SUSAN F. SMITH CENTER FOR WOMEN'S CANCERS
Dana-Farber Cancer Institute

HARVARD MEDICAL SCHOOL

Updates for HER2+ Breast Cancer

Wendy Y. Chen, MD, MPH
Dana-Farber Cancer Institute

DISCLOSURES

There are no financial disclosures relevant to this presentation.

Outline

- Metastatic breast cancer
  - Trastuzumab derutexacan
  - Tucatinib
  - Margetuximab
- Adjuvant treatment
  - APHINITY -pertuzumab
  - ATEMPT – TDM1 vs TH
  - KATHERINE – TDM1

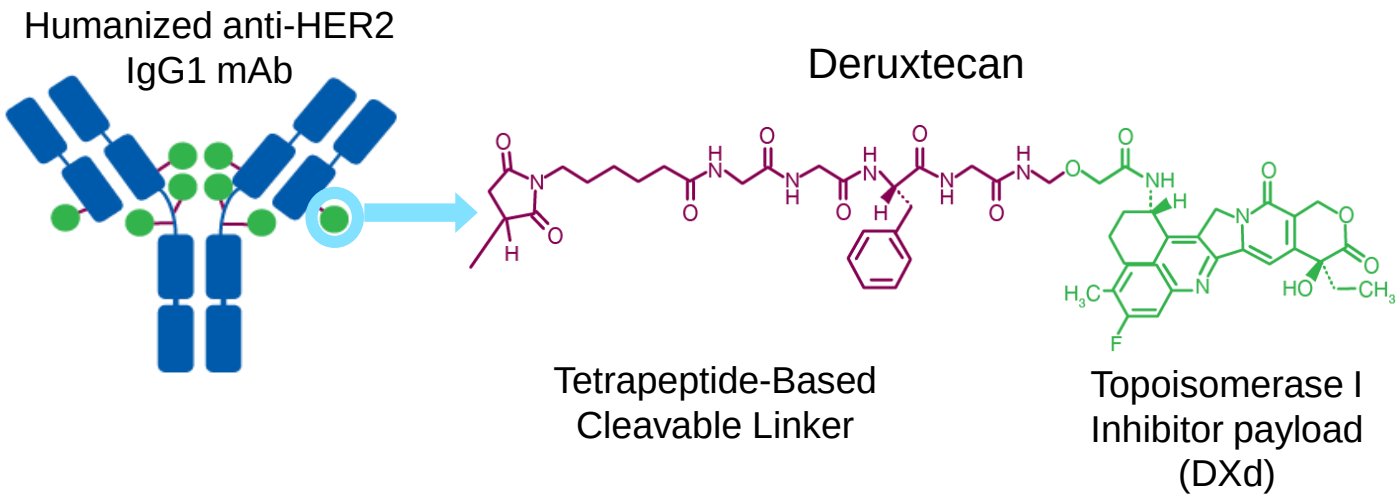
Trastuzumab Deruxtecan (DS-8201)

Antibody drug conjugate with 3 components:

- Humanized anti-HER2 IgG1 monoclonal antibody with same amino acid sequence as trastuzumab
- Potent topoisomerase I inhibitor payload (chemo)
- Tetrapeptide-based cleavable linker

Advantages compared to TDM1

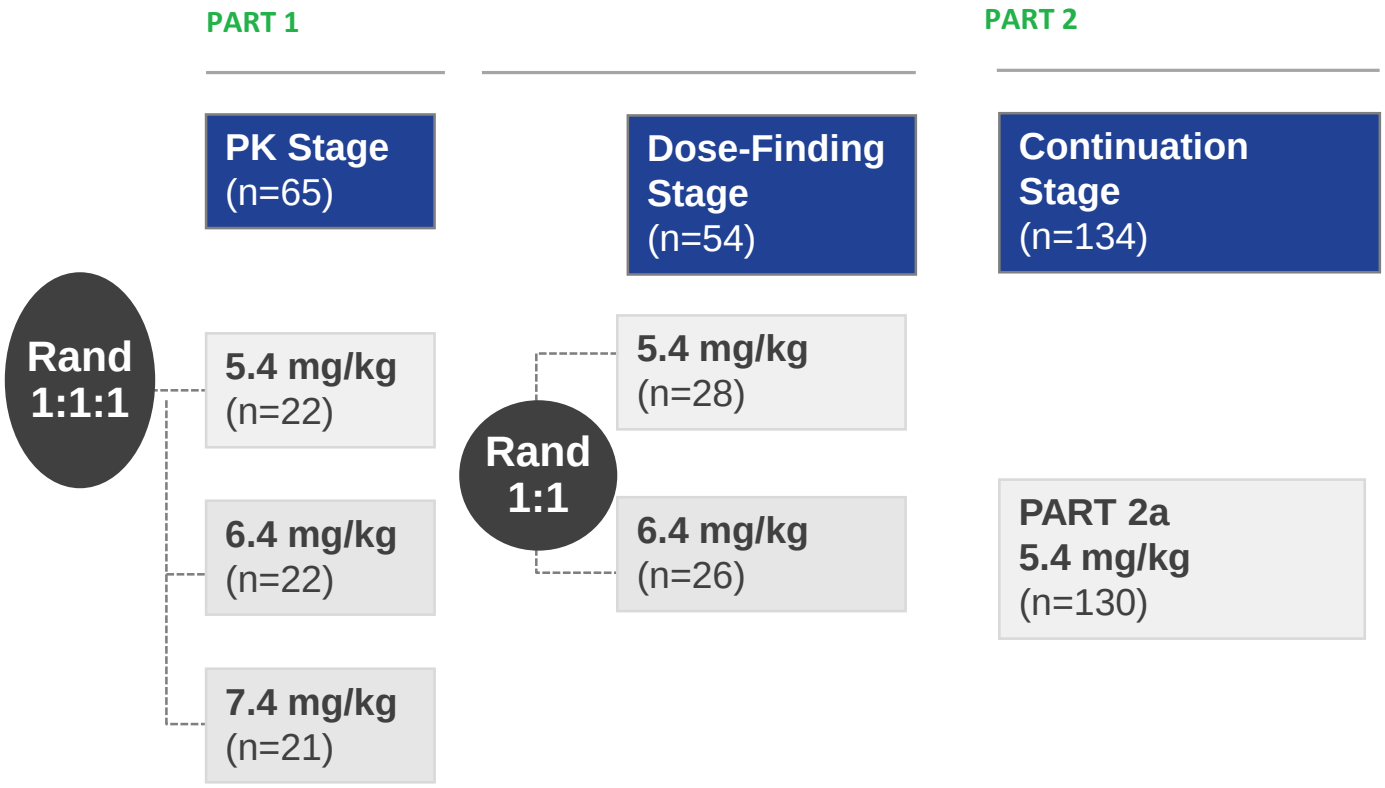
- Higher drug to antibody ratio, payload shorter half life and easily crosses cell membrane



DESTINY-Breast01: open-label,multicenter phase 2 study

Study population

- Unresectable and/or metastatic BC
- HER2-positive (centrally confirmed on archival tissue)
- Prior T-DM1
- Excluded patients with history of significant ILD
- Stable, treated brain metastases were allowed



Accelerated FDA approval December 20, 2019

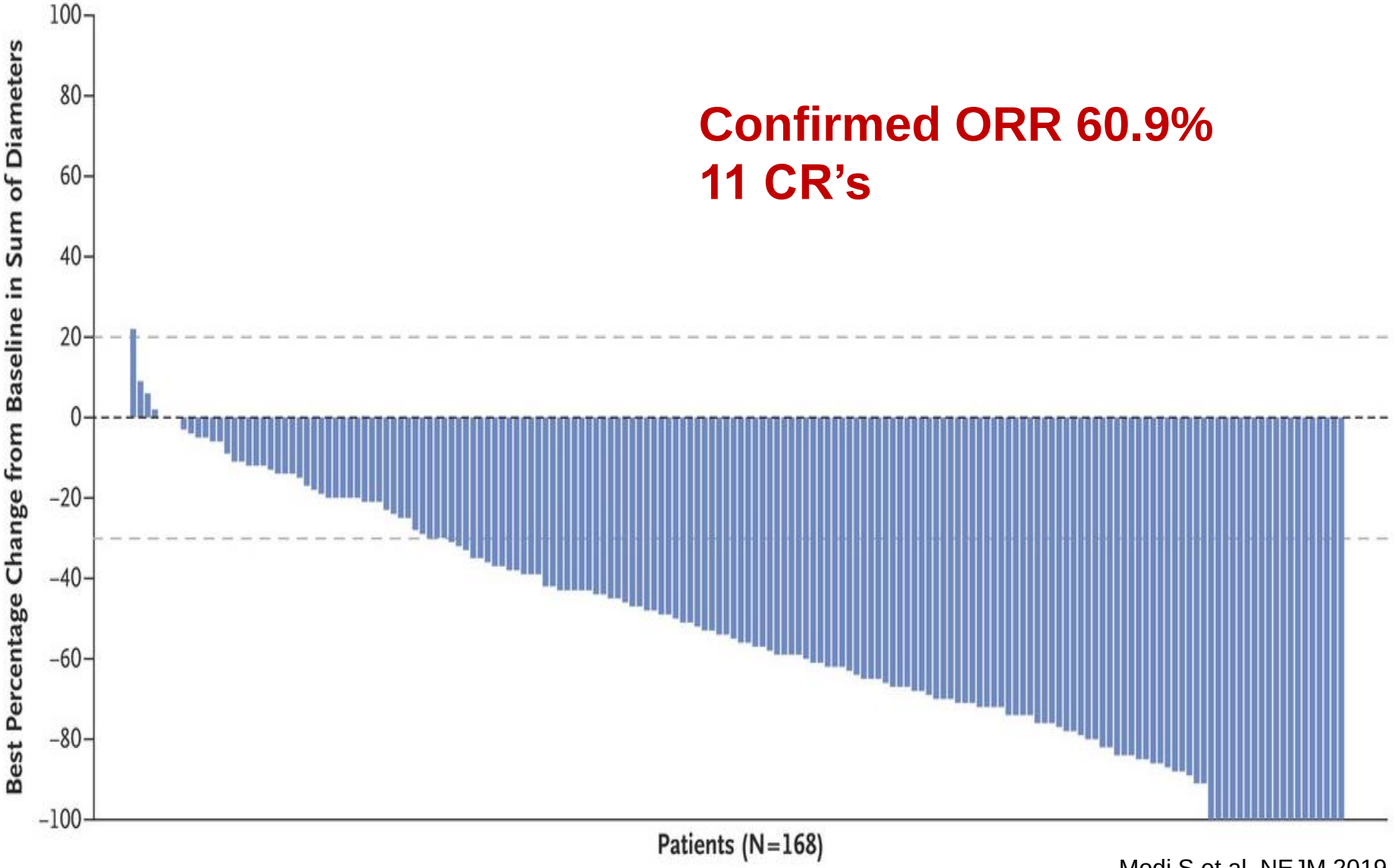
Modi S et al, NEJM 2019

DESTINY-Breast01: Patient characteristics

Age – median (range)	55 (28-96)
Hormone receptor status - no. (%)	
Positive	97 (53)
Negative	83 (45)
Unknown	4 (2)
Median no. of previous chemo (range)	6 (2-27)
Previous systemic therapy - no. (%)	
Trastuzumab	184 (100)
Trastuzumab emtansine	184 (100)
Pertuzumab	121 (66)
Other anti-HER2 therapy	100(54)
Hormone therapy	90(48)
Other systemic therapy	183(100)

Modi S et al, NEJM 2019

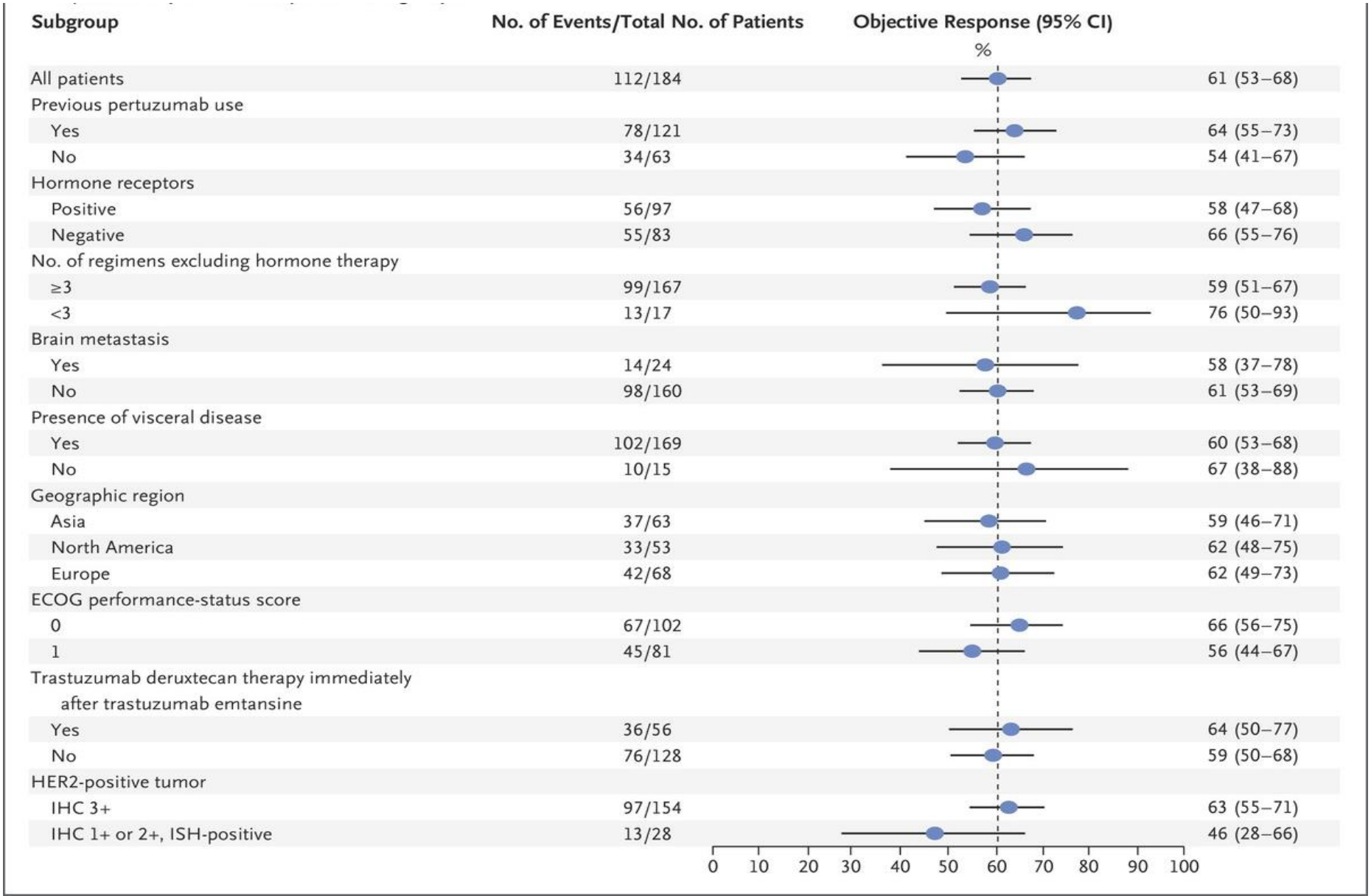
DESTINY-Breast01: Best change in tumor size



Confirmed ORR 60.9%
11 CR's

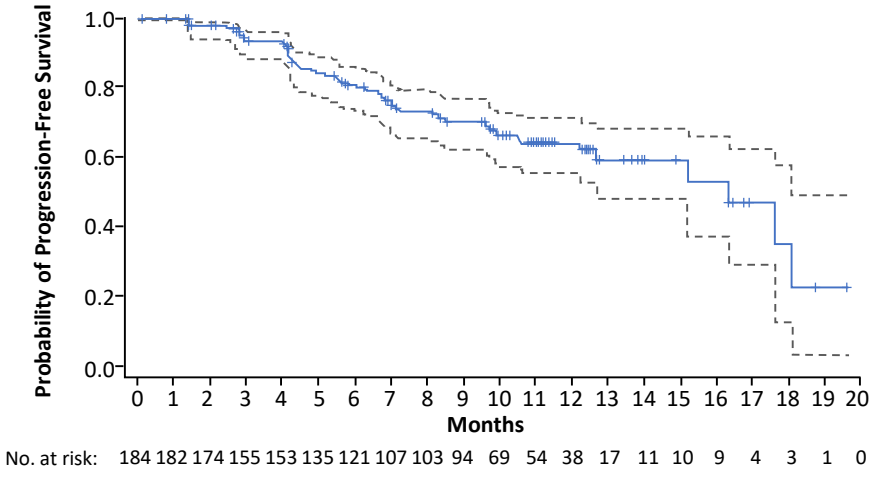
Modi S et al, NEJM 2019

DESTINY-Breast01: Subgroup analyses

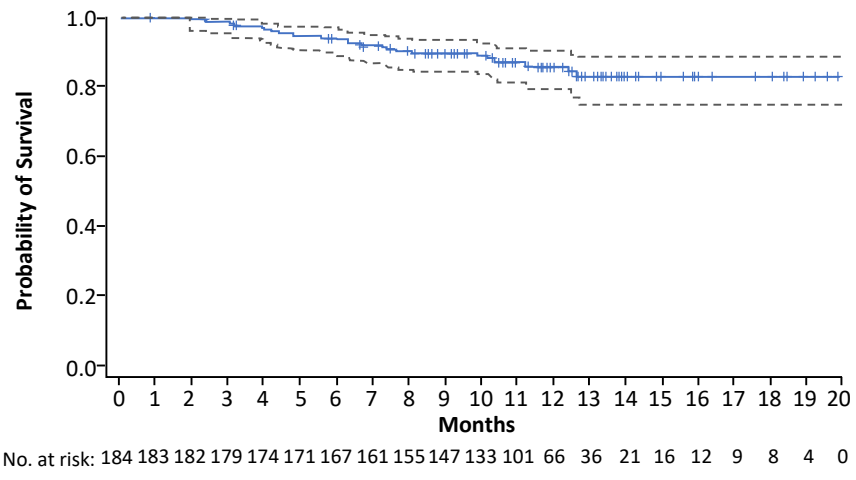


Progression-Free and Overall Survival

Progression-Free Survival
Median: 16.4 months (95% CI, 12.7-NE)



Overall Survival
Median: Not reached (95% CI, NE-NE)



- Median follow-up: 11.1 months (range 0.7-19.9)
- Median response duration: 14.8 months (95% CI 13.8-16.9)
- Median PFS in pts brain metastases (n=24): 18.1 months

Modi S et al, NEJM 2019

Table 2. Adverse Events in the Overall Population of 184 Patients.*

Adverse Events	Any Grade	Grade 3	Grade 4
	number of patients (percent)		
Any adverse event†	183 (99.5)	89 (48.4)	7 (3.8)
Nausea	143 (77.7)	14 (7.6)	0
Fatigue	91 (49.5)	11 (6.0)	0
Alopecia	89 (48.4)	1 (0.5)	0
Vomiting	84 (45.7)	8 (4.3)	0
Constipation	66 (35.9)	1 (0.5)	0
Decreased neutrophil count‡	64 (34.8)	36 (19.6)	2 (1.1)
Decreased appetite	57 (31.0)	3 (1.6)	0
Anemia§	55 (29.9)	15 (8.2)	1 (0.5)
Diarrhea	54 (29.3)	5 (2.7)	0
Decreased white-cell count¶	39 (21.2)	11 (6.0)	1 (0.5)
Decreased platelet count‖	39 (21.2)	7 (3.8)	1 (0.5)
Headache	36 (19.6)	0	0
Cough	35 (19.0)	0	0
Abdominal pain**	31 (16.8)	2 (1.1)	0
Decreased lymphocyte count††	26 (14.1)	11 (6.0)	1 (0.5)
Adverse events of special interest			
Interstitial lung disease‡‡	25 (13.6)	1 (0.5)	0
Prolonged QT interval	9 (4.9)	2 (1.1)	0
Infusion-related reaction	4 (2.2)	0	0
Decreased left ventricular ejection fraction§§	3 (1.6)	1 (0.5)¶¶	0

28 (15.2%) stopped rx due to AE: pneumonitis (n=11) and ILD (n=5)

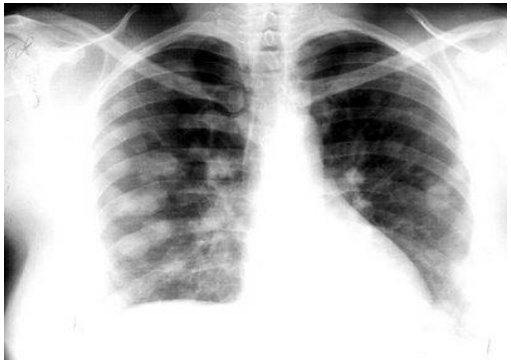
Adverse Events: Interstitial Lung Disease

Patients who received T-DXd 5.4 mg/kg (N=184)

	Grade 1	Grade 2	Grade 3	Grade 4	Grade 5	Any Grade/ Total
Interstitial lung disease	5 (2.7)	15 (8.2)	1 (0.5)	0	4 (2.2)	**25 (13.6)**

Among 25 ILD events:

- Median time to onset: 193 days (range 42-535)
- At data cutoff: 7 patients recovered, 2 recovering, 10 ongoing ILD, 2 unknown status, and 4 died
- Median duration from onset to recovery: 34 days (range 3-179)
- Of 4 fatal cases, death occurred 9-60 days after diagnosis



Modi S et al, NEJM 2019

Management Interstitial lung disease

- Grade 1 (radiographic changes but asymptomatic)
  - Hold drug
  - Steroids can be considered (0.5 mg/kg prednisone)
  - If resolved within 28 days, maintain dose
  - if resolved> 28 days from date of onset, reduce dose one level

- Grade 2 or higher (symptomatic)
  - Start corticosteroid (≥1 mg/kg prednisone or equivalent)
  - Upon improvement, follow by gradual taper (e.g., 4 weeks)
  - Permanently stop drug in patients who are diagnosed with any symptomatic ILD

FDA prescribing label

Trasutuzumab deruxtecan clinical pearls

- More nausea than with TDM1
  - Use 5-HT3 antagonist (e.g. ondansetron) day 1
  - After day 1, prn antiemetics
- Alopecia seen in 50%, though not usually grade 3
  - Unknown if scalp cooling beneficial
- Most dose reductions due to neutropenia
  - Starting dose 5.4 mg/kg, then 4.4, then 3.2
  - Febrile neutropenia rare
- LFTs and platelet issues less common than TDM1
- Act promptly if suspect interstitial lung disease!

FDA prescribing label

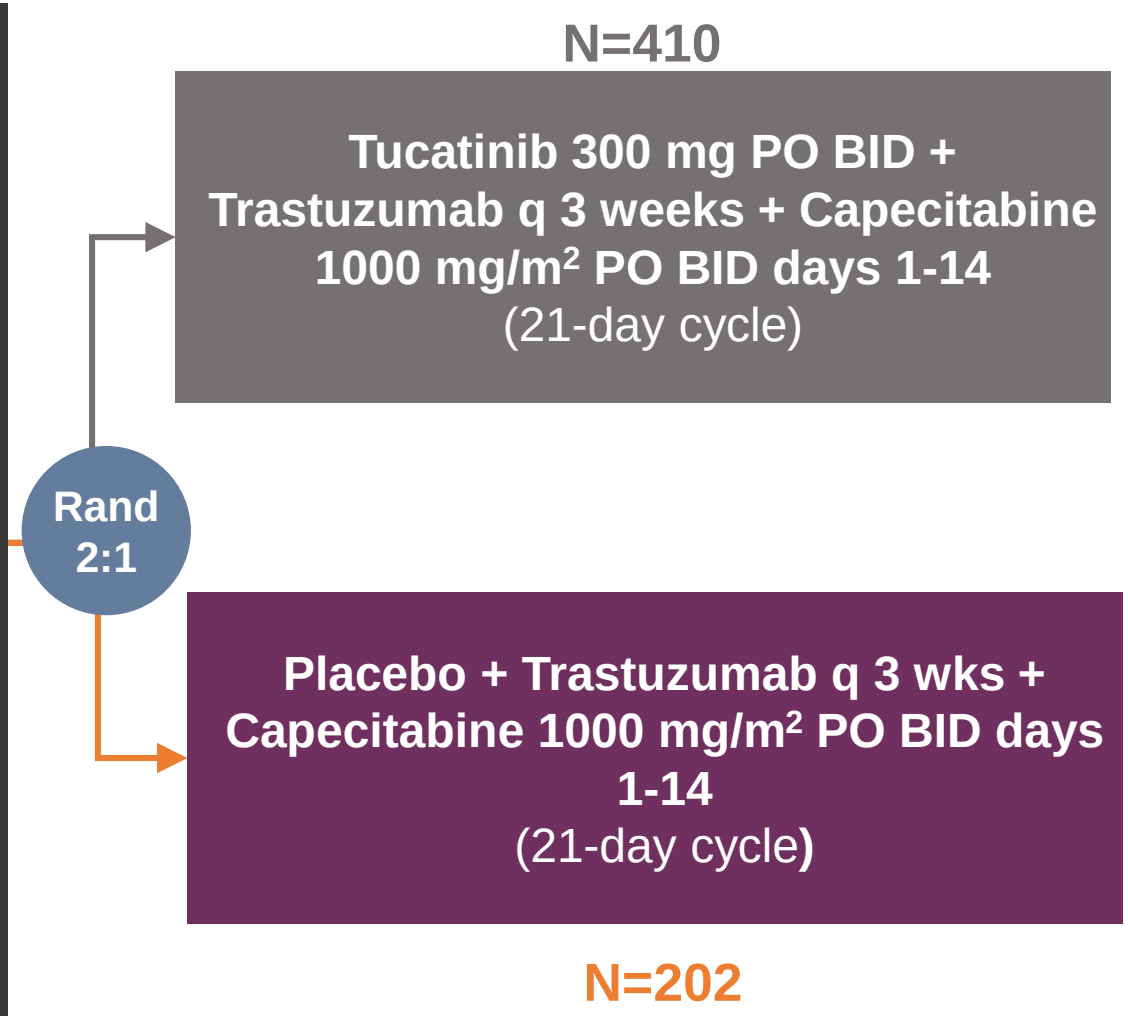
Tucatinib

- Potent and selective small molecule tyrosine kinase inhibitor against HER2
  - Highly selective for HER2 => less EGFR-related toxicities compared to dual inhibitors
  - Phase 1 single agent data had no treatment-related grade 3 diarrhea in heavily pretreated patients
- Preclinical data suggests synergy with capecitabine
- FDA approval pending

HER2CLIMB Trial Design

Key Eligibility Criteria

- HER2+ metastatic breast cancer
- Prior treatment with trastuzumab, pertuzumab, and T-DM1
- 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



Murthy R et al, NEJM 2019

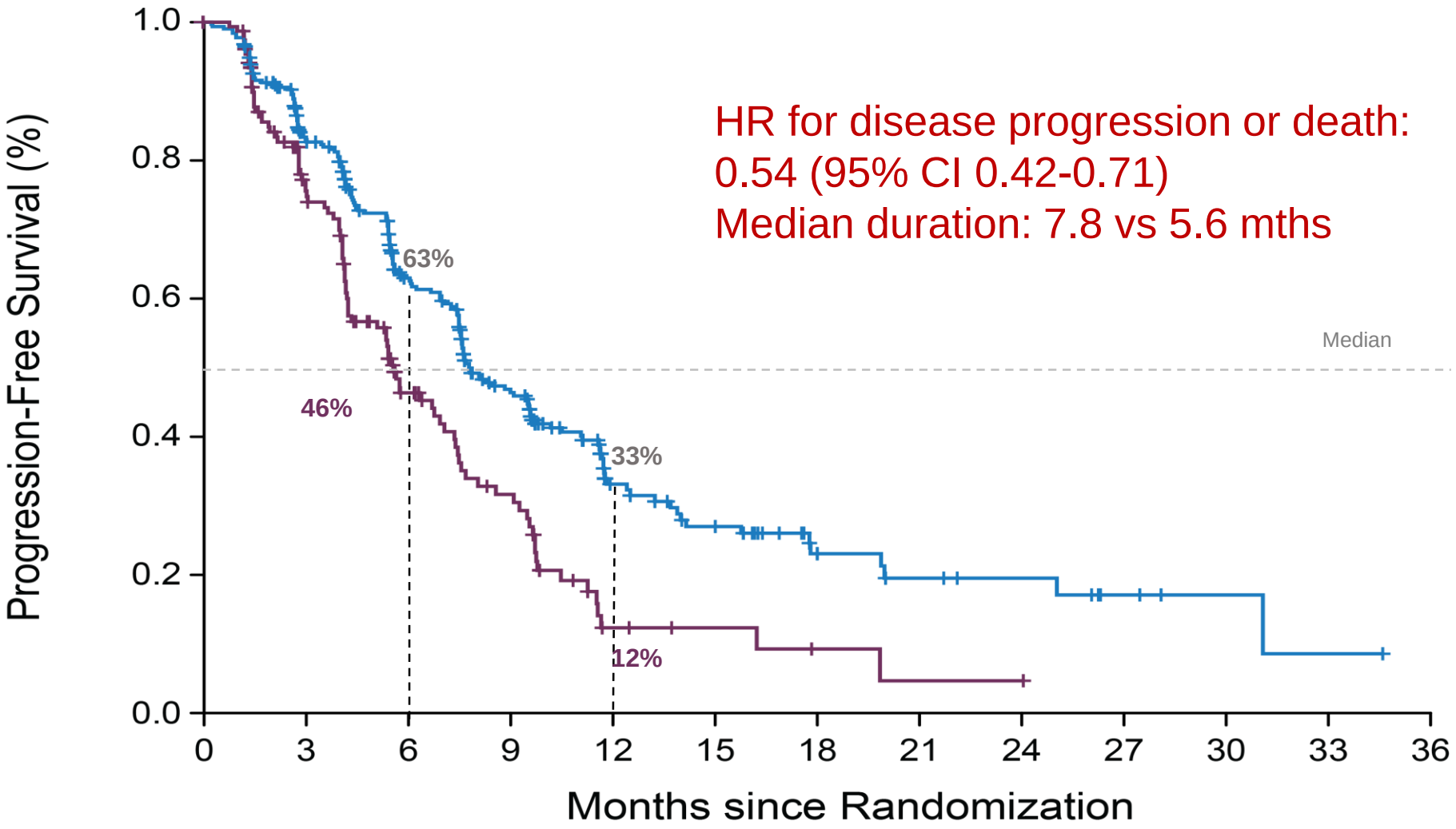
HER2CLIMB: Baseline patient characteristics

		TUC+Tras+Cape n=410	Plac+Tras+Cape n=202
Age (years), median (range)		55.0 (22-80)	54.0 (25-82)
ECOG performance status	0	204 (50)	94 (47)
	1	206 (50)	108 (54)
Stage IV at initial diagnosis		143 (35)	77 (39)
Hormone receptor status	ER and/or PR-positive	243 (60)	127 (63)
	ER and PR-negative	161 (40)	75 (37)
Prior lines of therapy, median (range)	Overall	4.0 (2-14)	4.0 (2-17)
	Metastatic setting	3.0 (1-14)	3.0 (1-13)
Presence/history of brain metastases		198 (48)	93 (46)
Treated, stable		118 (60)	55 (59)
Untreated		44 (22)	22 (24)
Treated, progressing		36 (18)	16 (17)

100% had prior pertuzumab and TDM1
6% had prior lapatinib

Murthy R et al, NEJM 2019

HER2CLIMB: Progression-Free Survival

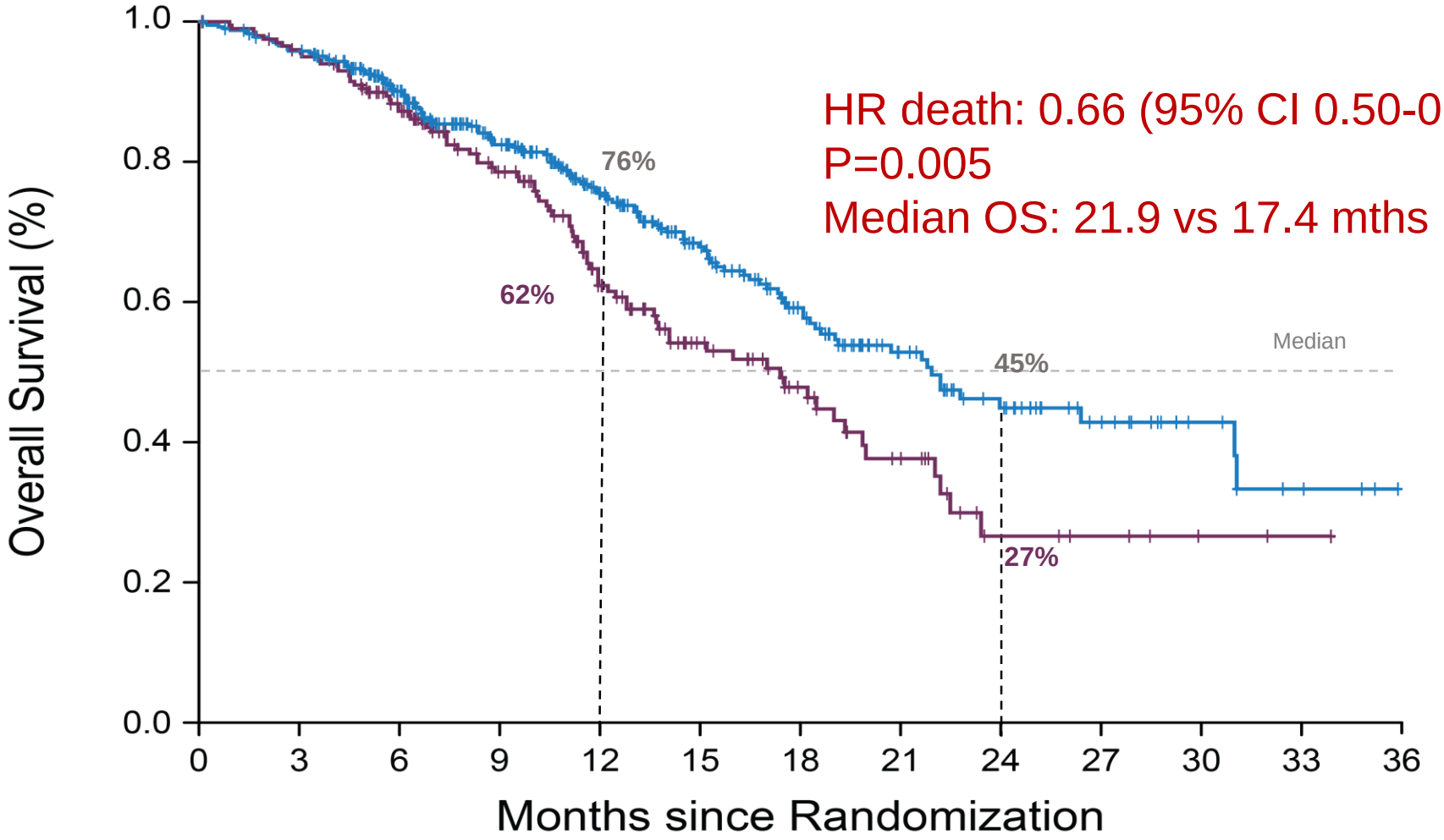


HR for disease progression or death:
0.54 (95% CI 0.42-0.71)
Median duration: 7.8 vs 5.6 mths

No. at Risk												
TUC+Tras+Cape	320	235	152	98	40	29	15	10	8	4	2	1	0
Pbo+Tras+Cape	160	94	45	27	6	4	2	1	1	0	0	0	0

Murthy R et al, NEJM 2019

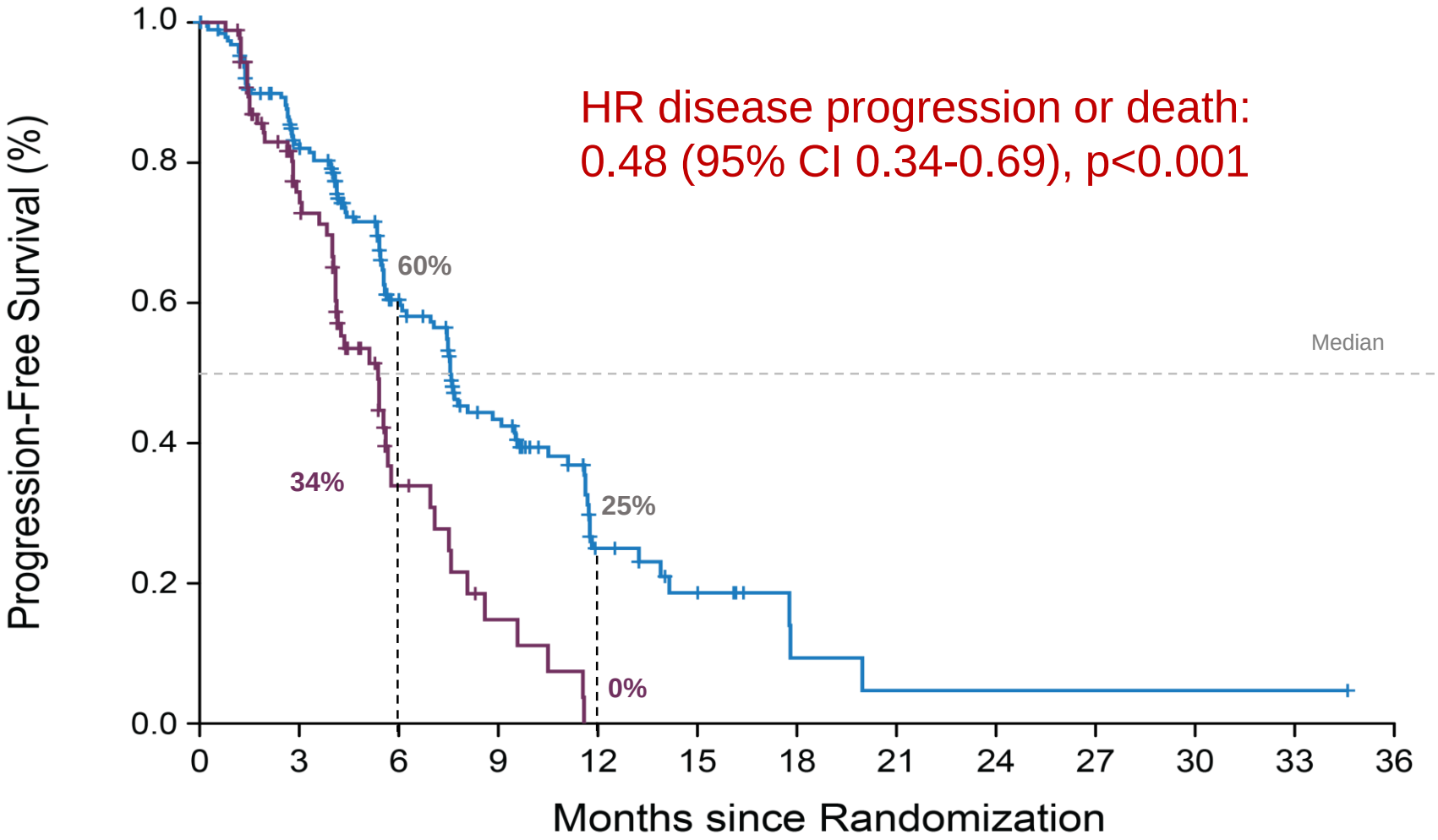
HER2CLIMB: Overall Survival



No. at Risk												
TUC+Tras+Cape	410	388	322	245	178	123	80	51	34	20	10	4	0
Pbo+Tras+Cape	202	191	160	119	77	48	32	19	7	5	2	1	0

Murthy R et al, NEJM 2019

HER2CLIMB: Progression-Free Survival for Patients with Brain Metastases (n=157)



Murthy R et al, NEJM 2019

HER2CLIMB: Adverse Events

Table 2. Most Common Adverse Events.*

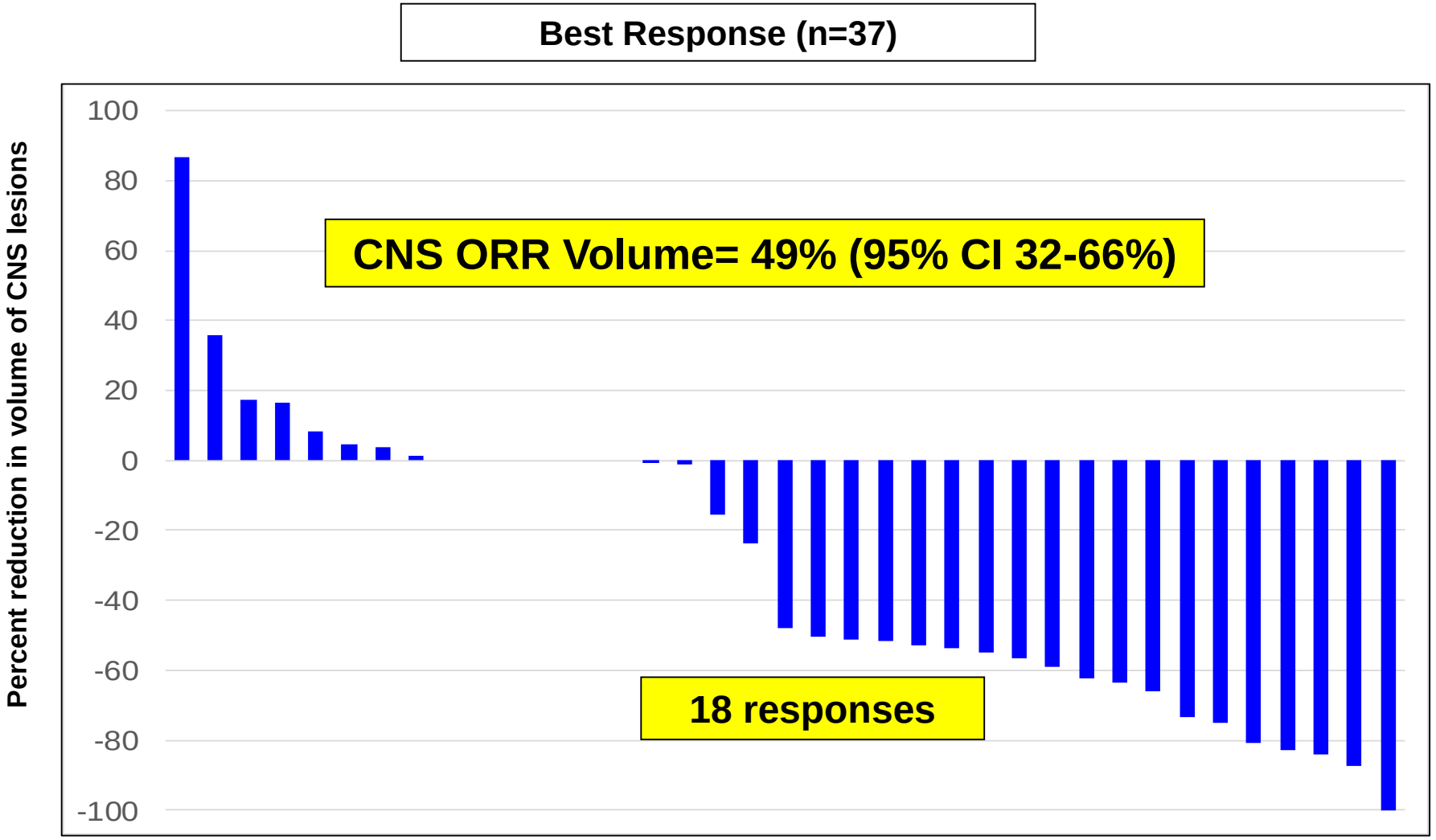
Event	Tucatinib-Combination Group (N = 404)		Placebo-Combination Group (N = 197)	
	Any Grade	Grade ≥3	Any Grade	Grade ≥3
	number of patients (percent)			
Any adverse event	401 (99.3)	223 (55.2)	191 (97.0)	96 (48.7)
Diarrhea	327 (80.9)	52 (12.9)	105 (53.3)	17 (8.6)
PPE syndrome	256 (63.4)	53 (13.1)	104 (52.8)	18 (9.1)
Nausea	236 (58.4)	15 (3.7)	86 (43.7)	6 (3.0)
Fatigue	182 (45.0)	19 (4.7)	85 (43.1)	8 (4.1)
Vomiting	145 (35.9)	12 (3.0)	50 (25.4)	7 (3.6)
Stomatitis	103 (25.5)	10 (2.5)	28 (14.2)	1 (0.5)
Decreased appetite	100 (24.8)	2 (0.5)	39 (19.8)	0
Headache	87 (21.5)	2 (0.5)	40 (20.3)	3 (1.5)
Aspartate aminotransferase increased	86 (21.3)	18 (4.5)	22 (11.2)	1 (0.5)
Alanine aminotransferase increased	81 (20.0)	22 (5.4)	13 (6.6)	1 (0.5)

Murthy R et al, NEJM 2019

Tucatinib clinical pearls

- Less diarrhea than neratinib
  - Antidiarrheal prophylaxis not mandated per protocol
- Active in CNS disease
  - On HER2 CLIMB, 48% had brain mets
  - Of those 18% were treated but progressing and 23% untreated

TBCRC 022: Neratinib + Capecitabine



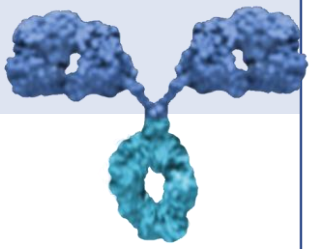
Neratinib + Capecitabine Endorsed by NCCN for HER2+ Brain Metastases

Freedman J Clin Oncol 2019

Margetuximab

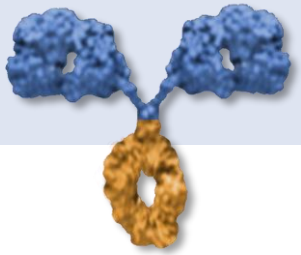
Trastuzumab

Fab:
- Binds HER2 with high specificity
- Disrupts signaling that drives cell proliferation and survival



Fc:
- Wild-type immunoglobulin G1 (IgG1) immune effector domains
- Binds and activates immune cells

Margetuximab



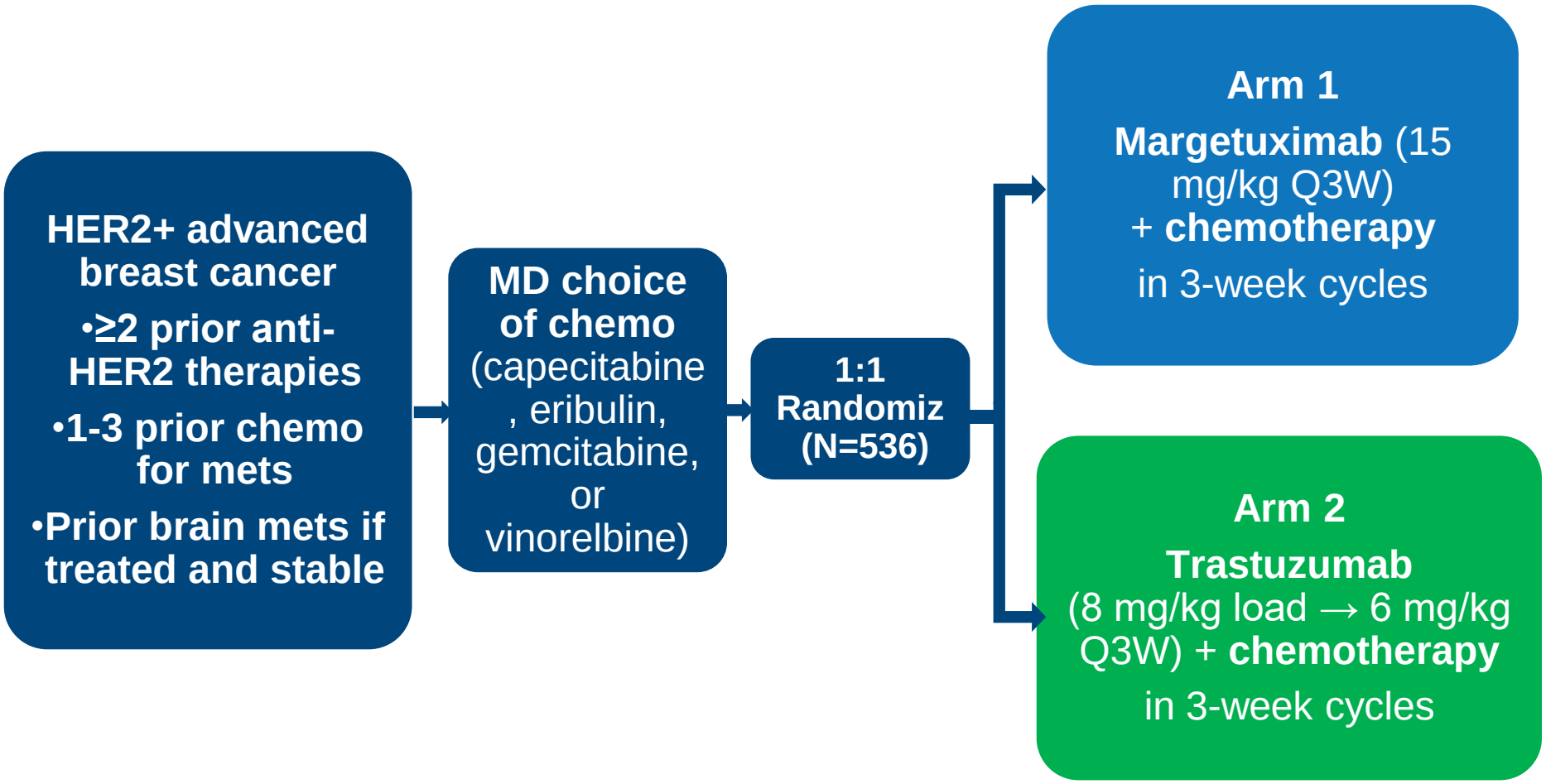
Fab:
- Same specificity and affinity
- Similarly disrupts signaling

Fc engineering:
- ⬆ Affinity for activating Fcγ RIIIA (CD16A)
- ⬇ Affinity for inhibitory Fcγ RIIB (CD32B)

Enhance innate immunity (antibody-dependent cellular cytotoxicity) and adaptive immunity (HER2-specific T-cell reactivity and antibodies)

Breast Cancer Res. 2011;Cancer Res. 2007

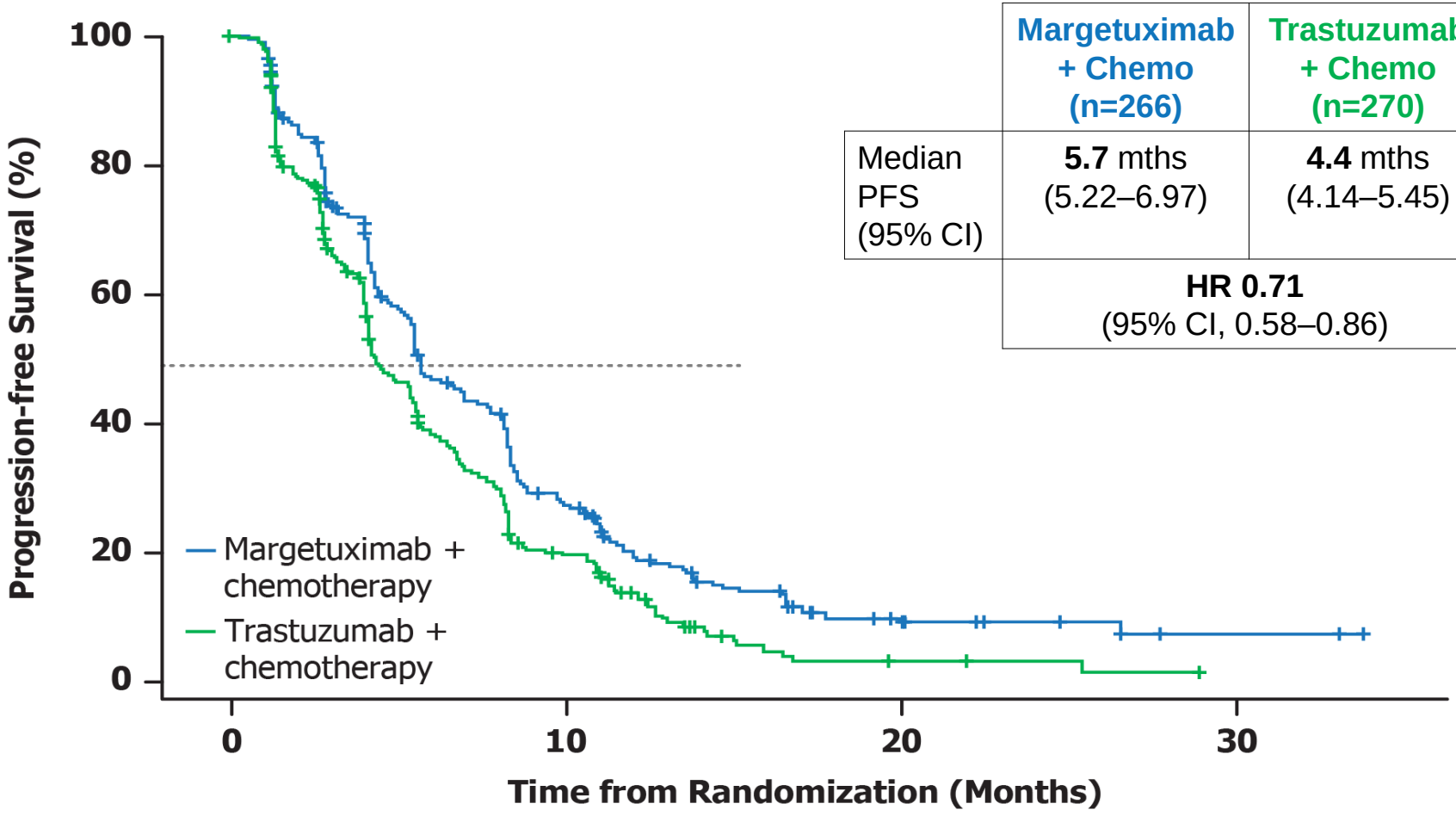
SOPHIA Study Design



SOPHIA patient characteristics: prior treatment

	Margetuximab + Chemo (n=266)	Trastuzumab + Chemo (n=270)
Settings of prior therapy		
Adjuvant and/or neoadjuvant	158 (59%)	145 (54%)
Metastatic only	108 (41%)	125 (46%)
Prior metastatic lines of therapy		
≤2	175 (66%)	180 (67%)
>2	91 (34%)	90 (33%)
Prior anti-HER2 therapy		
Trastuzumab	266 (100%)	270 (100%)
Pertuzumab	266 (100%)	269 (100%)
T-DM1	242 (91%)	247 (92%)
Lapatinib	41 (15%)	39 (14%)
Other HER2	6 (2%)	6 (2%)
Prior chemotherapy		
Taxane	252 (95%)	249 (92%)
Anthracycline	118 (44%)	110 (41%)
Platinum	34 (13%)	40 (15%)
Prior endocrine therapy	126 (47%)	133 (49%)

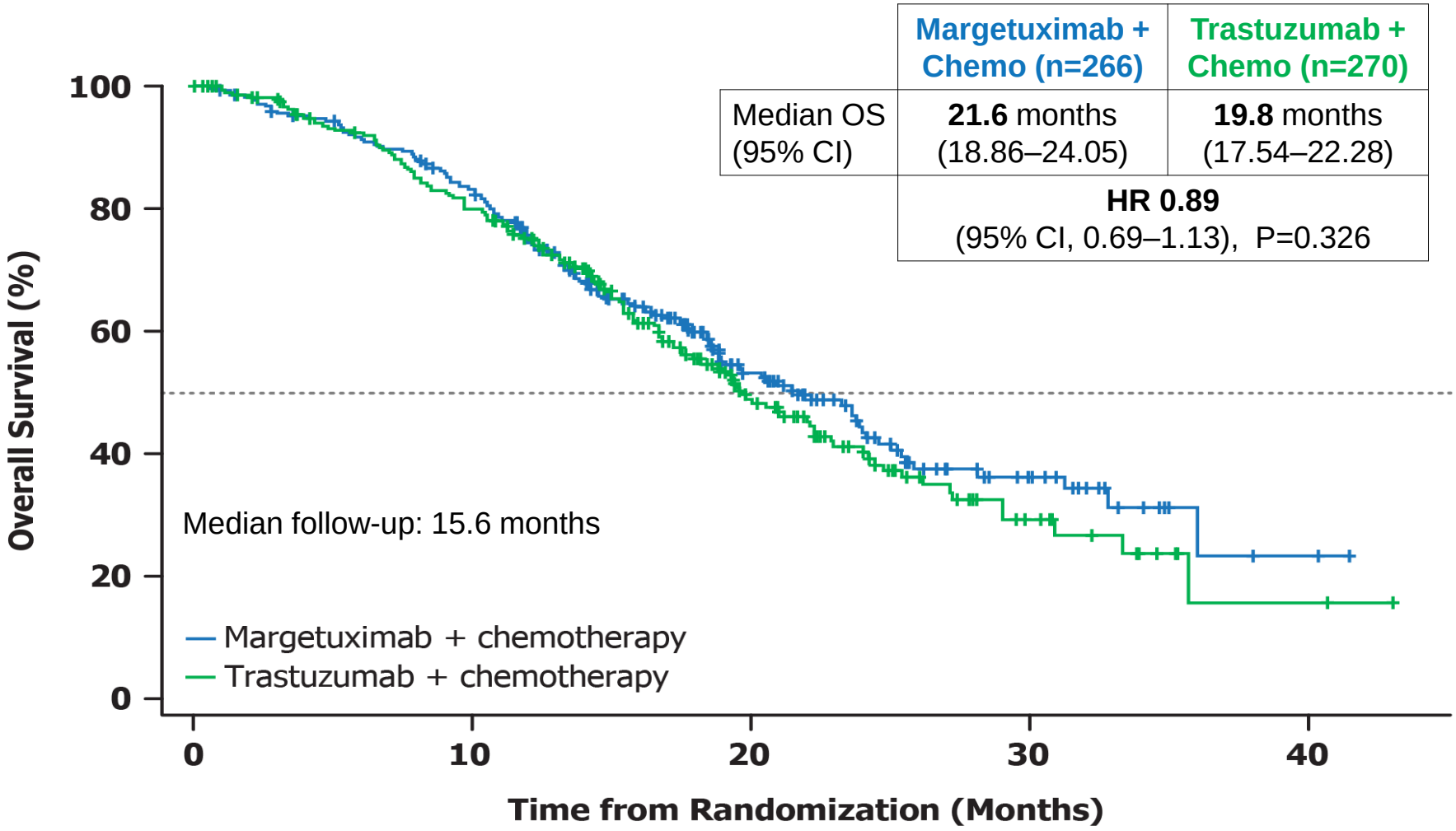
SOPHIA: Progression Free Survival



	Margetuximab + Chemo (n=266)	Trastuzumab + Chemo (n=270)
Median PFS (95% CI)	**5.7** mths (5.22–6.97)	**4.4** mths (4.14–5.45)
	HR 0.71 (95% CI, 0.58–0.86)	

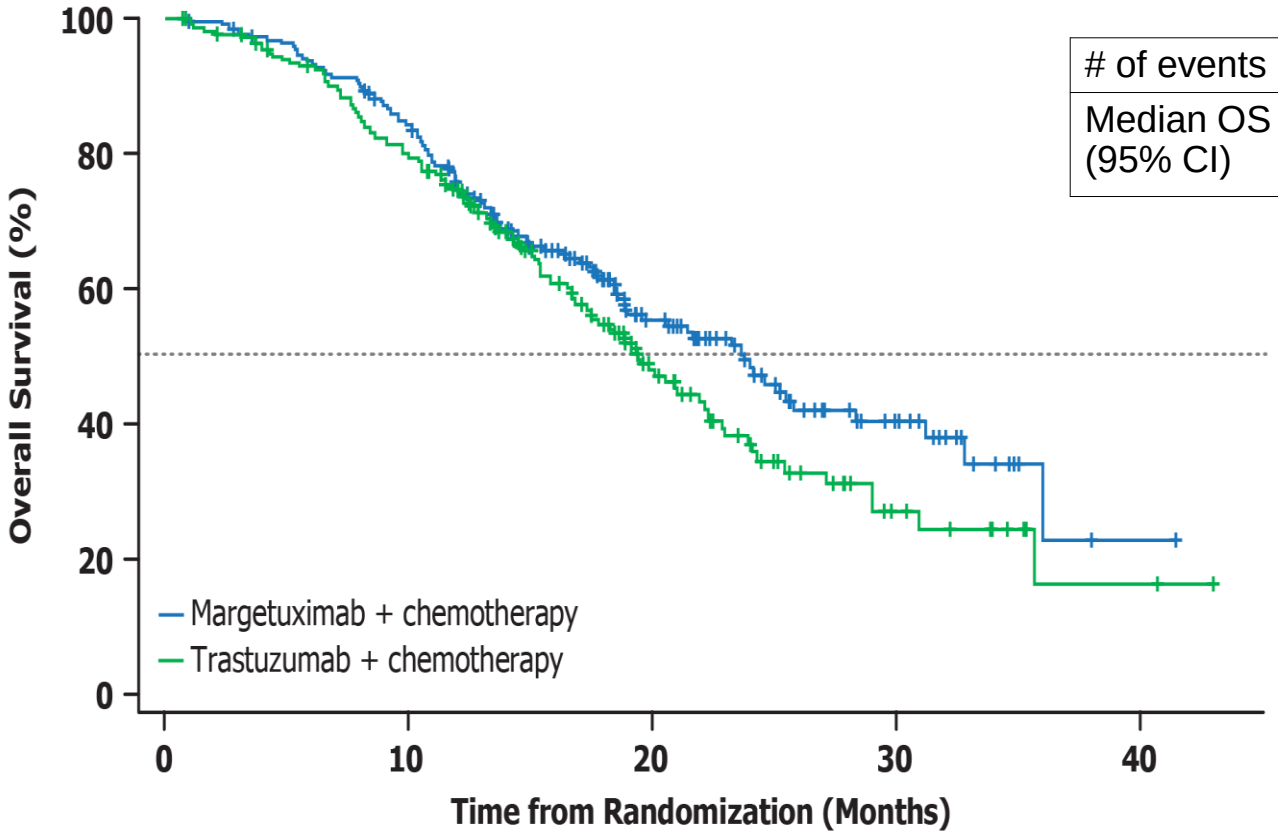
Margetuximab	266	210	137	100	62	36	25	14	11	6	5	3	2	2	0
Trastuzumab	270	192	108	72	42	20	8	4	3	2	2	1	0		

SOPHIA: Interim OS Analyses



SOPHIA: Pre-specified exploratory OS in CD16A-185 F carriers

CD16A-158F Carriers, FF or FV, n=437 of 506 (86%) genotyped



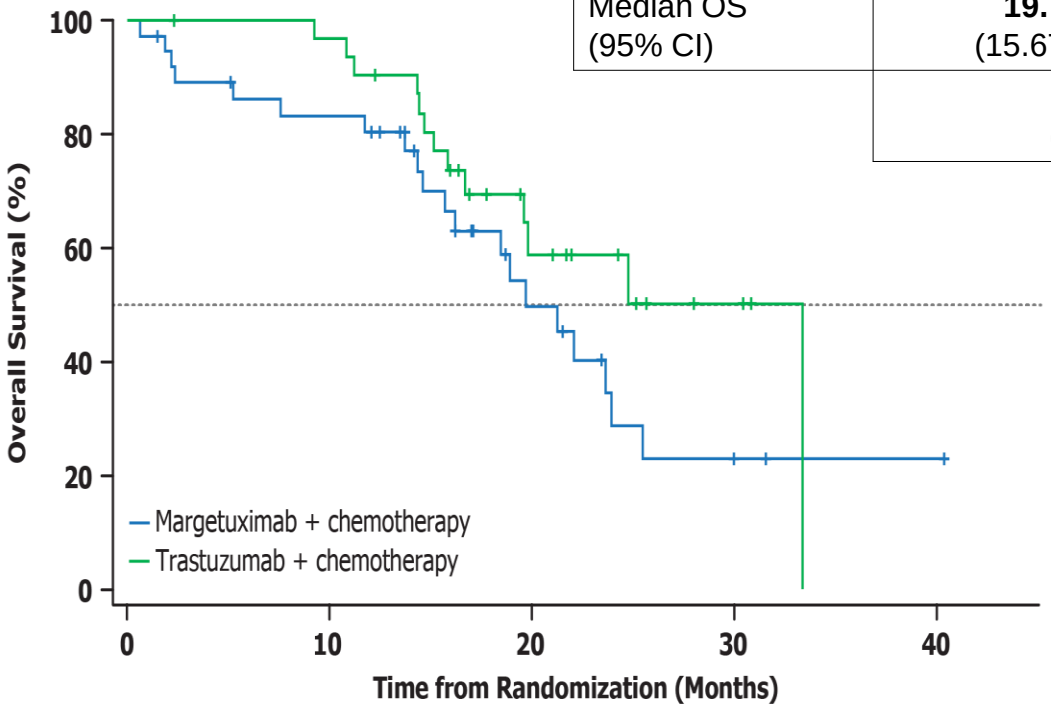
	Margetuximab + Chemo (n=221)	Trastuzumab + Chemo (n=216)
# of events	103	114
Median OS (95% CI)	**23.7** mths (18.89–28.32)	**19.4** mths (16.85–22.28)
	HR 0.79 (95% CI, 0.61–1.04), *P*=0.087	

Margetuximab	221	219	212	204	196	181	157	135	111	91	68	55	42	31	27	19	13	8	2	1	1	0
Trastuzumab	216	210	201	192	176	165	145	123	98	81	57	43	30	21	16	11	9	6	2	2	2	1	0

SOPHIA: Pre-specified exploratory OS in CD16A-158 VV homozygotes

CD16A-158VV Homozygotes, n=69 of 506 (14%) genotyped

	Margetuximab + Chemo (n=37)	Trastuzumab + Chemo (n=32)
# of events	20	13
Median OS (95% CI)	**19.7** mths (15.67–23.89)	**33.3** mths (16.66–33.31)
	HR 1.65 (95% CI, 0.82–3.32), P=0.157	



Margetuximab	37	34	32	30	29	29	27	23	19	15	11	9	5	4	4	3	1	1	1	1	0
Trastuzumab	32	32	31	31	31	30	28	27	20	14	11	8	8	4	3	3	1	0			

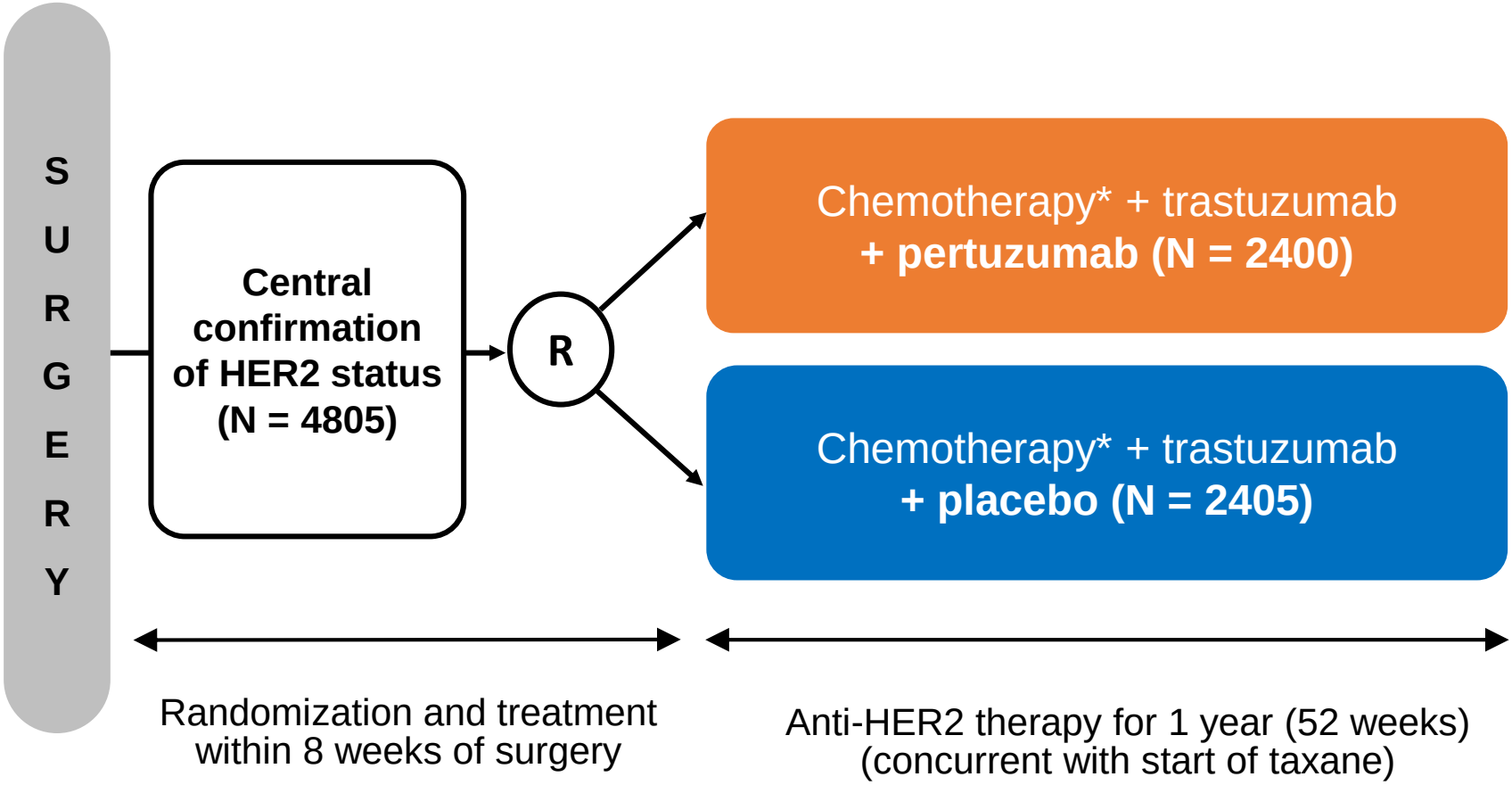
Unbalanced patient characteristics

Pt Characteristic	Margetuximab + Chemo (n=37)	Trastuzumab + Che (n=32)
Metastatic sites		
Brain, n(%)	8 (**22%**)	3 (**9%**)
Breast, n(%)	10 (**27%**)	5 (**16%**)
Liver, n(%)	16 (**43%**)	10 (**31%**)
Lung, n(%)	11 (**30%**)	13 (**41%**)
HER2 IHC 3+, n(%)	19 (**51%**)	18 (**56%**)
ECOG PS 1, n(%)	14 (**38%**)	16 (**50%**)
>60 yrs, n (%)	16 (**43%**)	5 (**16%**)
>2 prior metastatic lines, n(%)	15 (**41%**)	9 (**28%**)

Less favorable

Adjuvant treatment

APHINITY: Phase III trial trastuzumab + chemo +/- pertuzumab

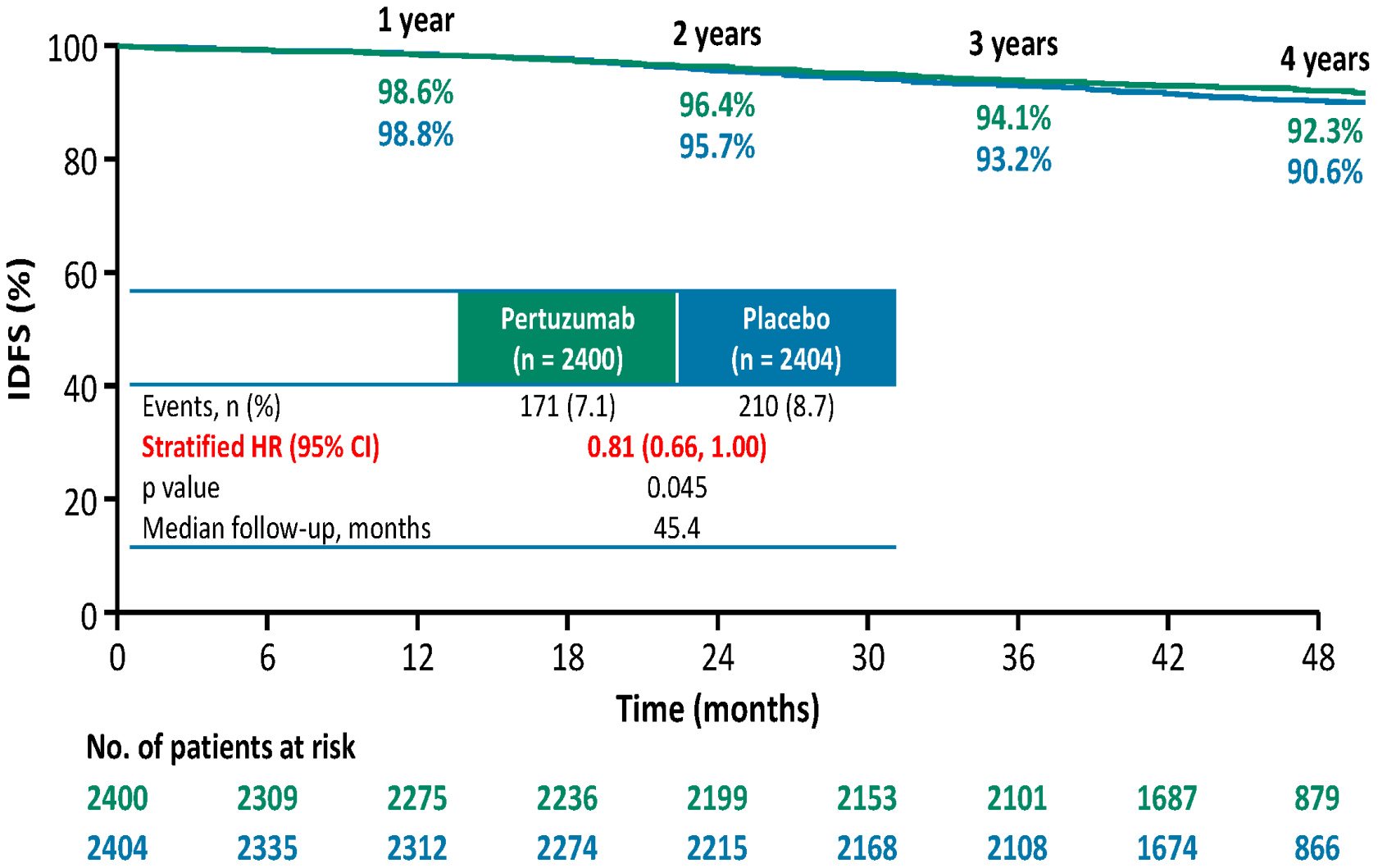


*CAF/CEF+ taxane; AC/EC + taxane; or docetaxel + carboplatin

=> 78% received anthracycline

von Minckwitz N Engl J Med 2017

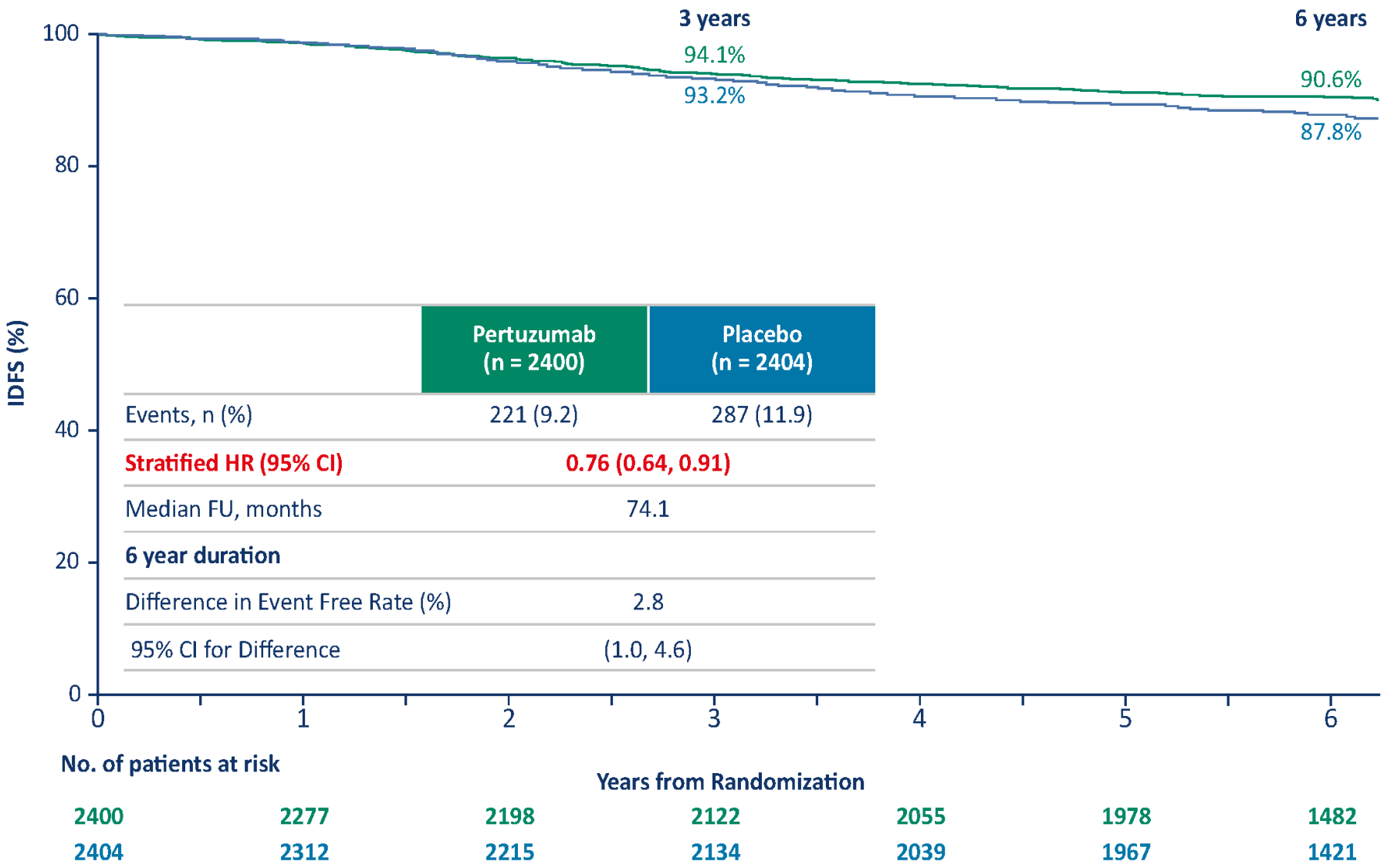
APHINITY primary analysis 2017 (median f/u 45.4 mths)



CI, confidence interval; FU, follow-up; HR, hazard ratio; IDFS, invasive disease-free survival.

Adapted from von Minckwitz G, *et al. N Engl J Med* 2017;

APHINITY Updated 2019 DFS descriptive analysis (median f/u 74.1 mths)

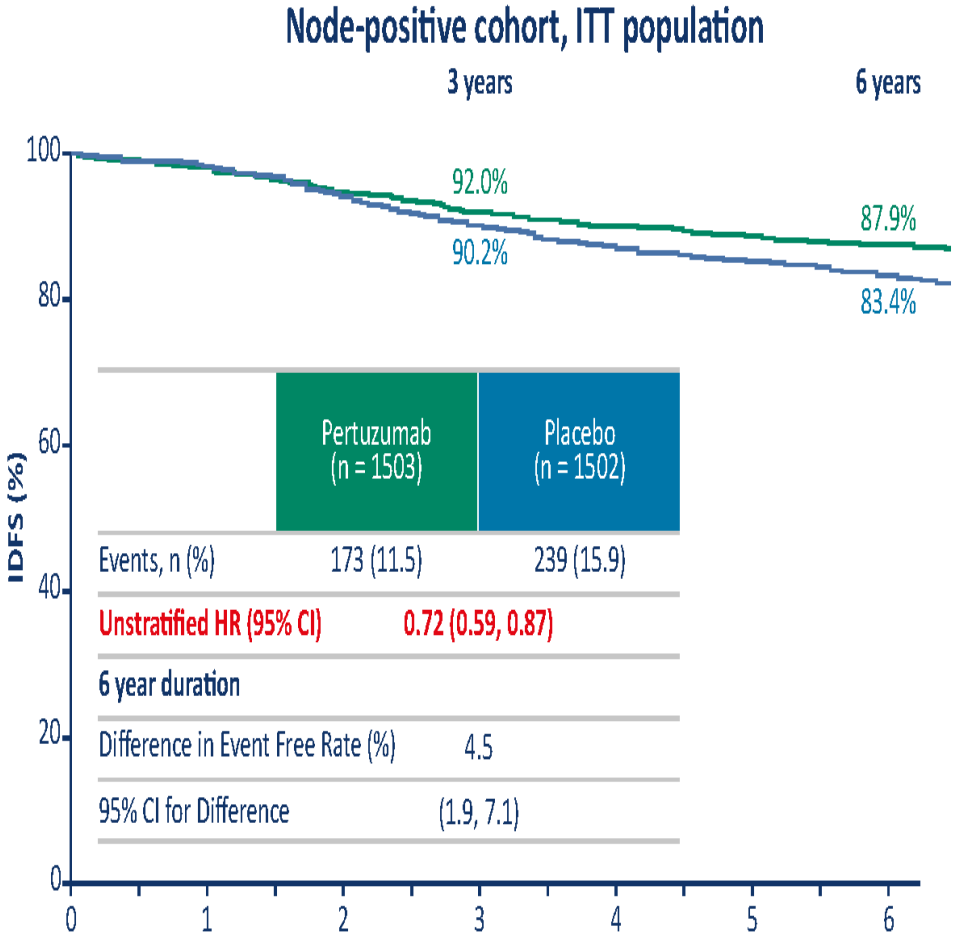


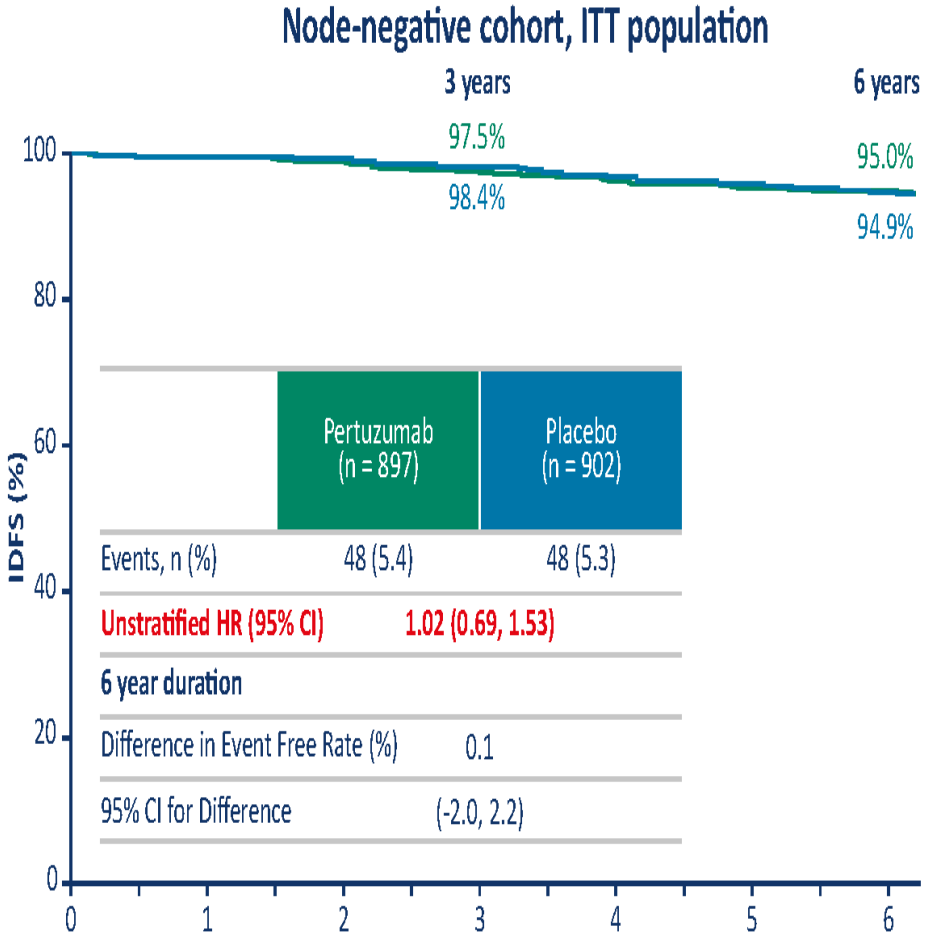
	Pertuzumab (n = 2400)	Placebo (n = 2404)
Events, n (%)	221 (9.2)	287 (11.9)
Stratified HR (95% CI)	**0.76 (0.64, 0.91)**	
Median FU, months	74.1	
6 year duration		
Difference in Event Free Rate (%)	2.8	
95% CI for Difference	(1.0, 4.6)	

Picart 2019, SABCS

APHINITY Updated 2019 DFS descriptive analysis by nodal status

Node positive cohort continues to derive benefit from addition of pertuzumab

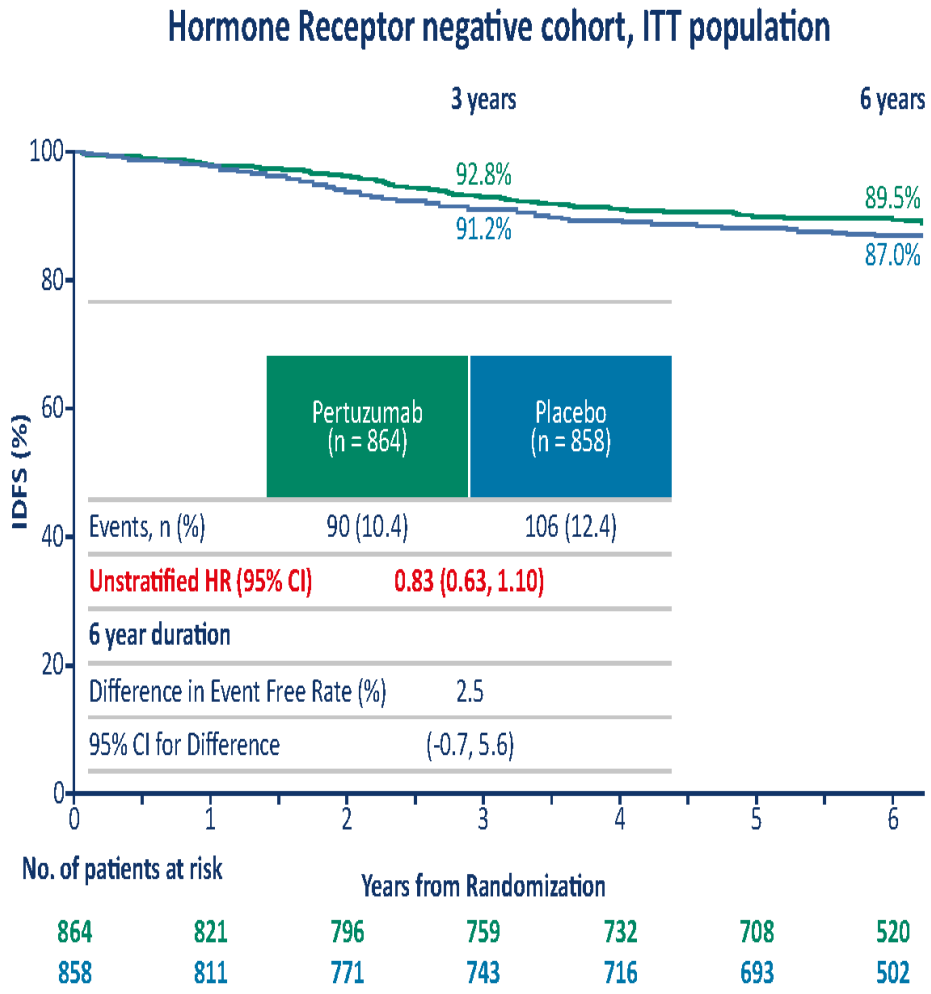


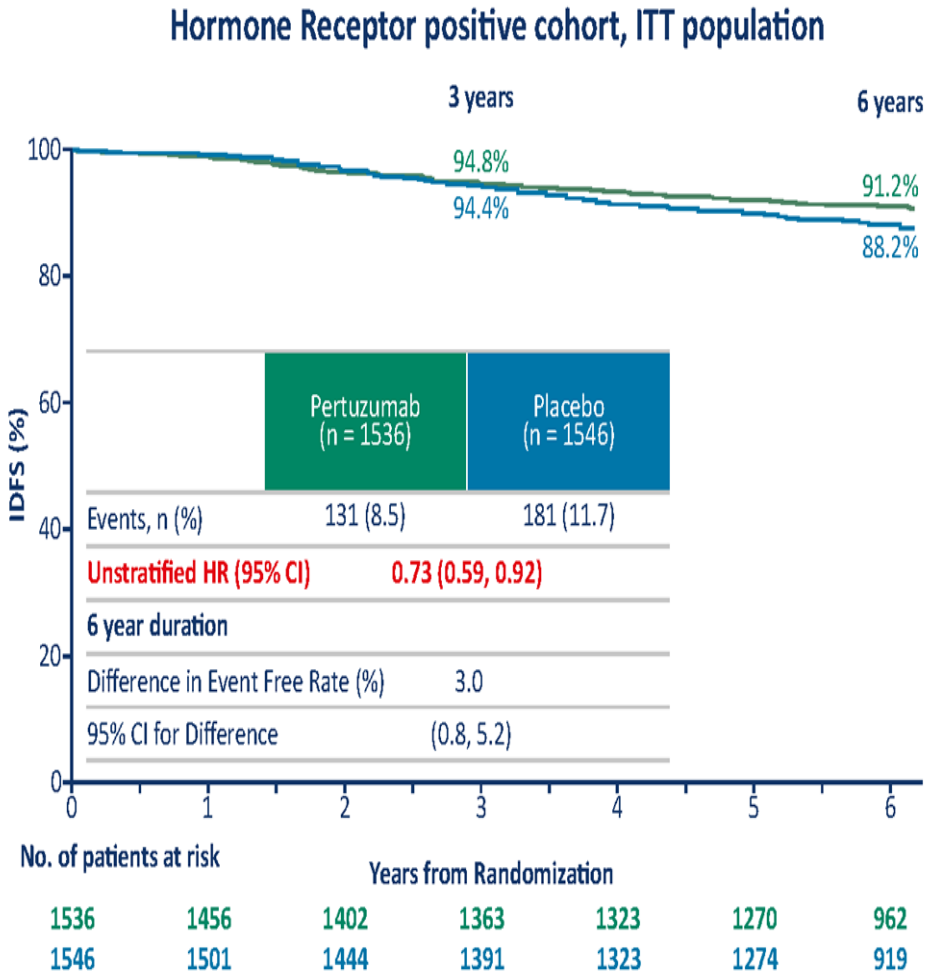


Picart 2019, SABCS

APHINITY Updated 2019 descriptive DFS analysis by hormone receptor status

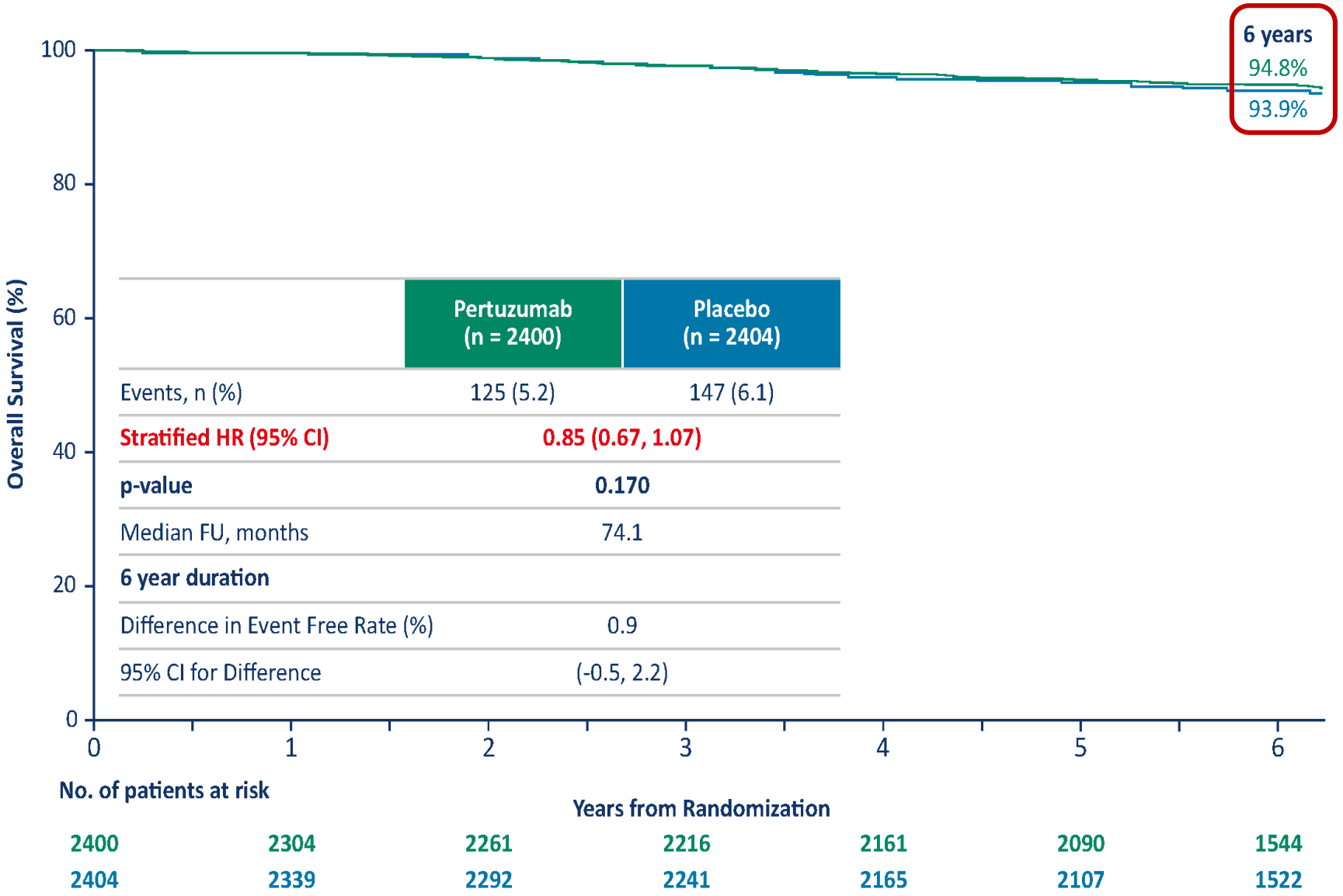
Treatment benefit of pertuzumab also seen in hormone positive cohort





Picart 2019, SABCS

APHINITY Interim OS analysis (median f/u 74.1 mths)

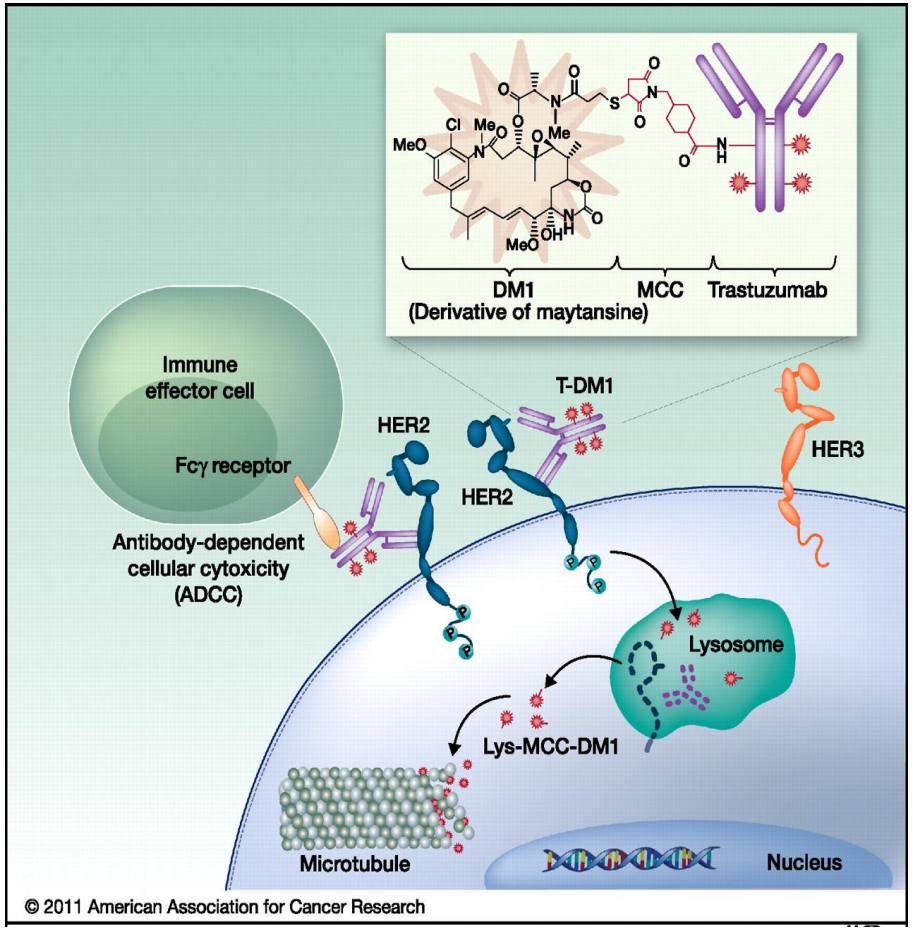


Picart 2019, SABCS

When to use pertuzumab?

- Adding pertuzumab to chemo + trastuzumab improves DFS in pts with node-positive disease regardless of hormone receptor status
- Most patients with HER2+ tumors >2cm receive preop therapy
  - Addition of pertuzumab improves pCR, but won't improve DFS in *all* patients (i.e. node negative patients)
  - ?Will pertuzumab impact on local therapy (rates of axillary dissection)?
- Administering preoperative pertuzumab to all patients may result in some overtreatment, but challenging to decide upfront which patients need pertuzumab

Trastuzumab Emtansine (T-DM1)

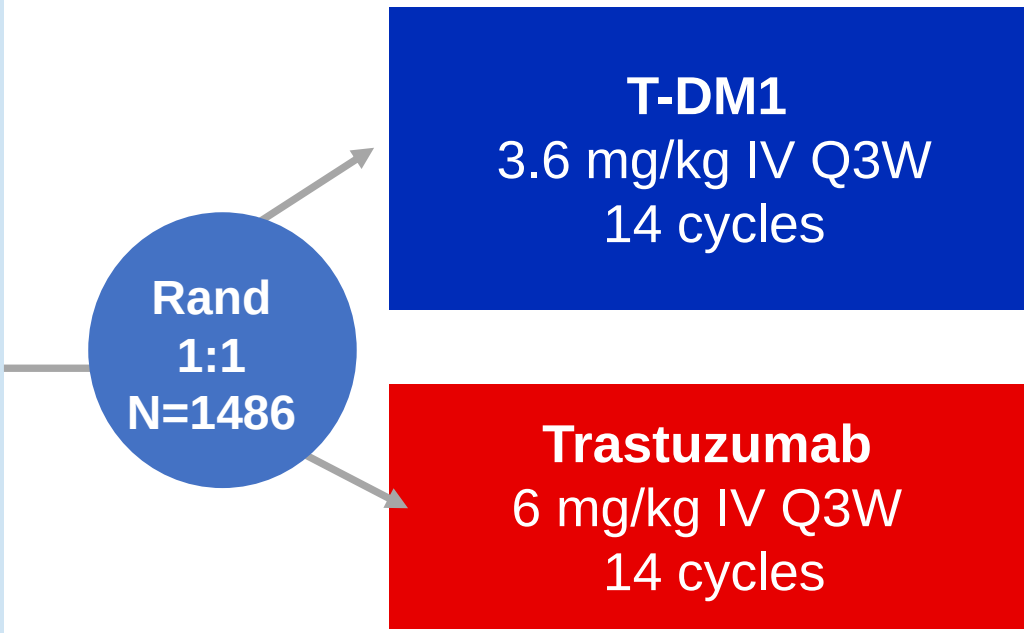


- **Antibody drug-conjugate**
  - **Trastuzumab linked to DM1, a microtubule inhibitor**
- **T-DM1 binds to HER2 with affinity similar to trastuzumab**

LoRusso Pet al, Clin Cancer Res 2011

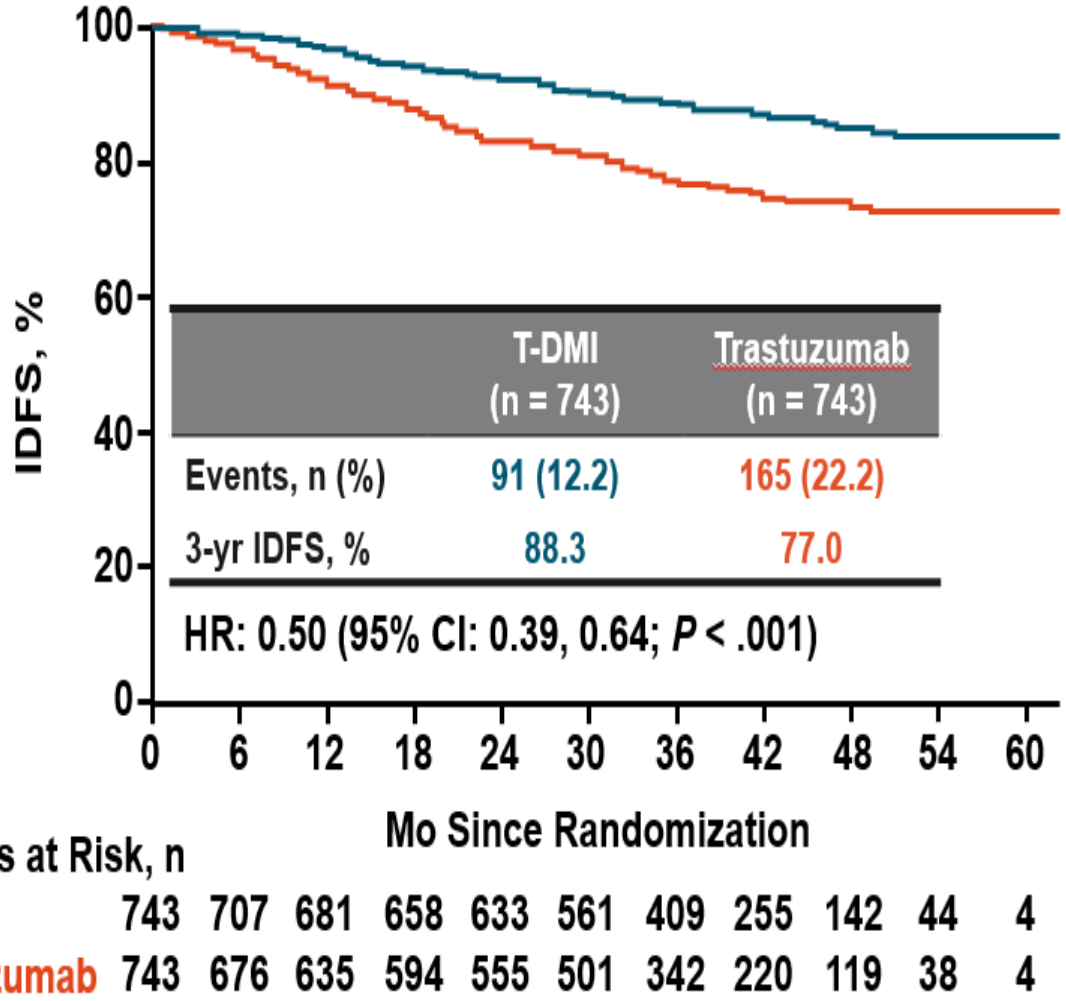
KATHERINE: Study Design

- cT1-4/N0-3/M0 at presentation (cT1a-b/N0 excluded)
- Neoadjuvant therapy:
  - Minimum 6 cycles of chemo
    - Minimum 9 wks of taxane
    - All chemo prior to surgery
  - Minimum 9 wks of trastuzumab
    - Second HER2-targeted agent allowed
- Residual invasive tumor in breast or axillary nodes (any amount)



von Minckwitz, N Engl J M 2019

KATHERINE: IDFS results



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

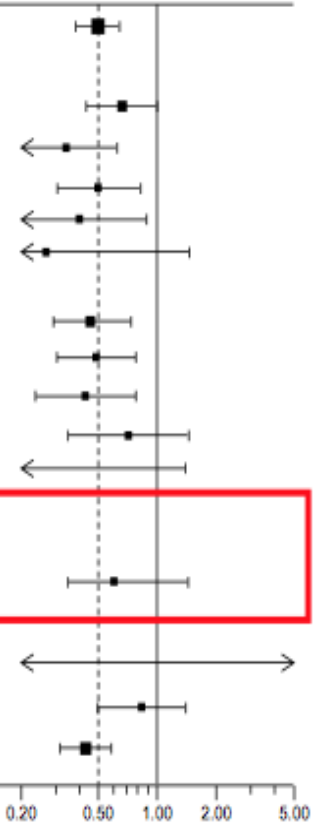
CNS events: *5.9% vs †4.3%

von Minckwitz G, *N Engl J Med.* 2019;380(7):617-628.

KATHERINE: Outcomes by residual disease

IDFS Subgroup Analysis (2)

Group	Total N	Trastuzumab (n=743) 3-Year IDFS	T-DM1 (n=743) 3-Year IDFS	Hazard Ratio	95% CI
All	1486	77.0	88.3	0.50	(0.39–0.64)
Primary tumor stage (at definitive surgery)					
ypT0, ypT1a, ypT1b, ypT1mic, ypTis	637	83.6	88.3	0.66	(0.44–1.00)
ypT1, ypT1c	359	75.9	91.9	0.34	(0.19–0.62)
ypT2	359	74.3	88.3	0.50	(0.31–0.82)
ypT3	108	61.1	79.8	0.40	(0.18–0.88)
ypT4^	23	30.0	70.0	0.29	(0.07–1.17)
Regional lymph node stage (at definitive surgery)					
ypN0	679	83.9	91.9	0.46	(0.30–0.73)
ypN1	433	75.8	88.9	0.49	(0.31–0.78)
ypN2	189	58.2	81.1	0.43	(0.24–0.77)
ypN3	67	40.6	52.0	0.71	(0.35–1.42)
ypNX	118	88.7	98.1	0.17	(0.02–1.38)
Residual disease ≤1 cm with negative axillary lymph nodes					
ypT1a, ypT1b or ypT1mic and ypN0	331	85.3	90.0	0.60	(0.33–1.12)
Central HER2 status by IHC*					
0/1+	25	83.9	100.0	<0.01	(0.00–NE)
2+	326	80.9	84.7	0.83	(0.50–1.38)
3+	1132	75.7	89.0	0.43	(0.32–0.58)



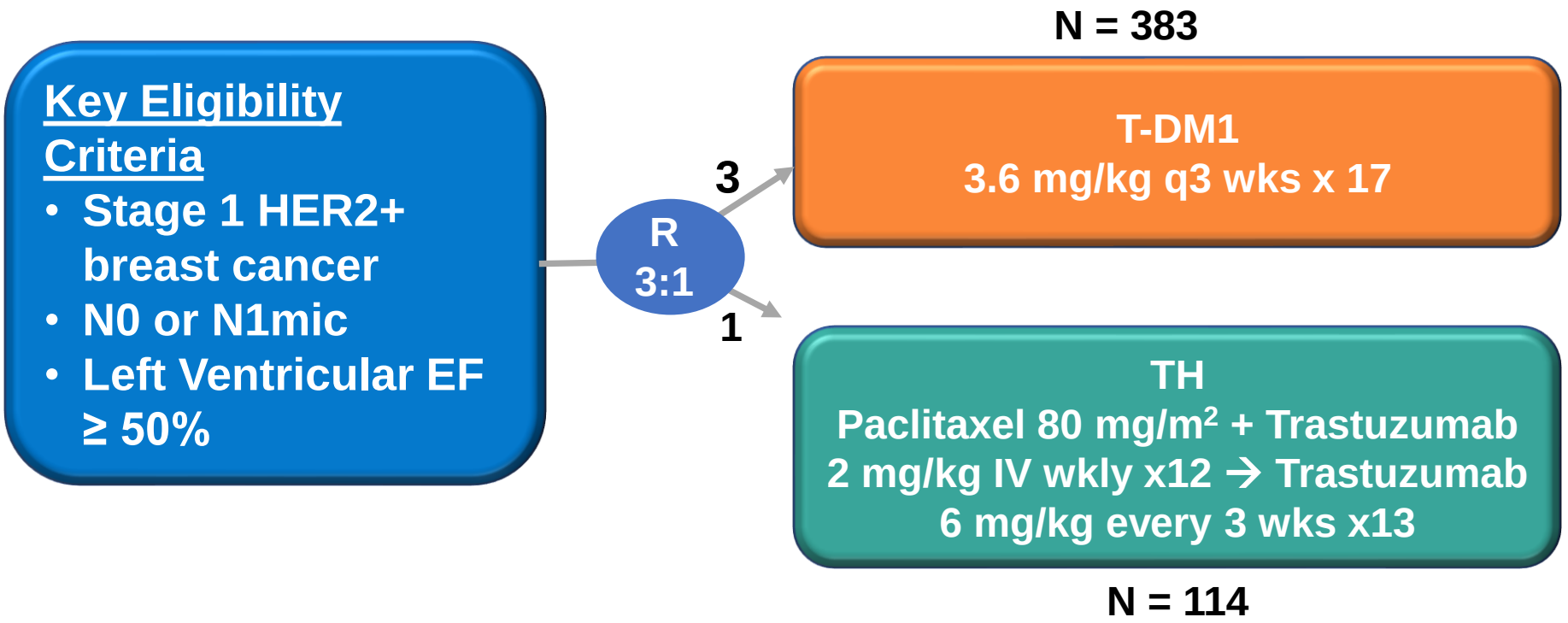
^Includes all ypT4 and 1 patient with ypTX; *Three patients had "unknown" HER2 IHC status.

Mano et al. SABCS 2019

KATHERINE: Unresolved issues

- What if T-DM1 had been compared to HP?
  - Given small benefits seen in APHINITY and large benefit seen in KATHERINE, seems highly likely that T-DM1 would be superior to HP
- Do the results apply to patients who received preoperative dual HER2-based therapy?
  - ~20% recv'd dual HER2 therapy with consistent benefit seen
- What is the optimal duration of T-DM1?
  - ~71% completed all 14 cycles (18% discontinued due to AEs)
  - More studies needed!

ATEMPT trial: TDM1 for Stage I HER2+?

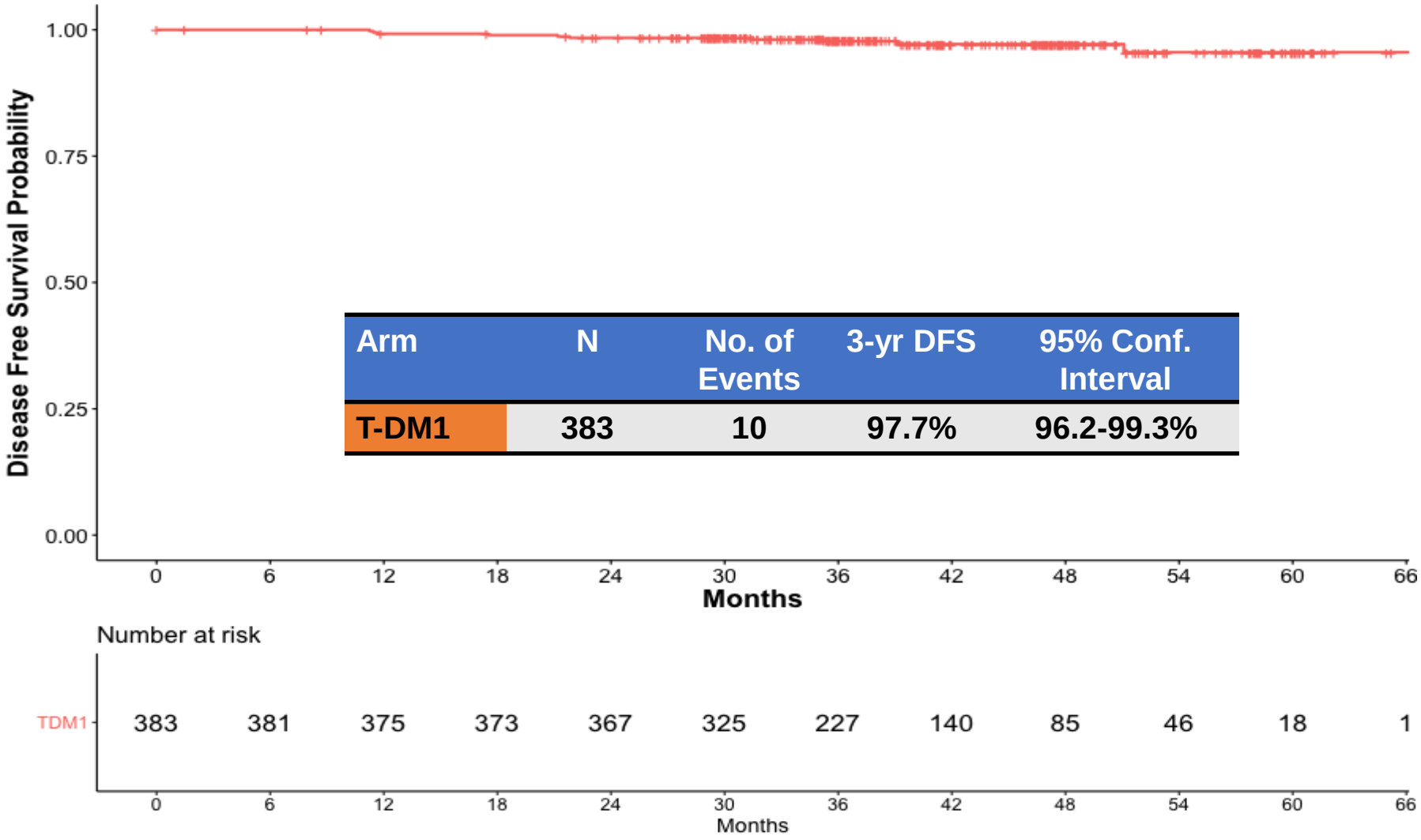


Study Endpoints

- **Co-primary Endpoints:**
  - **Evaluate 3 yr disease-free survival withT-DM1**
  - **Compare the incidence of clinically relevant toxicities (CRT) between the 2 arms**
    - **grade ≥3 non-hematologic toxicity**
    - **grade ≥2 neurotoxicity**
    - **grade ≥4 hematologic toxicity**
    - **febrile neutropenia**
    - **any toxicity requiring dose delay or discontinuation of protocol therapy**

***Study not powered to evaluate the efficacy of TH or to compare the efficacy of T-DM1 to TH**

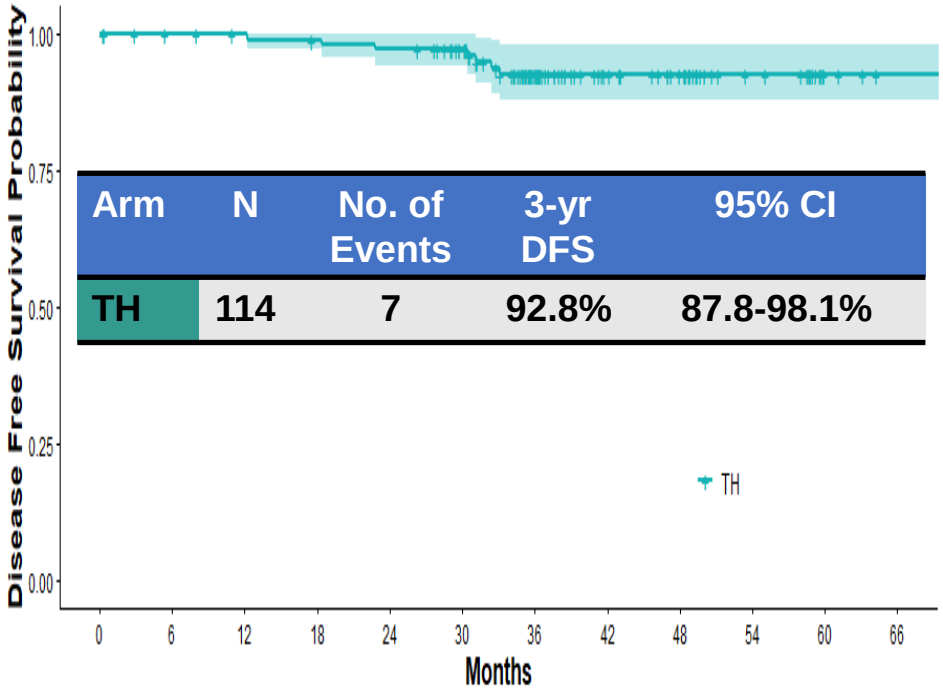
Disease-Free Survival: T-DM1



Arm	N	No. of Events	3-yr DFS	95% Conf. Interval
T-DM1	383	10	97.7%	96.2-99.3%

Disease-Free Survival: TH

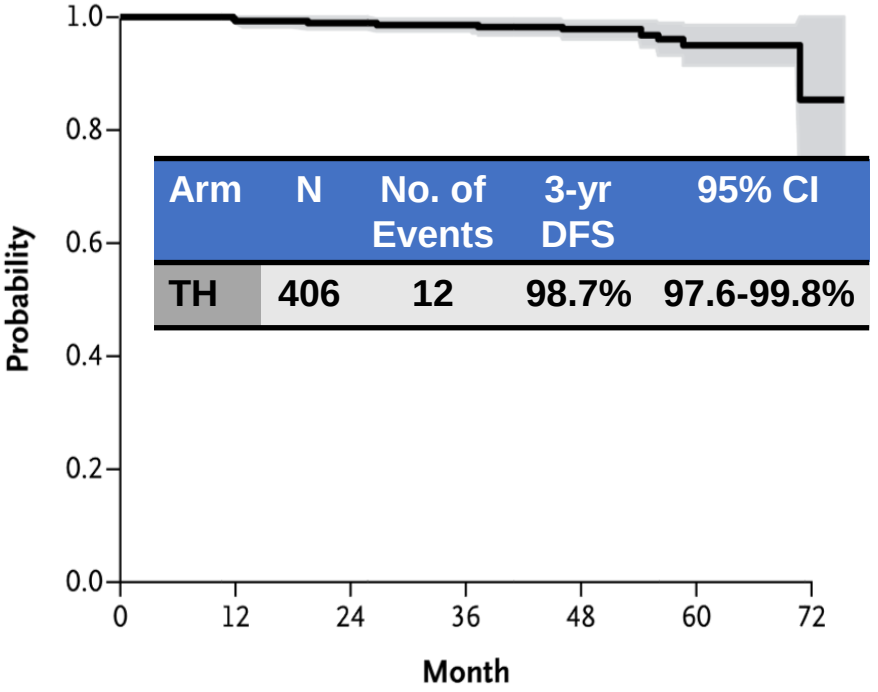
TH (ATEMPT Trial): n=114



Arm	N	No. of Events	3-yr DFS	95% CI
TH	114	7	92.8%	87.8-98.1%

Tolaney SABCS 2019

TH (APT Trial): n=406



Arm	N	No. of Events	3-yr DFS	95% CI
TH	406	12	98.7%	97.6-99.8%

Tolaney, NEJM 2015

ATEMPT: Clinically Relevant Toxicity

Clinically Relevant Toxicity	T-DM1 (n = 383) N (%)	TH (n = 114) N (%)
Grade ≥3 non-hematologic toxicity	37 (10%)	13 (11%)
Grade ≥ 2 neurotoxicity	42 (11%)	26 (23%)
Grade ≥4 hematologic toxicity	4 (1%)	0 (0%)
Febrile neutropenia	0 (0%)	2 (2%)
Any toxicity requiring dose delay	106 (28%)	30 (26%)
Any toxicity requiring early discontinuation	67 (17%)	7 (6%)
Total	176 (46%)	53 (46%)

Tolaney SABCS 2019

Treatment Related Adverse Events: Grade ≥2 by Arm

	T-DM1 (n = 383)	TH (n = 114)
Fatigue	84 (22%)	26 (23%)
Neuropathy	44 (11%)	27 (24%)
Neutropenia	13 (3%)	15 (13%)
Thrombocytopenia	43 (11%)	1 (1%)
Nausea	39 (10%)	8 (7%)
Hypertension	35 (9%)	7 (6%)
ALT increase	33 (9%)	5 (4%)
Headache	24 (6%)	4 (4%)
Bilirubin increase	21 (5%)	1 (1%)
Infusion related reaction	19 (5%)	12 (11%)
Arthralgia	18 (5%)	2 (2%)
Anemia	18 (5%)	2 (2%)

Treatment Related Adverse Events: Grade ≥2 by Arm

	T-DM1 (n = 383)	TH (n = 114)
Fatigue	84 (22%)	26 (23%)
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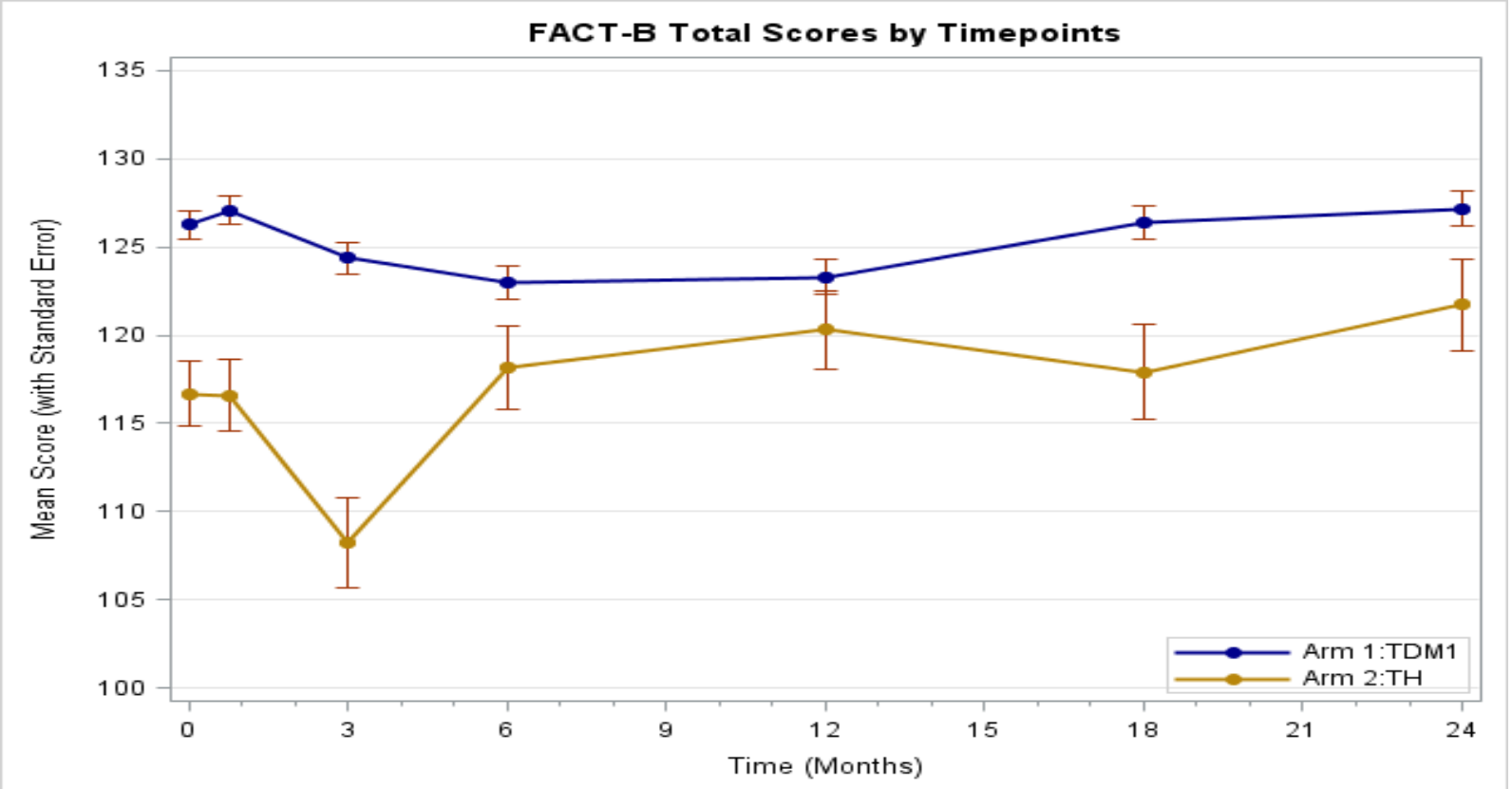
Arthralgia	18 (5%)	2 (2%)
Anemia	18 (5%)	2 (2%)

ATEMPT Trial: Quality of life (QOL)

- FACT-B
  - Baseline completed after randomization
  - Statistically worse QOL at baseline, 3+12 wks, and 18 months
  - Returned to baseline at 24 mths
  - Much less hair loss with TDM1



T-DM1

TH

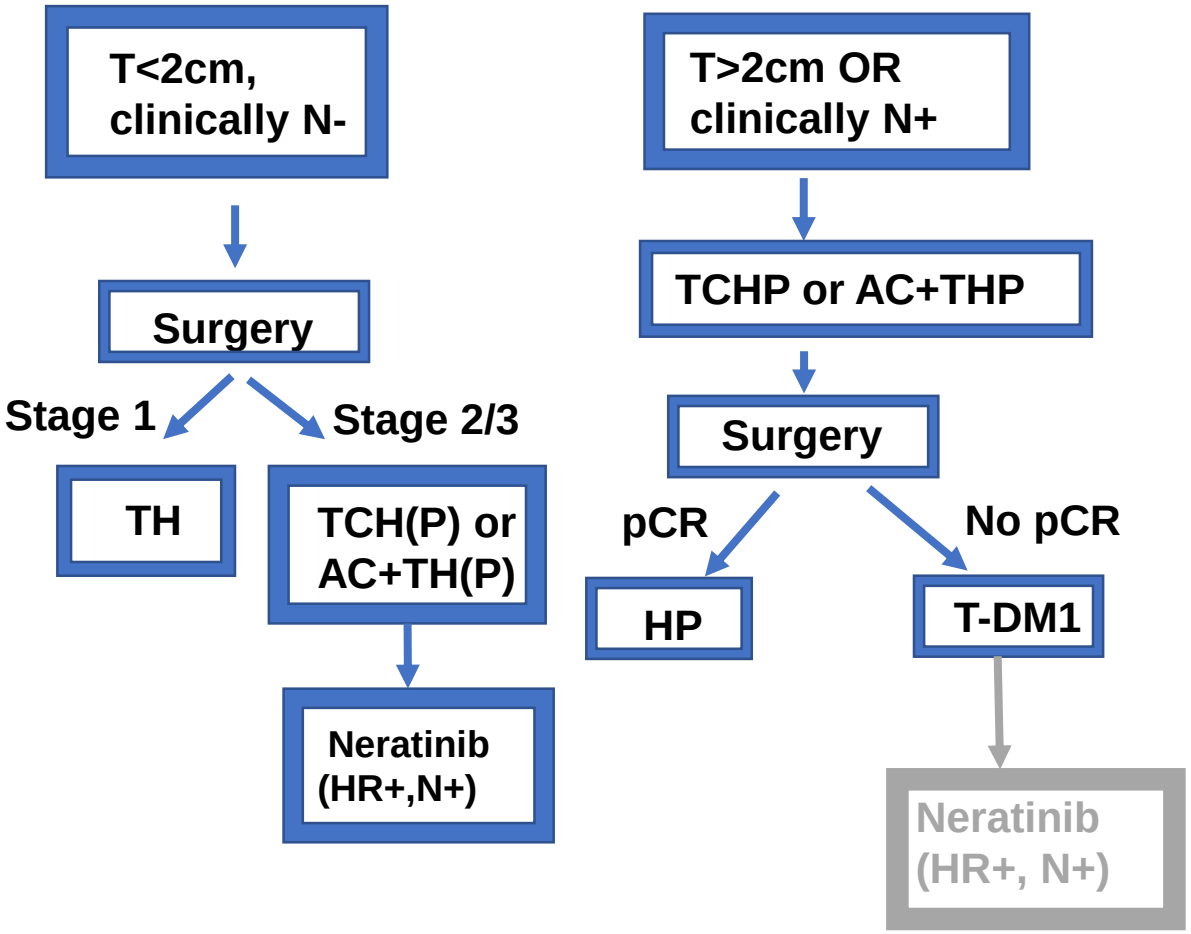
Partridge et al, SABCS 2019

Should patients with Stage I HER2+ disease get T-DM1?

- **T-DM1 x 1 year was associated with very few recurrences in the study population**
  - **3 year DFS 97.7% (95% CI: 96.2-99.3), RFI 99.1% (95% CI: 98.1-100)**
- **T-DM1 not associated with fewer clinically relevant toxicities than TH**
  - **No difference seen in overall incidence of clinically relevant toxicities (CRT) between two arms, but toxicity profiles differed for T-DM1 and TH**
  - **Not all toxicities captured in CRT endpoint (e.g. alopecia and patient reported outcomes (PROs). PROs generally favored T-DM1**
- **Given low event rate, T-DM1 may be alternative to TH for select patients with stage I HER2+ disease who are concerned about TH related side effects and understand potential T-DM1 toxicities**
- **Evaluation of shorter duration T-DM1 followed by trastuzumab should be considered**

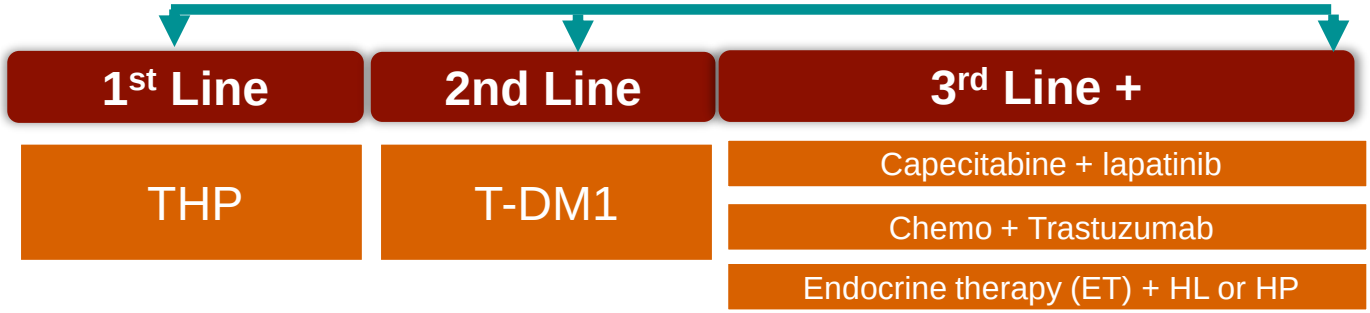
Summary: Adjuvant treatment

Preoperative therapy should be standard for all patients with clinical stage 2/3 disease



Summary – Metastatic breast cancer

ASCO 2018 Approach for Metastatic HER2+ Breast Cancer



Where are we headed?

Only one with survival benefit in metastatic setting

THANK YOU!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