Meet The Professor

Optimizing the Selection and Sequencing of Therapy for Patients with HER2-Positive Breast Cancer

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Associate Director, Susan F Smith Center for Women's Cancers
Director of Clinical Trials, Breast Oncology
Director of Breast Immunotherapy Clinical Research
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Commercial Support

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Dr Love — Disclosures

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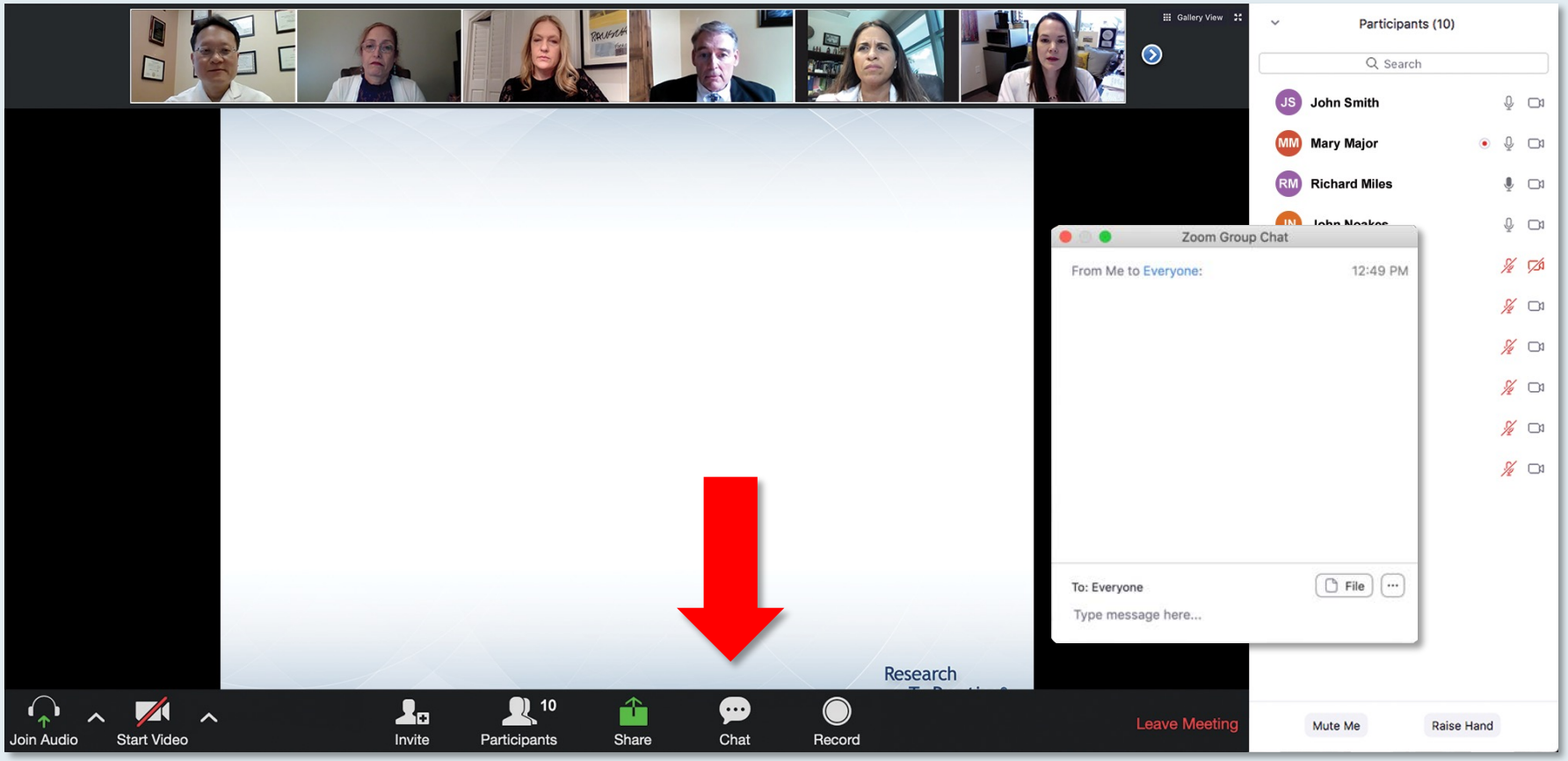

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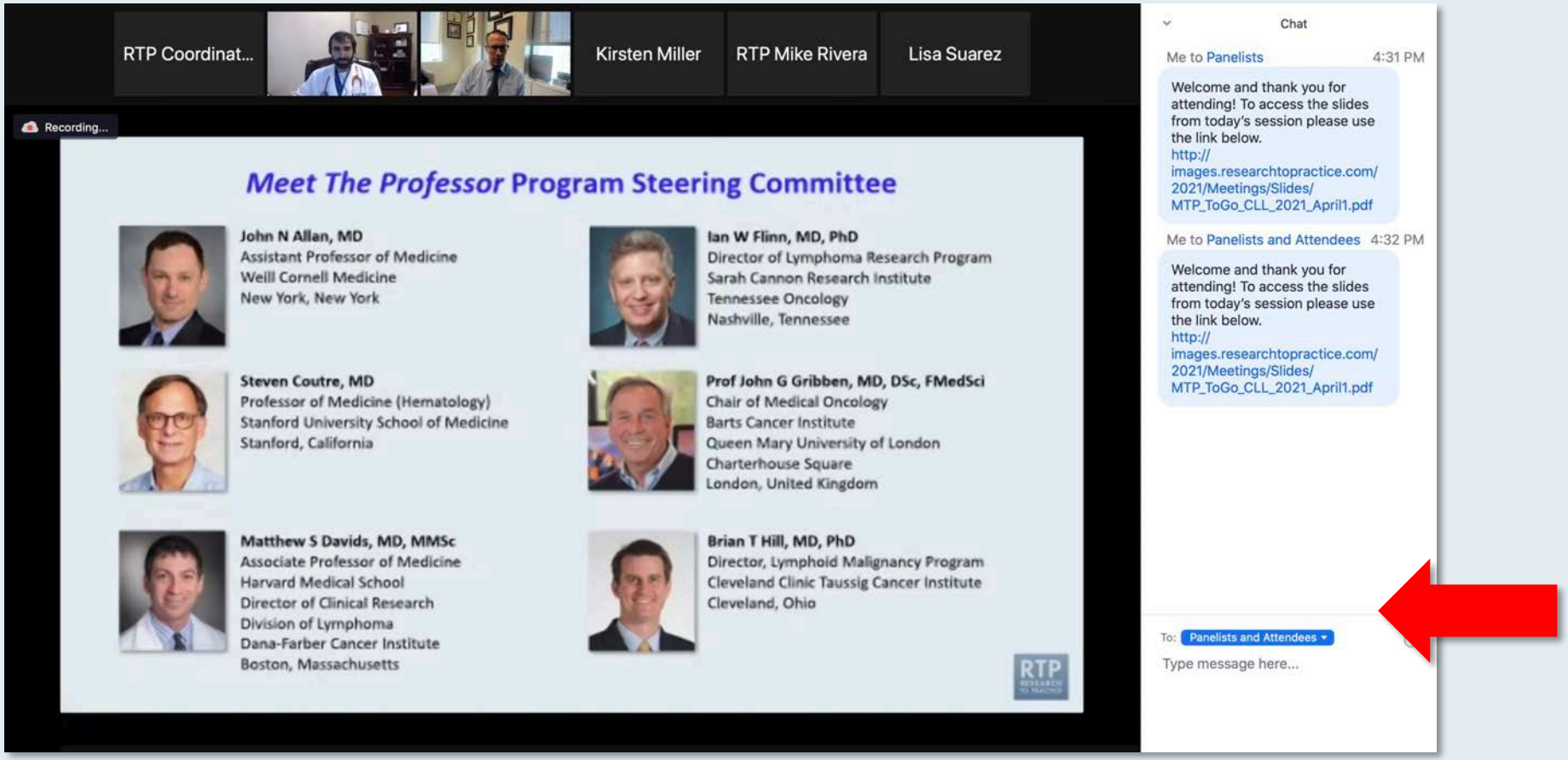

Drag the white line above the submission box up to create more space for your message.

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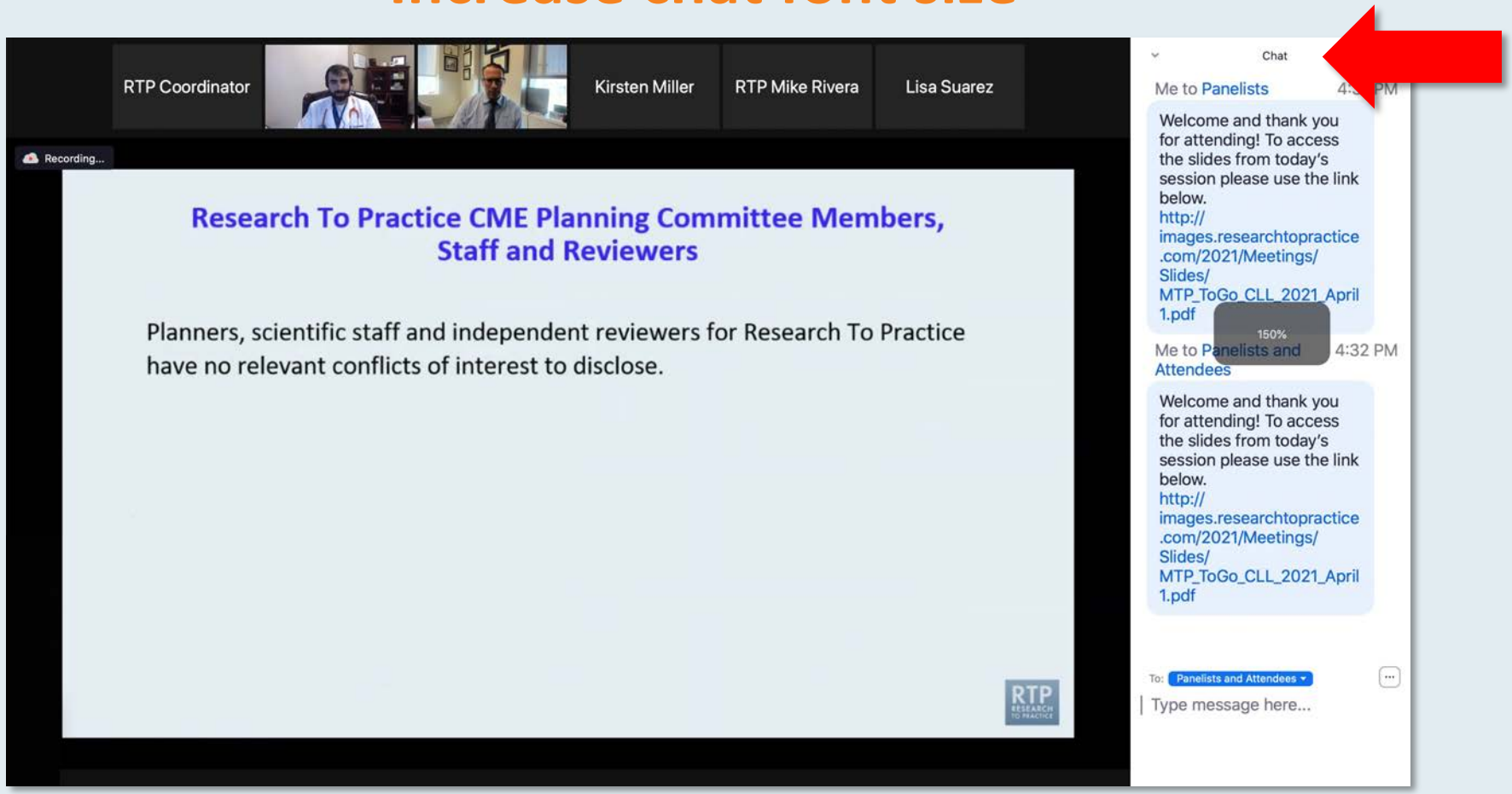

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WITH DR NEIL LOVE

Key Presentations on Breast Cancer from the 2021 ASCO Annual Meeting

DR SARA TOLANEY

DANA-FARBER CANCER INSTITUTE

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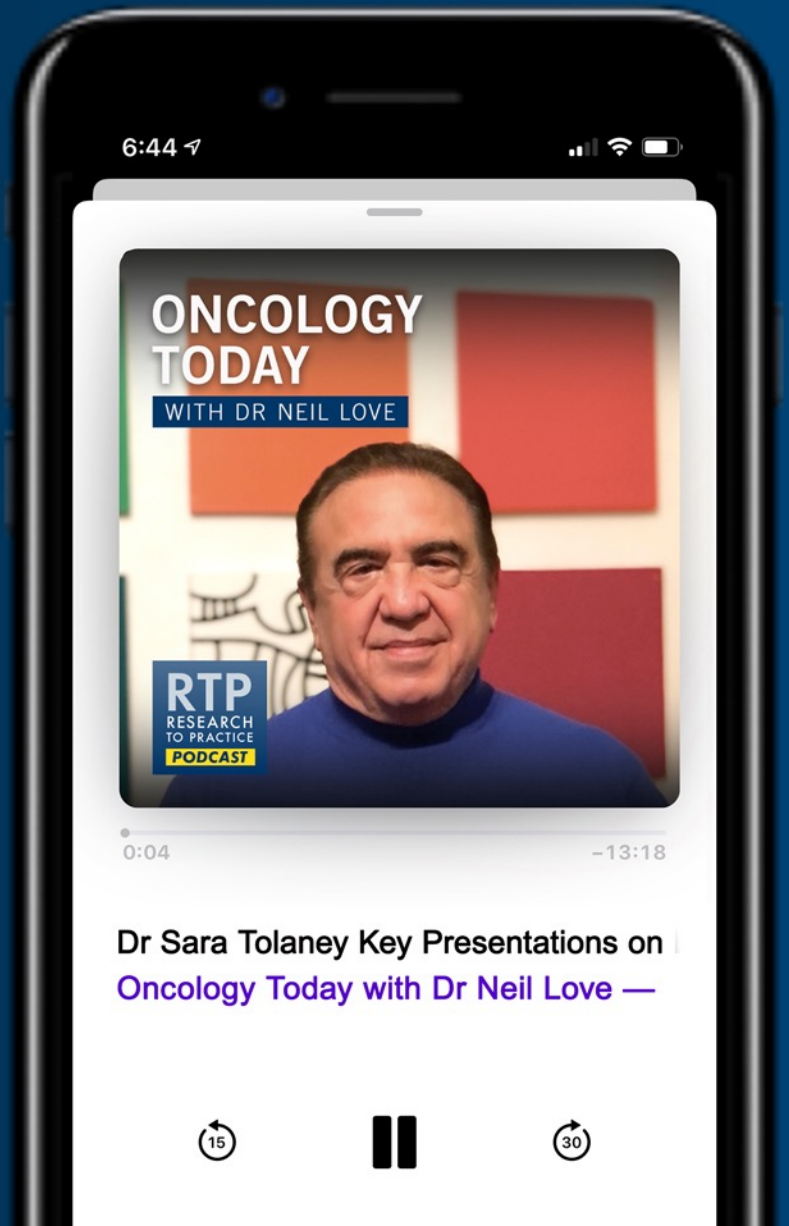

Fall Oncology Nursing Series

A Complimentary NCPD-Accredited Virtual Curriculum

Hodgkin and Non-Hodgkin Lymphomas

Thursday, September 23, 2021
5:00 PM – 6:00 PM ET

Faculty

John P Leonard, MD
Amy Goodrich, CRNP

Moderator

Neil Love, MD

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Meet The Professor

Immunotherapy and Novel Agents in Gynecologic Cancers

Friday, September 24, 2021
12:00 PM – 1:00 PM ET

Faculty

Martee L Hensley, MD, MSc

Moderator

Neil Love, MD

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Meet The Professor

Optimizing the Selection and Sequencing of Therapy for Patients with Advanced Gastrointestinal Cancers

Monday, September 27, 2021
5:00 PM – 6:00 PM ET

Faculty

Zev Wainberg, MD, MSc

Moderator

Neil Love, MD

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RESEARCH TO PRACTICE

Meet The Professor

Optimizing the Selection and Sequencing of Therapy for Patients with Triple-Negative Breast Cancer

Tuesday, September 28, 2021
5:00 PM – 6:00 PM ET

Faculty

Professor Peter Schmid, MD, PhD

Moderator

Neil Love, MD

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RESEARCH TO PRACTICE

Meet The Professor

Optimizing the Clinical Management of Hodgkin and Non-Hodgkin Lymphomas

Wednesday, September 29, 2021
5:00 PM – 6:00 PM ET

Faculty

Brad S Kahl, MD

Moderator

Neil Love, MD

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Meet The Professor

Optimizing the Selection and Sequencing of Therapy for Patients with Renal Cell Carcinoma

Friday, October 1, 2021
12:00 PM – 1:00 PM ET

Faculty

Hans Hammers, MD, PhD

Moderator

Neil Love, MD

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Identifying, Managing and Mitigating Therapy-Related Adverse Events in Patients with Chronic Lymphocytic Leukemia and Mantle Cell Lymphoma

A CME/MOC-Accredited Virtual Event

Monday, October 4, 2021
5:00 PM – 6:00 PM ET

Faculty

Richard R Furman, MD
Lindsey Roeker, MD

Consulting Cardiologist

Daniel J Lenihan, MD

Moderator

Neil Love, MD

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RESEARCH TO PRACTICE

Meet The Professor

Optimizing the Selection and Sequencing of Therapy for Patients with ER-Positive Breast Cancer

Wednesday, October 6, 2021
5:00 PM – 6:00 PM ET

Faculty

Virginia Kaklamani, MD, DSc

Moderator

Neil Love, MD

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Thank you for joining us!

CME and MOC credit information will be emailed to each participant within 5 business days.

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Associate Professor of Medicine
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Meet The Professor Program Participating Faculty

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Professor of Medicine
University of British Columbia
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Director, Breast Cancer Clinical Research Program
Co-Director, Santa Monica-UCLA Outpatient Oncology Practice
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Erika Hamilton, MD
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Reshma Mahtani, DO
Associate Professor of Medicine
Co-Leader, Breast Cancer Program
Sylvester Cancer Center
University of Miami
Miami, Florida

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Meet The Professor Program Participating Faculty

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Professor of Medicine
Director, Breast Oncology and Clinical Trials Education
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Helen Diller Family Comprehensive Cancer Center
San Francisco, California

Moderator
Neil Love, MD
Research To Practice
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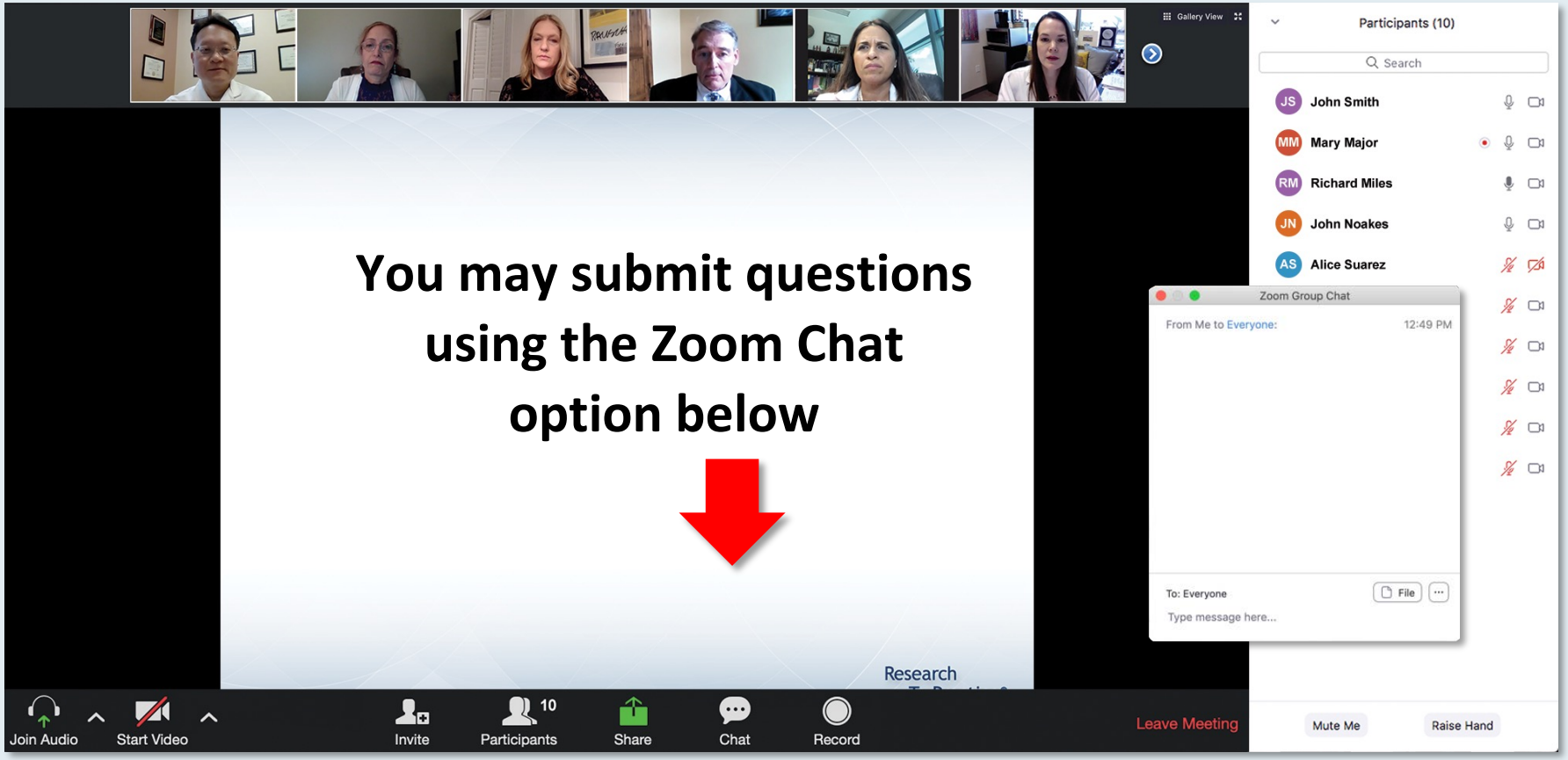

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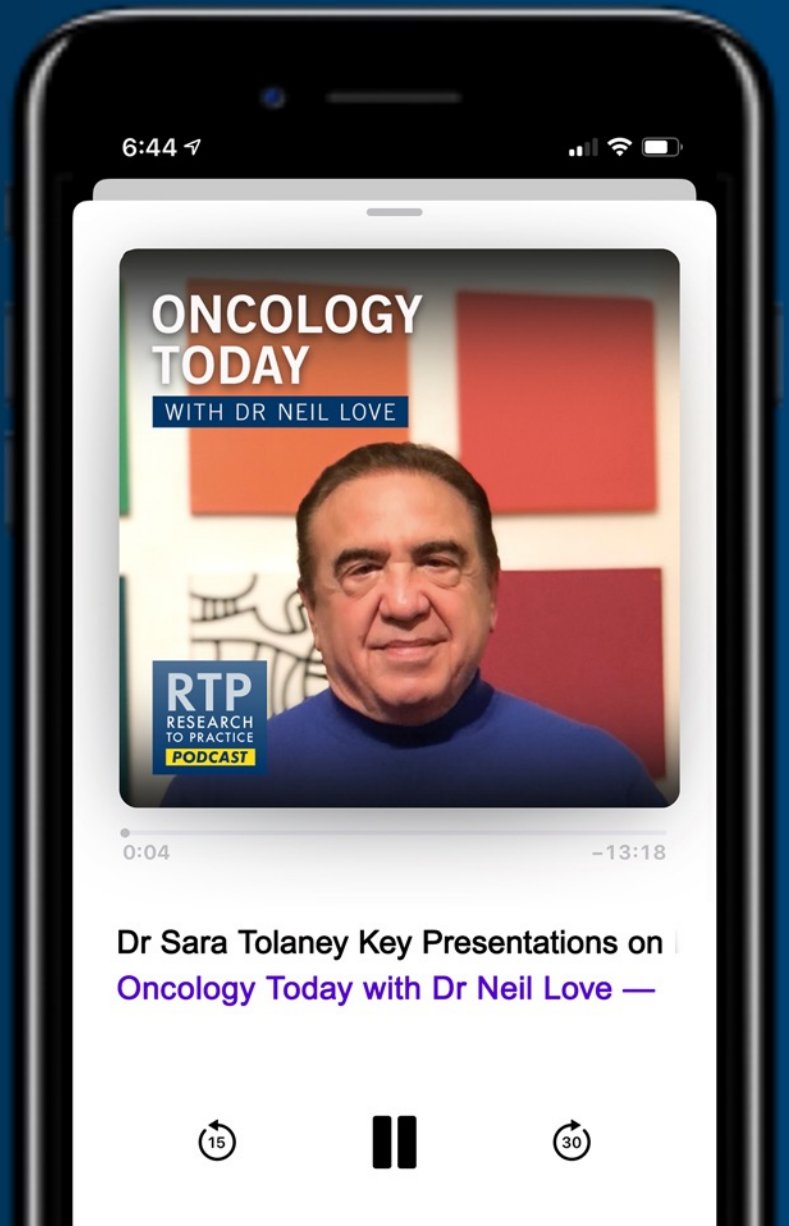

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Sulfi Ibrahim, MD
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Assistant Clinical Professor
City of Hope
Arcadia, California

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Meet The Professor with Dr Tolaney

Introduction: DESTINY-Breast03

MODULE 1: Case Presentations

- Dr Favaro: A 52-year-old woman with ER/PR-negative, HER2-positive breast cancer with bone, lung, liver and brain metastases
- Dr Ibrahim: A 74-year-old woman with ER-positive, PR-negative, HER2-positive metastatic breast cancer
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MODULE 2: Journal Club with Dr Tolaney

MODULE 3: Beyond the Guidelines

MODULE 4: Key Data Sets

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Trastuzumab Deruxtecan Significantly Improved PFS Over T-DM1 for HER2-Positive Metastatic Breast Cancer

Press Release – August 9, 2021

"Trastuzumab deruxtecan demonstrated superior progression-free survival (PFS) outcomes over trastuzumab emtansine (T-DM1) in patients with HER2-positive metastatic breast cancer, based on the phase 3 DESTINY-Breast03 trial (NCT03529110). The study's planned interim analysis identified a statistically significant and clinically meaningful improvement in the primary end point of PFS as assessed by an Independent Data Monitoring Committee (IDMC) for patients with HER2-positive, unresectable and/or metastatic breast cancer who received prior treatment with trastuzumab and a taxane.

Approximately 500 patients were enrolled in the DESTINY-Breast03 trial, who were randomized to either the experimental trastuzumab deruxtecan arm or the comparator T-DM1 arm. The primary end point was PFS assessed by IDMC, with secondary end points including overall survival (OS), objective response rate (ORR), duration of response, and PFS based on investigator assessment.

While patients treated with trastuzumab deruxtecan trended toward OS improvement, the data were immature. Furthermore, the safety profile was consistent with previously reported data regarding trastuzumab deruxtecan, with no new safety signals or grade 4/5 treatment-related interstitial lung disease events observed."

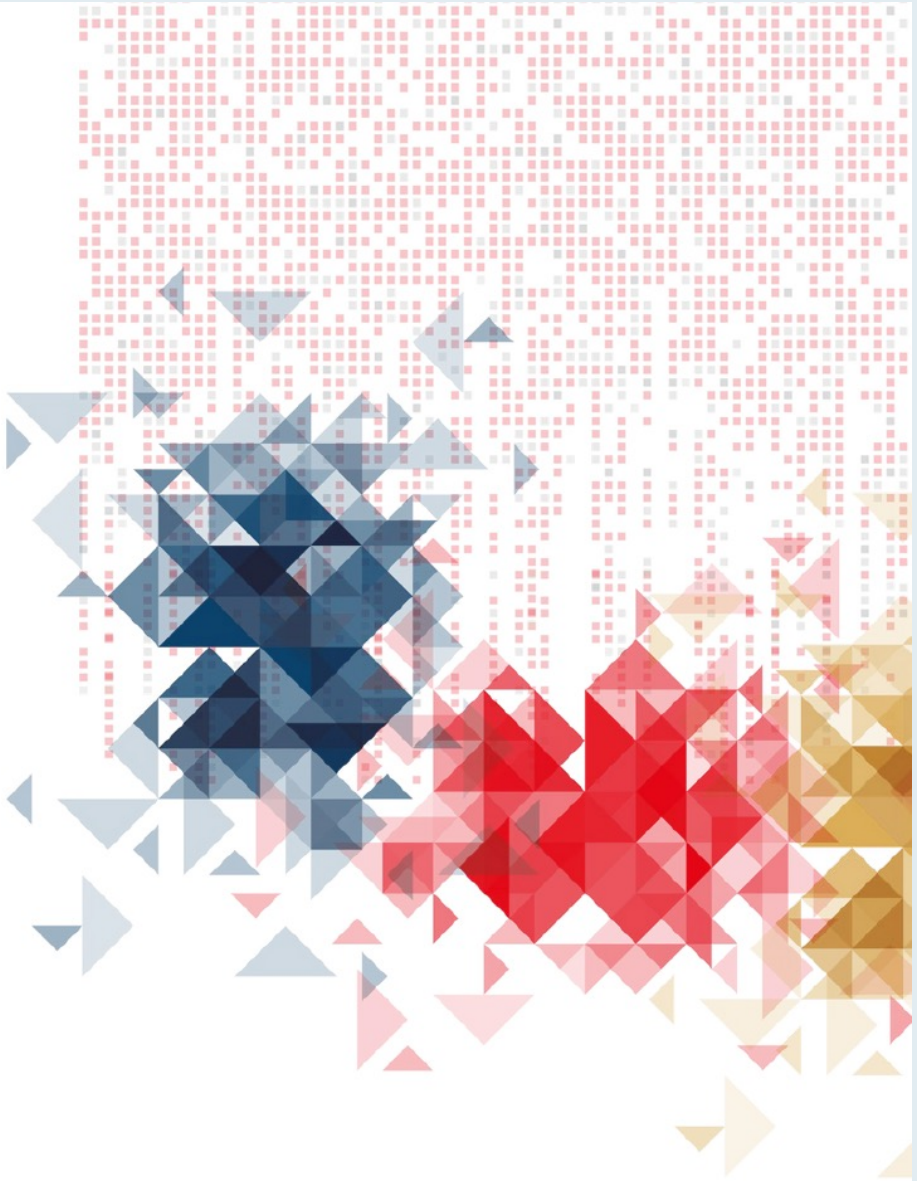
https://www.cancernetwork.com/view/trastuzumab-deruxtecan-significantly-improved-pfs-over-tdm-1-for-her2-metastatic-breast-cancer

2021 ESMO congress

Trastuzumab Deruxtecan (T-DXd) vs Trastuzumab Emtansine (T-DM1) in Patients With HER2+ Metastatic Breast Cancer: Results of the Randomized, Phase 3 Study DESTINY-Breast03

Javier Cortés, MD[a], Sung-Bae Kim, Wei-Pang Chung, Seock-Ah Im, Yeon Hee Park, Roberto Hegg, Min-Hwan Kim, Ling-Ming Tseng, Vanessa Petry, Chi-Feng Chung, Hiroji Iwata, Erika Hamilton, Giuseppe Curigliano, Binghe Xu, Caleb Lee, Yali Liu, Jillian Cathcart, Emarjola Bako, Sunil Verma, Sara Hurvitz
On behalf of the DESTINY-Breast03 investigators

[a]Medical Oncology, International Breast Cancer Center (IBCC), Quironsalud Group, and Vall d'Hebron Institute of Oncology (VHIO), Barcelona, Spain; Universidad Europea de Madrid, Faculty of Biomedical and Health Sciences, Department of Medicine, Madrid, Spain.



Abstract LBA1

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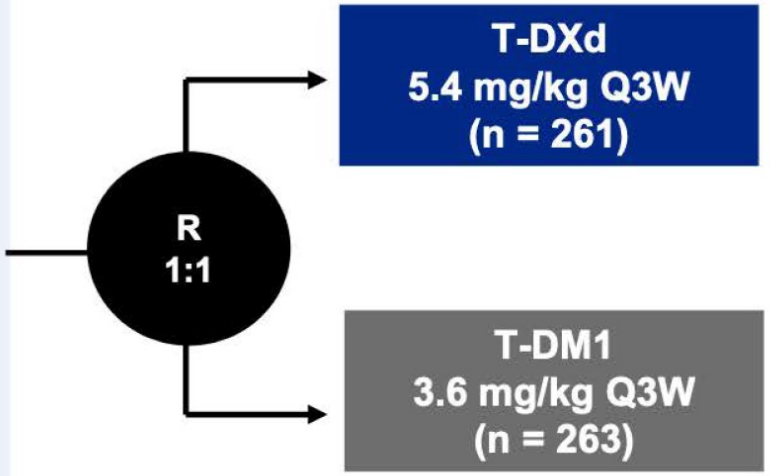
DESTINY-Breast03 Phase III Trial Schema

An open-label, multicenter study (NCT03529110)

Patients
- Unresectable or metastatic HER2-positive[a] breast cancer
- Previously treated with trastuzumab and taxane in advanced/metastatic setting[b]
- Could have clinically stable, treated brain metastases

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



Primary endpoint
- PFS (BICR)

Key secondary endpoint
- OS

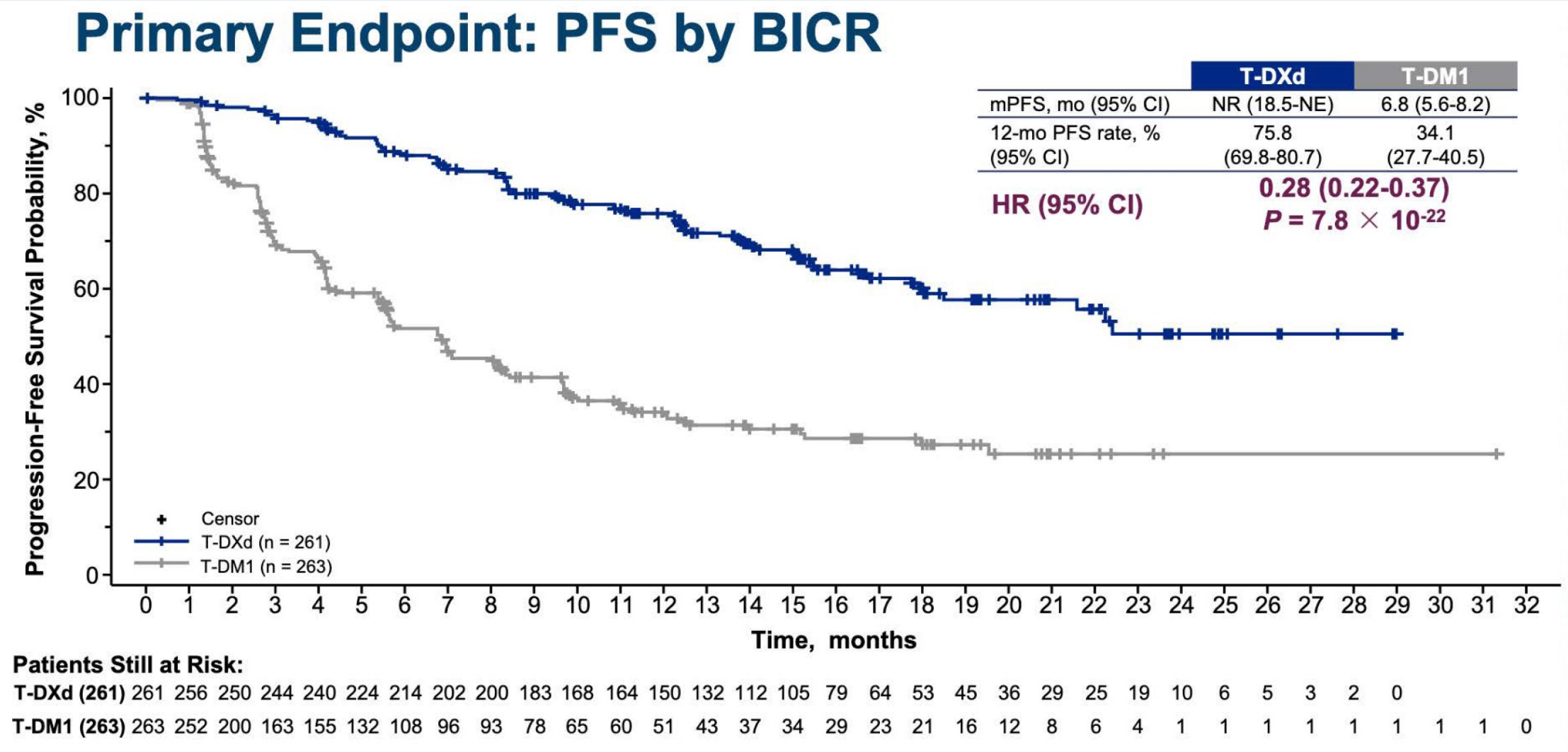
Secondary endpoints
- ORR (BICR and investigator)
- DOR (BICR)
- PFS (investigator)
- Safety

Interim analysis for PFS (data cutoff: May 21, 2021)
- Efficacy boundary for superiority: $P < 0.000204$ (based on 245 events)
- IDMC recommendation to unblind study (July 30, 2021)

Key secondary endpoint, OS: boundary for efficacy: $P < 0.000265$ (based on 86 events)

Cortés J et al. ESMO 2021;Abstract LBA1.

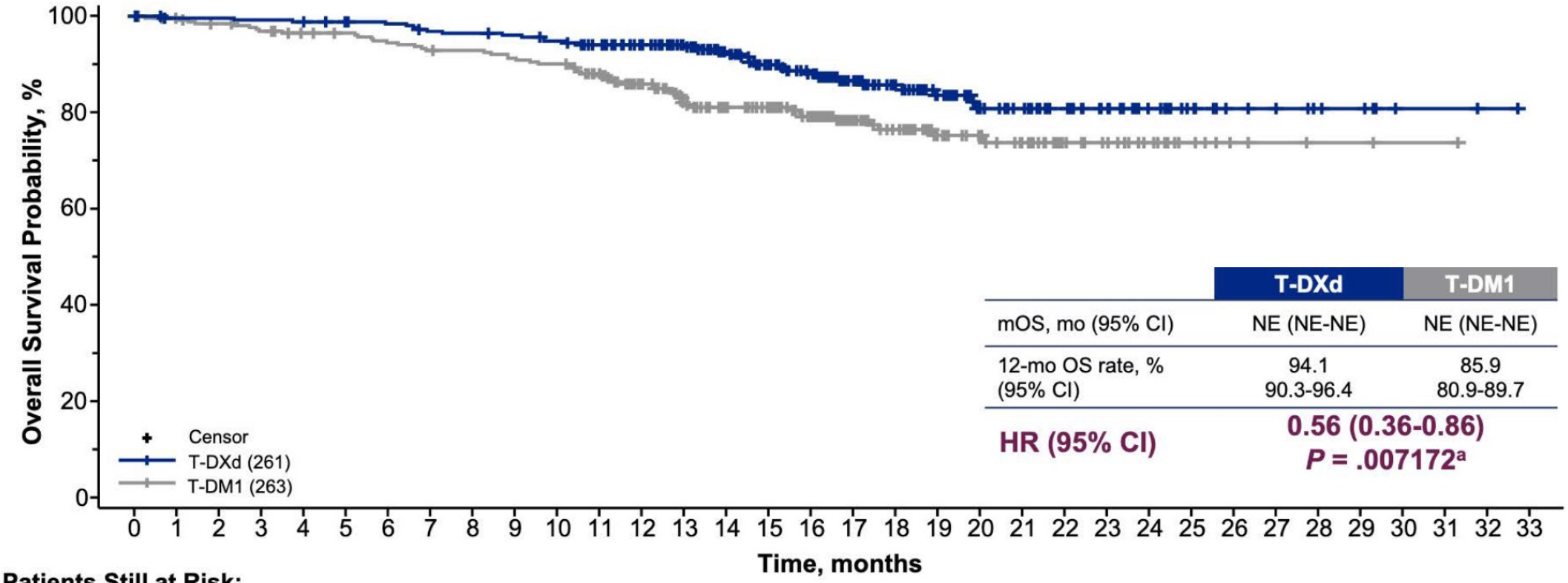
DESTINY-Breast03: PFS by BICR



Cortés J et al. ESMO 2021;Abstract LBA1.

DESTINY-Breast03: OS by BICR

Key Secondary Endpoint: OS



	T-DXd	T-DM1
mOS, mo (95% CI)	NE (NE-NE)	NE (NE-NE)
12-mo OS rate, % (95% CI)	94.1 90.3-96.4	85.9 80.9-89.7
HR (95% CI)	**0.56 (0.36-0.86)** *P* = .007172[a]	

Patients Still at Risk:

T-DXd (261)	261	256	256	255	254	251	249	244	243	241	237	230	218	202	180	158	133	108	86	71	56	50	42	33	24	18	11	10	7	6	2	2	1	0
T-DM1 (263)	263	258	253	248	243	241	236	232	231	227	224	210	188	165	151	140	120	91	75	58	52	44	32	27	18	11	5	4	3	3	1	1	0	

2021 ESMO congress

Early OS data with relatively few events (33 in the T-DXd arm, 53 in the T-DM1 arm)

[a]*P* = .007172, but does not cross pre-specified boundary of *P* < .000265

Cortés J et al. ESMO 2021;Abstract LBA1.

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DESTINY-Breast03: Adverse Events of Special Interest

Adjudicated as drug-related ILD/pneumonitis[a], n (%)						
n (%)	Grade 1	Grade 2	Grade 3	Grade 4	Grade 5	Any Grade
T-DXd (n = 257)	7 (2.7)	18 (7.0)	2 (0.8)	0	0	27 (10.5)
T-DM1 (n = 261)	4 (1.5)	1 (0.4)	0	0	0	5 (1.9)

- There were no grade 4 or 5 adjudicated drug-related ILD/pneumonitis events observed with T-DXd

LVEF decrease, n (%)						
n (%)	Grade 1	Grade 2	Grade 3	Grade 4	Grade 5	Any Grade
T-DXd (n = 257)	1 (0.4)[b]	6 (2.3)[c]	0	0	0	7 (2.7)
T-DM1 (n = 261)	0	1 (0.4)[c]	0	0	0	1 (0.4)

- In the T-DXd arm, all reported adverse events of LVEF decrease were asymptomatic and no cases of cardiac failure occurred

Cortés J et al. ESMO 2021;Abstract LBA1.

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Case Presentation – Dr Favaro: A 52-year-old woman with ER/PR-negative, HER2-positive breast cancer with bone, lung, liver and brain metastases

Dr Justin Favaro

- Docetaxel, trastuzumab and pertuzumab x 6 months → Brain metastases
- Whole brain radiation therapy, T-DM1 → CT stable, progression of brain metastases
- Tucatinib, capecitabine, trastuzumab

Question

- For patients with asymptomatic but progressive brain metastases, would you rely on tucatinib, capecitabine, trastuzumab to treat those brain metastases?

Case Presentation – Dr Ibrahim: A 74-year-old woman with ER-positive, PR-negative, HER2-positive metastatic breast cancer

Dr Sulfi Ibrahim

- Stage II ER-positive, PR-negative, HER2-positive right breast cancer
- Neoadjuvant TCHP (dose reduced due to toxicity), with residual disease in breast and lymph nodes
- Adjuvant radiation therapy → T-DM1 and letrozole → Develops lung, liver and bone metastases on T-DM1
- Stabilization of right femur due to impeding pathologic fracture
- Biopsy of bone lesion: Weakly ER-positive, HER2 IHC 2+, FISH-negative
- Trastuzumab deruxtecan, with clinical response and good tolerability

Questions

- How reliable is HER2 testing on a bone lesion?
- Is it reasonable to use trastuzumab deruxtecan in a patient like this who was HER2 positive before, but now has IHC 2+ on a bone lesion, but negative by FISH?

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Case Presentation – Dr Ibrahim: A 74-year-old woman with ER-positive, PR-negative, HER2-positive metastatic breast cancer (continued)

Dr Sulfi Ibrahim

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Case Presentation – Dr Stebel: A 63-year-old woman with 3.5-cm weakly ER/PR-positive, HER2-positive node-negative breast cancer

Dr Andrea Stebel

- Biopsy of *right* breast mass: Weakly ER/PR-positive, HER2-positive
- Neoadjuvant TCHP recommended
  - Mother died of breast cancer but patient attributes her death to the toxicity of chemotherapy
- Patient sought second opinion of Dr Stebel and team
- COVID vaccine on *right* side → Pre-surgery MRI: subcentimeter node in the *right* axilla
- Surgeon insists on biopsying the node: “reactive”

Case Presentation – Dr Partridge: A 40-year-old woman with localized ER-negative, HER2-positive breast cancer

Dr Ann Partridge

- Diagnosed with Grade 3 IDC with associated DCIS, ER negative/PR negative, HER2 positive 3+ by IHC
- Node-negative
- Enrolled in phase II MARGOT trial and received neoadjuvant paclitaxel with pertuzumab and margetuximab
- Bilateral mastectomies and left-sided SLNB revealed a pCR to treatment (RCB 0) with only residual high grade ER positive DCIS
- Restarted margetuximab/pertuzumab to complete a full year

Questions

- Is it appropriate to think about a de-escalation strategy for neoadjuvant therapy in the HER2-positive setting? Would you be comfortable treating a patient with only paclitaxel, trastuzumab, and pertuzumab, and then if she or he has a pCR only giving pertuzumab and trastuzumab in the adjuvant setting?

Case Presentation – Dr Yap: A 40-year-old woman with localized ER-positive, HER2-positive breast cancer

Dr Kelly Yap

- Diagnosed with Stage IIIA (cT4bN1M0) breast cancer
- ER 95%/PR 95%/HER2+ breast cancer
- Neoadjuvant TCHP → mastectomy/ALND r → ypT2N1a, RCB-II, ER 90%/PR-negative/ HER2-negative
- Adjuvant T-DM1 and radiation therapy
- Planning for adjuvant AI/OFS

Questions

- Is there a role for adjuvant neratinib for this patient?
- Given the toxicities associated with neratinib, is there a role for a dose-escalation approach? Do you administer a prophylactic anti-diarrheal agent, and if so, which one?
- If the patient has only minimal residual disease after neoadjuvant TCHP is there a role for T-DM1? Would the benefit of T-DM1 be less?

RTP RESEARCH TO PRACTICE

Case Presentation – Dr Parsons: A 36-year-old woman with ER/PR-positive, HER2-positive, node-positive inflammatory breast cancer

Dr Benjamin Parsons

- Presents with large area of peau d'orange change on her entire breast
- 9-cm ER/PR-positive, HER2-positive, node-positive breast cancer
- Neoadjuvant AC-THP, with immediate tumor reduction after 1 cycle, but residual disease at surgery

Questions

- Is TCHP enough therapy for inflammatory breast cancer?
- What strategy would you employ in the adjuvant setting? Would you offer adjuvant neratinib?
- Is there a role for adjuvant abemaciclib in patients with ER-positive, HER2-positive disease?
- If she had a BRCA mutation, would you offer adjuvant olaparib?

Meet The Professor with Dr Tolaney

Introduction: DESTINY-Breast03

MODULE 1: Case Presentations

- Dr Favaro: A 52-year-old woman with ER/PR-negative, HER2-positive breast cancer with bone, lung, liver and brain metastases
- Dr Ibrahim: A 74-year-old woman with ER-positive, PR-negative, HER2-positive metastatic breast cancer
- Dr Stebel: A 63-year-old woman with localized 3.5-cm weakly ER/PR-positive, HER2-positive node-negative breast cancer
- Dr Partridge: A 40-year-old woman with localized ER-negative, HER2-positive breast cancer
- Dr Yap: A 40-year-old woman with localized ER-positive, HER2-positive breast cancer
- Dr Parsons: A 36-year-old woman with ER/PR-positive, HER2-positive, node-positive inflammatory breast cancer

MODULE 2: Journal Club with Dr Tolaney

MODULE 3: Beyond the Guidelines

MODULE 4: Key Data Sets

RTP RESEARCH TO PRACTICE

Journal Club with Dr Tolaney – Part 1

- Exman P, Tolaney SM. **HER2-positive metastatic breast cancer: A comprehensive review.** *Clin Adv Hematol Oncol* 2021;19(1):40-50.
- Barroso-Sousa R, Tolaney SM. **Clinical development of new antibody-drug conjugates in breast cancer: To infinity and beyond.** *BioDrugs* 2021;35(2):159-74.
- Jackisch C et al. **Risk-based decision-making in the treatment of HER2-positive early breast cancer: Recommendations based on the current state of knowledge.** *Cancer Treat Rev* 2021;99:102229.
- Pernas S, Tolaney SM. **Management of early-stage human epidermal growth factor receptor 2-positive breast cancer.** *JCO Oncol Pract* 2021;17(6):320-30.
- Weis LN et al. **Tissue-agnostic drug approvals: How does this apply to patients with breast cancer?** *NPJ Breast Cancer* 2021;7(1):120.
- Tolaney SM et al. **Adjuvant trastuzumab emtansine versus paclitaxel in combination with trastuzumab for stage I HER2-positive breast cancer (ATEMPT): A randomized clinical trial.** *J Clin Oncol* 2021;39(21):2375-85.

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TO PRACTICE

Journal Club with Dr Tolaney – Part 2

- Tolaney SM et al. **Phase III study of trastuzumab deruxtecan (T-DXd) with or without pertuzumab vs a taxane, trastuzumab and pertuzumab in first-line (1L), human epidermal growth factor receptor 2-positive (HER2+) metastatic breast cancer (mBC): DESTINY-Breast09.** ESMO 2021;Abstract 328TiP.
- Pernas S, Tolaney SM. **Targeting HER2 heterogeneity in early-stage breast cancer.** *Curr Opin Oncol* 2020;32(6):545-54.
- Barroso-Sousa R et al. **Prospective study testing a simplified paclitaxel premedication regimen in patients with early breast cancer.** *Oncologist* 2021;[Online ahead of print].
- Brown JC et al. **The effects of a clinic-based weight loss program on health-related quality of life and weight maintenance in cancer survivors: A randomized controlled trial.** *Psychooncology* 2021;[Online ahead of print].
- Leone J et al. **Tumor subtypes and survival in male breast cancer.** *Breast Cancer Res Treat* 2021;188(3):695-702.
- Leone JP et al. **Survival in male breast cancer (MaBC) over the past three decades.** ASCO 2021;Abstract 569.

RTP RESEARCH TO PRACTICE

Meet The Professor with Dr Tolaney

Introduction: DESTINY-Breast03

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MODULE 2: Journal Club with Dr Tolaney

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RTP RESEARCH TO PRACTICE

Management of Metastatic HER2-Positive Breast Cancer

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TO PRACTICE

A 65-year-old woman with an ER-negative, HER2-positive IDC experiences disease recurrence in the liver 6 months after completing neoadjuvant TCHP followed by adjuvant T-DM1. Regulatory and reimbursement issues aside, what systemic treatment would you recommend?

1. Trastuzumab/pertuzumab/docetaxel
2. Neratinib + paclitaxel
3. Neratinib + capecitabine
4. Tucatinib + trastuzumab/capecitabine
5. Trastuzumab deruxtecan
6. Trastuzumab + capecitabine
7. Other

RTP
RESEARCH
TO PRACTICE

A 65-year-old woman with an ER-negative, HER2-positive IDC experiences disease recurrence in the liver 6 months after completing neoadjuvant TCHP followed by adjuvant T-DM1. Regulatory and reimbursement issues aside, what systemic treatment would you recommend?

 Dr Gelmon	Tucatinib + trastuzumab/ capecitabine	 Dr Mahtani	Tucatinib + trastuzumab/ capecitabine
 Dr Hamilton	Tucatinib + trastuzumab/ capecitabine	 Dr Rugo	Trastuzumab deruxtecan
 Dr Hurvitz	Tucatinib + trastuzumab/ capecitabine	 Dr Tolaney	Trastuzumab deruxtecan

RTP RESEARCH TO PRACTICE

A 65-year-old woman with an ER-negative, HER2-positive IDC experiences disease recurrence in the liver 6 months after completing neoadjuvant TCHP followed by adjuvant trastuzumab/pertuzumab. Regulatory and reimbursement issues aside, what systemic treatment would you recommend?

1. Trastuzumab/pertuzumab/docetaxel
2. T-DM1
3. Neratinib + paclitaxel
4. Neratinib + capecitabine
5. Tucatinib + trastuzumab/capecitabine
6. Trastuzumab deruxtecan
7. Trastuzumab + capecitabine
8. Other

RTP
RESEARCH
TO PRACTICE

A 65-year-old woman with an ER-negative, HER2-positive IDC experiences disease recurrence in the liver 6 months after completing neoadjuvant TCHP followed by adjuvant trastuzumab/pertuzumab. Regulatory and reimbursement issues aside, what systemic treatment would you recommend?

 Dr Gelmon	T-DM1	 Dr Mahtani	T-DM1
 Dr Hamilton	T-DM1	 Dr Rugo	T-DM1
 Dr Hurvitz	T-DM1	 Dr Tolaney	T-DM1

RTP RESEARCH TO PRACTICE

A 65-year-old woman with an ER-negative, HER2-positive IDC experiences disease recurrence in the liver and brain 18 months after completing neoadjuvant TCHP followed by adjuvant trastuzumab/pertuzumab. Regulatory and reimbursement issues aside, what systemic treatment would you recommend?

1. Trastuzumab/pertuzumab/docetaxel
2. T-DM1
3. Neratinib + paclitaxel
4. Neratinib + capecitabine
5. Tucatinib + trastuzumab/capecitabine
6. Trastuzumab deruxtecan
7. Trastuzumab + capecitabine
8. Other

RTP
RESEARCH
TO PRACTICE

A 65-year-old woman with an ER-negative, HER2-positive IDC experiences disease recurrence in the liver and brain 18 months after completing neoadjuvant TCHP followed by adjuvant trastuzumab/pertuzumab. Regulatory and reimbursement issues aside, what systemic treatment would you recommend?

 Dr Gelmon	Tucatinib + trastuzumab/ capecitabine	 Dr Mahtani	T-DM1
 Dr Hamilton	Tucatinib + trastuzumab/ capecitabine	 Dr Rugo	Tucatinib + trastuzumab/ capecitabine
 Dr Hurvitz	Tucatinib + trastuzumab/ capecitabine	 Dr Tolaney	Tucatinib + trastuzumab/ capecitabine

RTP RESEARCH TO PRACTICE

A 65-year-old woman with an ER-positive, HER2-positive IDC experiences recurrence in the liver and brain 18 months after completing neoadjuvant TCHP followed by adjuvant trastuzumab/pertuzumab and postadjuvant neratinib and is receiving adjuvant anastrozole. Regulatory and reimbursement issues aside, what systemic treatment would you recommend?

 Dr Gelmon	Tucatinib + trastuzumab/ capecitabine	 Dr Mahtani	T-DM1
 Dr Hamilton	T-DM1	 Dr Rugo	T-DM1
 Dr Hurvitz	Tucatinib + trastuzumab/ capecitabine	 Dr Tolaney	T-DM1

RTP RESEARCH TO PRACTICE

A 65-year-old woman with ER-negative, HER2-positive mBC receives first-line THP followed by second-line T-DM1 on disease progression. She now presents with further low-volume, asymptomatic progression but no evidence of CNS involvement. Regulatory and reimbursement issues aside, what systemic treatment would you recommend?

 Dr Gelmon	Tucatinib + trastuzumab/ capecitabine	 Dr Mahtani	Tucatinib + trastuzumab/ capecitabine
 Dr Hamilton	Tucatinib + trastuzumab/ capecitabine	 Dr Rugo	Trastuzumab deruxtecan
 Dr Hurvitz	Tucatinib + trastuzumab/ capecitabine	 Dr Tolaney	Trastuzumab deruxtecan

RTP RESEARCH TO PRACTICE

A 65-year-old woman with ER-negative, HER2-positive mBC receives first-line THP followed by second-line T-DM1 on disease progression. She now presents with further high-volume, moderately symptomatic progression but no evidence of CNS involvement. Regulatory and reimbursement issues aside, what systemic treatment would you recommend?

 Dr Gelmon	Tucatinib + trastuzumab/ capecitabine	 Dr Mahtani	Trastuzumab deruxtecan
 Dr Hamilton	Trastuzumab deruxtecan	 Dr Rugo	Trastuzumab deruxtecan
 Dr Hurvitz	Trastuzumab deruxtecan	 Dr Tolaney	Trastuzumab deruxtecan

RTP RESEARCH TO PRACTICE

At what grade of ILD would you permanently discontinue therapy with trastuzumab deruxtecan for a patient with HER2-positive mBC?

 Dr Gelmon	Grade 2	 Dr Mahtani	Grade 2
 Dr Hamilton	Grade 2	 Dr Rugo	Grade 2
 Dr Hurvitz	Grade 2	 Dr Tolaney	Grade 2

RTP RESEARCH TO PRACTICE

A 65-year-old woman with ER-negative, HER2-positive mBC receives first-line THP but after 1 year experiences disease progression, including 1 brain metastasis that is resected. Regulatory and reimbursement issues aside, what systemic treatment would you recommend next?

 Dr Gelmon	T-DM1	 Dr Mahtani	T-DM1
 Dr Hamilton	Tucatinib + trastuzumab/ capecitabine	 Dr Rugo	T-DM1
 Dr Hurvitz	Tucatinib + trastuzumab/ capecitabine	 Dr Tolaney	Tucatinib + trastuzumab/ capecitabine

RTP RESEARCH TO PRACTICE

A 65-year-old woman with ER-negative, HER2-positive mBC receives first-line THP but after 1 year experiences disease progression, including multiple brain metastases. Regulatory and reimbursement issues aside, what systemic treatment would you recommend next?

 Dr Gelmon	Tucatinib + trastuzumab/ capecitabine	 Dr Mahtani	Tucatinib + trastuzumab/ capecitabine
 Dr Hamilton	Tucatinib + trastuzumab/ capecitabine	 Dr Rugo	Tucatinib + trastuzumab/ capecitabine
 Dr Hurvitz	Tucatinib + trastuzumab/ capecitabine	 Dr Tolaney	Tucatinib + trastuzumab/ capecitabine

RTP RESEARCH TO PRACTICE

A 65-year-old woman with ER-negative, HER2-positive mBC receives first-line THP followed by second-line T-DM1 on disease progression. She now presents with a single brain metastasis that is resected with no other evidence of progression. Regulatory and reimbursement issues aside, what systemic treatment would you recommend?

 Dr Gelmon	Continue T-DM1	 Dr Mahtani	Continue T-DM1
 Dr Hamilton	Tucatinib + trastuzumab/ capecitabine	 Dr Rugo	Continue T-DM1
 Dr Hurvitz	Continue T-DM1	 Dr Tolaney	Continue T-DM1

RTP RESEARCH TO PRACTICE

A 65-year-old woman with ER-negative, HER2-positive mBC receives first-line THP followed by second-line T-DM1 on disease progression. She now presents with further disease progression, including multiple new brain metastases. Regulatory and reimbursement issues aside, what systemic treatment would you recommend?

 Dr Gelmon	Tucatinib + trastuzumab/ capecitabine	 Dr Mahtani	Tucatinib + trastuzumab/ capecitabine
 Dr Hamilton	Tucatinib + trastuzumab/ capecitabine	 Dr Rugo	Tucatinib + trastuzumab/ capecitabine
 Dr Hurvitz	Tucatinib + trastuzumab/ capecitabine	 Dr Tolaney	Tucatinib + trastuzumab/ capecitabine

RTP RESEARCH TO PRACTICE

Localized HER2-Positive Breast Cancer

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RESEARCH
TO PRACTICE

Which neoadjuvant systemic therapy, if any, would you generally recommend for a 65-year-old patient with a 2.5-cm ER-negative, HER2-positive, clinically node-negative IDC?

1. None
2. TCHP
3. TCH
4. Paclitaxel/trastuzumab
5. Paclitaxel/trastuzumab/pertuzumab
6. ACTH
7. Other

Which neoadjuvant systemic therapy, if any, would you generally recommend for a 65-year-old patient with a 2.5-cm ER-negative, HER2-positive, clinically node-negative IDC?

 Dr Gelmon	TCHP (TCH/pertuzumab) or ACTH/pertuzumab	 Dr Mahtani	TCHP
 Dr Hamilton	TCHP	 Dr Rugo	Paclitaxel/trastuzumab /pertuzumab
 Dr Hurvitz	TCHP	 Dr Tolaney	TCHP

RTP RESEARCH TO PRACTICE

A 65-year-old woman presents with a 3.4-cm ER-positive, HER2-positive IDC with biopsy-proven axillary nodes, receives neoadjuvant TCHP and at surgery is found to have 0.5 cm of residual tumor in the breast and no disease in the nodes. Regulatory and reimbursement issues aside, what adjuvant anti-HER2 therapy would you recommend?

1. Trastuzumab
2. Trastuzumab/pertuzumab
3. T-DM1
4. Trastuzumab → neratinib
5. Trastuzumab/pertuzumab → neratinib
6. T-DM1 → neratinib
7. Other

RTP
RESEARCH TO PRACTICE

A 65-year-old woman presents with a 3.4-cm ER-positive, HER2-positive IDC with biopsy-proven axillary nodes, receives neoadjuvant TCHP and at surgery is found to have 0.5 cm of residual tumor in the breast and no disease in the nodes. Regulatory and reimbursement issues aside, what adjuvant anti-HER2 therapy would you recommend?

 Dr Gelmon	T-DM1	 Dr Mahtani	T-DM1
 Dr Hamilton	T-DM1 or T-DM1 → neratinib	 Dr Rugo	T-DM1
 Dr Hurvitz	T-DM1 → neratinib	 Dr Tolaney	T-DM1

RTP RESEARCH TO PRACTICE

Meet The Professor with Dr Tolaney

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- Dr Yap: A 40-year-old woman with localized ER-positive, HER2-positive breast cancer
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MODULE 2: Journal Club with Dr Tolaney

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RTP RESEARCH TO PRACTICE

Management of Metastatic HER2-Positive Breast Cancer

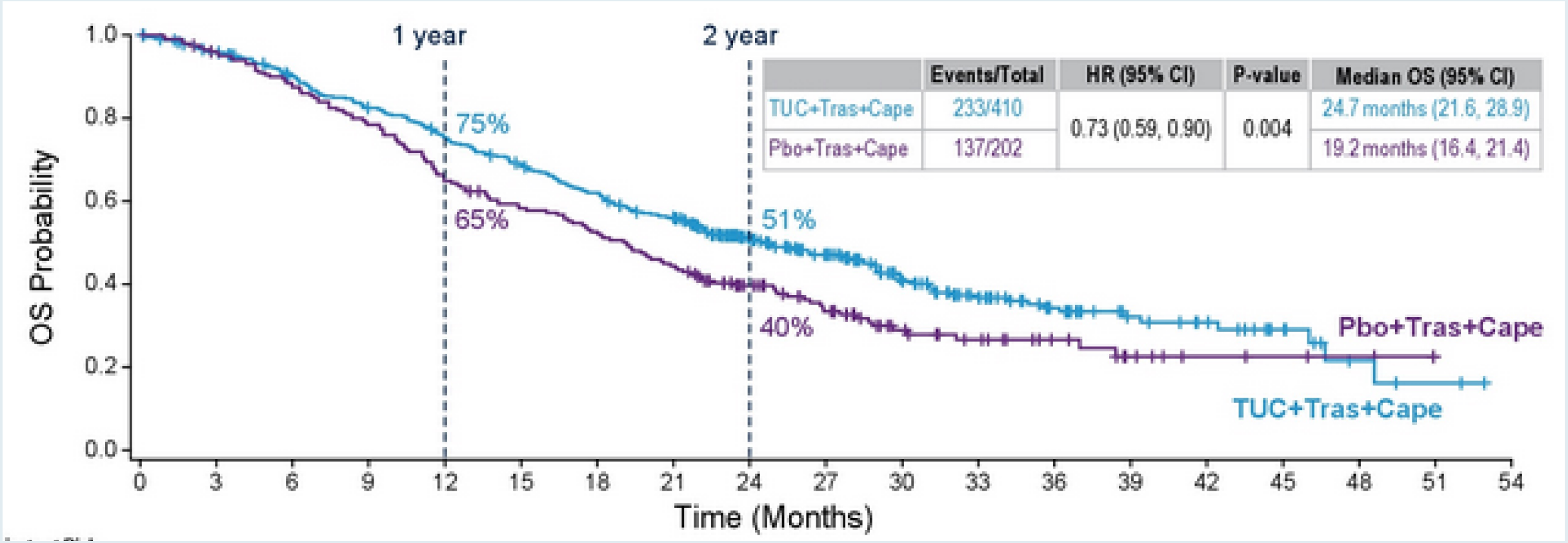
RTP
RESEARCH
TO PRACTICE

Updated Results of Tucatinib versus Placebo Added to Trastuzumab and Capecitabine for Patients with Pretreated HER2+ Metastatic Breast Cancer with and without Brain Metastases (HER2CLIMB)

Curigliano G et al.

ASCO 2021;Abstract 1043.

HER2CLIMB: Overall Survival

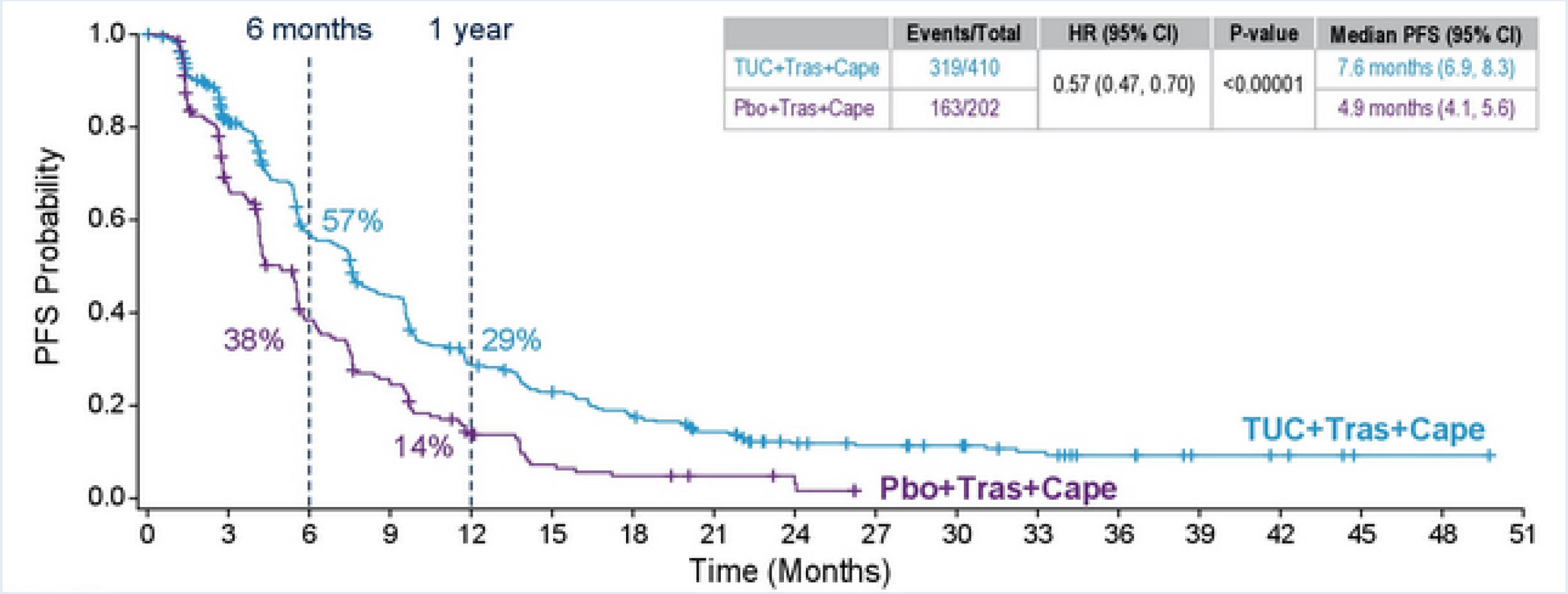


	Events/Total	HR (95% CI)	P-value	Median OS (95% CI)
TUC+Tras+Cape	233/410	0.73 (0.59, 0.90)	0.004	24.7 months (21.6, 28.9)
Pbo+Tras+Cape	137/202			19.2 months (16.4, 21.4)

Curigliano G et al. ASCO 2021;Abstract 1043.

RTP RESEARCH TO PRACTICE

HER2CLIMB: Progression-Free Survival



	Events/Total	HR (95% CI)	P-value	Median PFS (95% CI)
TUC+Tras+Cape	319/410	0.57 (0.47, 0.70)	<0.00001	7.6 months (6.9, 8.3)
Pbo+Tras+Cape	163/202			4.9 months (4.1, 5.6)

Curigliano G et al. ASCO 2021;Abstract 1043.

Tucatinib vs Placebo in Combination with Trastuzumab and Capecitabine for Patients with Locally Advanced Unresectable or HER2-Positive Metastatic Breast Cancer (HER2CLIMB): Outcomes by Hormone Receptor Status

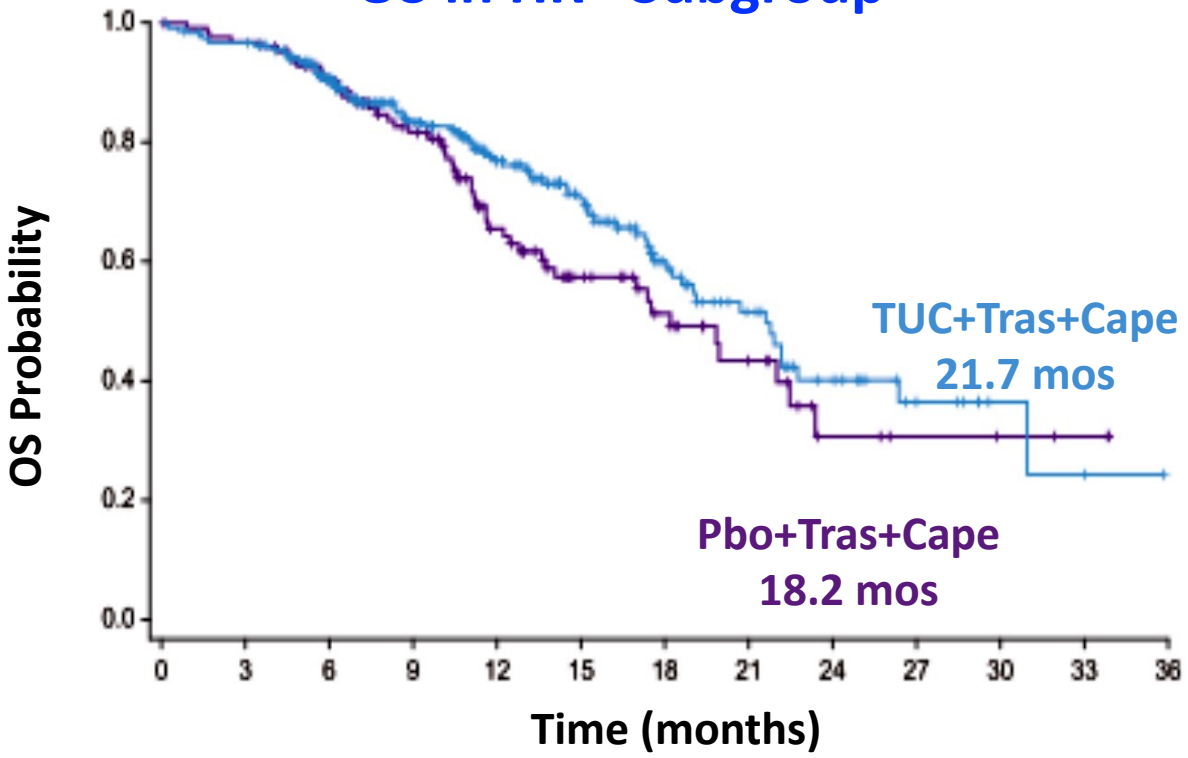
Hamilton E et al.

SABCS 2020;Abstract PD3-08.

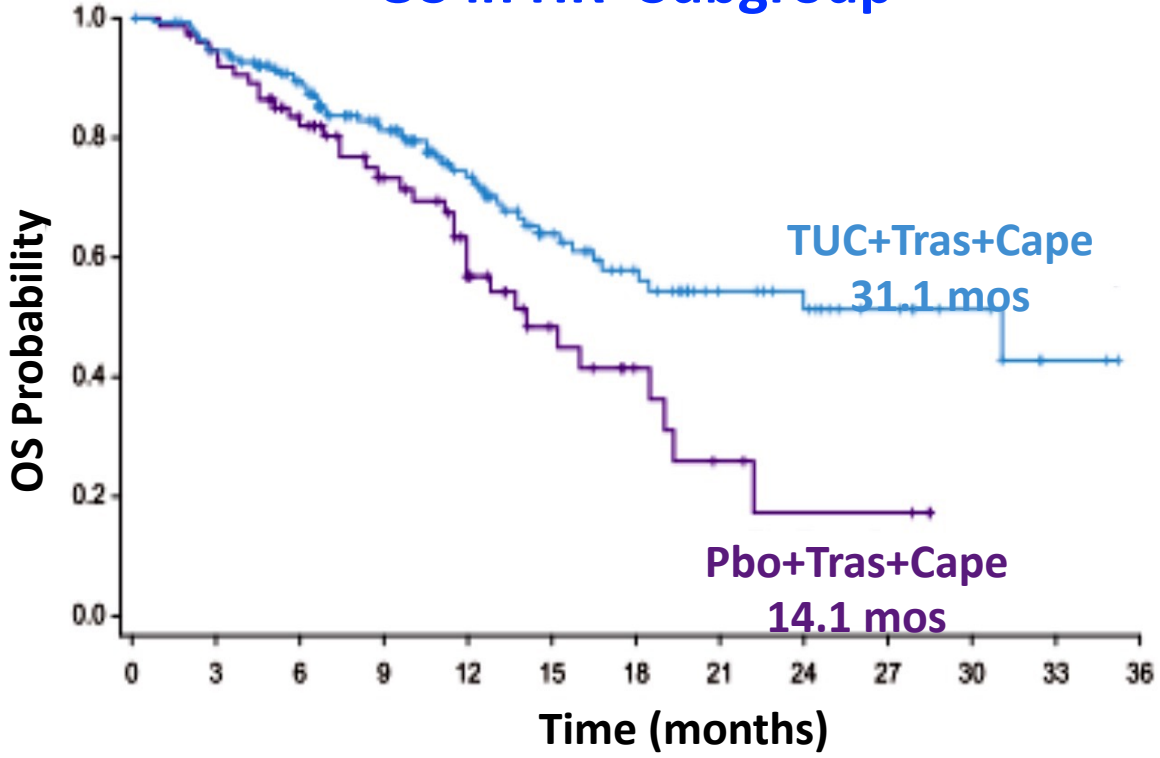
OS by HR Status in the Total Study Population

- Clinically meaningful improvement of OS was observed in patients on the tucatinib arm regardless of hormone receptor status.

OS in HR+ Subgroup



OS in HR- Subgroup



Hamilton E et al. SABCS 2020;Abstract PD3-08.

RTP RESEARCH TO PRACTICE

HER2CLIMB: Safety Outcomes

Select AE	Tucatinib (n = 404)		Placebo (n = 197)	
	Any grade	Grade ≥3	Any grade	Grade ≥3
Any	99.3%	55.2%	97.0%	48.7%
Diarrhea	80.9%	12.9%	53.3%	8.6%
PPE syndrome	63.4%	13.1%	52.8%	9.1%
Nausea	58.4%	3.7%	43.7%	3.0%
Fatigue	45.0%	4.7%	43.1%	4.1%
Vomiting	35.9%	3.0%	25.4%	3.6%
Stomatitis	25.5%	2.5%	14.2%	0.5%
Increased AST	21.3%	4.5%	11.2%	0.5%
Increased ALT	20.0%	5.4%	6.6%	0.5%

Murthy R et al. SABCS 2019;Abstract GS1-01; Murthy RK et al. *N Engl J Med* 2020;382(7):597-609.

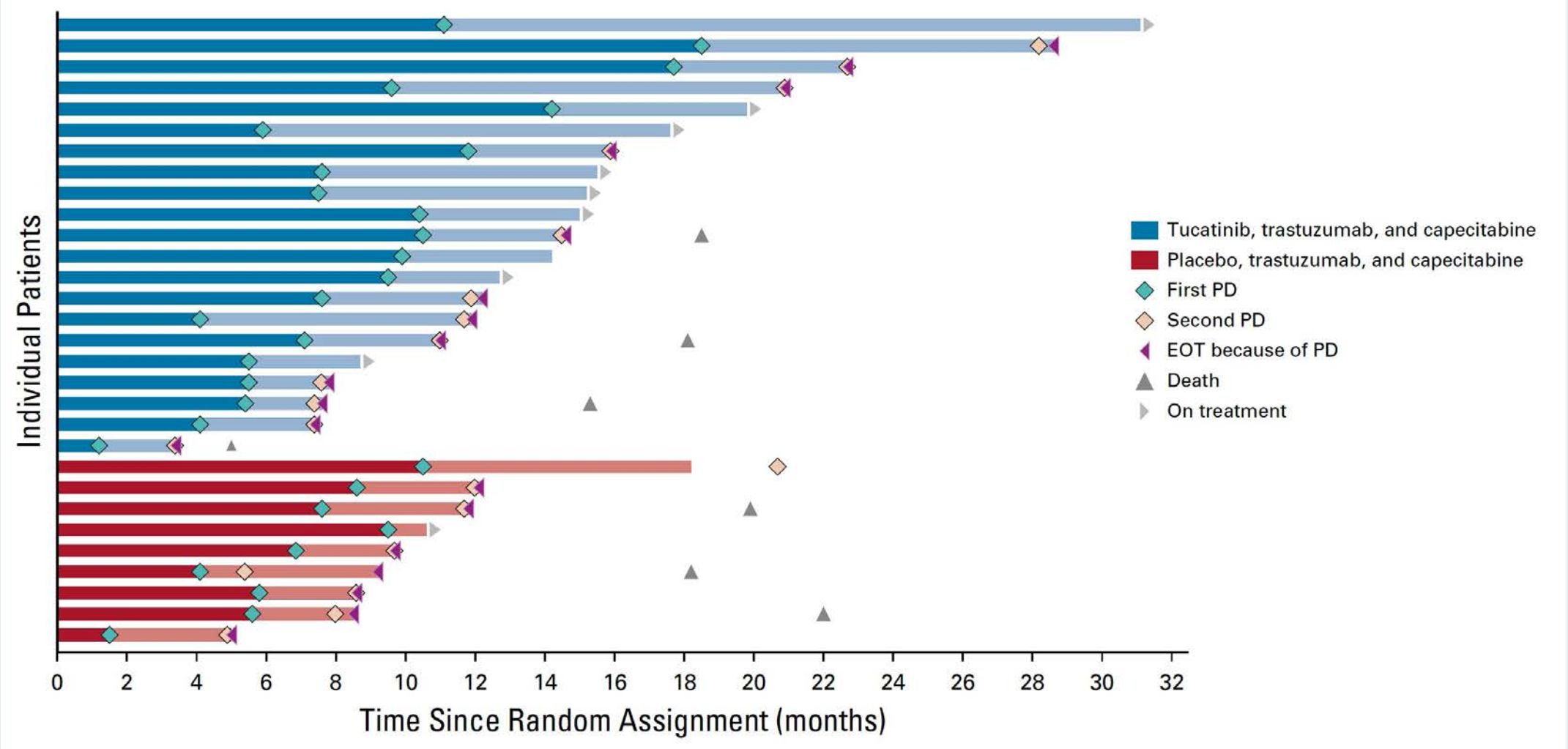
rapid communications

Intracranial Efficacy and Survival With Tucatinib Plus Trastuzumab and Capecitabine for Previously Treated HER2-Positive Breast Cancer With Brain Metastases in the HER2CLIMB Trial

Nancy U. Lin, MD[1]; Virginia Borges, MMSc, MD[2]; Carey Anders, MD[3]; Rashmi K. Murthy, MD, MBE[4]; Elisavet Paplomata, MD[5]; Erika Hamilton, MD[6]; Sara Hurvitz, MD[7]; Sherene Loi, MD, PhD[8]; Alicia Okines, MBChB, MD[9]; Vandana Abramson, MD[10]; Philippe L. Bedard, MD[11]; Mafalda Oliveira, MD, PhD[12]; Volkmar Mueller, MD[13]; Amelia Zelnak, MD[14]; Michael P. DiGiovanna, MD, PhD[15]; Thomas Bachelot, MD[16]; A. Jo Chien, MD[17]; Ruth O'Regan, MD[5]; Andrew Wardley, MBChB, MSc, MD[18]; Alison Conlin, MD, MPH[19]; David Cameron, MD, MA[20]; Lisa Carey, MD[21]; Giuseppe Curigliano, MD, PhD[22]; Karen Gelmon, MD[23]; Sibylle Loibl, MD, PhD[24]; JoAl Mayor, PharmD[25]; Suzanne McGoldrick, MD, MPH[25]; Xuebei An, PhD[25]; and Eric P. Winer, MD[1]

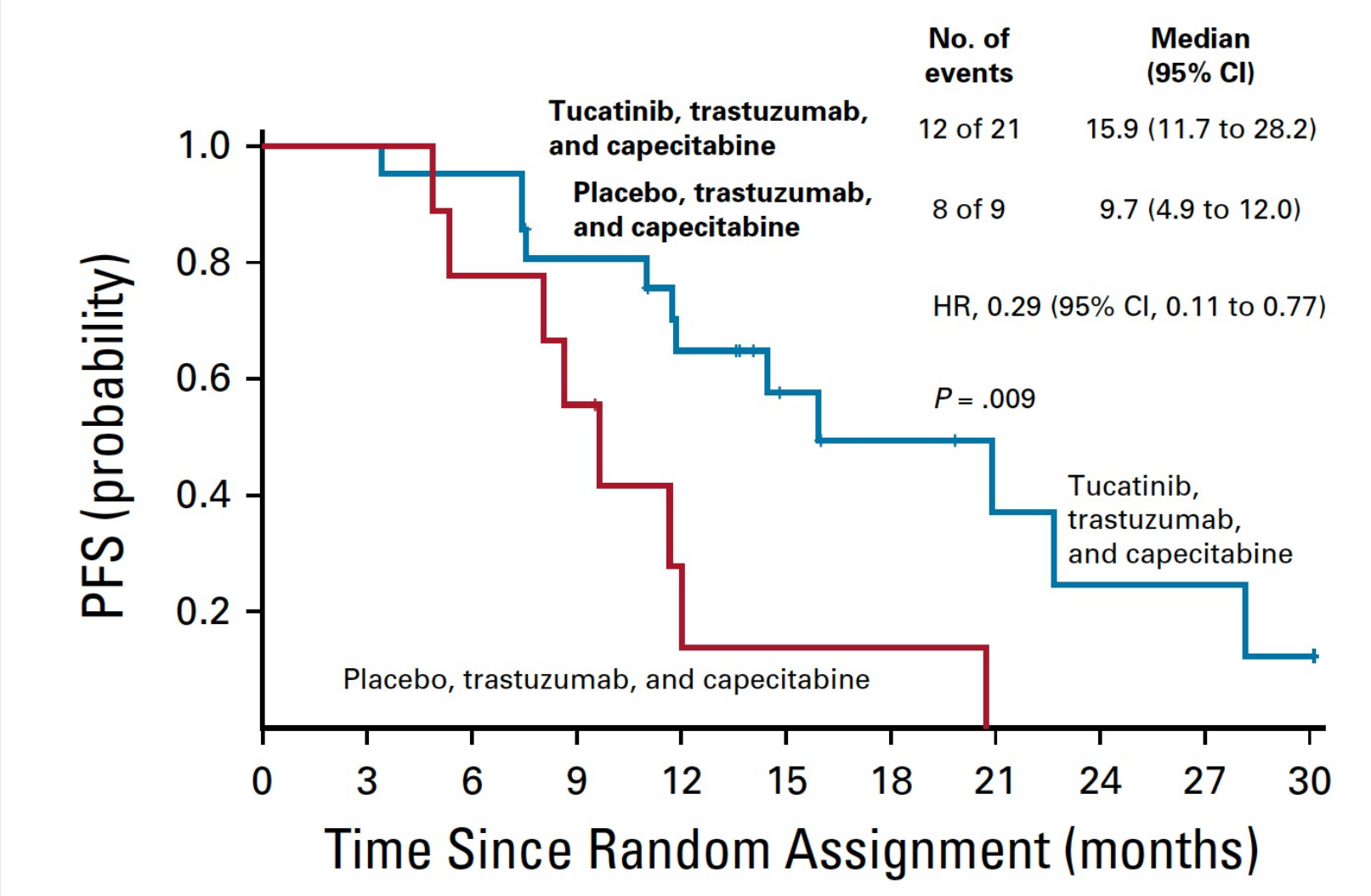
J Clin Oncol 2020;38(23):2610-9.

Duration of Treatment



Lin NU et al. *J Clin Oncol* 2020;38(23):2610-9.

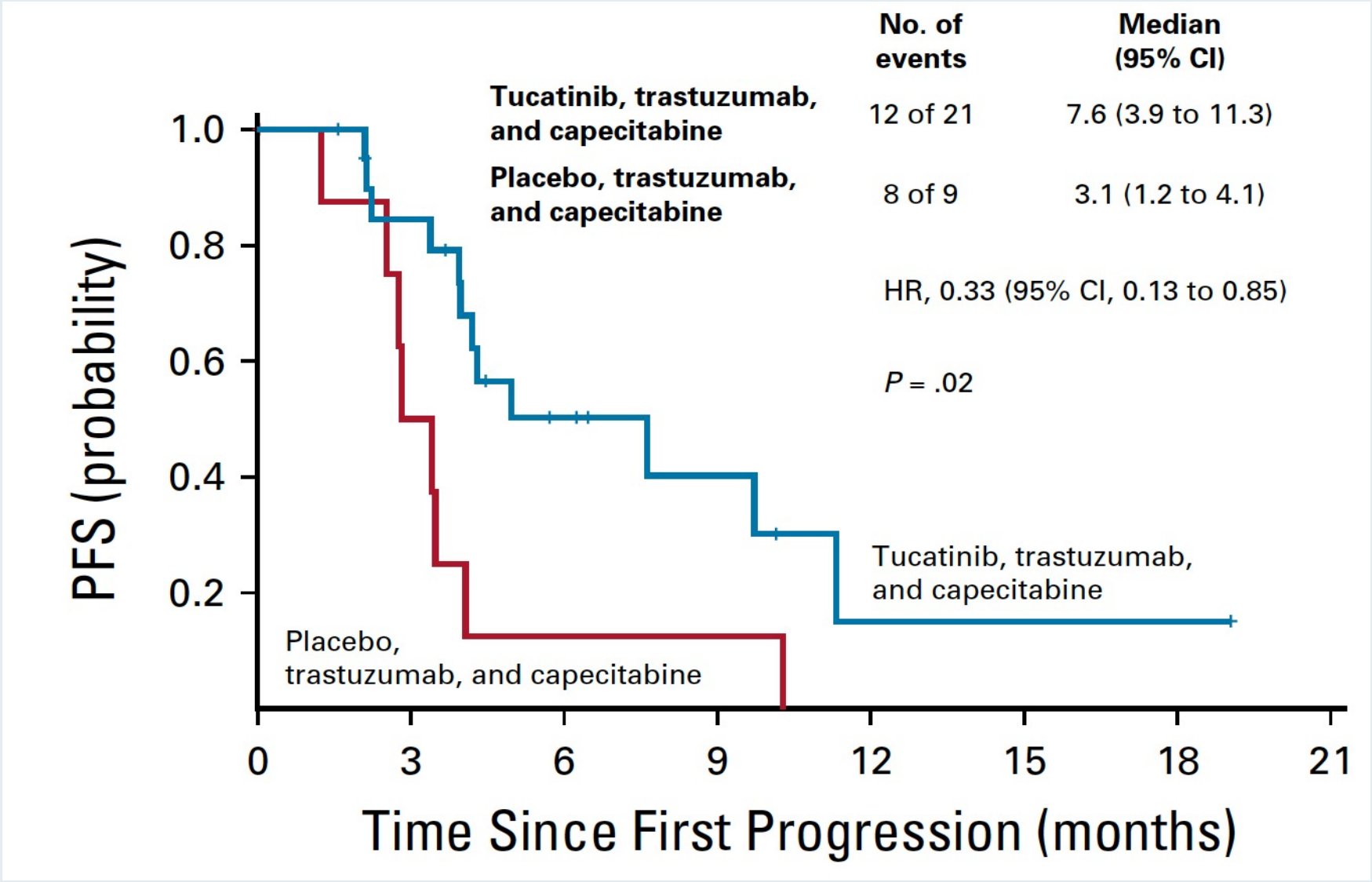
Time from Random Assignment to Second Disease Progression by Investigator Assessment or Death



Lin NU et al. *J Clin Oncol* 2020;38(23):2610-9.

RTP RESEARCH TO PRACTICE

Time from First PD to Second PD by Investigator Assessment or Death



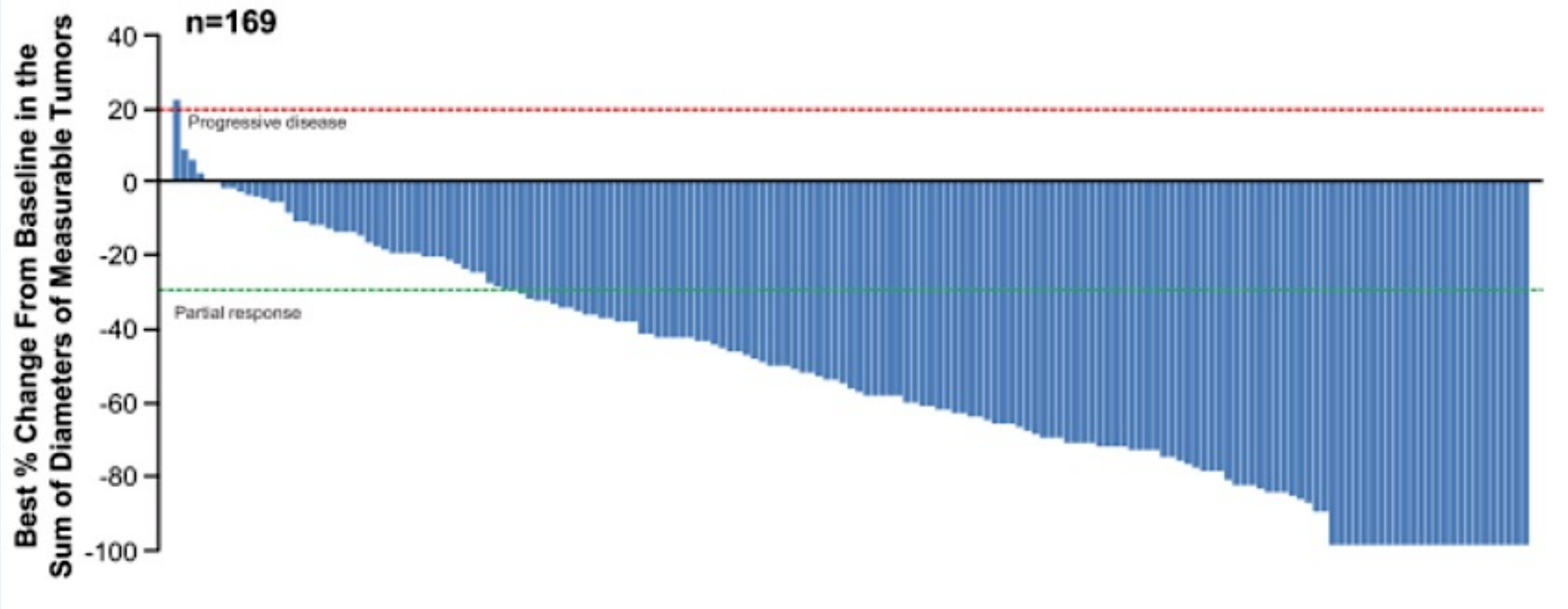
Lin NU et al. *J Clin Oncol* 2020;38(23):2610-9.

Updated Results from DESTINY-Breast01, a Phase 2 Trial of Trastuzumab Deruxtecan (T-DXd) in HER2-Positive Metastatic Breast Cancer

Modi S et al.

SABCS 2020;Abstract PD3-06.

DESTINY-Breast01: Best Percent Change in Tumor Size from Baseline



Modi S et al. SABCS 2020;Abstract PD3-06.

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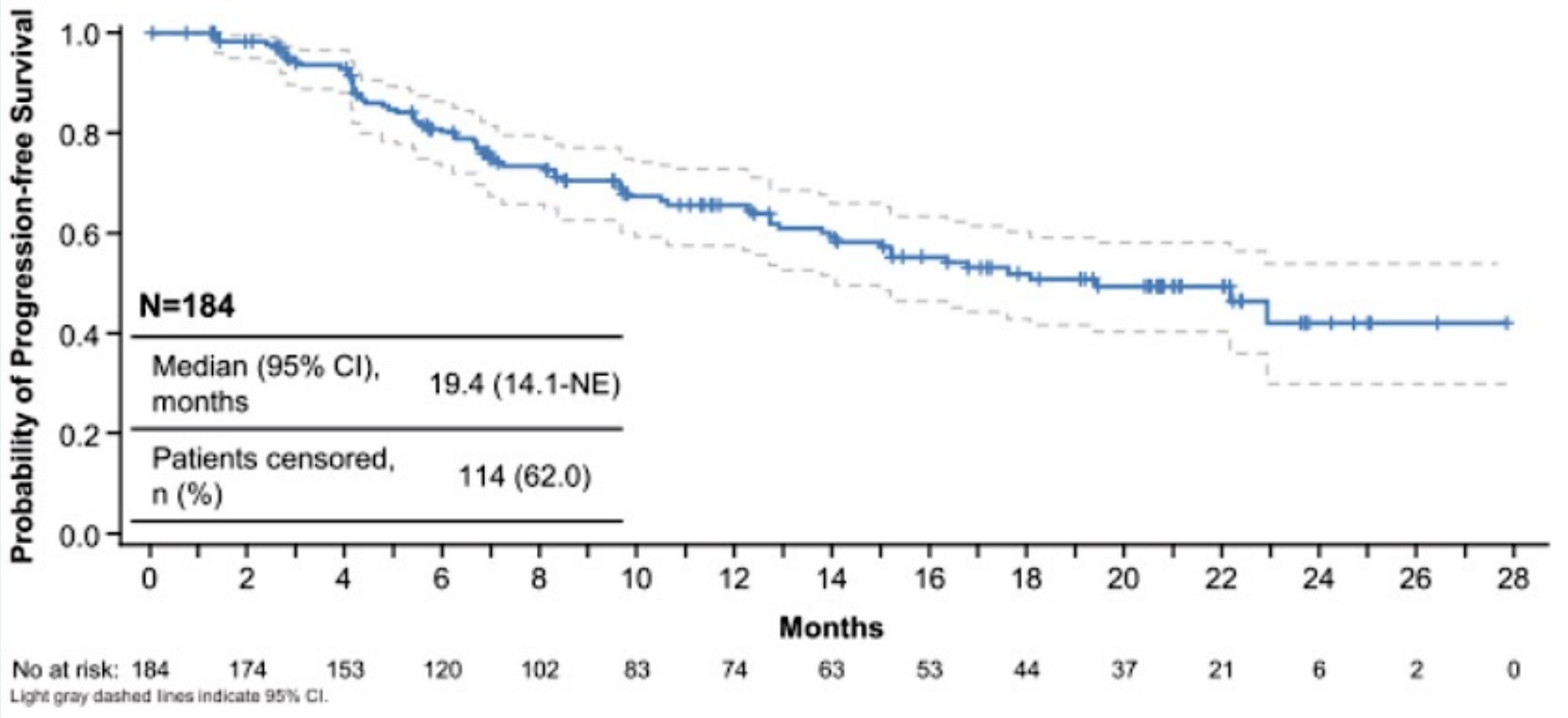
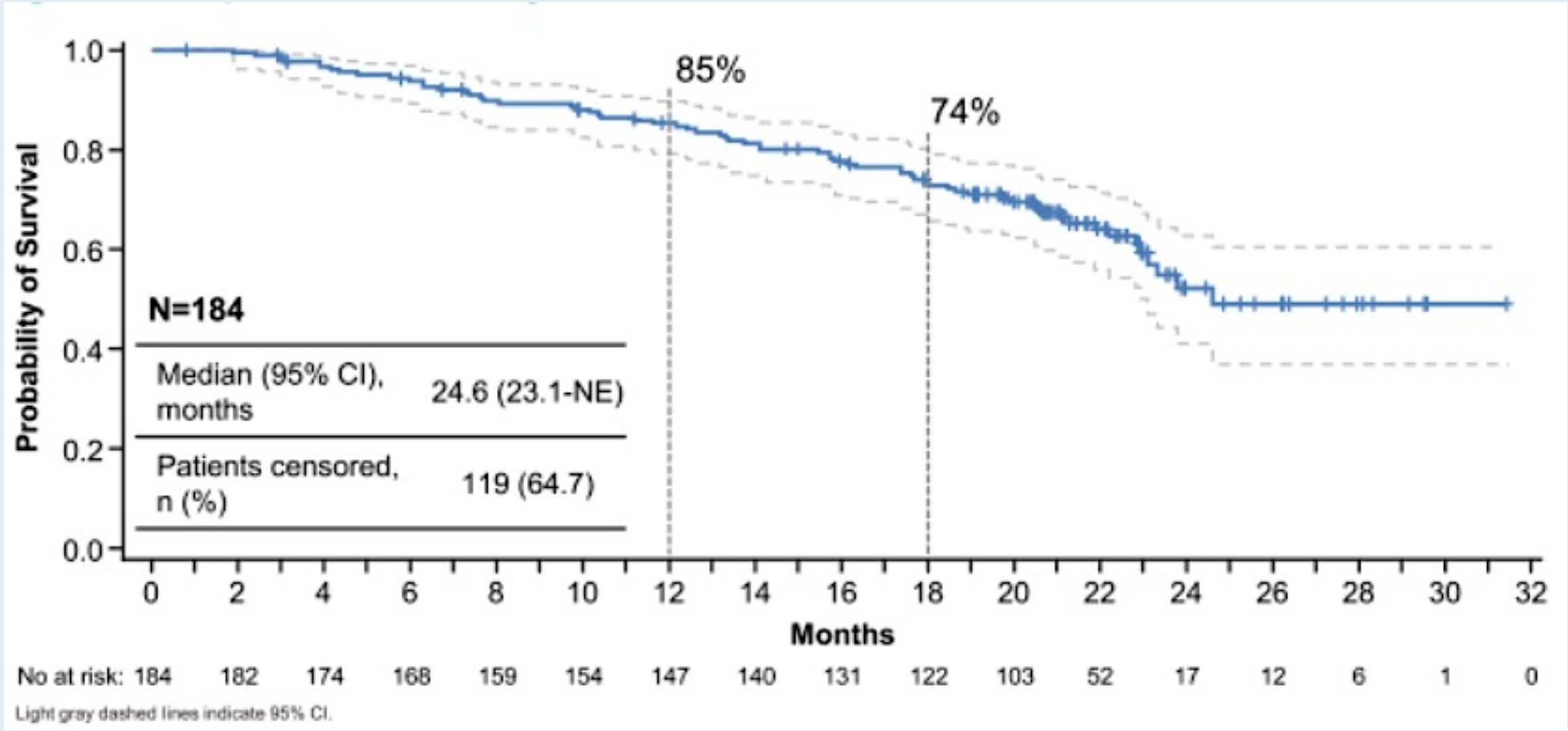
DESTINY-Breast01: Progression-Free Survival



Modi S et al. SABCS 2020;Abstract PD3-06.

RTP RESEARCH TO PRACTICE

DESTINY-Breast01: Overall Survival



Modi S et al. SABCS 2020;Abstract PD3-06.

RTP RESEARCH TO PRACTICE

DESTINY-Breast01: Safety

AEs of special interest (n = 184)	All grades	Grades 3 and 4
Interstitial lung disease	25 (13.6%)	1 (0.5%)
Prolonged QT interval	9 (4.9%)	2 (1.1%)
Infusion-related reaction	4 (2.2%)	0
Decreased left ventricular ejection fraction	3 (1.6%)	1 (0.5%)

- Most common Grade ≥3 AEs were decreased neutrophil count (21%), anemia (9%) and nausea (8%).

Modi S et al. *N Engl J Med* 2020;382(7):610-21.

Trastuzumab Deruxtecan (T-DXd) in Patients with HER2+ Metastatic Breast Cancer with Brain Metastases: A Subgroup Analysis of the DESTINY-Breast01 Trial

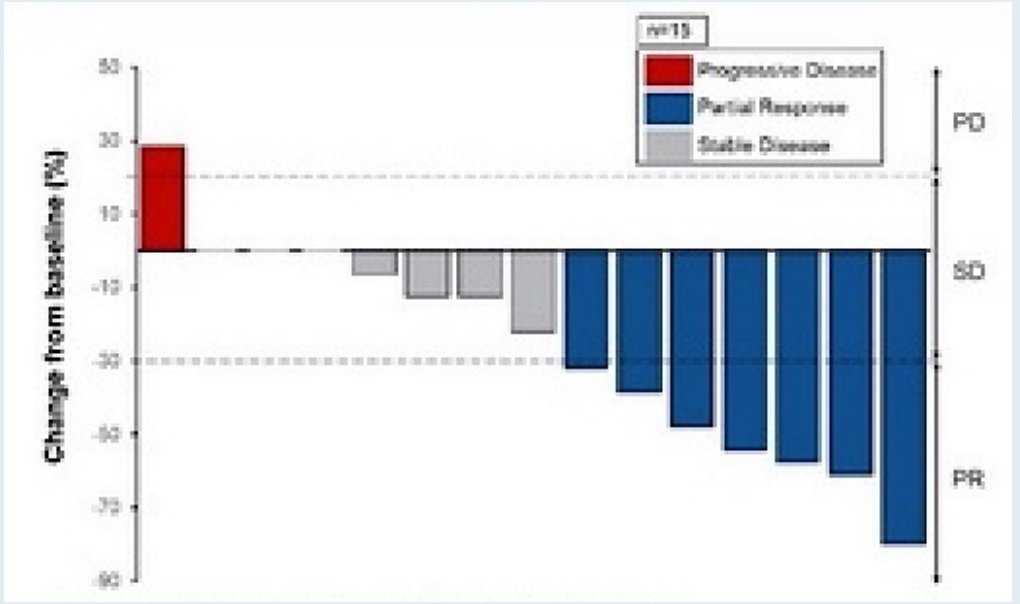
Jerusalem GHM et al.

ASCO 2021;Abstract 526.

DESTINY-Breast01: Clinical Activity Outcomes with Trastuzumab Deruxtecan

Endpoint	CNS Subgroup (n = 24)	All Patients (N = 184)
Confirmed ORR	58.3%	60.9%
Duration of response	16.9 mo	14.8 mo
Progression-free survival	18.1 mo	16.4 mo

Best Response in Brain Lesions in the CNS Subgroup



Jerusalem GHM et al. ASCO 2021;Abstract 526.

RTP RESEARCH TO PRACTICE

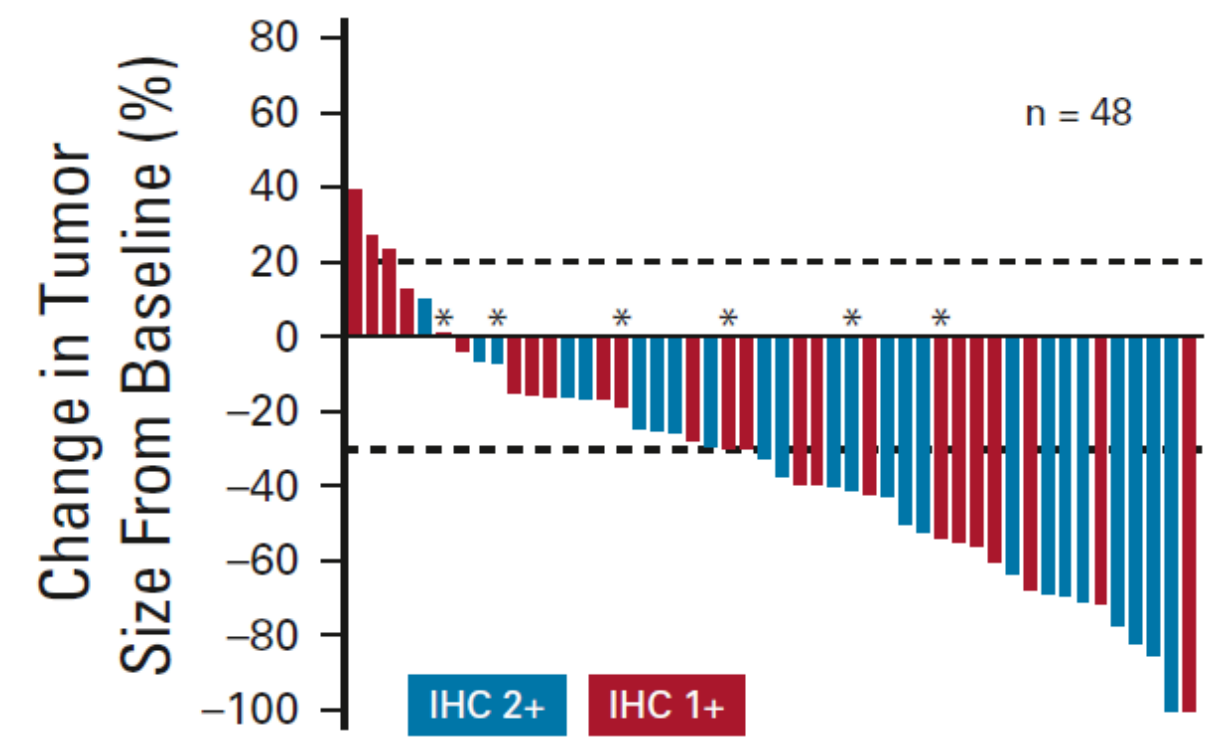
original reports

Antitumor Activity and Safety of Trastuzumab Deruxtecan in Patients With HER2-Low–Expressing Advanced Breast Cancer: Results From a Phase Ib Study

Shanu Modi, MD[1]; Haeseong Park, MD, MPH[2]; Rashmi K. Murthy, MD, MBE[3]; Hiroji Iwata, PhD, MD[4]; Kenji Tamura, MD, PhD[5]; Junji Tsurutani, MD, PhD[6]; Alvaro Moreno-Aspitia, PhD[7]; Toshihiko Doi, MD, PhD[8]; Yasuaki Sagara, MD[9]; Charles Redfern, MD[10]; Ian E. Krop, MD, PhD[11]; Caleb Lee, MD, PhD[12]; Yoshihiko Fujisaki, MS[13]; Masahiro Sugihara, PhD[13]; Lin Zhang, MD, PhD[12]; Javad Shahidi, MD[12]; and Shunji Takahashi, MD[14]

J Clin Oncol 2020;38(17):1887-96.

Effect of Trastuzumab Deruxtecan in Heavily Pretreated* HER2-Low Metastatic Breast Cancer



Clinical activity (by independent review)

ORR		
	Overall	37%
	HER2 2+	39%
	HER2 1+	36%
	ER+	40% (N = 47)
	ER-	14% (N = 7)
PFS		
	Overall	11.1 months

* Median of 7.5 prior regimens

Modi et al. *J Clin Oncol* 2020;38(17):1887-96.

Courtesy of Ian E Krop, MD, PhD

RTP RESEARCH TO PRACTICE

Final Overall Survival Results from the SOPHIA Study for Patients with HER2-Positive Metastatic Breast Cancer Did Not Demonstrate a Statistically Significant Advantage with Margetuximab Over Trastuzumab

Press Release – September 07, 2021

"Final overall survival (OS) results of the SOPHIA Phase 3 study in adult patients with metastatic HER2-positive breast cancer did not demonstrate a statistically significant advantage for margetuximab over trastuzumab.

The final OS analysis of the SOPHIA study was performed after 385 OS events occurred in the intent-to-treat (ITT) population. As per the study protocol, OS was defined as the number of days from randomization to the date of death (from any cause). The final OS analysis for the ITT population did not demonstrate a statistically significant advantage for margetuximab plus chemotherapy compared to that of patients who received trastuzumab plus chemotherapy (hazard ratio [HR]=0.95; 95% Confidence Interval [CI]: 0.77-1.17; P=0.62). In this overall ITT population, the median survival was 21.6 months in patients treated with margetuximab plus chemotherapy (N=266) compared to 21.9 months in patients treated with trastuzumab plus chemotherapy (N=270).

The safety profile at the time of the final OS analysis of SOPHIA was similar to what was previously reported."

https://www.globenewswire.com/news-release/2021/09/07/2292944/0/en/MacroGenics-Announces-Final-Overall-Survival-Results-from-SOPHIA-Study-of-MARGENZA-in-Patients-with-HER2-Positive-Metastatic-Breast-Cancer.html

Research

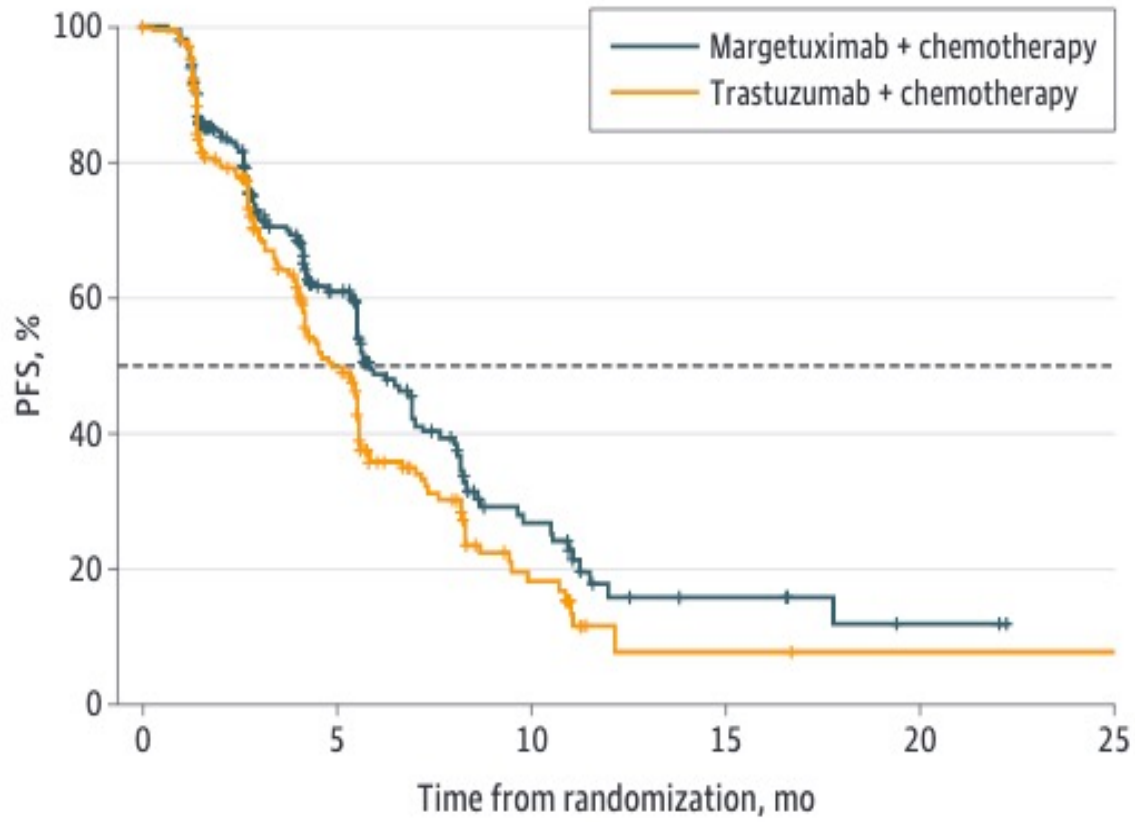
JAMA Oncology | Original Investigation

Efficacy of Margetuximab vs Trastuzumab in Patients With Pretreated ERBB2-Positive Advanced Breast Cancer
A Phase 3 Randomized Clinical Trial

Hope S. Rugo, MD; Seock-Ah Im, MD, PhD; Fatima Cardoso, MD; Javier Cortés, MD, PhD; Giuseppe Curigliano, MD, PhD; Antonino Musolino, MD, PhD, MSc; Mark D. Pegram, MD; Gail S. Wright, MD; Cristina Saura, MD, PhD; Santiago Escrivá-de-Romaní, MD; Michelino De Laurentiis, MD, PhD; Christelle Levy, MD; Ursa Brown-Glaberman, MD; Jean-Marc Ferrero, MD; Maaike de Boer, MD, PhD; Sung-Bae Kim, MD, PhD; Katarína Petráková, MD, PhD; Denise A. Yardley, MD; Orit Freedman, MD, MSc; Erik H. Jakobsen, MD; Bella Kaufman, MD; Rinat Yerushalmi, MD; Peter A. Fasching, MD; Jeffrey L. Nordstrom, PhD; Ezio Bonvini, MD; Scott Koenig, MD, PhD; Sutton Edlich, MS, PA; Shengyan Hong, PhD; Edwin P. Rock, MD, PhD; William J. Gradishar, MD; for the SOPHIA Study Group

JAMA Oncol 2021;[Online ahead of print].

SOPHIA: PFS by Central Blinded Analysis (ITT Population)

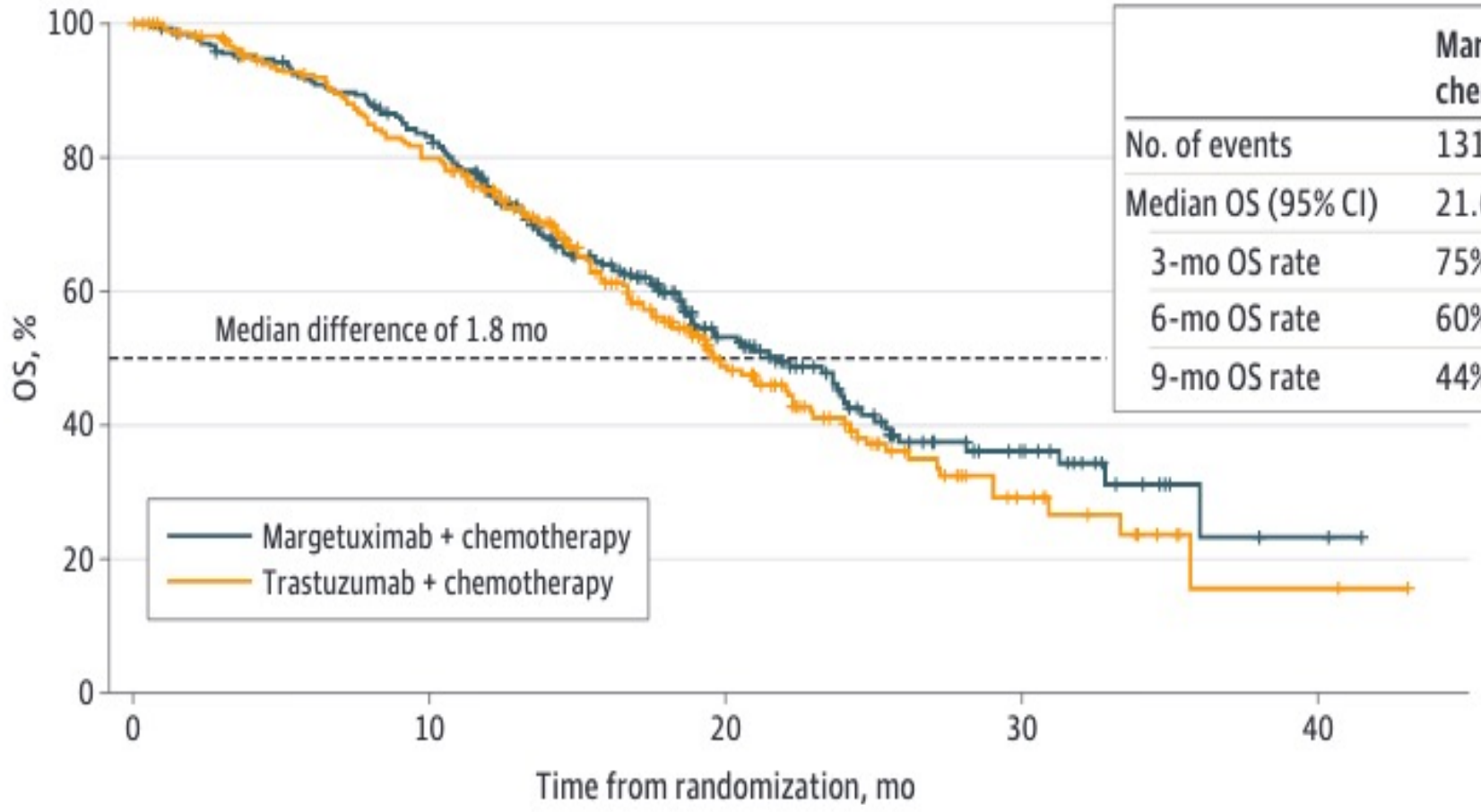


	Margetuximab + chemotherapy (n = 266)	Trastuzumab + chemotherapy (n = 270)
No. of events	130	135
Median PFS (95% CI)	5.8 mo (5.52-6.97)	4.9 mo (4.17-5.59)
3-mo PFS rate	72% (65%-77%)	70% (63%-76%)
6-mo PFS rate	48% (41%-56%)	36% (28%-44%)
9-mo PFS rate	30% (22%-38%)	22% (15%-30%)

HR by stratified Cox model, 0.76 (95% CI, 0.59-0.98)
Stratified log-rank $P = .03$
24% Risk reduction of disease progression[a]
Median follow-up, 2.8 mo

Rugo HS et al. *JAMA Oncol* 2021;[Online ahead of print].

SOPHIA: OS Analysis (ITT Population)



	Margetuximab + chemotherapy (n = 266)	Trastuzumab + chemotherapy (n = 270)
No. of events	131	139
Median OS (95% CI)	21.6 mo (18.86-24.05)	19.8 mo (17.54-22.28)
3-mo OS rate	75% (70%-80%)	75% (70%-80%)
6-mo OS rate	60% (53%-66%)	56% (49%-62%)
9-mo OS rate	44% (36%-51%)	40% (33%-48%)

HR by stratified Cox model, 0.89 (95% CI, 0.69-1.13)
Stratified log-rank $P = .33$
Median follow-up, 15.6 mo

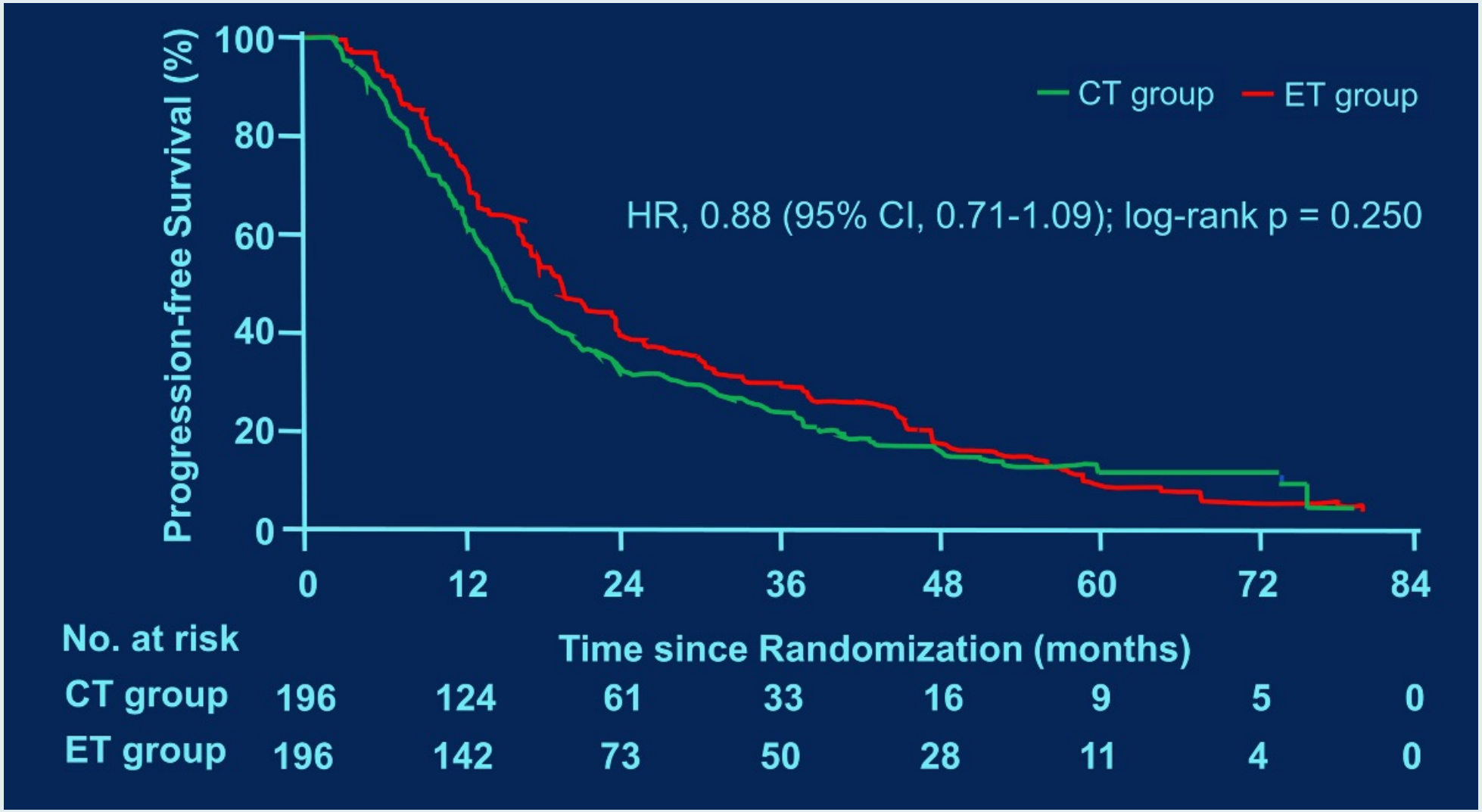
Rugo HS et al. *JAMA Oncol* 2021;[Online ahead of print].

Trastuzumab plus Endocrine Therapy or Chemotherapy as First-Line Treatment for Metastatic Breast Cancer with Hormone Receptor-Positive and HER2-Positive: The SYSUCC-002 Randomized Clinical Trial

Yuan Z et al.

ASCO 2021;Abstract 1003.

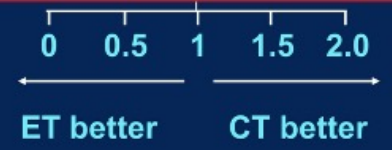
SYSUCC-002: Progression-Free Survival (Primary Endpoint)



Yuan Z et al. ASCO 2021;Abstract 1003.

SYSUCC-002: Subgroup Analysis of PFS

Subgroup	ET group (events/ n)	CT group (events/ n)	Hazard Ratio (95% CI)	p value
Age, years				0.146
≤ 40	29/31	30/42	1.14 (0.67, 1.91)	
> 40	151/165	135/154	0.80 (0.63, 1.00)	
Receptor status				0.099
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				0.487
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				0.904
AIs	74/83	66/83	0.98 (0.69, 1.15)	
ORMs	56/59	51/59	0.97 (0.70, 1.36)	
Metastasis number				0.851
< 2	127/140	111/139	0.89 (0.69, 1.15)	
≥ 2	53/56	54/57	0.86 (0.59, 1.27)	
Disease-free interval				0.016
≤ 24 months	59/64	64/78	1.39 (0.97, 1.98)	
> 24 months	71/78	53/64	0.77 (0.53, 1.10)	



Yuan Z et al. ASCO 2021;Abstract 1003.

Primary Outcome of the Phase III SYD985.002/TULIP Trial Comparing [vic-]Trastuzumab Duocarmazine to Physician's Choice Treatment in Patients with Pre-treated HER2-Positive Locally Advanced or Metastatic Breast Cancer

Manich E et al.

ESMO 2021;Abstract LBA15.

Conclusions: Treatment with [vic-]trastuzumab duocarmazine significantly improved PFS in comparison with standard physician's choice chemotherapy and may provide a new treatment option for patients with pre-treated locally advanced or metastatic HER2-positive breast cancer.

Select Ongoing Phase III Trials in Metastatic HER2-Positive Breast Cancer

Trial identifier	Estimated enrollment	Setting	Regimens	Estimated completion date
DESTINY-Breast09 (NCT04784715)	1,134	First line	• Trastuzumab deruxtecan • Trastuzumab deruxtecan + pertuzumab • Trastuzumab + pertuzumab + taxane	2029
HER2CLIMB-02 (NCT03975647)	460	Second line	• T-DM1 + tucatinib • Placebo + T-DM1	2024
DESTINY-Breast02 (NCT03523585)	600	Third line	• Trastuzumab deruxtecan • Physician's choice of capecitabine/trastuzumab or capecitabine/lapatinib	2024
DESTINY-Breast12	500	≤2 lines of therapy, presence or absence of BM	• Trastuzumab deruxtecan	2024

BM = brain metastases

www.clinicaltrials.gov. Accessed September 2021.

RTP RESEARCH TO PRACTICE

Localized HER2-Positive Breast Cancer

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TO PRACTICE

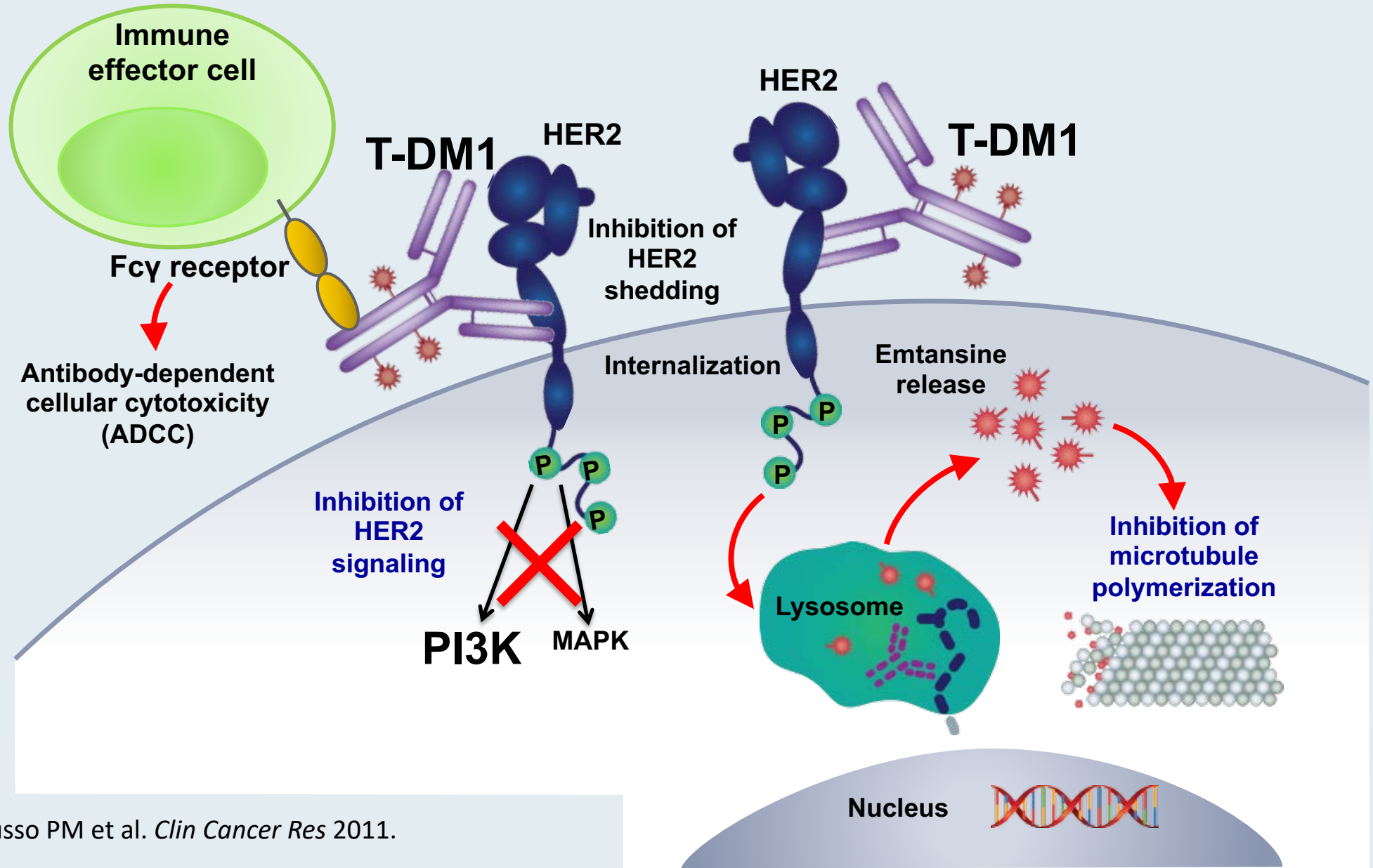
FDA-Approved Agents for Early-Stage HER2-Positive Breast Cancer

Agent	Setting	Pivotal trial(s)	Regimens	Year approved
Trastuzumab	Adjuvant HER2+ EBC, first line	NSABP-31 N9831 BCIRG 006 HERA	AC-T-placebo vs AC-T-H AC-T vs AC-H vs AC-T-H ACT vs ACT-H vs TC-H Observation vs trastuzumab	2006
Pertuzumab	Neoadjuvant HER2+, EBC	NeoSphere	TD vs PTD vs PT vs PD	2013
Pertuzumab	Adjuvant HER2+, EBC	APHINITY	Chemotherapy plus trastuzumab plus pertuzumab vs placebo	2017
Neratinib	Extended adjuvant treatment of HER2+ EBC	ExteNET	Placebo vs neratinib	2017
T-DM1	Adjuvant HER2+ EBC with residual disease after neoadjuvant taxane and trastuzumab-based treatment	KATHERINE	Trastuzumab vs T-DM1	2019

AC-H = doxorubicin, cyclophosphamide, and trastuzumab; AC-T, doxorubicin, cyclophosphamide, and paclitaxel; AC-T-H, doxorubicin, cyclophosphamide, paclitaxel, and trastuzumab; H, trastuzumab; PD, pertuzumab and docetaxel; PT, trastuzumab and pertuzumab; PTD, pertuzumab, trastuzumab, and docetaxel; TC, docetaxel and cyclophosphamide; TC-H, docetaxel, cyclophosphamide, and trastuzumab; TD, trastuzumab and docetaxel; THP, docetaxel, trastuzumab, and pertuzumab

Choong GM et al. *CA Cancer J Clin* 2020;70:355-374.

Trastuzumab Emtansine (T-DM1): Mechanisms of Action



Adapted from LoRusso PM et al. *Clin Cancer Res* 2011.

ARTICLE IN PRESS

ESMO GOOD SCIENCE BETTER MEDICINE BEST PRACTICE

Ann Oncol 2021;[Online ahead of print]

ANNALS OF ONCOLOGY driving innovation in oncology

ORIGINAL ARTICLE

Adjuvant T-DM1 versus trastuzumab in patients with residual invasive disease after neoadjuvant therapy for HER2-positive breast cancer: subgroup analyses from KATHERINE

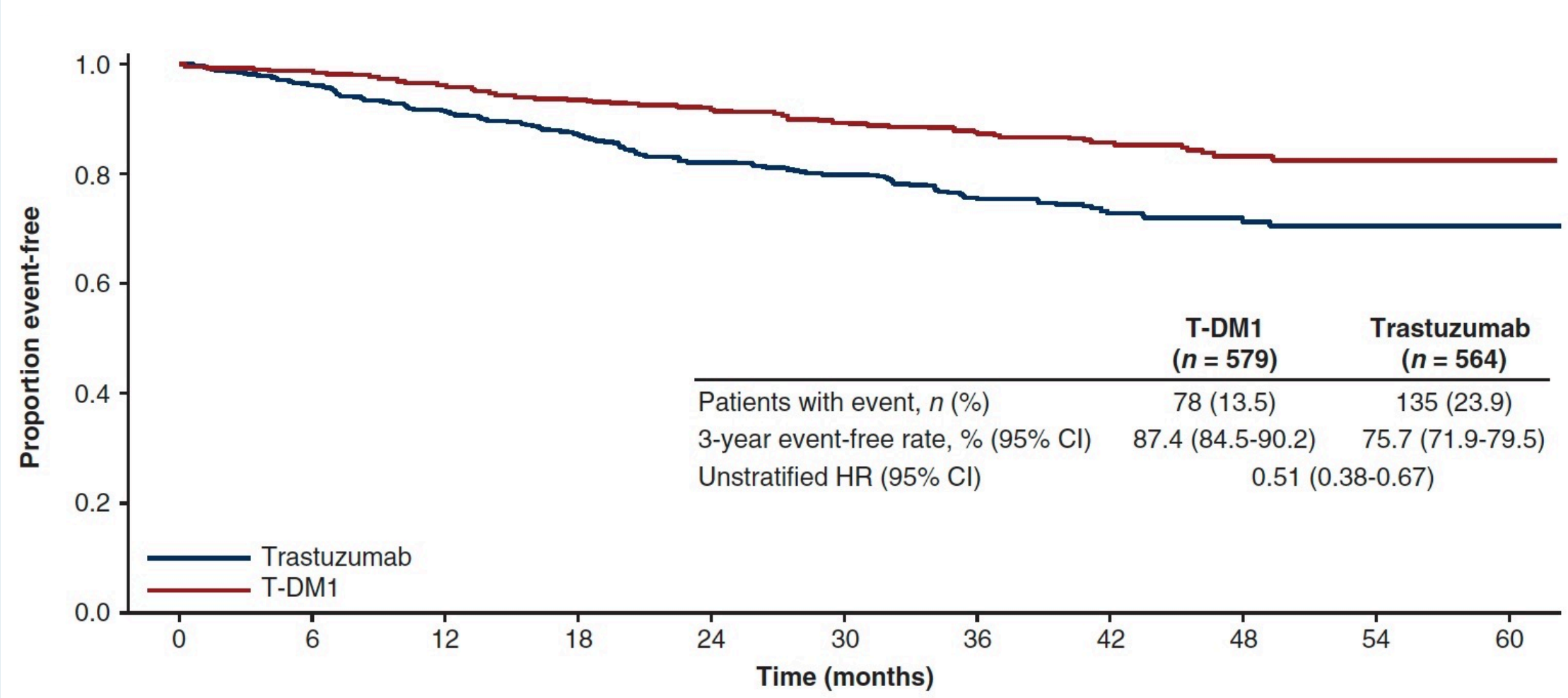
E. P. Mamounas[1,2*], M. Untch[3], M. S. Mano[4], C.-S. Huang[5], C. E. Geyer Jr[1,6], G. von Minckwitz[7], N. Wolmark[1,8], X. Pivot[9], S. Kuemmel[10,11], M. P. DiGiovanna[12], B. Kaufman[13], G. Kunz[7,14], A. K. Conlin[1,15], J. C. Alcedo[16], T. Kuehn[17], I. Wapnir[1,18], A. Fontana[19], J. Hackmann[7,20], J. Polikoff[1,21], M. Saghatchian[22], A. Brufsky[1,23], Y. Yang[24], M. Zimovjanova[25], T. Boulet[26], H. Liu[27], D. Tesarowski[28], L. H. Lam[28], C. Song[28], M. Smitt[28,29] & S. Loibl[7,30]

KATHERINE: Summary of Adverse Events Associated with T-DM1

Event	Trastuzumab (N = 720)	T-DM1 (N = 740)
Grade ≥3 adverse event	15.4%	25.7%
AE leading to drug discontinuation	2.1%	18.1%
Selected Grade ≥3 adverse event		
Decreased platelet count	0.3%	5.7%
Hypertension	1.2%	2.0%
Peripheral sensory neuropathy	0	1.4%
Decreased neutrophil count	0.7%	1.2%
Hypokalemia	0.1%	1.2%
Fatigue	0.1%	1.1%
Anemia	0.1%	1.1%

Von Minckwitz G et al. *N Engl J Med* 2019;380(7):617-28.

Time to First Invasive Disease-Free Survival Event for Patients Who Received Anthracycline-Based Neoadjuvant Therapy

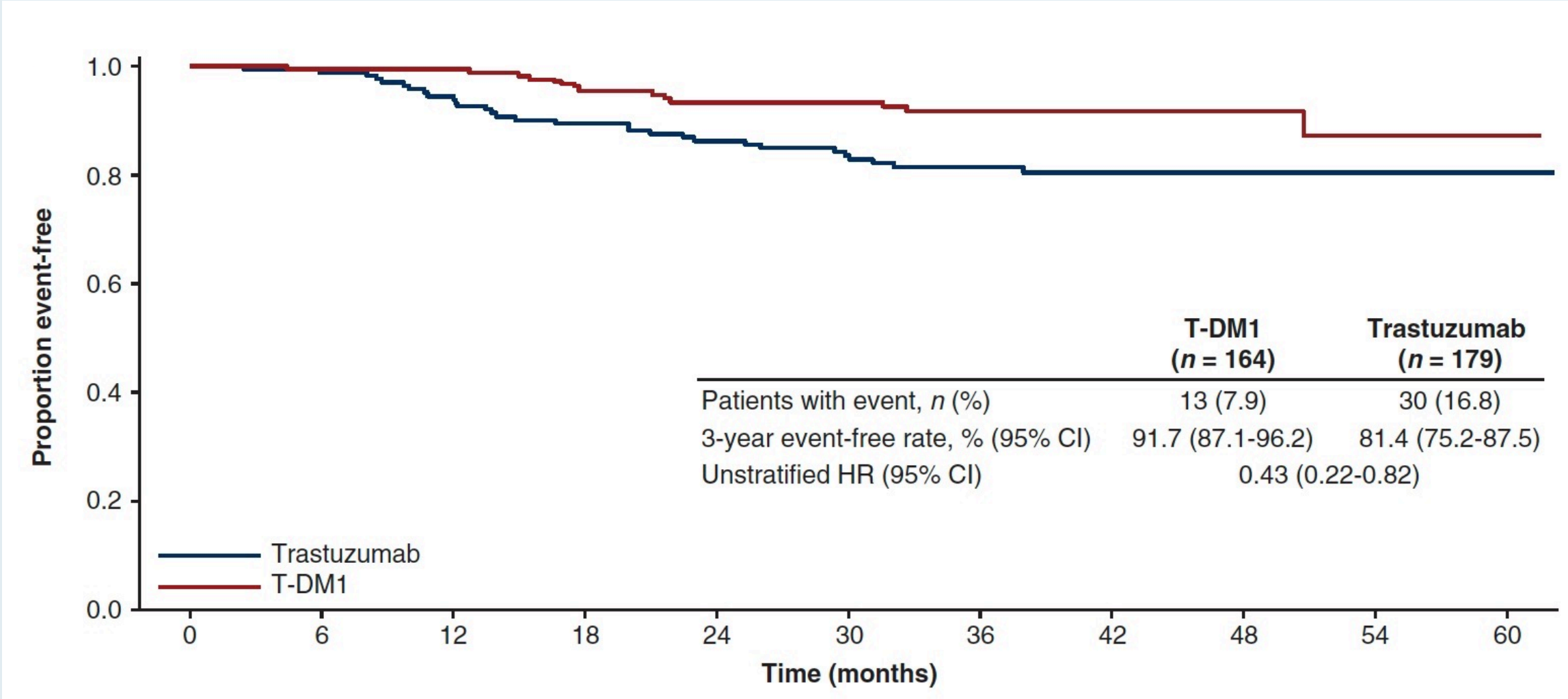


	T-DM1 (*n* = 579)	Trastuzumab (*n* = 564)
Patients with event, *n* (%)	78 (13.5)	135 (23.9)
3-year event-free rate, % (95% CI)	87.4 (84.5-90.2)	75.7 (71.9-79.5)
Unstratified HR (95% CI)	0.51 (0.38-0.67)	

Mamounas EP et al. *Ann Oncol* 2021;[Online ahead of print].

RTP RESEARCH TO PRACTICE

Time to First Invasive Disease-Free Survival Event for Patients Who Received Non-Anthracycline-Based Neoadjuvant Therapy



Mamounas EP et al. *Ann Oncol* 2021;[Online ahead of print].

RTP RESEARCH TO PRACTICE

original reports

Adjuvant Trastuzumab Emtansine Versus Paclitaxel in Combination With Trastuzumab for Stage I HER2-Positive Breast Cancer (ATEMPT): A Randomized Clinical Trial

Sara M. Tolaney, MD, MPH[1,2]; Nabihah Tayob, PhD[1]; Chau Dang, MD[3]; Denise A. Yardley, MD[4]; Steven J. Isakoff, MD, PhD[5]; Vicente Valero, MD[6]; Meredith Faggen, MD[1]; Therese Mulvey, MD[5]; Ron Bose, MD, PhD[7]; Jiani Hu, MSc[1]; Douglas Weckstein, MD[1]; Antonio C. Wolff, MD[8]; Katherine Reeder-Hayes, MD, MBA, MSc[9]; Hope S. Rugo, MD[10]; Bhuvaneswari Ramaswamy, MD[11]; Dan Zuckerman, MD[12]; Lowell Hart, MD[13]; Vijayakrishna K. Gadi, MD, PhD[14]; Michael Constantine, MD[1]; Kit Cheng, MD[15]; Frederick Briccetti, MD[1]; Bryan Schneider, MD[16]; Audrey Merrill Garrett, MD[17]; Kelly Marcom, MD[18]; Kathy Albain, MD[19]; Patricia DeFusco, MD[20]; Nadine Tung, MD[2,21]; Blair Ardman, MD[22]; Rita Nanda, MD[23]; Rachel C. Jankowitz, MD[24]; Mothaffar Rimawi, MD[25]; Vandana Abramson, MD[26]; Paula R. Pohlmann, MD, PhD, MSc[27]; Catherine Van Poznak, MD[28]; Andres Forero-Torres, MD[29]; Minetta Liu, MD[30]; Kathryn Ruddy, MD[30]; Yue Zheng, MSc[1]; Shoshana M. Rosenberg, ScD, MPH[1,2]; Richard D. Gelber, PhD[1,2]; Lorenzo Trippa, PhD[1,2]; William Barry, PhD[1]; Michelle DeMeo, BS[1]; Harold Burstein, MD, PhD[1,2]; Ann Partridge, MD, MPH[1,2]; Eric P. Winer, MD[1,2]; and Ian Krop, MD, PhD[1,2]

J Clin Oncol 2021;[Online ahead of print]

ATEMPT: Invasive Disease-Free Survival (iDFS) and Recurrence-Free Interval (RFI)

Outcome	T-DM1 (n = 383)	TH (n = 114)
Three-year iDFS	97.8%	93.4%
Three-year RFI	99.2%	94.3%

Tolaney SM et al. *J Clin Oncol* 2021;[Online ahead of print].

ATEMPT: Clinically Relevant Toxicity

Clinically Relevant Toxicity	T-DM1 (n = 383)	TH (n = 114)
Grade ≥3 nonhematologic toxicity	9%	11%
Grade ≥2 neurotoxicity	11%	23%
Grade ≥4 hematologic toxicity	1%	0%
Febrile neutropenia	0%	2%
Any toxicity requiring dose delay	28%	26%
Any toxicity requiring early discontinuation	17%	6%
Total	46%	47%

Tolaney SM et al. *J Clin Oncol* 2021;[Online ahead of print].

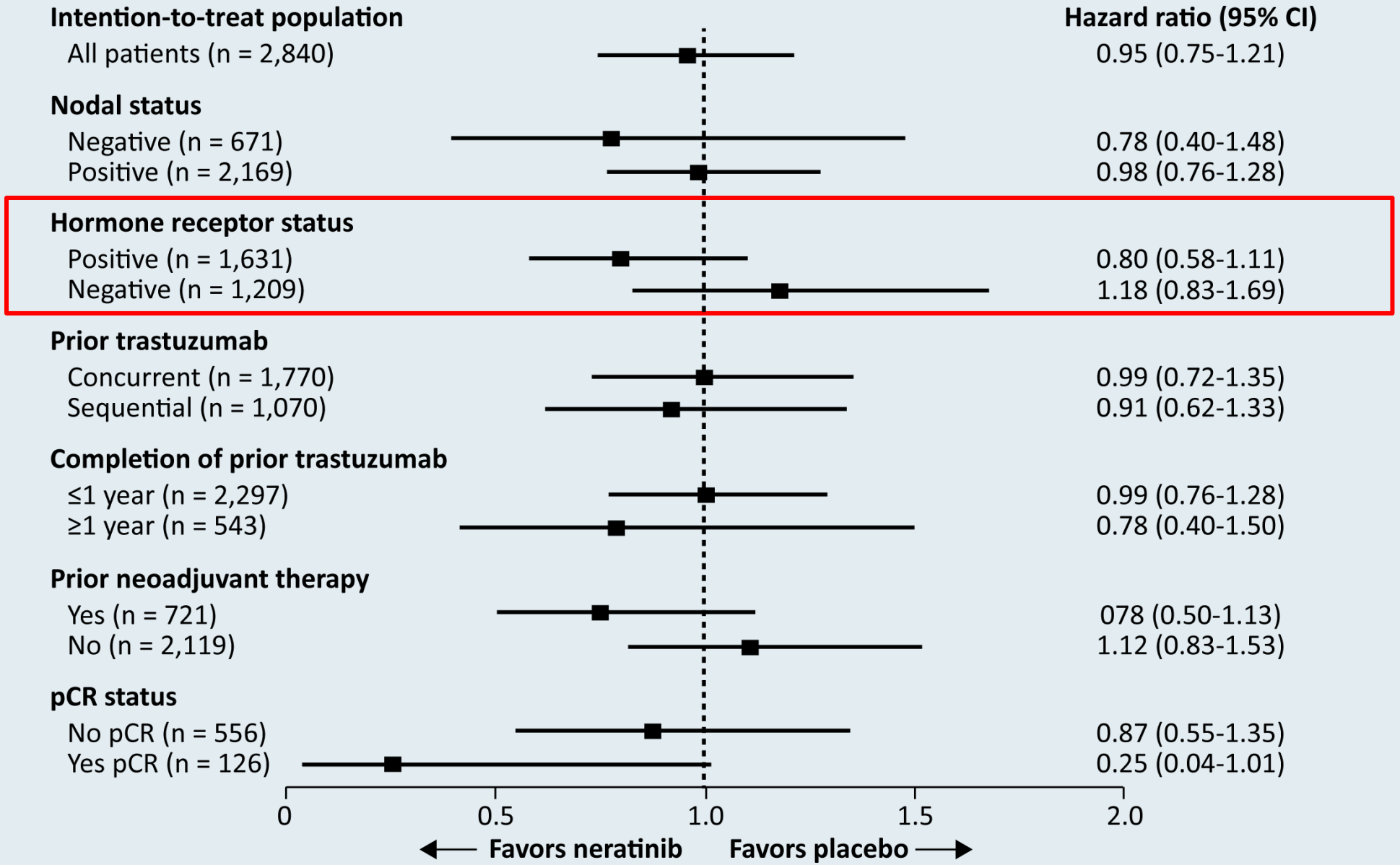
RTP RESEARCH TO PRACTICE

Continued Efficacy of Neratinib in Patients with HER2-Positive Early-Stage Breast Cancer: Final Overall Survival Analysis from the Randomized Phase 3 ExteNET Trial

Holmes FA et al.

SABCS 2020;Abstract PD3-03.

ExteNET: Final Overall Survival Analysis



Holmes FA et al. SABCS 2020;Abstract PD3-03.

ExteNET: Cumulative Incidence of CNS Recurrences

Population or subgroup	Events, n		Cumulative incidence of CNS recurrences, % (95% CI)	
	Neratinib	Placebo	Neratinib	Placebo
Intention-to-treat population (n = 2,840)	16	23	1.3 (0.8-2.1)	1.8 (1.2-2.7)
HR+/≤1-year population (EU indication) (n = 1,334)	4	12	0.7 (0.2-1.7)	2.1 (1.1-3.5)
Prior neoadjuvant therapy (n = 1,334)				
No (n = 980)	3	6	0.7 (0.2-2.0)	1.5 (0.6-3.0)
Yes (n = 354)	1	6	0.7 (0.1-3.3)	3.7 (1.5-7.4)
pCR status (n = 354)				
No (n = 295)	1	5	0.8 (0.1-4.0)	3.6 (1.3-7.8)
Yes (n = 38)	0	1	0 (NE)	5.0 (0.3-21.2)

Holmes FA et al. SABCS 2020;Abstract PD3-03.

ExteNET: CNS Disease-Free Survival at 5 Years

Population or subgroup	Events, n		Kaplan-Meier estimate at 5 years %, (95% CI)		Hazard ratio
	Neratinib	Placebo	Neratinib	Placebo	
Intention-to-treat population (n = 2,840)	29	42	97.5 (96-4-98.3)	96.4 (95.2-97.4)	0.73
HR+/≤1-year population (EU indication) (n = 1,334)	9	23	98.4 (96.8-99.1)	95.7 (93.6-97.2)	0.41
Prior neoadjuvant therapy (n = 1,334)					
No (n = 980)	7	10	98.2 (96.3-99.2)	97.5 (95.3-98.6)	0.70
Yes (n = 354)	2	13	98.7 (94.8-99.7)	91.2 (85.1-94.8)	0.18
pCR status (n = 354)					
No (n = 295)	2	10	98.4 (93.6-99.6)	92.0 (85.6-95.7)	0.24
Yes (n = 38)	0	3	100 (100-100)	81.9 (53.1-93.9)	0

Holmes FA et al. SABCS 2020;Abstract PD3-03.

RTP RESEARCH TO PRACTICE

CONTROL Trial: Strategies to Improve Neratinib Tolerability

Background: Neratinib is approved for extended adjuvant therapy in HER2-positive BC

- Neratinib poorly tolerated in ExteNET
  - Discontinuation rate: 17%
  - Grade 3 diarrhea: 40%

Objective: Improve GI tolerability of neratinib

Methods: **Sequential single arm interventions in patients treated with adjuvant therapy**

- Cohort 1 (L): Loperamide (n = 137)
- Cohort 2 (BL): Budesonide + loperamide (n = 64)
- Cohort 3 (CL or CL-PRN): Colestipol + loperamide (n = 136) or colestipol + as needed loperamide (n = 104)
- Cohort 4 (DE): Neratinib dose escalation; ongoing (n = 60)

Barcenas CH et al. *Ann Oncol* 2020;31(9):1223-30.

Treatment-Emergent Diarrhea in the ExteNET and CONTROL Studies

Outcome	ExteNET (*n* = 1408)	L (*n* = 137)	BL (*n* = 64)	CL (*n* = 136)	CL-PRN (*n* = 104)	DE (*n* = 60)
Treatment-emergent diarrhea incidence, *n* (%)						
No diarrhea	65 (5)	28 (20)	9 (14)	23 (17)	5 (5)	1 (2)
Grade 1	323 (23)	33 (24)	16 (25)	38 (28)	34 (33)	25 (42)
Grade 2	458 (33)	34 (25)	21 (33)	47 (35)	32 (31)	25 (42)
Grade 3	561 (40)	42 (31)	18 (28)	28 (21)	33 (32)	9 (15)
Grade 4	1 (<1)	0	0	0	0	0
Action taken, *n* (%)						
Dose hold	477 (34)	20 (15)	12 (19)	22 (16)	15 (14)	7 (12)
Dose reduction	372 (26)	10 (7)	3 (5)	10 (7)	12 (12)	2 (3)
Discontinuation	237 (17)	28 (20)	5 (8)	5 (4)	8 (8)	2 (3)
Hospitalization	20 (1)	2 (1)	0	0	0	0

Barcenas CH et al. *Ann Oncol* 2020;31(9):1223-30.

Select Ongoing Trials in Early-Stage HER2-Positive Breast Cancer

Trial identifier	Phase	Setting	Regimens	Estimated completion date
CompassHER2 pCR (NCT04266249)	II	Neoadjuvant and adjuvant	• Preoperative chemotherapy + trastuzumab/pertuzumab • *If pCR* → postoperative trastuzumab/pertuzumab • *If residual disease* → postoperative T-DM1 or T-DM1 + tucatinib	2023
DESTINY-Breast05 (NCT04622319)	III	High-risk, residual disease after neoadjuvant chemotherapy	• Trastuzumab deruxtecan • T-DM1	2027

www.clinicaltrials.gov. Accessed August 2021.

RTP RESEARCH TO PRACTICE

Fall Oncology Nursing Series

A Complimentary NCPD-Accredited Virtual Curriculum

Hodgkin and Non-Hodgkin Lymphomas

Thursday, September 23, 2021
5:00 PM – 6:00 PM ET

Faculty

John P Leonard, MD
Amy Goodrich, CRNP

Moderator

Neil Love, MD

RTP RESEARCH TO PRACTICE

Thank you for joining us!

CME and MOC credit information will be emailed to each participant within 5 business days.

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