Patterns of Care: Exploring How Community Oncologists Manage HR-Positive, HER2-Positive Metastatic Breast Cancer

A CME/MOC-Accredited Live Webinar

Wednesday, July 1, 2026

5:00 PM – 6:00 PM ET

Faculty

Lisa A Carey, MD, ScM, FASCO

Reshma L Mahtani, DO

Moderator

Neil Love, MD

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Faculty

Lisa A Carey, MD, ScM, FASCO
L Richardson and Marilyn Jacobs Preyer Distinguished
Professor for Breast Cancer Research
University of North Carolina at Chapel Hill
Deputy Director for Clinical Sciences
Lineberger Comprehensive Cancer Center
Chief Clinical Research Officer, Clinical Research Partners
UNC Health
Chapel Hill, North Carolina

Reshma L Mahtani, DO
Chief of Breast Medical Oncology
Miami Cancer Institute
Baptist Health South Florida
Miami, Florida

MODERATOR
Neil Love, MD
Research To Practice
Miami, Florida

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Dr Love — Disclosures

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Dr Carey — Disclosures

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Dr Mahtani — Disclosures

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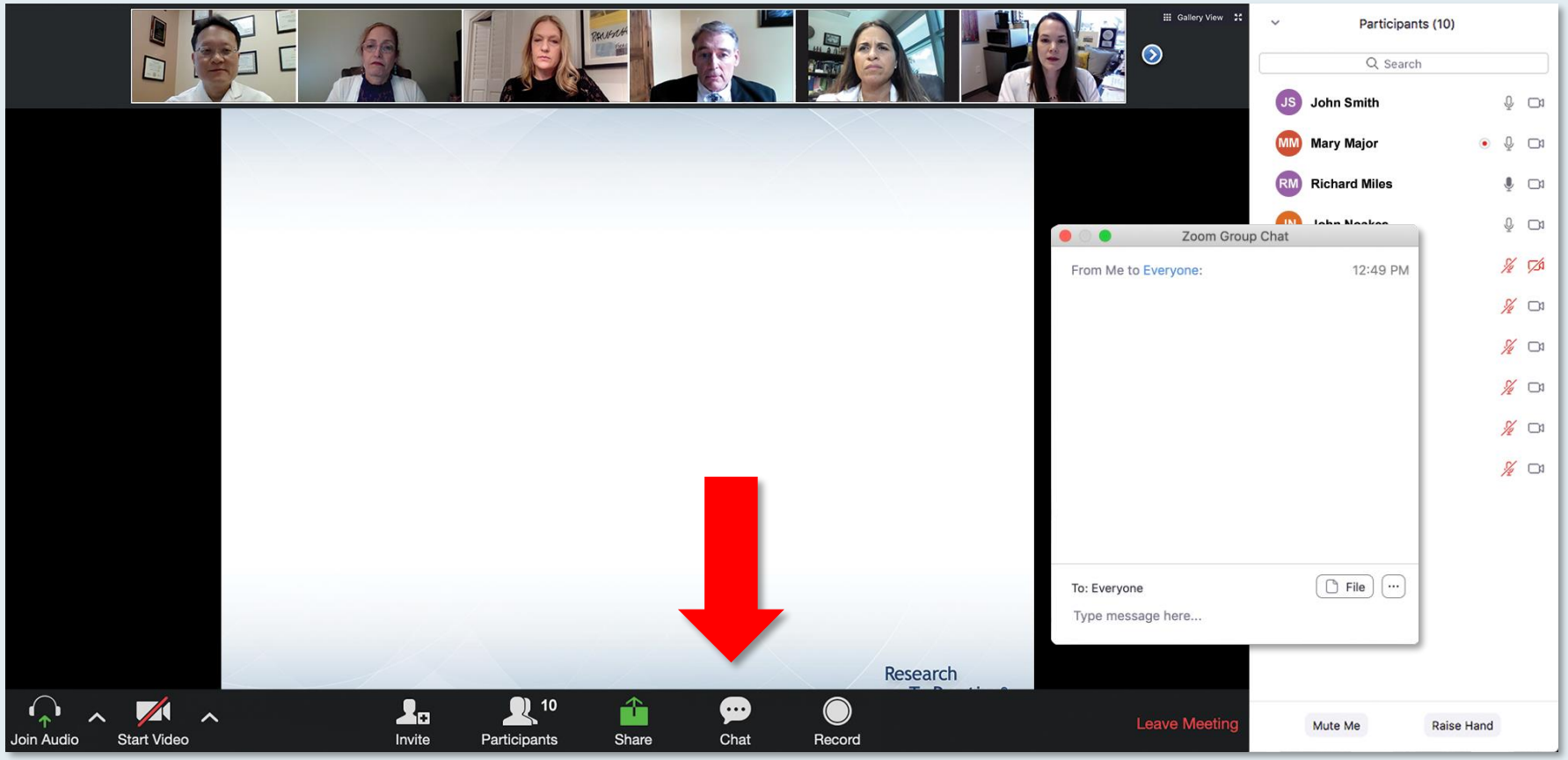

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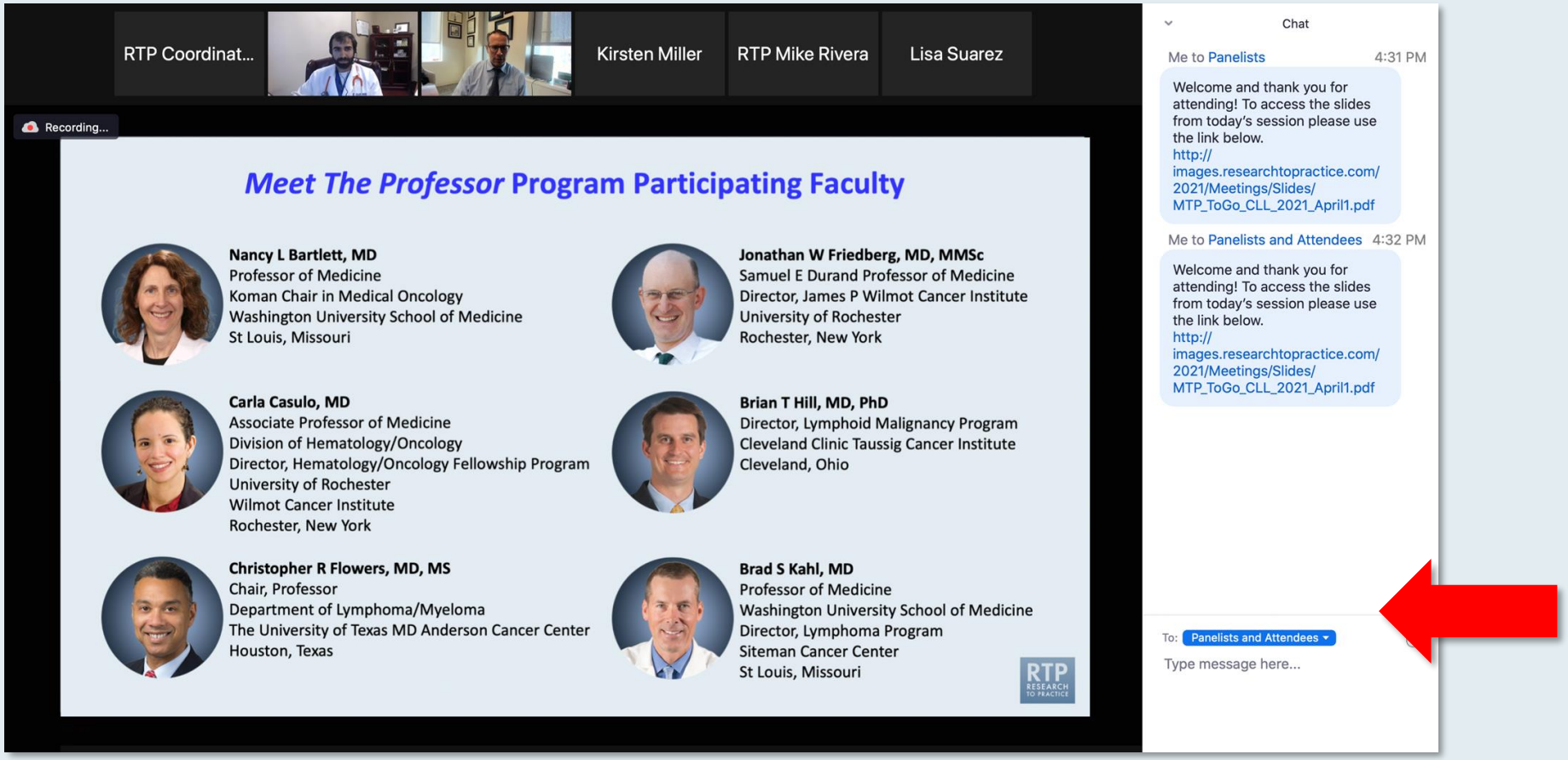

Drag the white line above the submission box up to create more space for your message.

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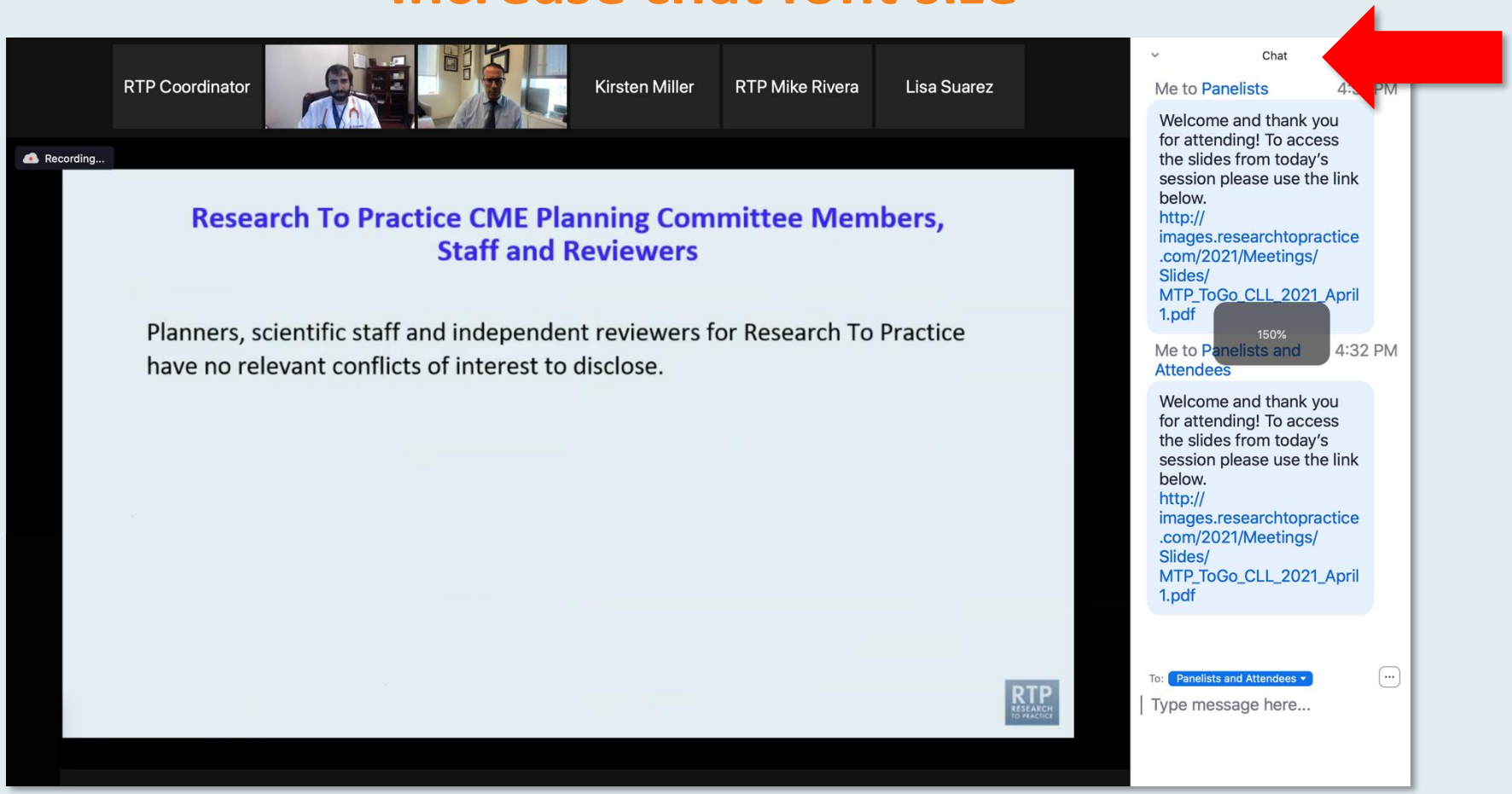

Press Command (for Mac) or Control (for PC) and the + symbol.
You may do this as many times as you need for readability.

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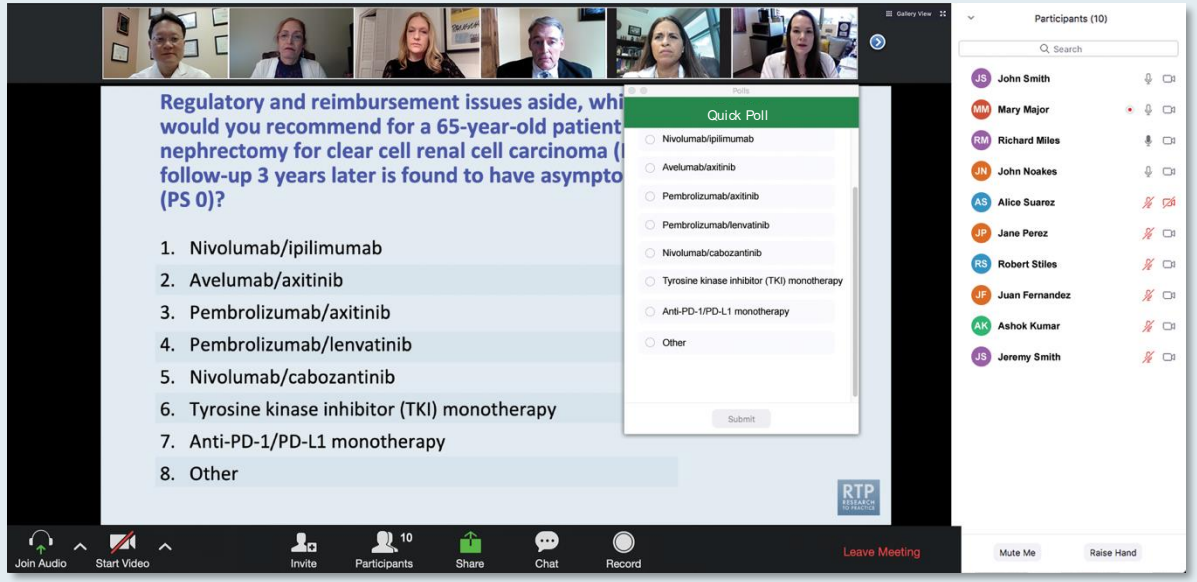

ONCOLOGY TODAY

WITH DR NEIL LOVE

HR-Positive Metastatic Breast Cancer — First- and Second-Line Therapy

SARA A HURVITZ, MD, FACP
FRED HUTCHINSON CANCER CENTER

VIRGINIA KAKLAMANI, MD, DSC
UT HEALTH SAN ANTONIO MD ANDERSON CANCER CENTER

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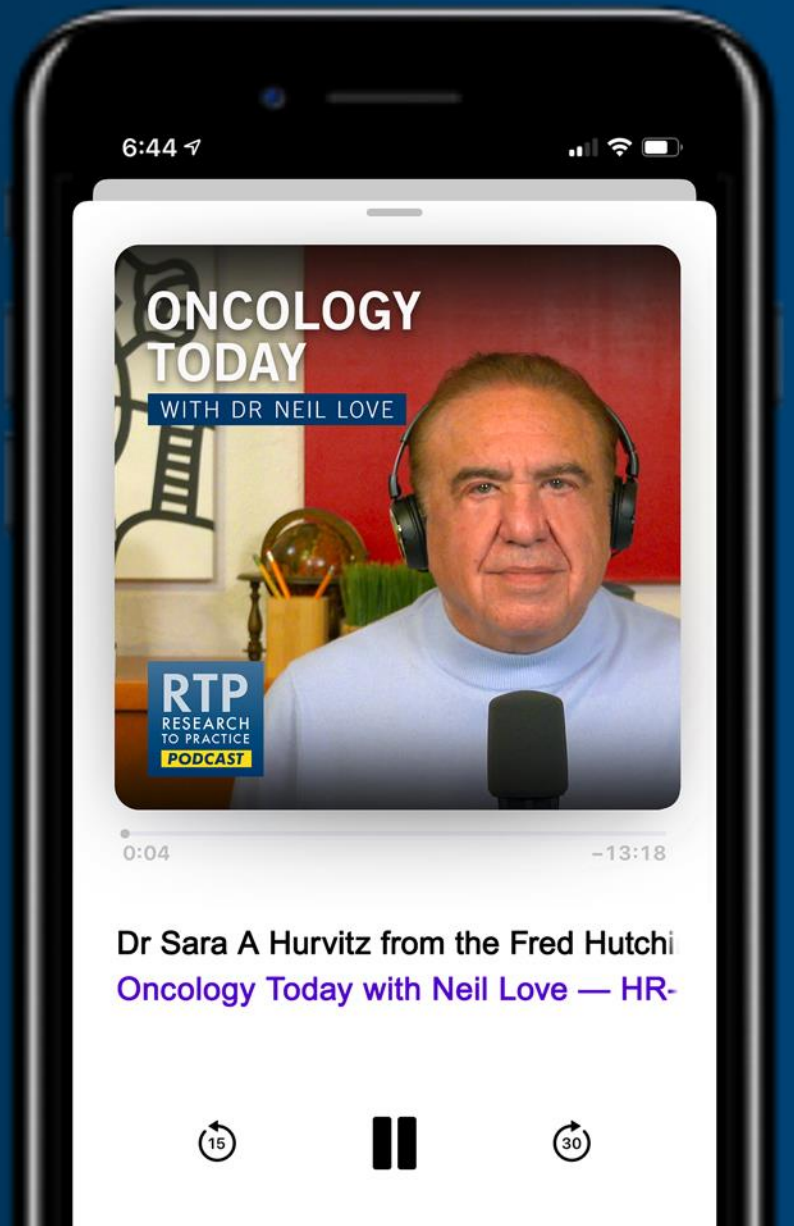

Year in Review: Clinical Investigator Perspectives on the Most Relevant New Datasets and Advances in Oncology

PI3K/AKT/mTOR Pathway in HR-Positive Metastatic Breast Cancer

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Hope S Rugo, MD

Moderator

Neil Love, MD

RTP Year in Review 2026

The Implications of Recent Datasets for the Current and Future Management of Genitourinary Cancers — An ASCO 2026 Review

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Matthew D Galsky, MD
Tian Zhang, MD, MHS

Moderator

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RTP RESEARCH TO PRACTICE

Patterns of Care: Exploring How Community Oncologists Manage Metastatic Triple-Negative Breast Cancer

A CME/MOC-Accredited Live Webinar

Tuesday, July 21, 2026

5:00 PM – 6:00 PM ET

Faculty

Professor Peter Schmid, FRCP, MD, PhD

Melinda Telli, MD, FASCO

Moderator

Neil Love, MD

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Join Us In Person or Virtually

Integrating New Advances into the Care of Patients with Cancer

A Multitumor Symposium in Partnership with the American Oncology Network

Saturday, August 22, 2026

JW Marriott Nashville | Nashville, Tennessee

Chronic Lymphocytic Leukemia
9:00 AM – 9:50 AM CT

Gastroesophageal Cancers
9:50 AM – 10:40 AM CT

Gynecologic Cancers
10:55 AM – 11:45 AM CT

Diffuse Large B-Cell Lymphoma
12:35 PM – 1:25 PM CT

Lung Cancer
1:25 PM – 2:15 PM CT

Moderator
Stephen “Fred” Divers, MD

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Grand Rounds

CME/MOC-Accredited Interactive Series

Regional Activities

Two Series

Optimizing the Use of Novel Therapies for Patients with Diffuse Large B-Cell Lymphoma

Optimizing Therapy for Patients with Hormone Receptor-Positive Localized Breast Cancer

Host a 1-hour session at your institution:
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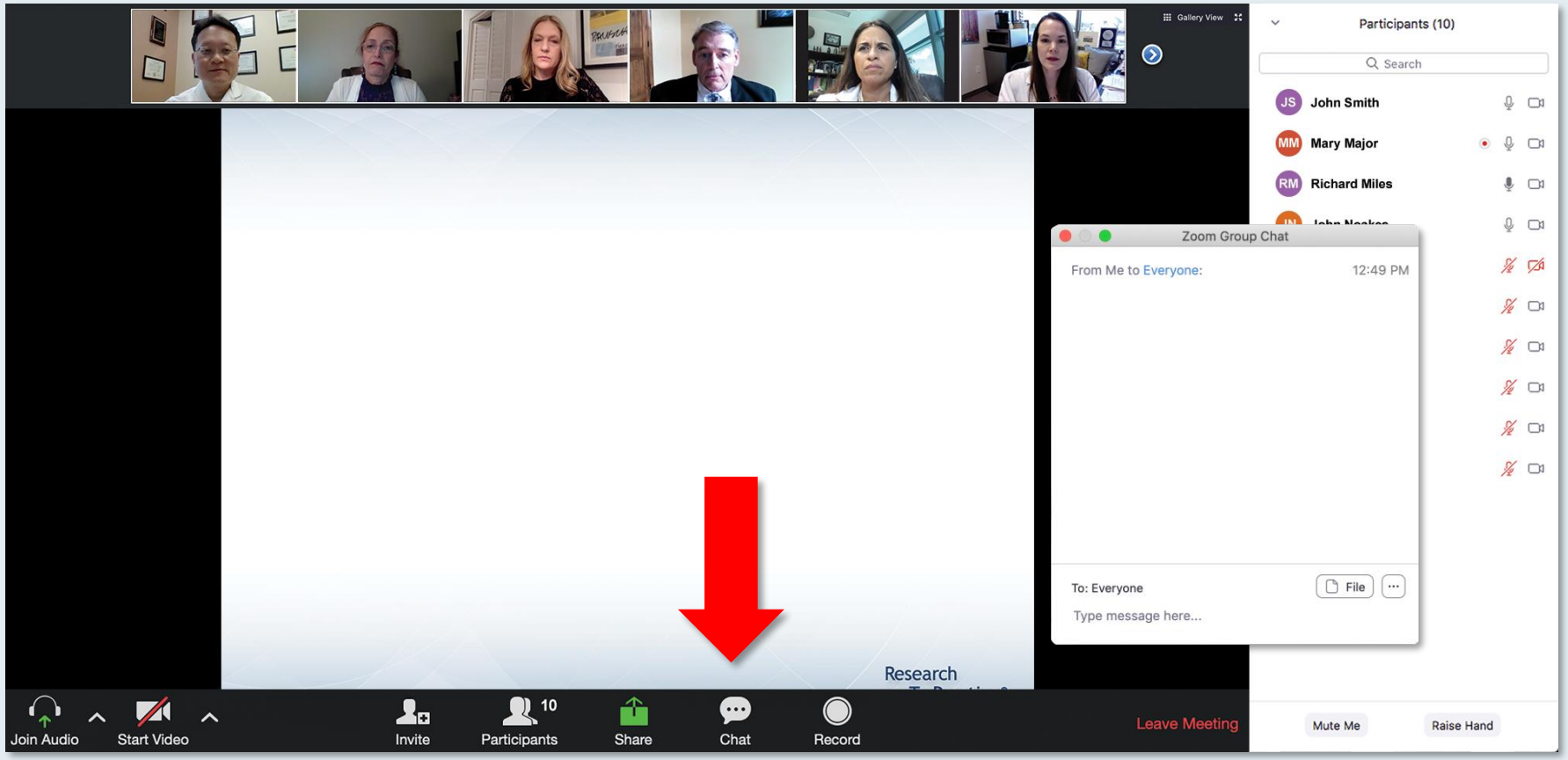

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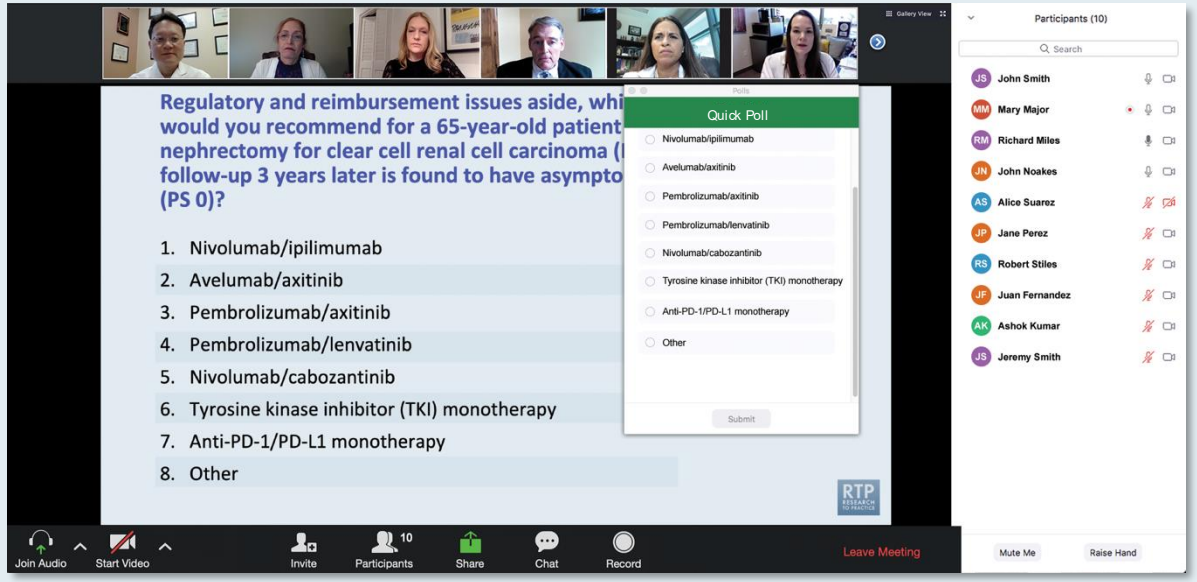

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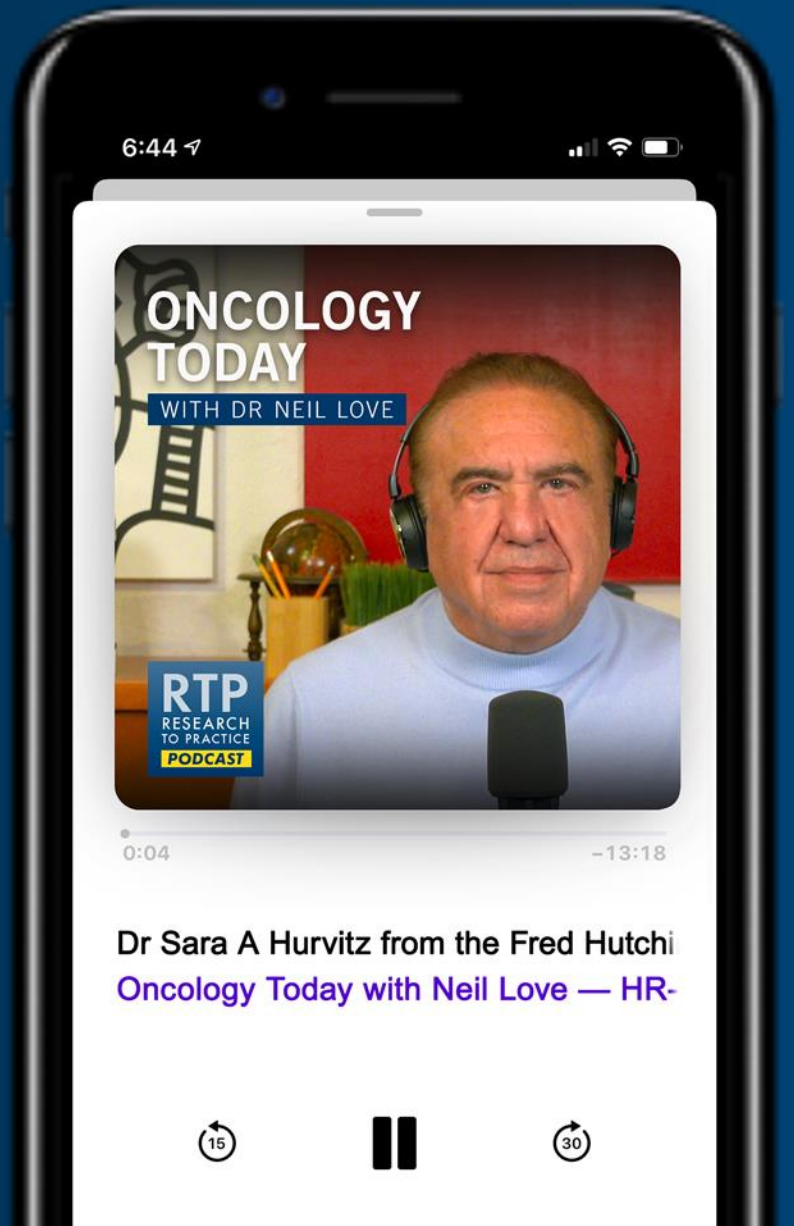

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Dr Carey — Disclosures

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Dr Mahtani — Disclosures

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Agenda

Introduction: HER2 History

Module 1: Cases from the GMO Survey

Module 2: Biology and Selection of First-Line Therapy for HR-Positive, HER2-Positive Metastatic Breast Cancer (mBC) — Dr Mahtani

Module 3: Faculty Case Presentations

Module 4: Patterns of Care Survey — Part 1

Module 5: Optimizing the Use of Up-Front Maintenance Therapy for HER2-Positive mBC — Dr Carey

Module 6: Faculty Case Presentations

Module 7: Patterns of Care Survey — Part 2

Optimizing the Selection of First-Line and Maintenance Therapy for Patients with HER2-Positive Metastatic Breast Cancer

Survey of 50 Community-Based General Medical Oncologists
March 10 to 13, 2026

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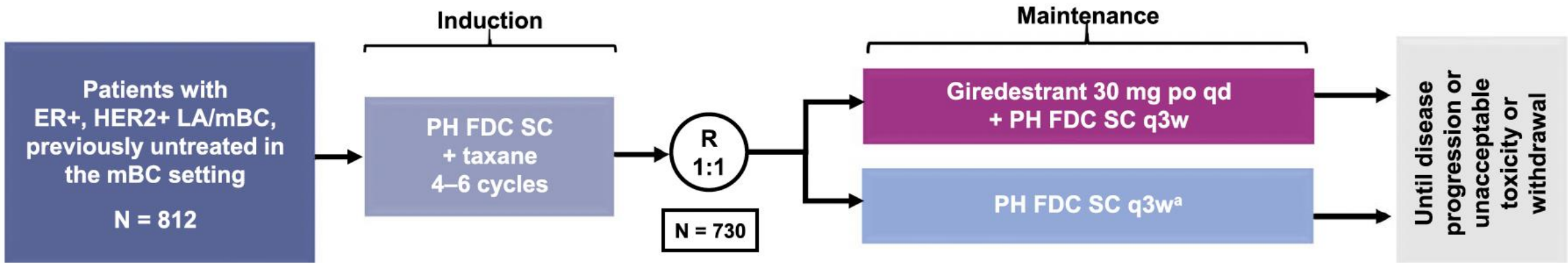
heredERA: An Ongoing Phase III Study of Giredestrant and the Fixed-Dose Combination of Pertuzumab and Trastuzumab for Subcutaneous Injection



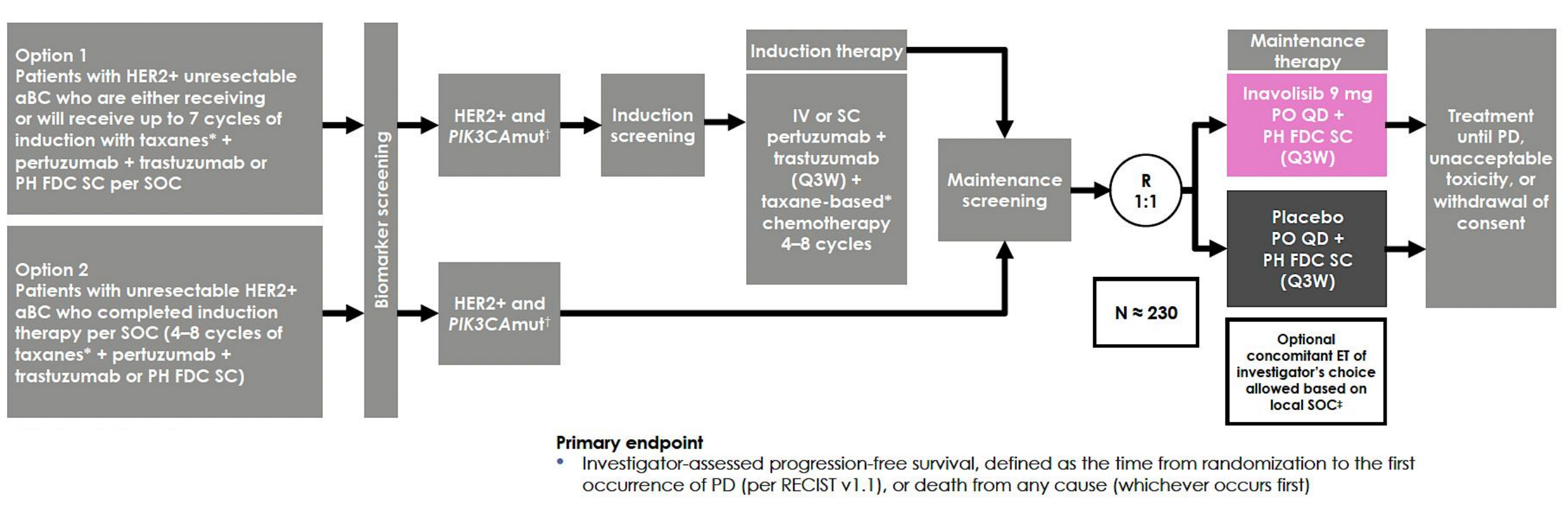
Stratification factors

- Site of disease (visceral vs. non-visceral).
- Type of stage IV presentation (de novo metastatic[b] vs. recurrent metastatic disease).
- Intention to give ET of investigator's choice (yes vs. no).
- OR during the induction therapy phase (PR/CR vs. SD [or non-CR/non-PD for participants with non-measurable disease]).

LA = locally advanced; PH FDC SC = fixed-dosed combination of pertuzumab and trastuzumab for subcutaneous injection

Kuemmel S et al. *BMC Cancer* 2024;24:641.

INAVO122: An Ongoing Phase III Study of Maintenance Inavolisib or Placebo with Pertuzumab and Trastuzumab for Patients with PIK3CA-Mutant, HER2-Positive Advanced Breast Cancer



Swain SM et al. ASCO 2024;Abstract TPS1124.

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Cases from General Medical Oncologists

70 yo woman

- **De novo HR+/HER2+ widely metastatic breast cancer including a solitary, asymptomatic brain metastasis.**
- **Started T-DXd + pertuzumab complicated by severe diarrhea requiring hospitalization and treatment interruption. Pertuzumab discontinued after 2 cycles, T-DXd continued. She responded to therapy at all sites including the brain.**

Would you rechallenge with pertuzumab + T-DXd? At what time point or degree of response would you switch to AI + Palbo + trastuzumab per PATINA? Is this your new standard?

Cases from General Medical Oncologists

43 yo woman

- **ER/PR+, HER2+ de novo metastatic breast cancer, minimally symptomatic bone and nodal metastases.**
- **1L induction THP for 6 cycles, then HP maintenance plus leuprolide and AI, remains NED for over 2 years.**
- **2 years of zoledronic acid.**

What 1L regimen and maintenance therapy would you use if she presented today? Would T-DXd + pertuzumab induction be appropriate? What about incorporating palbociclib into the endocrine therapy component given HR+ alongside HP maintenance per PATINA?

Cases from General Medical Oncologists

72 yo woman

- **ER/PR+, HER2+ metastatic breast cancer asymptomatic liver and bone metastases**
- **PMH: THP- HP + AI + palbo.**

Today would faculty consider T-DXd + Pertuzumab until best response, then Pertuzumab plus AI and palbo?
Any role for CT DNA monitoring to guide de-escalation or discontinuation of maintenance therapy in this setting?

Cases from General Medical Oncologists

56 yo woman

- **ER/PR-, HER2+, multiple sites of metastatic disease, including high burden visceral mets, bone and 7 small asymptomatic brain mets.**

What induction regimen would you recommend? Would you consider de-escalation after induction therapy? What about tucatinib/trastuzumab/pertuzumab as maintenance?
Any role for SRS or Gamma Knife?

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Biology and Selection of First-Line Therapy for HR-Positive, HER2-Positive mBC

Reshma L Mahtani, DO
Chief of Breast Medical Oncology
Miami Cancer Institute
Baptist Health South Florida
Miami, Florida

Crosstalk Between ER and HER2

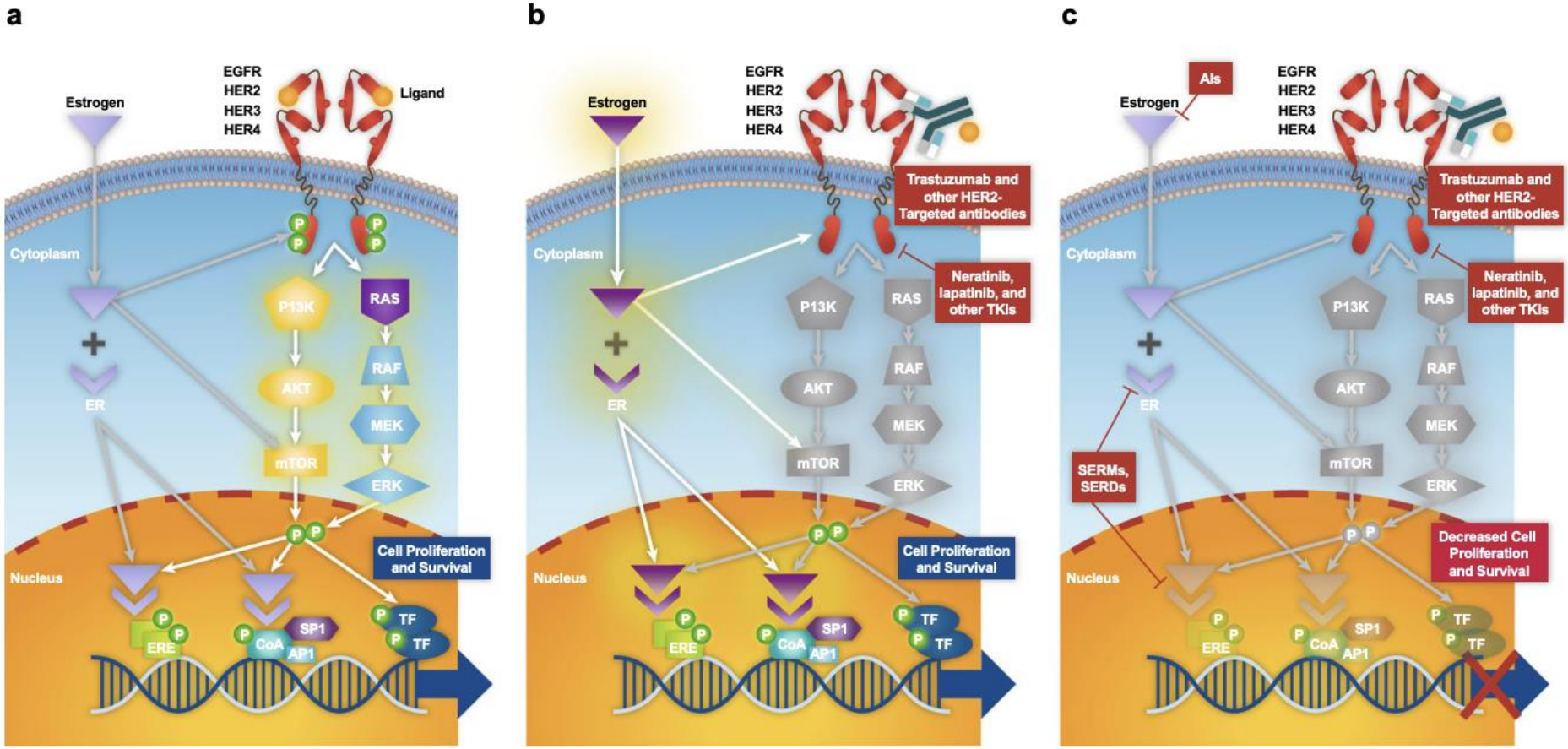


Fig. 1 Overview of estrogen receptor (ER) and human epidermal growth factor receptor 2 (HER2) signaling crosstalk. a HER2 overactivation results in downregulation of ER-regulated transcription and resistance to endocrine therapy. **b** Blockade of HER2 leads to activation of ER gene transcription via signaling crosstalk pathways as a compensatory mechanism for tumor growth and survival. **c** Inhibition of HER2 and ER pathways are both required to achieve effective HER2+/HR+ antitumor activity. Gray shading of the PI3K/AKT/mTOR and RAS/RAF/MEK/ERK signaling pathways in panels a and b indicate downregulation of these pathways. AI aromatase inhibitor, ER estrogen receptor, ERK extracellular signal-regulated kinase, HER2 human epidermal growth factor receptor 2, HR hormone receptor, MEK mitrogen-activated protein kinase kinase, mTOR mammalian target of rapamycin, P13K phosphatidylinositol 3-kinase, RAF rapidly accelerated fibrosarcoma, SERD selective estrogen receptor degrader, SERM selective estrogen receptor modulator, TKI tyrosine kinase inhibitor.

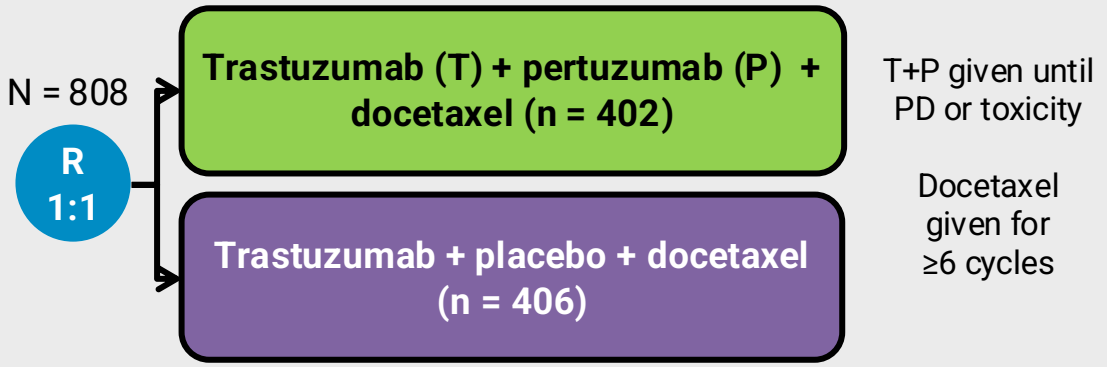
Pegram M, et al. NPJ Breast Cancer. 2023 May 31;9(1):45

Phase 3 CLEOPATRA Study of Pertuzumab, Trastuzumab, and Docetaxel

8-year follow-up

Key eligibility criteria

- HER2+ mBC
- ECOG PS 0–1
- of ≥50% at baseline
- Received no prior treatments for metastatic disease



Primary endpoint: IRC-assessed PFS

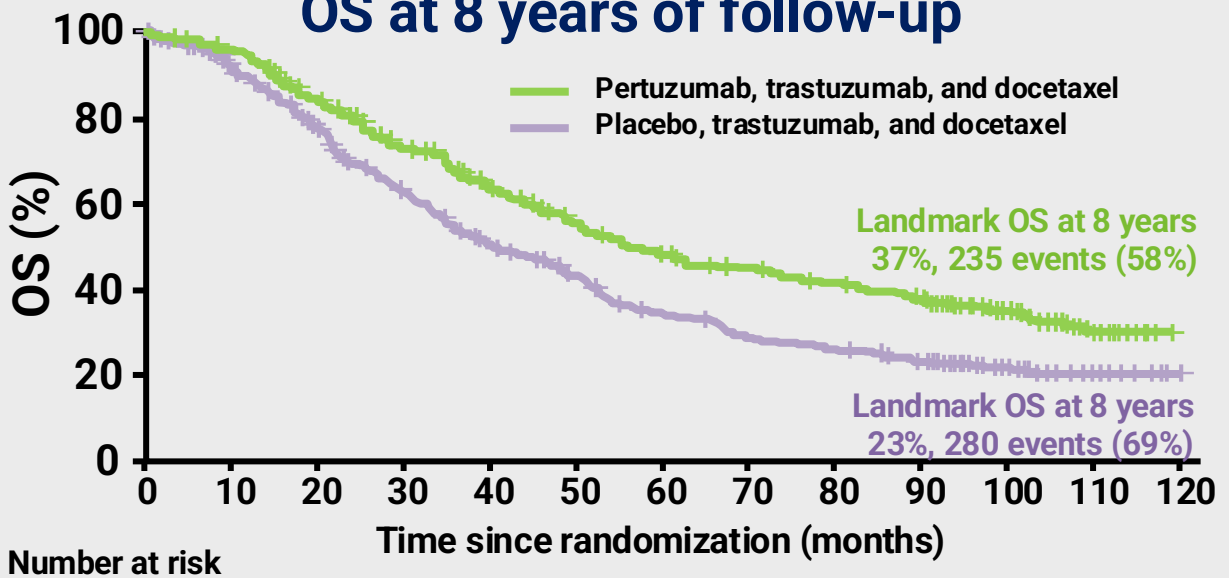
Key secondary endpoints: OS, INV-assessed PFS, ORR, DOR, safety, time to symptom progression

Data cutoff date: 11/23/2018.

DOR = duration of response; ECOG = Eastern Cooperative Oncology Group; HR = hazard ratio; INV = investigator; IRC = independent review committee; = left ventricular ejection fraction; ORR = objective overall response rate; PD = progressive disease; PFS = progression-free survival; PS = performance status; R = randomization.

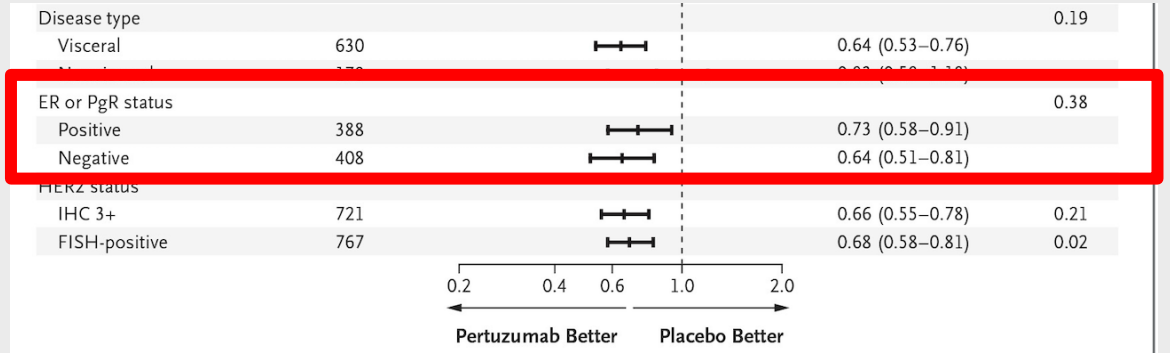
Swain SM, et al. *Lancet Oncol*. 2020;21:519-530.

OS at 8 years of follow-up

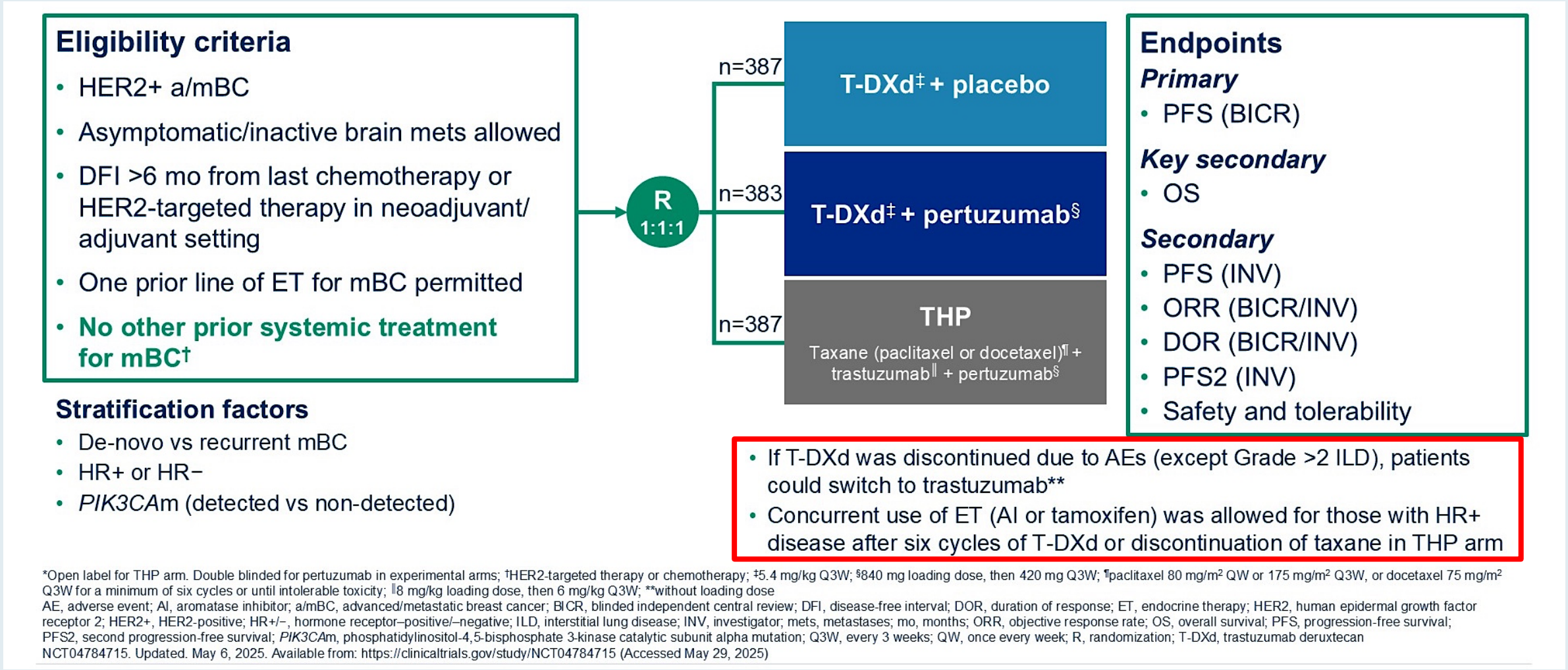


Number at risk							
P	402(0)	318 (23)	228 (41)	165 (50)	137 (56)	71 (102)	0 (167)
Placebo	406 (0)	289 (30)	181 (41)	115 (52)	88 (53)	44 (84)	1 (125)

Subgroup Analysis of OS



Phase III DESTINY-Breast09 Study Design



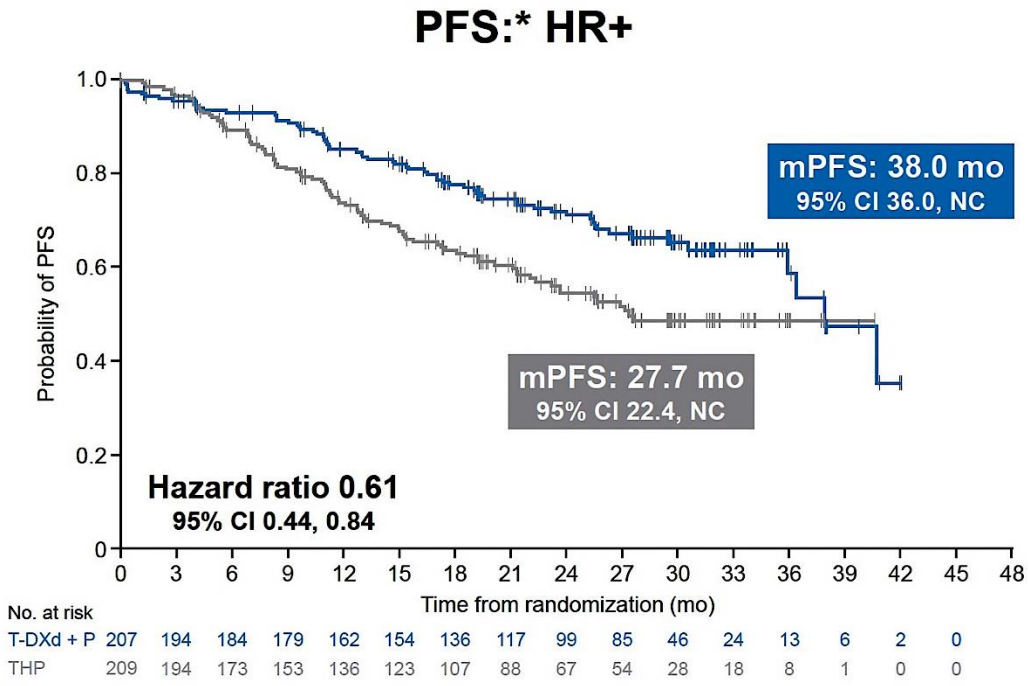
*Open label for THP arm. Double blinded for pertuzumab in experimental arms; †HER2-targeted therapy or chemotherapy; ‡5.4 mg/kg Q3W; §840 mg loading dose, then 420 mg Q3W; ¶paclitaxel 80 mg/m² QW or 175 mg/m² Q3W, or docetaxel 75 mg/m² Q3W for a minimum of six cycles or until intolerable toxicity; ‖8 mg/kg loading dose, then 6 mg/kg Q3W; **without loading dose

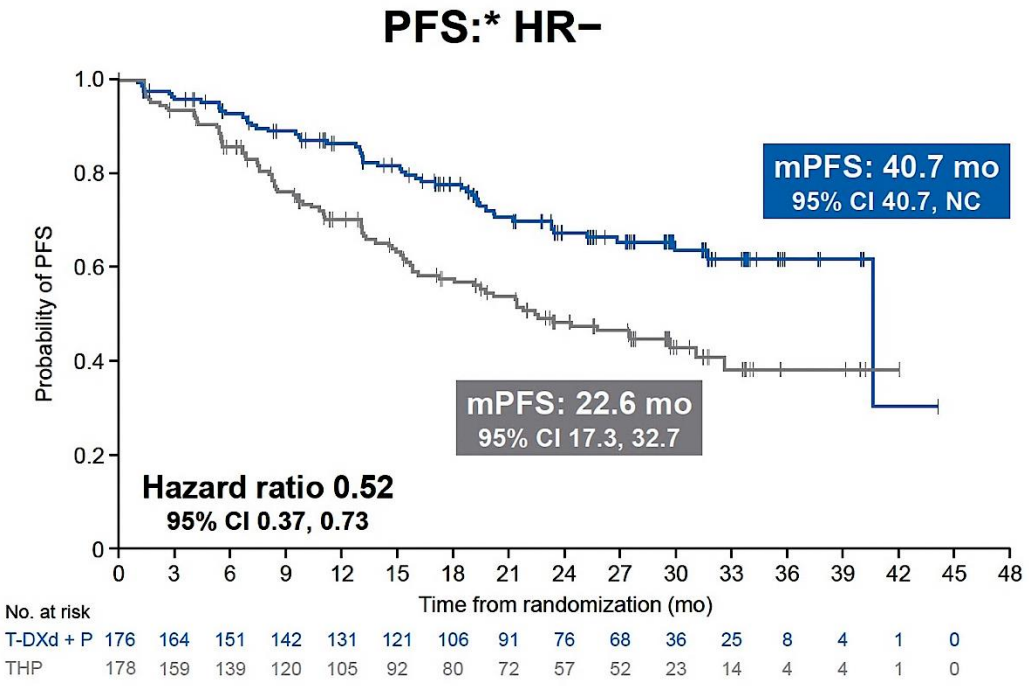
AE, adverse event; AI, aromatase inhibitor; a/mBC, advanced/metastatic breast cancer; BICR, blinded independent central review; DFI, disease-free interval; DOR, duration of response; ET, endocrine therapy; HER2, human epidermal growth factor receptor 2; HER2+, HER2-positive; HR+/−, hormone receptor–positive/–negative; ILD, interstitial lung disease; INV, investigator; mets, metastases; mo, months; ORR, objective response rate; OS, overall survival; PFS, progression-free survival; PFS2, second progression-free survival; *PIK3CA*m, phosphatidylinositol-4,5-bisphosphate 3-kinase catalytic subunit alpha mutation; Q3W, every 3 weeks; QW, once every week; R, randomization; T-DXd, trastuzumab deruxtecan

NCT04784715. Updated. May 6, 2025. Available from: https://clinicaltrials.gov/study/NCT04784715 (Accessed May 29, 2025)

Tolaney SM et al. ASCO 2025;Abstract LBA1008.

Phase III DESTINY-Breast09: PFS by HR Status





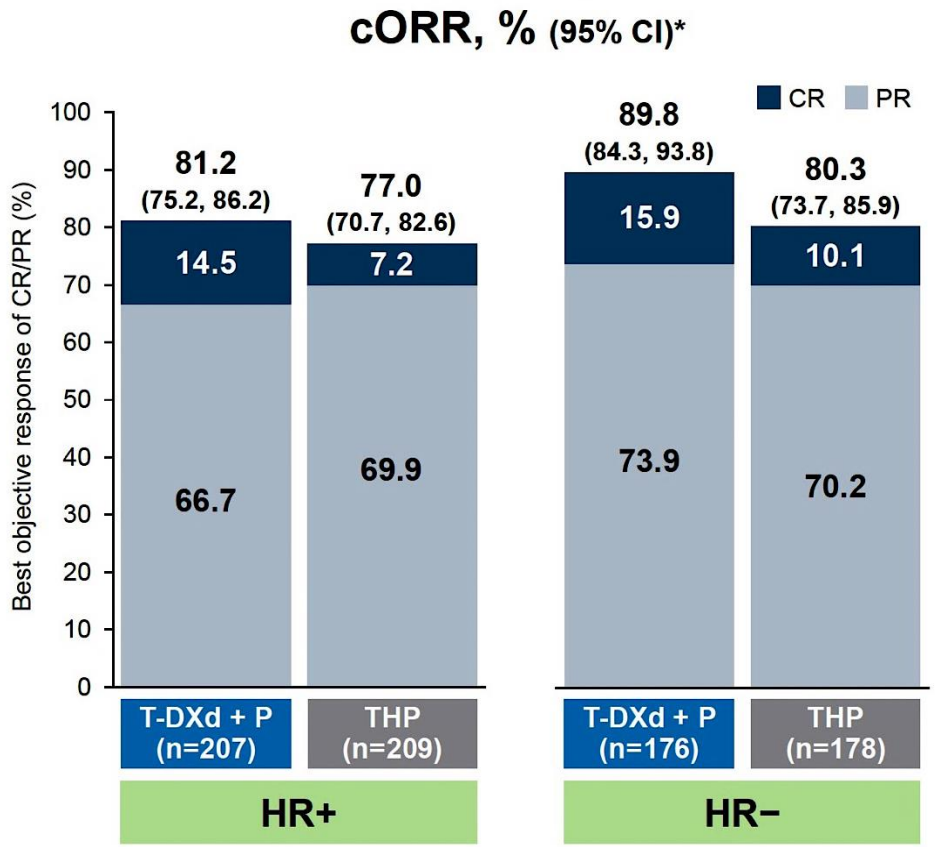
Patients with HR+ disease could receive concurrent ET after six cycles of T-DXd or discontinuation of taxane, which occurred in **13.5% (T-DXd + P)** versus **38.3% (THP)** of patients

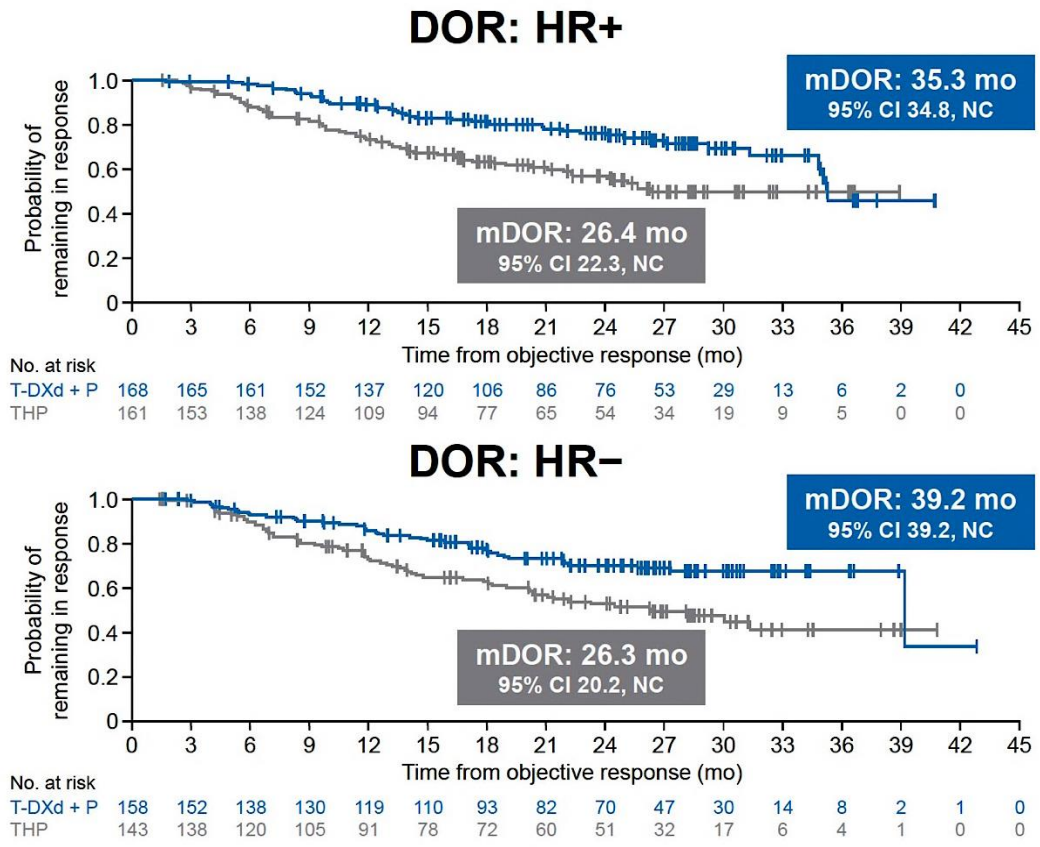
T-DXd + P demonstrated a clinically meaningful PFS benefit vs THP regardless of HR status

*By blinded independent central review
CI, confidence interval; ET, endocrine therapy; HR(+/−), hormone receptor(–positive/–negative); mPFS, median progression-free survival; mo, months; NC, not calculable; P, pertuzumab; PFS, progression-free survival; T-DXd, trastuzumab deruxtecan; THP, taxane + trastuzumab + pertuzumab

Loibl S et al. ESMO 2025;Abstract LBA18.

Phase III DESTINY-Breast09: Responses by HR Status





CR rates and DOR favored T-DXd + P vs THP regardless of HR status

*By blinded independent central review
CI, confidence interval; cORR, confirmed objective response rate; CR, complete response; DOR, duration of response; HR(+/−), hormone receptor(–positive/–negative); mDOR, median duration of response; mo, months; NC, not calculable; P, pertuzumab; PR, partial response; T-DXd, trastuzumab deruxtecan; THP, taxane + trastuzumab + pertuzumab

Loibl S et al. ESMO 2025;Abstract LBA18.

DESTINY-Breast09: Response Characteristics

T-DXd + P arm	CR (n=58) 15.4%	Deep PR* (n=141) 37.4%	PR (<80%) (n=127) 33.7%	SD/PD (n=51) 13.5%
Time to best response (median, mo) [95% CI]	**8.4 [5.6, 11.1]**	**9.6 [6.8, 11.0]**	**1.5 [1.4, 2.0]**	**NA**
Duration of best response (median, mo) [95% CI]	NC [35.1, NC]	39.2 [35.3, NC]	34.8 [22.8, NC]	NA
Patients remaining in best response, % [95% CI]				
12 mo	94.8 [84.8, 98.3]	91.3 [85.1, 95.0]	78.9 [70.1, 85.3]	NA
24 mo	85.0 [72.1, 92.3]	78.9 [70.4, 85.2]	60.4 [50.0, 69.3]	NA
Total treatment duration, (median, mo) [range][b]	28.0 [4.8–44.5]	25.4 [3.4–42.7]	20.6 [2.8–41.8]	4.4 [0.3–37.2]
PFS at 24 mo, % [95% CI]	**85.1 [72.2, 92.3]**	**80.0 [71.7, 86.1]**	**64.3 [54.3, 72.8]**	**35.5 [21.1, 50.2]**

- **80%** of patients (ITT) achieved maximal tumor reduction by 24 months
- Pts achieving CR and deep PR had the longest treatment duration, with responses deepening over time

THP arm	CR (n=33) 8.5%	Deep PR[b] (n=110) 28.4%	PR (<80%) (n=161)	SD/PD (n=68)
Time to best response (median, mo) [95% CI]	5.6 [2.8, 9.8]	8.2 [6.8, 9.6]	1.5 [1.4, 1.5]	NA
Duration of best response (median, mo) [95% CI]	31.3 [31.3, NC]	NC [22.3, NC]	20.1 [13.1, 30.1]	NA
Total treatment duration (median, mo), range[c]	28.1 (7.6–38.2)	20.2 (2.7–40.8)	17.9 (2.9–41.7)	5.9 (1.4–35.2)
PFS at 24 mo, % [95% CI]	76.7 [56.9, 88.2]	60.7 [50.3, 69.6]	48.5 [39.8, 56.6]	31.7 [18.6, 45.5]

In the THP arm, achieving deep PR was not associated with similar outcomes to achieving CR

***Deep PR: (≥80% to <100%)**

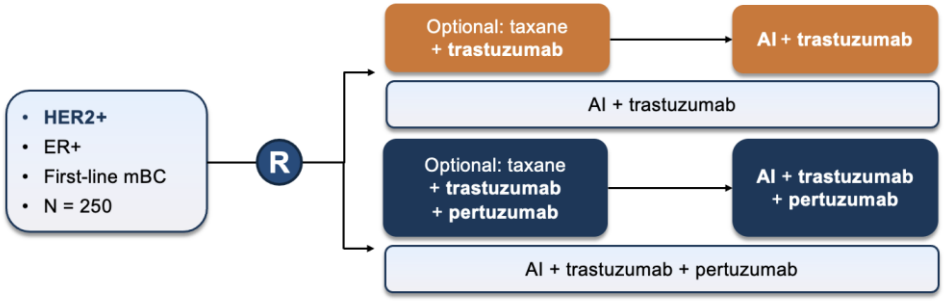
1L Trials in HER2+ MBC

Trial	Regimen	De Novo MBC (%)	Prior H(P)? (%)	HR+ Patients (%)	Endocrine therapy (%)	Brain mets (baseline) (%)	Median CNS PFS (M)	Median PFS & OS (months [M])
CLEOPATRA (2012) **N= 808**	Taxane + trastuzumab + placebo **(TH)** vs. taxane+ trastuzumab + **pertuzumab (THP)**	**54**	**H: 11** **P: N/A**	**48**	**Not permitted**	**Not eligible**	**N/A**	**mPFS: 18.5 vs. 12.4 M** (HR = 0.62) **mOS**: 56.5 vs. 40.8 M (HR = 0.68, P<0.001)
Destiny-Breast09 (2025) **N=770**	**T-DXd + P** vs. **T-DXd** + placebo vs. **THP**	**52**	**H: 27.9-28.7** **P: 6.2-8.1**	**54**	**T-DXd ± P: 13.5** **THP: 38.3**	**~5-7**	**Substantial benefit**	**mPFS: 40.7 vs. 26.9 M** **mOS** : immature (HR = 0.56)
PATINA (2024) **N= 518**	**Post THP:** maintenance **H(P)** + **palbociclib (Pb)** or placebo (Pbo)	**55**	**H ± P: 71**	**100**	**100**	**4**	**Risk CNS progression** 13.0 %- **Pb** 19.2 %- **Pbo** P-0.0378	**mPFS: 44.3 vs. 29.1 M** (HR = 0.75) **mOS** : immature
HER2CLIMB-05 (2025) **N=654**	**Post THP:** maintenance **HP** + **tucatinib** or placebo	**69.3**	**H: 60-67** **P: 16-19**	**~51-54**	**45.1**	**12.4**	**8.5 vs. 4.3M** (HR = 0.719)	**mPFS: 24.9 vs. 16.3 M** **mOS** : immature

Abbreviations: N/A, not applicable; H, trastuzumab, P, pertuzumab, M, months; OS, overall survival

Slide Credit: osullivan.ciara@mayo.edu

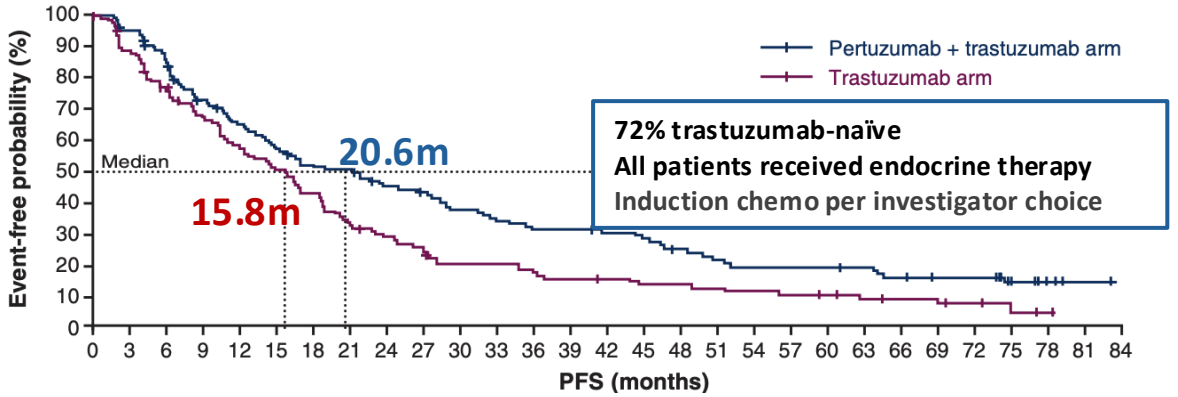
First Line Treatment for HER2+ mBC: PERTAIN Study



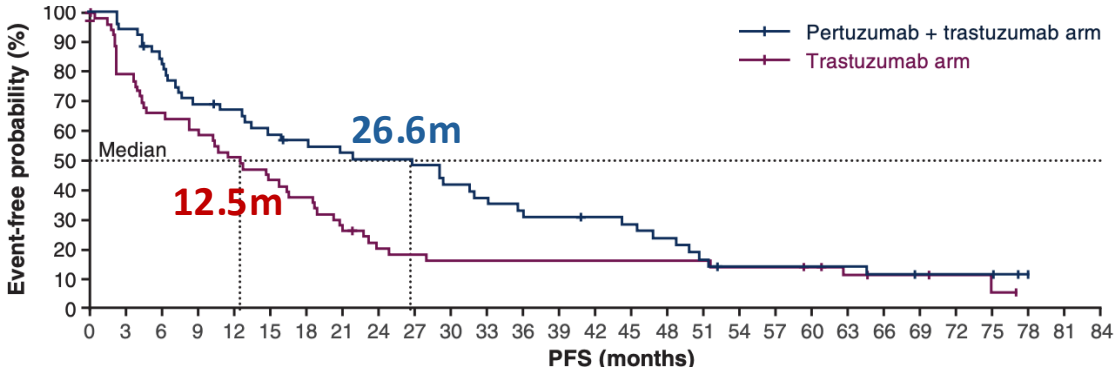
Primary endpoint: PFS

Key secondary endpoints: OS, ORR, CBR, DOR, time to response, safety, and QoL

ITT population:



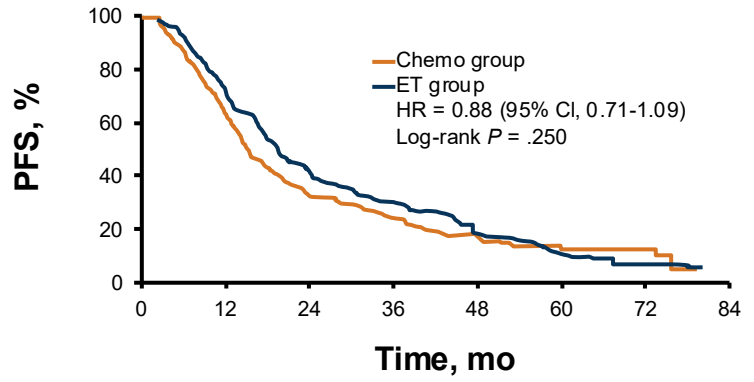
Pts chosen to not receive induction chemotherapy



(1) Gennari et al. Ann Oncol. 2021;32(12):1475-1495; (2) Arpino G, et al. Clin Cancer Res. 2023;29(8):1468-1476.

SYSUCC-002: Trastuzumab + ET or Chemotherapy as First-Line Treatment for HR+, HER2+ mBC

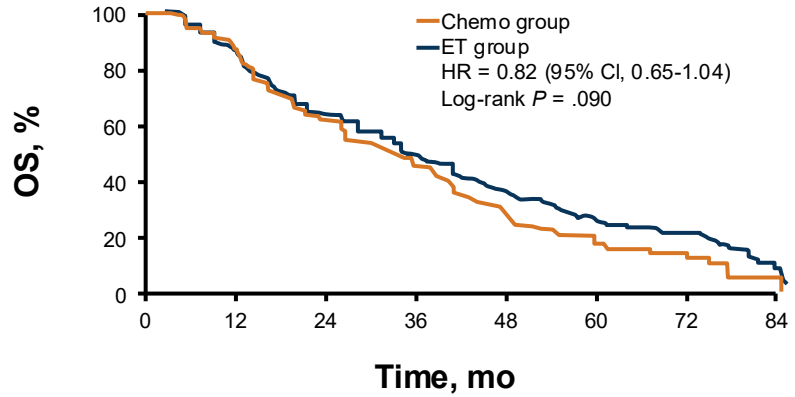
PFS (Primary Endpoint)



No. at Risk

Chemo	196	124	61	33	16	9	5	0
ET	196	142	73	50	28	11	4	0

Overall Survival



No. at Risk

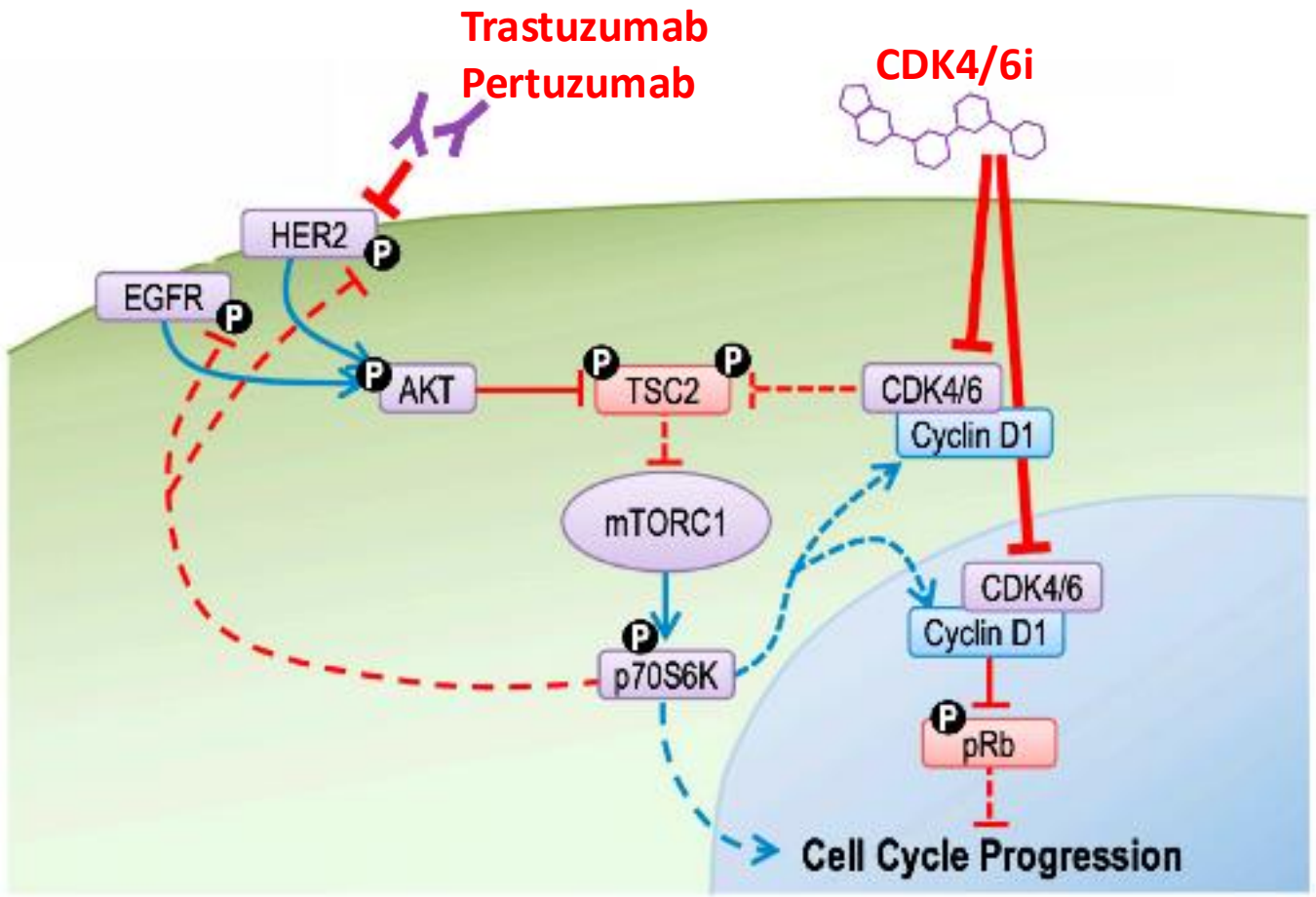
Chemo	196	166	114	66	28	16	6	0
ET	196	166	118	78	49	33	22	2

Subgroup Analyses of PFS

Subgroup	ET Group (Events/n)	Chemo Group (Events/n)	HR (95% CI)	*P*
Age, y				.146
≤40	29/31	30/42	1.14 (0.67-1.91)	
>40	151/165	135/154	0.80 (0.63-1.00)	
Receptor status				.099
ER and PR positive	143/157	128/157	0.90 (0.71-1.15)	
ER or PR positive	37/39	37/39	0.76 (0.48-1.20)	
Visceral involvement				.487
Yes	106/114	103/119	0.95 (0.72-1.25)	
No	74/82	62/77	0.80 (0.57-1.12)	
Previous adjuvant endocrine therapy				.904
AIs	74/83	66/83	0.98 (0.69-1.15)	
ORMs	56/59	51/59	0.97 (0.70-1.36)	
Metastasis number				.851
<2	127/140	111/139	0.89 (0.69-1.15)	
≥2	53/64	54/57	0.86 (0.59-1.27)	
DFS interval				**.016**
≤24 mo	59/64	64/78	1.39 (0.97-1.98)	
>24 mo	71/78	53/64	0.77 (0.53-1.10)	

Yuan Z et al. ASCO 2021. Abstract 1003; Hua X et al. Clin Cancer Res. 2022;28:637-645

Rationale for Blocking HER2 and CDK4/6 Pathways



Malumbres M et al. Cancer Cell 2016

- The cyclin D1-CDK4 axis is critical in HER2+ BC.
- Persistent **cyclin D1-CDK4 activity drives resistance** to the HER2 pathway blockade.
- **Dual inhibition of CDK4/6 and HER2 shows synergistic anti-tumor effects** in preclinical models by activating TSC2, leading to mTOR inhibition.

1. Yu Q, et al. *Nature*. 2001;411(6841):1017-1021.
2. Yu Q, et al. *Cancer Cell*. 2006;9(1):23-32.
3. Choi YJ, et al. *Cancer Cell*. 2012;22(4):438-451.
4. Goel S, et al. *Cancer Cell*. 2016;29(3):255-269.

CDK4/6 inhibition in HER2+ ABC

ASPIRE trial

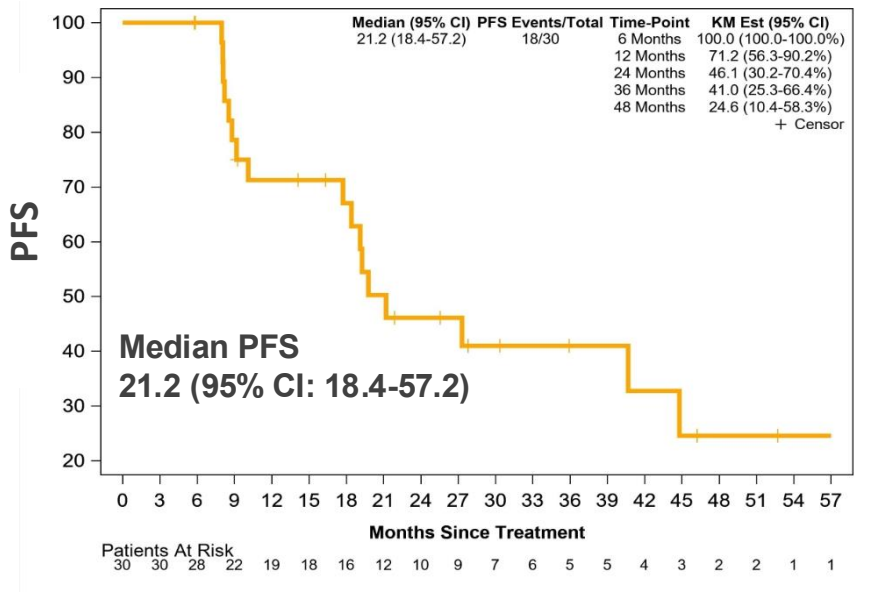
Key Eligibility Criteria

- Metastatic breast cancer with ER or PR positivity in ≥ 1% cells and HER2 positivity
- No prior systemic therapy for MBC
- Measurable or evaluable disease including bone metastasis only

- 57% recurrent disease
- 63.3% visceral disease

PHASE I N=3-12	PHASE II N=30-43
Palbociclib: PO at increasing doses (100mg, 125mg) on Days 1-21, followed by 7 days off using a 3+3 design	**Palbociclib:** PO at MTD (125mg) on Days 1-21, followed by 7 days off
Anastrozole: 1mg PO once daily	**Anastrozole:** 1mg PO once daily
Trastuzumab: 8mg/kg loading dose, followed by 6mg/kg q21 days	**Trastuzumab:** 8mg/kg loading dose, followed by 6mg/kg q21 days
Pertuzumab: 840mg/kg loading dose, followed by 420mg/kg q21 days	**Pertuzumab:** 840mg/kg loading dose, followed by 420mg/kg q21 days
Primary Endpoint Maximum Tolerated Dose (MTD)	**Primary Endpoint** • Clinical benefit rate (CBR): sum of complete response, partial response, and stable disease for ≥ 6 months **Secondary Endpoints** • Progression free survival (PFS) • Objective response rate (ORR) • Safety

Outcome	Patient Population (N=30)
Clinical benefit rate, % [95% CI]	**97%** [83, 100], p<0.0001
Objective response rate, % [95% CI]	**73%** [54, 88]
Complete Response	13% (4)
Partial Response	60% (18)
Stable Disease	23% (7)
Progressive Disease	0% (0)
Unevaluable	3% (1)
Median time to overall response, months [95% CI]	2.8 [2.7, 5.2]
Median duration of response, months [95% CI]	37.8 [14.0, Not Estimable]
Median follow up, months [95% CI]	30.3 [21.86,52.70]

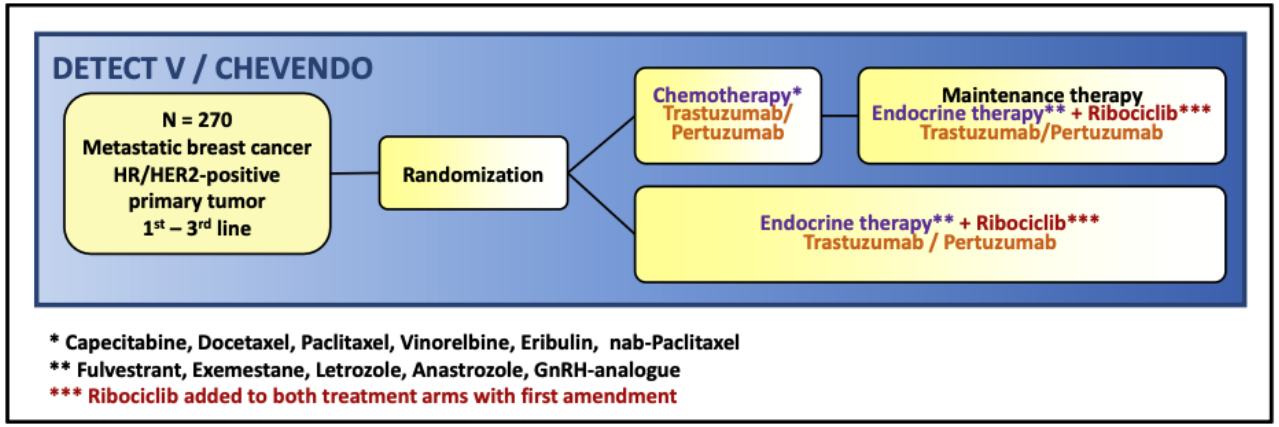


Patel R et al. SABCS 2023

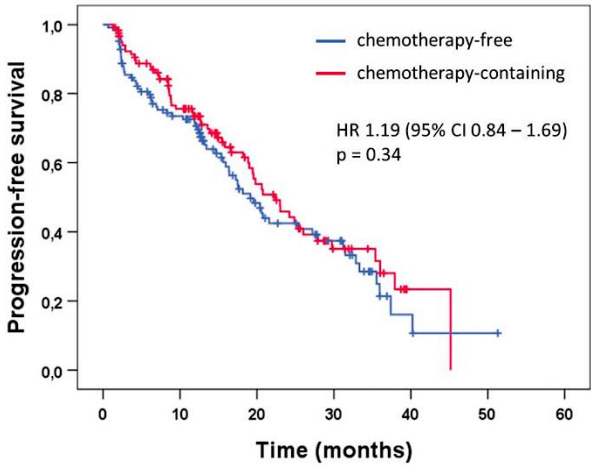
Slide credit: Otto Metzger

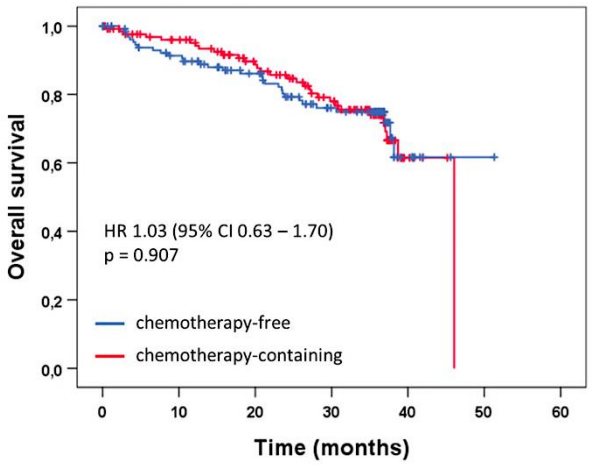
CDK4/6 inhibition in HER2+ ABC

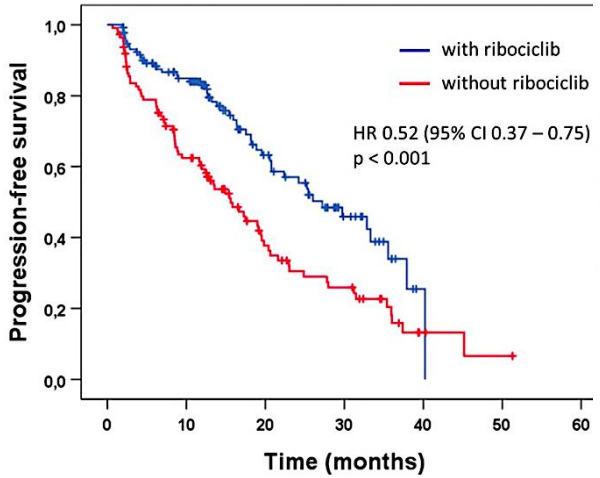
DETECT V trial

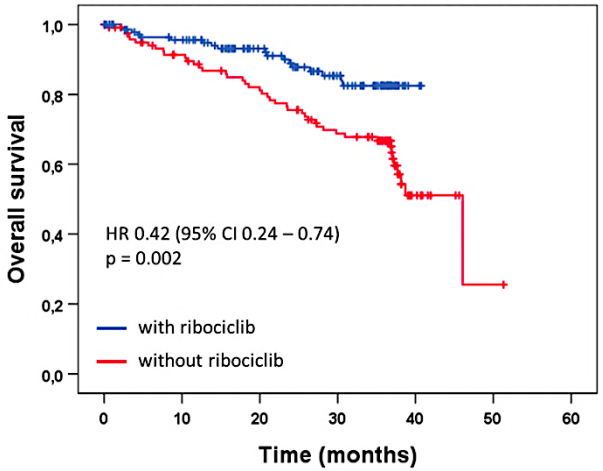


- After 124pts enrolled, amendment to add ribociclib in both treatment arms
- **76% pts treated in first line; 55% with visceral disease**
- **Primary endpoint:** tolerability; Secondary endpoints: PFS/OS









*Comparison of subsequent study cohorts, no randomized comparison

No differences in SAE but higher AEs grade 3/4 for ribo (neutropenia(74%), liver enzyme elevation)

Janni et al. ESMO 2024. 350MO.

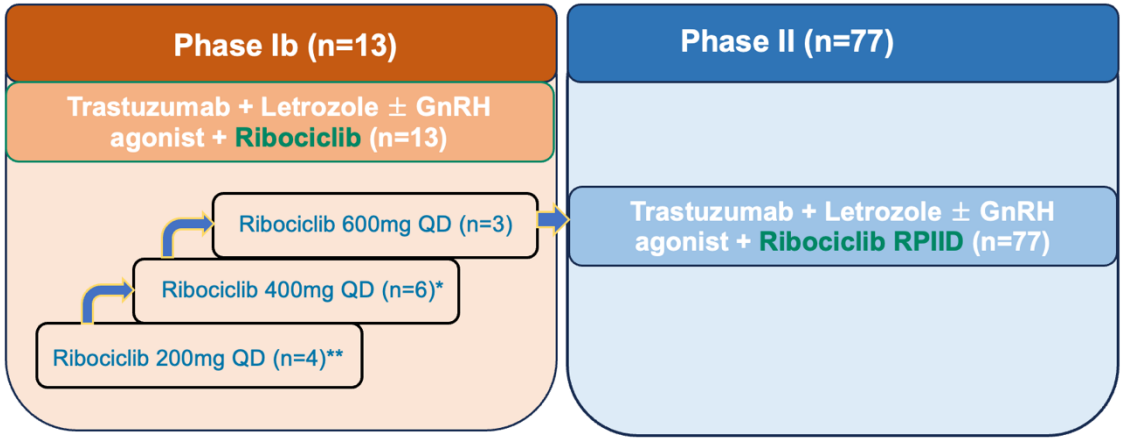
Slide credit: Otto Metzger

CDK4/6 inhibition in HER2+ ABC

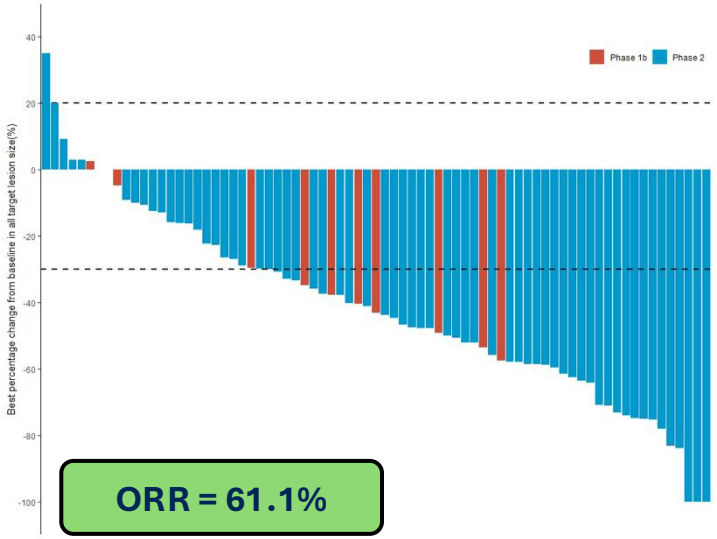
MINI trial – ASCO 2025

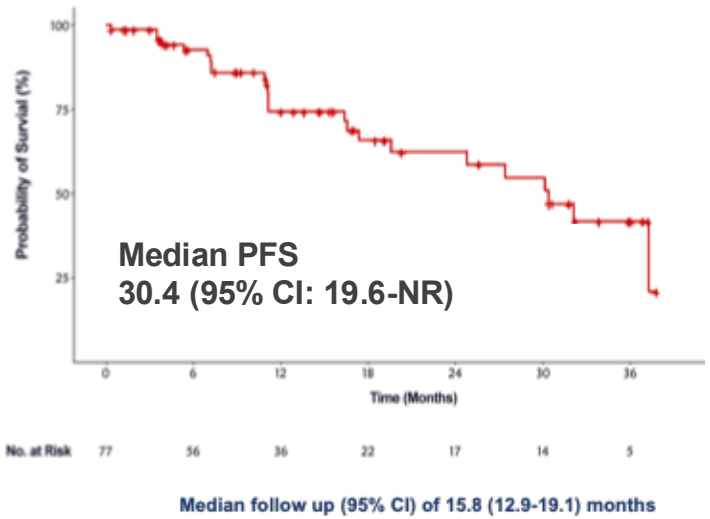
KEY ELIGIBILITY CRITERIA

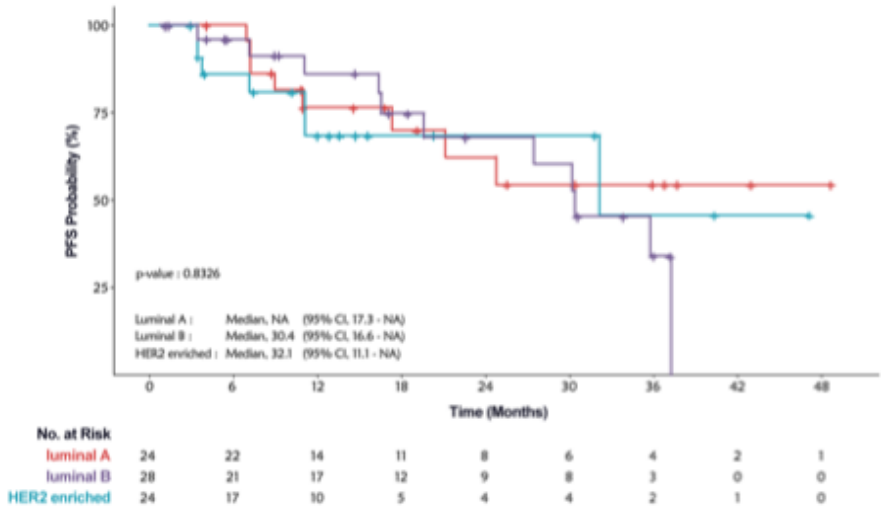
- Metastatic Breast Cancer
- HR+/HER2+
- Pre- or Postmenopause
- No prior systemic Tx for MBC
- Previous (neo) adjuvant trastuzumab or ET is not allowed unless
  - DFI > 12 mo from last Trastuzumab
  - Adjuvant ET > 2 years
- Stable CNS metastasis allowed
- Baseline LVEF within normal range



- **Primary endpoint:** Phase Ib – Determination RP2D; Phase II – PFS
- Secondary endpoints: OS, ORR, DoR, Safety
- **58.9% recurrent disease; 66.7% visceral disease**







Sohn J et al. ASCO 2025

Slide credit: Otto Metzger

Single vs. Dual HER2 Blockade + Endocrine Therapy in ABC

Endocrine therapy + Single anti-HER2					
TAnDEM	III	Trastuzumab + anastrozole *versus* anastrozole	HR+/HER2+ (207)	4.8 *versus* 2.4 ($p = 0.0016$)	28.5 *versus* 23.9 ($p = 0.325$)
EGF30008	III	Lapatinib + letrozole *versus* letrozole	HR+/HER2+ (219)	8.2 *versus* 3.0 ($p = 0.019$)	33.3 *versus* 32.3
eLEcTRA	III	Trastuzumab + letrozole *versus* letrozole	HR+/HER2+ (57)	14.1 *versus* 3.3 ($p = 0.23$)	Data not shown
Endocrine therapy + HP					
PERTAIN	II	Pertuzumab + trastuzumab + AI *versus* trastuzumab + AI	HR+/HER2+ (258)	18.9 *versus* 15.8 ($p = 0.007$)	60.2 *versus* 57.2
Trastuzumab ET vs. Trastuzumab Chemotherapy					
SYSUCC-002	III	Trastuzumab + ET *versus* trastuzumab + CT	HR+/HER2+ (392)	19.2 *versus* 14.8 ($p < 0.0001$)	33.9 *versus* 32.5 ($p = 0.094$)

Slide credit: Otto Metzger

1. Yu Q, et al. *Nature*. 2001;411(6841):1017-1021.
2. Yu Q, et al. *Cancer Cell*. 2006;9(1):23-32.
3. Liang Y, et al. *Ther Adv Med Oncol*. 2024;16:17588359231220501.

Agenda

Introduction: HER2 History

Module 1: Cases from the GMO Survey

Module 2: Biology and Selection of First-Line Therapy for HR-Positive, HER2-Positive Metastatic Breast Cancer (mBC) — Dr Mahtani

Module 3: Faculty Case Presentations

Module 4: Patterns of Care Survey — Part 1

Module 5: Optimizing the Use of Up-Front Maintenance Therapy for HER2-Positive mBC — Dr Carey

Module 6: Faculty Case Presentations

Module 7: Patterns of Care Survey — Part 2

Dr Mahtani: Case

- 56yo diagnosed with breast cancer in 2019
- S/P B/L mastectomy: Left: pT1aN0, ER 20%, P 5%, HER2 3+; Right: extensive DCIS spanning 4 cm, no invasive disease, ER 90%, PR 80%
- No adjuvant chemo/HER2 directed therapy
- Tamoxifen 2020-2025
- 3 months post discontinuation of tamoxifen presented with DOE while exercising, persistent cough, went to ER with worsening symptoms

Dr Mahtni: Case (Cont)

- Echo: large pericardial effusion, impending cardiac tamponade
- Emergent pericardial window and biopsy: IDC, ER 10%, PR 0, HER2 3+
- CT C/A/P: pleural effusion, multiple small lung nodules, no liver/bone mets
- Brain MRI (asymptomatic): no mets
- Started T-DXd + pertuzumab with rapid improvement after 2 cycles of therapy

Dr Carey: Case

- 59 yo patient with longstanding triple-positive mBC
- Six years without relapse, relapse bone-only

Key treatments:

  - ET + H then ET + HL (+ bone-directed Rx) x 10 years
  - Vinorelbine + HP (d/c for chemotherapy-induced peripheral neuropathy)
  - T-DXd (d/c for non-ILD AE)
  - AI + HP + palbociclib ongoing
- PS continues to be very good

Agenda

Introduction: HER2 History

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Module 7: Patterns of Care Survey — Part 2

Discussion Questions

In general, how you approach induction and maintenance therapy for a patient with HR-positive, HER2-positive mBC?

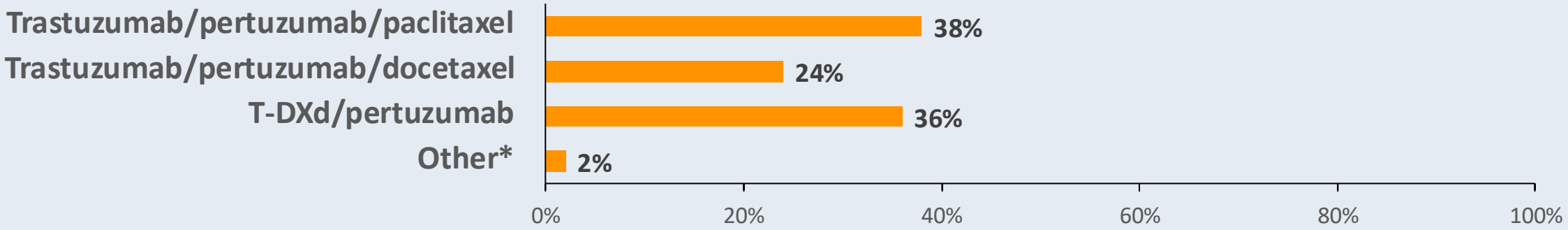
How do age, site(s) of metastases and tumor symptom status impact your approach?

RTP RESEARCH TO PRACTICE

A woman presents with de novo HR-positive, HER2-positive mBC. Regulatory and reimbursement issues aside, which first-line anti-HER2 induction therapy would you most likely recommend for each of the following scenarios?

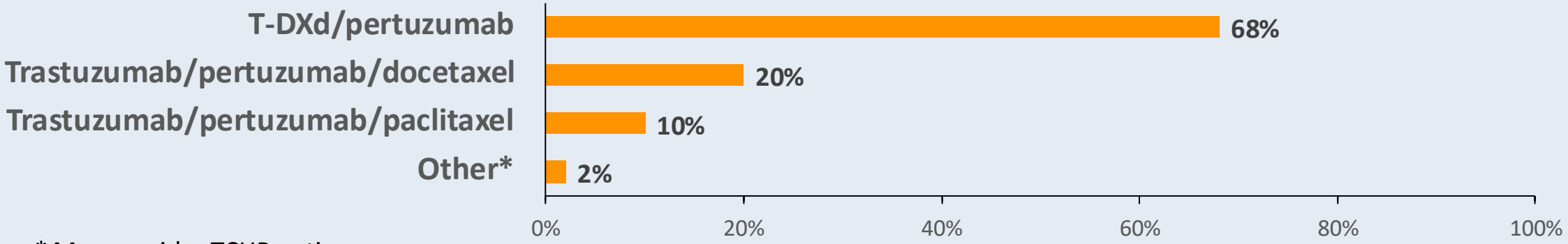
Age 65, PS 0

Asymptomatic bone metastases:



* OFS + CDK4/6i first then if pt develops symptomatic PD with measurable lesions, will give T-DXd

Symptomatic liver metastases:



* May consider TCHP option

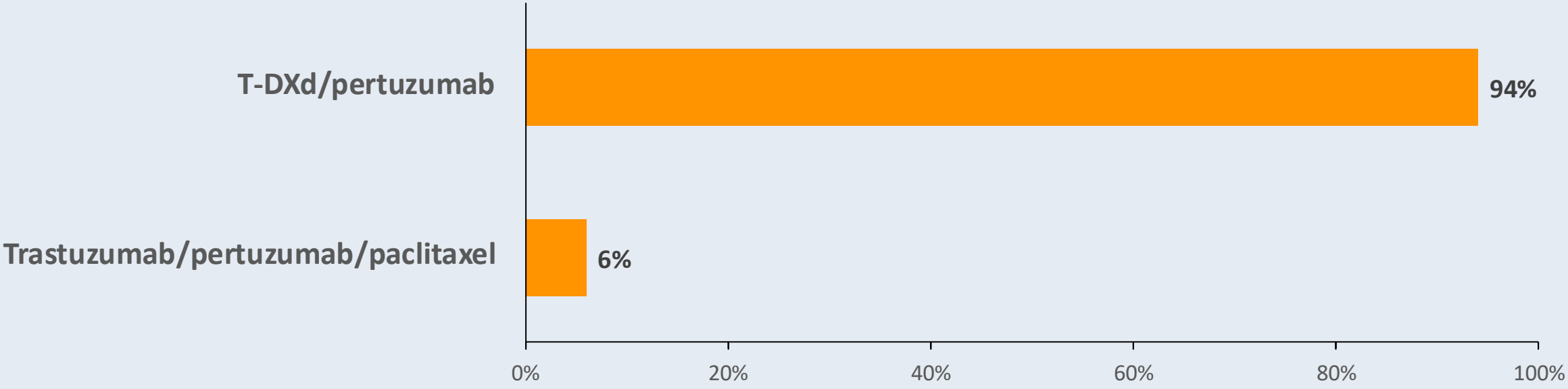
Survey of US-based general medical oncologists

RTP RESEARCH TO PRACTICE

A woman presents with de novo HR-positive, HER2-positive mBC. Regulatory and reimbursement issues aside, which first-line anti-HER2 induction therapy would you most likely recommend for each of the following scenarios? (continued)

Age 65, PS 0

Multiple brain metastases requiring SRS:

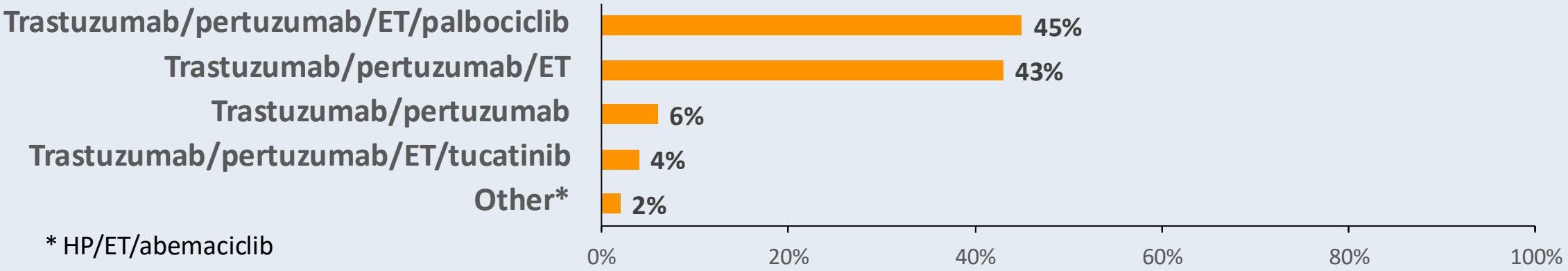


Survey of US-based general medical oncologists

A patient with HR-positive, HER2-positive mBC receives 6 cycles of THP as first-line induction therapy. Regulatory and reimbursement issues aside, which maintenance regimen would you recommend?

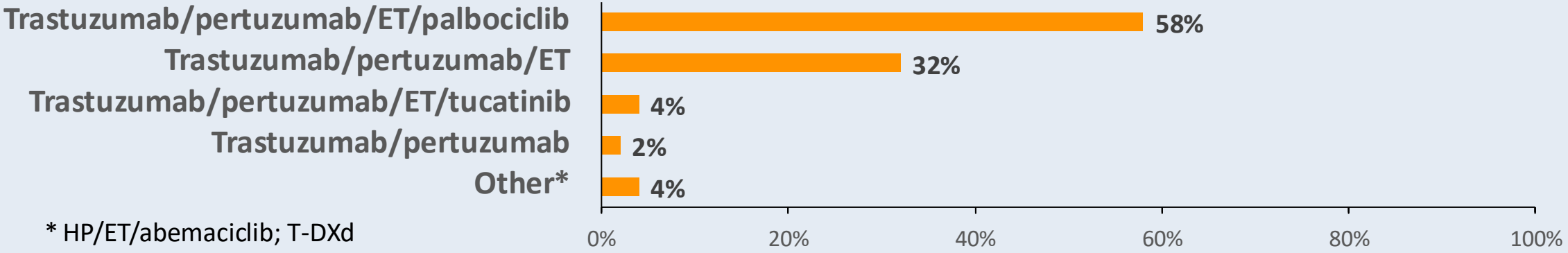
Age 65, PS 0

Achieved a complete response:



* HP/ET/abemaciclib

Achieved a partial response:



* HP/ET/abemaciclib; T-DXd

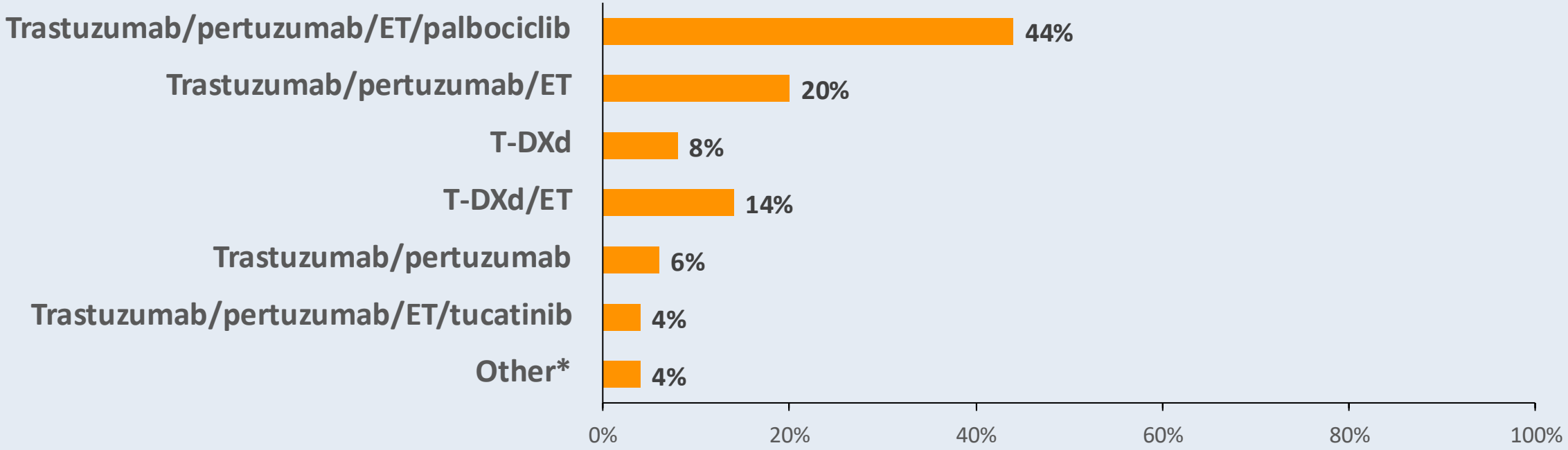
Survey of US-based general medical oncologists

RTP RESEARCH TO PRACTICE

A patient with HR-positive, HER2-positive mBC receives T-DXd/pertuzumab as first-line induction therapy. Regulatory and reimbursement issues aside, which maintenance regimen would you recommend?

Age 65, PS 0

Achieved a complete response:



* T-DXd/pertuzumab/ET

Survey of US-based general medical oncologists

RTP RESEARCH TO PRACTICE

A patient with HR-positive, HER2-positive mBC receives T-DXd/pertuzumab as first-line induction therapy. Regulatory and reimbursement issues aside, which maintenance regimen would you recommend?

Age 65, PS 0

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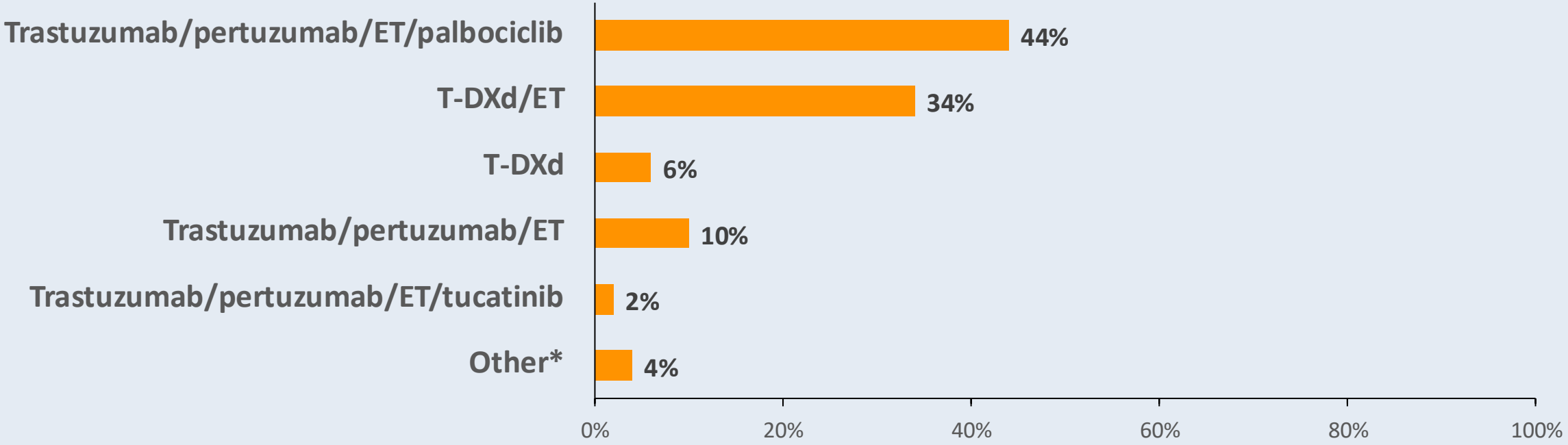
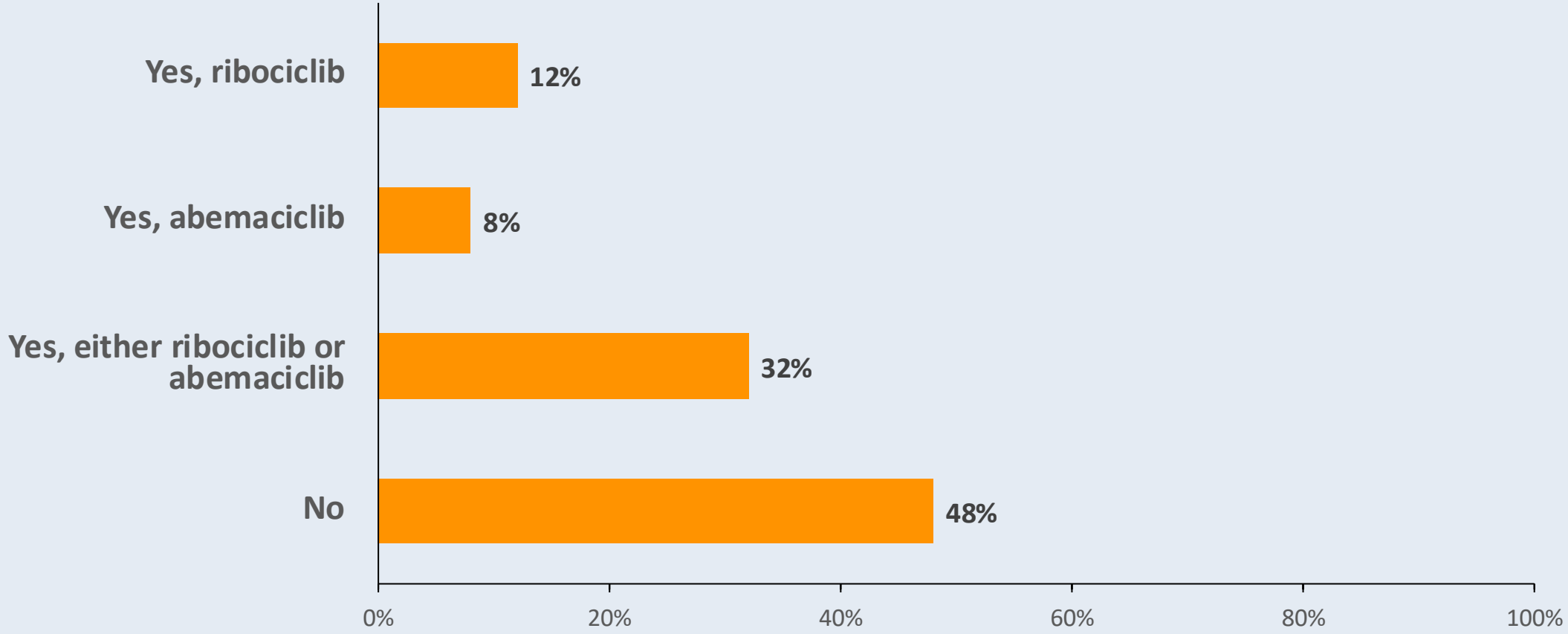


* T-DXd/P/ET; T-DXd/pertuzumab/ET

Survey of US-based general medical oncologists

RTP RESEARCH TO PRACTICE

Other than palbociclib, would you use any other CDK4/6 inhibitor in combination with maintenance HER2-targeted therapy and endocrine therapy after induction treatment for HR-positive, HER2-positive mBC?



Survey of US-based general medical oncologists

RTP RESEARCH TO PRACTICE

Discussion Questions

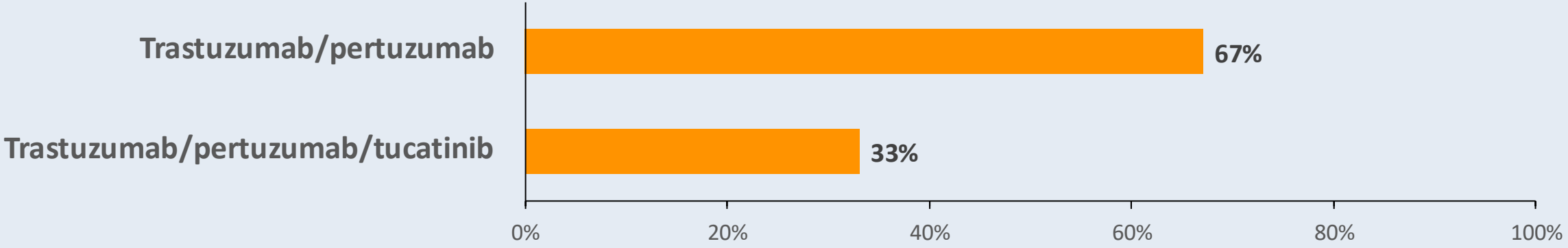
In general, how you approach induction and maintenance therapy for a patient with HR-negative, HER2-positive mBC?

How do age, site(s) of metastases and tumor symptom status impact your approach?

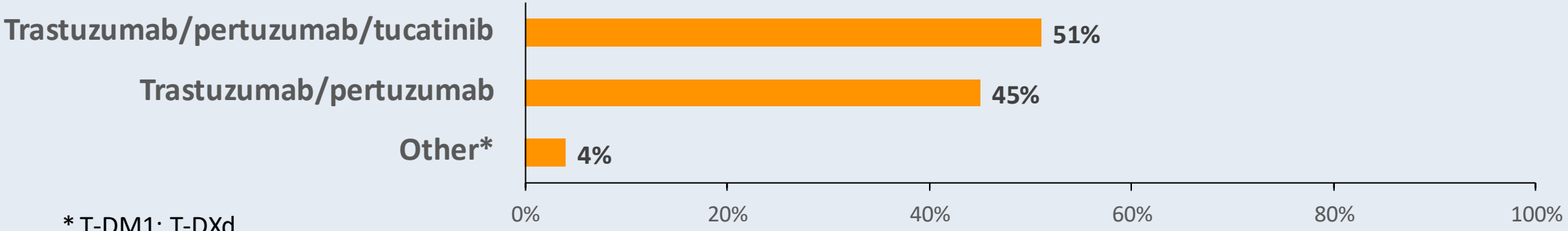
A patient with HR-negative, HER2-positive mBC receives 6 cycles of THP as first-line induction therapy. Regulatory and reimbursement issues aside, which maintenance regimen would you recommend?

Age 65, PS 0

Achieved a complete response:



Achieved a partial response:



* T-DM1; T-DXd

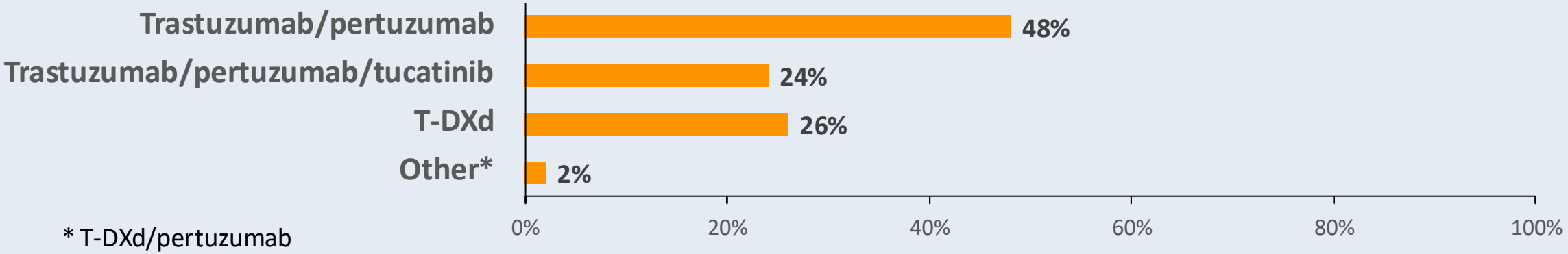
Survey of US-based general medical oncologists

RTP RESEARCH TO PRACTICE

A patient with HR-negative, HER2-positive mBC receives 6 cycles of T-DXd/pertuzumab as first-line induction therapy. Regulatory and reimbursement issues aside, which maintenance regimen would you recommend?

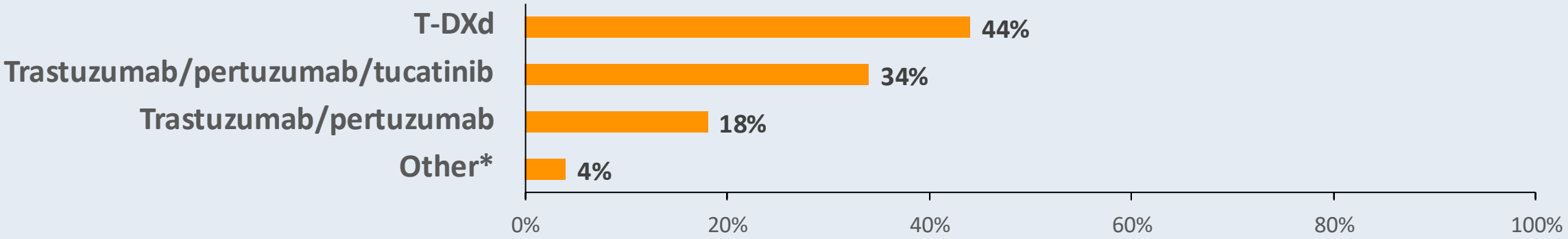
Age 65, PS 0

Achieved a complete response:



* T-DXd/pertuzumab

Achieved a partial response:

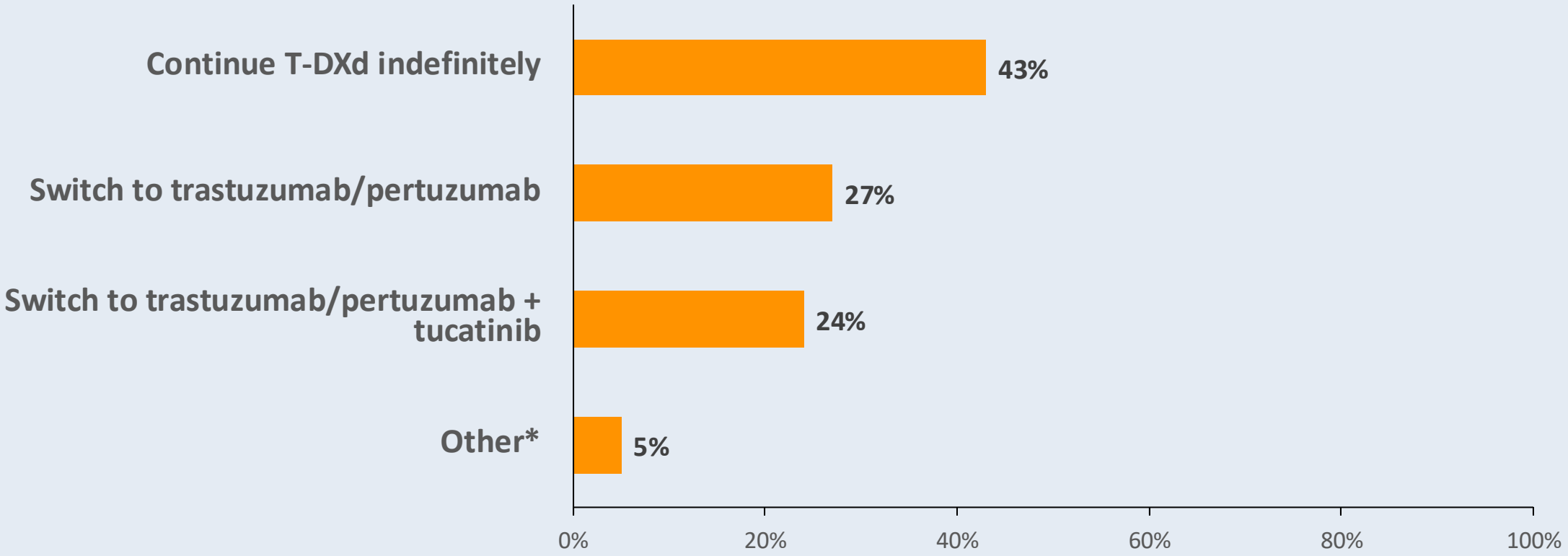


* T-DXd/pertuzumab

Survey of US-based general medical oncologists

RTP RESEARCH TO PRACTICE

A patient with de novo HR-negative, HER2-positive mBC is receiving first-line T-DXd and pertuzumab with response and reasonably good tolerability. Regulatory and reimbursement issues aside, what would be your most likely approach to maintenance therapy?



* Treat to maximum response and then switch to HER2CLIMB-05 regimen; Depends as above, any of these may be appropriate

Survey of US-based general medical oncologists

RTP RESEARCH TO PRACTICE

Agenda

Introduction: HER2 History

Module 1: Cases from the GMO Survey

Module 2: Biology and Selection of First-Line Therapy for HR-Positive, HER2-Positive Metastatic Breast Cancer (mBC) — Dr Mahtani

Module 3: Faculty Case Presentations

Module 4: Patterns of Care Survey — Part 1

Module 5: Optimizing the Use of Up-Front Maintenance Therapy for HER2-Positive mBC — Dr Carey

Module 6: Faculty Case Presentations

Module 7: Patterns of Care Survey — Part 2

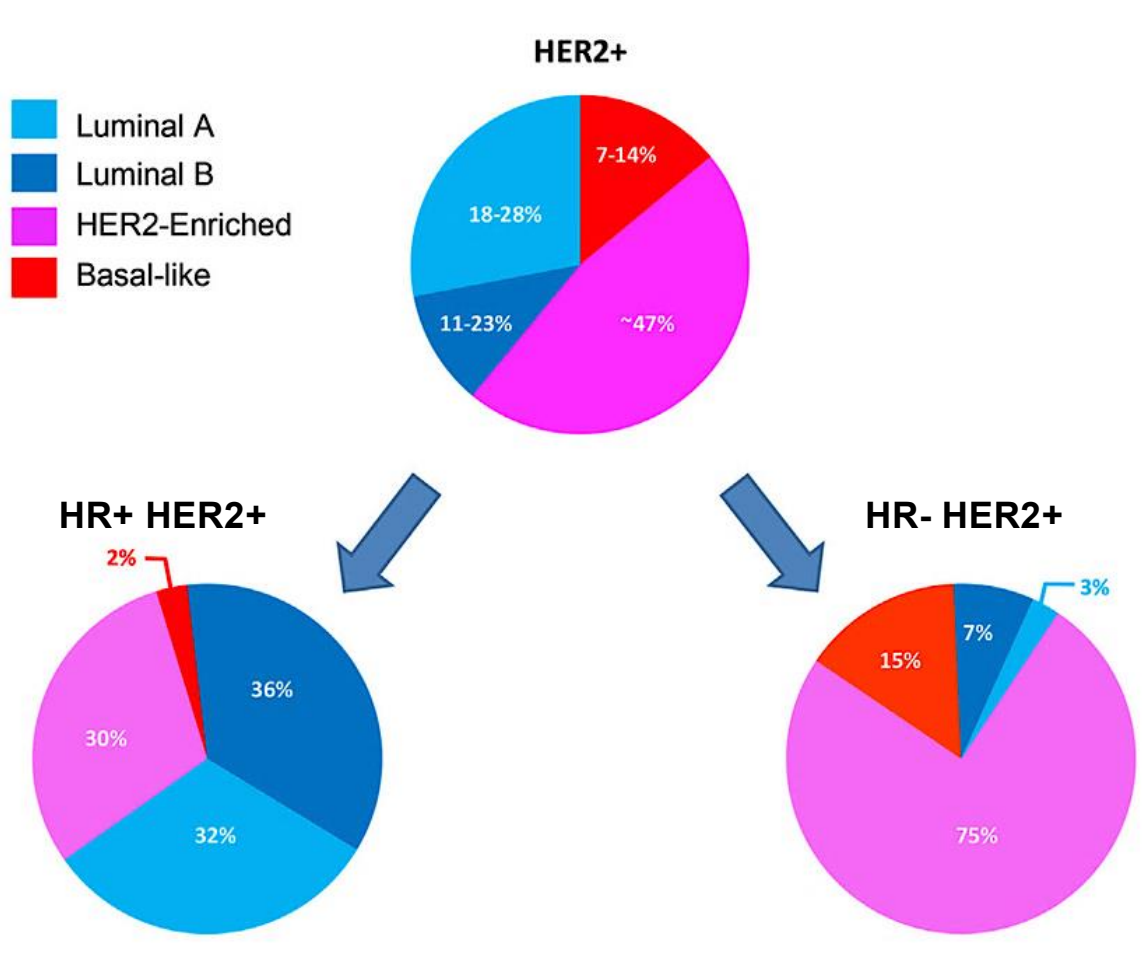
RTP RESEARCH TO PRACTICE

Optimizing the Use of Up-Front or Maintenance Therapy for HER2-Positive mBC, Including Patients with HR-Positive Disease

Lisa A Carey, MD, ScM, FASCO
UNC Lineberger Comprehensive Cancer Center
Chapel Hill, North Carolina

RTP RESEARCH TO PRACTICE

Molecular and Clinical Features of Triple-Positive Breast Cancer



Most triple-positive cases (68%) are "luminal"

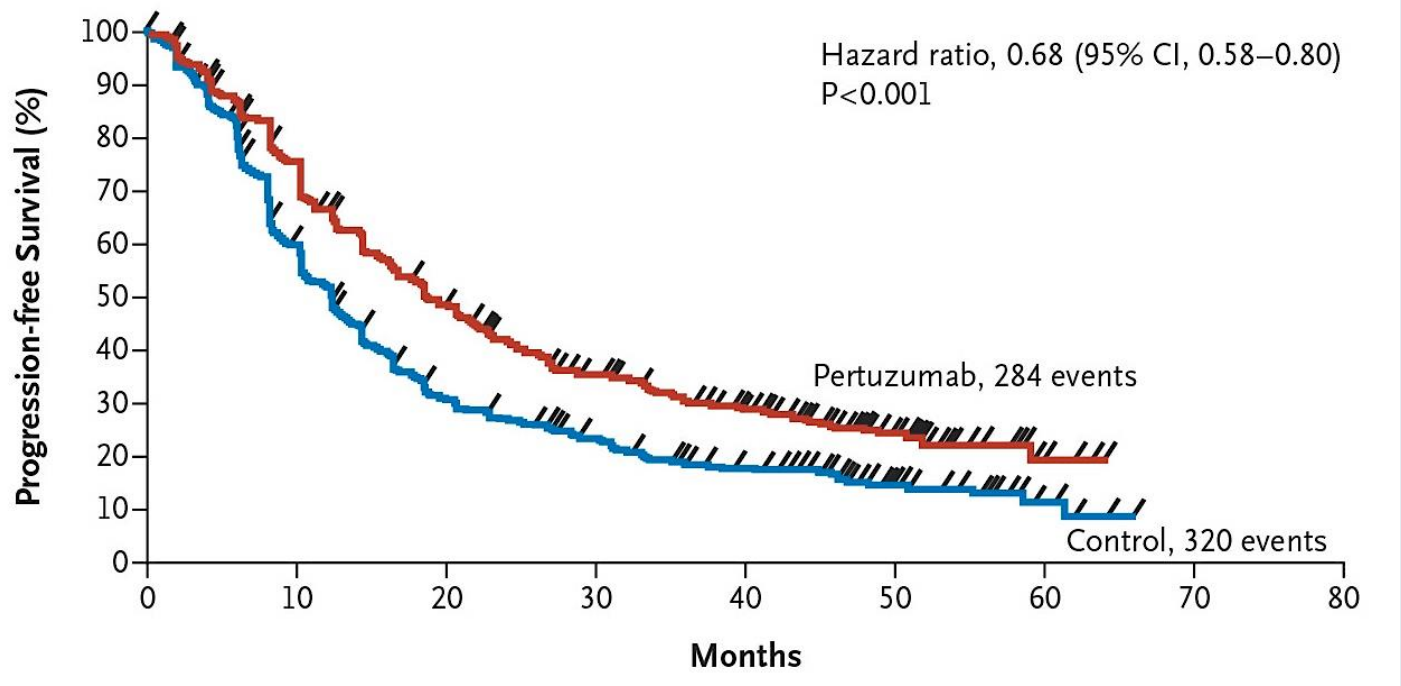
Compared to HR-negative, HER2-positive disease:

- **More likely to have late relapse, bone-only disease, better prognosis**
- **Less likely to have de novo, visceral or Grade 3 disease.**

Schettini et al. *Breast* 2021 October;59:339-50. Bischoff et al. *Clin Cancer Breast* 2026;26(2):93-104.

Phase III CLEOPATRA Trial: First-Line Treatment of HER2-Positive Breast Cancer

Benefit of pertuzumab added to first-line trastuzumab + taxane. THP = standard therapy for 10 years



PFS: 18.5 vs 12.4 mo
OS: 57.1 vs 40.8 mo

ER or PgR status			0.47
Positive	388	0.71 (0.53–0.96)	
Negative	408	0.61 (0.47–0.81)	

PFS = progression-free survival; OS = overall survival

Swain SM et al. *N Engl J Med* 2015;372(8):724-34; Swain SM et al. *Lancet Oncol* 2020;21:519-30; Miles D et al. *Ann Oncol* 2017;28(11):2761-7.

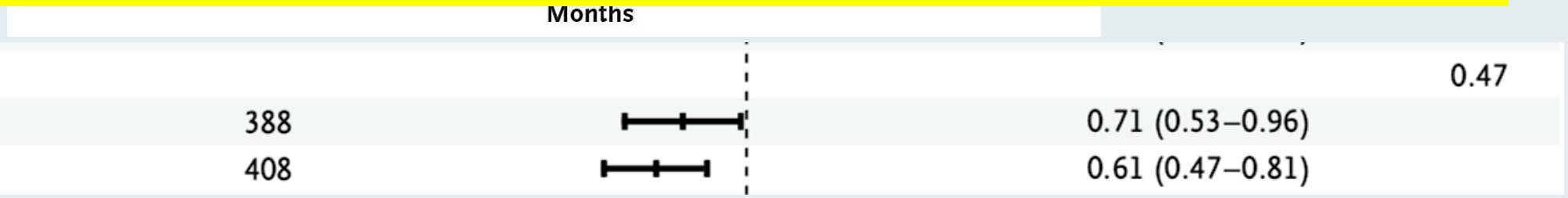
Phase III CLEOPATRA Trial: First-Line Treatment of HER2-Positive Breast Cancer

Benefit of pertuzumab added to first-line trastuzumab + taxane. THP = standard therapy for 10 years

Allowed discontinuation of taxane after 6 cycles (move to maintenance HP).
Post-hoc no outcome difference between 6 cycles THP and longer.

THP x 6 → HP became the norm

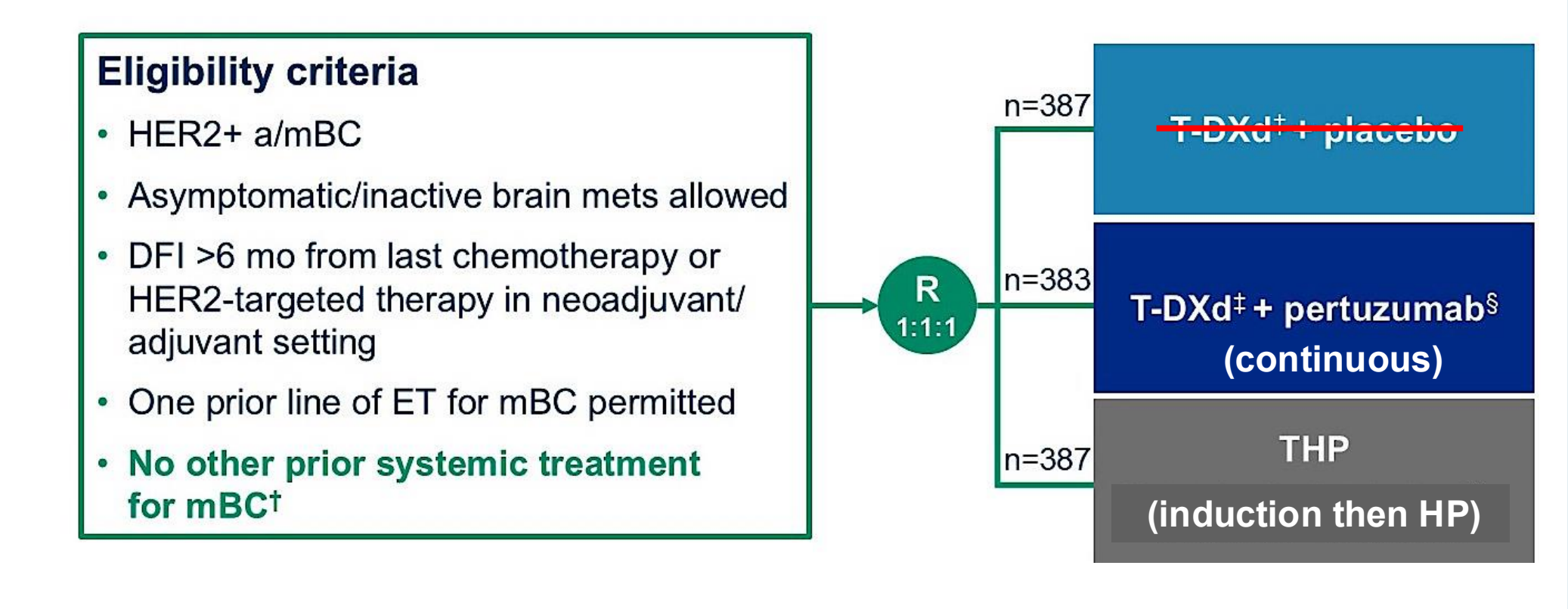
(CLEOPATRA not designed to test importance of induction therapy)



PFS = progression-free survival; OS = overall survival

Swain SM et al. *N Engl J Med* 2015;372(8):724-34; Swain SM et al. *Lancet Oncol* 2020;21:519-30; Miles D et al. *Ann Oncol* 2017;28(11):2761-7.

Phase III DESTINY-Breast09 Trial



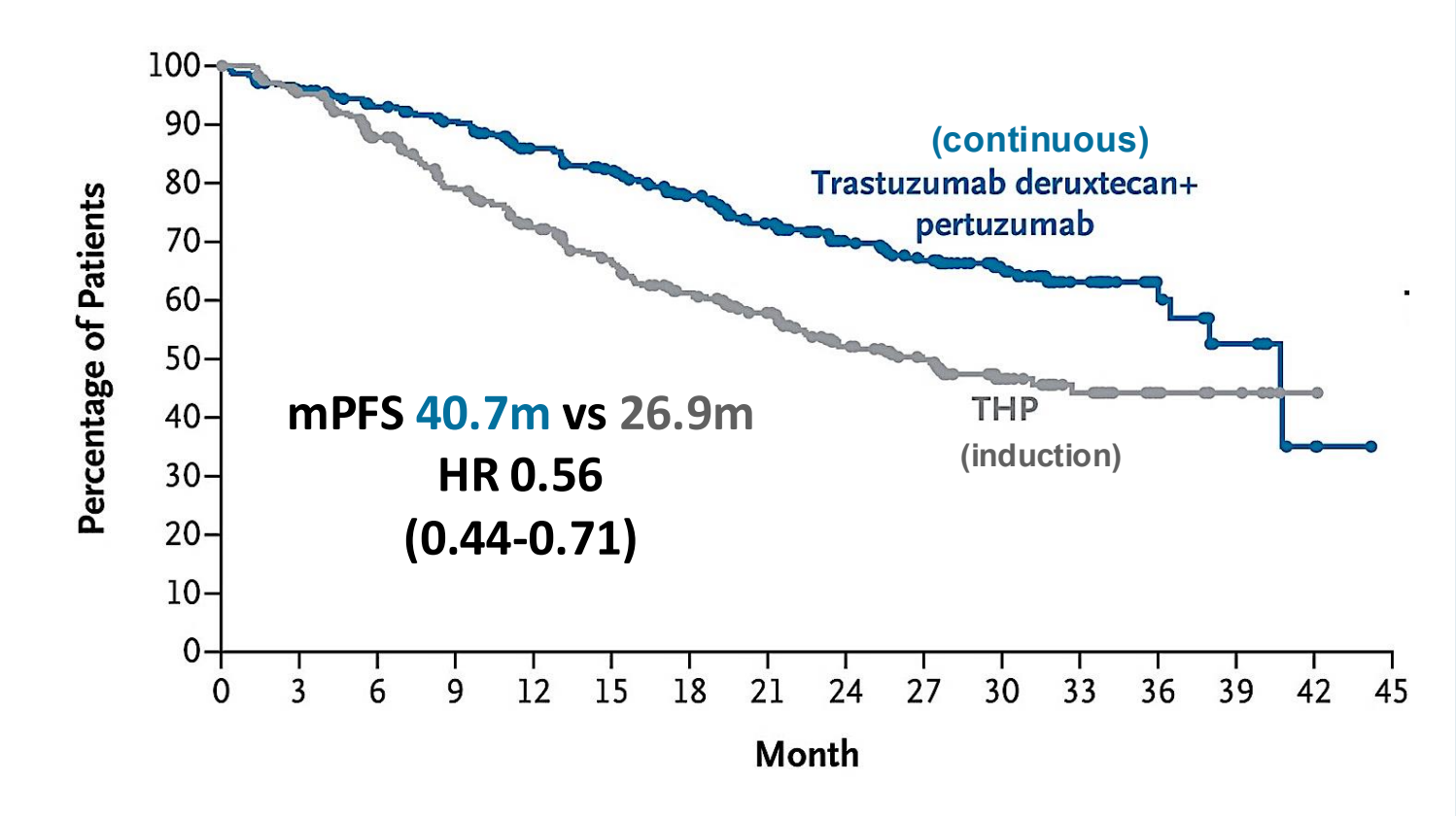
Triple-positive disease: ET allowed after 6 cycles of DXd, administered to 13%, or after taxane, administered to 38%

a/mBC = advanced or metastatic breast cancer; DFI = disease-free interval; ET = endocrine therapy; mBC = metastatic breast cancer; T-DXd = trastuzumab deruxtecan; THP = docetaxel/trastuzumab/pertuzumab

Tolaney SM et al. *N Engl J Med* 2026;394;551-62.

RTP RESEARCH TO PRACTICE

Phase III DESTINY-Breast09: Progression-Free Survival (PFS) by Blinded Independent Central Review



Similar effect in HR-positive (HR 0.61) and HR-negative (HR 0.52)

Toxicity as expected with T-DXd + pertuzumab: GI, fatigue, ANC, alopecia; ILD 12%, EF decline ~10%

mPFS = median progression-free survival; ANC = absolute neutrophil count, ILD = interstitial lung disease; EF = ejection fraction

Tolaney SM et al. *N Engl J Med* 2026;394;551-62.

RTP RESEARCH TO PRACTICE

Phase III DESTINY-Breast09: Progression-Free Survival by Blinded Independent Central Review

Approved 12/2025

Optimal regimen IF administering a chemotherapy-based regimen first

(Did not test induction strategy. Most clinicians plan to use as induction)

Similar effect in HR-positive (HR 0.61) and HR-negative (HR 0.52)

Toxicity as expected with T-DXd + pertuzumab: GI, fatigue, ANC, alopecia; ILD 12%, EF decline ~10%

mPFS = median progression-free survival; ANC = absolute neutrophil count, ILD = interstitial lung disease; EF = ejection fraction

Tolaney SM et al. *N Engl J Med* 2026;394;551-62.

RTP RESEARCH TO PRACTICE

What About "Maintenance" or Up-Front Nonchemotherapy Options?

- **CLEOPATRA trial established trastuzumab/pertuzumab as standard maintenance after THP.**
  - **Did not add ET to HP for triple-positive disease.**
- **PERTAIN trial: Good outcomes with ET + HP regardless of induction.**
- **PATINA and HER2CLIMB-05 trials have further optimized nonchemotherapy treatment.**
  - **Both required induction chemotherapy + anti-HER2 therapy for eligibility.**

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

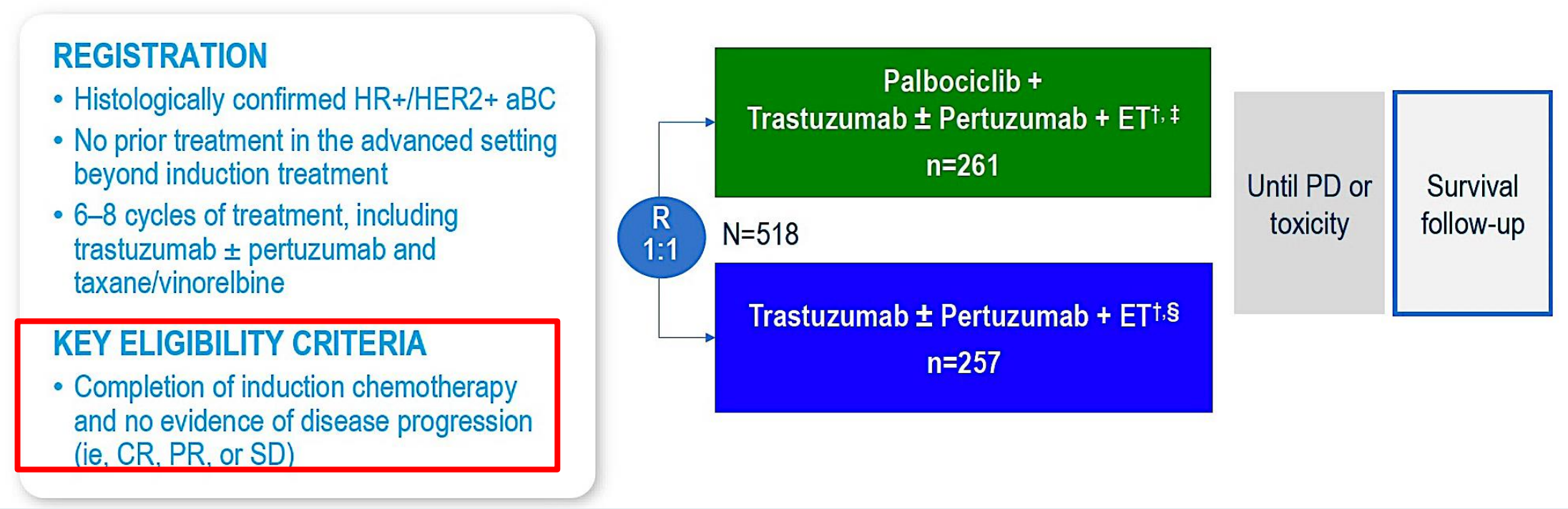
Palbociclib for Hormone-Receptor–Positive, HER2-Positive Advanced Breast Cancer

O. Metzger,[1] S. Mandrekar,[2] S. Goel,[3] J. Gligorov,[4,5] E. Lim,[6] E. Ciruelos,[7] S. Loibl,[8] T. Dockter,[2] X. Gonzàlez Farré,[9] P.A. Francis,[3] F. Lynce,[1] J. Lanzillotti,[10] C. DuFrane,[10] A. Wall,[2] C. Strand,[2] I. Krop,[11] I. Vaz-Luis,[12] D. Tripathy,[13] S. Loi,[3] A. Prat,[14] M. Goetz,[2] S. Escrivá-de-Romaní,[15] D. Porter,[16] J. Spoenlein,[17] D.G. Stover,[18] S. Sardesai,[18] P. Heudel,[19] M. Koehler,[20] C. Huang Bartlett,[21] A. Holynskyj,[21] P. Gopalakrishna,[21] E. Gauthier,[21] S. Delaloge,[12] K. Miller,[22] E.P. Winer,[11] L. Gianni,[23] A.H. Partridge,[1] A. DeMichele,[24] and L.A. Carey[25]

2026:394;451-62.

Phase III PATINA Trial: First-Line Therapy for Triple-Positive mBC

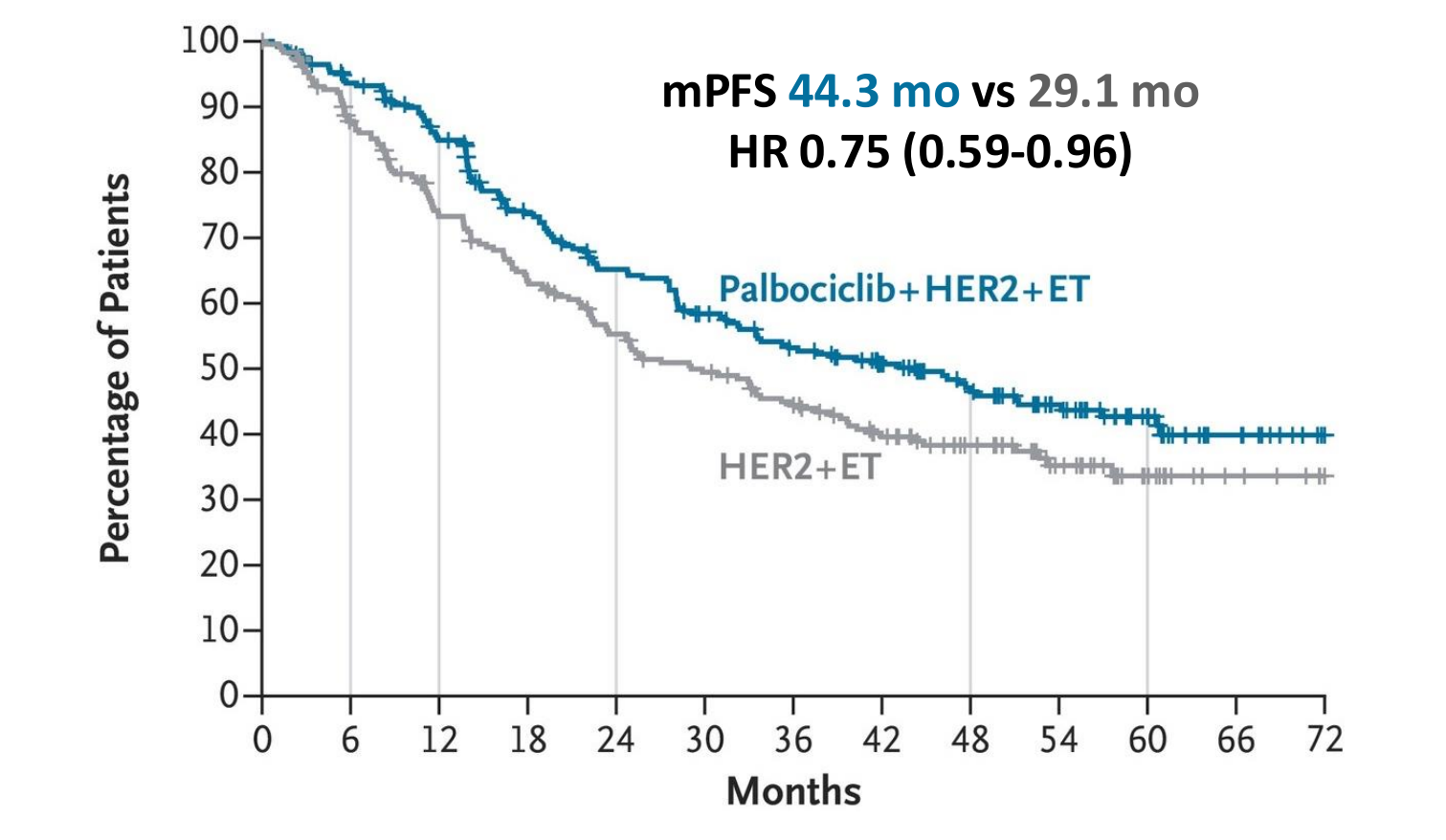
Tested addition of CDK4/6 inhibitor to maintenance ET + HP after induction chemotherapy + HP without disease progression



CR = complete response, PR = partial response; SD = stable disease

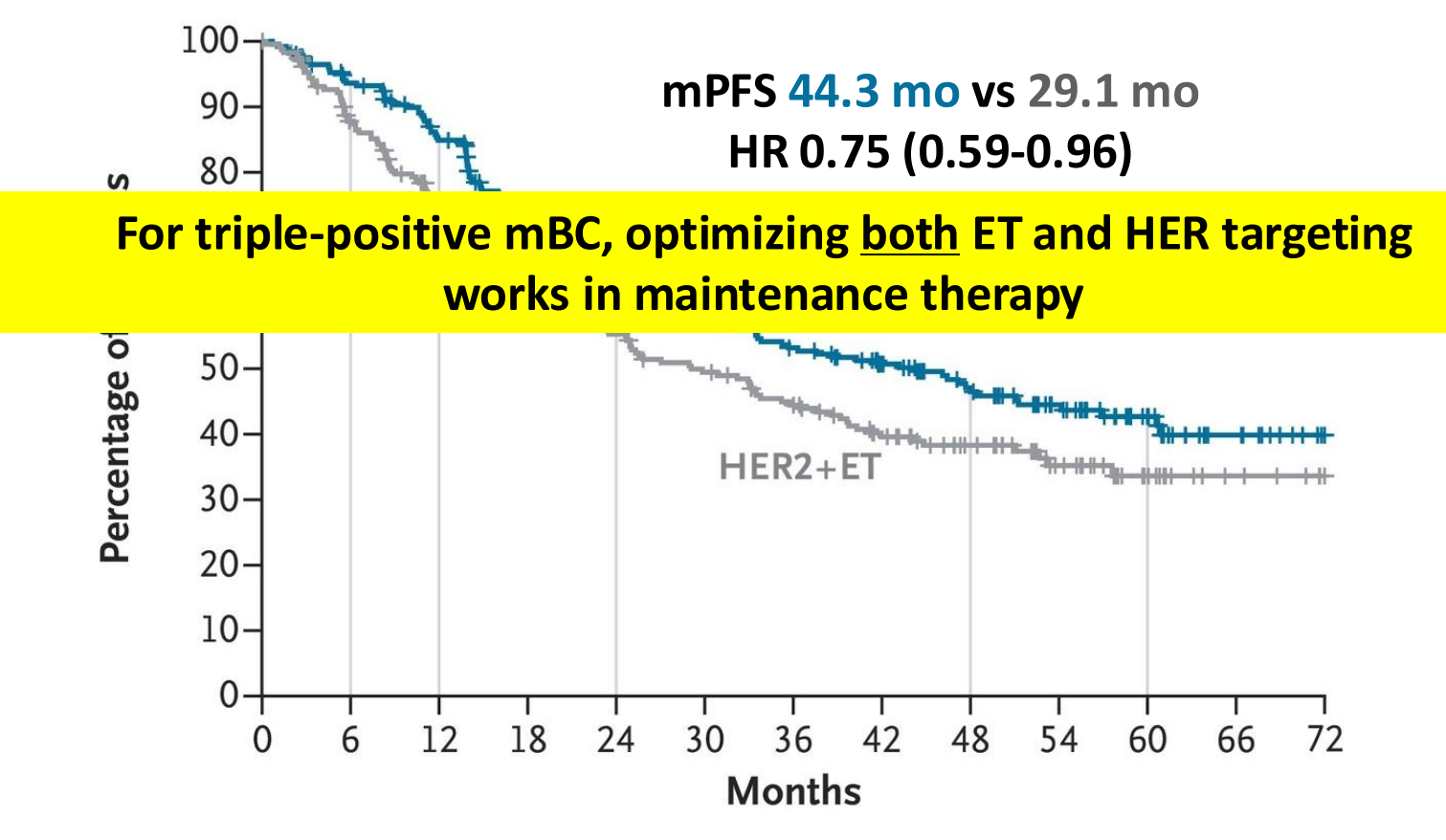
Metzger O et al. *N Engl J Med* 2026;394(5):451-62.

Phase III PATINA: Progression-Free Survival (Intention-to-Treat Population)



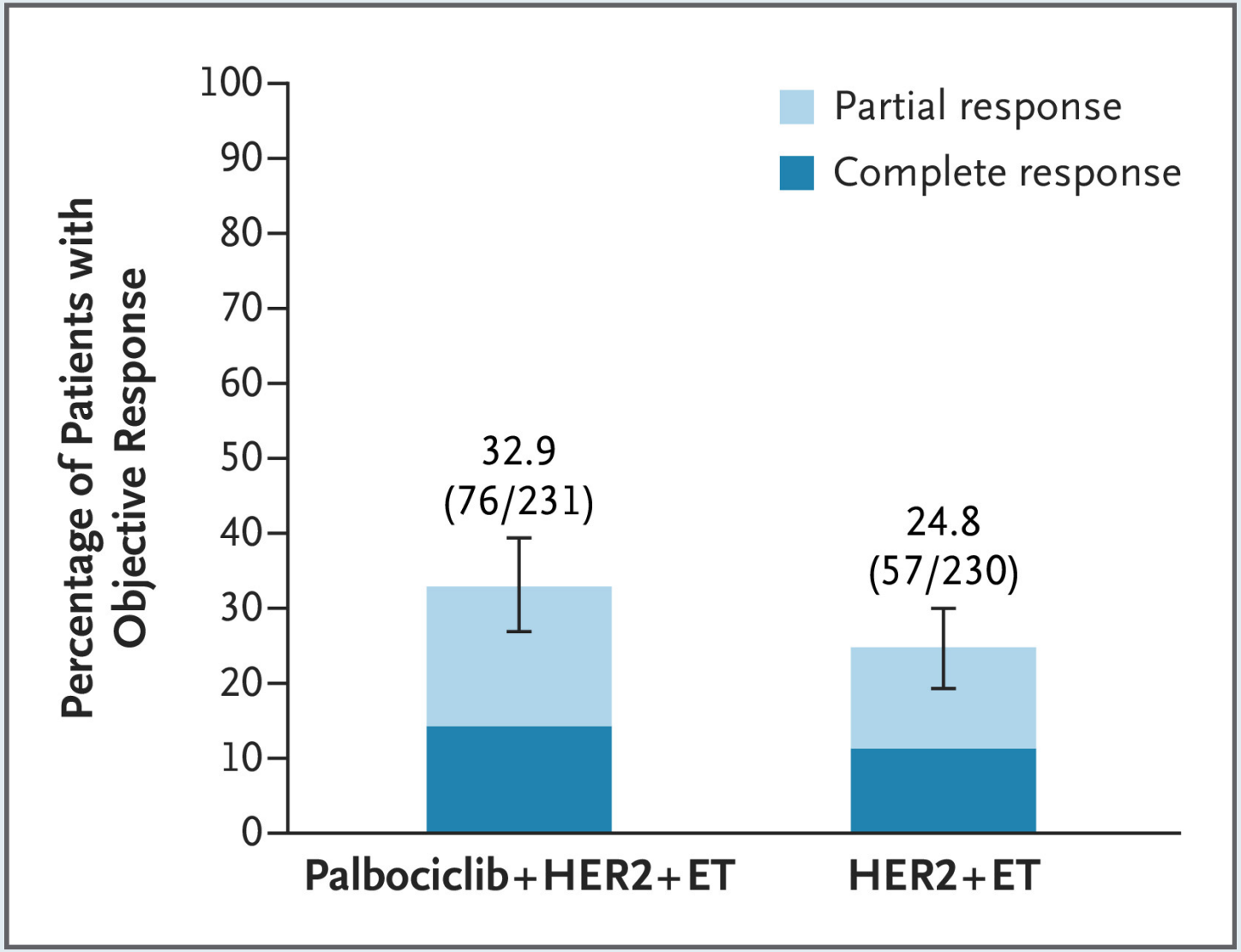
Metzger O et al. *N Engl J Med* 2026;394(5):451-62.

Phase III PATINA: Progression-Free Survival (Intention-to-Treat Population)



Metzger O et al. *N Engl J Med* 2026;394(5):451-62.

Phase III PATINA: Tumor Response



Metzger O et al. *N Engl J Med* 2026;394(5):451-62.

Phase III PATINA: Common Adverse Events

Adverse Events	Palbociclib+HER2+ET (N=261)		HER2+ET (N=248)	
	Any Grade	Grade ≥3	Any Grade	Grade ≥3
	number of patients (percent)			
Neutropenia†	203 (77.8)	158 (60.5)	19 (7.7)	5 (2.0)
Diarrhea	184 (70.5)	25 (9.6)	93 (37.5)	3 (1.2)
Fatigue†	140 (53.6)	13 (5.0)	99 (39.9)	0
Leukopenia†	99 (37.9)	42 (16.1)	12 (4.8)	2 (0.8)
Arthralgia	95 (36.4)	4 (1.5)	119 (48.0)	2 (0.8)
Anemia†	80 (30.7)	8 (3.1)	20 (8.1)	1 (0.4)
Nausea	77 (29.5)	1 (0.4)	38 (15.3)	1 (0.4)
Headache	67 (25.7)	4 (1.5)	45 (18.1)	2 (0.8)
Thrombocytopenia†	65 (24.9)	3 (1.1)	4 (1.6)	0
Abdominal pain†	62 (23.8)	4 (1.5)	19 (7.7)	5 (2.0)
Hot flush†	58 (22.2)	0	70 (28.2)	0
Rash†	58 (22.2)	0	42 (16.9)	0
Covid-19†	57 (21.8)	2 (0.8)	25 (10.1)	0
Pruritus	55 (21.1)	4 (1.5)	41 (16.5)	0
Stomatitis	54 (20.7)	5 (1.9)	11 (4.4)	0

Metzger O et al. *N Engl J Med* 2026;394(5):451-62.

FDA Approves Palbociclib with Trastuzumab, with or without Pertuzumab, and ET as Maintenance Therapy for HR-Positive, HER2-Positive mBC

Press Release: June 24, 2026

"On June 24, 2026, the Food and Drug Administration approved palbociclib in combination with trastuzumab, with or without pertuzumab, and endocrine therapy for the maintenance treatment of adults with HR-positive, HER2-positive locally advanced or metastatic breast cancer following induction treatment.

Efficacy was evaluated in PATINA (NCT02947685), a randomized, open-label trial in 518 patients with HR-positive, HER2-positive locally advanced or metastatic breast cancer who had no evidence of disease progression after induction treatment with a taxane and trastuzumab, with or without pertuzumab, for their advanced disease. Patients were randomized (1:1) to receive either palbociclib with trastuzumab, with or without pertuzumab, and endocrine therapy (fulvestrant or an aromatase inhibitor [anastrozole, letrozole, or exemestane]) or trastuzumab, with or without pertuzumab, and endocrine therapy alone. Patients received treatment until disease progression or unacceptable toxicity.

The palbociclib prescribing information includes warnings and precautions for neutropenia, interstitial lung disease/pneumonitis, and embryo-fetal toxicity."

https://www.fda.gov/drugs/resources-information-approved-drugs/fda-approves-palbociclib-trastuzumab-or-without-pertuzumab-and-endocrine-therapy-maintenance

SAN ANTONIO BREAST CANCER SYMPOSIUM®
UT Health San Antonio Mays Cancer Center
AACR American Association for Cancer Research
DECEMBER 9–12, 2025
HENRY B. GONZALEZ CONVENTION CENTER • SAN ANTONIO, TX

Central Nervous System Outcomes from the Phase III PATINA Trial (AFT-38)

Otto Metzger, MD
Medical Oncology, Dana-Farber Cancer Institute, Harvard Medical School, Boston, MA, USA

Abstract RF4-01

PATINA: Cumulative Incidence of CNS Progression or Death Among Patients without CNS Metastases at Baseline

	Palbociclib + anti-HER2 + ET (n = 250)	Anti-HER2 + ET (n = 248)
CNS PFS event (n)	35	48
Death	3	1
CNS progression	32	47
Cumulative risk of CNS progression or death (%)		
12 months	4.6%	6.9%
24 months	9.7%	15.7%
36 months	13.0%	19.2%

Metzger O et al. SABCS 2025;Abstract RF4-01.

RTP RESEARCH TO PRACTICE

BERLIN 2025 ESMO congress

Health-Related Quality of Life From the PATINA Trial (AFT-38): Impact of Adding Palbociclib to HER2 and Endocrine Therapy After Induction in HR+/HER2+ Metastatic Breast Cancer

I. Vaz-Luis[1], G. Mazza[2], J. Gligorov[3], E. Lim[4], E. Ciruelos[5], S. Loibl[6], A. DeMichele[7], B. Fruth[8], X.González Farre[9], P. Francis[10], F. Lynce[11], J. Chien[12], S. Delaloge[13], K. Miller[14], E. Winer[15], S.Mandrekar[16], S. Goel[17], L. Carey[18], A.H. Partridge[19], O. Metzger[20]

October 20th, 2025

[1]Department of Medical Oncology, Institut Gustave Roussy, Villejuif, France, [2]Biostatistics, Alliance Foundation Trials (AFT) Statistics and Data Center, Mayo Clinic, Scottsdale, AZ, United States of America, [3]Oncologie Médicale, UCBG; Tenon Hospital IUC AP-HP Sorbonne Université, Paris, France, [4]Medical Oncology, St. Vincent's Hospital; Garvan Institute of Medical Research, Sydney, Australia, [5]Medical Oncology, Hospital Universitario 12 de Octubre, Madrid, Spain, [6]Medicine and Research Dept., German Breast Group(GBG), Neu-Isenburg, Germany, [7]Hemato-Oncology Dept., University of Pennsylvania, Abramson Cancer Center, Philadelphia, PA, United States of America, [8]Biostatistics, Alliance Foundation Trials (AFT) Statistics and Data Center, Mayo Clinic, Scottsdale, AZ, USA, Rochester, United States of America, [9]Medical Oncology, Hospital Universitari General de Catalunya, Barcelona, Spain, [10]MedicalOncology Department, Peter MacCallum Cancer Center, Melbourne, Australia, [11]Breast Medical Oncology Dept., Dana Farber Cancer Institute, Boston, United States of America, [12]Breast Oncology, UCSF - University of California San Francisco, San Francisco, United States of America, [13]Breast Oncology Department, Institut Gustave Roussy, Villejuif, France, [14]Hematology and Oncology Department, Indiana University Simon Comprehensive Cancer Center, Indianapolis, IN, United States of America, [15]Medical Oncology, Yale University School of Medicine - Yale Cancer Center, New Haven, United States of America, [16]Biostatistics, Alliance Foundation (AFT), Boston, United States of America, [17]Cancer Research Department, Peter MacCallum Cancer Centre, Melbourne, Australia, [18]Medicine -Hematology/Oncology Dept., University of North Carolina (UNC) Lineberger Comprehensive Cancer Center, Chapel Hill, NC, United States of America, [19]Medical Oncology, Dana Farber Cancer Institute, Boston, United States of America, [20]Breast Oncology Department, Dana-Farber Cancer Institute, Boston, United States of America

PATINA: PRO Outcomes and Analysis

Primary PRO outcomes

- Patient-reported time to first symptom progression or death was defined as a single timepoint of ≥ 5-point worsening since baseline on the FACT-B TOI or death due to any cause, whichever occurred first.
- Definitive symptom progression or death was also analyzed ad hoc.
  - Patient-reported time to definitive symptom progression or death was defined as sustained deterioration of ≥ 5-point since baseline on the FACT-B TOI or death due to any cause, whichever occurred first.*

Secondary PRO outcomes

- Patient-reported HRQoL as assessed by FACT-B.
- General health status as assessed by EQ-5D-5L index values, VAS

Statistical Analyses

- Time to symptom progression was compared with log-rank test; Kaplan–Meier medians, 95% CIs, and hazard ratios.
- Mean differences between baseline and EOT and between arms (FACT-B and EQ-5D-5L) were evaluated with mixed-effects models including time, arm, and interaction.

PRO measures completion rates

Treatment arm, n/N (%)	Baseline	Year 1	Year 2	Year 3
Palbociclib + Anti-HER2 + ET	248/261 (95.0)	187/218 (85.8)	140/156 (89.7)	106/119 (89.1)
Anti-HER2 + ET	239/256 (93.4)	152/180 (84.4)	113/129 (87.6)	80/99 (80.8)

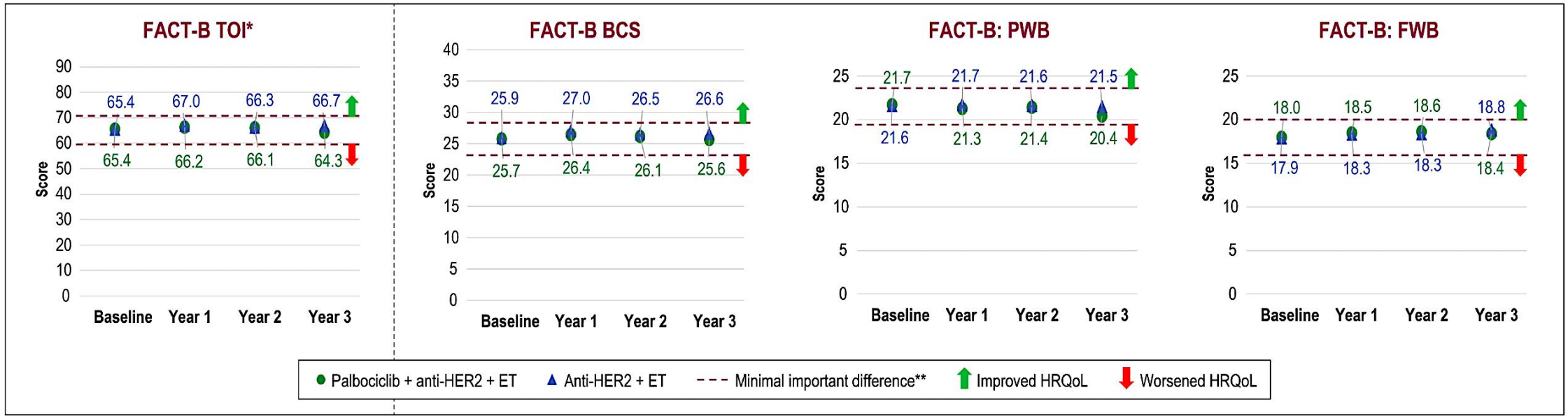
*The patient experiences a ≥ 5-point worsening since baseline on the FACT-B TOI that does not subsequently improve (to < 5-point worsening since baseline) until the final FACT-B assessment available for the patient OR the patient dies due to any cause.

BCS, Breast Cancer Subscale; CI, confidence interval; EOT, end of treatment; EQ-5D-5L, EuroQol 5D 5-Level questionnaire; ET, endocrine therapy; FACT-B, Functional Assessment of Cancer Therapy-Breast; FACT-G, Functional Assessment of Cancer Therapy-General; FACT-B TOI, FACT-B Trial Outcome Index; HER2, human epidermal growth factor receptor 2; HRQoL, health-related quality of life; PRO, patient-reported outcome; VAS, visual analogue scale.

Vaz-Luis I et al. ESMO 2025;Abstract 485MO.

PATINA: HRQoL Scores

FACT-B



HRQoL showed stability from baseline over time with **no significant or clinically meaningful differences** between treatment arms.

Global health status from EQ-5D-5L showed a similar pattern with **no significant or clinically meaningful differences**^ between treatment arms.

*Minimal important differences: FACT-B TOI (5 points); FACT-B Subscales (2 points); BCS (2 points).[1]

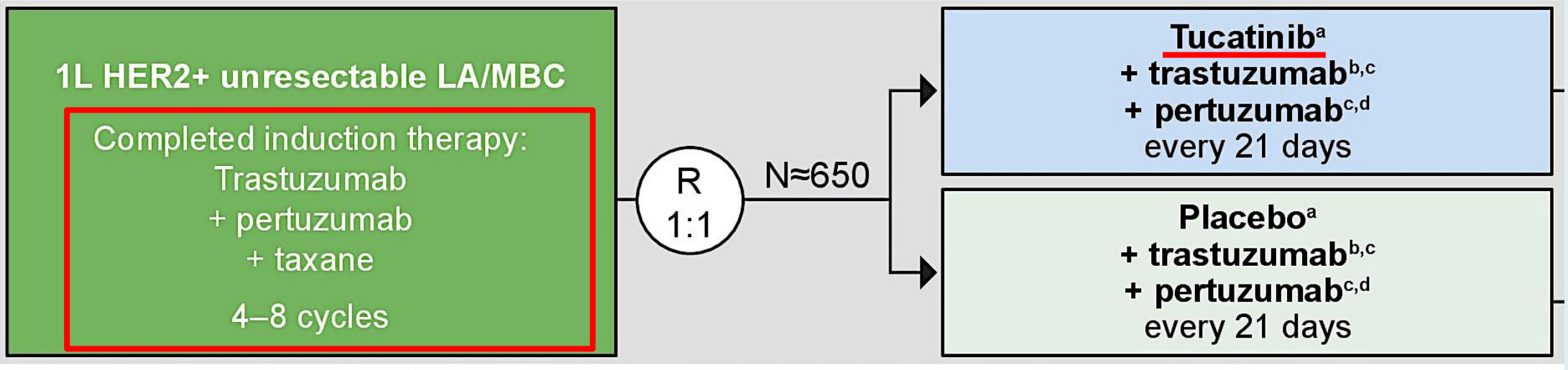
^Data not shown

BCS, Breast Cancer Subscale; EQ-5D, EuroQol 5 Dimension; ET, endocrine therapy; FACT-B TOI, Functional Assessment of Cancer Therapy-Breast Trial Outcome Index; FWB, Functional well-being; HER2, human epidermal growth factor receptor 2; HRQoL, health-related quality of life; PWB, Physical well-being.

Vaz-Luis I et al. ESMO 2025;Abstract 485MO.

Phase III HER2CLIMB-05 Trial Maintenance Regimen

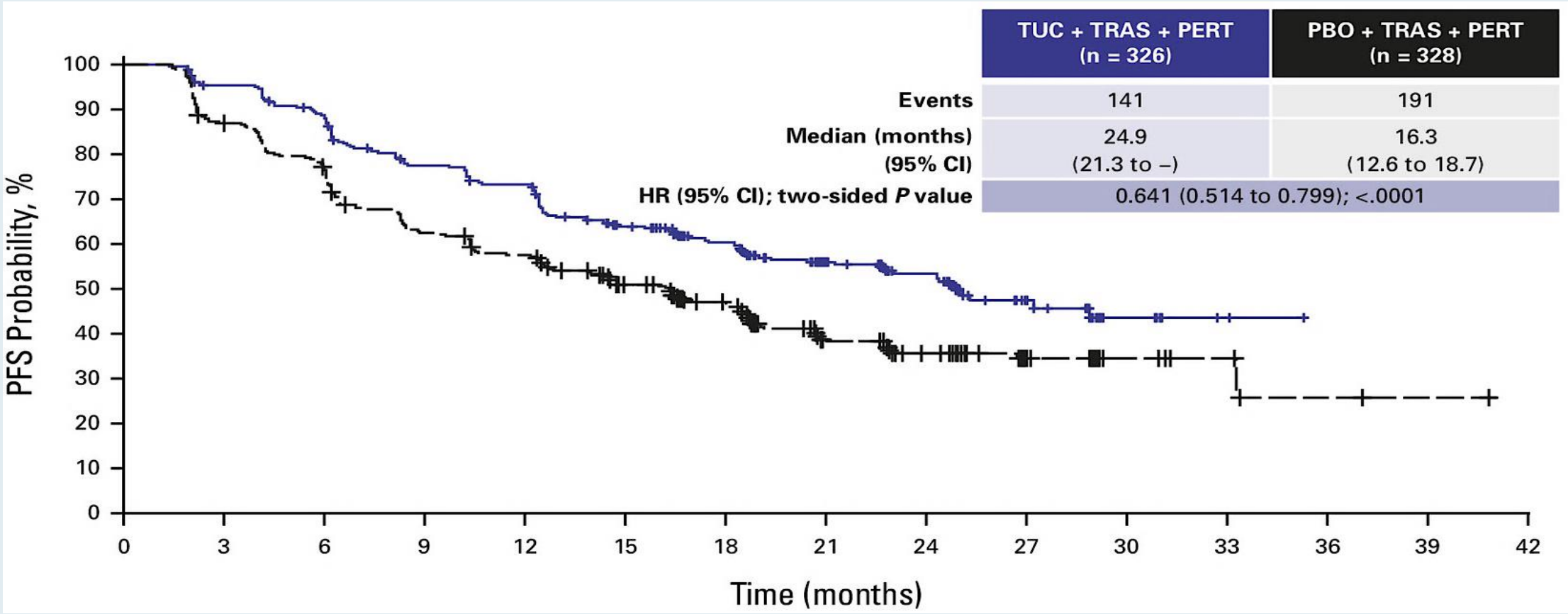
Tested addition of tucatinib to maintenance HP
after induction chemotherapy + HP without disease progression



(45% of patients with triple-positive disease also received ET)

Dieras V et al. *J Clin Oncol* 2025 December 10;44(17):1597-607.

Phase III HER2CLIMB-05: Investigator-Assessed PFS (Intention-to-Treat Population)



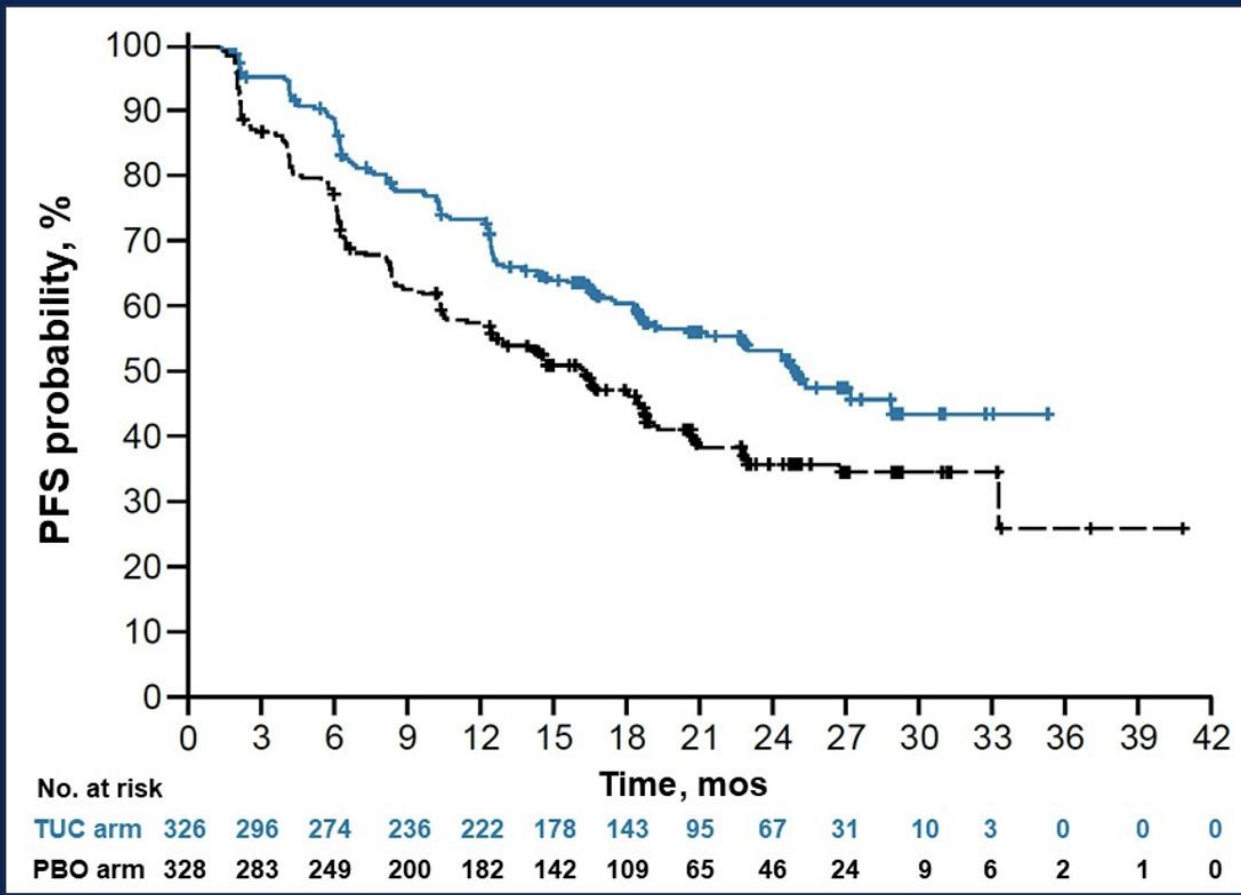
TUC = tucatinib; TRAS = trastuzumab; PERT = pertuzumab; PBO = placebo

PFS ~25 mo <u>regardless of HR status</u>

Toxicity as expected (more GI, transaminase with tucatinib added)

Dieras V et al. *J Clin Oncol* 2025 December 10;44(17):1597-607.

HER2CLIMB-05: Progression-Free Survival (PFS) in the Overall Population



	TUC + HP (n = 326)	PBO + HP (n = 328)
Events	141	191
Median PFS, mos (95% CI)	**24.9 (21.3–NE)**	**16.3 (12.6–18.7)**
HR (95% CI) *P*–value*	**0.641 (0.514–0.799); < 0.0001**	
	Δ of 8.6 months	
	n = 296	**n = 297**
cORR,† % (95% CI)	22.6 (18.0–27.8)	15.2 (11.3–19.7)
	n = 67	**n = 45**
Median DOR,† mos (95% CI)	20.9 (16.4–NE)	16.9 (12.3–NE)

In the primary HER2CLIMB-05 analysis with a median follow-up of ~23 months, addition of TUC to 1L maintenance HP vs control treatment extended PFS by nearly 9 months.[1]

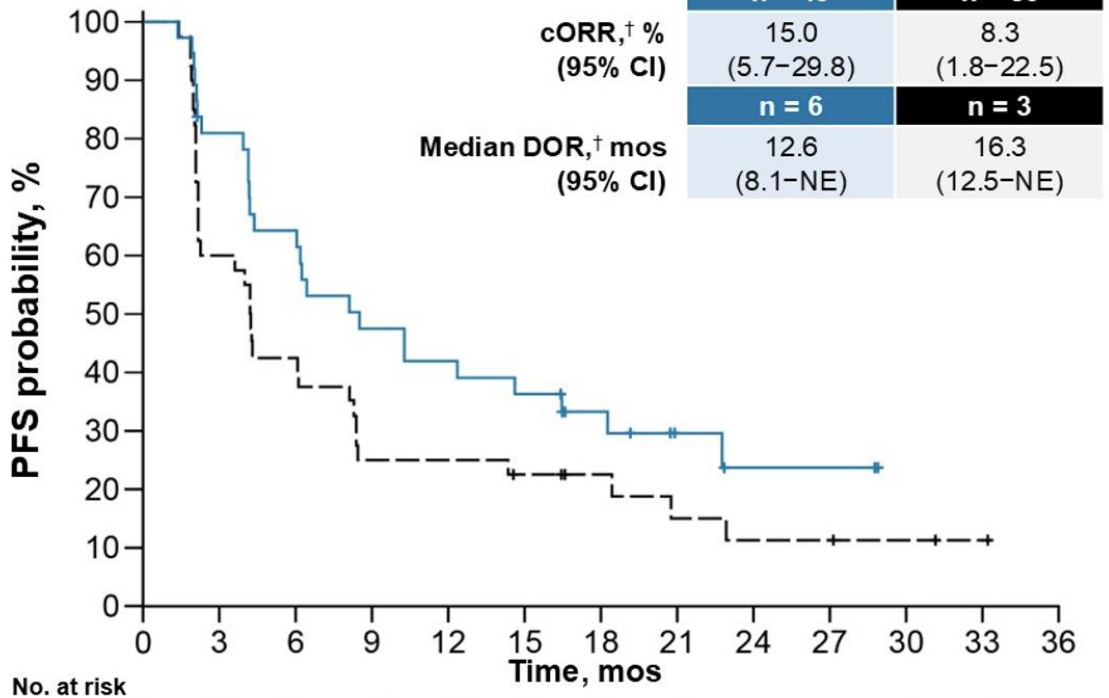
TUC = tucatinib; HP = trastuzumab and pertuzumab; PBO = placebo; cORR = confirmed objective response rate; DOR = duration of response; NE = not estimable

Hamilton E et al. ASCO 2026;Abstract 1005.

HER2CLIMB-05: PFS by Brain Metastases (BM) at Baseline

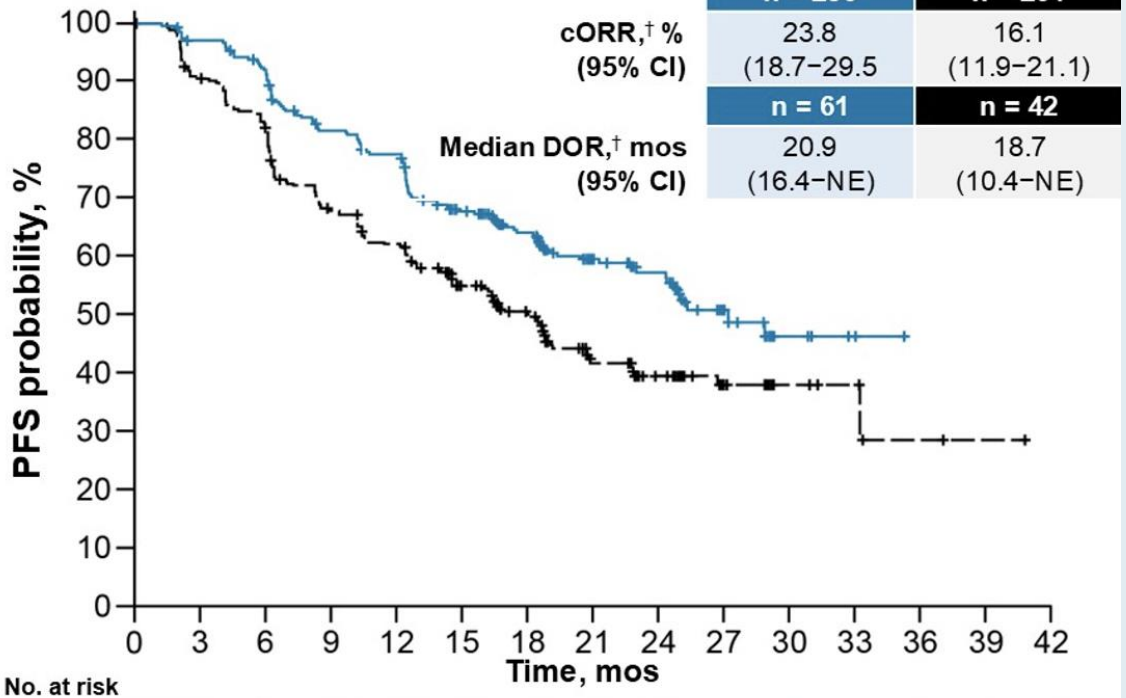
With baseline BM (12.4%)

	TUC + HP (n = 41)	PBO + HP (n = 40)
Events	26	34
Median PFS, mos (95% CI)	8.5 (4.2–16.5)	4.2 (2.2–8.1)
HR (95% CI); *P*–value*	0.640 (0.373–1.097); 0.1058	
	Δ of 4.3 months	
	n = 40	n = 36
cORR,† % (95% CI)	15.0 (5.7–29.8)	8.3 (1.8–22.5)
	n = 6	n = 3
Median DOR,† mos (95% CI)	12.6 (8.1–NE)	16.3 (12.5–NE)



Without baseline BM (87.6%)

	TUC + HP (n = 285)	PBO + HP (n = 288)
Events	115	157
Median PFS, mos (95% CI)	27.2 (24.3–NE)	18.1 (14.8–20.7)
HR (95% CI); *P*–value*	0.640 (0.503–0.816); 0.0003	
	Δ of 9.1 months	
	n = 256	n = 261
cORR,† % (95% CI)	23.8 (18.7–29.5	16.1 (11.9–21.1)
	n = 61	n = 42
Median DOR,† mos (95% CI)	20.9 (16.4–NE)	18.7 (10.4–NE)



Hamilton E et al. ASCO 2026;Abstract 1005.

Tucatinib combined with trastuzumab and pertuzumab as first-line maintenance therapy for HER2+ metastatic breast cancer: An in-depth safety analysis of HER2CLIMB-05

Dieras VC et al. ASCO 2026;Abstract 1042.

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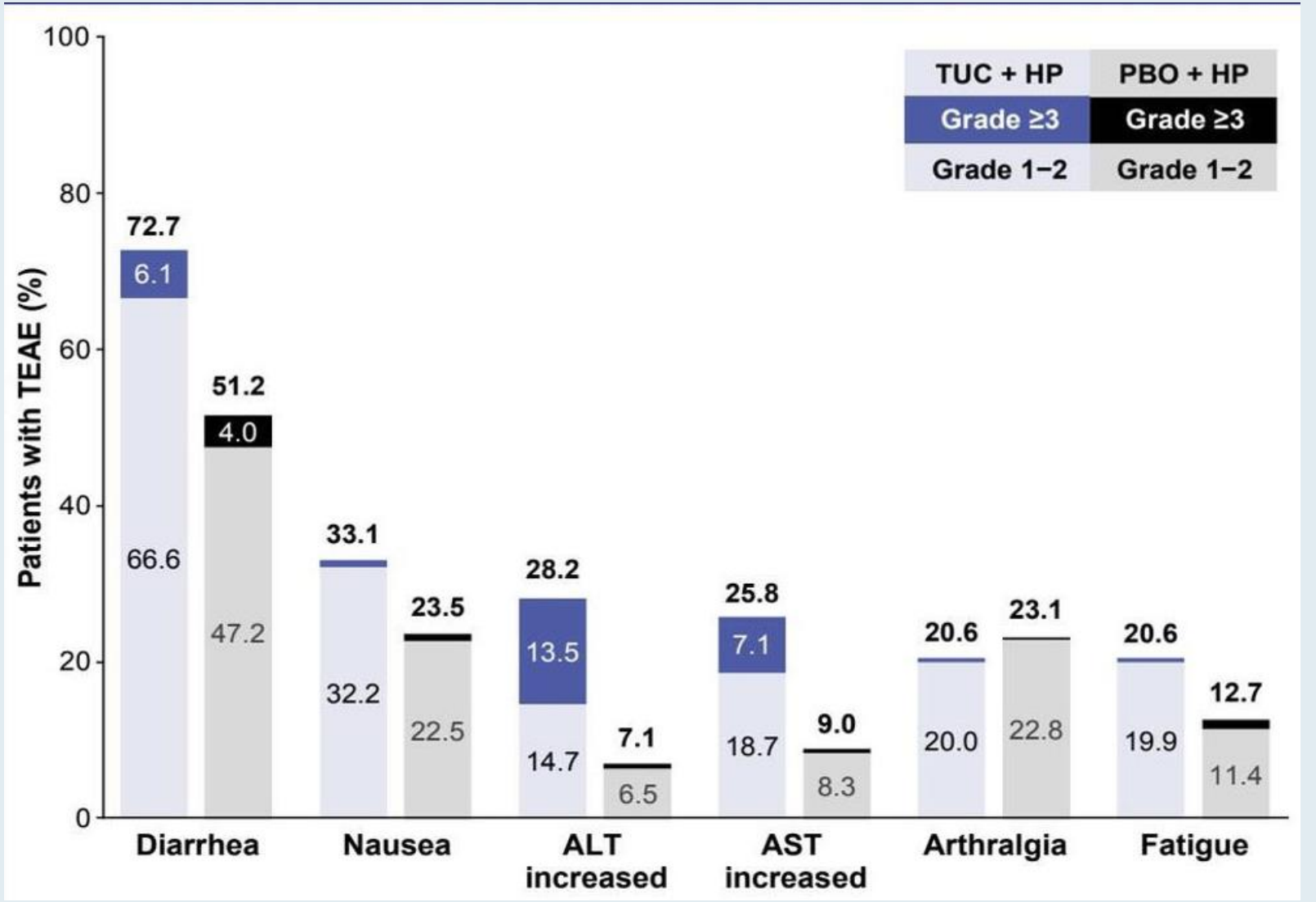
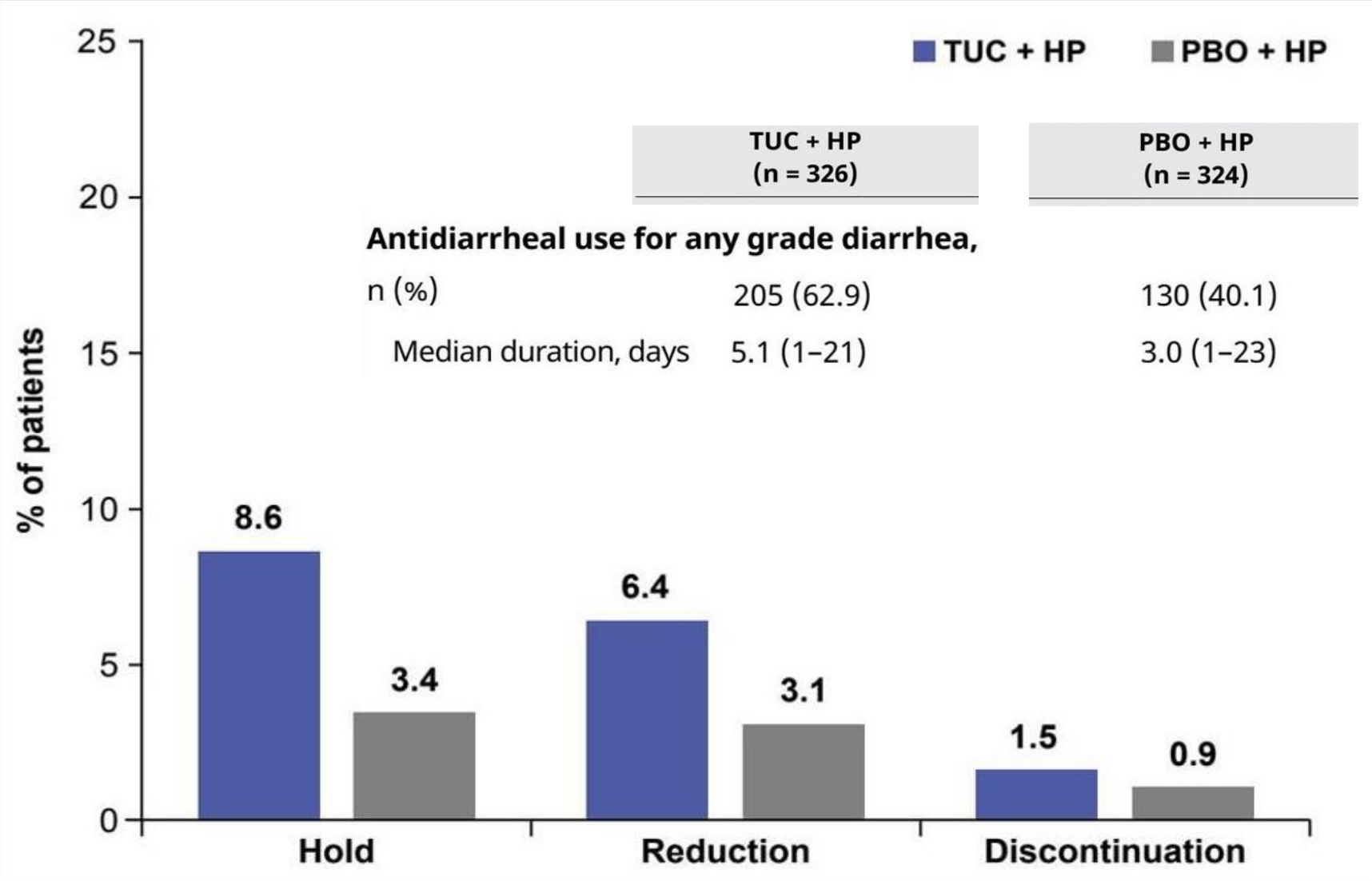
HER2CLIMB-05: Safety Overview



TEAE = treatment-emergent adverse event; ALT = alanine transaminase; AST = aspartate transferase

Dieras VC et al. ASCO 2026;Abstract 1042.

HER2CLIMB-05: Dose Modifications Due to Diarrhea



	TUC + HP (n = 326)	PBO + HP (n = 324)
Antidiarrheal use for any grade diarrhea,		
n (%)	205 (62.9)	130 (40.1)
Median duration, days	5.1 (1–21)	3.0 (1–23)

Dieras VC et al. ASCO 2026;Abstract 1042.

Treatment Considerations for First-Line HER2-Positive mBC

- **Conventional treatment is induction chemotherapy, including antibody-drug conjugates, with anti-HER2 therapy before a nonchemotherapy maintenance regimen.**
- **Nonchemotherapy regimens are now markedly more effective, calling into question the role of induction chemotherapy.**
- **Options:**
  - **Any HR status: Tucatinib + HP regardless of HR status.**
  - **Triple positive: ET + CDK4/6 inhibitor + HP.**
  - **PATINA outcomes are so favorable and molecular phenotype so strongly luminal that AI + palbociclib + HP may be favored for triple-positive disease.**

Agenda

Introduction: HER2 History

Module 1: Cases from the GMO Survey

Module 2: Biology and Selection of First-Line Therapy for HR-Positive, HER2-Positive Metastatic Breast Cancer (mBC) — Dr Mahtani

Module 3: Faculty Case Presentations

Module 4: Patterns of Care Survey — Part 1

Module 5: Optimizing the Use of Up-Front Maintenance Therapy for HER2-Positive mBC — Dr Carey

Module 6: Faculty Case Presentations

Module 7: Patterns of Care Survey — Part 2

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Dr Mahtani: Case

- 92yo with de novo triple-positive MBC
- PMHx: Osteopenia, HTN
- Underwent screening mammo in July 2024: right breast asymmetry noted, US confirmed 6mm suspicious lesion, no abnormal axillary nodes. Patient declined the suggested biopsy.
- May 2026: presented with painful right breast mass with nipple retraction, skin thickening. Repeat imaging confirmed 5.9cm mass with multiple suspicious axillary nodes.
- Biopsy: IDC, ER 80%, PR 60%, HER2 3+

Dr Mahtani: Case (Cont)

- PET: Multiple focal areas of abnormal uptake within the liver. Largest lesion 3.5cm. Right breast mass noted with abnormal uptake, multiple FDG avid axillary, subpectoral, mediastinal nodes
- Liver biopsy: confirmed mBC, triple positive; AST/ALT in the 200s
- Patient/family declined chemotherapy, consented to HP and “anything oral”
- Started HP, letrozole, palbociclib with initial improvement on exam after 3 months, falling LFTs (pending repeat imaging)
- Excellent tolerance to therapy

Dr Carey: Case

- 63 yo woman with triple-positive mBC in 2025 after an 8-year relapse-free interval
- Exemestane + palbociclib + HP + zoledronic acid
  - Fatigue and GI symptoms (diarrhea), declined dose reduction
  - Palliative RT at outset (spine, left pelvis) improved symptoms

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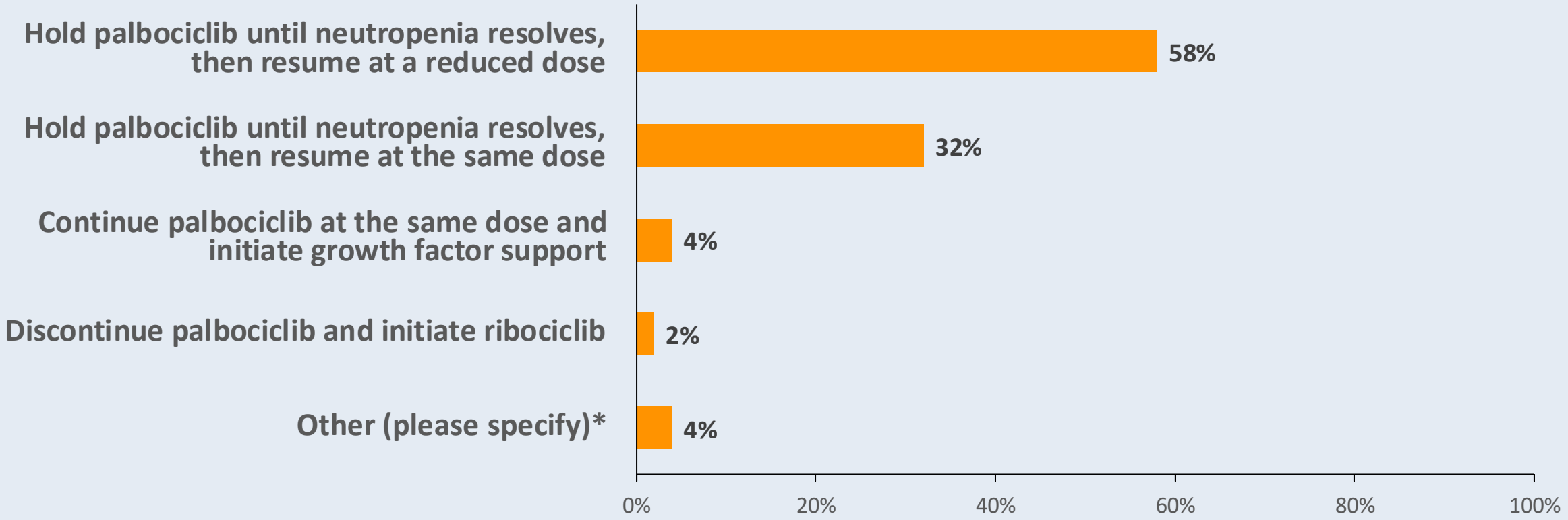
Module 7: Patterns of Care Survey — Part 2

A 65-year-old patient with HR-positive, HER2-positive mBC receives 6 cycles of THP as first-line induction therapy followed by HP/ET/palbociclib but develops asymptomatic moderate neutropenia (ANC = 750/µL) while receiving maintenance therapy. Regulatory and reimbursement issues aside, what would be your next course of action?



* ANC can run low on palbo but does not appear to increase infection, I would use lower threshold such as ANC < 500; Reduce dose and also change schedule

Survey of US-based general medical oncologists

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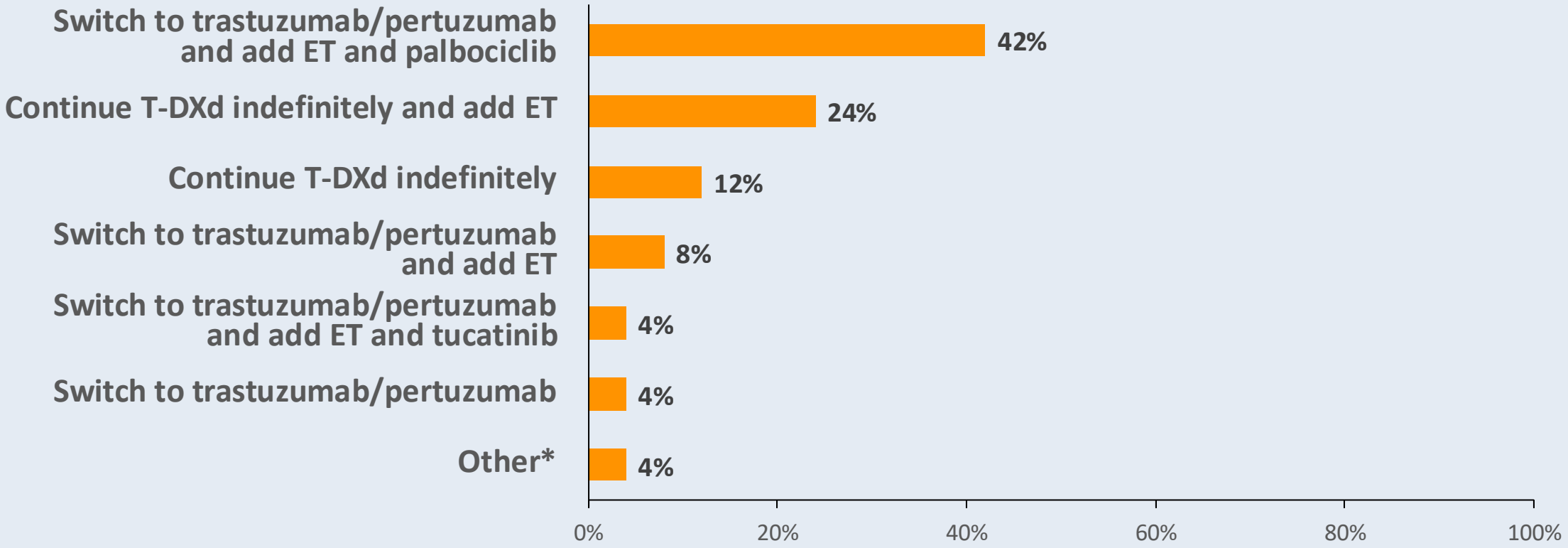
A patient with de novo HR-positive, HER2-positive mBC is receiving first-line T-DXd and pertuzumab with response and reasonably good tolerability. Regulatory and reimbursement issues aside, what would be your most likely approach to maintenance therapy?



* AI alone plus or minus palbociclib; Depends on patient age, comorbidities, burden of disease and degree of response

Survey of US-based general medical oncologists

RTP RESEARCH TO PRACTICE

Year in Review: Clinical Investigator Perspectives on the Most Relevant New Datasets and Advances in Oncology

PI3K/AKT/mTOR Pathway in HR-Positive Metastatic Breast Cancer

A CME/MOC-Accredited Live Webinar

Wednesday, July 15, 2026

5:00 PM – 6:00 PM ET

Faculty

Virginia Kaklamani, MD, DSc

Hope S Rugo, MD

Moderator

Neil Love, MD

RTP Year in Review 2026

Thank you for joining us!

Please take a moment to complete the survey currently up on Zoom. Your feedback is very important to us. The survey will remain open for 5 minutes after the meeting ends.

Information on how to obtain CME and ABIM MOC credit is provided in the Zoom chat room. Attendees will also receive an email in 1 to 3 business days with these instructions.

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