HER-2 Disease: Neo-, Adjuvant, Metastatic Setting

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WCS™ WINTER CANCER SYMPOSIUM

Disclosures

- Speaker Bureau: Merck, BMS, AbbVie, Eisai
- Research Support: AbbVie

Adjuvant/Neoadjuvant Treatment

Trastuzumab improves outcomes…

Study	Follow-up (yrs)	N	DFS		OS	
			HR	p value	HR	p value
HERA[1–4] CT±RT→T vs. CT±RT	1	3387	0.54	< 0.0001	0.76	0.26
	2	3401	0.64	< 0.0001	0.66	0.0115
	4	3401	0.76	< 0.0001	0.85	0.1087
	8	3399	0.76	< 0.0001	0.76	0.0005
	11	3399	0.76	< 0.0001	0.74	< 0.0001
NCCTG N9831/ NSABP B-31[5–7] AC→Tax+T→T vs. AC→Tax	2	3351	0.48	< 0.0001	–	–
	4	4045	0.52	< 0.001	0.61	< 0.001
	8.4	4046	0.60	< 0.0001	0.63	< 0.0001
	10	4046	0.60	< 0.001	0.63	< 0.001
BCIRG 006[8]						
AC→Tax + T vs. AC→Tax	5.4	3222	0.64	< 0.001	0.63	< 0.001
Tax+Cb→T vs. AC→Tax			0.75	0.04	0.77	0.04
AC→Tax + T vs. AC→Tax	10.3	3222	0.72	< 0.001	0.63	< 0.001
Tax+Cb→T vs. AC→Tax			0.77	0.0011	0.76	0.0075

AC, doxorubicin and cyclophosphamide; Cb, carboplatin; CT, chemotherapy; DFS, disease-free survival; HR, hazard ratio; OS, overall survival; RT, radiotherapy; T, trastuzumab; Tax, taxane.

Evolving Landscape: More or Less?

Escalate Treatment:

- Node positive
- LABC/Inflammatory
- no pCR

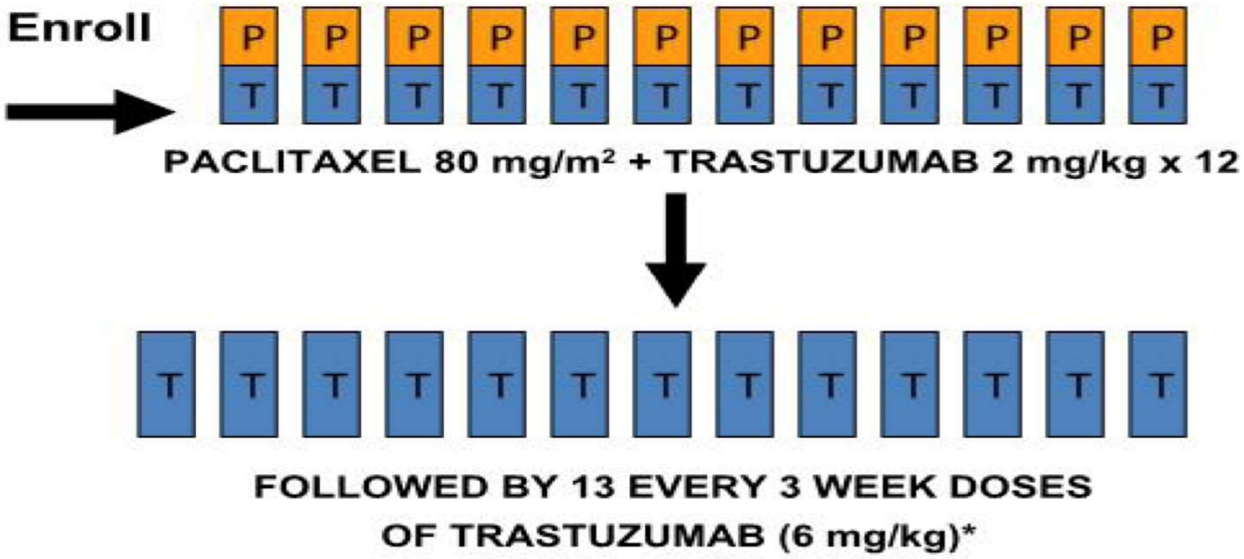
De-escalation of Treatment

- T1a/T1b/T1c
- Node Negative
- Patients achieving pCR

APT Trial: Study Design

HER2+
ER+ or ER-
Node Negative
≤ 3 cm

Planned N=400

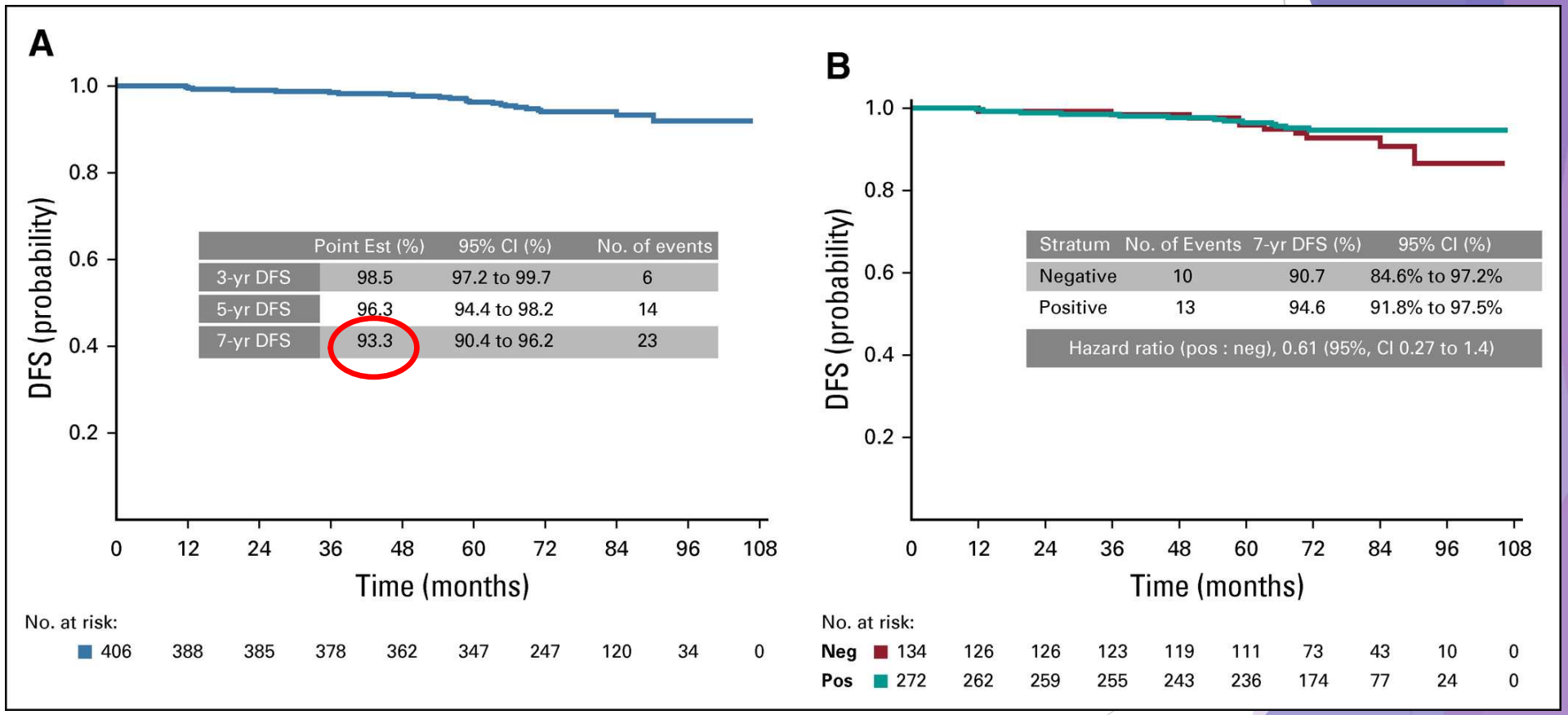


*Dosing could alternatively be 2 mg/kg IV weekly for 40 weeks
**Radiation and hormonal therapy was initaited after completion of paclitaxel

APT, adjuvant paclitaxel and trastuzumab

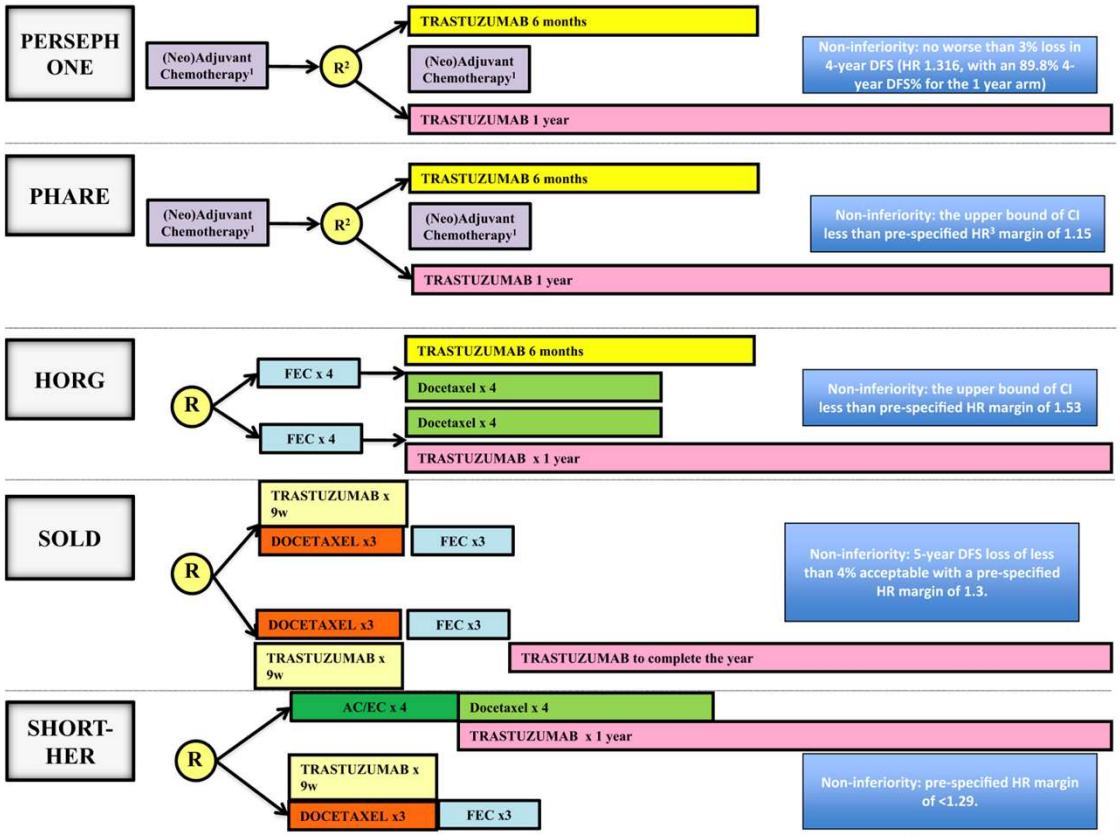
Tolaney SM, et al. *N Engl J Med.* 2015;372(2):134-141.

APT Trial Results



Duration of Trastuzumab

rom: PERSEPHONE: are we ready to de-escalate adjuvant trastuzumab for HER2-positive breast cancer?



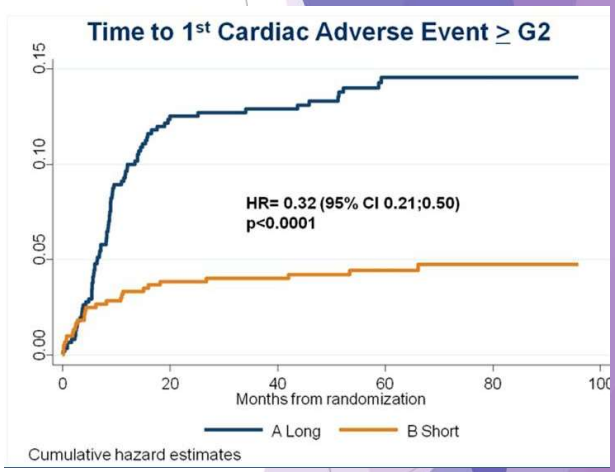
Pondé, N., Gelber, R.D. & Piccart, M. *npj Breast Cancer* **5,** 1 (2019).

Trial	Duration of trial[a]	Timing of randomization	Patient characteristics	Chemotherapy with anthracyclines and taxanes	Concomitant trastuzumab with chemotherapy	Patients (*n*)	Efficacy (short arm versus long arm)[b]	Notable Subgroup analysis favouring 1 year
6 months vs 12 months								
PERSEPHONE[8,15]	8 years	Within first 6 months	N−: 59% ER+: 69%	48%	47%	4089	11.6% vs 11.2% 4-year DFS events HR 1.07 (0.93–1.24)	Taxane-only concurrent chemothera and trend in ER-
PHARE[4]	6 years	At 6 months	N−: 55% ER+: 60%	74%	56%	3380	8.9% vs 6.2% 3.5-year DFS events: HR 1.28 (1.05–1.56)	Tumour size >2 cm and sequential chemothera trastuzumab
SOLD[6]	9 years	Previously to treatment	N−: 60% ER+: 66%	100%	100%	2,176	12.0% vs 9.5% 5-year DFS events: HR 1.39 (1.12–1.72)	lower docetaxel dose, trend ER- and LN1 of benefit in year arm
SHORT-HER[7]	9 years	Previously to treatment	N−: 51% ER+: 67%	100%	100%	1,253	14.6% vs 12.5% 5-year DFS events: HR 1.15 (0.91–1.46)	Stage III and N2/N3 significantly benefit from year

[a]From first patient in to initial presentation of results

[b]The confidence intervals are, respectively, 95% (HORG, PHARE) and 90% (SOLD, SHORT-HER, PERSEPHONE)

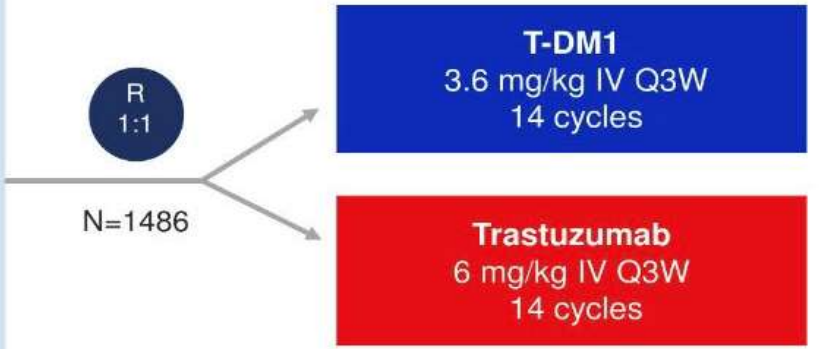
Pondé, N., Gelber, R.D. & Piccart, M. *npj Breast Cancer* **5,** 1 (2019).



KATHERINE STUDY: For Patients with noPCR after Neoadjuvant Therapy

KATHERINE Study Design

- cT1-4/N0-3/M0 at presentation (cT1a-b/N0 excluded)
- Centrally confirmed HER2-positive breast cancer
- Neoadjuvant therapy must have consisted of
  - Minimum of 6 cycles of chemotherapy
    - Minimum of 9 weeks of taxane
    - Anthracyclines and alkylating agents allowed
    - All chemotherapy prior to surgery
  - Minimum of 9 weeks of trastuzumab
    - Second HER2-targeted agent allowed
- Residual invasive tumor in breast or axillary nodes
- Randomization within 12 weeks of surgery



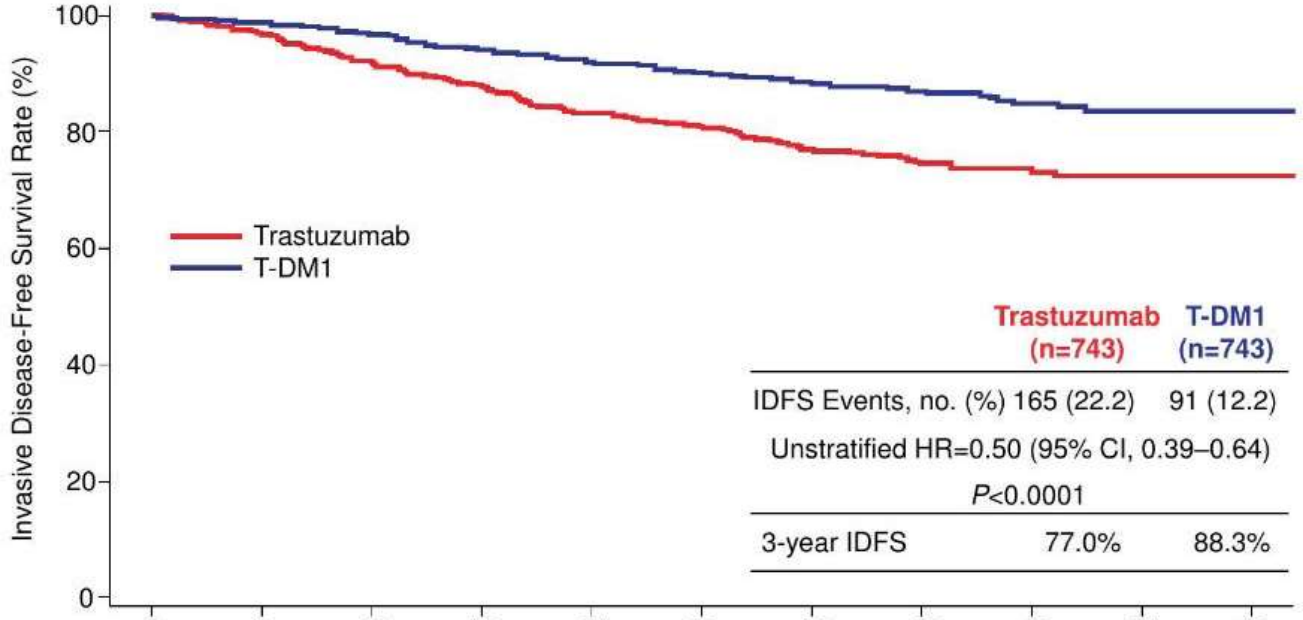
Radiation and endocrine therapy per protocol and local guidelines

Stratification factors:

- Clinical presentation: Inoperable (stage cT4 or cN2–3) vs operable (stages cT1-3N0-1)
- Hormone receptor: ER or PR positive vs ER negative and PR negative/unknown
- Preoperative therapy: Trastuzumab vs trastuzumab plus other HER2-targeted therapy
- Pathological nodal status after neoadjuvant therapy: Positive vs negative/not done

Katherine Study Results

Invasive Disease-Free Survival

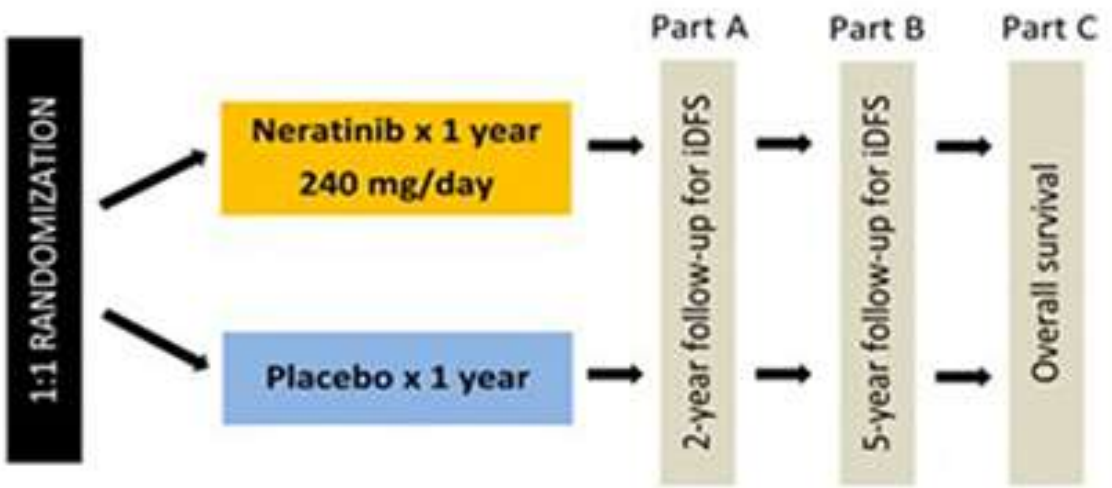


	Trastuzumab (n=743)	T-DM1 (n=743)
IDFS Events, no. (%)	165 (22.2)	91 (12.2)
Unstratified HR=0.50 (95% CI, 0.39–0.64)		
P<0.0001		
3-year IDFS	77.0%	88.3%

No. at Risk											
Trastuzumab	743	676	635	594	555	501	342	220	119	38	4
T-DM1	743	707	681	658	633	561	409	255	142	44	4

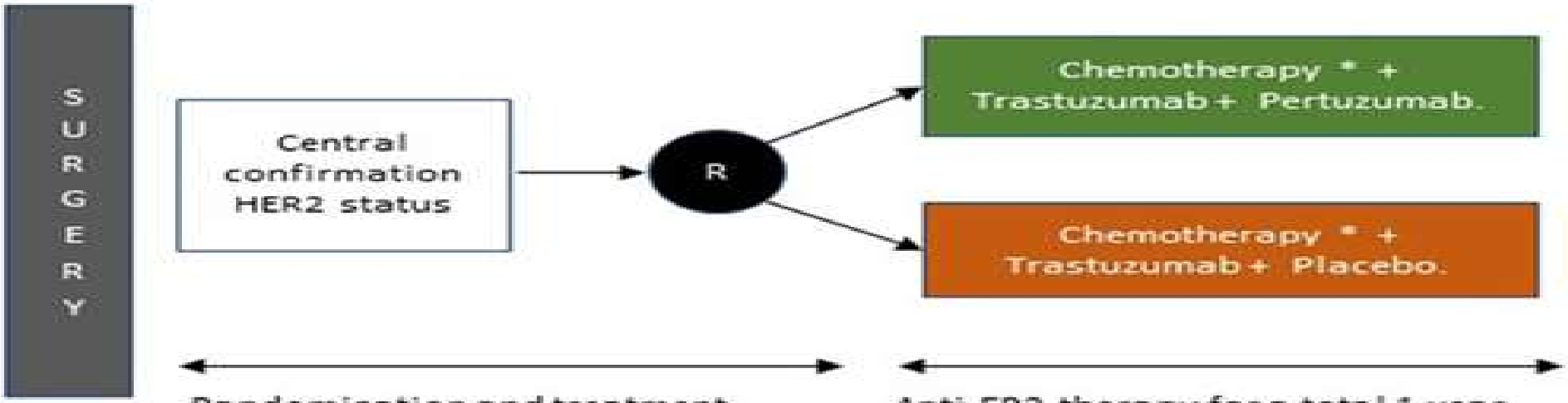
ExteNet Trial

- HER2+ Breast Cancer (local) by IHC 3+ or ISH amplification
- Prior adjuvant trastuzumab and chemotherapy completed 1 y prio study entry.
- Residual invasive disease after neoadujant therapy , +/- lymph node.
- N= 2840



Primary End point: invasive disease-free survival (iDFS)
Secondary endpoint: DFS-DCIS, time to distant recurrence, distant DFS, CNS metastases, overall survival, safety.

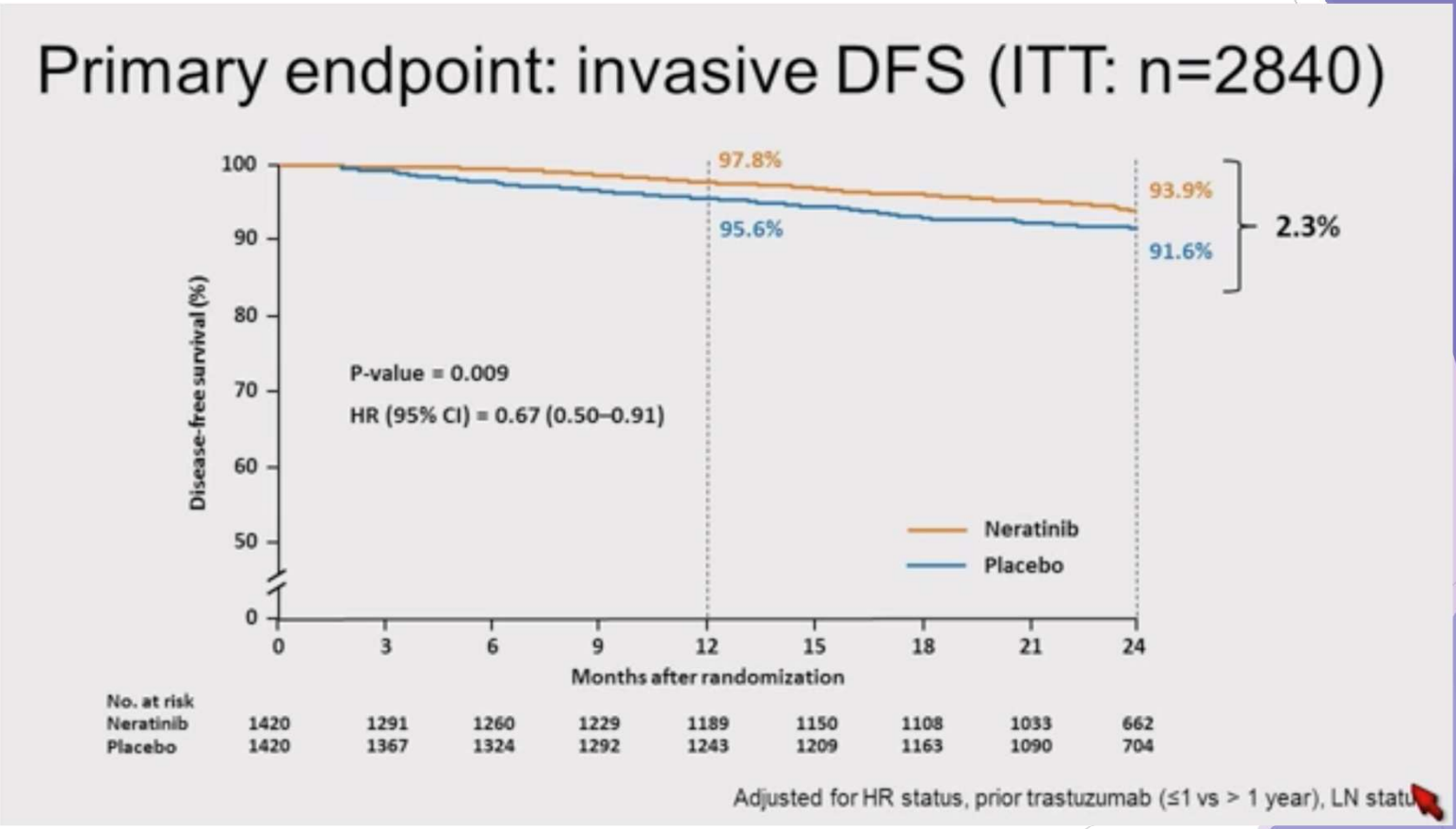
Aphinity Trial



* A number of standard anthracycline and non-anthracycline regimens were allowed.

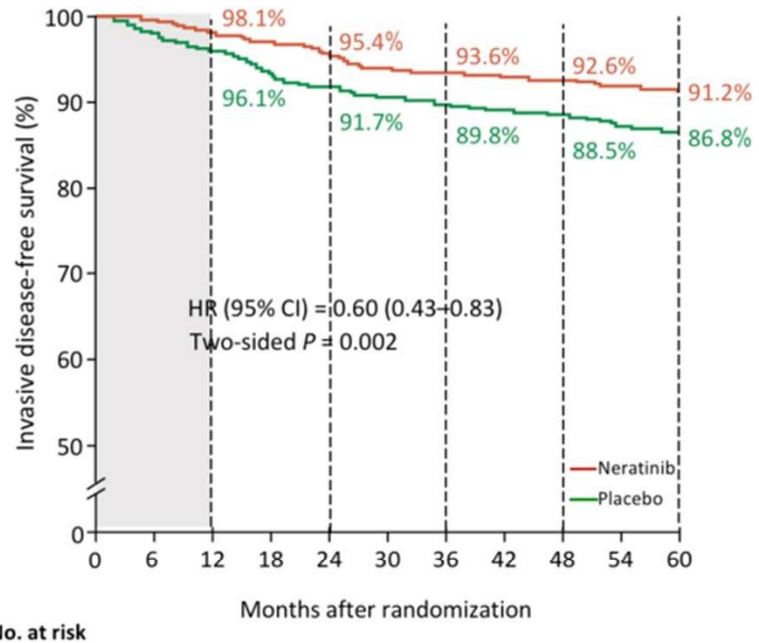
Primary endpoint: invasive-disease-free survival iDFS
Secondary endpoints: Overall survival, DFS (including DCIS), relapse-free interval, distant-relapse-free-interval, safety, health-related quality of life.

ExteNet Trial Results



ExteNET: iDFS by hormone receptor status

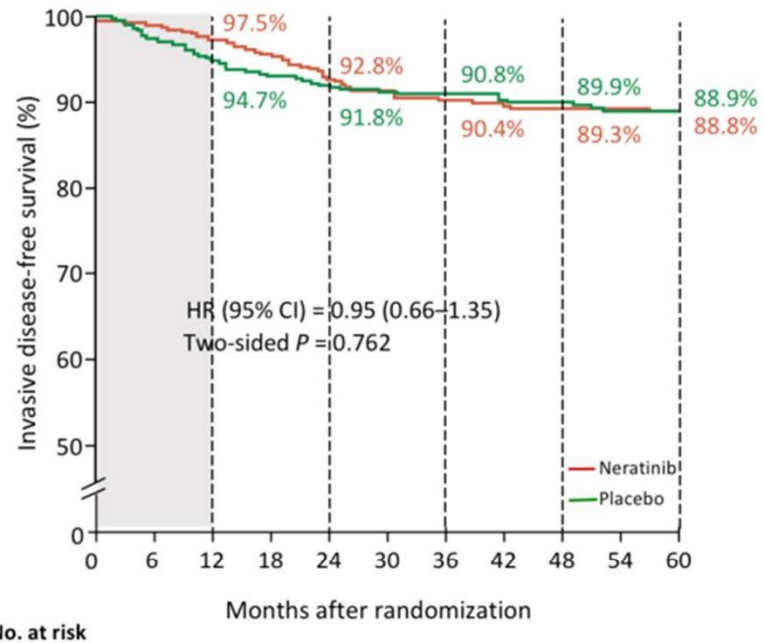
HR-positive subgroup



No. at risk

Neratinib	816	757	731	705	642	571	565	558	554	544	523
Placebo	815	779	750	719	647	581	567	556	551	542	525

HR-negative subgroup

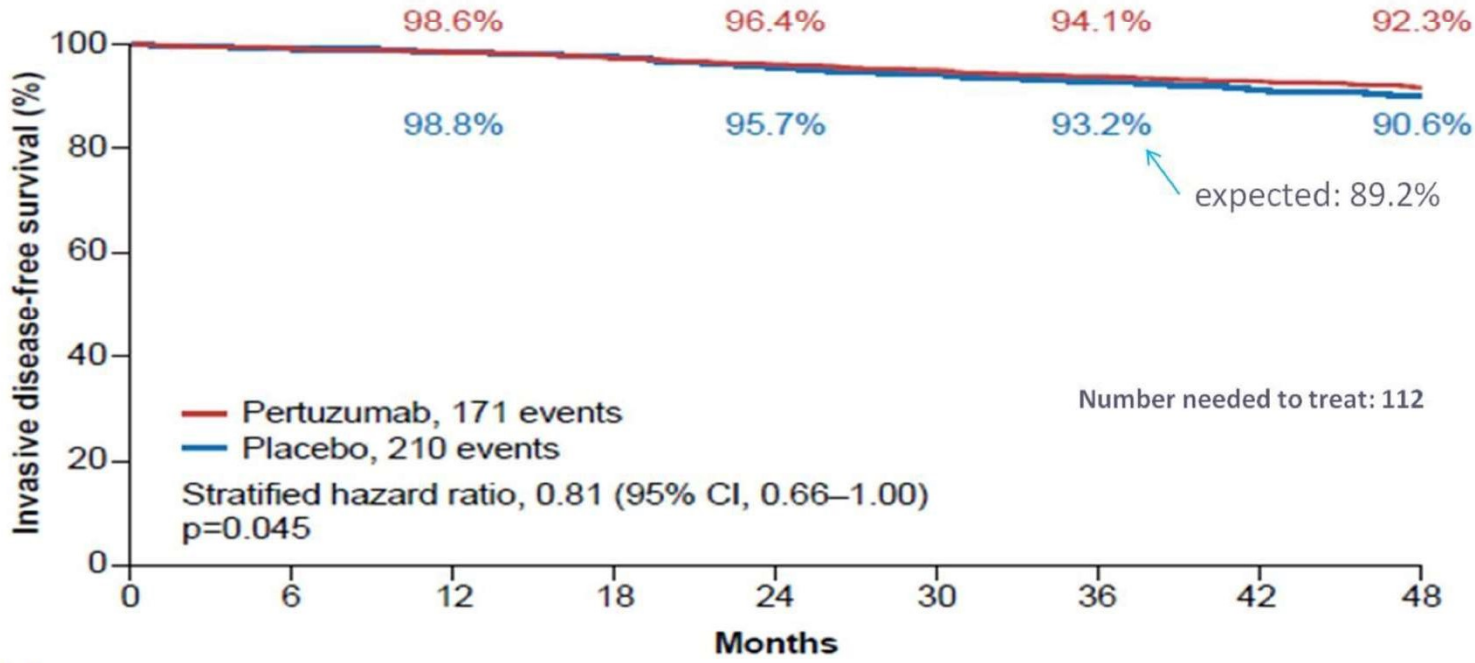


No. at risk

Neratinib	604	559	541	520	464	407	400	391	384	376	362
Placebo	605	575	548	529	495	448	444	435	427	416	402

Intention-to-treat population. Cut-off date: March 1, 2017

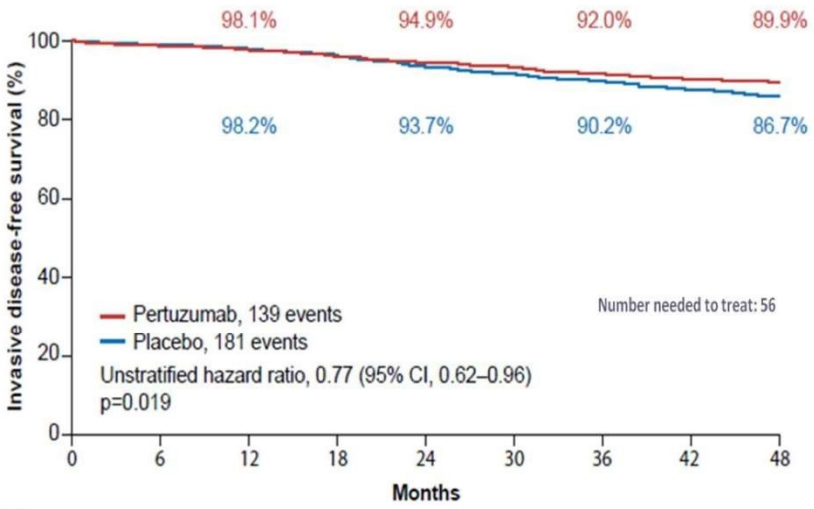
APHINITY: Intent-to-Treat Primary Endpoint Analysis Invasive Disease-free Survival



No. at Risk									
Pertuzumab	2400	2309	2275	2236	2199	2153	2101	1687	879
Placebo	2404	2335	2312	2274	2215	2168	2108	1674	866

BIG
Breast International Group

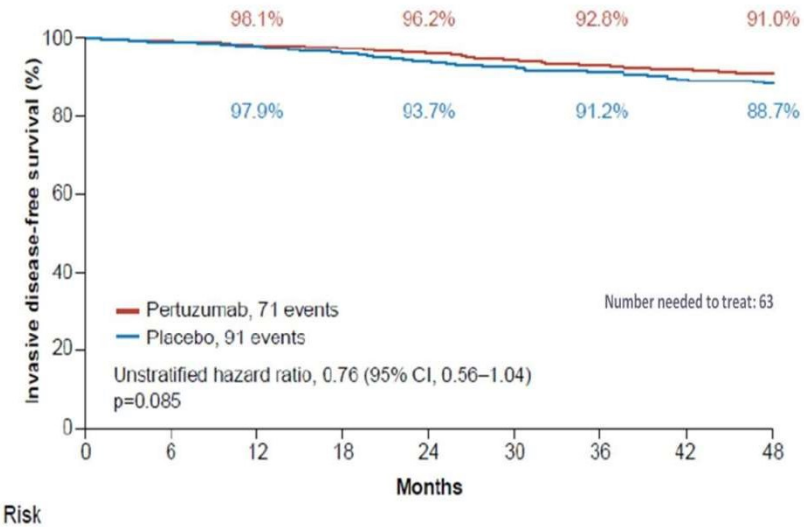
APHINITY: Node-positive Subgroup



No. at Risk									
Pertuzumab	1503	1444	1419	1387	1358	1327	1283	912	423
Placebo	1502	1453	1439	1408	1359	1319	1264	882	405

BIG
Breast International Group

APHINITY: Hormone Receptor-negative Subgroup



No. at Risk									
Pertuzumab	864	836	821	813	797	774	755	600	314
Placebo	858	827	811	793	771	758	730	569	302

BIG
Breast International Group

Adjuvant Dual Her2 Blockade

Patient characteristic	Neratinib	Pertuzumab
DFS	95.2 (HR+) vs 91.2% (HR–) DFS@ 2 years	92 vs 90% 3 years iDFS
Node positive	HR 0.70 in node + similar to ITT population[a]	1.8% Absolute DFS improvement
HR+	HR 0.51 for HR+ (improved outcome)	HR 0.81 (overall); 0.77 in high-risk node positive
HR–	No benefit	1.6% Absolute DFS improvement
Mechanism	PAN HER inhibition, MAPK, ERK, AKT downregulation	HER2 inhibition
Biomarker candidates	RB1CC1, HER3, FOXO3a, NR3C1, CCND1	CD8 TIL, anti-HER2 CD4+ T helper, high HER2 protein, HER2 and HER3 mRNA levels, PD1 for addition of IO
Ideal patient	High risk, node positive, HR+	High risk, node positive, HR–
Absolute DFS improvement	2.3% Absolute DFS improvement @ 2 years	0.9% Absolute iDFS improvement @ 3 years[a]
Cost (USD)	$120,000/year	$70,000/year

Ideal patient candidates for adjuvant neratinib vs pertuzumab in clinical setting outside of a clinical trial given no comparative studies between the drugs. These are considerations in HER2-positive high-risk patients.

HR, hormone receptor; DFS, disease-free survival; ITT, intention to treat; TIL, tumor-infiltrating lymphocytes; iDFS, invasive disease-free survival.

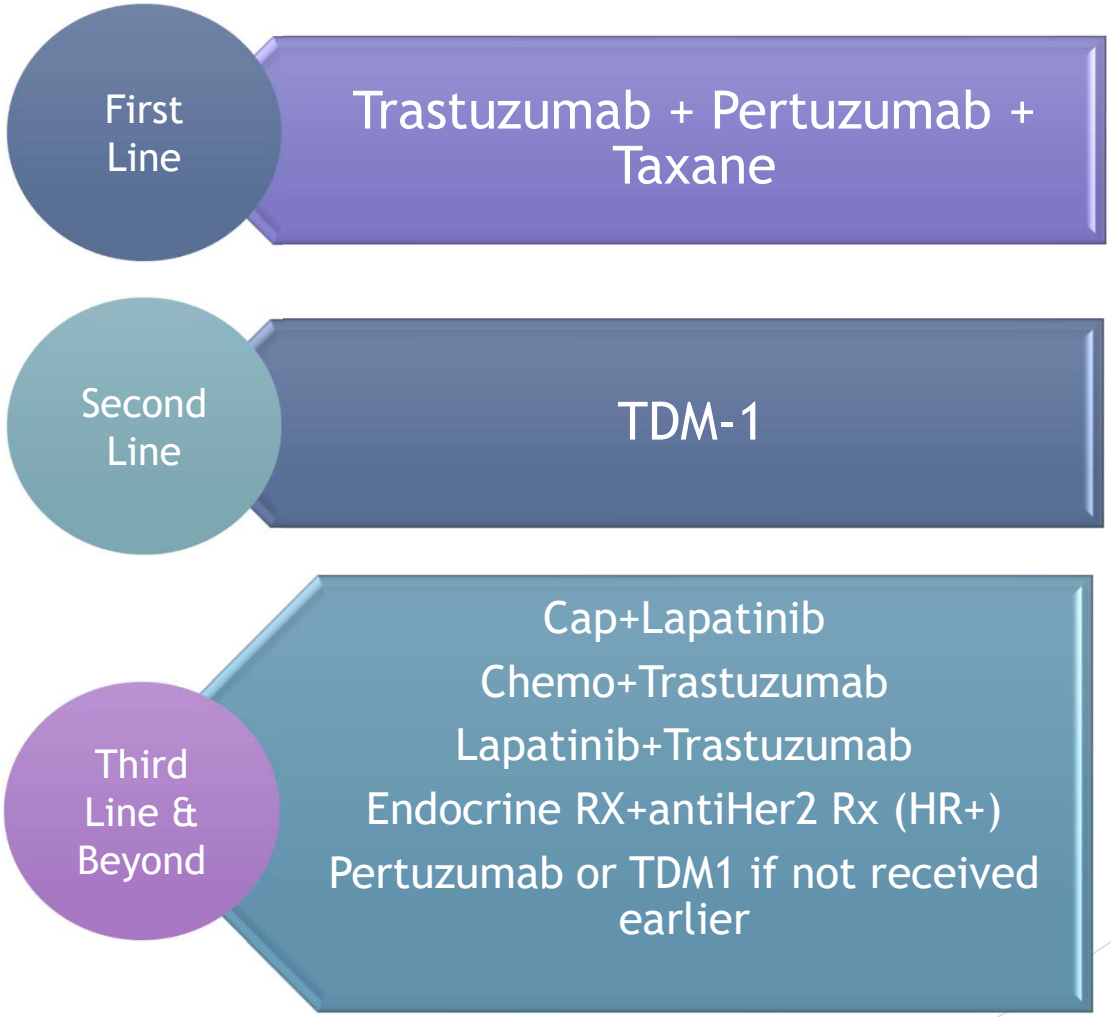
[a]2-Year. DFS based on LN status LN neg: 99.4 vs 99.2%, HR 0.82 (0.32–2.03); LN 1–3: 97.8 vs 96.5%, HR 0.66 (0.41–1.02); LN ≥ 4: DFS 97.8 vs 96.5%, HR 0.65 (0.41–1.01).

Bulbul A, et al. Front. Oncol., 30 May 2018

Metastatic Management

- Her2+ BC

Current Approach to MBC HER-2+ Disease



New and Emerging Therapies

PHENIX Study Design

Pyrotinib combined with capecitabine in women with HER2+ metastatic breast caNcer prevIously treated with trastuzumab and taXanes: a randomized phase 3 study

- **Double-blinded, multicenter, randomized phase 3 trial (NCT02973737)**
- **Primary objective:** the efficacy of pyrotinib plus capecitabine after failure of trastuzumab

Key eligibility criteria:

- Pathologically confirmed HER2-positive* metastatic breast cancer
- Disease progression during or after treatment with trastuzumab#, and were not amenable or available for trastuzumab or lapatinib treatment
- Prior taxane -containing regimen
- No. of lines of prior chemotherapy in the metastatic setting ≤ 2
- At least one measurable lesion
- ECOG performance status of 0 or 1

Randomization 2:1

Pyrotinib (400 mg, orally, qd) + Capecitabine (1000 mg/m^2, orally, bid on days 1–14 of each 21-day cycle)

Stratification:

- Metastatic sites at screening (visceral *versus* non-visceral)
- Hormone receptor status (ER- and/or PR-positive *versus* ER- and PR-negative)

Placebo (400 mg, orally, qd) + Capecitabine (1000 mg/m^2, orally, bid on days 1–14 of each 21-day cycle)

At progression

Investigator's choice of pyrotinib (400 mg, orally, qd)

Treatment until disease progression, unacceptable toxicity, patient withdrawal, or investigator decision.

- **Primary endpoint:** IRC-assessed PFS
- **Secondary endpoints:** ORR, DoR, DCR, CBR, OS, and safety profile

*__HER2-positive:__ immunohistochemistry 3+ and/or fluorescence in situ hybridization positive; #__Progression with trastuzumab:__ ≥2 cycles in the metastatic setting, or ≥3 months in adjuvant setting)

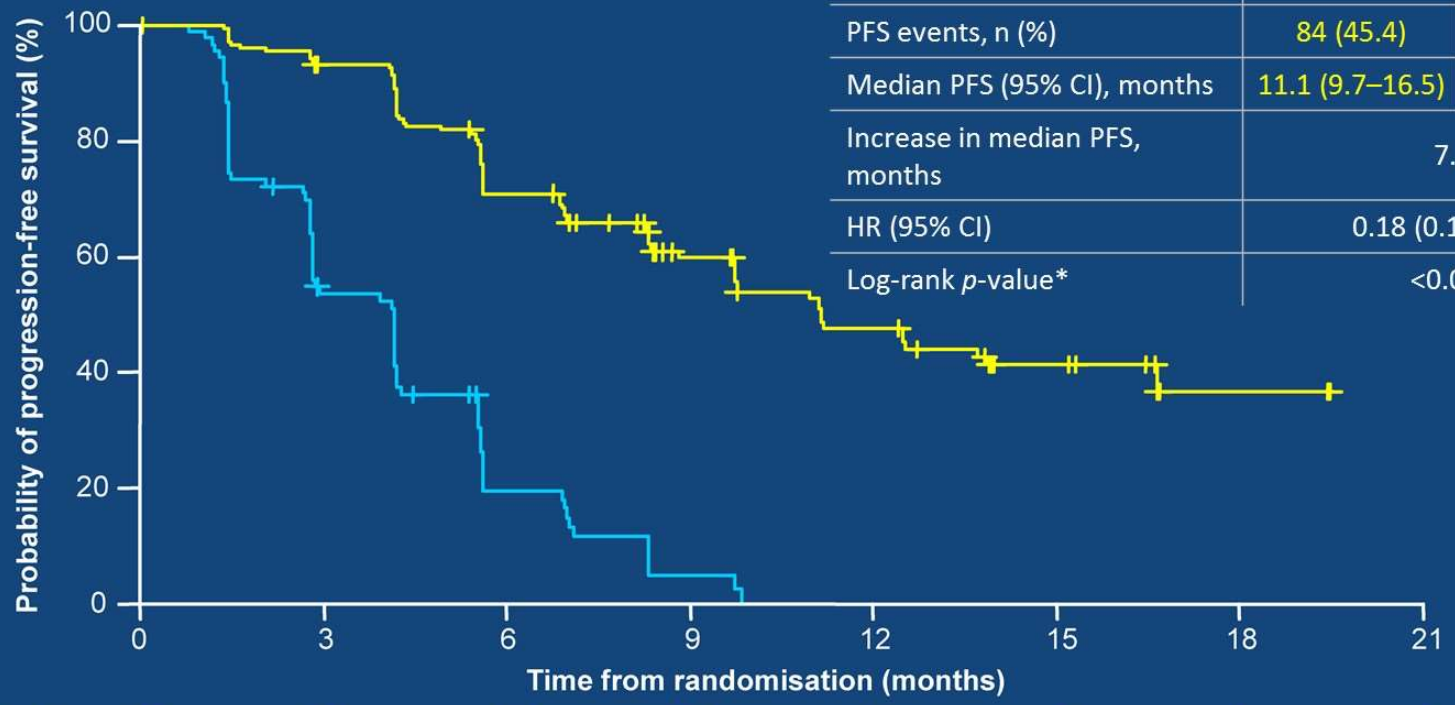
Abbreviations: IRC, independent review committee; DoR, duration of response; DCR, disease control rate; CBR, clinical benefit rate; OS, overall survival.

IRC-assessed PFS

FAS population, double-blind period

ORR, n (%; 95% CI)	68.6% (61.4–75.3)	16.0% (9.2–25.0)	<0.001

	Pyrotinib plus capecitabine	Placebo plus capecitabine
PFS events, n (%)	84 (45.4)	78 (83.0)
Median PFS (95% CI), months	11.1 (9.7–16.5)	4.1 (2.8–4.2)
Increase in median PFS, months	7.0	
HR (95% CI)	0.18 (0.13–0.26)	
Log-rank *p*-value*	<0.001	



No. at risk:

Pyrotinib plus capecitabine	185	159	113	71	41	13	3	0
Placebo plus capecitabine	94	43	14	2	0	0	0	0

*Stratified by metastatic sites and hormone receptor status

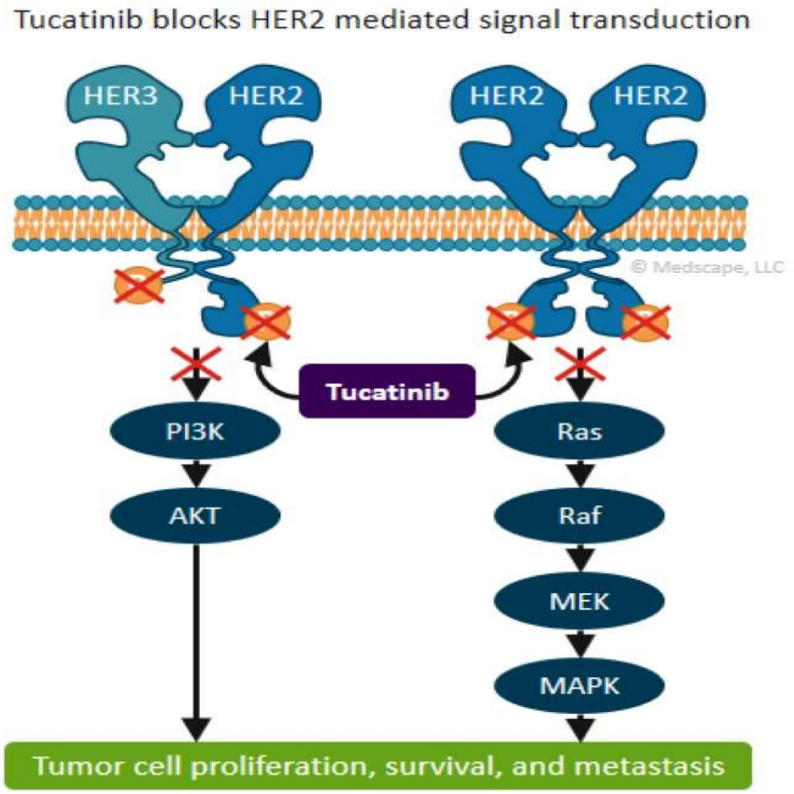
PHENIX TRIAL

- **Strengths**
  - Double-Blinded Trial
  - PFS benefit 11.1m; HR 0.18 *(Emilia TDM1 PFS 9.6m)*
  - ORR 68.6% *(Emilia TDM1 ORR 43%)*
  - Sequential single agent activity (ORR 38%)
  - Suggests activity in CNS

- **Potential Concerns/Questions**
  - Comparator is not standard second line regimen (capecitabine).
  - Will be interesting to learn about OS in this patient population.
  - G3 diarrhea in 30% of patients.

Tucatinib
Novel HER2-Specific TKI

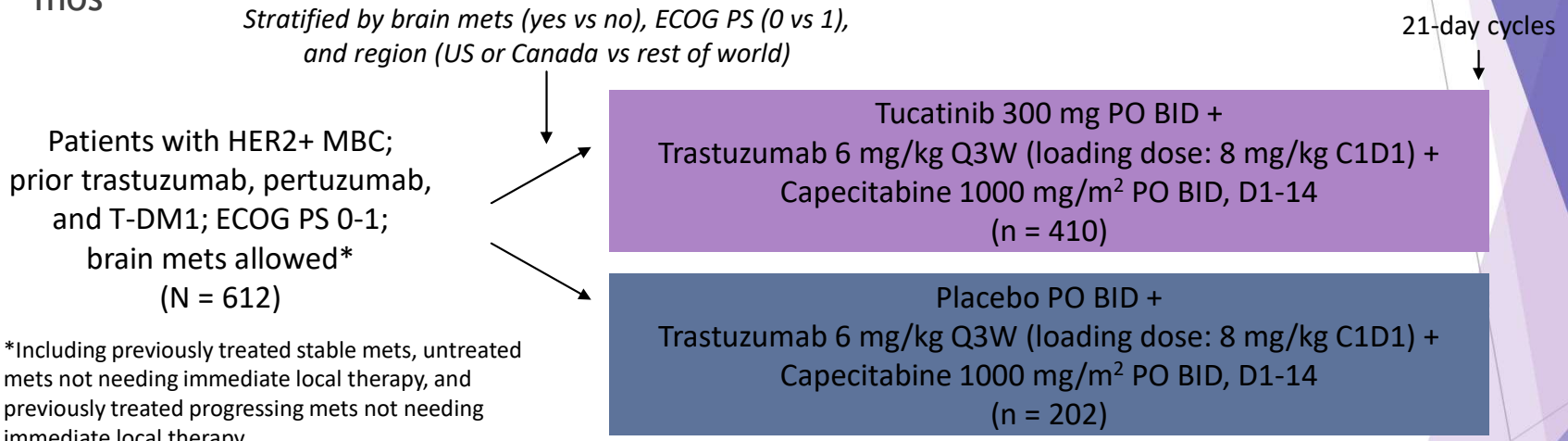
- Tucatinib is orally bioavailable, highly potent
- Highly selective for HER2 > EGFR
- Decreased potential for EGFR-related toxicities (eg, diarrhea, skin rash)
- Improved tolerability may lead to better compliance, higher dose intensity, and duration of treatment
- Superior activity compared with lapatinib or neratinib in preclinical models of brain metastases[a]
- Two phase 1 combination trials were conducted in patients with HER2-positive MBC
  - Tucatinib + T-DM1: mPFS 8.2 months; RR 47%[b]
  - Tucatinib + capecitabine + trastuzumab: mPFS 7.8 months, RR 61%[c]



a. Dinkel V, et al. AACR 2012. Abstract 852; b. Borges VF, et al. *JAMA Oncol*. 2018;4:1214-1220;
c. Hamilton E, et al. SABCS 2017. Abstract P5-20-01.

HER2CLIMB: Phase III Study Design

- Randomized, double-blind, placebo-controlled, active comparator phase III trial at 155 sites in 15 countries (February 2016 to May 2019); data cutoff: September 4, 2019; median f/u: 14.0 mos



*Including previously treated stable mets, untreated mets not needing immediate local therapy, and previously treated progressing mets not needing immediate local therapy.

Primary endpoint: PFS (RECIST v 1.1 by BICR) among first 480 randomized patients

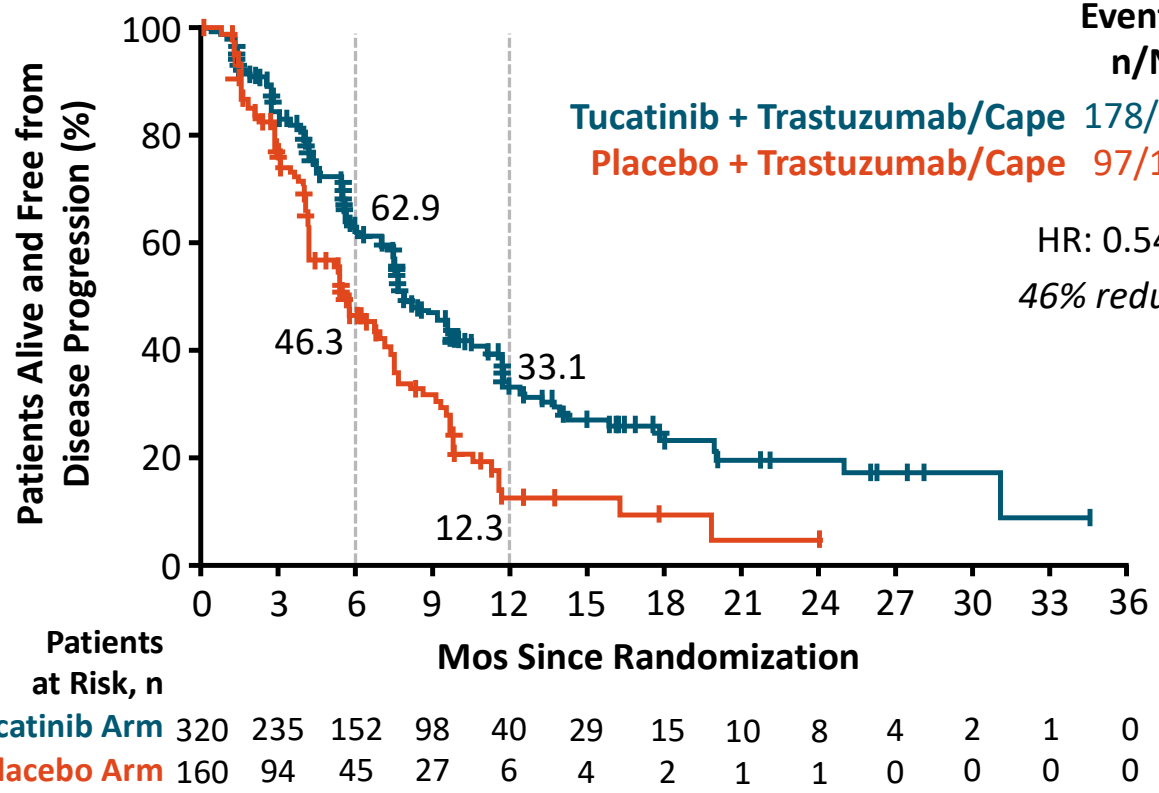
47%, which included 28% who had treated brain metastases and 19% who had progressive or untreated brain metastases

Secondary endpoints (total population): OS, PFS in patients w/ brain mets, ORR in patients w/ measurable disease, safety in patients who received ≥ 1 dose of study tx

Murthy. SABCS 2019. Abstr GS1-01. Murthy. NEJM. 2019;[E-pub].

Slide credit: clinicaloptions.com

HER2CLIMB: PFS (Primary Endpoint Population)



	Events, n/N	Median PFS, Mos (95% CI)	1-Yr PFS, % (95% CI)
Tucatinib + Trastuzumab/Cape	178/320	7.8 (7.5-9.6)	33 (27-40)
Placebo + Trastuzumab/Cape	97/160	5.6 (4.2-7.1)	12 (8-21)

HR: 0.54 (95% CI: 0.42-0.71; $P < .00001$)

46% reduction in risk of disease progression

Only 5.7% of the patients discontinued tucatinib because of adverse events.

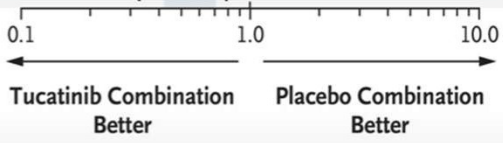
Murthy. SABCS 2019. Abstr GS1-01. Murthy. NEJM. 2019;[E-pub].

Slide credit: clinicaloptions.com

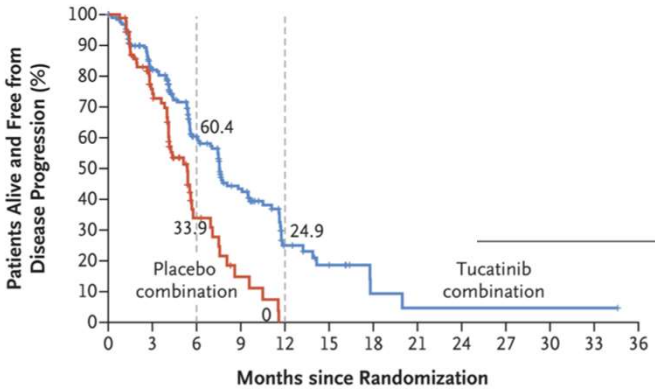
HER2CLIMB

B Subgroup Analysis of Progression-free Survival

Subgroup	No. of Events/ Total No.	Hazard Ratio for Disease Progression or Death (95% CI)
Total	275/480	0.54 (0.42–0.71)
Age		
≥65 yr	51/96	0.59 (0.32–1.11)
<65 yr	224/384	0.54 (0.41–0.72)
Race		
White	206/350	0.57 (0.42–0.77)
Nonwhite	69/130	0.46 (0.26–0.82)
Hormone-receptor status		
Positive for ER, PR, or both	172/289	0.58 (0.42–0.80)
Negative for ER and PR	103/191	0.54 (0.34–0.86)
Baseline brain metastasis		
Yes	138/219	0.46 (0.31–0.67)
No	136/260	0.62 (0.44–0.89)
ECOG performance-status score		
0	134/235	0.56 (0.39–0.80)
1	141/245	0.55 (0.38–0.79)
Geographic region		
United States and Canada	179/307	0.57 (0.41–0.78)
Rest of the world	96/173	0.51 (0.33–0.79)



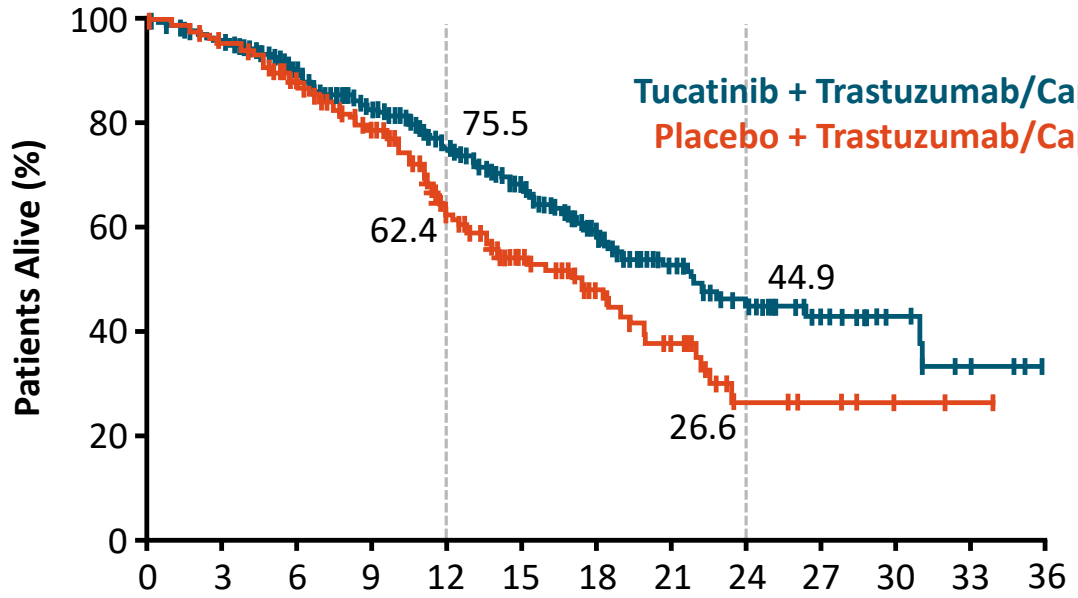
A Kaplan–Meier Estimates of Progression-free Survival among Patients with Brain Metastases



No. at Risk

Tucatinib combination	198	144	78	45	14	8	2	1	1	1	1	1	0
Placebo combination	93	49	12	4	0	0	0	0	0	0	0	0	0

HER2CLIMB: OS (Total Population)



	Events, n/N	Median OS, Mos (95% CI)	2-Yr OS, % (95% CI)
Tucatinib + Trastuzumab/Cape	130/410	21.9 (18.3-31.0)	45 (37-53)
Placebo + Trastuzumab/Cape	85/202	17.4 (13.6-19.9)	27 (16-39)

HR: 0.66 (95% CI: 0.50-0.88); *P* = .0048)

34% reduction in risk of death

Murthy. SABCS 2019. Abstr GS1-01. Murthy. NEJM. 2019;[E-pub].

Slide credit: clinicaloptions.com

Neratinib in HER2+ MBC: Study Design

- Pooled analysis of 3 multicenter phase II or III trials

NALA
Metastatic HER2+ BC, ≥ 2 lines of HER2-directed therapy for metastatic disease, asymptomatic and stable brain metastases permitted
(N = 621)

→ Neratinib 240 mg/day + Capecitabine 1500 mg/m^2 14/21 days*
(n = 307)

→ Lapatinib 1250 mg/day + Capecitabine 2000 mg/m^2 14/21 days
(n = 314)

NEfERT-T
Metastatic HER2+ BC, previously untreated recurrent and/or metastatic disease, asymptomatic and stable brain metastases permitted
(N = 479)

→ Neratinib 240 mg/day + Paclitaxel 80 mg/m^2 14/21 D1,8,15, Q28D
(n = 242)

→ Trastuzumab 4 mg/kg then 2 mg/kg QW +
Paclitaxel 80 mg/m^2 14/21 D1,8,15, Q28D (n = 237)

TBCRC 022
Metastatic HER2+ BC and measurable, progressive CNS metastases
(N = 37)

→ Neratinib 240 mg/day + Capecitabine 1500 mg/m^2 14/21 days*
(n = 37)

Awada. SABCS 2019. Abstr P2-20-01.

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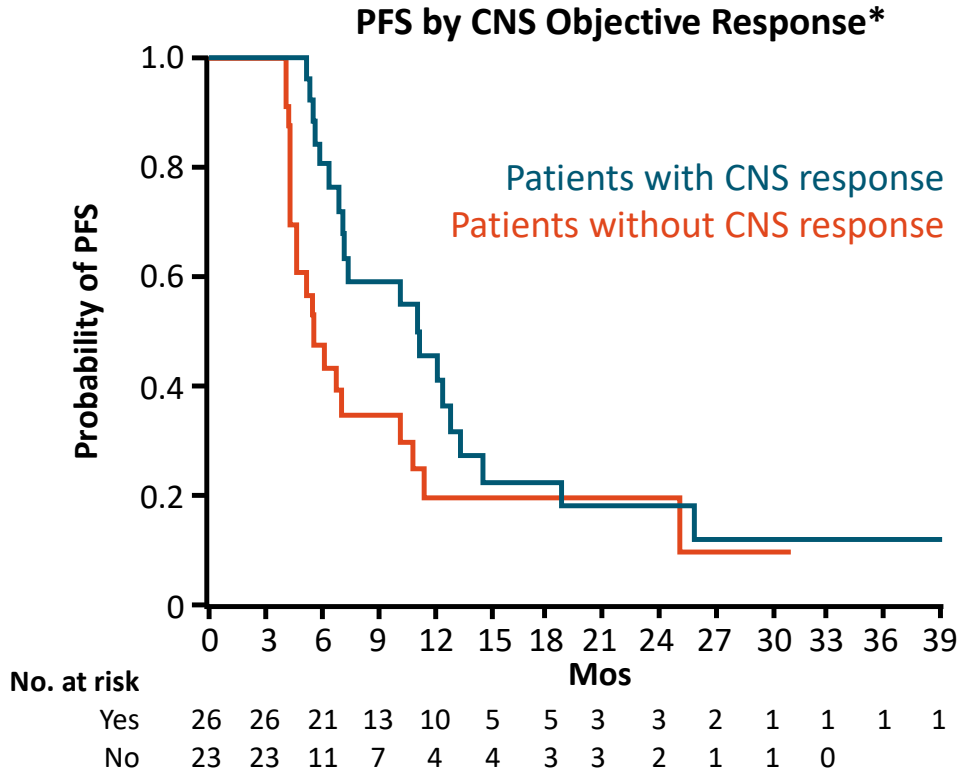
Neratinib in HER2+ MBC: PFS by CNS Objective Response (Combined Trials)



	Events, n (%)	Median PFS, Mos	HR (95% CI)	Log-Rank *P* Value
Patients with CNS response	20 (76.9)	11.3	0.58 (0.31-1.10)	.087
Patients without CNS response	19 (82.6)	5.6		

*PFS for CNS and systemic disease.

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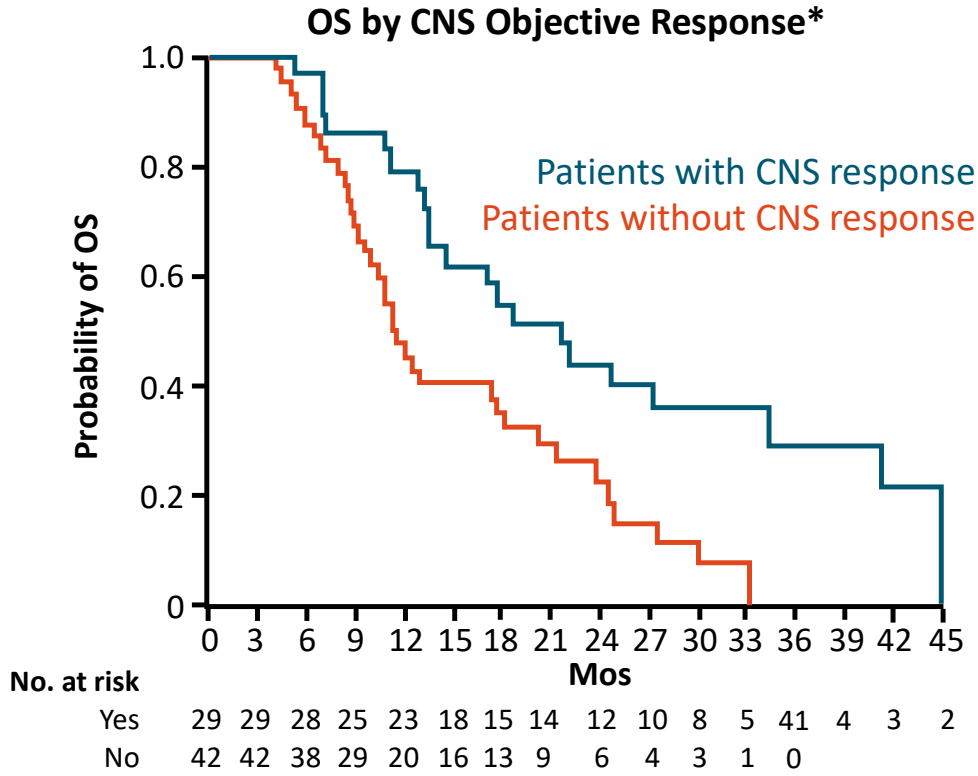
Neratinib in HER2+ MBC: OS by CNS Objective Response (Combined Trials)



	Events, n (%)	Median OS, Mos	HR (95% CI)	Log-Rank *P* Value
Patients with CNS response	21 (72.4)	27.1	0.43 (0.24-0.76)	.003
Patients without CNS response	36 (85.7)	11.5		

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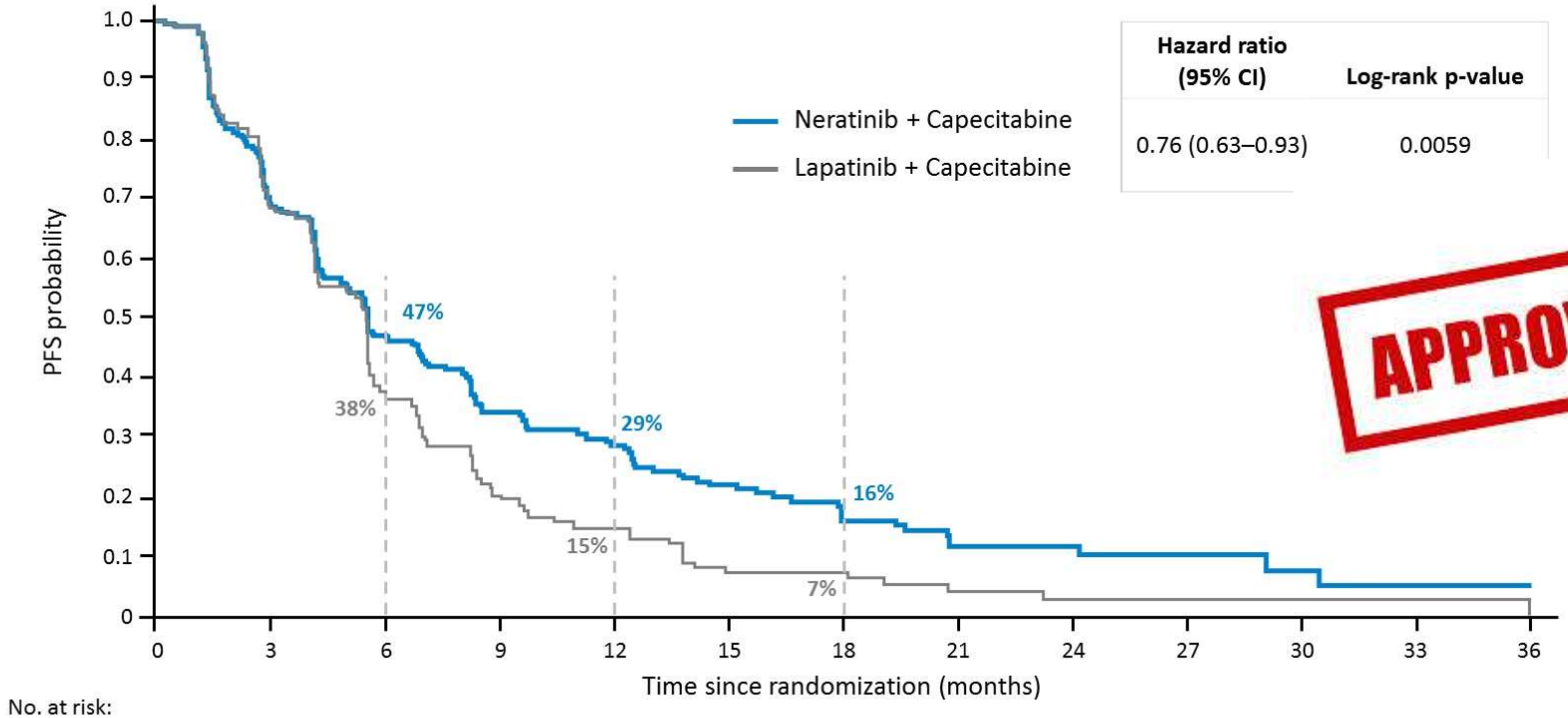
NALA

PFS (co-primary endpoint)



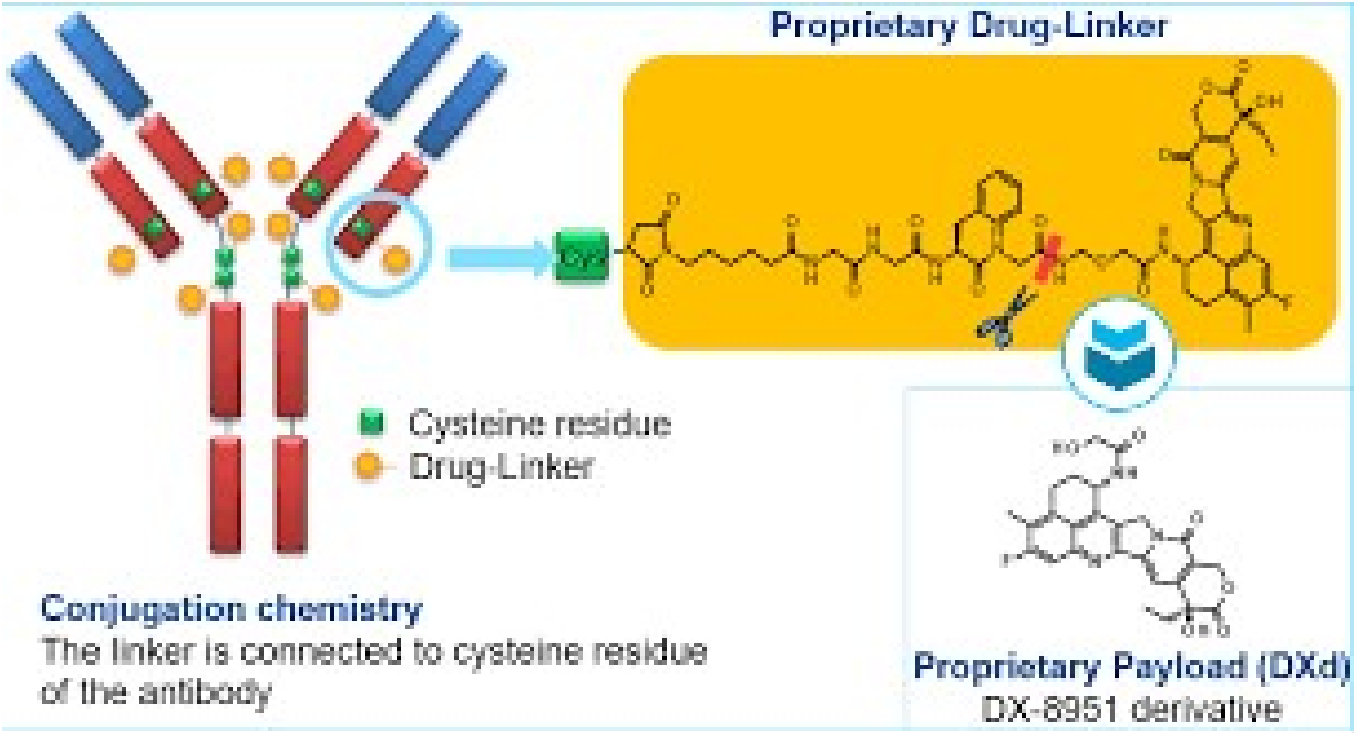
Hazard ratio (95% CI)	Log-rank p-value
0.76 (0.63–0.93)	0.0059

APPROVED

No. at risk:

N+C	307	183	113	69	54	35	20	13	9	7	3	2	2
L+C	314	183	82	39	24	9	8	3	2	2	2	2	1

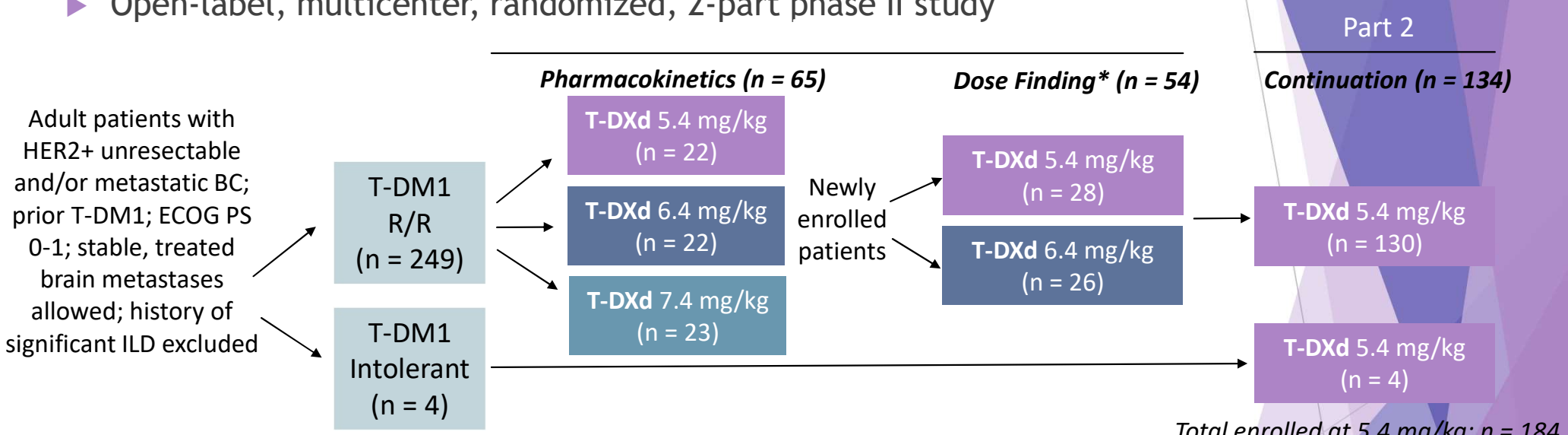
Trastuzumab Deruxtecan



ADC comprising a humanized HER2-targeted mAb with a tumor-selective cleavable tetrapeptide linker and a topoisomerase I inhibitor “payload”
It has a higher drug-to-antibody ratio than trastuzumab emtansine (8 to 1 vs. 3 to 1)

DESTINY-Breast01: Phase II Study Design

- Open-label, multicenter, randomized, 2-part phase II study



Primary endpoint: ORR by ICR (RECIST v1.1)

Secondary endpoints: investigator-assessed ORR, DCR, DoR, CBR, PFS, OS, PK, safety

Data cutoff: August 1, 2019

79 (42%) continuing treatment

105 (57.1%) d/c (mostly for PD, 28.8%)

Krop. SABCS 2019. Abstr GS1-03. Modi. NEJM. 2019:[Epub].

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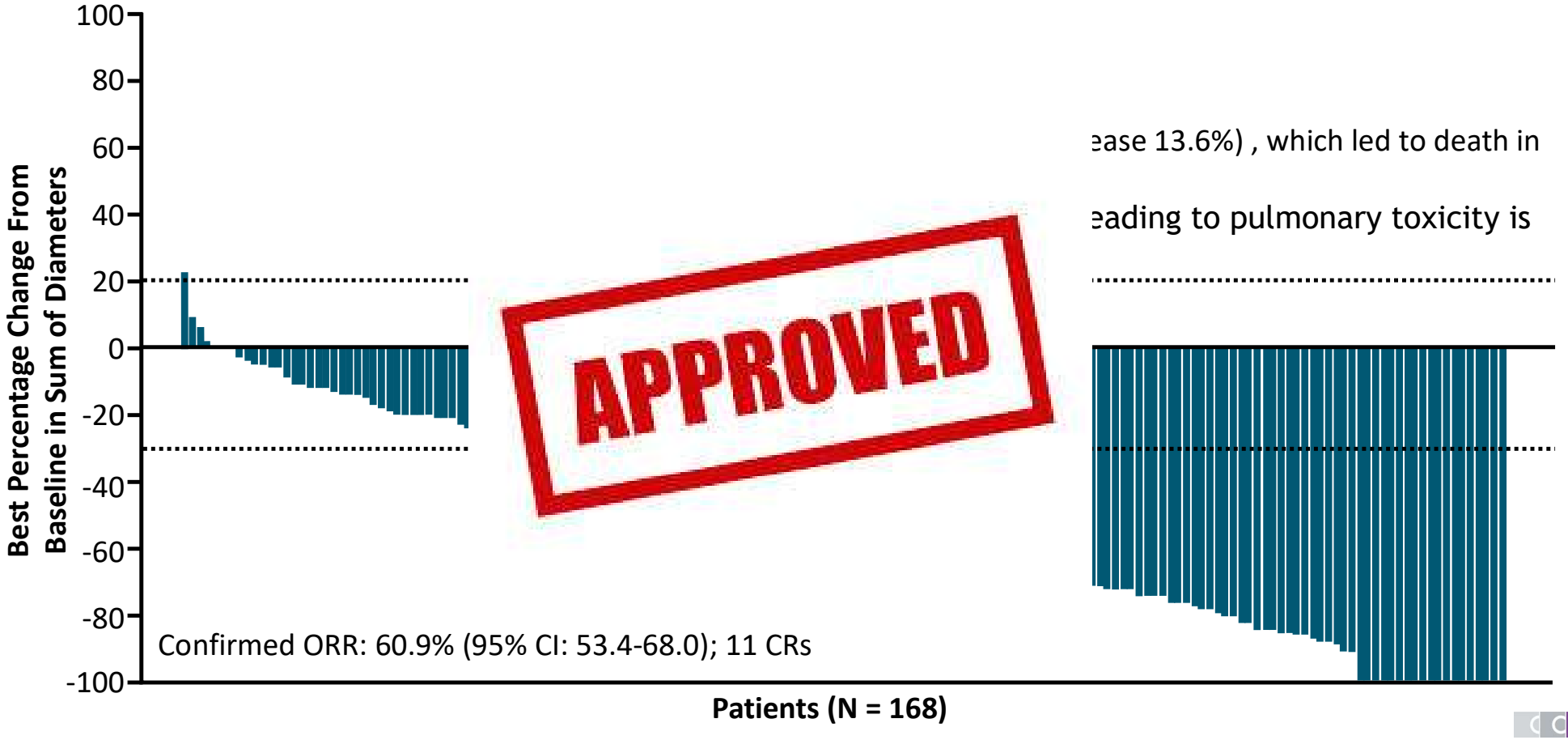
DESTINY-Breast01: Best Change in Tumor Size



ease 13.6%) , which led to death in

eading to pulmonary toxicity is

Krop. SABCS 2019. Abstr GS1-03. Modi. NEJM. 2019:[Epub].

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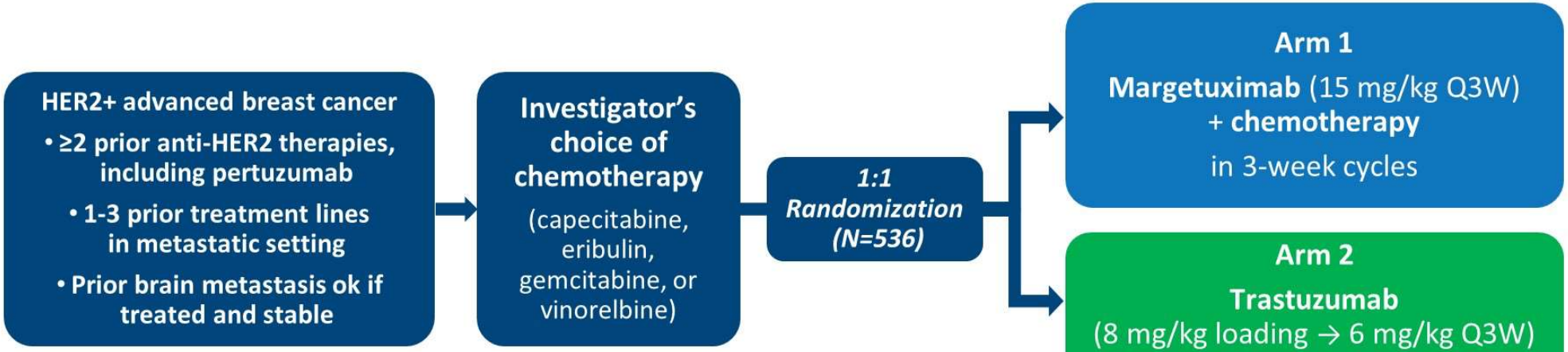
Study CP-MGAH22-04 (SOPHIA) Design[1,2]



Sequential Primary Endpoints	• **PFS** (by CBA; n=257; HR=0.67; α=0.05; power=90%) • **OS** (n=385; HR=0.75; α=0.05; power=80%)
Secondary Endpoints	• PFS (Investigator assessed) • Objective response rate (by CBA)
Tertiary/Exploratory Endpoints	• Clinical benefit rate (CBR), duration of response (DoR) • Safety profile, antidrug antibody • Effect of CD16A, CD32A, and CD32B on margetuximab efficacy

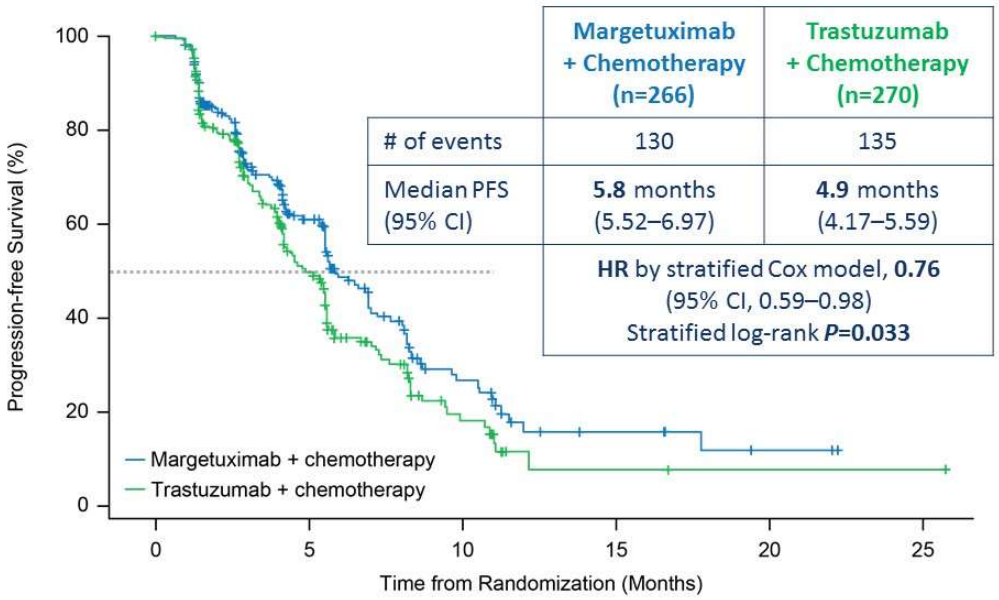
Stratification:
- Chemotherapy choice
- Prior therapies (≤2 *vs* >2)
- Metastatic sites (≤2 *vs* >2)

HR=hazard ratio; CBA=central blinded analysis.

1. Rugo HS, et al. *J Clin Oncol*. 2016;34(suppl 15):TPS630. 2. Clinicaltrials.gov. NCT02492711. www.clinicaltrials.gov/ct2/show/NCT02492711. Accessed April 8, 2019.

PFS Analysis in ITT Population

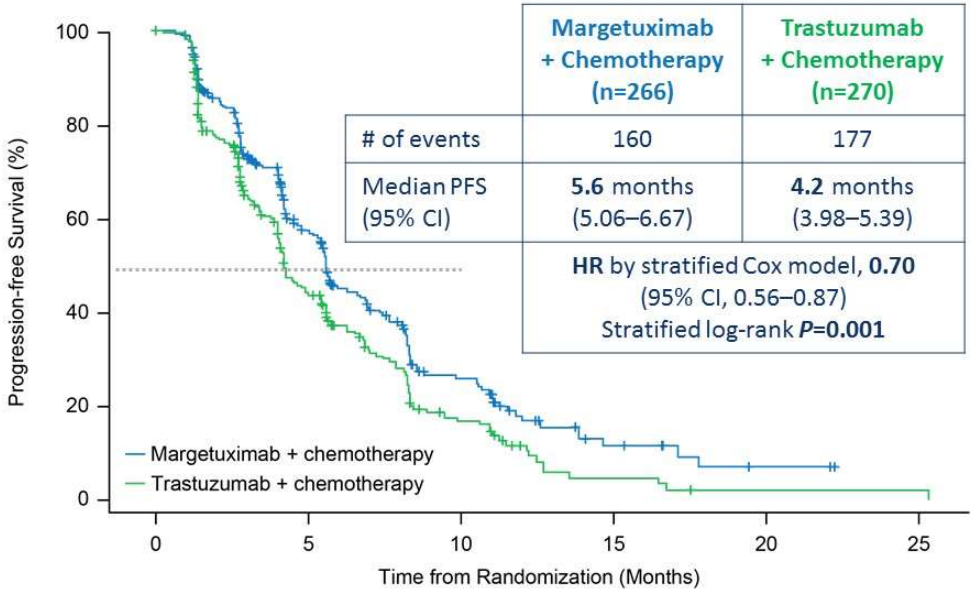
24% Risk Reduction of Disease Progression
Central Blinded Analysis (Primary Endpoint)



	Margetuximab + Chemotherapy (n=266)	Trastuzumab + Chemotherapy (n=270)
# of events	130	135
Median PFS (95% CI)	**5.8** months (5.52–6.97)	**4.9** months (4.17–5.59)
HR by stratified Cox model, **0.76** (95% CI, 0.59–0.98) Stratified log-rank ***P*=0.033**		

Margetuximab	266	174	94	45	21	8	6	4	2	0	
Trastuzumab	270	158	74	33	13	2	2	1	1	1	1

30% Risk Reduction of Disease Progression
Investigator Assessed (Secondary Endpoint)



	Margetuximab + Chemotherapy (n=266)	Trastuzumab + Chemotherapy (n=270)
# of events	160	177
Median PFS (95% CI)	**5.6** months (5.06–6.67)	**4.2** months (3.98–5.39)
HR by stratified Cox model, **0.70** (95% CI, 0.56–0.87) Stratified log-rank ***P*=0.001**		

Margetuximab	266	206	155	112	72	61	33	32	16	13	8	7	3	2	2	0		
Trastuzumab	270	184	130	87	59	45	25	21	10	5	4	3	1	1	1	1	1	0

- PFS analysis was triggered by last randomization on October 10, 2018, after 265 PFS events occurred

ITT population: N=536. CI=confidence interval.

SOPHIA Second Interim Survival Analysis: Response (ITT)

Outcome	Margetuximab + CT (n = 266)	Trastuzumab + CT (n = 270)	Nominal P Value
ORR*, n (%; 95% CI)	67 (25.2; 20.1-30.9)	37 (13.7; 9.8-18.4)	.0006
CBR†, n (%; 95% CI)	128 (48.1; 42.0-54.3)	96 (35.6; 29.9-41.6)	.0025
Best overall response, n (%)			
▪ CR	5 (1.9)	4 (1.5)	--
▪ PR	62 (23.3)	33 (12.2)	--
▪ SD	143 (53.8)	158 (58.5)	--
▪ PD	40 (15.0)	57 (21.1)	--
▪ Not evaluable/available	16 (6.0)	18 (6.7)	--
Median DoR, mos (95% CI)	6.9 (5.45-7.49)	7.0 (5.55-8.15)	.7400

*CR + PR. †CR + PR + SD > 6 mos.
Data cutoff: September 2019.

Rugo. SABCS 2019. Abstr GS1-02.

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Take home messages

- Anti Her2 therapy has led to a remarkable improvement of outcomes for patients with Her2 + BC
- Patient selection is key to determine right patients for a “more or less” approach
- Dual targeted therapy may provide greater benefit for some patients
- Emerging therapies in the metastatic setting show promise, especially for patients with brain metastasis