Meet The Professor

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

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Vice Chair, Oncology Care
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Commercial Support

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Dr Love — Disclosures

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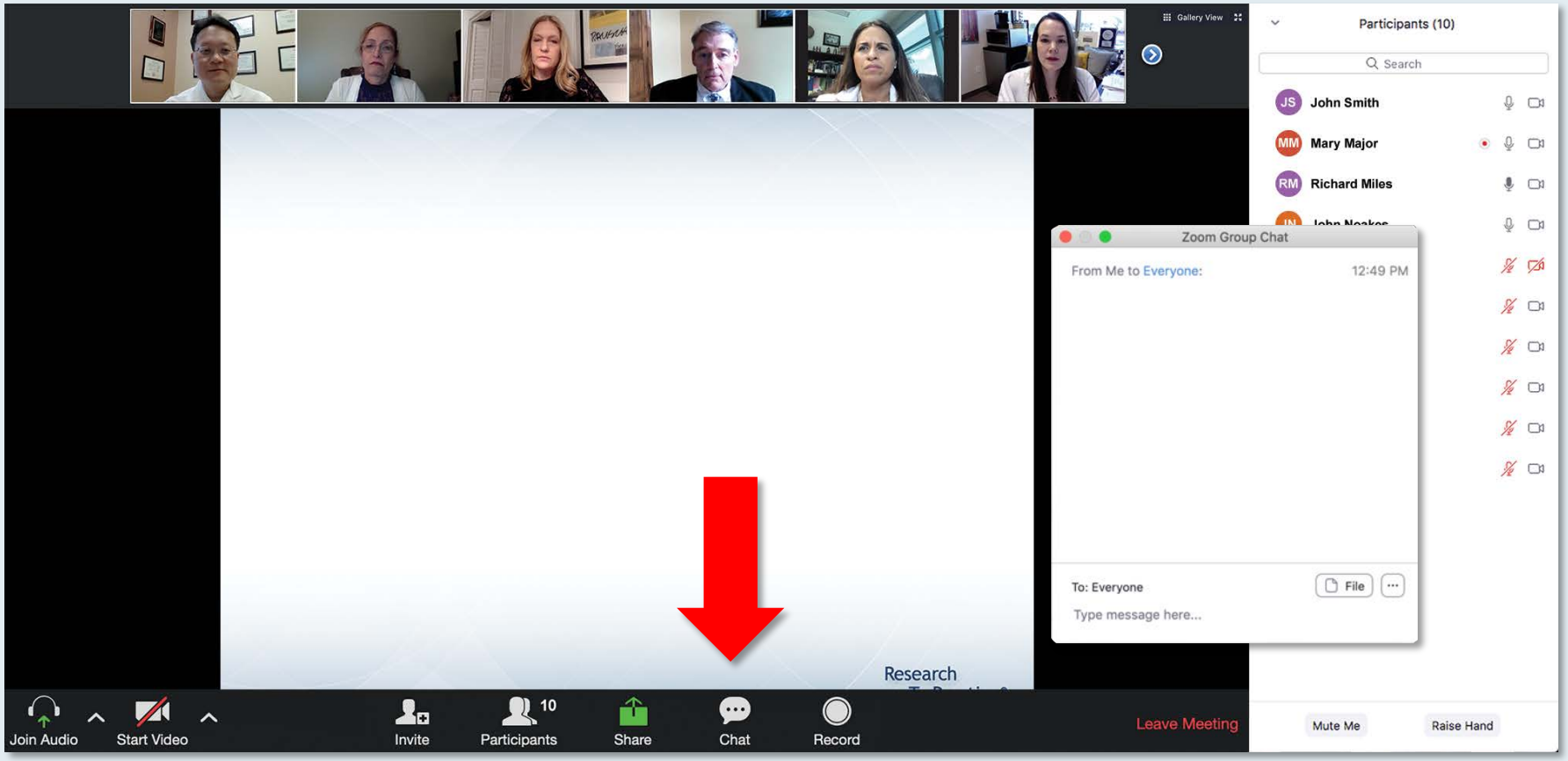

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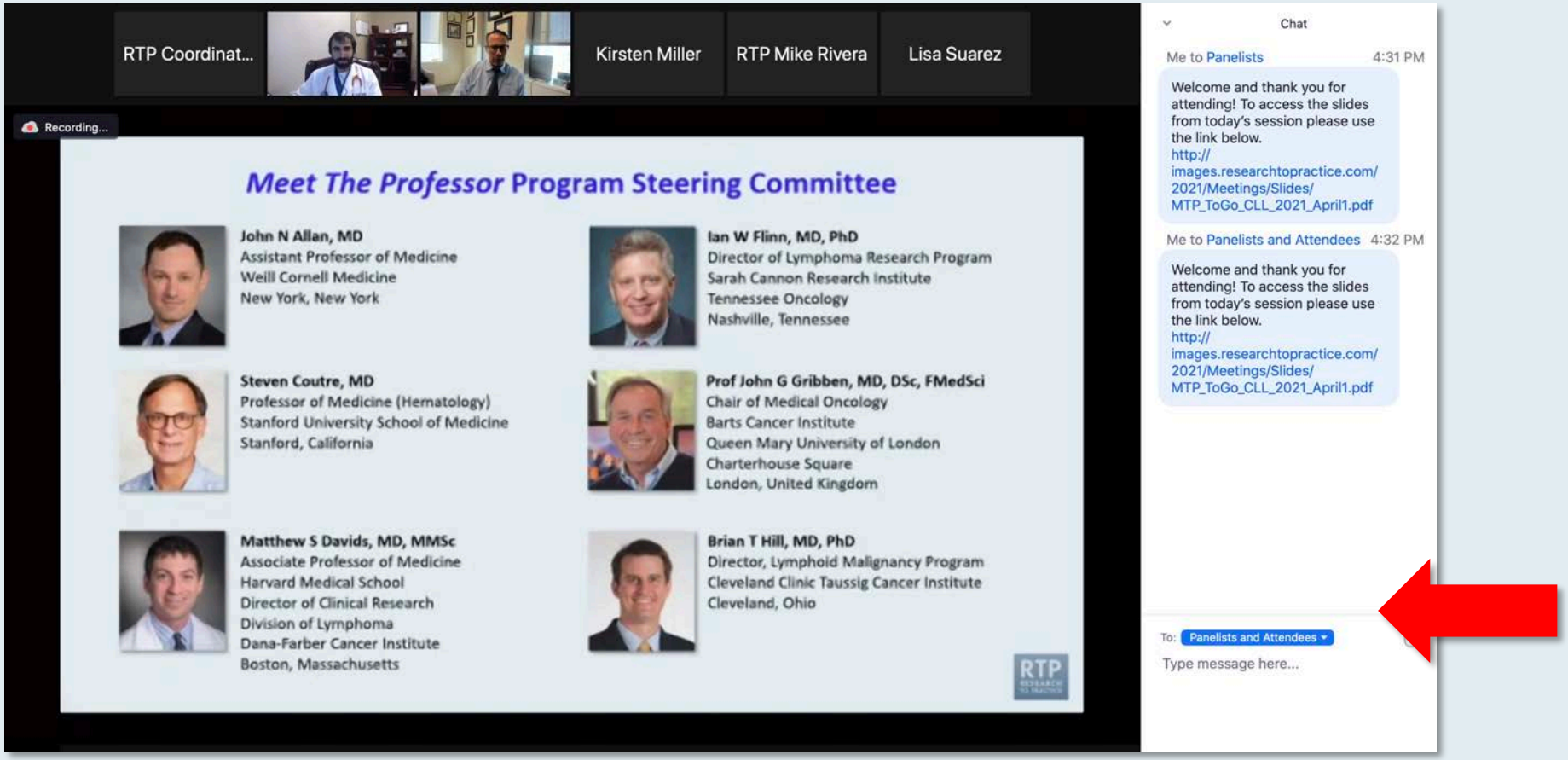

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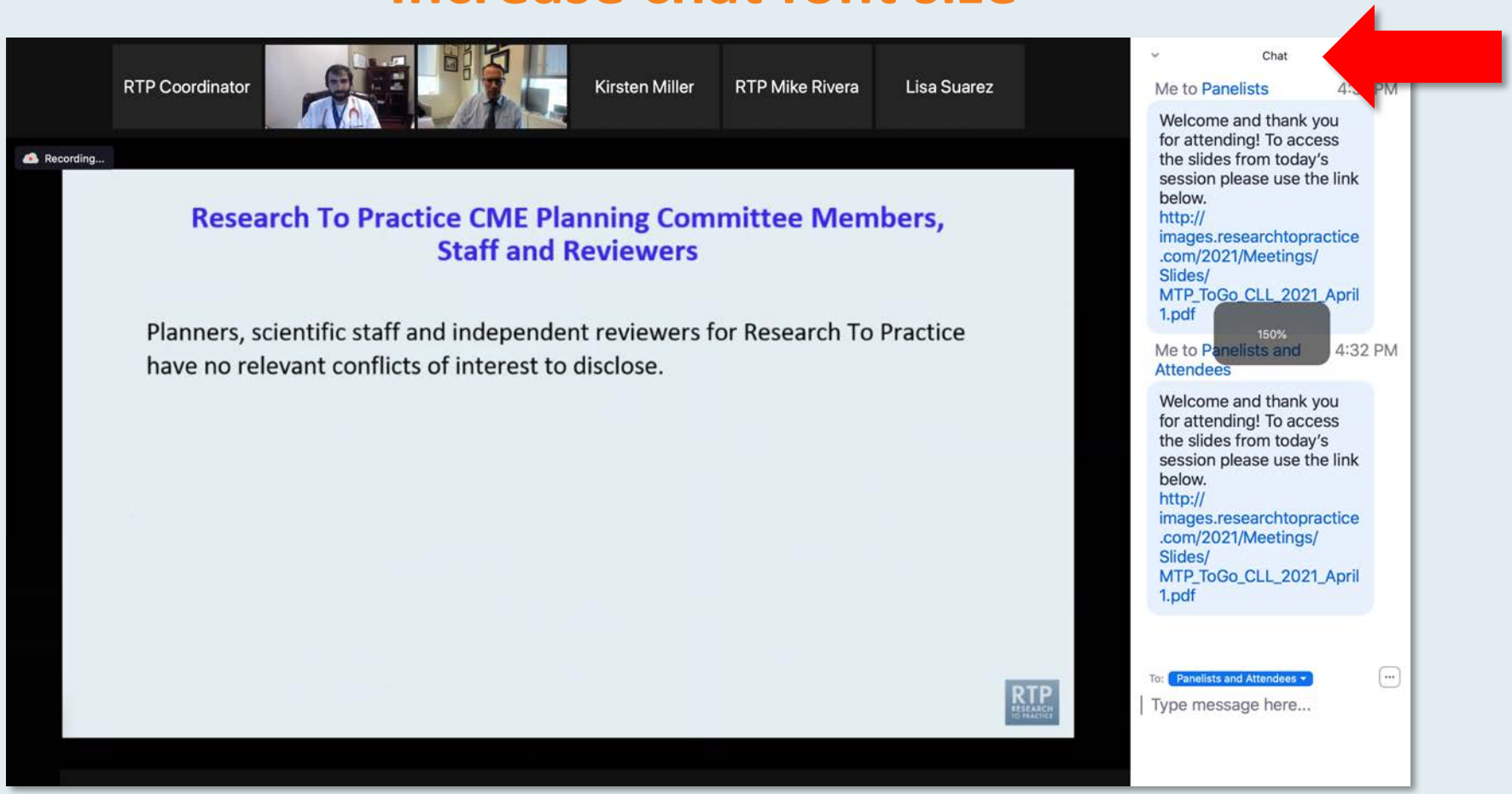

Press Command (for Mac) or Control (for PC) and the + symbol.
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Management of HER2-Low Breast Cancer

DR IAN KROP

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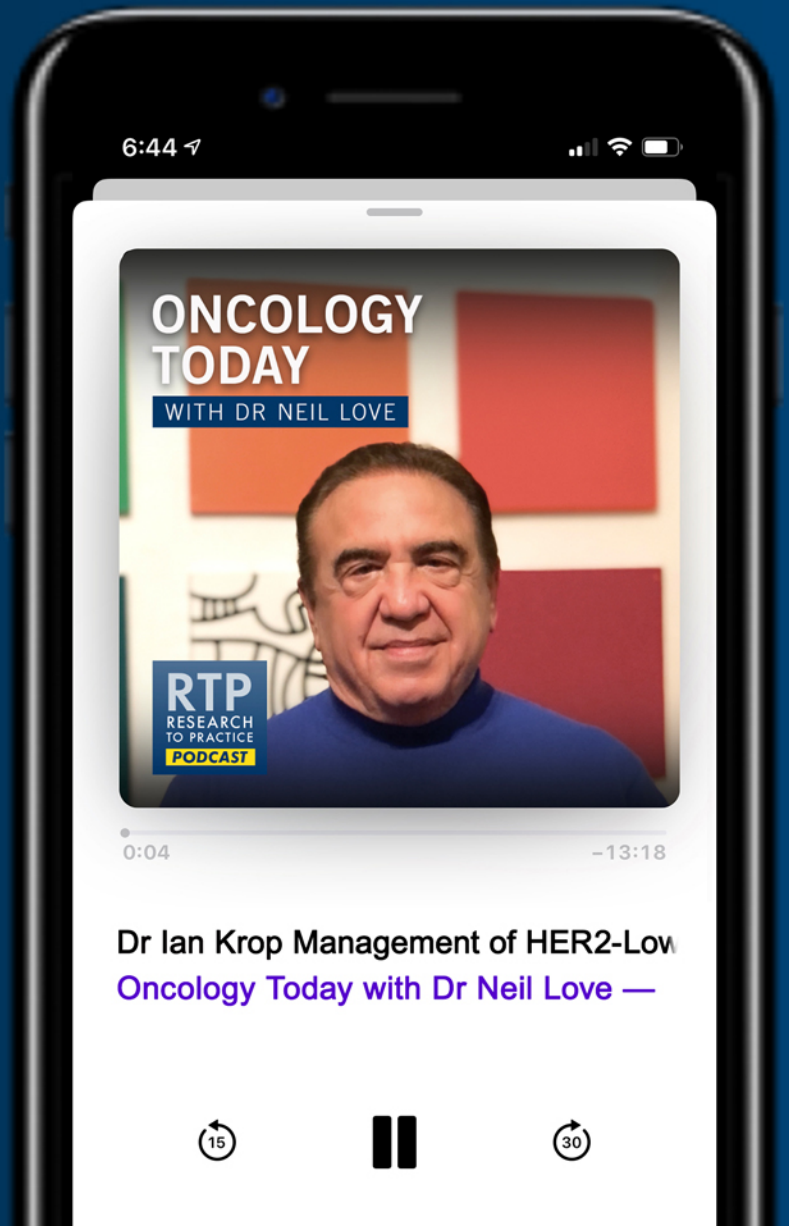

Year in Review: Clinical Investigator Perspectives on the Most Relevant New Data Sets and Advances in Oncology

Immunotherapy and Other Nontargeted Approaches for Lung Cancer

Thursday, January 13, 2022
5:00 PM – 6:00 PM ET

Faculty

Corey J Langer, MD

Anne S Tsao, MD, MBA

Moderator

Neil Love, MD

RTP Year in Review 2022

Beyond the Guidelines: Clinical Investigator Perspectives on the Management of Colorectal Cancer (Part 1 of a 3-Part Series)

Wednesday, January 19, 2022
10:15 PM – 11:45 PM ET

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Cathy Eng, MD
Christopher Lieu, MD
Alan P Venook, MD

Moderator

Kristen K Ciombor, MD, MSCI

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Beyond the Guidelines: Clinical Investigator Perspectives on the Management of Gastroesophageal Cancers (Part 2 of a 3-Part Series)

Thursday, January 20, 2022
9:15 PM – 10:45 PM ET

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Eric Van Cutsem, MD, PhD
Harry H Yoon, MD

Moderator

Samuel J Klempner, MD

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Richard S Finn, MD
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Chronic Lymphocytic Leukemia

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Jeff Sharman, MD

Moderator

Neil Love, MD

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Promising Investigational Agents and Strategies for Patients with Metastatic Non-Small Cell Lung Cancer Who Experience Disease Progression on Immune Checkpoint Inhibitor Therapy

Wednesday, January 26, 2022
5:00 PM – 6:00 PM ET

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Edward B Garon, MD, MS

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UPMC Hillman Cancer Center
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Karen A Gelmon, MD
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Erika Hamilton, MD
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Sarah Cannon Research Institute/Tennessee Oncology
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Professor of Medicine
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Reshma Mahtani, DO
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Helen Diller Family Comprehensive Cancer Center
San Francisco, California

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Associate Director, Susan F Smith Center
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Senior Physician
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Associate Professor of Medicine
Harvard Medical School
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Miami, Florida

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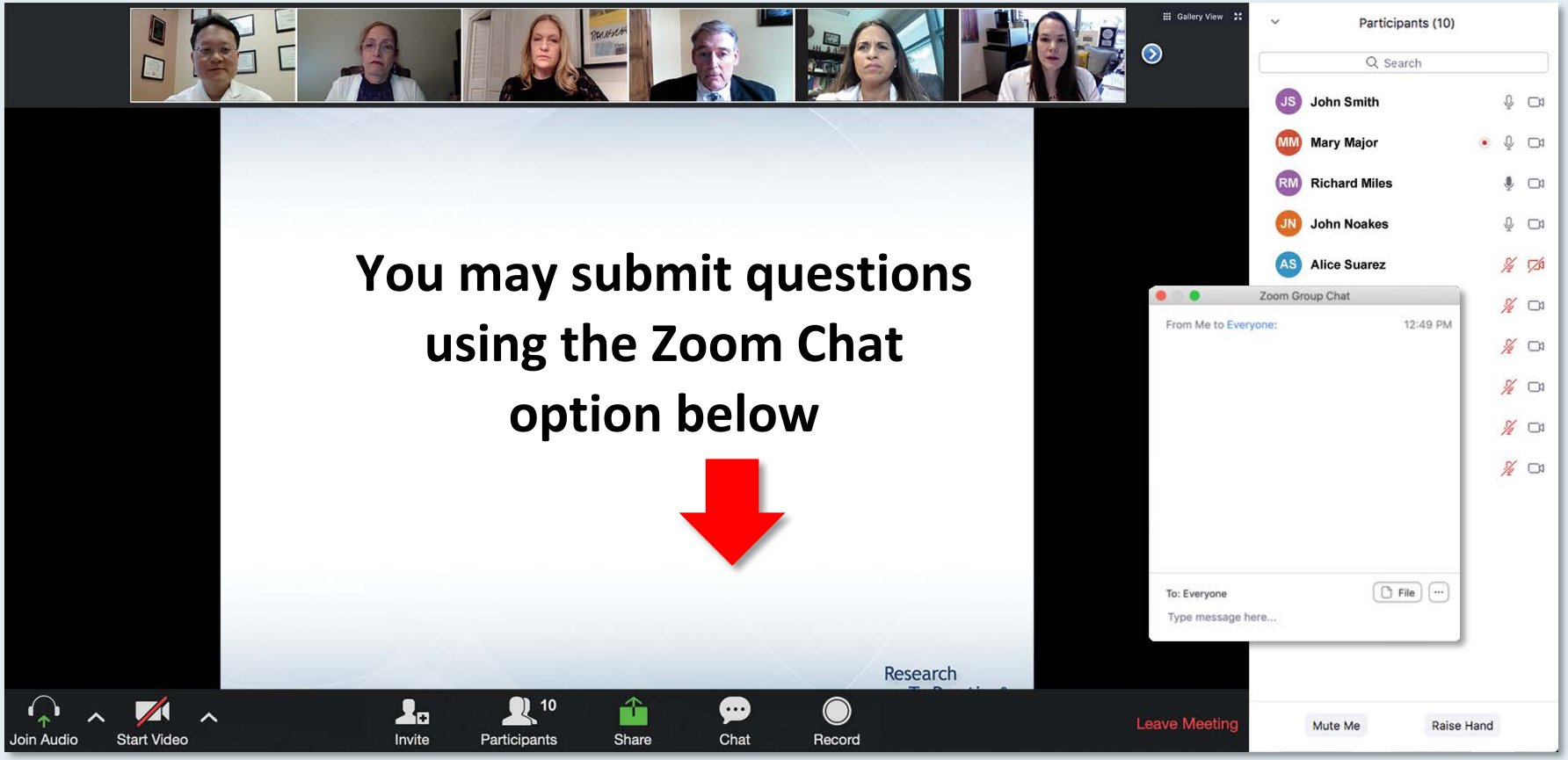

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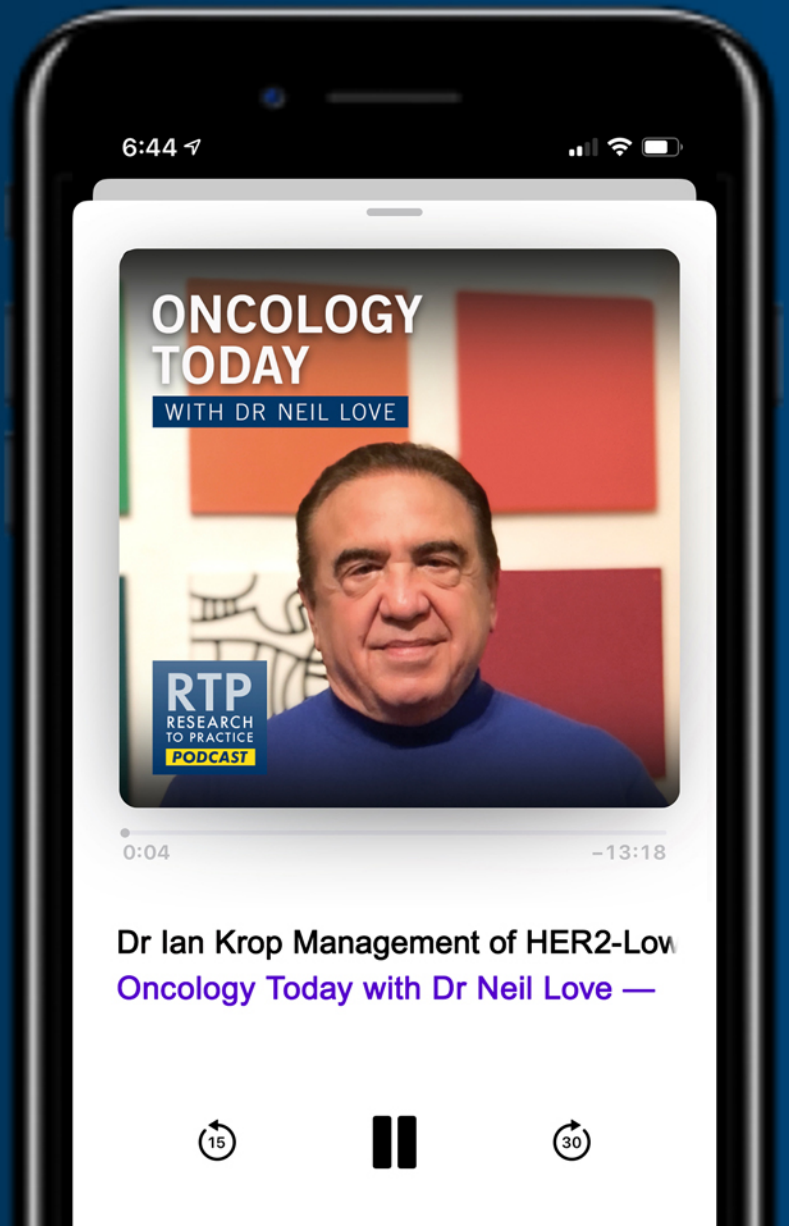

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Associate Professor
Weill Cornell Medical College
New York, New York

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	Trastuzumab deruxtecan
 Dr Hamilton	Tucatinib + trastuzumab/ capecitabine	 Dr Rugo	Trastuzumab deruxtecan
 Dr Hurvitz	Tucatinib + trastuzumab/ capecitabine	 Dr Tolaney	Trastuzumab/ pertuzumab/paclitaxel

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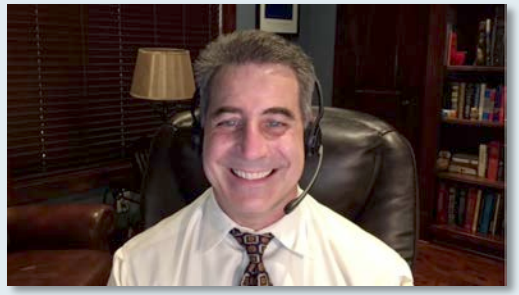
Real World Cases

Rohit Gosain, MD
UPMC Hillman Cancer Center
Jamestown, New York



Joseph Martins, MD
UT Health Science Center
Tyler, Texas

Arielle Heeke, MD
Levine Cancer Institute
Charlotte, North Carolina

Namrata I Peswani, MD
UT Southwestern Medical Center
Simmons Comprehensive
Cancer Center
Richardson, Texas

Gretchen G Kimmick, MD
Duke Cancer Institute
Durham, North Carolina

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Investigator Comments

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Sara M Tolaney, MD, MPH
Chief, Division of Breast Oncology
Associate Director, Susan F Smith Center for Women's Cancers
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Meet The Professor with Dr Traina

Introduction: HER2 Trials in Progress

MODULE 1: Case Presentations

- Dr Martins: A 60-year-old woman with de novo metastatic triple-positive breast cancer
- Dr Kimmick: A 62-year-old woman with metastatic triple-positive breast cancer
- Dr Peswani: A 58-year-old woman with localized triple-positive breast cancer
- Dr Heeke: A 58-year-old woman with multicentric node-positive breast cancer

MODULE 2: Investigator Comments

MODULE 3: SABCS® 2021

MODULE 4: Journal Club with Dr Traina

MODULE 5: Faculty Survey

MODULE 6: Appendix of Key Data Sets

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Select Ongoing Phase III Trials for 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
KATE3 (NCT04740918)	320	After prior trastuzumab +/- pertuzumab and taxane in the neo(adjuvant) or metastatic setting PD-L1-positive	• T-DM1 • T-DM1 + atezolizumab	2027
CompassHER2 RD (NCT04457596)	1,031	Postneoadjuvant residual disease	• Postneoadjuvant T-DM1 + tucatinib	2035

www.clinicaltrials.gov. Accessed September 2021.

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

Trial identifier	Estimated enrollment	Setting	Regimens	Estimated completion date
eMonarcHER (NCT04752332)	2,450	Adjuvant, high risk, node positive	• Abemaciclib + Standard ET • Standard adjuvant ET	2033
DESTINY-Breast05	1,600	Postneoadjuvant Residual disease	• T-DXd • T-DM1	2027
HER2CLIMB-02 (NCT03975647)	460	Second line	• T-DM1 + tucatinib • Placebo + T-DM1	2024

www.clinicaltrials.gov. Accessed September 2021.

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Select Trials in Progress for HER2-Positive Breast Cancer

- ESMO 2021: 330TiP Trastuzumab deruxtecan (T-DXd; DS-8201) in HER2-positive (HER2+) and HER2-low expressing (HER-LE) metastatic breast cancer (MBC) with brain metastases (BM) and/or leptomeningeal carcinomatosis (LMC): DEBBRAH
  Presenter: Marta Vaz Batista

- ESMO 2021: 331TiP HER2CLIMB-04 – Phase II trial of tucatinib + trastuzumab deruxtecan in patients with HER2+ locally advanced or metastatic breast cancer with and without brain metastases
  Presenter: Lisa Carey

- ESMO 2020: 353TiP HER2CLIMB-02 – A randomized, double-blind, phase III study of tucatinib or placebo with T-DM1 for unresectable locally advanced or metastatic HER2+ breast cancer
  Presenter: Sara Hurvitz

- ASCO 2021: TPS1099 Phase I/II study of radiation therapy followed by intrathecal trastuzumab/pertuzumab in the management of HER2+ breast leptomeningeal disease
  Presenter: Kamran A Ahmed

Select Trials in Progress for HER2-Positive Breast Cancer (Continued)

- SABCS 2020: OT-28-01 HER2CLIMB-02 – A randomized, double-blind, phase 3 study of tucatinib or placebo with T-DM1 for unresectable locally-advanced or metastatic HER2+ breast cancer
  Presenter: Sara Hurvitz

- SABCS 2020: OT-28-03 VICKI – A Phase Ib/II, randomized, placebo-controlled, study of venetoclax plus ado-trastuzumab emtansine (T-DM1) in patients (pts) with previously treated HER2-positive locally advanced (LA) or metastatic breast cancer (MBC)
  Presenter: Geoffrey Lindeman

- SABCS 2019: OT2-01-02 TBCRC049 – A phase II non-randomized study to assess the safety and efficacy of the combination of tucatinib and trastuzumab and capecitabine for treatment of leptomeningeal metastases in HER2 positive breast cancer
  Presenter: Rashmi K Murthy

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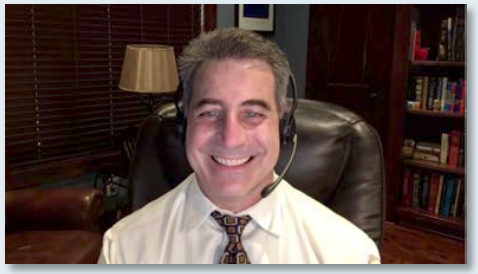
Case Presentation – Dr Martins: A 60-year-old woman with de novo metastatic triple-positive breast cancer



Dr Joseph Martins

- 2014: Palpable triple-positive breast mass, with numerous asymptomatic bone metastases
- Paclitaxel/trastuzumab/pertuzumab, with great response → Tamoxifen/trastuzumab/pertuzumab
- 2015: EF declined to 45%, trastuzumab discontinued, referred to Cardiology
  - Initiated Beta blocker and ACE inhibitor → EF returned to normal
- 2/2016: Anastrozole, but PD 2 months later → Trastuzumab/pertuzumab
- 2/2019: PD → T-DM1, discontinued anastrozole
- 4/2020: PD → Trastuzumab deruxtecan
- Serologic progression during unintended denosumab break; CA15-3 improved when resumed

Questions

- Would you or have you re-challenged a patient who experienced an EF decline on trastuzumab/pertuzumab, which subsequently returned to normal after treatment?
- What is the cardiac toxicity of other anti-HER2 agents?
- What treatment would you recommend next, particularly non-chemotherapy options?

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Case Presentation – Dr Kimmick: A 62-year-old woman with metastatic triple-positive breast cancer

Dr Gretchen Kimmick

- Triple-positive localized breast cancer, s/p adjuvant therapy
- Recurrence in bone but unable to verify ER/PR and HER2 status → Endocrine therapy alone
- Liver metastases → Trastuzumab/pertuzumab/fulvestrant → Worsening liver metastases

Questions

- What are your thoughts about endocrine therapy versus chemotherapy in a patient with metastatic disease? Do you start with anti-HER2 therapy and chemotherapy and then switch from chemotherapy to endocrine therapy after response?
- Our typical second-line therapy would be T-DM1, but with recent data would you use trastuzumab deruxtecan?
- Do we need to adjust her dose due to the liver disease?

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Case Presentation – Dr Peswani: A 58-year-old woman with localized triple-positive breast cancer

Dr Namrata Peswani

- Localized triple-positive left breast cancer, s/p neoadjuvant TCHP (severe diarrhea)
- Surgery → pT1cN1aM0 residual disease
- T-DM1 and concurrent RT, with Grade 3 pneumonitis after 6 months
- Patient refuses pertuzumab but agrees to trastuzumab alone

Questions

- Would you consider neratinib after completion of trastuzumab due to her residual disease?
- Would you consider T-DM1 again, since she has completed RT, or would that put her at too much risk for pneumonitis again?

Case Presentation – Dr Heeke: A 58-year-old woman with multicentric node-positive breast cancer

Dr Arielle Heeke

- Three left breast lesions, with biopsy-proven node-positive disease
  - ER/PR/HER2-negative
  - ER-positive, PR-negative, HER2-positive
  - ER/PR-negative, HER2-negative
- Staging CT CAP and bone scan: Negative
- Neoadjuvant AC → THP

Question

- For which patient would you opt for an anthracycline-based regimen when there's HER2-positive disease versus a traditional approach, which is an anthracycline-sparing regimen?

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Dr Sara Tolaney

DESTINY-Breast03

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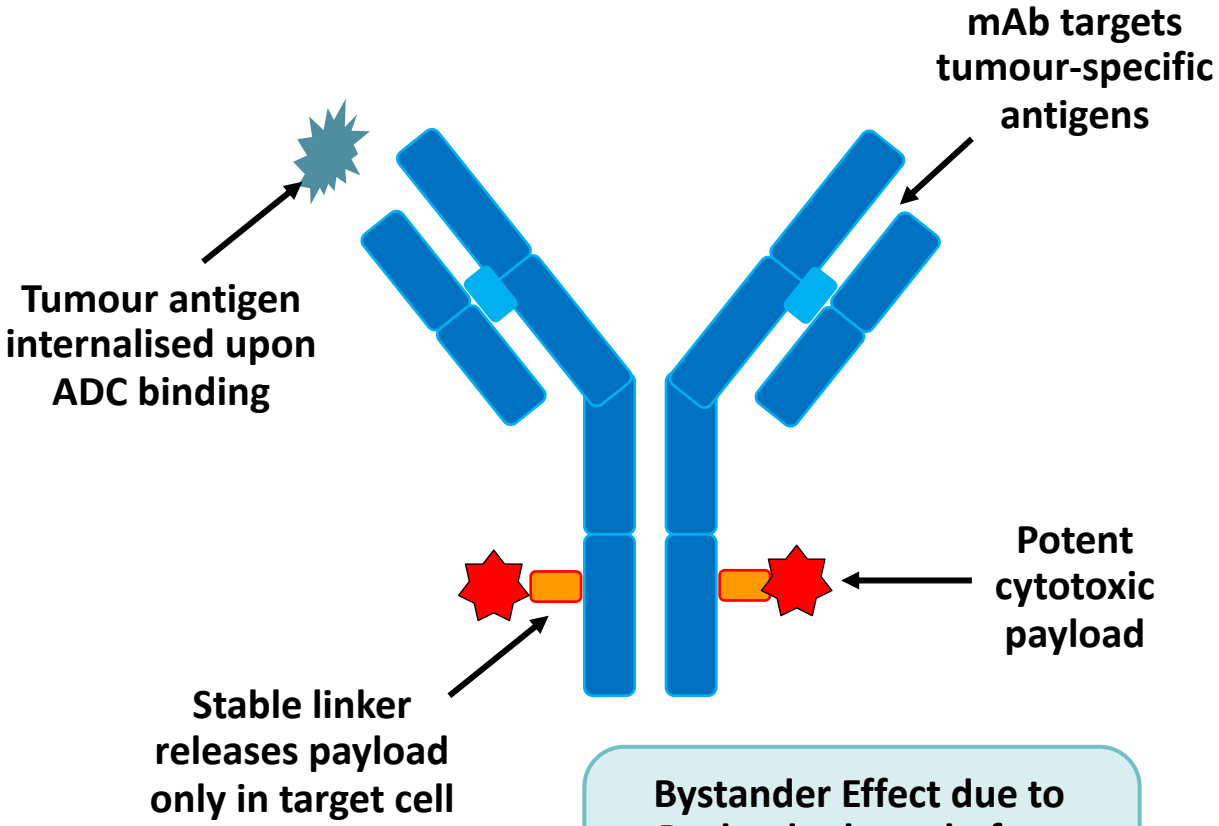
HER2-targeting Antibody Drug Conjugates (ADCs)



Bystander Effect due to Payload release before internalisation or membrane permeability

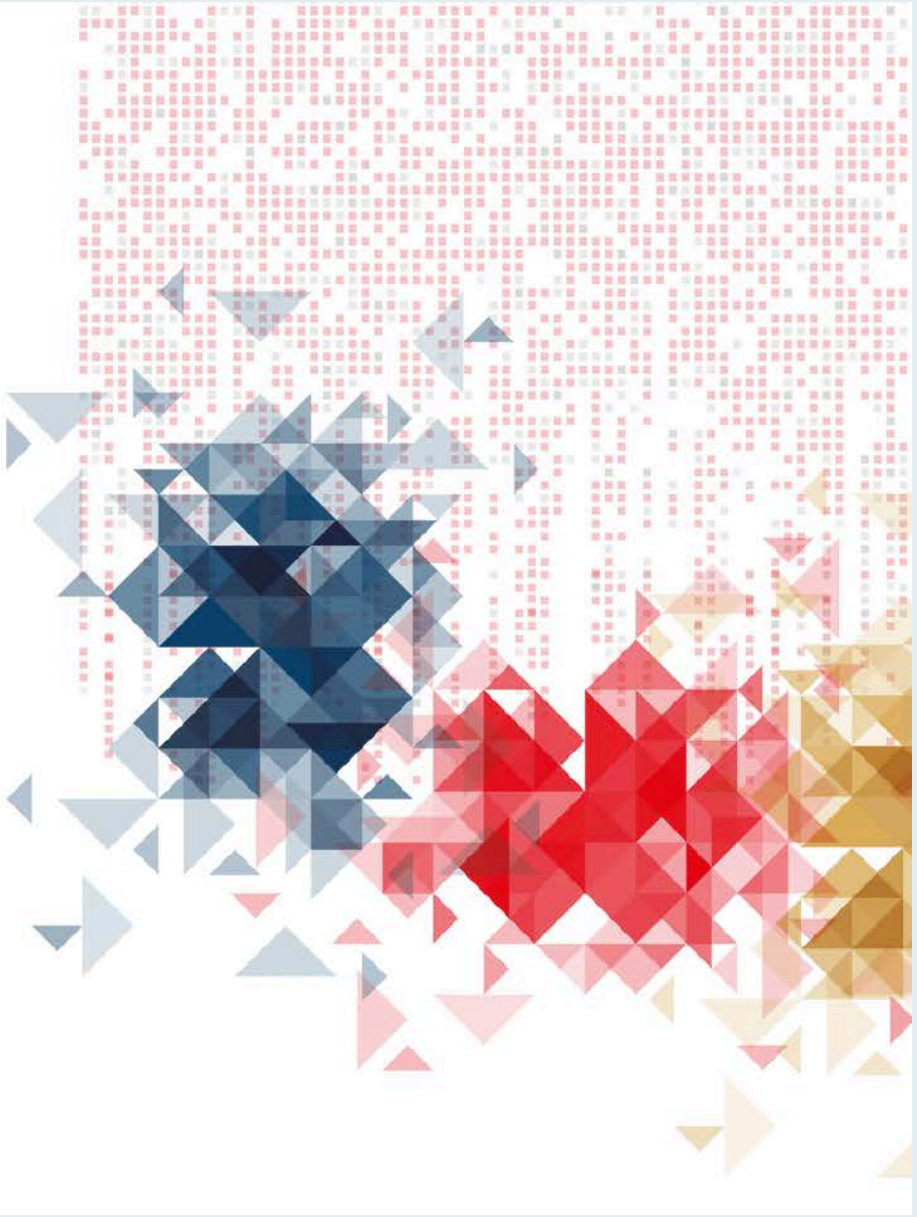
ADC Attributes	T-DM1[3-5]	T-DXd[1-4,a]
Payload MoA	Anti-microtubule	Topoisomerase I inhibitor
Drug-to-antibody ratio	~3.5:1	~8:1
Tumor-selective cleavable linker?	No	Yes
Evidence of bystander anti-tumor effect?	No	Yes

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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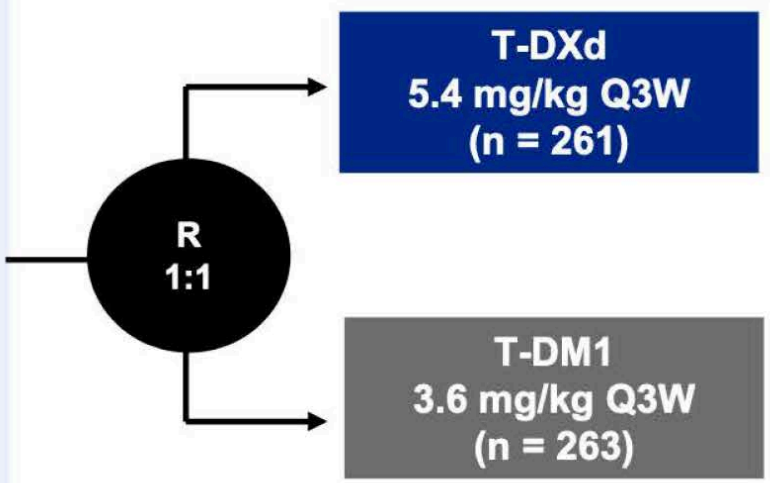
DESTINY-Breast03 Phase III Trial Schema

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

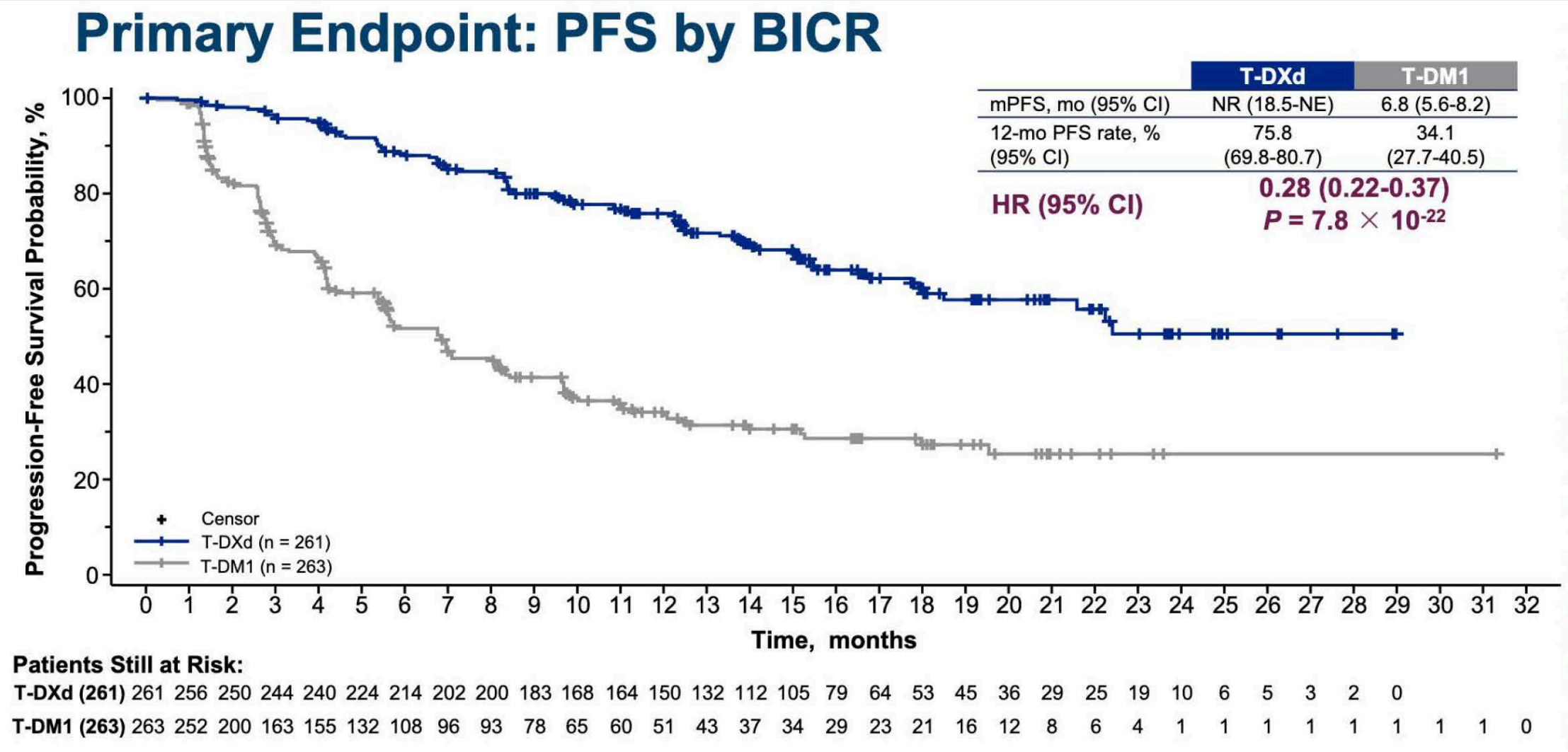
Secondary endpoints
- ORR (BICR and investigator)
- DOR (BICR)
- PFS (investigator)
- Safety

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.

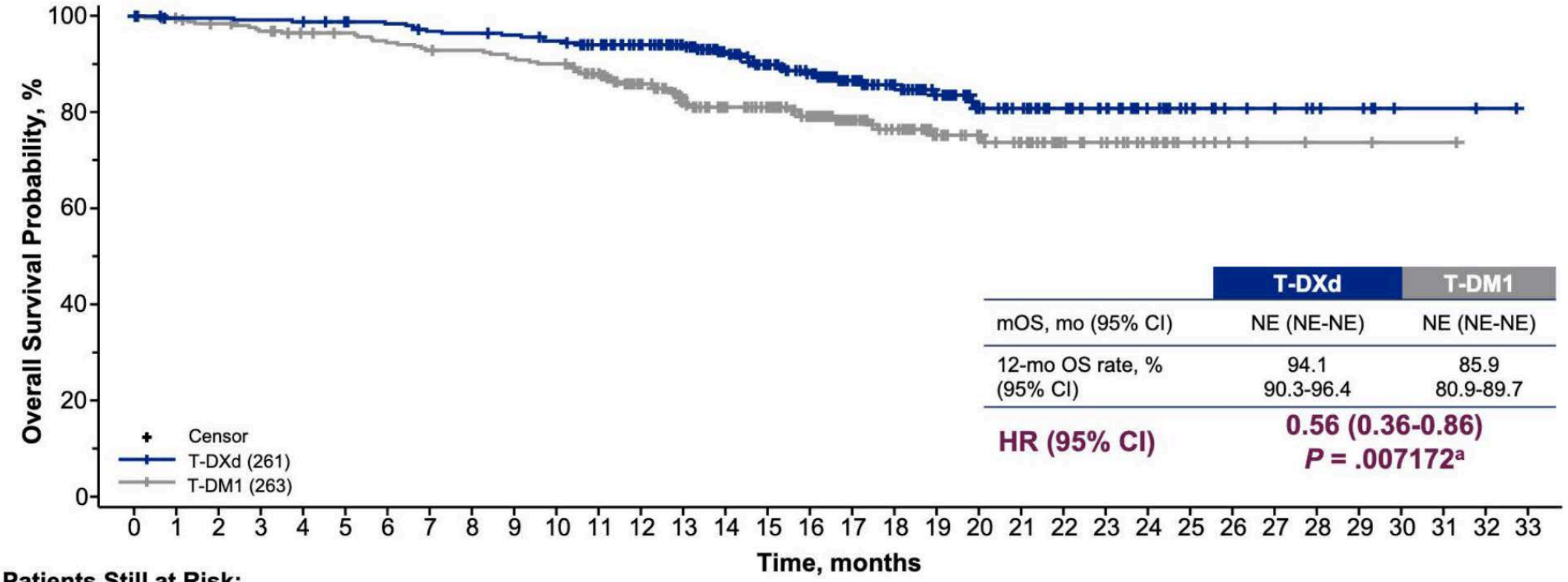
DESTINY-Breast03: Progression-Free Survival by BICR



Cortés J et al. ESMO 2021;Abstract LBA1.

DESTINY-Breast03: Overall Survival 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: Drug-Related Treatment-Emergent Adverse Events in ≥20% of Patients

System Organ Class Preferred term, n (%)	T-DXd (n = 257)		T-DM1 (n = 261)	
	Any Grade	Grade ≥3	Any Grade	Grade ≥3
Blood and lymphatic system disorders				
Neutropenia[a]	110 (42.8)	49 (19.1)	29 (11.1)	8 (3.1)
Anemia[b]	78 (30.4)	15 (5.8)	37 (14.2)	11 (4.2)
Leukopenia[c]	77 (30.0)	17 (6.6)	20 (7.7)	1 (0.4)
Thrombocytopenia[d]	64 (24.9)	18 (7.0)	135 (51.7)	65 (24.9)
Gastrointestinal disorders				
Nausea	187 (72.8)	17 (6.6)	72 (27.6)	1 (0.4)
Vomiting	113 (44.0)	4 (1.6)	15 (5.7)	1 (0.4)
Diarrhea	61 (23.7)	1 (0.4)	10 (3.8)	1 (0.4)
Constipation	58 (22.6)	0	25 (9.6)	0
General disorders				
Fatigue[e]	115 (44.7)	13 (5.1)	77 (29.5)	2 (0.8)
Investigations				
AST increased	60 (23.3)	2 (0.8)	97 (37.2)	13 (5.0)
ALT increased	50 (19.5)	4 (1.6)	71 (27.2)	12 (4.6)
Metabolism and nutrition disorders				
Decreased appetite	67 (26.1)	3 (1.2)	33 (12.6)	0
Skin and subcutaneous tissue disorders				
Alopecia[f]	93 (36.2)	1 (0.4)	6 (2.3)	0

Cortés J et al. ESMO 2021;Abstract LBA1.

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)

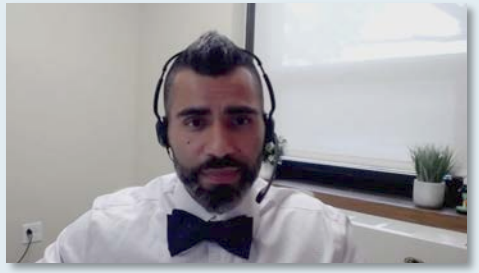
- There were no grade 4 or 5 adjudicated drug-related ILD/pneumonitis events observed with T-DXd

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.

Second Opinion: A 67-year-old woman with ER/PR-negative, HER2-positive mBC (Dr Gosain)



Dr Rohit Gosain

Dr Hope Rugo

- 5-cm ER/PR-negative, HER2-positive metastatic breast cancer (mBC)
- CT CAP: Multiple lung and liver lesions, biopsy-confirmed HER2-positive BC
- Paclitaxel/trastuzumab/pertuzumab (THP) → PD after 9 months → T-DM1
- Altered mental status after 6 months
- MRI: Multiple sub-centimeter brain lesions; Increase in size of lung and liver lesions

Question

- What treatment would you recommend for third-line therapy?

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Dr Hope Rugo

Third-line treatment for patients with CNS disease

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Dr Erika Hamilton

Management of tucatinib-associated adverse events

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HER2CLIMB: Safety Outcomes

Select adverse events	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.

Dr Sara Tolaney

Dr Hope Rugo

Tolerability of trastuzumab deruxtecan (T-DXd)

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Dr Hope Rugo

Trastuzumab deruxtecan (T-DXd) for HER2-low metastatic breast cancer

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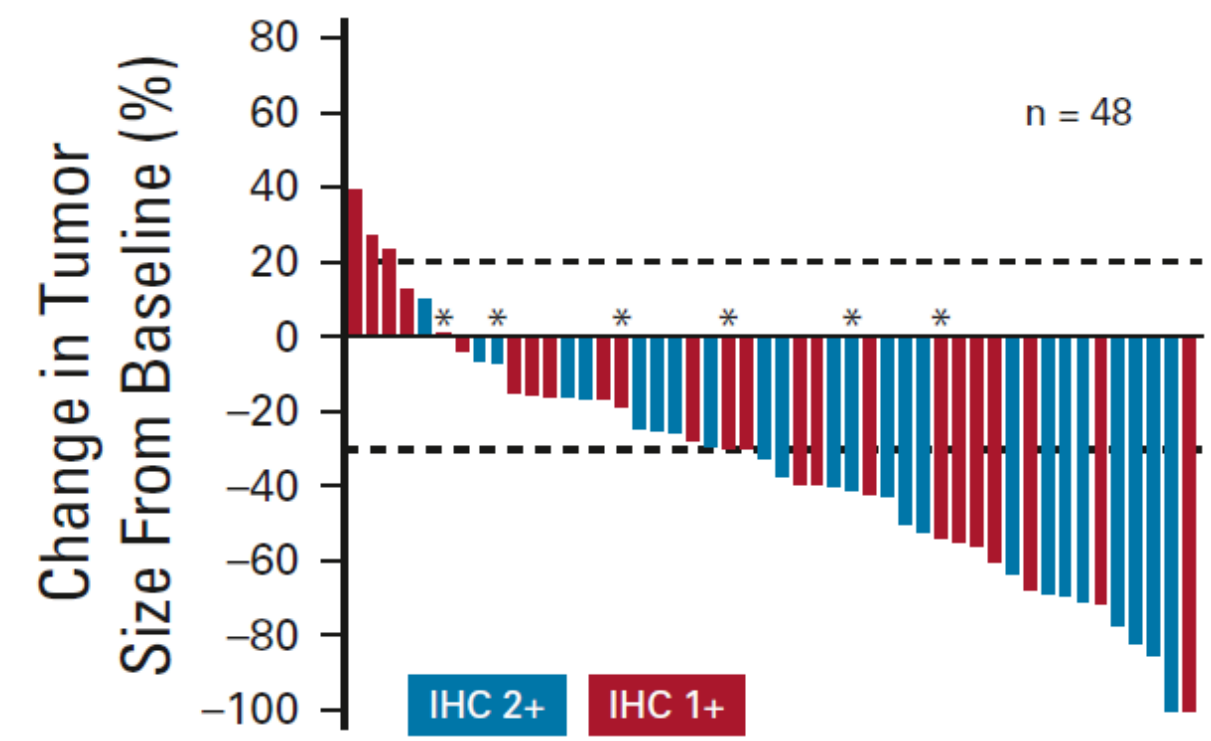
original reports

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 (Median 7.5 Prior Regimens)



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

ORR = objective response rate

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

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Dr Erika Hamilton

Trastuzumab deruxtecan (T-DXd) in combination with tucatinib

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Meet The Professor with Dr Traina

Introduction: HER2 Trials in Progress

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San Antonio Breast Cancer Symposium®, December 7-10, 2021

Trastuzumab Deruxtecan (T-DXd) Versus Trastuzumab Emtansine (T-DM1) in Patients With HER2+ Metastatic Breast Cancer: Subgroup Analyses From the Randomized Phase 3 Study DESTINY-Breast03

Sara A. Hurvitz, 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, Javier Cortes

On behalf of the DESTINY-Breast03 investigators

[a]Department of Medicine, David Geffen School of Medicine, University of California, Los Angeles, Jonsson Comprehensive Cancer Center, Los Angeles, CA USA

SABCS 2021;Abstract GS3-01.

San Antonio Breast Cancer Symposium®, December 7-10, 2021

Updated overall survival results from the phase 3 PHOEBE trial of pyrotinib versus lapatinib in combination with capecitabine in patients with HER2-positive metastatic breast cancer

Binghe Xu, MD

Cancer Hospital Chinese Academy of Medical Sciences, Beijing, China

On behalf of Min Yan, Fei Ma, Xichun Hu, Jifeng Feng, Quchang Ouyang, Zhongsheng Tong, Huiping Li, Qingyuan Zhang, Tao Sun, Xian Wang, Yongmei Yin, Ying Cheng, Wei Li, Xiaoyu Zhu, Chunxia Chen, Jianjun Zou, the PHOEBE Study Group

SABCS 2021;Abstract GS3-02.

San Antonio Breast cancer Symposium ®, December 7-10, 2021

Memorial Sloan Kettering Cancer Center

Genomic analysis of 733 HER2+ breast cancers identifies recurrent pathway alterations associated with anti-HER2 resistance and new therapeutic vulnerabilities

Emanuela Ferraro, Alison E. Smith, Anton Safonov, Paulino Tallon De Lara, Cristina Bernado, Enrique J. Arenas Lahuerta, Joaquín Arribas, David Solit, Jorge Reis-Filho, Neal Rosen, Larry Norton, Shanu Modi, Mark Robson, ChauT Dang, Giuseppe Curigliano, Sarat Chandarlapaty and Pedram Razavi

Presenter: Emanuela Ferraro, MD

Research Fellow, Breast Service, Department of Medicine

SABCS 2021;Abstract GS3-03.

RTP RESEARCH TO PRACTICE

San Antonio Breast Cancer Symposium®, December 7-10, 2021

Neratinib + fulvestrant + trastuzumab for hormone-receptor positive, *HER2*-mutant metastatic breast cancer, and neratinib + trastuzumab for *HER2*-mutant metastatic triple-negative disease: latest updates from the SUMMIT trial

Komal Jhaveri,[1] Haeseong Park,[2] James Waisman,[3] Jonathan W. Goldman,[4] Angel Guerrero-Zotano,[5] Valentina Boni,[6] Barbara Haley,[7] Ingrid A. Mayer,[8] Adam Brufsky,[9] Eddy Yang,[10] José A. García-Sáenz,[11] Francois-Clement Bidard,[12] John Crown,[13] Bo Zhang,[14] Aimee Frazier,[14] Irmina Diala,[14] Brian Barnett,[14] Lisa D Eli,[14] Hans Wildiers[15]

[1]Memorial Sloan Kettering Cancer Center, New York, NY; [2]Washington University School of Medicine, St. Louis, MO; [3]City of Hope Comprehensive Cancer Center, Duarte, CA; [4]UCLA, Santa Monica, CA; [5]Fundación Instituto Valenciano de Oncología, Valencia, Spain; [6]START Madrid-CIOCC, Hospital Universitario, Madrid Sanchinarro, Madrid, Spain; [7]UT Southwestern Medical Center, Dallas, TX; [8]Vanderbilt University Medical Center/Vanderbilt-Ingram Cancer Center, Nashville, TN; [9]Magee-Womens Hospital of UPMC, Pittsburgh, PA; [10]University of Alabama at Birmingham, Birmingham, AL; [11]Hospital Clínico San Carlos, Madrid, Spain; [12]Institut Curie, St. Cloud, France; [13]St. Vincent's University Hospital, Dublin, Ireland; [14]Puma Biotechnology Inc., Los Angeles, CA; [15]University Hospitals Leuven, Leuven, Belgium

SABCS 2021;Abstract GS4-10.

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Journal of Geriatric Oncology 13 (2022) 27–32

Contents lists available at ScienceDirect

Journal of Geriatric Oncology

Relationship between cognitive functioning and frailty in older breast cancer survivors

Tim A. Ahles [a,*], Elizabeth Schofield [a], Yuelin Li [a], Elizabeth Ryan [a], James C. Root [a], Sunita K. Patel [b], Katrazyna McNeal [a], Alexandra Gaynor [a], Heidi Tan [b], Vani Katheria [b], Jessica Vazquez [b], Tiffany Traina [c], Arti Hurria [d]

[a] Department of Psychiatry and Behavioral Sciences, Memorial Sloan Kettering Cancer Center, New York, NY, USA
[b] Departments of Population Science and Supportive Care Medicine, City of Hope Comprehensive Cancer Center, Duarte, CA, USA
[c] Department of Medicine, Memorial Sloan Kettering Cancer Center, New York, NY, USA
[d] Center for Cancer and Ageing, City of Hope Comprehensive Cancer Center, Duarte, CA, USA

2021 ASCO ANNUAL MEETING

Provision of subspecialized expert oncology opinions using a technology based platform: prospective pilot to facilitate access to care.

Tiffany A. Traina, Philip W. Kantoff, Matthew J. Matasar, Lara Dunn, Claire Frances Friedman, Martin H Voss, Andrew David Seidman, Oren Cahlon, Marjorie Glass Zauderer, Cole Manship, Emily Kauff, Gitika Srivastava, Naresh Ramarajan, Ghassan K. Abou-Alfa.

Memorial Sloan Kettering Cancer Center™

ASCO 2021;Abstract 6580.

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Meet The Professor with Dr Traina

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Management of Metastatic HER2-Positive Breast Cancer

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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	Trastuzumab deruxtecan
 Dr Hamilton	Tucatinib + trastuzumab/ capecitabine	 Dr Rugo	Trastuzumab deruxtecan
 Dr Hurvitz	Tucatinib + trastuzumab/ capecitabine	 Dr Tolaney	Trastuzumab/ pertuzumab/paclitaxel

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 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	Continue T-DM1	 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 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	Trastuzumab deruxtecan	 Dr Mahtani	Trastuzumab deruxtecan
 Dr Hamilton	Trastuzumab deruxtecan	 Dr Rugo	Trastuzumab deruxtecan
 Dr Hurvitz	Trastuzumab deruxtecan	 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 T-DM1. Regulatory and reimbursement issues aside, what systemic treatment would you recommend?

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

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	Trastuzumab deruxtecan
 Dr Hamilton	Tucatinib + trastuzumab/ capecitabine	 Dr Rugo	Trastuzumab deruxtecan
 Dr Hurvitz	Tucatinib + trastuzumab/ capecitabine	 Dr Tolaney	Trastuzumab/ pertuzumab/paclitaxel

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

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

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 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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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?

 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

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Meet The Professor with Dr Traina

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Management of Metastatic HER2-Positive Breast Cancer

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DESTINY-Breast03: Progression-Free Survival (PFS) and Objective Response Rate (ORR) with T-DXd versus T-DM1 by Subgroup

	PFS by BICR, HR (95% CI)	Absolute ORR difference T-DXd, T-DM1 (95% CI)
All patients (N = 524)	0.28 (0.22-0.37)	45.5 (37.6-53.4)
Hormone receptor		
Positive (n = 272)	0.32 (0.22-0.46)	47.3 (36.1-58.4)
Negative (n = 248)	0.30 (0.20-0.44)	43.2 (31.5-55.0)
Prior pertuzumab		
Yes (n = 320)	0.31 (0.22-0.43)	46.7 (36.5-56.9)
No (n = 204)	0.30 (0.19-0.47)	43.6 (30.5-56.7)
Prior lines of therapy		
0-1 (n = 258)	0.33 (0.23-0.48)	39.3 (27.3-51.2)
≥2 (n = 266)	0.28 (0.19-0.41)	51.6 (40.9-62.4)
Visceral disease		
Yes (n = 384)	0.28 (0.21-0.38)	48.3 (39.1-57.6)
No (n = 140)	0.32 (0.17-0.58)	39.1 (23.6-54.6)
Brain metastases at baseline		
Yes (n = 82)	0.25 (0.13-0.45)	46.9 (25.6-68.3)
No (n = 442)	0.30 (0.22-0.40)	45.5 (36.9-54.1)

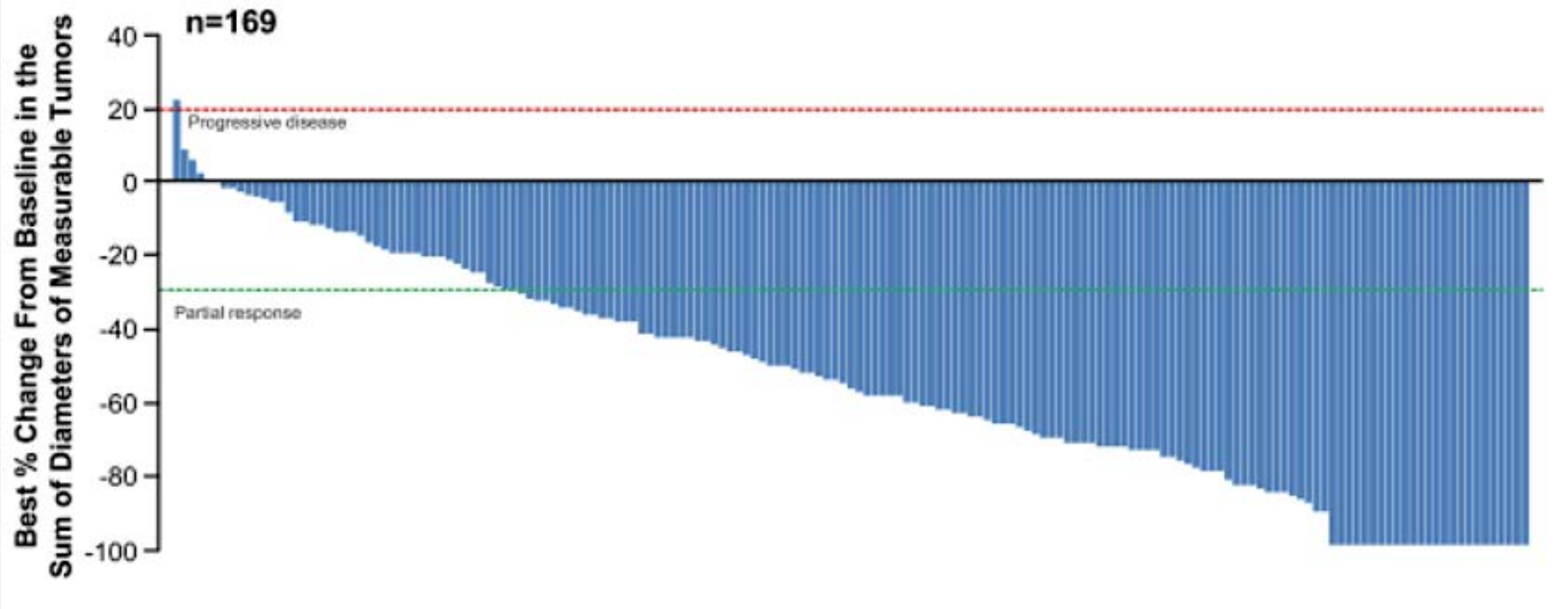
Hurvitz S et al. SABCS 2021;Abstract GS3-01.

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.

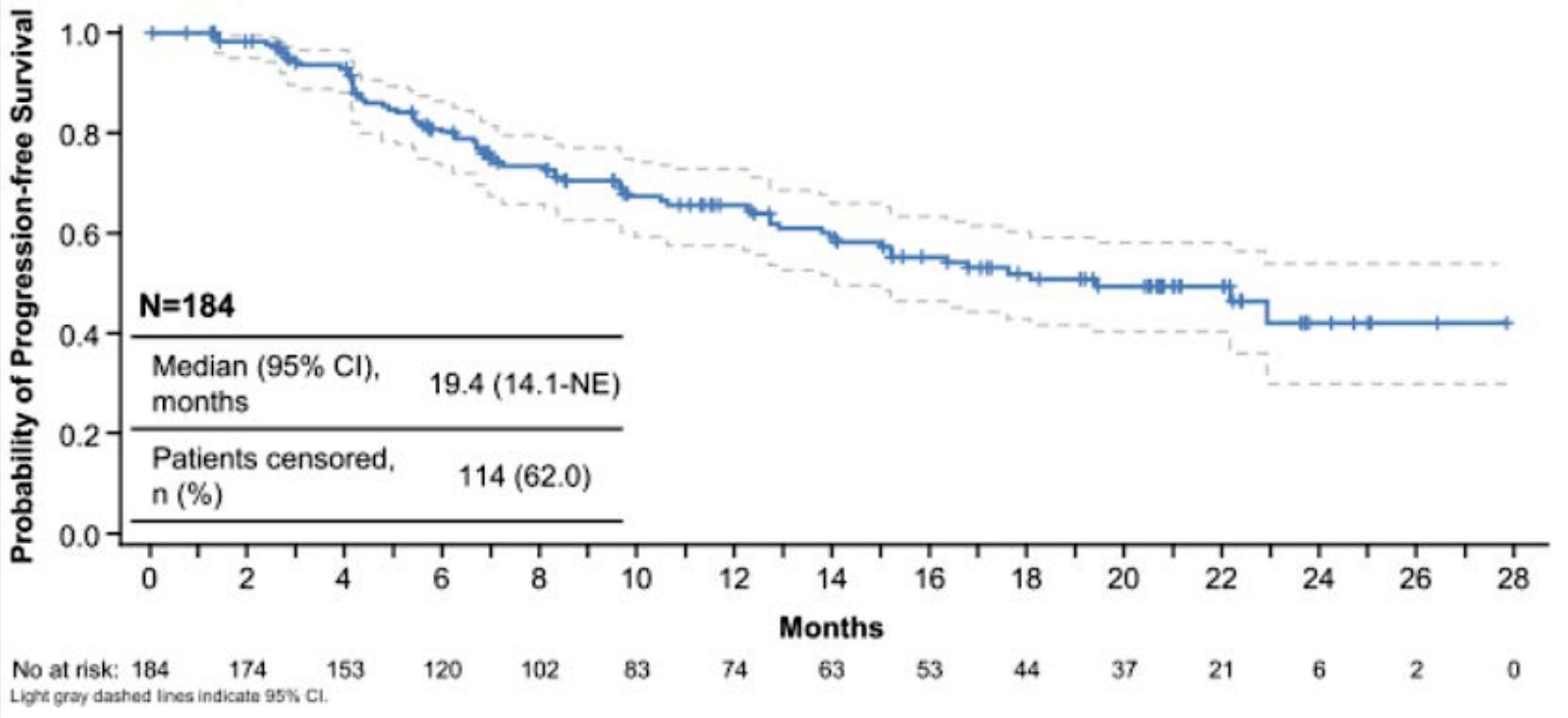
DESTINY-Breast01: Best Percent Change in Tumor Size from Baseline



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

RTP RESEARCH TO PRACTICE

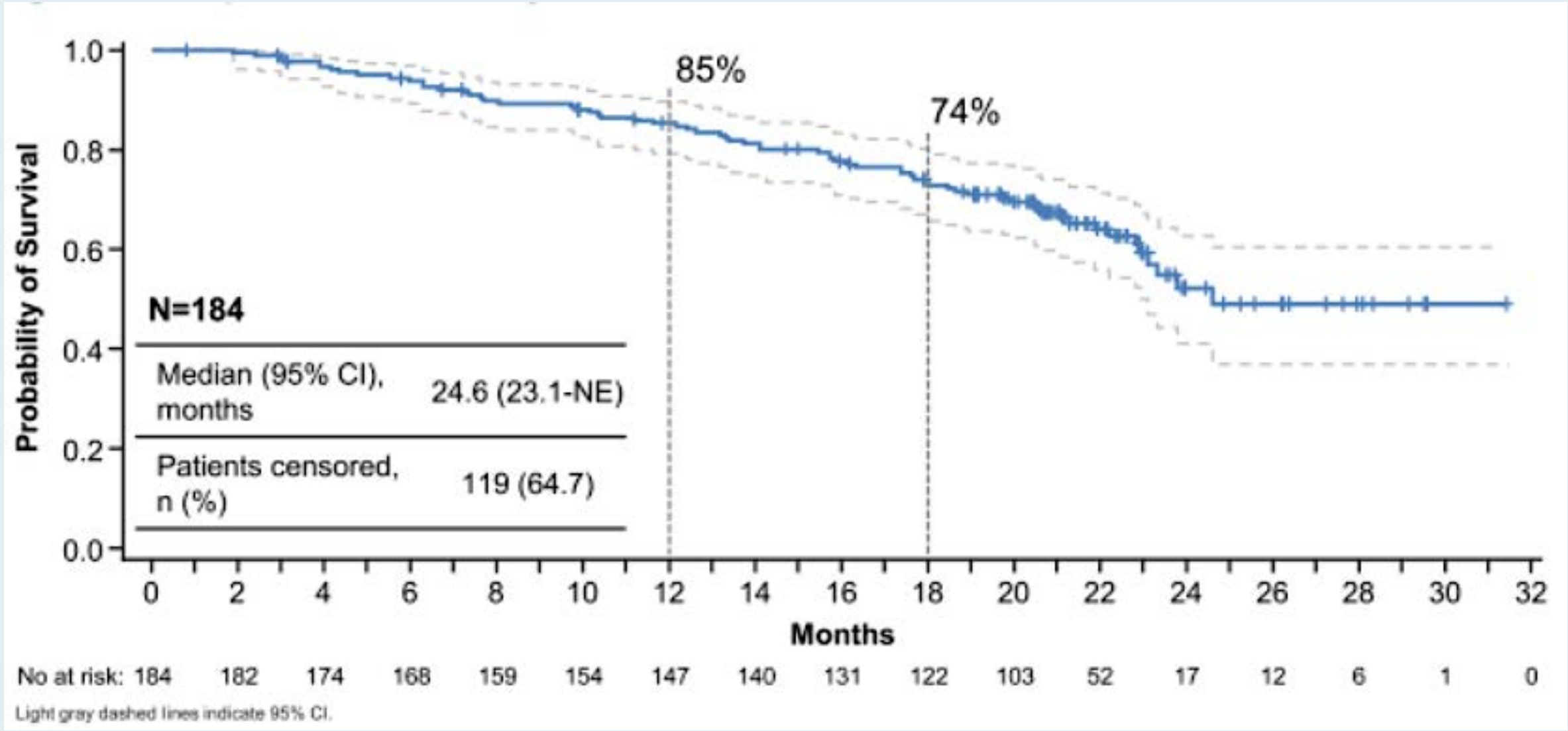
DESTINY-Breast01: Progression-Free Survival



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.

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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.

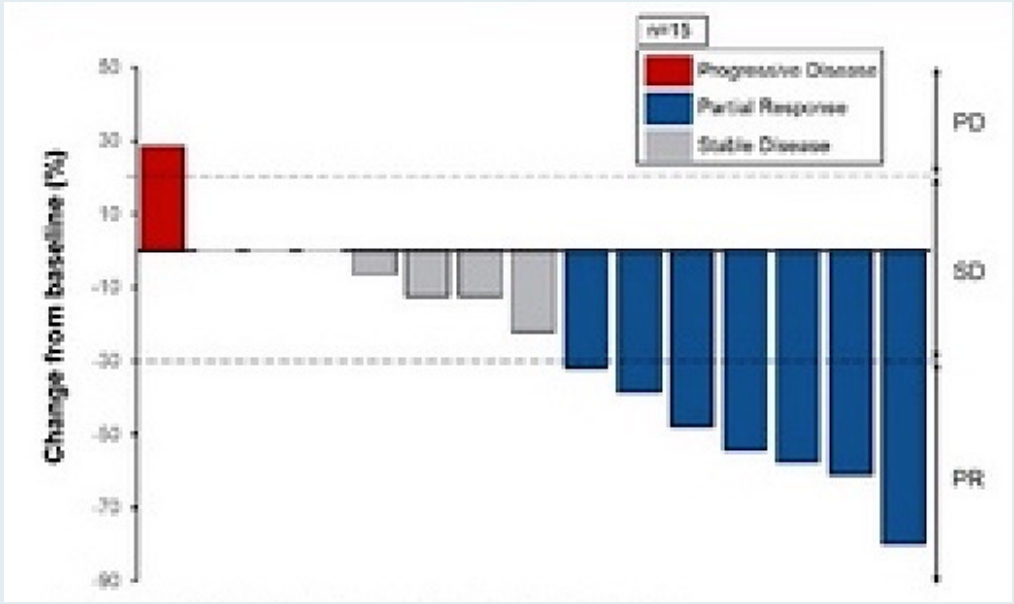
Trastuzumab Deruxtecan (T-DXd) in Patients with HER2+ Metastatic Breast Cancer with Brain Metastases: A Subgroup Analysis of the DESTINY-Breast01 Trial

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.

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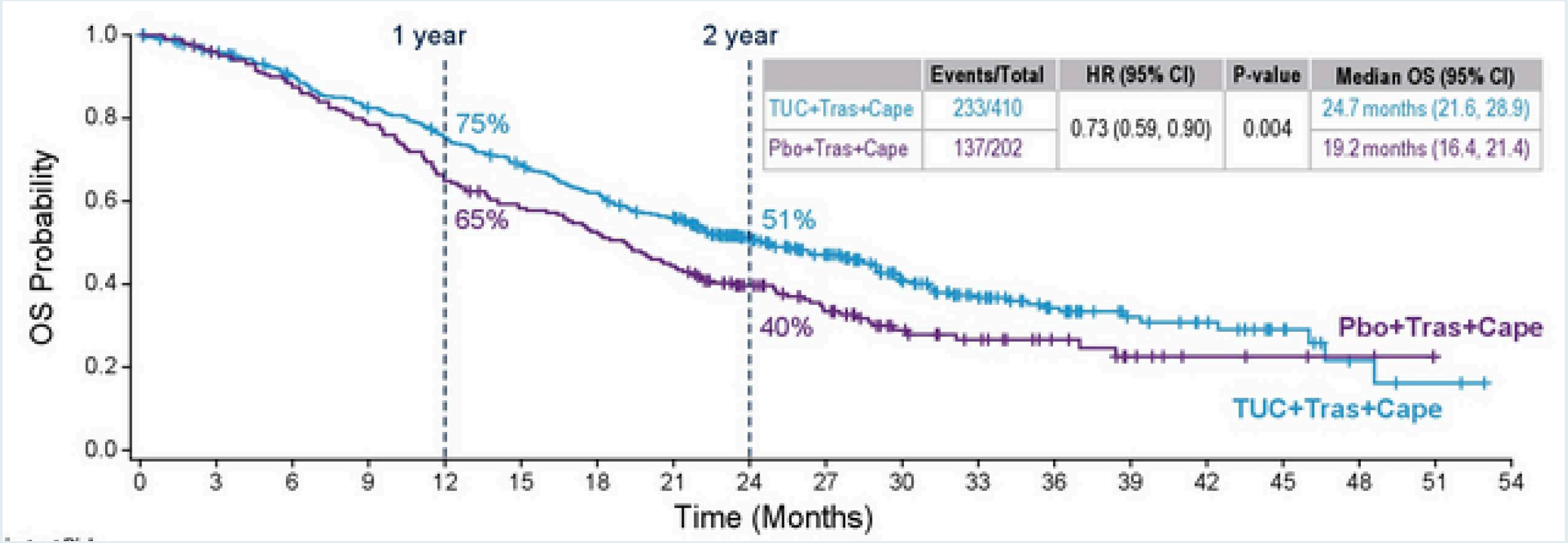
Updated Results of Tucatinib versus Placebo Added to Trastuzumab and Capecitabine for Patients with Pretreated HER2+ Metastatic Breast Cancer with and without Brain Metastases (HER2CLIMB)

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.

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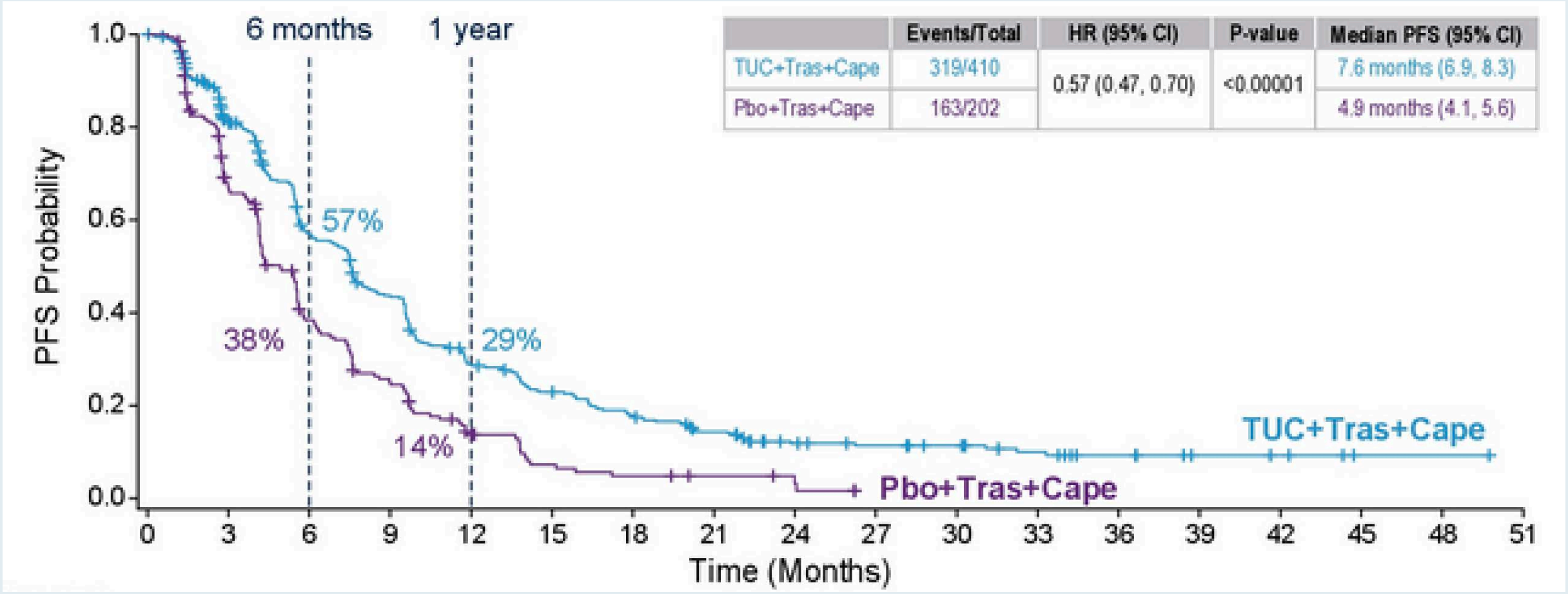
HER2CLIMB: Progression-Free Survival



	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.

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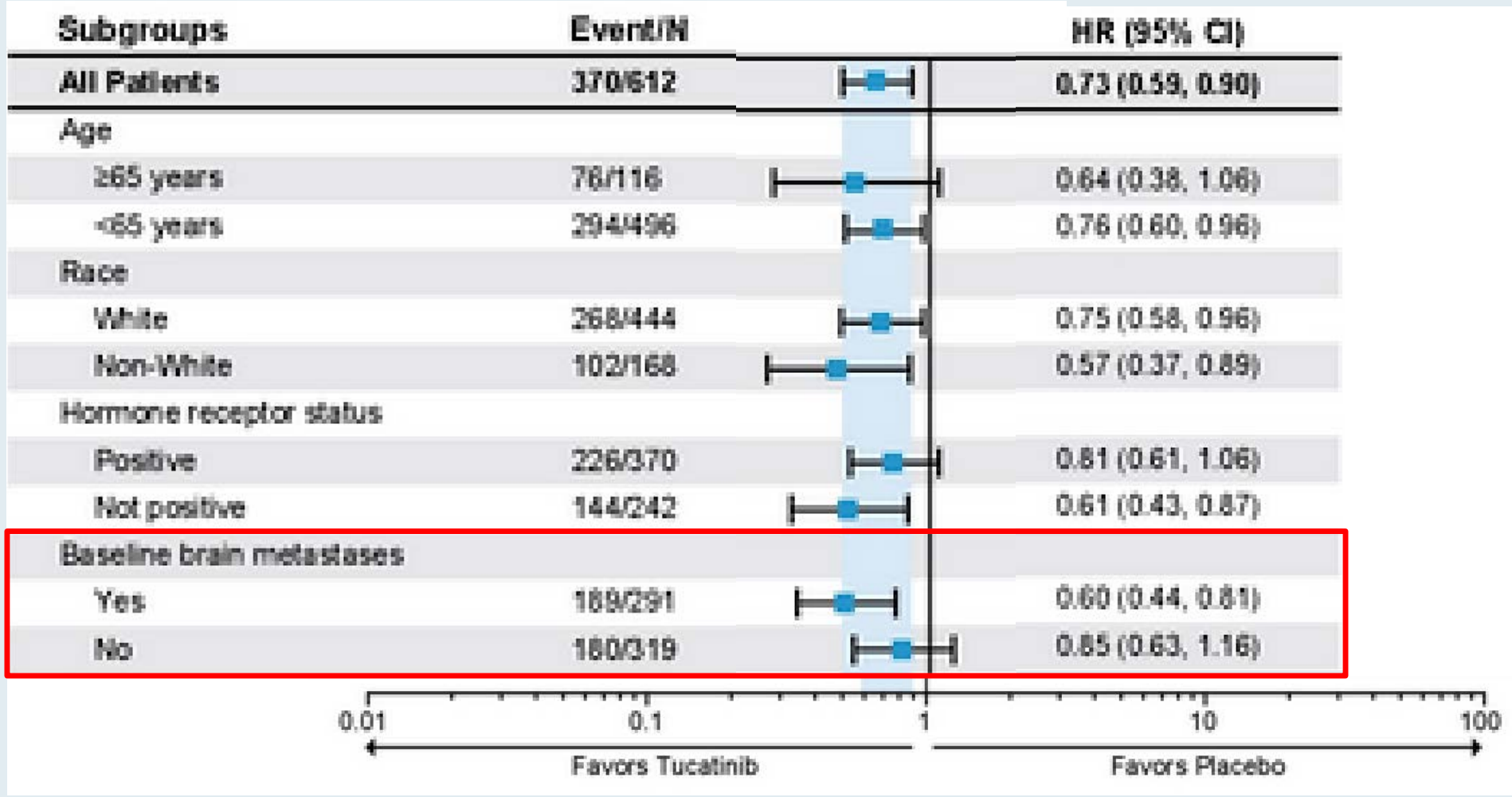
HER2CLIMB: Overall Survival for Patients with Baseline Brain Metastases



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

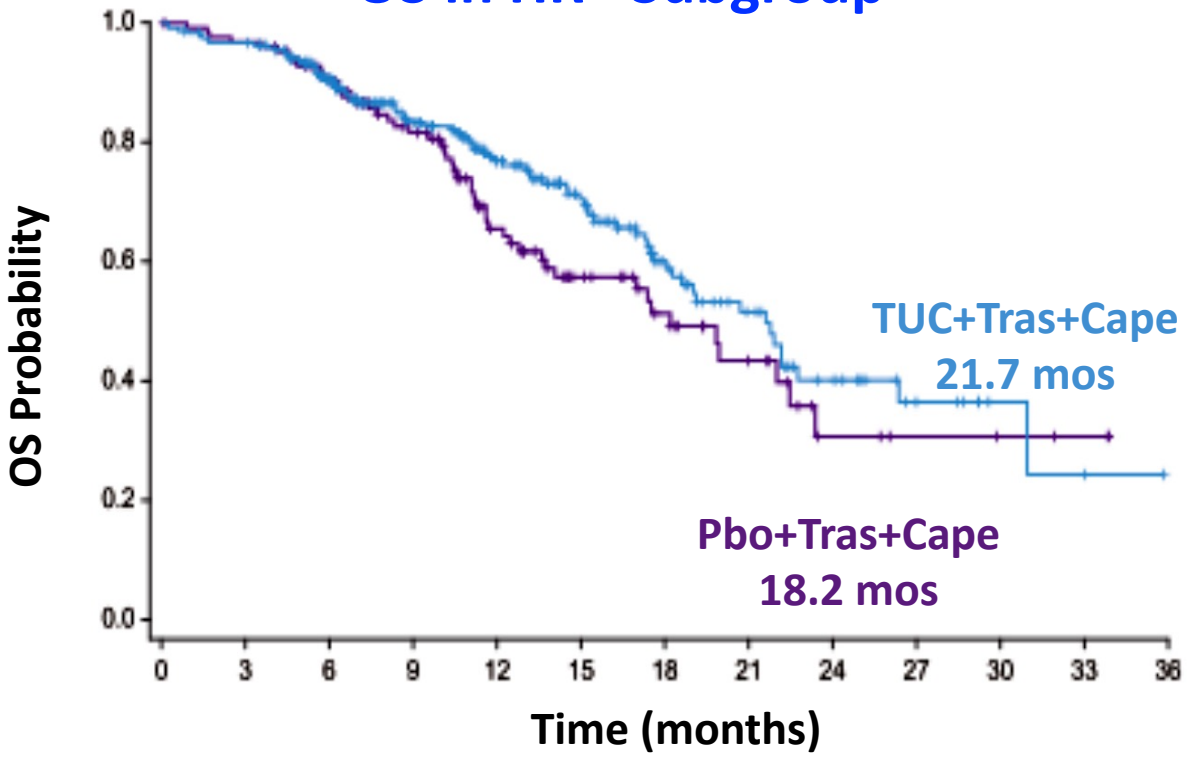
Hamilton E et al.

SABCS 2020;Abstract PD3-08.

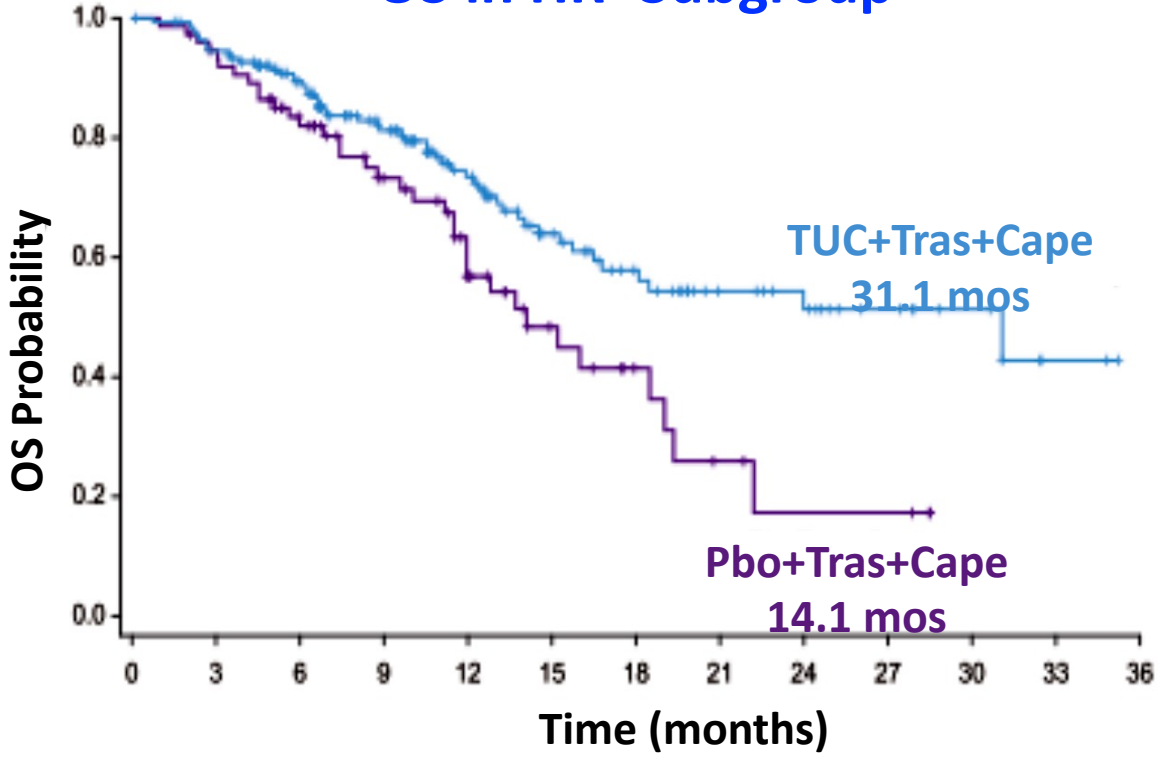
OS by HR Status in the Total Study Population

- 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

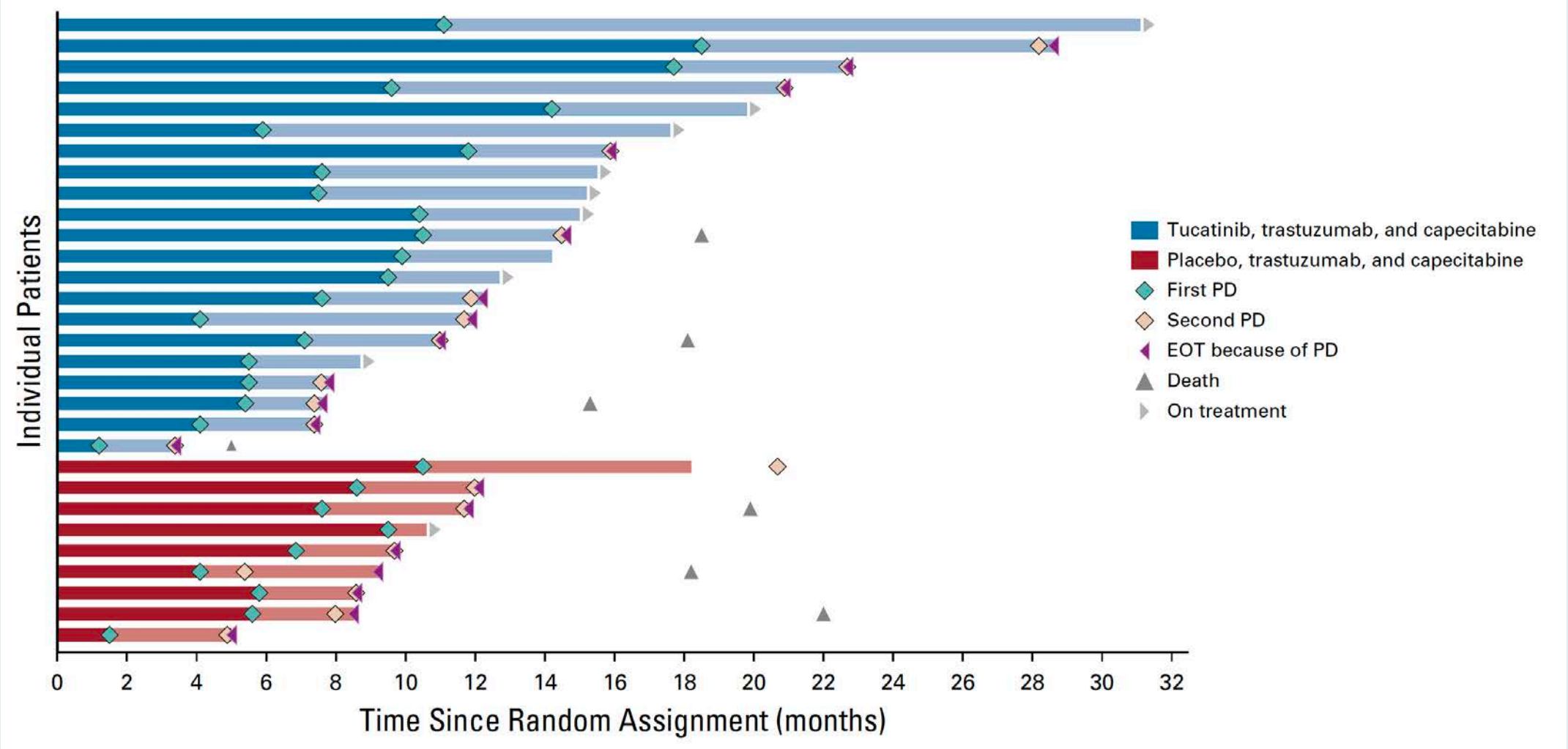
rapid communications

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]

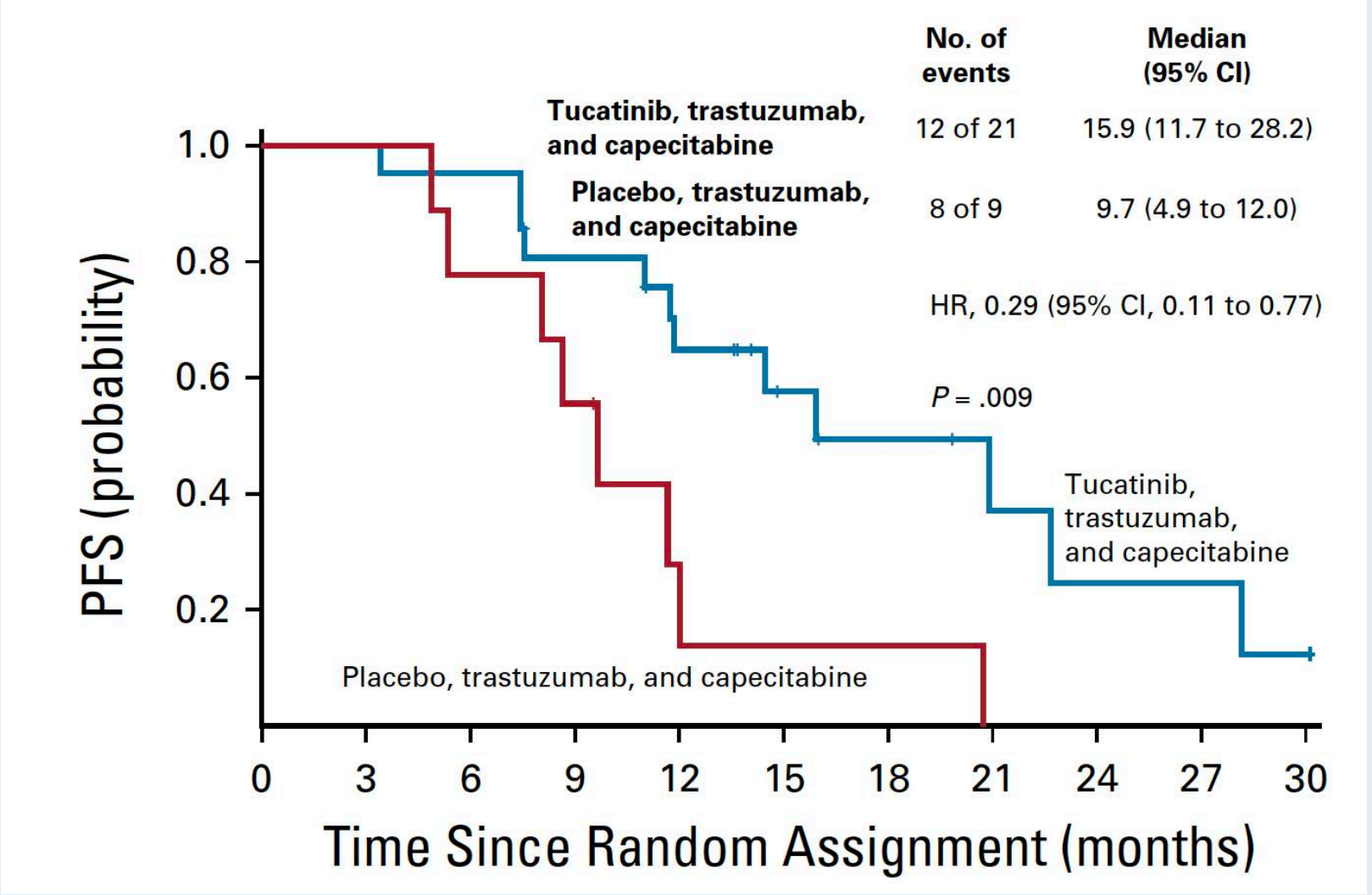
J Clin Oncol 2020;38(23):2610-9.

Duration of Treatment



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

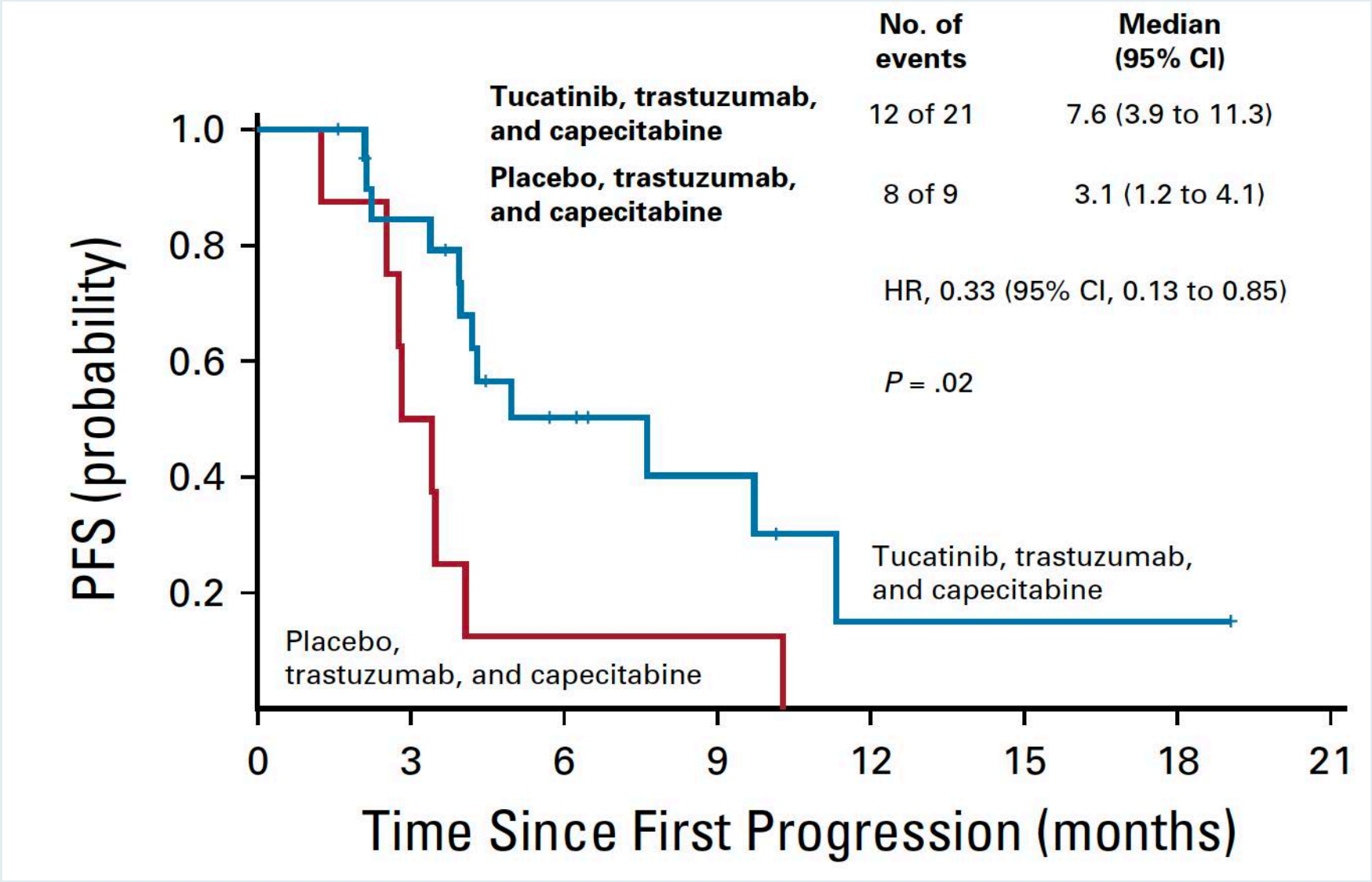
Time from Random Assignment to Second Disease Progression by Investigator Assessment or Death



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.

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

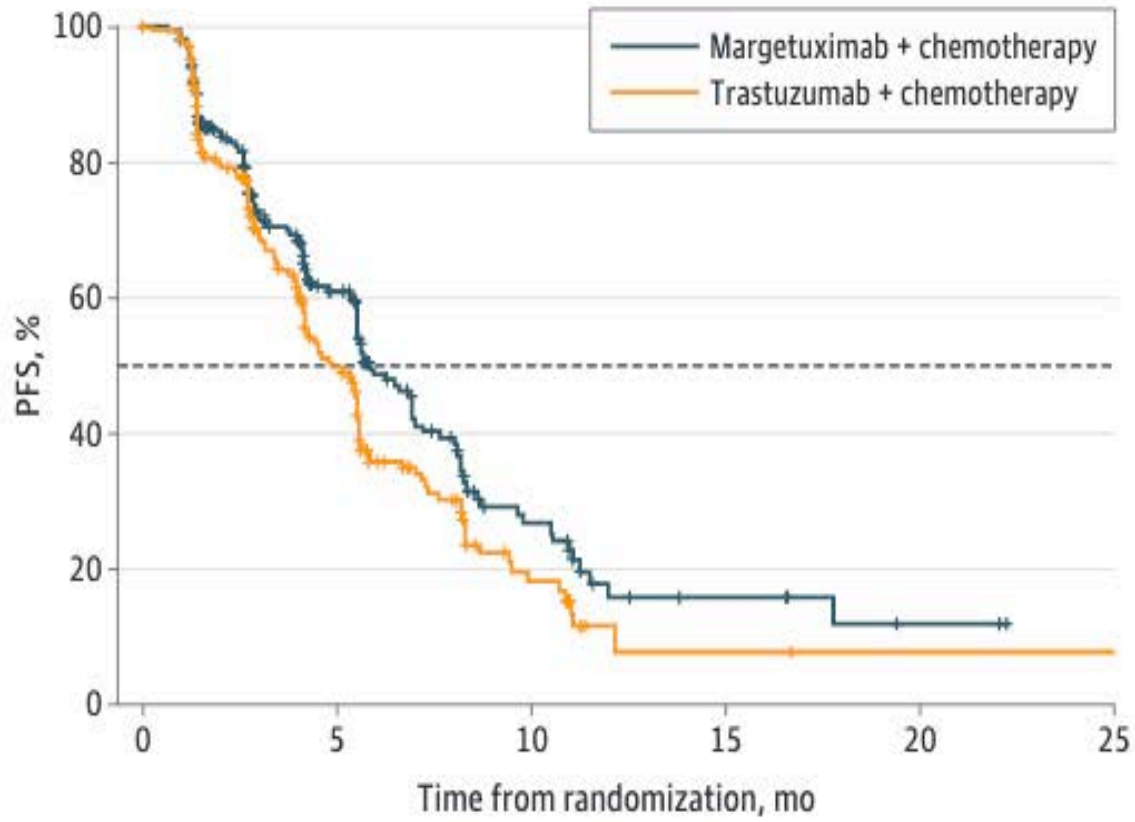
Efficacy of Margetuximab vs Trastuzumab in Patients With Pretreated ERBB2-Positive Advanced Breast Cancer

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)

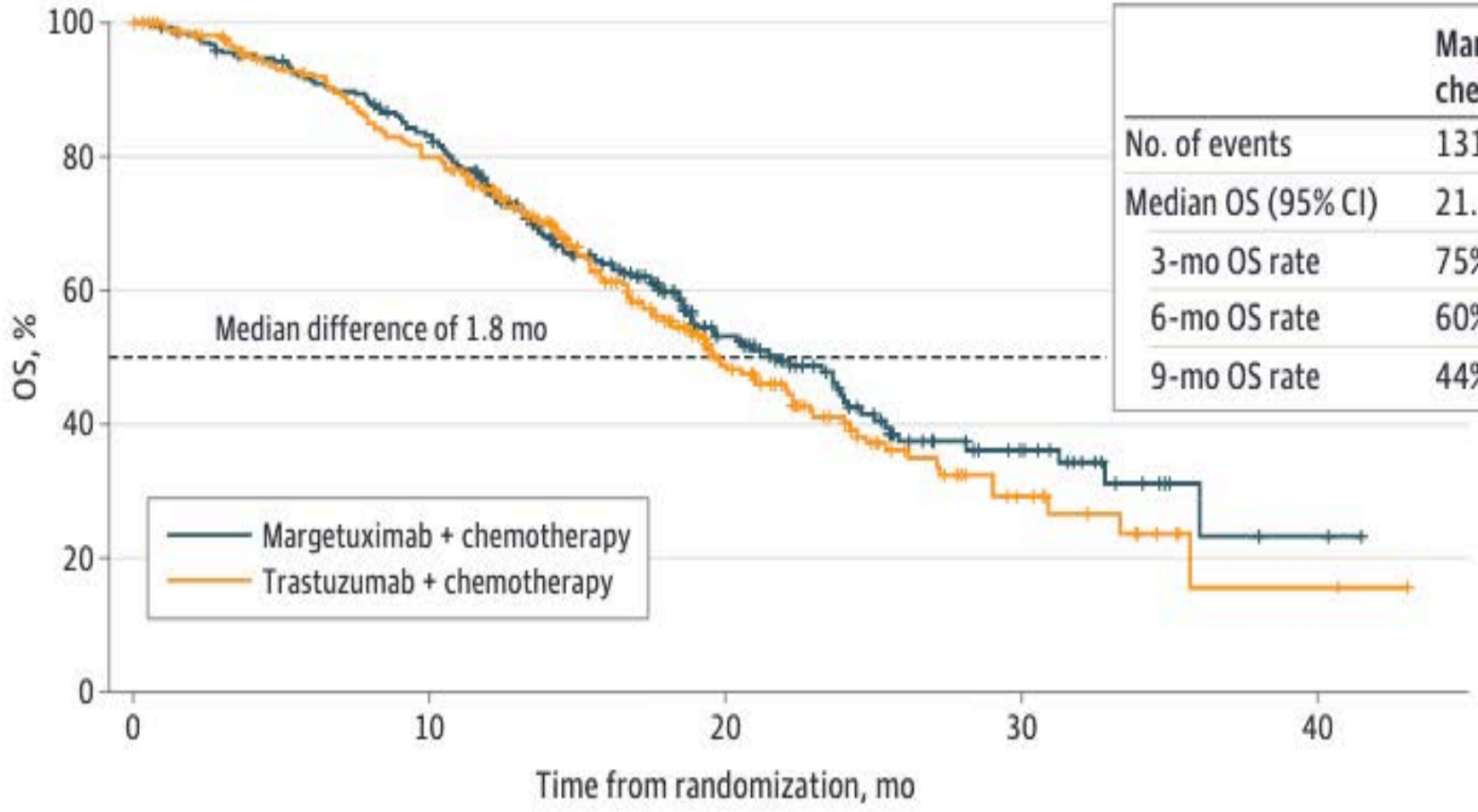


	Margetuximab + chemotherapy (n = 266)	Trastuzumab + chemotherapy (n = 270)
No. of events	130	135
Median PFS (95% CI)	5.8 mo (5.52-6.97)	4.9 mo (4.17-5.59)
3-mo PFS rate	72% (65%-77%)	70% (63%-76%)
6-mo PFS rate	48% (41%-56%)	36% (28%-44%)
9-mo PFS rate	30% (22%-38%)	22% (15%-30%)

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

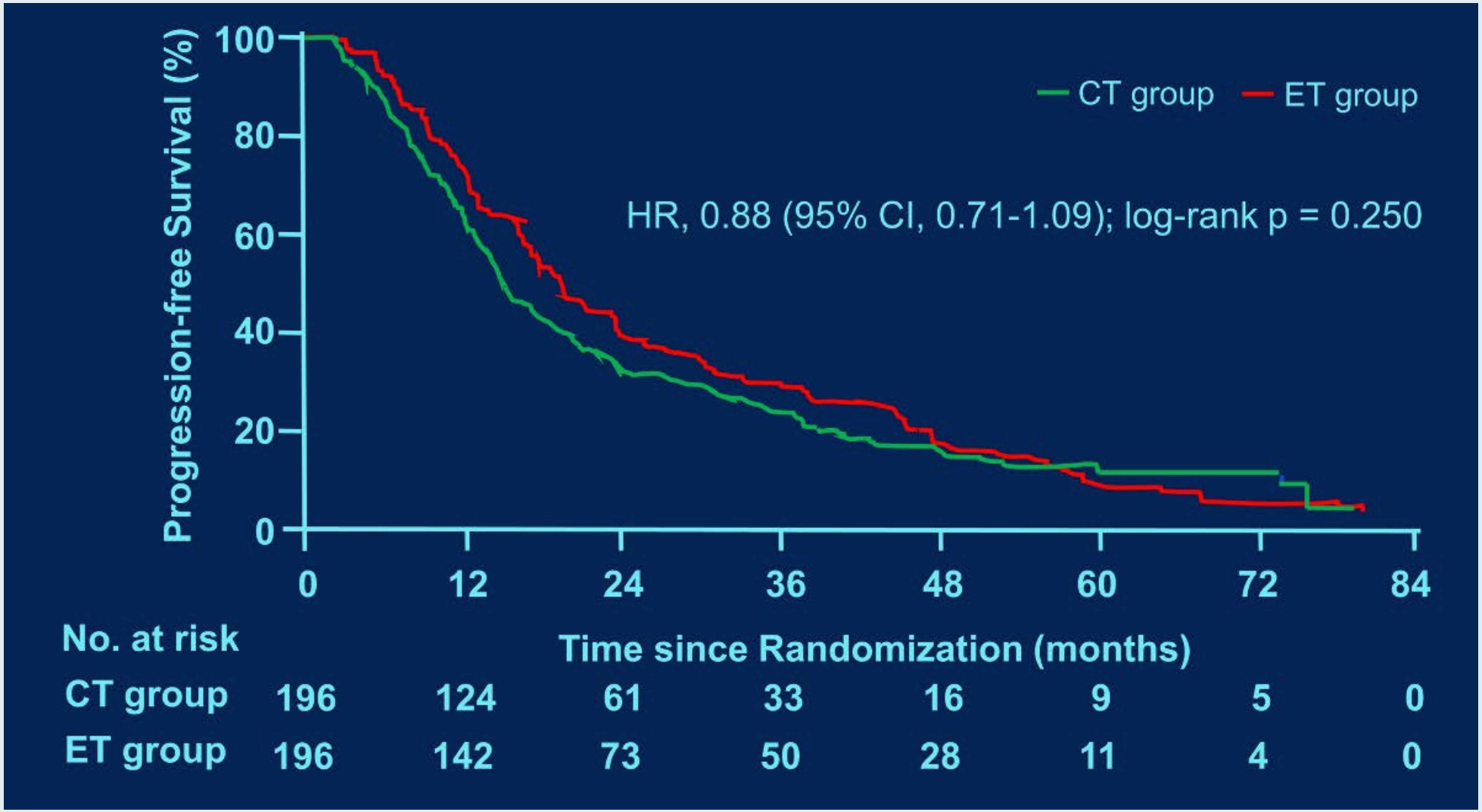
Rugo HS et al. *JAMA Oncol* 2021;[Online ahead of print].

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.

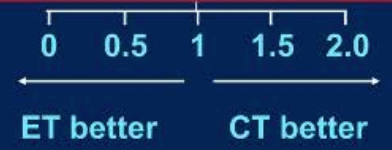
SYSUCC-002: Progression-Free Survival (Primary Endpoint)



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.

Localized HER2-Positive Breast Cancer

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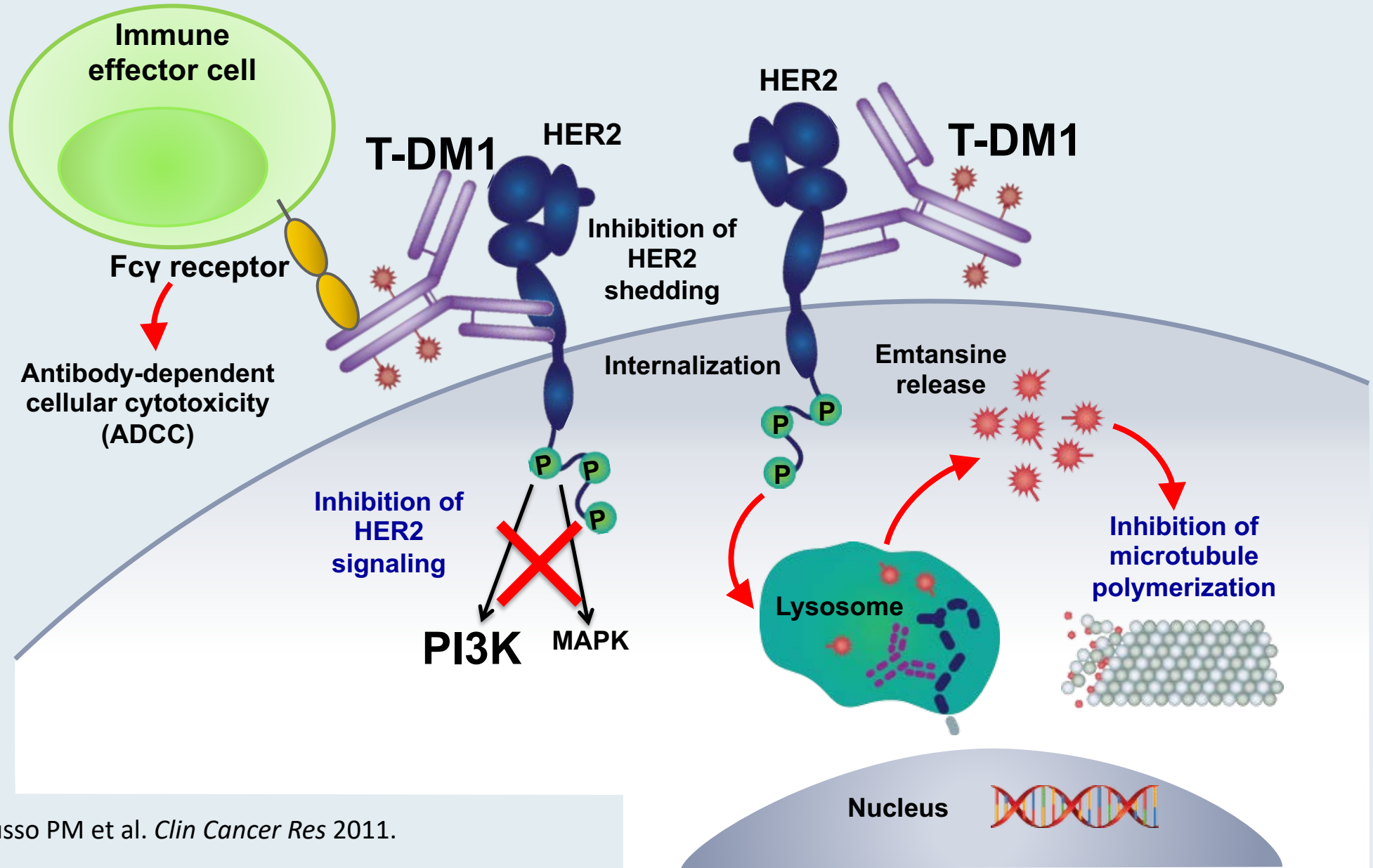
FDA-Approved Agents for Early-Stage HER2-Positive Breast Cancer

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

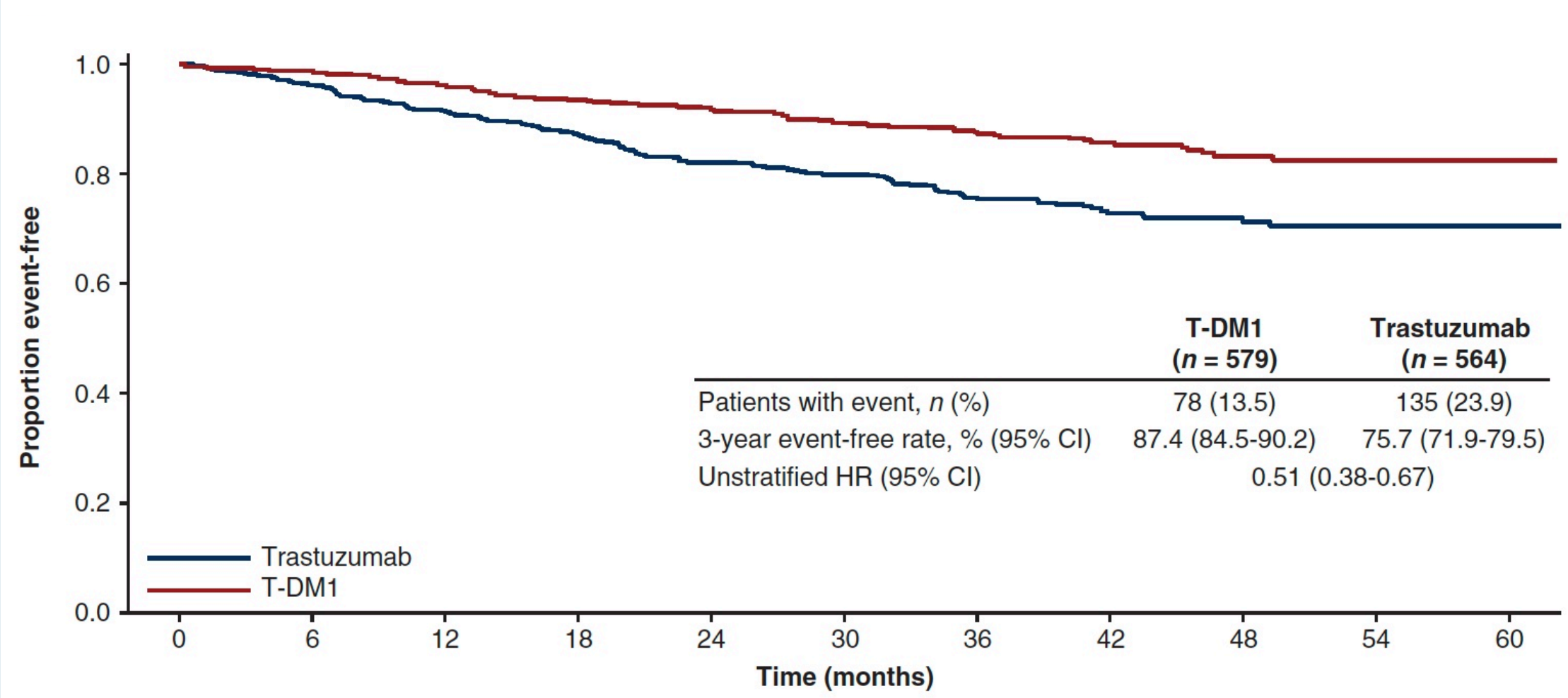
E. P. Mamounas[1,2*], M. Untch[3], M. S. Mano[4], C.-S. Huang[5], C. E. Geyer Jr[1,6], G. von Minckwitz[7], N. Wolmark[1,8], X. Pivot[9], S. Kuemmel[10,11], M. P. DiGiovanna[12], B. Kaufman[13], G. Kunz[7,14], A. K. Conlin[1,15], J. C. Alcedo[16], T. Kuehn[17], I. Wapnir[1,18], A. Fontana[19], J. Hackmann[7,20], 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.

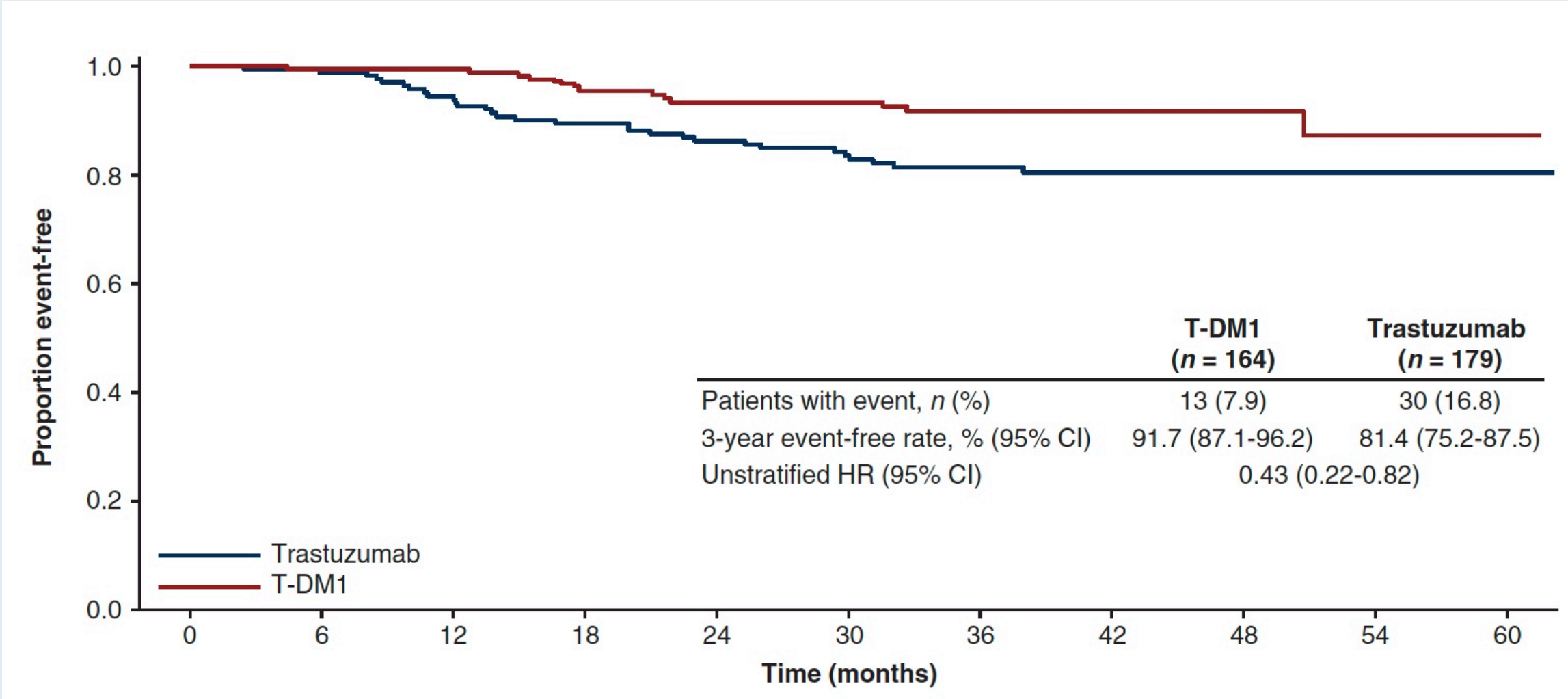
Time to First Invasive Disease-Free Survival Event for Patients Who Received Anthracycline-Based Neoadjuvant Therapy



	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].

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].

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KATHERINE: Central Nervous System Recurrence Events

	T-DM1 (n = 743)	Trastuzumab (n = 743)
Patients with CNS recurrence	45 (6.1%)	40 (5.4%)
At first IDFS event[a]	44 (5.9%)	32 (4.3%)
After first IDFS event[b]	1 (0.1%)	8 (1.1)
Patients with CNS as only event[c]	36 (4.8%)	21 (2.8%)
Median time to CNS recurrence	17.5 months	11.9 months

T-DM1 = trastuzumab emtansine; CNS = central nervous system; IDFS = invasive disease-free survival
CNS recurrence [a]within or [b]after 61 days of first IDFS event or at [c]any time

Mamounas EP et al. *Ann Oncol* 2021;32(8):1005-14.

original reports

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

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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].

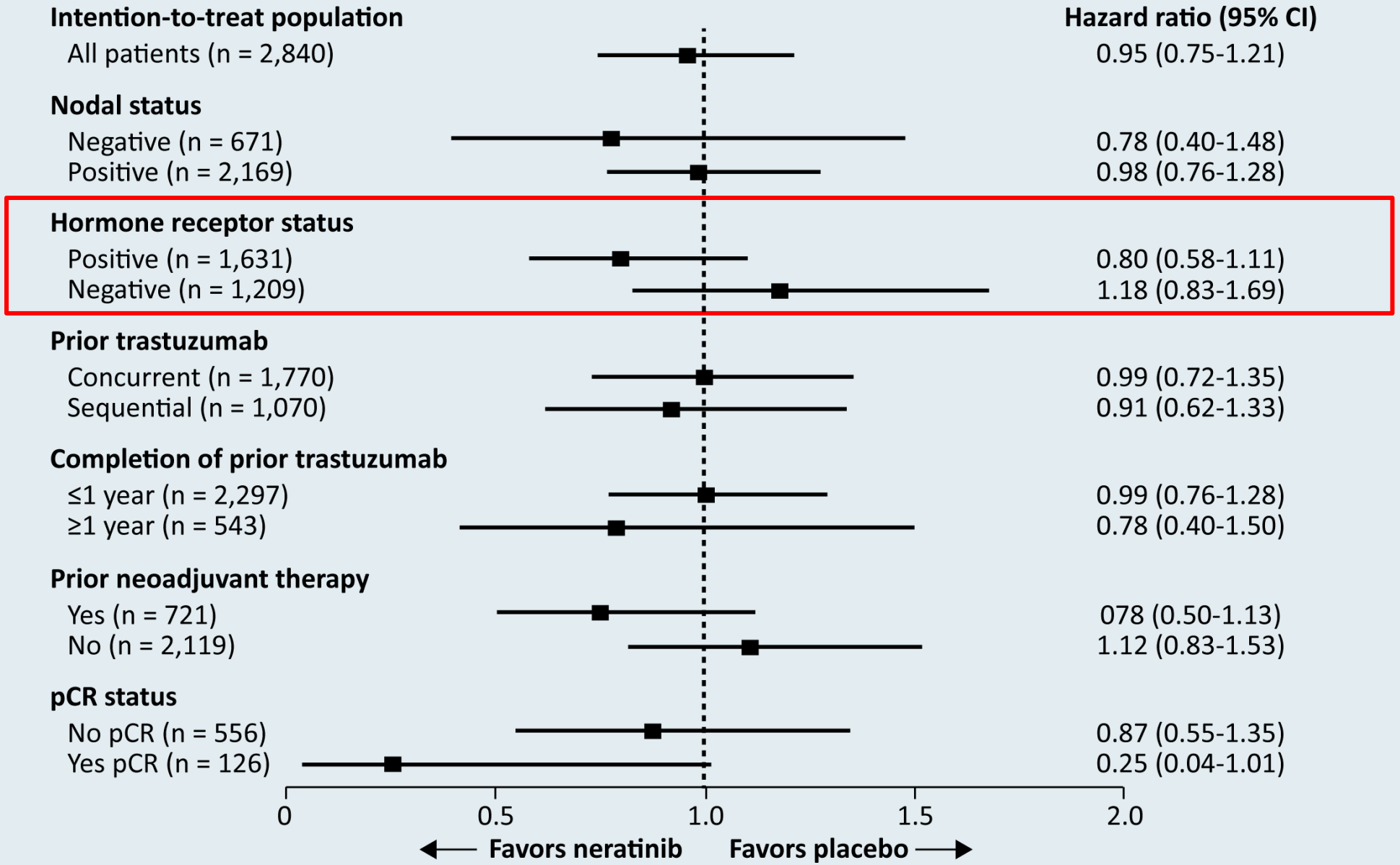
RTP RESEARCH TO PRACTICE

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

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

Immunotherapy and Other Nontargeted Approaches for Lung Cancer

Thursday, January 13, 2022
5:00 PM – 6:00 PM ET

Faculty

Corey J Langer, MD

Anne S Tsao, MD, MBA

Moderator

Neil Love, MD

RTP Year in Review 2022

Thank you for joining us!

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

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