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Global Breast Cancer Conference 2022

April 28 (Thu) - 30 (Sat), 2022
Grand Walkerhill Seoul, Korea

Abstract Book

한국유방암학회
Korean Breast Cancer Society

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*ePoster | Exhibition: Vista Lobby, Grand 1+2+3

April 29 (Fri)

Live Streaming

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*ePoster | Exhibition: Vista Lobby, Grand 1+2+3

🎧 현장에서만 한국어 통역이 제공됩니다.
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ASAN Medical Center, Korea

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Moderator **Komal Jhaveri**
Memorial Sloan Kettering Cancer Center, U.S.A.

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Chinese Academy of Medical Sciences, China

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Moderator **Jeong Eon Lee**
Samsung Medical Center, Korea

Moderator **Yen-Shen Lu**
National Taiwan Univ. Hospital, Taiwan

Speaker **Soo Kyung Ahn** *135*
EDUCATION AND DEVELOPMENTAL PROGRAM FOR YOUNG DOCTORS IN KOREA
Hallym Univ. Kangnam Sacred Heart Hospital, Korea

Speaker **Yen-Shen Lu** *136*
EDUCATION AND DEVELOPMENTAL PROGRAM FOR YOUNG DOCTORS IN TAIWAN
National Taiwan Univ. Hospital, Taiwan

Panelist **Wei-Pang Chung**
CONTINUOUS NETWORKING BETWEEN YOUNG DOCTORS IN TWO COUNTRIES
National Cheng Kung Univ. Hospital, Taiwan

Panelist **Yi-Fang Tsai**
CONTINUOUS NETWORKING BETWEEN YOUNG DOCTORS IN TWO COUNTRIES
Taipei Veterans General Hospital, Taiwan

Panelist **Jun-Won Min**
CONTINUOUS NETWORKING BETWEEN YOUNG DOCTORS IN TWO COUNTRIES
Dankook Univ. Hospital, Korea

Panelist **Hyun Yul Kim**
CONTINUOUS NETWORKING BETWEEN YOUNG DOCTORS IN TWO COUNTRIES
Pusan National Univ. Yangsan Hospital, Korea

Day 2 April 29 (Fri)

08:00-09:15 GBCC-SSO Joint Session RM 3(Walker Hall 1)

Moderator **Sang Uk Woo**
Korea Univ. Guro Hospital, Korea

Moderator **Christine Laronga**
Moffitt Cancer Center, U.S.A.

Speaker **Han-Byoel Lee** 142
CLINICAL TRIALS OF BREAST CANCER SURGERY IN KOREA & INTRODUCTION TO KBCSG
Seoul National Univ. Hospital, Korea

Speaker **Jennifer Plichta** 143
TRIALS IN BREAST CANCER LEAD BY SURGICAL ONCOLOGISTS IN THE US & INTRODUCTION TO SSO
Duke Univ. Medical Center, U.S.A.

Panelist **Jeong Eon Lee**
DISCUSSION ABOUT POTENTIAL COLLABORATIVE PROGRAMS AND STUDIES BETWEEN SSO AND KBCS
Samsung Medical Center, Korea

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

Novartis

Moderator **Nam Sun Paik**
Pohang SM Christianity Hospital, Korea

Speaker **Aditya Bardia** 171
THE EVOLVING LANDSCAPE OF HR+/HER2- BREAST CANCER TREATMENT
Massachusetts General Hospital Cancer Center, U.S.A.

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

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

Speaker **Walter Paul Weber** 4
DEFINING TODAY'S SURGICAL STANDARDS OF CARE IN PATIENTS WITH BREAST CANCER
Univ. Hospital Basel, Switzerland

10:30-11:45 Symposium 3 RM 1(Vista 1+2)

Translational Approach through Cancer Genomics and Biology

Moderator **Jeong-Yeon Lee**
Hanyang Univ. College of Medicine, Korea

Moderator **Alex Swarbrick**
Garvan Institute of Medical Research, Australia

Speaker **Jeong-Yeon Lee** 16
GENOMIC AMPLIFICATION LINKED TO THERAPEUTIC RESISTANCE IN BREAST CANCER
Hanyang Univ. College of Medicine, Korea

Speaker **Alex Swarbrick** 17
PARSING THE TUMOUR MICROENVIRONMENT OF BREAST CANCER USING INTEGRATED SINGLE-CELL AND SPATIALLY-RESOLVED MUTI-OMICS
Garvan Institute of Medical Research, Australia

Speaker **Rinath Jeselsohn** 19
GENOMICS RELATED TO TREATMENT AFTER CDK4/6 INHIBITORS IN HORMONE RECEPTOR POSITIVE BREAST CANCER
Dana-Farber Cancer Institute, U.S.A.

Day 2 April 29 (Fri)

10:30-11:45 **Panel Discussion 5** **RM 2(Vista 3)**

Obesity, Life Style Modification, and Exercise

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

Moderator **Pamela Goodwin**
Lunenfeld Tanenbaum Research Institute at Sinai Health System, Univ. of Toronto, Canada

Speaker **Pamela Goodwin** *60*
THE ROLE OF WEIGHT LOSS AND METFORMIN IN THE ADJUVANT TREATMENT OF BREAST CANCER
Lunenfeld Tanenbaum Research Institute at Sinai Health System, Univ. of Toronto, Canada

Speaker **Hyun Jo Youn** *62*
LIFE STYLE MODIFICATION OF BREAST CANCER SURVIVORS
Jeonbuk National Univ. Hospital, Korea

Speaker **Justin Y. Jeon** *63*
PHYSICAL ACTIVITY INTERVENTION IN WOMEN WITH BREAST CANCER
Yonsei Cancer Center, Korea

10:30-11:45 **Education Session 5** **RM 3(Walker Hall 1)**

Update in the Management of Adverse Events

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

Moderator **Toshiaki Saeki**
Saitama Medical Univ. International Medical Center, Japan

Speaker **Woo-Baek Chung** *85*
MANAGEMENT OF CARDIOTOXICITY OF BREAST CANCER
Seoul St. Mary's Hospital, Korea

Speaker **Eun Joo Yang** *86*
MANAGEMENT OF AIMSS (AROMATASE-INHIBITOR-ASSOCIATED MUSCULOSKELETAL SYNDROME)
Daerim St. Mary's Hospital, Korea

Speaker **Toshiaki Saeki** *87*
MANAGEMENT OF CHEMOTHERAPY INDUCED NAUSEA AND VOMITING (CINV)
Saitama Medical Univ. International Medical Center, Japan

10:30-11:45 **Oral Presentation 3** **RM 4(Walker Hall 2)**

Moderator **Yongsik Jung**
Ajou Univ. Hospital, Korea

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

Presenter **Huihui Li** *205*
PYROTINIB COMBINED WITH ALBUMIN-BOUND PACLITAXEL AS FIRST-LINE TREATMENT OF HER-2 POSITIVE METASTATIC BREAST CANCER: PRELIMINARY RESULTS OF A SINGLE-ARM, MULTICENTER PHASE 2 TRIAL
Shandong Cancer Hospital & Institute, China

Presenter **Ji Hyun Chang** *206*
AN EXPERT SURVEY REVEALS VARIOUS PRACTICE PATTERNS IN CLINICAL NODAL STAGING (N0, N1, N2A) ASSESSMENT PRIOR TO NEOADJUVANT CHEMOTHERAPY FOR BREAST CANCER: A KOSRO/KBCSG/KCSG COLLABORATIVE STUDY
Seoul National Univ. Hospital, Korea

Day 2 April 29 (Fri)

Presenter **Byung-Hee Kang** *207*
RADIOSENSITIVITY IS ASSOCIATED WITH ANTITUMOR IMMUNITY IN ESTROGEN RECEPTOR-NEGATIVE BREAST CANCER
Seoul National Univ. Bundang Hospital, Korea

Presenter **Tristen Park** *208*
PHENOTYPE AND FUNCTIONALITY OF TUMOR INFILTRATING LYMPHOCYTES AFTER RAPID EX-VIVO EXPANSION FROM CORE NEEDLE BIOPSIES OF TNBC TUMORS
Yale Univ. School of Medicine, U.S.A.

Presenter **Ju Hyeon Lee** *209*
SURVIVAL AFTER THE DIAGNOSIS OF SECONDARY PRIMARY MALIGNANCY IN BREAST CANCER PATIENTS, FOCUSING ON THE SECOND PRIMARY HEMATOLOGIC MALIGNANCY: A PROPENSITY SCORE MATCHING ANALYSIS
Korea Cancer Center Hospital, Korea

Presenter **Chi-Cheng Huang** *210*
PREVALENCE OF TUMOR GENOMIC ALTERATIONS IN HOMOLOGOUS RECOMBINATION REPAIR GENES AMONG TAIWANESE BREAST CANCERS
Taipei Veterans General Hospital, Taiwan

Presenter **Wonshik Chee** *211*
CAN A TECHNOLOGY-BASED INFORMATION AND COACHING/SUPPORT PROGRAM IMPROVE MULTIPLE DIMENSIONS OF QUALITY OF LIFE AMONG ASIAN AMERICAN BREAST CANCER SURVIVORS?
Emory University, U.S.A.

Presenter **Chun-Yu Liu** *212*
REGORAFENIB INDUCES DAMAGE-ASSOCIATED MOLECULAR PATTERNS, CANCER CELL DEATH AND IMMUNE MODULATORY EFFECTS IN A MURINE TRIPLE NEGATIVE BREAST CANCER MODEL
Taipei Veterans General Hospital, Taiwan

Presenter **Hee Kyung Ahn** *213*
A PHASE 2 STUDY OF NEOADJUVANT PERTUZUMAB, ATEZOLIZUMAB, DOCETAXEL AND TRASTUZUMAB IN HER2-POSITIVE EARLY BREAST CANCER (NEO-PATH, KCSG BR 18-23)
Gachon Univ. Gil Medical Center, Korea

10:30-11:45 ABCN Business Meeting RM 5(Art Hall)

Sharing Wisdom, Sharing Strength

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

Speaker **Joon Jeong**
LEGACY OF GBCC: BEYOND ASIA TOWARDS THE WORLD, NEW ERA OF GBCC
Gangnam Severance Hospital, Korea

Speaker **Philip Poortmans**
SHARING WISDOM, SHARING STRENGTH - MENTORSHIP AND INTERNATIONAL COLLABORATION
Iridium Netwerk & Univ. of Antwerp, Belgium

Speaker **Heejeong Kim**
KNOWLEDGE, ATTITUDE, PRACTICE BEHAVIORS AND BARRIERS FOR FERTILITY PRESERVATION
ASAN Medical Center, Korea

Discussion and Q&A

Day 2 April 29 (Fri)

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

Moderator **Kyung Hwan Shin**
Seoul National Univ. Hospital, Korea

Speaker **Philip Poortmans** *6*
OPTIMISING RADIATION THERAPY IN EARLY STAGE BREAST CANCER
Iridium Netwerk & Univ. of Antwerp, Belgium

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

Roche Korea

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

Speaker **Joyce O'Shaughnessy** *173*
TRANSFORMING THE TREATMENT JOURNEY FOR HER2+ BREAST CANCER PATIENTS
Baylor Univ. Medical Center, U.S.A.

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

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

Speaker **Mitch Dowsett** *8*
PRESURGICAL WINDOW STUDIES FOR DRUG DEVELOPMENT, STUDIES OF RESISTANCE AND PATIENT MANAGEMENT
Royal Marsden Hospital, UK

15:00-16:15 **Symposium 4** **RM 1(Vista 1+2)**

Immunotherapy in Breast Cancer

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

Moderator **Peter Schmid**
Bart's Cancer Institute, UK

Speaker **Hiroji Iwata** *20*
CURRENT STATUS OF IMMUNOTHERAPY: WHERE ARE WE?
Aichi Cancer Center Hospital, Japan

Speaker **Peter Schmid** *22*
BIOMARKER FOR IMMUNOTHERAPY: WHAT IS THE BEST?
Bart's Cancer Institute, UK

Speaker **Sherene Loi** *23*
CHALLENGE FOR IMMUNOTHERAPY IN BREAST CANCER: HOT OR COLD
Univ. of Melbourne, Australia

15:00-16:15 **Panel Discussion 6** **RM 2(Vista 3)**

Updates of Combined Management for Metastatic Breast Cancer

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

Moderator **Takayuki Ueno**
The Cancer Institute Hospital of JFCR, Japan

Day 2 April 29 (Fri)

Speaker **Sung Gwe Ahn** 65
TIMING OF BREAST SURGERY IN METASTATIC BREAST CANCER: IS IT REALLY NECESSARY TO PERFORM PALLIATIVE MASTECTOMY?
Gangnam Severance Hospital, Korea

Speaker **Takayuki Ueno** 66
CURRENT STATUS OF LOCOREGIONAL THERAPY IN ER+/HER2- OLIGOMETASTATIC BREAST CANCER
The Cancer Institute Hospital of JFCR, Japan

Speaker **Steven J. Chmura** 67
ROLE OF STEREOTACTIC ABLATIVE RADIOTHERAPY IN OLIGOMETASTATIC BREAST CANCER
Univ. of Chicago, U.S.A.

15:00-16:15 Education Session 6 RM 3(Walker Hall 1)

Psychologic Problem Management

Moderator **Jung Han Yoon**
Chonnam National Univ. Hwasun Hospital, Korea

Moderator **Hideko Yamauchi**
St. Luke's International Hospital, Japan

Speaker **Eun-Jung Shim** 88
PSYCHOLOGICAL INTERVENTIONS ON FATIGUE OF BREAST CANCER PATIENTS
Pusan National Univ. Hospital, Korea

Speaker **Seockhoon Chung** 89
ASSESSMENT AND MANAGEMENT OF INSOMNIA
ASAN Medical Center, Korea

Speaker **Hideko Yamauchi** 90
STANDARD OF CARE FOR BREAST CANCER DISTRESS
St. Luke's International Hospital, Japan

15:00-16:15 Oral Presentation 4 RM 4(Walker Hall 2)

Moderator **Hyeong-Gon Moon**
Seoul National Univ. Hospital, Korea

Moderator **Zisun Kim**
Soonchunhyang Univ. Hospital Bucheon, Korea

Presenter **Nora Jee-Young Park** 214
YAP1 PREDICTS PATHOLOGICAL COMPLETE RESPONSE TO NEOADJUVANT CHEMOTHERAPY IN LUMINAL BREAST CANCER PATIENTS
Kyungpook National Univ. School of Medicine, Korea

Presenter **Tae-Kyung Robyn Yoo** 215
POOR CLINICAL OUTCOME IN TRIPLE-NEGATIVE BREAST CANCER WITH LOW TUMOR-INFILTRATING LYMPHOCYTE SCORE AND NEGATIVE PD-L1 EXPRESSION
ASAN Medical Center, Korea

Presenter **Eva Blondeaux** 216
PREGNANCY AFTER BREAST CANCER: A SYSTEMATIC REVIEW AND META-ANALYSIS
IRCCS Ospedale Policlinico San Martino, Genova, Italy

Presenter **Jai Hyun Chung** 217
RECURRENCE AND CLINICOPATHOLOGIC CHARACTERISTICS OF BREAST CANCER IN BRCA-POSITIVE AND BRCA-NEGATIVE YOUNG WOMEN
Korea Univ. Guro Hospital, Korea

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Presenter **Kaori Terata** 218
MULTICENTER RETROSPECTIVE STUDY OF BREAST CANCER PATIENTS UNDERGOING FERTILITY PRESERVATION (BSTRO-02)
Akita Univ. Hospital, Japan

Presenter **Hyunji Jo** 219
LONG-TERM BREAST CANCER OUTCOMES OF PREGNANCY-ASSOCIATED BREAST CANCER IN A PROSPECTIVE COHORT
Samsung Medical Center, Korea

Presenter **Jieun Park** 220
C-MET-ENRICHED CIRCULATING TUMOR CELLS AS SIGNIFICANT INDEPENDENT PREDICTORS FOR PROGRESSION IN HR-POSITIVE HER2-NEGATIVE METASTATIC BREAST CANCER
Seoul National Univ., Korea

Presenter **Hakyoung Kim** 221
PROGNOSIS OF BREAST CANCER PATIENTS AFTER DEVELOPMENT OF CONTRALATERAL BREAST CANCER IN KOREA
ASAN Medical Center, Korea

15:00-16:15 Nursing Session 1 RM 5(Art Hall)

Challenges of Nursing Care Beyond a Pandemic

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

Moderator **Hye Sung Moon**
Ewha Womans Univ. Mokdong Hospital, Korea

Speaker **Jiyoung Choi** 148
THE EDUCATION FOR BREAST CANCER PATIENTS DURING COVID PANDEMIC
Seoul National Univ. Bundang Hospital, Korea

Speaker **In Jeong Cho** 150
SUPPORTIVE CARE POST PANDEMIC BREAST CANCER PATIENTS
Wonju Severance Christian Hospital, Korea

Speaker **Nayeon Kim** 151
EXPERIENCE OF EDUCATION FOR BREAST CANCER PATIENTS POST COVID-19
Samsung Medical Center, Korea

16:30-17:45 Symposium 5 RM 1(Vista 1+2)

Recent Updates for Surgery After Neoadjuvant Chemotherapy

Moderator **Sung Yong Kim**
Soonchunhyang Univ. Hospital Cheonan, Korea

Moderator **Emiel Rutgers**
Netherlands Cancer Institute, Netherlands

Speaker **Jeong Eon Lee** 24
DE-ESCALATION OF AXILLARY SURGERY AFTER NACT
Samsung Medical Center, Korea

Speaker **Peter C. Dubsky** 26
DE-ESCALATION OF BREAST SURGERY AFTER NACT
Hirslanden Klinik St. Anna, Switzerland

Speaker **Emiel Rutgers** 27
CAN WE SELECT PATIENTS IN WHOM WE CAN FOREGO ANY AXILLARY TREATMENT AFTER UP FRONT CHEMOTHERAPY?
Netherlands Cancer Institute, Netherlands

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16:30-17:45 **Panel Discussion 7** **RM 2(Vista 3)**

How to Apply Multigene Panel for ER+ EBC- Asia vs. Western

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

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

Speaker **Janice Tsang** *68*
MULTIGENE ASSAYS: WHAT EVIDENCE DO WE HAVE?
The Univ. of Hong Kong, Hong Kong

Speaker **Han-Byoel Lee** *69*
IS THERE ANY DIFFERENCE IN MULTIGENE ASSAYS DEVELOPED FROM ASIAN AND WESTERN COUNTRIES?
Seoul National Univ. Hospital, Korea

Speaker **Rebecca Dent** *70*
PRACTICAL APPLICATION OF MULTIGENE ASSAYS IN REAL CLINICAL SETTING (ASIA VS. WESTERN)
National Cancer Centre Singapore, Singapore

16:30-17:45 **Education Session 7** **RM 3(Walker Hall 1)**

Tailored Adjuvant Endocrine Therapy in ER+ Breast Cancer

Moderator **Se Jeong Oh**
The Catholic Univ. of Korea, Incheon St. Mary's Hospital, Korea

Moderator **Maria-Joao Cardoso**
Champalimaud Foundation, Portugal

Speaker **Maria-Joao Cardoso** *91*
OPTIMAL TREATMENT OPTIONS FOR HIGH RISK ER+ BREAST CANCER
Champalimaud Foundation, Portugal

Speaker **Sung Hoon Sim** *93*
EXTENDED ENDOCRINE THERAPY, OPTIMAL DURATION AND SEQUENCE
National Cancer Center, Korea

Speaker **Shin-Cheh Chen** *94*
OVARIAN SUPPRESSION WITH/WITHOUT ADJUVANT CHEMOTHERAPY IN HIGH-RISK PREMENOPAUSAL PATIENTS
Chang Gung Memorial Hospital, Taiwan

16:30-17:45 **Oral Presentation 5** **RM 4(Walker Hall 2)**

Moderator **Min Sung Chung**
Hanyang Univ. Seoul Hospital, Korea

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

Presenter **Jongho Cheun** *222*
EFFECT OF NEOADJUVANT VERSUS ADJUVANT CHEMOTHERAPY ON IPSILATERAL BREAST TUMOR RECURRENCE AFTER BREAST-CONSERVING SURGERY AND WHOLE-BREAST IRRADIATION
SMG-SNU Boramae Medical Center, Korea

Presenter **Seung Yeun Chung** *223*
THE IMPACT OF POSTOPERATIVE RADIATION THERAPY FOR ISCHEMIC HEART DISEASE IN BREAST CANCER PATIENTS USING NATIONWIDE CLAIM DATA
Ajou Univ. School of Medicine, Korea

Day 2 April 29 (Fri)

Presenter **Eunji Lo** 224
CDK9 IS A PROMISING THERAPEUTIC TARGET IN ER POSITIVE BREAST CANCER
Sungkyunkwan Univ. School of Medicine, Korea

Presenter **Heejoo Ko** 225
RISK ASSESSMENT OF LYMPHEDEMA IN BREAST CANCER PATIENTS USING AXILLARY-LATERAL THORACIC VESSEL JUNCTURE (ALTJ) DOSE: CLINICAL IMPLICATIONS FOR PERSONALIZED RADIOTHERAPY PLANNING
The Catholic Univ. of Korea, Korea

Presenter **Kangpyo Kim** 226
AUTOMATED CORONARY ARTERY CALCIUM (CAC) SCORING IN PATIENTS WITH BREAST CANCER TO ASSESS THE RISK OF HEART DISEASE FOLLOWING ADJUVANT RADIATION THERAPY (RT)
Yonsei Univ. College of Medicine, Korea

Presenter **Hwa Kyung Byun** 227
EVALUATION OF EARLY COSMETIC OUTCOME AND TOXICITY AFTER 5-FRACTION STEREOTACTIC PARTIAL BREAST IRRADIATION IN EARLY-STAGE BREAST CANCER: A PROSPECTIVE COHORT STUDY
Yonsei Cancer Center, Korea

Presenter **So-Hyun Yoon** 228
NOVEL NSDHL INHIBITOR (COMPOUND 9) HAS ANTI-CANCER ACTIVITY IN BREAST CANCER
Seoul National Univ., Korea

Presenter **Dong-Yun Kim** 229
THE IMPACT OF PM2.5 ON THE RADIATION-INDUCED PNEUMONITIS IN PATIENTS WITH BREAST CANCER
Seoul National Univ. Hospital, Korea

16:30-17:45 Nursing Session 2 (Korean) RM 5(Art Hall)

Return to Life Beyond Cure Among Young Women

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

Moderator **Soo Hyun Kim**
Inha Univ., Korea

Speaker **Ka Ryeong Bae** 152
WORKING YOUNG WOMEN WITH BREAST CANCER: FOR A LIFE THAT MAKES ME WHO I AM
National Cancer Center, Korea

Speaker **Eunji Cho** 153
HUMAN FLOURISHING IN ADOLESCENTS AND YOUNG ADULTS WITH CANCER
Vanderbilt Univ., Korea

Speaker **Jeehee Han** 155
FERTILITY PRESERVATION FOR WOMEN WITH BREAST CANCER
Chung-Ang Univ. College of Nursing, Korea

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

Lilly Korea

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

Speaker **Tomoyuki Aruga** 175
VERZENIO, POTENT CDK4/6 INHIBITOR, HOW TO OPTIMIZE HR+/HER2- MBC PATIENT WITH CDK4/6 INHIBITORS
Tokyo Metropolitan Cancer and Infectious Diseases Center Komagome Hospital, Japan

Day 3 April 30 (Sat)

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

MSD Korea

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

Speaker **Joyce O'Shaughnessy** 178
ONE GIANT LEAP FOR TRIPLE NEGATIVE BREAST CANCER
Baylor Univ. Medical Center, U.S.A.

09:00-10:15 **Symposium 6** **RM 1(Vista 1+2)**

Imaging Biomarkers for Precision Care

Moderator **Hak Hee Kim**
ASAN Medical Center, Korea

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

Speaker **Nola Hylton** 29
MR IMAGING BIOMARKERS FOR PREOPERATIVE TREATMENT AND NEOADJUVANT SYSTEMIC THERAPY
Univ. of California, San Francisco, U.S.A.

Speaker **Eun Sook Ko** 31
IMAGING BIOMARKERS FOR ASSESSING TUMOR HETEROGENEITY
Samsung Medical Center, Korea

Speaker **Jin You Kim** 33
THE ROLE OF IMAGING BIOMARKERS ON SURVIVAL PREDICTION
Pusan National Univ. Hospital, Korea

09:00-10:15 **Symposium 7** **RM 2(Vista 3)**

Advances Towards Personalized Radiotherapy

Moderator **Corey Speers**
Univ. of Michigan, U.S.A.

Moderator **Yong Bae Kim**
Yonsei Cancer Center, Korea

Speaker **Yong Bae Kim** 34
REGIONAL RT OTHER THAN AXILLA: THE LATEST ANSWER FROM KOREA
Yonsei Cancer Center, Korea

Speaker **Mariko Kawamura** 36
INDIVIDUALIZED RT ACCORDING TO IHC-BASED SUBTYPE
Nagoya Univ. Graduate School of Medicine, Japan

Speaker **Corey Speers** 38
PRECISION RADIATION ONCOLOGY: RT DECISION MAKING BASED ON GENOMIC BIOMARKERS
Univ. of Michigan, U.S.A.

Day 3 April 30 (Sat)

09:00-10:15 HBOC Session RM 3(Walker Hall 1)

Hereditary Breast/Ovarian Cancer Syndrome

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

Moderator **Ava Kwong**
The Univ. of Hong Kong, Hong Kong

Speaker **Ava Kwong** 110
SURGICAL OPTIONS IN HEREDITARY BREAST CANCER
The Univ. of Hong Kong, Hong Kong

Speaker **William Foulkes** 111
TEN GENES FOR HEREDITARY BREAST AND OVARIAN CANCER
McGill Univ., Canada

Speaker **Hongbeom Kim** 113
HEREDITARY PANCREAS CANCER
Seoul National Univ. Hospital, Korea

09:00-10:15 Junior Doctors Forum RM 4(Walker Hall 2)

Moderator **Byung Joo Chae**
Samsung Medical Center, Korea

Speaker **Matteo Lambertini** 145
HOW TO ESTABLISH YOURSELF IN THE BREAST CANCER SOCIETY AS A YOUNG DOCTOR/RESEARCHER
IRCCS Policlinico San Martino Hospital - Univ. of Genova, Italy

Speaker **Masakazu Toi** 146
FROM ASIA TO THE WORLD - HOW TO ENJOY WORK AT THE GLOBAL STAGE
Kyoto Univ. Hospital, Japan

09:00-10:15 Survivorship Session 1 RM 5(Art Hall)

Managing Side Effects of Endocrine Treatment for Breast Cancer

Moderator **Min Hyuk Lee**
Soonchunhyang Univ. Hospital Seoul, Korea

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

Speaker **Sung Gwe Ahn** 115
MUST-HAVE KNOWLEDGE ABOUT GNRH AGONIST FOR PATIENTS WITH BREAST CANCER
Gangnam Severance Hospital, Korea

Speaker **Seeyoun Lee** 116
BONE HEALTH IN BREAST CANCER PATIENTS
National Cancer Center, Korea

Speaker **Kyung Jin Eoh** 117
SEXUAL HEALTH AND REHABILITATION
Yongin Severance Hospital, Korea

Day 3 April 30 (Sat)

10:30-11:45 **Symposium 8** **RM 1(Vista 1+2)**

PARP Inhibitors in Breast Cancer: Current Status and Future Prospects

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

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

Speaker **Kan Yonemori** 39
IDENTIFYING TUMORS WITH DEFECTS IN DNA DAMAGE RESPONSE, HOMOLOGOUS RECOMBINATION, AND REPLICATION STRESS
National Cancer Center Hospital, Japan

Speaker **Seock-Ah Im** 40
CURRENT STATUS OF PARP INHIBITORS IN BREAST CANCER: NEOADJUVANT, ADJUVANT, AND METASTATIC SETTING
Seoul National Univ. Hospital, Korea

Speaker **Jung-Min Lee** 42
OVERCOMING RESISTANCE AND FUTURE DIRECTIONS
National Cancer Institute, U.S.A.

10:30-11:45 **Special Session 1** **RM 2(Vista 3)**

Multidisciplinary Case Approach - Oligometa Management

Moderator **Jee Suk Chang**
Gangnam Severance Hospital, Korea

Moderator **Takayuki Ueno**
The Cancer Institute Hospital of JFCR, Japan

Speaker **Jae Ho Jeong**
CASE PRESENTATION
ASAN Medical Center, Korea

Speaker **Soo Chin Lee**
CASE DISCUSSION
National Univ. Cancer Institute, Singapore

Speaker **Jee Suk Chang**
CASE DISCUSSION
Gangnam Severance Hospital, Korea

Speaker **Takayuki Ueno**
CASE DISCUSSION
The Cancer Institute Hospital of JFCR, Japan

10:30-11:45 **Special Session 2** **RM 3(Walker Hall 1)**

Bench to Bed Approach

Moderator **Wonshik Han**
Seoul National Univ. Hospital, Korea

Moderator **Duhee Bang**
Yonsei Univ., Korea

Day 3 April 30 (Sat)

Speaker **Hyunsook Lee** *96*
REVEALING THE ALTERNATIVE LENGTHENING OF TELOMERES PATHWAY BY THE DEPLETION OF BRCA2 AND THE APPLICATION OF TRIPLE NEGATIVE BREAST CANCER ORGANOIDS FOR PRECISION ONCOLOGY
Seoul National Univ., Korea

Speaker **Yongsub Kim** *97*
FUNCTIONAL ASSESSMENT OF PATIENT-DERIVED BRCA VARIANTS VIA CRISPR-MEDIATED GENOME EDITING
Univ. of Ulsan College of Medicine, Korea

Speaker **Duhee Bang** *98*
CELL-FREE TUMOR DNA AS A CANCER SURVEILLANCE STRATEGY: CURRENT AND FUTURE
Yonsei Univ., Korea

10:30-11:45 Junior Doctors Debate RM 4(Walker Hall 2)

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

Moderator **Veronique Km Tan**
National Cancer Centre Singapore, Singapore

Discussion

- LOCAL THERAPY: IS AXILLARY STAGING SURGERY NECESSARY FOR ALL EARLY BREAST CANCER PATIENTS (AGE < 70 YEARS)? - PROS
- LOCAL THERAPY: IS AXILLARY STAGING SURGERY NECESSARY FOR ALL EARLY BREAST CANCER PATIENTS (AGE < 70 YEARS)? - CONS
- SYSTEMIC THERAPY: HORMONE RECEPTOR-POSITIVE / HER2-NEGATIVE EARLY BREAST CANCER (PT1N1MIC, GR2), 45 YO, PREMENOPAUSAL: CHEMOTHERAPY OR NOT IN ADDITION TO ENDOCRINE THERAPY? - PROS
- SYSTEMIC THERAPY: HORMONE RECEPTOR-POSITIVE / HER2-NEGATIVE EARLY BREAST CANCER (PT1N1MIC, GR2), 45 YO, PREMENOPAUSAL: CHEMOTHERAPY OR NOT IN ADDITION TO ENDOCRINE THERAPY? - CONS

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Moderator **So-Youn Jung**
National Cancer Center, Korea

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Moderator **Seog Hyeon Youn**
Say-You Clinic, Korea

Moderator **So Yeon Park**
Seoul National Univ. Bundang Hospital, Korea

Speaker **Nora Jee-Young Park**
PATHOLOGIC REVIEW OF INTRADUCTAL LESIONS
Kyungpook National Univ. Chilgok Hospital, Korea

Speaker **Woo Jung Choi**
DIAGNOSTIC APPROACH OF INTRADUCTAL LESIONS
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Ramiyou Clinic, Korea

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Moderator **Beom Seok Kwak**
Dongguk Univ. Ilsan Hospital, Korea

Moderator **Sang Hoon Hahn**
Venus Breast & Thyroid Clinic, Korea

Speaker **Junho Kim**
HOW TO CHARGE PUBLIC MEDICAL INSURANCE OF BREAST DISEASE: ACCORDING TO THE CHART
Dr. Kim Breast Thyroid Clinic, Korea

Speaker **Hyewon Ro**
REVIEW ICD 10: BREAST DISEASE DIAGNOSTIC CODE
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Speaker **Jae Hong Kim**
FEASIBILITY OF HIGH RESOLUTION ULTRASONOGRAPHY AFTER AESTHETIC OR RECONSTRUCTIVE BREAST IMPLANT SURGERY
The W Clinic, Korea

Oral Presentation

Oral Presentation

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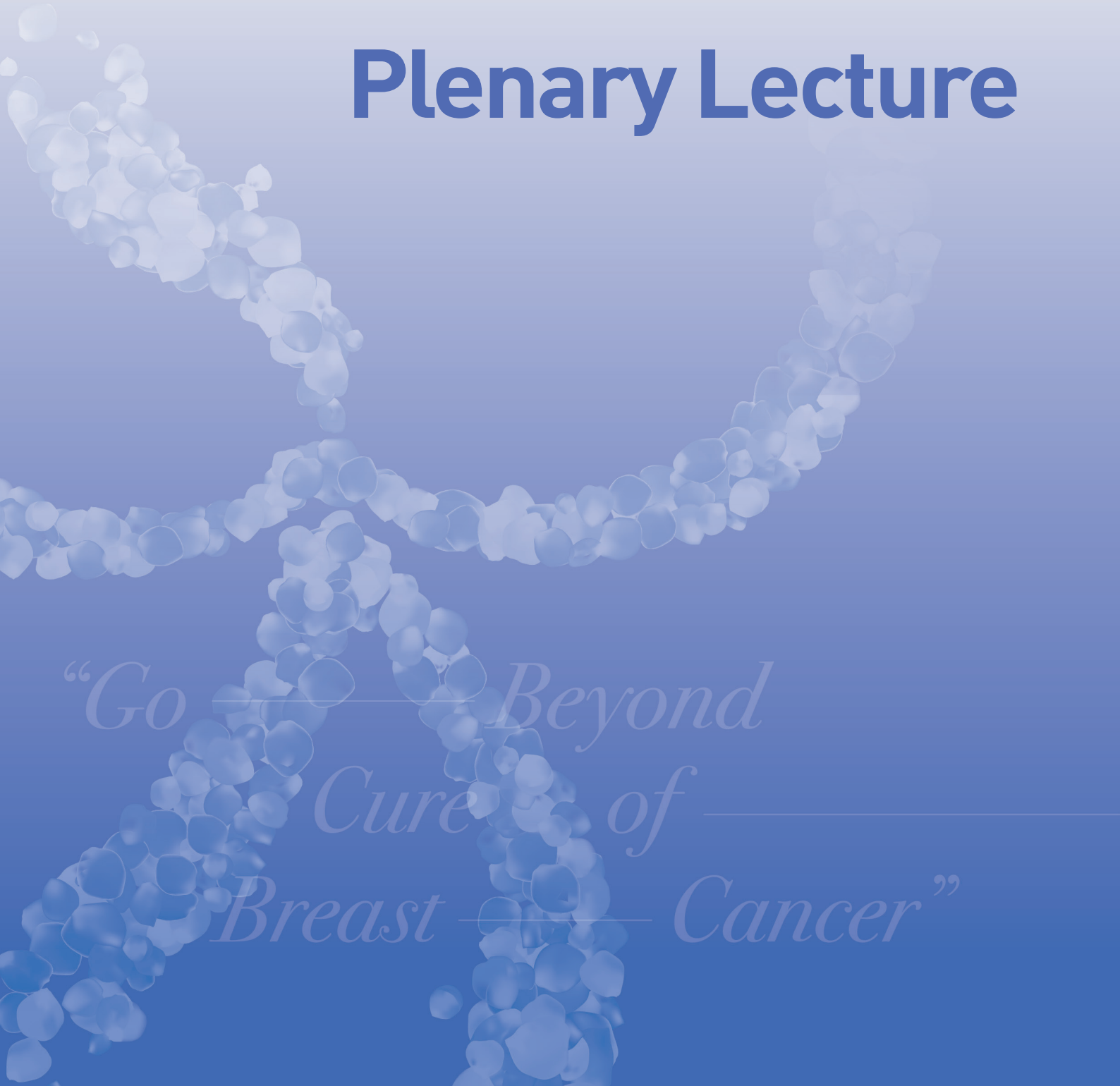

TARGETING HOMOLOGOUS RECOMBINATION DEFICIENT BREAST CANCER: MOVING FROM ADVANCED TO EARLY DISEASE

Andrew Tutt

Institute of Cancer Research, King's College London, Breast Cancer Research, United Kingdom

The therapeutic targeting of Homologous Recombination (HR) DNA repair deficiency (HRD) with the use of platinum chemotherapy and potent PARP1 trapping PARP inhibitors has been become standard practice because of trials conducted in the advanced disease setting. In the last year there has been much work on the development and further validation of biomarkers that can identify homologous recombination deficiency using germline and somatic sequencing of HR gene loci, mutational signatures driven by HRD and functional measures of HR such as RAD51 repair protein foci. There have also been several clinical trials investigating the role of both platinum agents, PARP inhibitors and combinations of both approaches that have moved from advanced disease to early breast cancer settings, using several PARP inhibitors of variable PARP1 trapping activity.

The OlympiA trial has recently published the first results of use of a PARPi, olaparib as an adjuvant therapy in a patient population selected using a biomarker of HR deficiency. This trial has influenced major changes in both in genetic testing and treatment guidelines in breast cancer. I will present recently updated result from OlympiA. I will review the latest results of several other relevant trials in my presentation and discuss how these approaches sit alongside other new therapy approaches available for the ER+ve and TNBC breast cancers that patients with germline BRCA1 and BRCA2 mutations develop. I will discuss some important "reverse translation" correlative biology initiatives within these trials and along "standard of care" patient journeys. I will show how these can be brought together with "forward translation" approaches using isogenic HR deficient models of BRCA1, BRCA2 and PALB2 deficient breast cancer and have the potential to inform the further optimisation of PARP inhibitor therapy. Finally, I will show development of some new approaches that target HR deficiency and may operate in settings where resistance to PARP inhibitors has developed.

HARNESSING THE VALUE AFFORDED BY WHOLE GENOME SEQUENCING OF BREAST CANCERS

Serena Nik-Zainal

Univ. of Cambridge, Department of Medical Genetics, United Kingdom

Whole genome sequencing permits exploration of the entirety of the cancer genome, per patient, revealing all causally-implicated driver mutations and mutational signatures that have arisen through carcinogenesis. Mutational signatures are the imprints of DNA damage and DNA repair processes that have been operative during tumorigenesis. First derived in breast cancers, they are biologically informative, reporting on the processes that have contributed to the developmental history of each patient's cancer. In this lecture, I shall provide an update on the field, focusing on validation of these abstract mathematical concepts, untangling the mechanisms underpinning mutation patterns in human breast cancers, and describing the new insights that we have gained through combinations of computational analysis and experiments in cell-based systems. We showcase how mutational-signature-based clinical algorithms have been developed, describe the path taken in translating these towards medical utility and for balance, highlight some of the hurdles that need to be navigated in this type of translational breast cancer research.

DEFINING TODAY'S SURGICAL STANDARDS OF CARE IN PATIENTS WITH BREAST CANCER

Walter Paul Weber

Univ. Hospital Basel, Department of Surgery, Switzerland

Current clinical practice is ideally informed by conclusive high-level scientific evidence. This abstract discusses two organizations that were founded to develop recommendations for clinical practice in case of missing or conflicting evidence and to identify research priorities: the Oncoplastic Breast Consortium (OPBC) and the St. Gallen International Breast Cancer Conference (SGIBCC).

The OPBC reflects a global consortium of oncologic, oncoplastic and plastic breast surgeons, radiation oncologists and patient advocates and currently consists of 730 members from 87 countries. At a precursor meeting in 2017, the German-speaking societies of senology called for standardization of oncoplastic breast conserving surgery (OPS) and discussed its goals and indications (BCRT 2017). The 2018 OPBC consensus conference revealed major heterogeneity in global breast reconstruction practice after skin- and nipple sparing mastectomy (BCRT 2018). This triggered the 2019 OPBC initiative to define knowledge gaps in oncoplastic surgery (Lancet Oncol. 2020), which identified type and timing of full breast reconstruction in the setting of planned adjuvant radiotherapy as the most important knowledge gaps. The 2021 OPBC initiative recommended autologous over implant-based breast reconstruction when radiation is planned due to lower risk of long-term complications and supported immediate and delayed-immediate reconstructive approaches. The third most important knowledge gap was the effect of oncoplastic surgery on local recurrence risk. This triggered the multicenter retrospective OPBC-01/iTOP2 study, which showed that large resection volumes in oncoplastic surgery increase the distance from cancer cells to the margin of the specimen, which reduces re-excision rates without affecting recurrence or survival (ASO 2021). The sixth most important knowledge gap referred to the indications for the use of prepectoral versus subpectoral implant-based breast reconstruction. This triggered the OPBC-02/PREPEC trial, which is a pragmatic multicenter randomized controlled trial designed to investigate quality of life two years after pre-versus sub-pectoral implant-based breast reconstruction. This trial has currently randomized 245 of a total of 372 patients at 22 breast centers in 6 countries (BMJ Open 2021). Finally, the OPBC initiated another Delphi process this year to identify uncertainties and controversies in axillary management. It currently leads OPBC-03/TAXIS, one of the most progressive axillary surgery de-escalation trials, which recruited 490 of the total sample size of 1500 patients at 28 sites around the world (Trials 2018). For this trial, we developed a new surgical concept called tailored axillary surgery that selectively reduces the tumor load in the axilla and remains

much less radical than axillary dissection (The Breast 2021).

While the OPBC was founded just a few years ago, the SGIBCC was held in 2021 already for the 17th time. More than 3'300 participants took part in this important bi-annual critical review of the "state of the art" in the multidisciplinary care of early-stage breast cancer, and 74 expert panelists from all continents discussed and commented on the 44 previously elaborated consensus questions as well as many key questions on early breast cancer diagnosis and treatment asked by the audience (Ann Oncol 2021). The Panel recommended completion axillary dissection for patients with residual macrometastases in the sentinel node after neoadjuvant chemotherapy, but many panelists felt axillary radiation could be an alternative to axillary dissection in case of lower volume disease. As with management of invasive breast cancer in older women, the Panel supported omission of radiation therapy in women > 70 years of age with DCIS bearing low risk features. A majority of the Panel felt that in women with ipsilateral in-breast cancer recurrence and/or 2nd primary breast cancer more than 5 years after initial surgery and radiation therapy, breast conservation with re-irradiation is appropriate option compared to mastectomy. Finally, the panel recommended a curative approach in selected patients with oligometastatic disease.

OPTIMISING RADIATION THERAPY IN EARLY STAGE BREAST CANCER

Philip Poortmans

Iridium Netwerk & Univ. of Antwerp, Department of Radiation Oncology, Belgium

As demonstrated by the EBCTCG meta-analyses, radiation therapy (RT) reduces any-recurrence risks and breast-cancer related mortality after mastectomy for node-positive disease and after breast conserving surgery. The relative risk reduction is partially independent from patient-, tumour- and treatment-related factors, while the absolute benefit depends to a large extent on the absolute risks without RT. Of note is an important interaction between systemic and locoregional treatments. The continuous improvements in outcomes after breast cancer diagnosis led to a quest for de-escalation of the overall treatment burden. In this, the decreased extent of axillary surgery further fuelled the increasing proportion of patients being eligible for nodal RT.

Against this background, RT evolves from the "one-size fits all" to a much more "tailor-made approach". Optimally, current tailoring of locoregional treatments involves decreasing number and size of target volumes, maintaining treatment focussed mainly at high-risk areas, while de-escalating treatment to low-risk areas. Within the multidisciplinary aspect of breast cancer treatment, this calls for integration of predictive and prognostic tools and looking into optimally combining less of both systemic and locoregional treatments to optimise tumour control while sparing normal tissues.

Not only distant but also locoregional recurrences risks depend on intrinsic tumour characteristics, including size, grade, endocrine and HER2 receptor status, proliferation rate and, with data becoming available slowly, prognostic and predictive profiles. All this can assist in predicting locoregional recurrence risks (and thereby indirectly the possible benefits of RT).

Currently, several trials are evaluating further de-escalation of locoregional treatments in patients with favourable intrinsic tumour types. Of interest in patients with intrinsic high-risk tumour types is the response to primary systemic therapy, with trials ongoing to de-escalate both axillary and local surgical as well as RT management after a favourable tumour response. Ongoing research also evaluates the predictive value of several proposed tools, including the available and mainly for selection of systemic treatments validated molecular and genomic profiles, the level of tumour infiltrating lymphocytes (TIL's), and the genomic adjusted radiation dose (GARD). Up to now, their clinical utility remains to be confirmed, preferably by integrating these tools in prospective clinical research.

Summary: while at present it remains challenging to reliably predict the benefit derived from RT at the individual patient's level, available data that are mainly based on retrospective analyses of older trials can already be used to start personalising RT indication, target volume selection and dose prescription for each individual patient. While doing so, we should avoid jeopardising the impressive improvements obtained in the outcomes after breast cancer diagnosis by precipitated de-escalating of treatments based on beliefs and assumptions rather than on solid evidence.

PRESURGICAL WINDOW STUDIES FOR DRUG DEVELOPMENT, STUDIES OF RESISTANCE AND PATIENT MANAGEMENT

Mitch Dowsett

Royal Marsden Hospital, Department of Pathology, United Kingdom

The interval between a patient being diagnosed with breast cancer and the time of excision is generally between 10 and 21 days and conventionally the patient receives no medical treatment in that period. However, this provides a "window of opportunity" for assessing the interaction between an intervention and the tumour while in situ. We and others have exploited this window for assessing the pharmacological dose-related activity and for identifying the responsive population of drugs under development for breast cancer (e.g. faslodex, arzoxifene) or drugs whose target population might be extended (eg lapatinib). It is essential that the drugs assessed pose no health risk to this mainly curable group of patients. This means that the value of such studies is sometimes not realised since once drug safety is established the priority is usually the conduct of conventional efficacy studies for registration purposes.

Hormonal agents are the most studied group of drugs in this situation. With these it has been established that the proportional reduction in malignant cell proliferation as measured by Ki67 staining is a measure of the degree of responsiveness to a given agent. In addition, the residual level of Ki67 after 2-3 weeks is related to the prognosis of the patient on the endocrine therapy and provides more information than baseline levels of Ki67. As such this 2-3 week value of Ki67 has now been used in several trials for recruiting patients with ER+ disease that are at high risk of recurrence due to incomplete responsiveness to the endocrine agent (e.g. ADAPT, ALTERNATE, POETIC-A).

The availability of Ki67 as a measure of pharmacological responsiveness provides a means of identifying those tumours that are at least partially resistant to therapy. We have used this scenario to study resistance mechanisms to aromatase inhibition making use of samples from the POETIC trial. Low levels of ER by IHC (1-10%) and ESR1 by rtPCR and RNAseq analysis were clearly associated with very poor Ki67 response and this questions the value of endocrine therapy in such tumours. Many growth factor signalling pathways were identified as associated with resistance in tumours with higher levels of ER but the dominant markers of resistance were associated with high levels of immune activity including high levels of tumour infiltrating lymphocytes. Detailed study of this relationship is needed to ensure that immune therapy is not detrimental to clinical outcome of patients with ER+ve disease.

Given the emphasis on RNAseq analysis for changes in gene expression due to treatment it is critical that the potential for artefactual changes is recognised. This is best done by the inclusion of a no treatment control arm.

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UPFRONT SURGERY VS. NEOADJUVANT SYSTEMIC THERAPY TO OPTIMIZE LOCOREGIONAL MANAGEMENT IN ER+/HER2- BREAST CANCER

Wonshik Han

Seoul National Univ. Hospital, Department of Surgery, Korea

The most important and well established benefit of neoadjuvant therapy for breast cancer patients is increased breast conservation rate. However, in luminal A type (ER+/HER2-) breast cancer, the response to neoadjuvant chemotherapy (NCT) is not as good as other subtype of breast cancer. In addition, with the advancement of multi-gene assay tools for this subtype, adjuvant chemotherapy is not needed at all in significant proportion of this subtype. Another option for these patients are neoadjuvant endocrine therapy (NET).

NET response (PEPI0, short term change of Ki67) can be a surrogate marker of long term prognosis to select who needs adjuvant chemotherapy. However, it seems that the response is not better marker than multigene assay. The most important advantage of NET or NCT in ER+/HER2- patients are to increase the possibility of breast conservation in BCS-ineligible or borderline patients, or to improve cosmetic outcome with decreased tumor size, especially in young patients. With individualized treatment (NET or NCT) using multigene assays, it is expected that BCS conversion rate (and hopefully QOL) will be increased overall.

BEYOND ENDOCRINE THERAPY FOR HIGH-RISK EARLY ER+/HER2- BREAST CANCER AFTER NEOADJUVANT CHEMOTHERAPY

Masakazu Toi, Masahiro Takada

Kyoto Univ. Hospital, Department of Surgery, Japan

The postoperative adjuvant therapy for high-risk ER+/HER2- breast cancer patients entered a period of major change in 2021. In high-risk cases determined by the anatomical staging or in cases where residual cancers were detected after neoadjuvant chemotherapy, the combined use of the postoperative CDK4/6 inhibitor abemaciclib and endocrine therapy (ET) showed a significant recurrence-reducing effect compared to ET alone. On the other hand, in patients with intermediate or high-risk cases or cases having residual diseases after neoadjuvant chemotherapy, the combined use of oral fluoropyrimidine S-1 and ET also showed a significant impact on reducing invasive disease recurrence compared with ET alone. These findings imply that two powerful novel therapies are going to be incorporated into practice of adjuvant therapy for ER+/HER2- patients having a high risk or a certain level of recurrence. Although these two treatments are different in terms of mode of action, administration period, and toxicity, they are treatments that can maintain high compliance and feasibility. The development and optimization of new treatment paradigm, including these two therapies, will further improve the prognosis of ER+/HER2- primary breast cancer patients.

VARIOUS TARGETED THERAPIES FOR ADVANCED ER+/HER- BREAST CANCER: TO WHOM SHOULD WE GIVE WHICH?

Komal Jhaveri

Memorial Sloan Kettering Cancer Center, Department of Medical Oncology, U.S.A.

Inhibitors of cyclin-dependent kinases 4 and 6 (CDK4/6) in combination with endocrine therapy have changed the natural history of hormone receptorpositive (HR+) metastatic breast cancer (MBC). Despite the unprecedented improvement in both median progression-free survival and overall survival that has been reported in the first- and second-line metastatic settings, the disease eventually progresses, and clinicians must choose a subsequent therapy.

There are several gaps in our current understanding of treatment options for HR-positive MBC including but not limited to optimal sequencing among others, that remain to be investigated. The studies leading to approval of everolimus (and alpelisib for tumors that harbor PIK3CA mutations) occurred before CDK4/6 inhibitors were available for clinical use. Treatment post-progression data from the phase III CDK4/6 inhibitor trials, single institution retrospective studies, real word data and non-randomized phase 2 trial provide some support for sequential use of combinations such as everolimus and exemestane or alpelisib plus endocrine therapy following progression on CDK4/6 inhibitor and ET. Other standard of care options includes PARP inhibitors for BRCA1 or BRCA2 mutation carriers, Pembrolizumab for MSI-high/dMMR tumors and NTRK inhibitors for rare secretory carcinomas of the breast that harbor NTRK fusions highlighting the importance of genomic profiling.

Novel drug development is crucial for HR+ HER2 negative MBC. Ongoing research efforts are focused on understanding mechanisms of resistance to CDK4/6 inhibitors, developing novel endocrine agents with or without CDK4/6 inhibitors, novel targeted therapies, and evaluating the role of antibody drug conjugates for this subtype of breast cancer. Data from the ongoing phase 3 trials evaluating triplet combinations and antibody drug conjugates in the metastatic setting are eagerly awaited and have the potential to further change the treatment paradigm of HR+/HER2- MBC.

ANTIBODY-DRUG CONJUGATES AND ENGINEERED ANTIBODIES

Yoon-Sim Yap

National Cancer Centre Singapore, Department of Medical Oncology, Singapore

In HER2-positive breast cancer, antibody-drug conjugates (ADCs) have dominated the arena of promising breakthrough treatments recently. ADCs have the potential to improve the therapeutic window by targeting the delivery of the potent cytotoxic agent (payload) to cancer cells expressing the antigen of interest. While Ado-trastuzumab emtansine (T-DM1) has been approved for clinical use in HER2+ advanced breast cancer since 2013, novel ADCs such as trastuzumab deruxtecan (T-Dxd) promise to improve the efficacy further with the higher drug antibody ratio, improved cleavable linker and bystander killer effect. Several new ADCs are currently being tested in clinical trials, some of which also enrol patients with HER2-low breast cancers. However, the efficacy and toxicity profiles vary, depending on the properties of the respective compounds.

There is also great interest in the development of engineered antibodies in HER2+ breast cancer. Although the activity of margetuximab in its registration SOPHIA trial was less impressive than that seen with ADCs, the role of engineered antibodies in selected patients in the right setting merit further research. Recent research efforts have focused on novel engineered antibodies such as bispecific antibodies, trispecific antibodies and even bispecific antibody drug conjugates. Most of these therapies are currently in the preclinical stage or early phase clinical trials. We will discuss the design of these ongoing trials, several of which involve combination therapies.

HER2 TARGETED TKI: OVERVIEW AND OVERCOMING RESISTANCE

Shaheenah Dawood

Mediclinic City Hospital, U.A.E.

A NEW PROMISE: HER2 VACCINES AND IMMUNOTHERAPY

Kyong Hwa Park

Korea Univ. Anam Hospital, Department of Medical Oncology (Internal Med), Korea

HER2 type cancer is one of the most immunogenic subtypes among breast cancers, and erbB2 protein is known as a tumor antigen that induces a natural anti-tumor immune response in patients with breast cancer.

It has been documented that interaction between the tumor cells and immune microenvironment determine the prognosis of patients with HER2 type breast cancer which has intrinsically aggressive tumor biology. Thus, the presence of CD8+ CTLs, but fewer regulatory T cells (Tregs) and Th17 cells were associated with a better prognosis. These findings implicated HER2 may represent a promising target for cancer immunotherapy.

Monoclonal antibodies targeting HER-2 were the first immunotherapeutics and have improved clinical outcomes of patients with HER2 type breast cancer. On top of the direct inhibition of signal transduction through binding to the extracellular domain of HER2 protein, all monoclonal antibodies (trastuzumab, pertuzumab, and trastuzumab-DM1) have immunologic mechanisms of ADCC in tumor cell killing. However, long-term use of the monoclonal antibodies is limited by cardiac safety, blood-brain barrier, and high cost.

Active immunotherapy using cancer vaccine has long been studied and a significant body of evidence is emerging recently. The immunotherapy using vaccine has advantages over monoclonal antibodies in terms of fewer administration, cost-effectiveness, and broad repertoire of immune responses. Among the vaccine platforms, peptide-based vaccines including MHC class I epitopes for the patients with specific HLA were the frontiers and clinical efficacy was demonstrated in both HER2 overexpressing and HER2 low (1+ - 2+) expressing tumors. Of note, those vaccines have shown synergy with trastuzumab, but no additional cardiac adverse events. To improve the immunogenicity of peptide vaccines, different adjuvants and delivery vectors are being explored in pre-clinical settings. Moreover, to overcome HLA restriction and short-lived immune response, large fragments of HER2 protein vaccines as protein or DNA vaccines are under active investigation. Also, combinations with 2 major immune checkpoint inhibitors (ICI; anti-PD1/PD-L1 and anti-CTLA4) are important areas of investigation and early data showed a potential to direct immune response after harnessing the immune system by the ICIs.

GENOMIC AMPLIFICATION LINKED TO THERAPEUTIC RESISTANCE IN BREAST CANCER

Jeong-Yeon Lee

Hanyang Univ. College of Medicine, Department of Pathology, Korea

Gene amplification is a critical genetic event that promotes oncogene overexpression and activation during tumor progression. Many recurrent amplicons have been found in breast cancer with clinical significance, but only HER2 gene amplification on chromosome 17q12 is being used as a diagnostic and therapeutic target for breast cancer treatment. Our studies have identified new targetable amplified genes that are associated with resistance to conventional therapies in different subtypes of breast cancer. First, we have demonstrated that genes co-amplified with HER2 on the 17q12 region are crucial determinants of response to anti-HER2 therapy in HER2+ breast cancer.

Approximately half of HER2+ breast cancers harbor co-amplification of HER2 and MEL-18 that was associated with the increased susceptibility to trastuzumab, while CDK12 amplification on the 17q12 was an alternative therapeutic target for trastuzumab-resistant breast cancer. Furthermore, our findings show that genes encoding histone modifiers, which are frequently amplified on 1q, 8p11-12, and 12p13 locus in breast cancer, play an important role in promoting metastatic progression or conferring resistance to hormonal therapy on ER+ breast cancer, indicating the interplay between genomic and epigenetic alterations. Taken together, these results highlight the crucial role of gene amplification in cancer progression and suggest the amplified genes as potential biomarkers and actionable molecular targets to overcome therapeutic resistance in the treatment of breast cancer.

PARSING THE TUMOUR MICROENVIRONMENT OF BREAST CANCER USING INTEGRATED SINGLE-CELL AND SPATIALLY-RESOLVED MUTI-OMICS

Alex Swarbrick[1], Sunny Z. Wu[2], Ghamdan AI-Eryani[2], Daniel Lee Roden[2]

[1]*Garvan Institute of Medical Research, Department of Radiology, Australia*
[2]*St Vincent's Clinical School, Faculty of Medicine, Australia*

Breast cancers are complex cellular ecosystems where heterotypic interactions play central roles in disease progression and response to therapy. However, our knowledge of the cellular composition and organization of breast cancer remains limited. We present a comprehensive single cell and spatially resolved transcriptomic atlas of human breast cancers.

The 10X Genomics Chromium platform was used to generate single cell transcriptomic data (scRNA-Seq) from more than 120,000 cells sampled from 26 breast cancers. CITE-Seq was employed to simultaneously generate protein measurements using a panel of 157 antibodies against immune, stromal and epithelial cell surface markers and analysed using Seurat. Using single cell signatures, we estimated the cellular composition of more than 2000 breast cancers in the Metabric cohort using deconvolution methods. Spatial transcriptomics was conducted on 12 frozen tissues (Luminal, Her2+ and triple negative breast cancer (TNBC)) using the 10X genomics Visium solution. We also used a novel Spatial Whole Transcriptome Panel, targeting 18,000+ genes on the Nanostring GeoMX platform, to profile T cells and malignant cells across multiple tissue niches from 16 TNBC FFPE cases.

Integrative scRNA-Seq analysis identifies recurrent gene modules driving neoplastic cell heterogeneity, including interferon signaling, estrogen receptor function and mutually exclusive patterns of proliferation versus EMT. We also develop a single cell classifier of intrinsic subtype (scSubtype) to reveal frequent intra-tumoral heterogeneity for breast cancer intrinsic subtypes.

CITE-Seq revealed immune profiles at high resolution, leading to the identification of novel macrophage populations with high expression of PD-L1 and PD-L2 immune checkpoint ligands and associations with clinical outcome. We also observe enrichment of exhausted and proliferative CD8 T cells in TNBC, with unique patterns of cell-surface checkpoint protein expression when compared to other subtypes. Targeted analysis using the GeoMX revealed spatial segregation of T cell phenotypes, with exhausted and proliferative CD8 T cells forming small clusters adjacent to tumor cells with high interferon pathway activity.

Analysis of scRNA-Seq data revealed that stromal cells generate diverse functions and cell surface protein expression through differentiation within 3 major lineages: fibroblast, endothelial and perivascular-like. Subsets of stromal cells had features associated with immune regulation and Visium data revealed that stromal-immune niches were spatially organized in tumors, offering insights into anti-tumor immune suppression by stromal cells.

Finally, deconvolution stratified >2000 breast cancer cases in Metabric into nine clusters, termed 'ecotypes', with distinct cellular compositions and clinical outcomes. This study provides a comprehensive atlas of the cellular architecture of breast cancer.

Keywords: Single cell, breast cancer, ecosystem, genomics

GENOMICS RELATED TO TREATMENT AFTER CDK4/6 INHIBITORS IN HORMONE RECEPTOR POSITIVE BREAST CANCER

Rinath Jeselsohn

Dana-Farber Cancer Institute, Department of Medical Oncology, U.S.A.

CDK4/6 inhibitors in combination have become the standard of care in hormone receptor positive metastatic breast cancer and improve progression free survival and overall survival. Despite the remarkable impact of this class of drugs, nearly all patients will ultimately develop resistance to CDK4/6 inhibitors. Currently there are no biomarkers to predict response to CDK4/6 inhibitors in the metastatic setting other than estrogen receptor positivity. Multiple pre-clinical studies have investigated the mechanisms of resistance to CDK4/6 inhibitors, and these can be categorized to; (i) Upstream adaptive mechanisms, such as activation of receptor tyrosine kinases. (ii) Aberrations of the CDK4/6 cyclin D-RB1 axis, such as RB1 genetic alterations and (iii) Downstream bypass mechanisms, such as cyclin E overexpression or amplification. In addition, many of the mechanism of resistance to endocrine treatment and CDK4/6 inhibitors converge, highlighting the role of improved ER blockade in the setting of CDK4/6 inhibitor treatment. Analyses of completed clinical trials are also shedding light on the mechanisms of resistance and guiding the development of novel treatment options. Currently there are several clinical trials testing novel approaches to overcome resistance to CDK4/6 inhibitors. These include, but not limited to the combination of CDK4/6 inhibitors with PI3Kinase inhibitors, CDK2/4/6 inhibitors, CDK2 inhibitors, CDK7 inhibitors, FGFR inhibitors and others. There are also several new oral endocrine treatments currently in clinical development.

In this presentation, I will review the mechanisms of resistance to CDK4/6 inhibitors and ongoing studies investigating clinical strategies to overcome resistance and improve outcomes in metastatic hormone receptor positive metastatic breast cancer.

CURRENT STATUS OF IMMUNOTHERAPY: WHERE ARE WE?

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Immunotherapy has been established as one of the standard treatments for many carcinomas, including breast cancer. Immune checkpoint inhibitors are categorized as anti-CTLA-4, anti-PD-1, and anti-PD-L1 antibodies, and then the anti-PD-1 and anti-PD-L1 antibodies have been confirmed to be effective in breast cancer. The effectiveness of immunotherapy depends on whether the immune response is cold or hot, and the type of cancer. Breast cancer is a cold tumor with low immunogenicity, so it was difficult to show efficacy with immune checkpoint inhibitors alone. Immunotherapy for breast cancer was established by combining chemotherapy with immune checkpoint inhibitor and by using PD-L1 expression as a biomarker to maximize the therapeutic effect.

In the Impassion130 study, the combination of Atezolizumab as the anti-PD-L1 antibody and nab-paclitaxel was more effective than nab-paclitaxel alone in the treatment of PD-L1 positive evaluated using SP142 antibody advanced or recurrent triple negative breast cancer (TNBC). PFS as the primary endpoint was 7.5 months versus 5 months, with statistically significant difference in favor of the combination therapy (hazard ratio (HR), 0.62; 95% CI, 0.49 to 0.78; $P < 0.001$).

In the KEYNOTE355 study, the combination of pembrolizumab (pembro) as the anti-PD-1 antibody and chemotherapy (paclitaxel or nab-paclitaxel or gemcitabine + carboplatin) was shown to be more effective than chemotherapy alone in TNBC with a CPS of 10 or greater evaluated using 22C3 antibody. PFS as the primary endpoint was 9.7 months versus 5.6 months, with statistically significant difference in favor of the combination therapy (HR 0.65, 95% CI 0-49-0-86 $p = 0.0012$).

In the KEYNOTE522 study, preoperative use of pembro in combination with chemotherapy (carboplatin+paclitaxel followed by AC/EC) increased the pCR rate from 40% to 58.7% and improved the 3-year EFS from 76.8% to 84.5% (HR: 0.63, $p = 0.00031$). Data from KEYNOTE355 and 522 showed similar trends in the Asian subset, and no significant increase in adverse events in the Asian population.

In many guidelines around the world, the combination of immune checkpoint inhibitor and chemotherapy is recommended as the first line treatment for PD-L1 positive recurrent triple negative breast cancer (TNBC). Furthermore, in perioperative TNBC, preoperative use of pembrolizumab (pembro) in combination with chemotherapy increased the pCR rate, and postoperative use of pembro for 9 cycles improved the DFS regardless of PD-L1 status. Pembro plus chemotherapy is expected to become a standard treatment for high risk TNBC in many countries, including Asia.

However, immunotherapy in breast cancer has many challenges. It is also questionable whether PD-L1 is a true biomarker or not. Is postoperative pembro really necessary in pCR cases? Whether it is better to add capecitabine or continue pembro for non pCR cases? How to turn a cold tumor into a hot tumor? How to combine with other drugs, especially antibody drug conjugate (ADC)? Many clinical questions remain to be answered for early and recurrence breast cancers.

Immunotherapy for breast cancer is still in its infancy, and it is necessary to make efforts to deliver optimal immunotherapy to optimal patients through the development of basic and clinical research.

BIOMARKER FOR IMMUNOTHERAPY: WHAT IS THE BEST?

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CHALLENGE FOR IMMUNOTHERAPY IN BREAST CANCER: HOT OR COLD

Sherene Loi

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Breast cancer has not traditionally been considered an immunogenic solid tumor. Recently approval of pembrolizumab in the early and late stage setting of triple negative breast cancer (TNBC) has challenged this belief. Checkpoint inhibitors that target the PD1/PDL1 pathway need to be combined with cytotoxic chemotherapy in breast cancer to be effective, but it is unclear if the combination is synergistic or just additive. Breast cancer contains far less mutations on average than other more immunogenic tumors, and its cause is largely related to hormonal factors rather than caricinogens or viruses. Therefore, optimizing immunotherapy for breast cancer is considered a different challenge, and the majority of breast cancers are considered to have a cold tumor immune microenvironment compared to other more immunogenic cancers such as melanoma and lung cancer. This particularly applies in the metastatic setting. In the advanced TNBC setting it is still unclear if we can create a new immune response, as at present, only patients with a pre-existing immune response respond to combinations of pembrolizumab and chemotherapy. In this talk, I will discuss reasons for this observation and new approaches being tested that are trying to change this for the benefit of our patients.

DE-ESCALATION OF AXILLARY SURGERY AFTER NACT

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In the surgical procedures of axillary lymph node(s) for the breast cancer patients, there are two purposes; One is to decrease the tumor burden in the axillary nodes in case of axillary lymph node metastasis and the other is to evaluate the precise status of lymph node and to guide the intensity of adjuvant systemic treatment. De-escalation of axillary surgery has become more popular as de-escalation of breast surgery has been possible with the help of an earlier diagnosis, more concise preoperative imaging evaluation, and proper application of neoadjuvant chemotherapy (NACT) with or without targeted agents. Although not for most of the advanced breast cancers with strong hormone receptor (HR) expression, there has been a remarkable increase in pCR rate after NACT in Her-2 expressing tumors and triple-negative breast cancers (TNBC). The expected pCR chances are over 50% after 6 cycles of TCHP in Her-2 positive tumors, and even higher up to 75% in HR-negative Her-2 positive tumors. In TNBC patients, the recently reported pCR rate is around 50% in the case of weekly paclitaxel plus carboplatin followed by classic AC 4 cycles, and it is even higher with the addition of novel immune checkpoint inhibitors.

Sentinel lymph node biopsy (SLNB) has gained wide popularity since its introduction to breast cancer about 30 years ago. In SLNB after NACT, there was an initial concern that fibrosis of lymphatic channels would result in unacceptably high false-negative rates (FNR). However, this hypothesis was not supported by clinical evidence. Nowadays, SLNB after NACT has been widely adopted in patients presenting as cN0. The next issue of SLNB after NACT was its feasibility for the patients with cN+ at initial diagnosis and with high suspicion of conversion to cN0 after NACT. With the accumulation of experiences, it has been known that SLN identification rates are lower than those observed in cN0 patients after NACT ranging from 79.5% to 92.7%, FNR decreased under the 10% threshold when 3 or more SLNs were obtained. In Samsung Medical Center, through the series of our retrospective studies of SLNB after NACT, we found out that the ypN0 chance is around 98% in case of pCR in the breast in Her-2 positive and TNBC patients if their initial axillary status is cN0, and a little over than 85% if the initial axillary status is cN1-2. In my humble opinion, the next question we should answer is the necessity of doing SLNB for patients with high suspicion pCR after NACT.

Like SOUND trial and NAUTILUS study, which are investigating the possibility of omission of SLNB in early breast cancer patients with cN0 in primary surgery setting, there are some studies searching for the chance of selective omission of SLNB after NACT in Her-2 positive and TNBC patients. ASICS study of

the Netherlands Cancer Institute is one of them which aims to find out the clinical outcome of omitting SLNB after NACT to avoid any possible short- and long-term morbidity from axillary surgical procedure in Her-2 positive and TNBC patients and cN0 patients with a very low risk of tumor-positive axillary lymph nodes. ASLAN study is another prospective, multi-center, single-arm observation study, activated in the Autumn of 2021 in search of a chance to avoid SLNB in case pf ypCR in the breast after a thorough pathological evaluation after BCS in Her-2 positive and TNBC patients and cN0-1 at the initial diagnosis. I hope we can get some clue in a few years.

DE-ESCALATION OF BREAST SURGERY AFTER NACT

Peter C. Dubsky

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Breast conservation is associated with excellent cosmetic outcomes and improved quality of life in early breast cancer patients. Neoadjuvant chemotherapy (NACT) is increasingly used in the treatment of patients with early-stage breast cancer, but few guidelines specifically address optimal locoregional therapy of the breast.

We have established an international consortium to discuss clinical evidence and to provide expert advice on technical management of patients with early-stage breast cancer. During a consensus meeting that included members from European scientific oncology societies, clinical trial groups, and patient advocates, statements were discussed and voted on. Based on these findings, the panel developed clinical guidance recommendations and a toolbox to overcome many clinical and technical requirements associated with the diagnosis, response assessment, surgical planning, and surgery of patients with early-stage breast cancer. During this presentation the implementation of optimal breast surgery after NACT will be discussed along these guidelines.

In addition, clinical research is ongoing with a goal to predict complete pathologic response (pCR) and omit breast surgery. The current failure to predict pCR in ongoing trials and future aims of research will be discussed.

CAN WE SELECT PATIENTS IN WHOM WE CAN FOREGO ANY AXILLARY TREATMENT AFTER UP FRONT CHEMOTHERAPY?

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Management of axillary lymph nodes in breast cancer has changed dramatically in the past decades and is changing continuously. Just an example: 20 years ago, over 80% of patients with invasive breast cancer had a full axillary lymph node dissection (ALND) as part of their treatment, nowadays it is less then 3%! Important insights in the biology of lymph nodes have led to these changes:

- Lymphatic spread to the LN is an orderly process, making the SN procedure a fully reliable staging procedure in N0 breast cancer
- Elective ALND does not impact on overall survival
- Prognostic relevance of nodal status is overtaken by the biology and metastatic potential of the primary tumor (for instance by gene signatures)
- Systemic treatment indication and type of treatment is largely determined by the biology of the primary tumor
- Systemic treatments have also impact on lymph node metastases

This latter observation has led to axilla preserving approaches in patients with proven N+ve breast cancer who are candidates for up front chemotherapy: in our experience up to 80% of patients with N+ve breast cancer could be spared a full ALND (1).

The next step is to see if patients with N0 breast cancer nd are candidates for up front systemic chemotherapy could be spared a SN procedure. To this end we performed a cohort study (2) in patients with cT1-3 cN0 breast cancer treated with neoadjuvant chemotherapy followed by breast surgery and sentinel node biopsy between 2013 and 2018. cN0 was defined by the absence of suspicious nodes on ultrasound imaging and PET/CT, or absence of tumour cells at fine-needle aspiration. Univariable and multivariable logistic regression analyses were performed to determine predictors of ypN0. Overall, 259 of 303 patients (85.5 per cent) achieved ypN0, with high rates among those with a radiological complete response (rCR) on breast MRI (95.5 per cent). Some 82 per cent of patients with hormone receptor-positive disease, 98 per cent of those with triple-negative breast cancer (TNBC) and all patients with human epidermal growth factor receptor 2 (HER2)-positive disease who had a rCR achieved ypN0. Multivariable regression analysis showed that HER2-positive (odds ratio (OR) 5·77, 95 per cent c.i. 1·91 to 23·13) and TNBC subtype (OR 11·65, 2·86 to 106·89) were associated with ypN0 status. In addition,

there was a trend toward ypN0 in patients with a breast rCR (OR 2·39, 0·95 to 6·77). The probability of nodal positivity after neoadjuvant chemotherapy was less than 3 per cent in patients with TNBC or HER2-positive disease who achieved a breast rCR on MRI. Other studies confirm these results: very low rates of positive SN after chemotherapy in cN0 patients, particularly TNBC and HER2 driven cancers. These results has led to 2 prospective studies where SN biopsy is omitted in cN0 patients and a rCR on imaging after chemotherapy: Omission of SLNB in Triple-negative and HER2-positive Breast Cancer Patients With rCR and pCR in the Breast After NAT- (NCT04101851 EUBREAST) and Avoiding Sentinel Lymph Node Biopsy in Breast Cancer Patients After Neoadjuvant Chemotherapy (ASICS) NCT04225858 The Netherlands Cancer Institute.

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MR IMAGING BIOMARKERS FOR PREOPERATIVE TREATMENT AND NEOADJUVANT SYSTEMIC THERAPY

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Preoperative, or neoadjuvant treatment of breast cancer, in which systemic therapy is administered prior to surgery, is used to downstage primary breast cancers while reducing the risk of distant recurrence[1-3]. Neoadjuvant treatment (NAT) often results in complete eradication of tumor by the time of surgery (pathologic complete response, or pCR) and it is now well-established that pCR confers excellent survival outcomes[4,5]. A recent meta-analysis of more than 27,000 patients concluded that achieving pCR after NAT is associated with significantly better event-free survival (EFS) and overall survival (OS), particularly for triple-negative and HER2+ breast cancer[6]. By contrast, women with substantial residual disease at surgery have much poorer outcomes, with recurrence rates of over 50% at 5 years[7]. Increased understanding of the relationship between NAT response and prognosis are fueling clinical trial efforts to determine the effectiveness of therapy as early as possible in the course of treatment. Imaging and tumor markers from biopsy and blood samples are all being developed as methods to monitor and measure the effects of NAT prior to surgery. These tests help to better characterize the heterogeneity of breast cancers and their response patterns, with the goal of tailoring treatments and improving individual outcomes.

Among imaging methods, magnetic resonance imaging (MRI) is particularly effective for visualizing the effects of neoadjuvant treatment on breast tumors. MRI has the potential to provide prognostic information and serve as a non-invasive imaging biomarker for predicting response. The American College of Radiology Imaging Network (ACRIN) 6657/I-SPY 1 trial found DCE-MRI functional tumor volume (FTV), a metric capturing the pattern of contrast enhancement following gadolinium injection, to be a robust measure of treatment response, predictive of pathologic and recurrence-free survival outcomes[8,9]. These findings led to the multi-center I-SPY 2 TRIAL, an adaptively-randomized phase II clinical trial of novel agents for breast cancer that incorporates MRI in its design[10].

A key element of I-SPY 1 was the demonstration that standardized quantitative contrast enhanced MRI methods were reproducible across multiple clinical sites, and that measures of FTV were predictive of pCR. These benchmarks underpinned the development of the I-SPY2 adaptive platform trial whose goal has been to accelerate phase II evaluation of targeted therapies. I-SPY 2 is predicated on the use of serial MRIs during treatment to monitor tumor response in near real-time. Since opening in 2010, 22 agents/combinations have entered the trial; twelve have completed accrual and seven have 'graduated' in

at least one tumor subtype. I-SPY 2 is also evaluating breast diffusion-weighted imaging (DWI) for prediction of response. This talk will discuss the use of MRI-based biomarkers to assess NAT response and to provide the early response assessments needed for individualization of treatment.

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IMAGING BIOMARKERS FOR ASSESSING TUMOR HETEROGENEITY

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Breast cancer is a heterogeneous disease presenting with variable histopathological and biological characteristics, different clinical outcomes, and different responses to systemic interventions, and this heterogeneity is observed intratumorally and intertumorally. In particular, intratumor heterogeneity can manifest both spatially and temporally (1). Spatial heterogeneity is thought to originate from variable, microenvironment-specific stresses and branched evolution from a common ancestor cell population into divergent subclonal populations (1). Temporal heterogeneity can be resulted from the dynamic progression and growth of cancer cells as well as in response to systemic therapy (1). As increased intratumor heterogeneity is reported to be associated with adverse clinical outcomes, it is getting much attention to detect "tumor heterogeneity" for accurate prediction of patients' prognosis (2).

Critical decisions during disease treatment are mostly made on the basis of markers acquired from tissue samples, typically obtained via core biopsy or surgical excision. More recently, commercial prognostic tests such as MammaPrint (Agendia BV) and Oncotype DX (Genomic Health, Inc.) have been developed and increasingly applied. All these prognostic and predictive markers need tissue sampling and these limited diagnostic tissue samples may undersample spatially heterogeneous breast tumors as well as miss temporal changes according to disease progression or exposure to therapy. Further, new commercial markers mentioned above are clinically limited by use in only specific breast cancer molecular subtypes (3) and importantly still expensive. Therefore, there is a clinical need to develop prognostic and predictive markers of intratumor heterogeneity that may augment established biomarkers for personalized disease diagnosis, staging, management, and to assess treatment response to neoadjuvant therapy.

Medical imaging is currently used for breast cancer diagnosis, staging, and treatment response assessment, providing a means for longitudinal, noninvasive, whole-tumor evaluation of disease burden. In addition to their fundamental impact on patient management, several radiological techniques have been shown to enable the identification of breast tumor heterogeneity.

In this lecture, I will briefly review imaging biomarkers for assessing tumor heterogeneity, focusing on MRI.

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THE ROLE OF IMAGING BIOMARKERS ON SURVIVAL PREDICTION

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Breast MRI is a key imaging technique for breast imaging. Several imaging features on preoperative MRI are correlated with poor clinical outcomes in patients with breast cancer. Breast MRI has potential to provide a wide range of biomarkers for survival prediction and for biomedical research. Research is ongoing to identify reliable MRI biomarkers that can guide clinicians in decision making and potentially enable personalized treatment for breast cancer. This presentation will 1) review the MRI features associated with clinical outcomes in breast cancer 2) discuss the role of breast imaging biomarkers in research and 3) discuss the potential clinical application of MRI imaging biomarker based on our clinical experience.

REGIONAL RT OTHER THAN AXILLA: THE LATEST ANSWER FROM KOREA

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For last two decades, substantial advances have been made regarding regional management for breast cancer. Sentinel node biopsy of the axilla have made it possible to de-escalate axillary node dissection and reduce the incidence of lymphedema. However, regarding management of regional node other than axilla, there has been still controversies until two landmark trials were published on 2015.

First, EORTC 22922/10925 trials reported the impact of overall survival (OS) of elective internal mammary and medial supraclavicular (IM-MS) irradiation. The results showed IM-MS irradiation reduced significantly 3.0% difference of disease-free survival (DFS), but was not converted to improved overall survival (1.6%) (1). Second, MA20 trial showed the similar results for regional radiotherapy to significantly improve disease-free survival (5.0%) and marginal effect on overall survival (1.0%) (2).

Confined to IM node irradiation (IMNI), French trial was the first trial to investigate the efficacy of irradiation of IMN on 10-year OS in breast cancer patients after mastectomy on 2013. The results showed the improvements of 3.3% by IMNI, although not statistically significant (3). On 2016, DBCG-IMN, prospective population-based cohort study, showed that IMNI was associated with an increase in OS of 3.7% at 8 years after treatment. Taken these trials together, IMNI showed modest improvement in DFS or OS (4).

KROG 0806 study was investigated to examine whether the inclusion of IMNI in regional nodal irradiation improves the outcomes in women with node-positive breast cancer (5). Patients were treated with contemporary therapy, such as taxane and trastuzumab and 3 dimensional conformal radiotherapy. This study recently confirmed IMNI showed 3.4% improvement on 7-year DFS rates like existing studies, although primary endpoint was unmet in this study. Despite the migration to earlier stage and introduction of more effective chemotherapy, IMNI would continue to improve survival in node-positive breast cancer.

Later, EBCTCG will publish the meta-analysis of the published studies to reveal the efficacy of IMN, and multicenter prospective phase III randomized controlled trial (POTENTIAL) ongoing in China will provide additional answer of IMNI (6).

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INDIVIDUALIZED RT ACCORDING TO IHC-BASED SUBTYPE

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In 2005, the Early Breast Cancer Trialists' Collaborative Group (EBCTCG) meta-analyses reported that one breast cancer death over the next 15 years could be avoided for every four local recurrences avoided and that most of the substantial absolute reductions in local recurrence risk involved the addition of radiotherapy. In 2011, the updated EBCTCG meta-analyses reported that after breast-conserving surgery, radiotherapy to the conserved breast halved recurrences and reduced breast cancer deaths by approximately one-sixth. Although they reported the importance of radiotherapy in terms of local control, they addressed that the local recurrence reduction by radiotherapy may be very little in some group of patients.

The adverse events associated with postoperative irradiation of breast cancer are often minor. However, some serious adverse events, including second cancer and cardiovascular event can occur in rare cases, and therefore, several clinical trials have suggested the omission of irradiation. However, there is a correlation between locoregional recurrence and breast cancer death, and local recurrence significantly reduces the quality of life of patients. Therefore, optimal postoperative therapy that reduces local recurrence and breast cancer deaths is desirable.

The Japanese breast cancer guidelines recommend that the appropriateness of irradiation should be determined by breast conservation and the number of lymph node metastases. After the 2014 EBCTCG meta-analyses, the Japanese breast cancer guidelines recommend regional irradiation for breast cancer patients with 1 to 3 positive lymph nodes who have undergone mastectomy, similar to other guidelines such as the NCCN and ASCO/ASTRO/SSO guidelines. However, there is significant debate regarding regional irradiation for 1 to 3 positive lymph nodes. In addition, since the publication of ACOSOG Z-11, EORTC10981-22023, and OTOASOR, axillary management of cN0 but pathologically positive or with micro-metastases has been widely discussed worldwide.

In the 2022 revision of the Japanese breast cancer guidelines, regional irradiation was discussed between surgeons and radiation oncologists in terms of axillary management. It was agreed that PMRT for 1 to 3 lymph node metastases should be described as follows: "Since the indication for irradiation of regional lymph nodes is not determined solely by the number of lymph node metastases, it should be performed after comprehensive consideration of other recurrence risks." Therefore, individualized treatment should also be considered in the field of radiotherapy.

Unfortunately, there is not much data on individualized treatment in the field of radiotherapy. When considering the treatment of patients, local and systemic therapy should not be considered separately, but should be considered as combined treatment. We learned from past data that the impact of the local therapy would be greater with the absence of today's systemic therapy. Therefore, we should be aware that the intensity of local treatment may vary depending on whether standard systemic therapy can be administered or not. Also, various clinical trials are currently underway, and there is much to be discussed, such as whether systemic or local therapy is more desirable for elderly patients.

In this session, I would like to summarize the current situation based on existing reports and deliver a presentation on the direction that we, radiation oncologists, should take in the future with my personal views.

PRECISION RADIATION ONCOLOGY: RT DECISION MAKING BASED ON GENOMIC BIOMARKERS

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Much as the development of molecularly based signatures (OncotypeDx, MammaPrint, ProSigna™, etc.) has revolutionized the decision-making process surrounding the need for adjuvant chemotherapy in women with early stage breast cancer, the development of prognostic and predictive signatures to determine the need and efficacy of radiation for women with breast cancer holds similar promise. While preliminary efforts to develop these signatures has been encouraging, much work remains in order to successfully translate these signatures into the clinic. In this educational session, we will review the current status of genomic-based signatures for radiation decision making. We will also review the barriers to clinical adoption and the molecularly stratified trials testing these signatures for treatment omission. Ultimately, for any of these tests to be translated into the clinic it will require demonstration of their accuracy and reproducibility as a test and perhaps more importantly, demonstration within the context of clinical trials of the utility of these tests at improving outcomes for women with breast cancer. While not yet realized, the ongoing development of these signatures holds much promise as the field seeks to finally realize "personalized medicine" as it relates to radiation treatment for women with breast cancer.

IDENTIFYING TUMORS WITH DEFECTS IN DNA DAMAGE RESPONSE, HOMOLOGOUS RECOMBINATION, AND REPLICATION STRESS

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PARP inhibitors have been shown to improve progression-free survival (PFS) compared to standard chemotherapy in patients with germline BRCA-mutated HER2-negative metastatic breast cancer and have become the standard of care. BRCA1/2 genes play an important role in homologous recombination repair in DNA damage response, and BRCA1/2 mutations cause homologous recombination deficiency (HRD) that result in sensitivity to PARP inhibitors. Since BRCA1/2 mutations are only one cause of HRD, identifying tumors with HRD is crucial for predicting patients who response to PARP inhibitors.

According to the results of the OlympiAD and EMBRACA trials, about 40% of patients with BRCA-mutated breast cancer did not respond, and most developed resistance to PARP inhibition. Therefore, there is also an unmet need to identify predictive factors for a response even in BRCA-mutated breast cancer. Currently, various assays have been developed to try to better define tumors with HRD.

We conducted a phase I/II trial of eribulin and olaparib for metastatic triple-negative breast cancer. The exploratory analysis of this study revealed that HRR-related gene mutations and high methylation levels are predictive factors for longer PFS in study treatment.

In this symposium, I will summarize the identification methods of HRD such as HRD score, mutational signature, methylation abnormalities, HRDetect, and RAD51 score.

CURRENT STATUS OF PARP INHIBITORS IN BREAST CANCER: NEOADJUVANT, ADJUVANT, AND METASTATIC SETTING

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One of main characteristics of cancer is partial loss of DNA damage repair (DDR) pathway resulting in increased DNA damage levels and replication stress. The poly-(ADP-ribose) polymerase inhibitor (PARPi) is the first DDR inhibitor incorporating into clinical practice, under the concept of synthetic lethality. PARPi have been tested in patients with BRCA1/2 germline mutations (gBRCA1/2mt) and shown clinical benefits in breast cancer with gBRCA1/2mt.

In OlympiAD trial, olaparib provided a significant benefit over treatment of physician's choice (TPC) single agent chemotherapy; median progression-free survival(PFS) was 2.8 months longer (7.0 mo vs. 4.2 mo; HR 0.58; 95% C.I., 0.43 - 0.80; $P < 0.001$) and the risk of disease progression or death was 42% lower with olaparib than with TPC. The objective response rate (ORR) was 59.9% in the olaparib and 28.8% in the TPC. Median OS was 19.3 mo. with olaparib vs. 17.1 mo. with TPC (HR 0.90, 95% CI 0.66-1.23; $P = 0.513$). HR for OS with olaparib vs. TPC in pre-specified subgroups were: prior chemotherapy for mBC [no (first-line): 0.51; yes (second/third-line): 1.13]; receptor status (triple negative: 0.93; hormone receptor positive: 0.86); prior platinum (yes: 0.83; no: 0.91). The prevalence of gBRCAmt in the OlympiAD Asian subgroup screened for study recruitment was 13.5%.

In EMBRACA trial, median PFS was significantly longer in the talazoparib than in the TPC (8.6 mo vs. 5.6 mo; HR for disease progression or death, 0.54; 95% C.I., 0.41 - 0.71; $P < 0.001$) with improvement of patient-reported outcomes (PRO). The ORR was higher in the talazoparib than in the TPC (62.6% vs. 27.2%; $P < 0.001$). HR for OS with talazoparib vs TPC was 0.848 (95% CI 0.670-1.073; $P = 0.17$); median PFS 19.3 mo vs. 19.5 mo. Kaplan-Meier survival percentages for talazoparib vs. TPC at 3 yr was 27% vs 21%. Most patients received subsequent treatments: for talazoparib and chemotherapy, 46.3%/41.7% received platinum and 4.5%/32.6% received a PARPi, respectively. Adjusting for subsequent PARP and/or platinum use, HR for OS was 0.756 (95% CI 0.503-1.029). Neoadjuvant talazoparib for 6 mo produced substantial activity with manageable toxicity. RCB-0 (pathologic complete response) rate was 53% and RCB-0/I was 63%. Eight patients (40%) had G3 anemia and required a transfusion, 3 patients had G3 neutropenia, and 1 patient had G4 thrombocytopenia.

In OlympiA trial, one year of adjuvant olaparib extended disease-free survival (DFS) in patients with high-risk, early-stage, HER2-negative breast cancer with gBRCA1/2mt. At 24 months of follow-up,

85.9% of patients treated with adjuvant olaparib were alive and free of recurrent invasive cancer and new second cancer (ie, invasive diseasefree survival) compared with 77.1% of placebo-treated patients. The estimated 3-year distant DFS rate was 87.5% for olaparib vs 80.4% with placebo. Adjuvant olaparib reduced the risk of invasive diseasefree recurrence by 42% compared with placebo. 43% reduction in distant DFS (ie, risk of metastatic breast cancer, new cancer, or death due to any cause [$P < .0001$]). The difference between arms was 7.1% at 3 years. The side effects were consistent with the safety profile of olaparib, and no new safety signals emerged during the trial. Grade 3 AEs were infrequent. Updated results of the planned second interim analysis, olaparib significantly improved OS. One year of adjuvant olaparib relative to placebo led to a statistically significant and clinically meaningful improvement in the HR for OS of 0.68 (98.5% CI 0.47-0.97; $p = 0.009$). This corresponds to a 32% reduction in risk for death with olaparib relative to placebo. At 4 years, the OS rate was 89.8% for patients treated with olaparib vs 86.4% for those on placebo. Based on the main results of OlympiA, various international guidelines, such as the ASCO/ESMO guidance for the management of hereditary breast cancer and the 2021 St Gallen International Consensus Guidelines for treatment of early breast cancer, have updated their recommendations for the adjuvant treatment of patients with hereditary, high-risk early breast cancer. Olaparib was approved by the FDA for the adjuvant treatment of patients with gBRCAmt HER2-negative high-risk early breast cancer who have already been treated with chemotherapy either before or after surgery. This approval will change the way patients with this type of cancer will be treated in the future. The OlympiA trial enrolled a total of 1,836 patients from over 600 hospitals and cancer centers in 23 countries worldwide, a global collaborative phase III trial coordinated by the Breast International Group (BIG), in partnership with NRG Oncology, the US NCI, Frontier Science & Technology Research Foundation (FSTRF), AstraZeneca and MSD.

OVERCOMING RESISTANCE AND FUTURE DIRECTIONS

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The past decade has witnessed the development and approval of numerous targeted cancer therapeutics. One such class of drugs, poly (ADP-ribose) polymerase (PARP) inhibitors (PARPis), has become a mainstay of therapy in BRCA-mutant breast cancer and other malignancies, including ovarian and BRCA-mutant prostate, and pancreatic cancers. However, a growing number of patients develop resistance to PARPis, highlighting the need to further understand the mechanisms of PARPi resistance and develop effective treatment strategies. Thus far, known key mechanisms of resistance against PARPis include restoration of the HR repair pathway, through BRCA-dependent means (e.g., reversion mutations and epigenetic upregulation of BRCA1), as well as BRCA-independent means (e.g., loss of negative regulators of HR like 53BP1 or REV7, or reversion mutations of non-BRCA HR pathway genes like RAD51C and PALB2). PARPi resistance may also arise independently of HR, including via replication fork protection, upregulation of survival pathways, drug efflux, and other mechanisms. Of note, these resistance mechanisms are not mutually exclusive, especially in the clinical setting. Individual patients may exhibit heterogeneous mechanisms of PARPi resistance simultaneously, suggesting that multiple molecular pathways act in parallel to confer clinical drug resistance.

To date, the results from early clinical trials for PARPi-resistant cancers have been somewhat limited and include heterogenous patient populations. Also worth noting is the fact that unlike platinum sensitivity or resistance, which is a relatively reliable clinical predictor of response to PARPis in ovarian cancer, there is no universal consensus as to what constitutes PARPi clinical resistance. Therefore, a biologically relevant consensus on what constitutes PARPi resistance in the clinic, as well as a unifying definition of replication stress, would aid greatly in standardizing results from clinical trials and facilitate more direct comparisons across different settings and development of biomarkers to identify subgroups of PARPi-resistant patients who may have benefit from such treatments. In addition, most clinical trials now incorporate pre- and on-treatment tissue biopsies and cell-free DNA to perform biomarker analyses, which will ultimately aid in furthering our knowledge of subsets of patients. As PARPi resistance continues to increase, tailoring clinical trials to PARPi-resistant patients and including PARPi-resistant subgroups within larger trials will be critically important in understanding the therapeutic combinations that best serve this unique but growing population.

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Panel Discussion

"Go Beyond Cure of Breast Cancer"

AI MEETS SURGEON, WHERE ARE WE AND HOW TO USE?

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Many studies have been conducted on the diagnosis and treatment of breast cancer, and based on this, if a more accurate diagnosis is made compared to the past, various treatment methods have been developed and applied to patients. Due to the nature of breast cancer, the stage, subtype, and menopause affect the decision of treatment method. Among the various treatment methods, a personalized precision treatment method with fewer side effects and the best results is being pursued.

Artificial intelligence in breast cancer surgery:
There are two main types of breast cancer surgery: total/partial mastectomy. The most important point in partial mastectomy is to completely remove the tumor while preserving the normal tissue as much as possible for good cosmetic results.

In order to lower breast cancer recurrence and obtain a good prognosis, it is important to obtain a tumor-free margin, and try to accurately target the tumor using multiple medical images.

There are technical limitations in tumor targeting: 1. The extent of the tumor on MRI cannot be quantitatively marked directly on the breast, and 2. It is difficult to track the area of the initial tumor when receiving neoadjuvant chemotherapy. Although these problems can be solved to some extent through 3D printing surgical guides or augmented reality tumor targeting methods, it is still difficult to segment a tumor and track tumor changes in MRI, and it consumes a lot of manpower and time. In addition, the results may be different depending on the difference in competency between individuals. The development and advancement of automatic tumor segmentation and automatic tumor tracking system using AI is expected to solve these problems.

APPLICATION OF AI-BASED BREAST IMAGING AND DIAGNOSIS

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Computer-aided diagnosis (CAD) has been a popular field of research and development in the past few decades. In CAD, machine learning methods and multidisciplinary knowledge and techniques are used to analyze patient information and predict outcome, which may provide decision support to physicians and improve the accuracy and efficiency of various patient care processes. The advances of the deep learning (DL) technology, or artificial intelligence (AI), in machine learning in recent years have brought major progresses to various applications such as speech and text recognition and computer vision. The potential of revolutionizing CAD via AI-based approach has spurred a new wave of efforts in research and development. Many studies have shown AI-based CAD performance superior to those of conventional techniques, and some reported AI-based models reaching comparable or even higher level of performance than physicians. A major area of AI-based CAD applications is breast imaging and cancer diagnosis. Numerous AI-based models have been proposed for lesion detection and characterization in various breast imaging modalities, including mammography, breast tomosynthesis, ultrasound, or MRI. AI-based models have been studied to be used as a concurrent reader to increase reading efficiency, or as a first reader for triaging or ruling-out cases and reducing radiologists' workload for breast cancer screening. AI-based CAD tools have also been proposed for cancer risk prediction, differentiation between malignant and benign lesions or between indolent and aggressive lesions, classification of cancer subtypes, prognosis prediction, and recurrence prediction. Despite the enthusiasm and high expectations, the development and translation of AI-based tools to clinical practice face many challenges, including the availability of large representative and diverse training data, validation of the generalizability to the populations, explainability of AI output, robust presentation of information to physicians in clinical workflow, training of user for proper use of the information, quality assurance of the model performance and reproducibility over time in clinical settings, and potential medicolegal issues if AI makes decision (e.g., ruling-out cases without physician inputs) rather than provides second opinion as decision support to physicians. In this talk, some of these important issues relevant to the development and adoption of AI-based tools in breast imaging and diagnosis will be discussed.

THE USE OF AI FOR PERSONALIZED RADIATION THERAPY

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The use of artificial intelligence (AI) is increasing in the field of radiation oncology for breast cancer. Personalized radiation therapy (RT) can be deployed by the assist of AI. Abstracts of literatures published for the last two years were collected by using searching terms as 'breast cancer radiation artificial intelligence'. The Word of Cloud analysis revealed that abstracts can be summarized to several words: segmentation, detection, classification, and imaging. Indeed, the use of AI in the radiation oncology can be classified into decision support, segmentation, treatment planning, and image guidance, which are intertwined with clinical oncology, radiation physics, and radiation biology.

When a term "personalized" indicates a patient, AI can be applied to predict RT-related cardiac side-effect through delineating cardiac substructures precisely. Also, AI can be used to detect and quantify cosmetic anomaly after RT in patients having reconstructed breast. In a mean time, when the term "personalized" is for a radiation oncologist, AI can be used to develop the model based on local contouring practices rather than based on atlas by other expertise. Even though training cases within an institution were small, the customized and personalized segmentation model can be developed easily by the assist of AI. In addition, the finalized model can be directly applied to datasets from other instructions without any preprocessing work in terms of image acquisition. By using the AI model, the clinical target volume or dose parameter for axillary RT can be extracted with a minimal variation. Lastly, when the term "personalized" contains both patient and radiation oncologist, AI is applicable for predicting spatial dose distribution in radiation physics or for natural language processing in a huge number of literatures regarding radiosensitivity in radiation biology.

Therefore, the use of AI in breast radiation oncology spans the field of clinical oncology, radiation physics, and radiation biology, along with all relevant RT-treated patients and radiation oncologists for personalized treatment.

LEVERAGING LARGE DATA BASES (SEER/NCDB) TO CREATE SCIENTIFIC RIGOR FOR CLINICAL TRIALS IN BREAST CANCER

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Utilizing large population data sets must be interpreted in the context of how the data is collected and what data is collected.

The National Cancer Database (NCDB) is a cancer registry of the American College of Surgeons and American Cancer Society that provides data from over 1500 CoC accredited Hospitals in the United States. The data contains demographics, treatment and oncologic outcomes.
The National Cancer Institute's Surveillance, Epidemiology and End Results (SEER) is a population data base that provides information and statistics to reduce the cancer burden in the United States. The SEER database has 18 different registries and encompasses nearly 30% of the US Population. SEER gives demographics, treatment and survival information.

These datasets can be used to look at questions in oncology that can help tailor future prospective clinical trials for definitive outcomes. We will discuss studies utilizing NCDB and SEER.

BREAST CANCER RESEARCH USING NATIONAL HEALTH INSURANCE DATABASE IN KOREA

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The National Health Insurance Service (NHIS) in Korea provides health insurance to almost all individuals in Korea, and the claim data and the reimbursement database has been established and managed by government. Therefore, the national cohort can be created using such information including follow up data. There are two institutions that can provide national healthcare information for academic purpose; the NHIS database and the Health Insurance Review and Assessment Service (HIRA) database.

Although the forms of database provided from each institutions is not similar, they manage the same health insurance system and population so that researchers can use either database for their own study purpose, whether they needs all-cause death information or only diagnosis and prescription information. The basic information such as date of birth, sex, and residence is shown in the electronic bills, and the economic status can be indirectly assumed from insurance eligibility. Diagnosis of disease can be shown as the International Classification of Disease 10th version (IDC-10) currently, along with drug prescription, imaging study, management, and the surgical treatment.

There are some limitations of research using Korean national health insurance database. The ICD-10 records dose not completely matched to each individuals' health status because there are missing data or coding error. Meticulous setup of operational definition for disease entity is important because the database is made for claim purpose and does not contain medical records, results from laboratory test, or imaging study results. The past history of disease or drug prescription history should be monitored for a sufficient time span if a new diagnosis of disease at some time point is required for creating study population or a primary endpoint.

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

CLINICOPATHOLOGICAL CHARACTERISTICS OF MALE BREAST CANCER IN JAPAN FROM THE NATIONAL CLINICAL DATABASE

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Background: Male breast cancer is a rare cancer. According to the Japanese Breast Cancer Society's Breast Cancer Registry, there were 613 cases of male breast cancer in 2016. It is only 0.6% of all cases of breast cancer incidence. Because of its rarity, there have been no comprehensive studies on characteristics of male breast cancer in Japan. Therefore, there has been few specific treatments developed for male breast cancer. In this study, we investigated the prevalence and clinicopathological characteristics of male breast cancer in Japan, using the most reliable domestic data, the National Clinical Database (NCD). NCD is a database that collects medical information on diseases, treatments, and surgeries in Japan. In collaboration and cooperation with academic societies and academic organizations, NCD maintain and manage the collected data. The data are used in domestic research to evaluate the standards of medical care and support clinical research. This study conducted with a collaboration with NCD and the registration committee of Japan Breast Cancer Society.

Methods: We investigated patients diagnosed with breast cancer in the Japanese National Clinical Database (NCD) between January 2012 and December 2018. We obtained age, sex, body mass index, performance status (PS), surgical procedure, family history, comorbidities, pathological factors, and perioperative systemic therapy from the NCD.

Result: A total of 594,316 cases of breast cancer, including 3,780 MBC (0.6%) and 590,536 female breast cancer (FBC) (99.4%), were evaluated. The median age at MBC and FBC diagnosis was 71 (4586, 5%-95%) and 60 years (3983) ($p < 0.001$), respectively. MBC patients had a higher clinical stage than FBC patients: 7.4% vs. 13.3% stage 0, 37.2% vs. 44.3% stage I, 25.6% vs. 23.9% stage IIA, 8.8% vs. 8.4% stage IIB, 1.9% vs. 2.4% stage IIIA, 10.1% vs. 3.3% stage IIIB, and 1.1% vs. 1.3% stage IIIC, respectively ($p < 0.001$). Breast-conserving surgery was more frequent in FBC (14.6% vs. 46.7%, $p = 0.02$). Axillary lymph node dissection was more frequent in MBC patients (32.9% vs. 25.2%, $p < 0.001$). Estrogen

receptor (ER)-positive disease was observed in 95.6% of MBC and 85.3% of FBC patients ($p < 0.001$). The HER2-positive disease rates were 9.5% and 15.7%, respectively ($p < 0.001$). Comorbidities were more frequent in MBC (57.3% vs. 32.8%) ($p < 0.001$). Chemotherapy was less common in MBC, while endocrine therapy use was similar in ER-positive FBC and MBC. Perioperative radiation therapy was performed in 14.3% and 44.3% of patients.

Conclusion: Japanese MBC had an older age of onset, were more likely to be hormone receptor-positive disease, and received less perioperative chemotherapy than FBC. This is the first comprehensive analysis using real-word data from a nationwide registry database in Japan of clinicopathological features and treatment trends in Japanese MBC patients.

HOW I PERFORM FERTILITY PRESERVATION IN BREAST CANCER PATIENTS

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Cancer diagnosis in young women is considered a public health problem requiring personalized approaches to manage the specific age-associated issues including the possible toxicities of anticancer therapies that may negatively impact on their quality of life. Thanks to improved survival rates, survivorship is now considered a crucial component in breast cancer care.

The use of anticancer treatments in premenopausal women can be associated with significant negative side effects such as the risk of developing premature ovarian insufficiency (POI) and subsequent infertility. Concerns about fertility preservation and future chance of achieving a pregnancy are prevalent issues affecting young women with newly diagnosed breast cancer. As recommended by major international guidelines, oncofertility counseling should be offered as early as possible to all young patients at risk of infertility and pregnancy following adequate treatment for breast cancer should not be discouraged. Hence, oncofertility counseling should be considered now as routine clinical practice before the patients start systemic anticancer treatments.

In young women with breast cancer, the main available strategies to preserve fertility include embryo/oocyte cryopreservation, cryopreservation of ovarian tissue and temporary ovarian suppression with gonadotropin-releasing hormone agonists (GnRHa) during chemotherapy. Embryo/oocyte cryopreservation is a standard strategy for fertility preservations in these patients and the first to be proposed. Ovarian tissue cryopreservation can be proposed to patients scheduled for therapies with a high risk of POI who cannot delay anticancer treatments or with contraindications to controlled ovarian stimulation. In breast cancer patients, use of temporary ovarian suppression with GnRHa during chemotherapy should now be proposed as a valid strategy to preserve ovarian function but it is not an alternative to cryopreservation strategies for fertility preservation.

Although many new safety and efficacy data have become available on the strategies for fertility preservation and several studies have shown the feasibility and safety of pregnancy after breast cancer, numerous challenges remain for these young patients considering to preserve fertility and to conceive following after the end of anticancer treatments. Hence, further research efforts in the field are warranted to acquire more robust data and try to address and solve the still unmet controversies in this field.

ONCO-FERTILITY MODULES AND CONSELING IN YOUNG WOMEN WITH BREAST CANCER: ASIAN EXPERIENCE

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Breast cancer is the most common cancer in women of reproductive age, approximately 6% of newly diagnosed breast cancer patients are under 40 years of age. Although the incidence of breast cancer in older than 40 years of age has been decreased after 2000, incidence of young breast cancer has remained stable for the past 30 years. Young patients with breast cancer have more biologically aggressive tumor, more commonly diagnosed at an advanced stage than older patients, and often have a worse prognosis. Young patients with breast cancer tend to receive intensive treatment like cytotoxic chemotherapy or long-term endocrine treatment for up to 10 years, resulting in temporary or permanent menopause. Accordingly, breast cancer survivors had the lowest fertility rate after cancer, and showed a 70% lower fertility rate than general cancer survivor. Several international guidelines recommended young women must be advised to have fertility counselling before starting breast cancer treatment. All patients who are interested in fertility preservation (FP) should immediately referred to the appropriate fertility specialist. However, there are unmet needs about fertility-related information for young patients with breast cancer. Young cancer patients also face serious decisional conflicts about FP at diagnosing cancer.

In Korea, the number of newly diagnosed patients with breast cancer increased from 6,234 per year in 2000 to 28,049 in 2018, more than tripled. A characteristic feature of Korean breast cancer is that women between the ages of 40 and 49 have the highest incidence of breast cancer, which is different from breast cancer in Western countries, where the incidence of breast cancer increases with age. Therefore, the proportion of premenopausal women in Korea is higher than in the Western countries. However, there are barriers in education and discussion for FP due to the time constraint of clinic and the lack of a multidisciplinary system, making it difficult to make patient-centered shared decision-making. Although FP consultations are being conducted at each hospital unit, there is no standardized protocol or referral system for FP in Korea. In this situation, the development of a shared decision-making program and standardized system for FP will be an important challenge. Therefore, we have developed the multidisciplinary shared decision making of FP in young women with breast cancer (MYBC) study and will evaluate the effect of shared decision-making program.

If the multidisciplinary shared decision-making program is effective, it can be implemented as part of the routine care to help decision about FP for patients with breast cancer who are of reproductive age.

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SHARED DECISION MAKING FOR FERTILITY PRESERVATION

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In the past, oncologists have needed to focus solely on cancer patients' survival and potential damage to life-dependent organs, such as cognitive impairment, and pulmonary and cardiac damage. For treating a newly diagnosed patient, oncologist major focus is to design the best treatment plan including establish a diagnosis, making the optimal treatment plan, discuss costs and refer to a support groups. But as cancer treatment and rates of cancer survivorship have improved in recent years, considering quality of life after cancer has become increasingly important. For premenopausal breast cancer esp. young breast cancer, The two things every oncologist needs to know about fertility, chemotherapy compromises future fertility. Fertility preservation techniques can help to mitigate this damage. Dramatic improvements in preserving fertility, We can freeze Embryos, Eggs and Ovarian tissue. Many young cancer survivors feel they received inadequate information on their fertility preservation options. Infertility is a source of long-term distress in survivors especially if this could have been prevented. Fertility preservation gives patients hope for a high quality life after cancer. Their future ability to have children will significantly improve their quality of life. Nowadays doctors and patients need to take proactive steps so called shared decision making (SDM) to preserve fertility before initiating cytotoxic therapy. Decisions should be made as early as possible. SDM features of Taipei-Veterans General Hospital Comprehensive Breast Health Center use 'user-friendly', developed web pages, APP and other models for patients to apply.

SDM should be patient-centered with knowledge, communication, and respect content. SDM in T-VGH emphasize 4 steps including understand: Compare the advantages and disadvantages of each appropriate treatment, thinking: The proportion of patient preferences, assessment: Confirm the patient's understanding and decision: Make medical decisions. After using the SDM aid, the number and extent of anxiety are significantly reduced. Use the SDM helper Substantially helpful to the patient.

In Taiwan, SDM is currently a key project in government cancer assessment. To promote the importance of fertility preservation, the Taiwan Breast Cancer Society has co-sponsored a consensus declaration on fertility preservation with a number of relevant societies, the National Health Agency and the Hope Foundation.

Doctor, why didn't you tell me to freeze my eggs? This is a question your survivors will ask you when their cancer is treated and they come for a 5-year follow up. Now we can not waste their golden opportunity anymore.

IS IT SAFE TO OMIT RADIOTHERAPY AFTER BREAST CONSERVING SURGERY IN ELDERLY PATIENTS?

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Radiation therapy is a standard therapeutic option in the post-operative setting for early breast cancer (EBC) patients after breast conserving surgery (BCS), providing a substantial benefit in reducing the risk of local relapse (IBTR) with a consequent survival gain. Nevertheless, the reduction in the burden related to treatment is becoming crucial in modern oncology for both local and systemic therapies and investigational efforts are being put forward by radiations oncologists to identify a subset of women at very low risk to be potentially omitted from post-operative irradiation after breast conservation. Clinical factors, classical pathological parameters and new predictive scores derived from gene expression and next generation sequencing techniques are being integrated in the quest toward a reliable low-risk profile for breast cancer patients. In main trials the option of whole breast irradiation (WBI) omission was addressed to a population selected by patient characteristics such as age (65 or 70 as in the PRIME II and CALGB 9343 trials), and tumor features such as size (T1 or favorable T2 tumors, except for the Toronto and British Columbia trial), hormonal receptor status (positive in most of the studies) and other histologic characteristics such as tumor grade, lymph vascular invasion and extensive intraductal component. Subset analysis, such as the one performed in the PRIME II trial, were not able to identify predictive factors for IBTR in this selected setting of patients. The addition of either WBI or tamoxifen after BCS lowers the local recurrence rate, with comparable effects as seen in the BASO II and German Breast Cancer Study Group trials. Combining WBI and Tamoxifen has addictive effect in preventing IBTR. No influence on survival was detected in any trial by the addition of WBI.

The challenge to identify the most suitable subset of EBC patient that can have WBI omitted after BCS is still ongoing. Probably, a comprehensive integration of features related to patient (age, comorbid conditions, life expectancy) and tumor, including either classical factors (size, hormonal receptor status, grade of differentiation and intrinsic subtyping) and genetic and molecular features, may enhance our ability to properly identify patients at low-risk of recurrence. New generation trials will, supposedly, help in answering this question. Nevertheless, the ideal treatment package for this potential low-risk patient subgroup still deserves investigation. Omission of WBI with no adjuvant endocrine treatment after BCS may consistently increase IBTR rate even in patients with this recurrence profile. Avoiding radiation in low-risk patients undergoing adjuvant endocrine therapy needs careful consideration as well.

For a patient population at low-risk of relapse, a de-escalation of the treatment package may include the

omission of endocrine therapy, instead of WBI, after BCS or even the omission of both the treatment approaches. Robust data on these options are lacking and prospective clinical studies are strongly demanded. The clinical question whether this subset of patients really needs adjuvant hormonal therapy is still pending. In this sense, a few trials are being initiated to fulfill this gap.

To our knowledge, the only trial combining a unique primary endpoint such as quality of life with a cost-effective biomarker assessment (luminal-like tumor based on IHC) is the phase 3 EUROPA trial (NCT04134598). This study will explore the role of exclusive breast irradiation vs exclusive endocrine-therapy after BCS for EBC women aged more than 70 years with luminal-like disease to determine which of these options may be better in terms of quality of life.

Overall, the side-effects of adjuvant systemic therapy may outweigh those of WBI, especially considering that hypofractionation, partial breast irradiation and refined delivery techniques have consistently decreased the radiation-burden in breast cancer patients. Composite endpoints evaluating not only IBTR rate and OS but also the toxicity profile of treatments, patient quality of life, psychosocial issues, and cost-effectiveness would be indicated to better tailor the clinical decision-making process in low-risk EBC patients.

SURVIVAL BENEFIT OF ADJUVANT CHEMOTHERAPY IN ELDERLY PATIENTS WITH MULTIPLE COMORBIDITIES

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As society ages, the number of older patients with breast cancer (BC) has been increasing all over the world. Limited data are available to provide the evidence for standard treatments of older BC because older patients are likely excluded from clinical trials due to their heterogeneous health backgrounds. Chemotherapy has survival benefits on breast cancer patients but must be considered about its adverse events. The clinical benefit of chemotherapy for older BC patients remains controversial due to their shorter life expectancy, intolerance to therapy, and concern for severe adverse events. Indeed, the rate of other causes of death in older BC patients was about a half in the Japanese Breast Cancer Registry, the magnificence of clinical benefit of chemotherapy on survival could be smaller than that of younger counterparts. Several studies demonstrated that comorbidities such as dementia, liver disease, chronic renal failure, congestive heart failure et al could be prognostic factors in older BC patients. National Comprehensive Cancer Network guidelines state that treatment should be individualized in patients over 70 years group, with consideration given to comorbid conditions. The Japanese Breast Cancer Society (JBCS) launched annual scientific research in 2018 to investigate the clinicopathological characteristics, treatments, and related prognosis of older Japanese female BC patients and discuss the clinical implications and future research with multidisciplinary team approaches for older patients.

To compensate for the lack of evidence of chemotherapy for older BC patients, several studies including us evaluated the efficacy of chemotherapy for them by analyzing the national clinical database. We reviewed 238,908 cases, diagnosed between 2004 and 2011, from the Japanese Breast Cancer Registry (JBCR). Among them, 56,093 patients with stage aged ≥55 were included in the analysis. The clinicopathological characteristics, treatments, and prognosis of patients aged ≥75 years (older: n=12,727) were compared to those of younger patients (65-74 years: n=17,860; 55-64 years: n=25,506) according to BC subtype. In the older group, 9.2% with a luminal (hormone receptor [HR]+/human epidermal growth factor receptor 2 [HER2]-), 32.9% with a triple-negative (TN, HR-/HER2-), and 27.4% with a HER2-positive (any-HR/HER2+) receptor were administered chemotherapy. In those with luminal cancer, the 5-year breast cancer-specific survival (BCSS) was approximately 95% in all age groups. Meanwhile, among those with TN and HER2- positive BC, the older group had a poorer BCSS. The 5-year overall survival (OS) was also poorer in the older group across all subtypes. Among older patients matched using clinicopathological factors, chemotherapy use was associated with improved OS

in the luminal and HER2-positive subtypes (PMID: 34293663). Although our data did not contain comorbidity status, JBCR has registered comorbidities since 2015. Future analysis will provide further information. Recently, Tamirisa et al reported node-positive, ER-positive older patients with BC and multiple comorbidities, receipt of chemotherapy was associated with improved overall survival by analyzing US National Cancer Database adjusted comorbidity status (PMID: 32672820). These data imply a survival benefit of chemotherapy for older BC patients.

On the other hand, we must consider that the individual goals and beliefs also differ among older patients in determining the treatment. Prolonging patient survival is not the only goal in treating older patients and sustaining a good quality of life is another important aspect of the treatment goal. The RESPECT trial (NCT01104935) prospectively evaluated the effect of trastuzumab monotherapy on the survival, adverse events, and quality of life (QOL) in older patients. Patients aged 70-80 years with stage I-IIIA HER2+ BC were randomized into the adjuvant trastuzumab-alone or trastuzumab with chemotherapy groups. Although the non-inferiority could not be confirmed, the low toxicity and more favorable health-related QOL outcomes favored trastuzumab monotherapy as an adjuvant treatment option for older patients.

The International Society of Geriatric Oncology and European Society of Breast Cancer Specialists recommended the comprehensive geriatric assessment (GA) to identify specific patient factors associated with a higher risk of treatment-related complications. There are several clinical trials performed to evaluate the efficacy of GA-driven intervention, it remains controversial. A new Japanese clinical trial on comprehensive GA to predict adverse events and prognosis is ongoing (UMIN000037454).

To determine treatment patterns of older patients with BC, especially administrating chemotherapy, it is important to share the process of decision-making with patients and their families, a multidisciplinary approach is warranted.

PREDICTION OF SEVERE TOXICITY IN OLDER ADULTS RECEIVING CHEMOTHERAPY FOR EARLY-STAGE BREAST CANCER

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Incidence of breast cancer continue to increase with age worldwide. Those with age of 70 years or older at diagnosis account for about 30% of all patients with breast cancer. Older adults have been under presented in clinical trials of perioperative chemotherapy for early-stage breast cancer because of several limitations such as comorbidities and functional decline of major organs. Although cancer specific survival benefits from chemotherapy in older patients are not as distinct as in younger patients, adjuvant chemotherapy can reduce the recurrence among subsets of older adults with high risk factors in early breast cancer based on limited data from registry based or pooled secondary analysis. Application of adjuvant or neoadjuvant chemotherapy is challenging for older adults due to the potential of a high risk of severe toxicities following anti-cancer chemotherapy. Chemotherapy toxicity should be predicted before administration of chemotherapy for older adults with cancer weighing a potential harm and benefit of chemotherapy. Conventional performance status is not objectively considered as a valid predictor of chemotherapy toxicity for older adults with cancer. Instead, incorporation of geriatric assessment has been issued to identify older adults with cancer at risk for chemotherapy toxicity, unlike measure of performance status commonly used in oncology practice. Several validated models predicting for grade 3-5 toxicity in older adults receiving systemic chemotherapy for solid cancers have been suggested. The Cancer and Aging Research Group-Breast Cancer (CARG-BC) score was developed to predict grade 3-5 chemotherapy toxicity in older adults with early-stage breast cancer. Three risk groups (low, intermediate, or high) were classified according to the risk score consistent with the probability of toxicity. The CARG-BC score was associated with hospitalizations, dose reductions, dose delays, early treatment discontinuation, and reduced relative dose intensity. Unlike palliative chemotherapy for metastatic breast cancer, in early-stage breast cancer, it is also necessary to predict the long-term or late adverse events from treatment. Because many noncytotoxic drugs of immunotherapy and targeted agents for early-stage breast cancer have been introduced recently in the clinical field, development of prediction models for adverse events would help physicians estimate and identify older adults who could suffer from toxicities of these drugs.

THE ROLE OF WEIGHT LOSS AND METFORMIN IN THE ADJUVANT TREATMENT OF BREAST CANCER

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Obesity is an adverse prognostic factor in early-stage breast cancer (BC), associated with a 20-35% higher risk of recurrence and death compared to normal weight. This association is present in all BC subtypes regardless of ER, PgR and HER2. The underlying physiology is complex, involving adipose tissue inflammation and systemic insulin resistance characterized by hyperinsulinemia, hyperglycemia and inflammation.

Lifestyle interventions involving diet, exercise and a behavioural component delivered in person or by phone lead to modest weight loss in the general population and in BC patients (5-10% on average) which is associated with a 25-40% reduction in metabolic markers. Reduced caloric intake is important for initial weight loss while physical activity enhances maintenance of weight loss. Bariatric surgery leads to even greater weight loss its effects on BC outcomes has not been studied. Evidence from the underpowered LISA randomized trial suggest weight loss may be associated with improved BC outcomes (HR 0.71, 95% CI 0.41-1.24, $P = 0.23$). The fully powered Alliance BWEL randomized trial has completed accrual and will provide definitive evidence regarding the effect of weight loss on BC outcomes, as well as insight into biologic mechanisms. Weight loss may be associated with other health benefits, including enhanced quality of life and reduced morbidity.

Metformin has been investigated as a potential adjuvant treatment in BC because it improves obesity-associated insulin resistance and may have additional direct anti-tumor effects. In some neoadjuvant window of opportunity studies it has reduced Ki67 and increased apoptosis. We recently reported results of CCTG MA.32, a Phase III randomized trial of metformin vs placebo in early BC. Significant beneficial effects of metformin on insulin, glucose, HOMA, leptin and hsCRP were observed. However, metformin did not improve IDFS or OS in ER/PgR positive (HR 1.01, 95% CI 0.84-1.21, $P = 0.93$ and HR 0.99, 95% CI 0.80-1.23, $P = 0.94$ respectively) or ER/PgR negative BC (HR 1.01, 95% CI 0.79-1.30, $P = 0.92$ and HR 0.89, 95% CI 0.64-1.23, $P = 0.46$ respectively). In exploratory analyses in HER2 + BC metformin was associated with improved IDFS (HR 0.64, 95% CI 0.43-0.95, $P = 0.03$ and OS (HR 0.53, 95% CI 0.30-0.98, $P = 0.04$); there was a significant interaction with the snp rs112112617 (a snp associated with enhanced glucose control by metformin in diabetes), those with any C allele having improved IDFS and OS with metformin and those with AA genotype showing no benefit (interaction $p = 0.05$

and 0.02 respectively).

At present, evidence to support the use of weight loss to improve BC outcomes in early BC is lacking; definitive trials are ongoing. Metformin is not beneficial in ER/PgR positive or negative BC; further research is needed to confirm potential beneficial effects in HER2 + BC.

LIFE STYLE MODIFICATION OF BREAST CANCER SURVIVORS

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As the survival rates of cancer patients are rising as a result of the increase of early diagnosis and advances in treatment modalities, the number of cancer survivors is growing. Compared to other types of cancers, breast cancer have better prognosis, and the 5-year and 10-year relative survival rates of Korean breast cancer patients have been reported to be 93.6% and 88.6%, respectively. There are about 259,000 breast cancer survivors in Korea, ranked 4th (12.1%) among total cancer survivors.

As breast cancer becomes a chronic condition rather than a life-threatening illness, physicians should know how to improve the quality of life and maintain the optimal lifestyle of breast cancer survivors. Many breast cancer survivors seek information from a variety of sources about behaviors that may reduce their risk of recurrence. Dramatic effects using lifestyle modifications have been demonstrated in breast cancer survivors. Several large studies have conclusively shown that health eating, active living and emotional resilience can significantly improve total health.

It is challenging to study lifestyle factors independently, because survivors who are more physically active often are leaner, eat a healthier diet and are typically less likely to drink excessive amounts of alcohol or smoke. Another limitation is the potential impact of lifestyle factors before diagnosis. Nevertheless, there is growing evidence that lifestyle modifications play an important role in determining rates of recurrence and prognosis among breast cancer survivors. Studies have shown that poor diet, obesity, and inactivity are linked to a higher risk of recurrence and mortality from breast cancer.

'Lifestyle medicine' is a powerful tool in the fight against breast cancer. Lifestyle medicine is a total-health approach to wellness that includes treating the mind, body, and spirit of breast cancer survivors. A paradigm shift to lifestyle medicine in breast cancer survivors must be implemented immediately.

PHYSICAL ACTIVITY INTERVENTION IN WOMEN WITH BREAST CANCER

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Physical activity has been shown to improve prognosis of breast cancer survivors. After Holmes et al. (2005) reported that breast cancer survivors, who participated in about 3 hours of walking (9 MET hour per week) exercise or more, are about 50% less likely to die from breast cancer, numerous other prospective cohort studies reported similar results. The most recent meta-analysis study which included 23,041 breast cancer survivors showed that all-cause mortality, breast cancer-specific mortality, and risk of recurrence reduced by 42%, 40% and 21%, respectively, were reduced among breast cancer survivors who were physically active (leisure) compared with those who were inactive. One of the reasons for anti-cancer effects of exercise for breast cancer include reduction in circulating insulin levels, inflammatory markers and immune function. We have also previously reported our meta-analysis data which reported that exercise significantly reduce circulating insulin levels in breast cancer survivors and exercise-induced reduction in circulating insulin levels were more evident among those with concurrent body weight reduction after exercise.

Contrary to ample evidence on the benefit of exercise for breast cancer prognosis, when breast cancer patients should start exercise after surgery is not fully studied. Furthermore, amount of tissue and muscle damage would vary after different types of breast cancer surgery (breast conserving surgery vs. total mastectomy with our without axillary lymph node dissection), yet, most studies do not specify what type of exercises or when these exercise should be implemented (after surgery). We recently followed 70 breast cancer survivors before surgery, 1 day, 7 day, 14 day, 1 month, 3 month and 6 month after surgery to identify their range of motion (ROM) and muscle strength in their shoulder. We observed that their shoulder ROM would recover up to 85% and strength up to 60% at 6 months after surgery. Interestingly, shoulder strength was significantly reduced in the arm where no surgery was performed as well, probably due to lack of usage. Then, we have developed a tailored exercise program according to their ROM, strength and pain levels, and applied exercise intervention starting on post-operative day 1. Thereafter, we educated breast cancer survivors exercise on the day of hospital discharge to help them continued exercise at home. Then, we educated breast cancer survivors four more times (7 days, 14 days, 1 month, 3 months after surgery) on the date of their follow up meeting with their surgeons. Interestingly, both shoulder ROM and strength of those who participated in this tailored exercise program recovered to the pre-surgery levels at 1 month post-surgery visit. At 6 month

follow-up, their shoulder strength levels were more than 150% of their pre-surgery levels. These improvements were seen among all breast cancer survivors regardless of type of surgery, neo-adjuvant and adjuvant chemo-radiation therapies. This study clearly demonstrated that immediate application of exercise during early post-surgery period prevent dysfunction and further even improve their shoulder function compared to their pre-surgery levels. Early implementation of exercise among breast cancer survivors would not only improve their prognosis, but also prevent dysfunctions in their shoulder as well as improve their quality of life.

TIMING OF BREAST SURGERY IN METASTATIC BREAST CANCER: IS IT REALLY NECESSARY TO PERFORM PALLIATIVE MASTECTOMY?

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There is a lack of consensus over the value of surgery as part of the treatment of metastatic breast cancer. The role of removal of the primary tumor in patients with metastatic disease has traditionally been relegated to palliation alone and not expected to have any impact on survival of the patient. However, evolving concepts of cancer biology and emerging evidence of a potential survival benefit from local surgery have raised the question of an expanded role for surgery in select patients with metastatic breast cancer. There are situations where it is still a potent option. Coordinated multidisciplinary care remains highly relevant in the setting of metastatic breast cancer, where surgical decisions should be made on an individual basis and may affect survival in select women. Accordingly, some recent studies have shown that surgery might have some role in improving the overall survival of stage IV breast cancer patients, thus opening to debate the role of mastectomy in metastatic breast cancer patients.

CURRENT STATUS OF LOCOREGIONAL THERAPY IN ER+/ HER2- OLIGOMETASTATIC BREAST CANCER

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Breast cancer with distant metastases is regarded as an evident status of systemic spread of the disease and systemic therapies are the main strategy for the treatment, the purpose of which is generally palliation. However, with the recent progress in systemic and local therapies, the prognosis of patients with metastatic breast cancer has been improved and some may expect long-term survival. In particular, the introduction of the concept of "oligometastases" has changed our views of metastatic disease. Oligometastases mean that tumors early in the chain of progression may have matastases limited in number and location, which is in contrast to micrometastases, which, although small in size, are extensive in number. This "oligometastatic state" indicates that some patients with metastases could be treated with curative intent using not only systemic treatment but also local treatment strategies. Indeed, some patients who underwent surgery or radiation therapy for distant metastatic lesions have been reported to show long-term survival. In this presentation, I would like to discuss current understanding of oligometastases and treatment strategies aiming at cure of the disease.

ROLE OF STEREOTACTIC ABLATIVE RADIOTHERAPY IN OLIGOMETASTATIC BREAST CANCER

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Oligometastatic breast cancer, which is typically defined as the presence of 1-5 metastases, represents an intermediate state between locally advanced and widely metastatic disease. Emerging research suggests that oligometastatic disease is characterized by a unique molecular signature that is distinct from widely metastatic disease, and additionally it carries a superior prognosis. Because oligometastatic disease exhibits a more limited capacity for widespread metastatic progression, it may be amenable to eradiation with aggressive ablative therapy to known metastases. Non-randomized data have shown long-term disease-free survival in patients with several different types of epithelial cancer after ablation of oligometastatic disease, including colon, lung, prostate, and breast cancer. Options for ablation include surgical excision, radiofrequency ablation, and hypofractionated image guided radiotherapy (HIGRT / SABR / SBRT).

Recently, the phase II SABR-COMET trial enrolled patient with cancer of multiple histologies and the presence of 1-5 metastases and randomized them to HIGRT vs. standard of care; it identified a notable survival advantage in favor of HIGRT furthering the need for Phase 3 trials. At present, there are multiple ongoing trials exploring the role of ablative therapy, most notably HIGRT, with or without immunotherapy, for the treatment of oligometastatic cancer. Many of these trials also seek to identify those patients more likely to benefit from ablative therapy through translational endpoints. These ongoing trials may offer patients improvement in both progression-free and overall survival.

This presentation will update the most recent data with regards to the (1) the biology of oligometastatic breast cancer, (2) lessons learned thus far, (3) trial design in this space, and (4) anticipated outcomes. We will detail the results of the NRG BR001 clinical trial and what that implies for design and rationale of both ongoing and future trials. In addition, we will preview the results of NRG BR002 that will be presented at ASCO 2022 and place this trial into the broader context. Finally, we will discuss what is reasonable to conclude about the role of SBRT / SABR / HIGRT as we await the definitive phase 3 trials.

MULTIGENE ASSAYS: WHAT EVIDENCE DO WE HAVE?

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Over the last 2 decades, we have witnessed breast cancer being transformed from "a common single disease" to "various rare heterogeneous entities" as demonstrated by various biological features in the molecular profile. From the era of personalized medicine to precision medicine, we had the FDA-approved molecular genomic assays available in the market and clinical practice in 2007 for early breast cancer patients. Through these 15 years, we have experienced the increasing number of available molecular genomic assays with clinical application for early breast cancer with prognostic and predictive value. These include but not limited to the Oncotype DX 21-gene assay, the MammaPrint 70-gene assay, the Prosigna PAM50 gene assay, the Endopredict 12-gene assay and Breast Cancer Index (BCI). In the context of hormone positive HER2 negative early breast cancer, while the main added value for these multi-gene assays being to identify specific selected patients who can be spared from the side effects of chemotherapy, despite the increasing number of various multi-gene assays, they are not interchangeable as these multigene assays provide different information and implication individually for different patient populations, with variability in predictive and prognostic value among these available assays.

This presentation will give an overview of the latest update and evidence available with regard to various multigene assays in hormone positive HER2 negative early breast cancer, their current limitations, potential expanding clinical utilities, and the still unanswered questions.

IS THERE ANY DIFFERENCE IN MULTIGENE ASSAYS DEVELOPED FROM ASIAN AND WESTERN COUNTRIES?

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Breast cancer is a heterogeneous disease with different biological and clinical characteristics among individual tumors. Along with standard clinicopathologic variables including patient age, tumor size, grade, and the number of metastatic lymph nodes, surrogate markers including estrogen receptor (ER), progesterone receptor (PR), and HER2 status to determine molecular subtypes of breast cancer are considered prognostic and predictive biomarkers. In particular, for ER-positive and HER2-negative breast cancers, various multigene expression assays have been developed and validated to have prognostic and/or predictive value. Such assays are widely used clinically per the treatment guidelines for early-stage breast cancer.

However, these genomic tests have been developed in the United States or Europe and may not completely reflect the characteristics of breast cancers in young women. The peak age in Western countries is much older and only about 15-30% of patients are premenopausal, whereas approximately half of the patients in Asia are premenopausal. This is potentially important, considering that the increased relapse and mortality rates are associated with young age among breast cancers with the luminal subtype. A comparative genomic analysis between predominantly premenopausal versus postmenopausal populations revealed higher proportions of luminal B subtypes and ER downregulation in ER-positive subtypes among younger women. On the other hand, several studies have shown favorable overall survival in Asian breast cancer patients compared to other ethnic groups. To better delineate the relapse risk in these populations, it is necessary to develop a multigene assay and validate it in a cohort comprising a higher proportion of young patients.

Several multigene assays have been developed and are being used in Asian countries, including the Curebest 95 in Japan, the RecurIndex in Taiwan, and the GenesWell BCT and OncoFREE in Korea. The characteristics and clinical evidence of these multigene assays will be introduced in comparison to those widely used globally, such as the Oncotype DX, Mammaprint, Endopredict, and PAM50.

PRACTICAL APPLICATION OF MULTIGENE ASSAYS IN REAL CLINICAL SETTING (ASIA VS. WESTERN)

Rebecca Dent

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Early-stage hormone receptor–positive and HER2 negative breast cancer is the most common subtype in patients presenting with early breast cancer. Standard clinical and pathologic tumour factors are routinely used to support decisions about adjuvant therapies and estimate prognosis. Genomic assays are now commercially available to aid in either further prognostication or in refining the potential benefit of adjuvant chemotherapy. These assays however included fewer younger patients and are not ethnically diverse. This presentation will review pivotal studies and global clinical practice guidelines with a special focus on age and ethnic diversity. Health Care Providers still struggle at how to best incorporate these assays into clinical practice to optimize clinic benefit while minimizing toxicities from systemic therapies.

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"Go Beyond Cure of Breast Cancer"

IMPLEMENTING RISK ASSESSMENT IN THE ROUTINE PRACTICE

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- The paradigm is changing from a uniform breast cancer screening to an individualized approach that considers the patient's risk factors.
- Risk factors for breast cancer vary from genetic to non-genetic host and environmental factors.
- Various risk models including various risk factors for breast cancer have been developed, but it is necessary to understand the clinical situation to which each model can be applied.
- This lecture provides a practical approach to the risk assessment process and includes an overview of the risk models along with recommendations for those at high risk for breast cancer.

NOVEL PARADIGMS FOR TAILORED SCREENING INCLUDING CONTRAST MAMMOGRAPHY AND MRI

Christopher E. Comstock

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Breast imagers now have many tools at their disposal to screen for breast cancer including mammography, ultrasound, contrast enhanced spectral mammography (CESM) and abbreviated breast MRI (AB-MR). CESM and AB-MR are vascular based imaging methods that are not limited by breast density. Enhancement and vascularity associated with breast cancers can be detected at a smaller size before they become evident on mammography or ultrasound. CEDM utilizes a dual energy mammographic technique and the injection of iodinated contrast to provide both a 2D mammographic image as well as a recombined image of the contrast distribution. AB-MR is a shortened contrast enhanced breast MRI protocol that allows centers to offer a low-cost breast MRI and expand access to screening MRI. However, in order to optimize outcomes, minimize costs and address patient preferences, a tailored approach to the implementation of these tools is needed. Incremental sensitivity increases over mammography of approximately 40%, 80% and 150% are seen with ultrasound, CEDM and AB-MR respectively in women with dense breasts at average risk. Patients at the highest risk of breast cancer should be imaged using the most sensitive modality. The choice of modality should also be balanced with the patient's concerns of contrast injections, cost and false positives. Education that helps both referring physicians and patients understand the strength and weakness of each modality will assist in the selection of the most appropriate test. This tailored approach, taking into consideration patient risk, breast density and testing preferences, will allow the most optimal implementation of these promising new breast cancer screening methods.

AI IN SCREENING AND DIAGNOSTIC BREAST IMAGING

Jung Hyun Yoon

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Artificial intelligence (AI)-based decision support systems for breast imaging have shown remarkable progress during the past decades. Currently, a variety of AI or deep learning (DL)-based computer assisted detection/diagnosis (CADe/CADx) algorithms are commercially-available with FDA approval for our everyday practice. Studies have shown promising results of AI-CAD in 1) improving lesion detection, 2) differential diagnosis of the detected lesion, and 3) reduction of reading time when integrated in our clinical workflow. During this lecture, we will review the results of current literature on AI-CAD when applied to different clinical settings, i.e., screening and diagnostic, and how this novel technique can be applied to precision medicine from deciding upon intensive screening according to individual breast cancer risk to predicting outcomes of breast cancer treatment.

PARTIAL BREAST IRRADIATION: A BEGINNER'S GUIDE

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Postoperative radiotherapy (RT) following breast conserving surgery has been known to increase the local control rate through multiple studies, as in NSABP B06, Milan, and DBCG. Some of the results in EBCTCG meta-analysis also demonstrated an improvement in survival with postoperative RT. Some changes have have taken place in postoperative radiotherapy in early breast cancer over the recent 10 years. Of those, the two major changes are the adoption of 1) hypofractionated RT, which takes about 3-4 weeks or less, compared with the 6-7 week course for conventionally fractionated RT, and 2) partial breast irradiation (PBI), which we will discuss in this lecture.

Originally, whole breast RT with or without tumor bed boost was performed for postoperative RT for early breast cancer or ductal carcinoma in situ. On the contrary, PBI targets are only near the tumor bed. There are largely three types of APBI: external beam RT, including 3D conformal RT and intensity modulated RT, brachytherapy, and intra-operative RT (IORT). As these modalities differ in their dosimetrical properties and treatment schedule, I will review the characteristics and studies of each modality.

Overall, the local recurrence-free survival and late effects follwing APBI in early-stage breast cancer are similar to that of whole breast RT, with small, if any, differences reported in some results. However, some of the long-term results from IORT studies reported poor local control rates greater than 10%, which could be considered unacceptable in early breast cancer patients. Therefore, special caution and longer-term follow-up are needed for patients with APBI including IORT.

HEART SPARING RT: A PRACTICAL CONSIDERATION

Shu-Lian Wang

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The priority of RT in breast cancer is disease control followed by reducing late effects, especially radiation-associated cardiac disease (RACD). The effective heart-sparing RT in practice include: limit dose to the heart through safely omission of RT, appropriate RT field and RT technique (such as DIBH, proton); respect the dose constraints of heart and cardiac substructures during treatment planning; and develop the heart atlas to improve the consistency of contour and dose reporting. After RT, multimodality biomarker and imaging-based diagnostic algorithm is required for early detection and intervention of cardiotoxicity.

ADVANCED TECHNIQUES IN BREAST RT: FROM IMRT TO PARTICLE THERAPY

Rachel Jimenez

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Approximately 60-70% of breast cancer (BC) patients receive radiation therapy (RT) as part of their care. Breast or chest wall RT improves locoregional control for BC and also improves BC survival in select populations. In recent years, there have been rapid developments in the technological delivery of radiotherapy with the utilization of volumetric arc therapy (VMAT) and proton beam radiotherapy (PBT), in particular, receiving increasing attention. These techniques, and others, hold distinct advantages over conventional 3-dimensional radiotherapy, but require more complex inverse planned treatment approaches. Therefore, the purpose of this talk is to discuss these recent advances in radiotherapy, including the specific technological and dosimetric advantages of novel radiation techniques like IMRT, VMAT, and proton therapy for breast cancer. This discussion will underscore the indications for these techniques as well as detail the specific patient populations most likely to benefit from them. The second goal of this talk will be to review the existing evidence for these advanced radiotherapy techniques in the treatment of breast cancer before highlighting gaps in the literature and future opportunities for additional research and insights.

NEOADJUVANT AND ADJUVANT TREATMENT FOR TRIPLE NEGATIVE BREAST CANCER

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Triple-negative breast cancer (TNBC) brings many challenges to clinical practice and research due to limited response to standard therapy, early recurrence, metastasis, and heterogeneous biology, resulting in reduced survival and difficulty in developing targeted therapies. Especially given the lack of available targets, including estrogen receptor (ER), progesterone receptor (PR), and human epidermal growth factor receptor (HER)2, there were no available effective targeted therapies in early-stage TNBC were offered for decades. This was a significant issue given the highest rate of recurrence and post-surgery progression compared to other molecular subtypes of breast cancer. Considering all these factors, TNBC has become a focus of a large proportion of breast cancer research over the last decade. Thanks to this effort, several new therapeutics have reshaped the treatment of TNBC. First, in the neoadjuvant space, pembrolizumab is now standard care in combination with systemic chemotherapies. Once the neoadjuvant pembrolizumab is used, it is continued for six months post-surgery as part of the adjuvant therapy. Before the checkpoint inhibitor, the adjuvant capecitabine was approved as standard therapy after showing an improved survival outcome.

Further, recently developed antibody-drug conjugate that has shown significant efficacy in the metastatic setting is also tested in neoadjuvant and adjuvant space as various combination regimens. As more therapeutics become available in the early-stage TNBC, creative combination strategies are tested. Yet, the up-scaling/down-scaling, precision tailoring approach is waiting for a prime time on TNBC. Here we will review the updates of recent neoadjuvant and adjuvant therapy guidelines and new discoveries in early-stage TNBC treatment

NEOADJUVANT AND ADJUVANT TREATMENT FOR HER2-POSITIVE BREAST CANCER

Joohyuk Sohn

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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.

Science is evolving even at this point. The introduction of new antibody drug conjugate (ADC) such as trastuzumab deruxtecan in metastatic breast cancer is shaking the definition of HER2 positivity as it is showing not only groundbreaking efficacy in HER2 positive BC but also outstanding data even in low HER2 BC (IHC 1 or 2 with ISH negative) which is previously considered HER2 negative disease. According to the results of trials in eBC with trastuzumab deruxtecan, all the aforementioned paradigms of treatments would be affected in near future.

USE OF MULTIGENE ASSAY IN HR+HER2- BREAST CANCER

Tom Wei-Wu Chen

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The adjuvant treatment of ER+/HER2- early stage breast cancer is sophisticated and complex. On the one hand, we do not want to over-treat the patients but on the other hand we also need to seriously consider adequate intensity of treatment for high-risk patients. The development of multi-gene assays provided another facet for clinicians to more reasonably predict the prognosis of these patients. Randomized studies with multi-gene assays have identified patients or subgroups who may benefit more from chemotherapy in the adjuvant setting. In this education session, we will discuss how the introduction of multi-gene assays in the early stage breast cancer had shifted our understanding of the pros and cons of chemotherapy in the adjuvant setting. Further, how could we integrate both clinical risk factors such as age and menopausal status and multi-gene assays reports to provide personalized advice regarding the optimal adjuvant treatment for each ER+/HER2 early stage breast cancer patient.

UPDATE ON MANAGEMENT OF PHYLLODES TUMORS OF THE BREAST

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Phyllodes tumors are rare and make up fewer than 1% of all breast tumors. It starts in the stroma, the connective tissue of the breast. Phyllodes tumors are most common in women in their 40s, but women of any age can have them.

Phyllodes tumors are often divided into three groups, based on microscopic findings. Benign (non-cancerous) phyllodes tumors account for more than half of all phyllodes tumors. These tumors are the least likely to grow quickly or to spread. Borderline tumors have features in between benign and malignant tumors. Malignant (cancerous) tumors account for about 25% of phyllodes tumors. These tend to grow the fastest and are the most likely to spread or recur after treatment.

Phyllodes tumors are usually felt as a firm, painless breast lump, but some may hurt. They tend to grow large quickly, and they often stretch the skin. The diagnosis can often be made with a core needle biopsy, but sometimes the entire tumor needs to be removed to know for sure that it's a phyllodes tumor, and whether it's malignant or not.

Phyllodes tumors typically need to be removed completely with surgery. If the tumor is found to be benign, an excisional biopsy might be all that is needed, as long as the tumor was removed completely. If the tumor is borderline or malignant, a wider margin usually needs to be removed as well. This might be done with breast conserving surgery. The entire breast might be removed with a mastectomy. Radiation therapy might be given to the area after surgery, especially if it's not clear that all of the tumors were removed.

Malignant phyllodes tumors are different from the more common types of breast cancer. They are less likely to respond to conventional treatment for breast cancer, such as hormone therapy or chemotherapy. Therefore, phyllodes tumors that have spread to other parts of the body are often treated more like soft tissue sarcomas than breast cancers. Metastasis can be seen in up to 22% of patients with malignant phyllodes at presentation with the most common site being the lung followed by bone, heart, and liver. Patients with metastasis have an overall poor prognosis, many dying within 3 years regardless of the systemic therapy regimen. There is no survival benefit to surgical excision of the breast primary in the setting of metastatic disease; however, palliative surgery could be performed on an individualized basis for local control if feasible.

OVERVIEW OF METAPLASTIC BREAST CANCER

Sunil Lakhani

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The WHO Tumour Classification 5th Ed (2019), defines Metaplastic breast cancer (MpBC) as 'a heterogeneous group of invasive breast carcinomas (IBCs) characterized by differentiation of the neoplastic epithelium towards squamous cells and/or mesenchymal-looking elements, including but not restricted to spindle, chondroid, and osseous cells'.

It is a rare and aggressive form of Triple Negative Breast Cancer (TNBC) with innate plasticity which supports differentiation into heterologous elements. The different morphologies are clonally related, and typically arise from an associated carcinoma but the signals initiating the diverse differentiation pathways remain unclear.

The pathological classification of metaplastic breast cancers is still descriptive and is broadly classified as monophasic (one metaplastic element) and biphasic (two or more elements). It can also be divided into epithelial only, pure sarcomatoid and mixed.

Epithelial only MpBC includes Low grade adenosquamous, Fibromatosis-like metaplastic carcinoma and pure squamous cell carcinomas. Sarcomatoid carcinomas include pure spindle cell and matrix producing carcinoma. Often, the tumours show a mixed epithelial-sarcomatous differentiation.

Molecular classifications put MpBC as 'basal-like' breast cancers; they express signatures consistent with an epithelial to mesenchymal transition, and express basal keratins. Prognostic differences between the different metaplastic presentations have been shown, with spindle fairing worst over squamous, and mesenchymal or matrix producing having the best outcome. We recently reported that those cases with increasing numbers of different morphologies present had a significantly worse prognosis than those with fewer morphologies. This fits with current ideas that increasing heterogeneity within a tumour, correlates with increasing therapeutic resistance. The 10-year overall survival is approx. 55%.

From the few genomics studies focussing on MpBC we have gleaned that metaplastic genome are neither highly mutated nor genomically unstable, and that the different morphologies have only subtly different genotypes. Overall, high levels of TP53 and PIK3CA mutations are detected and an apparent increase in WNT pathway alterations. Chondroid MBC have been shown to lack PIK3CA mutations and TERT promoter mutations; however, in general TNBC tend to have fewer PIK3CA mutations than ER positive tumours (20% v 40% in ER negative v positive). Given the clonal relatedness of the

different morphologies and the lack of a canonical or defining mutation or copy number alteration (a 'pathognomonic' alteration) to promote the differentiation lineages, it is likely that epigenetic changes play a role in the natural history of MpBC.

MpBC are managed according to standard protocols for TNBC, with systemic chemotherapy, but to limited benefit in early-stage tumours. MpBC are infrequently lymph node positive, however those with spread to lymph nodes respond better to chemotherapy. There are small pieces of evidence emerging that MpBC may be suitable candidates for immunotherapy, for example a dramatic response to combination pembrolizumab (an anti-PD-1 drug) and chemotherapy. Candidate biomarkers to identify the patients likely to benefit are yet to be appropriately defined, be they protein biomarkers or genetic (tumour mutation burden).

RECENT UPDATES IN PATHOLOGY OF LCIS, ALH, AND ADH

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For a long time, Atypical dental hyperplasia (ADH) and Atypical lobular hyperplasia (ALH) have been classified as precancerous lesions in breast, and LCIS as in situ carcinoma. Traditionally, diagnosis of ADH or ALH in core needle biopsies (CNB) was managed by excisional biopsies to lower the risk of underlining breast cancer or development of breast cancer in the future, and diagnosis of LCLIS was treated as in situ carcinoma.

Recent studies have established less than 5% chance of upgrade to ductal carcinoma in situ (DCIS) or invasive carcinoma at the time of surgical excision in women with classic-type LCIS. Furthermore, no difference in breast cancer rates existed among women with a core-biopsy diagnosis of classic-type LCIS managed with excision or observation. However, some special variants of LCIS, such as pleomorphic (PLCIS) and florid lobular carcinoma in situ (FLCIS) share morphological features like those of LCIS as well as the biological characteristics of DCIS.

ADH is a pathologically vague entity, but its clinical management should be managed promptly. ADH and low-grade ductal carcinoma in situ (DCIS) are morphologically indistinguishable and the distinction is based on a dimensional criterion, whose cut-off is set at 2 mm or at 2 contiguous duct spaces. Furthermore, during diagnosis, it can be challenging for pathologists to make a clear decision of these borderline lesions at the time of CNB given the small sample size and tissue fragmentation. Therefore, excisional biopsy of these borderline lesions is important, as the additional tissue sampled may allow for more definitive categorization as either ADH or DCIS. Many studies have concluded that diagnosis of ADH has a 5% chance of upgrading to ductal carcinoma in situ (DCIS) or invasive carcinoma at the time of surgical excision.

This presentation will focus on the concept and recent updates of lobular neoplasia (ALH, LCIS) and ADH.

MANAGEMENT OF CARDIOTOXICITY OF BREAST CANCER

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According to the national statistics of Korea, two most frequent causes of death in 2018 were cancer and cardiovascular disease. There are many evidences that both conditions share common risk factors and each affects the prognosis of the other. It is well known to cardiology society that some anti-cancer agents can cause acute and chronic cardiovascular toxic effect. There were many efforts to understand the pathophysiology of cardiotoxicity of anti-cancer agents and to diagnose early changes of cardiac function during chemotherapeutic periods. Cardiotoxicity is a well-known complication of anthracycline and trastuzumab, it is widely used in chemotherapy of breast cancer. There is diversity in clinical characteristics of patients including age, sex, co-morbidities, dose and infusion schedule of anthracycline and trastuzumab. Therefore, it is difficult to recommend preventive strategy of anthracycline-induced cardiotoxicity that can applied to any patients. The Individualized approach to each patient, such as the cardiotoxicity risk stratification before chemotherapy, are inevitable. Cardiotoxicity remains a major limitation in proper management of breast cancer patients treated with an anthracycline combined with trastuzumab. Extensive efforts have been made to determine the mechanism and treatment of cardiotoxicity. Because it is considered to cause irreversible damage to myocardium, prevention of cardiotoxicity is a more effective approach rather than treatment of cardiotoxicity after development of symptomatic or asymptomatic cardiac dysfunction. This article will review the outlines for pathophysiological mechanisms of cardiotoxicity and strategies for protection of myocardium from chemotherapeutic agents.

MANAGEMENT OF AIMSS (AROMATASE-INHIBITOR-ASSOCIATED MUSCULOSKELETAL SYNDROME)

Eun Joo Yang

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Breast cancer remains a significant threat to the health and wellness of women. Although advances in early detection and therapy have resulted in a 38% decrease in the breast cancer death rate, patients who develop metastatic disease need innovative approaches to breast cancer therapy that reduce relapse and death due to this disease. Aromatase inhibitors (AIs) are a key component in the chemoprevention and treatment of hormone receptor-positive (HR+) breast cancer. In recent years, accumulating data support a key role for the immune system in determining both response to standard therapy and long-term survival in breast cancer patients.

While the addition of AI therapy has improved cancer-related outcomes in the management of HR+ breast cancer, AIs are associated with musculoskeletal adverse effects known as the aromatase inhibitor-associated musculoskeletal syndrome (AIMSS) that limit its tolerability and use. AIMSS is mainly comprised of AI-associated bone loss and arthralgias that affect up to half of women on AI therapy and detrimentally impact patient quality of life and treatment adherence. Immune checkpoint inhibitors (ICI) associate with a wide range of immune-related adverse events (Ir-AE), including musculoskeletal manifestations.

This lecture aims to characterize the clinical features of AIMSS and ir-AE, and explore the syndrome's underlying mechanisms and management and rehabilitation strategies.

MANAGEMENT OF CHEMOTHERAPY INDUCED NAUSEA AND VOMITING (CINV)

Toshiaki Saeki

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Backgrounds: Chemotherapy induced nausea and vomiting (CINV) is a still great barrier to reach the optimal survival benefit of cancer patients. I will tach on a clinical study of new agents for CINV. Fosnetupitant (FN) is a phosphorylated prodrug of netupitant, which has high binding affinity and selectivity for the neurokinin 1 (NK1) receptor.

Methods: Patients scheduled to receive AC/EC were randomized 1:1 to receive FosNTP 235 mg or FosAPR 150 mg both in combination with intravenous palonosetron 0.75 mg and dexamethasone 9.9 mg on day 1. FosAPR regimen was included as an exploratory arm. The primary endpoint was the incidence rate of treatment-related adverse events (TRAEs) with FosNTP. Efficacy outcomes were evaluated as secondary endpoint.

Results: Overall 102 patients were randomized to FosNTP (N = 52) or FosAPR (N = 50), all of whom were treated with the study drug and evaluated for safety. The primary endpoint, the incidence rate of TRAEs in FosNTP arm was 21.2%. Similar data was shown in FosAPR arm (22.0%). TRAEs reported in 5% of patients were headache, diarrhea, urticaria, malaise, and decreased appetite in the FosNTP arm. Any-cause and treatment-related ISRs with FosNTP observed in 5.8% (all grade 1) and 0% of patients, respectively. The overall (0-120 hours) complete response rate standardized by age category was 45.9% (95% CI, 33.2%-58.6%) with FosNTP.

Conclusion: FosNTP demonstrated a favorable safety profile, with a very low risk of ISRs in the AC/EC setting.

PSYCHOLOGICAL INTERVENTIONS ON FATIGUE OF BREAST CANCER PATIENTS

Eun-Jung Shim

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Fatigue is one of the most distressing symptom affecting a considerable portion of patients with breast cancer. National Cancer Comprehensive Network (2021) defines cancer-related fatigue (CRF) as "a distressing, persistent, subjective sense of physical, emotional, and/or cognitive tiredness or exhaustion related to cancer or cancer treatment that is not proportional to recent activity and interferes with usual functioning". Multiple factors contribute to fatigue in patients with breast cancer and emotional distress is one of the major factors associated with CRF. Psychiatric symptoms such as depression, anxiety, and posttraumatic stress symptoms (e.g., intrusion, hyperarousal) are strongly associated with CRF. Psychological factors are also associated with worsening fatigue trajectories. These emotional distress appears to be associated with CRF directly and also indirectly via their associations with sleep disturbances, which is a strong and independent risk factor of CRF. Fatigue often co-occurs with these (i.e., depression and sleep disturbance), and studies suggest that managing them as part of symptom cluster (e.g., depression-sleep disturbance-fatigue) might be effective for CRF.

Important role of psychological factors in CRF provides rationale for psychological interventions on fatigue. In fact, NCCN fatigue guidelines (2021) suggested psychosocial interventions for CRF and recommended cognitive behavioral therapy (CBT)/behavioral therapy and psychoeducational therapies as psychosocial interventions with high level evidence. Moreover, given that fatigue is a subjective experience of patients, CBT appears to have promising potential as evidence-based interventions for CRF in patients with breast cancer. CBT for CRF aims to target perpetuating factors of fatigue, which includes excessive fear of disease recurrence, suboptimal coping with cancer and treatment, dysfunctional cognitions regarding fatigue (e.g., fatigue catastrophizing). CBT have been applied to treat fatigue among patients with breast cancer, and the majority of them supported CBT for fatigue as evidence-based intervention for CRF. Many CBT for fatigue are delivered on internet-based and tend to be brief, meeting the need for an accessible and more efficient evidence-based CRF treatments for patients with breast cancer. Recent CBT approach to CRF attempts to combine CBT with other therapeutic approaches such as bright light therapy or hypnosis. Moreover, psychoeducational therapies that assist patients with breast cancer to understand and cope with CRF also shown to be effective in CRF. Psychoeducational interventions usually includes guidance about patterns of fatigue and tailored interventions for self-management. Evidence also suggest that mindfulness-based interventions such as the Mindfulness-Based Stress Reduction for Breast Cancer was effective to improve psychological symptoms such as anxiety or fear of recurrence and severity and interference of fatigue among breast cancer survivors.

ASSESSMENT AND MANAGEMENT OF INSOMNIA

Seockhoon Chung

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Sleep disturbances or insomnia is a common psychiatric symptom which cancer patients frequently can suffer from. Although many cancer patients experience insomnia throughout the entire trajectory of the cancer diagnosis and treatment, only small number of patients will seek evidence-based treatment. Both cancer patients and healthcare providers often consider sleep problems as a normal reaction to cancer diagnosis and treatment. This is unfortunate because of the significant physical and psychological health ramifications of untreated, chronic sleep disturbances within a patient population already at high risk for the development of medical co-morbidities. Most of cancer patients can suffer cancer-related fatigue symptom, and fatigue is associated with depression or sleep disturbance. 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. Cancer patients who suffer insomnia also tend to be overconcerned about the negative consequences of poor sleep on their health. For example, "sleep during a specific time period (e.g., 10 pm to 2 am) is critical for immune functioning" or "poor sleep affects cancer progression," are common cancer-related dysfunctional beliefs about sleep observed among patients with cancer experiencing insomnia. 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 depression and sleep disturbance among cancer patients will be discussed. Especially, the Sleep Clinic for cancer patients, run in Asan Medical Center, will be presented.

STANDARD OF CARE FOR BREAST CANCER DISTRESS

Hideko Yamauchi

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Standard of Care for Breast Cancer Distress
-Butterflies and Roses-

Due to advancement of cancer treatment, the number of cancer survivors is increasing and our society needs to consider cancer survivorship. Cancer and its treatment largely affect not only survivors' life style but also their family's.

The peak of the breast cancer incidence rate had been at a younger age range in Asia than in Western countries. About half of breast cancer patients in Asia are diagnosed in their 30s50s. In Japan about 3% was diagnosed as a young breast cancer (less than 35 year old) especially. As individuals in this age range are considered the most active members in the society, it is important to support from multiple aspect.

As they are in the productive age, we have to discuss the influence for their reproductivity from cancer treatments. We have to assess the influence to working status, ie: the disability of work caused by fatigue, chemotherapy-induced cognitive disorder, and distorted appearance. Health care providers for cancer survivors should facilitate returning to work or keeping their job. If they have small children, the support for children whose parents were diagnosed cancer is very important.

We have been committing to provide standard of care for breast cancer distress and established support system. We should discuss how we can work together to develop better support systems for breast cancer distress and help their transformation from fragile butterflies to beautiful roses.

OPTIMAL TREATMENT OPTIONS FOR HIGH RISK ER+ BREAST CANCER

Maria-Joao Cardoso

Champalimaud Foundation, Department of Surgery, Portugal

Breast Cancer (BC) is the most common cancer in women, with HR+/HER2- BC being the most common subtype. Significant advances in the management of HR+/HER2- have been made over the past few decades with the currently available therapies while maintaining a good quality of life and avoiding any long-term sequalae.

There are classical prognostic factors that help determine the treatment strategy for HR+/HER2- BC, such as the anatomic staging (TN), the grade, ki67, lymphovascular invasion and the four immuno-chemistry markers. Several prognostic models have been created to calculate the risk of recurrences but none is used universally without criticisms Not all prognostic and predictive factors work equally for the prediction of early and late distant recurrence risk. Ideally, biomarkers and models of risk build on those biomarkers should be both prognostic and predictive. The recent genomic tests are actually used to establish the need for adjuvant chemotherapy in addition to endocrine treatment (ET).

However a clinically significant proportion of patients with high risk HR+/HER2- BC recurs even after receiving adjuvant chemo-endocrine therapy particularly those with high axillary burden.

Using a tailored risk approach to early HR+/HER2- BC and based on the efficacy of the combination of CDK4/6 inhibitors and ET in metastatic BC, this strategy is being tested in the adjuvant setting for patients with high-risk tumors in an attempt to overcome ET resistance.

The three CDK4/6 inhibitors currently approved for metastatic breast cancer (Palbociclib, Abemaciclib and Ribociclib) have been tested in different adjuvant trials with discordant results that still raise many questions related essentially to patient selection according to different risk definitions between the trials. Three trials PALLAS and PENELOPE-B (both with Palbociclib) and MonarchE (with Abemaciclib) have reported results at different stages of maturity, while a third trial, NATALEE is still ongoing (with Ribociclib). The German WSG ADAPT protocol is testing an individualised adjuvant decision-making strategy with Ribociclib for intermediate risk and ADAPT late with abemaciclib for high-risk BC patients.

Another attempt to overcome resistance to adjuvant ET was made with the use of Everolimus, an mTOR inhibitor, unfortunately unsuccessful.

In the rare subset of BRCA positive patients and according to the results of the OLYMPIA trial the addition of olaparib, a PARP-1 inhibitor, to standard ET improves DFS in patients with high-risk, early HR+/HER2- breast cancer.

Bone-modifying agents, when added to standard adjuvant ET, reduce the risk of bone metastasis, and produce a slight but statistically significant improvement in survival, an effect limited to postmenopausal women.

Quickly coming to this arena of defying resistance to ET the new group of oral SERDS are also being tested already in phase 3 trials in patients with high-risk, early HR+/HER2- breast cancer compared to standard ET. These agents with standard endocrine therapy have been already planned.

Up to now the available clinical and genomic tools are not capable to accurately identify those patients at high risk who will eventually relapse and are also not precise predictive factors for response to systemic therapies (endocrine therapy, chemotherapy).

Although residual disease after neoadjuvant treatment can be easily identified if macroscopic, minimal residual disease that can be responsible for late recurrences is difficult to detect. The use of liquid biopsies can help us in the future to identify those patients that can have additional treatment where there is still very low tumor burden.

EXTENDED ENDOCRINE THERAPY, OPTIMAL DURATION AND SEQUENCE

Sung Hoon Sim

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Since adjuvant endocrine therapy was established for hormone-positive breast cancer, there are a lot of treatment strategies for premenopausal or postmenopausal women. Many guidelines generally recommended aromatase inhibitor upfront or as a part of switch therapy after 2 or 3 year of tamoxifen. However, the recurrence rates after 5 years of tamoxifen still range from 19 up to 41%, depending on the tumor and nodal status of the primary tumor. For the reduction of late recurrence, extended endocrine therapy has been investigated. There are more than 8 trials evaluating extended endocrine therapy. Each trial has similar but different design with different primary outcome. It is not possible to draw a firm conclusion but it is clear that not all patients require the extended endocrine therapy. Most of trials did not show definite benefit from the therapy in disease free survival and overall survival. However, the group of patients with high risk including large tumor size or node positive disease had small benefits and can be a candidate for the treatment. The adverses effect of extended endocrine therapy is osteroporosis and increased bone fracture event. Therefore, the treatment should be individualized. Recent researches are focusing on the identification of biomarkers for the prediction of late disease recurrence. Some biomarkers under investigation include circulating tumor cells (CTCs), circulating tumor DNA (ctDNA), disseminated tumor cells (DTCs), and various types of scoring system or index tools. Further prospective studies are necessary to understand the role of biomarkers and to optimize the endocrine therapy.

OVARIAN SUPPRESSION WITH/WITHOUT ADJUVANT CHEMOTHERAPY IN HIGH-RISK PREMENOPAUSAL PATIENTS

Shin-Cheh Chen

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Breast cancer occurs in premenopausal women estimate about 50% of all breast cancer in Asia. Young age or very young breast cancer associated with high risk of relapse and death that is a big challenge to patients, family and the society.

The clinical characteristics of Asian premenopausal breast cancer patients include high percentage of ER (+) status, immune signature, different gene expression, esp. younger than 40 and the differences from western breast cancer will be presented.

The risk stratification strategy in premenopausal ER-positive breast cancer will help determine the efficacy and tailor optimal chemo-endocrine therapy. The risk factors are based on clinical, such as age, ER level, molecular subtypes, composite score, genomic expression assay and clinical trial definition.

Current adjuvant treatment options and recommendations are based mainly on SOFT and TEXT and other clinical trials with ovarian function suppression (OFS), tamoxifen and aromatase inhibitors (AI), the decisions of chemotherapy should weight the benefits against side effects.

The unresolved issues of OFS including timing of OFS, with or without chemotherapy, interval and prolonged OFS and combination with either Tamoxifen or AI will be explored.

The mechanism of chemotherapy is beyond OFS with direct cytotoxic effect on tumor cell. It improved the survival in high risk premenopausal women, esp. younger than 40 years breast cancer.

In summary, we proposed a treatment algorithm based on age and risk factors for optimal chemotherapy, OFS and hormonal therapy. The unsolved problems of very young (< 35 years), prolonged OFS, extended therapy and chemotherapy induced ovarian failure (CIOF) will be discussed.

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"Go Beyond Cure of Breast Cancer"

REVEALING THE ALTERNATIVE LENGTHENING OF TELOMERES PATHWAY BY THE DEPLETION OF BRCA2 AND THE APPLICATION OF TRIPLE NEGATIVE BREAST CANCER ORGANOIDS FOR PRECISION ONCOLOGY

Hyunsook Lee, Junyeop Lee, Jennifer J. Lee, So Young Joo, Sara Jeon

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Mice conditionally deficient in the breast cancer susceptibility gene, BRCA2, exhibit progressive telomere shortening leading to proliferative defect. Analysis of the MEFs revealed that BRCA2 deficiency resulted in breakdown of stalled replication forks, particularly at the lagging strand. As G-rich telomere can form G-quadruplex (G4), a four-stranded compact DNA structure, we asked whether the problem of lagging strand telomere synthesis upon loss of BRCA2 was associated with telomere G4. Here, we show a novel mode of BRCA2 interaction with the telomere G4. This unique way of BRCA2 with the telomere binding while replication remodels telomere G4, enabling RAD51-mediated restart of the fork, at the same time preventing from MRE11-mediated resection of the stalled replication forks. Cells depleted of BRCA2 exhibited significant telomeric damage and finally led to the induction of Break-induced replication (BIR), leading to the Alternative Lengthening of Telomeres (ALT). We provide evidence that the formation of LLPS (Liquid-liquid phase separation) is responsible for the instigation of BIR at telomeres. Lastly, we show the promise of culture of the organoids from the human triple negative breast cancers (TNBC) in collecting multi-omics information, which will let us to understand the pathways leading to TNBC.

FUNCTIONAL ASSESSMENT OF PATIENT-DERIVED BRCA VARIANTS VIA CRISPR-MEDIATED GENOME EDITING

Yongsub Kim

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Most of the human genetic diseases are caused by genomic changes such as substitutions, insertions, and deletions. Although advances in sequencing technology have led to the identification of many disease-associated variants and improved patient management, they have also unveiled a number of genetic variants that we are still not able to clearly define their disease association. Over the past decades, CRISPR-based genome editing tools have been developed and widely used for introducing genetic modification in living cells and organisms. Particularly, CRISPR-based base editors and prime editors enable precise genome writing and make it possible to elucidate the disease associations with patient-derived mutations. Using these systems, we have been studying several disease-causing genes and functions of their variants from patients. Here, I will introduce an application of the CRISPR-Cas9 system for functional analysis of BRCA variants. Although a number of BRCA variants are identified from cancer patients via genetic testing, it is still difficult to identify their pathogenicity. Using CRISPR-mediated base editors and prime editors, we introduced BRCA mutations in endogenous loci and analyzed their functions in a high-throughput manner. We identified a lot of the functions of BRCA variants of uncertain significance. We expect that our method will provide clues for the treatment of breast cancer with BRCA variants.

CELL-FREE TUMOR DNA AS A CANCER SURVEILLANCE STRATEGY: CURRENT AND FUTURE

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Recent studies on ctDNA have shown that the "liquid biopsy" is very attractive for monitoring of minimal residual cancers that cannot be sampled without invasive means. However, mutations from the tumor comprise only a small fraction of plasma DNA, and thus require very high-depth sequencing for reliable identification of minimal residual disease. In the presentation, we will discuss about what is optimal methods for the detection of MRD? Recently, we have actively explored mutation-based tissue informed methods; with colon cancer patient cohorts, we were able to predict relapse with high PPV. Furthermore, ctDNA based MRD analysis can be done without tissue and/or methylation-based means. We will also discuss about pros/cons of strategies implementing individualized panel, pre-designed targeted panel, or genome-wide analysis.

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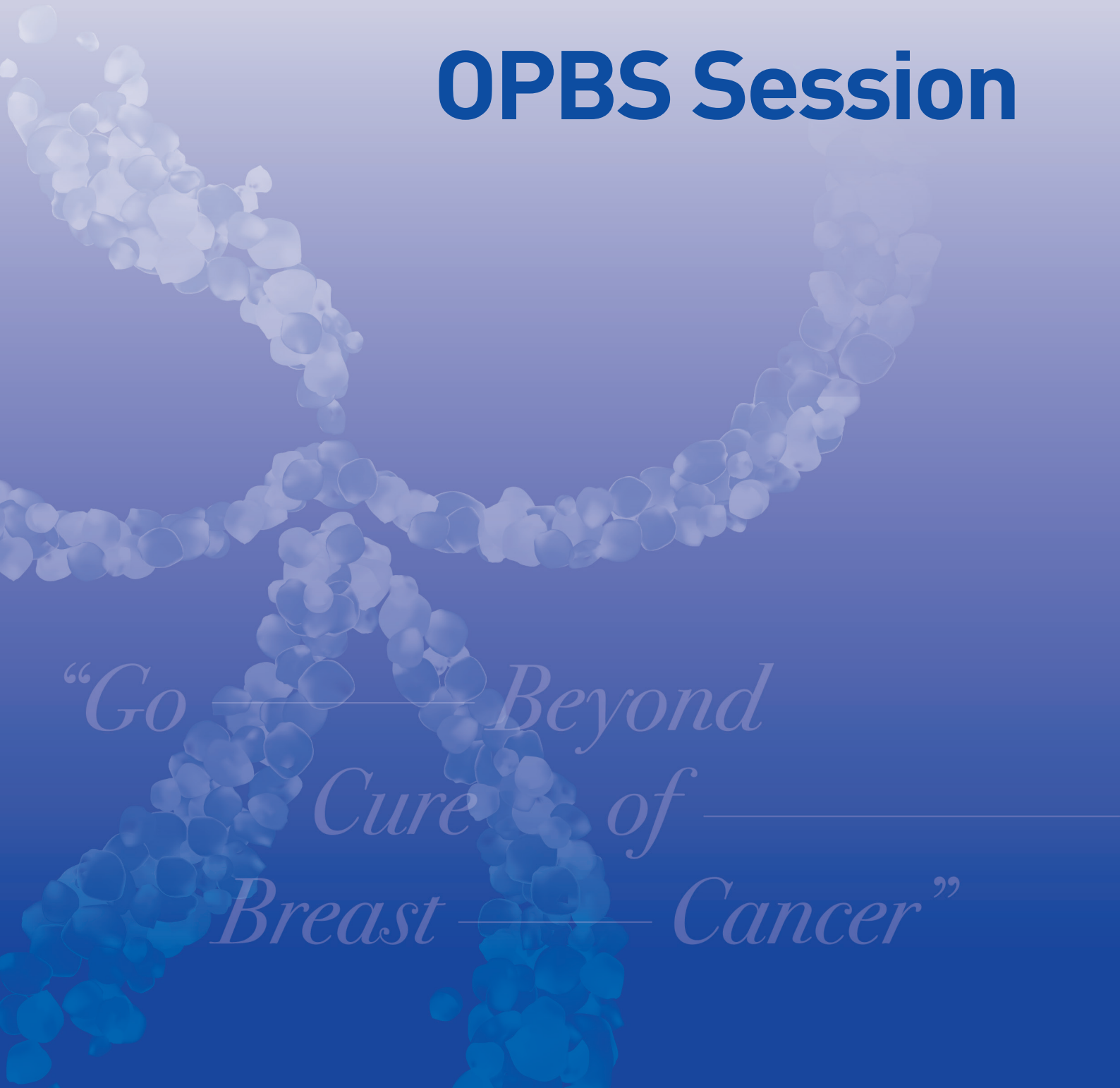

TRAINING THE ONCOPLASTIC BREAST SURGEON: AN INTERNATIONAL PERSPECTIVE

Patricia Lynn Clark

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With the development of multidisciplinary approaches to the treatment of breast cancer and better understanding of tumor biology, survival trends continue to improve. With greater survival, quality of life must now be considered in addition to extirpation of disease and primary oncologic management. In the late 1980's breast surgeons began to utilize principles of plastic surgery to prevent the aesthetic deformities that can result following traditional breast conservation surgery. Oncoplastic surgery techniques reconstruct the partial mastectomy defect, but training of surgeons and implementation of these techniques differs internationally as well as domestically. Training opportunities vary from a formal curriculum and certification in the UK, to development of independent training centers, to skill training through institutional or societal seminars and courses, to mentorship, and to individual surgeons traveling internationally to acquire these skills. The presentation will cover development of these training pathways in developed countries. Oncoplastic techniques are being implemented worldwide but training is not standardized. Each country can benefit from the experience of others. This information can be utilized to broaden and standardize training opportunities and implementation of oncoplastic surgery in much of the world.

EVIDENCE REVIEWS OF ONCOPLASTIC BREAST SURGERY

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Last decades, Oncoplastic breast surgery (OPBS) became more popular not only for partial breast reconstruction after breast conserving treatment (BCT), but also indicates for total breast reconstruction after various types of total mastectomy (TM). At the beginning of OPBS introduction, there are some concerns regards oncological safety especially for cancer recurrence in BCT.

Nowadays, with more evidence reviews on multilevel of literatures then such concerns are diminished in conventional OPBS techniques. Those conventional OPBS techniques are parenchymal relocation, oncoplastic level I II III, parenchymal substitution with loco-regional flap, distant free flap and expander implant-based technique. However, with novel method in OPBS technique especially when involve with tissue engineering, mesenchymal stem cell, scaffold and synthetic material the human research should be properly conducted.

Evidence reviews of OPBS, which evolve together with breast oncological management are essential for breast surgical oncologists, reconstructive surgeons and plastic surgeons.

OVERCOMING HURDLES IN ONCOPLASTIC BREAST SURGERY

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The oncoplastic surgical (OPS) methods can be appropriately categorized according to the breast and tumor size, the location of breast cancer, patient preference, and so on. Although the learning each surgical method can be acquired by watching at lectures or textbooks, it is difficult to learn about the complications or how to troubleshooting in OPS. The oncoplastic surgeons should learn how to prevent and treat complications based on the experiences of others, and make a better works on ways to minimize the complications with their own experiences. Also, the oncologic outcomes should be obtained within this process.

OPS hurdles can be divided into two main categories. The one is to make the oncologic result better and the other is to make the cosmetic result better. However, because the relationship between these two actually has a see-saw effect, it is the most important work to secure the optimized oncologic and cosmetic results, simultaneously. In order to overcome the oncological hurdles in breast cancer surgery, it is necessary to thoroughly analyze the preoperative images with the radiologists. Occasionally, although tumor size is small in ultrasound, there is diffuse microcalcifications in mammography or large size of non-mass enhancement in breast MR. If these are not identified before surgery, the surgeons may experience margin positivity during surgery and it would lead a certain change of oncoplastic surgical plan. Such an experience is not pleasant, the surgeons do not want to experience it. The OPS hurdles in a cosmetic point of view, they are frequently occur by movement range and softness of glandular tissue, skin elasticity, breast ptosis as well as unexpected margin positivity.

If you are a single oncoplastic surgeon, the better cosmetic outcomes including minimizing incision, natural breast shape, and obtaining symmetry can be achieved by overcoming the individual learning curve with increasing their skills. And if you work with plastic surgeon, you should discuss about the second, third surgical options with patient and plastic surgeon before surgery.

The oncological and cosmetic hurdles in oncoplastic surgery are not independent factors, but moves very organically. Therefore, the best way to overcome hurdles of OPS is a multidisciplinary approach in treating breast cancer.

PLASTIC SURGEON'S PERSPECTIVE FOR BETTER RECONSTRUCTION OUTCOMES

Ung Sik Jin

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Successful breast reconstruction after mastectomy requires close collaboration between breast and reconstructive surgeons to achieve optimal oncologic and aesthetic outcomes. Poor perfusion of mastectomy flap causes delayed wound healing, partial necrosis or even wound infection, which may consequently delay adjuvant anti-cancer therapies. While healthy mastectomy flap is crucial for reconstructive success, utilization of indocyanine green angiography provides gross information to assist the reconstructive procedure. In cases of poor mastectomy flap perfusion, partial sharp debridement of flap may enhance wound healing and tissue expander rather than implant insertion may be beneficial in implant-based reconstruction. In flap-based reconstruction, skin paddle from autologous flap may be spared for possible mastectomy flap necrosis. On the other hand, redundant mastectomy flap should be appropriately manipulated in cases of large ptotic breasts. Considering the tumor location, mastectomy incision may made following vertical reduction pattern or wide pattern if possible. Additional remnant skin after mastectomy may be used as dermal flap for implant coverage after de-epithelialization. Nipple-sparing mastectomy in large ptotic breasts may require further skin flap management of free nipple graft for appropriate nipple positioning. Appropriate assessment and manipulation of mastectomy flap can reduce complication and improve surgical outcomes.

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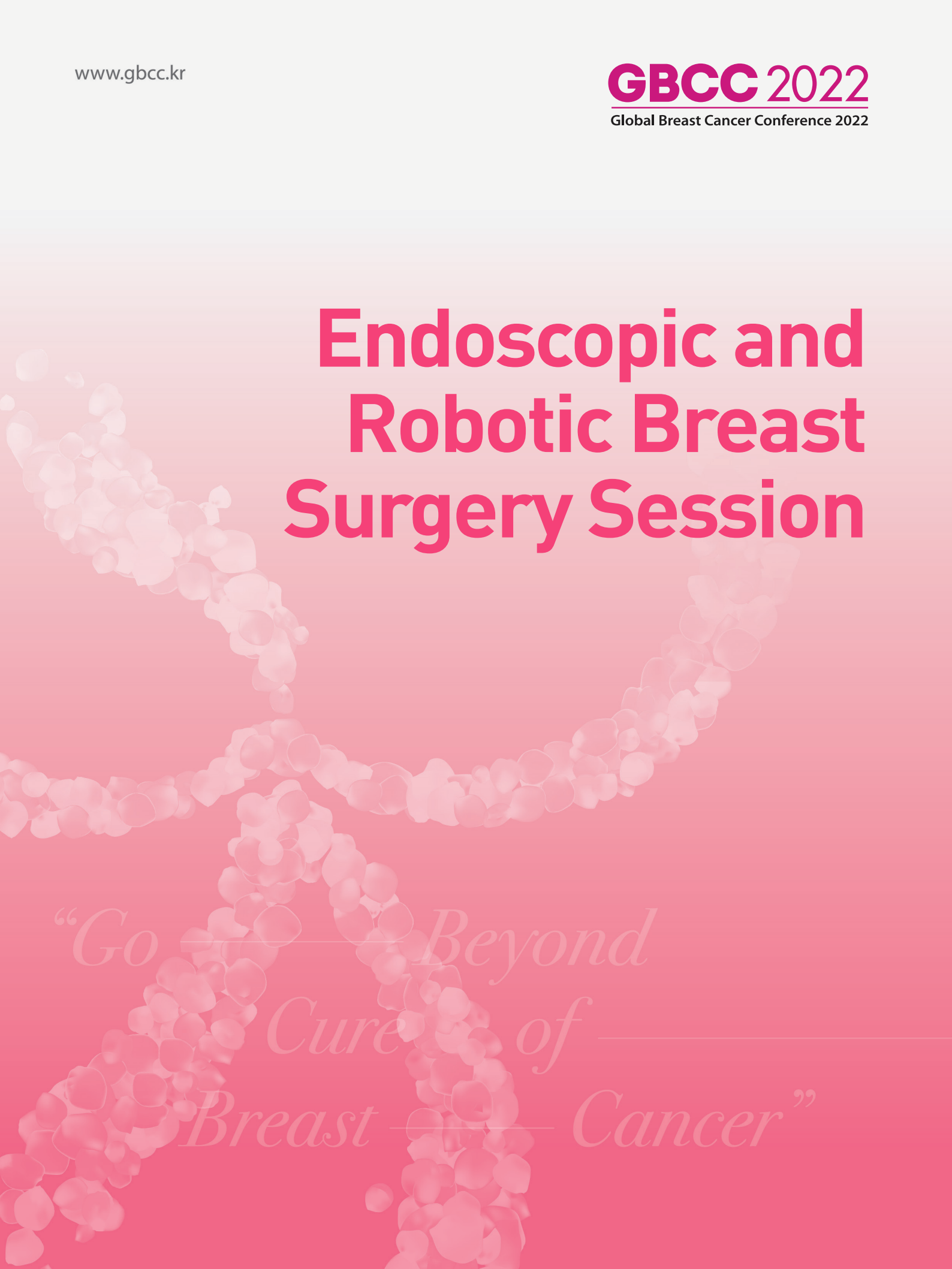
Endoscopic and Robotic Breast Surgery Session



BENEFITS AND DRAWBACKS: MULTI-PORT ROBOTIC MASTECTOMY

Hung-Wen Lai

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Minimal invasive surgery had become the main stream of operations, and new surgical innovations of NSM, like endoscopic assisted nipple sparing mastectomy (E-NSM) or robotic nipple sparing mastectomy (R-NSM), are emerging and increasingly applied in the surgical treatment of breast cancer. One of the aims of minimal access breast surgery is to decrease the wound length and hidden in more inconspicuous location, and therefore increase the patients' satisfaction.

R-NSM, which incorporated 3D imaging system and flexibility of robotic arm & instruments, was reported to have the potential to overcome the limitations of E-NSM and showed promising preliminary results. The widespread use of R-NSM, however, was limited to prolonged operation time and higher cost. New surgical innovations balancing efficacy, operation time, and medical cost are needed. E-NSM compared with R-NSM had the advantages of shorter operation time, less costly, and less instruments demanding. Single port 3D E-NSM, which is safe, efficient, not costly, and associated with good aesthetic result, is a promising new technique for breast cancer patients indicated for mastectomy, however, long-term oncologic safety follow-up still be needed.

In the presentation, the author would update the recent prospective studies available and compared the benefits and drawbacks of multi-port robotic mastectomy to conventional NSM and endoscopic assisted NSM.

BENEFITS AND DRAWBACKS: SINGLE-PORT ROBOTIC MASTECTOMY

Hyung Seok Park

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Robotic surgical systems have been evolving to efficiently deliver delicate surgeons' skills into the operation fields using 3-dimensional cameras and highly flexible robotic instruments via small endoscopic/laparoscopic incisions. Single-port surgery can minimize the number of incision sites and also provides feasible surgical environments for surgeons in various surgical fields.

For endoscopic mastectomy, multiple incisions were necessary to handle endoscopic instruments via trocas. During the initial period of endoscopic mastectomy, at least two incisions such as periareolar and axillary incisions were made to develop appropriate dissection for the breast and axillary tissue. After several modifications of endoscopic techniques in mastectomy, a technique via a single axillary incision using single-port access devices has been introduced to maximize surgical and cosmetic outcomes. However, because of the technical difficulty of endoscopic breast surgery, only surgeons in a few Asian countries have been able to apply endoscopic instruments in mastectomy.

Recently, Robot-assisted nipple-sparing mastectomy has been introduced to maximize surgical and cosmetic outcomes in women who undergo mastectomy and immediate breast reconstruction. At the beginning of robot-assisted nipple-sparing mastectomy, only multi-port robotic surgical systems such as da vinci Si, X, and Xi were available, thus, additional trocas or single-port access devices for gas-inflated techniques and self-retractors for gasless techniques were needed for making and maintaining the working-space. However, collisions between robotic instruments and/or patient's arms remain as one of the hurdles in performing robot-assisted nipple-sparing mastectomy in the early learning period because 3 or 4 endo-robotic instruments are inserted into the single 3-6 cm sized axillary incision.

To overcome these hurdles in robot-assisted nipple-sparing mastectomy, a recently introduced single-port robotic surgical system, the da vinci SP system, was first applied in robot-assisted nipple-sparing mastectomy by Park et al at Severance Hospital in 2018. The SP system delivers four endo-robotic instruments into the surgical field into 2.5 cm sized cannula, and the use of the SP system fits with surgeries in narrow spaces such as nipple-sparing mastectomy and thyroidectomy. The collision between instruments and/or the patient's arm can dramatically decrease in surgery using the SP system compared to the multi-port systems. Furthermore, flexible camera instruments provide better visualization of the surgical field, particularly the medial side of the breast which is the most difficult area to dissect in nipple-sparing mastectomy.

In this lecture, I will discuss the benefits and drawbacks of the SP system in mastectomy according to my personal experience and data from Severance Hospital.

RECENT UPDATES FOR ENDOSCOPIC MASTECTOMY WITH AXILLARY SURGERY

Chi Wei Mok

Changi General Hospital, Department of Surgery, Singapore

In this session, Asst Professor Mok will discuss and share on the recent updates on endoscopic mastectomy and axillary surgery. He will be giving an overview of the history of endoscopic mastectomy and axillary surgery while also sharing on the latest evidence supporting the use of these techniques. In addition, he will also be sharing his experience on technique innovations over the years.

ENDOSCOPIC/ROBOTIC-ASSISTED HARVEST OF LATISSIMUS DORSI FLAP FOR PARTIAL BREAST RECONSTRUCTION

Jung Dug Yang

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After partial mastectomy, partial breast reconstruction using the conventional latissimus dorsi (LD) muscle flap has some disadvantages such as leaving a long scar. To overcome these disadvantages of LD flap reconstruction, new surgical methods for minimizing skin incisions using endoscopic and robotic approach have been recently studied. Patients were selected according to the expected resected tumor weight, location of tumor, breast size, and patient preference, and only patients who agreed to the surgery were included.

Comparing with conventional approach, endoscopic and robotic approach have better results in donor site scar, recovery time. But learning curve and the operation time is long. Among them, LD flap harvest using an endoscope can reduce scarring and obtain patient satisfaction, but it has not been widely practiced because of the long learning curve and difficulty in confirming perspective and securing the field of view with a two-dimensional field of view. Comparing to endoscopic approach, robotic surgery is 3-dimensional imaging system and robotic arm and instruments are more flexible and better vision and wide range of motion.

In this presentation, current author will present surgical techniques and outcomes of endoscopic and robotic-assisted harvest of latissimus dorsi flap for partial breast reconstruction.

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HBOC Session

"Go Beyond Cure of Breast Cancer"

SURGICAL OPTIONS IN HEREDITARY BREAST CANCER

Ava Kwong

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Women who have inherited mutations in breast cancer susceptibility genes mutations such as BRCA1 and BRCA2 have substantially elevated risks of breast and ovarian cancer. With the emergence of next generation sequencing, more breast cancer susceptibility genes have been identified resulting in complexity in genetic counselling and decision making for management options more complex. Mutation carriers have various options, including extensive and regular surveillance, chemoprevention and risk-reducing surgery. Prophylactic surgery (bilateral mastectomy, bilateral salpingo-oophorectomy or a combination of both procedures) has proved to be the most effective risk-reducing strategy for breast cancer and ovarian cancer, but there are no randomised controlled trials able to demonstrate the potential benefits or harms of prophylactic surgery. Although it is not uncommon to perform mastectomy when a mutation carrier is encountered, breast conservation is not completely contraindicated. Based on the current knowledge, it is also reasonable to recommend prophylactic oophorectomy for BRCA1 or BRCA2 mutation carriers when childbearing is completed in order to reduce the risk of developing breast and ovarian cancer. In addition, women should be offered the options of intensive breast surveillance, chemoprevention apart from bilateral prophylactic mastectomy. The selection of the most appropriate surgical options with or without risk-reducing strategy however is not simple. The impact of risk-reducing strategies on cancer risk, survival, and overall quality of life are the key criteria considered for decision-making. Various other factors should be taken into consideration when evaluating individual mutation carriers' individual situation, namely woman's age, morbidity, type of mutation, and individual preferences and expectations. Strategies and existing guidelines will be reviewed and discussed.

The University of Hong Kong; Hong Kong Hereditary Breast Cancer Family Registry; Hong Kong Sanatorium and Hospital.

TEN GENES FOR HEREDITARY BREAST AND OVARIAN CANCER

William Foulkes

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The search for breast cancer susceptibility genes (BCSGs) has been a major activity of germline genetics-focused breast cancer researchers for the past 35 years. Linkage between the marker CMM86 and familial forms of breast cancer by Mary-Claire King in 1990 was the starting point for the search for BCSGs. In 1994, BRCA1 was finally isolated by Myriad Genetics (1), and one year later, BRCA2 was cloned by Michael Stratton and colleagues (2). After ten years of work it became clear that no other single gene could be contributing very substantially to the 60% of familial cases of breast cancer that remained unexplained (3). The same year, however, heralded the arrival of what could reasonably termed "BRCA3" PALB2. Notably, this gene was identified by David Livingston's group (4) based on its close physical relationship with BRCA2 - hence the name "Partner and Localizer of BRCA2". Not long after, three groups published strong evidence that PALB2 was a breast cancer susceptibility gene (5-7). PALB2 is implicated in homology directed DNA repair, and as seen for BRCA1 and BRCA2 (8,9), tumors arising in persons with germline pathogenic variants in PALB2 may respond to both old and new therapies (10) that target homologous recombination repair deficiency (HRD). These three form a group of established BCGS and have clear utility.

What of other candidate BCSGs? In 2015, Easton and colleagues set out a framework for determining if a candidate BCSG could be become established (11). This framework was helpful in interpreting the results of two large studies published in 2021 in the NEJM (12,13) and summarized by the current presenter in NRCO (14). In this latter News and Views piece, I argued that ten genes could reliably associated with breast cancer (or ovarian) cancer susceptibility. I recognize the candidacy of other genes that could be included in panels, especially for non-ductal breast cancers and non-serous ovarian cancers occur. Nevertheless, a core group of 10 genes (ATM, BARD1, BRCA1, BRCA2, BRIP1, CHEK2, PALB2, RAD51C, RAD51D and TP53) would likely capture 95%+ of the relevant variants. In my talk, I will also show data that strongly suggest that there are no more important BCSGs to be found (15,16), and we need to definitively move away from discovery projects, towards characterization and implementation of the known genes.

Thanks to Paz Polak for discussions and Clare Turnbull for sharing unpublished data that I will present.

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HEREDITARY PANCREAS CANCER

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Pancreatic cancer (PC) is the seventh and fifth leading cause of cancer-related mortality worldwide and in South Korea, respectively. PC has several clinical features such as non-specific symptoms, difficulty in early diagnosis, and lack of effective therapy as well as aggressive biological features. Many patients have distant metastases at the time of diagnosis; consequently, only 15-20% of patients can undergo potentially curative resection. Therefore, early detection and curative surgery at appropriate times are necessary in high-risk individuals.

The risk factors for PC include modifiable acquired factors (smoking, alcohol intake, diabetes mellitus, obesity, chronic pancreatitis) and unmodifiable inherited factors (family history of PC, inherited cancer syndromes). Unmodifiable inherited factors increase the risk of developing PC by two- to 132-fold compared to modifiable acquired factors that raise the risk by 1.2- to 13.3-fold. Therefore, it is important to screen the population with a genetic predisposition for PC early and to observe them continuously. A family history of PC increases the risk of developing PC. An increase in the number of first-degree relatives (FDR) diagnosed with PC is also associated with an increased risk of PC, from a 4.6-fold increased risk for a single affected FDR to a 32.0-fold increase for three or more affected FDRs. Familial pancreatic cancer (FPC), defined as at least one pair of FDRs with PC, accounts for 5-10% of total PC cases.

The population with genetic predisposition largely consists of high-risk individuals with FPC and inherited cancer syndromes. There has been no clear genetic cause in FPC, whereas in inherited cancer syndromes such as hereditary breast and ovarian cancer syndrome, Lynch syndrome, familial adenomatous polyposis, Peutz-Jeghers syndrome, hereditary pancreatitis, familial atypical multiple mole melanoma and so on, related genetic abnormalities and other associated cancers has been identified. In this presentation today, I would like to review the hereditary PC, especially the BRCA-related PC.

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Survivorship Session

"Go Beyond Cure of Breast Cancer"

MUST-HAVE KNOWLEDGE ABOUT GNRH AGONIST FOR PATIENTS WITH BREAST CANCER

Sung Gwe Ahn

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Gonadotrophin-releasing hormone (GnRH) agonists are increasingly being used for the treatment of breast cancer in women with functioning ovaries. They act by downregulating pituitary GnRH receptors, thereby suppressing the release of luteinising hormone (LH) and follicle stimulating hormone (FSH), which, in turn, reduce the main source of estradiol production in the ovaries. GnRH agonists have been shown to be as effective therapeutically as surgical ovarian ablation in pre- and perimenopausal women with advanced breast cancer. The combination of a GnRH agonist such as goserelin with selective estrogen receptor modulators (SERMs) or aromatase inhibitor, may be used to produce synergistic estrogen blockade. For a partner of GnRH agonist, the recent meta-analysis included data on 7030 premenopausal women included in the ABCSG 12, TEXT, SOFT, or HOBOE trials that compared an AI (anastrozole, exemestane, or letrozole) with tamoxifen, both given for 3~5 years, on a background of ovarian suppression with goserelin or triptorelin. Pooled analysis, with a median follow-up of 8 years, showed that treatment with an AI was associated with a significant 21% reduction in the risk for recurrence (defined as distant, locoregional, or new contralateral breast cancer) compared with tamoxifen. At SABCS 2021, updated analysis of the TEXT/SOFT trials was also presented, and in an analysis based on HER2 status and in the HER2-positive population, 12-year overall survival appeared to favor OS plus tamoxifen as compared to OS plus AI. While in the HER2-negative group who received chemotherapy, an absolute +3.3% improvement in overall survival in favor of OS plus exemestane was observed. Of note, similar data in the HER2-positive breast cancers was reported in HOBOE. In the light of increased morbidity with aromatase inhibitors and in the context of the reported data of the SOFT/TEXT trials, most patients are optimally treated with tamoxifen and ovarian function suppression (OFS). However, the option of aromatase inhibitors and OFS should be discussed on an individual basis.

BONE HEALTH IN BREAST CANCER PATIENTS

Seeyoun Lee

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Many breast cancer patients receive endocrine treatment according to hormone receptor status from their breast cancer. Some of the patients who receive endocrine treatment by aromatase inhibitor can suffer bone problems from the treatment. Unfortunately, some patients can undertreat their bone health during the endocrine treatment period. Therefore, we have to consider the multidisciplinary approach for bone health of breast cancer patients.

SEXUAL HEALTH AND REHABILITATION

Kyung Jin Eoh

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Sexual health, an essential component of emotional and physical well-being and quality of life, is often negatively impacted by malignancies and their treatment. Sexual function problems occur in 30-100% of cancer survivors. The prevalence of sexual health problems in female cancer survivors varies with cancer type and treatment modality, with gynecological cancer survivors having the highest prevalence (78%), but prevalence is also significant in breast and colorectal cancer patients (65% each). Sexual issues also span demographic characteristics, including age and cancer type, and are particularly prevalent among childhood cancer survivors.

In line with a conventional biopsychosocial model of sexual health, sexual issues during and after cancer exist in diverse ways depending on the effects of the cancer, the underlying physical condition, treatment, and the patient's psychosocial health, trauma, and cultural history. Survivors experience a variety of conditions, including arousal disorders, vaginal dryness/atrophy, decreased intensity, or frequency of orgasms, decreased sexual pleasure and desire, and dyspareunia, all of which can contribute to changes in body image and sexual self-esteem. Each of these aspects of sexual health can be affected by cancer and treatments including systemic chemotherapy, targeted drugs, immunotherapy, surgery, radiation therapy, and hormone therapy. Although pathophysiology is diverse, it includes anatomical, neurological, and hormonal changes such as sensory loss, early menopause, and psychological and social problems associated with cancer treatment and survival.

However, despite its high prevalence and potential to affect the quality of life of cancer survivors, many studies show that these concerns are not addressed in women living with or surviving cancer. Underdiagnosis and undertreatment can be attributed to communication barriers, lack of time or priorities, lack of knowledge/comfort with health providers, and, importantly, difficulties in treating these complex physical and psychological problems. It is important to recognize that treatment for the sexual condition and problems of cancer survivors is unique to the patient's specific interests, cancer type, treatment, preferences, relationships, mental health, and trauma history.

This presentation aims to summarize current studies evaluating interventions to improve sexual health (sexual function, body image, genitourinary and pelvic problems, and vasomotor symptoms) in female cancer survivors.

MEDICAL CONCERNS OF BREAST CANCER SURVIVORS

Su-Jin Koh

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Breast cancer is the most common primary malignancy and the second most common cause of cancer-related mortality among women worldwide. Long-term survival rates after a diagnosis of breast cancer are steadily rising. This is good news, but clinicians must also recognize that this brings new challenges to the medical community. Although breast cancer remains the most common cause of death after breast cancer diagnosis, other non-breast cancer causes of death, mainly heart and cerebrovascular diseases, represent a significant number of deaths among patients with breast cancer. These findings provide important insight into how breast cancer survivors should be counselled regarding future health risks. As breast cancer becomes a chronic condition rather than a life-threatening illness owing to advances in early diagnosis and more effective treatments, health care practitioners must recognize and manage the long-term sequelae of the constellation of therapeutic modalities. Survivors of breast cancer represent a unique and extremely complex group of patients; not only do they have the challenge of dealing with multiple long-term side effects of treatment protocols, but many are also forced to address the preexisting comorbidities of their therapies, which often include multiple other issues. Therapies have additional and/or additive side effects that may interfere with treatments directed toward the new primary diagnosis of breast cancer. Our mandate is to establish a smooth transition from patient with breast cancer to survivor of breast cancer while providing ongoing and future guidance.

ISSUES WITH FAMILY OF BREAST CANCER SURVIVORS

Juhee Cho

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A diagnosis of breast cancer is often a traumatic experience for a woman, creating an array of emotions such as fear, anger, and depression. Family members, including children and spouse, can also experience similar emotions. According to the American Psychological Association, when one member of a family has cancer, the whole family is affected. Considering that women do the bulk of kin-keeping within their families and are often the primary agents of familial socialization, a comparable number of families and their quality of life would be affected by breast cancer.

The diagnosis of breast cancer generates discomfort, changes in the lives of everyone involved feelings of loss, mutilation, indifference, prejudice, dependence, support, and resilience, which give life a new meaning. Family quality of life refers to individuals' perceived quality of family relationships such as satisfaction with family life, feelings about social support, perceived family strengths and weakness, and participation in family life.

Children can often sense emotional tension in the home, including anxiety, fear and uncertainty, brought on by a breast cancer diagnosis. Many professionals recommend telling children in language they can understand. Seeking the assistance of a mental health professional can help parents decide when and how to talk to their children. The dimension of the partner's mental health and hope as a way of adjusting to the diagnosis of their wife is very important. The men develop less depression and anxiety within such a care relationship with their wives, demonstrating greater acceptance of the caregiving role; however, going through the final stage characterizes a stressful moment that causes psychic suffering.

In this session, I would like to review how breast cancer impacts patients' family and their quality of life. I will also talk about patients' relationship with spouse and children. In addition, I will discuss about experience and burden of parents of young women with breast cancer considering increasing number of young women with breast cancer.

BARRIERS TO EMPLOYMENT OF BREAST CANCER SURVIVORS

Young Ae Kim

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In 2020, 2.3 million women were diagnosed with breast cancer worldwide. In the past five years, 7.8 million women were diagnosed with breast cancer, which was the most prevalent cancer type in the world. The incidence of breast cancer in women of all ages after puberty around the world is consistently increasing. In South Korea alone, 24,933 women were diagnosed with breast cancer in 2019, and it was the fifth most common cancer. The incidence of breast cancer has been increasing over the past two decades, and 258,172 women are currently living with a history of breast cancer.

In South Korea, the age of women diagnosed with breast cancer in 2019 is the highest in their 40s, followed by those in their 50s. Also, the highest employment rate is found in the same age group. However, there are wide-range of barriers for breast cancer survivors to return to work after cancer treatment during the most economically active period.

Barriers on return to work can be categorized into sociodemographic, disease-related, treatment-related, psychological, work-relate, policy and economic factors. In addition, conversation and support from the workplace also act as a part of barriers on returning to work. In Korea, there are laws and policies for cancer survivors, but the support system for direct job retention and supporting job search activities is insufficient. However, in other countries, cancer survivors receive job-related support in the same level as those who are handicapped.

Among the 667 breast cancer survivors aged 19 to 60 years, 82.3% were economically active before the diagnosis. Of these survivors, 25.5% were still engaged in the same type of economic activity, but 17.7% had reduced working hours and workload, 14.6% had other economic activities, and 36.1% were economically inactive.

Age was inversely related with engaging in economic activity. For instance, older survivors had stopped economic activity and younger survivors were on leave and had a plan to return to work. The economically active survivors before and after breast cancer diagnosis had a higher rate of no family members in need of care (69.3%). Those who stopped economic activity reported pain, discomfort, and feelings of anxiety or depression.

The group with a high score of 4 or higher in the distress measurement was the group with different

economic activities before cancer diagnosis, and the lowest was found in the group with the same economic activity before and after a cancer diagnosis.

Breast cancer survivors said that they were unaware of support systems and available information because they did not receive help related to economic activities in the community. They also reported that economic support and education for economic activities are needed.

52.1% of the general population reported that if the cancer survivor's job ability was low, the reason behind would be decreased physical strength. Among these general population, 43.8% reported that they would not hire cancer survivors.

Cancer survivors need support from multiple stakeholders such as medical staff, policy makers, employers as well as their families and colleagues for successfully returning to work.

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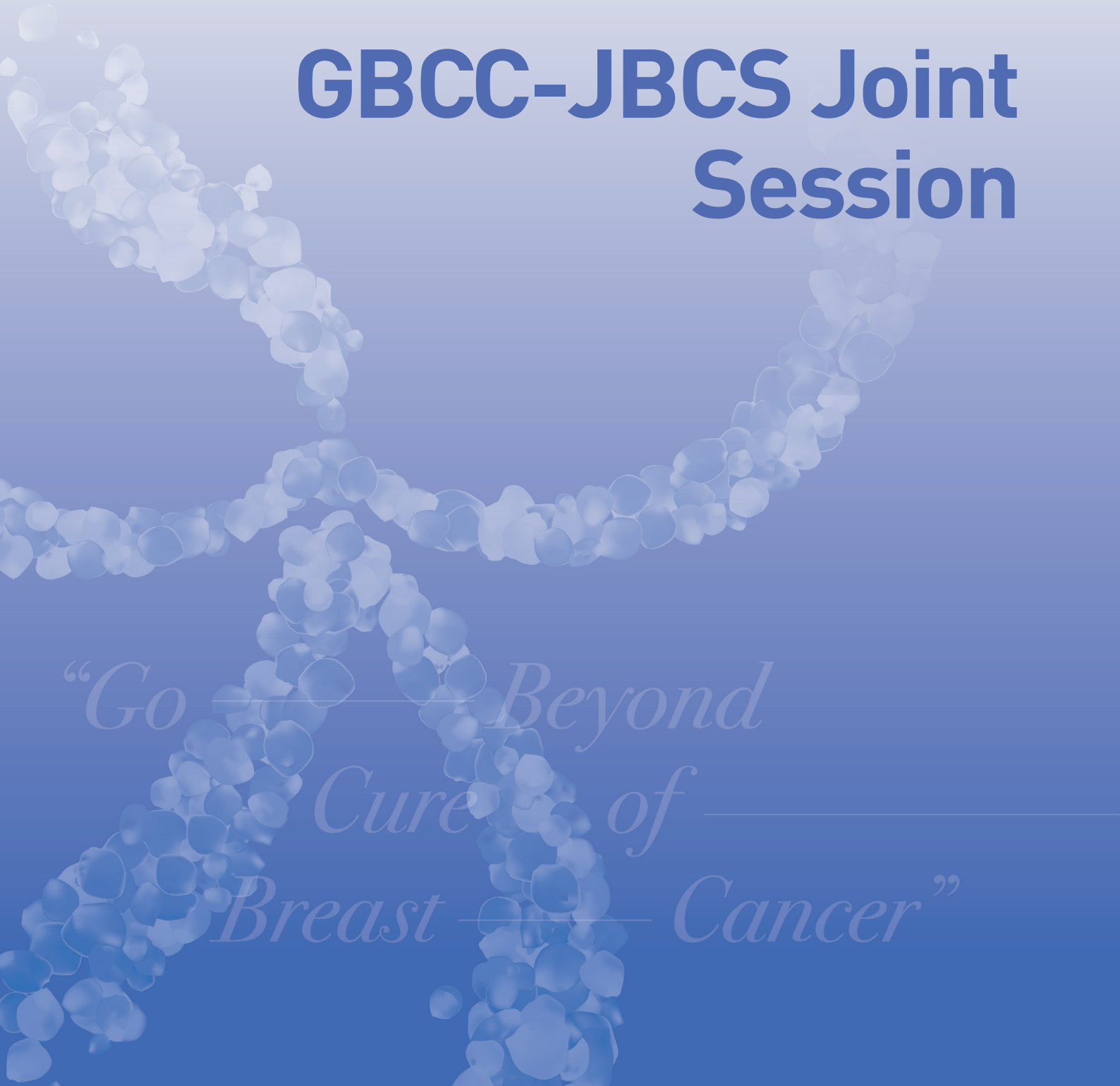

OMISSION OF SURGERY FOR PATHOLOGIC COMPLETE RESPONSE DIAGNOSED WITH MRI AND BIOPSY IN BREAST CANCER AFTER NEOADJUVANT CHEMOTHERAPY: OPTIMIST TRIAL

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Advances in chemotherapeutic and targeted agents have resulted in increased rates of pathologic complete response (pCR) rates after neoadjuvant systemic therapy (NST) for breast cancer. The pCR rates for triple-negative breast cancer (TNBC) and HER2-positive breast cancer are high as 50 and 70%, respectively. The results of large-scale meta-analyses suggest that patients with a pCR at surgery have favorable outcomes, with a 5-year disease-free survival rate of 85 to 90%.

In patients with residual tumor after NST, surgery has an important role in removing cancer and providing evidence for additional adjuvant systemic therapy, such as capecitabine for TNBC or TDM-1 for HER2-positive cancers. However, if a patient had achieved a pCR, the role of surgery may be limited to "pathologic confirmation" of no residual tumor. Early trials conducted in the 1970-90s omitting surgery resulted in higher rates of local recurrence without surgery and thus it is the standard treatment to offer breast and axillary surgery after NST. However, data from these studies suggested that when a complete clinical response is predicted with appropriate diagnostic methods, the local recurrence rates are comparable to those who receive a breast-conserving surgery.

Diagnostic imaging and biopsy techniques have improved greatly over the years. Recent feasibility and phase II studies evaluating the accuracy of imaging-guided biopsy to assess pCR in exceptional responders to NST have shown promising results. It is suggested that in patients with a radiologic complete response or minimal residual lesion of less than 1~2 cm on imaging, a sufficient number of tissues ($\geq$ 5~6 cores) sampled with a vacuum-assisted biopsy (VAB) using a 7~10 gauge needle could predict a pCR with a negative-predictive value of > 90% and a false-negative rate of < 10%.

In this talk, I will be introducing the OPTIMIST Trial, a multicenter, single-arm, non-inferiority trial evaluating the safety of omission of surgery for patients with a pCR diagnosed with MRI and VAB. It is planned to start enrolling patients by July, 2022. We will also seek collaboration opportunities between the KBCS and JBCS to expand the OPTIMIST Trial to a multinational study.

TRIALS OF SURGERY IN JAPAN

Hideo Shigematsu

National Cancer Center Hospital, Department of Surgery, Japan

Title: A single arm confirmatory study to evaluate the efficacy of non-surgical therapy for HER2 positive early breast cancer with clinical complete response after primary systemic therapy: (JCOG1806: AMATERAS-BC study)

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Background: Neoadjuvant systemic therapy (NST) has become the standard care of early breast cancer and pathological complete response (pCR) rates of 50-70% are reported in chemo-sensitive subtypes. Increasing use and high pCR rates of NST raise the question that omission of surgery may be one of the treatment options in case showing significant response to NCT. Because historical trials of omission of surgery following NCT in earlier era failed to show acceptable local control, appropriate patient selection and accurate prediction of pCR are warranted to proceed clinical trials of omission of surgery following NST. Regarding to this concept, there are currently two approaches for clinical trials evaluating omission of surgery following NST. First, rigorous patient selection and diagnostic procedure for extremely low false negative rate and high specificity are essential for omission of surgery. Second, foci of residual microscopic disease after NAC can be controlled by radiotherapy and additional systemic therapy. In accordance with the later concept, we started a single arm confirmatory study to evaluate the efficacy of non-surgical therapy for HER2 positive early breast cancer with clinical complete response after primary systemic therapy (JCOG1806: AMATERAS-BC study). This clinical trial has been registered at Japan Registry of Clinical Trials as jRCTs031190129 and conducted by the Japan Clinical Oncology Group (JCOG) Breast Cancer Study Group under public fund (National Cancer Center Research and Development Fund).

Methods: The key eligibility criteria are as follows: 1) Histologically confirmed as invasive HER2+ breast cancer. 2) cT1-2, N0, M0 (UICC 8th). 3) No ipsilateral BC. 4) Women aged 20-74 years. 5) ECOG

performance status 0 or 1. 6) Adequate hematologic and organ function. 7) Ejection fraction is over 50%. 8) Written informed consent. Prior to primary systemic therapy (PST), breast marker (Ultracore Twirl) is placed in the breast tumor. Six to eight courses of PST consisted with dual HER2 inhibitors (trastuzumab and pertuzumab) and/or cytotoxic agents are administered. After completion of PST, clinical complete response (cCR) is diagnosed with multimodal examination. cCR is defined as 1) Not palpable breast mass by physical examination, 2) No enhanced breast mass by enhanced MRI, 3) No breast mass by breast sonography and 4) No residual disease in core biopsy specimen. In pure HER2 subtype, core biopsy can be spared if there is no mass in both enhanced MRI and breast sonography. In cases with cCR, whole breast radiotherapy and boost radiation to tumor bed followed by 9 months dual HER2 inhibitors are administered as non-surgical therapy. Endocrine therapy is administered for luminal HER2 subtype. In non-cCR cases, standard surgical resection of breast tumor and axillary lymph node staging is performed and adjuvant therapy is administered in a physician's direction. The primary endpoint is a 3-year distant metastasis-free survival (DMFS), and the secondary endpoints are overall survival, relapse free survival, local recurrence and cosmetics outcome. Given the threshold and expected of DMFS at 3-year is 93% and 98% with a significance level 2.5% and 80% power, 170 cCR cases are statistically required. Assuming cCR rate of 50% in this study, 350 pts enrolment are required. First patient enrollment was done in November, 2019 and 206 pts have been enrolled as of February 28, 2022. Patient enrollment is expected to be completed by November, 2022, and primary endpoint is planned to be published in early 2026.

IMPACT OF POST-MASTECTOMY RADIOTHERAPY IN BREAST CANCER PATIENTS WITH EXCELLENT RESPONSE AFTER NEOADJUVANT CHEMOTHERAPY: A PHASE 3, MULTICENTER, RANDOMIZED, NON-INFERIORITY STUDY

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Neoadjuvant chemotherapy has been established in standard clinical practice for patients with locally advanced breast cancer or large operable disease, particularly in HER2+ breast cancer or triple-negative breast cancer. In previous randomized clinical trials, neoadjuvant chemotherapy has been found to be equally effective as adjuvant chemotherapy in prolonging survival. Furthermore, neoadjuvant chemotherapy has some potential clinical advantages, such as the conversion of mastectomy candidates to candidates for breast-conserving surgery and the improvement in cosmesis by reducing the size of lumpectomy in patients who are breast-conserving surgery candidates but present with large tumors. In addition, it can allow decreasing in unnecessary axillary lymph node dissection (ALND) because the previous pivotal studies showed that ALND could be omitted if no metastasis to three or more sentinel lymph nodes is noted after neoadjuvant chemotherapy.

Although radiotherapy has been shown to reduce locoregional recurrence (LRR) in breast cancer, the guideline for post-mastectomy radiotherapy (PMRT) is still unclear in patients who received neoadjuvant chemotherapy followed by mastectomy. Without a shred of robust evidence, several guidelines recommend a PMRT in patients with initial clinical tumor size larger than 5cm or suspicious axillary lymph node, regardless of response to neoadjuvant chemotherapy. However, PMRT induces acute and chronic complications such as capsular contraction, asymmetry, and reconstruction failure. Since the proportion of immediate breast reconstruction increases even in patients who received neoadjuvant chemotherapy followed by a mastectomy, unnecessary PMRT should be reduced.

The accumulating evidence suggests that achieving an excellent treatment response to neoadjuvant chemotherapy such as pathologic complete response (pCR) or residual cancer burden (RCB) class 0-I is highly associated with a favorable prognosis. These consistent outcomes have brought forward the hypothesis that PMRT can be omitted in patients who achieved excellent treatment response after neoadjuvant chemotherapy. However, there is a paucity of data for this issue. Our previous retrospective study revealed that the excellent treatment responders who underwent neoadjuvant chemotherapy followed by mastectomy had a favorable prognosis, regardless of PMRT: 5-year disease-free survival was the

same in patients with PMRT or without PMRT (91.0% vs. 91.0%, respectively).

In line with our previous data, a few other studies have recently reported that PMRT has no advantage in survival in patients who achieved excellent treatment response after neoadjuvant chemotherapy. Nevertheless, these reports have a critical limitation in that the evidence level is too low to apply in clinical practice due to the retrospective nature.

Accordingly, we designed a phase III, multicenter, randomized, non-inferiority study to identify whether PMRT can be omitted in patients with invasive breast cancer who achieved excellent response (pCR or RCB class o-I) after neoadjuvant chemotherapy. Here, we hope to share our protocol and discuss it together in this meeting. Also, we expect to proceed this clinical trial with the Japanese Breast Cancer Society (JBCS). Through this clinical trial, it is able to establish a new treatment guideline for de-escalating radiotherapy in neoadjuvant settings.

TRIALS OF RADIATION THERAPY IN JAPAN

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In Japan, there are not many large-scale clinical trials on radiation therapy (RT) for breast cancer. One reason for this may be that there are many small RT facilities in Japan and the number of patients treated at each facility is smaller than in other countries. No clinical trials on escalation are available as far as I know. I would like to introduce the Japanese clinical trials on de-escalation of in this section.

De-escalation in postoperative RT for breast cancer can be broadly classified into the following categories: accelerated partial breast irradiation (APBI), hypofractionated (HF) whole breast irradiation (WBI), omission of regional node irradiation including postmastectomy RT, and omission of WBI after breast-conserving therapy (BCS). Of these, the clinical trials conducted and planned in Japan will be presented.

1. APBI: A prospective multi-institutional feasibility study on accelerated partial breast irradiation using interstitial brachytherapy was conducted. Several small clinical trials of APBI are conducted, and unique clinical trials on radical irradiation without surgery using particle beams are ongoing.

2. Moderately hypofractionated WBI: A multicenter, prospective, single-arm, confirmatory trial of hypofractionated whole breast irradiation after breast-conserving surgery in Japan has been conducted by Japan Clinical Oncology Group (JCOG), and have been published.

3. Ultra-hypofractionated WBI: Although no clinical trial has yet been conducted in Japan, one clinical trial is planned by a group at Kyoto University Hospital and will expected to start soon.

4. Omission of WBI after BCS: Prospective study of wide excision and endocrine therapy WithOut RadioTHerapy (WORTH) for node-negative estrogen receptor positive early.

Breast cancer with histologically negative margins (WORTH trial) was conducted. Prospective intervention study of radiation therapy omission after partial mastectomy in invasive breast cancer which include young patients is ongoing.

RANDOMIZED, PHASE II TRIAL TO EVALUATE THE EFFICACY AND SAFETY OF ATEZOLIZUMAB PLUS CAPECITABINE ADJUVANT THERAPY COMPARED TO CAPECITABINE MONOTHERAPY FOR TRIPLE RECEPTOR-NEGATIVE BREAST CANCER WITH RESIDUAL INVASIVE CANCER AFTER NEOADJUVANT CHEMOTHERAPY

In Hae Park

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Triple negative breast cancer (TNBC), lack of ER, PR and HER2 expression, is known to have aggressive clinical features such as early recurrence, drug resistance, and frequent distant metastasis at the diagnosis. The most effective chemotherapy combinations used for early TNBC include anthracycline, taxanes, and/or platinum agents. Achieving a pathologic complete response (pCR) after neoadjuvant chemotherapy (NAC) provides important prognostic information and is considered as a surrogate endpoint in many clinical trials especially with TNBC. Patients with residual invasive disease after NAC have a high risk for early relapse and worse prognosis compared to those with pCR. Upon relapse, patients with metastatic TNBC have poor outcomes, with rapid progression and decreased overall survival (OS). Thus, there is a substantial need to improve the efficacy of neo/adjuvant treatment.

Therefore, patients who did not get pCR could be better candidates for additional adjuvant treatment because their risk of recurrence would be higher than those with pCR. The CREATE-X (capecitabine for residual cancer as adjuvant therapy) trial involved patients with HER2 negative breast cancer who did not have a pCR. This study showed that adjuvant capecitabine treatment improved 5-yr rate of disease-free survival of 74.1% compared to 67.6% in the control group. In the subgroup analysis, it appeared to be more beneficial in TNBC subtype (HR = 0.58, 95% CI, 0.39-0.87). Recently, KEYNOTE-522 study showed that anti-PD-L1 antibody (pembrolizumab) cooperated with neoadjuvant chemotherapy increased pCR rate in TNBC patients. In addition, adjuvant pembrolizumab also prolonged event free survival in non-pCR group. However, this study received many critics that adjuvant capecitabine was not administered for non-pCR patients as a standard treatment and the beneficial effect of immunotherapy was not noted for patients with pCR. Therefore, we need to elaborate the indication of immunotherapy for TNBC patients and evaluate the role of immunotherapy compared to standard capecitabine treatment.

This study is a phase II, multicenter, randomized open label trial of atezolizumab (anti-PD-L1 antibody) and capecitabine compared with capecitabine monotherapy in patients with TNBC who had residual disease after NAC. 284 patients will be enrolled from 15 sites in Korea with a primary objective to access the 5-yr invasive disease-free survival (IDFS) rate. Secondary objectives include 5-yr IDFS rate in PD-L1 positive population, distant relapse free survival (DRFS), overall survival (OS), and safety. Major inclusion and exclusion criteria are followings; 1) histologically confirmed TNBC, 2) received anthracycline and taxane based NAC followed by complete breast surgery, 3) residual disease after NAC must be ≥1 cm in the greatest dimension, and/or have macroscopically positive lymph nodes. The study is open with 13 patients enrolled at the time of submission. ClinicalTrials.gov Identifier: NCT03756298

TRIALS OF ER(+) CANCER IN JAPAN

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For luminal type early breast cancer, both escalating and de-escalating strategies are developed. NEOS is a phase III trial evaluating disease-free survival (DFS) between chemotherapy followed by endocrine therapy and endocrine therapy alone in luminal breast cancer patients who received neoadjuvant endocrine therapy (NET). This study showed that NET can be a standard of care, but clinical response to NET did not predict the benefit of adjuvant chemotherapy. So, the clinical question who should receive chemotherapy remains to be solved.

As an escalating strategy, we now use abemaciclib, S-1 and olaparib for high-risk patients based on monarchE, POTENT and OlympiA trials, respectively. We now have a clinical question whether we should select abemaciclib, S-1, or combination of them for luminal breast cancer, and the question is more complex for gBRCA-mutated luminal breast cancer.

Immune-checkpoint inhibitors for luminal breast cancer is another important topic. For metastatic luminal breast cancer, we conducted two clinical trials using nivolumab. WJOG9917B (NEWBEAT) is a phase II trial evaluating first-line therapy with paclitaxel + bevacizumab + nivolumab for HER2-negative metastatic breast cancer and showed high response rate (74%) in luminal type patients. Now, JCOG1919E (AMBITION) trial, a phase III trial comparing paclitaxel + bevacizumab + atezolizumab and paclitaxel + bevacizumab in patients with metastatic luminal breaset cancer, is ongoing. WJOG11418B (NEWFLAME) is a phase II trial evaluating endocrine therapy (letrozole or fulvestrant) + abemaciclib + nivolumab for metastatic luminal breast cancer. Unfortunately, this study was stopped due to safety concern, mainly liver toxicities and interstitial lung disease.

From now on, both escalation and de-escalation are important if we select appropriate patients. Individualization is most essential, and we need to conduct clinical trials to answer many clinical questions.

OVARIAN FUNCTION SUPPRESSION IN PREMENOPAUSAL WOMEN WITH NODE POSITIVE DISEASE AND LOW GENOMIC RISK: OPAL TRIAL

Tae-Kyung Robyn Yoo

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The recent publication of the RxPONDER trial presented some unexpected results regarding premenopausal women with hormone receptor-positive, one to three positive lymph nodes and genomic low-risk breast cancer. The addition of adjuvant chemotherapy resulted in a relative increase of 40% in invasive disease-free survival in this population, whereas no chemotherapy benefit was seen in postmenopausal women. The updated results of the MINDACT trial reports similar outcomes, showing a relative increase of 46% in distant metastasis-free survival in women of 50 years-old or younger with high clinical risk and low genomic risk undergoing adjuvant chemotherapy, compared to younger women not undergoing chemotherapy.

These results aroused a lively discussion on the role of chemotherapy in premenopausal women, debating whether chemotherapy benefit is mainly due to treatment-induced menopause or direct cytocidal effects. The low rate of ovarian function suppression in the endocrine only arm in both trials provoked this debate.

In this perception, we have designed a prospective randomized clinical trial to obtain an answer to this question. A MAMMPRINT test will be performed to premenopausal women with a hormone receptor-positive, HER2-negative, N1 breast cancer and genomic low-risk patients will be identified and enrolled. Participants who provide consent will be randomly assigned in a 1:1 ratio to receive chemoendocrine therapy or endocrine therapy only. Ovarian function suppression will be a necessity in the endocrine therapy only group. A sample of 1,774 patients would be needed to attain 80% power to detect non-inferiority at a one-sided significance level of 2.5% with a non-inferiority margin of 3%. An expected rate of distant metastasis-free survival at 5 years of 96.0% in the chemoendocrine therapy group is assumed, along with a dropout rate of 10%.

We anticipate to have a vivid discussion on this topic and discuss about the specifics of this clinical trial.

RANDOMIZED CONTROLLED TRIAL OF TRASTUZUMAB WITH OR WITHOUT CHEMOTHERAPY IN OLDER PATIENTS: RESPECT TRIAL

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As for clinical trials in Japan, we carried out the first randomized controlled trial comparing trastuzumab with or without chemotherapy in older patients (J Clin Oncol 38: 3743-52, 2020). This study was a treatment selection design in which a non-inferiority criterion was pre-defined. Patients were randomly assigned either trastuzumab monotherapy or trastuzumab plus chemotherapy of physician's choice from regimens prespecified in the protocol. As the primary endpoint 3-year disease-free survival was 89.5% with trastuzumab monotherapy versus 93.8% with trastuzumab plus chemotherapy (hazard ratio = 1.36; 95% confidence interval [CI], 0.72 to 2.58, $P = 0.51$). At 3 years, restricted mean survival time differed by -0.39 months between arms (95% CI, -1.71 to 0.93, $P = 0.56$). The grade 3 or 4 non-hematological adverse events occurred in 11.9% for trastuzumab monotherapy versus 29.8% for trastuzumab plus chemotherapy ($P = 0.0003$). Clinically-meaningful health-related quality of life (HRQoL) deterioration rate showed significant differences at 2 months (31% for trastuzumab monotherapy versus 48% for trastuzumab plus chemotherapy; $P = 0.016$) and at 1 year (19% versus 38%; $P = 0.009$). The primary objective of non-inferiority for trastuzumab monotherapy was not met; however, the observed survival outcome was favorable with lower toxicity and better HRQoL profile. Therefore, we concluded that trastuzumab monotherapy can be a reasonable option. As secondary endpoints, details on QOL, change of cognitive functioning, and cost-effectiveness were investigated. Detrimental effects of adjuvant chemotherapy on QoL, morale, and activity capacity lasted for 1 year but were not observed at 3 years; then care and social support for at least 1 year is required when standard chemotherapy is given (J Clin Oncol 39: 2452-62, 2021). On the other hand, the cognitive functioning did not demonstrate a negative impact of chemotherapy for at least 3 years (Breast Cancer Res Treat 188: 675-83, 2021). The base case analysis indicated that adjuvant treatment with trastuzumab plus chemotherapy was likely to be a cost-effectiveness choice (Clin Drug Investig, DOI: 10.1007/s40261-022-01124-y).

In this way, not only survival outcome but also adverse effects and QoL analysis are important to consider comprehensive balance assessment between benefits and harms in comparative studies. We show this trial in detail and discuss future perspective of clinical trials.

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"Go Beyond Cure of Breast Cancer"

EDUCATION AND DEVELOPMENTAL PROGRAM FOR YOUNG DOCTORS IN KOREA

Soo Kyung Ahn

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The substantial increase in the complexity of breast cancer care in the last few decades has resulted in significant improvements in survival rates and also in the quality of life of breast cancer survivors. Breast cancer is one of the most dynamic and innovative diseases in terms of changes in principles and guidelines for diagnosis and treatment. We need to evaluate emerging clinical data and evolving strategies for the diagnosis and treatment of breast cancer, and apply clinical trial data appropriately in order to optimize outcomes for individual patients. Therefore, it is very important to provide young doctors with education program offering proper and accurate information of breast cancer. The Korean Breast Cancer Society (KBCS) is running programs called the School of Breast Disease and Academy of Breast Clinicians, as well as regular symposium on systemic therapy and hereditary breast cancer. There are some external educational programs such as ultrasound guided intervention skills by the Korean Surgical Ultrasound Society, breast oncoplastic surgery education by the Korean Oncoplastic Breast Surgery Study group; KOPBS. Recently, education program about robot assisted breast cancer surgery is held by Korea Robot-Endoscopic minimal Access Breast Surgery study group; KoREa-BSG. We are hopeful that these programs for young doctors develop into collaborative study group and meaningful research.

EDUCATION AND DEVELOPMENTAL PROGRAM FOR YOUNG DOCTORS IN TAIWAN

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Taiwan breast cancer society (TBCS) provide educational program for young doctors who are interested in learning the knowledge about diagnosis and treatment for breast cancer. For young doctors who plan to pass the examination for breast cancer subspecialty, we provide specific education program for this purpose about one month before the examination every year. Besides the symposium such as Post San Antonio Cancer Symposium, annual meeting such as Taipei International Breast Cancer Symposium, Annual Meeting of the Taiwan Surgical Association, and Taiwan Joint Cancer Conference, we also established a breast cancer e-learning academy, by uploading a series of talk for updated topics in the cloud. The contents of the e-learning program are renewed every year. We also provide the real time online meet the expert meeting, by inviting the renowned international scholars to have a interactive lecture and discussion with young doctors. With the support from Health Promotion Administration, Ministry of Health and Welfare, we provide the regular learning programs for how to diagnose and manage the suspicious lesion detected by screening mammography to young breast cancer doctor as well as family medicine and Gynecology young doctors. We also generate the treatment guidelines, including following topics: HER2+ breast cancer neoadjuvant consensus, triple negative breast cancer consensus, elderly breast cancer consensus, HR+ metastatic breast cancer consensus, Taiwan BRCA testing consensus, early breast cancer neoadjuvant consensus, and consensus on controversial issues. During this talk, we will elaborate the content of these program.

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CURRENT STATUS AND FUTURE STRATEGY FOR SPORADIC AND HEREDITARY CHINESE BREAST CANCER IN ASIA

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Breast cancer was the second most common cancer globally in 2018, but it became the most common malignancy in 2020, according to the International Agency for Research on Cancer (IARC). In 2020, 2,206,771 patients were diagnosed with breast cancer (11.4% of all cancer cases), and the age-standardized incidence rate (ASR) of breast cancer was also the highest at 47.8. Among all breast cancers, the highest number of breast cancers occurred in Asia, accounting for 45.4% of all breast cancers with 1,026,171 cases.

In the 1990s, the ASR of breast cancer increased globally, but since the 2000s, it slowed down or even decreased in Europe and North America, but continued to increase in Asia. In western countries, the mortality of breast cancer is falling steadily and the five-year survival rate reaches 90% on average, but in Asian countries, it's increasing. Especially in those under the age of 50, increasing mortality is an important issue for both health care and social-economic aspects.

Breast cancer also increased steadily in Korea and during the year 2018, there were 23,547 patients with invasive breast cancer, approximately four times more than 5,848 patients in 2,000. By contrast, carcinoma in situ increased from 386 patients to 4,502, which was about 11 times more. One of the features of breast cancer observed commonly in Asian countries is that the affected age of breast cancer is lower than that in western countries. In 2018, the median age of breast cancer in Korea was 52.4, which was an increase of more than 47.0 in 2000, but yet lower than that in western countries. In Korea, with the expansion of screening breast examination as part of medical checkups, early-stage breast cancer increased gradually. In 2018, 91.8% of the entire patients with breast cancer were in stage 0, 1, and 2.

In Asian countries including Korea, the risk factors of breast cancer are changing with the fast-changing social-economic status. In particular, low birth rate, increase in women's age at first birth, lower age of the first menstruation, increase in obesity, an increase of female smoker and drinking is deeply related to the fast increase of breast cancer in Asia. Asian countries' the medical environment is different from western developed countries and there is a difference in the main features of breast cancer. Therefore, it is necessary to have a treatment strategy for breast cancer occurring in Asia as well as that in western countries.

OPTIMAL MANAGEMENT FOR CHINESE WOMEN WITH HEREDITARY BREAST CANCER

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Breast cancer is the most common malignant disease in Chinese women, with more than 420,000 new cases in year 2020, and breast cancer alone is account for approximately 20% of all new cancer cases in Chinese women, and it is the leading cause of cancer death in Chinese women younger than 45 years. Considering the large burden of health care in Chinese women with breast cancer, early detection and optimal treatment for these women are therefore extremely important.

Approximately 10% Chinese women with breast cancer may carry a germline pathogenic variant in breast cancer susceptibility genes (named as hereditary breast cancer). Women with hereditary breast cancer may exhibit a different clinical-pathological characteristics compared with those with sporadic breast cancer. Therefore, the treatment strategies of hereditary breast cancer is likely to be different from that of sporadic breast cancer.

BRCA1 and BRCA2 are the most important breast cancer susceptibility genes, and mutations in these genes are lead to a high-risk for development of breast cancer. In order to comprehensively understand the prevalence of BRCA1/2 germline mutations in Chinese women with breast cancer, we screened BRCA1/2 germline mutations in 8085 unselected Chinese women with breast cancer. The overall BRCA1/2 mutation rate was 5.3% in the entire cohort of 8085 patients. However, we observed that approximately one third BRCA1/2 mutations are novel in Chinese women that have not been previously reported in Caucasian women. We therefore conduct a kin-cohort study to investigate the estimated cumulative risks in Chinese women who carry a deleterious BRCA1 or BRCA2 mutation. We found that the estimated cumulative risks of breast cancer by age 70 years are 37.9% [95% confidence interval (CI) 24.154.4%] for BRCA1 mutation carriers and 36.5% (95% CI 26.751.8%) for BRCA2 mutation carriers in Chinese women, respectively. An additional study suggested that the 10-year cumulative risk of contralateral breast cancer in Chinese women with unilateral breast cancer was 15.5% (95% CI, 9.924.2) for BRCA1 carriers, 17.5% (95% CI, 10.928.0) for BRCA2 carriers and 3.2% (95% CI, 2.54.1) for noncarriers.

Therefore, women with a BRCA1 or BRCA2 mutation have a high risk of contralateral breast cancer after the primary unilateral breast cancer. Therefore, prophylactic contralateral mastectomy is an option for women with breast cancer who carry a BRCA1/2 mutation.

Breast conserving therapy (BCT) is a standard approach for the early-stage breast cancer patients, patients received a breast-conserving therapy have a good cosmetic outcome as well as similar or even

better survival when compared with those who received mastectomy. Whether BRCA1/2 mutation carriers should be treated with breast-conserving therapy is not fully elucidated. Therefore, we conducted a retrospective cohort study to compare the survival of patients who underwent BCT, mastectomy with radiotherapy, or mastectomy alone in a large series of 8396 unselected patients with breast cancer in which the BRCA1/2 mutations were determined. After a median follow-up of 7.5 years, both BRCA1 and BRCA2 carriers treated with BCT exhibited non-significantly better survival than those treated with mastectomy with radiotherapy or mastectomy alone after adjusting for clinicopathological factors and adjuvant therapy. Our findings suggested that BRCA1/2 carriers treated with BCT have at least comparable survival when compared with those treated mastectomy with radiotherapy or mastectomy alone, and BCT could be an option for BRCA1/2 mutation carriers when the tumor is clinically appropriate for BCT.

Neoadjuvant chemotherapy is widely used in the operable primary breast cancers and provides a platform to quickly evaluate the efficacy of the chemotherapy regimens. We investigated the associations between the BRCA1 mutation carriers and response to neoadjuvant anthracycline-based or taxane-based chemotherapy in Chinese women with BRCA1/2 mutated triple-negative breast cancers. We found that BRCA1 mutation carriers are extremely more sensitive to anthracycline-based neoadjuvant regimens than non-carriers (pCR rate, 57.1% versus 29.0%), but this is not case for taxane-based neoadjuvant regimens. Furthermore, BRCA1/2-mutated triple-negative breast cancers patients gain a survival benefit when carboplatin is added to standard anthracycline- taxane based neoadjuvant chemotherapy.

Taken together, these studies suggested that BRCA1/2 mutation carriers may be more likely to benefit from cisplatin or anthracycline-based neoadjuvant regimens but not from taxane-based regimens. These findings raise an interesting question that BRCA1/2 mutation status is not only a marker for evaluating breast cancer risk, but also a predictor for selecting the optimal neoadjuvant regimens as well. However, cautions are needed before the data are translated into clinical practice. Randomized prospective clinical trials are warranted to confirm these findings.

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CLINICAL TRIALS OF BREAST CANCER SURGERY IN KOREA & INTRODUCTION TO KBCSG

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Since the establishment of the Korean Breast Cancer Study Group (KBCSG) by the Korean Breast Cancer Society in 2007 to promote clinical research in Korea, it has approved 22 studies regarding important topics in breast cancer. Many of those studies attempted to address the needs of patients in Korea and the Asian region, reflecting the cultural differences and personal preferences in the area. There is a global trend to pursue de-escalation of surgical treatment, and there are a number of ongoing innovative trials in an effort to develop evidence of safety for doing less.

The PLATO (Personalized neoadjuvant strategy in ER+ HER2- breast cancer to increase BCS rate) trial aims to increase the BCS conversion rate after neoadjuvant systemic therapy for ER+/HER2- breast cancer. Neoadjuvant systemic therapy is decided according to genomic risk as determined by Mammaprint.

In Korea, the majority of the patients undergo frozen section biopsy for resection margins after BCS. The OFF-MAP (A randomized controlled trial for doing vs. omitting intraoperative frozen section biopsy for resection margin status in selected patients undergoing breast-conserving surgery) trial randomizes patients to evaluate resection margins during surgery with frozen section biopsy or not. It aims to provide evidence for omitting frozen section biopsies for patients who meet certain criteria.

In patients with clinically node-negative disease on physical examination and/or ultrasound, it is estimated that up to 95% of those patients actually do not have lymph node metastasis.The NAUTILUS (No axillary surgical treatment In clinically lymph node-negative patients after ultrasonography) trial is a multicenter, prospective randomized trial that compares omission of sentinel lymph node biopsy with standard axillary staging surgery. It will analyze the 5-year disease-free survival as the primary endpoint.

For exceptional responders to neoadjuvant chemotherapy with no residual tumor, surgical removal of the lesion in the breast and/or axillary lymph node may be an overtreatment and its role may be limited to pathological confirmation of pathologic complete response (pCR). The ASLAN (Avoid axillary sentinel lymph node biopsy after neoadjuvant chemotherapy) trial is a single arm, non-inferiority trial where surgery of the axilla is omitted for patients with a cN0-1 before neoadjuvant chemotherapy when a breast pCR after breast-conserving surgery. On the other hand, the OPTIMIST (Omission of surgery for predicted pCR patients wIth MRI and vacuum-assisted bIopsy in breast cancer after neoadjuvant chemotherapy) trial is a single arm, non-inferiority trial where breast surgery is omitted for patients with no residual tumor on vacuum-assisted biopsy in patients with a near radiologic complete response on MRI. The primary endpoint for both trials is 5-year disese-free survival.

The details of these ongoing studies will be introduced and possible collaboration opportunities between the Korean Breast Cancer Society and the Society of Surgical Oncology will be discussed.

TRIALS IN BREAST CANCER LEAD BY SURGICAL ONCOLOGISTS IN THE US & INTRODUCTION TO SSO

Jennifer Plichta

Duke Univ., Department of Surgery, U.S.A.

During this presentation, we will cover some of the significant trials and research conducted by oncologists and breast surgeons in the United States. We will review the results from recently published trials, such as the OlympiA and RxPONDER trials, which highlight the importance of both germline genetic testing and somatic/genomic testing. Given the ongoing controversary surrounding local-regional therapy for women with metastatic breast cancer, we will review the recently published findings from the ECOG-ACRIN 2108 trial. In addition, we will discuss the ongoing COMET trial, which is evaluating the potential de-escalation of care for patients with ductal carcinoma in situ. Furthermore, we will review some of the "Choosing Wisely" guidelines related to de-escalation of care and selective use of radiation and sentinel lymph node biopsy in the elderly. Lastly, a brief introduction the Society of Surgical Oncologists will also be provided.

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Junior Doctors Forum

"Go Beyond Cure of Breast Cancer"

HOW TO ESTABLISH YOURSELF IN THE BREAST CANCER SOCIETY AS A YOUNG DOCTOR/RESEARCHER

Matteo Lambertini

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Medical oncology in general and breast cancer more specifically are rapidly evolving. It is a fascinating field characterized by a continuous and fast development of innovative technologies, new biomarkers and effective anticancer therapies. Thus, it is crucial for all professionals to keep up to date. This could be more difficult for trainees and young oncologists, due to the several challenges they have to face on the top of their clinical duties, including the issues in being involved in research activities for those interested. Although problems may differ based on the country of origin, guidance is crucial for the career development of young oncologists and those interested in establishing themselves in the research field.

Several key factors should be considered by young oncologists for trying to establish themselves in the research field.

Firstly, developing research projects that can positively impact on the life of patients with cancer should be the starting point for all young oncologists interested in pursuing a career in academia. To achieve that, finding proper mentors and collaborators is key. Mentorship is crucial for career development and academic productivity. Identifying the right mentors for young oncologists may be challenging. Key features to be identified in the mentors should be competence, confidence and commitment. Moreover, it is important that young oncologists discuss, share ideas and collaborate closely by expanding their network of collaborators.

In order to do so, all young oncologists interested in pursuing a career in the research field should take advantage of the many opportunities offered by international scientific societies. Among them, many fellowship opportunities are made available free of cost upon acceptance by scientific societies. Indeed, a fellowship is a unique opportunity to strengthen research skills, knowledge and expertise of young oncologists by providing the time and infrastructure needed for implementing their research projects, finding new mentors and collaborators.

A final crucial component for young oncologists to establish themselves in the research field is motivation. The research environment is complex, competitive and time consuming with some successes but also several fails. Hence, being perseverant, following the rules, being fair and delivering the work should be considered key features for all young oncologists interested in working in the research environment.

FROM ASIA TO THE WORLD - HOW TO ENJOY WORK AT THE GLOBAL STAGE

Masakazu Toi

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It is important to take notes when you come up with something, or when you feel that you can expect various improvements by devising something. To realise that research, it is necessary not only to look at the literature and make a survey from various angles, but also to discuss with experts in each field. Current clinical studies and trials are made up of many parts and require multiple processes to be performed. Therefore, nothing can be achieved without a good research team. And it is important to be familiar with the steps to build a clinical study. In addition, research may not proceed as planned, so it is necessary to prepare backup plans. These studies essentially consist of strong scientific interests, curiosity, and solid methodologies. The scale of the study will be determined as needed. There are various situations, such as conducting research in one research unit, conducting joint research within a university, or conducting joint research with multiple institutions. When large-scale research or rapid research results are required, nation-wide research or global research will be devised. Young researchers often need supporters to carry out such large-scale research. In global research, many researchers gather. In many cases, unique and open-minded researchers from various backgrounds come together, which often leads to dynamic research. It is true that the research there will be fun and enrich you.

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Nursing Session

"Go Beyond Cure of Breast Cancer"

THE EDUCATION FOR BREAST CANCER PATIENTS DURING COVID PANDEMIC

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Many things have changed due to COVID-19, one of which is patient education.

Prior to COVID-19, in 2019, the Seoul National University Bundang Hospital Cancer Edu-Info Center regularly provided 20 lecture-type education and 25 participatory education for cancer patients, with a participation rate of 85 percent with 400 participants per month.

After COVID-19, face-to-face group education was completely suspended due to the hospital's COVID-19 prevention guidelines, and individual education was possible, but it was difficult to implement due to a lack of manpower.
Accordingly, the hospital actively utilized Hichart and conducted health lectures or delivered health information through YouTube channels.

High charts for breast cancer patients are "Concept and Treatment of Breast Cancer", "Guidance on Breast Cancer Surgery", and "Guidance on Breast Cancer Radiation Treatment". "Nutrition management of breast cancer patients", "arm exercise of breast cancer surgery patients", "genetic breast cancer counseling", "chemotherapy guidance", and "nutrition management of patients undergoing chemotherapy".

As such, even after COVID-19, information is provided through various channels, but educational program for the emotional and psychological support of cancer patients is insufficient.

In fact, I feel that the number of breast cancer patients complaining of psychological problems such as depression and anxiety has increased due to the destruction of daily life and disconnection of human relationships due to COVID-19.

Therefore, the Cancer Edu-Info Center started an educational program for emotional and psychological support for cancer patients in a non-face-to-face program, and it was art therapy, color therapy, aromatherapy, theater therapy, dance therapy, meditation with tea, and horticultural therapy programs.

Through the experience of operating non-face-to-face education programs for about a year and the educational evaluation of participants, advantages, disadvantages, and limitations could be identified.

First, the feeling emotional comfort and patient satisfaction than face-to-face programs, reduced.

The reason is that burns through communications with non-face-to-face online program is nonverbal signal to shape the emotion and attitude, there are limits. In addition, a lecturer in non-face-to-face, program participants actively interact, and it is hard to difficulties in ongoing education is transferred to the five participants.

Second, the participants' age imbalance and low participation rate were.
Patients in their 30s and 40s who are familiar with non-face-to-face programs actively participated, while patients in their 60s or older were reluctant to apply or applied, but often canceled without participating. Considering that the age group of cancer patients is old, it should not be missed that reverse discrimination and alienation can be brought about due to the difference between digital utilization ability and user competency to consume practical programs.

However, there were also advantages.
They also gave positive feedback that they participated in education that local patients wanted to participate in, but could not participate due to street restrictions, while implementing non-face-to-face education. In addition, some responded that they were able to participate comfortably at home even in situations where it was difficult to participate in education due to fatigue or poor condition during treatment.

Demand for non-face-to-face education programs initiated by COVID-19 is expected to settle at a higher level than before even if COVID-19 ends.
I think it is important to differentiate the advantages and disadvantages of non-face-to-face programs and educational program methods according to the age group to increase participation and create learning conditions in which specific classes are not alienated. It is necessary to develop a diversified program using the crisis brought about by the disaster as an opportunity.

SUPPORTIVE CARE POST PANDEMIC BREAST CANCER PATIENTS

In Jeong Cho

Wonju Severance Christian Hospital, Department of Nursing, Korea

Due to the spread of COVID-19, our society has entered an era of non-face-to-face (untact) which refrains us from contact with other people as much as possible. Patients diagnosed with breast cancer need a strong self-esteem to accept the current situation and the correct awareness, thought and behavior to control fear and anxiety of metastasis and recurrence. Patients diagnosed with breast cancer are treated through surgery, chemotherapy, radiation and targeted therapy. During that time, patients experience anxiety, depression, and decreased self-esteem. They receive emotional support through self-help groups, various physical activities, mentoring and art therapy as well as medical staff. Emphasizing social distancing, supportive care is restricted in the era of anxiety caused by COVID-19. In addition, the screening for breast cancer diagnosis is delayed and the importance of emotional support for breast cancer patients decreases. In the time of pandemic disease, patients in the process of diagnosing and treating breast cancer require discovering the ability to practice self-health management for treatment and prevention of recurrence as to improved quality of life that can overcome the moment of crisis.

EXPERIENCE OF EDUCATION FOR BREAST CANCER PATIENTS POST COVID-19

Nayeon Kim

Samsung Medical Center, Department of Nursing, Korea

When a woman receives the breast cancer diagnosis, education is vital in reducing anxiety, reducing side effect with cancer treatment, helping with self-management, and creating a sense of control. According to the result of several studies, patient education with breast cancer has been found to reduce repeat hospitalizations and visits to emergency departments and to improve quality of life. So, Breast cancer patient education is a critical aspect of quality cancer care. But COVID-19 created an immediate sense of urgency to integrate and deploy innovations in patient education into standard clinical care. COVID-19 changed the delivery of patient education early in the pandemic with a transition to increased cancer and COVID-19 communications, a widespread shift to virtual education and digital platforms, and changes to in-person practices within clinics, libraries, and resource centers. Virtual patient education and digital media can serve as important tools to help improve patient self-management and understanding of treatments. Thus, the disparities across these orientations suggest that a holistic, consistent, and well-articulated direction across the healthcare setting. In the absence of such a policy to collectively leverage digital transformations, differences in care will continue to be a concern.

WORKING YOUNG WOMEN WITH BREAST CANCER: FOR A LIFE THAT MAKES ME WHO I AM

Ka Ryeong Bae

National Cancer Center, Department of Nursing, Korea

Although the incidence rate of breast cancer in Korea is high, the mortality rate is very low. Recently, the survival rate was as high as 93.6%. In particular, the incidence rate of breast cancer among patients in younger age groups is high compared to other countries. As the number of young patients with breast cancer, who are working population, increases, enabling them to return to work healthily after cancer occurrences has become an important issue not only for the patients themselves but also for socioeconomic aspects. In addition, as the survival rate of cancer increases due to the early diagnosis and development of treatment technology and as the patients would need to live as cancer survivors for a long time after that, it is even more important for them to return to work. However, it has been reported that after the diagnosis of breast cancer, patients faced changes in employment status or difficulties related to employment. Access to information or education related to return after a breast cancer diagnosis has been limited in Korea. In addition, patients have many difficulties balancing between work and treatment because there is a lack of awareness and system to support cancer patients to maintain or return to work. Above all, when breast cancer patients return to work, they often have physical and mental difficulties leading to reduced ability on their work. So, patients will need to share their problems and find solutions with medical staff, health-related professionals, and even with colleagues, employers, and insurance companies for a long time after the end of cancer treatment. A policy and system that emphasizes both work and treatment are required for patients to continue economic activities after breast cancer treatment. And, social efforts are required to resolve social prejudice and discrimination against cancer patients.

HUMAN FLOURISHING IN ADOLESCENTS AND YOUNG ADULTS WITH CANCER

Eunji Cho

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Adolescents and young adults (AYA) with cancer deal with the difficulties of transition from pre-cancer to treatment trajectory while also transitioning from adolescence to young adulthood. Despite their complex suffering, these AYA are marginalized in age-appropriate care because neither pediatric nor adult health care settings are suitable for providing such services. While traditional oncology care prioritizes survival and symptom elimination, AYA health care should promote the capacity to deal with these patients' lifelong challenges and move toward the future. Targeted palliative and supportive intervention can benefit AYA with cancer by reducing multidimensional distress, promoting capacities to deal with difficulties, and enhancing overall well-being.

During this session, I will talk about the concept of human flourishing (i.e., complete well-being), which can serve as a framework for setting comprehensive health care goals and discuss how to apply this concept in AYA oncology nursing care. The National League for Nursing defines human flourishing as a lifelong existential journey toward self-actualization and fulfillment within the context of a larger community, based on experiences of hope, achievement, loss, suffering, and coping. They emphasized that nurses can guide individuals toward human flourishing by providing individualized, relationship-focused, culturally appropriate care. Despite ongoing national research priorities, there are significant gaps in AYA-specific research and intervention development to promote human flourishing.

My long-term goal is to develop a nurse-led palliative and supportive intervention that can reduce suffering and maximize human flourishing in AYA with cancer. As an initial step, we developed an "Expressive Storytelling to Share AYA Stories (i.e., ESSAY)", which guides AYA with cancer to reflect their experience following the Expressive Writing Framework and create their stories to share with specific audiences. The current study focuses explicitly on expressive storytelling to share AYA stories with their primary nurses ("ESSAY with nurses"). We have tested the prototype "ESSAY with nurses" through qualitative stakeholder interviews and a single group pre and post-test study. Preliminary data suggested "ESSAY with nurses" is feasible and acceptable for AYA with cancer. To further investigate the impact of "ESSAY with nurses" on multidimensional components of well-being in AYA with cancer, we will measure biological, physical, psychological, social, and spiritual parameters of human flourishing.

Upon completion of the study, we will accomplish a proof-of-concept of an innovative, evidence-based

nurse-led storytelling intervention utilizing the power of narratives and nurse-patient therapeutic relationships. In addition, these results will provide strong evidence of holistic nursing approaches to alleviate suffering and improve complete well-being in AYA with cancer, ultimately advancing palliative and supportive nursing care for this population.

FERTILITY PRESERVATION FOR WOMEN WITH BREAST CANCER

Jeehee Han

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Advances in cancer treatment have resulted in annual increases in the number and survival rates of cancer patients of reproductive age. In addition, due to the increase in the age at first marriage, many women have no concrete family plans at the time of their cancer diagnosis. However, cancer treatments, such as radiation therapy and chemotherapy can reduce or eliminate patient fertility. Fertility is a fundamental human desire; for cancer patients, reduced fertility is a critical issue that can cause serious psychological problems and decreased quality of life.

Recent improvements in reproductive technology have provided multiple options (e.g., sperm/oocyte, embryo, or tissue cryopreservation; hormone therapy, etc.) for patients to preserve their fertility before initiating cancer treatment. International guidelines recommend that oncologists inform patients of the possibility of infertility due to treatment, discuss issues with patients, and, if desired, refer patients to reproductive medicine experts before initiating cancer treatment regimens.

Nevertheless, many medical service providers and patients face difficulties in the decision-making process regarding the preservation of fertility. The patient difficulties include the fear of losing their fertility, limited time, lack of information, and communication with professional medical staff. Oncology medical staff also reported difficulties with insufficient knowledge regarding methods of fertility preservation, as well as access to fertility preservation resources.

In Korea, there are very few studies and interventions on decision-making on the preservation of fertility in cancer patients. Accordingly, it is necessary to confirm the decision-making needs of cancer patients along with the notification of the possibility of declining fertility and the status of access to information on preserving fertility, and a strategic approach to help them make their decisions is needed. In addition, the attributes that should be considered as key in this approach are the provision of detailed and practical information on fertility preservation, non-directive approaches to help patients' value judgments, emphasis on interactions through individualized consultations, establishing connections with available resources, and reinforcement of decision- making support resources.

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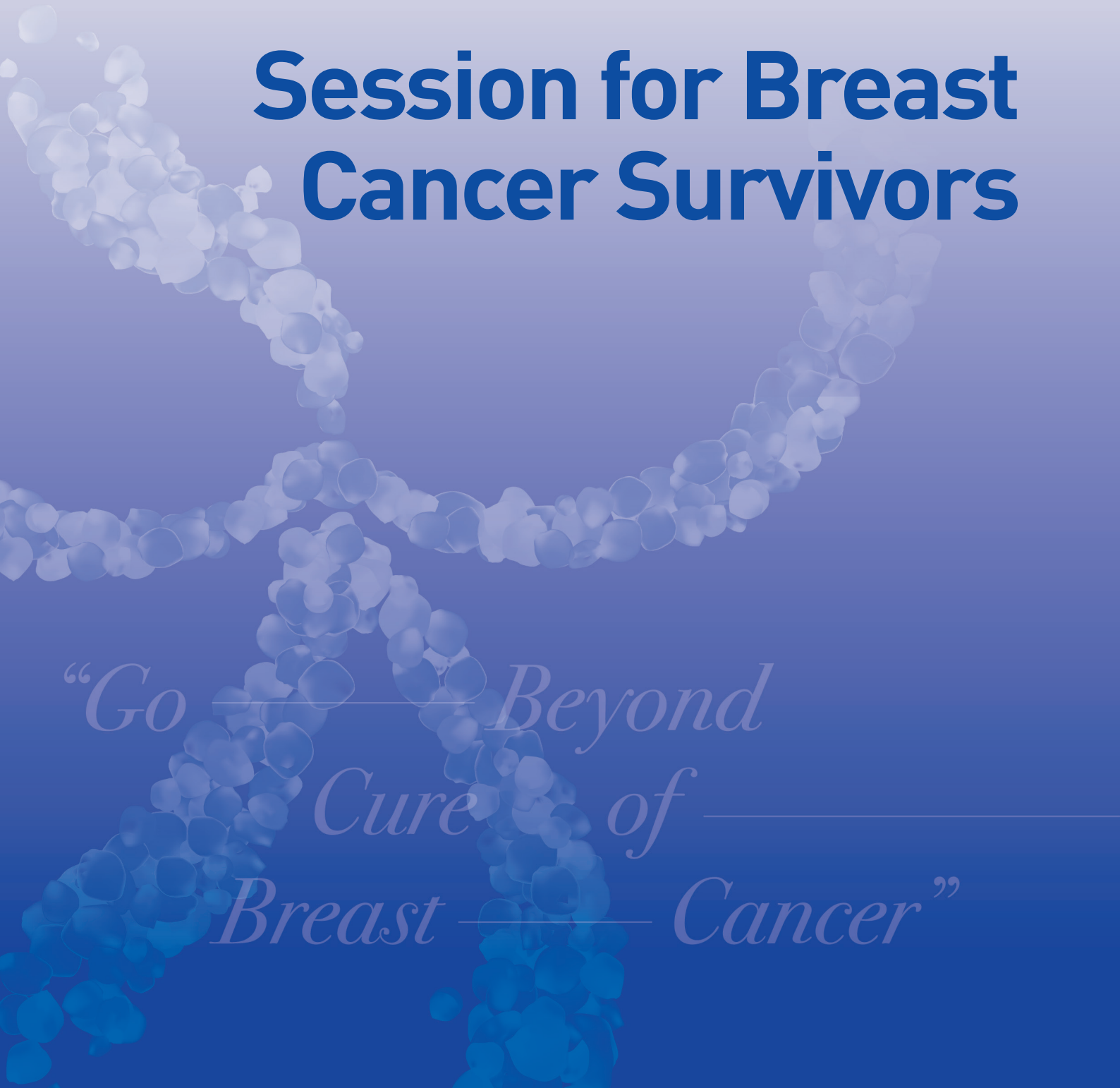

MANAGEMENT OF THE SIDE EFFECT OF HORMONE THERAPY

Seung Ah Lee

CHA Bundang Medical Center, Department of Surgery, Korea

Adjuvant endocrine therapy with either tamoxifen or aromatase inhibitors reduces breast cancer recurrence and improves survival outcomes in patients with hormone receptor-positive breast cancer. However, this therapy can cause side effects that have major consequences in terms of treatment adherence and patients' quality of life. Distressing side effects associated with adjuvant endocrine therapy include hot flashes, sexual dysfunction, weight gain, musculoskeletal symptoms, bone density loss, depression, cognitive dysfunction, and fatigue. Several clinical trials have shown the benefit of pharmacological interventions or non-pharmacological strategies for the management of side effects during adjuvant endocrine therapy.

Non-pharmacological interventions that patients can try before pharmacological treatment are physical exercise, acupuncture, cognitive behavioral therapy. Physical exercise improves musculoskeletal symptoms and fatigue caused by endocrine treatment. Also, acupuncture can be a complementary therapy for the control of musculoskeletal symptoms. Cognitive-behavioral therapy can be helpful for breast cancer survivors facing sexual dysfunction, hot flushes, and fatigue, however, this approach can be costly and time-consuming.

The symptoms for which pharmacological intervention is helpful are hot flashes and musculoskeletal symptoms. Several antidepressants (venlafaxine, duloxetine, paroxetine, sertraline) have been studied for the management of hot flushes, and although they have reduced hot flashes by 40-60%, these medications have significant side effects, such as dry mouth, decreased appetite, and nausea, constipation, and some medications can potentially reduce the bioavailability of tamoxifen.

There are many patients who suffer from more frequent and severe musculoskeletal symptoms in patients taking aromatase inhibitors (letrozole, anastrozole, exemestane) than in patients taking tamoxifen. Duloxetine helps to reduce aromatase inhibitors induced joint pain, is also effective in the treatment of hot flashes and has potentially positive effects on several symptoms (including depression) caused by estrogen deprivation, so it can be used considering its safety profile.

Sexual dysfunction in breast cancer survivors can arise from both physical change (vaginal dryness and dyspareunia), and psychosocial effects (decreased libido, changes in body image, and self-esteem) and

can be exacerbated by endocrine treatment. Local hormone-based therapies (estradiol releasing intravaginal tablets, low-dose vaginal inserts, estrogen-based vaginal creams) have been shown to be effective in treating vaginal symptoms related to estrogen deprivation, however, each is systemically absorbed with different rates. Currently, there is no formal evidence of increased risk of breast cancer recurrence with local vaginal estrogen therapy, but several studies have shown that these agents can cause an elevation of serum estradiol concentrations. So, non-hormonal approaches (virginal lubricant, virginal Lidocaine 4%) should be the first-line choices for the management of genitourinary symptoms in breast cancer survivors.

Endocrine therapy side-effects must be routinely assessed during treatment because several interventions are available to control or reverse them. This is crucial to increase treatment adherence and quality of life during adjuvant endocrine therapy. An individualized approach when choosing an intervention to control these symptoms is likely to have better chances of achieving a positive effect on oncological outcomes and quality of life.

BREAST RECONSTRUCTION AFTER BREAST CANCER SURGERY

Byung-Joon Jeon

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Reconstruction after breast cancer surgery can contribute to treatment by increasing the patient's self-esteem by restoring the deformed body and actively participating in the subsequent treatment process.

Reconstruction methods can be broadly divided into reconstruction using autologous tissue and reconstruction using implants. The method using autologous tissue can be divided into a method using belly fat and a method using back soft tissue. For reconstruction using an implant, there is a method in which the operation is completed at once by inserting the implant directly. And there is another method of additionally performing surgery in which a tissue expander is inserted at first to stretch the soft tissue and then replaces it with an implant.

Reconstruction method is selected in consideration of various factors such as the patient's preference, the size and shape of the breast, and the experience of the operator.

It is necessary to keep in mind that breast reconstruction usually requires several stages of surgery, and it is a cooperative process between the patient and the doctor that requires sufficient explanation and discussion to help the patient understand in this process.

PREVENTION AND REHABILITATION OF LYMPHEDEMA

Ji Sung Yoo

National Cancer Center, Department of Rehabilitation Medicine, Korea

Lymphedema is the abnormal accumulation of interstitial fluid which occurs as a consequence of malformation or acquired disruption of lymphatic circulation. Lymphedema of the upper extremity is considered one of the most chronic and distressing complications with breast cancer treatment.

A paradigm shift in lymphedema surveillance has occurred in the increased awareness to detect subclinical or early-stage lymphedema. This is happening because the surveillance and early identification strategies are more cost effective than waiting for symptoms or obvious swelling to occur. Additionally, because lymphedema is chronic and progressive condition, many survivors have become focused on precautions for the prevention of lymphedema.

There may be different treatment-related and modifiable risk factors according to each patient. Also, several management options can be considered for lymphedema patients according to their lymphedema status. Therefore, personalized management plans are needed.

Therefore, to increase awareness, I share information about prevention and rehabilitation of secondary lymphedema with breast cancer survivors.

BETTER DIET FOR BREAST CANCER SURVIVORS

Jung Eun Lee

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The observed large international variation, with incidence lower in developing countries than in Western countries, and the rapid upward trend in parts of Asia suggests the important roles of dietary factors in breast cancer development. Breast cancer outcomes have improved partly because of early detection, treatment improvement, and social support. Survival statistics based on the Korea Central Cancer Registry data linked to mortality data from the Ministry of the Interior reported that five-year survival rates for Korean breast cancer patients improved from 79.2% in 1993-1995 to 93.6% in 2015-2019. Survival improvements emphasize the importance of supportive care, diet, and quality of life for breast cancer survivors. Although there is limited evidence, several studies support that maintaining a healthy weight and healthy eating and engaging in regular physical activity improve breast cancer prognosis. The Pathways Study recently published the findings of four dietary quality indices and breast cancer survival. Breast cancer survivors who had better adherence to dietary quality indices (the American Cancer Society guidelines (ACS), the alternate Mediterranean Diet Index (aMED), the Dietary Approaches to Stop Hypertension (DASH), or the 2015 Healthy Eating Index (HEI)) had a 21-27% lower risk of mortality. The Nurses' Health Study reported that diabetes risk reduction diet (DRRD), characterized by higher intake of cereal fiber, coffee (caffeinated and decaffeinated), nuts, polyunsaturated:saturated fat ratio, and whole fruits, but lower intakes of glycemic index, trans-fat, SSBs/fruit juices, and red meat, was associated with a 20% lower risk of breast cancer-specific mortality.

This talk will summarize current guidelines and knowledge for breast cancer survivors including scientific research findings. Selected topic includes diet in early life, healthy weight, healthy dietary pattern, food database, and supplementation.

BETTER EXERCISE FOR BREAST CANCER SURVIVORS

Kyeong Eun Uhm

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Breast cancer is the most common cancer in women worldwide. Exercise has proven benefits for breast cancer patients in multiple aspects. Exercise improves survival in breast cancer, reduces the recurrence rate, and controls treatment-related side effects, while improving overall physical fitness and quality of life. Several studies in breast cancer survivors have demonstrated that being physically active after the diagnosis of breast cancer led to a 24-67% reduction in the risk of total deaths and a 50-53% reduction in the risk of breast cancer deaths when compared to a sedentary lifestyle. Both aerobic and resistance exercise are recommended. Recent guidelines recommended at least 2.5 to 5 hours of moderate-intensity or 1.25 to 2.5 hours of vigorous-intensity aerobic physical activity per week, two or more days a week of resistance training, and stretching of major muscle groups for cancer survivors. Additionally, breast cancer patients require progressive upper extremity exercises in a specific manner. Traditionally, upper extremity exercises were avoided in breast cancer patients with lymph node dissection and radiotherapy. However, recent studies have shown that upper body exercises do not have a negative impact on lymphedema. Exercise is safe and feasible for breast cancer survivors, and also could be a complementary treatment for achieving physical and psychological improvements.

BETTER MIND FOR BREAST CANCER SURVIVORS

Seo-Eun Cho

Gachon Univ. Gil Medical Center, Department of Psychiatry, Korea

Breast cancer has been the most commonly occurring cancer in Korean women since 2001. In particular, the breast cancer incidence rate is high among the relatively young age group (30 to 44 years), and most breast cancer patients are women in their 40s, 50s and 60s. The 5-year survival rate of breast cancer is over 90%. Although breast cancer is a kind of that has a significantly better treatment effect than other cancers, it is known that the patients suffer from greater distress compared to other cancer sufferers. Studies have shown that breast cancer survivors experience psychological and social stress by 40% more than those who have not been diagnosed with any cancer, even if they have survived for more than 5 years with no recurrence. Breast cancer survivors who may experience loss of breast, a symbol of femininity, are more likely to be stressed by the anxiety that their femininity may be lost or damaged, and thereby suffering psychological shock and physical pain. Many survivors feel severe depression due to not only hormonal changes during the menopausal transition but also the pain of being a cancer patient. It is reported that there are quite a few cases that lead to depression, and about 25% of patients are still suffering from severe stress even after two years of surgery. Stress and depression adversely affect cancer treatment outcomes. In addition, there are many difficulties in adapting, such as fear of cancer recurrence, which might come after completing cancer treatment successfully, and changes in life after cancer diagnosis. Diagnosis and treatment of breast cancer can be a huge stress in itself, and accompanied by psychological pain as well as physical pain. But the cancer survivors and their families usually focus only on the treatment of cancer and neglect to care about their feelings, causing lack of intervention in mental health issues. Even if there was emotional pain that required treatment, the appropriate intervention time was often missed due to negative perceptions and prejudices about consulting a psychiatrist or receiving psychosocial intervention. For breast cancer survivors, symptom-specific management for depression, anxiety, insomnia, and delirium is recommended, which are known to have a high prevalence among cancer patients, based on an accurate understanding of their disease, and continuous evaluation and therapeutic management are required. Breast cancer survivors should recognize that they are in an inevitable situation, live their lives within the boundaries of what they can do in that situation, and actively get help for themselves.

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BENEFITS OF SECONDARY PROPHYLAXIS WITH PEGFILGRASTIM FOR PATIENTS WITH BREAST CANCER: REAL WORLD DATA

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Adjuvant chemotherapy has its definite role for prolongation of survival in breast cancer. Maintenance of adequate dosage and period of adjuvant chemotherapy is important, considering relative dose intensity (RDI) of chemotherapeutic agents is associated to survival outcome in breast cancer. However, complication of cytotoxic chemotherapy such as febrile neutropenia is associated to decreased relative dose intensity (RDI) of chemotherapeutic agents and consequently related to reduced survival. Prophylaxis of grade 4 and febrile neutropenia can be achieved by use of pegfilgrastim. Pegfilgrastim is a long-acting form of filgrastim, administered by subcutaneous route. Randomized phase III trial showed single-administration of pegfilgrastim showed comparable efficacy compared to daily use of filgrastim, and therefore included in standard treatment guideline.

We conducted an observational study, investigating the clinical efficacy and adverse event of pegfilgrastim when used as secondary prophylaxis in Korean breast cancer women. More than 1,200 breast cancer patients were enrolled for analysis during 42 months of study period, and the incidence of febrile neutropenia, relative dose intensity, adverse events were analyzed. Less than 1% of patients experienced febrile neutropenia after secondary prophylaxis, comparable to previous reports. RDI was maintained over 85% in more than 90% of enrolled patients. The most common adverse event was bone pain, well controlled with oral medication.

In conclusion, pegfilgrastim showed comparable efficacy compared to previous prospective phase III trials with manageable toxicity profile.

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*Additional monitoring may be necessary based on the individual patient.
†As part of combination therapy with an AI or fulvestrant. Dosing for these combination partners should follow the dosing indications in the respective MFDS

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AI = aromatase inhibitor; ET = endocrine therapy; HR+/HER2- = hormone receptor-positive, human epidermal growth factor receptor 2–negative; LHRH = luteinising hormone-releasing hormone; mBC = metastatic breast cancer; SmPC = summary of product characteristics.

[안전성 정보] 임상시험에서 가장 빈번하게 보고된 이상반응은 호중구 감소증이었으며, 주기적인 혈액검사가 필요합니다. 호중구 감소증과 관련된 자세한 용량 조절 정보는 제품설명서를 참고해주세요.

[제품정보] 임랜스®캡슐 75mg, 100mg, 125mg **[유효성분]** 팔보시클립 **[효능·효과]** 이 약은 호르몬 수용체(HR)-양성 및 사람상피세포성장인자수용체2(HER2)-음성인 진행성 또는 전이성 유방암 치료에 아래와 같이 병용한다: 폐경 후 여성에서 일차 내분비 요법으로서 아로마타제 억제제와 병용 또는 내분비요법 후 질환이 진행된 여성에서 풀베스트란트와 병용 **[용법·용량]** 1. 권장용량 및 투여일정 이 약의 권장용량은 28일을 전체 주기로 하여, 1일 1회 125mg 캡슐을 21일간 연속하여 경구투여하고, 7일간 휴약한다. 이 약은 음식물과 함께 복용해야 한다. 이 약을 아로마타제 억제제와 투여할 경우, 아로마타제 억제제의 권장용량을 투여한다.(투여할 아로마타제 억제제의 허가사항 참조). 이 약과 풀베스트란트를 투여 시, 풀베스트란트의 권장용량은 1일 1회 500mg을 1일, 15일차, 29일차에 투여하며, 그 이후로는 한 달에 1번 투여한다(풀베스트란트 허가사항 참조). 환자가 매일 같은 시간에 이 약을 복용하도록 독려해야 한다. 환자가 이 약 복용 후 구토를 하거나 복용을 잊은 경우, 이 약 추가용량을 투여해서는 안 된다. 다음 용량의 투여는 예정된 복용시간에 이루어져야 한다. 이 약은 통째로 삼켜야 한다.(씹거나 으깨지 말 것. 삼키기 전 캡슐을 열지 말 것). 캡슐이 부서지거나 금이 가는 등 온전하지 않은 경우, 복용해서는 안된다. 이 약과 내분비 요법을 병용하는 폐경 전 및 폐경이행기(perimenopausal) 여성은 임상진료지침(local clinical practice)에 따라 황체형성호르몬분비호르몬 (LHRH) 작용제를 투여 받아야한다. **[사용상의 주의사항]** 1. 경고 1) 호중구감소증 이 약의 임상시험에서 호중구 수 감소가 관찰되었다. 이 약과 레트로졸(임상시험 1(PALOMA-1) 및 임상시험 2(PALOMA-2)) 또는 이 약과 풀베스트란트(임상시험 3(PALOMA-3))를 병용투여한 환자에서, 3등급 및 4등급의 호중구 수감소가 각각 56.1% 및 10.6%로 보고되었다. 3건의 무작위 임상시험에서 등급에 상관없이 호중구감소증의 첫 사례가 나타나기까지의 중앙값은 15일(12일~700일)이었고, 3등급 이상의 호중구감소증이 나타난 기간의 중앙값은 29일이었다. 이 약 투여를 시작하기 전, 각 투여주기의 시작 시, 처음 두 주기의 각 15일차 및 임상적으로 필요한 경우 전혈구 수를 모니터링 한다. 처음 6주기에서 최대 1등급 또는 2등급의 호중구감소증을 경험한 환자는 이 후의 주기에서 임상적으로 필요한 경우, 투여주기의 시작 전 및 매 3개월 마다 전혈구 수를 모니터링 한다. 각 투여 주기의 시작단계에서 투여 중단, 용량감소 또는 투여 지연은 3등급 또는 4등급의 호중구감소증이 나타난 환자에서 권장된다. 임상시험 3에서 호중구감소성 패혈증으로 인한 1건의 사망사례가 있었다. 의사는 환자가 모든 발열 증상을 즉시 보고하도록 교육해야 한다. 2) 베이-태아 독성 동물시험 및 이 약의 작용기전에 근거할 때, 이 약은 임부에 투여 시 태아에게 유해할 수 있다. 동물의 생식독성시험에서, 임신한 랫드 및 토끼에 이 약을 투여 시기관형성기에 AUC근거 사람 임상노출의 4배 이상 수준의 모체노출농도), 배태자 독성이 나타났다. 태아에 대한 잠재적 위험성을 임부에게 알린다. 가임 여성에게 이 약의 투여기간 및 마지막 용량 투여 후 최소 3주동안은 효과적인 피임법을 사용하도록 권고한다. 3) 간질성 폐질환 (Interstitial Lung Disease, ILD)/폐렴(pneumonitis) 이 약을 비롯한 사이클린-의존성 키나아제4/6(CDK 4/6) 억제제와 내분비요법을 병용할 경우, 중증의 생명을 위협하거나 치명적인 간질성 폐질환 및/또는 폐렴이 나타날 수 있다. 임상시험(PALOMA-1, PALOMA-2, PALOMA-3, n=872) 통합 분석에서, 이 약을 투여받은 환자의 1.4%가 간질성 폐질환/폐렴을 경험하였으며, 이 중 3등급은 0.1%이었고, 4등급 이상이거나 치명적인 경우는 보고되지 않았다. 시판 후 조사에서 간질성 폐질환/폐렴이 추가로 관찰되었으며, 사망사례가 보고되었다. 간질성 폐질환/폐렴의 증상(저산소증, 기침, 호흡곤란 등)이 있는지 환자를 모니터링한다. 새로운 또는 악화된 호흡기 증상이 있는 경우와 간질성 폐질환/폐렴의 발생이 의심되는 환자에서, 즉시 이 약 투여를 중단하고 검사를 실시한다. 중증 간질성 폐질환 또는 폐렴환자의 경우, 이 약 투여를 영구 중단한다. **[최종변경허가일]** 2020년 05월 21일 **※제품에 대한 자세한 정보는 최신의 제품설명서를 참고하시길 바라며 홈페이지(www.pfizer.co.kr)를 통해 확인하실 수 있습니다.**

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MAXIMIZING CLINICAL OUTCOME IN HR+HER2- METASTATIC BREAST CANCER PATIENTS: PALBOCICLIB & CDK4/6 INHIBITORS IN REAL-WORLD PRACTICE

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The advent of CDK4/6 inhibitors dramatically changed the course of metastatic breast cancer patient treatment. Efficacy and safety data of palbociclib in a various subgroups have been established in both RCT and real-world evidence. Cases of Palbociclib in different patient types have been accumulated in Korea since its reimbursement.

PALOMA Study, a pivotal study of palbociclib in combination with endocrine therapy, evaluated efficacy and safety of Palbociclib in 872 patients including various patients. Of note, the efficacy and safety of Palbociclib in patients with preexisting conditions were shown in the post hoc analysis of the PALOMA2 study. At baseline, 41.4% of patients had gastrointestinal disorders, 58.6% musculoskeletal disorders, 38.9% had metabolic disorders and 57.4% had vascular/cardiac disorders. For each patient group with underlying preexisting conditions, efficacy has remained stable showing superior efficacy in the palbociclib+ET combination group.[1] In post hoc analysis of PALOMA data, the long-term safety of palbociclib was analyzed. All grade and Grade 3/4 adverse events remained stable over long-term follow-up. Both hematologic and non-hematologic adverse events were stable after a 5-year follow-up. Through this study, Palbociclib proved its long-term safety profile.[2] In Korea, palbociclib was the first CDK4/6 inhibitor approved and reimbursed for HR+ HER2- metastatic breast cancer patients. Korean breast cancer patients, who are characterized by relatively younger age, are now able to continue their social life while receiving treatments.

Palbociclib also continuously showed clinical value in real-world evidence (RWE). One of these RWE is the FLATIRON study; this retrospective observational analysis collected data from more than 280 centers in the US and a total of 1430 patients were included for analysis. In this study, median rwPFS was 20.0 month in Palbociclib+letrozole with HR 0.58 (HR = 0.58; 95% CI 0.49-0.69, $P < 0.0001$). Median OS was not reached in Palbociclib+letrozole arm while letrozole showed mOS of 43.1 month (HR = 0.66; 95% CI 0.53-0.82, $P = 0.0002$). In the real-world setting, palbociclib showed its efficacy in heterogeneous populations.[3]

In addition, palbociclib is the only CDK4/6 inhibitor that was approved for male breast cancer patients

with HR(+) advanced breast cancer based on real-world data.

In summary, palbociclib in combination with endocrine therapy is an effective and safe treatment option in patients with HR(+) advanced breast cancer with various co-morbidities in real-world practice.

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THE EVOLVING LANDSCAPE OF HR+/HER2- BREAST CANCER TREATMENT

Aditya Bardia

Massachusetts General Hospital Cancer Center, Department of Medical Oncology, U.S.A.

Endocrine therapy with CDK4/6 inhibitor is the recommended 1st line treatment option for metastatic hormone receptor positive (HR+) breast cancer. Among post-menopausal women, improvement in progression-free survival has been observed with all 3 CDK4/6 inhibitors (palbociclib, ribociclib, abemaciclib) with aromatase inhibitor as 1st line therapy, and improvement in overall survival improvement with endocrine therapy and ribociclib in both pre-menopausal and post-menopausal HR+ MBC. CDK4/6 inhibitors have established, predictable, and manageable safety profiles based on clinical and real-world experience. Adverse effects observed with CDK4/6 inhibitor-based combinations are mostly low grade, reversible, and effectively managed with dose interruptions/reductions.

Biomarker testing is an emerging approach for profiling tumors and guiding therapeutic decisions. Data from various trials have demonstrated that PIK3CA mutations are common in patients with HR+, HER2 metastatic breast cancer. Pivotal results from SOLAR-1 demonstrated that the PI3Kα-selective inhibitor alpelisib is associated with improved clinical outcomes, and alpelisib is the first PI3K inhibitor approved in breast cancer and is the only therapy for ABC that specifically targets the effects of PIK3CA mutations. PIK3CA mutation testing using either tumor tissue or plasma ctDNA can identify patients who are likely to benefit from alpelisib. In addition, there have been number of oral SERDs in clinical development for metastatic ER+ breast cancer. In this presentation, we will review the current guidelines latest developments in management of HR+/HER2- breast cancer.

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pCR: pathological complete response, HER2: Human Epidermal Growth Factor Receptor 2, eBC: early breast cancer

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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.

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• 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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TRANSFORMING THE TREATMENT JOURNEY FOR HER2+ BREAST CANCER PATIENTS

Joyce O'shaughnessy

Baylor Univ. Medical Center, Department of Medical Oncology, U.S.A.

Combined administration of the anti-HER2 antibodies, trastuzumab and pertuzumab, has improved the outcomes of HER2+ breast cancer patients with stage II or III disease, and those receiving first-line therapy for metastatic disease. A subcutaneous fixed dose combination of pertuzumab plus trastuzumab, mixed with hyaluronidase, PH FDC SC, has been developed to provide an equally safe and efficacious, but more time-efficient formulation than IV administration. With PH FDC SC, 1200 mg/600 mg (15 ml) is given SC day 1 over 8 minutes, followed by 600 mg/600 mg (10 ml) every 3 weeks over 5 minutes, using pre-filled syringes. The FeDeriCa trial was a phase III non-inferiority trial that assessed the pharmacokinetics (PK), efficacy and safety of preoperative PH FDC SC vs IV P + H in combination with standard chemotherapy. The primary and secondary endpoints of pre-cycle 8 P and H serum Ctrough levels, respectively, of PH FDC SC showed non-inferiority compared with IV P + H; indeed the PH FDC SC trough levels exceeded those of IV P+H. The pCR rates obtained with PH FDC SC and IV P + H were almost identical at 59.7% and 59.5%, respectively. The safety profile of PH FDC SC was comparable to those of the P + H IV formulations, with no new safety signals identified.

In the PHranceSCa trial, HER2+ early breast cancer patients were treated with 3 cycles of adjuvant PH FDC SC followed by 3 cycles of IV P + H, or with the reverse order of the SC and IV formulations, having completed standard preoperative IV P + H plus chemotherapy and definitive surgery. 87% of the patients then chose to complete their adjuvant therapy with PH FDC SC, mainly because of "less time in clinic" and because they were "more comfortable during administration". In addition, 87% of health care professionals involved in PHranceSCa felt that PH FDC SC required less time and resource utilization for preparation and administration. Adverse event rates before and after switching formulations were similar. NCCN guidelines recommend the substitution of PH FDC SC for P + H IV for the treatment of HER2+ early and metastatic breast cancer.

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* HR+, HER2- advanced/metastatic breast cancer women에서 버제니오의 투여 적응증[1]

1) 호르몬 수용체(HR)-양성 및 사람 상피세포 성장인자 수용체 2(HER2)-음성인 진행성 또는 전이성 유방암이 있는 폐경 후 여성의 치료를 위한 일차 내분비 기반 요법으로서 아로마타제 억제제와 병용

2) 내분비 요법 후 질병이 진행된 호르몬 수용체(HR)-양성 및 사람 상피세포 성장인자 수용체 2(HER2)-음성인 진행성 또는 전이성 유방암 여성의 치료에 풀베스트란트와 병용†

†이 약과 풀베스트란트를 병용 투여 받은 폐경 전 및 폐경 이행기 여성들은 현재 임상진료지침(clinical practice standards)에 따라 생식샘자극 분비 호르몬 작용제를 투여 받아야 한다.

The first and the only CDK 4&6 inhibitor to significantly extend OS

in combination with fulvestrant regardless* of menopausal status (as of Feb.2021)[2-6]
(Median OS 46.7 vs 37.3 months; HR=0.757; 95% CI, 0.606-0.945; p = 0.01)

Consistent OS benefit in primary ET resistance and visceral disease in combination with fulvestrant[2,4]

[1.**Primary ET resistance:** Median OS 38.7 vs 31.5 months; HR = 0.686 (95% CI, 0.451-1.043)
2.**Visceral disease:** Median OS 40.3 vs 32.2months; HR = 0.675 (95% CI, 0.511-0.891)]

The only CDK inhibitor with **continuous dosing**[1,2,7,8]

(as of Feb.2021)

*pre- or perimenopausal women received a gonadotropin-releasing hormone agonist

Safety profile At the MONARCH2 analysis, the most common adverse events in the abemaciclib versus placebo arms were diarrhea (86.4% versus 24.7%), neutropenia (46.0% versus 4.0%), nausea (45.1% versus 22.9%), and fatigue (39.9% versus 26.9%).[3] At the MONARCH 3 interim analysis, the safety profile was consistent with previous reports. The most frequent grade ≥ 3 adverse events in the abemaciclib versus placebo arms were neutropenia (23.9% versus 1.2%), diarrhea (9.5% versus 1.2%), and leukopenia (8.6% versus 0.6%). Abemaciclib plus a nonsteroidal AI was an effective initial treatment with an acceptable safety profile for HR+, HER2- ABC.[3]

HR = Hormone receptor, **HER2** = Human epidermal growth factor receptor type 2, **CDK** = Cyclin dependent kinase, **OS** = Overall survival, **ITT** = Intention to treat, **ET** = Endocrine therapy

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[제품명] 버제니오정 50/100/150 밀리그램(아베마시클립)

[원료약품 및 그 분량]
1정(144.2밀리그램) 중 아베마시클립 50.00밀리그램, 1정(291.2밀리그램) 중 아베마시클립 100.00밀리그램
1정(432.6밀리그램) 중 아베마시클립 150.00밀리그램

[효능 · 효과]
- 호르몬 수용체 (HR)-양성 및 사람 상피세포 성장인자 수용체 2(HER2)-음성인 진행성 또는 전이성 유방암이 있는 폐경 후 여성의 치료를 위한 일차 내분비 기반 요법으로서 아로마타제 억제제와 병용
- 내분비 요법 후 질병이 진행된 호르몬 수용체 (HR)-양성 및 사람 상피세포 성장인자 수용체 2(HER2)-음성인 진행성 또는 전이성 유방암 여성의 치료에 풀베스트란트와 병용

[용법 · 용량]
1. 권장 용량 및 용법
- 풀베스트란트 또는 아로마타제 억제제와의 병용요법에서 이 약의 권장 용량은 150 mg을 1일 2회 경구 투여하는 것이다.
- 이 약과 병용 투여 시 사용되는 아로마타제 억제제의 권장 용량은 허가 사항을 참고한다.
- 이 약과 병용 투여 시 풀베스트란트의 권장 용량은 제 1일, 제 15일, 제 29일에 그리고 그 이후 한 달에 한 번 500 mg 투여이다. 풀베스트란트에 대한 허가사항을 참고한다. 이 약과 풀베스트란트를 병용 투여 받은 폐경 전 및 폐경 이행기 여성들은 현재 임상진료지침(clinical practice standards)에 따라 생식샘자극 분비 호르몬 작용제를 투여 받아야 한다.

질병 진행 또는 허용될 수 없는 독성이 나타날 때까지 치료를 계속한다. 이 약은 음식 섭취와 관계없이 투여할 수 있다.
매일 거의 동일한 시간에 이 약을 투여하도록 환자를 지도한다.
환자가 이 약을 토하거나 투여를 잊은 경우, 다음 계획된 시간에 다음 용량을 투여하도록 환자를 지도한다.
환자가 이 약 정제를 통째로 삼키게 하고 쪼개기 전 정제를 씹거나, 부수거나 분할하지 않도록 지도한다. 환자가 깨졌거나 금이 갔거나, 온전하지 않은 이 약의 정제를 투여하지 않도록 지도한다.

2. 용량 조절
이상반응에 따른 용량 조절 이상반응에 따른 권장되는 이 약의 용량 조절은 표 1-5에 제시하였다. 환자가 50 mg 1일 2회 용량에 내약성을 나타내지 못하는 경우 이 약 투여를 중단한다.

표 1: 이상반응에 대한 이 약의 용량 조절

용량 수준	풀베스트란트 또는 아로마타제 억제제와 병용 시 이 약의 용량
권장되는 시작 용량	150 mg 1일 2회
1차 용량 감소	100 mg 1일 2회
2차 용량 감소	50 mg 1일 2회
3차 용량 감소	해당사항 없음

표 2: 이 약의 용량 조절 및 관리 — 혈액학적 독성[a]

이 약 투여를 시작하기 전, 처음 2개월간 2주마다, 다음 2개월간 매달, 그리고 임상적으로 필요할 때마다 완전 혈구수를 모니터링한다.	
CTCAE 등급	이 약 용량 조절
1 또는 2 등급	용량 조절이 필요하지 않다.
3 등급	2 등급 이하로 독성이 소실될 때까지 투여를 보류한다. 용량 감소는 필요하지 않다.
3 등급 재발 또는 4 등급	2 등급 이하로 독성이 소실될 때까지 투여를 보류한다. 다음 낮은 용량으로 투여를 재개한다.

약어: CTCAE = Common Terminology Criteria for Adverse Events(이상반응에 대한 공통 용어 기준).
[a] 혈구 성장 인자가 필요한 경우, 혈구 성장 인자의 마지막 투여 후 최소 48시간 동안 그리고 독성이 등급 2 이하로 소실될 때까지 이 약의 투여를 보류한다.
성장 인자의 사용으로부지 이어진 독성에 대해 이미 실시된 경우가 아니라면 그다음 낮은 용량으로 재개한다. 성장 인자 사용은 현재 치료 가이드라인을 따른다.

표 3: 이 약의 용량 조절 및 관리 — 설사

무른 변의 정후가 처음 나타날 때 지시제 투여를 시작하고, 음료 섭취를 늘린다.	
CTCAE 등급	이 약 용량 조절
1 등급	용량 조절이 필요하지 않다.
2 등급	24시간 이내에 독성이 1 등급 이하로 소실되지 않으면, 소실될 때까지 투여를 보류한다. 용량 감소는 필요하지 않다.
최선 지지 치료에도 불구하고 동일한 용량을 재개한 후 지속되거나 재발한 2 등급	1 등급 이하로 독성이 소실될 때까지 투여를 보류한다. 다음 낮은 용량으로 투여를 재개한다.
3 또는 4 등급 또는 입원을 요하는 경우	1 등급 이하로 독성이 소실될 때까지 투여를 보류한다. 다음 낮은 용량으로 투여를 재개한다.

표 4: 이 약의 용량 조절 및 관리 — 간 독성

이 약 투여를 시작하기 전, 처음 2개월간 2주마다, 다음 2개월간 매달, 그리고 임상적으로 필요할 때마다 ALT, AST 및 혈청 빌리루빈을 모니터링한다.	
ALT 및 AST에 대한 CTCAE 등급	이 약 용량 조절
1 등급 (>ULN-3.0 x ULN) 2 등급 (>3.0-5.0 x ULN), 총 빌리루빈이 >2 x ULN로 상승하지 않음	용량 조절이 필요하지 않다.
지속적 또는 재발성 2 등급, 또는 3 등급 (>5.0-20.0 x ULN), 총 빌리루빈이 > 2 x ULN로 상승하지 않음	독성이 베이스라인 또는 1 등급 수준으로 소실될 때까지 투여를 보류한다. 다음 낮은 용량으로 투여를 재개한다.
AST 및/또는 ALT >3 x ULN의 상승과 총 빌리루빈 >2 x ULN 상승, 단, 담즙 정체는 없음	이 약 투여를 중단한다.
4 등급 (>20.0 x ULN)	이 약 투여를 중단한다.

약어: ALT = 알라닌 아미노전이효소, AST = 아스파르테이트 아미노전이효소, ULN = upper limit of normal(정상범위 상한).

표 5 : 간질성 폐질환(Interstitial Lung Disease, ILD)/간질성 폐렴(pneumonitis)에 대한 이 약 용량 조절

CTCAE 등급	이 약 용량 조절
1 또는 2 등급	용량 조절이 필요하지 않다.
최선 지지 치료에도 7일 이내에 베이스라인 또는 1 등급으로 소실되지 않는 지속적 또는 재발성 2 등급 독성	독성이 베이스라인 또는 1 등급 이하로 소실될 때까지 투여를 보류한다. 다음 낮은 용량으로 투여를 재개한다.
3 또는 4 등급	이 약 투여를 중단한다.

표 6 : 기타 독성'에 대한 이 약 용량 조절 및 관리

CTCAE 등급	이 약 용량 조절
1 또는 2 등급	용량 조절이 필요하지 않다.
최선 지지 치료에도 7일 이내에 베이스라인 또는 1 등급으로 소실되지 않는 지속적 또는 재발성 2 등급 독성	독성이 베이스라인 또는 1 등급 이하로 소실될 때까지 투여를 보류한다. 다음 낮은 용량으로 투여를 재개한다.
3 또는 4 등급	독성이 베이스라인 또는 1 등급 이하로 소실될 때까지 투여를 보류한다. 다음 낮은 용량으로 투여를 재개한다.

[a] 설사, 혈액학적 독성, 간독성 및 간질성 폐질환(Interstitial Lung Disease, ILD)/간질성 폐렴(pneumonitis) 제외

병용 투여되는 아로마타제 억제제 또는 풀베스트란트에 대한 용량 조절 및 기타 관련된 안전성 정보는 허가사항을 참고한다.

강력한 및 보통의 CYP3A 억제제 사용시 용량 조절
강력한 CYP3A 억제제인 케토코나졸의 병용 사용은 피한다.
권장되는 시작 용량이 150 mg 1일 2회인 환자들에서 케토코나졸 이외의 강력한 CYP3A 억제제의 병용 사용 시, 이 약의 용량을 100 mg 1일 2회로 줄인다. 이상반응으로 인해 용량을 100 mg 1일 2회로 줄였던 환자들의 경우, 이 약의 용량을 50 mg 1일 2회로 더 줄인다. 이 약을 투여 중인 환자가 CYP3A 억제제를 중단하는 경우, 이 약의 용량을(억제제의 3-5 반감기 경과 후) 강력한 억제제를 시작하기 전에 사용한 용량까지 증량한다. 보통의 CYP3A 억제제를 병용 사용할 경우, 이상 반응에 대하여 모니터링하고 필요한 경우, 표 1에 제시된 바와 같이 이 약의 용량을 50 mg씩 감소시킬 것을 고려한다.

중증 간 장애 환자에 대한 용량 조절
중증 간 장애 (Child Pugh-C) 환자의 경우, 이 약의 투여 빈도를 1일 1회로 줄인다.
중증 간 장애에 대한 병용 투여되는 아로마타제 억제제 또는 풀베스트란트에 대한 용량 조절 요건은 허가사항을 참고한다.

[경고] 1) 호중구 감소증 호중구 감소증은 MONARCH 3에서 이 약과 아로마타제 억제제를 병용 투여 받은 환자의 41%, MONARCH 2에서 이 약과 풀베스트란트를 병용 투여 받은 환자의 46%에서 발생하였다. 3 이상 등급의 호중구 수 감소(실험실 결과에 근거)는 MONARCH 3에서 이 약과 아로마타제 억제제를 병용 투여 받은 환자의 22%, MONARCH 2에서 이 약과 풀베스트란트를 병용 투여 받은 환자의 32%에서 발생하였다. MONARCH 3에서 3 이상 등급의 호중구 감소증의 첫 번째 발현까지 걸린 시간의 중앙값은 33일이었고, MONARCH 2에서는 29일이었다. MONARCH 3에서 3 이상 등급의 호중구 감소증 기간의 중앙값은 11일이었고, MONARCH 2의 경우 15일이었다. 이 약 투여를 시작하기 전 처음 2개월간 2주마다, 다음 2개월간 매달, 그리고 임상적으로 필요할 때마다 전혈구 수를 모니터링한다. 3 또는 4 등급의 호중구 감소증을 나타내는 환자에 대해서는 투여의 일시 중단, 용량 감소 또는 치료 주기 시작의 연기가 권장된다. 발열성 호중구 감소증은 MONARCH 시험들에서 이 약에 노출된 환자의 1% 미만에서 보고되었다. MONARCH 2에서 호중구 감소성 패혈증으로 인한 사망이 2건 관찰되었다. 환자가 발열이 나타나는 경우 담당 의료인에게 즉시 보고하도록 지도한다.

2) 배태자 독성 동물 시험으로부터의 결과 및 작용 기전에 근거할 때 이 약은 임신한 여성에게 투여 시 태아에게 유해할 수 있다. 동물 생식 독성 시험에서 거란 형성 기간에 임신한 랫드에게 아베마시클립을 투여한 결과 인체 최대 권장 용량에서의 곡선하 면적(AUC)에 근거한 인체 임상 노출과 유사한 모체 노출에서 최기 형성 및 태자 체중 감소를 나타냈다. 임신한 여성에게 태아에 대한 잠재적 위험을 알린다. 생식능력이 있는 여성에게 이 약을 투여하는 동안 그리고 마지막 투여 후 최소 3주 이상 효과적인 피임법을 사용하도록 지도한다.

3) 간질성 폐질환(Interstitial Lung Disease, ILD)/간질성 폐렴(pneumonitis) 이 약 또는 다른 CDK 4/6 억제제로 치료받은 환자들에게 중증, 생명을 위협하거나 치명적인 간질성 폐질환(ILD) 또는/및 간질성 폐렴(pneumonitis)이 발생할 수 있다. 임상시험(MONARCH 1, MONARCH 2 및 MONARCH 3)에서 이 약으로 치료받은 환자들 중 3.3%가 모든 등급의 간질성 폐질환 및 간질성 폐렴을 경험하였고, 0.6%가 3 또는 4등급, 그리고 0.4%가 치명적인 결과를 나타내었다. 시판 후 조사에서 간질성 폐질환 및 간질성 폐렴의 추가 사례들이 관찰되었고, 사망 사례들이 보고되었다. 간질성 폐질환 및 간질성 폐렴을 나타내는 폐 증상이 있는지 관찰하여야 한다. 증상은 저산소증, 기침, 호흡곤란, 방사선 검사상 간질성 침윤을 동반 포함할 수 있다. 이러한 증상들에 있어서 감염성, 종양성, 그리고 그 밖의 원인들은 적절한 조사에 의해 제외되어야만 한다.

지속적 또는 재발성 2등급의 간질성 폐질환 및 간질성 폐렴을 나타내는 환자들에 대해서는 투여의 중단 또는 용량 감소가 권장된다. 3등급 또는 4등급의 간질성 폐질환 또는 간질성 폐렴을 나타내는 모든 환자들은 영구적으로 이 약의 투여를 중단하여야 한다.

[다음 환자에게는 투여하지 말 것] 이 약은 유당을 함유하고 있으므로, 갈락토오스 불내증(galactose intolerance), Lapp 유당분해효소 결핍증(Lapp lactase deficiency) 또는 포도당-갈락토오스 흡수장애(glucose-galactose malabsorption) 등의 유전적인 문제가 있는 환자에게는 투여하면 안 된다.

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[신중투여] 1) 간질성 폐질환이 있는 환자 또는 간질성 폐질환 기왕력이 있는 환자(간질성 폐질환이 약화될 가능성이 있음)

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VERZENIO, POTENT CDK4/6 INHIBITOR, HOW TO OPTIMIZE HR+/HER2- MBC PATIENT WITH CDK4/6 INHIBITORS

Tomoyuki Aruga

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Cancer has been the leading cause of death in Japan since 1984. Among Japanese women, breast cancer is the most common type of cancer, with over 90,000 cases diagnosed annually. Furthermore, hormone receptor-positive, HER2-negative breast cancer, also known as luminal breast cancer (LBC), accounts for 60~70% of all breast cancer cases. In advanced LBC, hormone therapy is often administered if the disease is not life-threatening, but recently, combining hormone therapy with molecularly-targeted therapy has become the preferred treatment whereas in the past, hormone therapy alone was generally used.

Amid the emergence of new hormonal treatments, abemaciclib, a potent CDK4/6 inhibitor, was approved for use in Japan in November 2018 as a treatment for advanced LBC on the basis of the results of the Monarch 2 and Monarch 3 trials, both of which were global Phase III trials, and has shown unprecedented therapeutic efficacy in real-world clinical practice.

Monarch 3, which included de-novo Stage IV or recurrent LBC after completion of adjuvant hormone therapy, aimed to evaluate the efficacy of abemaciclib combined with letrozole as first-line therapy. The median PFS, the primary endpoint of the study, showed a statistically significant difference ($p = 0.00021$) with a hazard rate of 0.54 (95% CI: 0.41 to 0.72), demonstrating the efficacy of the drug.

The Monarch 2 trial also evaluated the efficacy of abemaciclib combined with fulvestrant in patients with advanced BC which progressed despite hormone therapy. Here again, the median PFS showed a statistically significant difference with a hazard rate of 0.553 (95% CI: 0.449-0.681). Subsequent reports from Monarch 2 also demonstrated that the median OS improved significantly by 46.7 months in the abemaciclib group versus 37.3 months in a placebo group, with a hazard ratio of 0.757 (95% CI: 0.606-0.945) ($p = 0.01$). The results astonished researchers around the world and gave hope to many patients, as statistically a significant improvement in OS is rarely verified in clinical trials for advanced LBC.

In real-world practice, however, controlling adverse events associated with abemaciclib use is important. Grade 3 or higher diarrhea occurs in about 15% of all patients receiving the drug, and hepatotoxicities, such as neutropenia, leukopenia, and anemia are often observed, their frequency and severity tending to be higher among East Asians. In actual clinical practice, patients for whom abemaciclib is recommended

should be made fully aware of potential adverse effects of the drug before use; during use, an effort should be made to record and report accurately any adverse effects to the attending physician even if this is not always possible because of the patient's lack of awareness, the physician's time constraints or other issues. In Japan, an instructional video book is provided with the drug to explain its characteristics, method of administration, the variety of potential adverse effects, and how to deal with them. In addition, patients can easily record adverse effects daily using a dedicated smartphone application and share this information with their healthcare providers to help accurately identify the adverse effects and prepare appropriate countermeasures. Furthermore, at our hospital we have established a patient support center providing easy access to outpatient counseling by nurses with relevant expertise, peer support from other breast cancer patients, and counseling by clinical psychologists to address the various psychological, social, and physical issues that may arise during treatment for advanced breast cancer.

The present seminar will cover the history of the development of cancer treatments in Japan, introduce data from the Monarch 2 and 3 clinical trials, review cases of abemaciclib use in actual clinical practice, and examine how we deal with side effects in our practice. I would also be happy to share with our Korean colleagues the evaluation of abemaciclib in Japan and discuss the measures implemented against its various adverse effects.

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* In the USA, this indication is approved under FDA's accelerated approval based on progression-free survival. Continued approval for this indication may be contingent upon verification and description of clinical benefit in the confirmatory trials.[4]
CPS = combined positive score; nab-paclitaxel = albumin-bound paclitaxel; FDA = Food and Drug Administration; PFS = progression free survival; HR = hazard ratio; CI = confidence interval; PD-L1 = programmed death-ligand 1

Study result

A. At the second interim analysis (data cutoff, Dec 11, 2019), median follow-up was 25.9 months (IQR 22.8-9.9) in the pembrolizumab -chemotherapy group and 26.3 months (22.7-9.7) in the placebo -chemotherapy group. Among patients with CPS of 10 or more, median PFS was 9·7 months with pembrolizumab - chemotherapy and 5.6 months with placebo -chemotherapy (HR for progression or death, 0.65, 95% CI 0.49 -0.86; one-sided p=0.0012 [primary objective met]).[1]

Study design

a. In this randomised, placebo-controlled, double-blind, phase 3 trial, patients (n=847) with untreated locally recurrent inoperable or metastatic triple-negative breast cancer were randomly assigned (2:1) to pembrolizumab 200 mg every 3 weeks plus chemotherapy (nab-paclitaxel; paclitaxel; or gemcitabine plus carboplatin, n=566) or placebo plus chemotherapy (n=281). Dual primary efficacy endpoints were progression-free survival and overall survival assessed in the PD-L1 CPS of 10 or more, CPS of 1 or more, and intention-to-treat populations.[1]

Reference 1. Cortes J, et al. Pembrolizumab plus chemotherapy versus placebo plus chemotherapy for previously untreated locally recurrent inoperable or metastatic triple-negative breast cancer (KEYNOTE-355): a randomised, placebo-controlled, double-blind, phase 3 clinical trial. *Lancet*. 2020 Dec 5;396(10265):1817-1828. **2.** 키트루다 허가사항. 식품의약품안전처 **3.** National Comprehensive Cancer Network. NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) Breast cancer. Version 3. 2021 **4.** Keytruda. FDA prescribing information.

키트루다® 주요 안전성 정보 **[제품명]** 키트루다®주 (펨브롤리주맙) 100 mg **[효능효과] 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 재발성 또는 전이성 또는 수술이 불가능한 두경부 편평상피세포암의 치료로서 단독 요법. **전형적 호지킨 림프종:** 불응성이거나 3차 이상의 치료 이후 재발한 전형적 호지킨 림프종의 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, 백금기반의 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 **신세포암:** 진행성 신세포암 환자에서의 1차 치료로서 엑시티닙과의 병용 요법. **자궁내막암:** 이전의 전신 요법이후 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:** PD-L1 발현 양성(CPS≥10)이며, 수술이 불가능한 국소 재발성 또는 전이성 삼중음성 유방암 환자의 치료로서 항암화학요법과의 병용요법 **[용법용량]** 이 약 200 mg을 매 3주마다 30분 동안 정맥 점적주입한다. 병용요법으로 투여하기 위해서는 해당 병용 약제의 허가사항을 참고한다. 이 약을 정맥주사용 화학요법제와 병용하여 투여하는 경우 이 약이 먼저 투여되어야 한다. **[금기] 다음 환자에는 투여하지 말 것:** 이 약 및 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 9%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 ; 폐렴증, 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:** 부신부전이 발병하는 시간의 중앙값은 5.3개월(범위: 26일 ~ 16.6개월)이었다. 지속기간의 중앙값은 아직 도달하지 않았다(범위: 4일 ~ 1.9+년). 부신부전으로 인해 이 약을 중단한 환자는 1명(<0.1%)이었다. 5명의 환자는 부신부전 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. **폐렴증:** 폐렴증이 발병하는 시간의 중앙값은 3.3개월(범위: 2일 ~ 19.3개월)이었다. 지속기간의 중앙값은 1.5개월(범위: 1일 ~ 17.2+개월)이었다. 폐렴증으로 인해 이 약을 중단한 환자는 36명(1.3%)이었다. 55명의 환자는 폐렴증 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. 41명의환자는 결장염 증상으로부터 회복하였다. **간염:** 간염이 발병하는 시간의 중앙값은 1.3개월(범위: 8일 ~ 21.4개월)이었다. 지속기간의 중앙값은 1.8 개월(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 약에 대한 항약물항체 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 폐렴증:** 이 약 투여 환자에서 치명적인 사례를 포함한 폐렴증이 보고되었다. 폐렴증의 징후와 증상에 대해 환자를 모니터링해야 한다. 폐렴증이 의심되면 방사선영상 검사를 실시한다. 중등증(2등급) 이상의 폐렴증의 경우 코르티코스테로이드를 투여(프레드니손으로 초회 용량 1-2 mg/kg/day 또는 이에 상응하는 양을 투여하고 이후 점감)한다. 중등증(2등급) 폐렴증의 경우 이 약 투여를 보류하며, 중증(3등급), 생명을 위협하는(4등급) 폐렴증 또는 재발성 중등증(2등급) 폐렴증의 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 단독투여 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. 단독요법으로 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%) 단독요법, 또는 두 약의 병용요법(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 부신부전(원발성 및 속발성)이 보고되었다. 이 약 투여 환자에서 뇌하수체염도 보고되었다. 부신부전 및 뇌하수체염 (뇌하수체기능저하증 포함)의 징후와 증상에 대해 환자를 모니터링한다. 코르티코스테로이드를 투여하고 임상적으로 필요한 경우 다른 호르몬 대체요법을 실시한다. 중등증(2등급) 뇌하수체염의 경우 이 약 투여를 보류하며, 중증(3등급) 내지 생명을 위협하는(4등급) 부신부전 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. 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]** 18세 미만의 소아 환자에 대한 안전성 및 유효성은 확립되지 않았다. **[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: 2021년 07월 23일 **※ 키트루다를 처방하시기 전에 제품설명서를 참조하시기 바랍니다.**

ONE GIANT LEAP FOR TRIPLE NEGATIVE BREAST CANCER

Joyce O'shaughnessy

Baylor Univ. Medical Center, Department of Medical Oncology, U.S.A.

Metastatic triple negative breast cancer (mTNBC) is associated with short survival of 12 to 18 months, and with a dirth of moleculary-targeted therapies. This is a highly heterogenous disease regarding natural history, sites and burden of metastases, and response to therapies, the molecular underpinnings of which are still being deciphered. Cytotoxic therapies, mono- or polychemotherapy, have been the mainstay of mTNBC therapy, but highly durable responses and prolonged survival accrue to a small minority of patients. In this context, the finding that the anti-PD-1 antibody, pembrolizumab, added to first-line chemotherapy, in patients with PD-L1+ mTNBC, significantly improved median overall survival, is an important step forward.

In the pivotal KN-355 trial it has been clearly shown that PD-L1-positivity, defined as a combined positive score (CPS) of >10 using the 22C3 antibody for IHC, is a requirement in selecting mTNBC patients who can benefit with improved survival from pembrolizumab. Approximately 17% of patients whose TNBCs are negative for PD-L1 expression using the SP-142 antibody have CPS >10 PD-L1 expression by 22C3. Thus it is important that patients' TNBCs be assessed for PD-L1 expression utilizing the 22C3 antibody.

Analysis of the Asian patient subpopulation in KN-355 showed CPS >10 PD-L1+ patients had substantially improved PFS of 5.6 mos with chemotherapy/placebo vs 17.3 mos with chemotherapy/pembrolizumab, HR 0.45 (0.22-0.91). The Asian and intent-to-treat populations had a very low incidence of serious immune-related adverse events with first-line pembrolizumab in KN-355, generally 2% or less. The NCCN guidelines have endorsed pembrolizmab as the preferred first-line therapy for CPS >10 PD-L1+ mTNBC patients.

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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 병용 화학요법실시후, 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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When BM from breast cancer weakens her bone,

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for their BETTER LIFE by PREVENTING BONE COMPLICATIONS

- **Denosumab significantly delayed time to first on-study SRE** by 18% compared with ZA.[1]
  [Median time to first SRE: Denosumab NE vs. ZA 26.4 months]
  [18% risk reduction, HR 0.82 (95% CI 0.71-0.95); *P*=0.01]
- Denosumab **reduced the risk of developing multiple SREs*** compared with ZA.[1]
  [23% risk reduction, RR 0.77 (95% CI 0.66-0.89); *P*=0.001]
- Denosumab **delayed time to pain** progression.[2]
  [Median time to moderate/severe pain: Denosumab 9.7 months vs. ZA 5.8 months, HR 0.78 (95% CI 0.67-0.92); *P*=0.0024]
- Denosumab showed clinically meaningful **improvement in HRQoL** of 10% patients.[3]
  [10% patient; average relative HRQoL improvement with denosumab vs. ZA]
- No dosing adjustment required for renal impairment.[1]

*Time to first and subsequent SREs.
SRE, skeletal-related event; **ZA,** zoledronic acid; **NE,** not estimated; **RR,** raito rate; **HRQoL,** health-related quality of life.
Reference 1. Stopeck AT, et al. *J Clin Oncol.* 2010;28:5132-5139. **2.** Cleeland CS, et al. *Cancer.* 2013:119;832-838. **3.** Martin M, et al. *Clin Cancer Res.* 201218 4841-9.

엑스지바®주 제품요약정보
[제품명] 엑스지바®주(데노수맙120밀리그램), **[효능효과]** 1. 다발성 골수종 및 고형암의 골전이 환자에서 골격계 증상 발생 위험 감소. 골격계 증상은 병리학적 골절, 뼈에 대한 방사선 조사, 척수압박, 뼈 수술을 말함. 2. 성인 및 골 성숙이 완료된 청소년에서 절제가 불가능하거나 수술적 절제가 중증의 이환을 일으킬 가능성이 있는 골거대세포종 치료. **[용법용량]** 이 약 1 바이알을 매 4주 간격으로 상완, 허벅지 위쪽 또는 복부에 피하 주사. 정맥내, 근내, 피내 투여되어서는 안된다. 필요시, 저칼슘혈증 치료 및 예방을 위해 칼슘과 비타민 D를 함께 복용. 골거대세포종의 경우 치료 첫 번째 달의 제8일째와 제15일째에 120mg을 추가로 투여한다. **[경고]** 턱뼈 괴사가 발생할 수 있다. **[다음 환자에게는 투여하지 말 것]** 이 약의 주성분 및 다른 성분에 대해 과민반응이 있는 환자, 중증의 치료받지 않은 저칼슘혈증 환자 **[약물이상반응]** [고형암의 골전이] 이 약을 투여 받은 환자에서 다타난 가장 흔한 약물이상반응(≥25%)은 피로/무력증(45%), 저인산혈증(32%), 구역(31%). 이 약을 투여 받은 환자에서 나타난 가장 흔한 중대한 약물이상반응은 호흡곤란. 이 약의 투여를 중단하게 한 가장 흔한 약물이상반응은 뼈괴사와 저칼슘혈증. [다발성골수종] 가장 흔한 약물이상반응(≥10%)은 설사, 구역, 빈혈, 등통증, 혈소판감소증, 말초 부종, 저칼슘혈증, 상기도 감염, 발진 및 두통. 가장 빈번하게 보고된 중대한 이상사례(어느 투여군에서든 ≥2%)은 폐렴, 형질세포 골수종, 발열, 열성 호중구감소증, 급성 신장 손상, 패혈증, 빈혈. 이 약의 투여를 중단하게 한 가장 흔한 약물이상반응(≥1%)은 턱뼈 괴사, [골거대세포종] 가장 흔한 약물이상반응(≥10%)은 관절통, 두통, 구역, 등 통증, 피로 및 사지통. 가장 흔하게 나타난 중대한 약물이상반응은 턱뼈 괴사와 골수염(발생률 0.7%)와 치아농양 또는 치아 감염(발생률 0.7%). **[일반적 주의]** 이 약 투여 중 프롤리아 프리필드시린지를 투여하면 안된다. 과민반응, 저칼슘혈증, 턱뼈 괴사, 비정형 전자하부 및 골간 대퇴골 골절, 뼈 성장 환자의 치료중단에 따른 고칼슘혈증, 치료 중단 후 다발성 척추 골절의 가능성이 있으므로 칼슘 수치 모니터링, 칼슘 및 비타민 D 섭취, 구강 검진, 통증 등의 골절의 징후 및 증상, 임신 여부 등을 모니터링하고, 필요시 치료 중단 등의 위험적 조치를 고려한다. **[보관 및 취급상의 주의사항]** 동결을 피하여 차광 냉장 (2-8°C) 보관. **[수입판매원]** 암젠코리아유한회사 (서울특별시 중구 을지로 5길 19, 20층). (개정일: 2019.10.23) ※**제품을 처방하시기 전 상세 제품설명서를 참고하여주시기 바랍니다.**

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KR-05518-XGA-2021-Feb

GC녹십자 JEIL 제일약품

건강예방문자 지금

[GC녹십자] 항암치료에 호중구감소증이 걱정된다면 뉴라펙 프리필드시린지주로 효과적으로 예방하세요.

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- 검증된 효과(단기간 내 회복)와 내약성

ref. 1) Lee KH, et al. Support Care Cancer 2016;24:1709-17.

NOVARTIS

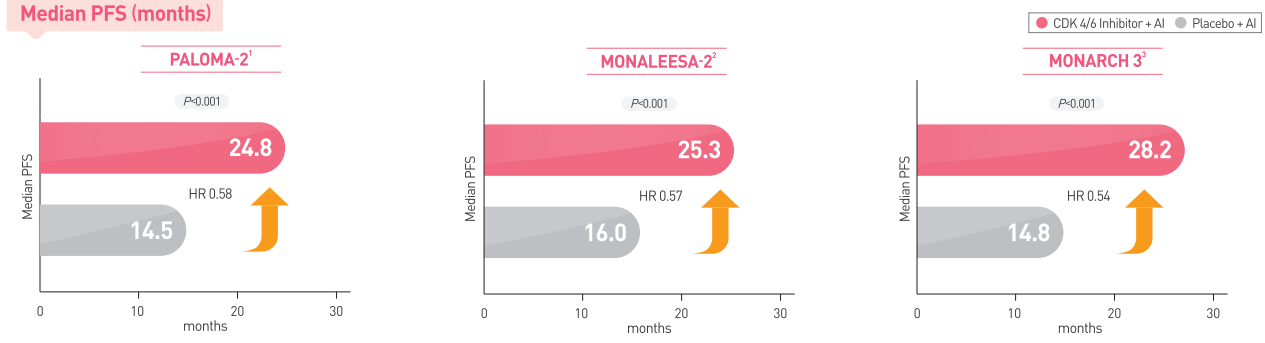
유한양행

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.

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KR2008B0211 FMR-P2.0-121202008

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- 루프린®은 **Microsphere 기술로 개발**되었으며[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 11.25 mg 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).

PRESCRIBING INFORMATION

루프린주 (Vial) 3.75 mg / 루프린 디피에스주 (DPS) 3.75 mg, 11.25 mg, 22.5 mg (류프로렐린아세트산염) [유효성분] 류프로렐린아세트산염 (JP) **[효능·효과] 1~2: 22.5 mg DPS / 1~5: 3.75 mg vial, 3.75 mg DPS, 11.25 mg 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 1회 3.75 mg/12주 1회 11.25 mg/24주 1회 22.5 mg을 피하주사한다. **3. 자궁내막증:** 보통 성인에는 4주 1회 3.75 mg (루프린주 3.75 mg: 체중 50 kg 미만의 환자에게는 1.88 mg을 투여)/12주 1회 11.25 mg을 피하주사하며, 초회 투여는 월경주기 1~5일째에 한다. **4. 자궁근종:** 보통 성인에는 4주 1회 1.88 mg 피하주사한다. (루프린주 3.75 mg에 한함) 단, 체중과다 환자, 자궁중대가 고도인 환자에는 4주 1회 3.75 mg/12주 1회 11.25 mg을 투여하며, 초회 투여는 월경주기 1~5일째에 한다. **5. 중추성 사춘기 조발증:** 1) 3.75 mg vial 보통 4주 1회 체중 kg당 30 μg을 피하주사하며, 증상에 따라 체중 kg당 90 μg까지 증량할 수 있다. 2) 3.75 mg DPS 보통 4주 1회 류프로렐린아세트산염으로서 체중 kg당 30 μg을 피하주사한다. 또한 증상에 따라 체중 kg당 90 μg까지 증량할 수 있다. 단, 이 제제는 1/2 시린지 용량 또는 1 시린지 용량 투여가 필요한 경우에 한하며, 남은 현탁 주사액은 폐기할 것 3) 11.25 mg DPS 용법·용량은 개인별로 조절되어야 하며, 권장 초기용량은 체중에 따라 조절한다. -체중 20 kg 이상의 소아: 1 mL (11.25 mg 류프로렐린아세트산염) 현탁액을 3개월마다 1회 피하주사한다. -체중 20 kg 미만의 소아: 이러한 드문 경우에는 중추성 사춘기 조발증의 임상적 활성도에 따라 다음의 용량을 투여한다. 0.5 mL (5.625 mg) 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 한다. 2. 남성 환자에서 심근경색, 급성심장사, 뇌졸중으로의 발생위험의 증가가 GnRH 작용제의 사용과 연관 있음이 보고되었다. 3. 앰플주사제는 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 (루프린주 3.75 mg에 한함) **• 다음 환자에는 투여하지 말 것** 1. 이 약의 성분, GnRH 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 22.5 mg 제외) 7. 진행성 뇌종양 소아 환자 (루프린주 3.75 mg에 한함) 8. 소아 (루프린디피에스주 22.5 mg에 한함) **• 다음 환자에는 신중히 투여할 것** 1. 자궁내막증, 자궁근종, 폐경전 유방암: 자궁에 정막하 근종이 있는 환자 2. 당뇨병 환자 3. 고혈압 환자 4. 우울증의 병력이 있는 환자 5. 젤라틴 함유제제 또는 젤라틴 함유 식품에 대해서 쇼크, 아나필락시양 증상 (두드러기, 호흡곤란, 구진부종, 후두부종 등) 등의 과민반응의 병력이 있는 환자 (단, 과민반응의 원인이 젤라틴인 것이 명확한 경우에는 투여해서는 안 됨) (루프린주 3.75 mg에 한함) **[저장방법]** 밀봉용기, 실온 (1~30℃) 보관 **[수입자]** 한국다케다제약 주식회사/서울특별시 송파구 올림픽로 300 롯데월드타워 37층 **[제조자]** Takeda Pharmaceutical Company Limited/Hikari Plant (Japan)

※ 이 내용은 허가사항을 요약한 것으로 자세한 정보는 제품의 첨부문서 또는 식약처 의약품 안전나라 (https://nedrug.mfds.go.kr)의 각 제품허가사항을 확인하십시오.

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.

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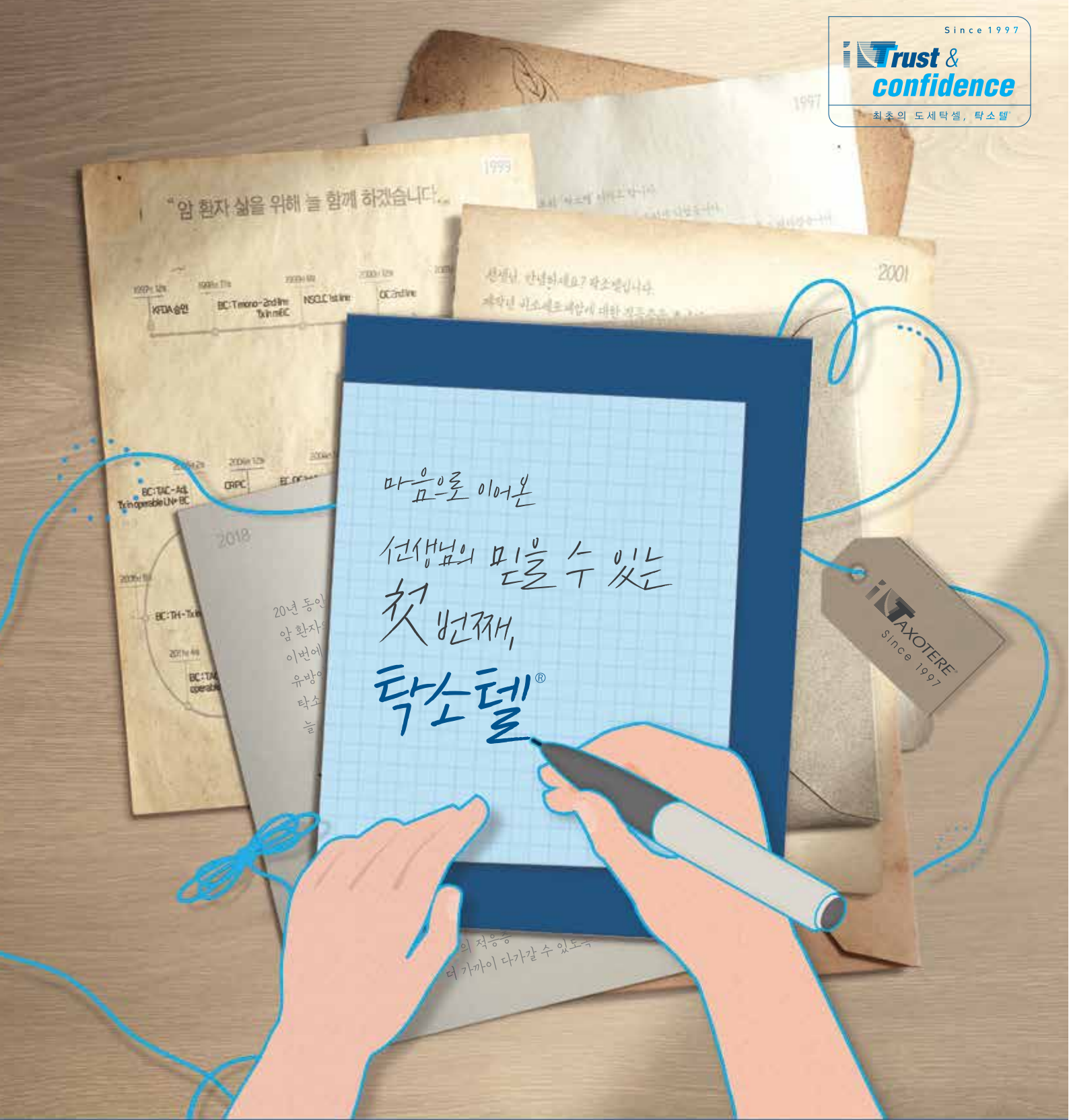

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탁소텔®1-바이알주(도세탁셀수화물) [효능·효과] 1. 유방암 • 국소적으로 진행된 또는 전이성 유방암 1) 독소루비신과 병용하여 국소적으로 진행된 또는 전이된 유방암의 1차 치료 2) HER2가 과발현(IHC 3+ 또는 FISH 양성)되고 화학요법 치료를 받은 경험이 없는 전이성 유방암에 트라스투주맙과 병용요법 3) 이전의 화학요법에 실패한 국소적으로 진행된 유방암 또는 전이성 유방암 4) 카페시타빈과 병용하여 안트라사이클린계 약물을 포함한 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 3. 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 단독요법 2) 시스플라틴 및 플루오로우라실과 병용하여 전이성 또는 국소재발성 위암의 1차 치료 7. 식도암: 진행성 또는 재발성 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 치료를 받은 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/m² 투여 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 1일차에 초기부하용량으로 트라스투주맙 4 mg/kg을 90분간 투여한 이후 1주마다 유지용량으로 2 mg/kg를 90분간 투여. (5주기의 8일차부터, 8주기까지) 도세탁셀은 5주기의 2일차에 투여하고 6~8주기에는 1일차에 투여. (3) 보조화학요법이 완료된후에트라스투주맙 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 주입. 도세탁셀 투여 1일 전, 전처치로 경구용 덱사메타손 8mg, 1일 2회 투여를 시작하며, 총 5회 동안 계속 복용. 2. 비소세포 폐암: 이 약 75 mg/m²을 매 3주마다 1시간동안 정맥 주사. 백금 유도체와 복합화학요법으로 치료시 최대 75 mg/m²으로 정맥 투여. 3. 전립샘암: 프레드니솔론과 병용시 이 약 75 mg/m²을 매 3주마다 1시간동안 정맥주사. 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: 수술이 불가능한 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, 낮은 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 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: 상용량은 성인에게 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. 2) 간장애 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 염성 호중구감소증, 감염, 혈소판감소증, 구내염, 모력증과 같은 중증의 이상반응이 나타날 위험이 높다. 3) 과민반응 4) 중증의 체액저류 5) 이차성 원발 악성종양 (급성 골수성 백혈병, 골수형성이상 증후군, 비호지킨 림프종 및 신장암 포함) 6) 소장결장염 및 호중구감소성 장염(맹장염) 7) 중앙응해증후군 **금기** 1) 이 약 및 이 약의 구성성분, 폴리소르베이트 80에 대해 중증의 과민반응의 병력이 있는 환자 2) 호중구수가 1,500 /mm³ 미만인 환자 3) 임부, 가임부 및 수유부 4) 중증 간기능장애 환자 5) 병용투여시, 병용약물에 금기인 환자(중증 신기능장애 환자, 파라플라틴, 백금화합물, 만니톨에 과민반응이 있는 환자 등) 6) 감염증의 합병증이 있는 환자 가) 감염성 발열이 의심되는 환자 나) 중증의 골수 억제가 있는 환자 **신중투여** 1) 골수억제가 있는 환자 2) 간기능장애 환자 3) 신기능장애 환자 4) 간질성 폐렴 또는 폐섬유증이 있는 환자 5) 부종이 있는 환자 6) 임신할 가능성이 있는 환자(남성 및 여성)(효과적인 피임법을 사용하여야 한다.) **※ 기타 자세한 내용은 제품설명서 또는 홈페이지를 참조하십시오.** 최종문안개정년월일: 2020.09.22

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* 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 4 주 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

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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 aARI20190501

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Global Breast Cancer Conference 2022

Oral Presentation

"Go Beyond Cure of Breast Cancer"

DISCRIMINATION OF HER2 LOW-POSITIVE WITH HER2 ZERO TUMORS WITH 21-GENE MULTIGENE ASSAY IN ER+HER2- BREAST CANCER

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Background: Recent studies suggest that breast cancers with low HER2 expression, which is defined as 1+ or 2+ of HER2 by immunohistochemistry (IHC), have distinct clinical course compared with those with HER2-zero tumors. Among ER+HER2- breast cancer, we compared genomic characteristics between HER2-low and HER2-zero using 21-gene multigene assay (Oncotype Dx).

Methods: We reviewed retrospectively 2,295 patients who underwent Oncotype DX test in two hospitals between 2013 and 2020. Patients were classified into two groups as the HER2-zero and HER2-low based on HER2 IHC and SISH test. In cases with HER2 2+, no amplification of HER2 gene was confirmed by silver *in situ* hybridization. High genomic risk was defined as cases with 21-gene recurrence score (RS) > 25.

Result: Of these, 944 (41.1%) were assigned in the HER2-zero, and 1351 (58.9%) were in the HER2-low. The averages of RS were 17.082 in the HER2-zero breast cancer and 18.503 in the HER2-low, respectively (P-value < 0.005). HER2 score identified by qRT-PCR was 8.912 in the HER2 zero group and was 9.337 in the HER2 low group (P < 0.005). When we compared a proportion of high RS between two groups, the high RS rate was 12.4% (117 of 944) in the HER2-zero, while it was 17.0% (230 of 1351) in the HER2-low (p = 0.002).

Conclusions: Within ER+HER2- breast cancer, HER2-low tumors have more chance to have high genomic risk than HER2-zero tumors. Further studies to discriminate survival outcome between the HER2-low and HER2-zero tumors are required.

LONG-TERM ONCOLOGIC OUTCOMES OF BRCA 1/2 MUTATIONS IN UNSELECTED TRIPLE-NEGATIVE BREAST CANCER PATIENTS IN SAMSUNG MEDICAL CENTER

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Background: Triple-negative breast cancer (TNBC) is known to have a relatively low risk of late recurrence compared to luminal type breast cancer. In the previous study about oncologic outcomes of BRCA 1/2 mutations in unselected TNBC patients in Korea, there were no significant differences between BRCA 1/2 carriers and non-carriers in recurrence and survival. However, BRCA 1/2 carriers showed worse contralateral breast cancer-free survival (CBCFS) than non-carriers. The median follow-up time was 53.6 months which was relatively short to analyze late recurrence. We hypothesized BRCA 1/2 carriers might have higher late recurrence rate than non-carriers and analyzed long-term oncologic outcomes in TNBC by the BRCA 1/2 mutations.

Methods: We conducted retrospective study of 953 TNBC patients with known BRCA1/2 mutation status who underwent surgery at Samsung Medical Center (SMC) between June 2008 and Jan 2016.

Result: Overall, 122 patients (12.8%) had BRCA 1/2 mutations: 91 (9.5%) were in BRCA 1, and 32 (3.4%) were in BRCA 2. The median follow-up duration was 80.9 months. There were no significant differences in disease-free survival, distant metastasis-free survival, overall survival, and breast cancer-specific survival (p-value = 0.301, 0.278, 0.412, and 0.079, respectively) between BRCA 1/2 carriers and non-carriers. However, there were worse CBCFS and ovarian cancer incidence in BRCA 1/2 carriers than non-carriers (p-value < 0.0001, respectively). BRCA 1/2 carriers showed significantly worse recurrence rate at 150 months than non-carriers.

Conclusions: In unselected TNBC patients with known BRCA 1/2 mutations, we found BRCA 1/2 carriers showed higher late recurrence rate than non-carriers.

ENHANCED REACTIVE OXYGEN SPECIES (ROS) IN BREAST CANCER IS ASSOCIATED WITH TUMOR AGGRESSIVENESS, IMMUNE RESPONSE AND WORSE SURVIVAL IN BREAST CANCER

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Background: Reactive oxygen species (ROS) are physiological oxygen derivative with high reactivity, and may be protective to cells by playing roles in cell signaling and homeostasis or may be harmful by causing irreversible damage to DNA. In this end, we hypothesized that ROS in tumor microenvironment (TME) is associated with worse breast cancer (BC) patient outcomes.

Methods: ROS pathway score was generated by Gene Set Variation Analysis of Hallmark ROS pathway gene sets and a total of 6,245 BC patients were analyzed.

Result: High ROS BC significantly enriched cell proliferation-related gene sets (MYC targets v1 and v2, G2M checkpoint, E2F targets), pro-cancer-related gene sets (DNA repair, unfolded protein response, MTORC1 signaling, PI3K/AKT/MTOR signaling, glycolysis, and oxidative phosphorylation), immune-related gene sets (inflammatory response, allograft rejection, interferon (IFN)-α and γ responses, complement, and IL6/JAK/STAT3 signaling), and infiltrated immune cells (CD4+ memory T cells, CD8+ T cells, Th1, dendritic cells, Tregs, Th2, M1 and M2 macrophages) and B-cells, as well as elevated cytolytic activity (CYT) consistently in two large cohorts. Cancer cells were the major source of ROS in BC TME of single cell sequence. High ROS was significantly associated with intratumor heterogeneity, homologous recombination defects, mutation rates and neoantigens. High ROS was significantly associated with clinical aggressiveness in AJCC stage, Nottingham grade and Ki67 expression, as well as worse overall survival in both GSE96058 and METABRIC, and with worse disease-specific survival in METABRIC.

Conclusions: Abundant ROS in breast cancer patients is associated with worse survival, abundant mutations, aggressive cancer biology, and immune response.

WHOLE GENOME SEQUENCING-BASED CIRCULATING TUMOR DNA PROFILING OF METASTATIC BREAST CANCER PATIENTS FOR MOLECULAR CHARACTERIZATION AND THERAPY RESPONSE PREDICTION

Min Hwan Kim[1], Gun Min Kim[1], Jin Mo Ahn[2], Won-Ji Ryu[3], Seul-Gi Kim[1], Jee Hung Kim[4], Tae Yeong Kim[3], Hyun Ju Han[3], Jee Ye Kim[5], Hyung Seok Park[5], Seho Park[5], Byeong-Woo Park[5], Seung Il Kim[5], Eun Hae Cho[2], Joohyuk Sohn[1]

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Background: Low-pass whole-genome sequencing (LP-WGS)-based circulating tumor DNA (ctDNA) analysis is a versatile tool for somatic copy number aberration (CNA) detection, and its clinical implication in breast cancer needs to be elucidated.

Methods: This study enrolled 207 treatment-nave metastatic breast cancer patients from Feb 2017 to September 2020 in Yonsei Cancer Center. The baseline (n = 207) and post-progression (n = 48) plasma samples were prospectively collected on first-line systemic therapy, and LP-WGS was employed for ctDNA somatic copy number alteration (CNA) analysis. The CNA burden of ctDNA was scored by "I-score" method, which was developed to measure genome-wide chromosomal instabilities.

Result: The baseline I-score ctDNA CNA burden was highest in triple-negative breast cancer (TNBC) patients among subtypes, and the patients were dichotomized by median I-score level. The high baseline ctDNA I-score was independently associated with poor overall survival with adjustment of tumor subtype, visceral metastasis, and disease status. The progression-free survival (PFS) on first-line therapy was also shorter in high baseline I-score patients. The patients were classified into five molecular clusters with distinct overall survival. Patients with BCL6 amplification on baseline ctDNA showed significantly shorter PFS on CDK4/6 inhibitor treatment, and emergence of FGFR1 amplification and MYC amplification was noted after CDK4/6 inhibitor treatment. The ctDNA shallowHRD score was highest in TNBC patients among subtypes, and TNBC patients with high shallowHRD score showed high response rate on platinum-based chemotherapy.

Conclusions: LP-WGS based ctDNA analysis provides a robust tool for non-invasive genomic clustering, therapy response prediction, and HRD estimation in metastatic breast cancer patients.

PRECLINICAL INVESTIGATION OF WEE1 INHIBITOR (AZD1775) IN PATIENT-DERIVED ORGANOIDS AND XENOGRAFT MODELS

Seungyeon Ryu[2,3,4,5], Hoe Suk Kim[2,3], Jung Eun Kim[6], So-Hyun Yoon[2,3,4,5], Sangeun Lee[2,3,4,5], Moonjou Baek[2,3,4,5], Han-Byoel Lee[1,2,3], Dong Woo Lee[6], Bosung Ku[6], Wonshik Han[1,2,3,4,5]

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Background: Breast cancer patient-derived organoids (PDO) and patient-derived xenografts (PDX) are useful tools to evaluate efficacy and experimental drug for personalized thearapeutic approaches, especially for triple negative breast cancer (TNBC) that lacks standard of care and targeted combination treatments. Herein, we evaluated multiple drug response in organoids using automated high-throughput screening system and investigated the therapeutic potency of targeting WEE1.

Methods: PDO were established using fresh surgical specimens of primary tumor of TNBC patients (N = 3; #207, #172, and #185). PDX were established by injecting PDO into NSG mice. PDX-derived organoids (PDXO) were established using tumor specimen of PDX. Western blot, immunofluorescent staining, and immunohistochemistry were performed. Cytotoxicity of 9 chemotherapeutic drugs and 13 targeted drugs including WEE1 inhibitor (AZD1775) was assessed by calcein AM staining. AZD1775 was administered by oral gavage (30 mg/kg) for 3-4 weeks in PDX mice.

Result: All PDO, PDX, and PDXO maintained ER-, PR- and HER2-negative characteristics of matched primary tumor. PDO and PDXO #207 of a 35-year old patient with metastatic TNBC were highly sensitive to AZD1775, but PDO and PDXO #172 and #185 were less sensitive. AZD1775 inhibited tumor growth and metastasis in PDX#207 mice ($P < 0.0079$), but was not sufficient to reduce tumor growth in PDX#172 and #185 mice. Additionally, PDO#207 were sensitive to mTOR (Everolimus), HDAC (Quisinostat), and ATP-competitive protein kinase (Saurosporine) inhibitors. We suggest that the combination with these targeted drugs may confer clinically meaningful benefit in patient #207 with metastatic TNBC.

Conclusions: This study may provide a preclinical tool to screen drug responses to standard of care and newly identified drugs for TNBC.

THE IMPACT OF STATIN USE AND BREAST CANCER RECURRENCE - A RETROSPECTIVE STUDY IN SINGAPORE

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Background: Statins, HMG-CoA reductase inhibitors, are commonly used cholesterol-lowering medications which are increasingly recognized to have anti-cancer properties. Most clinical evidence supports a protective effect of statin on reducing breast cancer recurrence, particularly in hormone-receptor positive breast cancers.

Methods: This is a retrospective study of patients diagnosed with breast cancer at the National Cancer Centre and Singapore General Hospital from 2005-2015. Statin use was defined as use after surgery. All statistical analyses were performed in Stata 16.1.

Result: A total of 7858 females with breast cancer were studied, 1353 (17.2%) were statin users, 6505 (82.8%) non-statin users, with a median follow-up of 8.67 years. Distribution of cancer stage, histology, molecular-subtypes and grades were similar in both groups. Estrogen-receptor (ER) positive (HR 0.57, 95% CI 0.43-0.76, $p < 0.001$) and HER2-negative (HR 0.74, 95% CI 0.57-0.96, $p = 0.026$) invasive cancers had a lower recurrence-risk in statin users. Statin users trended towards a long-term recurrence-risk reduction (all subtypes, HR 0.48, $p = 0.002$; ER-, HR 0.34, $p = 0.036$; HER2+, HR 0.10, $p = 0.002$). Disease-specific survival benefit was seen in statin users with ER+cancers (HR 0.69, 95% CI 0.51-0.95, $p = 0.023$), especially ER+ invasive cancers (HR 0.70, 95% CI 0.51-0.95, $p = 0.024$), but with no statistically significant benefit in overall survival for statin users (all subtypes).

Conclusions: This is the first known retrospective study on the effect of statin use and breast cancer recurrence in an Asian population. Similar to previous studies, statin use is associated with a risk-reduction in breast cancer recurrence, especially in patients who have ER+ and HER2- invasive breast cancer. Statin use is also associated with a reduced risk of breast cancer recurrence in all subtypes of breast cancer in the long term (> 6 years post-diagnosis).

CLINICAL CHARACTERISTICS AND PROGNOSIS OF METAPLASTIC CARCINOMA OF THE BREAST COMPARED WITH INVASIVE DUCTAL CARCINOMA: A PROPENSITY-MATCHED ANALYSIS

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Background: Metaplastic carcinoma of the breast (MpBC) is known as an aggressive histologic type of all breast cancers. Although MpBC has a poor prognosis and occupies an important proportion in breast cancer mortality, the clinical features of MpBC compared with invasive ductal carcinoma (IDC) are unknown in detail and treatment has also not been clearly identified.

Methods: We retrospectively reviewed medical record of cases of 155 MpBC patients and 16,251 IDC cases who underwent operation in single institution between Jan 1994 and Dec 2019. Both groups were matched at 1:4 by using propensity score matching (PSM). Finally, 120 were matched from 155 MpBC patients and 478 from 16,251 IDC patients. Disease-free survival and overall survival of MpBC and IDC patients after PSM were analyzed by Kaplan-Meier survival and multivariable Cox regression analysis was performed.

Result: The most common subtype of MpBC was triple-negative breast cancer and nuclear and histologic grade were higher than IDC. Multivariable Cox regression analysis indicated that MpBC was an independent prognostic factor for disease-free survival (HR = 2.240; 95% CI, 1.476-3.399, $p = 0.0002$) or overall survival (HR = 1.969; 95% CI, 1.147-3.382, $p = 0.0140$). However, survival analysis revealed that MpBC patients had no significantly worse disease-free survival (HR = 1.465; 95% CI, 0.882-2.432, $p = 0.1398$) or overall survival (hazard ratio [HR] = 1.542; 95% confidential interval [CI], 0.875-2.718, $p = 0.1340$) compared with IDC patients after PSM.

Conclusions: Although MpBC histologic type had poor prognostic factor compared with IDC, it might be treated according to the general treatment plan of invasive carcinoma rather than being treated aggressively.

THE IRRADIATION EFFECTS ON MALIGNANT PHYLLODES TUMOR OF THE BREAST IN A PATIENT-DERIVED XENOGRAFT MODEL

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Background: Wide excision is the primary treatment of choice for malignant phyllodes tumor (MPT); however, local treatment failure is often experienced even if sufficient resection margins are obtained. Therefore, the addition of radiation therapy (RT) after surgery is considered, however, questions remain regarding the role of RT on MPT. In this study, we investigate the effects of irradiation in MPT with a patient-derived xenograft model.

Methods: We irradiated the PDX model when the tumor reached 400 mm^2 in four fractions of 6 Gy daily (6 Gy × 4fractions, 2.0 Gy/min). The mice were euthanized when the tumor reached 1,000 mm^2 or after 15 days of irradiation. Histological and differential gene expression analyses were performed with resected tumors.

Result: The tumor growth was suppressed significantly in the irradiation group compared with the control group (n = 3, $P = 0.015$, Wilcoxon test). In histological evaluation, the irradiation group had a lower mitotic count (mitoses/10HPF, 2.3 ± 3.2 vs. 22.0 ± 11.1, $p = 0.04$), and showed a lower tendency of stromal cellularity and pleomorphism ($p = 0.057$, $p = 0.184$, respectively). There was no difference with stromal overgrowth. Neither irradiation group nor control group showed distant metastasis. Differentially Expressed Genes (DEGs, log2 fold change > |1| with p-value < 0.01) analysis identified significantly upregulated pathways in the irradiation group include: p53 signaling pathway and I-kappa B kinase/NF-kappa B signaling pathway.

Conclusions: This study provides the effects of irradiation in MPT. The irradiation group showed the shrinkage of tumor and upregulated p53 signaling pathway. The patient with MPT may benefit from postoperative RT.

MAMMOGRAPHIC BREAST FEATURES, RISK OF HEART DISEASES, AND MORTALITY OUTCOMES IN KOREAN WOMEN

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Background: This study aimed to evaluate the association of breast density and micro-calcification with heart disease risk and mortality risk in middle-aged women.

Methods: This cohort study used data from the National Health Insurance Service database and included women who underwent breast cancer screening between 2009 and 2014. Participants were followed up until 2020. Breast density and micro-calcification were obtained from mammographic results. Risk of heart diseases (including 16 sub-categories) and mortality outcomes (including death from any cause, cancer-related, and circulatory-related deaths) were defined according to the ICD-10 codes.

Result: Of the 6,889,171 women, the mean age was 54.1 ± 10.7. Presence of micro-calcification led to an increase in several heart diseases, including ischemic heart diseases (aHR 1.12, 95% CI 1.06-1.18), angina pectoris (1.08, 95% CI 1.02-1.15), chronic ischemic heart disease (1.21, 95% CI 1.09-1.35), atrial fibrillation (1.15, 95% CI, 1.03-1.29), heart failure (1.18, 95% CI 1.06-1.31), and stroke (1.07, 95% CI 1.03-1.12). Despite the increase in breast cancer, women with dense breasts had decreased risk of heart diseases, such as ischemic heart diseases (0.92, 95% CI 0.91-0.93), acute myocardial infarction (0.89, 95% CI 0.86-0.92), pulmonary (0.94, 95% CI 0.90-0.99), and cerebral infarction (0.95, 95% CI 0.93-0.96). An increased risk of all-cause mortality was observed in women with micro-calcification and decreased risk in women with dense breasts.

Conclusions: Micro-calcification and breast density assessed during mammography screening might be utilized to predict heart diseases and mortality beyond the benefits of breast cancer risk prediction.

CAPSULAR CONTRACTURE AFTER NIPPLE-SPARING MASTECTOMY AND IMMEDIATE PREPECTORAL VERSUS SUBPECTORAL IMPLANT-BASED BREAST RECONSTRUCTION

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Background: The frequency of prosthetic breast reconstruction has increased significantly. The development of implants and acellular dermal matrices (ADM) accelerated this trend. This study aimed to compare the capsular contracture (CC) in prepectoral versus subpectoral approach and discuss the effect of ADM in implant-based reconstruction.

Methods: Four hundred and thirty-three patients (478 breasts) underwent nipple-sparing or skin-sparing mastectomy followed by immediate implant-based reconstruction for invasive or in situ breast carcinomas between September 2007 to December 2018 were analyzed. A retrospective review was performed on patients who underwent prepectoral or subpectoral implant-based breast reconstruction in a single stage direct-to-implant or a two-stage tissue expander insertion. Fisher's exact test was used to analyses clinicopathological variables. Univariate and multivariate logistic regression was performed to assess the association between CC and variables.

Result: The 370 patients (77.4%) underwent subpectoral reconstruction and 108 (22.6%) underwent prepectoral. The CC occurred in 51(10.7%) patients. In these patients, mean capsular thickness was 0.26 ± 0.05 mm. A higher rate of CC was found for the subpectoral patients with partial ADM coverage than for the prepectoral patients with full ADM coverage (9.8% vs 90.2%; $p = 0.021$). The subpectoral reconstruction (OR 7.2; 95%CI 1.8-29.0; $p = 0.006$) and irradiation (OR 5.3; 95%CI 1.99-14.2; $p = 0.001$) and smaller implant (OR 0.9; 95%CI 0.98-0.99; $p = 0.002$) were significantly associated with an increased risk of CC. More patients in the subpectoral group were diagnosed with high grade of CC than prepectoral group (96.8% vs 3.2%; $p = 0.049$).

Conclusions: This study demonstrated that prepectoral reconstruction with ADM full coverage is a safe alternative for preventing CC.

SHOULD RESIDUAL MICROCALCIFICAIONS ON MAMMOGRAPHY BE REMOVED AFTER NEOADJUVANT CHEMOTHERAPY WITH TCHP FOR HER-2 POSITIVE BREAST CANCER

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Background: As neoadjuvant chemotherapy (NAC) is increasingly administered to locally advanced breast cancer patients, breast conserving surgery had become available for more breast cancer patients. However, even if tumor is reduced after NAC, it is not clear whether residual microcalcifications on mammography should be excised. The purpose of this study is to reduce unnecessary mastectomy by comparing the extent of calcification and the size of residual tumors in breast cancer patients after NAC with TCHP.

Methods: This study included patients diagnosed with HER-2 positive breast cancer and surgically treated after NAC with TCHP regimen at the Samsung medical center between June 2016 and December 2020. 658 patients were reviewed on the electronic medical records retrospectively, and 624 patients were enrolled.

Result: Of the 624 patients, 331 (53%) had residual invasive ductal carcinoma or intraductal carcinoma (pCR rate = 47%). There was no difference in the pCR rate according to residual microcalcifications (43.1% vs 50.5%, $p = 0.08$). There was a statistically significant difference in pCR rates according to HR status (32.8% vs 60.5%, $p < 0.05$). In 208 patients with suspected CR on MRI but residual microcalcifications on MMG after NAC, there was a statistically significant difference in the pCR rate according to HR status (41.9% vs 73.0%, $p < 0.05$), but no difference in the mastectomy rate (30.2% vs 32.8%, $p = 0.70$).

Conclusions: In the case of HR-/HER2+ breast cancer patients with suspected pCR on MRI after NAC with TCHP, unnecessary mastectomy can be reduced by confirming biopsy for residual microcalcifications.

ASSESSMENT OF QUALITY OF LIFE AND OBJECTIVE COSMETIC OUTCOME OF BREAST CONSERVING SURGERY WITH OR WITHOUT LATISSIMUS DORSI MINI-FLAP IN BREAST CANCER

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Background: Latissimus dorsi mini-flap (LDMF) with breast conserving surgery (BCS) was introduced as a useful volume replacement technique when the tumor is located in upper outer portion of breast and the tumor size is large requiring extensive excision of breast tissue. However few studies have assessed quality of life (QoL) and objective cosmetic outcome of LDMF in breast cancer surgery.

Methods: This study was a prospective cohort study of patients who underwent LDMF and BCS. AS a control, patients who underwent BCS without any volume replacement and the tumor size equal to or greater than 2.5 cm on the upper outer of the breast on preoperative imaging were enrolled. We compare QoL and cosmetic results using Breast Q questionnaire, BCCT.core and panel assessment of Harris scale.

Result: Pathologic tumor size was significantly larger in LDMF group (LDMF 3.92 cm vs BCS-only 3.01 cm, $p = 0.000$). Psychosocial well-being ($P = 0.024$), physical well-being ($P = 0.00$) were significantly better in the BCS-only group than in the LDMF group respectively. In the physicians assessment and BCCT.core assessment, there were no significant difference in the cosmetic outcome score between the two groups ($p = 0.884$, $p = 0.904$) respectively.

Conclusions: In conclusion, physician assessed cosmetic outcome of LDMF was equivalent to that of BCS without LDMF although the tumor size was significantly larger in patients with LDMF. There was also no significant difference between the two groups in the objective postoperative cosmetic result using BCCT.core. Because the average evaluation score of the LDMF group was slightly higher, oncoplastic surgery using LDMF is also sufficiently recommended.

ONLY TUMOR BIOLOGY IS CORRELATED WITH HIGHER LOCOREGIONAL RECURRENCE RATE IN PATIENTS UNDERGOING NIPPLE AREOLAR COMPLEX SPARING MASTECTOMY WITH IMMEDIATE IMPLANT RECONSTRUCTION

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Background: The rate of NAC sparing mastectomy with implant augmentation is rapidly increasing as the National Health Insurance covered reconstructive surgery for breast cancer patients from 2015. However, only few reports about oncologic safety have been reported and in the absence of large-scale data. We designed the study to analyze surgical outcomes.

Methods: We used the prospectively collected cohort data. Patients who underwent immediate implant reconstruction after nipple areola complex (NAC) sparing mastectomy at the National Cancer Center between January 2012 and December 2017 were enrolled.

Result: A total of 493 patients was analyzed. The mean age of the patients was 44.6 years, the mean BMI was 22.48 kg/m^2, and the number of bilateral cases was 52 (10.7%). 135 patients (27.8%) had multiple tumors. Median follow-up was 4.5 years. In the univariate cox-regression result, the overall 5-year recurrence rate was 20% regardless of subtype. When comparing recurrence-free survival for each subtype, the luminal A type had the best prognosis, and the recurrence rate was higher in TNBC in the early stages and in HER2 type in advanced stages.

Conclusions: Our results showed that NAC sparing mastectomy with immediate implant reconstruction had similar oncologic outcome in terms of overall survival or distant metastasis, however the locoregional recurrence was rather high. Even this is remediable problems we would admit that NAC sparing mastectomy is a bit different from traditional mastectomy. In case that we inevitably apply this operation to relatively young women with multifocal breast cancer, careful consideration would be needed.

EFFECTIVENESS OF PROPHYLACTIC LYMPHOVENOUS BYPASS IN REDUCTION OF BREAST CANCER-RELATED LYMPHEDEMA

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Background: Breast cancer-related lymphedema (BCRL) occurs in up to 40% undergoing axillary lymph node dissection (ALND). Prophylactic lymphovenous bypass (PLVB) is performed at the time of ALND. Our study aims to evaluate the effectiveness of PLVB.

Methods: We reviewed patients who underwent ALND from 5/2011 to 11/2020 at an academic cancer center. Physical therapy (PT) assessments were reviewed for limb measurements. BCRL was defined as circumference increase ≥ 2 cm.

Result: Of the 503 patients, 383 (76.1%) underwent ALND and 120 (23.9%) ALND+PLVB. ALND+PLVB patients were younger, less likely to have mastectomy, and more likely to receive neoadjuvant chemotherapy ($p < 0.0001$). Significantly more ALND+PLVB underwent preoperative PT (83.3% vs 31.6%, $p < 0.0001$), 3 months postoperative PT (57.5% vs 42.3%, $p = 0.004$), and 12 months postoperative PT (35.8% vs 16.7%, $p < 0.0001$). Overall BCRL at 3 months postop was 20.4%, with similar rates between ALND vs ALND+PLVB (17.6% vs 20%, $p = 0.605$); and 48.6% at 12 months (40.6% ALND vs 60.5% ALND+PLVB, $p = 0.04$). BCRL was less severe in ALND+PLVB (67% 1 site, 33% 2 sites in limb affected) compared to ALND (48% 1 site, 18% 2 sites, 18% 3 sites, 12% 4 sites, 3% 5 sites). Among ALND +PLVB, average number of LVB performed did not vary significantly by BCRL status (2.2 ± 1.36 no BCRL vs 1.9 ± 0.73 BCRL).

Conclusions: The rate of BCRL did not decrease significantly in ALND+PLVB, but the attrition rate for completing postoperative PT was high. PLVB tended to decrease the number of affected sites in BCRL. PLVB may play a critical role in mitigating the severity of lymphedema.

FOURTEEN-YEAR EXPERIENCE OF HIGH-RISK BREAST CANCER SURVEILLANCE FOR FEMALE BRCA MUTATION CARRIERS IN HONG KONG

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Background: Long-term results of high-risk breast cancer surveillance for BRCA mutation carriers are lacking in the literature, especially for Asian population. This study aimed to review our 14-year experience of high-risk surveillance and assess the outcome of cancer detection, breast cancer occurrence and mortality.

Methods: BRCA mutation carriers in Hong Kong Hereditary Breast Cancer Family Registry from January 2007 to December 2020 were reviewed. Surveillance program included biannual clinical examination, 6-monthly breast imaging with alternating contrast magnetic resonance imaging and a combination of mammogram and ultrasound.

Result: A total of 395 female BRCA mutation carriers who didn't have bilateral mastectomy were enrolled to our high-risk surveillance protocol with a median follow-up of 39.4 (range, 6~152) months. The uptake of risk-reducing mastectomy was 5%, and was particularly low in breast cancer-free patients, only 2%. The new breast cancer detection rate was 1.7% (34 cancers diagnosed from 1997 screening sessions). Early cancer detection was achieved with 88% diagnosed in stage 0/1 and a node negative rate of 94%, with minimal interval cancer occurrence. Overall breast-cancer specific mortality was 3%. Initially breast-cancer free patients who later developed breast cancer during surveillance, breast-cancer specific mortality was not observed. However, overall mortality of patients was largely dependent on ovarian cancer history.

Conclusions: Risk-reducing mastectomy is not popular among Chinese BRCA mutation carriers. High-risk breast cancer surveillance remained the core management and our 6-monthly breast imaging program could achieve early cancer detection with minimal interval cancer occurrence, and a low breast-cancer specific mortality. Further study with cost-effective analysis is warranted.

ADDED VALUE OF BLOOD-BASED 3-PROTEIN SIGNATURE AND DEEP LEARNING-BASED MAMMOGRAPHY AI-CAD TO BREAST ULTRASOUND IN WOMEN WITH DENSE BREASTS

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Background: We evaluate the combined use of blood-based 3-protein signature (Mastocheck) and deep learning-based mammography AI-CAD (Lunit INSIGHT MMG) to ultrasound (US) in women with dense breasts on mammography and needs supplemental screening.

Methods: Women who performed the whole-breast US and blood sampling to evaluate Mastocheck and those with dense breasts on mammography were evaluated. The AI-CAD values were retrospectively analyzed with Lunit INSIGHT MMG. We compared the diagnostic performance between US alone and the combined use of Mastocheck with US and AI-CAD with US.

Result: Among the 65 women with dense breasts on mammography, 40 (61.5%) were healthy individuals and 25 (38.5%) breast cancer patients. The addition of Mastocheck value to US improved diagnostic performance as follows: AUC of US was increased from 0.93 to 0.96, specificity and PPV were also increased from 70.0% to 95% and from 67.6% to 91.7%, respectively. Sensitivity was decreased from 100.0% to 88.0%. The addition of AI-CAD value to US improved diagnostic performance as follows: AUC of US was increased from 0.93 to 0.94, specificity and PPV were also increased from 70.0% to 100.0% and from 67.6% to 100.0%, respectively. Sensitivity was decreased from 100.0% to 60.0%.

Conclusions: The addition of Mastocheck provides a minimal decrease in sensitivity and a significant increase in specificity, whereas the addition of AI-CAD is excellent in terms of specificity but shows a significant decrease in sensitivity. Both novel techniques are effective tools that can be used with US to improve diagnostic performance in women with dense breasts.

THE PERCENTAGE OF UNNECESSARY MASTECTOMY DUE TO FALSE SIZE PREDICTION IN BREAST CANCER PATIENTS WHO UNDERWENT NEOADJUVANT CHEMOTHERAPY

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Background: In some patients who underwent TM after neoadjuvant chemotherapy (NCT), BCS could have been possible considering pathologic reports. We hypothesized that unnecessary mastectomy would be greater in patients receiving NCT than in those who do not.

Methods: We prospectively enrolled patients scheduled for TM due to large tumor size from May 2018 to 2021 at SNUH. Patients planned for TM by patient's choice, due to BRCA mutant, and inflammatory breast cancer were excluded. The size that BCS could've been tried was recorded before operation and compared with pathologic size, then unnecessary mastectomy due to false size prediction was calculated. (ClinicalTrials.gov : NCT04689529)

Result: Of 360 TM patients, 111 patients (30.8%) could've received BCS according to pathologic size. Unnecessary mastectomy in NCT vs. non-NCT group were 52.3% (62pts of 130) vs. 21.3% (49 pts of 230) (p-value < 0.001). In subgroup analysis, false size prediction in NCT vs. non-NCT group were 26.5% vs. 21.5% in hormone receptor positive, HER2 negative subtype (p-value_0.404), showing no difference, but 63.3% vs. 27.6% in HER2 positive (p-value_0.002), and 57.6% vs.13.3% in TNBC (p-value_0.004), showing significant difference. In 130 NCT patients, MR size 2 cm or more different with pathologic size in unnecessary mastectomy group vs non-unnecessary mastectomy group were 54.8% vs.16.4% (p-value < 0.001), and more than 2 cm size discrepancy of sonography were 22.6% vs.10.4% (p-value_0.062) respectively.

Conclusions: The size discrepancy of preoperative imaging and pathologic report was greater in NCT group especially in HER2 and TNBC subtype, and resulted in an unnecessary mastectomy. Preoperative MR imaging rather than sonography or microcalcification on mammography is the main cause for false prediction.

PYROTINIB COMBINED WITH ALBUMIN-BOUND PACLITAXEL AS FIRST-LINE TREATMENT OF HER-2 POSITIVE METASTATIC BREAST CANCER: PRELIMINARY RESULTS OF A SINGLE-ARM, MULTICENTER PHASE 2 TRIAL

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Background: Limited data have focused on the first-line regimen in HER2-positive metastatic breast cancer (MBC) progressed after adjuvant and/or neoadjuvant trastuzumab therapy. This study was to evaluate the efficacy and safety of pyrotinib combined with albumin-bound paclitaxel in the first-line treatment of HER2-positive MBC progressed after adjuvant and/or neoadjuvant trastuzumab therapy.

Methods: Patients with measurable lesion received pyrotinib (400 mg, po, qd) plus albumin-bound paclitaxel (200 mg, ivdrip, d1, d8, q21d) until disease progression or unacceptable toxicity. The primary endpoint was objective response rate (ORR). (ChiCTR1900027932)

Result: A total of 20 eligible patients (n = 20) were included from December 2019 to December 2021. The mean age was 53.7 years old and median follow-up time was 6.83 months (95% Cl, 5.01-8.66 months). Of the patients enrolled, 45% had visceral metastases; 45% had lymph node and soft tissue metastases; 5% had both visceral and lymph node metastases; 5% had brain metastases. Thirty-five percent of patients were hormone receptor positive and underwent endocrine therapy; postoperative radiotherapy was administered to 80% of patients. ORR was 68.4% and DCR was 78.9%, with 68.4% of patients with PR, 10.5% of patients with SD, and 21% of patients with PD. Grade 3 and higher adverse effects (AEs) occurred in 30% of the patients. Diarrhea (25%) was the most frequent AE, followed by leukocytopenia (15%), neutropenia (25%), and hand-foot syndrome (5%).

Conclusions: Pyrotinib combined with albumin-bound paclitaxel exhibits promising efficacy and acceptable safety in the first-line treatment of HER2-positive MBC progressed after adjuvant and/or neoadjuvant trastuzumab therapy.

Oral Presentation

AN EXPERT SURVEY REVEALS VARIOUS PRACTICE PATTERNS IN CLINICAL NODAL STAGING (N0, N1, N2A) ASSESSMENT PRIOR TO NEOADJUVANT CHEMOTHERAPY FOR BREAST CANCER: A KOSRO/KBCSG/KCSG COLLABORATIVE STUDY

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Background: Clinical nodal staging prior to neoadjuvant chemotherapy (NAC) is important for the choice of surgery and radiotherapy methods as well as NAC regimen. However, discrepancy exists between the clinical and pathological staging in the current American Joint Committee on Cancer (AJCC) staging and it makes clinical decision challenging. We aimed to investigate the current practice patterns regarding clinical nodal staging in breast cancer in the real-world setting.

Methods: From January to February 2022, board-certified oncologists were invited to participate in a web-based survey. The survey included 19 general questions and 3 case-based questions.

Result: 118 (44 surgical, 33 medical, and 41 radiation oncologists) completed the survey. The most frequently performed initial imaging study was ultrasonography. All responders referred to imaging studies in the nodal staging. 61 (51.6%) responders determined the stage strictly based on the radiology reports while 57 (48.3%) made their own decision while noting radiology reports. Of those who make their own decisions, 70.2% included the number of suspicious node(s). Of 73 involved in prescribing NAC, 57 (78.1%) responded that the reimbursement regulations in the selection of NAC regimens affects nodal staging in practice. In the case-based questions, high variability existed among clinicians in the same cases, especially when assessing cN0 versus cN1.

Conclusions: Diverse assessments among specialists due to the absence of clear harmonized staging system for the clinical nodal staging of breast cancer would lead to diverse practice patterns. Practical, harmonized, and objective methods for clinical nodal staging would be needed for appropriate treatment decisions and accurate outcome evaluation.

RADIOSENSITIVITY IS ASSOCIATED WITH ANTITUMOR IMMUNITY IN ESTROGEN RECEPTOR-NEGATIVE BREAST CANCER

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Background: This study evaluated radiosensitivity and the tumor microenvironment (TME) to identify characteristics of breast cancer patients who would benefit most from radiation therapy.

Methods: We analyzed 1,903 records from the Molecular Taxonomy of Breast Cancer International Consortium cohort using the radiosensitivity index (RSI) and gene expression deconvolution algorithms, CIBERSORT and xCell, that estimates the TME composition of tumor samples. In this study, patients were stratified according to TME and radiosensitivity. We performed integrative analyses of clinical and immuno-genomic data to characterize molecular features associated with radiosensitivity.

Result: Radiosensitivity was significantly associated with activation of antitumor immunity. In contrast, radioresistance was associated with a reactive stromal microenvironment. The immuno-genomic analysis revealed that estrogen receptor (ER) pathway activity was correlated with suppression of antitumor immunity. In ER-negative disease, the best prognosis was shown in the immune-infiltrated and radiosensitive group patients, and the worst was in the immune-excluded and radioresistant group patients. In ER-positive disease, immune signature and radiosensitivity had no prognostic significance.

Conclusions: Taken together, these results suggest that tumor radiosensitivity is associated with activation of antitumor immunity and a better prognosis, particularly in patients with ER-negative breast cancer.

PHENOTYPE AND FUNCTIONALITY OF TUMOR INFILTRATING LYMPHOCYTES AFTER RAPID EX-VIVO EXPANSION FROM CORE NEEDLE BIOPSIES OF TNBC TUMORS

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Background: Adoptive transfer of ex-vivo expanded tumor infiltrating lymphocytes (TILs) has resulted long-term durable responses in metastatic cancer. TILs were expanded from tissue specimens obtained via core needle biopsy (CNB) vs surgery in patients with triple negative breast cancer (TNBC).

Methods: Breast tumors were obtained from CNB (n = 7) or surgical resection (n = 6). After initial expansion, TILs underwent rapid expansion (REP) with IL-2 and irradiated PBMC feeders. Samples underwent analysis for cell counts, T cell subsets, memory (CCR7, CD45RA), activation (4-1BB) exhaustion (PD-1) and cytokine production.

Result: All 12 patients were females with TNBC, ages 31-86. Cell counts post initial expansion ranged from 3-215 × 10e6 cells. After REP, the average fold expansion was 1,479 (CNB) vs 1,110 (surgery). For expanded TILs, CD3+ cells averaged 97.8% (range: 95-99.1%) CNB vs 98.7% (98-99.1%) surgical. Average CD8 was 27% CNB (1.8- 56.9) vs. 11.6% surgical (0.6-27.5). CD4% was 69.2% (38-98.4%) CNB and 85.8% (66.6-99.1) surgical. TEM (CCR7-CD45RA-) was 92.20% (88.7-95.2) CNB vs 93.23% (87-96.5) surgical, with a significant portion of TCM (CCR7+CD45RA-) as 6.7% (3.1-8.9) CNB and 6% (3.1-12) surgical. TIL function was evaluated by cytokine secretion after PMA stimulation. INF-averaged 28% (11.5-47.5) CNB vs 34% (19.6-44.3) surgery. TNF was 43.97% (27.8-67.1) CNB vs 42.87% (30.4-49.6) surgery.

Conclusions: We report for the first time the expansion and characterization of TILs from core needle biopsies taken from TNBC lesions. This demonstrates the feasibility of CNBs as an alternative and less invasive technique for obtaining adequate tumor tissue for TIL growth in clinically relevant numbers for adoptive cell transfer.

SURVIVAL AFTER THE DIAGNOSIS OF SECONDARY PRIMARY MALIGNANCY IN BREAST CANCER PATIENTS, FOCUSING ON THE SECOND PRIMARY HEMATOLOGIC MALIGNANCY: A PROPENSITY SCORE MATCHING ANALYSIS

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Background: The survival of breast cancer patients has been improved, and the risk of developing second primary malignancies (SPM) is increasing. In this study, we investigated the overall survival (OS) of SPM in breast cancer patients according to the orgin-organs of SPM: thyroid, lung, female genital organ, digestive organ, and hematologic origin. Then, OS of the second primary hematologic malignancy (SPHM) was compared with that of metastatic breast cancer (MBC).

Methods: This retrospective study included patients who were diagnosed as primary breast cancer in the period 1998-2019. Of these patients, patients with any SPM were eligible for this analysis. First, OS of patients with SPM was analyzed. Next, OS of SPHM patients with or without breast cancer relapse was compared with that of patients with MBC matched by propensity score.

Result: The patients diagnosed as SPM without breast cancer relapse were 219 patients. Patients with SPM except patients with SPHM showed significant better OS than patients with MBC. The OS of patients with SPHM which was diagnosed as a first event was not statistically different from the patients with MBC (Hazard ratio 1.558, 95% confidence interval 0.856-2.839, $p = 0.147$). Next, the survival of 42 patients diagnosed SPHM with or without breast cancer relapse was compared with 84 patients with MBC matched by propensity score, and showed worse survival than MBC group (Hazard ratio 1.954, 95% confidence interval 1.045-3.654, $p = 0.036$).

Conclusions: Patients with SPHM showed worse OS than patients with MBC. Except the SPHM, patients diagnosed as SPMs showed better survival than the patients with MBC.

PREVALENCE OF TUMOR GENOMIC ALTERATIONS IN HOMOLOGOUS RECOMBINATION REPAIR GENES AMONG TAIWANESE BREAST CANCERS

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Background: Deleterious germline BRCA1/2 mutations are among the most highly pathogenic variants in hereditary breast and ovarian cancer syndrome. Recently, genes implicated in homologous recombination repair (HRR) pathways have been investigated extensively, as defective HRR genes may indicate potential clinical benefits from polyp ADP ribose polymerase (PARP) inhibitors beyond BRCA1/2 mutations.

Methods: We evaluated the prevalence of BRCA1/2 mutations as well as alterations in HRR genes with targeted sequencing. A total of 648 consecutive breast cancer samples were assayed, and HRR genes were evaluated for prevalence in breast cancer tissues.

Result: Among 648 breast cancers, there were 17 truncating and 2 missense mutations in BRCA1 and 45 truncating and 1 missense mutation in BRCA2, impacting 3% and 5% of the study population (collectively altered in 6%) with co-occurrence of BRCA1/2 in 7 breast cancers. On the other hand, HRR genes were altered in 122 (19%) breast cancers, while Talazoparib Beyond BRCA (TBB) trial-interrogated genes (excluding BRCA1/2) were mutated in 107 (17%) patients. Beyond BRCA1/2, the most prevalent HRR mutant genes came from ARID1A (7%), PALB2 (7%) and PTEN (6%). Collectively, 164 (25%) of the 648 Taiwanese breast cancer samples harbored at least one mutation among HRR genes.

Conclusions: The prevalence of BRCA1/2 mutations was far below one tenth, while the prevalence of HRR mutations was much higher and approached one-fourth among Taiwanese breast cancers. Further opportunities to take advantage of defective HRR genes for breast cancer treatment should be sought for the realization of precision medicine.

CAN A TECHNOLOGY-BASED INFORMATION AND COACHING/SUPPORT PROGRAM IMPROVE MULTIPLE DIMENSIONS OF QUALITY OF LIFE AMONG ASIAN AMERICAN BREAST CANCER SURVIVORS?

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Background: With the COVID19 pandemic, health care providers' interests in technology-based interventions have drastically increased. However, little is still known about the efficacy of technology-based interventions in improving the quality of life among cancer survivors. The purpose of this study was to explore the efficacy of a technology-based information and coaching/support program in improving multiple dimensions of quality of life among Asian American breast cancer survivors.

Methods: The study was a randomized clinical trial with repeated measures among 199 Asian American breast cancer survivors. The intervention group used the technology-based program that provided social media functions, online educational sessions, and online resources. Both the intervention and control groups used the American Cancer Society website on breast cancer. Multiple instruments included: questions on background characteristics and health/disease status and the Functional Assessment of Cancer Therapy Scale-Breast Cancer (FACT-B). The data were analyzed using separate intent-to-treat growth curve models.

Result: Although the change over time in the FACT-B scores was not significant in the mixed effect model, the fixed effect of time was significant ($\beta = -1.0476$, $p = .004$). The physical wellbeing scores ($\beta = -0.223$), the social wellbeing scores ($\beta = 0.111$), the emotional wellbeing scores ($\beta = -0.087$), the functional wellbeing scores ($\beta = 0.217$), and the breast cancer subscale scores ($\beta = -0.148$) showed a significant group * time interactive effect.

Conclusions: Future research needs to determine the factors that may increase the quality-of-life of Asian American breast cancer survivors by a technology-based intervention.

REGORAFENIB INDUCES DAMAGE-ASSOCIATED MOLECULAR PATTERNS, CANCER CELL DEATH AND IMMUNE MODULATORY EFFECTS IN A MURINE TRIPLE NEGATIVE BREAST CANCER MODEL

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Background: Damage associated molecular patterns (DAMPs), including calreticulin (CRT) exposure, high-mobility group box 1 protein (HMGB1) elevation and ATP release characterize immunogenic cell death (ICD) and may play a role in cancer immunotherapy.

Methods: The DAMPs were determined by western blot analysis, immunofluorescence microscopy and luminescent assay. The syngeneic 4T1 tumor bearing mice were used for *in vivo* study. Immunohistochemistry was used to assess the expression of DAMSs and infiltration of T cells. Mice splenic lymphocytes were harvested for subpopulations of immune cells.

Result: We demonstrated regorafenib, a multi-target angiokinase inhibitor previously known to suppress STAT3, induced DAMPs and cell death in TNBC cells. Regorafenib and a p-STAT3 inhibitor, SC-43, induced the expressions of HMGB1 and CRT, alongside with the release of ATP. Regorafenib-induced HMGB1 and CRT were reversed by ectopic STAT3 overexpression. In mice bearing syngeneic 4T1 tumors, regorafenib increased the expressions of HMGB1 and CRT, and effectively suppressed 4T1 tumor growth. Examining these 4T1 tumors revealed increased CD4+ as well as CD8+ tumor-infiltrating T cells in regorafenib-treated tumors. Moreover, regorafenib or programmed death-1 (PD-1) blockade using mice anti-PD1 monoclonal antibody reduced lung metastasis of 4T1 cells in immunocompetent mice. However, regorafenib did not further improve the tumor-suppressive effects of anti-mPD-1. Furthermore, analyzing mice splenic lymphocytes population revealed regorafenib treatment enhanced CD4 and CD8 positive T cells, increased antigen presenting ability of dendritic cells and suppressed regulatory T cells.

Conclusions: Regorafenib effectively reduced tumor growth and metastasis of TNBC in immunocompetent mice and increased tumor-infiltrating lymphocytes.

A PHASE 2 STUDY OF NEOADJUVANT PERTUZUMAB, ATEZOLIZUMAB, DOCETAXEL AND TRASTUZUMAB IN HER2-POSITIVE EARLY BREAST CANCER (NEO-PATH, KCSG BR 18-23)

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Background: Immune microenvironment and immune-mediated mechanism of action of anti-HER2 treatment suggested role of immunotherapy in HER2-positive breast cancer (BC). Therefore adding immunotherapy to neoadjuvant chemotherapy may increase efficacy with reduced toxicities. In this prospective phase 2 trial, we assessed the efficacy, safety, and biomarkers of neoadjuvant pertuzumab, atezolizumab, docetaxel and trastuzumab (PATH) in HER2-positive early breast cancer (EBC).

Methods: Eligible patients were with clinical stage II-III HER2-positive BC. Patients received six cycles of PATH combination chemotherapy every 3 weeks before primary surgery. Primary endpoint was pathologic complete response (pCR, defined as ypT0/isN0) rate. Tumor tissue was obtained before neoadjuvant treatment from all patients, and at surgery from the patients who did not achieve pCR. Targeted sequencing and whole transcriptome sequencing were performed and the association between pre-treament genomic features and pCR achievement was analyzed.

Result: Sixty-seven women were enrolled and surgery was performed in 65 patients. The pCR rate was 61.2% (41/67), which was higher in hormone receptor-negative and in PD-L1 positive disease. During the neoadjuvant treatment, the incidence of febrile neutropenia and grade 3/4 immune-related adverse events was 7.5% and 6.2%, respectively. ERBB2 amplification (94%), TP53 mutation (84%), PIK3CA mutation (43%) and MLL2 mutation (19%) were the most frequently detected mutations in pre-treatment samples. Pre-treatment Luminal subtype, MYC amplification, and MYC pathway mutations were enriched in patients with non-pCR.

Conclusions: Neoadjuvant PATH regimen showed favorable efficacy and safety profiles in stage II-III HER2-positive EBC, Luminal subtype and MYC amplification were associated with worse response. NEO-PATH provides evidence of combining immunotherapy and anti-HER2 treatment as a potential new therapeutic option.

YAP1 PREDICTS PATHOLOGICAL COMPLETE RESPONSE TO NEOADJUVANT CHEMOTHERAPY IN LUMINAL BREAST CANCER PATIENTS

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Background: The benefit of neoadjuvant chemotherapy (NAC) for patients with luminal breast cancer is unclear although 18F-FDG-PET can predict the pathologic complete response (pCR) to NAC in this subtype and may differentiate luminal A from luminal B subtype. YAP1 was previously identified to promote linage switching from luminal to basal/mesenchymal differentiation by suppressing luminal-specific gene expression. Therefore, we hypothesized tumoral expression of YAP1 might be associated with higher pCR to neoadjuvant chemotherapy (NAC) for patients with luminal breast cancer.

Methods: Luminal breast cancer patients were serially enrolled who underwent PET/CT at diagnosis and taxane and/or anthracycline-based NAC during Oct. 2010 and Aug. 2016. YAP1 expression was scored both quantitatively and qualitatively by immunohistochemical staining based on tissue microarray and then analyzed in association with clinical/pathological features including tumoral SUVmax of 18F-FDG-PET and outcomes after NAC such as pCR and survival.

Result: Among 145 enrolled patients, pCR was confirmed in 18 (12.4%) patients. The tumoral expression rate of YAP1 was 60.4% among 134 (92.4%) evaluable samples for scoring and significantly associated with HER2 expression (OR = 3.665; $P = 0.005$) and PR expression (OR = 0.411; $P = 0.015$). YAP1 was significantly associated with higher pCR (OR = 4.882; 95%CI = 1.006-23.690; $P = 0.049$) adjusted for age, clinical stage, and expressions of ER, HER2, and Ki67; furthermore, YAP1 expression was associated with a tumoral SUVmax of 18F-FDG-PET ($P = 0.04$). There was no survival difference, according to YAP1 expression.

Conclusions: YAP1 can be considered as a biomarker in predicting pCR after NAC in patients with luminal breast cancer without its prognostic value.

POOR CLINICAL OUTCOME IN TRIPLE-NEGATIVE BREAST CANCER WITH LOW TUMOR-INFILTRATING LYMPHOCYTE SCORE AND NEGATIVE PD-L1 EXPRESSION

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Background: We addressed the clinical outcomes and genomic characteristics in triple-negative breast cancer (TNBC) with low tumor infiltrating-lymphocyte (TIL) and negative PD-L1 expression in both neoadjuvant and adjuvant cohorts.

Methods: Core needle biopsy slides obtained at diagnosis were reviewed for the neoadjuvant cohort. Tissue microarrays constructed from surgical specimens were applied for the adjuvant cohort. The cut-off value for TIL score was 30%, and PD-L1 was evaluated using SP142 antibody and was considered positive when PD-L1 immune cells were identified in more than 1%. Tumors with both low TIL and negative PD-L1 were defined as double-negative tumors. Gene expression analysis was also performed in the adjuvant cohort.

Result: A total of 446 TNBC patients were included. Among them 274 (61.4%) patients underwent primary surgery and 172 (38.6%) patients had neoadjuvant chemotherapy. Patients with double-negative tumors had significantly poor recurrence-free survival rate compared to patients with either or both high TIL and positive PD-L1 tumors (HR 2.88, 95% CI 1.79 4.63.24, p-value < 0.001). Patients with double-negative tumors also had lower pathologic complete response rate (pCR) compared to other tumors (28.1% vs. 44.6%, p-value 0.024). Genomic analyses showed that immune gene signatures were significantly increased in tumors with either or both high TIL and positive PD-L1 compared to double-negative tumors.

Conclusions: TNBC patients with low TIL and negative PD-L1 tumors presented with lower pCR rate and higher recurrence rate. Either high TIL or PD-L1-positivity could identify patients with a good prognosis among early TNBC treated with chemotherapy.

PREGNANCY AFTER BREAST CANCER: A SYSTEMATIC REVIEW AND META-ANALYSIS

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Background: Patients and physicians are concerned about the potential detrimental effects of pregnancy after breast cancer (BC). In our systematic review and meta-analysis we aimed to provide updated evidence on reproductive outcomes and maternal safety of pregnancy following BC.

Methods: We conducted a systematic literature review and we identified studies including patients with a pregnancy after BC. We assessed likelihood of pregnancy after BC, reproductive outcomes, and maternal safety. We used random effects models to calculate pooled relative risks (RRs), odds ratios (ORs), and hazard ratios (HRs) with 95% CIs.

Result: We included 39 records out of 6,462 records identified, involving 8,093,401 women from the general population and 112,840 patients with BC. Compared with the general population, we found that BC survivors were significantly less likely to have a subsequent pregnancy (RR, 0.40; 95% CI, 0.32-0.49). Moreover, BC survivors had a significantly higher risk of caesarean section (OR, 1.14; 95% CI, 1.04-1.25), a higher risk of offspring with low birth weight (OR, 1.50; 95% CI, 1.31-1.73), preterm birth (OR, 1.45; 95% CI, 1.11-1.88), and small for gestational age (OR, 1.16; 95% CI, 1.01-1.33). Congenital abnormalities and other reproductive complications did not differ between BC survivors and general population. BC patients with a pregnancy after BC had better disease-free survival (HR, 0.66; 95% CI, 0.49-0.89) and overall survival (HR, 0.56; 95% CI, 0.45-0.68) compared to patients with BC without subsequent pregnancy.

Conclusions: Our results provide reassuring evidence on the safety of conceiving in BC survivors.

Oral Presentation

RECURRENCE AND CLINICOPATHOLOGIC CHARACTERISTICS OF BREAST CANCER IN BRCA-POSITIVE AND BRCA-NEGATIVE YOUNG WOMEN

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Background: There are reports of higher incidence of breast cancer recurrence associated with BRCA mutation. Young age is also known to be associated with higher recurrence rates. This study seeks to examine young breast cancer patients with BRCA mutation by comparing their clinicopathologic characteristics and recurrence to those without BRCA mutation.

Methods: From Jan 2010 to Jun 2020, 254 women of age 40 or less underwent breast cancer surgery at Korea University Guro Hospital, among which 124 patients were tested for BRCA mutation. The data of those patients were retrospectively collected. Kaplan-Meier estimation was used to determine the association between BRCA status and recurrence.

Result: 11 of 124 patients tested positive for BRCA. There was no significant difference between the BRCA-positive group and the BRCA-negative group in clinopathologic characteristics. The hazard ratio for recurrence in the BRCA-positive group compared with the BRCA-negative group was 2.140, but without significant difference (95 percent confidence interval, 0.91 to 5.796; $p = 0.13$). The ipsilateral breast recurrence-free survival and recurrence-free survival of the BRCA-positive group and the BRCA-negative group showed no significant difference ($p = 0.569$, $p = 0.126$, respectively).

Conclusions: Despite the hazard ratio of 2.140 for recurrence, this study did not show significant difference in ipsilateral breast recurrence-free survival and recurrence-free survival. This may indicate that young breast cancer patients with BRCA mutation may not need mastectomy over breast conserving surgery any more than those without BRCA mutation but may need to be closely followed postoperatively. Further studies with a large number of patients and long-term follow-up may be needed.

MULTICENTER RETROSPECTIVE STUDY OF BREAST CANCER PATIENTS UNDERGOING FERTILITY PRESERVATION (BSTRO-02)

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Background: In breast cancer (BC) treatment, it is recommended to provide information and implement fertility preservation (FP) for young BC patients who wish to raise children. However, the data on the timing, method, and effect on BC prognosis is insufficient.

Methods: BSTRO-02 is a multicenter, retrospective case series study with five university hospitals. We investigated the current state of FP, its efficacy, and safety of BC in the perioperative period.

Result: As of December 2021, 81 cases were examined (currently adding cases). Median age 35 years. Seven people in their 20s (9%), 64 people in their 30s (79%), 10 people in their 40s (12%). The stage was 0: 3%, I: 46%, II: 42%, III: 9%, and bilateral BC was found in 6%. The methods for FP have cryopreserved embryos 62% and cryopreserved oocytes 38%. As of 2021, 11 (14%) babies were born, of which 2 (14%) were from natural pregnancy and cryopreserved embryos (86%). Seven cases were found that were pregnant but did not give birth. Ten were children from patients in their thirties, and none had given birth over the age of 40. Recurrence was observed in 12 cases (15%), of which 4 had distant metastasis, 7 had local recurrence, and 1 had contralateral BC. All patients with local recurrence had undergone surgery.

Conclusions: In this retrospective study, 14% of BC patients who underwent FP gave birth. Most of them had cryopreserved embryos. We are currently investigating additional cases and will report the details of extensive data in Japan.

LONG-TERM BREAST CANCER OUTCOMES OF PREGNANCY-ASSOCIATED BREAST CANCER IN A PROSPECTIVE COHORT

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Background: Pregnancy transiently increases the risk of developing of breast cancer (BC). Considering peak age of BC in Asian is much younger than in Western population, the effect of pregnancy on BC may be different in Asia compared to Western countries. This study aimed to analyze the characteristics and clinical outcomes of pregnancy-associated breast cancer (PABC) in Korea.

Methods: We prospectively registered patients with young breast cancer (YBC) aged ≤ 40 years since May 2013 at Samsung Medical Center. We defined PABC as BC diagnosed during pregnancy or in the first postpartum year. We analyzed and compared the clinicopathological characteristics, obstetrical outcomes, and BC outcomes between PABC patients and non-PABC patients of the YBC cohort.

Result: We enrolled 1,492 patients in this cohort, and 1,364 patients were eligible. Among 1,364 women, 93 were PABC patients. Median age was 34 years for PABC. In PABC, lower incidence of hormone receptor expression (64.6% vs 74.6%) and higher frequency of HER2 overexpression (26.9% vs 17.6%) were observed compared with non-PABC. There was no maternal or fetal complication in all PABC patients. The 5-year overall survival (OS) rate was 82.9% in PABC and 92.4% in non-PABC ($p = 0.002$). The 5-year disease-free survival (DFS) rate was 71.7% in PABC and 82.7% in non-PABC. The hazard ratio of PABC versus non-PABC was 2.60 (95% CI, 1.49-4.54; $p = 0.001$) for OS and 1.83 (95% CI, 1.20-2.78; $p = 0.005$) for DFS.

Conclusions: The results showed worse OS and DFS for PABC patients compared with non-PABC patients in this prospective cohort.

C-MET-ENRICHED CIRCULATING TUMOR CELLS AS SIGNIFICANT INDEPENDENT PREDICTORS FOR PROGRESSION IN HR-POSITIVE HER2-NEGATIVE METASTATIC BREAST CANCER

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Background: Although hormone receptor (HR)-positive breast cancer generally shows favorable prognosis for endocrine therapy, overcoming its resistance is still a major challenge. cMET alterations are frequently observed in various cancers and have been reported to play a role in chemotherapy resistance and poor prognosis. This study aimed to evaluate whether cMET overexpressing circulating tumor cells (CTCs) can be detected in patient blood and whether cMET-enriched CTCs can be predictors of disease progression in HR-positive metastatic breast cancer (MBC) patients.

Methods: MBC patients were prospectively enrolled during standard treatment at Samsung Medical Center. Peripheral blood was collected after obtaining written informed consent. EpCAM and cMET-enriched CTCs were isolated using GenoCTC® with respective isolation kits. Cut-off values were calculated using maxstat R package, which estimates cutoff based on standardized log-rank statistic.

Result: Out of the 100 patients enrolled, analysis was performed on 93 patients with HR-positive MBC. Twenty-eight (30.1%, 28/93) patients had one or more cMET-enriched or EpCAM-enriched CTCs detected from 4 mL of blood each. Chi-squared test showed cMET-enriched CTCs were associated with HER-2 status ($p = 0.02$). Kaplan-Meier survival analysis showed significant association between cMET-enriched CTCs and progression-free survival (PFS) ($p = 0.0024$) in HR+/HER2- MBC (n = 63). However, high EpCAM-enriched CTC numbers were not statistically significant for PFS ($p = 0.39$). Multivariate Cox proportional-hazard model showed that cMET-enriched CTCs (HR = 4.21, 95% CI = 1.69-10.52, $p = 0.002$) were independent predictors for PFS in HR+/HER2- MBC.

Conclusions: cMET-enriched CTCs are significant independent predictors of disease progression in HR+HER2- MBC. This study addresses the potential of cMET inhibitors in treatment of HR+/HER2- MBC patients with cMET alteration.

PROGNOSIS OF BREAST CANCER PATIENTS AFTER DEVELOPMENT OF CONTRALATERAL BREAST CANCER IN KOREA

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Background: The rate of contralateral prophylactic mastectomy is increasing, despite survival benefit from contralateral prophylactic mastectomy is controversial. Purpose of this study was to investigate whether development of contralateral breast cancer (CBC) has influence on survival or recurrence.

Methods: In this retrospective study, we included patients who were diagnosed with a first primary unilateral non-metastatic breast cancer at Asan medical center between 1999-2013 followed through 2018. Patients were divided into CBC cohort and non-CBC cohort. Survival and recurrence of CBC cohort and non-CBC cohort was compared in whole study population and in subgroup analysis by breast cancer subtype.

Result: Over median range of 107 months, 418 patients developed CBC out of 16,251 patients. Development of CBC did not influence overall survival (OS) or breast cancer-specific survival (BCSS), but rate of breast cancer recurrence was two-fold higher than following a CBC diagnosis (hazard ratio 2.14; 95% CI 1.63-2.80). In subgroup analysis by subtype, hormone receptor (HR)-positive/human epidermal growth factor receptor 2 (HER2)-negative breast cancer showed higher risk for overall death following a CBC diagnosis (hazard ratio 1.88; 95% CI 1.14-3.10) whereas triple negative breast cancer showed lower risk (hazard ratio 0.42; 95% CI 0.19-0.95). BCSS showed similar pattern in subgroup analysis.

Conclusions: After adjusting for age of surgery, year of surgery, tumor characteristics and treatment, breast cancer recurrence was more than two-fold higher in CBC cohort. In subgroup analysis by subtype, HR-positive/HER 2-negative breast cancer had 1.88 times risk for overall death. Such information can be important when counseling patients who are considering contralateral prophylactic mastectomy.

EFFECT OF NEOADJUVANT VERSUS ADJUVANT CHEMOTHERAPY ON IPSILATERAL BREAST TUMOR RECURRENCE AFTER BREAST-CONSERVING SURGERY AND WHOLE-BREAST IRRADIATION

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Background: Early Breast Cancer Trialists' Collaborative Group conducted a large meta-analysis and reported that patients who underwent neoadjuvant chemotherapy (NAC) had higher ipsilateral breast tumor recurrence (IBTR) rate than those with adjuvant chemotherapy. However, since the study was conducted with patients treated two decades ago, the results could not reflect the advance in treatments and IBTR rate was much higher than in recent studies. Thus, we investigated the association between chemotherapy settings and IBTR rates in breast cancer patients.

Methods: We retrospectively reviewed the data of 5,307 patients who underwent breast conserving surgery followed by whole breast irradiation between January 2004 and December 2018 in a single institution. Patients who underwent mastectomy or omitted chemotherapy were excluded.

Result: The 1,473 patients who underwent NAC showed significantly higher IBTR rate than the 3,564 patients who underwent adjuvant chemotherapy (10-year risk: 4.5% vs. 4.0%; log-rank $p = 0.045$, hazard ratio 1.42 [95% CI, 1.01-1.99]). The difference was more evident for patients with hormone receptor (HR) positive and human epidermal growth factor receptor-2 (HER2) negative tumor (unadjusted $p = 0.001$, hazard ratio 2.27 [95% CI, 1.37-3.74; adjusted $p = 0.002$, hazard ratio 2.80 [95% CI, 1.45-5.42]), and the statistical significance was still remained after 1:1 propensity score matching ($p = 0.026$). In contrast, patients with other subtypes did not show significant differences between two groups.

Conclusions: Patients who underwent NAC for HR+/HER2- tumors carry increased risk of IBTR than those who underwent adjuvant chemotherapy. Our observation supports the need for considering tumor subtypes in initial treatment. In addition, more intensive surveillance would be needed for patients with HR+/HER2- tumors after NAC.

THE IMPACT OF POSTOPERATIVE RADIATION THERAPY FOR ISCHEMIC HEART DISEASE IN BREAST CANCER PATIENTS USING NATIONWIDE CLAIM DATA

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Background: This study aimed to analyze the effect of postoperative radiation therapy on ischemic heart disease (IHD) in patients with breast cancer using the Korean claim data of the National Health Insurance System (NHIS).

Methods: Between January 2011 and December 2018, we analyzed patients who received radiation therapy after breast-conserving surgery or mastectomy. Considering the risk factors, including the laterality of breast cancer, we investigated the effect of radiation therapy on the incidence rate of IHD.

Result: A total of 29,852 patients (14,773 left-sided patients and 15,079 right-sided patients) were selected. The incidence of IHD was higher in those with left-side than right-sided breast cancer ($p = 0.041$). Age (> 55 years), body mass index (BMI) (> 25 kg/m^2), histories of smoking, hypertension (HTN), diabetes mellitus (DM), and hyperlipidemia were significant adverse factors affecting the development of IHD. Anti-HER2 and aromatase inhibitors were unfavorable, but hormonal therapy was favorable. In subgroup analyses for each risk factor, patients with the risk factor showed higher IHD incidence rates compared to those without. In addition, laterality (left-sided versus right-sided breast cancer) increased the incidence of IHD significantly among those without each risk factor. In comparison, the laterality of breast cancer did not significantly affect the incidence of IHD in patients with the risk factor.

Conclusions: This study showed that patients without risk factors might be more vulnerable to increasing radiation to the heart. Active measures to reduce IHD risk can be considered for not only high-risk patients but also patients without risk or low-risk patients receiving radiotherapy.

ROLE OF CDK9 AS A PROMISING THERAPEUTIC TARGET IN ER POSITIVE BREAST CANCER CELLS

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Background: Despite improvements in endocrine therapy, approximately 30% of patients with estrogen receptor positive (ER+) breast cancer undergo adjuvant endocrine therapy eventually experience recurrence with distant metastasis. Therefore, we are aiming to identify novel targets to improve treatment efficiency for endocrine therapy-resistant patients.

Methods: To verify the roles of CDK9 and CCNT1 on breast cancer survival, we analyzed GSE9893 dataset including ER+ breast cancer patients. We established tamoxifen-resistant cells (TamR) using MCF7 cells and defined tamoxifen-sensitive cells (TamS) which are parental MCF7 cells. Levels of protein and mRNA expression were analyzed western blotting and real-time PCR, respectively. Cell-viability and cell-cycle were analyzed by MTT-assay and by flow cytometry. Tumorigenecity of established cells was evaluated through orthotopic xenografts.

Result: Levels of CDK9 and CCNT1 expression were associated with poor prognosis in ER+ breast cancer patients. Our results showed that levels of CDK9 expression were increased in TamR cells. So, we investigated the pharmacological effects of CDK9 inhibitors on TamS and TamR cells. Treatment of CDK9 inhibitors induced G2/M phase arrests while decreased cell growth in both TamS and TamR cells. Furthermore, we performed a CDK9 knock-out experiment in TamR cell lines. As expected, tumorigenecity of TamR with CDK9 loss was significantly decreased comparing to TamR with CDK9.

Conclusions: CDK9 expression is involved with the survival rate in ER+ breast cancer. Inhibition of CDK9 synergistically effects the endocrine therapy of ER+ breast cancers. Therefore, we suggest that the possibility that CDK9 could be a novel therapeutic target that can help the effective treatment of ER+ breast cancers.

RISK ASSESSMENT OF LYMPHEDEMA IN BREAST CANCER PATIENTS USING AXILLARY-LATERAL THORACIC VESSEL JUNCTURE (ALTJ) DOSE: CLINICAL IMPLICATIONS FOR PERSONALIZED RADIOTHERAPY PLANNING

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Background: To investigate whether dose exposure to the axillary-lateral thoracic vessel juncture (ALTJ) is associated with the risk of lymphedema in the context of other known risk factors.

Methods: 1,488 breast cancer patients from two institutions treated with multi-modal therapies were analyzed. ALTJ was manually delineated for individual patients then ALTJ dose-volume data were calculated by the treatment planning system. Decision tree, random forest model, and Cox's regression model were performed. Exposed doses to ALTJ were converted to biologically equivalent doses in 2 Gy fractions (EQD2).

Result: The 5-year cumulative incidence of lymphedema was 6.8%. In decision tree analysis, number of lymph nodes sampled was the most important factor and mean ALTJ dose was the second most important factor. First, decision tree model separated patients by the number of sampled nodes and among patients with ≤ 6 nodes sampled, patients were further seperated by ALTJ mean dose (≤ 35 vs > 35 Gy; 5-yr lymphedema rate: 1.0% vs 12.8%, $p < 0.001$). Cox's multivariate model showed a positive dose-response relationship between ALTJ mean dose and lymphedema risk (hazard ratio 1.2 per 10 Gy). In random forest, inclusion of dosimetric parameters of ALTJ to the model significantly increase the prediction performance (Harrell's c-index 0.91).

Conclusions: Radiation dose to ALTJ structure is a significant risk factor for lymphedema development, although surgical factor is the most important. These findings are particularly important for patients undergo sentinel node biopsy (≤ 6 nodes sampled). Contouring of ALTJ in breast RT planning should be incorporated in future prospective protocols, although external validation is necessary.

AUTOMATED CORONARY ARTERY CALCIUM (CAC) SCORING IN PATIENTS WITH BREAST CANCER TO ASSESS THE RISK OF HEART DISEASE FOLLOWING ADJUVANT RADIATION THERAPY (RT)

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Background: A novel biomarker is required to improve prediction of acute coronary events (ACEs) following adjuvant RT. We investigated the prognostic impact of coronary artery calcium scores (CAC) on the development of ACE in breast cancer patients in the context with cardiac exposure to radiation.

Methods: We evaluated women who underwent breast surgery for breast cancer who did (n = 511) or did not (n = 600) receive adjuvant RT between 2005 and 2013. A deep-learning-based algorithm was used for CAC scoring of each coronary artery and represented by Agatston scores. The endpoint was the effects of the CAC score and RT on the development of ACEs.

Result: In the RT and non-RT cohorts, 11.2% and 3.7% exhibited CAC scores > 0, respectively. With a median 9.3-year follow-up period, the cumulative ACE incidence was 0.7%. The CAC score was a significant risk factor for ACEs in the multivariate analysis ($P < .001$). The incidence rate of ACEs was 6.2% in the group with CAC scores > 0, significantly higher than the 0.2% rate in the group with CAC scores = 0 ($P < 0.001$). In the subgroup with CAC scores > 0, the 10-year cumulative incidence rates of ACEs were 0% [95% confidence interval (CI), 00], 3.7% [95% CI, 0.89-1.0], and 13.7% [95% CI, 0.74-0.99] for patients receiving mean heart doses of 0 Gy, 0-3 Gy, and > 3 Gy, respectively ($P = .133$).

Conclusions: CAC scores were a strong predictor of ACEs, especially if patients received adjuvant breast RT. Assessing CAC scores on simulation-CT should be an integral part of breast RT planning.

EVALUATION OF EARLY COSMETIC OUTCOME AND TOXICITY AFTER 5-FRACTION STEREOTACTIC PARTIAL BREAST IRRADIATION IN EARLY-STAGE BREAST CANCER: A PROSPECTIVE COHORT STUDY

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Background: We prospectively evaluated early toxicity and cosmetic outcomes in women undergoing 5-fraction stereotactic partial breast irradiation (S-PBI).

Methods: Women undergoing S-PBI or whole breast irradiation (WBI) for invasive carcinoma and/or carcinoma *in situ* were prospectively enrolled. S-PBI was delivered using a CyberKnife M6 with a dose of 30 Gy in five fractions. Patient-reported and physician-assessed adverse events were noted. Breast fibrosis was measured with a tissue compliance meter. Cosmetic outcomes were assessed using an automatic computer-based software (BCCT.core).

Result: Overall, 204 patients (n = 103, S-PBI; n = 101, WBI) were included. Fibrosis in uninvolved breast quadrants decreased over time following S-PBI for 12 months. However, this finding peaked at 6 months and further decreased at 12 months in the WBI group. Fibrosis in uninvolved breast quadrants at 6 months was significantly lower in the S-PBI group than in the WBI group ($P = 0.002$), while those of involved breast quadrants or scar sites were not significantly different between the groups. In the S-PBI group, patient-reported grade 3-4 events were 3% at 6 months and 0% at 12 months. Physician-assessed grade 34 events were 2% at 6 months and 0% at 12 months. Moreover, most cosmetic outcomes were excellent or good (82%) at 24 months after S-PBI with no significant cosmetic detriment from baseline ($P = 0.353$).

Conclusions: Patients who underwent S-PBI had less fibrosis in uninvolved breast quadrants compared with those who underwent WBI. Patients showed minimal toxicity with no detrimental cosmetic effect after S-PBI. Longer-term follow-up is ongoing and necessary.

NOVEL NSDHL INHIBITOR (COMPOUND 9) HAS ANTI-CANCER ACTIVITY IN BREAST CANCER

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Background: NAD(P) Dependent Steroid Dehydrogenase-Like (NSDHL) is an enzyme involved in post-squalene cholesterol biosynthesis. We recently suggested new insights into the critical role of the NSDHL involved in breast tumor growth and metastasis and its potential for targeted cancer therapy. Compound 9, a novel structure-based inhibitor of NSDHL, had been developed. This study aimed to investigate the anti-cancer potential of Compound 9 in breast cancer.

Methods: Compound 9 (10~100 uM) was investigated in several human breast cancer cell lines. Cell cycle analysis using DNA staining with PI, apoptosis analysis using annexin V/PI-labeling, synergistic cytotoxic analysis using crystal violet assay, transwell migration assay, western blot, immunofluorescent staining, and TEM image analysis were performed. NSG mice were used for orthotopic tumor models by injecting MDA-MB-231 cells.

Result: Time-dependent intracellular uptake of Compound 9 by breast cancer cells was observed. Compound 9 induced cytotoxic, anti-proliferative, and apoptotic effects and cell cycle arrest (G0/G1), and suppressed migration activity of breast cancer cells in a time- and dose-dependent manner. Combination with Compound 9 and paclitaxel led to synergistic cytotoxicity. Compound 9 increased the autophagy-related proteins (P62, LC3II) and autophagosome formation, but decreased the anti-apoptotic proteins (XIAP, BCL2). In orthotropic xenograft tumor models, the daily oral administration of Compound 9 suppressed tumor growth.

Conclusions: Our data show that Compound 9 triggers both autophagy and apoptosis and leads to anti-cancer activity, suggesting potential additional utility as an anti-cancer drug.

THE IMPACT OF PM2.5 ON THE RADIATION-INDUCED PNEUMONITIS IN PATIENTS WITH BREAST CANCER

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Background: Exposure to particulate matter (PM) air pollution has been associated with adverse effect on respiratory disease, but no study has investigated its impact on radiation-induced pneumonitis (RIP) in patients with breast cancer who received adjuvant radiation therapy (RT).

Methods: We conducted a retrospective review of 2,736 breast cancer patients who received postoperative RT between 2017 and 2020 in a single institution. Particulate matter data were retrieved from the open dataset in the 'Gyeonggi Data Dream'. We used the average, median and maximum values of the PM2.5 and PM10 measured during daytime when a patient visited to the hospital for RT.

Result: Overall incidence rate of RIP was 1.74%. There were no significant differences in average value of PM2.5 and number of RT fractions between RIP (+) and RIP (-) groups, but marginal differences were found in RT techniques (3-dimentional conformal RT vs. intensity modulated RT, $P = 0.053$) and proportion of PM2.5 value ≥ 35 ($\mu g/m^3$) ($P = 0.053$) between the two groups. After adjusting for age, RT technique, regional irradiation, fractionation and boost, the average value of PM2.5 was significantly associated with a higher risk of RIP ($P = 0.047$) when patients received ≥ 20 fractions of RT. Especially, PM2.5 ≥ 35 ($\mu g/m^3$) showed significant higher risk of RIP ($P = 0.014$) in patients with ≥ 20 fractions of RT after adjustment of aforementioned covariates.

Conclusions: This study is the first study to reveal the association between PM2.5 and RIP in breast cancer patients who received 20 fractions or more of postoperative RT.

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PREOPERATIVE INFLAMMATORY AND NUTRITION INDEXES PREDICT ARM LYMPHEDEMA IN 910 CHINESE BREAST CANCER PATIENTS UNDERGOING AXILLARY LYMPH NODE DISSECTION

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Background: Although the model Cleveland Clinic Risk Calculator (CCRC) has been widely used to assess the individual risk of arm lymphedema (ALE) in breast cancer patients undergoing axillary lymph node dissection (ALND), its accuracy in Chinese population remains to be proved. In addition, increasing evidence has clarified that preoperative inflammation and nutrition state might be associated with ALE, but their value for predicting ALE has not been assessed.

Methods: We retrospectively reviewed 910 breast cancer patients undergoing ALND from two independent cohorts. Best subset regression was used for feature selection and signature building. The risk score of ALE was calculated for each patient as a linear combination of selected predictors that were weighted by their respective coefficients.

Result: The results of our study demonstrated that the widely used model CCRC for predicting ALE was suboptimal in Chinese population, with an AUC of 0.661 at 1 years, 0.633 at 3 years, 0.651 at 5 years in the primary cohort, and 0.634 at 1 years, 0.628 at 3 years and 0.667 at 5 years in the validation cohort. Among the eleven systemic inflammation indexes in the primary cohort, seven variables were finally selected as risk factors to develop prediction model. The nomogram based on inflammation and nutrition markers possessed a stronger discrimination ability for ALE than the CCRC.

Conclusions: The nomogram based on preoperative inflammation and nutrition indexes possessed a strong discrimination ability for ALE, which may greatly help clinicians to identify patients at a high risk of ALE after ALND.

BARRIERS TO BRCA-RELATED FAMILY COMMUNICATION IN KOREA: THE DOCTOR-PATIENT-FAMILY NEXUS

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Background: As part of a larger study on Hereditary Breast-Ovarian Cancer (HBOC) family communication (K-CASCADE), this study aimed to explore barriers to BRCA-related family communication in Korea, from the perspective of carriers.

Methods: In-depth interviews were conducted with 22 women (17 affected, 5 unaffected carriers) across Korea, via face-to-face or telephone, between August 2020 and November 2021. Thematic analysis was done.

Result: Participants wished for sufficient information before disclosing their BRCA results and advocating for relatives seeking genetic testing (GT). Affected carriers were prone to experiencing stress because of the uncertain context of their own cancer trajectory. Barriers to BRCA-related family communication largely emerged at four levels: (1) receiving BRCA information from physicians (differences in intervening with respect to preventive approaches; unsatisfactory relaying of results); (2) processing BRCA implications (focused on their own cancer; burden of relaying and leading family talks; worry about foreseeable 'future of my family'); (3) disclosing and recommending GT (consideration of family member's life stage; family unaware of seriousness; wishing to avoid 'passing on this flaw'); and (4) cancer-related sociocultural barriers (unfamiliarity with hereditary cancer; differences in healthcare access).

Conclusions: As Korean women carrying BRCA pathogenic variants have tremendous difficulty transmitting genetic information to their family, disclosure should be framed as conveying useful news rather than bad news. Specific information, including the importance of GT, must be provided by healthcare professionals in a consistent way, with hands-on support for initiating and continuing family conversations so that patients do not feel isolated.

ASSOCIATION BETWEEN REPRODUCTIVE PATTERN AND BIOLOGIC SUBTYPE OF BREAST CANCER

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Background: Reproductive factors such as parity, menstrual pattern are known to be risk factors for breast cancer. But there is little study about the association between reproductive factors and breast cancer subtypes. The aim of this study was to investigate associations between reproductive factors and breast cancer subtypes, and whether these vary by age at diagnosis.

Methods: Reproductive risk factors (parity, age at first full-time pregnancy, number of childbirth, age at menarche, and menopausal status) from 1,195 patients with breast cancer were analyzed. The correlation between reproductive factors and subtype was analyzed by logistic regression analysis and chi-square test.

Result: Parity status was not associated with the breast cancer subtype. Nulliparity patients (119, 9.9%) were not associated with the aggressive subtypes or favor subtypes. First full-time pregnancy, number of childbirth, age at menarche were also not associated with breast cancer subtype. However, menopausal status was associated with the breast cancer subtype significantly ($p < 0.001$). Tripple negative type was more common in postmenopausal patients (16.1% vs 8.1%) and hormone receptor-positive breast cancer was less common in postmenopausal patients (73.6% vs 88.8%).

Conclusions: The triple-negative type was more common in postmenopausal breast cancer patients. However, reproductive factors (parity, age at first full-time pregnancy, number of childbirth, age at menarche) were not associated with the breast cancer subtype.

CONCEPTIONS OF RESPONSIBILITY TO COMMUNICATE GENETIC INFORMATION AND RISK ABOUT HEREDITARY BREAST AND OVARIAN CANCER: A SWISS-KOREAN QUALITATIVE COMPARATIVE ANALYSIS

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Background: This study aims to understand cultural differences and similarities between Swiss and Korean women carrying BRCA1 or BRCA2 pathogenic variants about their notions of responsibility to disclose genetic information and risk about hereditary cancer to relatives. Using qualitative data from the CASCADE study, an international cohort of hereditary breast and ovarian cancer (HBOC) families, we investigate the different issues encountered by Korean and Swiss families, with a focus on culturally diverging conceptions of responsibility and family.

Methods: In-depth qualitative interviews from 22 Korean and 57 Swiss HBOC cases were transcribed verbatim and were translated from Korean, French, Italian and Swiss German to English. Preliminary analysis has been done with 14 interviews using MaxQDA and a mind-mapping analysis tool by an interdisciplinary and bi-national team.

Result: Factors linked to Life Course Perspective, relatives' experiences with cancer and individual, relational and structural dimensions can either hinder or sustain the weight of responsibility. We identified several levels of responsibility and 4 models: 'overwhelming', 'leading', 'shared', and 'soft' responsibility. Differences between Swiss and Korean women were mainly identified in the model of 'shared' responsibility. Older Korean women discussed more often the topic of nuclear family solidarity, and issues regarding the Korean extended family system. Swiss and young Korean women refer more frequently to individual patterns of responsibility that are characteristic of the 'leading' and 'soft' models.

Conclusions: Capturing subtle cultural specificities regarding different conceptions of responsibility supports culturally appropriate interventions. Findings can be used in clinical practice to support genetic information disclosure.

THE INCIDENCE AND PROGNOSIS OF POSTPARTUM BREAST CANCER: A NATIONWIDE STUDY BY THE SMARTSHIP GROUP

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Background: The term 'pregnancy-associated breast cancer' is no longer used as it has been consistently reported that breast cancer during pregnancy and breast cancer after delivery (postpartum breast cancer) have different characteristics and prognosis. The purpose of this study is to define postpartum breast cancer by analyzing the incidence rate, related factors, and prognosis according to the timing of breast cancer.

Methods: Data from the Korean National Health Insurance Service were used to analyze 1,292,727 women aged 20-49 years who birthed their first child between 2007 and 2012.

Result: The annual incidence rate of breast cancer after delivery increased every year (7.7 per 10,000 person-years after 5 years, 19.36 per 10,000 person-years after 10 years). The risk of breast cancer was significantly higher (HR 1.15, 95% CI 1.05-1.27, $P=0.0037$) in women diagnosed with gestational diabetes, but that was not associated with overall survival (OS). Patients diagnosed with breast cancer within 5 years of delivery had a poorer prognosis than those diagnosed later (5-yr OS, <5 years: 91.1% vs. 5-10 yr: 96.0%). In multivariate analysis of OS, the HR of patients diagnosed within 5 years after delivery was 2.0 higher than that of patients diagnosed between 5 and 10 years.

Conclusions: Women diagnosed with gestational diabetes were at an increased risk of breast cancer. Breast cancer patients diagnosed within 5 years of delivery had a poorer prognosis than those diagnosed later. In this regard, careful screening for early diagnosis of high-risk patients and intensive research on new treatment strategies are needed.

DETERMINANTS FOR OR AGAINST UNDERGOING PROPHYLACTIC MASTECTOMY AND OOPHORECTOMY IN UNAFFECTED WOMEN WITH BRCA1/BRCA2 MUTATION IN SWITZERLAND: A MIXED-METHODS STUDY

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Background: Women carrying pathogenic variants in BRCA1 and BRCA2 have significantly higher risk of breast or ovarian cancer. Prophylactic surgeries (PS), such as mastectomy and/or salpingo-oophorectomy are documented cancer prevention methods, recommended by national and international guidelines. However, decisions for PS are not trivial, and women are often exposed to conflicting information from internet forums, websites, their social network, and even healthcare providers. There is limited evidence on how women with BRCA1/ BRCA2 pathogenic variants decide for or against PS.

Methods: Unaffected women with BRCA1/BRCA2 pathogenic variants (n = 109) completed a baseline survey as part of their participation to the Swiss CASCADE study, an open-family-based cohort focused on hereditary cancer. A subsample of unaffected women (n = 16) provided in-depth interviews. The survey and the interviews were designed to elicit factors influencing decisions for genetic testing and cancer risk management. Descriptive statistics and multivariate analysis identified the predictive value of demographic, clinical, and psychosocial variables. The narrative data was analyzed inductively using grounded theory method.

Result: Analyses are ongoing. Younger women (< 50 y.o.) and those with higher genetic literacy appear more likely to opt for prophylactic mastectomy. Women with children and those > 50 y.o. opt more often for salpingo-oophorectomy. Narrative data point to themes such as self-protection, responsibility towards children, self-image, relationship, sexuality, fertility, and adverse events.

Conclusions: Understanding reasoning and worries relating to PS, healthcare professionals will be able to improve consultations and better address age- and gender-specific concerns.

Poster Presentation

PREDICTING OPENNESS OF COMMUNICATION IN FAMILIES WITH HEREDITARY BREAST AND OVARIAN CANCER SYNDROME: A NATURAL LANGUAGE PROCESSING APPROACH

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Background: How patients communicate genetic information to their relatives is critical to ensuring dissemination of genetic information. Detailed information about patients' attitudes towards intrafamilial communication of cancer genetics and cancer risk can be also found in unstructured text notes in interviews. NLP has received great attention in the medical domain due to unique ability to extract and process narrative texts. We aimed to predict ease of communicating cancer risk among individuals from hereditary breast and ovarian cancer (HBOC) affected families by applying NLP techniques.

Methods: The ability of NLP techniques to identify levels of family communication in individuals with cancer risk associated with HBOC was evaluated following a multistep framework: (i) pre-processing, (ii) training, and (iii) performance evaluation. We measured the performance of the training and testing model using sensitivity, specificity, accuracy, positive predictive value or precision, negative predictive value, and area under the curve.

Result: Participant's age ranged from 32 to 76 years, 87.5% were female. In total, 34.4% had a prior diagnosis of breast or ovarian cancer; and 93.8% had tested positive for pathogenic variants. The overall sentiment is positive and varied between participants. Participants who have greater willingness to share each other and had a positive sentiment were more prone to communicate genetic risk. Being retired was associated with lower "ease of communication" scores, while being single was associated with higher "ease of communication" scores. The accuracy of the model on the validation set was 64% and, on the training, set 72%.

Conclusions: NLP models had a promising predictive value for communicating genetic risk in HBOC-affected families.

ASSOCIATIONS BETWEEN BREAST CANCER RISK FACTORS, BREAST CANCER RISK, AND BREAST DENSITY IN A COHORT OF KOREAN WOMEN: A MEDIATION ANALYSIS

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Background: Mammographic breast density is associated with breast cancer (BC) and other risk factors of BC. Thus, it might play a role as a mediator that influences the relationship between risk factors and BC risk.

Methods: The study population included Korean women between 40 and 74 years of age screened for breast cancer between 2009 and 2010 and followed up to 2020. Mediation analysis was used to calculate the mediation percent of dense breast density between the risk factors and breast cancer.

Result: 4,136,723 women (meanage, 53 ± 6 years) were analyzed. During follow-up (median 10.6 years), 69,225 women developed breast cancer. 31,041 (75.1%) in premenopausal women and 10,819 (38.8%) in postmenopausal women breast cancer development of dense breast density women was detected. The relationship between several risk factors and BC was mediated by breast density in both pre-and postmenopausal women, including height (proportion mediated 7.3%, $p < 0.001$ and 6.5%, $p < 0.001$, respectively), age at menarche (3.2% and 3.8%), family history of BC (4.3% and 11.1%), benign breast disease (8.4% and 14.7%), parity (10.5% and 13.9%), and breastfeeding (4.5% and 9.6%). In postmenopausal women, breast density also mediated the association between age at menopausal (3.8%, $p < 0.001$), and hormone replacement therapy (11.3%, $p < 0.001$).

Conclusions: Our findings suggest that the association between several BC risk factors and future risk is mediated by breast density, with different magnitudes and varied by menopausal status.

Poster Presentation

DOMESTIC MEDICAL TRAVEL FROM NON-SEOUL REGIONS TO SEOUL FOR BREAST CANCER TREATMENT: A NATIONWIDE COHORT STUDY

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Background: To investigate the annual frequencies and patterns of breast cancer treatment by region, assess the trend of domestic medical travel from non-Seoul regions to Seoul for initial treatment, and identify factors associated with medical travel in breast cancer patients.

Methods: A nationwide cohort study was performed using the Health Insurance Review and Assessment data of South Korea. Patients were classified according to the regions in which they underwent pathologic examination (Seoul vs. metropolitan cities vs. other regions). Frequencies of pathologic examinations, diagnosis, and treatment were analyzed according to regions. Domestic medical travel was analyzed according to cities and provinces, and factors associated with medical travel were investigated.

Result: A total of 150,709 breast cancer survivors who were diagnosed between 2010 and 2017 were included. The annual frequencies of pathologic exams, diagnosis, and treatment increased in all regions, and the difference in the frequencies of surgery between Seoul and non-Seoul regions increased over time. The rate of medical travel from non-Seoul regions to Seoul increased from 14.2% in 2010 to 19.8% in 2017. Approximately a quarter of patients from other regions traveled to Seoul, and over 40% of patients from Chungbuk, Gyeongbuk, and Jeju regions traveled to Seoul for treatment in 2017. Young age and other regions were significantly associated with the likelihood of domestic medical travel.

Conclusions: The number of patients traveling to Seoul for breast cancer treatment increased over time. Young age, comorbidities, and type of insurance were significant factors associated with medical travel.

COMPARISON OF THE PROGNOSTIC FACTORS ACCORDING TO TUMOR SIZE IN SMALL BREAST CANCER

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Background: Breast cancer most often affects women, with an increasing incidence worldwide. The incidence rate of breast cancer among women in Korea is also rising, and the rate of early breast cancer diagnosis has improved. The factors that determine the prognosis of breast cancer have been continuously studied. This study evaluated the prognosis of patients with breast cancer with a tumor size of less than 2 cm and the factors affecting the prognosis.

Methods: A retrospective study was conducted based on the medical records and imaging data of 345 patients diagnosed with breast cancer with a tumor size of 2 cm or less who underwent breast cancer surgery from 2010 to 2020. The patients were divided into two groups (T1ab/T1c) based on 1 cm tumor size and compared.

Result: Among various prognostic factors, axillary lymph node metastasis was found to be higher in the T1c group compared to the T1ab group (27.9% and 17.8%, respectively) but it was not statistically significant. Lymphovascular invasion was found in 29.9% of the T1c group with a relatively larger tumor size (1.0-2.0) and only in 15.3% of the T1ab group (less than 1.0), showing a statistically significant difference. An increase in tumor size is a poor prognostic factor that may increase the likelihood of lymph node metastasis and lymphatic vessel invasion, leading to increased recurrence or decreased survival.

Conclusions: Our analysis suggests that better treatment outcomes can be expected when the triggering factors for aggressive tendencies are identified in small-sized breast cancer and patients are introduced to active treatment.

FREQUENCY AND SPECTRUM OF GERMLINE VARIANTS OF UNCERTAIN SIGNIFICANCE IN A SRI LANKAN COHORT WITH HEREDITARY BREAST CANCER

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Background: Variants of uncertain significance (VUS) have been reported in about 10-40% of hereditary cancer patients undergoing germline genetic testing. However, there is paucity of data on the pattern of germline VUS in breast cancer predisposing genes in under-represented populations. This study aims to describe the frequency and spectrum of germline VUS identified in a Sri Lankan cohort with hereditary breast cancer.

Methods: Genomic data of 72 breast cancer affected patients from families with hereditary breast cancer who underwent germline genetic testing through Next-Generation Sequencing (NGS) analysis between January 2015 and December 2021 were maintained prospectively in a database and analyzed retrospectively. NGS data were subjected to bioinformatics analysis and variants were classified according to American College of Medical Genetics and Genomics and Association for Molecular Pathology standards and guidelines.

Result: Germline genetic variants were identified in 35/72 (48.6%) patients. Pathogenic/likely pathogenic variants were detected in 21/35 (60%) patients. VUS were identified in 14/35 (40%). 1 (7.1%) VUS was novel and remaining 13 (92.9%) were reported variants. Distribution of the VUS in high- and moderate-penetrant breast cancer predisposing genes were: APC:c.1564A>G;p.M522V- 1/14(7.14%), ATM:c.7502A>G;p.N2501S- 1/14(7.14%), BRCA1:c.3392A>G;p.D1131G- 1/14(7.14%), BRCA2:c.2488A>G;p.N830D, BRCA2:c.6231G>C;p.K2077N- 2/14(14.29%), BRIP1:c.3431A>G;p.E144G, BRIP1:c.3103C>T;p.R1035C- 2/14(14.29%), CDKN2A:c.377A>G;p.G126P- 1/14(7.14%), CHEK2:c.1630G>A;p.G544L- 1/14(7.14%), EPCAM:c.*261G>C- 1/14(7.14%), FANC1:c.3179T>C;p.I1060T- 1/14(7.14%), MET:c.840G>T;p.R280S- 1/14(7.14%), NF2:c.1522G>A;p.D508N- 1/14(7.14%), STK11:c.355A>G;p.N119D- 1/14(7.14%).

Conclusions: 40% of germline variants detected in affected patients were VUS. Functional evaluation and understanding the clinical significance of VUS in under-represented populations is necessary to improve the identification of potentially pathogenic variants that may be useful for patient clinical management in future.

Poster Presentation

METASTATIC AND SURVIVAL CHARACTERISTICS OF DE NOVO VERSUS RELAPSED BREAST CANCER IN FEMALE AGED>35-YEAR-OLD: A NATIONWIDE MULTICENTER STUDY BASED ON HOSPITAL POPULATION

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Background: It is uncertain how the metastatic and survival characteristics for de novo metastatic breast cancer (dnMBC) patients compared with relapsed metastatic breast cancer (rMBC) patients in cohort aged > 35-year-old.

Methods: All subjects diagnosed with metastatic breast cancer were enrolled from 21 hospitals in 7 geographical regions of China during 2012-2014. The rMBC patients were divided into 4 groups based on metastasis-free interval (< 12-month, 12~36-month, 36~60-month and > 60-month). Overall survival (OS) and post-distant relapsed survival (PDRS) were compared using Kaplan-Meier curves. Multivariable COX regression was applied to analyze the adjusted hazard ratios (aHRs) for OS and PDRS with different metastatic situations.

Result: A total of 3075 subjects aged > 35-year-old were included in this analysis. The proportion of dnMBC group and four rMBC groups were 17.3% (531), 9.9% (303), 36.2% (1114), 17.5% (538) and 19.2% (589) respectively. The dnMBC patients had a worse OS than rMBC individuals who relapsed later than 12 months (all $P < 0.001$). The < 12-month-rMBC and 12~36-month-rMBC showed a worse PDRS than dnMBC (both $P < 0.001$). For 12~36-month-rMBC individuals, bone (HR 0.49, 95% CI: 0.29-0.78) or liver (HR 0.58, 95% CI: 0.42-0.80) metastases might be a protective factor for OS compared with dnMBC, but not for < 12-month-rMBC group. Groups with < 12-month-rMBC and 12~36-month-rMBC did not show a significantly worse PDRS than dnMBC patients as for non-visceral metastases (HR < 12m 1.25, 95%CI: 0.45-3.47; HR12~36m 1.82, 95% CI: 0.94-3.54).

Conclusions: This research showed that de novo breast cancer had a better PDRS than those who relapsed within 36 months, but had a worse OS than patients relapsed later than 36 months.

Poster Presentation

INHIBITION OF MIF ENHANCES THE SENSITIVITY OF BREAST CANCER CELL TO EPIRUBICIN BY ACTIVATING NOX4/ROS PATHWAY

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Background: Macrophage migration inhibitory factor (MIF) is a widely reported pluripotent cytokines which participates in anti-inflammatory response, myocardial injury and tumor progression. Nevertheless, the studies of MIF on epirubicin resistance in BC are rare.

Methods: Immunohistochemistry, RT-PCR, and western blotting were used to analyze the expression of MIF in BC tissues. A series of in vitro experiments, including CCK8 assay, cell apoptosis assay, reactive oxygen species (ROS) detection and mitochondrial membrane potential (ψm) measurement, was conducted to elucidate the mechanisms via which MIF modulates the sensitivity of TNBC cells to epirubicin.

Result: In this study, we showed that MIF was over-expressed in BC tissues and cell lines, which was consistent with our bioinformatics analysis results. Furthermore, MIF expression was also closely related to TNM stage of BC. In the vitro assay, it was discovered that MIF knockdown increased the sensitivity of MDA-MB-231 and MDA-MB-468 cells to epirubicin. Moreover, MIF silencing combined with epirubicin treatment also increased ROS accumulation, which induced the mitochondrial pathways of apoptosis in BC. Since Nox4 plays a vital role in ROS production, we examined whether there was a correlation between MIF and Nox4 in oxidative stress of BC cells to epirubicin. Our results showed that MIF silencing increased the sensitivity of MDA-MB-231 and MDA-MB-468 cells to epirubicin by up-regulating Nox4 expression, which promoted ROS generation and induced the mitochondrial pathways of apoptosis.

Conclusions: In summary, our findings suggested that MIF silencing enhanced the sensitivity of BC cells to epirubicin by Nox4/ROS axis, which might provide a new strategy for overcoming drug-resistance of BC.

IS THE HUMAN PAPILLOMA VIRUS INVOLVED IN THE DEVELOPMENT OF BREAST PAPILLARY NEOPLASMS?

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Background: Human papilloma viruses (HPV) have been also shown to immortalize breast epithelium, with a possible role in breast cancer pathogenesis. A meta-analysis suggested that HPV infection is a risk factor for breast cancer. HPV may also be involved in breast papillary lesions. Vaccination against or treatment of HPV may have an impact in the prevention of these diseases. We examine the expression of p16 as a surrogate marker of HPV infection in papillary lesions and invasive breast cancer.

Methods: We looked at intraductal papillomas, triple negative breast cancers (TNBC) and non-papillary benign breast lesions diagnosed at the Singapore General Hospital from 2005-2015. Immunohistochemistry was performed on deparaffinized whole tissue sections, using p16 (E6H4). The slides were counterstained with haematoxylin was conducted, H-scores were determined. Mean H-scores were analysed with the unpaired t-test.

Result: P16 expression was higher in the stroma in both papillary and TNBC compared with the benign stroma ($p < 0.0001$), as was in the papillary epithelial cells compared to the epithelium ($p = 0.005$).

Conclusions: There is a significantly high expression of p16 protein, in papillary and TNBC compared with benign breast lesions. Further studies are needed to investigate its role in the causation pathway in breast papillary tumours.

Z-GUGGULSTERONE INHIBITS TUMOR PROGRESSION BY TARGETING CXCR4/CXCL12 SIGNALING AXIS IN AN ORTHOTOPIC TRIPLE NEGATIVE BREAST CANCER MODEL

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Background: CXCR4 receptor and its cognate ligand CXCL12 can play a critical role in metastasis. Triple negative breast cancer (TNBC) is an aggressive breast cancer sub-type exhibiting rapid proliferation and metastasis. Therefore, novel agents that can inhibit CXCR4/CXCL12 signalling axis might have potential in attenuation of growth and metastasis of TNBC.

Methods: The potential anticancer effects of Z-guggulsterone on the viability, migration, invasion, apoptosis was analyzed by MTT, and wound healing assays. The effect of this phytosteroid on CXCR4 regulation and in vivo tumor growth was also investigated using orthotopic mouse model. TNBC tissues obtained from patients (n = 204) and corresponding lymph nodes with tumor metastasis (n = 21) were also analyzed for CXCR4 levels.

Result: A total of 205 TNBC breast tumor tissue was examined for the expression of CXCR4 using the tissue microarray immunohistochemical analysis. We found that out of the 205 samples, 97 samples showed positive staining, 87 samples showed negative staining. Nuclear staining was found in 24 samples and cytoplasm staining was found in 71 samples and 21 samples were rejected for necrotic tumors. Moreover, out of 21 metastatic lymph node samples, 15 were positive while 6 were negative, 3 showed nuclear staining and 12 showed cytoplasmic staining. We also noted that guggulsterone can abrogate invasion, migration, modulate CXCR4 expression and can enhance anticancer effects of paclitaxel in orthotopic mouse model.

Conclusions: We prove the potential efficacy of guggulsterone as a novel CXCR4 antagonist with significant anticancer potential against TNBC.

STUDY OF THE BIOLOGICAL FUNCTIONS OF MUTANT NSDHL GENE IN BREAST CANCER CELLS

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Background: Cancer cells gain biologically worse phenotype by somatic mutations, while simultaneously influencing immune cell functions. We had identified somatic mutations of NAD(P) Dependent Steroid Dehydrogenase-Like (NSDHL) gene from breast tumors of patients with distant metastasis using whole-exome sequencing. This study aimed to explore whether NSDHL mutants contribute to a more aggressive phenotype of human breast cancer cells.

Methods: Breast cancer cell (ZR75-1) and macrophage (RAW264.7) were used. GFP-tagged NSDHL mutants were generated by subcloning the mutant NSDHL into lentiviral vector yielding an in-frame fusion 3' to GFP. CellTiter-Glo, transwell migration and wound healing assays, cell cycle analysis, qRT-PCR, western blot analysis and immunofluorescence staining were performed. Co-culture of two cell lines was used in vitro.

Result: Stable pools and clones expressing the GFP-tagged NSDHL mutants were selected by puromycin with subsequent FACS. In NSDHL mutant-transduced ZR75-1, there was no dramatic change in growth rate, but cell migration abilities were significantly increased compared with those of the parent and wild type NSDHL-transduced cells. The migration ability and M2 polarization markers (arginase1, FIZZ1, CD206, and YM-1) of RAW264.7 were significantly increased by co-culture of NSDHL mutant-transduced ZR75-1 as compared to the parent and wild type NSDHL-transduced cells.

Conclusions: The present data indicate that breast cancer cells harboring somatic mutants of NSDHL gene seem to display a more aggressive behavior by gaining biologically worse phenotype and directly recruiting M2 macrophages. Further study of the mechanisms underlying mutant NSDHL protein and gain-of-function will accelerate the development of targeted therapies for human cancer harboring mutant NSDHL.

UNDERSTANDING THE MOLECULAR SUBTYPES AND RESPECTIVE RADIOLOGICAL PHENOTYPES OF BREAST CANCER IN THE ERA OF PERSONALISED MEDICINE

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Background: Breast cancer is traditionally classified based on the clinicopathologic analysis of tumors. In recent two decades, identification of distinct gene expression profiling in different subtypes of breast cancers allows better prediction of tumor aggressiveness, prognostication, and implementation of personalized medicine. Importantly, associations with specific radiological phenotypes have been found in different molecular subtypes of breast cancer.

Methods: This presentation aims to provide a pictorial exhibit of distinctive imaging features of different molecular subtypes of breast cancer, with emphasis of their biological behaviors, therapeutic implication and clinical outcomes. Distinctive imaging characteristics of each molecular subtype of breast cancer are illustrated with pathological proven examples.

Result: Based on the gene expression profiling, breast cancers are reclassified into four major groups including luminal A, luminal B, HER2-enriched and basal-like subtypes. Characteristic radiological findings for each breast cancer molecular subtype on mammography, ultrasound and MR imaging are illustrated in details. The implication of the molecular classification of breast cancer in guiding personalized treatment is briefly discussed.

Conclusions: Breast cancers are now classified according to their molecular signatures. Understanding the genetic basis, imaging phenotypes and biological behaviors of different molecular subtypes is essential for breast cancer management in the era of personalized medicine.

CHOLESTEROL-LOWERING DRUGS DOWNREGULATE PROGRAMMED DEATH-LIGAND 1 (PD-L1) IN TRIPLE NEGATIVE BREAST CANCER CELLS

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Background: Statins, besides being powerful cholesterol-lowering drugs, have pleiotropic effects which includes anticancer activities by modulating anti-tumor immune response. Association of statin use with improved survival outcomes in triple-negative breast cancer (TNBC) has been reported, yet the tumor-selective mechanisms that mediate these clinical outcome remain largely unclear. Here, to elucidate the anti-cancer mechanism of statins in TNBC cells, we aimed to investigate the immunomodulatory effects of statins.

Methods: Thirteen human TNBC cell lines and mouse macrophage cell line and clinically approved drugs (statins: lovastatin and simvastatin) were used. Flow cytometry, western blot, qRT-PCR, Annexin V-PI assay, and transwell migration assay were performed. Co-culture of two cell lines, MDA-MB-231 with RAW 264.7 was used in vitro.

Result: Among thirteen TNBC cells, MDA-MB-231, HCC38, HCC70, and BT20 highly expressed endogenous/constitutive PD-L1. Statins suppressed the PD-L1 levels, along with decreased phosphorylation of AKT, ERK1/2, and STAT3 in breast cancer cells in a dose (1, 5, 10, 25 uM)- and time (8, 24 h)-dependent manner. In addition, statin exerted anti-proliferative and apoptotic actions in breast cancer cells. Conditioned medium of statin-treated breast cancer cells decreased migration of Raw 264.7 cells dose-dependently.

Conclusions: Our results indicate that statins exert direct anticancer activity by reducing PD-L1 expression, inducing apoptosis, impairing AKT, ERK1/2, and STAT3 signal pathways, and suppressing macrophage migration. Further study is needed to investigate in-depth molecular mechanism study by which statins regulate PD-L1 expression in TNBC and to confirm the safe and effective use of statins as an adjuvant therapy in TNBC.

REGULATION OF PAIRED BOX 2 IN BREAST CANCER METASTASIS BY EP2 RECEPTOR

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Background: Pro-tumorigenic actions of prostaglandin E receptors (EP1-EP4) have been shown in breast cancer and other solid tumors. Evidence suggest that EP2 receptor contributed to breast cancer progression and metastasis through different signaling pathways. This study aims to dissect the regulatory role of EP2 receptor in breast cancer metastasis.

Methods: A stable EP2-overexpressing cells were developed to study the tumor growth and metastasis in human xenograft breast cancer model. Correlation analysis and survival analysis were used to evaluate the relationship between EP2 and PAX2, and the correlation with clinical outcome of the patients respectively. In-silico prediction tool and luciferase reporting assay were used to identify the putative target of EP2.

Result: Higher expression of EP2 was seen in triple-negative breast cancer than other subtypes, and were associated with poor prognosis. Silencing of EP2 reduced tumorsphere generating ability and ABCG2 expression. In human xenograft breast cancer model, EP2-overexpressing cells promoted the growth of xenograft tumors and had more metastatic nodules. Various EMT-related gene expressions were altered in metastatic tumors of the xenografts. Moreover, PAX2 has been identified as the putative downstream target of EP2 by luciferase reporting assay. PAX2 expression significantly upregulated in tumor tissues and had a positive correlation between EP2 and PAX2 expression in paired primary tissues. Importantly, knockdown of PAX2 by RNA interference reduced cell proliferation and migration.

Conclusions: This study revealed a novel EP2-driven signaling cascade to promote cancer growth and metastasis through regulation of PAX2. Targeting EP2/PAX2 axis may offer a new treatment options for advanced breast cancer.

ESTABLISHMENT OF PATIENT-DERIVED ORGANOID OF BREAST CANCER

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Background: A patient-derived organoid (PDO) is an in vitro three-dimensional model which shows similar features in phenotypic and genetic aspects with primary tissue from patient. PDOs can provide a platform for drug sensitivity tests of tumors from individual patients, thus PDOs were recently introduced as an emerging tool for personalized medicine.

Methods: We obtained a total of 21 surgical specimens from 21 patients with breast cancer at the Yonsei Cancer Center, Severance Hospital, Seoul, Korea. One tissue specimen from a breast cancer patient-derived xenograft mouse model was also used for the establishment of PDO from April 2021 to December 2021. We dissociated the tissues and isolated breast cancer cells from the samples. We performed 3D-culture in basement membrane-like matrix and then growth media with supplements that was refreshed every 2-4 days. We defined establishment of PDOs as successful after 3 passaging.

Result: Among all 22 cases, 6 cases failed to culture or passage, however, 9 cases were successfully cultured over 3 passages. In addition, the remaining 7 cases are still in progress of establishment. Success rate of PDO was 60% (9/15). Subtypes of primary tumors of the PDO were 22.2% (2/9) of luminal A, 33.3% (3/9) of luminal B, 33.3% (3/9) of triple-negative, and 11.1% (1/9) of HER2. Pathologic evaluation using immunohistochemistry revealed that PDOs showed similar morphologic and immunohistochemical features with primary tumors.

Conclusions: PDOs can be a real-time platform for drug sensitivity and drug screening tests. PDO models would be available as a prominent tool for pre-clinical studies in breast cancer.

NK CELL ACTIVITY AND ANEMIA IN PATIENTS WITH BREAST CANCER

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Background: Breast cancer is associated with anemia, and the expression of several iron-related proteins, such as ferritin, hepcidin, and ferroportin, is not regulated in breast cancer cells. These changes may have a prognostic effect in patients with breast cancer. The Fanconi Anemia pathway is an important component of the DNA damage response involving 22 genes and plays an important role in cross-linking DNA strands and restoring genomic stability.

Methods: It has been reported that NK cells may be involved in immune surveillance for tumor spread. We investigated the relationship between anemia and NK cell activity in the treatment of breast cancer patients. We checked NK cell activity before and after treatment in 500 patients with breast cancer and also identified the relationship to anemia.

Result: In this study, NK cell activity was checked before treatment and 6 months after treatment, and the correlation with hemoglobin levels was confirmed. In addition, by checking the medical records of breast cancer patients, the association between body mass index and stage was confirmed, and the association with breast cancer prognosis was investigated.

Conclusions: This study investigated the relationship between the change in NK cell activity and the hemoglobin level during the treatment of breast cancer, and the prognosis was related. This study is valuable because it is important not only for the treatment of breast cancer but also for the self-healing and immunity of patients.

CORDYCEPS MILITARIS INDUCED THE IMMUNOGENIC CELL DEATH IN HUMAN AND MOUSE BREAST CANCER CELLS

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Background: Cordyceps militaris has been widely used as a traditional medicine in East Asia. Its effects against breast cancer have been reported previously. However, whether C. militaris-induced breast cancer cell death is immunogenic remains unelucidated. This study aimed to determine whether ethanolic extracts of C. militaris (CME) could induce immunogenic cell death (ICD) in breast cancer immunotherapy.

Methods: Human and mouse breast cancer cells were treated with various concentrations of CME for 72 hours and cytotoxicity was measured using the sulforhodamine B assay. Flow cytometry was used to assess cell death with annexin V/7-AAD staining and measure the surface exposure of damage-associated molecular pattern (DAMP) molecules including calreticulin, HSP70 and HSP90. Western blot for cleaved PARP was used to confirm apoptotic cell death. The immunogenicity of CME-induced dead cells was evaluated using the CFSE dilution assay.

Result: CME reduced the viability of human and mouse breast cancer cells. The IC50 was 25-50 μg/ml in human breast cancer cells and 10-50 μg/ml in mouse breast cancer cells at 72 hours. CME-treated breast cancer cells were positively stained by annexin V, cleaved PARP, and cleaved caspase 3/7 which were increased upon CME treatment. Surface exposure of DAMP molecules was increased in dose- and time-dependent manners. The CFSE dilution assay revealed that dendritic cells fed with CME-treated breast cancer cells successfully stimulated tumor-specific T cell proliferation without inhibiting DC function and T cell proliferation.

Conclusions: The CME can induce immunogenic and apoptotic cell death in breast cancer cells and it is a good candidate for cancer immunotherapy.

INVESTIGATION OF CD8+ T CELL-MEDIATED ANTI-TUMOR IMMUNE RESPONSE INDUCED BY CHEMOTHERAPY IN BREAST CANCER PATIENT

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Background: Neoadjuvant chemotherapy (NAC) is given preoperatively to shrink breast tumors prior to surgery. Recent studies showed that chemotherapy not only exerts a cytotoxic activity against tumor cells, but also elicits anti-tumor immune response by inducing immunologic cell death. In this study, we examined the change of characteristic of CD8+ T cells during and after NAC to evaluate the role of NAC on anti-tumor immune response.

Methods: We isolated peripheral blood mononuclear cells (PBMCs) sequentially before, during and after neoadjuvant chemotherapy from 106 breast cancer patients and performed immuno-phenotyping using flow cytometry. Ki67 and HLA-DR+ CD38+ cells were assessed for CD8+ T proliferation and activation. Also, we tracked the change of CD8+ T cell clones using bulk-TCR sequencing of CD8+ T cells. We investigated the relation between the pathologic response of NAC and the change of CD8+ T cell phenotypes or clonotypes during NAC.

Result: NAC induces lymphopenia in breast cancer patients. CD8+ T cells proliferate significantly after chemotherapy and the frequency of proliferating CD8+ T cells, especially in PD-1+EM+CD8+ T cell subpopulation, tends to be higher in pCR patients. Proliferation or activation features of CD8+ T cells is not limited to tumor-specific cells. Non-TAA-specific cells also showed similar characteristics. Changes in repertoire of CD8+ T cell clones after chemotherapy tends to be associated with pCR status.

Conclusions: NAC plays a role on the CD8+ T cell-mediated anti-tumor immune response and the measurement of peripheral CD8+ T cell characteristics during NAC may provide the better understanding of anti-tumor immune response in breast cancer patients.

FEASIBILITY OF ANOMALY SCORE DETECTED WITH DEEP LEARNING IN IRRADIATED BREAST CANCER PATIENTS WITH RECONSTRUCTION

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Background: We evaluated cosmetic outcomes of the reconstructed breast in breast cancer patients using anomaly score (AS) detected by generative adversarial network (GAN) deep learning algorithm.

Methods: A total of 251 normal breast images from patients who underwent breast-conserving surgery were used for training anomaly GAN network. GAN-based anomaly detection was used to calculate abnormalities as an AS with Z-score standardization. Then, we retrospectively reviewed 61 breast cancer patients who underwent mastectomy followed by breast reconstruction with autologous tissue or tissue expander. All patients were treated with adjuvant radiation therapy (RT) after breast reconstruction and computed tomography (CT) was performed three time points; before RT (Pre-RT), one year after RT (Post-1Y), and two years after RT (Post-2Y).

Result: Compared to Pre-RT, Post-1Y and Post-2Y demonstrated higher AS, indicating more abnormal cosmetic outcomes on paired-T test (Pre-RT vs. Post-1Y, $P=0.015$ and Pre-RT vs. Post-2Y, $P=0.011$). Pre-RT AS was significantly higher in patients having major breast complications ($P=0.016$). Autologous reconstruction showed better AS than tissue expander insertion at pre-RT (2.00 vs. 4.19, $P=0.008$) and post-2Y (2.89 vs. 5.00, $P=0.010$). Linear mixed effect model revealed that days after baseline were significantly associated with increasing AS ($P=0.007$). Also, the use of tissue expander was associated with steeper rise of AS, compared with autologous tissue ($P=0.015$). Fractionation regimen (conventional fractionation vs. hypofractionation) was not associated with the change of AS.

Conclusions: Anomaly score detected by deep learning might be feasible in predicting cosmetic outcomes of RT-treated patients with breast reconstruction. AS should be validated in clinical trial settings.

RECALL LATERALITY AND BILATERALITY: POSSIBLE NEW SCREENING MAMMOGRAPHY QUALITY METRICS

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Background: Current screening mammography quality metrics are important and helpful, but do not address all concerns. Never previously considered are a) whether the reader exhibits laterality bias, as evidenced by left versus right difference in recall, and b) among reports recommending recall, what an appropriate range of bilateral versus unilateral recall recommendations should be.

Methods: Five radiologists' screening mammography reports over two years at an academically affiliated, county hospital were tallied regarding laterality of recommended recall, and with respect to unilateral versus bilateral recalls advised. The chi-square (χ^2) statistic was applied to reports advising unilateral recall.

Result: Although as a group, no laterality bias was discovered, one radiologist evidenced a consistent bias over two years against left-breast findings, with a χ^2 p value of 0.07. Of reports recommending recall, the radiologists' annual range of portions that were bilateral was 10.2% to 23.3%; for the two years combined, the individual radiologists ranged from 13.6 to 17.9%. The group, two-year mean was 15.8%.

Conclusions: Laterality bias may exist in some screening mammogram readers, with many potential causes. Tendency to advise bilateral recall may reflect reader confidence level, experience level, and availability of prior exams with which to compare. How far unilateral recall recommendations may with high quality diverge from 50–50, left versus right, and what a high-quality range of bilateral (versus unilateral) recalls is, both have the potential to become valuable, quality metrics in screening mammography, and should be studied in a large group of radiologists.

IDENTIFYING THE MASQUERADING LESION- SONOGRAPHIC FEATURES OF TRIPLE NEGATIVE BREAST CANCERS

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Background: Triple-negative breast cancer (TNBC) is well known for its aggressive tumour behaviour, higher potential for distant metastases and recurrence. Meanwhile, they tend to exhibit benign imaging features which may offer false reassurance on imaging. Our study aims to identify distinguishing sonographic features of TNBC compared to non-TNBC based on features described in American College of Radiology Breast Imaging Reporting and Data System sonographic classification system.

Methods: This is a retrospective study. Sonographic images from 50 triple negative breast cancer (TNBC) and 52 non-TNBC, diagnosed during the period of 2016 to 2020 were reviewed by two reviewers simultaneously according to the 5th edition of Breast Imaging Reporting and Data System and result was reached by consensus.

Result: Triple-negative breast cancers were associated with higher tumour grades ($p < 0.001$), higher tumour (T) stage and larger tumour size ($p < 0.001$). They had higher incidence of the following features: oval or round in shape ($p = 0.006$), microlobulated in margin ($p = 0.006$), parallel in orientation ($p = 0.001$), presence of posterior acoustic enhancement ($p = 0.007$) and less architectural distortion ($p < 0.001$) when compared to non-TNBC.

Conclusions: Triple negative breast cancers (TNBC) have their own distinct sonographic features allowing them to be distinguished from their non-TNBC counterparts. These features are also commonly seen in benign pathologies such as fibroadenoma. Radiologists should remain alert when these commonly reassuring features are encountered on sonography in order to reach an early diagnosis of these aggressive tumours.

KNOWING THE FRAUD-PICTORIAL REVIEW OF BREAST CANCER MIMICS

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Background: A number of benign pathologies share imaging appearances of breast cancers, which cause diagnostic confusion and uncertainty when formulating treatment plan. This pictorial review aims to illustrate the range of breast mimickers and raise our awareness to prepare better for the discussion we may encounter in multidisciplinary breast meetings.

Methods: Images of breast mimicking conditions are retrieved from the institute's database (Prince of Wales Hospital, a local tertiary referring centre in Hong Kong) for review and discussion.

Result: Illustration of imaging findings of breast fibromatosis, granulomatous mastitis, diabetic mastopathy, lymphocytic mastopathy, fat necrosis, harmatoma, tubular adenoma, and pseudoangiomatous hyperplasia.

Conclusions: Awareness of the wide range of breast cancer mimics is required for optimal management (and avoid overtreatment) of patients presenting with breast lesions exhibiting malignant imaging features.

IS BREAST SCREENING NECESSARY BEFORE COSMETIC BREAST SURGERY?

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Background: Pre-operative breast screening is not a mandatory procedure for patients planning for a cosmetic breast surgery. Our study is to find out the necessity of breast screening prior to first or multiple cosmetic breast surgery.

Methods: Breast screening was done with consent including 542 women who visited a plastic surgery clinic for a cosmetic breast surgery during March 2017 to February 2019. Digital mammogram (MG) and high-resolution ultrasonography (HRUS) were done along with clinical examination.

Result: Total of 542 women were studied. Age ranged from 19 to 64 years old (median 28.9) and 498(92%) women were first timer for screening. All patients had MG and HRUS done. After HRUS, 123(22.7%) were found with abnormalities; Two (0.36%) patients were recommended for biopsy prior to cosmetic surgery, 55(10.1%) had biopsy done on the same day of cosmetic surgery. Core needle biopsy (CNB) was done on 24(4.4%), vacuum-assisted breast biopsy (VABB) was done on 15(2.8%), and excisional biopsy (EB) 7(1.3%). Thirty-four (6.3%) CNB, 15(2.8%) VABB, 8(1.47%) were done. Pathology showed 10(1.8%) fibrocystic change disease, 31(5.7%) fibroadenoma, 13(2.4%) fat necrosis, 1(0.2%) sclerosing adenoma, 1(0.2%) atypical ductal hyperplasia (ADH), 1(0.2%) invasive ductal carcinoma (IDC).

Conclusions: Even young women should be recommended for a breast screening before cosmetic surgery, especially if the patient has a family history of breast cancer. Women should highly consider a breast checkup at least using HRUS prior to breast cosmetic surgery for better management plans. Breast surgeon and plastic surgeon should have full cooperation of breast surgery considering both cosmesis and breast health management.

EFFECT OF CORONA VACCINE ON LYMPHADENOPATHY IN FOLLOW-UP PATIENTS AFTER BREAST CANCER SURGERY

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Background: The coronavirus disease 2019 (COVID-19) pandemic still affects many people worldwide, prompting urgent needs for effective vaccinations. Axillary lymph node recurrence is an important issue for patients undergoing follow-up after breast cancer treatment. The purpose of this study was to investigate the occurrence and characteristics of lymphadenopathy caused by the corona vaccine in these patients.

Methods: This study was conducted as a retrospective study, and the subjects were patients undergoing breast cancer treatment and follow-up at Department of Breast Surgery, Kosin University Gospel Hospital in accordance with the recommendations of the Korean Breast Association. 113 patients receiving up to two doses of Oxford-AstraZeneca (n = 44, 38.9%), Pfizer-BioN-Tech (n = 41, 36.3%), and Moderna (n = 28, 24.8%) vaccines were included. If lymphadenopathy occurred, chest CT was also checked.

Result: The number of patients with lymphadenopathy was 22 (19.5%), which was slightly higher than that reported after general corona vaccination (9-12%). There was no statistically significant difference in the incidence of lymphadenopathy according to the type of vaccine ($p = 0.137$). A statistical significance was found in the occurrence of lymphadenopathy according to the breast ($p = 0.004$) and axillary ($p = 0.014$) operation type. This is probably because problems related to systemic lymph nodes occur as the scope of operation increases, however, more in-depth research is needed.

Conclusions: The lymphadenopathy that occurs after corona inoculation is a new image interpretation conflict from the point of view of the medical staff monitoring the recurrence breast cancer of lymph nodes. But lymphadenopathy occurs after corona vaccination did not show a serious pattern that could obscure recurrence.

ROLE OF CTDNA FOR PREDICTING TUMOR RESPONSE IN BREAST CANCER PATIENTS AFTER NEOADJUVANT CHEMOTHERAPY

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Background: Next-generation sequencing to detect circulating tumor DNA (ctDNA) is non-invasive method for tumor genotyping and monitoring therapeutic response. Aim of this study is to evaluate role of ctDNA for predicting tumor response after neoadjuvant chemotherapy (NAC) and detecting minimal residual disease after surgery in breast cancer patients.

Methods: From December 2019 to August 2020, we collected ctDNA samples from 60 breast cancer patients. Plasma was collected prior to the initiation of NAC and after end of NAC. Library preparation and target capture were done using a commercial kit and custom target gene panel (Dxome) consisting of 49 cancer genes.

Result: Twenty-two patients achieved pathologic complete response (pCR), 38 patients achieved non-pCR. Prior to the start of NAC, ctDNA was detectable in 17 patients who achieved pCR and 33 patients among non-pCR group. Prior to NAC, TP53 mutations were the most prevalent (36.4%) followed by MUC16 mutations (31.8%), and PIK3CA (3/22, 13.6%) among patient who achieved pCR. Other genes were also detected as follows (FAT1, KDR, CDH1, NF1, NOTCH1, ERBB2, ARID1A, PTEN, EGFR, BRCA2, ESR1, TSC2, ALK). After NAC, ctDNA was detectable in 20 patients who achieved pCR and 37 patients among non-pCR group. Patients with pCR experienced rapid declines in ctDNA levels, whereas non-pCR showed residual ctDNA .

Conclusions: ctDNA is a sensitive marker for monitoring tumor response to NAC. ctDNA detection achieved a 75% detection rate at baseline. During NAC, ctDNA levels decreased quickly among pCR patients. However, a slow decrease of ctDNA level during NAC was strongly associated with residual disease.

PSYCHOSOCIAL BARRIERS AND FACILITATORS FOR CASCADE GENETIC TESTING IN HEREDITARY BREAST AND OVARIAN CANCER: A SCOPING REVIEW

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Background: Despite increased awareness of BRCA 1/2 genetic testing and its clinical availability for over 20 years, there is still significant underuse of cascade genetic testing in HBOC. This study aimed to synthesize evidence systematically and comprehensively on psychosocial barriers and facilitators for CGT in HBOC patients and their families.

Methods: This scoping review employed the methodological framework of Arksey and O'Malley's as outlined in the Joanna Briggs Institute manual. We used search terms including 'hereditary breast and ovarian cancer', 'cascade genetic testing' (search period: 2012~2021). Through searching databases including Ovid MEDLINE, Ovid EMBASE, CINAHL, and PsycINFO, and manual search, 447 studies were identified after excluding duplications. Each article was reviewed by two researchers independently, starting with title, abstract, and full-text to decide on eligibility. Finally, 18 studies were included. CASP, RoBANS 2.0, RoB 2.0, and MMAT were used to assess the quality of included studies. Extracted data were analyzed using Braun and Clarke's framework for thematic mapping.

Result: This study identified 3 themes and 12 subthemes of psychosocial barriers and facilitators for CGT: 1) common concepts (information; family dynamic; closeness; perception of cancer risk and testing; emotions and attitude); 2) facilitators (family support; belief of health protection; decisional empowerment; the sense of responsibility; self-efficacy; supportive health professionals); 3) barriers (negative reactions from family).

Conclusions: Different from other health-related behaviors, CGT reveals the genetic health status of the family and so could be affected by various family characteristics. To promote CGT in HBOC, healthcare providers need to be aware of common psychosocial concepts, strengthen facilitators, eliminate barriers and also consider family characteristics carefully.

COMPARISON OF MARGIN ASSESSMENT BETWEEN DIGITAL AND CONVENTIONAL SPECIMEN MAMMOGRAPHY IN BREAST CANCER

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Background: For patients with microcalcification or nonpalpable lesions, a specimen mammography is performed to determine margin involvement. The purpose of this study was to assess the feasibility, safety, and benefits of intraoperative digital specimen mammography (IDSM).

Methods: We conducted prospective randomized studies in 98 patients who underwent breast-conserving surgery from October 2021 to January 2022. The specimens were imaged in the operating room using a digital specimen mammography, or transported to the radiology department and imaged with a conventional specimen mammography (CSM).

Result: A total of 101 specimen mammography were performed in 98 patients with breast cancer. Of 101 cases, 76 cases were ISDM and 25 cases were CSM. A mean radiation dose of ISDM was 1.2 mSV (standard deviation [SD]: ± 2.1] and CSM was 0.82 [SD: 1.1]. Difference between two groups were not statistically significant (p-value 0.372). A delivery time was significantly shorter for the ISDM compared to CSM (3.1 ± 4.5 vs. 7.1 ± 2.8, p-value < 0.001). With 25 KVP and 20 mAS, the best image quality of breast lesions was obtained.

Conclusions: The intraoperaetive digital specimen mammography is a safe method, has the same quality images and reduces delivery time associated with specimen transport, potentially reducing surgical duration.

A CASE OF EXTENSIVE FAT NECROSIS OF THE BREAST SECONDARY TO TISSUE ISCHEMIA FROM SEVERE CALCIFIC VASCULAR DISEASE

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Background: Fat necrosis of the breast is a benign inflammatory process leading to saponification of fat. The clinical picture can simulate many conditions including cancer.

Methods: We report a case of an atraumatic fat necrosis in the breast occurring in an end stage renal failure patient with chronic hypercalcaemia. We describe the clinical presentation, radiological images and pathological findings of this case.

Result: A 61 years old lady with a background history of diabetes mellitus, hypertension, dyslipidemia and end-stage renal failure complicated by hypercalcaemia presented with a painful left breast lump. This was not preceded by trauma or symptoms of inflammation. On physical examination, there was a 2 cm firm irregular lump over the left breast 12 o'clock position. Mammography showed bilateral prominent vascular calcifications with no discrete mass or asymmetric density. Ultrasound demonstrated a vague 29 mm heterogeneously hyperechoic mass-like area of tissue with non-discrete margins at the left breast 12 o'clock position. Core biopsy of the breast lesion showed features of patchy fat necrosis without evidence of malignancy. Follow-up ultrasound showed an increasing size of the left breast 12 o'clock lesion thus excision biopsy was performed. Histology showed extensive vascular calcification with occlusion, and secondary infarction of breast fat. No malignancy was found.

Conclusions: We report a rare case of extensive fat necrosis of the breast secondary to tissue ischemia from severe calcific vascular disease resulting from renal failure with hypercalcaemia.

THE BLOOD LEVEL OF THIOREDOXIN 1 AS A BIOMARKER FOR THE MONITORING OF BREAST CANCER PATIENTS UNDERWENT SURGERY

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Background: CA15-3, CA27-29, and CEA are currently being used as biomarkers in breast cancer. Their performance is not satisfactory due to the low correlation between the biomarker levels and the treated patient's status. We have reported that blood Thioredoxin1 (Trx1) could be a specific biomarker to detect BC. Therefore, it would be interesting to study if the blood Trx1 level has the potential to be a monitoring biomarker for BC patients.

Methods: This study was approved by the IRB of the Chungnam National University Hospital. The blood from 20 patients was collected before operation and at the designated time points after the surgery such as 6, 12, and 18 months. We performed an immunoassay to quantify serum Trx1 (DxMe BC kit). Analysis was retrospectively compared to those from clinical information and treatment.

Result: The Trx1 level from BC patients before surgery was 30.53 ± 10.09 ng/ml (± SD). The Trx1 levels from the patients at 6, 12, and 18 months after surgery were 10.66 ± 7.67 ng/ml, 10.2 ± 6.81 ng/ml, and 7.02 ± 3.60 ng/ml, respectively. In comparison, the CEA and CA15-3 levels did not show any noticeable changes. Furthermore, the Trx1 level after surgery was not affected by clinical aspects of BC or therapy. The clinical sensitivity and specificity between pre-and post-surgery were 90.00%, 91.67%.

Conclusions: The blood Trx1 level decreased dramatically after surgery and it is likely to depend on the presence or absence of a tumor mass. Consequently, the blood Trx1 level has the potential as a monitoring biomarker to aid in the management of BC patients after treatment.

SP142 PD-L1 ASSAYS IN MULTIPLE SAMPLES FROM SAME PATIENTS WITH TRIPLE-NEGATIVE BREAST CANCER

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Background: PD-L1 examinations are companion diagnostics for the use of immune check-points blockades (ICBs) including atezolizumab and pembrolizumab in metastatic triple-negative breast cancer (TNBC). Since presence of discernible PD-L1 staining of any intensity covering ≥ 1% of tumor-infiltrating lymphocytes is considered as SP142 PD-L1 positive for atezolizumab, PD-L1 status between multiple samples from a patient could be discrepant. In this study, we evaluated PD-L1 status by SP142 using serially collected multiple samples from the same individuals with early or metastatic TNBC.

Methods: SP142 PD-L1 assays were performed in biopsied and surgical specimens from 82 patients with early TNBC. Of these, 51 patients received upfront surgery, whereas 31 underwent neoadjuvant chemotherapy (NAC) between biopsy and surgery.

Result: In 51 with upfront surgery, 15 (29.4%) had PD-L1+ on biopsied samples. However, after surgery, PD-L1+ rates in either biopsied or surgical specimens was 64.7% (33 of 51). Similarly, in 31 who had residual invasive cancer after NAC, PD-L1+ rate increased from 38.7% at baseline to 74.2% at surgery ($p = 0.0098$). Consequently, in 82 with early TNBC, multiple PD-L1 tests using both biopsied and surgical specimen raised PD-L1+ rate significantly than single test using biopsied samples (67.4% vs. 32.6%; $p = 0.0016$).

Conclusions: Our findings display heterogeneity of SP142 PD-L1 expression and lack of representativeness of biopsied samples in addressing PD-L1 status. Vigorous PD-L1 examination using available and multiple archived tumor samples may offer more opportunities for the use of ICBs for patients with TNBC.

EVALUATION OF TUMOR-DERIVED MICRO RNA SIGNATURE IN EXTRACELLULAR VESICLES FOR PREDICTING RELAPSE AND PROGNOSIS IN BREAST CANCER PATIENTS

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Background: Operable breast cancer (BC) shows good prognosis compared to other types of cancer, especially when the disease is identified at an initial stage and remains no residual tumors after surgery. Therefore, there is an obvious need to discover novel diagnostic biomarkers before BC reaches the incurable stage. This study aimed to identify optimal microRNA (miRNA) signatures to predict existence of BC through liquid biopsy.

Methods: Candidate miRNAs in BC-derived extracellular vesicles (BEVs) were selected from TCGA public datasets and previous exploratory study using plasma samples from a total of 82 individuals. In this study, quantitative real-time PCR (RT-qPCR) was used to validate miRNA expression profiles in BEVs obtained from plasma samples of 200 individuals, including normal controls, BC patients, and BC patients with recurrence.

Result: We isolated BEVs by immuno-capture using magnetic beads labeled with antibodies against EpCAM, CD49b, and CD51. Among thirteen candidate miRNAs, four differentially expressed miRNAs were markedly higher in BEVs. The multi-miRNA biomarker panel was optimized through logistic regression to establish a miRNA signature model that could predict the recurrence of BC with a high sensitivity and specificity. Furthermore, the miRNA signature also showed a differential expression scores between BC patients with better and worse prognoses.

Conclusions: In summary, the evaluation of differently expressed miRNAs in BEVs using plasma samples is valuable for detecting the minimal residual cancer that may be missed on imaging examinations, which can help predict recurrence. In clinical practice, the results showed that four miRNAs were significantly associated with prognosis in BC patients.

UNMASKING THE ELUSIVE MUCINOUS BREAST CANCERS: AN OFTEN UNDERDIAGNOSED CANCER

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Background: Mucinous Breast Cancers are a rare subtype of Breast Cancer, with favourable prognosis. It is usually radiologically well circumscribed, which leads to a possible delayed diagnosis and treatment. In addition, Mixed Mucinous Carcinomas (MMCs) and micropapillary subtypes may have more aggressive features and poorer prognosis.

Methods: Retrospective review of our prospective Breast Cancer Database, including all histologically proven mucinous Breast Cancers from March 2000 to Dec 2020. Radiological factors were analysed. Univariate and Multivariate analyses to assess factors that influence earlier biopsy of benign-looking lesions.

Result: We analysed 322 patients with Mucinous Breast Cancer. Of all the patients, 83.7% did not present with any asymmetry on mammogram. 15.0% of the patients were BIRADS 3 or less. Of these, 70.2% were symptomatic, with 29.8% picked up radiologically. There was a delay in diagnosis in 50% of the above cases. In particular, one case was only biopsied after the 7th imaging study. There was no difference in OS between those classified as BIRADS 1-3 compared to BIRADS 4-6.

Conclusions: In this large cohort or Mucinous Breast Cancers, 1 in 6 did not have any suspicious findings on initial assessment. Delay in diagnosis occurred in 50% of the cases. We could not identify any patient nor tumour factors that may influence the decision to obtain early histological diagnosis.

EVALUATION OF THE USEFULNESS OF THREE PROTEIN SIGNATURES (MASTOCHECK) IN FOLLOW-UP AFTER BREAST CANCER SURGERY

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Background: We developed three protein signatures (Mastocheck) for early diagnosis of breast cancer in a previous study. The purpose of this study is to evaluate whether the developed protein marker is useful for postoperative follow-up.

Methods: Patients were enrolled in prospective manner, and 111 patients were analyzed finally. All patients underwent blood test before surgery, 8 weeks after, and 6 months or 1 year after surgery. Of these, 53 patients underwent serial follow-up tests for one year after surgery from preoperative test. Changes in protein biomarkers were analyzed by period before and after surgery. Clinicopathological information was analyzed, and whether there was a significant correlation with changes in biomarkers was evaluated.

Result: A total of 111 patients were analyzed. 105 patients were followed up for an average of 8 weeks after surgery, and 53 patients were followed up for 6 months to 1 year after surgery. In the preoperative test, the diagnostic sensitivity of the biomarker was 73.0%. After 8 weeks of surgery, blood level of the biomarker were normalized in 67.6% of patients, and 86.8% were normalized in 6 months to 1 year follow-up after surgery. Similarly, the data of 53 patients measured serially showed that the sensitivity of preoperative tests was 73.6% and the accuracy of normalization in postoperative follow-up tests was 86.8%.

Conclusions: Blood protein signatures (Mastocheck) developed for early breast cancer diagnosis are normalized over time after surgery. Therefore, this is biological monitoring and could also be used for follow-up test after breast cancer surgery.

MANAGEMENT OF NON-PALPABLE LESIONS OF THE BREAST- CLINICO-RADIO-PATHOLOGICAL CORRELATION OF SONO-LOCALIZED EXCISION BIOPSIES- RETROSPECTIVE ANALYSIS

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Background: A thorough evaluation of breast imaging is necessary prior to planning breast conservation surgery in the routine diagnostic setting as well as in screening and follow-up setting. Non-palpable lesions need image guided biopsy depending on the index of radiological suspicion as assigned by the BIRADS reporting. We routinely sono-localize these lesions followed by excision biopsy other than offering USG guided trucut biopsy. We evaluated the outcome of such localization and open excision biopsy with respect to their BIRADS category to understand the yield of such minor surgical procedures.

Methods: We retrospectively analyzed the prospectively kept data of 520 patients who had an open biopsy for non-palpable lesions after ultrasound localization. We correlated the BIRADS category with the final histopathology report.

Result: Out of 520 patients, 393 had biopsy in the upfront diagnostic setting, 120 in the follow-up setting and 7 in the setting of benign breast diseases. The BIRADS category was 3, 4a, 4b and 4c in 51 (9.8%), 251 (48.3%), 123 (23.7%) and 95 (18.3%) patients respectively. Out of the 51 BIRADS 3 lesions, 100% were benign on histopathology. Whereas the incidence of malignancy was 7.5% (19/251), 32.5% (40/123) and 62.1% (59/95) for BIRADS 4a, 4b and 4c lesions respectively. The incidence of phyllodes tumors was 14/469 (2.9%) among all the BIRADS4 lesions.

Conclusions: We demonstrate a 100% specificity and NPV for B3 lesions which may be observed without a tissue diagnosis. Whereas the incidence of malignancy in other B4 lesions is in concordance with the world literature.

PATTERNS OF BREAST CANCER SECOND RECURRENCES IN PATIENTS AFTER MASTECTOMY

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Background: Little is known about second recurrences in breast cancer patients, especially in patients with mastectomy. We aimed to determine the incidence, patterns and timing of second recurrence in patients with mastectomy after their first recurrence.

Methods: Non stage IV breast cancer patients treated at a tertiary institution from 1st September 2005-31st October 2017 and developed first and second recurrences after mastectomy were retrospectively reviewed. We excluded patients with bilateral cancers and patients who were lost to follow-up. The demographics, pathological and recurrence data were collected from a prospectively maintained database and analysed.

Result: Of the 1841 mastectomy patients treated, 217 (11.8%) patients developed recurrences at a mean 39.8 months from first cancer diagnosis. 24, 8 and 185 had isolated chest wall recurrences (CWR), nodal and distant metastases respectively. Excluding 2 patients with CWR without surgery, second recurrences occurred in 3/22 (13.6%) and 3/8 (37.5%) in patients with CWR and nodal metastasis at 27.7 months (range: 5-42) and 32 months (range: 18-40) respectively. In both groups of patients, distant metastasis as second recurrence occurred within the 2 years after first recurrence while locoregional second recurrences occurred later.

Conclusions: In patients with mastectomy, second recurrences occurred in 20% of patients with locoregional first recurrence. Distant metastases manifesting as second recurrence occurred in the 2 year after first recurrence diagnosis. Restaging patients with second recurrences in their first 2 year of diagnosis could enable early prognostication and treatment of these metastatic patients with the newer treatments available in the metastatic setting to improve survival.

DEVELOPMENT OF GRANULOMATOUS MASTITIS IN A MALE BREAST AFTER COVID-19 VACCINATION

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Background: Idiopathic granulomatous mastitis (IGM) is a benign chronic inflammatory disorder of the breast tissue, with unknown etiology. IGM is extremely rare among the male gender. We described a rare case of idiopathic granulomatous mastitis in the male breast after coronavirus (COVID-19) vaccination.

Methods: A 28-year-old male patient presented with pain on the left shoulder, after COVID-19 vaccination on his left upper arm. One month after the COVID-19 vaccination, he presented a hard, painful mass in his left breast. His symptoms were not improved despite several surgical procedures and empirical antibiotics in the local clinic and he was referred to our hospital.

Result: Histopathology revealed gynecomastia with granulomatous mastitis from the excised specimen. The tissue was cultured and no microorganisms were identified. His symptom was improved after corticosteroid medication for 2 months without additional surgical procedure.

Conclusions: Granulomatous mastitis is extremely rare in male breast tissue. We reported a case of male granulomatous mastitis that may be related to COVID-19 and it was improved by corticosteroid medication.

ONCOLOGIC NECESSITY FOR COMPLETE REMOVAL OF RESIDUAL MICROCALCIFICATION AFTER NEOADJUVANT CHEMOTHERAPY IN BREAST CANCER

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Background: The authors evaluated the viability of cancer cells around the residual microcalcification in the case, which shows an obvious primary tumor shrinkage, but rarely changed the extent of microcalcification to confirm the necessity of mastectomy.

Methods: A total of 144 cases of locally advanced breast cancer with diffuse microcalcification were included. Although the mass had decreased enough to reduce the excision volume of breast, mastectomy had been needed due to the remained diffuse microcalcification. With the retrospective review, the breast specimen from five consecutive cases with the same condition were prospectively evaluated. The obtained breast specimens were sliced with 1 cm-intervals by a pathologist, and specimen mammography was performed with many pieces of breast specimen under the serial arrangement. Afterward, the pathologist confirmed the cancer cell viability of the residual microcalcifications observed in the specimen mammography.

Result: The incidence of the cases that the mastectomy was still needed after NAC due to still remaining diffuse microcalcification, even if the tumor size had decreased, were 49 cases (34.0%). In the prospective study, three cases (60%) showed pCR and the remained invasive carcinoma was less than 0.5 cm. However, there were the residual lesions with ductal carcinoma in situ around the microcalcification in every 5 cases (upto 3.8 cm).

Conclusions: Although invasive carcinomas were very small in size, there was ductal carcinoma in situ lesions around the diffuse microcalcification in every prospective case. Therefore, if the diffuse microcalcification remains after NAC, the complete removal of microcalcification would be necessary, even if the mass is almost disappeared after NAC.

SINGLE INCISION LATISSIMUS DORSI FLAP IN ROBOT ASSISTED MASTECTOMY WITH IMMEDIATE BREAST RECONSTRUCTION: A REPORT OF THREE CASES

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Background: Mastectomy using robot has preferred surgical approach for creating a precise, small incision. Although the latissimus dorsi flap technique is the only safe option for breast reconstruction after robot-assisted mastectomy. It is difficult to obtain sufficient tissue volume. This case aimed to report a reconstruction method that modified the extended latissimus dorsi flap design considering scar visibility and introduce a single-incision technique in three cases. This technique allows surgeons to design a latissimus dorsi flap as an extension of a robot-assisted mastectomy incision to prevent scar formation on the breast mound and perform breast reconstruction using autologous tissue to create a single scar.

Methods: Three patients who underwent surgery using a single incision technique that was modified by designing an extended latissimus dorsi flap as an extension of robot-assisted mastectomy incision, which formed no scar on the breast mound. We evaluated patient satisfaction, complications, and flap weight.

Result: The latissimus dorsi flap, which was initially created for robot-assisted mastectomy, was designed as an extension of the incision. Consequently, only a single scar was formed. Although the scar may be relatively long, this design does not require the use of an implant and can be covered by linings of underwear and the patient's arms.

Conclusions: Preparation for breast reconstruction that is tailored to an individual patient, if a patient who choose robot-assisted mastectomy to avoid scar on their breast mound specifically wants breast reconstruction using autologous tissue, the single incision latissimus dorsi flap is deemed as a useful modification that could complete both procedures.

ROBOTIC NIPPLE SPARING MASTECTOMY IN THE MANAGEMENT OF BREAST CANCER AND PROPHYLACTIC SURGERIES WITH SP SYSTEM

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Background: Robot-assisted nipple-sparing mastectomy (R-NSM) improves cosmetic outcomes over conventional nipple-sparing mastectomy (CNSM). However, data on the feasibility and safety of the R-NSM are limited. The aim of this study was to present the results of an early experience of R-NSM with the SP system.

Methods: Preliminary analysis of R-NSM using da Vinci SP system for breast cancer and prophylactic cases during the period October 2020 thru September 2021 from Asan Medical Center, Seoul, S Korea. Data on clinicopathologic characteristics, type of surgery, method of breast reconstruction, complications, and recurrence were analyzed to determine the performance and safety of R-NSM using the da Vinci SP system.

Result: During the period October 2020 thru September 2021, a total of 86 robotic breast surgery procedures were performed in 81 female patients with breast cancer (78 invasive, 8 non-invasive), and 2 patients who underwent surgery for prophylactic reasons. Five patients were bilateral, and 81 were unilateral. Immediate breast reconstruction (IBR) was performed in all patients. Autologous reconstruction was performed in 44 cases, and implants were used in 42 cases.

Conclusions: From our preliminary experience, R-NSM alone or combined with IBR is a safe procedure, with clinical outcomes results, and is promising new technology for breast cancer patients indicated for mastectomy.

THE ROLE OF PRE-OPERATIVE AXILLARY ULTRASOUND IN ASSESSMENT OF AXILLARY TUMOR BURDEN IN BREAST CANCER PATIENTS: A SYSTEMATIC REVIEW AND META-ANALYSIS

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Background: Recent studies have suggested that a significant proportion of patients with axillary nodal metastases diagnosed by pre-operative axillary ultrasound (AUS) guided needle biopsy was over-treated with axillary lymph node dissection (ALND). The role of routine AUS and needle biopsy in early breast cancer was questioned. This review aims to determine if pre-operative AUS could predict the extent of axillary tumor burden and the need for ALND.

Methods: PubMed and Embase literature databases were searched systematically for abnormal AUS characteristics and axillary nodal burden. Studies were eligible if they correlated the sonographic abnormalities in AUS with the resultant axillary nodal burden in ALND according to the ACOSOG Z0011 criteria.

Result: Eleven retrospective studies and one prospective study with 1658 patients were included. Sixty-five percent of patients with one abnormal lymph node in AUS and 56% of those with two had a low axillary nodal burden. Using one abnormal lymph node as the cut-off, the pooled sensitivity and specificity in prediction of axillary nodal burden were 66% (95% CI 63-69%) and 73% (95% CI 70-76%), respectively. Across the six studies that evaluated suspicious nodal characteristics, the increased nodal cortical thickness may be associated with high axillary nodal burden.

Conclusions: More than half of the patients with pre-operative positive AUS and biopsy-proven axillary nodal metastases were over-treated by ALND. Quantification of suspicious nodes and extent of cortical morphological changes in AUS may help identify suitable patients for sentinel lymph node biopsy.

DIFFERENT TYPES OF THE AXILLARY ACCESSORY BREAST

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Background: Accessory breast is defined as residual breast tissue that persists from normal embryologic development, common occurring in 2~6% women. It is most commonly located in the axilla. Different types of accessory breasts have their own characteristics and their surgical correction also varies depending on their types.

Methods: One thousand and forty-two patients who have been treated with accessory breast tissue from September 2017 to October 2021 at the Spring Day Clinic were analyzed retrospectively to its type (Spring Day Clinic's classification). Accessory breast excision and liposuction were performed on all cases by a single surgeon (Dr. Hwang).

Result: According to SDC's classification, type I was observed in 35.5% (361 patients), type II in 51.3% (534 patients), type III in 7.2% (82 patients), and type IV in 6.2% (65 patients) of all accessory breast patients. The mean amount of mammary tissue and liposuction was observed to increase depending on types except type IV. Higher grades of accessory breasts were more observed in married than in unmarried patients. Skin redundancy after surgery was more observed in high grade of accessory breast and married patients. Unlike other types, type IV of accessory breast did not differ between the married group and the unmarried group.

Conclusions: Accessory breast is natural tissue that grows and degrades according to hormonal changes and can be classified according to its shape. We can help patients with accessory breast by solving aesthetic problems and its cyclic pain through selective removal of the accessory breast according to its type.

VARIOUS TYPES OF GYNECOMASTIA SURGERY

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Background: Gynecomastia (GM) is a common condition that occurs in men at all ages. Patient with gynecomastia often present suffering from cosmetic and psychological problems. Only surgical treatment plays a very critical role in the treatment of gynecomastia. Since patients with gynecomastia have different characteristics and types from patient to patient, it is difficult to perform surgical correction in one way.

Methods: A thousand and four hundred patients who have been treated with gynecomastia from September 2017 to October 2021 at the Spring Day Clinic were classified into surgical methods according to their types of gynecomastia.

Result: The mean age was 26.3 years and the most frequent age group in gynecomastia patients was the twenties (53.6%). According to Simon's classification, there were 196 patients (14.0%) in type I, 1008 patients (72.0%) in type IIA, 186 patients (13.3%) in type IIB, and 10 patients (0.7%) in type III. According to a surgical method, there were 10 patients in liposuction only, 1370 patients in liposuction plus superficial mastectomy, 17 patients in staged operation, and 3 patients in total mastectomy using IMF with nipple-areolar complex free graft. It was found that the higher the Simoon's grade rating, the higher the tendency to require skin resection.

Conclusions: As society develops and economic prosperity makes people consider more of the aesthetic importance, proper treatment of gynecomastia can significantly help men's lives. Therefore, it is important to understand various methods of gynecomastia surgery and perform surgery tailored to each patient's characteristics.

ROBOT-ASSISTED BREAST CONSERVING SURGERY FOR EARLY BREAST CANCER PATIENTS

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Background: A traditional breast-conserving surgery (BCS) operation inevitably results in an external scar on the breast and axilla. Various attempts, including endoscopy-assisted breast surgery, has been successfully and reproducibly performed for improved cosmetic outcome. In an attempt to maximize esthetic effects, we performed robot-assisted BCS through an only axillary incision.

Methods: From Jan. 2021 to Dec. 2021, fifteen female patients underwent robot-assisted BCS. All patients underwent robot-assisted BCS with or without sentinel lymph node biopsy (SLNBx.) only a 2.5 cm axillary incision. All surgical procedures were performed in concordance with traditional BCS operations. Data on patient demographics, type of surgery, hospital stay, complications, and short-term postoperative outcomes were reviewed.

Result: Mean patient age was 53.7 ± 6.35 years, and mean tumor size was 1.6 ± 2.1 cm. Indications included in situ cancer in 7 cases and invasive cancer in 8 cases. Three patients underwent only BCS, and twelve patients underwent BCS+SLNBx. Two patients underwent axillary lymph node dissection. The mean operation time was 165.5 ± 8.2 minutes, and the mean hospital stay was 6.4 ± 5.3 days. No open conversion case was observed. One seroma with infection occurred postoperatively, and I & D performed. Two skin burn events during the operation occurred, and scar revision was performed. The operative scars the axilla became inconspicuous in a few weeks.

Conclusions: Our initial results show that robot-assisted BCS would be technically feasible, safe, and effective. This new technique can be a good alternative surgical option for BCS in early breast cancer patients.

PATIENT-REPORTED COSMETIC SATISFACTION AND DECISION REGRET AFTER BREAST CONSERVATION OR MASTECTOMY IN OLDER CHINESE BREAST CANCER PATIENTS

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Background: Few studies have investigated the optimal surgical management in older breast cancer patients, with many older patients opting for a mastectomy for simplicity's sake. The aim of this study was to compare the patient-reported cosmetic satisfaction and decision regret between breast-conserving surgery (BCS) and mastectomy in older Chinese patients.

Methods: Female Chinese patients equal to or older than 70 years of age at breast cancer diagnosis were recruited prospectively between September 2019 to June 2021. A questionnaire was administered to patients who were eligible for a BCS or mastectomy. Satisfaction of breast cosmesis was measured preoperatively and postoperatively at six months with the Chinese version of the BREAST-Q survey. Decision regret was characterized by the Decision Regret Scale at six months after the operation.

Result: Six-four patients were recruited, and fifty-six patients completed the questionnaires (participation rate 87.5%). Forty-three patients had a mastectomy (76.8%) and thirteen patients had BCS (23.2%). Patients who received a mastectomy were found to be less satisfied with the cosmetic outcome of their breasts at six months after the operation (BREAST-Q mean scores pre-op 71.61 vs. post-op 56.63, $p = 0.041$). Satisfaction of breast cosmesis remained similar in the group of patients who received a BCS ($p = 0.746$). Neither group demonstrated regret in their decision-making of the operation option ($p = 0.487$).

Conclusions: Elderly patients can show significant dissatisfaction with the cosmetic outcome after a mastectomy. It is crucial to engage the patients in discussion of surgical options to make an informed decision.

EFFECT OF TOPICAL TRANEXAMIC ACID ON SEROMA FORMATION IN A RAT MASTECTOMY MODEL

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Background: Seroma is the most common complication after mastectomy and reconstruction surgery, causing patient discomfort. Tranexamic acid is effective in reducing postoperative bleeding through intravenous and topical administration. The purpose of this study was to demonstrate the usefulness of the topical application of tranexamic acid to reduce seroma through a rat mastectomy model.

Methods: 48 SD rats were divided into four groups. After mastectomy and axillary lymph node dissection, 0.4 ml of normal saline was given to Group A in the dead space. In Group B, 0.4 ml of triamcinolone mixed solution was given. In Group C, 0.4 ml of tranexamic acid (10 mg/kg) mixed solution was given. In Group D, 0.4 ml of tranexamic acid (50 mg/kg) mixed solution was given. After conducting surgery, gross examination, assessment with micro CT and aspiration, and histopathologic assessment were implemented after 7, 14 days.

Result: No other complications were observed, such as wound infection and skin necrosis. In postoperative week 1, the volume of seroma in micro CT analysis and aspiration was checked in the order of Group A, D, C, and B. Group B and C showed statistically significantly lower values compared to Group A. In histopathologic analysis, the inflammation were observed more frequently in Group A, D and angiogenesis was more active in Group B, C.

Conclusions: In this study, topical application of tranexamic acid was as effective as compared to topical application of triamcinolone to prevent seroma. In addition, the stability of tranexamic acid was confirmed when a relatively high-dose of tranexamic acid was used.

SURGICAL OUTCOMES OF THE BREAST PHYLLODES TUMORS: ARETROSPECTIVE ANALYSIS OF 76 CASES

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Background: The recommended standard treatment for phyllodes tumor is extensive local resection, regardless of the tendency of malignancy. If positive, less recurrence and higher malignancy are likely to lead to better recurrence, but it is not well known about the criteria for how much ablation should be secured or the tendency to recur after incomplete ablation. We aimed to analyze the actual recurrence rate was sought to reduce over-treatment by resection surgery with little chance of recurrence.

Methods: All patients who underwent surgical resection for initially diagnosed with breast phyllodes tumor with all subtypes (benign, borderline and malignant) between August 2013 and September 2020 at our institution were included. In cases of phyllodes tumor recurrence, history of breast cancer, or postoperative follow-up loss were excluded.

Result: A total of 76 female patients were included with breast phyllodes tumors, of which 43 were benign, 29 borderlines, and four malignant. 67 wide excisions and nine mastectomies were performed. The tumor margin was 40 negative, 16 close (< 0.1 cm) and 20 positives. During a median follow-up of 30 months, local recurrence occurred in seven patients with a median time to recurrence of 36 months. The initial pathology was three benign, two borderline, and two malignant.

Conclusions: It reconfirmed that a wide resection is the only treatment of choice for all subtypes of phyllodes tumor. However, the lower the malignancy, the more likely it could have a chance to determine the timing of the re-operation by wait-and-see, even if the negative margin was not obtained in the first surgery.

ADJUVANT ENDOCRINE THERAPY COMBINED WITH ABEMACICLIB IN MONARCHE PATIENTS WITH HIGH-RISK EARLY BREAST CANCER: DISEASE CHARACTERISTICS AND ENDOCRINE THERAPY CHOICE BY MENOPAUSAL STATUS

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Background: MonarchE demonstrated that adjuvant abemaciclib, oral CDK4 & 6 inhibitor+endocrine therapy (ET) significantly improved invasive disease-free survival in HR+, HER2- high-risk early breast cancer (EBC) versus ET-alone. As prescribing practices for ET vary in younger patients, we present disease characteristics and ET choice in premenopausal patients (preM) enrolled in monarchE.

Methods: Patients with invasive, resected, HR+, HER2- node-positive, high-risk, EBC were randomly assigned 1:1 to adjuvant ET +/- abemaciclib in monarchE. Disease characteristics, prior chemotherapy, and ET patterns were examined by menopausal status at initial diagnosis: preM and postmenopausal patients (postM). ET choices for preM are further described by age.

Result: Of the 5637 patients, 43.5%/56.5% were preM/postM, with an even distribution between both arms. Median age for preM/postM was 44/59 years (y); 31.5% preM were ≤ 40 y. PreM had larger tumor size (abemaciclib+ET/ET-alone [N = 1227/1224]; ≥ 5 cm = 21/21%) vs postM (abemaciclib+ET/ET-alone [N = 1576/1605] = 15/14%). PreM had higher rates of neoadjuvant chemotherapy administration (abemaciclib+ET/ET-alone = 42/42%) vs postM (32/32%). Aromatase inhibitor (AI) use was higher in postM (abemaciclib+ET/ET-alone = 90/89%) vs preM (43/40%); tamoxifen use was higher in preM (57/59%) vs postM (10/11%). Among preM, AI use was highest in preM ≤ 40 y in both arms (abemaciclib+ET = 49.9%/ET = 49.4%) and tamoxifen use was highest in preM > 40 y to ≤ 50 y in both abemaciclib+ET (60.1%) and ET arms (65.0%).

Conclusions: PreM had larger tumors at baseline and were more likely to have received neoadjuvant chemotherapy, suggesting they may have a higher risk of recurrence than PostM. Previously presented at ESMO Congress 2021, "FPN (Final Publication Number):153P", "Shani Paluch-Shimon et al."- Reused with permission.

THE EFFICIACY AND SATETY OF INDOCYANIN GREEN-HYALURONIC ACID MIXURE FOR LOCALIZATION IN PATIENTS WITH NON-PALPABLE BREAST LESIONS: MULTICENTER, RANDOMIZED, OPEN-LABEL, PARALLEL PHASE 3 CLINICAL TRIAL

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Background: Early detection of tumor is increasing because of the popularization of breast cancer screening and the development of imaging techniques. As a result, suitable preoperative localization for non-palpable breast lesions is required for accurate diagnosis and treatment. This study aimed to evaluate the efficacy and safety of indocyanine green (ICG) for localization compared to charcoal, which is widely used.

Methods: This is a multicenter, randomized, open-label, parallel phase 3 clinical trial done at 4 centers in Korea. Female patients scheduled for surgery to remove non-palpable breast lesions were enrolled. One hundred nine patients were randomly assigned to the control group (charcoal 0.3~1 mL) or study group (ICG-hyaluronic acid mixture 0.2 mL).

Result: A total of 104 patients were eligible for per-protocol analysis (Control Group = 51, Study Group = 53). The accuracy of resection of resection was not inferior to the control group in the study group (86.79% vs 100%, 95% CI, 4.6-25.6, $p = 0.01$). There was no statistically significant difference between the two groups in the technical success rates (marking on breast; $p = 0.11$, marking on excised specimen; $p = 0.12$), and re-operation rate ($p = 1.00$). There was statistically significant difference in the histopathological accuracy (0.26 ± 0.13 vs 0.33 ± 0.17, $p = 0.01$) and the skin pigmentation rate (0.00% vs 30.77%, $p < 0.01$). There were no serious adverse events reported in either group.

Conclusions: When localization was performed using ICG, the accuracy on resection was not inferior to that of charcoal, although the resection area was smaller, and the skin pigmentation rate was significantly lower. In conclusion, ICG is effective and safe for the localization of non-palpable breast lesions.

A CASE OF BREAST CANCER IN BREAST AUGMENTATION BY INJECTING FREE LIQUID SILICONE

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Background: Breast augmentation surgery with an injection of free liquid silicone has been performed from the early 1960s but was abandoned by most practitioners because numerous complications have been reported, such as migration of silicone to other parts of the body, inflammation, discoloration, and the formation of granulomas, ulceration and fistulae, anaplastic large cell lymphoma, Silicone-Induced Granuloma, breast carcinoma.

Methods: In this case report, we describe an invasive breast carcinoma, diagnosed via core needle biopsy, in breast augmentation by injecting free liquid silicone ten years ago, including breast imaging findings on mammography and MRI, macroscopic and microscopic features.

Result: The nipple-sparing mastectomy was performed for two breasts that were injected with liquid silicone. In the right breast with adenocarcinoma, surgical margins above nipple-areolar were assessed intra-operatively by frozen section before immediate breast reconstruction was carried out in the same operation. TRAM flap procedure reconstructed for right breast and implant breast reconstruction for the left breast.

Conclusions: We received amazing post-operative results.

REAPPRAISAL OF ADEQUATE NEGATIVE MARGIN AFTER BREAST CONSERVING THERAPY IN YOUNG PATIENTS WITH INVASIVE BREAST CANCER

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Background: The current definition of adequate negative margin is "no ink on tumor". However, this definition is not validated in young patients with invasive breast cancer (IBC) because of a lack of evidence. This study examined the impact of resection margin width on ipsilateral breast tumor recurrence (IBTR) in young patients (< 40 years).

Methods: We analyzed 4,042 patients (median age, 48 years) with IBC who underwent breast-conserving therapy (partial mastectomy followed by whole breast irradiation and tumor bed boost) between 2006 and 2012. The impact of resection margin width was assessed by specified intervals (positive, < 1 mm, 1- < 2 mm, 2- < 3 mm, ≥ 3 mm). Most of the patients (98.0%) received systemic treatments.

Result: During the median follow-up period of 83 months, the 10-year estimated cumulative incidence of IBTR was 3.4% in all patients. The cumulative incidence of IBTR significantly decreased as resection margin width increased (positive, 12.6%; < 1 mm, 10.9%; 1- < 2 mm, 7.5%; 2- < 3 mm, 2.9%; ≥ 3 mm, 2.7%, $p < 0.01$). The impact of resection margin width on IBTR was more prominent in young patients (positive, 21.6%; < 1 mm, 13.9%; 1- < 2 mm, 10.8%; 2- < 3 mm, 5.7%; ≥ 3 mm, 5.8%, $p < 0.01$) than those ≥ 40 years (positive, 8.5%; < 1 mm, 8.0%; 1- < 2 mm, 4.4%; 2- < 3 mm, 2.7%; ≥ 3 mm, 2.1%, $p < 0.01$). Multivariate regression analysis revealed that resection margin width remained significant prognosticator all over the age groups.

Conclusions: IBTR excessively increased as resection margin width decreased in young patients with IBC. Therefore, the current definition of an adequate negative margin might not be appropriate in them.

THE USE BIPOLAR ELECTROSURGICAL IN SEROMA REDUCTION AFTER MASTECTOMY

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Background: Postmastectomy seroma formation is common and associated with increased morbidity. Use of pressure garments, immobilization of the ipsilateral upper limb, quilting, and use of sclerosing agents have been described to decrease seroma formation. Thus far, no method has been shown to be effective. We explore the use of Bipolar electrosurgical to reduce seroma formation through improved tissue adherence and hemostasis.

Methods: We compared the degree of seroma formation in 3 patients with Bipolar applied to the post -mastectomy with 10 patients who underwent without use of Bipolar.

Result: The amount of seroma formation (assessed by drain volume and volume of seroma fluid aspirated after drain removal) was compared between the two groups. Result: Median time to drain removal for the use of the Bipolar group is 7.5 days; 13.5 days for the control group. The median drain volume for the use of the Bipolar group is 130 mL; 250 ml for the control group. The median aspiration volume after drain removal for use of Bipolar group is 20.5 mL; 50.5 mL for the control group.

Conclusions: The use of Bipolar effectively reduces seroma formation. Bipolar electrosurgical has a good safety profile, is easy to use, and does not significantly increase the operative time. A follow-up prospective study of a larger scale is underway to analyze the cost and benefits of this technique.

ENDOSCOPIC NIPPLE SPARING MASTECTOMY

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Background: Conventional nipple-sparing mastectomy (NSM) is widely accepted approach patients with a benign diseases or early breast cancer. Compared to radical mastectomy, this technique presents better cosmetic outcomes but decrease in nipple sensitivity for incision into the nipple-areola complex (NAC). Endoscopic nipple-sparing mastectomy (ENSM) removes all breast tissue through the axillary incision used for insertion of breast implants and the sentinel lymph node biopsy in order to avoid an incision around the NAC area. In this case report, we intend to present our initial experience regarding the ENSM.

Methods: 48 years old female complained about pain in the left breast for a long period. Also pain migrates to the axilla. She had been complaining for the last 5 years. Moreover, several excisional biopsies were performed in the last 5 years. Pathological test evidenced Intracystic papilloma and Myoepithelial hyperplasia. We decided to perform ENSM with implant-based reconstruction (IBR).

Result: There was no complication that occurred during the operation. The patient recovered without any complications. Operation time was 315 mins, blood loss 10 ml. The pathological result showed. The patient had discharged on postoperative day 2, and during the 5 months of follow-up, she didn't complain of a change in sensitivity around the nipple.

Conclusions: ENSM, which avoids incision around the NAC, may result in a significant decrease in morbidity related to nipple sensation. Moreover, if combined with immediate reconstruction, the result is very satisfying for patients, particularly in young individuals. This novel approach might be a forthcoming trend in the near future.

DISAPPERANCE OF NONMASS ENHANCEMENT EXTENSION TO NIPPLE AFTER NEOADJUVANT CHEMOTHERAPY: PATHOLOGIC RESPONSE AND FEASIBILITY FOR NIPPLE-SPARING MASTECTOMY

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Background: To address whether nipple-sparing mastectomy (NSM) is feasible for patients with the disappearance of non-mass enhancement (NME) to the nipple after neoadjuvant chemotherapy (NAC), we compared pathologic response of nipple-areolar complex in patients undergoing nipple-sacrificing surgery and investigated oncologic outcome in patients with NSM who had NME to the nipple at initial diagnosis.

Methods: The patients were classified into four groups: E-E (NME extension to the nipple on pre-and-post), E-NE (NME extension to the nipple on pre, and disappeared NME on post), NE-E (NME non-extension to nipple on pre and NME extension to nipple on post), and NE-NE. Pathologic nipple invasion was assessed in patients who received nipple-sacrificing surgery. The oncologic outcome was investigated in patients with NSM who had NME to nipple before NAC.

Result: A total of 287 patients who underwent nipple-sacrificing surgery. There were 60 (20.9%) patients in the E-E, 134 (46.7%) patients in the E-NE group, 2 (0.7%) patients in the NE-E, and 91 (31.7%) patients in the NENE. The pathologic nipple invasion rates were 3.7% in the E-NE and 1.1% in the NENE, whereas they were 51.7% in the E-E and 50.0% in the NE-E. No pathologic nipple invasion was observed in the E-NE with radiologic breast complete response. Forty women who had NME to the nipple at baseline and received NSM had no relapse.

Conclusions: Pathologic nipple invasion was rare in patients with resolved NME extension to the nipple after NAC. Therefore, NSM could be an appropriate surgery for this population, especially in whom showed excellent NAC responses.

METHYLENE BLUE SENTINEL LYMPH NODE BIOPSY FOR BREAST CANCER LEARNING CURVE IN COVID-19 ERA: HOW MANY CASES ARE ENOUGH?

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Background: During the pandemic, there was an increased need to reduce the volume and duration of surgery. According to the Indonesian Board-Certified Oncologist Surgeon, the learning curve for evaluating the fellow breast surgeon in order to achieve this competency could have been shorter. The goal of this study is to see if the learning curve for SLN identification can be shortened, particularly during the COVID-19 pandemic & if imprint cytology can replace frozen section.

Methods: Fellow breast surgeons were taught to use methylene blue dye alone as a single agent to perform SLNB on breast cancer patients (operable primary tumour less than 5 cm and clinically negative ipsilateral axilla). Intraoperative assessment & completion of ALND were performed on the first setting for standardization with the attending surgeon. SLN identification was plotted on cumulative sum chart (CUSUM) limitations for evaluating the variability competency between attending surgeon & fellow surgeon based on a target identification rate of 85%.

Result: After 14 consecutive tests, the CUSUM plot positively identified SLN as a significant achievement level of competency. There was not a lot of difference between attending & fellow. Imprint cytology is inferior to frozen section cytology. The accuracy of imprint cytology is 73.9%, while the accuracy of frozen sections is 95.65%.

Conclusions: The CUSUM chart can be used to illustrate individual learning curves for breast surgery training by using an alternate indicator for the supervisor's inability to identify the SLN within 15 minutes. Regarding imprint as an alternative to the frozen section for identifying lymph node involvement, our findings show that the frozen section is still the gold standard for determining the disorder of axillary lymph nodes.

A MICRODOCHECTOMY FOR NIPPLE DISCHARGE USING NEAR-INFRARED INDOCYANINE GREEN FLUORESCENCE IMAGING-CASE REPORT

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Background: Nipple discharge is one of the most common breast-related outpatient visits. Recently, there are many cases of nipple secretion after procedures such as vacuum-assisted biopsy. If the discharge is not resolved even after sufficient time has passed, a surgical operation such as a microdochectomy should be performed. We report here an alternative method of using near-infrared ICG-fluorescence imaging with microdochectomy for nipple discharge.

Methods: A 43-year-old female patient visited our breast center with nipple discharge from her left breast. She had a vacuum-assisted biopsy 1 year ago and was discharged 3 months after the procedure. We observed the progress for 3 months, but there was no improvement. A galactogram was performed, and it was confirmed that the biopsy site with the cystic lesion and the duct were connected.

Result: We performed microdochectomy using near-infrared indocyanine green (ICG) fluorescence imaging. A silicone tube was inserted into the hole of the mammary duct that secretes discharge, and 1 mL of ICG solution was injected into the mammary duct under general anesthesia. After making a periareolar incision, the subcutaneous tissue was dissected to obtain a fluorescence image of the mammary duct with the boundary separated through a near-infrared fluorescence camera.

Conclusions: In conclusion, we were able to successfully apply fluorescence imaging to microdochectomy for the treatment of pathological papillary secretions. Using near-infrared ICG fluorescence imaging, pathological ducts can be detected more accurately, which is expected to reduce the operation time and scope.

INDOCYANINE GREEN FLUORESCENCE TECHNIQUE FOR SENTINEL LYMPH NODE BIOPSY IN EARLY BREAST CANCER: THE FIRST OF 30 CASES EXPERIENCE REPORT

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Background: Detection of a sentinel lymph node is the standard procedure to evaluate axillary lymph node status in breast cancer. Currently, the use of radiocolloid and blue dye for sentinel lymph nodes biopsy (SLNB) is common. However, the disadvantage of blue dye method is that the low detection rate and the radiocolloid method is invisible. It exposes the patients and health workers radiation. Recently, Indocyanine Green (ICG) has been proposed as an alternative SLNB agent. This study aimed to investigate the accuracy and safety of ICG guided sentinel lymph nodes biopsy.

Methods: A total of 30 women diagnosed stage 0 to IIA breast cancer with clinical axillary lymph nodes negative were analyzed. The primary endpoint was the identification rate and sensitivity rate. The secondary endpoint was false-negative rate-related factors. The early ICG-related complications were observed postoperatively.

Result: All 89 lymph nodes were removed in 30 cases. The identification rate of SLNs was 100%, with a mean of 2,97 SLNs per patient. The false-negative rate was 6.7% (2/30), with the sensitive rate was 93.3%. There are no differences in the false-negative rate in comparing the number of SLNs, location of the tumor, histology, and tumor subtype. The false-negative rate of SLNB seems to be closely related to the BMI > 25. No acute or chronic allergic reaction was observed in this study. However, 19 patients (19/30) who received breast-conserving surgery and skin-sparing mastectomy reported temporary skin staining.

Conclusions: ICG fluorescence technique for detection of SLNs in breast cancer was found to be a valid, feasible, and surgeon-friendly method in clinical practice.

EARLY ONCOLOGIC OUTCOMES OF ROBOT-ASSISTED NIPPLE-SPARING MASTECTOMY COMPARED TO CONVENTIONAL NIPPLE-SPARING MASTECTOMY

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Background: Since 2015, robotic surgical systems have been introduced and widely used for performing nipple-sparing mastectomy (NSM). However, the oncologic outcomes have not been well evaluated. The study aimed to evaluate early oncologic outcomes of robot-assisted nipple-sparing mastectomy (RNSM) with immediate breast reconstruction (IBR) compared to conventional nipple-sparing mastectomy (CNSM).

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. Patient clinicopathological features and early oncologic outcomes were analyzed using the Chi-square test, the Kaplan-Meier curves, and log-rank tests.

Result: The mean age of the patients was 44 years in the RNSM group and 46 years in the CNSM group ($p = 0.017$). Bilateral NSM was performed in 25 patients of the CNSM group and 24 patients of the RNSM group, of which contralateral risk-reducing mastectomy was performed in 16 patients (64%) of the CNSM group and 12 patients (50%) of the RNSM group ($p = 0.322$). Three-quarters of all patients were pathologic stage 0-I. Overall, 12.7% received neoadjuvant chemotherapy, and post-mastectomy radiotherapy was performed in 20.2%. Clinicopathological variables such as germline mutation, histology, subtype, histologic grade, and stage did not show significant differences. With a median follow-up of 36 months, there were no significant differences in disease-free survival ($p = 0.604$).

Conclusions: RNSM with IBR is a safe and feasible surgical procedure in selected women with early breast cancer comparable to CNSM with IBR in terms of early oncologic outcomes.

COMPARISON OF SURVIVAL OUTCOMES FOR SURGERY OF THE PRIMARY TUMOR IN RELATION TO SYSTEMIC THERAPY RESPONSE AND TREATMENT SEQUENCE IN DE NOVO STAGE IV BREAST CANCER

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Background: Our study aimed to evaluate the effect of surgery on survival of patients with de novo stage IV breast cancer according to their response to chemotherapy and treatment sequence.

Methods: We retrospectively analyzed data from 371 patients which were categorized into systemic therapy [ST] alone, ST followed by surgery, and upfront surgery with following ST. We assessed the response after three to four cycles of ST except the upfront surgery cohort. Patients were grouped into complete response [CR], partial response [PR], and progressive disease or stable disease [SD] of the primary tumor. We analyzed overall survival of those subgroups. The statistical analysis was performed using the time-varing covariate cox model to control potential confounders.

Result: At a median follow-up of 43 months, three-year overall survival was 46.7% in the ST alone group, 79.8% in the ST + surgery group, and 63.0% in the upfront surgery + ST group. The adjusted hazard ratio [HR] for surgery was 0.64 (95% CI 0.44-0.93, $p = 0.02$) compared to ST alone. The HRs for surgery were 0.58 (95% CI 0.21-1.60, $p = 0.29$) in the CR group, 0.42 (95% CI 0.27-0.65, $p < 0.001$) in the PR group, and 0.44 (95% CI 0.25-0.77, $p = 0.004$) in the SD group.

Conclusions: This study suggested that surgery of the primary tumor regardless of timing prolonged survival compared to ST alone and provided survival benefit for patients whose response to ST were either PR or SD. For optimal management, a tailored surgical decision should be made on the basis of coordinated multidisciplinary team approach.

EARLY EXPERIENCE OF VOLUME REPLACEMENT USING ACELLULAR DERMAL MATRIX FOR BREAST CONSERVING SURGERY

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Background: Acellular dermal matrix (ADM) in various surgery have become increasingly popular, particularly for oncoplastic breast surgery. We evaluated the postoperative outcome of breast-conserving surgery with volume replacement using ADM.

Methods: Data were collected retrospectively in 12 patients of breast conserving surgery with volume replacement using an ADM from January 2020 to January 2022. After partial mastectomies for the removal of breast cancer with clear resection margins, the defects were filled with $3 \times 4 \times 0.3$, $4 \times 6 \times 0.3$, and $4 \times 8 \times 0.3$ cm sized ADM, depending on defect size. Postoperative complications were evaluated.

Result: One (8.3%) patient was diagnosed with ductal carcinoma in situ (DCIS), and 11 (91.76%) were invasive ductal carcinoma. Mean resected weight was 36.99 (6.5-69) g. We did not insert any drain tube for the patients. There was no postoperative complication, such as infection, seroma, and bleeding. After radiation therapy, some patients complained of foreign body sensation at the surgical site, they improved within a few months.

Conclusions: The ADM for volume replacement during breast-conserving surgery can be a safe option based on postoperative outcome.

COMPARISON OF POSTOPERATIVE COMPLICATION RATES BETWEEN MINIMAL ACCESS NSM AND CONVENTIONAL NSM (KOREA-BSG 2)

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Background: For breast cancer patients, nipple-sparing mastectomy (NSM) is a method that can minimize aesthetic loss along with appropriate oncological treatment. In the past, NSM was performed using the incision method, but NSM using endoscopes and robots is also increasing recently. There are very few studies on the advantages and disadvantages of this minimal access NSM (M-NSM) compared to the conventional NSM (C-NSM). In this study, we tried to analyze whether there is a difference in complications between M-NSM and C-NSM.

Methods: This study is a multicenter retrospective study. From January 2018 to December 2020, data related to clinical pathologic factors of breast cancer patients and complications within 3 months after surgery were collected from 21 institutions in Korea.

Result: A total of 1587 cases of NSM were performed to breast cancer patients at 17 institutions for 3 years, and it consisted of 243 M-NSM cases (endoscope 29 cases, robot 214 cases) and C-NSM 1344

cases. Although more patients with lower ptosis grades were included in the M-NSM group (normal ptosis; M-NSM 66.67% vs. C-NSM 48.05%), there was no significant difference in mean specimen weight (p-value = 0.0001; 47.95 mm vs. 77.51 mm) and pathologic stage. On the other hand, mean incision size was significantly smaller in M-NSM (p-value = 0.0001; 47.95 mm vs. 77.51 mm), and nipple-areolar complex (NAC) necrosis and seroma were also significantly less in M-NSM.

Conclusions: Compared to C-NSM, M-NSM did not significantly increase complications and less NAC necrosis and seroma. In conclusion, in terms of complications, M-NSM is not inferior to C-NSM.

TRENDS OF AXILLARY SURGERY IN BREAST CANCER PATIENTS WITH LN METASTASIS

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Background: According to the results of the SENTINA, SN FNAC and ACOSOG Z1071 trial, de-escalation of axillary surgery after neoadjuvant chemotherapy (NAC) has been increased in patients with axillary lymph node (ALN) metastasis before NAC. Despite the luminal type of breast cancer known as a less aggressive tumor, the rate of omitting axillary lymph node dissection (ALND) after NAC in patients with luminal type is lower than that with other types. The aim of this study is to review the trends of axillary surgery by time, subtype in patients with ALN metastasis.

Methods: From January 2009 to July 2019, there were 2525 breast cancer patients who were biopsy proven metastasis ALN who underwent axillary surgery in Samsung Medical Center. There were 1152 patients (45.6 %) who received NAC and 1373 patients (54.4 %) without NAC. We analyzed the ratio of sentinel lymph node biopsy (SLNB) and ALND by time, subtype and with or without NAC.

Result: In 2009-2012, all subtypes were significantly higher ALND rate than SLNB rate ($p < 0.014$). The ALND rate of all subtypes gradually decreased in 2013-2019 ($p < 0.001$). The ratio of SLNB was significantly lower in the HR+/HER2- type (13.6 %) compared to other types (46.6 %) during the period of 2017-2019($p < 0.001$). In the patient group receiving NAC, HR+/HER2-type had a significantly higher ALND rate than other types (84.1%; 60.8%; 62.3%; 70.7%; $p < 0.001$).

Conclusions: SLNB rate of patients with ALN metastasis has increased over time, but ALND rate of HR+/HER2- type has not decreased.

MINIMALLY INVASIVE BREAST SURGERY FOR BENIGN AND MALIGNANT BREAST DISEASE: EARLY EXPERIENCE FROM MALAYSIA

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Background: The objective of this study is to describe the feasibility of a minimally invasive surgical approach to treat benign and malignant breast disease. Evolution of breast surgery has tremendously occurred with the direction towards aesthetically sensible following the improvement of survival of malignant breast disease. The extension of the importance of aesthetic outcome has included in benign breast condition that needed removal of breast such as in gynacomastia. Assessment of feasibility of using endoscopic approach for patients underwent mastectomy through lateral chest wall or axillary incision has been performed.

Methods: We retrospectively selected 38 patients (10 breast cancer and 28 gynaecomastia) treated with endoscopic mastectomy via single incision between January 2017 and February 2021. All patients were cosmetically satisfied with to have as little scarring as possible. The following data were collected: demography, breast tissue volume removed, tumor location, incision site, time of surgery, complication, and histopathological reports.

Result: Among the analyzed cases, the median age of 40.92 years. Average surgical incision length were 3.8 cm (3 cm-5 cm). There were 1 case of haematoma in benign breast disease group. There was no immediate complication in malignant breast disease group. Majority of the patients gave satisfactory to excellent score after surgery. There was no reported local recurrence in the endoscopic mastectomy cases after 4 years of followup.

Conclusions: Endoscopic mastectomy technique offered reasonably feasible technique with better aesthetic and good satisfaction in benign and malignant breast disease patients. Longer followup studies to be conducted to assess longterm outcome of the technique.

STRATIFICATION OF AXILLARY LYMPH NODE METASTASIS RISK WITH BREAST MAGNETIC RESONANCE IMAGING IN BREAST CANCER

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Background: To develop a model based on the standard breast magnetic resonance imaging (MRI) features of breast tumor to stratify patients by different burden of axillary lymph node (ALN) metastasis in breast cancer.

Methods: All eligible patients underwent breast surgery with sentinel lymph node biopsy and/or ALN dissection as well as breast MRI scan before surgery. Patients with zero, one to three and more than three pathologically positive lymph nodes were classified as no, low and heavy axillary metastasis burden, respectively. Preoperative factors significantly correlated with axillary burden in the univariate analysis with $\chi 2$ test were put into the ordinal logistic regression analysis to develop a predicting model. The accuracy and sensitivity of axillary burden stratification were calculated based on this model, which was validated by an independent group of patients.

Result: Five preoperative factors including tumor size, margin, ADC value, MRI ALN status, and time-signal intensity curve (TIC) were significantly correlated with ALN burden in the univariate analysis. A model incorporating the above five factors was developed, yielding the total accuracy of 73.1% in the test set and 82.5% in the validation set. The sensitivity to predict patients with no, low and heavy ALN burden was 96.4%, 8.0% and 61.5%, respectively in the test set and 94.3%, 64.3% and 62.5%, respectively in the validation set.

Conclusions: A simple model based on the standard breast MRI features may be helpful for the preoperative stratification of axillary metastasis burden in patients with newly diagnosed breast cancer.

SURVIVAL BENEFIT FROM AXILLARY SURGERY IN PATIENTS AGED 70 YEARS OR OLDER WITH CLINICALLY NODE-NEGATIVE BREAST CANCER: A POPULATION-BASED PROPENSITY-SCORE MATCHED ANALYSIS

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Background: Elderly breast cancer patients have a good prognosis and most of them die from disease other than breast cancer. This study aimed to compare survival outcomes in breast cancer patients ≥ 70 years old received breast surgery with or without axillary surgery.

Methods: A total of 3,032 breast cancer patients ≥ 70 years old receiving breast surgery were included from the Korean Breast Cancer Registry. Patients were divided into two groups according to axillary surgery. To minimize bias caused by retrospective analysis, we used propensity score matching of demographics and treatment factors. We compared the 5-year overall survival (OS) and breast cancer-specific survival (BCSS).

Result: After 3:1 propensity score matching, 542 patients received breast with axillary surgery and 182 patients received breast surgery alone. Of all patients, 374 (51.7%) had pathologic T1 stage and received mastectomy. 31.2% of patients received chemotherapy, 19.6% received radiation therapy. OS and BCSS rates after 5 years in axillary surgery group were 86.9% and 94.7%, respectively. In patients without axillary surgery, OS and BCSS rates were 85.2% and 96.7%, respectively. The hazard ratios of axillary surgery for OS and BCSS were 0.778 (95% CI 0.545-1.111, $p = 0.167$) and 1.5 (95% CI 0.661-3.407, $p = 0.332$), respectively, indicating no significant difference between two groups.

Conclusions: Our study demonstrated that axillary surgery in elderly patients would not provide additional survival benefit in terms of OS and BCSS compared with breast surgery alone. Our findings suggest that axillary surgery could be omitted in elderly patients with clinically node negative breast cancer.

NON-SENTINEL NODE METASTASIS PREDICTION DURING SURGERY IN PATIENTS WITH BREAST CANCER WITH ONE TO THREE POSITIVE SENTINEL NODE(S)UP ON FROZEN BIOPSY RESULT FOLLOWING NEOADJUVANT CHEMOTHERAPY

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Background: Our goal was to develop a tool that could accurately predict the possibility of non-sentinel lymph node metastasis (NSLNM) during surgery, allowing a surgeon to decide the extent of further axillary lymph node dissection (ALND) intraoperatively for patients with one to three positive sentinel lymph node(s) (SLN) after neoadjuvant chemotherapy (NAC).

Methods: In a retrospective analysis of the Asan Medical Center (AMC) database, we included 558 patients' records who were treated between 2005 and 2019. Using chi-square and logistic regression with a bootstrapped, backward elimination method, 13 factors were assessed for their utility in predicting NSLNM. Based on the results of the univariate analysis for statistical significance, the number of positive SLN(s), number of frozen nodes, progesterone receptor (PR) positivity and clinical N stage were selected for the multivariate analysis and used to generate a nomogram for predicting residual nodal disease. The resulting nomogram was validated using a more recent, different time window patient group at the AMC.

Result: We designed a nomogram to predict NSLNM that included four components: number of SLN(s), number of frozen nodes, PR positivity and clinical N stage prior to NAC. The area under the receiver operating characteristics curve value of this formula was 0.709 (95% CI, 0.6580.761) for the development set and 0.715 (95% CI, 0.6340.796) for the validation set.

Conclusions: This newly developed AMC nomogram may be useful to a surgeon for intraoperative guidance in determining the extent of further axillary surgery.

APPLICATION ABOUT SENTINEL LYMPH NODE BIOPSY SURGERY IN LOCALLY ADVANCED BREAST CANCER WHO RECEIVED PREOPERATIVE CHEMOTHERAPY: QUESTIONNAIRE STUDY

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Background: In patients with local advanced breast cancer, if the metastasis of the axillary lymph nodes after neoadjuvant chemotherapy shows a complete response, studies are being applied clinically sentinel node biopsy (SNB) instead of the axillary lymph node dissection (ALND). This study is aimed to evaluate application in clinical practice regarding SNB among clinically node-negative patients after neoadjuvant chemotherapy for breast cancer with axillary node metastasis conducting a survey of breast surgeons.

Methods: We conducted a survey among 1,160 members of the Korean Breast Cancer Society from December 2020 to November 2021. The questionnaire comprised total 14 questions about axillary surgery. The inclusion criteria of the questionnaire were selected from surgeons performing breast cancer surgery.

Result: The response rate was 11.6% (135/1,160). Methods for the evaluation of axillary stage in patients with axillary metastatic breast cancer after neoadjuvant chemotherapy were that they would perform SNB rather than ALND (96.3% for SNB versus 3.7% for ALND). Mapping methods showed that 64 (48.1%) had dual methods (dye and Radioactive isotope (RI)) and 41 (31.8%) had RI method. After mapping breast cancer surgery with indocyanine green fluorescence, 25 (18.7%) people performed SNB surgery with near-infrared camera. If the Sentinel lymph node was not detected, 53% performed ALND, and 43.3% performed ALN sampling. In the absence of sentinel node metastasis with SNB, the proportion of respondents indicating that they would not perform additional ALND was 67.7%.

Conclusions: This study show that axillary node surgery has changed more minimal surgery among clinically node-negative patients after neoadjuvant chemotherapy for breast cancer with node metastasis.

THE IMPACT OF IMMEDIATE LYMPHO-VASCULAR ANASTOMOSIS AFTER AXILLARY LYMPH NODE DISSECTION ON THE PREVENTION OF BREAST CANCER RELATED LYMPHEDEMA: THE INITIAL SURGICAL OUTCOMES

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Background: Breast cancer related lymphedema (BCRL) affects 20~45% of breast cancer survivors after surgical intervention. BCRL is associated with decreased patient quality-of-life measures, increased susceptibility to infection, and increased medical expenditure. This study was to evaluate the impact of preventive lympho-vascular anastomosis (LVA) on the incidence of postoperative lymphedema.

Methods: Breast cancer patients who were candidates for axillary lymph node dissection (ALND) were prospectively enrolled. Preventive LVA was performed by microsurgical technique at the completion of ALND. Surveillance at 1, 3, 6, 9, 12, 18, and 24 postoperative months was planned to identify the occurrence of lymphedema, and patient reported outcomes regarding BCRL symptoms were measured. The lymphedema was defined as more than 2 cm difference of both arm circumferences and bio-impedance analysis (BIA) ratio measurement.

Result: From April 2020 to January 2022, twenty node-positive breast cancer patients underwent ALND with immediate preventive LVA. The median patient age was 46 years (range, 32~59), and body mass index was 22.46 kg/m^2 (range, 18.8~42.57). The median removed lymph nodes was 17 (range, 11~68), and the median operation time (ALND+LVA) was 92 minutes (range, 80~149). There was no postoperative complication such as hematoma, bleeding, or infection related to LVA. All the enrolled patients received chemotherapy and 52.9% underwent radiotherapy. None of the patients developed lymphedema during the follow-up period (median 12 months, range 1~18).

Conclusions: The initial result of immediate LVA suggested that it was a promising and safe approach for the prevention of BCRL. Long term follow-up data with a larger cohort study will be needed.

AXILLARY MANAGEMENT OF BREAST CANCER PATIENTS WITH ISOLATED CHEST WALL RECURRENCE AFTER MASTECTOMY

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Background: NCCN guidelines on the axillary management of breast cancer patients with isolated chest wall recurrence after mastectomy is unclear. Though sentinel lymph node biopsy (SLNB) is possible and may be considered, there is limited data on its usefulness. We aimed to determine if axillary restaging surgery was required in this group of patients who developed operable isolated chest wall recurrences after mastectomy.

Methods: Breast cancer patients treated at a tertiary institution from 1st September 2005- 31st October 2017 and developed isolated chest wall invasive recurrences after mastectomy were retrospectively reviewed. We excluded patients with bilateral cancers, concurrent regional or distant metastases, patients without surgery for their chest wall recurrences and patients who were lost to follow-up. The demographics, pathological data and second recurrences were collected from a prospectively maintained database and compared between patients with axillary lymph node dissection (ALND), SLNB and no axillary operation.

Result: Of the 1,841 patients who underwent mastectomy, 26 (1.4%) patients developed isolated chest wall recurrences. 22 eligible patients were analysed. The mean age at diagnosis of the recurrence was 54.7 years (range: 37-84). One, two and nineteen patients had ALND, SLNB and no axillary operation respectively. On mean follow-up of 38.3 months, no axillary recurrences were noted.

Conclusions: In breast cancer patients with isolated chest wall recurrences after mastectomy, axilla restaging surgery can be safely omitted with no increased axillary recurrences on medium term follow-up. This finding could refine existing guidelines in the management of the axilla for patients with chest wall recurrences after mastectomy.

ONCOLOGIC OUTCOME OF IMMEDIATE BREAST RECONSTRUCTION AFTER MASTECTOMY IN BREAST CANCER PATIENTS: A SYSTEMATIC REVIEWS AND META-ANALYSIS

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Background: We performed a comprehensive systematic review of the literature and a meta-analysis of the oncologic outcome of immediate breast reconstruction (IBR) after mastectomy and mastectomy only. The aim of this study was to analyse the impact of IBR on the prognosis of patients with breast cancer.

Methods: A systematic search of MEDLINE and EMBASE was performed using the key words of breast cancer, mastectomy, IBR. Inclusion criteria was studies reporting survival data of patients after mastectomy only and mastectomy with IBR. Event-free survival (EFS), Breast cancer specific survival (BCSS) and overall survival (OS) were considered markers of oncologic outcome. The impact of IBR on survival was measured by the effect size of hazard ratio (HR). Data from each study were analysed using Review Manager.

Result: Sixteen studies with 22833 cases of IBR and 60266 cases of mastectomy were included this study. The pooled HR for EFS was 0.83 (95% confidence interval [CI]; 0.63 - 1.09, $p = 0.18$). Patients who underwent IBR after mastectomy had similar EFS. Furthermore, patients receiving IBR had better BCSS (HR = 0.68; 95% CI: 0.61 to 0.76, $p < 0.001$) and OS (HR = 0.68; 95% CI: 0.57 to 0.80, $p < 0.001$) as those of mastectomy only patients.

Conclusions: There data provided that IBR after mastectomy has a similar EFS and better BCSS, OS than mastectomy only. Our meta-analysis suggested IBR is a feasible and safe treatment option for patients with breast cancer.

DOUBLE-PEDICLE TRAM FLAP FOR BREAST RECONSTRUCTION: A SINGLE CENTER EXPERIENCE

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Background: For autologous traverse rectus abdominal muscle, flap reconstruction (TRAM) flap breast reconstruction, either unipedicle or double-pedicle TRAM flap can be used to reconstruct unilateral post mastectomy defect. Unipedicle TRAM flap is suitable for patient with no risk factor for partial flap necrosis and limited tissue needed for breast reconstruction while double-pedicle technique should be used in low and intermediate risk patient and more volume of tissue needed for breast reconstruction. The Double-pedicle TRAM flap breast reconstruction is rarely done by breast surgeon as it requires long operative time, increased difficulty in abdominal wall closure and greater difficulty in shaping the breast.

Methods: To compare the immediate morbidity of patients who had unipedicle and double-pedicle TRAM flap by single breast surgeon.

Result: TRAM flap were performed on 16 patients with breast cancer; 12 patients had unipedicle TRAM flap and 4 patients had double-pedicle TRAM flap. Significant factors for partial flap necrosis in both groups included obesity, prior irradiation and small vessel disease due to either smoking, diabetes mellitus and high risk of vessel thrombosis post COVID-19 infection. None of the double-pedicle groups had immediate complications post operation, while 55% of the patients in the unipedicle groups had partial flap necrosis and required second operation for wound debridement and flap remodeling.

Conclusions: Patients at increased risk of flap necrosis should be offered double-pedicle TRAM flap to allow larger and safer reconstruction. Double-pedicle TRAM flap is a useful option to the free TRAM flap with acceptable complication rates and elimination of the requirement of microsurgical technical expertise.

BOOMERANG LATISSIMUS DORSI FLAP IN TOTAL BREAST RECONSTRUCTION: REPORT OF THREE CASES

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Background: The latissimus dorsi flap is one of the most useful techniques for autologous breast reconstruction in Asia. However, for reconstruction of moderate to large volume breasts, it is difficult to achieve the desirable volume and projection. Although there is the option of concurrent application of an latissimus dorsi flap and a small silicone implant, this may lead to larger volume than desired; furthermore, an increasing number of patients prefer reconstruction with autologous tissue alone.

Methods: Flap was harvested with a transverse incision along the brassiere line and a vertical incision under the arm. Then, after tunneling to the breast, the autologous reconstructed breast was created. Total of 3 patients who underwent the boomerang latissimus dorsi flap were evaluated. Mastectomy method, flap design, size, and weight, mass weight, postoperative outcome and complications were evaluated.

Result: There were no severe intraoperative or postoperative complications. Seromas were observed in the donor site of the boomerang latissimus dorsi flap and healing was successful. Donor site incision was 1.5 to 1.6 times longer than that of the classic latissimus dorsi flap.

Conclusions: The boomerang latissimus dorsi flap is considered a useful autologous flap that can be applied for breast reconstruction in patients with large breast volume who want to avoid implants. Satisfactory outcomes were achieved for the reconstructed breast, primary closure was possible at the donor site and the length of recovery period was similar to classic latissimus dorsi flaps.

SIMULTANEOUS NIPPLE RECONSTRUCTION IN AUTOLOGOUS BREAST RECONSTRUCTION

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Background: Reconstruction of the nipple-areola complex is the final step in surgical restoration of the breast. Nipple-areola reconstruction was previously done after an interval of several months using variable techniques, often resulting in low projection and flattened breast mound over time. We present algorithm of simultaneous nipple reconstruction that leaves adequate residual projection and naturally shaped breast mound.

Methods: Forty patients underwent a skin-sparing mastectomy and nipple excision between October 2016 and December 2020. In the control group, 21 patients underwent delayed nipple reconstruction for 6 months after breast reconstruction. The experimental group of 19 patients underwent nipple and breast reconstruction simultaneously. We collected relevant information and photographs of nipple profiles of both groups in the preoperative, postoperative 6-month, and postoperative 1-year time periods. We also examined the ratio between the reconstructed and contralateral nipples.

Result: Scores regarding patient satisfaction questionnaire averaged higher in experimental groups (simultaneous nipple reconstruction) to every category. The control group's scores gradually declined over time and the experimental group showed lesser decline. At the 1-year postoperative follow-up, the mean projection of the immediately reconstructed nipple was approximately the same as the contralateral nipple at 91%, whereas the delayed reconstructed nipple resulted in a 77% ratio.

Conclusions: Nipple reconstruction should no longer be considered as a secondary complement to immediate breast reconstruction. The nipple appears to be essential component of breast reconstruction for patient. Simultaneous nipple reconstruction with immediate breast reconstruction is a simple and reliable technique, giving stable aesthetic results over time.

SURFACE TOPOGRAPHY OF SILICONE BREAST IMPLANTS IMPACTS CAPSULE FORMATION: A COMPARATIVE STUDY BETWEEN SMOOTH, MACROTEXTURE AND NANOTEXTURE TYPE IMPLANT

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Background: Capsular contracture remains one of the major problems following silicone breast implantation. Although the surface structure of the implant has been known to affect the capsular contracture, the associated mechanism has yet to be determined. This study thus aimed to investigate capsule formation and capsular contracture using three types of implants with different surface topographies in vivo.

Methods: Three types of implants (i.e., smooth, macrotexture, and nanotexture) with different surface topographies were inserted in a total of 48 Wistar rats. After 4 and 12 weeks, the samples were analyzed via histological, immunohistochemical, and Western blot examination. To identify implant movement, the degree to which implant position changed was measured. The surface topography was characterized using scanning electron microscopy on a three-dimensional confocal laser scanning microscope.

Result: Hematoxylin eosin staining showed that the nanotexture type implant promoted significant decreases in capsule thickness at 12 weeks, while Masson trichrome staining showed decreased collagen fiber density with the same implant type. Immunohistochemical and Western blot examination revealed reduced fibrosis markers (macrophage, myofibroblast, and transforming growth factor beta-1) in the nanotexture surface implant. Meanwhile, implant location evaluation found that the nanotexture- and smooth surface implants had significantly increased movement.

Conclusions: The nanotexture surface implant had been found to reduce capsule formation given that it minimizes the effects of factors related to foreign body reaction and has better biocompatibility compared to smooth and macrotexture surface implants.

PREPECTORAL BREAST RECONSTRUCTION WITH COMPLETE ANTERIOR COVERAGE OF IMPLANT USING A LARGE ONE-PIECE SQUARE SHAPED ADM

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Background: Although, in some studies on prepectoral direct-to-implant (DTI) using acellular dermal matrix (ADM), several methods have been reported using large ADM in a purpose of full coverage of prosthesis, not many studies reported anterior coverage of prosthesis. In this study, prepectoral DTI was conducted through complete anterior coverage piece square shaped ADM. This study aim to introduce our prepectoral DTI technique, to identify functional, cosmetic outcome compared to classical subpectoral DTI technique.

Methods: The anterior coverage method has been used for 20 breasts among 20 consecutive patients. Prepectoral pocket formation starts with insetting the ADM over the pectoralis muscle in interrupted sutures. Suture was made in Superior first, and medial, inferior border, then prosthesis was inserted through lateral aspect, and then lateral border suture was made. Postoperative complications, breast symmetry was evaluated by using Vectra H2 3D scanner.

Result: A total of 36 breast cancer patients undergone skin-sparing mastectomy from January 2019 to December 2020, prospective cohort study was conducted on 16 patients who received subpectoral implant insertion (21 breasts), 20 patients who received anterior coverage prepectoral implant insertion (20 breasts). No statistical significance was found in both groups regarding all complications. Mean drain removal period was 10.5238 ± 2.4823 and 8.65 ± 3.0655 respectively, there was statistical significance. 3D scan shown that more symmetric in anterior coverage group; however, no statistical significance was found.

Conclusions: Considering stability, faster recovery time, and cosmetic aspect, anterior coverage may be one good option in performing breast reconstruction for breast cancer patients who have undergone mastectomy.

ONCOLOGIC OUTCOMES AFTER IMPLANT-BASED IMMEDIATE BREAST RECONSTRUCTION FOLLOWING MASTECTOMY: COMPARISON BASED ON IMPLANT SURFACE TEXTURE

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Background: Potential association between textured implant and increased cancer recurrence has been raised in immediate breast reconstruction following mastectomy. We investigated oncologic outcomes of breast cancer according to the surface type of implants used in breast reconstruction with a long-term follow-up in a large cohort.

Methods: A retrospective cohort study was performed on breast cancer patients who underwent immediate implant-based breast reconstruction after mastectomy at Seoul National University Hospital between 2010 - 2019. Primary breast cancer patients with more than 2 years follow-up after implant insertion were included. The main out comes determined were locoregional recurrence-free interval (LRRFI) and disease-free interval (DFI).

Result: We analyzed total 899 patients of median age 44.9 years (macrotextured implant, 327; microtextured implant, 524; smooth implant, 71). During median follow-up of 51.2 months, the LRRFI ($p = 0.091$) was not significantly different following implant surface texture type. However, textured implant group showed inferior DFS compared to smooth implant ($p = 0.001$).

Conclusions: Textured surface implant resulted in higher overall recurrence of breast cancer. Locoregional relapse was not significantly affected by implant surface texture.

IMMEDIATE BREAST RECONSTRUCTION AFTER NIPPLE SKIN SPARING MASTECTOMY COMBINATION WITH INTRAOPERATIVE RADIATION THERAPY BY INTRABEAM SYSTEM

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Background: Purpose of this study to be effectineve assessement of combination of these procedures in the oncological field as well as aesthetic result.

Methods: 36 patients were performed nipple sparing mastectomy and immediately breast reconstruction with TRAM flap or implant. Intraoperative radiation therapy (IORT) provided a point source of low energy 6-8 Gy of Intrabeam system. The applicator was inserted inside the remaining tissue under nipple areolar after removing the whole breast. After completing IORT, breast reconstruction surgery would be done.

Result: All patient is age ranged from 41-50, there is 31 patients (58.3%) confirming that axillary metastasis with 1-3 lymph nodes, 100% frozen section biopsy at the remaining tissue under nipple areolar is negative. 34 patients (91.6%) using the intraoperative radiation therapy with dose from 6-8 Gy during time 2'01"- 3'45". Complication of radiation in 1 patient (2.8%) with necrose in part of nipple aerolar. Complication of breast reconstruction following nipple sparing mastectomy in 2 patients (5.6%) with infection and seroma. Assessment of the aesthetic results showed that 94.4% having the excellent score. There is no local recurrence, no recurrence in the nipple, no distant metastasis in 30 patients was being follow up in 24 months.

Conclusions: Combination of these novel approaches brings to the effectiveness in oncology field as well as aesthetic result.

THE SAFETY AND EFFICACY OF SVF-ASSISTED LIPOTRANSFER IN BREAST RECONSTRUCTION AFTER MASTECTOMY

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Background: Surgery to reconstruct the breasts can be done immediately or delayingly after the mastectomy. There are several common techniques to complete the treatment including implant reconstruction, flap reconstruction and lipo-transfer. Lipo-transfer has been concerned over the past decades, which is expected to bring the softest and most natural feelings for the patients. However, the unpredictable resorption of the fat graft is still a matter of controversy. In recent years, many physicians have mentioned to the concept CAL (cell-associated lipo-transfer) as the most promising procedure to resolve all the problems of the traditional lipo-transfer. SVF (stromal-vascular fraction) isolated from the lipo-aspirates, autologous, containing the amount of adipose-derived stem cells (ADSCs), fibroblasts, growth factors... can promote angiogenesis, cell regeneration, which is believed having big potential to increase survival rate and lower fat loss volume. Therefore, we applied for a clinical trial using SVF-assisted lipo-transfer in breast reconstruction.

Methods: There would be 30 patients chosen in the clinical trial. All of the case were suffered from mastectomy surgery due to the breast cancer and all will be the delayed reconstructions. They will be examined in clinical, lab work and medical imaging depending on their current situation. The patients will do liposuction surgery, send half of the fat volume to the lab do produce SVF, then we mix the fat and SVF purified as ratio 1:1. The mixture will be injected to the treatment area.

Result: To be announced.

Conclusions: SVF-assisted lipo-transfer in breast reconstruction after mastectomy would be taken into consideration a potential treatment method.

APPLICATIONS AND EXPERIENCES OF PROFUNDUS ARTERY FLAP AND SMALL DEEP INFERIOR EPIGASTRIC IN TAIWAN

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Background: As breast cancer continues to rise in Asian countries, breast reconstruction surgery has played a role in helping breast cancer patients regain their confidences and improve their quality of life. The purpose of this study is to compare the use of the PAP and small DIEP flap for autologous breast reconstruction, its impact on the donor site and the aesthetic outcomes of each flap.

Methods: A retrospective study was conducted on patients who underwent either immediate PAP flap or small DIEP flap reconstruction after mastectomy from 2011 to 2021. Patients with flap weight ≤300 g were included. Patient's demographic data, flap characteristics, breast and donor complications, and number of revisions were reviewed.

Result: 28 patients including seventeen PAP flaps and eleven DIEP flaps were enrolled. The PAP flap was smaller in diameter and shorter in pedicle length. There was no significant difference in the donor site morbidity between these two groups. The average revision times of the PAP flap was significantly higher than the small DIEP flap.

Conclusions: A shorter width of the PAP flap negatively affected the breast appearance because it increased the difficulty of shaping. This explained the high demand for aesthetic revisions of the PAP flap. A short pedicle length of the PAP flap often limited the ability to create a ptotic breast. Since the PAP flap did not sacrifice abdominal tissue, young women who were worried about abdominal muscle weakness during future pregnancies could opt the PAP flap as alternative source for breast reconstruction.

ONCOLOGIC OUTCOME OF IMMEDIATE BREAST RECONSTRUCTION FOLLOWING TOTAL MASTECTOMY IN IPSILATERAL BREAST TUMOR RECURRENCE PATIENT

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Background: Immediate breast reconstruction (IBR) after total mastectomy (TM) has gradually increased in breast cancer patient. Even though the indications for IBR have been broadened, only a few evidence reported feasibility of IBR in ipsilateral breast tumor recurrence (IBTR) patients. This study aimed to analyze the oncologic outcomes between TM only and IBR following TM in IBTR patients.

Methods: We retrospectively reviewed IBTR patients after breast conserving surgery who underwent TM with or without IBR between 2008 and 2018. We excluded 3rd recurrence patients and delayed reconstruction patients. We divided the patients into two groups: those who underwent TM only and those who underwent IBR following TM.

Result: Overall, 123 IBTR patients were enrolled (75 - TM only vs. 48 - TM with IBR). There was no significant difference on clinicopathologic characteristics between two groups, except more advanced pathologic T stage at first surgery in TM group ($p = 0.042$). There was no significant difference in locoregional recurrence, distant metastasis, and recurrence free survival between two groups ($p = 0.480$, $p = 0.160$, and $p = 0.119$). TM with IBR group showed better overall survival ($p = 0.040$). TM with IBR group showed significantly more complication rate ($p = 0.011$) (2 partial necrosis, 1 infection: TM group vs. 2 implant rupture, 2 partial dehiscence, 2 bleeding, 1 contracture, 1 partial nipple necrosis, 1 infection: TM with IBR group).

Conclusions: Our results suggest that IBR following TM could be a feasible treatment option for patients with IBTR patients.

IS TILOOP BRA MESH ABLE TO MINIMIZE IMPLANT EXTRUSION AND CAPSULAR CONTRACTURE IN PREPECTORAL IMMEDIATE BREAST RECONSTRUCTION?

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Background: In prepectoral immediate breast reconstruction (IBR), the mastectomy flap is usually too thin to support the inserted implant resulting in complications, especially implant extrusion. The prepectoral pocket also has higher rate of capsular contracture. Additional use of internal support showed encouraging results regarding these complications. This study is to report our case series of prepectoral IBR with additional use of the TiLoop Bra titanium-coated polypropylene mesh (TCPM).

Methods: The consecutive patients with breast tumors underwent mastectomy with prepectoral IBR using implant and TCPM by the senior surgeon (V.L.) at Siriraj hospital between 2018-2019 were reviewed. Demographic data and history of radiotherapy in each patient were collected. The primary outcomes focus on the major complications of implant extrusion and capsular contracture. Also, additional surgical interventions to correct the complications were reported.

Result: There are 12 women (age between 22-57 years old) with breast tumors underwent unilateral or bilateral mastectomy with prepectoral IBR using implant and TCPM. The mean follow-up was 1 year and 3 months (the longest follow-up of 2 years and 1 month). There was no implant extrusion. According to modified Baker classification, all 4 patients with a history of adjuvant radiotherapy developed capsular contracture grade III-IV and 2 of them (50%) required additional revision breast surgery to subpectoral reconstruction.

Conclusions: TCPM provides strong support to the implant and minimizes tension at the lower pole of the mastectomy flap. It is a good option in prepectoral IBR in selected patients who do not need radiotherapy.

NEAR-MAXIMUM RIB DOSE IS THE MOST RELEVANT RISK FACTOR FOR IPSILATERAL SPONTANEOUS RIB FRACTURE: A DOSIMETRIC ANALYSIS OF BREAST CANCER PATIENTS AFTER RADIOTHERAPY

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Background: Spontaneous rib fracture (SRF) is a common late complication in treated breast cancer patients. This study evaluated the incidence and risk factors of ipsilateral SRF after radiotherapy (RT) in breast cancer patients. In addition, we identified dosimetric parameters that were significantly associated with ipsilateral SRF.

Methods: We retrospectively reviewed 2,204 patients with breast cancer who underwent RT between 2014 and 2016, and were followed up with bone scans. We evaluated clinical risk factors for ipsilateral SRF. Dose-volume histogram analysis was also performed for patients (n = 538) whose dosimetric data were available. All ipsilateral ribs were manually delineated, and dosimetric parameters of the ribs were converted into the equivalent dose in 2 Gy fractions (EQD2).

Result: Ipsilateral SRF occurred in 14.5% of patients 3 years after RT. The median time to develop ipsilateral SRF was 15 months. In multivariate analysis of all patients, a hypofractionated dose scheme and abnormally low bone density were significant clinical risk factors for ipsilateral SRF. In dosimetric analysis, near-maximum rib dose (D2cc) best predicted ipsilateral SRF. The cutoff value of D2cc was EQD2 52 Gy, as determined by receiver operating characteristic analysis. In multivariate analysis including dosimetric variables, D2cc EQD2 $\geq$ 52 Gy was the only significant risk factor for ipsilateral SRF.

Conclusions: Our data demonstrated that near-maximum rib dose was the best dosimetric parameter to predict ipsilateral SRF in RT-treated breast cancer patients. Additionally, we suggest that the dose for the rib be constrained to D2cc EQD2 $<$ 52 Gy to minimize the risk of ipsilateral SRF.

PMRT WITHOUT BOLUS IS FEASIBLE

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Background: To investigate the efficacy and toxicity of postmastectomy radiation therapy (PMRT) and estimate the actual skin surface dose when bolus was routinely omitted.

Methods: We reviewed medical charts of patients who received PMRT between February 2012 and September 2019. The 3-year locoregional recurrence (LR), distant metastasis (DM), and breast cancer mortality (BCM) were analyzed using the Kaplan-Meier method. Adverse events were evaluated based on CTCAE ver. 5.0. Re-calculation of the plans was performed using Acuros External Beam algorithm (Valian Eclipse) to estimate the actual skin surface dose delivered within PTV (skin_PTV).

Result: One hundred two patients were treated with the median follow-up of 43.5 months (1.0114). Ten patients had a skin invasion, and 56 had four or more lymph node metastases at surgery. Thirty-nine patients received chemotherapy prior to surgery. The prescription dose was 50 Gy in all patients except one had 10 Gy boost. Three patients received PMRT with bolus, 1 with skin invasion had 5-mm bolus on chest wall, and 2 with implant-based reconstruction had 2 mm body shell on the reconstructed breast. Photon beams of 4/4+10/6 MV were used 85/16/1 patients, respectively. The 3-year cumulative incidence of LR, DM and BCM was 1%, 21% and 8%. No Grade 3 or greater adverse events were found. The median skin_PTV D98% and PTV D2cc were 42.9 Gy (range: 38.6-46.5) and 53.7 Gy (range: 50.1-57.9), respectively.

Conclusions: Actual skin dose without bolus was around 85% of prescribed dose. However, the incidence of LR was low. PMRT without bolus may be feasible.

RE-IRRADIATION DOSE NOT INCREASE THE RISK OF LYMPHEDEMA IN PATIENTS WITH LOCOREGIONALLY RECURRENT BREAST CANCER

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Background: There is limited data on subsequent lymphedema (SL) after salvage treatment for locoregional recurrent breast cancer. Nonetheless, physicians hinder performing radiotherapy (RT) at locoregional recurrence to prevent SL. In this context, we conducted the study to evaluate the risk of SL.

Methods: We reviewed patients with locoregional recurrent breast cancer between 2003 to 2017. A board certified rehabilitation physician confirmed SL based on arm volume measurements by an infrared optoelectronic volumetric. To exclude potential malignant lymphedema, competing risk analysis considering death and second locoregional recurrence was performed.

Result: Among 214 patients, most patients had local (n = 113) recurrences followed by regional (n = 73) failures. And re-RT was performed in 72(33.6%); complete mastectomy/node dissection and taxane-based chemotherapy were performed in 116(54.2%) and 70(32.7%), respectively. With a median follow-up of 41.4 months, 51(23.8%) experienced SL; 3-year cumulative incidence of SL was 19.0%. Patients with SL received more extensive axillary dissection at diagnosis (median, 14 vs. 6), had frequent initial lymphedema (17.6% vs. 5.5%), shorter disease-free interval (median, 26.6 vs. 41.0 months), and frequent low axillar recurrences (39.2% vs. 12.3%) (all $p < 0.05$). Multivariable analysis revealed that axillar level I recurrence (HR 2.08), taxane-based salvage chemotherapy (HR 2.36), and initial lymphedema (HR 5.82) were associated with SL. However, re-RT with regional node irradiation ($p = 0.095$) or low axillar re-RT ($p = 0.120$) were not related to SL.

Conclusions: Salvage re-RT for locoregional recurrent breast cancer did not increase the risk of SL. Instead, close surveillance for SL is needed for patients with low axillar recurrence initial lymphedema and treated with taxane-based salvage chemotherapy.

ROLE OF PHOTODYNAMIC THERAPY AND CHEMOTHERAPY IN MURINE BREAST CANCER CELLS

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Background: The biomedical photodynamic principle is based on the light-induced and photosensitizermediated killing of unwanted or harmful cells by overproducting of reactive oxygen species. The purpose of this study was to investigate the action of different nanoemulsions designed to encapsulate methylsulfonyl Zn phthalocyanine, a polyvalent and hydrophobic photosensitizer used in photodynamic therapy, and cyclophosphamide, a well-known chemotherapeutic agent used to treat aggressive breast cancer cells.

Methods: Murine breast cancer cells (Py2T) were incubated with nanoemulsions for two hours at various concentrations and were subjected to cell viability tests to find the concentration dependence profile. Thereafter, the in vitro phototoxic effect was evaluated in the presence of visible laser light irradiation. Less than 10% of Py2T viable cells were observed when photodynamic therapy and chemotherapy were combined at a 1.0 J · cm-2 laser light dose with 1.0 μM methylsulfonyl Zn phthalocyanine and 0.5 μM cyclophosphamide.

Result: The cell death assay and cell cycle arrest analysis confirmed the therapy efficiency demonstrating an increase in the apoptosis rate and in the cell cycle arrest on G2. Additionally, 20 genes related to apoptosis and 28 target genes of anti-cancer drugs were overexpressed. Four genes related to apoptosis and four target genes of anti-cancer drugs were downregulated in Py2T cells after treatment with nanoemulsion with methylsulfonyl Zn phthalocyanine and cyclophosphamide associated with photodynamic therapy.

Conclusions: It can be concluded that nanoemulsions loaded with methylsulfonyl Zn phthalocyanine and cyclophosphamide to be considered as promising formulations for photodynamic therapy and chemotherapeutic use in breast cancer treatment.

INITIAL EXPERIENCE OF ULTRA-HYPOFRACTIONATED WHOLE BREAST IRRADIATION FOR THE TREATMENT OF BREAST CANCER WITH VOLUMETRIC MODULATED ARC THERAPY

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Background: Based on the 5-year results of Fast-Forward trial, ESTRO-ACROP endorsed the consensus guideline on a 1-week regimen as one of an alternative schedule for whole breast irradiation (WBI). Double trouble issue in large fraction breast irradiation is among several concerns for clinical implementation. Herein we report the initial experience in the adjuvant WBI for breast cancer using ultra-hypofractionation via volumetric modulated arc therapy (VMAT).

Methods: Patients with breast cancer who received ultra-hypofractionated WBI (26 Gy/5 fractions in 5 days) via VMAT followed by sequential tumor bed boost (10 Gy or 16 Gy in 2-Gy fractions) at our institution were retrospectively analyzed. The study endpoints were acute and subacute (within 1 month of RT completion) toxicities. Acute and subacute toxicities were compared with our historical controls (doi: 10.1002/ijc.33525).

Result: Between 2020/06 and 2021/09, 469 patients with the pT1-2N0 disease were treated with VMAT-based ultra-hypofractionated WBI. The median PTV D95 was 98%. The maximum PTV dose (D1) was 102%. Grade 2 acute and subacute toxicities were 1% (3 pain, 2 dermatitis and 1 edema) and 0.2% (one pain), respectively, which is lower than historical controls (2501 patients treated with 3D-conformal conventional fractionated WBI, 11% and 1%, respectively). One patient (0.2%) had grade 3 toxicity (breast abscess and fistula, which required draining and suture closure in the outpatient clinics).

Conclusions: Ultra-hypofractionation (5.2 Gy fraction) delivered with high conformity of dose to a breast target via VMAT was feasible and acute toxicity was relatively low, although longer follow-up is needed.

OMISSION OF AXILLARY LYMPH NODE DISSECTION IN PATIENTS WITH YPN+ BREAST CANCER AFTER NEOADJUVANT CHEMOTHERAPY: A RETROSPECTIVE, MULTICENTER STUDY (KROG 21-06)

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Background: We evaluated the impact of omitting axillary lymph node dissection (ALND) on oncologic outcomes in breast cancer patients with residual nodal disease after neoadjuvant chemotherapy (NAC).

Methods: Medical records of patients who received NAC followed by surgical resection and had residual nodal disease were retrospectively reviewed. A total of 1273 patients from 12 institutions were included, and all patients received postoperative radiotherapy. Regarding axillary surgery, 1103 patients (86.6%) underwent ALND, and 170 patients (13.4%) underwent sentinel lymph node biopsy (SLNBx) alone. Univariate and multivariate analyses were performed for disease-free survival (DFS) and overall survival (OS) before and after propensity score matching.

Result: The median follow-up duration was 75.3 months (range, 2.5 - 182.7). Axillary recurrences occurred in 4.7% of SLNBx group (8 patients) and 4.8% of ALND group (53 patients). Before matching, the 5-yr OS rate was inferior in patients undergoing ALND (93.3% in SLNBx group vs. 86.6% in ALND group, $p = 0.002$) on univariate analysis, but not on multivariate analysis ($p = 0.325$). After matching, 148 and 285 patients were included in SLNBx and ALND group, respectively. There were no significant differences in DFS (5-yr rate, 75.8% in SLNBx group vs. 78.1% in ALND group, $p = 0.858$) and OS (5-yr rate, 93.6% in SLNBx group vs. 91.5% in ALND group, $p = 0.243$).

Conclusions: SLNBx alone did not compromise the oncologic outcomes in patients with residual nodal disease after NAC. Omitting ALND could be a viable option for axillary management in patients treated with NAC and postoperative radiotherapy.

EFFICACY AND SAFETY OF 4AC-4P DOSE-DENSE REGIMEN IN ADJUVANT CHEMOTHERAPY OF BREAST CANCER IN VIET NAM NATIONAL CANCER HOSPITAL

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Background: In breast cancer, the 4AC-4P dose-dense regimen, in which treatment is given every two weeks rather than every three weeks, is associated with better DFS outcomes and similar tolerability. Although demonstrated in several trials, the utility of this dose-dense schedule has not been adequately investigated in Vietnam.

Methods: Eligible patients with stage II-III breast cancer were treated with Doxorubicin (60 mg/m^2) and Cyclophosphamide (600 mg/m^2) followed by Paclitaxel 175 mg/m^2 every two weeks for a total of 8 cycles with Peg-filgrastim subcutaneous injections at least 24 hours after each cycle. Disease-free survial, overall survial, and adverse events were investigated in this study.

Result: Data for 152 patients were analyzed. All patients completed the schedule. The median disease-free survival estimated by Kaplan Meier was 39.2 months (95% CI 38.1-40.3). The 1-year, 2-year, and 3-year disease-free survival rates were 100%, 98.7%, 97.4% respectively. The median overall survival was 40.2 months (95% CI 39.5-41.7). The 1-year, 2-year, 3-year overall survival rates were 100%; 100%; 99.3% respectively. Grade 3-4 leukopenia, grade 3-4 neutropenia, and febrile neutropenia rates were 13.8%, 6.4%, 4.9% respectively. There was no severe anemia and thrombocytopenia.

Conclusions: Adjuvant chemotherapy of 4AC-4P in the dose-dense regimen followed by G-CSF support was effective and safe for early breast cancer patients.

MANAGEMENT OF CHEMOTHERAPY-INDUCED NAUSEA AND VOMITING (CINV)-RESULTS FROM A FOSNETUPITANT STUDY FOR BREAST CANCER PATIENTS

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Background: Chemotherapy-Induced nausea and vomiting (CINV) is a still great barrier to reaching the optimal survival benefit of cancer patients. I will tach on a clinical study of new agents for CINV. Fosnetupitant (FN) is a phosphorylated prodrug of netupitant, which has high binding affinity and selectivity for the neurokinin 1 (NK1) receptor.

Methods: Patients scheduled to receive AC/EC were randomized 1:1 to receive FosNTP 235 mg or FosAPR 150 mg both in combination with intravenous palonosetron 0.75 mg and dexamethasone 9.9 mg on day 1. FosAPR regimen was included as an exploratory arm. The primary endpoint was the incidence rate of treatment-related adverse events (TRAEs) with FosNTP. Efficacy outcomes were evaluated as secondary endpoint.

Result: Overall, 102 patients were randomized to FosNTP (N = 52) or FosAPR (N = 50), all of whom were treated with the study drug and evaluated for safety. The primary endpoint, the incidence rate of TRAEs in FosNTP arm was 21.2%. Similar data was shown in FosAPR arm (22.0%). TRAEs reported in 5% of patients were headache, diarrhea, urticaria, malaise, and decreased appetite in the FosNTP arm. Any-cause and treatment-related ISRs with FosNTP was observed in 5.8% (all grade 1) and 0% of patients, respectively. The overall (0-120 hours) complete response rate standardized by age category was 45.9% with FosNTP.

Conclusions: FosNTP demonstrated a favorable safety profile, with a very low risk of ISRs in the AC/EC setting.

THE SAFETY AND EFFICACY OF DOSE-DENSE DOXORUBICIN AND CYCLOPHOSPHAMIDE FOLLOWED BY PACLITAXEL AS POSTOPERATIVE ADJUVANT THERAPY IN VIETNAMESE PATIENTS WITH BREAST CANCER

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Background: Breast cancer (BC) is the most common cancer and the first cause leading to cancer-related death in Vietnamse women. Every 2-week (dose-dense) adjuvant doxorubicin and cyclophosphamide (AC) followed by paclitaxel (T) has been improved outcomes for BC patients (pts) globally. The aim of this study was to evaluate the adverse envents (AEs) and the results of dose-dense adjuvant ACT regimen in Vietnamese women with BC.

Methods: Pts with operable, histologically confirmed stage 2 and 3 BC were received 4 cycles of dose-dense doxorubicin 60 mg/m^2 plus cyclophosphamide 600 mg/m^2 followed by 4 cycles of dose-dense paclitaxel 175 mg/m^2. Peg-filgrastim was required routinely during chemotherapy. The endpoints of interest were overall survival (OS), disease-free survival (DFS), and toxicities.

Result: From December 2016 to June 2018 in National Cancer Hospital Vietnam 152 Vietnamese pts were enrolled. The median age was 49 years (range from 27 to 60 years). 100% pts completed 8 cycles of dose-dense adjuvant ACT therapy. No treatment-related dose reductions and dose interruption occurred. The most common grade ≥3 taxane-related AEs were hypersensitivity reactions and neuropathy, whereas the majority of toxicities during AC therapy were fatigue, nausea and neutropenia. With the median follow-up time of 37 months, DFS was 39.2 months and OS was 40.2 months.

Conclusions: Dose-dense adjuvant ACT chemotherapy with prophylactic filgrastim was feasible option in Vietnamese pts with operable BC. This study suggested that it may be a potentially preferred treatment for BC pts, particularly for women with high-risk features.

THE IMPACT OF NEOADJUVANT CHEMOTHERAPY ON CLINICAL OUTCOMES AND BREAST CONSERVATION IN PATIENTS WITH ER-POSITIVE HER2-NEGATIVE BREAST CANCER

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Background: This study aimed to evaluate the response of neoadjuvant chemotherapy (NAC) and the effect of NAC on prognosis in patients with ER-positive, HER2-negative breast cancer. We also evaluated the rate of breast-conserving surgery (BCS) conversion in patients who had difficulty in BCS at the time of initial diagnosis.

Methods: We retrospectively reviewed the medical records of 198 patients with ER-positive, HER2-negative breast cancer who received NAC at Seoul National University Bundang Hospital from 2005 to 2014. The pathologic complete response (pCR) was defined as ypT0N0 and ypTisN0. Disease-free survival (DFS) and overall survival (OS) were estimated using the Kaplan-Meier method.

Result: Of 198 patients, pCR was observed in 11 patients (5.6%). In univariable and multivariable analyses, only histologic grade 3 was an independent predictive factor for pCR (HR 3.36, 95% CI 0.842-13.398; $p = 0.09$). The median follow-up period was 65 months (range 0.8-138.0 months). The 5-year DFS (88.9% vs. 81.7%; $p = 0.369$) and OS (100% vs. 95.2%; $p = 0.318$) for pCR and non-pCR groups were not statistically different. In univariable analysis, higher clinical and pathologic T stage was associated with poor OS and DFS. Higher clinical N stage affected poor OS. In multivariable Cox regression analysis, the clinical T stage was an independent prognostic factor for DFS (HR 3.357, $p = 0.002$). In 63 patients with NAC for BCS conversion, 87.3% successfully underwent BCS.

Conclusions: Although NAC yielded a low pCR rate and no association between pCR and prognosis in patients with ER-positive, HER2-negative breast cancer, NAC could be considered for BCS conversion by reducing tumor size.

THE INFLUENCE OF PSYCHOLOGICAL INTERVENTION OF ACCEPTANCE COMMITMENT THERAPY (ACT) ON TNF-A LEVELS AND ITS IMPACT ON ANTHRACYCLINE BASED NEOADJUVANT CHEMOTHERAPY RESPONSE IN LOCALLY ADVANCED BREAST CANCER

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Background: In developing countries, breast cancer patients usually come to health facility in advanced stage. One of the reasons of the delay is the anxiety and fear of surgery or side effects of chemotherapy/radiotherapy. This study assessed the effect of psychological intervention through Acceptance Commitment Therapy (ACT) on TNF-A levels and its response to anthracycline-based neoadjuvant chemotherapy in locally advanced breast cancer (LABC) patients.

Methods: This is an experimental study with double-blind randomized control trial design. We recruited LABC women who received anthracycline-based neoadjuvant chemotherapy. ACT intervention was given 3 sessions in the treatment group. Stress level scores was measured using Acceptance and Action Questionnaire-II (AAQ-II). TNF-A levels were measured before and after the treatment, as well as evaluating chemotherapy responses.

Result: ACT reduced TNF-A levels by an average of 1.21 pg/ml from 5.42 ± 1.99 pg/ml to 4.22 ± 1.58 pg/ml ($p = 0.026$). The Pearson correlation test showed that TNF-A levels were positively correlated with stress levels score AAQ-II ($p = 0.043$). There were 17 (56.7%) and 13 (43.33%) patients with positive and negative response after neoadjuvant chemotherapy. In the treatment group, the positive response was higher than the control group (80.0% vs. 33.3%) ($p = 0.027$). Positive chemotherapy responses had lower TNF-A levels (3.84 ± 1.42) than negative responses (6.62 ± 2.48) ($p = 0.001$).

Conclusions: The treatment group by ACT psychological intervention reduced the stress level of the patients. Stress levels was positively correlated with levels of TNF-A. TNF-A decrease improved the response of anthracycline-based neoadjuvant chemotherapy.

DELAYED INITIATION OF ADJUVANT CHEMOTHERAPY DOES AFFECT SURVIVAL IN BREAST CANCER PATIENTS, STUDY FROM TAIWAN CANCER REGISTRATION DATABASE

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Background: Adjuvant chemotherapy is an important backbone preventing recurrence in high-risk group. The consensus of chemotherapy starting time should not beyond 40 days after surgery so as not to affect the cytotoxic effect. However, the optimal time of chemotherapy administration for breast cancer patients is not definitely defined. In Taiwan, adjuvant chemotherapy is reimbursed in national health insurance and every breast cancer patient could receive this adjuvant treatment regardless of their income. Thus, we want to review the real-world data of impaction of delayed chemotherapy initiation in Taiwan.

Methods: Form 2011~2017, there were 27931 breast cancer patients underwent chemotherapy with complete data of cancer histology, stage, immunohistochemistry result, time between surgery to chemotherapy initiation, time of recurrence, and survival status in database. Time to chemotherapy initiation is categorized into four groups: within 30 days, 31~60 days, 61~90 days, more than 90 days.

Result: In general population underwent chemotherapy, our preliminary data showed delayed initiation of chemotherapy did not affect the overall survival in 31~60 days ($p = 0.379$, HR = 1.045) and 61~90 days ($p = 0.257$, HR = 1.150), but significant difference in more than 90 days group ($p = 0.000$, HR = 1.934). In triple negative and triple positive subgroup, the impaction of delayed initiation in survival is more prominent. Margin status and number of lymph node metastasis were also important factor affecting overall survival. More detailed date will be discussed in the subsequent presentation.

Conclusions: When adjuvant chemotherapy is justified in breast cancer patients, delayed initiation of chemotherapy (especially more than 90 days) does impact the overall survival.

LONG-TERM OUTCOMES OF BREAST CANCER PATIENTS WITH PATHOLOGIC COMPLETE RESPONSE AFTER NEOADJUVANT CHEMOTHERAPY

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Background: Patients who achieved pathologic complete response (pCR) after neoadjuvant chemotherapy (NCT) for breast cancer show significant better survival outcomes than those with residual disease. However certain proportion of patients still experience any type of recurrence or cancer-related death. We analyzed risk factors of poor survival outcome and recurrence pattern of patients who achieved pCR after NCT.

Methods: We retrospectively reviewed 732 patients who had pCR after NCT and curative surgery from 2008 to 2018. pCR is defined as both ypT0N0 and ypTisN0. We used several clinico-pathological factors including age, grade, receptor status and clinical stage to find any risk factors for poor survival outcomes of iDFS, DMFS and OS.

Result: Mean age at diagnosis was 47.8 ± 10.7, with whom 533 (72.8%) had clinically positive nodes and 286 (39.1%) had clinical stage III. 187 (25.5%) had residual in-situ disease. During the median follow up period of 58.3 (3.7-129.0) months, total 50 (6.8%) invasive disease events and 20 (2.7%) death had occured. There was no clinical factors associated with iDFS. However, higher clinical stage was associated with more distant metastasis (hazard ratio 2.84 (95% CI 1.31-6.2), $p = 0.008$). Residual in-situ disease (ypTisN0) (hazard ratio 3.07 (95% CI 1.15-8.17), $p = 0.025$) and higher clinical stage (hazard ratio 4.95 (95% CI 1.737-14.10), $p = 0.003$) were associated with worse survival.

Conclusions: Overall, patients with pCR showed favorable long-term survival. No significant factors were associated with poor disease free survival. Initial stage and residual in-situ disease were associated with poor survival outcome.

EFFICACY OF LIMITED DOSE MODIFICATIONS FOR PALBOCICLIB-RELATED GRADE 3 NEUTROPENIA IN HORMONE RECEPTOR POSITIVE METASTATIC BREAST CANCER

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Background: Frequent neutropenia hinders uninterrupted palbociclib treatment in hormone receptor (HR)-positive breast cancer patients. Previously, we reported the safety of palbociclib dose maintenance for afebrile grade 3 neutropenia. Herein, we compared efficacy outcomes in multicenter cohorts of metastatic breast cancer (mBC) patients who received palbociclib following conventional dose modification or limited modified schemes regarding afebrile grade 3 neutropenia.

Methods: HR-positive, human epidermal growth factor receptor 2-negative mBC patients (434) who received palbociclib with letrozole as first-line therapy were analyzed and classified into four groups based on neutropenia grade and afebrile grade 3 neutropenia management: Group 1 (maintained palbociclib dose, limited scheme), Group 2 (dose delay or reduction, conventional scheme), Group 3 (no afebrile grade 3 neutropenia event), and Group 4 (grade 4 neutropenia event). Primary and secondary endpoints were progression-free survival (PFS) between Groups 1 and 2 and PFS, overall survival, and safety profiles among all groups, respectively.

Result: At follow-up (median 23.7 months), Group 1 (2-year PFS: 67.9%) showed significantly longer PFS than Group 2 (2-year PFS: 55.3%; $P = 0.036$). This trend was maintained across all subgroups and upon adjustment for age, disease status, visceral metastasis, and number of organ involvements (hazard ratio 0.665, $P = 0.044$). Overall toxicity profiles were similar between the two groups. Febrile neutropenia occurred in only one patient in Group 1 and two patients in Group 2, without mortality.

Conclusions: Limited dose modification for palbociclib-related grade 3 neutropenia may lead to longer PFS than the conventional dose scheme without increasing toxicities.

ELACESTRANT, AN ORAL SERD, VS INVESTIGATOR'S CHOICE OF ENDOCRINE MONOTHERAPY FOR ER+/HER2- MBC FOLLOWING PROGRESSION ON PRIOR ENDOCRINE AND CDK4/6 INHIBITOR THERAPY: RESULTS OF EMERALD PHASE 3 TRIAL

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Background: Patients (pts) with ER+/HER2-advanced/metastatic breast cancer (mBC) progressing after 1st-line therapy have a poor prognosis. Elacestrant, an oral selective estrogen receptor degrader (SERD), demonstrated activity in early studies.

Methods: EMERALD (NCT03778931) enrolled pts with ER+/HER2-mBC who had 1-2 lines of endocrine therapy, CDK4/6i pretreatment, and ≤ 1 chemotherapy. Pts were randomized to elacestrant

(400 mg orally daily) or standard of care (SOC; fulvestrant or aromatase inhibitor). Primary endpoints were progression-free survival (PFS) in all pts and pts with mESR1.

Result: 477 pts were enrolled (n = 228 with mESR1). Demographics were well-balanced between groups; heavily pre-treated [70% visceral metastasis, 43% received 2 prior lines]. There was a 30% reduction in the risk of progression or death in the elacestrant arm in all pts (Hazard ratio [HR] = 0.70[95% Confidence interval [CI]: 0.55-0.88]; *P* = 0.0018), and a 45%(HR = 0.55[95% CI: 0.39-0.77]; *P* = 0.0005) reduction in pts with mESR1. Interim overall survival (OS) analysis demonstrated a trend in favor of elacestrant in all pts (HR = 0.75[95% CI: 0.54-1.04]; *P* = 0.0821) and in pts with mESR1(HR = 0.59 [95% CI: 0.36-0.96]; *P* = 0.0325). Common treatment-related adverse events (TRAEs) with elacestrant vs SOC included nausea (25.3% vs 8.7%), vomiting (11% vs 2.6%), and fatigue (11% vs 7.9%), mostly grade 1/2, and TRAEs leading to discontinuation were infrequent (3.4% vs 0.9%).

Conclusions: Elacestrant is the first oral SERD demonstrating a statistically significant and clinically meaningful improvement of PFS vs SOC in the overall population and in pts with mESR1. Elacestrant was well tolerated and has the potential to become the new SOC for pts with ER+/HER2-mBC.

RISK OF DEVELOPING DEPRESSION FROM ENDOCRINE TREATMENT: A NATIONWIDE COHORT STUDY OF WOMEN ADMINISTERED TREATMENT FOR BREAST CANCER IN KOREA

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Background: There are many articles about the relationship between endocrine treatment and depression in breast cancer. Although a large prospective study reported no difference on the mood of depression with receiving tamoxifen, there are still limited long-term follow-up data of depression in breast cancer. The purpose of this study was to evaluate the relationship between endocrine treatment and depression by using retrospective population-based registry.

Methods: This nationwide population-based cohort study used data obtained in a 14-year period between 2007 and 2021 in the Korean National Health Insurance claims database. All female breast cancer patients diagnosed between 2009 and 2010 were included. Patients without receiving endocrine treatment constituted the control group. The main study outcome was the risk of developing depression according to endocrine treatment.

Result: From a total of 123,681 patients with breast cancer, patients without underwent surgery were excluded. Data for 11,109 patients receiving endocrine treatment and 6,615 controls were analyzed before matching. After matching for comorbidities and age, either group comprised 6,532 patients. The mean and median follow-up period was 113.31 and 119.71 months. Before and after matching, endocrine treatment was not a significant risk factor for developing depression ($p = 0.7295$ and $p = 0.2668$). In addition, endocrine treatment was not a significant factor for increasing suicide attempt ($p = 0.6381$ and $p = 0.8366$).

Conclusions: Using longitudinal nationwide population-based cohort, this study showed endocrine treatment in breast cancer patients was not a risk factor for depression. This finding provide a basis for physician to reduce excessive concern about the risk of developing depression associated with endocrine treatment.

REAL WORLD EXPERIENCE OF CDK4/6 INHIBITORS ASSOCIATED NEUTROPENIA AND PHARMACOKINETICS STUDY OF PALBOCICLIB IN A PATIENT WITH PERITONEAL DIALYSIS

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Background: CDK4/6 inhibitors have shown great efficacy in prolonging survival and is current standard of care for hormone positive (HR(+)) metastatic breast cancer (mBC). Despite well tolerability and ease of use, the most common side effect of CDK4/6 inhibitors is myelosuppression, with neutropenia the most prevalent adverse effect, especially for palbociclib and ribociclib. Studies have proposed genetic factors predisoposing to neutropenia, including Duffy antigen polymorphisms, ABCB1 and ERCC1 polymorphisms, CDK6 polymorphisms, and others. Subgroup studies from PALOMA trials have suggested that Asian patients receiving palbociclib have higher rates of neutropenia, although the exact explanation is unknown.

Methods: We conducted a retrospective analysis of 94 patients who received palbociclib for HR(+) mBC at the Taipei Veterans General Hospital. Clinical features, incidence and time course of neutropenia were analyzed. We also analyze pharmacokinetics of a patients with peritoneal dialysis who developed neutropenia on palbociclib.

Result: In our study, both progression free survival (PFS) and overall survival (OS) were not reached in 1st line subgroup, which could be explained by the relatively short follow up time (20.2 months), as PALOMA-2 reported a median PFS of 27.6 months. We observed a high incidence of neutropenia (96.8% all grade, 82% grade 3/4). We also identified high prevalance of SNPs in Taiwanese patients potentially associated with palbociclib associated neutropenia. We also quantified palbociclib levels from blood and peritoneal fluid and analyzed phamaokinetics in a patient with peritoneal dialysis.

Conclusions: Palbociclib is associated with a higher incidence of neutropenia in Taiwanese patients. Genetic factors may play a role in this phenomenon.

REAL WORLD EXPERIENCE IN TRASTUZUMAB BIOSIMILARS FOR BREAST CANCER IN TAIWAN

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Background: Apart from generics, biosimilars are interchangeable biological medicines of the same safety, quality, and efficacy in the treatment of cancers and immunological diseases. With regard to breast cancer specifically, trastuzumab, the reference monoclonal antibody biologic, has been the standard of care for early and advanced HER2-positive breast cancer since 1998. By offering the same effectiveness with lower price, the utilization of trastuzumab biosimilars could relieve the burdens of patients and government medical expenses, as well as expanding patient's access to HER2 targeted therapy. This study provides an experience in utilization of trastuzumab biosimilars from Kaohsiung Veterans General Hospital.

Methods: We included a total of 79 patients with HER2-positive breast cancer treated with trastuzumab biosimilars from February, 2020 to December, 2021. There are 28 cases in neoadjuvant groups, 16 cases in adjuvant groups, and 35 cases in metastatic groups.

Result: In the neoadjuvant group, ten patients reached pathologic complete response (pCR) after surgery. pCR rate was 40%. In the metastatic group, first-line treatment with pertuzumab and trastuzumab biosimilars had better disease control rate. In the adjuvant group, we still need a longer period of time to investigate. No adverse events of cardiac toxicity were presented.

Conclusions: In our preliminary experiences, the affordability and safety of trastuzumab biosimilar are presented. The efficacy of biosimilar trastuzumab is noted in neoadjuvant settings. For metastatic settings, dual blockade results in better disease control. For adjuvant settings, we still need longer time to follow up.

ADJUVANT TARGET THERAPY FOR PATIENTS WITH HER2 POSITIVE BREAST CANCER ACHIEVING PATHOLOGICAL COMPLETE RESPONSE AFTER NEOADJUVANT THERAPY

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Background: Neoadjuvant chemotherapy (NAC) is the accepted approach for women with locally advanced breast cancer for downsize. The clinical benefit of adjuvant dual blockade as trastuzumab and pertuzumab remained unknown in patients achieving pathological complete response (pCR). The aim of this study is to analyze the effect of adjuvant dual blockade and single blockade therapy in HER2 positive breast cancer patients achieving pCR after NAC.

Methods: A retrospective study was analyzed from 2010 to 2019, and a total of 441 invasive HER2 positive breast cancer patients underwent mastectomy or breast conserving surgery (BCS) after NAC at Linkou Chang Gung Memorial Hospital were enrolled.

Result: The median follow-up time was 39.7 months. The median age was 50 years-old (range 29-93). pCR was achieved in 186 (42.2%) patients. One hundred forty patients (31.7%) receiving neoadjuvant chemotherapy dual blockade (trastuzumab + pertuzumab) and 69 patients (49.2%) achieved pCR while 117 patients (38.9%) achieved pCR receiving single blockade in total 301 patients, respectively ($p = 0.039$). Of 69 pCR patients with neoadjuvant dual blockade therapy, adjuvant dual blockade therapy was given in 24 patients (34.8%). Four patients (16.7%) of 24 patients recured in adjuvant dual blockade setting while compared 5 patients (11.1%) of 45 patients, respectively ($p = 0.1354$). Two deaths (4.4%) in adjuvant single blockade therapy were observed while no death (0%) was found in adjuvant dual blockade therapy ($p = 0.473$).

Conclusions: Our findings concluded that there was no significant difference between adjuvant dual blockade therapy and adjuvant single blockade therapy in HER2 positive breast cancer patients achieving pCR after NAC.

PATHOLOGIC COMPLETE RESPONSE RATE ANALYSIS OF HORMONE RECEPTOR NEGATIVE BREAST CANCER WITH RADIOLOGIC COMPLETE RESPONSE AFTER NEOADJUVANT CHEMOTHERAPY

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Background: We performed this study to analyze the predictive factors of complete response (CR) rate in hormone receptor negative breast cancer after neoadjuvant chemotherapy in Korea during the last 12 years (2007-2019).

Methods: We retrospectively anlyzed 315 patients with axillary lymph node positive and hormone receptor negative breast cancer who received neoadjuvant chemotherapy before surgery. We reviewed the collected database including clinical manifestations, MRI finding after neoadjuvant chemotherapy, surgical methods, pathology report after surgery, types of adjuvant therapy, presence or absence of recurrence.

Result: There were 50 cases (15.9%) of radiologic CR in the breast and axilla MRI image after neoadjuvant chemothrepy and among them 15 (9.7%) of pathologic CR cases. Out of all patients, 154 cases (48.9%) of HER2 subtype and 161 cases (51.1%) of triple negative subtype. Multivariate logistic regression demonstrated that pathologic complete response (pCR) was significantly associsted with age ($p = 0.009$) and HER2 positivity ($p = 0.001$). Trastuzumab combination therapy was used in all HER2 positive patients, and the use of Pertuzumab ($p = 0.172$) did not have a statistically significant relationship with pCR.

Conclusions: Recently, Trastuzumab-included regimen is used in neoadjuvant chemotherapy for HER2-positive breast cancer. Its effectiveness has been proven in previous studies. We confirmed that age and HER2 positivity is the predictive factor of pathologic CR among radiologic CR patients.

ENTELON IMPROVES TRASTUZUMAB RESISTANCE THROUGH INHIBITING FN1 ESPRESSION IN HER2 POSITIVE BREAST CANCERS

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Background: Fibronectin (FN) plays an important role on cell adhesion, metastasis in various types of cancer. Here, we investigated the function of FN expression on HER2+ breast cancer cells. Furthermore, we studied the pharmacological effect of Entelon on the regulatory mechanism of FN in trastuzumab-resistant (TR) cells.

Methods: We established an acquired trastuzumab-resistant cells derived from BT474 cells. Profiles of gene expression were analyzed by RNA sequencing. Levels of mRNA and protein expression were analyzed by real-time PCR and western blotting. Tumorigenecity was analyzed using orthotopic xenograft mouse models.

Result: Using the RNA sequencing, the expression of FN was significantly increased in TR cells compared to parental cells. Aberrant FN expression was related with poor prognosis in HER2-positive (HER2+) breast cancer patients. FN expression directly enhanced cell adhesion and migration abilities. While investigating the mechanism of FN regulation, FN expression levels were increased by EGFR overexpression whereas this induction was decreased by neratinib. We investigated the pharmacological effect of Entelon on EGFR and/or HER2 signaling pathway. As a result, FN expression was significantly decreased by Entelon treatment in TR breast cancer cell lines. EGF/EGFR signaling axis was suppressed by Entelon treatment. Finally, we observed that the tumorigenecity by FN was significantly reduced by Entelon.

Conclusions: FN expression is associated with the survival of HER2+ breast cancer patients. FN expression is regulated by EGFR signaling pathway but not by HER2 signaling pathway. Furthermore, Entelon downregulates FN expression through suppression of EGFR expression. Therefore, we suggest that Entelon will be a promising drug to escape trastuzumab resistance.

ENHANCED MULTIMODAL CANCER THERAPY WITH PLATELET MEMBRANE-BASED BIOMIMETIC NANOSYSTEM

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Background: Cancer is still one of the major challenges in the world. In recent years, a large number of new drug delivery nanocarriers have been developed. However, the materials themselves often have toxic and side effects. This reason seriously hinders the further development of drug loading system. Therefore, it is crucial to construct a safe and effective drug carrier.

Methods: Herein, we constructed Platelet (PLT)-poly (lactic-co-glycolic acid) (PLGA)-based nano platform and encapsulated photosensitizer indocyanine green (ICG) and chemotherapeutic drug doxorubicin (DOX).

Result: This biomimetic nano carrier with multimodal therapeutic effect promotes the effective delivery of DOX to tumor cells by 808 nm light. In addition, PLT membrane modified nanocarriers have the ability of tumor targeting, reducing immune clearance and prolonging blood circulation time. The outcomes of the in vitro and in vivo anticancer therapy demonstrated that the as-fabricated therapy system exhibited strong therapeutic effect.

Conclusions: Since each component in the system has been clinically approved, the as-proposed therapy system has the potential for practical applications in clinical cancer treatment. This study will open a new avenue for potential applications of PLT in clinical anticancer therapy.

EFFECTS OF RUXOLITINIB AND CALCITRIOL COMBINATION TREATMENT ON VARIOUS MOLECULAR SUBTYPES OF BREAST CANCER

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Background: The anticancer effects of ruxolitinib and calcitriol against breast cancer have been reported in our previous study, in luminal B subtype MCF7-HER18 breast cancer cells in vitro However, the effect of ruxolitinib and calcitriol combination treatment on various molecular subtypes of breast cancer remains unexplored.

Methods: In this study, we used MCF-7, SKBR3, and MDA-MB-468 cells to investigate the effect of ruxolitinib and calcitriol combination treatment on cell proliferation, apoptosis, cell cycle, and cell signaling markers, in vitro and in vivo.

Result: Our results revealed a synergistic anticancer effect of ruxolitinib and calcitriol combination treatment in SKBR3 and MDA-MB-468 cells, but not in MCF-7 cells in vitro, via cell proliferation inhibition, apoptosis induction, cell cycle arrest, and alteration of cell signaling protein expression, including cell cycle-related (cyclin D1, CDK1, CDK4, p21, and p27), apoptosis-related (c-caspase and c-PARP), and cell proliferation-related (c-Myc, p-p53, and p-JAK2) proteins. Furthermore, in the MDA-MB-468 xenograft mouse model, we demonstrated the synergistic anti-tumor effect of ruxolitinib and calcitriol combination treatment, including alteration of c-PARP, cyclin D1, and c-Myc expression, without significant drug toxicity.

Conclusions: The combination exhibited a synergistic effect in HER2-enriched and triple-negative breast cancer subtypes. In conclusion, our results suggest different effects of the combination treatment of ruxolitinib and calcitriol depending on the molecular subtype of breast cancer.

THE EFFECT OF COMBINED CISPLATIN WITH B-CATENIN INHIBITOR IN TRIPLE NEGATIVE BREAST CANCER CELLS

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Background: Triple Negative Breast Cancer (TNBC) is the most aggressive breast cancer subtype, characterized by limited treatment options and poor prognosis. Poly-(ADP)-ribose polymerase inhibitors (PARPi) and platinum-based chemotherapeutic drugs are current therapies for TNBC with BRCA loss. The Wnt/β-catenin signaling pathway is a developmental signaling cascade that plays a prominent role in cancer. The β-catenin small-molecule inhibitor, ICG-001, is proposed to prevent β-catenin in the nucleus from being able to perform CBP-dependent stemness-related transcription during canonical Wnt/β-catenin signaling pathway. In this study, we investigate the combinatory effect of platinum and β-catenin inhibitor in BRCA mutant TNBC cells and to explore potential mechanisms.

Methods: HCC1937 is a human TNBC cell line with BRCA1 mutation. These cells were treated with cisplatin and/or ICG-001. Cell viability was measured using the Cell Counting Kit-8 (Enzo Life Sciences) according to the manufacturer's protocol and Western blot analysis was used for exploration of mechanisms of synergy with 2 drugs.

Result: HCC1937 cells showed increasement β-catenin expression with cisplatin treatment in dose dependent manner compared with other type of TNBC cell lines. Also they showed synergistic effect in terms of cell proliferation with cisplatin and ICG-001 treatment. Increased γH2AX and decreased β-catenin activity were observed with the combination 2 drugs therapy.

Conclusions: We suggest that β-catenin inhibitor and cisplatin combination resulted into significant regression of tumor growth in BRCA mutant TNBC cells.

ENTELON PREVENTS TUMORIGENESIS THROUGH ANTI-INFLAMMATION IN TRIPLE-NEGATIVE BREAST CANCER MODELS

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Background: Interleukin-1 (IL1) is a proinflammatory cytokine and contributes to tumor invasion, angiogenesis and metastasis. IL1 is upregulated in several types of cancers, including breast, lung and melanoma. Triple-negative breast cancer (TNBC) is a heterogenous disease without clinically approved therapeutic target drugs against IL1. Here, we focused on the pharmacological effect of Entelon (ETL) on the tumorigenesis of TNBC by IL1A.

Methods: Clinical significance of IL1A in TNBC was analyzed through the Kaplan-Meier (KM) plotter database. An orthotopic xenograft model was used to verify the effect of ETL. Secreted proteins were analyzed by Proteome Profiler Mouse Cytokine Array and Human Quantikine ELISA. Levels of various genes mRNA and protein expression were analyzed real-time PCR, western blotting and immunohistochemistry assay.

Result: Clinically, IL1A induction is related with poor prognosis of TNBC patients. We found that IL1A expression enhanced the cell growth and invasiveness of TNBC and also increased a variety of chemokines such as CCL2 and IL8. Induction of IL1A was suppressed by the ETL treatment. ETL inhibited the MEK/ERK and PI3K/AKT signaling pathway and suppressing the lung metastasis of TNBC cells through downregulation of IL1A.

Conclusions: Aberrant IL1A induction elicited tumor growth and invasiveness in the TNBC models. IL1A expression level plays a pivotal role in the recurrence of breast cancer and could be a target of TNBC treatment. We proved that ETL reduced the basal IL1A level by inhibiting MEK/ERK- or PI3K/AKT-signaling pathway in TNBC. Thus, we will further strive to change the drug repositioning of ETL by demonstrating its drug efficacy by inhibiting IL1A.

PROGNOSTIC VALUE OF SUVMAX IN BREAST CANCER: A SYSTEMATIC REVIEW AND META-ANALYSIS

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Background: The aim of the present study was to assess the prognostic capability of SUVmax measured in the primary tumor and axillary lymph nodes by pretreatment ^{18}F-FDG PET/CT and to analyze outcomes according to the molecular breast cancer subtypes through meta-analysis.

Methods: A systematic review of the literature using PubMed and EMBASE showed a total of 16 eligible studies meeting inclusion criteria of 3713 patients with breast cancer. The databases were systematically searched using keywords for breast cancer, PET/CT, and SUVmax; the extracted studies reported at least one form of survival data, event-free survival and overall survival. Comparative analyses of the pooled hazard ratios for EFS and OS were performed to assess their correlations with SUVmax.

Result: The pooled HRs of high SUVmax in the primary tumor and ALN were 3.29 (95% CI 2.145.06; I2 = 82%; $P < 0.00001$; I2 = 82%) and 3.72(95% CI 1.1512.01; I2 = 92%; $P = 0.03$), respectively. Patients with higher SUVmax demonstrated a poorer survival prognosis. Furthermore, comparative analyses according to the molecular subtypes demonstrated that the SUVmax in the primary tumor or ALN can be a predictive parameter in patients with the luminal subtype disease. Subtype analysis results indicated a significant association of the luminal group, with a HR of 2.92 (95% CI 1.655.17; I2 = 8%; $P = 0.0002$).

Conclusions: SUVmax from pretreatment is a significant prognostic factor for EFS in patients with breast cancer. Despite several limitations, correlation with molecular subtype (luminal type) was demonstrated. Considering as limitations due to sample size and heterogeneity, further researches including large-scale prospective studies is required to investigate more precise prognostic capabilities.

EVALUATION OF USEFULNESS OF HOUNSFIELD UNIT, A QUANTITATIVE MEASUREMENT TO INTERPRET COMPUTED TOMOGRAPHY, AS A PROGNOSTIC FACTOR IN PATIENTS WITH BREAST CANCER

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Background: Angiogenesis is associated with poor survival. However, previous clinical studies assessing anti-angiogenesis methods demonstrated no clear overall survival benefits due to the lack of appropriate biomarkers. This study aimed to identify biomarkers that reflect tumor angiogenesis and serve as prognostic factors.

Methods: Patients with stage I-III breast cancer who completed the planned treatment were assessed. Data were retrospectively collected from the Wonju Severance Christian Hospital database of Yonsei University and the Korean National Cancer Center database.

Result: A total of 624 patients were enrolled. Patients were divided into two groups based on the cut-off value, 37.14% of the proportional ratio between the maximum Hounsfield unit (HU) of the tumor and maximum HU of the aortic arch (maximum tumor-aorta ratio, TAR). The Kaplan-Meier curve and log-rank test revealed that the high TAR group exhibited significantly worse overall survival rate ($p < 0.001$), and distant relapse-free survival rates ($p = 0.001$). The Cox proportional hazard model indicated that T stage (T2-T3), lymph node metastasis, ER negativity, and high TAR were significant risk factors for overall mortality.

Conclusions: TAR measured by computed tomography before treatment is a potential prognostic factor for overall and distant relapse-free survival in patients with breast cancer. TAR might be a potential biomarker for patients who will benefit from anti-angiogenesis agents.

HIGH BMI (≥25KG/M2) AS A RISK FACTOR FOR HIGH 21-GENE RECURRENCE SCORE (>20) IN YOUNG ER+HER2- BREAST CANCER

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Background: Several lines of evidence suggested that body mass index (BMI) might interact with 21-gene recurrence score (RS) in ER+ breast cancer. We aimed to assess the association between RS and BMI according to age groups.

Methods: We retrospectively identified 2,298 patients with ER+HER2- breast cancer who underwent Oncotype DX test from two hospitals. High BMI was defined as 25 kg/m^2 or greater. In premenopausal women, High RS was defined as greater than 20. The interaction between RS and BMI, and young age (≤ 45) was tested. A binary logistic model was used to identify risk factors for high RS.

Result: In all patients, RS was not correlated with BMI. In postmenopausal, the relationship between RS and BMI showed an inverse weak correlation, whereas it tended to be positively correlated in premenopausal. Among women who were 45 years of age or younger (n = 776), RS and BMI correlated significantly (Perason's R, 0.119). The Pinteraction of the correlations between RS and BMI was significant with age. Of these young patients, the proportion of patients with a RS greater than 20 was significantly higher in patient with high BMI than in those with normal BMI (46% vs 27%). Additionally, in multivariable analysis, high BMI was demonstrated to be a risk factor for high RS (Odds Ratio [OR], 1.96; 95% CI, 1.22-3.16; P = 0.006).

Conclusions: In young women who were 45 years of age or younger, high BMI was a risk factor for high RS. Our findings suggest that increasing BMI might be associated with higher genomic risk in young ER+ breast cancer.

INFLUENCE OF THE LIVER TO SPLEEN RATIO BY THE PREOPERATIVE LOW-DOSE COMPUTED TOMOGRAPHY ON THE PROGNOSIS OF BREAST CANCER

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Background: This study investigated the prevalence of fatty liver disease in breast cancer patients by the liver to spleen (L/S) ratio using preoperative computed tomography (CT) scans, and also analyzed the prognostic role of the preoperative L/S ratio in breast cancer.

Methods: We utilized data of 933 consecutive primary breast cancer patients with preoperative low-dose CT who received surgery for primary invasive breast cancer at Seoul National University Boramae Medical Center. Fatty liver was diagnosed by traditional standard using the attenuation ratio of liver and spleen less than 1.0.

Result: The low L/S ratio group showed worse overall survival compared to the high L/S ratio group ($p = 0.007$). The L/S ratio was a significant prognostic factor by both univariable analysis (Hazard ratio [HR], 2.104; 95% Confidence interval [CI], 1.213-3.651) and multivariable analyses (HR, 1.869; 95% CI, 1.014-3.446). The L/S ratio was a significant prognostic indicator in patients who received lumpectomy, radiation therapy, chemotherapy, anti-HER2 therapy. The low L/S ratio group showed lower body mass index (BMI), glutamic oxaloacetic transaminase (GOT), and glutamic pyruvic transaminase (GPT) compared to the high L/S ratio group, and the low L/S ratio showed a negative correlation with BMI, GOT, and GPT.

Conclusions: The preoperative L/S ratio was a significant independent prognostic factor in breast cancer regarding overall survival, and the low L/S ratio group showed a worse prognosis compared to the high L/S group. As a surrogate marker of nonalcoholic fatty liver disease, the preoperative L/S ratio could be usefully utilized for prognostication of breast cancer patients in a clinical setting.

MACHINE LEARNING-BASED RADIOMICS MODELS FOR THE PREDICTION OF LOCOREGIONAL RECURRENCE IN PATIENTS WITH BREAST CANCER

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Background: Locoregional recurrence (LRR) is the predominant pattern of relapse after definitive treatment of breast cancer. We aimed to develop machine learning (ML)-based radiomics models for the prediction of LRR in patients with breast cancer, using preoperative magnetic resonance imaging (MRI).

Methods: Data of localized breast cancer patients who underwent preoperative MRI between January 2013 and December 2017 were collected. Propensity score matching (PSM) was performed to adjust for clinical factors between patients with/without LRR. Images were taken from T2-weighted with/without fat-suppressed and contrast-enhanced T1-weighted with fat-suppressed MRI. We designed 6 ML-based models and compared the performance of each: 4 single classifiers, 1 ensemble of 4 single classifiers, and 1 trained with meta-learning. Meta-learning consists of Logistic Regression re-training using probability values obtained from 3 classifiers consisting of MLP, Kneighbors, and GaussianNB.

Result: After PSM, there were 28 patients with LRR and 86 patients without LRR (total 114 patients). Of these, 80 patients were randomly selected to train the models, and the remaining 34 patients were used to evaluate performance of the trained models. Among 5,064 features obtained from each patient, 420 features were selected. Four single classifiers and ensemble model performed poorly (Area Under the Curve [AUC] range 0.39-0.61). Meta-learning showed superior performance compared to previous models (AUC 0.74, accuracy 73.5%, sensitivity 75.0%, specificity 73.1%).

Conclusions: We developed radiomics model using preoperative MRI with meta-learning to predict breast cancer patients at high LRR risk prior to treatment. This model should be further validated with large numbers of patients.

OUTCOMES IN METAPLASTIC BREAST CANCER PATIENS

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Background: This study evaluated the outcomes of metaplastic breast cancer, a rare and aggressive subtype of breast cancer.

Methods: A retrospective study of female patients diagnosed with metaplastic breast cancer between January 2001 to August 2020.

Result: Of 170 identified patients, 148 (87.1%) were non-metastatic and 22 (12.9%) were metastatic at diagnosis. 77.6% (n = 132) of patients presented with ≥ cT2 disease, and 67.6% (n = 115) were cN0. Majority of patients had triple negative (64.7%, n = 110), ER/PR weakly positive and HER2 negative (10.6%, n = 18) cancers, and 74.1% (n = 126) of all patients had grade 3 disease. Analysis was done for patients that completed curative treatment with no synchronous or previous cancers (n = 127, 75%). With a median follow-up of 48 months, there were 34 cancer related deaths and 44 disease recurrences. The 4-year overall survival (OS) and disease free survival (DFS) were 50.4% and 37.8% respectively. On multivariate analysis, patients that received adjuvant radiotherapy (RT) had better OS and DFS with hazard ratios of 0.23 (95% Confidence interval [CI]; 0.08-0.71, $p = 0.01$) and 0.22 (95% CI; 0.08-0.57, $p < 0.005$) respectively, whereas there was no impact of histological subtype, pathologic stage, type of surgery or chemotherapy use on OS and DFS.

Conclusions: Patients with metaplastic breast cancer have generally poor OS and DFS. RT is associated with improved survival.

Poster Presentation

CLINICAL SIGNIFICANCE OF HER2-LOW EXPRESSION IN EARLY BREAST CANCER: A NATIONWIDE STUDY FROM THE KOREAN BREAST CANCER SOCIETY

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Background: There is an increasing interest in HER2-low breast cancer with promising data from clinical trials using novel anti-HER2 antibody-drug conjugates. We explored the differences in clinicopathological characteristics and survival outcomes between HER2-low and HER2-IHC 0 breast cancer.

Methods: Using nationwide data from the Korean Breast Cancer Registry between 2006 and 2011, 30,491 patients with stages I to III breast cancer were included in the analysis: 9,506 (31.2%) in the HER2-low group and 20,985 (68.8%) in the HER2-IHC 0 group. Kaplan-Meier and Cox proportional hazards regression survival analysis were used to compare breast cancer-specific survival (BCSS) between the two groups.

Result: HER2-low breast cancer was more frequent in patients with hormone receptor (HR)-positive breast cancer than in those with triple-negative breast cancer (TNBC). Within HR-positive breast cancer, HER2-low breast cancer was associated with fewer T4 tumors, higher histological grade, and a negative lymphatic invasion. Within TNBC, HER2-low breast cancer was associated with a high lymph node ratio and positive lymphatic invasion. HER2-low breast cancer was associated with a lower Ki-67 labeling index. HER2-low breast cancer showed significantly better BCSS than HER2-IHC 0 breast cancer in HR-positive breast cancer and TNBC. In multivariate analysis, the impact of low HER2 expression on BCSS was significant only in TNBC (hazard ratio, 0.67; 95% confidence interval, 0.49-0.92; $p = 0.017$).

Conclusions: These findings suggest that the biology and clinical impact of low HER2 expression can differ according to the hormone receptor status and HER2-low breast cancer may be a distinct disease entity with a different prognosis.

THE EFFECTS OF SMARTPHONE BASED BREAST SELF-EXAMINATION APPLICATION PROGRAM IN KOREAN WOMEN: THE PINK ROAD APPLICATION

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Background: Breast cancer is the most common malignancy in Korean women. Above all, early detection of breast cancer is very important and it is necessary to help the breast self-examination (BSE) more easily and conveniently. The purpose of this study was to verify the effects of smartphone-based BSE application program in Korean women.

Methods: The study design was one group pretest-posttest experimental research. The one group pretest-posttest experimental study was carried out to verify knowledge on breast cancer, beliefs on BSE: perceived benefits, perceived barriers, and confidence, and compliance of BSE practice. The data were collected through the self-reported questionnaires from August 2020 to January 2021 among 25 women in Korea. All participants installed the smartphone-based BSE application program and used it for 6 months. The application consists of the educational video of BSE, Q&A, and interactive Chabot. This application sent an alarm according to the participant's menstrual cycle during the study period to encourage about BSE. Data were analyzed with Wilcoxon Signed Ranks test using SPSS/WIN 25.0.

Result: The participants were significantly improvement on knowledge on breast cancer ($Z = -3.48$, $p < .001$), confidence ($Z = -2.70$, $p = .007$), and compliance of BSE practice ($Z = -2.49$, $p = .013$) after provided smartphone-based BSE application program.

Conclusions: The research results showed that this BSE application education is effective in knowledge of breast cancer and compliance of BSE practice. It is necessary to provide useful educational measures that can be easily used to detect breast cancer early and improve the BSE practice rate.

PREDICTION FOR RECURRENCE FREE SURVIVAL WITH DEEP LEARNING-BASED MAMMOGRAPHIC ANALYSIS IN PATIENTS WITH HORMONE RECEPTOR-POSITIVE BREAST CANCER

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Background: We analyzed pre and post-endocrine treatment mammographic density using deep learning (DL)-based model, and developed a model to predict individual recurrence free survival (RFS) with these results and other clinical information of patients with hormone receptor-positive breast cancer.

Methods: Overall, 7,332 patients with hormone receptor-positive breast cancer who received endocrine treatment, and had both a baseline and a follow-up mammograms were eligible for analysis. The mammographic density of pre and post-endocrine treatment were predicted by DL-based model on the mammograms of the breast unaffected by breast cancer. Survival analysis was performed by using Cox proportional hazards regression model with a recurrence as the end point, and prediction for RFS was performed by random survival forest model with patient and tumor characteristics as well as change in mammographic density.

Result: During a median follow-up period of 77 months (range, 13-157 months), 119 patients (1.6%) died, of whom 77 (1.1%) died of breast cancer, and 455 patients (6.2%) experienced recurrence. Women who experienced a relative density reduction of more than 20% between baseline and follow-up mammograms had a reduced risk of recurrence of 20% (hazard ratio, 0.800; 95% confidence interval [CI], 0.6440.994) compared to women with a 20% decrease or less. The model to predict RFS showed good discrimination, with a C-index of 0.7990 (95% CI, 0.79320.8049).

Conclusions: Our prediction model with DL-based mammographic analysis on pre- and post-endocrine treatments showed good performance and may be used as a guidance in endocrine treatment for hormone receptor-positive breast cancer.

BREAST CANCER STEM CELL MARKER AND TUMOR SUPPRESSOR MIRNAS (MIR-200A, MIR-200B, MIR-205 AND MIR-145) IN BREAST CARCINOMA: A ROUTE TOWARDS PRECISION MEDICINE

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Background: Breast cancer is a complex disease with heterogeneity and several studies have been conducted to explore differentially expressed miRNA in carcinogenesis. Tumor suppressor miRNAs (miR 200a, miR 200b, miR 205 and miR 145) are involved in various signalling pathways and promote carcinogenesis and Cancer stem cells (CSCs) noticed as the driving force of tumorigenesis and metastases. Thus, my objective was to explore relationship of expressed miRNAs and Cancer Stem Cells in breast cancer patients before and after chemotherapy.

Methods: 39 Breast Cancer samples were recruited after pathological approval and ethical clarification. miRNAs were quantified on real-time PCR by using exiqon cDNA and Sybr green kit. The validated miRNAs primer were purchased from exiqon and Qiagen. CSCs (CD44+/CD24-) were characterized by using CD44 and CD24 conjugated antibodies on BD flow cytometer.

Result: Breast Cancer Stem Cell marker CD44+/CD24- were significantly reduced after three cycle of chemotherapy (Average % & Mean counts: 7.60% & 590 Vs 3.22% & 291). However, the highest frequency of cells with expression of CD44-/CD24+ were observed and remain almost unchanged after 3 cycle of chemotherapy (Average % & Mean counts: 33.68% & 23,953 Vs 32.63% & 21,648). The Breast cancer patients showed significant ($p < 0.5$) down-regulated expression of miR 21 (Mean Cq 27.95 ± 1.63 Vs 26.51 ± 1.00) after 3 cycle of standard chemotherapy.

Conclusions: This study had shown the all tumor suppressor miRNAs 205 showed higher expression with decrease in mean count of CSCs (CD44+/CD24- in patients positively responding therapy. So this and similar type of study may help in guiding more precise treatment of chemotherapy with gene therapy in near future.

PROGNOSTIC RELEVANCE AND ANTITUMOR OR IMMUNITY OF NSD3 OVEREXPRESSION IN THE BREAST CANCER

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Background: Nuclear receptor-binding SET domain protein (NSD), a histone methyltransferase, is known to play an important role in cancer pathogenesis. The WHSC1L1 (Wolf-Hirschhorn syndrome candidate 1-like 1) gene, encoding NSD3, is highly expressed in breast cancer, but its role in the development of breast cancer is still unknown. The purpose of this study was to analyze the survival rates and immune responses of breast cancer patients with WHSC1L1 overexpression and to validate the results using gradient boosting machine (GBM) in breast cancer.

Methods: We investigated the clinicopathologic parameters, proportions of immune cells, pathway networks and in vitro drug responses according to WHSC1L1 expression in 456, 1,500 and 776 breast cancer patients from the Hanyang University Guri Hospital, METABRIC and TCGA, respectively.

Result: WHSC1L1 overexpression was associated with poor prognosis, decreased CD8+ T cells and high CD274 expression (encoding PD-L1). In the pathway networks, WHSC1L1 was indirectly linked to the regulation of the lymphocyte apoptotic process. The GBM model with WHSC1L1 showed improved prognostic performance compared with the model without WHSC1L1. We found that VX-11e, CZC24832, LY2109761, oxaliplatin and erlotinib were effective in inhibiting breast cancer cell lines with WHSC1L1 overexpression.

Conclusions: WHSC1L1 overexpression could play potential roles in the progression of breast cancer, and targeting WHSC1L1 could be a potential strategy for the treatment of breast cancer.

CHARACTERISTICS AND PROGNOSIS OF POSTPARTUM BREAST CANCER

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Background: Postpartum breast cancer (PPBC) is a breast cancer diagnosed within 5-10 years postpartum owing to its unique biological attributes and its prognosis. PPBC is a not well-established subset of breast cancer, and only few studies address its poorer prognosis. To improve clinical practice and patient outcomes of PPBC, we need further understanding of the disease. The aim of this study is to analyze characteristics and overall survival rate of PPBC patients in Korean population, and to figure out the chronological difference of prognosis of PPBC, and provide better data into the clinical care of young women's breast cancer (YWBC).

Methods: The Korean Breast Cancer Society registry was retrospectively reviewed to identify PPBC patients diagnosed between January 2000 and December 2014. Patients ages were 20 to 50 when they were surgically treated, and all of the patients were married with known menopausal status. Patients with childbirth experiences had their delivery under 50 years of age, and had 3 or less children. A total of 32,628 breast cancer patients were ultimately eligible for the analysis.

Result: Our data showed that PPBC < 5 had worse survival rate compared to nulliparous and PPBC more than 5 years (5-year cumulative survival; PPBC < 5 89%, nulliparous 97.3, 5 ≤ PPBC10 93%). In multivariate analysis, PPBC < 5 was associated with worse survival rate (HR 1.55, 95% CI 1.148-2.094, $p = 0.004$) after adjustment for age on operation, breast cancer stage, ER and HER2 status, Ki-67 level, and chemotherapy.

Conclusions: We demonstrated that patients with breast cancer diagnosed within first five years after parturition confers worse survival rate.

PROGNISIS CHANGES IN AUTOMATED MAMMOGRAPHIC BREAST DENSITY COULD BE RELATED TO THE PATHOLOGICAL RESPONSE OF BREAST CANCER PATIENTS AFTER NEOADJUVAN CHEMOTHERAPY

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Background: Mammographic density is one of the independent risk factors for breast cancer, which may change after neoadjuvant chemotherapy (NCT). The aim of this study was to evaluate the percentage of changes in volumetric breast density (Vbd%) using automated volumetric breast density (Vbd) measurement as a predictive marker of the pathological response after NCT.

Methods: 327 breast cancer patients treated between January 2014 and December 2016 were reviewed. Automated Vbd measurement provided Vbd. Vbd% was calculated by a formula as follow; (preoperative Vbd minus baseline Vbd/baseline Vbd) x 100 (%). Three groups were divided according to Vbd%; $<-20\%$, $-20\% \leq \sim \leq 20\%$, and $>20\%$ as decreased, stable, and increased groups, respectively. No evidence of invasive carcinoma in the breast and metastatic tumors in the axillary and regional lymph nodes at surgical pathology were considered to be an achievement of pathologic complete remission (pCR) after NCT.

Result: The interval between baseline and preoperative mammograms was ranged from 79 to 250 days (median, 170 days). Decreased group showed significantly lower the volume of fibroglandular tissue and volumetric breast density than stable group. Decreased group showed younger age, premenopausal women, no history of full term delivery and larger tumor size. In multivariate analysis, decreased group had lower probability of pCR after NCT independently.

Conclusions: The percentile of changes in Vbd after NCT was closely related to the pathological response of breast cancer and had predictive value for NCT. The need for additional adjuvant treatment cannot be overlooked in patients with decreased change in Vbd after NCT.

GROWTH PATTERN OF HEPATIC METASTASIS AS A PROGNOSTIC INDEX IN BREAST CANCER LIVER METASTASIS

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Background: Breast cancer with liver metastasis (BCLM) patients frequently develop hepatic failure owing to extensive liver metastasis compared to other solid cancers, but there are no clinicopathologic or radiologic parameters for estimating the prognosis of BCLM. We analyzed the relationship of radiologic and clinicopathologic characteristics with survival outcomes in BCLM patients.

Methods: Between January 2009 to May 2019, baseline and final abdomen CT scan or liver MRI of BCLM patients were reviewed. The pattern of liver metastasis was classified as oligometastasis (3 or less metastatic lesions), non-confluent mass formation, confluent mass formation, infiltrative and pseudocirrhosis. Thirty-one surgical or biopsy specimens for liver metastasis were immunostained for L1 adhesion molecule (L1CAM), Yes-associated protein 1/Transcriptional co-activator with PDZ-binding motif (YAP/TAZ) and β1-integrin.

Result: Among the 156 patients, 77 initially presented with oligometastasis, 58 with nonconfluent mass-forming pattern, 14 with confluent mass formation, and 7 with infiltrative liver metastasis. Patients with confluent or infiltrative liver metastasis showed inferior liver metastasis-associated survival (LMOS) compared to others (median 24.00 vs. 51.37 months, $P = 0.001$). Positive staining for L1CAM in BCLM cells was associated with inferior survival and positive YAP/TAZ staining associated to pattern of final liver metastasis.

Conclusions: Initial hepatic metastasis pattern was associated with LMOS, especially confluent mass forming, and infiltrative liver metastasis associated to poor survival outcome. Positive staining for YAP/TAZ or L1CAM was associated with pattern of final liver metastasis or LMOS.

CLINICAL SIGNIFICANCE OF CD73+ TUMOR INFILTRATING LYMPHOCYTES IN BREAST CANCER

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Background: CD73 is an ecto-enzyme that promotes tumor immune escape through the production of immunosuppressive extracellular adenosine in the tumor microenvironment. The purpose of this study was to investigate the relationship between CD-73 positive tumor infiltrating lymphocytes (TIL) expression and clinicopathological factors in breast cancer and their effects on prognosis.

Methods: This study included 472 patients with primary invasive breast cancers who were treated in our hospital, from 2010 to 2017. Tissue microarray blocks were constructed from formalin fixed paraffin-embedded primary breast tumor samples. We assessed CD73 protein expression on TIL and stromal cells and investigated the associations between CD73 protein expression and other adenosine pathway factors with clinic-pathological features, and prognosis.

Result: CD73 TIL was expressed in 27.8% of patients. There was no association with the expression of CD73 TIL and stromal CD73. The expression of CD73+ TIL was statistically significantly higher in HER2 positive breast cancer (34.1% vs 16.8%), ER negative (61.1% vs 79.2%), and PR negative (53.4% vs 71.3%) breast cancer (each p value < 0.001). As well, CD73+ TIL was associated with the expression of ADAR (49.6% vs 28.2%, p value < 0.001). The expression of CD73+ TIL was a good prognostic factor in HER2-positive breast cancer. (Kaplan Meier curve, positive 0.01) However, the expression of CD73+ TIL in premenopausal ER (-) breast cancer acted as a rather bad prognostic factor, which was not statistically significant (Kaplan Meier curve, p value 0.103).

Conclusions: CD73+ TIL shows high expression in HR(-), HER2(+) breast cancer, and has different prognostic effects depending on breast cancer subtype.

THE COMBINATION OF KI67 AND PR IS AN IMPORTANT PROGNOSTIC FACTOR IN BREAST CANCER WITH ER+/HER2- AT AGE ≤50 AND >50 YEARS: INTERPRETATION OF THE DISCORDANT STATUS BETWEEN KI67 AND PR

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Background: The aim of our study intends to identify the combination of Ki67 and PR can play a role as an important prognostic factor in breast cancer with ER+/HER2-.

Methods: We retrospectively selected 2756 patients. Ki67 was divided by Ki67 ≤5% (Low), 5% < Ki67 < 30% (Intermediate), and Ki67 ≥ 30% (High). PR was divided into low and high based on 20% (PR ≥ 20% Good, PR < 20% Bad). In this group, we made four combinations of Ki67 and PR with Low/Good (LG) group (Ki67 ≤5% /PR ≥ 20%), Low/Bad and Intermediate/Good (LB/IG) group (Ki67 ≤5% /PR < 20%, and 5% < Ki67 < 30% /PR ≥ 20%), Intermediate/Bad and High/Good (IB/HG) group (5% < Ki67 < 30% /PR < 20%, and Ki67 ≥ 30% /PR ≥ 20%) and High/Good (HG) group (Ki67 ≥ 30% / PR < 20%).

Result: Among all patients, 1401 patients under 50 and 1355 after 50 years. In under 50, the four groups, LG, LG/IB, IB/HG, and HB, were 423, 643, 264, and 71, and in after 50 were 306, 631, 320, and 98, respectively. In univariate analysis, the four groups showed significant survival curves both under 50 and after 50. In multivariate analysis, a significant and proportional increased HR was observed in both under 50 and after 50, and a similar pattern was observed (Age ≤ 50 HR; LG vs LB/IG, IB/HG, HB = 1.136 $p = 0.645$, 2.150 $p = 0.008$, 3.628 $p < 0.001$, Age > 50 HR; 1.329 $p = 0.394$, 2.281 $p = 0.015$, 3.078 $p = 0.005$).

Conclusions: The combination of Ki67 and PR can be evaluated as an important prognostic factor in breast cancer with ER+/HER2- both under 50 and after 50 years. And discordant status between Ki67 and PR, LB/IG group has a good prognosis and IB/HG group can predict a poor prognosis.

ASSESSMENT HIGH KI67 (>=20%) ER+HER2-BREAST CANCER WITH 21-GENE MULTIGENE ASSAY (ONCOTYPE DX)

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Background: The Ki67 immunohistochemistry (IHC) with a cut-off of 20% by MIB-1 PharmDx assay has been approved as companion diagnostics for adjuvant abemaciclib in high risk ER+HER2- breast cancer. We addressed genomic risk profile of locally addressed high Ki67 (≥ 20%) ER+HER2- breast cancer using 21-gene multigene assay (Oncotype DX test).

Methods: We collected clinical and pathologic information in 2,294 patients who underwent Oncotype DX test from two hospitals. High genomic risk was defined as higher 21-gene recurrence score (≥ 26). Ki67 IHC examination with cut-off of 20% was performed locally using MIB-1.

Result: The Ki67 IHC assigned 870 (38%) as the high and 1,424 (62%) as the low groups. In the high Ki67, 263 (30%) had high genomic risk, whereas 84 (6%) of the low Ki67 had it ($p < 0.0001$). Average 21-gene recurrence score was significantly higher in the high Ki67 than in the low Ki67. Progesterone receptor (PR) positive and histologic grade 1-2 rates were significantly higher in the high Ki67 and genomic low than in the genomic high groups.

Conclusions: About two-thirds of high Ki67 tumors had low genomic risk by 21-gene multigene assay. Tumors with high Ki67 but lower Oncotype DX score tend to have PR positivity. In high Ki67 and PR+ tumors, multigene assay would be useful to address whether these tumors are truly genomic high risk.

CLOSE/POSITIVE MARGINS OF NIPPLE-AREOLAR SPARING MASTECTOMIES: DOES IT AFFECT BREAST CANCER RECURRENCE?

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Background: Nipple-areolar sparing mastectomies (NSM) are controversial over the superficial margin as they preserve the skin compared to conventional mastectomy. Since most of the breast parenchyma is removed, the lateral margin is not relevant, but there is an issue with the deep margin. Close/positive superficial or deep margins may affect local recurrence or the prognosis of breast cancer. Existing research reports on this are insufficient. We analyzed the relationship between the status of superficial or deep margins and breast cancer recurrence in patients who underwent NSM.

Methods: A retrospective analysis was performed on 962 patients who underwent NSM for invasive breast cancer at Asan Medical Center from 2003 to 2015.

Result: The available resection margin (RM) count was 895 for superficial RM and 903 for deep RM. Local recurrence (LR) on the skin was 9% (9 of 100 positive superficial RM cases), and chest wall was 6.52% (3 of 46 positive deep RM cases). There were 6 patients with simultaneous recurrence of skin and chest wall. Among them, 1 patient had both positive superficial and deep RM and another had positive superficial and negative deep RM. In study, *p*-values of skin and chest wall LR according to the superficial RM and deep RM are 0.71 and 0.35 respectively.

Conclusions: Close/positive superficial or deep margins in NSM do not affect LR, so additional surgery is not always required.

LACTATE DEHYDROGENASE AS A SURROGATE MARKER FOR BOTH PCR AND SURVIVAL IN BREAST CANCER PATIENTS WHO UNDERWENT NEOADJUVANT CHEMOTHERAPY

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Background: Glucose metabolism in cancer cells produces various glycolytic metabolites, which can affect cancer progression and treatment outcome. Herein we evaluated the association of glucose transporters and enzymes involved in glucose metabolism with clinic-pathological factors and outcomes in breast cancer patients who underwent neoadjuvant chemotherapy (NAC).

Methods: We selected 7 target transporters and enzymes (GLUT1, hexokinase 2, lactate dehydrogenase, MCT1, MCT4, IGF1RA, and IGF1RB) involved in glucose metabolism. Their tumoral expressions were scored both quantitively and qualitatively based on tissue microarrays and immunohistochemistry as previously described (Pinheiro et al., 2010) and then evaluated in relationships with pretreatment clinical/pathological characteristics and treatment outcomes including findings of 18F-FDG PET/CT, pathologic complete response (pCR), and relapse in breast cancer(stage IIA-IIIC) patients who underwent anthracycline or taxane-based NAC.

Result: Of the 236 enrolled patients, 145(61.4%), 44(18.6%), and 47(19.9%) were luminal, HER2-enriched, and TNBC subtypes. Pathologic CR was determined 50(21.2%) and 57(24.2%) relapses, 42(17.8%) distant relapses, and 28 deaths were observed during median follow-up duration of 64.0 (32.3-114.9) months. The expression rates of the target molecules were 76.0, 31.1, 42.1, 54.9, 67.9, 78.4, and 49.8% for GLUT1, hexokinase 2 (HK2), lactate dehydrogenase (LD), MCT1, MCT4, IGF1RA, and IGF1RB, respectively. Among target molecules in glucose metabolism, LD was significantly associated with pCR (OR = 0.251; $p = 0.016$) and distant disease-free survival (HR = 2.29; $P = 0.019$). Plus, LD expression shows a trend for a high SUVmax of primary tumor 18F-FDG PET/CT (OR = 1.797 $P = 0.060$).

Conclusions: Tumoral expression of lactate dehydrogenase can be considered as a predictive marker for pCR to NAC and plus prognostic marker for survival in patients with breast cancer.

ANALYSIS OF THE PIK3CA MUTATION EXPRESSION THROUGH NGS IN ER POSITIVE AND HER2 NEGATIVE BREAST CANCER

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Background: PIK3CA gene mutation common in breast cancer. This mutation appear to play an important role in oncogenesis, or the process of cancer developing in the first place. PIK3CA mutations may be associated with resistance to treatments for breast cancer.

Methods: Next Generation Sequencing (NGS) was used to analyze somatic mutations in breast cancer. Expression of the PIK3CA mutation was detected through NGS. From January 2018 to December 2018, we studied patients who underwent surgery at Kosin University Gospel Hospital.

Result: Among 157 lumen-like breast cancer, the expression of PIK3CA mutation ratio was 85/157(54%). The expression rate of PIK3CA was 68/119(57%) in luminal A type and 17/38(44%) in luminal B type. In NGS, two or more mutations were detected in 35% and 53% of luminal A and luminal B, respectively. Among several mutations, PIK3CA mutation was found in 43% of luminal A type and 23% of luminal B type, respectively.

Conclusions: The expression rate of the PIK3CA mutation analyzed in this study was higher than the generally known 30-40%. Expression of the PIK3CA mutation was more frequent in luminal breast cancer than in other types such as HER2 type and TNBC. The expression rate was higher in luminal type A, which had a relatively good prognosis, than in luminal type B. This is thought to be related to the prognosis of breast cancer with PIK3CA mutations. Currently, therapeutic agents targeting PIK3CA mutation have been developed and used. This study is expected to be helpful in the management and future treatment of high-risk patients.

NOMOGRAM FOR PREDICTION POSITIVE RESECTION MARGIN AFTER BREAST-CONSERVING SURGERY FOLLOWING NEOADJUVANT CHEMOTHERAPY

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Background: The desire for breast-conserving surgery (BCS) is one of the indications for neoadjuvant chemotherapy (NAC) in breast cancer. Negative resection margin (RM) after BCS is the most important risk factor of local recurrence. We aimed to suggest variables associated with positive RM on BCS following NAC for proper surgical planning.

Methods: We reviewed the medical records of patients who initially received BCS after NAC from 2000 to 2018 at a single institution. We compared clinicopathologic variables between patients with negative vs positive resection margins using the chi-square test. Multivariate logistic regression analysis was used to analyze independent risk factors of positive resection margins.

Result: Of a total 1581 patients, 109 had a positive RM. hormone receptor positive ($P < 0.0001$), pre-NAC tumor size on MRI ($P = 0.015$), >0.5 cm difference in pre-NAC tumor size between MRI and ultrasound ($P < 0.0001$), post-NAC tumor size on MRI ($P < 0.0001$), and lobular component on needle biopsy ($P < 0.0001$) were significantly different between the negative and positive RM groups. On multivariate logistic regression analysis, hormone receptor positive (OR 2.193, $P = 0.034$), lobular component on needle biopsy (OR 4.814, $P = 0.010$), >0.5 cm difference in pre-NAC tumor size between MRI and ultrasound (OR 2.370, $P = 0.009$), and post-NAC tumor size on MRI (OR 1.266, $P = 0.010$) were significantly different between the groups.

Conclusions: We identified 4 variables associated with positive RM after BCS following NAC. They will be useful in optimizing individual surgical plans, including the need for intraoperative frozen biopsy.

DIFFERENCE OF HORMONE RECEPTOR AND INVASIVENESS CONCORDANCE IN SYNCHRONOUS AND METACHRONOUS BILATERAL BREAST CANCER

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Background: The aim of this study was to analyze the association of hormone receptors and invasiveness concordance in patients with synchronous bilateral breast cancer (SBC) and metachronous breast cancer (MBC).

Methods: Patients diagnosed with SBC or MBC in Korea University Guro Hospital between March 2008 and February 2020 were retrospectively reviewed and included. Clinicopathologic features, molecular subtype status concordance, and prognosis were compared in patients with SBC and MBC.

Result: Totally, 60 SBC and 39 MBC were included. Hormone receptor concordance was higher in the SBC group compared to MBC (86.4% vs 59.0%). MBC had more both invasiveness than SBC (74.4% vs 48.3%).

Conclusions: Both invasiveness was higher in MBC than SBC group. MBC had less hormone receptor disconcordance than SBC. This might affect to poor prognosis.

THE OCCURRENCE OF CHEMOTHERAPY-INDUCED ALTERED TASTE IN BREAST CANCER PATIENTS AND ITS ASSOCIATION WITH WEIGHT LOSS

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Background: Altered taste of foodstuffs is frequently experienced by breast cancer (BC) patients during chemotherapy. It has been linked to worsening BC morbidity and mortality due to weight loss. It is unclear whether altered taste is associated with other gastrointestinal (GIT) symptoms including oral dryness, oral mucositis, and nausea. This study aimed to describe the occurrence pattern of chemotherapy-induced altered taste and its association with GIT symptoms and weight loss.

Methods: This study recruited 140 BC patients who were diagnosed from 2018 to 2021. Chemotherapy-induced altered taste, oral dryness, oral mucositis, and nausea were recorded using Common Terminology Criteria for Adverse Events (CTCAE) v4 after third chemotherapy cycle (T1), sixth cycle (T2), and three months after chemotherapy completion (T3). Weight loss was defined as > 5% decline of body weight at mid-chemotherapy cycle compared to baseline. Logistic regression was used to analyse the association related to altered taste.

Result: Altered taste was reported by 79.3% of BC patients at T1. Its occurrence increased up to 89.8% at T2 and markedly declined at T3 (15.3%). Altered taste at T1 was significantly associated with nausea ($p = 0.018$), while altered taste at T2 was significantly associated with oral dryness ($p = 0.017$). There is no significant association between altered taste and oral mucositis ($p > 0.05$). BC patients who suffered from altered taste had higher incidence of weight loss (95.8% vs. 4.2%, $p = 0.057$).

Conclusions: This study demonstrated the frequent yet transient occurrence of chemotherapy-induced altered taste. Altered taste was associated with oral dryness and nausea, and also tend to increase weight loss risk.

DETERMINANTS OF CLINICALLY SIGNIFICANT WEIGHT GAIN DURING AND AFTER BREAST CANCER CHEMOTHERAPY: A HOSPITAL-BASED STUDY IN YOGYAKARTA, INDONESIA

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Background: Breast cancer ranks highest in incidence and ranks second in mortality rates among other malignancies among Indonesian women. It was recently shown that weight gain of ≥ 5% following chemotherapy for breast cancer was associated with lower survival and increased recurrence. This study aims to identify sociodemographic and clinicopathological predictors that contribute to clinically significant weight gain in breast cancer patients.

Methods: We included 140 female breast cancer patients who were registered in a prospective study determining chemotherapy toxicities and their relationship with the survival. Secondary data regarding demographic, clinical, and treatment variables were obtained from the study database. Patients body weight were documented during chemotherapy, at the end of chemotherapy, 1 month, 2 months, 3 months and 6 months after chemotherapy. Multivariate logistic regression analysis was performed to explore the association between determinants and incidence of ≥ 5% weight gain.

Result: Thirty one out of 140 study participants (22%) experienced ≥ 5% weight gain upon measurement during the course of follow up period. Analysis indicates that pretreatment body mass index (BMI) and neutrophil-to-lymphocyte ratio (NLR) were significantly associated with lower incidence of ≥ 5% weight gain (OR = 0.88, 95% CI = 0.79-0.99, $p = 0.033$; OR = 0.61, 95% CI (0.41-0.91), $p = 0.016$; respectively).

Conclusions: The result of this study may provide a framework for identifying person at risk for clinically significant weight gain during and after breast cancer therapy, and promote weight gain prevention program which has the potential to increase survival rates.

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THE PATTERN OF CARE FOR BRAIN METASTASIS FROM BREAST CANCER OVER THE PAST 10 YEARS IN KOREA: A MULTICENTER RETROSPECTIVE STUDY (KROG 16-12)

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Background: We aimed to investigate manifestations and patterns of care for patients with brain metastasis (BM) from breast cancer (BC) and compared their overall survival (OS) from 2005 through 2014 in Korea.

Methods: We retrospectively reviewed 600 BC patients with BM diagnosed between 2005 and 2014. The median follow-up duration was 12.5 months. We categorized the patients into three groups according to the year when BM was initially diagnosed [group I (2005-2008), 98 patients; group II (2009-2011), 200 patients; and group III (2012-2014), 302 patients].

Result: Over time, the median age at BM diagnosis increased by 2.2 years (group I, 49.0 years; group II, 48.3 years; and group III, 51.2 years; $p = 0.008$). The percentage of patients with extracranial metastasis was 73.5%, 83.5%, and 86.4% for group I, II, and III, respectively ($p = 0.011$). The time interval between

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BC and BM was prolonged in patients with stage III primary BC (median, 2.4 to 3 years, $p = 0.029$). As an initial brain-directed treatment, whole-brain radiotherapy alone decreased from 80.0% in 2005 to 41.1% in 2014. Meanwhile, stereotactic radiosurgery or fractionated stereotactic radiotherapy alone increased from 13.3% to 34.7% during the same period ($p = 0.005$). The median OS for group I, II, and III was 15.6, 17.9, and 15.0 months, respectively, with no statistical significance.

Conclusions: The manifestations of BM from BC and the pattern of care have changed from 2005 to 2014 in Korea. However, the OS has remained relatively unchanged over the 10 years.

CHANGES IN SYMPTOM CLUSTERS OVER TIME AMONG ASIAN AMERICAN BREAST CANCER SURVIVORS RECEIVING TECHNOLOGY-BASED ONLINE COACHING/SUPPORT PROGRAM

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Background: Asian American breast cancer survivors experience a complex array of co-occurring symptoms. In-person survivorship programs have shown to be effective in reducing symptom clusters despite their barriers such as lack of accessibility and cultural sensitivity. While technology-based online programs are presumed to overcome such barriers, there is limited understanding on symptom clusters especially among those receiving the intervention.

Methods: This secondary analysis used the data from a randomized controlled trial of 199 Asian American breast cancer survivors. The symptoms were measured using the Memorial Symptom Assessment Scale. An exploratory factor analysis was conducted to group symptoms that are highly prevalent and correlated. Each symptom cluster was assigned a clinically meaningful name based on the characteristics of the included symptoms.

Result: The types of symptom clusters differed between the control and the intervention group. At baseline, the intervention group experienced the psychological/sexual cluster, anticholinergic/pain cluster, and appetite/itching cluster. At post 1-month, they experienced the anticholinergic/somatic cluster, psychological (mood)/sexual cluster, and psychological (CNS) cluster. At post 3-month, they experienced the psychological (mood & CNS) cluster, anticholinergic/pain/somatic cluster, and psychological (CNS)/skin/hair/GI cluster. In contrast, the control group experienced the psychological/GI/skin/hair cluster, somatic/sexual/pain cluster, anticholinergic cluster at baseline, psychological (mood)/somatic cluster, psychologica l (CNS) cluster, anticholinergic/sexual cluster at post 1-month, and psychological (mood) cluster, psychological (CNS)/anticholinergic/skin cluster, and somatic/pain cluster at post 3-month.

Conclusions: Clinicians should understand the different symptom cluster experience over time between the two groups. In addition, they should take a more symptom cluster targeted assessment and management in clinical practice to reduce symptom burden and improve patient health outcomes.

PREDICTION OF BREAST CANCER-RELATED LYMPHEDEMA RISK AFTER POSTOPERATIVE RADIOTHERAPY VIA MULTIVARIABLE LOGISTIC REGRESSION ANALYSIS

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Background: We identified novel clinical and dosimetric prognostic factors affecting breast cancer-related lymphedema after postoperative radiotherapy (RT) and developed a multivariable logistic regression model to predict lymphedema in these patients.

Methods: A total of 580 patients with unilateral breast cancer were retrospectively reviewed. All patients underwent breast surgery and postoperative RT with or without systemic treatment in 2015. With available RT plan data, 532 patients were randomly divided into the train (N = 372) and test (N = 160) cohort with a 7:3 ratio to generate and validate lymphedema prediction models, respectively. An area under the curve (AUC) value was estimated to compare models.

Result: The median follow-up duration was 5.4 years. One-hundred-four (17.9%) patients experienced lymphedema and cumulative incidence of it as follows: 1-year, 10.5%; 3-year, 16.4%; and 5-year, 17.6%, respectively. Multivariate analysis showed that body mass index ≥ 25 kg/m^2 (hazard ratio [HR] 1.845), dissected lymph nodes ≥ 7 (HR 1.041), taxane-based chemotherapy (HR 4.200), and the interval between surgery and RT < 1 month (HR 1.568) were significantly associated with lymphedema development. The multivariable logistic regression model using the above factors as well as the minimum dose of axillary level I and supraclavicular lymph node was established with an AUC of 0.761 and 0.794 in the train and test cohort, respectively.

Conclusions: Our study demonstrated that the shorter interval from surgery to RT and other established clinical factors increased lymphedema risk. Combining them with two dosimetric parameters, we suggest the multivariable logistic regression model for breast cancer-related lymphedema prediction after RT.

ELEVATION OF CA 15-3 WITHIN NORMAL RANGE INCREASES THE RISK OF BREAST CANCER RECURRENCE IN KOREAN WOMEN: A LONGITUDINAL RETROSPECTIVE COHORT STUDY

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Background: CA15-3 is extensively used in the clinical practice of breast cancer (BC) as serum tumor markers. We hypothesized that the changes of CA 15-3 within normal ranges could affect recurrence of BC and analyzed between elevation of CA 15-3 within normal ranges and BC recurrence.

Methods: We conducted a retrospective cohort study using the de-identified data for the events of recurrence, and visits extracted from DARWIN-C (Clinical Data Warehouse of Samsung Medical Center).

Result: The mean age of study participants (N = 11,452) was 49.3 years. The proportion of participants with 1standard deviation (SD) or more elevated CA15-3 comparing previous exam during follow-up was 23% (N = 2,666). During the follow-up of 5.8 years, 790 patients occurred recurrence. The fully-adjusted HR for recurrence comparing participants with stable CA15-3 to those elevated CA15-3 was 1.75 (95% CI = 1.52, 2.02). In addition, if the CA15-3 elevated 1SD or more, the risk was much higher (HR = 6.86, 95% CI = 5.80, 8.11) than these of patient without CA15-3 elevated 1SD or more. In the sensitivity analysis, even within under 30 of CA15-3, the recurrence risk was consistent that the risk was higher in participants who had elevated CA15-3 than these who were not. The association between elevated levels of CA15-3 and incidence of recurrence was observed in all subtypes, and the association was stronger in patient with N+ compared to patient with N0 (P value for interaction < 0.001).

Conclusions: We demonstrated the changes of CA 15-3 within normal ranges affect recurrence of BC.

DEPRESSION CARE MODEL WITH THE APPROACH OF LIFE IN MEANINGS-CENTER WITH MINDFULNESS FOR BREAST CANCER SURVIVORS

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Background: The review and meta-analysis studies revealed that there were about 30-40% of breast cancer women with depressive symptoms. Therefore, over 15 years, our team examined the depression associated factors of breast cancer survivors among meaning in life, attachment styles in close relationship, diurnal cortisol patterns. The depression programs were then developed and examined its effects on enhancing their well-being.

Methods: The prospective longitudinal studies were conducted to identified the factors associated with depression of breast cancer survivors. Based the findings, body-mind-spirit holistic theory and mindfulness theory, the mindfulness integrated with body-mind-spirit (BMS) group therapy was developed and examined using RCT design for its effects for breast cancer survivors. BMS consists of a healthy lifestyle and holistic empowerment strategies in particular meaning reconstruction such as exploring the meanings of 'loss and gain' on their life road, practicing 'letting go' of attachments and desires, and learning to love others. Mindfulness components include mindful breathing, guided imagery, individual and interactive meditation, mindful touching with loving kindness.

Result: The long-term follow up studies showed that among the associated factors of sleeping problems, attachment styles, cortisol levels at night, meaning in life was the main predictor of breast cancer survivors' depression. Mindfulness integrated with BMS could improve the causes of depression such as attachment styles, meaning in life, and stablishing cortisol levels at night.

Conclusions: Mindfulness integrated into holistic body-mind-spirit therapy contributes to a holistic depression care model for breast cancer survivors.

VALIDATION OF A NOMOGRAM FOR PREDICTING THE RISK OF LYMPHEDEMA FOLLOWING CONTEMPORARY TREATMENT FOR BREAST CANCER: A LARGE MULTI-INSTITUTIONAL STUDY (KROG 20-05)

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Background: We previously constructed a nomogram for predicting the risk of arm lymphedema following contemporary breast cancer treatment. This nomogram should be validated in several patients with different background characteristics before use. Therefore, we aimed to externally validate the nomogram in a large multi-institutional cohort.

Methods: Overall, 8835 patients who underwent breast cancer surgery during 2007-2017 were identified. Data of variables in the nomogram and arm lymphedema were collected. The nomogram was validated externally using C-index and integrated area under the curve (iAUC) with 1000 bootstrap samples and by calibration plots.

Result: Overall, 1377 patients (15.6%) developed lymphedema. The median time from surgery to lymphedema development was 11.4 months. Lymphedema rates at 2, 3, and 5 years were 11.2%, 13.1%, and 15.6%, respectively. Patients with lymphedema had significantly higher body mass index (median, 24.1 kg/m^2 vs. 23.4 kg/m^2) and a greater number of removed nodes (median, 17 vs. 6) and more frequently underwent taxane-based chemotherapy (85.7% vs. 41.9%), total mastectomy (73.1% vs. 52.1%), conventionally fractionated radiotherapy (71.9% vs. 54.2%), and regional nodal irradiation (70.7% vs 22.4%) than those who did not develop lymphedema (all $P < 0.001$). The C-index of the nomogram was 0.7887, and iAUC was 0.7628, indicating good predictive accuracy. Calibration plots confirmed that the predicted lymphedema risks were well correlated with the actual lymphedema rates.

Conclusions: This nomogram, which was developed using factors related to multimodal breast cancer treatment and was validated in a large multi-institutional cohort, can well predict the risk of breast cancer-related lymphedema.

THE RISK OF VENOUS THROMBOEMBOLISM RELATED TO BREAST CANCER IN KOREAN POPULATION

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Background: Breast cancer is a well-known risk factor for venous thromboembolic disease. However, the incidence of venous thromboembolic disease related to breast cancer in Korean population is still unknown. We aimed to investigate cumulative incidence of venous thromboembolic disease for breast cancer patients during follow-up.

Methods: We retrospectively reviewed electronic medical records of breast cancer patients who underwent surgery between 2012 and 2017. We identified patients diagnosed with deep vein thrombosis or pulmonary thromboembolism.

Result: We identified 1340 breast cancer patients. The median of follow up periods was 68 months. There were 24 (1.8%) patients were diagnosed with thromboembolic disease. Among 24 patients, 7 (29.2%) were diagnosed with only deep vein thrombosis; 12 (50.0%) had only pulmonary thromboembolism; 5 (20.8%) had both deep vein thrombosis and pulmonary thromboembolism.

Conclusions: The risk of thromboembolism in Korean breast cancer patients is very low. Pharmacologic prophylaxis should be selectively applied for the high-risk patients.

THE INCIDENCE AND RISK FACTORS FOR VENOUS THROMBOEMBOLISM IN ASIAN WOMEN WITH EARLY BREAST CANCER

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Background: The risk of venous thromboembolism is increased in cancer patients (pts), and VTE is the second leading cause of death in cancer. The incidence of VTE in breast cancer (BC) has been expected as lower than that of other cancers. Since early BC has good prognosis generally, VTE events can be fetal for BC pts. Reports about those of BC are quite scarce. The aim of this study is to investigate the incidence and risk factors of VTE in early BC women of Asia.

Methods: We reviewed database of 1032 stage 0-3 BC pts underwent primary breast surgery from 2014-2018. Age, BMI, stage, D-dimer results before initial treatment, types of systemic therapy, the incidents of VTE events within the follow up period retrieved, and the risk factors of VTE were assessed.

Result: Median age: 61 (26-91), median BMI: 22.5 (14.6-43.2) kg/m^2, median follow up times: 60 (0-98) months, stage 0: 125 (12%), 1: 388 (38%), 2: 398 (39%), 3: 121 (11%). Abnormal D-dimer elevation (> = 1.1 μg/mL) was shown in 167 pts (16%, median D-dimer: 1.5 (1.1-16.5)) before initial treatment. VTE found in 21 pts (2%, median Dd: 2.6 (1.2-13.8)). Only one patient died from fatal pulmonary embolism (PE) following anticoagulant therapy. Additional 20 pts developed VTE after initiation of BC treatment (2%), included 5 pts with concurrent PE. VTE occurred during perioperative chemotherapy or chemoterapy after their recurrence in 55% (11/20) pts. Factors significantly correlated with VTE included older age and chemotherapy. Other factors such as stage, BMI, endocrine therapy did not appear to be correlated in this study ($p > 0.05$).

Conclusions: Age and chemotherapy are possible risk factors of VTE for early BC patients.

IMAGING SURVEILLANCE OF BREAST CANCER AFTER PRIMARY TREATMENT: A RETROSPECTIVE NATIONWIDE STUDY IN KOREA BY THE STUDY OF SMARTSHIP GROUP

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Background: After primary treatment of breast cancer, patients still have concerns of recurrence. Early detection and treatment of recurrence are believed to be better for controlling disease. However, the effect of early detection of recurrence on survival is debated. The type and frequency of imaging surveillance after primary treatment of breast cancer vary by doctor and hospital. The aim of this study is to evaluate the impact of imaging surveillance on survival.

Methods: Using the Korean National Health Insurance Service database, we created retrospective female breast cancer cohort by analyzing annual newly diagnosed cases from 2004 to 2009 with sufficient follow-up period in Korea. To evaluate the effect of imaging surveillance on survival, we analyzed the correlation between annual frequency of imaging surveillance (0 vs. < 1 vs. ≥ 1) and overall survival by imaging type.

Result: A total of 40,500 patients were included. Mammography was the only imaging test that was statistically significantly associated with improved survival. The mortality rate per 1,000 person-years were 27.53, 13.50 and 8.14 in the '0', '< 1' and '≥ 1' groups, respectively. Hazard ratio (HR) decreased with increase in annual frequency of mammography (HR, 1.00, ref. in '0' group, HR, 0.49, 95% CI, 0.44-0.54 in '< 1' group, and HR, 0.29, 95% CI, 0.26-0.32 in '≥ 1' group). Even in the chemotherapy group under 65 years of age, mammography was the only imaging test that was significantly associated with improved survival.

Conclusions: Annual mammographic surveillance was associated with better survival. However, other imaging tests were not associated with better survival.

YOUNG FILIPINO BREAST CANCER PATIENTS HAVE WORSE SURVIVAL OUTCOMES

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Background: This study aims to evaluate the impact of age as an adverse factor in breast cancer presentation, recurrence, and survival.

Methods: A retrospective review was done in a single institution in the Philippines on all patients with confirmed invasive breast cancer Stage I-III from January 1, 2010, to December 31, 2018. Clinicopathologic characteristics and type of treatment management were recorded. Outcomes of overall survival and disease-free survival were assessed.

Result: A total of 524 female breast cancer patients were included in the study, 81 (15.5%) were aged ≤ 40 while 443 (84.5%) were > 40 years old. In comparison to their older counterpart, young Filipino breast cancer patients had invasive ductal carcinoma ($P = 0.0210$), higher stage (III) at diagnosis ($P = 0.0130$), higher grade (III) of differentiation ($P = 0.0034$), and are mostly triple negative ($P = 0.0098$). Treatment profile of young Filipino breast cancer patient showed majority of them had adjuvant chemotherapy ($P = 0.0322$) and radiation ($P = 0.0014$). All these factors contributed to a lower 5-year disease free (31.1% vs 66.8%, $P = 0.000$) and 5-year overall survival rate (61.1% versus 77.1%, $P = 0.464$).

Conclusions: Our study showed earlier disease recurrence of breast cancer in young women but no significant difference in overall survival compared with > 40 years old breast cancer patients. Thus diligent follow-up must be emphasized for this population group to detect early recurrence and prevent mortality.

THE OPTIMIZATION OF BREAST CANCER SURVIVORSHIP CARE IN KWONG WAH HOSPITAL (KWH) - A 7 YEARS REVIEW OF THE LONG TERM NURSE CLINIC

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Background: Due to the advances in screening and cancer treatment, there is no doubt breast cancer patients have better survival rate and lower risk of recurrence. After active treatment, there is a transition to survivorship phase. However, patients still carry the label of breast cancer survivors and have psychological stress on disease recurrence and health problem. Therefore, patients are referred to long term nurse clinic for follow up after discharged from doctor clinic. This review aimed to evaluate the service of long term nurse clinic in KWH.

Methods: In long term nurse clinic, patients would complete the Memorial Symptoms Assessment Scale questionnaires on arrival. Breast care nurse (BCN) would perform general health and clinical breast assessment, provide psychological support, promote self-management and breast awareness, monitor of disease recurrence and refer to other specialty if necessary. Survivorship care plan would be made with patients and follow up was coordinated.

Result: Since 2014, more than 1000 breast cancer survivors with over 4000 attendances were reviewed. < 3% cases referred back to surgeons and < 2% cases confirmed local recurrence or 2nd primary cancer.

Conclusions: In summary, breast cancer survivors still experience a variety of physical and psychological consequences. So, cancer care does not end after treatment. BCN has the privilege to provide education, support and advocacy for breast cancer survivors. The continuity of care improves nurse-patient relationship and survivors are willing to come back yearly for follow up. Moreover, long term nurse clinic can also share part of the caseload of doctor clinic.

EARLY LEARNINGS OF INFORMATION NEEDS OF BREAST CANCER PATIENTS AND ADDRESSING THOSE NEEDS THROUGH REMOTE NURSE SUPPORT

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Background: Through this research, Lunit is seeking to identify unmet information needs of breast cancer patients and caregivers and the feasibility to fulfill this need through remote nurse support.

Methods: 383 Breast Cancer patients and caregivers participated in an online survey from 10/21/2021-11/7/2021 to understand various needs throughout their cancer journey. 8 self-selected Breast Cancer patients and caregivers asked 25 questions through remote nurse support. Interactions took place based on patient preference, either phone or via text-based responses, starting 12/20/2021 and is ongoing. The answers to patient questions were drafted by nurses and reviewed by a team of medical doctors to ensure delivery of clinically sound information.

Result: Respondents reported a range of needs across the cancer journey. Specifically information on understanding the treatment (85.3%) and understanding the cancer (84.1%) were directly reflected in the remote nurse support, with nearly half of the questions related to understanding their treatment plan, and almost a third of the questions related to understanding the cancer the patient has. All of the service participants reported high satisfaction for the support and provided qualitative feedback that indicates strengthened confidence in their treatment.

Conclusions: We are seeing early evidence of the value remote nurse support can deliver which empowers the patient and their caregivers to feel more confidence in an otherwise difficult situation that is out of their control. We see an opportunity to explore the clinical benefits of the service to validate the true value of this service.

DETERMINATION OF CUT-OFF POINT USING BIO-IMPEDANCE SPECTROSCOPY FOR THE EARLY DETECTION OF BREAST CANCER-RELATED LYMPHEDEMA

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Background: Deteriorating quality of life in patients with breast cancer-related lymphedema (BCRL) can be substantial. Bio-impedance spectroscopy (BIS) is a useful tool for early diagnosis of lymphedema, however, data of BIS in breast cancer is limited. Here, we aimed to evaluate BIS according to lymphedema in breast cancer and determine the diagnostic cut-off value.

Methods: This study is a prospective cohort study of 146 patients in Seoul St Mary's hospital between March 2021 and January 2022. Breast cancer patients with clinically diagnosed BCRL and without BCRL were enrolled. Arm circumferences, volume, and BIS (S770, Inbody Co., Korea) measurements were taken once at the time of enrollment.

Result: Total 146 patients were enrolled, 72 patients with BCRL and 74 patients for the control group. BCRL patients had significantly higher impedance values at 1 kHz and 5 kHz, and extracellular water (ECW) ratio (ECW of the arm with breast cancer/ECW of contralateral arm). Among those, the ECW ratio was the strongest factor that discriminates lymphedema patients from non-BCRL patients (area under curve 0.827, 95% confidence interval 0.759-0.895, $p < 0.001$). The optimal cut-off point of the ECW ratio was 1.046 (4.6% increase) with 75.7% sensitivity and 75% specificity. Also, the ECW ratio showed a significant positive correlation with upper limb volume (Pearson correlation = 0.415, $p < 0.001$).

Conclusions: BIS is an efficient and easy diagnostic tool for lymphedema, and it might be used for early detection at a subclinical stage, reducing further morbidities when provided with early intervention.

MACHINE DEEP LEARNING APPLICATION, BASED ON COMPUTED TOMOGRAPHY IMAGES, FOR 3-DIMENSIONAL LYMPH EDEMA FIBROSIS QUANTIFICATION

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Background: In lymphedema patients, cytokine-mediated inflammatory cascades always occur such that fibrosis involves whole limbs. If collagen deposits, it disturbs QOLs and managements of patients in never-stop manner. However, no method has yet been approved for detecting lymphedema fibrosis before its progression. To gain this goal, verification of CT-based quantification of suprafascial microscopic fibrosis has been tried.

Methods: First, cross-sectional validation study had been conducted to 19 unilateral lymphedema patients for development of CT reticulation indexes (CTRIs) digitally subtracted from cross-sectional images by narrowing window-width of absorptive values (Hounsfield unit). Second, convolution neural network-based deep learning verification trial has been tried to cross-sectional CT images for recognition of every pixel as 6 classes.

Result: Maximal, mean, minimal CTRIs were significantly correlated with lymphedema duration, International Society of Lymphedema stages, bio-impedance ratio, and limb circumference difference ratio. Based on ROC analysis, maximal CTRI discriminated against lymphoscintigraphic stage IV (sensitivity: 0.78 and specificity: 0.60). The machine learning was trained with 784 images (4 mini batch; 70 epochs; 16 image depth; ADAM optimizer), and then tested with 36 images. Accuracy and intersection over union were 84.43% and 48.02% for the suprafascial reticulated pattern, 88.92% and 87.82% for the fat, 77.66% and 71.11% for the vessel, 99.66% and 95.74% for the muscle and bone, and 99.99% and 99.99% for the background.

Conclusions: The manual-processed prototype CTRIs could quantify inaccessible deep-located fibrosis and discriminate deep lymphatic system dysfunction. The current deep learning could differentiate the suprafascial fibrosis enough to kick off a clinical trial.

PREVALENCE OF BREAST CANCER RELATED LYMPHEDEMA AFTER BREAST CANCER TREATMENT IN A SINGLE SINGAPORE TERTIARY CENTRE AND ITS ASSOCIATED IMPACT ON QUALITY-OF-LIFE OUTCOMES (QOL)

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Background: Breast cancer related lymphedema (BCRL) represents a major adverse effect of breast cancer treatment. It can lead to pain, infections, loss of sensibility, strength and mobility of the affected arm which is associated with reduced arm function, and reduced quality of life (QOL). However, local data on prevalence of BCRL is sparse. This is mainly due to a lack of consistency in definition of breast cancer related lymphedema and measurements criteria. There is also no validation of QOL questionnaires which could be used as clinical outcome measure and assessment of treatment efficacy in our local population.

Methods: This cross-sectional study aims to determine the prevalence of lymphedema using patients' subjective complaints, objective arm circumference measurements and clinicians' independent assessments. 462 patients who were treated and on follow up for breast cancer surveillance in Changi General Hospital Breast Centre were recruited by convenient sampling. We ascertained the QOL of patients with lymphedema via an adapted questionnaire. The 3 lymphedema measurement criteria were analysed for concordance and diagnostic accuracy for clinically significant BRCL.

Result: Of the 3 criteria used, the prevalence of BCRL defined by arm circumference measurements was the highest at 16.7% (n = 88/462), whereas clinicians' assessment was the lowest at 6.4% (n = 30/462). When using any of the diagnostic criteria, the cumulative prevalence was 33.7% (n = 159). Quality of life assessment showed statistically significant differences in domains of function, appearance, mood and symptoms in patients with BCRL.

Conclusions: Clinicians may underestimate the prevalence of BCRL and its associated QOL impact without adjunctive tools.

A TECHNOLOGY-BASED SUPPORT PROGRAM: IS IT EFFECTIVE FOR ASIAN AMERICAN BREAST CANCER SURVIVORS?

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Background: A technology-based support program was designed to effectively provide support for Asian American breast cancer survivors in order to improve their survivorship experience. The purpose of the study was to examine the effectiveness of the program on the survivorship experience of this specific population.

Methods: This study used a randomized repeated measures control group design. A total of 199 Asian American breast cancer survivors were included (104 in the intervention group and 95 in the control group). The technology-based program included interaction platforms for participants and interventionists, being culturally tailored to three sub-ethnic groups (Chinese, Korean, and Japanese). To investigate the effectiveness of the program, internet questionnaires were repeatedly administered at pre-test, post 1-month, and post 3-months. The questionnaires included questions on background and disease-related factors, the Support Care Needs Survey-34, the Memorial Symptom Assessment Scale, and the Functional Assessment of Cancer Therapy Scale-Breast Cancer. Separate intent-to-treat growth curve models were used to analyze the data.

Result: Support care needs and psychological and physical symptom distress significantly decreased over time in the mixed-effect model using first-order autoregressive covariance structure (all $p < .01$). Yet, the effects on the quality-of-life scores were not significant over time.

Conclusions: This study presents the effectiveness of a technology-based support program in improving the survivorship experience, specifically support care needs and psychological and physical symptom distress of Asian American Breast Cancer survivors. Further study is needed to explore significant factors that may increase the quality-of-life among this specific population.

ANALYSIS OF EDUCATIONAL NEEDS FOR DEVELOPMENT OF PRACTICAL TRAINING PROGRAMS FOR SAFETY MANAGEMENT OF ANTICANCER DRUGS OF NURSES HANDLING ANTICANCER DRUGS IN GENERAL HOSPITALS

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Background: This study aimed to identify the priorities of anticancer drug safety management education needs for clinical nurses through need analysis.

Methods: Research design is a cross-sectional study. Data collection was performed from 10 to 30 April, 2021. The participants were 225 nurses working at one general hospital in C region. The questionnaire consists of 'knowledge on anticancer drug safety management', 'importance of anticancer drug safety management', and 'implementation of anticancer drug safety management'. Data was analyzed using t-test and one-way ANOVA. In order to identify the priorities of anticancer drug safety management education needs, the need analysis was conducted by using Borich's educational need equation and the Locus focus model. Highly ranked priorities on both methods proposed as the highest priorities.

Result: As a result, 2 items of 'personal protective equipment', 1 item of 'Spill protocol', and 1 item of 'medication' were highly ranked on both methods. The selected items by Locus for Focus model show that clinical nurses at general hospital need anticancer drug safety management education contents associated with personal protective equipment, spill protocol, and medication by priority.

Conclusions: The results show that anticancer drug safety management educational needs should be considered when developing anticancer drug safety management education program for clinical nurses in the future. The anticancer drug safety management education program should focus especially on the first quadrant (HH sector) of Locus for Focus model.

THE EFFECTS OF A TECHNOLOGY-BASED PROGRAM ON SUPPORT CARE NEEDS AMONG ASIAN AMERICAN BREAST CANCER SURVIVORS

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Background: With the recent ongoing global COVID-19 pandemic, the importance of a technology-based program for cancer survivors is emerging. Furthermore, technology-based programs are known to decrease the support care needs of cancer survivors, especially racial/ethnic minorities. The purpose of this study was to investigate the effects of a technology-based program on support care needs among Asian American breast cancer survivors.

Methods: This randomized controlled trial included 199 female Asian American breast cancer survivors, randomly assigned to either technology-based information and coaching/support program (n = 104) or control (n = 95). The participants were recruited through online and offline communities/groups for Asian Americans. Participants completed questionnaires at baseline (T0), 1 month (T1; after intervention) and 3 months (T2). Study measures included background characteristics and the Supportive Care Needs Survey Short Form 34 (SCNS). Effectiveness was analyzed with growth curve models according to the intention-to-treat principle.

Result: There were significant decreases in the SCNS scores over time in both groups ($p < .001$). No significant interactive effects of group and time were found on psychological needs, information needs, and sexual needs, but significant effects on physical needs ($\beta = -0.166$, $p < .001$) and support needs ($\beta = -0.066$, $p < .001$). In other words, the technology-based program significantly decreased physical needs and support needs of Asian American breast cancer survivors.

Conclusions: Future research is needed to identify additional variables that could help reduce the support care needs of breast cancer survivors during the cancer survival process.

ELEVATION OF CA 15-3 WITHIN NORMAL RANGE INCREASES THE RISK OF BREAST CANCER RECURRENCE IN KOREAN WOMEN: A LONGITUDINAL RETROSPECTIVE COHORT STUDY

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Background: This study aimed to examine the characteristics of research conducted on non-pharmacological interventions for breast cancer patients with cancer-related cognitive impairment (CRCI) and identify the primary effects of non-pharmacological interventions through a systematic literature review and meta-analysis.

Methods: A systematic review was conducted according to the Preferred Reporting Items for Systematic Review and Meta-Analyses statement. Databses such as Ovid-MEDLINE, EMBASE, and CINAHL were searched between May and April 2021 using the key terms of breast cancer, cognition disorders, and their possible variations. Risk of bias and effect size were also evaluated.

Result: A total of 3,683 studies was searched. After exclusions, 20 articles were included in the systematic review and 15 articles were included in the meta-analysis. Among the non-pharmacological interventions for breast cancer patients, cognitive behavior intervention was the most common with ten published papers (50.0%), followed by physical exercise with seven papers (35.0%). The meta-analysis indicated that non-pharmacological interventions had a significant effect on subjective cognitive function and immediate recall, execution capacity, and processing speed among objective cognitive functions.

Conclusions: Non-pharmacological interventions can improve subjective cognitive functioning among breast cancer patients undergoing cancer treatment. CRCI can negatively affect the daily life and quality of life of breast cancer patients. Therefore, it is necessary to provide non-pharmacological interventions by screening patients at high risk of CRCI. The findings can help breast cancer patients recover and adapt to their daily lives, prevent health problems, and maximize their quality of life by providing information on non-pharmacological interventions.

CONCEPT ANALYSIS OF BODY ACCEPTANCE IN BREAST CANCER WOMEN: APPLICATION OF HYBRID MODEL

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Background: Breast cancer is the most common cancer in women worldwide. Women undergo drastic body alterations following breast cancer and its treatments. Despite body acceptance having recently been highlighted as the key to body image improvement, there is no comprehensive and clear definition of it. Therefore, this study aimed to analyze the concept of body acceptance in breast cancer women.

Methods: This study employed a hybrid model, which comprises three phases. In the initial theoretical phase, attributes and working definitions of body acceptance were identified through an extensive literature review. Following this, during the fieldwork phase, in-depth interviews were conducted with five breast cancer women to elucidate the concept and to verify attributes derived from the first phase. Lastly, in the final analytic phase, the results were compared and integrated.

Result: Three core attributes extracted in the theoretical phase as "acknowledgment", "normalization", and "overcoming". Moreover, three themes emerged in the fieldwork phase, including "confronting and acknowledging the given body realities", "resuming daily life in harmony with the altered body", and "embracing body changes and designing a healthy future". In the third phase, definitive attributes and the conceptual definition of body acceptance were presented.

Conclusions: This study provides insights and improves our understanding of body acceptance among women within the context of breast cancer by clarifying the concept. This may encourage health professionals to develop an effective intervention for breast cancer women and consequently facilitate its provision in practice. Ultimately, this may offer a useful framework that guides the acceleration of further research into body acceptance.

PREOPERATIVE DECISION CONFLICT AND ANXIETY IN BREAST CANCER

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Background: This study is to investigate the degree of decision conflict and anxiety among breast cancer patients before surgery. This is a cross-sectional descriptive study conducted to understand how decision conflict and its sub-elements are correlated with anxiety.

Methods: Data collection was conducted in 2021 at a hospital in Seoul with a total of 75 breast cancer patients who were about to undergo surgery. The Decision Conflict Scale (DCS) was used to identify decision conflict, and STAI-X was used to figure out state-specific anxiety.

Result: First, the degree of decision conflict and anxiety experienced by breast cancer patients before surgery were high, and the anxiety level of subjects with severe decision conflict was significantly higher. Second, the correlation between the degree of decision conflict and the degree of anxiety experienced by breast cancer patients had a significant positive correlation with the higher the total score of the decision conflict, the higher the anxiety. In detail, correlations were shown in the order of satisfaction with treatment decision, perceived uncertainty, support experienced in the decision-making process, clarity of one's own value, and satisfaction with information about choice. However, satisfaction with information was not found to be related to anxiety.

Conclusions: The degree of decision conflict and anxiety experienced by breast cancer patients right before surgery is so severe that intervention is urgently needed. It seems to be necessary to develop and implement a holistic program in consideration of sub-factors constituting decision conflict in order to lower both decision conflict and anxiety.

THE DEVELOPMENT OF MINDFULNESS MEDITATION SMARTPHONE APPLICATION: FOCUSING ON FAMOUS PAINTING APPRECIATION

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Background: Breast cancer survivors experience adversity and stress as they experience the treatment process and recovery after cancer diagnosis. Mindfulness meditation is effective in reducing stress, pain, and relaxation in breast cancer survivors through being aware of myself and paying attention to this moment.

Methods: This study is a study to develop a smartphone application that provides mindfulness meditation focusing on appreciation of famous paintings. The mindfulness meditation application was developed as a three-step process as follows. Step 1: Development of mindfulness meditation education video, Step 2: Design of Application, and Step 3: Evaluation.

Result: First, mindfulness meditation education video content centered on appreciation of famous paintings was developed. In the video production stage, six educational videos of about 18 to 30 minutes were produced, including mindfulness meditation skills, sound healing meditation, meditation for pain relief, and self-regulation meditation skills. The smartphone application design was completed in a hybrid type compatible with both IOS and Android. In the evaluation phase, usability evaluation of the application was verified by expertise using application evaluation scale. The results showed content truth 19.13 ± 1.28, accessibility and convenience 24.87 ± 1.73, speed and connection 15.0, overall impression 14.8 ± 0.85.

Conclusions: The mindfulness meditation smartphone application developed in this study is expected to be effective in relieving pain and stress in breast cancer survivors and psychosocial adaptation after cancer diagnosis.

DISTINCT COGNITIVE FUNCTION PROFILES ARE ASSOCIATED WITH A HIGHER PRE-SURGERY SYMPTOM BURDEN IN PATIENTS WITH BREAST CANCER

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Background: Cancer-related cognitive impairment (CRCI) is a common symptom in patients with breast cancer. In our previous study of 397 women with breast cancer, we identified three groups of patients with distinct CRCI profiles (i.e., High, Moderate, Low-moderate attentional function). Compared to the other two classes, Low-moderate class was younger, had more comorbidities, and lower functional status. In this study, we expand on this work and evaluate for differences among these latent classes in the severity of psychological (depression, anxiety) and physical (fatigue, decrements in energy, sleep disturbance, pain) symptoms prior to surgery.

Methods: CRCI was assessed using the Attentional Functional Index from prior to through six months after surgery. Lower AFI scores indicate higher levels of CRCI. Psychological and physical symptoms were assessed with valid instruments. Parametric and non-parametric tests were used to evaluate for differences in symptom severity scores among the latent classes.

Result: Approximately 60% of patients experienced CRCI (i.e., Moderate and Low-Moderate classes). Significant differences were found among the three classes in the severity of trait and state anxiety, depressive symptoms, fatigue, and sleep disturbance (i.e., High < Moderate < Low-moderate). In addition, compared to the other two classes, the Low-moderate class reported higher pain interference scores.

Conclusions: These findings suggest that women with clinically meaningful levels of persistent CRCI have a relatively high symptom burden prior to surgery. Clinicians need to routinely perform preoperative assessments of CRCI and associated symptoms and initiate therapeutic interventions.

COMPARING DISEASE-SPECIFIC AND GENERIC QUALITY OF LIFE IN KOREAN BREAST CANCER SURVIVORS

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Background: Quality of life (QOL) has become an important indicator for evaluating patients' symptoms and their overall life satisfaction. However, selecting the appropriate instrument for QOL measurement is challenging, and few studies have compared disease-specific and generic QOL measures and how they reflect the impact of cancer-related symptoms on QOL in breast cancer survivors (BCS). We examined QOL in Korean BCS using both disease-specific and generic instruments and compared their representation of how anxiety, depression, sleep, fatigability, and posttraumatic growth impact QOL.

Methods: This study analyzed follow-up data for the BLESS study (Better Life after cancer, Energy, Strength, and Support), a 12-week exercise adherence RCT of 40 BCS in South Korea. Their QOL was assessed using both the Functional Assessment of Cancer Therapy-Breast (FACT-B) and Quality of Life Index (QLI).

Result: FACT-B and QLI scores revealed that Korean BCS had low levels of QOL. Both FACT-B and QLI scores were significantly related to anxiety, depression, sleep, fatigability, and posttraumatic growth in the participants. Notably, multivariate regression analysis of FACT-B and QLI scores showed different predictors for QOL: with the FACT-B, depression was the only significant predictor; whereas with QLI, posttraumatic growth was the only significant predictor.

Conclusions: The selection of a given QOL instrument may affect the overall findings and interpretation of the impacts of related symptoms. The FACT-B should be considered for studies of symptoms such as depression, while the QLI is more appropriate for examining overall QOL and posttraumatic growth.

DEVELOPMENT AND APPLICATION OF THE MOBILE-BASED VIRTUAL BREAST CANCER WOMEN NURSING SIMULATION TRAINING CONTENT: A MIXED METHODS STUDY

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Background: Nursing clinical practice education faces a new paradigm with mobile education through experiences taking care of virtual patients. The purpose of this study is to evaluate the efficacy of the mobile-based virtual breast cancer women nursing simulation training content on nursing students' knowledge, self-efficacy, learning flow, confidence, and satisfaction to explore the nursing students' virtual patient care experiences.

Methods: A mixed-method approach using the convergent design was used to explore students' cancer care knowledge, self-efficacy, learning flow, confidence and satisfaction, and learning experiences. Quantitative data through online questionnaires and qualitative data through focused group interviews were simultaneously collected, merged, and analyzed.

Result: In this study, a virtual breast cancer women nursing module was developed for the simulation training of nursing students by IBSTECH. Its content for practical education was implemented to enable mobile-based simulation training and a virtual medical record, in which the students experienced caring for a virtual breast cancer woman. Survey results indicated positive outcomes in knowledge, self-efficacy, learning flow, confidence, and satisfaction. The experience acquired by caring for virtual breast cancer women was derived with two core themes and five sub-themes, where it was found that the students "experienced taking care of virtual breast cancer women, and learned nursing care as if it were real."

Conclusions: The mobile-based virtual breast cancer women nursing simulation training content allowed nursing students to upgrade their skills by experiencing a fun and practical environment as a new learning method.

THE RELATIONSHIP BETWEEN PERCEIVED STRESS AND UNCERTAINTY IN BREAST CANCER PATIENT

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Background: This study was conducted to investigate the relationship between perceived stress and uncertainty in breast cancer patients.

Methods: A total of 54 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 perceived stress and uncertainty were 18.20 ± 3.89, and 95.91 ± 13.19. As perceived stress, there were no significant differences by cancer period, cancer stage, breast surgery, chemotherapy, radiotherapy and other treatment. But there was a significant difference in perceived stress according to the presence or absence of pain ($t = 3.165$, $p = .003$) and physical discomfort ($t = 3.623$, $p = .001$). As the uncertainty, there were no significant differences by breast cancer characteristics. There were significantly positive correlations between perceived stress and uncertainty ($r = .302$, $p = .027$).

Conclusions: The stress perception of breast cancer patients was confirmed as pain and physical discomfort rather than other cancer-related characteristics. Also, the higher the uncertainty, the higher the perception of stress in breast cancer patients. Therefore, it is suggested that strategies of clinical intervention for relieving pain and physical discomfort, furthermore it is managed strengthening emotional support and clarifying communications with breast cancer patients.

EFFECTS OF MOBILE APPS ON IMPROVING LIFESTYLE AND QUALITY OF LIFE IN POSTOPERATIVE BREAST CANCER PATIENTS: P4CANCERMDNET STUDY

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Background: Physical activity (PA) of a patient with a breast cancer diagnosis is associated with improved quality of life, but many breast cancer survivors do not meet the recommended level of PA. This study aims to evaluate the effect of digital health intervention using mobile apps to promote PA and quality of life in postoperative breast cancer patients. This study will also identify effective digital intervention methods and perform an economic analysis. The main hypothesis states that the use of mobile healthcare apps will improve health-related quality of life (HRQOL), promote PA, and reduce healthcare costs.

Methods: The promotion of better lifestyle with precise and practicable digital healthcare in postoperative cancer patients through multi-disciplinary network (P4CancerMDnet) study is a prospective four-group randomized controlled trial with a concurrent cost-utility evaluation. Patients are randomly assigned to the three different mobile app intervention groups or control group using a 1:1:1:1 ratio. The intervention groups are encouraged to use the assigned mobile app. The targeted outcomes are HRQOL, markers of metabolic health, and quality-adjusted life year. Outcomes will be measured at 6- and 12-month follow-ups.

Result: Recruitment was undertaken between November 2020 and September 2021. Patient follow-up is ongoing and outcome variables are being investigated.

Conclusions: This study will contribute to a better lifestyle and HRQOL through digital health care for postoperative breast cancer patients. The findings are expected to provide evidence on the effectiveness of mobile apps for breast cancer survivors.

FACTORS ASSOCIATED WITH SURGICAL EXCISION AND RECURRENCE IN PAPILLARY LESIONS OF THE BREAST

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Background: Incidental benign solitary papilloma with imaging concordance may be offered close follow-up. The purpose of this study was to investigate the factors for surgical excision and the recurrence of benign papillary lesions.

Methods: The patients with papilloma or papillary findings in the pathologic reports were reviewed from 2001 to 2020 in a single institution. The objective was to determine the factors with upgrading to invasive cancer or in situ. Another objective was to find factors associated with recurrence of papilloma in the patients who have a history of papilloma with or without atypia.

Result: Among 264 cases of total patients, the upgrade rate to malignancy was 7.6% (20/264). According to the pathologic differences, the upgrade rates were 4.3% and 22.0% for papilloma without atypia and with atypia, respectively ($p < 0.001$). Size on radiologic finding ($p = 0.006$) and BIRADS category ($p = 0.049$) were associated with upgrading the papilloma without atypia. The multivariate analysis showed that tumor size was only related to upgrading to malignancy (odds ratio [OR] = 8.09, $p = 0.040$). The mean follow-up period was 53.4 months for recurrence of benign papilloma. Multivariate Cox regression model represented that body mass index was significantly associated with recurrence of benign papilloma after adjusting for factors (OR 1.12; 95% CI 1.01-1.24; $p = 0.034$).

Conclusions: The result of this study for upgrading was similar to those of other studies, and no additional factors for excision were found. There are few studies related to the recurrence of benign papilloma. Follow-up may be recommended for patients at high risk of benign papilloma recurrence through additional analysis.

PLEOMORPHIC LOBUAR CARCINOMA IN SITU COMPOSED OF SIGNET-RING CELLS MIMICKING DUCTAL CARCINOMA IN SITU WITH PAPILLARY PATTERN

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Background: Carcinoma cells having various amount of intracytoplasmic mucin displacing the nuclei to the cell periphery are regarded as signet-ring cells. While some forms of invasive or in situ carcinoma of the breast may be partly composed of signet-ring cells, breast carcinoma entirely composed of signet-ring cells is extraordinarily rare.

Methods: We report a rare case of pleomorphic lobular carcinoma in situ (LCIS) composed predominantly of signet-ring cells with papillary pattern mimicking ductal carcinoma in situ (DCIS).

Result: A 58-year-old woman presented with a mass in the left breast detected on ultrasonography. Fourteen years ago, the patient has undergone right breast conserving surgery for invasive ductal carcinoma. Ultrasonography revealed an irregular parallel angular hypoechoic mass measuring 1.5 cm in the left 10 o'clock breast, which exhibited slow growth over the past 2 years. Ultrasound-guided core needle core biopsy was done. Microscopically, the tumor was composed of epithelial cells supported by fibrovascular stroma. The space between fibrovascular stalks were filled with discohesive epithelial cells. The majority (>70%) of tumor cells showed a feature of signet-ring cell differentiation. Some of the nuclei of signet-ring cells was round shape with intermediate-grade atypia. Within the signet-ring cells, mucicarmine and PAS stains demonstrated intracytoplasmic mucin. E-cadherin immunohistochemistry demonstrated absent staining within the tumor cells. After surgical excision, the final diagnosis was a pleomorphic LCIS without any high-risk pathological features, including invasive carcinoma and DCIS.

Conclusions: We report a case of pleomorphic LCIS composed predominantly of signet-ring cells with papillary pattern.

PREOPERATIVE TRANSCATHETER ARTERIAL EMBOLIZATION FOR CONTROLLING BLEEDING AND TREATMENT FROM CHEMORESISTANT ADVANCED BREAST CANCER: A CASE REPORT

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Background: The severe bleeding from the ulcerating focus of the locally advanced breast cancer is one of the rare but most challenging issues. Especially, if the breast cancer is chemoresistant, the treatment options are limited.

Methods: We herein report a case of transcatheter arterial embolization (TAE) in an inflammatory breast cancer with persistent bleeding during neoadjuvant chemotherapy (NAC).

Result: A 74-year-old woman had been diagnosed with right breast cancer at other hospital, but she refused to treat. After one year, she visited our hospital, complained about spontaneous bleeding from the huge protruding mass with ulceration in the breast. Imaging studies including MRI and contrast-enhanced CT revealed a huge enhancing mass, measuring 11 cm with skin invasion involving right whole breast, and multiple enlarged axillary lymph nodes. She was at stage IIIC (cT4N2M0), clinically. After six cycles of systemic NAC, tumor size and ulceration were unchanged, hemorrhage and exudate continued. She had chronic anemia need for intermittent transfusion. She was deemed to be unsuitable for surgery, because of the large tumor extent and spontaneous bleeding from multiple sites. For hemostatic purpose, TAE was performed. After obtaining left subclavian and axillary angiography, tumor feeders from internal thoracic, thoracoacrominal, lateral thoracic and thoracodorsal arteries were selectively embolized using Embosphere and Histoacryl. On completion angiogram, there were no visible tumor stainings. Three weeks later, she underwent definite total mastectomy with axillary lymph node dissection and skin graft to defect.

Conclusions: The application of embolization in optional patients can be an alternative to facilitating surgery.

CAUTIOUSNESS IN DETERMINING THE BIOPSY METHOD OF AXILLARY LYMPH NODE ENLARGEMENT: CASE REPORT

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Background: Enlarged lymph node in axillary area is symptom that is frequently encountered. In order to differentiate the cause of axillary lymph node enlargement, especially for malignant diseases, various examinations are performed. Blood test, imaging tests such as CT, ultrasound, PET-CT and biopsy are performed to determine the cause of the lymph node enlargement. The biopsy methods of lymph node include FNA, CNB, incisional biopsy and excisional biopsy.

Methods: Case report a-54-year-old male visited the OPD with enlarged left lymph node. The patient had no symptoms. No specific findings were observed on physical examination. The lesion observed on the chest CT was an enhanced lesion about 5 cm. We did ultrasound for axillary area. About 5 cm-sized isoechoic oval mass with hypervascularity. Lesion was difficult to differentiated from mass and enlarged lymph node only morphologic feature. We did core needle biopsy for lesion. The result was atypical stromal cells with fibrosis. We performed excisional biopsy under general anesthesia to differentiate malignant disease. The lesion was removed well, but bleeding occurred after surgery and compression was applied. Bleeding stopped after compression.

Result: Castleman's disease was reported for excisional biopsy. After confirming that there is no more lymph node enlargement on the other imaging examinations, chest CT, abdominal CT, neck CT and PET-CT, follow-up observation will be performed.

Conclusions: Excisional biopsy is often needed to differentiate axillary lymph nodes for the diagnosis of malignant disease, especially breast cancer. However, for diagnostic purposes, it should also be considered to obtain tissue in a less invasive method in consideration of side effect.

KS10076, STAT3 INHIBITOR, ENHANCES RADIATION SENSITIVITY VIA ROS-MEDIATED ER STRESS PATHWAY IN TRIPLE-NEGATIVE BREAST CANCER CELLS

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Background: Triple-negative breast cancer (TNBC), the most aggressive and deadly in breast cancer, is known to be resistant to radiation therapy (RT). Previous publications have alluded that a typical cause of this resistance due to STAT3, which is activated during RT. However, the mechanistic basis of how STAT3 causes resistance has not yet been fully understood. Here, we found KS10076 acted as a new STAT3 inhibitor, reversing radioresistance by increasing ROS-induced ER stress.

Methods: Cell viability assay was used to investigate the viability of breast cancer cells (MDA-MB-468, MDA-MB-231, HCC-1937, SK-BR-3, MDA-MB-453, MCF-7) following treated RT. Flow cytometry was used to determine ROS generation and apoptosis. Then Western blot was used to find whether p-STAT3 regulates the radiation sensitivity for inducing ER stress. Finally, the efficacy of radiation combined with KS10076 was assessed in vivo.

Result: Ionizing radiation promoted p-STAT3 expression and activation in TNBC cells. We found that cells with high expression of p-STAT3 could not induce ER stress due to lack of ROS generation. The combination treatment of KS10076 and radiation caused a significant decrease in p-STAT3, resulting in ER stress by maximizing ROS in TNBC cells. Moreover, it was confirmed that the occurrence of ER stress caused apoptosis and autophagy. Taken together, the combined anti-tumor effects of KS10076 and irradiation were significantly enhanced toxicity in TNBC cells.

Conclusions: Our data support the possibility of using a combination of KS10076 and radiation treatment in TNBC. Furthermore, STAT3 may be a potential target protein inducing ER stress for TNBC treatment.

COMPREHENSIVE CLINICAL CHARACTERIZATION OF PATIENTS WITH BRCA1:C.5017_5019DEL GERMLINE VARIANT

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Background: We present the clinicopathological characteristics, clinical outcomes, and family history of breast or ovarian acner in 17 patients with the BRCA1:c.5017_5019del variant and provide evidence for the re-classificaion of this variant.

Methods: This study included breast or ovarian cancer patients tested for BRCA1/3 genes between January 2008 and Jun 2020 at 10 medical centers in Korea. We retrospectively reviewed 17 probands from 15 families who had the BRCA1:c.5017_5019del variant according to the elecgtronic medical records.

Result: We present 17 patients from 15 families identified as having BRCA1:c.5017_5019del and a total of 19 cases of breast cancer and 14 cases of ovarian cancer in these families. Of ten breast cancer patients with this variant, 8 (80%) patients showed familiy history of breast or ovarian cancer, 7 (70%) patients had a cancer diagnosis prior to 50 years of age and 5 (50%) patients were categorized into th triple-negative breast cancer subgroup. Of the 17 patients with this variant, 7 patients had ovarian cancer, so the ratio of breast-to-ovarian cancer was 1.3:1. Also. the ovarian cancer patients with this variant showed strong family histories of breast and/or ovarian cancer.

Conclusions: We represented clinical evidence for the reclassification of BRCA1:c.5017_5019del as an LPV. Reclassificaion as an Likely pathogenic variant (LPV) could result in the prophylactic treatment and medical surveillance of provands, family testing recommendations, and appropriate genetic counseling of the families.

CAN TISSUE STIFFNESS MEASURED USING SHEAR-WAVE ELASTOGRAPHY REPRESENT LYMPHEDEMA IN BREAST CANCER?

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Background: Lymphedema causes skin and subcutaneous fibrosis. However, quantitative methods for estimating the severity of fibrosis due to lymphedema have not been established. We evaluated skin stiffness using shear-wave elastography (SWE) and aimed to identify stiffness-associated factors in patients with breast cancer-related lymphedema.

Methods: Thirty-six women (mean age, 57.5 ± 1.78 years; range, 39-77 years) were retrospectively recruited for this study. The mid-arm and mid-forearm circumferences were measured. The percentage differences in arm and forearm circumferences were used as an indicator of the severity of lymphedema at the time of SWE measurement and the measurement taken when the symptoms were most severe.

Result: Not subcutaneous tissues but cutaneous tissues of the affected arm and forearm showed a significant increase in shear-wave velocity compared with those of the unaffected side. However, shear-wave velocity was not correlated with the severity of lymphedema as a percentage difference when symptoms were most severe. Body mass index and lymphedema duration showed no significant correlation with the shear-wave velocity of cutaneous tissues on the affected upper extremities.

Conclusions: SWE can adequately estimate cutaneous fibrosis between the affected and unaffected limbs in patients with breast cancer-related lymphedema. However, evaluation of subcutaneous fibrosis is limited. Therefore, SWE can be an effective tool for evaluating cutaneous fibrosis in patients with breast cancer-related lymphedema.

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