Cancer Conference Update: What Happened at the 2020 San Antonio Breast Cancer Symposium®

Session 2: Management of HER2-Positive Breast Cancer

Monday, March 8, 2021
5:00 PM – 6:00 PM ET

Faculty

Mark D Pegram, MD

Moderator

Neil Love, MD

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Commercial Support

This activity is supported by educational grants from AstraZeneca Pharmaceuticals LP, Daiichi Sankyo Inc, Genentech, a member of the Roche Group, Puma Biotechnology Inc and Seagen Inc.

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Dr Love — Disclosures

Dr Love is president and CEO of Research To Practice. Research To Practice receives funds in the form of educational grants to develop CME activities from the following commercial interests: AbbVie Inc, Acerta Pharma — A member of the AstraZeneca Group, Adaptive Biotechnologies Corporation, Agendia Inc, Agios Pharmaceuticals Inc, Amgen Inc, Array BioPharma Inc, a subsidiary of Pfizer Inc, Astellas, AstraZeneca Pharmaceuticals LP, Aveo Pharmaceuticals, Bayer HealthCare Pharmaceuticals, BeiGene Ltd, Biodesix Inc, bioTheranostics Inc, Blueprint Medicines, Boehringer Ingelheim Pharmaceuticals Inc, Bristol-Myers Squibb Company, Celgene Corporation, Clovis Oncology, Daiichi Sankyo Inc, Dendreon Pharmaceuticals Inc, Eisai Inc, EMD Serono Inc, Epizyme Inc, Exact Sciences Inc, Exelixis Inc, Five Prime Therapeutics Inc, Foundation Medicine, Genentech, a member of the Roche Group, Genmab, Gilead Sciences Inc, GlaxoSmithKline, Grail Inc, Guardant Health, Halozyme Inc, Helsinn Healthcare SA, ImmunoGen Inc, Incyte Corporation, Infinity Pharmaceuticals Inc, Ipsen Biopharmaceuticals Inc, Janssen Biotech Inc, administered by Janssen Scientific Affairs LLC, Jazz Pharmaceuticals Inc, Karyopharm Therapeutics, Kite, A Gilead Company, Lexicon Pharmaceuticals Inc, Lilly, Loxo Oncology Inc, a wholly owned subsidiary of Eli Lilly & Company, Merck, Merrimack Pharmaceuticals Inc, Myriad Genetic Laboratories Inc, Natera Inc, Novartis, Novocure Inc, Oncopeptides, Pfizer Inc, Pharmacyclics LLC, an AbbVie Company, Prometheus Laboratories Inc, Puma Biotechnology Inc, Regeneron Pharmaceuticals Inc, Sandoz Inc, a Novartis Division, Sanofi Genzyme, Seagen Inc, Sirtex Medical Ltd, Spectrum Pharmaceuticals Inc, Sumitomo Dainippon Pharma Oncology Inc, Taiho Oncology Inc, Takeda Oncology, Tesaro, A GSK Company, Teva Oncology, Tokai Pharmaceuticals Inc and Verastem Inc.

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Research To Practice CME Planning Committee Members, Staff and Reviewers

Planners, scientific staff and independent reviewers for Research To Practice have no relevant conflicts of interest to disclose.

Dr Pegram — Disclosures

Consulting Agreements	AstraZeneca Pharmaceuticals LP, Daiichi Sankyo Inc, Genentech, a member of the Roche Group, MacroGenics Inc, Merck, Novartis, Odonate Therapeutics, Pfizer Inc, Puma Biotechnology Inc, Samsung Bioepis, Seagen Inc, Zymeworks
Contracted Research	AstraZeneca Pharmaceuticals LP, Daiichi Sankyo Inc, Pfizer Inc, Zymeworks
Data and Safety Monitoring Board/Committee	Roche Laboratories Inc
Employment (Spouse)	Loxo Oncology Inc, a wholly owned subsidiary of Eli Lilly & Company

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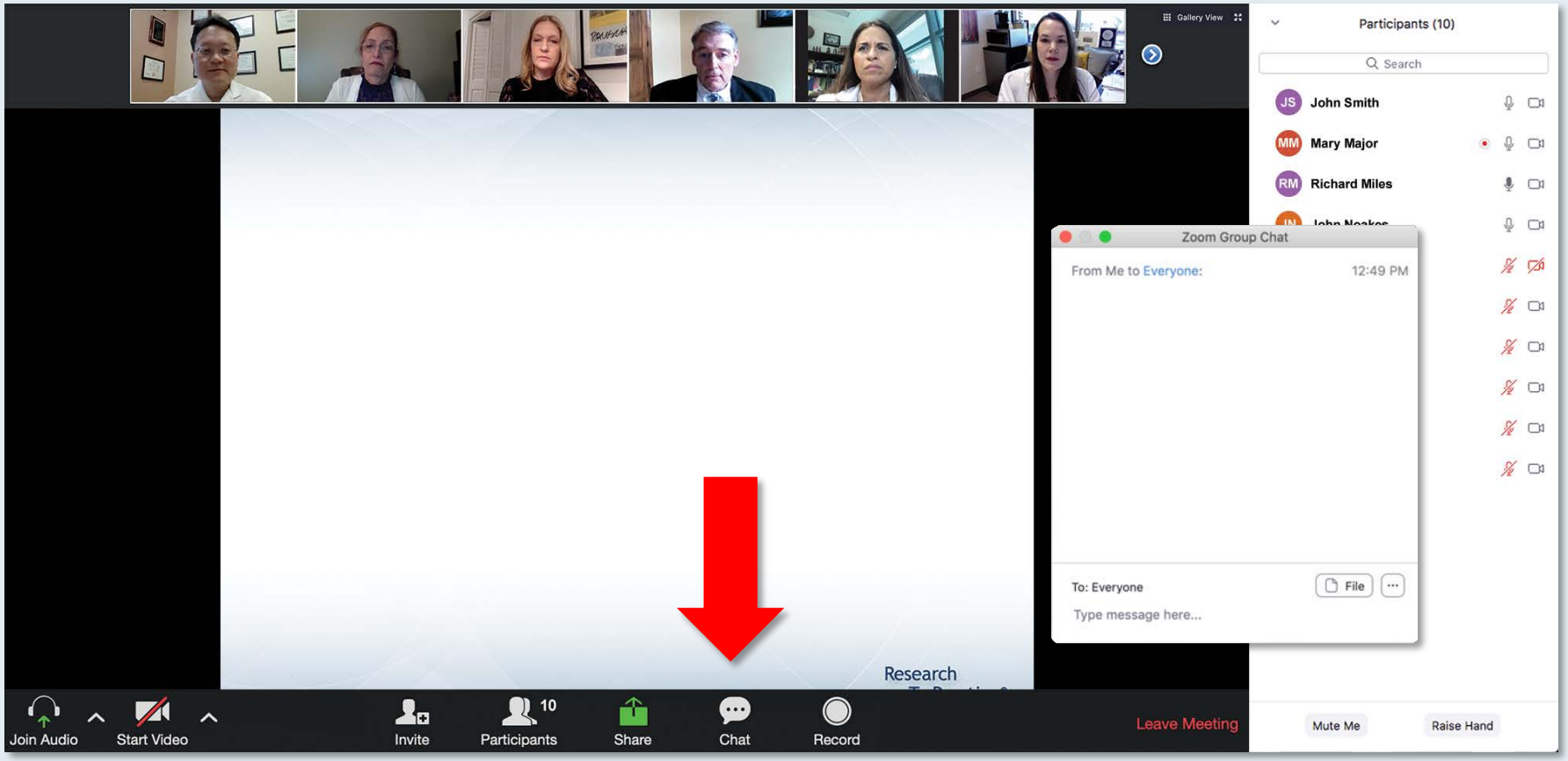
We Encourage Clinicians in Practice to Submit Questions



Feel free to submit questions now before the program begins and throughout the program.

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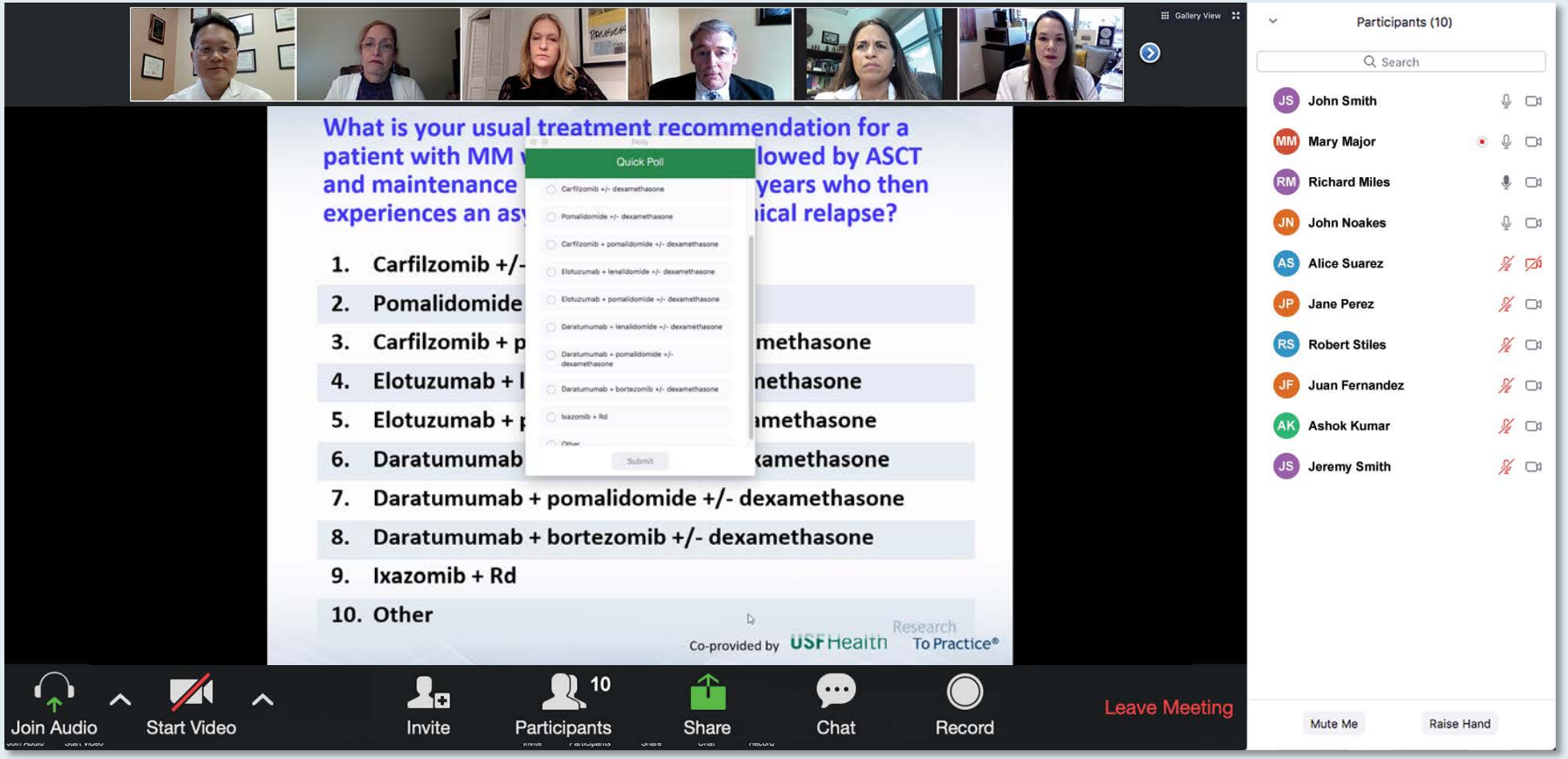
How to answer poll questions



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ONCOLOGY TODAY

WITH DR NEIL LOVE

Newly Approved Agents in HER2-Positive Metastatic Breast Cancer

DR MARK PEGRAM
STANFORD UNIVERSITY SCHOOL OF MEDICINE

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Data + Perspectives: Investigators Discuss the Effects of Emerging Research on the Care of Patients with Acute Myeloid Leukemia

Wednesday, March 10, 2021
7:00 PM – 8:00 PM ET

Faculty

Alexander Perl, MD
Eunice S Wang, MD

Moderator

Neil Love, MD

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Meet The Professor

Management of Chronic Lymphocytic Leukemia

Thursday, March 11, 2021
5:00 PM – 6:00 PM ET

Faculty

Steven Coutre, MD

Moderator

Neil Love, MD

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Dissecting the Decision: Clinical and Nursing Investigators Provide Practical Perspectives on Key Issues in Cancer Care

Part 1 — Acute Myeloid Leukemia

Tuesday, March 16, 2021
5:00 PM – 6:00 PM ET

Faculty

Rhonda Hewitt, MSN, ANP, AOCNP
Mark Levis, MD, PhD

Moderator

Neil Love, MD

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Meet The Professor

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

Wednesday, March 17, 2021
5:00 PM – 6:00 PM ET

Faculty

Alan P Venook, MD

Moderator

Neil Love, MD

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Dissecting the Decision: Clinical and Nursing Investigators Provide Practical Perspectives on Key Issues in Cancer Care

Part 2 — HER2-Positive Breast Cancer

Thursday, March 18, 2021
5:00 PM – 6:00 PM ET

Faculty

Jamie Carroll, APRN, MSN, CNP
Sara Hurvitz, MD

Moderator

Neil Love, MD

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Cases from the Community: Investigators Discuss the Role of PARP Inhibition in the Care of Actual Patients with Ovarian Cancer

Saturday, March 20, 2021
3:00 PM – 4:00 PM CT (4:00 PM – 5:00 PM ET)

Faculty

Susana Banerjee, MBBS, MA, PhD
Richard T Penson, MD, MRCP
Shannon N Westin, MD, MPH

Moderator

Neil Love, MD

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Thank you for joining us!

CME credit information will be emailed to each participant within 3 business days.

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Beyond the Guidelines: Clinical Investigator Perspectives on the Management of HER2-Positive Breast Cancer

Thursday, December 10, 2020
8:30 PM – 10:00 PM ET

Faculty

Carey K Anders, MD
Erika Hamilton, MD
Sara Hurvitz, MD
Mark D Pegram, MD
Sara M Tolaney, MD, MPH

Moderator

Neil Love, MD

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Beyond the Guidelines: Clinical Investigator Perspectives on the Management of HER2-Positive Breast Cancer — December 10, 2020

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Presentation Library

HER2-Positive Breast Cancer, Thursday, December 10, 2020

Considerations in the Care of Patients with Localized HER2-Positive Breast Cancer (BC) Receiving Neoadjuvant Systemic Therapy
Mark D Pegram, MD

Download Slides

Adjuvant and Extended-Adjuvant Therapy for Patients with Localized HER2-Positive BC
Sara M Tolaney, MD, MPH

Download Slides

Optimizing the Management of HER2-Positive Metastatic BC (mBC)
Sara Hurvitz, MD

Download Slides

Treatment of HER2-Positive Brain Metastases
Carey K Anders, MD

Download Slides

Incidence and Management of Adverse Events Associated with HER2-Targeted Therapies
Erika Hamilton, MD

Download Slides

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HER2-Positive Breast Cancer Survey Participants

1. Carey K Anders, MD
2. Aditya Bardia, MD, MPH
3. Joanne L Blum, MD, PhD
4. Adam M Brufsky, MD, PhD
5. Howard A Burris III, MD
6. Harold J Burstein, MD, PhD
7. Lisa A Carey, MD
8. Charles E Geyer Jr, MD
9. Matthew Goetz, MD
10. Erika Hamilton, MD
11. Sara Hurvitz, MD
12. Virginia Kaklamani, MD, DSc
13. Hannah M Linden, MD
14. Eleftherios P Mamounas, MD, MPH
15. P Kelly Marcom, MD
16. Jennifer M Matro, MD
17. Kathy D Miller, MD
18. Rita Nanda, MD
19. Ruth O'Regan, MD
20. Joyce O'Shaughnessy, MD
21. Mark D Pegram, MD
22. Lajos Pusztai, MD, DPhil
23. Joseph A Sparano, MD
24. Sandra M Swain, MD
25. Sara M Tolaney, MD, MPH

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Faculty

Mark D Pegram, MD
Susy Yuan-Huey Hung Endowed Professor of Oncology
Director, Clinical and Translational Research Unit
Associate Dean for Clinical Research Quality
Stanford University School of Medicine
Associate Director for Clinical Research
Stanford Comprehensive Cancer Institute
Stanford, California

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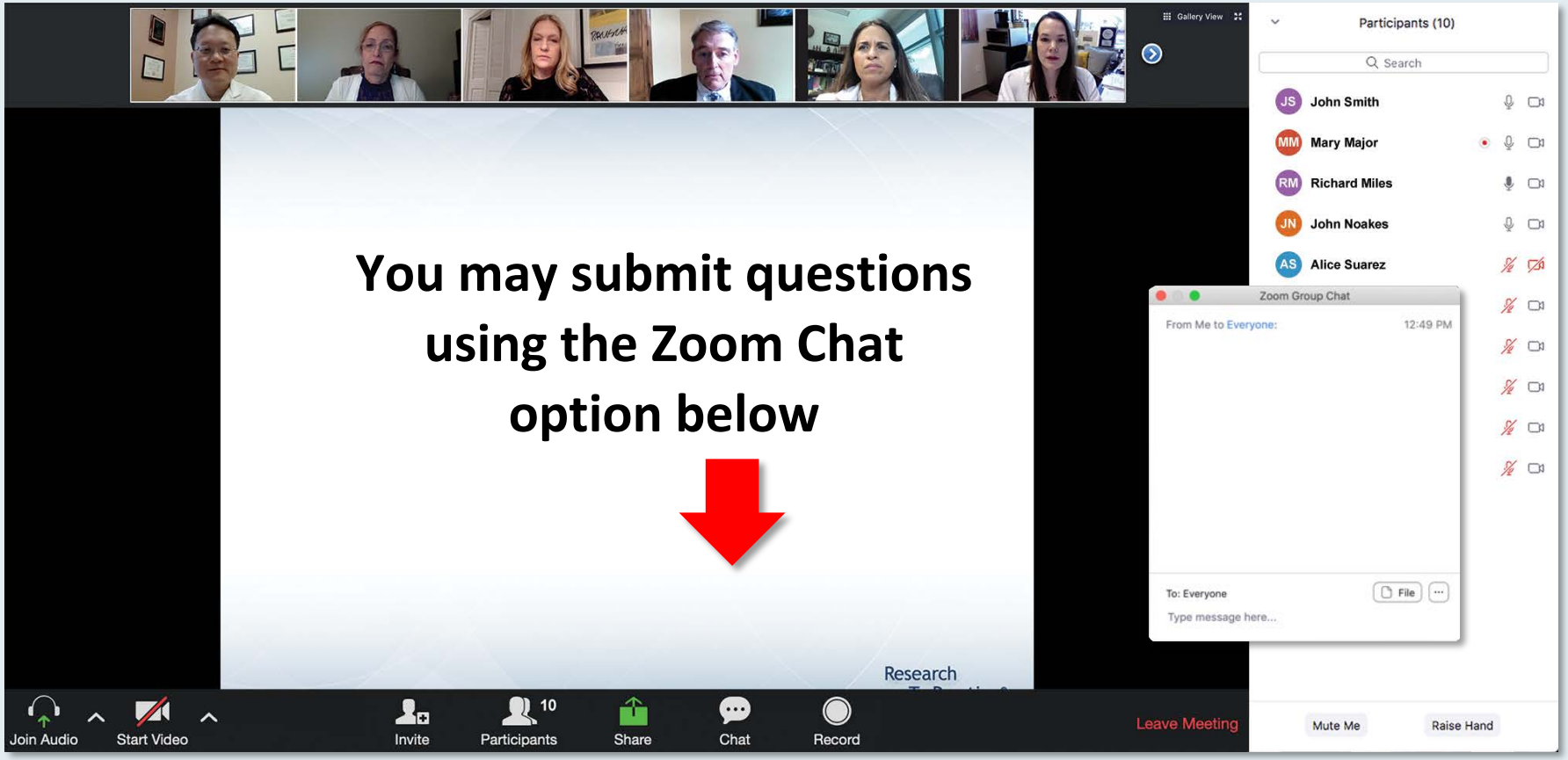
We Encourage Clinicians in Practice to Submit Questions



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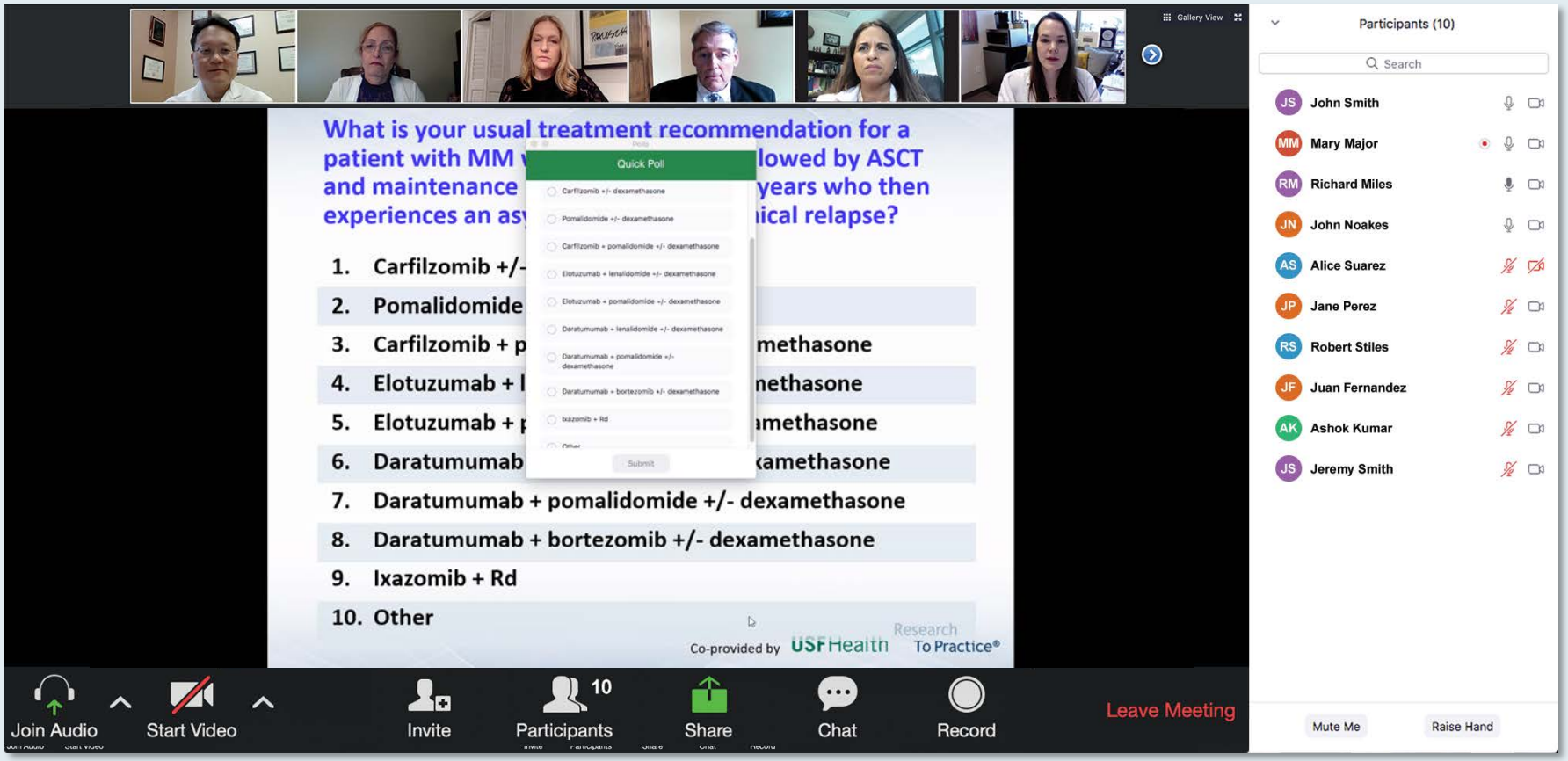

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ONCOLOGY TODAY

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Newly Approved Agents in HER2-Positive Metastatic Breast Cancer

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Alan B Astrow, MD
Chief, Hematology/Medical Oncology
NewYork-Presbyterian Brooklyn Methodist Hospital
Professor of Clinical Medicine
Weill Cornell Medical College
Brooklyn, New York

Estelamari Rodriguez, MD, MPH
Voluntary Assistant Professor of Clinical Medicine
Associate Director, Community Outreach
Sylvester Comprehensive Cancer Center
University of Miami Miller School of Medicine
Miami, Florida

Philip Glynn, MD
Director, Medical Oncology
Mercy Medical Center
Springfield, Massachusetts

Kelly Yap, MD
Assistant Clinical Professor
City of Hope
Arcadia, California

Yanjun Ma, MD
Tennessee Oncology
Murfreesboro, Tennessee

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Agenda

Module 1: Case Presentations

- Dr Rodriguez: A 49-year-old woman who received neoadjuvant TCHP, currently awaiting surgery
- Dr Yap: A 55-year-old woman with Stage I HER2-positive breast cancer
- Dr Glynn: A 45-year-old woman who received postoperative T-DM1 after neoadjuvant TCHP
- Dr Rodriguez: A 39-year-old woman with localized disease and a positive cervical node on PET scan

Module 2: SABCS 2020 Review — Localized Disease

Module 3: Case Presentations

- Dr Astrow: A 70-year-old woman with a 10-cm Grade III, ER/PR-negative, HER2-positive IDC and pleural metastases
- Dr Ma: An 87-year-old woman with pretreated HER2-positive metastatic breast cancer now with negative (low) HER2
- Dr Glynn: A 60-year-old woman with malignant pericardial effusion
- Dr Yap: A 43-year-old woman who develops brain metastases after prior TCHP

Module 4: SABCS 2020 Review — Metastatic Disease

Agenda

Module 1: Case Presentations

- Dr Rodriguez: A 49-year-old woman who received neoadjuvant TCHP, currently awaiting surgery
- Dr Yap: A 55-year-old woman with Stage I HER2-positive breast cancer
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Module 4: SABCS 2020 Review — Metastatic Disease

Case Presentation – Dr Rodriguez: A 49-year-old woman who received neoadjuvant TCHP, currently awaiting surgery

Dr Estelamari Rodriguez

- Presented with a palpable lump on the lateral aspect of the left breast, had stabbing pain near the location of the palpable lump and in the nipple
- 6/2020: Diagnostic mammogram: 2.8 x 1.9 cm mass in the upper outer quadrant of the left breast
- Pathology confirmed multifocal left breast invasive ductal carcinoma
- 1/2021: Patient completed neoadjuvant chemotherapy with TCHP x 6
  - Course complicated by port related infection and sepsis
- Left breast mass and left axillary lymphadenopathy have resolved and are no longer palpable
- Patient is awaiting surgery this month
- **Plan:** Resume trastuzumab and pertuzumab (subQ) to complete one year of treatment

Questions

- For a patient that has good response, if you find residual disease at the time of surgery, what is the next course of treatment systemically?
- Although this patient was BRCA-negative, I have seen some new data of possible use of adjuvant olaparib in BRCA-positive patients. In a patient with HER2-positive breast cancer how do we integrate that data? Are we thinking that in the future we may have to offer these patients that are BRCA positive/HER2 positive both types of treatment?

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OlympiA Trial: Olaparib Crosses Superiority Boundary for Invasive Disease-Free Survival versus Placebo at Planned Interim Analysis

Press Release: February 17, 2021

“The Phase 3 OlympiA trial for olaparib will move to early primary analysis and reporting following a recommendation from the Independent Data Monitoring Committee (IDMC).
Based on the planned interim analysis, the IDMC concluded that the trial crossed the superiority boundary for its primary endpoint of invasive disease-free survival (iDFS) versus placebo in the adjuvant treatment of germline *BRCA*-mutated (g*BRCA*m), high-risk human epidermal growth factor receptor 2 (HER2)-negative early-stage breast cancer following definitive local treatment and neoadjuvant or adjuvant chemotherapy.

Andrew Tutt, global chair of the OlympiA Phase 3 trial and professor, Institute of Cancer Research and Kings College London, said, "We are delighted that our global academic and industry partnership has been able to help investigate a possible personalized treatment for women with hereditary breast cancer. The most common cause of hereditary breast cancer is an inherited mutation in the BRCA1 or BRCA2 genes, which also may cause the disease to develop at a significantly earlier age than is usual. The OlympiA trial has allowed us to go beyond using genetic testing to identify patients who are at risk of this disease and explore the potential of olaparib to prevent disease recurrence for these patients. We look forward to analyzing and presenting the full results of the trial at a forthcoming medical meeting."

https://finance.yahoo.com/news/independent-data-monitoring-committee-concludes-115500394.html

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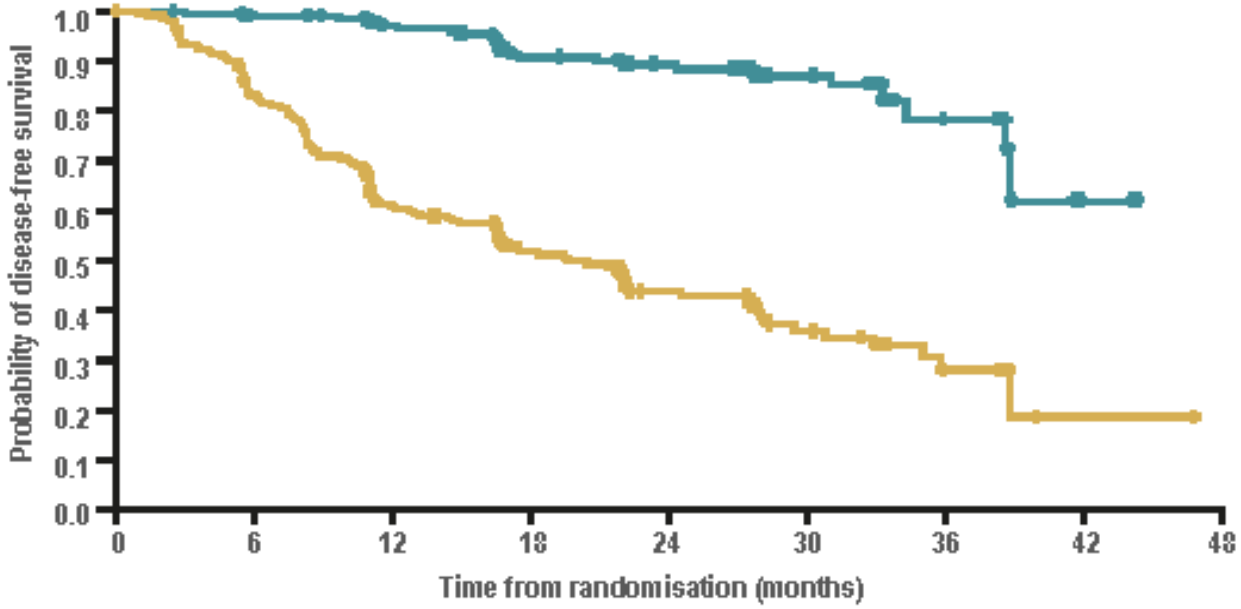
ADAURA: Osimertinib improves DFS versus placebo in resected EGFRm NSCLC

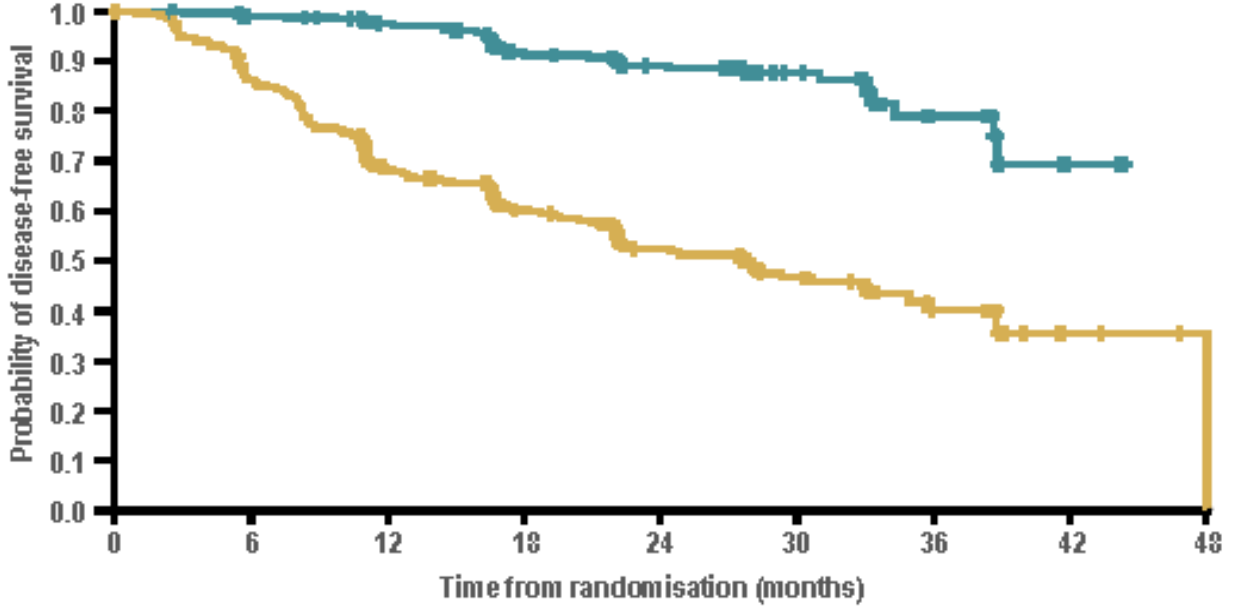
Primary population: Stage II/IIIA



No. at risk									
Osimertinib	233	219	189	137	97	52	18	2	0
Placebo	237	190	127	82	51	27	9	1	0

	Median DFS, months (95% CI)	HR (99.06% CI)
– Osimertinib	NR (38.8, NC)	0.17 (0.11, 0.26) P<0.0001
– Placebo	19.6 (16.6, 24.5)	

Overall population: Stage IB/II/IIIA



No. at risk									
Osimertinib	339	313	272	208	138	74	27	5	0
Placebo	343	287	207	148	88	53	20	3	1

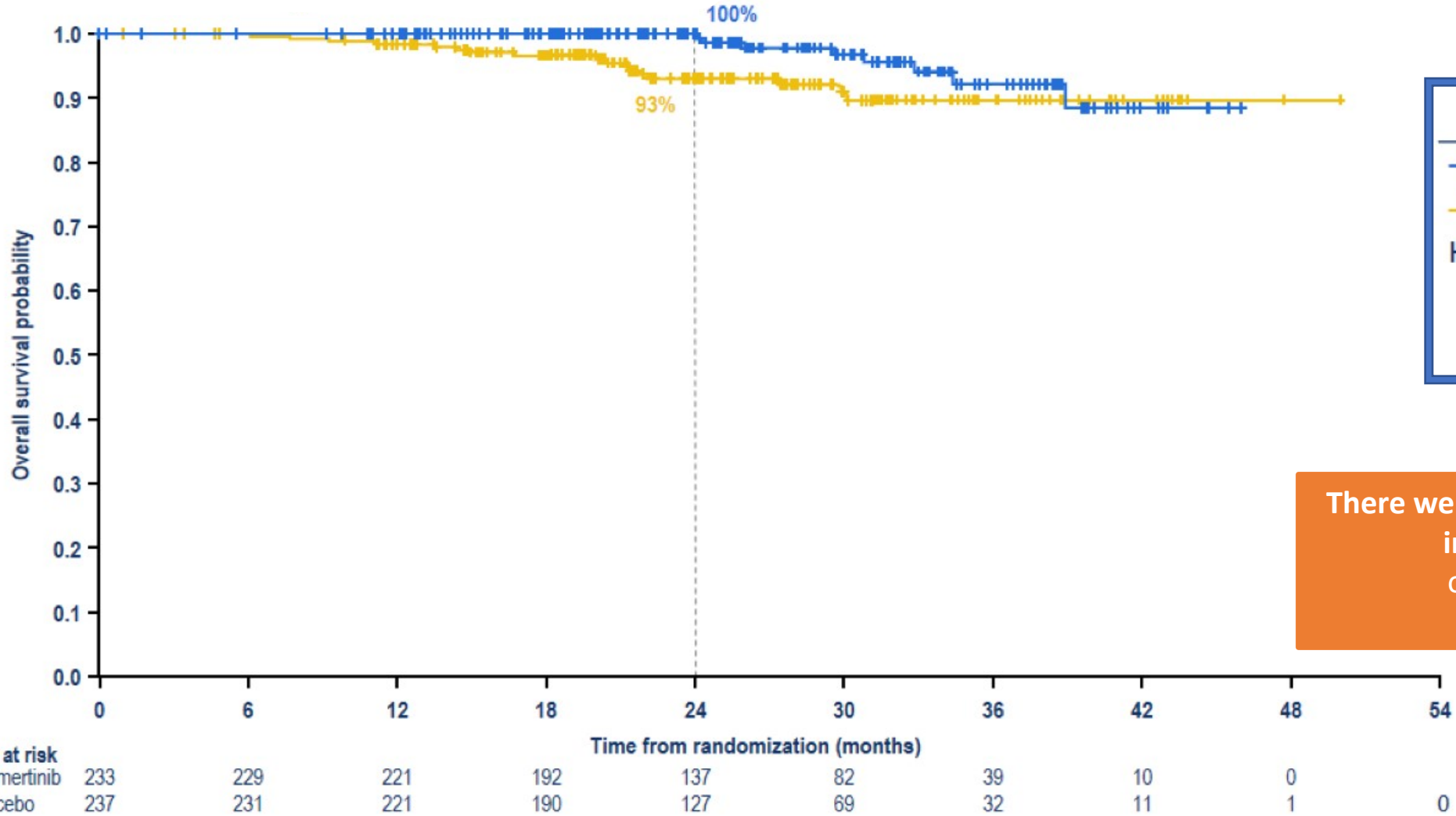
	Median DFS, months (95% CI)	HR (99.12% CI)
– Osimertinib	NR (NC, NC)	0.20 (0.14, 0.30) P<0.0001
– Placebo	27.5 (22.0, 35.0)	

VIRTUAL 2020 ESMO congress

Courtesy of Roy S Herbst, MD, PhD

CI, confidence interval; NC, not calculable; HR, hazard ratio; NR, not reached
ADAURA data cut-off: 17 January, 2020

ADAURA: Early snapshot: overall survival in patients with stage II/IIIA disease



Median OS, months (95% CI)	
– Osimertinib	NR (NC, NC)
– Placebo	NR (NC, NC)
HR (95% CI)	**0.40 (0.18, 0.90)**

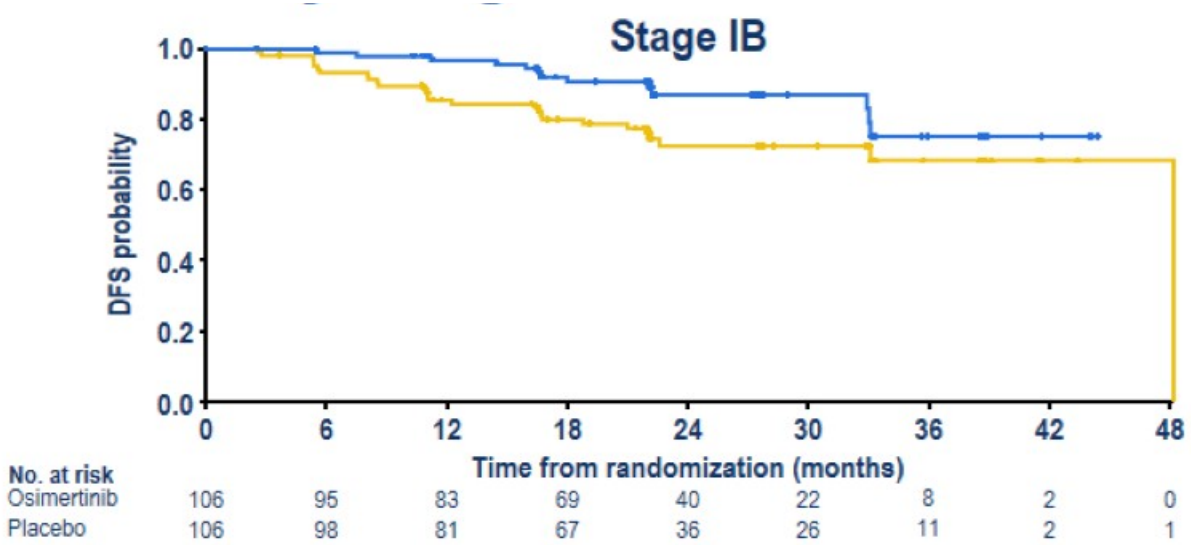
Maturity 5%:
osimertinib 3%, placebo 7%

There were a small number of deaths in stage IB patients:[2]
osimertinib 1 death,
placebo 2 deaths

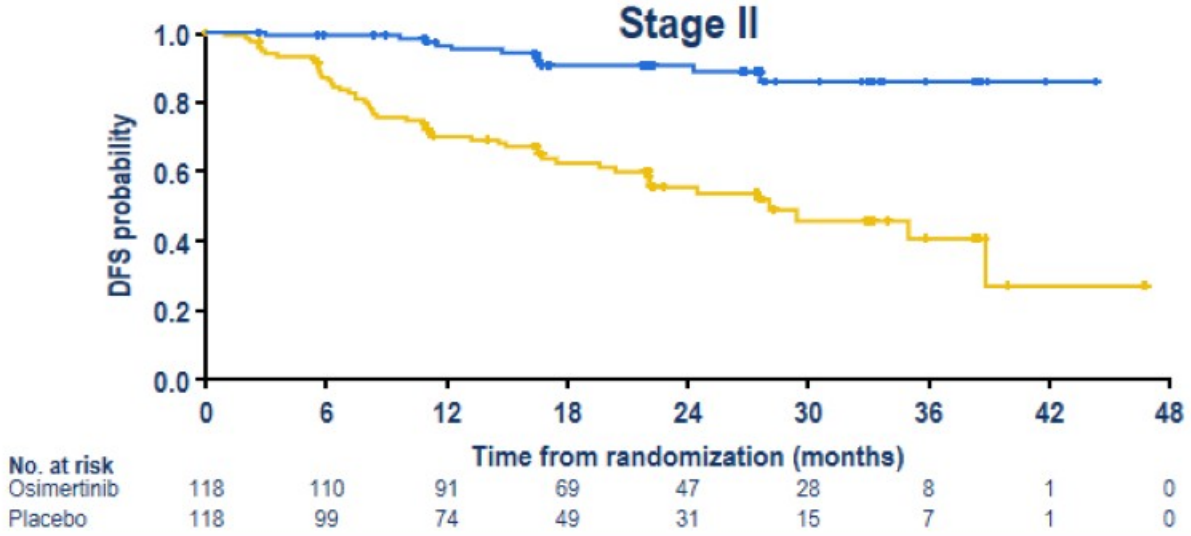
Courtesy of Roy S Herbst, MD, PhD

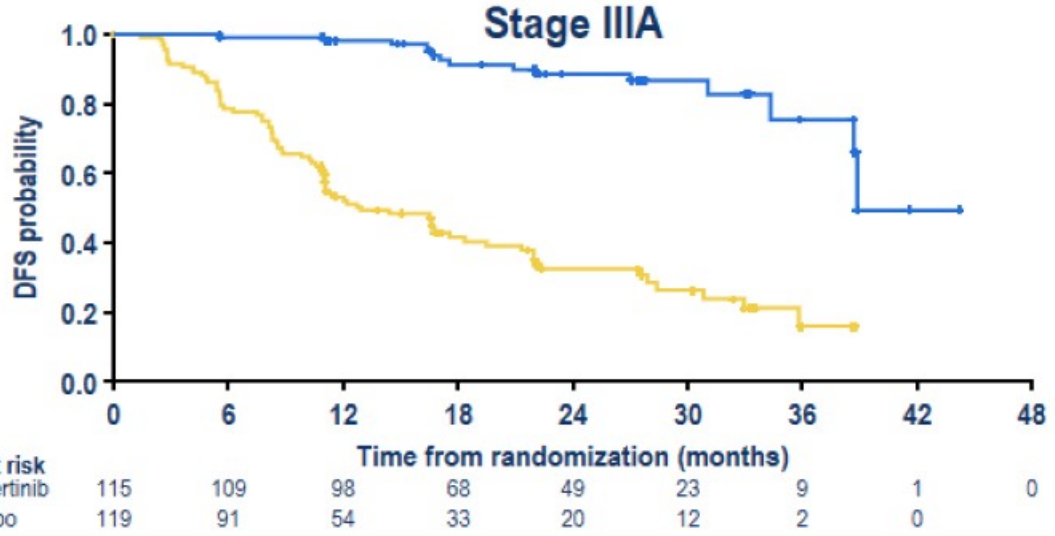
ADAURA data cut-off: January 17, 2020.
Median follow-up: osimertinib 26.1, placebo 24.7 months.
Tick marks indicate censored data.

ADAURA: DFS by stage



	Stage IB	Stage II	Stage IIIA
2 year DFS rate, % (95% CI)			
– Osimertinib	87 (77, 93)	91 (82, 95)	88 (79, 94)
– Placebo	73 (62, 81)	56 (45, 65)	32 (23, 42)
Overall HR (95% CI)	0.50 (0.25, 0.96)	0.17 (0.08, 0.31)	0.12 (0.07, 0.20)





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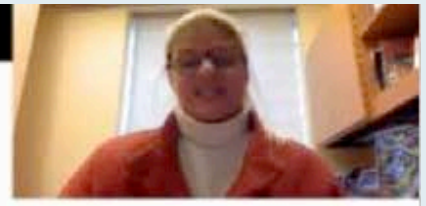


San Antonio Breast Cancer Symposium*, December 8-11, 2020

Do you remember 2005?

The NEW ENGLAND JOURNAL of MEDICINE

OCTOBER 6, 2011

Adjuvant Trastuzumab in HER2-Positive Breast Cancer

ORIGINAL ARTICLE

Trastuzumab plus Adjuvant Chemotherapy for Operable HER2-Positive Breast Cancer

The NEW ENGLAND JOURNAL of MEDICINE

OCTOBER 20, 2005

Trastuzumab after Adjuvant Chemotherapy in HER2-Positive Breast Cancer

"The results are simply stunning. They're not evolutionary, they're revolutionary." NEJM 2005

Traina T et al. SABCS 2020;Spotlight Session SS3. Used with permission from Dr Traina.

The NEW ENGLAND JOURNAL of MEDICINE

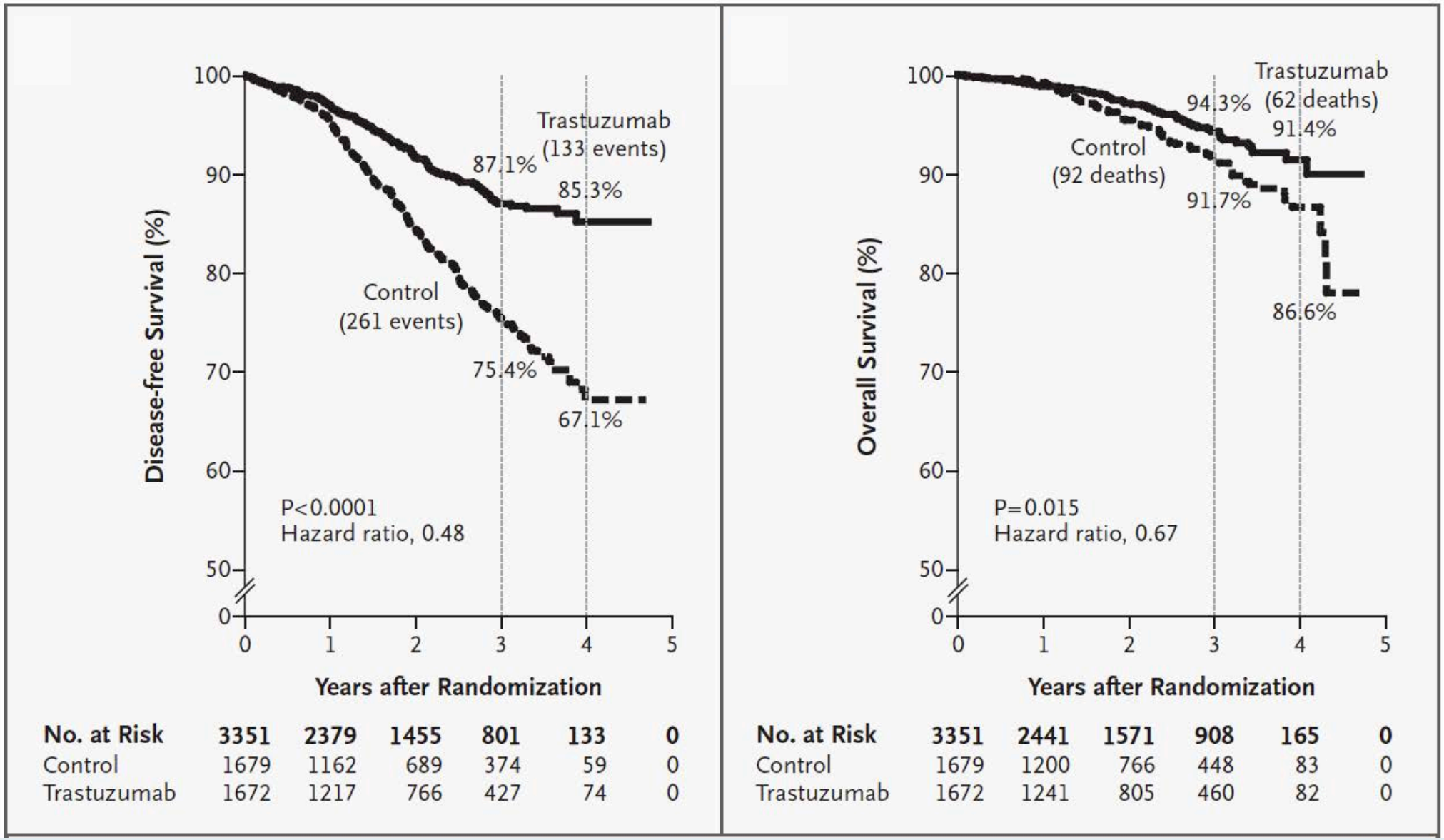
ORIGINAL ARTICLE

Trastuzumab plus Adjuvant Chemotherapy for Operable HER2-Positive Breast Cancer

Edward H. Romond, M.D., Edith A. Perez, M.D., John Bryant, Ph.D., Vera J. Suman, Ph.D., Charles E. Geyer, Jr., M.D., Nancy E. Davidson, M.D., Elizabeth Tan-Chiu, M.D., Silvana Martino, D.O., Soonmyung Paik, M.D., Peter A. Kaufman, M.D., Sandra M. Swain, M.D., Thomas M. Pisansky, M.D., Louis Fehrenbacher, M.D., Leila A. Kutteh, M.D., Victor G. Vogel, M.D., Daniel W. Visscher, M.D., Greg Yothers, Ph.D., Robert B. Jenkins, M.D., Ph.D., Ann M. Brown, Sc.D., Shaker R. Dakhil, M.D., Eleftherios P. Mamounas, M.D., M.P.H., Wilma L. Lingle, Ph.D., Pamela M. Klein, M.D., James N. Ingle, M.D., and Norman Wolmark, M.D.

N Engl J Med 2005;353:1673-84.

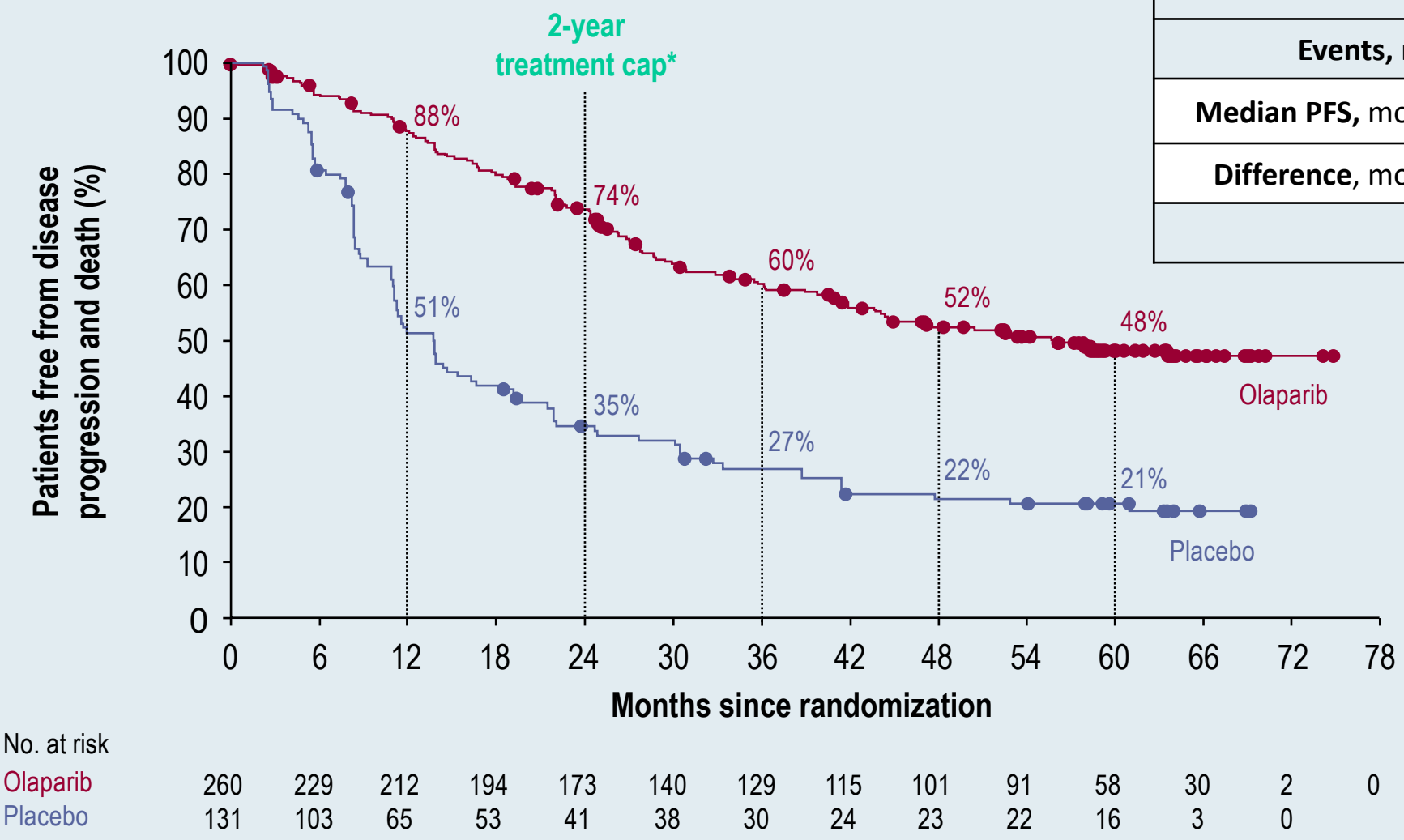
NSABP-B-31/NCCTG N9831: Survival



Romond EH et al. *N Engl J Med* 2005;353:1673-84.

SOLO-1: Updated PFS (60 Months Follow-Up)

	Olaparib (N=260)	Placebo (N=131)
Events, n (%)	118 (45)	100 (76)
Median PFS, months	**56.0**	**13.8**
Difference, months	42.2	
	HR 0.33 (95% CI 0.25–0.43)	



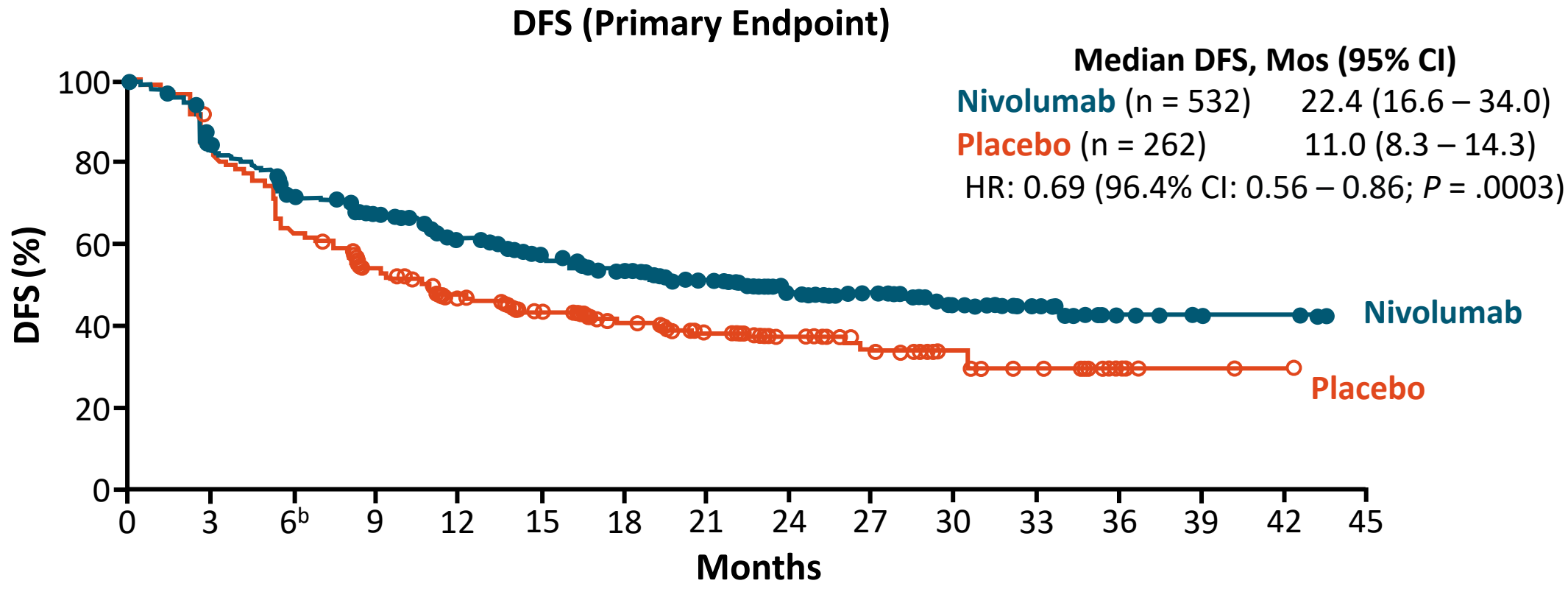
Median treatment duration:
Olaparib, 24.6 months
Placebo†, 13.9 months

Banerjee S et al. ESMO 2020;Abstract 811MO.

RTP RESEARCH TO PRACTICE

CheckMate 577: Adjuvant Nivolumab Following Neoadjuvant CRT/Resection in Esophageal/GEJ Cancer

- Randomized phase III trial of **adjuvant nivolumab** vs **placebo** following neoadjuvant CRT + surgical resection* for pts with stage II/III **esophageal/GEJ adenocarcinoma/SCC** (N = 794)

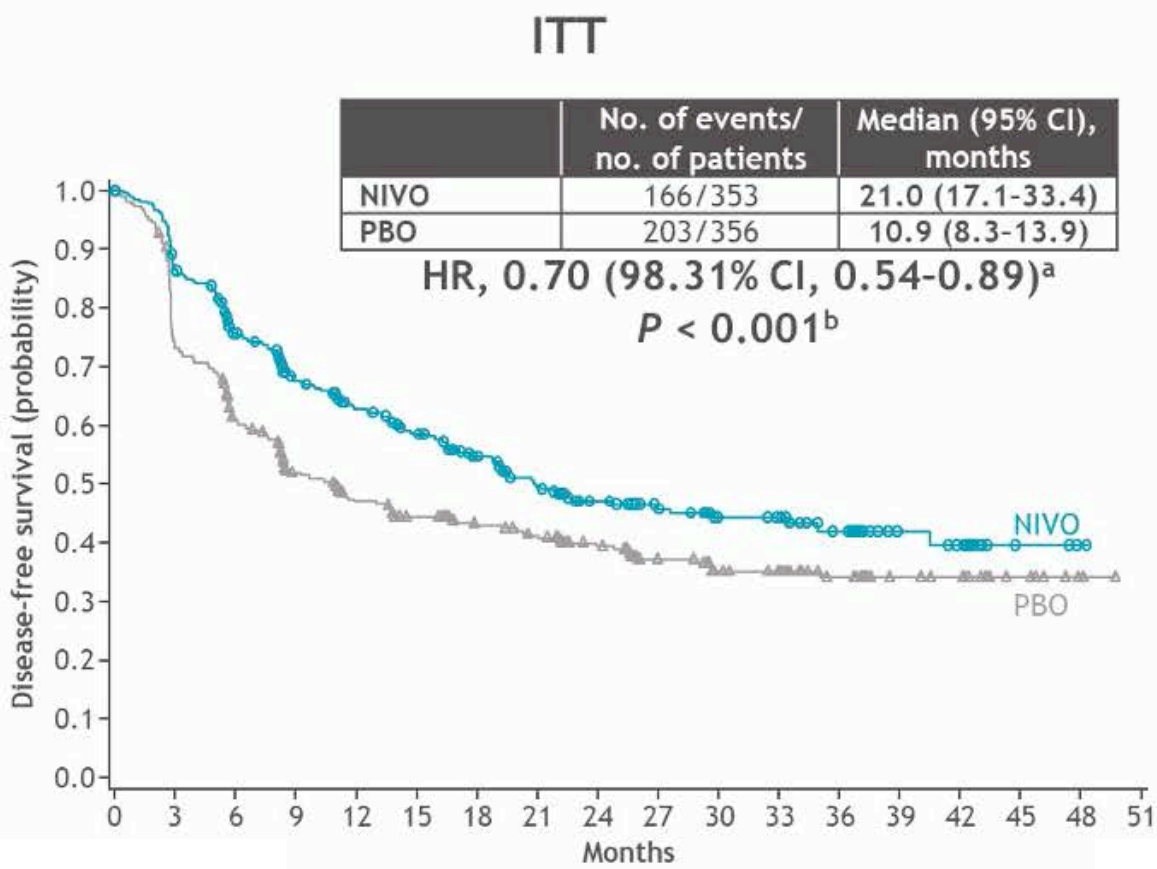


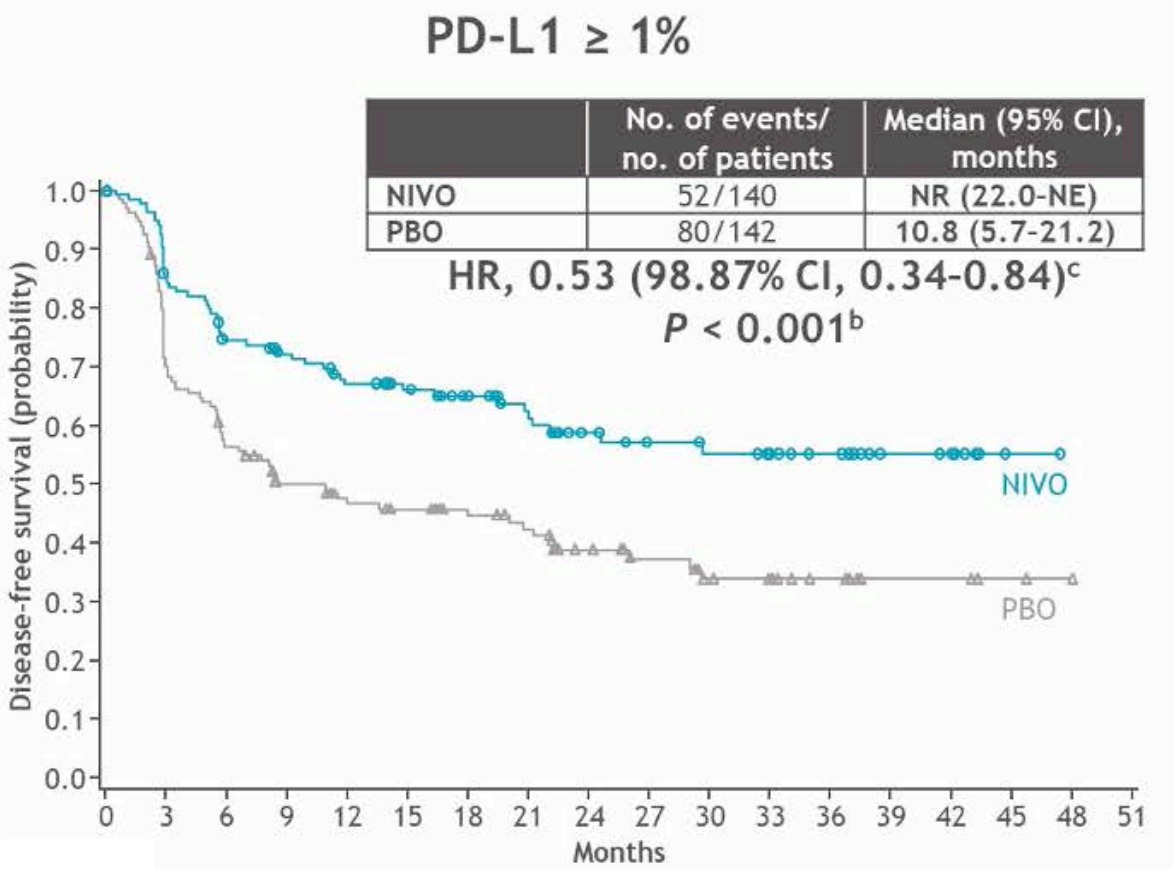
*Residual pathologic disease ≥ ypT1 or ≥ ypN1.

Kelly. ESMO 2020. Abstr LBA9.

Courtesy of Zev Wainberg, MD, MSc

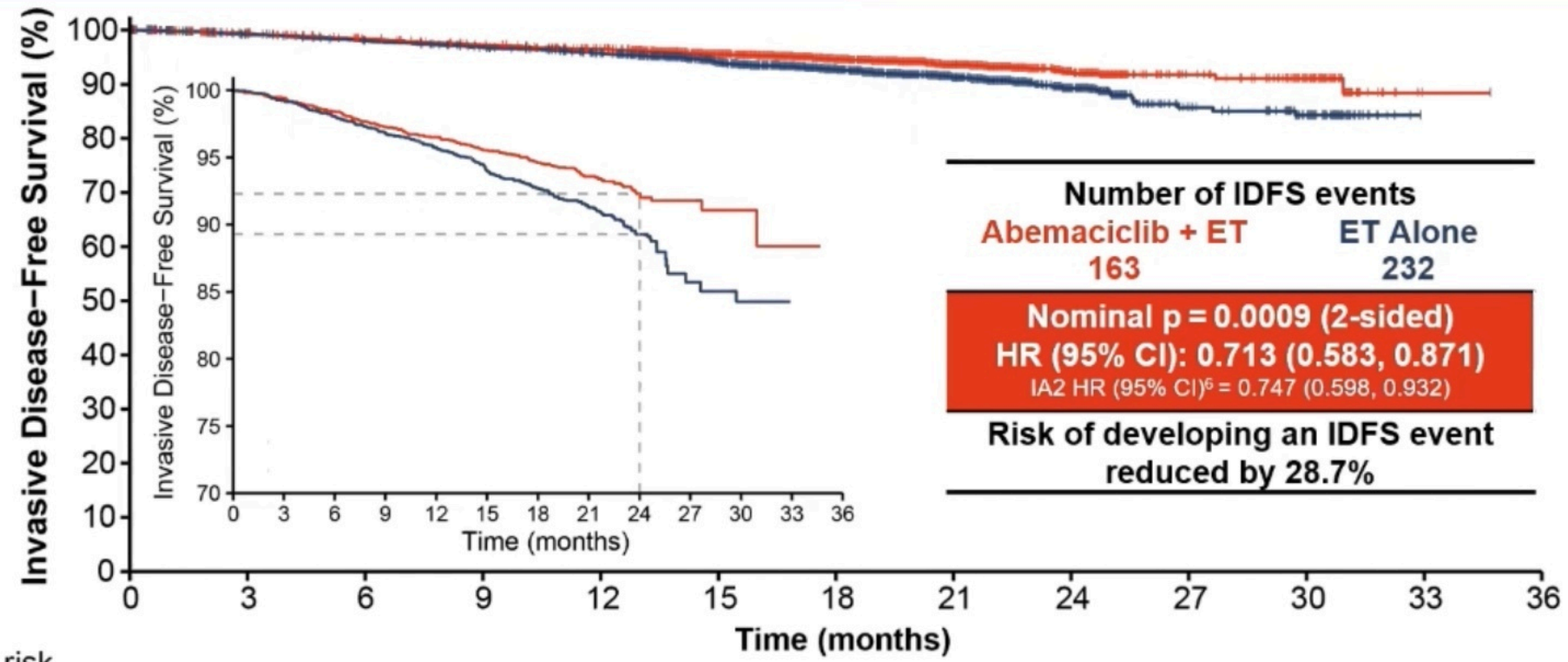
CheckMate 274: Adjuvant Nivolumab for High-Risk Muscle-Invasive Urothelial Bladder Carcinoma – Disease-Free Survival





Bajorin DF et al. Genitourinary Cancers Symposium 2021;Abstract 391.

monarchE: Invasive Disease-Free Survival at Primary Outcome Analysis



Statistically significant and clinically meaningful improvement in IDFS with greater treatment benefit at PO analysis

Two-year IDFS rates were 92.3% in the abemaciclib + ET arm and 89.3% in the ET arm - 3.0% difference

[6]Johnston SD et al JCO 2020

O'Shaughnessy JA et al. SABCS 2020;Abstract GS1-01.

Case Presentation – Dr Yap: A 55-year-old woman with Stage I HER2-positive breast cancer

Dr Kelly Yap

- Presented with Stage I ER/PR-negative, HER2-positive breast cancer
- Patient had 3 positive core biopsies, largest of which was 4 mm
- No residual disease present post lumpectomy/SLNB

Questions

- Is there a role for adjuvant chemotherapy in a patient with HER2-positive breast cancer that is less than 1 cm, meaning T1a or bN0? And if so, which regimen would be best? Would it be the combination of paclitaxel with trastuzumab or T-DM1?
- Would the faculty's recommendation for adjuvant chemotherapy differ between hormone receptor positive versus hormone receptor negative HER2 breast cancer that is less than 1 cm?

Case Presentation – Dr Glynn: A 45-year-old woman who received postoperative T-DM1 after neoadjuvant TCHP

Dr Philip Glynn

- Originally diagnosed with infiltrating ductal carcinoma of the left breast with lobular features
- Patient was treated with neoadjuvant TCHP
- Subsequent surgery demonstrated a PT2Y, N0 (ITC positive) carcinoma
  - Patient transitioned to radiation therapy → T-DM1 plus tamoxifen

Questions

- How would the faculty maximize her hormonal therapy?
- What would be the role of neratinib in a patient like this and what would be the most efficacious way to offer this agent to minimize toxicities?

Case Presentation – Dr Rodriguez: A 39-year-old woman with localized disease and a positive cervical node on PET scan

Dr Estelamari Rodriguez

- 11/2020: Noted some palpable abnormality in the right breast in the upper medial quadrant
- Diagnostic mammogram: 3 small slightly spiculated nodules corresponding to the area of palpable abnormality
- PET CT: Multiple FDG avid lesions within the right breast, compatible with malignancy; multiple (at least 6) FDG avid bilateral cervical lymph nodes, indeterminate in etiology
- **Treatment plan**: Under development

Questions

- Would the faculty biopsy cervical nodes to complete staging?
- What is the recommended neoadjuvant chemotherapy for HER2-positive disease?
- How would the faculty address fertility concerns in a young woman with HER2-positive breast cancer that requires chemotherapy?
- Do you have any concerns with transitioning to subq regimens containing trastuzumab and pertuzumab?
- What kind of radiation fields would the faculty use in a patient such as this one?

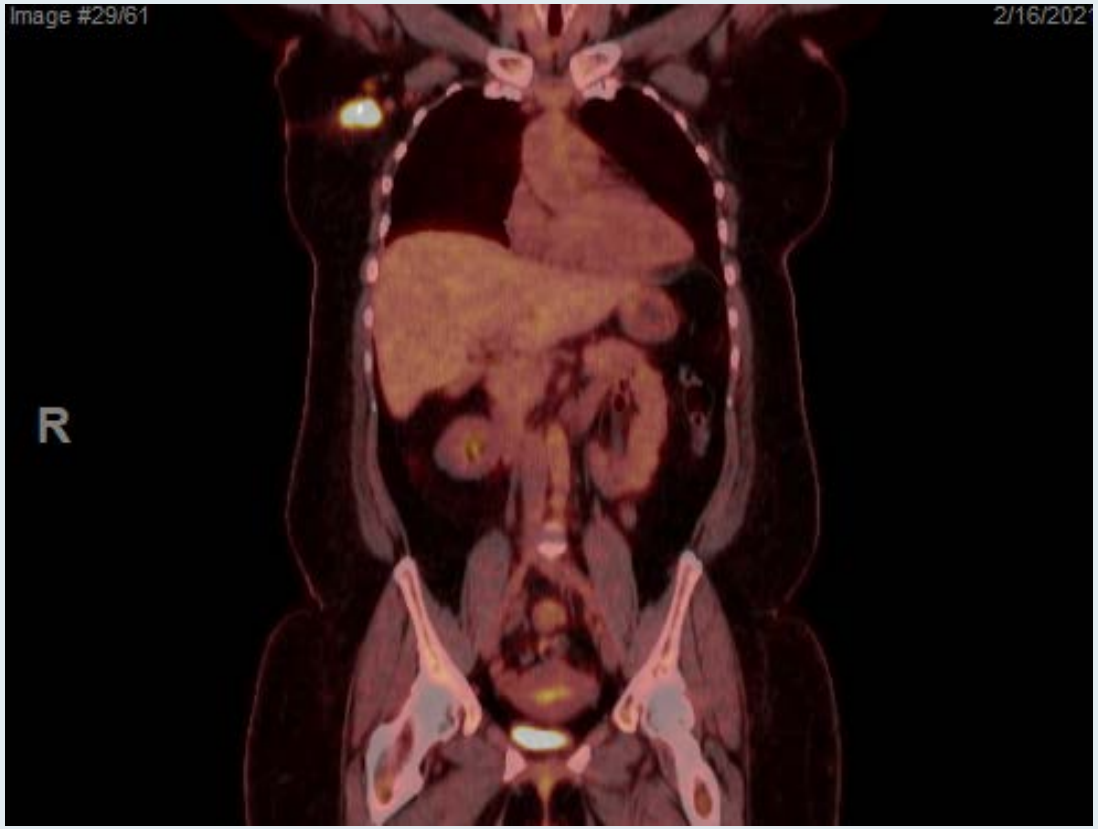
RTP RESEARCH TO PRACTICE

Case Presentation – Dr Rodriguez: A 39-year-old woman with localized disease and a positive cervical node on PET scan

Dr Estelamari Rodriguez

PET CT: Right Breast

PET CT: Pectoral and Cervical Lymph Node Involvement



RTP RESEARCH TO PRACTICE

Agenda

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- Dr Rodriguez: A 49-year-old woman who received neoadjuvant TCHP, currently awaiting surgery
- Dr Yap: A 55-year-old woman with Stage I HER2-positive breast cancer
- Dr Glynn: A 45-year-old woman who received postoperative T-DM1 after neoadjuvant TCHP
- Dr Rodriguez: A 39-year-old woman with localized disease and a positive cervical node on PET scan

Module 2: SABCS 2020 Review — Localized Disease

Module 3: Case Presentations

- Dr Astrow: A 70-year-old woman with a 10-cm Grade III, ER/PR-negative, HER2-positive IDC and pleural metastases
- Dr Ma: An 87-year-old woman with pretreated HER2-positive metastatic breast cancer now with negative (low) HER2
- Dr Glynn: A 60-year-old woman with malignant pericardial effusion
- Dr Yap: A 43-year-old woman who develops brain metastases after prior TCHP

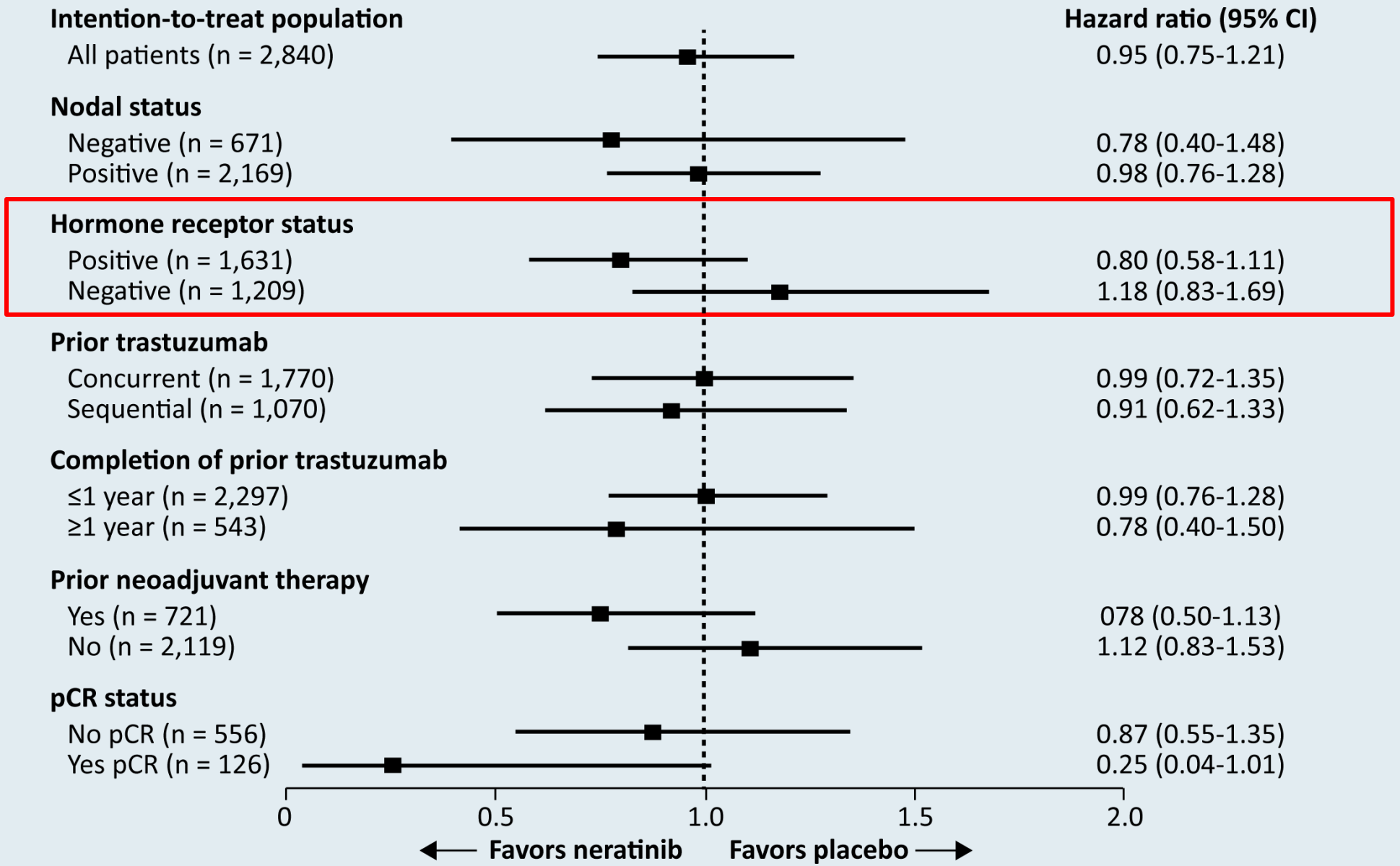
Module 4: SABCS 2020 Review — Metastatic Disease

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

The DAPHNe Trial: A Feasibility Study of Chemotherapy De-Escalation Based on Response to Neoadjuvant Paclitaxel-HP (THP) in HER2-Positive Breast Cancer

Waks AG et al.

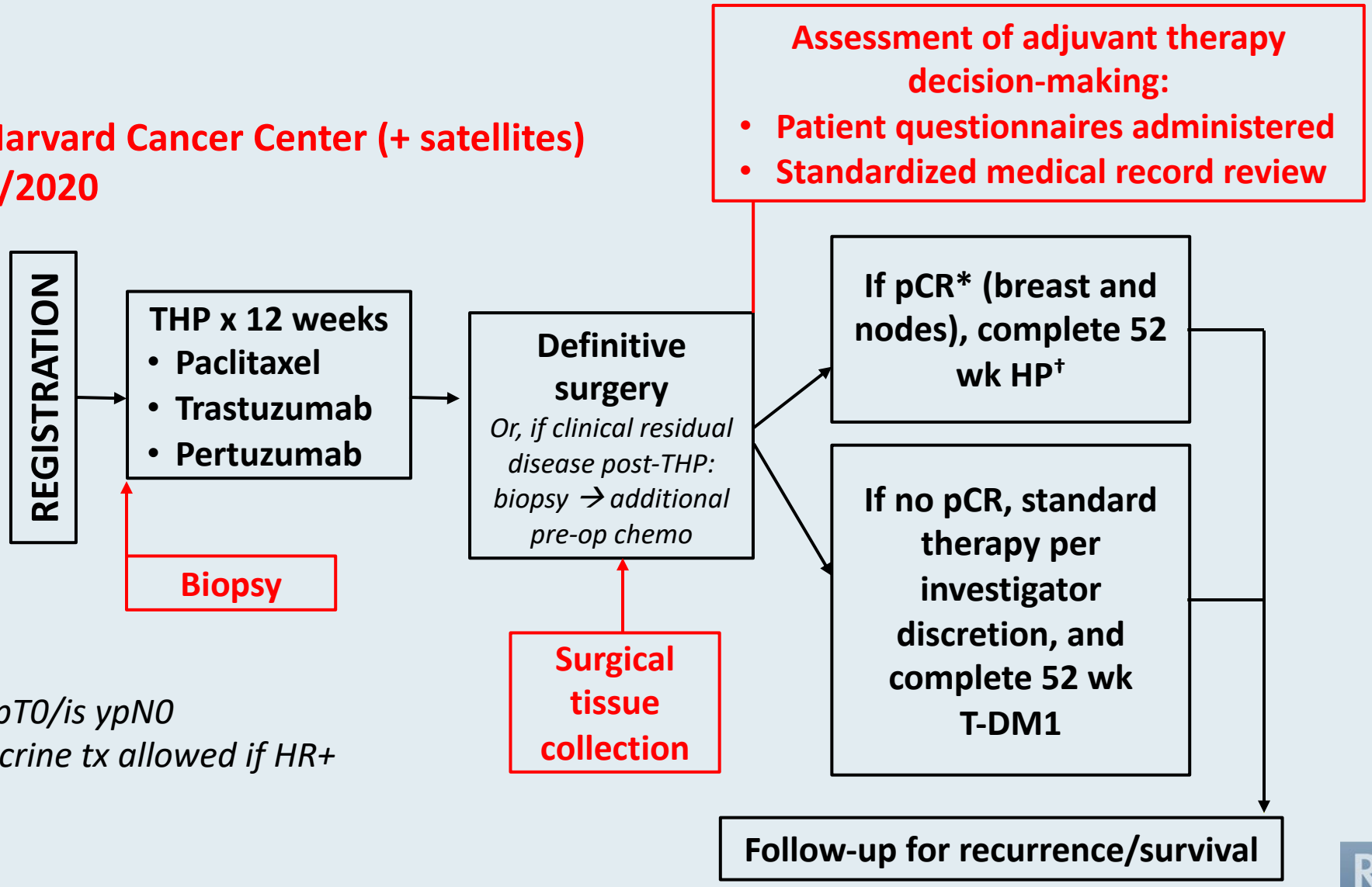
SABCS 2020;Abstract PD3-05.

DAPHNe: Trial of Chemotherapy De-escalation

TRIAL SCHEMA

Open at Dana-Farber/Harvard Cancer Center (+ satellites)
Enrollment 11/2018 - 1/2020

Eligibility:
- Anatomic Stage II-III HER2+ breast cancer
- Breast tumor ≥1.5 cm
- ER/PR pos or negative



** pCR defined as ypT0/is ypN0*
† Concurrent endocrine tx allowed if HR+

Waks AG et al. SABCS 2020;Abstract PD3-05.

RTP RESEARCH TO PRACTICE

Key Ongoing Phase III Trials for Localized HER2-Positive Breast Cancer

Study identifier	n	Randomization	Estimated primary completion
DESTINY-Breast05	1,600	• Trastuzumab deruxtecan (T-DXd) • Trastuzumab emtansine (T-DM1)	December 2025
CompassHER2 RD	1,031	• T-DM1 • T-DM1 + tucatinib	January 2028
IMpassion050	453	• ddAC-PacHP + atezolizumab • ddAC-PacHP + placebo	April 2021
TACT2	4,400	• Epirubicin-CMF • Accelerated epirubicin-CMF • Epirubicin-capecitabine • Accelerated epirubicin-capecitabine	September 2024
HR-BLTN-III-EBC	1,192	• Adjuvant trastuzumab → pyrotinib • Adjuvant trastuzumab → placebo	July 2022

www.clinicaltrials.gov; Accessed March 2021.

RTP RESEARCH TO PRACTICE

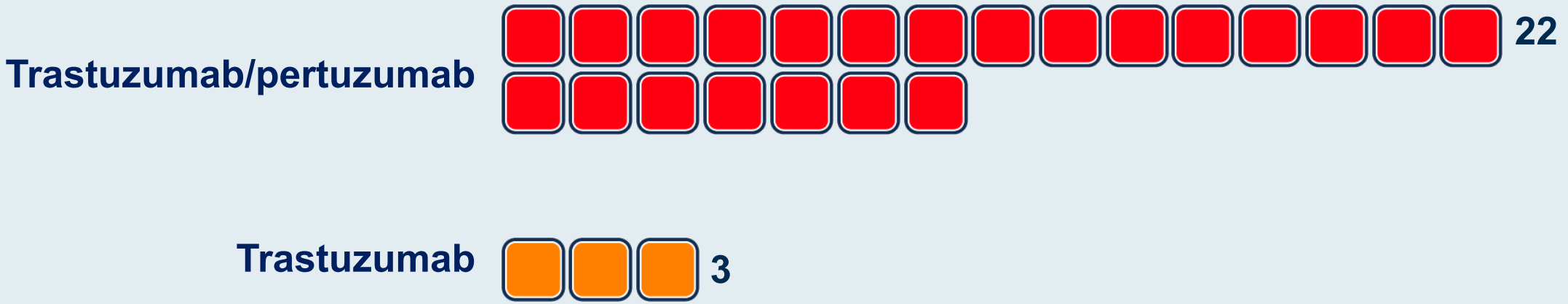
Which neoadjuvant systemic therapy, if any, would you generally recommend for a 65-year-old patient with a 2.5-cm, ER-negative, HER2-positive, clinically node-negative infiltrating ductal carcinoma (IDC)?

1. None
2. Paclitaxel/trastuzumab
3. Paclitaxel/trastuzumab/pertuzumab
4. ACTH (doxorubicin/cyclophosphamide/paclitaxel/trastuzumab)
5. ACTHP (ACTH/pertuzumab)
6. TCH (docetaxel/carboplatin/trastuzumab)
7. TCHP (TCH/pertuzumab)
8. Other

A 65-year-old woman presents with a 3.4-cm, ER-negative, HER2-positive IDC with biopsy-proven axillary nodes and receives neoadjuvant TCHP. Regulatory and reimbursement issues aside, what adjuvant anti-HER2 therapy would you recommend if at surgery the patient were found to have a pathologic complete response?

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

A 65-year-old woman presents with a 3.4-cm, ER-negative, HER2-positive IDC with biopsy-proven axillary nodes and receives neoadjuvant TCHP. Regulatory and reimbursement issues aside, what adjuvant anti-HER2 therapy would you recommend if at surgery the patient were found to have a pathologic complete response?



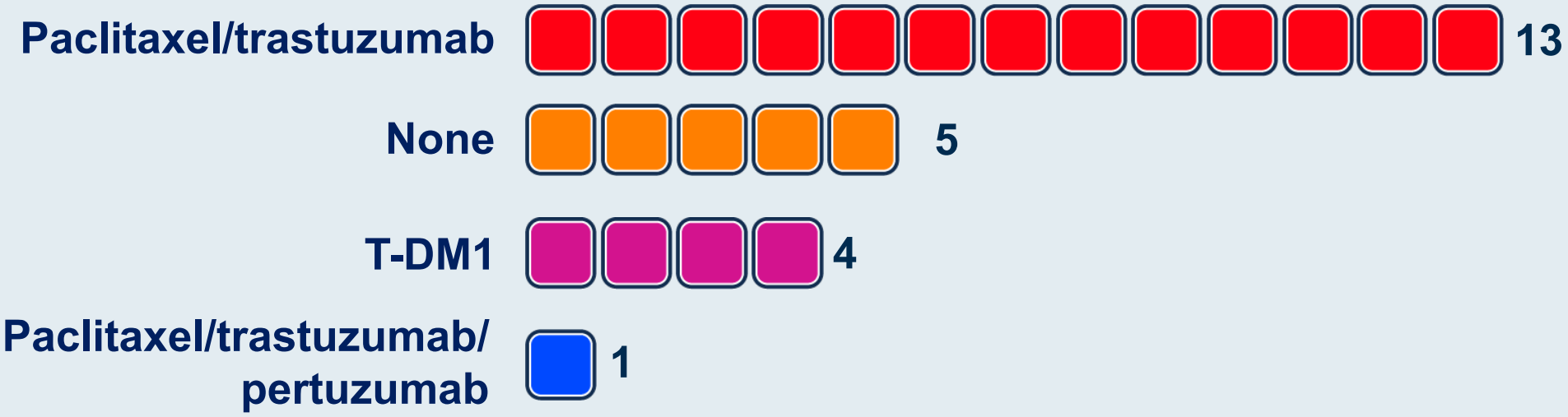
Survey of 25 Breast Cancer Clinical Investigators

An 80-year-old woman presents with a 0.6-cm, ER-negative, HER2-positive, node-negative IDC. Regulatory and reimbursement issues aside, what adjuvant systemic therapy would you recommend?

1. None
2. Paclitaxel/trastuzumab
3. Paclitaxel/trastuzumab/pertuzumab
4. TCH
5. TCHP
6. T-DM1
7. Other

Regulatory and reimbursement issues aside, what adjuvant systemic therapy would you recommend for a patient with an ER-negative, HER2-positive, node-negative IDC with the following characteristics?

Age: 80, Tumor size: 0.6 cm



Survey of 25 Breast Cancer Clinical Investigators

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- Dr Yap: A 43-year-old woman who develops brain metastases after prior TCHP

Module 4: SABCS 2020 Review — Metastatic Disease

Case Presentation – Dr Astrow: A 70-year-old woman with history of mild dementia presents with a 10-cm Grade III, ER/PR-negative, HER2-positive IDC and pleural metastases

Dr Alan Astrow

- History of stroke and mild dementia
- Presents with 10 cm left breast mass
- PET-CT: supraclavicular, internal mammary, mediastinal, hilum nodes; hypermetabolic left pleural-based metastases and a single left pulmonary nodule
- Treatment: THP x 12 weeks → trastuzumab/pertuzumab to complete 1 year
- Follow-up PET-CT: complete resolution of lymphadenopathy and the pleural-based metastases
- Difficult for patient to come to clinic
  - Her medical problems contributed to decision to stop the treatment after a year

Question

- How would the faculty approach this situation? Should she still be on trastuzumab/pertuzumab? Should I switch her to T-DM1 or just leave her alone since she's doing well?

RTP RESEARCH TO PRACTICE

Case Presentation – Dr Ma: An 87-year-old woman with pretreated HER2-positive metastatic breast cancer now with negative (low) HER2

Dr Yanjun Ma

- Treatments always dose-reduced due to fragile health
- 6/2020: Rebiopsy indicates loss of HER2 expression (FISH negative, IHC 2+)
  - No response to carboplatin → aggressive disease progression
- 7/2020: 7th line sacituzumab govitecan at 80% dose
- 8/2020: 8th line trastuzumab deruxtecan (T-DXd) with equivocal HER2 expression, good initial efficacy
- 1/2021: Patient experienced disease progression

Questions

- Are there any newer agents on the horizon other than T-DXd for patients with HER2 equivocal status?
- Also, at this point, for patients like this would the faculty want to shift to triple negative options, or would they continue targeting HER2?

Case Presentation – Dr Glynn: A 60-year-old woman with malignant pericardial effusion

Dr Philip Glynn

- 11/2008: Initial diagnosis – ER/PR-positive, HER2-negative IDC
  - Received multiple treatments, including hormonal therapy, carboplatin/gemcitabine, capecitabine, *nab*-paclitaxel
- 7/2020: Patient developed liver metastases, recurrence of pericardial effusion
  - Biopsy: HER2-positive disease
- Treated with T-DM1
  - Performance status improved, tolerating treatment well
- 2/2021: Patient inquires about treatment break

Question

- Given that this patient did not exhibit any impairments in her quality of life, I advised her we should continue therapy, but what are the faculty's thoughts on this case?

RTP RESEARCH TO PRACTICE

Case Presentation – Dr Yap: A 43-year-old woman who develops brain metastases after prior TCHP

Dr Kelly Yap

- Presented with Stage IIA (cT3N1M0) ER/PR-negative, HER2-positive breast cancer
- Patient was treated with neoadjuvant TCHP → pCR
- Brain metastases identified ~5 months after completion of 1 year of adjuvant HER2-targeted therapy
  - Treated with SRS, no other systemic disease

Questions

- What would be the best approach for this patient at her first recurrence with brain-only metastases? Would a treatment with known CNS activity such as tucatinib be recommended at that point?
- If the patient experiences a second recurrence in the brain, would you treat with systemic treatment or with another SRS? If treating with systemic therapy, what would be the best option?
- Should we follow the NCCN Guidelines of using T-DM1 as the next line of treatment? Or should we pick a regimen that has known CNS activity, such as the tucatinib/capecitabine/trastuzumab combination or trastuzumab deruxtecan?

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Module 4: SABCS 2020 Review — Metastatic Disease

RTP RESEARCH TO PRACTICE

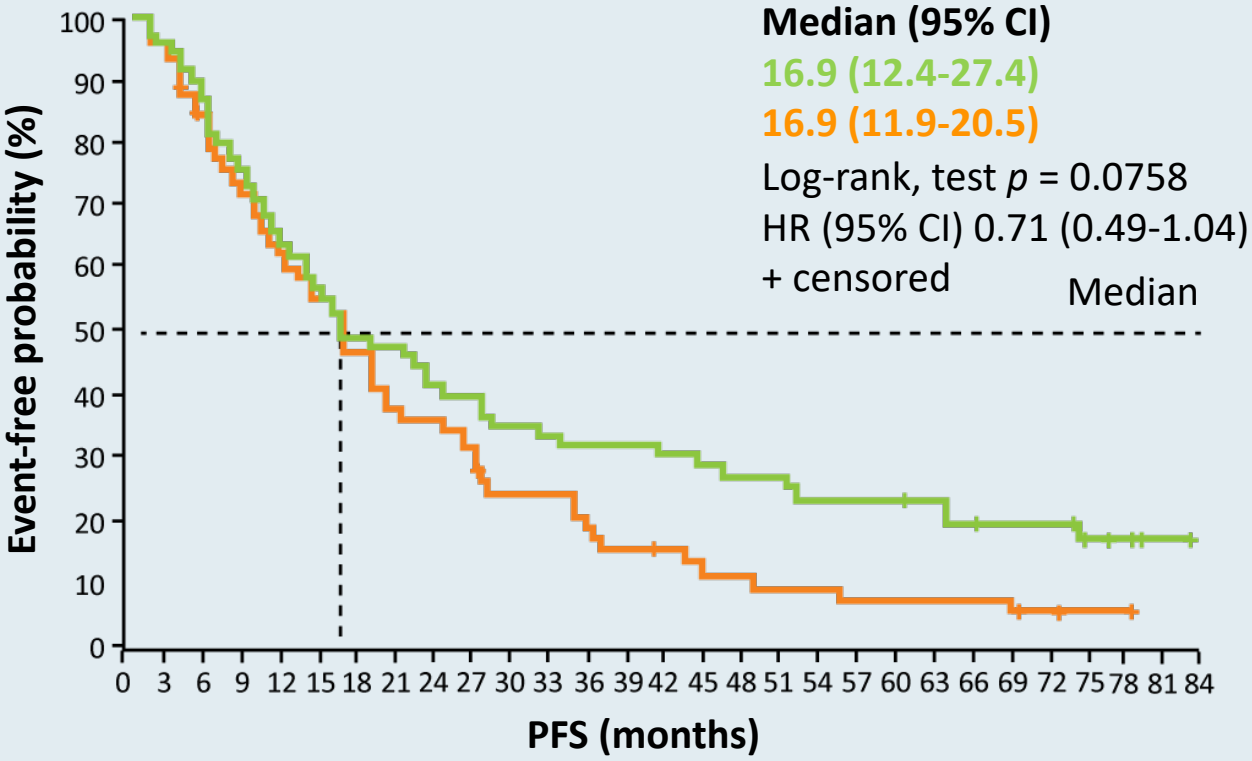
Final Analysis of PERTAIN: A Randomized, Two-Arm, Open-Label, Multicenter Phase II Trial Assessing the Efficacy and Safety of First-Line Pertuzumab Given in Combination with Trastuzumab plus an Aromatase Inhibitor in Patients with HER2-Positive and Hormone Receptor-Positive Metastatic or Locally Advanced Breast Cancer

Arpino G et al.

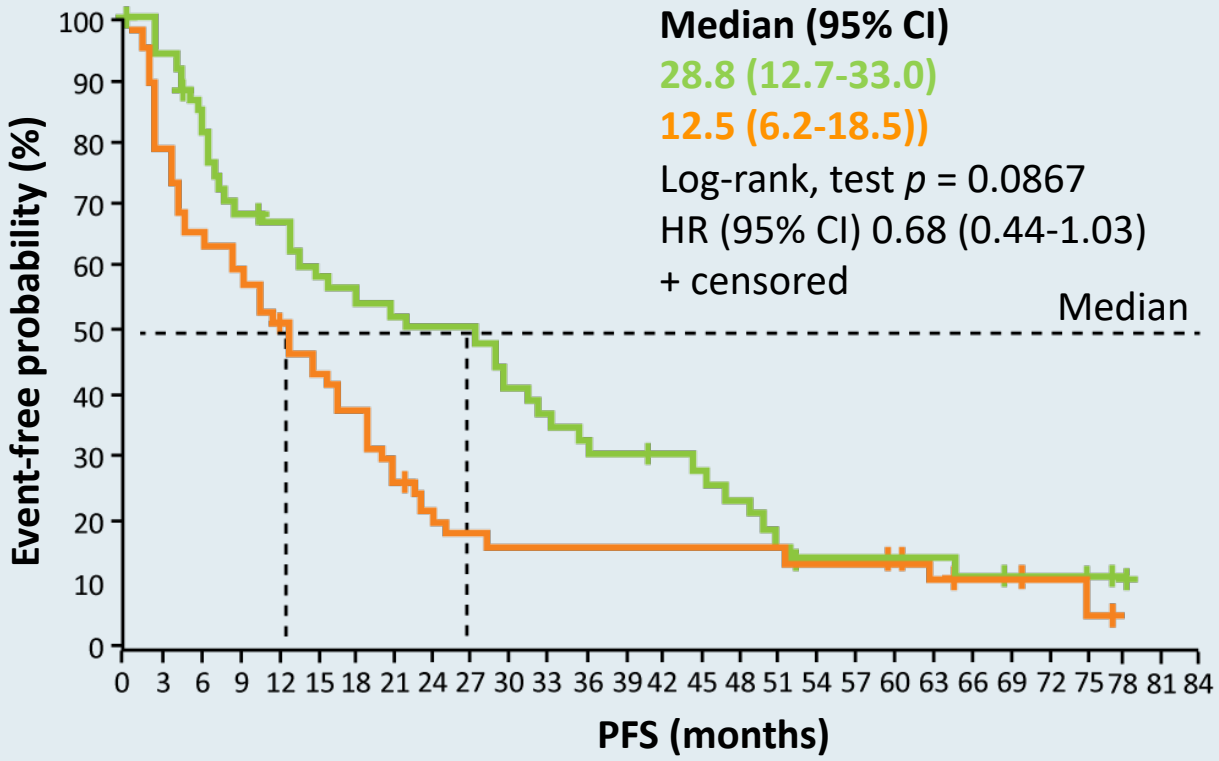
SABCS 2020;Abstract PD3-02.

PERTAIN: Progression-Free Survival

Received Induction Therapy



No Induction Therapy



Arpino G et al. SABCS 2020;Abstract PD3-02.

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

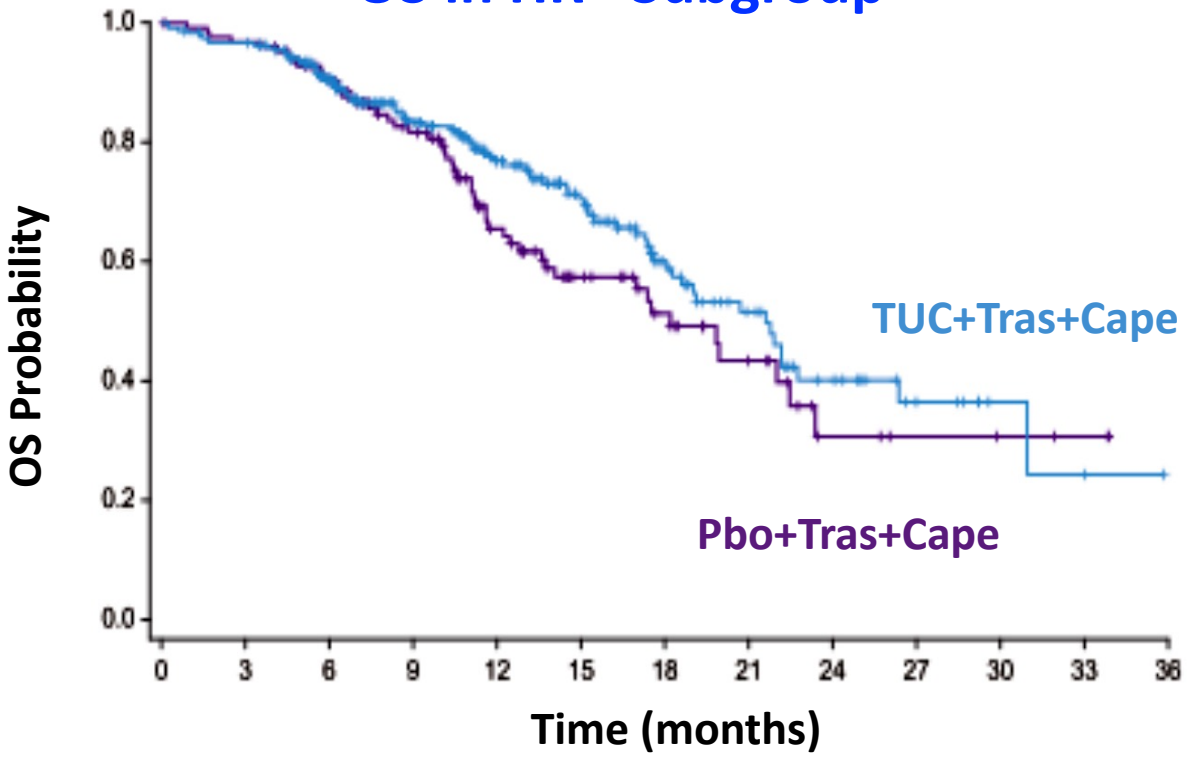
Hamilton E et al.

SABCS 2020;Abstract PD3-08.

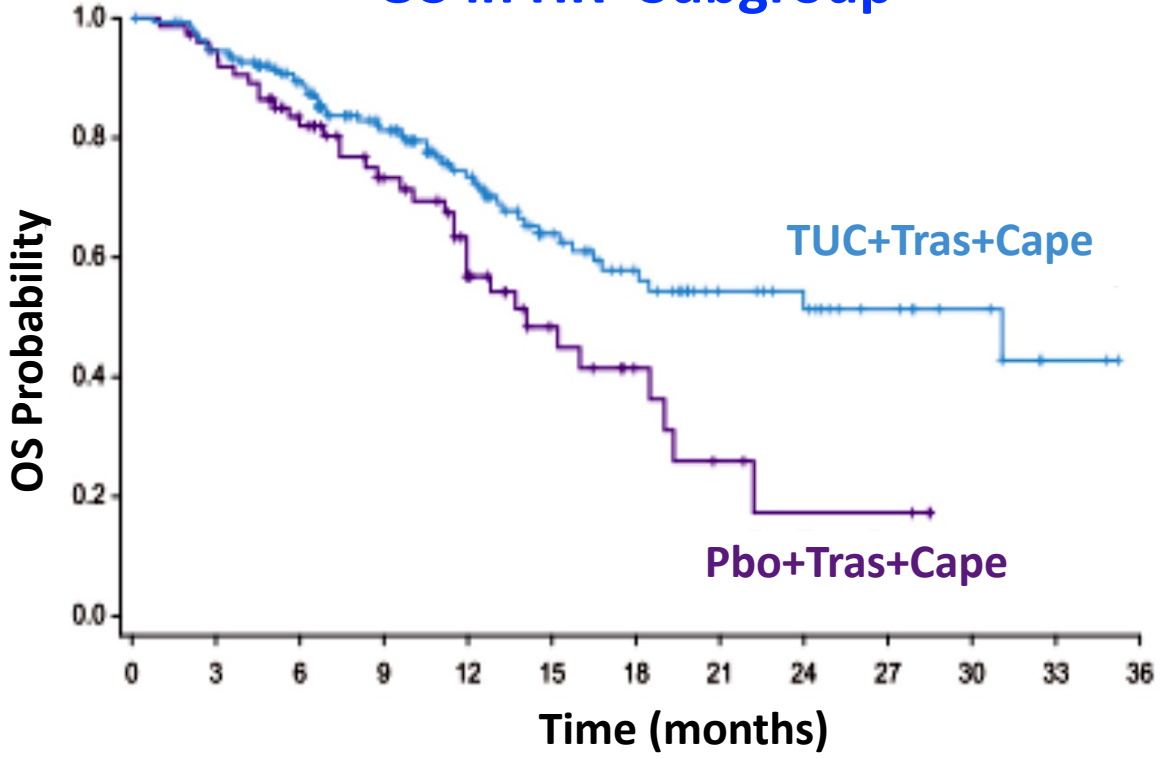
OS by HR Status in the Total Study Population

- 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.

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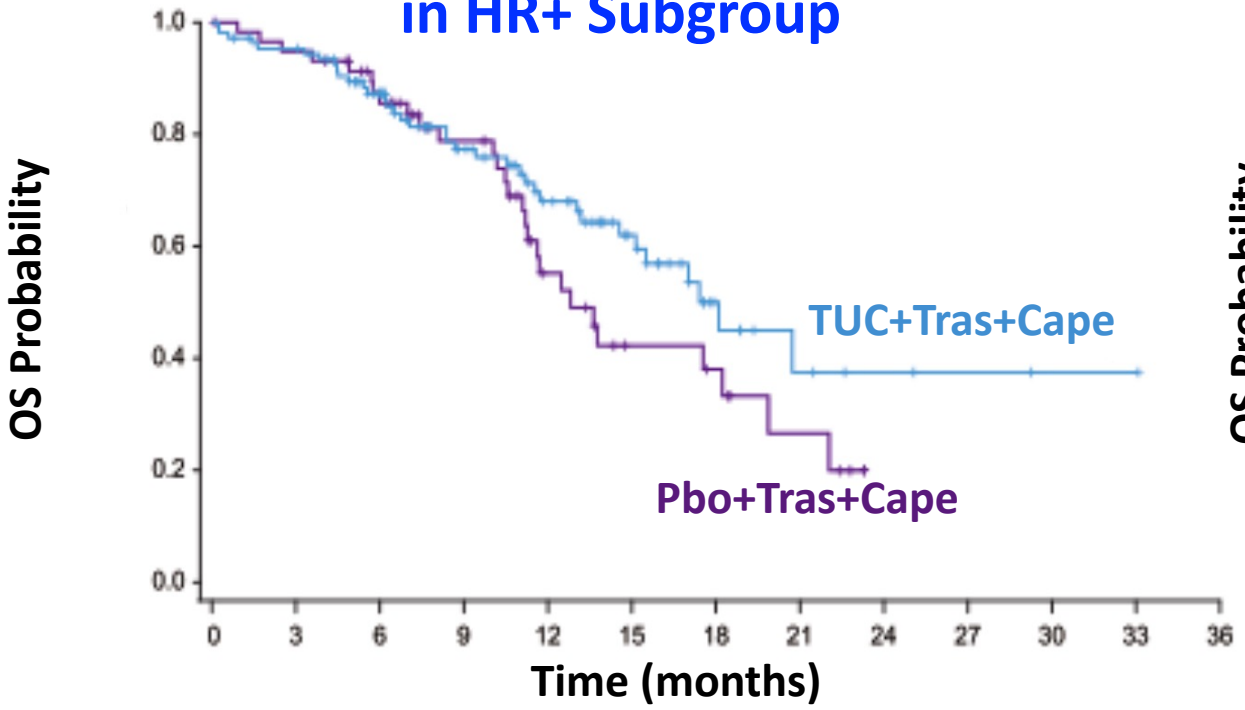
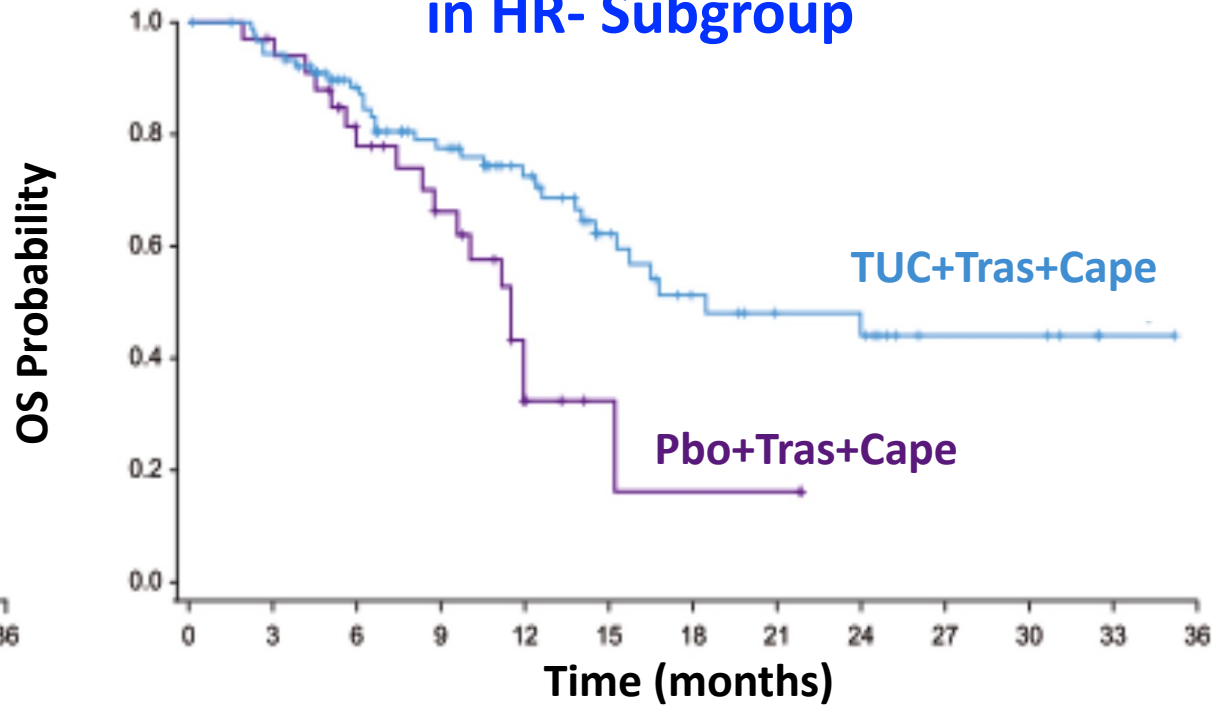
OS by HR Status in Patients with Baseline Brain Metastases

- OS was numerically improved in patients with brain metastases in the tucatinib arm in both hormone receptor subgroups.

OS in Patients with Brain Metastases in HR+ Subgroup



OS in Patients with Brain Metastases in HR- Subgroup



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

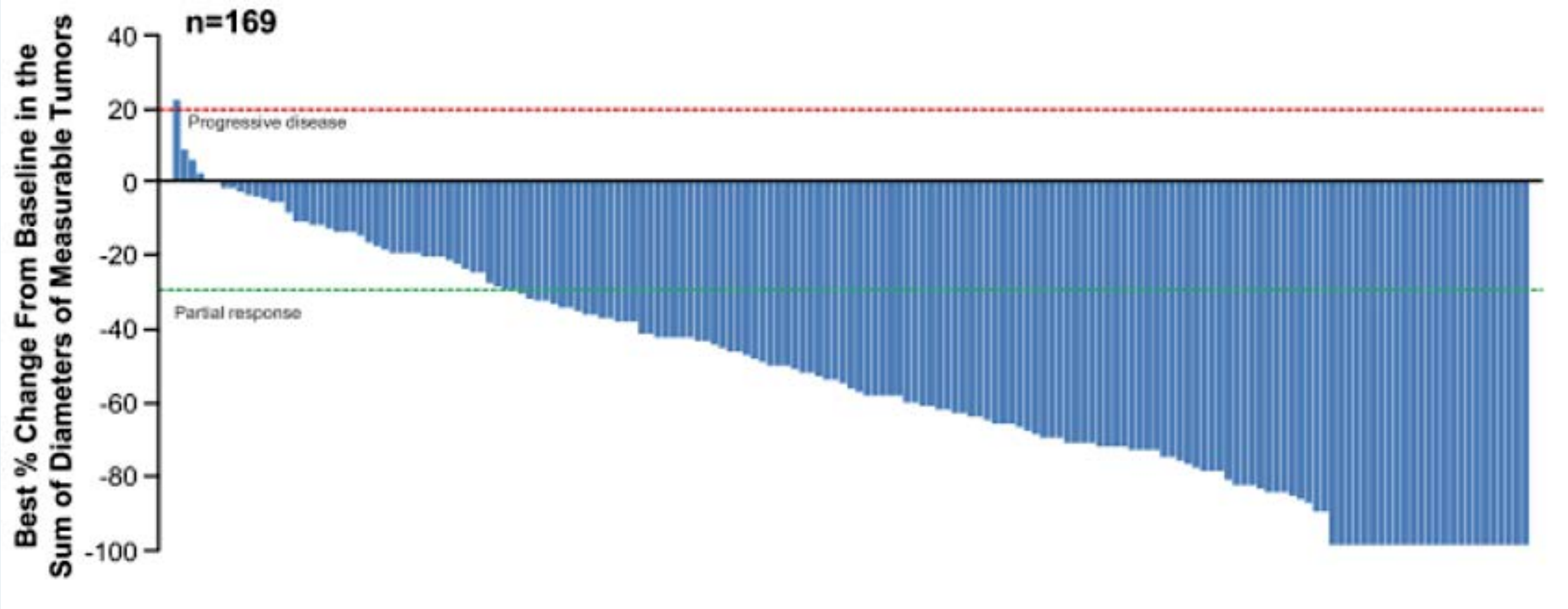
RTP RESEARCH TO PRACTICE

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 Percentage Change in Tumor Size from Baseline



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

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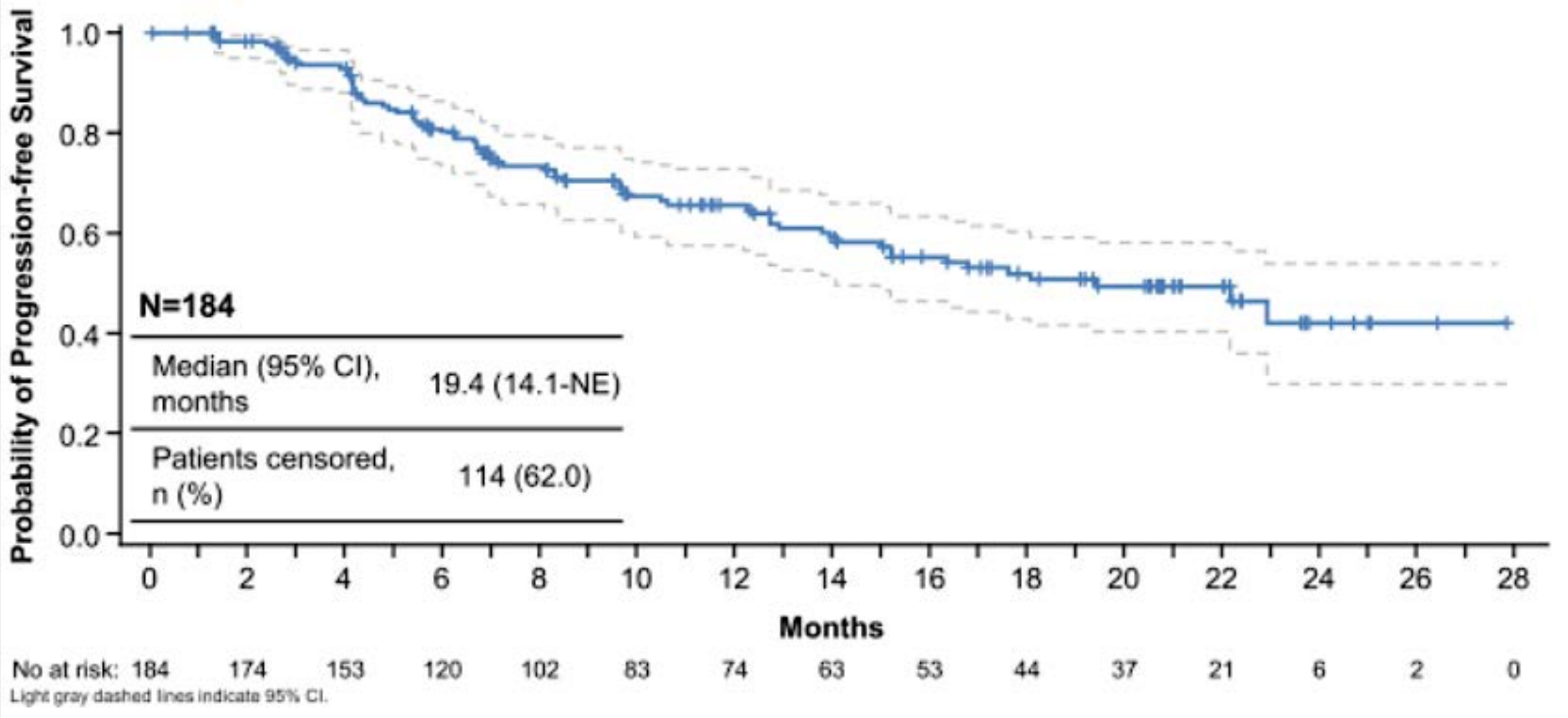
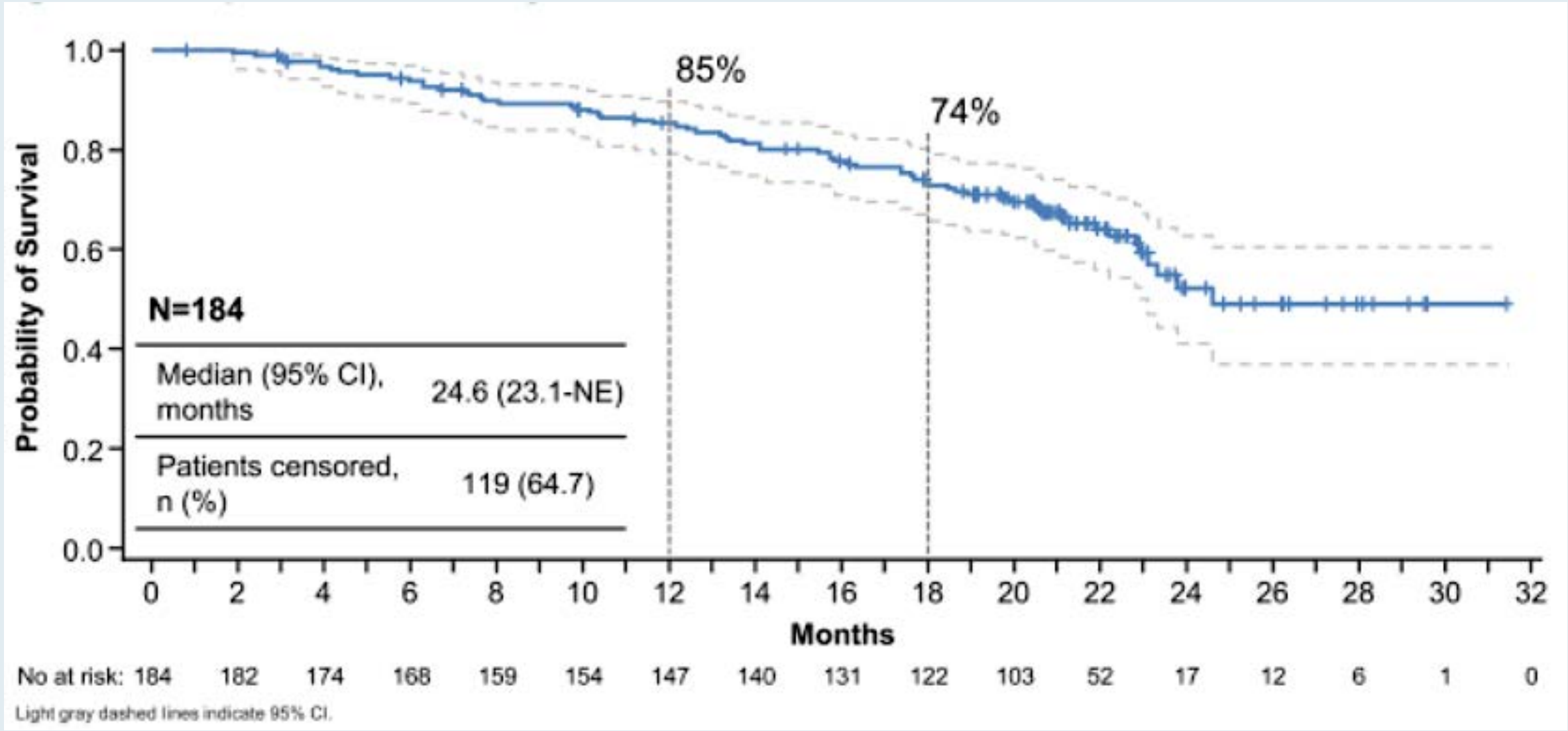
DESTINY-Breast01: Progression-Free Survival



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.

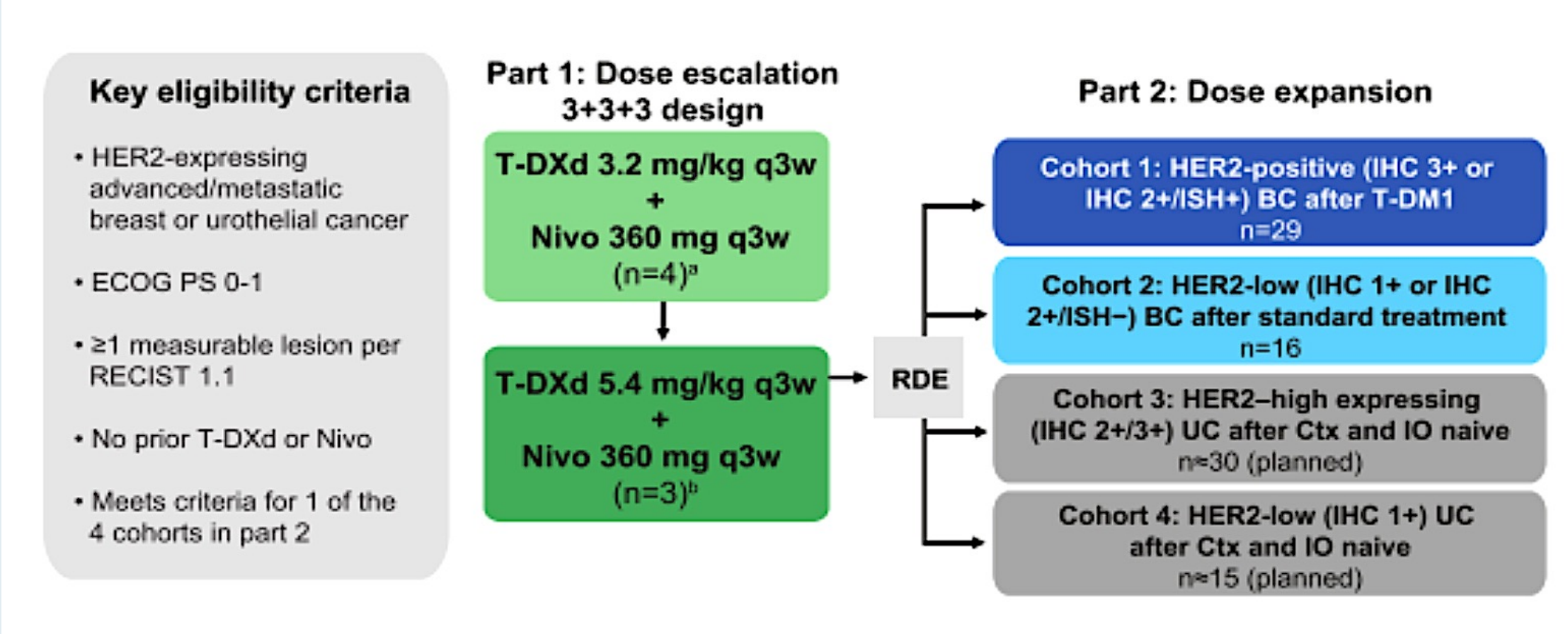
RTP RESEARCH TO PRACTICE

Trastuzumab Deruxtecan (T-DXd; DS-8201) with Nivolumab in Patients with HER2-Expressing, Advanced Breast Cancer: A 2-Part, Phase 1b, Multicenter, Open-Label Study

Hamilton E et al.

SABCS 2020;Abstract PD3-07.

T-DXd with Nivolumab: Trial Schema



Hamilton E et al. SABCS 2020;Abstract PD3-07.

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

RTP
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TO PRACTICE

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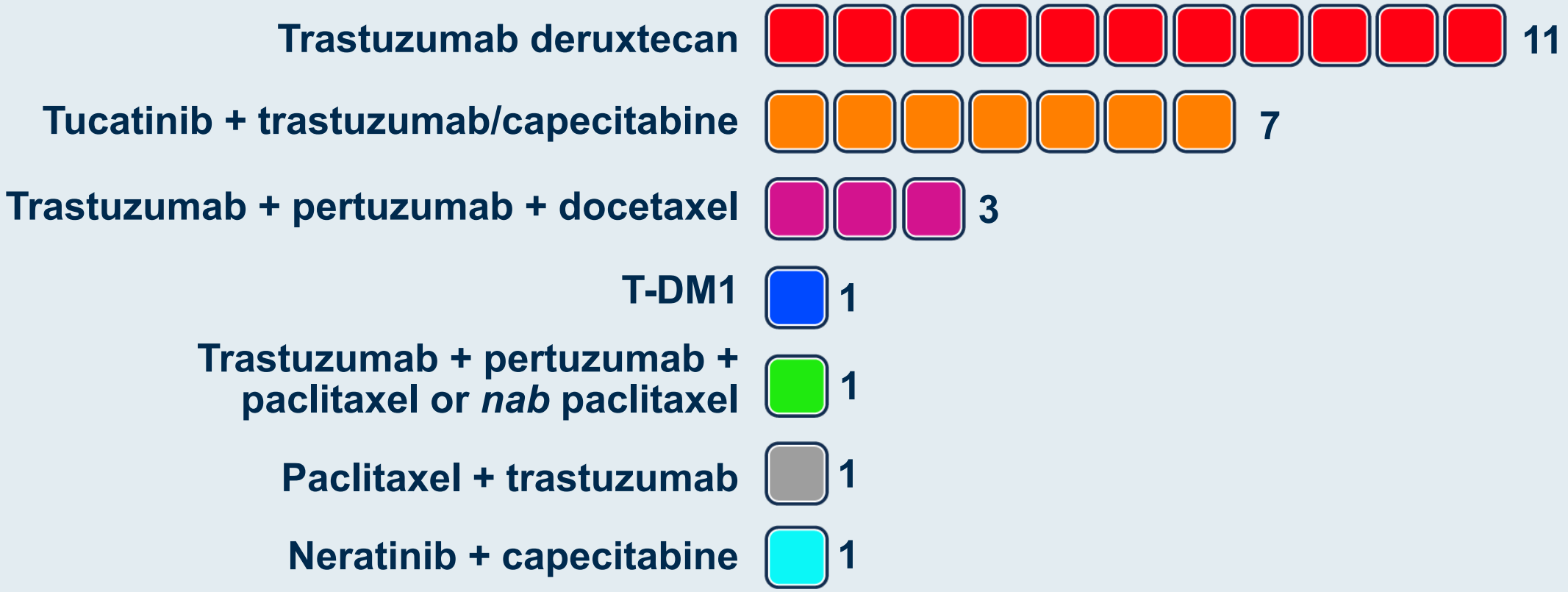
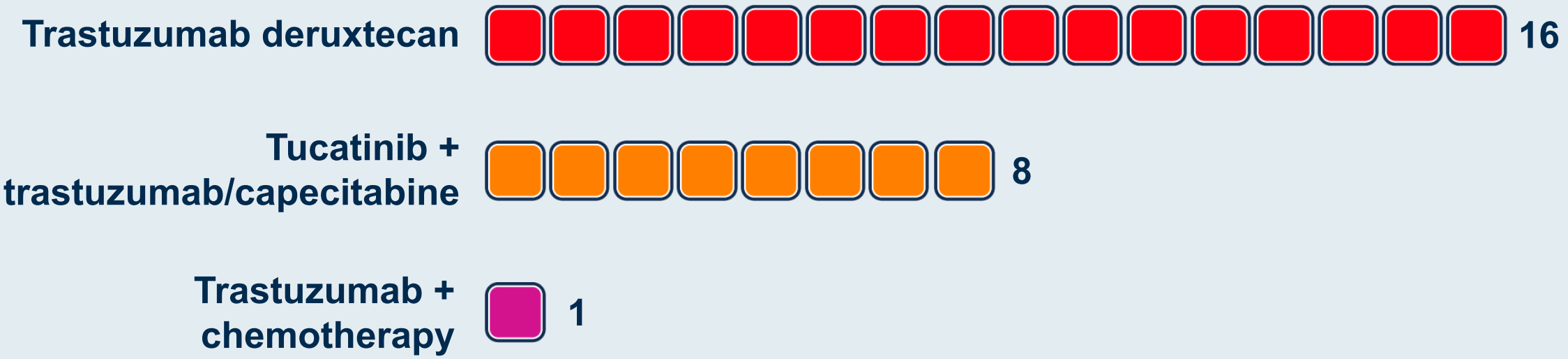


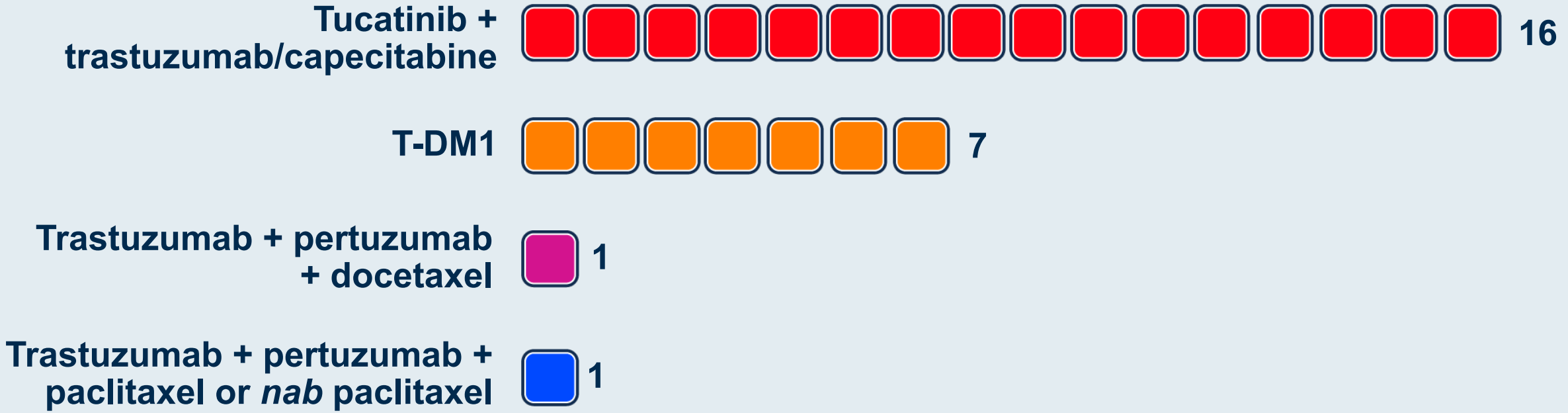
Survey of 25 Breast Cancer Clinical Investigators

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



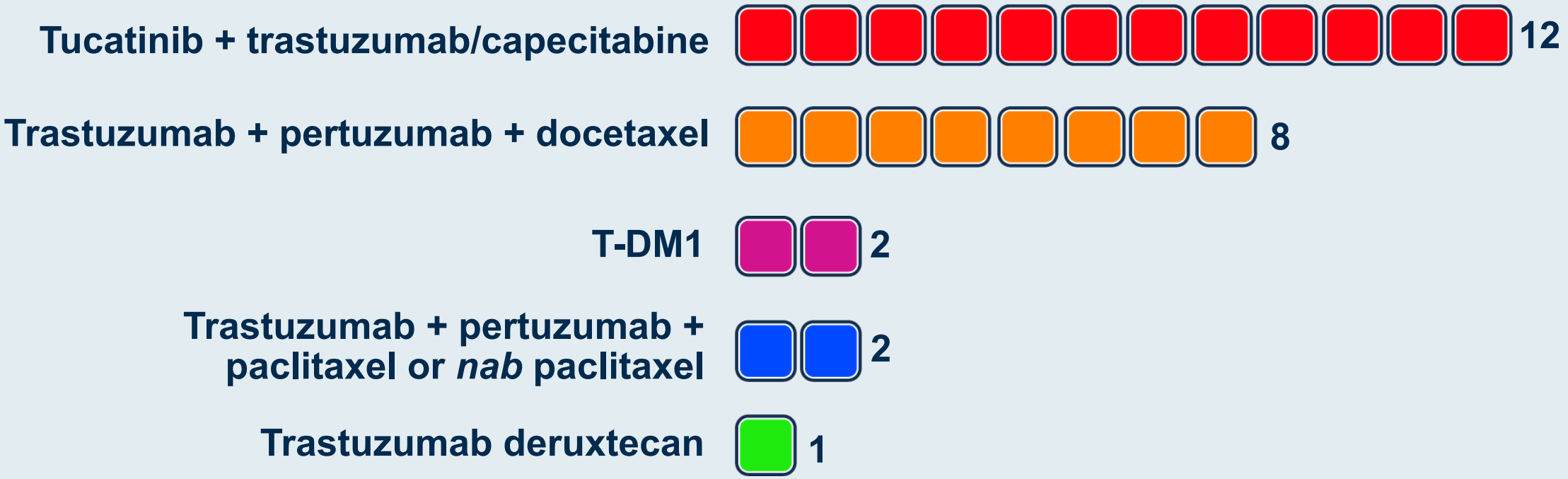
Survey of 25 Breast Cancer Clinical Investigators

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



Survey of 25 Breast Cancer Clinical Investigators

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?



Survey of 25 Breast Cancer Clinical Investigators

Data + Perspectives: Investigators Discuss the Effects of Emerging Research on the Care of Patients with Acute Myeloid Leukemia

Wednesday, March 10, 2021
7:00 PM – 8:00 PM ET

Faculty

Alexander Perl, MD
Eunice S Wang, MD

Moderator

Neil Love, MD

RTP RESEARCH TO PRACTICE

Thank you for joining us!

CME credit information will be emailed to each participant within 3 business days.

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