Meet The Professor

Optimizing the Management of ER-Positive and Triple-Negative Breast Cancer

Tuesday, March 7, 2023
5:00 PM – 6:00 PM ET

Faculty

Sara M Tolaney, MD, MPH

Moderator

Neil Love, MD

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Commercial Support

This activity is supported by educational grants from AstraZeneca Pharmaceuticals LP, Exact Sciences Corporation, Sanofi, and TerSera Therapeutics LLC.

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 companies: AbbVie Inc, Adaptive Biotechnologies Corporation, ADC Therapeutics, Agios Pharmaceuticals Inc, Alexion Pharmaceuticals, Amgen Inc, Array BioPharma Inc, a subsidiary of Pfizer Inc, Astellas, AstraZeneca Pharmaceuticals LP, Aveo Pharmaceuticals, Bayer HealthCare Pharmaceuticals, BeiGene Ltd, BeyondSpring Pharmaceuticals Inc, Blueprint Medicines, Boehringer Ingelheim Pharmaceuticals Inc, Bristol-Myers Squibb Company, Celgene Corporation, Clovis Oncology, Coherus BioSciences, CTI BioPharma Corp, Daiichi Sankyo Inc, Eisai Inc, Elevation Oncology Inc, EMD Serono Inc, Epizyme Inc, Exact Sciences Corporation, Exelixis Inc, Five Prime Therapeutics Inc, Foundation Medicine, G1 Therapeutics Inc, Genentech, a member of the Roche Group, Genmab US Inc, Gilead Sciences Inc, Grail Inc, GSK, Halozyme Inc, Helsinn Healthcare SA, ImmunoGen Inc, Incyte Corporation, Ipsen Biopharmaceuticals Inc, Janssen Biotech Inc, administered by Janssen Scientific Affairs LLC, Jazz Pharmaceuticals Inc, Karyopharm Therapeutics, Kite, A Gilead Company, Kronos Bio Inc, Lilly, Loxo Oncology Inc, a wholly owned subsidiary of Eli Lilly & Company, MEI Pharma Inc, Merck, Mersana Therapeutics Inc, Mirati Therapeutics Inc, Natera Inc, Novartis, Novartis Pharmaceuticals Corporation on behalf of Advanced Accelerator Applications, Novocure Inc, Oncopeptides, Pfizer Inc, Pharmacyclics LLC, an AbbVie Company, Puma Biotechnology Inc, Regeneron Pharmaceuticals Inc, Sanofi, Seagen Inc, Servier Pharmaceuticals LLC, SpringWorks Therapeutics Inc, Sumitomo Dainippon Pharma Oncology Inc, Taiho Oncology Inc, Takeda Pharmaceuticals USA Inc, TerSera Therapeutics LLC, Tesaro, A GSK Company, TG Therapeutics Inc, Turning Point Therapeutics Inc, Verastem Inc, and Zymeworks Inc.

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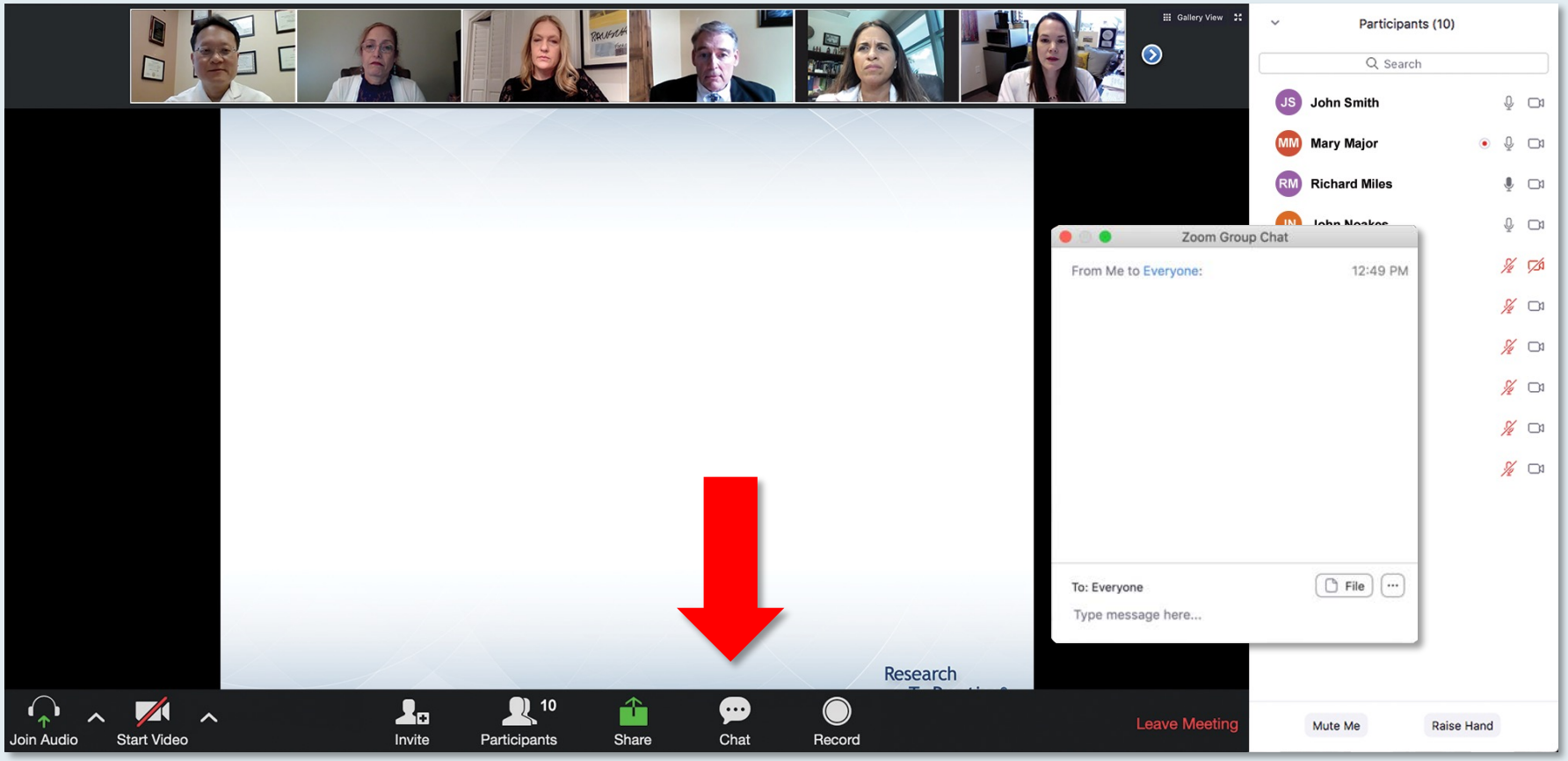
Planners, scientific staff and independent reviewers for Research To Practice have no relevant conflicts of interest to disclose.

Dr Tolaney — Disclosures

Consulting Agreements	4D Pharma PLC, Aadi Bioscience, ARC Therapeutics, AstraZeneca Pharmaceuticals LP, Bayer HealthCare Pharmaceuticals, BeyondSpring Pharmaceuticals Inc, Blueprint Medicines, Bristol-Myers Squibb Company, CytomX Therapeutics, Daiichi Sankyo Inc, Eisai Inc, Ellipses Pharma, Genentech, a member of the Roche Group, Gilead Sciences Inc, Incyte Corporation, Infinity Pharmaceuticals Inc, Lilly, Menarini Group, Merck, Myovant Sciences, Novartis, OncoSec Medical, OncXerna Therapeutics Inc, Pfizer Inc, Reveal Genomics, Sanofi, Seagen Inc, Stemline Therapeutics Inc, Umoja Biopharma, Zentalis Pharmaceuticals, Zetagen, Zymeworks Inc
Contracted Research	AstraZeneca Pharmaceuticals LP, Bristol-Myers Squibb Company, Cyclacel Pharmaceuticals Inc, Eisai Inc, Exelixis Inc, Genentech, a member of the Roche Group, Gilead Sciences Inc, Lilly, Merck, NanoString Technologies, Nektar, Novartis, Pfizer Inc, Sanofi, Seagen Inc

We Encourage Clinicians in Practice to Submit Questions



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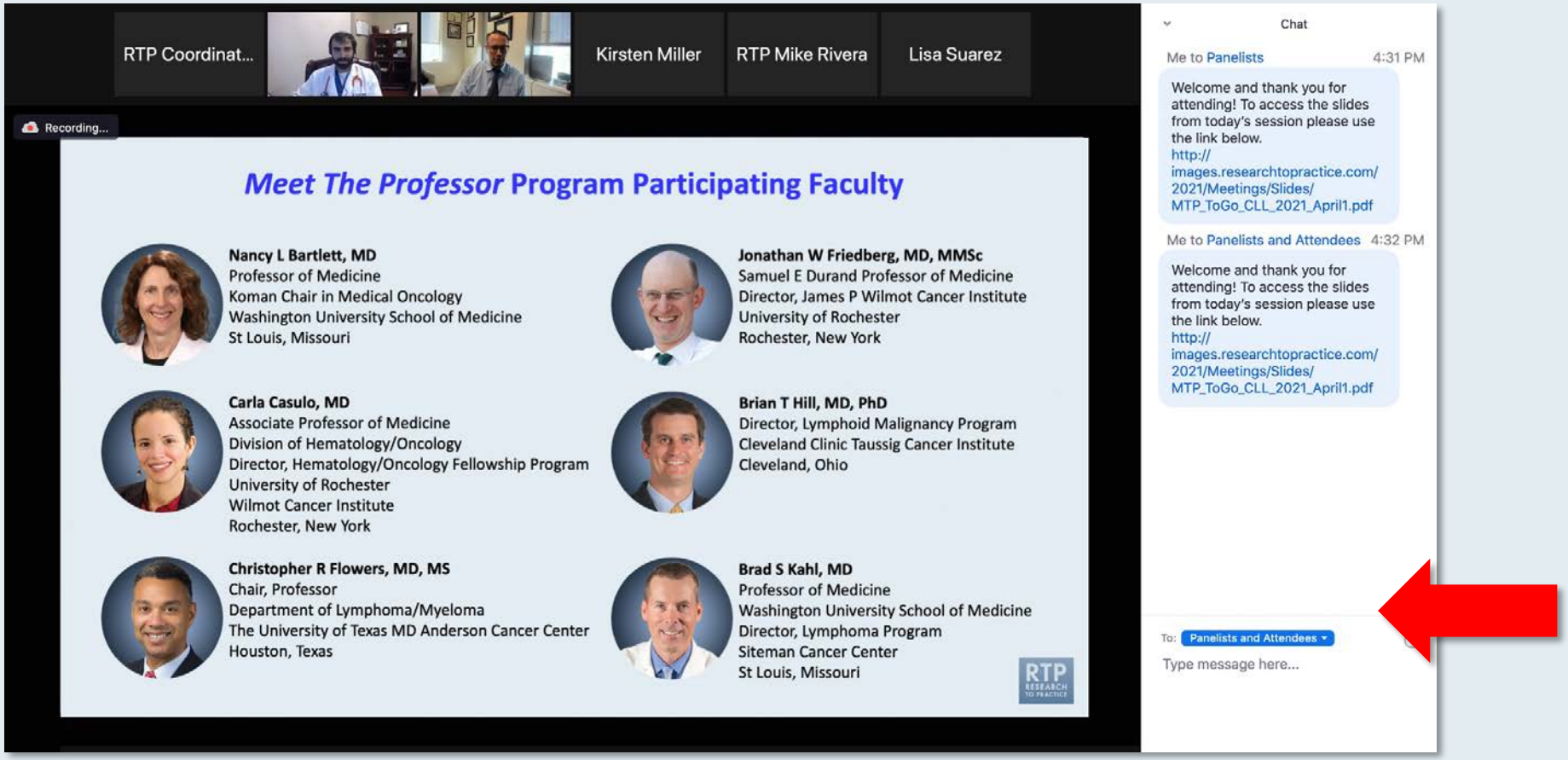

Drag the white line above the submission box up to create more space for your message.

RTP RESEARCH TO PRACTICE

Familiarizing Yourself with the Zoom Interface

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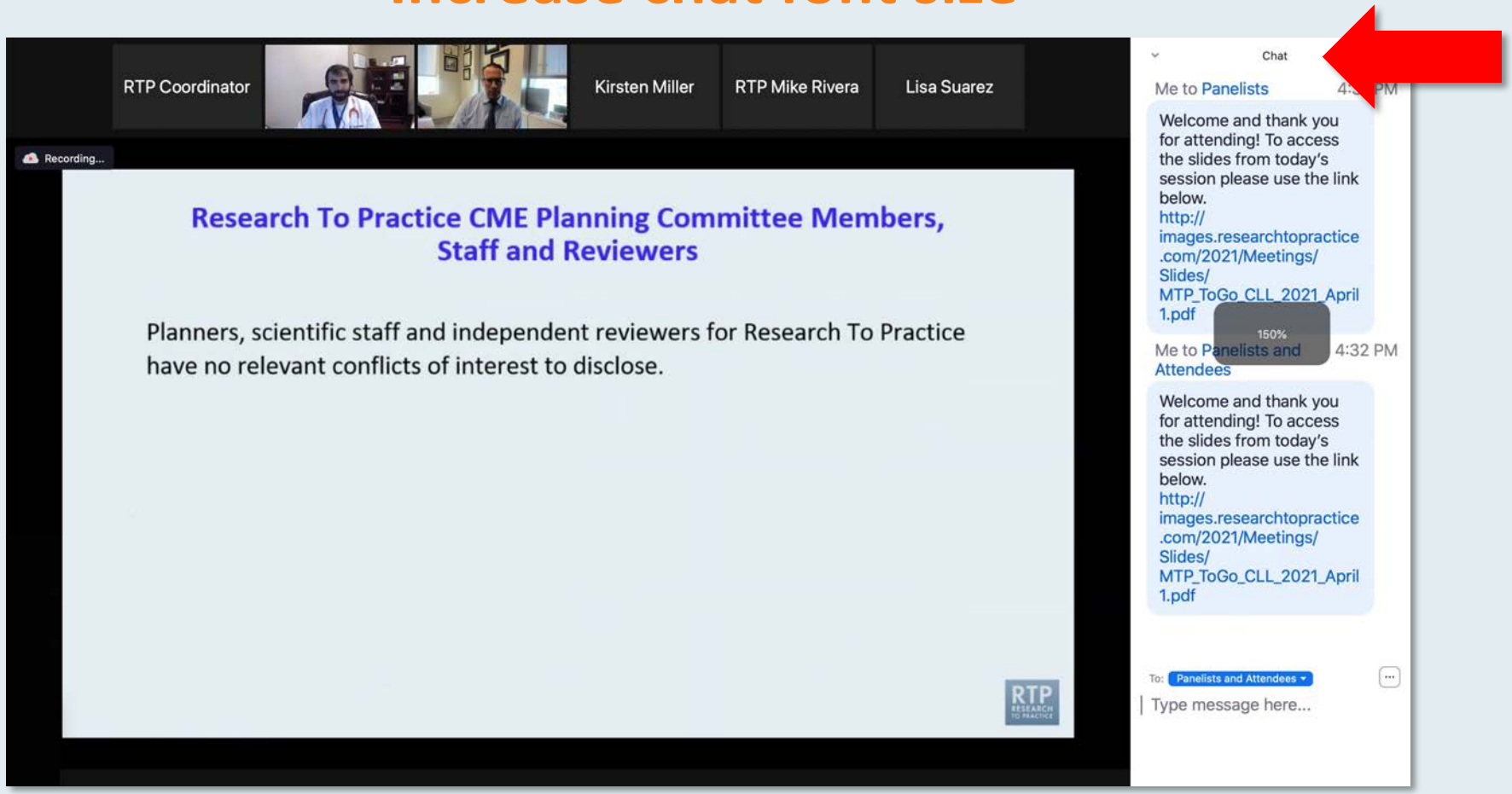

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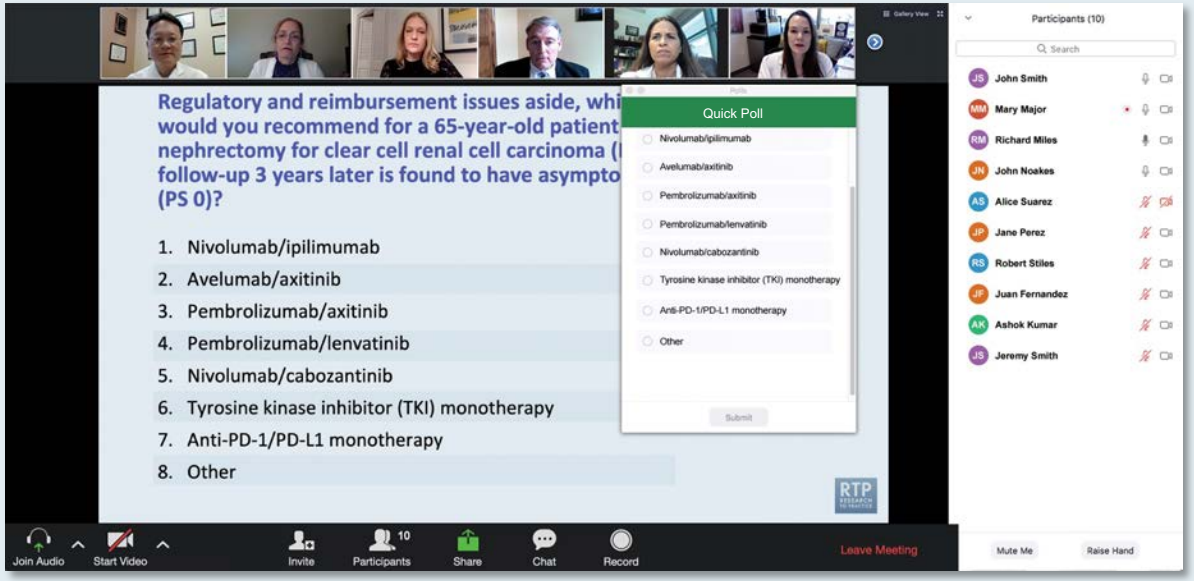
You may do this as many times as you need for readability.

Clinicians in the Audience, Please Complete the Pre- and Postmeeting Surveys



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ONCOLOGY TODAY

WITH DR NEIL LOVE

Special Edition — Management of ER-Positive Breast Cancer

DR ERICA MAYER
DANA-FARBER CANCER INSTITUTE

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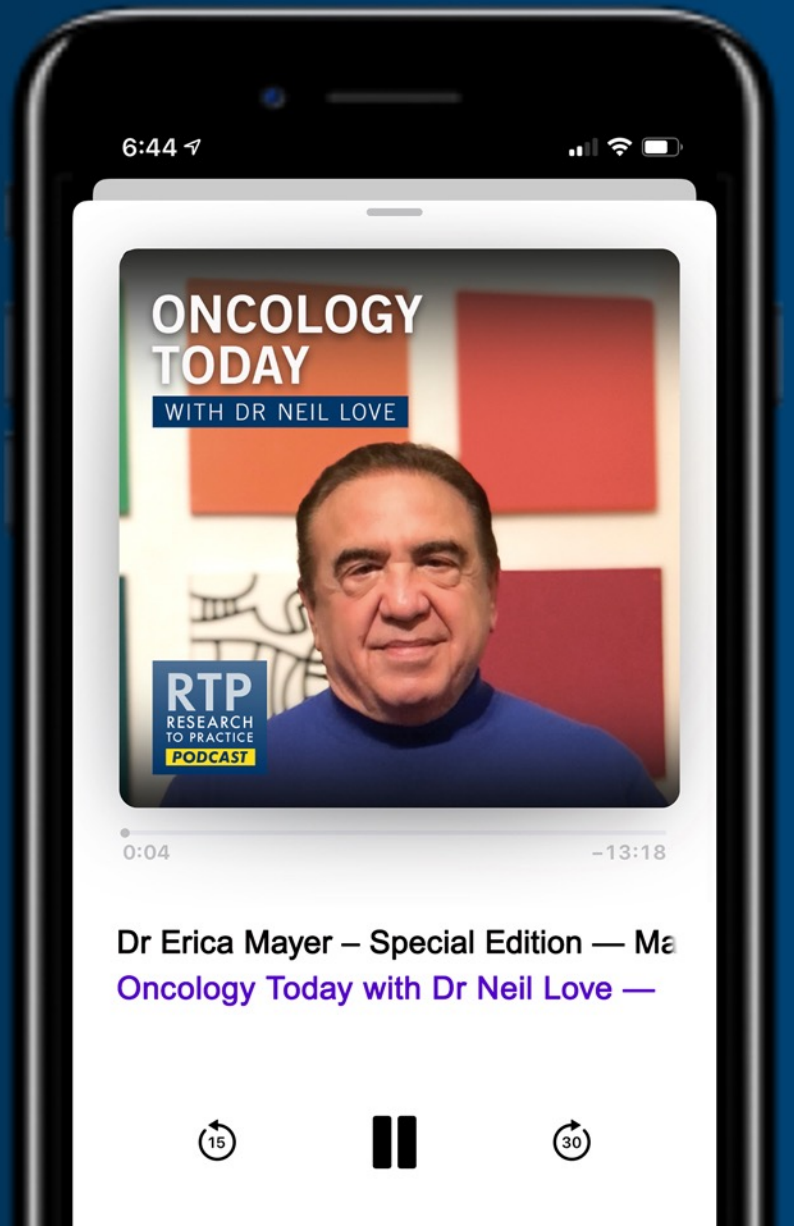

Cases from the Community: Investigators Discuss Available Research Guiding the Care of Patients with Gastroesophageal and Hepatobiliary Cancers — A 2023 Post-ASCO GI Webcast

A CME/MOC-Accredited Virtual Event

Wednesday, March 8, 2023

5:00 PM – 6:00 PM ET

Consulting Clinical Investigators

Lipika Goyal, MD, MPhil

Zev Wainberg, MD, MSc

Faculty Panel

Eric H Lee, MD, PhD

Neil Morganstein, MD

Swati Vishwanathan, MD

Moderator

Neil Love, MD

RTP RESEARCH TO PRACTICE

Meet The Professor
Optimizing the Management of Colorectal Cancer

Wednesday, March 22, 2023
5:00 PM – 6:00 PM ET

Faculty

John Strickler, MD

Moderator

Neil Love, MD

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Cases from the Community: Investigators Discuss Available Research Guiding the Care of Patients with Ovarian Cancer

Part 1 of a 2-Part CME Symposium Series Held in Conjunction with the 2023 Society of Gynecologic Oncology (SGO) Annual Meeting on Women's Cancer®

Sunday, March 26, 2023

11:45 AM – 1:15 PM ET

Faculty

Mansoor Raza Mirza, MD

Amit M Oza, MD

Richard T Penson, MD, MRCP

Moderator

Joyce F Liu, MD, MPH

RTP RESEARCH TO PRACTICE

Cases from the Community: Investigators Discuss Available Research Guiding the Care of Patients with Endometrial Cancer

Part 2 of a 2-Part CME Symposium Series Held in Conjunction with the 2023 Society of Gynecologic Oncology (SGO) Annual Meeting on Women's Cancer®

Monday, March 27, 2023

11:45 AM – 1:15 PM ET

Faculty

Robert L Coleman, MD

Matthew A Powell, MD

Brian M Slomovitz, MD

Moderator

Shannon N Westin, MD, MPH

RTP RESEARCH TO PRACTICE

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

A Multitumor CME/MOC-Accredited Live Webinar Series

Acute Myeloid Leukemia and Myelodysplastic Syndromes

Tuesday, April 4, 2023
5:00 PM – 6:00 PM ET

Faculty

Uma Borate, MD, MS

Andrew H Wei, MBBS, PhD

Moderator

Neil Love, MD

RTP Year in Review 2023

Meet The Professor

Optimizing the Management of ER-Positive and Triple-Negative Breast Cancer

Wednesday, April 12, 2023
5:00 PM – 6:00 PM ET

Faculty

Sara A Hurvitz, MD

Moderator

Neil Love, MD

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Thank you for joining us!

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

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Meet The Professor

Optimizing the Management of ER-Positive and Triple-Negative Breast Cancer

Sara M Tolaney, MD, MPH
Chief, Division of Breast Oncology
Associate Director, Susan F Smith Center
for Women's Cancers
Senior Physician
Dana-Farber Cancer Institute
Associate Professor of Medicine
Harvard Medical School
Boston, Massachusetts

Meet The Professor Program Participating Faculty

Sara A Hurvitz, MD
Professor of Medicine
Director, Breast Cancer Clinical Trials Program,
Division of Hematology-Oncology
David Geffen School of Medicine at UCLA
Medical Director, Clinical Research Unit
Jonsson Comprehensive Cancer Center
Santa Monica, California

Kathy D Miller, MD
Ballvé-Lantero Professor
Division of Hematology/Oncology
Associate Director for Clinical Research
The Indiana University Melvin and Bren Simon Cancer Center
Indianapolis, Indiana

Komal Jhaveri, MD
Associate Attending Physician
Breast Medicine Service and Early Drug Development Service
Section Head, Endocrine Therapy Research Program
Clinical Director, Early Drug Development Service
Department of Medicine
Memorial Sloan Kettering Cancer Center
Assistant Professor of Medicine
Weill Cornell College of Medicine
New York, New York

Ann Partridge, MD, MPH
Vice Chair of Medical Oncology
Director, Program for Young Women with Breast Cancer
Director, Adult Survivorship Program
Dana-Farber Cancer Institute
Professor of Medicine
Harvard Medical School
Boston, Massachusetts

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Meet The Professor Program Participating Faculty

Melinda Telli, MD
Associate Professor of Medicine
Stanford University School of Medicine
Director, Breast Cancer Program
Stanford Cancer Institute
Stanford, California

MODERATOR
Neil Love, MD
Research To Practice
Miami, Florida

Sara M Tolaney, MD, MPH
Chief, Division of Breast Oncology
Associate Director, Susan F Smith Center for Women's Cancers
Senior Physician
Dana-Farber Cancer Institute
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Harvard Medical School
Boston, Massachusetts

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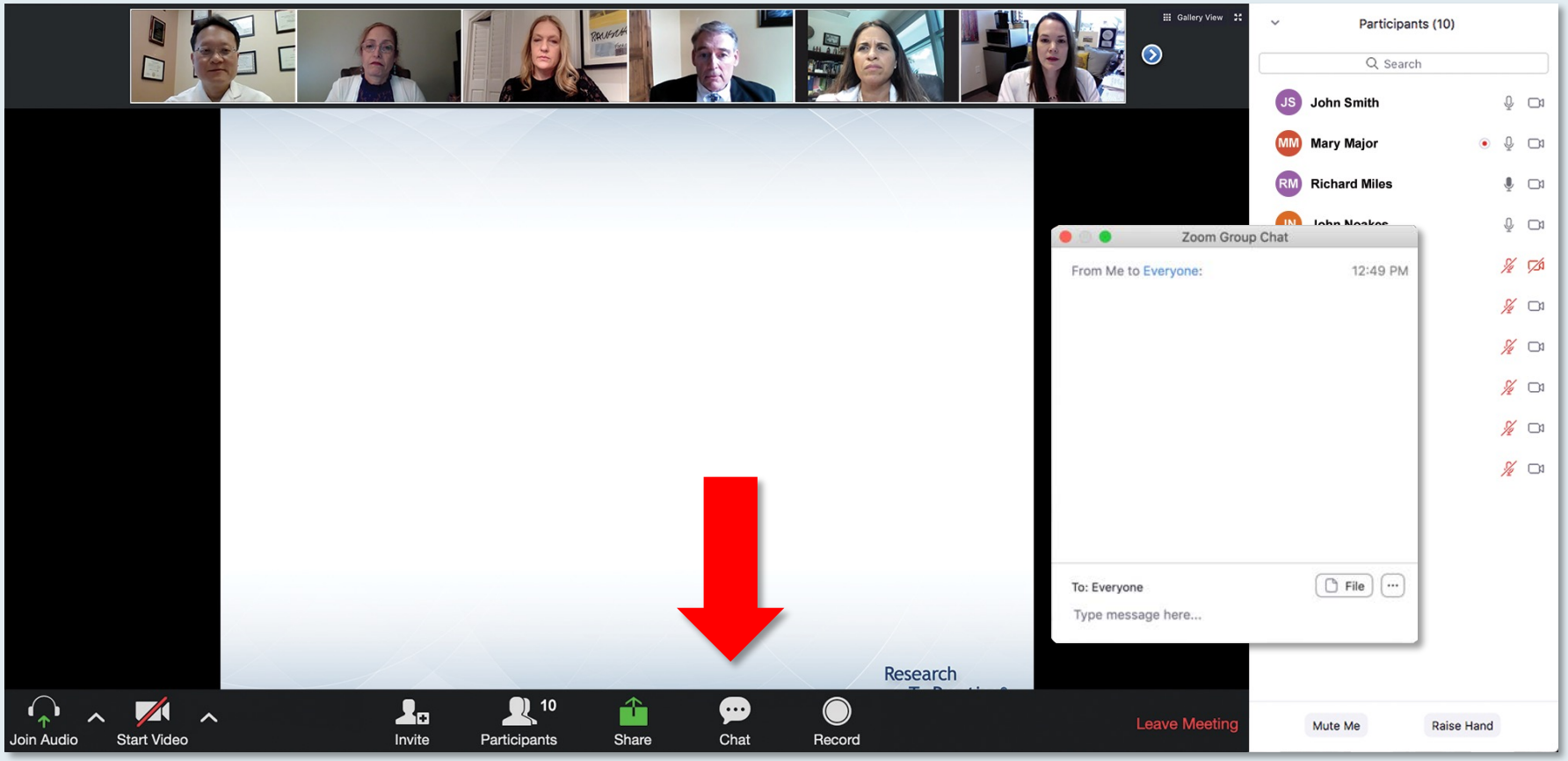
We Encourage Clinicians in Practice to Submit Questions



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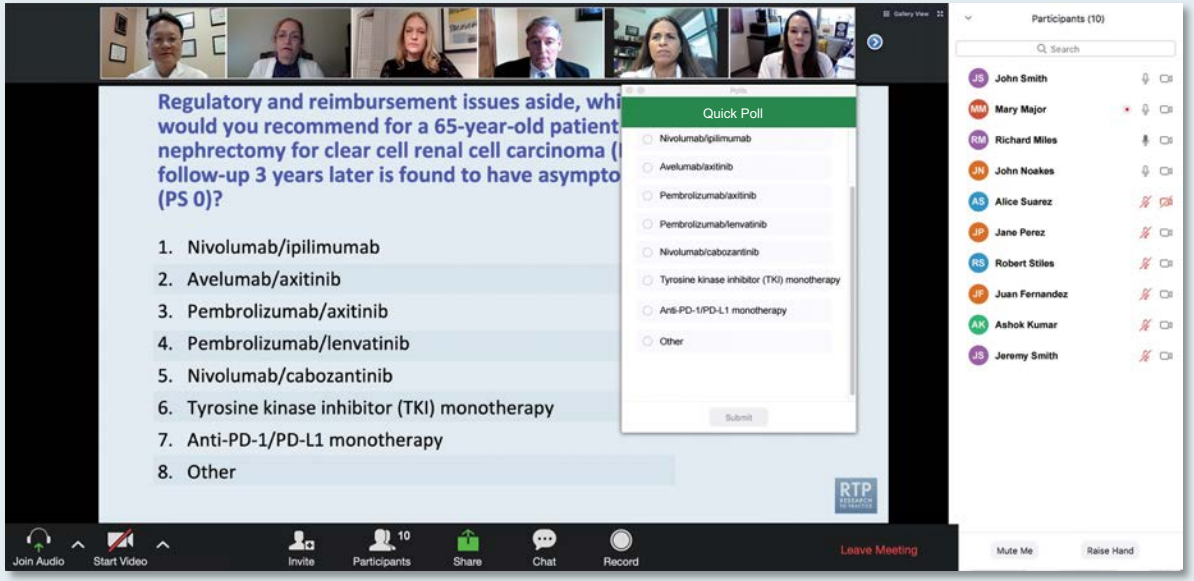

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DANA-FARBER CANCER INSTITUTE

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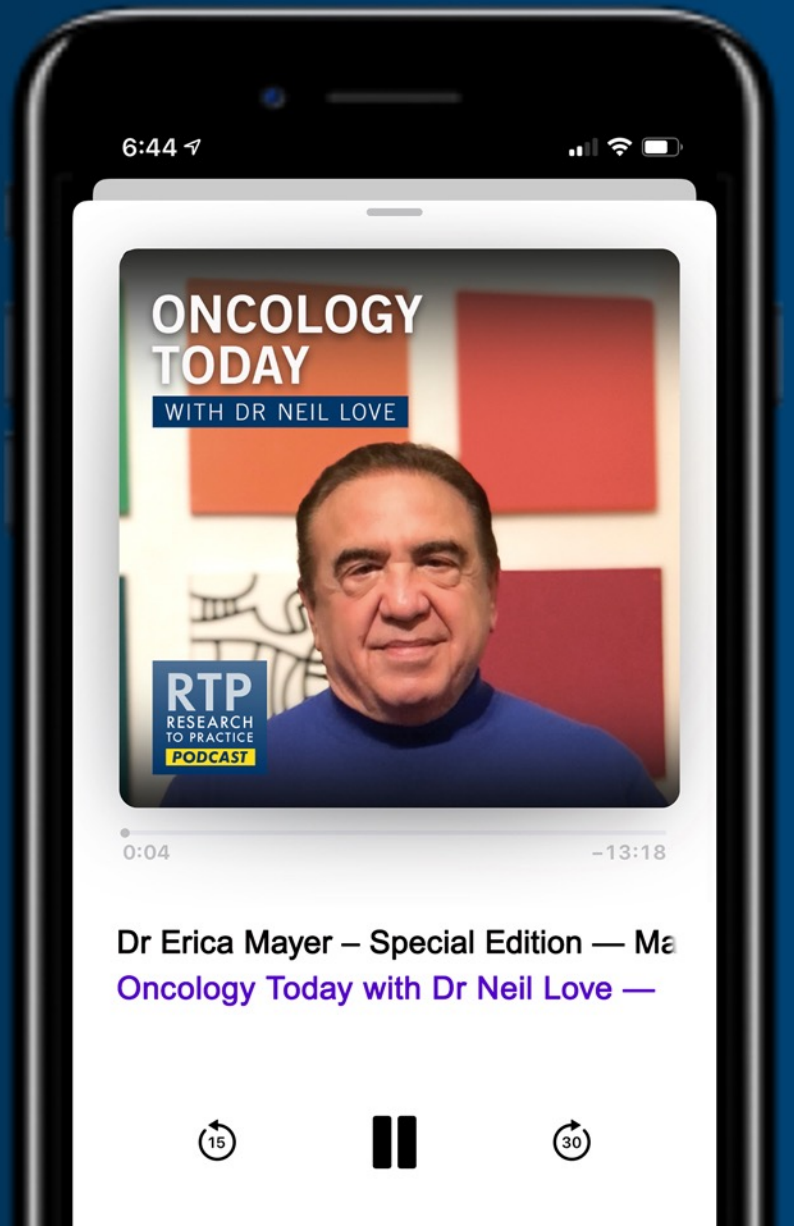

Meet The Professor

Optimizing the Management of ER-Positive and Triple-Negative Breast Cancer

Sara M Tolaney, MD, MPH
Chief, Division of Breast Oncology
Associate Director, Susan F Smith Center
for Women's Cancers
Senior Physician
Dana-Farber Cancer Institute
Associate Professor of Medicine
Harvard Medical School
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Dr Tolaney — Disclosures

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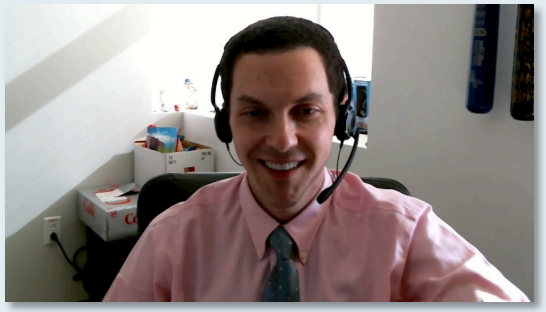
Laila Agrawal, MD
Norton Cancer Institute
Louisville, Kentucky

Nick Leasure, MD
Tower Health Reading
West Reading, Pennsylvania

Alan B Astrow, MD
NewYork-Presbyterian Brooklyn Methodist Hospital
Weill Cornell Medical College
Brooklyn, New York



Jeremy Lorber, MD
Cedars-Sinai Medical Center
Beverly Hills, California

Ranju Gupta, MD
Lehigh Valley Health Network
Bethlehem, Pennsylvania

Henna Malik, MD
Texas Oncology
Houston, Texas

Zanetta S Lamar, MD
Florida Cancer Specialists
Naples, Florida

Richard Zelkowitz, MD
Hartford HealthCare Cancer Institute
Bridgeport, Connecticut

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Meet The Professor with Dr Tolaney

Introduction: Male Breast Cancer

MODULE 1: Hormone Receptor-Positive Breast Cancer

MODULE 2: Triple-Negative Breast Cancer

MODULE 3: Appendix

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Meet The Professor with Dr Tolaney

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OXFORD

JNCI: Journal of the National Cancer Institute, 2023, 00(0), 1–8

Advance Access Publication Date: December 30, 2022

Article

Survival in male breast cancer over the past 3 decades

José P. Leone, MD,[1,*] Rachel A. Freedman, MD, MPH,[1] Julieta Leone, MD,[2] Sara M. Tolaney, MD, MPH,[1] Carlos T. Vallejo, MD,[2] Bernardo A. Leone, MD,[2,†] Eric P. Winer, MD,[1,3] Nancy U. Lin, MD,[1] Michael J. Hassett, MD, MPH[1]

Mortality Risks Over 20 Years in Men with Stage I-III Hormone Receptor-Positive Breast Cancer

Leone JP et al.
SABCS 2022;Abstract PD6-08.

Cancer 2022;128:3796-803.

Original Article

Efficacy of neoadjuvant chemotherapy in male breast cancer compared with female breast cancer

José Pablo Leone, MD [1]; Michael J. Hassett, MD[1]; Julieta Leone, MD[2]; Sara M. Tolaney, MD, MPH[1]; Carlos T. Vallejo, MD[2]; Bernardo A. Leone, MD; Eric P. Winer, MD[1]; and Nancy U. Lin, MD[1]

editorials

Can a Late Interception by Circulating Tumor DNA Deliver a Win in Estrogen Receptor–Positive Early Breast Cancer?

David W. Cescon, MD, PhD[1]; Kevin Kalinsky, MD[2]; and Angela M. DeMichele, MD, MSCE[3]

J Clin Oncol 2022 Aug 1;40(22):2395-2397

rapid communications

Circulating Tumor DNA and Late Recurrence in High-Risk Hormone Receptor–Positive, Human Epidermal Growth Factor Receptor 2–Negative Breast Cancer

Marla Lipsyc-Sharf, MD[1,2]; Elza C. de Bruin, PhD[3]; Katheryn Santos, BS[1]; Robert McEwen, PhD[3]; Daniel Stetson, MS[4]; Ashka Patel, BS[1]; Gregory J. Kirkner, MPH[1]; Melissa E. Hughes, MSc[1]; Sara M. Tolaney, MD, MPH[1,2]; Ann H. Partridge, MD, MPH[1,2]; Ian E. Krop, MD, PhD[1,2,5]; Charlene Knape, MT[6]; Ute Feger, PhD[6]; Giovanni Marsico, PhD[7]; Karen Howarth, PhD[7]; Eric P. Winer, MD[1,2,5]; Nancy U. Lin, MD[1,2]; and Heather A. Parsons, MD, MPH[1,2]

J Clin Oncol 2022;40:2408-19

JC JOURNAL CLUB RTP RESEARCH TO PRACTICE

Meet The Professor with Dr Tolaney

Introduction: Male Breast Cancer

MODULE 1: Hormone Receptor-Positive Breast Cancer – Part 1

- Dr Astrow: 32-year-old premenopausal woman with T1cN0 ER/PR-positive, HER2-negative, gBRCA2-mutant IDC with an Onco*type* DX® Recurrence Score® (RS) of 30 receives adjuvant chemotherapy followed by leuprolide/letrozole but wishes to discontinue treatment to attempt pregnancy
- Dr Gupta: 38-year-old woman with T2N0 ER/PR-positive, HER2-negative IDC; RS of 35; has severe menopause after adjuvant TC, TAH/BSO and letrozole
- Dr Lamar: 53-year-old postmenopausal woman with bilateral ER-positive, HER2-negative breast cancer; RS on the left is low and on the right is 30 but the tumor is 4 mm
- Dr Leasure: 42-year-old premenopausal woman with a 5-cm ER/PR-positive (100%), HER2-negative Grade I IDC

MODULE 2: Triple-Negative Breast Cancer

MODULE 3: Appendix

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Case Presentation: 32-year-old premenopausal woman with T1cN0 ER/PR-positive, HER2-negative, gBRCA2-mutant IDC with an Onco*type* DX Recurrence Score (RS) of 30 receives adjuvant chemotherapy followed by leuprolide/letrozole but wishes to discontinue treatment to attempt pregnancy

Dr Alan Astrow (Brooklyn, New York)

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Clinicopathological Characteristics, Treatment Patterns and Disease Outcomes of Germline BRCA1/2 Carriers with Early Stage HER2-Negative Breast Cancer and Potential Eligibility for Adjuvant Olaparib

Morganti S et al.

SABCS 2022;Abstract P2-01-02.

J Clin Oncol 2021 September 10;39(26):2959-61.

ASCO rapid recommendations

Adjuvant PARP Inhibitors in Patients With High-Risk Early-Stage HER2-Negative Breast Cancer and Germline *BRCA* Mutations: ASCO Hereditary Breast Cancer Guideline Rapid Recommendation Update

Nadine M. Tung, MD[1]; Dana Zakalik, MD[2]; and Mark R. Somerfield, PhD[3]; for the Hereditary Breast Cancer Guideline Expert Panel

ASCO Rapid Recommendations Updates highlight revisions to select ASCO guideline recommendations as a response to the emergence of new and practice-changing data. The rapid updates are supported by an evidence review and follow the guideline development processes outlined in the ASCO Guideline Methodology Manual. The goal of these articles is to disseminate updated recommendations, in a timely manner, to better inform health practitioners and the public on the best available cancer care options.

ASCO 2021 Adjuvant PARP Inhibitor Updated Recommendations

- **For patients with localized, HER2-negative breast cancer** with high risk of recurrence and germline BRCA1 or BRCA2 pathogenic or likely pathogenic variants, 1 year of adjuvant olaparib should be offered after completion of (neo)adjuvant chemotherapy and local treatment, including radiation therapy.
- **For those who underwent surgery first**, 1 year of adjuvant olaparib should be offered for patients with triple-negative breast cancer and tumor size >2 cm or any involved axillary nodes.
- **For those with hormone receptor (HR)-positive disease**, 1 year of adjuvant olaparib should be offered to those with at least 4 involved axillary lymph nodes.
- **For patients who received neoadjuvant chemotherapy**, 1 year of adjuvant olaparib should be offered to patients with triple-negative breast cancer and any residual cancer; **for patients with HR-positive disease**, 1 year of adjuvant olaparib should be offered to patients with residual disease and a clinical stage, pathologic stage, estrogen receptor and tumor grade score ≥3.

Tung NM et al. *J Clin Oncol* 2021;39(26):2959-61.

Regulatory and reimbursement issues aside, in general, what would you recommend as adjuvant therapy for a patient with TNBC, a germline BRCA mutation and a PD-L1 combined positive score (CPS) of 1 who has residual disease after neoadjuvant chemotherapy? Does level of PD-L1 expression have any bearing on your response?

	Adjuvant therapy	PD-L1 expression a factor?
 Dr Hurvitz	Olaparib for 1 year*	No
 Dr Jhaveri	Olaparib + pembrolizumab	No
 Dr Miller	Capecitabine + olaparib for 1 year*	No
 Dr Partridge	Olaparib for 1 year + or followed by pembrolizumab	No
 Dr Telli	Olaparib for 1 year*	No
 Dr Tolaney	Olaparib for 1 year*	No

*If patient received neoadjuvant pembrolizumab, I would complete pembrolizumab in combination with olaparib

Regulatory and reimbursement issues aside, have you attempted or would you attempt to access olaparib as part of adjuvant therapy for a patient with a germline PALB2 mutation and TNBC who has residual disease after neoadjuvant chemotherapy?

Case Presentation: 38-year-old woman with T2N0 ER/PR-positive, HER2-negative IDC; RS of 35; has severe menopausal symptoms after adjuvant TC, TAH/BSO and letrozole

Dr Ranju Gupta (Bethlehem, Pennsylvania)

RTP RESEARCH TO PRACTICE

Inside the Issue — Exploring the Current Role of Ovarian Suppression in the Management of Breast Cancer

Wednesday, February 8, 2023
5:00 PM – 6:00 PM ET

Faculty

Kathy D Miller, MD
Ann Partridge, MD, MPH

Moderator

Neil Love, MD

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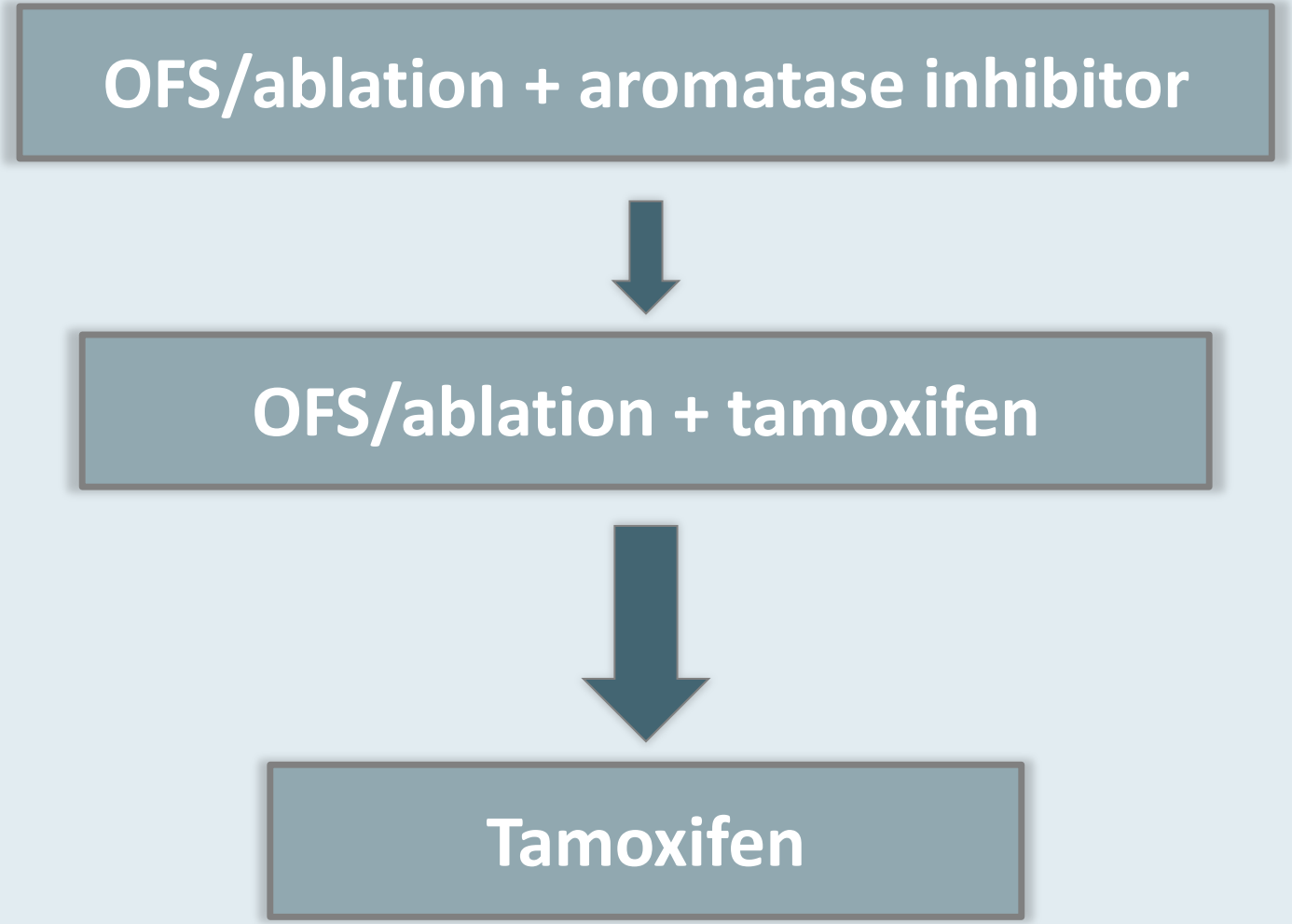
Hierarchy of Endocrine Therapy for Premenopausal Women



OFS = ovarian function suppression

RTP RESEARCH TO PRACTICE

clinical trial updates

Adjuvant Endocrine Therapy in Premenopausal Breast Cancer: 12-Year Results From SOFT

Prudence A. Francis, MD[1,2,3]; Gini F. Fleming, MD[4]; István Láng, MD[5,6]; Eva M. Ciruelos, MD, PhD[7]; Hervé R. Bonnefoi, MD[8]; Meritxell Bellet, MD[9]; Antonio Bernardo, MD[10]; Miguel A. Climent, MD[11]; Silvana Martino, DO[12]; Begoña Bermejo, MD, PhD[13,14]; Harold J. Burstein, MD, PhD[15]; Nancy E. Davidson, MD[16]; Charles E. Geyer Jr, MD[17]; Barbara A. Walley, MD[18]; James N. Ingle, MD[19]; Robert E. Coleman, MD, MBBS, FRCP[20,21,22]; Bettina Müller, MD[23]; Fanny Le Du, MD[24]; Sibylle Loibl, MD, PhD[25,26]; Eric P. Winer, MD[15,27,28]; Barbara Ruepp, PharmD[29]; Sherene Loi, MD, PhD[30]; Marco Colleoni, MD[31]; Alan S. Coates, MD[32]; Richard D. Gelber, PhD[33]; Aron Goldhirsch, MD[34]; and Meredith M. Regan, ScD[35]; for the SOFT Investigators and the International Breast Cancer Study Group (a division of ETOP IBCSG Partners Foundation)

J Clin Oncol 2023 March 1;41(7):1370-5.

clinical trial updates

Adjuvant Exemestane With Ovarian Suppression in Premenopausal Breast Cancer: Long-Term Follow-Up of the Combined TEXT and SOFT Trials

Olivia Pagani, MD[1,2]; Barbara A. Walley, MD[3]; Gini F. Fleming, MD[4]; Marco Colleoni, MD[5]; István Láng, MD, PhD[6,7]; Henry L. Gomez, MD, PhD[8,9]; Carlo Tondini, MD[10]; Harold J. Burstein, MD, PhD[11]; Matthew P. Goetz, MD[12] ; Eva M. Ciruelos, MD, PhD[13]; Vered Stearns, MD[14]; Hervé R. Bonnefoi, MD[15]; Silvana Martino, DO[16]; Charles E. Geyer Jr, MD[17]; Claudio Chini, MD[18]; Fabio Puglisi, MD, PhD[19]; Simon Spazzapan, MD[20]; Thomas Ruhstaller, MD[21]; Eric P. Winer, MD[22,11]; Barbara Ruepp, PharmD[23]; Sherene Loi, MD, PhD[24]; Alan S. Coates, MD[25]; Richard D. Gelber, PhD[26]; Aron Goldhirsch, MD[27,†]; Meredith M. Regan, ScD[28]; and Prudence A. Francis, MD[29,30]; for the SOFT and TEXT Investigators and the International Breast Cancer Study Group (a division of ETOP IBCSG Partners Foundation)

J Clin Oncol 2023 March 1;41(7):1376-82.

RTP RESEARCH TO PRACTICE

editorials

Back to the Beginning: The Role of Ovarian Suppression in Management of Hormone Sensitive Breast Cancer in Premenopausal Women

Roisin M. Connolly, MBBCh, MD[1] and Kathy D. Miller, MD[2]

J Clin Oncol 2023 March 1;41(7):1339-41.

RTP RESEARCH TO PRACTICE

Back to the Beginning: The Role of Ovarian Suppression

"Ovarian suppression with an aromatase inhibitor should become the preferred initial hormone therapy recommendation for all premenopausal women with high-risk (ie, grade 3, T2, and age , 35 years) ER-positive breast cancer. We favor a stepwise approach, first initiating and evaluating toxicity with ovarian suppression alone and then adding an aromatase inhibitor. Should toxicity be intolerable, reversion to tamoxifen alone, or with continued ovarian suppression remains an option and is certainly preferable to discontinuation of all antiestrogen therapies. Ovarian suppression should not be considered a mandate for patients with lower risk disease where the long-term toxicities outweigh the benefits."

Connolly RM, Miller KD. *J Clin Oncol* 2023 March 1;41(7):1339-41.

RTP RESEARCH TO PRACTICE

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RTP RESEARCH TO PRACTICE

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RTP RESEARCH TO PRACTICE

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Connolly RM, Miller KD. *J Clin Oncol* 2023 March 1;41(7):1339-41.

RTP RESEARCH TO PRACTICE

HER2 and estrogen receptor status drive decisions regarding the use of neoadjuvant chemotherapy

Neil Love, MD[1], Kimberly L Blackwell, MD[2], Eleftherios P Mamounas, MD, MPH[3], Jonathan Moss, BS[1], Kathryn Ziel, PhD[1]

[1] Research To Practice, Miami, FL; [2] Duke Cancer Institute, Durham, NC; [3] UF Cancer Center at Orlando Health, Orlando, FL

BACKGROUND:

Neoadjuvant chemotherapy (NC) is widely utilized to facilitate breast-conserving surgery and is considered equivalent to adjuvant chemotherapy with regard to recurrence-free and overall survival. However, controversy exists about specific indications for NC and its effects on other outcomes, particularly related to surgery in the breast and axilla. Limited data are available about the NC recommendations of breast cancer clinical investigators (CI).

METHODS:

In May 2015, a 139-item survey was sent to 96 US-based surgical (S) and medical oncology (MO) CI from a proprietary database to assess their practice patterns. A modest honorarium was offered.

RESULTS:

The assessment was completed by 60 CI (28 S and 32 MO; 64% of those sent the survey). Most (87%) recommend NC to patients with estrogen receptor-negative/HER2-negative (ER-/HER2-) and HER2-positive (HER2+) tumors larger than 2 cm or with biopsy-proven axillary node involvement.

For such patients with HER2+ tumors, MO routinely (96%) use pertuzumab (P) with trastuzumab (T) combined with NC — either docetaxel/carboplatin (56%), a taxane and doxorubicin (25%), paclitaxel (14%) or docetaxel (4%). For patients with these higher-risk HER2+ tumors not receiving NC, 52% of MO use P in the adjuvant setting, either during chemotherapy or during chemotherapy and continuing for a year.

There was more heterogeneity and less use of NC in patients with ER-positive (ER+)/HER2- tumors, and 47% of MO will use genomic profiling (generally the 21-gene Recurrence Score®) to facilitate this decision in select situations. Globally, for the 36 defined scenarios that were evaluated, recommendations of S and MO were similar, although S were somewhat more likely to recommend NC (70%) than MO (63%).

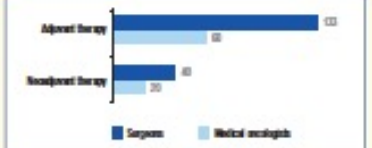
S typically employ post-NC sentinel node biopsy (SNB; 87%), even for patients with initial axillary node involvement, and only proceed to axillary dissection if the SNB is positive.

CONCLUSIONS:

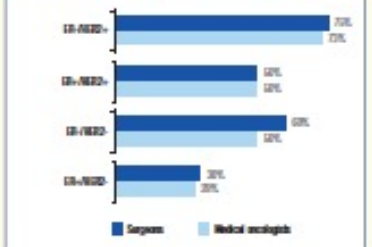
- S and MO consider ER and HER2 (as well as tumor size and axillary node status) essential factors in NC decisions and generally recommend NC to patients with HER2+ or ER-/HER2- tumors larger than 2 cm or with axillary node involvement.
- Two years after P (in combination with NC/T) became the first agent approved in the neoadjuvant setting, it is now commonly used in both adjuvant and neoadjuvant treatment scenarios.
- The approach to ER+/HER2- tumors is different than the algorithms used for HER2+ and ER-/HER2- disease, with much less use of NC. A substantial fraction of CI will use genomic profiling to assist in decision-making for some patients.
- Although clinical research evidence has not demonstrated a long-term advantage with neoadjuvant versus adjuvant chemotherapy in terms of risk of recurrence or death, the fact that S generally use post-NC SNB to decide on axillary dissection suggests that one advantage of this therapeutic approach is downstaging of the axilla.
- The tumor marker-based algorithms generated by this assessment will be useful in educating and assisting community-based physicians, and an online point-of-care tool based on this information is being evaluated.

This project was supported by an unrestricted educational grant to Research To Practice from Genomic Health Oncology. The authors did not receive direct reimbursement from this grant.

1 NUMBER OF PATIENTS IN YOUR PRACTICE IN THE PAST YEAR RECEIVING ADJUVANT OR NEOADJUVANT CHEMOTHERAPY



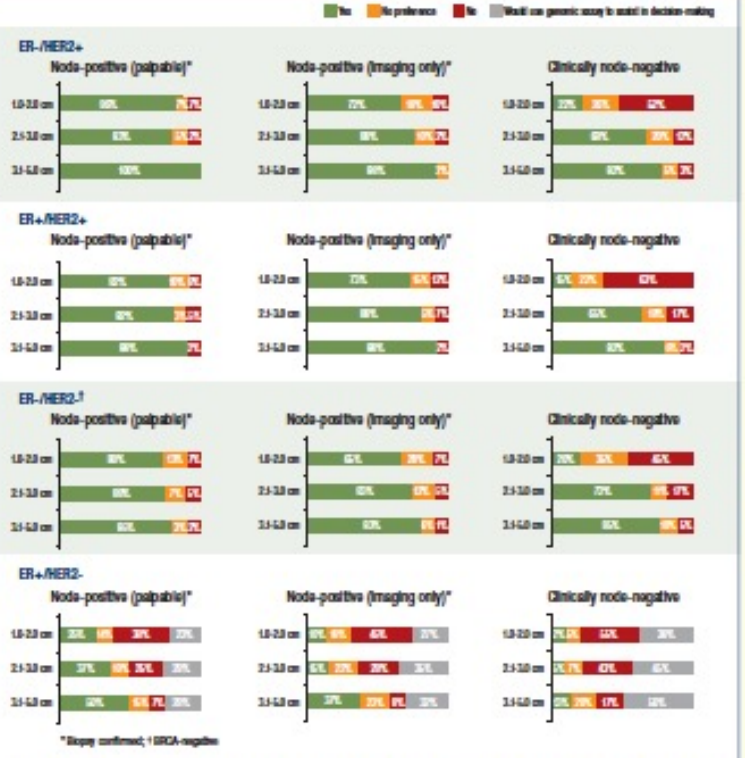
2 A PATIENT WITH LOCALIZED IDC DESIRES BREAST-CONSERVING SURGERY, BUT THE TUMOR IS TOO LARGE TO ACHIEVE A GOOD COSMETIC RESULT. WHAT IS THE APPROXIMATE CHANCE THAT NEOADJUVANT SYSTEMIC THERAPY WILL SHRINK THE TUMOR ENOUGH FOR SUCCESSFUL BREAST CONSERVATION?



3 THREE MOST COMMONLY RECOMMENDED NEOADJUVANT CHEMOTHERAPY REGIMENS (MEDICAL ONCOLOGISTS)

Tumor subtype	Chemotherapy regimen
ER-/HER2+ or ER+/HER2+	• Docetaxel/carboplatin/trastuzumab/pertuzumab • AC→ paclitaxel + trastuzumab/pertuzumab • Paclitaxel + trastuzumab + pertuzumab
ER-/HER2-	• Dose-dense AC followed (or preceded) by weekly paclitaxel • AC followed (or preceded) by paclitaxel or docetaxel • AC followed by carboplatin/paclitaxel
ER+/HER2-	• Dose-dense AC → paclitaxel (q2wk) • AC→ paclitaxel (q3wk) • TC or TAC

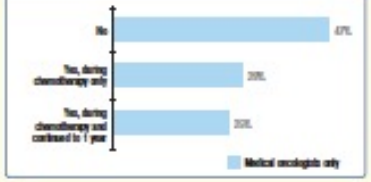
4 A HER2/ER-DRIVEN ALGORITHM FOR NEOADJUVANT CHEMOTHERAPY (COMBINED DATA FOR SURGEONS AND MEDICAL ONCOLOGISTS)



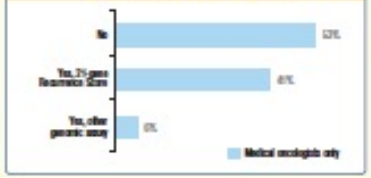
*Biopsy confirmed; †BRCA-negative

- Patients with ER-negative/HER2-negative or HER2-positive tumors greater than 2 cm or with biopsy-proven axillary node involvement generally receive neoadjuvant chemotherapy. There is heterogeneity in the clinical approach in this subset in the use of neoadjuvant chemotherapy in patients with tumors smaller than 2 cm with no clinical nodal involvement.
- Patients with ER-positive/HER2-negative breast cancer of any tumor size either don't generally receive neoadjuvant chemotherapy or have a 21-gene Recurrence Score assay performed to aid in the decision.

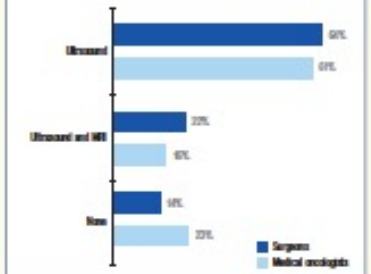
5 DO YOU USE PERTUZUMAB IN THE ADJUVANT SETTING OUTSIDE OF A CLINICAL TRIAL?



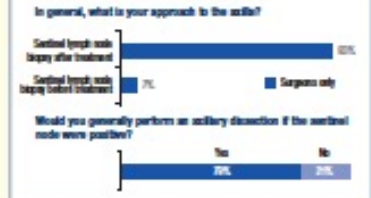
6 FOR PATIENTS WITH ER-POSITIVE/HER2-NEGATIVE DISEASE, DO YOU UTILIZE A GENOMIC ASSAY TO ASSIST IN YOUR DECISION-MAKING REGARDING NEOADJUVANT THERAPY?



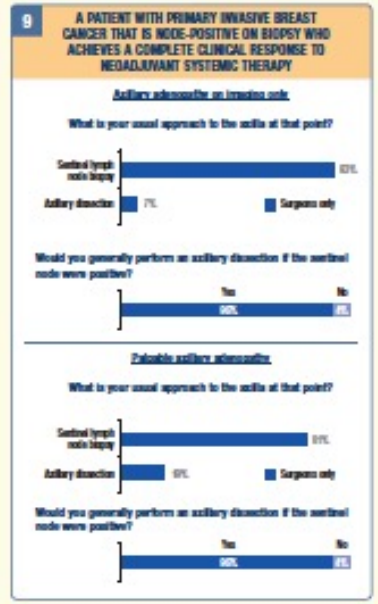
7 FOR A PATIENT BEING CONSIDERED FOR NEOADJUVANT SYSTEMIC THERAPY WITH A CLINICALLY NEGATIVE AXILLA, WHAT KIND OF IMAGING, IF ANY, SHOULD BE DONE ON THE AXILLA?



8 A PATIENT WITH INVASIVE PRIMARY BREAST CANCER AND CLINICALLY NEGATIVE AXILLA WHO IS GOING TO UNDERGO NEOADJUVANT SYSTEMIC THERAPY



9 A PATIENT WITH PRIMARY INVASIVE BREAST CANCER THAT IS NODE-POSITIVE ON BIOPSY WHO ACHIEVES A COMPLETE CLINICAL RESPONSE TO NEOADJUVANT SYSTEMIC THERAPY



Love N et al. SABCS 2015;Abstract P1-14-20.

Which adjuvant treatment would you most likely recommend for a 30-year-old premenopausal woman with 1-cm ER-positive, HER2-negative, node-negative localized breast cancer and the RS below?

	RS = 8 ET	RS = 20 ET
 Dr Hurvitz	Tamoxifen	OFS/ablation and tamoxifen
 Dr Jhaveri	Tamoxifen	Discuss OFS with tamoxifen/AI
 Dr Miller	OFS/ablation	OFS/ablation
 Dr Partridge	Tamoxifen	OFS/ablation and letrozole
 Dr Telli	Tamoxifen	OFS/ablation and exemestane
 Dr Tolaney	Tamoxifen	OFS/ablation and letrozole

ET = endocrine therapy; OFS = ovarian function suppression; AI = aromatase inhibitor

Which adjuvant treatment would you most likely recommend for a 30-year-old premenopausal woman with 1.5-cm ER-positive, HER2-negative, node-negative localized breast cancer and the RS below?

	RS = 8 ET	RS = 20 ET
 Dr Hurvitz	Tamoxifen	OFS/ablation and tamoxifen
 Dr Jhaveri	Tamoxifen	Discuss OFS with tamoxifen/AI
 Dr Miller	OFS/ablation	OFS/ablation
 Dr Partridge	Tamoxifen	OFS/ablation and letrozole
 Dr Telli	Tamoxifen	OFS/ablation and exemestane
 Dr Tolaney	Tamoxifen	OFS/ablation and exemestane

Which adjuvant treatment would you most likely recommend for a 30-year-old premenopausal woman with 2-cm ER-positive, HER2-negative, node-negative localized breast cancer and the RS below?

	RS = 8 ET	RS = 20 ET
 Dr Hurvitz	OFS/ablation and tamoxifen	OFS/ablation and tamoxifen
 Dr Jhaveri	Tamoxifen	Discuss OFS with tamoxifen/AI
 Dr Miller	OFS/ablation	OFS/ablation
 Dr Partridge	OFS/ablation and letrozole	OFS/ablation and letrozole
 Dr Telli	Tamoxifen	OFS/ablation and exemestane
 Dr Tolaney	Tamoxifen	OFS/ablation and letrozole

Which adjuvant treatment would you most likely recommend for a 30-year-old premenopausal woman with 2.5-cm ER-positive, HER2-negative, node-negative localized breast cancer and the RS below?

	RS = 8 ET	RS = 20 ET
 Dr Hurvitz	OFS/ablation and tamoxifen	OFS/ablation and tamoxifen
 Dr Jhaveri	Discuss OFS with tamoxifen/AI	OFS/ablation and AI
 Dr Miller	OFS/ablation	OFS/ablation
 Dr Partridge	OFS/ablation and letrozole	OFS/ablation and letrozole
 Dr Telli	Tamoxifen	OFS/ablation and exemestane
 Dr Tolaney	Tamoxifen	OFS/ablation and letrozole

Which adjuvant ET would you most likely recommend for a 30-year-old premenopausal woman with ER-positive, HER2-negative localized breast cancer with 1 positive node and the RS below?

	RS = 8 ET	RS = 20 ET
 Dr Hurvitz	OFS/ablation and anastrozole	OFS/ablation and anastrozole
 Dr Jhaveri	OFS/ablation + tamoxifen	OFS/ablation + anastrozole
 Dr Miller	OFS/ablation + tamoxifen or letrozole	OFS/ablation + tamoxifen or letrozole
 Dr Partridge	OFS/ablation + tamoxifen or + letrozole	OFS/ablation + letrozole
 Dr Telli	OFS/ablation + exemestane	OFS/ablation + exemestane
 Dr Tolaney	OFS/ablation + letrozole	OFS/ablation + letrozole

For premenopausal patients (age 40-50 years) with ER-positive, HER2-negative localized breast cancer who are about to receive adjuvant chemotherapy, do you generally offer the option of using OFS during chemotherapy in the following clinical scenarios?

	For fertility preservation	For ovarian function preservation
 Dr Hurvitz	Yes	Yes
 Dr Jhaveri	No*	Yes
 Dr Miller	Yes	No
 Dr Partridge	No	Yes
 Dr Telli	Yes, for select younger patients	No
 Dr Tolaney	No	Yes

*Fertility specialist discusses with patient

Case Presentation: 53-year-old postmenopausal woman with bilateral ER-positive, HER2-negative breast cancer; RS on the left is low and on the right is 30 but the tumor is 4 mm

Dr Zanetta Lamar (Naples, Florida)

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Case Presentation: 42-year-old premenopausal woman with a 5-cm ER/PR-positive (100%), HER2-negative Grade I IDC

Dr Nick Leasure (West Reading, Pennsylvania)

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TO PRACTICE

comments and controversies

Impact of RxPONDER and monarchE on the Surgical Management of the Axilla in Patients With Breast Cancer

Elizabeth A. Mittendorf, MD, PhD[1,2]; Tari A. King, MD[1,2]; and Sara M. Tolaney, MD, MPH[2,3]

J Clin Oncol 2022 October 10;40(29):3361-4.

JC JOURNAL CLUB RTP RESEARCH TO PRACTICE

Is there a role for the Oncotype DX Breast Recurrence Score Genomic Assay in Estrogen Receptor-low Positive Breast Cancer?

Julia Giordano[1,2], Monica McGrath[1,2], Beth Harrison[3], Olga Kantor[1,2,4], Harold Burstein[2,4,5], Halley Vora[1,2], Sara M. Tolaney[2,4,5], Tari A. King[1,2,4], Elizabeth A. Mittendorf[1,2,4]

Dana-Farber Cancer Institute | BWH BRIGHAM AND WOMEN'S HOSPITAL | HARVARD MEDICAL SCHOOL

DANA-FARBER/BRIGHAM AND WOMEN'S CANCER CENTER

ASCO 2022;Abstract 564.

JC JOURNAL CLUB | RTP RESEARCH TO PRACTICE

Indication Broadened for Abemaciclib in HR-Positive, HER2-Negative, High-Risk Localized Breast Cancer

Press Release: March 3, 2023

"The US Food and Drug Administration (FDA) approved an expanded indication for abemaciclib, in combination with endocrine therapy (ET), for the adjuvant treatment of adult patients with hormone receptor-positive (HR+), human epidermal growth factor receptor 2-negative (HER2-), node-positive, early breast cancer (EBC) at a high risk of recurrence. High risk patients eligible for abemaciclib can now be identified solely based on nodal status, tumor size, and tumor grade (4+ positive nodes, or 1-3 positive nodes and at least one of the following: tumors that are ≥5 cm or Grade 3). This expanded adjuvant indication removes the Ki-67 score requirement for patient selection.

This label expansion is supported by four-year data from the Phase 3 monarchE trial of adjuvant abemaciclib in combination with ET, which showed a deepened benefit in invasive disease-free survival (IDFS) beyond the two-year treatment course with adjuvant abemaciclib. The absolute difference in IDFS between treatment groups increased over time."

https://finance.yahoo.com/news/u-fda-broadens-indication-verzenio-195800378.html?guccounter=1

RTP RESEARCH TO PRACTICE

ASCO Rapid Recommendation Update for Abemaciclib for HR-Positive, HER2-Negative, Node-Positive Localized Breast Cancer

- Abemaciclib with endocrine therapy (ET; tamoxifen or an aromatase inhibitor) is FDA approved for adjuvant treatment of HR-positive, HER2-negative, node-positive localized breast cancer with high risk of recurrence **and a Ki-67 score ≥20%**.
- Based on analyses reported by Harbeck and colleagues, the panel recommends that abemaciclib for 2 years with ET for 5 years or longer may be offered to the broader intent-to-treat population of patients with resected HR-positive, HER2-negative, node-positive localized breast cancer at high risk of recurrence, defined as having >4 positive axillary lymph nodes **or** as having 1 to 3 positive axillary lymph nodes and 1 or more of the following features: histologic Grade III, tumor size >5 cm **or Ki-67 index >20%**.
- Despite similar hazard ratios in favor of abemaciclib regardless of Ki-67 status, relatively few low Ki-67 tumors were reported in monarchE. When discussing treatment options with patients, the potential benefits (improved IDFS) should be weighed against the potential harms (treatment toxicity, financial cost).

Harbeck N et al. *Ann Oncol* 2021;32(12):1571-81.
https://www.asco.org/practice-patients/guidelines/breast-cancer#/11081

European Journal of Cancer 173 (2022) 20–29

Available online at www.sciencedirect.com

ScienceDirect

journal homepage: www.ejcancer.com

Original Research

Estimating long-term mortality in women with hormone receptor-positive breast cancer: The 'ESTIMATE' tool☆,☆☆

José P. Leone [a,*], Noah Graham [a], Sara M. Tolaney [a], Bernardo A. Leone [b,2], Rachel A. Freedman [a], Michael J. Hassett [a], Julieta Leone [b], Carlos T. Vallejo [b], Eric P. Winer [a,1], Nancy U. Lin [a], Nabihah Tayob [a]

Which adjuvant endocrine therapy (ET) would you most likely recommend for a 30-year-old premenopausal woman with node-negative, ER-positive, HER2-negative localized breast cancer and the Recurrence Score® (RS) below? Would you recommend adjuvant chemotherapy?

	RS = 8		RS = 20	
	ET	Chemotherapy?	ET	Chemotherapy?
 Dr Hurvitz	OFS/ablation + tamoxifen, or Tam alone if small tumor	No	OFS/ablation + tamoxifen	Yes, but OFS/ablation as alternative
 Dr Jhaveri	Tamoxifen	No	OFS/ablation + tamoxifen or letrozole	Yes, but OFS/ablation as alternative
 Dr Miller	OFS/ablation + anastrozole	No	OFS/ablation + anastrozole	Yes, but OFS/ablation as alternative
 Dr Partridge	Tamoxifen +/- OFS/ablation	No	OFS/ablation + letrozole	Yes, but OFS/ablation as alternative
 Dr Telli	Tamoxifen	No	OFS/ablation + exemestane	No
 Dr Tolaney	Tamoxifen	No	OFS/ablation + letrozole	Yes, but OFS/ablation as alternative

OFS = ovarian function suppression

Which adjuvant ET would you most likely recommend for a 30-year-old premenopausal woman with ER-positive, HER2-negative localized breast cancer with 1 positive node and the RS below? Would you recommend adjuvant chemotherapy?

	RS = 8		RS = 20	
	ET	Chemotherapy?	ET	Chemotherapy?
 Dr Hurvitz	OFS/ablation + tamoxifen	Yes, but OFS/ablation as alternative	OFS/ablation + anastrozole	Yes
 Dr Jhaveri	OFS/ablation + tamoxifen or letrozole	Yes, but OFS/ablation as alternative	OFS/ablation + tamoxifen or letrozole	Yes
 Dr Miller	OFS/ablation + anastrozole	No	OFS/ablation + anastrozole	Yes, but OFS/ablation as alternative
 Dr Partridge	OFS/ablation + tamoxifen or + letrozole	Yes, but OFS/ablation as alternative	OFS/ablation + letrozole	Yes, but OFS/ablation as alternative
 Dr Telli	OFS/ablation + exemestane	Yes, but OFS/ablation as alternative	OFS/ablation + exemestane	Yes
 Dr Tolaney	OFS/ablation + letrozole	No	OFS/ablation + letrozole	Yes

OFS = ovarian function suppression

Meet The Professor with Dr Tolaney

Introduction: Male Breast Cancer

MODULE 1: Hormone Receptor-Positive Breast Cancer – Part 2

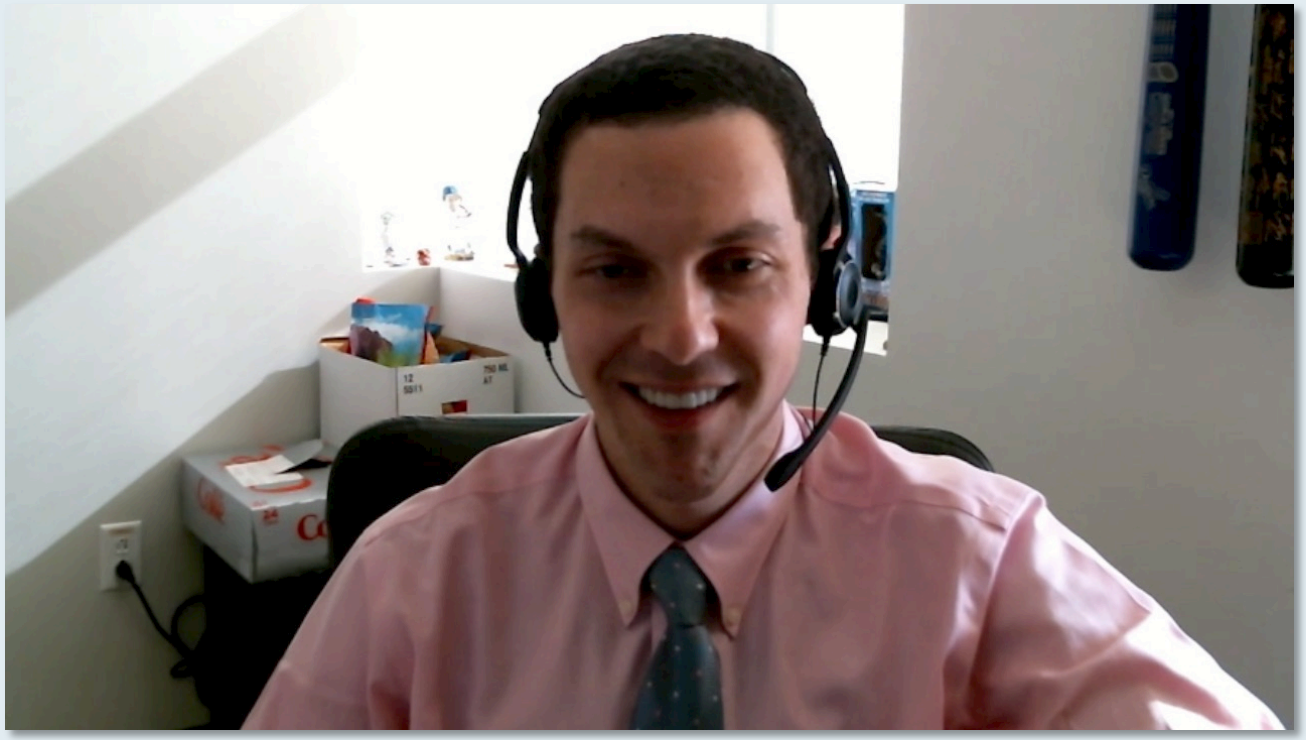
- Dr Lorber: 42-year-old premenopausal woman (gBRCA2) with Stage IIB ER/PR-positive, HER2-low (IHC 1+) IDC treated with adjuvant tamoxifen develops extensive mets and receives OFS, letrozole and palbociclib
- Dr Malik: 72-year-old woman with multiregimen-recurrent ER/PR-positive, HER2-low (IHC 1+) metastatic breast cancer receives T-DXd

MODULE 2: Triple-Negative Breast Cancer

MODULE 3: Appendix

RTP RESEARCH TO PRACTICE

Case Presentation: 42-year-old premenopausal woman (gBRCA2) with Stage IIB ER/PR-positive, HER2-low (IHC1+) IDC treated with adjuvant tamoxifen develops extensive mets and receives OFS, letrozole and palbociclib



Dr Jeremy Lorber (Beverly Hills, California)

RTP RESEARCH TO PRACTICE

Breast Cancer Research and Treatment (2022) 192:303–311

CLINICAL TRIAL

Factors leading to alpelisib discontinuation in patients with hormone receptor positive, human epidermal growth factor receptor-2 negative breast cancer

Yee-Ming M. Cheung[1,2] · Grace E. Cromwell[1] · Sara M. Tolaney[3] · Le Min[1] · Marie E. McDonnell[1]

Alpelisib Treatment Details

Alpelisib therapy	$n=62$ *n* (%)
Median exposure to alpelisib (days, IQR)	97 (29–189)
Dose reduction	28 (45)
Median dose of alpelisib (mg, IQR)	250 (250–300)
Permanent cessation of alpelisib	
Yes	53 (85.5)
No	7 (14.5)
Reason for cessation	
Progression	26 (42)
Adverse effect other than hyperglycemia	17 (27.4)
Rash	9 (52.9)
Gastrointestinal (diarrhea, decreased appetite and abdominal discomfort)	7 (41.2)
Anaphylaxis	1 (5.9)
Hyperglycemia	9 (14.5)
Died	2 (3.2)
Reason for early cessation ($\leq$30 days)	
Progression	1 (1.7)
Adverse effect other than hyperglycemia	8 (14.5)
Hyperglycemia	6 (10.9)
Died	0 (0)

IQR Interquartile range, *n* number

Cheung Y-MM et al. *Breast Cancer Res Treat* 2022;192:303-11.

Hyperglycemia During Alpelisib Treatment

Hyperglycemia during alpelisib	*n* = 55 *n* (%)
Hyperglycemia in the diabetes range (peak RBG > 200)	24 (39)
Median post-alpelisib HbA1c (%, IQR)	6.2 (5.5–6.9)
Median post-alpelisib RBG (mg/dL, IQR)	121 (107–153)
Median peak RBG during alpelisib (mg/dL, IQR)	190 (152–298)
Median time to peak RBG during alpelisib (days, IQR)	27 (14–63.5)
Anti-diabetic agents commenced	*n* = 28 (%)
Metformin	21 (75)
Thiazolidinediones	1 (3.6)
Sulfonylurea	4 (14.3)
Insulin	10 (35.7)
GLP-1 analogue	1 (3.6)
SGLT2 inhibitor	1 (3.6)
Other	1 (3.6)
Referral to endocrinology	
Yes	13 (46.4)
No	13 (46.4)
Nurse practitioner	2 (7.2)

GLP-1 Glucagon-like peptide, *HbA1c* hemaglobin A1c, *IQR* inter-quartile range, *n* number, *SGLT2* sodium-glucose co-transporter-2, *SD* standard deviation, *RBG* random blood glucose

Cheung Y-MM et al. *Breast Cancer Res Treat* 2022;192:303-11.

Capivasertib and Fulvestrant for Patients with Aromatase Inhibitor-Resistant Hormone Receptor-Positive/Human Epidermal Growth Factor Receptor 2-Negative Advanced Breast Cancer: Results from the Phase III CAPItello-291 Trial

Turner NC et al.

SABCS 2022;Abstract GS3-04.

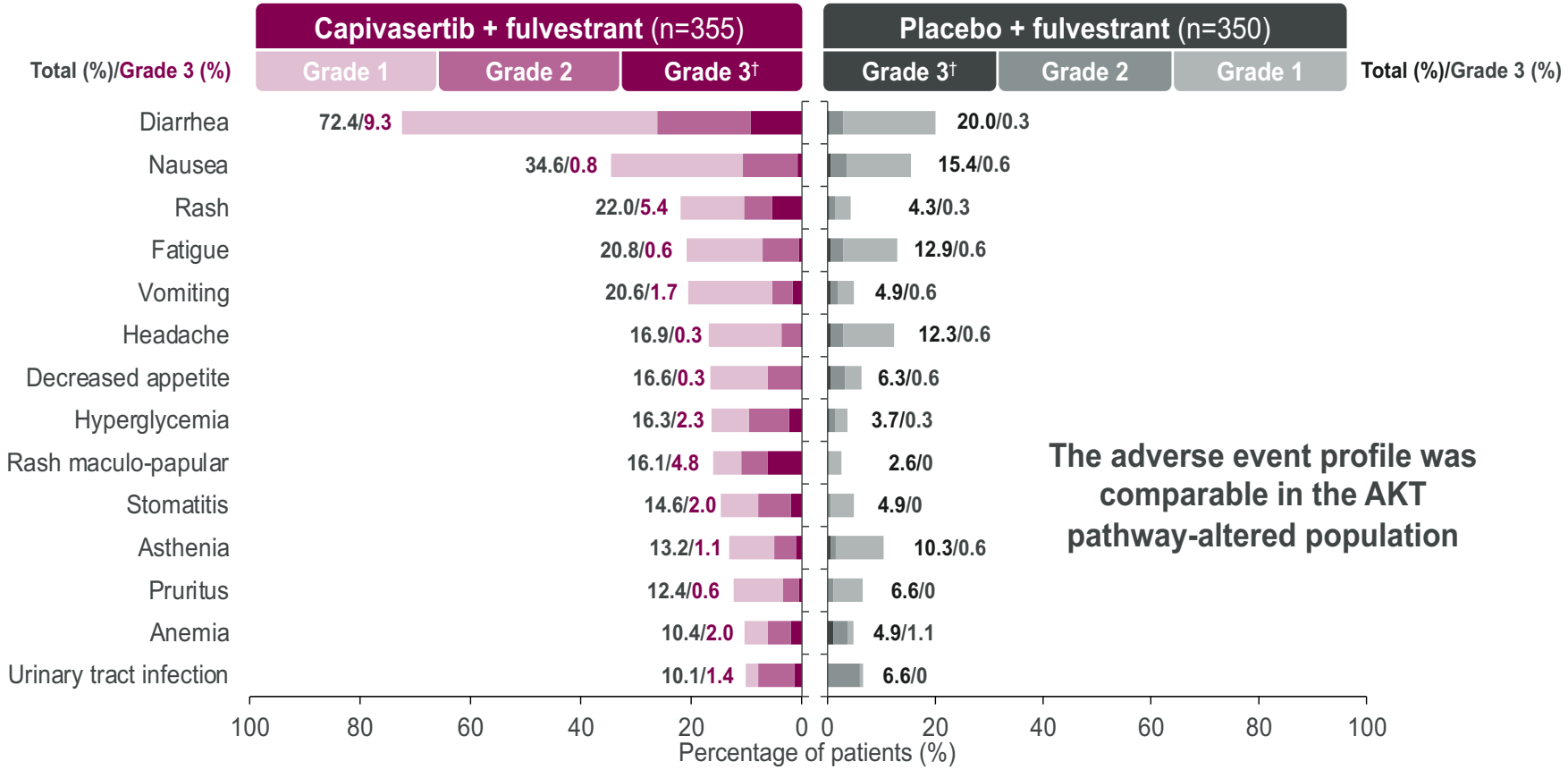
CAPItello-291: Overall Response per Investigator Assessment

	Overall population		AKT pathway-altered population	
	Capivasertib + fulvestrant	Placebo + fulvestrant	Capivasertib + fulvestrant	Placebo + fulvestrant
Patients with measurable disease at baseline	310	320	132	124
Objective response rate; n (%)	71 (22.9)	39 (12.2)	38 (28.8)	12 (9.7)
Odds ratio (95% CI)	2.19 (1.42, 3.36)		3.93 (1.93, 8.04)	

Turner NC et al. SABCS 2022;Abstract GS3-04.

CAPItello-291: Safety

Adverse events (>10% of patients) – overall population



The adverse event profile was comparable in the AKT pathway-altered population

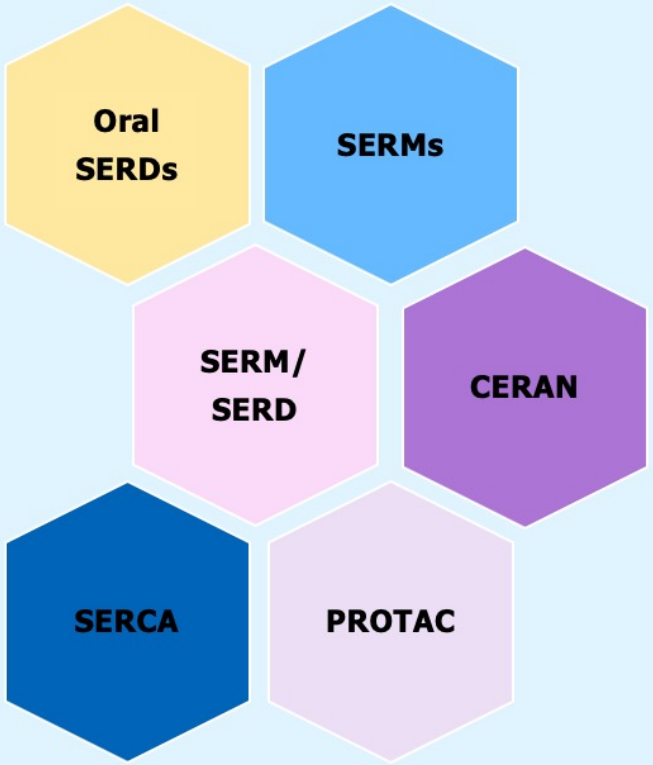
Adverse events of any grade related to rash (group term including rash, rash macular, maculo-papular rash, rash papular and rash pruritic) were reported in 38.0% of the patients in the capivasertib + fulvestrant arm (grade ≥3 in 12.1%) and in 7.1% of those in the placebo + fulvestrant group (grade ≥3 in 0.3%). †All events shown were Grade 3 except one case of Grade 4 hyperglycemia in the capivasertib + fulvestrant arm.

Turner NC et al. SABCS 2022;Abstract GS3-04.

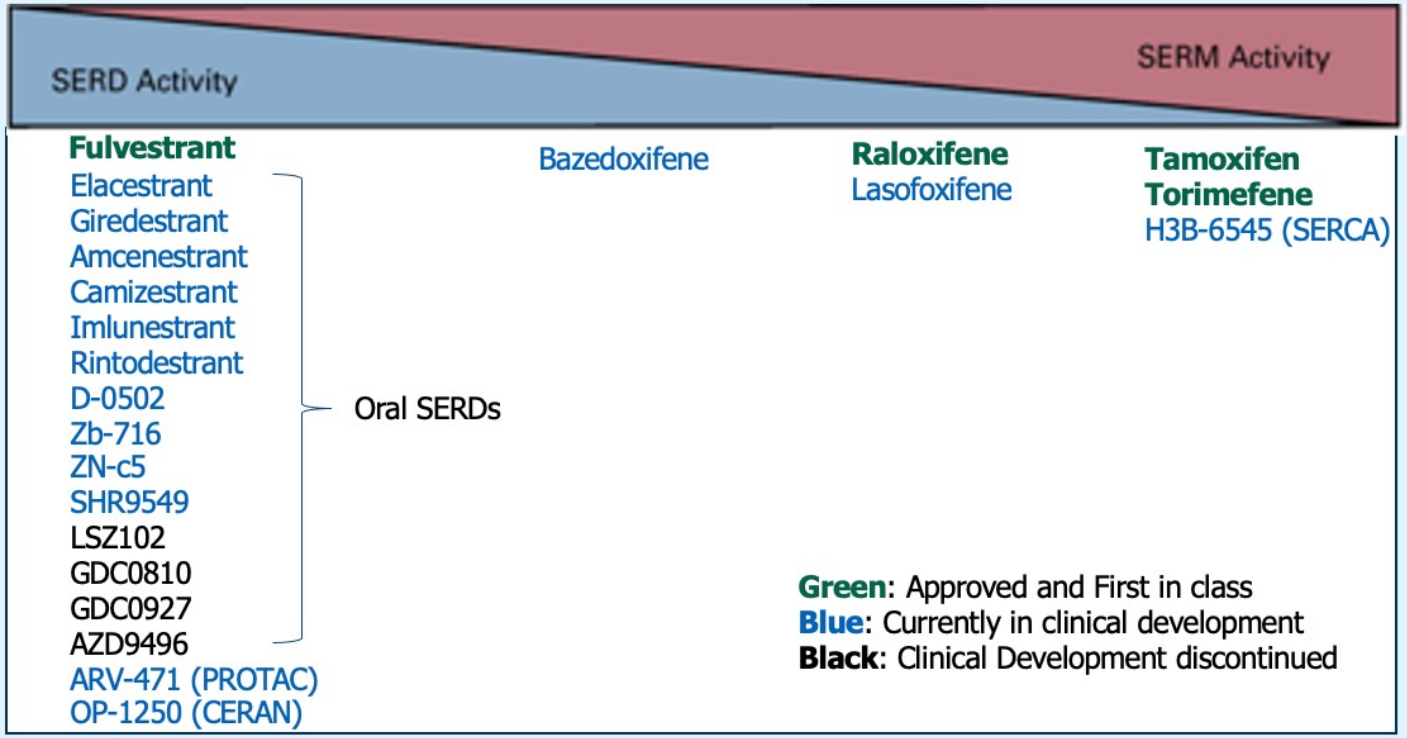
San Antonio Breast Cancer Symposium®, December 7-10, 2021

Novel ER Targeting Agents

Ultimate Goal: Downregulate ERα with an agent that has an optimal Therapeutic Index



Adapted from McDonnell et al JCO 2021

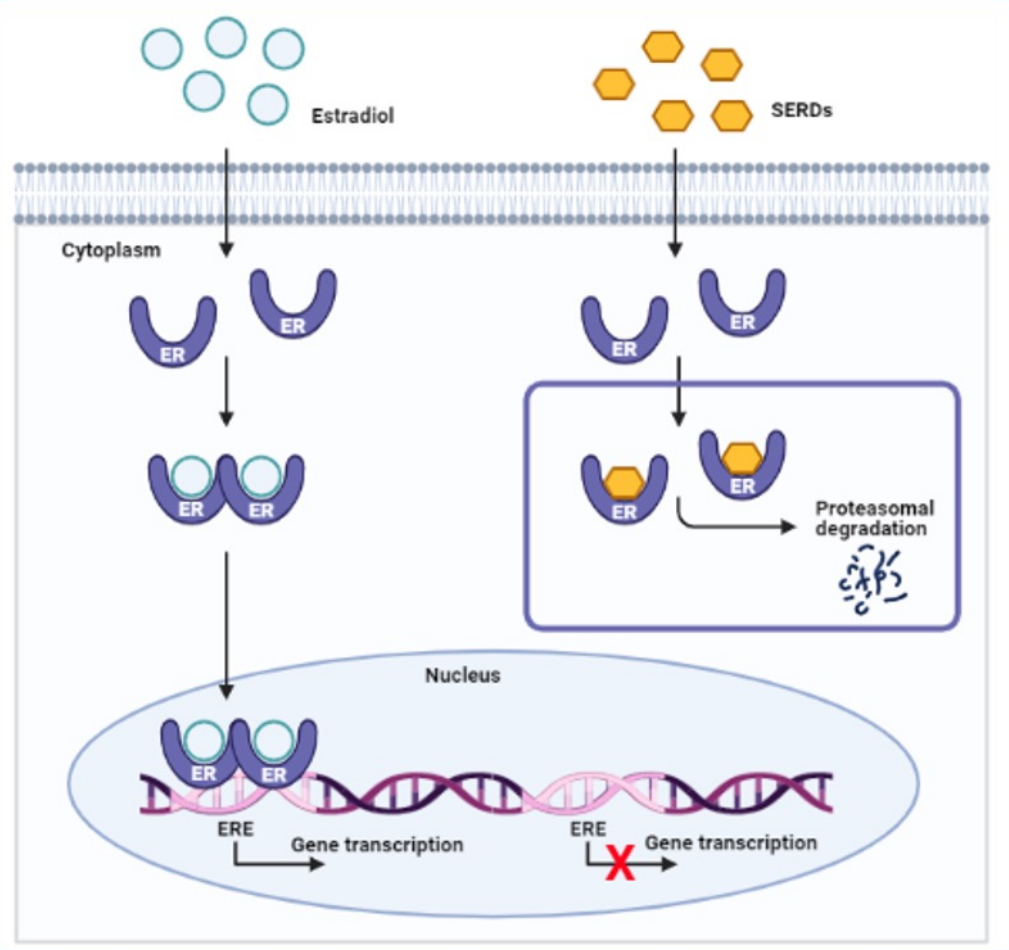


SERCA: Serum ER Covalent Antagonist; CERAN: Complete ER Antagonist; PROTAC: Proteolysis Targeting Chimera

Jhaveri K et al. SABCS 2022;Abstract TF-1.

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

Oral Selective Estrogen Receptor Degraders (SERDs)



Key Advantages

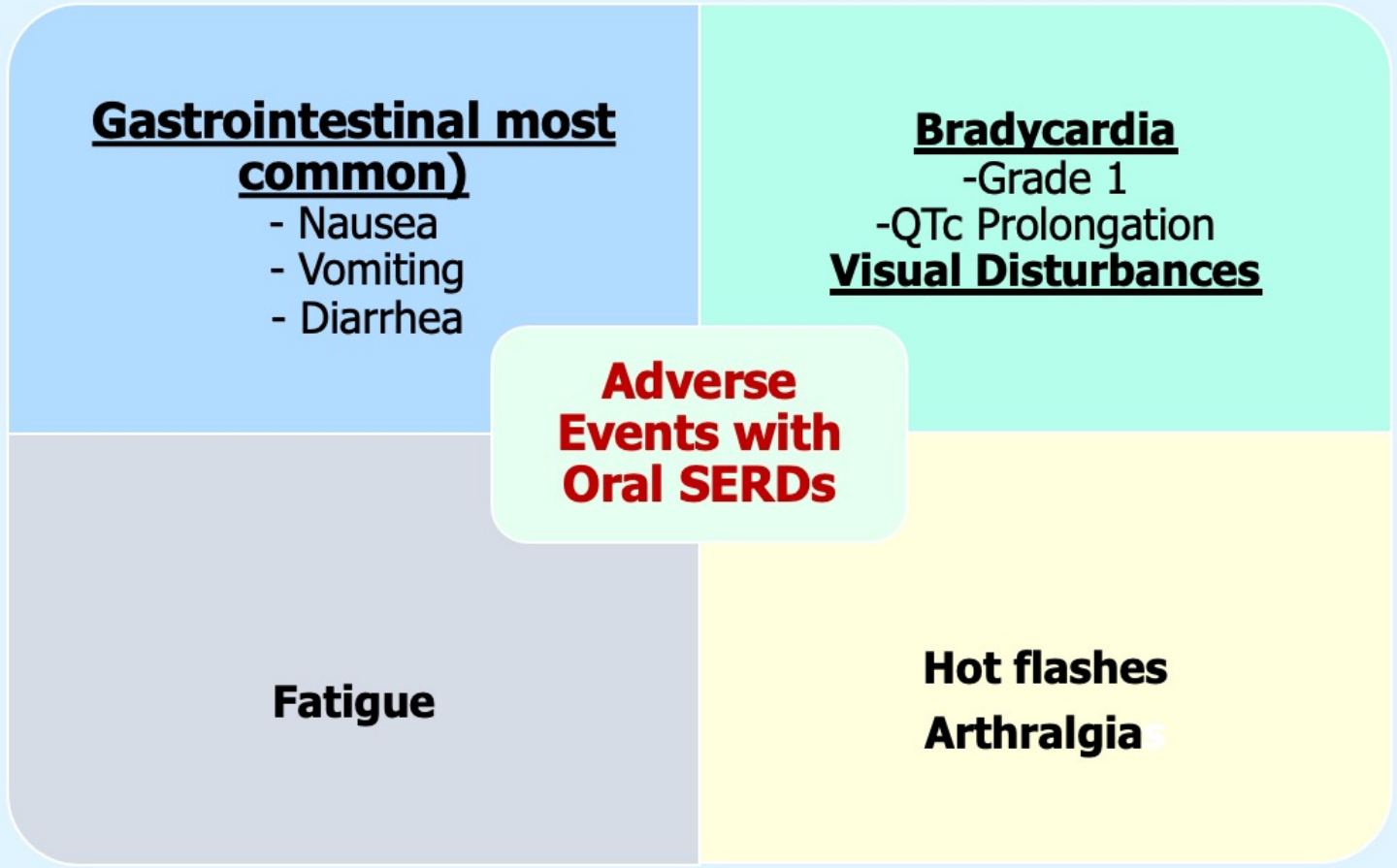
- Oral Formulation
- High Potency
- Activity against endocrine resistant and *ESR1* mutant models including Y537S

Shomali M, et al. Mol Cancer Ther. 2021;20(2):250–62.

Jhaveri K et al. SABCS 2022;Abstract TF-1.

RTP RESEARCH TO PRACTICE

Safety: Oral SERDs



Jhaveri K et al. SABCS 2022;Abstract TF-1.

Key Takeaways for Oral SERDs

Oral SERDs are ACTIVE in metastatic setting

1) Work post CDK4/6 inhibitors and fulfill an unmet need
   - PFS post CDK4/6i with single agent Fulvestrant is ~2 months (**Lindemann et al ASCO2021**)
2) Superior to current approved ET in 2/3L metastatic setting (**Bardia et al SABCS2021**). New SOC?
3) Effective in *ESR1* WT and in patients whose tumor harbor *ESR1* mutation
4) Safe and tolerable

Jhaveri K et al. SABCS 2022;Abstract TF-1.

San Antonio Breast Cancer Symposium®, December 6-10, 2022

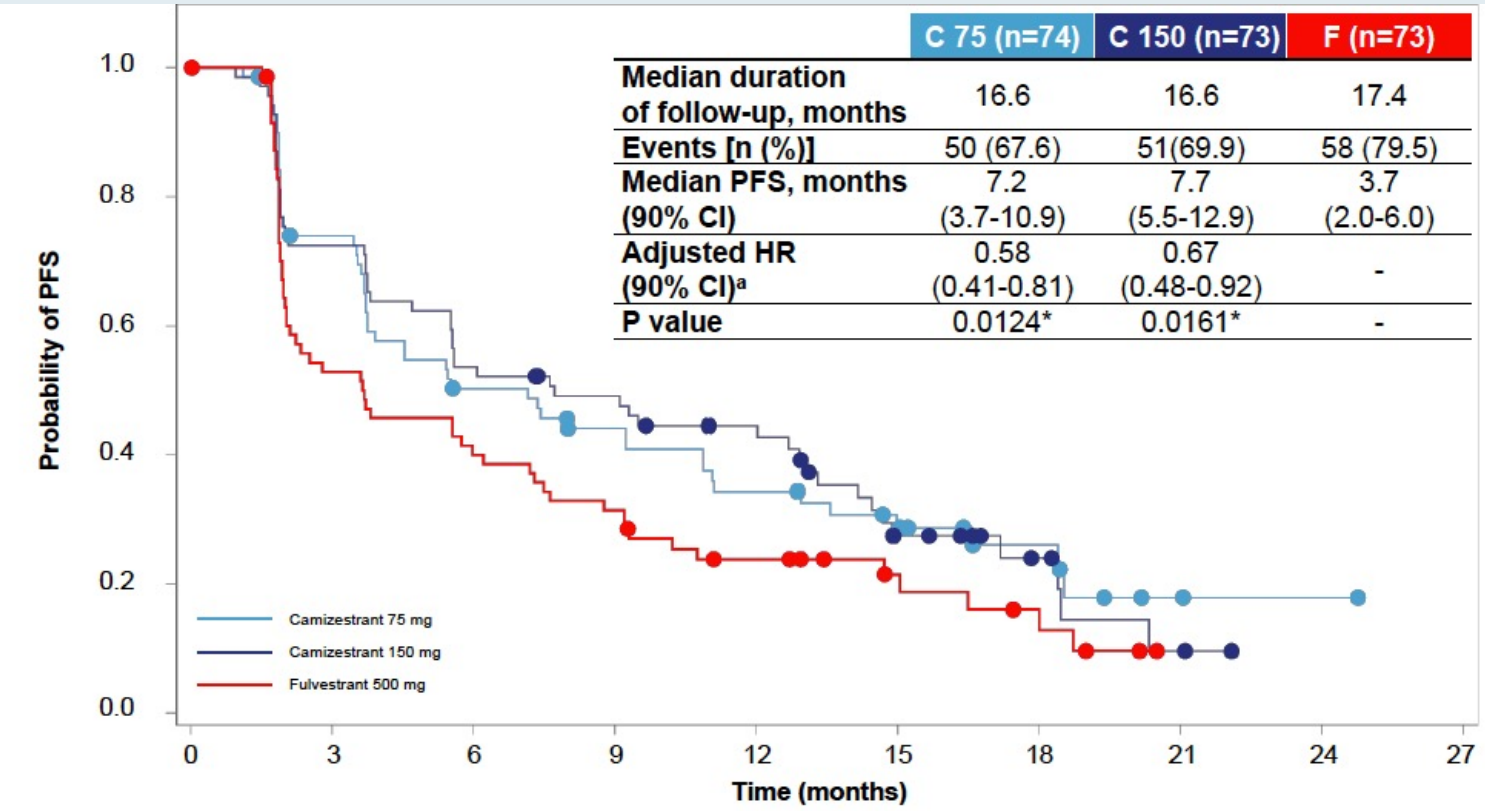
Abstract GS3-02

Camizestrant, a next-generation oral SERD *vs* fulvestrant in post-menopausal women with advanced ER-positive HER2-negative breast cancer: Results of the randomized, multi-dose Phase 2 SERENA-2 trial

Mafalda Oliveira, MD, PhD[1], Denys Pominchuk, PhD[2], Zbigniew Nowecki MD[3], Erika Hamilton, MD[4], Yaroslav Kulyaba, MD[5], Timur Andabekov, PhD[6], Yevhen Hotko, MD[7], Tamar Melkadze, MD[8], Gia Nemsadze, MD, PhD[9], Patrick Neven, MD[10], Yuriy Semegen, MD[11], Vladimir Vladimirov, MD[12], Claudio Zamagni, MD[13], Hannelore Denys, MD, PhD[14], Frédéric Forget, MD[15], Zsolt Horvath, MD, PhD[16], Alfiya Nesterova, MD, PhD[17], Maxine Bennett, PhD[18], Bistra Kirova, MBChB, MSc[19], Teresa Klinowska, PhD[20], Justin P O Lindemann, MBChB, MB[18], Delphine Lissa, PharmD, PhD[18], Alastair Mathewson, PhD[18], Christopher J Morrow, PhD[18], Zuzana Traugottova, MD[21], Ruaan van Zyl, PhD[22], Ekaterine Arkania, MD[23]

[1]Medical Oncology Department, Vall d'Hebron University Hospital and Breast Cancer Group, Vall d'Hebron Institute of Oncology, Barcelona, Spain; [2]Medical Center Verum, Kyiv, Ukraine; [3]The Maria Sklodowska Curie Memorial Cancer Center and Institute of Oncology, Warsaw, Poland; [4]Sarah Cannon Research Institute/Tennessee Oncology, Nashville, TN, USA; [5]Makiivka City Hospital of Donetsk Region, Makiivka, Ukraine; [6]AV Medical Group, St Petersburg, Russian Federation; [7]Central City Hospital, Uzhgorod National University, Uzhgorod, Ukraine; [8]Oncology and Hematology Department, Academician Fridon Todua Medical Center – Research Institute of Clinical Medicine Tbilisi, Georgia; [9]The Institute of Clinical Oncology, Tbilisi, Georgia; [10]Multidisciplinary Breast Center, University Hospitals Leuven – Campus Gasthuisberg, Leuven, Belgium; [11]Bukovynsky Clinical Oncology Center, Chernivtsi, Ukraine; [12]Pyatigorsky Oncology Dispensary, Pyatigorsk, Russia; [13]IRCCS Azienda Ospedaliero-Universitaria di Bologna, Bologna, Italy; [14]Department of Medical Oncology, Ghent University Hospital, Belgium; [15]Centre Hospitalier de l'Ardenne-Site de Libramont, Libramont-Chevigny, Belgium; [16]Center of Oncoradiology, Bács-Kiskun County Teaching Hospital, Kecskemét, Hungary; [17]Republican Clinical Oncology Dispensary of the Ministry of Health of the Republic of Tatarstan, Russian Federation; [18]Research and Early Development, Oncology R&D, AstraZeneca, Cambridge, UK; [19]Oncology Patient Safety, Oncology R&D, AstraZeneca, Cambridge, UK; [20]Late Development, Oncology R&D, AstraZeneca, Cambridge, UK; [21]Parexel International, Prague, Czech Republic; [22]Parexel International, Bloemfontein, South Africa; [23]Helsicore Israeli Georgian Medical Research Clinic, Tbilisi, Georgia.

SERENA-2 Primary Endpoint: PFS by Investigator Assessment



	C 75 (n=74)	C 150 (n=73)	F (n=73)
Median duration of follow-up, months	16.6	16.6	17.4
Events [n (%)]	50 (67.6)	51(69.9)	58 (79.5)
Median PFS, months (90% CI)	7.2 (3.7-10.9)	7.7 (5.5-12.9)	3.7 (2.0-6.0)
Adjusted HR (90% CI)[a]	0.58 (0.41-0.81)	0.67 (0.48-0.92)	-
P value	0.0124*	0.0161*	-

C 75	74	50	33	27	21	14	7	2	1	0
C 150	73	50	37	32	25	12	6	2	0	
F	73	37	28	22	14	8	5	0		

*Statistically significant; [a]HRs adjusted for prior use of CDK4/6i and liver/lung metastases

CDK4/6i: CDK4/6 inhibitor; CI: confidence interval; HR: hazard ratio; PFS: progression-free survival

In the overall population, camizestrant produces a statistically significant and clinically meaningful improvement in PFS for both 75 and 150 mg camizestrant doses over fulvestrant

Oliveira M et al. SABCS 2022;Abstract GS3-02.

RTP RESEARCH TO PRACTICE

Discontinuation of the Amcenestrant Clinical Development Program

Press Release: August 17, 2022

"[Manufacturer] is discontinuing the global clinical development program of amcenestrant, an investigational oral selective estrogen receptor degrader (SERD). The decision is based on the outcome of a prespecified interim analysis of the Phase 3 AMEERA-5 trial evaluating amcenestrant in combination with palbociclib compared with letrozole in combination with palbociclib in patients with estrogen receptor-positive (ER+)/human epidermal growth factor receptor 2-negative (HER2-) advanced breast cancer.

An Independent Data Monitoring Committee (IDMC) found that amcenestrant in combination with palbociclib did not meet the prespecified boundary for continuation in comparison with the control arm and recommended stopping the trial. No new safety signals were observed. Trial participants will be transitioned to letrozole in combination with palbociclib or another appropriate standard of care therapy, as determined by their physician.

All other studies of amcenestrant, including in early-stage breast cancer (AMEERA-6), will be discontinued."

https://www.sanofi.com/en/media-room/press-releases/2022/2022-08-17-05-30-00-2499668

RTP RESEARCH TO PRACTICE

Select Ongoing Phase III Trials of Oral SERDs in Development for HR-Positive Advanced Breast Cancer (ABC)

Trial	N	Randomization	Setting	Est primary completion
SERENA-4	1,342	• Camizestrant + palbociclib • Anastrozole + palbociclib	Untreated ABC	August 2026
persevERA	978	• Giredestrant + palbociclib • Letrozole + palbociclib	Untreated ABC	April 2024
SERENA-6	302	• Camizestrant + (palbociclib or abemaciclib) • (Anastrozole or letrozole) + (palbociclib or abemaciclib)	Detectable ESR1 mutation w/o PD during 1st-line AI + CDK4/6i	Sept 2023
EMBER-3	860	• Imlunestrant • Imlunestrant + abemaciclib • Investigator's choice of ET	ABC previously treated with ET + CDK4/6i	April 2024
evERA	320	• Giredestrant + everolimus • Exemestane + everolimus	ABC previously treated with ET + CDK4/6i	July 2024
heredERA	812	• Giredestrant + pertuzumab/trastuzumab/hyaluronidase-zzxf • Pertuzumab/trastuzumab/hyaluronidase-zzxf	Untreated ER+, HER2+ ABC after first-line pertuzumab/trastuzumab/ hyaluronidase-zzxf + taxane	August 2026

SERD = selective ER degrader

www.clinicaltrials.gov. Accessed November 2022.

RTP RESEARCH TO PRACTICE

Ongoing Phase III Trials of Adjuvant Oral SERDs for HR-Positive, HER2-Negative Localized Breast Cancer

Study	N	Setting	Randomization
lidERA	4,100	• Node-negative or node-positive	• Giredestrant +/- LHRH agonist • ET of physician's choice +/- LHRH agonist
EMBER-4	6,000	• Elevated risk of recurrence after definitive treatment • Completion of at least 2 years and up to 5 years of ET • Previous adjuvant CDK4/6i or PARPi allowed	• Imlunestrant • ET of physician's choice
EORTC-2129-BCG	220	• Elevated risk of recurrence after definitive treatment • Completion of at least 2 years and up to 7 years of ET • ctDNA-positive • Previous adjuvant CDK4/6i or PARPi allowed	• Elacestrant • Tamoxifen or aromatase inhibitor at time of ctDNA detection

ctDNA = circulating tumor DNA

www.clinicaltrials.gov. Accessed January 2023.

RTP RESEARCH TO PRACTICE

In general, which CDK4/6 inhibitor do you recommend in combination with endocrine therapy as first-line treatment for women with ER-positive, HER2-negative metastatic breast cancer if they are…?

	Postmenopausal	Premenopausal
 Dr Hurvitz	Ribociclib	Ribociclib
 Dr Jhaveri	Ribociclib	Ribociclib
 Dr Miller	Palbociclib	Palbociclib
 Dr Partridge	No preference	Ribociclib
 Dr Telli	No preference – decision based on patient characteristics, side effect profile	Ribociclib
 Dr Tolaney	Ribociclib	Ribociclib

Following the recent FDA approval of the oral SERD elacestrant for postmenopausal women or men with ER-positive, HER2-negative, ESR1-mutated advanced breast cancer with disease progression after at least 1 line of endocrine therapy, in what situations, if any, do you plan to use this agent?

 Dr Hurvitz	ESR1 mutation, after CDK4/6i and probably after a line of everolimus or alpelisib + fulvestrant, prolonged benefit from CDK4/6i	 Dr Partridge	Second line
 Dr Jhaveri	ESR1 mutation, duration of response to CDK4/6i >12 months*	 Dr Telli	Most likely third-line
 Dr Miller	As oral therapy rather than fulvestrant	 Dr Tolaney	ESR1 mutation, after progression on CDK4/6i + AI with prolonged benefit*

*Also PIK3CA wild type

Case Presentation: 72-year-old woman with multiregimen-recurrent ER/PR-positive, HER2-low (IHC 1+) metastatic breast cancer receives T-DXd

Dr Henna Malik (Houston, Texas)

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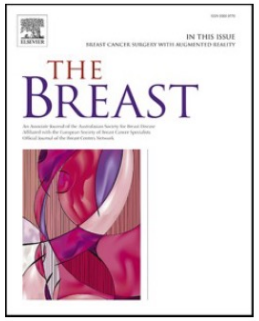
The Breast 67 (2023) 116–123

Contents lists available at ScienceDirect

The Breast

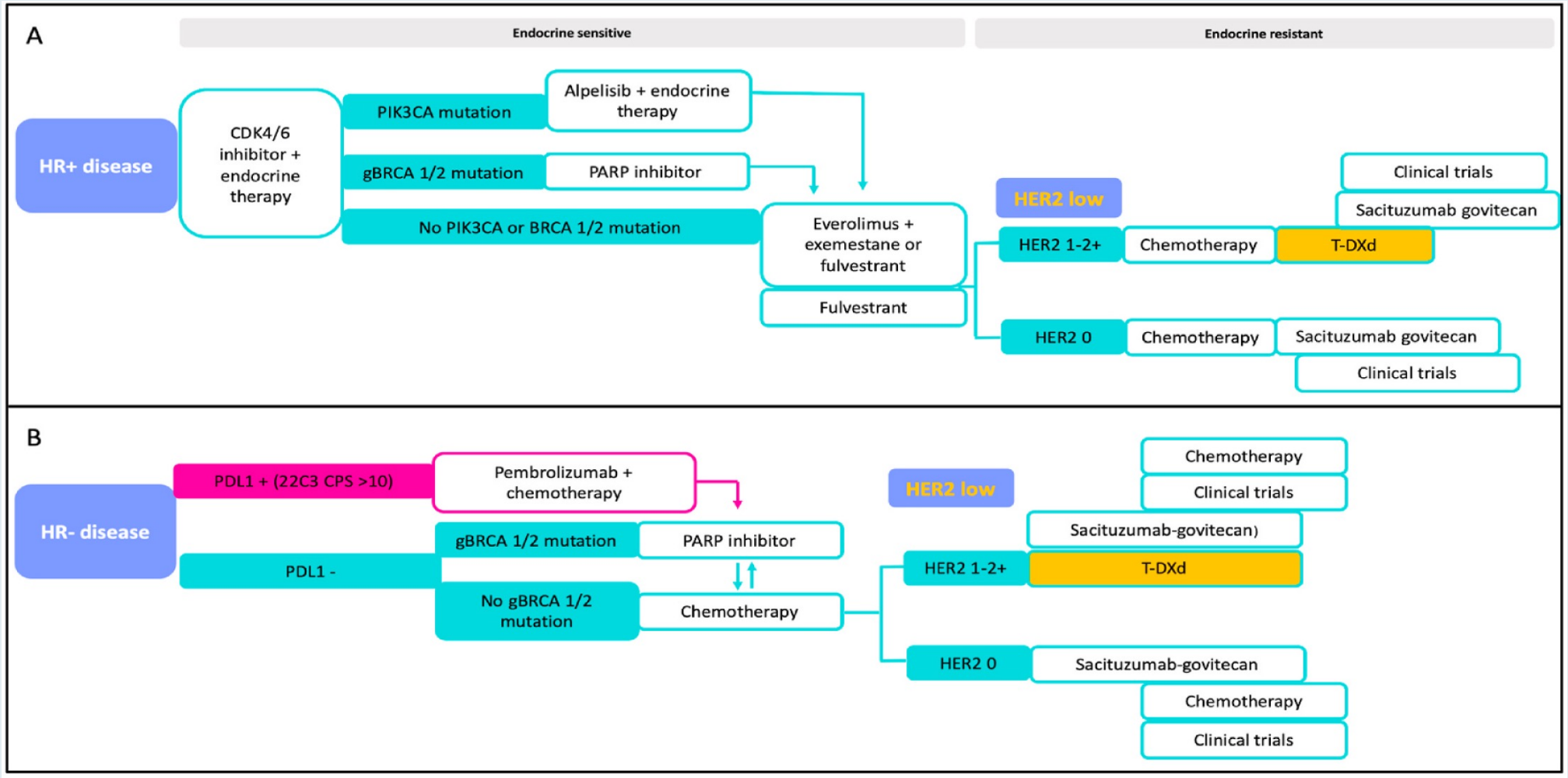
journal homepage: www.journals.elsevier.com/the-breast



How I treat HER2-low advanced breast cancer

Ilana Schlam [a], Sara M. Tolaney [b], Paolo Tarantino [b,c,*]

Proposed Treatment Algorithm for Hormone Receptor-Positive and Hormone Receptor-Negative HER2-Low Breast Cancer



Schlam I et al. *The Breast* 2023;67:116-23.

Expert Review of Anticancer Therapy

January 24, 2023;[Online ahead of print].

ISSN: (Print) (Online) Journal homepage: https://www.tandfonline.com/loi/iery20

The efficacy of trastuzumab-deruxtecan for the treatment of patients with advanced pretreated HER2-low breast cancer

Ilana Schlam, Sara M. Tolaney & Paolo Tarantino

JAMA Oncol 2022 September 15;[Online ahead of print].

Clinical Review & Education

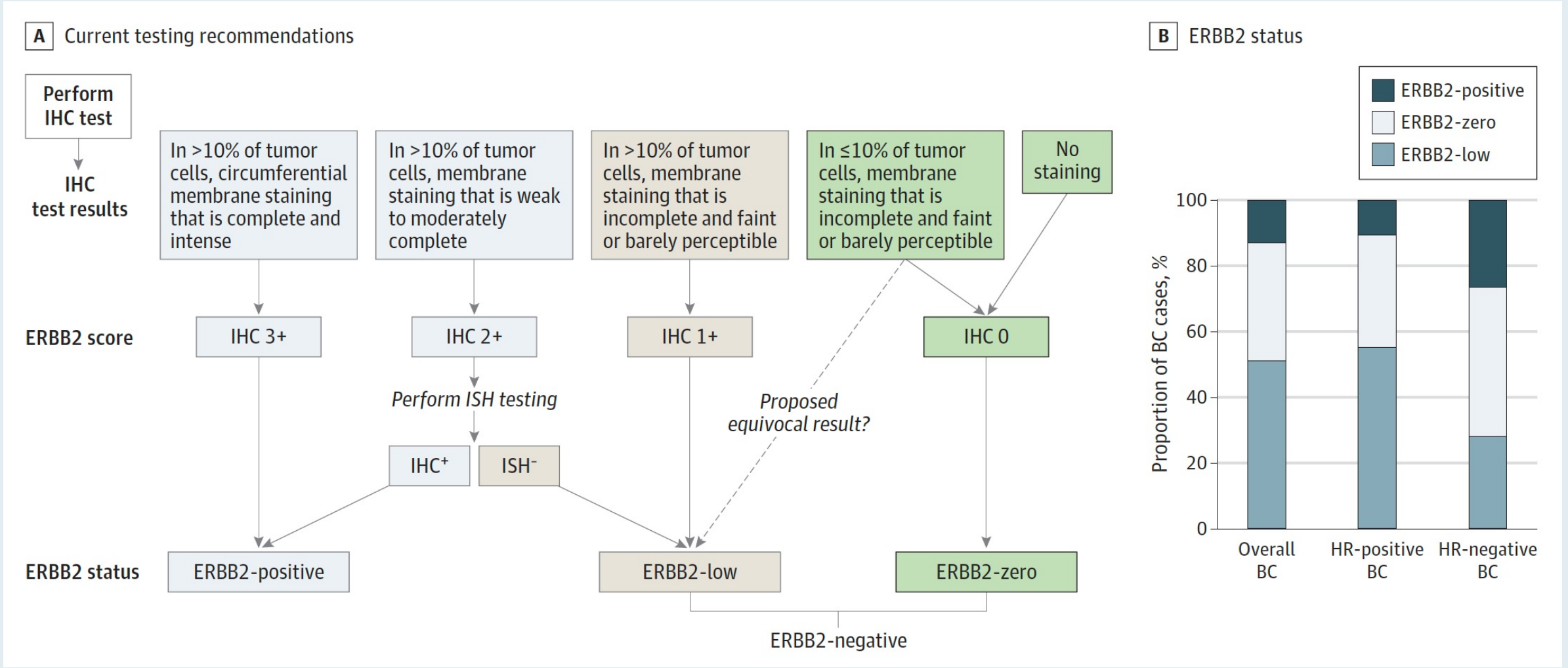
JAMA Oncology | Review

An Overview of Clinical Development of Agents for Metastatic or Advanced Breast Cancer Without *ERBB2* Amplification (HER2-Low)

Aleix Prat, MD, PhD; Aditya Bardia, MD, MPH; Giuseppe Curigliano, MD, PhD; M. Elizabeth H. Hammond, MD; Sibylle Loibl, MD, PhD; Sara M. Tolaney, MD, MPH; Giuseppe Viale, MD

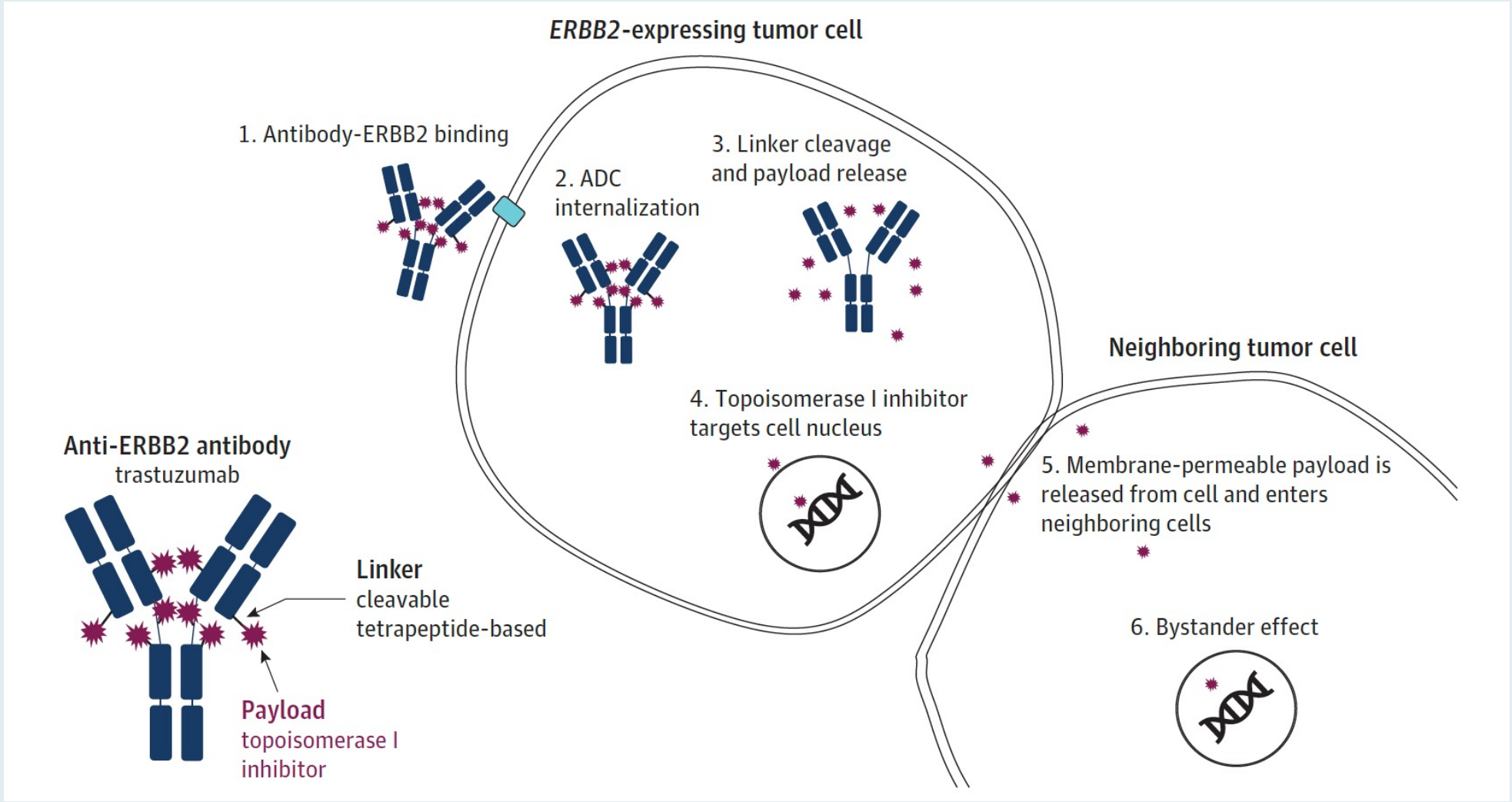
JC JOURNAL CLUB RTP RESEARCH TO PRACTICE

Testing for ERBB2 (HER2) Status in Breast Cancer



Prat A et al. *JAMA Oncol* 2022 September 15;[Online ahead of print].

Mechanism of Action of Trastuzumab Deruxtecan



Prat A et al. *JAMA Oncol* 2022 September 15;[Online ahead of print].

JAMA Oncol 2022 August 1;8(8):1177-83.

Research

JAMA Oncology | Original Investigation

Prognostic and Biologic Significance of ERBB2-Low Expression in Early-Stage Breast Cancer

Paolo Tarantino, MD; Qingchun Jin, MPH; Nabihah Tayob, PhD; Rinath M. Jeselsohn, MD; Stuart J. Schnitt, MD; Julie Vincuilla, BS; Tonia Parker, BS; Svitlana Tyekucheva, PhD; Tianyu Li, MS; Nancy U. Lin, MD; Melissa E. Hughes, MSc; Anna C. Weiss, MD; Tari A. King, MD; Elizabeth A. Mittendorf, MD, PhD; Giuseppe Curigliano, MD, PhD; Sara M. Tolaney, MD, MPH

Comprehensive Genomic Characterization of HER2-Low Breast Cancer

Tarantino P et al.
SABCS 2022;Abstract HER2-05.

Regulatory and reimbursement issues aside, what would be your most likely next therapy for a symptomatic patient with ER-positive, HER2-low breast cancer and diffuse bone pain who has experienced disease progression on adjuvant AC → T followed by an AI, then a CDK4/6 inhibitor and fulvestrant for metastatic disease?

 Dr Hurvitz	Depends on duration of response to CDK4/6 inhibitor*	 Dr Partridge	T-DXd
 Dr Jhaveri	Chemotherapy	 Dr Telli	Capecitabine
 Dr Miller	Capecitabine	 Dr Tolaney	Capecitabine

*If disease controlled ≥12 mo, would try another line of hormone therapy with everolimus or alpelisib; if disease controlled <12 mo, would use capecitabine

RTP RESEARCH TO PRACTICE

Meet The Professor with Dr Tolaney

Introduction

MODULE 1: Hormone Receptor-Positive Breast Cancer

MODULE 2: Triple-Negative Breast Cancer (TNBC)

- Dr Agrawal: 45-year-old woman with node-positive localized TNBC has residual disease after neoadjuvant pembrolizumab/chemotherapy and surgery
- Dr Zelkowitz: 46-year-old woman with TxN1 BRCA-WT TNBC

MODULE 3: Appendix

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Case Presentation: 45-year-old woman with node-positive localized TNBC has residual disease after neoadjuvant pembrolizumab/chemotherapy and surgery

Dr Laila Agrawal (Louisville, Kentucky)

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TO PRACTICE

Case Presentation: 46-year-old woman with TxN1 BRCA-WT TNBC

Dr Richard Zelkowitz (Bridgeport, Connecticut)

RTP RESEARCH TO PRACTICE

Hematol Oncol Clin North Am 2023 Feb;37(1):133-50.

Role of Immunotherapy in Early- and Late-Stage Triple-Negative Breast Cancer

Stefania Morganti, MD[a,b,c,d,e], Sara M. Tolaney, MD, MPH[a,b,c,*]

npj | Breast Cancer

February 18, 2022;8(1):23

www.nature.com/npjbcancer

PERSPECTIVE OPEN

Immunotherapy for early triple negative breast cancer: research agenda for the next decade

Paolo Tarantino[1], Chiara Corti[1,2], Peter Schmid[3], Javier Cortes[4,5,6,7], Elizabeth A. Mittendorf[8,9], Hope Rugo[10], Sara M. Tolaney[11,12], Giampaolo Bianchini[13], Fabrice Andrè[14] and Giuseppe Curigliano[1,2] ✉

MEETING REPORTS

Immunotherapy for the Treatment of Triple-Negative Breast Cancer

PRESENTED BY SARA M. TOLANEY, MD, MPH, AND LINDSAY SHAW, ANP-BC, AOCNP®

J Adv Pract Oncol 2022;13(3):298-301.

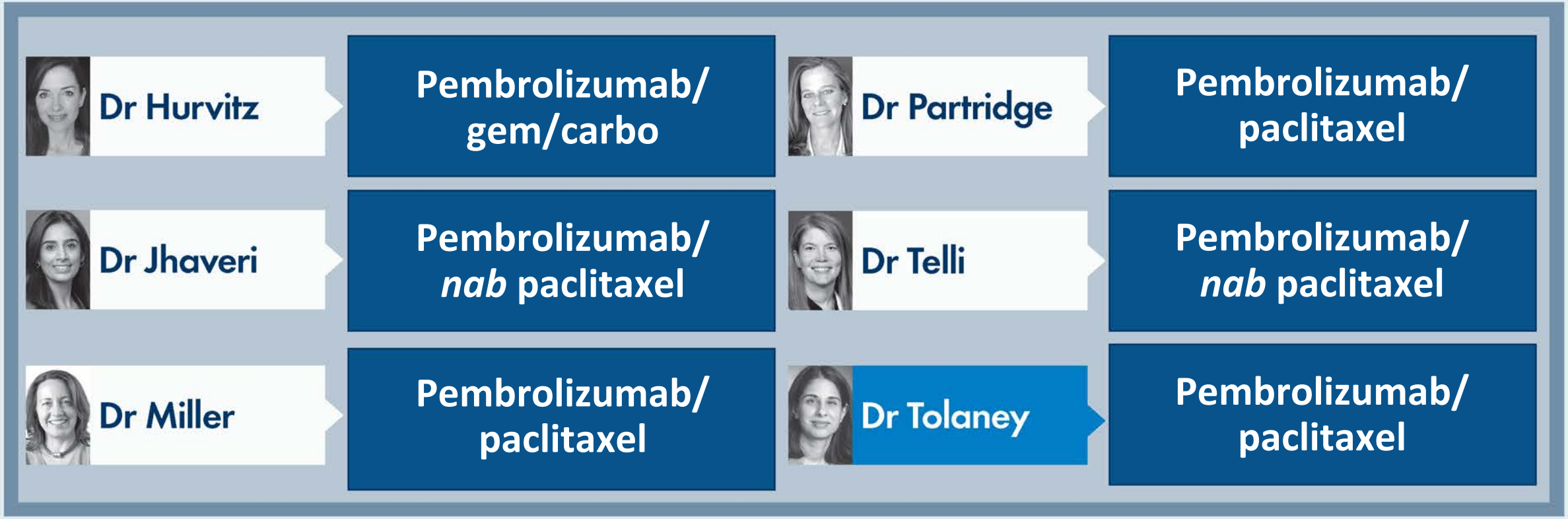
JC JOURNAL CLUB RTP RESEARCH TO PRACTICE

What would be your preferred treatment approach for a 60-year-old patient with a germline BRCA mutation and de novo metastatic TNBC and the following PD-L1 CPS?

	PD-L1 CPS 0	PD-L1 CPS >10
 Dr Hurvitz	Nonplatinum chemotherapy	Pembrolizumab/*nab* paclitaxel
 Dr Jhaveri	Olaparib	Pembrolizumab/*nab* paclitaxel
 Dr Miller	Olaparib or talazoparib – coin flip	Pembrolizumab/paclitaxel
 Dr Partridge	Olaparib	Olaparib
 Dr Telli	Single agent PARPi or induction chemo → PARPi maintenance*	Pembrolizumab/gem/carbo
 Dr Tolaney	Olaparib	Pembrolizumab/gem/carbo

CPS = combined positive score; PARPi = PARP inhibitor; gem/carbo = gemcitabine/carboplatin; * Olaparib or talazoparib

What would be your preferred treatment approach for a 60-year-old patient with BRCA wild-type de novo metastatic TNBC with a PD-L1 CPS of >10?



CPS = combined positive score; gem/carbo = gemcitabine carboplatin

RTP RESEARCH TO PRACTICE

Meet The Professor with Dr Tolaney

Introduction

MODULE 1: Hormone Receptor-Positive Breast Cancer

MODULE 2: Triple-Negative Breast Cancer

MODULE 3: Appendix

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HR-Positive Localized Breast Cancer

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RESEARCH
TO PRACTICE

San Antonio Breast Cancer Symposium – December 6-10, 2022

Trial Assigning IndividuaLized Options for TReatment (TAILORx): An Update Including 12-Year Event Rates

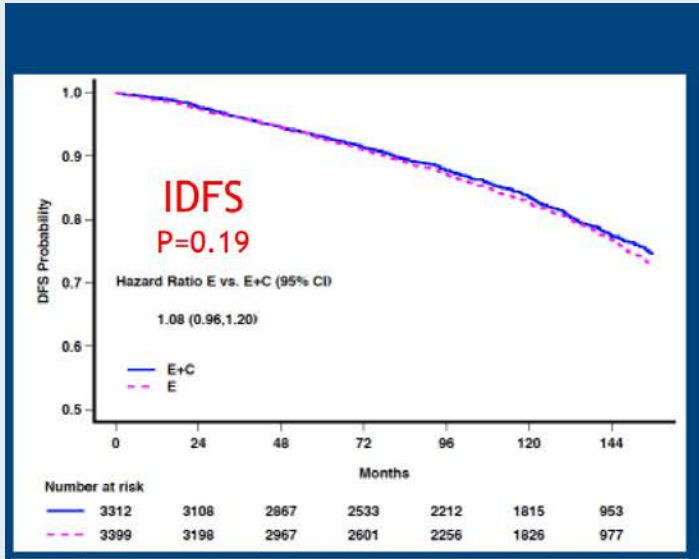
Abstract GS1-05

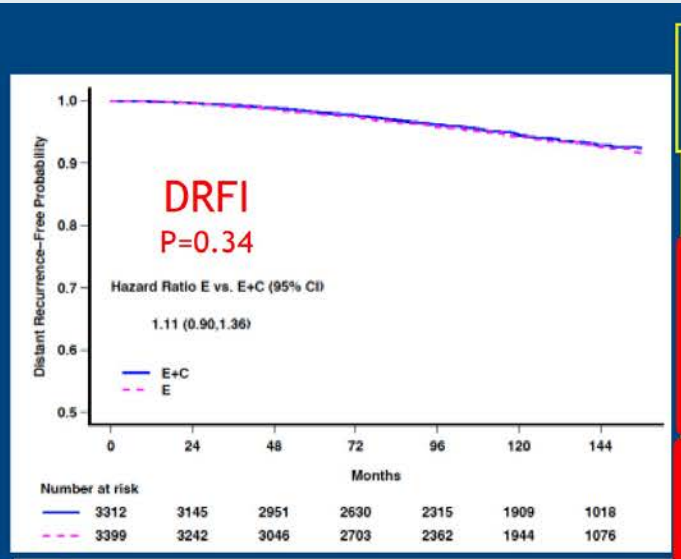
Joseph A. Sparano, Robert J. Gray, Della F. Makower, Kathy S. Albain, Daniel F. Hayes, Charles E. Geyer, Elizabeth Claire Dees, Matthew P. Goetz, John A. Olson, Jr., Tracy G. Lively, Sunil Badve, Thomas J. Saphner, Timothy J. Whelan, Virginia Kaklamani, & George W. Sledge, Jr.

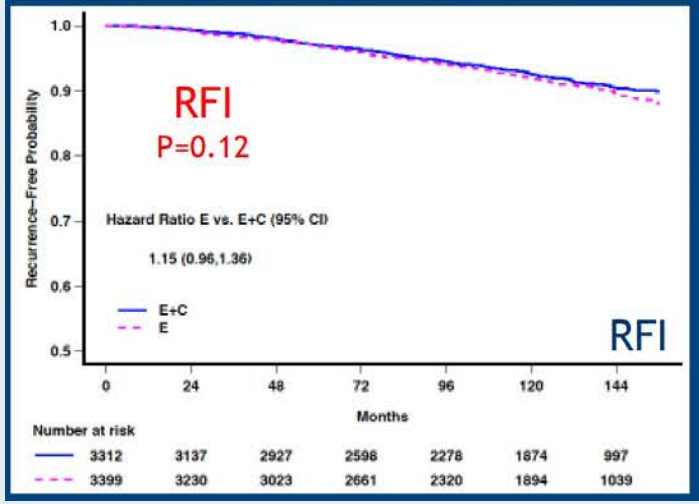
on behalf of the TAILORx Investigators

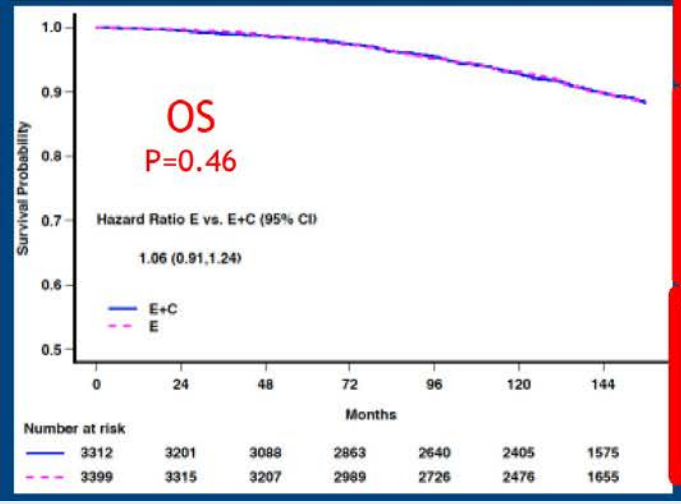
Funding: U.S. NIH/NCI U10CA180820, U10CA180794, UG1CA189859, UG1CA190140, UG1CA233160, UG1CA23337, UG1CA189869; U.S. Postal Service Breast Cancer Stamp Fund; Canadian Cancer Society Research Institute grants 015469, 021039; Breast Cancer Research Foundation, Komen Foundation.

TAILORx Updated Analysis: Kaplan-Meier Curves in RS 11-25 Arms (ITT Population)









Primary trial conclusions unchanged:
ET non-inferior to CET (N=6711)

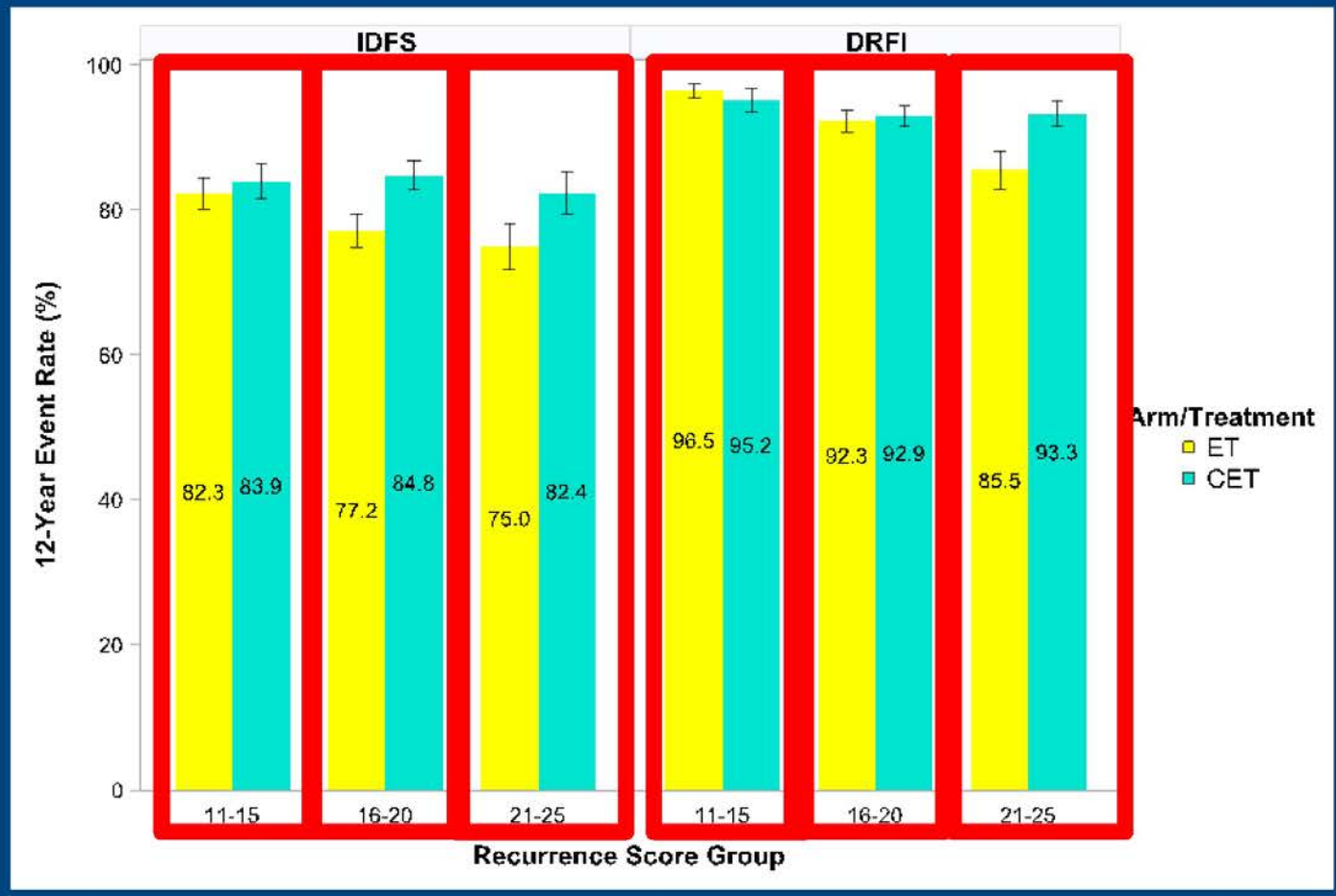
Event	Hazard Ratio: Arm B vs. C (95% CI)
IDFS	Primary analysis: 1.08 (0.94, 1.24, p=0.26) Updated analysis: 1.08 (0.96, 1.20)
DRFI	Primary analysis: 1.10 (0.85,1.41, p=0.48) Updated analysis: 1.11 (0.90, 1.36)
RFI	Primary analysis: 1.11 (0.90, 1.37, p=0.33) Updated analysis: 1.15 (0.96, 1.36)
OS	Primary analysis: 0.99 (0.79, 1.22, p=0.89) Updated analysis: 1.06 (0.91, 1.24)

IDFS = invasive disease-free survival; DRFI = distant recurrence-free interval; RFI = recurrence-free interval; OS = overall survival

Sparano JA et al. SABCS 2022;Abstract GS1-05.

TAILORx Updated Analysis: Event Rates in RS 11-25 Arms and Age ≤50 Years (ITT Population)

- No chemo benefit for RS 11-15
- Marginal benefit for RS 16-20
- Evident benefit for RS 21-25



Sparano JA et al. SABCS 2022;Abstract GS1-05.

RTP RESEARCH TO PRACTICE

Abstract VP1-2022

ESMO VIRTUAL PLENARY

PRE-SPECIFIED EVENT DRIVEN ANALYSIS OF OVERALL SURVIVAL (OS) IN THE OLYMPIA PHASE III TRIAL OF ADJUVANT OLAPARIB (OL) IN GERMLINE *BRCA1/2* MUTATION (*gBRCAm*) ASSOCIATED BREAST CANCER

Andrew Nicholas James Tutt[1], Judy Garber[2], Richard D. Gelber[2], Kelly-Anne Phillips[3], Andrea Eisen[4], Oskar Thor Jóhannsson[5], Priya Rastogi[6], Karen Yongzhi Cui[7], Seock-Ah Im[8], Rinat Yerushalmi[9], Adam Matthew Brufsky[10], Maria Taboada[11], Giovanna Rossi[12], Greg Yothers[13], Christian Singer[14], Luis E. Fein[15], Niklas Loman[16], David Cameron[17], Christine Campbell[18], Charles Edward Geyer Jr[19]

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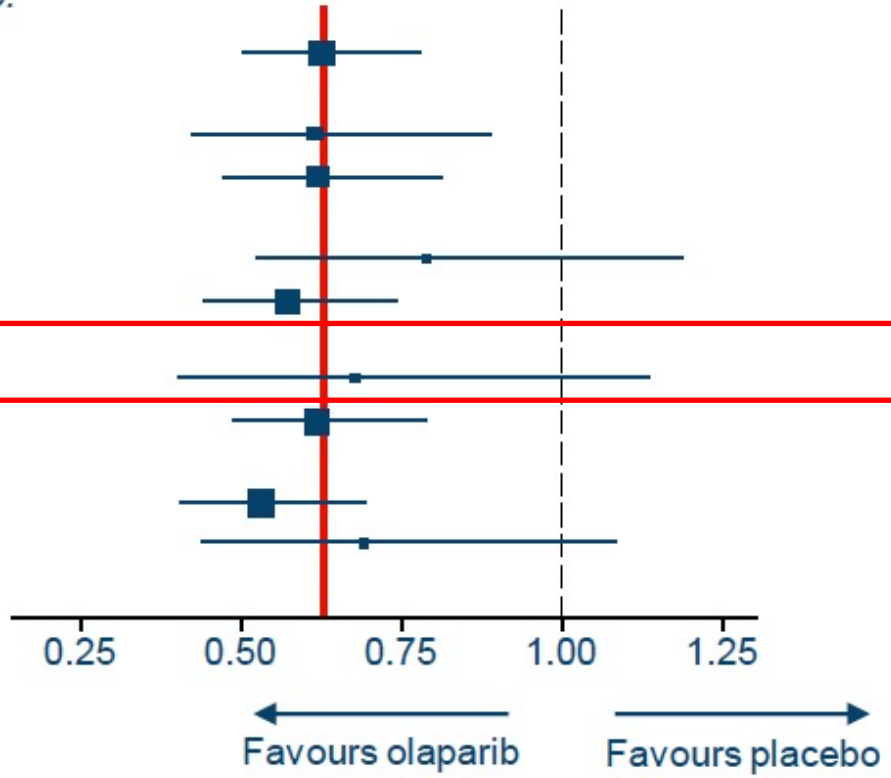
RTP RESEARCH TO PRACTICE

OlympiA: IDFS (Primary Endpoint) – Subgroup Analysis

Subgroup	Olaparib	Placebo	Stratified hazard ratio for invasive disease-free survival (95% CI)	P value for heterogeneity
	No. of patients with an invasive disease event/total no.			
All patients	134 / 921	207 / 915	0.628 (0.504, 0.779)	NA
Prior chemo				0.977
Adjuvant	46 / 461	75 / 455	0.618 (0.425, 0.888)	
Neoadjuvant	88 / 460	132 / 460	0.622 (0.473, 0.813)	
Prior platinum				0.197
Yes	42 / 247	51 / 238	0.791 (0.523, 1.187)	
No	92 / 674	156 / 677	0.575 (0.443, 0.742)	
HR status				0.754
HR+/HER2-	25 / 168	34 / 157	0.680 (0.402, 1.134)	
TNBC	109 / 751	173 / 758	0.620 (0.487, 0.787)	
BRCA				0.615
BRCA1	83 / 579	149 / 588	0.533 (0.406, 0.695)	
BRCA2	34 / 235	44 / 216	0.693 (0.440, 1.082)	
BRCA1/2 both	0 / 2	0 / 3	NC	



IDFS = invasive disease-free survival

Tutt ANJ et al. ESMO Virtual Plenary 2022;Abstract VP1-2022.

VOLUME 36 · NUMBER 19 · JULY 1, 2018

JOURNAL OF CLINICAL ONCOLOGY

ASCO SPECIAL ARTICLE

Fertility Preservation in Patients With Cancer: ASCO Clinical Practice Guideline Update

Kutluk Oktay, Brittany E. Harvey, Ann H. Partridge, Gwendolyn P. Quinn, Joyce Reinecke, Hugh S. Taylor, W. Hamish Wallace, Erica T. Wang, and Alison W. Loren

- Sperm, oocyte, and embryo cryopreservation are considered standard practice and are widely available
- There is conflicting evidence to recommend gonadotrophin-releasing hormone agonists (GnRHa) and other means of ovarian suppression for fertility preservation
- The Panel recognizes that, when proven fertility preservation methods are not feasible, and in the setting of young women with breast cancer, GnRHa may be offered to patients in the hope of reducing the likelihood of chemotherapy-induced ovarian insufficiency
- GnRHa should not be used in place of proven fertility preservation methods

RTP RESEARCH TO PRACTICE

The NEW ENGLAND JOURNAL of MEDICINE

2015;372(10):923-32

ORIGINAL ARTICLE

Goserelin for Ovarian Protection during Breast-Cancer Adjuvant Chemotherapy

Halle C.F. Moore, M.D., Joseph M. Unger, Ph.D., Kelly-Anne Phillips, M.D., Frances Boyle, M.B., B.S., Ph.D., Erika Hitre, M.D., David Porter, M.D., Prudence A. Francis, M.D., Lori J. Goldstein, M.D., Henry L. Gomez, M.D., Carlos S. Vallejos, M.D., Ann H. Partridge, M.D., M.P.H., Shaker R. Dakhil, M.D., Agustin A. Garcia, M.D., Julie Gralow, M.D., Janine M. Lombard, M.D., John F. Forbes, M.B., B.S., Silvana Martino, D.O., William E. Barlow, Ph.D., Carol J. Fabian, M.D., Lori Minasian, M.D., Frank L. Meyskens, Jr., M.D., Richard D. Gelber, Ph.D., Gabriel N. Hortobagyi, M.D., and Kathy S. Albain, M.D., for the POEMS/S0230 Investigators

- Among 135 patients with complete primary endpoint data, the ovarian failure rate was 8% in the goserelin group and 22% in the chemotherapy-alone group (odds ratio 0.30, two-sided $p = 0.04$)
- Owing to missing primary endpoint data, sensitivity analyses were performed, and the results were consistent with the main findings

Moore HCF et al. *N Engl J Med* 2015;372(10):923-32.

Localized Triple-Negative Breast Cancer (TNBC)

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VOLUME 36 · NUMBER 19 · JULY 1, 2018

JOURNAL OF CLINICAL ONCOLOGY

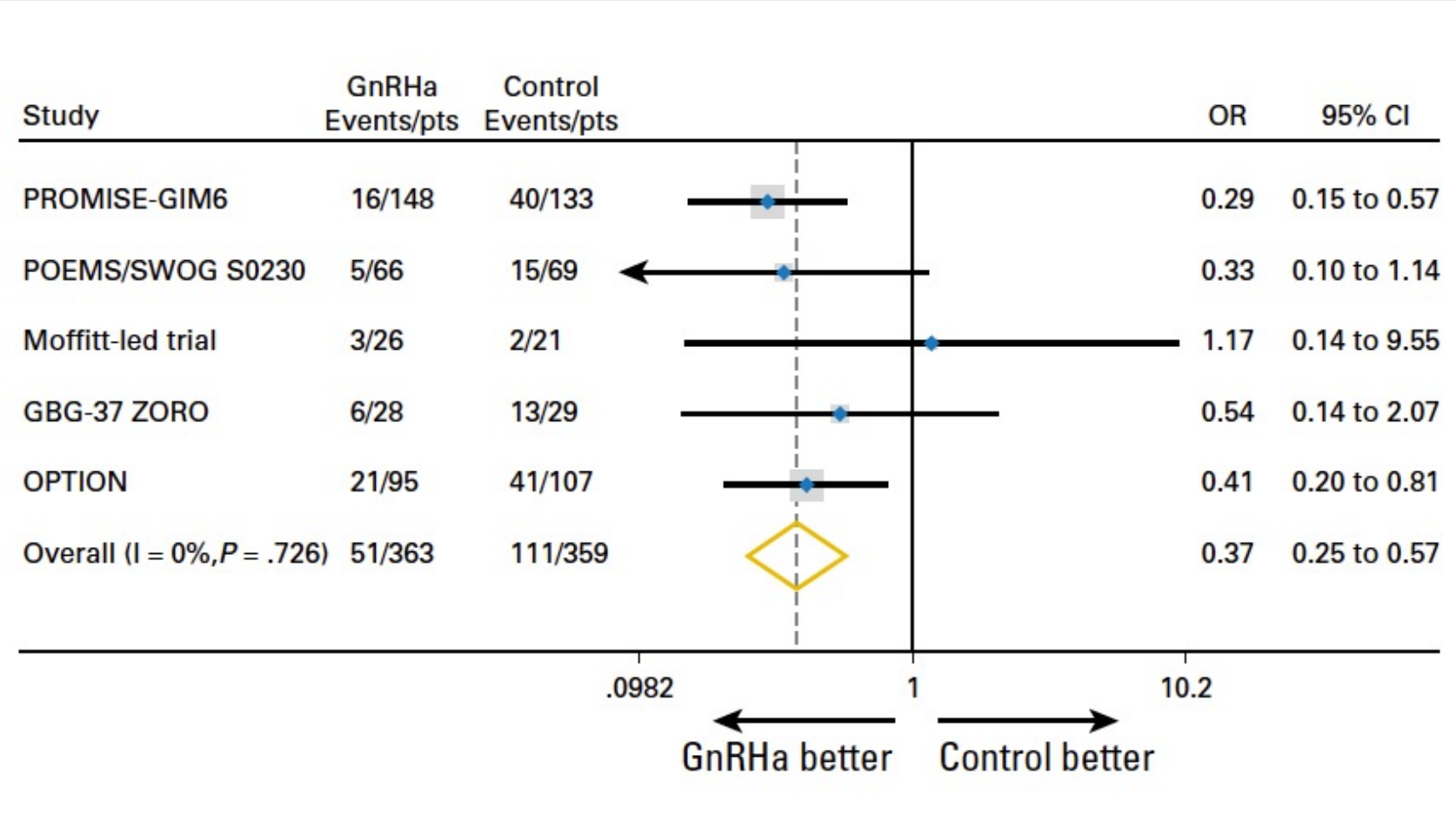
REVIEW ARTICLE

Gonadotropin-Releasing Hormone Agonists During Chemotherapy for Preservation of Ovarian Function and Fertility in Premenopausal Patients With Early Breast Cancer: A Systematic Review and Meta-Analysis of Individual Patient–Level Data

Matteo Lambertini, Halle C.F. Moore, Robert C.F. Leonard, Sibylle Loibl, Pamela Munster, Marco Bruzzone, Luca Boni, Joseph M. Unger, Richard A. Anderson, Keyur Mehta, Susan Minton, Francesca Poggio, Kathy S. Albain, Douglas J.A. Adamson, Bernd Gerber, Amy Cripps, Gianfilippo Bertelli, Sabine Seiler, Marcello Ceppi, Ann H. Partridge, and Lucia Del Mastro

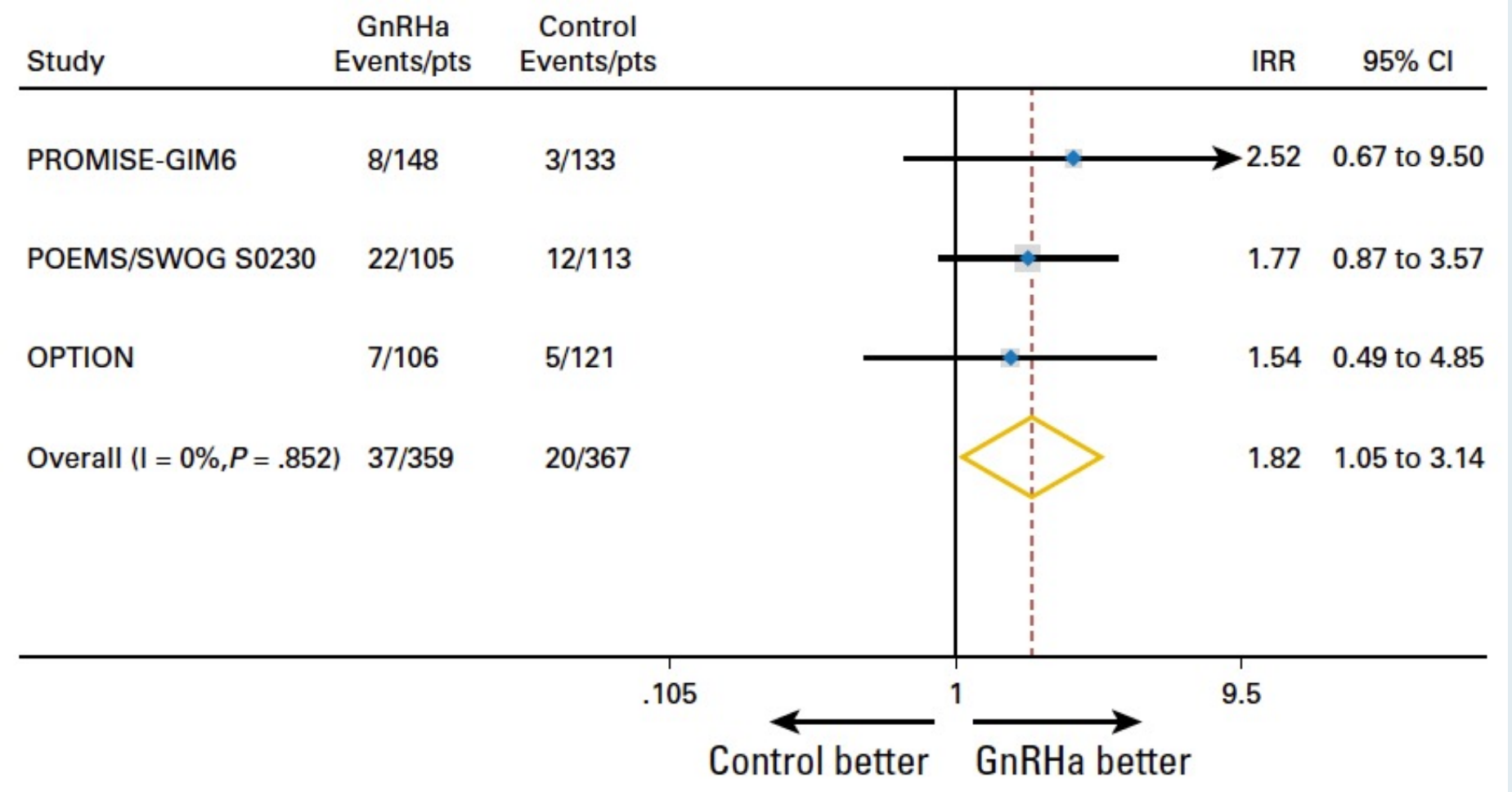
Meta-analysis of Gonadotropin-Releasing Hormone Analogues During Chemotherapy for Localized Breast Cancer: Premature Ovarian Insufficiency by Trial

- 873 randomized patients from 5 major trials were included in the meta-analysis



Lambertini M et al. *J Clin Oncol* 2018;36(19):1981-90.

Meta-analysis of Gonadotropin-Releasing Hormone Analogues During Chemotherapy for Localized Breast Cancer: Post-treatment Pregnancies by Trial



Lambertini M et al. *J Clin Oncol* 2018;36(19):1981-90.

HR-Positive Metastatic Breast Cancer

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San Antonio Breast Cancer Symposium®, December 6-10, 2022

Abstract GS3-01

EMERALD phase 3 trial of elacestrant versus standard of care endocrine therapy in patients with ER+/HER2- metastatic breast cancer: updated results by duration of prior CDK4/6i in metastatic setting

Bardia A,[1*] Bidard FC,[2*] Neven P,[3] Streich G,[4] Montero AJ,[5] Forget F,[6] Mouret-Reynier MA,[7] Sohn JH,[8] Taylor D,[9] Harnden KK,[10] Khong H,[11] Kocsis J,[12] Dalenc F,[13] Dillon P,[14] Babu S,[15] Waters S,[16] Deleu I,[17] Garcia-Saenz J,[18] Bria E,[19] Cazzaniga M,[20] Aftimos P,[21] Cortes J,[22] Tonini G,[23] Tarek Sahmoud,[24] Habboubi N,[24] Grzegorzewski KJ,[24] **Kaklamani V**[25**]

*=Co-first
**=Presenting author

1. Massachusetts General Hospital Cancer Center, Harvard Medical School, Boston, MA, USA; 2. Institut Curie, Paris and Saint Cloud, France 3. Universitaire Ziekenhuizen (UZ) - Leuven Cancer Institute, Leuven, Belgium; 4. Centro Médico Austral, Buenos Aires, Argentina; 5. University Hospitals Seidman Cancer Center- Case Western Reserve University, Cleveland, OH, USA; 6. Centre Hospitalier de l'Ardenne - Site de Libramont, Libramont-Chevigny, Belgium; 7. Centre Jean Perrin, Clermont-Ferrand, France; 8. Yonsei Cancer Center, Yonsei University Health System -Medical Oncology, Seoul, Republic of Korea; 9. Universite catholiqué de Louvain, CHU UCL Namur—Site Sainte-Elisabeth, Namur, Belgium; 10. Inova Schar Cancer Institute, Fairfax, VA, USA; 11. Moffit Cancer Center & Research Institute, Tampa, FL, USA; 12. Bács-Kiskun Megyei Kórház, Kecskemét, Hungary; 13. Institut Claudius Regaud, IUCT-Oncopole, Toulouse, France; 14. University of Virginia Cancer Center, Charlottesville, VA, USA; 15. Fort Wayne Medical Oncology and Hematology, Fort Wayne, IN, USA; 16. Velindre Cancer Centre, Cardiff, UK; 17. AZ Nikolaas, Sint-Niklaas, Belgium; 18. Instituto de Investigación Sanitaria Hospital Clinico San Carlos (IdISSC), Madrid, Spain; 19. Fondazione Policlinico Universitario Agostino Gemelli IRCCS, Università Cattolica del Sacro Cuore, Roma, Italy; 20. Ospedale San Gerardo-ASST Monza, Monza, Italy; 21. Institut Jules Bordet – Université Libre de Bruxelles, Brussels, Belgium; 22. International Breast Cancer Center (IBCC), Quiron Group, Barcelona, Spain; 23. Menarini Group, Florence, Italy; 24. Stemline Therapeutics/Menarini Group, New York, NY, USA; 25. University of Texas Health Sciences Center, San Antonio, TX, USA

EMERALD: PFS Analyses by CDK4/6 Inhibitor Duration

Duration of CDK4/6i	<6 months		6-12 months		12-18 months		≥18 months	
All patients	**Elacestrant (n = 29)**	**SOC ET (n = 29)**	**Elacestrant (n = 52)**	**SOC ET (n = 46)**	**Elacestrant (n = 52)**	**SOC ET (n = 40)**	**Elacestrant (n = 98)**	**SOC ET (n = 119)**
Median PFS	3.6 mo	1.9 mo	1.9 mo	1.9 mo	3.5 mo	1.8 mo	5.5 mo	3.3 mo
Patients with ESR1 mutations	**Elacestrant (n = 9)**	**SOC ET (n = 8)**	**Elacestrant (n = 25)**	**SOC ET (n = 21)**	**Elacestrant (n = 23)**	**SOC ET (n = 25)**	**Elacestrant (n = 55)**	**SOC ET (n = 56)**
Median PFS	1.9 mo	1.9 mo	1.9 mo	1.8 mo	5.5 mo	1.8 mo	8.6 mo	2.1 mo

Bardia A et al. SABCS 2022;Abstract GS3-01.

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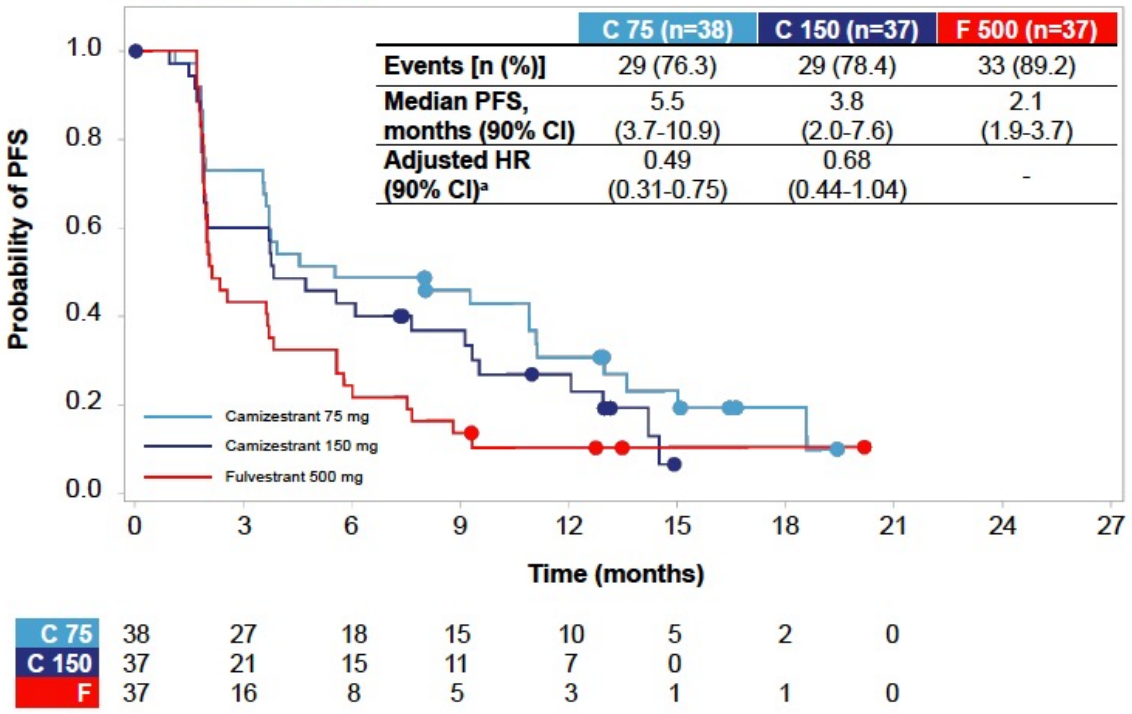
SERENA-2: PFS by Prior CDK4/6 Inhibitor Use

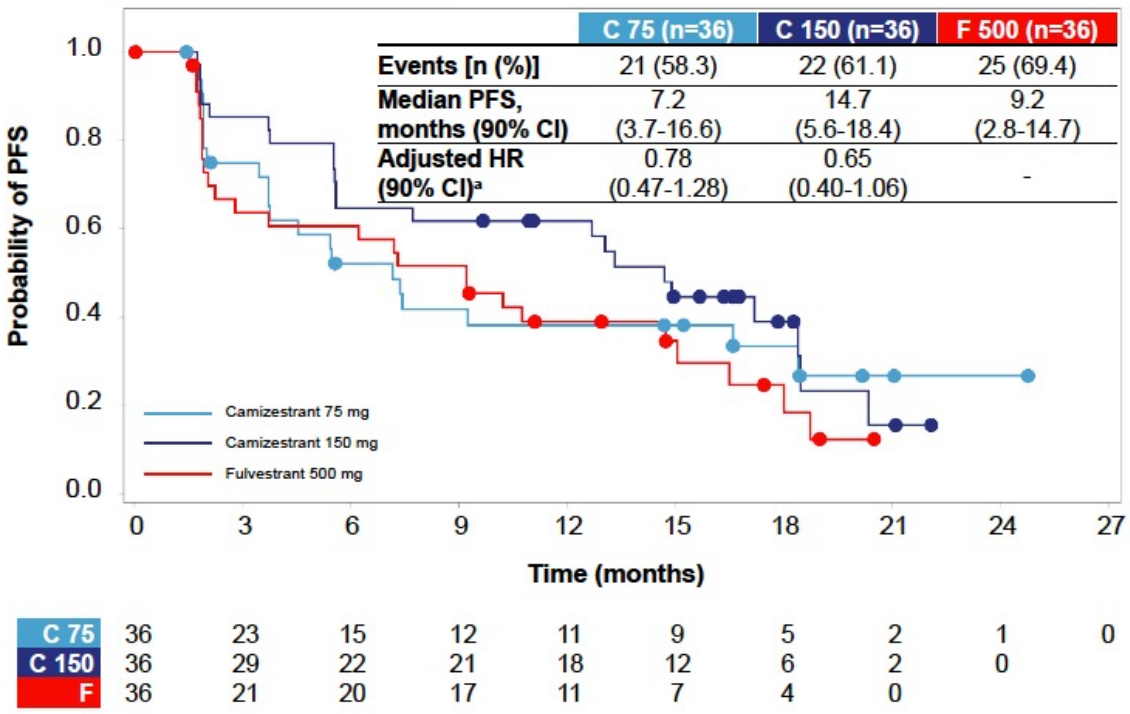
Prior CDK4/6i



	C 75 (n=38)	C 150 (n=37)	F 500 (n=37)
Events [n (%)]	29 (76.3)	29 (78.4)	33 (89.2)
Median PFS, months (90% CI)	5.5 (3.7-10.9)	3.8 (2.0-7.6)	2.1 (1.9-3.7)
Adjusted HR (90% CI)[a]	0.49 (0.31-0.75)	0.68 (0.44-1.04)	-

C 75	38	27	18	15	10	5	2	0
C 150	37	21	15	11	7	0		
F	37	16	8	5	3	1	1	0

No prior CDK4/6i



	C 75 (n=36)	C 150 (n=36)	F 500 (n=36)
Events [n (%)]	21 (58.3)	22 (61.1)	25 (69.4)
Median PFS, months (90% CI)	7.2 (3.7-16.6)	14.7 (5.6-18.4)	9.2 (2.8-14.7)
Adjusted HR (90% CI)[a]	0.78 (0.47-1.28)	0.65 (0.40-1.06)	-

C 75	36	23	15	12	11	9	5	2	1	0
C 150	36	29	22	21	18	12	6	2	0	
F	36	21	20	17	11	7	4	0		

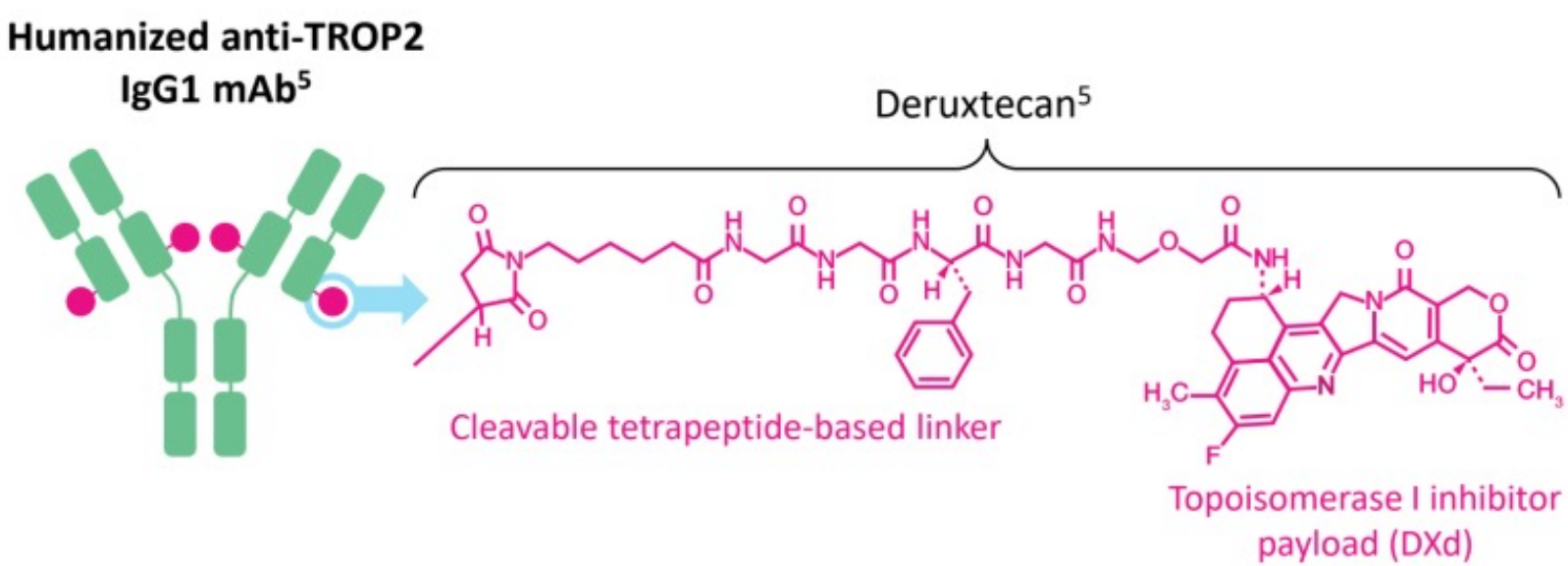
- In the sub-population of patients previously treated with CDK4/6i + endocrine therapy, camizestrant at both doses produces a clinically meaningful improvement in PFS over fulvestrant

[a]HRs adjusted for liver/lung metastases

CI: confidence interval; CDK4/6i: CDK4/6 inhibitor; HR: hazard ratio; PFS: progression-free survival

Oliveira M et al. SABCS 2022;Abstract GS3-02.

Datopotamab Deruxtecan Mechanism of Action



7 Key Attributes

- Payload mechanism of action: topoisomerase I inhibitor[5-7,a]
- High potency of payload[5-7,a]
- Optimized drug to antibody ratio ≈4[5,a,b]
- Payload with short systemic half-life[5-7,a,b]
- Stable linker-payload[5-7,a]
- Tumor-selective cleavable linker[5-7,a]
- Bystander antitumor effect[6,8,a]

[a] The clinical relevance of these features is under investigation.
[b] Based on animal data.

Meric-Bernstam F et al. SABCS 2022;Abstract PD13-08.

RTP RESEARCH TO PRACTICE

2022 ASCO ANNUAL MEETING **Abstract LBA3** DESTINY-Breast04

Trastuzumab deruxtecan (T-DXd) vs treatment of physician's choice in patients with HER2-low unresectable and/or metastatic breast cancer: Results of DESTINY-Breast04, a randomized, phase 3 study

Shanu Modi Memorial Sloan Kettering Cancer Center, Memorial Hospital, New York, NY, USA

June 5, 2022

Additional authors: William Jacot, Toshinari Yamashita, Joo Hyuk Sohn, Maria Vidal, Eriko Tokunaga, Junji Tsurutani, Naoto Ueno, Yee Soo Chae, Keun Seok Lee, Naoki Niikura, Yeon Hee Park, Xiaojia Wang, Binghe Xu, Dhiraj Gambhire, Lotus Yung, Gerold Meinhardt, Yibin Wang, Nadia Harbeck, David Cameron

On behalf of the DESTINY-Breast04 investigators

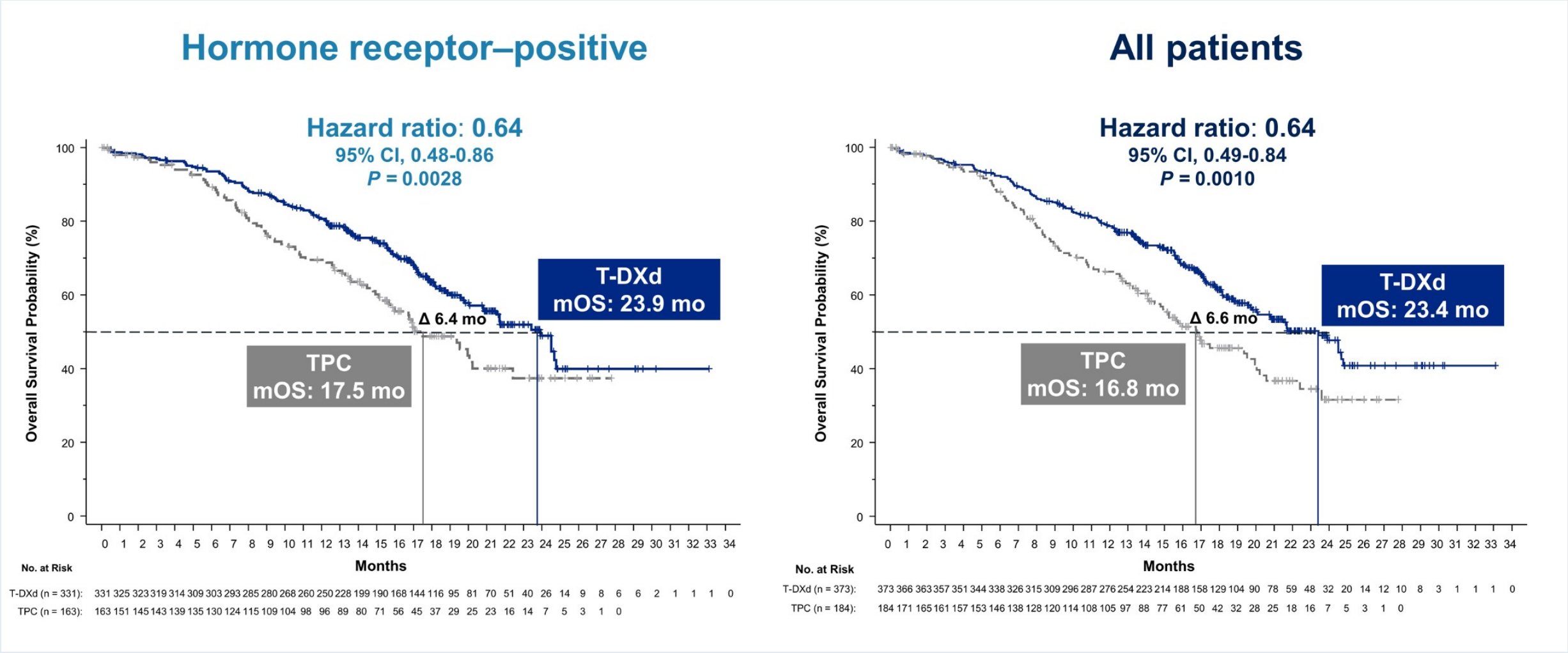
The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812 JULY 7, 2022 VOL. 387 NO. 1

Trastuzumab Deruxtecan in Previously Treated HER2-Low Advanced Breast Cancer

S. Modi, W. Jacot, T. Yamashita, J. Sohn, M. Vidal, E. Tokunaga, J. Tsurutani, N.T. Ueno, A. Prat, Y.S. Chae, K.S. Lee, N. Niikura, Y.H. Park, B. Xu, X. Wang, M. Gil-Gil, W. Li, J.-Y. Pierga, S.-A. Im, H.C.F. Moore, H.S. Rugo, R. Yerushalmi, F. Zagouri, A. Gombos, S.-B. Kim, Q. Liu, T. Luo, C. Saura, P. Schmid, T. Sun, D. Gambhire, L. Yung, Y. Wang, J. Singh, P. Vitazka, G. Meinhardt, N. Harbeck, and D.A. Cameron, for the DESTINY-Breast04 Trial Investigators*

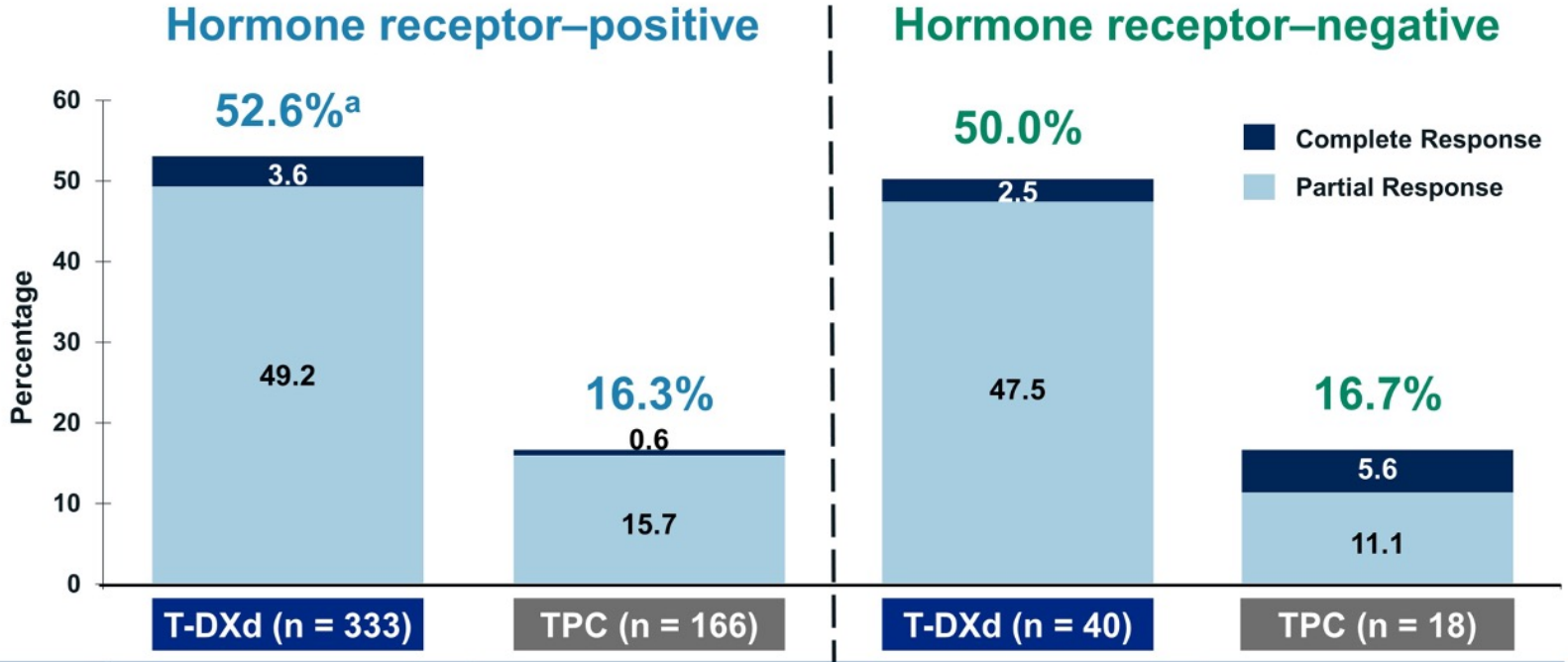
DESTINY-Breast04: OS for HR-Positive and All Patients



mOS = median overall survival

Modi S et al. ASCO 2022;Abstract LBA3. Modi S et al. *N Engl J Med* 2022 July 7;387(1):9-20.

DESTINY-Breast04: Confirmed Objective Response Rate



	T-DXd (n = 333)	TPC (n = 166)	T-DXd (n = 40)	TPC (n = 18)
Progressive disease, %	7.8	21.1	12.5	33.3
Not evaluable, %	4.2	12.7	7.5	5.6
Clinical benefit rate,[b] %	71.2	34.3	62.5	27.8
Duration of response, months	10.7	6.8	8.6	4.9

Modi S et al. ASCO 2022;Abstract LBA3. Modi S et al. *N Engl J Med* 2022 July 7;387(1):9-20.

DESTINY-Breast04: Response and Survival with T-DXd in the HR-Negative Population

	All patients			Hormone-receptor negative		
	T-DXd (N = 373)	TPC (N = 184)	HR (*p*-value)	T-DXd (N = 40)	TPC (N = 18)	Hazard ratio
Median PFS	9.9 mo	5.1 mo	0.5 (<0.001)	8.5 mo	2.9 mo	0.46
Median OS	23.4 mo	16.8 mo	0.64 (0.001)	18.2 mo	8.3 mo	0.48
Objective response rate	52.3%	16.3%	—	50.0%	16.7%	—

Modi S et al. *N Engl J Med* 2022 July;387(1):9-20.

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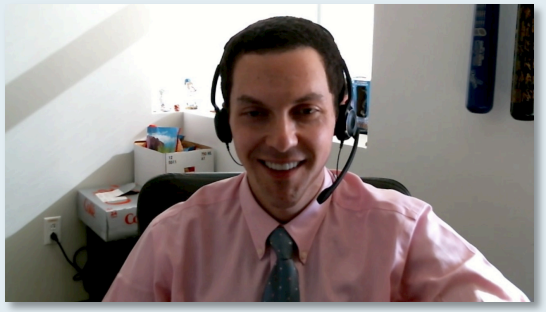

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Cases from the Community: Investigators Discuss Available Research Guiding the Care of Patients with Gastroesophageal and Hepatobiliary Cancers — A 2023 Post-ASCO GI Webcast

A CME/MOC-Accredited Virtual Event

Wednesday, March 8, 2023

5:00 PM – 6:00 PM ET

General Medical Oncologists

Eric H Lee, MD, PhD

Neil Morganstein, MD

Swati Vishwanathan, MD

Moderator

Neil Love, MD

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Thank you for joining us!

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

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

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