediction of the patient's final outcome and guidance for further treatment. Contrast enhanced MRI is most accurate imaging modality to evaluate the residual tumor extent (sensitivity: 63-88%, specificity: 54-91%, overestimation: 6-19%, underestimation: 7-28%)

Microcalcifications remains an area of difficulty in the interpretation for the evaluation of response to the neoadjuvant chemotherapy. Microcalcifications frequently persist after chemotherapy, which contributes to disagreement between the clinical and radiological response. Change in the number of microcalcifications is an unreliable indicator of response. Not all residual calcifications represent carcinoma, but also represent successfully treated cancer with calcified and necrotic material in tumor bed.

Current treatment guidelines require excising calcifications seen on preoperative mammography because they are believed to represent the total tumor burden]; this sometimes prompts a larger lumpectomy or a mastectomy in a patient who otherwise has responded well to NAC, even if a complete resolution of enhancement is achieved on MRI.

Although there were not many studies on this topic, previous studies that support the standard guideline and studies that suggest surgery according to MR enhancement will be reviewed. A few studies suggested that ER-breast cancers or nonluminal HER2+ breast cancers with remnant calcifications and no MR enhancement may be considered candidates for breast conservation.

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OPTIMAL DECISIONS ON ADJUVANT ENDOCRINE AND CHEMOTHERAPY USING MULTIGENE ASSAYS

Chi-Cheng Huang

Taipei Veterans General Hospital, Department of Surgery, Taiwan

The overall survival of breast cancer gradually decreases as the stage of the cancer increases. Regardless of stage, there are still patients with recurrence, metastasis or even death, indicating a gap which traditional pathology-based prognostic factors fail to explain. Therefore, many polygenic prognostic markers based on gene expression patterns have been proposed in the past decades to augment pathology reports, such as PAM50 (Prosigna), 21-gene Recurrence Score (Oncotype DX), 70-gene signature (MammaPrint), 11-gene signature (EndoPredict) and so on. Some of which have been commercialized and adopted in clinical guidelines of important international societies. Since 2016, ASCO has also formulated clinical guidelines for these prognostic biomarkers. In 2017, ESMO guideline for early stage hormone receptor-positive, HER2-negative breast cancer without regional lymph node spread also agreed that the implementation of chemotherapy in addition to endocrine therapy should base on these multi-gene expression biomarkers, except those of pT1a/T1b, N0, grade I, and strong estrogen receptor expression.

Most of these gene expression signatures provide additional predictive/prognostic power beyond traditional pathological factors. Specifically, the prognostic (most markers)/predictive (only a few) power of gene expression assays are based on polygenic tests to evaluate the prognosis of patients, or the risk of recurrence and metastasis at the molecular level. Multi-gene expression assays are used to answer questions for early breast cancers: do small tumors without lymph node metastasis need cytotoxic chemotherapy to prevent further recurrence? These assays also identify the real high-risk group of patients and appropriate chemotherapy should be applied, even with potential side effects, and for low-risk patients, chemotherapy can be safely waived without a compromise in outcome. A polygenic gene expression assay is based on the relative expression of its constituent genes and defines the prognostic risk score with a specific algorithm. At present, multi-gene expresion assays for breast cancer can strengthen but not replace the traditional pathological features such as ER, PR, HER2, grade, Ki-67, anatomical stage and age (pre-/post-menopausal status).

In this presentation, we will update the state-of-the-art multi-gene expression assays for hormone receptor positive breast cancers, as well as recent advances in determining the application of extended endorine therpay, paving the way for personalized medicine for early stage endocrine-responsive breast cancer. In addition, novel applications such as omission of local adjuvant radiotherapy and the discremination between endocrine sensitivity and chemotherapy sensitivity will be highlighted.

CLINICAL PARAMETERS AS ALTERNATIVES TO GENOMIC ASSAYS

Jong Won Lee

ASAN Medical Center, Breast Cancer Center, Department of Surgery, Korea

Genomic assays such as Oncotype DX (ODX) and Mammaprint (MMP) in hormone receptor-positive, HER2-negative breast cancer are considered independent prognostic and predictive markers to avoid unnecessary chemotherapy. The number of assays being performed is increasing, but the assays still take a long time to get results and are expensive for many eligible patients. Efforts to build nomograms to predict the results of the assays have been made based on both nation-based datasets and institution-based experiences. Studies showed the correlation between the assays' results and commonly available clinicopathological variables such as ER, progesterone receptor (PR), HER2, and Ki67 on immunohistochemistry; tumor size and grade on conventional pathology; and age at diagnosis, new radiologic parameters, and so on. In this talk, we are going to review the various clinical nomograms presented as alternatives to genomic assays and share insights into the more tailored use of genomic assays in terms of healthcare expenditures as well as acceptable clinical outcomes

INTERPRETATION OF GENOMIC ASSAYS IN PREMENOPAUSAL WOMEN

Kevin Kalinsky

Winship Cancer Institute of Emory Univ., Department of Hematology and Medical Oncology, U.S.A.

In this presentation, data from the large, randomized trials with genomic assays will be reviewed, including TailorX, RxPONDER, and MINDACT. There will be a focus on the premenopausal population. Limitations of these trials will be discussed, including the limited percentage of premenopausal patients who received optimal endocrine therapy with ovarian function suppression. The presentation will also cover the question of whether the chemotherapy benefit seen in the premenopausal population is due to tumor biology differences between pre- and post-menopausal women or exclusively due to the amenorrhea experienced by premenopausal women who are administered chemotherapy. Future randomized trials to address this issue will also be reviewed.

BREAST RADIOTHERAPY DURING PREGNANCY

Stefanie Corradini

Univ. Hospital, LMU Munich, Department of Radiation Oncology, Germany

The use of radiotherapy for breast cancer treatment during pregnancy is a controversial topic, with many clinicians being cautious and avoiding the procedure whenever possible. Technological advancements in radiation oncology, such as intensity modulated and image guided radiation delivery, have been introduced since the 1990s to enhance the efficacy and tolerance of radiation treatment. However, the potential health effects on the fetus from radiation exposure through advanced radiotherapy techniques are not yet clear in terms of short- and long-term outcomes. The objective of this talk is to provide a comprehensive overview of the limited evidence available from current literature on the feasibility and clinical outcomes of modern radiotherapy procedures for the treatment of pregnant women.

RISK OF CONTRALATERAL BREAST CANCER AFTER BREAST RADIOTHERAPY IN YOUNG WOMEN

Seung Won Seol

Univ. of Pennsylvania, Department of Radiation Oncology, U.S.A.

Adjuvant radiotherapy after breast-conserving surgery has become a vital component of the breast cancer treatment paradigm as it reduces the risk of local recurrence significantly and improves breast cancer-specific survival. However, radiation for breast cancer also exposes surrounding healthy tissues including the contralateral breast to low-dose scatter, which may increase the risk of secondary malignancy. Although most of the available data using modern radiation techniques do not suggest a significant increase in the risk of developing contralateral breast cancer, there is some evidence suggesting a slightly increased risk in younger patients (age < 45 years at diagnosis) or patients with genetic susceptibility. This session will introduce data comparing the incidences of contralateral breast cancer in patients who received adjuvant radiation with those who did not receive radiation, and review the suggested patient-related factors and treatment-related factors in the literature that may affect the risk. While the reported risks can be related to using older radiotherapy techniques and the benefit of radiation far outweighs the risk, it is important to consider these potential risks and use techniques that minimize scattered doses to the contralateral breast.

HEART DISEASE AFTER BREAST RADIOTHERAPY IN YOUNG WOMEN

Ji Hyeon Joo[1,2]

[1]*Pusan National Univ. Yangsan Hospital, Department of Radiation Oncology, Korea,*
[2]*Pusan National Univ. School of Medicine, Department of Radiation Oncology, Korea*

Breast-conserving therapy, involving lumpectomy and breast irradiation, is a well-established treatment option for early-stage breast cancer. However, radiation therapy (RT) can cause incidental exposure of the heart to radiation, increasing the risk of radiation-induced heart disease. The risk of coronary artery disease (CAD) increases progressively with the mean heart dose, particularly after left-sided breast irradiation, and can lead to ischemic heart disease, pericardial effusion, transient ischemia, congestive heart failure, and myocardial infarction.

Long-term follow-up and monitoring for cardiac complications are crucial for young breast cancer survivors, especially those who have or will receive known cardiotoxic agents such as an anthracycline or trastuzumab. A recent study on the effects of RT on younger breast cancer patients shows that the cumulative incidence of CAD over 27 years is higher in left-sided breast cancer patients than in right-sided patients. Among women aged 25-39 years, the incidence of CAD was 6% in left-sided breast cancer patients and 0% in right-sided breast cancer patients.

It is recommended that all patients undergoing radiation or cardiotoxic cancer therapy receive a baseline comprehensive cardiovascular history and physical exam. The presence of coronary artery calcification is a strong and independent predictor of heart disease events, providing a clinically useful tool for assessing the risk of radiation-induced heart disease. To minimize heart irradiation, several techniques can be employed, such as hypofractionation, partial breast irradiation, breathing control, intensity-modulated RT, volumetric modified arc therapy, or proton therapy.

In conclusion, breast-conserving therapy is an effective treatment for early-stage breast cancer, but the incidental exposure of the heart to radiation can cause long-term cardiac complications. Close monitoring and evaluation of cardiac health are essential for young breast cancer survivors, and healthcare providers should employ techniques to minimize heart irradiation during RT.

SYSTEMIC TREATMENT FOR HER2-POSITIVE EARLY BREAST CANCER

Jee Hung Kim

Yonsei Univ. College of Medicine, Department of Medical Onocology, Korea

HER2-positive breast cancer is an aggressive disease in which survival is close to triple-negative breast cancer rather than hormone receptor (HR) positive breast cancer in the natural course of the disease. However, anti-HER2-based targeted therapies in combination with chemotherapy have dramatically changed the prognosis, which is now comparable to HR-positive disease. This achievement is still moving forward. The first thing in the clinic we think about when HER2-positive early breast cancer (EBC) patients came in is to decide whether neoadjuvant chemotherapy (NACT) or surgery would be offered first to the patient. If it is low-risk EBC with clinically node-negative disease and tumor size < 2 cm, upfront surgery is usually advised followed by adjuvant chemotherapy with trastuzumab +/- pertuzumab, depending on pathologic LN status. If it is high-risk EBC (the tumor size ≥ 2 cm, and/or node-positive disease), NACT with anti-HER2 targeted agents will be suggested to the patients, followed by surgery. In this case, pathologic LN status could tailor the following therapies if there is a pathological complete response (pCR: ypT0/is, ypN0), anti-HER2 targeted agents will be continued to complete 1 year of therapy. If it is non-pCR after surgery, trastuzumab emtansine (T-DM1) therapy should be considered for 14 cycles because it significantly improved invasive disease-free survival compared to trastuzumab. Extended therapy with neratinib could be considered for patients who have completed 1 year of trastuzumab when it is an ER+HER2+high risk disease. However, these suggestions should be discussed with patients considering the local reimbursement system, patients' age, co-morbidities, and preferences.

SYSTEMIC TREATMENT FOR HER2-POSITIVE METASTATIC BREAST CANCER

Soo Chin Lee

National Univ. Cancer Institute, Department of Hematology-Oncology, Singapore

HER2 inhibition is a crucial cornerstone in the systemic therapy of HER2-positive breast cancer. Dual anti-HER2 blockade with pertuzumab + trastuzumab combined with taxanes has been the standard first-line treatment for HER2+ metastatic breast cancer (MBC) since 2012 and remains unchallenged for more than a decade. Trastuzumab emtansine (T-DM1) was approved as the preferred second-line treatment based on the EMILIA trial in 2013 but its position is recently challenged by a newer antibody drug conjugate, trastuzumab deruxtecan (T-DXd). Compared to T-DM1, T-DXd has a higher drug-antibody ratio, has a tumor-selective cleavable linker and induces bystander anti-tumor effects. T-DXd led to remarkable objective responses in almost 80% of previously treated patients and prolonged median PFS by almost 3.5 fold from 7 months to 24 months compared to T-DM1 in the phase III randomized DESTINY Breast03 trial. These promising data have been quickly embraced by the oncology community with NCCN and ESMO revising their guidelines to recommend T-DXd as the preferred second-line treatment over T-DM1. Notably, the median PFS of T-DXd of 24 months in the treated setting is longer than the median PFS of 18 months with first-line pertuzumab + trastuzumab + taxanes in the CLEOPATRA trial, underscoring the potential of T-DXd to challenge the current first-line therapy. Indeed, first-line T-DXd is being evaluated in the DESTINY Breast09 trial and results are eagerly awaited. Another new agent that is changing the treatment landscape of HER2+ MBC is the small molecule tyrosine kinase inhibitor tucatinib, which has shown highly promising CNS activity in the HER2Climb trial. CNS disease occurs commonly in HER2+ MBC and is traditionally managed with local intervention such as radiotherapy or surgery. However, there is increasing evidence that some drugs have CNS activity and systemic therapies such as tucatinib-based combinations are now accepted as viable treatment options for CNS disease in HER2+ MBC, particularly in patients who progress both extra- and intra-cranially. Two other new HER2-directed therapies, neratinib and margetuximab, were approved for refractory disease in 2020, adding to our treatment armamentarium. The availability of these new agents is revolutionizing the management of HER2+ MBC. However, these new drugs are expensive and not yet available in all countries or affordable to most patients. Co-ordinated efforts by the oncology community, pharma and national healthcare systems would be crucial to expand patient access to promising new drugs to truly achieve improvements in patient outcomes in the real world.

OVERVIEW AND MANAGEMENT OF ADVERSE EVENTS OF ANTI-HER2 ADCS

Makiko Ono

The Cancer Institute Hospital of JFCR, Department of Medical Oncology, Japan

The prognosis of HER2-positive breast cancer has improved dramatically due to anti-HER2 treatment over the past 20 years. Anti-HER2 monoclonal antibodies had played a key role and nowadays biotechnological development has led to a new type of drug, antibody-drug conjugates (ADCs) which are composed of a monoclonal antibody, a linker and a payload. The ADC targeting HER2 which was firstly approved for metastatic HER2-positive breast cancer was ado-trastuzumab emtansine (T-DM1) and several novel anti-HER2 ADCs have been developed. T-DM1 consists of trastuzumab, a thioether uncleavable linker and DM1 of a microtubule inhibitor. In EMILIA trial, T-DM1 significantly improved progression-free survival (PFS) and overall survival (OS) compared with the combination treatment with capecitabine and lapatinib in advanced HER2-positive breast cancer patients who were previously treated with trastuzumab and taxane. The most common severe adverse events with T-DM1 are thrombocytopenia, liver dysfunction, and anemia. Fam-trastuzumab deruxtecan (T-Dxd), which is constituted of trastuzumab, a cleavable tetrapeptide linker and a topoisomerase inhibitor of exatecan derivative as a payload has been approved for metastatic HER2+ and HER2-low breast cancer. In DESTINY-Breast03, T-DXd significantly prolonged PFS and OS compared with T-DM1 in advanced HER2-positive breast cancer patients previously treated with trastuzumab and taxane. The most common severe adverse events occurred more frequently in T-DXd compared with T-DM1 and were interstitial lung disease (ILD), neutropenia, and gastrointestinal disorders with T-DXd. In earlier drug development for T-DXd, patients had fatal ILD, however, in the phase III trial there were no fatal ILD cases. That means investigators became more careful and the education for ILD was important for investigators and patients. In addition, since gastrointestinal disorders often impair QOLs of patients, the management of those are quite important as well. In this session, adverse events of anti-HER2 ADCs including T-DM1, T-DXd and other drugs under development will be summarized and the management of those will be discussed.

BASIC TECHNOLOGY OF LIQUID BIOPSY

Eunhae Cho

GC Genome, Genome Research Center, Korea

The circulating tumor DNA (ctDNA) and intact circulating tumor cells (CTCs) are two of the components that are targeted during a liquid biopsy. In this topic, I would like to focus primarily on ctDNA. In terms of use, liquid biopsy technology is expanding from panel testing for selection of anticancer drugs to early cancer detection and MRD detection. Currently most techniques are panel testing based on the mutations and CNVs for selection of anticancer drugs. In the field of MRD, three major companies are providing testing service. Natera's first MRD testing, Signatera is a testing that detects personalized mutations for each individual with tissue sequencing. Guardant Reveal is the first liquid only test to detect MRD in colon, breast and lung cancer. C2i Genomics uses WGS for MRD detection. In the field of early diagnosis, cf-WGS or methylation analysis are being developed. Grail that specializes in the developing blood tests for early cancer detection, services Galleri, a multi-cancer early detection test. Freenome, a healthcare AI company that uses machine learning algorithms to analyze cell free DNA, RNA and proteins in the blood for early cancer detection. GC genome is also developing early cancer detection using cf-WGS and I will present the preliminary data.

CLINICAL UTILITY OF DETECTION OF EARLY RECURRENCE OR MINIMAL RESIDUAL DISEASE USING LIQUID BIOPSY IN EARLY BREAST CANCER

Kan Yonemori

National Cancer Center Hospital, Department of Medical Oncology, Japan

Liquid biopsies, particularly those involving circulating tumor DNA (ctDNA) from patient blood, are rapidly emerging as important and minimally invasive genotyping tools for patients with cancer. Liquid biopsies have been widely used for genomic profiling in patients with advanced cancer and also show potential for detecting minimal residual disease (MRD). MRD is defined as cancer that persists after treatment and cannot be detected with current medical imaging modalities. It is a strong prognostic biomarker for poor outcomes in various tumor types, including breast cancer. Thus, the detection of MRD, in addition to established clinicopathological risk factors, has the potential to identify patients at high risk of metastatic relapse. Several MRD assays have been developed, but the standard assay has not yet been determined. Since the amount of ctDNA is minimal in early-stage solid tumors, highly sensitive assays are needed. Multiple interventional trials based on MRD detection using ctDNA testing to guide treatment are ongoing. MRD-based treatment strategies may dramatically change the future of breast cancer treatment. However, there are some caveats to MRD-based treatment strategies for clinical application.

In this symposium, I will summarize the current evidence of MRD detection using ctDNA and discuss future perspectives for clinical application.

CURRENT ADVANCES OF LIQUID BIOPSY IN TUMOR BURDEN DYNAMICS, RESPONSE MONITORING AND PROGNOSTIC MARKER IN METASTATIC BREAST CANCER

Jisun Kim

ASAN Medical Center, Department of Surgery, Korea

Liquid biopsy enables to dissect heterogeneity of tumors which can profoundly affect response to specific therapy. Most metastatic breast cancer patients have undergone several lines of treatment, and under those selective pressure, metastatic tumors tend to acquire mutations leading to acquisition of new subclones. While one-time tissue analyses may not sufficiently display the dynamics of the subclones, noninvasive liquid biopsy enables tracking and monitoring the process of clonal evolution while treatment from real time analyses. This talk will mainly cover liquid biopsy analyzing circulating tumor DNA (ctDNA) and circulating tumor cells (CTCs). Though extensive level of investigations in ctDNA and CTC analysis, evidences on clinical utility in guiding therapy are yet limited.

PI3K inhibitor has been shown to be effective in PIK3CA mutated tumors. Tumors with PIK3CA mutation found in either tumor and/or plasma are candidates for PI3K inhibitor (eg. Alpellisib) by applying PCR based method- or sequencing. PCR based method analyzes specific 10-20 known hotspot mutations and sequencing method analyzes the whole exonic region of the gene. Currently, PCR based method has been approved for both using both tumor and plasma, while sequencing method is limited to tumor tissue.

ESR1 mutation is the most common cause of endocrine resistance and arise during long term estrogen deprivation. Recent phase lll trial analyzed the oral SERD in metastatic HR positive HER2 negative patients with previous 1-2 lines of endocrine therapy. Progression free survival was prolonged for overall population and patients with ESR1 mutations (47.8% of overall population) displayed most benefit and lead to update in 2023 guideline for using Elacestant for ESR1 mutated breast cancer patients. ESR1 mutation was analyzed in plasma DNA by using Guardant360 CDx. Another recent phase lll trial randomizing patients to switch to fulvestrant + CDK4/6i from aromatase inhibitor + CDK4/6i at time of plasma ESR1 mutation positive or stay on AI + CDK4/6i, reported longer progression survival for early switch to fulvestrant. Evidences for using other novel agents of immune checkpoint inhibitors, PARP inhibitors, TRK inhibitors etc. depending on liquid biopsy is still growing as methods with higher sensitivity, specificity is being introduced.

While liquid biopsy technology holds promise in metastatic disease for its ability to potentially identify

patients and guide decisions, however, to date, neither the identification nor measurement of dynamic changes of allelic frequencies and cell number to direct therapy has been prospectively shown to improve patients' outcome. Whats more, the relevant correlation nor comparison between each methods and pipelines have not been evaluated, and among which are the most accurate and reliable in each of clinical setting, accompanied by the development of new drugs, are far more to be investigated.

SURVEILLANCE STRATEGY OVERVIEW IN KOREA

Hyeong-Gon Moon

Seoul National Univ. Hospital, Department of Surgery, Korea

Breast cancer is the most common malignancy in Korean women and, more importantly, the incidence rate is continuously rising. As the breast cancer is a malignant disease with relatively high overall survival rate, there are also a large number of breast cancer survivors who have completed their initial multimodal treatment.

Several decades ago, two prospective randomized trials have demonstrated that radiologic surveillance for distant metastasis in asymptomatic breast cancer patients does not improve the overall survival of the breast cancer patients. The results of these randomized trials, along with the palliative nature of the treatment for patients who developed distant metastasis, have led to the current international guidelines that recommend against the use of radiologic exams for distant organs in asymptomatic patients.

However, in reality, there are significant differences in the surveillance policies among different institutions and physicians in terms of using various radiologic modalities for asymptomatic breast cancer patients. Additionally, recent development in new therapeutic arsenals for metastatic breast cancer patients have raised the possibility of improved survival of metastatic breast cancer patients when the treatment is initiated at earlier levels.

To address this issue, our team has started a multicenter retrospective study to investigate the current status on the use of the radiologic exams for distant metastasis in Korea. Multiple researchers from the Korean Breast Cancer Survivor Research Group have participated in the study. Also, we have launched a prospective trial investigating the attitude and decision of Korean breast cancer patients with regard to the metastasis surveillance during the asymptomatic phase. The preliminary findings of these studies will be presented.

POST-OPERATIVE SURVEILLANCE AND MANAGEMENT FOR BREAST CANCER PATIENTS IN TAIWAN

An-Chieh Feng

Tri-Service General Hospital, Department of General Surgery, Taiwan

Breast cancer is the most commonly diagnosed female cancer in Taiwan. There were 16,325 women newly diagnosed as having breast cancer in 2019 and more than 2,000 women died from breast cancer each year.

To better understand the current postoperative surveillance strategy in Taiwan, we designed a questionnaire and completed by 62 physician members in Taiwan Breast Cancer Society from the north, middle and south part of Taiwan. In the questionnaire, there are mainly four categories including physician profiles, image studies, serological studies and hormone therapy related studies. For the image and serological studies, we further divided these sections into carcinoma in situ and invasive disease.

By analyzing the data, we aim to demonstrate the current real world practice in breast cancer postoperative surveillance among different physician groups, hospital scales and disease severities under the unique health insurance system in Taiwan.

THE STATE-OF-THE-ART RISK PREDICTION TOOLS AND HOW THEY APPLY TO ASIAN BREAST CANCER SCREENING PROGRAMS

Jingmei Li

Genome Institute of Singapore, Department of Women's Health and Genetics, Singapore

In the light of health screening programs, chronic conditions such as diabetes and cardiovascular diseases have established markers such as blood glucose, cholesterol, or pressure measurements to flag individuals at high risk for interventions. Screening for common cancers, such as breast cancer, is not risk stratification, but rather, the early detection of tumors. The diagnosis of breast cancer early through mammography screening has been shown to reduce deaths from the disease. However, mammography is not without harm. False positive tests and overdiagnosis of tumors that may never advance into a clinical stage that endangers life are commonly cited downsides of mammography screening. In Asia, the benefits of mammography screening are further impeded by the lack of organized screening programs and low screening attendance rates.

Risk stratification for breast cancer helps to optimize resource allocation by targeting screening toward those who will benefit from it the most. Family history is commonly used in the clinic to assess individual breast cancer risk. However, many high-risk women who could potentially benefit from timely interventions are missed by information from only family history. Many tools that take into account both genetic and non-genetic risk factors are available to stratify women according to their individual risk of developing breast cancer. Understanding the proportions of high-risk women flagged by different breast cancer risk prediction tools helps support their implementation in breast cancer screening programs.

In the Singapore Breast Cancer Cohort study comprising 7,600 Asian breast cancer patients diagnosed between ages 30 and 75 years, individuals with a priori high breast cancer risk were identified using the following criteria: 1) family history, 2) Gail model (non-genetic), 3) breast cancer predisposition genes (rare, germline, protein-truncating genetic variants [PTV] in ATM, BRCA1, BRCA2, CHEK2, PALB2, BARD1, RAD51C, RAD51D, or TP53), and 4) polygenic risk score (PRS, aggregated score of 313 known common genetic risk variants).

Over half of the breast cancer patients (53%, n = 4,041) were considered high risk by one or more classification criteria. PRS and the Gail model identified 2,774 (36%), and 1,592 (21%) patients to be at

high risk, based on a five-year absolute risk cut-off of 1.3%, equivalent to that of an average 50-year-old woman recommended to start mammography screening. Family history and PTV carriership identified 1,247 (16%) and 385 (5%) high-risk individuals. In a subset of 3,227 women aged below the recommended screening age of 50 years, the four tools examined identified 769 (24%), 325 (10%), 470 (15%), and 213 (7%), unique patients who were considered at high risk, respectively.

However, the correlation between absolute risks estimated by genetic (PRS and non-genetic (Gail model) models was low ($r = 0.27$). For younger women, genetic risk predictors (PRS and PTVs) together identified 745 (59% of 1276) high-risk individuals who were not flagged by the non-genetic risk predictors (Gail model and family history).

The findings suggest that risk-based breast cancer screening programs may benefit from a multi-pronged approach that includes PRS, pathogenic variants in breast cancer predisposition genes, family history, and other recognized risk factors. There are other remaining issues regarding optimal risk thresholds, how participants are informed of risk assessment findings, and how future policies may be shaped before the potential of precision screening for breast cancer is realized.

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Debate Session

"Go Beyond Cure of Breast Cancer"

ROLE OF PLATINUM AGENT IN EARLY TRIPLE NEGATIVE BREAST CANCER - PROS.

Jieun Lee

The Catholic Univ. of Korea, Seoul St. Mary's Hospital, Department of Medical Oncology, Korea

In Early triple negative breast cancer (TNBC), achievement of pathologic complete response (pCR) is related to improvement of overall survival. To increase the pCR rate during neoadjuvant chemotherapy, escalation of chemotherapy based on a combination regimen with platinum agent has been the focus in recent years. The combination of platinum with conventional anthracycline and taxane based regimen has improved the pCR rate from approximately 35% to over 50%. The rationale of using platinum in TNBC is based on the biology of TNBC. In tradition, platinum was considered in gBRCA mutant patients. In gBRCA mutant breast cancer, platinum inhibits DNA repair mechanism and induce cancer cell apoptosis. Sporadic TNBC patients may show similar tumor biology to gBRCA mutant breast cancer, and this is called BRCAness. BRCAness of TNBC may be associated to improved response to platinum in neoadjuvant setting, and this is one of a biological basis of using platinum in TNBC patients.

Combination of platinum agents can be considered in patients who need rapid local control before surgery, and achievement of improved pCR is a strong rationale of using platinum in TNBC patients.

ROLE OF PLATINUM AGENT IN EARLY TRIPLE NEGATIVE BREAST CANCER - CONS.

Min Hwan Kim

Yonsei Univ. College of Medicine, Department of Medical Oncology, Korea

Although there is no definitive clinical trial data demonstrating the survival gain by adding platinum agent (carboplatin) to (neo)adjuvant chemotherapy in early triple-negative breast cancer (TNBC) yet, the neoadjuvant carboplatin is now widely used for treatment of stage II-III TNBC patients in Republic of Korea. However, the presenter raises a scientific concern on routine use of carboplatin in early TNBC patients for following reasons.

1) There is no multicenter study result to show the survival gain of adding carboplatin using EFS or DFS as a dedicated primary endpoint yet. Despite the increased pCR rate by carboplatin, there was inconsistency in EFS outcome between GeparSixto and CALGB40603 study. We are waiting for the upcoming survival result of PEARLY and NRG BR-003 phase III trial.
2) Carboplatin causes a significant hematologic and non-hematologic toxicities that may lead inferior dose intensity and survival outcome.
3) In ECOG-ACRIN EA1131 trial that tested capecitabine versus carboplatin in adjuvant treatment of non-pCR TNBC patients, platinum did not improve outcomes in patients with basal subtype TNBC and was associated with more severe toxicity. This trial suggests the role of carboplatin may be replaced by less toxic capecitabine.
4) For BRCA1/2 mutant patients, there was no difference in pCR by carboplatin use in Brightness trial, and this result negates role of carboplatin in BRCA1/2 mutant patients.
5) A recent Indian single-center trial presented in SABCS 2023, the carboplatin improved EFS and pCR only in patients aged $\leq$ 50, but no in patients aged $>$ 50.

Therefore, the presenter suggests future direction for selective carboplatin use in early TNBC who essentially benefit from the platinums

1) More delicate HRD diagnostics need to be developed, including WGS, ctDNA, RNA signature based HRD detection.
2) ctDNA-based molecular residual disease (MRD) assay may guide escalation of (neo)adjuvant therapy of TNBC.
3) The differential benefit of carboplatin by patient age needs to be judged in multiple patient context.
4) The relationship between carboplatin use and anti-immune response (TIL or pembrolizumab response) needs to be interrogated by clinical and translational studies in early TNBC.

GENOMIC RISK VS. CLINICAL RISK IN EARLY-STAGE, HR+ BREAST CANCER - GENOMIC RISK

Dae-Won Lee

Seoul National Univ. Hospital, Department of Internal Medicine, Korea

In hormone receptor (HR) positive breast cancer, adjuvant endocrine therapy and chemotherapy reduces risk of recurrence after curative surgery. However, the added benefit of adjuvant chemotherapy is low in patients with relatively small tumor size, low grade, and lymph node negative disease. Studies show that multigene assays can predict local recurrence, distant recurrence, and survival in hormone receptor positive breast cancer. Oncotype DX and MammaPrint are among the most studied assays and have been clinically validated for predicting the benefit of adjuvant chemotherapy after surgery. In the prospective TAILORx trial, HR-positive, human epidermal growth factor receptor 2 (HER2)-negative, lymph node-negative breast cancer with a midrange Oncotype DX recurrence score (RS) of 11 to 25 and were randomly assigned to receive either chemoendocrine therapy or endocrine therapy alone. In post-menopausal patients with RS 11-25, there was no difference in invasive disease free survival (iDFS), distant recurrence, and overall survival (OS) regardless of chemotherapy use. However, patients with ≤ 50 years old with RS of 16-25 had superior iDFS and lower distant recurrence when treated with chemotherapy. Similar finding was shown in the RxPONDER trial which included HR-positive, HER2-negative, lymph node-positive (1-3), and a RS score of 25 or lower. Five year iDFS between endocrine therapy only arm and chemoendocrine therapy arm was similar in the postmenopausal patients. However, premenopausal patients who received chemoendocrine therapy had longer iDFS and distant relapsefree survival. These findings show that genomic risk could predict chemotherapy benefit especially in post-menopausal patients. Although chemotherapy showed benefit in pre-menopause women with RS score under 25, the role of adding ovarian function suppression without chemotherapy in these patients needs to be answered.

While extended endocrine therapy reduces cancer recurrence, the benefit is modest with increased side effects. Recent evidences suggests that multigene assays may predict benefit from extended endocrine therapy. The NSABP B-42 study enrolled patients with HR-positive breast cancer treated with 5 years of treatment with an aromatase inhibitor or tamoxifen followed by an aromatase inhibitor. Patients were randomly assigned to receive 5 years of letrozole of placebo. The utility of MammaPrint assay was studied in this population showing statistically significant extended hormone therapy benefit in MammaPrint Low risk but not in MammaPrint High risk. The benefits were profound in non-UltraLow MammaPrint Low patients. Similar findings was identified in patients enrolled in the IDEAL

trial which included HR-positive postmenopausal patients treated with five years of any endocrine therapy. Patients were randomly allocated to either 2.5 or 5 years of letrozole in the IDEAL trial. These results show that multigene assays may have potential role in selecting patients with extended endocrine therapy in early stage HR-positive breast cancer.

GENOMIC RISK VS. CLINICAL RISK IN EARLY-STAGE, HR+ BREAST CANCER - CLINICAL RISK

Tae-Kyung Robyn Yoo

ASAN Medical Center, Department of Surgery, Korea

The use of multigene assays in hormone receptor-positive, HER2-negative early breast cancer resulted in reduced use of adjuvant chemotherapy without increase in oncologic outcomes. Whereas multigene assays can guide and assist the physician decision for adjuvant chemotherapy, it cannot be a tool that "decides" the use of it. Clinical risk is still a powerful tool in deciding a patient's adjuvant treatment.

The recent studies (TAILORx, RxPONDER and MINDACT) investigating the role of multigene assay demonstrated the clinical utility of these tests, but it is also careful to apply the results of these recent studies in all patients. These studies include a low proportion of patients with T3/4 tumors or high grade tumors, very young patients (< 40 years old) and patients with multiple metastatic lymph nodes or multicentric cancers. We still lack evidence in using multigene assays in all clinical situations within the indication of each study.

These three studies have commonly shown chemotherapy benefit in young women (or premenopausal women) regardless of genomic risk status. However, all three studies have a very low rate of ovarian function suppression in the only endocrine group, not being able to differentiate whether the chemotherapy benefits from its cytotoxic effect or indirect endocrine effect. Futures studies such as the NGR BR009 trial is to be started to answer this question.

Multigene assays present with high discrepancies among each other when distinguishing low/high risk. The preliminary results of the OPTIMA trial showed 60% of disagreement among different multigene assays in risk categorization. This result is biologically understandable as all multigene assays differ in included gene sets, but in a clinical perspective, it is quite confusing. It also means that there is no ultimate discriminator of risk for patients and emphasizes the need for clinical risk assessment.

Clinical factors are not excluded but actually included in assessing patient's risk with multigene assays. The MINDACT trial was designed to assess clinical factor first to decide whether to proceed with a multigene assay. Sparano et al also included clinical factors to the Oncotype DX test to identify premenopausal women who could benefit for more effective therapy. The Endopredict and BCI test includes clinical factors in their algorithm.

However, the major limitation of assessing clinical risk is that it includes many factors that are frequently

mixed up with high and low risk features. An alternative approach to assist clinical decision would be to evaluate endocrine responsiveness by giving endocrine therapy preoperatively for 2 weeks and assess Ki67 change which was applied in the ADAPT trial.

In conclusion, although multigene assays are helpful in guiding adjuvant treatment decisions, it is clear that it cannot be the ultimate decision tool. Clinical risk is a powerful tool that must be included and highly considered in our everyday clinic decisions.

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OPBS Session

"Go Beyond Cure of Breast Cancer"

ONCOPLASTIC BREAST SURGERY: WHERE ARE WE?

Ho Yong Park

Kyungpook National Univ. Chilgok Hospital, Department of Surgery, Korea

According to the latest statistics of the Korean Breast Cancer Society, the rate of partial mastectomy (PM) in 2019 was 68.6% and that of total mastectomy (TM) was 30.4%. Although PM had increased rapidly since 2000 due to the increase in early breast cancer and the development of radiotherapy, there are still advanced breast cancers requiring TM, and with the development of imaging techniques such as MRI, which can make early diagnosis of a wide extent of breast cancers and multiple breast cancers.

A standardized classification system for breast surgery that incorporates oncoplastic techniques is needed. Here, I classified the surgical techniques for breast cancer treatment into five groups according to the extent of surgery and reconstructive methods, i.e. conventional breast-conserving surgery, partial mastectomy with volume displacement, partial mastectomy with volume replacement, simple mastectomy and total mastectomy with immediate reconstruction. I will show the oncological outcomes for each of the five groups.

According to 5-year oncological results from patients with breast cancer who underwent breast surgery with reconstruction between 2008 and 2013. In total, 1469 patients had 1504 breast surgeries performed. There were 35 cases (2.3%) of locoregional recurrence and 85 cases (5.7%) of distant metastasis, and the 5-year overall survival rate was 98.6%.

I will also introduce current our study aimed to compare 10-year oncological outcomes of ipsilateral breast tumor recurrence (IBTR) disease-free survival (DFS) and overall survival (OS) following conventional and oncoplastic breast conserving surgery using volume displacement and replacement techniques. Between 2009 and 2013, 539 consecutive patients who underwent breast conservation surgery including 174 oncoplastic and 376 conventional procedures were analysed. There was no difference in IBTR-free survival when performing OBCS after stratifying by high-grade tumors, larger tumors (T2/3) and node positive, hormone receptor positive, or triple negative breast tumors. The main findings of this study were that there was an overall low rate of IBTR (OBCS 1.8% vs CBCS 2.4%)

Since April 2015, post-mastectomy breast reconstruction has been covered by the Korean National Health Insurance Service (NHIS). The post-mastectomy breast reconstruction rate increased from 19.4% in 2015 to 53.4% in 2018. In 2015, implant reconstruction was performed in 60.1 % and autologous reconstruction in 39.8%; these trends increased to70.2% and 29.7% in 2018. For implant-based reconstructions, the rates of direct-to-implant and tissue-expander breast reconstructions (first

stage) were similar in 2018.

With the recent trend of de-escalating axillary surgery, clinical research results have been reported. Axillary lymph node dissection (ALND) is optionally omitted if BCS and adjuvant radiotherapy is planned even if there are 1 or 2 axillary lymph node metastases in the sentinel lymph node biopsy (SLNB). ALND is the standard treatment for surgery in case of pathologically confirmed axillary lymph node metastasis prior to neoadjuvant chemotherapy, but over the past decade, breast surgeons have been trying to reduce postoperative complications such as lymphedema by omitting ALND with the favorable response of neoadjuvant chemotherapy.

Targeted axillary sampling (TAS) is a new surgical concept for the assessment of axillary lymph node status in breast cancer that is hypothesized to be more effective at minimizing postoperative morbidities than axillary lymph node dissection (ALND), provided the metastatic axillary lymph node can be accurately detected without missing data; however, the oncologic outcomes over long-term follow-up have not been sufficiently investigated.

According to our retrospective analysis to evaluate the 10-year oncologic outcomes in T1-3N1 breast cancer after TAS, there was no statistically significant difference in oncologic outcomes, including locoregional recurrence, distant metastasis, and overall survival. Furthermore, the incidence of lymphedema on the ipsilateral arm was significantly higher in the ALND group.

Some group reported that the incidence rate of nipple invasion confirmed at pathologic examination was 86% in the Nonmass enhancement extension(NME) to the nipple at MRI. These results suggest that nipple invasion by NME at breast MRI should be considered a contraindication for NSM. But, In patients with no clinical or no direct radiographic evidence of nipple involvement by tumor, rates of microscopic tumor involvement on final pathology range from 2.5% to 10% in therapeutic mastectomies and 0% to 3% in prophylactic mastectomies.

Rates of new or recurrent tumor in the retained nipple and areola are extremely low when a clear nipple/areola margin is obtained.

So, if we carefully evaluate the nipple involvement with new surgical technique, we can preserve the nipple even though NME be at MRI.

ADVANCED SURGICAL TECHNIC FOR SUCCESSFUL OPBS IN BREAST CANCER

Visnu Lohsiriwat

Siriraj Hospital, Mahidol Univ., Department of Surgery, Thailand

Oncoplastic Breast Surgery techniques have rapidly evolved in last decades. The advance technique is developed according to the progression of oncological treatment, not only the surgical technique but also adjuvant chemotherapy, immunotherapy, targeted treatment and radiotherapy. There are four aspects that may be the focal points recently. 1) The Implant based reconstruction technique which may involve in two main categories; the new implant generation and the supportive matrix. 2) The autologous reconstruction technique which correlates to precision of flap anatomy. Then the perforator flaps and microsurgical flaps are now revisited to diminished the donor site morbidities. 3) The tissue engineering is a key of future success in breast reconstruction. The combination in knowledge of cells, signaling and matrices are the promising step for in vitro cellular expansion. 4) New AI and mechanic technologies assisted surgery can facilitate the preoperative planning, intra operative decision and post operative monitoring process with better outcomes.

EVALUATION OF BREAST SYMMETRY AND COSMESIS FOR DENSE BREAST

Jung Ho Lee

The Catholic Univ. of Korea Bucheon St. Mary's Hospital, Department of Plastic and Reconstructive Surgery, Korea

Symmetry is one of the main purposes of breast reconstruction. Compared to Western women, Asian women are generally smaller with lower body mass index, and have denser breasts. In addition, they have a higher risk of leaving unsightly scars on the donor site. For these reasons, implant-based breast reconstruction has become more popular among Asian patients. However, for patients with small breasts, it is difficult to find a suitable implant because most of them were designed according to the shape and volume of Western breasts. Even if the smallest implant is used, the reconstructed breast often looks bigger than the contralateral side. Therefore, contralateral augmentation is often needed for achieving better contour and symmetry. In this presentation, I will present considerations for the breast reconstruction of patients with small and dense breasts.

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Endoscopic and Robotic Breast Surgery Session

"Go Beyond Cure of Breast Cancer"

CHALLENGES OF ROBOT BREAST SURGERY: IS THERE A ROLE FOR ROBOT BREAST SURGERY OUTSIDE OF CLINICAL TRIAL?

Moo Hyun Lee

Keimyung Univ. School of Medicine, Department of Surgery, Korea

Robot-assisted surgery has emerged as a promising modality in various surgical fields, offering minimally invasive procedures that can reduce patient discomfort and recovery time. In particular, robotic nipple sparing mastectomy is a rising trend in the surgical treatment of breast cancer, as it aims to minimize scar length and location inconspicuously, thereby increasing patient satisfaction. However, there are still several challenges associated with robot breast surgery that must be addressed before it can be widely adopted. These include the lack of evidence of oncologic outcomes, the absence of a standardized training system for robot breast surgery, and the significant cost barrier to adoption. Thus, further research is needed to establish the safety and effectiveness of robot breast surgery beyond clinical trials, including long-term studies evaluating recurrence rates, survival rates, and quality of life. Moreover, there is a need to standardize surgical procedures and develop comprehensive training programs to ensure that surgeons possess the necessary skills and expertise to safely perform robot-assisted procedures. In this lecture, we will discuss the strategies and plans for overcoming these challenges and advancing the field of robot breast surgery.

CHALLENGES OF ENDOSCOPIC BREAST SURGERY: IS IT JUST A BRIDGE FOR ROBOT BREAST SURGERY?

Chi Wei Mok

Changi General Hospital, Singhealth Duke NUS Breast Centre, Division of Breast Surgery, Department of Surgery, Singapore

Minimally invasive breast surgery techniques started with endoscopic breast surgery in the late 1990's. Subsequently there were many technique modifications and improvement over the years. Owing to the increasing demand for improved aesthetic outcomes, robotic breast surgery was first performed in 2015. In this talk, Asst Prof Mok will share his unique experience where he started off as both an endoscopic as well as robotic breast surgeon whereas most breast surgeons performed either one of the two. He will also share his thoughts on the differences, strengths and weaknesses of both techniques as well as whether endoscopic breast surgery is just a bridge to robotic breast surgery.

CURRENT STATUS OF ROBOT BREAST SURGERY

Wen-Ling Kuo

Chang Gung Memorial Hospital, Department of General Surgery, Taiwan

Robotic mastectomy is an innovative breast surgical approach driven by the advancement in instrument mechanics and the unmet need encountered in small incision total mastectomy. With the feasibility proved, breast surgeon's vision and surgeon-controlled instruments can travel and perform dissection freely around the three-dimensional contour of a dome-shaped surgical plane in the breast pocket, through a small or concealed incision. The increased instrumental range of motion also allows fine dissection along the anatomical microstructure of the breast which is often invisible with bare eye.

Multi-arm surgical robotic system has been commercially available and applied in robotic mastectomy since 2014. The docking of multiple robotic arms works through a third-party single port device and the wrists of rigid instruments allow 270-degree range of motion. However, collision of robotic arms outside the surgical space can be encountered from time to time and require an assistant's help to adjust the arms. Single-arm robot is the next-generation surgical system under several clinical trials investigating its clinical feasibility and safety in mastectomy. In Korea, it has been available for mastectomy since 2019. Instruments and camera with multi-level wrist and elbow joints are controlled by the instrument drives on a single robotic arm. The camera has greater range of motion to provide better vision of the surgical field, and the collision of instruments only happens within the surgical space, which can be monitored and adjusted by the surgeon from the console. With the appropriate adjustment of instruments and camera, blind spots can be fully avoided.

To answer the question whether a new surgical approach with extra cost is likely to become a reasonable alternative to the conventional procedure, the cost, benefit, and safety must be weighed. Although improved cosmetic and patient-reported outcomes of robotic mastectomy are shown by many recent reports, the magnitude of difference can also be challenged by endoscopic or carefully conducted open approach. In the USFDA 2021 update about caution with robotically-assisted device for mastectomy, monitoring of long-term clinical outcomes such as cancer recurrence, disease-free survival, and overall survival. Therefore, comparison of surgical complication rates and cancer-related outcomes between robotic and conventional mastectomy, such as margin-positive rate, local-regional recurrence rate, ipsilateral breast recurrence rate, distant metastasis rate, or even breast cancer-related death is highly anticipated.

Breast surgeons interested in robotic mastectomy should engage themselves in the training and credentialing of robotic mastectomy. They also appreciate the overcome of learning curves and work under appropriate mentoring programs. Each robotic mastectomy should be registered with its surgical complications and oncological results being monitored.

ROBOT SURGERY FOR BREAST RECONSTRUCTION

Jesse Selber

Corewell Health, Department of Plastic Surgery, U.S.A.

Robotic Breast Surgery

Applications in robotic breast surgery will permit the entire continuum of the surgical treatment and reconstruction of breast cancer to be performed with robotic involvement in every step. The robotic Nipple Sparing Mastectomy with robotic lymph node sampling or dissection is safe, reproducible and effective. Robotic breast reconstruction can be performed using the Robotic DIEP technique, or robotic assisted latissimus dorsi flap. If a DIEP is selected, the microvascular anastomosis can be performed using one of the new microsurgical robots that enhance and scale human motion for greater precision. And finally, prophylactic lymphovenous bypass can be performed taking advantage of the super-microsurgical features and instrumentation of these new robotic devices.

The final state is a more controlled, precise robotic extirpative procedure with a minimally invasive robotic flap harvest that saves donor site morbidity, and a robotic microvascular and microlymphatic anastomosis that are more precise and reliable than the equivalent manual procedure.

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HBOC Session

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MRI SCREENING AND BREAST CANCER MORTALITY IN BRCA1/2 CARRIERS

Steven Narod[1,2], Joanne Kotsopoulos,[1,2] Jacek Gronwald[3], Tomasz Huzarski[3], Pal Moller[4], Tuya Pal[5], Ellen Warner[6], Raymond Kim[7], Christian F Singer[8], Beth Karlan[9], Amber Aeilts[10], Charis Eng[11], Andrea Eisen[6], Louise Bordeleau[12], William D Foulkes[13], Nadine Tung[14], Fergus Couch[15], Robert Fruscio[16], Teresa Ramon Y Cajal[17], Susan Neuhausen[18], Dana Zakalik[19], Cezary Cybulski[3], Olufunmilayo Olopade[20], Kelly Metcalfe[1,21], Ping Sun[1], Jan Lubinski[3]

[1]Women's College Hospital, Research Institute, Canada, [2]Dalla Lana School of Public Health, Univ. of Toronto, Department of Public Health - Epidemiology, Canada, [3]International Hereditary Cancer Center, Pomeranian Medical Univ., Poland, [4]Oslo Univ. Hospital, The Norwegian Radium Hospital, Department for Medical Genetics, Norway, [5]Vanderbilt Univ., Department of Medicine, U.S.A., [6]Sunnybrook Odette Cancer Center and Univ. of Toronto, Department of Medical Oncology, Canada, [7]Univ. Health Network, Univ. of Toronto, Division of Medical Oncology and Hematology, Princess Margaret Cancer Centre, Canada, [8]Medical Univ. of Vienna, Department of Obstetrics and Gynecology and Comprehensive Cancer Center, Austria, [9]Univ. of California, David Geffen School of Medicine, Department of Obstetrics and Gynecology, U.S.A., [10]The Ohio State Univ. Medical Center, Comprehensive Cancer Center, Division of Human Genetics, U.S.A., [11]Cleveland Clinic, Genomic Medicine Institute, Center for Personalized Genetic Healthcare, U.S.A., [12]Juravinski Cancer Centre, Department of Oncology, Canada, [13]McGill Univ., McGill Program in Cancer Genetics, Department of Oncology, Canada, [14]Beth Israel Deaconess Medical Center, Cancer Risk and Prevention Program, U.S.A., [15]Mayo Clinic, Division of Experimental Pathology and Laboratory Medicine, Department of Laboratory Medicine and Pathology, U.S.A., [16]Univ. of Milan Bicocca, Department of Medicine and Surgery, Italy, [17]Univ. Hospital of Santa Creu i Sant Pau, Department of Medical Oncology, Spain, [18]City of Hope, Division of Biomarkers of Early Detection and Prevention, U.S.A., [19]Beaumont Hospital, Cancer Genetics Program, U.S.A., [20]Univ. of Chicago, Department of Medicine and Human Genetics, U.S.A., [21]Univ. of Toronto, Bloomberg School of Nursing, Canada

Background: MRI surveillance is offered as screening to women at high risk of breast cancer due to a mutation in BRCA1 or BRCA2. MRI is a sensitive screening test, but the impact of MRI surveillance on reducing mortality has not been defined.

Materials and Methods: Women with a BRCA1 or BRCA2 mutation were identified from an international registry. There were 2832 women who were between age 30 and 70 and who were cancer-free at baseline who were included in this prospective analysis. Subjects completed a baseline questionnaire between 2000 and 2015 and a follow-up questionnaire every two years thereafter. Subjects who had an MRI more than one year prior to enrollment in the study or who had a bilateral mastectomy prior to enrollment were excluded. Women were followed from the date of the baseline questionnaire or age 30 until age 75, last follow-up or death from breast cancer. Women were considered exposed after entering an MRI screening program. Cox proportional hazards modelling was used to estimate the hazard ratio (HR) and 95% confidence intervals (CI) for breast cancer mortality and all-cause mortality associated

with entering an MRI screening program.

Results: In the cohort, 2078 of the 2832 women (73%) had one or more screening MRIs. After a mean follow-up of 8.9 years, 464 women (16%) developed breast cancer and 45 women (1.6%) died of breast cancer. The age-adjusted hazard ratio for breast cancer mortality associated with entering an MRI program was 0.35 (95% CI 0.19-0.79; $P = 0.001$). The age-adjusted hazard ratio for all-cause mortality was 0.55 (95% CI 0.38-0.79; $P = 0.001$).

Conclusion: Among women with a BRCA1 or BRCA2 mutation, MRI surveillance is associated with a significant reduction in breast cancer mortality, compared to conventional screening

GENETIC COUNSELING AND TESTING FOR BREAST AND OVARIAN CANCER IN ASIA

Ava Kwong

The Univ. of Hong Kong, Department of Surgery, Hong Kong

About 5 to 10% of breast cancer and 10 to 15% of ovarian cancer are hereditarily related. The genes BRCA1 and BRCA2 have been well-proven as highly associated with these hereditary breast and ovarian cancers. The rate of BRCA mutation of hereditary breast and ovarian cancers syndrome (HBOC) in Asia varies from 17% to 28%. In comparison, the BRCA mutation rate of the general population in Asia varies from 0.18% to 0.52%. The mutation spectrum has been found differently across ethnicity. An average of 9.6% of BRCA1 and 7.9% of BRCA2 mutations identified in Chinese are commonly seen in other Asian populations. A systematic study on BRCA variation identified in the Asian population from 40 Asia countries found two common pathogenic BRCA mutations.

Beyond BRCA, more genes and mutation variants associated with breast and ovarian cancers are being discovered. The list of genes includes: CHEK2, ATM, PALB2, BARD1, RAD51C, RAD51D, BRIP1 and TP53. The most commonly mutated genes for HBOC patients are PALB2. Among Asian countries, Korea showed the highest mutation frequency among these genes in HBOC patients. The mutation spectrum for general breast cancer patients showed completely different pictures. Mutations are mostly found in those moderate to low penetrance genes but not high penetrance genes. In our recent study, high penetrance genes (BRCA1/2, CDH1, PALB2, PTEN and TP53) mutations were only found in 10.60% of the HBOC patients and 6.67 % of the random breast cancer cohort but were not found not in the normal cohort. ATM, BRIP1, RAD51C and RAD51D mutations were identified in all cohorts. It was also noted that RAD51C and RAD51D mutations showed conflicting penetrance. An unexpectedly high mutation rate of 2.0% was found in the normal cohort, but it was only 0.36% and 0.33% in HBOC patients and random breast cancer cohorts, respectively.

Guidelines for genetic testing have always been a hot topic to discuss. Testing on a confined approach or universal testing on all patients with breast cancer met with controversy when next-generation sequencing technology became widely used and affordable. The balance between the positive detection rate and resources was, in fact, a worldwide issue applicable to any country providing or planning to provide such genetic service. The subsequence spinout procedures, such as surveillance cancer screenings, prophylactic surgery and caring, genetics counseling on related family members and reproductive planning supports, demand more resources for health care.

Genetic counseling and early surveillance of the diseases have been proven essential for risk assessment and early cancer detection, both for affected patients and cancer-free mutation carriers. We established the Hereditary Breast Cancer Family Registry in 2007. Collaborating with the Hospital Authority in Hong Kong, we offered genetic services and surveillance programs to HBOC Chinese patients. We were focusing not only on routine genetic testing, counseling and management services but also on evaluating disease management practices and generating new research findings targeting the Chinese cohort with hereditary breast and ovarian cancer. We have recruited over 4700 HBOC patients, identifying over 750 pathogenic BRCA mutation carriers. In this lecture, we will share our data from the Hong Kong cohort and review the effectiveness of current practices on genetic testing criteria, surveillance programs, early cancer detection rate and genetic counseling status in Hong Kong and other Asian countries. The data will provide insights into disease management, genetic testing, and counseling on heredity breast and ovarian cancer in other Asian countries.

HEREDITARY PROSTATE CANCER

Jae Hoon Chung

Samsung Medical Center, College of Nursing, Korea

Hereditary prostate cancer is a type of prostate cancer that has a strong genetic component. It is estimated that 5-10% of prostate cancers are hereditary, meaning that they are caused by mutations in genes that are passed down from generation to generation in a family.

The most well-known genes associated with hereditary prostate cancer are the BRCA1 and BRCA2 genes. Mutations in these genes are also associated with an increased risk of breast and ovarian cancer in women. Other genes that have been linked to hereditary prostate cancer include HOXB13, ATM, CHEK2, and MSR1.

Men who have a family history of prostate cancer are at an increased risk of developing the disease themselves. The risk is even higher if multiple family members have been affected, and if the cancer was diagnosed at a younger age.

The clinical features of hereditary prostate cancer are similar to those of non-hereditary forms of the disease. Moreover, there was no difference in diagnosis, treatment and prognosis between hereditary and non-hereditary prostate cancer. However, there are some differences.

1. Younger age at diagnosis: Men with hereditary prostate cancer are more likely to be diagnosed with prostate cancer at a younger age (before age 55) compared to men with sporadic prostate cancer.
2. Aggressive feature.
3. Family history of cancer: prostate, breast, and ovarian cancer.
4. Multiple affected family members: hereditary prostate cancer tends to cluster in families, with multiple members affected by prostate cancer.
5. Ethnicity: Men of African descent are more likely to have hereditary prostate cancer.
6. Response to treatment: hereditary prostate cancer may be more likely to have treatment-resistant tumors, which can make it more difficult to control the cancer.

Genetic testing can play an important role in prostate cancer, especially in hereditary prostate cancer.

1. Personalized treatment: Genetic testing can help identify genetic changes in prostate cancer cells that may help guide treatment decisions. For example, testing for the androgen receptor gene may help predict response to hormone therapy.

2. Family screening: Genetic testing can be used to identify family members who may be at increased risk for prostate cancer due to a known genetic mutation. Early identification of at-risk individuals can help with increased surveillance or preventive interventions.
3. Clinical trials: Genetic testing can be used to identify individuals who may be eligible for clinical trials of new treatments or therapies.

Germline mutation of prostate cancer.

1. BRCA1 and BRCA2: Mutations in the BRCA1 and BRCA2 genes are well-known to increase the risk of breast and ovarian cancers in women, but they also increase the risk of prostate cancer in men. Men with mutations in these genes are at higher risk for developing aggressive forms of prostate cancer and may benefit from increased surveillance and/or preventive interventions.
2. HOXB13: Mutations in the HOXB13 gene have been found to be associated with an increased risk of prostate cancer in some families. These mutations are relatively rare, but individuals with a family history of prostate cancer may be tested for mutations in this gene.
3. DNA repair genes: Mutations in genes involved in DNA repair, such as ATM, CHEK2, and RAD51D, have been associated with an increased risk of prostate cancer in some studies.
4. Lynch syndrome genes: Lynch syndrome is an inherited condition that increases the risk of several types of cancer, including prostate cancer. Mutations in genes such as MLH1, MSH2, and MSH6 have been associated with Lynch syndrome and an increased risk of prostate cancer.

Information about germline genetic scan have impact on treatments available for patients with hereditary prostate cancer, and inform screening and testing for their family members. Ongoing research in this field will lead to continued advancement in how we treat patients with prostate cancer and their families.

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Survivorship Session

"Go Beyond Cure of Breast Cancer"

BUILDING ESMO CANCER REGISTRIES IN ASIA

Rolf Stahel[1], Les Mery[2], Aude Bardot[2], Ravindran Kanesvaran[3], Toh Chee Keong[3], Donsuk Pongnikorn[4], Naiyarat Prasongsook[5], Susanna Hilda Hutajulu[6], Cosphiadi Irawan[7], Azizah Ab Manan[8], Muthukkumaran Thiagarajan[9], Patumrat Sripan[10], Solange Peters[11], Hans Storm[12], Freddie Bray[2], Ross A Soo[13]

[1]ETOP IBCSG Partners Foundation, Department of Surgical Sciences and Section for Breast Surgery, Switzerland, [2]International Agency for Research on Cancer, Section of Cancer Surveillance, France, [3]National Cancer Center, Department of Medical Oncology, Singapore, [4]Lampang Cancer Hospital, Cancer Registry Unit, Thailand, [5]Phramongkutklao Hospital, Department of Internal Medicine and Medical Oncology, Thailand, [6]Universitas Gadjah Mada / Dr. Sardjito General Hospital, Faculty of Medicine, Public Health and Nursing, Division of Hematology and Medical Oncology, Department of Internal Medicine, Indonesia, [7]Faculty of Medicine, Universitas Indonesia/ Dr. Cipto Mangunkusumo General Hospital, Division of Hematology and Medical Oncology, Department of Internal Medicine, Indonesia, [8]National Cancer Institute, Ministry of Health Malaysia, Malaysian National Cancer Registry Department, Malaysia, [9]Kuala Lumpur Hospital, Department of Radiotherapy and Oncology, Malaysia, [10]Chiang Mai Univ., Chiangmai, Research Institute for Health Sciences, Thailand, [11]Centre Hospitalier Universitaire Vaudois, Department of Medical Oncology, Switzerland, [12]Danish Cancer Society, Danish Cancer Society, Denmark, [13]National Univ. Hospital, Department of Hematology-oncology, Singapore

The Evaluating Medical Oncology Outcomes (EMOO) in Asia Study was designed to establish a clinical annotated population-based cancer registry in a collaboration between the European Society of Medical Oncology (ESMO), the International Agency for Research on Cancer (IARC), and partner institutions in Indonesia, Malaysia and Singapore and Thailand. More specifically, the study aimed to examine lung cancer incidence, alongside diagnostic and clinical information and outcomes for patients diagnosed in the years 2017-2019.

Recognizing the paucity of real-world data on cancer from Southeast Asian countries and appreciating the importance to promote development in the region the initiative to this project was started at ESMO Asia 2016. An initial meeting in August 2017 in Singapore brought together representatives from oncological societies and registries from Indonesia, Malaysia, Singapore and Thailand, the Danish Cancer Society, IARC and ESMO and a decision was taken focus on defined regions and lung cancer as the pilot project. In addition to population-based registry data, clinical indicators were selected and governance was established. In July 2019, the final study protocol was approved. Ethics approval for the study was obtained through the IARC's institutional review board and locally from each participating site. Prior to the commencement of data collection, a two-day in-person training workshop on the definitions and methods with representatives from each participating site was held in September 2019. Implementation of the study was overseen by local Principal Investigators and by an Advisory Committee comprised of representatives from ESMO and IARC. Site visits were held to introduce the

study to key stakeholders and finalize any required adjustments. Funding for the study was provided by ESMO.

Two methods were used as sources for case finding. The first involved subnational population-based cancer registries in Lampang (Thailand), Penang (Malaysia) and Yogyakarta (Indonesia) to produce a listing of incident lung cancer cases among residents from each respective geographic area. The second method of case finding was specific to Singapore, where the national population-based registry was not accessible to the study. Here, inclusion was restricted to consenting patients participating in the Lung Cancer Consortium Singapore National Lung Cancer Research Study, an open-based clinical research platform.

3,413 lung cancer cases registered in the database. As for the Lampang, Penang and Yoyakarta this represents 162%, 49% and 53% the number of expected cases. The average age at diagnosis was 66 years, 62% of patients were male, 38% female. Diagnosis was based on pathological findings in 87% of cases (histology 73% and cytology 27%) and on clinical and/or /imaging findings only in 13%. Small cell lung cancer (SCLC) was diagnosed in 6% and non-small cell lung cancer (NSCLC) in 92%. Overall, one-year survival was 48.3% (95%CI 46.6-50.1). Performance status at diagnosis was 0-1 in 55% with a range from 16% in Yogyakarta to 87% in Singapore, 2 in 22%, 3 in 14%, 4 in 3% and unknown in 5%, Smoking status included current smokers in 21%, ever smokers in 27%, never smokers in 40%, and unknown in 12%.

Detailed analyses were performed for patients with documented pathological diagnosis, including 168 patients with SCLC and 2702 patients with NSCLC, of which 82% were of non-squamous histology. Data on stage distribution from SCLC was available for 153 patients and included 26% with stages I-III and 74% with stage IV. The respective actuarial 1-year survival was 63% and 32%. Data on stage distribution from patients with NSCLC was available for 2,534 patients and included stage I/II in 17%, stage III in 14% and stage IV in 69%. The respective actuarial 1-year survival by stage was 93%, 64% and 47%. The survival by stage varied between the regions ranging from 57-96% for stage I and II, 40-96% for stage III and 29-67% for stage IV. The pattern of further diagnostic work-up in terms of biomarker testing for advanced non-squamous NSCLC, treatment patterns by stage and according to regions, and outcome according to regions will be reported.

The EMOO in Asia Study demonstrates the feasibility of the establishment of a clinically annotated population-based registry for lung cancer in four regions in South-East Asia. The findings highlight the heterogeneity of patients' access to diagnostic work-up and treatment. Although by design retrospective in nature, clinically annotated population-based registries provide a unique tool to identity and document disparities and thus allow to rationally address issues in the respective health systems.

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GENETIC RISK FACTORS OF BREAST CANCER IN ASIAN WOMEN

Wei Zheng

Vanderbilt Univ. School of Medicine, Department of Epidemiology, U.S.A.

Breast cancer is the most commonly diagnosed malignancy among women in most Asian countries. Genetic factors play a critical role in the etiology of both familial and sporadic breast cancers. To date, most studies investigating genetic factors for breast cancer risk are conducted in European-ancestry women. Given the differences in genetic architectures and lifestyle and environmental exposures between Asians and other populations, studies are needed in Asian women to investigate unique genetic risk factors for breast cancer in this population. Over the past 25 years, we have conducted multiple large-scale studies in Asian countries, including the Asia Breast Cancer Consortium that includes over 127,000 breast cancer cases and controls recruited from more than 25 studies in multiple Asian countries. These studies have identified large numbers of novel genetic associations and improved the understanding of breast cancer genetics and biology. We have also demonstrated that the utility of polygenic risk scores, along or in combination with known risk factors, in predicting breast cancer risk in Asian women. Proper use of genetic data will undoubtedly accelerate the pace of discovery of the genetic and biologic basis of breast cancer, leading to the development of cost-efficient prevention strategies.

COLLABORATIONS OF COHORT STUDY IN SOUTHEAST ASIAN COUNTRIES

Susanna H. Hutajulu

Universitas Gadja Mada, Division of Hematology and Medical Oncology, Department of Internal Medicine, Indonesia

Cancer registries have a critical role in cancer surveillance and control. The most essential registry type is the population-based cancer registry (PBCR) which collects data from all regional health facilities and from the vital statistics. Despite Indonesia having a high number of cancer cases among other Asian countries, a nationwide PBCR was only recently initiated in 2016 to cover 14% of the country's population. Yogyakarta province, one of the appointed regional PBCRs, has three catchment areas out of five districts with a two million population for the registry denominator. The catchment districts included Sleman, Kota Yogyakarta, and Bantul. Ideally, 92 health facilities are involved in the registry network. Our hospital functions as the central data office, performing training, coordination, supervision and data verification at the regional level. We used the IARC-developed Canreg 5 as a data collection tool comprising demographic, tumor and follow-up data. Our activity is supported mainly by the annual budget of Dr. Sardjito General Hospital and the Faculty of Medicine, Public Health and Nursing, Universitas Gadjah Mada. We also are supported by the Provincial Health offices, the Ministry of Health, and the International Agency for Research on Cancer (IARC). The local PBCR faced challenges especially during the initiation phase of development, including a lack of legality decree and advisory power for regional implementation, funding, personnel, and training. All obstacles resulted in a low data collection coverage (35%) based on national estimation, although it was comparable with other regions and even the national PBCR achievement.

Yogyakarta PBCR reached its pivotal point of development when it was involved in the Evaluation of Medical Oncology Outcome (EMOO) study in Asia, a collaboration of cohort study involving Yogyakarta PBCR (Indonesia), Lampang PBCR (Thailand), Penang PBCR (Malaysia), and a nation-wide clinical registry (Singapore). The EMOO study was initiated and funded by the European Society for Medical Oncology (ESMO) and conducted in collaboration with the IARC/WHO and the Danish cancer registry. The study focused on lung cancer because it is the third most frequent cancer and is the highest cause of mortality globally. After consolidation meetings across study sites, a study protocol was established to include incidence, clinical, population, and mortality datasets. Activities in all study sites included data access, data collection, data analysis, and reporting. During the EMOO study period, our local PBCR took important steps toward community empowerment alongside lung cancer registry

development. Stronger legality was achieved upon decree and agreement signing to refresh the local legal foundation. Training on lung cancer registry variables and PBCR strengthening were supported by the ESMO and IARC. With additional staff numbers, we reorganized personnel and activities across the province.

For the main EMOO study, the four study sites collected more than 3,000 lung cancer cases altogether. Yogyakarta PBCR has contributed almost 20% of the cases identified. Recently, the study group released its first joint publication on diagnostic workup and systemic treatment for metastatic non-small cell lung cancer. We are looking forward to seeing the impact of this publication, and more to come, on the patient management.

Upon the EMOO study completion, we can see the direct impact of these activities on the Yogyakarta PBCR output. Data quality has quickly improved. Morphology verification, a quality parameter, increased from around 60% to more than 75%, passing the WHO standard. However, other quality variables still need to be improved. Currently, we have stronger connection and more support from relevant stakeholders. Data collection methods are performed in various ways, either passive, active, or combining both methods resulting in a more effective activity. Significantly higher involvement of hospitals and health facilities made total participation close to 100%. These have speeded up the overall data collection coverage to almost 90% based on the local estimation.

More specifically, the Yogyakarta PBCR has collected 4,268 data on breast cancer cases in the region diagnosed from 2008-2019. The majority of cases were diagnosed at a late stage. Using joinpoint analysis, we observed a significantly increasing trend in breast cancer incidence, with peak incidence at the 45-64 age group. To determine the geographical variation of breast cancer incidence, we used a geographical information system and found a significant positive spatial autocorrelation of breast cancer incidence in the province. Further, using Local Indicators of Spatial Association analysis, we identified a high-high cluster comprised of several subdistricts within the central area of Kota Yogyakarta. These findings potentially inform higher authorities for resource allocation and public health efforts to reduce disease and mortality in the high-risk areas and develop more targeted prevention and early detection programs.

MANAGEMENT OF LYMPHEDEMA AND SHOULDER PAIN

Seung Hyun Chung

National Cancer Center, Department of Rehabilitation, Korea

The cause of shoulder problems in breast cancer patients is not well understood. Some studies have suggested that shortening of the pectoralis minor muscle may be a contributing factor, but there is no consensus on the exact mechanism and how to prevent it. Shoulder problems commonly observed in breast cancer patients include shoulder impingement syndrome, frozen shoulder, myofascial pain syndrome, and unknown discomfort. Other upper extremity problems include axillary web syndrome, tingling and numbness in the hands due to pectoralis minor muscle syndrome, and chest and flank pain.

Due to the wide range of problems that occur, it is difficult to attribute all of them to a single cause. Therefore, it is reasonable to assume that there are multiple causes and that the different stages of the disease process are the result of a combination of factors.

Shoulder impingement syndrome is classified into static cause and dynamic cause, and shoulder impingement syndrome in breast cancer patients is judged to be a dynamic case. Dynamic shoulder instability causes damage to the shoulder rotator cuff muscles, and excessive joint mobilization exercises or incorrect movements continue to superimpose the damage and ultimately cause rotator cuff damage. Therefore, the principle of prevention and treatment is to identify and improve dynamic instability around the scapula and train to perform correct movements. In addition, repetitive shoulder joint ROM exercises should not be recommended before safe and correct movement skills are completed after breast cancer surgery.

Frozen shoulder is thought to occur after cumulative damage to the shoulder, which is not directly caused by the breast cancer treatment, but rather the accumulation of damage from subsequent excessive joint motion, shoulder instability, and the accumulation of unsafe motion.

Myofascial pain syndrome is caused by abnormal positioning and movement of the scapula at rest and in motion. Shortening of the pectoralis minor muscle, shoulder instability, shoulder impingement syndrome, and rounded shoulder posture are all contributing factors, and it is important to identify and address these causes and not treat the pain procedure without treating the cause.

Brachial plexus compression caused by shortening of the pectoralis minor muscle is a type of thoracic outlet syndrome, and stretching of the pectoralis minor muscle and proper positioning of the scapula is the key to treatment.

An important principle in preventing shoulder problems and lymphedema is shoulder-centered upper extremity use. When using or moving the upper extremities, the movement should start at the shoulder and move to the elbow hand. To achieve this, a target specified rehabilitation program should be designed to practice correct patterns, stretch shortened muscles and fascias, and strengthen weakened shoulder stabilizer muscles.

MANAGEMENT OF COGNITIVE FUNCTION

Eun-Jung Shim

Pusan National Univ., Department of Psychology, Korea

Cancer-related cognitive impairment (CRCI) is a prevalent concern for patients with breast cancer. Approximately one in four patients with breast cancer experiences cognitive impairment during the course of therapy. The main cognitive functions affected include memory, attention, concentration, executive function and processing speed. Although the link between CRCI and chemotherapy is the most commonly studied, a variety of factors - from cancer therapies to disease-related biological factors - appear to contribute to CRCI. Other factors that may exacerbate subjective CRCI include psychological distress, depression, sleep problems and fatigue. CRCI affects various aspects of quality of life and can even influence treatment adherence and treatment decisions. Therefore, appropriate assessment and treatment of CRCI is warranted. The American Cancer Society and American Society of Clinical Oncology guidelines for the care of breast cancer survivors recommend assessment and treatment of CRCI and the treatable factors that contribute to it. In terms of assessment, both subjective and objective assessment of CRCI would be helpful. The Functional Assessment of Cancer Therapy-Cognition (FACT-Cog) is a commonly used measure for assessing subjective cognitive function in cancer patients. The Patient's Assessment of Own Functioning Inventory assesses a spectrum of cognitive abilities commonly experienced by patients with breast cancer patients. A neuropsychological assessment is required to objectively evaluate CRCI. Examples of neuropsychological tests recommended by the International Cognition and Cancer Task Force include the Hopkins Verbal Learning Test-Revised, the Trail Making Test, and the Controlled Oral Word Association of the Multilingual Aphasia Examination. In terms of intervention, patient education about CRCI is recommended. In addition, there is evidence on the effectiveness of cognitive rehabilitation or training to improve CRCI. Web-based or mobile applications for cognitive rehabilitation or training are increasingly available but have yet to be tested in patients with breast cancer. Physical activity and pharmacological treatment for CRCI require further evidence but appear promising.

MANAGEMENT OF ADVERSE EFFECTS FROM RECENTLY APPROVED BREAST CANCER DRUGS

Yoon-Sim Yap

National Cancer Centre Singapore, Department of Medical Oncology, Singapore

Several new drugs have been approved over the past 5 years for breast cancer in both the early and advanced settings. Although certain drugs such as CDK inhibitors may be well tolerated with mainly asymptomatic neutropenia, there may be other adverse effects such as transaminitis, pneumonitis, thromboembolic events and prolonged QT prolongation. PI3K inhibitors may be complicated by toxicities such as hyperglycaemia and rash, among others. The most common toxicities associated with PARP inhibitors are haematologic, but may also lead to more serious complications such as myelodysplasia and leukaemia. Similarly, although immune checkpoints inhibitor are generally well tolerated, a small percentage of patients may develop lifethreatening side effects which need prompt management with multidisciplinary input. Last but not least, the use of antibody drug conjugates also warrants caution with early detection and management of complications such as pneumonitis. We will discuss the frequency, workup and management of the various adverse effects. Education of both healthcare professionals and patients is important to maximise the benefit risk ratio of these new agents.

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"Go Beyond Cure of Breast Cancer"

PRESENT AND FUTURE PERSPECTIVES IN KOREA

So-Youn Jung

National Cancer Center, Department of Surgery, Korea

The first infection case of the coronavirus SARS-CoV-2 (COVID-19) was detected in Korea on January 20, 2020. For more than 3 years, we, breast oncologists, have concerned that compromises to cancer care during the pandemic era would result in delay of breast cancer diagnosis and treatment, and lower survival of breast cancer patients and survivors. Compared to the past, multidisciplinary team approach has needed for the adequate treatment and care for breast cancer patients.

In this session, we will evaluate the epidemiology of breast cancer in Korea, before and after the first detection of Covid-19, review the experts' recommendations and guidelines for breast cancer screening and treatment based on Korea health-care system and multidisciplinary team approach for breast cancer patients during pandemic era, and plan the future direction for the next pandemics.

PRESENT AND FUTURE PERSPECTIVES IN JAPAN

Akihiko Shimomura

National Center for Global Health and Medicine, Department of Breast and Medical Oncology, Japan

Under the COVID-19 epidemic, the treatment and palliative care of patients with metastatic breast cancer (MBC) have been subject to many restrictions. In the face of new challenges such as telemedicine and infection prevention procedures, a holistic medical perspective is essential to maintain the quality of life of patients.

Patients with MBC often suffered from pain, nausea, or fatigue; appropriate symptom management is necessary even during the COVID-19 epidemic. Adverse event management of systemic therapy and supportive care for symptom management should be provided, but adequate medical care may not be provided due to limitations on medical resource. In addition, the risk of COVID-19 infection should be taken into account when establishing a medical care system.

In the COVID-19 epidemic, telemedicine should be utilized. Telemedicine can provide online medical care, telehealth, and self-management support applications. This will allow patients to recuperate at home. However, telemedicine also needs to relieve urgent symptoms and accurately assess the patient's condition.

Family members and caregivers of MBC patients also bear an emotional burden. Therefore, appropriate support for family members and caregivers is also necessary. In some cases, telemedicine can be used to reduce the burden on family members and caregivers. It is also important to respect the opinions and wishes of family members and caregivers and to build a cooperative relationship with them. Furthermore, during periods of high numbers of infected patients, visits to hospitalized patients are often restricted, and emotional support for patient families with limited prognosis is necessary.

For MBC patients, it is important to improve their quality of life in their recuperation; the COVID-19 epidemic revealed new problems such as mental isolation and stress. Providing appropriate information and ensuring communication are also important to improve patients' quality of life.

During the COVID-19 epidemic, infection prevention measures are necessary. It is known that the risk of COVID-19 infection and severe illness is high during cancer treatment because the immune system may be weakened. Therefore, measures such as hand washing, wearing masks, and maintaining social distance are necessary. Healthcare workers are also at risk of infection and must pay sufficient attention to infection control measures.

Especially in the terminal phase, symptoms such as pain, nausea, and anxiety may intensify. Appropriate palliative care can alleviate patients' symptoms and provide psychological support, thereby reducing their physical and mental suffering. It is important to respect the wishes of the patient and family and provide appropriate medical and psychological care despite limitations.

Appropriate medical care for MBC patients is required even under the COVID-19 epidemic. Appropriate symptom palliation, use of telemedicine, support for family and caregivers, quality of life, infection prevention measures, and end-of-life care are all necessary. This can be achieved by taking a holistic medical perspective, respecting the wishes of patients and their families, and practicing multidisciplinary medical care.

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BREAST CANCER REGISTRY FROM THE KOREAN BREAST CANCER SOCIETY

Jaihong Han

National Cancer Center, Department of Surgery, Korea

1. Korea breast cancer statistics

Worldwide, breast cancer is the fastest growing cancer and the most common female cancer. It accounts for 24.2% of all female cancers. Mortality is also the highest, reaching 15%. Breast cancer in Korea has doubled over the past 10 years, with 25,868 cases occurring in 2016, with the highest incidence rate among Asian countries at 59.8% per 100,000 people. Although the incidence rate is high, the mortality rate is as low as 6%. In 2017, 22,395 patients with invasive breast cancer and 4,139 patients with intraepithelial carcinoma occurred, a 4.3-fold increase compared to 17 years ago.

2. History of Korea breast cancer society(KBCS) registry

1) Korea Central Cancer Registry (KCCR)

It started in 1980 and was based on hospital-centered cancer registries and regional cancer registries. However, important information such as surgical method and stage, clinical features, and recurrence record are missing. Therefore, it was mainly used as an objective basis for evaluating the effectiveness of the national cancer control project and promoting cancer control policies.

2) Korea Breast Cancer Society Registry (KBCS)

Accordingly, KBCS was created in 1997, and as the first project, Nationalwide data collection of breast cancer patients in Korea every two years. Off-line sheet questionnaires were used. In 2001, the on-line registry program began to be used.

3. The role of KBCS registry

1) Research

Using this data, doctors at many hospitals across the country were able to write research papers and publish them in domestic and international journals. When researchers (breast cancer surgeons) write a research plan and request data, the academic society examines it and provides the necessary data.

2) Statistics

It also publishes Korea breast cancer statistics every year.

4. The current problem of KBCS registry

1) Privacy policy or privacy act) : death data

As the Personal Information Protection Act has been strengthened, there are restrictions on data collection and export of each hospital. In addition, the death data was regularly updated through the previous National Statistical Office, but this also became difficult.

2) IRB (Institutional Review Board)

Research regulations for data collection and export from patients have been strengthened, making data collection difficult.

3) Difficulties in data collection (manpower problem, low participation of each hospital)

In addition, the quantity and quality of data are declining due to the lack of manpower to organize and input data for each hospital.

5. The future of KBCS registry

1) Link to national database

Recently, the cancer data collection business is in full swing around the country through the K-cancer project, etc., but there is still a long way to go.

2) Automatic data extraction

In particular, automatic data extraction from hospital EMR through a program is being considered, but it is less sophisticated than manual work.

NATIONWIDE TAIWANESE BREAST CANCER STUDY

Ching-Hung Lin

National Taiwan Univ. Hospital, Department of Medical Oncology, Taiwan

Three nationwide databases have been frequently used in cancer studies in Taiwan. Taiwan Cancer Registry (TCR) established in 1979 reports all newly diagnosed malignancies. In 2002, the reporting form was modified and included more detailed clinicopathological and treatment information. In 1995, Taiwan launched a single-payer mandatory enrollment National Health Insurance Program, and Taiwan's National Health Research Institutes established and continue to maintain National Health Insurance research database (NHIRD) for public research purposes since 2002. In addition, Taiwan National Death Certificate Database included cause of death certification and ICD coding after 1994.

Using nationwide databases, three topics of breast cancer studies involving epidemiology and pathological features, pregnancy associated issues, and treatment and side effect will be presented in this meeting. Regarding epidemiology, the incidence of female invasive breast cancer in young Asian women has been rapidly increasing in many East Asian countries. The Westernized lifestyle was thought to be the major reason behind this trend and that emerging young (or premenopausal) breast cancer in East Asia was considered as the mirror image of its Western counterpart. However, our previous findings indicated that there existed major discrepancies between young breast cancer patients in Taiwan and their Western counterparts. These findings were further validated in a nationwide population-based study in Taiwan and in a collaborative study in East Asia. In addition, using TCR database, we found that the incidence of type I uterine cancer and endometrioid subtype of ovarian cancer, estrogen-related malignancies, had also been rapidly increasing in young women in Taiwan. The findings provided a clue for further studies to explore endogenous estrogen or xenoestrogen as causative factors of the breast carcinogenesis in young Taiwanese women.

The pregnancy-associated breast cancer, usually defined as breast cancer diagnosed during pregnancy and within 1-2 years after delivery, have been increasing in East Asia. Using the nationwide data, we found an increased risk of mortality for patients diagnosed within a year postpartum in estrogen receptor-positive cancers. Our another showed that that pregnancy after breast cancer diagnosis was associated with lower mortality than that of nonpregnant patients with breast cancer, and the inverse association was more pronounced for those who became pregnant more than 3 years after diagnosis.

Regarding the treatment and side effect, we found that, in contrast to other ethnicity, the risks of developing deep vein thrombosis and pulmonary embolism were not increased in Asian early breast

cancer patients receiving adjuvant tamoxifen. In contrast to the findings in basic research, our nationwide study using NHIRD and TCR database showed that concomitant use of GC improved survival in patients receiving adjuvant anthracycline-based chemotherapy for stage IIII breast cancer. Although this presentation cannot cover all the nationwide breast cancer studies in Taiwan, we believe that the use of nationwide databases is a precious tool to answer some important clinical questions, and international studies can have greater impact.

KOREAN BREAST CANCER STUDY USING NATIONAL INSURANCE BIG DATA

Sungmin Park

Chungbuk National Univ. Hospital, Department of Surgery, Korea

The National Health Insurance Service (NHIS) is the governmental organization for healthcare insurance in Korea. Under the supervision of the Ministry of Health and Welfare, the NHIS functions as a single insurer that provides health insurance to all Korean citizens. The NHIS operates the National Health Insurance Program, through which the NHIS pays for healthcare services in all healthcare institutions, which provides the NHIS with information about treatments for various medical diseases. Public users can access these data through the National Health Insurance Sharing Service (NHISS), which has been established to facilitate political decisions and academic research conducted using the NHIS data. Although the NHIS data can be a valuable source, in the field of breast cancer research, the utility has not been investigated thus far.

In breast cancer research, the Study of Multi-disciplinAry Teamwork for breast cancer survivorship (SMARTSHIP) group has performed analysis using the NHIS database with support from the Korean Breast Cancer Society. From creating a nationwide cohort of newly diagnosed breast cancer patients applied with a washout period of two years and the specialized code of V193 for cancer, subsequent retrospective studies are ongoing using the NHIS database.

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KBCS GUIDELINES OF SCREENING AND CURRENT STATUS

Young-Joon Kang

The Catholic Univ. of Korea, Incheon St. Mary's Hospital, Department of Surgery, Korea

South Korea has adopted the Korean National Cancer Screening Program of breast cancer screening with biennial mammography for all women 40 years and older since 2002 and for asymptomatic women aged 40 to 69 years since 2015 (Grade B recommendation), which has a moderate level of evidence to reduce breast cancer mortality significantly. Compared with the Western guideline, the Korean guideline shows a difference in that it includes the 40s age group. In a meta-analysis of the results of a randomized controlled comparative clinical trial, the breast cancer screening group using mammography had a 19% lower breast cancer mortality rate than the control group, which was statistically significant.

Combined ultrasound screening has been widely used for Korean women because of the high prevalence of dense breast. East Asia widely uses breast ultrasound as the primary screening modality for young women. It was recommended that additional tools such as clinical breast examination or breast ultrasound can be implemented according to the decision of the clinician because there is insufficient evidence to recommend or oppose screening by clinical breast examination and breast ultrasound.

Randomized controlled trials and Korean cohort studies have statistically shown that mammography-based breast cancer screening for asymptomatic women in their 40s and 50-69 years lower breast cancer mortality rates. No studies have been conducted targeting women in their 30s, and statistically significant results have not been observed for women aged 70 and above. When examining the effect of screening intervals on breast cancer mortality reduction, a significant decrease was observed when screening was conducted at less than 24 months intervals for women aged 39-49. Both less and over 24-month screening intervals effectively reduced mortality rates for women aged 50-69 years, but the effect was insignificant for those aged 70 and over. Cohort studies on mammography-based breast cancer screening published since 2011 mostly recommended a biennial screening interval.

The harms of mammography include psychological stress and radiation exposure. The reports on the extent of psychological harm vary depending on the literature. Based on cumulative radiation exposure over a lifetime, it is estimated that the benefits of screening outweigh the harms of radiation exposure in women aged 40 and over. It is difficult to conclude overtreatment.

The positive predictive value (PPV) of breast ultrasound, a complementary test to mammography, was

insufficient to support its standard use as a screening tool when the guideline was updated. The PPV of breast ultrasound as a screening test for breast cancer ranged from 0.7% to 82.8%. However, a direct comparison was difficult due to the diversity of subject characteristics and criteria for tissue confirmation. Various PPVs were reported depending on the papers when breast ultrasound was added after a negative mammography result. Breast ultrasound sensitivity was reported to be 50.0-100.0%, and specificity was 64.37-99.7% in subjects with dense breasts when mammography results were negative. Overall, cancer detection rates increased when breast ultrasound was performed. However, the increase was less than 1%. Few studies have been conducted on the effectiveness of clinical breast examination as a screening test, making it difficult to make an accurate decision.

Each item was scored for the evaluation of breast cancer screening evidence, with higher scores given to items with greater importance. Scores ranged from 1 to 9, and the guidelines were updated based on the scores obtained for each item. Breast cancer mortality, stage shift, false-positive, interval cancer rate, and unnecessary biopsies or surgeries were considered 'critical outcomes' with a score of 7 or higher.

Since then, several studies on breast cancer diagnosis using MRI or breast ultrasound have been published in Korea and abroad, and it is expected that it will have an impact on breast cancer screening.

CACA GUIDELINES OF SCREENING AND CURRENT STATUS

Yongsheng Wang

Shandong Cancer Hospital & Institute, Breast Cancer Center, China

KOREAN RECOMMENDATIONS FOR PREVENTION AND RISK MANAGEMENTS

Yoo Seok Kim

Chosun Univ. Hospital, Department of Breast Surgery, Korea

Breast cancer is currently one of the most common cancers in women worldwide.

To date, it is difficult to suggest a complete prevention method for breast cancer because the cause of breast cancer has not been clearly defined. However, a lifestyle modification that avoids risk factors known to increase the risk of breast cancer will have some effect on preventing cancer development. Based on this, I would like to review about Korean recommendations for prevention and risk managements and discuss this.

CHINESE RECOMMENDATIONS FOR PREVENTION AND RISK MANAGEMENTS

Junjie Li

Fudan Univ. Shanghai Cancer Center, Department of Breast Surgery, China

1. Breast cancer burden in China.
2. Current guidelines of breast cancer screening, diagnose and prevention in China.
3. Differences in incidence rate, risk factors, screening mode, prevention methods between China and western countries.

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MANAGEMENT OF HEREDITARY BREAST CANCER IN THE U.S.

Tolga Ozmen

Massachusetts General Hospital, Department of Surgery, Division of Gastrointestinal and Oncologic Surgery, U.S.A.

The concept that breast cancer can be inherited was first described in the 19th century. Since then, accumulating evidence confirmed inheritability of breast cancer, and established family history as a risk increasing factor in breast cancer. Today, we know that 15% of breast cancer patients have at least one family member diagnosed with breast cancer. The American Cancer Society reports that about 5-10% of breast cancers are thought to be hereditary with most common genetic mutations being BRCA 1 and BRCA 2.

Women with a BRCA 1 or BRCA 2 mutation have a much higher risk of developing breast cancer in comparison to the general population. These patients also have a significantly higher risk of developing cancer in contralateral breast. It is very important to quantify the increased risk, since this is strongly affected by the age of the patient and type of genetic mutation. Nevertheless, once diagnosed, treatment of breast cancer in this group of patient follows the same track as general population and includes surgery, radiation and systemic therapy options as endocrine therapy and chemotherapy. Options for reducing risk and treatment of breast cancer should be discussed thoroughly with the patient and personalized according to the patient's own risk and preferences.

Management of hereditary breast cancer varies among different cultures and countries. Although there are professional society guidelines pointing out clearly the screening-, risk reduction- and treatment recommendations in hereditary breast cancer, there are still differences among countries in complying with these guidelines. Some of these discrepancies are caused by infrastructure shortcomings and some due population's own culture and beliefs.

In this presentation, I will summarize the current status of genetic testing in United States including the obstacles against genetic testing. I will also discuss the extent to which the United States is complying with recommended risk reducing strategies. Finally, I will conclude with the treatment of hereditary breast cancer in the United States.

MANAGEMENT OF HEREDITARY BREAST CANCER IN EUROPE

Isabel T. Rubio

Clinica Universidad de Navarra, Department of Breast Surgical Oncology, Spain

Approximately 510% of breast cancers are associated with a pathogenic germline variant in one of several different genes. And over 50% of these pathogenic variants are mutations in the BRCA 1 and 2 genes.

In the last two decades, improvements in sequencing and multigene panel testing have increased the detection of susceptibility germline mutations that increases risk for breast cancer and other malignancies. These genes are divided in high-penetrance genes such as BRCA1/2, PALB2, CDH1, PTEN and TP53 and moderate penetrance genes as well, as ATM, CHEK2 and NF1.

It has recently demonstrated that the prevalence of 12 established breast cancer-predisposition genes (ATM, BARD1, BRCA1, BRCA2, CDHS1, CHEKs, NF1, PALB2, PTEN, RAD51C and TP53) is closer to 5% among women with breast cancer and that high penetrance genes confer a 5- to 20-fold lifetime increased risk of breast cancer and moderate penetrance genes confer a 1.5- to 5-fold increased risk. Studies of the prevalence of hereditary breast cancer are largely based on high-risk genes in individuals of Caucasian/European ancestry.

When assessing risk, it is important to incorporate the pathogenic variant along with individual risk factors such as age and family history to balance risks and benefits of the different interventions.

There are several strategies to reduce cancer risk in women with an increased risk of hereditary breast cancer and these includes imaging screening, prophylactic surgeries as breast risk-reducing mastectomy (BRRM) and risk-reducing salpingo-oophrectomy (RRSO) for ovarian cancer and chemoprevention.

The intensive screening in the presence of a pathogenic variant in BRCA1, BRCA2 or PALB2, include breast MRI as one of the essential components of screening programs.

Risk reducing mastectomy (RRM) reduces the risk of breast cancer by 90%. With the increasing use of nipple sparing mastectomy (NSM) and immediate breast reconstruction, that has shown very low rates of breast cancer occurrence (< 1 %) in retrospective and prospective studies, there has been an increase uptake of RRM. The INSPIRE International Registry on NSM showed that there was a significant improvement in emotional functioning after NSM which may be explained by their relief after the decision to undergo RR surgery. RRM is the most effective method for reducing breast cancer risk

among BRCA1/2 carriers and can also be discussed in pathogenic variants in other high risk genes as TP53, PTEN, and PALB2.

There are many international differences in the uptake of RRM, reflecting probably cultural differences and also the way it is discussed by the clinicians.

In Europe the uptake of RRM varies between 25% -50%. A study done by the Manchester group have confirmed that losing a mother or sister to breast cancer at younger ages, having children or a breast biopsy after a false positive screen were all independently associated with uptake of BRRM in BRCA1/2 carriers and noncarriers.

The third option would be the use of tamoxifen and raloxifene, and aromatase inhibitors (anastrozole and exemestane) that have shown to reduce breast cancer incidence by 30% to 60%, although not approved in all European countries for this use.

It is important to test and identify women at high risk for breast cancer because it will allow for discussions about prevention. If testing is done in breast cancer patients, it can be considered a failure of prevention, as the patient has already a cancer diagnosis.

In this case, there has been recently a shift toward breast conservation in patients with breast cancer and a pathogenic variant. In women with non-metastatic breast cancer and a pathogenic variant (except TP53), breast conservation + radiation therapy may be a safe alternative to mastectomy.

Discussions about surgical risk reduction and treatment for breast cancer should be individualized based on risks and patient's preferences

MANAGEMENT OF HEREDITARY BREAST CANCER IN ASIA

Sung-Won Kim

Daerim St. Mary's Hospital, Department of Surgery, Korea

Breast cancer is the most frequent female cancer that remains the leading cause of cancer death in women globally, which amounted to 25% of all new cancers and 15% of all cancer deaths. Genetic predisposition is one of the major risk factors in breast cancer which constitutes 5%10% of all breast cancers. About 20%40% of inherited breast cancers are attributed to deleterious mutations in the breast cancer-associated genes BRCA1 and BRCA2. Women who have BRCA germline mutations are at an increased risk of developing breast and ovarian cancers. Meta-analyses indicate that BRCA1 and BRCA2 carriers have a 57%65% and 45%49% probability of developing breast cancer over lifetime, respectively. BRCA1/2 germline mutations are more common in patients with a family history of breast or ovarian cancer, personal history of breast cancer at young age, or triple-negative phenotype (for BRCA1 only). The prevalence of these genetic mutations varies among ethnic groups and countries. However, most studies of hereditary breast cancer have been on Caucasians in Europe and North America.

Asians make up 60% of the world population. Although the incidence is low compared with Western countries, breast cancer is the most prevalent female cancer in Asia, and its incidence is continuously increasing. Asian patients develop breast cancer at younger age than their Caucasian counterparts. Thus, the contributions of BRCA1/2 germline mutations to breast cancer incidence are expected to differ between Asians and Caucasians. In addition to the age of onset, epidemiological aspects of breast cancer are quite different between patients in Asia and those in the West. The different racial background leads to different genetic backgrounds, which in turn, may result in different breast cancer phenotypes.

The reported prevalence of BRCA1/2 germline mutations in Asian patients with familial breast cancer ranges from 8.0% to 31.8% and in those with early-onset breast cancers from 2.8% to 21.4%. The prevalence of BRCA1/2 mutations in familial breast cancer in Asians is similar to that of African and Hispanic Americans but lower than Ashkenazi-Jews and North Americans of Caucasian descent. The prevalence of BRCA1/2 mutations in early-onset breast cancer in Asians is similar to that of Caucasians and African Americans. It has been reported that BRCA2 mutations have a higher incidence in Asians with the exception of Indians and Pakistanis, whereas BRCA1 mutations are more prominent in other ethnicities. In a recent study from a Chinese cohort, BRCA mutations were identified in 9.1% of cases with at least one risk factor for hereditary breast cancer, 3.5% of sporadic patients, and 0.38% of healthy

controls. In Western countries, the estimated cumulative risk of breast cancer to the age of 70 years in BRCA1and BRCA2 mutation carriers ranges from 72%87% and 71%84%, respectively. The estimated cumulative risk of breast cancer to the age of 70 years is 72.1%66.3% and 78%80% for BRCA1 and BRCA2 mutation carriers in Korea and Japan, respectively.

Current treatment recommendations for BRCA-associated breast cancer are similar to sporadic breast cancers, which mainly include surgery, radiotherapy, and chemotherapy. However, as chemotherapeutic regimens are becoming increasingly tumor-specific, it is possible that patients with BRCA mutations will be treated differently in the future. Recently, for example, various clinical trials have investigated polyadenosine diphosphate-ribose polymerase (PARP) inhibitor treatment for advanced breast cancer patients with germline BRCA1/2 mutation. Among the various PARP inhibitors, olaparib and talazoparib, which reached phase III clinical trials, showed a significant benefit over standard chemotherapy with respect to progression-free survival. Thus, it is important to determine the clinical characteristics and tumor pathological features of BRCA-associated cancers that may affect treatment recommendations.

Most studies on Asian patients have focused on the incidence and prevalence of BRCA mutation in high-risk women and their families, and few studies have investigated the clinicopathological features of BRCA-associated breast cancer. The management of HBC in Asian countries still has significant gaps in the health care system, with some countries having well-developed systems for genetic testing, cancer screening and risk reduction, while others do not. However, all countries are working towards improving their approaches to address HBOC, and it is likely that the landscape will continue to evolve in the coming years.

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HOW TO BE A HAPPY SURGICAL ONCOLOGIST

Peter C. Dubsky

Hirslanden Klinik St. Anna, Department of Surgery, Switzerland

Physician burn out is real- multiple studies have shown the increased risk of health care workers in comparison to the general population. Severe physical and psychological exhaustion, loss of quality of life and loss of professional satisfaction are a common experience in both junior doctors. In oncology, many of us experience first-hand fear, pain and death of patients on a daily basis; many oncology residents will see more deaths in a week than soldiers. Deterioration of professional satisfaction and quality of life will have negative consequences in patient care. Unhappy oncologists are terrible doctors.

This presentation is based on the simple premise that it is possible to acknowledge the many negative factors in our profession and work actively on experiences that can cause happiness. The content will be highly unscientific and is based on the experience of the presenter and a multitude of human beings that have made life and work a thing to be relished every day.

GLOBAL MINDSET OF A BREAST CANCER SURGEON

Jeong Eon Lee

Samsung Medical Center, Department of Surgery, Korea

We are already living in a globalized world. The recent COVID crisis has shown that great problems may arise when globalization is suddenly disrupted.

Breast cancer is the most common cancer in women worldwide, with about 2 million newly diagnosed patients annually. Among them, more than half of breast cancers occur in Asia. One of the characteristics of Asian breast cancer is that the proportion of premenopausal and postmenopausal women is similar, as the proportion of young women is relatively high compared to that of the West.

Asia has a fair amount of geographical, economic, religious, and racial diversity. In Northeast Asia, Japan is providing the most advanced research results almost simultaneously with the developed Western countries. South Korea and Taiwan are working hard to follow global standards. It seems like China is a bit independently developing its own medical treatments. In Southeast Asia, Singapore, Vietnam, Thailand, Malaysia, Indonesia, and the Philippines differ from each other in political, cultural, and economic viewpoints. However, We Asian countries share the same phenomenon. In other words, in Asian countries, the proportion of young women is high and the incidence of breast cancer is increasing.

Because different treatments are being developed for each subtype of breast cancer, it is difficult to produce good results by conducting independent research even in large hospitals. Even if the country is not large, there are countries that have produced good research results, such as Austria, Germany, and Spain. Asian surgeons must gain experience by participating in international clinical studies. And, through cooperation, clinical studies targeting Asian women should be sought in the future.

Also, we need to find our roles to improve the levels of medical healthcare providers and our own patients who are surviving breast cancer. It must be helpful to share our experiences and to learn about the good and bad things about each country's medical system.

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THE IMPACT OF CHEMOTHERAPY ON COGNITIVE IMPAIRMENTS: EVIDENCE AND IMPLICATIONS

Hee-Ju Kim

The Catholic Univ. of Korea, College of Nursing, Korea

Background: The impact of chemotherapy on cognitive impairment has been a focus of debate among oncology researchers, requiring more robust evidence, particularly, from longitudinal data. Therefore, we conducted two separate systematic reviews focused on only longitudinal studies: one for subjective cognitive impatient (SCI); and the other for the objective cognitive impairment (OCI). Studies on subjective and objective cognitive impairments have different design issues and can provide the different level of evidence on cognitive impairment.

Purposes: Each systematic reviews aimed to synthesize the evidence from longitudinal studies on the effects of chemotherapy on cognitive function and to examine potential moderators and methodological issues.

Methods: We extracted the data from Pubmed, EMBASE, CINAHL, PsychInfo, and the Cochrane library. We synthesized and analyzed the data by the type of control groups used (pretreatment baseline, healthy controls, cancer controls) and by the measurement time points to examine the time course of the impact of chemotherapy.

Results: A substantial trend was found in findings across 38 studies on SCI; and also across 42 studies on OCI. The prevalence as well as severity of SCI tended to worsen after initiating chemotherapy, and also in comparison to baseline and to control groups. The impact of chemotherapy on SCI appears to be acute, with improvement after the completion of treatment. Psycho-neurological factors of, depression, and fatigue, were consistent moderators of SCI. In the review of OCI, there was significant deteriorations in cognitive function after initiating chemotherapy, compared to a control group or the baseline. The most affected cognitive domain was memory. At least, a subsample experienced marked declines in cognitive function after initiating chemotherapy. Education, IQ, and regimen were important moderators of OCI. Major methodological concerns were the measurement: the wide range of measures and the unclear domains.

Implications: Findings from longitudinal studies support that chemotherapy negatively impacts patients' self-perceptions of their cognitive function/impairment as well as objectively assessed cognitive function. The impact of chemotherapy appears to be limited to subsample. The mechanisms and

significance of chemotherapy-associated cognitive impairment needs additional evidence. The risk factors should be further examined. Clinicians need to aware that impairment in cognitive function could interfere with patients' daily-life functioning, such as treatments or job-related decision making. They also need to assess the levels of cognitive impairment.

THE COGNITIVE IMPAIRMENT IN BREAST CANCER PATIENTS UNDERGOING THERAPY

Hyejin Cho

Ewha Womans Univ. Seoul Hospital, Department of Nursing, Korea

After diagnosis, breast cancer goes through several stages of treatment, including surgery, chemotherapy, target therapy, radiation therapy, and endocrine therapy, depending on the stage and subtype, which causes various side effects. Among them, Cancer-related cognitive impairment(CRCI) refers to changes or impairments in cognitive function associated with a cancer diagnosis and/or its treatment. This occurs in approximately 1675% of patients. Although it lasts months to years after treatment completion, resulting in discomfort in daily life, impairment in social and occupational functions, and decreased quality of life, and contributes to mortality in the long run, because of strong subjective aspect and inconsistent prevalence, the importance was not recognized. Therefore, through a review of various literature, we would like to find out about CRCI of breast cancer.

Most breast cancer surgeries are performed under general anesthesia, and

new cognitive impairment arising after a surgical procedure is called Post-Operative Cognitive Dysfunction (POCD). POCD is usually transient and can appear in all ages, but it is more common in older people. Three months later, about 12.7% of the patients over age 60 still had POCD. Its pathogenesis is multifactorial, with the

immune response to surgery probably acting as a trigger. Factors that elevate the risk of POCD include old age, pre-existing cerebral, cardiac, and vascular disease,

alcohol abuse, low educational level, and intra- and postoperative complications. POCD is associated with poorer recovery and increased utilization of social financial

assistance. It is also associated with higher mortality.

The American Cancer Society defines Chemotherapy-related cognitive impairment as: increased forgetfulness, trouble concentrating and remembering details, difficulty with multitasking and word finding, and taking longer to finish tasks. Current longitudinal studies suggest that approximately 40% of breast cancer patients have evidence of cognitive impairment prior to cancer treatment, up to 75% exhibit cognitive decline during treatment, and 35%60% exhibit cognitive decline following completion of chemotherapy. Aging, Pre-Morbid Cognitive Functioning, Pre-Existing Cognitive Impairment(MCI

or dementia), Endocrine therapy and targeted therapy are risk factors of Chemotherapy-related cognitive impairment.

Endocrine therapy forms the backbone of systemic therapy for the ER+ breast cancer. Estrogen receptors are found throughout the brain and are predominantly present in the cerebellum, ventral tegmental area (VTA), hippocampus, amygdala, frontal cortex, the raphe nuclei of the midbrain, hypothalamus and thalamus. Aromatase, an enzyme that catalyses the conversion of androgens to oestradiol, is widely distributed throughout the cerebral cortex, hippocampus, hypothalamus and midbrain. Objective deficits using neuropsychological testing have been reported to occur in 32% to 64% of persons receiving endocrine therapy, while self-reported cognitive symptoms have been reported in 45% of patients in one study. Risk factors include lower cognitive reserve, lower educational status, increasing age, ethnicity, depression, fatigue, anxiety and APOE e4 allele. Overall, there is no difference in the global measures of cognition, however impairments are reported in specific domains, including memory, particularly verbal memory as opposed to visual memory or working memory, and fluency.

Trastuzumab, the first humanized mono-clone antibody, selectively targets HER2 on cancer cells and provides successful survival benefits in HER2+ breast cancers. However, the long term treatment of Trastuzumab can cause CRCI. Coello suggested that up-regulation of IL-6 levels after long Trastuzumab treatment is a major cause of CRCI.

Under-diagnosis and under-treatment of CRCI is very common. Therefore, assessment before treatment using screening tools is recommended. The FACT-Cog, a patient reported outcome measure that takes 15-20min to complete, are easy to utilize. Referral for formal neuropsychological assessment, exercise, self-management, formal cognitive rehabilitation is needed for the breast patient.

BENEFICIAL EFFECTS OF EXERCISE ON CANCER-RELATED COGNITIVE IMPAIRMENT WITH BREAST CANCER PATIENTS

Seung-Soo Baek

Sangmyung Univ., Department of Exercise Physiology, Korea

Exercise increases hippocampal neurogenesis and improves short-term memory and learning ability. Breast cancer patients experience Cancer-Related Cognitive Impairment (CRCI), which can develop into mid- to long-term symptoms which can interfere with their daily lives. Exercise, a representative non-pharmaceutical intervention, has recently been reported to improve the cognitive function of CRCI breast cancer patients through several exercise-related studies. However, there is still no agreement on the optimal exercise components affecting cognitive function improvement in CRCI breast cancer patients, making it challenging to form a practical exercise program that can be proposed clinically. The effect of improving cognitive ability such as executive function, memory, and verbal function of CRCI breast cancer patients according to exercise components was verified. PubMed, ScienceDirect, MEDLINE, and Google scholar databases from inception to 31 December 2022 were utilized for searching studies related to research purposes. Meta-analysis was conducted with Comprehensive Meta-Analysis 2.0 using the random-effect model. Meta-analysis of 14 studies showed that exercise improves global cognition(ES = 0.28, $p = 0.00$), executive function(ES = 0.29, $p = 0.00$), memory(ES = 0.24, $p = 0.00$), and verbal function(ES = 0.48, $p = 0.00$) in breast cancer patients with CRCI. The walking-based exercise was effective, and the improvement of cognitive function in breast cancer patients with CRCI was effective in exercise for more than 30 minutes per session, five times a week, and was efficient in moderate-intensity exercise for more than eight weeks and 120-150 minutes a week. Exercise is an effective intervention in improving cognitive function in CRCI breast cancer patients. Moderate-intensity walking-based exercise was effective in global cognition, executive function, memory, and verbal function, and differences were observed according to the components of exercise intervention. Based on the results of this study, it is possible to organize and set up a customized exercise program considering the characteristics of breast cancer patients. Exercise can be used therapeutic strategies as safe and economical intervention for CRCI breast cancer patients.

Keywords: Cognitive-related Cognitive Impairment, Breast cancer, Cognition, Exercise, Meta-analysis

AN OVERVIEW OF GENETIC COUNSELING FOR HEREDITARY BREAST AND OVARIAN CANCER SYNDROME

Bom-Yi Lee

Daerim St. Mary's Hospital, Breast Care Center, Korea

Hereditary Breast and Ovarian Cancer (HBOC) Syndrome is a genetic condition that significantly increases the risk of developing breast and ovarian cancer. The syndrome is inherited in an autosomal dominant pattern, which means that an individual with a pathogenic or likely pathogenic variant in one of the relevant genes has a 50% chance of passing the variant to their offspring. The most common genetic variants associated with HBOC Syndrome are found in the BRCA1 and BRCA2 genes. When these genes are altered, the risk of developing breast and ovarian cancer is significantly increased. Other susceptibility genes, such as TP53, PTEN, PALB2, CDH1, STK11, CHEK2, and ATM, have also been associated with an increased risk of breast cancer.

Individuals with a family history of breast and/or ovarian cancer may be at increased risk of developing these cancers due to a genetic variant. A family history of male breast cancer, pancreatic cancer, or aggressive prostate cancer may also indicate an increased risk. Women with a personal history of ovarian cancer may also be at increased risk. Individuals with HBOC Syndrome may be at increased risk of developing these cancers at a younger age and/or in both breasts. The management of HBOC Syndrome involves a combination of cancer screening and risk reduction strategies. Screening may include mammography, breast MRI, and transvaginal ultrasound. Some individuals may also choose to undergo risk-reducing surgeries, such as prophylactic mastectomy or salpingo-oophorectomy.

Genetic testing is available for individuals who are at risk for HBOC Syndrome. The decision to undergo genetic testing should be made in consultation with a healthcare professional who is trained in genetics and counseling. Genetic testing may have important implications for an individual's healthcare decisions, as well as for their family members. Genetic counseling is an important tool for individuals and families who may be at risk for HBOC Syndrome. The goal of genetic counseling is to help individuals understand their potential risk of developing cancer, and to provide them with the information and support they need to make informed decisions about their healthcare. One of the key components of genetic counseling for HBOC Syndrome is the assessment of a personal and/or family history. The counselor will typically look for patterns of cancer such as a number of cases of breast or ovarian, metastatic prostate or pancreatic cancer in the family, or cases of cancer at age 40 or younger, cases of cancer in both breasts, triple-negative breast cancer diagnosed at age 60 or younger or cases of

ovarian cancer. If the counselor determines that the personal and family history suggests a high risk of HBOC Syndrome, they may recommend BRCA1 and BRCA2 genetic testing. If a genetic counselor suspects that a patient has a hereditary cancer syndrome based on their personal or family medical history, a multi-gene panel test for the susceptibility genes of hereditary cancer may be also recommended to confirm the diagnosis. The decision to recommend a multi-gene panel test for hereditary cancer syndrome will depend on a number of factors, including the patient has a strong family history of certain cancers, the patient has a suspected hereditary cancer syndrome, and/or the patient has had a negative result on a targeted genetic test. It is important to note that while multi-gene panel tests can provide a more comprehensive analysis of a patient\'s risk for hereditary cancer, and it may also detect genetic variants that have uncertain clinical significance. Additionally, the results of genetic testing may have important implications for an individual\'s healthcare decisions, as well as for their family members.

Therefore, the decision to recommend genetic testing should be made in consultation with a healthcare professional who is trained in genetics and counseling. The genetic counselor should help the patient understand the potential benefits and limitations of testing, the emotional and psychological implications of testing, and provide support throughout the testing process.

GENETIC COUNSELING FOR HEREDITARY BREAST CANCER PATIENTS

Ji Hye Yang

ASAN Medical Center, Department of Surgery, Korea

The NSGC (National Society of Genetic Counselors) defined genetic counseling as the process of helping people understand and adapt to the medical, psychological, and familial implications of the genetic contributions to disease.

About 10% of breast cancers are hereditary. Mutations in the BRCA1 and BRCA2 genes are responsible for two thirds of hereditary breast cancer, being the most well-known cause of inherited cancer predisposition. Also, additional non-BRCA genes have been identified as predisposing for breast cancer: ATM, CHEK2, PALB2, PTEN, TP53, and others.

BRCA1 and BRCA2 are called tumor suppressor genes. Inheritance pattern is dominant and autosomal. The cumulative breast cancer risk to age 80 years is 72% for BRCA1 and 69% for BRCA2 carriers. The cumulative ovarian cancer risk to age 80 years is 44% for BRCA1 and 17% for BRCA2 carriers. BRCA testing was performed for about 1000 patient by every year.

Next generation sequencing (NGS) and the recent discovery of the new genes permit multi gene panel testing. The number of multi-gene panel testing is increasing.

These multi-gene panels usually include high and moderate penetrance genes and some low risk genes. However, there are several details to consider when recommending testing, such as the large number of variants of unknown significance (VUS), The clinical actions or guidelines for moderate gene have not been sufficiently established.

Multi gene panel testing can be considered if the patient has a personal or family history that suggests various hereditary breast cancers, or if the patient is a high-risk group for hereditary breast cancer with no mutations detected in single-gene testing. But not all genetic variant information that can be included in a multi-gene panel is clinically useful. So, Multi-gene panel testing should always be preceded and followed by appropriate genetic counseling.

Genetic counseling process involves.
- Risk assessment: Evaluating Family history and Medical records.
- Pre-Test Genetic Counseling & Pedigree Construction

- Genetic Testing: Blood sample
- Post-Test Genetic Counseling & Follow Up Care

The patient is identified by predicting the possibility of mutant through risk assessment. Pre-test genetic counseling is conducted through face-to-face counseling and pedigree construction. Post-test counseling should include an explanation of results, options for managing risk, as well as discussion of the implications for other family members. If a mutation is identified, it allows for targeted mutation testing in at-risk family members. The transmission of genetic information to a patient's family is usually accomplished by communication between the patient and each relative. Therefore, it is necessary to provide resources to patients to help them communicate. Studies show that women who had undergone genetic counseling had a higher satisfaction with the genetic process. Therefore, it is important that all patients who undergo genetic testing have an appropriate pre- and post-test genetic counseling.

THE PROCESS OF CHOOSING CANCER RISK-REDUCING OPTIONS IN WOMEN WITH HEREDITARY BREAST CANCER: A GROUNDED THEORY STUDY

Sun-Young Park

Daegu Catholic Univ., College of Nursing, Korea

Background: Despite already being diagnosed with breast cancer, women with BRCA1 or 2 pathogenic variants are recommended to undergo risk-reducing surgeries (RRS) such as a risk-reducing salpingo-oophorectomy (RRSO) or contralateral prophylactic mastectomy (CPM) in order to reduce further cancer occurrence. Choosing options to reduce cancer risk is challenging for women as the advantages and disadvantages of each choice vary and can have profound effects on their lives. In order for informative and effective genetic counseling, we need a better understanding of how women with hereditary breast cancer perceive and experience the choosing process of cancer risk-reducing options, as well as their attitudes and social contexts. However, little is known about how this decision-making process occurs, especially for Korean women with hereditary breast cancer.

Objective: This study aimed to explore the experiences and the socio-cultural context throughout choosing cancer risk-reducing options among women with hereditary breast cancer in Korea.

Methods: Based on Strauss and Corbin's (1998) grounded theory approach, we conducted in-depth interviews with 17 women with hereditary breast cancer who were identified with BRCA1 or 2 pathogenic variants and had experienced choosing cancer risk-reducing options. Between March and December of 2021, participants were recruited through an online community titled "Breast Cancer Story", following approval by the National Cancer Center Institutional Review Board (IRB No. NCC 2021-0058). Theoretical sampling was conducted based on the constant comparative method, and categories were developed and arranged using MAXQDA software. Data was analyzed using open coding, axial coding, and selective coding according to Strauss & Corbin's method (1998).

Results: Participants in this study were between the ages of 29 and 55; following a cancer diagnosis, BRCA results were generally confirmed within two months (range: 0-7 months). Between the 17 interviewees, RRSO was performed on eight women; five women were scheduled for RRSO; and four women chose surveillance after delaying RRSO. Also, CPM was performed on six women; seven undertook surveillance; and four women were not indicated for CPM (multiple or malignant tumor(s), etc.). None of the participants chose chemoprevention.

In total, 10 categories and 27 subcategories emerged from the 68 open codes. The core category was "navigating optimal trajectories for preserving myself", which means there was a conflict between the incompatible values of preserving "cancer-free health" and "myself as a whole". This "conflicting" phenomenon, was affected by "choosing within a given time frame", "added burden of choice by medical process", "lack of reliable and detailed information", and "drifting between various opinions". The intervening conditions that influence participants' action/interaction strategies were "recognizing who the decision-maker is" and "accepting negative opinions from others about CPM". Women's action/interaction strategies to cope with conflicts were "seeking the standard of choice", "evaluating and predicting the results of choosing and reflecting them in my case", and "refining the decision". Finally, the result of coping was making the right decision for me" and " leaving CPM aside". The hypothetical relation statement was the conflict that can be reduced by providing women with enough time to consider their options, constructing a medical system that provides BRCA test results promptly, and providing detailed and professional information.

Conclusions: Women with hereditary breast cancer experience "inner conflicting" as they search for the most optimal way to "preserve themselves", which involves trying to prevent unwanted consequences from choosing risk-reduction options. According to this study, the decision-making process for RRS in Korean women is influenced significantly by the patriarchy between women and physicians, physicians' one-way instructions, as well as communication with healthcare professionals. As such, it will be necessary to develop and implement a shared decision-making model between Korean healthcare professionals and patients that takes into account Korea's socio-cultural milieu. Our findings also align with the notion that Korea's perception of CPM is more negative than that of the West. Choosing cancer risk-reduction options involves a complex and subjective evaluation process that is affected by interpersonal and individual factors, which consider their situation and values, and occur for a long time before surgery. Healthcare professionals should therefore provide customized counseling in consideration of the various factors that affect choices in order to find individual values and preferences.

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MANAGEMENT AFTER RADIATION THERAPY

Hwa Kyung Byun

Yongin Severance Hospital, Department of Radiation Oncology, Korea

Radiation therapy is a crucial part of breast cancer treatment. While it can improve treatment outcomes, it is also associated with both acute and late side effects, which depend on the radiation dose, technique, and area being treated. Acute side effects include skin reactions, fatigue, breast swelling, and breast pain, while late side effects include arm lymphedema, radiation pneumonitis, and heart toxicity. Managing these toxicities is crucial to improving patients' quality of life. Skin reactions can cause redness, darkening, soreness, itching, and sunburn-like appearance with peeling and blistering. It is important to moisturize the skin during and after radiation therapy, apply sunscreen when going out, and avoid irritating the skin. Arm lymphedema is another common side effect, caused by damage to the lymphatic system during axillary surgery or regional node irradiation, resulting in swelling of the arm, hand, and fingers. Management involves physical therapy, compression garments, and lymphatic drainage massage. Sometimes, treatment to the breast or chest wall area can cause inflammation of the lung behind the treatment area, leading to radiation pneumonitis, which can cause a dry cough or shortness of breath. This condition usually heals by itself over time, but may require corticosteroids and supportive care. Heart toxicity is a rare but serious late toxicity of breast radiation therapy, which can damage the heart muscle and increase the risk of heart disease. Management involves monitoring cardiac function, lifestyle changes, and treatment with medications. In conclusion, breast cancer radiation therapy can result in both acute and late toxicities, which require close monitoring and management. Healthcare providers must be vigilant in monitoring for these toxicities and implementing appropriate management strategies to improve patient quality of life.

MANAGEMENT AFTER CHEMOTHERAPY

Hyehyun Jeong

ASAN Medical Center, Department of Oncology, Korea

1) Treatment overview of early breast cancer patients and its long-term complications

Treatment strategies in early-stage breast cancer patients include neoadjuvant and/or adjuvant chemotherapy, surgery, and radiation therapy, followed by 5-10 years of adjuvant endocrine therapy with or without ovarian function suppression in hormone receptor-positive breast cancer patients, or adjuvant HER2-targeted therapy such as trastuzumab, pertuzumab, or T-DM1 in HER2-positive breast cancer patients. In addition, the neoadjuvant/adjuvant use of an immune checkpoint inhibitor, pembrolizumab, has recently been implemented in clinical practice in triple-negative breast cancer patients. All these therapies take essential parts in the treatment of patients with breast cancer and significantly improved survival outcomes, and adequate survivorship care and management of long-term complications of their previous treatment gained significant interest.

2) Common or important adverse events during adjuvant systemic treatment (other than endocrine treatments)

A. Chemotherapeutic agents epirubicin and doxorubicin, and HER2-targeted agent trastuzumab is associated with an increased risk of cardiac dysfunction. Cardiovascular monitoring is necessary.

B. Capecitabine is associated with cutaneous adverse events such as hand-foot syndrome. Dose interruption may be necessary. Other supportive measures, such as urea cream, topical antibiotics, topical steroids, and lifestyle modifications, may be helpful

C. Pembrolizumab is associated with an increased risk of immune-related adverse events (irAEs), including various systems such as the skin, endocrine system, liver, lung, gastrointestinal tract, etc.

D. During treatment, patients are encouraged to report relevant symptoms.

3) Menopausal symptoms

A. Women can experience menopausal symptoms if chemotherapy results in premature cessation of ovarian function or as an adverse effect of endocrine therapies.

B. Vasomotor symptoms occur in 20-40% of women treated with antihormone therapies and can have a significant impact on the quality of life. Systemic hormone therapy is not recommended due to the increased risk of recurrence. Lifestyle modifications, such as dressing in layers, using cooling aids, and avoiding spicy foods, caffeine, and alcohol, may help. Nonhormonal medications, including venlafaxine, gabapentin, clonidine, and oxybutynin, may help decrease the severity of menopausal symptoms.

C. Sexual complaints are common in breast cancer survivors, with multiple causes contributing to this condition, such as decreased libido, mood problems, body image concerns, as well as vaginal dryness and dyspareunia (often associated with aromatase inhibitor use). Treatments include pharmacologic remedies, including nonhormonal, water-based lubricants and moisturizers for vaginal dryness, management of menopausal symptoms, and psycho-educational support.

4) Musculoskeletal symptoms and bone health

A. Systemic therapies for breast cancer have been associated with the development of musculoskeletal symptoms, especially aromatase inhibitor use. Symptoms include joint pain, stiffness, tenosynovitis, myalgia, and muscle weakness. Symptomatic relief may require acetaminophen or NSAIDs. Exercise, acupuncture, and duloxetine have shown benefits in managing aromatase inhibitor-associated musculoskeletal symptoms. Switching medications or taking a brief treatment break may be necessary.

B. Up to 80% of patients with breast cancer experience bone loss. The risk of osteoporosis is associated with clinical factors such as chemotherapy-induced early menopause, ovarian function suppression, the use of anti-estrogen therapies (especially aromatase inhibitors), advanced age, low BMI, family history of osteoporotic fracture, and smoking. Regular bone densitometry monitoring is necessary. Lifestyle modifications including regular physical activity, cessation of smoking, and limiting alcohol intake are recommended. Adequate intake of calcium and vitamin D is also recommended. Pharmacologic options include bisphosphonates and denosumab.

5) Metabolic effects and obesity

A. Aromatase inhibitor use is associated with increased cholesterol levels and may increase the risk of diabetes. Lipid levels should be monitored as indicated.

B. Obesity is a common problem in breast cancer survivors and a risk factor for poor outcomes. Obesity is associated with a 35-40% increased risk of breast cancer recurrence and death, especially in hormone receptor-positive breast cancer patients. The 2015 ASCO survivorship guideline recommends adequate dietary management and physical activity (aim for ≥ 150 minutes of moderate or 75 minutes of vigorous aerobic exercise per week, and strength training exercise at least 2 days per week) for breast cancer survivors.

6) Other long-term complications of chemotherapy include cognitive impairment, fatigue, peripheral neuropathy (especially after taxane use), and, although rare, an increased risk of leukemia/myelodysplastic syndrome.

7) The survivorship care plan should include information on the risk of late effects of treatment and what to watch for based on the type of cancer and treatment received. Survivors should be assessed for the presence of these physical and psychosocial effects and referred to appropriate providers and services. It is also recommended to include caregivers, spouses, or partners in usual breast cancer survivorship care and support.

SURVEILLANCE AFTER TREATMENT AND SCREENING OF FAMILY MEMBERS

Hyeong-Gon Moon

Seoul National Univ. Hospital, Department of Surgery, Korea

Breast cancer is the most common malignancy in Korean women and, more importantly, the incidence rate is continuously rising. As the breast cancer is a malignant disease with relatively high overall survival rate, there are also a large number of breast cancer survivors who have completed their initial multimodal treatment.

Several decades ago, two prospective randomized trials have demonstrated that radiologic surveillance for distant metastasis in asymptomatic breast cancer patients does not improve the overall survival of the breast cancer patients. The results of these randomized trials, along with the palliative nature of the treatment for patients who developed distant metastasis, have led to the current international guidelines that recommend against the use of radiologic exams for distant organs in asymptomatic patients.

However, in reality, there are significant differences in the surveillance policies among different institutions and physicians in terms of using various radiologic modalities for asymptomatic breast cancer patients. Additionally, recent development in new therapeutic arsenals for metastatic breast cancer patients have raised the possibility of improved survival of metastatic breast cancer patients when the treatment is initiated at earlier levels.

To address this issue, our team has started a multicenter retrospective study to investigate the current status on the use of the radiologic exams for distant metastasis in Korea. Multiple researchers from the Korean Breast Cancer Survivor Research Group have participated in the study. Also, we have launched a prospective trial investigating the attitude and decision of Korean breast cancer patients with regard to the metastasis surveillance during the asymptomatic phase.

In today's talk, I will share the historical studies dealing with the breast cancer surveillance and try to educate the survivors how the principles have come the the present conclusions. Additionally, the preliminary findings of these studies will be introduced to help the survivors understand the current practices in Korea.

BETTER SLEEP FOR BREAST CANCER SURVIVORS

Seockhoon Chung

ASAN Medical Center, Department of Psychiatry, Korea

Breast cancer patients can suffer from psychiatric symptoms such as depression, anxiety, or insomnia. Especially, sleep disturbances are common complaints of breast cancer patients throughout the trajectory of cancer diagnosis and treatment. Both patients and their healthcare providers often consider sleep problems as a normal reaction to cancer diagnosis and treatment. However, reducing sleep problem might improve their quality of life, and we should explore sleep problems of cancer patients for their better life. Patients spend a lot of time lying in bed during daytime, and it may impair the sleep-wake cycle and decrease sleep quality at night. Time in bed within 24 hours (TIB/d), rather than time in bed (TIB), can be a useful sleep index for cancer patients who spend their time sleeping during the day. They also tend to be overconcerned about the negative consequences of poor sleep on their health. Such catastrophic thinking and pressure to sleep may lead them to go to bed earlier than their habitual sleep time before the diagnosis of cancer and try to fall asleep even though they are not sleepy. In this talk, the prevalence, etiology, and management of sleep disturbance among breast cancer patients will be discussed. Especially, the Sleep Clinic for cancer patients, run in Asan Medical Center, will be presented.

FERTILITY PRESERVATION FOR BREAST CANCER SURVIVORS

Hee Jeong Kim

ASAN Medical Center, Department of Surgery, Korea

Women of childbearing age who are diagnosed with breast cancer may be so focused on starting cancer treatment that they do not think about getting pregnant and miss their chance to conceive. It is well known through numerous reports that it is possible to safely maintain a pregnancy and give birth to a healthy baby after breast cancer treatment. However, some breast cancer treatments can lead to a decrease in fertility.

Therefore, it is important to discuss fertility preservation methods from the time of developing a breast cancer treatment plan, considering the impact of breast cancer treatment on fertility. Although there may be many concerns to consider when developing a breast cancer treatment plan, it is possible to prepare for future pregnancy together without affecting the outcome of breast cancer treatment by simultaneously undergoing appropriate fertility preservation treatment, which can be completed within two weeks if necessary.

Impact of cancer treatment on fertility:

Chemotherapy

Chemotherapy can cause problems not only in treating cancer but also in normal bodily functions. Some chemotherapy drugs used to treat breast cancer can damage the ovaries and blood vessels, leading to the loss of follicles, which can interfere with ovulation and the production of female hormones. This can lead to temporary or permanent menopause.The impact of chemotherapy on the ovaries should be considered based on factors such as the age and ovarian function of the patient, as well as the type and dose of chemotherapy.

Radiation therapy

Radiation therapy is the use of X-rays to treat cancer, and the radiation delivered to the ovaries can affect the cells that make up the ovaries.

Hormone therapy

Hormone therapy is taken for a minimum of 5 years, and high-risk patients are recommended to take it for 10 years. Hormone therapy interferes with the action of female hormones or suppresses the production of female hormones, making it difficult to conceive during the treatment period.

Therefore, if a patient wants to get pregnant during hormone therapy, temporary discontinuation of

treatment may be considered after consulting with the patient and their caregiver, taking into account the risk of recurrence.

Recently, there have been reports of breast cancer patients who stopped hormone therapy after about 2 years of treatment following breast cancer surgery and attempted pregnancy before resuming hormone therapy.

Preservation of Fertility before Cancer Treatment

Oocyte Cryopreservation

Cryopreservation is the most basic and reliable method for preserving fertility. Oocyte cryopreservation is a method that can be performed in unmarried women. Ovarian stimulation is induced with follicle-stimulating hormone to induce superovulation, and then oocytes are collected. The induction of superovulation can be started at any time regardless of the menstrual cycle, and since the procedure is usually completed within two weeks, it does not affect the scheduled breast cancer treatment schedule.

Embryo Cryopreservation

For married women, embryo cryopreservation is an option. As with oocyte cryopreservation, oocytes are collected after superovulation induction, fertilized with the spouse's sperm, and the resulting embryos are cryopreserved. This is the same method as preserving remaining embryos after in vitro fertilization treatment for infertile couples, and the success rate of pregnancy is high.

Ovarian Tissue Cryopreservation

This is a method of freezing healthy ovarian tissue before cancer treatment and thawing it at the desired time of pregnancy. Ovarian tissue can be obtained by laparoscopic surgery or can be collected during surgery for cancer treatment. Ovarian tissue cryopreservation has the advantage of not requiring a period of ovarian stimulation or drug administration, and a large number of follicles can be cryopreserved. It can also be performed in prepubescent young women who cannot undergo superovulation induction for oocyte collection.

Ovarian Protection Injections

To preserve ovarian function, a gonadotropin-releasing hormone agonist is administered as an injection. The injection suppresses ovarian function and protects it from the toxic effects of chemotherapy. and its effectiveness is not yet clear.

As a breast cancer survivor, it is important to know that becoming pregnant after cancer treatment does not negatively affect cancer prognosis. Therefore, it is crucial to consider fertility preservation before cancer treatment, and survivors should not be afraid to pursue fertility-preserving treatments. Despite barriers such as lack of understanding, economic support, and medical environment, efforts should be made to eliminate them and make shared decisions with a multidisciplinary team for a better quality of life after breast cancer treatment. Adequate information on fertility preservation should be provided to patients in a timely manner, and an early referral to a fertility specialist is key to success.

HEALTH SUPPLEMENTS FOR BREAST CANCER SURVIVORS

Jung Eun Lee

Seoul National Univ., Department of Food and Nutrition, Korea

Breast cancer is the most frequently diagnosed cancer among women in Korea and worldwide. Several studies reported that cancer survivors tend to use dietary supplements more than individuals with no history of cancer. Our research team also found a higher prevalence of supplement use among Korean cancer survivors compared with age-matched individuals in the general population. In that study, among female cancer survivors, the dietary supplement use rate was the highest in breast cancer survivors (55.9%). Also, in our study of Korean breast cancer survivors, we investigated the proportion of supplemental use, the contribution of supplement use to total nutrient intake, the prevalence of inadequate nutrient intake, and the factors associated with supplement use. Given the high proportion of supplement use among Korean breast cancer survivors and limited evidence in Korea, it is essential to examine the dietary supplements that Korean breast cancer survivors take and whether their nutrient levels are adequate. This talk will present guidelines suggested by accredited organizations and information on Dietary Reference Intakes for Koreans, health functional foods regulated by the Ministry of Food and Drug Safety, databases of foods and functional foods, and a few case reports.

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[제품명] 키트루다®주 (펨브롤리주맙) 100 mg [효능 · 효과] 흑색종: 1. 수술이 불가능하거나 전이성인 흑색종의 치료 2. 완전 절제술을 받은 림프절 침범을 동반한 흑색종의 수술 후 보조요법(adjuvant) 치료 **비소세포폐암:** 1. EGFR 또는 ALK 변이가 없는 전이성 비편평 비소세포폐암 환자에서의 1차 치료로서 페메트렉시드 및 백금 화학요법과의 병용 요법 2. 전이성 편평 비소세포폐암 환자에서의 1차 치료로서 카보플라틴 및 파클리탁셀(혹은 알부민 결합 파클리탁셀)과의 병용 요법 3. PD-L1 발현 양성(Tumor Proportion Score(TPS) ≥50%)으로서, EGFR 또는 ALK 변이가 없는 진행성 비소세포폐암 환자에서의 1차 치료 4. PD-L1 발현 양성(TPS ≥1%)으로서, 백금 기반 화학요법제 치료 도중 또는 이후에 진행이 확인된 진행성 비소세포폐암의 치료. 다만 EGFR 또는 ALK 변이가 확인된 환자는 이 약을 투여하기 전에 이러한 변이에 대한 승인된 치료제를 투여한 후에도 질병의 진행이 확인된 경우여야 한다. **두경부암:** 1. 전이성 또는 수술이 불가능한 재발성 두경부 편평상피세포암 환자에서의 1차 치료로서 PD-L1 발현 양성(CPS ≥1)인 환자에서의 단독 요법, 백금 및 플루오로우라실(5-FU) 화학요법과의 병용 요법 2. PD-L1 발현 양성(TPS ≥50%)으로서, 백금 기반 화학요법제 치료 도중 또는 이후에 진행이 확인된 전이성 또는 수술이 불가능한 재발성 두경부 편평상피세포암의 치료로서 단독 요법. **전형적 호지킨 림프종:** 자가조혈모세포이식에 실패하거나, 자가조혈모세포이식이 치료 옵션이 아닌 경우 최소 두 가지 이상의 이전 요법에 실패한 재발성 또는 불응성인 전형적 호지킨 림프종 성인 및 2세 이상의 소아 환자의 치료. **요로상피암:** 1. PD-L1 발현 양성(Combined Positive Score(CPS) ≥10)이며 시스플라틴 기반 항암화학요법이 불가능한 국소 진행성 또는 전이성 요로상피암의 치료 2. 백금 기반 화학요법제 치료 도중 또는 이후에 진행이 확인되거나, 백금 기반의 수술 전 보조요법(neoadjuvant) 또는 수술 후 보조요법(adjuvant) 치료 12개월 이내에 진행이 확인된 국소 진행성 또는 전이성인 요로상피암의 치료. 3. 방광 절제술이 불가능하거나 시행을 선택하지 않았으며, 유두종 유무에 상관없이 상피내암을 동반한 BCG-불응 고위험 비근침습성 방광암의 치료 **식도암:** PD-L1 발현 양성(CPS ≥10)으로서, 수술이 불가능한 국소 진행성 또는 전이성 식도암이나 HER-2 음성인 위식도 접합부 선암(병변의 중심(epicenter)이 위식도 접합부 1-5 cm 위에 위치) 환자에서의 1차 치료로서 백금 및 플루오로피리미딘 기반 화학요법과의 병용 요법 **신세포암:** 1. 진행성 신세포암 환자에서의 1차 치료로서 엑시티닙과의 병용 요법 2. 진행성 신세포암 환자에서의 1차 치료로서 렌바티닙과의 병용 요법 **자궁내막암:** 이전의 전신 요법 이후 진행이 확인되고 수술적 치료 또는 방사선 치료가 부적합한, 고빈도-현미부수체 불안정성(MSI-H, microsatellite instability high) 또는 불일치 복구 결함(dMMR, mismatch repair deficient)이 없는 진행성 자궁내막암 치료로서 렌바티닙과의 병용 요법 **고빈도-현미부수체 불안정성(MSI-H)암:** 이전의 치료를 받은 후 진행하였고 만족스러운 대체 치료 옵션이 없는, 고빈도-현미부수체 불안정성(MSI-H) 또는 불일치 복구 결함(dMMR)을 나타내며 수술이 불가능하거나 전이성인 자궁내막암, 위암, 소장암, 난소암, 췌장암, 담도암 환자의 치료 **고빈도-현미부수체 불안정성(MSI-H) 직결장암:** 고빈도-현미부수체 불안정성(MSI-H) 또는 불일치 복구 결함(dMMR)을 나타내며 수술이 불가능하거나 전이성인 직결장암 환자의 치료 **삼중음성 유방암:** 1. 고위험 조기 삼중음성 유방암 환자의 치료로서 수술 전 보조요법(neoadjuvant)으로 항암화학요법과 병용 요법, 그리고 이어서 수술 후 보조요법(adjuvant)으로 단독 요법 2. PD-L1 발현 양성(CPS≥ 10)이며, 수술이 불가능한 국소 재발성 또는 전이성 삼중음성 유방암 환자의 치료로서 항암화학요법과의 병용 요법 **[용법 · 용량]** 이 약 200 mg을 매 3주마다 30분 동안 정맥 점적주입한다. 전형적 호지킨 림프종 소아 환자에서 이 약의 권장용량은 2 mg/kg(최대 200 mg)이다. 병용 요법으로 투여하기 위해서는 해당 병용 약제의 처방정보를 참고한다.(사용상의 주의사항 14. 임상시험 정보 항 참고) 이 약을 정맥주사용 화학요법제와 병용하여 투여하는 경우 이 약이 먼저 투여되어야 한다. 고위험 조기 삼중음성 유방암에서 수술 전 보조요법으로 항암화학요법과 병용하여 매 3주마다 200mg 8 회 또는 매 6주마다 400mg 4회 투여한다. 수술 후 보조요법으로 이약을 매 3주마다 200mg 9 회 또는 매 6주마다 400mg 5회 투여한다. **[금기] 다음 환자에는 투여하지 말 것** 이 약 및 그 구성 성분에 과민증인 환자 **[신중투여] 다음 환자에는 신중히 투여할 것** 자가면역질환이 있거나 만성적 혹은 재발성 자가면역질환의 기왕력이 있는 환자 **[약물이상반응] 1) 임상시험에서 보고된 이상사례** 대조 및 비대조 임상시험에서 총 2799명을 대상으로 이 약의 안전성을 분석하였다. 치료 기간의 중앙값은 4.2개월(범위: 1일 ~ 30.4개월)이었고, 6개월 이상 치료받은 환자는 1153명, 1년 이상 치료 받은 환자는 600명이었다. 환자의 5%가 치료 관련 약물이상반응으로 이 약 투여를 중단하였다. 최종 투여 후 90일째까지 보고된 치료 관련 중대한 이상사례(SAE)는 이 약을 투여 받은 환자의 10%에서 발생하였다. 발생한 치료 관련 중대한 이상사례 중 가장 흔하게 발생한 이상사례는 다음과 같다; 폐염증, 결장염, 설사, 발열. 치료 관련 중대한 이상사례로 자가면역성 간염과 부신기능저하증도 보고되었다. **2) 시판 후 이상사례** 이 약의 시판 후 사용 동안 아래와 같은 이상사례가 확인되었다. 이러한 이상사례는 불특정한 인구에서 자발적으로 보고되었기 때문에 발생빈도를 확실히 추정하거나 이 약 노출과의 상관관계를 확립하기 어렵다. 눈 장애: 보그트-고야나기-하라다 증후군, 면역계 장애: 혈구 탐식성 림프 조직구증 **3) 면역-매개 약물이상반응 내분비병증:** 부신 부전이 발병하는 시간의 중앙값은 5.3개월(범위: 26일 ~ 16.6개월)이었다. 지속기간의 중앙값은 아직 도달하지 않았다(범위: 4일 ~ 1.9+년). 부신 부전으로 인해 이 약을 중단한 환자는 1명(<0.1%)이었다. 5명의 환자는 부신 부전 증상으로부터 회복하였다. 뇌하수체염이 발병하는 시간의 중앙값은 3.7개월(범위: 1일 ~ 11.9개월)이었다. 지속기간의 중앙값은 4.7개월(범위: 8+일 ~ 12.7+개월)이었다. 뇌하수체염으로 인해 이 약을 중단한 환자는 4명(0.1%)이었다. 7명의 환자는 뇌하수체염 증상으로부터 회복하였다. 갑상선기능항진증이 발병하는 시간의 중앙값은 2.1개월(범위: 3일 ~ 15.0+개월)이었다. 지속기간의 중앙값은 1.8개월(범위: 1일 ~ 12.8개월)이었다. 갑상선기능항진증으로 인해 이 약을 중단한 환자는 2명(<0.1%)이었다. 71명의 환자는 갑상선기능항진증 증상으로부터 회복하였다. 갑상선 저하증이 발병하는 시간의 중앙값은 3.5개월(범위: 1일 ~ 18.9개월)이었다. 지속기간의 중앙값은 아직 도달하지 않았다(범위: 2일 ~ 27.7+개월). 갑상선 저하증으로 이 약을 중단한 환자는 1명(<0.1%)이었다. **폐염증:** 폐염증이 발병하는 시간의 중앙값은 3.3개월(범위: 2일 ~ 19.3개월)이었다. 지속기간의 중앙값은 1.5개월(범위: 1일 ~ 17.2+개월)이었다. 폐염증으로 인해 이 약을 중단한 환자는 36명(1.3%)이었다. 55명의 환자는 폐염증 증상으로부터 회복하였다. **결장염:** 결장염이 발병하는 시간의 중앙값은 3.5개월(범위: 10일 ~ 16.2개월)이었다. 지속기간의 중앙값은 1.3개월(범위: 1일 ~ 8.7+개월)이었다. 결장염으로 인해 이 약을 중단한 환자는 15명(0.5%)이었다. 41명의 환자는 결장염 증상으로부터 회복하였다. **간염:** 간염이 발병하는 시간의 중앙값은 1.3개월(범위: 8일 ~ 21.4개월)이었다. 지속기간의 중앙값은 1.8개월(범위: 8일 ~ 20.9+개월)이었다. 간염으로 인해 이 약을 중단한 환자는 6명(0.2%)이었다. 15명의 환자는 간염 증상으로부터 회복하였다. **신장염:** 신장염이 발병하는 시간의 중앙값은 5.1개월(범위: 12일 ~ 12.8개월)이었다. 지속기간의 중앙값은 3.3개월(범위: 12일 ~ 8.9+개월)이었다. 신장염으로 인해 이 약을 중단한 환자는 3명(0.1 %)이었다. 5명의 환자는 신장염 증상으로부터 회복하였다. **4) 면역원성** 이 약 2 mg/kg을 매 3주마다 투여하거나 200 mg을 매 3주마다 투여하거나 10 mg/kg을 매 2주 또는 3주마다 투여한 임상시험에 참여한 환자 중에서 이 약 치료 중 항약물항체 존재 여부를 평가한 2034명의 환자 중 36명(1.8%)에게서 양성이 보고되었고, 이 중 9명(0.4%)의 환자에서는 펨브롤리주맙에 대한 중화 항체가 양성이었다. 항-펨브롤리주맙 결합 또는 중화 항체 발생에 따라 약동학 또는 안전성 프로파일이 변경된다는 증거는 확인되지 않았다. **5)** 국내 시판 후 수집된 중대한 이상사례 분석 · 평가 결과 확인된 이상사례는 다음과 같다. 다만, 이로써 곧 해당성분과 다음의 이상사례 간에 인과관계가 입증된 것을 의미하는 것은 아니다. 감염: 폐렴(pneumonia) **[일반적 주의]** 1) 면역-매개 약물이상반응 **① 면역-매개 폐염증:** 이 약 투여 환자에서 치명적인 사례를 포함한 폐염증이 보고되었다. 폐염증의 징후와 증상에 대해 환자를 모니터링해야 한다. 폐염증이 의심되면 방사선영상 검사를 실시한다. 중등증(2등급) 이상의 폐염증의 경우 코르티코스테로이드를 투여(프레드니손으로 초회 용량 1-2 mg/kg/day 또는 이에 상응하는 양을 투여하고 이후 점감)한다. 중등증(2등급) 폐염증의 경우 이 약 투여를 보류하며, 중증(3등급), 생명을 위협하는(4등급) 폐염증 또는 재발성 중등증(2등급) 폐염증의 경우에는 이 약 투여를 영구 중단한다. **② 면역-매개 결장염:** 이 약 투여 환자에서 결장염이 보고되었다. 결장염의 징후와 증상에 대해 환자를 모니터링해야 한다. 중등증(2등급) 이상의 결장염의 경우 코르티코스테로이드를 투여(프레드니손으로 초회 용량 1-2 mg/kg/day 또는 이에 상응하는 양을 투여하고 이후 점감)한다. 중등증(2등급) 또는 중증(3등급)의 결장염의 경우 이 약 투여를 보류하며, 생명을 위협하는(4등급) 결장염의 경우 이 약 투여를 영구 중단한다. **③ 면역-매개 간염 (이 약) 및 간독성 (이 약과 엑시티닙 병용 요법):** 면역-매개 간염 이 약 투여 환자에서 간염이 보고되었다. 간 기능의 변화(치료 시작 시점, 치료 기간 중에는 정기적으로 실시 및 임상 평가를 토대로 필요한 경우 실시)와 간염의 증상에 대해 환자를 모니터링해야 한다. 코르티코스테로이드를 투여(프레드니손으로 초회 용량을 2등급 간염의 경우 0.5-1 mg/kg/day, 3등급 이상의 간염의 경우 1-2 mg/kg/day 또는 이에 상응하는 양을 투여하고 이후 점감)하고 간 효소 상승의 중증도에 따라 이 약 투여를 보류 또는 중단한다. 엑시티닙과의 병용 시 간독성 이 약의 단독 투여 시와 비교하여 이 약과 엑시티닙의 병용 투여 시에는 예상되었던 발생률보다 높은 빈도의 3등급 및 4등급의 ALT 및 AST 상승과 같은 간독성이 발생할 수 있다. 치료를 시작하기 전과 치료하는 동안 정기적으로 간 효소를 모니터링해야 한다. 단독 요법으로 사용될 때에 비해 간 효소를 더 자주 모니터링할 것을 고려한다. 간 효소 상승 시 이 약 및 엑시티닙의 투여를 일시 중단하고, 필요 시 코르티코스테로이드의 투여를 고려한다(용법용량 참고). 이 약과 엑시티닙의 병용 투여 시 3등급 및 4등급의 ALT 증가(20%) 및 AST 증가(13%)가 보고되었다. ALT 증가가 발병하는 시간의 중앙값은 2.3개월(범위: 7일 ~ 19.8개월)이었다. ALT 증가인 환자들 중 59%는 전신 코르티코스테로이드를 투여받았다. ALT가 정상 상한치의 3배 이상인 환자들(2~4등급, n=116) 중 94%에서 ALT가 0~1등급으로 회복되었다. 이 약(3%) 또는 엑시티닙(31%) 단독 요법, 또는 두 약의 병용 요법(50%)으로 재투여한 92명의 환자들 중 55%는 ALT가 정상 상한치의 3배 초과로 상승하는 재발을 보이지 않았다. **④ 면역-매개 신장염:** 이 약 투여 환자에서 신장염이 보고되었다. 신기능의 변화에 대해 환자를 모니터링한다. 중등증(2등급) 이상의 신장염의 경우 코르티코스테로이드를 투여(프레드니손으로 초회 용량 1-2 mg/kg/day 또는 이에 상응하는 양을 투여하고 이후 점감)한다. 중등증(2등급) 신장염의 경우 이 약 투여를 보류하며, 중증(3등급) 내지 생명을 위협하는(4등급) 신장염의 경우 이 약 투여를 영구 중단한다. **⑤ 면역-매개 내분비병증:** 이 약 투여 환자에서 부신 부전(원발성 및 속발성)이 보고되었다. 이 약 투여 환자에서 뇌하수체염도 보고되었다. 부신 부전 및 뇌하수체염(뇌하수체기능저하증 포함)의 징후와 증상에 대해 환자를 모니터링한다. 코르티코스테로이드를 투여하고 임상적으로 필요한 경우 다른 호르몬 대체요법을 실시한다. 중등증(2등급) 부신 부전 또는 뇌하수체염의 경우 이 약 투여를 보류하며, 중증(3등급) 내지 생명을 위협하는(4등급) 부신 부전 또는 뇌하수체염의 경우 이 약 투여를 보류 또는 중단한다. 이 약 투여 환자에서 당뇨병성 케토산증을 포함하는 제1형 당뇨병이 보고되었다. 고혈당증 또는 다른 당뇨병의 징후와 증상에 대해 환자를 모니터링해야 한다. 제1형 당뇨병의 경우 인슐린을 투여하고 중증의 고혈당증의 경우 대사조절에 도달할 때까지 이 약 투여를 보류한다. 이 약 투여 환자에서 갑상선기능항진증, 갑상선 저하증 및 갑상선염을 포함하는 갑상선 장애가 보고되었으며 치료 중 언제라도 발생할 수 있다. 그러므로 갑상선 기능의 변화(치료 시작 시점, 치료 기간 중에는 정기적으로 모니터링 및 임상 평가를 토대로 필요한 경우 모니터링)와 갑상선 장애의 임상적 징후와 증상에 대해 모니터링해야 한다. 갑상선 저하증의 경우 호르몬 대체요법을 실시한다. 갑상선기능항진증은 티오나마이드 및 베타 차단제로 적절히 관리한다. 중증(3등급) 또는 생명을 위협하는(4등급) 갑상선기능항진증의 경우 투여를 일시 또는 영구 중단한다. **⑥ 중증의 피부반응:** 이 약 투여 환자에서 면역-매개의 중증의 피부반응이 보고되었다. 중증의 피부반응이 의심되면 환자를 모니터링하고 다른 원인들을 배제한다. 약물이상반응의 중증도에 따라 이 약 투여를 보류 또는 영구 중단하고 코르티코스테로이드를 투여한다(용법용량 참고). 이 약 투여 환자에서 스티븐스-존슨 증후군(SJS)과 독성표피괴사용해증(TEN)이 보고되었으며, 일부는 치명적인 경과를 보였다. 스티븐스-존슨 증후군 또는 독성표피괴사용해증의 징후 또는 증상이 있으면, 이 약 투여를 보류하고 보다 전문적인 평가와 치료를 위한 기관에 위탁한다. 만약 스티븐스-존슨 증후군 또는 독성표피괴사용해증이 확진되면, 이 약 투여를 영구 중단한다(용법용량 참고). **⑦ 기타 면역-매개 약물이상반응:** 이 약을 투여받은 환자 2799명 중 1% 미만(별도의 표시가 없는 경우)에서 다음의 임상적으로 중요한 면역관련 약물이상반응이 확인되었다: 관절염(1.5%), 포도막염, 근염, 길랑-바레증후군, 중증근무력증(악화 포함), 혈관염, 췌장염, 용혈성 빈혈, 사르코이드증, 뇌염, 척수염. 다음은 이 약의 다른 임상시험 또는 시판 후 사용에서 보고되었다: 심근염, 경화성 담관염. 면역-매개 약물이상반응 중 일부는 중증이었으며 임상시험 중 또는 시판 후 사용에서 보고되었다. **⑧ 이식 관련 약물이상반응:** 시판 후 사용에서 이 약을 투여받은 환자에서 고형 장기 이식 거부가 보고되었다. 이 약은 고형 장기 이식 거부의 위험성을 증가시킬 수 있다. 이러한 환자에게 투여할 경우, 이 약 투여에 따른 유익성 대비 이식 거부 가능성에 따른 위험성을 고려해야 한다. 이 약을 투여받은 동종이형 조혈모세포이식수술(HSCT) 이력이 있는 환자에서 치명적인 이식편대숙주질환(GVHD)을 포함한 급성 이식편대숙주질환이 보고되었다. 이식 수술 후 이식편대숙주질환을 경험한 환자들은 이 약 투여 이후 이식편대숙주질환의 위험이 증가할 수 있다. 동종이형 조혈모세포이식수술 이력이 있는 환자에서는 이 약 투여에 따른 유익성 대비 이식편대숙주질환의 위험성을 고려해야 한다. **[상호작용]** 이 약에 대해 공식적인 약동학적 약물 상호작용 연구는 수행된 바 없다. 펨브롤리주맙은 혈액에서 이화작용을 통해 소실되므로 대사적 약물-약물 상호작용은 예상되지 않는다. 이 약의 약력학적 활성 및 유효성이 저해될 가능성이 있으므로 이 약 투여를 시작하기 전에 전신 코르티코스테로이드 또는 면역억제제의 사용을 피해야 한다. 하지만 이 약 투여를 시작한 이후에 면역-매개 약물이상반응의 치료를 위해서는 전신 코르티코스테로이드 또는 면역억제제를 사용할 수 있다. 이 약을 화학요법제와 병용하여 투여할 때, 예방적 항구토제 및/또는 화학요법제와 관련된 약물이상반응 완화의 목적으로 코르티코스테로이드를 전처료로 사용할 수 있다. **[임부, 수유부, 가임여성]** 1) 임부 및 가임여성: 이 약의 임신 중 투여에 관한 안전성은 확립되어 있지 않으므로 임부 또는 임신하고 있을 가능성이 있는 여성에게는 투여하지 않는다. 2) 수유부: 이 약이 사람 모유로 분비되는지 여부는 알려지지 않았다. 인간 IgG는 모유 중으로 이행되므로 수유부에게 투여하는 경우에는 수유를 중단하도록 한다. **[소아]** 소아 환자에서 이 약의 안전성 프로파일은 성인에서와 유사하였다. 가장 빈번한 약물이상반응(적어도 20%의 소아 환자에서 보고됨)은 발열, 구토, 두통, 복통, 빈혈, 기침 그리고 변비였다. **[고령자]** 전반적으로 고령자(65세 이상)와 65세 미만 성인 간에 안전성 또는 유효성의 차이는 보고되지 않았다. 이 환자군에서 용량 조절은 필요하지 않다. **[신장애 환자]** 경증 또는 중등증 신장애 환자에게는 용량 조절이 필요하지 않다. 중증 신장애 환자를 대상으로 한 이 약에 대한 연구는 수행된 바 없다. **[간장애 환자]** 경증 간장애 환자에게는 용량 조절이 필요하지 않다. 중등증 또는 중증 간장애 환자를 대상으로 한 이 약에 대한 연구는 수행된 바 없다. 작성일자: 2022년 7월 13일

※ 키트루다를 처방하시기 전에 제품설명서를 참조하시기 바랍니다.

*고위험 조기 삼중음성 유방암 환자의 치료로서 수술 전 보조요법(neoadjuvant)으로 항암화학요법과 병용 요법, 그리고 이어서 수술 후 보조요법(adjuvant)으로 단독요법 (2022년 7월 기준)

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PEMBROLIZUMAB FOR MORE TOMORROWS IN TNBC

Yen-Shen Lu

National Taiwan Univ. Hospital, Department of Medical Oncology, Taiwan

Neoadjuvant pembrolizumab combined with chemotherapy followed by adjuvant pembrolizumab led to a significantly higher percentage of patients with early TNBC having a pathological complete response (pCR), and resulted in a significant improvement in event-free survival among patients with previously untreated stage II or III triple-negative breast cancer (TNBC). The event free survival was 37% lower with pembrolizumab–chemotherapy than with placebo–chemotherapy. The addition of pembrolizumab before and after surgery for a total duration of approximately 1 year led to a lower risk of distant recurrence. The prolongation of event-free survival with pembrolizumab was observed across all the subgroups. The higher percentage of patients with a pCR with the addition of pembrolizumab to neoadjuvant chemotherapy was independent of PD-L1 expression. In this talk, the speaker will further discuss about, (1) why pembrolizumab also works for PDL1- patients in early triple negative breast cancer? (2) for ICI, why neoadjuvant works better? (3) why adjuvant ICI is still needed? and (4) does Asian benefit more, or less, from pembroizumab treatment. In general, the results of KN 522 study support the use of pembrolizumab plus platinum-, taxane-, and anthracycline-containing neoadjuvant chemotherapy, followed by adjuvant pembrolizumab after surgery, as a standard treatment regimen for patients with high-risk, early TNBC, regardless of tumour PD-L1 expression status.

PALBOCICLIB: ADDED VALUE OF LONG-TERM EFFICACY, SAFETY AND REAL-WORLD DATA

Kyung-Hun Lee

Seoul National Univ. Hospital, Department of Medical Oncology, Korea

CDK4/6 inhibitors have played a significant role in treating patients with hormone receptor (HR)-positive, human epidermal growth factor receptor 2 (HER2)-negative advanced breast cancer. Palbociclib, the first CDK4/6 inhibitor, has been clinically available since 2015.

In PALOMA-2 trial, Palbociclib showed more than 2 years of median progression free survival (PFS) in the first line setting. Median PFS of Palbociclib in combination with letrozole was 27.6 months and placebo arm showed median PFS of 14.5 months (HR = 0.563 (95% CI: 0.461-0.687); $p < 0.0001$).

PALOMA-3 trial also showed Palbociclib's efficacy in combination with fulvestrant with improvement in overall survival of 34.8 months (28.8-39.9) versus 28.0 months (23.5-33.8) in the placebo group through updated exploratory analysis (stratified HR = 0.81; 95% CI, 0.65-0.99).

In addition, Palbociclib, with the longest experience in the class, has established reliable efficacy and safety in the real-world settings. P-REALITY X, a real-world study designed to evaluate effectiveness of first line Palbociclib in combination with aromatase inhibitor (AI) with total database of 2,888 patients with HR+/HER2- metastatic breast cancer from more than 280 centers in US has shown median overall survival of 49.1 months (45.2-57.7) in Palbociclib arm compared to 43.2 months (37.6-48.0) in AI arm after stabilized inverse probability treatment weighting (HR = 0.76 [95% CI, 0.65-0.87]; P < 0.0001).

Palbociclib also have shown its long-term safety profile. A long-term analysis of Palbociclib plus endocrine therapy after 5 years demonstrated that it has a consistent and stable safety profile without cumulative or delayed toxicities, while many treatments for breast cancer are associated with long-term or latent adverse events.

Quality of life (QoL) is another key consideration. FACT-B questionnaire was used to assess patient reported health-related quality of life (HRQoL) in PALOMA-2 study. In a post-hoc analysis, improvement in pain scores was observed in Palbociclib plus letrozole group compared to placebo group (-0.256 vs -0.098; $p = 0.0183$).

Overall, Palbociclib in combination with endocrine therapy showed reliable efficacy and safety profile in patients with HR+HER2- advanced breast cancer in both RCTs and real-world practices.

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TAKE HOPE FURTHER FOR HR+HER2-HIGH-RISK EARLY BREAST CANCER PATIENTS WITH ABEMACICLIB

Nadia Harbeck

LMU Univ. Hospital, Department of Breast Center, Germany

In HR+ HER2- early breast cancer (eBC), patients with high locoregional tumor burden still have an increased risk for recurrence despite (neo-)adjuvant chemotherapy and endocrine therapy (ET). Monarch-E (NCT03155997) is a randomized multicenter trial evaluating the benefit of two years of abemaciclinb in addition to ET vs. ET alone in pre- and postmenopausal patients with node-positive high-risk HR+ HER2- eBC. Patients were eligible if they had either 4 or more involved axillary lymph nodes (LN) or 1-3 LN and either tumor size >/=5 cm or G3 or Ki67 >/=20%. The most recent 42-month follow-up of Monarch-E demonstrated a significant and clinically meaningful benefit in iDFS and dRFS even after patients had finished their 2-year abemaciclib treatment period. Four-year absolute benefit was 6.4% for iDFS (HR 0.66) and 5.9% for dRFS (HR 0.66), both favoring the abemaciclib arm. Even though Ki67 was a prognostic factor in this trial, it was not predictive for abemaciclib benefit. The safety profile of abemaciclib was consistent with that known from the metastatic setting. With its approval based on the Monarch-E results, abemaciclib has become standard of care for high-risk HR+ HER2- eBC and offers increased chances for cure for these patients. Open clinical questions include optimal management of patients with high-risk HR+ HER2- eBC and gBRCAmut. The ongoing WSG-ADAPTlate trial addresses the question whether abemaciclib can also overcome secondary endocrine resistence and patients will also benefit from adjuvant abemaciclib 1-6 years after the start of their adjuvant ET.

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ABC, advanced breast cancer; **AI,** aromatase inhibitor; **CDK4/6,** cyclin-dependent kinase 4/6; **ET,** endocrine therapy; **GnRHa,** gonadotropin-releasing hormone agonist; **HR,** hazard ratio; **mOS,** median overall survival; **OS,** overall survival.

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Keun Seok Lee

National Cancer Center, Center for Breast Cancer, Korea

CDKs regulate cell proliferation by interacting with cyclins. When the Rb/CDK4/CDK6/cyclin D pathway is activated, it facilitates cancer cell growth, contributing to endocrine resistance. Combining CDK4/6 inhibitors with endocrine therapies has shown improved outcomes in terms of progression-free survival (PFS) and/or overall survival, suggesting their role in overcoming endocrine resistance. The lecture will provide updated survival outcomes from clinically available CDK4/6 inhibitors.

Chemotherapy has long been considered necessary for patients with aggressive diseases, such as visceral crisis, defined as the presence of metastases that compromise vital organ functions. The RIGHT Choice trial showed that patients treated with ribociclib plus endocrine therapy had significantly longer PFS compared to those treated with combination chemotherapy. The lecture will discuss further implications of the RIGHT Choice trial in managing patients with aggressive diseases.

Although CDK4/6 inhibitors are effective in reversing endocrine resistance, resistance to these inhibitors can occur through multiple molecular resistance mechanisms, including gene amplification (e.g. ESR1, CDK4, CDK6, and p16), pathway activation (e.g. cyclinD1-CDK4/6-Rb, PI3K-AKT-mTOR), and epigenetic alterations. Strategies to overcome these resistance mechanisms will be discussed.

Additionally, switching to or continuing with a different CDK4/6 inhibitor shows promise in overcoming resistance to previously used inhibitors. In the MAINTAIN trial, the addition of ribociclib to endocrine therapy improved PFS in patients who had progressed on a CDK4/6 inhibitor. However, combining palbociclib with fulvestrant beyond progression on a prior CDK4/6 inhibitor did not significantly improve PFS compared to fulvestrant alone in the PACE trial. Given these conflicting results, a better understanding of the mechanisms driving post-CDK4/6 inhibitor and endocrine therapy resistance is needed. Future directions regarding the optimal treatment sequence for patients who have progressed on a CDK4/6 inhibitor and endocrine therapy will be discussed based on the current evidence.

보건의료전문가용

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ENHERTU®
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HER2+ 절제 불가능 또는 전이성 유방암 치료에 새롭게 승인 받은 HER2 표적 항체약물접합체[1]
HER2+ 진행성 또는 전이성 위암 치료에 최초로 승인 받은 HER2 표적 항체약물접합체[1,2]

EXTEND HER2+ EXPECTATIONS

이전에 두 개 이상의 항 HER2 기반의 요법을 투여 받은
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ENHERTU® achieved unprecedented efficacy with consistent and durable responses in HER2+ mBC patients[3]

DESTINY-Breast01[3]

16.4 months mPFS with ENHERTU®
(95% CI: 12.7, NR), n=184

60.9% ORR with ENHERTU®
(95% CI: 53.4, 68.0), n=112/184

이전에 항 HER2 치료를 포함하여 두 개 이상의 요법을 투여 받은
국소 진행성 또는 **전이성 HER2 양성 위** 또는 **위식도접합부 선암종**의 치료[1]

ENHERTU® is the first and only HER2-directed treatment to surpass 1 year mOS in AGC following a trastuzumab-based regimen[2,4-6] (2022년 9월 19일 현재)

DESTINY-Gastric01[4]

12.5 months mOS with ENHERTU®
(95% CI: 9.6, 14.3), n=125

51% ORR with ENHERTU®
(95% CI: 42, 61), n=61/119

DESTINY-Breast01: A single-arm trial of 184 females with HER2+ unresectable and/or mBC who had received ≥2 prior anti-HER2 therapies. Patients received ENHERTU® 5.4 mg/kg IV once every 3 weeks until disease progression or unacceptable toxicity. The primary endpoint was confirmed ORR assessed by ICR using RECIST v1.1. Secondary endpoints included DOR and PFS.[3]

DESTINY-Gastric01: A multicenter, open-label, randomized, Phase 2 trial in Japan/South Korea of 188 adult patients with HER2+ locally advanced or metastatic gastric or GEJ adenocarcinoma who had progressed on ≥ 2 prior regimens, including trastuzumab, a fluoropyrimidine- and a platinum-containing chemotherapy regimen. Patients in the ENHERTU® arm received 6.4 mg/kg IV once every 3 weeks until disease progression, death, withdrawal of consent, or unacceptable toxicity. The primary efficacy outcome measure was ORR assessed by ICR based on RECIST v1.1. OS was a key secondary endpoint. PFS and DOR were additional secondary outcome measures.[4]

HER2, human epidermal growth factor receptor 2; **mBC**, metastatic breast cancer; **mPFS**, median progression-free survival; **ORR**, objective response rate; **CI**, confidence interval; **NR**, not reached; **mOS**, median overall survival; **AGC**, advanced gastric cancer; **ICR**, independent central review; **RECIST**, Response Evaluation Criteria in Solid Tumors; **DOR**, duration of response; **GEJ**, gastroesophageal junction.

References 1. 엔허투®주(트라스투주맙데룩스테칸) 제품설명서. 식품의약품안전처, 2022. **2**. 식품의약품안전처. 의약품 안전나라, https://nedrug.mfds.go.kr/searchDrug. Accessed on Sep 19, 2022. **3**. Modi, Shanu, et al. "Trastuzumab deruxtecan in previously treated HER2-positive breast cancer." *New England Journal of Medicine* 382.7 (2020): 610-621. **4**. Shitara, Kohei, et al. "Trastuzumab deruxtecan in previously treated HER2-positive gastric cancer." *New England Journal of Medicine* 382.25(2020):2419-2430. **5**. Curea, Fabiana G., et al. "Current targeted therapies in HER2-positive gastric adenocarcinoma." *Cancer Biotherapy & Radiopharmaceuticals* 32.10 (2017): 351-363. **6**. Zhao, Dan, Samuel J. Klempner, and Joseph Chao. "Progress and challenges in HER2-positive gastroesophageal adenocarcinoma." *Journal of Hematology & Oncology* 12.1 (2019):1-13.

엔허투®주 Product Information

전문의약품

[제품명] 엔허투®주 100 mg (트라스투주맙데룩스테칸) **[원료약품 및 그 분량]** 1바이알(616.97 mg) 중 트라스투주맙데룩스테칸(별규) 107 mg **[효능·효과]** 1. 이전에 두 개 이상의 항 HER2 기반의 요법을 투여 받은 절제 불가능한 또는 전이성 HER2 양성 유방암 환자의 치료 2. 이전에 항 HER2 치료를 포함하여 두 개 이상의 요법을 투여 받은 국소 진행성 또는 전이성 HER2 양성 위 또는 위식도접합부 선암종의 치료 **[용법·용량]** 초기 용량은 90분간 정맥 내 주입한다. 이전의 투여에서 내약성이 우수한 경우, 이 약의 다음 용량은 30분간 주입할 수 있다. 환자가 주입 관련 증상이 있다면, 이 약의 주입속도를 늦추거나 중단시켜야 한다. 심각한 주입 반응의 경우에는 이 약의 투여는 영구적으로 중단되어야 한다. 예방 또는 관리를 위해 환자의 내약성에 따라 국내 진료 지침에 따라 항구토제를 투여할 수 있다. 이 약을 사용하기 전에 HER2 유전자 변이 양성임을 확인한다. 1. 용량: 1) 전이성 유방암: 이 약의 권장 용량은 질병 진행 또는 허용할 수 없는 독성이 나타날 때까지 매 3주 1회(21일 주기) 5.4 mg/kg을 정맥 내 주입하는 것이다. 2) 국소 진행성 또는 전이성 위암: 이 약의 권장 용량은 질병 진행 또는 허용할 수 없는 독성이 나타날 때까지 매 3주 1회(21일 주기) 6.4 mg/kg을 정맥 내 주입하는 것이다. 2. 투여방법 : 이 약은 정맥용으로 사용한다. 의료전문가가 재구성하고 희석하여 정맥 점적 주입(intravenous infusion)으로 투여해야 한다. 이 약은 급속 정맥 주입(intravenous push or bolus)으로 투여해서는 안 된다. **[사용상 주의사항]** 1. 경고 : 1) 투약 오류를 예방하기 위해서는 조제 및 투여 중인 약품이 이 약트라스투주맙데룩스테칸이며, 트라스투주맙 또는 트라스투주맙엠탄신이 아닌지를 확인하기 위해 바이알 라벨을 확인하는 것이 중요하다. 이 약을 트라스투주맙 또는 트라스투주맙엠탄신을 대신하거나 함께 투여해서는 안된다. 2) 간질성 폐질환/폐염증 : 이 약 투여 시 치명적 사례를 포함한 간질성 폐질환 및 폐염증이 보고되었다. 기침, 호흡곤란, 발열, 기타 새로운 또는 악화되는 호흡기 증상을 모니터링하고 즉시 조사한다. 2등급 이상의 간질성 폐질환/폐염증이 있는 모든 환자는 이 약의 투여를 영구적으로 중단한다. 3) 배태아독성 : 임신 중 이 약에 노출될 경우 태아에 해를 끼칠 수 있다. 환자에게 이러한 위험과 효과적인 피임의 필요성을 설명해야 한다. 2. 다음 환자에는 투여하지 말 것 : 이 약 또는 이 약의 구성성분에 과민반응이 있는 환자 3. 약물이상반응 : 1) 전이성 유방암 : DESTINY-Breast01 및 DS8201-A-J101 연구에서 가장 흔한 이상반응(빈도≥20%)은 오심(79.9%), 피로(60.3%), 구토(48.7%), 탈모증(46.2%), 변비(35.9%), 식욕 감소(34.6%), 빈혈(33.8%), 중성구 감소증(32.5%), 설사(30.8%), 혈소판 감소증(23.1%), 기침(21.4%), 백혈구 감소증(20.5%) 및 두통(20.1%)이었다. 2) 국소 진행성 또는 전이성 위암 : DESTINY-Gastric01에서 이 약 6.4 mg/kg으로 치료한 환자에게서 발생한 가장 흔한 이상반응(빈도≥20%)은 중성구 감소증(63.2%), 오심(63.2%), 식욕 감소(60.0%), 빈혈(57.6%), 피로(55.2%), 혈소판 감소증(39.2%), 백혈구 감소증(37.6%), 설사(32.0%), 구토(26.4%), 변비(24.0%), 발열(24.0%), 탈모증(22.4%) 및 림프구 감소증(21.6%)이었다. **[개정년월일]** 2022년 9월 30일 **[제조원]** Daiichi Sankyo Chemical Pharma Co., Ltd., Tatebayashi Plant, Lonza AG, Daiichi Sankyo Chemical Pharma Co., Ltd, Onahama Plant, Baxter Oncology GmbH, Daiichi Sankyo Europe GmbH.

※ 보다 자세한 정보는 식품의약품안전처 의약품 안전나라(http://nedrug.mfds.go.kr) 또는 제품설명서 전문을 참고하시기 바랍니다.

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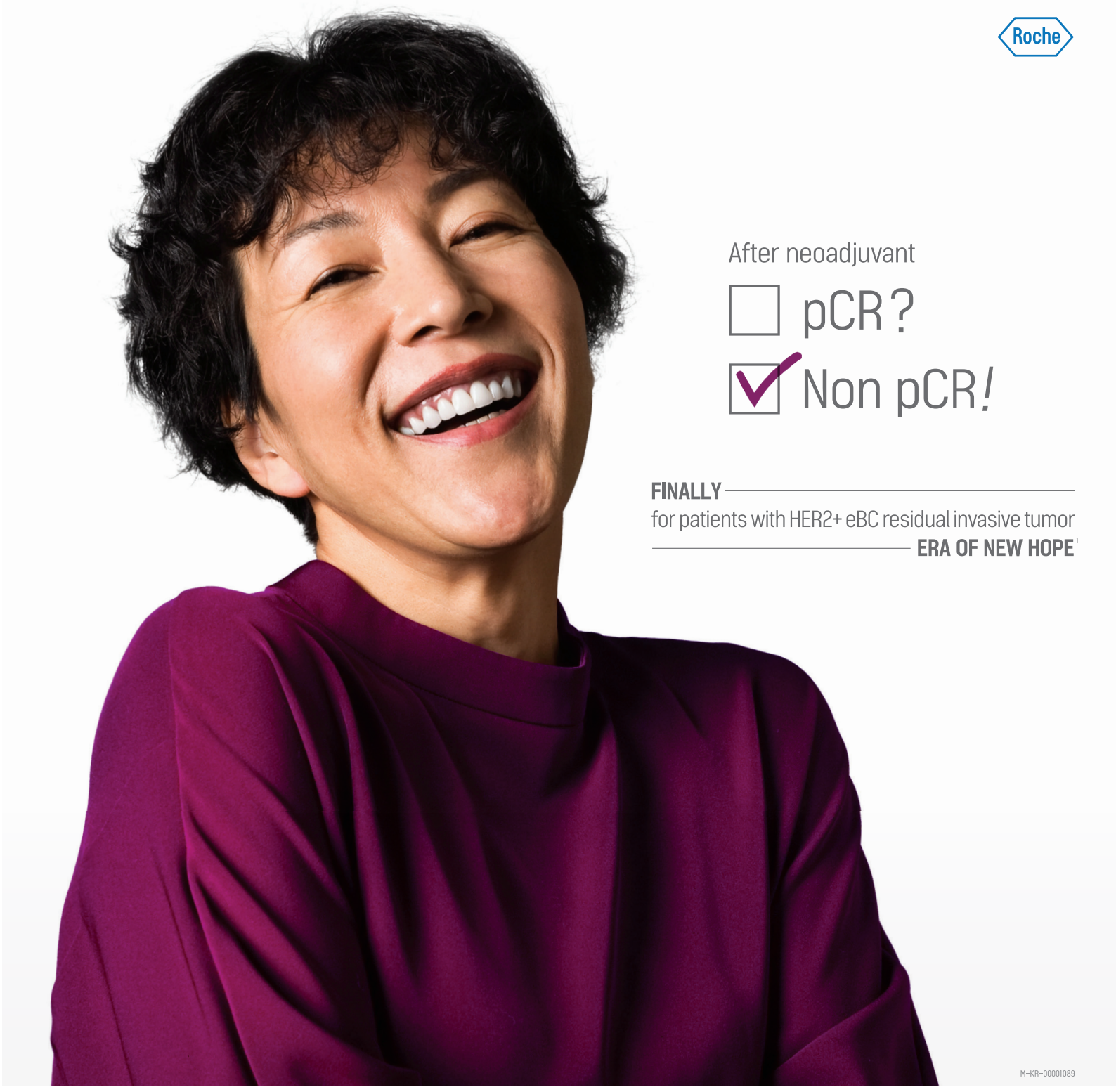
ENHERTU, THE GAME CHANGER IN HER2+ MBC TREATMENT: FROM CLINICAL TRIAL TO CLINICAL PRACTICE

Min Hwan Kim

Yonsei Univ. College of Medicine, Department of Medical Oncology, Korea

Recent advances in cancer biology led to the development of molecularly targeted agents for cancer therapeutics. While traditional monoclonal antibody or small-molecule-based targeting agents for oncogenic mutations are reaching their limits, a new strategy targeting cancer-related membrane proteins using antibody-drug conjugates (ADCs) is showing promising successes across tumor types. The HER2-positive metastatic breast cancer is majorly incurable disease despite the use of HER2-targeting agents, such as trastuzumab, pertuzumab, and lapatinib, because of frequent drug resistance, and patients eventually die from the breast cancer after several lines of systemic chemotherapy. This clinical unmet need calls for rigorous investigation into the efficacy of a new HER2-directed ADC, trastuzumab deruxtecan (T-DXd) both in HER2-positive (or amplified) or low-HER2 expressing in metastatic breast cancers. The T-DXd contains high drug-to-antibody ratio with hydrolyzable linker-payload system and exerts strong bystander cytotoxic effects. The efficacy and the safety of T-DXd was firstly tested in Destiny Breast01, which showed objective response rate (ORR) of 60.9% and progression-free survival (PFS) of 16.4 months in heavily-treated HER2-positive breast cancer patients. (median 6 previous cancer therapy) This remarkable efficacy was further validated in Destiny Breast02 and 03 trials, and T-DXd is now established as standard treatment for HER2-positive metastatic breast cancer patients in ≥2nd line of treatment. In Destiny Breast02 trial, 608 HER2-positive metastatic breast cancer patients who were previously treated with T-DM1 received T-DXd (experimental) or treatment of physician's choice [Trastuzumab/Capecitabine or Lapatinib /Capecitabine] in 2:1 randomization. The T-DXd showed superior ORR (69.7% vs. 29.2%) and PFS (17.8 months vs. 6.9 months, hazard ratio [HR] = 0.3589, $p < 0.001$) compared with treatment of physician's choice. Additionally, T-DXd patients had a significantly longer overall survival time of 39.2 months, while physician\'s choice patients had an overall survival time of 26.5 months. The rate of drug-related TEAEs associated with discontinuation was 14.4% in the T-DXd arm [including pneumonitis (6.2%) and ILD (3.2%)] and 5.1% in the TPC arm [including palmar-plantar erythrodysesthesia (1.5%)] In the Destiny Breast03 trial, 524 HER2-positive advanced breast cancer patients with previous treatment with trastuzumab and taxane were 1:1 randomized to receive T-DXd and T-DM1. In this 2nd line trial, T-DXd showed about four times longer median PFS compared to T-DM1 (28.8 months vs. 6.8 months, HR = 0.33, $p < 0.001$), which is even longer than median PFS shown in the 1st line CLEOPATRA trial

(18.7 months). Especially, T-DXd also showed much higher intracranial response rate than T-DM1 (63.9% vs. 33.4%) showing robust activity against brain metastasis. However, we should note that treatment-emergent adverse events (TEAE) led to T-DXd discontinuation in 51 (20%) patients that include pneumonitis (15 [6%] patients), interstitial lung disease (13 [5%]), and pneumonia (five [2%]). Therefore, early detection and careful management of T-DXd-induced pneumonitis is strongly warranted in the whole treatment courses. The ENHERTU (T-DXd) is now approved by KFDA for "treatment of HER-positive metastatic or unresectable breast cancer patients who received at least one line of HER2-targeted therapy" and started the important mission to save the lives of HER2-positive breast cancer patients. We welcome this innovative moment for HER2-positive breast cancer treatment and expect future academic and regulatory progresses in ENHERTU treatment landscape.



Indication for Kadcyla eBC[2] Monotherapy for the adjuvant treatment of adult patients with HER2-positive early breast cancer who have residual disease after pre-operative systemic treatment that included a taxane and HER2 targeted therapy

pCR: pathological complete response, HER2: Human Epidermal Growth Factor Receptor 2, eBC: early breast cancer

Reference 1. von Minckwitz G, Huang C-S, Mano MS, et al. Trastuzumab emtansine for residual invasive HER2-positive breast cancer. N Engl J Med. 2019;380:617-628, 2. Kadcyla_Korean PI (Kadcyla-2022-02-03-1.0)

Kadcyla inj (Trastuzumab emtansine) prescription medicine [Active Ingredient and Quantitative Composition] Kadcyla inj 100mg: Trastuzumab emtansine 106mg as an active ingredient in 1vial (433.8mg), Kadcyla inj 160mg: Trastuzumab emtansine 171mg as an active ingredient in 1vial (700.7mg) [Pharmaceutical Form] White to off white sterile powder for concentrate for infusion solution which is filled in colorlessness vial. After reconstitution with solution, dissolved as liquid with colorlessness or clear or slightly turbid light yellow [Therapeutic Indications] • Metastatic Breast Cancer (MBC): HER2-positive, unresectable locally advanced or metastatic breast cancer who have received prior treatment with trastuzumab and a taxane as separately or in combination. Patients should have either: • Received prior therapy for locally advanced or metastatic disease, or • Developed disease recurrence during or within six months of completing adjuvant therapy • Early Breast Cancer (EBC): Monotherapy for the adjuvant treatment of adult patients with HER2-positive early breast cancer who have residual invasive disease after pre-operative systemic treatment that included a taxane and HER2 targeted therapy [Dosage and Administration] • Schedule and dosage: The recommended dose of Kadcyla is 3.6 mg/kg given as an intravenous infusion every 3 weeks (21-day cycle). Administer the initial dose as a 90-minute intravenous infusion. Patients should be observed during the infusion and for at least 90 minutes following the initial dose for fever, chills, or other infusion related reactions. The infusion site should be closely monitored for possible subcutaneous infiltration during drug administration. If prior infusions were well tolerated, subsequent doses of Kadcyla may be administered as 30 minute infusions and patients should be observed during the infusions and for at least 30 minutes after infusion. The infusion rate of Kadcyla should be slowed or interrupted if the patient develops infusion-related symptoms. Discontinue Kadcyla for life threatening infusion reactions. Medications to treat allergic / anaphylactic-like reactions, as well as emergency equipment, should be available for immediate use. • Delayed or Missed dose: If a planned dose of Kadcyla is missed, it should be administered as soon as possible: do not wait until the next planned cycle. The schedule of administration should be adjusted to maintain a 3-week interval between doses. The infusion may be administered at the rate the patient tolerated the most recent infusion. • Dose modifications: Management of symptomatic adverse events may require temporary interruption, dose reduction, or treatment discontinuation. Kadcyla dose should not be re-escalated after a dose reduction is made. • Dose reduction schedule: Starting dose: 3.6mg/kg, first dose reduction: 3mg/kg, second dose reduction: 2.4mg/kg, requirement for further dose reduction: Discontinue treatment (as per guideline provided in Table 2. Dose reduction guideline in Kadcyla prescribing information) • Duration of treatment: Patients with MBC should receive treatment until disease progression or unmanageable toxicity. Patients with EBC should receive treatment for a total of 14 cycles unless there is disease recurrence or unmanageable toxicity. • Method of administration: Kadcyla must be reconstituted and diluted by a healthcare professional and administrated as an intravenous infusion. Should not administer as an intravenous push or bolus. If diluted in 0.9% Sodium Chloride Injection, a 0.2 or 0.22 micron in-line polyethersulfone (PES) filter is required for administration. [Warnings and Precautions] • Contraindications: Kadcyla is contraindicated in patients with a known hypersensitivity to Kadcyla or any of the excipients. • Warning: 1) Kadcyla should not be administered instead of or in combination with Trastuzumab-containing product (e.g Herceptin Inj, (Monoclonal antibody, genetic recombination)) 2) Hepatotoxicity: Serious hepatobiliary disorders, including hepatic failure and some with a fatal outcome have been observed in patients treated with trastuzumab emtansine. Serum transaminases and concomitant total bilirubin should be monitored prior to initiation of the first treatment and initiation of every other treatments. 3) Cardiotoxicity: Patients treated with Kadcyla could be at risk of decreased Left ventricular ejection fraction (LVEF). Testing LVEF should be performed prior to initiation of treatment with Kadcyla. Kadcyla treatment should be discontinued when there is clinically significant decrease in LVEF. 4) Embryotoxicity: Exposure to this medication could be embryotoxic including fatal outcomes with embryo / Fetus. Should explain patients with embryotoxicity and effective contraception while receiving Kadcyla. [Precaution for Use] 1. Pregnancy, Lactation and Fertile women 1) Contraception in males and females: Women of childbearing potential should use effective contraception while receiving trastuzumab emtansine and for 7 months following the last dose of trastuzumab emtansine. Male patients or their female partners should also use effective contraception 2) Pregnancy: There are no data from the use of trastuzumab emtansine in pregnant women. Trastuzumab, a component of trastuzumab emtansine, can cause fatal harm or death when administered to a pregnant woman. In the post marketing setting, cases of oligohydramnios, some associated with fatal pulmonary hypoplasia, have been reported in pregnant women receiving trastuzumab. Animal studies of maytansine, a closely related chemical entity of the same maytansinoid class as DM1, suggest that DM1, the microtubule inhibiting cytotoxic component of trastuzumab emtansine, is expected to be teratogenic and potentially embryotoxic. Administration of trastuzumab emtansine to pregnant women is not recommended and women should be informed of the possibility of harm to the fetus before they become pregnant. Women who become pregnant must immediately contact their doctor. If a pregnant woman is treated with trastuzumab emtansine, close monitoring by a multidisciplinary team is recommended. 3) Lactation: It is not known whether trastuzumab emtansine is excreted in human milk. Since many medicinal products are excreted in human milk and because of the potential for serious adverse reactions in breast-feeding infants, women should discontinue breast feeding prior to initiating treatment with trastuzumab emtansine. Women may begin breast feeding 7 months after concluding treatment. 4) Fertility: No reproductive and developmental toxicology studies have been conducted with trastuzumab emtansine.

Kadcyla-2022-02-03-1.0

• If a patient becomes pregnant while receiving Kadcyla or within 7 months following the last dose of Kadcyla, health care providers and patients should immediately report Kadcyla exposure to Roche Korea (02-3451-3600). • Additional information may be requested regarding pregnancy period and the first year of the infant. This will allow Roche to understand more about the safety of Kadcyla and provide adequate information to health authorities, health care providers, and patients. • Please contact Roche Korea (02-3451-3600) for more detailed product information and product-related adverse events reports. • The most recent prescribing information is on Roche Korea homepage (www.roche.co.kr).

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GRASIN® PFS
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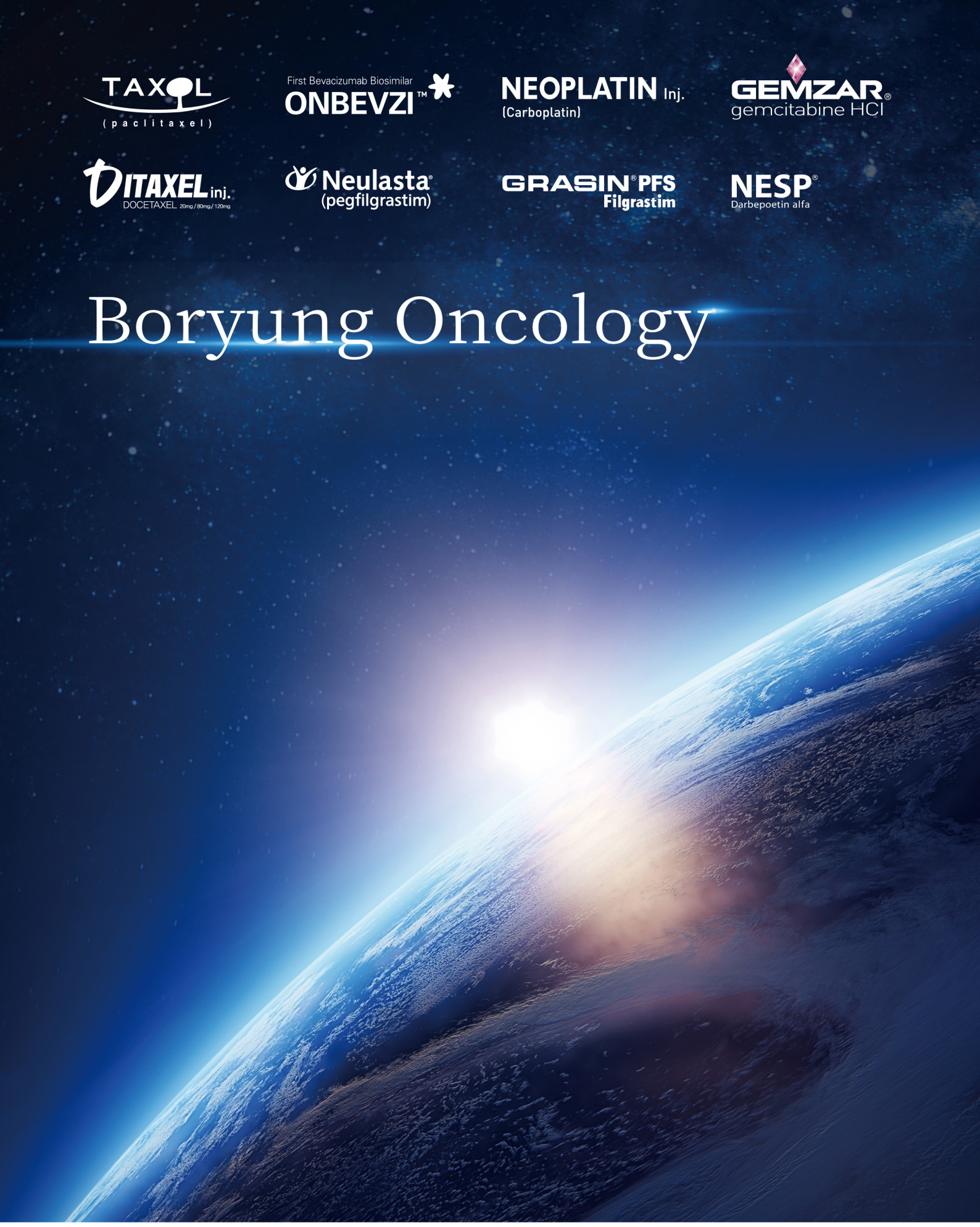

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[제품명] 허쥬마®주 150mg, 440mg(트라스투주맙) (단클론항체, 유전자재조합) [주성분] 트라스투주맙(단클론항체, 유전자재조합) [효능 · 효과] HER2(Human Epidermal growth factor Recepotr 2 protein) 양성 조기 유방암 · 전이성 유방암 · 전이성 위암 [용법 · 용량] 트라스투주맙 치료를 시작하기 전 HER2 시험이 필수적이다. 트라스투주맙은 자격을 갖춘 전문 의료인에 의해 투여되어야 한다. 투여 전 투여하려는 제형이 환자에 처방된 것이 맞는지 제품라벨을 확인하여야 한다. 이 약은 정맥주사용이다. 투약 오류를 방지하기 위해 조제해 투여하는 약이 캐싸일라(트라스투주맙엠탄신)가 아닌 트라스투주맙이 맞는지 바이알 라벨을 확인해야 한다. 유방암 • 전이성 유방암 : HER2 양성 전이성 유방암 환자 치료에 다음과 같이 투여한다. 이 약 단독요법 및 파클리탁셀, 도세탁셀, 아로마타제 억제제와의 병용요법 시 이 약의 권장용량은 다음과 같다. 1) 1주 요법 : 초기부하용량 : 권장 초기부하용량은 4mg/kg이다. 유지용량 : 권장 유지용량은 매주 2mg/kg이며 초기부하용량 투여 1주일 후부터 투여를 시작한다. 2) 3주 요법 : 초기부하용량 : 권장 초기부하용량은 8mg/kg이다. • 유지용량 : 권장 유지용량은 6mg/kg이며 초기부하용량 투여 3주 후부터 투여를 시작한다. 도세탁셀과 파클리탁셀의 병용요법 : 이 약의 최초 투여시에는 이 약 투여 다음날에 파클리탁셀 또는 도세탁셀을 투여한다. 최초 투여에 내약성이 우수한 경우, 이후 투여시에는 이 약 투여후 즉시 파클리탁셀 또는 도세탁셀을 투여할 수 있다. 아로마타제 억제제와의 병용요법 : 이 약과 아로마타제 억제제는 첫날에 모두 투여한다(투여순서는 상관없음). 조기 유방암 : 다음의 2가지 투여요법중 선택하여 투여할 수 있다. 1) 3주 요법 : 초기 부하용량으로 8mg/kg을 투여하고 이후 매 3주마다 유지용량으로 6mg/kg을 투여한다. 2) 1주 요법 : 안트라싸이클린과 싸이클로포스파미드 병용화학요법실시후, 초기부하용량으로 4mg/kg을 투여하고 이후 1주 마다 2mg/kg을 유지용량으로 투여한다. 이때는 파클리탁셀과 병용투여한다. 전이성 위암 • 3주 요법 : 초기 부하용량으로 8mg/kg을 투여하고 이후 매 3주마다 유지용량으로 6mg/kg을 약 90분에 걸쳐 점적주입 한다. 초기 부하 용량에 내약성이 우수한 경우 유지용량은 30분에 걸쳐 주입할 수 있다. 유방암(조기 유방암 및 전이성 유방암) 및 전이성 위암 : 전이성 유방암이나 전이성 위암환자는 질병진행시까지 이 약을 투여한다. 조기 유방암의 경우는 1년 동안 또는 질병재발까지 이 약을 투여해야한다. 조기 유방암 치료를 1년 넘게 지속하는 것은 권장되지 않는다. [사용상의 주의사항] 이 약은 허셉틴주(트라스투주맙)(단클론항체, 유전자재조합)를 대조약으로 한 동등생물의약품이다. 1. 경고 1) 심기능 장애(Cardiac dysfunction): 트라스투주맙 투여 시 울혈성 심부전[뉴욕심장학회(NYHA) 2~4등급] 또는 무증상 심기능 장애의 위험이 증가한다. 심질환 위험성이 큰 환자(고혈압, 입증된 관상동맥질환, 울혈성 심부전, 이완기 장애, 55% 미만 LVEF, 고령자) 투여 시 주의를 기울여야 한다. 2) 주입관련 반응, 알러지양 반응 및 과민 반응 3) 폐 이상사례 4) 벤질알코올은 미숙아에게서 치명적인 가쁜 호흡증상과 연관이 있는 것으로 보고되었다.(허쥬마주 440mg에 한함) 2. 다음 환자에는 투여하지 말 것 1) 트라스투주맙, 설치류 유래 단백 또는 이 약의 구성성분에 과민반응 병력이 있는 환자 2) 진행성 악성종양에 의한 중증 안정 시 호흡곤란 또는 산소보충이 필요한 환자 3) 신생아, 미숙아(벤질알코올을 함유하고 있다, 허쥬마주 440mg에 한함) ※셀트리온 제약 홈페이지 www.celltrionph.com 또는 전화 080-850-3611(~2)에서 확인하실 수 있습니다.
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- 폐경 전 호르몬 수용체 양성, 림프절 양성인 유방암 환자에서 수술 후 루프린® DPS주 11.25 mg 보조 요법은 **CMF* 보조 화학 요법**과 **동등한 Recurrence-Free Survival**을 나타냄[2]

루프린®은 Microsphere 기술로 개발되었으며[3], 투여 직후 환자의 불편감이 적었던 것으로 나타났습니다.[4]

*CMF, Cyclophosphamide / Methotrexate / Fluorouracil

[1]Study summary: An open-label, randomized controlled pilot study to evaluate the safety and efficacy of leuprorelin 11.25mg subcutaneously administered every-3-months for 2 versus 3 or more, up to 5 years, together with daily tamoxifen for 5 years in premenopausal endocrine-responsive breast cancer patients. Primary endpoints were disease-free survival (DFS) and safety. Adjuvant leuprorelin treatment for 3 or more years with tamoxifen showed a survival benefit and safety profile similar to that for 2 years in premenopausal endocrine-responsive breast cancer patients. **[2]Study summary:** A randomized phase III trial was performed to compare the Leuplin 3 month (n=299) and chemotherapy with CMF (n=300) in pre- or perimenopausal patients with ER-positive, node-positive breast cancer. The primary study objective was to compare RFS between both treatment groups. With a median follow-up of 5.8 years, recurrence-free survival was similar for patients treated with Leuplin 3M or CMF (hazard ratio [HR], 1.19; 95% CI, 0.94 to 1.51; P=0.15) Chemotherapy-related adverse effects were more common with CMF, whereas symptoms of estrogen suppression were initially more pronounced with Leuplin 3M. **[4]Study summary:** A crossover trial was conducted to compare patient comfort and tolerability between two commonly used LH-RH analogues: goserelin acetate and leuprorelin acetate. A total of 50 patients were randomised into two groups, each receiving 6-monthly injections of leuprorelin acetate (a liquid presentation) and goserelin acetate (a depot pellet) and crossing over between treatments. Patients completed a simple visual analogue score for the discomfort felt from the injections. An analysis of variance model was used, and the results found that patients do tolerate leuprorelin acetate (0.589) better than goserelin acetate (1.343) (P <0.001).

References. 1. Shiba E, et al. A randomized controlled study evaluating safety and efficacy of leuprorelin acetate every-3-months depot for 2 versus 3 or more years with tamoxifen for 5 years as adjuvant in premenopausal patients with endocrine-responsive breast cancer. Breast Cancer. 2016 May;23(3):499-509. **2.** Schmid P, et al. Leuprorelin Acetate Every-3-Months Depot Versus Cyclophosphamide, Methotrexate and Fluorouracil As Adjuvant Treatment in Premenopausal Patients With Node-Positive Breast Cancer : The TABLE Study. J Clin Oncol. 2007 Jun 20;25(18):2509-15. **3.** Okada H. One-and three-month release injectable microspheres of the LH-RH super agonist leuprorelin acetate. Adv Drug Deliv Rev. 1997 Oct 13;28(1):43-70. **4.** Williams G et al. Randomised crossover trial to assess the tolerability of LHRH analogue administration. Prostate Cancer Prostatic Dis. 2003;6(2):187-9.

Prescribing Information

루프린주 (Vial) 3.75mg / 루프린 디피에스주 (DPS) 3.75mg, 11.25mg, 22.5mg (류프로렐린아세트산염) [유효성분] 류프로렐린아세트산염 (JP) **[효능 · 효과]** (1)~(5) 3.75mg vial, 3.75mg DPS, (1) 진행성 전립선암 (2) 폐경전 유방암 (3) 자궁내막증 (4) 과다월경, 하복통, 요통 및 빈혈 등을 수반한 자궁근종에서 근종핵의 축소 및 증상의 개선 (5) 중추성 사춘기 조발증 **[용법 · 용량] (1) 진행성 전립선암 (2) 폐경전 유방암** 보통 성인에는 류프로렐린아세트산염으로서 4주 1회3.75mg/12주 1회 11.25mg/24주 1회 22.5mg을 피하주사한다. **(3) 자궁내막증** 보통 성인에는 4주 1회3.75mg (루프린주 3.75mg: 체중 50 kg 미만의 환자에게는 1.88 mg을 투여)/12주 1회 11.25mg을 피하주사하며, 초회투여는 월경주기 1~5일째에 한다. **(4) 자궁근종** 보통 성인에는 4주 1회1.88mg 피하주사한다. (루프린주 3.75mg만 해당) 단, 체중과다 환자, 자궁종대가 고도인 환자에는 4주 1회 3.75 mg/12주 1회 11.25mg을 투여하며, 초회투여는 월경주기 1~5일째에 한다. **(5) 중추성 사춘기 조발증** · 3.75mg vial 보통 4주 1회 체중 kg당 30 ㎍을 피하주사하며, 증상에 따라 체중 kg당 90 ㎍까지 증량할 수 있다. · 3.75mg DPS 보통 4주 1회 류프로렐린아세트산염으로서 체중 kg당 30 ㎍을 피하주사한다. 또한 증상에 따라 체중 kg당 90 ㎍까지 증량할 수 있다. 단, 이 제제는 1/2 시린지 용량 또는1시린지 용량 투여가 필요한 경우에 한하며, 남은 현탁 주사액은 폐기할 것 · 11.25mg DPS 용법용량은 개인별로 조절되어야 하며, 권장 초기용량은 체중에 따라 조절한다. –체중 20kg 이상의 소아: 1mL (11.25mg 류프로렐린아세트산염) 현탁액을 3개월마다 1회 피하주사한다. –체중 20kg 미만의 소아: 이러한 드문 경우에는 중추성 사춘기 조발증의 임상적 활성도에 따라 다음의 용량을 투여한다. 0.5Ml (5.625mg) 현탁액을 3개월마다 1회 피하주사하며, 남은 현탁 주사액은 폐기한다. 체중 증가를 관찰하여야 한다. **사용상의 주의사항 [경고]** 1)전이성 척추 손상이나 요로폐쇄증을 수반한 환자는 치료 초기 몇 주 동안 세심하게 관찰하여야 한다2)남성환자에서 심근경색, 급성심장사, 뇌졸중으로의 발생위험의 증가가 GnRH 작용체의 사용과 연관 있음이 보고되었다. 3)맴플주사제는 용기 절단 시 유리 파편이 혼입되어 부작용을 초래할 수 있으므로 사용 시 유리 파편 혼입이 최소화될 수 있도록 신중하게 절단 사용하되, 특히 어린이, 노약자에게 사용 시에는 각별히 주의할 것 (루프린주3.75mg에 한함) **[다음 환자에는 투여하지 말 것]** 1)이 약의 성분, LHRH 유사약물에 대해 과민반응의 병력이 있는 환자 2)임부 또는 임신하고 있을 가능성이 있는 여성 및 수유부 3)호르몬 비의존성 전립선암 환자 4)양쪽 고환 절제술을 받은 후, 이 약에 의해 더 이상 테스토스테론의 감소를 기대할 수 없는 환자 5)진단된 뇌하수체 샘종 환자 6)자궁내막증, 자궁근종, 중추성사춘기조발증: 원인불명의 질출혈이 있는 환자 (루프린디피에스주 22.5mg 제외) 7)진행성 뇌종양 소아 환자 (루프린주 3.75mg만 해당) 8)소아 (루프린디피에스주 22.5mg 만 해당) **[다음 환자에는 신중히 투여할 것]** 1)자궁내막증, 자궁근종, 폐경전 유방암: 자궁에 점막하 근종이 있는 환자 2)당뇨병 환자 3)고혈압 환자 4)우울증의 병력이 있는 환자 5) 젤라틴 함유제제 또는 젤라틴 함유 식품에 대해서 속, 아나필락시양 증상 (두드러기, 호흡곤란, 구진부종, 후두부종 등) 등의 과민반응의 병력이 있는 환자 (단, 과민반응의 원인이 젤라틴인 것이 명확한 경우에는 투여해서는 안됨) (루프린주3.75mg에 한함) **[저장방법]** 밀봉용기, 실온 (1~30℃)보관 **[수입자]** 한국다케다제약 주식회사/서울특별시 송파구 올림픽로 300 롯데월드타워 37층 [Pharmaceutical Company Limited/Hikari Plant (Japan)] ***이 내용은 허가사항을 요약한 것으로 자세한 정보는 제품의 첨부문서 또는 의약품통합정보시스템 (https://nedrug.mfds.go.kr)를 확인하십시오.**

C-KPROM/KR/LEU/0609 Date of preparation/Mar/2022

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텔®1-바이알주(도세탁셀수화물) [효능·효과] 1. 유방암 • 국소적으로 진행된 또는 전이성 유방암 1) 독소루비신과 병용하여 국소적으로 진행된 또는 전이된 유방암의 1차 치료 2) HER2가 과발현(IHC 3+ 또는 FISH 양성)되고 화학요법 치료를 받은 경험이 없는 전이성 유방암에 트라스투주맙과 병용요법 3) 이전의 화학요법에 실패한 국소적으로 진행된 유방암 또는 전이성 유방암 4) 카페시타빈과 병용하여 안트라사이클린계 약물을 포함한 화학요법에 실패한 국소적으로 진행된 유방암 또는 전이성 유방암 • 수술 후 보조요법 1) 독소루비신과 시클로포스파미드와 병용하여 다음 환자의 수술 후 보조요법 (TAC regimen) (1)림프절 양성의 수술 가능한 유방암 (2)림프절 음성의 수술 가능한 유방암(고위험인자가 하나 이상 있는 환자(종양크기>2cm, 연령<35세, 호르몬수용체음성, 종양분화도2~3)) 2) 독소루비신과 시클로포스파미드 사용 후, 트라스투주맙과 병용하여, HER2가 과발현된 수술 가능한 유방암 환자의 수술 후 보조요법 (AC-TH regimen) 3) 카보플라틴과 트라스투주맙과 병용하여, HER2가 과발현된 수술 가능한 유방암 환자의 수술 후 보조요법 (TCH regimen) 4) 시클로포스파미드와 병용하여 수술가능한 유방암 환자의 수술 후 보조요법 (1cm≤원발종양크기<7cm) (TC regimen) 2. 비소세포폐암: 백금화학요법제로 치료효과를 얻지 못한 환자들을 포함한 국소적으로 진행된 비소세포폐암 또는 전이성 비소세포폐암 1) 전립샘암: 프레드니솔론과 병용하여 안드로겐 비의존성(호르몬불응성) 전이성 전립샘암 4. 난소암: 카보플라틴과 병용하는 1차요법제로서 진행된 또는 전이된 상피성 난소암 5. 두경부암: 시스플라틴 및 플루오로우라실과 병용하여 국소 진행성 두경부 편평세포암의 유도화학요법 6. 위암 1) 진행성 및 전이성 또는 국소재발성 위암의 1차 치료 2) 시스플라틴 및 플루오로우라실과 병용하여 전이성 또는 국소재발성 식도 편평세포암 **[용법·용량]** 1. 유방암 • 국소적으로 진행된 또는 전이성 유방암 1) 유방암에 대한 일차적 요법에서 독소루비신(50 mg/m²)과 병용시 도세탁셀로서 75 mg/m²을 투여. 2) 화학요법 치료가 적이 없는 HER2 과발현 전이성 유방암에 트라스투주맙과 병용요법제로 사용하는 경우, 이 약으로서 100 mg/m²를 매 3주마다 60분에 걸쳐 점적정맥주사. 3) 이전 화학요법에 실패한 유방암에서는 도세탁셀 75~100 mg/m²을 매 3주마다 1시간 동안 정맥 투여. 4) 카페시타빈과 병용하여 안트라사이클린계 약물을 포함한 화학요법에 실패한 국소적으로 진행된 유방암 또는 전이성 유방암에서는 3주마다 이 약 75 mg/m² 투여하면서 카페시타빈을 2주간 1일 2회, 1회 1,250 mg/m² 투여하고(식후 30분 이내) 1주간 휴약하는 것(3주를 주기로 함)이 권장. **• 수술 후 보조요법** 1) TAC regimen: 매 3주마다 독소루비신 50 mg/m²과 시클로포스파미드 500 mg/m²을 1시간 후 이 약 75 mg/m²를 6주기 투여. 2) AC-TH regimen: (1) AC: 1~4 주기(3주/1주기)동안 매 3주마다, 독소루비신 (A) 60 mg/m² 투여하고, 시클로포스파미드 (C) 600 mg/m² 투여. (2) TH: 5~8 주기(3주/1주기)동안 매 3주마다 도세탁셀 (T) 100 mg/m²를 1시간 동안 투여하고, 트라스투주맙 (H)은 매주 5주기의 기부하용량으로 트라스투주맙 4 mg/kg을 90분간 투여한 이후 1주마다 유지용량으로 2 mg/kg를 30분간 투여. (5주기의 8일차부터, 8주기까지) 도세탁셀은 5주기의 2일차에 투여하고 6~8주기에는 1일차에 투여. (3) 보조화학요법이 완료된 후에 트라스투주맙 6 mg/kg를 단독요법으로 3주마다 30분간 투여. 트라스투주맙은 총 1년간 투여. 3) TCH regimen(1-6주기) (1) 도세탁셀 및 카보플라틴: 3주마다 도세탁셀 (T) 75 mg/m²를 1시간 동안 투여 및 카보플라틴 (C) AUC 6 mg/mL/min를 30~60분간 투여하며, 1주기에는 2일차에 투여, 2~6주기에는 1일차에 투여. (2) 트라스투주맙: 1일차에 초기부하용량으로 트라스투주맙 4 mg/kg을 90분간 투여한 이후 1주마다 유지용량으로 2 mg/kg를 30분간 투여. (3) 보조화학요법이 완료된 후에 트라스투주맙 6 mg/kg를 3주마다 30분간 투여. 트라스투주맙은 총 1년간 투여. 4) TC regimen: 3주를 1주기로 하여 4주기 동안, 매 주기의 1일차에 도세탁셀 75 mg/m²을 1시간 이상 주입하고, 시클로포스파미드 600mg/m²을 30~60분간 정맥 투여. 3. 전립샘암: 프레드니솔론과 병용시 이 약 75 mg/m²을 매 3주마다 1시간동안 정맥 주사. 프레드니솔론은 1일 2회, 1회 5mg을 지속적으로 경구투여. 4. 난소암: 진행된 또는 전이된 상피성 난소암에 대한 1차 요법으로 카보플라틴과 병용하여 3주마다 이 약 75 mg/m² 1시간동안 정맥주사 후 즉시 카보플라틴 AUC 6.0 mg/mL·min 을 30~60분간 정맥주사. 5. 두경부암 1) 방사선요법 전의 유도화학요법: 수술 또는 방사선요법과 병용하여 국소 진행성 두경부 편평세포암의 유도화학요법시 이 약75mg/m²을 1시간동안 정맥주사한 후, 시스플라틴 75mg/m²을 1시간 이상 정맥주사(제 1일). 그 후 플루오로우라실을 750mg/m²/day로 5일동안 연속 정맥주사. 3주를 1주기로 하여 4주기 동안 투여. 2)화학방사선요법 전의 유도화학요법: 국소 진행성(절제 불가능한 국소 재발 또는 외과적 치료 및 장기 보존) 두경부 편평세포암의 유도화학요법시 이 약75mg/m²을 1시간동안 정맥주사한 후, 시스플라틴 100mg/m²을 30분~3시간 동안 정맥주사(제 1 일). 그 후 플루오로우라실을 1,000mg/m²/day로 연속 정맥주사(제1일~제4일). 3주를 1주기로 하여 3주기 동안 투여. 6. 위암 1) 단독요법: 이 약 75 mg/m²을 매 3주마다 1시간동안 정맥 주사. 2) 시스플라틴 및 플루오로우라실과 병용투여: 이 약 75 mg/m²을 1시간 동안 정맥주사 후, 시스플라틴 75 mg/m²을 1~3시간 동안 정맥주사. 시스플라틴 정맥주사가 끝난 후부터 플루오로우라실을 750 mg/m²/day 용량으로 5일동안 연속주입(1주기). 3주마다 같은 방법으로 투여. 7. 식도암: 상기 요법에게 1일 1회 이 약 70 mg/m²을 1시간 이상 3~4주 간격으로 정맥 주사하며, 환자의 상태에 따라 적절히 감량. **[사용상의 주의사항]** 경고 1) 간기능의 이상이 있고, 고용량을 받는 경우, 이전 백금을 기본으로 한 치료경험이 있는 비소세포폐암 환자 중 단독으로 100mg/m²을 투여 받는 경우 이 약과 관련된 사망 건수가 증가하였다. 장애 환자: 이 약 100mg/m²을 단독으로 투여받은 환자 중에서 혈청 아미노전달효소(ALT 또는/그리고 AST)가 ULN보다 1.5배 이상 높고, 혈청 ALP가 ULN보다 2.5배 이상 높은 경우에는 사망으로 이어질 수 있는 치명적인 패혈증, 위장관 출혈과 열성 호중구감소증, 감염, 혈소판감소증, 구내염, 무력증과 같은 중증의 이상반응이

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- ASCO guideline update recommends standard duration of ovarian suppression up to 5 years[1]
- ARIMIDEX demonstrates comparable efficacy compared to letrozole in either DFS or OS, with no new safety concerns identified[1,2]

* 호르몬요법이 적합한 폐경기전 및 주폐경기 여성의 진행성 유방암
** 폐경기 이후 여성의 진행성 유방암(이 요법 이전의 타목시펜 치료시 임상반응을 나타내지 않는 에스트로겐 수용체 음성인 환자에서, 이 약의 유효성은 입증되지 않았다.)

† Study design: phase IIIb, open-label, multicenter trial conducted across 271 international centers. postmenopausal women with HR-positive were randomly assigned 1:1 to receive either adjuvant letrozole (2.5 mg) or anastrozole (1 mg) once per day until disease recurrence/relapse or for a maximum of 5 years.

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전문의약품

PRODUCT INFORMATION

졸라덱스 데포주사 (초산고세렐린) 【 성분 · 함량 】 이 약 1 프리필드실린지 (18.0 mg) 중 유효성분: 고세렐린아세트산염 (별규) 3.78 mg(고세렐린으로서 3.6 mg)첨가제: 락타이드/글리콜라이드공중합체 18.0 mg프리필드시린지 **【 성 상 】** 1회용 실린지 어프리케이터 속에 살균된 흰색–미황색의 원주형 데포가 들어있으며 이 속에 고세렐린아세트산염(고세렐린으로서 3.6mg)이 생체내에서 분해되는 매트릭스에 분산되어 있다. **【 효능 · 효과 】** 1. 호르몬요법이 적합한 전립선암 2. 호르몬요법이 적합한 폐경기전 및 주폐경기 여성의 진행성 유방암 3. 조기유방암의 보조요법: 에스트로겐 수용체(ER) 양성인 폐경기전 및 주폐경기 여성의 조기 유방암에 대한 표준 화학 요법의 대체요법 4. 자궁내막증 5. 자궁내막조직의 퇴축: 자궁내막 제거나 절제 전에 자궁내막을 얇게 함을 목적으로 투여함 6. 자궁근종: 자궁근종을 가진 빈혈환자에서 수술 전 철분요법과 병행하여 환자의 혈액상태를 개선함을 목적으로 투여함 7. 보조생식술: 배란촉진 과정 시 뇌하수체 억제 목적 **【 용법 · 용량 】** 성인: 고세렐린으로서 3.6 mg 을 28 일 간격으로 전방복벽에 피하주사한다. 신장애, 간장애 환자나 고령자의 경우에도 용량을 조절할 필요는 없다. 1. 전립선암, 유방암: 호르몬요법이 적합한 전립선암 또는 유방암의 관리에 고세렐린으로서 3.6 mg 1 데포를28 일마다 전방복벽에 피하주사한다. 국소진행 전립선암에 있어서 방사선요법과 병용하는 보조 호르몬요법의 경우 36 개월로 사용이 제한된다. 2. 자궁내막증: 자궁내막증을 이 약으로서 6 개월 이상 치료한 임상자료가 없으므로 치료기간은 6 개월 이하가 되도록 한다. 뼈 무기질 밀도 감소의 우려가 있으므로 반복적인 치료는 하지 않도록 한다. 이 약 투여 시 호르몬 대체요법(에스트로겐 및 프로게스테론 제제)을 병행하면 뼈 무기질 밀도 감소 및 혈관운동성 증상이 감소된다. 3. 자궁내막조직의 퇴축: 자궁내막의 퇴축을 목적으로 투여할 때는 4주 또는 8 주간 치료한다. 자궁의 크기가 큰 환자에게 투여 시 또는 적당한 수술 일정을 결정하기 위해서 2 번째 데포를 투여할 수 있다.4. 자궁근종: 자궁근종에 의한 빈혈이 있는 여성에게는 고세렐린으로서 3.6 mg 에 철분을 보충하여 수술 전3 개월까지 투여할 수 있다.5. 보조생식술: 에스트라디올 농도가 초기 황체기 수준이(약 150 pmol/L) 되도록 뇌하수체를 억제하기 위해 고세렐린으로서 3.6 mg 1 데포를 투여한다. 이는 7~21 일 사이에 일어난다. 뇌하수체가 억제되면 생식샘자극호르몬(gonadotrophin)으로 배란을 촉진시킨다. 이 약에 의한 뇌하수체 억제는 일정하여 일부 경우, 성선자극호르몬 요구량이 증가될 수 있다. 적당한 시기의 황체기에 성선자극호르몬을 중지하고 사람융모성생식샘자극호르몬(hCG)을 투여하여 배란시킨다. 치료관찰, 난자 회수 및 임신기법은 각 병원의 일반적 방법에 따른다. **【 사용상의 주의사항 】** 1. 경고: 전이성 척추 손상(metastatic vertebral lesion)이나 요로폐쇄증을 수반한 환자는 치료 초기 몇 주 동안 세심하게 관찰하여야 한다. 2. 다음 환자에는 투여하지 말 것.1) 이 약의 성분 및 LHRH 유사약물에 대하여 과민반응 환자 2) 임부 및 수유부 3) 호르몬 비의존성 전립선암 환자 4) 양쪽 고환 절제술을 받은 후, 이 약에 의해 더 이상 테스토스테론의 감소를 기대할 수 없는 환자 5) 원인 불명의 질 출혈 환자 6) 소아 7) 진단된 뇌하수체 샘종 환자 3. 다음 환자에는 신중히 투여할 것. 보조생식술의 경우: 다낭포성 난소 환자 문헌개정연월일: 2020 년 8 월 5 일 수입자: 한국아스트라제네카, 서울시 강남구 영동대로 517 아셈타워 21 층, 전화: (02) 2188-0800 공동판매자: 알보젠코리아주식회사, 서울시 영등포구 국제금융로 10 2IFC 13 층, 전화: (02) 2047-7700 aZOL20200924

전문의약품

PRODUCT INFORMATION

아리미덱스 정(아나스트로졸) Arimidex tablet (Anastrozole) 【성분 · 함량】 1정(약 103mg)중 주성분 : 아나스트로졸 (별규) 1.0mg **【성상】** 백색의 원형 필름코팅정 **【효능 · 효과】** 1. 폐경기 이후 여성의 진행성 유방암의 치료(이 요법 이전의 타목시펜 치료시 임상반응을 나타내지 않는 에스트로겐 수용체 음성인 환자에서, 이 약의 유효성은 입증되지 않았다.) 2. 호르몬 수용체 양성인 폐경기 이후 여성의 조기 유방암의 보조 치료. 조기 유방암의 보조 요법으로 2~3 년간 타목시펜을 투여 받아온 호르몬 수용체 양성인 폐경기 이후 여성 환자의 조기 유방암의 보조 치료. **【용법 · 용량】** • 성인 : 아나스트로졸로서 1일 1회 1mg을 경구투여한다. • 소아 : 18세 이하 소아에게는 투여하지 않는다. • 신장애 환자 : 경증 또는 중등도의 신장애 환자는 용량을 변경할 필요가 없다. 중증 신기능장애 환자(크레아티닌청소율이 30 mL/min 이하인 환자)에서는 이 약을 투여하지 않는다. • 간장애 환자 : 경증의 간장애 환자는 용량을 변경할 필요가 없다. 중등도 이상의 간장 질환자에서는 이 약을 투여하지 않는다. **【사용상의 주의사항】** 1. 경고 1) 이 약은 폐경기 이전의 여성에게는 안전성 및 유효성이 입증되지 않았기 때문에 사용하지 않아야 한다. 폐경기 상태가 의심스러운 경우 폐경기 여부를 생화학적으로 확인 하여야 한다. 2) 이 약은 중등도 또는 중증의 간장애 및 중증의 신장애 환자(크레아티닌 클리어런스가 30mL/min 이하)에 대해서는 시험되지 않았다. 3) 이 약은 순환 에스트로겐을 낮추므로 골무기질 밀도를 감소시켜서 골절의 위험을 증가시킬 수 있다. 4) 골다공증 및 골다공증 위험이 있는 환자에게 치료 시작 및 그 후 일정한 간격으로 골밀도에 대하여 시험(예, DEXA scanning)하여야 한다. 골다공증 치료 및 예방법이 적절하게 시행되어야 하고 주의 깊게 모니터링 해야 한다. 5) LHRH 계열과 아나스트로졸 병용에 대한 연구가 이루어지지 않았다. 이 병용요법을 임상에서 사용해서는 안된다. 2. 다음의 환자에는 투여하지 말 것. 1) 폐경기 이전의 여성 2) 임부 또는 임신하고 있을 가능성이 있는 여성, 수유부 3) 중증의 신장애 환자 (크레아티닌청소율이 30mL/min 이하인 환자) 4) 중등도 이상의 간장애 환자 5) 이 약 또는 이 약의 구성성분에 과민반응이 있다고 알려진 환자 6) 타목시펜 병용투여 환자 또는 에스트로겐을 함유하는 요법중인 환자(이 약의 약리작용을 감소시키기 때문에 병용해서는 안된다.) 7) 이 약은 락토오스를 포함하고 있다. 드물게 나타나는 갈락토오스 불내성(galactose intolerance), Lapp유당분해효소 결핍증(Lapp lactase deficiency) 또는 포도당–갈락토스 흡수장애(glucose–galactose malabsorption) 등의 유전적인 문제가 있는 환자에게는 투여하면 안 된다. **【저장방법】** 밀폐용기, 30℃ 미만에서 보관 수입자 : 한국아스트라제네카

aAR(20190501

KR-8604 (Exp. 2023-06 (Prep. 2021-06)

AstraZeneca

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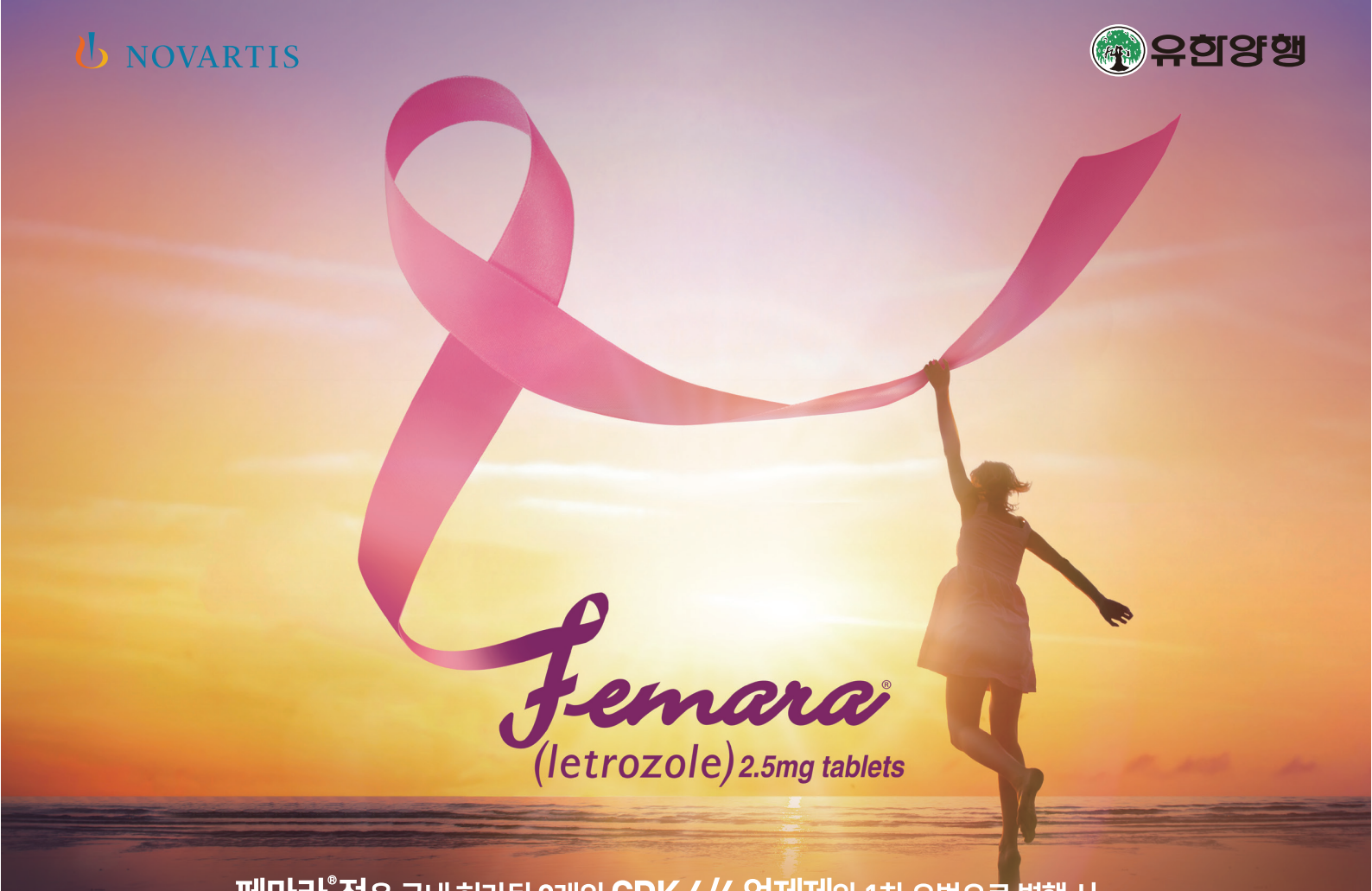
NOVARTIS

유한양행

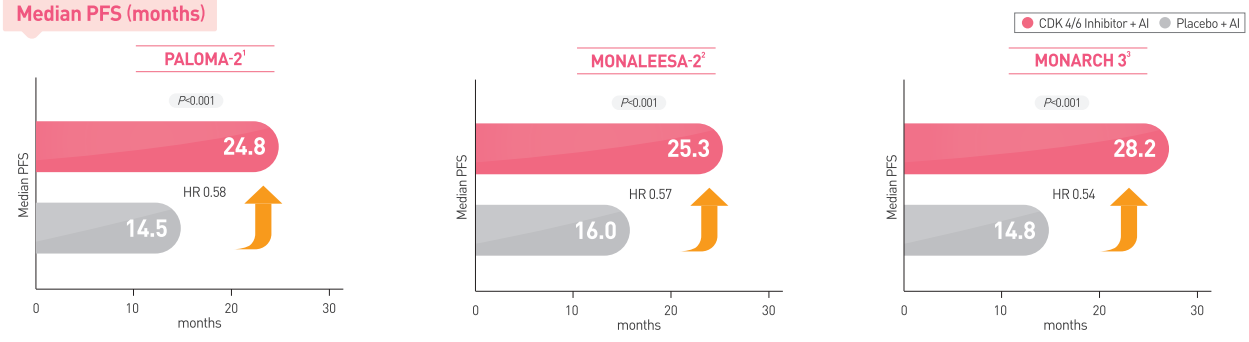


페마라®정은 국내 허가된 3개의 CDK 4/6 억제제와 1차 요법으로 병행 시, 아로마타제 단독 요법 대비 통계적으로 유의한 PFS 개선 효과를 보였습니다.[1-3]

Study	CDK 4/6 Inhibitor	Aromatase Inhibitor	Study Population	Line of Therapy	Sample Size
PALOMA-2[1]	Palbociclib	Letrozole	Postmenopausal women with HR+/HER2- ABC and no prior systemic treatment for ABC; (neo) adjuvant ET permitted if disease-free interval>12 months from therapy completion	1st line	666
MONALEESA-2[2]	Ribociclib	Letrozole		1st line	668
MONARCH 3[3]	Abemaciclib	Letrozole or Anastrozole		1st line	493

Phase III studies of CDK 4/6 inhibitors in breast cancer

Median PFS (months)



Study design

- [PALOMA-2][1] 2:1 무작위배정, 이중맹검, 위약대조 시험으로 폐경 후 HR+/HER2- 전이성 유방암에서 전이 후 선행치료경험이 없는 환자 666명을 대상으로 palbociclib 125 mg qd (3주 투약 후 1주간 휴약) 또는 위약을 letrozole 2.5 mg qd와 병용하여 1차 평가변수로 PFS, 2차 평가변수로 OS, OR 및 안전성을 평가한 임상 3상 연구
- [MONALEESA-2][2] 1:1 무작위배정, 이중맹검, 위약대조 시험으로 폐경 후 HR+/HER2- 재발 혹은 전이된 유방암 환자 668명을 대상으로 1차 치료로 ribociclib 600 mg 또는 위약을 letrozole 2.5 mg qd와 병용하여 1차 평가변수로 PFS, 2차 평가변수로 OS, ORR 및 안전성을 평가한 임상 3상 연구
- [MONARCH 3][3] 2:1 무작위배정, 이중맹검, 위약대조 시험으로 폐경 후 HR+/HER2- 진행성 유방암 환자 493명을 대상으로 초기 내분비 요법으로서 abemaciclib 150 mg bid 또는 위약을 letrozole 2.5 mg qd 혹은 anastrozole 1 mg qd와 병용하여 1차 평가변수로 PFS, 2차 평가변수로 OS, 반응기간 및 안전성을 평가한 임상 3상 연구

ABC, advanced breast cancer; **AI,** aromatase inhibitor; **BID,** twice a day; **CDK,** cyclin-dependent kinase; **ET,** endocrine therapy; **HER2-,** human epidermal growth factor receptor 2 negative; **HR,** hazard ratio; **HR+,** hormone receptor positive; **OR,** overall response; **ORR,** overall response rate; **OS,** overall survival; **PFS,** progression-free survival; **QD,** once a day.

References 1. Finn RS, et al. *N Engl J Med*. 2016;375:1925–36. **2.** Hortobagyi GN, et al. *Ann Oncol*. 2018;29(7):1541-1547. **3.** Johnston S, et al. *NPJ Breast Cancer*. 2019;5:5.

[Product Information]

처방하시기전 QR코드 또는 식품의약품안전처 의약품통합정보시스템 (http://nedrug.mfds.go.kr)을 통해상세 제품정보를 참조하시기 바랍니다.

페마라®정 (레트로졸)

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GBCC 2023
Global Breast Cancer Conference 2023

Oral Presentation

"Go Beyond Cure of Breast Cancer"

BREAST CANCER IN ADOLESCENT & YOUNG ADULT (AYA) AGE GROUP HAS A SPECIFIC BIOLOGICAL FEATURE AND POOR OUTCOME COMPARED TO OTHER GENERATIONS

Masanori Oshi[1,2], Akimitsu Yamada[1], Mahato Sasamoto[1], Shinya Yamamoto[3], Kazutaka Narui[3], Takashi Ishikawa[4], Kazuaki Takabe[2], Itaru Endo[1]

[1]Yokohama City Univ. Graduate School of Medicine, Department of Breast Surgery, Japan, [2]Roswell Park Comprehensive Cancer Center, Department of Surgical Oncology, U.S.A., [3]Yokohama City Univ. Medical Center, Department of Breast

Background: Different characteristics of breast cancer (BC) have been reported for different age groups. However, there is still unknown on the clinicopathological and biological features regarding the differences.

Methods: BC patients were categorized into four age groups; adolescent and young adult (AYA) (15-39 years), perimenopausal (40-55), menopausal (55-65), and old (65 and more). Clinicopathological analysis was performed using a cohort from two Yokohama city university hospitals (YCU; n = 4,562), and large public databases (METABRIC; n = 1,903, GSE96058; n = 3,273). Biological features were analyzed using gene set variation analysis and the xCell algorithm using mRNA expression in public databases using.

Result: AYA had significantly poorer disease-specific survival (DSS) than other groups in 2 cohorts ($p = 0.010$ and $p = 0.002$, respectively). The survival difference was more pronounced in ER-positive/HER2-negative (Luminal) BC patients. AYA BC group had larger tumor size, higher rates of node metastasis and PgR positivity (all $p < 0.001$) while it did not observe among the other groups. In Luminal subtype, AYA BC significantly had higher enhancement in cell proliferation-related gene sets (G2M checkpoint, E2F targets, and MYC target v1) as well as in MTORC1, unfolded protein response, and PI3K/ACT/MTOR signaling when compared to the other age groups. In HER2-negative subtypes, AYA BC showed significantly high activated BRCAness ($p \leq 0.002$ and $p \leq 0.023$, respectively) compared to other age groups.

Conclusions: Biological difference was found in BC between AYA group and the others. This could play a pertinent role in the difference of outcome in each age group. It is necessary to elucidate these differences and develop the treatment strategies which are specific to the AYA BC.

CONSECUTIVE GAIN AND LOSS IN BODY WEIGHT AND WAIST CIRCUMFERENCE WITH RISK OF SUBSEQUENT BREAST CANCER IN KOREAN WOMEN

Thi Xuan Mai Tran[1,3], Soyeoun Kim[1,3], Huiyeon Song[4], Boyoung Park[1,2]

[1]Hanyang Univ. College of Medicine, Department of Preventive Medicine, Vietnam, [2]Hanyang Univ., Hanyang Institute of Bioscience and Biotechnology, Korea, [3]Hanyang Univ., Institute for Health and Society, Korea, [4]Hanyang Univ., Department of Epidemiology and Biostatistics, Korea

Background: This study investigated the association between longitudinal changes in weight and waist circumference and breast cancer risk according to menopausal status.

Methods: This prospective cohort study used data from the population-based Korean National Health Insurance Service (NHI) database. The study population included women aged ≥40 years who consecutively underwent three biennial breast cancer screenings between 2009-2014 and were followed up until 2020. The percentage changes in weight and waist circumference during the three screenings were calculated and categorized into five groups based on the level of increase or decrease in these two factors. Hazard ratios (HRs) and 95% confidence intervals (95% CI) for breast cancer risk were calculated and adjusted for other factors.

Result: Of 691,253 premenopausal and 1,519,211 postmenopausal women, 9,485 and 12,553 cases were identified, respectively, during a median 6.9 follow-up years. Postmenopausal women with two consecutive weight gains had an increased risk of breast cancer risk (HR = 1.11, 95% CI = 1.01 to 1.22); meanwhile, consecutive weight loss was associated with a decreased risk (HR = 0.84, 95% CI = 0.76 to 0.93). Single time and continuous decreases in waist circumference were associated with a decreased risk (HR = 0.91, 95% CI = 0.85 to 0.98, and HR = 0.84, 95% CI = 0.760.93), while single time and continuous increases were associated with an increased risk (HR = 1.08, 95% CI = 1.01 to 1.15, and HR = 1.13, 95% CI = 1.04 to 1.22). Single weight gain was associated with the increased breast cancer risk in premenopausal women (HR = 1.07, 95% CI = 1.01 1.13).

Conclusions: Our findings suggest a dose-response relationship between weight, waist circumference change, and the risk of future breast cancer.

THE BURDEN OF BREAST CANCER IN YOGYAKARTA SPECIAL REGION, INDONESIA FROM 2008-2019: A TEMPORAL TREND ANALYSIS OF THE POPULATION-BASED CANCER REGISTRY DATA

Herindita Puspitaningtyas[1], Juan Adrian Wiranata[2], Bryant Ng[3], Susanna Hilda Hutajulu[4], Nungki Anggorowati[5], Guardian Yoki Sanjaya[6], Lutfan Lazuardi[6], Patumrat Sripan[7]

[1]Universitas Gadjah Mada, Doctorate Program of Health and Medical Science, Faculty of Medicine, Public Health and Nursing, Indonesia, [2]Universitas Gadjah Mada, Master of Clinical Epidemiology Postgraduate Program, Faculty of Medicine, Public Health and Nursing, Indonesia, [3]Universitas Gadjah Mada, Medicine Study Program, Faculty of Medicine, Public Health and Nursing, Indonesia, [4]Universitas Gadjah Mada/ Dr. Sardjito General Hospital, Division of Hematology and Medical Oncology, Department of Internal Medicine, Faculty of Medicine, Public Health and Nursing, Indonesia, [5]Universitas Gadjah Mada/ Dr. Sardjito General Hospital, Department of Anatomical Pathology, Faculty of Medicine, Public Health and Nursing, Indonesia, [6]Universitas Gadjah Mada, Department of Health Policy and Management, Faculty of Medicine, Public Health and Nursing, Indonesia, [7]Research Institute for Health Sciences, Chiang Mai Univ., Thailand

Background: Breast cancer (BC) remains the most frequent cancer, with increasing incidence worldwide. This study aimed to elucidate the dynamic change of BC incidence in the local population.

Methods: We extracted 4,268 data of 2008-2019 female BC from the Yogyakarta Population-based cancer registry, comprising ≥ 20 years-old residents of three out of five districts of Yogyakarta Special Region (Sleman, Yogyakarta, Bantul). We calculated the age-standardized rate (ASR) using regional (2014) and world population data. Using Joinpoint regression, we described the average annual percent change (AAPC) of the incidence and compared the trend of early-onset BC (EOBC) vs. late-onset BC (LOBC).

Result: The ASR of BC in the three districts during 2008-2019 was 41.35 per 100,000 person-year. The ASR of EOBC was lower than LOBC (ASR = 29.42 and 61.46, respectively). In Sleman and Yogyakarta, the peak incidence shifted from 50-54 in 2008-2013 to 60-64 age group in 2014-2019. The shift was also identified from 55-59 to 50-54 and 60-64 age groups in Bantul. Although increasing trend of BC was apparent in all districts (AAPC Sleman = 18.21, Yogyakarta = 18.77, Bantul = 8.94), significant increase was identified during 2012-2017 in Sleman and Yogyakarta (AAPC = 36.09 and 34.05). In Sleman, we found a significant increase in EOBC during 2013-2017 and LOBC during 2012-2017 (AAPC = 38.71 and 37.48).

Conclusions: Our results display a steady increase in BC incidence in the region during the last 12 years. We also identify a shift towards older age group in the local population. This finding may serve as basis for reinforcement of BC screening and early detection programs, especially towards older women.

AUGMENTING BREAST CANCER SCREENING EFFICIENCY BY MAXIMIZING DETECTION OF NORMAL MAMMOGRAMS USING AN ARTIFICIAL INTELLIGENCE ALGORITHM

Serene Si Ning Goh[1], Du Hao[2], Meng Ling Feng[2], Mikael Hartman[1,2], Yin Jin[3], Jiajun Qiu[3], Wei Zhang[3], Julian Euma Ishii-Rousseau[4], Tomoyuki Fujioka[5], Wei-Cheng Wong[6], Chang-Fu Kuo[6], Chi-Tung Cheng[6], Sira Sriswasdi[7], Yothin Rakvongthai[8], Jirarat Jirarayapong[8], Sze Yiun Teo[9], Yien Sien Lee[9]

[1]National Univ. of Singapore, Department of Surgery, Singapore, [2]National Univ. of Singapore, Saw Swee Hock School of Public Health, National Univ. Health System, Singapore, [3]West China Hospital, Sichuan Univ., West China Biomedical Big Data Center, China, [4]Tokyo Medical Univ., Department of Global Health Promotion, Japan, [5]Tokyo Medical Univ., Department of Radiology, Japan, [6]Chang Gung Memorial Hospital, Centre for Artificial Intelligence Research in Medicine, Taiwan, [7]Chulalongkorn Univ., Center for Artificial Intelligence in Medicine, Research Affairs, Faculty of Medicine, Thailand, [8]Chulalongkorn Univ., Department of Radiology, Thailand, [9]KK Women's and Children's Hospital, Department of Radiology, Singapore

Background: Population-wide screening mammography has shown reduction in breast cancer mortality. However, the high volume of mammograms, most of which are normal, and the requirement for double-reading lead to longer work hours and increased boredom for radiologists. Artificial intelligence (AI) offers a promising solution as evidenced by studies in Caucasian populations. Comparatively, breast density and clinical profile may differ in Asians. To date, there is a paucity of data evaluating AI models in populations from the Asian-Pacific (APAC) regions.

Methods: We conducted a multi-center study involving six medical centers in the APAC region. Inclusion criteria were mammograms from women aged 40 years and above. Exclusion criteria were 1) Patients with computed radiography (CR) instead of full field digital mammograms (FFDM) 2) Patients with no histopathological results 3) Patients with breast surgery or implant(s) prior to mammography.

Result: A total of 11,028 mammograms were evaluated. Demographics, radiological and histological findings between centers were comparable. Up to 87.4% of patients had dense breasts. BI-RADS 3 was the most frequent category for benign cases whilst BI-RADS 4 was the most frequent category for malignant cases. A high overall ROC-AUC performance of 0.902 was achieved, comparable to the current state-of-the-art AI models and consistent across the APAC populations. Up to 57% of normal mammograms were estimated to be safely excluded from human reading, assuming a missed cancer rate of 5% (compared to the current standard of 12%).

Conclusions: These findings allow policymakers to leverage on the AI model to improve efficiency of breast cancer screening.

THE EFFECT OF MAMMOGRAPHIC BREAST DENSITY ON DIAGNOSTIC OUTCOMES IN MEN

Hwan Lee

Univ. of Pennsylvania, Department of Radiology, U.S.A.

Background: Reports on mammographic density and BI-RADS assessment in males are scarce in the literature. We examined the relationship between mammographic density and outcomes of diagnostic mammograms in males.

Methods: A total of 1,268 diagnostic mammograms with digital breast tomosynthesis performed in men at a single institution were retrospectively reviewed. Mammographic density was described in ACR BI-RADS classes. Each BI-RADS assessment of the mammograms was classified as true positive, true negative, false positive, or false negative.

Result: The most common mammographic density was almost entirely fatty (65.3%), followed by scattered fibroglandular density (30.3%), heterogeneously dense (3.7%), and extremely dense (0.7%). For almost entirely fatty breasts, mammographic BI-RADS was 3 in 3.4% and 4-5 in 5.6%. For scattered fibroglandular density breasts, BI-RADS assessment was 3 in 2.6% and 4-5 in 6.0%. For heterogeneously or extremely dense breasts, BI-RADS assessment was 3 in 8.9% and 4-5 in 7.1%. The number of false negative examinations was 1 for almost entirely fatty breasts, 1 for scattered fibroglandular density breasts, and 0 for dense breasts. The overall PPV2 was 24.7%: 19.6% (9/46) for almost entirely fatty breasts, 34.8% (8/23) for scattered fibroglandular density breasts, and 25% (1/4) for dense breasts.

Conclusions: Mammographic density in men was generally low. Dense breasts were more likely to be assigned BI-RADS 3 assessment. A very low number of missed cancer cases and reasonable PPV2 of 25% were observed in males, without a clear relationship to breast density. Overall, the results suggest clinical value of diagnostic mammography in males across all breast density classes.

DRUG-RESISTANT EXTRACELLULAR VESICLES PREDICT TUMOR RESPONSE IN BREAST CANCER PATIENTS RECEIVING NEOADJUVANT CHEMOTHERAPY

Jee Ye Kim, Min Woo Kim, Sol Moon, Suji Lee, Young Kim, Hyojung Lee, Joon Ye Kim, Seung Il Kim

Yonsei Univ. College of Medicine, Department of Surgery, Korea

Background: Predicting tumor response after neoadjuvant chemotherapy (NAC) is critical for predicting prognosis and deciding the treatment strategy in breast cancer (BC) patients. Therefore, we aimed to validate the clinical feasibility of miRNA and protein markers in exosomes for predicting tumor response during NAC.

Methods: Drug-resistant clones were generated from three BC cell lines. Profiling of drug-resistant BC identified potential drug resistance-related biomarkers. We isolated tumor exosomes and validated that drug-resistant biomarkers were also significant in exosomes released from drug-resistant tumor cells. The putative drug-resistant exosomal markers were validated in plasma samples from 72 BC patients, including 42 individuals showing no tumor response and 30 individuals showing a complete response.

Result: Compared with wild-type and drug-resistant exosomes, 5 EV miRNAs (miR-125b, miR-146a, miR-484, miR-1246, and miR-1260b) and 3 exosomal proteins (MDR1, MRP1, and BCRP) were confirmed as biomarkers contributing to the acquisition of drug resistance. The optimal combination of drug-resistant exosomal markers represented the best performance to differentiate tumor response. We also analyzed The GEO datasets to identify target genes of exosomal mRNAs related to drug resistance. The miRNA-target gene networks correlated highly with cell mitosis, metabolism, drug transport, and immune response.

Conclusions: Our study suggests that drug-resistant exosomal markers effectively predict tumor response, which can be clinically applicable. Moreover, drug-resistant exosomal markers seem to increase with repeated drug treatment in the tumor exosome population. This approach allows real-time monitoring of drug-resistant exosomal marker alterations potentially sensitive to targeted therapy or associated with treatment resistance in patients with BC during NAC.

DEEP LEARNING-BASED QUANTITATIVE ESTIMATION OF LYMPHEDEMA-INDUCED FIBROSIS USING THREE-DIMENSIONAL COMPUTED TOMOGRAPHY IMAGES

Chang Ho Hwang[1], Hyewon Son[2], Suwon Lee[2], Kwangsoo Kim[3], Kyo-In Koo[2]

[1]Chungnam National Univ. College of Medicine, Department of Physical and Rehabilitation Medicine, Korea, [2]Univ. of Ulsan, Major of Biomedical Engineering, Department of Electrical, Electronic and Computer Engineering, Korea, [3]Hanbat National Univ., Department of Electronics and Control Engineering, Korea

Background: In lymphedema, proinflammatory cytokine-mediated progressive cascades always occur, leading to macroscopic fibrosis. However, no methods are practically available for measuring lymphedema-induced fibrosis before its deterioration. Technically, Computed tomography (CT) can visualize fibrosis in superficial and deep locations. For standardized measurement, verification of deep learning (DL)-based recognition was performed.

Methods: A cross-sectional, observational cohort trial was conducted. After narrowing window width of the absorptive values in CT images, SegNet-based semantic segmentation model of every pixel into 5 classes (air, skin, muscle/water, fat, and fibrosis) was trained (65%), validated (15%), and tested (20%). Then, 4 indices were formulated and compared with the standardized circumference difference ratio (SCDR) and bioelectrical impedance (BEI) results.

Result: In total, 2138 CT images of 27 chronic unilateral lymphedema patients were analyzed. Regarding fibrosis segmentation, the mean boundary F1 score and accuracy were 0.868 and 0.776, respectively. Among 19 subindices of the 4 indices, 73.7% were correlated with the BEI (partial correlation coefficient: 0.420-0.875), and 13.2% were correlated with the SCDR (0.406-0.460). The mean subindex of Index 2 ((P_(Fibrosis in Affected)-P_(Fibrosis in Unaffected))/P_(Limb in Unaffected)) presented the highest correlation.

Conclusions: DL has potential applications in CT image-based lymphedema-induced fibrosis recognition. The subtraction-type formula might be the most promising estimation method.

PROGNOSTIC VALUE OF THE NGS-BASED MULTIGENE ASSAY TO PREDICT DISTANT METASTASIS IN HORMONE RECEPTOR-POSITIVE, HER2-NEGATIVE BREAST CANCER: ANALYSIS OF THE DEVELOPMENT COHORT WITH A FOLLOW-UP OF 95 MONTHS

Eunhye Kang[1], Young-Won Lee[2], Wonshik Han[1], Sae Byul Lee[2], Han-Byoel Lee[1]

[1]Seoul National Univ. Hospital, Breast Care Center, Department of Surgery, Korea,
[2]ASAN Medical Center, Department of Surgery, Korea

Background: The NGS-based multigene assay OncoFREE provides prognostic information for hormone receptor-positive, HER2-negative breast cancer according to the Decision Index™ (DI ≤ 20 [low-risk] vs. > 20 [high-risk]). It was developed and verified using samples tested for Oncotype DX. We aimed to validate the prognostic ability of OncoFREE in these samples using their long-term survival data.

Methods: We analyzed 339 patients who received endocrine therapy among the 343 patients used to develop and verification of OncoFREE. Distant metastasis-free survival (DMFS) rates were estimated using the KaplanMeier method, and the log-rank test was performed to assess differences in DMFS rates in each risk group.

Result: The patients were classified into 234 (68.9%) low- and 105 (31.1%) high-risk groups. At a median follow-up of 95 months, the five- and 10-year DMFS estimates for low- vs. high-risk groups were 99.1% vs. 95.2% and 98.0% vs. 91.9% (HR 3.39, *p*-value 0.045), respectively. For 271 patients without adjuvant chemotherapy, the five- and 10-year DMFS estimates for low- vs. high-risk groups were 99.5% vs. 96.5% and 98.8% vs. 90.1% (HR 5.59, *p*-value 0.034), respectively. In 61 patients who were pN1, 45 and 16 were classified as low- and high-risk. All low-risk patients, including 32 patients with age ≤ 50, had not received chemotherapy, and there was no distant recurrence.

Conclusions: We validated the prognostic ability of OncoFREE to predict the distant recurrence risk in early breast cancer using long-term survival data. OncoFREE-low pN1 patients had no distant recurrence without chemotherapy.

FEASIBILITY AND HEALTH OUTCOMES OF HOME-BASED AEROBIC AND RESISTANCE TRAINING IN INDONESIAN BREAST CANCER PATIENTS

Yufi Kartika Astari[1], Yayi Suryo Prabandari[2], Bagas Suryo Bintoro[2], Rakhmat Ari Wibowo[3], Mardiah Suci Hardianti[4], Anggoro Budi Hartopo[5], Susanna Hilda Hutajulu[4], Matthew John Allsop[6], Shaunna Burke[7]

[1]Universitas Gadjah Mada, Faculty of Medicine, Public Health and Nursing, Division of Hematology and Medical Oncology, Department of Internal Medicine, Indonesia, [2]Universitas Gadjah Mada, Faculty of Medicine, Public Health and Nursing, Department of Health Behavior, Environment, and Social Medicine, Indonesia, [3]Universitas Gadjah Mada, Faculty of Medicine, Public Health and Nursing, Department of Physiology, Indonesia, [4]Dr Sardjito General Hospital, Division of Hematology and Medical Oncology, Department of Internal Medicine, Indonesia, [5]Dr Sardjito General Hospital, Department of Cardiology and Vascular Medicine, Indonesia, [6]Univ. of Leeds, Leeds Institute of Health Sciences, School of Medicine, Faculty of Medicine and Health, United Kingdom, [7]Univ. of Leeds, School of Biomedical Sciences, United Kingdom

Background: Moderate-intensity aerobic and resistance training (A&RT) can improve physical function and quality of life in breast cancer (BC) patients. Physical activity studies for people with BC have generally been conducted in Western populations. Home-based interventions, an alternative to supervised programs, can be affordable and accessible. For the first time in Indonesia, this study aimed to assess the feasibility and health outcomes of A&RT in a home-based setting.

Methods: Forty-eight stage I-III hormonal positive BC patients undergoing hormonal treatment, aged 39-68 years, who had completed primary treatment, were approached in a single arm pre-post intervention study of a 12-week home-based A&RT intervention. Interventions included a pedometer-based aerobic walking program and resistance training using therapeutic bands. Feasibility measures included recruitment rate (>75%), retention rate (>75%), and adherence rate (>75%). Modified Bruce treadmill test was used to measure health outcomes including test duration and aerobic capacity represented by maximal volume oxygen uptake (VO2max) pre- and post-intervention.

Result: From 48 eligible patients, 36 patients (75%) agreed to participate. After 12 weeks, 32 participants completed the whole intervention (i.e. retention rate of 89%). Participants (n=25;78%) adhered to resistance training and aerobic training (n=17;53%). No baseline characteristics significantly influenced patient adherence. However, patients >52 years had lower adherence to resistance training ($p=0.075$). The home-based intervention significantly increased test duration (+1.1 minutes, $p=0.001$) and aerobic capacity (VO2max) (+2.3 ml/kg/min, $p=0.043$).

Conclusions: We observed that a 12-week home-based intervention is feasible to implement and can significantly improve patients' health outcomes.

GENOMIC CHARACTERIZATION OF HORMONE RECEPTOR-POSITIVE ADVANCED BREAST CANCER WITH HIGH TUMOR MUTATIONAL BURDEN: FRESH-FROZEN TISSUE GENOMIC ANALYSIS FROM MUTATION-1 STUDY (KCSG BR17-04)

Min Hwan Kim[1], Yohan Yang[2], Eunyoung Kim[3], Yong Wha Moon[4], Gun Min Kim[1], Seul-Gi Kim[4], Yeesoo Chae[5], Jieun Lee[6], Jae Ho Jeong[7], Kyung-Hun Lee[8], Han Jo Kim[9], Joo Young Jung[10], Su-Jin Koh[11], Kyoung Eun Lee[12], Hee-Jun Kim[13], Kyong Hwa Park[14], Seungtaek Lim[15], Yeon Hee Park[16], Sangwoo Kim[2,3], Joohyuk Sohn[1]

[1]Yonsei Univ. College of Medicine, Department of Medical Oncology, Korea, [2]Yonsei Univ. College of Medicine, Department of Biomedical Systems Informatics, Korea, [3]Yonsei Univ. College of Medicine, Department of Biomedical Systems Informatics, Brain Korea 21 Plus Project for Medical Science, Korea, [4]CHA Bundang Medical Center, Department of Medical Oncology, Korea, [5]Kyungpook National Univ. Chilgok Hospital, Department of Medical Oncology, Korea, [6]The Catholic Univ. of Korea, Seoul St. Mary's Hospital, Department of Medical Oncology, Korea, [7]ASAN Medical Center, Department of Medical Oncology, Korea, [8]Seoul National Univ., Department of Medical Oncology, Korea, [9]Soonchunhyang Univ. College of Medicine, Department of Medical Oncology, Korea, [10]Dongtan Sacred Heart Hospital, Department of Medical Oncology, Korea, [11]Ulsan Univ. Hospital, Department of Medical Oncology, Korea, [12]Ewha Womans Univ. School of Medicine, Department of Medical Oncology, Korea, [13]Chung-Ang Univ. College of Medicine, Department of Medical Oncology, Korea, [14]Korea Univ. Anam Hospital, Department of Medical Oncology, Korea, [15]Wonju Severance Christian Hospital, Department of Medical Oncology, Korea, [16]Sungkyunkwan Univ. School of Medicine, Department of Medical Oncology, Korea

Background: Here we report genomic landscape of 117 hormone receptor (HR)-positive metastatic breast cancer (MBC) patients who were included in the pre-screening tissue genomic analysis of MUTATION-1 study to explore the clinical implication of tumor mutational burden (TMB).

Methods: The MUTATION-1 study performed prescreening in HR-positive MBC patients with whole exome sequencing (WES) and RNA-seq of fresh-frozen tissues. Patients who met upper 30% of TMB received durvalumab plus tremelimumab.

Result: The 117 patients with prescreening WES and RNA-seq data showed diverse TMB and the most frequently mutated gene included PIK3CA, TP53, ESR1, GATA3, and MAP3K1. The patients were classified according to their dominant mutational signatures: APOBEC (25.6%), HRD (41.0%), clockwise (28.2%), SBS8, and SBS17. The APOBEC patients showed higher TMB and higher mutation prevalence in PIK3CA, ARID1A, and NF1 compared with other patients. The high TMB positively correlated with time from MBC diagnosis to biopsy. Tumors with TMB ≥ 5 mut/Mb were exclusively found in patients diagnosed as MBC ≥ 36 months before the timing of biopsy. The high TMB (≥ 3.16 mut/Mb) patients showed upregulation of G2/M checkpoint, MYC, E2F1, and MTORC1 signature. In the tumor microenvironment analysis by CIBESORT, PIK3CA mutant patients showed lower score of cytotoxic T cell than others.

Conclusions: The high TMB in HR+ breast cancer was associated with longer time duration from MBC diagnosis to biopsy, high APOBEC signature, and cell cycle/MYC signature gene upregulation.

BROWN ADIPOCYTE FACILITATES BREAST CANCER INVASIVENESS VIA CELL FUSION

Shihang Hu, Vivian Yvonne Shin, Sze Keong Tey, Hei Lam Agnes Wong, Ava Kwong

The Univ. of Hong Kong, Department of Surgery, Hong Kong

Background: Adipose tissue plays an important role in the tumor microenvironment of breast cancer (BC), however the underlying mechanisms of BC progression driven by adipocytes are not fully elucidated. This study aims to understand the interaction involve steps of BC initiation and growth at cellular and molecular levels.

Methods: Brown adipocytes (BAT) and white adipocytes (WAT) differentiated from preadipocytes, and adipose-derived stem cell (ASC) were co-cultivated with hormone receptor-positive breast cancer cell (MCF7). The invasiveness of cancer cells, the cells movement, mitochondrial and molecular signatures of the co-cultivation system were investigated. The functional role of adipocytes on BC was explored in a xenograft tumor mouse model.

Result: MCF7 co-cultured with all adipocytes showed a higher tumor activity than MCF7 alone in terms of proliferation, migration and invasiveness, among which with BAT had the highest effect (4 folds increase, $p < 0.0001$). Morphologically, adipocyte-MCF7 cell-cell fusion was observed. And the fused cell proportion was significantly higher in BAT-MCF7 than in WAT-MCF7 and ASC-MCF7 co-cultivation systems. In addition, the mitochondrial mass content in the cancer cells co-cultured with BAT was more increased and was associated with a higher cancer proliferative capacity. Furthermore, the tumorigenic potential of the fusion hybrid was validated in the xenograft tumor mouse model, in which the in vivo tumor growth of fused cells was significantly higher than that of the MCF7 alone.

Conclusions: BAT have the highest potential of promoting BC progression by direct cell fusion and increasing mitochondrial content of the cancer cells.

COMBINATION OF LOCAL RADIOTHERAPY AND ANTI-GLUCOCORTICOID-INDUCED TUMOR NECROSIS FACTOR RECEPTOR (GITR) THERAPY AUGMENTS PD-L1 BLOCKADE-MEDIATED ANTI-TUMOR EFFECTS IN MURINE BREAST CANCER MODEL

Jun Yeong Song[1,2], Min Guk Han[4], Mi Hyun Kang[5], Min Ji Kim[4], In Ah Kim[2,3]

[1]Seoul National Univ. Hospital, Department of Radiation Oncology, Korea, [2]Seoul National Univ. College of Medicine, Department of Radiation Oncology, Korea, [3]Seoul National Univ. Bundang Hospital, Department of Radiation Oncology, Korea, [4]Seoul National Univ. College of Medicine, Department of Tumor Biology, Korea, [5]Seoul National Univ. Bundang Hospital, Medical Science Research Institute, Korea

Background: Whether local radiotherapy (RT) and anti-glucocorticoid-induced tumor necrosis factor receptor (GITR) agonist increase the efficacy of PD-L1 blockade in triple-negative breast cancer (TNBC) need to be elucidated.

Methods: We analyzed the METABRIC cohort to examine the role of GITR in breast cancer patients. The 4T1 murine TNBC model with primary and secondary tumors was used to investigate the efficacy of PD-L1 blockade, local RT, anti-GITR agonist, and their combination strategies. Tumor growth was assessed by tumor volume and in vivo bioluminescence imaging, and metastatic lung nodule counts were analyzed to evaluate the systemic effect. Flow cytometry and immunohistochemistry staining were performed to examine the proportions and phenotypes of CD8+ T cells and regulatory T cells (Tregs) in tumor and spleen. Plasma levels of cytokines were measured by ELISA.

Result: In METABRIC cohort, patients with high expression of TNFRSF18, encoding GITR, showed significantly better survival compared to those with low expression. The addition of both local RT and anti-GITR agonist to PD-L1 blockade significantly reduced the tumor growth and lung metastasis. The benefit of this triple combination treatment over PD-L1 blockade was accompanied by increased CD8+ T cells and decreased Tregs in the tumor microenvironment. Furthermore, splenic CD8+ T cells and plasma levels of inflammatory cytokines were increased and splenic Tregs were decreased by the triple combination treatment compared to PD-L1 blockade alone.

Conclusions: The combination of local RT and anti-GITR agonist significantly enhanced the anti-tumor immune responses induced by PD-L1 blockade and provide preclinical rationale for the combination treatment.

COMPARISON OF TRANSCRIPTOME PROFILES BETWEEN HER2-LOW AND HER2-ZERO BREAST CANCER

Po-Hsiang Huang[1], Chia-Lang Hsu[2], Yuan-Ching Chang[3], Wen-Hung Kuo[4], Jyh-Cherng Yu[5], Ming-Yang Wang[6], Sung-Chao Chu[7], Kuo-Ting Lee[8], Ming-Jenn Chen[9], Dar-Ren Chen[10], Ming-Hsin Yeh[11], Chiao Lo[4], Ming Chao[12], Dwan-Ying Chang[1], I-Chun Chen[13], Wei-Wu Chen[1], Wei-Li Ma[1], Guo-Shiou Liao[5], Chiun-Sheng Huang[4], Ching-Hung Lin[13], Yen-Shen Lu[1]

[1]National Taiwan Univ. Hospital, Department of Medical Oncology, Taiwan, [2]National Taiwan Univ. Hospital, Department of Medical Research, Taiwan, [3]MacKay Memorial Hospital, Department of Surgery, Taiwan, [4]National Taiwan Univ. Hospital, Department of Surgery, Taiwan, [5]Tri-Service General Hospital, Department of Surgery, Taiwan, [6]National Taiwan Univ. Cancer Center, Department of Surgery, Taiwan, [7]Hualien Tzu Chi Hospital, Department of Hematology and Oncology, Taiwan, [8]National Cheng Kung Univ. Hospital, Department of Surgery, Taiwan, [9]Chi Mei Medical Center, Department of Surgery, Taiwan, [10]Changhua Christian Hospital, Comprehensive Breast Cancer Center, Taiwan, [11]Chung Shan Medical Univ. Hospital, Department of Breast and Thyroid Surgery, Taiwan, [12]National Taiwan Univ. Hsin-Chu Hospital, Department of Surgery, Taiwan, [13]National Taiwan Univ. Cancer Center, Department of Medical Oncology, Taiwan

Background: Prior studies yielded conflicting results on whether HER2-low [HER2 immunohistochemistry (IHC) 1+ or 2+ without gene amplification] tumors are biologically distinct. We evaluated the differences in gene expression between HER2-low and HER2-zero (IHC 0) breast cancer.

Methods: We prospectively collected tumor samples from patients with early breast cancer who underwent surgery at nine hospitals in Taiwan during 2018-2020. RNA sequencing was performed on fresh samples (RNA-seq cohort). The NanoString nCounter BC360 analysis was done on fixed specimens (BC360 cohort). Gene set enrichment analysis of the RNA-seq cohort was conducted to identify HER2-low enriched signaling. Tumor immune infiltration was evaluated using cell type-specific transcriptomic markers. The findings were then validated in the BC360 cohort and The Cancer Genome Atlas (TCGA cohort).

Result: There were 406 tumors in the RNA-seq cohort (HER2-low, n = 300; HER2-zero, n = 106), 613 tumors in the BC360 cohort (HER2-low, n = 395; HER2-zero, n = 218), and 480 tumors in the TCGA cohort (HER2-low, n = 420; HER2-zero, n = 60). The distribution of intrinsic subtypes was not significantly different between HER2-low and HER2-zero in HR+ tumors. However, lower proportions of basal subtypes were found in HR-, HER2-low tumors. Transcriptomic analysis of the RNA-seq cohort showed that HER2-low tumors demonstrated lower expression of E2F targets, MYC targets, G2M checkpoint, mTORC1, and interferon-gamma signaling. No difference in infiltrating immune cells was found between HER2-low and HER2-zero tumors. The BC360 and TCGA cohorts further validated the results.

Conclusions: HER2-low tumors were associated with lower expression of cell cycle and proliferation-related gene sets.

GERMLINE MUTATIONS RELATED TO COMPLETE REMISSION AFTER NEOADJUVANT THERAPY DETECTED BY MULTIGENE PANELS IN PATIENTS WITH TRIPLE-NEGATIVE BREAST CANCER

Jee Hyun Ahn[1], Ji Soo Park[2], Suk Jun Lee[1], Jieon Go[1], Jee Ye Kim[1], Seho Park[1], Seung Il Kim[1], Byeong-Woo Park[1], Min Hwan Kim[3], Gun Min Kim[3], Joohyuk Sohn[3], Hyung Seok Park[1,2]

[1]Yonsei Univ. College of Medicine, Department of Surgery, Korea, [2]Yonsei Univ. College of Medicine, Cancer Prevention Center, Korea, [3]Yonsei Univ. College of Medicine, Department of Medical Oncology, Korea

Background: Triple-negative breast cancer (TNBC) is a frequent phenotype of BRCA-mutant tumors. Tumors with BRCAness may exhibit characteristics of BRCA-mutant tumors and are expected to respond to similar treatments. Next-generation sequencing (NGS) is a method of sequencing multiple cancer susceptibility genes simultaneously, which is more efficient and cheaper than conventional genetic testing.

Methods: A total of 149 women with TNBC were recruited from December 2015 to November 2018 at Yonsei Cancer Center. Among them, 104 patients received neoadjuvant chemotherapy (NCT). Targeted genes related to hereditary cancers were sequenced using the 65-gene NGS panel and pathogenic and likely pathogenic variants were confirmed by Sanger sequencing. We analyzed pathologic complete remission (ypCR) according to pathogenic and likely pathogenic variants.

Result: The median age of the patients was 47 (range, 27-69) years. Nineteen (12.8%) of 149 patients had 19 pathogenic or likely pathogenic variants in six genes, including BARD1 (n = 2), BRCA1 (n = 9), BRCA2 (n = 5), CHEK2 (n = 1), RAD51C (n = 1), RAD51D (n = 2). Among the 104 patients with NCT, 43 (28.9%) of 104 patients achieved ypCR (pathogenic or likely pathogenic variants; 9, 0.06% vs. non-variants; 34, 79.1%). Among the 104 patients with NCT, 14 (9.3%) patients had pathogenic or likely pathogenic variants. Nine of 14 patients with pathogenic or likely pathogenic variants of the genes, including BARD1 (n = 2), BRCA1 (n = 4), BRCA2 (n = 1), RAD51 (n = 2), achieved ypCR ($p = 0.066$).

Conclusions: Patients with TNBC and germline pathogenic or likely pathogenic mutations could be analyzed by NGS. The NGS panel test has the potential to identify BRCAness mutations that predict ypCR in TNBC.

EXPLORATION OF MELK AS A DOWNSTREAM OF DEL-1 & DRUGGABLE TARGET IN TNBC

In Hee Lee[1], Soo Jung Lee[1], Byeongju Kang[2], Jeeyeon Lee[2], Jin Hyang Jung[2], Ho Yong Park[2], Ji-Young Park[3], Nora Jee-Young Park[3], Jieun Kang[4], Eun Ae Kim[5], Yee Soo Chae[1]

[1]Kyungpook National Univ. Chilgok Hospital, Department of Medical Oncology, Korea, [2]Kyungpook National Univ. Chilgok Hospital, Department of Surgery, Korea, [3]Kyungpook National Univ. Chilgok Hospital, Department of Pathology, Korea, [4]Kyungpook National Univ. Hospital, Cell and Matrix Research Institute, Korea, [5]Kyungpook National Univ. School of Medicine, Exosome Convergence Research Center, Korea

Background: In our previous study, Del-1 was a promising predictive marker for breast cancer. However, the Del-1 downstream targets and biological effectors remain unknown. We used RNA-seq to analyze the transcriptome and examine tumor tissue MELK expression.

Methods: To evaluate the expression levels of Del-1 and MELK, mRNA levels in several breast cancer cell lines were analyzed. Due to the heterogeneity of TNBC, eight different cell lines were analyzed (BT20, MDA-MB-468, HCC-1806, DU4475, BT549, MDA-MB-231, HS578T, MDA-MB-453). OTS167 was treated for inhibition of MELK. To further investigate the relationship between DEL-1 and MELK, the researchers performed dual inhibition of DEL-1 & MELK. Plus, we examined MELK expression in breast cancer tissue (n = 354).

Result: Del-1 and MELK expression were significantly increased in TNBC cell lines. Expression of Del-1/MELK was dramatically enhanced in MB 468, HCC-1806, and MB 231. Three cell lines were transfected with Del-1-specific siRNA. Del-1 knockdown HCC-1806 & MDA-MB 231 cells significantly decreased MELK expression, suggesting the relation between Del-1 and MELK. OTS 167 significantly inhibits breast cell proliferation and promotes cell apoptosis (MBA-MB-468, $p < 0.001$). Furthermore, the cell viability decreased and the degree was the greatest in MBA-MB 468, basal-like 1. To further investigate the relationship between DEL-1 and MELK, the researchers inhibited DEL-1 and then MELK. Dual inhibition significantly reduced cell viability in MDA-MB468 and MDA-MB 231, with the basal-like 1 cell lines showing the most significant effect. Tumor tissue MELK expression was associated with age, tumor size, ER/PR expression, Ki 67, and molecular tumor subtype. DMFS was significantly associated with MELK expression ($p = 0.042$)

Conclusions: In this study, we sought to investigate the association between De1-1 and MELK in TNBC and tumor tissue. We found that MELK is downstream of Del-1 and is a promising target, especially in the basal-like 1.

SYMPTOM CLUSTER AND PREDICTORS OF GENERAL CHEMOTHERAPY TOXICITY IN PATIENTS WITH BREAST CANCER: EXPLORATORY FACTOR ANALYSIS (EFA) AND A CHI-SQUARE AUTOMATIC INTERACTION DETECTOR (CHAID) DECISION TREE

Juan Adrian Wiranata[1], Yufi Kartika Astari[2], Susanna Hilda Hutajulu[2], Mardiah Suci Hardianti[2], Kartika Widayati Taroeno-Hariadi[2], Johan Kurnianda[2], Ibnu Purwanto[2], Bagas Suryo Bintoro[3]

[1]Universitas Gadjah Mada, Master of Clinical Epidemiology Postgraduate Program, Faculty of Medicine, Public Health and Nursing, Indonesia, [2]Universitas Gadjah Mada/ Dr Sardjito General Hospital, Division of Hematology and Medical Oncology, Department of Internal Medicine, Faculty of Medicine, Public Health and Nursing, Indonesia, [3]Universitas Gadjah Mada, Department of Health Behavior, Environment, and Social Medicine, Faculty of Medicine, Public Health and Nursing, Indonesia

Background: Previous studies have shown that cancer patients are able to experience ≥8 chemotherapy toxicities and each symptom can influence the others. Exploration of symptom clusters and identifying patients with a higher risk of developing more toxicity is a potential guide for developing symptom management strategies.

Methods: We performed a symptom cluster analysis of 23 general (nonhaematological) toxicities using EFA in 213 stage I-IV breast cancer patients undergoing first-line chemotherapy. Secondary data on chemotherapy toxicity were obtained from the adapted version of Common Terminology Criteria for Adverse Events (CTCAE) version 4.0 in a patient-reported manner. Symptom clusters were assessed after the first cycle of chemotherapy (T1), mid-chemotherapy (T2), and at the end of chemotherapy (T3). Prediction modelling using a CHAID decision tree was conducted to assess the sociodemographic, clinical, and treatment predictors of experiencing a total item of general toxicity above average cumulatively throughout chemotherapy.

Result: Four symptom clusters were identified at T1 and T3, and three were identified at T2. Nausea-vomiting-anorexia and anxiety-depression symptom clusters persisted throughout chemotherapy. The highest probability of experiencing a total item of symptoms above average (> 13) from the decision tree analysis was highest education degree of junior to senior high school with at least one comorbidity condition (65.6%; X2 = 3.919; $P = 0.048$).

Conclusions: Gastrointestinal and psychological symptom clusters were persistent throughout chemotherapy. Patients with education attainment of junior to senior high school with comorbidity had the highest probability of experiencing > 13 symptom items during chemotherapy program. Our findings may provide insights into developing treatment strategies that simultaneously manage cluster symptoms.

B-CELL MEDIATED IMMUNITY PREDICTS SURVIVAL OF ER-POSITIVE BREAST CANCER

Byung-Hee Kang[1], Seungbok Lee[2], Bum-Sup Jang[3], Han-Byoel Lee[4], Wonshik Han[4], In Ah Kim[1,5]

[1]Seoul National Univ. Bundang Hospital, Department of Radiation Oncology, Korea, [2]Seoul National Univ. Hospital, Department of Genomic Medicine, Korea, [3]Seoul National Univ. Hospital, Department of Radiation Oncology, Korea, [4]Seoul National Univ. College of Medicine, Department of Surgery, Korea, [5]Seoul National Univ. College of Medicine, Department of Radiation Oncology, Korea

Background: Estrogen receptor-positive (ER+) breast cancer (BC) is the most prevalent type of BC, which is a highly heterogeneous condition that shows different treatment responses and risks of relapse by the patient. Considering that comprehensive molecular classification can greatly aid precision treatments, we aimed to define molecular subtypes for ER+ BC representing the tumor microenvironment.

Methods: We analyzed RNA-seq data of 113 BC samples and classified them according to the PAM50 intrinsic subtypes using gene expression profiles. We further focused on 48 luminal-type patients and conducted principal component and differential expression analyses for subclassification. The Cancer Genome Atlas (TCGA) Breast cancer RNA-Seq 1,048 patients were utilized as a validation dataset to verify the classification.

Result: The principal component analysis clearly divided 48 luminal BC patients into two subgroups, separate from the luminal A and B classification. The top differentially expressed genes between the subgroups were distinctly characterized by immunoglobulin and B cell-related genes We could divide TCGA ER+ BC patients into two subgroups based on the expression of the B cell-related gene set. Patients with high B cell immune activity were shown to have better prognoses than patients with low B cell immune activity.

Conclusions: Our transcriptomic approach allowed us to define a novel molecular phenotype for ER+ BC, reflecting the B cell immune activity and can help predict prognosis. Although further research is required, B cell immunity for ER+ BC patients may be helpful for identifying patients who are good responders to chemotherapy or immunotherapy.

IMPROVEMENT OF DIAGNOSTIC ACCURACY OF BREAST CANCER USING MULTI-PROTEIN SIGNATURE MARKERS THROUGH MACHINE LEARNING

Yumi Kim[1], Jung Min Park[1], Chan Seok Yoon[1], Sungsoo Kim[2,3], Hyeon Seok Shin[3], Kyung-Geun Ahn[2], Wonshik Han[4], Dong-Young Noh[1,5]

[1]CHA Gangnam Medical Center, Department of General Surgery, Korea, [2]Bertis Inc., Manufacturing and Technology Division, Korea, [3]Bertis Inc., Bio Convergence Research Institute, Korea, [4]Seoul National Univ. College of Medicine, Department of Surgery, Korea, [5]Bertis Inc., Biomarker Research Institute, Korea

Background: We have developed a 3-protein signature blood marker (Mastocheck) for early diagnosis of breast cancer. The purpose of this study is to improve the performance of the previously developed blood markers.

Methods: Blood from 196 breast cancer patients and 196 healthy control groups were prospectively collected. Through the development of a biomarker detectable library, PepQuant, peptides that are optimal for MS/MS detection were selected. After chemically synthesizing these were quantified by multiple reaction monitoring (MRM). Seven final proteins were derived by applying the PepQuant library for breast cancer biomarker discovery and verification. Machine learning algorithms was trained as protein candidates identified between breast cancer patients and healthy controls.

Result: The sensitivity, specificity, and accuracy of Mastocheck, were 69.4%, 83.7%, and 76.5%, respectively, The false positive rate (FPR) and the false negative rate (FNR) were 16.3% and 30.7%. The positive predictive value (PPV) and negative predictive value (NPV) were 81.0% and 73.2%. During the study when 7-protein signature was combined with an artificial intelligence (AI) for the analysis, the sensitivity, specificity, and accuracy were 88.3%, 83.2%, and 85.7%, showing superior performance compared to Mastocheck. The FPR and FNR were 16.8% and 11.7%, indicating that the FNR was improved by 20% compared to Mastecheck. In addition, the PPV and NPV were also improved to 84.0% and 87.6%.

Conclusions: Through the collection of new prospective samples, the study confirmed that the diagnostic performance of Mastocheck was repeatedly maintained. In addition, breast cancer diagnosis using 7-protein signatures with AI model showed that breast cancer diagnosis can be remarkably improved.

IMPACT OF RESIDUAL MICROCALCIFCATIONS ON PROGNOSIS AFTER NEOADJUVANT CHEMOTHERAPY IN BREAST CANCER PATIENTS

Eun Young Kim[1], Sung Yoon Jang[2], Jong Han Yu[2]

[1]Kangbuk Samsung Hospital, Department of Surgery, Korea, [2]Samsung Medical Center, Department of Surgery, Korea

Background: Residual microcalcifications after neoadjuvant chemotherapy (NAC) are challenging for deciding extent of surgery and questionable for impact on prognosis. We investigated changes in the extent and patterns of microcalcifications before and after NAC and correlated them with pathologic response and survival outcome.

Methods: We retrospectively collected data for patients with breast cancer with suspicious looking microcalcifications who underwent NAC between 2015 and 2018. Patients were classified into four groups according to pathologic response and residual microcalcifications on breast: patients with breast non-pathologic complete response (pCR) with residual microcalcifications (group 1, n = 25), patients with breast non-pCR without residual microcalcifications (group 2, n = 196), patients with breast pCR with residual microcalcifications (group 3, n = 13) and patients with breast pCR without residual microcalcifications (group 4, n = 89).

Result: A total of 323 patients were analyzed. The median follow-up time was 70 months. There were no differences in the extent, morphology, and distribution of microcalcifications according to pathologic response and subtype after NAC ($p > 0.05$). Radiologic response on MRI was significantly different according to pathologic response and subtype ($p < 0.05$). HER2+ subtype (OR 3.193, $p < 0.001$), post-NAC tumor size ≥ 1 cm on MRI (OR 4.886, $p < 0.001$) and radiologic CR on MRI (OR 37.037, $p = 0.001$) were predictors of pCR. The 5-year LRFS, DFS and OS were not different among four groups.

Conclusions: HER2+ subtype, tumor size ≥ 1cm on MRI after NAC, radiologic CR on MRI were significant predictive factors for pCR. Residual microcalcifications in patients who achieved pCR does not negatively affect long term local recurrence.

IS AGE AN INDEPENDENT FACTOR OF LATE RECURRENCE AMONG YOUNG BREAST CANCER PATIENTS WITH ESTROGEN RECEPTOR POSITIVE/HER2 NEGATIVE?

Dong Seung Shin[1,2], Jai Min Ryu[1,2], Jun-Hee Lee[3], Janghee Lee[4,5], Eunhye Kang[6], Jong-Ho Cheun[7], Han-Byoel Lee[6], Sung Gwe Ahn[8]

[1]Samsung Medical Center, Department of Surgery, Korea, [2]Samsung Medical Center, Department of Breast Surgery, Korea, [3]Soonchunhyang Univ. Hospital Seoul, Department of Surgery, Korea, [4]Dongtan Sacred Heart Hospital, Department of Surgery, Korea, [5]Yonsei Univ. Graduate School, Department of Medicine, Korea, [6]Seoul National Univ. Hospital, Department of Surgery, Korea, [7]SMG-SNU Boramae Medical Center, Department of Surgery, Korea, [8]Gangnam Severance Hospital, Department of Surgery, Korea

Background: Young breast cancer (YBC) is known to have a poor prognosis, especially ER+/ HER2-. Late recurrence of ER+/HER2- BC has been recognized for many years. However, there was little data about the effect of age on late recurrence among YBC. We analyzed factors that affect late distant metastasis among ER+/HER- breast cancer younger than 45 years.

Methods: We retrospectively reviewed patients, age ≤ 45, no distant metastasis (DM) within 5 years, unilateral, no neoadjuvant chemotherapy, more than 2 years endocrine therapy, ER+HER2- BC who received primary surgery at Samsung Medical Center, Gangnam Severance Hospital, and Seoul National University Hospital between January 2000 and December 2011. We categorized into 3 groups by age: 21-35, 36 -40, and 41-45 years (groups I, II, and III). We analyzed factors related to late recurrence, especially age, from 5 years after the surgery.

Result: Of those 2,772, 370 (13.3%), 885 (31.9%), and 1,517 (54.7%) were categorized as group I, II, and III, respectively. The median follow-up duration was 130.3 months. Group I had a poorer histologic grade and received chemotherapy more than groups II/III. Between the three groups, the younger group had a significantly worse RFS, LRFS, and DMFS, but not OS ($P < .0001$, $P < .0001$, $P < .0001$, and $P = 0.1726$, respectively). In a multivariate analysis, the HR for DMFS showed lower in group II/III than in group I (HR = 0.536, $P = 0.0056$, 95% CI 0.344~0.833 and HR = 0.324, $P < .0001$, 95% CI 0.207~0.507). Axillary surgery type, pT, and histologic grade were additional risk factors for DMFS.

Conclusions: We demonstrated age is an independent factor for late recurrence even in YBC with ER+/HER2-.

STROMAL TUMOR INFILTRATING LYMPHOCYTES (TIL) AS A POTENTIAL PROGNOSTIC BIOMARKER FOR RECURRENCE IN LOCALLY ADVANCED BREAST CANCER (LABC) PATIENTS

Dannu Novriandhika[1], Desak Gede Agung Suprabawati[2], Dwi Hari Susilo[2], Dyah Fauziah[3], Priangga Adi Wiratama[3]

[1]Medical Faculty Airlangga Univ., Dr Soetomo General Hospital Surabaya, Department of Surgery, Indonesia, [2]Medical Faculty Airlangga Univ., Dr Soetomo General Hospital Surabaya, Department of Surgical Oncology, Indonesia, [3]Medical Faculty Airlangga Univ., Dr Soetomo General Hospital Surabaya, Department of Anatomical Pathology, Indonesia

Background: Tumor-infiltrating lymphocytes (TIL) serves as the host adaptive immune response in breast cancer. TIL has the potential to be an independent prognostic factor in breast cancer patients. In this study, we aimed to examine the association between stromal TIL and recurrence in locally advanced breast cancer patients.

Methods: A cohort retrospective study was conducted using medical records of female breast cancer patients with locally advanced breast cancer. We collected patients' data, including demographic data from the medical record. Stromal TIL was examined following the recommendations of the International TIL Working Group 2014.

Result: 75 samples were included with an average age of 49.5 ± 8.4. Ductal carcinoma was the most common histological type (88.0%). Luminal B Her2-negative was the predominant breast cancer subtype (32.0%). There was a significant association between Stromal Tumor-infiltrating lymphocytes (TIL) and disease-free survival ($P = 0.001$). The optimal cut-off to determine the recurrence of breast cancer was 15%. The sensitivity, specificity, PPV, NPV, and accuracy of TIL to predict the 24-month disease-free survival (DFS) were 80.5%, 82.4%, 84.6%, 77.8%, and 81.3%, respectively. Every 10% increase in TIL percentage could raise the DFS by 5.45 months ($p = 0.001$). Patients with high TIL values had higher survival than those with low TIL values.

Conclusions: There was a significant correlation between the stromal TIL and the recurrence rate. The pre-therapy stromal TIL percentage can be employed as a potential biomarker to predict breast cancer recurrence, particularly in the first two years.

DEVELOPMENT OF BREAST CANCER RISK PREDICTION MODEL INCORPORATING POLYGENIC RISK SCORE AND NONGENETIC RISK FACTORS IN KOREAN WOMEN

Jihye Choi[1], Tae-Woong Ha[2], Hye-Mi Choi[2], Han-Byoel Lee[3], Hee-Chul Shin[4], Woosung Chung[2], Wonshik Han[3]

[1]National Medical Center, Department of General Surgery, Korea, [2]DCGen, Co., Ltd, Korea, [3]Seoul National Univ. College of Medicine, Department of Surgery, Korea, [4]Seoul National Univ. Bundang Hospital, Korea, Department of Surgery, Korea

Background: To develop a breast cancer prediction model for Korean women using published polygenic risk scores (PRSs) combined with non-genetic risk factors (NGRFs).

Methods: Thirteen PRS models generated from single or multiple combinations of the Asian and European PRSs were evaluated in 39,263 Korean women. Area under the curve (AUC) and increase in odds ratio (OR) per standard deviation (SD) were compared for each PRS. The PRSs with the highest predictive power were combined with NGRFs and an integrated prediction model was then established using the iCARE tool. The absolute breast cancer risk was stratified in 29,840 women with available follow-up data.

Result: European PRS performed better than Asian PRS. PRS38_ASN+PRS190_EB, a combination of Asian and European PRSs, showed the highest AUC among PRSs with an OR per SD increase of 1.46 (95% CI: 1.32-1.62) and AUC of 0.620. Compared with the average risk group (35-65%), women in the top 5% were at a 2.44-fold high risk of breast cancer. Incorporating NGRFs yielded a modest increase in the AUC. The effect of incorporating NGRF was greater in women beyond the age of 50. In PRS38_ASN+PRS190_EB+NGRF, the average absolute risk was 5.04%. Lifetime absolute risk at 80 years for women in the top 5% was 10.00 %, while in the lowest 5% was at 2.19%.

Conclusions: Combined Asian and European PRSs were predictive of breast cancer in Korean women. Incorporation of NGRFs further enhanced the predictive performance. Our findings support the use of these models in personalized screening and prevention of breast cancer in Korean women.

LONG-TERM PROGNOSTIC VALUE OF THE GENESWELL BCT SCORE IN ASIAN WOMEN WITH HORMONE RECEPTOR-POSITIVE/HER2-NEGATIVE EARLY BREAST CANCER

Youngwon Lee[1], Sae Byul Lee[1], Fujiki Yoshitaka[2], Kashiwaba Masataka[2], Ohi Yasuyo[2], Gyungyub Gong[3], Jeong Eon Lee[4,5], Young Kee Shin[6,7], Mi Jeong Kwon[8,9], Sagara Yasuaki[2], Uiree Jo[3]

[1]ASAN Medical Center, Department of Breast Surgery, Korea, [2]Sagara Hospital, Department of Breast and Thyroid Surgical Oncology, Japan, [3]ASAN Medical Center, Department of Pathology, Korea, [4]Sungkyunkwan Univ. School of Medicine, Department of Health Sciences and Technology, Samsung Advanced Institute for Health Sciences and Technology (SAIHST), Korea, [5]Samsung Medical Center, Department of Surgery, Korea, [6]Seoul National Univ., Laboratory of Molecular Pathology and Cancer Genomics, Research Institute of Pharmaceutical Sciences and College of Pharmacy, Korea, [7]Seoul National Univ., Department of Molecular Medicine and Biopharmaceutical Sciences, Graduate School of Convergence Science and Technology, Korea, [8]Kyungpook National Univ., Vessel-organ Interaction Research Center, College of Pharmacy, Korea, [9]Kyungpook National Univ., BK21 Four Community-based Intelligent Novel Drug Discovery Education Unit, College of Pharmacy and Research Institute of Pharmaceutical Sciences, Korea

Background: Accurate risk prediction of late recurrence is required to make optimal treatment decisions after endocrine therapy in hormone receptor (HR)-positive/human epidermal growth factor receptor 2 (HER2)-negative early breast cancer. The GenesWell BCT assay (Gencurix) was validated to predict the 10-year risk of distant metastasis. However, its long-term prognostic significance is unclear.

Methods: We evaluated the long-term prognostic value of the GenesWell BCT assay in 366 Asian women with HR-positive/HER2-negative breast cancer. The 15-year distant metastasis-free survival (DMFS) rates for women from Korean (Asan Medical Center) and Japanese sites (Sagara hospital) were compared according to their risk stratification based on the BCT score. We further evaluated the risk of late recurrence 5-15 years after surgery based on the BCT score classification.

Result: According to the BCT score, patients from Japan and Korea were categorized as BCT low risk (83.6%) and high risk (16.4%) for distant metastasis. The 15-year DMFS rate was significantly lower in the BCT high-risk than in the BCT low-risk group ($P < 0.001$), and the BCT risk group was an independent prognostic factor for 15-year DMFS (hazard ratio, 4.59; 95% confidence interval 2.139.88; $P < 0.001$). Moreover, the BCT score was a significant predictor of both early (0-5 years) and late (5-15 years) recurrence and added prognostic information to traditional clinical prognostic factors.

Conclusions: The BCT score can identify patients at low risk for late recurrence who may not require adjuvant chemotherapy or extended endocrine therapy.

ESTABLISHING THE CORRELATION OF AN 8-GENE SET OF IMMUNE-RESPONSE GENE EXPRESSION PROFILING WITH PATHOLOGICAL COMPLETE RESPONSE NEOADJUVANT CHEMOTHERAPY IN PRIMARY BREAST CANCER PATIENTS

Chun-Yu Liu[1,3,5], Chi-Cheng Huang[3], Yi-Fang Tsai[3,5], Ta-Chung Chao[3,5], Yen-Shu Lin[2,3], Chin-Jung Feng[3], Jiun-I Lai[3,5], Ji-Lin Chen[3], Yen-Jen Chen[2,3,5], Jen-Hwey Chiu[2,3,5], Chih-Yi Hsu[4,5], Ling-Ming Tseng[2,3,5]

[1]Taipei Veterans General Hospital, Department of Medicine, Taiwan, [2]Taipei Veterans General Hospital, Department of Surgery, Taiwan, [3]Taipei Veterans General Hospital, Comprehensive Breast Health Center, Taiwan, [4]Taipei Veterans General Hospital, Department of Pathology, Taiwan, [5]National Yang Ming Chiao Tung Univ., School of Medicine, Taiwan

Background: Neoadjuvant chemotherapy (NACT) has been widely adopted as downstaging and/or chemosensitivity testing for patients with primary breast cancers. Patients responding to NACT achieve pathological complete response (pCR) are associated with good prognosis for breast cancer. This study aimed to establish potential biomarkers of pCR in patients with breast cancer receiving NACT by assessing the gene expression profiling of tumor-immune interaction-related genes.

Methods: Pre-treatment tissues from breast cancer patients were collected for 400-targeted gene expression assay. The differentially expressed genes between patients achieving pCR and non-pCR were measured. In silico analyses were performed to explore the correlation of genes with outcomes.

Result: Patients achieving pCR were associated with lower tumor stage and HER2 positive. NGS data revealed that eight immune-response genes, including KLRK1, IGJ, CD69, CD40LG, MS4A1, CD1C, KLRB1, and CA4, were upregulated in tissues from patients achieving pCR. In silico analysis showed that patients with high expression of 8-gene had better relapse-free survival in chemotherapy setting. Patients with high expression of pCR-related genes had better response to treatment. The expression of pCR-related gene was negatively correlated with IC50 value of drugs, suggesting these genes were associated with drug sensitivity. These pCR-related genes were downregulated in breast tumor tissues compared to normal tissues. Moreover, the expression of pCR-related genes was positively correlated with infiltration of immune cells.

Conclusions: These results demonstrate that eight pCR-related genes were associated with better clinical outcome and drug response. The expression of 8-gene set of immune-response gene may act as a prognostic biomarker for breast cancer patients receiving NACT.

MIR-606 INHIBITS THE GROWTH AND METASTASIS OF TRIPLE-NEGATIVE BREAST CANCER BY TARGETING STANNIOCALCIN 1

Isaac Kim[1], Sujin Choi[2], Hyun-Ju An[2], Kwanbum Lee[1], Seung Ah Lee[1], Seung Ki Kim[1], Soonchul Lee[3]

[1]CHA Bundang Medical Center, Department of Surgery, Korea, [2]CHA Bundang Medical Center, Biologist, Korea, [3]CHA Bundang Medical Center, Department of Orthopaedic Surgery, Korea

Background: Triple-negative breast cancer (TNBC) is associated with poor prognosis. However, treatments for TNBC are limited, with poor outcomes. MicroRNAs (miRNAs) are small non-coding RNAs that regulate gene expression. This study aimed to identify differentially expressed miRNAs in patients with breast cancer, and investigate the functional role of the identified miRNA, targets, and effects both in vitro and in vivo.

Methods: We investigated the functional role of the novel miR-606 in TNBC cells by transfecting cells with miR-606 mimics. We evaluated the cell proliferation, migration, invasion, tumor sphere-formation abilities and apoptosis of TNBC cells. We investigated the expression of miR-606 and stanniocalcin 1 (STC1), a direct target gene of miR-606, in patients with TNBC and healthy individuals using the Cancer Genome Atlas (TCGA). In addition, we investigated the targets of miR-606 and its effects on tumor growth and in a mouse xenograft model. Furthermore, we investigated the metastasis of miR-606 in a mouse tail vein injection model.

Result: Transfection with miR-606 suppressed TNBC cell proliferation, migration, invasion, and tumor sphere-formation ability. Moreover, miR-606 induced apoptosis in TNBC cells. The expression of miR-606 was downregulated and that of STC1 was upregulated in patients with TNBC compared with those in healthy individuals. Moreover, intratumoral injections of miR-606 mimic suppressed tumor growth in MDA-MB-231 xenografts. In addition, MDA-MB-231 cells transfected with miR-606 showed decreased lung metastatic nodules in a mouse tail vein injection model.

Conclusions: Our results suggest a novel tumor-suppressor function for miR-606 in TNBC and its potential applications in the development of anticancer miRNA therapeutics.

THE EFFECT OF PROGESTERONE RECEPTOR EXPRESSION LEVEL TO PREDICT PROGNOSIS OF ESTROGEN RECEPTOR POSITIVE/ HER2 NEGATIVE YOUNG BREAST CANCER: A SINGLE-CENTER PROSPECTIVE COHORT STUDY

Youngji Kwak[1], Jai Min Ryu[1], Sung Yoon Jang[1], Joon Young Choi[1], Hyunjun Lee[1], Dong Seung Shin[1], Yeon Hee Park[2], Ji-Yeon Kim[2], Jin-Seok Ahn[2], Byung-Joo Chae[1], Jonghan Yu[1], Jeong Eon Lee[1], Seok Won Kim[1], Seok Jin Nam[1]

[1]Samsung Medical Center, Department of General Surgery, Korea, [2]Samsung Medical Center, Department of Medical Oncology, Korea

Background: Hormone receptor (HR) status which is composed of estrogen receptor (ER) and progesterone receptor (PR) status correlates response to endocrine therapy in breast cancer. Although ER expression levels affect the prognosis of breast cancer, there are not enough studies about PR expression levels especially in young breast cancer.

Methods: A prospective cohort study has been conducted to identify young breast cancer patients with invasive carcinoma and diagnosed less than 40 years old between 2013 and 2018. We investigated the clinicopathologic features and prognosis of the patients with ER+ and HER2- patients and strong-PR, low-PR, and PR-negative which was stratified PR levels as positive cell proportion over 10%, 1~10% and below 1%. Statistical analysis were executed using SAS.

Result: Among the 458 patients, 386 (84.3%), 26 (5.7%), and 46 (10.0%) were categorized as strong-PR, low-PR and PR-negative. Median F/U duration was 58.6 months. Compared strong-PR, patients with low-PR and PR-negative were more likely to have high Ki-67 and high nuclear grade ($p < 0.0001$). Low-PR group received chemotherapy more than PR-negative group ($p < 0.0001$). Low-PR (76.4%, 76.3%) and PR-negative group (74.8%, 77.4%) had worse DFS ($p = 0.0033$) and DMFS ($p = 0.0007$) compared with strong-PR (87.5%, 92.5%). Low-PR patients had even worse DMFS than PR-negative. There was a difference in OS ($p < 0.0001$) between strong-PR and low-PR (97.4% vs. 92.2%). In strong-ER patients, low-PR patients had the lowest DFS even lower than PR-negative patients (68.0% vs. 76.0%, $p = 0.0090$).

Conclusions: In ER+/ HER2- young breast cancer patients, low-PR patients had aggressive clinicopathologic characteristics, and showed significant worse DFS, DMFS, OS than strong-PR patients, even worse DMFS than PR-negative patients.

ELUCIDATING THE MUTATIONAL LANDSCAPE OF PI3K PATHWAY AMONG INDIAN BREAST CANCER CASES

Rahul Kumar[1], Usha Agrawal[2], Svs Deo[3], Sandeep Mathur[4], Ajay Gogia[5], Pranay Tanwar[1]

[1]All India Institute of Medical Sciences, Laboratory Oncology Unit, India, [2]National Institute of Pathology, Department of Pathology, India, [3]All India Institute of Medical Sciences, Department of Surgery, India, [4]All India Institute of Medical Sciences, Department of Pathology, India, [5]All India Institute of Medical Sciences, Department of Medical Oncology, India

Background: Breast cancer (BC) is a heterogeneous group of malignant neoplasia of the epithelial cell. The alteration of PI3K-Akt signalling pathway is mainly responsible for the pathogenesis of breast cancer. However, their prevalence remains unknown among the Indian population. Therefore in this study, we aim to investigate somatic mutation profile of the genes involved in the PI3K-Akt pathway by performing whole exome sequencing (WES).

Methods: In this study, we enrolled 45 primary BC patients after taking informed consent. DNA was extracted from 45 fresh tumor tissues and matched blood samples followed by library preparation and WES. Somatic mutation analysis for PI3K-Akt pathway was done by using an in-house developed script.

Result: The PI3K signalling pathway has been shown to be frequently affected in 43 out of 45 samples. A total of 24 genes were found to be mutated, of which 14 are oncogenes and 9 are tumor suppressor genes. The most common mutated oncogenes of this pathway are PIK3CA, EIF4EBP1, MTOR, AKT1 and PIK3CB with a somatic mutation rate of 44.4%, 28.9%, 22.2%, 11%, 11% respectively while tumor suppressor genes are TSC2, TSC1, INPP4B, PIK3R1 24.4%, 22.2%, 15.6%, 11.2%. In addition, DEPDC5 was mutated in 6.6% cases which acts as a passenger gene.

Conclusions: In our study, we found several tumor suppressors and oncogenes that were predominantly mutated in our cohort and plays a crucial role in PI3K-Akt signalling pathway. Moreover, the current understanding of these genes can be utilized as potential targeted candidate genes which can be used for diagnosis and prognosis purposes.

NATIONAL PATTERNS OF HOSPITAL ADMISSION VS. HOME RECOVERY FOLLOWING MASTECTOMY FOR BREAST CANCER

Leah Kim, Miranda Moore, Eric Schneider, Joseph Canner, Pavan Anant, Elena Graetz, Judy Ruo Zhu, Melanie Lynch, Gregory Zanieski, Alyssa Gillego, Monica Valero, Ellie Proussaloglou, Elizabeth Berger, Mehra Golshan, Rachel Greenup, Tristen Park

Yale Univ. School of Medicine, Department of Surgery, U.S.A.

Background: Home recovery (HR) after mastectomy may save costs, promote faster recovery, and improve patient experience. We examined US national patterns of care and perioperative outcomes for women post-mastectomy, comparing HR to hospital admission.

Methods: Using MarketScan commercial claims data (2017-2019), we identified women ≥ 18 years old who underwent mastectomy with/without non-autologous reconstruction for breast cancer or genetic cancer risk. Mastectomies were classified as HR or hospital admission (inpatient stays > 1 calendar day). Comorbidities, receipt of chemo/immunotherapy, and complications were measured perioperatively. Characteristics were compared by encounter type using chi-square tests. Logistic regression calculated the odds of any complication, age adjusted, accompanying LN procedure, reconstruction, neoadjuvant chemo- and/or immunotherapy, and select comorbidities.

Result: Of 14,744 mastectomies, 34% involved patients recovering at home while 66% had hospital admission. HR patients had lower rates of ALND (4.1 vs. 27.5%, $p < 0.001$) and similar rates of non-autologous reconstruction (59.6 vs. 60.1%, $p = 0.544$). Rates of neoadjuvant chemotherapy (19.9 vs. 21.1%, $p = .093$) and immunotherapy (3.6 vs. 3.8%, $p = 0.486$) were similar. Complications were lower among HR patients including hematomas (0.7 vs. 1.5%, $p < 0.001$) and wound complications (8.7 vs. 10.0%, $p = 0.009$). In multivariable analysis, odds of any complication were 15% lower for HR patients (aOR: 0.85, 95% CI: 0.77-0.94, $p = 0.001$). Unplanned emergency department visits were similar (6.8 vs. 7.4%, $p = 0.18$); yet fewer re-admissions (2.5 vs. 3.9%, $p < 0.001$) occurred in HR.

Conclusions: HR is a safe and non-inferior alternative to inpatient admission for clinically appropriate women post-mastectomy. These results prompted the development and initiation of a HR pathway at our institution.

IMPACT OF DISTANCE BETWEEN TUMOR AND NIPPLE ON SURVIVAL OUTCOMES IN BREAST CANCER

Jong-Ho Cheun[1], Eunhye Kang[2], Jung Whan Chun[2], Hong-Kyu Kim[2], Han-Byoel Lee[2], Hyeong-Gon Moon[2], Wonshik Han[2], Ki-Tae Hwang[1]

[1]*SMG-SNU Boramae Medical Center, Department of Surgery, Korea,*
[2]*Seoul National Univ. Hospital, Department of Surgery, Korea*

Background: Mastectomy is usually recommended for centrally located tumors regarding the possibility of nipple invasion. Although there's no difference in survival outcomes according to tumor locations, central tumor has more chance of main lactiferous duct invasion, resulting in tumor cell can migration to periphery. Thus, we investigated locoregional recurrence (LRR) according to the tumor-to-nipple distance (TND).

Methods: We retrospectively collected the data of patients who underwent breast cancer surgery between 2004-2018 from two institutions. Patients who underwent neoadjuvant chemotherapy were excluded. TND was obtained from preoperative MRI records.

Result: Totally 9,014 patients were included and median TND was 3.4 (0.0-15.0) cm. For all, restricted cubic spline curve showed that the hazard risk of LRR increased with shorter TND. While breast-conserving surgery (BCS) group showed apparently increasing pattern, mastectomy group showed constant risk according to TND. Thus, we conducted survival analysis for 5,455 patients who underwent BCS. We set the cutoff for TND as 2.5cm as it showed the lowest p-value for LRR rate. Compared to those with TND > 2.5cm, patients with TND ≤ 2.5cm showed significantly lower LRR (HR, 1.83; 95% CI, [1.37-2.46], $p < 0.001$) and distant metastasis (DM) (HR, 1.53; 95% CI, [1.16-2.02], $p = 0.002$) rates. Overall survival was not different between two groups ($p = 0.405$). Cox-regression analysis revealed that TND still impacts LRR (HR, 1.52; 95% CI, [1.11-2.09], $p = 0.010$) but not DM. Importantly, TND still remained significant factor affecting LRR when analyzed as continuous variable (HR, 1.04; 95% CI, [1.02-1.06], $p < 0.001$). Prognostic impact of shorter TND was more evidence in patients with high mammographic density.

Conclusions: BCS can be conducted for central tumors regarding oncologic safety. However, if there's a fear of recurrence and reluctance to re-operation, mastectomy would be good choice.

THE IMPACT OF CAVITARY MARGIN SHAVING OF BREAST CONSERVING SURGERY: THE ONCOLOGICAL OUTCOME

Dabin Kim[1], Zisun Kim[1], Sung Mo Hur[1], Susie Chin[2], Cheol Wan Lim[1]

[1]*Soonchunhyang Univ. Hospital Bucheon, Department of Surgery, Korea,*
[2]*Soonchunhyang Univ. Hospital Bucheon, Department of Pathology, Korea*

Background: Cavitary margin shaving (CMS) is well known to reduce margin positivity and re-excision rate after breast conserving surgery (BCS). We aimed to analyze oncological outcome of CMS.

Methods: 890 female patients with non-metastatic breast cancer were prospectively collected and received CMS during BCS from October, 2012 to December, 2020. Intraoperative frozen section margin analysis was carried out and re-excision was done if necessary. Permanent section margin analysis was also conducted, and some of the patients with positive margin underwent re-excision; and others were given whole breast radiation therapy with boost.

Result: The mean ± SD age of the patients was 52.53 ± 9.90 years and mean follow-up period was 56.77 ± 25.91 months. 196 (22.02%) patients had carcinoma in situ, and 694 (77.98%) had invasive cancer. Neoadjuvant chemotherapy was given in 59 (6.63%) patients. There were 191 (21.46%) cases which reported margin positivity in intraoperative frozen section analysis, and re-excision was done in 148 cases. There were 115 (12.92%) cases with permanent section margin positivity and 10 cases underwent additional re-excision; 105 patients underwent whole breast radiation therapy with boost. Local recurrence and distant metastasis occurred in 17 (1.91%) and 26 (2.92%) patients, respectively. Patients who had cancer-associated microcalcification or who received neoadjuvant chemotherapy were associated with higher risk of local recurrence.

Conclusions: CMS reduced local recurrence after BCS, compared to conventional reported rate of local recurrence (2.5~5.5%). More sufficient margin or mastectomy should be considered in patients who have cancer-associated microcalcification or who received neoadjuvant chemotherapy.

FUNCTIONALITY BETWEEN BREAST CONSERVATION SURGERY VS. MASTECTOMY: SHORT TERM OUTCOME FROM A SINGLE INSTITUTION

Lorraine Ma[1], Kwan Yin Li[2], Mei Lin Yip[1], Suet Ying Lee[1], Chi Yee Choi[1], So Fan Yeung[2], Ka Ying Fung[1]

[1]*Pamela Youde Nethersole Eastern Hospital, Department of Surgery, Hong Kong,*
[2]*Pamela Youde Nethersole Eastern Hospital, Department of Physiotherapy, Hong Kong*

Background: Breast conservation surgery (BCS) had been gaining popularity in recent years for aesthetic reasons. However, little interests had been paid on its impact on functionality. We hypothesized that BCT would perform functionally better than mastectomy.

Methods: From July 2021 to June 2022, data of all patients who attended post-operative physiotherapy were collected. Shoulder active range of forward flexion, abduction and hand group power at first visit post-operatively and 3 months post-operatively were measured.

Result: 112 patients had post-operative physiotherapy in our unit. 83 patients underwent mastectomy and 28 patients underwent BCS. At post-operative first visit, shoulder forward flexion and abduction was better in BCS group, 138 degrees vs. 119 degrees ($p < 0.001$) and 137 degrees vs. 107 degrees ($p < 0.001$) respectively. At post-operative 3 months, abduction in BCS group still outperformed mastectomy (153 degrees vs. 143 degrees ($p = 0.01$)) while shoulder forward flexion showed no significant difference (154 degrees vs. 149 degrees ($p = 0.8$)). There was no statistical significant difference between grip power in both groups at post-operative first visit (16 kg BCS vs. 14 kg mastectomy ($p = 0.087$)) and post-operative 3 months (16 kg in BCS and 15kg in mastectomy ($p = 0.425$))

Conclusions: BCS had provided better active range of motion for patients post-operatively compared with mastectomy in the short-term.

COMPARISON OF GRADE 3 POSTOPERATIVE COMPLICATION RATES OF ROBOT-ASSISTED NIPPLE-SPARING MASTECTOMY ACCORDING TO ROBOTIC SURGICAL SYSTEM VERSION

Jieon Go[1], Jee Hyun Ahn[1], Jeea Lee[2], Jee Ye Kim[1], Hyung Seok Park[1]

[1]Severance Hospital, Department of Surgery, Korea, [2]Eulji Univ. Medical Center, Department of Surgery, Korea

Background: The purpose was to analyze postoperative outcomes of robot-assisted nipple-sparing mastectomy (RNSM) with immediate breast reconstruction (IBR), compare differences from conventional nipple-sparing mastectomy (CNSM), and evaluate the results of each robotic surgical system.

Methods: A total of 401 patients with breast cancer who underwent RNSM (n = 162) or CNSM (n = 239) with IBR at Severance Hospital between Jan 2016 and Dec 2020 were retrospectively reviewed. The da Vinci Si (9, 5.6%), Xi (96, 59.3%), and SP (57, 35.2%) were applied to RNSM. Patient baseline characteristics, intra-operative details, and grade 3 postoperative complications within 30 days after surgery (G3-Cx-PO30D) were analyzed.

Result: The mean age of the patients who received RNSM was significantly lower at 44 years ($p = 0.017$). Regarding breast ptosis, a greater number of patients with normal to mild ptosis were included in the RNSM group (RNSM 94.4% vs. CNSM 70.3%, $p < 0.001$). For operation time, RNSM took only 50 minutes longer than CNSM ($p < 0.001$) and there was no significant difference among the robotic surgical systems. G3-Cx-PO30D were evaluated, and fewer complications occurred in the RNSM group (RNSM 4.3% vs. CNSM 29.3%, $p < 0.001$). According to robot surgical system, procedures with the SP showed less grade 3 complications than those with multiport systems (0% vs. 6.7%, $p = 0.053$). Of G3-Cx-PO30D, partial skin necrosis was the most common cause in the RNSM group.

Conclusions: RNSM with IBR is a feasible surgical procedure regardless of the robotic surgical systems. RNSM using the SP system might show a better outcome in terms of G3-Cx-PO30D.

COMPARISON OF LONG-TERM ONCOLOGICAL OUTCOMES OF CENTRAL LUMPECTOMY AND CONVENTIONAL BREAST-CONSERVING SURGERY FOR INVASIVE BREAST CANCER

Jijung Jung[1], Jong-Ho Cheun[2], Hong-Kyu Kim[1,4], Han-Byoel Lee[1,3,4], Hyeong-Gon Moon[1,3,4], Ki-Tae Hwang[1,2], Wonshik Han[1,3,4]

[1]Seoul National Univ., Department of Surgery, Korea, [2]Seoul Metropolitan Government Seoul National Univ. Boramae Medical Center, Department of Surgery, Korea, [3]Biomedical Research Institute, Seoul National Univ. Hospital, Department of Surgery, Korea, [4]Cancer Research Institute, Seoul National Univ., Department of Surgery, Korea

Background: Central lumpectomy (CL) is a breast-conserving surgery (BCS) technique that involves excision of the nipple-areolar complex with breast tumor in centrally located breast cancers. We aimed to investigate the long-term clinical outcomes of CL in comparison with conventional BCS (cBCS).

Methods: Patient records who underwent BCS with clear resection margins for invasive breast cancer between 2004 and 2018 were retrospectively reviewed. Of the total 6,533 patients, 106 (1.6%) underwent CL. Median follow-up duration was 73.4 months.

Result: The CL group showed a significantly higher ipsilateral breast tumor recurrence (IBTR) rate than the conventional BCS group (10-year IBTR rate: 5.8% vs. 3.1%, $p=0.004$) and after adjusting for other variables (hazard ratio (HR), 2.65; 95% confidence interval (CI), 1.07-6.60, $p=0.048$). However, regional recurrence, distant metastasis, and overall survival rates were not significantly different between the two groups. We performed 1:3 propensity score matching (PSM) yielding 99 and 297 patients in the CL and cBCS groups, respectively. However, CL showed significantly higher IBTR rate than the cBCS group (HR, 3.27; 95% CI, 0.94-11.36; $p=0.048$). Lastly, when analyzing 2,213 patients whose tumors were located within 3 cm of the nipple, the CL group showed a significantly higher IBTR than the cBCS group before and after PSM.

Conclusions: CL showed higher IBTR rate compared to cBCS while other survival outcomes were comparable. For centrally located tumors, CL may be considered for patients preferring breast preservation. However, shared decision-making with patients regarding the risk of IBTR and need for careful surveillance is critical.

RISK FACTOR OF SKIN AND NIPPLE-AREOLAR COMPLICATION AND ONCOLOGIC SAFETY IN DIFFERENT APPROACH NIPPLE SPARING MASTECTOMY: A LONG-TERM FOLLOW-UP IN A SINGLE MEDICAL CENTER

Ruoh Yun Gau, Hsu-Huan Chou, Shin-Cheh Chen

Chang Gung Memorial Hospital, Department of Surgery, Taiwan

Background: The aim of the study is to investigate the peri-operative outcome and oncologic safety of nipple-sparing mastectomy (NSM) by comparing different approach including conventional (CON), trans-axillary conventional (TAC), robotic (ROB) and endoscopic (END) surgery, with or without reconstruction.

Methods: We retrospectively reviewed 558 patients from 2008 to 2020 receiving NSM at Chang Gung Memorial Hospital. The patients were grouped in four different approach types NSM. The peri-operative outcome focused on skin and nipple-areolar complex (NAC) after NSM and reconstruction.

Result: In the consecutive cases of 12 years, the patients received CON, TAC, ROB and END approach NSM were 402 (72.0%), 69 (12.4%), 50 (9.0%) and 37 (6.6%) respectively. Significantly higher proportion of cases in combination with free flap reconstruction was found in ROB group (70.0%), while the END cases were combined with implant reconstruction mostly (43.2%). On the contrary, patients with TAC approach NSM had the lowest reconstruction rate. The overall complication of skin and NAC after operation was found more in ROB and END group (38.0% and 27.0%, respectively), comparing with CON and TAC group (18.8%, 10.1%, respectively) ($p = 0.001$). By logistic multivariate analysis, minimal invasive approach and implant reconstruction were independently related to skin and NAC complication. There was no difference in oncologic outcome including locoregional recurrence, distant metastasis rate and overall survival.

Conclusions: There was significant difference in patient preference on surgical approach and combined breast reconstruction in NSM. The different type of NSM had impact on the peri-operative skin and NAC outcome, which was also affected by different reconstructive surgery.

LONG-TERM ONCOLOGICAL OUTCOMES OF ONCOPLASTIC BREAST-CONSERVING SURGERY AFTER A 10-YEAR FOLLOW-UP: A SINGLE CENTER EXPERIENCE AND SYSTEMATIC LITERATURE REVIEW

Byeongju Kang[1], Jun Xian Hing[1,2,3], Hee Jung Keum[1], Jeeyeon Lee[1], Jin Hyang Jung[1], Wan Wook Kim[1], Jung Dug Yang[4], Joon Seok Lee[4], Ho Yong Park[1]

[1]Kyungpook National Univ. Chilgok Hospital, Department of Surgery, Korea, [2]Changi General Hospital, Department of Surgery, Singapore, [3]Singapore Health Services Pte Ltd., [3]Singhealth Duke-nus Breast Centre, Singapore, [4]Kyungpook National Univ. Chilgok Hospital, Department of Plastic Surgery, Korea

Background: While many studies reported the oncological outcomes of oncoplastic breast-conserving surgery (OBCS), there were inherent differences in the study population, surgeons' expertise, and classifications of techniques used. There were also limited studies with long-term follow-up oncological outcomes beyond 5 years. This current study aimed to compare long-term oncological outcomes of ipsilateral breast tumor recurrence (IBTR) disease-free survival (DFS) and overall survival (OS) following conventional and oncoplastic breast-conserving surgery using volume displacement (VD) and replacement techniques.

Methods: Between 2009 and 2013, 539 consecutive patients who underwent breast conservation surgery including 174 oncoplastic and 376 conventional procedures were analyzed. A systematic review of studies with at least five years of median follow-up was performed to compare long-term oncological outcomes.

Result: At a median follow-up of 82.4 months, there were 23 (4.2%) locoregional recurrences, 17 (3.2%) metachronous contralateral breast cancer, 26 (4.8%) distant metastases, and 13 (2.4%) deaths. The hazard ratio of OBCS for IBTR, DFS, and OS was 0.78 (95% confidence interval [CI] 0.21 2.94, $p = 0.78$), 1.59 (95% CI, 0.88 to 2.87, $p = 0.12$), and 2.1 (95% CI, 0.72 to 5.9, $p = 0.17$) respectively. The 10-year IBTR-free, DFS, and OS rate were 97.8%, 86.2%, and 95.7% respectively.

Conclusions: There remained a dearth of well-balanced comparative studies with sufficient long-term follow-up, and our study reported long-term oncological outcomes for OBCS which were favorable of either VD or replacement techniques.

OCCULT LYMPH NODE METASTASES IN CLINICALLY NODE-NEGATIVE (CN0) BREAST CANCER PATIENTS REFERRED FOR NEOADJUVANT THERAPY (NAT).

Si Ying Tan[1,2], Jun Ma[3], Zewen Zhang[3], Fuh Yong Wong[5], Benita Kiat Tee Tan[4], Veronique Kiak Mien Tan[1,2], Tira Jing Ying Tan[3]

[1]Singapore General Hospital, Department of Surgical Oncology, Singhealth Duke- NUS Breast Centre, Singapore, [2]National Cancer Centre Singapore, Department of Surgical Oncology, Singhealth Duke-NUS Breast Centre, Singapore, [3]National Cancer Centre Singapore, Department of Medical Oncology, Singapore, [4]Sengkang General Hospital, Department of Surgery, Singapore, [5]National Cancer Centre Singapore, Department of Radiation Oncology, Singapore

Background: Lymph node involvement in Breast Cancer (BC) is associated with a worse prognosis. No guidelines exist for treatment of cN0 patients with pathological evidence of treatment response in the lymph nodes, resulting in heterogeneous adjuvant management.

Methods: A prospective study of supportive care needs of Breast Cancer patients referred for neoadjuvant therapy at the SingHealth group of hospitals. Consecutive females aged above 21 recruited from 2019-2020. Patients with cN0 disease were reviewed for histological evidence of response to treatment.

Result: Of the 119 patients, 28 were TNBC, 71 were HER2+ and 20 were ER+HER2-. 50 (42%) had cN0 disease. All had pathologically node-negative (ypN0) disease on final histology. 5 had pathological evidence of scarring suggestive of occult disease which had responded to NAT. All had pre-NAT axilla and cross-sectional imaging (CT or PET-CT). None underwent pre-NAT breast MRI. Of these five, all Her2+ (n = 3) patients achieved pCR. The two ER+Her2- patients had residual disease. Two underwent axillary clearance and radiation therapy to the chest wall only, one for cT4N0M0 ER+PR+Her2- disease, the other, cT2N0M0 ER-Her2+ disease, as the sentinel node could not be identified, and lymph node scarring was reported. Three were not referred for discussion of radiotherapy. A significant proportion of samples 12 (24%) had no documentation of response status.

Conclusions: The implications of occult metastases which had responded to NAT and benefit of further axillary adjuvant therapy needs to be addressed in further follow up of this prospective database. Pathological evidence of treatment response in nodes should be routinely reported by histopathologists.

COMPARATIVE MICROBIOME ANALYSIS OF THE CONTRACTED BREAST CAPSULE USING NEXT GENERATION SEQUENCING

Tae Hyun Park[1], Min-Ji Kim[2], Yeon-Kyeong Lee[2], Joon Seok Lee[1], Jeeyeon Lee[3], Ho Yong Park[3], Jae-Ho Shin[2], Jung Dug Yang[1]

[1]Kyungpook National Univ. School of Medicine, Department of Plastic Surgery, Korea, [2]Kyungpook National Univ., Department of Applied Biosciences, Korea, [3]Kyungpook National Univ. School of Medicine, Department of Surgery, Korea

Background: Of all the potential aetiology of capsular contracture, the leading theory of is that subclinical infection by bacterial biofilm. However, recent studies are limited by culture method, so it is restricted to the cultivable fraction of bacteria. Microbiome of the capsule was analyzed using the most advanced sequencing technology, next generation sequencing (NGS). The aim of this study is to characterize the microbiome of the breast capsules using NGS and to estimate the origin of the bacteria found.

Methods: 25 normal and contracted breast capsules were collected during implant removal or replacement. Ipsilateral skin samples were collected by swabbing method. We analyzed them by dividing them into 2 groups, Healthy Capsule (HC) and Contracted Capsule (CC), according to the baker grade. NGS was performed with an Illumina MiSeq. Data analysis was processed by a Quantitative Insights into Microbial Ecology 2 (QIIME2) pipeline.

Result: Beta-diversity analysis shows capsules are distributed completely different clusters with skin ($p < 0.05$). There was no relationship between the microbial structure of the capsule and the skin. In taxonomic analysis, bacterial composition of the two specimens were significantly different. In HC, several bacteria, including breast normal flora, were evenly distributed, whereas in CC, colonies dominated by opportunistic pathogens.

Conclusions: This study presented new perspectives on biofilm theory. We suggests the possibility that the endogenous bacteria of breast tissue play a role. And opportunistic pathogen dominates the microbiome as capsular contracture progresses. By understanding changes in the breast microbiome around the implant, it may be possible to prevent, or treat capsular contracture.

FACTORS RELATED TO PREGNANCY RATE AND TIMING AFTER BREAST CANCER TREATMENT IN YOUNG PATIENTS

Young-Jin Lee[1], Young Joo Lee[2], Tae-Kyung Yoo[1], Sae Byul Lee[1], Jisun Kim[1], Il Yong Chung[1], Beom Seok Ko[1], Jong Won Lee[1], Byung Ho Son[1], Hee Jeong Kim[1]

[1]*ASAN Medical Center, Department of Surgery, Korea,*
[2]*The Catholic Univ. of Korea, Seoul St. Mary's Hospital, Department of Surgery, Korea*

Background: Because of young patient's desire to give birth, fertility is the most important concern for young breast cancer patients when deciding on treatment. In order to plan pregnancy after treatment, it is important to know the time needed to pregnant and the pregnancy rate after treatment, but not much is known about it. The aim of this study was to determine these outcomes in a cohort of young survivors.

Methods: We evaluated patients treated from December 2010 to September 2020, aged 18-40 years old at diagnosis having at least one pregnancy. We analyzed the time and rate of pregnancy from surgery according to age at diagnosis, stage, hormone receptor (HR) status, breast surgery, reconstruction, adjuvant treatment (chemo, hormone, radiation, and targeted therapy).

Result: A total of 1033 patients were included, representing 115 patients who were pregnant. The median time from breast surgery to pregnancy was 3.2 years. Our analysis showed differences in pregnancy rates for age at diagnosis ($P = .002$), HR status ($P = .015$), hormonal therapy ($P = .004$), and total mastectomy ($P = .044$), and among them, there was a significant difference in pregnancy timing only for HR (2.53 versus 3.42, $P = .009$) and hormonal therapy (2.39 versus 3.56 years, $P < .001$). In multivariate analysis, age at diagnosis rate (HR 0.57, 95% CI 0.39-0.82, $P = .003$) significantly associated with pregnancy and none of treatments was associated.

Conclusions: The findings of this study suggest that factors other than age at diagnosis do not interfere with pregnancy after breast cancer treatment. Additionally HR positive and hormonal therapy may delay the timing of pregnancy.

PRELIMINARY EFFICACY OF NEOADJUVANT NAB-PACLITAXEL AND PEMBROLIZUMAB-CONTAINING REGIMENS IN EARLY STAGED TRIPLE NEGATIVE BREAST CANCER (ETNBC) THERAPY

Sum Lung Jeffrey Wong[1], Roland Leung[1], Gerry Kwok[1], Josephine Tsang[1], Bryan Li[1], Thomas Yau[1], Tsz Kok Yau[3], Lawrence Pui Ki Li[4], Peter Ho Keung Choi[5], Chun Chung Yau[5], Dacita Suen[2], Ava Kwong[2], Joanne Wing Yan Chiu[1]

[1]Queen Mary Hospital, Department of Medical Oncology, Hong Kong, [2]Queen Mary Hospital, Department of Breast Surgery, Hong Kong, [3]OncWell Integrated Cancer Centre, Department of Radiation Oncology, Hong Kong, [4]Alpha Oncology Centre, Department of Radiation Oncology, Hong Kong, [5]Comprehensive Oncology Centre, Hong Kong Sanatorium & Hospital, Department of Radiation Oncology, Hong Kong

Background: The KEYNOTE-522 regimen yielded a pathological complete response (pCR) rate of 65%. Yet clinical evidence suggests that nab-paclitaxel is more effective than paclitaxel in metastatic TNBC and when used with immunotherapy. The optimal taxane and pembrolizumab-containing regimen in eTNBC is unknown.

Methods: Consecutive patients (pts) with untreated stage II-III TNBC were offered neoadjuvant pembrolizumab (IV 2mg/kg or 200mg Q3wk for 8 cycles), in combination with nab-paclitaxel/paclitaxel and carboplatin for 4 cycles followed by anthracycline-cyclophosphamide (AC) for 4 cycles. The pCR rate was documented. Treatment-related adverse events (TRAEs) were assessed according to CTCAE v4.0.

Result: Thirty-seven pts with a median age of 51 (range 33-70) were included. 59% and 41% of pts had stage II and III disease respectively. 65% (n = 24) of pts received nab-paclitaxel, half of which omitted AC (n = 12) due to good response (42%), toxicities (50%) or progressive disease (8%). Three out of the 13 paclitaxel pts omitted AC, due to good response, toxicities, or comorbidities. Most patients (97%) received curative resection. The overall pCR rate was 57%. The pCR rates of nab-paclitaxel and paclitaxel pts were 67% and 39% respectively. The pCR rates of AC-free (n = 15) and AC-exposed patients (n = 22) were 60% and 55% respectively. Amongst AC-free patients who used nab-paclitaxel, the pCR rate was 67%. Grade > = 3 TRAE was observed in 78% of all patients.

Conclusions: Pts receiving nab-paclitaxel had a numerically higher pCR rate despite higher rates of AC omission. There may be opportunities for treatment de-escalation without compromising efficacy.

DP103-REGULATED P53-SUMO/ACETYLATION SWITCH DETERMINES RESPONSE TO DOCETAXEL IN ERα-POSITIVE BREAST CANCER

Alan Prem Kumar

National Univ. of Singapore, Department of Pharmacology, Singapore

Background: Given that molecular determinants responsible for docetaxel resistance are not known, there is an unmet need to identify robust biomarkers to predict drug sensitivity. Our group recently identified, DP103, a DEAD-box RNA helicase, to be elevated in aggressive breast cancer. This research aimed to investigate the mechanism underlying DP103-mediated docetaxel activity and if DP103 could serve as docetaxel-responsive marker in metastatic breast cancer.

Methods: Transcriptomic and immunohistochemical analyses on retrospective breast cancer biopsies obtained from a phase II randomized trial were evaluated for DP103 expression baseline, and post-docetaxel cycles. Cell based assays were employed to decipher the mechanism. Protein docking analysis and simulation dynamics evaluated interaction surfaces and binding energy between DP103 and p53.

Result: Clinical data show DP103 expression decreased progressively in response to docetaxel therapy cycles in ERα-positive patients and associated with positive response, while non-decreased DP103 patients showed poor response. Cell based experiments indicated DP103 modulated cells' sensitivity to docetaxel via p53. Docking predicted direct interactions for DP103 at p53's DNA-binding domain. Docetaxel chemosensitivity involves DP103-mediated activation of ERα via suppression of p53 which, in turn, increased expression of DP103 via a positive feedback loop.

Conclusions: Our study show for the first time DP103 acts as a "master switch" that controls p53 activation. These findings suggest targeting DP103 to relieve its interaction with p53 offers a therapeutic opportunity to enhance docetaxel sensitivity of ERα-positive breast cancer patients.

KEY REGULATORS OF CHOLESTEROL AND LIPID METABOLISM AGGRAVATE BREAST CANCER

Sakshi Shukla, Archna Singh

All India Institute of Medical Sciences, Department of Biochemistry, India

Background: One of the most common malignancies is breast cancer (BC). Through hormonal alterations, insulin resistance, and changes in lipid metabolism, obesity is a risk factor for BC. NR1H3 (nuclear receptor subfamily 1, group H, member 3), PPARG (Peroxisome Proliferator-Activated Receptor Gamma), and SRB1 (sterol regulatory element-binding protein 1) are key regulators of cholesterol and lipid metabolism. We correlated the expression profiles of these markers in the setting of BC.

Methods: Transcriptomic and proteomic expression of NR1H3, SRB1 and PPARG was evaluated in BC cell lines by qRT-PCR and western blotting respectively. Clinicopathological parameters were assessed in clinical BC cohort. In silico analysis of differential proteomic and transcriptomic expression was evaluated through the human protein atlas and The Cancer Genome Atlas (TCGA). Overall survival (OS) and Disease Free survival (DFS) were plotted against these markers in BC.

Result: The results demonstrate variable mRNA and protein expression of NR1H3, SRB1, and PPARG in BC cell lines. The TCGA data analysis reveals considerably lower expression of these markers in tumor compared to matched TCGA normal and GTEx data. This gene downregulation persisted across the BC subtypes. In the TCGA cohort, high-expression groups showed a link with poor OS and DFS. Additionally, it has been found that low NR1H3 expression is a poor OS prognostic indicator.

Conclusions: Taken together we provide insights into the intricate relationships between lipid metabolism regulators on the onset, progression, and aggressiveness of BC. We suggest evaluating dietary factors and pharmaceutical targeting of lipid metabolism regulators to aid the existing therapy regimen.

PATTERN AND COMPLICATION OF RECONSTRUCTED BREAST CANCER PATIENTS WHO RECEIVED POSTMASTECTOMY RADIOTHERAPY IN THE NATIONAL HEALTH INSURANCE SERVICE COHORT

Hyejo Ryu[1,2], Kyung Hwan Shin[1,2], Ji Hyun Chang[1,2], Bum-Sup Jang[1,2]

[1]*Seoul National Univ. College of Medicine, Department of Radiation Oncology, Korea,*
[2]*Seoul National Univ. Hospital, Department of Radiation Oncology, Korea*

Background: We aimed to analyze the nationwide pattern of reconstruction in breast cancer patients who received postmastectomy radiotherapy (PMRT) and to compare complications according to fractionation.

Methods: We used the National Health Insurance Service (NHIS) claim data to analyze breast cancer patients who received PMRT and underwent reconstruction between 2015 and 2020. The primary endpoint was grade ≥ 3 complication which involved hospital admission to the department of plastic surgery due to wound infections (ICD-10; T81.3), dehiscence (T81.4), fat necrosis (N64.1), or mechanical complication of breast prosthesis (T85.4). Propensity score matching was used to constitute the matched cohort between the hypofractionated fractionation (HF) and the conventional fractionation (CF).

Result: Altogether 4,553 patients were analyzed: 1,395 (30.6%) in the HF group and 3,158 (69.4.%) in the CF group. The use of HF increased from 20.1% in 2015 to 42.2% in 2020. Immediate implant reconstruction (36.8%) method was the most frequently used, followed by immediate autologous (33.3%) and two-stage implant reconstruction methods (19.6%). In the matched cohort (N = 2,276), the complication rate was not significantly different between the HF group and the CF group (2.6% [30/1,138] vs. 3.5% [40/1,138], $P = 0.311$) with the median follow-up of 30.9 months (6.0-82.1). The most frequent complication was wound dehiscence (44.3%) followed by wound infection (27.1%). HF was not associated with major complications (odds ratio 0.73, 95% CI 0.5-1.1, $P = 0.128$).

Conclusions: In a nationwide cohort, the complication rate was not significantly different between the HF group and the CF group. However, consultation for fractionation regimen in reconstructed breasts may be still required.

MULTIDIMENSIONAL LONGITUDINAL ASSESSMENT OF TOXICITY AND COSMESIS AFTER HYPOFRACTIONATED WHOLE-BREAST RADIOTHERAPY FOR BREAST CANCER AMONG A PROSPECTIVE COHORT OF KOREAN WOMEN: A PRELIMINARY RESULT

Nalee Kim[1], Haeyoung Kim[1], Won Kyung Cho[1], Won Park[1], Seok Won Kim[2], Seok Jin Nam[2], Jeong Eon Lee[2], Jonghan Yu[2], Byung Joo Chae[2], Sei Kyung Lee[2], Jai Min Ryu[2]

[1]*Samsung Medical Center, Department of Radiation Oncology, Korea,*
[2]*Samsung Medical Center, Department of Surgery, Korea*

Background: Hypofractionated breast whole-breast radiotherapy (HypoRT) has been conceived as a standard. Although intensity-modulated RT (IMRT) is widely used for HypoRT, no prospective data is available for Koreans. We started a prospective cohort study in June 2021 to assess adverse events after HypoRT. This preliminary analysis is aimed to report acute/subacute toxicities.

Methods: Until December 2022, 152 patients were enrolled and available for the analysis. Toxicities were assessed by physician's examination and patient-reported outcomes (PRO) using BREAST-Q. Each patient's cosmesis was graded by two blinded physicians based on photographs. Skin fibrosis was quantified using FibroMeterTM. All assessments were made at baseline (t0), during HypoRT (t1), at 2-3 weeks (t2), 6 months after HypoRT (t3).

Result: Most (99%) had pTis-2 disease. IMRT and 3-dimensional conformal RT (3D-CRT) were used in 48.0% and 52.0%, respectively. Physicians recorded grade 2 toxicities in 10.5%, 12.5%, and 6.1% at t1-t3. Within t2, IMRT was associated with lower rates of dermatitis/hyperpigmentation than 3D-CRT. At t2, PRO was worst for hyperpigmentation/dryness/irritation/thickness/sensitivity, but most of the domains recovered at t3. Except for hyperpigmentation, there was no difference in PRO between 3D-CRT and IMRT. Excellent/good cosmesis based on photographs was observed in 74.3%, 71.5%, 46.8%, and 68.8% during t0-t3. IMRT exhibited better cosmesis than 3D-CRT at t1 and t2 ($p < 0.05$). A mild/marked change of cosmesis was pronounced after 3D-CRT at t1-t2 ($p < 0.001$). There was no significant change in skin fibrosis during t0-t3.

Conclusions: HypoRT for breast cancer resulted in minimal toxicities with a recovery within t3. Also, IMRT showed better outcomes regarding toxicities and cosmesis than 3D-CRT.

IMPACT OF SURGICAL FACTORS ON AESTHETIC OUTCOME AFTER BREAST CONSERVATION THERAPY: A PROSPECTIVE COHORT STUDY

Shraddha Kenekar, Tabassum Wadasadawala, Rima Pathak, Rajiv Sarin, Revathy Krishnamurthy, Vani Parmar, Nita Nair, Shalaka Joshi, Omkar Salvi, Kp Namita Umesh, Sonal Chavan

Tata Memorial Centre, Department of Radiation Oncology, India

Background: Overall cosmetic outcome relies on patient, tumor, treatment factors and method by which cosmetic assessment's done.

Methods: In 377 patients planned for adjuvant radiotherapy (RT) after breast conserving surgery (BCS) at Tama Memorial Centre, patient and physician rated overall cosmesis using Vos et al subjective assessment scoring system at baseline (pre-RT), 6 months and 1 year was carried out. Currently, we report only baseline cosmetic outcome and factors impacting the same. Univariate and multivariate analysis was carried out using Chi square test and linear regression modeling respectively in IBM-SPSSv25.

Result: The median size of breast, tumor bed and breast-tumor ratio were 700cc (130-1775), 80cc (17.9-237) and 11.68% (1.88-55.14) respectively. Tumor was in UOQ, UIQ, LOQ, LIQ and central quadrant in 46.9%, 25.5%, 9.5%, 9.5% and 8.5% respectively. Open cavity surgery was done in 71% and oncoplasty in 29%. 23% patients presented with primary surgery that was done outside. Rate of re-excision was 12.5% in overall cohort and 54% patients operated outside had inadequate excision. 4.5% patients had post-operative complications like surgical site infection, hematoma/seroma. Proportion of excellent-good (EG) cosmesis by physician was 80% and by patients was 74%. Slight concordance (kappa-0.206, p-value < 0.001) was observed between the two. On multivariate analysis, overall cosmesis by physician was affected by breast size (p-0.040, OR-0.999 & CI-0.999-1.0), type of cavity (p-0.010, OR-2.462 & CI-1.24-4.86) and BCS outside (p-0.030, OR-0.509 & CI-0.276-0.936). According to patient reported outcome, breast-tumor ratio (p-0.038, OR-1.04 & CI-1.002-1.079) and post-operative complication (p-0.025, with OR-3.2 & CI-1.15-8.85) were predominant factors affecting overall cosmesis in multivariate analysis.

Conclusions: Smaller breast size, lower breast-tumor ratio and oncoplastic breast surgery had favorable cosmesis at baseline according to physician. Patients presenting with inadequate surgery and requiring re-excision had unfavorable cosmesis according to physician. Patients having lower breast-tumor ratio and no post-operative complications had favorable cosmesis at baseline according to patient reported outcome.

BIODEGRADABLE AND REDOX-RESPONSIVE NANOPARTICLE PLATFORM WITH TROP2 ANTIBODY LINKAGE FOR RNA INTERFERENCE TARGETING LNCRNA MNX1-AS1 TO REDUCE RADIO-RESISTANCE IN TRIPLE NEGATIVE BREAST CANCER

Qingjian Li, Ruilin Lei, Zhuofei Bi

Sun Yat-sen Memorial Hospital, Department of Medical Oncology, China

Background: Radio-resistance, the major cause of treatment failure, relapse and metastasis of triple negative breast cancer (TNBC), is partially induced by aberrant expression of long noncoding RNA (lncRNA). Trop2 is a transmembrane glycoprotein overexpressing in TNBC and targeting lncRNA is the promising therapeutic strategy as well as radiation can trigger redox reaction, therefore, we constructed a biodegradable and redox-responsive nanoparticle (NP) platform linking Trop2 antibody for RNA interference targeting lncRNA MNX1-AS1 which could enhance radio-resistance of TNBC.

Methods: We constructed a biodegradable and redox-responsive NP platform that consists of a solid poly (disulfide amide) (PDSA)/cationic lipid core and a lipid-poly (ethylene glycol) (lipid-PEG) shell for systemic small interfering RNA (siRNA) targeting lncRNA MNX1-AS1 and with Trop2 antibody linkage in TNBC cells. The NP platform is highly responsive to the concentrated glutathione (GSH) in the cytoplasm induced by radiation and further trigger intracellular siRNA release.

Result: We identified lncRNA MNX1-AS1 was up-regulated in radio-resistant TNBC. The NP platform with Trop2 antibody linkage efficiently suppressed MNX1-AS1 expression and increased radio-sensitivity in TNBC notably in vitro and in vivo. Meanwhile, a durable blood circulation, high tumor accumulation, an impressive synergistic anticancer effect with radiation and negligible toxicities were observed in vivo.

Conclusions: Our findings revealed a promising therapeutic strategy to radio-resistant TNBC that targeting MNX1-AS1 by a novel biodegradable and redox-responsive NP platform with Trop2 antibody linkage. It shows an encouraging synergistic anticancer effect with radiation and provides an original approach to overcome the radio-resistance in TNBC.

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Poster Presentation

"Go Beyond Cure of Breast Cancer"

RELATIONSHIP BETWEEN GERMLINE MUTATION AND FAMILY HISTORY IN A HIGH RISK BREAST CANCER CHINESE COHORT

Ava Kwong[1,2,3], Cecilia Ys Ho[4], Wing Pan Luk[5], Ling Hiu Fung[5], Chun Hang Au[4], Edmond Sk Ma[4]

[1]The Univ. of Hong Kong, Department of Surgery, Hong Kong, [2]Hong Kong Hereditary Breast Cancer Family Registry, Hong Kong, [3]Hong Kong Sanatorium & Hospital, Department of Surgery, Hong Kong, [4]Hong Kong Sanatorium & Hospital, Department of Molecular Pathology, Hong Kong, [5]Hong Kong Sanatorium & Hospital, Department of Research, Hong Kong

Background: Risk factors including young onset (Dx ≤ 45), triple negative, male or bilateral breast cancer are listed as selection criteria in many international guidelines for identification of germline mutation. Family history is the major consideration for screening cancer-free high-risk subjects. This study reviewed the association between germline mutation and family history to provide insight for local screening practice.

Methods: This study cohort comprised 3797 high-risk Chinese breast cancer patients. 841 (22.1%) patients who did not fulfill the above-listed risk factors were further analyzed for the relationship between germline mutation and family history.

Result: The aggregated pathogenic mutation rate of the 6 HBOC genes (BRCA1, BRCA2, PTEN, TP53, PALB2 and CDH1) increased with numbers of family member (FM) having a young onset of breast cancer ≤ 50 (YOBC), from 4.6% (no FM) to 17.8% (>1 FM). The increase was also higher in patients with relatively younger onset (46-50) than those with the late-onset group (>50), from 5.9% to 25.0% and 3.4% to 13.8% respectively. Among FM positive for YOBC, a history of ovarian cancer increased the positive rate from 9.8% to 50.0%. Compared to FM negative for YOBC, mutation rate was 78% higher in patients with only one FM with YOBC but nearly 3 folds higher in patients with more than one FM with YOBC.

Conclusions: A higher mutation rate is associated with positive FM for YOBC. While the detection rate is not as high as other cancer-related factors, a positive FM for YOBC is confirmed as a useful selection criterion for screening cancer-free subjects.

DELAY IN PRESENTATION IN OLDER BREAST CANCER PATIENTS DURING THE COVID-19 PANDEMIC

Dacita Suen, Ava Kwong

The Univ. of Hong Kong, Department of Surgery, Hong Kong

Background: The first case of COVID-19 in Hong Kong was reported on January 23, 2020. The purpose of this study was to examine the impact of the COVID-19 pandemic on the pattern of breast cancer presentation, functional assessment, cognition status, and treatment variations among older women in Hong Kong.

Methods: Patients aged 70 or older with newly diagnosed early operable breast cancer who attended a university affiliated breast center between August 2018 and July 2021 were included. Every study participant was subjected to a comprehensive geriatric assessment by the research team. A comparison was made between those who presented before and after the onset of COVID-19.

Result: Among the 122 patients recruited, half (61) presented before the onset of COVID-19 and half (61) after. In the group who presented after the onset, there were significantly more patients presenting with symptoms (75.4% vs. 91.8%) and fewer with screening (24.6% vs. 8.2%) ($p = 0.011$). These patients had larger tumors and more advanced overall staging although not statistical significance. The two groups did not differ significantly in terms of breast operations (mastectomy or breast conservation surgery) or treatment sequence (upfront surgery or neoadjuvant systemic therapy). Patients presented after the onset scored better in functional and cognition status ($p < 0.005$), psychological evaluation ($p = 0.015$) and social assessment ($p = 0.005$).

Conclusions: COVID-19 has caused a delay in presentation in older breast cancer patients, and those who presented after the onset were more robust. Long-term follow-up is needed to assess its impact on recurrence and survival.

THE ANALYSIS OF THE RISK FACTOR OF YOUNG BREAST CANCER USING URINE MICROBIOME

Jeongshin An[1,2], Hyungju Kwon[1], Woosung Lim[1], Byung-In Moon[1]

[1]*Ewha Womans Univ. Mokdong Hospital, Department of Surgery, Korea,*
[2]*Ewha Womans Univ. Mokdong Hospital, Institute of Convergence Medicine Research, Korea*

Background: Breast cancers with estrogen receptors account for more than 70% of all patients with breast cancer. The microbiome involved in the metabolism of estrogen is called estrobolome. This study aims to find the cause of breast cancer in young patients, focusing on the estrobolome.

Methods: In this study, 183 breast cancer patients were involved, and urine samples were collected. Among them, 22 were under 39 years, and 161 were more than 40 years. Isolation of bacterial extracellular vesicles and circulating cell-free DNA extraction was performed from urine samples. The sequencing of 16S rRNA gene variable regions was done by the next-generation sequencer MiSeq, Illumina. Sequencing results were assigned through taxonomic alignment and analyzed according to age and estrobolome.

Result: In young and elderly patients with breast cancer, there were statistical differences in several bacteria, especially in estrobolome, Bifidobacterium spp. and Bacteroides spp., which were more abundant in younger patients. The estrobolome tended to be higher in younger patients because of its association with estrogen levels. In particular, Bifidobacterium is known as a beneficial bacterium and is a popular strain in various supplements and probiotic drinks. However, it suggests that additional studies on the flip side of these strains may be needed.

Conclusions: In this study, we focused on young patients with breast cancer and estrobolome to discover the microbiome that could cause young breast cancer. Bacteria, which is known to be beneficial to healthy people, can also be a risk factor for breast cancer when it is in excess.

BIOELECTRICAL IMPEDANCE ANALYSIS (BIA) CAN BE USED AS TOOLS FOR TARGET PREVENTATIVE MEASURES TO IMPROVE THE OVERALL HEALTH STATUS AND PROGNOSIS OF EARLY BREAST CANCER PATIENT AFTER CHEMOTHERAPY

Yohana Danoe Gordy, Dimyati Achmad

Hasan Sadikin General Hospital, Department of Surgery / Faculty of Medicine Universitas Padjadjaran, Indonesia

Background: Early Breast Cancer (EBC) is associated with excellent prognosis and cure is achieved in most patients who treated with surgery, chemotherapy and hormonal therapy. The majority of patients experience weight changes after EBC diagnosis with negative consequences on self-image, quality of life and overall health. This condition associated with a higher proportion of fat mass and especially with increased amount of visceral fat. The aim of study is to explored the effects treatment of breast cancer on body composition during and after the treatment.

Methods: We studied 50 EBC patients before chemotherapy, after the second cycle of chemotherapy and three months after the end of chemotherapy. Body composition parameters were evaluated using bioelectrical impedance analysis (BIA).

Result: Three months after the end of chemotherapy the fat mass had increased from 22.04 ± 7.15% to 23.92 ± 7.33% ($P = 0.026$) and visceral fat volume had increased by 17% from 2.36 ± 1.75l to 2.77 ± 1.94l ($P = 0.013$). There was a decrease in muscle mass in all breast cancer patients after the second cycle of chemotherapy (-1.33 ± 2 kg on average; $P = 0.005$). The changes in body composition varied according to distinct baseline fat mass.

Conclusions: Treatment of EBC was associated with increase of fat mass, visceral fat, and body mass index. In this research also observed decrease in muscle mass and total body water. Our results suggest that BIA could help to target preventative measures to improve the overall health status and prognosis of breast cancer patient.

GEOGRAPHIC DISPARITIES OF BREAST CANCER INCIDENCE IN YOGYAKARTA, INDONESIA: ANALYSIS USING GLOBAL MORAN'S I STATISTIC AND LOCAL INDICATORS OF SPATIAL ASSOCIATION (LISA)

Bryant Ng[1], Herindita Puspitaningtyas[2], Juan Adrian Wiranata[3], Susanna Hilda Hutajulu[4], Nungki Anggorowati[5], Guardian Yoki Sanjaya[6], Lutfan Lazuardi[6], Patumrat Sripan[7]

[1]Universitas Gadjah Mada, Medicine Study Program, Faculty of Medicine, Public Health and Nursing, Indonesia, [2]Universitas Gadjah Mada, Doctorate Program of Health and Medical Science, Faculty of Medicine, Public Health and Nursing, Indonesia, [3]Universitas Gadjah Mada, Master of Clinical Epidemiology Postgraduate Program, Faculty of Medicine, Public Health and Nursing, Indonesia , [4]Universitas Gadjah Mada/ Dr Sardjito General Hospital, Division of Hematology and Medical Oncology, Department of Internal Medicine, Faculty of Medicine, Public Health and Nursing, Indonesia, [5]Universitas Gadjah Mada/ Dr Sardjito General Hospital, Department of Anatomical Pathology, Faculty of Medicine, Public Health and Nursing, Indonesia, [6]Universitas Gadjah Mada, Department of Health Policy and Management, Faculty of Medicine, Public Health and Nursing, Indonesia , [7]Chiang Mai Univ., Research Institute for Health Sciences, Thailand

Background: Breast cancer (BC) is the cancer type with the highest incidence worldwide and in Indonesia. In Indonesia, there is limited research on the spatial analysis of BC incidence, which can help guide targeted public health interventions based on geographic location. This study aims to examine spatial disparities of BC incidence in Yogyakarta province, Indonesia.

Methods: BC case data from 2008 to 2019 from Yogyakarta's population-based cancer registry were used with population data of the year 2014 to calculate the Age-Standardized Rate (ASR) of breast cancer in 48 subdistricts of 3 catchment districts of Yogyakarta province (Sleman, Kota Yogyakarta and Bantul). Analyses using global Moran's I statistic and Local Indicators of Spatial Association (LISA) were conducted to confirm and measure spatial autocorrelation and to identify potential clusters and outliers.

Result: The median ASR of the subdistricts was 41.9, and the range was 15.3-70.4. We found a significant positive spatial autocorrelation of BC incidence among the subdistricts ($I = 0.581$, $p < 0.001$). There were 11 subdistricts in the central area of Kota Yogyakarta which are high-high clusters and 6 subdistricts in Bantul and Sleman districts, located southeast of the catchment area, which are low-low clusters. There were no high-low or low-high outliers.

Conclusions: BC incidence in Yogyakarta province was highly clustered. Our findings can inform public health decision making and resource allocation. The results may also contribute to a further exploration of the relationship of BC incidence and environmental factors.

THE BREAST CANCER RISK ASSESSMENT TOOL (BCRAT) AND APPLICABILITY TO FILIPINO WOMEN IN A SINGLE TERTIARY INSTITUTION: A RETROSPECTIVE STUDY

Paulino Patriccia Anne Mae, Tison Nicola Raphaela, Que Raissa Maxine

Univ. of Santo Tomas Hospital, Department of Surgery, Philippines

Background: The diagnostic accuracy of the BCRAT has not been fully evaluated yet in the Filipino population. The purpose of this study is to analyze the applicability of this model to Filipino ethnic groups using data gathered from a single tertiary hospital in Manila. The results will help Filipino women enrich their awareness on breast cancer and understand the different risk factors associated with the disease. Most importantly, it will aid health care professionals in identifying women with a high risk for breast cancer, who may benefit more from closer follow ups and targeted screening.

Methods: A total of 420 out of 1024 breast cancer patient records were included from the hospital records from January 2016 to December 2021. BCRAT database sheet were filled up for each patient. 5 year risk and lifetime risk for breast cancer were calculated using the BCRAT online calculator. Data gathered were analyzed statistically thereafter.

Result: The median five-year risk of developing breast cancer among the participants was 1.10% (IQR = 0.80% to 1.50%), while the average five-year risk was 1.20% (IQR = 1.00% to 1.50%). Categorizing the five-year risk, results showed that most of the participants had an average risk of developing breast cancer in the next five years (79.29%), and only 20.71% had high risk for breast cancer development in 5 years.

Conclusions: The BCRAT calculator, when applied to Filipino women, underestimates the risk for breast cancer. Further validation studies which can be of prospective nature may be done to determine applicability of the BCRAT to Filipino women.

INCIDENCE AND PEAK OCCURRING TIME OF CONTRALATERAL BREAST CANCER RELATED TO AGE; YOUNGER WOMEN VERSUS OLDER WOMEN

Hakyoung Kim[1], Hee Jeong Kim[2], Tae In Yoon[3], Seonok Kim[4], Sae Byul Lee[2], Jisun Kim[2], Il Yong Chung[2], Beom Seok Ko[2], Jong Won Lee[2], Byung Ho Son[2]

[1]Dongguk Univ. Ilsan Hospital, Department of Surgery, Korea, [2]ASAN Medical Center, Department of Surgery, Korea, [3]Dongnam Institute of Radiological and Medical Science, Department of Surgery, Korea, [4]ASAN Medical Center, Department of Clinical Epidemiology and Biostatics, Korea

Background: One of the important risk factors for developing contralateral breast cancer (CBC) is diagnosis of primary breast cancer at young age. The purpose of this study is to compare incidence and peak occurring period of CBC according to the age at surgery of primary breast cancer.

Methods: In this retrospective study, we included patients who were diagnosed with unilateral non-metastatic breast cancer at Asan Medical Center, Korea, between 1999-2013 followed through 2018. Patients were divided into two groups according to the age at surgery of primary breast cancer; younger group (≤ 35 years) versus older group (> 35 years). Cumulative incidence and hazard rate which demonstrates annual risk for developing CBC at certain time frame were compared in whole population and in subgroup divided by cancer subtype

Result: In total of 16,251 patients, 347 out of 14,933 in older group and 71 out of 1,318 in younger group developed CBC. Younger group showed significantly higher incidence of CBC with the 10-year cumulative incidence 7.1% compared with 2.9% in older group, with p-value < .0001. Hazard rate for CBC differed according to the subtype of primary cancer. In hormone receptor positive, human epidermal receptor-2 negative subtype annual risk increased continuously in both younger and older group. In hormone receptor negative, human epidermal receptor-2 positive subtype, annual risk peaked before 5 years since the primary breast cancer surgery in younger group whereas in older group peak was about 2 years later.

Conclusions: Such information can be important when counseling patients who are considering contralateral prophylactic mastectomy.

ANALYSIS OF THE ASSOCIATION BETWEEN THE RISK OF BREAST DISEASES AND UTERINE FIBROIDS BY USING NATIONAL HEALTH INSURANCE DATA

Geumhee Gwak[1], Jin-Sung Yuk[2], Seung-Woo Yang[2], Sang-Hee Yoon[2], Myoung Hwan Kim[2], Yong-Soo Seo[2], Yujin Lee[1], Yilseok Joo[1], Jungbin Kim[1], Sam-Youl Yoon[1], Hyunjin Cho[1], Keunho Yang[1]

[1]Inje Univ. Sanggye Paik Hospital, Department of Surgery, Korea, [2]Inje Univ. Sanggye Paik Hospital, Department of Obstetrics and Gynecology, Korea

Background: The purpose of this study was to investigate the incidence of benign breast disease (BBD), carcinoma in situ (CIS), and breast cancer (BC) in women treated for uterine fibroids (UFs) compared to women who were not treated for UFs.

Methods: We selected women who were treated for UFs and women without UFs between 20 and 50 years old using national health insurance data from 2011 to 2020. We analyzed independent variables such as age, socioeconomic status, region, Charlson comorbidity index, delivery status, menopausal status, menopausal hormone therapy, endometriosis, hypertension, diabetes mellitus, and dyslipidemia in the UF and non-UF group.

Result: There were 190,583 and 439,940 participants in the UF and control groups, respectively. Compared with those of the control group, the RRs of BBD, CIS, and BC were increased in the UF group. The hazard ratios (HRs) of BBD, CIS, and BC in the UF group were 1.335 (95% CI 1.299-1.372), 1.796 (95% CI 1.542-2.092), and 1.3 (95% CI 1.198-1.41), respectively. When we analyzed the risk of BC according to age at inclusion, UFs group had the increased risk of BCs in all age groups in comparison with control group. Women with low SES (HR 0.514, 95% CI 0.36-0.734) and living in rural areas (HR 0.889, 95% CI 0.822-0.962) had a lower risk of BC.

Conclusions: Our study showed that women with UFs had a higher risk of BBD, CIS, and BC than those without UFs. This result suggests that women with UFs should be more conscious of BC than those without UFs.

BILATERAL BREAST CANCER IN YOUNG WOMEN IN AN ASIAN POPULATION

Hui Wen Chua[1,2], Faith Qi Hui Leong[1,2], Ngaserin Ng Hui Na Sabrina[1,2], Yirong Sim[2,5], Tan Jing Ying Tira[3], Ngeow Yuen Tie Joanne[3], Fuh Yong Wong[4], Tan Kian Mien Veronique[2,5], Tan Kiat Tee Benita[2,5]

[1]Sengkang General Hospital, Department of General Surgery, Singapore, [2]Singhealth Duke-NUS Breast Centre, Department of Surgery, Singapore, [3]National Cancer Centre Singapore, Department of Medical Oncology, Singapore, [4]National Cancer Centre Singapore, Department of Radiation Oncology, Singapore, [5]National Cancer Centre Singapore, Department of Surgery, Singapore

Background: 13.6% of breast cancer in Singaporean women are below 40. They do not qualify for screening and are diagnosed when symptomatic and abnormalities detected in the other breast, leading to diagnosis of synchronous bilateral breast cancer (BBC). Metachronous BBC are usually found during surveillance. We aim to investigate the incidence and outcomes of BBCs in young women with characteristic survivorship issues.

Methods: A retrospective study on patients in SingHealth Joint Breast Cancer Registry between January 1998 and December 2017. Of 2610 women < 40 years old at diagnosis, 97 women had bilateral cancers. Interval of 6 months and greater between the diagnosis of index and contralateral breast cancer was categorized as metachronous BBC.

Result: 35% were synchronous and 65% metachronous. Mean age of diagnosis of index cancer for both groups was similar; 35.5 (synchronous) and 36 (metachronous). Invasive ductal carcinoma was more common, and no differences in tumour biology between sides. Tumours with synchronous BBC were more likely ER/PR positive (84.6% vs. 64.9% in metachronous), less likely HER2 positive (9.5% vs. 24.5%) and triple negative (11.1% vs. 27.3%). More than 55% of BBC patients opted for breast conserving surgeries. A greater proportion of patients with synchronous breast cancer elected for reconstruction surgeries (30% vs. 10%). Synchronous BBC had worse prognosis and higher recurrence compared to metachronous.

Conclusions: Young women with breast cancer are a unique group with medical and psychosocial challenges. Healthcare providers need to be cognizant in order to provide well-rounded care. Establishing protocols would be helpful to facilitate multi-disciplinary care.

MAKING THE RIGHT CHOICE. HOW UNAFFECTED WOMEN CARRYING BRCA1/BRCA2 GERMLINE PATHOGENIC VARIANTS DECIDE FOR PROPHYLACTIC MASTECTOMY TO REDUCE CANCER RISK

Reka Schweighoffer[1], Monica Aceti[1], Carla Pedrazzani[1,2], Nicole Buerki[3], Pierre Chappuis[4], Rossella Graffeo-Galbiati[5], Veronique Membrez[6], Christian Monnerat[7], Manuela Rabaglio[8], Olivia Pagani[9], Sheila Unger[10], Maria Katapodi[1], Maria Caiata-Zufferey[2]

[1]Univ. of Basel, Department of Clinical Research, Switzerland, [2]Univ. of Applied Sciences and Arts of Southern Switzerland, Department of Business Economics, Health and Social Care, Switzerland, [3]Univ. Hospital Basel, Department of Womens Clinic and Gynecological Oncology, Switzerland, [4]Geneva Univ. Hospital, Department of Oncogenetics, Switzerland, [5]Institute of Oncology (IOSI) and Breast Unit (CSSI) of Southern Switzerland, Department of Oncology, Switzerland, [6]Hpital du Valais, Institut Central (ICH), Department of Medical Genetics, Switzerland, [7]Jura Hospital, Department of Oncology, Switzerland, [8]Inselspital Bern, Department of Oncology, Switzerland, [9]Istituto Oncologico della Svizzera Italiana Ospedale Regionale Bellinzona e Valli, Department of Oncology, Switzerland, [10]Centre Hospitalier Universitaire Vaudois, Service of Medical Genetics, Switzerland

Background: For women at high risk of breast cancer, prophylactic surgery is an alternative to intensive surveillance to preserve their health. Risk-reducing mastectomy (RRM) strongly reduces the risk of breast cancer, but meanwhile it can cause several physical and psychosocial issues. The choice between intensive surveillance and RRM therefore appears to be particularly difficult and highly personalized. Literature reveals that to date, little is known about the underlying mechanisms of the decision-making process of unaffected hereditary breast and ovarian cancer (HBOC) carrying women for RRM.

Methods: Data was acquired from biographical qualitative interviews conducted in Switzerland within two studies and with 30 women carrying BRCA1/BRCA2 mutations who underwent RRM and have no prior cancer history.

Result: The decision-making process is influenced by several factors that include women's identity and moral values, risk perception based on lay theories, stage in their life course, family configuration, and experiences with intensive surveillance. Importantly, we observed that to take their decision, women engage in three interlocking crucial processes: thinking of RRM as an obligation, de-dramatizing RRM, and building consensus around it.

Conclusions: We conclude that RRM is more the result of a complex interaction between the woman and her context that an intimate and private choice. Health professionals should be aware of this decision-making process and help women to govern it.

Poster Presentation

BREAST CANCER AWARENESS AMONG FEMALE RESIDENTS IN SURAKARTA, INDONESIA

Asticha Erlianing Sari[1], Agus Jati Sunggoro[2]

[1]*Sebelas Maret Univ., Department of Internal Medicine, Indonesia,*
[2]*Sebelas Maret Univ., Department of Medical Oncology, Indonesia*

Background: Breast cancer is the most prevalent cancer worldwide and leading cause of cancer death among female. In 2020, there were 396,914 cases in Indonesia with more than 22,000 deaths. Female physicians have an important role in identifying early breast cancer, as well as promoting awareness regarding breast cancer to general public. This study determines the awareness level of breast cancer in female physicians in Surakarta, Indonesia.

Methods: It was performed as cross-sectional study in Moewardi Hospital, Surakarta, Indonesia from November 2022 - January 2023. The population included female residents of all years in all speciality program. Data collection had been done by Breast Cancer Awareness Scale-Indonesia (BCAS-I) questionnaire.

Result: A total of 103 participants took part in the study. Ninety two (89.3%) participants had satisfactory knowledge about the warning signs of breast cancer. On the question on the risk factors, 101 (98%) participants were assessed to have adequate knowledge. Seventy two (69%) participants had negative responses to health behavior related to breast cancer awareness inspite of the adequate knowledge. Barriers to breast cancer screening were mostly because of their busy lives and lack of time to see a doctor.

Conclusions: The awareness about warning signs and risk factors of breast cancer in female residents was more than satisfactory but the behavior related to breast cancer awareness was still inadequate. More efforts are needed through conducting breast screening programme and promoting both awareness and behavior about breast cancer.

CLINICOPATHOLOGIC CHARACTERISTICS AND DISPARITIES OF TREATMENTS IN MALE BREAST CANCER PATIENTS ACCORDING TO AGE DISTRIBUTION

Chihwan Cha[1], Bomin Kim[2], Min Sung Chung[1]

[1]*Hanyang Univ. Seoul Hospital, Department of Surgery, Korea,*
[2]*Hanyang Womens Univ., Department of Health Administration, Korea*

Background: We aimed to investigate the clinicopathologic characteristics and type of treatments of male breast cancer (MBC) according to age distribution from a Korean Breast Cancer Registry.

Methods: We retrospectively reviewed the data of patients with MBC who received curative surgery between 2005 and 2014. Clinicopathologic features including family history, disease stage, history of other cancer, hormone receptor status, HER2 status and Ki-67 index were compared between two groups by age 60.

Result: Of all 403 patients, 193 (47.9%) were younger than 60 years old. Twenty-three (5.7%) patients had family history, and 12 (3.0%) had history of other cancer. There was no difference in family history ($p = .654$) and other cancer history ($p = .302$) between two groups. Although there was no difference in disease stage ($p = .131$), and lymph node metastasis ($p = .513$), older patients (age >60) received more mastectomy and axillary node dissection than younger (90.9% vs. 74.1%, $p < .001$; 67.5% vs. 50.5%, $p = .005$, respectively). Regarding the prognostic factors, there was no differences in hormone receptor/HER2 status ($p = .686$) and Ki-67 index ($p = .639$) between two groups. However, older patients were less likely to receive both chemotherapy and radiotherapy than younger (51.5% vs. 61.4%, $p = .052$; 21.9% vs. 33.1%, $p = .031$, respectively).

Conclusions: In the treatment of MBC, there were considerable disparities of the extent of surgery and the use of radiotherapy according to age distribution. Older patients (age >60) tend to receive more radical surgery and lesser adjuvant treatment compared with younger.

GERMLINE BRCA MUTATION STATUS AND RESPONSE TO NEOADJUVANT SYSTEMIC THERAPY IN BREAST CANCER

Hyunyou Kim[1], Jung Whan Chun[2], Mary Rose Mendoza[1], Ji Young You[1], Seung Pil Jung[1], Eun-Shin Lee[1]

[1]*Korea Univ. Anam Hospital, Department of Surgery, Korea,*
[2]*Seoul National Univ. Hospital, Department of Surgery, Korea*

Background: It remains inconclusive whether germline BRCA (gBRCA) mutation affects the response of neoadjuvant systemic therapy in breast cancer. Here, we present a retrospective analysis which estimated the pathologic complete response (pCR) rate in breast cancer patients according to gBRCA1/2 mutation status.

Methods: We reviewed a total of 442 breast cancer patients who underwent gBRCA1/2 tests and received neoadjuvant chemotherapy in 2 institutions between 2001 and 2022. Chemotherapy response was compared between patients with or without deleterious BRCA1/2 mutation and we assessed the association of the pCR rate and clinical characteristics of the patients. For pCR rates, the ypT0/is ypN0 definition was used as a primary end point.

Result: We detected pathogenic BRCA1/2 mutations in 145 (32.8%) of the 442 patients, 83 (18.8%) in BRCA1 and 62 (14.0%) in BRCA2. Overall pCR rate was 34.6% (153/442). The pCR rate was 37.9% (55/145) and 33.0% (98/297) for gBRCA1/2 carriers and non-carriers, respectively. Germline BRCA1/2 mutation status was not significantly different from a pCR rate (OR:0.806, 95% CI = 0.533-1.219, $p = 0.306$). With respect to the demographic and clinicopathological characteristics, higher pCR rate observed in breast cancer with hormone-receptor negative (OR:2.845, 95%CI 1.791-4.520, $p < 0.001$) and HER2 negative (OR:2.823, 95%CI = 1.6-4.984, $p < 0.001$) tumor and high ki-67 level (OR:2.165, 95%CI 1.347-3.480, $p = 0.001$), irrespective of gBRCA1/2 mutation.

Conclusions: In this analysis, patients with gBRCA1/2 mutations showed no significantly different response in neoadjuvant systemic therapy. Further large-scale analysis with survival data may provide robust evidence on the impact of the gBRCA1/2 mutation status for breast cancer patients.

EVALUATION OF SECOND-HIT PATTERNS IN JAPANESE BREAST CANCER PATIENTS WITH GERMLINE BRCA1/2 MUTATIONS

Yukino Kawamura[1,7], Kotaro Mori[2], Fumihiko Takeuchi[2,3], Junko Kawano[4], Yasuaki Sagara[3,4], Norihiro Kato[2,3,5], Chikako Shimizu[1], Akihiko Shimomura[1,2,7], Akira Hida[6]

[1]National Center for Global Health and Medicine, Department of Medical Oncology, Japan, [2]National Center for Global Health and Medicine, Department of Genetic Medicine, Japan, [3]National Center for Global Health and Medicine, Department of Gene Diagnositics and Therapeutics, Research Institute, Japan, [4]Sagara Hospital, Department of Breast Surgery, Japan, [5]National Center for Global Health and Medicine, Medical Genomic Center, Research Institute, Japan, [6]Matsuyama City Hospital, Department of Pathology and Diagnosis, Japan, [7]Juntendo Univ. Cooperative Graduate School National Center for Global Health and Medicine Research Course in Advanced Medical Specialties, Japan

Background: While not all carriers of germline BRCA1/2 mutations (gBRCA1/2m) develop breast cancer, de novo mutations occurring in the contralateral allele may cause carcinogenesis (so-called second-hit). Patterns of second-hit remain unclear in Japanese breast cancer patients with gBRCA1/2m.

Methods: Japanese breast cancer patients with gBRCA1/2m who had undergone surgery for the primary tumor at two institutions from April 2010 to March 2020 were enrolled. Clinical information including gBRCA1/2m was collected from electronic medical records. Somatic BRCA1/2 mutations (sBRCA1/2m) found in the surgical specimen were compared to known gBRCA1/2m. Next-generation sequencing was performed to detect sBRCA1/2m with AmpliSeq for Illumina BRCA Panel. The identified variants were annotated using VarSeq (Golden Helix). To estimate the pathogenicity of variants, we referred to ClinVar. Loss of heterozygosity (LOH) was considered if the somatic variant-allele frequency (VAF) was >0.6.

Result: A total of 22 patients were enrolled. The median age was 43 years. 12 (54.5%) had BRCA1 mutations, and 10 (45.5%) had BRCA2 mutations. Of these, 16 (72.7%) were triple-negative breast cancer, and none were HER2-positive. 10 of the 22 cases showed only the same variant as the gBRCA1/2m, 8(36.4%) had LOH (VAF$>$ 0.6). 2 cases (9.1%) showed several sBRCA1/2m in addition to the same variant as gBRCA1/2m, one of which had VAF>0.6. In other 2 cases, gBRCA1/2m and sBRCA1/2m did not match. 5 (22.7%) cases showed only benign variant. In the remaining 3 cases, no significant variants were found.

Conclusions: LOH was the most frequent pattern of second-hit of gBRCA1/2m in Japanese breast cancer patients.

Poster Presentation

HETEROLOGOUS SARCOMATOUS DIFFERENTIATION OF PHYLLODES TUMOR: CASE SERIES AND LITERATURE REVIEW

Tushar Parmeshwar

AIIMS Bibinagar, Department of Surgery, India

Background: Phyllodes tumour is rare with 2-3% incidence of all fibroepithelial and < 1% of all breast neoplasm. Malignant Phyllodes Tumors (MPTs) form only 10%-15% of subgroup. MPTs can have further malignant differentiation resulting in rare heterologous sarcomatous differentiation and pose a diagnostic dilemma.

Methods: Two females aged 40yrs and 56yrs presented with breast lump and were diagnosed with PT. Demographic and clinical data were collected and each case reviewed for the clinical features, prior treatment history, radiological imaging, histopathological and immunohistochemical details, disease stage, outcome and follow-up. On histopathology, 40yrs old female had PT with liposarcoma. Second 56yrs female had MPT with rhabdomyosarcoma. An in-depth review of literature was done.

Result: Association of Phyllodes and heterologous sarcomatous differentiation is rare. Presence of rhabdomyosarcoma in MPT is extremely rare and has been reported in only 4 cases till date. Phyllodes tumors form a spectrum from absolutely benign to borderline to frankly malignant tumors based on histological characteristics that comprise degree of stromal cellularity, atypia, mitoses, presence of stromal overgrowth, malignant heterologous element and tumour border. Heterologous sarcomatous transformation towards liposarcoma, fibrosarcoma, angiosarcoma, osteosarcoma, chondrosarcoma, and rhabdomyosarcoma are seen.

Conclusions: Heterologous differentiation in PT must be kept in mind. Meticulous histopathological sampling along with subtyping of the heterologous sarcomatous components needs considerations. Due to its rarity and paucity of literature there are no clear-cut guideline for surgical management and targeted therapy of these patients with resultant prognostication.

DNA DAMAGE RECOVERY AND CHEMOSENSITIVITY TO OLAPARIB AND CISPLATIN IN BREAST CANCER CELLS WITH MUTATION ON BRCT DOMAIN OF BRCA1 PROTEIN

Ji Soo Park[1,2], Jiyoung Kim[3], You Keun Shin[4,5,6], Se Eung Oh[4,5,6], Ik Jae Lee[7], Hei-Cheul Jeung[4,5,6]

[1]Yonsei Univ. College of Medicine, Cancer Prevention Center, Yonsei Cancer Center, Korea, [2]Yonsei Univ. College of Medicine, Department of Medical Oncology, Korea, [3]Univ. of Seoul, Department of Life Science, Korea, [4]Yonsei Univ. College of Medicine, Cancer Metastasis Research Center, Korea, [5]Yonsei Univ. College of Medicine, Songdang Institute for Cancer Research, Korea, [6]Gangnam Severance Hospital, Department of Medical Oncology, Korea, [7]Yonsei Univ. College of Medicine, Department of Radiation Oncology, Korea

Background: BRCA1 increases a homologous recombination process responded to double-strand break of breast cancer cells. However, it is not well known whether the DNA recovery and chemosensitivity are different according to the location of BRCA1 mutation.

Methods: Using the BRCA1-mutated and wild type breast cancer cell lines, HCC1937 (5382insC), MDA-MB-436 (5396+1G > A), SUM149PT (2288delT), MDA-MB-231 (wild), and MCF7 (wild), we assessed recovery efficiency to irradiation, binding efficacy of the partners with BRCT domain, and chemosensitivity to olaparib and cisplatin in cell lines.

Result: HCC1937 cells had worse recovery potency to irradiation compared to other cells. Intranuclear location of BACH1/BRIP1 was decreased in BRCA1-mutated cells than BRCA1-wild type cells. Intranuclear expression of abraxas was decreased, and late apoptotic-necrotic portion was increased in HCC1937 cells than others. In MTT assay, BRCA1-mutated breast cancer cells with mutation on BRCT domains (HCC1937, MDA-MB-436) showed higher sensitivity to olaparib and cisplatin.

Conclusions: The mechanism of response to DNA break and chemosensitivity of breast cancer cells are possibly influenced by the location of BRCA1 mutation. To find the prognostic and predictive meaning of these characteristic, well-controlled preclinical and clinical studies are needed.

HEXASACCHARIDE GLOBO-H AS A THERAPEUTIC TARGET FOR ANTIBODY-DRUG CONJUGATE OBI-999 IN TRIPLE-NEGATIVE BREAST CANCER

Jangsoon Lee[1], Youngjin Gi[1], Yu-Jung Chen[3], Ming-Chen Yang[3], Ming-Tain Lai[3], Debu Tripathy[1], Naoto Ueno[2]

[1]UT MD Anderson Cancer Center, Department of Cancer Medicine, U.S.A., [2]Univ. of Hawai'i Cancer Center, Cancer Biology Program, U.S.A., [3]OBI Pharma, Inc, Pharmaceutical Company, Taiwan

Background: Globohexaosylceramide (Globo-H) is a tumor-associated carbohydrate antigen overexpressed in various cancers, including breast cancer. OBI-999, comprising a humanized anti-Globo-H antibody bound to monomethyl auristatin E (MMAE, anti-mitotic agent) by a ThioBridge™ linker, has shown antitumor effects in various cancers. This preclinical project evaluated the therapeutic efficacy of OBI-999 in triple-negative breast cancer (TNBC) in vitro and in vivo.

Methods: Globo-H expression was determined using fluorescence-activated cell sorting or immunohistochemistry analysis. The antiproliferation effect of OBI-999 was examined using sulforhodamine B staining and spheroid formation assays. Caspase 3/7 activity and Western blot analysis were used to confirm OBI-999-mediated apoptosis. Mammary fat pad xenograft models were used to evaluate the antitumor effect of OBI-999.

Result: Thirty percent of TNBC tissue samples from patient-derived xenografts (44 cases) were membrane Globo-H-positive (H-score ≥ 1). OBI-999 reduced the viability of Globo-H-positive TNBC cell lines ($P < .05$), and the half-maximal inhibitory concentration of OBI-999 was 9.5 to 152 nM. OBI-999 also induced caspase 3/7 activity and cleaved poly-ADP-ribose polymerase and phospho-H2AX expression, indicating that TNBC cell death is caused by inducing DNA damage response-mediated apoptosis. In SUM149 TNBC xenograft (H-score, 60), OBI-999 led to dose-dependent tumor growth inhibition (TGI; 1 mg/kg, 45.5% TGI, $P < .0001$; 3 mg/kg, 66.7% TGI, $P < .0001$). In TNBC patient-derived xenografts BCM-0132 (H-score, 110), OBI-999 led to tumor shrinkage (3 mg/kg, 144.6% TGI, $P < .0001$).

Conclusions: OBI-999 significantly reduces Globo-H-positive TNBC tumor growth by inducing apoptosis. Our data justify clinical trials targeting Globo-H for patients with advanced TNBC (NCT04084366).

INFLUENCE OF STATINS ON PD-L1 EXPRESSION IN TRIPLE NEGATIVE BREAST CANCER

Sangeun Lee[1,2,3,4], Ju Hee Kim[4], A Young Park[1,2,3,4], Han-Byeol Lee[3,4,5], Wonshik Han[1,2,3,4,5,6]

[1]Seoul National Univ., College of Medicine Interdisciplinary Program in Cancer Biology, Korea, [2]Seoul National Univ., Integrated Major in Innovative Medical Science, Korea, [3]Seoul National Univ., Cancer Research Institute, Korea, [4]Seoul National Univ. Hospital, Biomedical Research Institute, Korea, [5]Seoul National Univ. College of Medicine, Department of Surgery, Korea, [6]Seoul National Univ., Genomic Medicine Institute, Medical Research Center, Korea

Background: In addition to the original purpose of statins as cholesterol-lowering drugs, they have pleiotropic effects including anti-tumor activity. Based on the fact that TNBC has increased expression of PD-L1, immunotherapeutic approaches are being developed. It has recently been proposed that statins have an impact on the PD-L1 expression in tumor cells, but it is unclear if statins influence PD-L1 expression in TNBC. Therefore, we examined the influence of statins on PD-L1 expression and basic anti-cancer effects in TNBC.

Methods: We used human TNBC cell lines and clinically approved statins. Flow cytometry, western blot, qRT-PCR, the Annexin V-PI assay, and transwell migration and invasion were carried out.

Result: Among thirteen TNBC cell lines, MDA-MB-231, HCC38, and HCC70 have high expression of PD-L1, and Hs578T and MDA-MB-468 have low expression of PD-L1. Statins decreased PD-L1 expression in high-expressing PD-L1 cell lines while increasing PD-L1 expression in low-expressing PD-L1 cell lines in a dose- and time-dependent manner. The phosphorylation of STAT3 showed the same tendency as changes in PD-L1 by statins. Inhibition of phosphorylation of AKT was observed in all the examined cell lines, regardless of PD-L1 changes by statins. Statins induced apoptosis and inhibited cell motility and EMT in MDA-MB-231.

Conclusions: Our findings show statins control PD-L1 expression via STAT3 signaling rather than AKT signaling. Further research is required to fully understand the molecular mechanism by which statins regulate the expression of PD-L1 in TNBC and to confirm the safety and efficacy of using statins in combination therapy with immune checkpoint inhibitors.

EFFECT OF PD-L1 EXPRESSION ABOUT IMMUNE CHECKPOINT INHIBITOR IN TRIPLE-NEGATIVE BREAST CANCER

A Young Park[1,2,3,4], Ju Hee Kim[3], Sangen Lee[1,2,3,4], Hong Kyu Kim[5], Han-Byoel Lee[2,3,5,6], Wonshik Han[1,2,3,4,5,6,7]

[1]Seoul National Univ. College of Medicine, Interdisciplinary Program in Cancer Biology, Korea, [2]Seoul National Univ. College of Medicine, Cancer Research Institute, Korea, [3]Seoul National Univ. Hospital, Biomedical Research Institute, Korea, [4]Seoul National Univ. College of Medicine, Integrated Major in Innovative Medical Science, Korea, [5]Seoul National Univ. Hospital, Department of Surgery, Korea, [6]Seoul National Univ. College of Medicine, Department of Surgery, Korea, [7]Seoul National Univ. College of Medicine, Genomic Medicine Institute, Medical Research Center, Korea

Background: Among breast cancers, only 20% of triple-negative breast cancer (TNBC) subtypes show a therapeutic effect to immunotherapy, but still many patients do not respond and have severe side effects. For this, we studied the effect of PD-L1 expression on the immune checkpoint inhibitor in TNBC.

Methods: Statistical analysis of actual breast cancer patients was conducted using the TCGA and METABRIC datasets. Association of breast cancer T stage and N stage according to PD-L1 mRNA expression was analyzed. To confirm the role of PD-L1 according to the difference in PD-L1 expression level, PD-L1 overexpressing breast cancer cell lines were established.

Result: We found that the expression of PD-L1 is high in the basal subtype of breast cancer. However, the relationship between T stage and N stage for PD-L1 was not statistically significant. To determine the functional importance of PD-L1 in breast cancer, we established 4T1-PD-L1-overexpressing breast cancer cell lines. We confirmed that overexpression of PD-L1 promotes cancer cell proliferation, migration, and invasion, but in the orthotopic tumor mouse model, there was no significant difference in tumor growth compared to the control group. However, we found a relationship between the anti-PD-L1 effect and PD-L1 expression.

Conclusions: We found a positive correlation between high PD-L1 expression in cancer cells and tumor growth, and anti-PD-L1 response according to PD-L1 expression was also observed. Our findings show that the expression level of PD-L1 in breast cancer has a significant effect on the immune checkpoint inhibitor effect. We need to further investigate the role of PD-L1 in breast cancer.

RESULTS OF THE FIRST MOBILE BUS MAMMOGRAPHY SCREENING FOR BREAST CANCER

Khiem Pham, Tung Nguyen

EMCAS Plastic Surgery Hospital, Department of Plastic Surgery, Vietnam

Background: There are several strategies to prevent breast cancer, including clinical examination, mammography, MRI scan, and gene test. The preventative campaign in Vietnam has not been carried out regularly and there is no established protocol. Patients with breast cancer frequently enter hospitals in the latter stages of the disease. In order to participate in the early detection of breast cancer, we decided on a cost-free surveillance bus as the best option given the local circumstances, including convenient access, parking space reservations, synchronized medical devices on board, processing information-communication to the public.

Methods: The mobile bus included a clinical examination, an ultrasound, and a SIEMENS mammography machine. We screened 400 DEUSCHE HAUS employees for breast cancer with the mammogram using three criteria: over age 40, prior fybroids or cysts, or a family history of breast cancer. We analyzed the results and informed the patients two days later whether they need further testing to confirm the diagnosis.

Result: Out of 400 respondents, 169 women meet the three criteria. We identified 8 cases requiring further testing to confirm the diagnosis. Our screening rate of 4.7% (8/169) for Vietnamese women is higher than that of previous literature, which is 0.26%.

Conclusions: The preliminary findings from the mobile bus screening for breast cancer in HCM City are encouraging. This community screening program will lessen hospital costs, patients' psychological suffering, and their financial burden. Future studies should test on a larger and more diverse population.

ANATOMICAL VIEW OF THORACODORSAL ARTERY VARIANTS USING COMPUTED TOMOGRAPHY ANGIOGRAPHY

Hyun Geun Cho[1], Byungju Kang[2], Jeong Yeop Ryu[1], Kang Young Choi[1], Jung Dug Yang[1], Ho Yun Chung[1], Byung Chae Cho[1], Jeeyeon Lee[2], Ho Yong Park[2], Joon Seok Lee[1]

[1]*Kyungpook National Univ. Hospital, Department of Plastic Surgery, Korea,*
[2]*Kyungpook National Univ. Hospital, Department of Surgery, Korea*

Background: The latissimus dorsi (LD) muscle has a dominant pedicle with one thoracodorsal artery and receives sufficient blood by segmental circulation through several perforators. Thus, it is widely used in various reconstructive surgeries. We are reporting on the patterns of the thoracodorsal artery analyzed by chest CT angiography.

Methods: We analyzed the preoperative chest CT angiography results of 350 patients scheduled to undergo LD flap breast reconstruction following complete mastectomy for breast cancer between October 2011 and October 2020.

Result: 700 blood vessels were classified according to the KNUPS TDA classification, 388, 126 , 91, 57, and 38 vessels were classified as Type I, II, III, IV, and V, respectively. Among 350 patients, 205 patients showed matching types for Lt. and Rt. vessels, whereas 145 patients showed mismatching types. For 205 patients with matching types, the distribution by type was 134, 30, 30, 7, and 4 patients with Type I, II, III, IV, and V, respectively. For 145 patients with mismatching types, the distribution by different combinations was 48, 25, 28, 19, 2, 9, 7, 3, 1, and 3 patients with Types I+II, I+III, I+IV, I+V, II+III, II+IV, II+V, III+IV, III+V, and IV+V, respectively.

Conclusions: While there is some diversity in the vascular anatomical structures of the LD flap, the dominant vessel can be found in a similar location in almost all cases and no flap had absence of a dominant vessel. Therefore, in surgical procedures using the thoracodorsal artery as the pedicle, preoperative radiological confirmation is not absolutely necessary; however, due to variants, performing the surgery with an understanding of this aspect should lead to good outcomes.

COMPARISON OF CONCORDANCE OF TUMOR SIZE MEASURED BY ULTRASONOGRAPHY, MRI, AND PATHOLOGY

Jaeyeon Woo[1], Sinae Kim[2], Seeyoun Lee[1], So-Youn Jung[1], Eun-Gyeong Lee[1], Ran Song[1], Youngmi Kwon[3], Yunju Kim[4], Bo Hwa Choi[4], Jai Hong Han[1]

[1]National Cancer Center, Department of Surgery, Korea, [2]Research Institute of National Cancer Center, Biostatics Collaboration Team, Korea, [3]National Cancer Center, Department of Pathology, Korea, [4]National Cancer Center, Department of Radiology, Korea

Background: In breast cancer, preoperative evaluation of tumor size is important in obtaining negative margins and oncoplastic surgery. Although there have been many studies comparing the accuracy of preoperative imaging modalities, each study has different results. In this study, we compared the tumor size measured by ultrasonography (USG), magnetic resonance imaging (MRI), and pathology.

Methods: We reviewed patients who had a single mass in USG and underwent surgery between March 2016 and February 2019. Patients with multiple lesions or positive surgical margins-, and those who had undergone neoadjuvant chemotherapy were excluded. For each examination, the largest diameter of the tumor was measured. Intraclass Correlation Coefficient (ICC) and Bland-Altman plot were used as statistical analyses to compare the concordance of tumor size.

Result: A total of 996 patients were analyzed and divided into subgroups according to menopausal status (premenopausal vs. postmenopausal), MRI features (mass vs. non-mass enhancement; NME), and pathological subtypes (ductal vs. lobular). In all patients, MRI (ICC: 0.721; 95% CI, 0.656-0.771) showed a higher concordance with pathologic than USG (ICC: 0.602; 95% CI, 0.560-0.641). In the Bland-Altman plot, USG showed that the larger the tumor size, the greater the difference from the pathologic, but the difference was relatively constant regardless of the tumor size in MRI. In subgroups, the postmenopausal and mass groups showed higher concordance than the others. In pathologic subtypes, USG showed higher concordance in ductal than lobular, whereas MRI showed the opposite result.

Conclusions: Since the tumor size concordance differs depending on the clinicopathologic characteristics of the patient, this should be considered in the surgical plan.

BREAST CANCER LITERACY AS A MEDIATOR OF THE RELATIONSHIP BETWEEN PERCEIVED SUSCEPTIBILITY, PERCEIVED BARRIERS, AND PERCEIVED STIGMA AND CLINICAL BREAST EXAMINATION UPTAKE AMONG WOMEN IN GHANA

Agani Afaya[1], Hyeonkyeong Lee[2], So Yoon Kim[3], Chang Gi Park[4], Min Kyeong Jang[1], Sue Kim[2]

[1]Yonsei Univ. College of Nursing, Department of Nursing, Korea, [2]Yonsei Univ. College of Nursing, Mo-im Kim Nursing Research Institute, Korea, [3]Yonsei Univ. College of Medicine, Department of Medical Law and Ethics, Korea, [4]College of Nursing, Univ. of Illinois, Department of Population Nursing Science, U.S.A.

Background: Previous research has identified breast cancer (BC) awareness/literacy as a significant antecedent to BC screening uptake among women. Clinical breast examination (CBE) is the most accessible BC screening method in Ghana, yet it is underused. This study aimed to examine BC literacy as a mediator of the relationship between BC perceptions and the uptake of CBE among women in Ghana.

Methods: Previous research has identified BC awareness/literacy as a significant antecedent to BC screening uptake among women. CBE is the most accessible BC screening method in Ghana, yet it is underused. This study aimed to examine BC literacy as a mediator of the relationship between BC perceptions and the uptake of CBE among women in Ghana.

Result: The level of BC literacy was somewhat low (Mean = 3.65, ± SD = .33). The mediation analysis showed significant direct and indirect effects of women's perception of BC on CBE uptake through women's BC literacy. The association between BC perceptions and CBE uptake remained significant after controlling for BC literacy, indicating that BC literacy strongly and partially mediated the effect of perceived barriers (B = -0.19, SE = 0.06, 95%CI [-0.34, -0.07]), perceived susceptibility (B = 0.07 SE = 0.02, 95%CI [0.02, 0.13]), and perceived stigma (B = 0.70, SE = 0.19, 95%CI [0.34, 1.13]) on CBE uptake.

Conclusions: As BC literacy mediates the effects of BC perception on CBE uptake in Ghanaian women, clinicians and policymakers should consider implementing public health intervention programs that target increasing Ghanaian women's BC literacy in order to improve CBE uptake.

GENE MUTATION DIAGNOSIS BY DETECTING CIRCULATING TUMOR DNA USING NOBLE CRISPR/CAS9 SYSTEM IN BREAST CANCER PATIENTS

Hong-Kyu Kim[1], Hamin Jeong[2], Changjin Lim[1], Eunhye Kang[1], Ji-Jung Jung[1], Hyun Su Yeoh[1], Hyunjeung Choi[3], Sunghyeok Ye[3], Junseok W. Hur[3], Han-Byoel Lee[1], Hyeong-Gon Moon[1], Wonshik Han[1]

[1]Seoul National Univ. Hospital, Department of Surgery, Korea, [2]Seoul National Univ. Hospital, Biomedical Research Institute, Korea, [3]GeneCker, Inc., Korea

Background: Due to the limitations of tissue biopsy, clinical demand for liquid biopsy has increased. However, the limitation of low-frequency mutations in circulating tumor DNA (ctDNA) makes it difficult to utilize it. This study aims to investigate the potential of enhancing the sensitivity of liquid biopsy in early breast cancer by utilizing a novel CRISPR/Cas9 system.

Methods: High fidelity CRISPR/Cas9 system (GC-Cas9) engineered by GeneCker is capable of effectively detecting single-base mutations at all 20 positions within a single guide RNA target sequence. In this study, we investigated whether GC-Cas9 could enhance the sensitivity of liquid biopsy in early breast cancer patients to a level comparable to that of tissue biopsy.

Result: We extracted somatic mutations with high frequency from the COSMIC database and constructed mutation clusters based on genomic coordinates to create a panel. From these clusters, we identified 16 clusters that can be targeted by a single gRNA, consisting of genes such as PIK3CA, TP53, ERBB2, ESR1, GATA3, CDH1, KRAS, PTEN, SF3B1, and AKT1. We compared tissue genomic DNA and plasma cfDNA samples from four stage II breast cancer patients and found that some mutations were not detectable in the plasma samples without enrichment, but were detected after enrichment with GC-Cas9 in three cases. One case had no driver mutation.

Conclusions: This study demonstrates the potential for improving the clinical utility of liquid biopsy in the diagnosis of breast cancer. The mutation clusters we identified through the COSMIC database provide a basis for further investigation of other cancer types with a similar mutational profile.

COMPARISON OF LONG TERM ONCOLOGIC OUTCOME OF SENTINEL LYMPH NODE MAPPING METHODS, DYE-ONLY VERSUS DYE AND RADIOISOTOPE IN BREAST CANCER FOLLOWING NEOADJUVANT CHEMOTHERAPY

Changjin Lim, Eunhye Kang, Ji-Jung Jung, Hyun Su Yeoh, Jung Whan Chun, Hong-Kyu Kim, Han-Byoel Lee, Hyeong-Gon Moon, Wonshik Han

Seoul National Univ. Hospital, Department of Surgery, Korea

Background: In patients who received neoadjuvant chemotherapy (NCT), false-negative rate of sentinel lymph node biopsy (SLNB) is higher than in upfront surgery. It has been suggested that dual mapping method using dye and isotope (DUAL) could reduce false-negative rate compared with dye-only method (DYE) in NCT patients. However, long term outcome of either method is unclear.

Methods: This retrospective single-institution cohort study included 2,175 patients who underwent breast cancer surgery with SLNB after NCT. Indigo carmine was used for the dye method and Tc99m-antimony trisulfate for isotope. To compare long term outcomes, pathologic N0 patients were selected from both groups and 1:2 propensity score matching (PSM) was performed with matching variables of clinical T and N stage, and pathologic T stage (DYE, 280; DUAL, 560).

Result: The median follow-up duration was 6.3 years. There was no significant difference in patient characteristics between the two groups including clinical T stage, percentage of pCR, and tumor subtype. The median number of harvested sentinel nodes was 6.70 and 6.67 in DYE and DUAL group, respectively ($p = 0.908$). Multivariate logistic regression revealed that the mapping methods were not significantly associated with lymph node-positive rate ($p = 0.527$). After PSM, the 5-year axillary recurrence rate (DYE 3.3% vs. DUAL 2.8%; $p = 0.831$), and 5-year disease-free survival (DYE 88.4% vs. DUAL 89.1%; $p = 0.870$) were similar between the two groups.

Conclusions: Dye alone for SLNB was not inferior to dual mapping regarding long term oncological outcome in breast cancer patients who received NCT.

THE EFFICIENCY OF ULTRASOUND-GUIDED VACUUM-ASSISTED BREAST BIOPSY (VABB) IN THE DIAGNOSIS AND TREATMENT OF FOCAL LESIONS OF THE BREAST AT THE BREAST CENTER OF VINMEC TIMES CITY INTERNATIONAL HOSPITAL

Huong Nguyen-Thu, Anh Nguyen-Thi-Ngoc, Tien Nguyen-Cong

Vinmec Times City International Hospital, Department of Radiology, Vietnam

Background: The purpose of this study is to investigate the efficiency of ultrasound-guided vacuum-assisted breast biopsy (VABB) in the diagnosis and treatment of focal lesions of the breast in our institution.

Methods: In the period January to December 2022, 435 lesions classifieds B3 were removed and 23 lesions classifieds B4 were biopsied by VABB (428 local anesthesia and 30 anesthesia). All patients with diagnosed cancer underwent surgery. The patients with histopathological benign lesions were under follow-up by ultrasound (1 month, 3 months, and 6 months).

Result: Specimens for histopathological examination were obtained from 435 lesions, 100% benign lesions (380 fibroadenomas, 29 fibrocystic changes, 8 usual ductal hyperplasia, 5 fibroadenomas with intraductal papilloma, 3 fibroadenomas with atypical ductal hyperplasia, 7 intraductal papilloma, 2 phyllodes tumors, 1 granulomatous inflammation). In 23 lesions that were biopsied, 8/23 (34.8%) were malignant lesions (5 fibrocystic changes, 5 fibroadenomas, 2 chronic inflammations, 3 atypical lobular hyperplasia, 8 infiltrating ductal carcinoma). 435/435 lesions (100%) were entirely removed during the VABB. One week after VABB, the hematoma of 25/435 (5.7%) patients needed aspiration (aspiration if with the largest diameter of the hematoma ≥ 30 mm), the mean diameters of hematoma in those patients were 34.2 mm (30–58.5mm), 100% patients no need analgesia after intervention (VAS 0-2 points).

Conclusions: VABB is a minimally invasive and efficient method for the diagnosis and treatment of breast focal lesions. It can be one method alternative to an open surgical biopsy.

ADENOMYOEPITHELIOMA OF THE RIGHT BREAST: A CASE REPORT

Justine Vigo[1], Raphael Simpliciano[1], Celestine Marie Trinidad[1], Patriccia Anne Mae Paulino[2], Nicola Raphaela Tison[2]

[1]*Univ. of Santo Tomas Hospital, Department of Pathology, Philippines,*
[2]*Univ. of Santo Tomas Hospital, Department of Surgery, Philippines*

Background: Among the breast tumors, adenomyoepitheliomas (AMEs) represent one of the rarest entities. It is a biphasic tumor with epithelial and myoepithelial components with benign to low malignant potential. Due to their rarity, their non-specific and variable clinical and radiographic presentation, diagnosis relies on histomorphology. Treatment would encompass wide surgical excision with negative margins.

Methods: This is a case of a 77-year-old female presenting with a movable, non-tender, right breast mass in the periareolar region. Mammography and ultrasound showed a well-marginated fairly dense mass and a well marginated lobulated heterogeneous solid mass located at the retro-areloar area, respectively. Core needle biopsy of the mass revealed ductal epithelial proliferation with tubular features. Mastectomy was performed.

Result: Histomorphologic findings disclosed a well-circumscribed and lobulated proliferation of epithelial cells arranged in sheets, tubular structures, and focal papillary patterns. The tubular structures are seen to be lined by a double layer of inner round to ovoid cells and abluminal round to spindle-shaped cells. The cells exhibited diffuse expression of cytokeratin in luminal cells and expression of SMA and p63 in the outer myoepithelial cells. The case was signed out as a case of AME of the breast.

Conclusions: AME is a rare and entity which radiologists, surgeons, and pathologists should be aware of. The possibility of malignant transformation in this generally benign condition should always be kept in mind amidst making the diagnosis and treatment planning. Excisional lumpectomy is usually the treatment of choice for small, benign forms while mastectomy is more recommended for malignant forms of AME.

DIAGNOSTIC ACCURACY OF A THREE-PROTEIN SIGNATURE IN WOMEN WITH SUSPICIOUS BREAST LESIONS: A MULTICENTER PROSPECTIVE TRIAL

Eun-Shin Lee[1], Yumi Kim[2], Dong-Young Noh[2], Hyeong-Gon Moon[3]

[1]Korea Univ. Anam Hospital, Department of Surgery, Korea, [2]CHA Gangnam Medical Center, Department of Surgery, Korea, [3]Seoul National Univ. College of Medicine, Department of Surgery, Korea

Background: Mammography screening have been proven to detect breast cancers in early stage and reduce mortality, although it has shown low accuracy in young women or women with dense breasts. Blood-based diagnostic tool might overcome the drawbacks of mammography. This prospective study assessed the diagnostic performance of three-protein signature in patients with moderately to highly suspicious lesion.

Methods: Between August, 2019 and September, 2020, the three-protein signature values were prospectively obtained using blood from women with moderately to highly suspicious lesion for breast malignancy before their tumor biopsy. Additionally, the blood samples of the women who had clear or benign mammography were collected for the assay.

Result: This trial (MAST; KCT0004847) was a prospective multicenter observational trial. Three-protein signature values were obtained using serum and plasma from women with suspicious lesions for breast malignancy before tumor biopsy. Additionally, blood samples from women who underwent clear or benign mammography were collected for the assays. Among 642 participants, the sensitivity, specificity, and overall accuracy values of the three-protein signature were 74.4%, 66.9%, and 70.6%, respectively, and the concordance index was 0.698 (95% C.I. 0.656, 0.739). The sensitivity of the three-protein signature was consistent across different cancer stages and subtypes. The diagnostic performance was not biased by the demographic and medical features of the participants.

Conclusions: The present trial showed an accuracy of 70.6% for the three-protein signature. Considering the value of blood-based biomarkers for the early detection of breast malignancies, further evaluation of this proteomic assay is warranted in larger, population-level trials.

CLASSIFICATION OF MOLECULAR SUBTYPES OF BREAST CANCER IN WHOLE-SLIDE HISTOPATHOLOGICAL IMAGES USING A DEEP LEARNING ALGORITHM

Hyung Suk Kim[1], Kyueng-Whan Min[2], Jong Soo Kim[3]

[1]Hanyang Univ. College of Medicine, Department of Surgery, Korea, [2]Hanyang Univ. Medical Center, Department of Pathology, Korea, [3]Hanyang Univ. College of Medicine, Institute for Software Convergence, Hanyang Univ., Korea

Background: Classification of molecular subtypes of breast cancer is widely used in clinical decision-making, leading to different treatment responses and clinical outcomes. We classified molecular subtypes using a novel deep learning algorithm in whole-slide histopathological images (WSIs) with invasive ductal carcinoma of the breast.

Methods: We obtained 1,094 breast cancer cases with available hematoxylin and eosin-stained WSIs from the TCGA database. We applied a new deep learning algorithm for artificial neural networks (ANNs) that is completely different from the back-propagation method developed in previous studies.

Result: Our model based on the ANN algorithm had an accuracy of 67.8% for all datasets (training and testing), and the area under the receiver operating characteristic curve was 0.819 when classifying molecular subtypes of breast cancer. In approximately 30% of cases, the molecular subtype did not reflect the unique histological subtype, which lowered the accuracy. The set revealed relatively high sensitivity (70.5%) and specificity (84.4%).

Conclusions: Our approach involving this ANN model has favorable diagnostic performance for molecular classification of breast cancer based on WSIs and could provide reliable results for planning treatment strategies.

EVALUATING THE IMPACT OF CLINICAL FACTORS ON THE DIAGNOSTIC PERFORMANCE OF DIFFUSE OPTICAL SPECTROSCOPIC IMAGING FOR BREAST CANCER

Yeji Kwon, Min Jung Kim

Severance Hospital, Department of Radiology, Korea

Background: To compare the diagnostic performance of diffuse optical spectroscopic imaging/discrete multi-wavelength near-infrared spectrum (DOSI/DMW-NIRS) for breast malignancy according to clinical factors.

Methods: This study was approved by the Institutional Review Board of Severance Hospital. Informed consent was obtained from all participants. A total of 62 women with 62 breast lesions (37 malignant, 25 benign) biopsied under US guidance were included. DOSI/DMW-NIRS was used to quantify the chromophores (HbO2, HHb, THC, StO2, water, lipid, and TOI) of lesions and then the computed chromophore ratios were compared to those of contralateral normal breasts. Lesions were categorized by demographic (age, BMI, bra cup size, and menstrual cycle phase) and sonographic variables (tumor diameter, depth, distance from nipple, vascularity, breast thickness, and BI-RADS category), and areas under the curve (AUCs) were compared between subgroups.

Result: TOI showed the highest AUC value (0.904, 95%CI:0.831-0.977) for diagnosing breast malignancy among the 7 chromophore values, with no significant difference in diagnostic performance among all subgroups ($p > 0.05$). The diagnostic performance of water differed according to breast thickness ($p = 0.033$) and distance from nipple ($p = 0.011$). The diagnostic performance of THC and HbO2 differed according to BMI ($p = 0.0119$ and 0.0056, respectively) and menstrual cycle ($p = 0.011$ and 0.006, respectively).

Conclusions: The TOI ratio evaluated with DOSI/DMW-NIRS shows strong diagnostic performance regardless of demographic and sonographic parameters, suggesting that it has the potential to be universally applied to the general population.

PREVALENCE OF PATHOGENIC BRCA 1/2 GERMLINE MUTATION ACCORDING TO PD-L1 STATUS IN EARLY TRIPLE-NEGATIVE BREAST CANCER

Yoonwon Kook, Seung Ho Baek, Min Ji Kim, Jung Hyun Kim, Sohyun Moon, Seung Eun Lee, Sung Gwe Ahn, Joon Jeong, Soong June Bae

Gangnam Severance Hospital, Department of Surgery, Korea

Background: Clinical activity of immune-checkpoint inhibitors (ICIs) has been confirmed in triple-negative breast cancer (TNBC) with PD-L1 expression while patients harboring pathogenic BRCA 1/2 germline mutation can benefit from PARP inhibitors. However, there is limited data on the incidence of pathogenic BRCA 1/2 germline mutation according to PD-L1 status in early TNBC.

Methods: In this study, we retrospectively included 209 patients with early TNBC for whom tumor-infiltrating lymphocytes (TILs), PD-L1 status (VENTANA SP142 PD-L1 IHC assay), and germline BRCA status were available. We defined high TILs as ≥ 20% and positive PD-L1 expression as ≥ 1% of tumor area.

Result: A total of 208 patients, 29 (13.9%) had pathogenic BRCA 1/2 germline mutation (22 BRCA1-mutation, 7 BRCA2-mutation), 107 (51.4%) had high TILs, and 80 (38.3%) had positive PD-L1 expression. There was no difference in the prevalence of pathogenic BRCA 1/2 germline mutation according to PD-L1 status: it was confirmed in 10 of 80 (12.5%) in patients with positive PD-L1 expression, and 19 of 128 (14.8%) in patients with negative PD-L1 expression ($p = 0.635$). The incidence of pathogenic BRCA 1/2 germline mutation was similar according to TILs: 14.9% (15 of 101) in low TILs, and 13.1% (14 of 107) in high TILs ($p = 0.713$).

Conclusions: The prevalence of pathogenic BRCA germline mutation was not associated with PD-L1 and TILs status in early TNBC. Future work is needed to determine which treatment outstands among the ICIs, PARP inhibitors, or combination therapy in patients with TNBC who have both positive PD-L1 expression and pathogenic BRCA germline mutation.

SILICONE LYMPHADENOPATHY OF THE AXILLA: A POTENTAL FOR MISDIAGNOSIS AS METASTATIC CARCINOMA ON FINE NEEDLE ASPIRATION CYTOLOGY

Ji Shin Lee[1], Nah Ihm Kim[1], Min Ho Park[2]

[1]*Chonnam National Univ. Hwasun Hospital, Department of Pathology, Korea,*
[2]*Chonnam National Univ. Hwasun Hospital, Department of Surgery, Korea*

Background: Axillary silicone lymphadenopathy is a well-known rare complication of breast implant insertion. If silicone lymphadenopathy is not considered in the initial differential diagnosis due to lack of a history of silicone breast implants, it may be misdiagnosed as malignant lymphadenopathy.

Methods: We report a case of axillary silicone lymphadenopathy, initially misdiagnosed as a metastatic carcinoma by fine-needle aspiration cytology (FNAC).

Result: A 45-year-old woman presented to local clinic complaining of a mass, located in the right axillary area. The axillary mas was diagnosed as metastatic carcinoma with atypical clear cells having clear vacuoles by FNAC. She referred to our clinics. Ultrasound guided FNAC and core-needle biopsy were performed on right axillary lymph node. Cytological examination showed several clusters and single cells with microvacuoles in a background of lymphocytes. The microvacuoles compressed the nuclei and gave the impression of a signet ring cell or a lipoblast. The vacuoles had refractile, non-birefringent, and colorless particles. Multinucleate giant cells containing vacuoles were frequently observed. The histiocytic nature of epithelioid cells and multinucleate giant cells was confirmed by their positive reaction for CD68. These cytological and histological findings were typical of a silicone lymphadenopathy. She had undergone bilateral breast augmentation with a silicone prosthesis 10 years previously for cosmetic purposes. Subsequent ultrasonographic and MRI showed bilateral intracapsular rupture of the breast implants and several enlarged lymph nodes in the both axillae.

Conclusions: Cytopathologists need to know the unique cytological appearance of silicone lymphadenopathy, which is sufficiently characteristic to consider breast implant history.

HEALTH-SEEKING BEHAVIOR RETURNING TO NORMALCY OVERCOMING COVID-19 THREAT IN BREAST CANCER

Eun-Gyeong Lee[1], Yireh Han[3], Dong-Eun Lee[4], Hyeong-Gon Moon[5,6], Hyoung Won Koh[7], Eun-Kyu Kim[7], So-Youn Jung[1,2]

[1]National Cancer Center, Center of Breast and Thyroid Cancer, Korea, [2]National Cancer Center, Cancer Healthcare Research Branch, Korea, [3]Korea Cancer Center Hospital, Department of Surgery, Korea, [4]National Cancer Center, Research Core Center, Korea, [5]Seoul National Univ. College of Medicine, Department of Surgery, Korea, [6]Seoul National Univ., Cancer Research Institute, Korea, [7]Seoul National Univ. Bundang Hospital, Department of Surgery, Korea

Background: The coronavirus disease 2019 (COVID-19) outbreak has significantly impacted the diagnosis and treatment of breast cancer. Our study investigated the change in diagnosis and treatment of breast cancer with the progress of COVID-19 pandemic.

Methods: The study group comprised 6514 recently diagnosed breast cancer patients between January 1, 2019, and February 28, 2021. The patients were divided into two groups: pre-COVID-19 period (3182; January 2019 to December 2019) and COVID-19 pandemic period (3332; January 2020 to February 2021). Clinicopathological information related to the first treatment after breast cancer diagnosis was retrospectively collected and analyzed in the two groups.

Result: Among the 6514 breast cancer patients, 3182 were in the pre-COVID-19 period and 3332 were in the COVID-19 pandemic period. According to our evaluation, the least breast cancer diagnosis (21.8%) was seen in the first quarter of 2020. The diagnosis increased gradually except for the fourth quarter in 2020. While early-stage breast cancer was diagnosed 1601 (48.05%) during the COVID-19 pandemic ($p = 0.001$), the number of surgical treatments increased 4.64% ($p < 0.000$), and the treatment time was slightly shorter 2 days ($p = 0.001$). The breast cancer subtype distribution was not statistically different between the pre-COVID-19 and COVID-19 period groups.

Conclusions: In the early stages of the pandemic, the number of breast cancer cases temporarily decreased; however, they stabilized soon, and no significant differences could be identified in the diagnosis and treatment when compared to the period before the pandemic.

SHOULD A BRCA GERMLINE TEST BE PERFORMED IN ALL TRIPLE-NEGATIVE BREAST CANCER PATIENTS UNDER THE AGE OF 60?

Seung Ho Baek[1,2], Soong June Bae[1,2], Yoonwon Kook[1,2], Ji Soo Jang[1,2], Sohyun Moon[1,2], Minji Kim[1,2], Seungeun Lee[1,2], Jung Hyun Kim[1,2], Sung Gwe Ahn[1,2], Joon Jeong[1,2]

[1]*Gangnam Severance Hospital, Department of Surgery, Korea,*
[2]*Yonsei Univ. College of Medicine, Institute for Breast Cancer Precesion Medicine, Korea*

Background: As the criterion for BRCA germline test in Triple-negative breast cancer (TNBC) patients was extended to 60 years of age, the BRCA test implementation rate has increased dramatically. However, whether these extended criteria really increased BRCA germline mutation detection is controversial. We aim to confirm the effectiveness of extended criteria of BRCA germline test in the real world.

Methods: After the test criteria were extended in 2020, there are 883 patients who underwent the BRCA germline test in the Gangnam Severance Hospital. Of these, two hundred and fifteen patients checked the BRCA mutation because they were diagnosed with TNBC. We verified the prevalence of BRCA germline mutation in TNBC subgroup according to age at diagnosis.

Result: Among those who underwent BRCA germline test after diagnosed as TNBC, 28 patients were confirmed to have the BRCA mutation (13.02%). When we divided this group by age, the prevalence of BRCA mutation was 11.94% and 8.42% of those diagnosis age was 41-50 and 51-60 years old. Among these, the prevalence of BRCA mutation in the group for which TNBC was the only criterion for the BRCA test was 6.82% (3/44) and 5.8% (4/69), respectively.

Conclusions: In this cohort, the prevalence of the BRCA germline mutation in patients whose age of diagnosis was between 41 and 60 and who did not meet any other BRCA test criteria other than TNBC was not higher than that of all breast cancer population. Through the further analysis of this study, we could pick up a new group that should undergo BRCA germline test.

EFFECTS OF AI MAMMOGRAPHY FOR WOMEN YOUNGER THAN 40 OF AGE WITH HETEROGENEOUSLY DENSE BREAST

Azzaya Terbish[1], Shirnen Odnasan[2], Odbayar Barkhas[3]

[1]Breast Clinic of Ulaanbaatar, Department of Radiology, Mongolia, [2]Breast clinic of Ulaanbaatar, Department of Surgery, Mongolia, [3]National Cancer Center of Mongolia, Department of Surgery, Mongolia

Background: Breast cancer is 4th most common primary cancer among women in Mongolia, about 250-300 new cancer patients are reported every year and 76% of the total patients are over the age of 40, leading to a 5 year of survival rate of 57%. The main reason behind late diagnoses and stages are largely due to lack of availability of mammography and early screening program. We examined potential change in cancer detection using an AI mammography for women younger than 40 of age with heterogeneously dense breast to improve screening throughout the country.

Methods: Total of 2,450 women are included in this study, 41 were diagnosed with breast cancer. All patients had complete four-six view, digital mammography-grams were acquired using Lunit Insight AI software.

Result: By statistics of American Cancer Society, about 20–30% of women with breast cancer have tumors that are missed by mammogram screening. Women with high density breast and fibrotic tissue, there could be a high incidence of un-detecting suspicious lesions. However, AI offers the opportunity to mark a better distinction between normal and cancerous lesions regardless of the breast density and tissue which minimizes the risk of missing early cancers for radiologist.

Conclusions: AI performed better in detecting malignant lesions with heterogeneously dense breast. AI proved its value as second reader. This will help to increase early detection rate for younger women and lowers breast cancer mortality in Mongolia. However, mammography technicians play very important role since the quality of mammograms are extremely essential for AI to perform as well.

BREAST METASTASIS FROM ENDOMETRIAL CLEAR CELL CARCINOMA: A CASE REPORT AND REVIEW OF THE LITERATURE

Li En Amadora Choo, Llewellyn Shao-Jen Sim, Kesavan Sittampalam, Wei Chong Tan, Amos Zhi En Tay, Ravichandran Nadarajah, Veronique Kiak Mien Tan, Yirong Sim

[1]*Singapore General Hospital, Department of Surgery, Singapore*

Background: Metastasis to the breast from extra-mammary malignancies are rare, accounting for less than 1% of all breast cancers. Endometrial cancer, a common gynecological malignancy, often spreads to the pelvis, abdominal lymph nodes, peritoneum or the lungs. Endometrial metastasis to the breast is extremely rare, and while there have been isolated case reports of endometrial serous carcinoma with breast metastasis, it has not been reported in the case of clear cell carcinoma.

Methods: We present a rare case of a 70 year old Chinese lady who had a metastatic endometrial clear cell carcinoma with metastasis to the breast, mimicking an inflammatory breast cancer clinically. We reviewed the current literature and describe the challenges in differentiating primary from metastatic breast lesions, as well as clinical, radiological and histopathological features that may help to differentiate the two.

Result: Tumour metastasis to the breast via lymphatic or hematogenous route can affect their radiological features: the former mimicking inflammatory breast cancer and the latter with features similar to benign breast lesions. Regardless, histological features with immunohistochemical staining is still the gold standard in diagnosing metastatic breast lesions and determining their tissue of origin.

Conclusions: Breast metastases from extra-mammary malignancies are uncommon and it is even rarer for endometrial clear cell carcinoma to spread to the breast. Nonetheless, this case highlights the importance of keeping an open mind and engaging a multidisciplinary team for the care of complex patients.

BREAST CANCER METASTASIS TO UTERUS DURING ADJUVANT TAMOXIFEN TREATMENT: A CASE REPORT AND REVIEW OF THE LITERATURE

Jong-Min Baek, Ohjoon Kwon, Min Jong Song, Tae Jung Kim

The Catholic Univ. of Korea, Yeouido St. Mary's Hospital, Department of Surgery, Korea

Background: Uterine metastases from breast cancers are rare. But breast cancer is the most frequent primary site of metastasis to the uterine corpus. We report a rare case of uterine metastasis from invasive ductal carcinoma with review of the literature.

Methods: A 50-year-old premenopausal woman was diagnosed with uterine metastasis from breast cancer. Five years prior to her presentation, she was diagnosed with breast cancer and underwent a partial resection of her right breast for stage IIIA invasive ductal carcinoma. She underwent adjuvant chemotherapy, radiotherapy, and under five years of tamoxifen therapy. She presented with a incidental lung mass under follow-up and high SUV uptake was seen on uterine myometrium. She was diagnosed as primary lung cancer. Lobectomy for upper lobe of left lung was completed and biopsy for uterus myometrium was done. Lung cancer was diagnosed as stage I and there was no adjuvant therapy. Pathology for uterus was confirmed as metastatic carcinoma from invasive breast ductal carcinoma. She underwent a total hysterectomy with bilateral salpingo-oophorectomy.

Result: Lung cancer was diagnosed as stage I and there was no adjuvant therapy. Pathology for uterus was confirmed as metastatic carcinoma from invasive breast ductal carcinoma. She underwent a total hysterectomy with bilateral salpingo-oophorectomy. A histopathological examination, including immunohistochemistry, confirmed metastatic invasive ductal carcinoma, infiltrating uterine myometrium. The CDK4/6 inhibitor with aromatase inhibitor treatment was started.

Conclusions: We report a rare metastatic pattern of invasive ductal carcinoma with review of uterine metastasis from breast cancer.

COMPARING OUTCOMES FOLLOWING BREAST CONSERVING SURGERY WITH RADIOTHERAPY VERSUS MASTECTOMY IN PATIENTS WITH PAGET'S DISEASE OF THE BREAST (PDB): A SYSTEMATIC REVIEW AND META-ANALYSIS

Serene Si Ning Goh, Nicolas Li Xun Syn, Rui En, Cheryl Lim, Celene Wei Qi Ng

National Univ. of Singapore, Department of Surgery, Singapore

Background: Our study provides an updated systematic review and meta-analysis comparing outcomes following breast conserving surgery (BCS) followed by radiotherapy (RT) versus mastectomy (TM) in the treatment of PDB.

Methods: Studies prior to May 2021 comparing mastectomy versus BCS and RT for PDB were included. Primary outcomes were overall survival (OS) and local recurrence (LR). As the prognosis of PDB-DCIS and PDB-IDC differs, they were analyzed separately. Meta-regression was utilized to adjust for imbalance in proportion of IDC among patients selected to undergo BCS or mastectomy.

Result: The pooled hazard ratio (HR) for OS for BCS with RT versus mastectomy was 0.68 (0.45, 1.01). The pooled relative risk (RR) for LR for BCS versus mastectomy was 2.01 (1.12, 3.60). The adjusted HR for BCS with or without RT vs. mastectomy for patients with PDB-DCIS is 0.28 (0.22-0.36) and 0.14 (0.10, 0.20) respectively. The adjusted HR for BCS alone with or without RT vs. mastectomy for patients with PDB-IDC is 1.64 (1.04, 2.58) and 0.84 (0.57, 1.25) respectively. The adjusted RR for LR of patients with DCIS who underwent BCS with or without RT as compared to mastectomy were 0.72 (0.11,4.5) and 1.38 (0.09, 21.2) respectively. The adjusted RR for LR for patients with PDB-IDC who underwent BCS with or without RT as compared to mastectomy was 26.8 (1.6, 456) and 51.8 (6.8, 391).

Conclusions: For PDB-DCIS, BCS with RT has comparable LR and OS rates compared to mastectomy. For PDB-IDC, BCS with RT has higher LR rates but comparable OS rates compared to mastectomy.

SINGLE AXILLARY INCISION ENDOSCOPIC ASSISTED NIPPLE-SPARING MASTECTOMY WITH AUTOLOGOUS RECONSTRUCTION IN EARLY BREAST CANCER PATIENTS: PRELIMINARY EXPERIENCE AND RESULT

Hsu-Huan Chou[1], Hsiu-Pei Tsai[1], Ming-Hui Cheng[2], Jung-Ju Huang[2], Hui-Yu Ho[1], Wen-Ling Kuo[1], Chi-Chang Yu[1], Shih-Che Shen[1], Chia-Hui Chu[1], Shin-Cheh Chen[1]

[1]*Linkou Chang Gung Memorial Hospital, Department of General Surgery, Taiwan,*
[2]*Linkou Chang Gung Memorial Hospital, Department of Plastic Surgery, Taiwan*

Background: The aim of the study is to investigate the feasibility and short term of the peri-operative outcomes of single axillary incision endoscopic assisted nipple-sparing mastectomy (SAIE-NSM) with autologous reconstruction in early breast cancer patients.

Methods: We retrospectively reviewed 43 patients from 2018 to 2022 receiving SAIE-NSM at Linkou Chang Gung Memorial Hospital. Four procedures of contralateral prophylactic mastectomy (CPM) were included and total of 46 breast surgery were analyzed. The peri-operative and short term oncological outcomes including after SAIE-NSM and autologous reconstruction were collected.

Result: Among all breast procedures, the overall complication rate was 26.1%. Twelve of 46 SAIE-NSM procedures combined with autologous reconstruction and deep inferior epigastric artery perforator (DIEP) flap were performed in nine breasts including one bilateral seperated DIEP reconstruction. One profunda artery perforator (PAP) flap was performed. The recipient's vessels were anastomosed to thoracodorsal vessels via an axillary wound. There was no significant difference in terms of the complication rate in the autologous reconstruction group (25%) and in implant or tissue expander-based reconstruction (24.1%). There were 3 complications of 12 SAIE-NSM with autologous reconstructions, 2 of 3 complications were the loss of DIEP due to repeat thrombus which not related to mastectomy and the last one was nipple ischemia. No nipple loss was found in autologous reconstruction procedures. The median follow-up time is 20.0 months. There was no locoregional recurrence, distant metastasis or any deaths.

Conclusions: Single axillary incision endoscopic assisted nipple-sparing mastectomy with autologous reconstruction was a feasible and safe procedure with similar complication rates compared with implant-based reconstruction.

SAFETY OUTCOMES OF ADVANCED ENERGY DEVICES IN BREAST AND AXILLARY LYMPH-NODE SURGERY: A SINGLE-CENTER EXPERIENCE

Young-Jin Lee, Young-Won Lee, Tae-Kyung Yoo, Sae Byul Lee, Jisun Kim, Il Yong Chung, Hee Jeong Kim, Jong Won Lee, Byung Ho Son, Beom Seok Ko

ASAN Medical Center, Department of Surgery, Korea

Background: The Harmonic Scalpel (HS) is a advanced energy device. There are limited data on its use in sentinel lymph-node biopsy (SNB) and axillary lymph-node dissection (ALND) followed by mastectomy and breast reconstruction. The aim of this study was to verify safety outcomes in patients undergoing breast and axillary surgery with HS.

Methods: We retrospectively analyzed the safety outcomes of 509 patients who underwent mastectomy and reconstruction with SNB or ALND with HS. We compare two groups of patients with less than 5 lymph nodes retrieved and with more than 6 nodes. The primary outcome measure was the surgical complications (post-operative bleeding, hematoma, infection, skin necrosis). Secondary outcome measures evaluated were total operation time, hospital days, readmission, Jackson-Pratt (JP) drain tube placement day, drain amount in the first 3 days, and aspiration after discharge.

Result: There were 273 patients in less than 5 lymph nodes group and 236 patients in more than 6 lymph nodes group. Surgical complications were not significantly different between two groups (2 versus 7 cases, $P = .057$). There were statistically significant differences in drain amount in the first 3 days (414ml versus 460ml, $P = .038$) and total operation time (251 hours versus 277 hours, $P = .020$) observed between two groups. There was equivalent rate of hospital days ($P = .154$), JP placement day ($P = .498$), readmission ($P = .772$) and seroma aspiration at clinic ($P = .865$).

Conclusions: This study's findings suggest that there is no difference in the safety outcomes between the two groups with the use of advanced energy device for breast cancer surgery with axillary approach.

LYMPHOVASCULAR INVASION AS A PROGNOSTIC FACTOR IN BREAST CANCER: INDEPENDENT FROM NODE METASTASIS AND MOLECULAR SUBTYPES

Suk Jun Lee

Yonsei Univ. College of Medicine, Department of Surgery, Korea

Background: Lymphovascular invasion (LVI) is a well-known poor prognostic factor in early breast cancer. However, the impact of LVI in association with breast cancer subtypes and node status remains unknown. In this study, we aim to evaluate the clinical significance of LVI on recurrence and long-term survival in patients with early breast cancer by comparing groups according to subtypes and node status.

Methods: We retrospectively reviewed medical records of 14,456 breast cancer patients who underwent breast cancer surgery between January 2010 and December 2017. Data on patient and clinicopathological information were collected. Patients were classified as luminal A, luminal B, HER2-positive and triple negative breast cancer (TNBC) according to the St. Gallen consensus guideline. Primary endpoint was disease-free survival (DFS) and overall survival (OS), and univariable and multivariable analyses were performed to identify prognostic factors related to DFS and OS.

Result: At a median follow-up of 94 months, the median OS and DFS was 92 and 90 months, respectively. The expression rate of LVI was 8.4%. LVI had negative impact on DFS and OS regardless of lymph node status. In addition, Median DFS of LVI positive and negative patients were 90 and 86 months, respectively ($p = 0.007$). LVI was related to higher recurrence and lower survival in luminal A, HER2-positive and TNBC subtypes. The Cox proportional hazard model showed that LVI was a significant prognostic factor for both DFS and OS.

Conclusions: The presence of lymphovascular invasion is an independent poor prognostic factor in early breast cancer patients regardless of node status and molecular subtypes.

COMPARISON OF 3-D ENDOSCOPIC NIPPLE-SPARING MASTECTOMY AND CONVENTIONAL NIPPLE-SPARING MASTECTOMY FOR BREAST CANCER, INITIAL EXPERIENCE

Young Jin Choi, Sungmin Park

Chungbuk National Univ. Hospital, Department of Surgery, Korea

Background: Recently, a single-port 3-dimensional (3D) videoscope system for endoscopic nipple-sparing mastectomy (NSM) were reported. It allows for better visualization of the planes and reducing the invasiveness. The main purpose of this study was to investigate the feasibility and safety of 3D endoscopic NSM (E-NSM) in patients with breast cancer by comparing 3D E-NSM and conventional NSM (C-NSM).

Methods: The medical records of patients who underwent single-port 3D E-NSM for breast cancer and C-NSM during the period of January 2017 to Novemner 2022 in a single institution were retrospectively collected and analyzed. We retrieved the records of 98 patients who underwent NSM with permanent silicone implants and divided them into the 3D E-NSM group (41 patients) and the C-NSM group (57 patients), depending on the use of the endoscopic device. We also analyzed demographic information, pathology, operative time, and complications.

Result: No significant differences were observed between the 2 groups based on demographic information, postoperative pathological data, mean length of hospital stay. Compared to the C-NSM group, the 3D E-NSM group had a significantly longer mean operative time (122.8 ± 28.4 minutes versus 90.2 ± 26.2 minutes, $P = 0.02$) and had a significantly less total complications (4% versus 12%, $P < 0.001$). Compared with C- NSM group, 3D E- NSM group showed less nipple ischemia (4.4% versus 8.4%) and skin necrosis (2.2% versus 5.1%). Implant loss was reported reported in one patient of C-NSM group.

Conclusions: The results showed that 3D E-NSM was feasible and safe with less postoperative complications in patients with breast cancer.

VALIDATION STUDY ON THE OSCAR SCORE FOR CONSERVATIVE TREATMENT OF DCIS

Michael Co, Ava Kwong

The Univ. of Hong Kong, Department of Surgery, Hong Kong

Background: Retrospective studies have suggested that conservative treatment is oncologically safe for selected low-risk DCIS patients. However, oncologic safety is not the only consideration in DCIS treatment planning. An OSCAR score was developed to aid DCIS treatment planning, and this is a validation study of the OSCAR score.

Methods: OSCAR scores for conservative treatment and surgical treatment were calculated for patients with DCIS treated between 2020 and 2022. (https://poetic-pastelito-f1b352.netlify.app). Decision regret scale (AM O' Connor) was used to evaluate patients' level of regret to their treatment received. Breast Q questionnaire version 20 and post-treatment patient satisfaction score were obtained four weeks after the surgery / treatment decision. Correlation between the OSCAR scores and patient satisfaction was evaluated by Pearson correlation coefficient.

Result: 70 patients with low-risk DCIS were recruited for the study within the 3-year recruitment period. 9 patients had pre-operative OSCAR score in favour of conservative treatment, all patients decided for conservative treatment. 61 patients had pre-operative OSCAR score in favour of surgical treatment, of which all patients decided for surgical treatment (100% score-decision concordance). Positive correlation between the differential OSCAR score and patient satisfaction was demonstrated (Pearson correlation coefficient R = 0.768). One patient in the operation group expressed regret of the decision due to surgical complication. None of the patients who received conservative treatment expressed regret. Amongst the 61 patients who received surgical treatment, the median Breast-Q score was 13 (Range 7-25).

Conclusions: OSCAR score is a useful clinical score to guide DCIS treatment decision.

OFF-THE-SHELF VOLUME REPLACEMENT IN BREAST-CONSERVING SURGERY: OXIDIZED REGENERATED CELLULOSE (ORC) FOR UPPER INNER QUADRANT DEFECTS

Celene Ng[1,2], Kristjan Asgeirsson[2], Hazem Khout[2], Nadia Gilani[2], Douglas Macmillan[2]

[1]*National Univ. Hospital, Department of Breast Surgery, Singapore,*
[2]*Nottingham Breast Institute, Department of Surgery, United Kingdom*

Background: Despite innovations in oncoplastic surgery, managing cancers in the cosmetically sensitive upper inner quadrant (UIQ), where even small volume excisions can leave obvious deformities. The traditional approach via a peri-areola incision requires extensive subcutaneous dissection, often results in displacement of the nipple after radiotherapy, and closure of the defect by parenchymal mobilisation is troublesome due to the thin and tapering nature of the breast. Volume replacement is usually the technique of choice, but this requires additional scarring and expertise.

Methods: Wide local excision (WLE) was performed via an inframammary fold incision, with lateral crease incisions used in those without ptosis. A dilute local anaesthetic and adrenaline solution was infiltrated at the incision site, around the planned WLE and in between. Dissection proceeded in the prepectoral plane, towards and posterior to the cancer, enabling palpation of planned margins. Lateral and inferior margins were then defined to the subcutaneous plane, which was then dissected superficial to the cancer before completing superior and medial margins. The WLE defect was then loosely filled with 2-4 pieces of a thin woven form of oxidized regenerated cellulose (ORC). Patients were photographed 1 year after surgery.

Result: Eight patients with UIQ disease were managed using ORC. Mean tumour diameter and weight was 14 mm and 18 g respectively. One patient developed a seroma and underwent aspiration. One year after surgery, the typical appearance was of a subtle, shallow-volume deficiency in the UIQ.

Conclusions: Inframammary or lateral skin crease incision with ORC provides a simple and low-cost technique to overcome the challenge of WLE defects in the UIQ.

ENDOSCOPY-ASSISTED BREAST CONSERVING SURGERY FOR EARLY BREAST CANCER PATIENTS

Sehyun Paek, Woosung Lim, Byung-In Moon

Ewha Womans Univ. Medical Center, Department of Surgery, Korea

Background: A traditional breast conserving surgery (BCS) operation inevitably results in an external scar on breast and axilla. Various attempts have been tried for improved cosmetic outcome. In an attempt to maximize esthetic effects, we performed endoscopy-assisted BCS through only axillary incision.

Methods: Three female patients underwent endoscopy-assisted BCS. All patients underwent endoscopy-assisted BCS with sentinel lymph node biopsy (SLNBx.) through only 3 cm axillary incision. All surgical procedures were performed in concordance with traditional BCS with SLNBx. operation. Data on patient demographics, type of surgery, hospital stay, complications, and short-term postoperative outcomes were reviewed.

Result: Mean patient age was 54.3 years and mean tumor size was 0.8 cm. Two patients underwent BCS with SLNBx., and one patient underwent axillary lymph node dissection through elongated axillary incision. The mean operation time was 135 minute and the mean hospital stay was 8.7 days. No open conversion was observed and all procedures were technically successful without any complications. The operative scars in axilla became inconspicuous in a few weeks.

Conclusions: Our initial results show that endoscopy-assisted BCS would be technically feasible, safe, and effective. This technique can be a good alternative surgical option for BCS in early breast cancer patients.

ENDOSCOPIC MASTECTOMY AND IMMEDIATE FREE ABDOMINAL-BASED FLAP RECONSTRUCTION: A PRELIMINARY EXPERIENCE DESCRIBING AN APPROACH TO THE "AESTHETICALLY SCARLESS" MASTECTOMY

Sabrina Ngaserin[1,2], Allen Wei-Jiat Wong[3], Faith Qi-Hui Leong[1,2], Jia Jun Feng[3], Yee Onn Kok[3], Benita Kiat-Tee Tan[1,2]

[1]Sengkang General Hospital, Breast Service, Department of Surgery, Singapore, [2]SingHealth Duke-NUS Breast Centre, Department of Surgery, Singapore, [3]Sengkang General Hospital, Plastic, Reconstructive & Aesthetic Surgery Service, Department of Surgery, Singapore

Background: Endoscopic total mastectomy (ETM) is predominantly offered with reconstruction utilizing prostheses, latissimus dorsi flap, omental flap, lipofilling, or a combination of techniques. Common approaches include periareolar, inframammary, axillary or mid-axillary line incisions, which limit the technical ability to perform autologous flap inset and microvascular anastomoses, as such the ETM with free abdominal-based flap reconstruction as not been robustly explored.

Methods: 12 female patients with breast cancer received ETM and abdominal-based flap reconstruction at Sengkang General Hospital Breast Centre. Clinical-radiological-pathological characteristics, type of surgery, complications, rate of recurrence, and aesthetic outcomes were reviewed.

Result: Mean age was 53.4 years old (36-65 years). 33.3% of cancers were stage I, 58.4% stage II, and 8.3% stage III. Mean tumor size was 35.4mm (1-67 mm). Mean specimen weight was 458.75g (242-800g). 92.3% successfully received endoscopic NSM and 7.7% underwent conversion to SSM after carcinoma was reported on frozen section of the nipple base. Mean operative time for ETM was 139 minutes (92-198 minutes); average ischemic time was 37.3 minutes (22-50 minutes). No cases required re-exploration, no flap failure occurred, margins were clear, no skin or nipple-areolar complex ischemia or necrosis developed. In the aesthetic outcome evaluation, 16.7% were excellent, 75% good, 8.3% fair, and 0% unsatisfactory. No recurrence was observed.

Conclusions: ETM and immediate Pedicled TRAM or Free AFR, can be a safe means of achieving an "aesthetically scarless" mastectomy and reconstruction. The approach imposes minimal limits to patient breast size and habitus, can maximize inclusiveness and patient satisfaction.

EARLY RESULTS OF PATIENTS WITH NEOADJUVANT CHEMOTHERAPY AND NEOADJUVANT RADIOTHERAPY IN THE TREATMENT OF LOCALLY ADVANCED BREAST CANCER

Enver Ozkurt[1], Mustafa Tukenmez[2], Mahmut Muslumanoglu[2], Selman Emiroglu[2], Neslihan Cabioglu[2], Abdullah Igci[2], Vahit Ozmen[1], Kamuran Ibis[3], Seden Kucucuk[3]

[1]Istanbul Florence Nightingale Hospital, Department of Surgery, Republic of Turkiye , [2]Istanbul Univ., Istanbul Faculty of Medicine, Department of Surgery, Republic of Turkiye , [3]Istanbul Univ., Istanbul Faculty of Medicine, Department of Radiation Oncology, Republic of Turkiye

Background: Neoadjuvant chemotherapy (NCT) is widely used for locally advanced cases. As the key factor is pathologic complete response (pCR), several physicians tried administering radiotherapy before surgery to increase response rates. In this single center prospective observational study on non-complete responder patients after NCT, we aim to present the initial results and complication rates of additional neoadjuvant radiotherapy (NART).

Methods: Clinical T1-3, N+, non-metastatic patients who will receive NCT were registered. After the final dose of the chemotherapy, patients were evaluated clinically and radiologically. Non-complete responder patients received NART according to the guidelines.

Result: Between January 2017 and January 2019, 37 patients received NART. Following NART (after NCT) and surgery, pCR was achieved for 7 (18.9%) patients in the breast and for 14 (37.8%) patients in the axilla. Human epidermal growth factor receptor positive/triple negative cases were significantly relevant with complete response in breast and axilla ($p = 0.029$) following NART. Post-surgical infection was detected in 11 (29.7%). Factors significantly effecting surgical site infection was BMI of greater than 25 kg/m2 ($p = 0.036$). The implant loss rate was 16.7% (n = 2). There was no radiotherapy related early ≥ grade 3 toxicity.

Conclusions: This is the first study presenting the effect of NART for patients that initially received NCT and did not achieve clinical complete response. This study demonstrated that NART for non-complete responder patients, improves pCR rates in the breast and in the axilla allowing almost 38% of the patients to be converted to BCS, and lowering axillary lymph node dissection rates without the elevation of major complications.

INTRAOPERATIVE FROZEN SECTION MARGIN POSITIVE IN BREAST-CONSERVING SURGERY; CURRENT STATUS AND WAYS TO REDUCE IT

Jin Lee, Beom Seok Ko, Tae-Kyung Yoo, Sae Byul Lee, Jisun Kim, Il Yong Chung, Hee Jeong Kim, Jong Won Lee, Byung Ho Son

ASAN Medical Center, Department of Breast Surgery, Korea

Background: There have been many analyzes of permanent resection margin (PM) in breast conserving surgery (BCS) but few studies have organized the data of intraoperative frozen section margin (FM). We were aimed to focus more on FM and organize the data including FM.

Methods: A single center, retrospective study was conducted. The electronic medical records of the patients who underwent BCS for breast cancer between January 2015 and December 2015 in Asan Medical Center were reviewed. We investigated the rate of positive FM and the difference in operation time according to the result of FM. Also, we analyzed various patient and tumor related factors which can affect the result of resection margin (RM) including FM.

Result: 1,110 patients were included in the analysis. FM evaluation was done in 56.5% (627/1110). The rate of positive FM was 12.4% (78/627). The operation time was significantly longer when additional resection was done for positive FM (112.7 ± 32.6 min vs. 74.7 ± 22.9 min, $p < .001$). By univariate analysis, multiplicity, non-mass enhancement (NME) on magnetic resonance imaging (MRI), maximum diameter on MRI, T3, N2-3, invasive lobular carcinoma (ILC), presence of extensive intraductal component (EIC) and presence of ductal carcinoma in situ (DCIS) were factors significantly associated with the result of RM while after multivariate analysis, multiplicity, ILC and presence of EIC showed statistical significance.

Conclusions: The operation time was significantly longer when additional resection was done for positive FM. Further data collection and organization is needed for standardized predictive tool for FM.

BENEFITS OF PECS BLOCK AS PART OF THE ENHANCED RECOVERY AFTER SURGERY (ERAS) PROTOCOL FOR BREAST CANCER SURGERY IN AN ASIAN INSTITUTION A RETROSPECTIVE COHORT STUDY

Teh Mei Sze[1], Kavinya Diana[1], Tania Omia[1], Lim Woon Lai[2], Beh Zhiyuan[2], Taib Nur Aishah[1]

[1]Univ. Malaya Medical Centre, Department of Surgery, Malaysia, [2]Univ. Malaya Medical Centre, Department of Anaesthesilogy, Malaysia

Background: Regional analgesia techniques have been increasingly used for post-operative pain management following mastectomy. We aimed to evaluate the analgesic benefits of pectoral nerve (PECS) block incorporated in the enhanced recovery after surgery (ERAS) protocol in patients undergoing mastectomy in University Malaya Medical Centre, Malaysia.

Methods: This was a single centre, cohort study evaluating 335 women who have undergone unilateral mastectomy between January 2017 to March 2020 in Malaysia. Regional anaesthesia was given pre-operatively via ultrasound guided pectoral and intercostal nerves block (PECSII).

Result: Utilization of regional anaesthesia increased from 11% in 2017 to 43% in 2020. Opiod consumption was 3mg lower and length of stay was half a day shorter in the regional anaesthesia group and these were statistically significant. However, pain score and post-operative nausea and vomiting (PONV) were similar.

Conclusions: This study highlights the importance of regional analgesia (PECS block) as a component of ERAS protocol for mastectomy in an Asian hospital. Although there was statistical significance of lower opioid consumption, the overall pain score and PONV remained unchanged while the length of hospital stay was shortened. Therefore, daycare surgery may be feasible in a selected group of patients undergoing mastectomy and could imply overall cost benefits.

INFLUENCE OF IRRADIATION ON CAPSULES OF SILICONE IMPLANTS COVERED WITH ACELLULAR DERMAL MATRIX IN MICE

Jung Ho Lee[1], Joon Seok Lee[1], Jeong Yeop Ryu[1], Kang Young Choi[1], Ho Yun Chung[1], Byung Chae Cho[1], Jeeyeon Lee[2], Ho Yong Park[2], Jung Dug Yang[1]

[1]*Kyungpook National Univ. Hospital, Department of Plastic Surgery, Korea,*
[2]*Kyungpook National Univ. School of Medicine, Department of Surgery, Korea*

Background: In advanced breast cancer, radiotherapy is recommended as adjuvant therapy following breast reconstructive surgery. This inevitably led to growing concerns over possible complications of radiotherapy on implants. In this experimental animal study, we investigated the utility of acellular dermal matrix (ADM) wraps around implants as preventive management for radiotherapy complications.

Methods: Black mice were assigned to groups that either received radiation or did not: groups A and B underwent surgery using implants without radiotherapy; while groups C, D underwent surgery using implants with radiotherapy for one and three months, respectively. The 0.8 cm-diameter hemispheric silicone implants were inserted on the back of each mouse, and implants wrapped by ADM were inserted on the right back. The Clinic 23EX LINAC model was used for irradiation at 10Gy. The samples were evaluated by gross assessment, histological, immunohistochemical analysis, and the Western blot.

Result: In a H&E staining, membrane thickness is smallest in group A, followed by groups C, D, and B. In a Masson trichrome histological analysis, collagen fibers became less dense and more widespread over time in the groups that received an ADM. Immunohistochemistry findings were similarly constant. However, the expression of TGF-b1 was increased in the irradiated groups, whereas it was decreased in the non-irradiated groups over time.

Conclusions: Radiotherapy was shown to increase risk factors for capsular contracture, including inflammatory response, pseudoepithelium, thinning of membrane, and TGF-b1 expression over time; however, using ADM as a barrier between implant and tissue was shown to be effective in alleviating these risks.

DAY SURGERY-BREAST ONCOLOGICAL SURGERY-A PRELIMINARY REPORT

Lin Zar Chi[1], Yun Le Linn[2], Chi Wei Mok[1]

[1]*Changi General Hospital, Department of Surgery, Singapore,* [2]*MOHH, Department of Surgery, Singapore*

Background: Breast oncological surgery (BOS) have been reported to be performed in day surgery (DS) settings in some centres, although its uptake has been poor due to concerns of postoperative pain, nausea and vomiting. We review our preliminary experience with performing DS-BOS and compare the outcomes and quality of recovery (QOR) with patients who underwent inpatient (IP) BOS.

Methods: Consecutive patients who underwent DS-BOS between January and July 2022 were included. Patients received preoperative education and counselling by dedicated breast care nurses. Multimodal perioperative and intraoperative analgesia was given. Patients were discharged on the same day with video and/or physical consultation on the first and fourth postoperative day. Clinical outcomes and QoR were assessed and compared with a similar cohort of patients who underwent IP-BOS.

Result: 13 patients underwent DS-BOS and 19 patients underwent IP-BOS. 8/13 (61.5%) underwent mastectomy and 5/13 (38.4%) underwent breast conserving surgery. 10/13 (76.9%) had sentinel lymph node biopsy performed and 3/13 (23.0%) had axillary clearance. There were no complications, conversion to inpatient stay or readmissions within 24 hours. Postoperative pain and postoperatie nausea and vomiting were minimal and not significantly different from IP-BOS. There was an overall improvement in QoR-15 scores assessed preoperatively, on POD1 and POD4, $p < .05$.

Conclusions: BOS may safely be performed as a DS procedure. Appropriately selected patients who are well counselled and receive multimodal analgesia may enjoy the benefit of recovering from their homes, allowing for inpatient beds to be redirected/conserved where needed.

DEVELOPMENT OF A SURGICAL METHOD-PREDICTION MODEL ACCORDING TO "TUMOR OCCUPANCY SCORE" ON MAMMOGRAMS OR MRI

Hyung Jin Kim, Chan Sub Park, Min-Ki Seong, Yireh Han, Hyun-Ah Kim

Korea Cancer Center Hospital, Department of Surgery, Korea

Background: In clinical practice, the choice of breast-conserving surgery (BCS) or total mastectomy for women with breast cancer is based only on subjective criteria. The absence of objective prediction models complicates the planning of surgical clinical trials. The aim of this study was to develop a mammography (MMG)- or MRI-based model (reflecting the three-dimensional structure of the breast) to predict which surgical method a clinician is likely to choose.

Methods: A total of 144 patients who underwent surgery for breast cancer in 2016 in one center was included in this retrospective study. Breast mammograms and MRIs were divided according to imaginary triangles. The "tumor occupancy score (TOS)" was calculated by multiplying the number of tumor-occupied triangles. Receiver operating characteristic curves were constructed to evaluate the prediction model according to MMG, MRI, and tumor size. Cut-off values were chosen as those yielding the highest sensitivity and specificity.

Result: For the MMG model, the area under the curve (AUC) for a cut-off TOS of 7 was 0.894 (95% confidence interval [CI] = 0.813-0.974, $p < 0.001$). The sensitivity and specificity were 0.833 and 0.815, respectively. For the MRI model, the AUC for a cut-off TOS of 13 was 0.912 (95% CI = 0.848-0.976, $p < 0.001$). The AUC for tumor size was 0.647 (95% CI = 0.487-0.808, $p = 0.051$).

Conclusions: The TOS may be predictive of which surgical method a clinician will choose for patients with breast cancer. It may be useful when protocols for surgical clinical trials are being drafted.

EFFECT OF BREAST SILICONE IMPLANT TOPOGRAPHY ON BACTERIAL ATTATCHMENT AND GROWTH : AN IN VITRO STUDY

Hyunbin Kim[1], Jong Ho Lee[1,3], Jeong Yeop Ryu[1], Joon Seok Lee[1], Kang Young Choi[1], Ho Yun Chung[1], Byung Chae Cho[1], Koeun Kim[2], Young Ju Lee[2], Hee Kyung Jin[3], Jae-Sung Bae[4], Jung Dug Yang[1]

[1]*Kyungpook National Univ. School of Medicine, Department of Plastic and Reconstructive Surgery, Korea,*
[2]*Kyunbpook National Univ., College of Veterinary Medicine and Zoonoses Research Institute, Korea,*
[3]*Kyungpook National Univ., College of Veterinary Medicine, Korea,*
[4]*Kyungpook National Univ. School of Medicine, Department of Physiology, Korea*

Background: The mechanisms underlying capsular contracture remain unclear. Emerging evidence supports the inflammation hypothesis, according to which bacteria from an adherent biofilm cause chronic inflammation and collagen deposition on the implant and trigger capsular contracture. Our goal was to evaluate the effect of different types of breast implants on the growth of Staphylococcus aureus, S. epidermidis, and Pseudomonas aeruginosa, which are commonly found in biofilms in infection.

Methods: Bacteria were grown in tryptic soy broth at 37˚C for 2, 6, and 24 h and subsequently incubated for 24 h on 12 shell sections of smooth, nano-, and macrotextured breast implants. After incubation, the solutions were ultrasonicated and bacterial numbers were determined by serial dilution. S. aureus were fixed, washed with phosphate-buffered saline, dehydrated in ethanol, and coated with a platinum film to visualize the presence of biofilms by scanning electron microscopy.

Result: The numbers of S. aureus and S. epidermidis attached to the smooth and nanotextured surface implants were significantly lower than those on the macrotextured surface for all incubation times, whereas the number of P. aeruginosa was non-significantly lowest on the nanotextured surface after 24-h incubation. Biofilms on smooth and nanotextured implant surfaces showed patchy patterns on scanning electron microscopy in contrast to the continuous pattern detected on macrotextured implants.

Conclusions: Nanotextured breast implants may limit bacterial growth and thus prevent capsular contracture.

TECHNICAL APPROACH AND CLINICAL OUTCOMES OF DELAYED TWO-STAGE TISSUE EXPANDER/IMPLANT BREAST RECONSTRUCTION: A SINGLE-INSTITUTION EXPERIENCE

Myeong Jae Kang[1], Jung Ho Lee[1], Hyeon Jun Jeon[2], Jeong Yeop Ryu[1], Joon Seok Lee[1], Kang Young Choi[1], Ho Yun Chung[1], Byung Chae Cho[1], Jeeyeon Lee[3], Ho Yong Park[3], Jung Dug Yang[1]

[1]Kyungpook National Univ. School of Medicine, Department of Plastic Surgery, Korea, [2]Liting Plastic Surgery Clinic, Department of Plastic Surgery, Korea, [3]Kyung Hee Univ. School of Medicine, Department of Surgery, Korea

Background: Immediate breast reconstruction after mastectomy is challenging in some patients due to medical or oncological reasons. Delayed two-stage tissue expander/implant breast reconstruction is a reliable option for these patients. However, limited data regarding operation techniques, outcomes, and complication rates have been reported. This study reports our experience with two-stage tissue expander/implant reconstruction in delayed breast reconstruction.

Methods: This retrospective study included 32 patients (34 breasts) who underwent delayed two-stage tissue expander/implant breast reconstruction at our institution from January 2018 to July 2022. The techniques of the procedure are summarized, and the reconstruction outcomes and complication rates one year after the reconstruction were evaluated.

Result: The mean time from mastectomy to expander insertion was 210 ± 25 days, and 8.2 ± 2.3 additional expansions were required prior to the implant insertion. The mean time of tissue expansion was 187 ± 15 days, and the mean volume of expansion was 495 ± 31 ml. No major complications requiring reoperation occurred, and patients were highly satisfied with the surgical results.

Conclusions: Delayed two-stage tissue expander/implant breast reconstruction results in satisfactory outcomes. A consensus regarding the operative technique is necessary, and two-stage tissue expander/implant breast reconstruction is a safe and effective option for delayed breast reconstruction.

COMPARISON OF INTRA-OPERATIVE SPECIMEN IMAGING IN BREAST SURGERY WITH MOZART 3D SPECIMEN TOMOSYNTHESIS SYSTEM VERSUS CONVENTIONAL SPECIMEN RADIOGRAPHY: AN EARLY INSTITUTIONAL EXPERIENCE

Ee Wen Lim, Pallavi Basu, Chi Wei Mok

Changi General Hospital, Department of Surgery, Singapore

Background: Breast specimen radiography is essential to ensure adequate excision especially non-palpable lesions. Traditionally this is performed in radiology unit and assessed by radiologist (conventional specimen radiography). However, it has been shown that intra-operative specimen imaging allows for satisfactory assessment and shorter total operative time. We designed an observational study to evaluate the performance and safety of intra-operative specimen radiography (ISR) compared to conventional specimen radiography (CSR).

Methods: All patients who underwent excision of breast lesions between November 2021 and June 2022 in our institution with ISR were included. ISR was performed using the MOZART 3D Specimen Tomosynthesis System. After specimen delivery, ISR was performed by breast surgeons after which, specimens were sent to radiology for CSR. The primary aim was to assess the time taken for evaluation of adequacy of excision via ISR compared to CSR (performance) and whether assessment by surgeons were concordant with that by radiologists (safety).

Result: A total of 32 specimens were assessed from 30 patients via ISR from November 2021 to June 2022. Mean time taken for final image to be ready for viewing was 1.9 minutes in ISR and 14.4 minutes in CSR ($p < 0.05$). Mean time taken to make a decision on adequacy of surgery was 1.8 minutes in ISR and 25.4 minutes in CSR ($p < 0.05$). Both surgeons and radiologists were able to identify lesion of interest within specimens with 100% concordance.

Conclusions: Intraoperative specimen imaging assessment by surgeons using ISR is a safe and reliable technique with shorter total operative time.

INTERNAL MAMMARY LYMPH NODE SENTINEL NODE BIOPSY IN CLINICALLY EARLY BREAST CANCER - A FEASIBILITY STUDY

Veronica Alcantara[1], Qing Ting Tan[1], Jayne Michelley Adolfo Lim[2], Yien Sien Lee[3], Sze Yiun Teo[3], Mihir Ananta Gudi[4], Kok Yen Evan Lee Woo[1]

[1]KK Women's and Children's Hospital, Breast Department, Singapore, [2]Asian Hospital and Medical Center, Department of Surgery, Philippines, [3]KK Women's and Children's Hospital, Department of Radiology, Singapore, [4]KK Women's and Children's Hospital, Department of Pathology, Singapore

Background: Internal mammary lymph node (IMLN) metastasis is an important prognosticator in breast cancer. Up to 17% of axillary lymph node (ALN) negative patients have IMLN metastasis (IMLNm). IMLN sentinel node biopsy (SNB) is not routinely performed and occult IMLNm may be missed. Upstaged IMLNm patients may benefit from improved therapeutic decisions and better eventual outcomes.

Methods: This study was funded by KKH Health Fund Research Grant. Clinically node negative patients with unilateral invasive breast cancers were prospectively recruited. Peritumoural injection of 2mCi Tc99 sulphur colloid and lymphoscintigraphy was performed. Patients with scintigraphic "hotspots" or gamma probe signal over the IMLN region (IMLN+) underwent IMLN and ALN SNB with frozen section (FS).

Result: From 2019 to 2021, eight patients were recruited. Two were IMLN+. One IMLN was harvested in each patient. Both were negative for metastasis on FS and final histology. One IMLN+ patient had an ALN micrometastasis. Two patients without IMLN SNB had an ALN macrometastasis and subsequent ALN dissection. No peri-operative complication was reported. Mean operative time for IMLN SNB patients was 173 minutes (vs. 165 minutes). Mean follow-up was 24.6 months. There was no reported local, nodal or distant recurrence.

Conclusions: IMLN SNB is safe and does not significantly increase operative time. However increased cost and patient reluctance for an additional surgical procedure limits its acceptance as part of routine nodal staging for clinically early breast cancer. Larger studies over a longer duration are needed to assess cost-effectiveness and impact on recurrence and survival.

IN-VIVO SURGICAL LIGHTING - ACHIEVING OPTIMAL ILLUMINATION IN MINIMAL ACCESS BREAST SURGERY

Jun Xian Jeffrey Hing

Changi General Hospital, Department of Breast Surgery, Singapore

Background: Insufficient lighting in a deep and narrow cavity significantly impairs the precision of dissection in minimal access breast surgery (MABS), which aims to reduce length of incisions and site them in remote, inconspicuous area for better aesthetic outcomes. Adjusting of the operating theatre lights to achieve optimal illumination is a traditional bane faced by many surgeons. Alternatives include the use of lighted retractors, or headlights. This study highlights the effectiveness of Klaros, a freely bendable light-emitting diode light strip developed for in-vivo surgical lighting and demonstrates its versatility to light up deep and narrow surgical cavities encountered in MABS.

Methods: Between 2022 to 2023, consecutive breast surgeries that were conducted with the use of Klaros were analysed. Minimal access breast surgery performed included oncoplastic breast conservation surgery as well as skin and/or nipple sparing mastectomies. Incision placement, extent of skin flap dissection, tumour excision, axillary and reconstructive procedures were performed in standard fashion.

Result: Intraoperative photographs of surgeons' view with Klaros demonstrated superior lighting, reduction in shadows and glares. With each dissection field, the frequency and time needed for adjustments of the Klaros were considerably lesser than conventional operating lights. Duration and ease to set up the Klaros was also better, compared to the lighted retractor. None of the cases required extension of the incisions for increased exposure, additional use of headlights and/or lighted retractors.

Conclusions: The study highlights the application of an innovative in-vivo surgical lighting device in MABS with significant ease of setup and improved versatility compared to conventional light sources.

CRYOTHERAPY FOR BREAST B3 FIBROEPITHELIAL LESION: A FIRST REPORTED CASE AND LITERATURE REVIEW

Geok Hoon Lim[1], Mooi Tai Cham[1], Ruey Pyng Ng[1], Mihir Gudi[3], Sze Yiun Teo[2], Sien Yien Lee[2], Chee Hao Lester Leong[4]

[1]KK Women's and Children's Hospital, Breast Department, Singapore, [2]KK Women's and Children's Hospital, Department of Radiology, Singapore, [3]KK Women's and Children's Hospital, Department of Pathology, Singapore, [4]Singapore General Hospital, Department of Radiology, Singapore

Background: Cryotherapy has been described for the treatment of fibroadenomas and selected early breast cancers. However, the use of cryotherapy for B3 fibroepithelial lesions (FELs), diagnosed on percutaneous biopsy, has not been described. These FELs usually warranted an excision since there is a risk of benign phyllodes tumour which may not be diagnosed on biopsy. We aimed to report the outcome of cryotherapy for a patient with a breast B3 FEL on biopsy and conduct a literature review. This is the first such reported case, to the best of our knowledge.

Methods: In a prospective trial (ClinicalTrials.gov Identifier: NCT04571307), patients with B3 FEL on percutaneous biopsy were recruited. We excluded patients with tumour size >3cm. Cryotherapy was performed under local anaesthesia and the patient was monitored after cryotherapy for recurrence. Pain score, return to work and cosmetic outcomes were recorded too.

Result: A 23 years old lady underwent cryotherapy with no complications. Pain score was minimal (0-1) after the procedure and at 2 weeks' review. Return to work was possible one day after cryotherapy. The patient also reported excellent cosmetic outcome with minimal scar. At 4 months' follow-up, imaging revealed cryotherapy changes.

Conclusions: Cryotherapy for breast B3 FELs is safe and feasible on short term follow-up. It avoided the disadvantages associated with surgery and offered an excellent cosmetic outcome. Our findings suggest that cryotherapy may be considered as an alternative to surgery in selected patients. This finding awaits further validation with longer follow-up and larger studies.

EFFECT OF LANGER'S AXILLARY ARCH ON PREOPERATIVE EVALUATION OF AXILLARY NODES IN BREAST CANCER PATIENTS

Eunhye Kang, Ji-Jung Jung, Hyun Su Yeoh, Changjin Lim, Jung Whan Chun, Hong-Kyu Kim, Han-Byoel Lee, Wonshik Han, Hyeong-Gon Moon

Seoul National Univ. Hospital, Breast Care Center, Department of Surgery, Korea

Background: Langer's axillary arch (LAA) is a muscle in axilla region and relatively common variation. LAA may cover some of axillary lymph node (LN), and impede exposure of axillary space. So, patients with LAA muscle may have insufficient preoperative evaluation and incomplete removal of axillary LN. This study evaluated whether there are differences in preoperative axillary staging and clearance of axillary LN according to presence of LAA.

Methods: We reviewed medical records of the patients with newly diagnosed breast cancer at SNUH from Jan to Oct 2022. The presence of LAA muscle was determined by preoperative chest CT.

Result: During the study period, axillary surgery was performed in 649 cases. LAA was observed in 56 cases (8.6%). There was no difference in axilla surgery method and N stage between LAA group and non-LAA group. In non-LAA group, the sensitivity, specificity, and overall accuracy of preoperative sonographic axilla node staging was 60.0%, 80.1%, and 75.2%, respectively. However, in LAA group, it was 41.2%, 71.8%, and 62.5%, respectively. In terms of axilla surgery, the number of removed lymph node was similar between the two groups ($p = 0.575$). However, in patiets who underwent ALND, the number of dissection nodes in LAA group was significantly smaller (13.5 for non-LAA, 8.5 for LAA, $p = 0.004$).

Conclusions: In patients with LAA muscle, accuracy of ultrasonography evaluating the axillary LN was lower, and also had fewer of lymph nodes removed during surgery. Therefore, it is necessary to recognize the presence of LAA for adequate evaluation and accurate removal of axillary lymph nodes.

TEN-YEAR ONCOLOGIC OUTCOMES IN T1-3N1 BREAST CANCER AFTER TARGETED AXILLARY SAMPLING: A RETROSPECTIVE STUDY

Byeongju Kang[1], Jeeyeon Lee[1], Jin Hyang Jung[1], Wan Wook Kim[1], Heejung Keum[1], Yee Soo Chae[2], Soo Jung Lee[2], Ji-Young Park[3], Nora Ji-Young Park[3], Tae-Du Jung[4], Ho Yong Park[1]

[1]Kyungpook National Univ. Chilgok Hospital, Department of Surgery, Korea, [2]Kyungpook National Univ. Chilgok Hospital, Department of Medical Oncology, Korea, [3]Kyungpook National Univ. Chilgok Hospital, Department of Pathology, Korea, [4]Kyungpook National Univ. Chilgok Hospital, Department of Rehabilitation Medicine, Korea

Background: Targeted axillary sampling (TAS) is a new surgical concept for the assessment of axillary lymph node status in breast cancer, which is hypothesized to be more effective at minimizing postoperative morbidities than axillary lymph node dissection (ALND), provided the metastatic axillary lymph node can be accurately detected without missing data. However, the oncologic outcomes over long-term follow-up have not been sufficiently investigated. This is a retrospective analysis to evaluate the 10-year oncologic outcomes in T1-3N1 breast cancer after TAS.

Methods: Between 2008 and 2013, 230 female patients with cT1-3N1 breast cancer underwent breast and axillary surgery (ALND, n = 171; TAS, n = 59) at our institute. After TAS was applied, additional axillary radiotherapy was performed. Various postoperative complications, including postoperative seroma, lymphedema, and 10-year oncological outcomes, were evaluated and compared between the ALND and TAS groups.

Result: Although overall survival during the 10-year follow-up period was better in the TAS group, there was no statistically significant difference in oncologic outcomes, including locoregional recurrence, distant metastasis, and overall survival ($p = 0.395$, 0.818, and 0.555, respectively). And the incidence of lymphedema on the ipsilateral arm was significantly higher in the ALND group ($p < 0.001$).

Conclusions: The 10-year oncological outcomes of TAS were not inferior to those of conventional ALND in T1-3N1 breast cancers. However, the incidence of lymphedema was significantly higher in the ALND group.

TUMOR BED LOCALIZATION AND TARGETED AXILLARY DISSECTION IN NODE-POSITIVE BREAST CANCER POST-NEOADJUVANT CHEMOTHERAPY A TOTALLY MAGNETIC APPROACH

Chi Mei Vivian Man[1], Michelle Cheung[2], Grace Ng[2], Leanne Han Qing Chin[2], Tina Poy Wing Lam[2], Ava Kwong[1]

[1]*Queen Mary Hospital, Department of Surgery, Hong Kong,*
[2]*Queen Mary Hospital, Department of Radiology, Hong Kong*

Background: Pre-chemotherapy marking of breast tumor and biopsy-proven positive axillary lymph node is essential to ensure safe breast conservative surgery and targeted axillary dissection following neoadjuvant chemotherapy. In this prospective feasibility trial, we describe a totally magnetic technique in breast cancer surgery after neoadjuvant chemotherapy.

Methods: From October 2020, 21 patients with clinical T1-3N1 primary breast cancers planning neoadjuvant chemotherapy were recruited. A total of 27 magnetic markers were placed to the breast tumors and 21 to the most abnormal biopsy-proven positive axillary lymph node before commencement of chemotherapy. Subsequent operation was performed with magnetic marker localization and superparamagnetic iron oxide (SPIO)-guided sentinel lymph node biopsy. Primary endpoint was magnetic seed retrieval rate. Secondary endpoints were rate of positive margin, percentage of patients requiring completion axillary dissection, and the level of satisfaction from radiologists and surgeons.

Result: The overall magnetic marker retrieval rate was 97.9% (47/48), with a 100% success rate in localizing the marked axillary lymph node. Twenty patients (95.2%) had simultaneous successful sentinel lymph node mapping with SPIO. The mean number of lymph nodes retrieved in targeted axillary dissection was 3.4. Eleven patients (52.4%) achieved nodal pathological complete response and avoided completion axillary dissection. None of the patients required re-excision of margins. A high satisfaction score was reported from radiologists and surgeons towards the ease of insertion and detection of magnetic markers, respectively.

Conclusions: A totally magnetic technique is feasible for simultaneous breast tumor localization and targeted axillary dissection. It allows high clinicians' satisfaction and simpler administrative logistics.

NODAL RESPONSE TO NEOADJUVANT CHEMOTHERAPY IN NODE-POSITIVE BREAST CANCER

Andrea Lee, Vivian Man, Ava Kwong

Queen Mary Hospital, Department of Surgery, Hong Kong

Background: Increase in nodal complete pathological response (pCR) after neoadjuvant chemotherapy (NAC) in clinically node-positive breast cancer patients has paved way towards less invasive axillary treatment strategies such as targeted axillary dissection. Patient selection is important. This study aims to identify factors that predict complete nodal response in an Asian cohort.

Methods: Retrospective analysis of a prospectively maintained database in our tertiary hospital was conducted from 2012-2020. Patients with invasive breast cancer, lymph node involvement, no metastasis, and who underwent NAC were included.

Result: Of the 299 patients analyzed, 150 (50.2%) patients achieved nodal pathological complete response (pCR). 72 (24.1%) patients achieved overall pCR, 81 (27.1%) breast pCR, 221 (73.9%) overall partial response, and 6 (2.0%) experienced overall progressive disease. Lack of multicentricity, molecular subtype including triple negative subtype and human epidermal growth factor receptor 2 (HER2) positivity, and type of NAC regimen were correlated with nodal pCR (all $p < 0.05$). MRI tumor response, and PET-CT nodal response were predictors of nodal pCR (all $p < 0.05$).

Conclusions: Similar to the breast, HER2 positivity and triple negative subtypes predicts better response in the axilla. This group of patients may benefit most from pre-treatment nodal clipping and subsequent targeted axillary dissection. Pre-operative assessment by MRI and PET-CT is more useful in predicting nodal response than mammography and ultrasound.

REMOVAL OF 1 OR 2 METASTASIZED SENTINEL LYMPH NODES SHOW SAME PROGNOSIS WITH N0 STAGE IN T1 BREAST CANCER PATIENTS WHO UNDERWENT SENTINEL LYMPH NODE BIOPSY

Hyoung Won Koh[1], Eunyoung Kang[1], Eun-Kyu Kim[1], So Yeon Park[2], Hee-Chul Shin[1]

[1]Seoul National Univ. Bundang Hospital, Department of Surgery, Korea, [2]Seoul National Univ. Bundang Hospital, Department of Pathology, Korea

Background: Currently ongoing trials such as NAUTILUS and SOUND trials are constructed based on assumption that prognostic value of sentinel lymph node (SLN) metastasis is minimal in an era of modern medicine. In this study, we aimed to investigate the significance of SLN metastasis on prognosis.

Methods: We retrospectively reviewed the medical records of 1,234 patients with T1 breast cancer who underwent upfront breast conservation surgery (BC) with SLN biopsy (SLNBx). All patients underwent SLNBx after proven cN0. To better identify the significance of SLN positivity on regional and systemic recurrence free survival (RS-RFS), we excluded local recurrences in survival analysis.

Result: Among all patients, the overall rate of sentinel lymph node metastasis was 15.5%, highest in T2 (26.5%), and lowest in T1mic (0%). Kaplan-Meier curve showed lower RS-RFS in SLN-positive group ($p = 0.002$), but no difference was found between T stage (data not shown). After propensity score matching for T stage, histologic grade, pathologic subtype and completion of RT, SLN-positive group still showed lower RS-RFS ($p = 0.016$) and subgroup analysis according to pT stage revealed no significant difference of RS-RFS in pT1 patients (T1mic to T1b, P = NA; pT1c, $p = 0.2$), but showed significance in pT2 patients ($p = 0.04$).

Conclusions: In T1 breast cancer patients found with 1 or 2 metastasize SLN, surgical resection result in equivalent prognosis with T1N0 breast cancer patients.

LONG TERM OUTCOME IN BREAST CANCER PATIENTS WITH MINIMAL NODAL METASTASIS TREATED WITH SENTINEL LYMPH NODE BIOPSY AFTER NEOADJUVANT CHEMOTHERAPY

Sue Zann Lim[1,2], Tae-Kyung Yoo[2], Sae Byul Lee[2], Jisun Kim[2], Il Yong Chung[2], Beom Seok Ko[2], Jong Won Lee[2], Byung Ho Son[2], Sei-Hyun Ahn[2], Seonok Kim[3], Hee Jeong Kim[2]

[1]Singapore General Hospital, Department of Breast Surgery, Singapore, [2]ASAN Medical Center, Department of Surgery, Korea, [3]ASAN Medical Center, Department of Clinical Epidemiology and Biostatistics, Korea

Background: We have long accepted sentinel lymph node biopsy (SLNB) alone as the treatment for breast cancer patients with minimal nodal metastasis including isolated tumour cells or micrometastasis who underwent primary breast surgery. However there is minimal evidence on the oncological safety of omitting axillary lymph node dissection (ALND) in patients found to have minimal nodal metastasis on SLNB following neoadjuvant chemotherapy (NAC). We aim to compare the long term outcome of post NAC patients with minimal nodal metastasis, receiving SLNB alone versus ALND.

Methods: Patients who underwent NAC and found to have minimal nodal metastasis on surgery from January 2014 to December 2018 were identified from the Asan Medical Center database. Primary endpoint was axillary recurrence rate (ARR) and secondary endpoints were disease-free survival (DFS) and overall survival (OS). These outcomes were reported for patients who had SLNB alone versus ALND.

Result: Following NAC, 213 patients with minimal nodal metastasis were identified. 95 (44.6%) patients received SLNB only while 118 (55.4%) patients had ALND. At a median follow up of 65 months, ARR was 8.4% in the SLNB only group and 3.4% in the ALND group ($p = 0.125$). There were no statistically significant difference in DFS and OS (log rank $p = 0.773$ and 0.619 respectively). Among the SLNB cohort, the DFS and OS were significantly better in patients with axillary radiotherapy (log rank $p = 0.014$ and 0.033 respectively).

Conclusions: Our findings suggest that ALND may be safely omitted in patients with minimal nodal metastasis following NAC and axillary radiotherapy may confer survival benefit.

COMPARISON CLINICAL TRIAL OF THE KOREAN SURGICAL ULTRASONIC ENERGY DEVICE (DISEALOR) VERSUS HARMONIC SCALPEL IN AXILLARY LYMPH NODE DISSECTION

Hee Yeon Kim[1], Kyung Do Byun[1], Ku Sang Kim[2], Jin Hyuk Choi[2], Sung Ui Jung[2], Hee Seung Lee[2], Eun Hwa Park[3], Youn Jung Cha[3], Seok Won Lee[4], Hyun Yeol Kim[5], Yun Ju Jung[5], Woon Won Kim[6], Jung Sun Lee[6], Tae Hyun Kim[1]

[1]Inje Univ. Busan Paik Hospital, Department of Surgery, Korea, [2]Kosin Univ. Gospel Hospital, Department of Surgery, Korea, [3]Dong-A Univ. College of Medicine, Department of Surgery, Korea, [4]Pusan National Univ. Hospital, Department of Surgery, Korea, [5]Pusan National Univ. Yangsan Hospital, Department of Surgery, Korea, [6]Inje Univ. Haeundae Paik Hospital, Department of Surgery, Korea

Background: In this era of de-escalating systemic axillary surgery, axillary lymph node dissection (ALND) stands still as a crucial therapeutic strategy in controlling locally advanced breast cancer. Diverse advanced surgical apparatuses are widely used to aid ALND. This study demonstrates multi-center randomized controlled study on evaluating the efficacy and safety of Korean surgical ultrasonic energy device Disealor versus Harmonic scalpel in ALND.

Methods: This randomized controlled trial was done from August 2021 to April 2022. A total of 64 breast cancer patients from 6 institutions receiving ALND were enrolled and randomly allocated to group A (ALND by Disealor) and group B (ALND by Harmonic). Efficacy and safety of both procedures were compared by total amount of wound drain and time to drain removal.

Result: 64 consecutive patients were enrolled in the study. Total drain amount was not statistically different between the Disealor group and the Harmonic group (mean difference; -48.51 ml, CI; -195.04-98.03 ml, $p = 0.51$). The time to drain removal did not differ significantly in two groups (mean difference; -0.51 day, CI; -2.50-1.48 days, $p = 0.61$). Weight and age were significantly associated with the total drain amount ($p = 0.009$ and $p = 0.02$ respectively). Pathological lymph node stage, weight and age were associated with time to drain removal ($p = 0.003$, $p = 0.02$, and $p = 0.06$ respectively).

Conclusions: This study is the first multicenter randomized controlled trial to compare advanced hemostasis devices in ALND. In axillary surgery of breast cancer patients requiring ALND, Disealor manifested non-inferior lymphatic sealing and hemostasis compared to Harmonic scalpel.

CLIPPED NODES IN NODE-POSITIVE BREAST CANCER PLANNED FOR NEOADJUVANT CHEMOTHERAPY: SENTINEL OR NON-SENTINEL LYMPH NODES?

Seung Ho Baek[1,2], Soong June Bae[1,2], Yoonwon Kook[1,2], Ji Soo Jang[1,2], Sohyun Moon[1,2], Minji Kim[1,2], Seungeun Lee[1,2], Jung Hyun Kim[1,2], Joon Jeong[1,2], Sung Gwe Ahn[1,2]

[1]*Gangnam Severance Hospital, Department of Surgery, Korea,*
[2]*Yonsei Univ. College of Medicine, Institute for Breast Cancer Precision Medicine, Korea*

Background: The choice of axilla surgery in clinically node-positive breast cancer patients who have undergone neoadjuvant chemotherapy (NACT) is controversial. Targeted axillary dissection (TAD), which could lower a false-negative rate of sentinel lymph node biopsy (SLNB) through clipping the most enlarged lymph node prior to NACT, has been preferred axillary surgery in this setting. We aimed to identify clipped nodes whether they are sentinel or non-sentinel lymph nodes in patients treated with TAD after NACT.

Methods: From 2017 to 2023, thirty-two patients with clinically node-positive cancer underwent breast cancer surgery and TAD after NACT in the Gangnam Severance Hospital. A single clip was inserted into the most suspicious node with a guidance of ultrasonography. In 26 patients, a metastatic status of clipped node was pathologically confirmed. In 6 patients, clipping into the most suspicious node was done without a pathologic confirmation.

Result: Excluding nine patients whose clipped node status was not confirmed, status of clipped nodes was determined as SLN or non-SLN in 23 patients. More than half of clipped nodes in these (12/23) were identified as non-SLNs. Subsequent ALND was performed in 6 patients. One patient had negative SLN but positive clipped non-SLN. Thus, in 6 patients with ALND, the false-negative rate of SLNB was 16.7%.

Conclusions: In this study, more than half of clipped nodes were identified as non-SLNs. Our findings support a rationale why TAD could omit ALND securely when both SLNs and clipped nodes turns out to be negative in clinically node-positive breast cancer treated with NACT.

FEASIBILITY OF OMITTING SENTINEL LYMPH NODE BIOPSY DURING MASTECTOMY IN BREAST CANCER PATIENTS WITH PRESUMPTIVE DUCTAL CARCINOMA IN SITU DIAGNOSIS

Geok Hoon Lim[1], Zhiyan Yan[1], Qing Ting Tan[1], Mingjia Wang[1], John Allen[2], Jinnie Pang[1]

[1]*KK Women's and Children's Hospital, Breast Department, Singapore,*
[2]*Duke-NUS Medical School, Centre for Quantitative Medicine, Singapore*

Background: Nodal involvement in ductal carcinoma in situ (DCIS) is rare. In patients with DCIS diagnosis prior to mastectomy, a sentinel lymph node biopsy (SLNB) is performed during mastectomy, to avoid the risk of reoperation and the non-identification of SLN subsequently, should there be an upgrade to invasive cancer on final histology. We aimed to study the feasibility of omitting SLNB in patients with DCIS diagnosis before mastectomy but subsequently upgraded to invasive cancer/ DCIS microinvasion (DCISM) after mastectomy and determine the risk factors associated with the upgrade.

Methods: Patients with pure DCIS diagnosis before mastectomy were reviewed retrospectively. We excluded patients with DCISM or invasive cancer known before mastectomy and bilateral cancers. Patients' demographics, radiological and pathological data pre-mastectomy were analysed.

Result: 189 patients were included. The mean age was 53.8 (range: 29-85) years old. 64.4% presented with symptoms, with breast lump as the commonest symptom. 36.0% and 15.3% upgraded to invasive cancer and DCISM on mastectomy respectively. Palpable tumour ($p = 0.0036$), larger size on ultrasound ($p = 0.0283$), tumour seen on mammogram and ultrasound ($p = 0.0082$), ultrasound-guided biopsy ($p < 0.0001$), higher grade DCIS on biopsy ($p = 0.0350$) and no open biopsy/lumpectomy before mastectomy ($p < 0.0001$) were associated with invasive cancer/DCISM upgrade. Nodal involvement was 8.47% and was associated with invasive cancer ($p < 0.0001$).

Conclusions: In patients with presumptive diagnosis of DCIS undergoing mastectomy, the upgrade to invasive cancer/DCISM was 51.3%. Despite the high upgrade rate, nodal involvement was low. The above risk factors could be used to select patients for an avoidance of SLNB during mastectomy.

CAN WE OMIT THE DRAIN AFTER AXILLARY APPROACH USING AN ENERGY DEVICE WITH BREAST CONSERVING SURGERY?

Youngwon Lee, Young-Jin Lee, Tae-Kyung Yoo, Sae Byul Lee, Jisun Kim, Il Yong Chung, Hee Jeong Kim, Jong Won Lee, Byung Ho Son, Beom Seok Ko

ASAN Medical Center, Department of Breast Surgery, Korea

Background: Energy device is commonly used with breast cancer surgery, especially with axillary approach during breast conserving surgery, and there are previous reports regarding outcomes with different kinds of energy device. The study was aimed to figure out effects on utilizing energy device with any axillary approaches on breast conserving surgery.

Methods: From January 2020 to August 2021, patients who underwent breast conserving surgery with energy device from January 2020 to August 2021 in Asan Medical Center were enrolled. The study estimated number of retrieved axillary lymph nodes, presence and amount of drain, operation time, complications, volume of estimated blood loss (EBL) and length of stay for both sentinel node biopsy (SNB) and axillary lymph node dissection (ALND) groups.

Result: 298 patients were included for the analysis, and 73.15% (218/298) had SNB only while 26.85% (80/298) had ALND. There was no significant difference between SNB and ALND groups in operation time [minutes(min); $p = 0.104$], hospital day ($p = 0.704$), and existence of complications ($p = 0.458$) and re-admission due to complications ($p = 0.223$), and EBL ($p = 0.118$). Although there were only 14.77% (44/298) with drain for both SNB and ALND, there were significant differences on presence (5.5% vs. 40.0%, $p < 0.001$) and amount of drain (24.68 vs. 104.18 ml, $p < 0.001$), and length of waiting day before drain removal also showed statistical difference (0.29 vs. 2.16, $p < 0.001$).

Conclusions: Utilizing energy devices for any axillary approaches on breast conserving surgery may allow the omission of drain insertion.

MODIFIED CHEST WALL LATERAL INTERCOSTAL ARTERY PERFORATOR (MCW-LICAP) FLAP: A VERSATILE FLAP IN THE ERA OF ONCOPLASTIC BREAST SURGERY

Chi Wei Mok, Francis Yee, Ee Wen Lim, Yert Li Melissa Seet, Jun Xian Hing

Changi General Hospital, Department of Surgery, Singapore

Background: Breast reconstruction following oncological resection is becoming more common in recent years. In some ladies, implant reconstruction is not ideal due to significant implant visibility or palpability. Autologous reconstruction addresses the limitations of implant reconstruction but results in potential donor site morbidities. To date, there is no clear advantage ascribed to any technique. With appropriate selection, patients with adequate lateral mammary fold have the option of reconstruction with MCW-LICAP flap. We present our techniques and outcomes from a series of 29 patients who underwent MCW-LICAP flap.

Methods: A retrospective review of consecutive patients who underwent curative resection for breast cancer with immediate MCW-LICAP flap reconstruction, between July 2018 to April 2022 was conducted. The techniques used with its variations along with video demonstrations are presented.

Result: A total of 29 patients underwent 34 procedures. Nineteen breast conserving surgeries and 15 mastectomies were completed, and immediate reconstruction performed in all cases. Twenty-three patients had MCW-LICAP, 1 with a Stacked intercostal artery perforator (STICAP) flap, and 5 had MCW-LICAP combined with a Goldilocks mastectomy. There were no cases of complications requiring re-operation. All patients had acceptable time to adjuvant therapy with a median of 36 days. Learning curve analysis showed a significant reduction in operative time after the 6th case.

Conclusions: In our preliminary experience, MCW-LICAP flap is a safe, reliable, and versatile oncoplastic reconstruction option.

A FEASIBILITY STUDY AND AESTHETIC OUTCOME OF A HYBRID IMMEDIATE FAT-ENRICHED LATISSIMUS DORSI FLAP IN BREAST RECONSTRUCTION POST MASTECTOMY IN A TERTIARY BREAST CENTRE

Teoh Li Ying[1], See Mee Hoong[1], Alya Shaqirah Azraq[2], Soh Wei Qi[1], Lee Chen Hoi[1], Tan Qing Yi[1], Teh Mei Sze[1], Lim Yin Cheng[3], Suniza Jamaris[1], Lai Lee Lee[4]

[1]Univ. Malaya Medical Centre, Department of Surgery, Malaysia, [2]Univ. of Malaya, Faculty of Medicine, Malaysia, [3]Univ. of Malaya, Department of Social and Preventive Medicine, Malaysia, [4]Univ. of Malaya, Department of Nursing Science, Malaysia

Background: Latissimus dorsi (LD) flap is a reliable flap. It provides a natural reconstructed breast but often associated with inadequate volume. The aim of this study is to observe the feasibility of the hybrid fat-enriched LD flap (FELD) method and to assess the patients' cosmetic outcome and satisfaction.

Methods: This is a prospective cohort study among breast cancer patients who undergo mastectomy and FELD. A five-view photographic assessment and Aesthetic Item Scale (AIS) were done at the first, sixth and 12th month. Hopwood's Body Image Scale (BIS) was used at the sixth and 12th month. The study was approved by local institution's Medical Advisory Committee (MAC).

Result: 23 patients were included in this study. 11 patients underwent skin-sparing mastectomy (SSM), 11 underwent nipple-sparing mastectomy (NSM) and 1 patient had delayed reconstruction after a modified radical mastectomy. An average of 311 mililitres of fat (SD + 175.7) was harvested and injected an average of 232 mililitres of fat (SD + 98.8) to the flap. The median duration for the fat harvesting procedure was 68 minutes. Learning curve is achievable after the ninth case. There were no unsatisfactory AIS scores among the SSM or NSM patients in the first year except for the delayed reconstructed patient. There is a decrease in the BIS mean scores at 6 months and 12 months indicating patients' self-esteem improves with time.

Conclusions: FELD is an acceptable hybrid method for immediate reconstruction following mastectomy. The procedure provides an extra option of symmetrisation without the need for immediate contralateral reduction surgery.

SMALL VOLUME FREE TISSUE TRANSFER FOR MICROSURGICAL BREAST RECONSTRUCTIONS-FLAP SELECTIONS AND OUTCOMES

Cheng Feng Chu, Wei-Chuan Hsieh, Wen-Ling Kuo, David Cheong Chon Fok Fok, Jung-Ju Huang

Chang Gung Memorial Hospital, Department of Plastic Surgery, Taiwan

Background: Perforator flaps has been used in post mastectomy breast reconstruction for decades. In Asia, women tend to be thinner with smaller volume of possible donor site such as DIEP or PAP flap. Microsurgical breast reconstruction will require specific approaches. The safety and efficacy of small volume free tissue transfer for breast reconstruction will be described in this study.

Methods: We conducted a retrospective chart review between 2008 to 2021. Total 265 patients using either DIEP flap or PAP flap for breast reconstruction. In both groups, the patients were divided into subgroups by the first, second and third quartile(Q) of the flap-elevated size and flap-used size. Donor site complications and recipient site early or late complications are calculated.

Result: Eighteen out of the 265 patients (6.8%) received breast reconstruction using free PAP flaps and the rest 247 (93.2%) were abdominal-based free flaps. The usage of free PAP flaps is significantly more often in patients with smaller BMI. The flap-used size between 1st and 3rd quartile has significant higher odds ratio (2.72) of recipient site complication compared to those smaller than first quartile ($P < 0.05$). Aesthetic outcomes are compatible with similar revision or contralateral breast touch up rate.

Conclusions: The safety and efficacy of small volume free flaps in both PAP and DIEP groups are as good as larger volume ones. BMI has strong correlation to flap choice. The result suggesting microsurgical breast reconstruction can be performed safely with compatible results in patients have small volume of free tissue as along as adequate flap size can be obtained.

VIDEOENDOSCOPIC NIPPLE-SPARING MASTECTOMY VERSUS CONVENTIONAL NIPPLE/SKIN SPARING MASTECTOMY FOR BREAST CANCER

Mustafa Tukenmez[1], Baran Mollavelioglu[1], Selman Emiroglu[1], Erol Kozanoglu[2], Neslihan Cabioglu[1], Mahmut Muslumanoglu[1]

[1]*Istanbul Univ. Faculty of Medicine, Department of Surgery, Republic of Turkiye,*
[2]*Istanbul Univ. Faculty of Medicine, Department of Plastic Surgery, Republic of Turkiye*

Background: Nipple-Sparing Mastectomy (NSM) and Skin-Sparing Mastectomy (SSM) have become standard methods in the treatment of breast cancer in recent years. On the other hand, Videoendoscopic Single-Port Nipple-Sparing Mastectomy (V-NSM) is a less invasive technique that can be performed with a single axillary incision. In this study, we aimed to compare the surgical and oncological results of NSM, SSM and VNSM.

Methods: Between February 2012 and January 2022, 103 patients (NSM:47, SSM:18, V-NSM:38), were included in the study. Clinicopathological features, operation times, complications, and follow-up data were analyzed.

Result: The median age was 42 (range: 26-66) years, and the median BMI was 42 (range: 18-40). Median age (41 vs. 44; $p = 0.012$) and median BMI (24 vs. 23; $p = 0.010$) were lower in the V-NSM group. The mean operation time was 180 minutes for V-NSM and 120 minutes for NSM and SSM groups. In the V-NSM group bilateral surgery was performed in 24% of the patients (24% vs. 8%; $p = 0.047$) and the median hospital stay was 2 days (2 days vs. 3 days $p = 0.001$). Major complications such as implant loss or flap necrosis were recorded in 8 patients (7.8%). The median follow-up was 46 (range: 6-136) months. Local recurrence occurred in 5 patients (4.9%) during follow-up. There was no statistically significant difference in the complication and recurrence rates of the patients who underwent VNSM ($p > 0.05$).

Conclusions: V-NSM may provide similar oncological outcomes as NSM and SSM with better cosmetic results and decreased hospital stay in breast cancer patients. V-NSM could be a safe alternative method in selected breast cancer patients.

AN EARLY EXPERIENCE OF MICROVASCULAR BREAST RECONSTRUCTION IN MONGOLIA

Battsengel Byambasuren[1], Bold Altangerel[1], Gan-Erdene Badamraa[2], Unubold Enkhbaatar[2], Denis Skuratov[2]

[1]*Intermed Hospital, Department of Surgery, Mongolia,*
[2]*National Cancer Center of Mongolia, Department of Plastic Surgery, Mongolia*

Background: Reconstructive micro surgery is an important adjunct to breast cancer management. The study evaluated single institute experience of microvascular free tissue transfer for breast reconstruction.

Methods: The retrospective study included consecutive patients who were treated with microvascular breast reconstruction at the National Cancer Center of Mongolia from 2017.

Result: A total of 18 free flap reconstructions were performed in 18 patients. Deep inferior epigastric artery perforator free flaps were used in most cases (55.5%) whereas anterolateral thigh free flap (27.7%). The overall complication rate was 38.8% and consisted partial flap necrosis (22.2%) postoperative bleeding (11.1%). There was no total flap necrosis in all cases.

Conclusions: Mastectomy have been performed for many years in Mongolia, reconstruction following mastectomy has only been a consideration more recently. The breast reconstruction only been expected for advanced breast cancer patients due to large amount of defect following cancer ablative surgery. Previously the reconstruction team tend to use latissimus dorsi flap, pedicled TRAM flap to avoid complications following micro anastomosis. However, eventually, we experience that the risk of flap necrosis is low if the micro anastomosis has been successfully done. Therefore, currently, we prefer and frequently use free TRAM flap, DIEP flap, ALT free flaps for breast reconstruction to minimize postoperative complications such as abdominal wall bulges and partial flap necrosis.

DERMOGLANDULAR ROTATION FLAP (BUROW'S TRIANGLE) FOR UPPER INNER QUADRANT BREAST CANCER: A CASE SERIES AND REVIEW OF LITERATURE

Nor Safariny Ahmad, Shahizzat Fahmi Badrolhisham

Breast & Endocrine Surgery Centre, Department of Surgery, Malaysia

Background: Oncoplastic breast conserving surgery in the treatment of breast cancer has replaced mastectomy in most cases. However, the classic conservative surgery can present unfavourable aesthetic results for tumor at upper inner quadrant (UIQ) of the breast. Dermoglandular rotation flap (Burow's triangle) is a good solution for UIQ tumor because it provides high local control rates and cause minimum breast deformities, leading to a better aesthetic result.

Methods: To report cases of patients with UIQ breast cancer who underwent dermoglandular flap rotation surgery by single surgeon.

Result: Four patients had oncoplastic dermoglandular rotation flap surgery combined with sentinel lymph node dissection or axillary clearance for their UIQ breast cancer. The average age of patients was 39 years old. The aesthetic result was evaluated based on patient satisfaction, complication post-operative and oncological resection margin. All patients postoperative without any complications and margin were clear of any tumor cell and patient were satisfy with result.

Conclusions: The use of oncoplastic dermoglandular rotation flap techniques for no man's island UIQ breast tumor allows extensive resections in breast conserving surgery, leading to a satisfying symmetry and a good aesthetic result without the need of symmetrization, with low postoperative complication rates and high rates of free surgical margins.

DELAYED RECONSTRUCTION FOR PARTIAL MASTECTOMY DEFECT BY LATISSIMUS DORSI FLAP WITH CONTRALATERAL MASTOPEXY

Orgilbold Enkhbat, Odbaatar Myagmar, Battsengel Byambasuren, Khurelbaatar Sainbaatar, Bold Altangerel

Intermed Hospital, Department of Thoracic Surgery, Mongolia

Background: The ideal method of breast reconstruction should be safe, reliable, and have minimal donor-site morbidity and provide adequate size, shape, and volume to the reconstructed breast. The latissimus dorsi (LD) flap is known as the safest method for breast reconstruction and has a reliable blood supply with adequate soft tissue.

Methods: A 38-year-old female patient visited Intermed hospital with early ductal cell carcinoma of the left breast in 2019. Operation of lower outer quadrantectomy was performed and subsequently patient received 30 Gy adjuvant radiation treatment with 4 cycles of concurrent chemotherapy. Cancer treatment is done in 2019 without any complications. After cancer treatment, the patient's chief complaint was asymmetry of breasts due to moderate ptosis of the right breast and reduced left breast volume. Therefore, we performed right mastopexy with the inverted-T technique and volume replacement of the left breast by a pedicled LD flap in 2022.

Result: The wound healed primarily, and the patient was discharged post-operatiopn 7th day with an acceptable aesthetic outcome. Post-operation seroma developed and managed with aspiration by weekly 3 times at the outpatient clinic.

Conclusions: The goal was to recreate a breast with aesthetic contours symmetric with that opposite breast rather than simply reconstructing a breast mound. Ease of harvest from adequate soft tissue and low incidence of complication rate was reason to choose the LD flap.

COMPREHENSIVE ANALYSIS OF CLINICAL FACTORS AND DOSIMETRIC PARAMETER FOR PREDICTING SUBSEQUENT ARM LYMPHEDEMA FOLLOWING SALVAGE REPEAT IRRADIATION IN LOCOREGIONAL BREAST CANCER

Hyunju Shin, Haeyoung Kim, Won Kyung Cho, Nalee Kim, Won Park

Samsung Medical Center, Department of Radiation Oncology, Korea

Background: This study aimed to investigate risk factors for subsequent arm lymphedema (SAL) including dosimetric parameters in patients treated with salvage repeated radiation therapy (RT) for locoregional breast cancer.

Methods: We retrospectively reviewed 65 patients who received salvage repeated RT for locoregional recurrent breast cancer between 2003 and 2017. Regional nodal areas were divided into 7 subregions and retrospectively contoured. RT plans for each patient were merged to evaluate dose-volume histogram of each nodal area. Dosimetric analysis was performed using equivalent dose in 2Gy fractions (EQD2).

Result: Salvage repeated RT was combined with salvage surgery and taxane-based chemotherapy in 34 (52.3%) and 29 patients (44.6%), respectively. Total number of RT course were 2 in 59 patients (90.6%) and 3 in 6 (9.4%). Median EQD2 of accumulated prescription dose was 113.0 Gy (interquartile range [IQR] 105.0-121.6). Median follow-up was 30.4 months (IQR 19.3-52.5). Fifteen patients (23.1%) experienced SAL with a median interval of 6.43 months (IQR 13.3-16.5) after secondary RT. In multivariate analysis for SAL without dosimetric parameters, salvage taxane-based chemotherapy remained significant (HR, 4.19; $P = 0.041$). After incorporating dosimetric parameters, a model including lateral to axillary-lateral thoracic vessel junction (ALTJ) V30Gy ≥ 55.8% (HR 5.35; $P = 0.001$) and salvage taxane-based chemotherapy (HR, 4.73; $P = 0.021$) was adopted as the final optimal model.

Conclusions: Salvage repeated RT induced SAL in 23.1% of the patients. Early consult of patients with the above risk factors to the department of rehabilitation or constraining dose of lateral to ALTJ in RT planning could be helpful to reduce SAL.

IMPACT OF THE NEW ESTRO-ACROP TARGET VOLUME DELINEATION GUIDELINE ON BREAST-RELATED COMPLICATIONS AFTER IMPLANT-BASED RECONSTRUCTION AND POSTMASTECTOMY RADIOTHERAPY

Jung Bin Park[1], Bum-Sup Jang[1], Ji Hyun Chang[1], Jin Ho Kim[1], Ki Yong Hong[2], Ung Sik Jin[2], Hak Chang[2], Yujin Myung[3], Jae Hoon Jeong[3], Chan Yeong Heo[3], In Ah Kim[4], Kyung Hwan Shin[1]

[1]Seoul National Univ. Hospital, Department of Radiation Oncology, Korea, [2]Seoul National Univ. Hospital, Department of Plastic Surgery, Korea, [3]Seoul National Univ. Bundang Hospital, Department of Plastic Surgery, Korea, [4]Seoul National Univ. Bundang Hospital, Department of Radiation Oncology, Korea

Background: The European Society for Radiotherapy and Oncology Advisory Committee in Radiation Oncology Practice (ESTRO-ACROP) updated a new target volume delineation guideline for postmastectomy radiotherapy (PMRT) after implant-based reconstruction. This study aimed whether this change has impact on breast-related complications.

Methods: We retrospectively reviewed patients who underwent PMRT after tissue expander or permanent implant insertion from 2016 to 2021. In total, 412 patients were included; 277 received RT by the new ESTRO-ACROP target delineation (ESTRO-T), and 135 received RT by conventional target delineation (CONV-T). The primary endpoint was comparison of major breast-related complication (infection, capsular contracture, deformity and necrosis requiring re-operation or re-hospitalization).

Result: The median follow-up was 29.5 months (range, 0.3-76.8). The 3-year incidence rate of major complication were 11.6% in the ESTRO-T group, and 14.7% in the CONV-T groups; it did not show a difference between the groups ($P = 0.55$). In multivariate analyses, target delineation is not significantly associated with the major complications (HR = 0.93; $P = 0.83$). There was no significant difference between the ESTRO-T and CONV-T groups in any breast-related complications (3-year incidence, 37.3% vs. 29.4%, respectively; $P = 0.28$). Symptomatic RT-induced pneumonitis rates were 2.7% in the ESTRO-T and 2.2% in the CONV-T group. One local recurrence occurred in the ESTRO-T group, which was within the ESTRO-target volume.

Conclusions: Target volume delineation according to the new ESTRO-ACROP guideline did not reduce the risk of breast-related complications. As the dosimetric benefits have been reported, further analyses are necessary to evaluate whether it could be connected to better clinical outcomes.

DOSIMETRIC COMPARISON OF VOLUMETRIC ARC THERAPY AND HELICAL TOMOTHERAPY IN PATIENTS WITH BILATERAL BREAST CANCER

Gail Wan Ying Chua[1], Bryan Shihan Ho[1], Rehena Ganguly[2], Pearl Cheah[3], Yan Yee Ng[1], Zubin Master[1], Grace Kusumawidjaja[1]

[1]National Cancer Centre Singapore, Department of Radiation Oncology, Singapore, [2]Duke-NUS Medical School, National Univ. of Singapore, Singapore, [3]Transmedic Group, Department of Physics, Singapore

Background: Radiotherapy treatment of bilateral breast cancer poses technical challenges with regards to dose coverage and sparing of organs at risk (OAR). As we shifted from using helical tomotherapy (HT) to volumetric arc therapy (VMAT) to treat these patients, we aimed to compare the dosimetric characteristics of these techniques.

Methods: 10 patients with synchronous bilateral breast cancer received radiotherapy to the chest wall and regional nodes (supraclavicular fossa and internal mammary chain) to a dose of 40.05Gy in 15 daily fractions, using VMAT technique. HT plans were generated for each patient. Dosimetric data were summarized and compared using paired T-test, evaluating Planning Target Volume (PTV) coverage and doses to OAR: lungs, heart, thyroid, spinal cord, brachial plexus and oesophagus.

Result: Mean patient age was 61 years (43-84). Majority of patients (80%) were ER+ PR+ and HER2-. 4 patients underwent breast reconstruction. Both techniques provided good PTV dose distribution and OAR sparing. There was no significant difference in VMAT and HT plans for mean heart dose. VMAT plans showed significantly lower V25Gy heart dose on average ($p = 0.04$). No significant difference was observed in VMAT and HT plans for mean lung dose or V20Gy lung dose. V5Gy lung dose was slightly lower in HT plans, approaching statistical significance ($p = 0.08$). All techniques fulfilled cord, oesophagus, thyroid and brachial plexus constraints.

Conclusions: Both techniques met OAR constraints and resulted in acceptable PTV coverage. VMAT plans resulted in significantly lower V25Gy heart dose. HT plans showed slightly better control over low dose spillage in lungs, approaching statistical significance.

CURCUMIN ENHANCES RADIOSENSITIVITY OF BREAST CANCER BY DOWN-REGULATING PNKP EXPRESSION AND IMPEDING NHEJ PATHWAY

Qingjian Li, Zhiwei Yang, Zhuofei Bi

Sun Yat-sen Memorial Hospital, Department of Medical Oncology, China

Background: Radiotherapy is an important part of the comprehensive treatment of breast cancer, radioresistance is the main course of recurrence and death. Curcumin, derivative of the spice turmeric, has been found to improve radiosensitivity of tumor cells, but the underlying mechanism how curcumin enhance radiosensitivity of breast cancer remains unknown.

Methods: By adding curcumin, we found that sensitivity of MDA-MB-231 to ionizing radiation was enhanced. Through colony formation and apotosis experiment, curcumin showed the synergistic cytotoxicity effect with radiotherapy. As shown by immunoblotting, the expression of PNKP protein and NHEJ pathway in MDA-MB-231 cells was significantly reduced with the addition of curcumin.

Result: In this study, curcumin was found to reduce the stability of PNKP protein by upregulating its ubiquitination, thus hindered the repair process of NHEJ pathway to repair DNA damage in time, and ultimately enhanced the sensitivity of breast cancer to radiotherapy.

Conclusions: Our study found that curcumin impeded the repair process of NHEJ pathway by reducing the stability of PNKP protein via ubiquitination, and explored the possibility of curcumin as a radiotherapy sensitizer for breast cancer, and further expand the application of traditional herbal medicine in breast cancer treatment.

STEREOTACTIC PARTIAL BREAST IRRADIATION FOR LOW-RISK EARLY-STAGE BREAST CANCER IN KOREA: AN UPDATE WITH 767 PATIENTS

Yong Bae Kim, Jong Won Park, Hwa Kyung Byun, Jee Suk Chang

Yonsei Cancer Center, Department of Radiation Oncology, Korea

Background: In this article, we hereby report the survival outcome after stereotactic partial breast irradiation (S-PBI) using Cyberknife M6 in same population, with an updated data of 767 early breast cancer patients in Korea.

Methods: We reviewed 767 consecutive early breast cancer patients treated with S-PBI at our institution between 2015.11 and 2021.12. Patients were selected based on the American society for Radiation Oncology (ASTRO), American Brachytherapy Society, American Society of Breast Surgeons, and Groupe Europen de Curiethrapie-European Society for Therapeutic Radiology and Oncology guidelines. Gold fiducials were inserted for tracking which allows image-guided radiotherapy. A dose of 34Gy in 10 fractions and 30Gy in 5 fractions were used for S-PBI.

Result: Median follow-up was 39.7 months. Ipsilateral breast tumor recurrence (IBTR) was observed in 9 cases; true & marginal recurrences in 3 cases and elsewhere recurrences in 6 cases. Disease-specific survival (DSS) at 5 years was 99.2%. Patients were categorized as "suitable" (74.3%) or "cautionary" (23.9%) according to 2017 the ASTRO guidelines. Median planning target volume (PTV) and PTV-to-whole breast volume ratio was 70.5 mL (interquartile range, 55.0-103.9 mL) and 16.3% (13.0-19.1%), respectively. Median PTV V95%, PTV Dmax, and ipsilateral breast V50% were 98.0% (96.0-98.8%), 106.3% (104.2-107.4%), and 36.0% (28.3-40.1%), respectively. No acute toxicity ≥ grade 2 was reported, except grade 2 induration in 6 breasts.

Conclusions: Very low 5-year IBTR and high 5-year DSS can be achieved in early breast cancer patients treated with S-PBI while treatment-related acute toxicity is very scarce and dosimetric outcome is excellent. Upcoming prospective study (NCT03568981) may approve these results.

IMPACT OF POSTMASTECTOMY RADIATION THERAPY ON BREAST CANCER PATIENTS ACCORDING TO PATHOLOGIC NODAL STATUS AFTER MODERN NEOADJUVANT CHEMOTHERAPY

Dowook Kim[1,2], Jin Ho Kim[1,2], In Ah Kim[2,3], Ji Hyun Chang[1,2], Kyung Hwan Shin[1,2]

[1]Seoul National Univ. Hospital, Department of Radiation Oncology, Korea, [2]Seoul National Univ. College of Medicine, Department of Radiation Oncology, Korea, [3]Seoul National Univ. Bundang Hospital, Department of Radiation Oncology, Korea

Background: The utility of postmastectomy radiation therapy (PMRT) for breast cancer patients after neoadjuvant chemotherapy (NAC) is highly controversial. This study evaluated the impact of PMRT according to pathologic nodal status after modern NAC.

Methods: We retrospectively reviewed 682 patients with clinical stage II-III breast cancer who underwent NAC and mastectomy from 2013 to 2017. In total, 596 (87.4%) patients received PMRT, and 86 (12.6%) did not. We investigated the relationships among locoregional recurrence-free survival (LRRFS), disease-free survival (DFS), overall survival (OS), and various prognostic factors. Subgroup analyses were also performed to identify patients who may benefit from PMRT.

Result: The median follow-up duration was 67 months. In ypN+ patients (n = 368, 51.2%), PMRT showed significant benefits in terms of LRRFS, DFS, and OS (all $p < 0.001$). In multivariate analyses, histologic grade (HG) III ($p = 0.002$), lymphovascular invasion (LVI) ($p = 0.045$), and ypN2-3 ($p = 0.02$) were significant risk factors for poor LRRFS. In ypN1 patients with more than two prognostic factors among luminal/HER2-negative subtype, HG I-II, and absence of LVI, PMRT had no significant effect on LRRFS ($p = 0.18$). In ypN0 patients (n = 351, 48.8%), PMRT was not significantly associated with LRRFS, DFS, or OS. However, PMRT showed better LRRFS in triple-negative breast cancer (TNBC) patients ($p = 0.03$).

Conclusions: PMRT had a major impact on treatment outcomes in patients with residual lymph nodes following NAC and mastectomy. Among ypN0 patients, PMRT may be beneficial only for those with TNBC.

Poster Presentation

PATTERNS AND LONGITUDINAL CHANGES IN THE PRACTICE OF BREAST CANCER RADIOTHERAPY IN KOREA: KOREAN RADIATION ONCOLOGY GROUP 22-01

Hae Jin Park[1], Kyubo Kim[2], Yong Bae Kim[3], Jee Suk Chang[3], Kyung Hwan Shin[4]

[1]Hanyang Univ. College of Medicine, Department of Radiation Oncology, Korea, [2]Ewha Womans Univ. School of Medicine, Department of Radiation Oncology, Korea, [3]Yonsei Univ. College of Medicine, Department of Radiation Oncology, Korea, [4]Seoul National Univ. College of Medicine, Department of Radiation Oncology, Korea

Background: Nationwide survey analyzed contemporary practice patterns in breast cancer radiotherapy (RT) and assessed longitudinal changes over 5 years in Korea.

Methods: The survey consisted of 44 questions related to six domains: hypofractionated (HypoFx) whole breast RT, accelerated partial breast RT (APBI), regional nodal irradiation (RNI), RT for ductal carcinoma in situ (DCIS), postmastectomy RT (PMRT), and tumor bed boost.

Result: In total, 70 radiation oncologists from 61 institutions participated in the survey. HypoFx RT was used by 62 respondents (89%), which has significantly increased from 36% in 2017. The HypoFx RT was commonly administered at 40-42.5 Gy in 15-16 fractions. APBI was used by 12 respondents (17%), which has increased from 5% in 2017. The use of RNI did not change significantly: ≥ pN2 (6%), ≥ pN1 (33%), and ≥ pN1 with pathological risk factors (61%). However, the indications for use of internal mammary lymph node (IMN) irradiation have expanded. In particular, the rates of routine treatment of IMN (6% to 11%) and treatment in cases of ≥ pN2 (14% to 27%) have doubled. With regard to DCIS, the use of hypoFx RT increased to 75% from 25%, and the omission of RT after breast-conserving surgery decreased to 38% from 48% in 2017. The use of hypoFx RT for PMRT also increased to 36% from 8% in 2017.

Conclusions: The adoption of HypoFx RT after breast-conserving surgery in invasive breast cancer and DCIS has increased significantly, whereas that for PMRT has increased moderately, compared to 2017. Further studies are required to determine the optimal use of RNI.

DOSE-VOLUME PARAMETER PREDICTING HYPOTHYROIDISM AFTER REGIONAL NODAL IRRADIATION USING VOLUMETRIC MODULATED ARC THERAPY FOR BREAST CANCER

Taeryool Koo

Hallym Univ. Sacred Heart Hospital, Department of Radiation Oncology, Korea

Background: To evaluate the association between the thyroid dysfunction and thyroid radiation dose in regional nodal irradiation (RNI) using volumetric modulated arc therapy (VMAT) for breast cancer.

Methods: We reviewed medical data of 67 breast cancer patients who received curative surgery followed by adjuvant radiotherapy of the breast/chest wall and regional lymph nodes using VMAT between 2018 and 2021. All the patents had normal thyroid functional test (TFT) results, including thyroid stimulating hormone (TSH), T3, and free-T4 (fT4). We checked TFT results performed after the completion of VMAT. Subclinical hypothyroidism was defined by the increased TSH with or without the decreased level of fT4 and T3. Dose-volume histogram parameters (DVHPs) including the mean dose and relative thyroid volume receiving at least 10 Gy, 20 Gy, 30 Gy, and 40 Gy were calculated.

Result: The median follow-up time was 23.2 months. The 3-year locoregional failure-free survival, progression-free survival, and overall survival rates were 96.3%, 94.7%, and 96.2%, respectively. The mean thyroid dose was 21.4 Gy (range = 11.529.4 Gy). Subclinical hypothyroidism was noted in 14 patients (20.9%) and the median time to the event was 4.1 months. Among the DVHPs, relative volume receiving ≥ 20 Gy (V20Gy) was associated with subclinical hypothyroidism, the 2-year rates were 24.8% and 59.1% in patients with V20Gy ≤ 46.3% and > 46.3%, respectively.

Conclusions: Considerable numbers of breast cancer patient experienced subclinical hypothyroidism after VMAT for RNI. The thyroid should be considered as the organ at risk for VMAT plans, and V20Gy could be a useful dose-volume constraint.

PMRT FOLLOWING RECONSTRUCTIVE SURGERY FOR BREAST CANCER : TOXICITY ANALYSIS ACCORDING TO TYPE OF RECONSTRUCTION

Dong-Yun Kim[1], Eonju Park[2], Chan Yeong Heo[2], Ung Sik Jin[2], Eun-Kyu Kim[3], Wonshik Han[3,4], Kyung Hwan Shin[1], In Ah Kim[1,4,5]

[1]Seoul National Univ. College of Medicine, Department of Radiation Oncology, Korea, [2]Seoul National Univ. College of Medicine, Department of Plastic Surgery, Korea, [3]Seoul National Univ. College of Medicine, Department of Surgery, Korea, [4]Seoul National Univ. College of Medicine, Cancer Research Institute, Korea, [5]Seoul National Univ. Bundang Hospital, Department of Radiation Oncology, Korea

Background: This study aimed to compare major breast complication(s) according to the types of reconstruction surgery in breast cancer patients who underwent mastectomy followed by adjuvant radiation therapy (RT).

Methods: We retrospectively reviewed 393 patients who received breast reconstruction following mastectomy in two institutions. The patients underwent reconstruction using either autologous tissues or implants, which were classified according to whether they were immediate or delayed from the time of mastectomy. In addition, delayed reconstruction was subdivided into 2-stages or 1-stage surgery depending on whether expander insertion was performed first.

Result: The median follow-up time was 31.0 months. There was a significant difference in incidence of major breast complication between autologous and implant reconstruction ($P = 0.014$). However, as a result of analysis by classification into immediate and delayed reconstruction, there was no significant difference in the major complications of autologous tissue and implant in both cases. RT-associated factors such as fractionation (conventional vs. hypofractionation) did not affect the complication rates in all types of breast reconstruction surgery. Subgroup analyses for the three most frequently used reconstruction types showed significantly different major complication rates; 9.6% in immediate autologous, 17.5% in delayed 2-stages implant, and 19.5 % in delayed autologous ($P = 0.021$). Among immediate autologous reconstructions, there was no difference in the incidence of major complications between latissimus dorsi flap and transverse rectus abdominis muscle flap.

Conclusions: Immediate reconstruction using autologous tissue showed the lowest major complication rate and might be a good choice when incorporating with RT in breast cancer patients who have undergone reconstruction after mastectomy.

ADAPTIVE RADIOTHERAPY FOR ANATOMICAL CHANGE OF THE BREAST DURING WHOLE BREAST IRRADIATION

Kyung Ran Park[1], Sangwook Lim[1], Dong Hyun Lee[2], Jin Hyuk Choi[3], Sung Ui Jung[3], Chang Wan Jeon[4]

[1]Kosin Univ. College of Medicine, Department of Radiation Oncology, Korea, [2]Kosin Univ. Gospel Hospital, Department of Radiation Oncology, Korea, [3]Kosin Univ. College of Medicine, Department of Surgery, Korea, [4]Good Gang-an Hospital, Department of Surgery, Korea

Background: To investigate the dosimetric effect of anatomical changes in the breast on planning target volume (PTV) during whole-breast irradiation (WBI) for adaptive radiotherapy (ART).

Methods: Patients who underwent field-in-field radiation therapy and ART during WBI were reviewed. ART was performed when the maximum misalignment of the breast skin contour was ≥ 5 mm on treatment imaging using an electronic portal image (EPI). To analyze the various dosimetric parameters, the initial plans were applied to the resimulation computed tomography (re-CT) images and were compared with those on the initial CT.

Result: Twenty-two patients underwent ART, according to our guidelines. The comparison of the initial plans between initial CT and re-CT revealed that areas with under 85% of the prescribed dose within the PTV were present in eight out of the 22 patients, and volume with under 85% ranged from 0.2 to 23 cc (median, 1.6 cc). In the PTV, the minimum dose ($p = 0.000$), volume receiving at least 95% of the prescribed dose ($p = 0.009$), and conformity index ($p = 0.009$) significantly decreased; however, the maximum dose ($p = 0.014$) and homogeneity index ($p = 0.004$) significantly increased. There were no statistically significant differences in the mean PTV dose or the mean lung and heart doses.

Conclusions: Anatomical changes significantly decreased PTV dose coverage. Our results suggest that a misalignment of ≥ 5 mm in the breast skin contour in patients on EPI makes the dose distribution in the PTV unacceptable for treatment; therefore, ART is desirable.

IS IT APPROPRIATE TO SELECT PATIENTS FOR PRIMARY PROPHYLACTIC USE OF PEGFILGRASTIM BASED ON THE RISK OF FEBRILE NEUTROPENIA?

Kazutaka Narui[1], Takashi Ishikawa[2], Ikumi Takashima[3], Kosuke Kashiwabara[3], Yukari Uemura[4], Yuichiro Kikawa[5], Naruto Taira[6], Hirofumi Mukai[7]

[1]Yokohama City Univ. Medical Center, Department of Breast and Thyroid Surgery, Japan, [2]Tokyo Medical Univ., Department of Breast Surgery and Oncology, Japan, [3]Univ. of Tokyo Hospital, Clinical Research Promotion Center, Japan, [4]National Center for Global Health and Medicine, Department of Data Science, Japan, [5]Kansai Medical Univ., Department of Breast Surgery, Japan, [6]Kawasaki Medical Univ., Department of Breast Surgery, Japan, [7]National Cancer Center Hospital East, Department of Medical Oncology, Japan

Background: Febrile neutropenia (FN), a major hematologic adverse event in perioperative chemotherapy for breast cancer, is more prevalent among Asian than Caucasian populations. Guidelines for hematopoietic growth factor recommend considering primary prophylaxis by PEG-G based on chemotherapy regimen and patient risk factors. We verified the appropriateness these guidelines for patient selection.

Methods: In the CSPOR-BC FN study conducted from 2015 to 2017 as prospective multicenter study in Japan, 477 patients were prospectively surveyed for FN, defined as ≥ 37.5℃ and grade 4 neutropenia. The analysis was performed to find cut-off values for age and pretreatment neutrophil count as risk factors.

Result: The incidence of FN was 28.7% (137 cases). In the multivariate analysis of risk factors of FN, the regimen (TC), age (≥ 65), low pretreatment neutrophil count, and no primary prophylaxis with PEG-G were significant. Among them, two patient risk factors were analyzed. Age ≥ 65 was a significant risk factor by logistic regression analysis (OR = 2.24, 95% CI: 1.34-3.75), however, considering the age of 65 as the cutoff for FN, sensitivity, specificity, and AUC of ROC curve were 28.4%, 83.8%, and 0.5195, respectively, indicating low discriminative ability. Next, pretreatment neutrophil count was also a risk factor at 1000/μl (OR = 0.8, 95% CI: 0.67-0.95), even with the cut-off of 2436/μl optimized from the ROC curve. The sensitivity, specificity, and AUC were 27.6%, 83.8%, and 0.5561, respectively, indicating low discriminative ability.

Conclusions: These results indicate that it is inappropriate to select patients for primary prophylactic use of PEG-G by evaluating the existing risk of FN with respect to each patient.

HIGH HER2/CEP17 RATIO IS ASSOCIATED WITH BETTER TREATMENT OUTCOMES IN ADVANCED HER2-POSITIVE BREAST CANCER TREATED WITH PERTUZUMAB, TRASTUZUMAB, AND DOCETAXEL REGARDLESS OF HER2 2+ OR 3+ RESULTS

Dae-Won Lee[1,2,3], Jeongmin Seo[1], Jiwon Koh[4], Han Suk Ryu[4], Kyung-Hun Lee[1,5], Tae-Yong Kim[1], Seock-Ah Im[1,2,3,5]

[1]Seoul National Univ. Hospital, Department of Internal Medicine, Korea, [2]Seoul National Univ. College of Medicine, Department of Translational Medicine, Korea, [3]Seoul National Univ. College of Medicine, Department of Internal Medicine, Korea, [4]Seoul National Univ. Hospital, Department of Pathology, Korea, [5]Seoul National Univ., Cancer Research Institute, Korea

Background: This study investigated the association between HER2/CEP17 ratio and treatment outcomes in patients with advanced HER2-positive breast cancer.

Methods: This is a single center retrospective study. Patients with advanced HER2-positive breast cancer treated with first-line pertuzumab, trastuzumab, and docetaxel were included. The association between HER2/CEP17 ratio and treatment outcome was assessed.

Result: A total of 165 patients were included in this study with a median follow-up duration of 28.0 months. The correlation between HER2/CEP17 ratio and treatment outcome was assessed in 88 patients. Thirty-five patients had archival HER2 ISH result and additional ISH test was performed in 53 patients who did not have previous ISH results (IHC 3+ patients). Cox proportional hazard analysis revealed that HER2/CEP17 ratio is correlated with PFS (HR 0.23, $p < 0.001$). When dichotomized by the median HER2/CEP17 ratio, patients with higher HER2/CEP17 ratio had significantly longer PFS (37.5 vs. 17.4 months, $p = 0.003$) and numerically higher ORR (54.5% vs. 34.1%, $p = 0.085$). Multivariate analysis revealed that HER2/CEP17 ratio is an independent prognostic factor for PFS (HR 0.72, $p = 0.001$). HER2/CEP17 ratio was associated with PFS in both HER2 IHC 1+/2+ patients (HR 0.12, $p = 0.037$) and IHC 3+ patients (HR 0.18, $p = 0.001$).

Conclusions: This is the first study to report that higher HER2/CEP17 ratio is associated with longer PFS in HER2-positive advanced breast cancer patients treated with dual HER2 blockade. In addition, this study identified the prognostic role of ISH even in patients with HER2 IHC 3+. ISH could be helpful even in patients with HER2 IHC 3+ to predict treatment outcome.

EFFICACY AND SAFETY NEOADJUVANT CHEMOTHERAPY PACLITAXEL AND CARBOPLATIN FOLLOW BY DOXORUBICIN AND CYCLOPHOSPHAMIDE (TC+AC) IN TRIPLE-NEGATIVE BREAST CANCER (TNBC)

Anh Dinh

National Cancer Center Hospital, Department of Medical Oncology, Vietnam

Background: TNBC is associated with a higher risk of recurrence and a worse overall prognosis than other breast cancer subtypes. In Vietnam, neoadjuvant chemotherapy (NACT) followed by surgery has become a standard treatment for patients with stage I-III TNBC.

Methods: Patients and methods: 31 cases with TNBC stage I-III were investigated in this prospect and retrospect study, treated by chemotherapy with paclitaxel (weekly for 12 doses) plus carboplatin (every 3 weeks for four cycles) followed by doxorubicin and cyclophosphamide every 2 weeks for four cycles at Vietnam National Cancer Hospital from 2020 - 2022. The primary endpoint was the complete pathological response (pCR). The secondary endpoint was acute toxicity (safety).

Result: Women with stage I-III TNBC who received TC-AC chemotherapy and then surgery at Vietnam National Cancer Hospital were included in the analysis. The median age was 41 ± 58,5 (range 30 -71 years). Of these 31 patients, 5 (16.1%) were at stage I, 7 (22.6%) were at stage II and 19 (61.3%) were at stage III. Total pathological complete response (tpCR) was achieved in 14 (45.2%) of the evaluated patients. There was no significant association between pathological response rates and age, tumor grade, hormone receptor status, and Ki-67 expression. Grade 3 or 4 hematological toxicity occurred in 8 patients (25.8 %) with anemia. Grade 3 or 4 non-hematological toxicity is hepatotoxicity in 12 patients (38.7%).

Conclusions: These findings support the TC-AC neoadjuvant chemotherapy for early-stage TNBC with improvement in pCR and manageable safety profile.

CHEMOTHERAPY-INDUCED NAUSEA AND VOMITING IN PATENT UNDERGOING ANTHRACYCLINE-CONTAINING CHEMOTHERAPY: ANALYSIS OF EXACERBATING FACTORS

Winnie Yeo, Horatio Yeo, Christopher Yip, Victoria Yeo, Jonathan Ko, Claudia Yip, Nicole Ngai, Frankie Mo

The Chinese Univ. of Hong Kong, Department of Clinical Oncology, Hong Kong

Background: Anthracycline-based chemotherapy has been considered to be highly emetogenic. Current international guidelines recommend use of NK1-receptor antagonist, 5HT3-receptor antagonist, corticosteroids with or without olanzapine as optimal antiemetic prophylaxis. However, a proportion of the patients still develop chemotherapy-induced nausea and vomiting (CINV) despite such optimal antiemetic prophylaxis. In this study, we aimed to determine associated factors related to CINV development in patients who received anthracycline-containing chemotherapy.

Methods: Data from female patients who had early stage breast cancer and who received doxorubicin and cyclophosphamide (neo)adjuvant chemotherapy were included. They were previously enrolled into one of the three prospective antiemetic studies. Majority of them received contemporary antiemetic prophylaxis. Control of CINV was defined as CR (no vomiting and no use of rescue medication) in the acute (0-24 hours after the start of doxorubicin and cyclophosphamide administration) and delayed (24-120 hours). Multivariate logistic regression models were used to predict risk factors associated with the occurrence of CINV.

Result: Three hundred and three Chinese patients were included. Multivariate analysis revealed that in the acute phases, obesity (OR 2.83, $p = 0.003$), history of motion sickness (OR 0.34, $p = 0.0002$) and BSA (OR 0.56, $p = 0.45$) were found to be associated with CR. For the delayed phase, obesity (OR 2.09, $p = 0.019$), history of motion sickness (OR 0.49, $p = 0.017$) and contemporary antiemetic regimens (OR 3.80, $p < 0.0001$) were associated with CR.

Conclusions: The current analysis confirmed the previously reported risk factors are important for CINV in patients receiving anthracycline-containing chemotherapy in the presence of contemporary antiemetics regimens.

REVIEW OF CLINICAL RESPONSE IN LOCALLY ADVANCED AND ADVANCED STAGE BREAST CANCER ON VARIOUS REGIMENTS OF CHEMOTHERAPY AND SUBTYPES: A HOSPITAL BASED STUDY IN TERTIARY CARE HOSPITAL, INDONESIA

Suyatno Suyatno[1,2], Salsabila Yasmine Dyahputri[1]

[1]*Haji Adam Malik General Hospital, Department of Surgery, Indonesia,*
[2]*Univ. of Sumatera Utara, Surgical Oncology Division, Department of Surgery, Indonesia*

Background: Chemotherapy is the most used systemic therapy in locally advanced and advanced-stage breast cancer, not only for TNBC, Her-2 type, and luminal B but also partly for luminal A. In Haji Adam Malik (HAM) Hospital, a tertiary care hospital, most breast cancer patients are in stages III and IV, hence chemotherapy is given to most patients. In this review, we will examine the clinical response of breast cancer according to various chemotherapy regimens and subtypes of breast cancer.

Methods: A review of the medical records and clinical examination in the Surgical Oncology Division, Department of Surgery, HAM Hospital in Medan, Indonesia was conducted. RECIST criteria were used to assess the clinical response.

Result: In 2022, 107 patients met the criteria for this study including 23 Luminal A, 56 Luminal B, 19 Her-2 type, and 9 TNBC. General clinical responses; CR (complete response), PR (partial response), SD (stable disease), PD (progressive disease) consecutively are: 2 cases (1.9%), 55 cases (51.4%), 20 cases (18.7%), and 30 cases (28%). A total of 13 chemotherapy regimens were administered; AT (Paclitaxel/Doxorubicin), TP (Docetaxel/Cisplatin), CEF (Cyclophosphamide/Epirubicin/5FU), and AC (Doxorubicin/Cyclophosphamide) were given the most. Cumulative complete and partial response for AT: 64.5%, TP: 28.6%, CEF: 53%, and AC: 58.3%. Based on subtype, cumulative complete and partial response for TNBC 66.7%, Luminal A 60%, Her-2 type 52.6%, and Luminal B 48.2%. On regiments AT, TP, CEF, AC consecutively, benefit response (CR+PR+SD) of luminal A 9/9(100%), 2/5(40%), 3/5(60%), 2/2(100%); luminal B 9/11(81.8%), 8/15(53.3%), 2/4(50%), 4/6(66.7%); TNBC: 5/5(100%), 3/3(100%), 1/1(100%), 0% and Her-2 type: 5/6(83.3%), 1/1(100%), 4/4(100%), 2/3(66.7%).

Conclusions: Paclitaxel plus Doxorubicin had the highest complete and partial response, and also benefit response in all subtypes of breast cancer, including TNBC.

SURVIVAL OF BREAST CANCER PATIENTS IN INTERMED HOSPITAL, MONGOLIA

Khurelbaatar Sainbaatar

Intermed Hospital of Mongolia, Department of Surgery, Mongolia

Background: Nowadays neoadjuvant chemotherapy offers advantages, particularly in terms of tumor reduction as well as improved prognosis. This study aimed to investigate the effect of the time from diagnosis to breast cancer surgery on breast cancer patients prognosis.

Methods: Patients who were confirmed with breast cancer in Intermed Hospital between November 2016 and November 2019 were included in this study. All patients, including those who received neoadjuvant chemotherapy and those who received immediate surgical treatment and adjuvant chemotherapy. We conducted a COX regression analysis to identify prognostic factors of breast cancer associated with the period from diagnosis to treatment.

Result: The patients were followed up until November 2016 and the median follow-up time was 3 years. A total of 73 patients with breast cancer were enrolled in the study. The patients ranged in age from 32 to 72 years old, with an average age of 55 years. There were four events in the groups, which of 29 cases Luminal A (39.7%), Luminal B - 11 cases (15%), Her2 11 cases (15%) and triple negative breast cancer 22 cases (30 %). In the neoadjuvant treatment was 13 cases, the most pathological stage was pT2 than surgery types were modified radical mastectomy 53 cases and breast conserving surgery 20 cases. Among 2 patients for whom treatment was adjusted after recurrence and metastasis, 71 patients remained recurrence-free during the follow-up period.

Conclusions: After adjusting treatment according most patients remained progression-free during the follow-up period. Furthermore, we will describe impact of neoadjuvant chemotherapy for proper management of breast cancer patients.

ROLE OF AN ORAL ANTIMETABOLITE AGENT TEGAFUR ON TRIPLE-NEGATIVE BREAST CANCER FOR THE ADJUVANT PURPOSE

Tserenyudon Shirchinjav, Bold Altangerel

Intermed Hospital of Mongolia, Department of Thoracic Surgery, Mongolia

Background: The worldwide incidence of breast cancer is being diagnosed rapidly over the last few decades. Especially, triple-negative breast cancer (TNBC) that accounts for approximately 15 percent of breast cancers diagnosed worldwide. Our main goal is to evaluate the role of oral Tegafur on stage II-III recurrence of TNBC in the first 3 years after diagnosis.

Methods: We selected women who were diagnosed with TNBC during the last 3 years period at Intermed hospital of Mongolia. The patients who are diagnosed with stage II or III TNBC are administered neoadjuvant chemotherapy with or without, and adjuvant regimens such as AC-T or TC, followed by oral fluoropyrimidine are adopted. There were a total of 10 women on oral tegafur at 400 mg to 500 mg per day that is dosed on their BSA status for 1 year. 9 patients crossed over to the treatment and 1 patient abandoned a research project.

Result: The result from an interim analysis presented the initial result that taking oral fluoropyrimidine was superior to chemotherapy standard only in patients. During the period, recurrence and metastases were not shown by CT scan, and during the first 3 years, overall survival was improved compared to another analysis of Mongolia.

Conclusions: In conclusion, oral fluoropyrimidine Tegafur might play important role in disease-free survival rate and disease recurrence for patients with triple-negative breast cancer. The short-term study will attempt to further elucidate the role of oral antimetabolite agents in the triple-negative population of Mongolia.

THE KI-67 MARKER TO CHEMOTHERAPY SENSITIVITY IN BREAST CANCER

Batmunkh Bilguunzaya

Intermed Hospital of Mongolia, Department of Thoracic, Mongolia

Background: This study aimed to explore the Ki-67 expression in chemotherapy sensitivity breast cancer.

Methods: Patients who were confirmed with Breast cancer in Intermed Hospital between January 2019 and January 2022 were included in this study. The expression of Ki-67 detected by immunohistochemistry, the first-line rescue treatment was recorded for all patients.

Result: The patients were followed up from December 2022, and an average follow-up period was three years. A total of 23 patients with breast cancer enrolled in the study. The patients ranged in age from 39 to 82 years old, with an average age of 62 years. The pathological stage of the total cases was pT1-pT2 and 16 patients received chemotherapy. There are 23 patients, of which 12 (52%) had Ki-67 > 20% and 11 (47%) Ki-67 < 20%. The Ki-67 > 20% of patients, 11 of them were estrogen receptor-positive and 12 patients with Ki-67 < 20% were identified too. There were 14 (60%) cases of lymph node metastases.

Conclusions: In this study, the sensitivity to chemotherapy was determined by Ki-67 marker. If the Ki-67 marker is > 20%, docetaxel is highly sensitive to chemotherapy. Also, estrogen receptor positivity further increases sensitivity. The chemotherapy regiment was docetaxel, doxorubicin, and cyclophosphamide in patients with lymph node metastases, and doxorubicin and cyclophosphamide in patients without lymph node metastases. During the follow-up period, no recurrence and metastasis was detected, and the sensitivity to chemotherapy was high. Further studies will compare it to hormone therapy.

MOLECULAR PROFILING IN BREAST CANCER IDENTIFIES ANDROGEN RECEPTOR ISOFORM AR-V7 AS CRITICAL PREDICTOR OF TUMOR AGGRESSIVENESS AND OUTCOME

Tryambak Srivastava[1], Joyeeta Talukdar[1], Sandeep R Mathur[2], Anurag Srivastava[3], Rajinder Parshad[3], Svs Deo[4], Ruby Dhar[1], Subhradip Karmakar[1]

[1]All India Institute of Medical Sciences, Department of Oncology, India, [2]All India Institute of Medical Sciences, Department of Pathology, India, [3]All India Institute of Medical Sciences, Department of Surgery, India, [4]All India Institute of Medical Sciences, Department of Surgical Oncology, India

Background: Around 15-20% of Breast Cancer (BrCa) are Triple Negative BrCa (TNBC) with a lack of targetable therapies and the lowest 5-year survival rate. Androgen Receptor (AR) is present in up to 80% of BrCa and 30% of TNBC with better clinical outcomes. Apart from the putative full-length AR (AR-FL), Ligand Binding Domain (LBD) truncated AR variant (AR-V7) shows variable expression. In metastatic prostate cancer, AR-V7 is constitutively present and is known to contribute towards castration resistance.

Methods: We correlated AR-V7 expression and clinical profile in BrCa patients from India. Preclinical studies were conducted in cell lines MDA-MB-231, MCF7, and MDA-MB-453. Histopathologically validated patients undergoing surgical intervention were recruited with informed consent. Tumor and matched control tissue from the recruited cohort were checked for ARVs expression at mRNA and protein levels. Endpoint evaluation of stimulation and knockdown studies was carried out by qRT-PCR and Western Blotting & Immunohistochemistry.

Result: The AR-V7 was upregulated in HER2-positive MDA-MB-453 cells. The expression ratio of AR-V7 and AR-FL was, however, elevated in MDA-MB-231 cells. Stimulation of cells with AR ligands induces an Epithelial-mesenchymal transition (EMT) like phenotype. Interestingly, AR knockdown studies also support the role of AR-V7 in EMT. Aligning with the preclinical findings, the higher expression of AR-V7 among the AR-positive TNBC subtype correlates with aggressive clinical features and higher pathological grades.

Conclusions: Our data support the attribution of AR-V7 in yielding poor clinical outcomes in TNBC cohorts. The study recommends screening of AR-V7 to ascertain poor prognosis and as a target for therapeutic intervention.

FACTORS ASSOCIATED WITH LATE BREAST CANCER RECURRENCE AFTER COMPLETION OF FIVE-YEAR ENDOCRINE THERAPY

Mary Rose Mendoza[1], Hyunyou Kim[2], Jung Whan Chun[3], Ji Young You[2], Wonshik Han[3], Seung Pil Jung[2], Eun-Shin Lee[2]

[1]Bicol Medical Center, Department of Surgery, Philippines, [2]Korea Univ. Anam Hospital, Department of Surgery, Korea, [3]Seoul National Univ. Hospital, Department of Surgery, Korea

Background: Endocrine therapy (ET) for five years substantially reduces recurrence rates and increases survival in patients with estrogen-receptor (ER) positive breast cancer. Recently, large-scale clinical data has shown a further benefit of extending ET up to 10 years instead of stopping at five years. We evaluated demographic and clinical factors associated with late recurrence after 5-year completion of ET.

Methods: This retrospective analysis used medical records of 1,058 ER-positive breast cancer patients who underwent curative operation in two institutions and completed scheduled endocrine therapy with no recurrence in 5 years between 2001 and 2014. The associations of demographic and clinical-pathological factors with patients' outcomes were determined.

Result: The mean follow-up period was 13.2 years (ranging from 5.6 to 23.3 years). All-type of recurrence rate was 12.5% and 69 (6.5%) patients had distant metastasis after five years of ET. The distant recurrence was related to the initial TN (Tumor/Node) status ($p < 0.001$) and the kind of ET regimen (tamoxifen (TMX) versus aromatase inhibitors, $p = 0.038$). Distant recurrence-free survival showed a statistically significant difference according to the initial TN stage ($p < 0.001$) and tumor grade ($p = 0.017$) in the Kaplan-Meier analysis. Tumor diameter of more than 2 cm and metastasis in axillary lymph nodes were significantly related to poor outcomes in Cox regression analyses (tumor size HR 3.770, 95%CI:1.993-7.130, $p < 0.001$ and LN metastasis HR 2.105, 95%CI:1.201-3.691, $p < 0.001$).

Conclusions: After 5 years of adjuvant ET, TN stages and tumor grade predicted late relapse and survival from breast cancer. Risk factors reported herein may provide insights to optimize decision-making regarding extended ET.

THE SAFETY AND EFFICACY OF ENDOCRINE THERAPY PLUS CDK4/6 INHIBITORS IN VIETNAMESE PATIENTS WITH METASTATIC BREAST CANCER HORMONE RECEPTOR-POSITIVE HER2/NEU-NEGATIVE

Hang Hoang

K Hospital, Department of Medical Oncology, Vietnam

Background: Breast cancer (BC) is the most common cancer among women worldwide. Approximately 5% of BC patients (pts) have metastases and four subtype of BC were categorized including HR-positive Her2-negative. Endocrine therapies (ET) combined with CDK4/6 inhibitors (CDK4/6i) showed clinical benefit with acceptable safety profile. We first evaluate the toxicities and efficacy of these available options in pts with metastatic breast cancer (mBC).

Methods: Postmenopausal pts with HR-positive Her2-negative mBC were assigned. All were treated with ET combined with CDK4/6i (palbociclib 125 mg or ribociclib 600 mg once daily on 21 days off 7 days) until PD or unacceptable toxicities. Dose reduction and treatment discontinuation were allowed. Primary outcomes were ORR and safety. Secondary outcomes were PFS and OS.

Result: A total of 61 pts were analyzed with the mean age of 54. ORR was 45.9% and clinical benefit rate (CBR) was 77.0%. We found the significant differences in ORR when compared fulvestrant group to AI group and differences between CDK4/6i front-line and subsequent treatment. No differences in ORR between palbociclib and ribociclib as well as pts with presence or absence of visceral metastatic disease. Median PFS was 17 months and median OS was not reached. PFS at 1-year and 2-year were 56.7% and 10.0% respectively. Most common toxicities were fatigue, neutropenia and hypertransaminase including 16.2% pts experienced dose reduction but no treatment discontinuation was detected.

Conclusions: This is the first report in Vietnam showing that CDK4/6i plus ET improves ORR and PFS in pts with HR-positive, HER2-negative mBC and the safety profile is acceptable.

ANALYSIS OF LONG TERM CLINICAL OUTCOMES OF MICROINVASIVE BREAST CANCER REGARDING CANCER SUBTYPES AND HER2 EXPRESSION

Soo-Young Lee, Tae-Kyung Yoo, Jisun Kim, Il Yong Chung, Beom Seok Ko, Hee Jeong Kim, Jong Won Lee, Sae Byul Lee

ASAN Medical Center, Department of Surgery, Korea

Background: The clinical behavior, prognosis and management of microinvasive breast cancer (MiBC) is controversial and the difference of the disease free survival (DFS) between the subtypes and the role of human epidermal growth factor receptor 2 (HER2) expression is unclear.

Methods: We analyzed 1530 patients with T1micro (tumor size = 0.1 cm), node-negative breast cancer who had undergone breast conserving surgery or total mastectomy between 2001-2020, at Asan Medical Center.

Result: Among the 4 subtypes, hormone receptor (HR)+/HER2-, HR+/HER2+, HR-/HER2+ and HR-/HER2-, HR-/HER2+ was the most prevalent of all, being 38.5%. For median follow-up of 74 months (0-271months), 103 patients (6.7%) had recurrent tumor, and 95(6.2%) of them had local recurrence. The DFS and local recurrence-free survival (LRFS) were the worst in HR-/HER2+ group. The 5-year DFS of HR-/HER2+ group was 92.2%, while it was 97.1% for HR+/HER2- group ($p = 0.024$). The 5-year LRFS of HER2 negative were better than HER2 positive MiBC, being 97.1% and 93.8%($p = 0.010$). In a multivariate analysis, HER2 positivity was adverse prognostic factor to the local recurrence (HR = 2.406, 95% CI 1.317-4.394, $p = 0.004$, adjusted).

Conclusions: HER2 overexpression was significantly associated with adverse clinicopathologic parameters and increased risk of the local recurrence in MiBC. Through more understanding of the clinical behavior of HER2 in MiBC, tailored adjuvant therapy for these patients would be enabled.

WHAT IS THE BEST TIME TO CHECK TUMOR VASCULARITY AS A BIOMARKER IN PATIENTS WITH PREOPERATIVE SYSTEMIC TREATMENT AGAINST BREAST CANCER, BEFORE OR AFTER SYSTEMIC TREATMENT?

Hyang Suk Choi[1], Kwangmin Kim[1], Seok Hanhn[2], In-Jeong Cho[1], Hany Noh[1], Seung Taek Lim[3], Jong-In Lee[3], Airi Han[1]

[1]Wonju Severance Christian Hospital, Department of Sugery, Korea, [2]Inje Univ. Haeundae Paik Hospital, Department of Radiology, Korea, [3]Wonju Severance Christian Hospital, Department of Medical Oncology, Korea

Background: Tumor vascularity plays a fundamental role in cancer prognosis. Preoperative systemic approach can serve as a platform for translational research regarding many topics, including tumor vascularity. This study aimed to investigate which tumor vascularity, before or after systemic treatment, can affect patients' prognosis.

Methods: Female patients with breast cancer who received preoperative chemotherapy due to breast cancer between 2003 and 2018 at Wonju Severance Hospital, Korea, were included. Clinocopathological characteristics were collected. Hounsfield units (HU) on contrast-enhanced computed tomography (CT) was used as a marker indicating tumor vascularity. Tumor to aortic arch ratio (TAR) of HU was applied to enhance objectivity of measurement. Patients were categorized according to the cut-off values retrieved from the receiver operating characteristic curve. Kaplan-Meier curves were generated to compare recurrence-free interval (RFI) and overall survival.

Result: The final cohort included 162 patients. Initial TAR was 0.38 ± 0.103 (0.184-0.946) and TAR after completion of preoperative systemic treatment was 0.29 ± 0.094(0.677-0.298). Difference between TAR of immediate before surgery and first clinical presentation was -0.0860 ± 094 (-0.386-0.176). TAR was decreased in 122 (75.3%) patients. Initial TAR was significantly correlated with recurrence free survival ($p = 0.002$). However, TAR after preoperative systemic treatment ($p = 0.221$) or delta TAR (area under receiver operating characteristics = 0.498) were not significant. Interestingly, initial TAR was significant only in patients with decreased TAR after preoperative systemic treatment ($p = 0.005$).

Conclusions: Initial TAR showed better performance as predictive marker than the TAR evaluated after completion of preoperative systemic treatment. Another interesting finding is that TAR is significantly related with patients' RFI only when TAR decreased after completion of preoperative systemic treatment.

Poster Presentation

RISK FACTORS FOR TRASTUZUMAB-INDUCED CARDIOTOXICITY IN HER2-POSITIVE BREAST CANCER: A SYSTEMATIC REVIEW AND META-ANALYSIS

Asdi Wihandono[1], Ottofianus Alvedo Hewick Kalangi[1], Desak Gede Agung Suprabawati[1], Yohana Azhar[2]

[1]Medical Faculty Airlangga Univ., Dr. Soetomo General Hospital Surabaya, Department of Surgical Oncology, Indonesia, [2]Dr. Hasan Sadikin General Hospital Bandung, Department of Surgical Oncology, Indonesia

Background: Trastuzumab has been proven to improve disease-free and overall survival in patients with human epidermal growth factor receptor 2 (HER2)-positive breast cancer. However, the main side effect of trastuzumab is the increased risk of cardiac dysfunction. This meta-analysis aims to clarify the association between cardiovascular risk factors with trastuzumab-induced cardiotoxicity (TIC).

Methods: A systematic search of PubMed, Scopus, SAGE, and The Cochrane Library proceeded with the terms "trastuzumab," "cardiotoxicity," "risk factors," and "breast cancer," as well as the medical subject headings. Relevant studies were analyzed using the Newcastle-Ottawa Scale (NOS). Statistical analysis was conducted to calculate the odd ratio and 95% confidence interval (CI) using a fixed-effects or random-effect model.

Result: A total of 12 studies involving 6768 patients treated with trastuzumab were included. Overall, 1097 suffered cardiotoxicity. Patients with hypertension (OR = 1.16; 95%CI: 1.00, 1.34; $P = 0.05$) and diabetes mellitus (OR = 1.30; 95%CI: 1.03, 1.62; $P = 0.03$) were significant associated with TIC. However, hyperlipidemia (OR = 1.13; 95%CI: 0.84, 1.51; $P = 0.41$) and obesity (OR = 1.33; 95%CI: 0.90, 1.96; $P = 0.15$) were insignificantly associated with the development of TIC.

Conclusions: TIC incidence increases in HER2-positive breast cancer patients with cardiovascular risk factors such as hypertension, hyperlipidemia, diabetes mellitus, and obesity. Hypertension and diabetes mellitus were significantly associated with TIC. Nevertheless, hyperlipidemia and obesity were insignificantly associated with TIC in this study. Screening for cardiovascular risk factors can reduce the incidence of cardiotoxicity in breast cancer patients receiving trastuzumab therapy, and cardiac function should be carefully monitored.

THE CHANGE OF BRCA TESTING NUMBER IN SAMSUNG MEDICAL CENTER AFTER KOREAN NATIONAL INSURANCE COVERAGE EXPANSION AND ADDITIONAL INVOLVEMENTS OF GENETIC COUNSELORS

Sung Yoon Jang[1,2], Jai Min Ryu[1,2], Hyunjun Lee[1,2], Dong Seung Shin[1,2], Joon Young Choi[1,2], Youngji Kwak[1,2], Seok Jin Nam[1,2], Seok Won Kim[1,2], Jeong Eon Lee[1,2], Jonghan Yu[1,2], Byung-Joo Chae[1,2], Boo Yeon Jung[3], Mina Kim[3]

[1]Samsung Medical Center, Department of General Surgery, Korea, [2]Samsung Medical Center, Department of Breast Surgery, Korea, [3]Samsung Medical Center, Breast Cancer Center, Korea

Background: Relatively high prevalence of BRCA1/2 mutations in Korean triple negative breast cancer (TNBC)-patients diagnosed under the age of 60 was analyzed through previous study from our center, and this result brought out the expansion of Korean national insurance coverage (NIC) on BRCA testing. The purpose of this study is to evaluate the increase of BRCA gene mutation tests not only after NIC expansion but also after additional recruitment of genetic counselor in SMC.

Methods: This is a single-institution retrospective review. Total of 7299 patients received breast cancer surgery from August, 2019 to December, 2021 in SMC, were divided into 3-groups according to the time marks: before NIC expansion (group 1), after NIC expansion (group 2), and after genetic counselor's involvemen (group 3). The BRCA testing numbers were assessed with Fisher's exact test. Statistical analyses were performed using IBM-SPSS statistical software version 27.0. A statistical significance was accepted for P-values of < 0.05.

Result: Each group showed statistically significant increase in BRCA gene mutation test number. BRCA testing numbers in TNBC-patients diagnosed under the age of 60 increased from 0.8% in group1 to 5.2% and 15.3% in groups 2 and 3 respectively. 584 of the follow-up patients were newly tested for BRCA mutation under new insurance criteria, and BRCA detection rate was 7.7%.

Conclusions: The NIC expansion and additional involvement of genetic counselors together led to a significant increase in number of effective BRCA tests to newly diagnosed breast cancer patients, especially in TNBC patients under the age of 60. The genetic counselor's role is very important especially in recalling follow-up patients for genetic tests under expanded insurance criteria.

LONG-TERM SURVIVAL OUTCOME AFTER AXILLARY RECURRENCE IN PRIMARY STAGE I/II BREAST CANCER PATIENTS ACCORDING TO SUBTYPE

Changjin Lim, Jung Whan Chun, Hong-Kyu Kim, Han-Byoel Lee, Hyeong-Gon Moon, Wonshik Han

Seoul National Univ. Hospital, Department of Surgery, Korea

Background: With the current trend of de-escalation of axillary surgery in early breast cancer, there is a worry for potential worse outcome with axillary recurrence (AR). However, previous studies that evaluated the survival in patients after AR predated the use of recent treatment. This study assessed the survival outcome and patterns of AR according to subtype in contemporary treatment era.

Methods: This retrospective single-institution cohort study included 6,177 (stage I, 2,548; stage II, 3,629) breast cancer patients operated between 2005 and 2013. 158 cases had regional recurrences. Of those, 41 cases had isolated AR. The median follow-up was 7.5 years.

Result: Regional recurrence rate was higher TNBC than other subtypes in univariate and multivariate analysis (Luminal A, 1.9%, Luminal B, 2.2%, HER2, 2.6%, TNBC, 4.8%; $p < 0.05$). However, there was no difference in isolated AR between subtypes (Luminal A, 0.8%, Luminal B, 0.7%, HER2, 1.0%, TNBC, 1.3%; $p = 0.564$). The median time to AR after surgery was 8.7 years (range, 3.615.8 years). 7-year overall survival was worse in patients who had AR as the first recurrence event compared with other patients (78.5% vs. 95.9%; $p < 0.001$). However, in ER+/HER2- patients, 7-year overall survival was not different between the groups (AR 96.2% vs. non-AR group 97.3%; $p = 0.178$).

Conclusions: Patients who had AR showed worse overall survival than other patients. However, in ER+/HER2- patients, comparable survival outcome was observed with appropriate salvage treatment after AR.

HEPATITIS A VIRUS CELLULAR RECEPTOR 2 (HAVCR2)/T-CELL IMMUNOGLOBULIN MUCIN RECEPTOR 3 (TIM3) AND ITS ASSOCIATION WITH TUMOUR IMMUNE MICROENVIRONMENT IN BREAST CANCER

Xiao-Shan Cao[1,2,3], Bin-Bin Cong[1,2], Wen-Guo Jiang[2], Tracey-A Martin[2]

[1]Shandong Cancer Hospital & Institute, Breast Cancer Center, China, [2]Cardiff Univ. School of Medicine, Cardiff China Medical Research Collaborative, United Kingdom, [3]Tianjin Medical Univ., Department of Medical Oncology, China

Background: Hepatitis A Virus Cellular Receptor 2 (HAVcR2), also known as T-cell Immunoglobulin Mucin receptor 3 (TIM3) has been shown to be a player in the immune microenvironment and may be a useful target in immunotherapy in renal cell carcinoma. The present study aimed to characterize if HAVcR2/TIM3 has role in the immune microenvironment in immunotherapy in breast cancer and if it has an impact on the single agent immune therapy, unknown in breast cancer.

Methods: Kaplan-Meier plotter and Tumor Immune Estimation Resource were applied to illustrate correlation of HAVcR2/TIM3 with the prognosis and immune infiltration of breast cancer.

Result: High HAVcR2/TIM3 levels indicated a worse overall survival (OS) (HR = 1.59, 95%CI:1.26-2.01, $P < 0.05$) in breast cancer. HAVcR2/TIM3 significantly correlated with immune infiltration in breast cancer, especially with B cells, CD8+ T cells, CD4+ T cells, macrophages, neutrophils and dendritic cell ($P < 0.05$), together with immune markers PDCD1 and CTLA4 ($P < 0.05$). A decrease of HAVcR2/TIM3 in type 1 T-helper cells, natural killer T-cells and enrichment of macrophages, regulatory T-cells, type 2 T-helper cells significantly improved the prediction of OS ($P < 0.05$). Furthermore, HAVcR2/TIM3 decrease in B cells was correlated with worse OS ($P < 0.05$).

Conclusions: HAVcR2/TIM3 is closely correlated with breast cancer immune microenvironment and may serve as a potential tumour immunotherapy target for breast cancer.

Poster Presentation

CLINICAL FACTORS ASSOCIATED WITH BREAST CANCER SPECIFIC SURVIVAL OF STAGE III BREAST CANCER : A NATIONWIDE STUDY FROM THE KOREAN BREAST CANCER SOCIETY

Juneyoung Ahn, Yongseon Kim, Yong-Seok Kim

The Catholic Univ. of Korea, Uijeongbu St. Mary's Hospital, Department of Breast Surgery, Korea

Background: In the current era early breast cancers are well-treated by surgery and adjuvant therapy. On the other hand, advanced breast cancer is still challenging area for clinicians. AJCC 8th edition upgraded the staging of breast cancer by adding prognostic factors, but undiscovered area still remains. We tried to figure out whether the size of the tumor (T stage) or number of metastatic lymph nodes (N stage) affects more on the prognosis. And we also compared the survival between breast cancer subtypes within the same TNM stage group.

Methods: Nationwide data between 2005 and 2014 from the Korean Breast Cancer Registry was collected. 9376 patients with stages III breast cancer were included in the analysis: 5099 (54.4%) were luminal A type, 1218 (13.0%) were luminal B type, 1442 (15.4%) were HER2 overexpressed type, and 1617 (17.3%) were triple negative type. KaplanMeier and Cox proportional hazards regression survival analysis were used to compare breast cancer-specific survival (BCSS) between the groups.

Result: HER2 overexpressed type and triple negative type shown more advanced stage than luminal type with worse overall survival and BCSS. These tendency was repeated within the same specific stages (3A, 3B, 3C). T4N0 group shown no significant difference in survival compared to T1N3 group (hazard ratio, 1.10; 95% confidence interval, 0.70-1.73; $p = 0.693$).

Conclusions: These findings suggest that breast cancer subtype is a solid factor for predicting prognosis, whereas effect of tumor size or number of metastatic lymph node within the stage is unclear. Further research should be done.

THE EFFICIENCY OF EVALUATING CONVENTIONAL RISK FACTORS IN PREDICTING THE OUTCOME OF GENESWELL BREAST CANCER TEST (BCT) IN EARLY BREAST CANCER PATIENTS

Ji Hye Kim, Jai Hyun Chung, Yong Yeup Kim, Woo Young Kim, Jae Bok Lee, Sang Uk Woo

Korea Univ. Guro Hospital, Department of Breast and Endocrine Surgery, Korea

Background: Hormone receptor (HR) positive and human epidermal growth factor receptor-2 (HER2) negative subtype is the most common subtype in breast cancer, accounting for around 65% of all breast cancer in Korea. GenesWell Breast Cancer Test (BCT) is a multigene assay developed in Korea to predict the risk of lifelong distant recurrence in patients with early breast cancer. The aim of this study was to identify the risk factors that may predict the outcome of GenesWell BCT.

Methods: GenesWell BCT score was obtained from 2 different groups of patients, all of whom underwent curative surgery for early breast cancer in Korea University Guro Hospital. In one group, the outcome was retrieved retrospectively from patients who underwent surgery from January 2012 until December 2017, and already received another gene expression assay, particularly Oncotype DX. Patients in the other group were enrolled prospectively from January 2021 until December 2022.

Result: A total of 108 patients was enrolled in this study. Fifty-five patients (50.9%) had already received Oncotype Dx test and subsequent treatment, while 53 patients (49.1%) were prospectively enrolled. Sixteen patients were classified as high risk group according to GenesWell BCT. After performing logistic regression analysis, patients with different T stage and N stage showed statistically significant difference in predicting high risk group on GenesWell BCT.

Conclusions: In this study, advanced pathological stage, including increased tumor size and presence of metastatic lymph node, was associated with high risk BCT score.

NDUFAF6 EXPRESSION MIGHT BE A NOVEL PROGNOSTIC FACTOR FOR BREAST CANCER

Xiao-Shan Cao[1,2], Bin-Bin Cong[1]

[1]*Shandong Cancer Hospital & Institute, Breast Cancer Center, China,*
[2]*Tianjin Medical Univ., Department of Medical Oncology, China*

Background: NDUFAF6 (NADH: Ubiquinone Oxidoreductase Complex Assembly Factor 6), also known as C8orf38, is a protein coding gene expressed in various tumor types, which has been proved to be a potential prognosis biomarker and target in hepatocellular carcinoma, but not clear in breast cancer. This study aimed to characterized the role of NDUFAF6 in breast cancer, hoping to find a novel prognosis biomarker of breast cancer.

Methods: The Cancer Genome Atlas was used to evaluate expression and functional role of NDUFAF6. UALCAN and Kaplan-Meier plotter were applied to illustrate correlation of NDUFAF6 with the prognosis of breast cancer.

Result: NDUFAF6 was significantly overexpressed in breast cancer compared with normal tissues ($P < 0.05$). It was also significantly upregulated in luminal like breast cancer compared to triple negative breast cancer ($P < 0.05$). Premenopausal breast cancer women were also significantly overexpressed than postmenopausal women ($P < 0.05$). N2 was significantly overexpressed in breast cancer compared with N0, N1 and N3 ($P < 0.05$). TP53-Mutant was significantly overexpressed than TP53-NonMutan ($P < 0.05$). There was no statistical difference among different breast cancer stages. NDUFAF6 upregulation was an independent indicator of shorter overall survival (OS) (HR:1.72, 95%CI:1.242.38, $P = 0.0011$). By performing univariate analysis, we found that lymph node negative, HER2 negative, Nottingham histologic grade 3 and high NDUFAF6 expression were risk factors of shorter OS ($P < 0.05$).

Conclusions: NDUFAF6 gene was valuable gene with the potential to be prognosis biomarkers and targeted therapies in breast cancer.

CLINICAL IMPACT OF KI67 CHANGES IN LOCALLY ADVANCED BREAST CANCER AFTER NEOADJUVANT CHEMOTHERAPY: A SINGLE CENTER EXPERIENCE

Desak Gede Agung Pramesti Devi[1], Desak G. A. Suprabawati[1], I Wayan Sudarsa[2]

[1]Medical Faculty Airlangga Univ., Dr Soetomo General Hospital Surabaya, Department of Surgical Oncology, Indonesia, [2]Medical Faculty Udayana Univ., Prof I.G.N.G. Ngoerah General Hospital Denpasar, Department of Surgical Oncology, Indonesia

Background: Locally Advanced Breast Cancer still become the highest stage present in developing countries, associated with unfavorable prognosis and its managements requires multimodal therapy. Data from our hospital showed that more than 70% of patients were diagnosed with LABC at first encounter. Achieving pathological complete response (pCR) after neoadjuvant chemotherapy (NAC) is known to have a better long-term outcome. Ki67 has been extensively investigated as a promising predictive and prognostic factor in breast cancer, but the role of Ki67 changes before and after NAC remains unclear. The aim of our study was to investigate the clinical role of Ki67 change in patients not achieving pCR.

Methods: LABC patients without pCR after standard NAC with anthracycline were analyze. Clinical and immunohistochemical characteristics before and after NAC were obtained retrospectively. Changes in Ki67 and NAC response were analyzed.

Result: A total 66 subjects were analyzed. We determined 2 groups with good clinical response and poor clinical response using RECIST 1.1 criteria. Our study showed that a decreased > 12.5% in Ki67 expression after NAC were correlated with good clinical response (p 0.007; OR 4.67 (95%CI 1.45-15.08). In multivariate analysis, decreased in Ki67 were strongly correlated to response in NAC than low post treatment Ki67 expression (p 0.037, $p < 0.05$). We were able to observe 3 years survival in 50 patients. 72% (23 out of 32) patients who had a decreased < 12.5% in Ki67 had recurrence within 3 years.

Conclusions: Decrease in Ki67 greater than 12.5% after anthracycline-based NAC was correlated with good clinical response of in LABC.

CLINICAL SIGNIFICANCE OF RESIDUAL TUMOR IN BREAST CANCER AFTER PRIMARY SYSTEMIC TREATMENT

Sae Fujioka[1,2], Koji Takada[2], Wataru Goto[2], Yukie Tauchi[2], Kana Ogisawa[2], Tamami Morisaki[2], Yoko Mizuyama[1], Shinichiro Kashiwagi[2]

[1]*Kashibaseiki Hospital, Department of Breast Surgery, Japan,*
[2]*Osaka Metropolitan Univ. Graduate School of Medicine, Department of Breast Surgical Oncology, Japan*

Background: Residual tumor after primary systemic therapy (PST) has been shown to affect prognosis. Therefore, additional treatment to improve the prognosis in non-pCR cases is a clinical issue. Non-pCR is treated as the same efficacy assessment regardless of the presence or absence of residual lymph node metastasis (ypN+). However, considering factor N, which is a strong prognostic factor, ypN+ cases may have worse prognosis than ypT+ cases. We intended to create a new index using the T factor and N factor of residual disease, and clinically verified the residual disease form after primary systemic therapy.

Methods: From 327 breast cancer patients who underwent PST, total of 174 patients, excluding those who acquired pCR and those who omitted axillary lymph node dissection (ALND), were included in this study. We used the T and N factors to classify residual disease types.

Result: The pCR acquired cases had significantly better prognosis than the non-pCR cases (disease-free survival DFS: $p < 0.001$, log-rank / cancer-specific survival CSS: $p = 0.010$, log- rank). Prognostic analysis showed that the ypT+ and ypN+ groups had significantly worse DFS ($p = 0.001$, log-rank) and CSS ($p = 0.001$, log-rank) than the ypT+ or ypN+ groups. Further univariate and multivariate analyzes showed that ypT+ and ypN+ were poor prognostic factors contributing to DFS ($p = 0.002$, HR: hazard ratio 0.382) ($p = 0.001$, HR 0.346).

Conclusions: Patients with residual T and N factors after PST for breast cancer had poor prognosis. This suggests that it may serve as a reference index for the indication criteria for additional treatment after PST.

MOLECULAR SUBTYPING OF BREAST CANCER INTRINSIC TAXONOMY WITH OLIGONUCLEOTIDE MICROARRAY AND NANOSTRING NCOUNTER

Yen-Jen Chen

Taipei Veterans General Hospital, Department of Surgery, Taiwan

Background: Breast cancer intrinsic subtypes have been identified based on the transcription of a predefined gene expression (GE) profiles and algorithm (prediction analysis of microarray 50 gene set, PAM50). The present study compared molecular subtyping with oligonucleotide microarray and NanoString nCounter assay.

Methods: The whole study protocol (CGH-P101091) was approved by IRB of Cathay General Hospital. Enrolled subjects were those operated between 2010 and 2014. A total of 109 Taiwanese breast cancers (24 with adjacent normal breast tissues) were assayed with Affymetrix Human Genome U133 plus 2.0 microarrays and 144 were assayed with the NanoString nCounter while 64 patients were assayed for both platforms.

Result: Subtyping with the nearest centroid (single sample prediction (SSP)) was performed, and 16 out of 24 (67%) matched normal breasts were categorized as the normal breast-like subtype. For 64 breast cancers assayed for both platforms, 41 (65%, one unclassified by microarray) were predicted with an identical subtype, resulting in a fair κ statistic of 0.60. Taking nCounter subtyping as the gold standard, prediction accuracy was 43% (3/7), 81% (13/16), 25% (5/20), and 100% (20/20) for basal-like, human epidermal growth factor receptor II (HER2)-enriched, luminal A and luminal B subtypes predicted from microarray GE profiles.

Conclusions: Microarray identified more luminal B cases from luminal A subtype predicted by nCounter. It is not uncommon to use microarray for breast cancer molecular subtyping for research. Our study showed that fundamental discrepancy existed between distinct GE assays, and cross-platform equivalence should be carefully appraised when molecular subtyping was conducted with oligonucleotide microarray.

ASSOCIATION OF RESIDUAL DUCTAL CARCINOMA IN SITU WITH BREAST CANCER OUTCOME AFTER NEOADJUVANT CHEMOTHERAPY

Eunju Shin, Jisun Kim, Tae-Kyung Yoo, Il Yong Chung, Beom Seok Ko, Hee Jeong Kim, Jong Won Lee, Byung Ho Son, Sae Byul Lee

ASAN Medical Center, Department of Breast Surgery, Korea

Background: In breast cancer, pathological complete reactions (pCR) after neoadjuvant chemotherapy (NAC) are closely related to overall. However, there is a controversy over whether the definition of the pCR should exclude or allow the presence of residual duct cancer (DCIS). We aim to clarify the association of residual DCIS in surgical specimens after neoadjuvant chemotherapy for breast cancer with survival outcome.

Methods: We retrospectively analyzed 326 patients with pCR (pT0 or pTis) who underwent breast surgery after neoadjuvant chemotherapy for breast cancer at single institution between January 2008 and December 2014. The overall survival (OS), disease free survival (DFS), local recurrence free survival (LRFS) were compared between the two groups and analyzed survival according to operation type.

Result: Of the 326 participants with pCR, 101 (31.0%) had residual DCIS. At a median follow-up of 65.3 months, group with residual DCIS patients had worse 5-year OS rate of 90.5% compared to 88.0% of group without residual DCIS patients ($p = 0.024$). There were also no significant difference in OS based on presence or absence of residual DCIS in the group underwent breast conserving surgery ($p = 0.995$). The group without residual DCIS had a higher OS than the group with residual DCIS in the group underwent total mastectomy ($p = 0.010$). Similar trends in DFS and LRFS analysis.

Conclusions: The presence or absence of DCIS can be as an important surrogate for adjuvant treatment after neoadjuvant chemotherapy.

HIGH ACCURACY OF PNACLAMP PIK3CA DETECTION KIT IN HORMONE RECEPTOR-POSITIVE, HER2-NEGATIVE BREAST CANCER

Bokyung Ahn[1], Hee Jin Lee[1], Jisun Kim[2], Sae Byul Lee[2], Sungwook Jung[3], Gyungyub Gong[1]

[1]ASAN Medical Center, Department of Pathology, Univ. of Ulsan College of Medicine, Korea, [2]ASAN Medical Center, Department of Breast Surgery, Univ. of Ulsan College of Medicine, Korea, [3]ASAN Medical Center, Department of Medical Science, AMIST, Univ. of Ulsan College of Medicine, Korea

Background: Detection of PIK3CA mutation is essential for advanced/metastatic hormone receptor-positive (HR+)/HER2- post-menopausal breast cancer patients who progressed after endocrine therapy since these patients can benefit from the FDA-approved, α-specific phosphatidylinositol 3-kinase inhibitor, PIQRAY (alpelisib) along with fulvestrant. In the present study, overall performance of PNAClamp™ PIK3CA Mutation Detection Kit was compared to the Therascreen PIK3CA detection kit.

Methods: Tissue only (n = 133) or with matched plasma samples (n = 146) of HR+/HER2- breast cancer patients who underwent surgical resection at Asan Medical Center during 2016 to 2022 were either prospectively collected or obtained from the Bio-Resource Center.

Result: PIK3CA mutation was prevalent in 45.5% (126/277) of the HR+/HER2- breast cancer patients for both detection methods. Positive and negative concordance rates between the two devices using the tissue were 96.9% [95% CI, 92.13 - 99.14] and 97.4% [95% CI, 93.40 - 99.28], respectively. Positive and negative concordance rates between the two devices using the plasma were 96.6% [95% CI, 88.29 - 99.59] and 96.6% [95% CI, 90.25 - 99.28], respectively. Discrepant results between the tissue and plasma were observed in 2.1% (3/146) and 4.1% (6/148) of the cases using PNAClamp™ and Therascreen, respectively, with an overall κvalue of 78.9. In detail, there were discrepant cases were 2 (tissue +/plasma-), and 1(-/+) for PNAClamp™, and 4 (+/-) and 2(-/+) for Therascreen.

Conclusions: PNAClamp™ is highly concordant with Therascreen analysis in detecting PIK3CA mutation for HR+/HER2- breast cancer patients. Our study results show that PNAClamp™ can be a suitable companion diagnostic tool for PIK3CA mutation detection.

THE UPDATE PREDICT BREAST CANCER PROGNOSTICATION IN 91,182 PATIENTS USING KOREAN BREAST CANCER REGISTRY DATA

Jungsun Lee[1], Minkyung Oh[2]

[1]*Inje Univ. Haeundae Paik Hospital, Department of Surgery, Korea,*
[2]*Inje Univ. College of Medicine, Department of Pharmacology, Korea*

Background: PREDICT is a widely used online prognostication and treatment benefit for patients with early breast cancer. This has been criticized due to underestimation of overall survival in for either young patients or hormone receptor positive breast cancers. The aim of this study was to conduct an independent validation exercise of the most up to version of the PREDICT algorithm (version 2.2) using real-world outcomes from the Korean Breast Cancer Registry Data.

Methods: Patients data were obtained for Korean Breast Cancer Registry (KBCR) records with a diagnosis of operable invasive breast cancer diagnosed in the period between January 2001 and December 2014. Prognostic scores were calculated using the PREDICT version2.2 algorithm. External validity was assessed by statistical analysis of discrimination and calibration. Calibration was assessed by comparing the predicted number of deaths to the observed number of deaths across relevant subgroups by Hosemr-Lemeshow test. Discrimination was assessed by area under the receiver-operator curve (AUC).

Result: A total 91,182 eligible cases were selected from 125,423 individual records. AUC statistics ranged from 0.73 to 0.78. Calibration results did not show close agreement between predicted and observed deaths, especially observed deaths were lower than predicted deaths among sub-groups. The 5-year complete follow-up sample reported some overestimation (11.76%), even the 10 year complete follow-up sample displayed more overestimation (22.45%).

Conclusions: Validation results suggests that the PREDICT tool remains irrelevant for contemporary Asian patients with operable breast cancer, especially in term of a long term survival.

CLINICAL OUTCOME OF ADJUVANT CAPECITABINE ACCORDING TO RESIDUAL CANCER BURDEN INDEX IN PATIENTS WITH RESIDUAL TRIPLE NEGATIVE BREAST CANCER AFTER NEOADJUVANT CHEMOTHERAPY

Yoonwon Kook, Ji Soo Jang, Seung Ho Baek, Min Ji Kim, Jung Hyun Kim, Sohyun Moon, Seung Eun Lee, Soong June Bae, Sung Gwe Ahn, Joon Jeong

Gangnam Severance Hospital, Department of Surgery, Korea

Background: Capecitabine is the standard treatment for triple negative breast cancer (TNBC) patient with residual disease (RD) after neoadjuvant chemotherapy (NAC) and surgery. However, there are few data on the predictive markers of capecitabine response. Residual Cancer Burden (RCB) is a validated tool to evaluate RD. We investigated whether capecitabine response can be predicted by looking into recurrence in patients who underwent adjuvant capecitabine versus observation according to RCB grade.

Methods: Non-metastatic TNBC patients with quantified RD by RCB from Gangnam Severance Hospital were included. They were divided into two cohorts either by adjuvant capecitabine or no adjuvant treatment. Patients with other systemic therapy were excluded. Recurrence free survival (RFS, months) was estimated using Kaplan-Meier test.

Result: 113 patients (Capecitabine 76 observation 37) with a median follow-up of 31 months were included. RFS for RCB 1 could not be estimated. In RCB 2, meadian RFS of the capecitabine cohort and the observation cohort were 74m versus 70m ($p = 0.636$) while for RCB 3, it was 32m versus 23m ($p = 0.465$). Exploratory analyses for clinicopathologic factors including baseline clinical and post-operative pathologic TNM stage, grade, TILs, and Ki-67 were done. None were predictive of capecitabine response in both univariate and multivariate analyses.

Conclusions: RCB was not able to delineate better or worse response to adjuvant capecitabine with statistical significance. However, it is important to note that patients with RCB 3 had distinctly differential RFS numerically by 32m versus 23m. Further investigation with maturation of data and larger number is warranted to determine possible indications of tailoring adjuvant treatment.

THE SIGNIFICANCE OF LOW HER2 EXPRESSION ON LATE RECURRENCE-FREE SURVIVAL (≥5 YEARS) IN ER-HER2- BREAST CANCER

Janghee Lee[1,2], Yeonjoo Kwon[1], Jung Ho Park[3], Sanghwa Kim[3], Young Ah Im[1], Hee-Joon Kang[1], Doyil Kim[3]

[1]Dongtan Sacred Heart Hospital, Department of Surgery, Korea, [2]Yonsei Univ. College of Medicine, Department of Medicine, Korea, [3]Hallym Univ. Sacred Heart Hospital, Department of Surgery, Korea

Background: As the results of the Destiny breast-04 trial were announced in 2022, research and interest in low HER2 expression have gradually increased. The Purpose of our study was to analyse the significance of low HER2 expression in ER-HER2- breast cancer patients.

Methods: We retrospectively identified patients who were diagnosed and treated for ER-HER2- breast cancer at Hallym University Sacred Heart Hospital and Dongtan Sacred Heart Hospital. The primary object of our study was to compare recurrence-free survival (RFS) according to the expression of HER2. For analysis, Kaplan-Meier survival curve was applied, and a multivariate Cox proportional hazard model was used to variable associated with RFS.

Result: A total of 350 ER-HER2- breast cancer patients were enrolled in the study. Among the patients in our cohort, approximately 80% were PR-negative and 90% received neoadjuvant or adjuvant chemotherapy. In Kaplan-Meier survival analysis, patients with HER2-1+ showed worse recurrence outcome than those with HER2-0 or HER2-2+ ($P = 0.023$). HER2-1+ was also a significant risk factor for poor RFS in multivariate analysis (HR, 1.91; 95% CI, 1.06-3.46; $P = 0.032$). Furthermore, HER2-1+ did not affect early recurrence within 5 years ($P = 0.643$), but had a negative effect on the late recurrence after 5 years ($P < 0.001$).

Conclusions: Patients with HER2-1+ had a poorer RFS compared to patients with HER2-0 or HER2-2+ patients. In particular, HER2-1+ was associated with increased late recurrence after 5 years. Further research on the mechanism underlying these results will be needed.

A SURVEY OF CLINICIANS ON THE USE OF ADJUVANT THERAPY FOR PREMENOPAUSAL WOMEN WITH BREAST CANCER

Youngwon Lee[1], Sae Byul Lee[1], Sei-Hyun Ahn[2], Tae-Kyung Yoo[1], Jisun Kim[1], Il Yong Chung[1], Hee Jeong Kim[1], Beom Seok Ko[1], Jong Won Lee[1], Byung Ho Son[1]

[1]*ASAN Medical Center, Department of Breast Surgery, Korea,*
[2]*Ewha Womans Univ. Mokdong Hospital, Department of Surgery, Korea*

Background: Considering prognostic stage with anatomic stage, clinicians decide whether to perform multigene assay, adjuvant chemotherapy, or additional ovarian suppression as a result of genetic information for hormone receptor (HR) positive, HER2 negative, early-staged, premenopausal patients. We aimed to find out the tendency of adjuvant therapy in practice.

Methods: From April to May of 2022, clinicians of the Korean Breast Cancer Society (KBCS) replied a web-based survey. The survey included 62 questionnaires with multiple choices, and questions were mainly about decision makings at each condition.

Result: 92 clinicians replied to the survey, and 91.3% were breast surgeons. 96.8% replied to perform chemotherapy for 35-year-old patients with pT2N0, Ki-67 50%, compared to 50.7% for pT1N0, Ki-67 10%, without ODX result, and only 35.6% answered with 47-year-old patients under same conditions. 84.3% chose chemotherapy with ODX RS 21, while 49.1% answered with ODX RS 16. About endocrine therapy, clinicians tended to choose TMX plus OFS than AI plus OFS for 5 years with adjuvant chemotherapy regardless of genomic and clinical risk. When the same patients didn't receive adjuvant chemotherapy, more clinicians replied to adjust AI plus OFS compared to those with adjuvant chemotherapy. Additionally, it showed longer duration of additional OFS to TMX with high clinical and genomic risk, and the duration of OFS became relatively shorter with older patients.

Conclusions: The decision-making regarding adjuvant therapy should be considered with clinical risk, genomic risk and age of each patient, and clinicians should consult with patients in detail about adverse effects and compliance in advance.

PIBF1 AS AN IMMUNOMODULATORY FACTOR IN BREAST CANCER AND PROGNOSTIC MARKER ACCORDING TO BREAST CANCER SUBTYPE

Eunju Shin[1], Tae-Kyung Yoo[1], Sae Byul Lee[1], Jisun Kim[1], Il Yong Chung[1], Beom Seok Ko[1], Hee Jeong Kim[1], Jong Won Lee[1], Jewon Ryu[3], Sang-Wook Lee[2], Byung Ho Son[1]

[1]ASAN Medical Center, Department of Surgery, Korea, [2]Univ. of Ulsan College of Medicine, Department of Radiation Oncology Asan Medical Center, Korea, [3]ASAN Medical Center, Department of Convergence Medicine, Korea

Background: With the increase in breast cancer, interest in the characteristics of tumor cells that enable prediction of prognosis after treatment has increased. Progesterone-induced blocking factor 1 (PIBF1) is described as immuno-modulators molecules involved in pregnancy, and malignant tumors can escape from maternal immunity by producing PIBF1. Studies on the association between breast cancer and PIBF1 are still lacking, especially related to prognosis in patients.

Methods: Samples, obtained from 469 patients underwent surgery between 2008 and 2013, were divided into two groups, TNBC and non-TNBC. Anti-PIBF1 antibody was used for immunohistochemical detection of the PIBF1 protein in tissues, whose sections were analyzed with cut-off value of 3 (intensity plus proportion). Kaplan-Meier survival analysis was used to assess the probability of overall survival (OS).

Result: We detected high PIBF1 expression in the non-TNBC group compared with TNBC group ($P < 0.001$). And we studied related factors, that in non-TNBC group, high PIBF1 expression is related to low histologic grade ($P = 0.015$), ER+, PR+, HER2- ($P < 0.001$), on the other hand, in TNBC group it is related to low Ki-67 ($P = 0.021$). Similarly, we found that high expression of PIBF1 in the non-TNBC group is related to the good OS ($P = 0.013$), but not in the TNBC group.

Conclusions: The existence of PIBF1 expression in breast cancers may lead new visions for prognosis and adjuvant therapy of breast cancer. As a result, non-TNBC cells have greater levels of expression of PIBF1 than TNBC according to immunohistochemistry and high levels of PIBF1 also have relations with better prognosis factors in non-TNBC group. Further research is needed to understand the clinical importance of this finding.

EVALUATION OF TREATMENT RESPONSE FOLLOWING NEOADJUVANT CHEMOTHERAPY IN STAGE III BREAST CANCER AND ITS OUTCOME

Wei Wen Ang, Sherwin Kuah

Tan Tock Seng Hospital, Department of Surgery, Singapore

Background: Neoadjuvant chemotherapy (NAC) is known to improve survival and pathological complete response (pCR) is a good prognostic indicator. At our unit, many women prefer to have surgery done upfront and in fact many try to avoid chemotherapy. Consequently most women undergoing NAC have more advanced Stage III disease. In this study we evaluate pathological response after NAC and identify predictors of response.

Methods: A retrospective review was done of 696 patients with Stage III breast cancer diagnosed and treated from 2006 to 2013 at two institutions. 253 (36.3%) of these patients received NAC. We defined pCR as no invasive carcinoma in breast and lymph nodes. Factors such as receptor positivity were assessed. Patients were followed up for a minimum of 5 years for overall survival and recurrence.

Result: 21 out of 253 women (8.3%) had pCR, of which 8 (3.1%) had residual in situ tumor. Women with pCR or residual in situ tumor had largely similar clinical and pathological parameters. Compared to women with residual invasive cancer, women with pCR or only residual DCIS were more likely to be ER/PR-negative ($p < 0.001$) and Her2-positive ($p < 0.001$). They had also more likely to have received trastuzumab as part of the neoadjuvant regimen ($p < 0.001$). At the 5 year mark, 21 patients presented with isolated local recurrences. Of which 8 were in those who received NAC.

Conclusions: Women with ER/PR-negative Her2-positive tumours had better response with NAC and were more likely to achieve pCR. However, there was no change in overall survival or 5 year recurrence rates.

THE USE OF ART THERAPY FOR BREAST CANCER PATIENTS IN AN ASIAN POPULATION – A PILOT STUDY

Melissa Seet, Su-Ming Tan

Changi General Hospital, Department of Surgery, Singapore

Background: Positive psychological outcomes have been demonstrated using Art therapy for cancer patients in Western populations. However, in Asia, it remains understudied and underutilized in breast cancer patients. This study aimed to explore the use of Art therapy in an Asian population.

Methods: Between Dec 2021 and July 2022, seven newly diagnosed, non-metastatic breast cancer patients, mean age of 51 years old (range 48 to 63), underwent a series of eight monthly themed group art therapy sessions in Singapore. Pre- and post-intervention questionnaires assessing the quality of life (The World Health Organization Quality of Life – BREF (WHOQOL-BREF)), measuring depressive symptomology (Centre for Epidemiologic Studies Depression Scale (CES-D)), and looking at coping methods after a stressful life event (Coping Orientation to Problems Experienced Inventory (Brief-COPE)) were obtained. Primary endpoints included an improvement of post-intervention scores from baseline.

Result: WHOQOL-BREF psychological domain scores revealed significant improvement, from pre-intervention mean score (61.3) to post-intervention score (77.0) ($p < 0.05$). CES-D demonstrated a decrease of depressive symptomology mean score of 41.2 to 32.3 ($p < 0.05$). All patients demonstrated an increased utilization of positive problem-focused coping strategy ($p < 0.05$) with a corresponding decrease in maladaptive coping methods ($p < 0.05$).

Conclusions: This pilot study suggests that Art therapy is effective in improving psychological functioning, and equipping breast cancer patients with coping strategies that may allow them to improve their quality of life in the long term.

IS THERE A SURVIVAL DIFFERENCE BETWEEN MALE AND FEMALE BREAST CANCER SUBTYPES ACCORDING TO THE PROGNOSTIC STAGING SYSTEM? A POPULATION-BASED COHORT STUDY

Fatih Aydogan[1], Ahmet Necati Sanli[2], Deniz Esin Tekcan Sanli[3], M. Kadri Altundag[4]

[1]Memorial Bahcelievler Breast Health Center and Kirklareli Univ. Medical School, Breast Health Center, Republic of Turkiye, [2]Abdulkadir Yuksel State Hospital, Department of General Surgery, Republic of Turkiye, [3]Gaziantep Univ., Department of Radiology, Republic of Turkiye, [4]MKA Breast Cancer Clinic, Department of Medical Oncology, Republic of Turkiye

Background: Due to the low incidence of male breast cancer, there is no prospective study comparing survival with female breast cancer. In retrospective studies investigating the difference in survival, there are conflicting results. It was aimed to compare overall and breast cancer-specific survival in male and female breast cancer subtypes according to the prognostic staging system.

Methods: Between 2010 and 2018, male and female breast cancers were compared in terms of age at diagnosis, race, laterality, hormone receptor and HER-2 positivity, molecular subtype, grade, and stage using the SEER Database of the US National Cancer Institute. The stage has been rearranged according to the 8th edition of the AJCC. In addition, overall survival (OS) and breast cancer-specific survival (BCSS) were compared according to gender.

Result: 243,150 patients were included in the study. 0.7% of all breast cancers were male breast cancer. In the whole population, OS and BCSS rates were significantly higher in females than in males ($p < 0.001$, $p < 0.001$, respectively). In the whole population, gender, age, race, surgical status, grade, estrogen receptor, progesterone receptor, Her2 receptor, molecular subtype, and stage were found to significantly affect OS and BCSS.

Conclusions: Breast cancer-specific mortality is significantly higher in male breast cancers, especially in the early stage, compared to female breast cancers. The high mortality of male breast cancers can be explained by the fact that the disease is detected at an older age, differences in tumor biology, and disease of heart-related death are higher.

THE ASSOCIATION OF TAMOXIFEN USE AND RISK OF CATARACT IN BREAST CANCER PATIENTS : A POPULATION-BASED STUDY IN TAIWAN

Cheng-Wei Chou[1], Ching-Heng Lin[2], Chih-Chiang Hung[3]

[1]Taichung Veterans General Hospital, Department of Medical Oncology, Taiwan, [2]Taichung Veterans General Hospital, Department of Medical Research, Taiwan, [3]Taichung Veterans General Hospital, Department of Surgery, Taiwan

Background: Tamoxifen is widely used in hormone-positive breast cancer patients. In the adjuvant setting, the use of tamoxifen might continue up to ten years. Possible ocular side effects had been reported in several trials. We retrospectively studied the potential association of tamoxifen use and the cataract risk.

Methods: Newly diagnosed female breast cancer were retrieved from the Taiwan National health insurance research database from 2000-2005 with follow up till the end of 2013. We matched patients receiving cataract surgery with non-cataract surgery patients according to age, index date, and the time interval in both groups for comparison.

Result: Among 23957 female breast cancer patients, a total of 1235 patients receiving cataract surgery were enrolled and matched with patients without cataract surgery. Age, time interval between breast cancer and index date were not significantly different in both groups. Although, comorbidities including hypertension, diabetes, hyperlipidemia, and ischemic heart disease were higher in the patients with cataract surgeries ($P < 0.05$). Multiple regression analyses showed an adjusted odds ratio of 1.46 (95% CI:1.11-1.91, $P = 0.006$) in the prolonged exposure of tamoxifen (more than 3 years) to develop a higher risk of cataract requiring surgery. Among the comorbidities, diabetes was also an important risk factor for developing cataract requiring surgery (adjust odds ratio:1.78, 95% CI:1.43-2.21, $P < 0.001$).

Conclusions: Among the breast cancer survivors, diabetes and long-term use of tamoxifen are associated with significantly higher risks for developing cataract requiring surgery. From our population-based study, active surveillance for ocular problems should be considered in the subgroups of breast cancer patients.

A MOBILE APP-BASED SHOULDER EXERCISE PROGRAM FOLLOWING BREAST RECONSTRUCTION: A PILOT STUDY INVESTIGATING FEASIBILITY

Soo Kim[1], Rhonda Loeppky[1], Angelica Lang[2]

[1]*Univ. of Saskatchewan, School of Rehabilitation Science, Canada,*
[2]*Univ. of Saskatchewan, Canadian Centre for Health and Safety in Agriculture, Canada*

Background: As many as 50% of cancer patients who've undergone mastectomy elect to have breast reconstruction. Despite the numerous benefits for quality of life, shoulder dysfunction post-reconstruction remains a problem for many. Based on observed kinematic changes post-reconstruction in a recent study, our team developed a tailored shoulder exercise program for a mobile app (ShAPP). The aim of this project was to explore the feasibility of ShAPP for a larger study.

Methods: A convenience sample of women post-reconstruction (n = 11) were recruited and randomized into 2 groups: education (control) or exercise. The education group had access to educational material on the app, and the exercise group, a 6-week (3X/week) evidence-informed upper extremity exercise program. Measures of shoulder pain, fatigue, and quality-of-life, as well as satisfaction were collected at 0, 3 and 6 weeks on the app. Planned analysis included descriptive statistics and repeated measures two-way ANOVA ($p < 0.05$).

Result: Participants enjoyed using the app (60%), found it easy to use (50%), and would consider participating in a longer program (75%). No adverse events were reported. No significant differences in pre-post measures were found but the final sample posed limitations. Drop-out rate was greater in the exercise group (n = 4).

Conclusions: Experiences with this version of ShAPP were overall positive. Drop-out rates likely reflected variability in time from surgery and lack of monitoring. The design for our larger study was informed from this pilot; participants were standardized to be 6-weeks post-op, monitored by a physical therapist remotely, and the length of the program was increased to 8 weeks.

IMPACT OF SYMPTOM CLUSTERS ON QUALITY OF LIFE OUTCOMES IN CANCER SURVIVORS

Jinhee Park[1], Heejun Kim[1,4], Junghee Yoo[3], Eunae Chun[3], Sunhyoung Bae[1], Yoojin Jung[1], Misun Chun[2]

[1]Ajou Univ. College of Nursing, Department of Nursing, Korea, [2]Ajou Univ. School of Medicine, Department of Radiation Oncology, Korea, [3]Ajou Univ. Hospital, Geyonggi Regional Cancer Center, Korea, [4]Ajou Univ. College of Nursing, Ajou Hospital, Korea

Background: This study aims to classify symptom clusters in cancer survivors using latent profile analysis (LPA) and determine the differences in quality of life based on symptom clusters.

Methods: Data from 871 adult cancer survivors who were enrolled in the Integrated Supportive Care Centers for Cancer Survivors between April 2020 and July 2022 were retrospectively analyzed. IBy means of the Mplus statistical software, symptom clusters were classified using finite Gaussian mixture model-based LPA. ANOVA was used to examine the differences in quality-of-life scores by symptom cluster.

Result: To investigate the symptom clusters, the analysis model included five symptoms: sleep disorders, anxiety, depression, pain, and fatigue. The LPA results revealed five symptom clusters. Class 1 (14.1%), the "high symptom cluster," was a group with overall high symptoms scores. Class 2 (48.3%), the "stable symptom cluster," was a group that had the lowest levels of all symptoms scores. Class 3 (18.8%), the "psychologically dependent symptom cluster," was a group with high scores for depression and anxiety. Class 4 (11.9%), the "average symptom cluster," was a group that had intermediate levels of overall symptoms scores. Class 5 (6.9%), the "highest symptom cluster," was a group with the highest scores of all symptoms. The class 2 showed the highest level of quality of life.

Conclusions: High-level symptoms experienced by cancer survivors may reduce their quality of life. Therefore, for cancer survivors to return to their daily lives after treatment, it is necessary to determine the severity of symptoms and provide personalized management based on the symptom cluster.

FACTORS INFLUENCING THE INTENTION TO INFORM IN HEREDITARY BREAST AND OVARIAN CANCER SYNDROME: THE K-CASCADE COHORT

Yeeun Kim[1], Yun Ji Jo[3], Jihye Kim[1], Agani Afaya[1], Maria C. Katapodi[2], Sue Kim[3]

[1]Yonsei Univ. College of Nursing, General Graduate Program, Korea, [2]Univ. of Basel, Department of Clinical Research, Switzerland, [3]Yonsei Univ. College of Nursing, Mo-im Kim Nursing Institute, Korea

Background: Cancer genetic testing is recommended for families with Hereditary Breast and Ovarian Cancer syndrome (HBOC) and family communication is an important first step. This study aimed to identify the factors that influence intention to inform a family member of HBOC.

Methods: This study is a descriptive study of baseline data from the K-CASCADE cohort of 257 HBOC index cases from the K-CASCADE cohort. Data were collected from March 2021 to December 2022. Family coherence, family support in illness, living alone, knowledge of breast cancer, genetic affinities, perceived cancer risk, education, and coping with stressful events were investigated. Using STATA version 16.1 zero-inflated negative binomial regression was done to analyze influencing factors between the intention and non-intention group and within the intention group.

Result: The rate of index cases who had intention to inform at least one relative was 32.3% and 67.7% for non-intention (zero relatives). Compared to the non-intention group, the intention group had higher perceived cancer risk (B = -0.36, 95%CI [-0.69, -0.036]), and higher family support in illness (B = -1.27, 95%CI [-2.44, -010]). Within the intention group, those who lived with family (B = -1.24, 95%CI [-2.27, -0.21]) and those who had higher genetic affinity (B = -0.15, 95%CI [-0.29, -0.01]) expressed greater intention to invite one more family member to the HBOC study.

Conclusions: Intervention programs considering the beliefs of cancer occurrence and exploring the family support systems will be imperative to improve Korean probands' intention to inform at-risk family members about HBOC.

CONVENTIONAL STANDARD-SIZED COTTON OR CUSTOMIZED HAND-KNITTED EXTERNAL BREAST PROSTHESIS AFTER MASTECTOMY: A MIXED-METHODS EVALUATION OF BREAST CANCER PATIENTS' PREFERENCES

Ruey Pyng Ng[1], John C Allen[2], Yen Yen Chia[1], Geok Hoon Lim[3]

[1]KK Women's and Children's Hospital, Department of Nursing, Singapore, [2]Duke-NUS Medical School, Office of Clinical Sciences, Centre for Quantitative Medicine, Singapore, [3]KK Women's and Children's Hospital, KK Breast Department, Singapore

Background: In breast cancer patients undergoing mastectomy without reconstruction, an external breast prosthesis could aid patients' recovery, improve body image and confidence by helping to regain a symmetrical chest appearance when dressed. However, external breast prosthesis preferences among Asian breast cancer patients was not previously studied. We aimed to compare patients' experience with the conventional commercially manufactured standard-sized (small, medium, large, extra-large) versus customized hand-knitted external breast prosthesis after unilateral mastectomy at a tertiary hospital. This is the first such study in Asian women, to our knowledge.

Methods: In this prospective study, participants used the conventional prosthesis followed by the customized one consecutively for at least 3 months before they were administered an identical questionnaire at 3 and 6 months respectively. The questionnaire assessed the patients' experience with the prosthesis on aspects of comfort, body image and satisfaction etc. Patients were also invited for in-depth interviews.

Result: Of 155 eligible patients, 148 patients participated with a response rate of 95.5%. 99 (67%) participants preferred the customized prosthesis, while 38 (25.7%) did not. 11 (7.4%) participants were undecided. Seventeen participants underwent in-depth interviews until data saturation on major qualitative themes was achieved. More patients experienced excessive sweating ($p < 0.0001$) and higher level of discomfort ($p = 0.0195$) with the conventional prosthesis as compared to the customized prosthesis.

Conclusions: Customized external breast prostheses could be an alternative to the conventional ones for breast cancer patients with mastectomy, with additional benefits of less sweating and more comfort perceived.

THE RELATIONSHIP BETWEEN KNOWLEDGE AND MEDICATION ADHERENCE TO ADJUVANT ENDOCRINE THERAPY IN BREAST CANCER PATIENTS

Ji Sook Kang[1], Unjong Choi[2], Eun Jeong Kim[3]

[1]Wonkwang Univ. School of Medicine, Department of Nursing, Korea, [2]Wonkwang Univ. Hospital, Department of Surgery, Korea, [3]Wonkwang Univ. Hospital, Department of Nursing, Korea

Background: This study was conducted to investigate the relationship between knowledge and medication adherence to adjuvant endocrine therapy in breast cancer patients

Methods: A total of 190 breast cancer patients in a university hospital located in J province were included, who agreed to participate in this study completed a self-report Questionnaire. The collected data were analyzed by descriptive analysis, t-test, ANOVA and Pearson's correlation using SPSS 26.0 statistical program.

Result: The average score of knowledge and medication adherence to hormonal therapy were 41.85 ± 5.41 (maximum-48), and 6.24 ± 2.22 (maximum-9). As knowledge hormonal therapy, there were significant differences by age ($F = 15.82$, $p < .001$), education level ($F = 17.69$, $p < .001$), monthly income ($F = 7.86$, $p < .001$) and comorbidity ($t = -3.94$, $p < .001$). As medication adherence for hormonal therapy, there were also significant by age ($F = 6.48$, $p < .001$), education level ($F = 7.38$, $p < .001$), monthly income ($F = 8.77$, $p < .001$), occupational status ($t = 4.69$, $p < .001$) and perceived health status ($F = 10.86$, $p < .001$). There were no significant correlations between knowledge and medication adherence to adjuvant endocrine therapy in breast cancer patients ($r = .072$, $p = .326$).

Conclusions: The medication adherence for hormonal therapy of breast cancer patients has nothing to do with knowledge for hormonal therapy. Therefore, we need to explore the various variables that promote medication adherence to adjuvant endocrine therapy in breast cancer patients. And it is suggested that strategies of physical, emotional and social approach with breast cancer patients

DEVELOPMENT OF THE NURSING METAVERSE SIMULATION MODULE FOR BREAST CANCER WOMEN'S PRE AND POST-OPERATIVE NURSING CARE

Jiyoung Kang[1,2]

[1]*Jeju National Univ., College of Nursing, Korea,* [2]*Jeju National Univ., Research Institute of Health and Nursing, Korea*

Background: Nursing practice education faces a new paradigm with metaverse learning through experiences taking care of virtual patients. This study aims to develop the metaverse-based nursing simulation module for breast cancer women's pre and post-operative nursing care. The researcher applied the developed nursing metaverse practical simulation training content to 30 nursing students and explored their immersive learning experiences.

Methods: Nursing metaverse simulation contents using gamification elements were developed according to the steps of assessment, design, development, implementation, and evaluation based on the conceptual framework of three-dimensional nursing simulation education. A convergent parallel mixed-methods design using online surveys and individual interviews was used to explore students' learning flow experience.

Result: The nursing metaverse platform was developed to enable integrated and continuous virtual experiential learning by reflecting scope of practice, complexity, and student competency. This content was implemented to enable metaverse simulation training, medical order, nursing record, communication using sbar, nurse chatting, applied nursing process, and debriefing. Learners enter the metaverse space through avatars, and 1 professor, 1 trainer, and up to 8 students can participate simultaneously. Students stated that the platform was vivid and valuable because they could learn about the breast cancer patients' pre and post-operative nursing processes in a fun and realistic way while continuously integrating care for the patients.

Conclusions: The oncology nursing metaverse learning content allowed students to embrace their holistic learning by experiencing a fun, practical, and immersive environment as a new learning tool.

A RANDOMIZED, DOUBLE-BLIND, PLACEBO-CONTROLLED STUDY OF OLANZAPINE FOR CINV DURING T-DXD TREATMENT IN HER2 POSITIVE METASTATIC BREAST CANCER PATIENTS: WJOG14320B (ERICA)

Hitomi Sakai[1], Junji Tsurutani[1], Takamichi Yokoe[2], Chiyo K Imamura[1], Koji Matsumoto[3], Tsutomu Iwasa[4], Yasutaka Chiba[5], Yuji Hirakawa[6], Toshimi Takano[7]

[1]Showa Univ. School of Medicine, Advanced Cancer Translational Research Institute, Japan, [2]Keio Univ. School of Medicine, Department of Surgery, Japan, [3]Hyogo Cancer Center, Department of Medical Oncology, Japan, [4]Kindai Univ. Faculty of Medicine, Department of Medical Oncology, Japan, [5]Kindai Univ. Hospital, Clinical Research Center, Japan, [6]Daiichi Sankyo Co., Ltd, Oncology Medical Science Department, Japan, [7]The Cancer Institute Hospital of Japanese Foundation for Cancer Research, Department of Breast Medical Oncology, Japan

Background: Nausea and vomiting are commonly reported adverse effects in trastuzumab deruxtecan (T-DXd) therapy. Nausea of any grade was reported in 77.7% of patients and vomiting in 45.7% in the DESTINY-Breast01 trial. Olanzapine at 5 mg has been shown to reduce the risk of delayed nausea and vomiting in patients undergoing highly emetogenic chemotherapy in the J-FORCE study. We focus on the efficacy of olanzapine in the management of persistent nausea and vomiting in T-DXd treatment and start to conduct ERICA study.

Methods: ERICA (jRCTs031210410) is a randomized, double-blind, placebo-controlled study of prophylactic olanzapine for patients with HER2 positive metastatic breast cancer with T-DXd treatment. Patients are randomly assigned to receive either olanzapine 5 mg on day1-6 or placebo with 5-HT3 receptor inhibitor and dexamethasone on day1. The primary endpoint is complete response (CR) rate (no emesis and no rescue medications) during 24120 hours post-T-DXd administration). The secondary endpoints include CR rate during 0-24, 0-120, 120-504, and 0-504 hours, complete control rate, total control rate, the rate of no nausea, Quality of life (EORTC QLQ C-30), other symptoms, including diarrhea, constipation, abdominal pain, bloating, decreased appetite, fatigue, and insomnia assessed by PRO-CTCAE, and safety. An electronic PRO (ePRO) system is used to capture patients' symptoms.

Result: NA.

Conclusions: This study is currently open and actively recruiting at institutions in West Japan Oncology Group (WJOG). Funding: Daiichi Sankyo Co., Ltd The study protocol was presented at the 30th Annual Meeting of the Japanese Breast Cancer Society (EP17-4, Trial in Progress). This is an Encore Presentation.

A RANDOMIZED CONTROLLED TRIAL USING SURGICAL GLOVES TO PREVENT CHEMOTHERAPY-INDUCED PERIPHERAL NEUROPATHY BY PACLITAXEL IN BREAST CANCER PATIENTS (AIUR TRIAL)

Young-Joon Kang[1], Chang Ik Yoon[2], Jong Min Baek[3], Yong-Seok Kim[4], Ye Won Jeon[5], Jiyoung Rhu[6], Dooreh Kim[2], Se Jeong Oh[1], Huieun Ju[1], Jae Pak Yi[1]

[1]The Catholic Univ. of Korea, Incheon St. Mary's Hospital, Department of Surgery, Korea, [2]The Catholic Univ. of Korea, Seoul St. Mary's Hospital, Department of Surgery, Korea, [3]The Catholic Univ. of Korea, Yeouido St. Mary's Hospital, Department of Surgery, Korea, [4]The Catholic Univ. of Korea, Uijeongbu St. Mary's Hospital, Department of Surgery, Korea, [5]The Catholic Univ. of Korea, St. Vincent's Hospital, Department of Surgery, Korea, [6]The Catholic Univ. of Korea, Bucheon St. Mary's Hospital, Department of Surgery, Korea

Background: Chemotherapy-induced peripheral neuropathy (CIPN) is the most common non-hematological, dose-limiting, adverse effect of paclitaxel. No treatment for CIPN can be strongly recommended; prevention is of major importance. Cryotherapy, compression therapy, and exercise therapy can be considered for prevention, but no definitive recommendations. This is because larger sample-sized studies are needed to confirm the efficacy and clarify risks. We plan to use two normal-sized gloves for compression therapy to reduce discomfort and increase adherence to the procedure.

Methods: The clinical trial is a multicenter, randomized controlled, open-label study that will be conducted at six university hospitals. Eligible participants are women aged 19-69 years with histologically or clinically stage II-III breast cancer who will receive paclitaxel chemotherapy for at least 12 weeks. The primary outcome of the study is to demonstrate the preventive effect of compression therapy using surgical gloves as measured by the change in the neurotoxicity component of the Functional Assessment of Cancer Therapy-Taxane questionnaire.

Result: The statistical methods proposed in the trial design are appropriate for the type of data expected. For nominal variables such as clinical pathological factors, the chi-squares test or Fisher's exact test will be used for evaluation, and for numerical variables, Student's t-test or corresponding non-parametric method such as Mann-Whitney U-test will be used to analyze. If necessary, important variables will be analyzed through stratification or logistic regression. The trial aims to enroll 126 women, including a drop-off rate of 10%.

Conclusions: The study has not started recruiting participants.

PREDICTORS OF SURVIVAL IN PATIENTS WITH BRAIN METASTASIS SECONDARY TO BREAST CANCER

Atlal Abusanad[1], Omar Iskanderani[1], Reem Ujami[1], Omalkhair Abualkair[2], Rolina Alwassia[1]

[1]*Faculty of Medicine, King Abdulaziz Univ., Department of Medical Oncology, Saudi Arabia,*
[2]*Dr. Sulaiman Al Habib Hospital, Department of Medical Oncology, Saudi Arabia*

Background: Breast cancer (BC) is the most common malignancy in women from Saudi Arabia. Data on the pattern and outcome of brain metastasis (BM) in breast cancer patients is yet to be reported to inform the local practice.

Methods: A retrospective cohort study included BC patients with BM was conducted. Survival, factors influencing survival and the risk of death were examined. A p-value of less than 0.05 was considered statistically significant.

Result: 111 patients with BM due to BC were analyzed. All are female with a mean age 50.28 ± 11.61 years. IDC (93%), grade III (71%), tumor > T2 (64%) and N+ve (60%) BC were the majority. HER2-positive/ HR-negative was 21%, HER2/HR- positive was 16%, HR-positive/HER2-negative was 31%, triple negative breast cancer (TNBC) was 22.5% and unknown in 10%. 60% had metastases on presentation with 41% had both skeletal and visceral. Brain lesions > three were reported in nearly half of the cohort. Whole brain radiotherapy (WBRT), surgical resection and SRS were reported in 84%, 16% and 22%, respectively. The mean survival time was 3.31 years with a maximum of 4.23 years and a minimum of 2.39 years. Patients with HR or HER2-positive BC had a significant longer survival ($p = 0.039$, 0.033 respectively). The presence of visceral metastases increased the likelihood of death in BC patients with BM up to 6 folds ($p = 0.031$).

Conclusions: Mortality was associated with the presence of extracranial metastases, particularly visceral metastases in this cohort. Longer survival was seen with specific subtypes (HER2 and HR-positive), suggesting advancements in systemic treatments against these subtypes.

BRCA TESTING RATE IN KOREAN BREAST CANCER PATIENTS: A NATIONWIDE STUDY

Yunghuyn Hwang, Tae-Kyung Yoo, Sae Byul Lee, Jisun Kim, Hee Jeong Kim, Beom Seok Ko, Jong Won Lee, Byung Ho Son, Il Yong Chung

ASAN Medical Center, Department of Breast Surgery, Korea

Background: As the understanding of breast cancer gene (BRCA) increases, the indications of tests are increasing and the management methods for mutation carriers are also evolving. However, not all eligible patients benefit from BRCA testing. In this study, we investigated the distribution of BRCA testing rates in Korea through national insurance claim data.

Methods: Health Insurance Review & Assessment Service (HIRA) claim data of Korean patients diagnosed with breast cancer from 2008 to 2018 was collected. Of the HIRA's BRCA test reimbursement criteria, which data could be secured were age (less than 40 years of age). Comparisons were made according to year and region. The primary outcome was the ratio of those who were tested among those who were indicated.

Result: From January 2010 to December 2017, of the 163,208 first-diagnosed breast cancer patients, 18,308 were women under the age of 40. Of these, 6119 patients underwent the BRCA test, accounting for 33.4% of the subjects. BRCA testing rate increased gradually over time from 6.8% in 2010 to 64.5% in 2017. BRCA testing rate in 2017 was very high at 83.4% in Seoul, whereas the testing rates in metropolitan cities and others were relatively low at 40.9% and 49.7%, respectively.

Conclusions: BRCA testing rate has increased over time and it was higher in Seoul than in metropolitan cities or others. Additional research is needed on the causes of the difference in testing rates between regions.

COMPARISON OF DIFFERENT COMBINATION OF RECIPIENT VESSELS FOR BIPEDICLED DIEP ON UNILATERAL BREAST RECONSTRUCTION

Chiafang Chen, Jung Ju Huang

Chang Gung Memorial Hospital, Department of Plastic Surgery, Taiwan

Background: The deep inferior epigastric artery perforator (DIEP) flap is currently the most common flap for breast reconstruction. Based on bilateral deep inferior epigastric artery perforators, the DIEP flap can be supplied by either side of artery to provide adequate perfusion. However, in Asian patients, due to low BMI and smaller abdomen size, we now included bilateral pedicles to get more well-perfused soft tissue for reconstruction. Previously, we used retrograde and antegrade IMA to anastomosed to two perforators. Due to the development of robotic-assisted mastectomy, the lateral approach and short incision is difficult for IMA based anastomosis. In this study, we tried to compared if the substitute recipient arteries of thoracodorsal artery and lateral thoracic artery are as reliable as internal mammary artery (IMA) for breast reconstruction.

Methods: Collecting patient receiving robotic-assisted mastectomy and DIEP flap reconstruction in our hospital. Compared the flap utilization rates, surgery duration, vascular complications and postop fat necrosis of with traditional mastectomy excision and IMA based DIEP flap reconstructions.

Result: We had total 45 patients received bipedicled DIEP flap reconstruction. The surgery duration and flap utilization rates were similar in two groups. The exploration rate was similar in two groups. Only 1 patient in robotic-assisted group had medial and inferior pole fat necrosis, the incidence rate was statistically non-significant in two groups.

Conclusions: Combination of thoracodorsal and lateral thoracic artery as the recipient arteries were as reliable as IMA to supply the DIEP flap. The laterally based characteristics made them a better choice in bipedicled DIEP flap reconstruction for robotic-assisted mastectomy cases.

FLUORESCENCE-GUIDED SURGERY FOR ROTOBIC-ASSISTED BREAST-CONSERVING SURGERY IN BREAST CANCER: A CASE REPORT

Jun-Hee Lee, Jihyoun Lee, Min-Hyuk Lee

Soonchunhyang Univ. Hospital Seoul, Department of Surgery, Korea

Background: Since robotic breast cancer surgery was introduced in 2016, the number has been steadily increasing. However, compared with mastectomy, robotic-assisted breast-conserving surgery (RA-BCS) is not routinely being performed for several reasons. If tumor is located near to skin, it is difficult to obtain oncologic safety margin and if the resection margin is positive, reoperation is not easy because positive margin site is far from the robotic incision site. Therefore, localization of the tumor is very important in RA-BCS for proper and sufficient resection. We planned surgery using fluorescence with indocyanine green (ICG) and identified the tumor margin using firefly mode which is detecting fluorescence in da Vinci system.

Methods: Here we report some cases about RA-BCS in breast cancer. Tumor localization is performed by inserting a needle into tumor, and then intraoperative ultrasonography-guided ICG injection was performed to mark the margin. The tumor is excised around the area marked with ICG by looking green fluorescence while running firefly mode.

Result: After checking the inserted needle, we identified the margin around the tumor through ICG and resected cylindrically. The direction of the lump was set with clips at superior and lateral portion, and frozen biopsy was performed. After surgery, the shape of both breasts was almost the same and natural, both patient and the medical team were satisfied with no scar on breast.

Conclusions: Although there are still many hurdles for RA-BCS to be successfully performed, it would be possible to secure an oncologic safety margin comparable to conventional BCS through tumor localization using fluorescence.

MALIGNANT PHYLLODES TUMOUR CO-EXISTING WITH INVASIVE DUCTAL CARCINOMA AND DUCTAL CARCINOMA IN-SITU: A RARE ENTITY

Jung Ah Lee[1], You Chan Shin[1], Gail Chua[2], Evan Woo[3], Gudi Mihir[4]

[1]KK Women's and Children's Hospital, Department of Breast Surgery, Singapore, [2]National Cancer Centre Singapore, Department of Radiation Oncology, Singapore, [3]KK Women's and Children's Hospital, Department of Plastic Surgery, Singapore, [4]KK Women's and Children's Hospital, Department of Pathology, Singapore

Background: Breast malignant phyllodes tumor is known to be rare, accounting for around 1% of all breast malignancies. It is even more rare to have co-existing malignancies on ipsilateral breast.

Methods: We report a case of a patient who was diagnosed with malignant phyllodes tumor with co-existing invasive ductal carcinoma (IDC) and ductal carcinoma in situ (DCIS).

Result: Patient visited hospital complaining of a right breast large lump, and mammogram and ultrasound revealed a 11 cm sized well circumscribed mass. Core needle biopsy was performed and histology was reported as a cellular fibroepithelial lesion and benign phyllodes could not be excluded. Wide excision for right breast lump was performed and the lump was diagnosed with a 9.5 cm sized malignant phyllodes tumor with low grade DCIS. Patient underwent right skin sparing mastectomy and sentinel lymph node biopsy with transverse rectus abdominis myocutaneous flap reconstruction. Final histology revealed a 2.4 cm sized IDC without lymph node metastasis or any residual malignant phyllodes tumor. Patient completed chemotherapy, radiation therapy and has been free of recurrences and distant metastasis for 2.5 years.

Conclusions: Concurrent malignant phyllodes tumor with IDC and DCIS is extremely rare and there are no standardized treatments or known prognosis. Such patients should be treated with care for each malignancy.

INVASIVE LOBULAR CARCINOMA PRESENTING AS CHYLOUS ASCITES: A CASE REPORT

Jung Ho Park[1], So Eun Ahn[1], Sanghwa Kim[1], Yong Joon Suh[1], Ho Young Kim[2], Doyil Kim[1]

[1]*Hallym Univ. Sacred Heart Hospital, Department of Surgery, Korea,*
[2]*Hallym Univ. Sacred Heart Hospital, Department of Medical Oncology, Korea*

Background: Chylous ascites can be caused by disruption of mesenteric lymphatic channel, which include congenital anomaly, surgery, trauma, and malignancy. Although chylous ascites frequently occur after gastrointestinal procedures, there is no report of chylous ascites caused by breast cancer.

Methods: A 50-year-old woman presented with severe abdominal distension and swollen leg. She had dyspepsia and abdominal distension for two months. She had a erythematous lesion on her breast for 1 year. Physical examination revealed a 5-cm extent skin thickening with redness and multiple sub-centimeter nodules, which are suggestive of inflammatory breast cancer. Punch biopsy revealed invasive lobular carcinoma. Palliative docetaxel was administrated, and a pigtail catheter was inserted to drain ascites. The ascites changed into white color after diet, suggesting chylous ascites. Endoscopic examination showed a diffusely depressed lesion on stomach, and it was confirmed metastatic invasive lobular carcinoma from breast.

Result: After multiple cycles of cytotoxic chemotherapy, the amount of ascites decreased.

Conclusions: Herein, we present a rare case of chylous ascites caused by breast cancer with gastrointestinal metastases.

UNEXPECTED PULMONARY METASTASIS TO BREAST: A RARE BUT IMPORTANT DIAGNOSIS

Sean Sw Park[1,2], Shawn Ng[1,2], Rita Poon[1]

[1]*Gosford Hospital, Department of Surgery, Australia,* [2]*The Univ. of Newcastle, Department of Surgery, Australia*

Background: While it is common for breast cancers to metastasise to the lungs, pulmonary metastasis to the breast is very rare with an incidence of 0.5-3%. Since the presenting symptoms of the primary and secondary breast cancers are similar, clinical differentiation between the two can be challenging. However, making an accurate diagnosis between the two is of paramount significance as the management and prognosis are vastly different.

Methods: We report such a case in a 61-year-old lady on the background of a previous T2N1M0 left breast cancer, which was a grade III, ER/PR positive and HER2 negative invasive ductal carcinoma. The cancer was treated with a combination of surgery and immunotherapy. Subsequently, 4 years later, she presented with dyspnoea with a pulmonary nodule, the histopathology of which revealed a poorly differentiated adenocarcinoma.

Result: A new right breast lesion was also found, which demonstrated a high-grade triple negative carcinoma on core biopsy without metastatic burden on PET CT. With negative BRCA genes and discordant breast pathology, a pulmonary metastatic lesion to the breast was suspected. The morphology, immunohistochemistry, and molecular testing were compared between the lung and breast lesions, which demonstrated similar cancer profiles with positive CK 7, 8 and 18, as well as KRAS mutation. Given that the patient had a solitary metastasis with ECOG status of 1, a wide local excision was performed, followed by immunotherapy.

Conclusions: This case illustrates that a high index of clinical suspicion in unusual disease pattern remains the key to accurate diagnosis and decision making for secondary breast cancer.

POROCARCINOMA CLINICALLY AND HISTOPATHOLOGICALLY MIMICKING PAGET DISEASE OF THE NIPPLE: AN EXTRAORDINARY CASE REPORT

Phatcharawan Prastiviset[1], Panitta Sittinamsuwan[2], Mongkol Boonsripitayanon[1], Pongthep Pisarnturakit[1]

[1]Head, Neck and Breast Surgery, Faculty of Medicine Siriraj Hospital, Department of Surgery, Thailand, [2]Pathology, Faculty of Medicine Siriraj Hostpital, Department of Pathology, Thailand

Background: Porocarcinoma is a very rare type of adnexal skin carcinoma that confused with other skin carcinoma. It arises from the intra-epidermal portion of the eccrine sweat glands. To date, few cases of porocarcinoma in the breast have been published.

Methods: Report rare interesting case.

Result: We presented a rare case of primary breast porocarcinoma in 59-year-old woman, presented with left nipple ulcer without breast mass and axillary lymph node lymphadenopathy. Mammogram and ultrasound showed skin thickening of left nipple. Incisional biopsy at left nipple was performed and demonstrated a carcinoma with squamoid differentiation and basaloid neoplastic cell with cuticular differentiation, compatible with porocarcinoma. Immunohistochemistry for estrogen receptor was 10%, progesterone receptor was negative, HER-2 negative, Ki-67% was up to 90%. Additional immunostaining demonstrated that the neoplastic cells mark with Gata-3, p40, CK19 and EMA. CK7 highlighted cuticular differentiation. We performed wide excision included left nipple ulcer and sentinel lymph node biopsy were negative. Patient was received adjuvant endocrine and radiotherapy without chemotherapy. Overall, the treatment was successful. Now, the patient is no recurrence for one year.

Conclusions: Porocarcinoma is very rare and not common site in breast or nipple region. Our patient's manifestation was not similar in the previous published literature. Porocarcinoma can present mimic like Paget disease, it may be prone to misdiagnosis. Tissue biopsy and immunohistochemistry are keyword for diagnosis. Complete excision and axillary surgical staging are the mainstay of treatment. Adjuvant radiotherapy should be used to assist in local control. The rule of endocrine therapy is depend on hormonal receptors status.

AN UNUSUAL SITE FOR BREAST CLIP MIGRATION

Yien Sien Lee[1], Benson Wen Guang Ang[2], Geok Hoon Lim[2]

[1]*KK Women's and Children's Hospital, Department of Radiology, Singapore,*
[2]*KK Women's and Children's Hospital, Department of Surgery, Singapore*

Background: Clip migration following breast biopsy is a known complication. The migrated clip is usually found within the breast. We describe a rare case of delayed clip migration to the skin following MRI guided biopsy of the breast, highlighting its natural history of presentation and treatment.

Methods: A 48 year old patient with BRCA2 mutation presented for high risk screening. MRI breasts showed ductal enhancement in the lower central left breast. The lesion had no sonographic or mammographic correlate. In view of patient's BRCA mutation status, decision was made to proceed with MRI-guided vacuum assisted biopsy with 10G needle. The procedure was performed uneventfully and an UltraCor Twirl marker was deployed at the biopsy site.

Result: 2 months after biopsy, patient noticed a skin lump at the biopsy site. 4 months later, clip migration to the skin was confirmed on imaging.

Conclusions: The migrated clip would get caught on clothing resulting in painful tugging of the breast during dressing. Hence clip was excised, 1 year after excision, the patient remained well.

NIPPLE ADENOMA: A CASE REPORT

Youn Jung Cha, Eunhwa Park

Dong-A Univ. Hospital, Department of General Surgery, Korea

Background: Nipple adenoma (NA) is a rare benign breast disease. It most commonly affects women in their fourth decades of life. Due to the rarity of the disease, the exact incidence rate has not been established. NA presents clinically with palpable nodule on the nipple, nipple erosion with discharge, nipple enlargement, nipple deformity. NA can be misdiagnosed with other proliferative diseases including Paget's disease. Histological confirmation is essential to exclude other proliferative disease. Treatment is surgical excision.

Methods: Here we report a rare case of benign breast disease.

Result: A 37-year-old woman presented with a red-colored tumor on her right nipple for 10 months, with the nipple erosion and bloody nipple discharge. The patient was recommended for breast ultrasonography and mammography. Benign calcification was found on mammography. There were no lesions that could cause nipple discharge on ultrasonography. Punch biopsy was performed for diagnosis. The biopsy result was NA. For treatment, surgical excision of the NA with complete resection of the nipple and part of the surrounding areola was performed. Part of the areola was left to obtain a cosmetically satisfactory result.

Conclusions: NA is a very rare benign disease involving the major lactiferous ducts. It is clinically resembling Paget's disease of the nipple or malignant breast disease. Early diagnosis is important since it allows for less invasive surgery. The purpose of reporting this case is to highlight the possibility of this rare benign disease, which may be easily overlooked clinically and also demands careful histopathological examination for its correct diagnosis.

EXTENSIVE THROMBOSIS CAUSING SUPERIOR VENA CAVA SYNDROME IN A PATIENT WITH BREAST CANCER

Jihye Choi[1,2], Hokyun Noh[2], Byeonghun Oh[2], Kwang Woo Choi[2]

[1]*Seoul National Univ. College of Medicine, Department of General Surgery, Korea,*
[2]*National Medical Center, Department of General Surgery, Korea*

Background: Although patients with breast cancer typically have an elevated venous thromboembolic risk, massive thrombosis causing superior vena cava (SVC) syndrome is uncommon, with only a few cases reported in literature. We highlight a case of SVC syndrome in a breast cancer patient with multiple potential thromboembolic risk factors.

Methods: A 64-year old female with left-sided, stage IV HER2+ inflammatory breast cancer (cT4dN2M1, liver single) presented with suddenly developed facial edema, left arm swelling and dyspnea. The patient could hardly speak, and oral intake was impossible due to severe laryngeal edema. She had received 15 cycles of pertuzumab and trastuzumab through chemoport in right internal jugular vein (IJV). She also underwent concurrent palliative radiotherapy after palliative MRM (ypT2N1aM1). On CT angiography, thrombosis was extensively filling Rt and Lt IJV, innominate vein, brachiocephalic vein and SVC.

Result: Patient was immediately treated with enoxaparin. Head elevation, oxygen, fluid and salt restriction was applied. We decided to reserve the chemoport because the other vascular approach was not readily available due to both IJV occlusion and obesity (BMI28). After two weeks of anticoagulation, her symptoms were much relieved. After 5 months of apixaban, thrombosis is being successfully treated to date, without neither chemoport removal nor any invasive treatments.

Conclusions: In addition to risks contributed by the cancer itself, thromboembolic risk in patients with breast cancer may further be complicated by concomitant anti-cancer treatments, underlying general conditions and indwelling catheters. Although rare, clinicians should recognize the possibility of SVC syndrome in patients with breast cancer, as early diagnosis and treatment can prevent catastrophic complications.

ACCESSORY BREAST CANCER IN THE ANTERIOR CHEST WALL: A CASE REPORT

Soeun Park, Young Up Cho

CHA Ilsan Medical Center, Department of Surgery, Korea

Background: Accessory breasts occur as a result of incomplete regression of the mammary ridges. Accessory breast tissue can exist anywhere along this region, most commonly developing in the axilla or inframammary fold. Accessory breast cancer on chest wall has been reported rarely, and there is no specific guideline for treatment.

Methods: Case presentation: A 37-year-old Korean woman visited our clinic after diagnosed as ductal carcinoma in situ (DCIS) of left breast on vacuum-assisted breast excision. About 2 cm palpable masses were observed on both sides of lower anterior chest wall, and the left mass showed low suspicious feature on ultrasound. During partial mastectomy, the chest wall masses were resected together.

Result: A final pathology report identified the left chest wall mass as invasive ductal carcinoma, the right chest wall mass as fibroadenoma, and the left breast mass as DCIS. Sentinel lymph node biopsy showed one nodal metastasis of all three lymph nodes. Following surgery, she is receiving chemotherapy.

Conclusions: Accessory breasts apart from breasts are apt to be ignored by clinicians. The ectopic tissue along the mammary ridge should be carefully considered as accessory breast, and the potential for malignancy should be considered.

MACHINE LEARNING CLASSIFICATION OF TRIPLE NEGATIVE BREAST CANCER USING TRANSCRIPTOMICS DATA

Rohit Kumar Verma, Ashutosh Singh

Shiv Nadar Institution of Eminence, Department of Life Sciences, India

Background: Breast cancer is one of the complex cancers with several molecular types and subtypes. Triple negative breast cancer (TNBC), is more aggressive and has a greater recurrence rate than other kinds of breast cancer. Classifying TNBC from non-TNBC is a key medical need. Here in this study, we classified the TNBC to non-TNBC using gene expression data.

Methods: In this work, we analyzed the data from The Cancer Genome Atlas (116 TNBC and 979 non-TNBC samples) for protein coding (PC) and non-coding genes (NC). Different strategies for developing and validating classification models are used to get the best features (genes). Here we have evaluated the performance of most of the ML-based classification algorithms using features selected as an ensemble approach at different threshold levels to train the models for classifying the TNBC from non-TNBC.

Result: Here in this study, we found 55 protein coding genes and 66 non-coding genes using different Machine Learning (ML) model as a classifier and among which the Support Vector Machine with accuracy 98.13% for PC and 98.81% for NC genes was able to classify into TNBC and non-TNBC. The top classifiers further validated using qRTPCR.

Conclusions: RNA expression data can be used to distinguish TNBC from non-TNBC using appropriate ML model. Our findings suggest that using 55 protein coding genes and 66 non-coding genes can classify TNBC and non-TNBC. TNBC is characterized by low expression of the estrogen receptor (ER), progesterone receptor (PR), and HER2. In contrast, non-TNBC typically expresses one or more of these receptors.

BREAST TISSUE SIGNATURE RECOGNITION: USING HYPERSPECRAL IMAGING TECHNIQUES AND SIGNAL INTENSITY DECAY CURVES IN IVIM-MR IMAGING

Si-Wa Chan[1,2], Guan-Yuan Chen[3], Chein-I Chang[4], Yen-Chieh Ouyang[3], Chin-Yao Lin[5], Chih-Chiang Hung[6], Kuo-Chung Wang[6], Chih-Yean Lum[6]

[1]Taichung Veterans General Hospital, Department of Radiology, Taiwan, [2]National Chung Hsing Univ., Department of Post Baccalaureate Medicine, College of Medicine, Taiwan, [3]National Chung Hsing Univ., Department of Electrical Engineering, College of Electrical Engineering and Computer Science, Taiwan, [4]Univ. of Maryland, Department of Computer Science and Electrical Engineering, U.S.A., [5]Buddhist Tzu Chi Medical Foundation & School of Medicine, Department of Surgery, Taichung Tzu Chi Hospital, Taiwan, [6]Taichung Veterans General Hospital, Department of Breast Surgery, Taiwan

Background: Delayed contrast-enhanced breast MRI provides a non-invasive digital biomarker with good spatial resolution and reproducibility for early detection of breast cancer. Two major challenging problems arise in DCE-MRI. The first is that even breast DCE-MRI has demonstrated high sensitivity in tumor detection, but remains a challenge in distinguishing benign from malignant. Another problem is that contrast media injected under blood microperfusion is toxic and may cause idiosyncratic reactions in a small number of people. Different from traditional anatomical MRI, this paper proposes to use apparent diffusion coefficient (ADC) and intra-voxel incoherent motion (IVIM) parameters to distinguish malignant breast lesions from benign lesions.

Methods: MR imaging for this research was generated on a 3T MR system. Axial IVIM imaging was acquired by using echo planar imaging (EPI) single spin echoes, and these images covered both breasts. Application of spectral pre-saturation inversion recovery and diffusion sensitization in the anterior-posterior direction with weighting factors b of 0~2500 sec/mm^2.

Result: We can identify breast tumors and different types of breast tissue by measuring their quantitative parameters and generate signal intensity decay maps. The results of the quantitative parameters were made into boxplots, showing that the quantitative values of glands and fat were distributed differently for different breast types.

Conclusions: In this study, we investigated the differences between breast tumors and examined their location. We introduced hyperspectral processing to analyze diffusion-weighted imaging (DWI) at different b values. For breast tumor detection, we use kernel constrained energy minimization (KCEM), iterative kernel constrained energy minimization (IKCEM) and deep neural network (DNN) for tumor detection and 3D-ROC to evaluate the performance of our detector.

THE ASSOCIATION WITH GRANULOCYTE-COLONY STIMULATING FACTOR TREATMENT AND RISK OF BRAIN METASTASIS IN PATIENTS WITH DE NOVO STAGE IV BREAST CANCER

Yun-Sheng Tai, Shyh-Yau Wang, Henry Wc Leung

An-Nan Hospital, China Medical Univ., Department of Surgery, Taiwan

Background: Severe neutropenia, or febrile neutropenia is a life-threatening event that can be treated by administration of G-CSF. Over the past 15 years, G-CSF may support tumor progression by mobilizing tumor-associated neutrophils, thereby promoting tumor dissemination and metastasis in preclinical models. None of the studies published to date have revealed evidence of increased tumor progression associated with the use of G-CSF during chemotherapy in the clinical setting. We therefore aim to assess the association between G-CSF use and the later incidence of brain metastasis.

Methods: We identified patients with de novo stage IV breast cancer from 1 January 2014 to December 2020. Logistic regression models were used to test the association between variables.

Result: A total of 1412 patients with de novo stage IV breast cancer were included in the final analysis. Among those, 51 patients have treated with at least one dose of G-CSF (3.6%) for neutropenia caused by chemotherapy. Brain metastases were diagnosed in 19 of 1412 patients (1.35 %). Eight of 19 patients (42.1%) showed the risk of brain metastases related to G-CSF treatment and 11 patients did not treat with G-CSF showed brain metastases. In univariate and multivariate logistic regression models, G-CSF user showed insignificantly increased risk of brain metastasis (OR 3.227 [95%CI: 0.725-14.325]; $P = 0.124$).

Conclusions: In our study, we observed that the use of G-CSF showed insignificantly increased risk of brain metastasis in patients with de novo Stage IV breast cancer. We need further clinical studies or big data observation study with comprehensive design to confirm our preliminary results.

DISTALLY BASED LYMPHATIC PREVENTATIVE HEALING APPROACH (DLYMPHA) A MODIFICATION OF THE CLASSIC APPROACH TO REDUCE LYMPHODEMA POST AXILLARY CLEARANCE

Allen Wei-Jiat Wong[1], Benita K T Tan[1,2], Nadia H S Sim[1], Coeway B Theng[1], Shermaine Loh[1], Hui Wen Chua[1,2], Sabrina Ngaserine[1,2]

[1]*Sengkang General Hospital, Department of Surgery, Singapore,*
[2]*Singhealth Duke NUS Breast Centre, Department of Surgery, Singapore*

Background: Lymphatic Microsurgical Preventive Healing Approach (LYMPHA) is a well-known approach to reduce lymphedema following axillary clearance for breast cancer. There are oncological safety concerns for proximal lymphaticovenular anastomosis (LVA) in the axilla. High axillary venous pressure gradients and potential damage from radiotherapy may affect the long-term patency of the anastomoses. To mitigate these issues, LYMPHA was performed in the distal arm.

Methods: Patients planned for axillary clearance were offered Distally based LYMPHA (dLYMPHA) in the same sitting. Superficial lymphatic vessels were mapped using indocyanine green and Iso-sulfan blue. An infrared vein finder was used to locate veins adjacent to the mapped lymphatics. LVA was performed distal to the axilla. Lymphatic diameter was recorded. Volumetry and presence of pitting odema was recorded pre- and post-operatively.

Result: 113 patients underwent axillary clearance from 2018 to 2022. 78 anastomoses (3/arm) were successfully performed in 26 patients. 19 patients in the dLYMPHA group received adjuvant radiotherapy. After 6-months, 1 patient (3.84%) in the dLYMPHA group developed lymphedema, versus 15 patients (17.2%) without dLYMPHA ($p = 0.018$). The mean arm volume for patients without dLYMPHA increased by 6 % (1803.7 ml to 1910.7 ml) but decreased in the dLYMPHA group by 8% (1775.1 ml to 1638.6 ml) post-operatively. There is arm volume reduction of 5% for every increase in 0.1mm of lymphatic diameter ($p = 0.05$).

Conclusions: Distally based LYMPHA is a feasible and promising method to prevent lymphedema following axillary clearance.

PREVALENCE OF BRCA1, BRCA2, AND PALB2 GENOMIC ALTERATIONS AMONG TAIWANESE BREAST CANCER PATIENTS WITH TUMOR-ONLY TARGETED SEQUENCING: EXTENDED DATA ANALYSIS FROM THE VGH-TAYLOR TRIAL

Han Fang Cheng[1,2], Chi Cheng Huang[1,2], Yi Fang Tsai[1,2], Chun Yu Liu[1,2,3,4], Chih Yi Hsu[1,5], Pei Ju Lien[1], Yen Shu Lin[1,2], Ta Chung Chao[1,2,4], Chin Jung Feng[1,2], Yen Jen Chen[1,2], Jen Hwey Chiu[1,2], Ling Ming Tseng[1,2,6]

[1]Taipei Veterans General Hospital, Comprehensive Breast Health Center, Department of Surgery, Taiwan, [2]National Yang Ming Chiao Tung Univ., Faculty of Medicine, School of Medicine, Taiwan, [3]Taipei Veterans General Hospital, Department of Transfusion Medicine, Taiwan, [4]Taipei Veterans General Hospital, Department of Medical Oncology, Taiwan, [5]Taipei Veterans General Hospital, Department of Pathology and Laboratory Medicine, Taiwan, [6]Taipei Veterans General Hospital, Department of Surgery, Taiwan

Background: Several HR genes are well-established cancer susceptibility genes with clinically actionable pathogenic variants (PVs). Among all, deleterious BRCA1 and BRCA2 mutations are the most highly pathogenic genetic variants in hereditary breast and ovarian cancer syndrome, which are proved to be exquisitely sensitive to PARP (poly ADP ribose polymerase) inhibitors as well. Further investigations for more "druggable" HR targets are ongoing. Developing an Asian-based genetic profiling database for breast cancer is an urgent need to improve the treatment outcomes and survival. In current analysis, we further extended the number of enrolled subjects and evaluated the prevalence of genetic alterations in BRCA1, BRCA2, and PALB2.

Methods: A total of 924 consecutive samples from 879 Taiwanese breast cancer patients were assayed with targeted sequencing (Thermo Fisher Oncomine Comprehensive Assay v3), and we evaluated BRCA1, BRCA2, and PALB2 mutation profiles and frequencies.

Result: Among 924 assays, the prevalence of genomic alterations were 3%, 5%, and 8% in BRCA1, BRCA2, and PALB2, respectively. Collectively, pathogenic genetic alterations annotated by both Oncomine and ClinVar were noted in 9.8% or 91 samples (assays). Mutually exclusivity analysis revealed the co-occurrence among these 3 genes. The most prevalent pathologic variants were I887fs for PALB2 mutation, S2186fs, fT912fs, K654fs, and E33* for BRCA2 mutation, and K654fs for BRCA1 mutation.

Conclusions: Our results revealed the mutational frequencies of BRCA1, BRCA2, and PALB2 with a commercial targeted sequencing panel. The prevalence of BRCA1, BRCA2, and PALB2 genomic alterations were 3%, 5%, and 8%, respectively. Co-occurrence among these 3 genes was observed.

SIDE EFFECTS OF POLYACRYLAMIDE GEL MAMMOPLASTY: A CASE REPORT AND REVIEW OF LITERATURE

Seung Yeon Ko[1], Han Seong Kim[2]

[1]*Korea Univ. Ansan Hospital, Department of Surgery, Korea,*
[2]*Eunpyeong Yonsei Hospital, Department of Surgery, Korea*

Background: Polyacrylamide gel was widely used for injection augmentation mammoplasty in Korea. In particular, aquafilling gel (Biomedica. spol, s,r,o, Czech Republic) is typically used. Aquafilling gel is a hydrophilic gel composed of 98% sodium chloride solution (0.9%) and 2% cation copolyamide. However, the safety of this procedure remained controversial.

Methods: Herein, we report a 30-year-old woman with a history of augmentation mammoplasty by aquafilling gel injection developed breast pain and engorgement. She gave birth three months before the symptoms. So we initially suspected puerperal mastitis. But it was not a typical aspect. Magnetic resonance imaging showed septated fluid containing lesions and increased vascularity on breast parenchyma in bilateral breasts. Aquafilling gel was also observed inside the pectoralis muscle of both breasts.

Result: She was treated via surgical intervention for removal of necrotic infected tissue and filler, as well as massive irrigation. After the partial mastectomy, there were no complications. This case showed that the aquafilling gel can cause inflammation and had infiltrated the pectoralis muscle fibers.

Conclusions: Augmentation mammoplasty is one of the most popular esthetic operations in the world. Aquafilling gel is easy to inject and is natural looking. But once a complication occurs, treatment is difficult. Also, aquafilling gel itself has not yet been proven to be safe, such as long-term toxicity of the gel material and its effect on surrounding tissues. So more research on this subject should be done. Hence, sufficient evidences of long-term safety must be accumulated and proved, until which time the aesthetic use of the unapproved filler must be restricted.

THE INFLUENCE OF COPING ON THE DECISION TO PURSUE GENETIC TESTING AMONG INDIVIDUALS FROM FAMILIES WITH HEREDITARY BREAST AND OVARIAN CANCER SYNDROME

Emina Ricciardi[1], Reka Schweighoffer[2], Mahesh Sarki[2], Maria C. Katapodi[2], CASCADE Consortium

[1]Univ. of Basel, Department of Psychology, Switzerland, [2]Univ. of Basel, Department of Medicine / Division for Clinical Research, Switzerland

Background: Hereditary breast and ovarian cancer syndrome (HBOC) is caused by pathogenic germline variants on BRCA1, BRCA2 and other genes which follow an autosomal dominant pattern of inheritance and confer an increased risk for multiple cancer types. In European countries, for example, the risk for developing breast cancer under 80 years is 72% for BRCA1 carriers and 69% for BRCA2 carriers. For index cases and for family members who are potential HBOC-associated variant carriers, dealing with HBOC means lifelong surveillance, which is often nerve-wracking and tedious. Moreover, genetic testing can cause a lot of stress, as individuals have to deal with their significantly increased cancer risk, if tested positive. A lifelong ability to manage stressors on this journey is needed. Therefore, it is crucial to focus on coping in psychosocial care of HBOC families. To date, little is known about the impact of coping on the decision to pursue genetic testing procedures so far.

Methods: This study uses quantitative data from the Swiss CASCADE study. A principal component analysis is conducted to identify the validity structure of the Brief COPE questionnaire.

Result: Different coping styles and strategies are investigated to understand the influence of coping on the decision-making process for genetic testing. Expected results reveal differences between active and passive coping styles.

Conclusions: Results will be discussed after final analysis.

WAITING TIME FOR BREAST CANCER TREATMENT IN KOREA: A NATIONWIDE COHORT STUDY

Young-Jin Lee[1], Jae Ho Jeong[2], Jinhong Jung[3], Tae-Kyung Yoo[1], Sae Byul Lee[1], Jisun Kim[1], Beom Seok Ko[1], Hee Jeong Kim[1], Jong Won Lee[1], Byung Ho Son[1], Il-Yong Chung[1]

[1]ASAN Medical Center, Department of Surgery, Korea, [2]ASAN Medical Center, Department of Medical Oncology, Korea, [3]ASAN Medical Center, Department of Radiation Oncology, Korea

Background: This study was conducted with an aim to analyze the waiting time for initial treatment after breast cancer diagnosis, and to determine factors that influence treatment delay in South Korea.

Methods: This nationwide retrospective cohort study was conducted using the Health Insurance Review and Assessment data. The participants were classified according to regions where biopsy and treatment were performed (Seoul-Seoul, Metro-Metro, Other-Other, Metro-Seoul, Other-Seoul). Waiting time was analyzed according to regional subgroup, year of diagnosis, and treatments. Multivariable logistic regression models were performed to identify factors associated with treatment delay (after 30 days of diagnosis).

Result: A total of 133,514 participants who were newly diagnosed between January 2010 and December 2017 were included. The median waiting time for initial treatment in the total population had increased from 8 days, in 2010, to 14 days, in 2017. In the Seoul-Seoul group, the waiting time had increased from 10 days, in 2010, to 16 days, in 2017. Although the median waiting times were approximately 10 days in the Metro-Metro and Other-Other groups, the times were 27 and 24 days, in 2017, in the Metro-Seoul and Other-Seoul group, respectively. The proportions of delayed upfront surgery were higher in the Metro-Seoul (48.4%) and Other-Seoul group (36.3%) than in the Metro-Metro (9.6%) and Other-Other (6.0%) groups. Medical history and treatment at tertiary hospital were factors related to delayed surgery.

Conclusions: Waiting time in patients who seek breast cancer surgeries in Seoul has been increasing rapidly. Further studies are needed to evaluate the effect of this phenomenon on treatment outcome.

IMMEDIATE TRANSVERSE RECTUS ABDOMINIS MUSCULOCUTANEOUS FLAP RECONSTRUCTION SURGERY OF THE BREAST FOR DUCTAL CARCINOMA IN SITU (DCIS) AT THE NATIONAL CANCER CENTER OF MONGOLIA

Odbayar Barkhas, Shirnen Odnasan, Bayart-Uils Baya

National Cancer Center of Mongolia, Department of Surgery, Mongolia

Background: Oncoplastic surgery is still in the developmental phase in Mongolia. In The National cancer center of Mongolia (NCC), it has been 3 years since we have started introducing pedicled flaps (LD or muscle sparing TDAP, LICAP, and TRAM) harvested from the back, belly, lumbar and/or the axillary region reconstruction after mastectomy.

Methods: Under general anesthesia, right nipple-sparing mastectomy was performed along with the sentinel lymph node dissection. After removing the breast specimen, tissue was marked and immediately sent to the pathological unit for margin evaluation by the frozen sectioning. Emergency histological examination demonstrated that the malignant cells infiltrated the nipple-areolar margin. In terms of lymph nodes, frozen section evaluation did not find lymphatic metastasis, so further radical dissection was not necessary. Thus, we extended our approach to simple mastectomy followed by the transverse-abdominis rotational flap reconstruction.

Result: Operative time was 362 minutes. Intraoperative blood loss was 40ml. We had mobilized the patient on a day after surgery. Oral intake was started first day after surgery. Hospital stay was 10 days. Patient has recovered uneventfully. Pathological TNM stage (AJCC 8th edition; 2022): pT1bN0Mx.

Conclusions: Mongolia recently introduced reconstruction surgeries in the breast cancer treatments to improve the quality of patient's lives and deliver enhanced outcomes. But, long-term practice and experiences are much needed. In order to significantly improve the quality of surgery treatments in breast cancer, opportunities must be provided to surgeons to learn from best practices and mentorship around the world.

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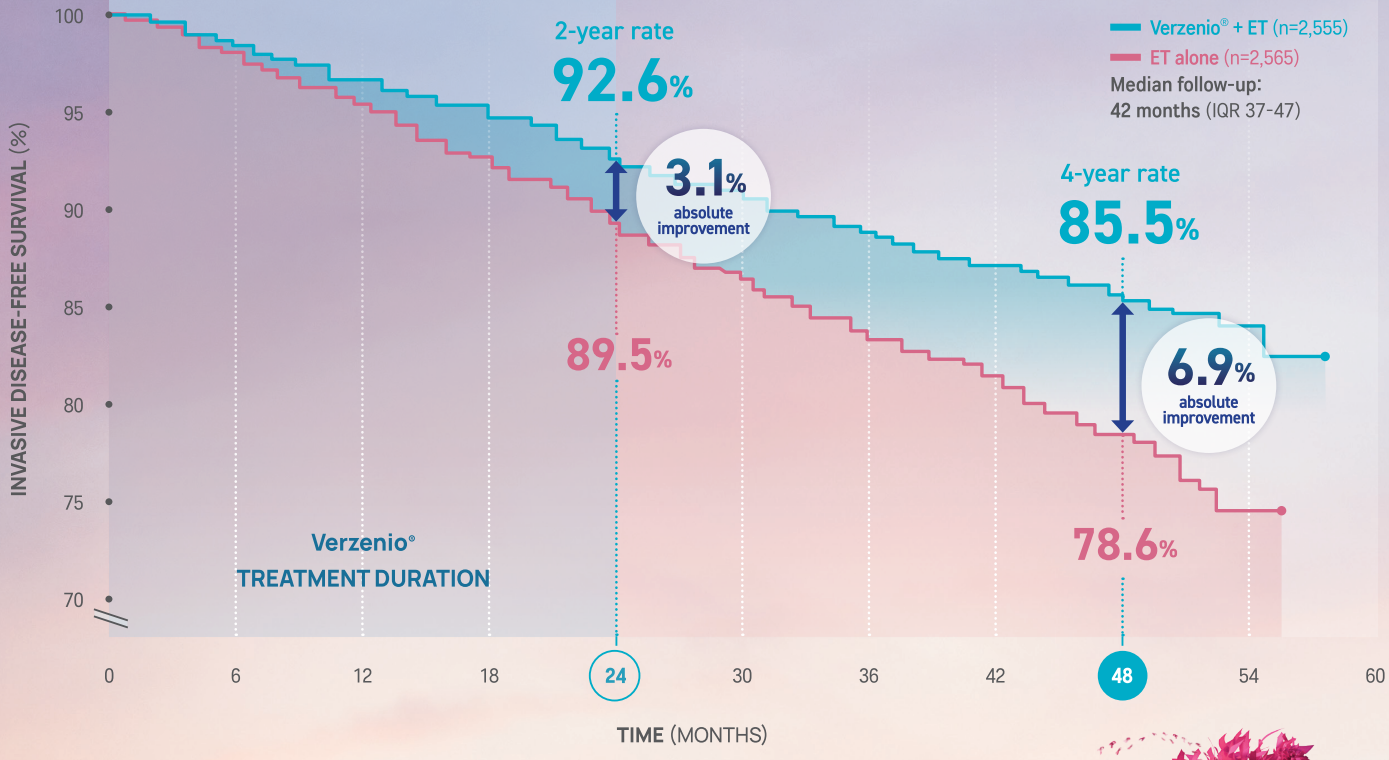

Verzenio Indication[2]

1. HR+, HER2-인 진행성 또는 전이성 유방암이 있는 폐경 후 여성의 치료를 위한 일차 내분비 기반 요법으로서 아로마타제 억제제와 병용
2. 내분비 요법 후 질병이 진행된 HR+, HER2-인 진행성 또는 전이성 유방암 여성의 치료에 풀베스트란트와 병용*
3. HR+, HER2-, 림프절 양성의 재발 위험이 높은 조기 유방암이 있는 성인 환자의 보조 치료로서 내분비 요법과 병용, 폐경 전 또는 폐경 이행기 여성에서, 아로마타제 억제제 내분비 요법은 LHRH 작용제와 병용

*풀베스트란트를 병용 투여 받은 폐경 전 및 폐경 이행기 여성들은 현재 임상진료지침(clinical practice standards)에 따라 생식샘자극 분비 호르몬 작용제를 투여 받아야 한다.

버제니오정50밀리그램 제품상세정보 자세히보기

버제니오정100밀리그램 제품상세정보 자세히보기

버제니오정150밀리그램 제품상세정보 자세히보기

IDFS: Invasive disease-free survival, **HR+:** hormone receptor positive, **HER2-:** human epidermal growth factor receptor 2 negative, **EBC:** early breast cancer, **ET:** endocrine therapy, **LHRH:** Luteinizing hormone releasing hormone, **IQR:** interquartile range

Reference 1. Johnston SRD, *et al. Lancet Oncol.* 2022 Dec 5;S1470-2045(22)00694-5, **2.** 버제니오 식약처 허가사항(식약처 의약품통합정보시스템 https://nedrug.mfds.go.kr/) [Revised on 2022-11-18].

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