SUSAN F. SMITH CENTER FOR WOMEN'S CANCERS

Dana-Farber Cancer Institute

HARVARD MEDICAL SCHOOL

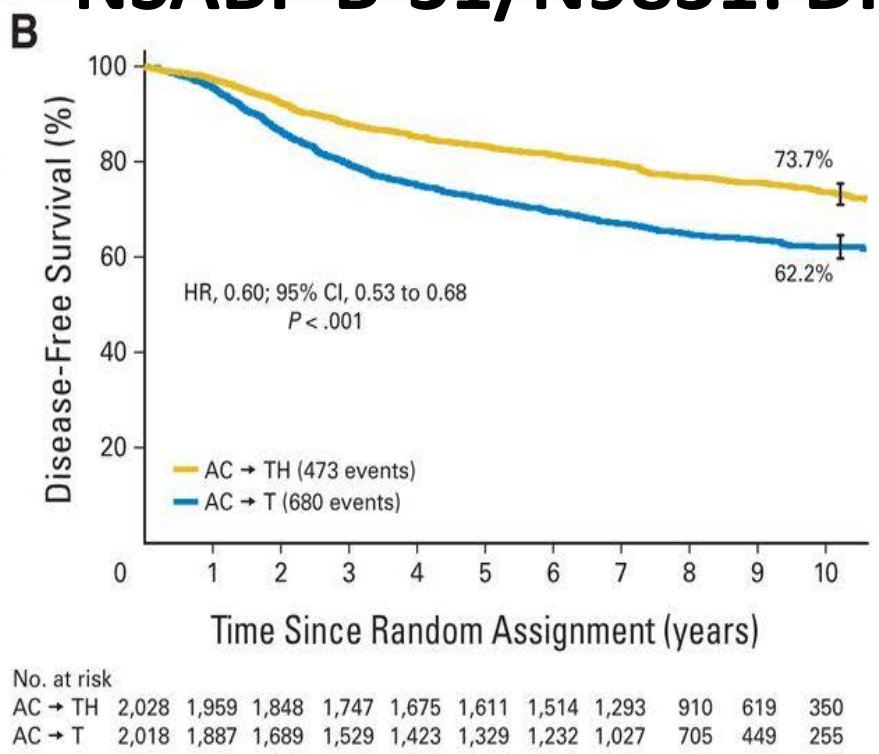
ADJUVANT AND EXTENDED-ADJUVANT THERAPY FOR PATIENTS WITH LOCALIZED HER2+ BREAST CANCER

Sara M. Tolaney

Dana-Farber Cancer Institute

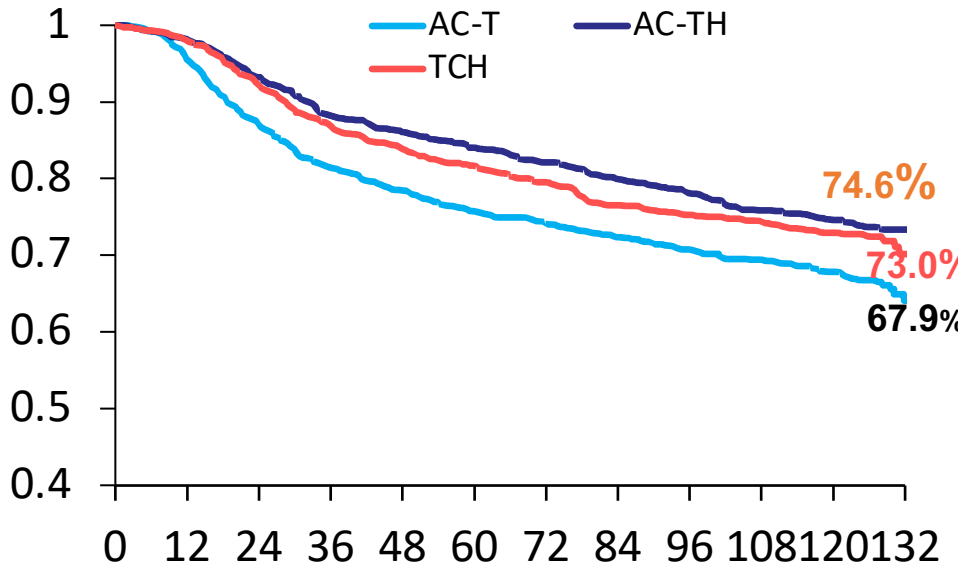
ADJUVANT TRASTUZUMAB: LONG TERM OUTCOMES

NSABP B-31/N9831: DFS



Perez E et al, J Clin Oncol 2014

BCIRG-006: DFS



Slamon D et al, SABCS 2015

~25% of patients recur with 10 years of follow-up

Courtesy of Sara M Tolaney, MD, MPH

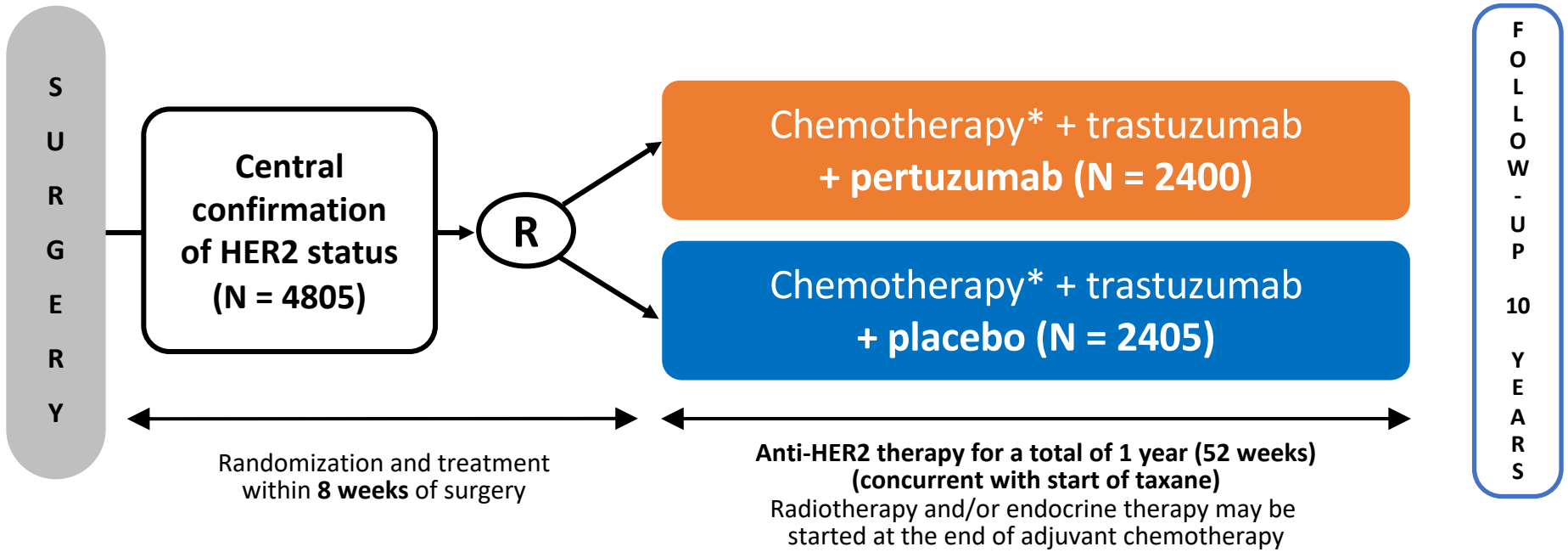
NEOADJUVANT PERTUZUMAB/TRASTUZUMAB (3 REGIMENS FDA APPROVED 9/2013)

	NEOSPHERE[1]	TRYPHAENA[2]	TRYPHAENA[2]
Treatment	Pertuzumab, Trastuzumab, Docetaxel THP x 4 FEC x 3 post-op)	Docetaxel/Carbo/ Trastuzumab/ Pertuzumab TCHP x 6	 FEC x 3 → THP x 3
N	107	77	75
ypT0/is ypN0 (%)	39.3	63.6	54.6

1. Gianni L, et al. Lancet Oncol. 2012
2. Schneeweiss A, et al. Ann Oncol. 2013

Courtesy of Sara M Tolaney, MD, MPH

APHINITY: A PHASE III ADJUVANT STUDY INVESTIGATING THE BENEFIT OF PERTUZUMAB WHEN ADDED TO TRASTUZUMAB + CHEMOTHERAPY

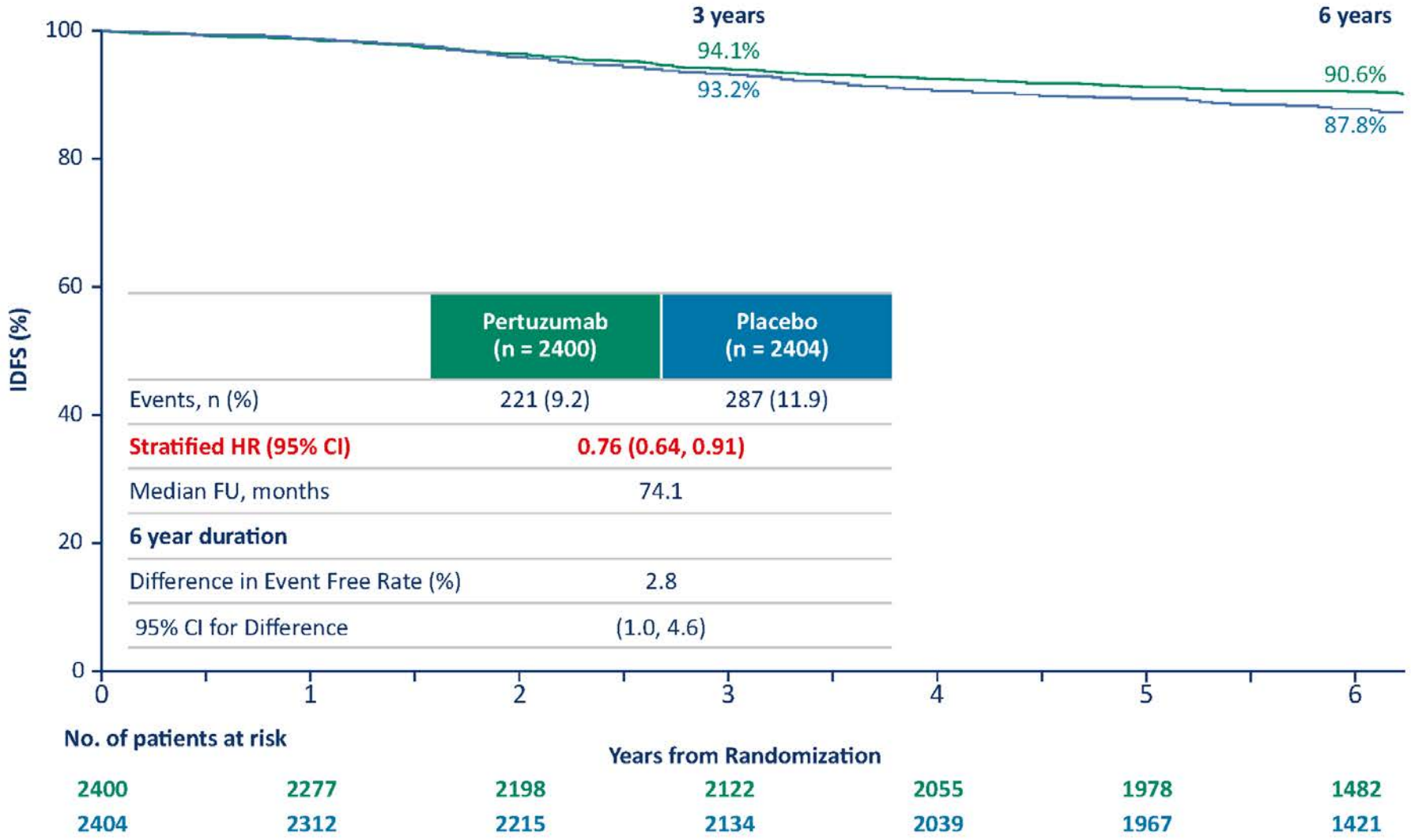


* Standard anthracycline or non-anthracycline (TCH) regimens were allowed: 3–4 x FEC (or FAC) → 3–4 x TH; 4 x AC (or EC) → 4 x TH; 6 x TCH

- **Primary endpoint:** IDFS (APHINITY definition differs from STEEP definition)
- **Secondary endpoints:** 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

Courtesy of Sara M Tolaney, MD, MPH

APHINITY UPDATED ANALYSIS: IDFS (ITT POPULATION) 74.1 MONTHS MEDIAN FU



Δ=2.8%

Piccart M et al, SABCS 2019

Courtesy of Sara M Tolaney, MD, MPH

APHINITY UPDATED ANALYSIS: IDFS BY SUBGROUPS 74.1 MONTHS MEDIAN FU

	PERTUZUMAB	PLACEBO	DIFFERENCE	HAZARD RATIO
ITT	90.6%	87.8%	2.8%	0.76
HR+	91.2%	88.2%	3.0%	0.73
HR-	89.5%	87.0%	2.5%	0.83
Node +	87.9%	83.4%	4.5%	0.72
Node -	95.0%	94.9%	0.1%	1.02

- **BENEFIT SEEN IN HR+/HR- AND NODE POSITIVE**
- **NO BENEFIT IN NODE NEGATIVE**
- **NO OS BENEFITS YET SEEN**

Piccart M et al, SABCS 2019

Courtesy of Sara M Tolaney, MD, MPH

WHEN DO WE THEN GIVE PERTUZUMAB?

- Most patients with HER2+ tumors >2cm or clinically node positive disease receive preoperative therapy
- The addition of pertuzumab improves pCR, but will not improve DFS in *all* patients (ie. not node negative patients)
- Administration of preoperative pertuzumab to all patients may result in some overtreatment, but challenging to discern which patients need pertuzumab upfront

Courtesy of Sara M Tolaney, MD, MPH

IS ANTHRACYCLINE-BASED CHEMOTHERAPY NECESSARY?

BCIRG006: 10.3 YRS FOLLOW-UP

Outcome	AC → T (n = 1073)	AC → TH (n = 1074)	TCH (n = 1075)
DFS, % (n/N) HR (95% CI)	67.9 (328/1073) 1	74.6 (269/1074) 0.72 (0.61-0.85); *P* < .0001	73.0 (279/1075) 0.77 (0.65-0.90); *P* = .0011
OS, % (n/N) HR (95% CI)	78.7 (203/1073) 1	85.9 (141/1074) 0.63 (0.51-0.79); *P* < .0001	83.3 (167/1075) 0.76 (0.62-0.93); *P* = .0075
DFS in LN+ pts, % (n/N) HR (95% CI)	62.2 (265/764) 1	69.6 (217/764) 0.72 (0.61-0.87); *P* < .001	68.4 (224/766) 0.75 (0.63-0.90); *P* = .0018

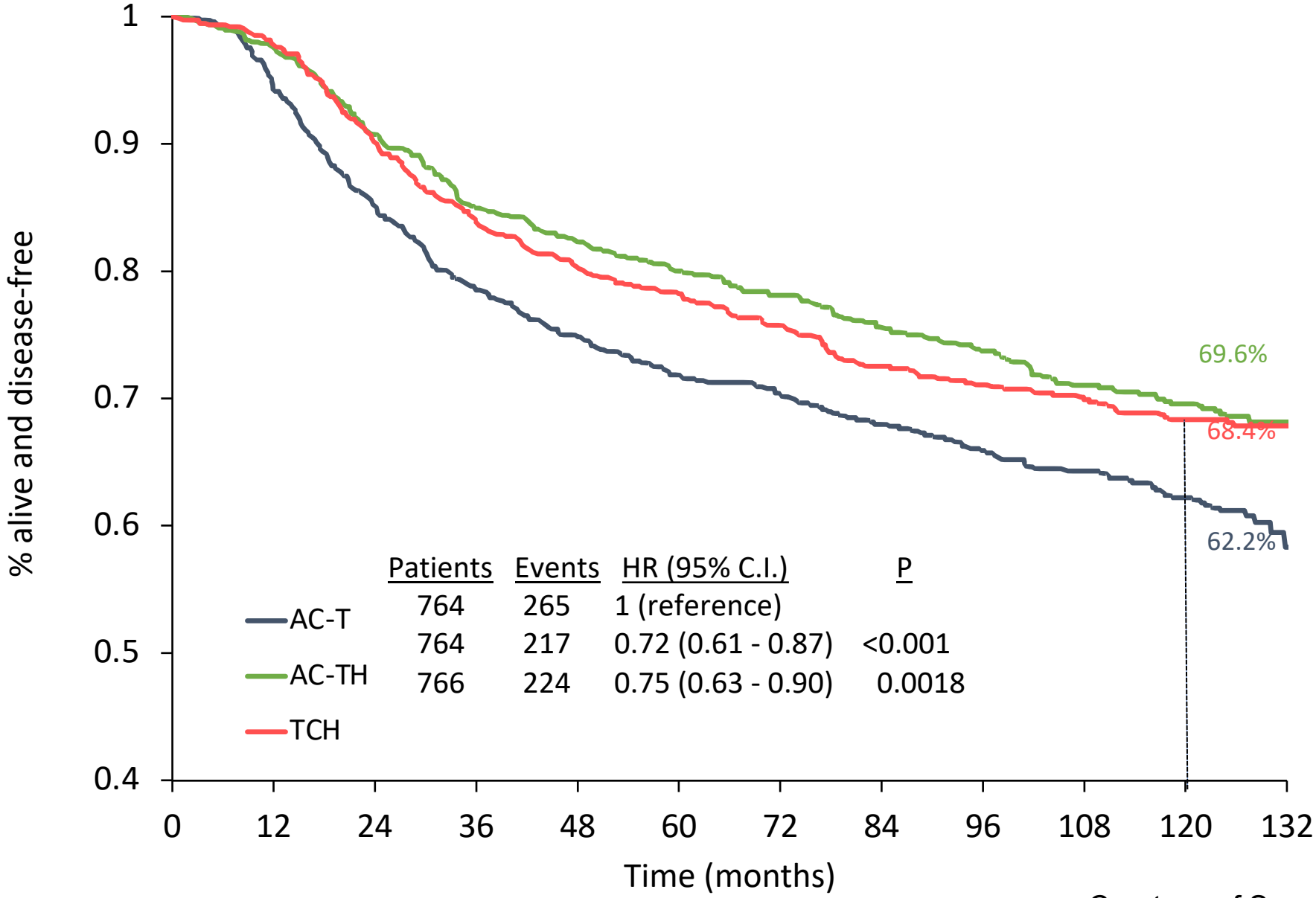
TCH ASSOCIATED WITH LESS CARDIAC TOXICITY AND NUMERICALLY FEWER CASES OF SECONDARY LEUKEMIA

Slamon D et al, SABCS 2015

Courtesy of Sara M Tolaney, MD, MPH

BCIRG 006: DFS LYMPH NODE POSITIVE

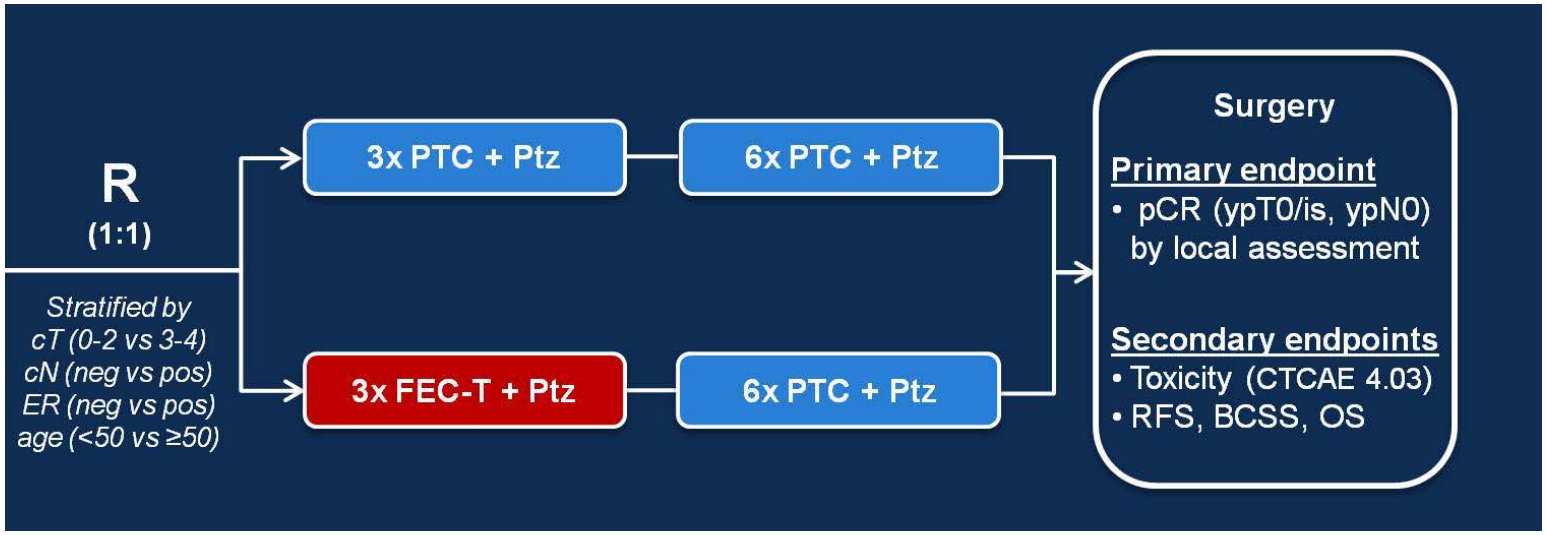
NO ADVANTAGE FOR ANTHRACYCLINES EVEN IN THE HIGH RISK GROUP

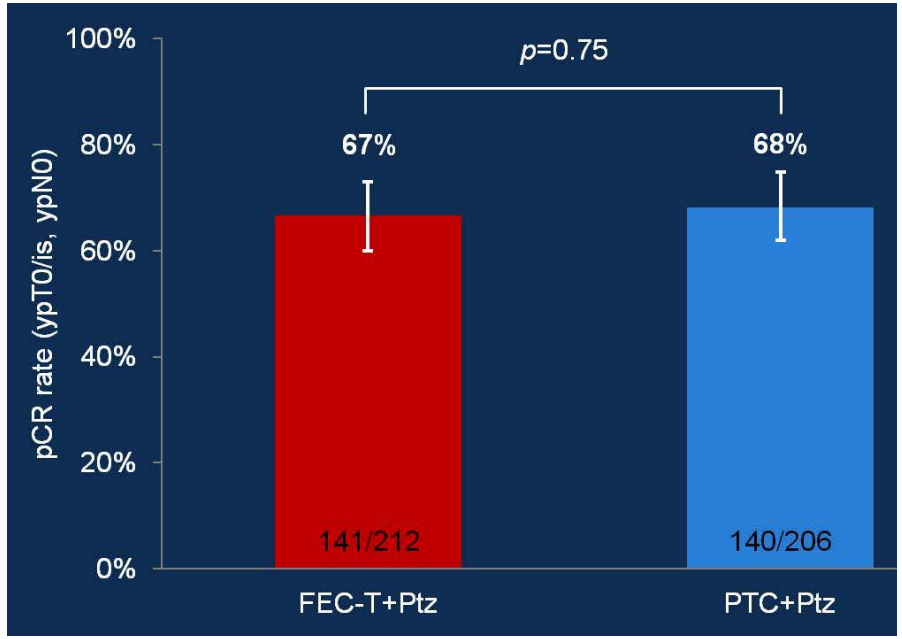


Slamon et al, SABCS 2015

Courtesy of Sara M Tolaney, MD, MPH

SUBSTITUTING ANTHRACYCLINE WITH TAXANE: TRAIN-2



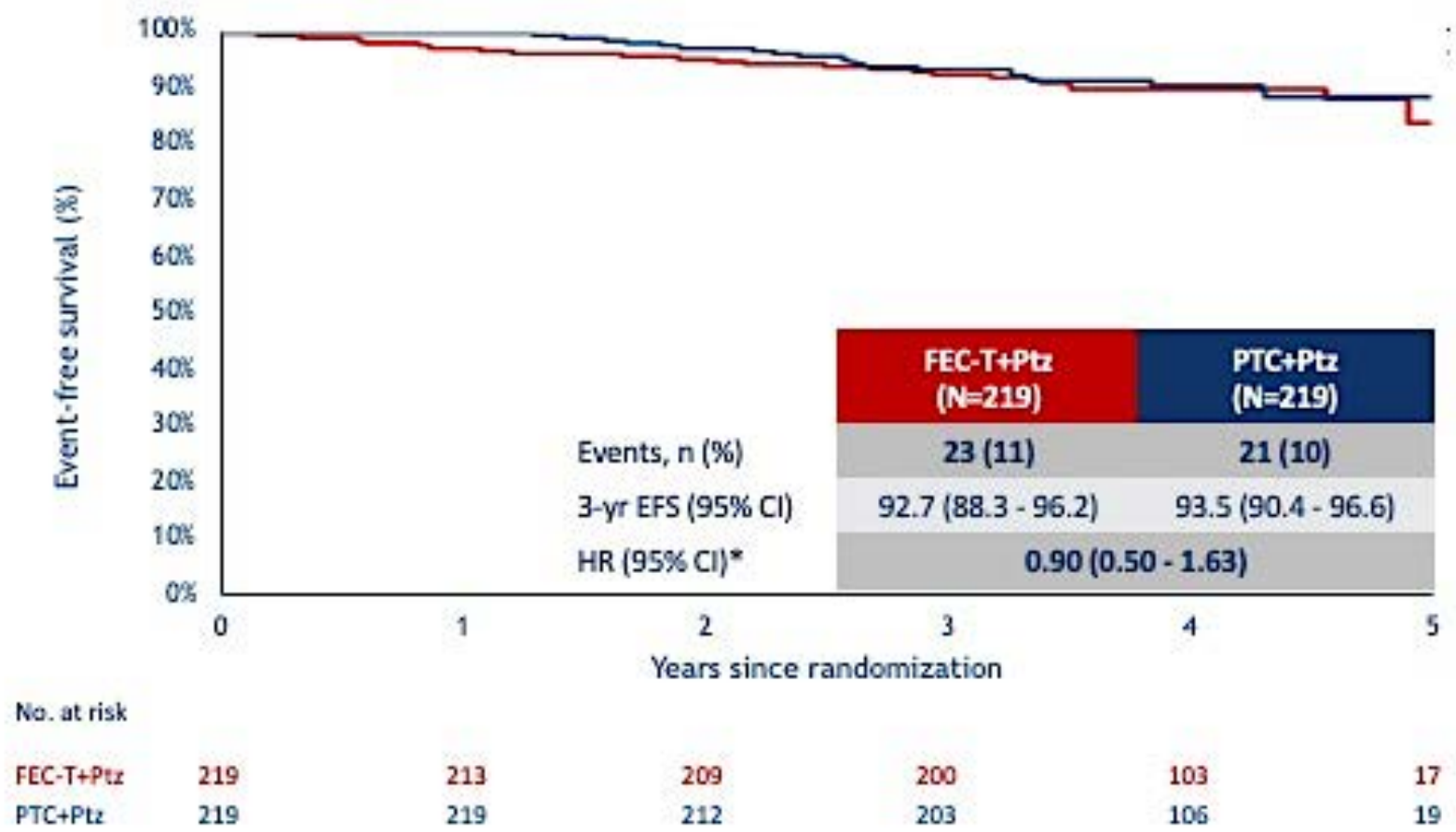


- 64% node positive, 42% HR negative
- pCR was consistent across all subgroups
- More pts completed 1 year trastuzumab in PTC/Ptz arm (97% vs 89%)
- Significantly more grade 3/4 febrile neutropenia (10% vs 1%) in anthracycline arm

Van Ramshorst MS, et al. ASCO 2017, Lancet Oncol 2018

Courtesy of Sara M Tolaney, MD, MPH

TRAIN-2: EFS

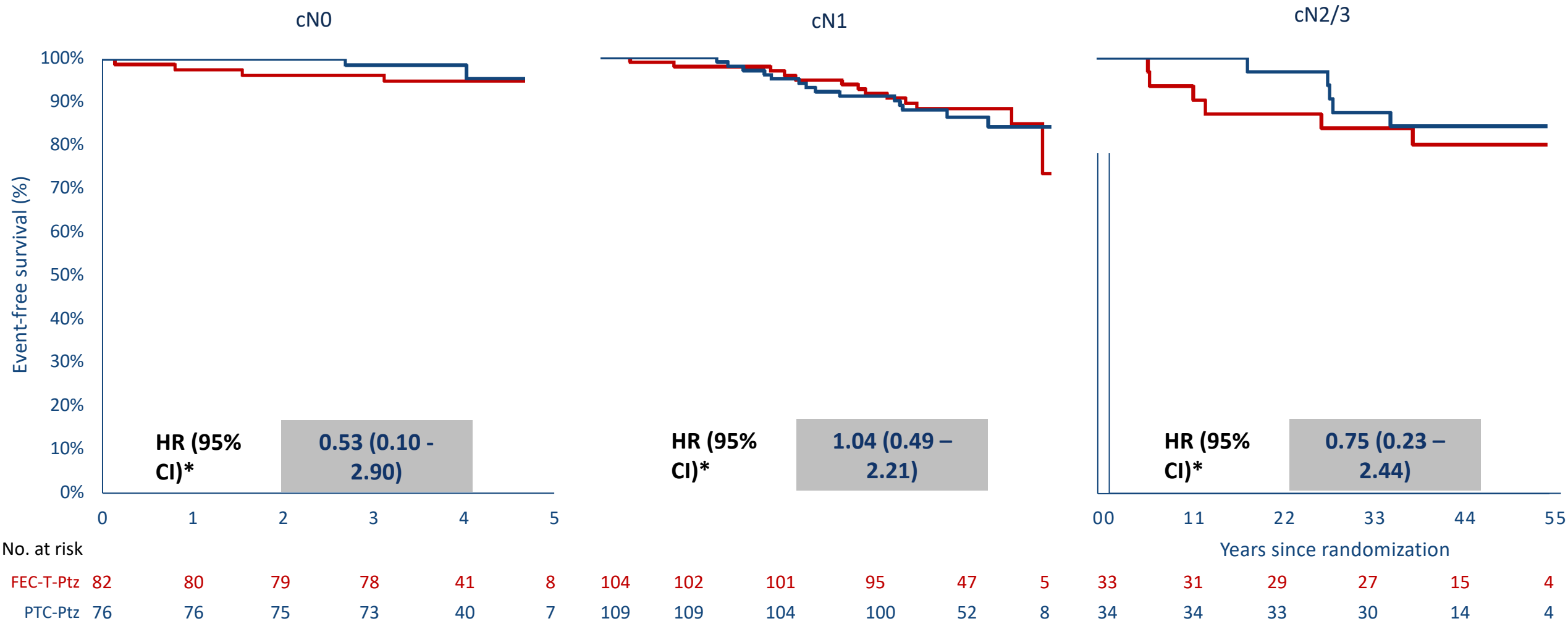


- Significantly less cardiac toxicity PTCPtz
- 2 leukemia in FEC-arm

Van der Voort A et al, ASCO 2020

Courtesy of Sara M Tolaney, MD, MPH

EFS TRAIN-2 BY NODAL STATUS



*HR <1 favors PTC+Ptz

Van der Voort A et al, ASCO 2020

Courtesy of Sara M Tolaney, MD, MPH

ANTHRACYCLINE CAN BE SUBSTITUTED WITH TAXANE-BASED HER2 DIRECTED THERAPY

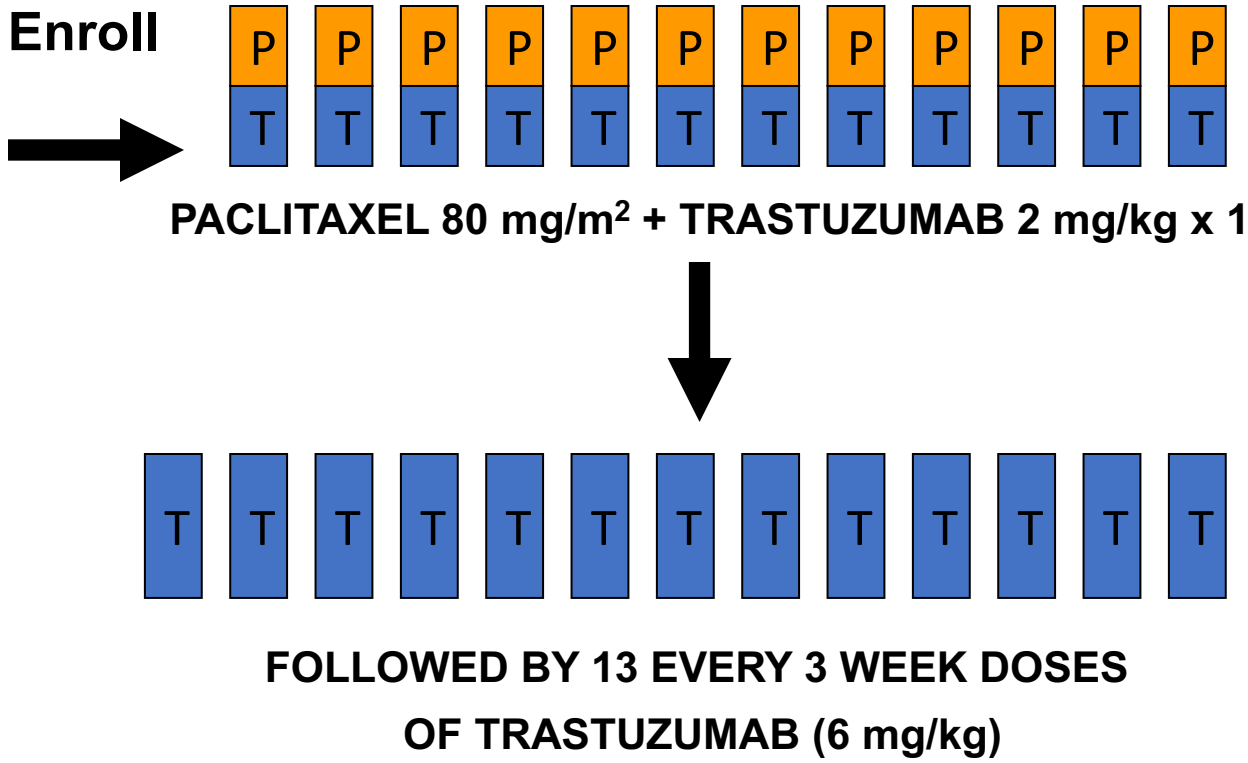
- BCIRG-006 and TRAIN-2 demonstrate similar long term outcomes with taxane-based therapy as with anthracycline-based therapy, even in high risk node-positive patients
- Less cardiac toxicity and numerically less leukemia
- Hard to justify use of anthracyclines in era of HER2-directed therapies

Courtesy of Sara M Tolaney, MD, MPH

WHAT ABOUT STAGE 1 HER2+ PATIENTS?
APT TRIAL: STUDY DESIGN

HER2+
ER+ or ER-
Node Negative
≤ 3 cm

Planned N=400

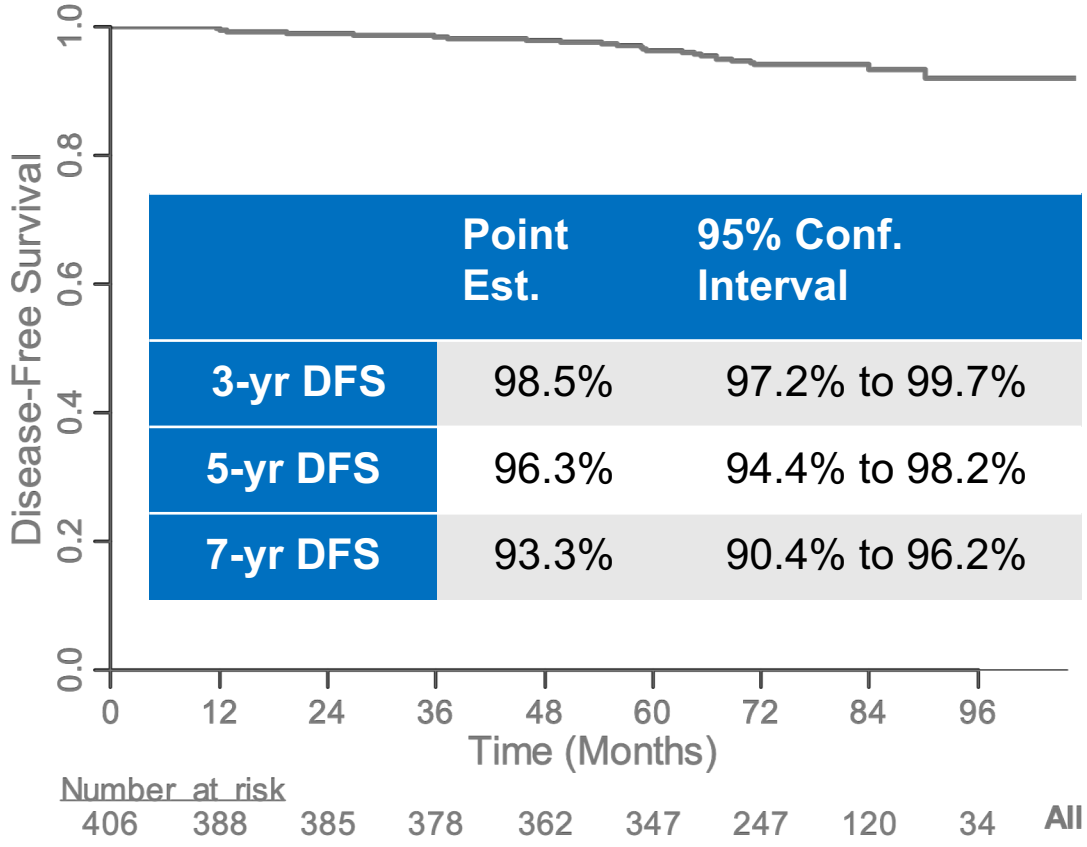


Tolaney SM et al, NEJM 2015
Tolaney SM et al, JCO 2019

Courtesy of Sara M Tolaney, MD, MPH

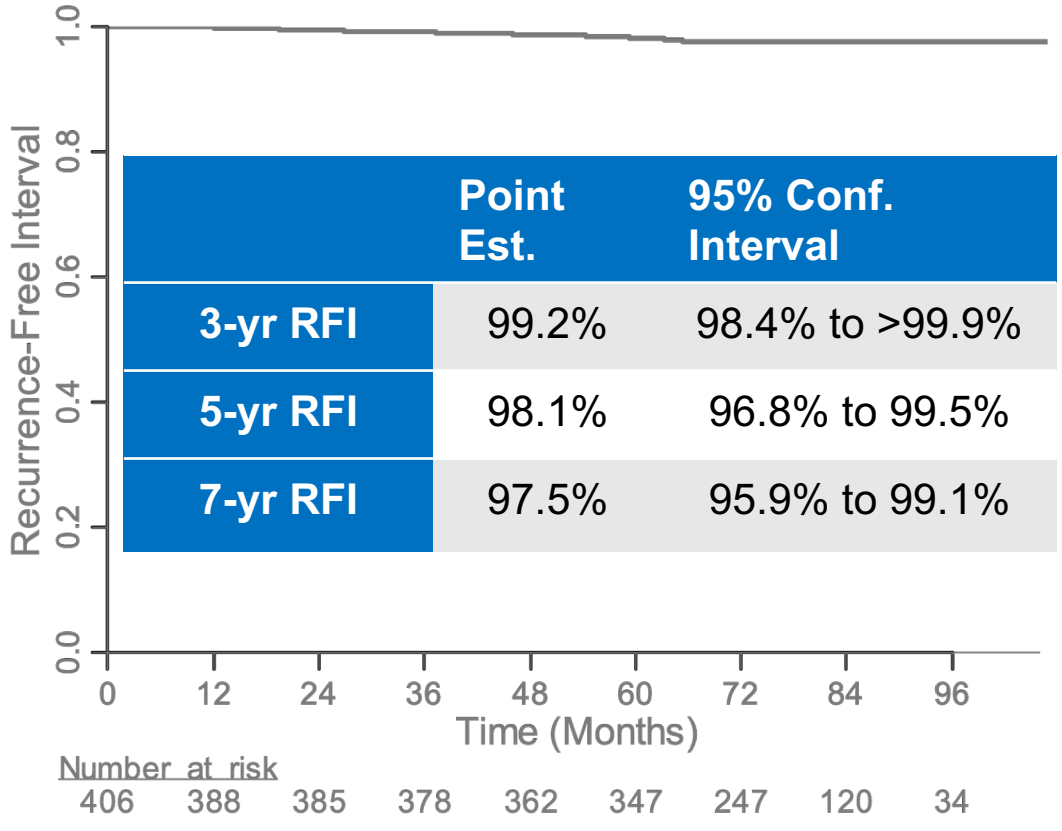
APT: OUTCOMES AT 7 YRS

DISEASE-FREE SURVIVAL



	Point Est.	95% Conf. Interval
3-yr DFS	98.5%	97.2% to 99.7%
5-yr DFS	96.3%	94.4% to 98.2%
7-yr DFS	93.3%	90.4% to 96.2%

RECURRENCE-FREE INTERVAL



	Point Est.	95% Conf. Interval
3-yr RFI	99.2%	98.4% to >99.9%
5-yr RFI	98.1%	96.8% to 99.5%
7-yr RFI	97.5%	95.9% to 99.1%

RFI Events=
- **Invasive Local/Regional Recurrence**
- **Distant Recurrence**
- **Death from Breast Cancer**

Tolaney SM et al, JCO 2019

Courtesy of Sara M Tolaney, MD, MPH

Does T-DM1 have a role for Stage I HER2+ Disease? ATEMPT Trial

Key Eligibility Criteria

- Stage 1 HER2+ breast cancer
  - HER2 centrally tested (ASCO CAP 2013 guidelines)
- N0 or N1mic
- Left Ventricular EF ≥ 50%
- No prior invasive breast cancer
- ≤90 days from last surgery

N = 497

R 3:1

3

1

N = 383

T-DM1

3.6 mg/kg IV q3 wks x 17

N = 114

TH

Paclitaxel 80 mg/m^2 IV + Trastuzumab 2 mg/kg IV wkly x12 → Trastuzumab 6 mg/kg every 3 wks x13

Stratification factors:

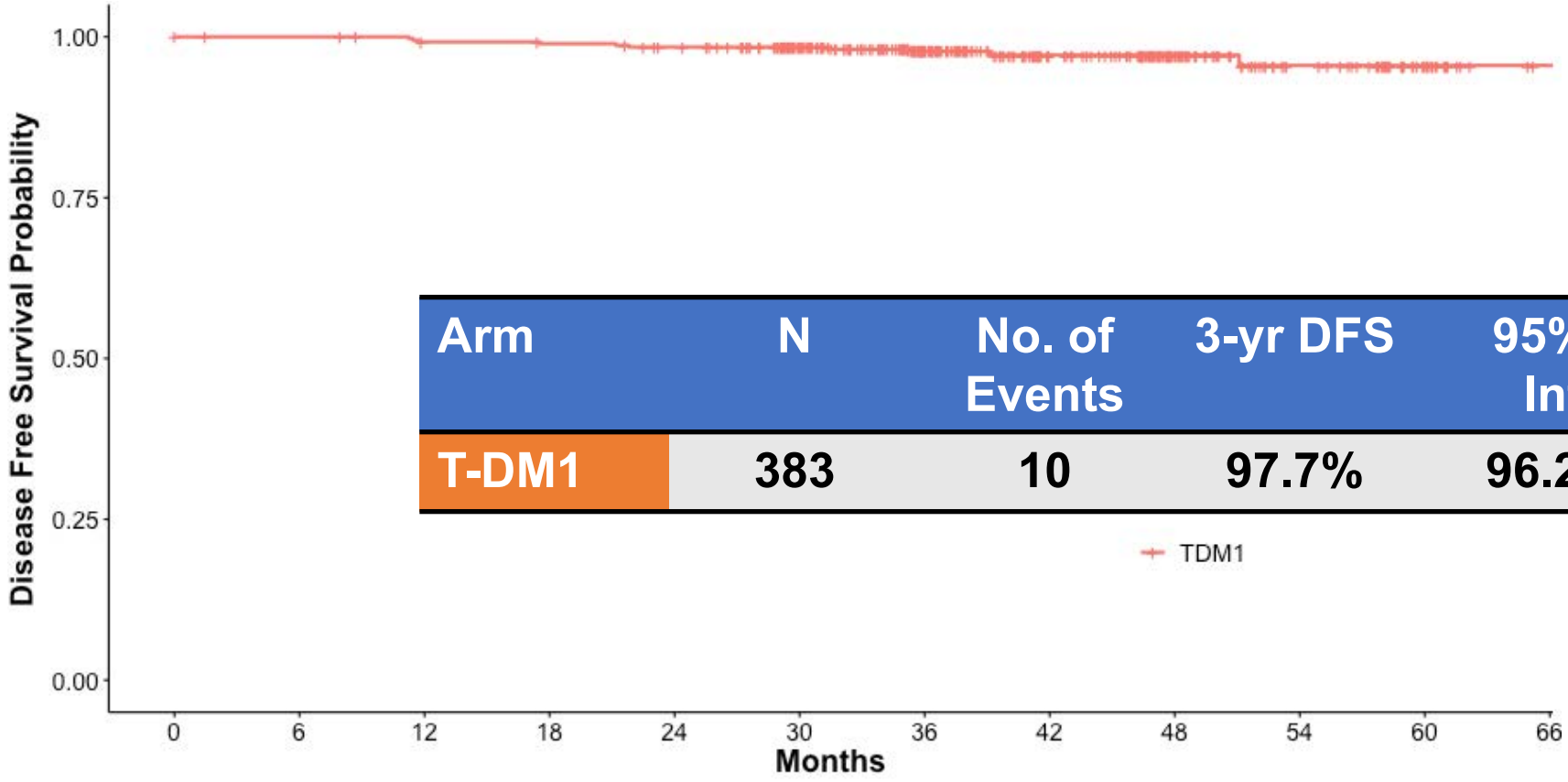
- Age (<55, ≥55)
- Planned radiation (Yes/No)
- Planned hormonal therapy (Yes/No)

***Radiation and endocrine therapy could be initiated after 12 weeks on study therapy**

Tolaney S et al. SABCS 2019

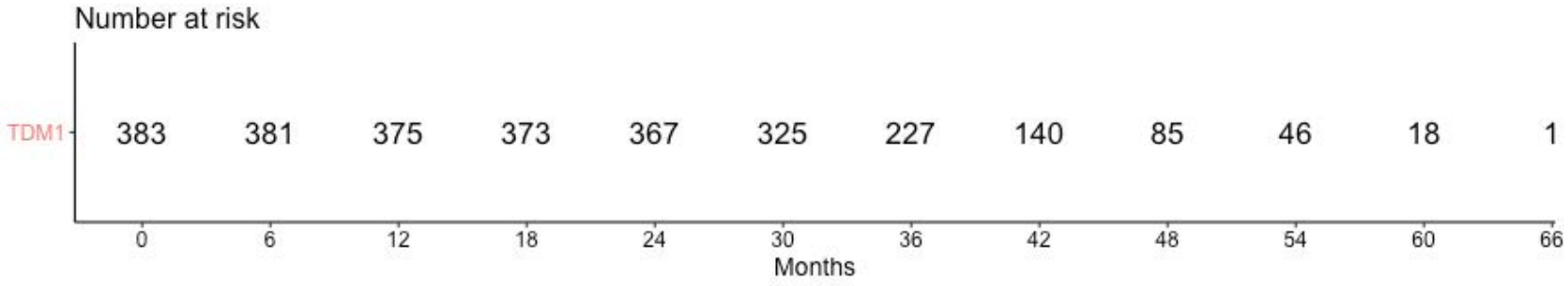
Courtesy of Sara M Tolaney, MD, MPH

ATEMPT: DISEASE-FREE SURVIVAL FOR T-DM1



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

p<0.0001



Tolaney S et al. SABCS 2019

Courtesy of Sara M Tolaney, MD, MPH

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%)

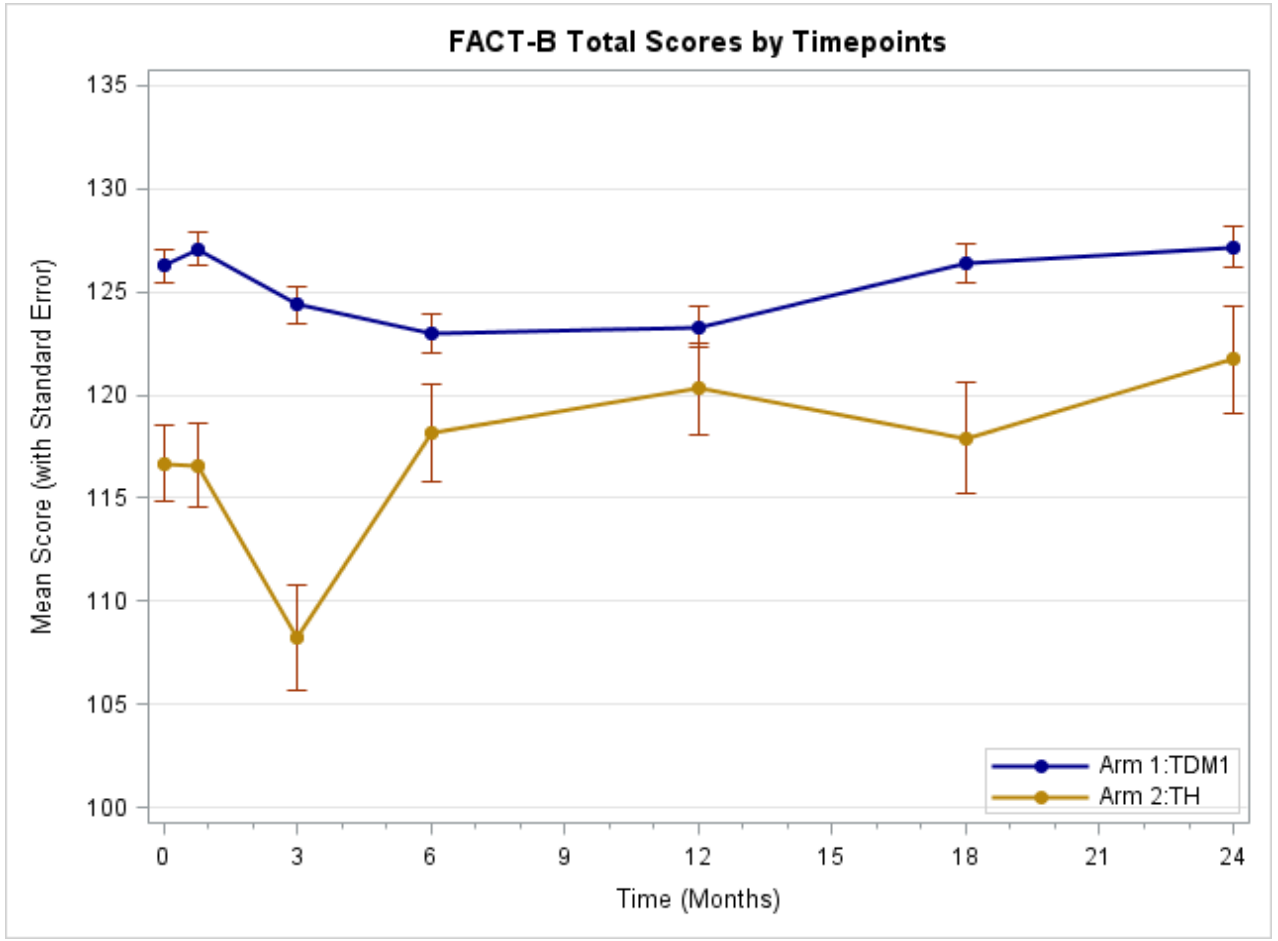
p=0.91

Tolaney S et al. SABCS 2019

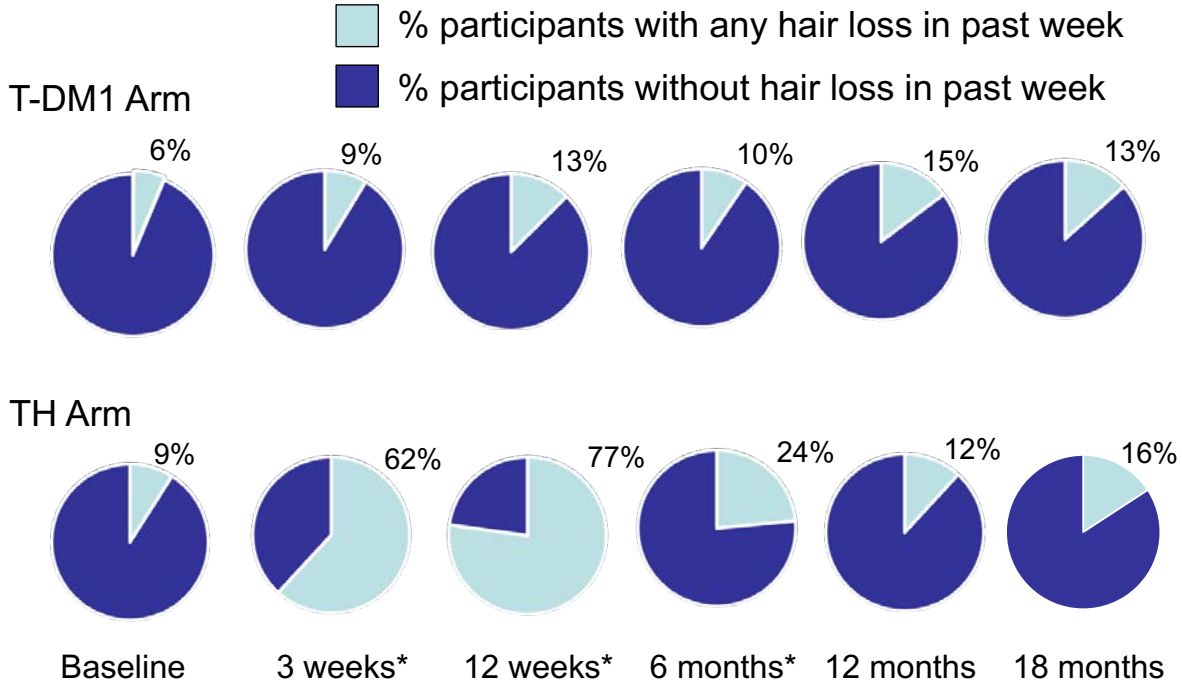
Courtesy of Sara M Tolaney, MD, MPH

ATEMPT TRIAL: PROS

QUALITY OF LIFE



Alopecia



- * Indicates statistically significantly ($p<0.05$) greater hair loss at timepoint for TH vs. T-DM1

Partridge et al, SABCS 2019

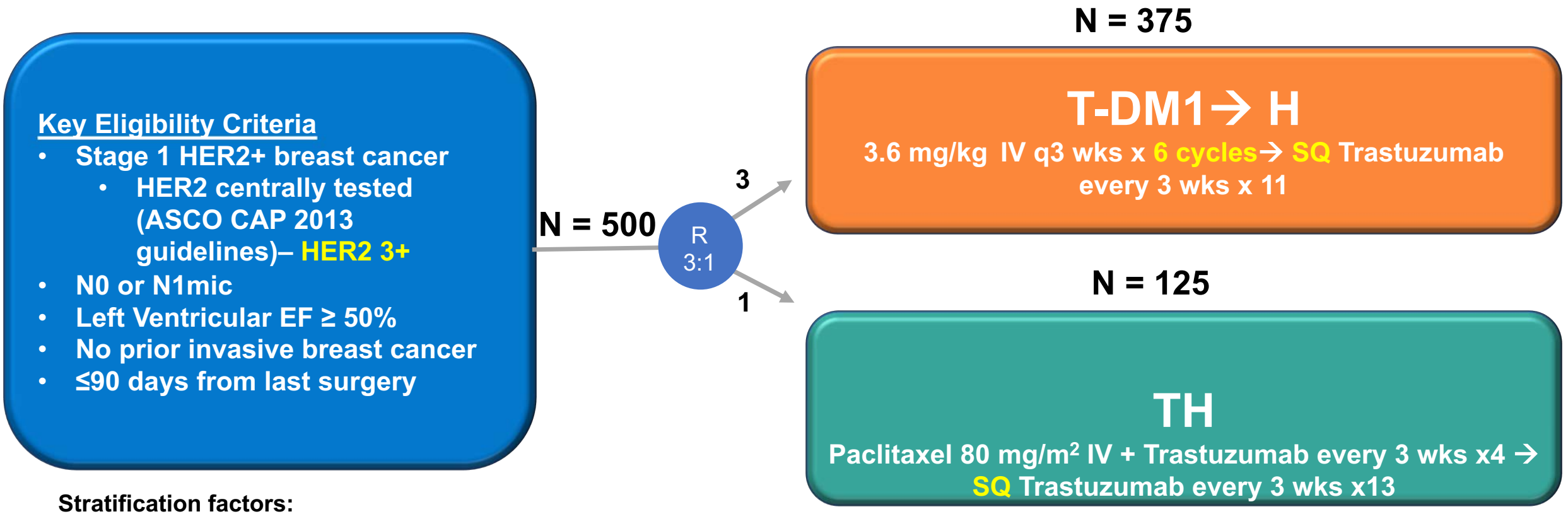
Courtesy of Sara M Tolaney, MD, MPH

WHICH PATIENTS WITH STAGE I HER2+ DISEASE SHOULD GET T-DM1?

- **T-DM1 for 1 year was associated with very few recurrences in patients with Stage I HER2+ disease**
  - **3 year DFS 97.7% (95% CI: 96.2-99.3), RFI 99.1% (95% CI: 98.1-100)**
- **T-DM1 was not associated with significantly fewer clinically relevant toxicities than TH**
- **No difference seen in the overall incidence of clinically relevant toxicities (CRT) between the two arms, but there were differences in toxicity profiles between T-DM1 and TH**
- **Not all toxicities are captured in the CRT endpoint, including alopecia, and patient reported outcomes (PROs) should be considered when assessing tolerability (generally favored T-DM1)**
- **Given the low event rate seen in this trial, T-DM1 may be an alternative to TH**

Courtesy of Sara M Tolaney, MD, MPH

PLANNED STUDY: ATEMPT 2.0



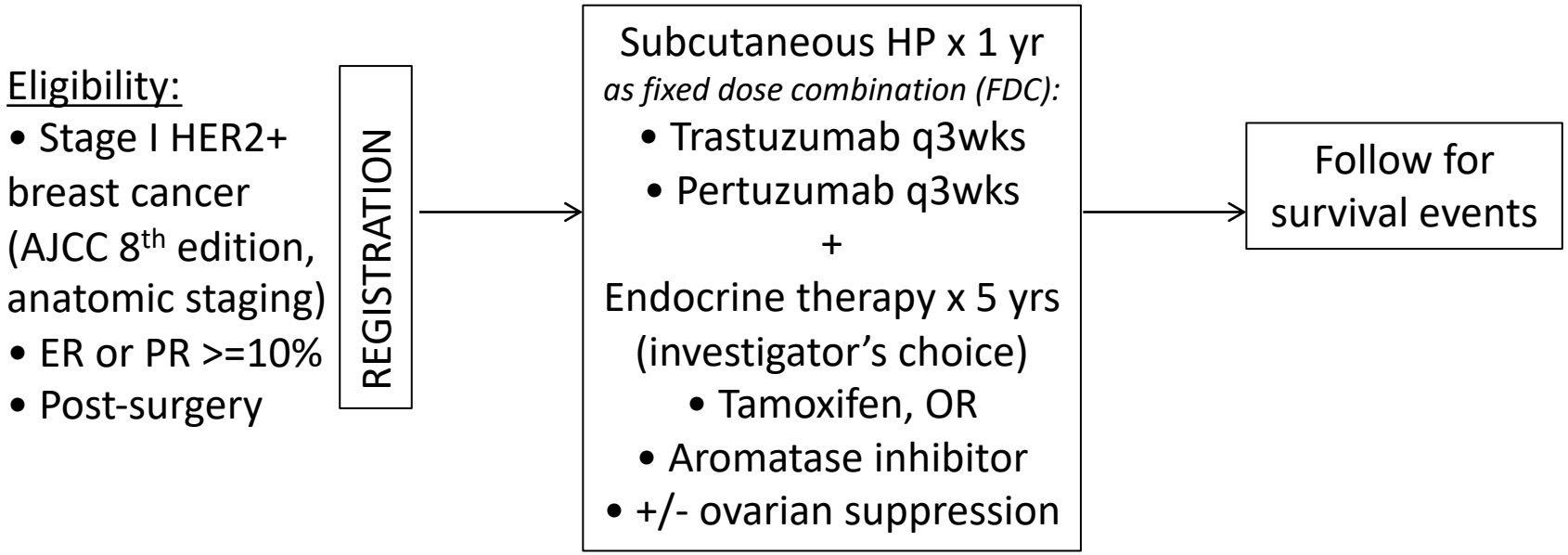
Stratification factors:

- **Age (<55, ≥55)**
- **Planned radiation (Yes/No)**
- **Planned hormonal therapy (Yes/No)**

***Radiation and endocrine therapy could be initiated after 12 weeks on study therapy**

Courtesy of Sara M Tolaney, MD, MPH

PLANNED STUDY: A SINGLE ARM PHASE II STUDY OF ADJUVANT ENDOCRINE THERAPY, SUBCUTANEOUS PERTUZUMAB, AND TRASTUZUMAB FIXED-DOSE COMBINATION FOR PATIENTS WITH ANATOMIC STAGE I HORMONE RECEPTOR-POSITIVE, HER2-POSITIVE BREAST CANCER (ADEPT)



PI: Ada Waks

Courtesy of Sara M Tolaney, MD, MPH

CAN WE SHORTEN THE DURATION OF TRASTUZUMAB?

Trial	Tmab Duration	Chemotherapy	N	DFS, %	Status/Results
SOLD[1]	9 wks vs 1 yr	DTX x 3 + FEC x 3	2174	5 yrs: 88 vs 90.5	Noninferiority not reached, cardiac tox better with shorter
Short-HER[2]	9 wks vs 1 yr	DTX x 3→FEC x 3 vs AC x 4→TX x 4	1254	5 yrs: 85.4 vs 87.5	Noninferiority not reached, cardiac tox better with shorter
PHARE[3]	6 vs 12 mos	Investigator choice (~90% anthracycline based)	3384	7.5 yrs: 78.8 vs 79.6 (*P* = .39)	Noninferiority not reached, cardiac tox better with shorter
Hellenic Oncology[4]	6 vs 12 mos	ddFEC/D	481	3 yrs: 93.3 vs 95.7 (*P* = .137)	Noninferiority not reached
PERSEPHONE	6 vs 12 mos	Investigator choice	4089	4 yrs: 89.4 vs 89.8 (*P* = .01)	Cardiac outcomes published 2016[5]; noninferiority demonstrated (ASCO 2018[6])

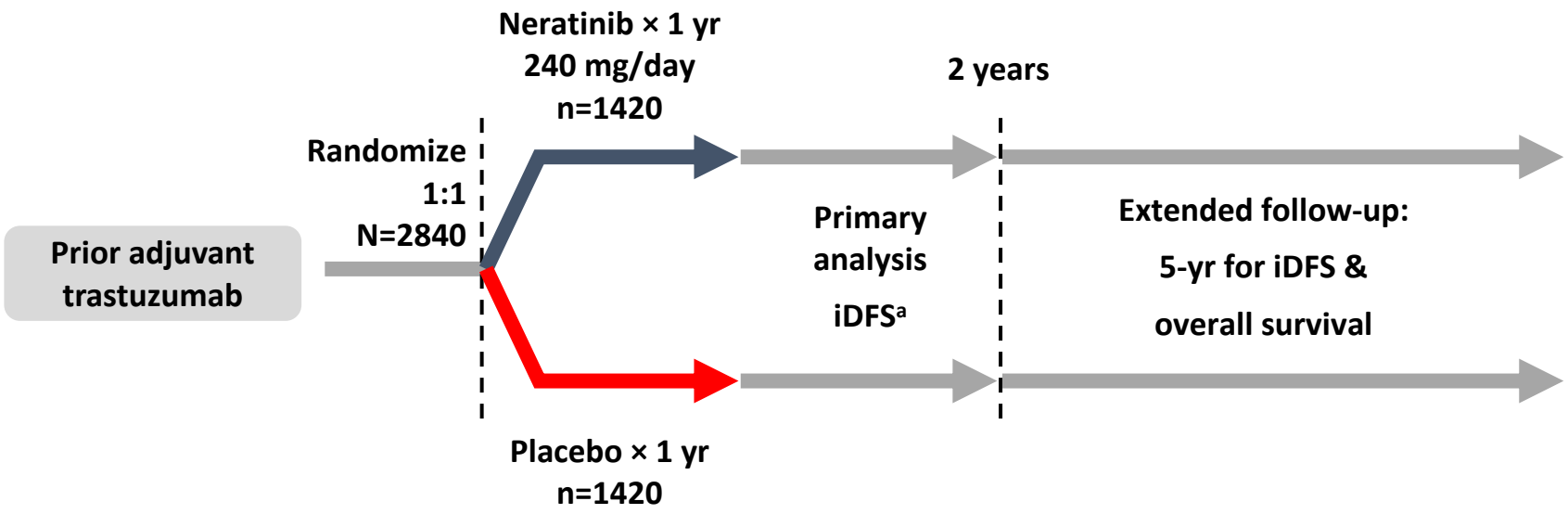
1. Joensuu. JAMA Oncol. 2018;4:1199. 2. Conte. Ann Oncol. 2018;29:2328. 3. Pivot. Lancet Oncol 2013;14:74. 4. Mavroudis. Ann Oncol 2015;26:1333
5. Earl. Br J Cancer. 2016;115:1462. 6. Earl. ASCO 2018. Abstr. 506.

ONE YEAR OF TRASTUZUMAB REMAINS THE STANDARD

(stopping early for toxicity in patients with lower risk disease unlikely to have significant impact on outcomes)

Courtesy of Sara M Tolaney, MD, MPH

ADDING NERATINIB: ExteNET STUDY



Primary endpoint: invasive disease-free survival (iDFS)[a]

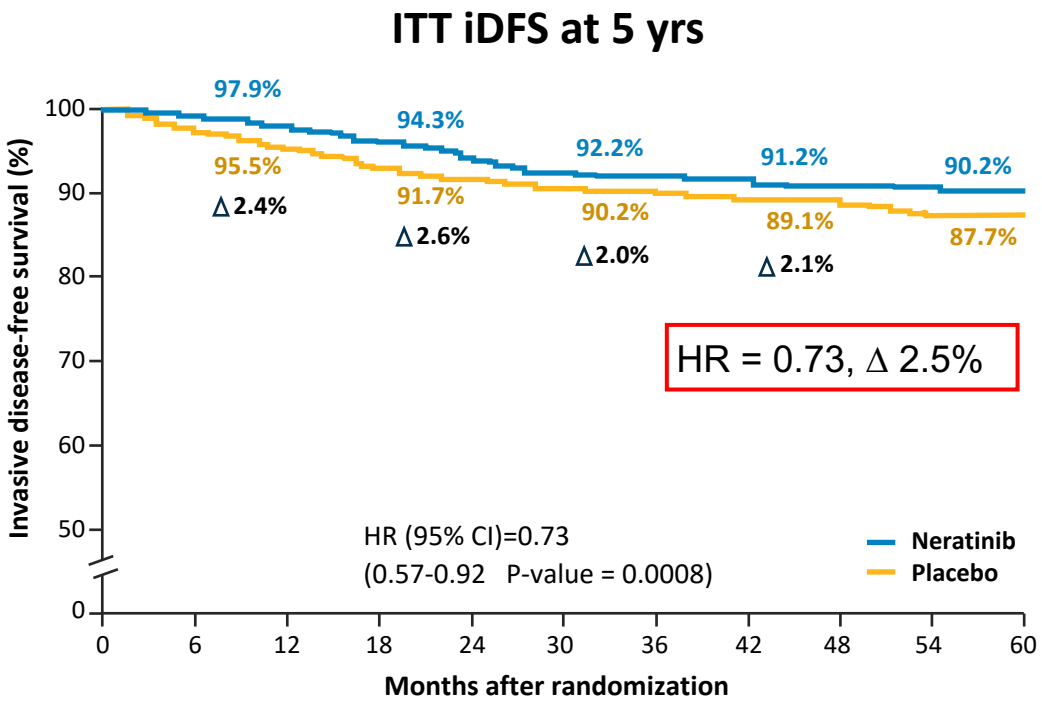
Secondary endpoints: overall survival, DFS-DCIS, distant DFS, time to distant recurrence, CNS metastases, safety,

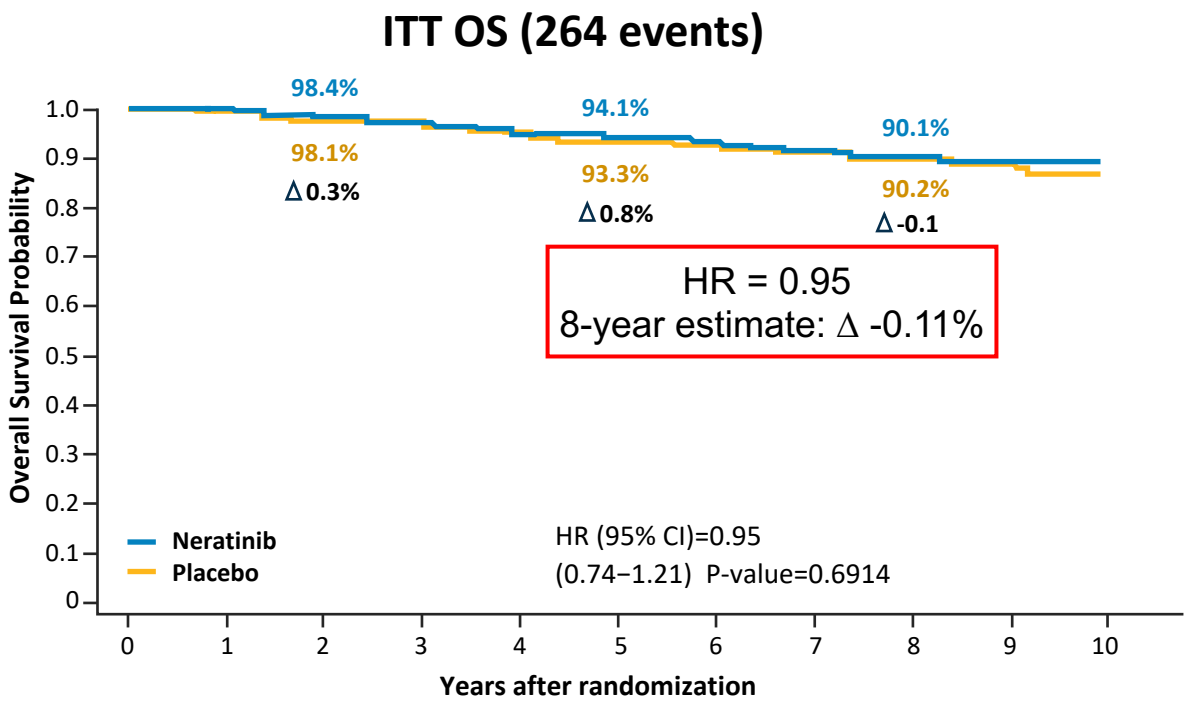
Stratification: nodes 0, 1-3 vs 4+, ER/PR status, concurrent vs sequential trastuzumab

Study blinded: Until primary analysis; OS remains blinded

Courtesy of Sara M Tolaney, MD, MPH

ExteNET iDFS and OS Intent-To-Treat Population (N=2,840)





No. at risk

Neratinib	1420	1316	1272	1225	1106	978	965	949	938	920	885
Placebo	1420	1354	1298	1248	1142	1029	1011	991	978	958	927

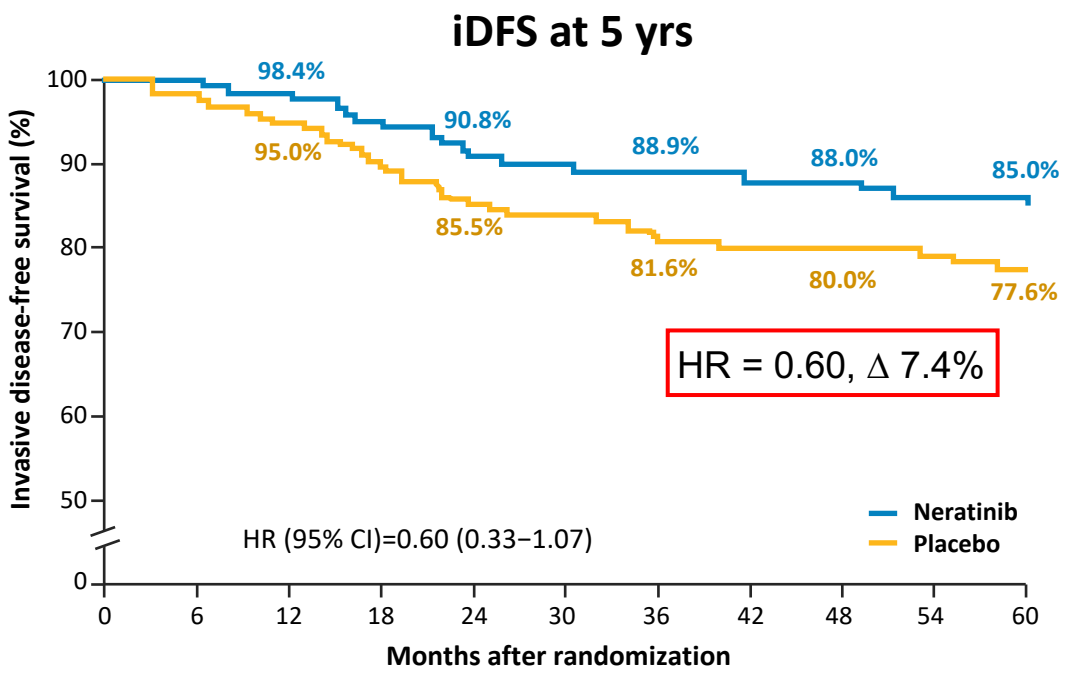
No. at risk

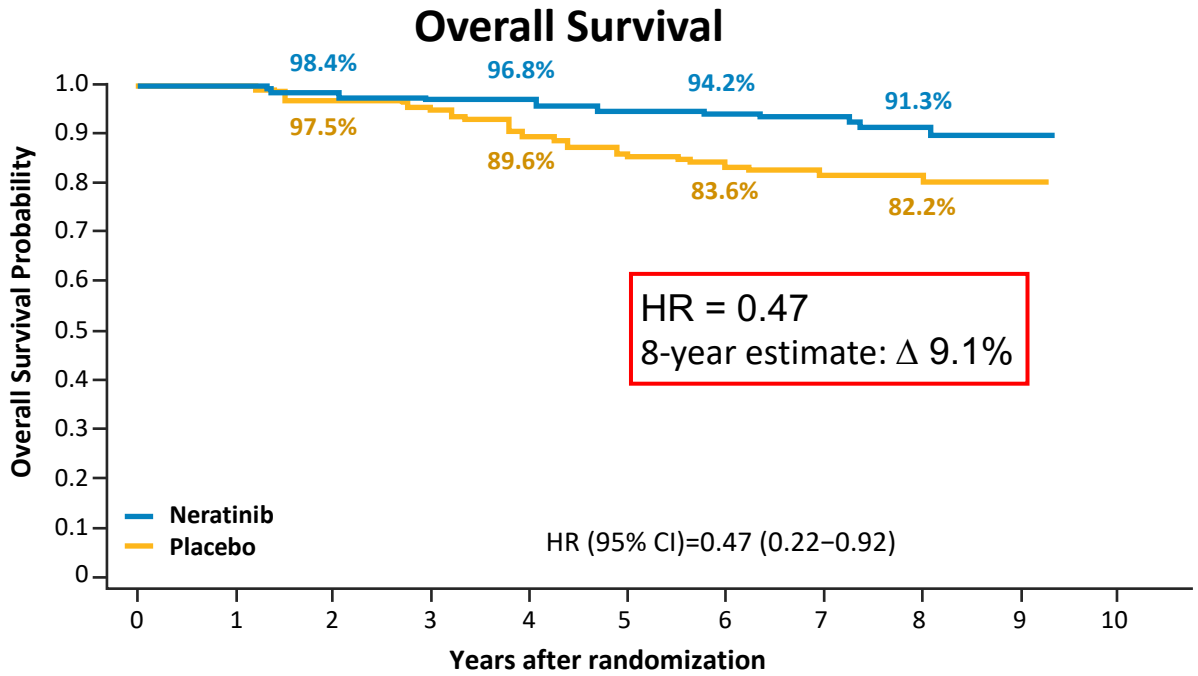
Neratinib	1420	1364	1309	1213	1118	1168	1123	1041	746	218	0
Placebo	1420	1384	1341	1249	1223	1199	1166	1086	796	221	0

Martin et al. Lancet Oncol. Dec 2017;18(12):1688-1700

Courtesy of Sara M Tolaney, MD, MPH

ExteNET: No pCR Post Neoadjuvant Therapy HR+, ≤1 Year from Trastuzumab (N=295)





No. at risk

Neratinib	131	126	121	113	100	94	93	91	91	88	84
Placebo	164	159	151	143	125	107	103	99	99	98	94

No. at risk

Neratinib	131	126	121	116	113	110	106	100	60	14	0
Placebo	164	161	156	143	135	129	123	115	65	12	0

Chan, A. Clin Breast Cancer. 2020. Online ahead of print.

Courtesy of Sara M Tolaney, MD, MPH

Descriptive Analysis: Cumulative Incidence of CNS recurrences at first site of mets at 5 years HR+/≤1-year population (*n*=1334)

Subgroup	Cumulative Incidence of CNS recurrences at 5 years, %	
	Neratinib	Placebo
	%	%
All patients (*n*=1334)	0.7	2.1
Prior neoadjuvant therapy		
No (*n*=980)	0.7	1.5
Yes (*n*=354)	0.7	3.7
pCR status[1]		
No (*n*=295)	0.8	3.6
Yes (*n*=38)*	0	5

*Small Ns

1. Among the 354 patients who had received neoadjuvant therapy, 295 had no pCR, 38 patients achieved a pCR, and 21 patients had no outcome reported

CI, confidence interval; CNS, central nervous system; NE, not estimated; pCR, pathologic complete response

Courtesy of Sara M Tolaney, MD, MPH

To date no agent has shown a difference in CNS Recurrences as first site of metastasis

Trial Population	CNS Recurrences, %	CNS Recurrences, %
ALLTO (3 years) ITT, L+T , T->L, L, T* (N=5190)	Trastuzumab: 2	Trastuzumab +Lapatinib: 2
APHINITY (3 years) ITT (N=4,805)	Placebo: 2	Pertuzumab: 2
KATHERINE (3 years) ITT (high risk, No pCR) (N=1,486)	Trastuzumab: 5.4	T-DM1: 6.1

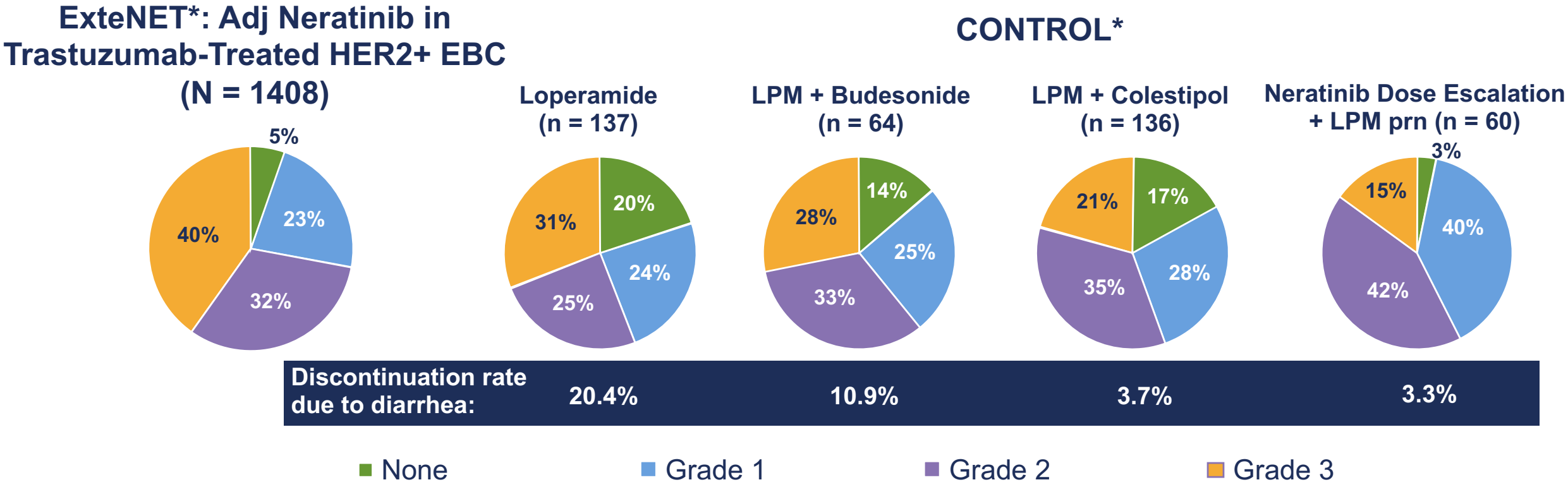
Caveat: Cross Trial Comparisons
Patients in KATHERINE are at higher risk of recurrence

Piccart-Gebhart JCO 2016; 34(10)
von Minckwitz et al. N Engl J Med. 2017;377:122-131.
von Minckwitz et al. N Engl J Med. Feb 14 2019;380(7).

*ALTTO reported the same rate for all 4 arms, 2 are shown here

Courtesy of Sara M Tolaney, MD, MPH

ANTIDIARRHEAL PROPHYLAXIS REDUCES DIARRHEA WITH NERATINIB: CONTROL TRIAL



PREVENTIVE STRATEGIES REDUCED GRADE ≥3 DIARRHEA COMPARED TO EXTENET

Chan et al, SABCS 2019
Chan at al, Lancet Oncol 2016
Hurvitz S, SABCS 2017

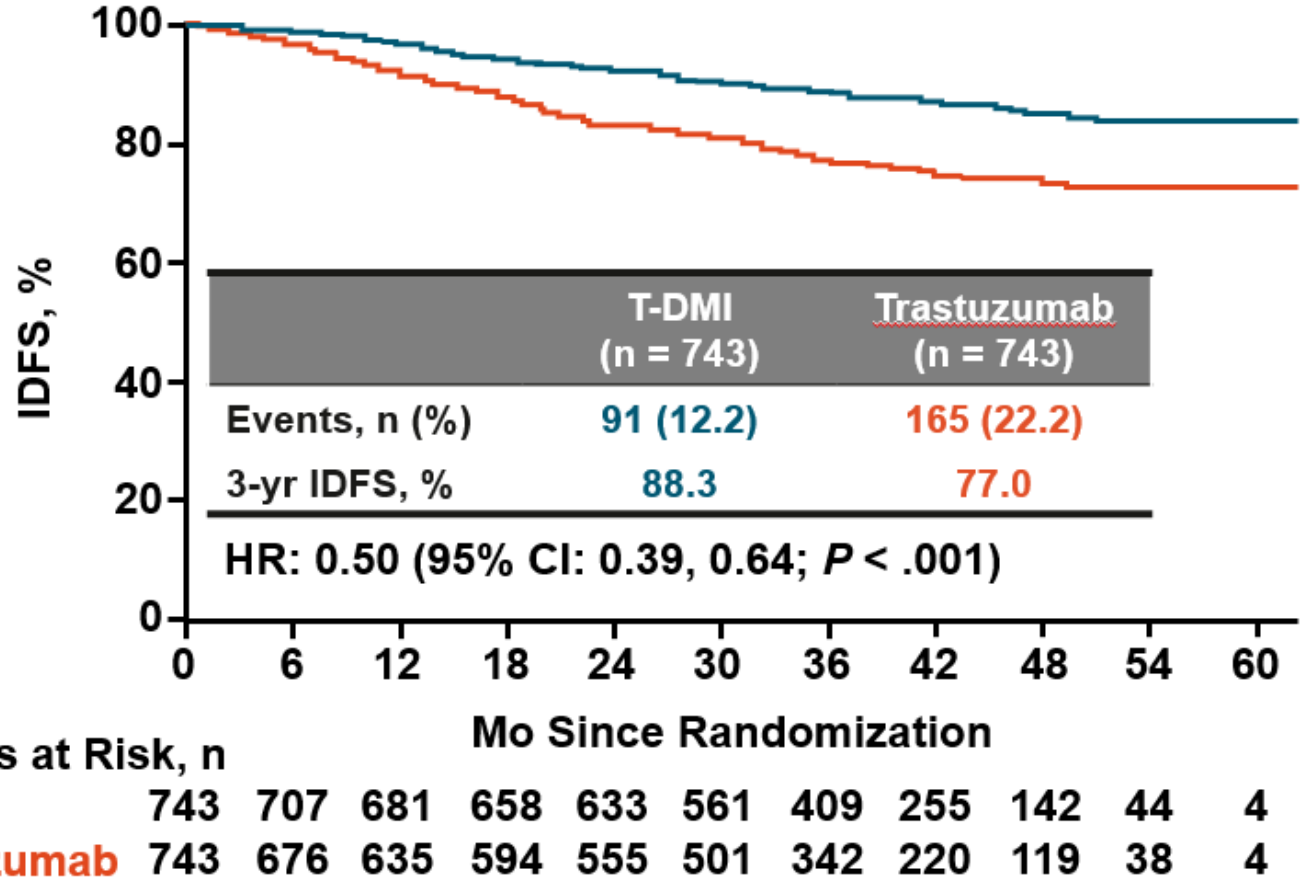
Courtesy of Sara M Tolaney, MD, MPH

WHEN SHOULD WE GIVE NERATINIB?

- Benefit seen in patients with high risk HR+ HER2+ disease (larger benefit in patients with residual disease after preoperative therapy)
- Challenge is lack of data in patients who have previously received pertuzumab and/or T-DM1
- Must also weigh potential benefit with toxicity (~40% grade 3/4 diarrhea)
    - All patients should receive prophylactic anti-diarrheals (OR can consider a dose escalation approach)

Courtesy of Sara M Tolaney, MD, MPH

RESPONSE TO NEOADJUVANT TREATMENT CLEARLY IDENTIFIES HIGH RISK PATIENTS FOR TREATMENT WITH T-DM1 (KATHERINE)



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

CNS events: *5.9% vs †4.3%.

Geyer C, et al. SABCS 2018
von Minckwitz G, et al. *N Engl J Med.* 2019

Courtesy of Sara M Tolaney, MD, MPH

CAN WE IMPROVE UPON THE KATHERINE TRIAL OF T-DM1?

- 3 yr iDFS for N+ pts: 83%.
- No improvement in rates of CNS recurrence
- May want to consider further treatment escalation with future studies:
  - Add on strategies: T-DM1 + tucatinib (being explored in COMPASS-RD)
  - Substitution strategies: Trastuzumab deruxtecan (DS-8201a)

Courtesy of Sara M Tolaney, MD, MPH

COMPASSHER2 TRIALS

Eligibility:
Stage II or IIIA HER2+ BC (T2-3, N0-2)

- cN0 eligible if ≥ 2.0 cm
- cN1-2 eligible ≥ 1.5cm
- ER+ and ER- eligible

REGISTRATION

Preoperative Phase: all patients

THP x 4 Cycles
Paclitaxel qwk x12
OR
Docetaxel q3 wk x4
with
Trastuzumab (H)
& Pertuzumab (P) q3 wk x4

* nab-pacl allowed

SURGERY

Eligibility
HER2+ RD
ER- & ER+
(ER+ must be N+)
(~30% of A011801 expected to come from EA1181)

Arm A: pCR (no invasive disease)

pCR (ypT0/Tis ypN0) *40%*

EA1181
CompassHER2-pCR

- Complete 1 yr HP
- Radiation and endocrine Rx (if appropriate)

ECOG-ACRIN cancer research group
Reshaping the future of patient care

No pCR *60%*

A011801
CompassHER2-RD

Alliance for Clinical Trials in Oncology

Grp 1: pre-op THP-> AC, Cb/HP x 4
Grp 2: pre-op TCHP, *AC-THP* -> no further chemo

Registration

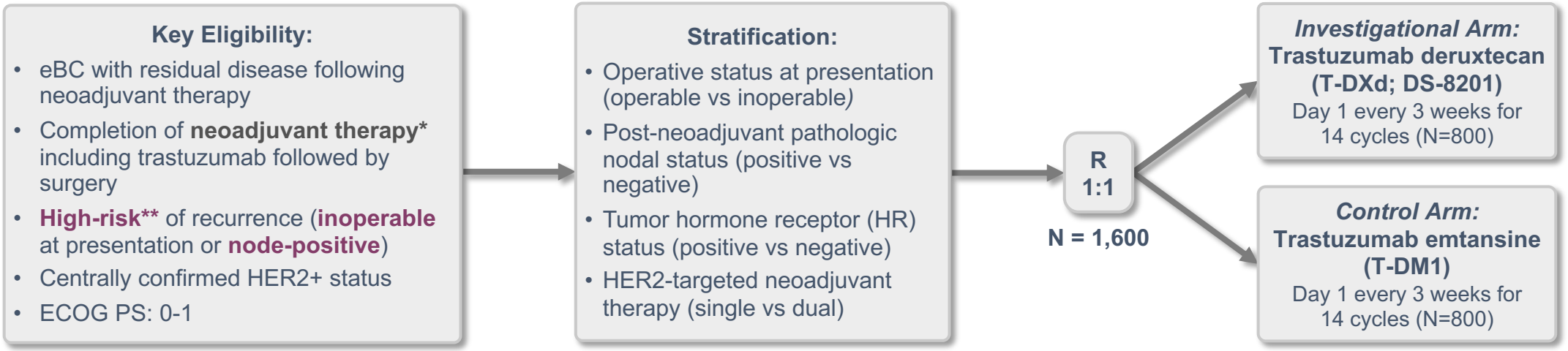
R

- T-DM1 x 14 doses
- T-DM1/tucatinib x 14 doses

Courtesy of Sara M Tolaney, MD, MPH

DESTINY-Breast05 (DS8201-A-U305) Study Design

T-DXd vs. T-DM1 in high-risk HER2-positive early breast cancer patients with residual invasive disease following neoadjuvant therapy



***Neoadjuvant therapy** to include at least 16 weeks of total systemic treatment in the preoperative setting, including:

- At least 9 weeks of HER2-targeted therapy including **trastuzumab** (with or without pertuzumab) and,
- At least 9 weeks of **taxane** therapy

****High-risk definitions:**

- **Inoperable:** Inoperable breast cancer at presentation with residual invasive cancer in the breast or axillary nodes following neoadjuvant therapy.
- **Node-positive:** Metastatic disease in axillary node(s) following neoadjuvant therapy irrespective of presence or absence of residual invasive cancer in the breast.

Additional Notes: Randomization within 12 weeks of surgery; adjuvant radiotherapy and/or endocrine therapy per protocol and local guidelines.

Endpoints:

- **Primary:**
  - **IDFS** (Invasive disease-free survival)
- **Secondary:**
  - **DFS** (Disease-free survival)
  - **DRFI** (Distant recurrence-free interval)
  - **BMFI** (Brain metastases-free interval)
  - **OS** (Overall survival)
  - **Adverse events**
- **Exploratory:**
  - **PROs** (Patient reported outcomes; QoL)
  - **Biomarkers** associated with efficacy/safety
  - **PK** associated with efficacy/safety

eBC=early breast cancer; ECOG PS=Eastern Cooperative Oncology Group performance status; HER2=Human epidermal growth factor receptor 2; PK=pharmacokinetics; QoL=quality of life R=randomization

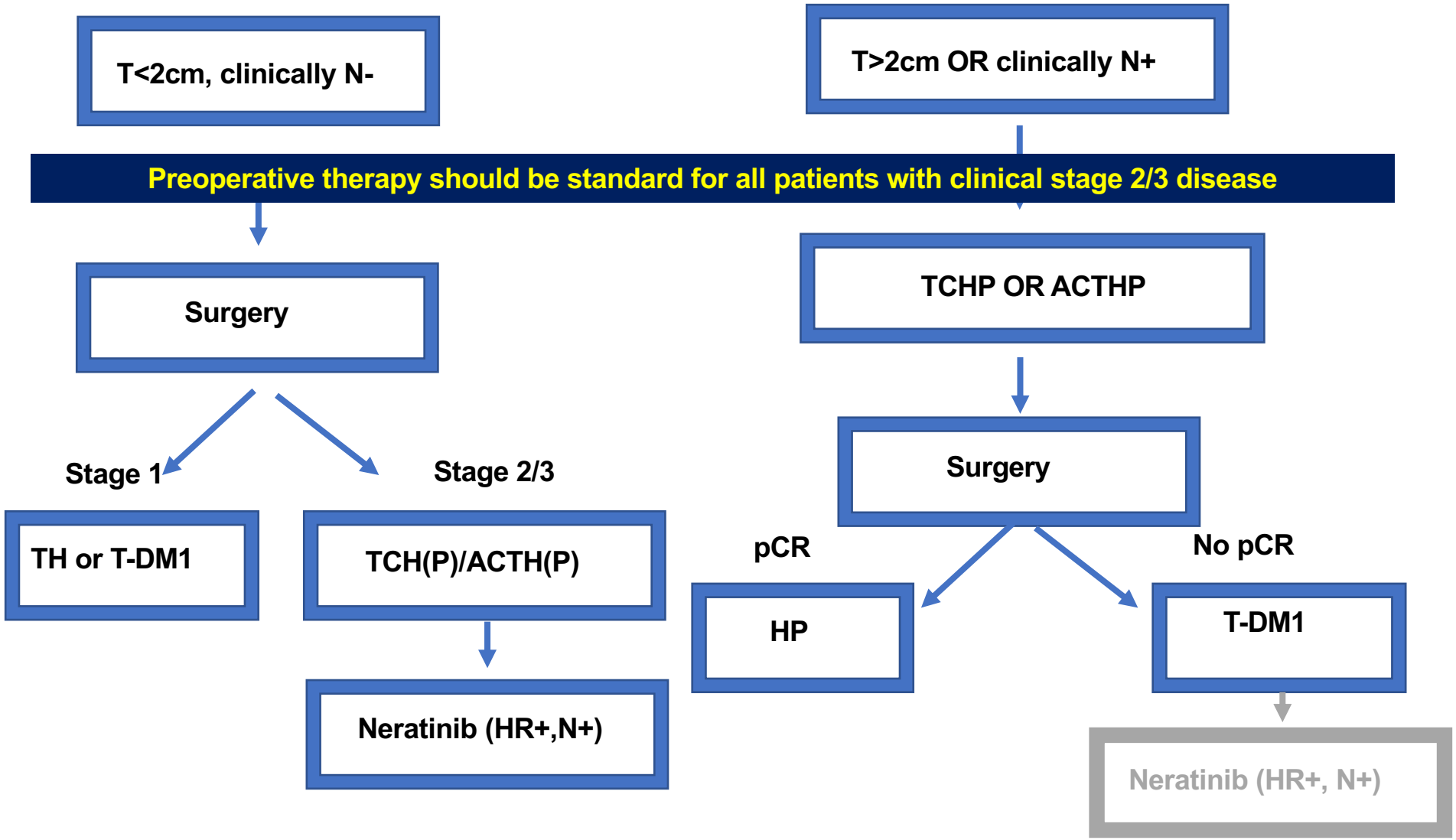
Courtesy of Sara M Tolaney, MD, MPH

FUTURE DIRECTIONS: SELECT ONGOING CLINICAL TRIALS

Trial Name	Phase	Setting	Treatment Arms	Primary Endpoint
IMpassion050	III	Neoadjuvant; T2-4, N1-3, M0 with known HER2, HR, PD-L1 status	AC + Atezolizumab → THP + Atezolizumab vs AC + Pbo → THP + Pbo	pCR
APTneo	III	Neoadjuvant; Early high-risk (T1c-2N1 or T3N0) or LA disease suitable for neoaj tx	TCHP vs TCHP + Atezolizumab vs AC + Atezolizumab → TCHP + Atezolizumab	EFS
PALTAN	II	Neoadjuvant; Stage II-III ER+ HER2+ (tumor ≥ 2 cm)	Palbociclib + letrozole + Tmab +/- goserelin	pCR
NA-PHER2	II	Neoadjuvant; early ER+ HER2+ (tumor > 1.5 cm)	Tmab + Pmab + Palbociclib +/- fulvestrant	Ki67
MARGOT	II	Neoadjuvant; Stage II-III (tumor > 1.5 cm); CD 16A FF or FV	Taxane + Tmab/Pmab vs Taxane+ Margetuximab +Pmab (TMP)	pCR

Courtesy of Sara M Tolaney, MD, MPH

Current Approach for Treatment of HER2+ breast cancer: 2020



Courtesy of Sara M Tolaney, MD, MPH

SUMMARY

- Understanding that we can change long term outcomes by adapting adjuvant therapy based on response to preoperative therapy is a paradigm shift for HER2+ breast cancer
    - End of an era of purely adjuvant trials for developing novel strategies to improve outcomes
    - Important for all patients with HER2+ tumors >2 cm or clinically node positive disease to receive preoperative trastuzumab and pertuzumab based chemotherapy
    - All patients who fail to achieve a pCR should receive adjuvant T-DM1
- Extending adjuvant therapy with 1 yr of neratinib can benefit some patients, particularly those with HR+ disease at high risk of recurrence
    - No data in patients with prior pertuzumab and T-DM1
- Patients with stage I HER2+ breast cancer can receive adjuvant TH or T-DM1
- Future studies are looking at both escalation and de-escalation strategies

Courtesy of Sara M Tolaney, MD, MPH

CASES

CASE 1

- 36 yo premenopausal woman presented with a right-sided palpable 3.5 cm L breast mass. Imaging confirmed finding, and biopsy demonstrated grade 3 invasive ductal carcinoma, ER-, PR-, HER2 3+.
- No palpable right-sided axillary adenopathy, and no abnormal nodes on ultrasound

Recommended preop TCHP x 6 cycles

Had difficulties with diarrhea and fatigue, requiring loperamide

Surgery revealed pCR

Now on adjuvant HP with intermittent diarrhea

Courtesy of Sara M Tolaney, MD, MPH

CASE 2

- 72 yo woman found to have a 1.1 cm mammographic abnormality on screening
- Biopsy reveals ER-, PR-, HER2 3+ IDC
- Undergoes lumpectomy and SN biopsy: 1.2 cm IDC, 0/1 SN

Started therapy with adjuvant T-DM1

Has had mild elevation in LFTs, but tolerating therapy well now 6 months in

Courtesy of Sara M Tolaney, MD, MPH

CASE 3

- 43 yo premenopausal woman presented with a palpable 4.5cm L breast mass with a palpable axillary lymph node
- Biopsy revealed grade 2 IDC, ER+, PR+, HER2 2+, FISH 3.5
- Received preop TCHP
- Underwent lumpectomy and SN biopsy: residual 2.5 cm of disease, with 2/4 SN involved; underwent completion axillary dissection with no additional positive nodes
- Received adjuvant T-DM1 x 14 cycles, and adjuvant radiation

Started recently on neratinib with dose-escalation strategy

Courtesy of Sara M Tolaney, MD, MPH