What Clinicians Want to Know About the Management of Triple-Negative Breast Cancer

A CME/MOC-Accredited Live Webinar

Thursday, June 20, 2024
5:00 PM – 6:00 PM ET

Faculty

Kevin Kalinsky, MD, MS
Heather McArthur, MD, MPH

Moderator

Neil Love, MD

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Faculty

Kevin Kalinsky, MD, MS
Professor
Department of Hematology and Medical Oncology
Emory University School of Medicine
Director, Glenn Family Breast Center
Director, Breast Medical Oncology
Winship Cancer Institute of Emory University
Atlanta, Georgia

MODERATOR
Neil Love, MD
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Miami, Florida

Heather McArthur, MD, MPH
Associate Professor
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Clinical Director, Breast Cancer Program
Komen Distinguished Chair in Clinical Breast Cancer Research
UT Southwestern Medical Center
Dallas, Texas

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Dr Love — Disclosures

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Dr Gupta — Disclosures
Consulting Faculty

No relevant conflicts of interest to disclose.

Dr Kumar — Disclosures
Consulting Faculty

No relevant conflicts of interest to disclose.

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This educational activity contains discussion of non-FDA-approved uses of agents and regimens. Please refer to official prescribing information for each product for approved indications.

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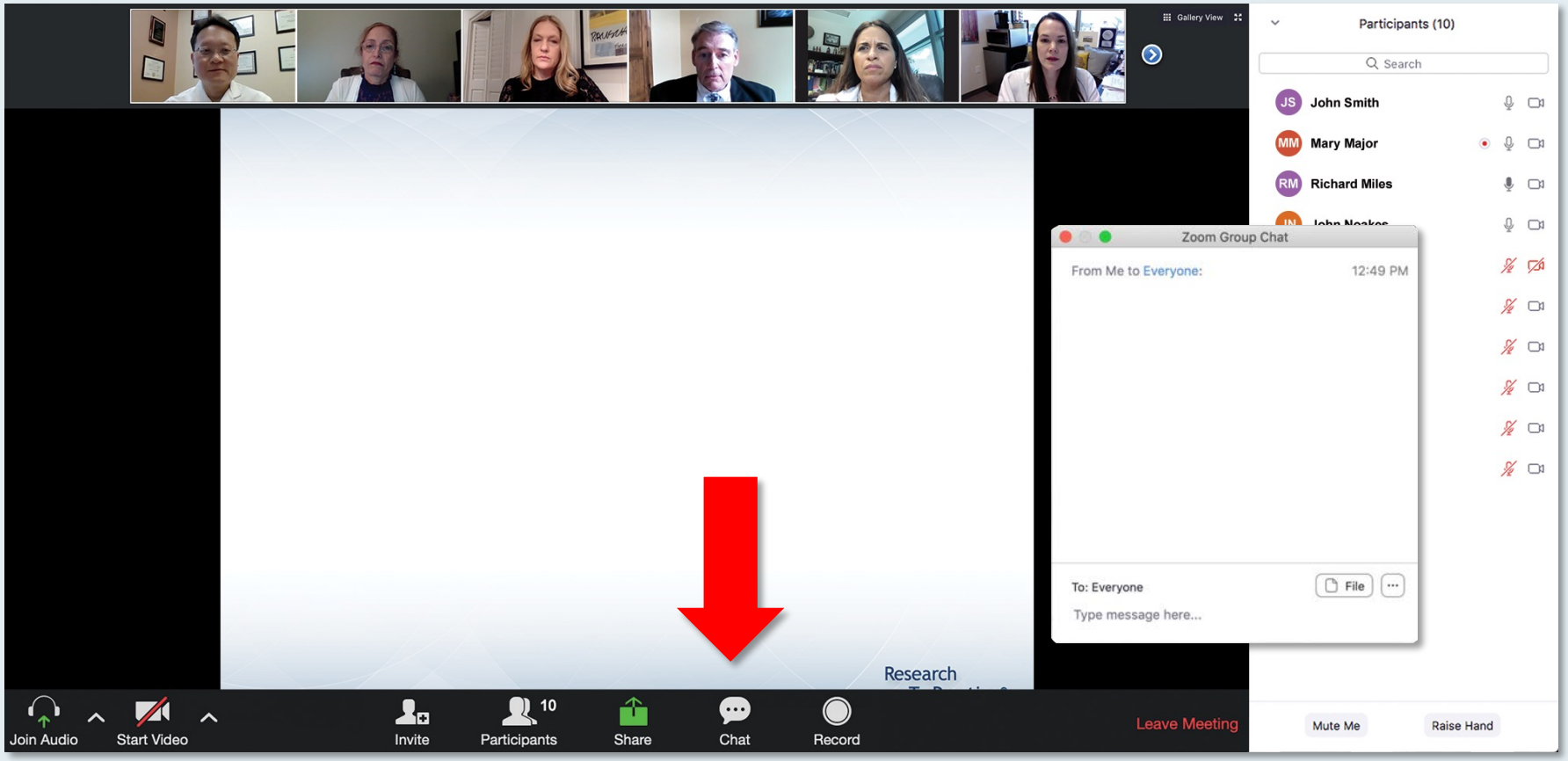

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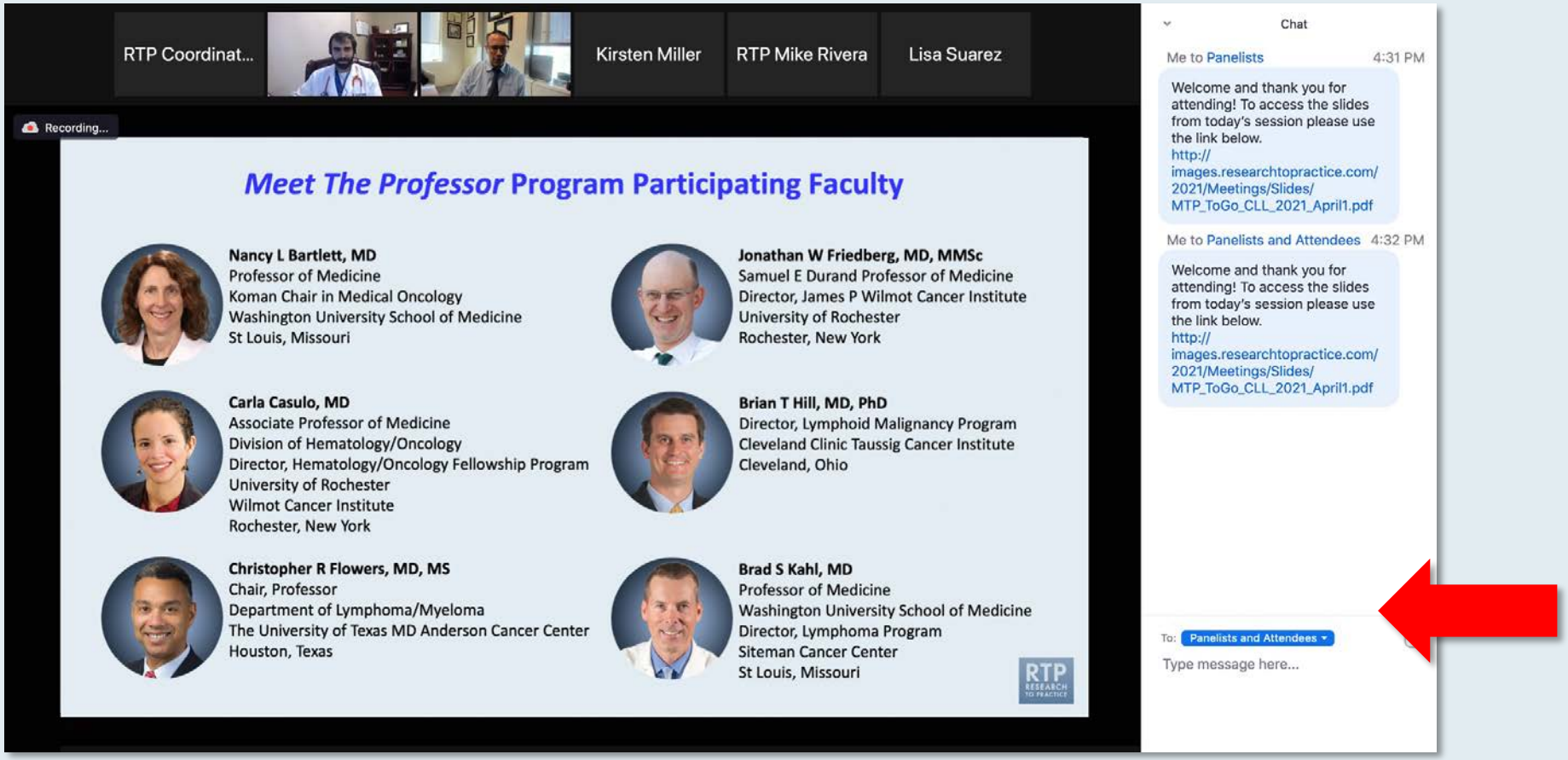

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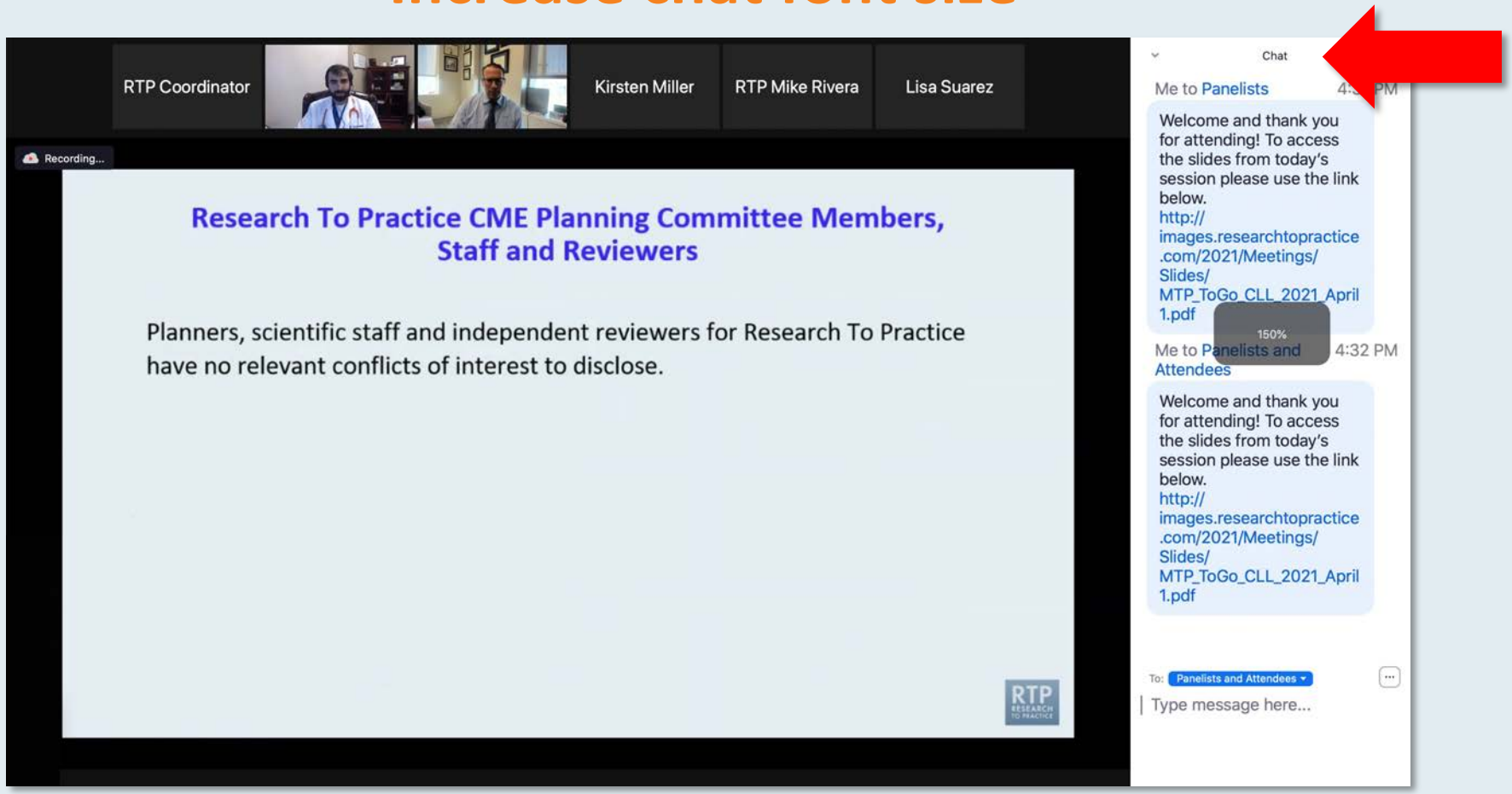

Press Command (for Mac) or Control (for PC) and the + symbol.
You may do this as many times as you need for readability.

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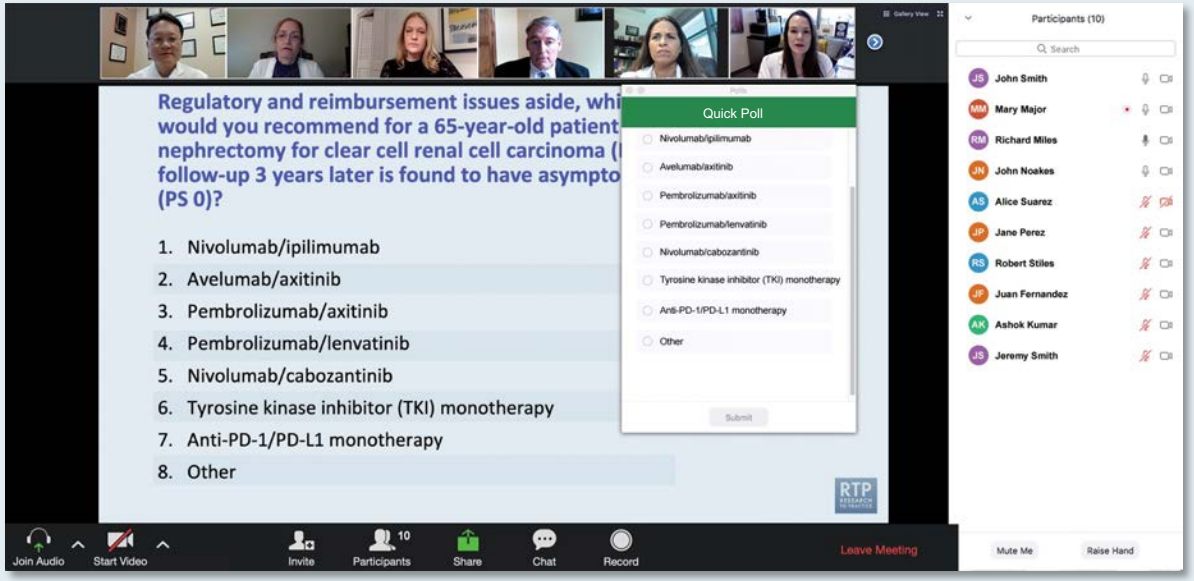

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WITH DR NEIL LOVE

Striving for Consensus: Exploring the Current Role of Ovarian Suppression in the Management of Breast Cancer

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NORTHWESTERN MEDICINE
FEINBERG SCHOOL OF MEDICINE

DR ERICA MAYER
DANA-FARBER CANCER INSTITUTE

DR VIRGINIA KAKLAMANI
UT HEALTH SAN ANTONIO
MD ANDERSON CANCER CENTER

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MASSACHUSETTS GENERAL HOSPITAL

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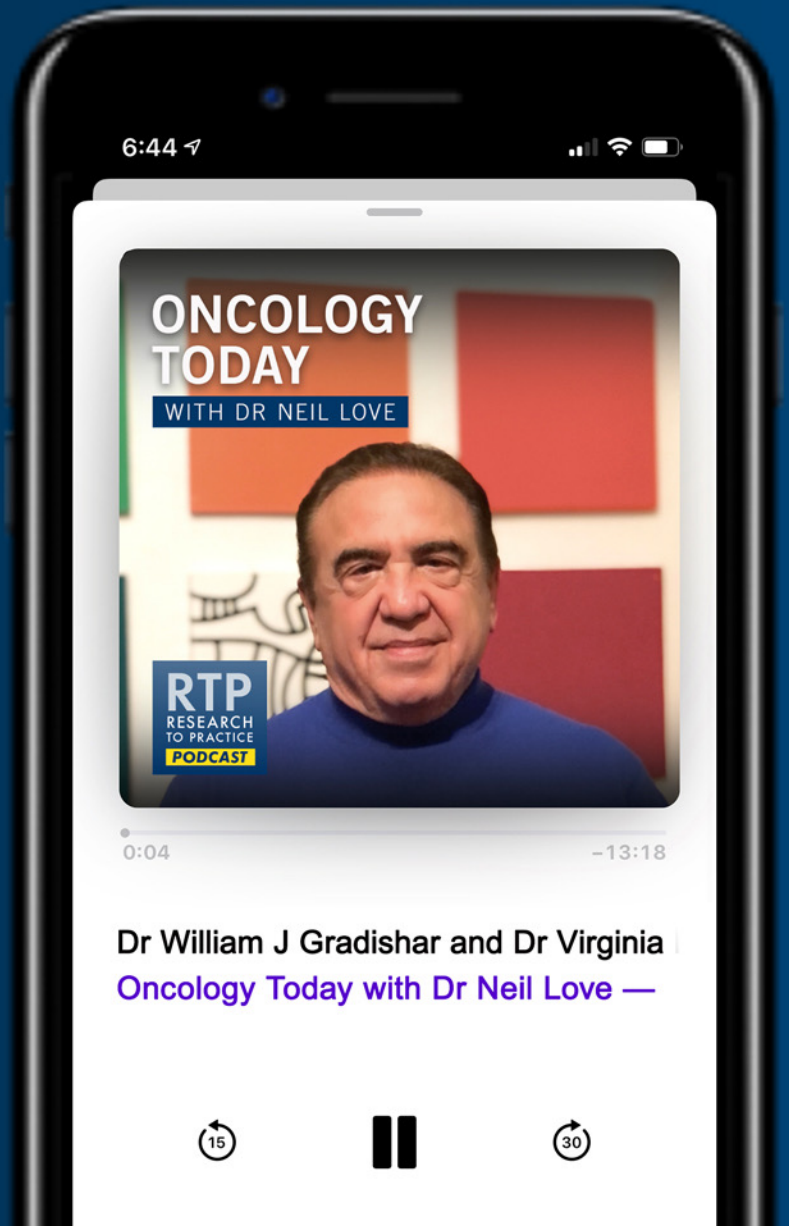

Year in Review: Gynecologic Oncology

A CME/MOC-Accredited Live Webinar

Tuesday, June 25, 2024
5:00 PM – 6:00 PM ET

Faculty

Dana M Chase, MD

Moderator

Neil Love, MD

RTP Year in Review 2024

Year in Review: Multiple Myeloma

A CME/MOC-Accredited Live Webinar

Tuesday, July 9, 2024
5:00 PM – 6:00 PM ET

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Jesús G Berdeja, MD
Thomas Martin, MD

Moderator

Neil Love, MD

RTP Year in Review 2024

Inside the Issue: Integrating Antibody-Drug Conjugates into the Management of HR-Positive and Triple-Negative Metastatic Breast Cancer

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Sara M Tolaney, MD, MPH

Moderator

Neil Love, MD

RTP RESEARCH TO PRACTICE

Inside the Issue: Integrating ALK-Targeted Therapy into the Management of Localized Non-Small Cell Lung Cancer

A CME/MOC-Accredited Live Webinar

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Professor Solange Peters, MD, PhD
Professor Ben Solomon, MBBS, PhD

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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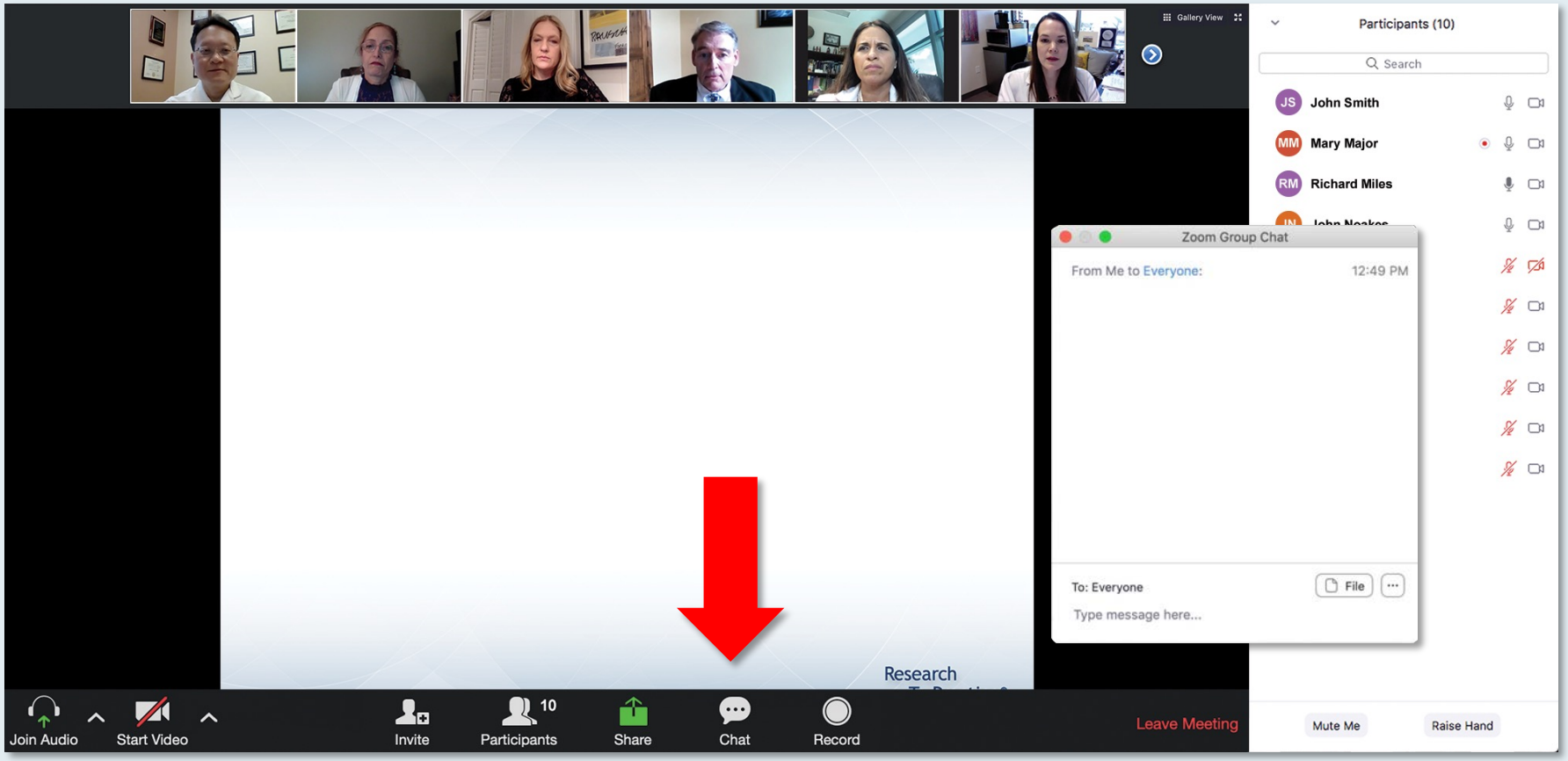

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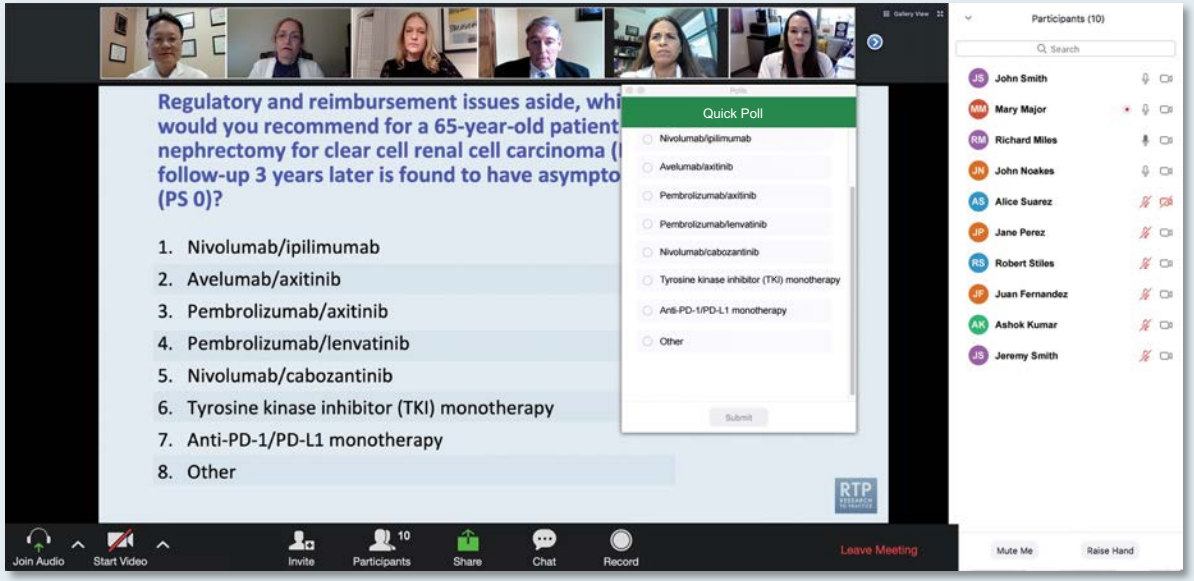

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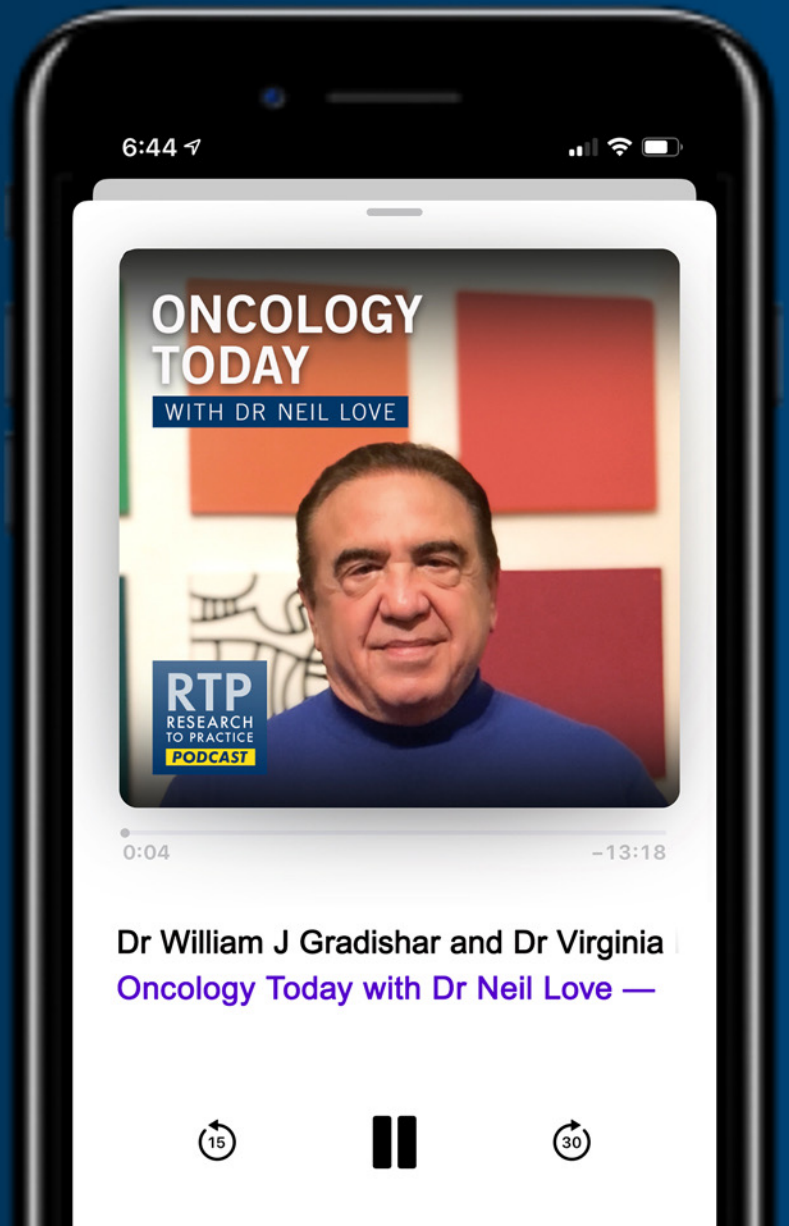

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Dr Kalinsky — Disclosures
Faculty

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Dr Gupta — Disclosures
Consulting Faculty

No relevant conflicts of interest to disclose.

Dr Kumar — Disclosures
Consulting Faculty

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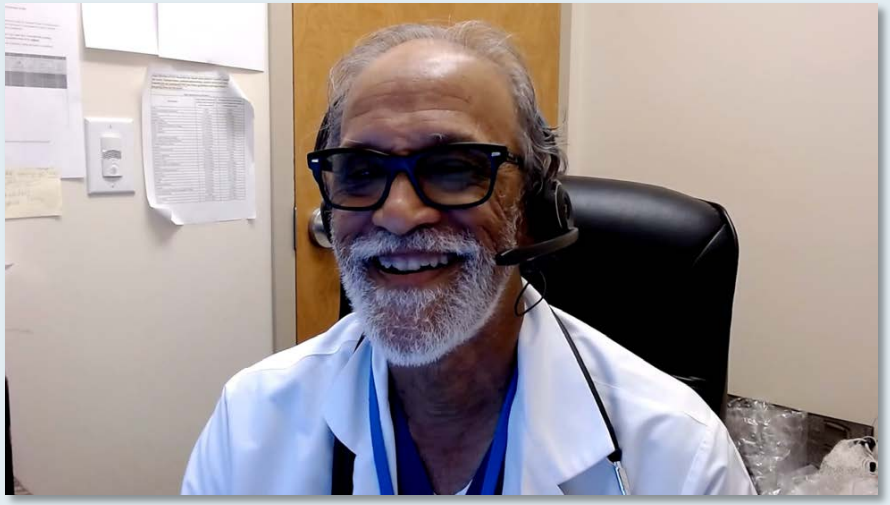
Consulting Faculty

Ranju Gupta, MD
Lehigh Valley Topper Cancer Institute
Bethlehem, Pennsylvania



Kapisthalam (KS) Kumar, MD
Florida Cancer Specialists & Research Institute
Trinity, Florida

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Agenda

Cases and Questions from Drs Gupta and Kumar

- **Dr Gupta**: 86-year-old woman with a 2.7-cm residual tumor after neoadjuvant pembrolizumab/ chemotherapy for localized TNBC
- **Dr Kumar**: Approach to neoadjuvant therapy and defining residual disease; PD-L1 status and efficacy of pembrolizumab in the localized and metastatic settings
- **Dr Kumar**: 65-year-old woman with node-positive TNBC and a single lung metastasis who receives neoadjuvant therapy based on the KEYNOTE-522 trial
- **Dr Kumar**: 70-year-old woman with localized TNBC and residual disease after poorly tolerated neoadjuvant pembrolizumab/chemotherapy and lumpectomy
- **Dr Gupta**: 69-year-old woman with widely metastatic ER-negative, HER2-low disease after multiple lines of treatment – CDH1 and ERBB2-V697L mutations, MSS, TMB 3 mut/Mb
- **Dr Kumar**: Adjuvant therapy selection for patients with localized TNBC with a BRCA mutation and residual disease; risk of AML/MDS associated with PARP inhibitor therapy
- **Dr Gupta**: 73-year-old woman who develops recurrent metastatic ER-negative, HER2-low breast cancer after *nab* paclitaxel/atezolizumab and receives sacituzumab govitecan
- **Dr Gupta**: 54-year-old woman with TNBC chest wall metastatic recurrence after fulvestrant/abemaciclib for ER-positive, HER2-negative breast cancer – PIK3CA mutation

Case Presentation: 86-year-old woman with a 2.7-cm residual tumor after neoadjuvant pembrolizumab/ chemotherapy for localized TNBC

Dr Ranju Gupta (Bethlehem, Pennsylvania)

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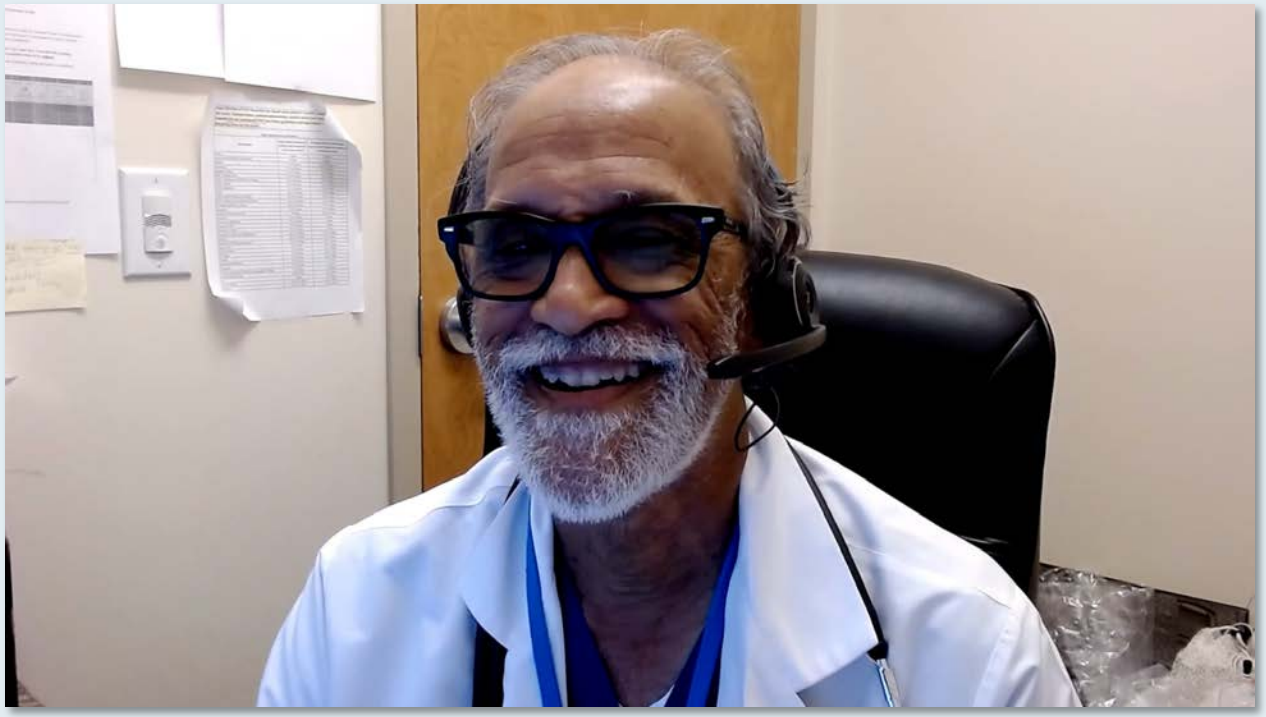
Question and Comments: Approach to neoadjuvant therapy and defining residual disease; PD-L1 status and efficacy of pembrolizumab in the localized and metastatic settings



Dr KS Kumar (Trinity, Florida)

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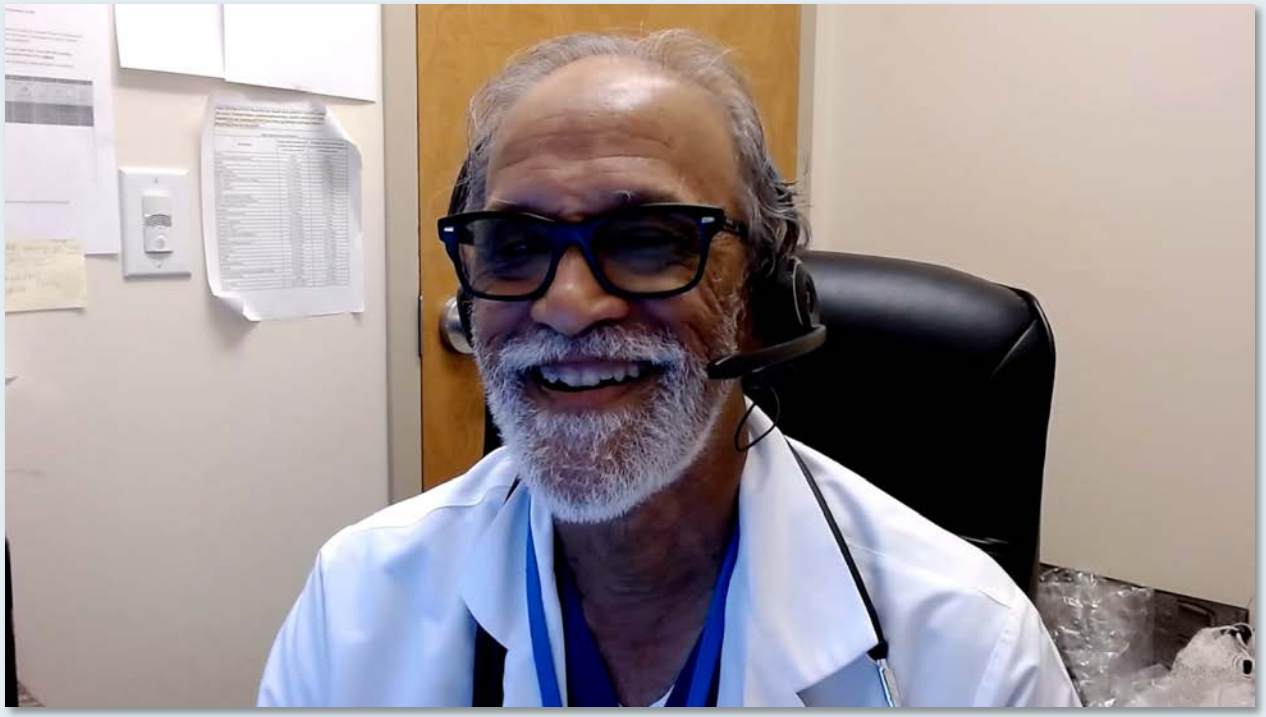
Case Presentation: 65-year-old woman with node-positive TNBC and a single lung metastasis who receives neoadjuvant therapy based on the KEYNOTE-522 trial



Dr KS Kumar (Trinity, Florida)

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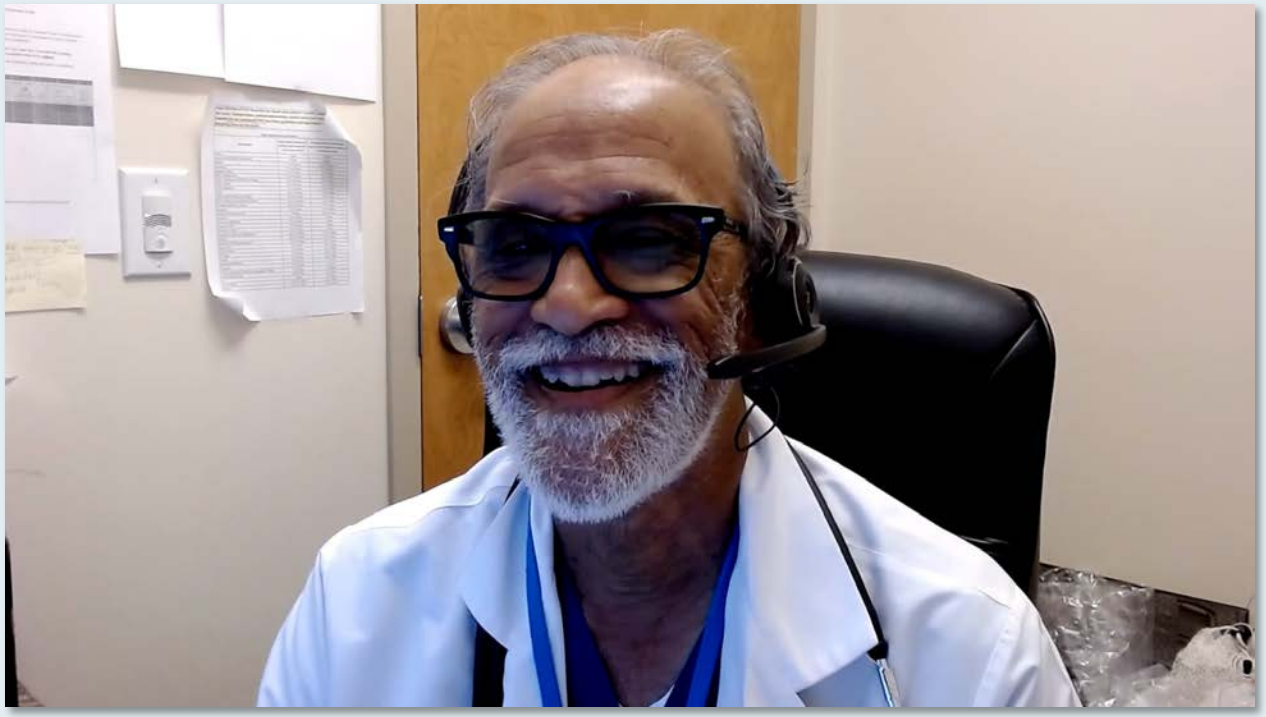
Case Presentation: 70-year-old woman with localized TNBC and residual disease after poorly tolerated neoadjuvant pembrolizumab/chemotherapy and lumpectomy



Dr KS Kumar (Trinity, Florida)

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2022;386(6):556-67

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Event-free Survival with Pembrolizumab in Early Triple-Negative Breast Cancer

P. Schmid, J. Cortes, R. Dent, L. Pusztai, H. McArthur, S. Kümmel, J. Bergh, C. Denkert, Y.H. Park, R. Hui, N. Harbeck, M. Takahashi, M. Untch, P.A. Fasching, F. Cardoso, J. Andersen, D. Patt, M. Danso, M. Ferreira, M.-A. Mouret-Reynier, S.-A. Im, J.-H. Ahn, M. Gion, S. Baron-Hay, J.-F. Boileau, Y. Ding, K. Tryfonidis, G. Aktan, V. Karantza, and J. O'Shaughnessy, for the KEYNOTE-522 Investigators*

Neoadjuvant Pembrolizumab or Placebo Plus Chemotherapy Followed by Adjuvant Pembrolizumab or Placebo for Early-Stage Triple-Negative Breast Cancer: Updated Event-Free Survival Results From the Phase 3 KEYNOTE-522 Study

Peter Schmid[1]; Javier Cortes[2]; Rebecca Dent[3]; Lajos Pusztai[4]; Heather McArthur[5]; Sherko Kümmel[6]; Carsten Denkert[7]; Yeon Hee Park[8]; Rina Hui[9]; Nadia Harbeck[10]; Masato Takahashi[11]; Theodoros Foukakis[12]; Marie-Ange Mouret-Reynier[13]; Marta Ferreira[14]; Seock-Ah Im[15]; Michael Untch[16]; Peter A. Fasching[17]; Fatima Cardoso[18]; Yu Ding[19]; Wilbur Pan[19]; Konstantinos Tryfonidis[19]; Joyce O'Shaughnessy[20]

SABCS 2023;Abstract LB01-01.

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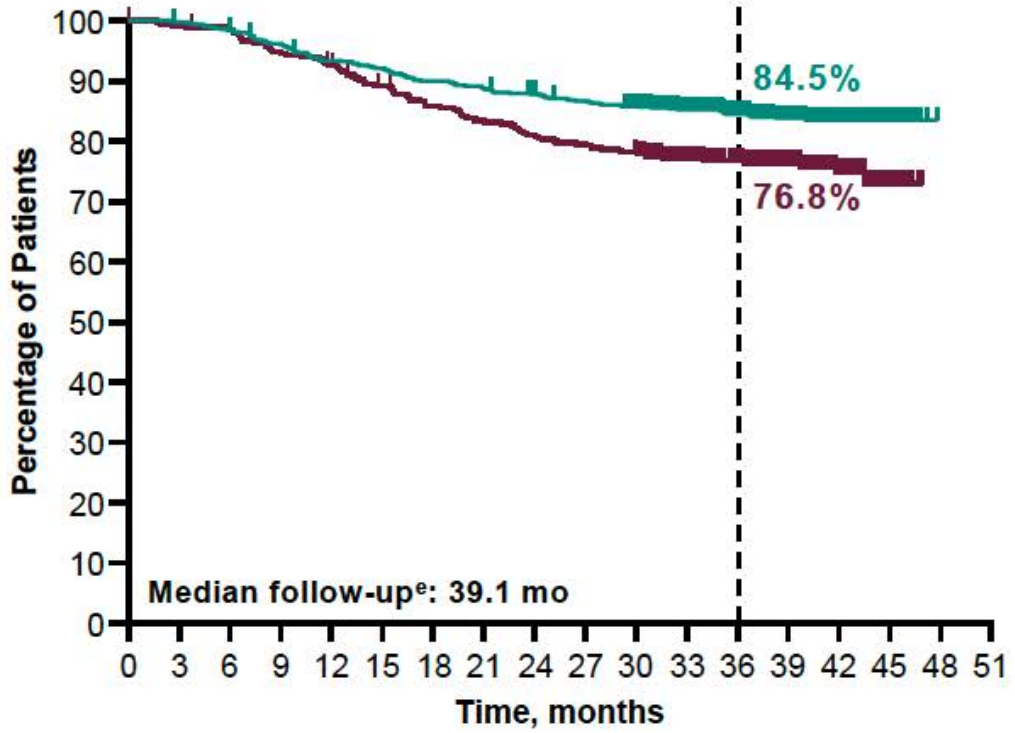
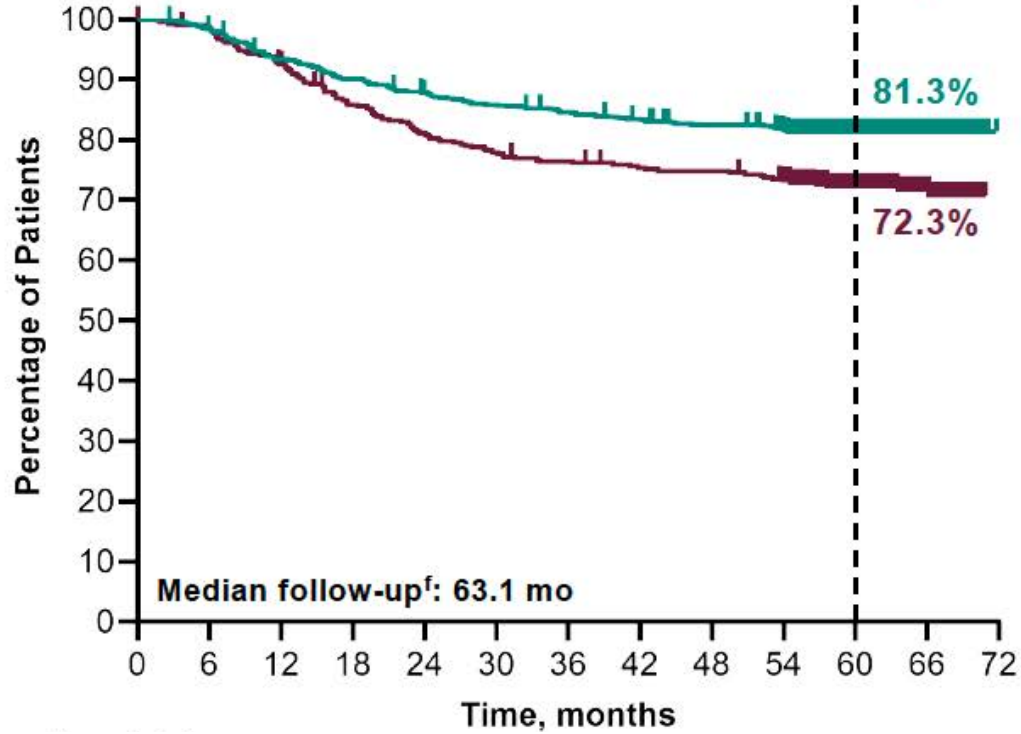
KEYNOTE-522: Event-Free Survival (EFS) by Interim Analysis

IA4[a]	Events	HR (95% CI)	*P* value
Pembro + Chemo/Pembro	15.7%	0.63[c] (0.48–0.82)	0.00031[d]
Placebo + Chemo/Placebo	23.8%		



IA6[b]	Events	HR (95% CI)
Pembro + Chemo/Pembro	18.5%	0.63[c] (0.49–0.81)
Placebo + Chemo/Placebo	27.7%	



IA4 = fourth prespecified interim analysis; IA6 = sixth prespecified interim analysis

Schmid P et al. SABCS 2023;Abstract LB01-01; *N Engl J Med* 2022;386(6):556-67.

Phase III KEYNOTE-522 Trial Meets Overall Survival Endpoint for Patients with High-Risk Early-Stage TNBC

Press Release: May 28, 2024

"**New OS results build on the pathological complete response and event-free survival data previously reported from the KEYNOTE-522 trial.**

Today [it was] announced that the Phase 3 KEYNOTE-522 trial evaluating pembrolizumab ... met its overall survival (OS) endpoint, in combination with chemotherapy as pre-operative (neoadjuvant) treatment and then continuing as a single agent after surgery (adjuvant) for the treatment of patients with high-risk early-stage triple-negative breast cancer (TNBC). At a pre-specified interim analysis conducted by an independent Data Monitoring Committee, pembrolizumab demonstrated a statistically significant and clinically meaningful improvement in OS compared to pre-operative chemotherapy.

The safety profile of pembrolizumab was consistent with that observed in previously reported studies; no new safety signals were observed. Results will be presented at an upcoming medical meeting and shared with regulatory authorities."

https://www.merck.com/news/merck-announces-phase-3-keynote-522-trial-met-its-overall-survival-os-endpoint-in-patients-with-high-risk-early-stage-triple-negative-breast-cancer-tnbc/

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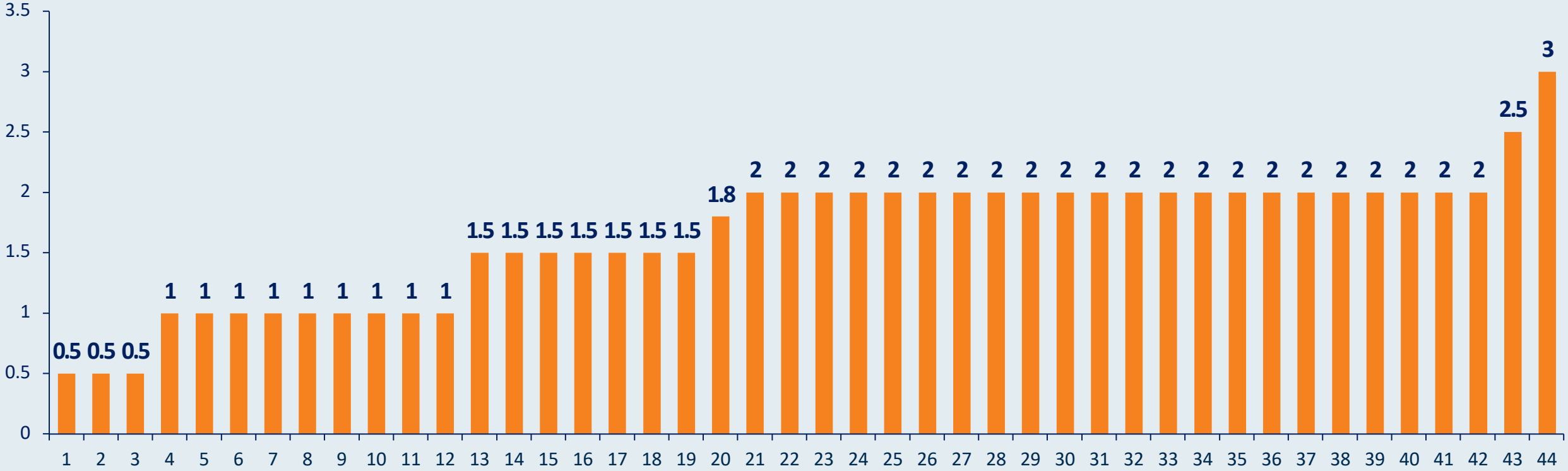
For a patient with localized triple-negative breast cancer (TNBC) and clinically negative axilla, what is the smallest size of tumor for which would you generally recommend neoadjuvant chemotherapy/pembrolizumab → adjuvant pembrolizumab?

Median: 2 cm

Range: 0.5-3 cm



Survey of US-based general medical oncologists

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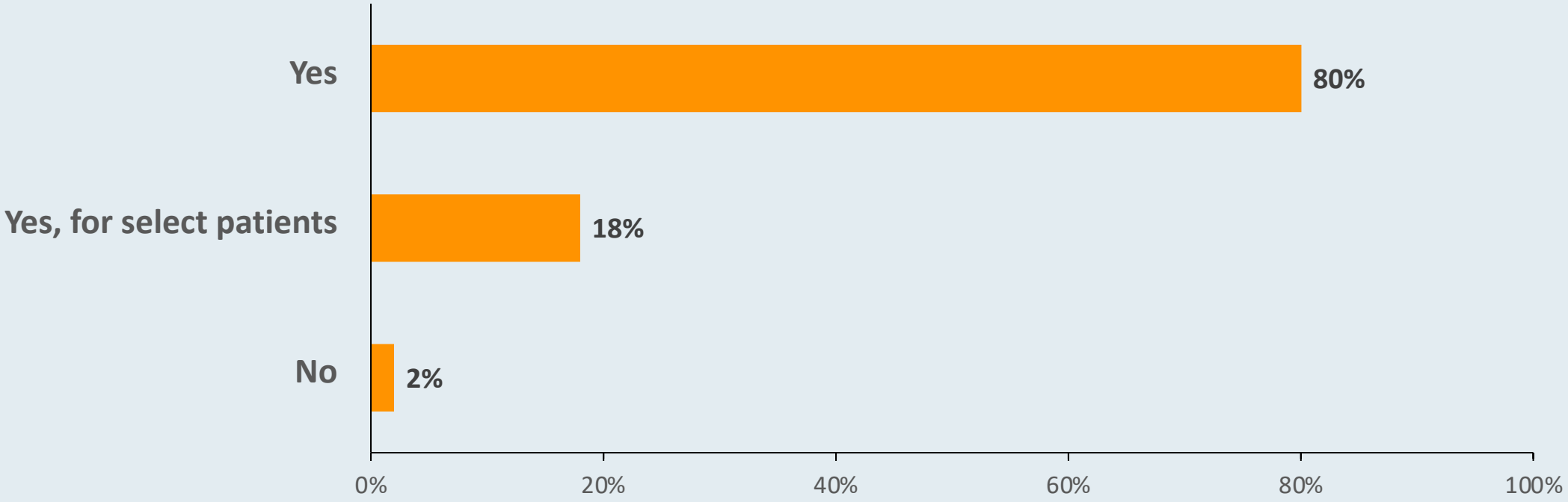
Do you generally administer adjuvant pembrolizumab to patients with localized TNBC who receive neoadjuvant chemotherapy/pembrolizumab and are found at surgery to have a pathologic complete response?



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MADRID 2023 ESMO congress

Trastuzumab Deruxtecan (T-DXd) Versus Treatment of Physician's Choice (TPC) in Patients With HER2-Low Unresectable and/or Metastatic Breast Cancer: Updated Survival Results of the Randomized, Phase 3 DESTINY-Breast04 Study

Presentation 376O

Shanu Modi,[1] William Jacot, Hiroji Iwata, Yeon Hee Park, Maria Jesus Vidal Losada, Wei Li, Junji Tsurutani, Khalil Zaman, Naoto Ueno, Aleix Prat, Konstantinos Papazisis, Hope S. Rugo, Nadia Harbeck, Seock-Ah Im, Michelino De Laurentis, Cecilia Orbegoso Aguilar, Lotus Yung, Fu-Chih Cheng, Yingkai Cheng, David Cameron

On behalf of the DESTINY-Breast04 investigators

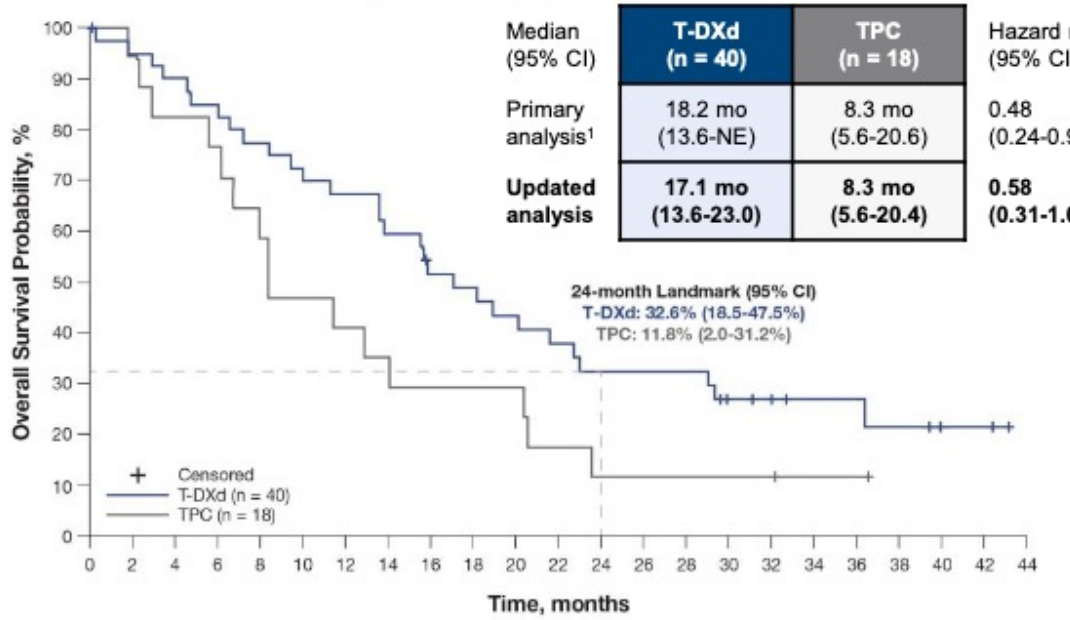
[1]Memorial Sloan Kettering Cancer Center, New York, NY, USA

Madrid, Spain, October 20-24, 2023

DESTINY-Breast04: Exploratory Analyses of Efficacy in the HR-Negative Cohort

Overall Survival

Median (95% CI)	T-DXd (n = 40)	TPC (n = 18)	Hazard ratio (95% CI)
Primary analysis[1]	18.2 mo (13.6-NE)	8.3 mo (5.6-20.6)	0.48 (0.24-0.95)
Updated analysis	**17.1 mo (13.6-23.0)**	**8.3 mo (5.6-20.4)**	**0.58 (0.31-1.08)**



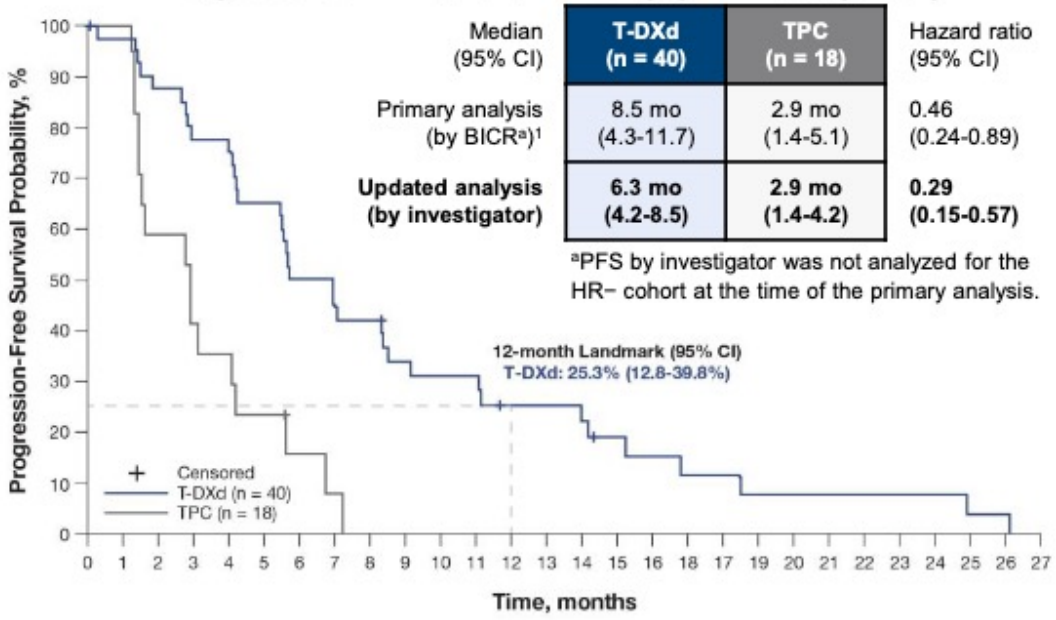
Patients still at risk:

T-DXd (n = 40)	40	38	36	34	31	28	26	23	19	18	16	14	12	12	12	8	7	5	5	4	2	2	0
TPC (n = 18)	18	16	14	13	10	8	7	6	5	5	5	3	2	2	2	2	2	1	1	0	0	0	0

Progression-Free Survival (by Investigator)

Median (95% CI)	T-DXd (n = 40)	TPC (n = 18)	Hazard ratio (95% CI)
Primary analysis (by BICR[a])[1]	8.5 mo (4.3-11.7)	2.9 mo (1.4-5.1)	0.46 (0.24-0.89)
Updated analysis (by investigator)	**6.3 mo (4.2-8.5)**	**2.9 mo (1.4-4.2)**	**0.29 (0.15-0.57)**

[a]PFS by investigator was not analyzed for the HR− cohort at the time of the primary analysis.



Patients still at risk:

T-DXd (n = 40)	40	39	35	31	30	26	19	17	16	12	11	11	8	8	7	5	4	3	3	2	2	2	2	2	2	1	1	0
TPC (n = 18)	18	17	10	7	6	4	2	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0

- There was a 42% reduction in risk of death and 71% reduction in risk of disease progression or death for HR− patients receiving T-DXd compared with TPC

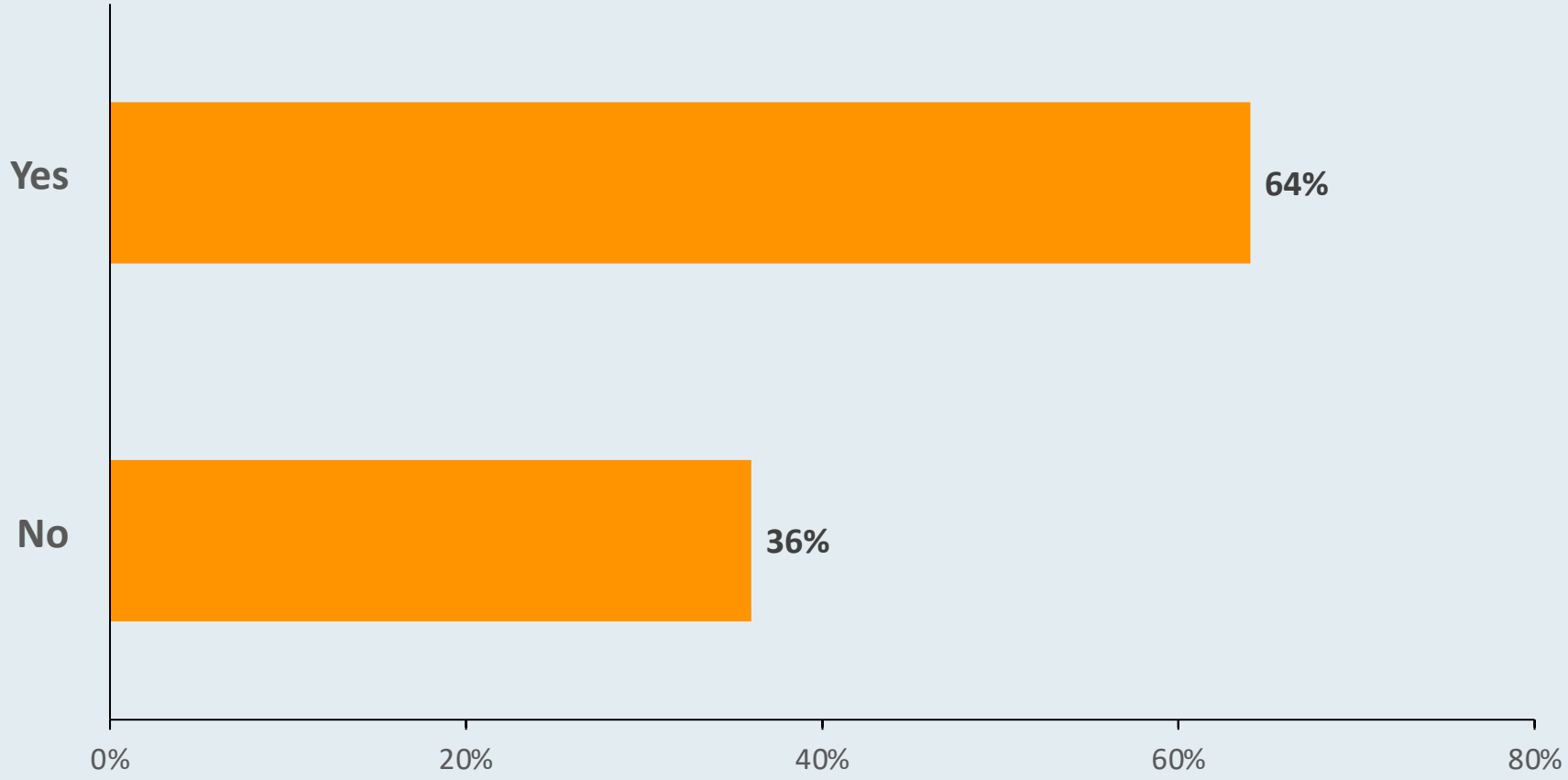
BICR, blinded independent central review; HR, hormone receptor; mo, month; NE, not evaluable; OS, overall survival; T-DXd, trastuzumab deruxtecan; TPC, treatment of physician's choice.

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

Modi S et al. ESMO 2023;Abstract 376O.

RTP RESEARCH TO PRACTICE

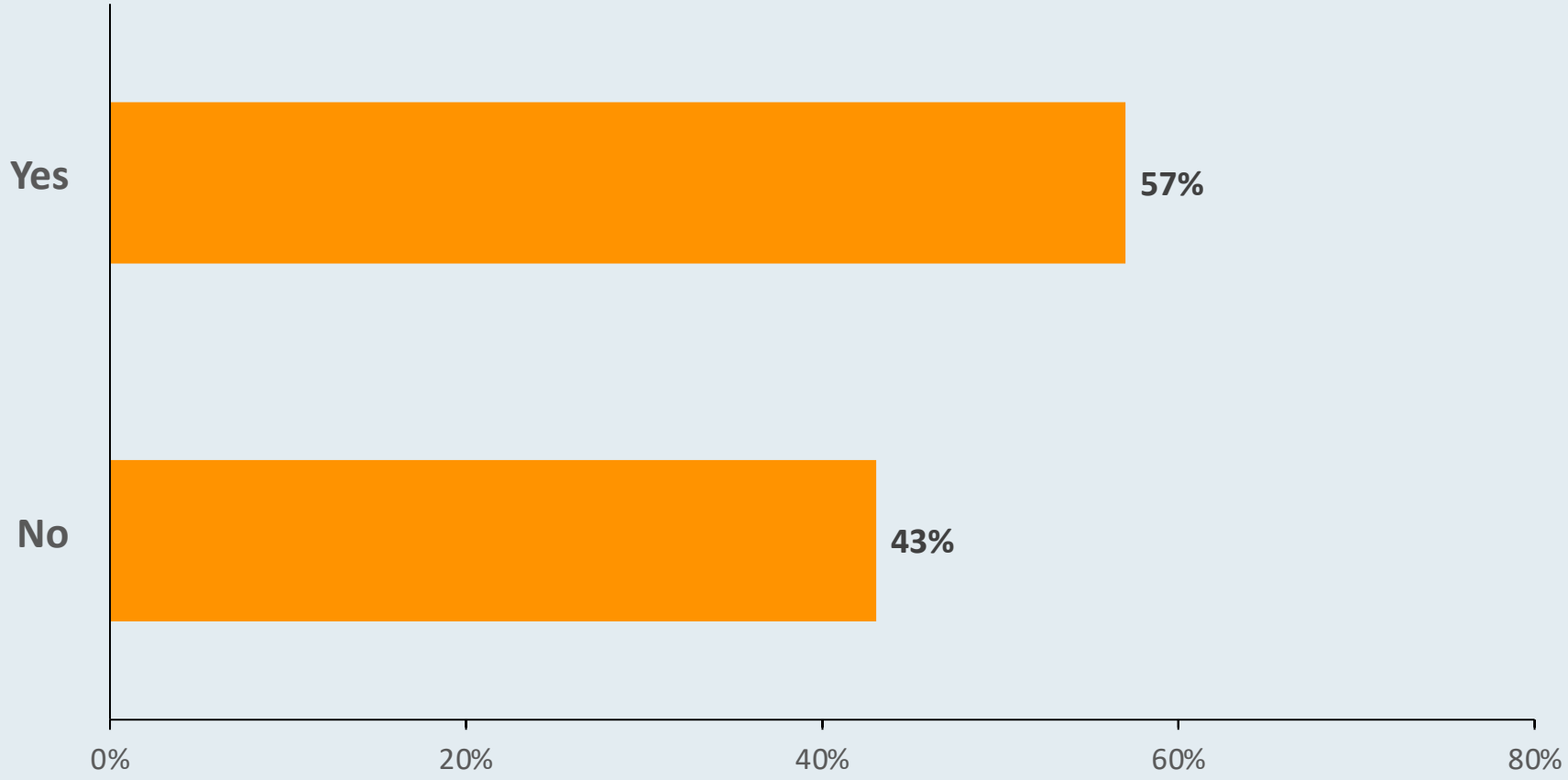
Regulatory and reimbursement issues aside, would you offer trastuzumab deruxtecan to a patient with ER-negative, HER2-ultralow (IHC >0 but <1+) mBC?



Survey of US-based general medical oncologists

RTP RESEARCH TO PRACTICE

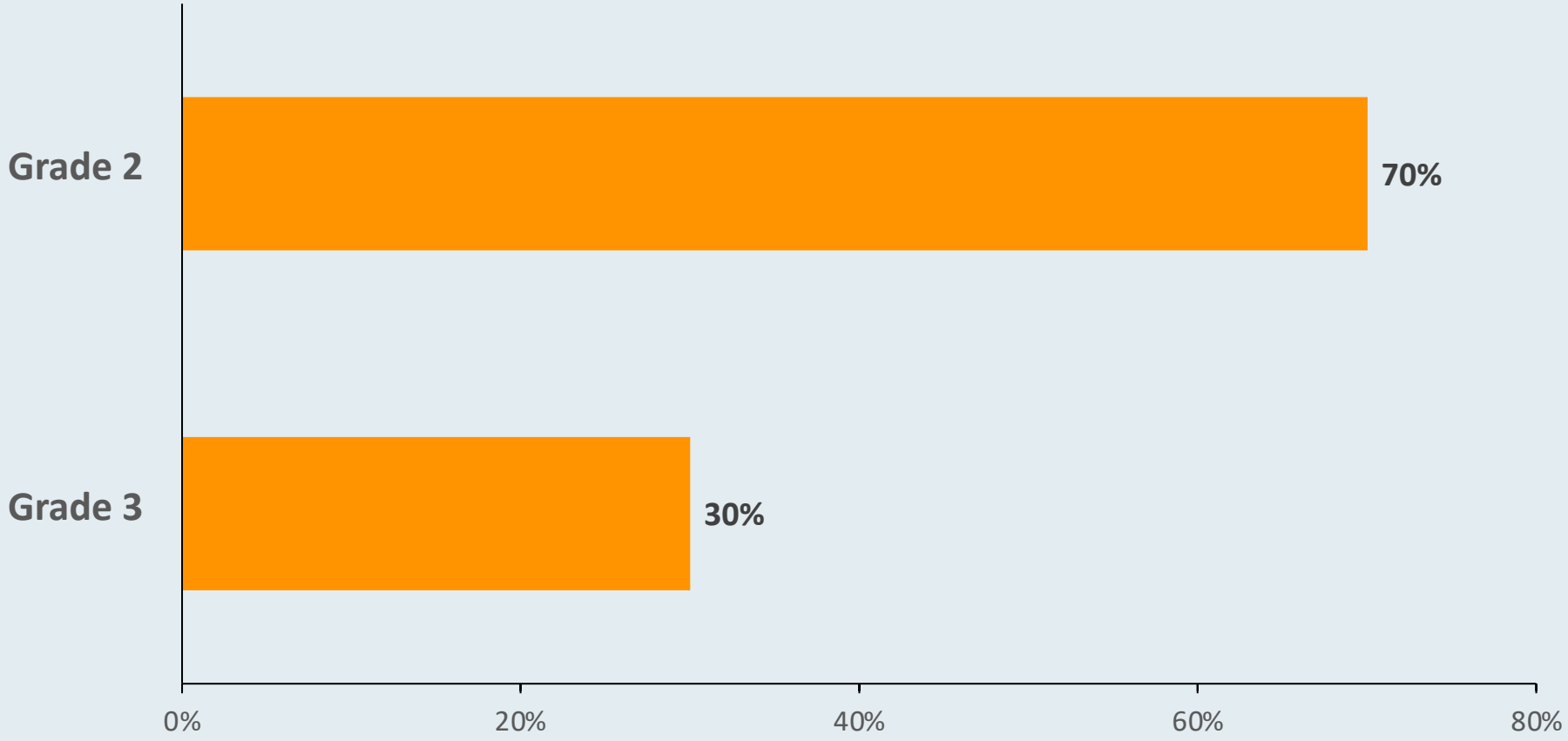
Regulatory and reimbursement issues aside, would you offer trastuzumab deruxtecan to a patient with HER2 IHC 0 mBC with a HER2 mutation?



Survey of US-based general medical oncologists

RTP RESEARCH TO PRACTICE

What grade of interstitial lung disease (ILD) would lead you to permanently discontinue treatment with trastuzumab deruxtecan?



Survey of US-based general medical oncologists

RTP RESEARCH TO PRACTICE

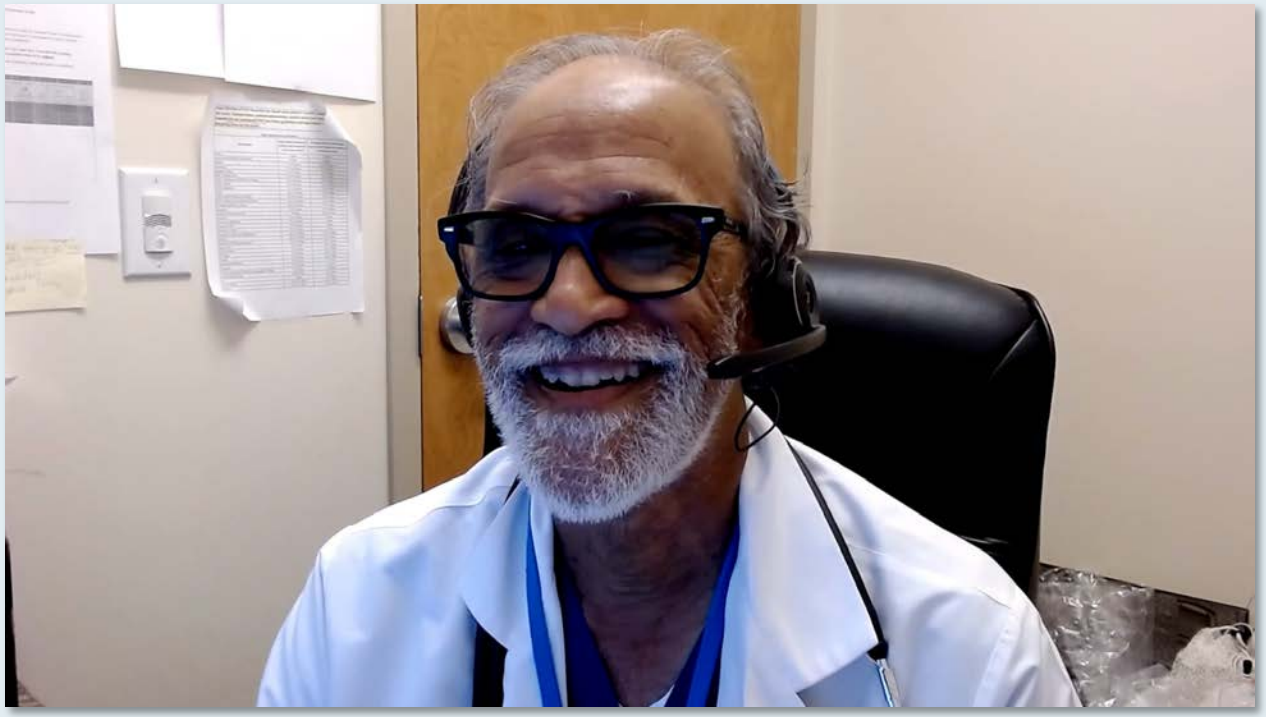
Questions for the faculty related to the use of trastuzumab deruxtecan for HR-negative, HER2-low or HER2-ultralow mBC

- Any concerns for usage of T-DXd in patients with HER2 mutations aside from simply expression?
- HER2 ultralow is not tested in routine clinical practice. Should we start requesting this and treating based on HER2 ultralow?
- Would you move T-DXd to the first line? In what context?
- Would using trastzumab deruxtecan after multiple lines of chemotherapy increase pneumonitis risk as opposed to use in early lines?
- In which scenarios do you rechallenge with T-DXd after documented pneumonitis?
- How do you use trastuzumab deruxtecan in patients with HER2 ultralow mBC?
- How do you manage Grade 2 ILD?
- What is the best way to test for pulmonary toxicity? If only mild SOB, would you test?
- How long do I continue the imaging tests to monitor for the history of Grade 1 ILD?
- When would you consider using trastuzumab deruxtecan? 2nd line or 3rd line? Would you consider repeat biopsy and repeat HER2 status determination before T-DXd?
- Can we use sacituzumab govitecan immediately after T-DXd or do we have to use chemotherapy followed by an ADC?
- When can you stop treatment?

Survey of US-based general medical oncologists

RTP RESEARCH TO PRACTICE

Question and Comments: Adjuvant therapy selection for patients with localized TNBC with a BRCA mutation and residual disease; risk of AML/MDS associated with PARP inhibitor therapy



Dr KS Kumar (Trinity, Florida)

RTP
RESEARCH
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Patient-Reported Outcomes in OlympiA: A Phase III, Randomized, Placebo-Controlled Trial of Adjuvant Olaparib in g*BRCA1/2* Mutations and High-Risk Human Epidermal Growth Factor Receptor 2–Negative Early Breast Cancer

Patricia A. Ganz, MD[1,2]; Hanna Bandos, PhD[3]; Tanja Španić, PhD, DVM[4,5]; Sue Friedman, DVM[6]; Volkmar Müller, MD[7]; Sherko Kuemmel, MD, PhD[8,9]; Suzette Delaloge, MD[10]; Etienne Brain, MD, PhD[11]; Masakazu Toi, MD, PhD[12,13]; Hideko Yamauchi, MD[14]; Eduardo-M. de Dueñas, MD, PhD[15,16]; Anne Armstrong, MD[17]; Seock-Ah Im, MD[18]; Chuan-gui Song, MD[19]; Hong Zheng, MD, PhD[20]; Tomasz Sarosiek, MD[21]; Priyanka Sharma, MD[22]; Cuizhi Geng, MD[23]; Peifen Fu, MD[24]; Kerstin Rhiem, MD[25]; Heike Frauchiger-Heuer, MD[26]; Pauline Wimberger, MD[27,28,29,30,31,32]; Daphné t'Kint de Roodenbeke, MD[33]; Ning Liao, MD[34]; Annabel Goodwin, MD[35]; Camille Chakiba-Brugère, MD[36]; Michael Friedlander, MD, PhD[37]; Keun Seok Lee, MD, PhD[38]; Sylvie Giacchetti, MD[39]; Toshimi Takano, MD[40]; Fernando Henao-Carrasco, MD[41]; Shamsuddin Virani, MD[42]; Frances Valdes-Albini, MD[43]; Susan M. Domchek, MD[44]; Charles Bane, MD[45]; Edward C. McCarron, MD[46]; Monica Mita, MD[47]; Giovanna Rossi, MD[48]; Priya Rastogi, MD[49,50]; Anitra Fielding, MBChB[51]; Richard D. Gelber, PhD[52,53]; Elsemieke D. Scheepers, MSc[54]; David Cameron, MD[55]; Judy Garber, MD[56]; Charles E. Geyer, MD[49]; and Andrew N.J. Tutt, PhD, MBChB[57,58]

***J Clin Oncol* 2024 April 10;42(11):1288-300.**

Author conclusions: *Treatment-emergent symptoms from olaparib were limited, generally resolving after treatment ended. Olaparib- and placebo-treated patients had similar functional scores, slowly improving during the 24 months after (neo)adjuvant chemotherapy, and there was no clinically meaningful persistence of fatigue severity in olaparib-treated patients.*

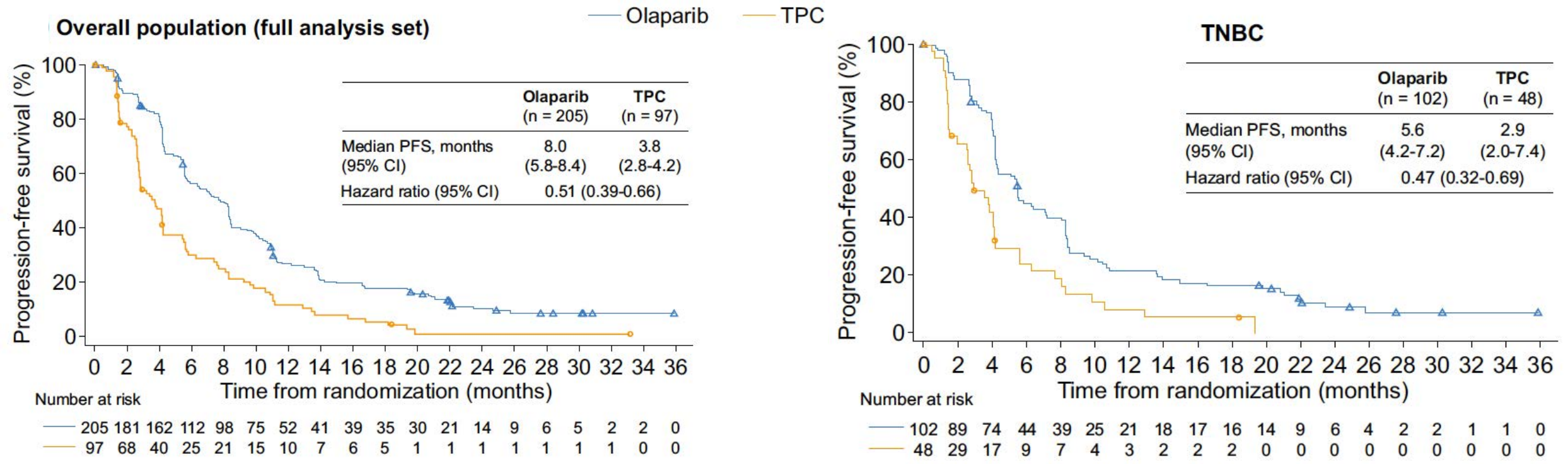
Olaparib efficacy in patients with germline BRCA-mutated, HER2-negative metastatic breast cancer: Subgroup analyses from the phase III OlympiAD trial

Elżbieta Senkus[1] | Suzette Delaloge[2] | Susan M. Domchek[3] | Pierfranco Conte[4] | Seock-Ah Im[5] | Binghe Xu[6] | Anne Armstrong[7,8] | Norikazu Masuda[9] | Anitra Fielding[10] | Mark Robson[11] | Nadine Tung[12]

Int J Cancer 2023 August 15;153(4):803-14.

RTP RESEARCH TO PRACTICE

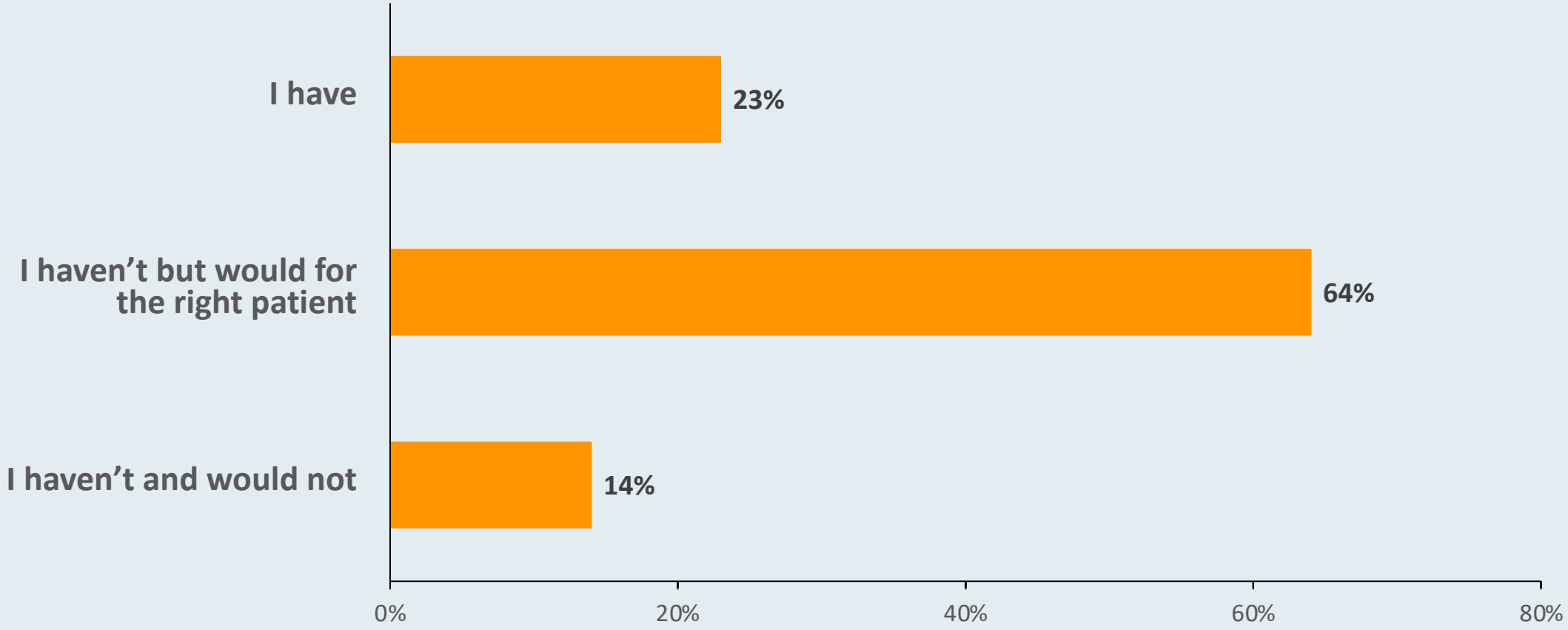
OlympiAD Subgroup Analyses: Investigator-Assessed PFS in the Overall and TNBC Patient Populations



Senkus E et al. *Int J Cancer* 2023 August 15;153(4):803-14.

RTP RESEARCH TO PRACTICE

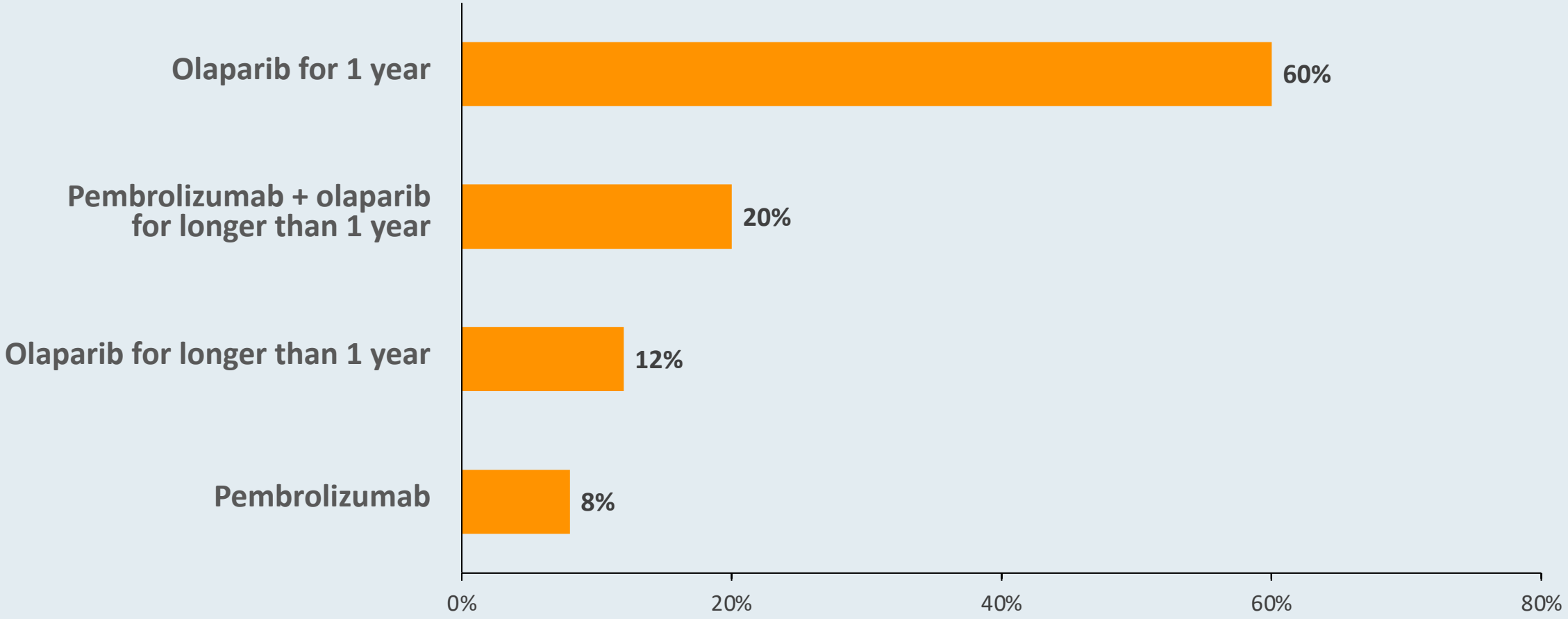
Regulatory and reimbursement issues aside, have you combined or would you combine olaparib with adjuvant pembrolizumab for a patient with a germline BRCA mutation and PD-L1-positive TNBC who had residual disease after neoadjuvant chemotherapy/pembrolizumab?



Survey of US-based general medical oncologists

RTP RESEARCH TO PRACTICE

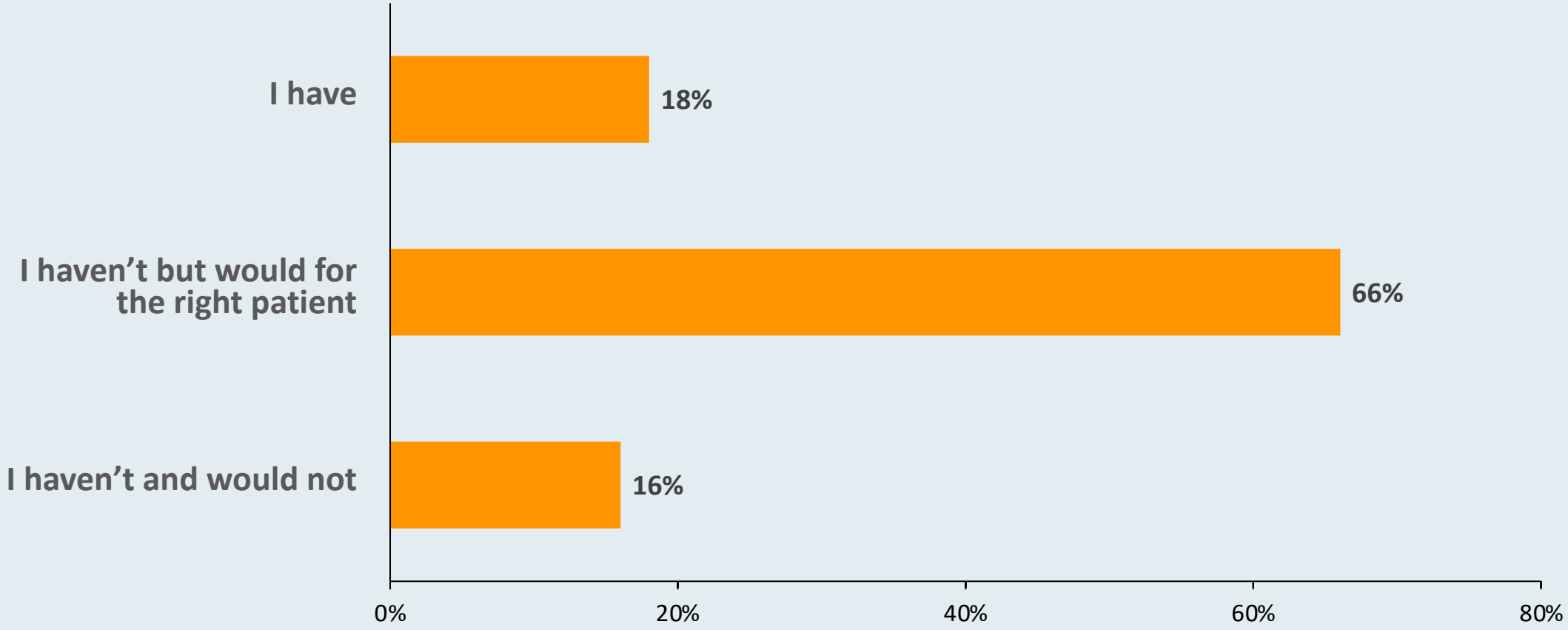
Regulatory and reimbursement issues aside, in general what would you recommend as adjuvant therapy for a patient with TNBC, a germline BRCA mutation and a PD-L1 combined positive score of 1 who has residual disease after neoadjuvant chemotherapy?



Survey of US-based general medical oncologists

RTP RESEARCH TO PRACTICE

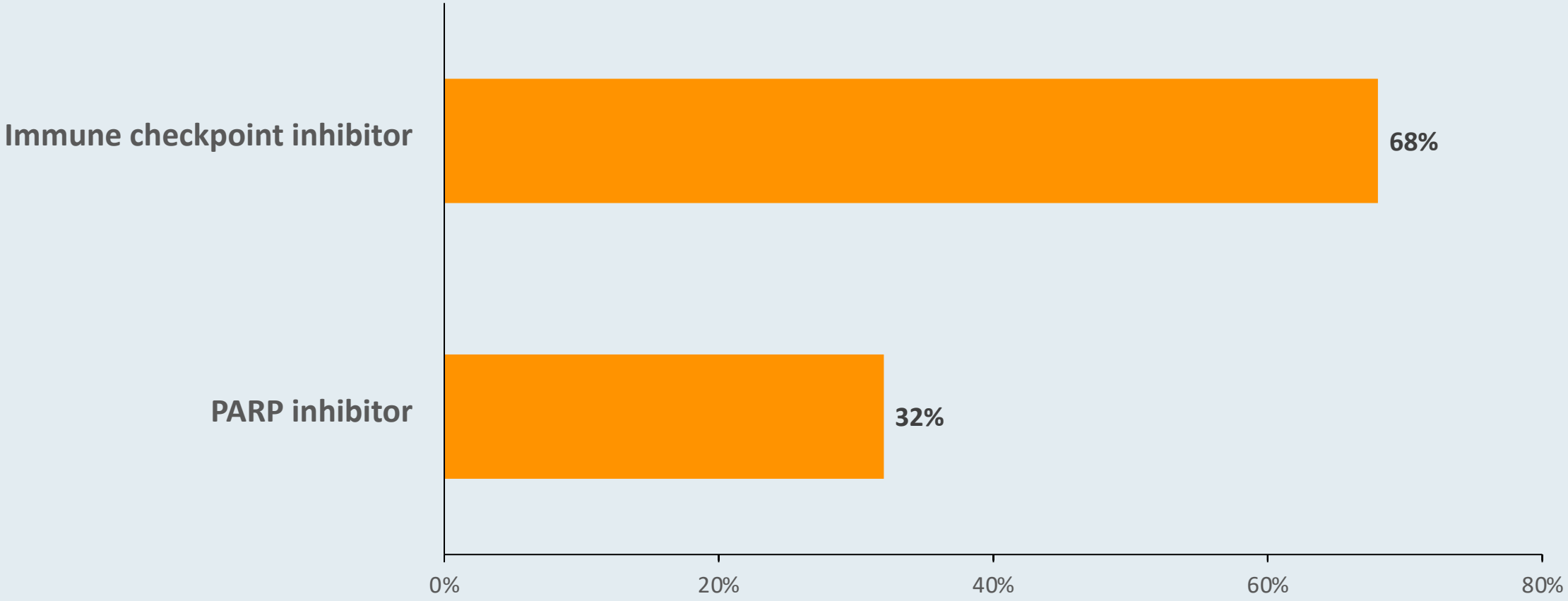
Regulatory and reimbursement issues aside, have you attempted or would you attempt to access olaparib as part of adjuvant therapy for a patient with a germline PALB2 mutation and TNBC who had residual disease after neoadjuvant chemotherapy?



Survey of US-based general medical oncologists

RTP RESEARCH TO PRACTICE

For a patient with PD-L1-positive metastatic TNBC (mTNBC) and a germline BRCA mutation, which type of agent do you generally administer first?



Survey of US-based general medical oncologists

RTP RESEARCH TO PRACTICE

Case Presentation: 73-year-old woman who develops recurrent metastatic ER-negative, HER2-low breast cancer after *nab* paclitaxel/atezolizumab and receives sacituzumab govitecan

Dr Ranju Gupta (Bethlehem, Pennsylvania)

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Clinical Trial Updates

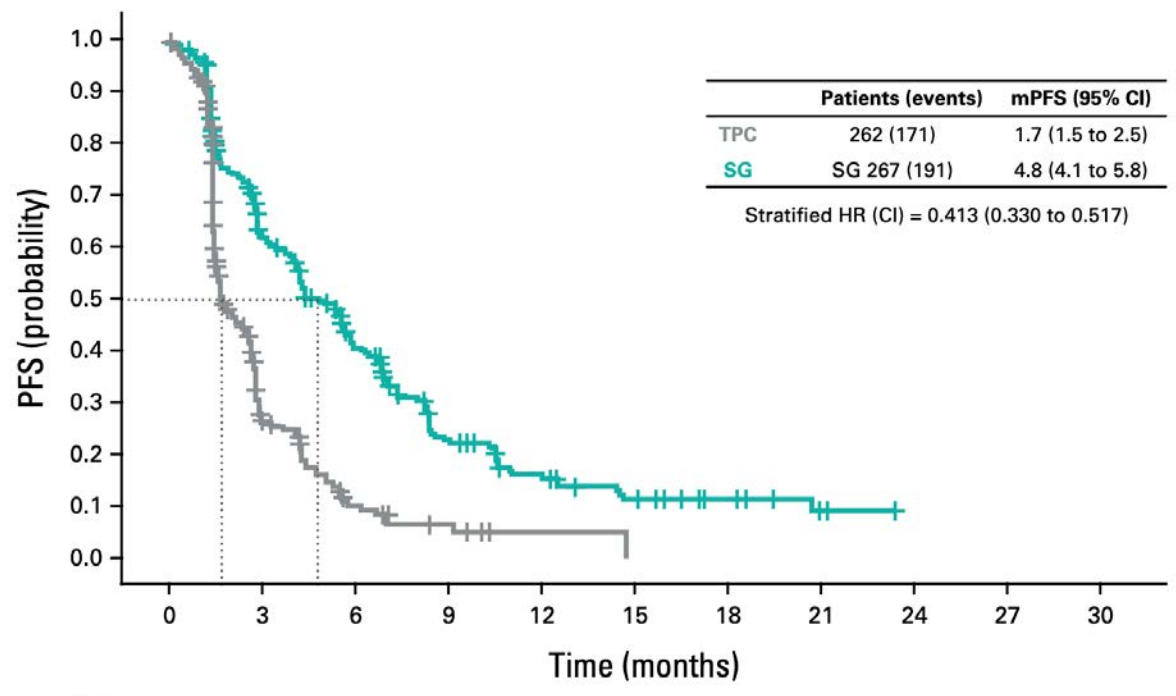
Final Results From the Randomized Phase III ASCENT Clinical Trial in Metastatic Triple-Negative Breast Cancer and Association of Outcomes by Human Epidermal Growth Factor Receptor 2 and Trophoblast Cell Surface Antigen 2 Expression

Aditya Bardia, MD, MPH[1]; Hope S. Rugo, MD[2]; Sara M. Tolaney, MD, MPH[3]; Delphine Loirat, PhD, MD[4]; Kevin Punie, MD[5]; Mafalda Oliveira, MD, PhD[6]; Adam Brufsky, MD, PhD[7]; Kevin Kalinsky, MD, MS[8]; Javier Cortés, MD, PhD[9]; Joyce O' Shaughnessy, MD[10]; Véronique Diéras, MD, MPH[11]; Lisa A. Carey, MD, ScM[12]; Luca Gianni, MD[13]; Martine Piccart-Gebhart, MD, PhD[14]; Sibylle Loibl, MD, PhD[15]; Oh Kyu Yoon, PhD, MBA[16]; Yang Pan, PhD[16]; Scott Hofsess, MS[17]; See-Chun Phan, MD[16]; and Sara A. Hurvitz, MD, FACP[18]

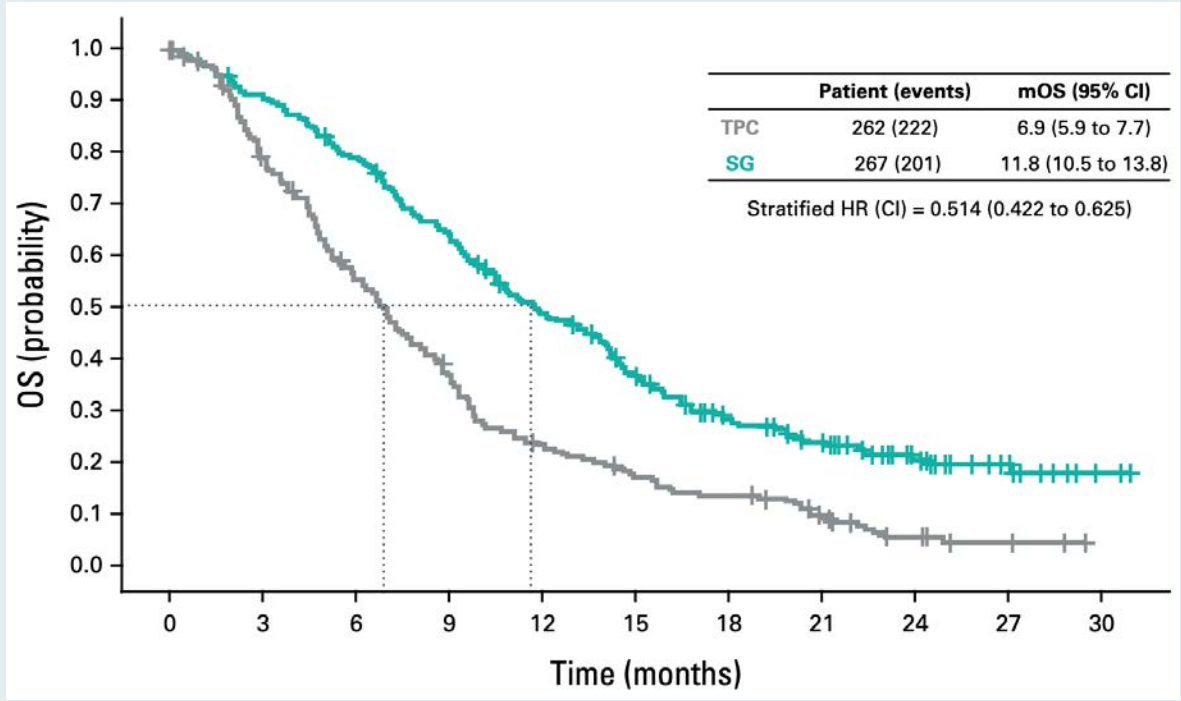
J Clin Oncol 2024;42:1738-44.

ASCENT Final Results: Sacituzumab Govitecan (SG) versus Treatment of Physician's Choice (TPC) for Relapsed/Refractory Metastatic TNBC

Progression-free survival (ITT population)



Overall survival (ITT population)



- **TROP2 subgroups analysis:** SG improved progression-free survival (PFS) in comparison to TPC in each TROP2 expression quartile (n = 168); a trend was observed for improved overall survival (OS) across quartiles.

Bardia A et al. *J Clin Oncol* 2024;42:1738-44.

RTP RESEARCH TO PRACTICE

ASCENT Final Results: Select Treatment-Emergent Adverse Events (TEAEs) with Sacituzumab Govitecan (SG) for Metastatic TNBC

TEAE[a]		SG (n=258)		TPC (n=224)	
		All grade (%)	Grade ≥ 3 (%)	All grade (%)	Grade ≥ 3 (%)
Hematologic	Neutropenia[b]	165 (64)	135 (52)	98 (44)	76 (34)
	Anemia[c]	103 (40)	24 (9)	62 (28)	13 (6)
	Leukopenia[d]	43 (17)	27 (11)	27 (12)	13 (6)
	Febrile Neutropenia	15 (6)	15 (6)	6 (3)	6 (3)
Gastrointestinal	Diarrhea	168 (65)	30 (12)	38 (17)	2 (1)
	Nausea	161 (62)	8 (3)	68 (30)	1 (< 1)
	Vomiting	87 (34)	5 (2)	36 (16)	3 (1)
	Constipation	96 (37)	1 (< 1)	52 (23)	0
	Abdominal Pain	54 (21)	7 (3)	18 (8)	3 (1)
	Stomatitis	27 (11)	2 (1)	14 (6)	0

- Overall, the safety profile of SG was manageable, with ≤5% of treatment-related discontinuations because of adverse events and no treatment-related deaths.
- The safety profile was consistent across all subgroups.

Bardia A et al. *J Clin Oncol* 2024;42:1738-44.

RTP RESEARCH TO PRACTICE

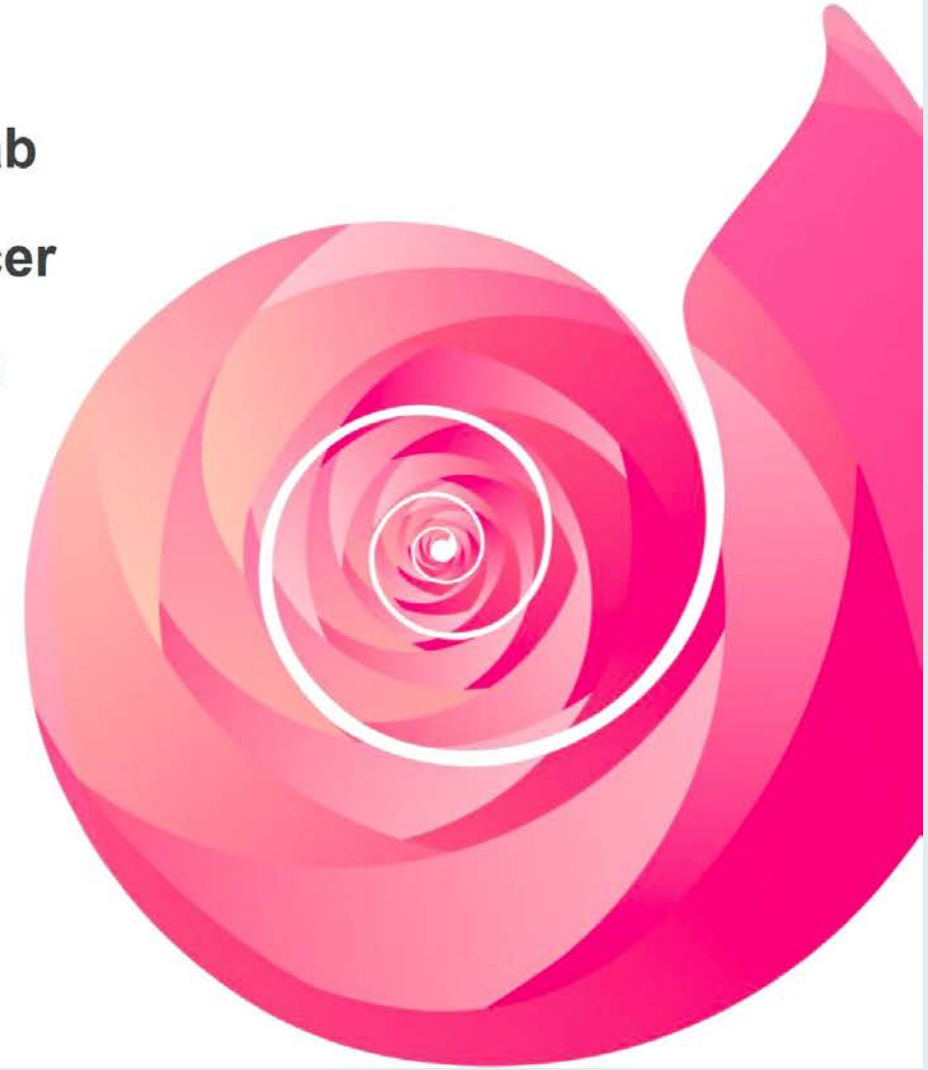
2024 ESMO BREAST CANCER

Annual Congress

181O: Interim analysis (IA) of the atezolizumab (atezo) + sacituzumab govitecan (SG) arm in patients (pts) with triple-negative breast cancer (TNBC) in MORPHEUS-pan BC: A phase Ib/II study of multiple treatment (tx) combinations in pts with locally advanced/metastatic BC (LA/mBC)

Peter Schmid,* Sherene Loi, Luis de la Cruz-Merino, Rinat Yerushalmi, Seock-Ah Im, Amir Sonnenblick, Maria Martinez-Garcia, Irene Moreno, Laura Kennedy, Kristin L. Griffiths, Richard Schwab, Fiona Young, Laura Liao, Kelly DuPree, Sung-Bae Kim

*** Barts Cancer Institute, Queen Mary University of London, UK**

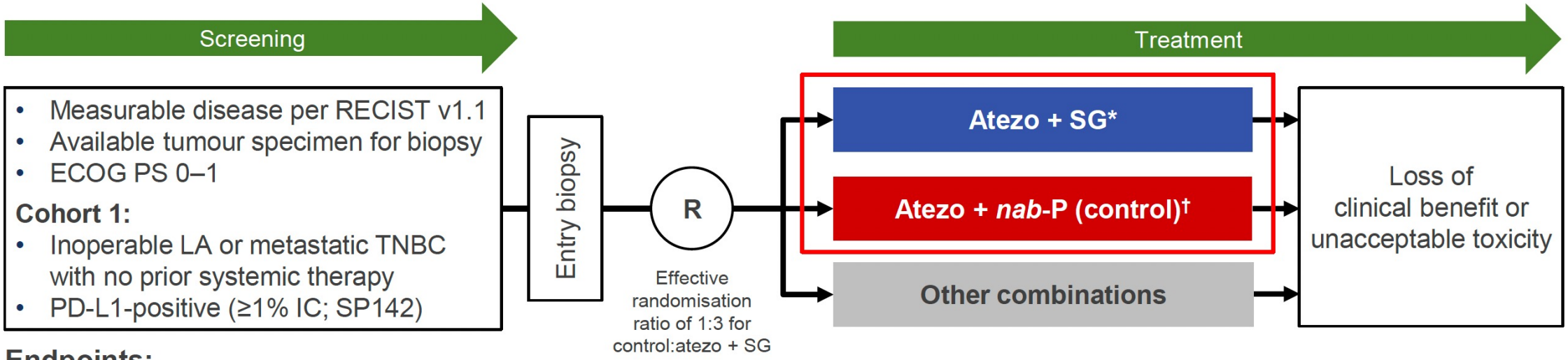


ESMO GOOD SCIENCE BETTER MEDICINE BEST PRACTICE

RTP RESEARCH TO PRACTICE

MORPHEUS-Pan BC Study Design

Phase Ib/II, open-label, multicentre, randomised, umbrella study of multiple treatment combinations in LA/mBC (NCT03424005)



Endpoints:

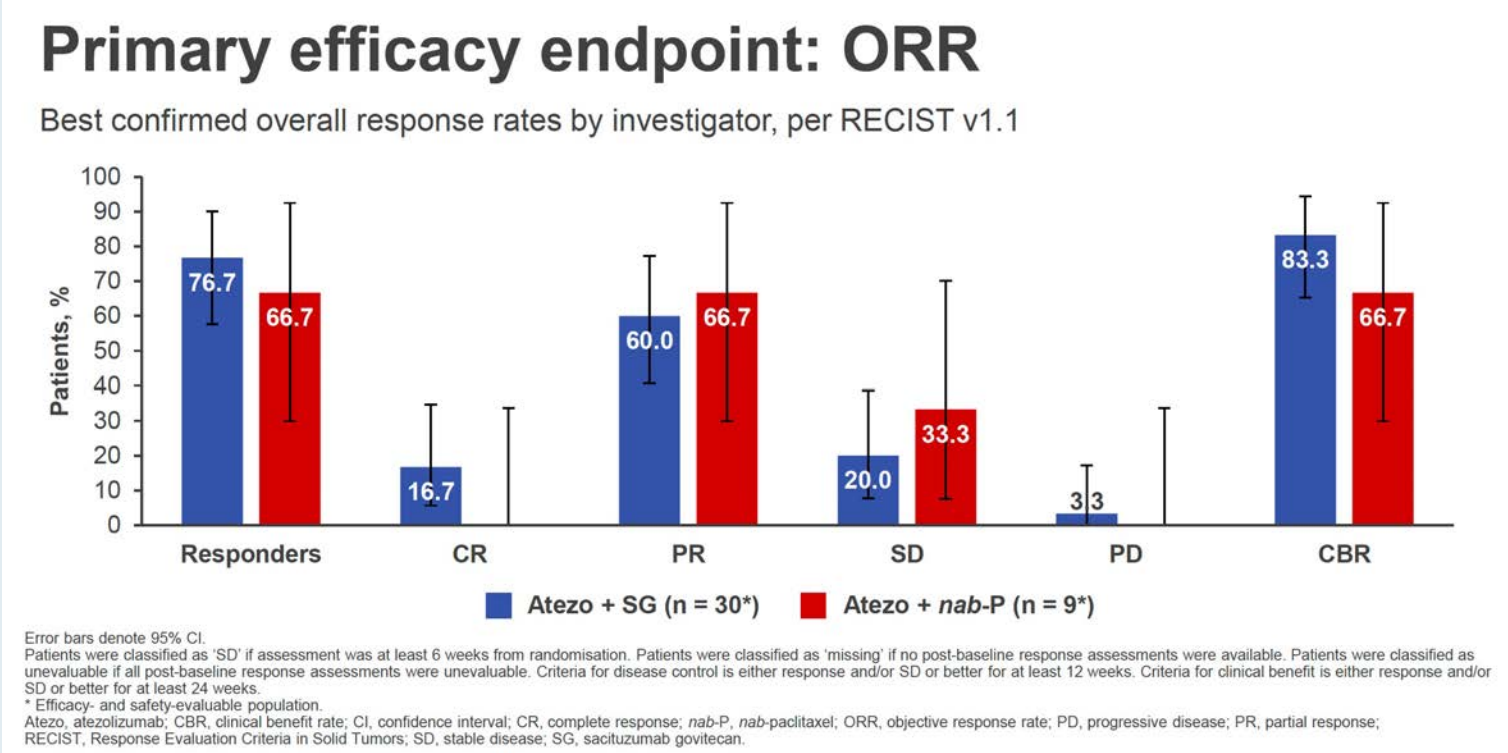
- Primary: ORR, safety
- Secondary: PFS, DCR, OS, DOR

Baseline tumours were evaluated for Trop-2, CD8 immune phenotype and stromal TILs for associations with response

Target enrolment: n = 30 in the atezo + SG arm.
* Atezo 1200 mg IV D1 and SG 10 mg/kg IV D1 and 8 (21-D cycles); † Atezo 840 mg IV D1 and 15 and *nab*-P 100 mg/m² IV D1, 8, 15 (28-D cycles).
Atezo, atezolizumab; BC, breast cancer; D, day; DCR, disease control rate; DOR, duration of response; ECOG PS, Eastern cooperative Oncology Group performance score; IC, immune cells; IV, intravenous; LA, locally advanced; *nab*-P, *nab*-paclitaxel; ORR, objective response rate; OS, overall survival; PD-L1, programmed death-ligand 1; PFS, progression-free survival; R, randomised; RECIST, Response Evaluation Criteria in Solid Tumors; SG, sacituzumab govitecan; TIL, tumour-infiltrating lymphocyte; TNBC, triple-negative breast cancer.

Schmid P et al. ESMO Breast Cancer Congress 2024;Abstract 181O.

MORPHEUS-Pan BC: Results Summary

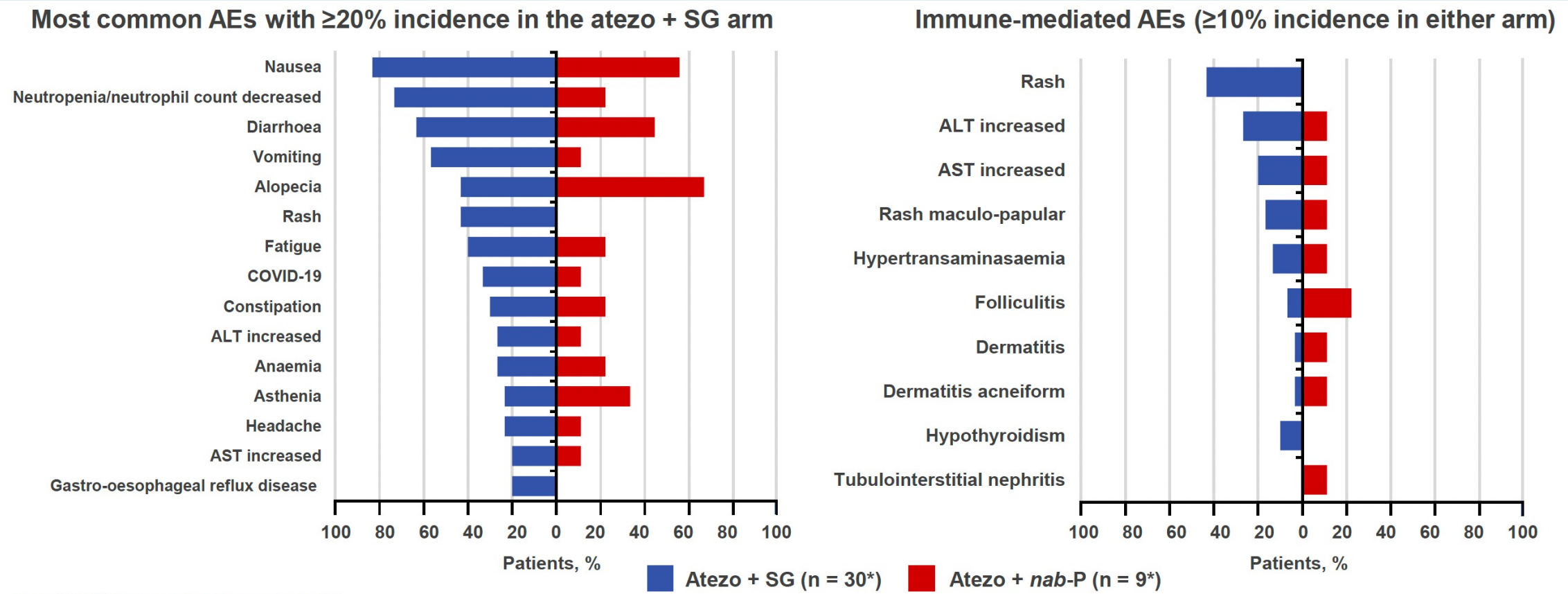


- PFS and OS data were immature but showed a trend toward benefit with atezolizumab + SG.
- The SG treatment benefit was seen across all TROP2 expression levels, with a trend toward higher response rates with higher TROP2

Schmid P et al. ESMO Breast Cancer Congress 2024;Abstract 181O.

RTP RESEARCH TO PRACTICE

MORPHEUS-Pan BC: Most Common Adverse Events (AEs) and Immune-Related AEs of Special Interest with Atezolizumab and Sacituzumab Govitecan

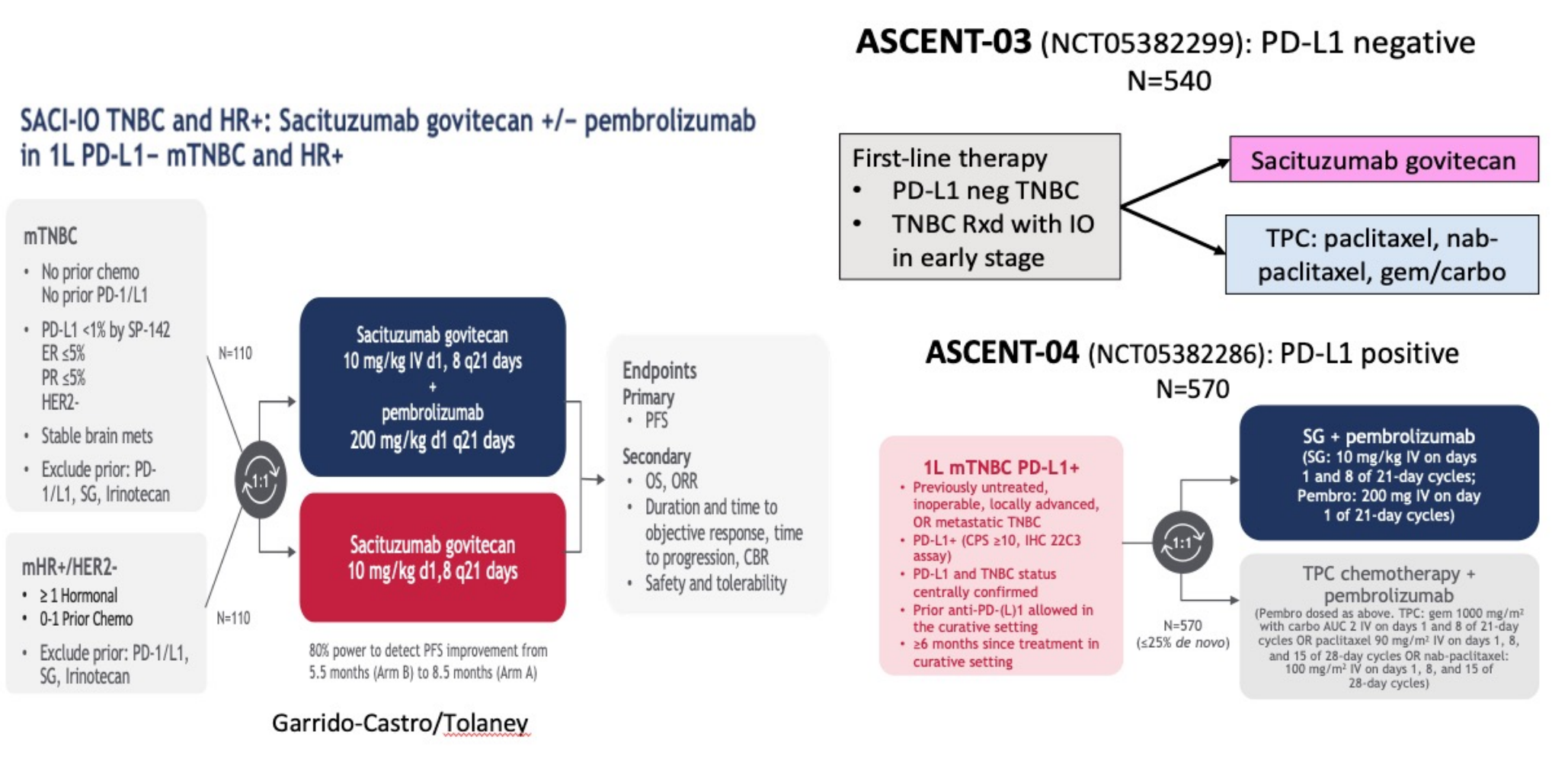


Use of G-CSF in one patient (for neutropenia).
* Efficacy- and safety-evaluable population.
AE, adverse event; AESI, adverse event of special interest; ALT, alanine aminotransferase; AST, aspartate aminotransferase; atezo, atezolizumab; G-CSF, granulocyte-colony stimulating factor; *nab*-P, *nab*-paclitaxel; SG, sacituzumab govitecan.

Schmid P et al. ESMO Breast Congress 2024;Abstract 181O.

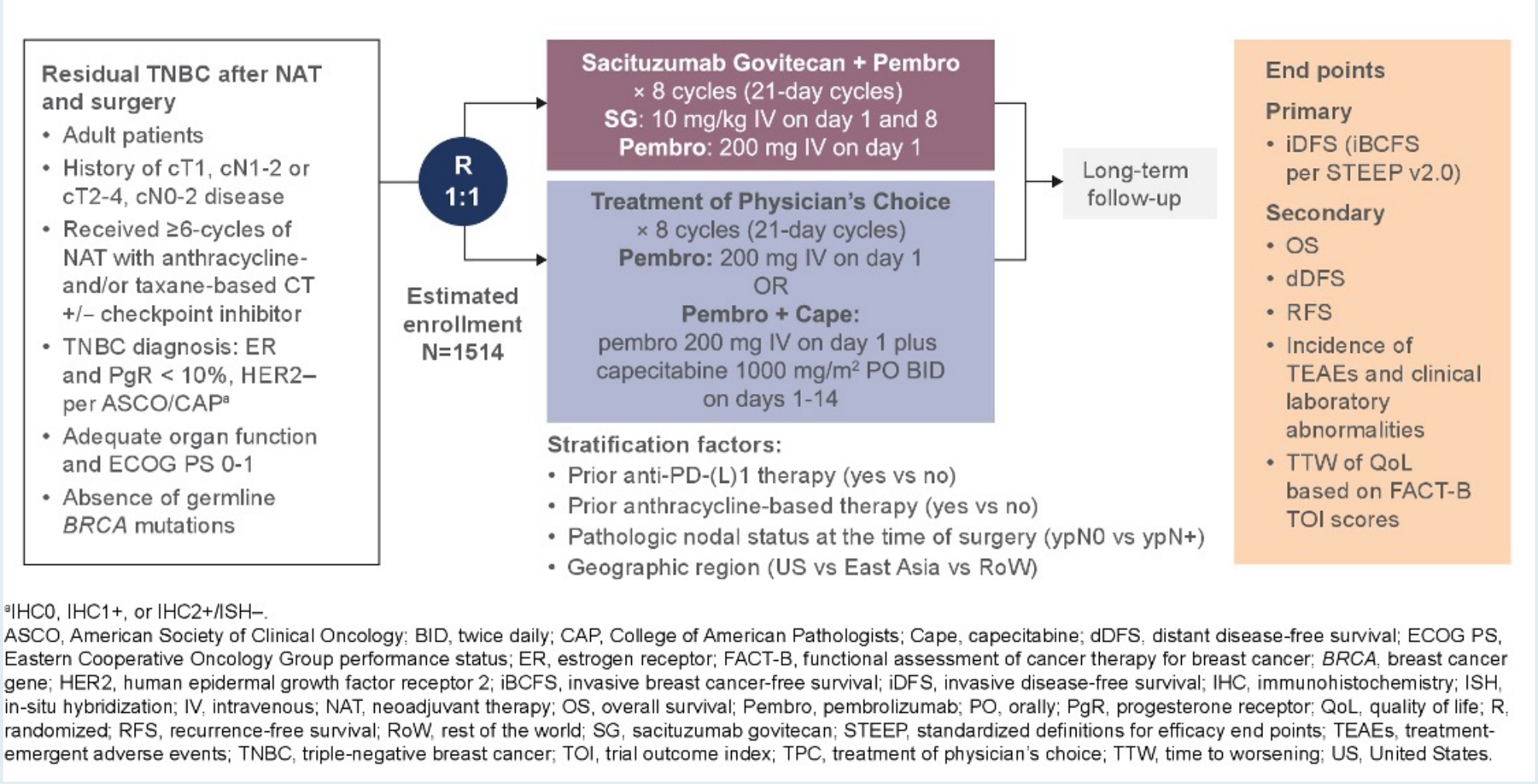
RTP RESEARCH TO PRACTICE

Ongoing Trials of Sacituzumab Govitecan as First-Line Treatment for Metastatic TNBC (mTNBC)



Courtesy of Joyce O'Shaughnessy, MD.

ASCENT-05/OptimICE-RD (AFT-65): An Ongoing Phase III Trial of Adjuvant Sacituzumab Govitecan with Pembrolizumab for Patients with TNBC and Residual Disease After Neoadjuvant Therapy and Surgery



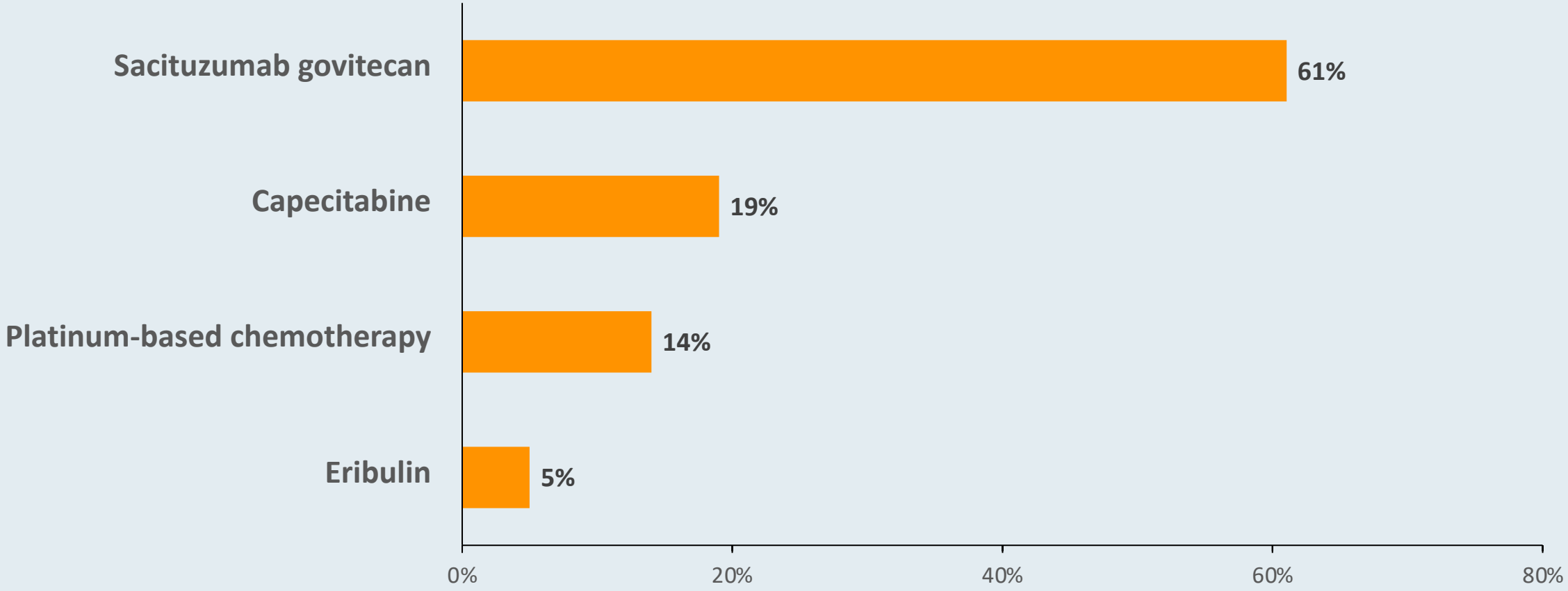
[a]IHC0, IHC1+, or IHC2+/ISH–.

ASCO, American Society of Clinical Oncology; BID, twice daily; CAP, College of American Pathologists; Cape, capecitabine; dDFS, distant disease-free survival; ECOG PS, Eastern Cooperative Oncology Group performance status; ER, estrogen receptor; FACT-B, functional assessment of cancer therapy for breast cancer; *BRCA*, breast cancer gene; HER2, human epidermal growth factor receptor 2; iBCFS, invasive breast cancer-free survival; iDFS, invasive disease-free survival; IHC, immunohistochemistry; ISH, in-situ hybridization; IV, intravenous; NAT, neoadjuvant therapy; OS, overall survival; Pembro, pembrolizumab; PO, orally; PgR, progesterone receptor; QoL, quality of life; R, randomized; RFS, recurrence-free survival; RoW, rest of the world; SG, sacituzumab govitecan; STEEP, standardized definitions for efficacy end points; TEAEs, treatment-emergent adverse events; TNBC, triple-negative breast cancer; TOI, trial outcome index; TPC, treatment of physician's choice; TTW, time to worsening; US, United States.

Tolaney SM et al. ASCO 2023;Abstract TPS619.

RTP RESEARCH TO PRACTICE

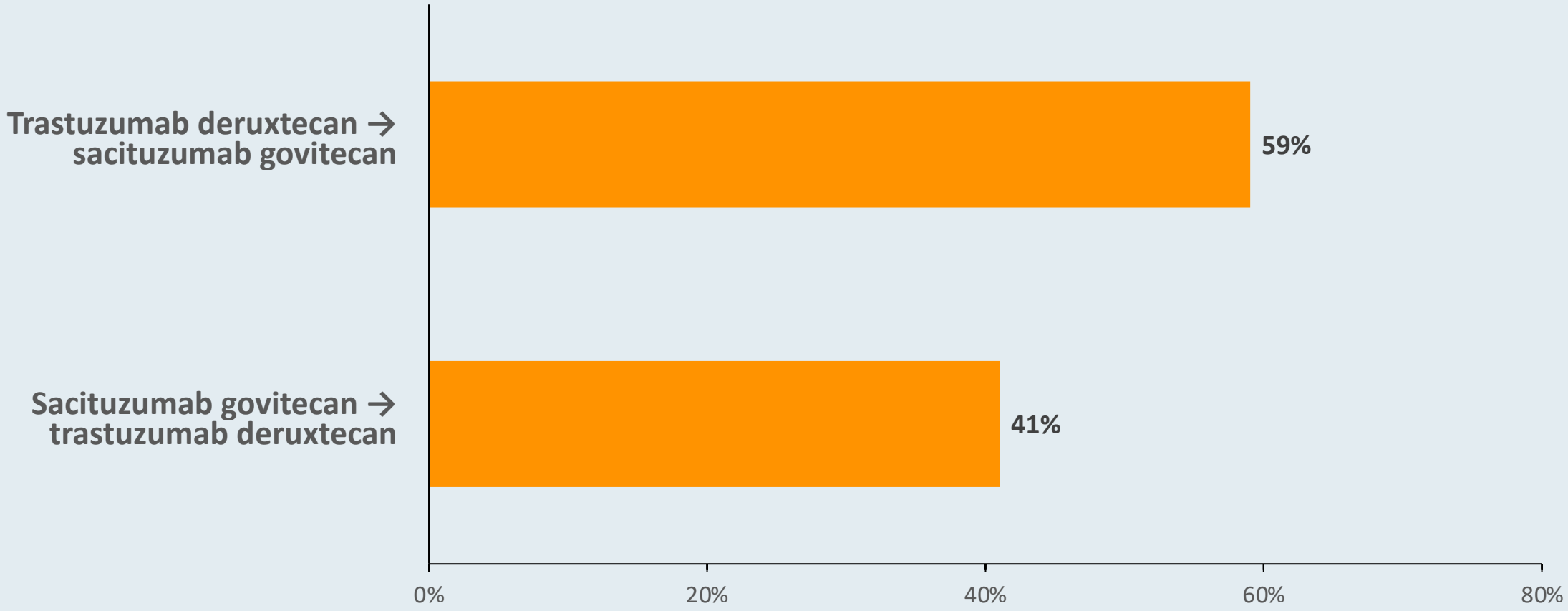
Regulatory and reimbursement issues aside, which next line of therapy would you recommend to a patient with BRCA wild-type TNBC who received neoadjuvant chemoimmunotherapy and developed metastatic disease while receiving adjuvant immunotherapy?



Survey of US-based general medical oncologists

RTP RESEARCH TO PRACTICE

How do you generally sequence trastuzumab deruxtecan and sacituzumab govitecan for a patient with ER-negative, HER2-low metastatic breast cancer (mBC) who is eligible to receive both?



Survey of US-based general medical oncologists

RTP RESEARCH TO PRACTICE

Questions for the faculty related to the use of sacituzumab govitecan for mTNBC

- Could you review general issues seen in clinic with sacituzumab govitecan (after already adding G-CSF and maximizing anti-emetic premeds)?
- How do you dose in elderly/frail patients? Do you start at a lower dose if worried about tolerability?
- How do you sequence a different ADC now that multiples are available? How do you sequence TROP2-directed ADC, HER3 ADC, HER2 ADC?
- Should sacituzumab be brought in as front-line therapy as opposed to later lines of chemotherapy?
- Should any other agent be considered before sacituzumab govitecan?
- For a patient who is HER2 low, would investigators use sacituzumab govitecan or T-DXd?
- Any pearls to mitigate side effects?
- When do I change to T-DXd if tolerance is poor to sacituzumab and response less than optimal?
- How often do you see Grade 3 or more diarrhea?
- Is growth factor mandatory for sacituzumab govitecan?
- How do you manage the fatigue associated with sacituzumab govitecan?
- Can we ever discontinue therapy if a patient has a good response?

Survey of US-based general medical oncologists

RTP RESEARCH TO PRACTICE

Original Reports | Breast Cancer

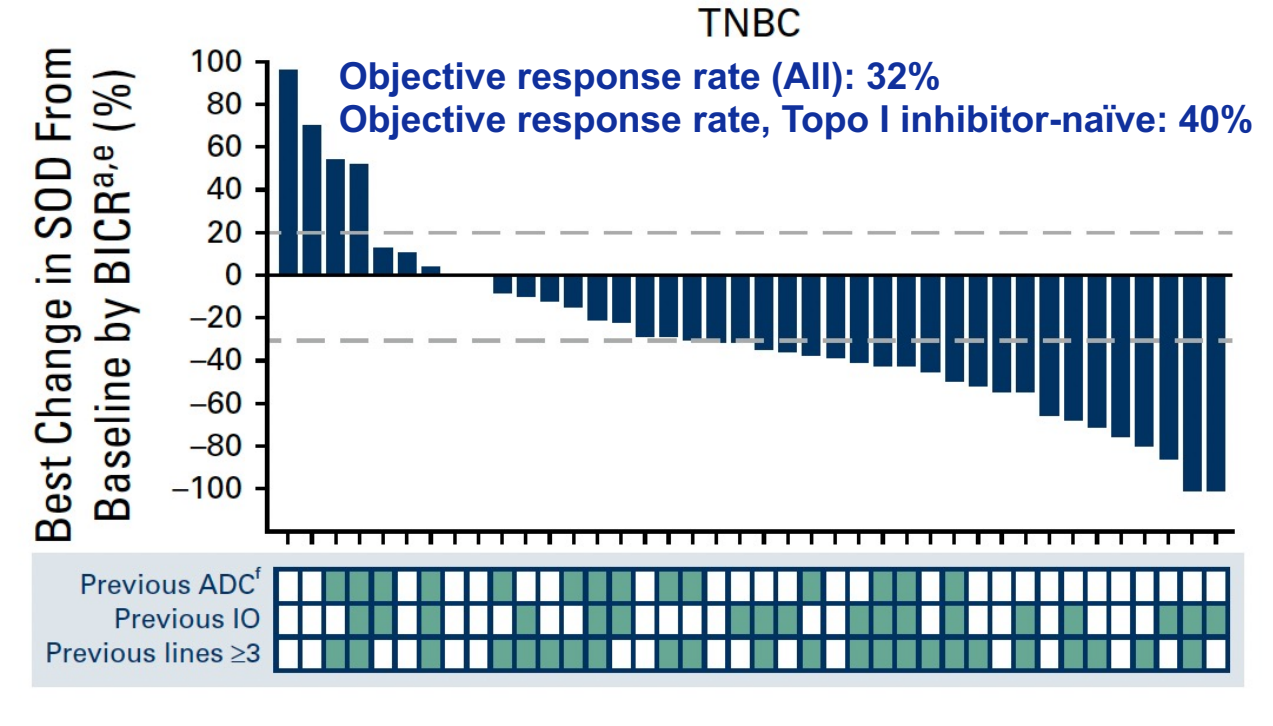
Datopotamab Deruxtecan in Advanced or Metastatic HR+/HER2– and Triple-Negative Breast Cancer: Results From the Phase I TROPION-PanTumor01 Study

Aditya Bardia, MD, PhD[1]; Ian E. Krop, MD, PhD[2,3]; Takahiro Kogawa, MD, PhD[4]; Dejan Juric, MD[1]; Anthony W. Tolcher, MD[5,6,7]; Erika P. Hamilton, MD[8,9]; Toru Mukohara, MD, DMedSci[10]; Aaron Lisberg, MD[11]; Toshio Shimizu, MD, PhD[12,13]; Alexander I. Spira, MD[14]; Junji Tsurutani, MD, PhD[15]; Senthil Damodaran, MD, PhD[16]; Kyriakos P. Papadopoulos, MD[17]; Jonathan Greenberg, MD, MA, BA[18,19]; Fumiaki Kobayashi, PhD, MS[20]; Hong Zebger-Gong, MD, PhD[19]; Rie Wong, BS[21]; Yui Kawasaki, PhD[18]; Tadakatsu Nakamura, MS[20]; and Funda Meric-Bernstam, MD[16]

J Clin Oncol 2024 April 23;[Online ahead of print].

RTP RESEARCH TO PRACTICE

TROPION-PanTumor01: Response and PFS with Dato-DXd for TNBC



	All patients (N = 44)	Topo I inhibitor naïve (N = 30)
Median PFS	4.4 mo	7.3 mo

Bardia A et al. *J Clin Oncol* 2024 April 23;[Online ahead of print].

RTP RESEARCH TO PRACTICE

MADRID 2023 ESMO congress

Datopotamab Deruxtecan (Dato-DXd) + Durvalumab (D) as First-Line (1L) Treatment for Unresectable Locally Advanced/Metastatic Triple-Negative Breast Cancer (a/mTNBC)

Updated Results From BEGONIA, a Phase 1b/2 Study

Professor Peter Schmid, FRCP, MD, PhD

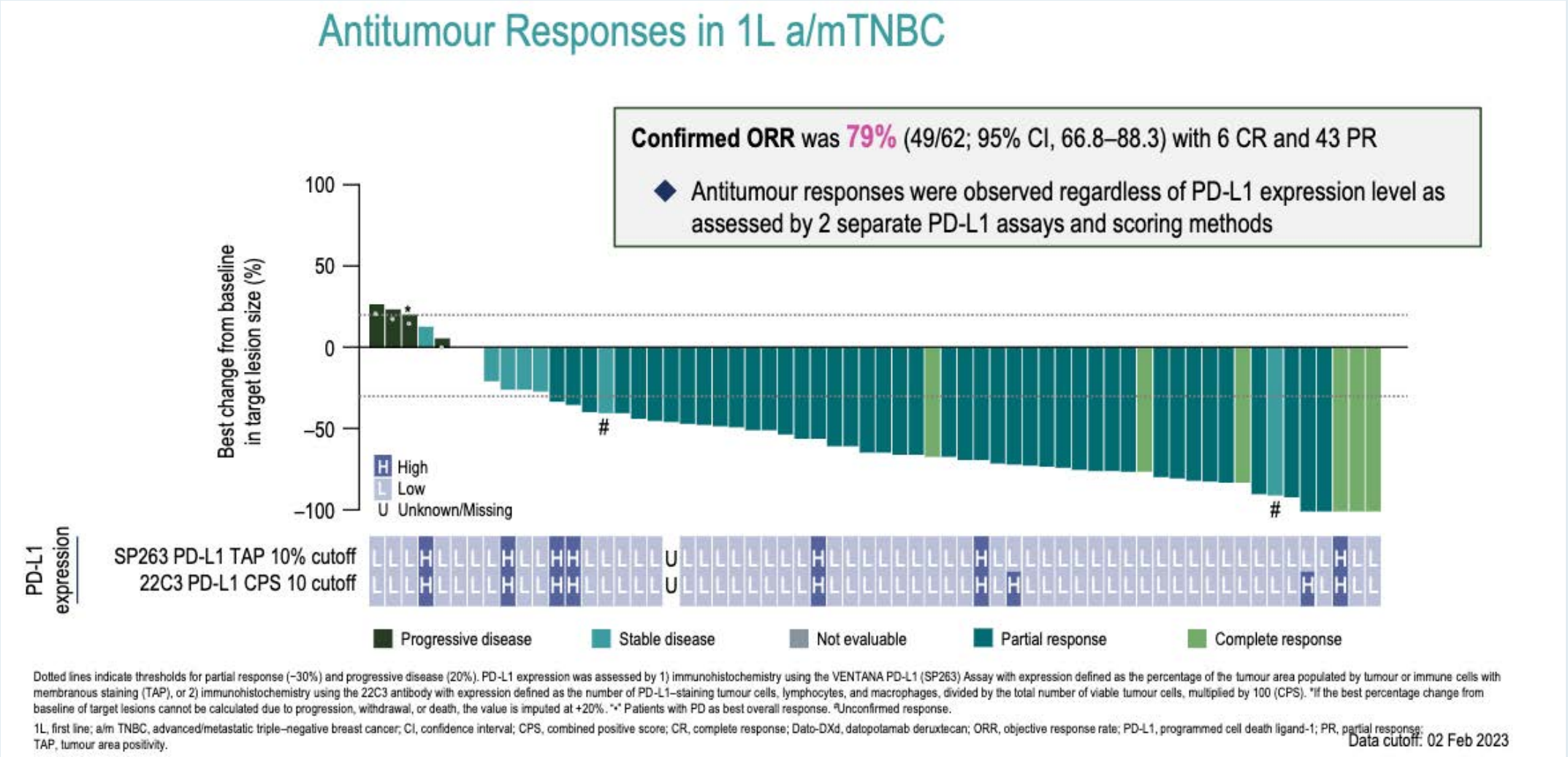
Barts Cancer Institute, Queen Mary University of London, London, UK

P. J. Wysocki,[1] C. X. Ma,[2] Y. H. Park,[3] R. Fernandes,[4] S. Lord,[5] R. D. Baird,[6] C. Prady,[7] K. H. Jung,[8] J. Asselah,[9] R. Huisden,[10] R. Stewart,[10] K. Heider,[10] P. Vukovic,[10] N. Denduluri,[11] Z. Nowecki[12]

[1]Jagiellonian University Medical College, Krakow, Poland; [2]Washington University School of Medicine, St. Louis, MO, USA; [3]Samsung Medical Center, Sungkyunkwan University School of Medicine, Seoul, Korea; [4]Schulich School of Medicine & Dentistry, Western University, London Health Sciences Centre, London, Ontario, Canada; [5]University of Oxford, Oxford, UK; [6]Cancer Research UK Cambridge Centre, Cambridge, UK; [7]Sherbrooke University, Centre intégré de cancérologie de la Montérégie, CISSS Montérégie Centre, Greenfield Park, Quebec, Canada; [8]Asan Medical Center - University of Ulsan, College of Medicine, Seoul, Korea; [9]McGill University Health Centre, Montreal, Québec, Canada; [10]AstraZeneca, Cambridge, UK; [11]AstraZeneca, Gaithersburg, MD, USA; [12]Maria Skłodowska-Curie National Research Institute of Oncology, Warsaw, Poland

RTP RESEARCH TO PRACTICE

BEGONIA: Updated Antitumor Activity of Dato-DXd and Durvalumab



Dotted lines indicate thresholds for partial response (−30%) and progressive disease (20%). PD-L1 expression was assessed by 1) immunohistochemistry using the VENTANA PD-L1 (SP263) Assay with expression defined as the percentage of the tumour area populated by tumour or immune cells with membranous staining (TAP), or 2) immunohistochemistry using the 22C3 antibody with expression defined as the number of PD-L1–staining tumour cells, lymphocytes, and macrophages, divided by the total number of viable tumour cells, multiplied by 100 (CPS). #If the best percentage change from baseline of target lesions cannot be calculated due to progression, withdrawal, or death, the value is imputed at +20%. "•" Patients with PD as best overall response. [a]Unconfirmed response.

1L, first line; a/m TNBC, advanced/metastatic triple–negative breast cancer; CI, confidence interval; CPS, combined positive score; CR, complete response; Dato-DXd, datopotamab deruxtecan; ORR, objective response rate; PD-L1, programmed cell death ligand-1; PR, partial response; TAP, tumour area positivity.

Data cutoff: 02 Feb 2023

Schmid P et al. ESMO 2023;Abstract 379MO.

RTP RESEARCH TO PRACTICE

Questions for the faculty related to the use of datopotamab deruxtecan for mTNBC

- Any pearls for side effects management?
- Where do you see datopotamab deruxtecan being sequenced?
- How do you sequence this ADC in the context of T-DXd?
- With it targeting TROP2 but having a deruxtecan payload, will datopotamab deruxtecan have any benefit after using sacituzumab govitecan and T-DXd?
- How do you anticipate using the drug (patient selection)?
- How do you sequence therapy, and any words on mechanism of resistance?
- In which line can we use datopotamab deruxtecan for HER2 IHC=0 or IHC=1 patients?
- What's the efficacy of datopotamab deruxtecan vs sacituzumab govitecan?
- In which patients would you use it and how do you sequence it?
- Would you use datopotamab deruxtecan up front before T-DXd?
- How far away are we from routine TROP2 H score in mTNBC to guide care?
- Without a head to head, would the faculty prefer datopotamab deruxtecan over T-DXd for HER2 ultralow disease?
- Is there any data to support the use of datopotamab deruxtecan for patients previously treated with sacituzumab govitecan?
- Difference between T-DXd and datopotamab deruxtecan? How to use both optimally?

Survey of US-based general medical oncologists

RTP RESEARCH TO PRACTICE

2024 ASCO ANNUAL MEETING

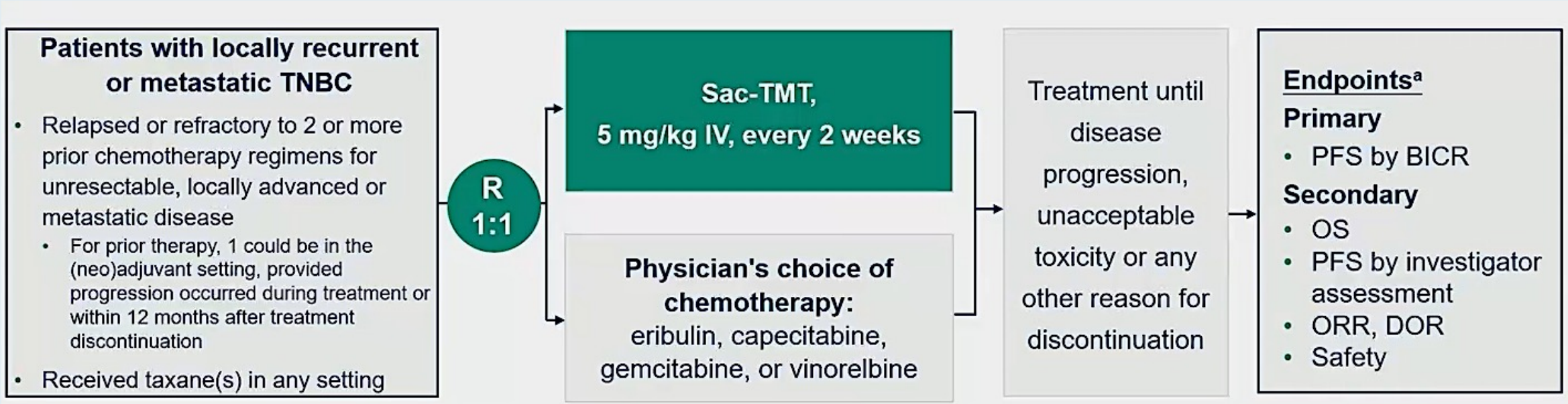
Abstract 104

Sacituzumab Tirumotecan (Sac-TMT, Also Known as SKB264/MK-2870) in Patients With Previously Treated Locally Recurrent or Metastatic Triple-Negative Breast Cancer (TNBC): Results From the Phase III OptiTROP-Breast01 Study

Binghe Xu,[1] Yongmei Yin,[2] Ying Fan,[1] Quchang Ouyang,[3] Lihua Song,[4] Xiaojia Wang,[5] Wei Li,[6] Man Li,[7] Xi Yan,[8] Shusen Wang,[9] Tao Sun,[10] Yue'e Teng,[11] Xianjun Tang,[12] Zhongsheng Tong,[13] Zhengkui Sun,[14] Xiaoping Jin,[15] Yina Diao,[15] Gesha Liu,[15] Junyou Ge[15]

[1]Cancer Hospital Chinese Academy of Medical Sciences, Beijing, China; [2]Jiangsu Province Hospital, Nanjing, China; [3]Hunan Cancer Hospital, Changsha, China; [4]Shandong Cancer Hospital, Jinan, China; [5]Zhejiang Cancer Hospital, Hangzhou, China; [6]The First Hospital of Jilin University, Changchun, China; [7]The Second Hospital of Dalian Medical University, Dalian, China; [8]West China Hospital of Sichuan University, Chengdu, China; [9]Sun Yat-sen University Cancer Center, Guangzhou, China; [10]Liaoning Cancer Hospital & Institute, Shenyang, China; [11]The First Hospital of China Medical University, Shenyang, China; [12]Chongqing University Cancer Hospital, Chongqing, China; [13]Tianjin Medical University Cancer Institute & Hospital, Tianjin, China; [14]Jiangxi Cancer Hospital, Nanchang, China; [15]Sichuan Kelun-Biotech Biopharmaceutical Co., Ltd., Chengdu, China

OptiTROP-Breast01 Phase III Trial Design



Stratification factors

- Line of prior therapy (2–3 vs >3)
- Presence of liver metastases (yes vs no)

Tumor assessment

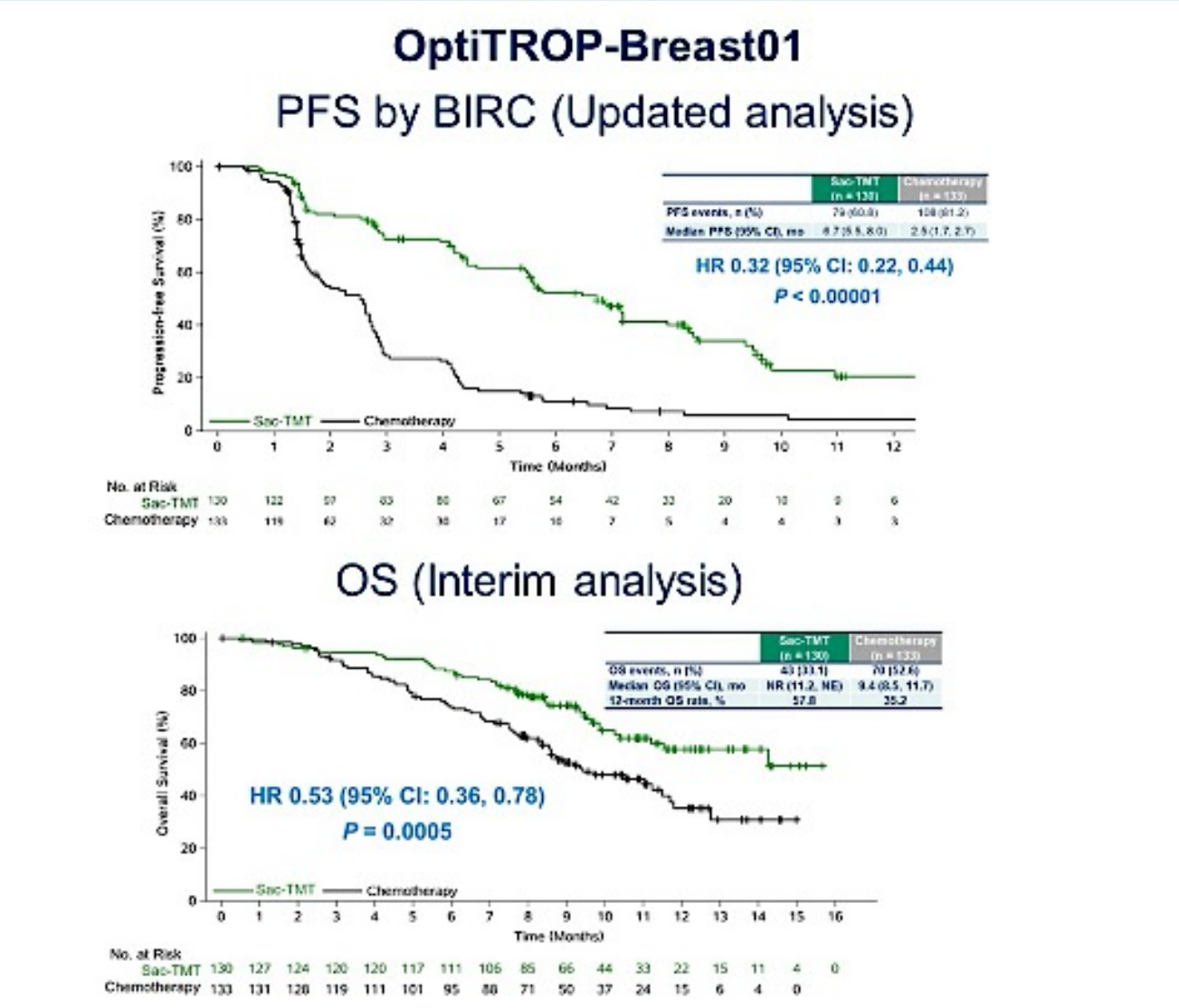
- Every 6 weeks for the first year and every 12 weeks afterward.

[a]Tumor response was assessed using RECIST version 1.1.

BICR, blinded independent central review; DOR, duration of response; IV, intravenous; ORR, objective response rate; OS, overall survival; PFS, progression-free survival; R, randomization; RECIST, Response Evaluation Criteria in Solid Tumors; TNBC, triple-negative breast cancer.

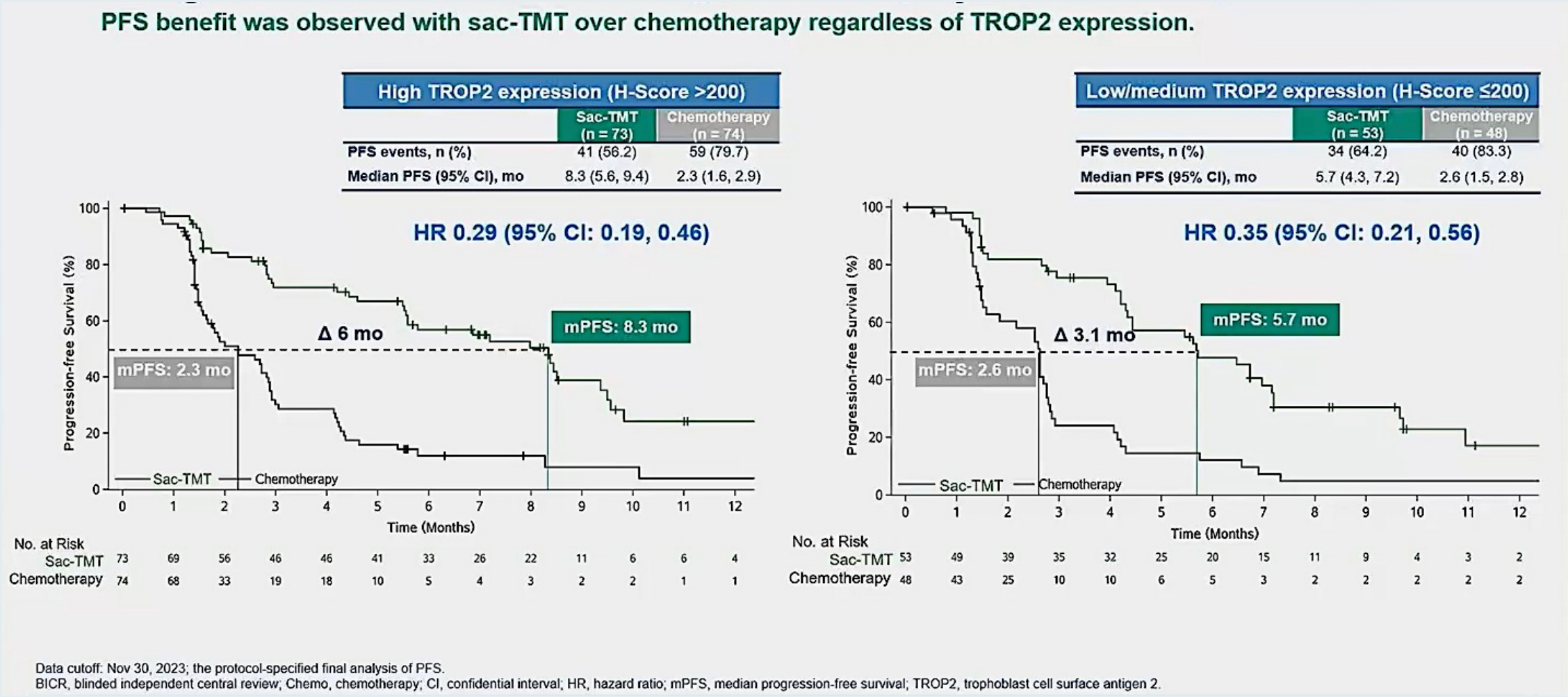
Xu B et al. ASCO 2024;Abstract 104.

OptiTROP-Breast01: Sacituzumab Tirumotecan Efficacy in the ITT Population



Xu B et al. ASCO 2024;Abstract 104.

OptiTROP-Breast01: PFS with Sacituzumab Tirumotecan (by BICR) by TROP2 Expression



Data cutoff: Nov 30, 2023; the protocol-specified final analysis of PFS.
BICR, blinded independent central review; Chemo, chemotherapy; CI, confidential interval; HR, hazard ratio; mPFS, median progression-free survival; TROP2, trophoblast cell surface antigen 2.

Xu B et al. ASCO 2024;Abstract 104.

RTP RESEARCH TO PRACTICE

Original Reports | Breast Cancer

Patritumab Deruxtecan (HER3-DXd), a Human Epidermal Growth Factor Receptor 3–Directed Antibody-Drug Conjugate, in Patients With Previously Treated Human Epidermal Growth Factor Receptor 3–Expressing Metastatic Breast Cancer: A Multicenter, Phase I/II Trial

Ian E. Krop, MD, PhD[1]; Norikazu Masuda, MD, PhD[2]; Toru Mukohara, MD, DMedSci[3]; Shunji Takahashi, MD, PhD[4]; Takahiro Nakayama, MD, PhD[5]; Kenichi Inoue, MD, PhD[6]; Hiroji Iwata, MD, PhD[7]; Yutaka Yamamoto, MD, PhD[8]; Ricardo H. Alvarez, MD, MSc[9]; Tatsuya Toyama, MD, PhD[10]; Masato Takahashi, MD[11]; Akihiko Osaki, MD, PhD[12]; Shigehira Saji, MD, PhD[13]; Yasuaki Sagara, MD, MPH[14]; Joyce O'Shaughnessy, MD[15]; Shoichi Ohwada, PhD[16]; Kumiko Koyama, PhD[16]; Tatsuya Inoue, MD, PhD[17]; Li Li, PhD[18]; Parul Patel, MS[18]; Joseph Mostillo, PharmD[18]; Yoshimi Tanaka, MA[18]; David W. Sternberg, MD, PhD[18]; Dalila Sellami, MD[18]; and Kan Yonemori, MD, PhD[19]

J Clin Oncol 2023;41(36):5550-60.

U31402-A-J101: Clinical Activity of Patritumab Deruxtecan Across Breast Cancer Subtypes

	HR+/HER2− (n = 113)	TNBC (n = 53)	HER2+ (n = 14)
Outcome (BICR per RECIST 1.1)	HER3-High[a] and HER3-Low	HER3-High[a]	HER3-High[a]
Confirmed ORR (95% CI), %[b]	30.1 (21.8 to 39.4)	22.6 (12.3 to 36.2)	42.9 (17.7 to 71.1)
Best overall response, %[c]			
PR	30.1	22.6	42.9
SD	50.4	56.6	50.0
PD	11.5	17.0	7.1
NE	8.0	3.8	0
DCR (95% CI), %	80.5 (72.0 to 87.4)	79.2 (65.9 to 89.2)	92.9 (66.1 to 99.8)
CBR (95% CI), %	43.4 (34.1 to 53.0)	35.8 (23.1 to 50.2)	50.0 (23.0 to 77.0)
DOR, median (95% CI), months	7.2 (5.3 to NE)	5.9 (3.0 to 8.4)	8.3 (2.8 to 26.4)
PFS, median (95% CI), months	7.4 (4.7 to 8.4)	5.5 (3.9 to 6.8)	11.0 (4.4 to 16.4)
Six-month PFS rate (95% CI), %	53.5 (43.4 to 62.6)	38.2 (24.2 to 52.0)	51.6 (22.1 to 74.8)
OS, median (95% CI), months	14.6 (11.3 to 19.5)	14.6 (11.2 to 17.2)	19.5 (12.2 to NE)

BC = breast cancer; BICR = blinded independent central review; CBR = clinical benefit rate; DCR = disease control rate; DOR = duration of response; HER2 = human epidermal growth factor receptor 2; HER2+ = HER2-positive; HER2- = HER2-negative; HER3 = human epidermal growth factor receptor 3; HR + = hormone receptor-positive; IHC = immunohistochemistry; NE = not estimable; ORR = objective response rate; OS = overall survival; PD = progressive disease; PFS = progression-free survival; PR = partial response; SD = stable disease; TNBC = triple-negative breast cancer.

[a] HER3-high includes patients assessed as IHC 2+/3 + or ≥75% HER3 membrane positivity.

[b] 95% exact binomial CI (by the Clopper-Pearson method).

[c] No patients had a complete response.

Krop IE et al. *J Clin Oncol* 2023;41(36):5550-60.

RTP RESEARCH TO PRACTICE

Questions for the faculty related to the use of patritumab deruxtecan for HER3-expressing mBC

- How to test for HER3 accurately, can we use in HER2 failures?
- Do we need to check expression of HER3?
- This drug was studied in EGFR-mutated lung cancer — has HER3 expression been correlated with response in breast cancer?
- Does patritumab deruxtecan function similar to T-DM1 or T-DXd in terms of the requirement for HER3 expression level?
- Is there a difference if HER3 is negative?
- Can this be used in sequence after trastuzumab deruxtecan?
- How do you sequence this ADC and T-DXd?
- Can you use the drug earlier?
- Who would be best candidates for this?
- What's the best sequence of therapy?
- For HER3 positive and HER2 low mBC how would you sequence T-DXd and patritumab?
- What would be the optimal way to sequence this drug? Is there benefit to sequencing this after trastuzumab deruxtecan failure?
- What are the adverse effects of this medication?
- Any advice for side effects management?

Survey of US-based general medical oncologists

RTP RESEARCH TO PRACTICE

2024 ASCO ANNUAL MEETING

Abstract 1005

Enfortumab Vedotin in the HR+/HER2− and Triple-Negative Breast Cancer Cohorts of EV-202

Antonio Giordano, MD, PhD;[1] Arif Ali Awan, MD;[2] Justine Yang Bruce, MD;[3] Hope S. Rugo, MD;[4] Jennifer R. Diamond, MD;[5] Yelena Novik, MD;[6] Joaquina Baranda, MD;[7] Kei Muro, MD, PhD;[8] Makiko Ono, MD;[9] Rita Nanda, MD;[10] Jason Kaplan, MD;[11] Seema Gorla, MD;[11] Shubin Liu, MSc;[11] Michele Wozniak, PhD;[11] Anthony Lee, PharmD;[12] Tiffany Traina, MD[13]

[1]Dana-Farber Cancer Institute, Harvard Medical School, Boston, MA, USA; [2]Ottawa Hospital Research Institute, Ottawa, Canada; [3]University of Wisconsin Carbone Cancer Center, Madison, WI, USA; [4]University of California, San Francisco, CA, USA; [5]University of Colorado Cancer Center, Aurora, CO, USA; [6]NYU Langone Health, New York, NY, USA; [7]University of Kansas Medical Center, Westwood, KS, USA; [8]Aichi Cancer Center Hospital, Nagoya, Japan; [9]Cancer Institute Hospital, Tokyo, Japan; [10]The University of Chicago Medicine, Chicago, IL, USA; [11]Astellas Pharma, Inc., Northbrook, IL, USA; [12]Pfizer Inc., Bothell, WA, USA; [13]Memorial Sloan Kettering Cancer Center, New York, NY, USA

EV-202: Conclusions

- EV demonstrated antitumor activity in both the HR+/HER2- BC and TNBC cohorts, though the prespecified ORR threshold was not met
- Safety in both cohorts was manageable and consistent with previous reports
- Nectin-4 was highly expressed in both cohorts, and expression was similar between responders and non-responders
- Based on the totality of the data, we are evaluating potential future development opportunities for EV in BC

Giordano A et al. ASCO 2024;Abstract 1005.

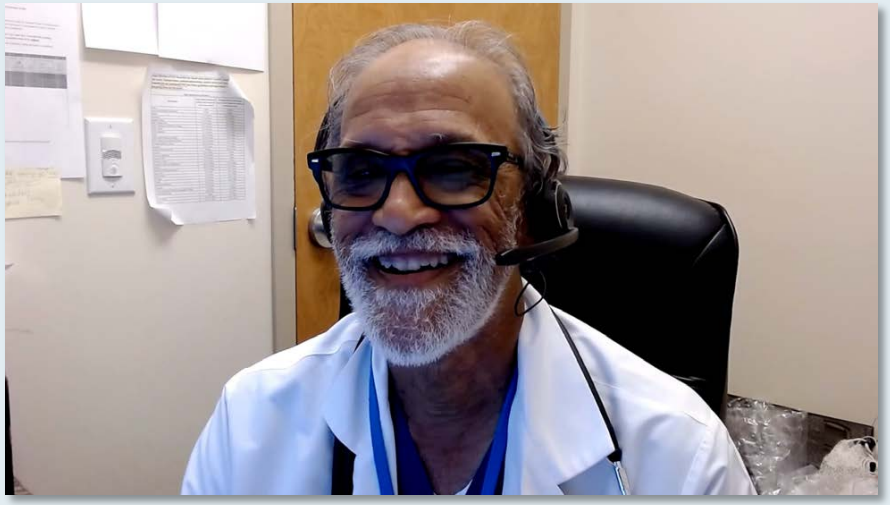
Case Presentation: 54-year-old woman with TNBC chest wall metastatic recurrence after fulvestrant/abemaciclib for ER-positive, HER2-negative breast cancer – PIK3CA mutation

Dr Ranju Gupta (Bethlehem, Pennsylvania)

RTP
RESEARCH
TO PRACTICE

Consulting Faculty

Ranju Gupta, MD
Lehigh Valley Topper Cancer Institute
Bethlehem, Pennsylvania



Kapisthalam (KS) Kumar, MD
Florida Cancer Specialists & Research Institute
Trinity, Florida

RTP
RESEARCH
TO PRACTICE

Year in Review: Gynecologic Oncology

A CME/MOC-Accredited Live Webinar

Tuesday, June 25, 2024
5:00 PM – 6:00 PM ET

Faculty

Dana M Chase, MD

Moderator

Neil Love, MD

RTP Year in Review 2024

Thank you for joining us!

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

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

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