What Clinicians Want to Know: First-Line and Maintenance Therapy for Patients with ER-Positive, HER2-Positive Metastatic Breast Cancer

A CME/MOC-Accredited Live Webinar

Wednesday, March 18, 2026

5:00 PM – 6:00 PM ET

Faculty

Virginia F Borges, MD, MMSc
Ian E Krop, MD, PhD

Moderator

Neil Love, MD

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Faculty

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Professor of Medicine with Tenure
Robert F and Patricia Young Connor Endowed Chair
in Young Women's Breast Cancer Research
Deputy Division Head, Medical Oncology
Co-Director, Diane O'Connor Thompson
Breast Center
Co-Director, Breast Cancer Research Program
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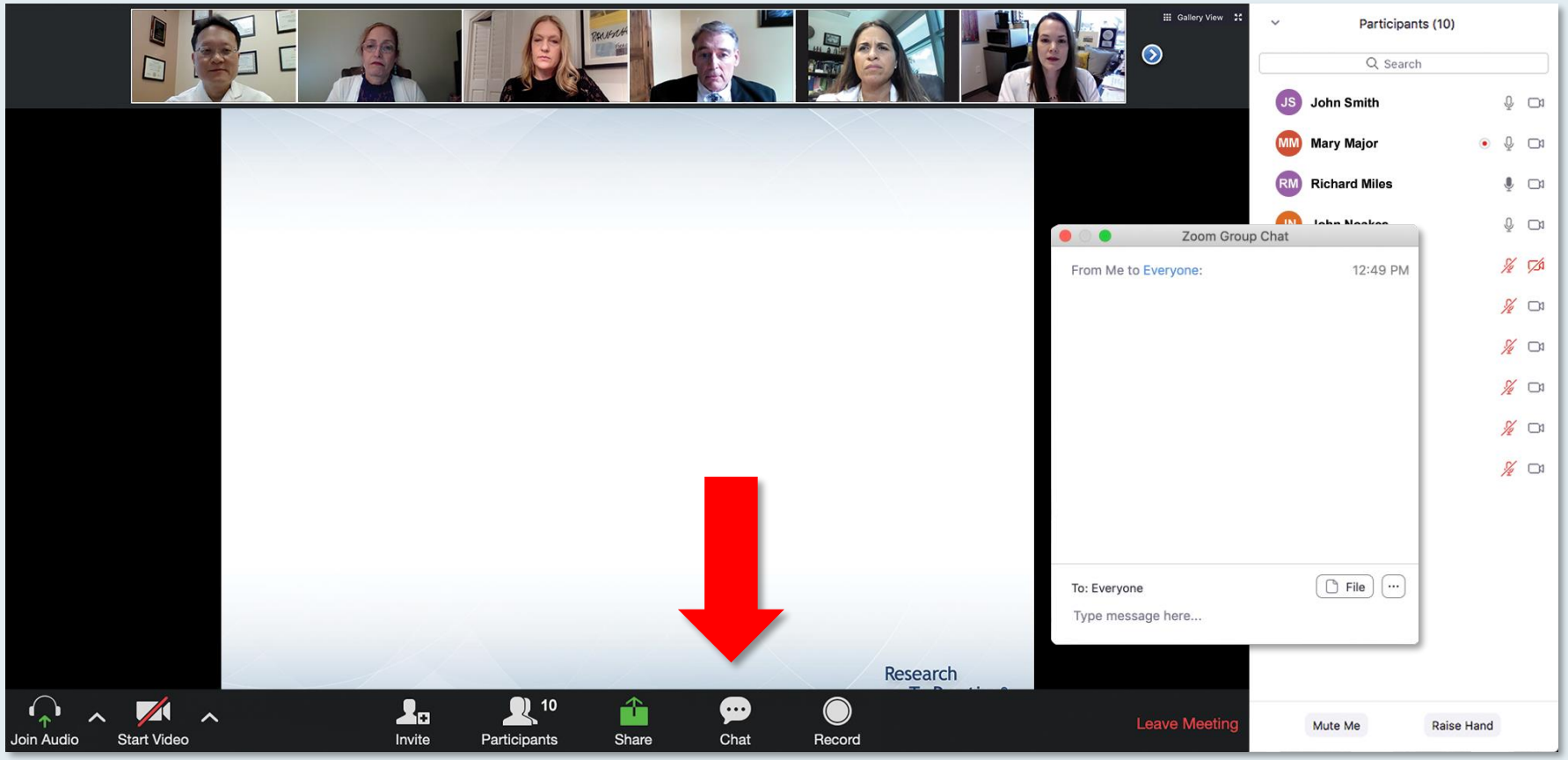

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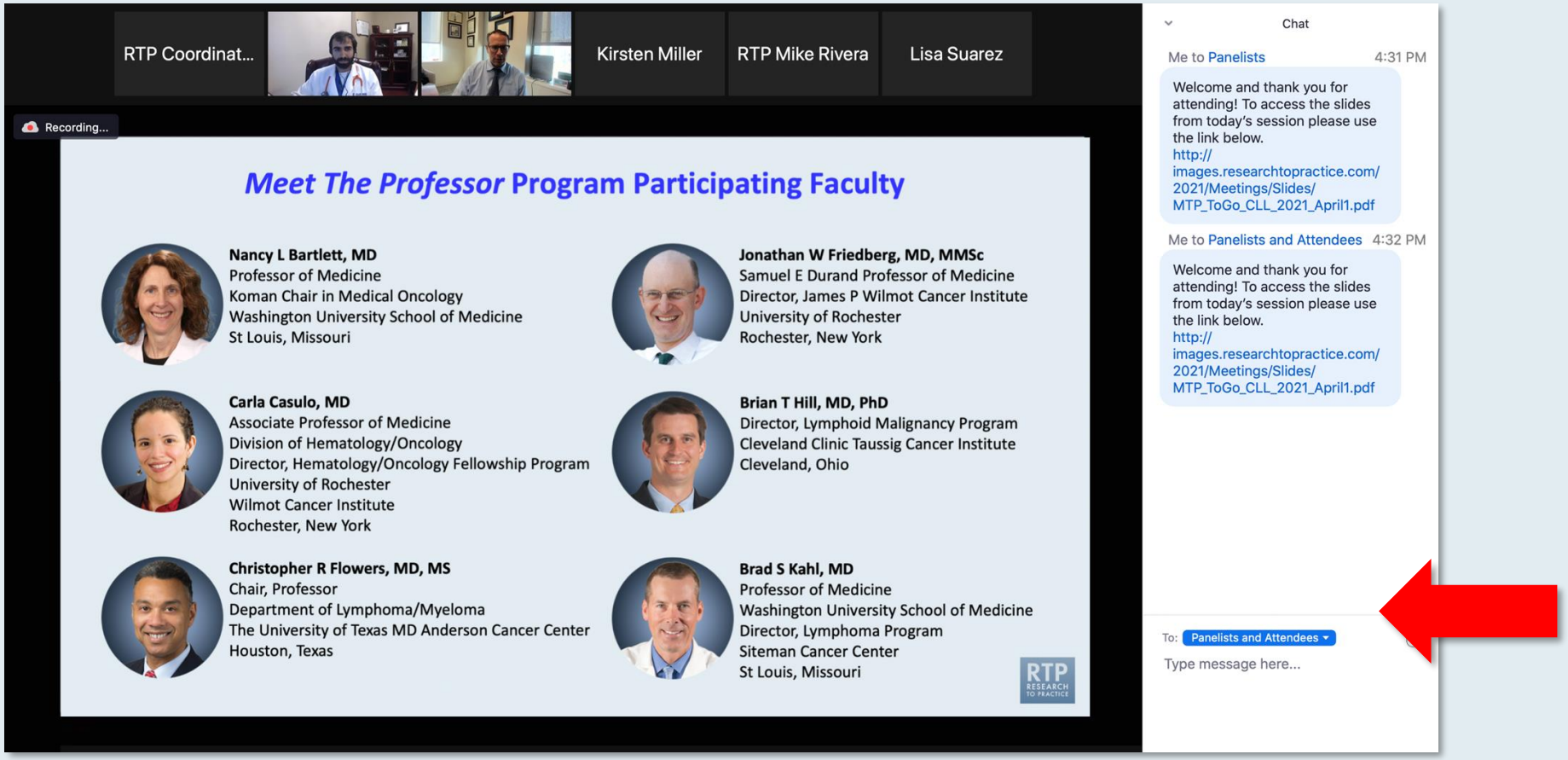

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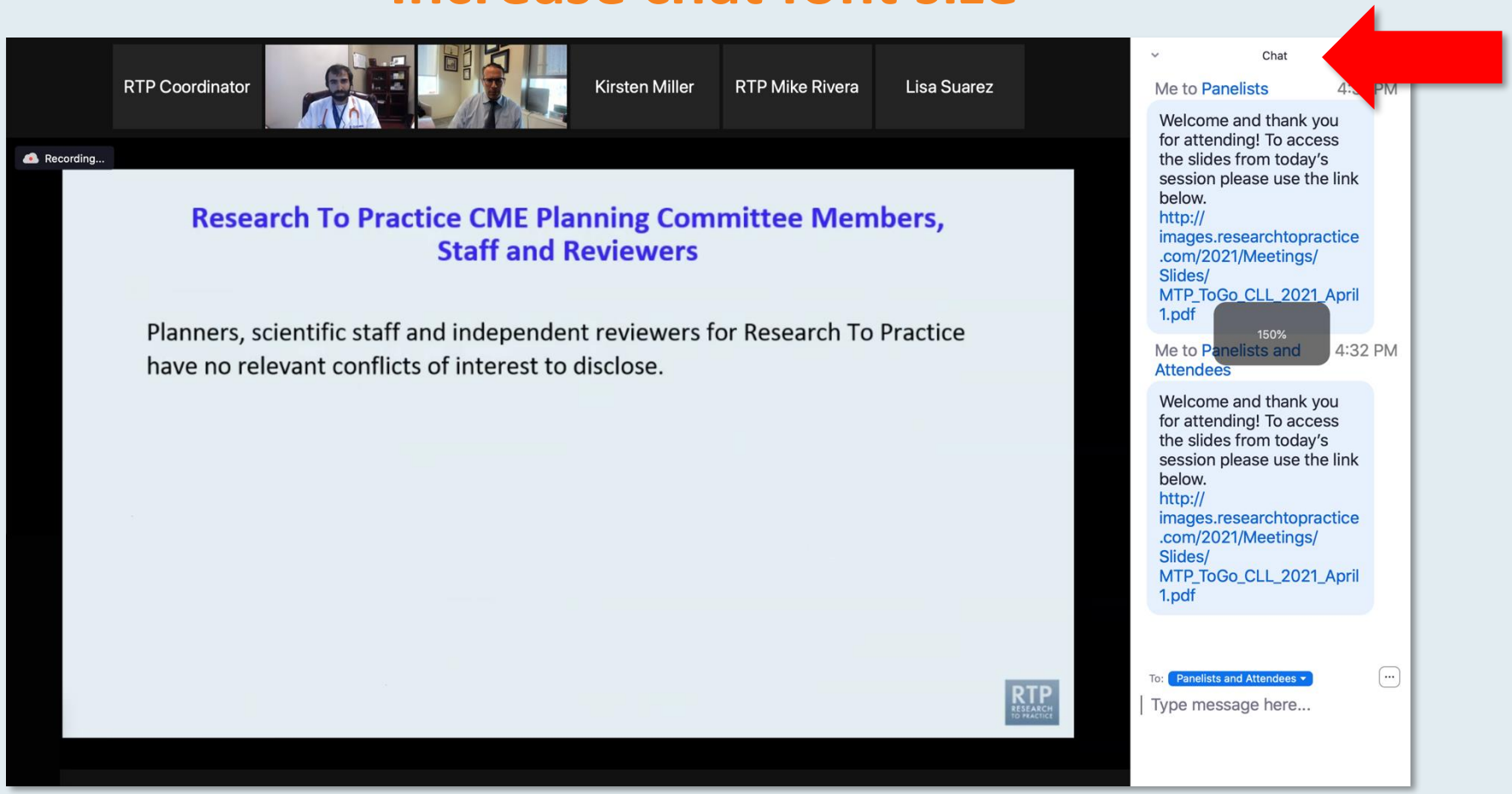

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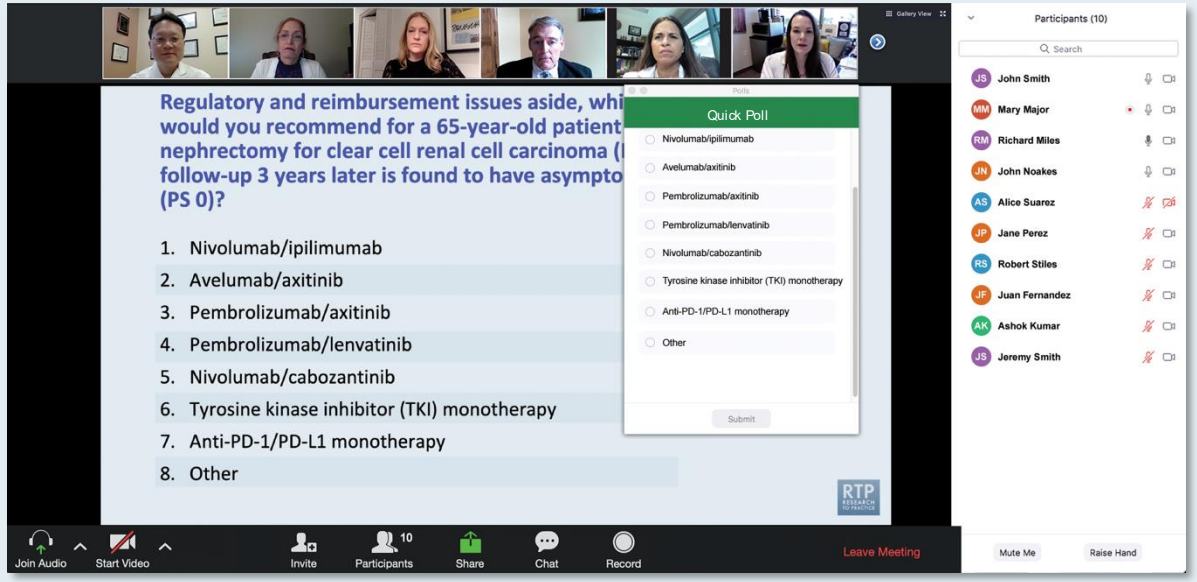

Endocrine-Based Therapy for HR-Positive Breast Cancer — Proceedings from a San Antonio 2025 Symposium Series

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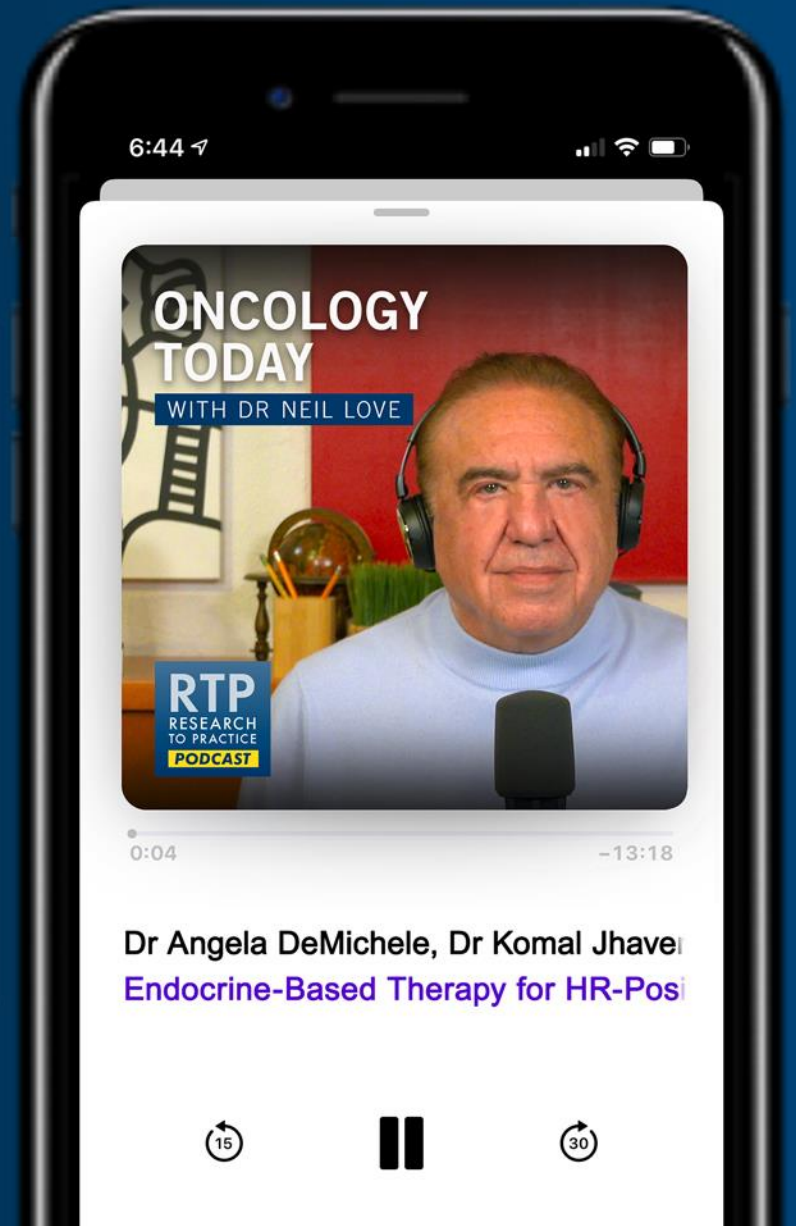

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Year in Review: Clinical Investigator Perspectives on the Most Relevant New Datasets and Advances in Oncology

Prostate Cancer

A CME/MOC-Accredited Live Webinar

Wednesday, March 25, 2026
5:00 PM – 6:00 PM ET

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Moderator

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Erica Mayer, MD, MPH, FASCO

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EGFR-Mutant Non-Small Cell Lung Cancer

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Tuesday, April 7, 2026
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Optimizing Treatment for Patients with Relapsed/Refractory Chronic Lymphocytic Leukemia

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

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A Multitumor CME/MOC-, NCPD- and ACPE-Accredited Educational Conference Developed in Partnership with Florida Cancer Specialists & Research Institute

Friday to Sunday, April 24 to 26, 2026

The Ritz-Carlton Orlando, Grande Lakes | Orlando, Florida

Moderated by Neil Love, MD

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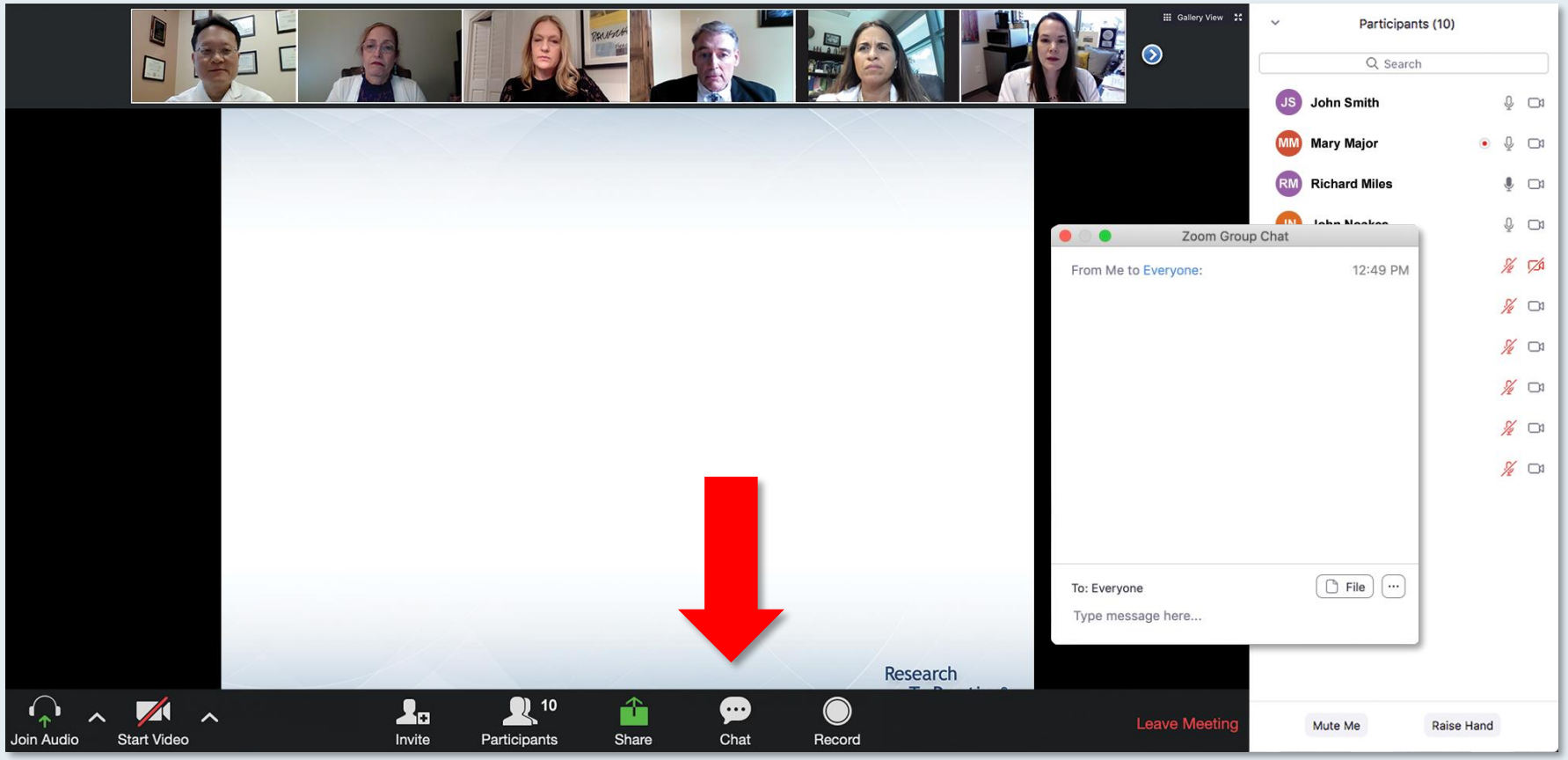

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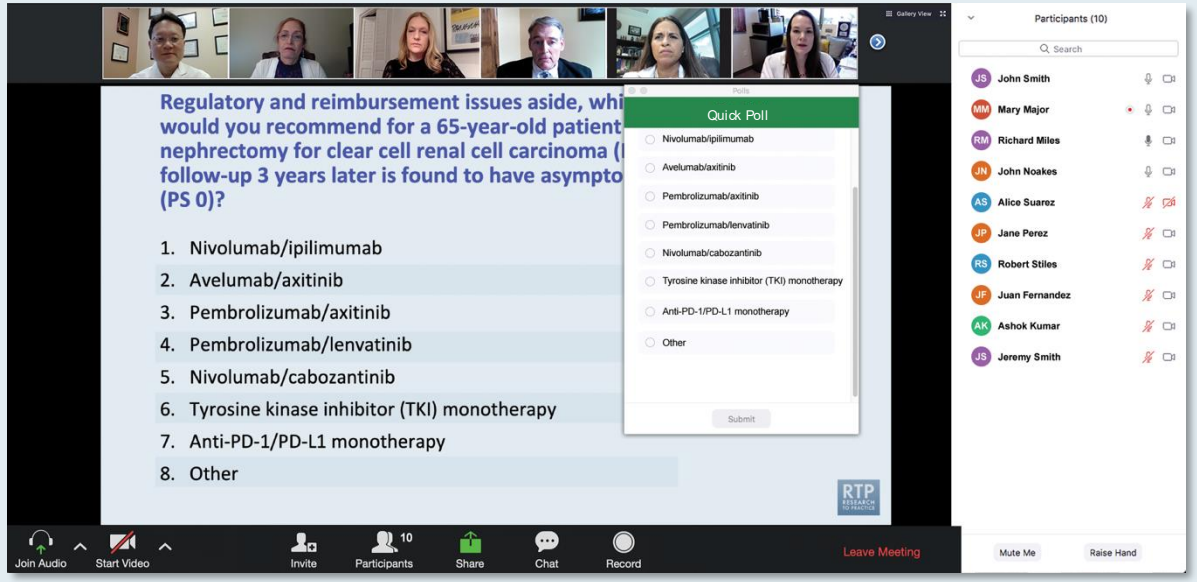

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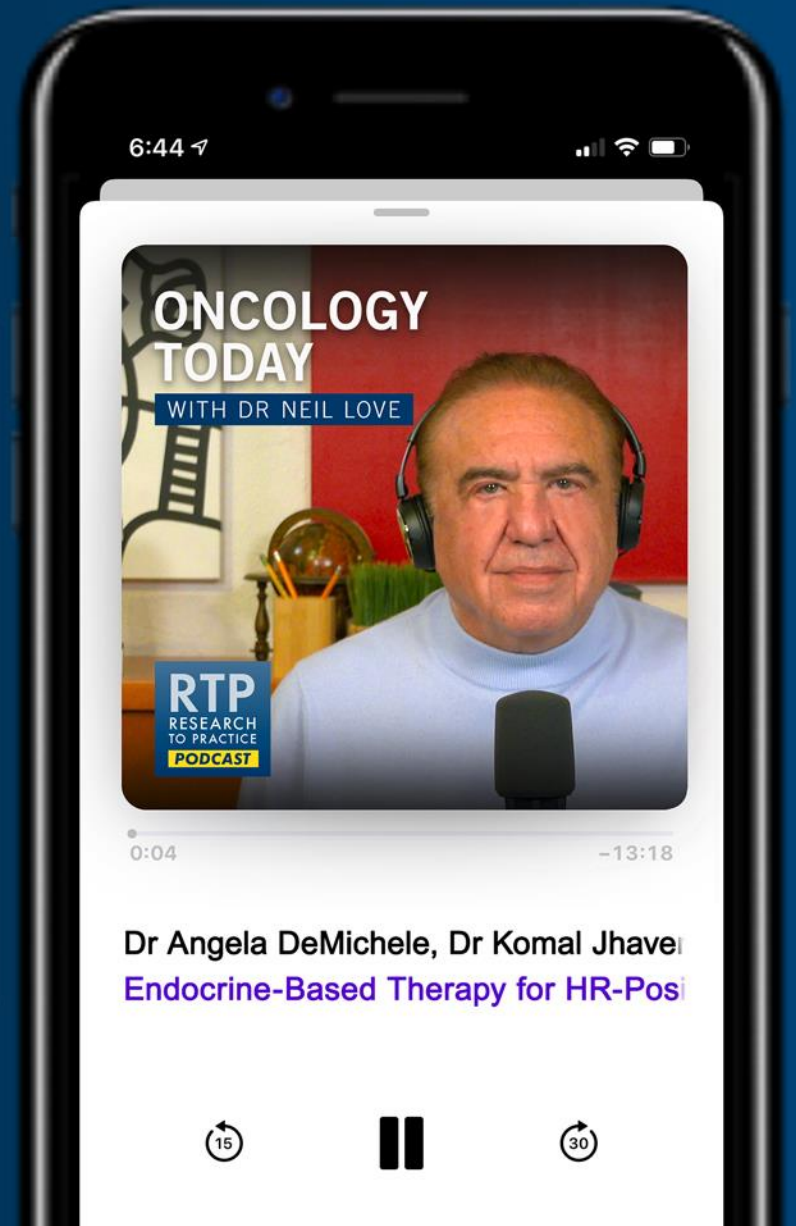

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Module 1: Cases from the GMO Survey

Module 2: First-Line Therapy for Metastatic HER2-Positive Disease

Module 3: Cases from the GMO Survey

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Module 4b: Maintenance Therapy for HR-Negative, HER2-Positive Disease

Module 5: Ongoing Clinical Trials Attempting to Address These Decisions

Module 6: Cases from the GMO Survey

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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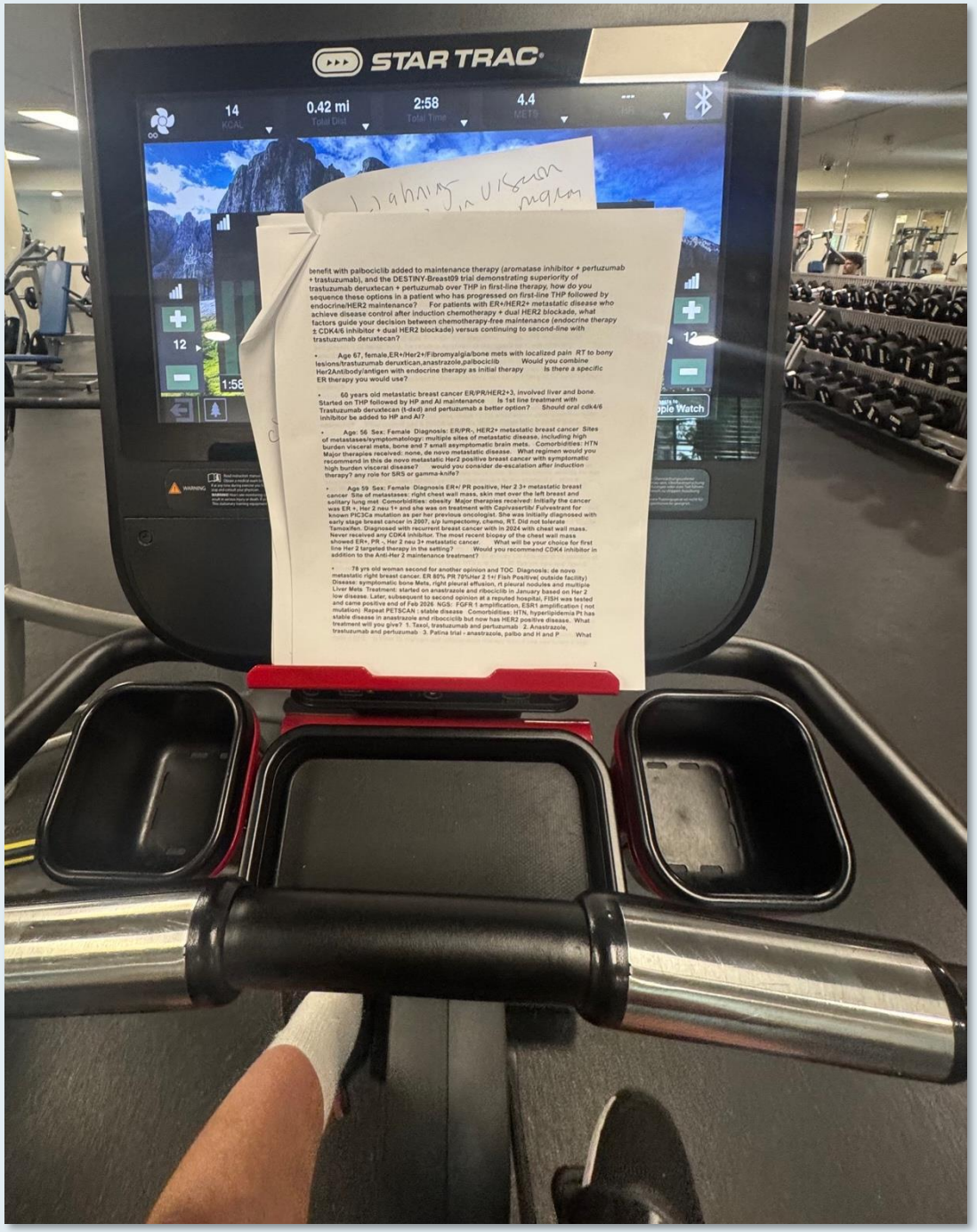
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benefit with palbociclib added to maintenance therapy (aromatase inhibitor + pertuzumab + trastuzumab), and the DESTINY-Breast09 trial demonstrating superiority of trastuzumab deruxtecan + pertuzumab over THP in first-line therapy, how do you sequence these options in a patient who has progressed on first-line THP followed by endocrine/HER2 maintenance? For patients with ER+/HER2+ metastatic disease who achieve disease control after induction chemotherapy + dual HER2 blockade, what factors guide your decision between chemotherapy-free maintenance (endocrine therapy ± CDK4/6 inhibitor + dual HER2 blockade) versus continuing to second-line with trastuzumab deruxtecan?
Age 67, female,ER+/Her2+/Fibromyalgia/bone mets with localized pain RT to bony lesions/trastuzumab deruxtican,anastrazole,palbociclib Would you combine Her2Antibody/antigen with endocrine therapy as initial therapy Is there a specific ER therapy you would use?
60 years old metastatic breast cancer ER/PR/HER2+3, involved liver and bone. Started on THP followed by HP and AI maintenance Is 1st line treatment with Trastuzumab deruxtecan (t-dxd) and pertuzumab a better option? Should oral cdk4/6 inhibitor be added to HP and AI?
Age: 56 Sex: Female Diagnosis: ER/PR-, HER2+ metastatic breast cancer Sites of metastases/symptomatology: multiple sites of metastatic disease, including high burden visceral mets, bone and 7 small asymptomatic brain mets. Comorbidities: HTN Major therapies received: none, de novo metastatic disease. What regimen would you recommend in this de novo metastatic Her2 positive breast cancer with symptomatic high burden visceral disease? would you consider de-escalation after induction therapy? any role for SRS or gamma-knife?
Age 59 Sex: Female Diagnosis ER+/ PR positive, Her 2 3+ metastatic breast cancer Site of metastases: right chest wall mass, skin met over the left breast and solitary lung met Comorbidities: obesity Major therapies received: Initially the cancer was ER +, Her 2 neu 1+ and she was on treatment with Capivasertib/ Fulvestrant for known PIC3Ca mutation as per her previous oncologist. She was initially diagnosed with early stage breast cancer in 2007, s/p lumpectomy, chemo, RT. Did not tolerate Tamoxifen. Diagnosed with recurrent breast cancer with in 2024 with chest wall mass. Never received any CDK4 inhibitor. The most recent biopsy of the chest wall mass showed ER+, PR -, Her 2 neu 3+ metastatic cancer. What will be your choice for first line Her 2 targeted therapy in the setting? Would you recommend CDK4 inhibitor in addition to the Anti-Her 2 maintenance treatment?
78 yrs old woman second for another opinion and TOC Diagnosis: de novo metastatic right breast cancer. ER 80% PR 70%Her 2 1+/ Fish Positive(outside facility) Disease: symptomatic bone Mets, right pleural effusion, rt pleural nodules and multiple Liver Mets Treatment: started on anastrazole and ribociclib in January based on Her 2 low disease. Later, subsequent to second opinion at a reputed hospital, FISH was tested and came positive end of Feb 2026. NGS: FGFR 1 amplification, ESR1 amplification (not mutation) Repeat PETSCAN : stable disease Comorbidities: HTN, hyperlipidemia Pt has stable disease in anastrazole and ribociclib but now has HER2 positive disease. What treatment will you give? 1. Taxol, trastuzumab and pertuzumab 2. Anastrazole, trastuzumab and pertuzumab 3. Patina trial - anastrazole, palbo and H and P What

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Review Article

CDK4/6 Inhibitors in HER2-positive Metastatic Breast Cancer

Hervé Bischoff, Thierry Petit

Abstract

HR +/HER2 + breast cancer (BC) represents a unique clinical entity distinct from HR−/HER2 + BC, with specific molecular characteristics and resistance mechanisms. The interaction between estrogen receptor (ER) and HER2 signaling pathways promotes tumor growth and therapeutic resistance, highlighting the need for tailored approaches. This review focuses on the clinical and molecular features of HR + /HER2 + metastatic BC, with an emphasis on recent data exploring the integration of CDK4/6 inhibitors (CDK4/6i) into anti-HER2 therapeutic strategies. Key findings from metastatic trials are summarized. HR + /HER2 + metastatic BC is characterized by a predominance of luminal molecular subtypes, associated with distinct patterns of metastatic spread and prolonged progression-free survival compared to nonluminal subtypes. Despite the efficacy of dual HER2 blockade, resistance remains a challenge, driven by crosstalk between ER and HER2 pathways. CDK4/6i disrupt the cell cycle at the G1/S checkpoint and have shown promise in overcoming resistance, inducing sustained senescence, and improving outcomes in luminal subtypes. Recent trials suggest that CDK4/6i may play a key role in maintenance therapy and chemotherapy-free regimens for selected patients with HR + /HER2 + metastatic BC. The integration of CDK4/6 inhibitors into anti-HER2 treatment strategies represents a promising approach to address the unique biology of HR + /HER2 + BC. Molecular profiling and personalized treatment strategies are essential to optimize patient outcomes and reduce unnecessary toxicity.

Clin Breast Cancer 2026;26(2):93-104.

Changes in Features of Triple-Positive Breast Cancer (TPBC) Compared to ER-Negative, HER2-Positive Disease

Late relapse (DFI ≥60 months) ↑

Bone-only metastases ↑

Median OS ↑

De novo metastatic disease ↓

Visceral metastases ↓

Grade 3 tumors ↓

Adapted from Bischoff et al. *Clin Cancer Breast* 2026;26(2):93-104.

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Questions About Biology and Therapeutic Implications

- How do you explain the interaction between the HER2 and ER pathways in normal tissue and in breast cancer (BC), and what potential synergies occur?
- What is known about the relative efficacy of anti-HER2 therapy in HR-positive versus HR-negative HER2-positive BC?
- Does this explain the differential effect of neratinib seen in the ExteNET trial?

Questions About Biology and Therapeutic Implications

- **What is known about the relative efficacy of endocrine therapy in HER2-positive versus HER2-negative, HR-positive BC?**
- **What outcomes have been reported with the use of CDK inhibitors in HER2-positive disease?**

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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

69 yo woman

- **Presents with a palpable left neck node 12/22.**
- **Biopsy: ER+HER2+ metastatic lobular cancer.**
- **No breast mass and mammo is negative; staging shows multiple bone mets and upper endoscopy reveals a gastric polyp containing lobular cancer.**
- **HP/paclitaxel and after 12 weeks switched to letrozole and palbociclib in June 2023. She remains well with no toxicity on maint subcut HP/palbo and letrozole with a stable bone scan. She continues zoledronic acid for her bone mets.**

Have you seen lobular cancers metastasize to the stomach?
After a negative endoscopy in 5/23, would you repeat any further endoscopies?

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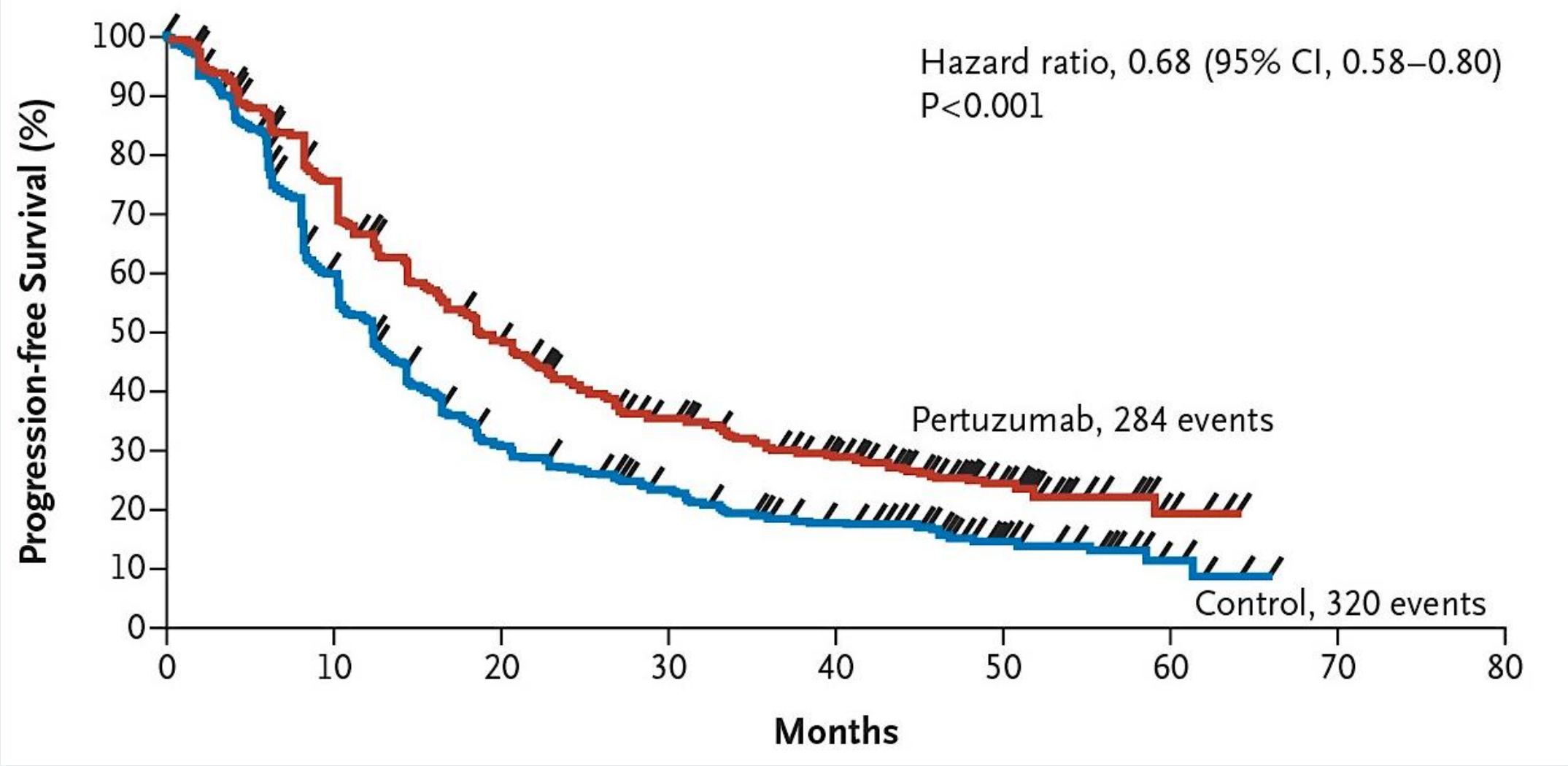
Questions About First Line Induction Treatment

- **What is your usual first-line therapy for metastatic HER2-positive disease?**
- **What duration of treatment do you usually employ, assuming the patient has acceptable treatment tolerance?**
- **How do you factor in prior adjuvant and/or neoadjuvant anti-HER2 therapy?**

Questions About First Line Induction Treatment

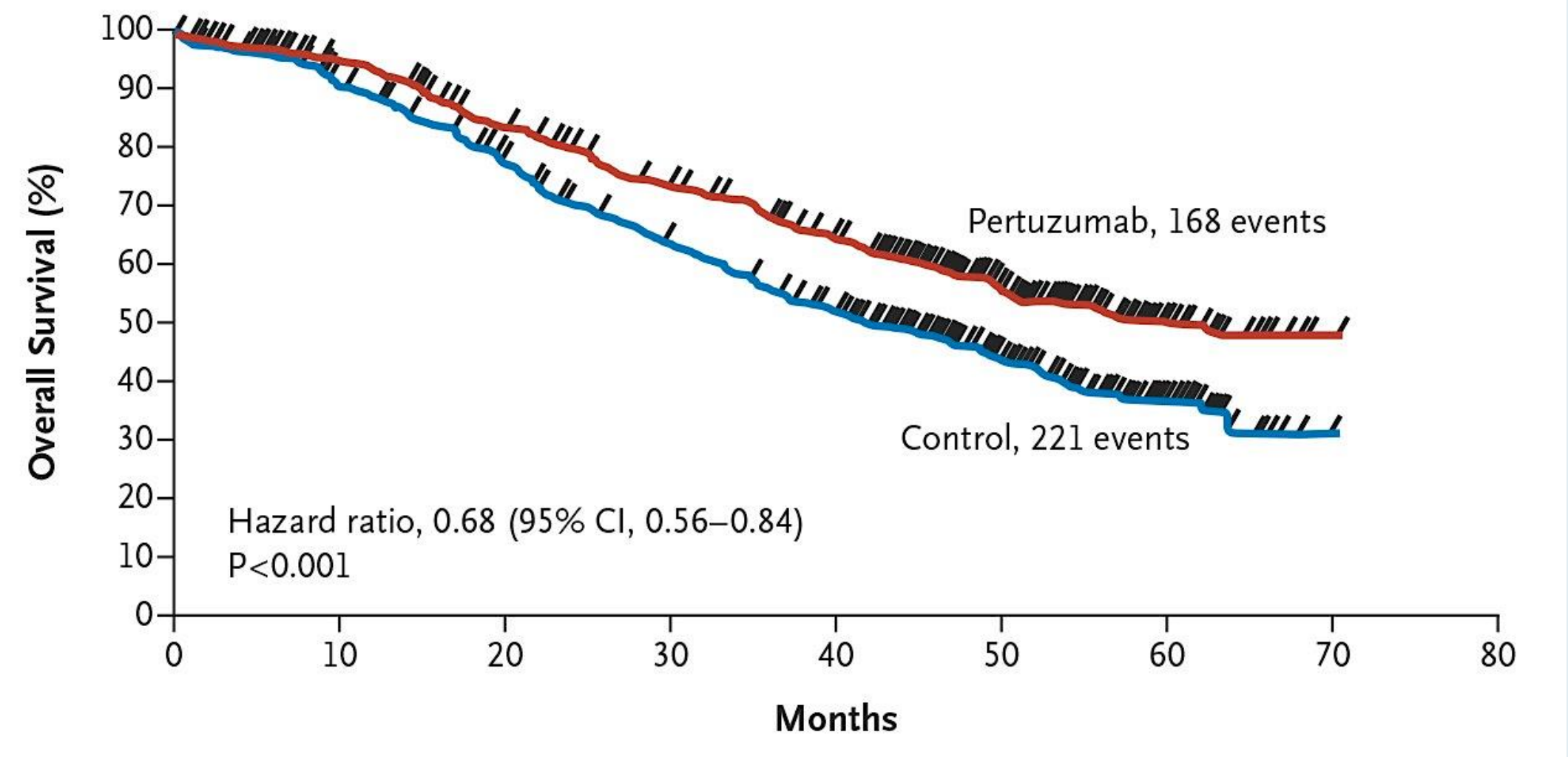
- Does your approach change if the patient is younger (40) or older (85)?
- Does your approach change based on the degree of symptomatology?
- Does your approach change based on location of metastatic disease (eg, visceral, bone only, CNS)?
- How does HR status affect your approach?

Phase III CLEOPATRA: Final Progression-Free Survival



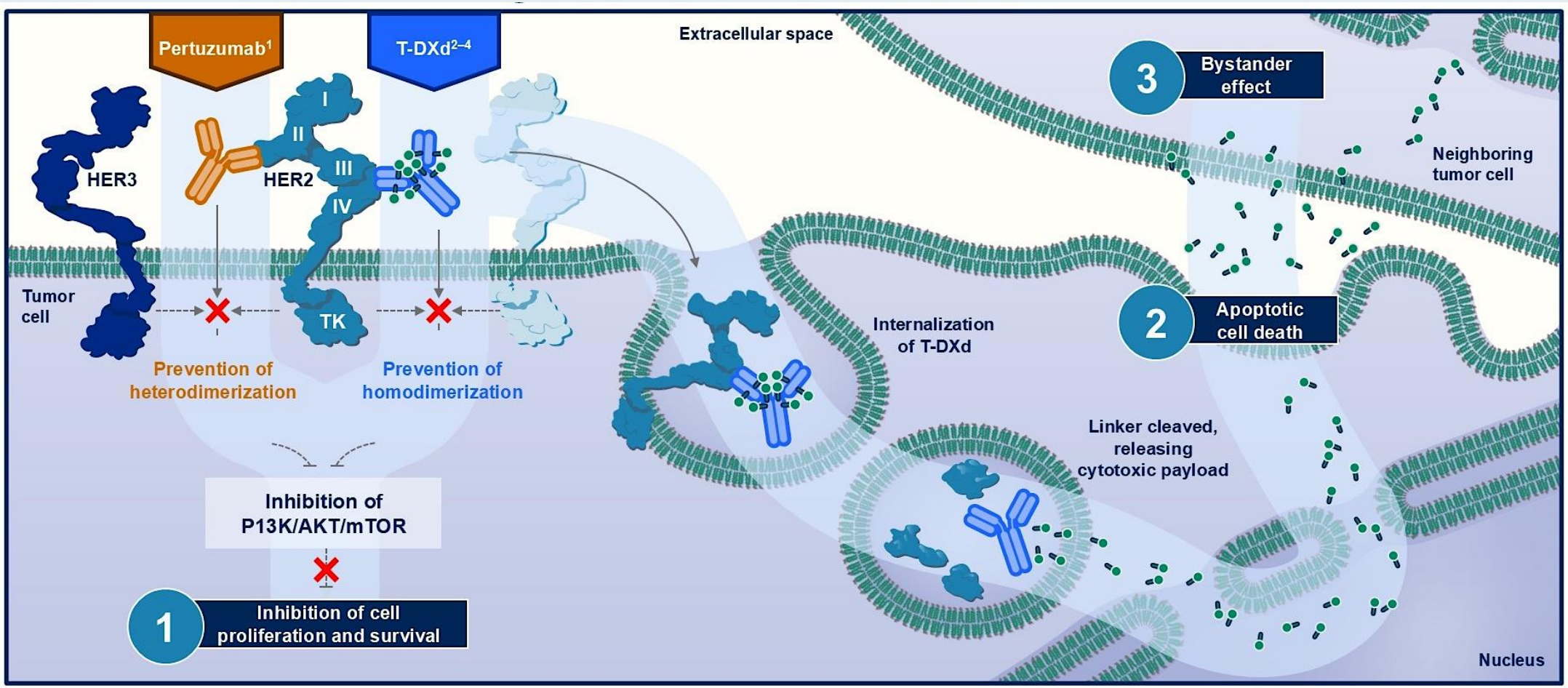
Swain SM et al. *N Engl J Med* 2015 February 19;372(8):724-34.

Phase III CLEOPATRA: Final Overall Survival



Swain SM et al. *N Engl J Med* 2015 February 19;372(8):724-34.

Rationale for Pertuzumab and T-DXd Combination Therapy

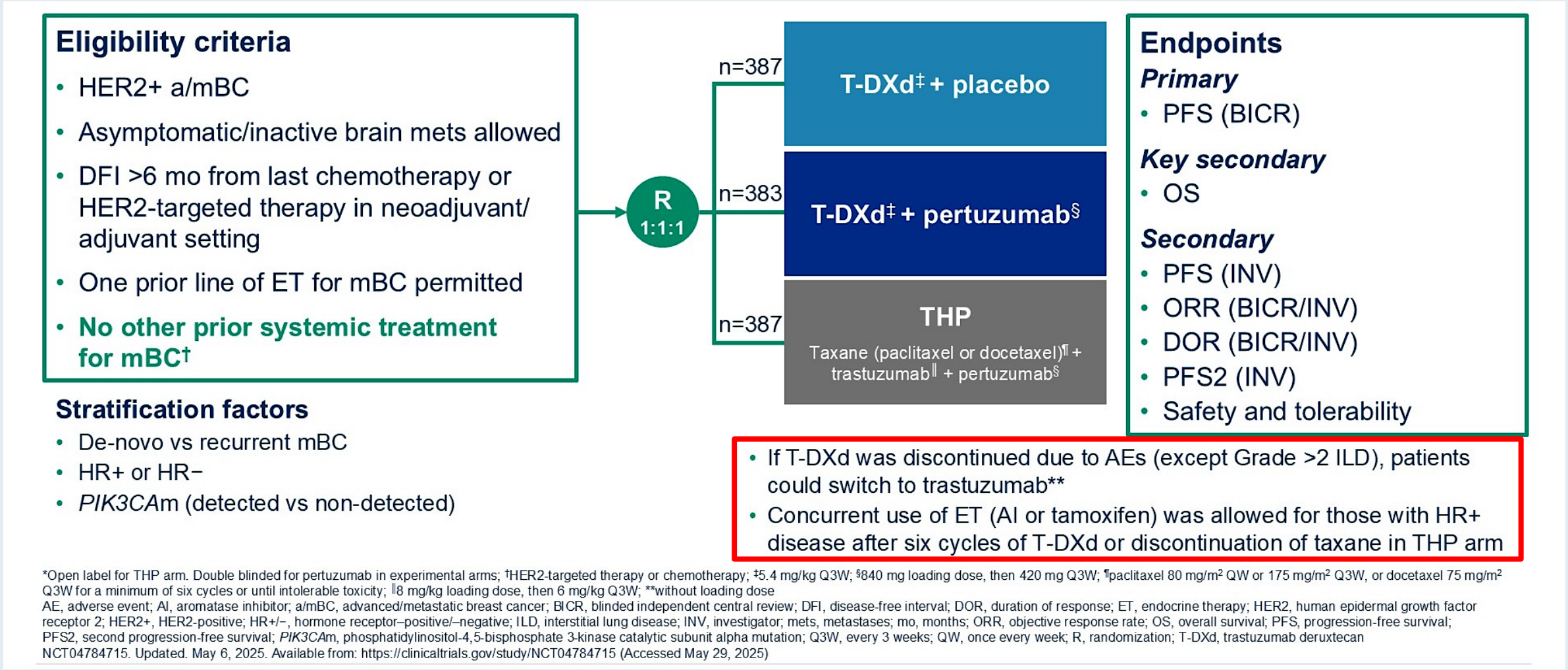


AKT, protein kinase B; HER2/3, human epidermal growth factor receptor 2/3; mTOR, mammalian target of rapamycin; P13K, phosphoinositide 3-kinase; T-DXd, trastuzumab deruxtecan; TK, tyrosine kinase

1. Nami B, et al. *Cancers (Basel)*. 2018;10:342; 2. Nakada T, et al. *Chem Pharm Bull (Tokyo)*. 2019;67:173-185; 3. Ogitani Y, et al. *Clin Cancer Res*. 2016;22:5097–5108; 4. Geng W, et al. *Eur J Pharmacol*. 2024:977:176725

Tolaney SM et al. ASCO 2025;Abstract LBA1008.

Phase III DESTINY-Breast09 Study Design



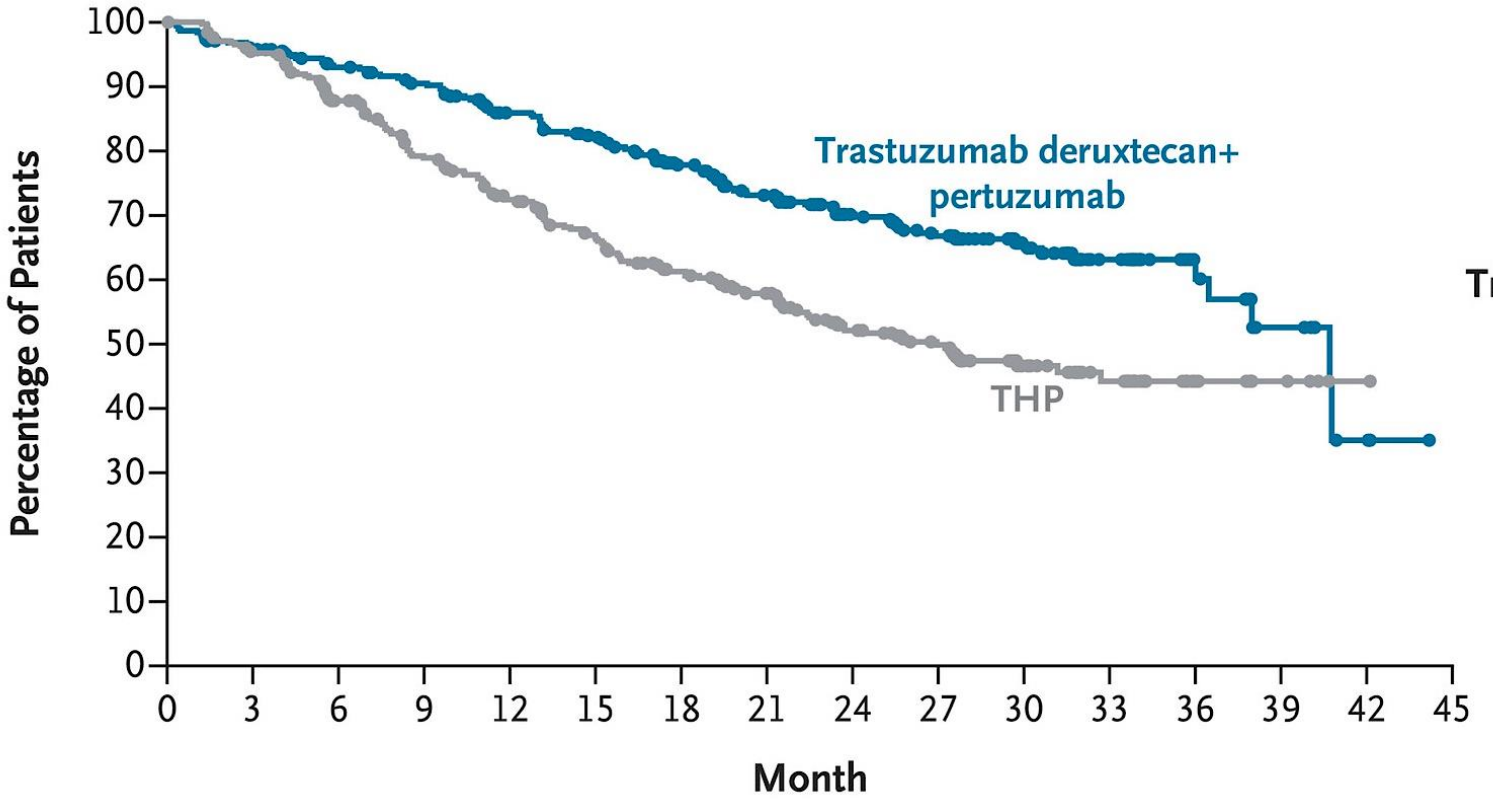
*Open label for THP arm. Double blinded for pertuzumab in experimental arms; †HER2-targeted therapy or chemotherapy; ‡5.4 mg/kg Q3W; §840 mg loading dose, then 420 mg Q3W; ¶paclitaxel 80 mg/m² QW or 175 mg/m² Q3W, or docetaxel 75 mg/m² Q3W for a minimum of six cycles or until intolerable toxicity; ‖8 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: Progression-Free Survival (Blinded Independent Central Review)

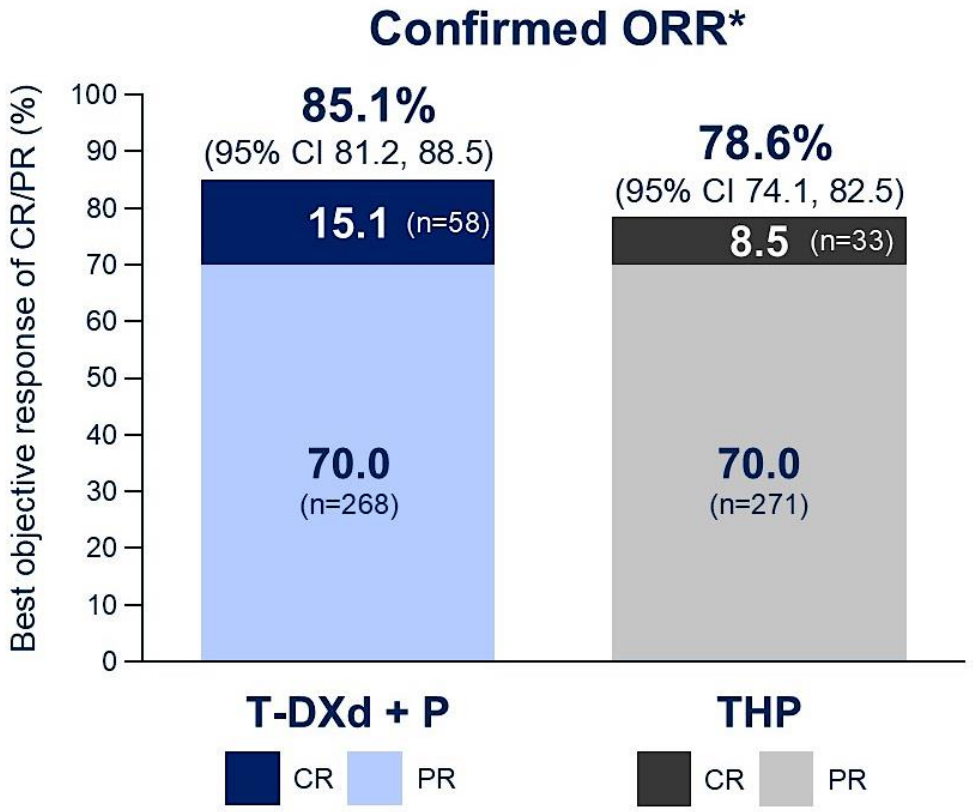


	No. of Patients	Median Progression-free Survival (95% CI)
		mo
Trastuzumab Deruxtecan+ Pertuzumab	383	40.7 (36.5–NC)
THP	387	26.9 (21.8–NC)

Hazard ratio for disease progression or death, 0.56 (95% CI, 0.44–0.71)
P<0.00001 (prespecified P-value boundary for superiority, 0.00043)

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

Phase III DESTINY-Breast09: Efficacy



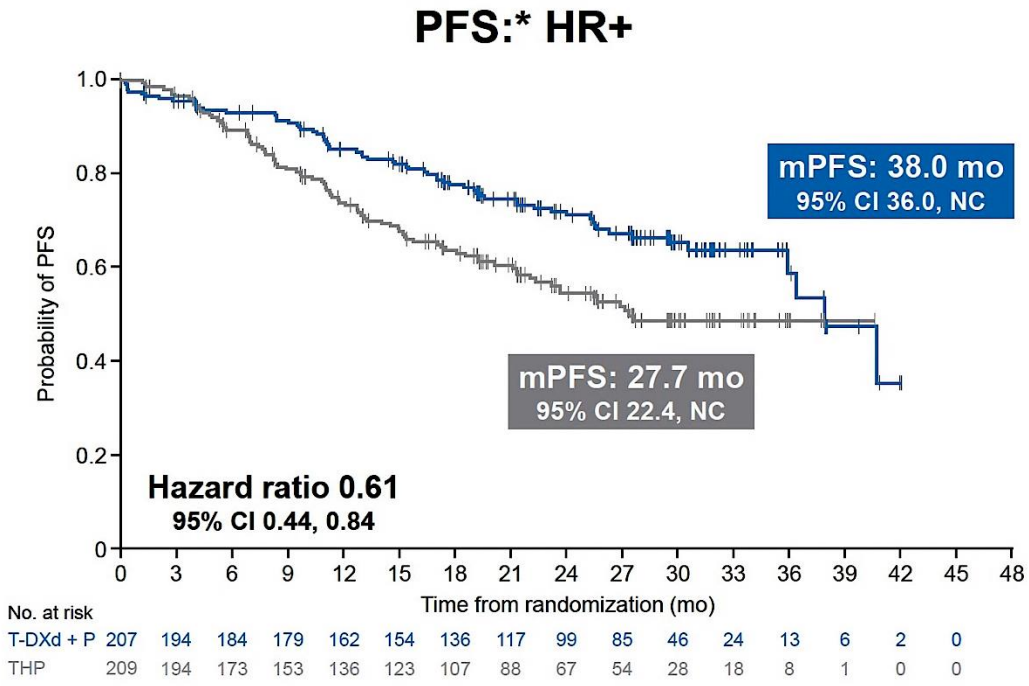
	T-DXd + P (n=383)	THP (n=387)
Median DOR, mo (95% CI)	39.2 (35.1, NC)	26.4 (22.3, NC)
Remaining in response at 24 mo (%)	73.3	54.9
Stable disease, n (%)	38 (9.9)	56 (14.5)

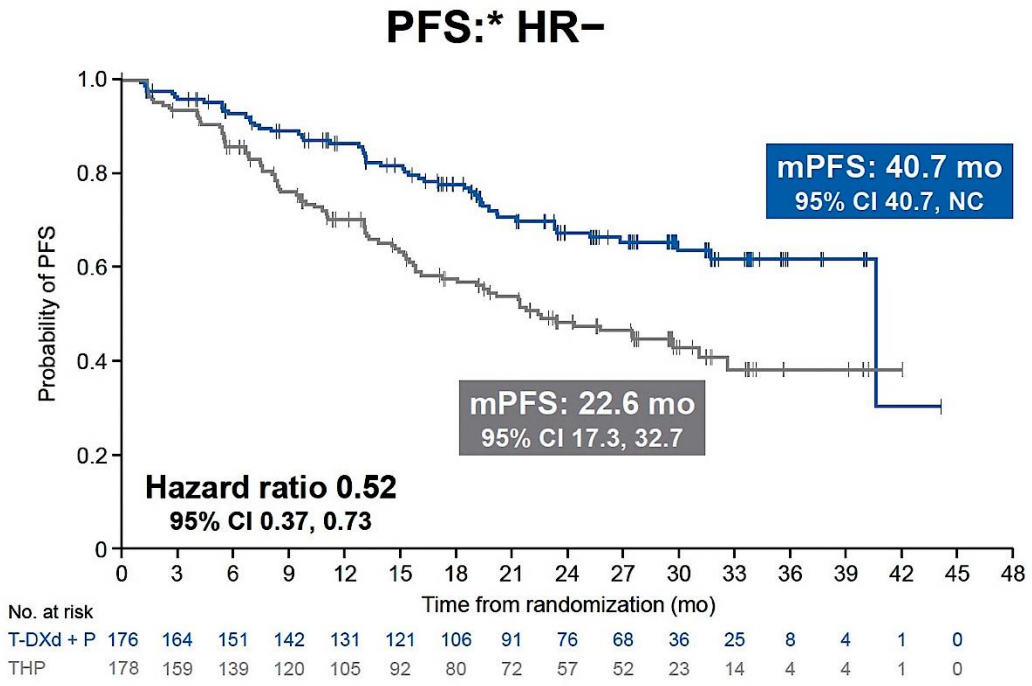
Response rates were greater with T-DXd + P vs THP and were durable

*Based on RECIST v1.1; response required confirmation after 4 weeks
BICR, blinded independent central review; CI, confidence interval; CR, complete response; DOR, duration of response; mo, months; NC, not calculable; ORR, objective response rate; P, pertuzumab; PR, partial response; RECIST, Response Evaluation Criteria in Solid Tumours; T-DXd, trastuzumab deruxtecan; THP, taxane + trastuzumab + pertuzumab

Tolaney SM et al. ASCO 2025;Abstract LBA1008; Tolaney SM et al. *N Engl J Med* 2026;394;551-62.

Phase III DESTINY-Breast09: PFS by HR Status





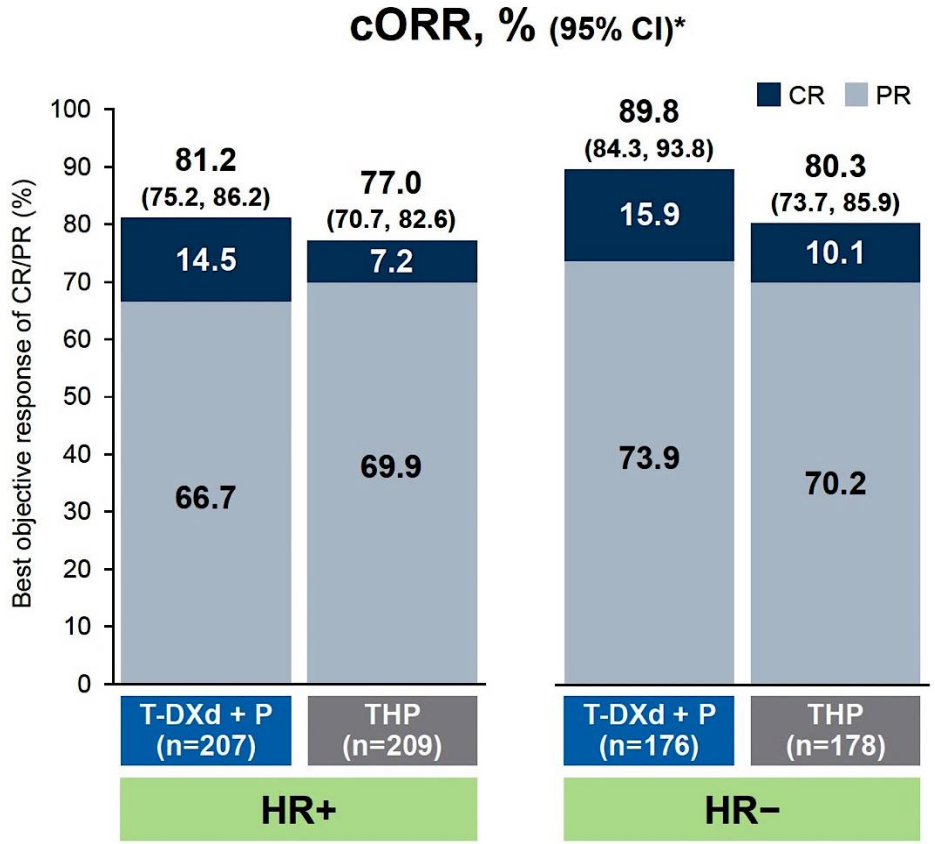
Patients with HR+ disease could receive concurrent ET after six cycles of T-DXd or discontinuation of taxane, which occurred in **13.5% (T-DXd + P)** versus **38.3% (THP)** of patients

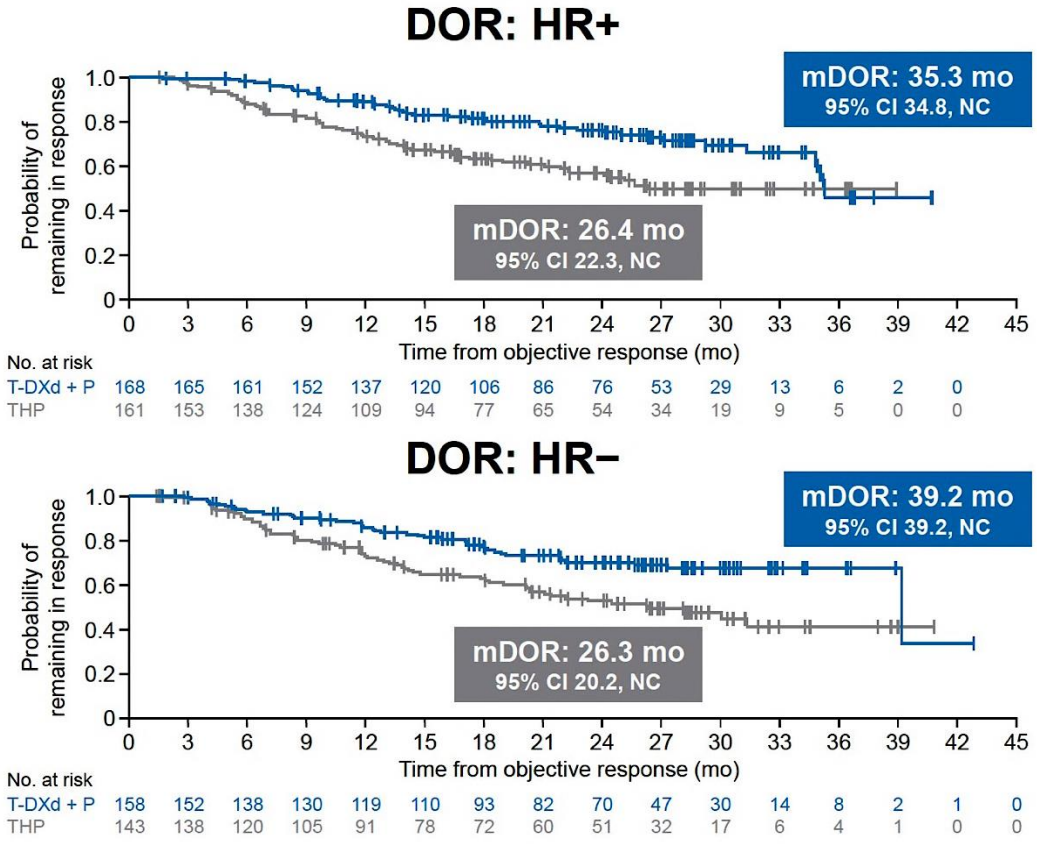
T-DXd + P demonstrated a clinically meaningful PFS benefit vs THP regardless of HR status

*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



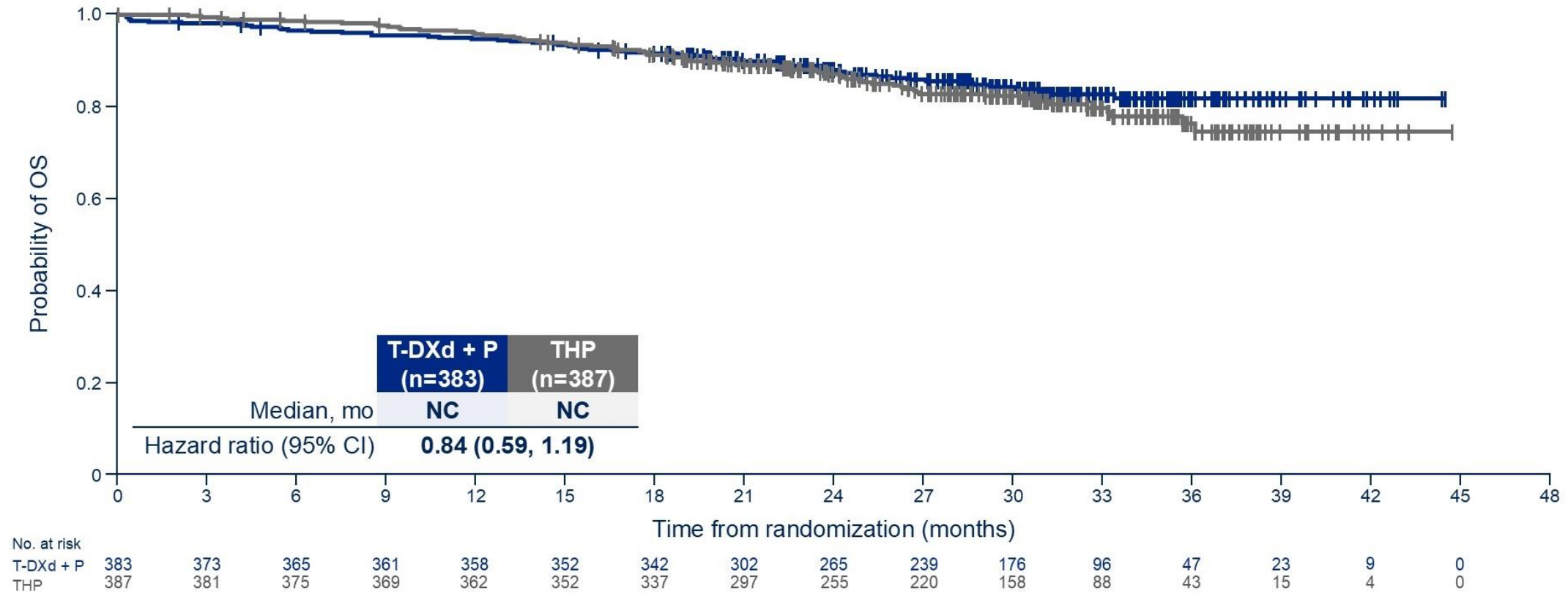


CR rates and DOR favored T-DXd + P vs THP regardless of HR status

*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.

Phase III DESTINY-Breast09: Overall Survival (16% Maturity)

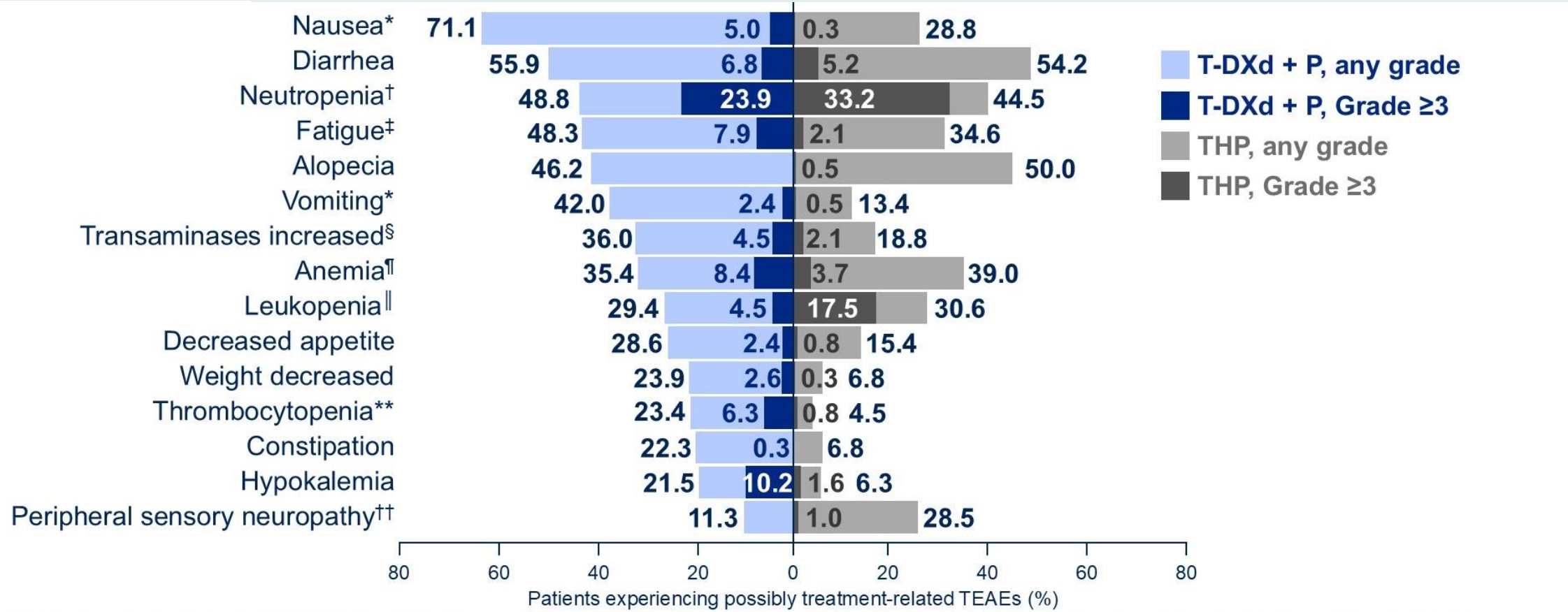


Early OS data suggest a positive trend favoring T-DXd + P over THP

CI, confidence interval; OS, overall survival; NC, not calculable; P, pertuzumab; T-DXd, trastuzumab deruxtecan; THP, taxane + trastuzumab + pertuzumab

Tolaney SM et al. ASCO 2025;Abstract LBA1008.

Phase III DESTINY-Breast09: Common Adverse Events



*Antiemetic prophylaxis was recommended but not mandated by protocol; †neutropenia (grouped term) includes: neutropenia and neutrophil count decreased; ‡fatigue (grouped term) includes: fatigue, asthenia, malaise, and lethargy; §transaminases increased (grouped term) includes: transaminases increased, aspartate aminotransferase increased, alanine aminotransferase increased, gamma-glutamyltransferase increased, liver function test abnormal, hepatic function abnormal, and liver function test increase; ¶anemia (grouped term) includes: anemia, hemoglobin decreased, hematocrit decreased, and red blood cell count decreased; ‖leukopenia (grouped term) includes: leukopenia and white blood cell count decreased; **thrombocytopenia (grouped term) includes: platelet count decreased and thrombocytopenia; ††peripheral sensory neuropathy (grouped term) includes: neuropathy peripheral, peripheral sensory neuropathy, and polyneuropathy
P, pertuzumab; T-DXd, trastuzumab deruxtecan; TEAE, treatment-emergent adverse event; THP, taxane + trastuzumab + pertuzumab

Tolaney SM et al. ASCO 2025;Abstract LBA1008.

Phase III DESTINY-Breast09: Adverse Events of Special Interest

Adjudicated drug-related ILD/pneumonitis*

n (%)	Grade 1	Grade 2	Grade 3	Grade 4	Grade 5	Any grade
T-DXd + P (n=381)	17 (4.5)	27 (7.1)	0	0	2 (0.5)	46 (12.1)
THP (n=382)	2 (0.5)	2 (0.5)	0	0	0	4 (1.0)

Left ventricular dysfunction†

n (%)	Grade 1	Grade 2	Grade 3	Grade 4	Grade 5	Any grade
T-DXd + P (n=381)	4 (1.0)	30 (7.9)	7 (1.8)	1 (0.3)	0	42 (11.0)
THP (n=382)	1 (0.3)	19 (5.0)	7 (1.8)	0	0	27 (7.1)

Safety analysis set
*Adjudicated drug-related ILD/pneumonitis (grouped term) includes: chronic obstructive pulmonary disease, interstitial lung disease, organizing pneumonia, pneumonia, and pneumonitis, †left ventricular dysfunction (grouped term) includes: potential heart failure, cardiac failure, cardiac failure chronic, ejection fraction decreased, left ventricular dysfunction, and right ventricular failure
ILD, interstitial lung disease; P, pertuzumab; T-DXd, trastuzumab deruxtecan; THP, taxane + trastuzumab + pertuzumab

Tolaney SM et al. ASCO 2025;Abstract LBA1008; Tolaney SM et al. *N Engl J Med* 2026;394;551-62.

FDA Approves Fam-Trastuzumab Deruxtecan-nxki with Pertuzumab for Unresectable or Metastatic HER2-Positive Breast Cancer

Press Release: December 15, 2025

"On December 15, 2025, the Food and Drug Administration approved fam-trastuzumab deruxtecan-nxki in combination with pertuzumab for the first-line treatment of adults with unresectable or metastatic HER2-positive (IHC 3+ or ISH+) breast cancer as determined by an FDA-approved test.

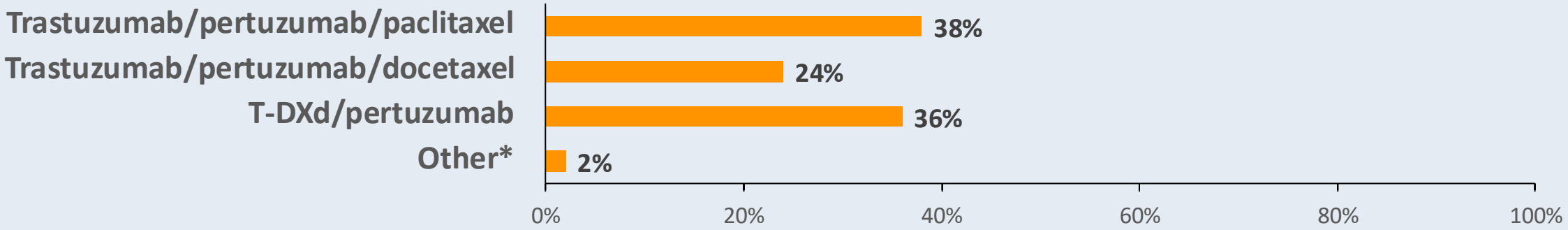
Efficacy was evaluated in DESTINY-Breast09 (NCT04784715), a randomized, three-arm, multicenter, global trial that enrolled 1157 adults with HER2-positive advanced or metastatic breast cancer who had not received prior chemotherapy or HER2-targeted therapy or had received neoadjuvant or adjuvant HER2-targeted therapy more than six months before the diagnosis of advanced or metastatic disease."

https://www.fda.gov/drugs/drug-approvals-and-databases/fda-approves-fam-trastuzumab-deruxtecan-nxki-pertuzumab-unresectable-or-metastatic-her2-positive

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?

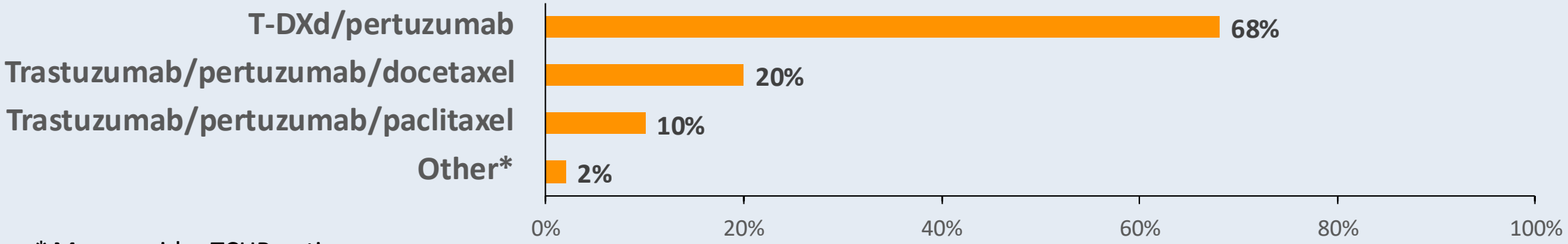
Age 65, PS 0

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

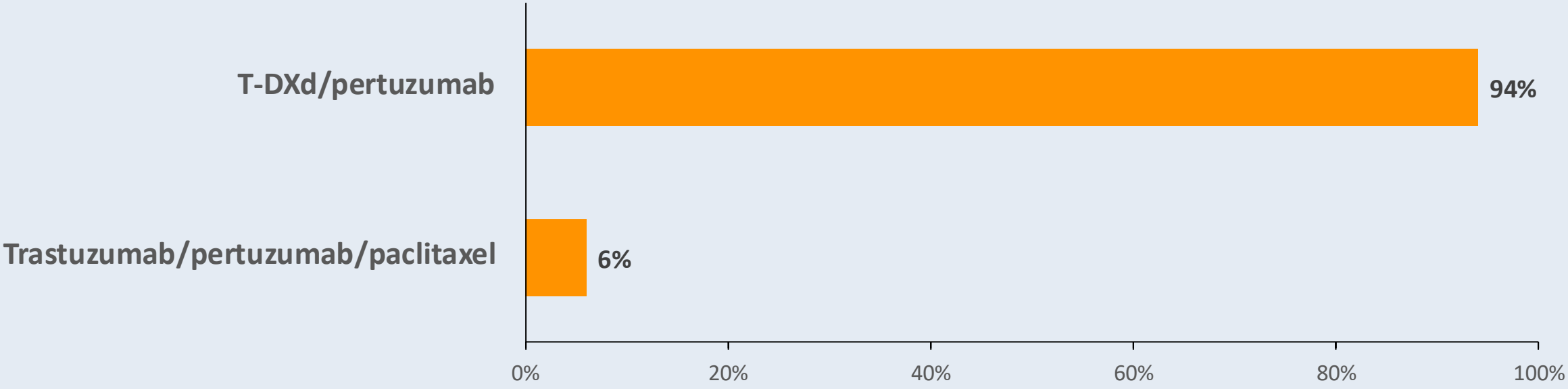
Survey of US-based general medical oncologists

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

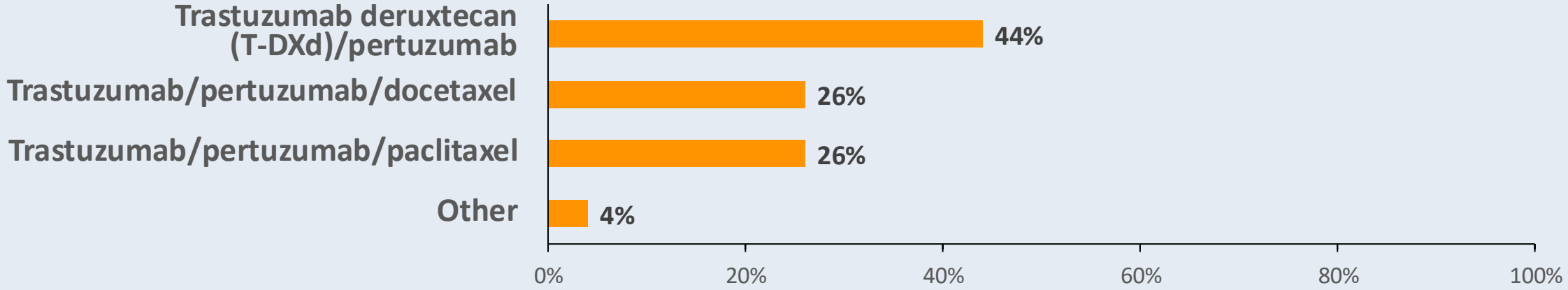
Multiple brain metastases requiring SRS:



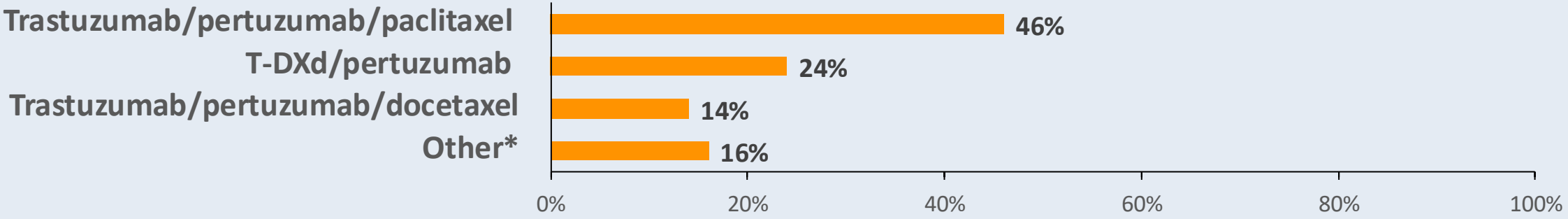
Survey of US-based general medical oncologists

A woman presents with de novo HR-positive, HER2-positive metastatic breast cancer (mBC). Regulatory and reimbursement issues aside, which first-line anti-HER2 induction therapy would you most likely recommend for each asymptomatic bone metastases?

Age 40 (premenopausal), PS 0



Age 85, PS 1



* Trastuzumab + chemotherapy (+/- pertuzumab); Trastuzumab + ET; Trastuzumab/pertuzumab and consider adding AI if low-volume disease; AI + CDK4/6i first and ONLY if pt develops symptomatic PD will give THP

Survey of US-based general medical oncologists

RTP RESEARCH TO PRACTICE

Agenda

Introduction: Biology of "Triple-Positive" Breast Cancer; Implications for Therapeutic Development

Module 1: Cases from the GMO Survey

Module 2: First-Line Therapy for Metastatic HER2-Positive Disease

Module 3: Cases from the GMO Survey

Module 4a: Maintenance Therapy for HR-Positive, HER2-Positive Disease

Module 4b: Maintenance Therapy for HR-Negative, HER2-Positive Disease

Module 5: Ongoing Clinical Trials Attempting to Address These Decisions

Module 6: Cases from the GMO Survey

Cases from General Medical Oncologists

52 yo woman

- **ER/PR-, HER2+**
- **Comorbidities: HTN, syncope, GERD, depression.**
- **Original diagnosis: ER/PR-, HER2+ stage IIB T1N1M0.**
- **Neoadjuvant TCHP; Adjuvant radiation/HP.**
- **Surveillance for 2 years, then progression to asymptomatic bone metastases.**
- **Treated with THP and HP maintenance.**

If she presented today would you use T-DXd/pertuzumab? What about tucatinib/HP maintenance?

Cases from General Medical Oncologists

86 yr old woman

- **Hx DCIS, presents with weight loss. CT scans show liver masses — biopsy ER/PR neg, HER2 2+, FISH negative, high grade IDC, palpable right breast mass ER/PR negative, HER2 2+ FISH+**
- **KPS 90**

Would you treat as HER2+ disease given breast FISH+, liver 2+?
Any experience with T-DXd in older patients?
Recommendations for initial dose reduction?
Hold pertuzumab cycle 1, add if tolerated?
Maintenance HP/tucatinib?

Cases from General Medical Oncologists

49 yo woman

- **Triple-positive breast cancer with liver and bone mets.**
- **6 cycles of THP, then HP maintenance (subcut) plus letrozole w T-DXd is an option now for front line therapy. However, the indication is a forever treatment, aka we cannot de-escalate off chemo.**
- **Would investigators use a similar approach — 6 cycles of T-DXd, followed by maintenance HP? Or would they do T-DXd until intolerance or progression? That to me would seem to increase long term risk for pneumonitis.**
- **This patient actually achieved excellent response on maintenance HP for ~2 years. She then developed new liver mets, biopsied still HER2+ IHC 3+. I have changed therapy to T-DXd. Pt stays on letrozole too.**

What would investigators do in this scenario?

RTP RESEARCH TO PRACTICE

Agenda

Introduction: Biology of "Triple-Positive" Breast Cancer; Implications for Therapeutic Development

Module 1: Cases from the GMO Survey

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Module 4b: Maintenance Therapy for HR-Negative, HER2-Positive Disease

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Module 6: Cases from the GMO Survey

RTP RESEARCH TO PRACTICE

Questions About Maintenance Therapy for HR-Positive, HER2-Positive Disease

- What is your usual approach to maintenance therapy for a patient with HR-positive, HER2-positive metastatic disease?
- What duration of maintenance therapy do you employ, assuming the patient has acceptable treatment tolerance?
- How do you factor in prior adjuvant endocrine treatment?
- How do you factor in prior HER2-targeted treatment?

Questions About Maintenance Therapy for HR-Positive, HER2-Positive Disease

- Does your approach vary if the patient is younger (40) or older (85)?
- Does tucatinib currently have a role in this setting?
- If you are using a CDK inhibitor, do you prefer palbociclib?
- For patients receiving palbociclib, how do you manage neutropenia?

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(5):451-62.

Phase III PATINA Study Design

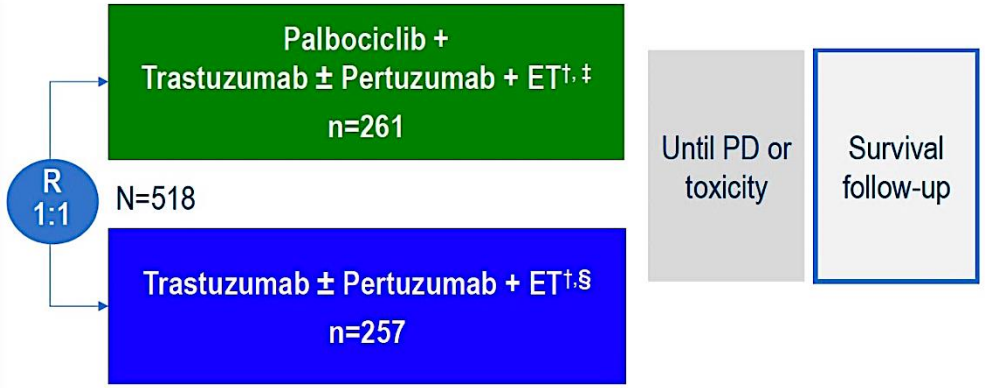
Objective: To evaluate the addition of palbociclib to anti-HER2 and ET for patients with HR+/HER2+ breast cancer

REGISTRATION

- Histologically confirmed HR+/HER2+ aBC
- No prior treatment in the advanced setting beyond induction treatment
- 6–8 cycles of treatment, including trastuzumab ± pertuzumab and taxane/vinorelbine

KEY ELIGIBILITY CRITERIA

- Completion of induction chemotherapy and no evidence of disease progression (ie, CR, PR, or SD)



Primary Outcome

- Investigator-assessed PFS

Secondary Outcomes

- OS
- 3- and 5- year survival probabilities
- ORR / DOR / CBR
- Safety
- PRO
- Incidence of CNS mets

Stratification Factors

- Pertuzumab use (yes vs no)
  - The non-pertuzumab option is limited to up to 20% of the population
- Prior anti-HER2 therapy in the (neo)adjuvant setting (yes vs no, including de novo)‖
- Response to induction therapy (CR or PR vs SD) by investigator assessment‖
- Type of ET (fulvestrant vs aromatase inhibitor)

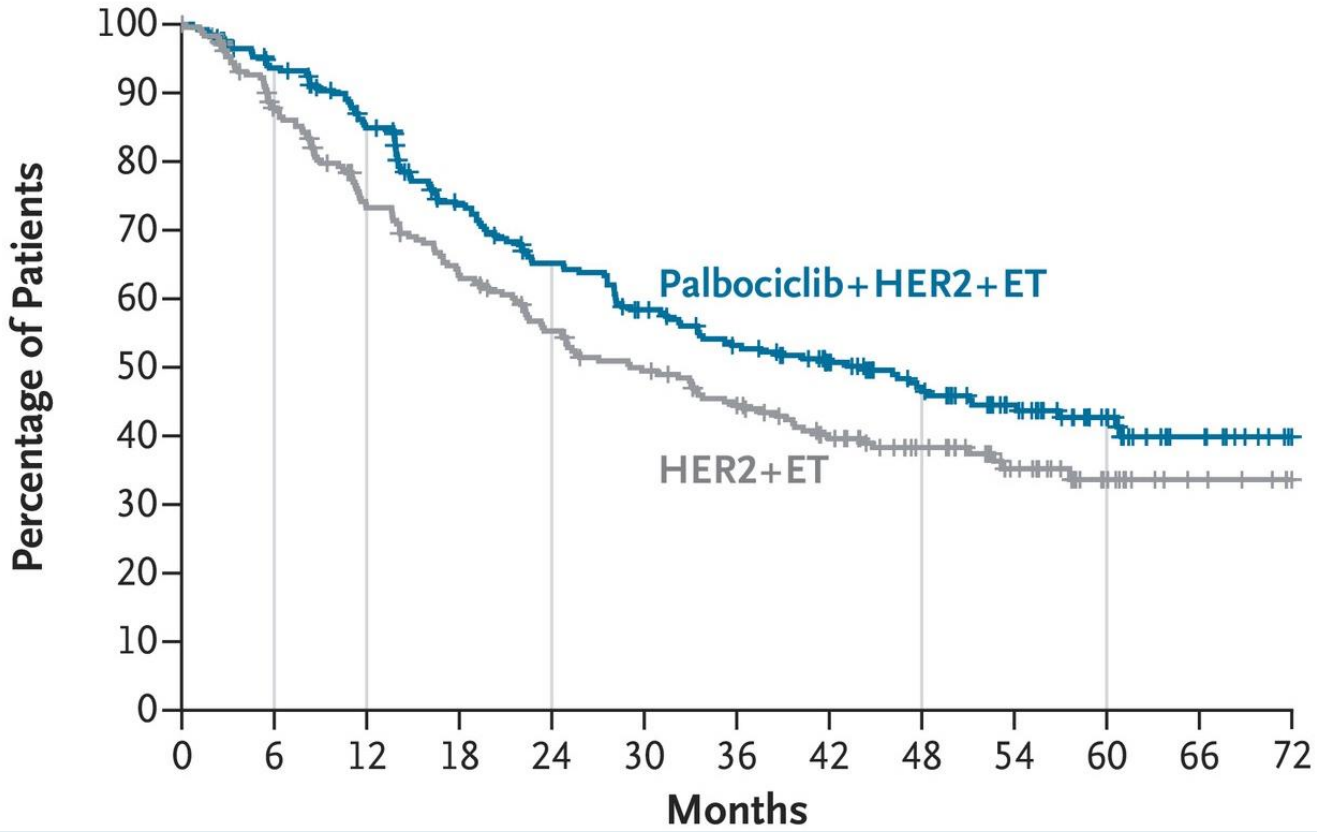
Data cutoff for final PFS analysis: October 15, 2024.

*Study enrollment period was June 2017 until 2021 across the United States, France, Germany, Italy, Portugal, Spain, Australia, and New Zealand. DSMB recommendation to release study data occurred on December 2, 2024. †Trastuzumab and pertuzumab were administered per SOC. ET options included an aromatase inhibitor or fulvestrant. ‡All patients included in the primary and secondary analyses. §Nine patients withdrew before starting treatment and were not included in the safety analysis. All patients were included in the ITT analysis. ‖Factors used in stratified analyses. CBR, clinical benefit rate; CNS, central nervous system; CR=complete response; DOR, duration of response; DSMB=Data and Safety Monitoring Board; ET=endocrine therapy; HER2, human epidermal growth factor receptor 2; HR, hormone receptor; mBC, metastatic breast cancer; mets, metastases; OS, overall survival; ORR, objective response rate; PD, progressive disease; PFS, progression-free survival; PR, partial response; PRO, patient-reported outcome; R, randomization; SD, stable disease; SOC, standard of care.

References: 1. https://clinicaltrials.gov/study/NCT02947685. Accessed September 11, 2025; 2. Metzger O, *et al.* SABCS 2024. Presentation GS2-12.

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

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

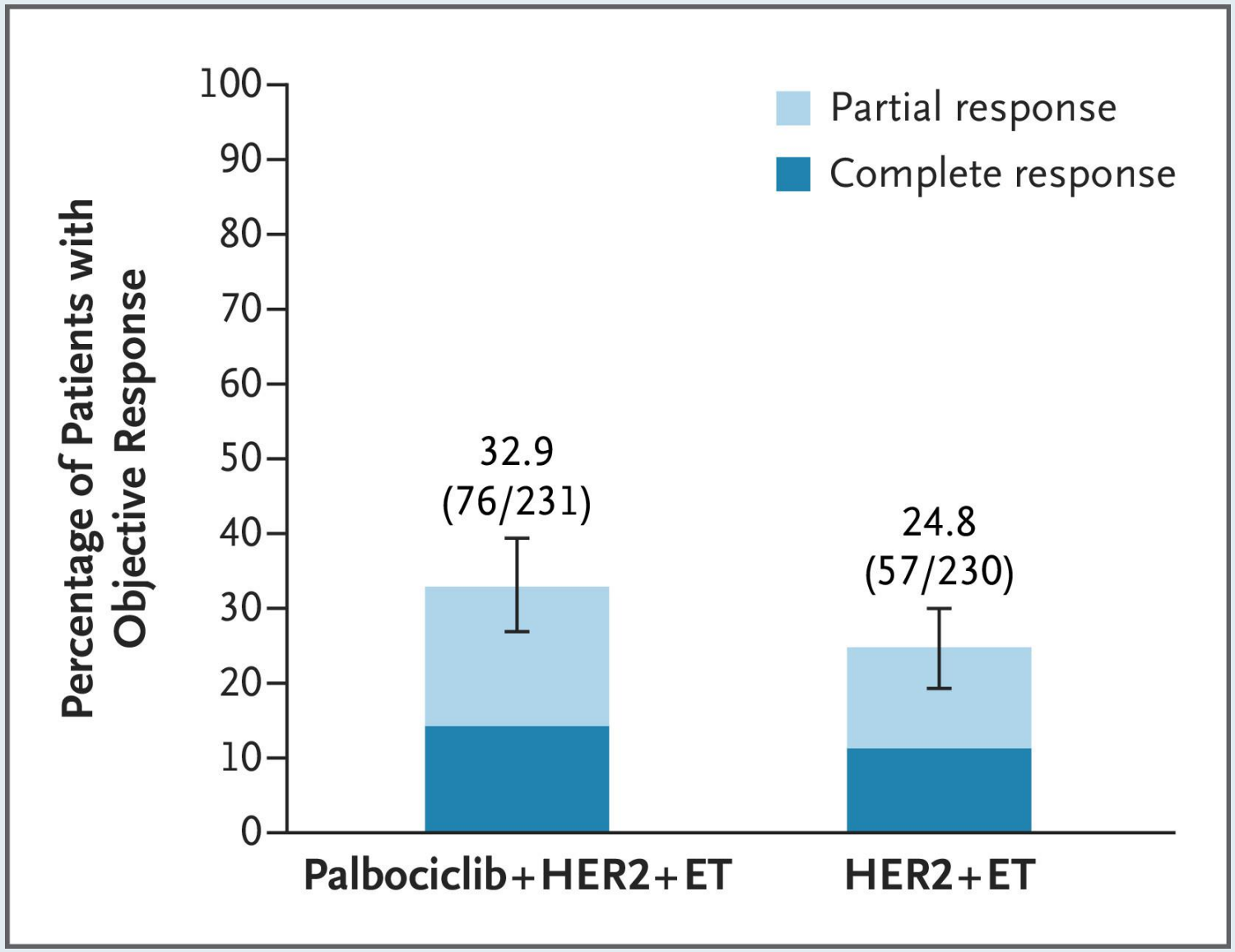


	No. of Events/Total No. of Patients	Median Progression-free Survival (95% CI)
		mo
Palbociclib+HER2+ET	127/261	44.3 (32.4–56.8)
HER2+ET	135/257	29.1 (23.3–38.6)

Hazard ratio for disease progression or death, 0.75 (95% CI, 0.59–0.96)
Two-sided unstratified P=0.02 by log-rank test

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.

PATINA: Select Baseline Characteristics of All Patients

Characteristic	Total (N = 518)
Age — yr	
Median (IQR)	53.4 (44.2–61.4)
Range	28.7–84.3
Menopausal status — no. (%)	
NA because of male sex	3 (0.6)
Postmenopausal	320 (61.8)
Premenopausal	192 (37.1)
Missing data	3 (0.6)

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

RTP RESEARCH TO PRACTICE

PATINA: Select Baseline Characteristics of All Patients (Continued)

Characteristic	Total (N=518)
Progesterone-receptor status — no. (%)§	
Negative	154 (29.9)
Positive	359 (69.3)
Unknown	2 (0.4)
Missing data	3 (0.6)
HER2 assessment — no. (%)§¶	
2+, ISH amplified	130 (25.1)
3+	384 (74.1)
Missing data	4 (0.8)

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

PATINA: Select Baseline Characteristics of All Patients (Continued)

Characteristic	Total (N = 518)
Site of metastases — no. (%)‖	
Central nervous system	20 (3.9)
Nonvisceral	117 (22.6)
Visceral	379 (73.6)
Missing data	2 (0.4)
Number of cycles of induction treatment	
Median (IQR)	6.0 (6.0–7.0)
Range	4.0–8.0
Missing data	3 (0.6)
De novo metastatic disease — no. (%)**	
No	233 (45.0)
Yes	282 (54.4)
Missing data	3 (0.6)

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

PATINA: Select Baseline Characteristics of All Patients (Continued)

Characteristic	Total (N = 518)
Previous adjuvant or neoadjuvant anti-HER2 therapy — no. (%)††	
No	346 (66.8)
Yes	169 (32.6)
Missing data	3 (0.6)
Best response to induction therapy by investigator assessment — no. (%)††‡‡	
Complete or partial response	363 (70.1)
Stable disease	152 (29.3)
Missing data	3 (0.6)

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

PATINA: Select Baseline Characteristics of All Patients (Continued)

Characteristic	Total (N = 518)
Receipt of dual anti-HER2 therapy — no. (%)††	
No	29 (5.6)
Yes	487 (94.0)
Missing data	2 (0.4)
Type of endocrine therapy — no. (%)††	
Aromatase inhibitor	470 (90.7)
Fulvestrant	44 (8.5)
Missing data	4 (0.8)

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

Phase III PATINA: Select 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
Mucosal inflammation	52 (19.9)	4 (1.5)	10 (4.0)	0

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

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

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

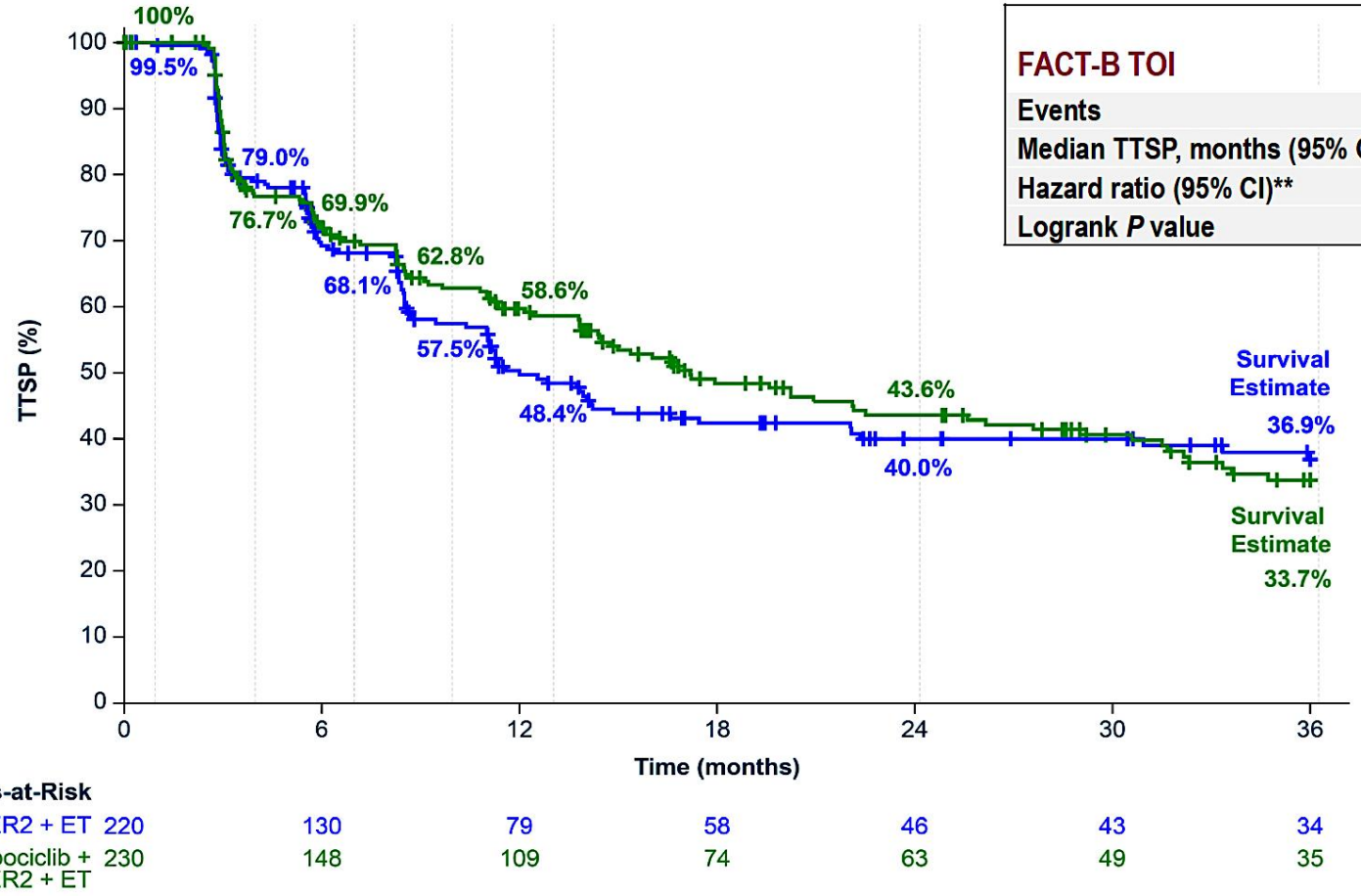
Treatment arm, n/N (%)	Baseline	Year 1	Year 2	Year 3
Palbociclib + Anti-HER2 + ET	248/261 (95.0)	187/218 (85.8)	140/156 (89.7)	106/119 (89.1)
Anti-HER2 + ET	239/256 (93.4)	152/180 (84.4)	113/129 (87.6)	80/99 (80.8)

*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: Time to First Symptom Progression or Death



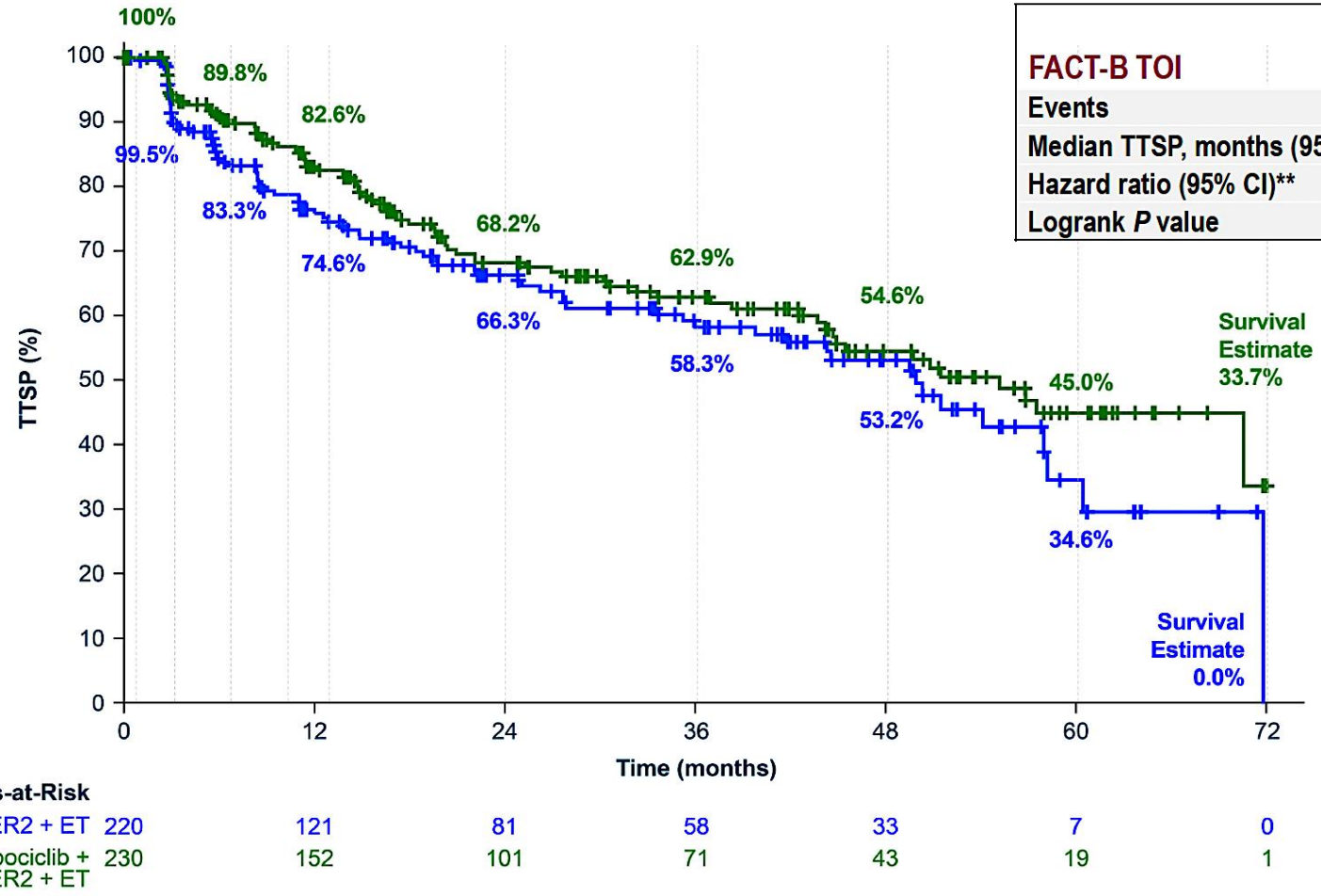
FACT-B TOI	Palbociclib + anti-HER2 + ET	Anti-HER2 + ET
Events	123/230	114/220
Median TTSP, months (95% CI)*	**17.2** (13.9–27.6)	**12.0** (11.1–22.0)
Hazard ratio (95% CI)**	0.93 (0.72–1.20)	Reference
Logrank *P* value	0.5904	

There was **no difference observed** between treatment arms in the time to first symptom progression or death.

TTSP = time to symptomatic progression

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

PATINA: Time to Definitive Symptom Progression or Death



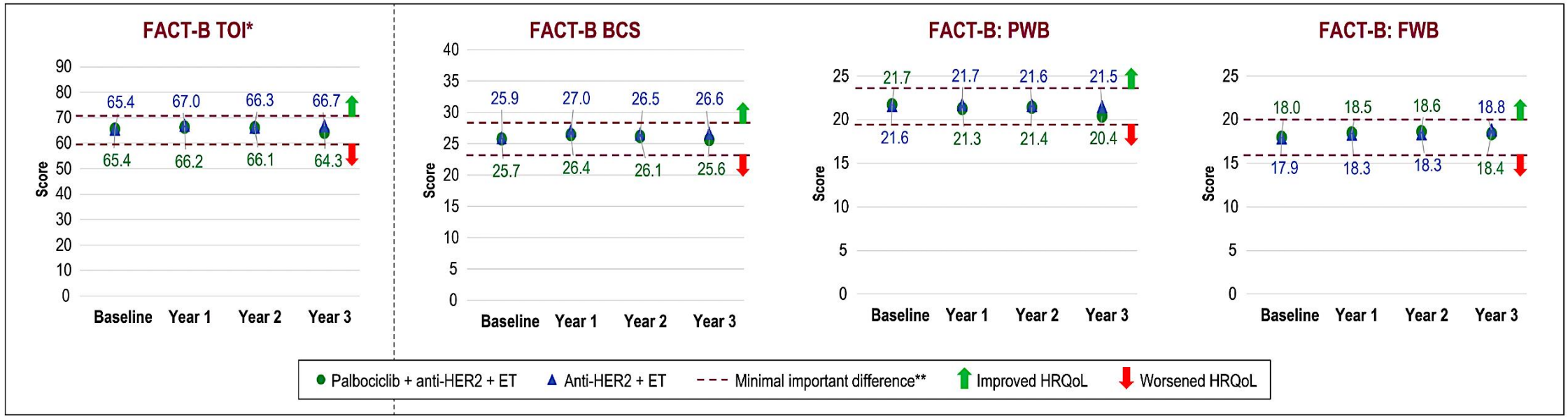
FACT-B TOI	Palbociclib + anti-HER2 + ET	Anti-HER2 + ET
Events	81/230	83/220
Median TTSP, months (95% CI)*	**55.2** (44.7–NE)	**49.9** (39.8–60.4)
Hazard ratio (95% CI)**	0.80 (0.59–1.08)	Reference
Logrank *P* value	0.1484	

There was **no difference observed** between treatment arms in the time to definitive symptom progression or death.

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.

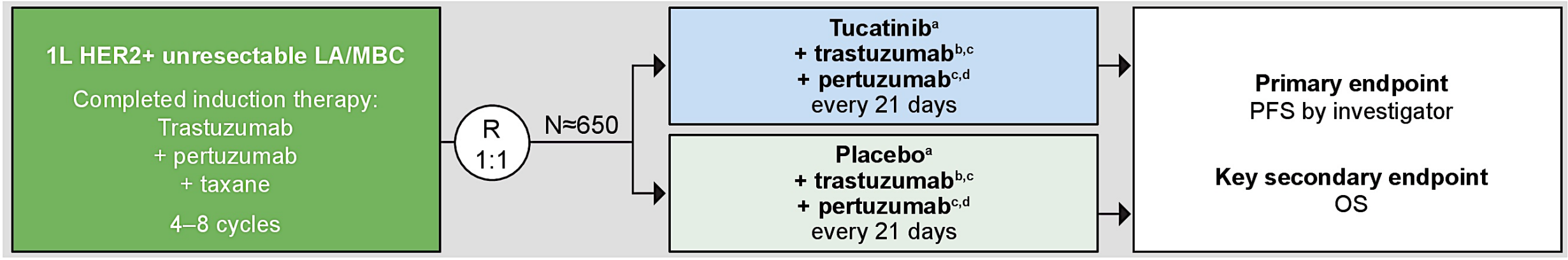
*Minimal important differences: FACT-B TOI (5 points); FACT-B Subscales (2 points); BCS (2 points).[1]

^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 Study Design



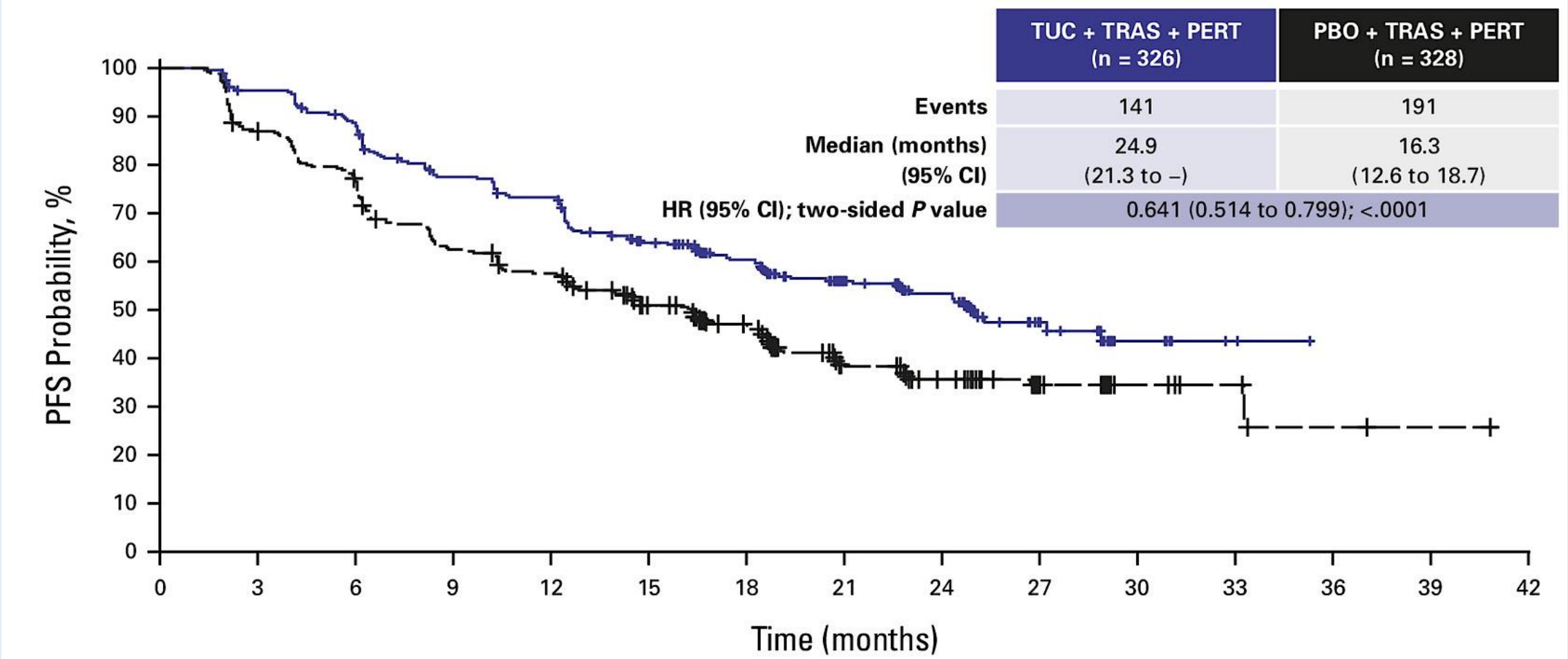
Randomization will be stratified by diagnosis (de novo vs recurrent MBC), hormone receptor status (positive vs negative), and presence or history of BMs (yes vs no).

Patients are permitted to receive up to 2 cycles of carboplatin during the start of induction therapy in combination with trastuzumab, pertuzumab, and taxane.

[a]Tucatinib/placebo 300 mg will be administered PO from Cycle 1 Day 1 onward, BID on each day of study treatment. [b]IV trastuzumab will be given at a dose of 6 mg/kg once every 21 days. Alternatively, trastuzumab may be administered as an SC dose, at a fixed dose of 600 mg once every 21 days. SC trastuzumab does not require a loading dose. [c]A fixed dose of trastuzumab + pertuzumab (600 mg pertuzumab, 600 mg trastuzumab, and 20,000 units hyaluronidase) can be administered every 21 days by SC administration, in lieu of trastuzumab and pertuzumab administered IV individually. [d]Pertuzumab 420 mg will be administered every 21 days intravenously over 30-60 minutes.

Hamilton EP et al. ASCO 2023;Abstract TPS1115.

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

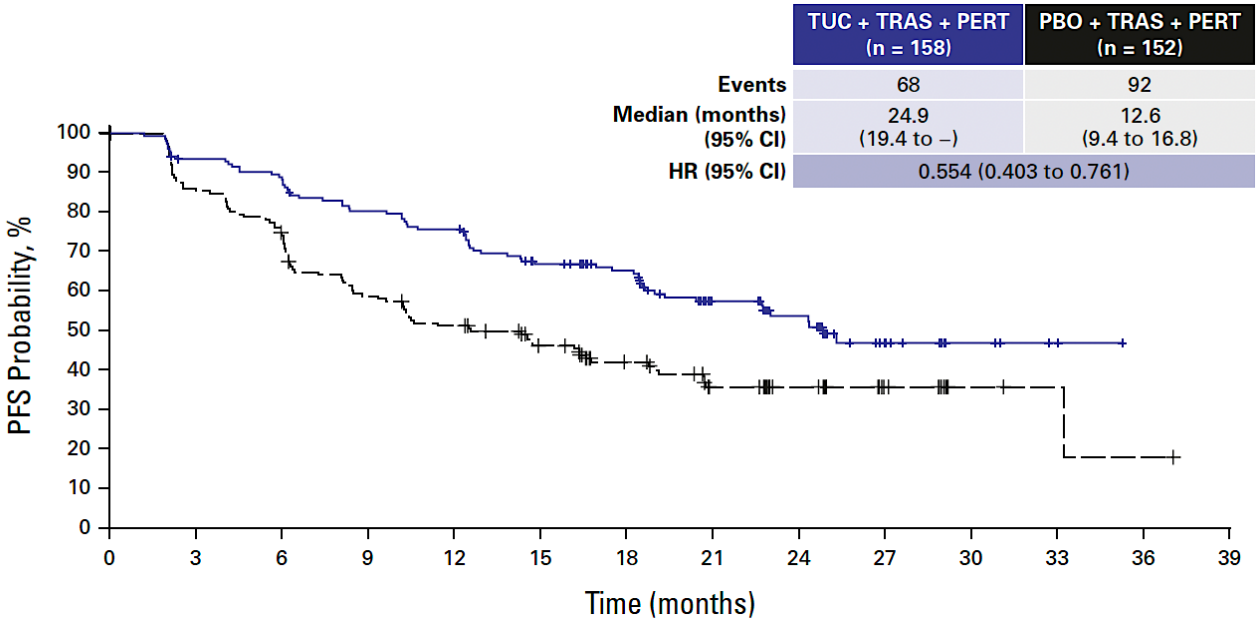


TUC = tucatinib; TRAS = trastuzumab; PERT = pertuzumab; PBO = placebo

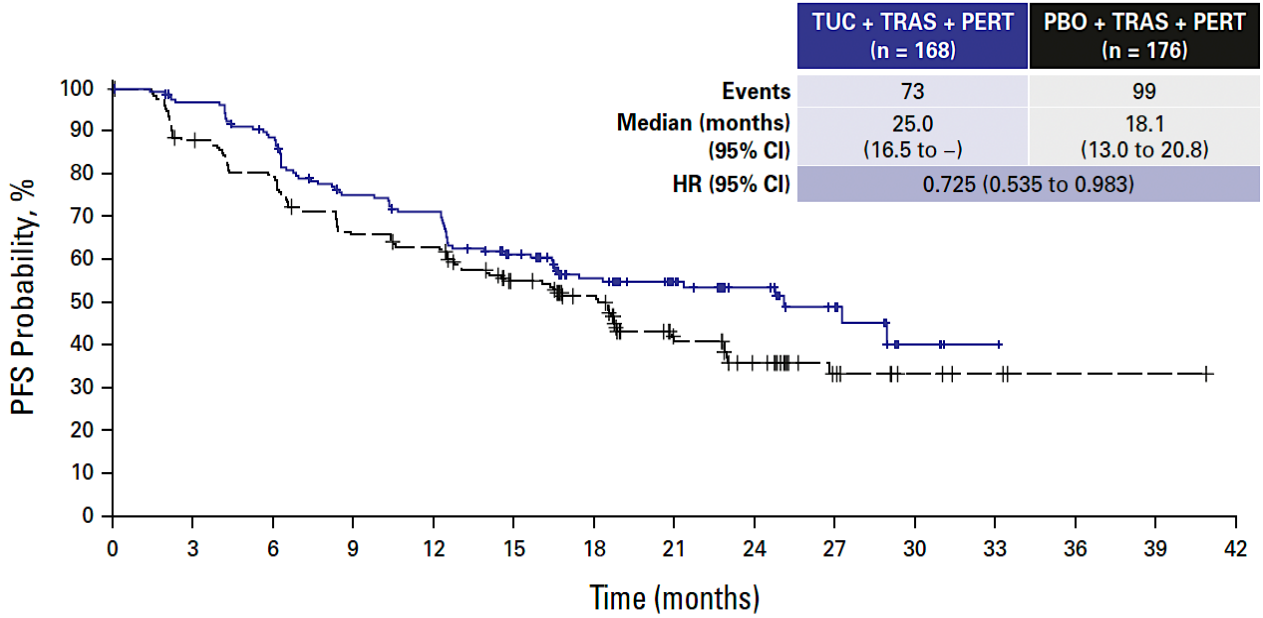
Dieras V et al. *J Clin Oncol* 2025; December 10;[Online ahead of print].

Phase III HER2CLIMB-05: Investigator-Assessed PFS by HR Status

HR-negative

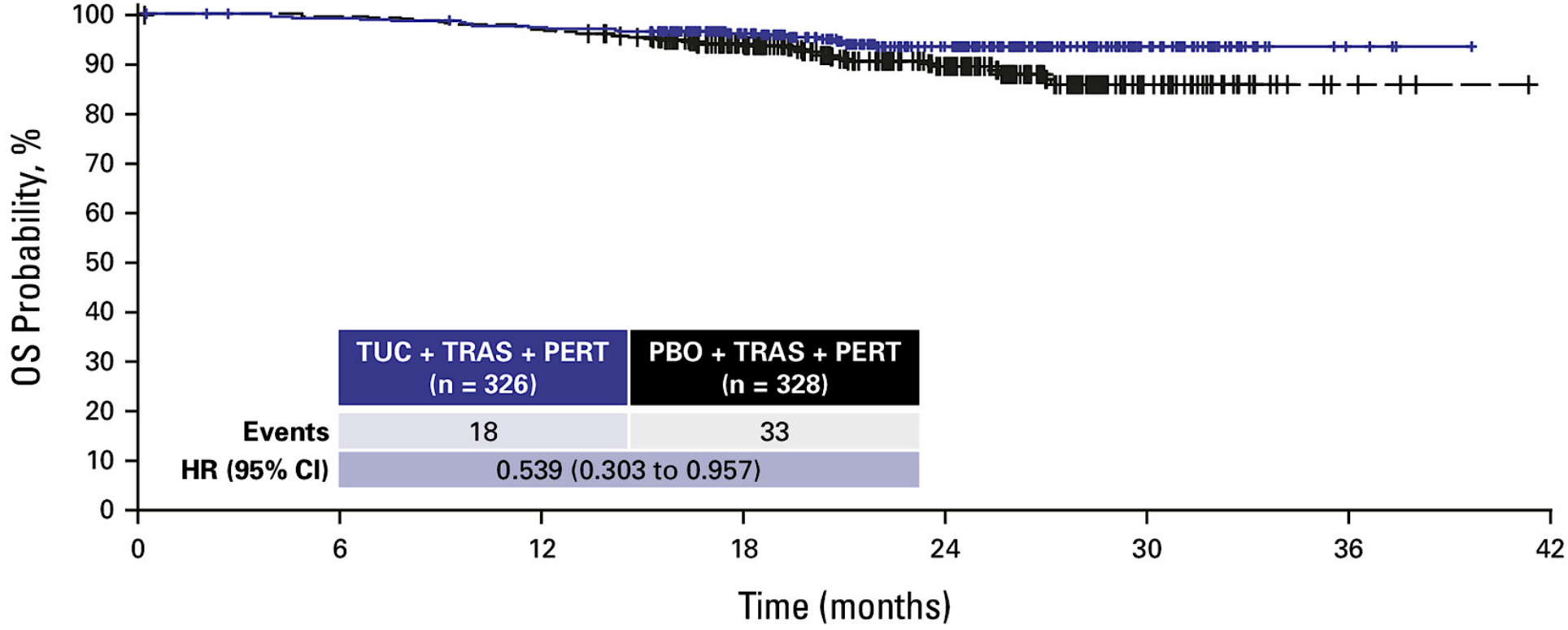


HR-positive



Dieras V et al. *J Clin Oncol* 2025; December 10;[Online ahead of print].

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



TUC + TRAS + PERT								
No. at risk	326	321	314	255	152	43	4	0
No. censored	0	3	4	59	156	265	304	308
PBO + TRAS + PERT								
No. at risk	328	326	317	249	151	41	4	0
No. censored	0	1	1	60	148	254	291	295

Dieras V et al. *J Clin Oncol* 2025; December 10;[Online ahead of print].

Phase III HER2CLIMB-05: Safety and Common Adverse Events

Safety Parameter	TUC + TRAS + PERT (n = 326), No. (%)	PBO + TRAS + PERT (n = 324), No. (%)
Patients with TEAE		
Any	323 (99.1)	313 (96.6)
Grade ≥3	138 (42.3)	79 (24.4)
Serious TEAE	55 (16.9)	26 (8.0)
Leading to death	1 (0.3)[a]	1 (0.3)

	TUC + TRAS + PERT (n = 326), No. (%)		PBO + TRAS + PERT (n = 324), No. (%)	
TEAE	All Grades	Grade ≥3	All Grades	Grade ≥3
Any	323 (99.1)	138 (42.3)	313 (96.6)	79 (24.4)
Diarrhea	237 (72.7)	20 (6.1)	166 (51.2)	13 (4.0)
Nausea	108 (33.1)	3 (0.9)	76 (23.5)	3 (0.9)
ALT increased	92 (28.2)	44 (13.5)	23 (7.1)	2 (0.6)
AST increased	84 (25.8)	23 (7.1)	29 (9.0)	2 (0.6)
Arthralgia	67 (20.6)	2 (0.6)	75 (23.1)	1 (0.3)
Fatigue	67 (20.6)	2 (0.6)	41 (12.7)	4 (1.2)
Vomiting	64 (19.6)	1 (0.3)	45 (13.9)	1 (0.3)

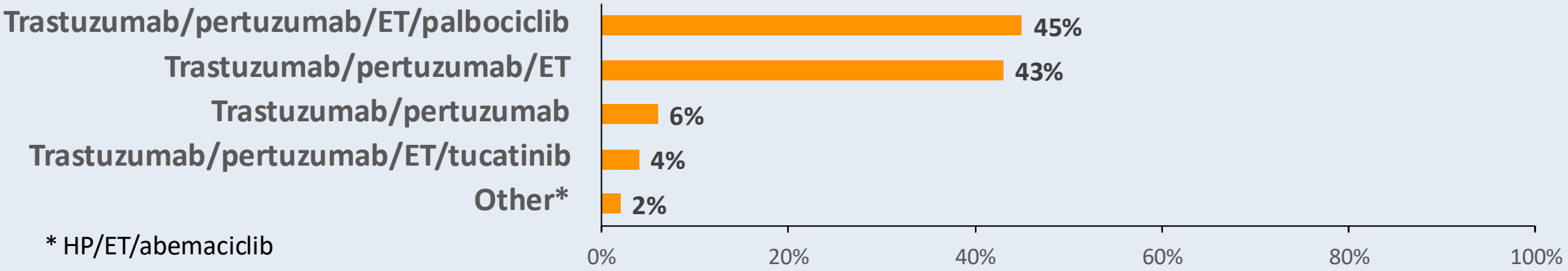
TEAE = treatment-emergent adverse event

Dieras V et al. *J Clin Oncol* 2025; December 10;[Online ahead of print].

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?

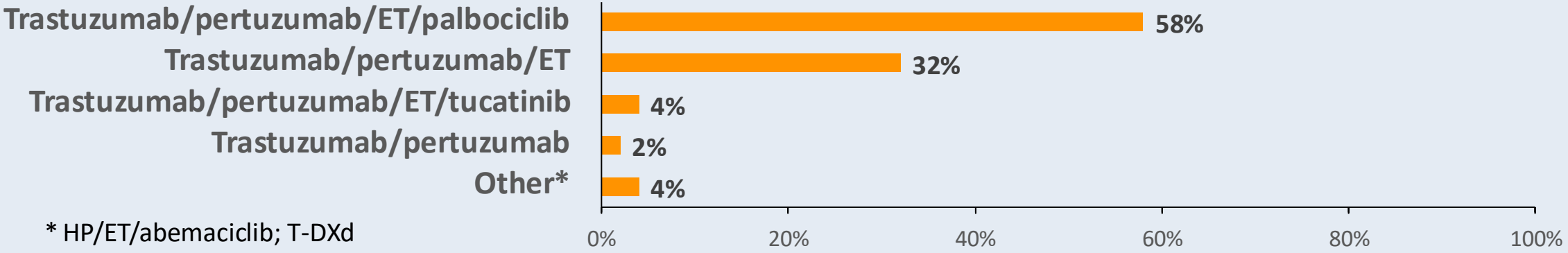
Age 65, PS 0

Achieved a complete response:



* HP/ET/abemaciclib

Achieved a partial response:



* HP/ET/abemaciclib; T-DXd

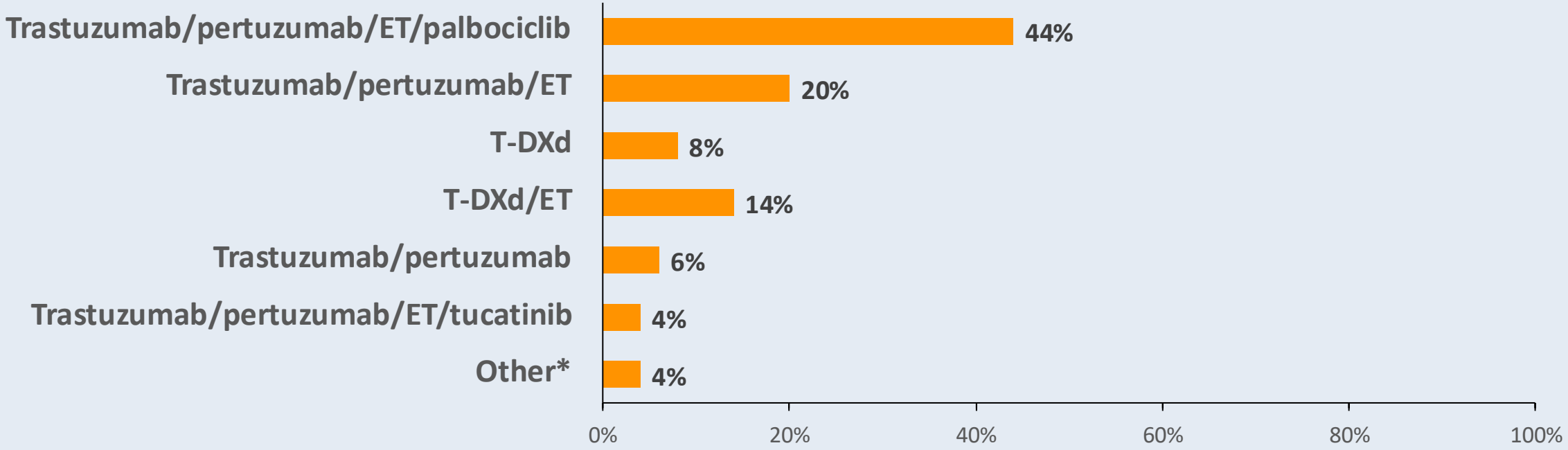
Survey of US-based general medical oncologists

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

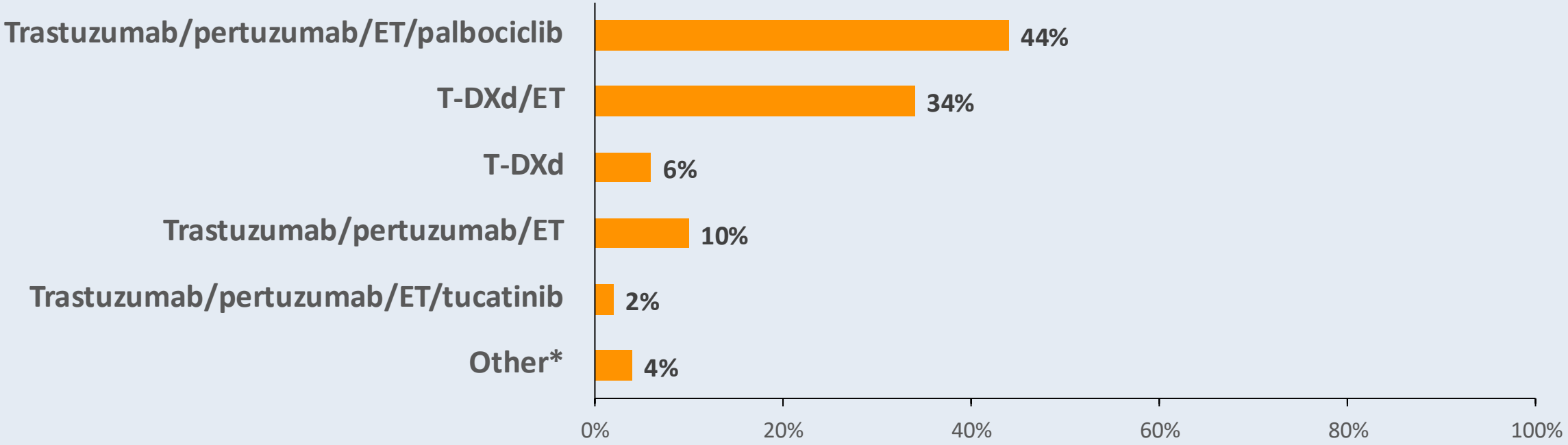
Survey of US-based general medical oncologists

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

Achieved a partial response:

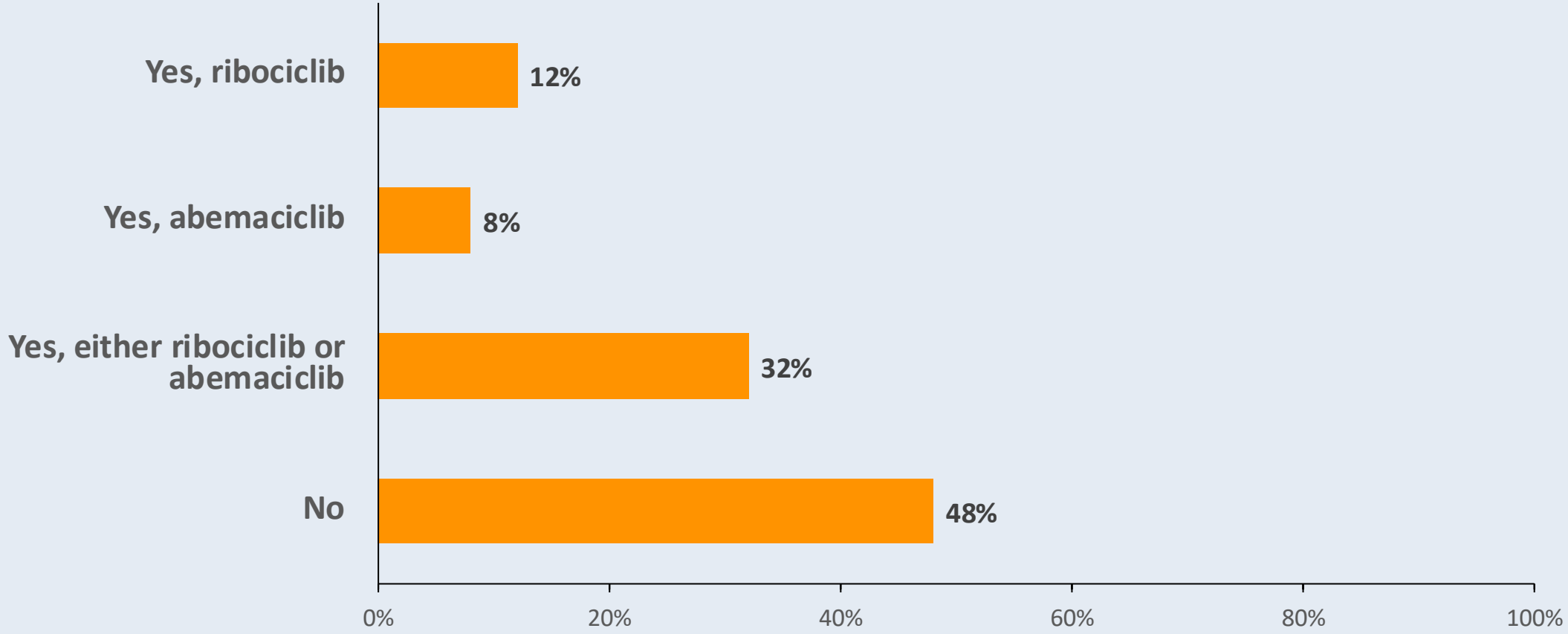


* T-DXd/P/ET; T-DXd/pertuzumab/ET

Survey of US-based general medical oncologists

RTP RESEARCH TO PRACTICE

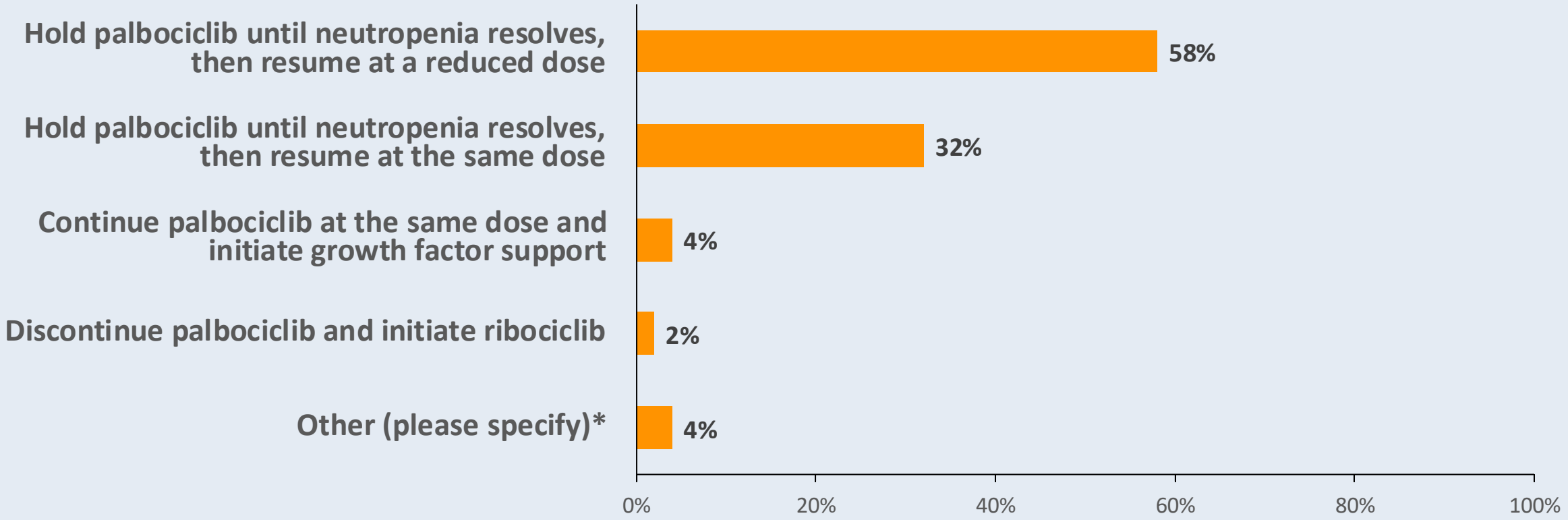
Other than palbociclib, would you use any other CDK4/6 inhibitor in combination with maintenance HER2-targeted therapy and endocrine therapy after induction treatment for HR-positive, HER2-positive mBC?



Survey of US-based general medical oncologists

RTP RESEARCH TO PRACTICE

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?

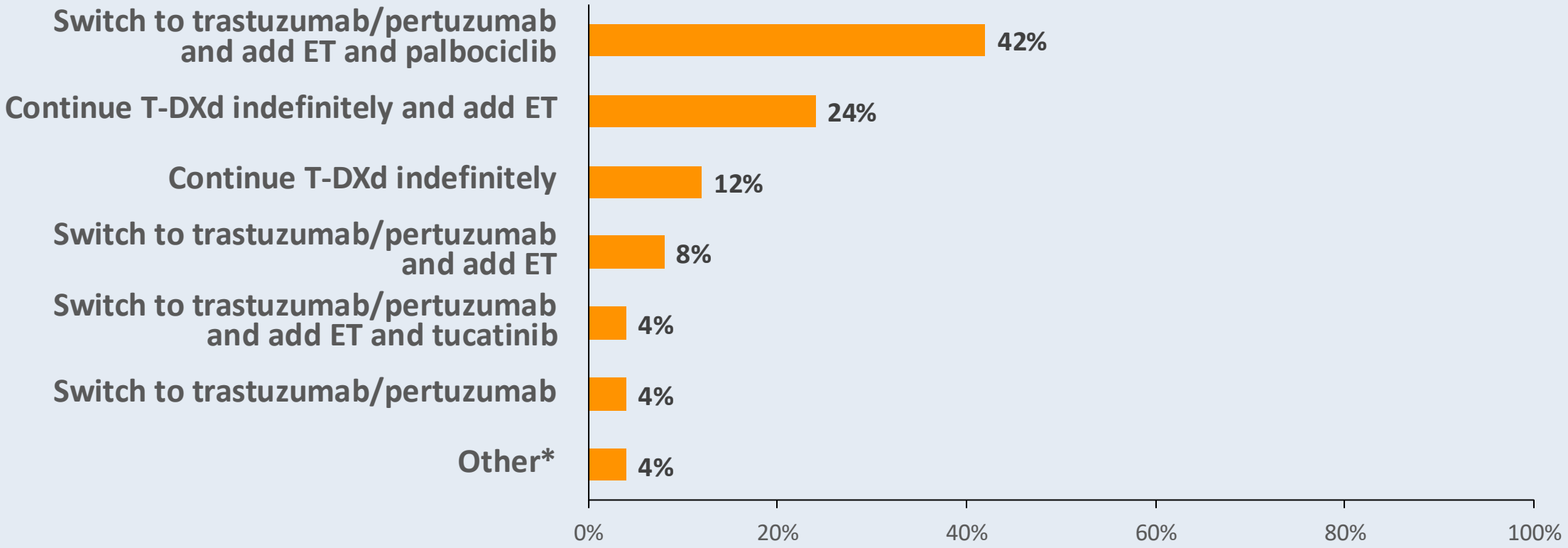


* ANC can run low on palbo but does not appear to increase infection, I would use lower threshold such as ANC < 500; Reduce dose and also change schedule

Survey of US-based general medical oncologists

RTP RESEARCH TO PRACTICE

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

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RTP RESEARCH TO PRACTICE

Agenda

Introduction: Biology of "Triple-Positive" Breast Cancer; Implications for Therapeutic Development

Module 1: Cases from the GMO Survey

Module 2: First-Line Therapy for Metastatic HER2-Positive Disease

Module 3: Cases from the GMO Survey

Module 4a: Maintenance Therapy for HR-Positive, HER2-Positive Disease

Module 4b: Maintenance Therapy for HR-Negative, HER2-Positive Disease

Module 5: Ongoing Clinical Trials Attempting to Address These Decisions

Module 6: Cases from the GMO Survey

Questions About Maintenance Treatment for HR-Negative, HER2-Positive Disease

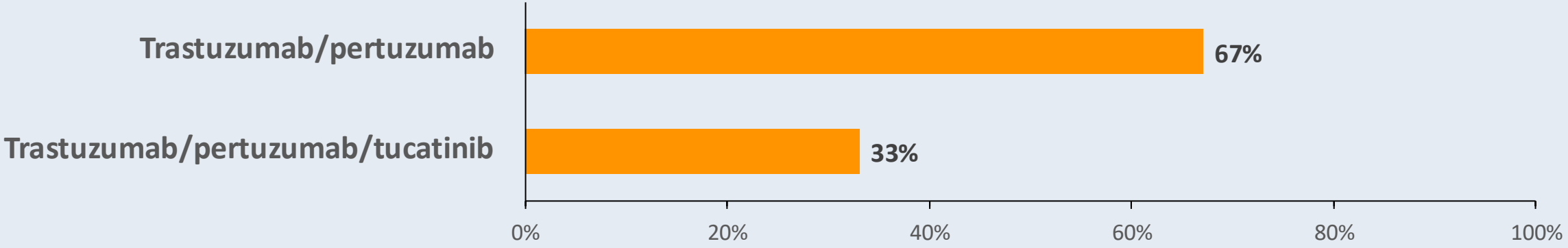
- What is your usual approach to maintenance therapy for a patient with HR-negative, HER2-positive metastatic disease?
- How, if at all, does your choice of induction therapy impact your approach to maintenance?
- What duration of maintenance therapy do you employ, assuming the patient has acceptable treatment tolerance?
- Does your approach change if the patient is younger (40) or older (85)?
- In what situations, if any, are you recommending tucatinib in this setting?

RTP RESEARCH TO PRACTICE

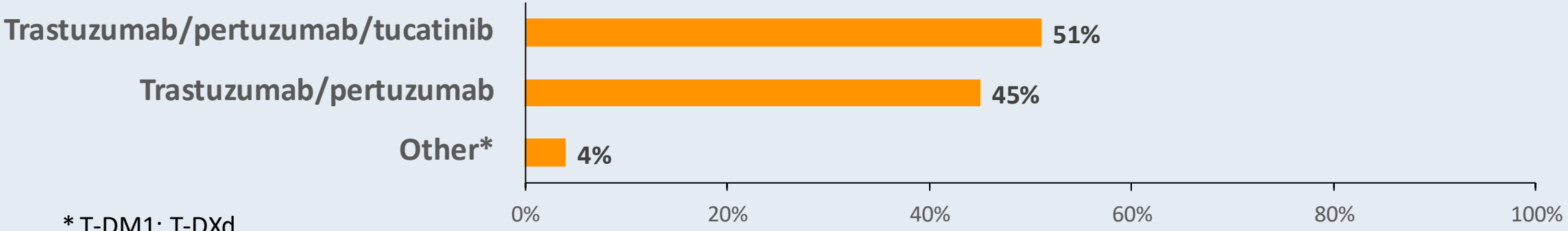
A patient with HR-negative, HER2-positive mBC receives 6 cycles of THP as first-line induction therapy. Regulatory and reimbursement issues aside, which maintenance regimen would you recommend?

Age 65, PS 0

Achieved a complete response:



Achieved a partial response:



* T-DM1; T-DXd

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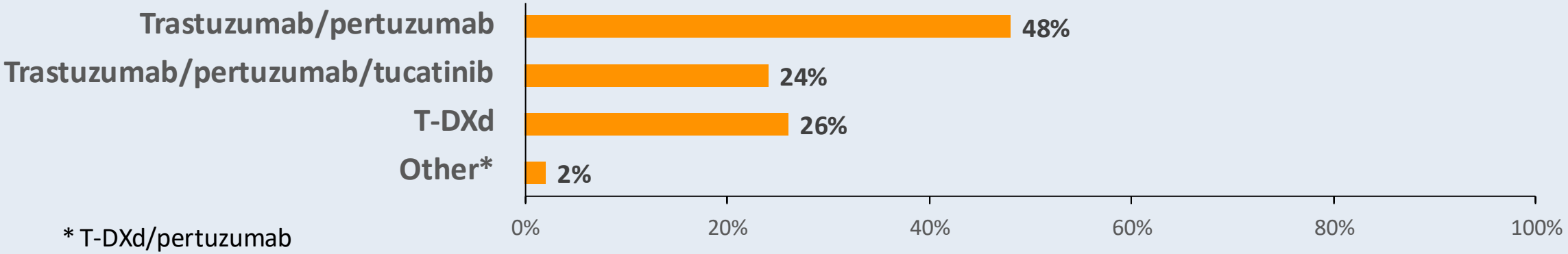
RTP RESEARCH TO PRACTICE

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?

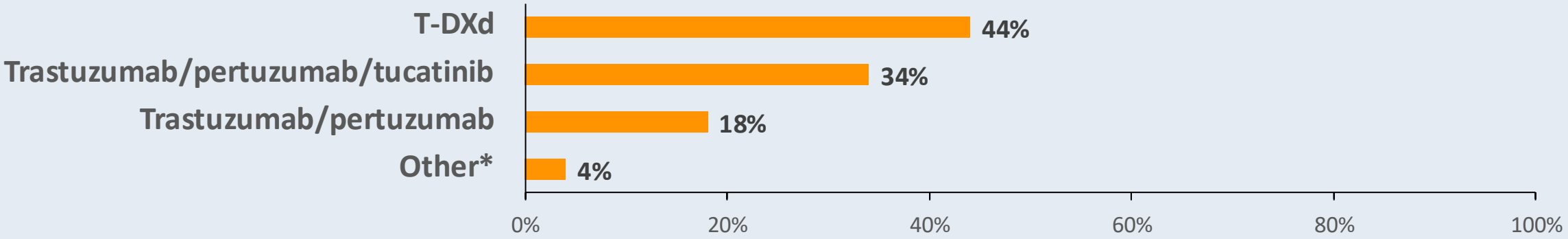
Age 65, PS 0

Achieved a complete response:



* T-DXd/pertuzumab

Achieved a partial response:



* T-DXd/pertuzumab

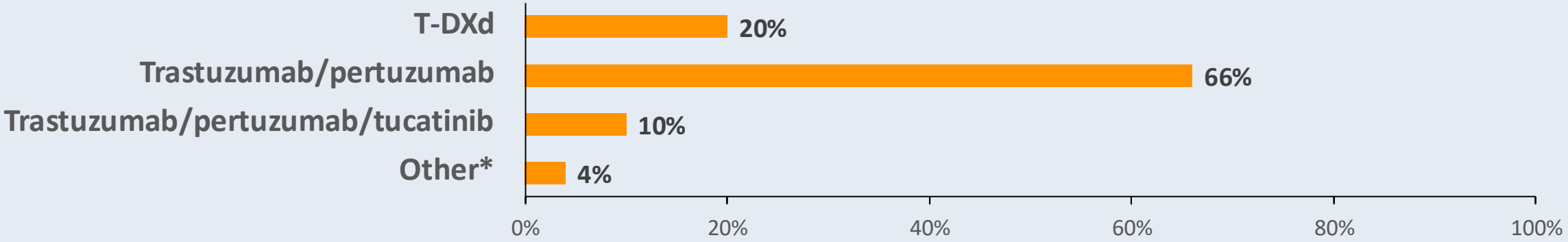
Survey of US-based general medical oncologists

RTP RESEARCH TO PRACTICE

A patient with 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?

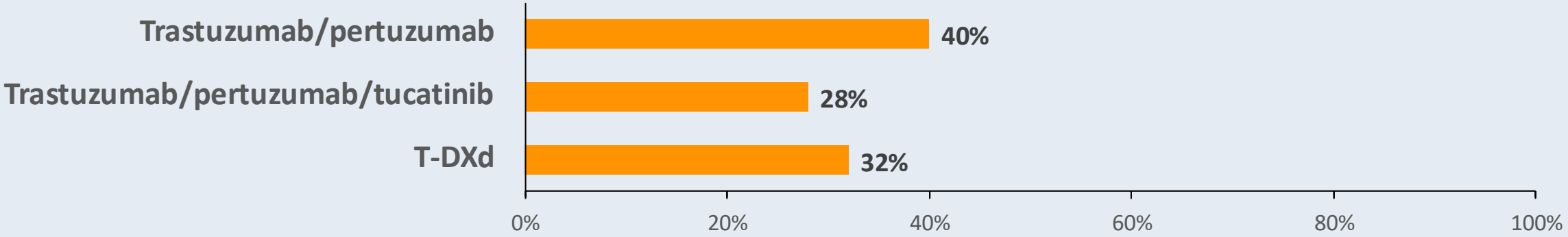
Age 85, PS 1

Achieved a complete response:



* Trastuzumab only; Capecitabine trastuzumab

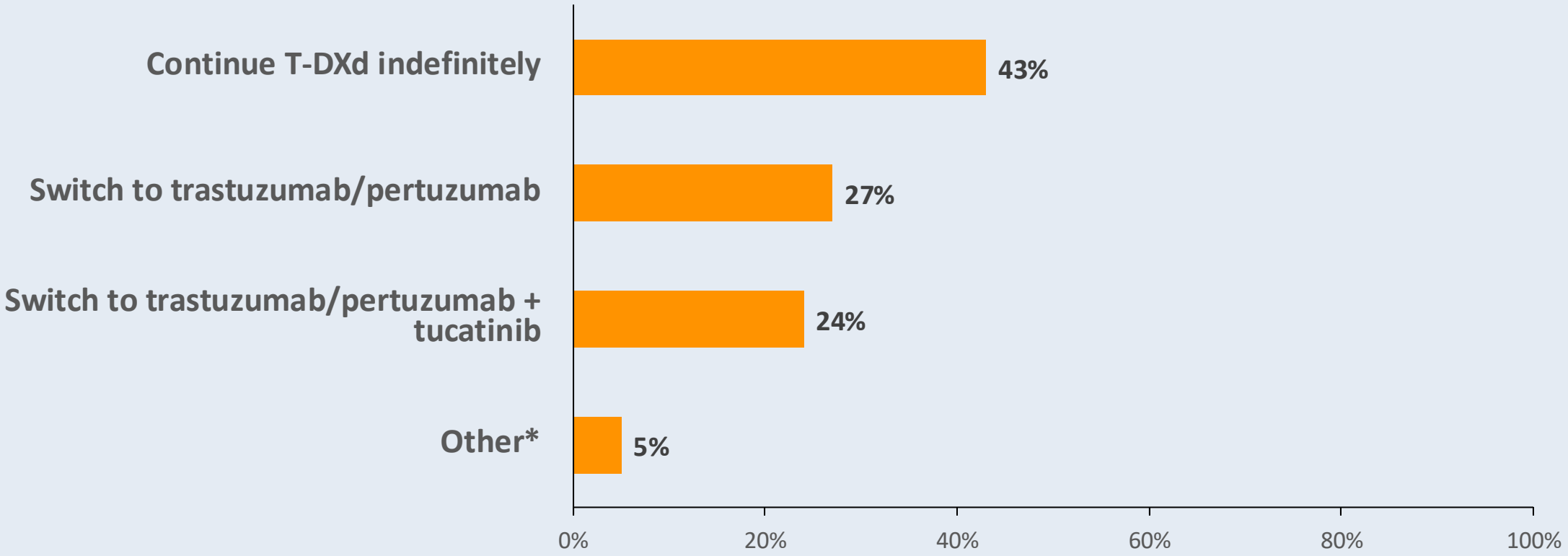
Achieved a partial response:



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

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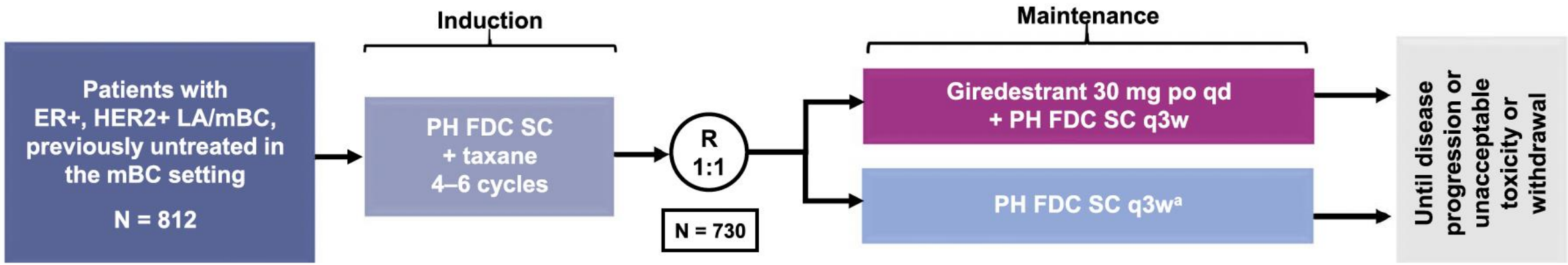
Module 5: Ongoing Clinical Trials Attempting to Address These Decisions

Module 6: Cases from the GMO Survey

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



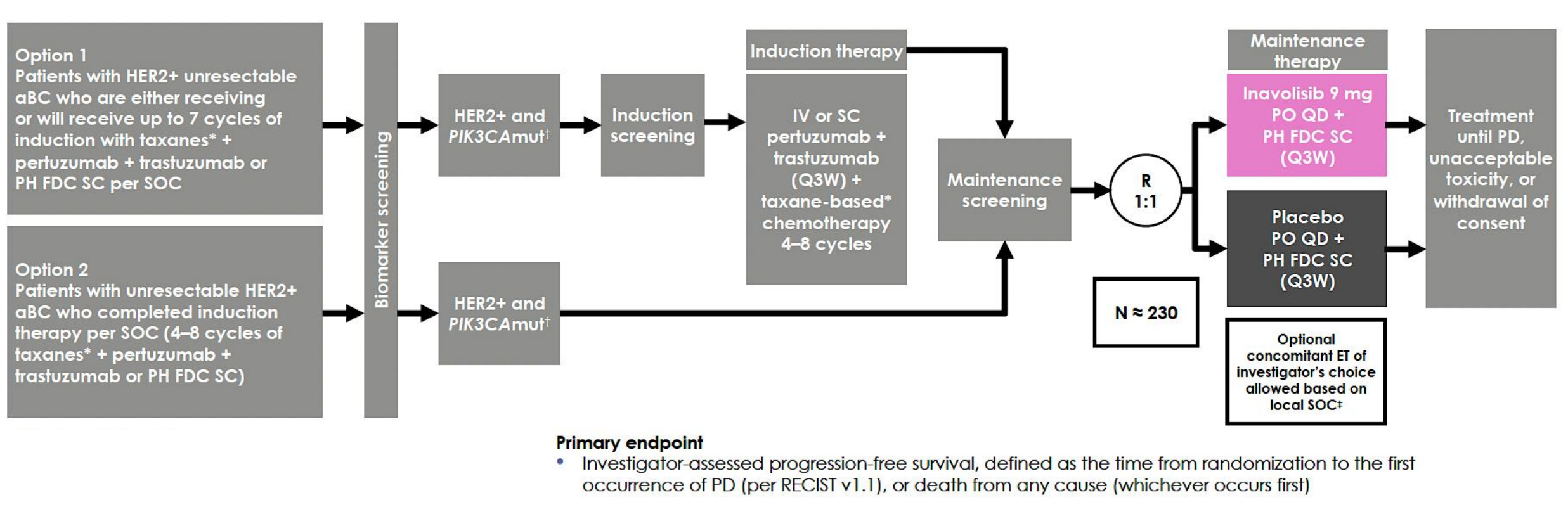
Stratification factors

- 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.

Select Other Ongoing Trials in the Front-Line Setting for HR-Positive, HER2-Positive mBC

Trial identifier	Phase	Status	Intervention
NCT03304080	I/II	Active, not recruiting	Anastrozole + palbociclib + trastuzumab + pertuzumab
FAVOR (NCT04337658)	III	Not yet recruiting	Pertuzumab + trastuzumab + fulvestrant Pertuzumab + trastuzumab + capecitabine
NCT04646759	III	Recruiting	Fulvestrant + pyrotinib Capecitabine + pyrotinib

www.clinicaltrials.gov. Accessed March 2026.

RTP RESEARCH TO PRACTICE

Agenda

Introduction: Biology of "Triple-Positive" Breast Cancer; Implications for Therapeutic Development

Module 1: Cases from the GMO Survey

Module 2: First-Line Therapy for Metastatic HER2-Positive Disease

Module 3: Cases from the GMO Survey

Module 4a: Maintenance Therapy for HR-Positive, HER2-Positive Disease

Module 4b: Maintenance Therapy for HR-Negative, HER2-Positive Disease

Module 5: Ongoing Clinical Trials Attempting to Address These Decisions

Module 6: Cases from the GMO Survey

RTP RESEARCH TO PRACTICE

Cases from General Medical Oncologists

59 yo woman

- **Early stage breast cancer in 2007 (ER+, HER2 1+) s/p lumpectomy, chemo, RT. Did not tolerate tamoxifen.**
- **Metastatic disease 2024 with chest wall mass: multiple therapies including capivasertib/ fulvestrant (PIK3+).**
- **Most recent biopsy of the chest wall mass: ER+, PR-, HER2 3+.**

What will be your next treatment? No prior CDK. Would you recommend CDK4 and anti-HER2 maintenance treatment?

RTP RESEARCH TO PRACTICE

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?
Any role for SRS or Gamma Knife?

Cases from General Medical Oncologists

78 yr old woman (second opinion)

- **De novo metastatic right breast cancer. ER 80% PR 70% HER2 1+/FISH positive.**
- **Symptomatic bone Mets, right pleural effusion, rt pleural nodules and multiple liver Mets.**
- **Treatment: anastrozole and ribociclib.**
- **FISH was tested and was positive (end of Feb 2026).**
- **NGS: FGFR1 amplification, ESR1 amplification (not mutation).**
- **Pt has stable disease in anastrozole and ribociclib but now has HER2 positive disease.**

What treatment will you give?

1. **Paclitaxel, trastuzumab and pertuzumab**
2. **Anastrozole, trastuzumab and pertuzumab**
3. **PATINA trial — anastrozole, palbo and H and P**

What is the significance of ESR1 amplification? Same as ESR1 mutation?

RTP RESEARCH TO PRACTICE

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

52 year old woman

- **Triple-positive inflammatory breast cancer.**
- **Neoadjuvant TCHP, mastectomy, axillary dissection with positive nodes, radiation and T-DM1.**
- **Relapsed 2 years later with intracranial-only disease.**
- **Very symptomatic in terms of headaches and unilateral weakness.**
- **This patient got HER2CLIMB regimen (plus brain RT given so symptomatic). This was prior to T-DXd trial.**

Would you use T-DXd/pertuzumab now?

RTP RESEARCH TO PRACTICE

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?

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

Prostate Cancer

A CME/MOC-Accredited Live Webinar

Wednesday, March 25, 2026
5:00 PM – 6:00 PM ET

Faculty

Andrew J Armstrong, MD, ScM
Scott T Tagawa, MD, MS

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, ABIM MOC and ABS 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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