GBCC2016
Global Breast Cancer Conference 2016
www.gbcc.kr
April 28 (Thu) - 30 (Sat), 2016
The Shilla Jeju Hotel, Jeju Island, Korea

Better Thinking for Better Life:
Exploring Advancing and Transforming Cancer Care

SAMSUNG MEDICAL CENTER

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Physician Scientist's View

Innovative Clinical Trial in the Era of Genomics

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Breast Cancer Center

Medical Oncology

Samsung Medical Center

Seoul, Korea

Contents

- Overview of precision medicine
- Genomics-driven clinical trials
- ***Oncoseq*** in patients with refractory MBC in SMC
- Incorporation of immune-oncology into precision medicine

Cell 2010

Leading Edge
Essay

Genetic Heterogeneity in Human Disease

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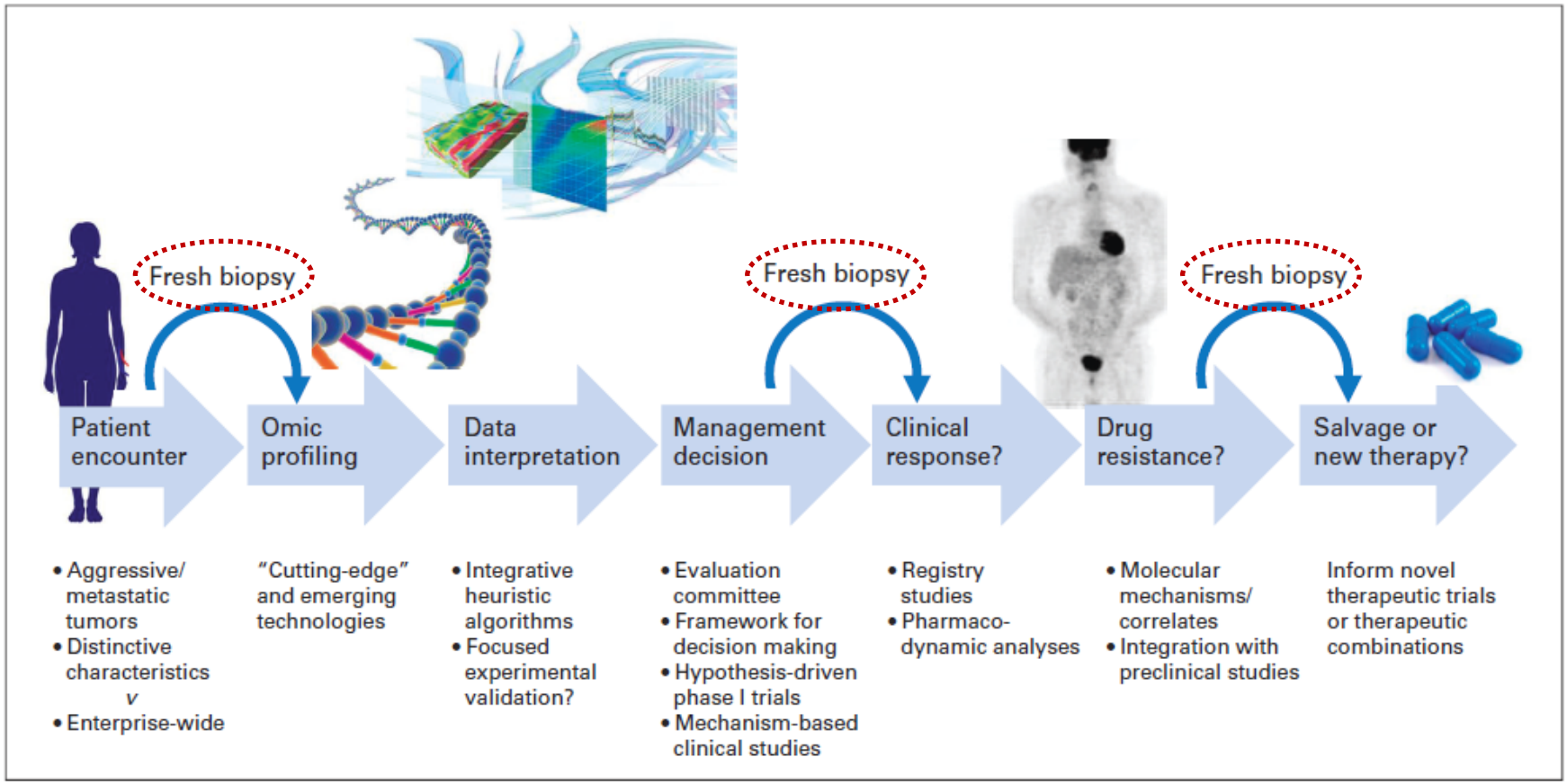
DOI 10.1016/j.cell.2010.03.032

Strong evidence suggests that rare mutations of severe effect are responsible for a substantial portion of complex human disease. Evolutionary forces generate vast genetic heterogeneity in human illness by introducing many new variants in each generation. Current sequencing technologies offer the possibility of finding rare disease-causing mutations and the genes that harbor them.

"Happy families are all alike; each unhappy family is unhappy in its own way."

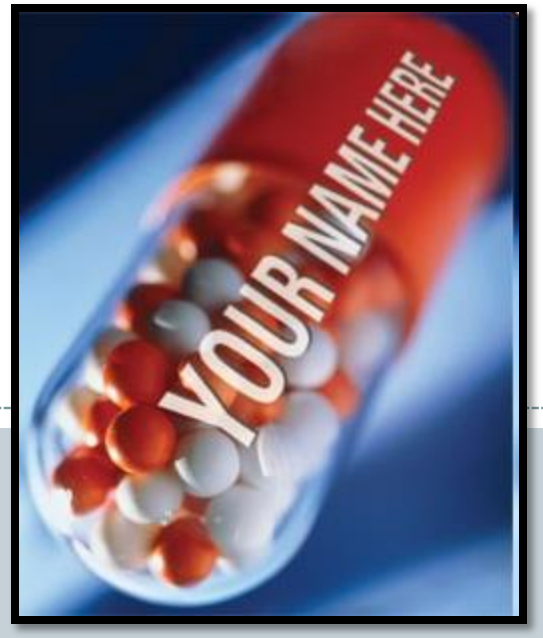
Leo Tolstoy, *Anna Karenina*

Enabling Components for Genomics-driven Cancer Medicine



Levi A, Garraway. J Clin Oncol 31:1806-1814, 2013.

"Tonight, I'm launching a new **Precision Medicine** Initiative to bring us closer to curing diseases like cancer and diabetes — and to give all of us access to the personalized information we need to keep ourselves and our families healthier."—



Nixon Signs $1.6 Billion Cancer Bill, Names Man to Head Fight

WASHINGTON (UPI)—President Nixon today signed into law a $1.6 billion program to find a cure for

the act was "a milestone in the long and difficult effort

Declaring War Against Cancer

- The signing of the National Cancer Act of 1971 by then U.S. President Richard *Nixon* is viewed as the beginning of the *war on cancer.*

President Richard Nixon signs the National Cancer Act, Dec. 23, 1971, launching a $1.6 billion federal crusade to conquer cancer. (AP)

AACR
American Association for Cancer Research
FINDING CURES TOGETHER™

PROJECTGENIE
Genomics Evidence Neoplasia Information Exchange

JOHNS HOPKINS MEDICINE
THE SIDNEY KIMMEL COMPREHENSIVE CANCER CENTER

CPCT
Center for Personalized Cancer Treatment

DANA-FARBER CANCER INSTITUTE

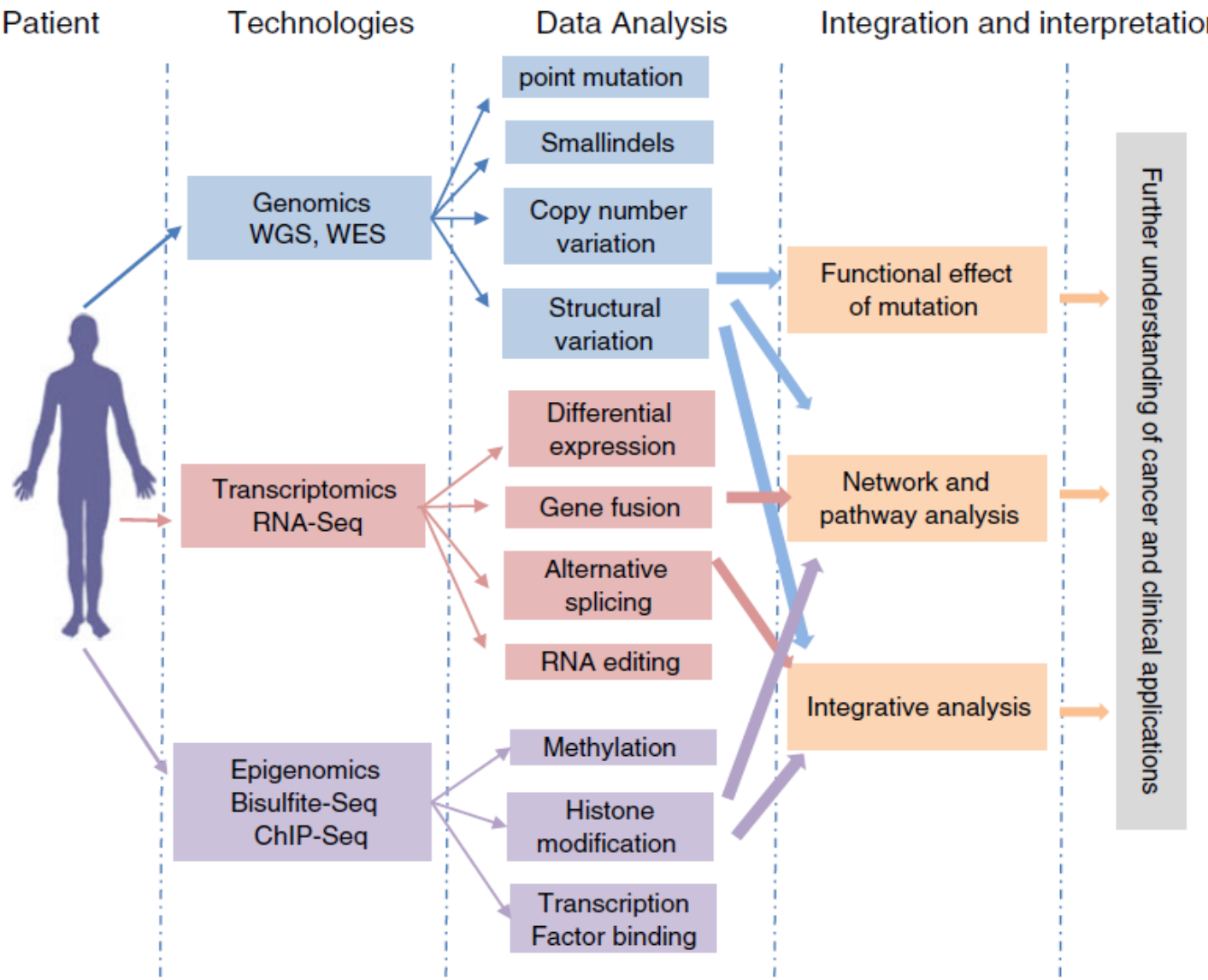
Princess Margaret Cancer Centre UHN

VANDERBILT-INGRAM CANCER CENTER

GUSTAVE ROUSSY
CANCER CAMPUS GRAND PARIS

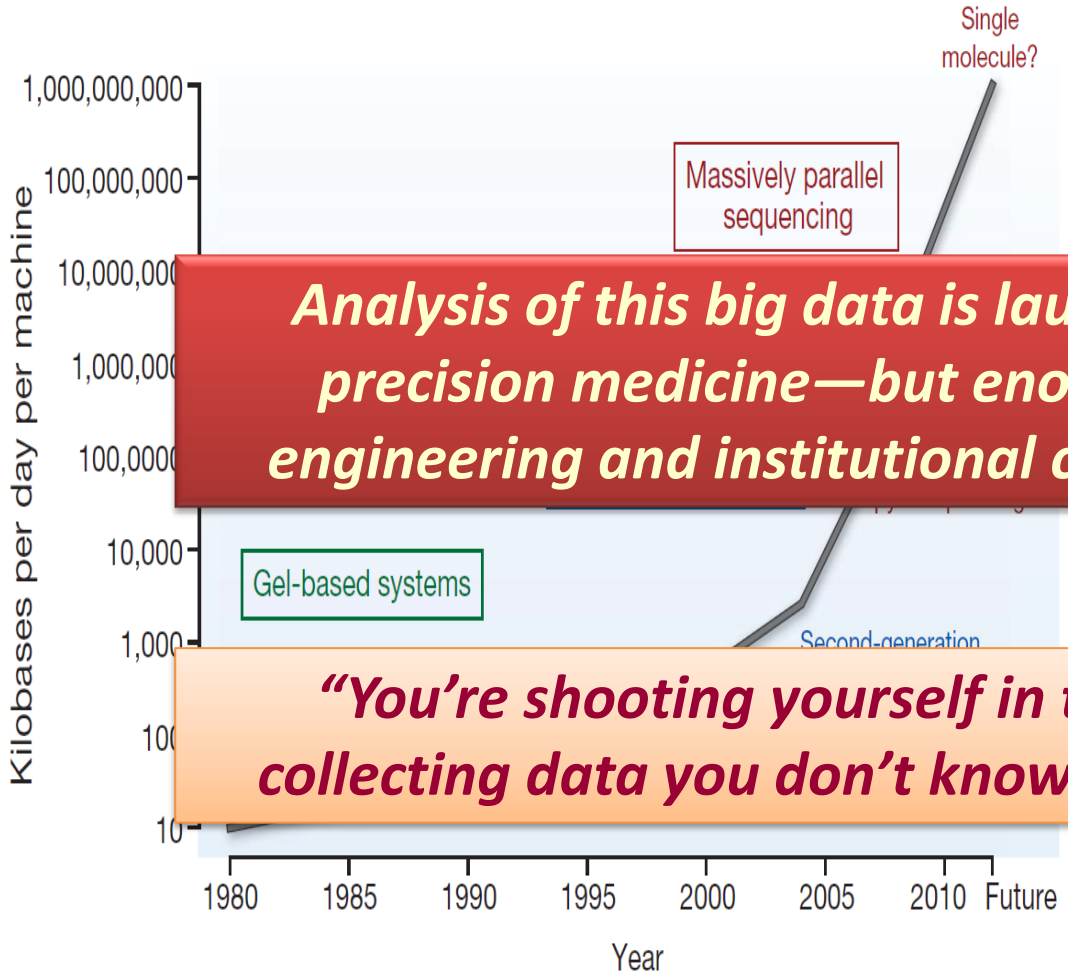
Memorial Sloan-Kettering Cancer Center

The workflow of integrating omics data in cancer research and clinical application



Shyr and Liu Biological Procedures Online 2013, 15:4

'Genomic Tsunami'



Analysis of this big data is launching the era of precision medicine—but enormous scientific, engineering and institutional challenges remain.

"You're shooting yourself in the foot if you're collecting data you don't know how to interpret."

Nature 2009, 458; 719-724

November 2015 / Vol 527 / Issue No 7576

Breast Cancer Treatment in 10 years

- **Predictions**
  - The era of HER2 is almost over.
  - BRCA testing will become ubiquitous.
  - We will continue to target proliferation and survival pathways.
  - Cancer genomics will become ubiquitous, but we won't like what we find.
  - We will need to do something different.

Sledge G, ASCO POST 9/11/2013

Norman Sharpless of the University of North Carolina works with IBM Watson Health to analyse DNA data.

CANCER

Reshaping the cancer clinic

Big data's war on cancer is still in the early stages, but the front line is advancing.

CancerLinQ

Briefing for Yeon Hee Park
April 21, 2016

ASCO CancerLinQ Newsletter

CancerLinQ Completes Agreements with Over Thirty-Five "Vanguard" Practices; Benefits for Practices Who Sign Up by June 1, 2016

CancerLinQ LLC is working with "vanguard" practices to begin implementing CancerLinQ™. In addition, ASCO is encouraging more of its members to have their practices become early adopters of CancerLinQ. Practices who sign up before June 1, 2016, will receive benefits.

LEARN MORE ABOUT BECOMING AN EARLY ADOPTER

In late 2015, the ASCO is expecting to launch CancerLinQ, a platform designed to deliver clinical benefits by analyzing aggregated electronic health records from thousands of oncology practices.

"Much of what we know about treating cancer comes from clinical trials that enroll just 3% of the patients diagnosed with cancer every year,"

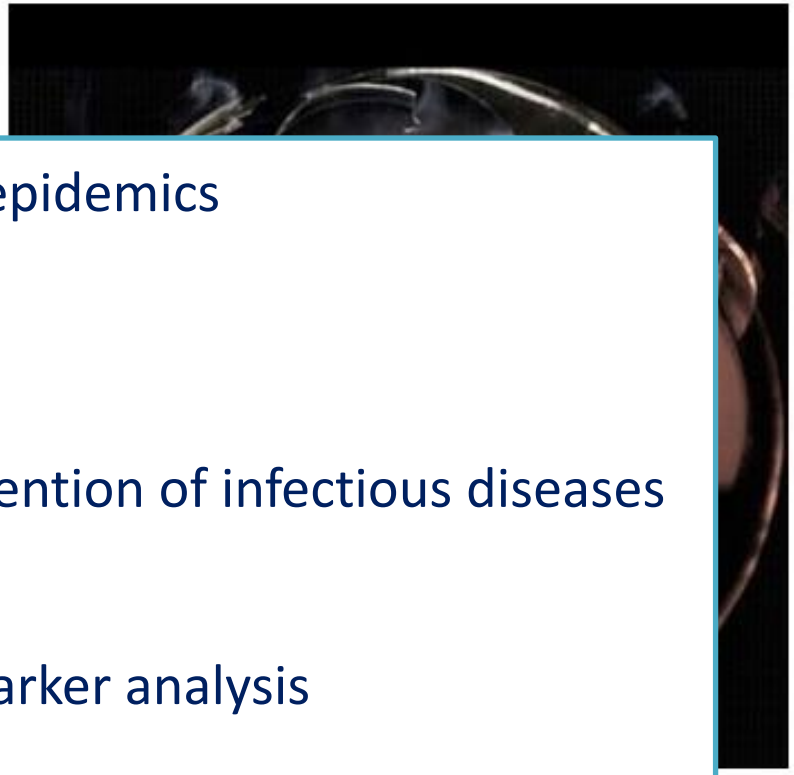
"With CancerLinQ, we're trying to learn from the remaining 97% who don't participate in these studies."

Nature 2015 / Vol 527 / Issue No 7576

Amazing Science: Top 10 Medical Innovations for 2016

October 28, 2015 / By News Wire Team

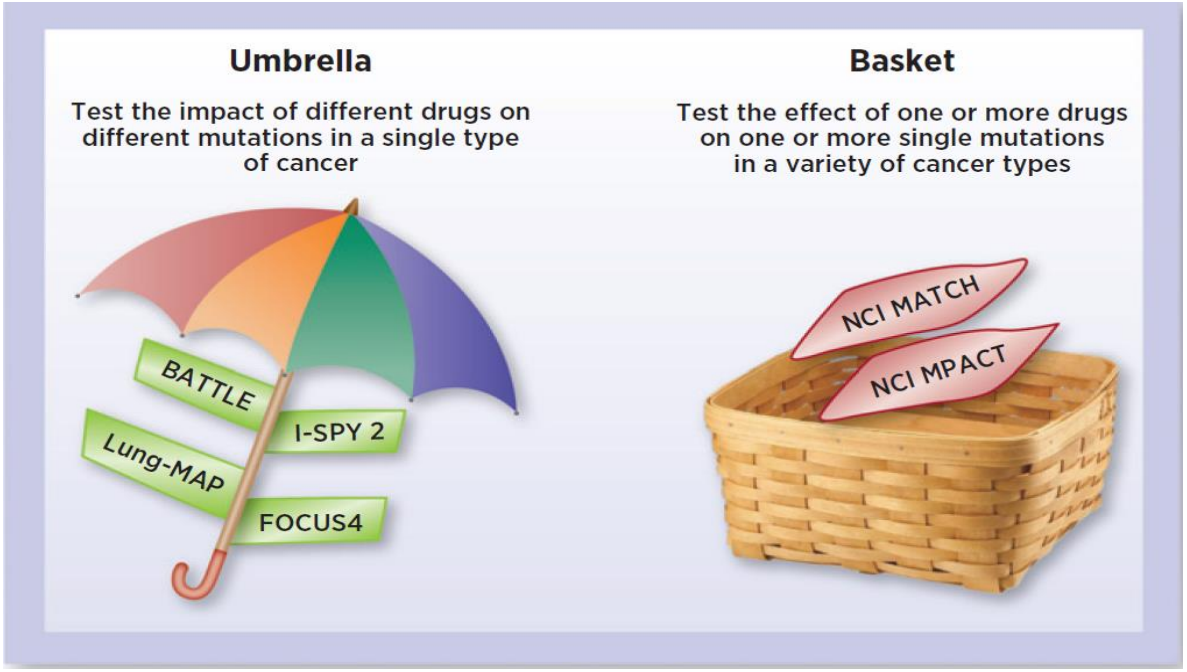
Take a look at the top 10 medical innovations from Cleveland Clinic's 2016 Medical Innovation Summit.



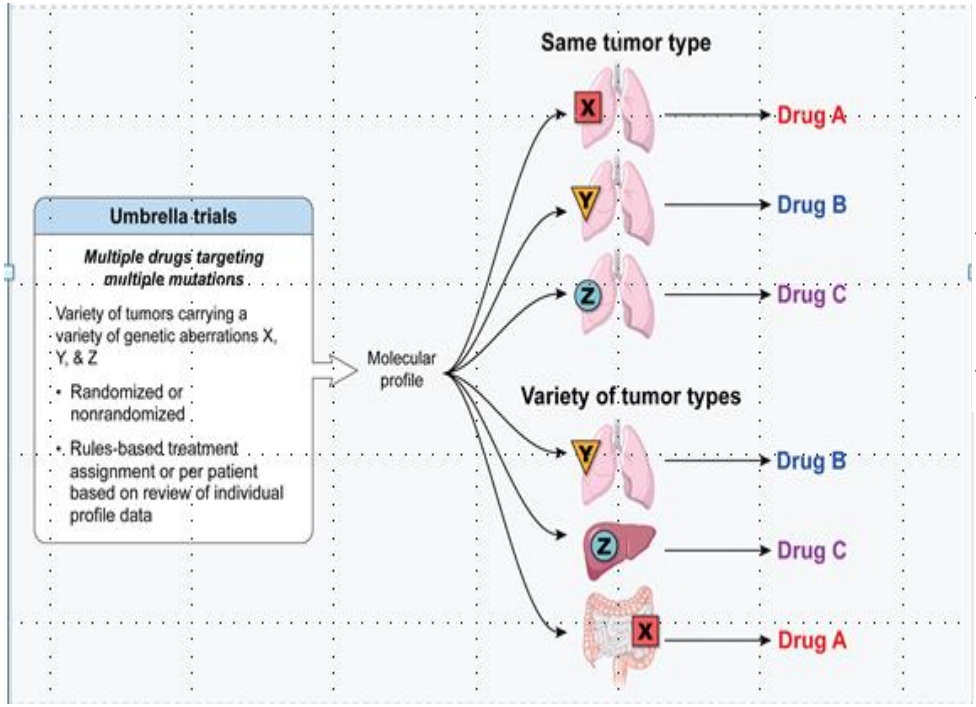
1. Vaccines to prevent public health epidemics
2. ***Genomic directed clinical trials***
3. Gene editing using CRISPR
4. Water purification system for prevention of infectious diseases
5. Cell-free fetal DNA testing
6. Cancer screening via protein biomarker analysis
7. Naturally controlled artificial limbs
8. First-ever treatment for HSDD
9. Frictionless remote monitoring
10. Neurovascular stent retriever

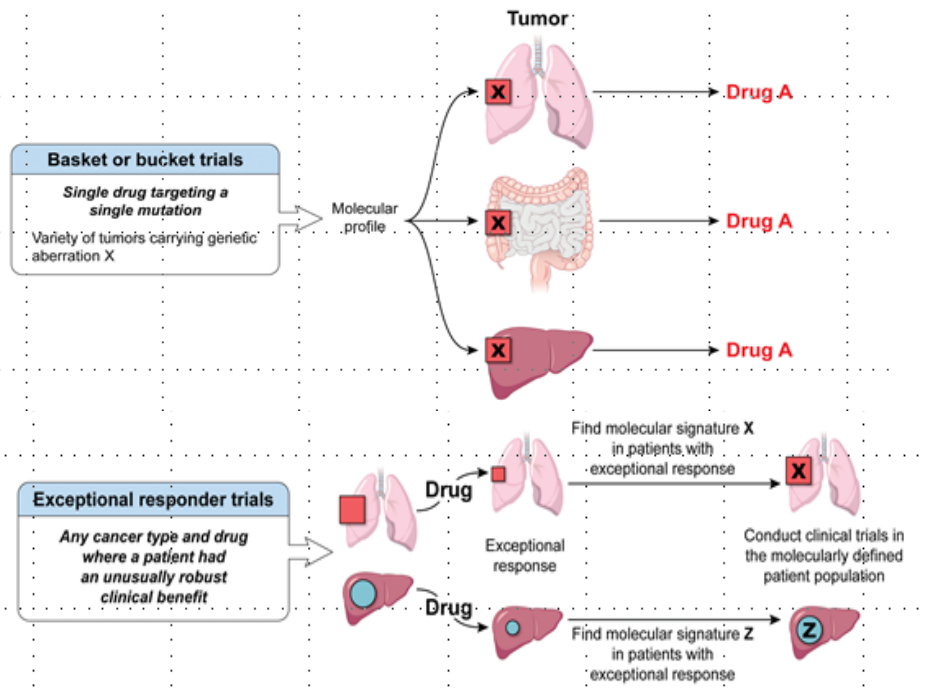
Randomized trial designs with integral biomarkers

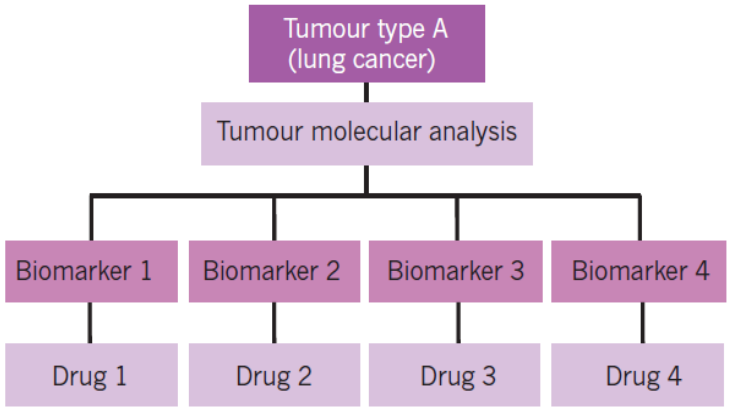
- Basket design
- Umbrella design
- Enrichment design with biomarker
- Stratified design according to with or without biomarker
- Hybrid design

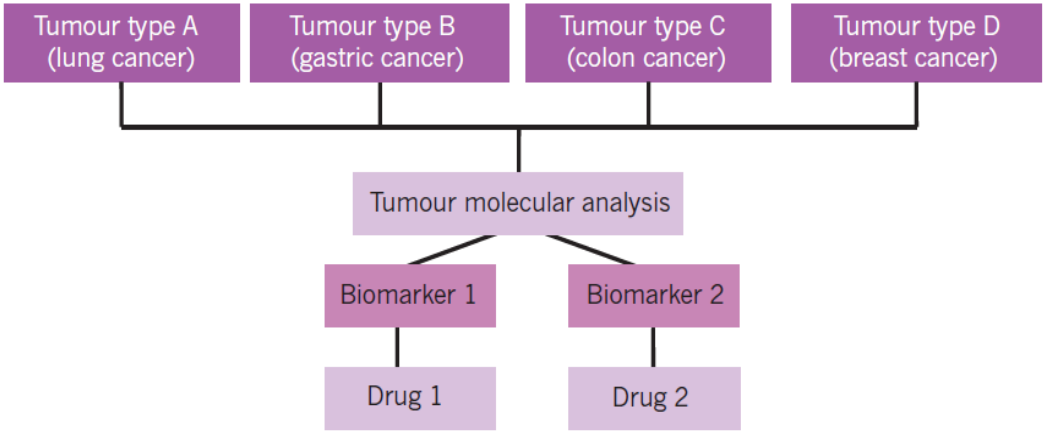


Clinical trial designs utilizing molecular profiling









Nature 2015, 526; 361-370; JNCI J Natl Cancer Inst, (2015) 107(4): djv003

Precision-medicine clinical trials

Study	Tumour	Phase/design	Location	Arms	Patients†	Clinical trial ID	References
Bisgrove	All	Phase II, non-randomized	United States	N/A	84	NCT00530192	19
IMPACT	All	Phase I	United States	N/A	1,144	NCT00851032	20
MOSCATO 01	All	Phase I	France	N/A	420	NCT01566019	21
Lung-MAP	Squamous lung	Phase II/III, randomized	United States	5	10,000	NCT02154490	49
BATTLE	NSCLC	Umbrella, route to four phase II randomized	United States	4	300	NCT00409968 (umbrella) NCT00411671 NCT00410189	31, 66, 67
BATTLE-2	NSCLC	Phase II randomized	United States	4	450	NCT01248247	N/A
BATTLE-FL	NSCLC	Phase II randomized	United States	4	225	NCT01263782	N/A
I-SPY 2	Breast cancer	Phase II randomized	United States	8	800	NCT01042379	68, 69
NCI-MPACT	All	Phase II stratified, non-randomized	United States	6	700	NCT01827384	70
NCI-MATCH	Solid	Phase II stratified, non-randomized	United States	20	3,000	Umbrella, route to phase II‡	48
V-BASKET	All	Phase II stratified, non-randomized	Global	2	160	NCT01524978	71
CREATE	Selected	Phase II stratified, non-randomized	European Union	6	582	NCT01524926	N/A
WINTHER	All	Stratified, non-randomized	European Union	2	200	NCT01856296	72
SHIVA	All	Phase II stratified, controlled	France	10	1,000	NCT01771458	38
MOST	All	Phase II stratified, randomized	France	5	560	NCT02029001	N/A
SAFIR 02 Lung	NSCLC	Phase II stratified, randomized	France	8	650	NCT02117167	73
SAFIR 02 Breast	Breast cancer	Phase II stratified, randomized	France	18	460	NCT02299999	N/A
Lung MATRIX	NSCLC	Phase II stratified, non-randomized	United Kingdom	21§	2,000‖	EudraCT 2014-000814-73	65
FOCUS 4	Colorectal cancer	Phase II/III randomized	United Kingdom	4	643	EudraCT 2012-005111-12	74
IMPaCT	Pancreatic cancer	Phase II stratified, randomized	Australia	4	90	ACTRN 12612000777897	47

"Master protocol" or "Platform protocol"

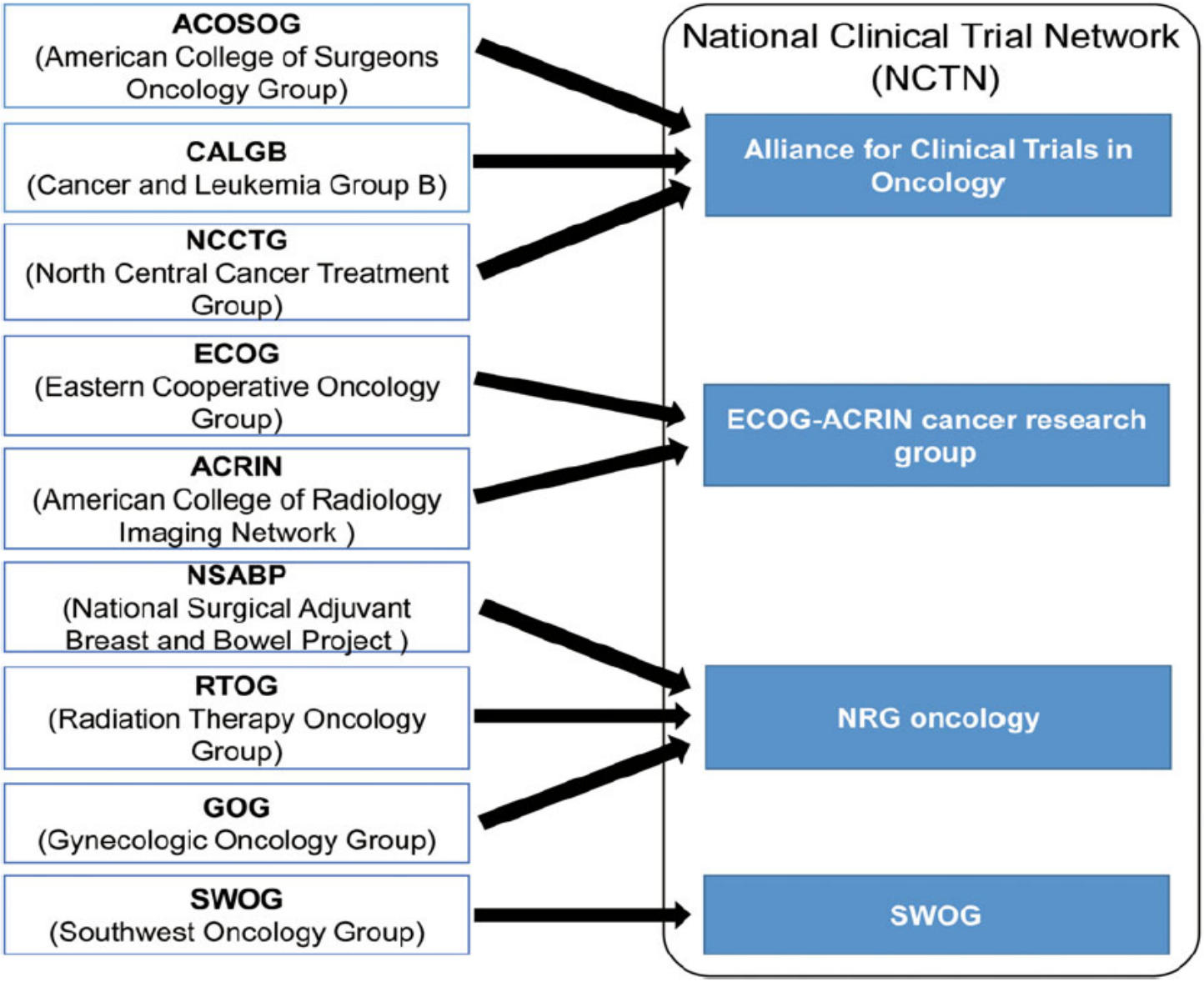
Nature 2015, 526; 361-370

Screening programmes that feed into precision-medicine trials

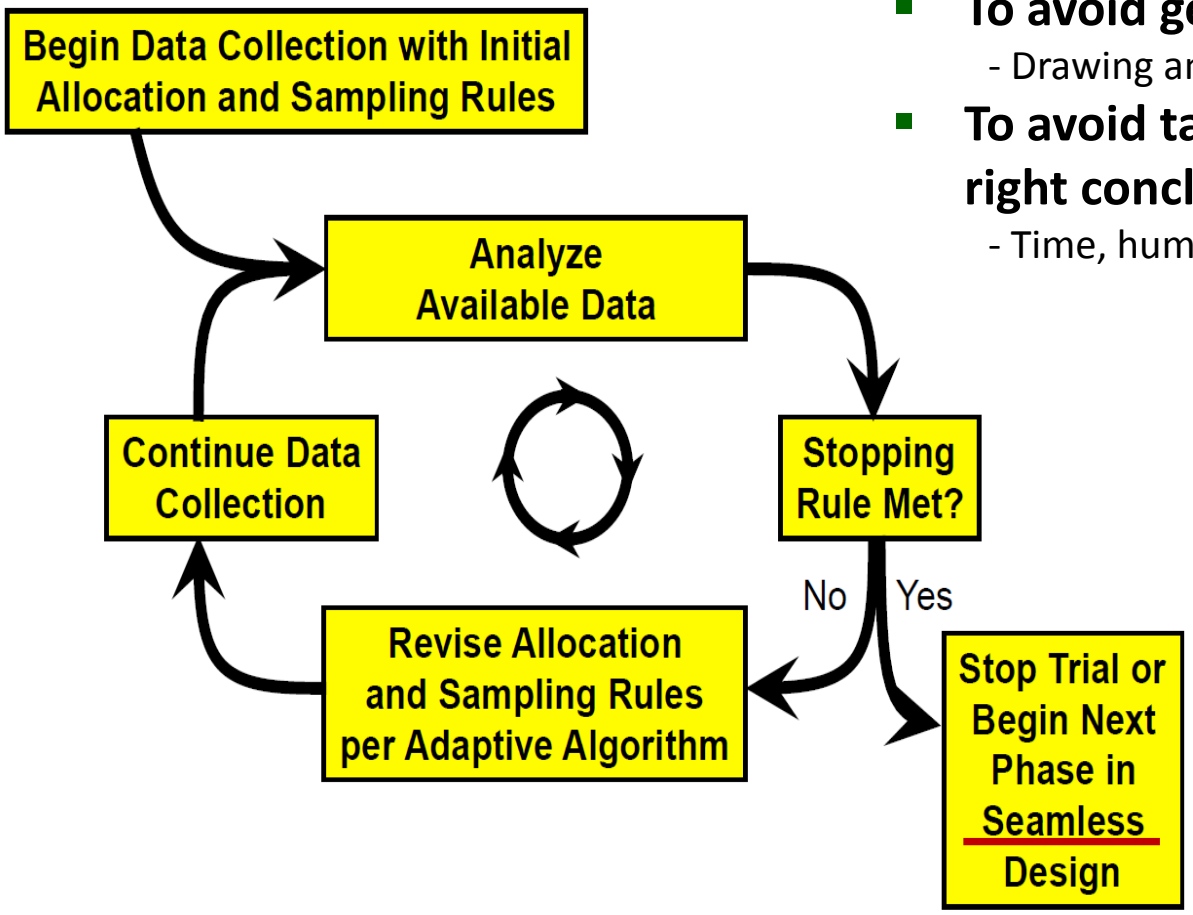
I-SPY	Breast cancer	Phase II, diagnostic study	United States	Genomic, imaging	221	NCT00043017
NCI-MATCH	Solid	Screening, route to phase II	United States	NGS¶	3,000	N/A
VIKTORY	Gastric cancer	Screening, route to phase II	Asia	NGS, other#	600	NCT02299648
LC-SCRUM	NSCLC	Screening, route to phase II/III	Asia	As needed**	Open††	N/A
AURORA	Breast cancer	Screening, route to phase I/II/III	European Union	NGS, other‡‡	1,300	NCT02102165
SPECTAColor	Colorectal cancer	Screening, route to phase I/II/III	European Union	NGS	2,600	NCT01723969
SPECTALung	Lung	Screening, route to phase I/II/III	European Union	NGS	500§§	NCT02214134
MOSCATO	All	Screening, route to phase I/II	France	CGH array, sequencing	1,050	NCT01566019
SAFIR 01	Breast cancer	Screening, route to phase I/II	France	CGH, sequencing, gene expression array	423	NCT01414933
CRUK SMP1	Selected	Screening, feasibility	United Kingdom	Bespoke panel	9,000	N/A

Nature 2015, 526; 361-370

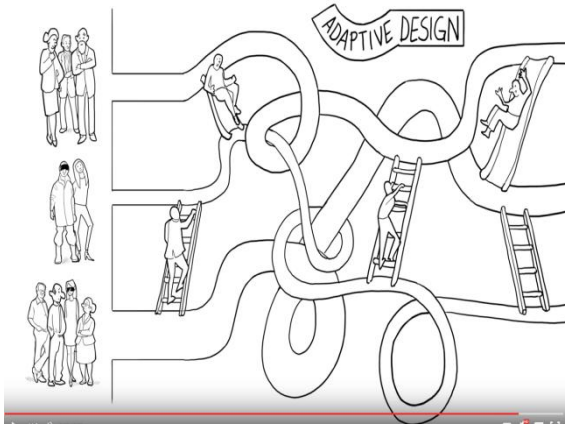
The NCI National Clinical Trials Network (NCTN) structure



Adaptive Bayesian Clinical Trial Design



- **To avoid getting the wrong answer!**
  - Drawing an incorrect qualitative conclusion
- **To avoid taking too long to draw the right conclusion**
  - Time, human subjects, and resources



Clinical trials testing large panel of genes for treatment decision

Trial	Technology	n screened	Matched therapy	Outcome
SAFIR01[1] (brea	CGH /	423	55 (13%)	30% OR and/or ths
MOSCA				
MDACC[3]	11-50 genes	2 000	83 (4%) (P1 trials)	Not available
Princess Margaret[4]	48 genes	1595	64 (4%)	22% OR
T-Gen[5]	Gene expression	86	66*	27% PFS ratio of ≥ 1.3
SHIVA[6]	NGS	741	195[$]	hazard ratio 0·88, 95% CI 0·65–1·19, p=0·41

No evidence from large clinical trial that sequencing large panel of genes improves outcome!!

Is it a new generation of garbage-in/garbage-out???

1. Andre, Lancet Oncol, 2014 , 2. Ferte, AACR, 2014, 3. Meric-Bernstam, JCO, 2015, 4. Bedard, ENA, 2015, 5. Von Hoff, JCO, 2010, 6. Letourneau, Lancet Oncol, 2015

Lessons from Genome Profiling Clinical Trials

- ***Why these trials failed ?***
  - **Drugs are not bioactive and/or not well matched to alterations.**
  - **Method for driver identification is *not* optimal**: validated and robust tools to interpret biology at the individual level were not available

- ***Rare mutations are….rare.***
  - Uncommon and rare mutations make it very hard to do studies to get drugs approved.
  - ***RCT(randomized clinical trials) vs. SOC (standard of care)*** can be very difficult: Unappealing to pts and their doctors

Oncoseq Project for Patients with Refractory MBC in SMC

Screening program for 'N of 1 trial' experience in SMC for patients with MBC

- ***Genomic platform for the treatment of the patients with refractory malignancies in SMC based on multi-omics***
- **2012-**
- **WES, WTS, CancerSCAN (targeted sequencing)**

Work flow for NGS

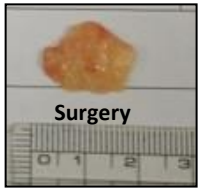
BC Lab

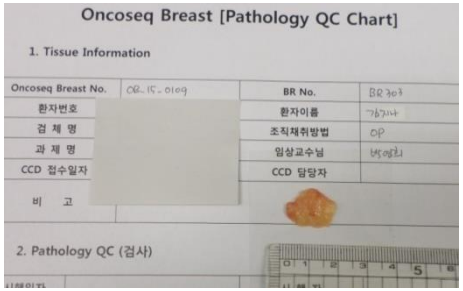
Informed Consent

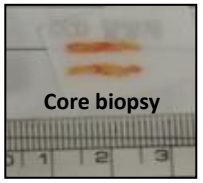
Tissue delivery

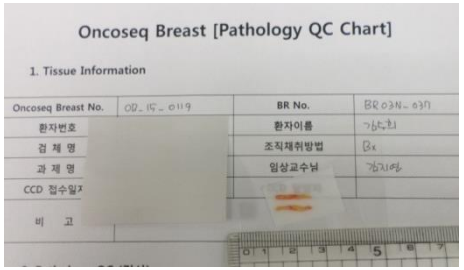
Surgery

Core biopsy





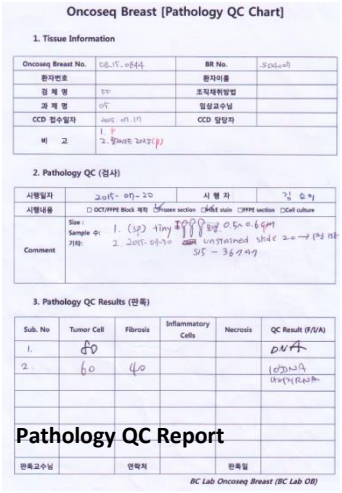




CCD

Pathology QC

DNA/RNA extraction

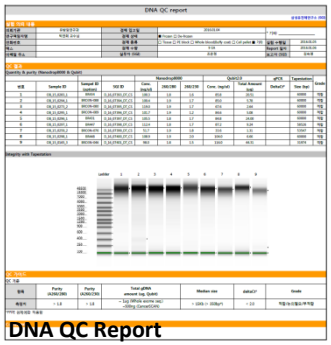


Pathology QC Report

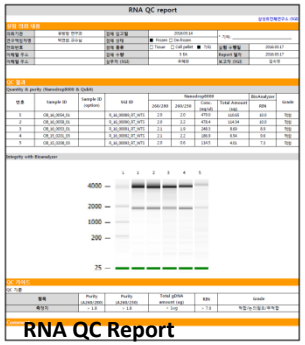
SGI

DNA/RNA QC

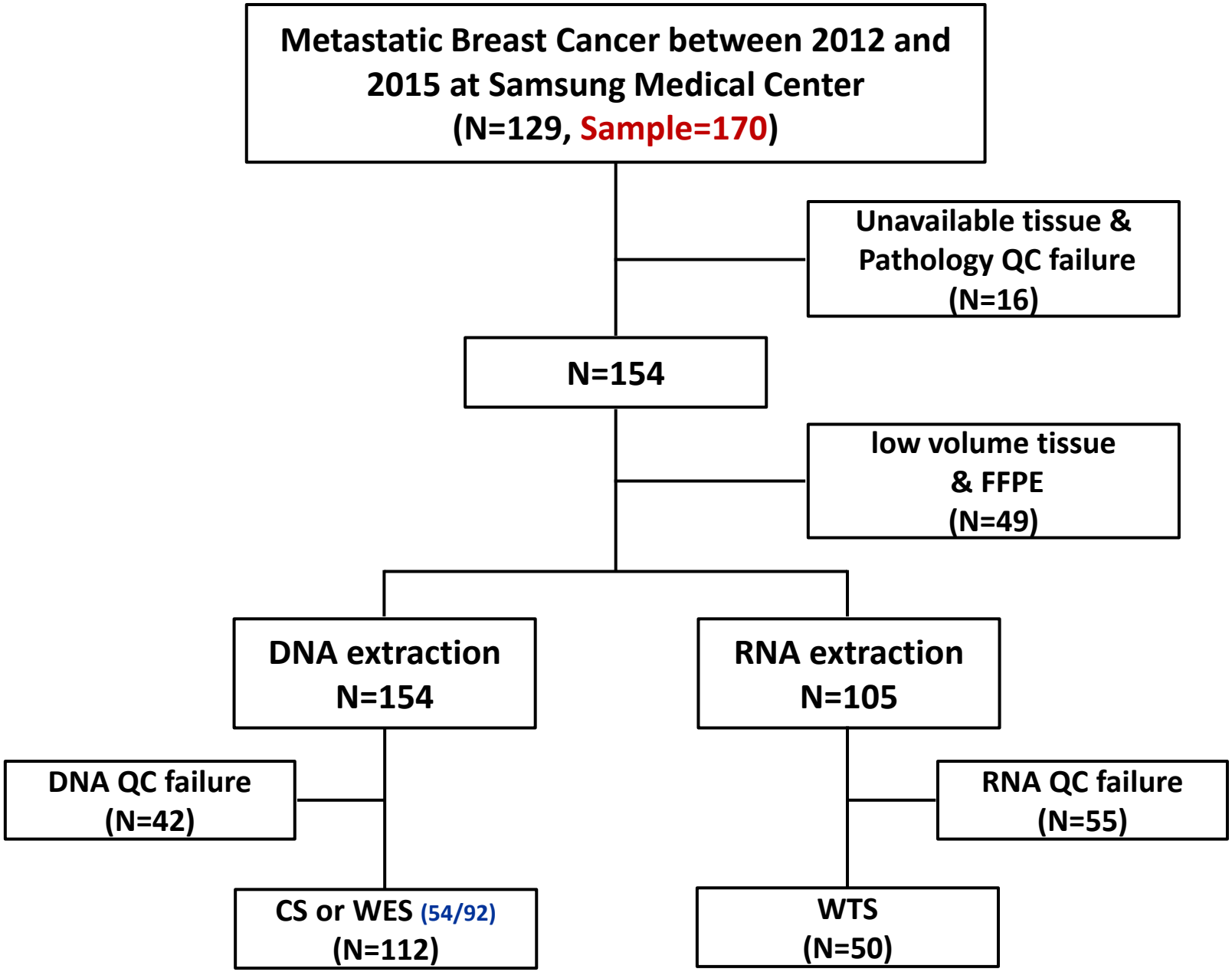
NGS



DNA QC Report

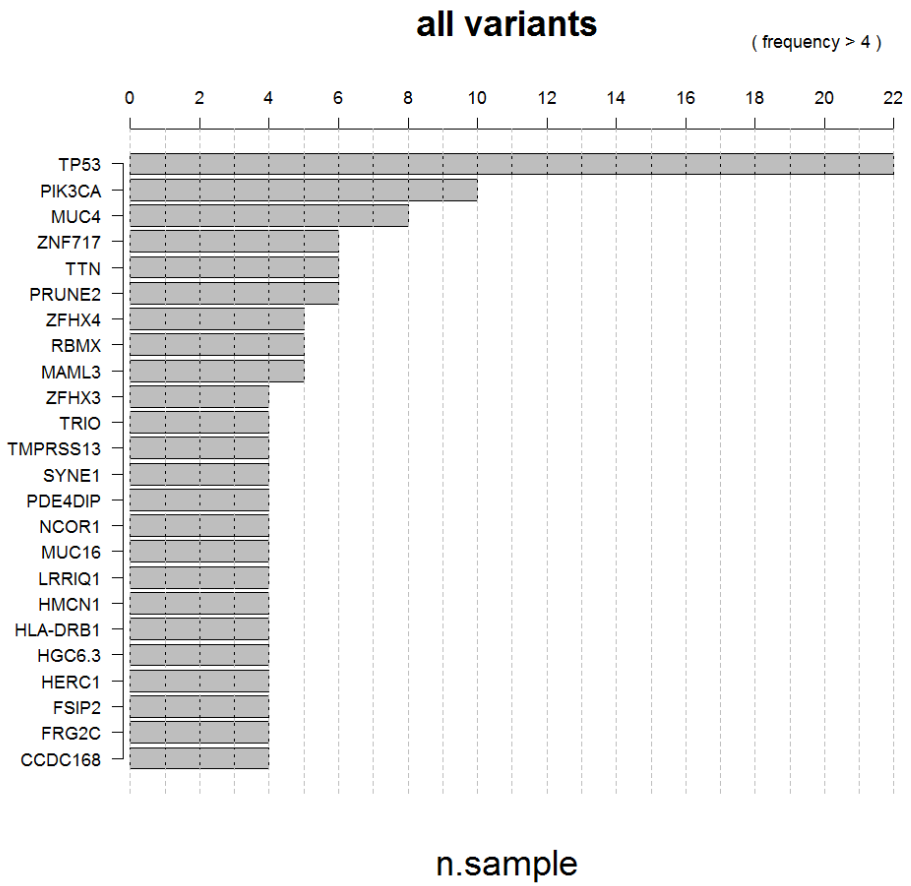


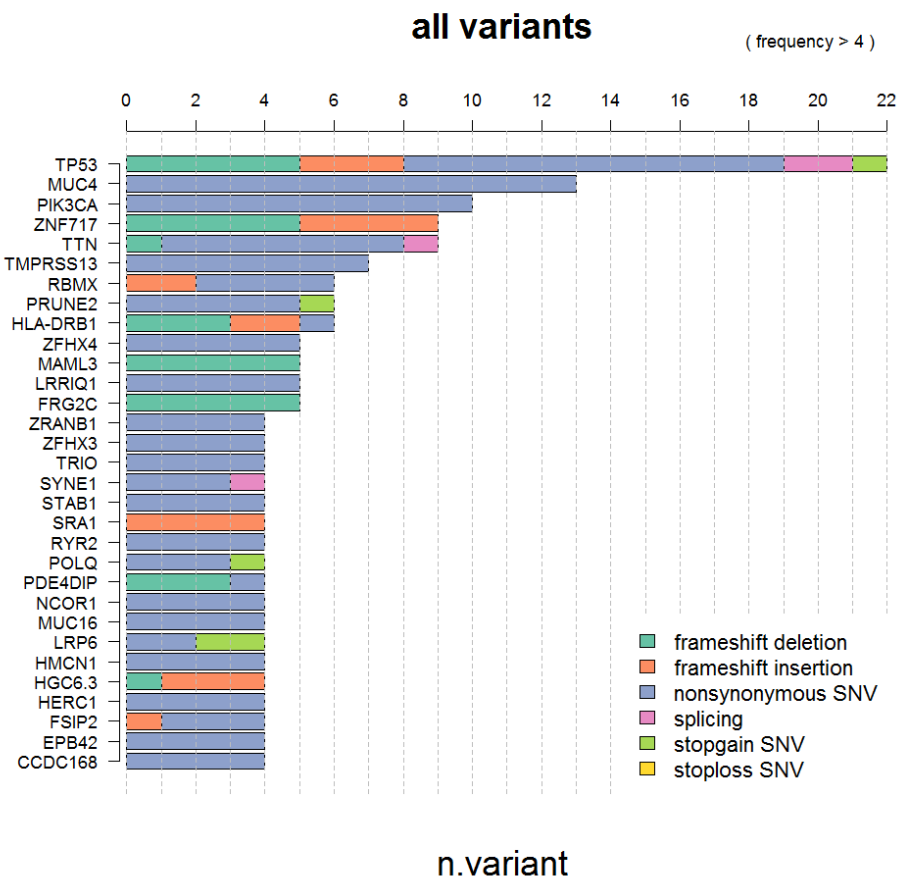
RNA QC Report

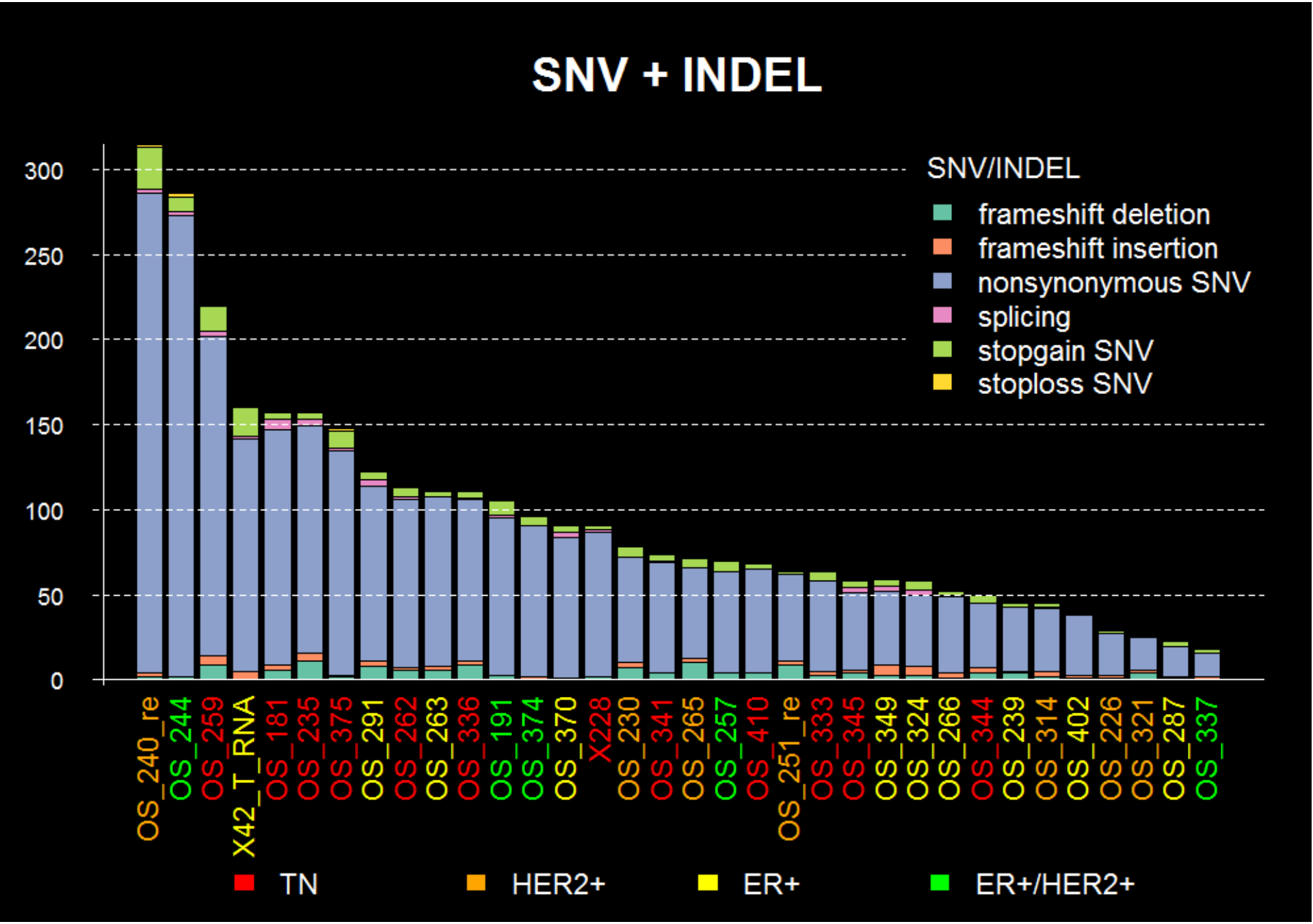

Metastatic Breast Cancer between 2012 and 2015 at Samsung Medical Center (N=129, Sample=170)
Unavailable tissue & Pathology QC failure (N=16)
N=154
low volume tissue & FFPE (N=49)
DNA extraction N=154
RNA extraction N=105
DNA QC failure (N=42)
RNA QC failure (N=55)
CS or WES (54/92) (N=112)
WTS (N=50)

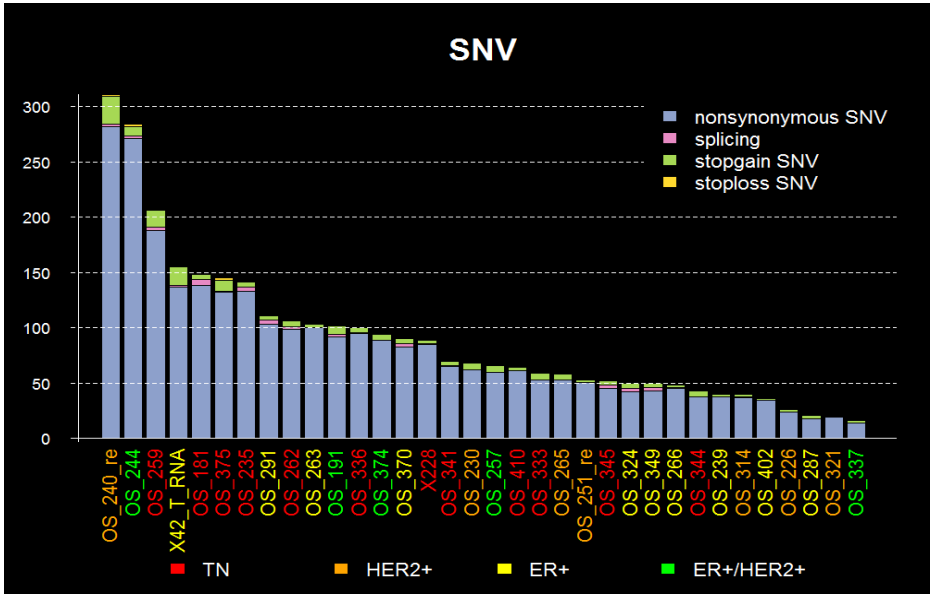
MBC WES (WTS paired 34 samples)

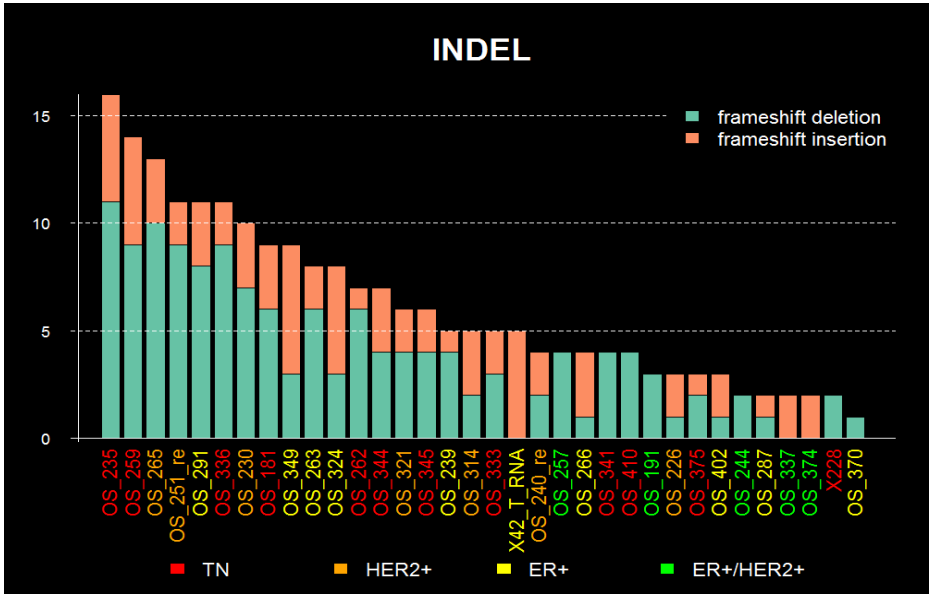
- Final mutation data : SNV 3,069 + indel 209 = 3,278
- Most frequent variant : TP53 (n=22 / SNV=14, indel=8)
- 2nd : PIK3CA (n=10, SNV=10)



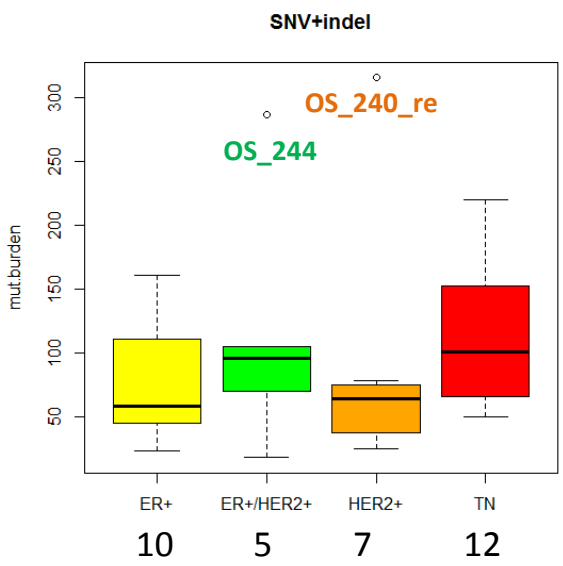


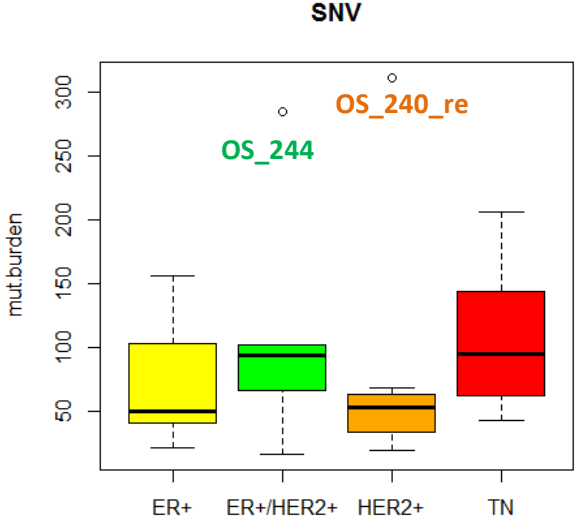

SNV + INDEL
SNV/INDEL
frameshift deletion
frameshift insertion
nonsynonymous SNV
splicing
stopgain SNV
stoploss SNV
300
250
200
150
100
50
0
OS_240_re
OS_244
OS_259
X42_T_RNA
OS_181
OS_235
OS_375
OS_291
OS_262
OS_263
OS_336
OS_191
OS_374
OS_370
X228
OS_230
OS_341
OS_265
OS_257
OS_410
OS_251_re
OS_333
OS_345
OS_349
OS_324
OS_266
OS_344
OS_239
OS_314
OS_402
OS_226
OS_321
OS_287
OS_337
TN
HER2+
ER+
ER+/HER2+

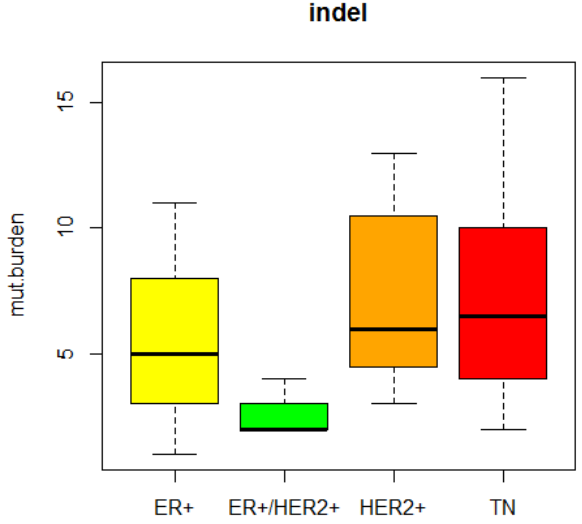




- TN samples have more SNVs than other groups, especially HER2+.
- ER+/HER2+ samples have fewer indels than other groups.







Case 1.
Medical history (F/36)

Rt breast ca(pT2(3cm)N(3/8))(ER-/PR-/HER2-)(2007.8)
s/p Rt PM with ALND
s/p AC #4 + paclitaxel #4 + Radiotherapy (2007.10.1-2008.4.28)
- progression on lung (multiple hematogeneous lung metastses) (NED :2Y7M)
s/p palliative PG #20 (2010.03.04-2011.04.18) with CR -> PD
s/p capecitabine #3 (2011.10.24-2012.02.06) -> PD (Pleura)
s/p GP #6 (2012.03.12-2012.07.03) -> SD -> PD
s/p DC #14 (2013.12.16-2014.10.2) -> PR -> PD (Pleura, lung)
s/p eribulin #7 (2015.1.8-2015.6.4) -> SD -> PD
s/p vinorelbine #2 (2015.6.25-2015.7.23)
s/p VATS pleural biopsy and talc pleurodesis, Lt. (2015.8.19)
: metastatic carcinoma, ER/PR/HER2 (+(3)/-/-)ki-67(2+),EGFR(-), AR (-) DDK4/FGFR1 fusion, FGFR1 amplification (+)
s/p CMF #1 (2015.9.7)
- progression on CNS
s/p WBRT 30Gy/10Fx's (2015.9.16-2015.9.30)
s/p pazopanib (2015.11.20-2016.01.03) with SD

CNV 6 rows

Class	Gene	Drug	Position	CNV	Log2Ratio	Copy No.	Known
C1	FGFR1	Fibroblast growth factor receptor 1 (DB08577)	8p11.23-p11.22	Amp.	1.28	4.9	Known
C1	FGFR1	Fibroblast growth factor receptor 1 (DB08577)	8p11.23-p11.22	Amp.	1.28	4.9	Known
C2	MYC		8q24.21	Amp.	1.07	4.2	Known
C3	GPR124		8p11.23	Amp.	1.29	4.9	Unknown
C3	WHSC1L1		8p11.2	Amp.	1.31	5.0	Unknown
NA	ZNF703		8p11.23	Amp.	1.25	4.8	NA

Translocation 2 rows

Class	ChrA	GeneA	DrugA	BreakpointA	Direction	ChrB	GeneB	DrugB	BreakpointB	Total reads
T3	8	DKK4		42233274 [E2(4)]	A->B	8	FGFR1	Fibroblast growth factor receptor 1 (DB08577)	38303524 [I2(18)]	118
T3	6	GPSM3		Not_estimated [I1(8)]	B->A	6	NOTCH4		32163541 [I-121(30)]	10

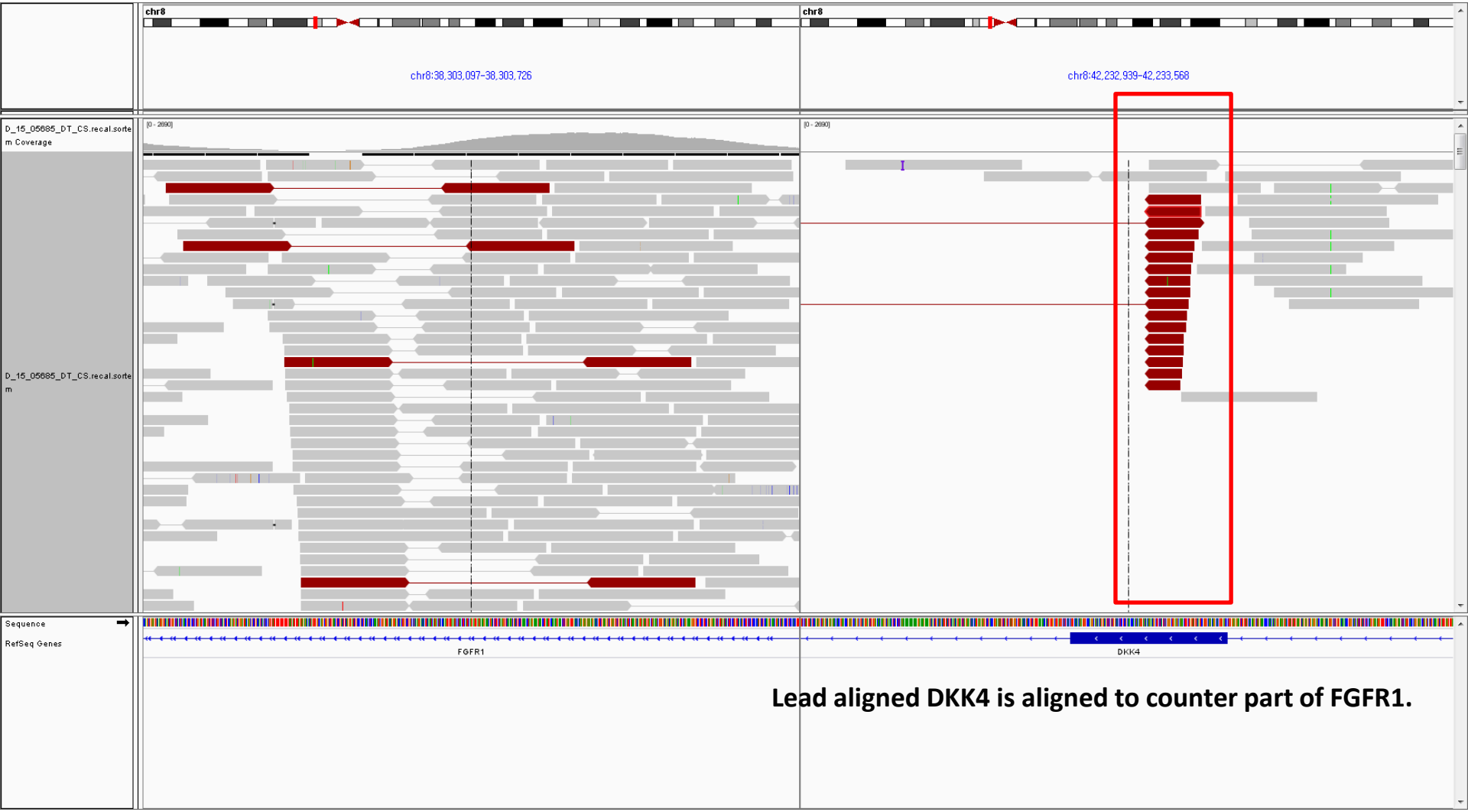
FGFR1

- Fibroblast growth factor receptor 1
- Chr8:38,411,139-38,468,834
- FGFR1 amplification
  - SCLC, SqCC of lung, Breast cancer
- TACC1-FGFR1 (FGFR1-TACC1)
  - Glioblastoma, Prostate cancer, bladder cancer

DKK4

- Dickkopf WNT Signaling Pathway Inhibitor 4
- Chr8:42,229,586-42,236,674

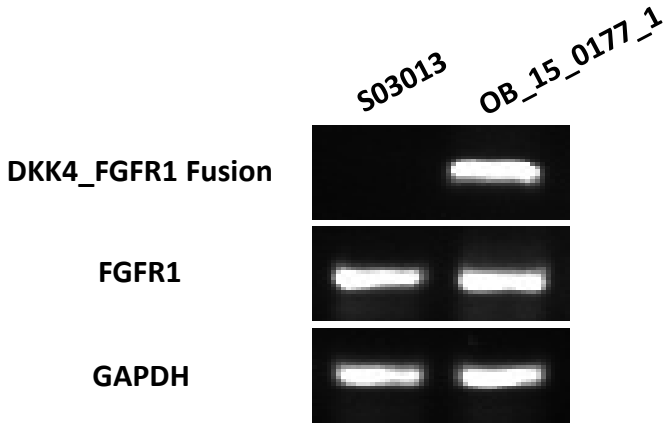
IGV bam file



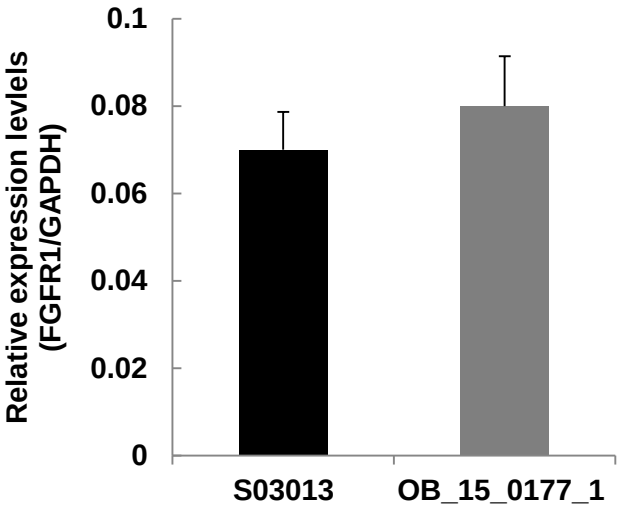
Lead aligned DKK4 is aligned to counter part of FGFR1.

Class	ChrA	GeneA	DrugA	BreakpointA	Direction	ChrB	GeneB	DrugB	BreakpointB
T3	8	DKK4	-	42233274 [E2(4)]	A->B	8	FGFR1	Fibroblast growth factor receptor1 (DB08577)	38303524 [I2(18)]

1. RT-PCR

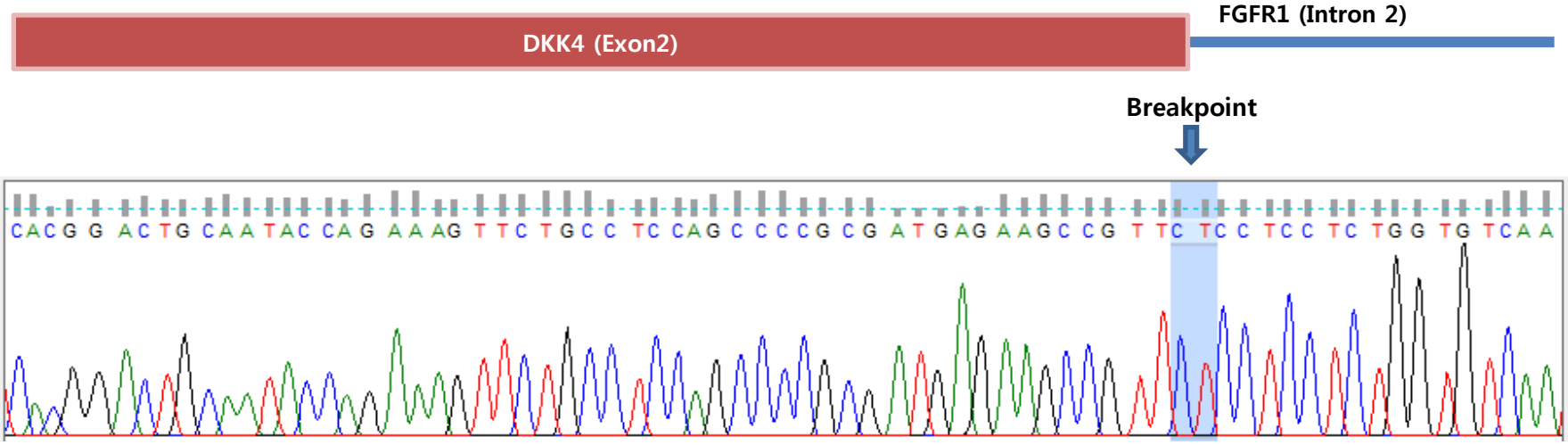


2. Q-PCR

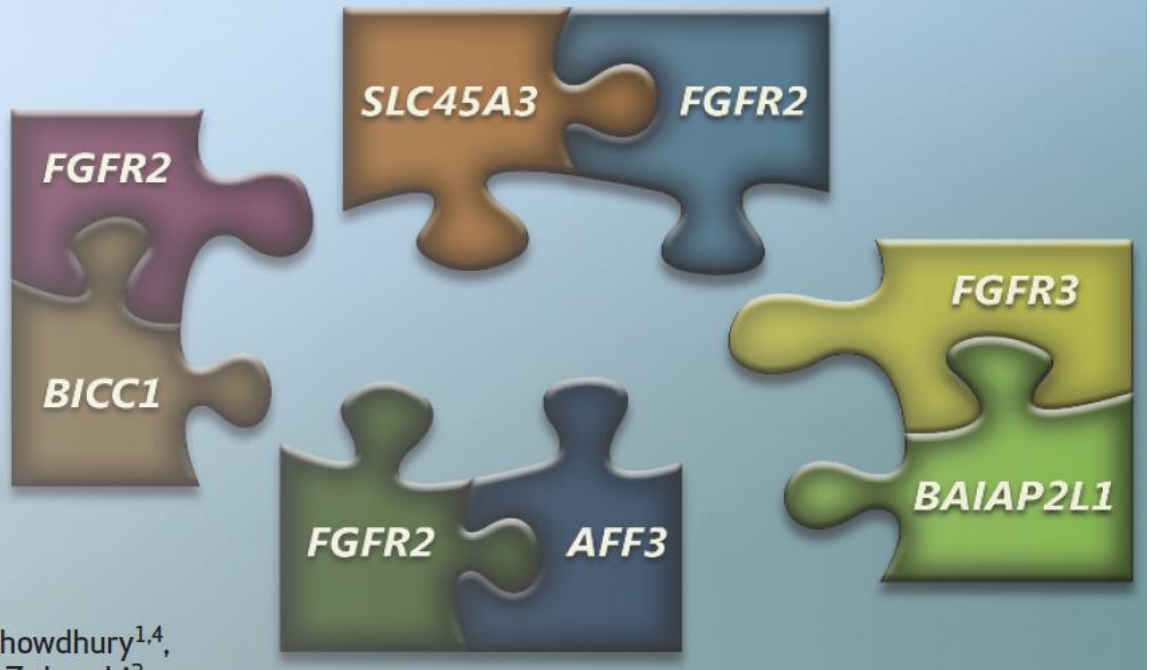


S03013 : FGFR1 CN amplification
OB_15_0177_1 : DKK4-FGFR1 fusion

3. Sequencing



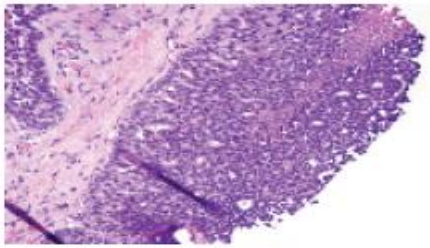
Identification of Targetable FGFR Gene Fusions in Diverse Cancers

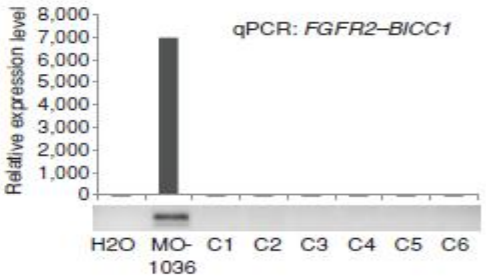


Yi-Mi Wu[1,2], Fengyun Su[1,2], Shanker Kalyana-Sundaram[1,2], Nickolay Khazanov[10], Bushra Ateeq[1,2], Xuhong Cao[1,7], Robert J. Lonigro[1,8], Pankaj Vats[1,2], Rui Wang[1,2], Su-Fang Lin[11], Ann-Joy Cheng[12], Lakshmi P. Kunju[1,2], Javed Siddiqui[1,2], Scott A. Tomlins [1,2], Peter Wyngaard [10], Seth Sadis[10], Sameek Roychowdhury[1,4], Maha H. Hussain[3], Felix Y. Feng[1,4,8], Mark M. Zalupski[3]

Case 1: MO_1036

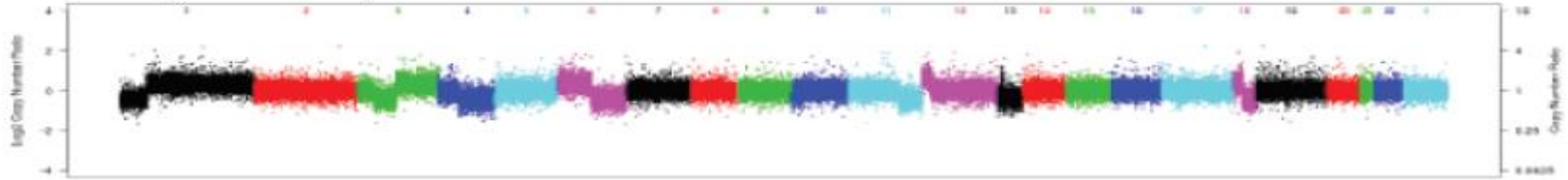
Patient	34-year-old female
Cancer type	Cholangiocarcinoma
SNVs	8 mutations (*ARID1A, PBRM1*)
Gene fusions	8 fusions (*FGFR2–BICC1*)





FGFR2–BICC1 fusion (1663 a.a.)

Gene copy number ratios by chromosome



Aberrant *FGFR* signalling occurs by diverse mechanisms in many cancer types

Amplification

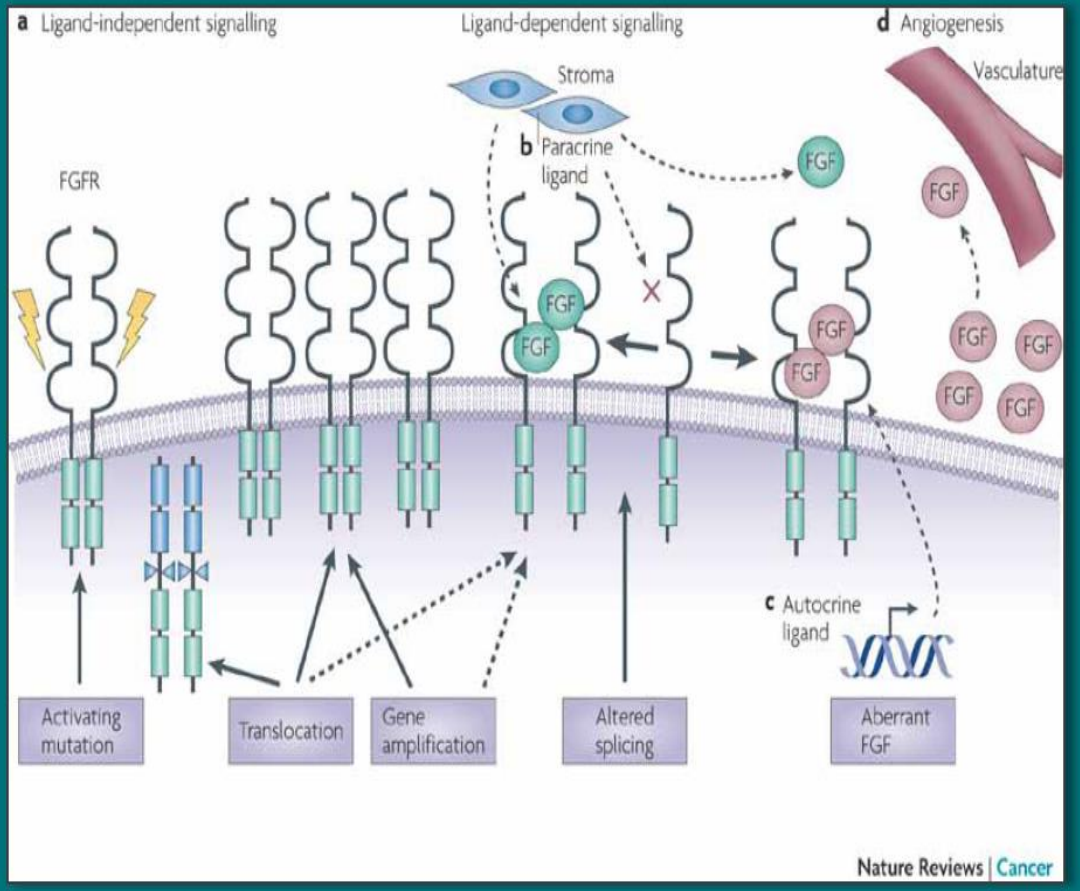
FGFR1	ER+ breast cancer (9-23%) SqNSCLC (10-20%)
FGFR2	Gastroesophageal (9%)

Fusion

FGFR2	Cholangiocarcinoma (15%)
FGFR3	Bladder (6%) Glioblastoma (3-7%)

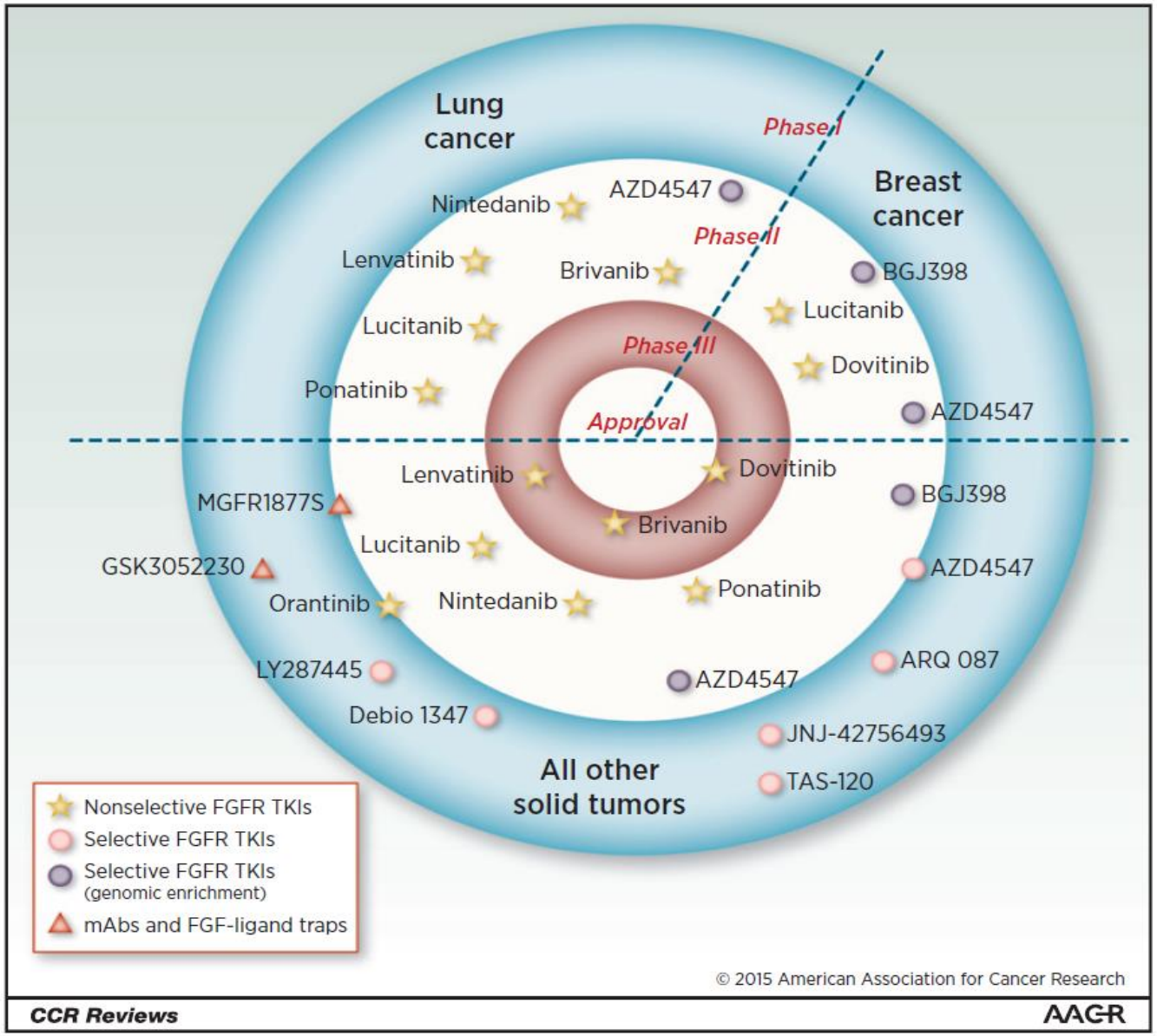
Mutation

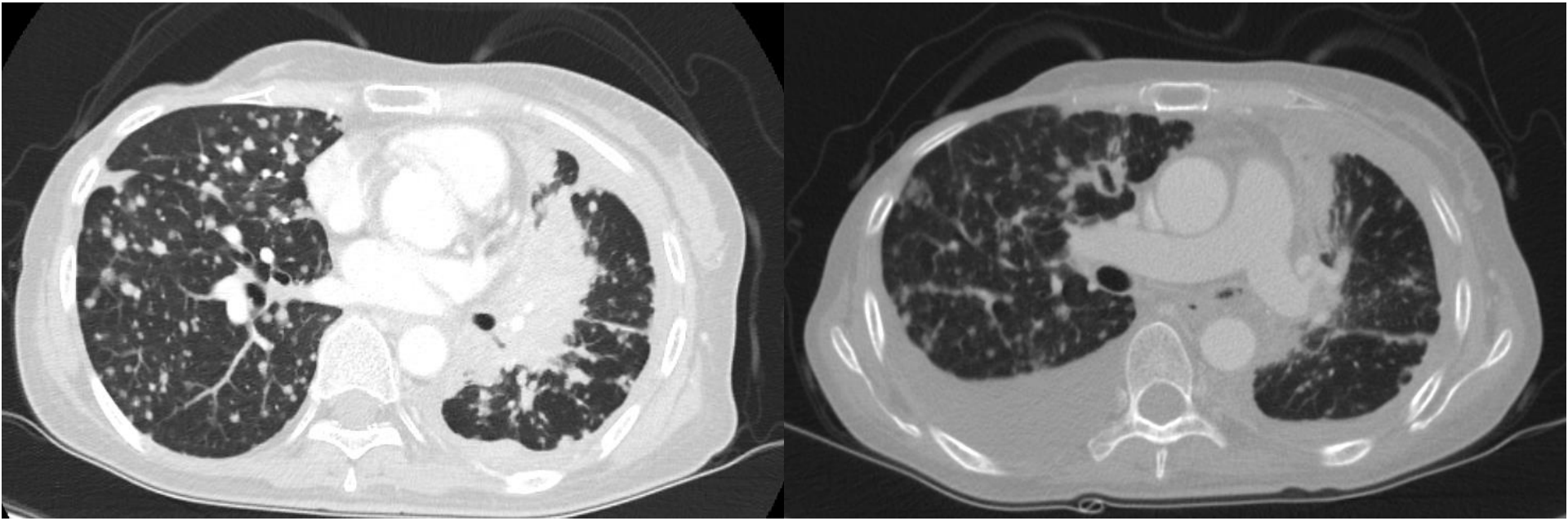
FGFR1	Endometrial (12%)
FGFR3	Bladder (10%-60%)



Turner N, Grose, R. Nature Reviews Cancer 10, 116-129

Selected overview of clinical trials evaluating **FGFR signaling**–targeted therapies currently under development





2015.11.19 → 2016.01.04

Pazopanib treatment

Case 2
Medical history (F/47)

breast ca with M/stomach, peritoneum, bone & ovary at 2008
(ER+/PR+/HER2-)

s/p palliative ECX #1 (mis-diagnosed as AGC)

s/p palliative AC #7 (2008.10.08-2009.02.20)

s/p docetaxel #10 (2009.03.17-2009.09.28)

s/p AI + goserelin (2009.12.16-2013.12.30) -> PD (Peritoneal carcinomatosis)

s/p PG #12 (2013.1217-2014.08.18)

s/p tamoxifen (2014.11.10-2015.05.03)

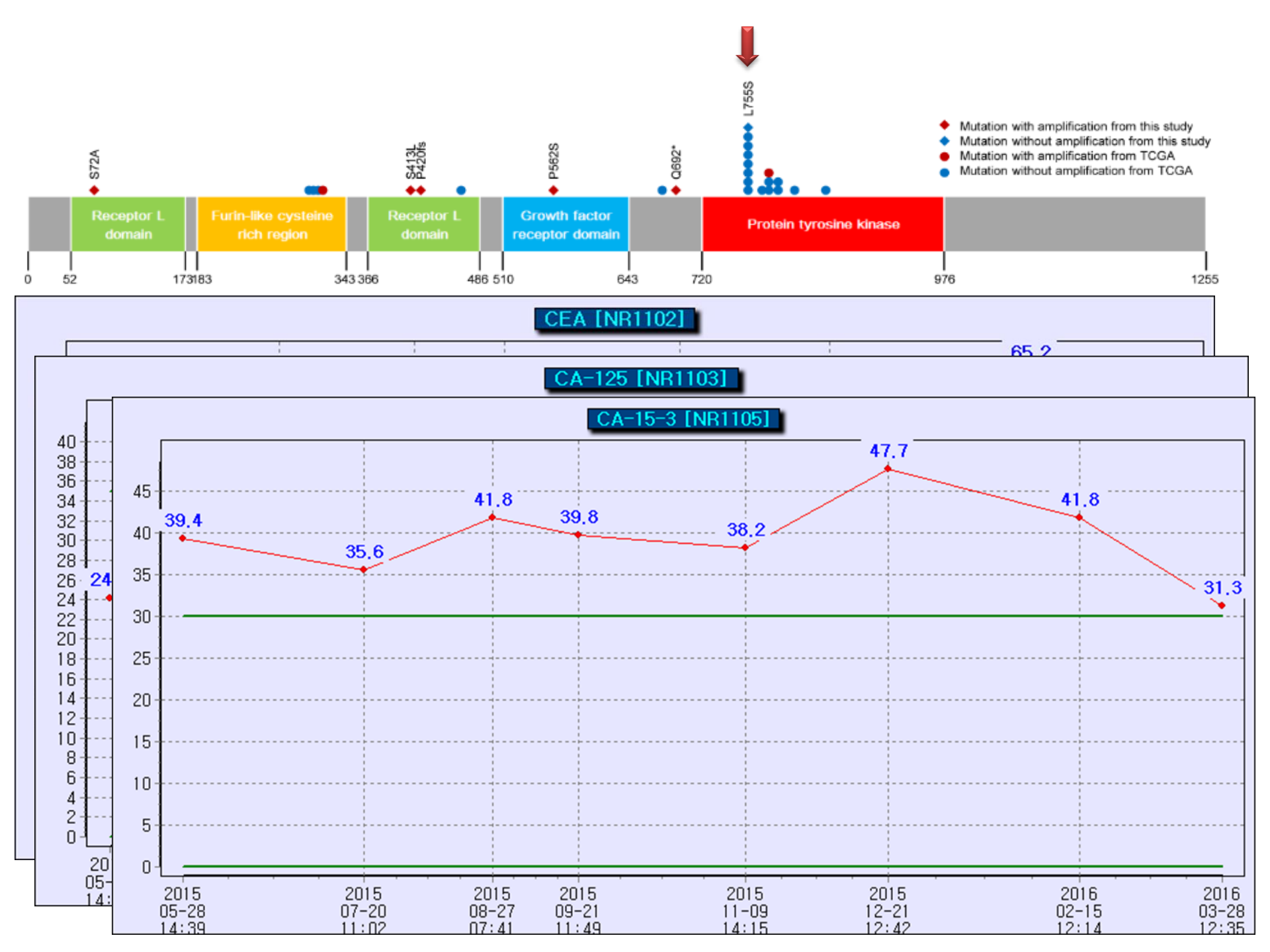
s/p eribulin #11 (2015.5.4-2015.12.28) -> SD -> PD

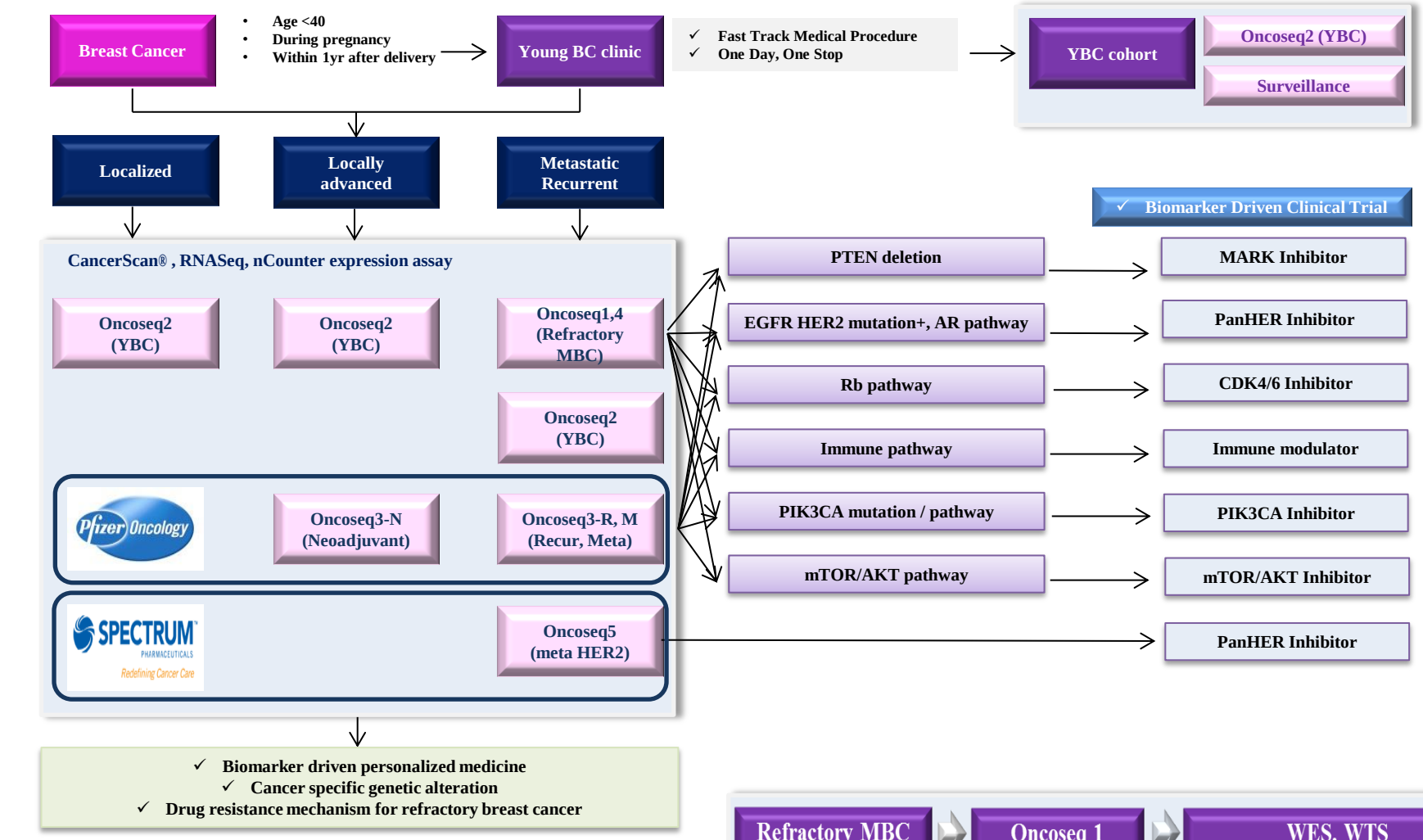
s/p US guided peritoneum biopsy

: metastatic carcinoma, ER/PR/HER2 (+(5)/-/-)

HER2 mutation (TKD L755S)

On poziotinib (2016.02.22)


S72A
S413L
P420fs
P562S
Q692*
L755S
Mutation with amplification from this study
Mutation without amplification from this study
Mutation with amplification from TCGA
Mutation without amplification from TCGA
Receptor L domain
Furin-like cysteine rich region
Receptor L domain
Growth factor receptor domain
Protein tyrosine kinase
0
52
173
183
343
366
486
510
643
720
976
1255
CEA [NR1102]
CA-125 [NR1103]
CA-15-3 [NR1105]
39.4
35.6
41.8
39.8
38.2
47.7
41.8
31.3
2015 05-28 14:39
2015 07-20 11:02
2015 08-27 07:41
2015 09-21 11:49
2015 11-09 14:15
2015 12-21 12:42
2016 02-15 12:14
2016 03-28 12:35



Breast Cancer Precision Medicine Scheme in SMC

Refractory MBC	Oncoseq 1	WES, WTS
YBC	Oncoseq 2	CancerSCAN, WES
Neoadjuvant	Oncoseq 3-N	CancerSCAN, WTS, nCounter
Recurrent	Oncoseq 3-R	CancerSCAN, WTS, nCounter
Metastatic 1st line	Oncoseq 3-M	CancerSCAN, WTS, nCounter

Current Limitations of Genomics-driven Clinical Trials Using Multi-Omics

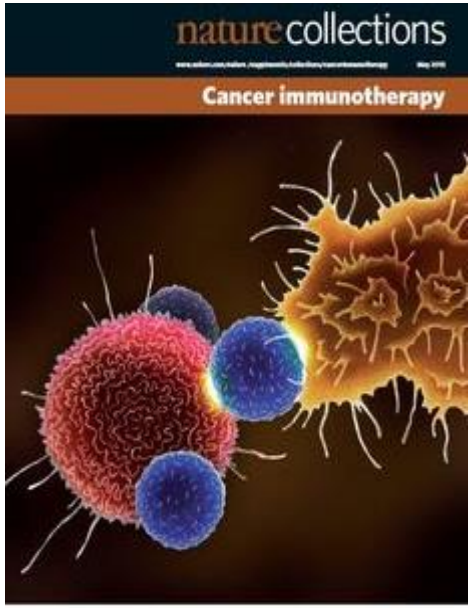
- *Real target?* : **oncogenic driver mutation << passenger mutations**
- **Druggable target??**
- Clinical application of **Bioinformatics**
- Need functional genomics
- Challenging **adaptive clinical trial design**
- Intra- and/or inter-tumoral **Heterogeneity**
- ***Evolving by-pass tracks*** → **Resistance** to target
- Cancer pathway **Complexity**: multiple targets, cross-talk between pathways

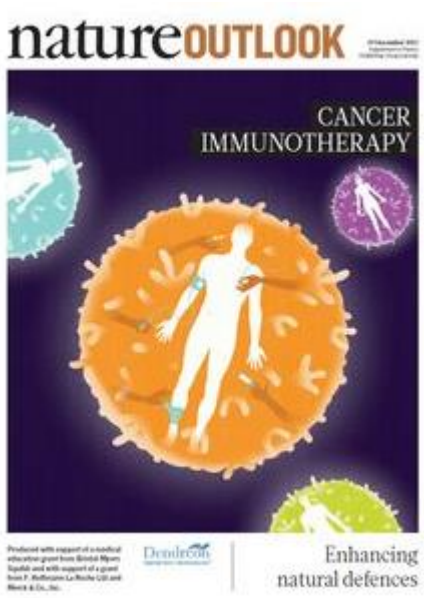
Hope for the Future

- **Treatments to date improve outcomes**
  - in both curative and metastatic settings
- **Clinical trials continue to push the frontier**
  - to better treatments and outcomes
- **Genetic testing of tumor tissue (and now blood!)**
  - helps us understand the driving forces in a cancer
  - Clinical trials testing targeted therapies are ongoing
- **Immunotherapy holds great promise**
  - to better clinical outcomes
  - Clinical trials assessing how to best do this are ongoing

ASCO Plenary 2015

- Insights into immune checkpoint blockade
- CheckMate trial of immunotherapy in melanoma
- Childhood Cancer Survivor Report
- Case for preventive neck lymph node surgery
- Risks of whole-brain radiation therapy





Panacea for Progress or Pandora's Box?

Room 354, Morial Convention Center

Clinical Trials Design: Part 2

Chairperson: Elizabeth M. Jaffee, Baltimore, MD

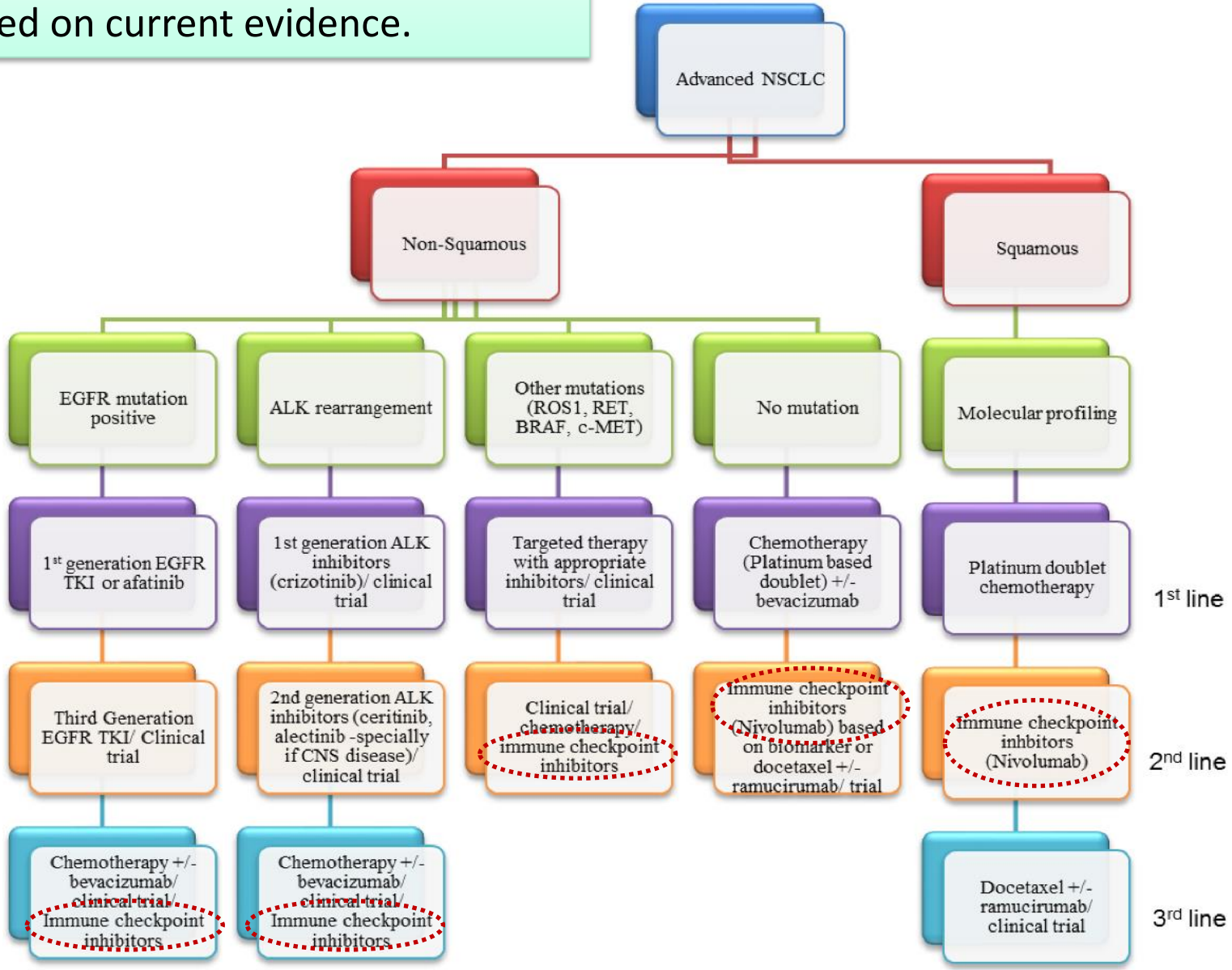
10:15 a.m. **Successes and challenges in designing combination immunotherapy clinical trials for breast cancer.** Leisha A. Emens, Baltimore, MD

10:45 a.m. **Issues faced by industry in developing safe and effective combination immunotherapies.** Ira Mellman, South San Francisco, CA

11:15 a.m. **Statistical challenges in designing combination immunotherapy clinical trials.** Katy Simonsen, Princeton, NJ

11:45 a.m. **FDA's point of view on trial designs for accelerating combination immunotherapies across multiple tumor types.** Tatiana Prowell, Silver Spring, MD

A likely algorithm for incorporating different therapies into the management of ***NSCLC*** based on current evidence.



Cancers **2015**, *7*(3), 1815-1846; doi:10.3390/cancers7030864

Incorporation of immune-oncology into precision medicine

New Orleans Theater B, Morial Convention Center

Genomics-guided Immunotherapy

Chairperson: Catherine J. Wu, Boston, MA

1:00 p.m. **Introduction**

1:10 p.m. **Tumor-host coevolution: Therapeutic implications.** Catherine J. Wu, Boston, MA

1:40 p.m. **Immunogenomics and precision cancer medicine.** Eliezer Van Allen, Brookline, MA [SY18-02]*

2:10 p.m. **RNA based individualized cancer immunotherapy.** Ugur Sahin, Mainz, Germany **(not eligible for CME credit)**

Immunogenomics to search *Neo-antigen, 'inflammed' types, and proper combination* *therapeutic strategies*

NEWS FEATURE

Cocktails for cancer with a measure of immunotherapy

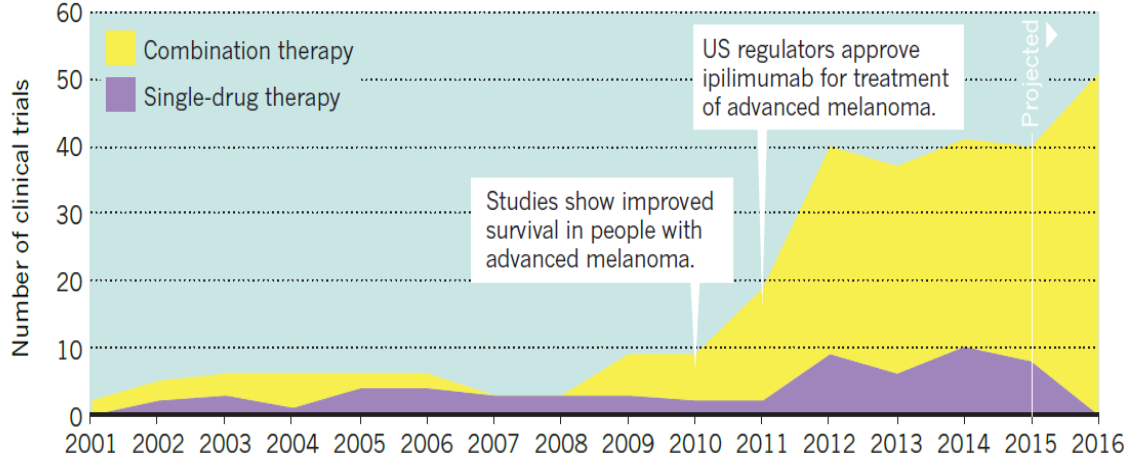
THE PERFECT BLEND

The next frontier in cancer immunotherapy lies in combining it with other treatments. Scientists are trying to get the mix just right.

BY HEIDI LEDFORD

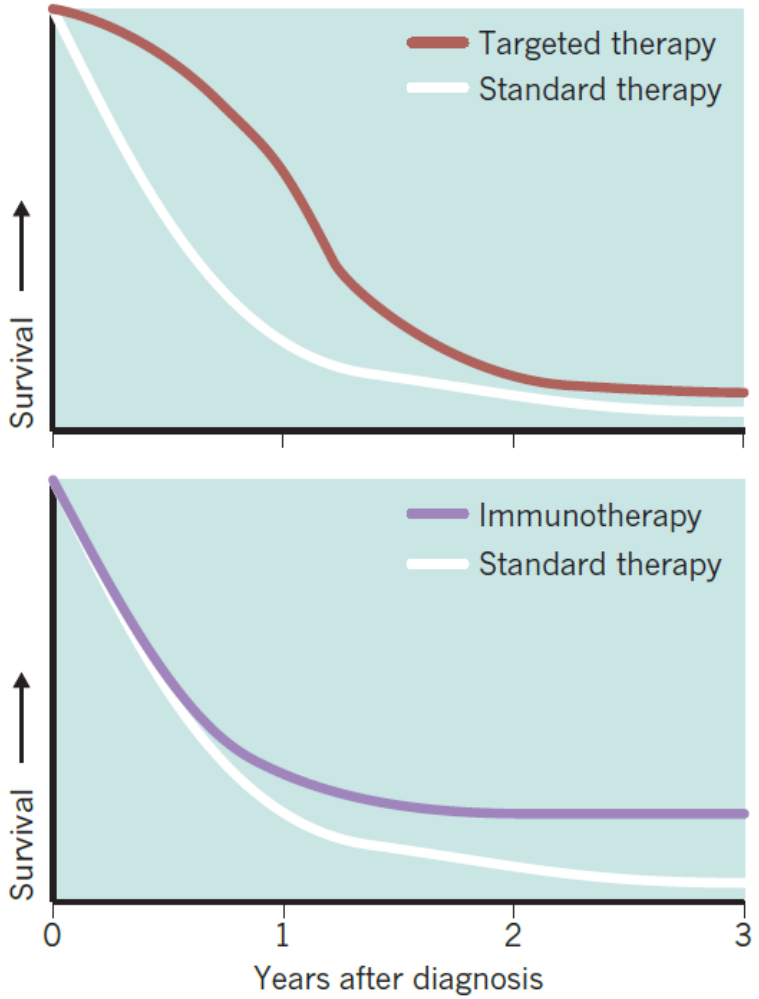
COMBINATORIAL EXPLOSION

Ipilimumab, the first approved checkpoint inhibitor, has been tested in dozens of clinical trials since 2001. And like many other drugs in its class, it is increasingly being tested in combination with other therapies.



DESPERATELY SEEKING SURVIVAL

Patients generally respond well to targeted therapies (top), which are directed at specific mutations in a cancer, but only for a short time. Checkpoint immunotherapies (bottom) do not help as many people, but those they do help tend to live longer. Oncologists are trying to get the best out of both strategies by combining the drugs.

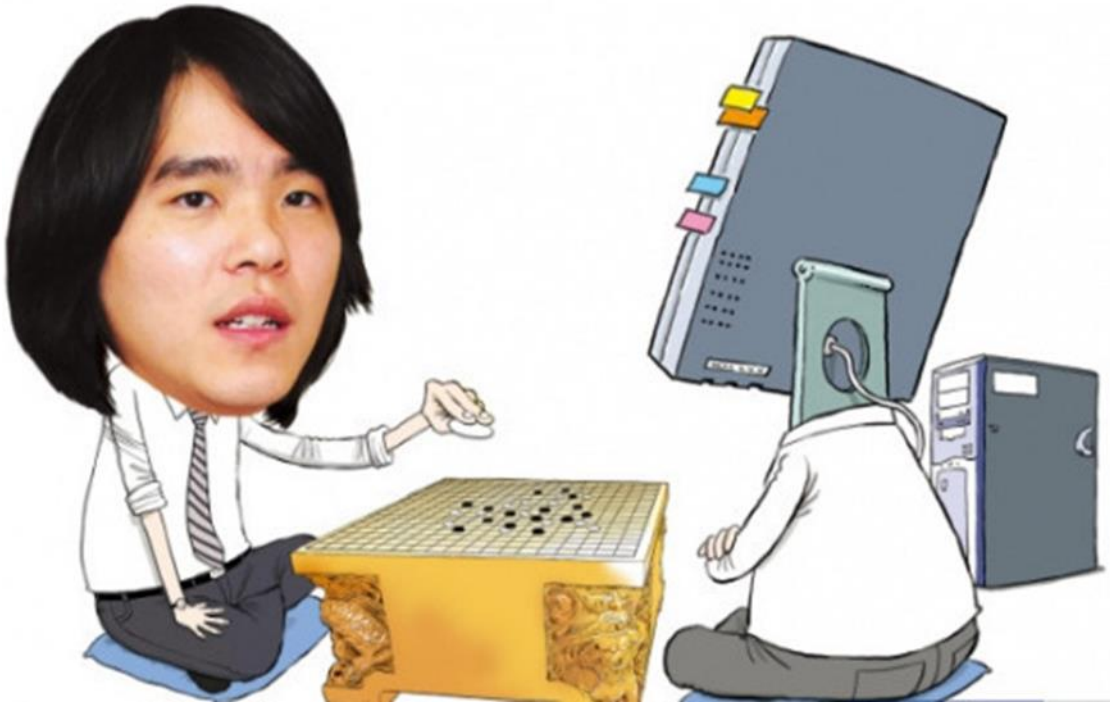


Nature 2016, 532; 162-164

Acknowledgements

- Surgeon
  - Seok-Jin Nam
  - Jeong Eon Lee
  - Seok Won Kim
  - Jong Han Yu
  - Se Kyung Lee
  - Su Yeon Bae
- CRC
  - In Kyung Jung
  - Eun-Ji Lee
- Our lab
  - Hae Hyun Jung
  - Jee Eun Lim
  - Ji-Yeon Kim
- SGI
  - Woong-Yang Park
  - Kyung Hee Park
  - Woosung Jung
- PI
  - Young-Hyuck Im

SAMSUNG MEDICAL CENTER



Thank You!