Breast Cancer Review

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January 21st, 2023

Disclosures

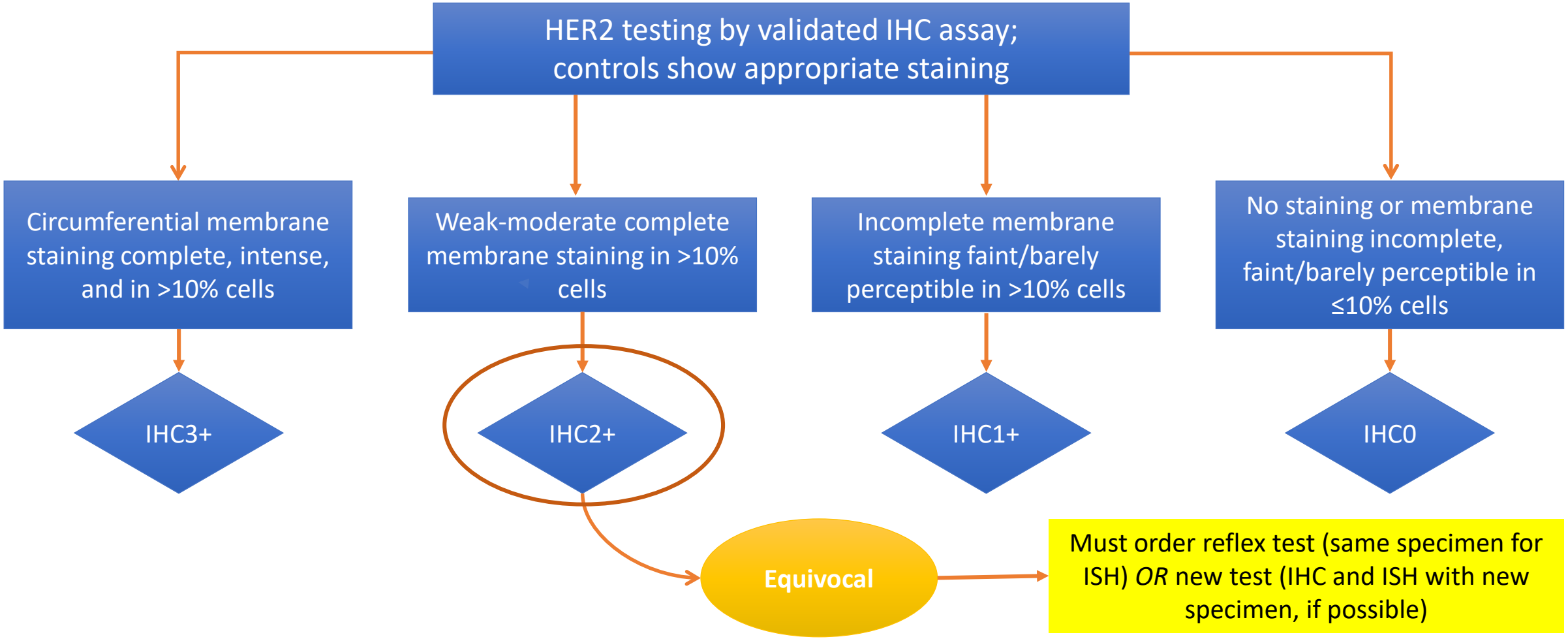
- Consulting / Advisory Board:
  - Gilead
  - Daischi Sankyo
  - AstraZeneca

Outline

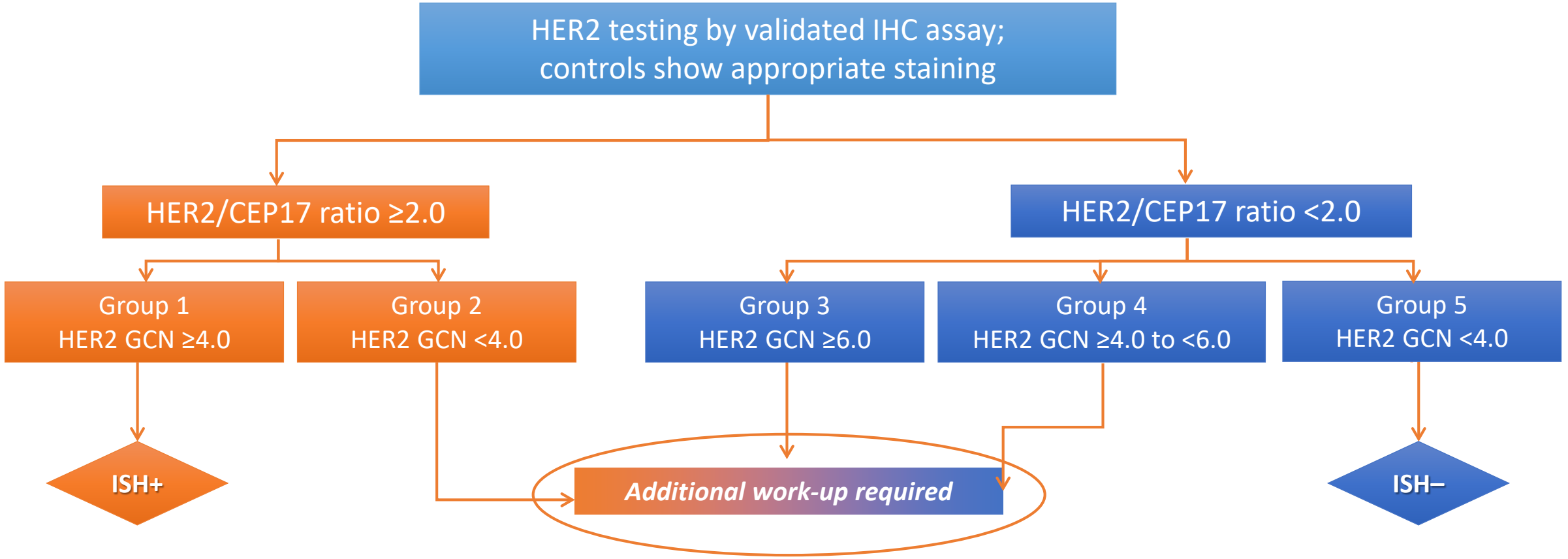
- HER2 Positive Breast Cancer
  - DESTINY Breast 02
  - Destiny Breast 03
  - HER CNS Metastases
  - Aphinity update
  - Neoadjuvant T-DxD
- TNBC
  - ASCENT Trial
  - Tropion-01 Update
  - KEYNOTE-522 irAEs
  - Carboplatin

HER2 POSITIVE BREAST CANCER

ASCO/CAP Algorithm for IHC Testing

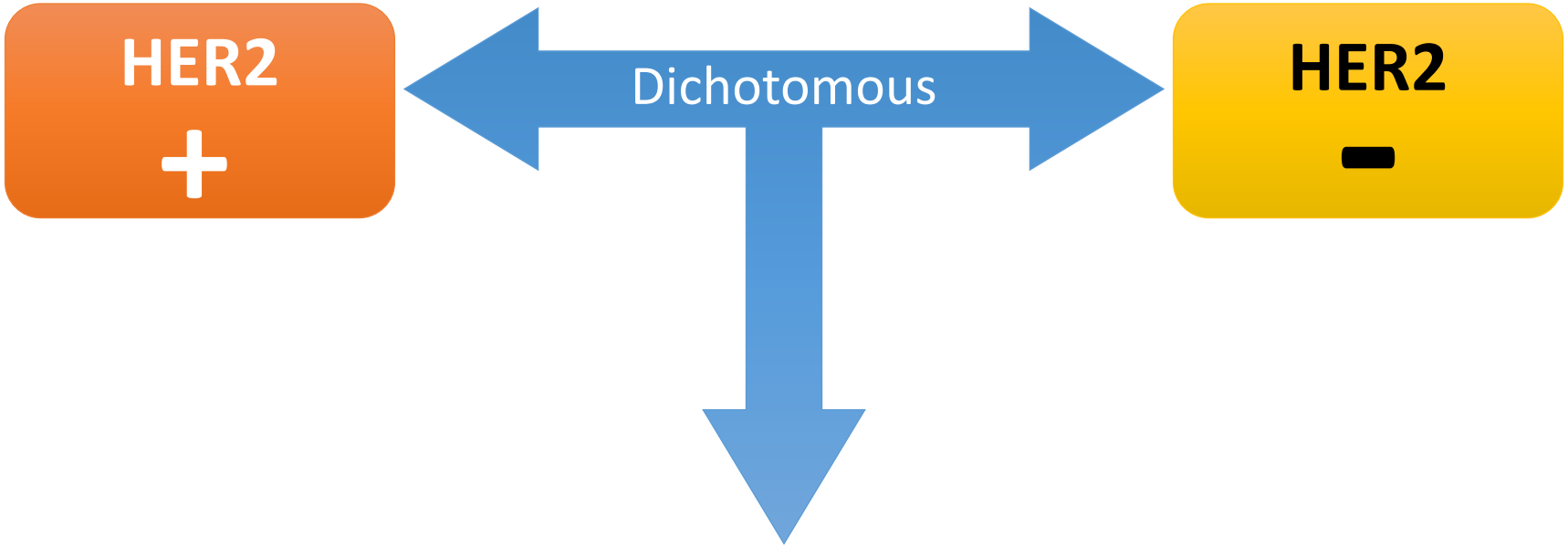


ASCO/CAP Algorithm for ISH Testing



- **NCCN 2020 endorses ASCO/CAP guideline**
- Equivocal results stratified through sequential IHC and ISH testing

Paradigm Shift in HER2 Status



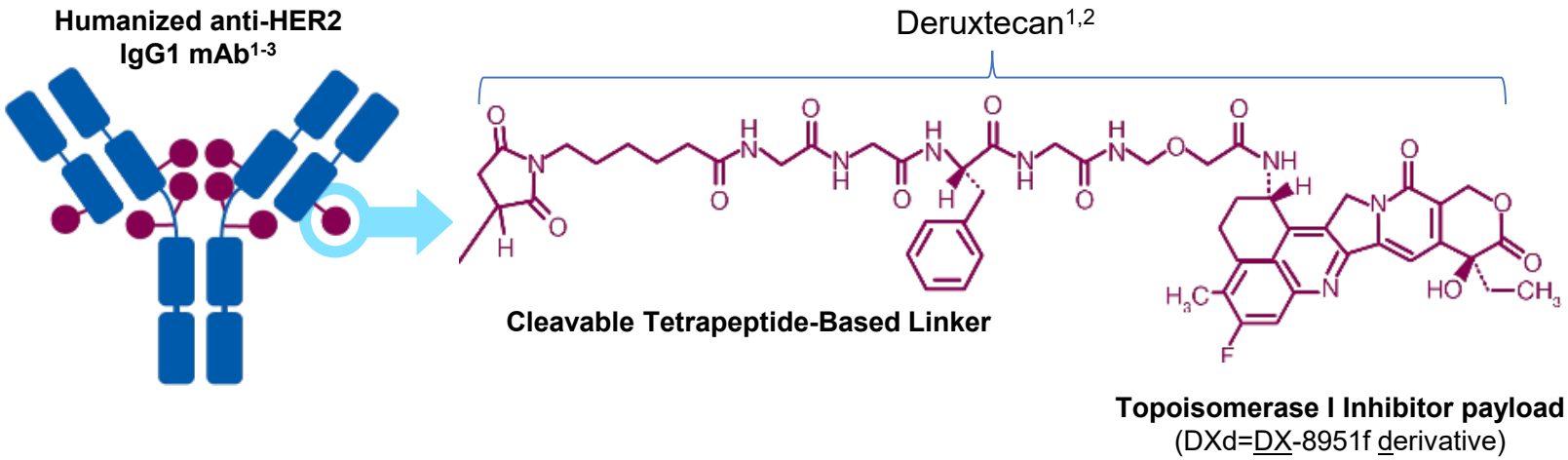
- HER2 expression as continuum
- Accommodates HER2 low expression and emerging treatment options

Metastatic HER2+ Breast Cancer
Trastuzumab Deruxtecan

ENHERTU Structure

T-DXd is an ADC composed of 3 components[1,2]:

- A humanized anti-HER2 IgG1 mAb with the same amino acid sequence as fam-trastuzumab deruxtecan-nxki, covalently linked to:
- A topoisomerase I inhibitor payload, an exatecan derivative, via
- A tetrapeptide-based cleavable linker



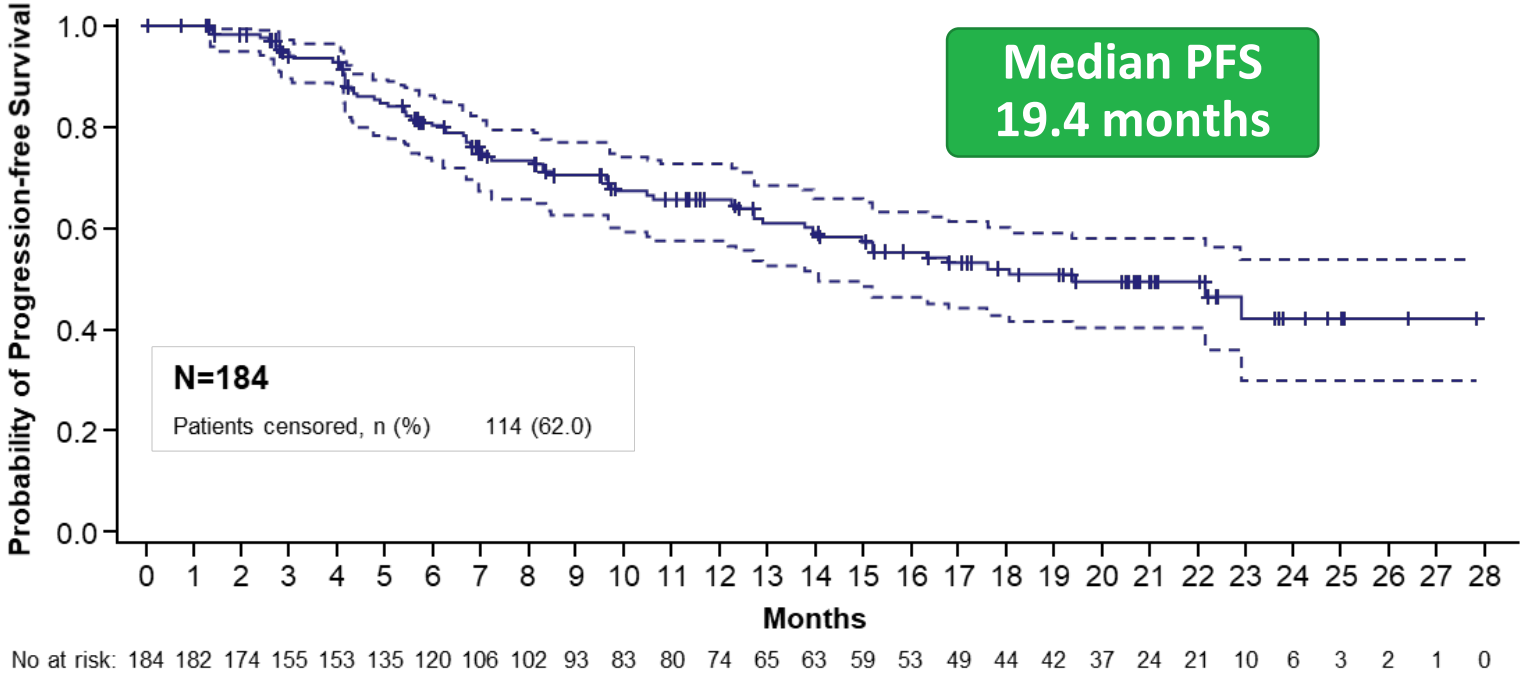
- Payload mechanism of action: topoisomerase I inhibitor[1,2,a]
- High potency of payload[1,2,a]
- High drug to antibody ratio ≈ 8[1,2,a]
- Payload with short systemic half-life[1,2,a]
- Stable linker-payload[1,2,a]
- Tumor-selective cleavable linker[1,2,a]
- Membrane-permeable payload[1,4,a]

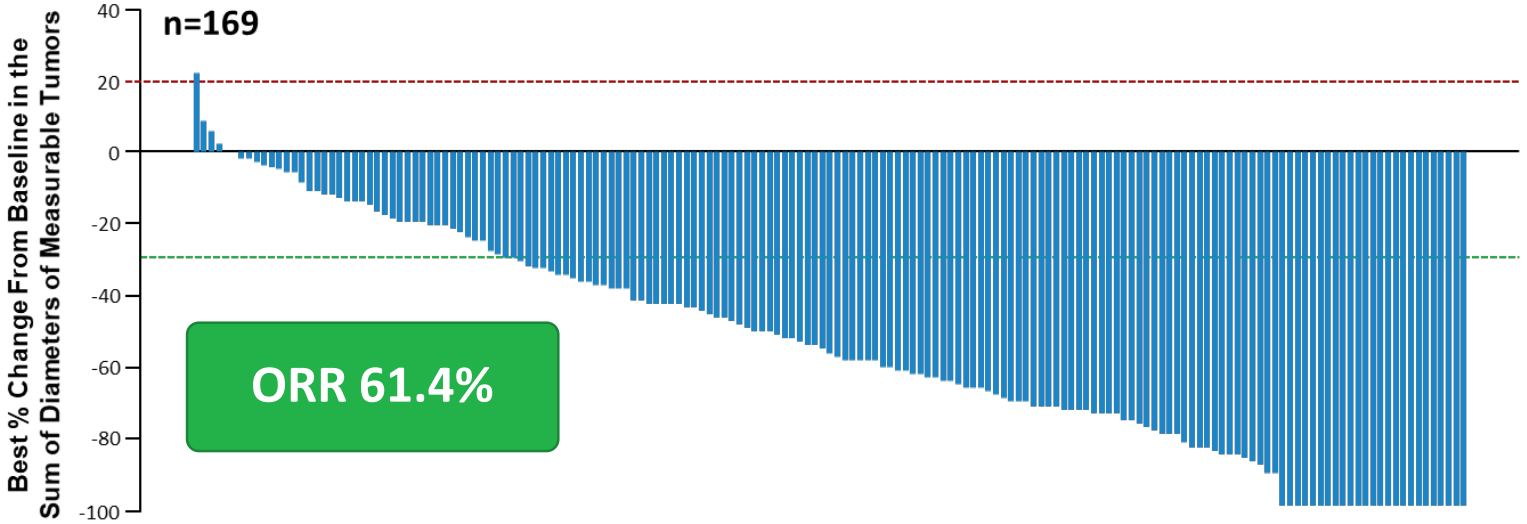
ADC, antibody-drug conjugate; HER2, human epidermal growth factor receptor 2; IgG1, immunoglobin; mAb, monoclonal antibodies; T-DXd, fam-trastuzumab deruxtecan-nxki.
[a]The clinical relevance of these features is under. investigation

1. Nakada T, et al. *Chem Pharm Bull (Tokyo)*. 2019;67(3):173-185. **2.** Ogitani Y, et al. *Clin Cancer Res*. 2016;22(20):5097-5108. **3.** Trail PA, et al. *Pharmacol Ther.* 2018;181:126-142. **4.** Ogitani Y, et al. *Cancer Sci*. 2016;107(7):1039-1046.

DESTINY BREAST – 01

- Phase 2 study
- Pre-treated population
  - Pertuzumab (65%)
  - T-DM1 (100%)
- Interstitial Lung Disease
  - All grades: 15.2%
  - Grade 5: 2.7%





Trastuzumab deruxtecan versus trastuzumab emtansine in patients with HER2-positive metastatic breast cancer: Updated results of the randomized, phase 3 study DESTINY-Breast03

Presentation ID: GS2-02

Sara A. Hurvitz,[a] Roberto Hegg, Wei-Pang Chung, Seock-Ah Im, William Jacot, Vinod Ganju, Joanne Wing Yan Chiu, Binghe Xu, Erika Hamilton, Srinivasan Madhusudan, Hiroji Iwata, Sevilay Altintas, Jan-Willem Henning, Giuseppe Curigliano, José Manuel Perez-Garcia, Anton Egorov, Yali Liu, Jillian Cathcart, Shahid Ashfaque, Javier Cortés

On behalf of the DESTINY-Breast03 investigators

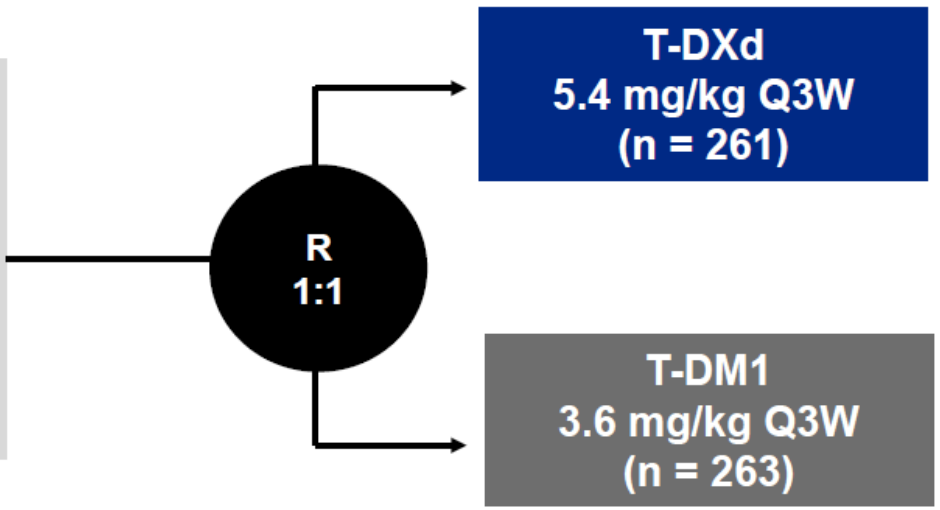
[a]Department of Medicine, David Geffen School of Medicine, University of California, Los Angeles and Jonsson Comprehensive Cancer Center, Los Angeles, CA, USA

Updated OS Analysis of DESTINY-Breast03

Randomized, open-label, multicenter study (NCT03529110)

Patients (N = 524)

- Unresectable or metastatic HER2-positive[a] breast cancer
- Previously treated with trastuzumab and a taxane in metastatic or (neo)adjuvant setting with recurrence within 6 months of therapy[b]



Primary endpoint

- PFS (BICR)

Key secondary endpoint

- OS[c]

Secondary endpoints

- ORR (BICR and investigator)
- DoR (BICR)
- Safety

Stratification factors

- Hormone receptor status
- Prior treatment with pertuzumab
- History of visceral disease

The prespecified OS interim analysis was planned with 153 events.[d] At the time of data cutoff (July 25, 2022), 169 OS events were observed and the *P* value to achieve statistical significance was 0.013

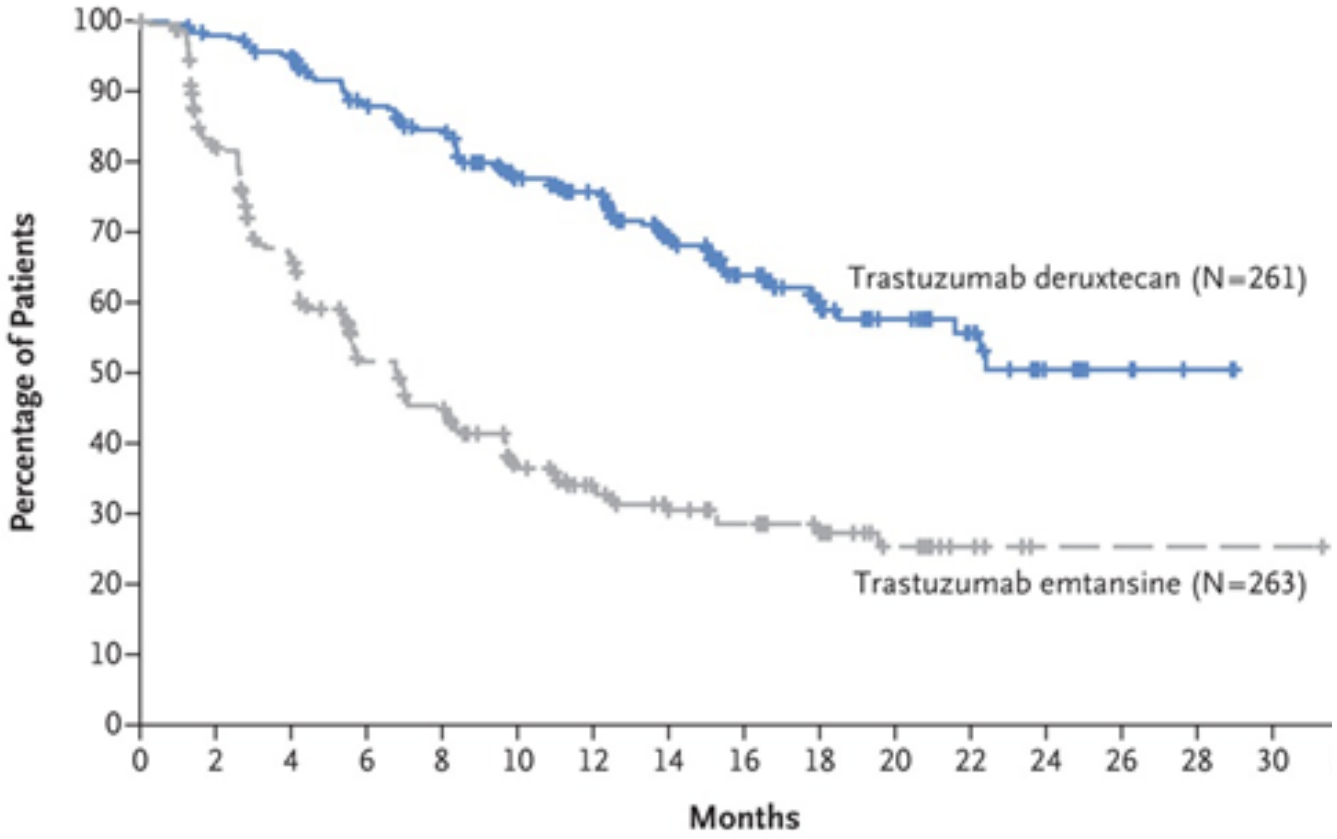
BICR, blinded independent central review; DoR, duration of response; HER2, human epidermal growth factor receptor 2; IHC, immunohistochemistry; ISH, in situ hybridization; ORR, objective response rate; OS, overall survival; PFS, progression-free survival; Q3W, every 3 weeks; R, randomization; T-DM1, trastuzumab emtansine; T-DXd, trastuzumab deruxtecan.
[a]HER2 IHC 3+ or IHC 2+/ISH+ based on central confirmation. [b]Progression during or within 6 months after completing adjuvant therapy involving trastuzumab and a taxane. [c]80% powered at 2-sided significance level of 5%. [d]Information fraction of 61%, with a *P* value boundary to reach statistical significance of 0.008. The *P* value was recalculated based on the actual OS events at the data cutoff.

Baseline Characteristics

	T-DXd n = 261	T-DM1 n = 263
Age, median (range), years	54.3 (27.9-83.1)	54.2 (20.2-83.0)
Female, n (%)	260 (99.6)	262 (99.6)
Region, n (%)		
Europe	54 (20.7)	50 (19.0)
Asia	149 (57.1)	160 (60.8)
North America	17 (6.5)	17 (6.5)
Rest of World	41 (15.7)	36 (13.7)
HER2 status (IHC[a]), n (%)		
3+	234 (89.7)	232 (88.2)
2+	25 (9.6)	30 (11.4)
1+ | Not evaluable	1 (0.4) | 1 (0.4)	0 | 1 (0.4)
ECOG PS, n (%)		
0	154 (59.0)	175 (66.5)
1	106 (40.6)	87 (33.1)
Missing	1 (0.4)	1 (0.4)
Positive hormone receptor status, n (%)	131 (50.2)	134 (51.0)
Baseline brain metastases, n (%)	43 (16.5)	39 (14.8)
History of visceral disease, n (%)	184 (70.5)	185 (70.3)

ECOG PS, Eastern Cooperative Oncology Group performance status; HER2, human epidermal growth factor receptor 2; IHC, immunohistochemistry; T-DM1, trastuzumab emtansine; T-DXd, trastuzumab deruxtecan.
[a]HER2-status as evaluated by central laboratory.

DESTINY BREAST 03 - PFS



No. at Risk

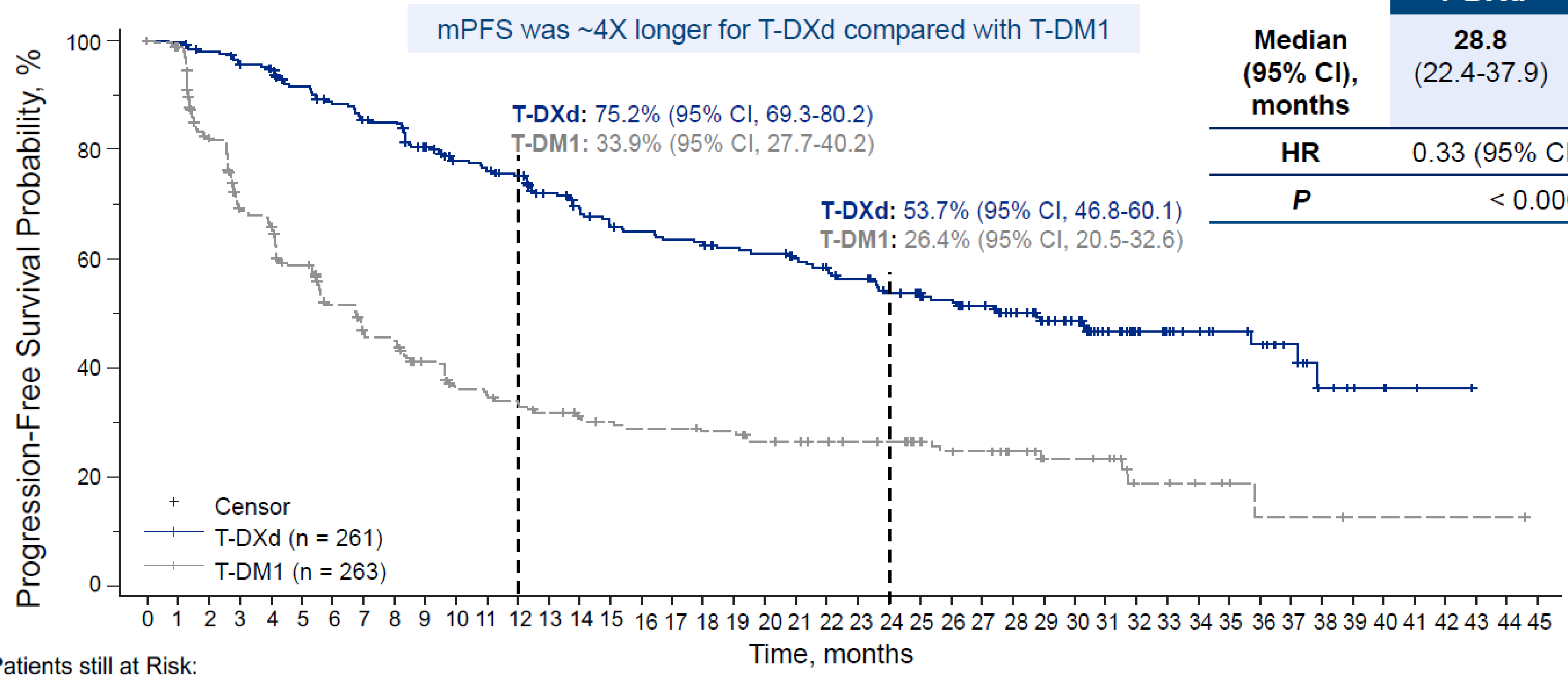
Trastuzumab deruxtecan	261	250	240	214	200	168	150	112	79	53	36	25	10	5	2
Trastuzumab emtansine	263	200	155	108	93	65	51	37	29	21	12	6	1	1	1	1

PFS	T-DxD	T-DM1
Median	**NR (18.5 – NE)**	6.8 (5.6 – 8.2)
12 months	**75.8% (69.8 – 80.7%)**	34.1 (27.7 – 40.5)
	p<0.001	

Cortes et al, NEJM 2022

DESTINY BREAST 03 – PFS Update SABCS 2022

Updated Primary Endpoint: PFS by BICR



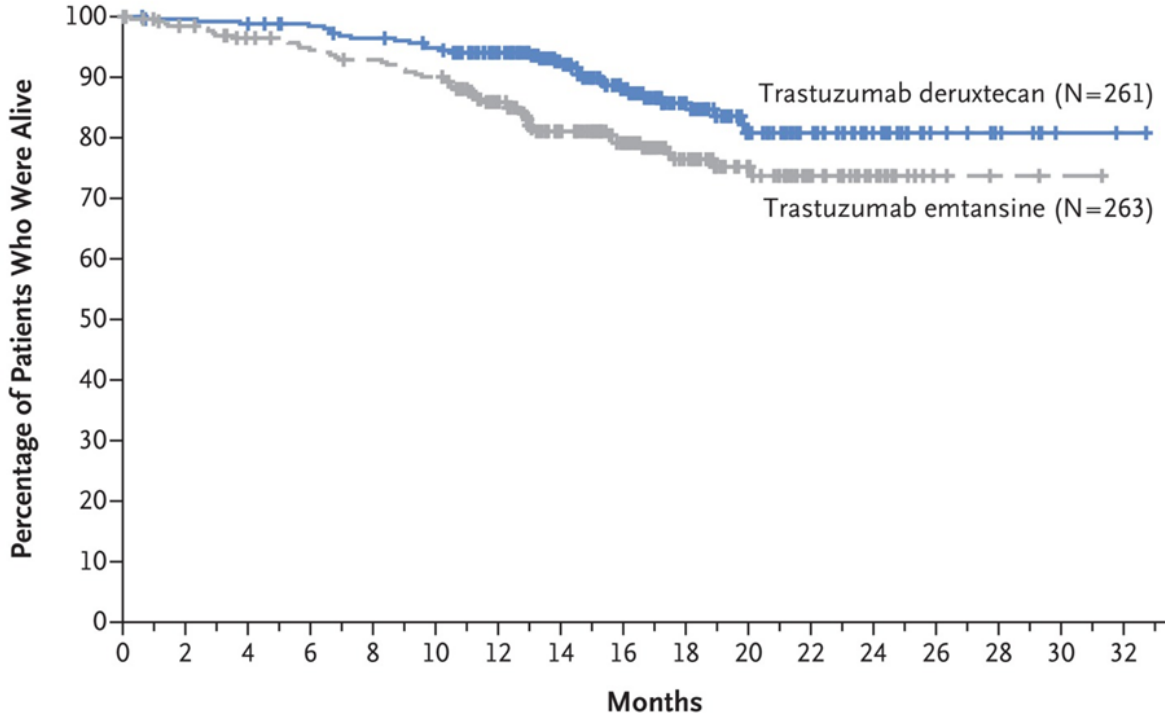
	T-DXd	T-DM1
Median (95% CI), months	**28.8** (22.4-37.9)	**6.8** (5.6-8.2)
HR	0.33 (95% CI, 0.26-0.43)	
P	< 0.000001[a,b]	

Patients still at Risk:

	0	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23
T-DXd	261	256	250	244	240	225	216	207	205	191	176	173	167	154	146	140	134	131	130	125	123	117	113	107
T-DM1	263	253	201	164	156	134	111	99	96	81	69	67	63	58	54	51	49	49	47	47	42	41	39	37

	24	25	26	27	28	29	30	31	32	33	34	35	36	37	38	39	40	41	42	43	44	45
T-DXd	99	96	90	82	73	64	55	41	32	28	23	20	18	13	7	5	4	2	1	0		
T-DM1	36	32	28	27	22	19	15	14	8	7	6	4	2	2	2	1	1	1	1	1	1	0

DESTINY BREAST 03 – OS Interim Analysis



No. at Risk

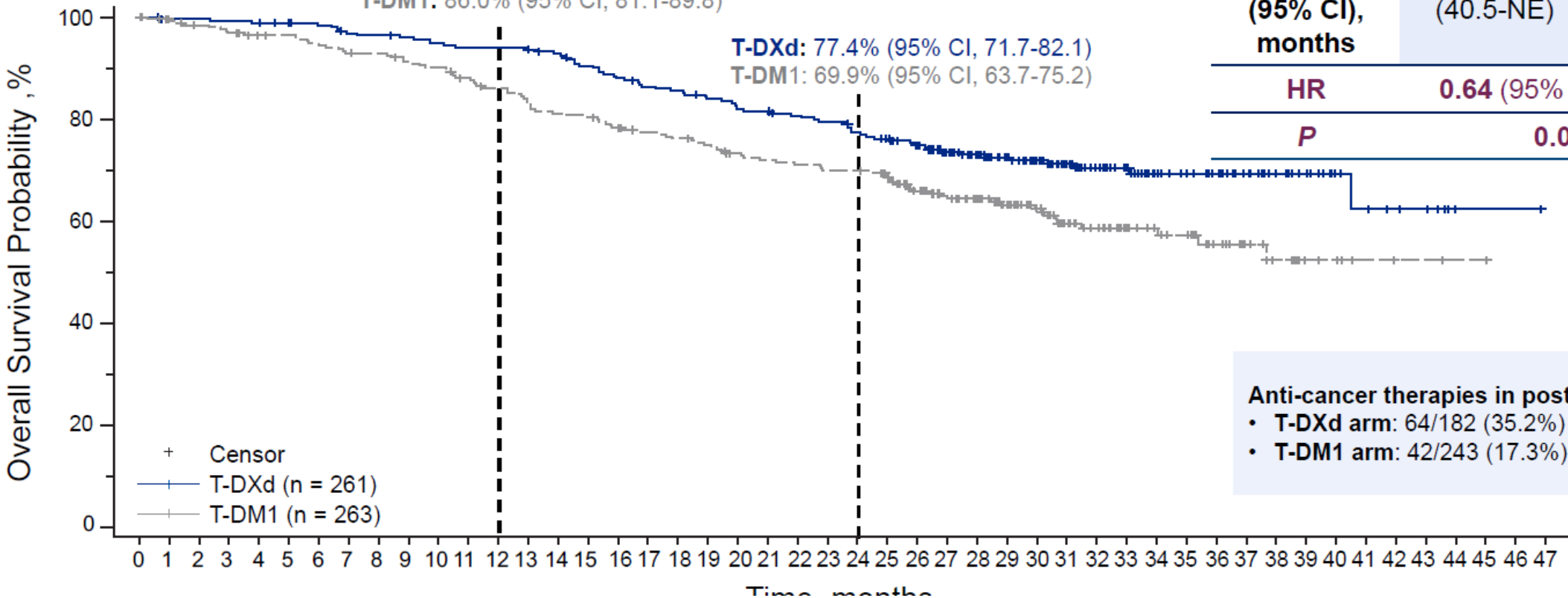
Trastuzumab deruxtecan	261	256	254	249	243	237	218	180	133	86	56	42	24	11	7	6	2	2	1	0
Trastuzumab emtansine	263	253	243	236	231	224	188	151	120	75	52	32	18	5	3	3	1	1	0	

OS	T-DxD	T-DM1
Median	**NE**	NE
12 months	**94.1% (90.3 - 96.4%)**	85.9 (80.9 – 89.7%)
	p=0.007	

Cortes et al, NEJM 2022

DESTINY BREAST 03 – OS Update SABCS 2022

Key Secondary Endpoint: Overall Survival

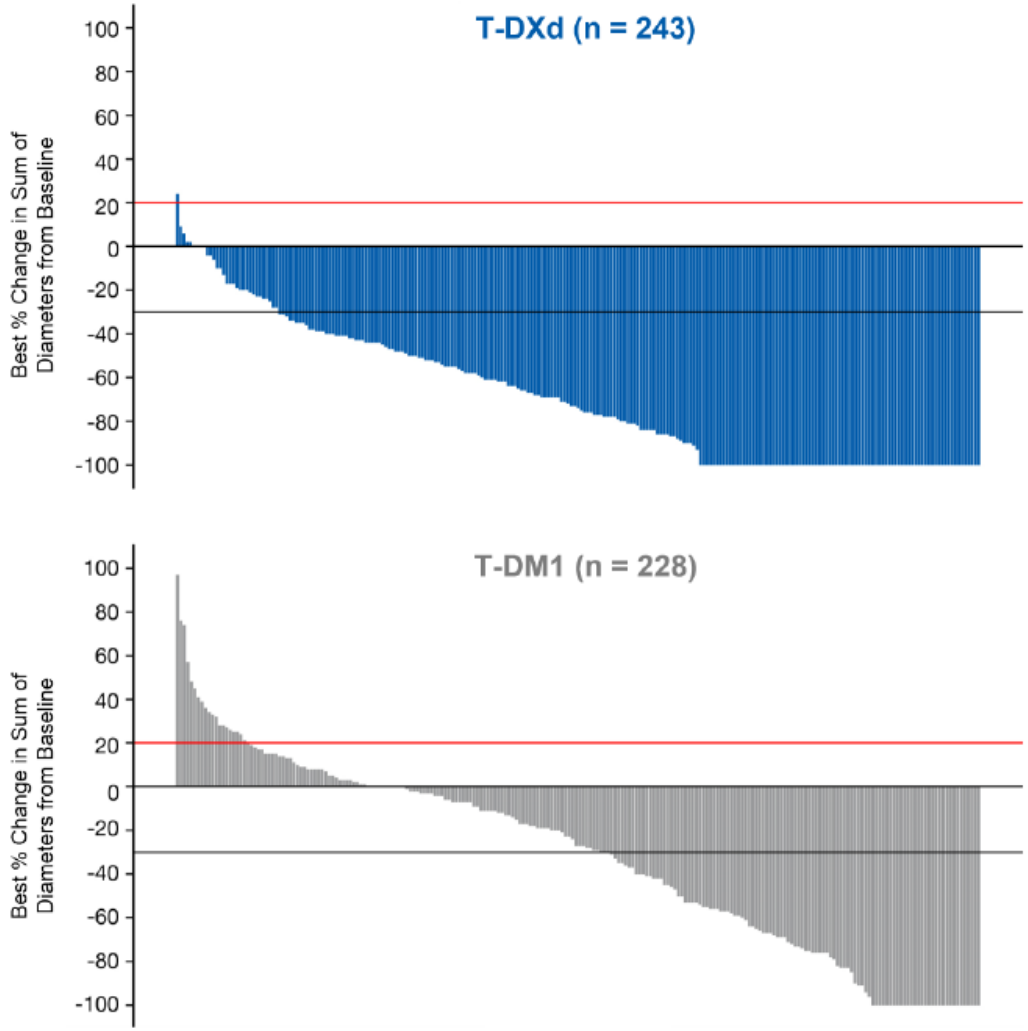


	T-DXd	T-DM1
Median (95% CI), months	**NR** (40.5-NE)	**NR** (34.0-NE)
HR	**0.64** (95% CI, 0.47-0.87)	
P	**0.0037**[a,b]	

Anti-cancer therapies in post-trial setting:

- **T-DXd arm**: 64/182 (35.2%) received T-DM1
- **T-DM1 arm**: 42/243 (17.3%) received T-DXd

Confirmed ORR and Other Efficacy Endpoints



	T-DXd n = 261[a]	T-DM1 n = 263[a]
Confirmed ORR by BICR		
n (%)	205 (**78.5**)	92 (**35.0**)
[95% CI]	[73.1-83.4]	[29.2-41.1]
Nominal *P* value	< 0.0001	
CR, n (%)	55 (**21.1**)	25 (**9.5**)
PR, n (%)	150 (57.5)	67 (25.5)
SD, n (%)	47 (18.0)	110 (41.8)
PD, n (%)	3 (1.1)	47 (17.9)
NE, n (%)	6 (2.3)	14 (5.3)
CBR, n (%) [95% CI]	233 (89.3) [84.9-92.8]	122 (46.4) [40.2-52.6]
Nominal *P* value	< 0.0001	
mDoR by BICR, months (95% CI)	**36.6** (22.4-NE)	**23.8** (12.6-34.7)

BICR, blinded independent central review; CBR, clinical benefit rate; CR, complete response; mDoR, median duration of response; NE, not evaluable; ORR, objective response rate; PD, progressive disease; PR, partial response; SD, stable disease; T-DM1, trastuzumab emtansine; T-DXd, trastuzumab deruxtecan.
Red line at 20% indicates progressive disease; black line at −30% indicates partial response.
[a]Only patients with measurable disease at baseline and at least 1 postbaseline target lesion assessment were included.

DESTINY BREAST 03 – Safety

Most Common TEAEs in ≥20% of Patients

System Organ Class Preferred Term, n (%)	T-DXd n = 257		T-DM1 n = 261	
	Any grade	Grade ≥3	Any grade	Grade ≥3
Blood and lymphatic system disorders				
Anemia	95 (37.0)	24 (9.3)	51 (19.5)	17 (6.5)
Platelet count decreased	64 (24.9)	20 (7.8)	114 (43.7)	52 (19.9)
White blood cell count decreased	60 (23.3)	16 (6.2)	16 (6.1)	2 (0.8)
Gastrointestinal disorders				
Nausea	198 (77.0)	18 (7.0)	79 (30.3)	1 (0.4)
Vomiting	133 (51.8)	4 (1.6)	28 (10.7)	2 (0.8)
Constipation	96 (37.4)	0	51 (19.5)	0
Diarrhea	83 (32.3)	3 (1.2)	21 (8.0)	2 (0.8)
General disorders				
Fatigue	79 (30.7)	15 (5.8)	53 (20.3)	2 (0.8)
Headache	61 (23.7)	1 (0.4)	40 (15.3)	0
Investigations				
Neutrophil count decreased	79 (30.7)	41 (16.0)	30 (11.5)	8 (3.1)
Aspartate aminotransferase increased	72 (28.0)	2 (0.8)	108 (41.4)	14 (5.4)
Alanine aminotransferase increased	59 (23.0)	4 (1.6)	83 (31.8)	12 (4.6)
Metabolism and nutrition disorders				
Decreased appetite	78 (30.4)	4 (1.6)	46 (17.6)	1 (0.4)
Weight decreased	58 (22.6)	6 (2.3)	23 (8.8)	2 (0.8)
Skin and subcutaneous tissue disorders				
Alopecia	102 (39.7)	1 (0.4)[a]	9 (3.4)	0

T-DM1, trastuzumab emtansine; T-DXd, trastuzumab deruxtecan; TEAE, treatment-emergent adverse event.
Adverse events were managed according to the protocol. [a]Cases of alopecia reported during the study were graded based on the clinical judgement of the investigator. 1 case of alopecia was categorized as grade 3 by the investigator despite grade 3 alopecia not being recognized by the NCI Common Terminology criteria. The event outcome was reported as recovered by the investigator.

DESTINY BREAST 03 – Safety

- Interstitial Lung Disease / Pneumonitis (N=39)
  - Grade 1-2: N=37
  - Grade 3: N=2
  - No Grade 4-5 events

Hurvitz et al, SABCS 2022

Trastuzumab deruxtecan vs physician's choice in patients with HER2+ unresectable and/or metastatic breast cancer previously treated with trastuzumab emtansine: Primary results of the randomized phase 3 study DESTINY-Breast02

Presentation ID: GS2-01

Ian Krop,[a] Yeon Hee Park, Sung-Bae Kim, Giuliano Borges, Sercan Aksoy, Joaquin Gavila Gregori, Rebecca Roylance, Elgene Lim, Rinat Yerushalmi, Flora Zagouri, Francois P. Duhoux, Tanja Fehm, Toshimi Takano, Anton Egorov, Iris Wu, Jillian Cathcart, Changan Chu, Fabrice André

On behalf of the DESTINY-Breast02 investigators

[a]Yale Cancer Center, New Haven, CT, USA

DESTINY-Breast02

Randomized phase 3, open-label, multicenter study (NCT03523585)

Key eligibility criteria[a]

- Centrally confirmed HER2-positive (IHC 3+ or IHC 2+/ISH+) unresectable or metastatic breast cancer
- Documented radiographic progression after most recent treatment
- Previously treated with T-DM1

Stratification factors

- Hormone receptor status
- Prior treatment with pertuzumab
- History of visceral disease

R 2:1

T-DXd
5.4 mg/kg Q3W
(n = 406)

TPC
Per label (n = 202)
- Trastuzumab / Capecitabine
or
- Lapatinib / Capecitabine

Primary endpoint
- PFS (BICR[b])

Key secondary endpoint
- OS

Secondary endpoints
- ORR (BICR[b])
- DoR (BICR[b])
- PFS (investigator)
- Safety

Exploratory endpoints
- CBR (BICR[b])
- PFS2[c] (investigator)

At data cutoff (June 30, 2022), the median duration of follow-up[d] was:
- **21.5 months** (range, 0.1-45.6 months) in the T-DXd arm
- **18.6 months** (range, 0-45.7 months) in the TPC arm

Protocol-prespecified statistical analysis plan

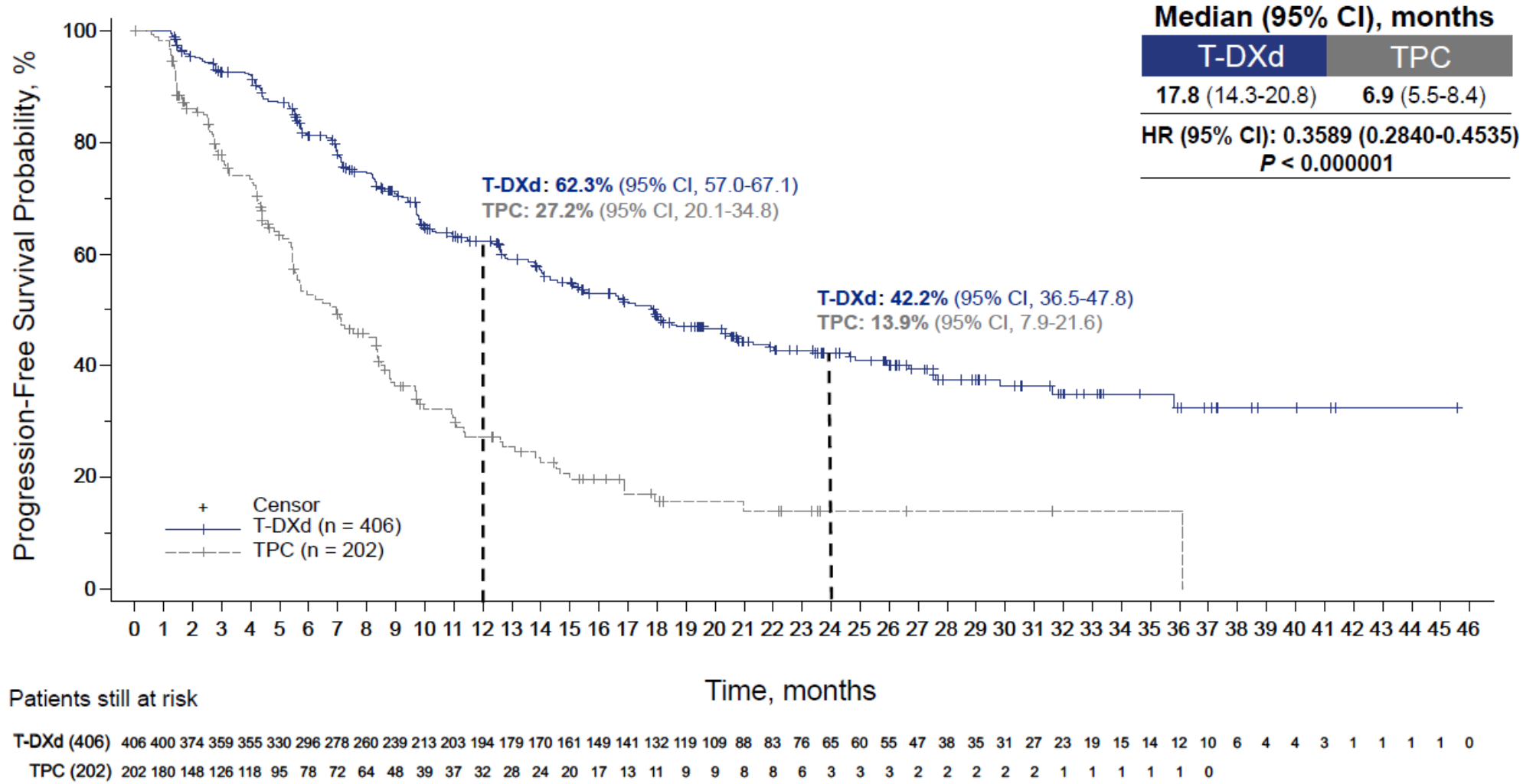
- Primary analysis planned for ~372 BICR PFS events observed or 18 months from the last patient randomized, whichever came first
- Group sequential testing was used to compare OS between treatment groups hierarchically, provided PFS was significant

BICR, blinded independent central review; CBR, clinical benefit rate; DoR, duration of response; HER2, human epidermal growth factor receptor 2; IHC, immunohistochemistry; ISH, in situ hybridization; mRECIST, modified Response Evaluation Criteria in Solid Tumors version 1.1; ORR, objective response rate; OS, overall survival; PFS, progression-free survival; PFS2; progression-free survival on the next line of therapy; Q3W, every 3 weeks; R, randomization, T-DM1, trastuzumab emtansine; T-DXd, trastuzumab deruxtecan; TPC, treatment of physician's choice.
[a]Patients with clinically inactive brain metastases and patients with treated brain metastases that were no longer symptomatic and who require no treatment with corticosteroids or anticonvulsants could be included. [b]BICR assessed per mRECIST 1.1. [c]PFS2 was defined as the time from date of randomization to the first documented progression on the next line of therapy or death due to any cause, whichever came first. [d]Duration of follow up is defined as study duration = the date last known alive minus date of randomization plus 1.

Baseline Characteristics

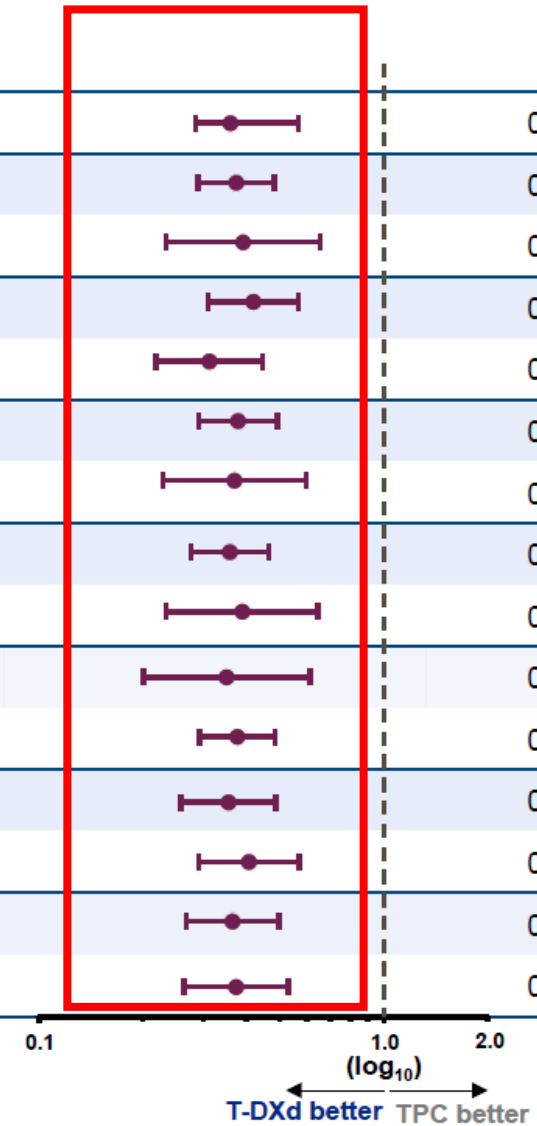
	T-DxD (N=406)	TPC (N=202)
HR-positive	238 (58.6%)	118 (58.4%)
Brain Mets	74 (18.2%)	36 (17.8%)
Visceral Disease	316 (77.8%)	160 (79.2%)
Prior Trastuzumab	404 (99.5%)	202 (100%)
Prior T-DM1	404 (99.5%)	202 (100%)

Primary Endpoint: PFS by BICR



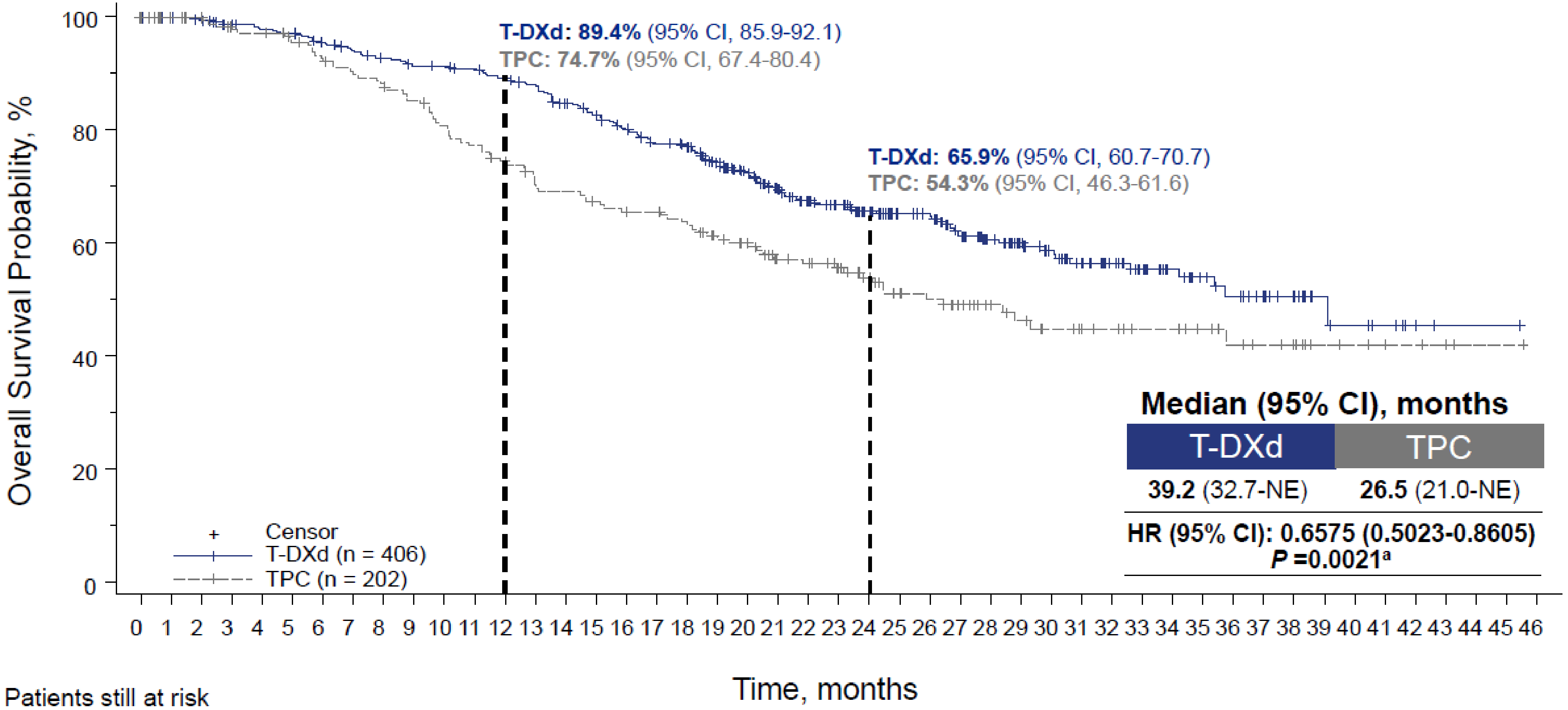
PFS in Key Subgroups

		Number of Events		Median PFS, mo (95% CI)		HR (95% CI)
		T-DXd	TPC	T-DXd	TPC	
All patients		200/406	125/202	17.8 (14.3-20.8)	6.9 (5.5-8.4)	0.36 (0.28-0.45)
Age	<65	160/321	101/164	17.9 (14.1-20.8)	7.1 (5.5-8.6)	0.37 (0.29-0.48)
	≥65	40/85	24/38	16.8 (12.7-NE)	6.7 (4.3-8.4)	0.39 (0.23-0.65)
Hormone receptor status	Positive	115/238	71/118	18.0 (15.1-21.3)	8.5 (6.5-10.0)	0.42 (0.31-0.57)
	Negative	84/165	53/83	17.0 (12.3-24.6)	5.3 (4.3-6.7)	0.31 (0.22-0.45)
Prior pertuzumab treatment[a]	Yes	155/318	95/156	17.8 (14.0-20.8)	6.2 (5.0-8.4)	0.38 (0.29-0.49)
	No	45/88	30/46	18.0 (13.9-26.7)	8.3 (5.5-12.6)	0.37 (0.23-0.60)
Visceral disease[a]	Yes	164/316	98/160	15.6 (12.8-20.3)	5.7 (5.3-7.2)	0.36 (0.28-0.46)
	No	36/90	27/42	29.8 (16.8-NE)	9.8 (6.2-12.6)	0.39 (0.23-0.64)
Baseline brain metastases	Yes	44/74	20/36	13.9 (11.1-18.0)	5.6 (3.3-8.1)	0.35 (0.20-0.61)
	No	156/332	105/166	18.7 (15.1-24.8)	7.1 (5.5-8.6)	0.38 (0.29-0.48)
Prior lines of therapy[b]	<3	105/212	66/104	16.6 (13.8-24.6)	7.0 (4.6-8.6)	0.35 (0.26-0.49)
	≥3	95/194	59/98	18.2 (14.3-22.0)	6.9 (5.5-8.8)	0.41 (0.29-0.57)
ECOG PS	0	101/228	75/121	24.6 (15.3-31.6)	8.1 (5.7-9.7)	0.36 (0.27-0.50)
	1	98/177	50/81	15.1 (11.5-18.0)	5.4 (4.3-7.5)	0.37 (0.26-0.53)



ECOG PS, Eastern Cooperative Oncology Group performance status; HR, hazard ratio; mo, months; PFS, progression-free survival; T-DXd, trastuzumab deruxtecan; TPC, treatment of physician's choice.
[a]Subgroup values are derived from baseline. [b]Lines of prior systemic therapy not including hormone therapy.

Key Secondary Endpoint: OS



Patients still at risk

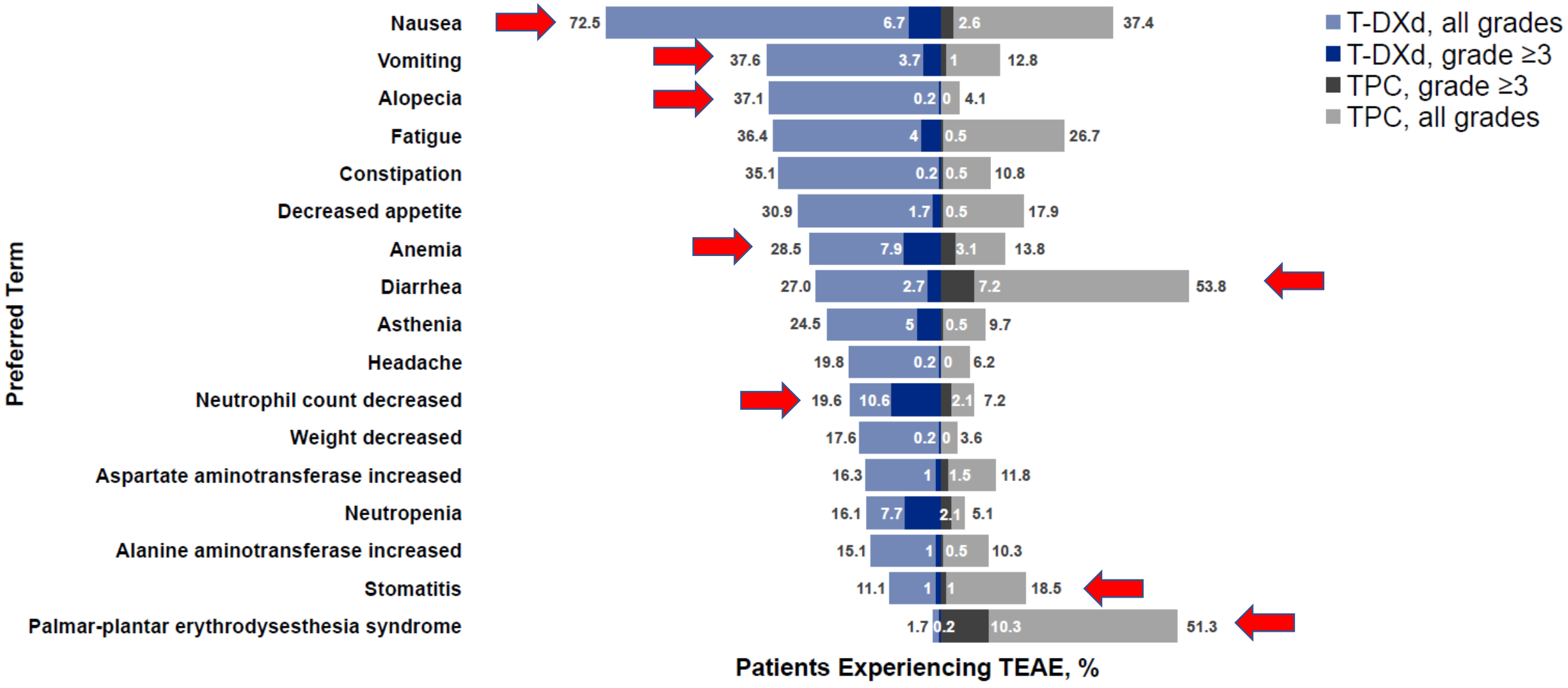
T-DXd (406)	406	404	400	390	385	382	374	366	357	352	350	346	339	331	317	306	295	282	277	257	234	215	196	183	160	144	139	122	104	93	82	72	63	51	40	34	29	25	19	10	8	6	3	1	1	1	0
TPC (202)	202	192	187	182	178	173	167	161	157	151	142	136	130	124	118	114	111	110	106	95	89	79	76	72	61	53	50	46	38	33	29	28	25	22	22	18	15	13	12	7	6	5	4	3	1	1	0

In the TPC arm

- **69.3% (140/202) of patients received a new systemic anticancer treatment**
- **25.7% (52/202) of patients received T-DXd in the post-trial setting**

[a]The boundary for statistical significance is 0.0040. HR, hazard ratio; mo, month; NE, not estimable; OS, overall survival; T-DXd, trastuzumab deruxtecan; TPC, treatment of physician's choice.

Most Common TEAEs (≥15% of Patients in Either Treatment Arm)



T-DXd, trastuzumab deruxtecan; TEAE, treatment-emergent adverse event; TPC, treatment of physician's choice.

Adverse Events of Special Interest: ILD and LV Dysfunction

Adjudicated as Drug-related ILD[a]						
n (%)	Grade 1	Grade 2	Grade 3	Grade 4	Grade 5	Any Grade
T-DXd (n = 404)	11 (2.7)	26 (6.4)	3 (0.7)	0	2 (0.5)	42 (10.4)
TPC (n = 195)	0	0	1 (0.5)	0	0	1 (0.5)

- Median time to onset of adjudicated drug-related ILD was 209.5 days (range, 41-638 days) with T-DXd

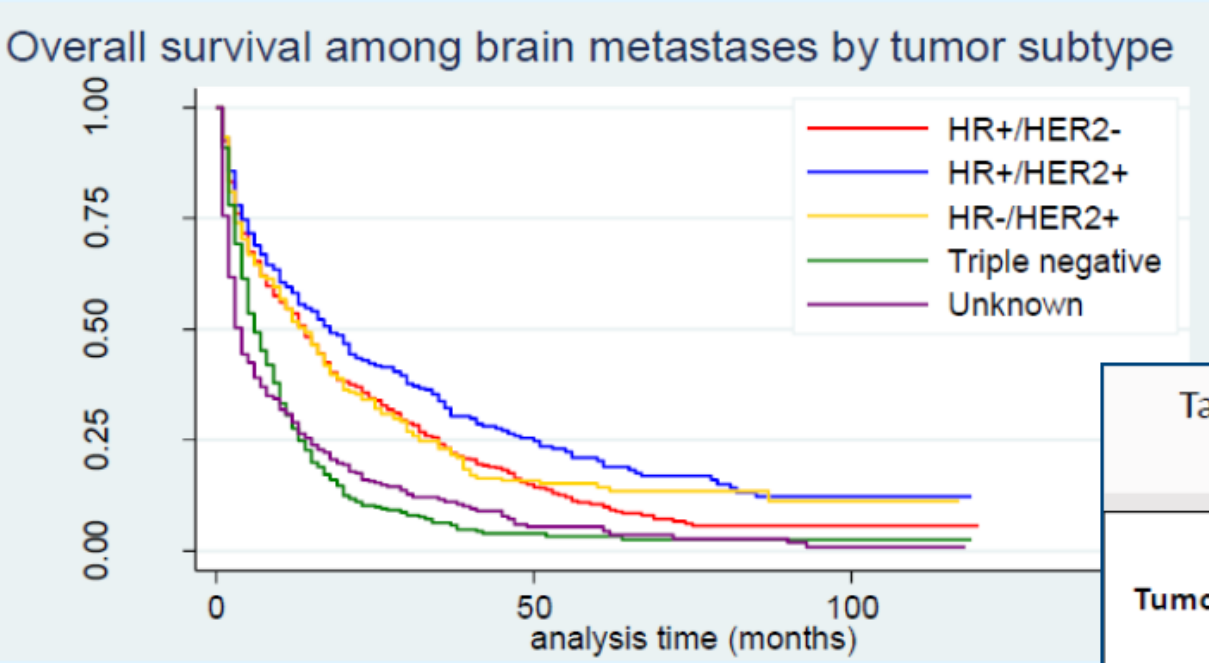
LV dysfunction[b]

- In the T-DXd arm, 18 (4.5%) patients experienced an LV dysfunction event[c]
  - 2 (0.5%) patients had a grade ≥3 event
- In the TPC arm, 3 (1.5%) patients experienced an LV dysfunction[d]
  - 1 (0.5%) patient had a grade ≥3 event

ILD, interstitial lung disease; LV, left ventricular; T-DXd, trastuzumab deruxtecan; TPC, treatment of physician's choice.
[a]The safety analysis set includes all randomly assigned patients who received at least 1 dose of study treatment. [b]Left ventricular dysfunction included preferred terms of acute left ventricular failure, acute right ventricular failure, cardiac failure, cardiac failure acute, cardiac failure chronic, cardiac failure congestive, chronic left ventricular failure, chronic right ventricular failure, ejection fraction decreased, left ventricular failure, right ventricular failure, ventricular failure, and left ventricular dysfunction. [c]17 ejection fraction decreased (2 grade ≥3), 1 LV dysfunction (grade 1). [d]1 ejection fraction decreased (grade 1), 2 cardiac failure (1 grade ≥3).

Metastatic HER2+ Breast Cancer - Brain Metastases

Subtype-specific Survival following BCBrM Diagnosis



- Among those with HER2+ BCBrM, 10 – 20% living 5 – 8 years after diagnosis of de novo Stage IV BC
- Underscores need to focus on QOL and Neurocognition

Table 4. OS and survival rate at 2, 5, and 8 years by tumor subtype among all pts with BM at initial BC diagnosis

Tumor Subtype	Median OS in months (95% CI)	% OS at 2 years (95% CI)	% OS at 5 years (95% CI)	% OS at 8 years (95% CI)
HR+/HER2-	14 (12-16)	34.4 (30.7-38.2)	10.6 (7.9-13.7)	5.5 (3.3-8.6)
HR+/HER2+	18 (13-22)	42.2 (36.4-48)	20.3 (15.1-26.1)	12.2 (7.6-18)
HR-/HER2+	14 (11-17)	34.2 (27.9-40.6)	14.3 (9.5-20)	11.2 (6.2-17.9)
Triple Negative	6 (5-8)	10.27 (7.1-14.1)	3.2 (1.4-6.2)	2.6 (1.0-5.5)
Unknown	4 (3-4)	15.68 (11.7-20.1)	5.4 (2.8-9.1)	0.9 (1-4.2)
All patients	10 (9-11)	28.3 (26.2-30.5)	10.5 (8.9-12.3)	5.9 (4.4-7.7)

Avilo, J et al. SABCS 2022.

TUCATINIB – HER2 CLIMB

HER2CLIMB Trial Design

Key Eligibility Criteria

- HER2+ metastatic breast cancer
- Prior treatment with trastuzumab, pertuzumab, and T-DM1
- ECOG performance status 0 or 1
- Brain MRI at baseline
  - Previously treated stable brain metastases
  - Untreated brain metastases not needing immediate local therapy
  - Previously treated progressing brain metastases not needing immediate local therapy
  - No evidence of brain metastases

R* (2:1)

N=410

Tucatinib + Trastuzumab + Capecitabine
(21-day cycle)

Tucatinib 300 mg PO BID
+
Trastuzumab 6 mg/kg Q3W (loading dose 8 mg/kg C1D1)
+
Capecitabine 1000 mg/m^2 PO BID (Days 1-14)

N=202

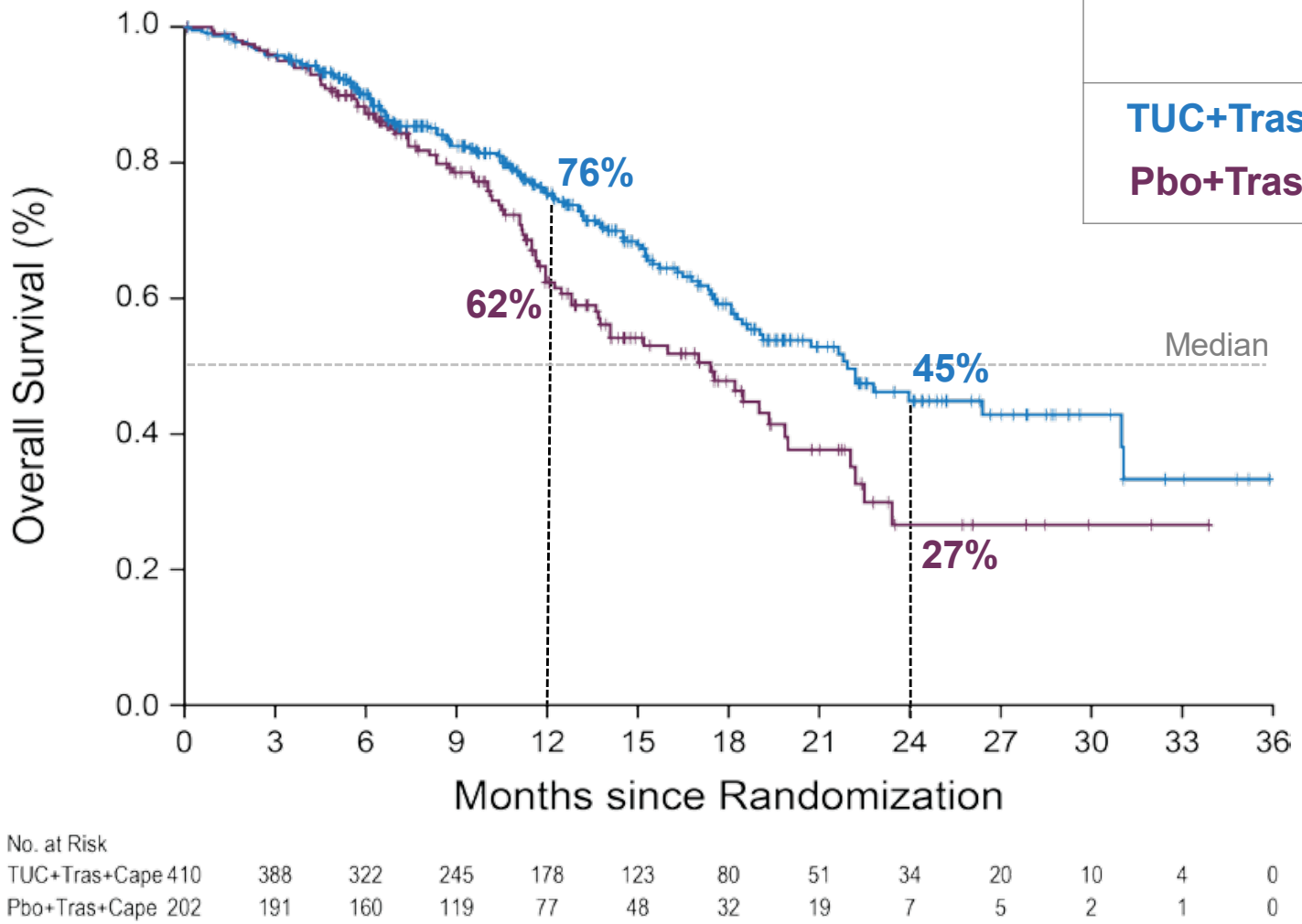
Placebo + Trastuzumab + Capecitabine
(21-day cycle)

Placebo
+
Trastuzumab 6 mg/kg Q3W (loading dose 8 mg/kg C1D1)
+
Capecitabine 1000 mg/m^2 PO BID (Days 1-14)

*Stratification factors: presence of brain metastases (yes/no), ECOG status (0 or 1), and region (US or Canada or rest of world)

https://clinicaltrials.gov/ct2/show/NCT02614794

HER2 CLIMB - OS



	Events N=612	HR (95% CI)	P Value
TUC+Tras+Cape	130/410	0.66 (0.50, 0.88)	0.00480
Pbo+Tras+Cape	85/202		

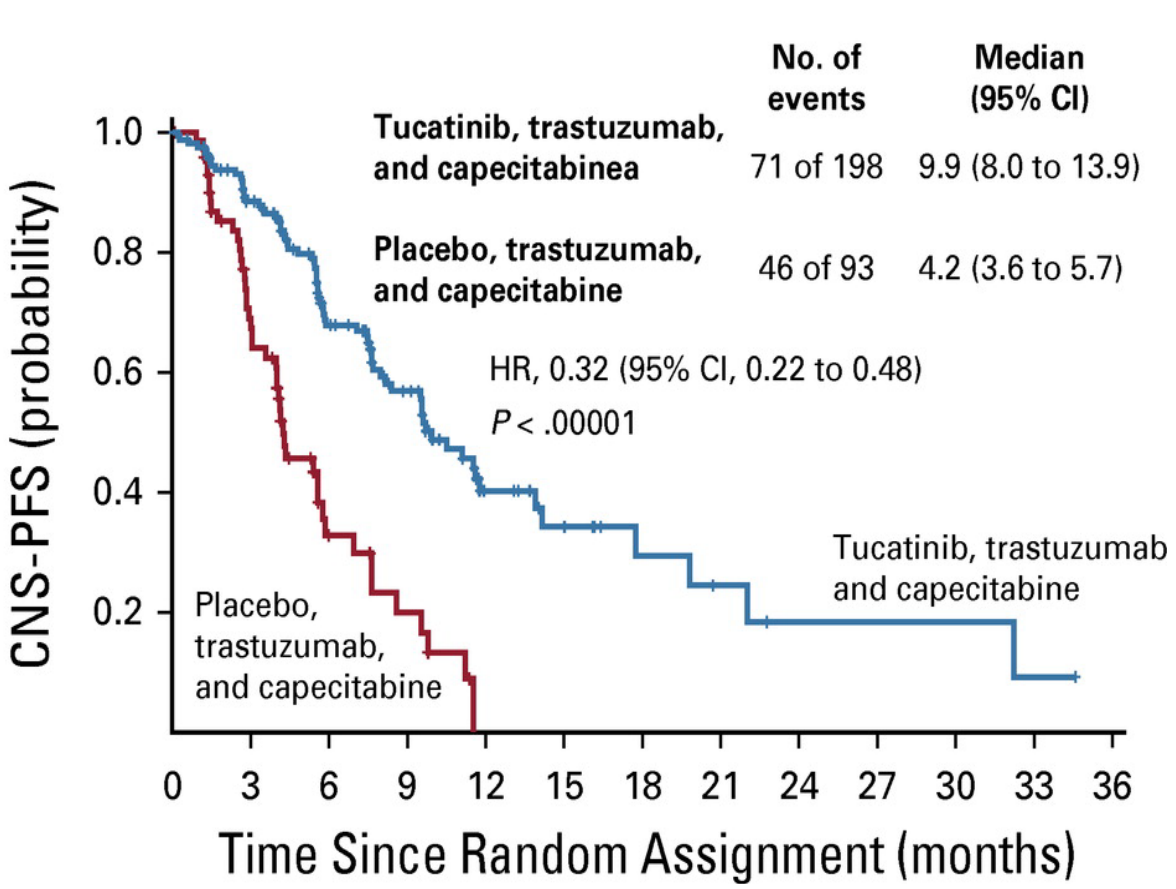
Median OS (95% CI):

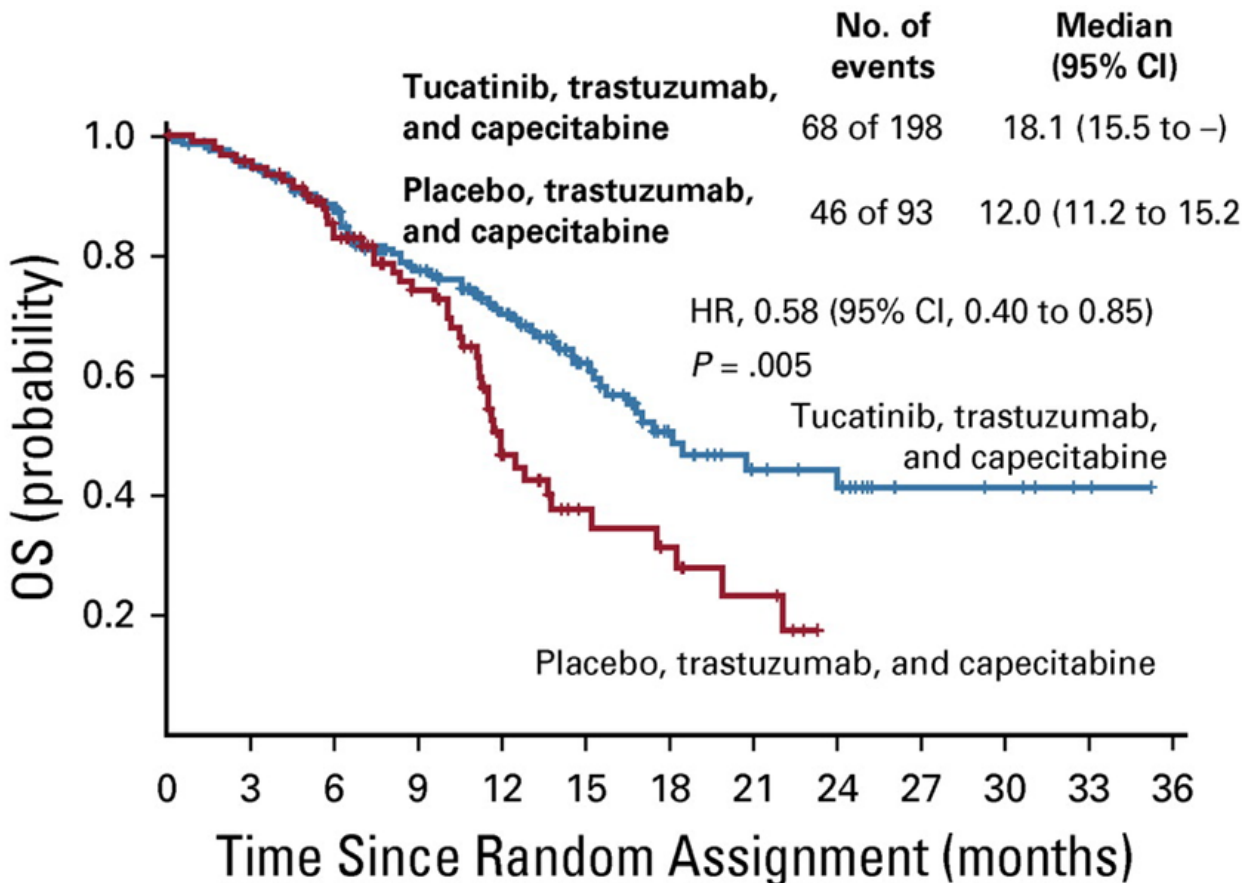
Tucatinib	Placebo
21.9 months (18.3 – 31.0)	17.4 months (13.6 – 19.9)

HER2 CLIMB – Baseline Demographics

Characteristic, n (%)	Tucatinib (n=410)	Placebo (n=202)
Female	407 (99)	200 (99)
Age (years), median (range)	55.0 (22, 80)	54.0 (25, 82)
Presence/history of brain metastases	198 (48)	93 (46)
Treated, stable	118 (59.6)	55 (59.1)
Untreated	44 (22.2)	22 (23.7)
Treated, progressing	36 (18.2)	16 (17.2)

HER2 CLIMB – PFS / OS (Brain Met Subgroup)

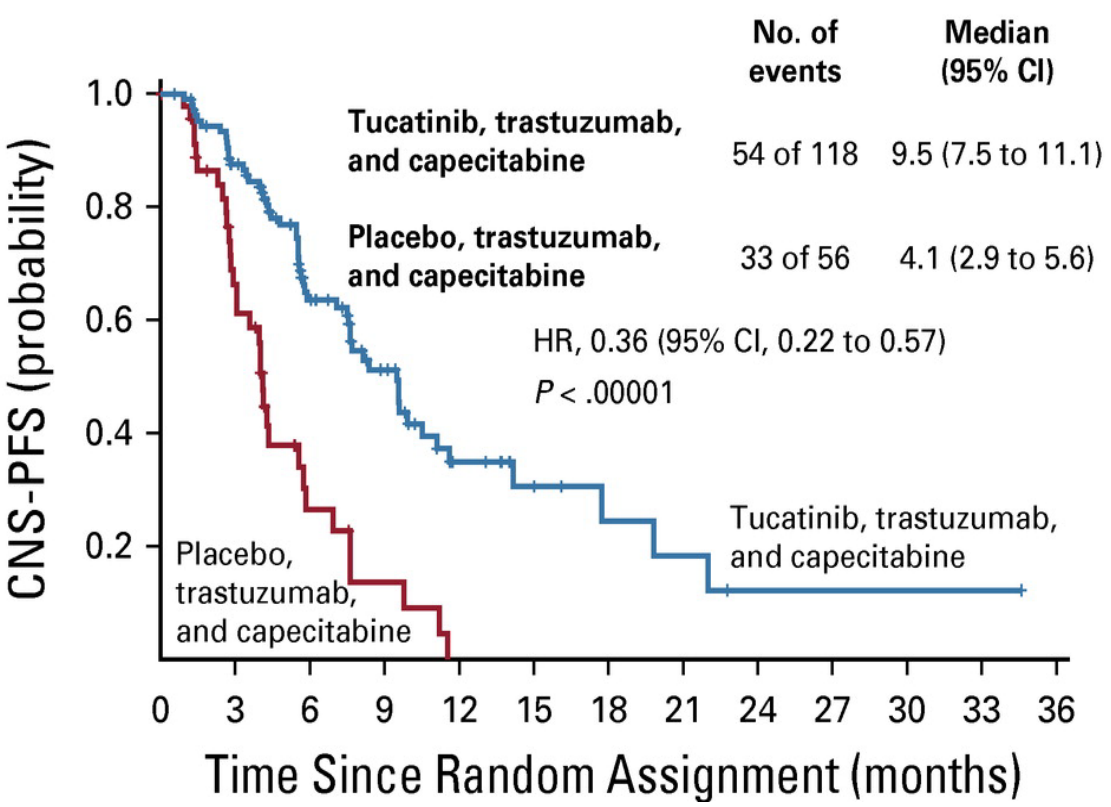




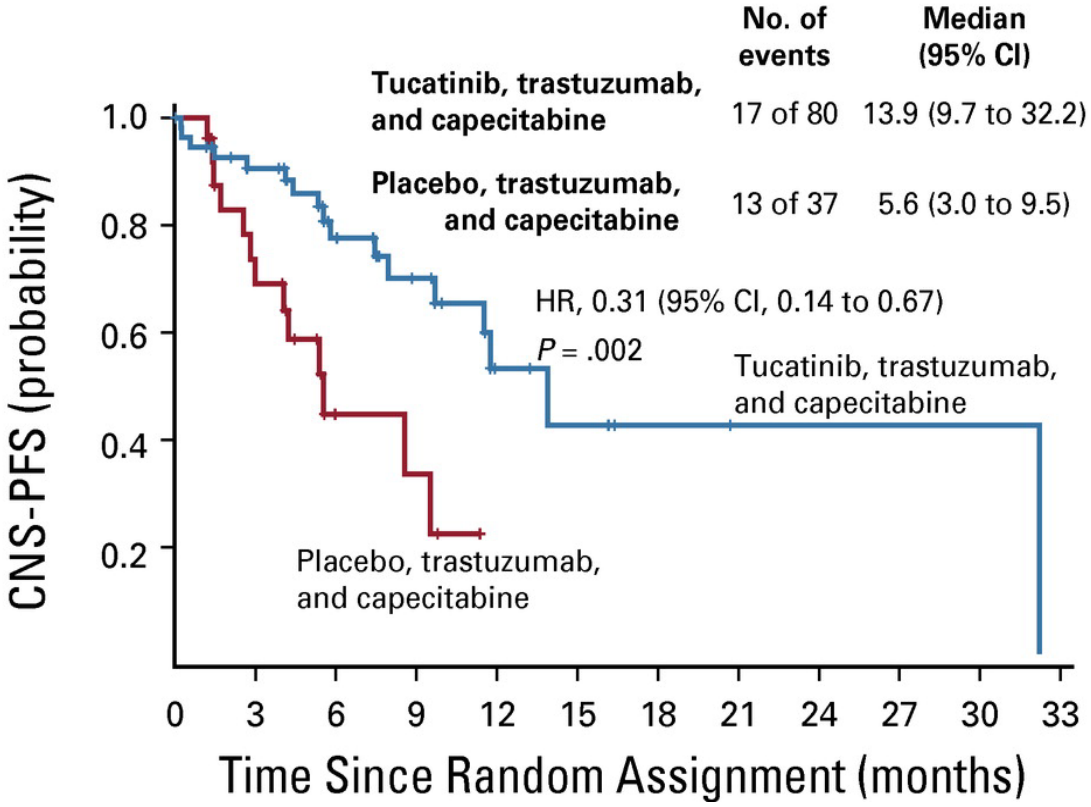
Lin et al, JCO 2020

HER2 CLIMB – PFS / OS (Brain Met Subgroup)

Active Brain Mets



Stable Brain Mets



Lin et al, JCO 2020

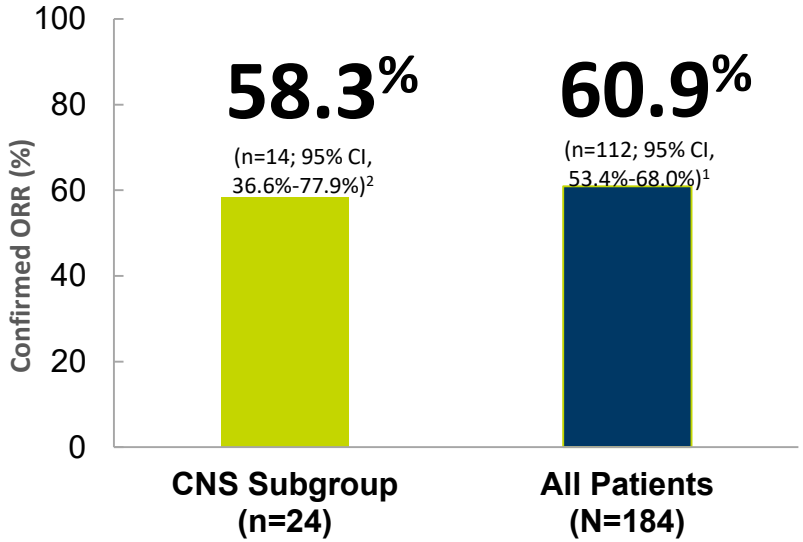
INTRACRANIAL EFFICACY – Trastuzumab Deruxtecan

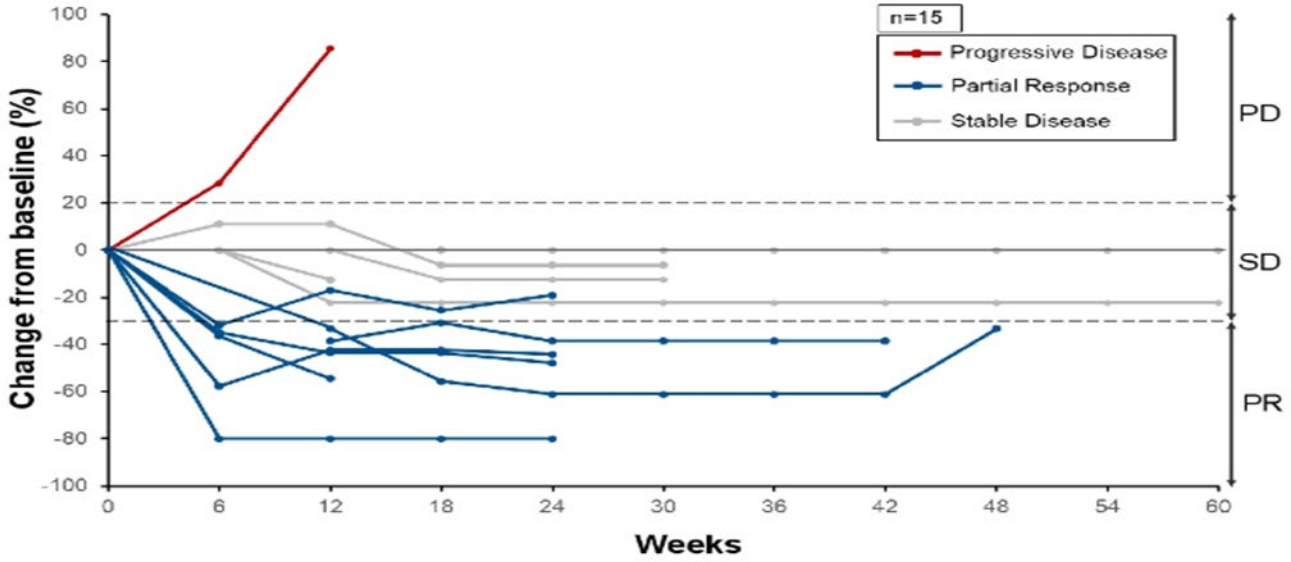
DESTINY BREAST 01 – CNS Subgroup

Baseline Criteria	CNS Subgroup[a] (n=24)	All Patients (N=184)
Age, median (range), years	58.0 (33-85)	55.0 (28-96)
ECOG performance status 0/1/2, %	62.5/37.5/0	55.4/44.0/0.5
HR positive/negative/unknown, %	37.5/58.3/4.2	52.7/45.1/2.2
Presence of visceral disease, %	100	91.8
Median prior therapies, n (range)	6 (3-16)	6 (2-27)

DESTINY BREAST 01 – CNS Subgroup

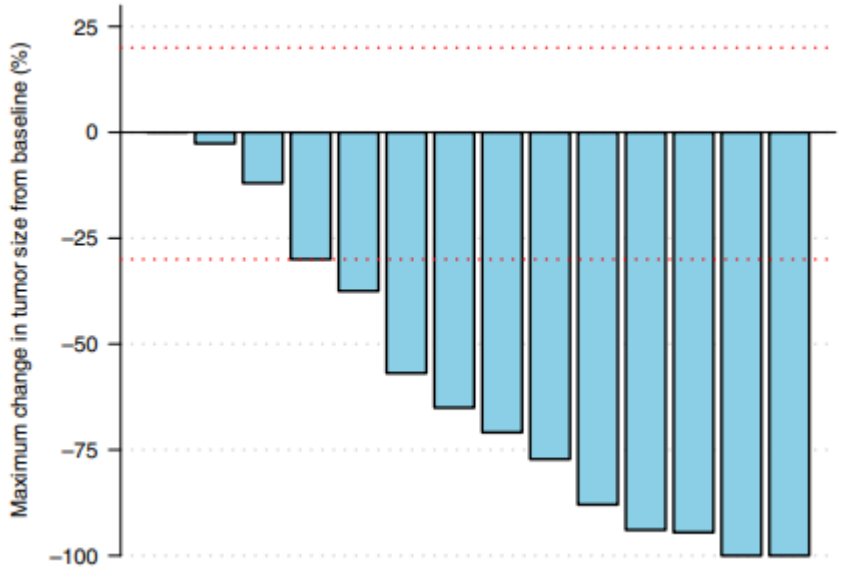
ITT Analysis	CNS Subgroup (n=24)	All Patients (N=184)
Complete response, % (n)	4.2 (1)	6.0 (11)
Partial response, % (n)	54.2 (13)	54.9 (101)
Stable disease, % (n)	33.3 (8)	36.4 (67)
Disease control rate, % (n)	91.7 (22)	97.3 (179)
Median DOR (CR or PR), months (95% CI)	16.9 (5.7-16.9)	14.8 (13.8-16.9)
Median PFS, months (95% CI)	18.1 (6.7-18.1)	16.4 (12.7-NE)



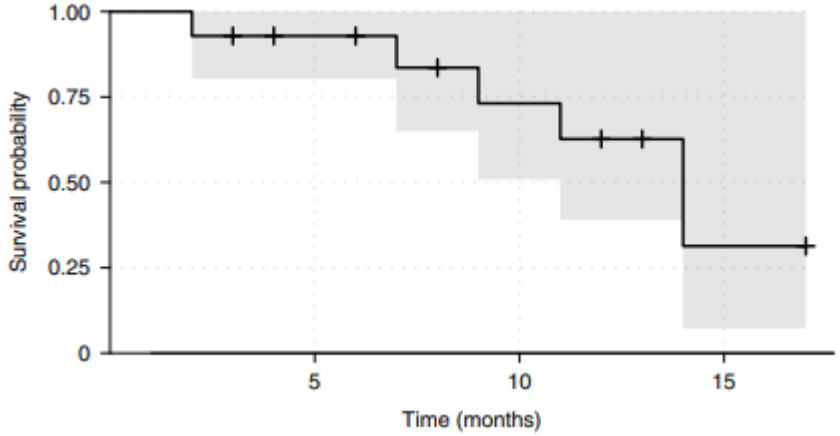


TUXEDO-1 Trial

- N=15 patients
  - Untreated brain mets (40%)
  - Primary brain mets after local therapy (60%)
- Efficacy (RANO-BM Criteria)
  - Intracranial RR 73.3%
    - 2 CR (13.3%)
    - 9 PR (60%)
- No extracranial progression as first site of progressive disease
- No impact on QOL and cognitive function



Response Rate
73.3%



Median PFS
14 months

Preusser et al, Nature Medicine 2022

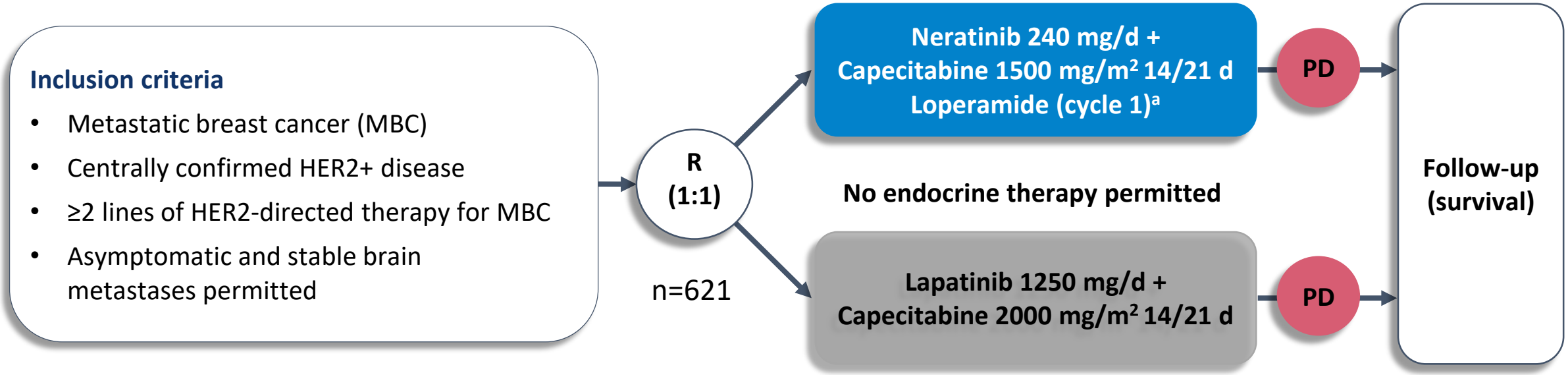
T-DxD in Brain Metastases

Study	Type	IC-ORR
TUXEDO-1 Bartsch et al 2022	Phase 2	73% (11/15; RANO-BM)
Kabraji et al 2022	Retrospective	70% (7/10; RANO-BM)
Yamanaka et al 2022	**Retrospective**	**54% (20/37; RECIST)**
DEBBRAH(c2/3) Perez-Garcia et al 2022	Phase 2	46% (6/13; RANO-BM)

O'Brien, SABCS 2022

NERATINIB–NALA

NALA – Study Design



Stratification variables

- Number of prior HER2 therapies for MBC
- Disease location
- HR status
- Geographic location

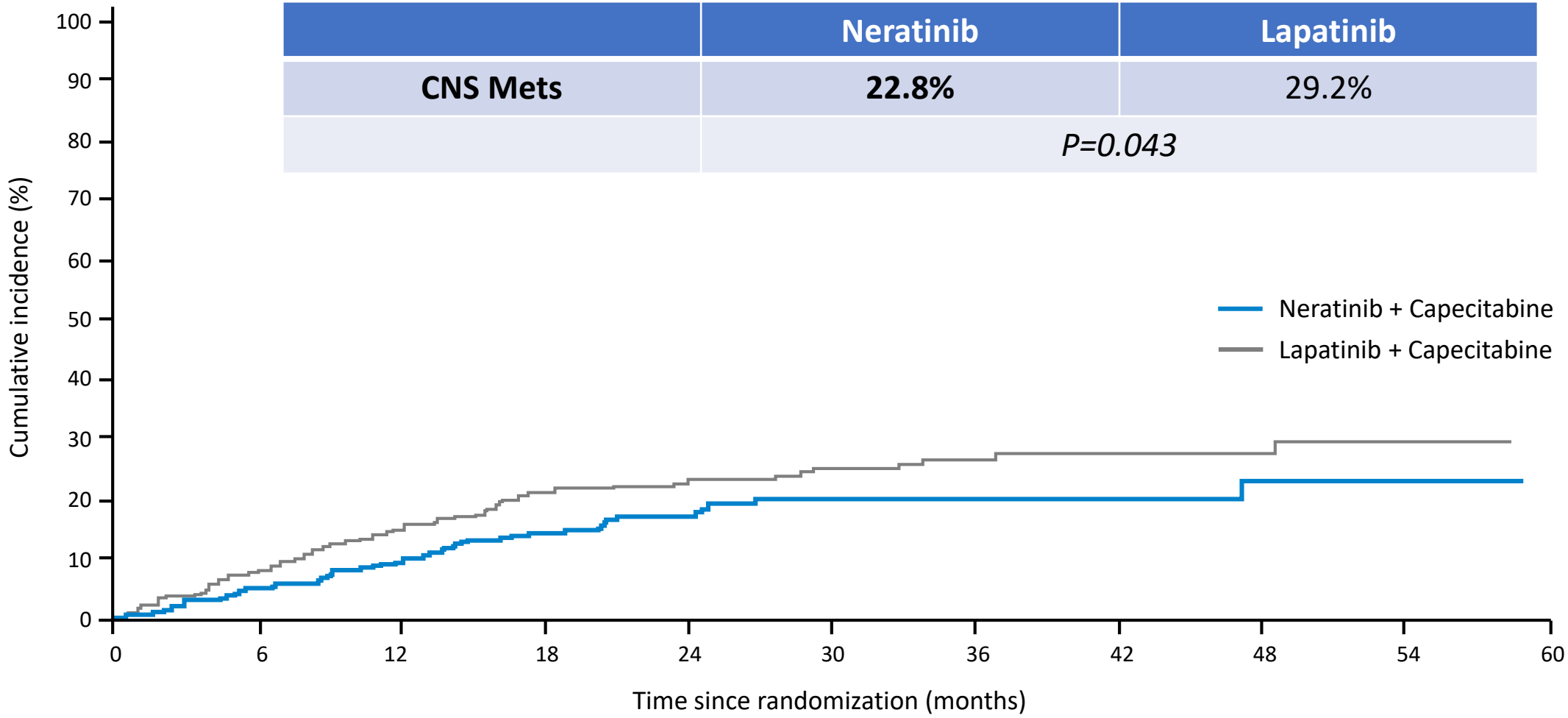
Endpoints

- Co-primary: PFS (centrally confirmed) and OS
- Secondary: PFS (local), ORR, DoR, CBR, intervention for CNS metastases, safety, health outcomes

Loperamide 4 mg with first dose of neratinib, followed by 2 mg every 4 h for first 3 d, then loperamide 2 mg every 6–8 h until end of Cycle 1. Thereafter as needed

NALA – Brain Mets

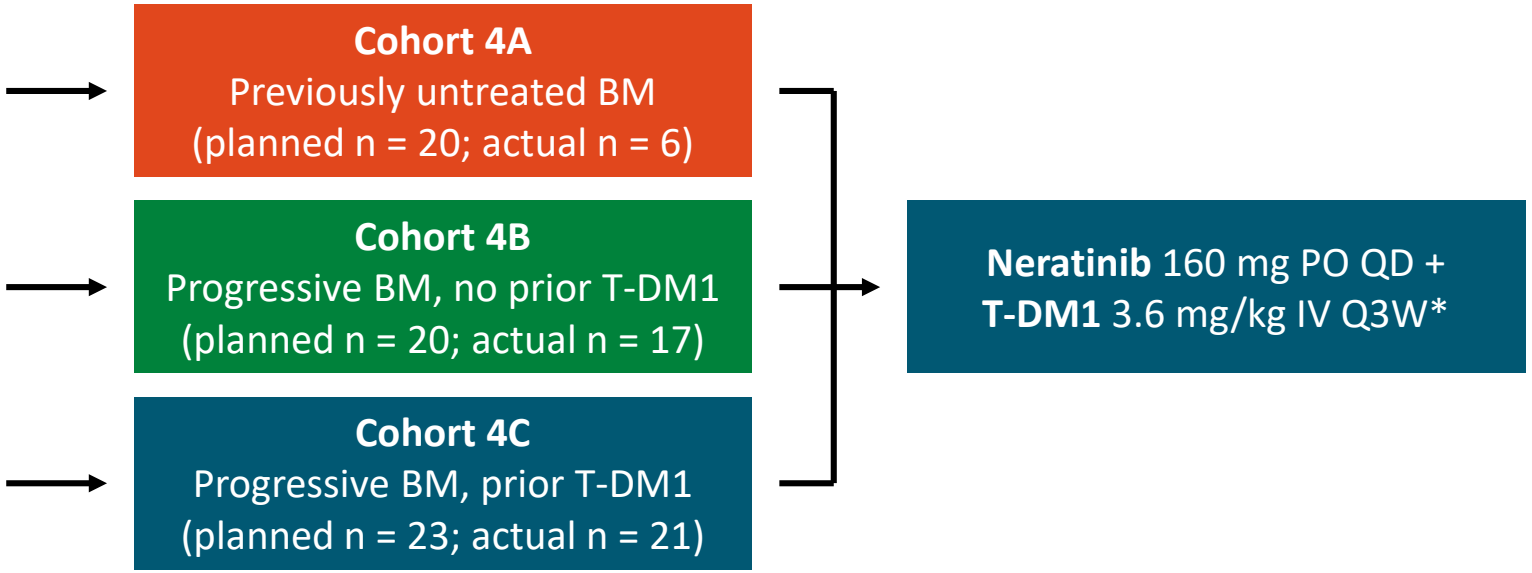
	Neratinib	Lapatinib
CNS Mets	**22.8%**	29.2%
	P=0.043	



Neratinib and ado-Trastuzumab-Emtansine (T-DM1) for HER2+ BCBM: TBCRC Trial 022

Cohort 4

- HER2+ MBC
- Measurable parenchymal BM
- ECOG PS 0-2
- No prior neratinib



*Diarrhea prophylaxis with colestipol and loperamide mandated during cycle 1.

- **Primary endpoint:** RANO-BM in each cohort
- Correlative analyses including PROs for GI toxicity

Freedman. SABCS 2022. Abstr PD7-03. NCT01494662.

Slide credit: clinicaloptions.com

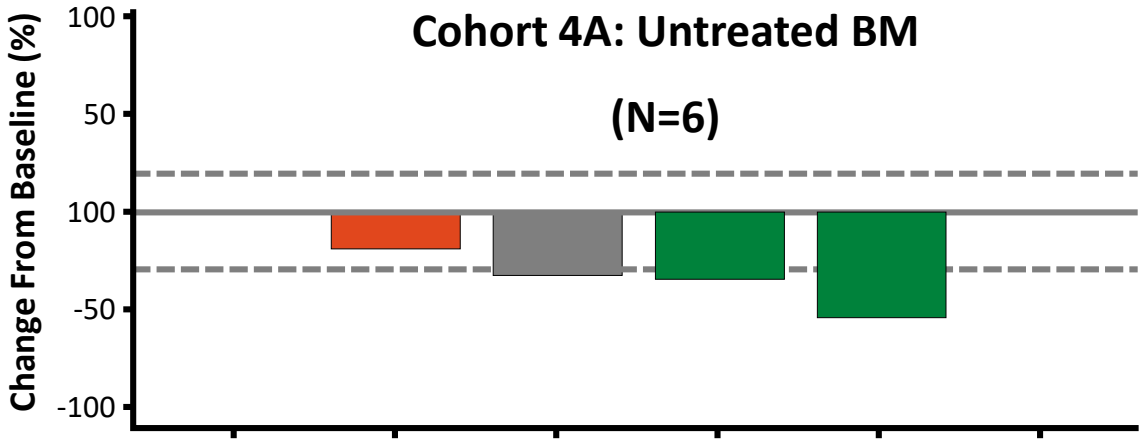
Neratinib and ado-Trastuzumab-Emtansine (T-DM1) for HER2+ BCBM: TBCRC Trial 022

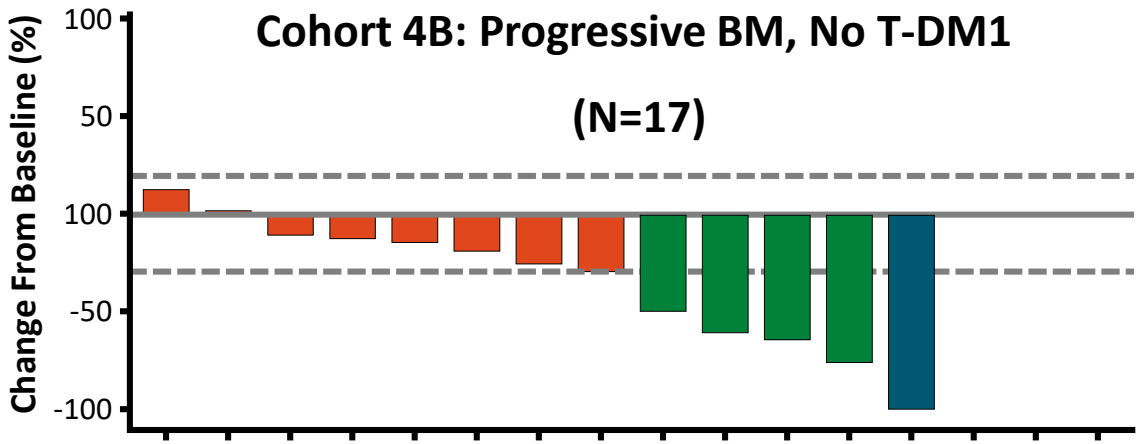
Characteristic, n (%)	Cohort 4A: Untreated BM (n = 6)	Cohort 4B: Progressive BM, No T-DM1 (n = 17)	Cohort 4C: Progressive BM, Prior T-DM1 (n = 21)
Median age, yr (range)	52 (44-65)	48 (42-59)	48 (35-68)
Non-White race	2 (33.0)	3 (17.6)	1 (4.8)
No. prior CT lines for MBC			
▪ 1	1 (16.7)	9 (52.9)	0
▪ 2	1 (16.7)	4 (23.5)	6 (28.6)
▪ ≥3	1 (16.7)	3 (17.6)	15 (71.4)
▪ Missing	3 (50)	1 (5.9)	0
Prior CNS surgery	0	7 (41.2)	7 (33.3)
Prior WBRT	0	12 (70.6)	11 (52.4)
Prior SRS	1 (16.7)	12 (70.6)	10 (47.6)

- Median no. prior lines of CT for MBC: 2 (range: 0-10)
- No patient previously received Tucatinib
- In cohort 4B, ~70% of patients had been treated with WBRT and SRS
- In cohort 4C, ~50% of patients had been treated with WBRT and SRS

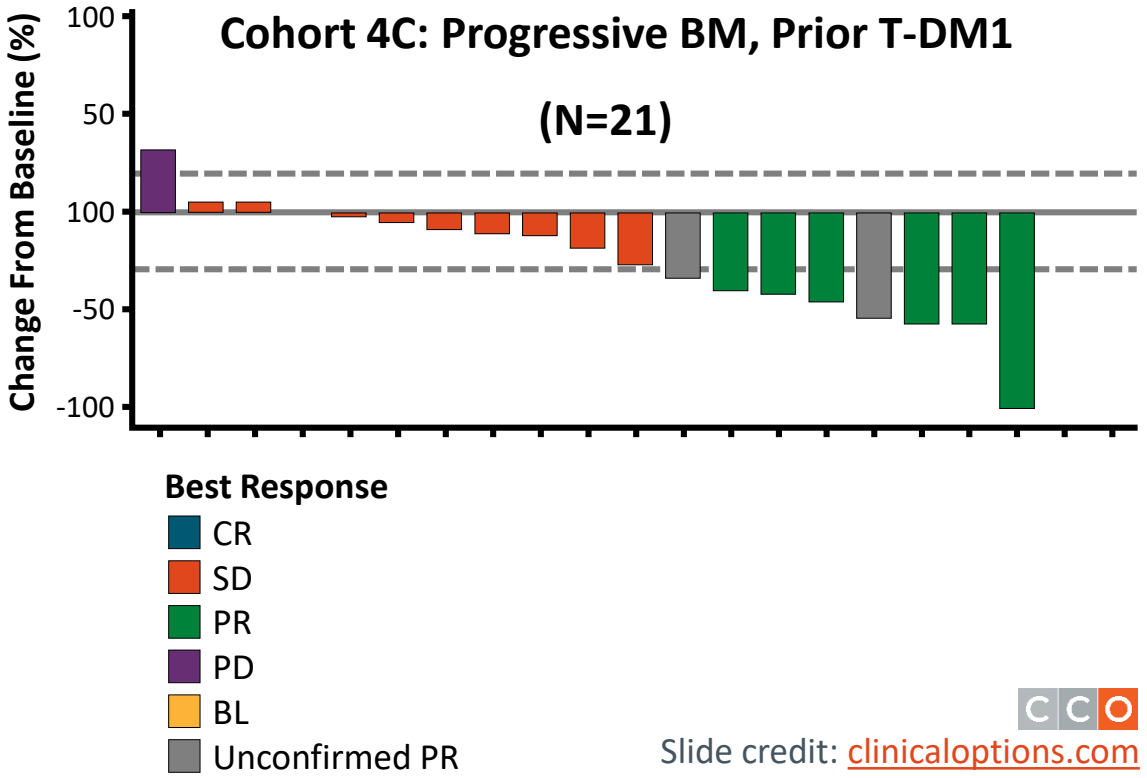
Freedman. SABCS 2022. Abstr PD7-03.

Slide credit: clinicaloptions.com



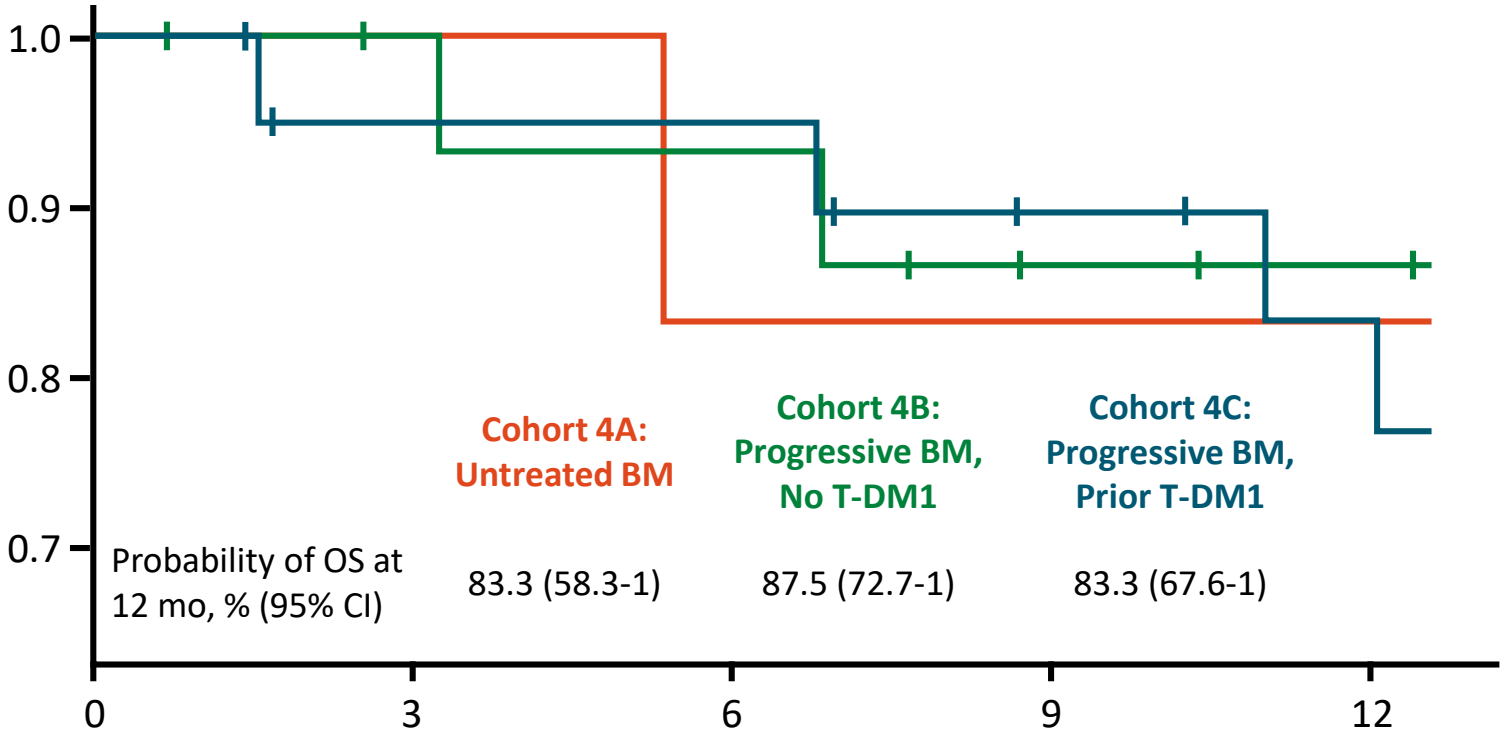


Best RANO-BM CNS Response, n (%)	Cohort 4A:	Cohort 4B:	Cohort 4C:
CNS ORR%	33.3 (4.3-77.7)	29.4 (10.3-56.0)	28.6 (11.3-52.2)
CNS CR + PR + SD ≥6 mo, %	50.0 (11.8-88.2)	35.3 (14.2-61.7)	33.3 (14.6-57.0)



Slide credit: clinicaloptions.com

TBCRC 022: OS



Patients at Risk, n					
Cohort 4A	6	6	5	5	5
Cohort 4B	17	15	14	11	10
Cohort 4C	21	18	18	15	13

Freedman. SABCS 2022. Abstr PD7-03. Reproduced with permission.

Slide credit: clinicaloptions.com

TBCRC 022: Safety

AE, n (%)	Cohort 4 (N = 44)	
	Grade 2	Grade 3
Diarrhea	14 (32)	10 (23)
Fatigue	11 (25)	1 (2)
AST increased	6 (14)	3 (7)
Nausea	7 (16)	1 (2)
ALT increased	2 (5)	2 (5)
Anorexia	5 (11)	--
Platelet count decreased	4 (9)	1 (2)
Vomiting	4 (9)	--
Abdominal pain	3 (7)	--
Dehydration	1 (2)	2 (5)
Dyspepsia	3 (7)	--

AE, n (%)	Cohort 4 (N = 44)	
	Grade 2	Grade 3
GERD	3 (7)	--
Hypokalemia	--	3 (7)
Mucositis oral	3 (7)	--
Anemia	--	2 (5)
Generalized muscle weakness	2 (5)	--
Peripheral sensory neuropathy	1 (2)	1 (2)

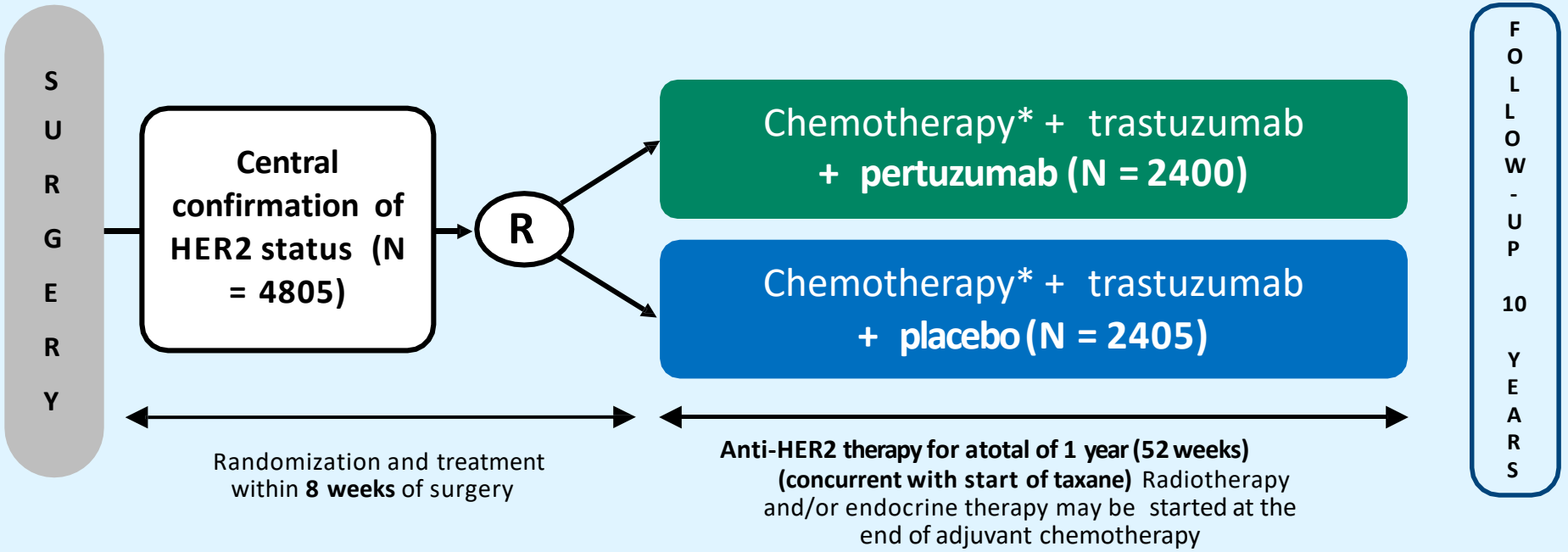
- 1 grade 4 event reported (ALT increased)
- Despite diarrhea prophylaxis, more than one half of patients had grade 2/3 diarrhea

Freedman. SABCS 2022. Abstr PD7-03.

Slide credit: clinicaloptions.com

Early Stage HER2+ Breast Cancer
APHINITY Trial Update

APHINITY TRIAL – Adjuvant Pertuzumab

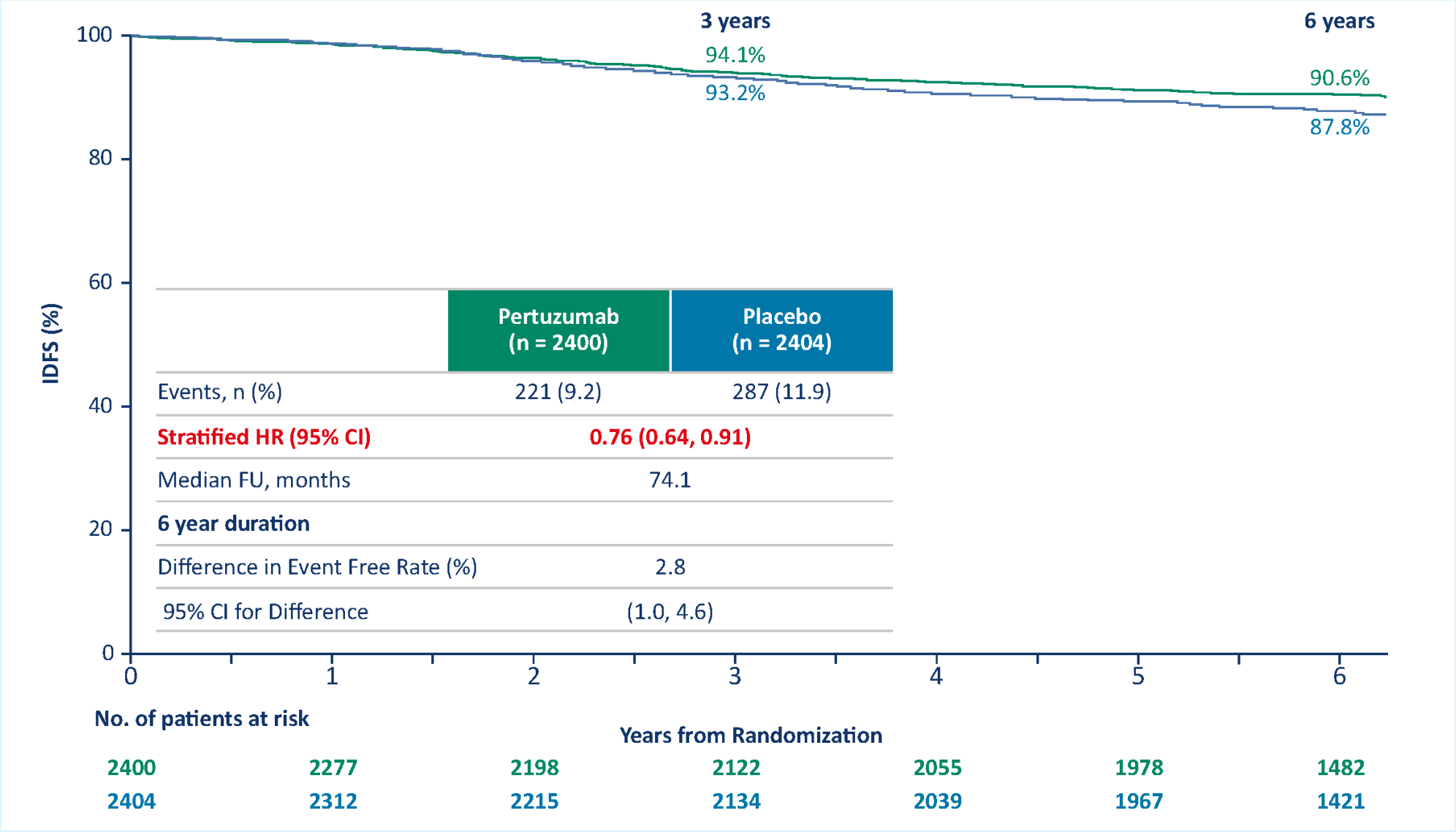


* Standard anthracycline or non-anthracycline (TCH) regimens were allowed: 3–4 x FEC (or FAC) → 3–4 x TH; 4 x AC (or EC) → 4 x TH; 6 x TCH

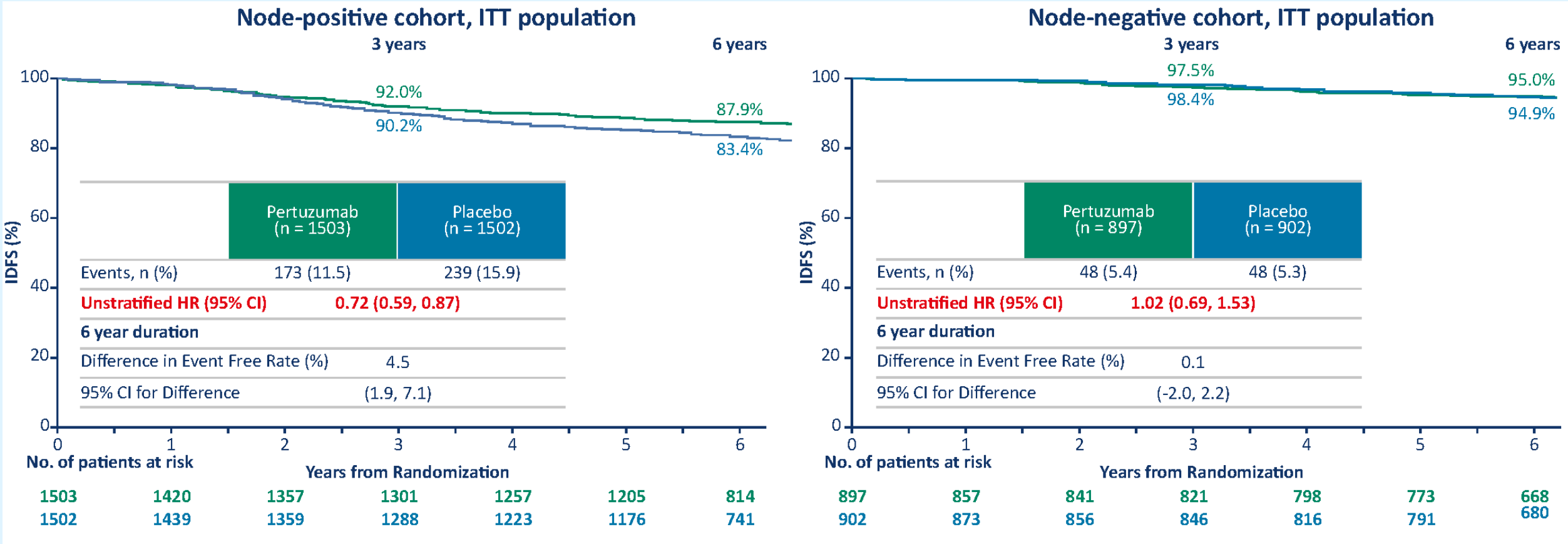
- **Primary endpoint:** IDFS (APHINITY definition differs from STEEP definition)
- **Secondary endpoint:** IDFS with 2nd primary non-breast primary cancers included, DFS, OS, RFI, DRFI, safety, and HRQoL
- **Stratification factors:** nodal status, HR status, chemotherapy regimen, geographic region, Protocol version (A vs. B)
- **Clinical cut off date (CCOD)** at the time of primary analysis was 19 Dec 2016, median follow up of 45.4 months

von Minckwitz et al, N Engl J Med 2017

APHINITY TRIAL – 6 year IDFS



APHINITY TRIAL – 6 year IDFS



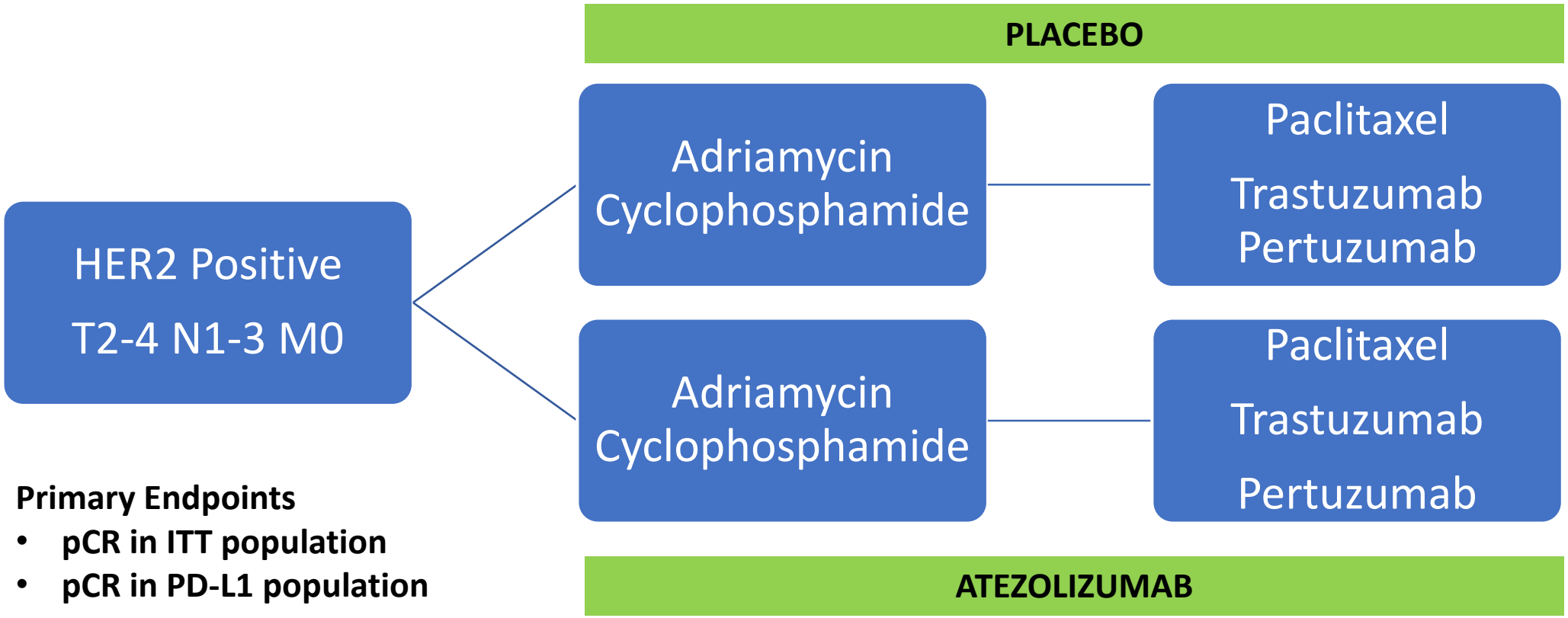
San Antonio Breast Cancer Symposium®, December 10-14, 2019

APHINITY TRIAL – 8 year update

	Pertuzumab	Placebo	
Overall Survival (ITT)	92.7%	92.0%	HR 0.83 p=0.078
Overall Survival (Node Negative)	96.4%	95.5%	HR=0.99
IDFS (ITT)	88.4%	85.8%	HR 0.77 95% 0.66-0.91
IDFS (Node Positive)	86.1%	81.2%	HR 0.72 95% CI 0.66 – 0.91

Early Stage HER2+ Breast Cancer Immune Checkpoint Blockade IMPASSION-050

IMPASSION 050 - Schema

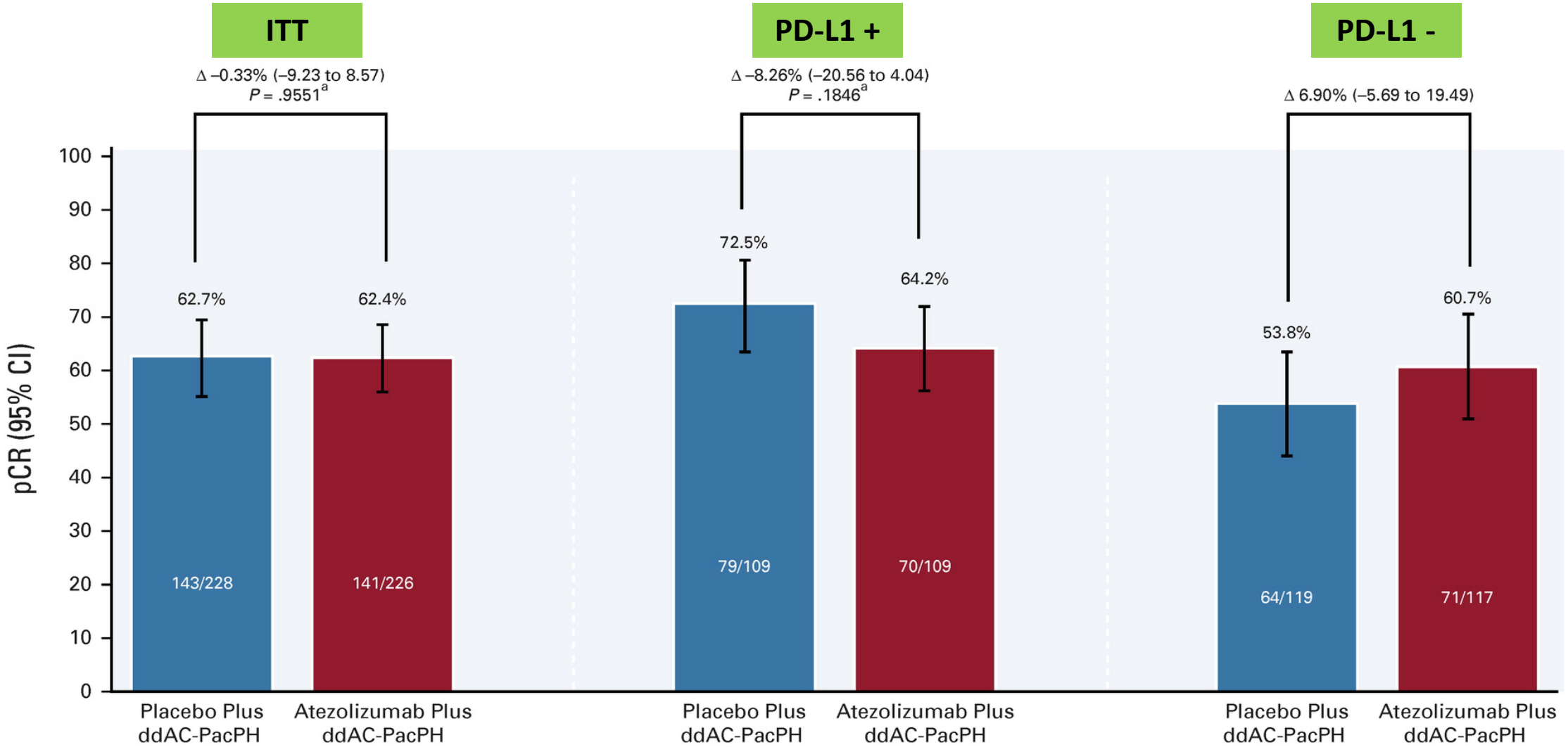


Primary Endpoints

- **pCR in ITT population**
- **pCR in PD-L1 population**

Zhang et al, JCO 2022

IMPASSION 050 - Results



Zhang et al, JCO 2022

IMPASSION 050 - Safety

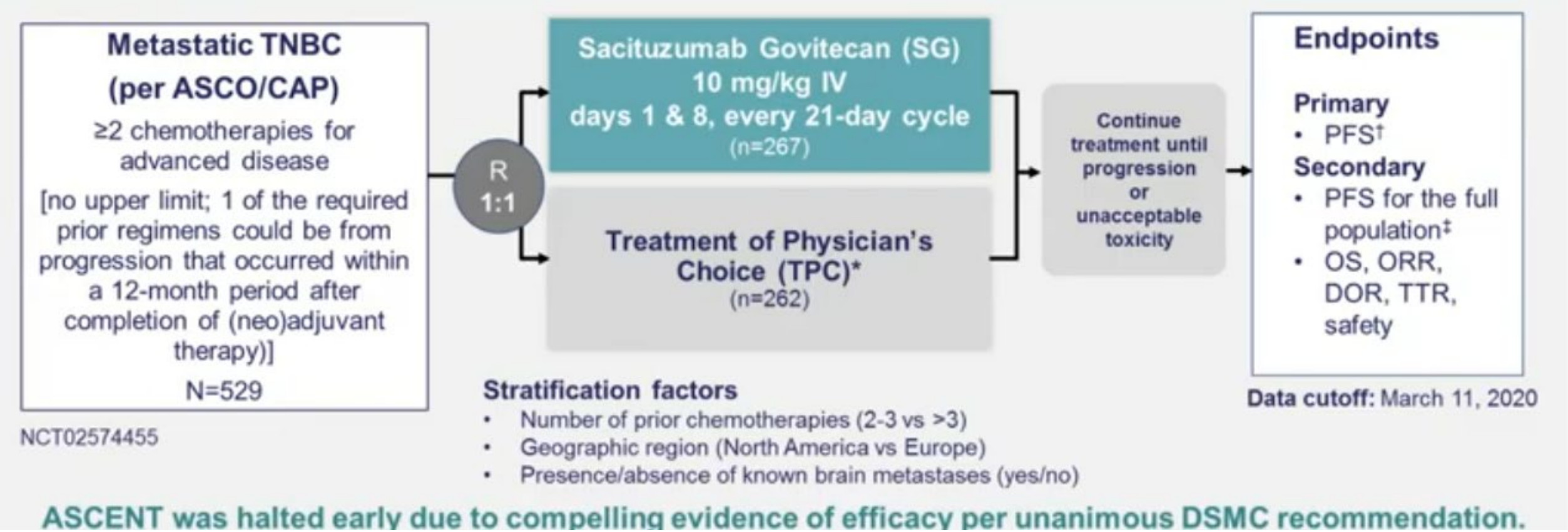
- Atezolizumab vs Placebo
  - Higher incidence of Grade 3-4 adverse events
  - Higher incidence of serious adverse events
  - Deaths (n=5) in the Atezolizumab arm (Neoadjuvant phase)
  - Expected higher rate of immune related adverse events

Zhang et al, JCO 2022

TRIPLE NEGATIVE BREAST CANCER

SACITUZUMAB GOVITECAN

ASCENT Trial – Sacituzumab Govitecan

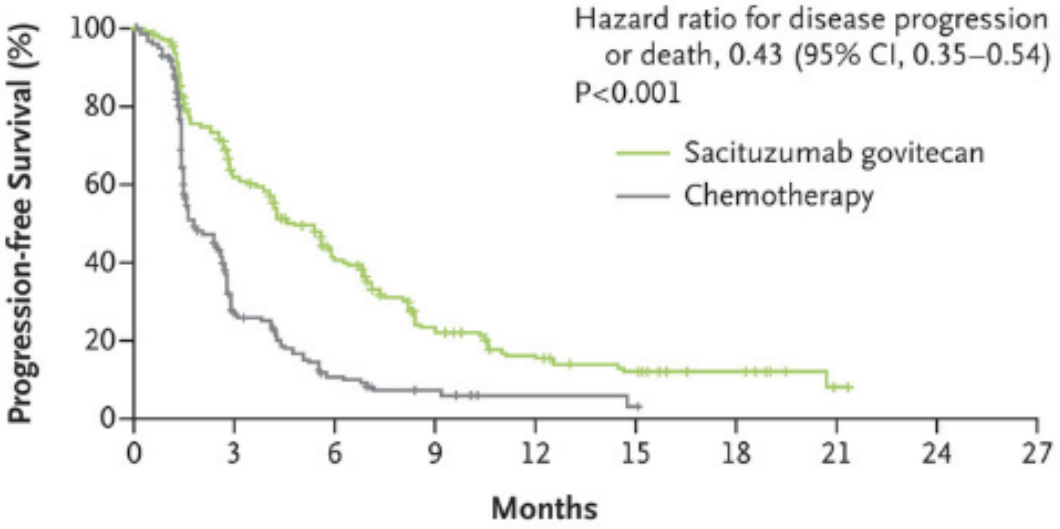


Bardia NEJM 2021

ASCENT Trial – Sacituzumab Govitecan

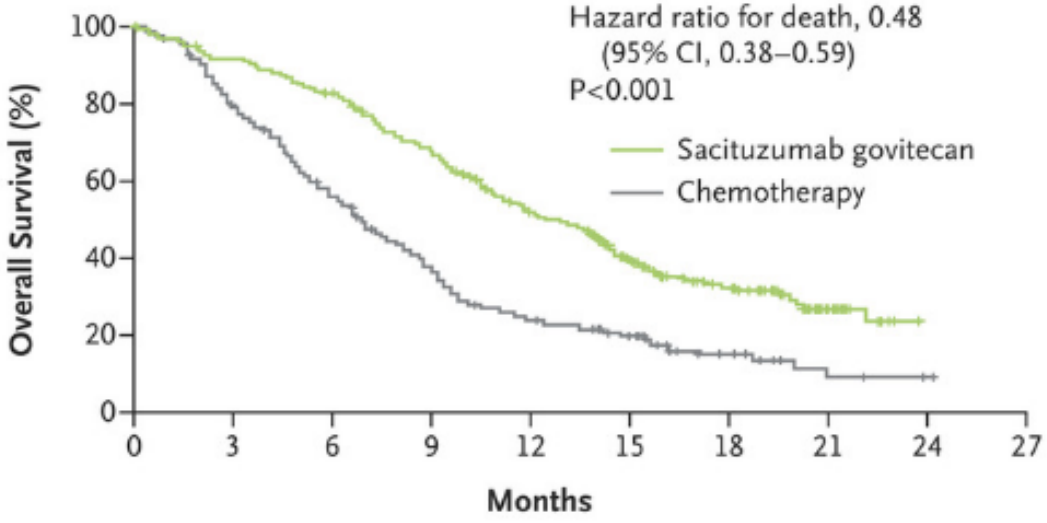
PFS

	No. of Patients	No. of Events	Median Progression-free Survival
			mo (95% CI)
Sacituzumab Govitecan	267	190	4.8 (4.1–5.8)
Chemotherapy	262	171	1.7 (1.5–2.5)



OVERALL SURVIVAL

	No. of Patients	No. of Events	Median Overall Survival
			mo (95% CI)
Sacituzumab Govitecan	235	155	12.1 (10.7–14.0)
Chemotherapy	233	185	6.7 (5.8–7.7)



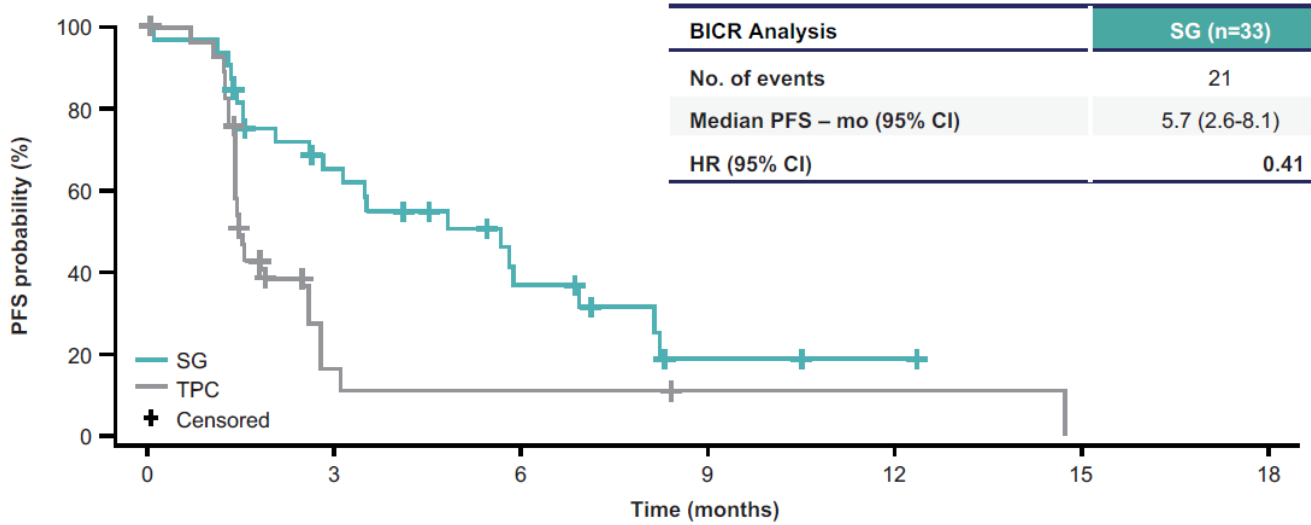
Bardia NEJM 2021

ARTICLE OPEN

Sacituzumab govitecan as second-line treatment for metastatic triple-negative breast cancer—phase 3 ASCENT study subanalysis

- Subgroup Analysis
  - Sacituzumab Govitecan (n=33/235)
  - TPC (n=32/233)
- Most common 1L metastatic therapies
  - Carboplatin, Gemcitabine, Capecitabine
- Safety profile similar to overall ASCENT trial
  - Most common SG TRAEs: Neutropenia, Diarrhea, Alopecia

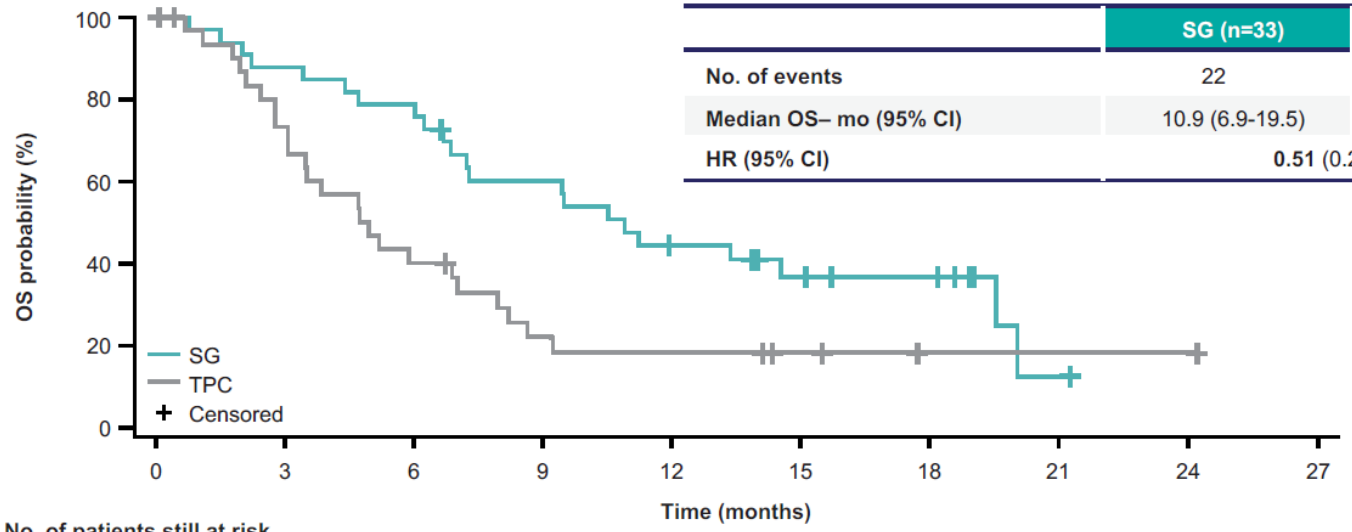
Carey et al NPJ Breast 2022



BICR Analysis	SG (n=33)	TPC (n=32)
No. of events	21	23
Median PFS – mo (95% CI)	5.7 (2.6-8.1)	1.5 (1.4-2.6)
HR (95% CI)	**0.41** (0.22-0.76)	

No. of patients still at risk

SG	33	32	23	19	16	12	8	6	5	2	2	1	1	0	0	0
TPC	32	28	8	3	2	2	2	2	2	1	1	1	1	1	1	0



	SG (n=33)	TPC (n=32)
No. of events	22	24
Median OS– mo (95% CI)	10.9 (6.9-19.5)	4.9 (3.1-7.1)
HR (95% CI)	**0.51** (0.28-0.91)	

No. of patients still at risk

SG	33	32	31	29	28	26	26	21	19	19	17	15	13	13	11	9	7	7	7	4	2	1	0	0	0	0
TPC	32	29	27	22	17	14	12	10	8	6	5	5	5	5	5	3	2	2	1	1	1	1	1	1	1	0

Carey et al NPJ Breast 2022

Health-related quality of life in the phase III ASCENT trial of sacituzumab govitecan versus standard chemotherapy in metastatic triple-negative breast cancer

- EORTC QLQ-C30
  - Sacituzumab Govitecan (n=236)
  - TPC (n=183)
- Quality of life instrument on day 1 of each cycle
- TPC (Capecitabine, eribulin, vinorelbine, or gemcitabine)

Loibl et al EJC 2023

Health-related quality of life in the phase III ASCENT trial of sacituzumab govitecan versus standard chemotherapy in metastatic triple-negative breast cancer

- SG superior to TPC with longer time to clinically meaningful worsening scores in
  - Physical functions: 22.1 vs 12.1 weeks
  - Role functioning: 11.4 vs 7.1 weeks
  - Fatigue: 7.7 vs 6.0 weeks
  - Pain: 21.6 vs 9.9 weeks
- SG inferior to TPC
  - Nausea/ vomiting scores
  - Diarrhea

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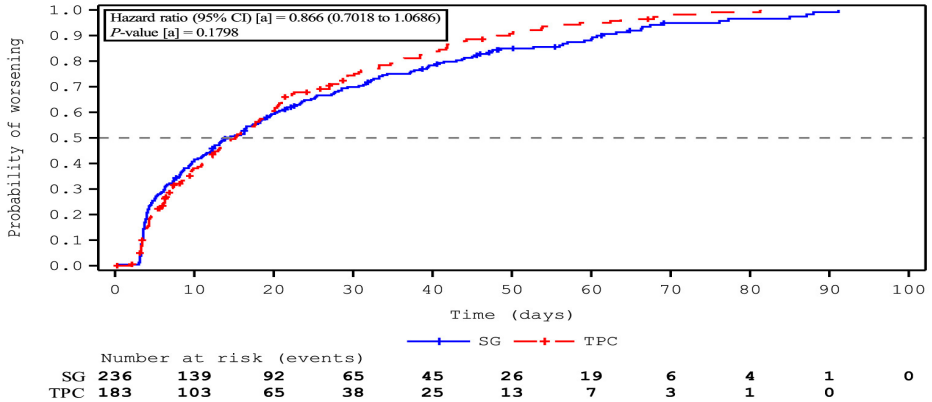
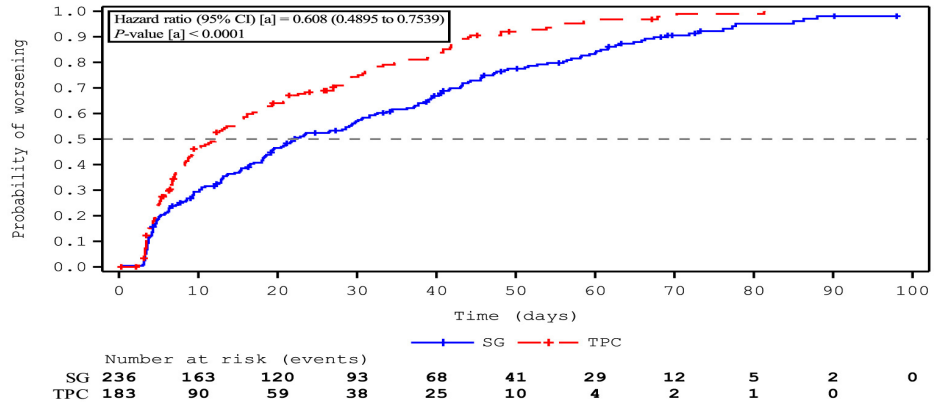
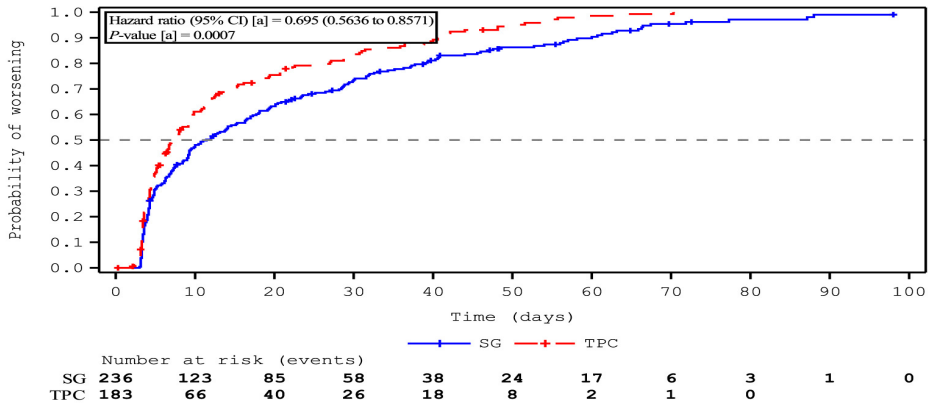
Global health status/QoL



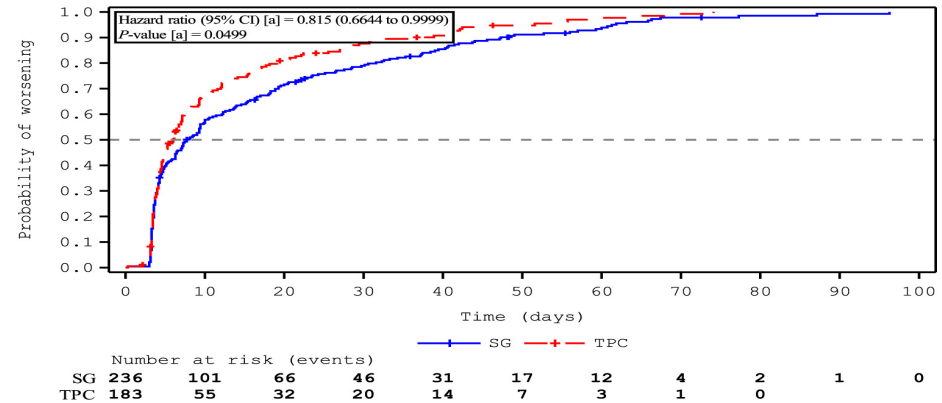
Physical functioning



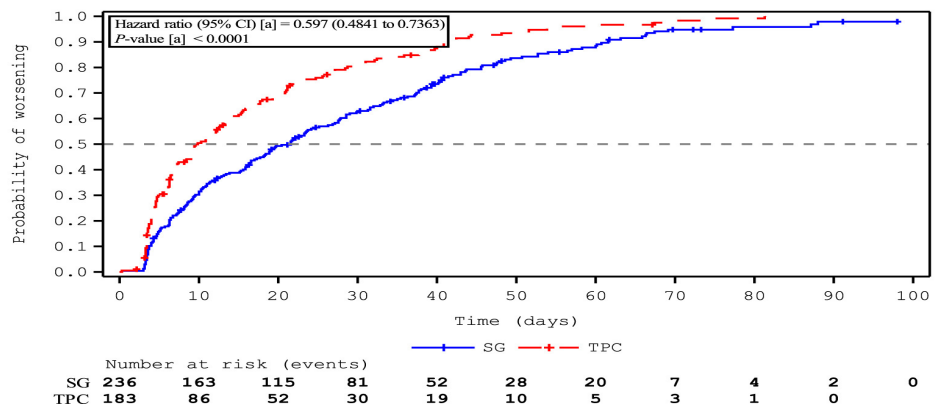
Role functioning



Fatigue



Pain



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CARBOPLATIN

San Antonio Breast Cancer Symposium®, December 6-10, 2022

Addition of platinum to sequential taxane-anthracycline neoadjuvant chemotherapy in patients with triple-negative breast cancer: A phase III randomized controlled trial

Sudeep Gupta, M.D., D.M.; on behalf of

Nita S Nair, Rohini W Hawaldar, Vaibhav Vanmali, Vani Parmar, Seema Gulia, Jaya Ghosh, Shalaka Joshi, Rajiv Sarin, Tabassum Wadasadawala, Tejal Panhale, Sangeeta Desai, Tanuja Shet, Asawari Patil, Garvit Chitkara, Sushmita Rath, Jyoti Bajpai, Meenakshi Thakur, and Rajendra A Badwe.

Breast Cancer Working Group, Tata Memorial Centre, Mumbai

Funded by Tata Memorial Centre, Mumbai

TMC Neoadjuvant Platinum TNBC Study

- TNBC (1% cutoff for ER & PR)
- No evidence of M1
- Fit for anthracycline
- T1-T4, N0-3

R

Platinum
Pacli+Carbo → AC/EC

Control
Pacli → AC/EC

Surgery → Radiotherapy

Breast conserving surgery
OR
Mastectomy

Stratification

Menopausal Status
(Pre+Peri, Post)

Clinical Stage
OBC (cT_{1-3},N_{0-1}, M_0)
LABC (cT_4/N_{2-3}, M_0)

Platinum Arm:
Paclitaxel 100/m2 + Carboplatin (AUC-2) once per week X 8w*
followed by
[Doxorubicin (60/m2) or Epirubicin (90/m2)] + Cyclo (600/m2) every 2 weeks or 3 weeks X 4 cycles

Control Arm: Same as above, without carboplatin

*Gupta S, et al. Single agent weekly paclitaxel as neoadjuvant chemotherapy in locally advanced breast cancer: a feasibility study. Clin Oncol (R Coll Radiol). 2012 Nov;24(9):604-9

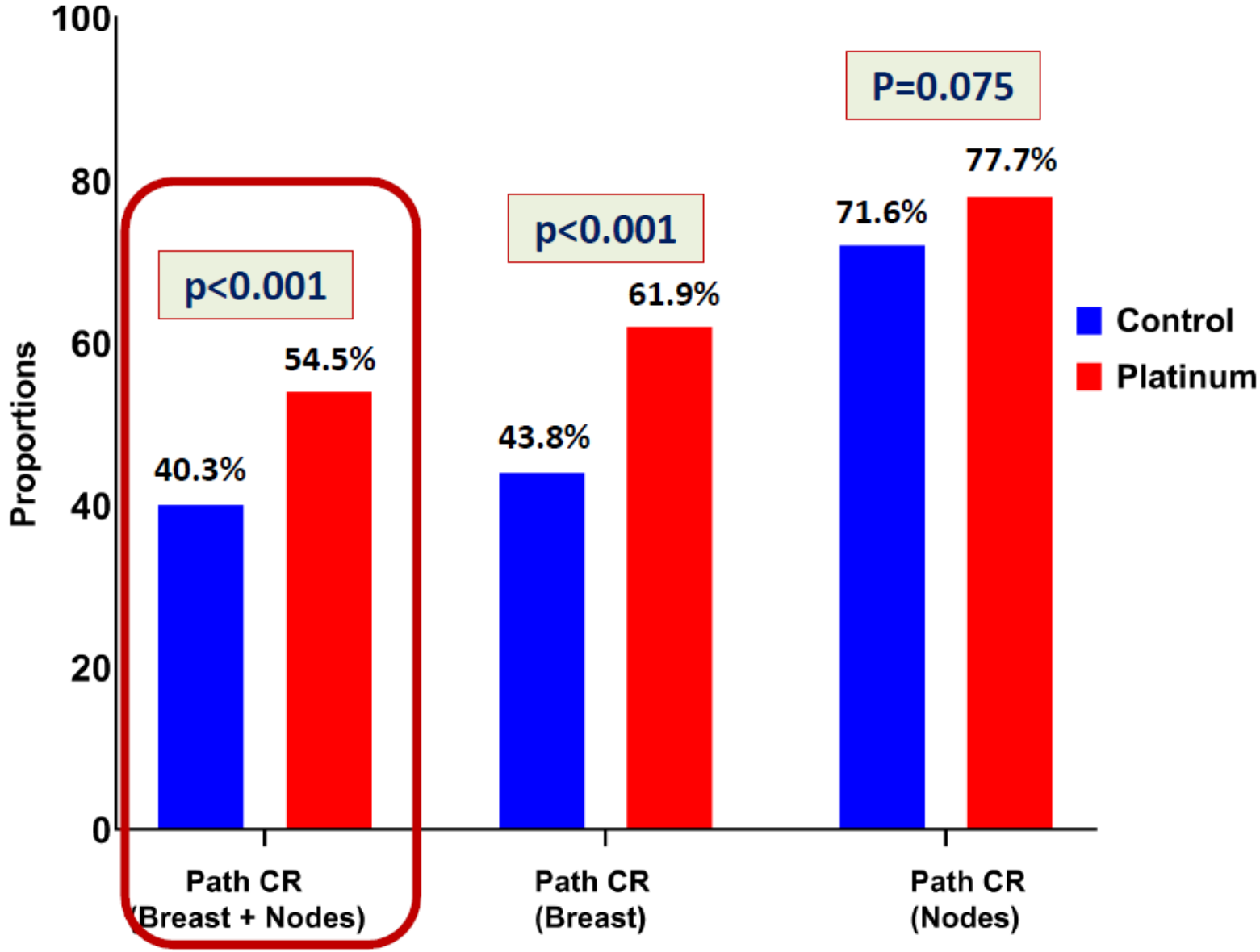
Patient & Tumor Characteristics

	Control Arm (N=356)	Platinum Arm (N=361)	Total (N=717)
Age (years)			
Median (Range)	46 (26-69)	46 (25-67)	46 (25-69)
≤ 50 years	245 (68.8%)	255 (70.6%)	500 (69.7%)
> 50 years	111 (31.2%)	106 (29.4%)	217 (30.3%)
Menopausal Status			
Pre- or Peri-menopausal	209 (58.7%)	209 (57.9%)	418 (58.3%)
Post-menopausal	147 (41.3%)	152 (42.1%)	299 (41.7%)
Family History of Any Cancer			
Yes	72 (20.2%)	62 (17.2%)	134 (18.7%)
No	284 (79.8%)	299 (82.8%)	583 (81.3%)

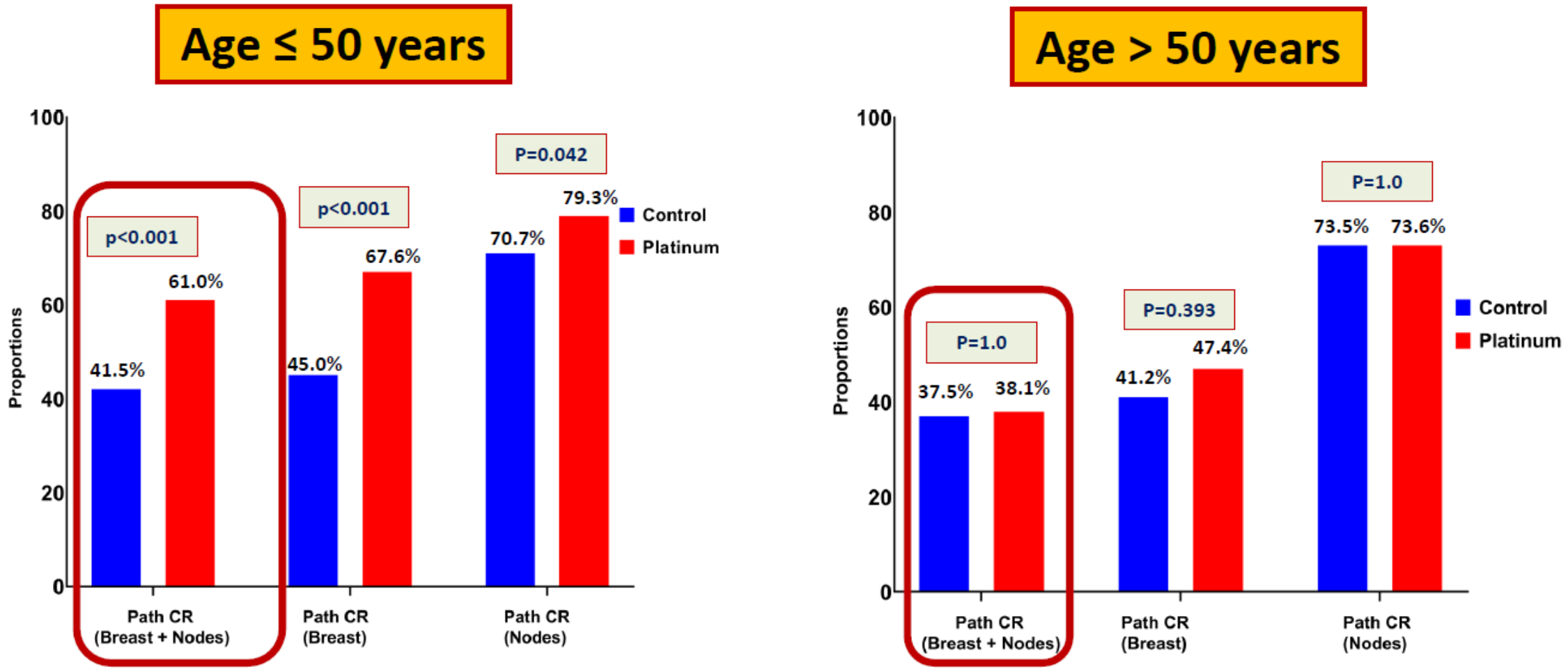
Patient & Tumor Characteristics

	Control Arm (N=356)	Platinum Arm (N=361)	Total (N=717)
Clinical Stage (pre-NACT)			
Operable (cT1-3, N0-1)	142 (39.9%)	143 (39.6%)	285 (39.7%)
Locally Advanced (cT4 / N2-3)	214 (60.1%)	218 (60.4%)	432 (60.3%)
Clinical Node Status (pre-NACT)			
Negative	39 (11.0%)	41 (11.4%)	80 (11.2%)
Positive	317 (89.0%)	320 (88.6%)	637 (88.8%)
Clinical T-size (pre-NACT) (cm)			
Median (Range)	6.0 (1.2-20.0)	6.0 (1.5-20.0)	6.0 (1.2-20.0)
≤ 5 cm	79 (22.2%)	81 (22.4%)	160 (22.3%)
> 5 cm	277 (77.8%)	280 (77.6%)	557 (77.7%)

ITT: Pathological Response to NACT by Rx-Arm



Pathological Response to NACT by Age & Rx-Arm

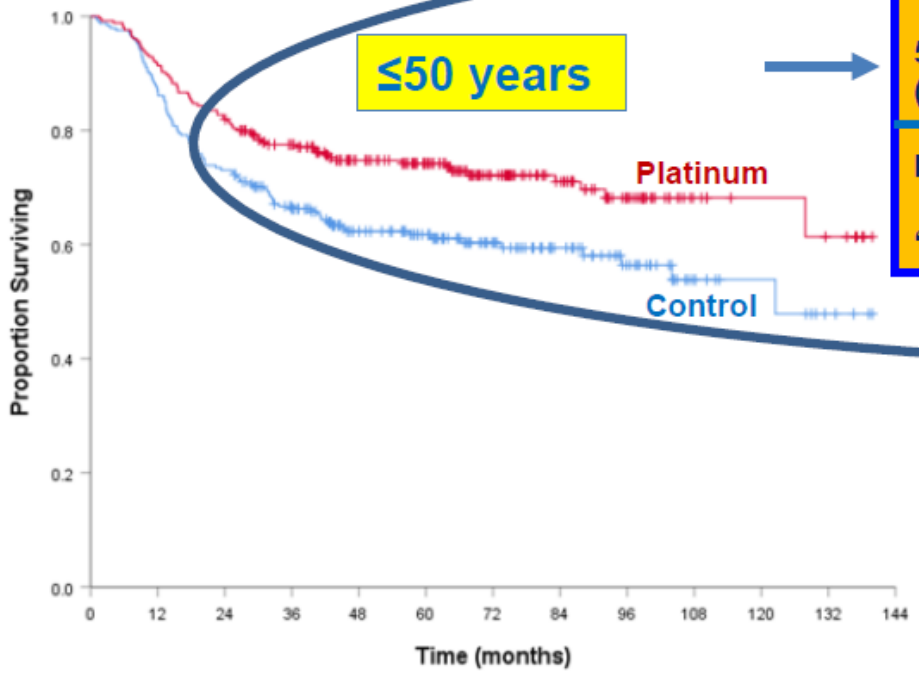


Multivariable (binary logistic) analysis for factors affecting pCR: Rx-Arm X Age interaction significant in a model including Rx-Arm, Age, cT size, cN status, Family History

Event-free Survival in Younger and Older Patients

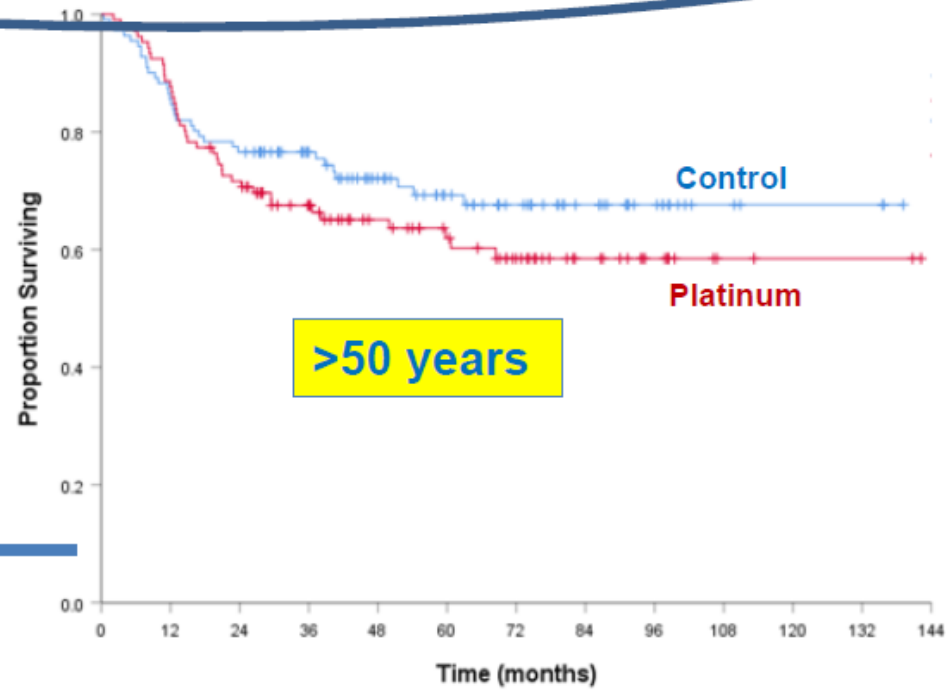
≤50 years

	Platinum	Control
5-year EFS (95% CI)	74.2% (68.71 - 79.69%)	61.7% (55.43 - 67.97%)
HR (95% CI)	0.642 (0.473 - 0.871)	
'p'	0.004	



Control	245	213	179	149	115	98	69	49	32	14	9	4
Platinum	255	233	209	180	145	122	85	62	37	14	10	8

>50 years

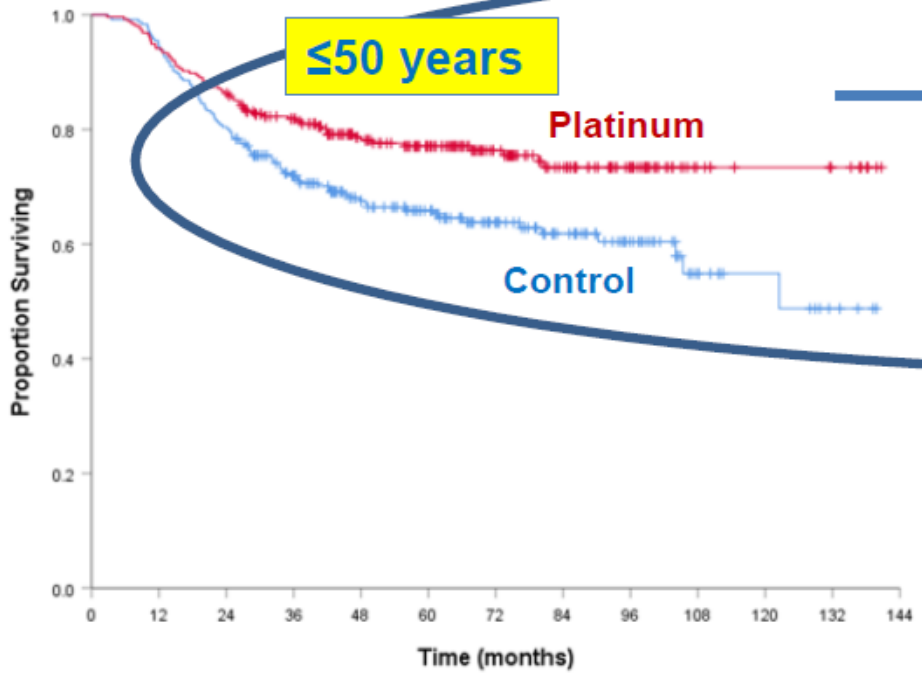


	Platinum	Control
5-year EFS (95% CI)	62.0% (52.2 - 71.8%)	69.3% (60.28 - 78.32%)
HR (95% CI)	1.309 (0.825-2.076)	
'p'	0.253	

Control	111	95	85	69	54	43	32	21	13	5	3	3
Platinum	106	93	75	59	45	37	27	17	10	3	2	2

Overall Survival in Younger and Older Patients

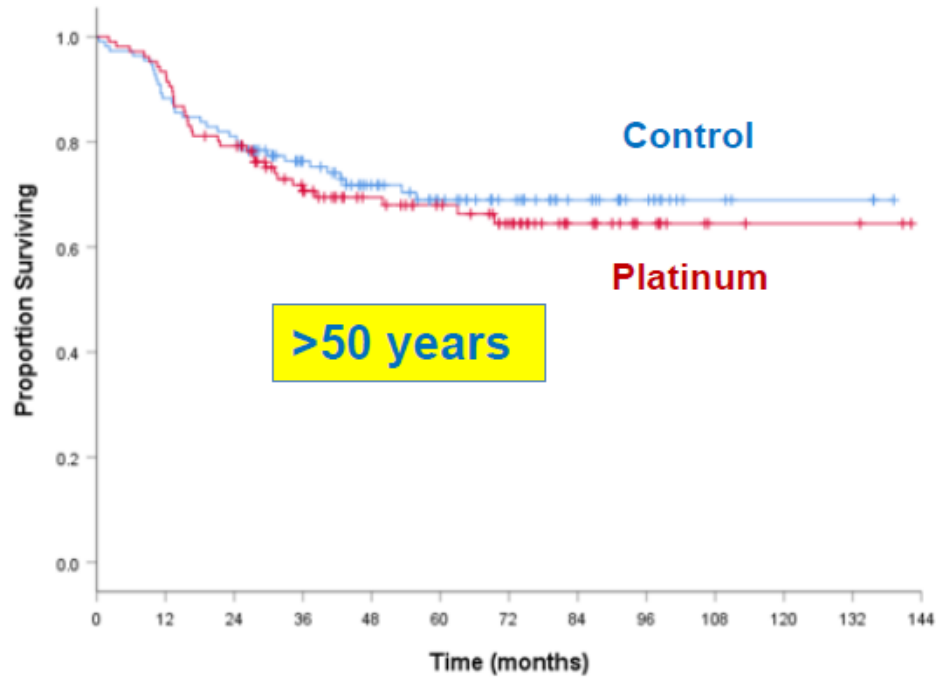
≤50 years



	Platinum	Control
5-year OS (95% CI)	77.1% (71.81 - 82.39%)	65.9% (59.82 - 71.98%)
HR (95% CI)	0.611 (0.440 - 0.848)	
'p'	0.003	

Control	245	232	197	160	125	104	74	53	35	15	9	4
Platinum	255	240	220	190	153	127	91	64	40	15	11	9

>50 years



	Platinum	Control
5-year OS (95% CI)	68.0% (58.79 - 77.21%)	68.9% (59.69 - 78.11%)
HR (95% CI)	1.132 (0.698 - 1.835)	
'p'	0.615	

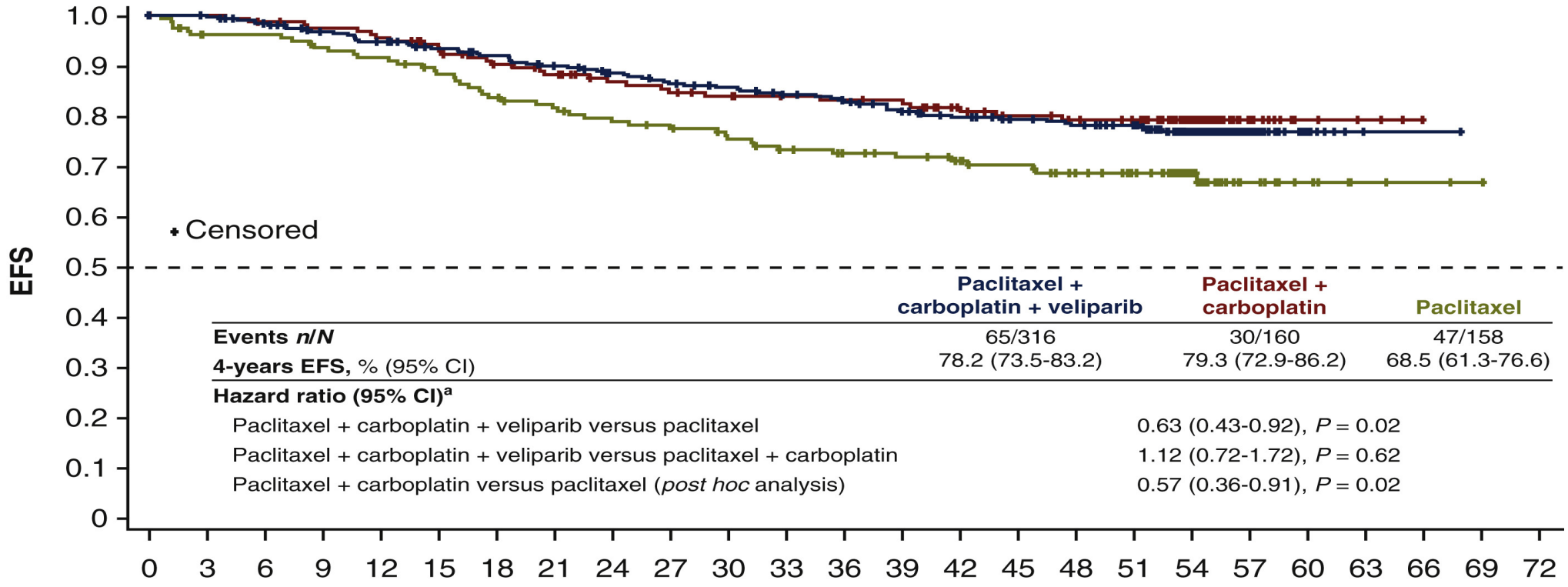
Control	111	98	90	69	54	43	32	21	13	5	3	3
Platinum	106	99	83	62	48	41	31	19	11	4	3	3

Conclusion

- Addition of Carboplatin improved pCR, PFS, and OS
  - Benefit seems to be limited to younger / pre-perimenopausal women
- Patients who achieve a pCR have excellent outcomes regardless of age / menopausal status
- Pitfalls
  - Paclitaxel 8 weeks
  - No pembrolizumab used. Now standard since KEYNOTE-522
  - No adjuvant capecitabine

ORIGINAL ARTICLE

Long-term efficacy and safety of addition of carboplatin with or without veliparib to standard neoadjuvant chemotherapy in triple-negative breast cancer: 4-year follow-up data from BrighTNess, a randomized phase III trial



	Paclitaxel + carboplatin + veliparib	Paclitaxel + carboplatin	Paclitaxel
Events *n/N*	65/316	30/160	47/158
4-years EFS, % (95% CI)	78.2 (73.5-83.2)	79.3 (72.9-86.2)	68.5 (61.3-76.6)
Hazard ratio (95% CI)[a]			
Paclitaxel + carboplatin + veliparib versus paclitaxel		0.63 (0.43-0.92), *P* = 0.02	
Paclitaxel + carboplatin + veliparib versus paclitaxel + carboplatin		1.12 (0.72-1.72), *P* = 0.62	
Paclitaxel + carboplatin versus paclitaxel (*post hoc* analysis)		0.57 (0.36-0.91), *P* = 0.02	

Number of patients at risk

P + C + V	316	311	301	290	283	273	266	257	248	241	235	228	222	213	206	199	195	188	130	28	9	1	1	0
P + C	160	157	154	151	148	143	134	129	121	118	115	112	111	110	102	97	94	91	55	13	5	3	0	
P	158	147	147	142	139	132	125	120	115	112	107	102	98	95	91	87	80	74	41	12	7	3	2	1	0

Geyer et al, Annals 2022

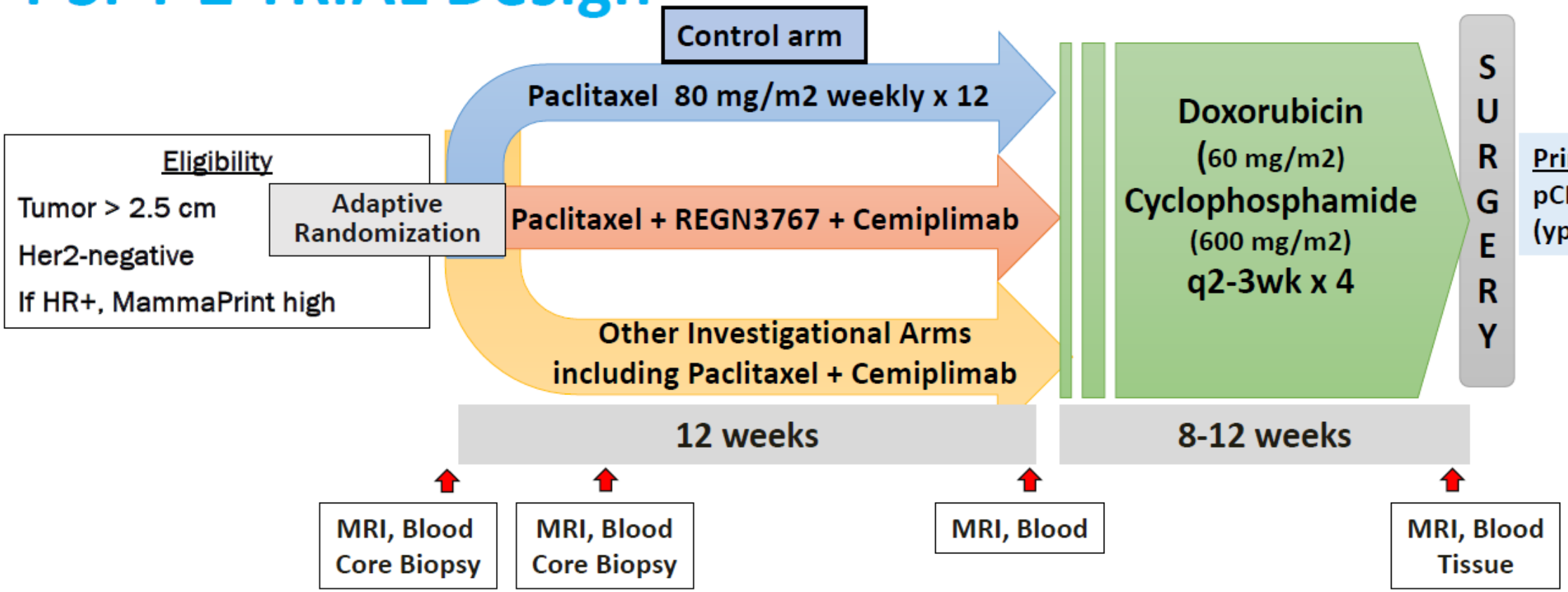
NEW AGENTS

Evaluation of anti-PD-1 Cemiplimab plus anti-LAG-3 REGN3767 in Combination with Paclitaxel in Early-Stage, High-Risk HER2-negative Breast Cancer: Results from the Neoadjuvant I-SPY 2 TRIAL

Claudine Isaacs, Rita Nanda, Christina Yau, Jo Chien, Megna Trivedi, Erica Stringer-Reasor, Christos Vaklavas, Judy Boughey, Amy Sanford, Anne Wallace, Amy Clark, Alexandra Thomas, Kathy Albain, Laura Kennedy, Tara Sanft, Kevin Kalinsky, Heather Han, Williams N, Mili Arora, Anthony Elias, Carla Falkson, Smita Asare, Ruixiao Lu, Maria Pitsiouni, Amy Wilson, Jane Perlmutter, Hope S Rugo, Richard Schwab, Frasier Symmans, Nola Hylton, Laura Van 't Veer, Douglas Yee, Angela DeMichele, Don Berry, Laura Esserman

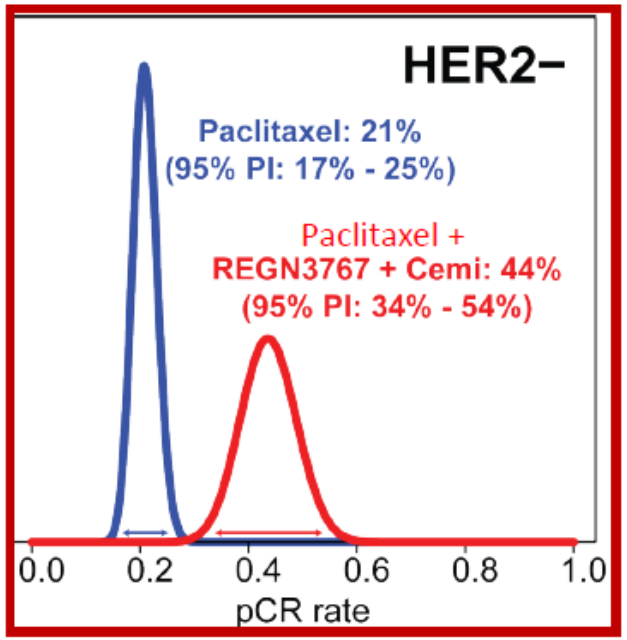
on behalf of the I-SPY 2 TRIAL Consortium

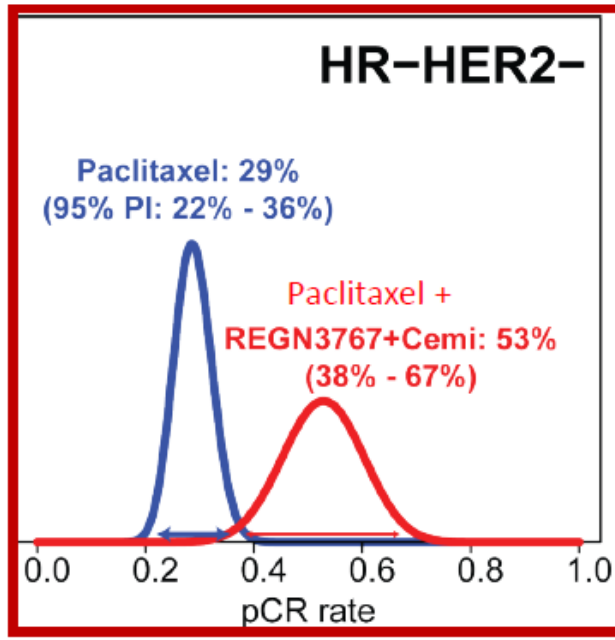
I-SPY 2 TRIAL Design

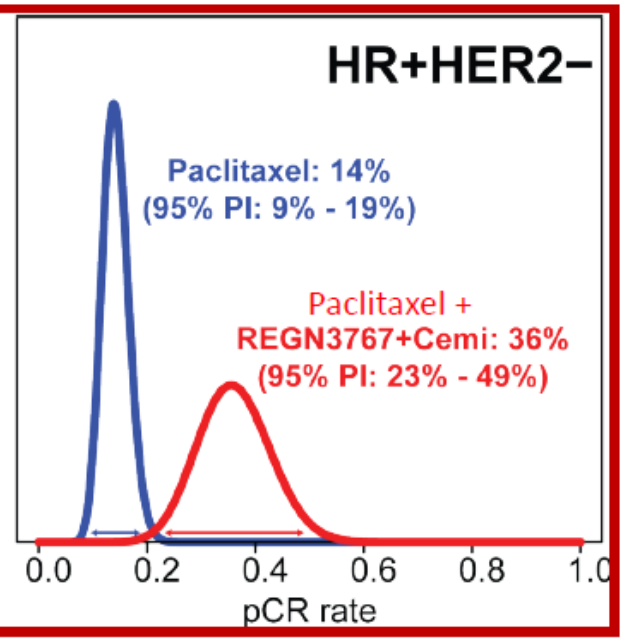


Agent	Dose	Route	Treatment Week
REGN3767	1600 mg q3wks	IV	wk 1,4,7,10
Cemiplimab	350 mg q3wks	IV	wk 1,4,7,10
Paclitaxel	80 mg/m^2 q1wk	IV	wk 1–12

Efficacy Analysis



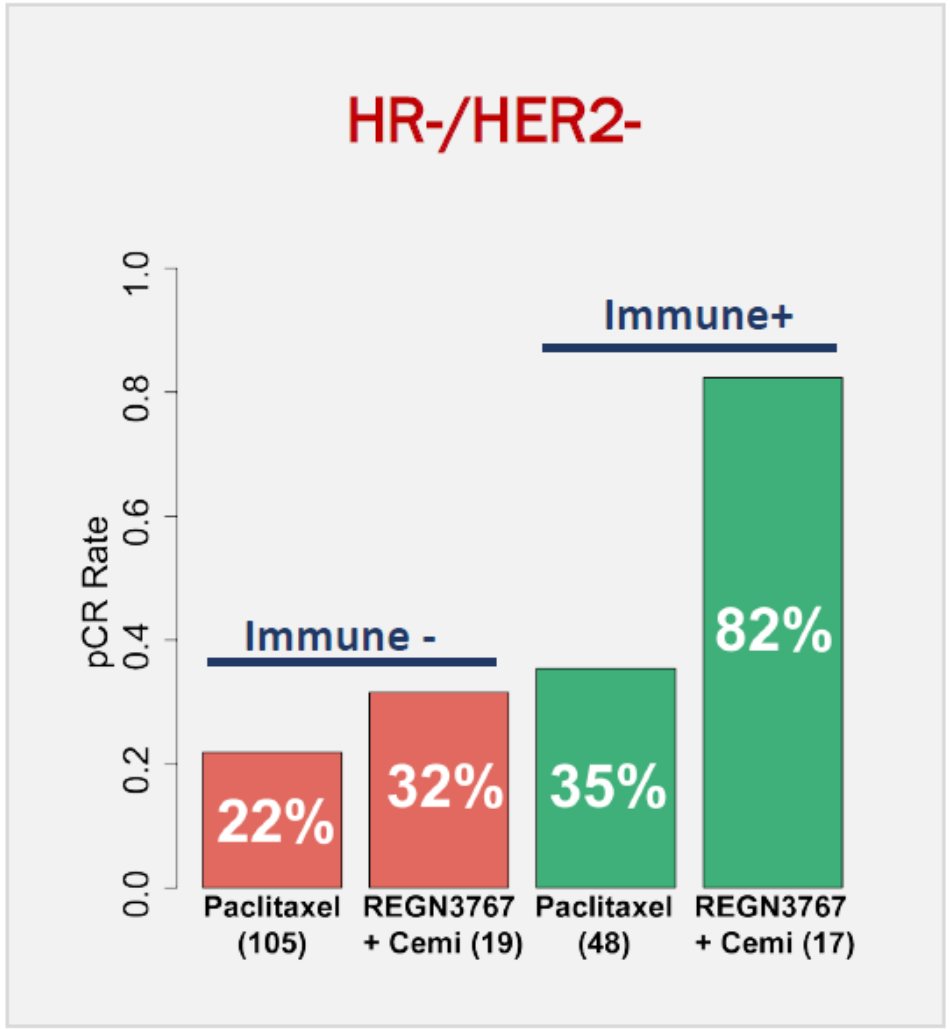


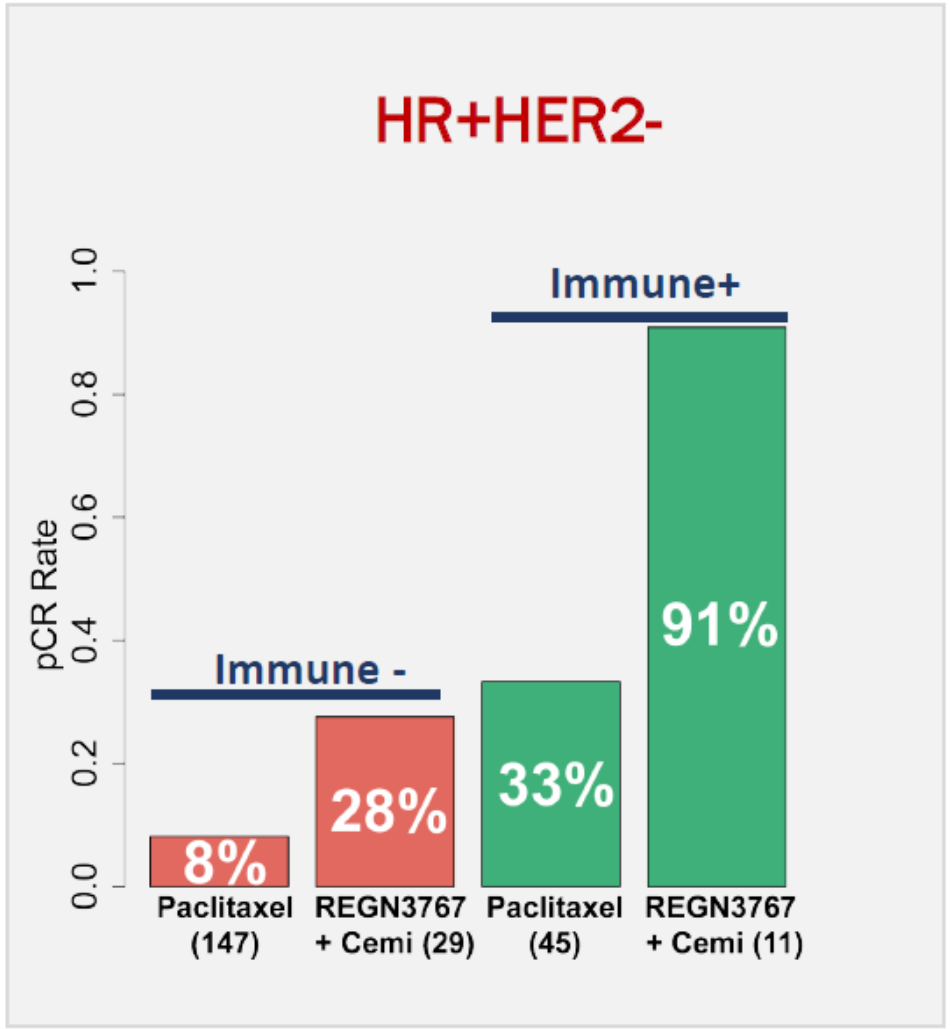


Signature	Estimated pCR Rate (95% Probability Interval)		Probability Pac + REGN3767 + Cemi Superior to Control	Predictive Probability of Success in Phase 3 (relative to Control)
	Pac + REGN3767 + Cemi (n=76)	Control (n=350)		
HER2-	44% (34% - 54%)	21% (17% - 25%)	>0.999	0.955
HR-HER2-	53% (38% - 67%)	29% (22% - 36%)	0.999	0.915
HR+HER2-	36% (23% - 49%)	14% (9% - 19%)	>0.999	0.940

Pac + REGN3767 + Cemiplimab graduated in all 3 eligible biomarker signatures by demonstrating increased pCR

pCR by HR status and Immune Subtype





Observed (not modeled) pCR rates are shown
345 control and 76 cemi+REGN3767 of primary efficacy analysis population have ImPrint data

Immune-Related Adverse Events (irAEs)

40 (53%) patients in REGN3767 + Cemi arm experienced irAE

irAE	Grade 1/2	Grade 3	All Grade
Hypothyroidism	24 (32%)	0 (0%)	24 (32%)
Adrenal insufficiency/ Hypophysitis	10 (12%)	6 (5%)	16 (21%)
Type 1 diabetes mellitus	0	3 (4%)	3 (4%)
Autoimmune hepatitis	0	2 (3%)	2 (3%)
Pneumonitis	2 (3%)	0 (0%)	2 (3%)
Renal failure acute	1 (1%)*	1 (1%)	2 (3%)

1 case of arthritis (G3)
1 case of immune-related Rash maculo-papular (G3)
1 case of thyroiditis (G2)
No Grade 4+ irAEs

Based on available data as of October 15th, 2022

Conclusions

- Cemiplimab + REGN 3767 effective in HR+ and TNBC tumors
- Immune signature identifies greatest benefit from ICB
- Increased incidence of immune related adverse events

THANK YOU