



Associazione Italiana di Oncologia Medica
SEZIONE REGIONE LAZIO

POST SAN ANTONIO BREAST CANCER SYMPOSIUM 2018



— 28 Gennaio 2019 —

POLICLINICO UMBERTO I - ROMA

Aula Bignami (Patologia Generale)
Viale Regina Elena 324

Recent clinical and biological insights in HER-2 positive Breast Cancers: Liquid Biopsy for biomarkers identification.

Prof. Francesco Cognetti
Istituto Nazionale Tumori
'Regina Elena'
Roma

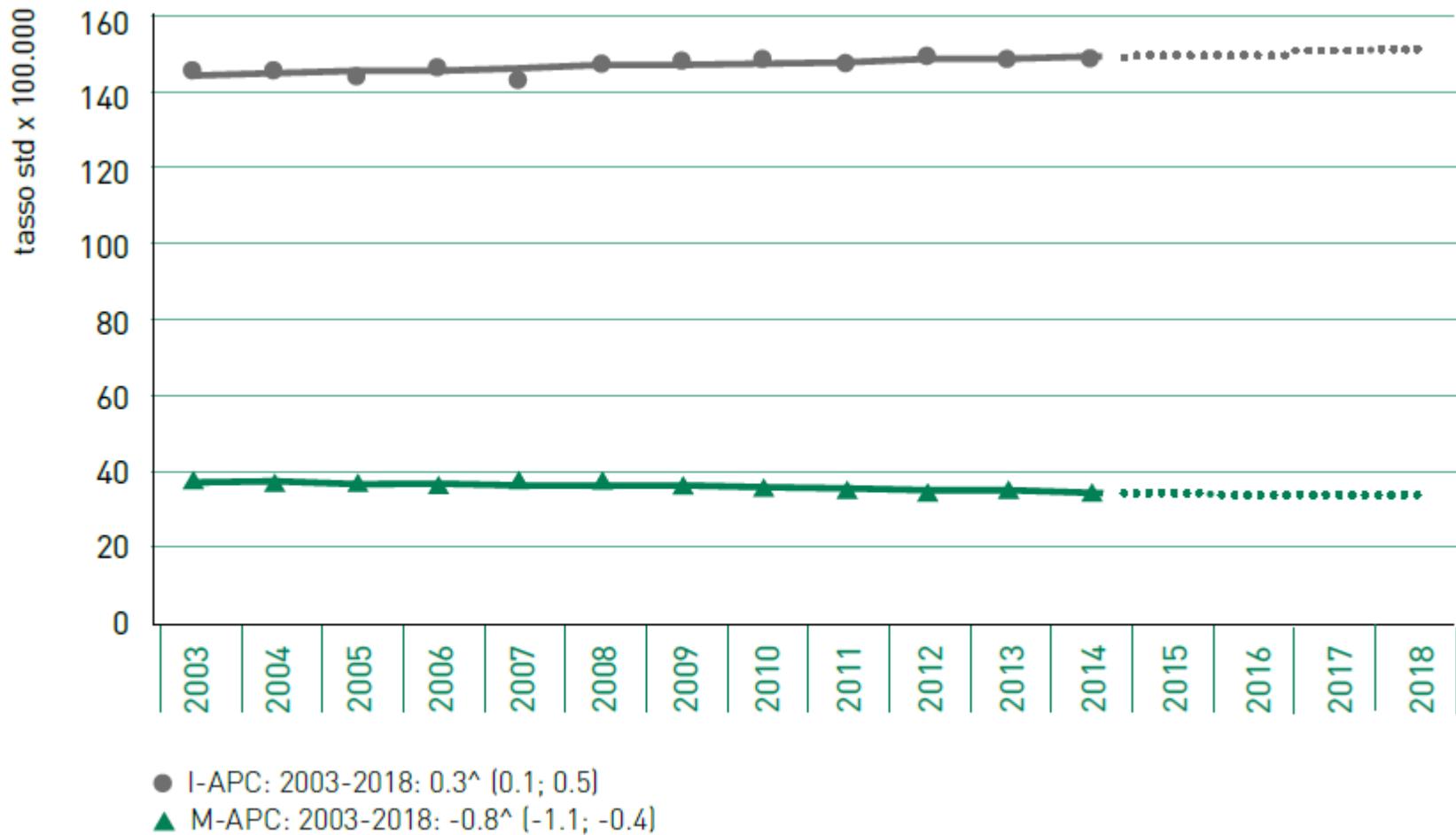
IRE INSTITUTO NAZIONALE TUMORI
REGINA ELENA
ISG INSTITUTO SERRATOLOGICO
SAN GALlicano
ISTITUTO DI RICERCA E CURA A CARATTERE SCIENTIFICO

Breast Cancer in Italy

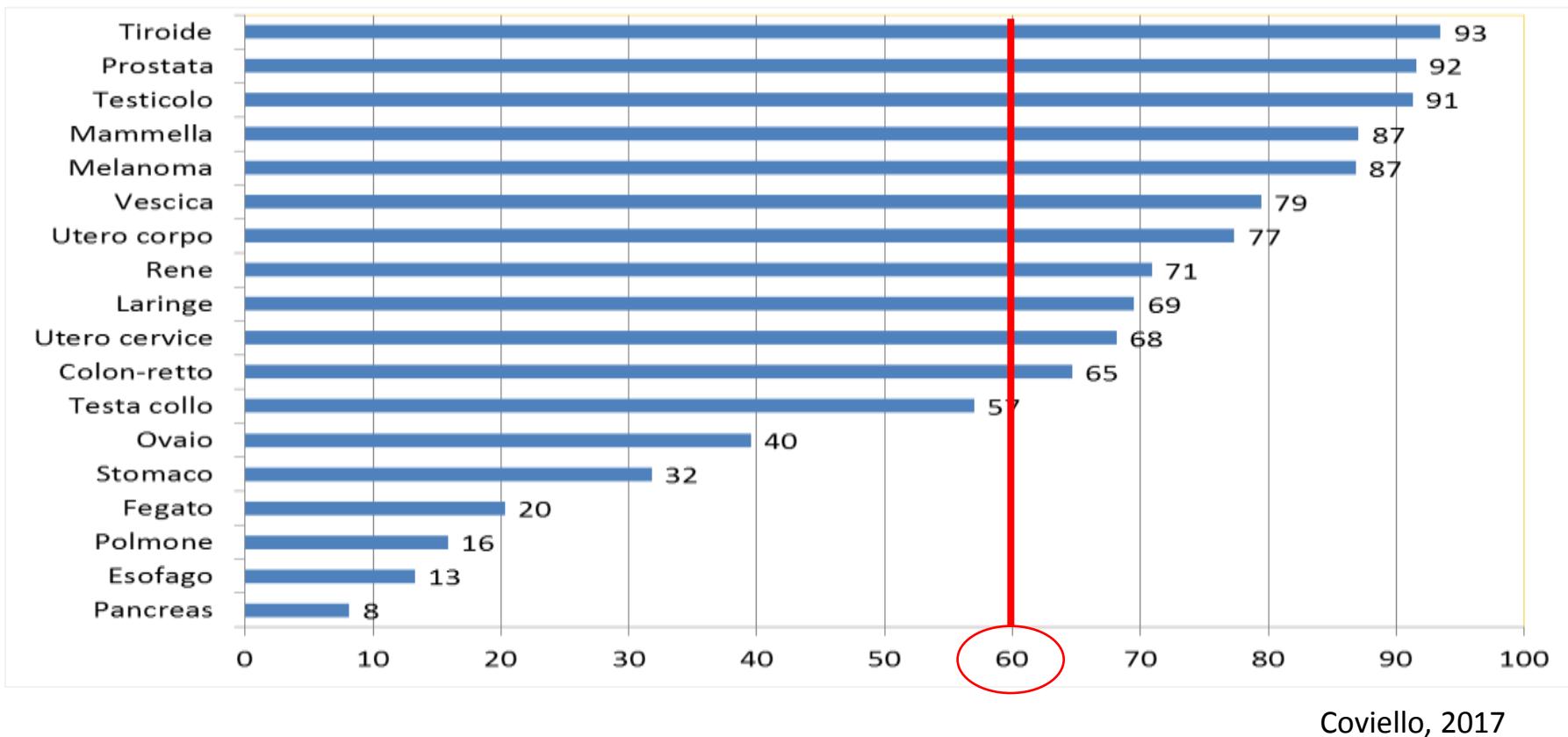
- It is estimated that in 2018, in Italy, were diagnosed with just over 373,000 new cases of malignancy, of which about 178,000 in women.
- Breast cancer accounts for 29% of female neoplasms.
- In 2018 about 52,800 new cases of female breast carcinomas were diagnosed in Italy.
- About 800,000 women live in Italy with a diagnosis of breast cancer.
- Breast cancer is the leading cause of cancer death for women in all age groups. In 2015 there were 12,274 deaths due to breast cancer.

- Approximately one third of patients with primary breast cancer will eventually develop disseminated disease;
- About 10% of patients are metastatic at diagnosis.

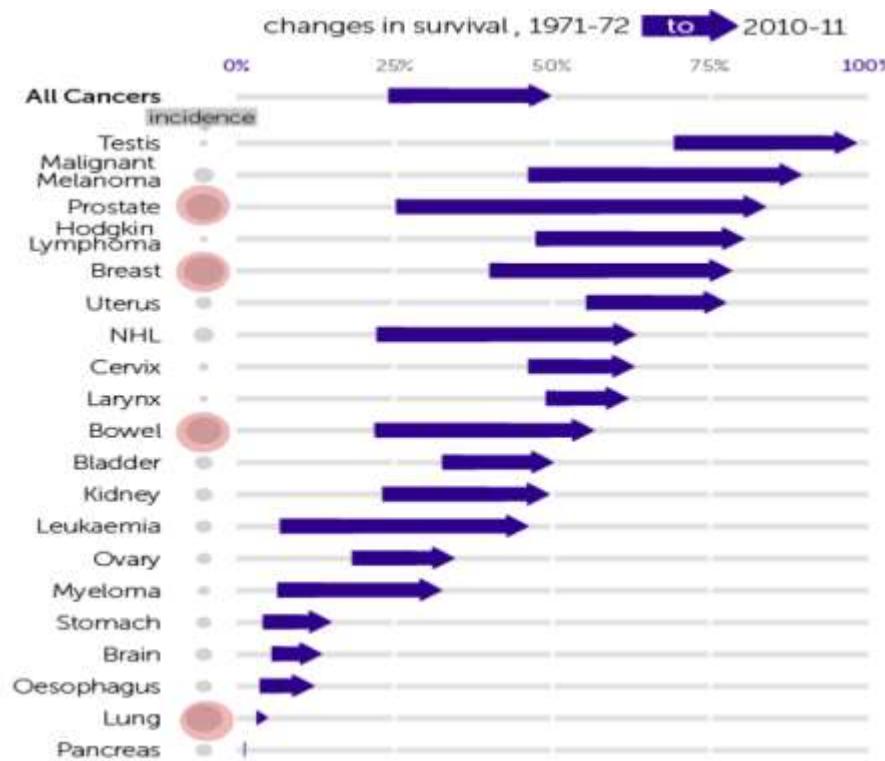
Breast Cancer: Incidence and Mortality Trends in Italy



Sopravvivenza per sede



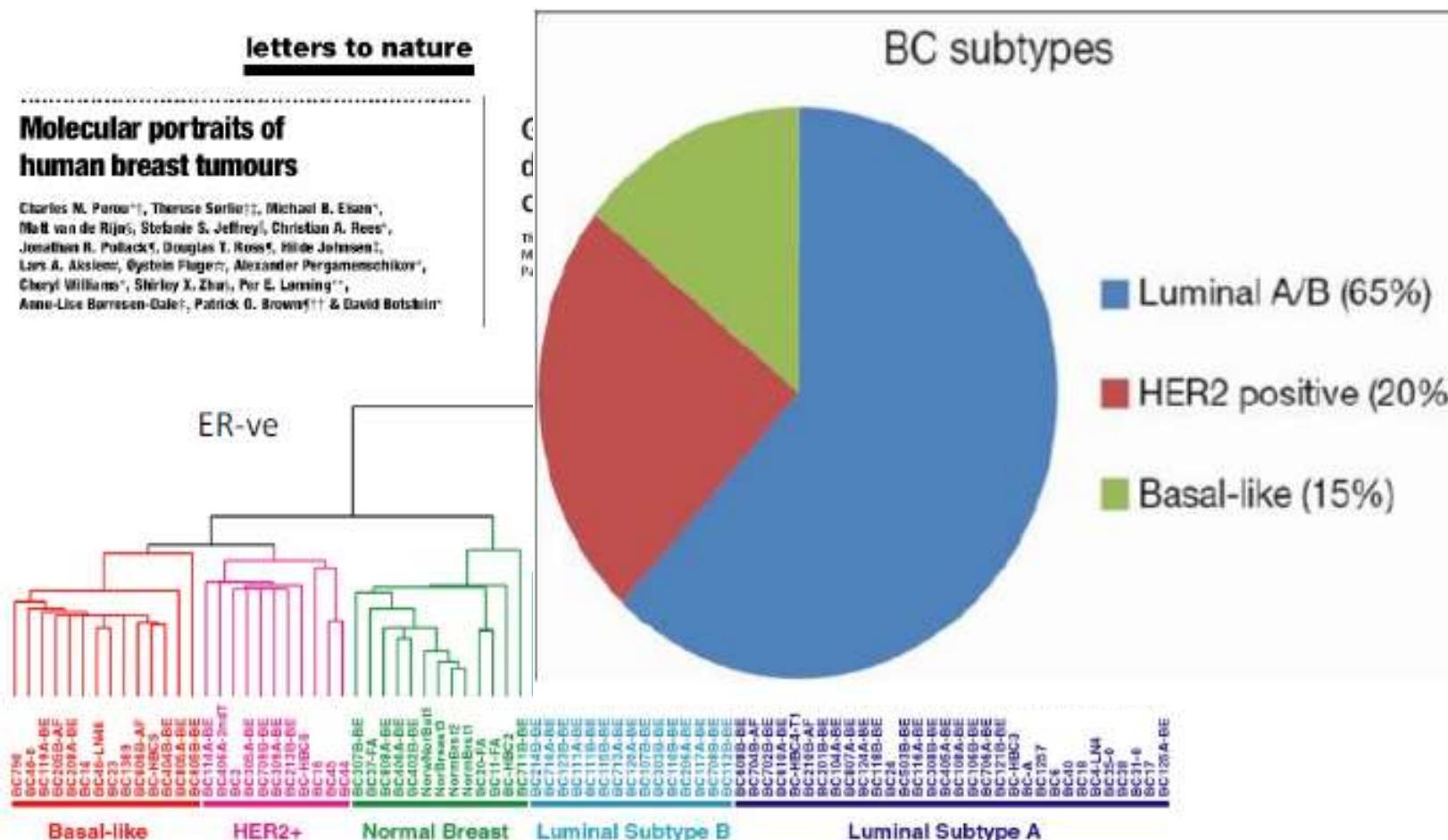
England 10-year net survival changes in ~ 40 years



Source: cruk.org/cancerstats

Breast cancer is many disease!

MOLECULAR CLASSIFICATION OF BREAST CANCER

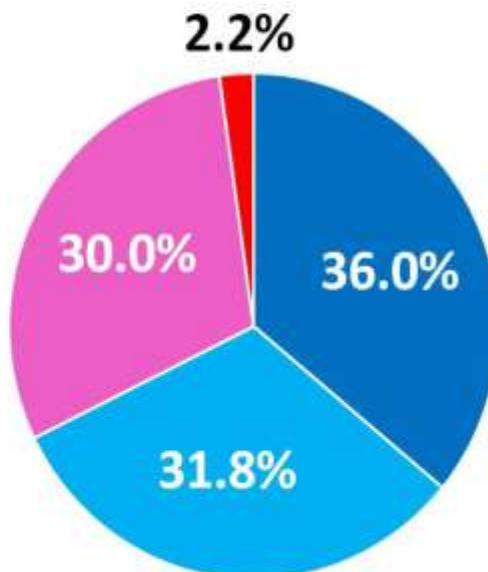


Intrinsic Subtype Heterogeneity in Clinically HER2+ disease

Basal-like ■
HER2-enriched ■
Luminal A ■
Luminal B ■

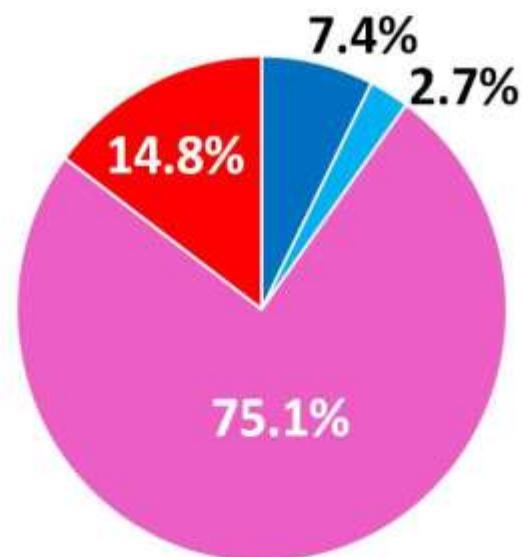
ER+/HER2+

N=1,648



ER-/HER2+

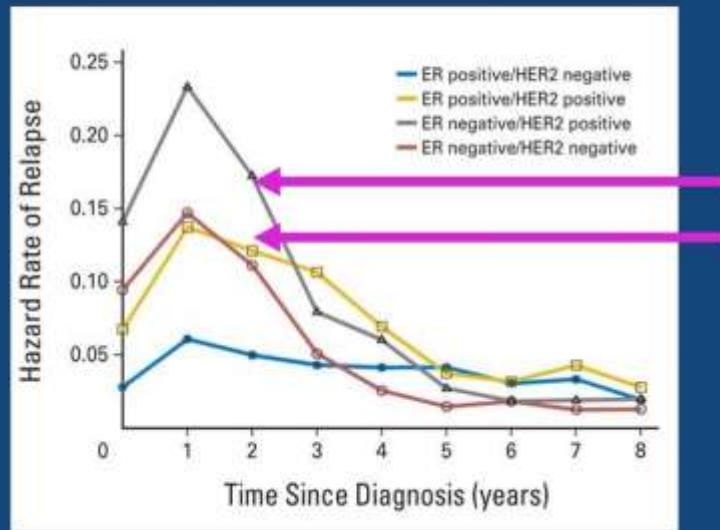
N=1,213



Courtesy Aleix Prat

Poor prognosis of HER2-positive Disease (without trastuzumab)

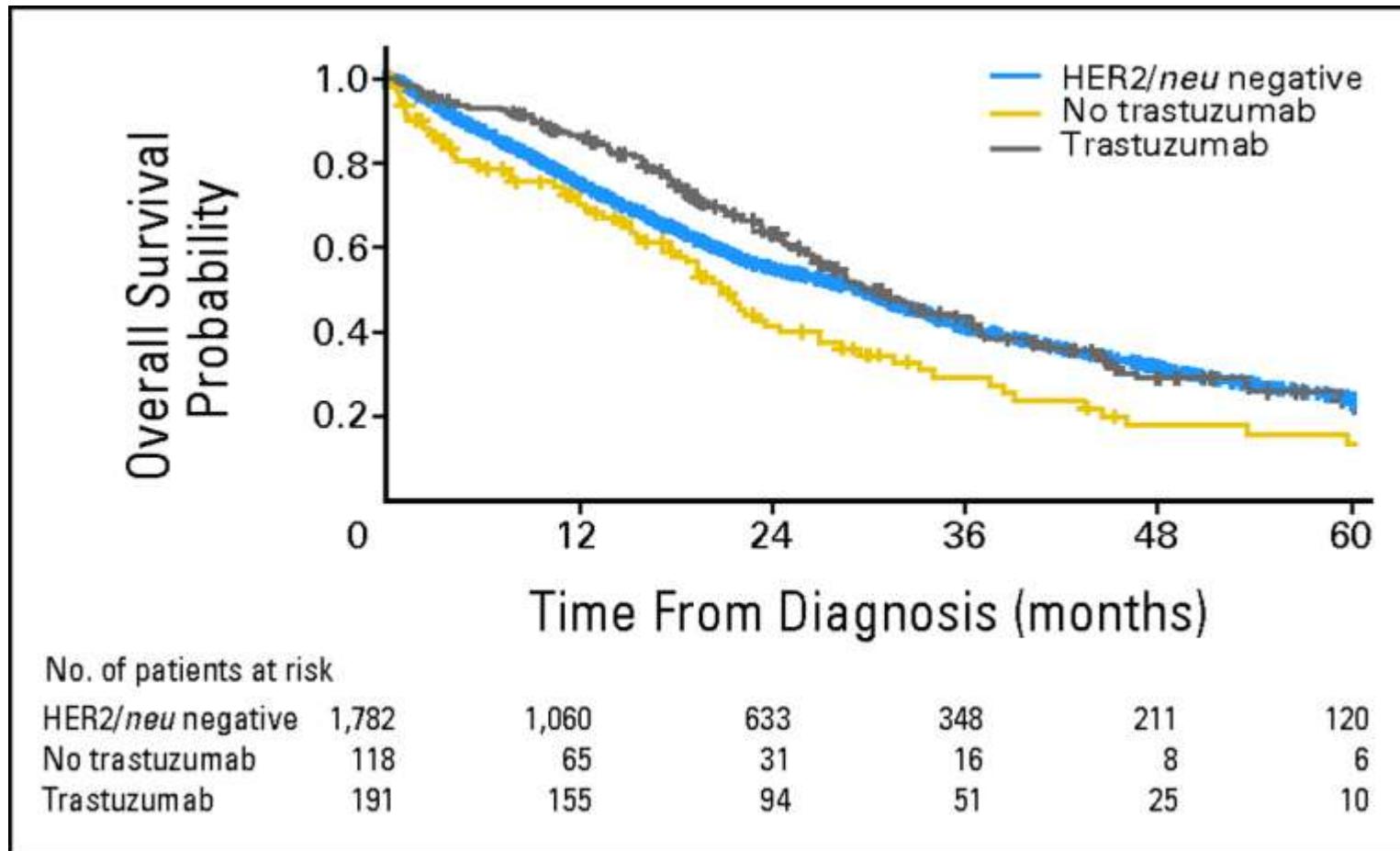
HER2+ Behavior



Without HER2-targeting
Frequent and early relapse
Visceral and CNS involvement

Sites	Bone	Soft Tissue	Viscera
Triple negative	13%	13%	74%
ER+	39%	7%	54%
HER2+	7%	12%	81%
CNS - 25-40%			

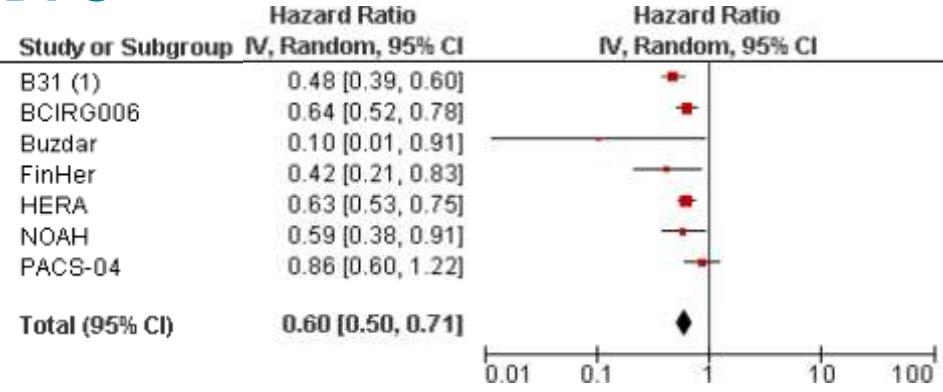
Trastuzumab has changed the landscape and natural history of HER2+ BC



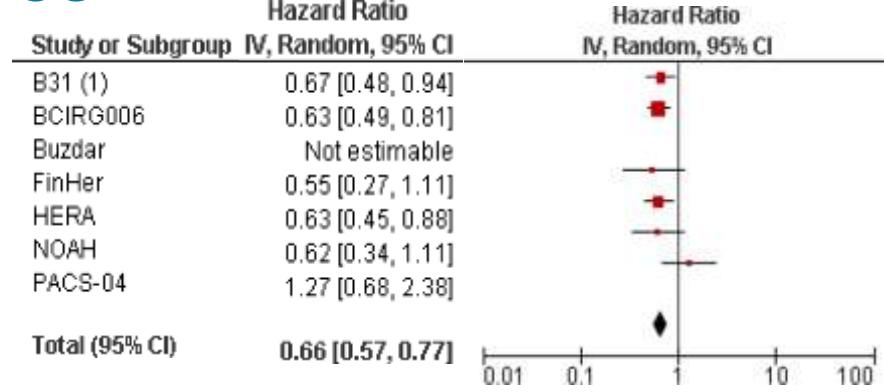
Dawood, S. et al. J Clin Oncol; 28:92-98 2010

Trastuzumab for HER2+ Early BC: Systematic Review of Pivotal Trials

DFS



OS



- EBC: Risk of death reduction of approx. 40%.

STANDARD:
1 year of trastuzumab concurrent with chemotherapy

Dual HER2-Inhibition in Neoadjuvant Trials

Trial	Experimental Anti-HER2	pCR with Trastuzumab	pCR with Dual inhibition
NeoSphere	Pertuzumab	29%	46%
NeoALTTO	Lapatinib	30%	51%
CALGB 40601	Lapatinib	40%	51%*
NSABP B41[#]	Lapatinib	52%	62%*
TRYPHAENA^{\$}	Pertuzumab	NA	55-64%

* Not statistically significant, # Received AC-T, \$ No single anti-HER2 arm

Phase III Study of Trastuzumab Emtansine (T-DM1) vs Trastuzumab as Adjuvant Therapy in Patients with HER2-Positive Early Breast Cancer with Residual Invasive Disease after Neoadjuvant Chemotherapy and HER2-Targeted Therapy Including Trastuzumab: Primary Results from **KATHERINE (NSABP B-50-I, GBG 77 and Roche BO27938)**

Charles E. Geyer, Jr., Chiun-Sheng Huang, Max S. Mano, Sibylle Loibl, Eleftherios P. Mamounas,
Michael Untch, Norman Wolmark, Priya Rastogi, Andreas Schneeweiss, Andrés Redondo, Hans H. Fischer,
William Jacot, Alison K. Conlin, Claudia Arce-Salinas, Irene L. Wapnir, Christian Jackisch, Michael P. DiGiovanna,
Peter A. Fasching, John P. Crown, Pia Wülfing, Zhimin Shao, Elena Rota Caremoli, Haiyan Wu, Lisa H. Lam,
David Tesarowski, Melanie Smitt, Hannah Douthwaite, Stina M. Singel, and Gunter von Minckwitz,
on behalf of the KATHERINE investigators



ORIGINAL ARTICLE

Trastuzumab Emtansine for Residual Invasive HER2-Positive Breast Cancer

[von Minckwitz G et al, N Engl J Med.](#) 2018 Dec 5. doi: 10.1056/NEJMoa1814017

Rationale for KATHERINE Study Design

- HER2-positive early breast cancer patients with residual invasive disease following neoadjuvant chemotherapy combined with HER2-targeted therapy have an increased risk of recurrence and death¹⁻⁵
- T-DM1 is active in HER2-positive metastatic breast cancer following prior exposure to taxanes and HER2-targeted therapy⁶⁻⁹
- A phase 2 study demonstrated that administration of T-DM1 following an anthracycline-containing regimen was feasible in patients with EBC¹⁰
- KATHERINE investigated whether substituting adjuvant T-DM1 for trastuzumab would improve outcomes for patients with residual invasive cancer following neoadjuvant therapy

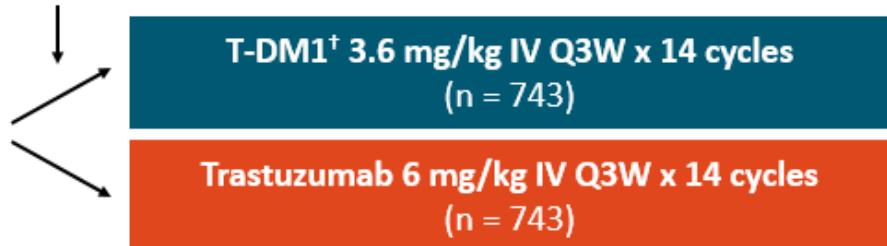
¹Untch et al. *J Clin Oncol* 2011;29:3351; ²Cortazar et al. *Lancet* 2014;384:164; ³de Azambuja et al. *Lancet Oncol* 2014;15:1137; ⁴Gianni et al. *Lancet Oncol* 2014;15:540; ⁵Schwarzweiss et al. *Eur J Cancer* 2018;99:27; ⁶Vermia et al. *N Engl J Med* 2012;367:1783; ⁷Krop et al. *Lancet Oncol* 2014;15:689; ⁸Dimes et al. *Lancet Oncol* 2017;18:743; ⁹Krop et al. *Lancet Oncol* 2017;18:743; ¹⁰Krop et al. *J Clin Oncol* 2016;33:1136.

KATHERINE: Trastuzumab Emtansine vs Trastuzumab as Adjuvant Therapy for HER2+ EBC

- International, randomized, open-label phase III study

Stratified by clinical stage, HR status, single vs dual neoadjuvant HER2-targeted therapy, pathological nodal status after neoadjuvant therapy

Patients with HER2+ EBC (cT1-4/N0-3/M0) who had residual invasive disease in breast or axillary nodes after neoadjuvant chemotherapy plus HER2-targeted therapy* at surgery
(N = 1486)



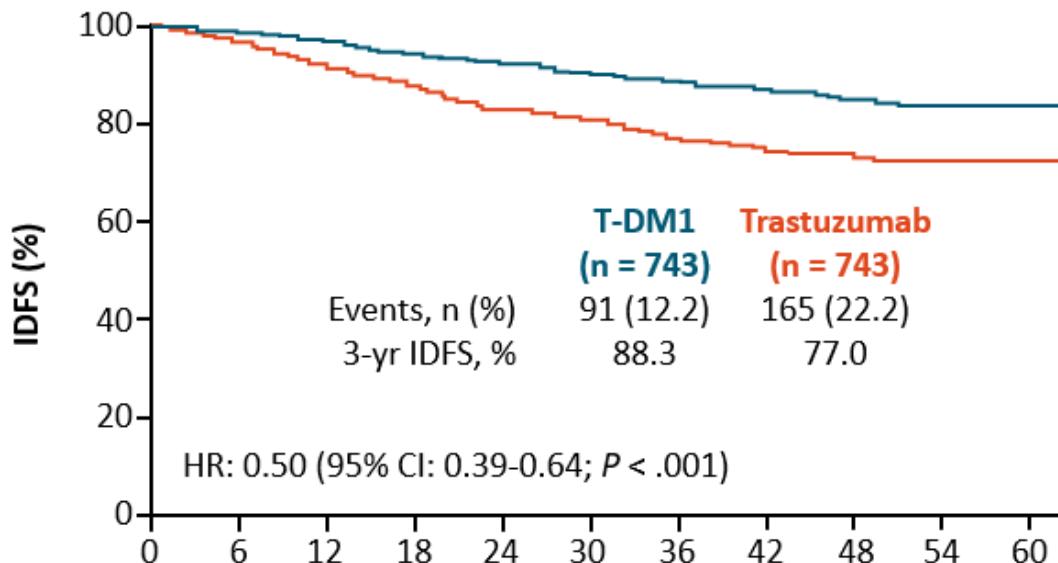
Randomization occurred within 12 wks of surgery; radiotherapy and/or endocrine therapy given per local standards. *Minimum of 9 wks taxane and trastuzumab. [†]Patients who d/c T-DM1 for toxicity allowed switch to trastuzumab to complete 14 cycles.

- Primary endpoint: IDFS
- Secondary endpoints including: distant recurrence-free survival, OS, safety

Geyer. SABCs 2018. Abstr GS1-10. von Minckwitz. NEJM. 2018;[Epub].

Slide credit: clinicaloptions.com

KATHERINE: IDFS



Patients at Risk, n		Mos Since Randomization										
		0	6	12	18	24	30	36	42	48	54	60
T-DM1	743	707	681	658	633	561	409	255	142	44	4	
Trastuzumab	743	676	635	594	555	501	342	220	119	38	4	

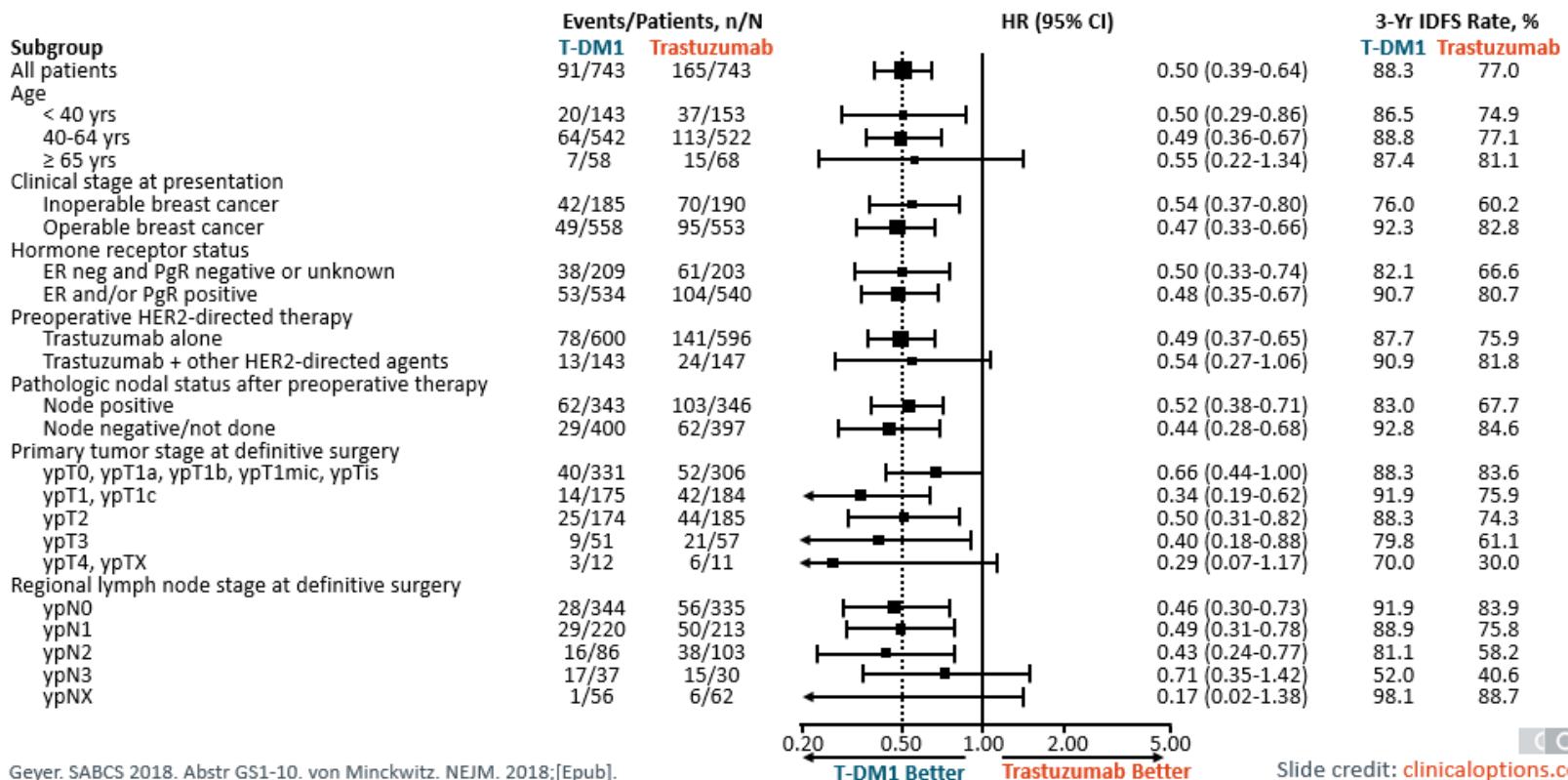
First IDFS Event, %	T-DM1	T
Any	12.2	22.2
Distant recurrence	10.5*	15.9†
Locoregional recurrence	1.1	4.6
Contralateral breast cancer	0.4	1.3
Death without prior event	0.3	0.4

CNS events: *5.9% vs †4.3%.

Geyer. SABCS 2018. Abstr GS1-10. von Minckwitz. NEJM. 2018;[Epub].

Slide credit: clinicaloptions.com

KATHERINE: IDFS by Subgroup

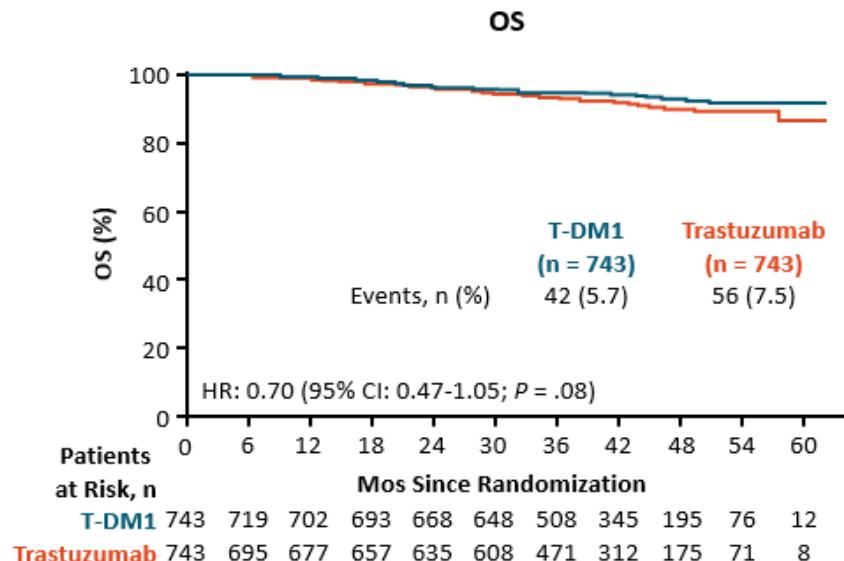
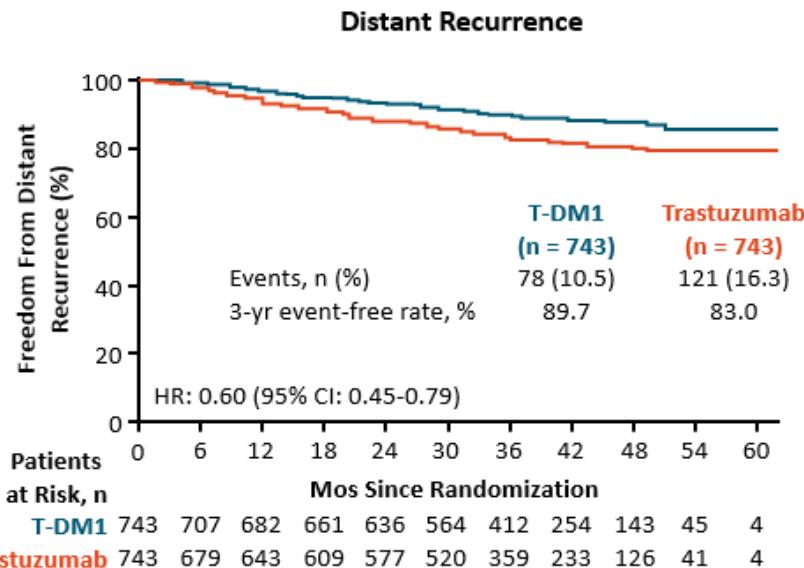


Geyer. SABCS 2018. Abstr GS1-10. von Minckwitz. NEJM. 2018;[Epub].



Slide credit: clinicaloptions.com

KATHERINE: Secondary Endpoints



Geyer. SABCS 2018. Abstr GS1-10. von Minckwitz. NEJM. 2018;[Epub].



Slide credit: clinicaloptions.com

KATHERINE Summary and Conclusions

- Adjuvant T-DM1 demonstrated both a statistically significant and clinically meaningful improvement in IDFS compared with trastuzumab
 - Unstratified HR=0.50; 95% CI 0.39–0.64; $P<0.0001$
 - 3-year IDFS rate improved from 77.0% to 88.3% (difference=11.3%)
- Benefit of T-DM1 was consistent across all key subgroups including HR status, extent of residual invasive disease, and single or dual HER2-targeted neoadjuvant therapy
- The safety data were consistent with the known manageable toxicities of T-DM1, with expected increases in AEs associated with T-DM1 compared to trastuzumab
- Additional follow-up will be necessary to evaluate the effect of T-DM1 on OS
- The KATHERINE data will likely form the foundation of a new standard of care in this population and increase the use of neoadjuvant therapy in HER2-positive EBC

Dual Inhibition in Adjuvant Setting: Aphinity trial

Resected
HER2+
(N = 4805)

R

Chemotherapy* +
trastuzumab
+ pertuzumab

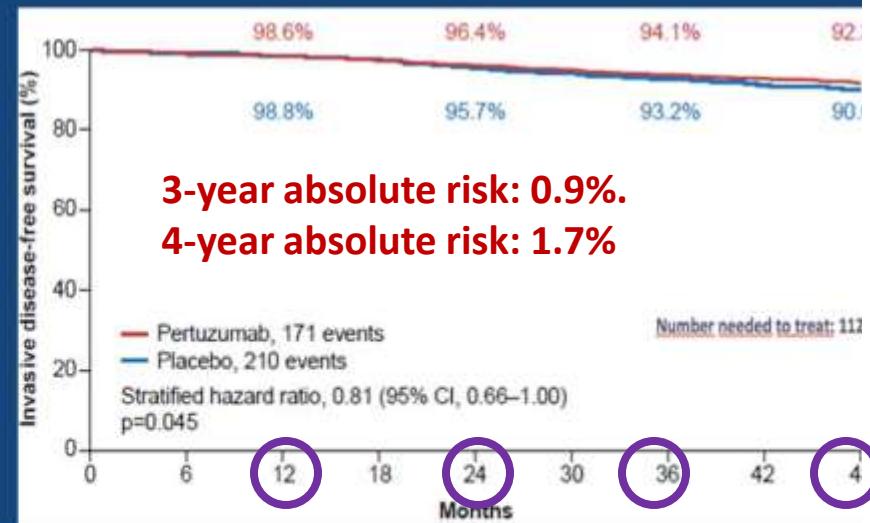
Chemotherapy* +
trastuzumab
+ placebo

*several concurrent and sequential chemo designs

iDFS = 92.3% vs 90.6%
Met prespecified statistical endpoints
FDA approval 2017

Significant yes, but meaningful?

Von Minckwitz et al, NEJM 2017



Hormone-receptor status							0.54
Positive	100/1536	119/1546			0.86 (0.66–1.13)	94.8	94.4
Negative	71/864	91/858			0.76 (0.56–1.04)	92.8	91.2

Absolute
Difference

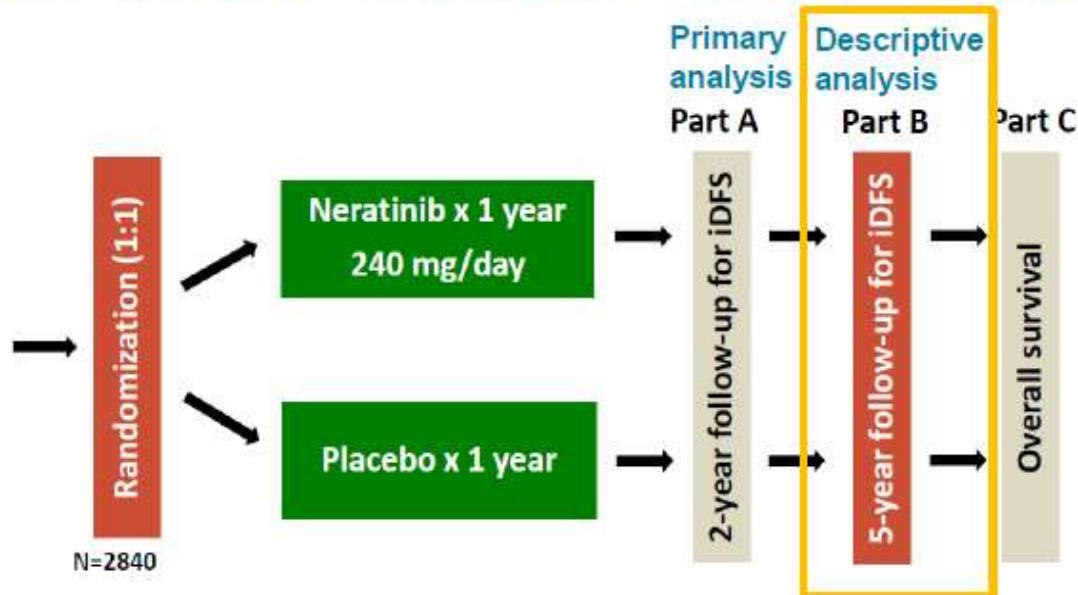
HR- : 1.6%
Node- 0.9%

HR+ : 0.4%.
Node + : 1.8%

NEJM 2017

ExteNET: Neratinib vs Placebo As Extended Adjuvant Therapy After Trastuzumab in Operable HER2+ Breast Cancer

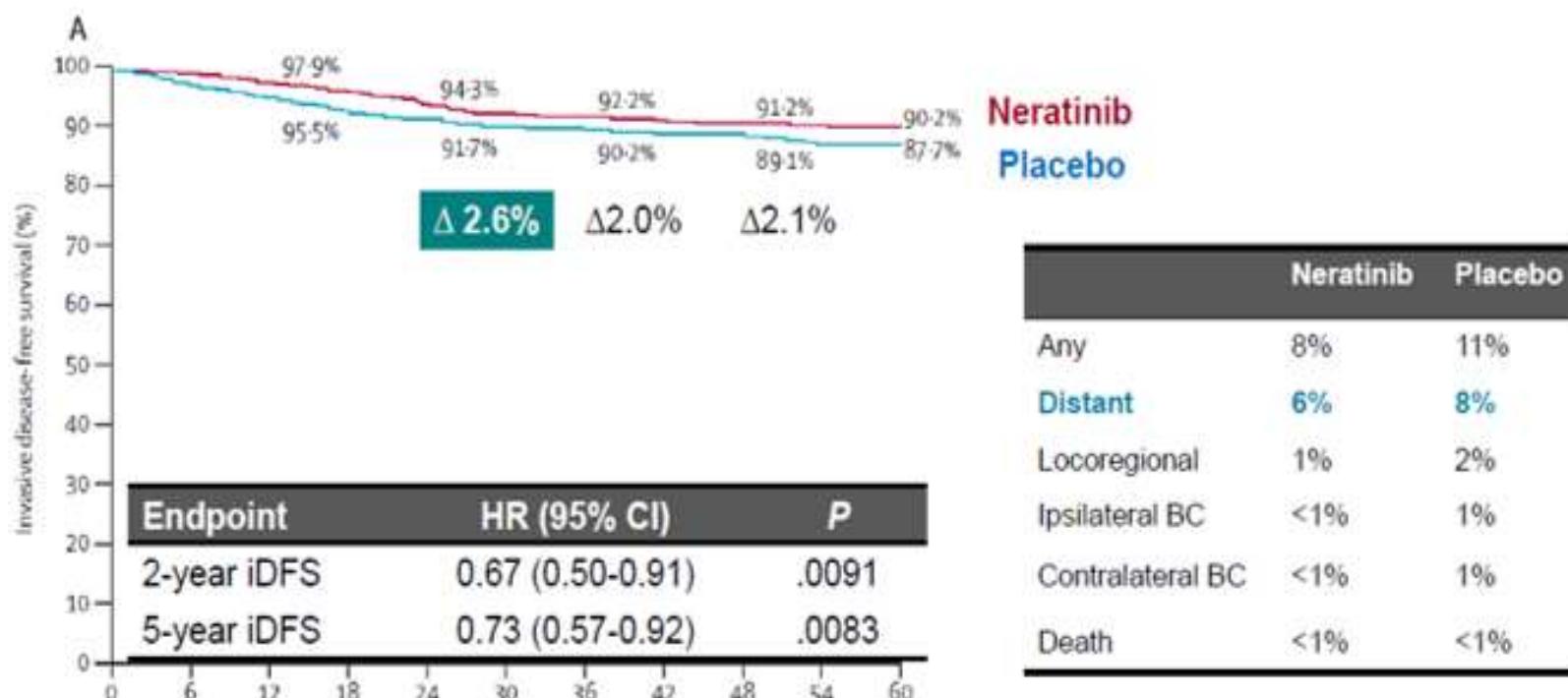
- HER2+ breast cancer
 - IHC 3+ or ISH amplified (locally determined)
 - Prior adjuvant trastuzumab + chemotherapy
 - Lymph node +/-, or residual invasive disease after neoadjuvant therapy
- Stratified by: nodal status, hormone receptor status, concurrent vs sequential trastuzumab



- Primary endpoint: Invasive disease-free survival (iDFS)
- Secondary endpoints: DFS-DCIS, time to distant recurrence, distant DFS, CNS recurrences, OS, safety
- Other analyses: Biomarkers, health outcome assessments (FACT-B, EQ-5D)
- Endocrine adjuvant therapy given to patients with HR-positive tumors according to local practice

Chan, et al. *Lancet.* 2016;17(3):367-377. National Institutes of Health. <https://clinicaltrials.gov/ct2/show/NCT00878709>. Accessed 18 October 2018.

ExteNET: iDFS at 5 Years



Chan, et al. *Lancet*. 2016;17(3):367-377. Martin M, et al. *Lancet Oncol*. 2017;18(12):1688-1700.

Challenges

- At 10 years, the risk of disease relapse after modern trastuzumab-based adjuvant therapy is high
 - ~20% of patients with node-negative disease
 - One-fourth to one-third of patients with node-positive disease
- De novo resistance to first-line therapy (THP) in ~4% of patients (bad disease!)
- Resistance develops to systemic therapy in the vast majority of patients with MBC, with < 40% survival at 5 years and < 30% survival at 7 years after diagnosis
- More than 30% of patients with *HER2*-positive MBC develop CNS metastases, an area of unmet need

Treating HER2+: Triumph of Incrementalism

Metastatic disease approvals

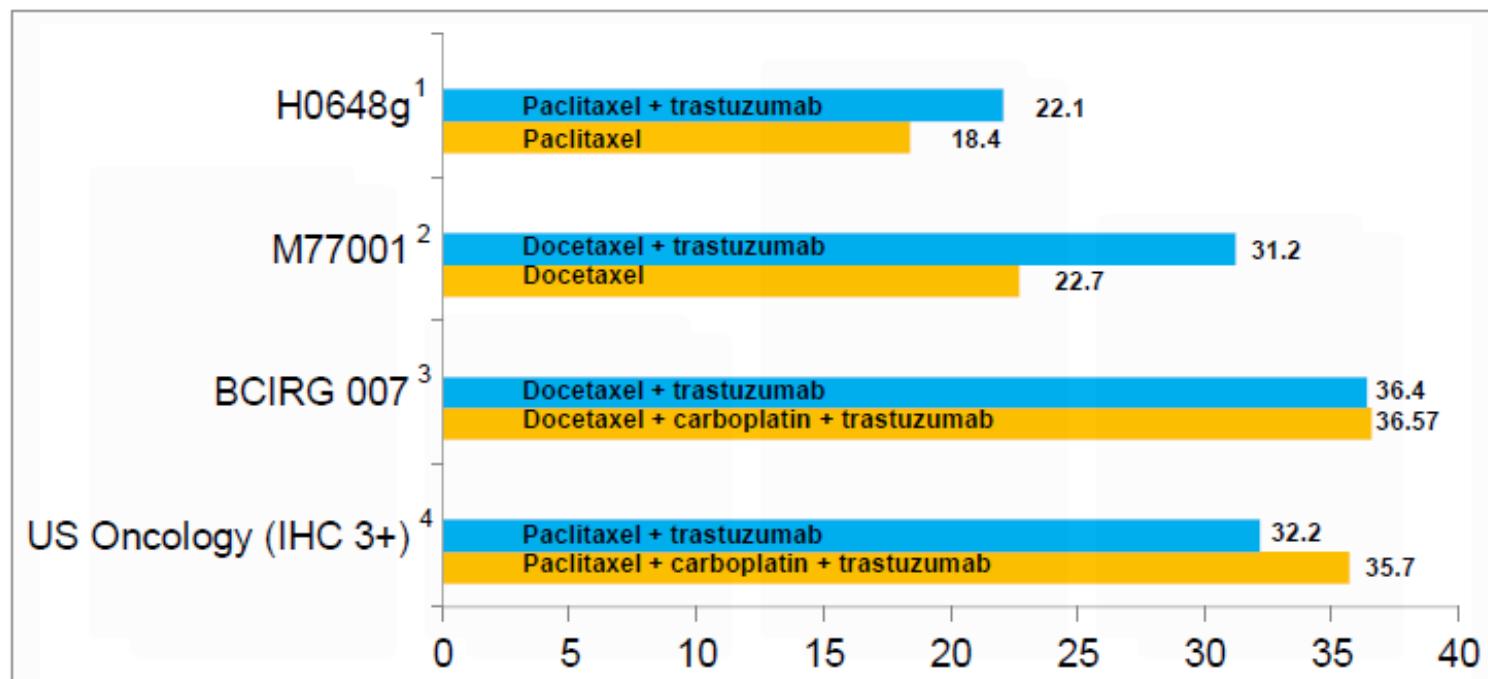
Trastuzumab 1 st line	Lapatinib > 1 st line	Pertuzumab (added) 1 st line	T-DM1 > 1 st line
1998	2005	2012	2013

(Neo)adjuvant approvals

Trastuzumab (H)	Pertuzumab (added to H)	Neratinib (after H)
2005	2013 - 2018	2018

Slamon et al, NEJM 2001; Geyer et al, NEJM 2006; Swain et al, NEJM 2015; Verma et al, NEJM 2012; Perez et al, JCO 2011; von Minckwitz et al, NEJM 2017; Martin et al, Lancet Oncol 2017

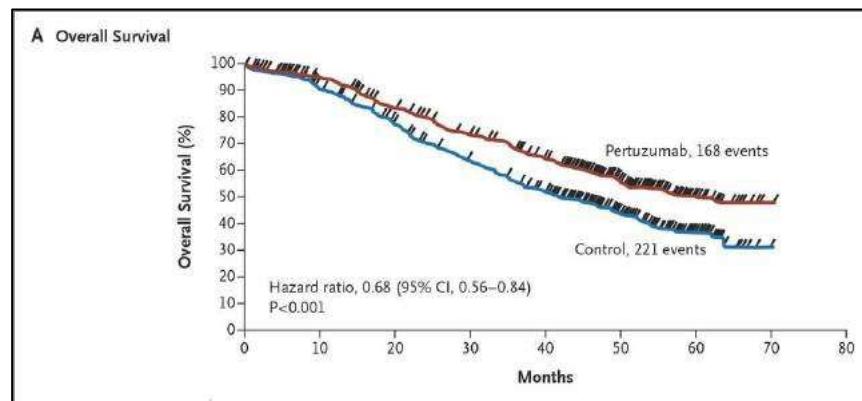
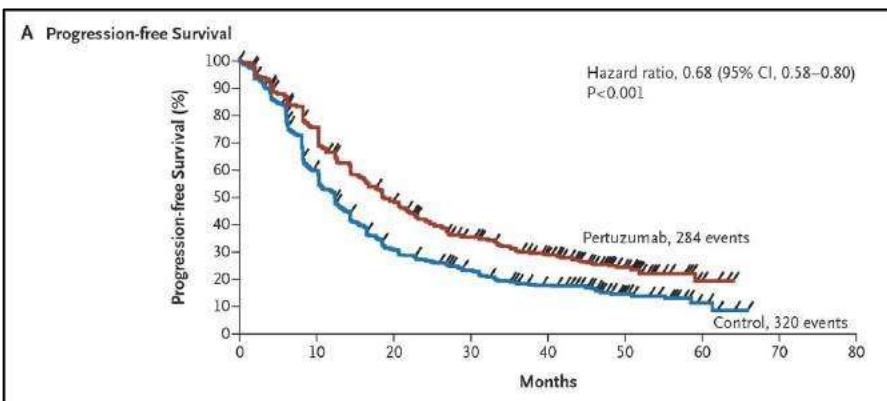
Trastuzumab Prolongs Survival in Women With First-Line HER2/neu + mBC



IHC, immunohistochemistry

1. Slamon DJ, et al. *N Engl J Med.* 2001;344(11):784-792. 2. Marty M, et al *J Clin Oncol.* 2005;23(19):4265-4274. 3. Pegram MD, et al. *J Clin Oncol.* 2007;25(18_suppl): Abstract LBA1008. 4. Robert N, et al. *J Clin Oncol.* 2006;24(18):2786-2792.

CLEOPATRA: First-line Trastuzumab + Pertuzumab vs. Trastuzumab (mFU 50 mos)



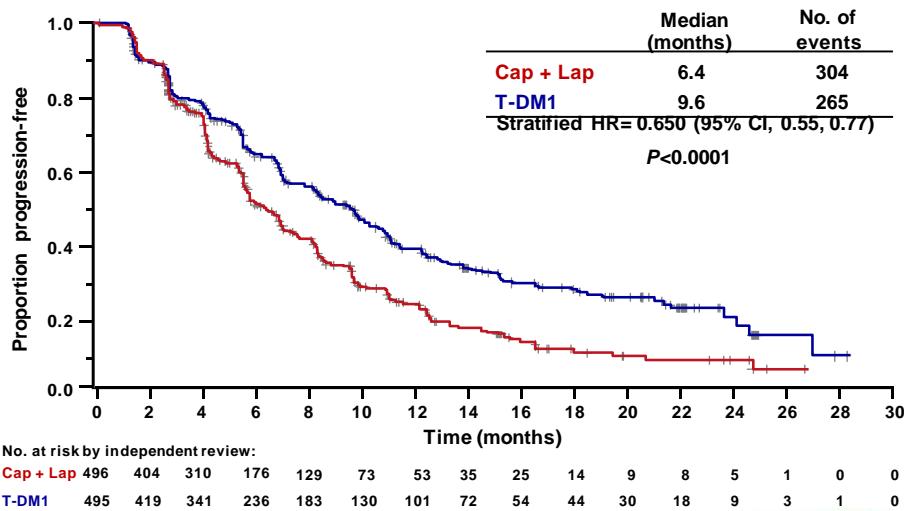
	Pertuzumab + trastuzumab+docetaxel	Placebo + trastuzumab+docetaxel	Hazard ratio	P-value
ORR ¹	80.2%	69.3%		0.0001
PFS ²	18.7 months	12.4 months	0.68	<0.0001
OS ²	56.5 months	40.8 months	0.66	0.0001

Most common adverse events ≥Grade 3 in the pertuzumab+trastuzumab+docetaxel group:
 Neutropenia (48.9%), febrile neutropenia (13.8%), leukopenia (12.3%), and diarrhea (7.9%)
 Long term cardiac safety maintained

1. Baselga et al, N Eng J Med 2012; 2. Swain S et al, NEJM 2015

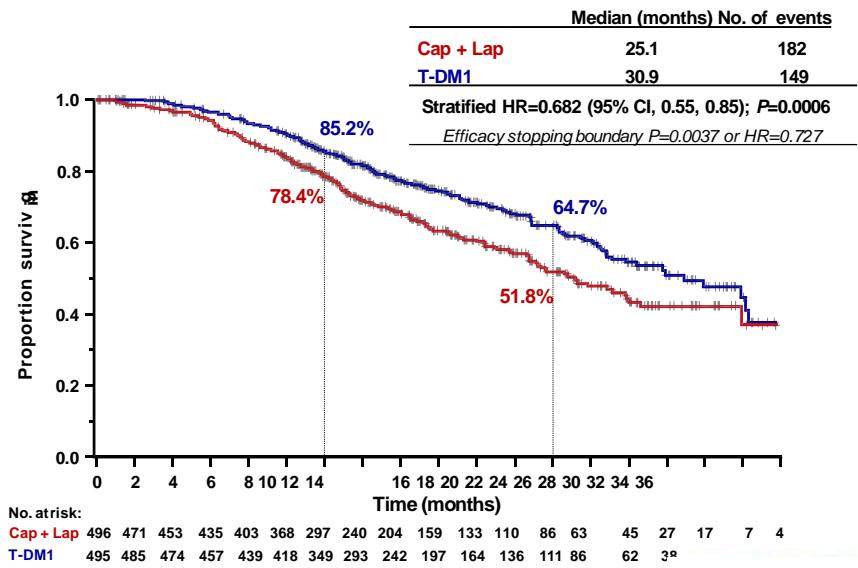
EMILIA: T-DM1 vs. Lapatinib Plus Capecitabine in Second-line

Progression-Free Survival by Independent Review



Unstratified HR = 0.66 (P < 0.0001).

Overall Survival: Confirmatory Analysis



Data cut-off July 31, 2012; Unstratified HR = 0.70 (P = 0.0012).

	T-DM1	Lapatinib + capecitabine	Hazard ratio	P-value
PFS	9.6 months	4.6 months	0.65	<0.001
OS	30.9 months	25.1 months	0.68	<0.001

HER2-Directed Therapy: Role of T-DM1

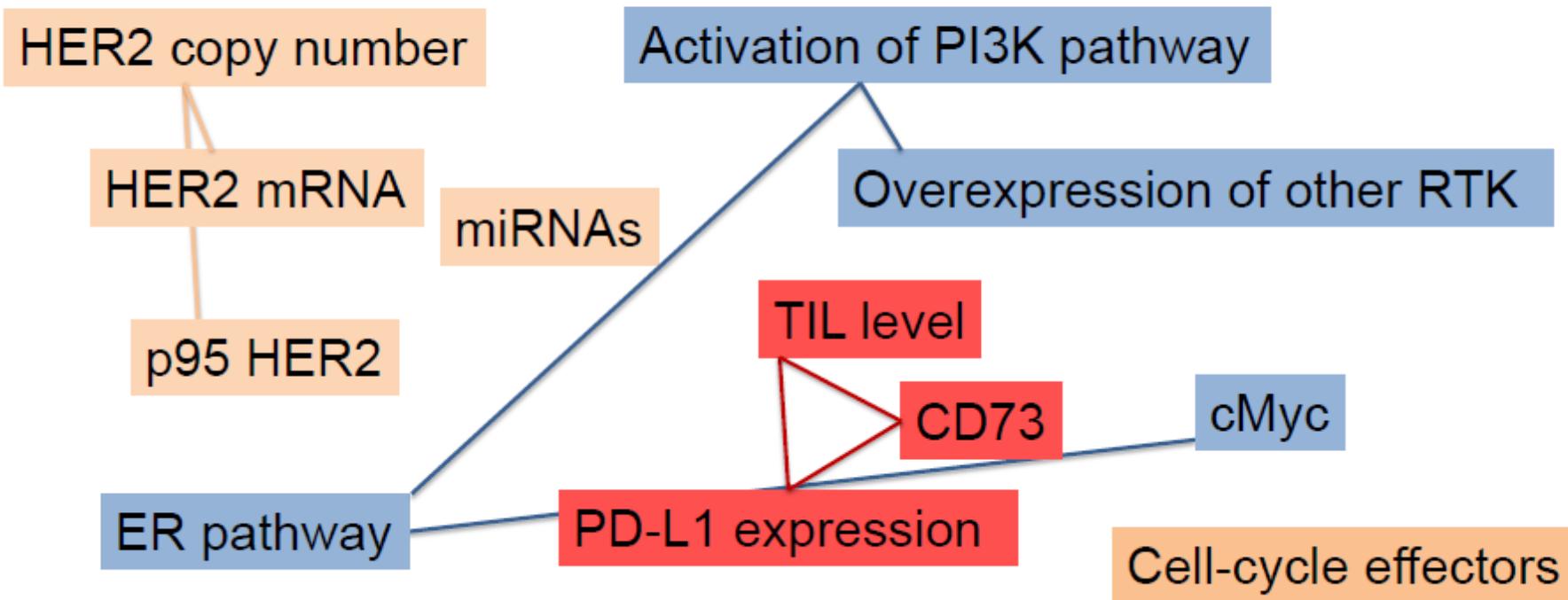
- T-DM1's approval was for *HER2*-positive MBC previously treated with trastuzumab and a taxane based on EMILIA
- Activity of T-DM1 after failure of trastuzumab and pertuzumab; CLEOPATRA and PHEREXA trial
- Exploratory analysis of patients receiving T-DM1 after discontinuing study assigned treatment

Study	No T-DM1 (median OS)	T-DM1 (median OS)
Cleopatra HT + placebo	39.6	46.2
Cleopatra HTP	61.4	49-NR
PHEREXA HC	23.7	40.1
PHEREXA HCP	32.8	38.3

- Median duration of T-DM1: Cleopatra: 7.1 mo (0-44); PHEREXA: 4.2 mo (0-22)
- Data limited but evidence of T-DM1 clinical activity in patients progressing on pertuzumab and trastuzumab
- However, the patient described had already failed T-DM1, so what next?

Key Predictors of Sensitivity/Resistance to HER2-Targeting Agents

Demonstrated biomarkers linked to sensitivity/resistance to anti-HER2 agents

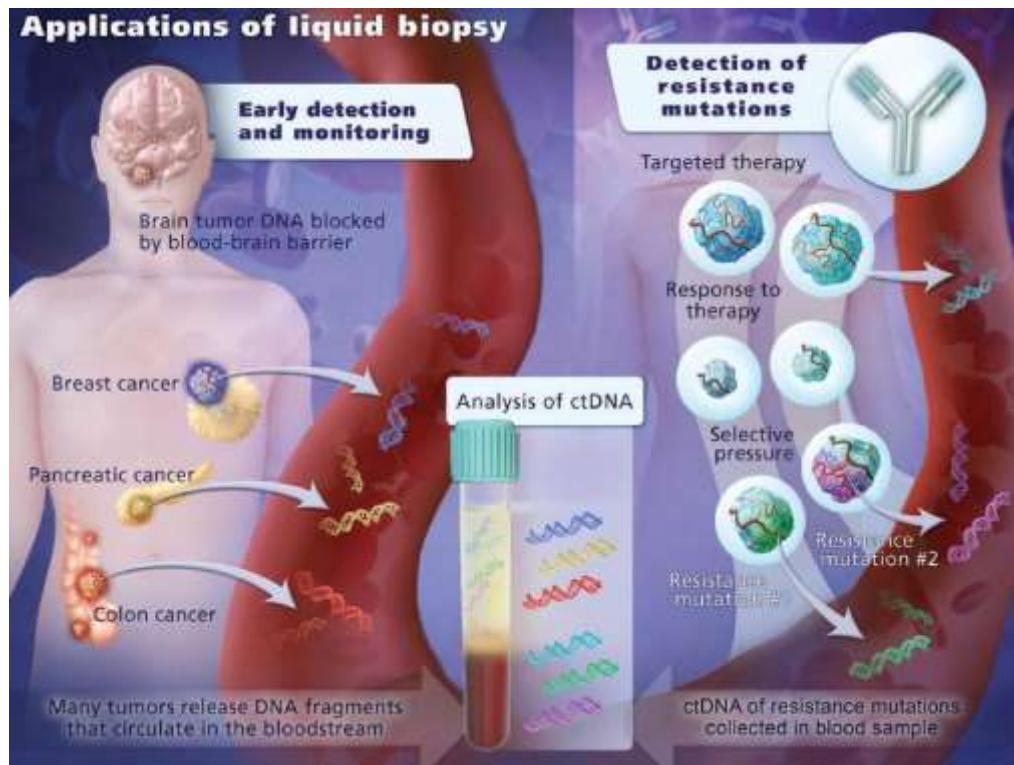


Mechanisms of Resistance to HER2-Directed Therapy

- Not just one mechanism or pathway to account for *HER2* therapy resistance
 - *HER2*+ breast cancer has a number of resistance pathways
- Resistance mechanisms intrinsic to the target
 - *HER2* expression as a predictor of response
 - $\Delta 16_HER2$ splice variant, p95-*HER2* resistance that involves parallel bypass signaling pathways
 - Constitutive activation of the PI3K/AKT pathway, IGF-1R
 - T-DM1 agnostic to *PIK3CA* mutational status
- Resistance that involves defects in apoptosis and host factors
 - Tolerance to antibody-dependent cell-mediated cytotoxicity (ADCC)
 - Polymorphisms in Fc γ RIII, CD137 agonist antibodies
- CDK inhibition to overcome resistance in *HER2*+ breast cancer
- Brain metastases remain a challenge

How can we improve early detection of Resistance to HER2- Directed Therapy?

Liquid biopsies open a complete new perspective

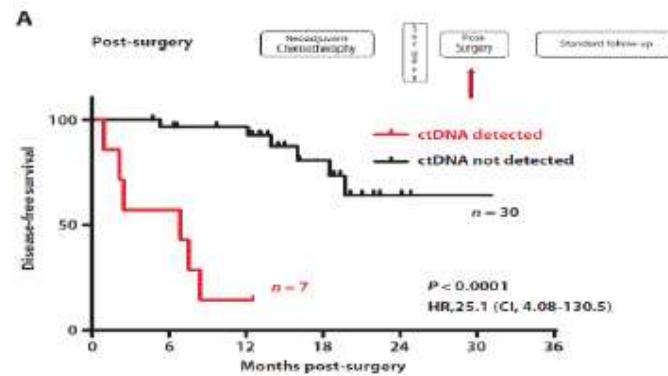
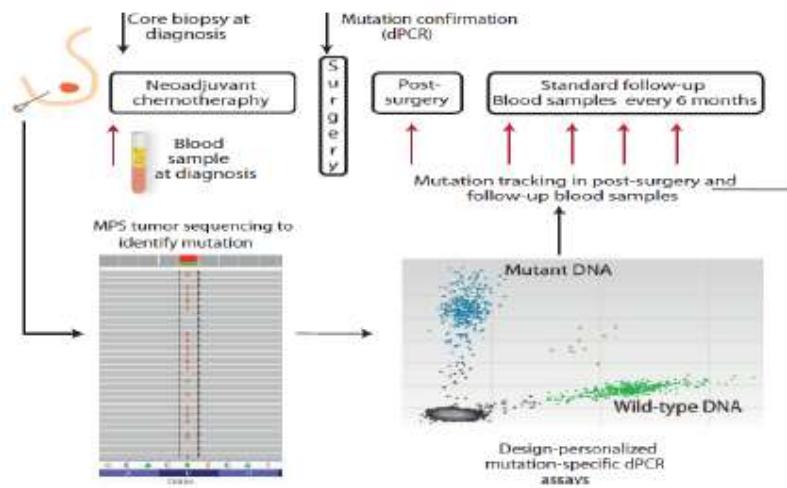


Liquid biopsies open a complete new perspective

- ctDNA is a direct measurement of cancer DNA, rather than an indirect measure of the effects of cancer
 - Higher specificity
 - Participate to early detection of cancer
 - Allow monitoring of minimal residual disease
- Ultra-deep sequencing to detect ctDNA
 - Can improve signal to noise ratio
 - Increase detection of more mutations/amplifications per sample

Liquid biopsies in resectable disease (breast cancer)

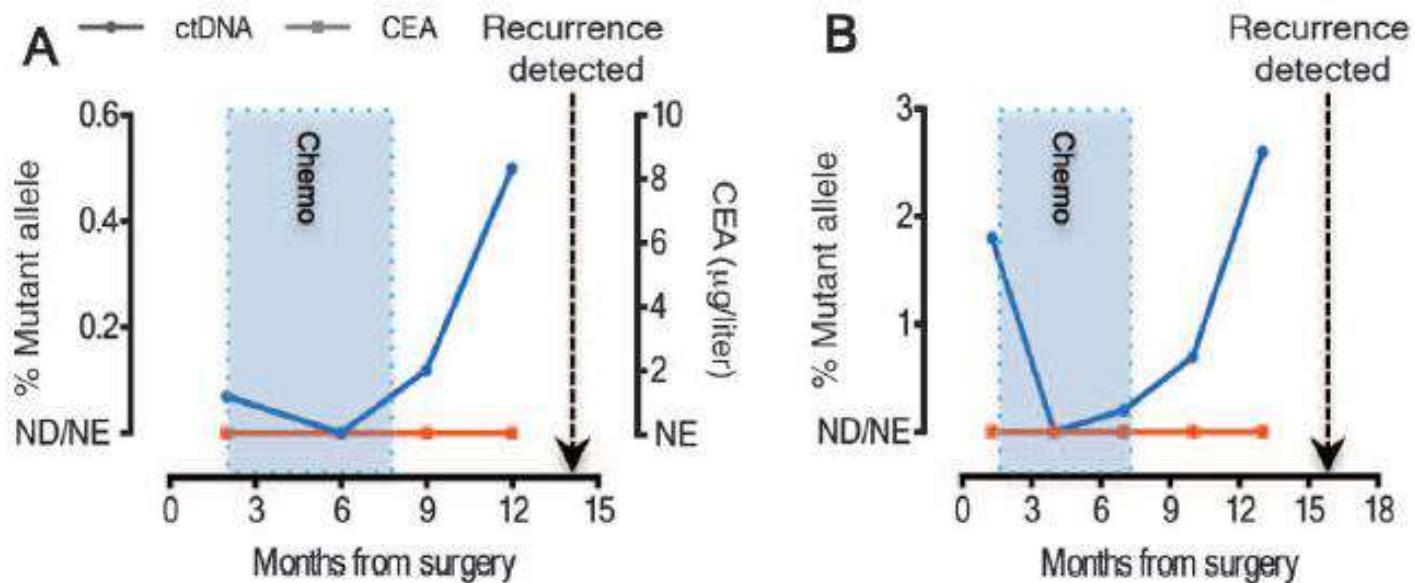
Surgically resected BC post-CT



Garcia-Murillas I, STM 2015

Liquid biopsies in resectable disease (colorectal cancer)

Stage II colorectal cancer



Tie J, et al. STM 2016



SABCS, December 4-8, 2018

Spotlight Session: Biomarkers in Clinical Trials Liquid Biopsy

San Antonio Breast Cancer Symposium®
Wednesday December 5th, 2018



SABCS, December 4-8, 2018



I-SPY2 Trial

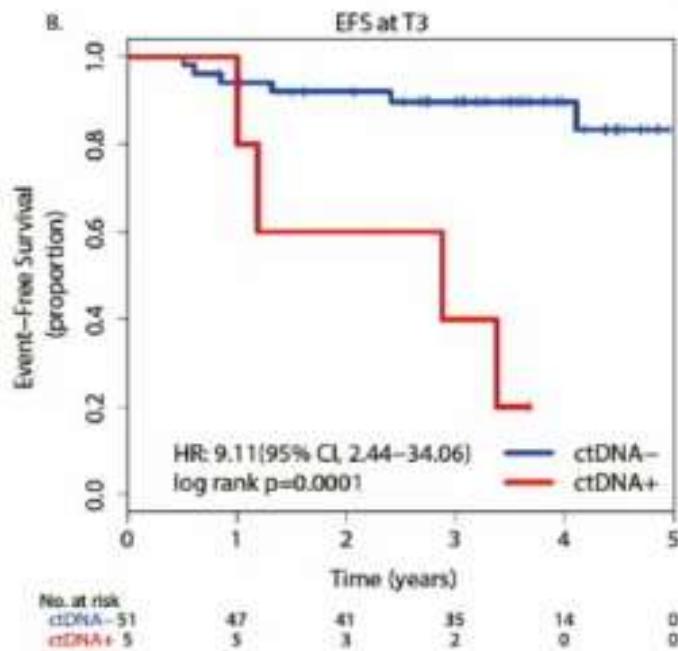
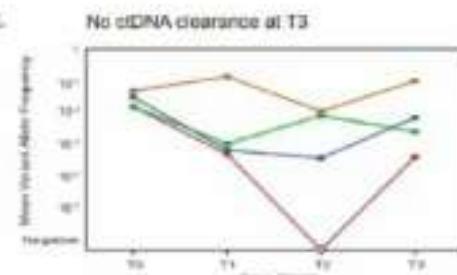
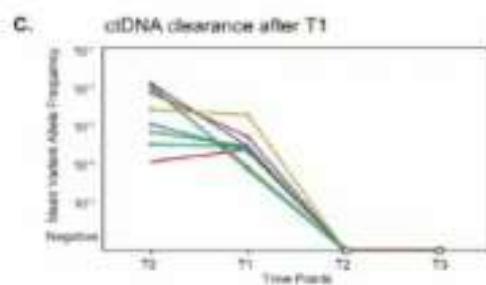
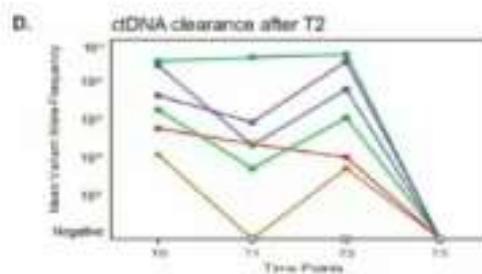
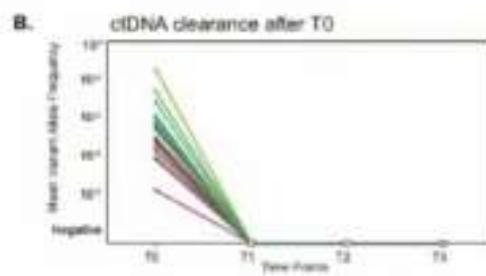


Personalized Serial Circulating Tumor DNA (ctDNA) Analysis in High-Risk Early Stage Breast Cancer Patients to Monitor and Predict Response to Neoadjuvant Therapy and Outcome in the I-SPY 2 TRIAL

Mark Jesus M. Magbanua¹, Lamorna Brown-Swigart¹, Gillian L. Hirst¹, Christina Yau¹, Denise Wolf¹, Aye Aye Ma¹, Elizabeth Bergin¹, Sara Venters¹, Nola Hylton¹, Himanshu Sethi², Hsin-Ta Wu², Raheleh Salari², Svetlana Shchegrova², Antony Tin², Sarah Sawyer², Maggie Louie², Jonathan Keats³, Winnie Liang³, Lori Cuyugan³, Daniel Enriquez³, Debasish Tripathy⁴, Amy Jo Chien¹, Andres Forero⁵, Angela DeMichele⁶, Minetta Liu⁷, Amy Delson¹, Smita Asare¹, Bernhard G. Zimmermann², Cheng-Ho Jimmy Lin², Laura Esserman¹, Laura van 't Veer¹, I-SPY 2 Consortium¹

¹University of California San Francisco, San Francisco, CA; ²Natera, San Carlos, CA; ³TGEN, Phoenix, Arizona; ⁴MD Anderson Cancer Center, Houston, Texas;
⁵ University of Alabama, Birmingham, Alabama; ⁶University of Pennsylvania, Philadelphia, Pennsylvania; ⁷Mayo Clinic, Rochester, Minnesota.

ctDNA clearance and clinical outcome



Strengths and weaknesses

- This study confirms previous studies^{1,2} demonstrating that ctDNA detection following neoadjuvant treatment is associated with poor outcome.
- Is ctDNA adding prognostic information to pCR status for predicting event-free survival?
- Larger studies are needed to evaluate the sensitivity and specificity of different ctDNA assays to predict relapse.
- Studies demonstrating clinical utility are needed (e.g. ctDNA elimination as surrogate endpoint in drug development³).

¹Garcia-Murillas I et al STM 2015

²Chen YH et al NPG Breast 2017

³Ignatiadis M et al Ann Oncol 2018

LiqERBcept: the GIM21 project

id: GIM21

Funding

Chairman of the project



Francesco Cognetti



Alessandra Fabi

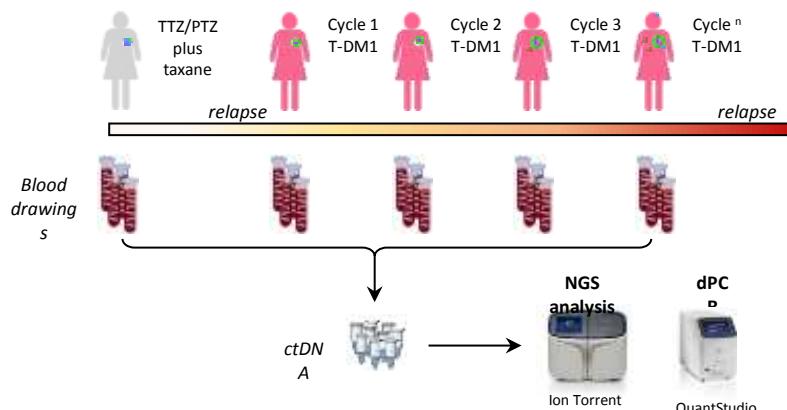
Patrizio Giacomini

Project PIs

PI(s)	City	Center(s)
A. Fabi	RM	IRCSS Istituto Nazionale Tumori Regina Elena
C. Tondini	BG	A.O. Papa Giovanni XXIII
L. Moscetti	MO	A.O.U. Modena
L. Del Mastro	GE	IRCSS A.O.U. San Martino IST
P. Marchetti	RM	A.O.U. Sant'Andrea
G. De Placido	NA	Università degli Studi Federico II

Aims of the project

- ❖ Application of liquid biopsy for longitudinal cancer monitoring
- ❖ Anticipation of relapse or early evaluation of response to T-DM1
- ❖ Identification of additional 'actionable' mutations
- ❖ Liquid biopsy vs clinical imaging



Kick-off:
November
2018

LiqERBcept: the GIM21 project

Sponsor e Centro coordinatore

Sponsor	
Promotore	Consorzio Oncotech c/o Dipartimento di Medicina Clinica e Chirurgia – Oncologia Università degli Studi di Napoli “Federico II” 80131 Napoli Prof. Sabino De Placido

Centro	
Study Chairman	Prof. Francesco Cognetti Regina Elena National Cancer Institute
Study coordinators	Dr. Alessandra Fabi: clinical issues
	Dr. Patrizio Giacomini: laboratory assessment and liquid biopsy
Statistician	Dr. Diana Giannarelli
Central Laboratory Responsible person	Dr. Patrizio Giacomini Oncogenomics and Epigenetics

Disegno dello studio

studio in aperto, prospettico,
interventistico, non farmacologico



Treatment with TDM1

PD

Dose: 3,6 mg / Kg ogni 21 giorni

I pazienti saranno trattati fino a progressione della malattia, tossicità inaccettabile, ritiro del consenso o morte, a seconda di cosa accada per primo, come da pratica clinica

Disegno dello studio

- Si tratta di uno studio in aperto, prospettico, interventistico, non farmacologico
- Gli effetti di T DM1 saranno monitorati dalla **combinazione di Next Generation Sequencing (NGS, tessuto tumorale) e Biopsia Liquida (LB, sangue)** per rilevare eventi molecolari (aberrazioni genetiche, principalmente mutazioni) associati a (o causativi di) recidiva e resistenza primaria/adattativa al blocco di HER2
- Saranno selezionati per lo studio circa **45 pazienti** con neoplasia mammaria metastatica HER2-positiva candidati a ricevere Trastuzumab Emtansine (TDM1) come da pratica clinica. Gli effetti di T-DM1 saranno monitorati durante tutta la storia clinica dei pazienti (tessuti archiviati, raccolta del sangue, biopsie mirate).
- Gli effetti di T DM1 saranno monitorati dalla combinazione di Next Generation Sequencing (NGS, tessuto tumorale) e Biopsia Liquida (LB, sangue) per rilevare eventi molecolari (aberrazioni genetiche, principalmente mutazioni) associati a (o causativi di) recidiva e resistenza primaria/adattativa al blocco di HER2.

Obiettivi dello studio

OBIETTIVI PRIMARI	OBIETTIVO SECONDARIO
<p>Sono stati definiti tre obiettivi principali:</p> <p>1. Rilevazione delle mutazioni dell'elenco (sono definite come quelle rilevate nelle biopsie tissutali da una o entrambe le lesioni primarie e dalla recidiva più recente, quando disponibile) e di mutazioni acquisite associate alla resistenza nel sangue.</p> <p>2) Identificazione delle relazioni temporali tra indicatori molecolari di recidiva (mutazioni dell'elenco) e letture convenzionali (criteri RECIST) che portano alla predizione della risposta/anticipazione della ricaduta.</p> <p>3) Rilevazione di mutazioni de novo che si verificano durante il trattamento con T-DM1</p>	<p>1) Specificità e Sensitività della biopsia liquida come definite di routine nella pratica clinica patologica</p> <p>2) Investigare se si verifichino mutazioni durante il trattamento con T-DM1</p>



SABCS, December 4-8, 2018

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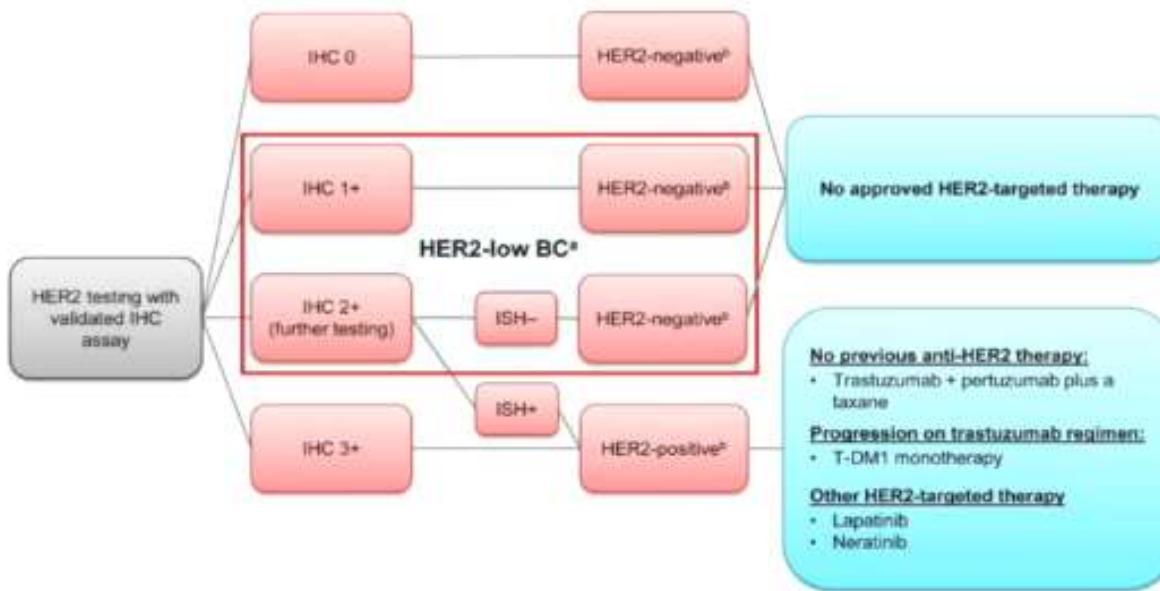
P6-17-02

Trastuzumab deruxtecan (DS-8201a) in subjects with HER2-low expressing breast cancer: Updated results of a large phase 1 study

Modi S, et al.

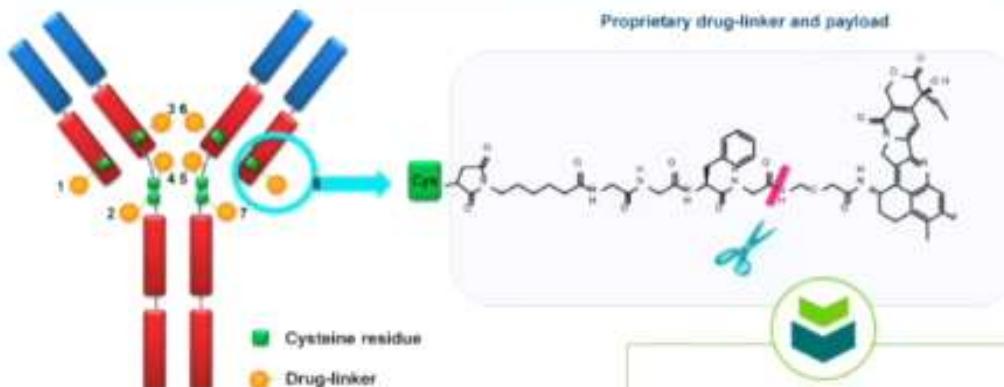
Memorial Sloan-Kettering Cancer Center, New York, NY

Overview of Breast Cancer Treatment Strategies with HER2-Targeted Therapy Based on HER2 Status^a



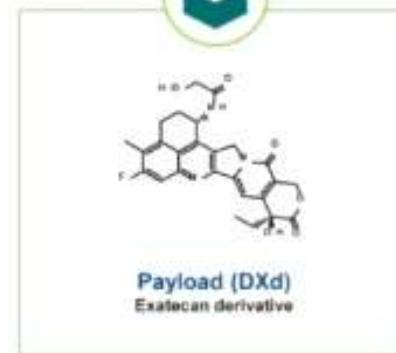
^aHER2-low breast cancer population assessed in current study; currently undefined by HER2-testing guidelines.
^bHER2 status according to ASCO/CAP guidelines.⁴
 ASCO/CAP, American Society of Clinical Oncology/College of American Pathologists; BC, breast cancer; HER2, human epidermal growth receptor 2; IHC, immunohistochemistry; ISH, in situ hybridization; T-DM1, ado-trastuzumab emtansine.

Structure of [Fam-] Trastuzumab Deruxtecan



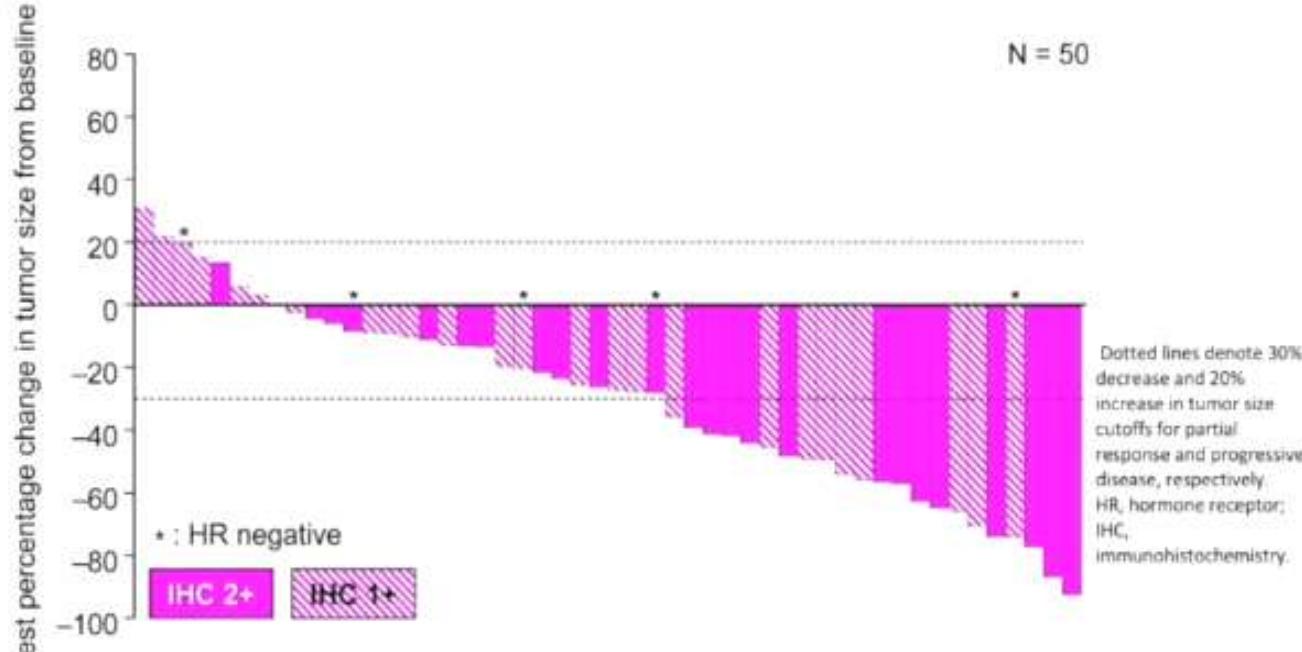
Conjugation chemistry

The linker is connected to the cysteine residue of the antibody



Modi S. et al. 2018 SABCS® Abstract P6-17-02

Best Percentage Change in Tumor Size from Baseline by IHC Status (October 12, 2018 Data Cutoff)



Modi S, et al. 2018 SABCS® Abstract P6-17-02

Conclusions

- ❖ The natural history of patients with early and metastatic HER2+ breast cancer has changed due to trastuzumab treatment.
- ❖ Resistance mechanisms in HER2-targeted treatments play an important role.
- ❖ Risk stratification based on pathologic response after neoadjuvant treatment allows for a more personalized treatment and a more rational resource allocation.
- ❖ Novel treatments in MBC HR2+ disease are showing great promise and, in the future, may add to the currently available options.
- ❖ New scientific insights and a spur of technological innovations, make prospects for success greater than ever.
- ❖ Breast cancer is many diseases and precision medicine aims at selecting the right therapy
- ❖ Liquid Biopsy in the future could drive treatments.



Associazione Italiana di Oncologia Medica
SEZIONE REGIONE LAZIO

POST SAN ANTONIO BREAST CANCER SYMPOSIUM 2018



— 28 Gennaio 2019 —

POLICLINICO UMBERTO I - ROMA

Aula Bignami (Patologia Generale)
Viale Regina Elena 324



Prof. Francesco Cognetti
Istituto Nazionale Tumori
'Regina Elena'
Roma

IRE  **ISG**
ISTITUTO NAZIONALE TUMORI
REGINA ELENA  **SAN GALLICANO**
ISTITUTO DI RICERCA E CURA A CARATTERE SCIENTIFICO