Meet The Professor

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

Professor Peter Schmid, FRCP, MD, PhD
Centre Lead
Centre for Experimental Cancer Medicine
Barts Cancer Institute
London, United Kingdom

Commercial Support

This activity is supported by educational grants from AstraZeneca Pharmaceuticals LP, Gilead Sciences Inc and Merck.

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, Blueprint Medicines, Boehringer Ingelheim Pharmaceuticals Inc, Bristol-Myers Squibb Company, Celgene Corporation, Clovis Oncology, Coherus BioSciences, Daiichi Sankyo Inc, Eisai Inc, Epizyme Inc, Exact Sciences Inc, Exelixis Inc, Five Prime Therapeutics Inc, Foundation Medicine, G1 Therapeutics Inc, Genentech, a member of the Roche Group, Gilead Sciences Inc, GlaxoSmithKline, Grail Inc, 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, Lilly, Loxo Oncology Inc, a wholly owned subsidiary of Eli Lilly & Company, Merck, Novartis, Novocure Inc, Oncopeptides, Pfizer Inc, Pharmacyclics LLC, an AbbVie Company, Puma Biotechnology Inc, Regeneron Pharmaceuticals Inc, Sanofi Genzyme, Seagen Inc, Servier Pharmaceuticals LLC, Sumitomo Dainippon Pharma Oncology Inc, Taiho Oncology Inc, Takeda Oncology, Tesaro, A GSK Company, TG Therapeutics Inc, Turning Point Therapeutics Inc and Verastem Inc.

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Prof Schmid — Disclosures

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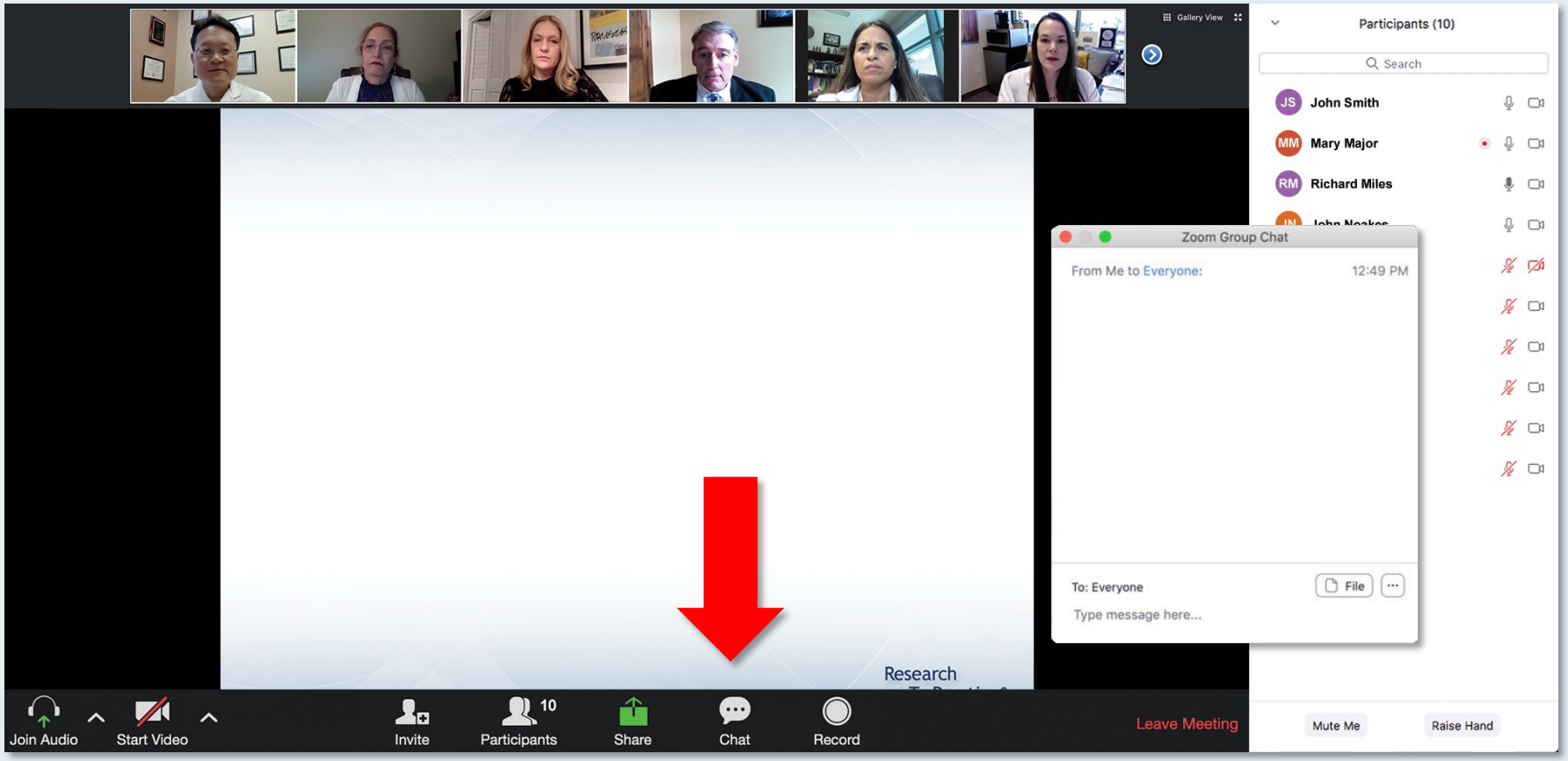
Contracted Research	Astellas, AstraZeneca Pharmaceuticals LP, Genentech, a member of the Roche Group, Medivation Inc, a Pfizer Company, Novartis, OncoGenex Pharmaceuticals Inc, Roche Laboratories Inc
Spouse Employment/Salary	Roche Laboratories Inc

We Encourage Clinicians in Practice to Submit Questions



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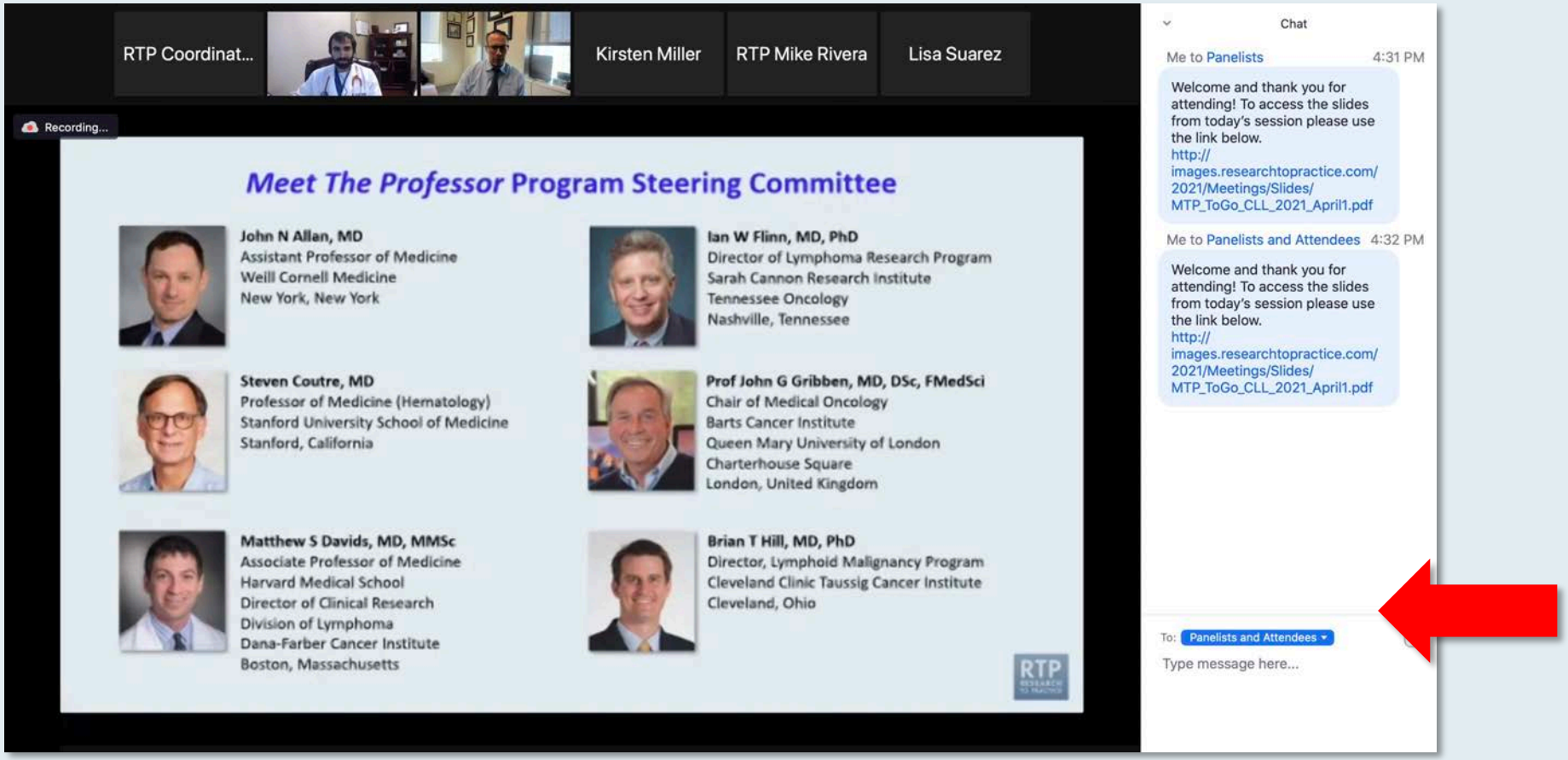

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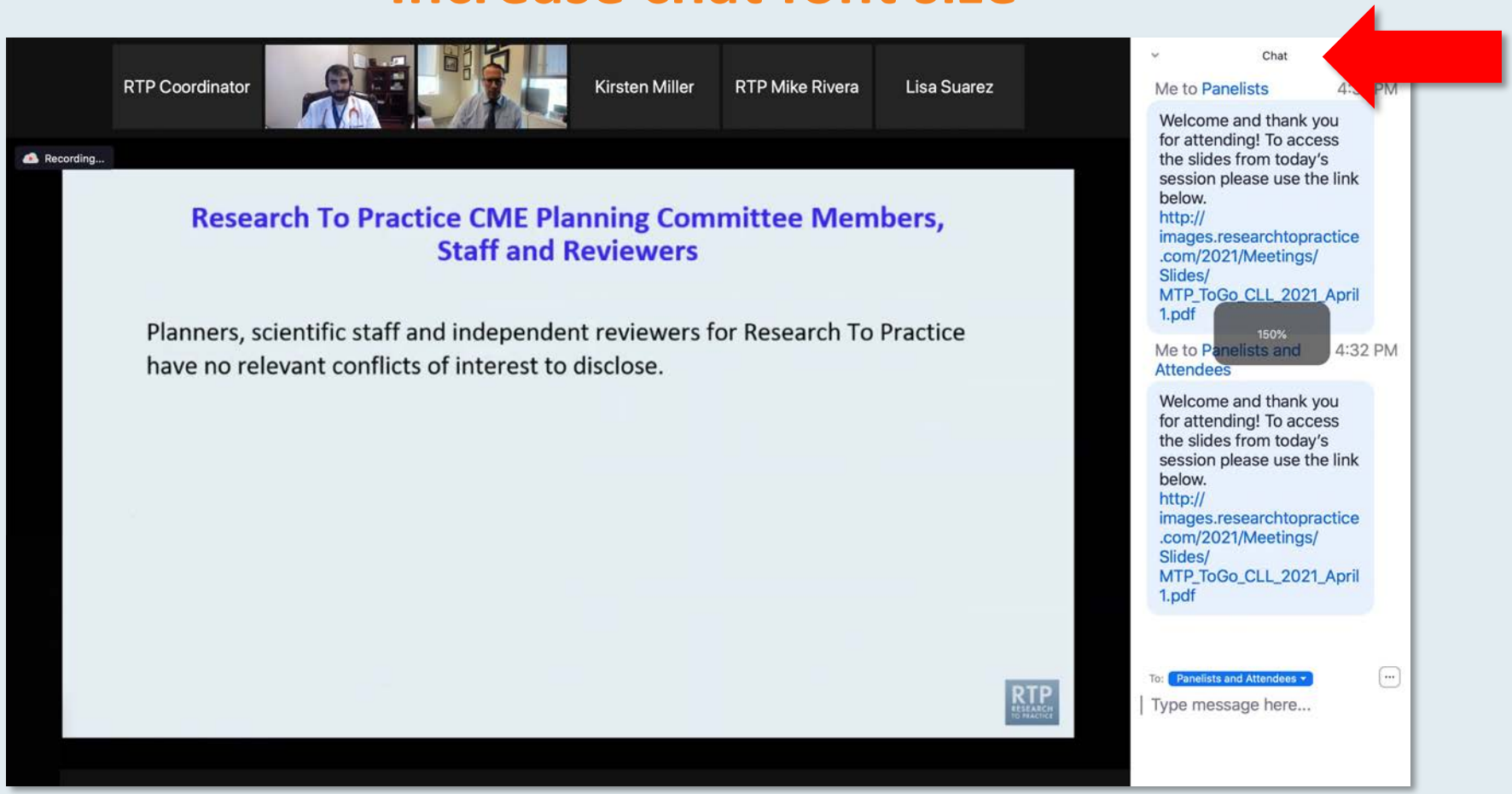

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Key Presentations on Breast Cancer from the 2021 ASCO Annual Meeting

DR SARA TOLANEY

DANA-FARBER CANCER INSTITUTE

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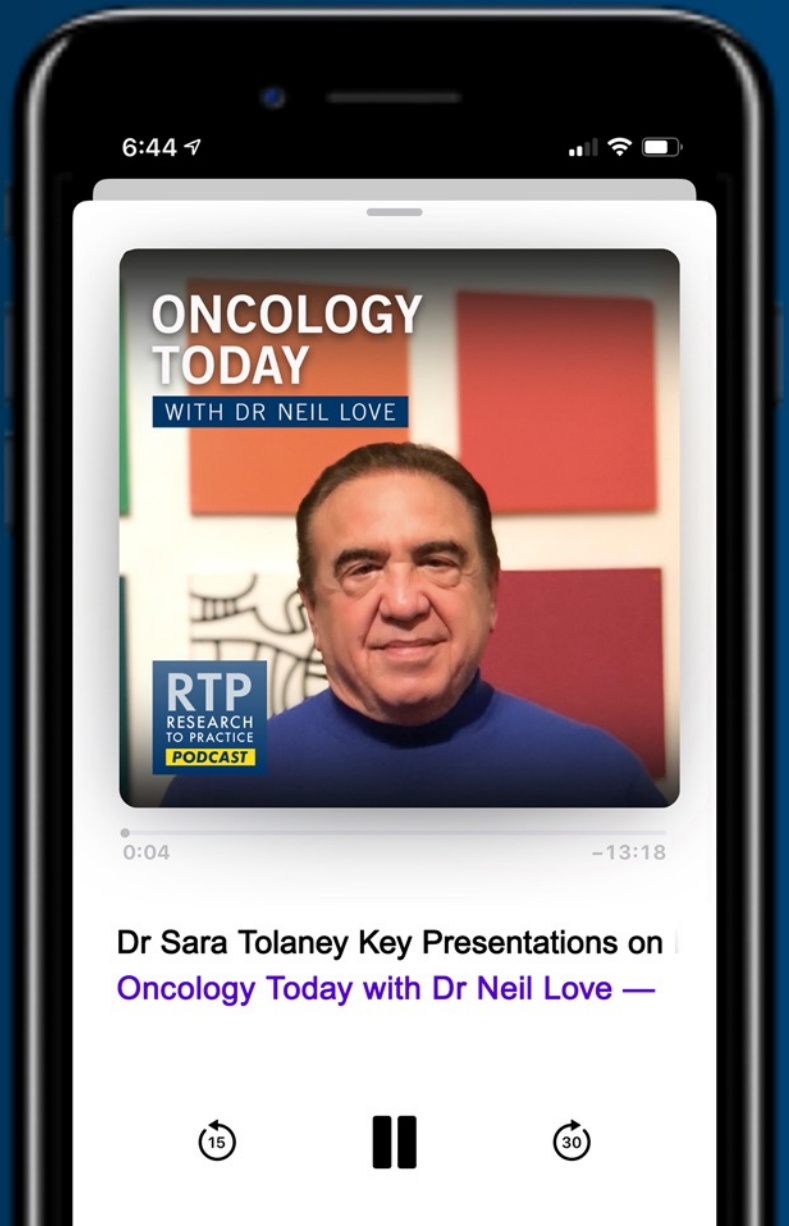

Meet The Professor

Optimizing the Clinical Management of Hodgkin and Non-Hodgkin Lymphomas

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

Faculty

Brad S Kahl, MD

Moderator

Neil Love, MD

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Meet The Professor

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

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

Faculty

Hans Hammers, MD, PhD

Moderator

Neil Love, MD

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

A CME/MOC-Accredited Virtual Event

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

Faculty

Richard R Furman, MD
Lindsey Roeker, MD

Consulting Cardiologist

Daniel J Lenihan, MD

Moderator

Neil Love, MD

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RESEARCH TO PRACTICE

Meet The Professor

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

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

Faculty

Virginia Kaklamani, MD, DSc

Moderator

Neil Love, MD

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Fall Oncology Nursing Series

A Complimentary NCPD-Accredited Virtual Curriculum

Hodgkin and Non-Hodgkin Lymphomas

Thursday, October 7, 2021
5:00 PM – 6:00 PM ET

Faculty

Stephen M Ansell, MD, PhD
Robin Klebig, APRN, CNP, AOCNP

Moderator

Neil Love, MD

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Meet The Professor

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

Friday, October 8, 2021
12:00 PM – 1:00 PM ET

Faculty

Eileen M O'Reilly, MD

Moderator

Neil Love, MD

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

Monday, October 11, 2021
5:00 PM – 6:00 PM ET

Faculty

Elizabeth R Plimack, MD, MS

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Meet The Professor

Immunotherapy and Novel Agents in Gynecologic Cancers

Tuesday, October 12, 2021
5:00 PM – 6:00 PM ET

Faculty

Shannon N Westin, MD, MPH

Moderator

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RESEARCH TO PRACTICE

Recent Advances and Future Directions in Oncology: A Daylong Multitumor Educational Webinar in Partnership with Florida Cancer Specialists

A CME-MOC/NCPD Accredited Virtual Event

Saturday, October 23, 2021
9:30 AM – 4:30 PM ET

Faculty

Tanios Bekaii-Saab, MD
Kristen K Ciombor, MD, MSCI
Brad S Kahl, MD
Mark Levis, MD, PhD
Mark D Pegram, MD
Daniel P Petrylak, MD
Noopur Raje, MD
David Sallman, MD
Lecia V Sequist, MD, MPH

Additional faculty to be announced.

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 Program Participating Faculty

Aditya Bardia, MD, MPH
Director, Breast Cancer Research Program
Associate Professor
Harvard Medical School
Attending Physician
Massachusetts General Hospital
Boston, Massachusetts

Sara Hurvitz, MD
Professor of Medicine
David Geffen School of Medicine at UCLA
Director, Breast Cancer Clinical Research Program
Co-Director, Santa Monica-UCLA Outpatient Oncology Practice
Santa Monica, California

Erika Hamilton, MD
Director, Breast and Gynecologic Research Program
Sarah Cannon Research Institute/Tennessee Oncology
Nashville, Tennessee

Rita Nanda, MD
Director, Breast Oncology
Associate Professor of Medicine
Section of Hematology/Oncology
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Chicago, Illinois

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Meet The Professor Program Participating Faculty

Joyce O'Shaughnessy, MD
Celebrating Women Chair in Breast Cancer Research
Baylor University Medical Center
Director, Breast Cancer Research Program
Texas Oncology
US Oncology
Dallas, Texas

Charles L Vogel, MD
Breast Medical Oncology
Baptist Health South Florida
Miami Cancer Institute
Plantation, Florida

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Research To Practice
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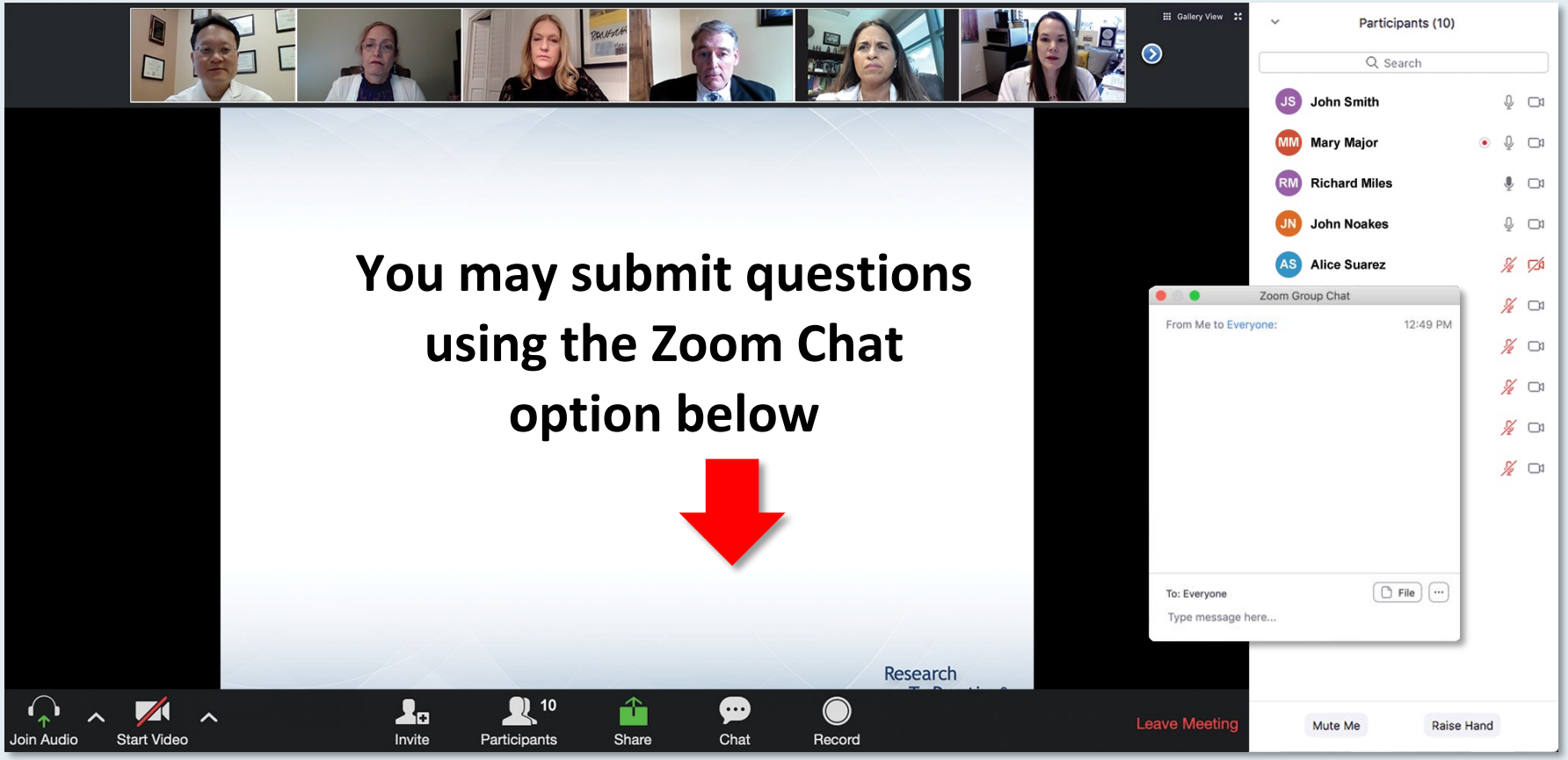

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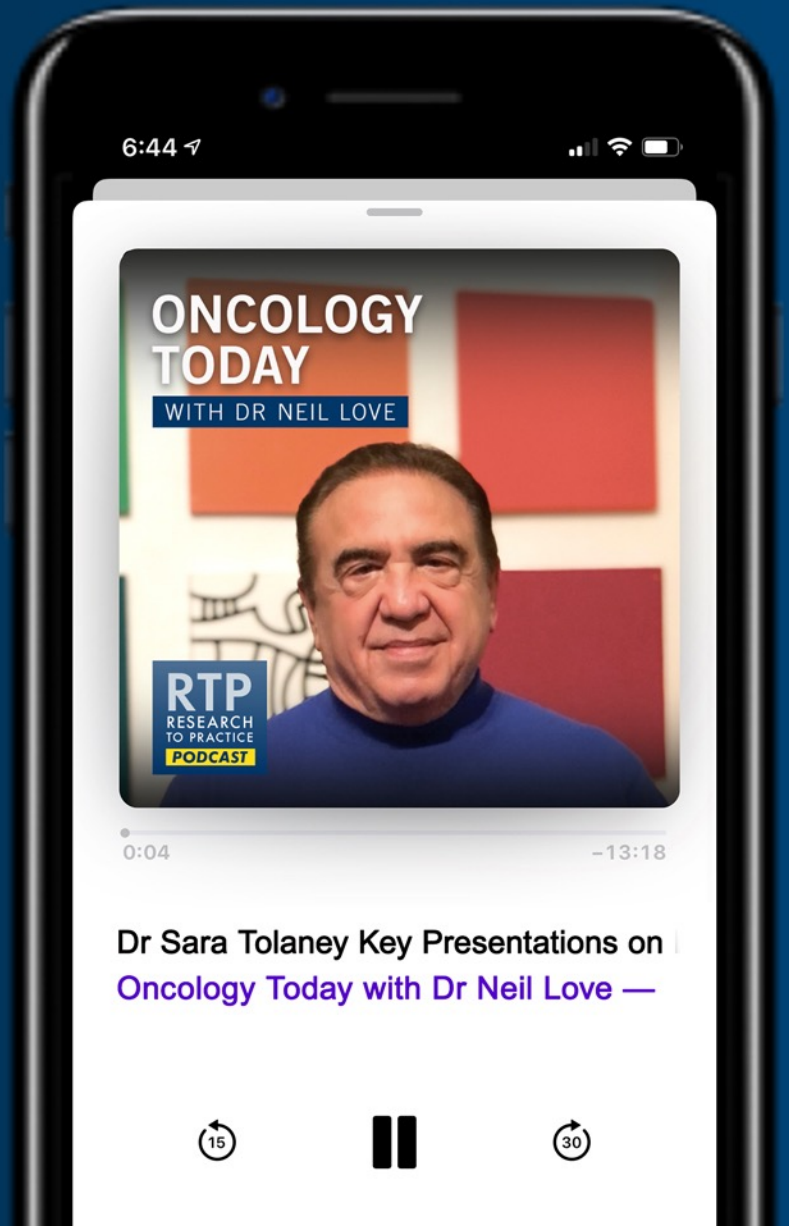

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Recent Advances and Future Directions in Oncology: A Daylong Multitumor Educational Webinar in Partnership with Florida Cancer Specialists

Module 1: Breast Cancer – 9:30 AM – 10:20 AM

Module 2: Lung Cancer – 10:30 AM – 11:20 AM

Module 3: Gastrointestinal Cancers – 11:30 AM – 12:20 PM

Module 4: Genitourinary Cancers – 12:30 PM – 1:20 PM

Module 5: CLL and Lymphomas – 1:30 PM – 2:20 PM

Module 6: Multiple Myeloma – 2:30 PM – 3:20 PM

Module 7: AML and MDS – 3:30 PM – 4:20 PM

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Professor Peter Schmid, FRCP, MD, PhD
Centre Lead
Centre for Experimental Cancer Medicine
Barts Cancer Institute
London, United Kingdom

Mamta Choksi, MD
Florida Cancer Specialists and
Research Institute
New Port Richey, Florida

Kapisthalam (KS) Kumar, MD
Physician Partner
Florida Cancer Specialists
New Port Richey, Florida

Ranju Gupta, MD
Attending Physician
Co-Director, Cardio-Oncology Program
LVPG Hematology Oncology Associates
Lehigh Valley Health Network
Bethlehem, Pennsylvania

Joseph Martins, MD
Associate Professor of Medicine
UT Health Science Center
Tyler, Texas

Nikesh Jasani, MD
Texas Oncology-Cypress
Houston, Texas

Andrea Stebel, MD
Newport Breast Care
Newport Beach, California

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Meet The Professor with Prof Schmid

MODULE 1: ESMO 2021 Review

MODULE 2: Case Presentations

- Dr Jasani: A 60-year-old Jehovah's Witness with metastatic TNBC – PD-L1 >1%
- Dr Martins: A 54-year-old woman with node-positive TNBC
- Dr Gupta: A 48-year-old nurse with TNBC and a germline BRCA2 mutation
- Dr Choksi: A 73-year-old woman with MSS TNBC and suspected bone metastases
- Dr Kumar: A 53-year-old Jehovah's Witness with localized TNBC
- Dr Stebel: A 45-year-old woman with locally recurrent TNBC

MODULE 3: Beyond the Guidelines

MODULE 4: Journal Club with Prof Schmid

MODULE 5: Other Key Data Sets

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ESMO 2021 Review

- Schmid P et al. **KEYNOTE-522: Phase 3 study of pembrolizumab + chemotherapy vs placebo + chemotherapy as neoadjuvant treatment, followed by pembrolizumab vs placebo as adjuvant treatment for early triple-negative breast cancer (TNBC).** ESMO 2021;Abstract VP7_2021.
- Rugo HS et al. **KEYNOTE-355: Final results from a randomized, double-blind phase III study of first-line pembrolizumab + chemotherapy vs placebo + chemotherapy for metastatic TNBC.** ESMO 2021;Abstract LBA16.
- Marmé F et al. **Phase III post-neoadjuvant study evaluating sacituzumab govitecan (SG), an antibody drug conjugate in primary HER2-negative breast cancer patients with high relapse risk after standard neoadjuvant treatment: SASCIA.** ESMO 2021; Abstract 199TiP.

ESMO 2021 Review

- Tsai M et al. **Weekly ladiratuzumab vedotin monotherapy for metastatic triple-negative breast cancer.** ESMO 2021;Abstract 259P.
- Martin M et al. **Outcomes of patients (pts) who had received prior platinum (PP) therapy in the phase III EMBRACA trial of talazoparib (TALA) vs physician's choice of chemotherapy (PCT) in patients with germline BRCA1/2 mutated (gBRCA1/2mut) advanced breast cancer (ABC).** ESMO 2021;Abstract 272P.

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Case Presentation – Dr Jasani: A 60-year-old Jehovah's Witness with metastatic TNBC – PD-L1 >1%

Dr Nikesh Jasani

- Massive chest wall disease which extended into the right, reconstructed breast, and mediastinal, supraclavicular lymph node involvement and pleural effusion, PD-L1 >1%
- *Nab*-paclitaxel/atezolizumab, with minimal response, continued PD
- Sacituzumab govitecan, with clinical and radiographic response
  - Neutropenia addressed by growth factor support

Case Presentation – Dr Martins: A 54-year-old woman with node-positive TNBC

Dr Joseph Martins

- PMH: Tetralogy of Fallot, s/p multiple cardiac surgeries in childhood
  - EF: 50-55%
- 6/2017: TNBC, s/p mastectomy and axillary node dissection (T2N2), with 6 of 17 positive lymph nodes
- Docetaxel/carboplatin

Questions

- Have you encountered patients with Tetraology of Fallot and breast cancer to whom you have administered doxorubicin?
- Is there a survival advantage associated with neoadjuvant chemotherapy, or is its primary value an in vivo assessment of tumor responsiveness?

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Case Presentation – Dr Gupta: A 48-year-old nurse with TNBC and a germline BRCA2 mutation

Dr Ranju Gupta

- Nurse and colleague with triple-negative breast cancer and a germline BRCA2 mutation
- S/p neoadjuvant AC → Carboplatin/paclitaxel, with 1.5-mm residual disease in one node
- Enrolled on SWOG-1418 and receives adjuvant pembrolizumab x 1 year → Observation
- Patient calls inquiring about eligibility for olaparib

Case Presentation – Dr Choksi: A 73-year-old woman with MSS TNBC and suspected bone metastases

Dr Mamta Choksi

- 5/2020 Mammogram/US/Biopsy: 4.4-cm high-grade, ER/PR-negative, HER2-negative carcinoma, with lymphovascular invasion
- PET/CT staging denied → CT C/A/P: multifocal, left breast and axillary, mediastinal, hilar LAD
  - Clinical stage: T2N1/2M0, inflammatory characteristics
- 6/2020: AC → dd paclitaxel
- 10/2020 CT: Improvement in breast but possible bone involvement unconfirmed with further workup
- 12/2020 CT-guided bone biopsy: Negative
- 12/2020: After completion of chemotherapy, 2-2.5-cm residual disease in breast, erythematous changes over left breast, CEA increased from 13.8 to 17.4

Questions

- If she has residual disease based on the final pathology after surgery, what is the next treatment option you would recommend?
- What do we know about checkpoint inhibitor/chemotherapy regimens, especially in patients with triple-negative inflammatory breast cancer?

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Case Presentation – Dr Kumar: A 53-year-old Jehovah's Witness with localized TNBC

Dr KS Kumar

- PMH: Primary biliary cirrhosis of the liver, Child-Pugh A; Massive GI bleeding 3 years ago, with varices treated with iron, epoetin-alfa and TIPS procedure; Scleroderma
- Presents with 2-cm mass in the right breast → Biopsy-confirmed TNBC

Questions

- How would you manage this patient for whom it would be difficult to administer neoadjuvant chemotherapy? Would you proceed to surgery and then offer adjuvant chemotherapy?
- What are your thoughts about adjuvant immunotherapy for this patient in light of her underlying autoimmune disease?

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Case Presentation – Dr Stebel: A 45-year-old woman with locally recurrent TNBC

Dr Andrea Stebel

- Large left breast cancer, with nodal involvement, TNBC, BRCA1/2 wild type
- Neoadjuvant FEC → docetaxel per PACS 0 → Mastectomy, with pCR → RT
- After 2 years, developed subcutaneous lesions outside the area of radiation ports
  - Biopsy and NGS: PD-L1-negative, no actionable mutations
- *Nab*-paclitaxel/carboplatin, with complete resolution of skin lesions
- Six months later, developed new skin lesions around radiation ports, with plans for RT to the site
- Eribulin

Questions

- What other markers can be looked for?
- Other than standard chemotherapy, what are her next options for treatment?
- Should all patients with TNBC be treated with extended adjuvant capecitabine?

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A 45-year-old woman who completed dose-dense AC-T and radiation therapy 3 years ago for localized TNBC now presents with low-volume metastatic disease to the lung and bones. What type of biomarker assessment would you recommend?

 Dr Bardia	PD-L1, Germline BRCA, NGS
 Dr Hamilton	PD-L1, Germline BRCA, NGS
 Dr Nanda	PD-L1, Germline BRCA, NGS
 Dr O'Shaughnessy	PD-L1, Germline BRCA, NGS
 Dr Vogel	PD-L1, Germline BRCA, NGS

NGS = next-generation sequencing

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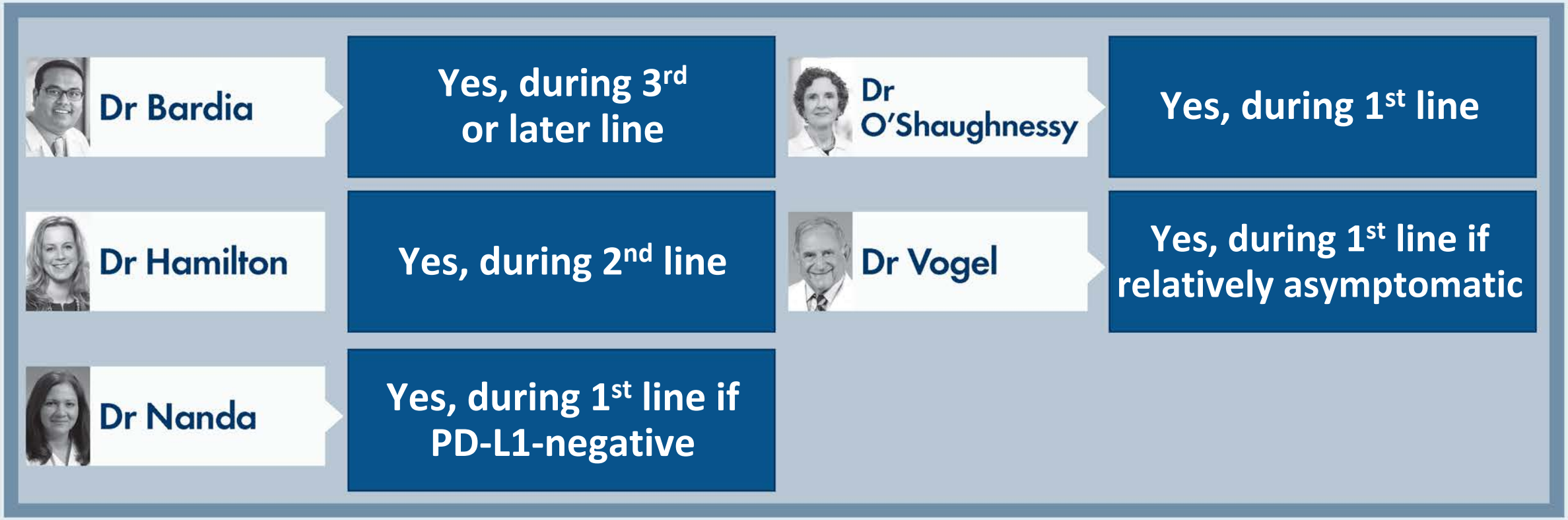
If a patient with TNBC and a germline BRCA1/2 mutation received olaparib as part of adjuvant therapy on a clinical trial and then developed metastatic disease 3 years later, would you attempt to administer a PARP inhibitor during a subsequent line of treatment?



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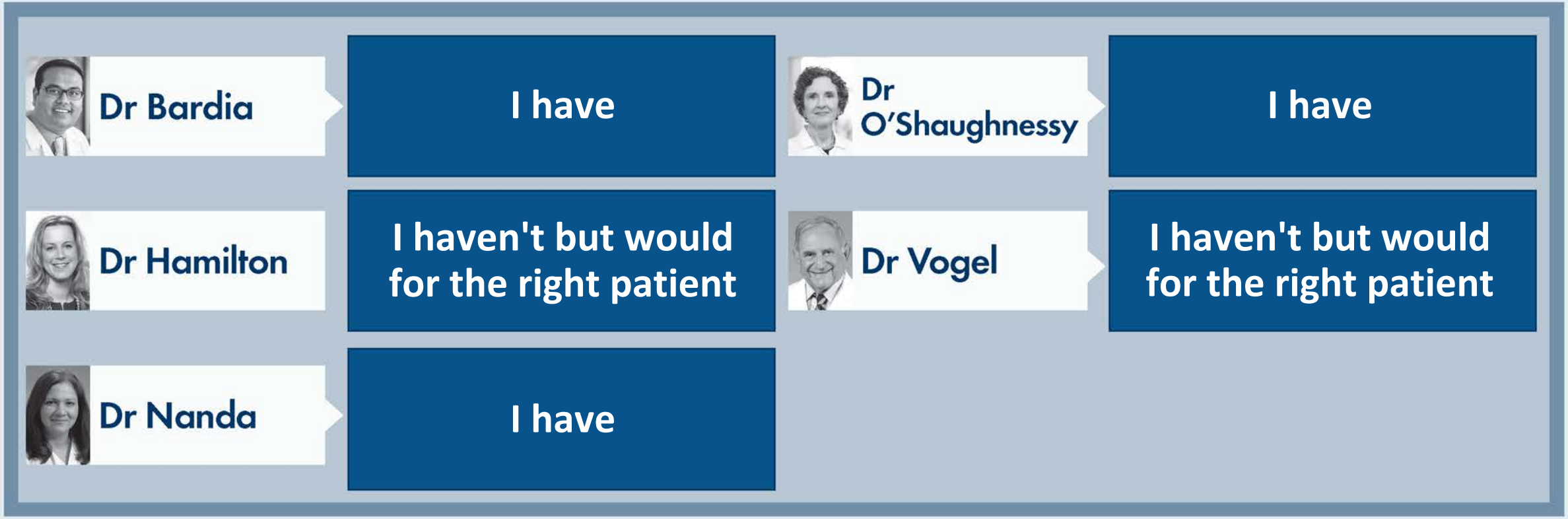
Regulatory and reimbursement issues aside, have you attempted or would you attempt to access a PARP inhibitor for a patient with metastatic TNBC and a somatic BRCA mutation?

 Dr Bardia	I have	 Dr O'Shaughnessy	I have
 Dr Hamilton	I have	 Dr Vogel	I haven't but would for the right patient
 Dr Nanda	I have		

Regulatory and reimbursement issues aside, have you attempted or would you attempt to access a PARP inhibitor for a patient with metastatic TNBC and a germline PALB2 mutation?



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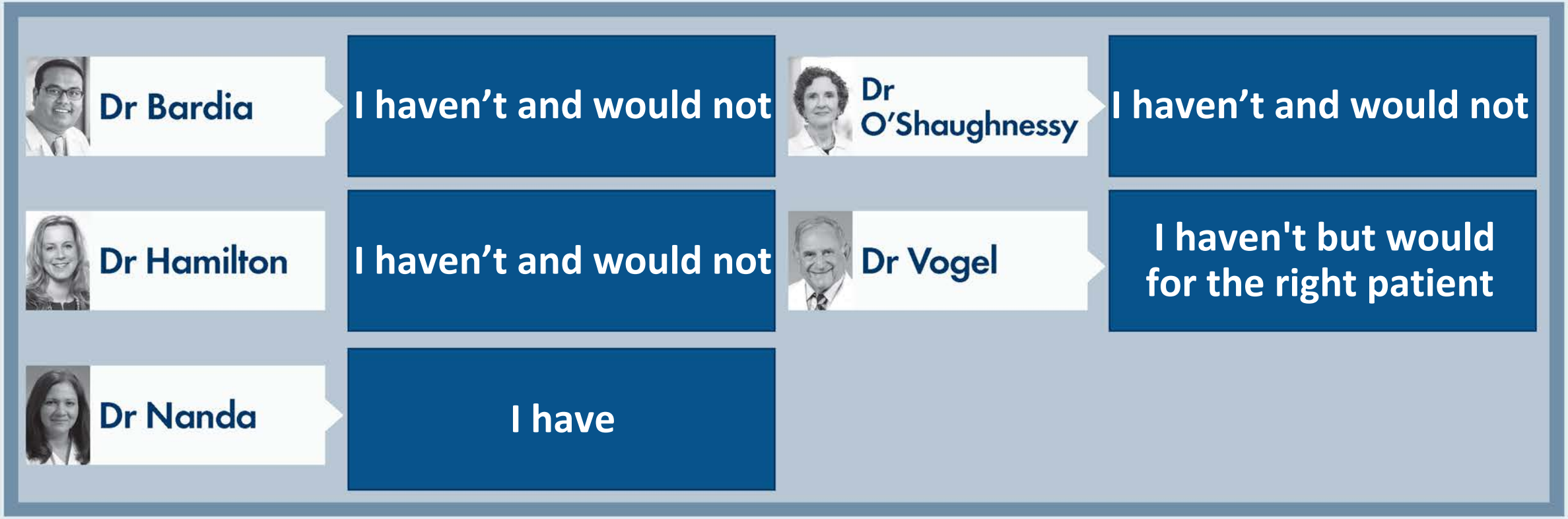
Regulatory and reimbursement issues aside, have you attempted or would you attempt to access a PARP inhibitor for a patient with metastatic TNBC and a germline ATM mutation?



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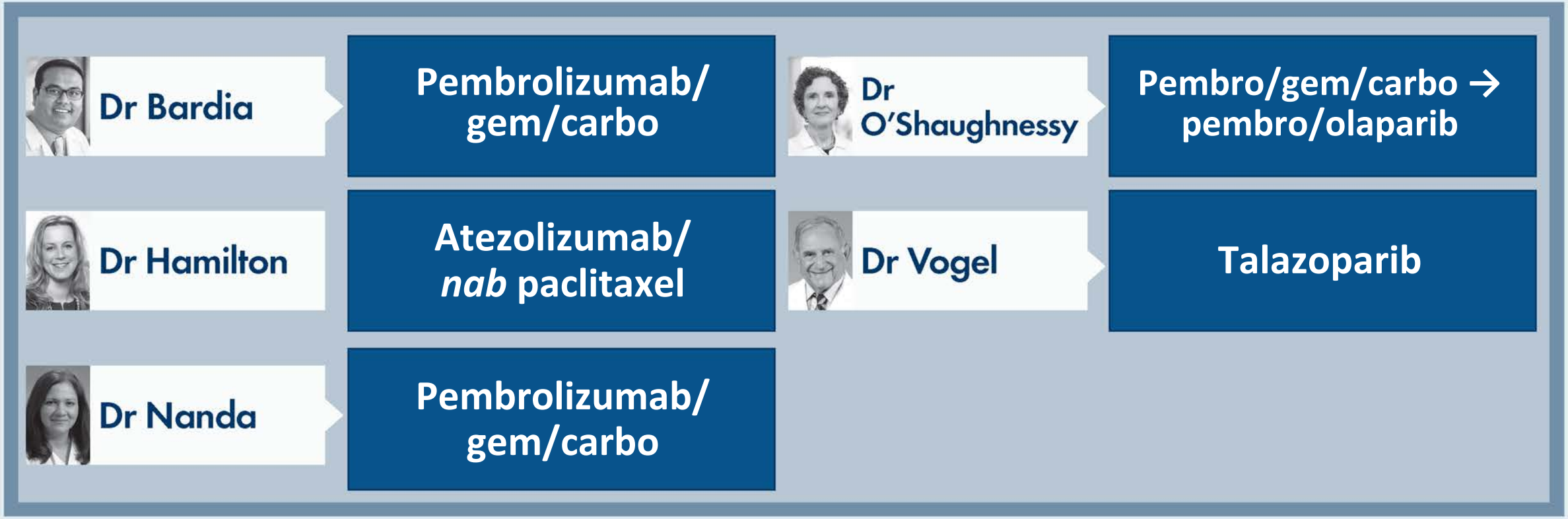
What would be your preferred treatment approach for a 60-year-old patient with a BRCA germline mutation and de novo metastatic TNBC that is PD-L1-positive?



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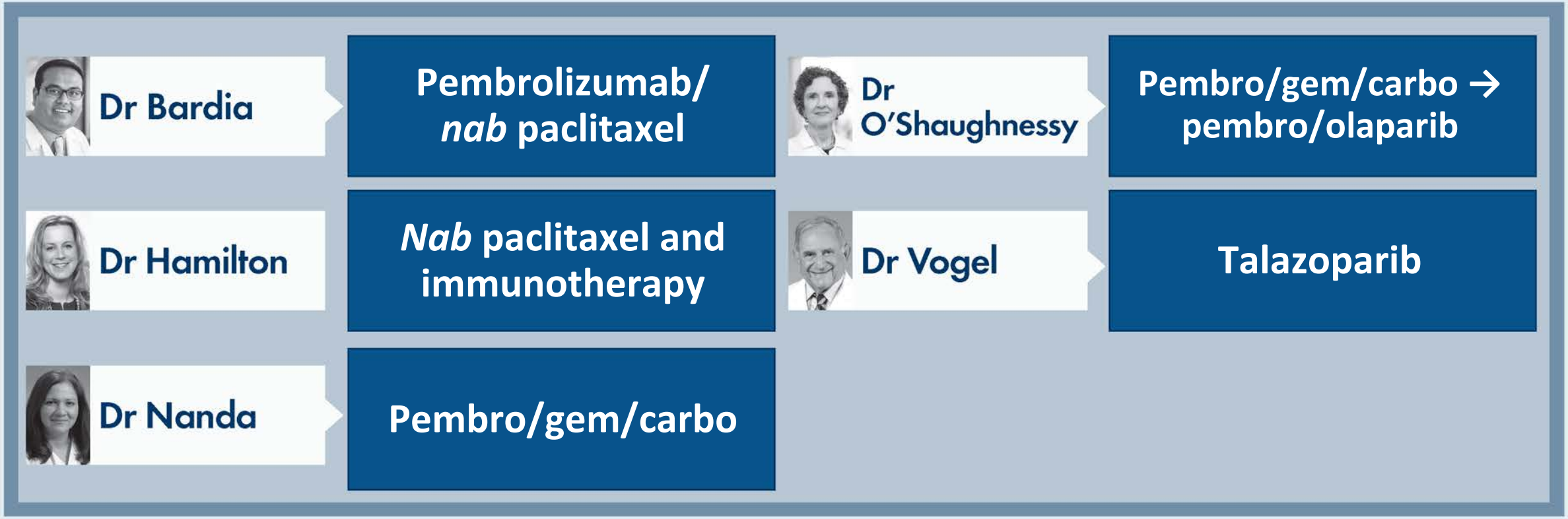
A 60-year-old woman with TNBC and a germline BRCA1 mutation (PD-L1 CPS >10) receives neoadjuvant carboplatin/paclitaxel/pembrolizumab → AC/ pembrolizumab and achieves a pathologic complete response. Three years after completion of adjuvant pembrolizumab, she develops metastatic TNBC (PD-L1 CPS >10). Which first-line treatment would you generally recommend?



Gem = gemcitabine; carbo = carboplatin

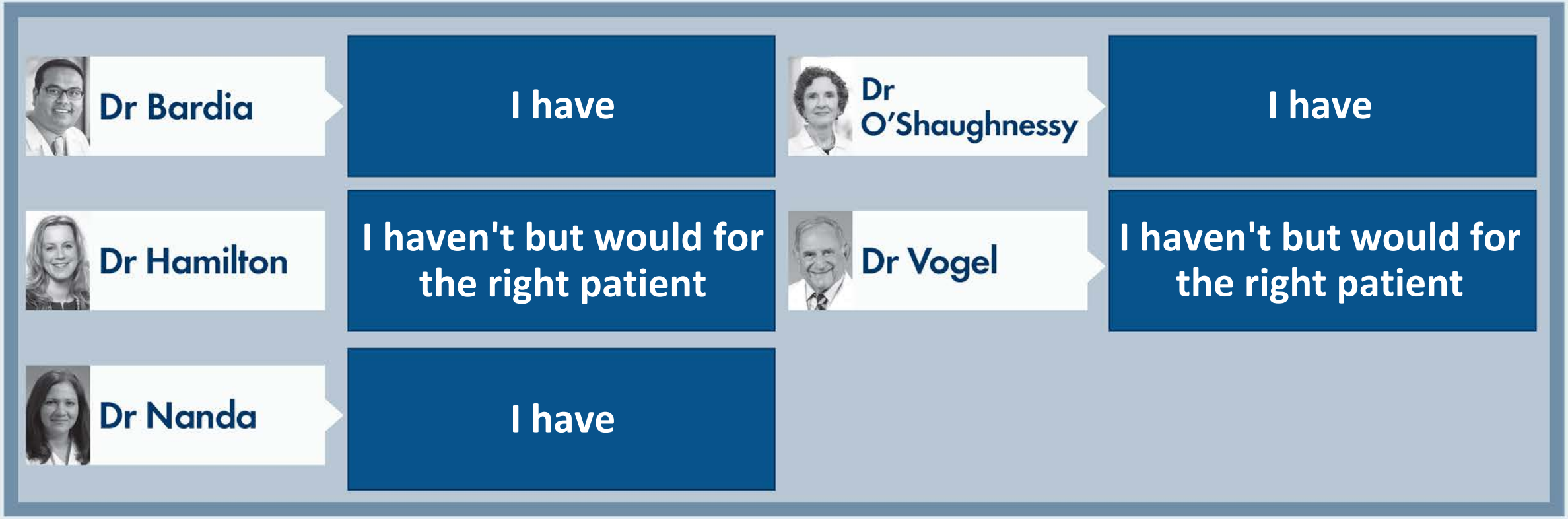
RTP RESEARCH TO PRACTICE

Regulatory and reimbursement issues aside, have you attempted or would you attempt to access olaparib as part of neoadjuvant therapy for a 45-year-old patient with a germline BRCA2 mutation and a 6-cm TNBC with negative axillary nodes on biopsy (PD-L1 10%)?

 Dr Bardia	I haven’t and would not	 Dr O’Shaughnessy	I haven’t and would not
 Dr Hamilton	I haven’t and would not	 Dr Vogel	I haven't but would for the right patient
 Dr Nanda	I haven't but would for the right patient		

RTP RESEARCH TO PRACTICE

Regulatory and reimbursement issues aside, have you attempted or would you attempt to access an anti-PD-1/PD-L1 antibody as part of neoadjuvant therapy for a 45-year-old patient with a germline BRCA2 mutation and a 6-cm TNBC with 3 positive axillary nodes on biopsy (PD-L1 10%)?



RTP RESEARCH TO PRACTICE

If olaparib receives FDA approval as adjuvant therapy for patients with germline BRCA mutations, would you incorporate it as adjuvant therapy for a patient who was also receiving neoadjuvant/adjuvant pembrolizumab?

RTP RESEARCH TO PRACTICE

A 60-year-old woman with BRCA1/2 wild-type TNBC and PD-L1 CPS >10 receives neoadjuvant carboplatin/paclitaxel/pembrolizumab → AC/pembrolizumab and achieves a pathologic complete response. Three years after completion of adjuvant pembrolizumab, she develops metastatic TNBC (BRCA1/2 wild type, PD-L1 CPS >10). Which first-line treatment would you generally recommend?

 Dr Bardia	Pembrolizumab/ *nab* paclitaxel
 Dr Hamilton	Atezolizumab/ *nab* paclitaxel
 Dr Nanda	Pembrolizumab/ *nab* paclitaxel
 Dr O'Shaughnessy	Pembrolizumab/ gem/carbo
 Dr Vogel	Atezolizumab/ *nab* paclitaxel

RTP RESEARCH TO PRACTICE

What treatment would you recommend next for a 60-year-old woman who received adjuvant carboplatin/paclitaxel, developed metastatic TNBC (BRCA wild type, PD-L1-positive) and experienced disease progression after 7 months of first-line atezolizumab/*nab* paclitaxel?

Dr Bardia

Sacituzumab govitecan

Dr O'Shaughnessy

Sacituzumab govitecan

Dr Hamilton

Sacituzumab govitecan

Dr Vogel

Sacituzumab govitecan

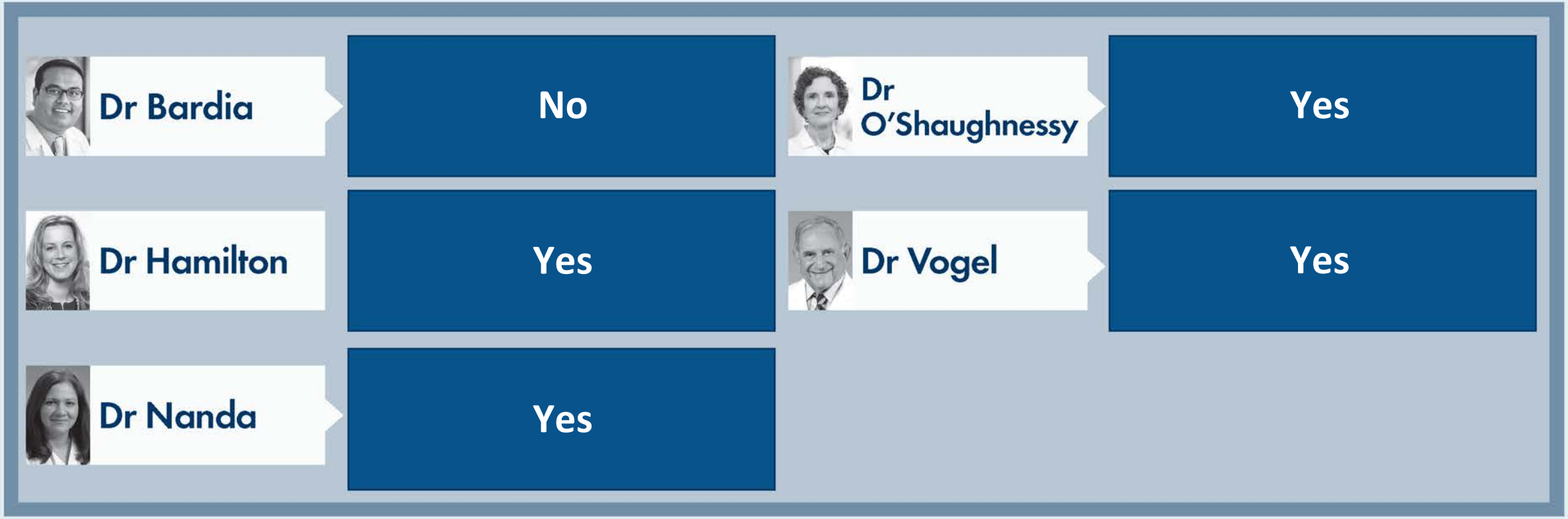
Dr Nanda

Sacituzumab govitecan

RTP RESEARCH TO PRACTICE

For a patient with localized TNBC and PD-L1 CPS ≥1, would you generally recommend neoadjuvant chemotherapy/ pembrolizumab → adjuvant pembrolizumab if they had…

3.0-cm tumor, N0?



RTP RESEARCH TO PRACTICE

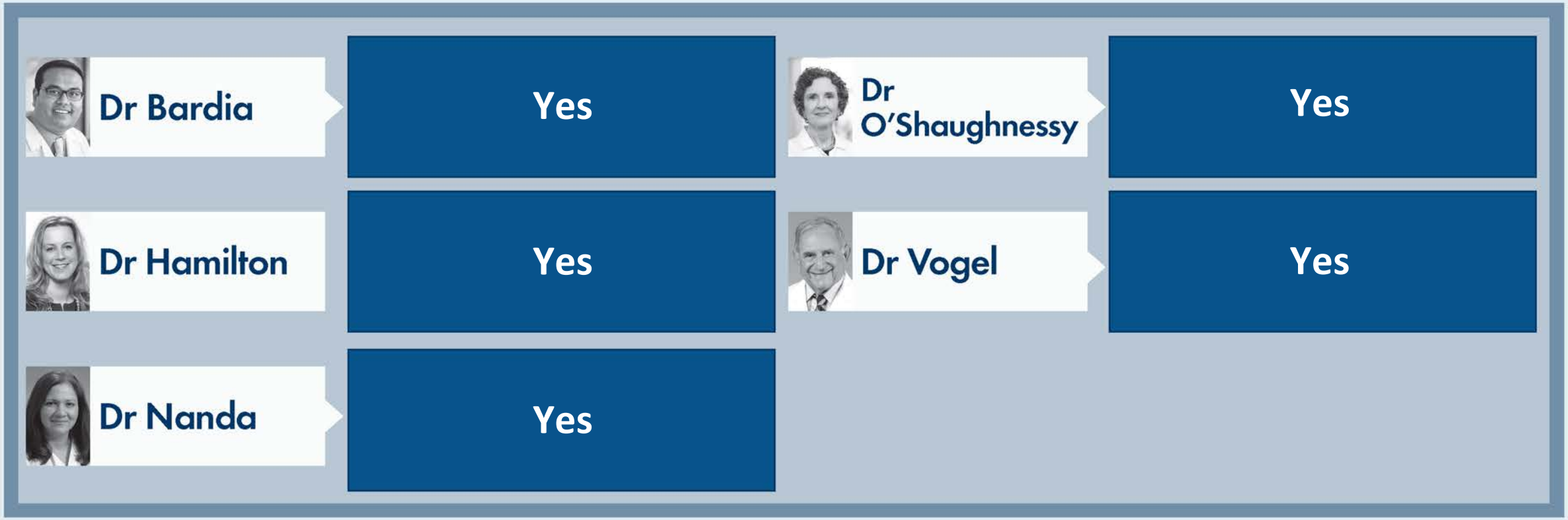
For a patient with localized TNBC and PD-L1 CPS ≥1, would you generally recommend neoadjuvant chemotherapy/ pembrolizumab → adjuvant pembrolizumab if they had…

6.0-cm tumor, N0?

RTP RESEARCH TO PRACTICE

For a patient with localized TNBC that was PD-L1-negative, would you generally recommend neoadjuvant chemotherapy/ pembrolizumab → adjuvant pembrolizumab if they had…

6.0-cm tumor, N0?



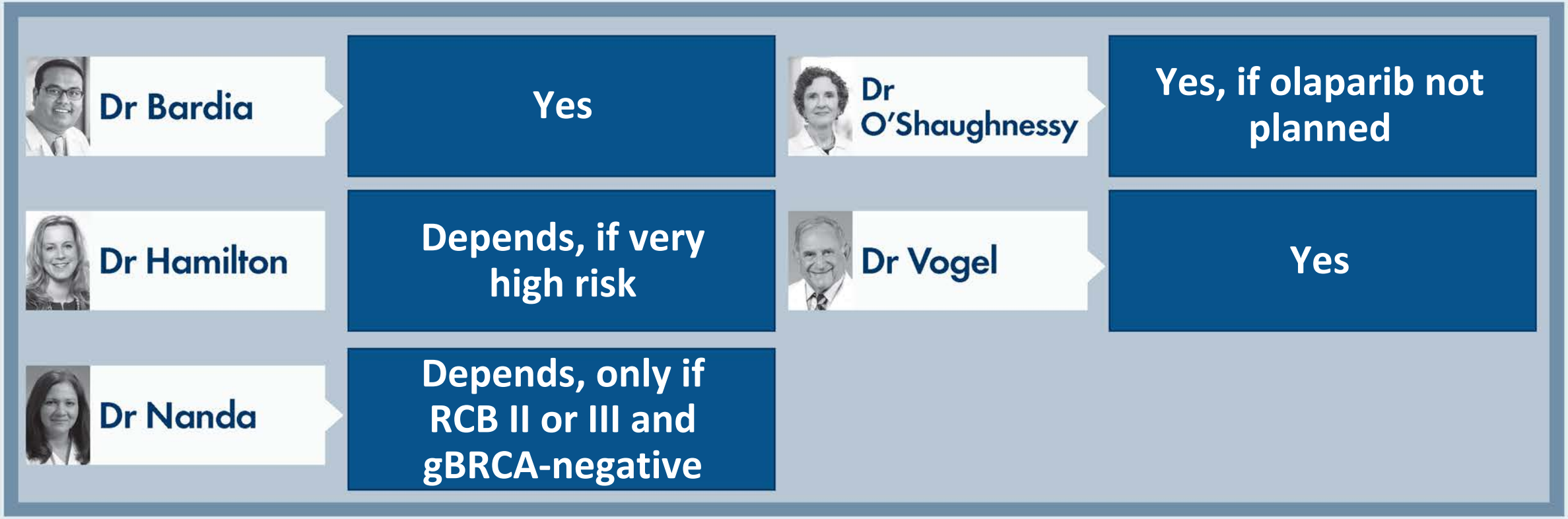
RTP RESEARCH TO PRACTICE

When administering neoadjuvant/adjuvant pembrolizumab, which schedule of pembrolizumab would you generally use?

 Dr Bardia	400 mg q6wk	 Dr O'Shaughnessy	200 mg q3wk neoadj, 400 mg q6wk adj
 Dr Hamilton	200 mg q3wk neoadj, 400 mg q6wk adj	 Dr Vogel	200 mg q3wk neoadj, 400 mg q6wk adj
 Dr Nanda	200 mg q3wk neoadj, 400 mg q6wk adj		

RTP RESEARCH TO PRACTICE

Would you likely include adjuvant capecitabine along with pembrolizumab if the patient had residual disease after neoadjuvant chemotherapy/pembrolizumab?



RCB = residual cancer burden

RTP RESEARCH TO PRACTICE

Meet The Professor with Prof Schmid

MODULE 1: ESMO 2021 Review

MODULE 2: Case Presentations

- Dr Jasani: A 60-year-old Jehovah's Witness with metastatic TNBC – PD-L1 >1%
- Dr Martins: A 54-year-old woman with node-positive TNBC
- Dr Gupta: A 48-year-old nurse with TNBC and a germline BRCA2 mutation
- Dr Choksi: A 73-year-old woman with MSS TNBC and suspected bone metastases
- Dr Kumar: A 53-year-old Jehovah's Witness with localized TNBC
- Dr Stebel: A 45-year-old woman with locally recurrent TNBC

MODULE 3: Beyond the Guidelines

MODULE 4: Journal Club with Prof Schmid

MODULE 5: Other Key Data Sets

RTP
RESEARCH
TO PRACTICE

Journal Club with Prof Schmid

- Huang M et al. **Association of pathologic complete response with long-term survival outcomes in triple-negative breast cancer: A meta-analysis.** *Cancer Res* 2020;80(24):5427-34.
- Schmid P et al. **ARB: Phase II window of opportunity study of preoperative treatment with enzalutamide in ER+ve and TNBC.** ESMO 2021;Abstract 208P.
- Hall PE, Schmid P. **Emerging drugs for the treatment of triple-negative breast cancer: A focus on phase II immunotherapy trials.** *Expert Opin Emerg Drugs* 2021;26(2):131-47.
- Emens LA et al. **Atezolizumab and nab-paclitaxel in advanced triple-negative breast cancer: Biomarker evaluation of the IMpassion130 study.** *J Natl Cancer Inst* 2021;113(8):1005-16.
- Schmid P et al. **BEGONIA: Phase 1b/2 study of durvalumab (D) combinations in locally advanced/metastatic triple-negative breast cancer (TNBC)—Initial results from arm 1, d+paclitaxel (P), and arm 6, d+trastuzumab deruxtecan (T-DXd).** ASCO 2021;Abstract 1023.

RTP
RESEARCH
TO PRACTICE

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MODULE 3: Beyond the Guidelines

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RTP RESEARCH TO PRACTICE

Pivotal Phase III Trials Supporting the FDA Approvals of Olaparib and Talazoparib for Metastatic Breast Cancer with a Germline BRCA Mutation

Trial	Eligibility	Randomization	Primary endpoint
OlympiAD[1] (n = 302)	• HER2-negative metastatic BC – ER+ and/or PR+ or TNBC • Deleterious or suspected deleterious gBRCA mutation • Prior anthracycline and taxane • ≤2 prior chemotherapy lines in metastatic setting	• Olaparib • Physician's choice – Capecitabine – Eribulin – Vinorelbine	• PFS by blinded independent central review
EMBRACA[2] (n = 431)	• HER2-negative locally advanced or metastatic BC • Germline BRCA1 or BRCA2 mutation • ≤3 prior cytotoxic chemotherapy regimens • Prior treatment with a taxane and/or anthracycline unless medically contraindicated	• Talazoparib • Physician's choice – Capecitabine – Eribulin – Gemcitabine – Vinorelbine	• PFS by blinded independent central review

[1] Robson M et al. *N Engl J Med* 2017;377(6):523-33. [2] Litton JK et al. San Antonio Breast Cancer Symposium 2017;Abstract GS6-07; www.clinicaltrials.gov. Accessed August 2019.

RTP RESEARCH TO PRACTICE

OlympiAD and EMBRACA: Efficacy Summary

	OlympiAD [1-3]	EMBRACA [4-6]
HR (PFS)	0.58	0.54
HR (PFS) ER/PR-positive	0.82	0.47
HR (PFS) TNBC	0.43	0.60
HR (OS)	0.84	0.76
ORR	59.9% (vs 28.8% TPC)	67.6% (vs 27.2% TPC)

TPC = treatment of physician's choice

Cross-trial comparisons are challenging in terms of determining the relative efficacy and tolerability of treatments

[1] Robson M et al. *N Engl J Med* 2017;377(6):523-33. [2] Robson M et al. *Ann Oncol* 2019;30(4):558-66. [3] Robson M et al. San Antonio Breast Cancer Symposium 2019;Abstract PD4-03. [4] Litton JK et al. *N Engl J Med* 2018;379(8):753-63. [5] Litton JK et al. San Antonio Breast Cancer Symposium 2017;Abstract GS6-07. [6] Rugo HS et al. ASCO 2018;Abstract 1069.

OlympiAD and EMBRACA: Adverse Event and Quality of Life Summary

	OlympiAD [1,2]	EMBRACA [3,4]
Serious AEs Grade ≥3	36.6% (vs 50.5% TPC)	25.5% (v. 25.4% TPC)
Anemia Grade ≥3	16.1%	39.2%
Neutropenia Grade ≥3	9.3%	20.9%
Thrombocytopenia Grade ≥3	2.4%	14.7%
MDS/AML	0	0
Nausea (any grade)	58.0%	48.6%
Alopecia (any grade)	3.4%	25.2%
Dose modification/reduction due to AE	25.4% (vs 30.8% TPC)	66% (vs 60% TPC)
Treatment discontinuation due to AE	4.9% (vs 7.7% TPC)	5.9% (vs 8.7% TPC)

Cross-trial comparisons are challenging in terms of determining the relative efficacy and tolerability of treatments

[1] Robson M et al. *N Engl J Med* 2017;377(6):523-33. [2] Robson M et al. *Ann Oncol* 2019;30(4):558-66. [3] Litton JK et al. *N Engl J Med* 2018;379(8):753-63. [4] Litton JK et al. San Antonio Breast Cancer Symposium 2017;Abstract GS6-07.

J Clin Oncol 2021;[Online ahead of print].

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.

2021 Updated Recommendations

- For patients with early-stage, 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;[Online ahead of print].

N Engl J Med 2021;384:2394-405

The NEW ENGLAND JOURNAL of MEDICINE

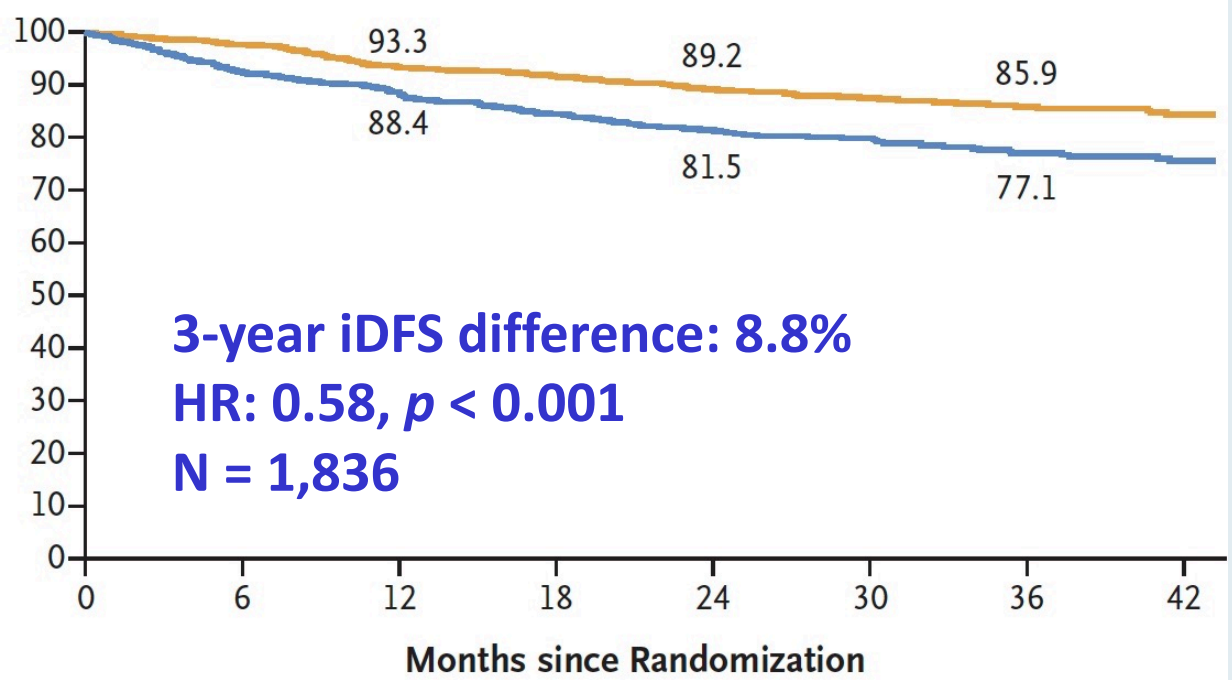
ORIGINAL ARTICLE

Adjuvant Olaparib for Patients with *BRCA1*- or *BRCA2*-Mutated Breast Cancer

A.N.J. Tutt, J.E. Garber, B. Kaufman, G. Viale, D. Fumagalli, P. Rastogi, R.D. Gelber, E. de Azambuja, A. Fielding, J. Balmaña, S.M. Domchek, K.A. Gelmon, S.J. Hollingsworth, L.A. Korde, B. Linderholm, H. Bandos, E. Senkus, J.M. Suga, Z. Shao, A.W. Pippas, Z. Nowecki, T. Huzarski, P.A. Ganz, P.C. Lucas, N. Baker, S. Loibl, R. McConnell, M. Piccart, R. Schmutzler, G.G. Steger, J.P. Costantino, A. Arahmani, N. Wolmark, E. McFadden, V. Karantza, S.R. Lakhani, G. Yothers, C. Campbell, and C.E. Geyer, Jr., for the OlympiA Clinical Trial Steering Committee and Investigators*

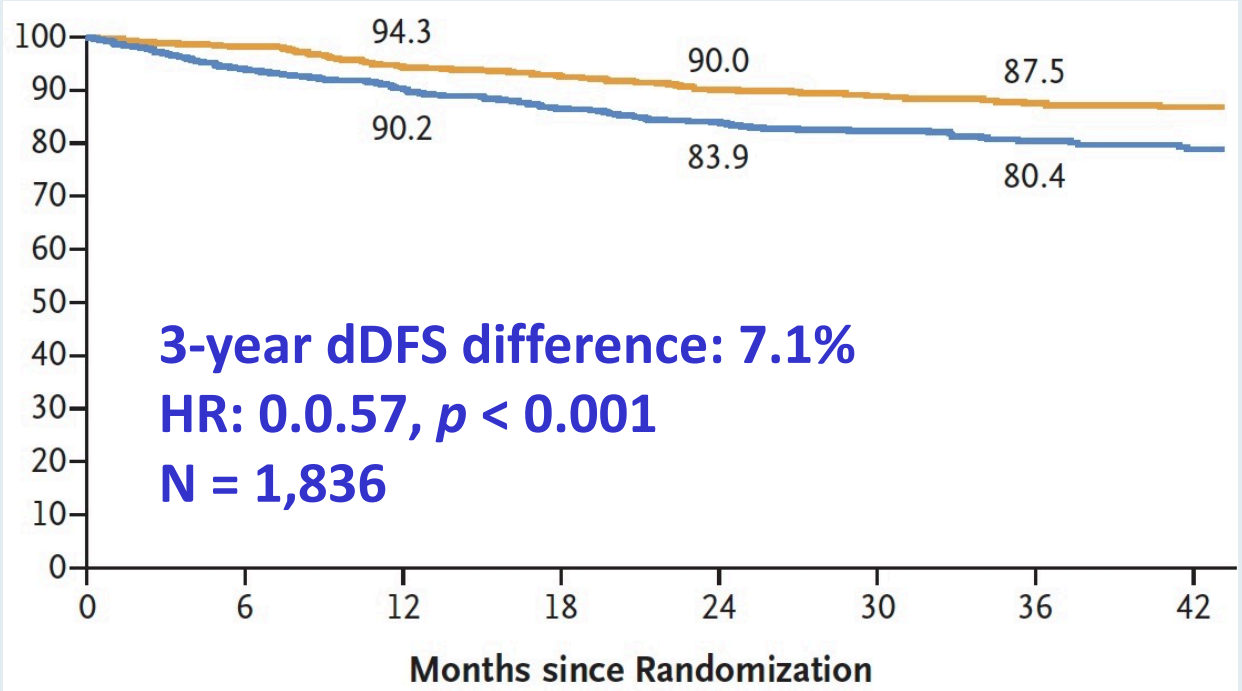
OlympiA: Invasive and Distant Disease-Free Survival

Invasive DFS



3-year iDFS difference: 8.8%
HR: 0.58, $p < 0.001$
N = 1,836

Distant DFS



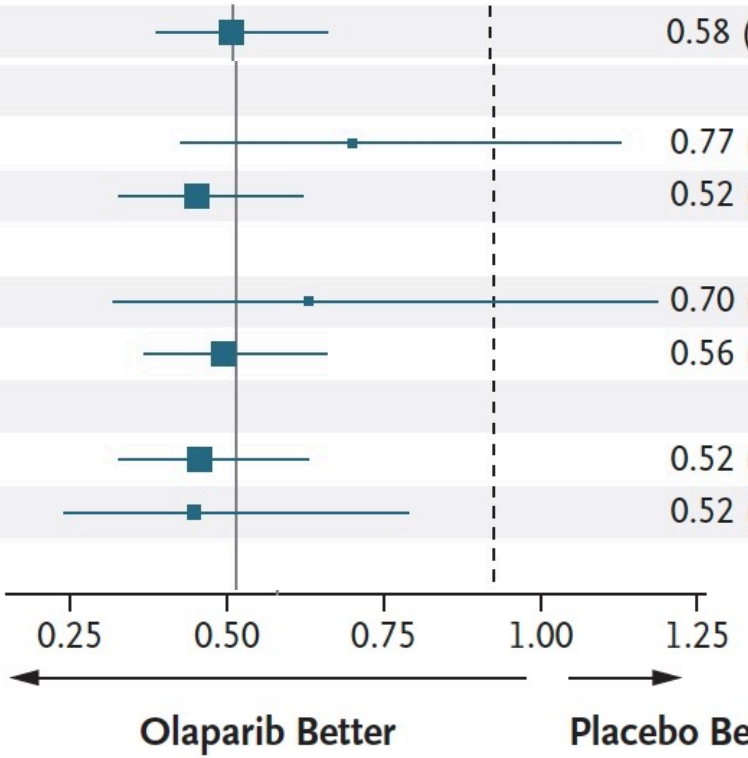
3-year dDFS difference: 7.1%
HR: 0.0.57, $p < 0.001$
N = 1,836

Tutt ANJ et al. *N Engl J Med* 2021;384:2394-405.

RTP RESEARCH TO PRACTICE

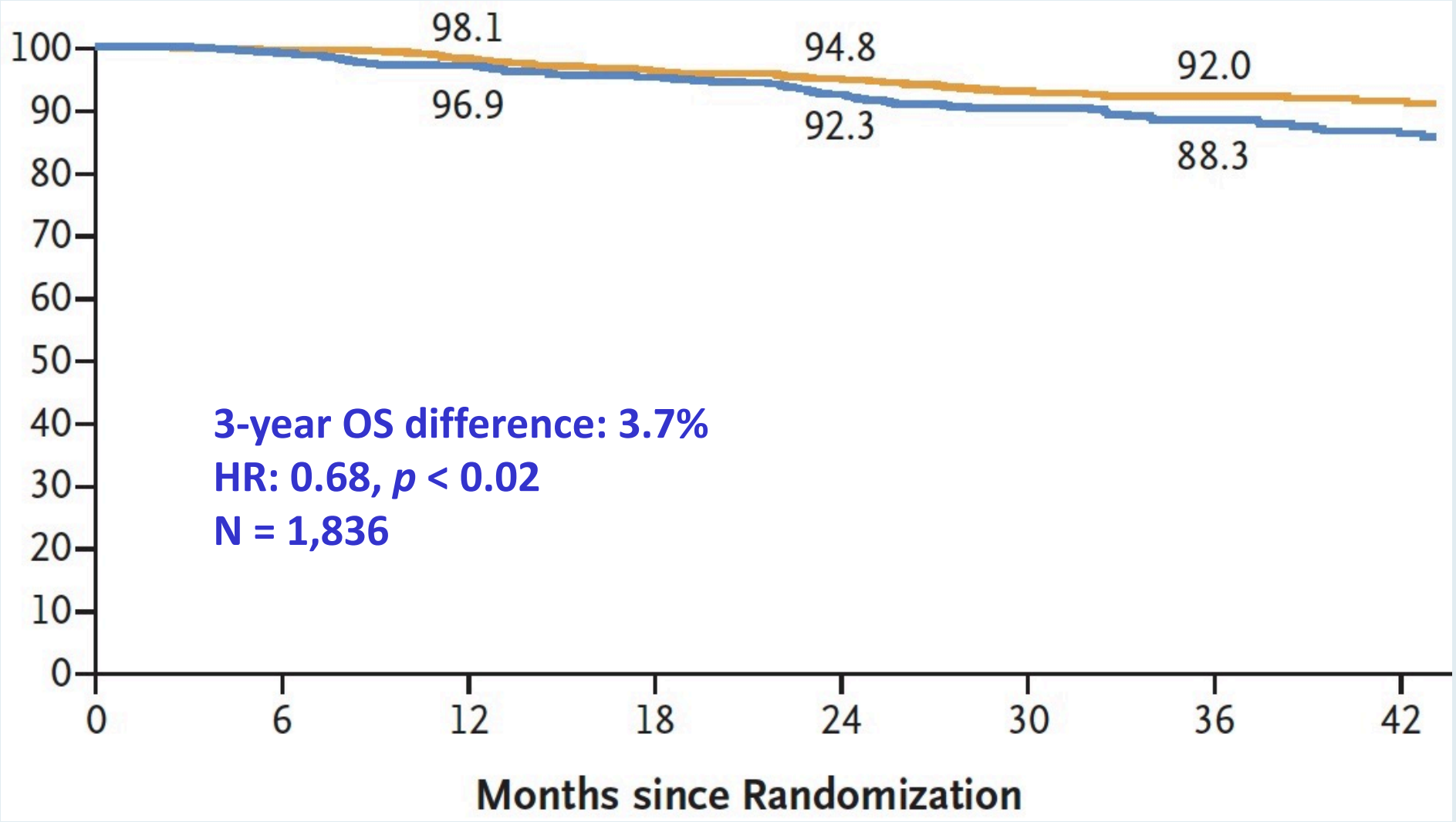
OlympiA: 3-Year Invasive DFS

Subgroup	Olaparib	Placebo	3-Yr Invasive Disease–free Survival		Stratified Hazard Ratio for Invasive Disease or Death (95% CI)
			Olaparib	Placebo	
	no. of patients with an event/total no.		%		
All patients	106/921	178/915	85.9	77.1	0.58 (0.46–0.74)
Previous platinum-based chemotherapy					
Yes	34/247	43/239	82.0	77.0	0.77 (0.49–1.21)
No	72/674	135/676	87.3	77.1	0.52 (0.39–0.69)
Hormone-receptor status					
HR+ and HER2–	19/168	25/157	83.5	77.2	0.70 (0.38–1.27)
TNBC	87/751	153/758	86.1	76.9	0.56 (0.43–0.73)
Germline *BRCA* mutation					
BRCA1	70/558	126/558	85.0	73.4	0.52 (0.39–0.70)
BRCA2	22/230	38/209	88.6	78.0	0.52 (0.30–0.86)
BRCA1 and *BRCA2*	0/1	0/3	NC	NC	NC



Tutt ANJ et al. *N Engl J Med* 2021;384:2394-405.

OlympiA: Overall Survival



Tutt ANJ et al. *N Engl J Med* 2021;384:2394-405.

RTP RESEARCH TO PRACTICE

OlympiA: Summary of Adverse Events

Adverse Event	Olaparib (N = 911)	Placebo (N = 904)
	no. of patients (%)	
Any adverse event	835 (91.7)	753 (83.3)
Serious adverse event	79 (8.7)	76 (8.4)
Adverse event of special interest†	30 (3.3)	46 (5.1)
MDS or AML	2 (0.2)	3 (0.3)
Pneumonitis‡	9 (1.0)	11 (1.2)
New primary cancer§	19 (2.1)	32 (3.5)
Grade ≥3 adverse event	221 (24.3)	102 (11.3)
Grade 4 adverse event¶	17 (1.9)	4 (0.4)
Adverse event leading to permanent discontinuation of olaparib or placebo‖	90 (9.9)	38 (4.2)
Adverse event leading to death**	1 (0.1)	2 (0.2)

Tutt ANJ et al. *N Engl J Med* 2021;384:2394-405.

2021 ASCO ANNUAL MEETING

Abstract 505

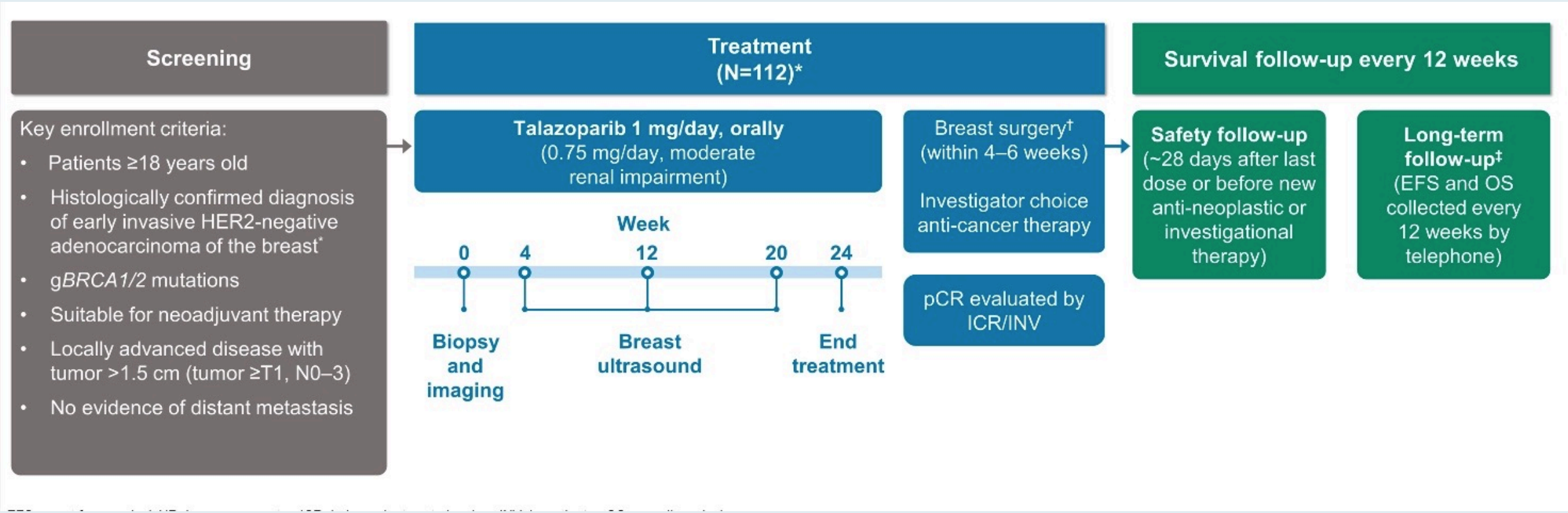
NEOADJUVANT TALAZOPARIB IN PATIENTS WITH GERMLINE *BRCA1/2* MUTATION-POSITIVE, EARLY HER2-NEGATIVE BREAST CANCER: RESULTS OF A PHASE 2 STUDY

Jennifer K. Litton,[1] J. Thaddeus Beck,[2] Jason M. Jones,[3] Jay Andersen,[4] Joanne L. Blum,[5] Lida A. Mina,[6] Raymond Brig,[7] Michael Danso,[8] Yuan Yuan,[9] Antonello Abbattista,[10] Kay Noonan,[11] Jayeta Chakrabarti,[12] Akos Czibere,[13] William F. Symmans,[1] Melinda L. Telli[14]

[1]The University of Texas MD Anderson Cancer Center, Houston, TX, USA; [2]Highlands Oncology Group, Fayetteville, AR, USA; [3]Avera Cancer Institute, Sioux Falls, SD, USA; [4]Compass Oncology, West Cancer Center, Tigard, OR, USA; [5]Texas Oncology-Baylor Charles A. Sammons Cancer Center, US Oncology Network, Dallas, TX, USA; [6]Banner MD Anderson Cancer Center, Gilbert, AZ, USA; [7]Brig Center for Cancer Care and Survivorship, Knoxville, TN, USA; [8]Virginia Oncology Associates, Norfolk, VA, USA; [9]City of Hope Comprehensive Cancer Center and Beckman Research Institute, Duarte, CA, USA; [10]Pfizer Oncology, Milan, Italy; [11]Pfizer Inc., Groton, CT, USA; [12]Pfizer, Walton Oaks, Surrey, UK; [13]Pfizer Inc., Cambridge, MA, USA; [14]Stanford University School of Medicine, Stanford, CA, USA

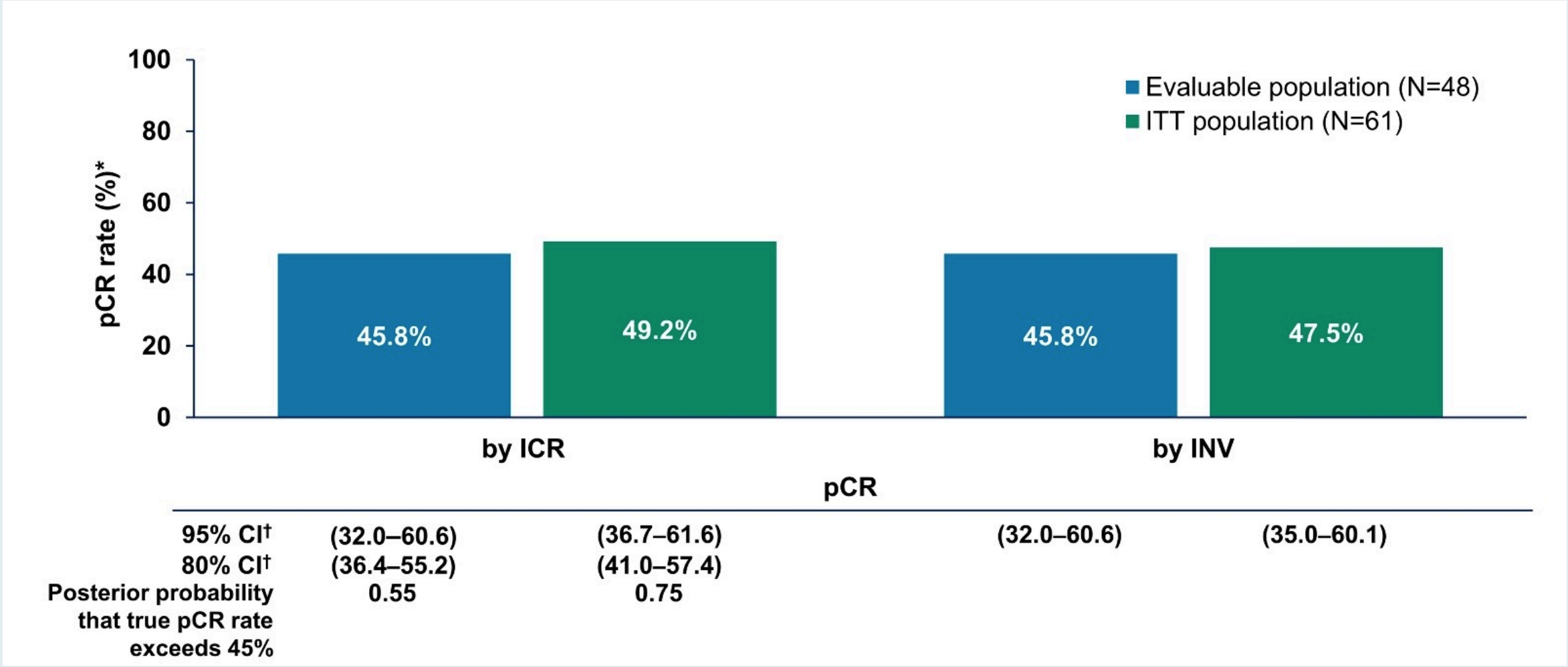
June 6, 2021

NEOTALA: Multicenter Phase II Study Schema



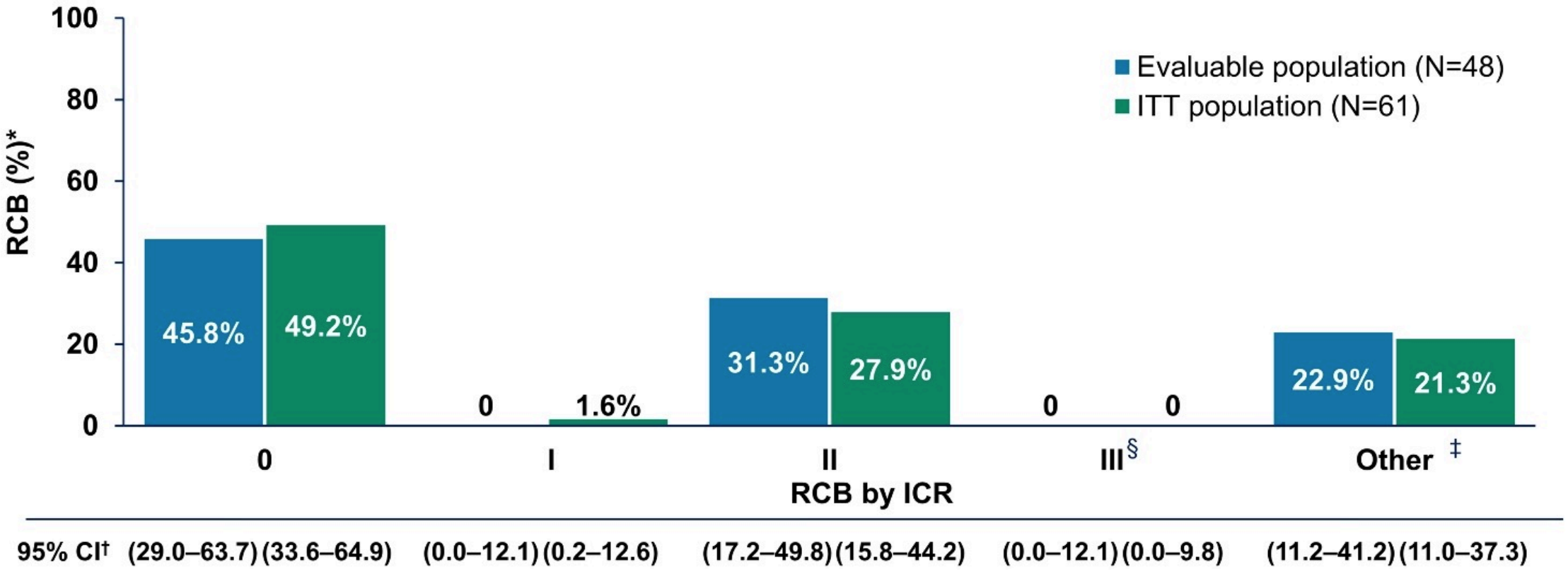
Litton JK et al. ASCO 2021;Abstract 505.

NEOTALA: Pathologic Complete Response



Litton JK et al. ASCO 2021;Abstract 505.

NEOTALA: Residual Cancer Burden



Litton JK et al. ASCO 2021;Abstract 505.

Phase III KEYNOTE-355 Trial Met Primary Endpoint of Overall Survival for Patients with Metastatic Triple-Negative Breast Cancer Whose Tumors Expressed PD-L1 (CPS ≥10)

Press Release – July 27, 2021

"Positive overall survival (OS) results [were announced] from the pivotal Phase 3 KEYNOTE-355 trial evaluating pembrolizumab in combination with chemotherapy for the treatment of patients with metastatic triple-negative breast cancer (mTNBC). Findings from the final analysis show first-line treatment with pembrolizumab in combination with chemotherapy (*nab*-paclitaxel, paclitaxel or gemcitabine/carboplatin) demonstrated a statistically significant and clinically meaningful improvement in OS compared with chemotherapy alone in patients with mTNBC whose tumors expressed PD-L1 (Combined Positive Score [CPS] ≥10). No new safety signals were identified. These OS results will be presented at an upcoming medical meeting and submitted to regulatory authorities."

https://www.joplinglobe.com/region/national_business/merck-announces-phase-3-keynote-355-trial-met-primary-endpoint-of-overall-survival-os-in/article_c2d17a73-33cf-5d36-8201-85b5fa2bb130.html

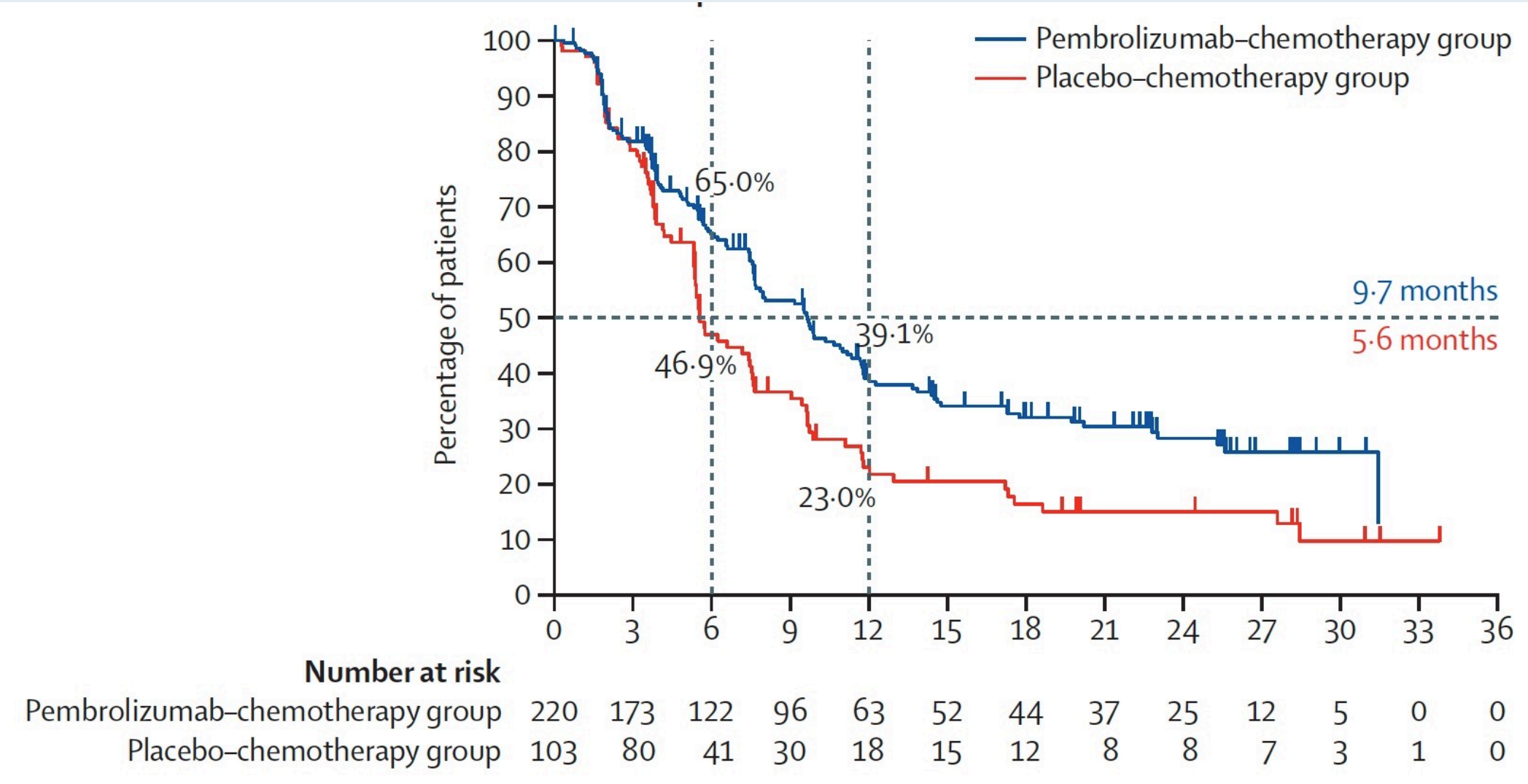
RTP RESEARCH TO PRACTICE

Lancet 2020;396:1817-28

Pembrolizumab plus chemotherapy versus placebo plus chemotherapy for previously untreated locally recurrent inoperable or metastatic triple-negative breast cancer (KEYNOTE-355): a randomised, placebo-controlled, double-blind, phase 3 clinical trial

*Javier Cortes, David W Cescon, Hope S Rugo, Zbigniew Nowecki, Seock-Ah Im, Mastura Md Yusof, Carlos Gallardo, Oleg Lipatov, Carlos H Barrios, Esther Holgado, Hiroji Iwata, Norikazu Masuda, Marco Torregroza Otero, Erhan Gokmen, Sherene Loi, Zifang Guo, Jing Zhao, Gursel Aktan, Vassiliki Karantza, Peter Schmid, for the KEYNOTE-355 Investigators**

KEYNOTE-355: Progression-Free Survival (Combined Positive Score ≥10)



Cortes J et al. *Lancet* 2020;396:1817-28.

Withdrawal of Accelerated Approval of Atezolizumab in Combination with Chemotherapy for Unresectable Locally Advanced or Metastatic TNBC

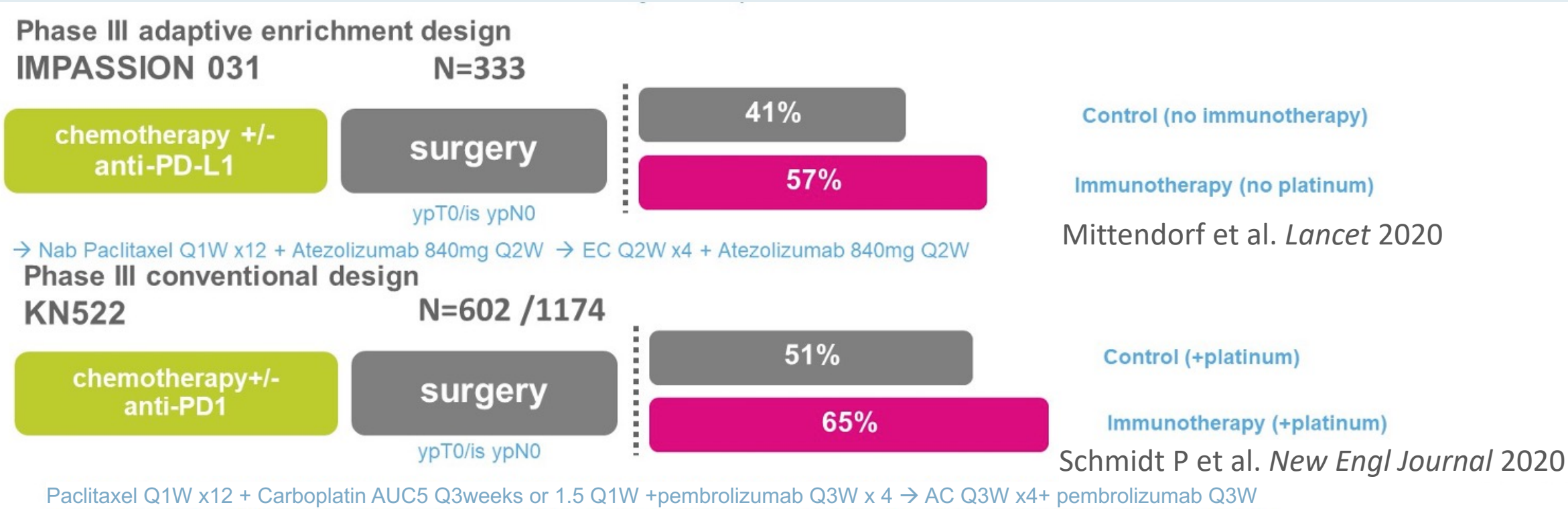
Press Release – August 27, 2021

Accelerated approval has been voluntarily withdrawn in the United States for atezolizumab in combination with chemotherapy (*nab* paclitaxel) for the treatment of unresectable locally advanced or metastatic TNBC in adult patients whose tumors express PD-L1 as determined by an FDA-approved test.

The decision was made in consultation with the FDA after failure of the confirmatory IMpassion131 trial to meet its primary endpoint of PFS for the initial (first-line) treatment of mTNBC in the PD-L1-positive population.

https://www.gene.com/media/press-releases/14927/2021-08-27/genentech-provides-update-on-tecentriq-u

Phase III Studies of Neoadjuvant Chemotherapy with Anti-PD-1/PD-L1 Antibodies: IMPASSION 031 and KEYNOTE-522



Mittendorf et al. *Lancet* 2020

Schmidt P et al. *New Engl Journal* 2020

Loibl S et al. ASCO 2021;Abstract 506.

RTP RESEARCH TO PRACTICE

Primary Endpoints of Phase III Studies of Neoadjuvant Immunotherapy with Chemotherapy

Change in pCR rate	Overall	PD-L1-positive	PD-L1-negative
KEYNOTE-522[1] (Pembrolizumab + CT vs Placebo + CT)	+13.6%	+14%	+18%
IMpassion 031[2] (Atezolizumab + CT vs Placebo + CT)	+17%	+20%	+14%

pCR = pathologic complete response

Event-free survival	Median FU	Events	HR
KEYNOTE-522[3] (Pembrolizumab + CT vs Placebo + CT)	39.1 mo	15.7% vs 23.8%	0.63
IMpassion 031[2] (Atezolizumab + CT vs Placebo + CT)*	20.6 mo	10.3% vs 13.1%	0.76

*IMpassion 031 not powered for event-free survival, disease-free survival or overall survival

[1] Schmid et al. *NEJM* 2020; [2] Mittendorf et al. *Lancet* 2020; [3] Schmid et al. ESMO 2021 Virtual Plenary

FDA Approves Pembrolizumab for High-Risk Early-Stage Triple-Negative Breast Cancer

Press Release – July 26, 2021

"The Food and Drug Administration approved pembrolizumab for high-risk, early-stage, triple-negative breast cancer (TNBC) in combination with chemotherapy as neoadjuvant treatment, and then continued as a single agent as adjuvant treatment after surgery.

FDA also granted regular approval to pembrolizumab in combination with chemotherapy for patients with locally recurrent unresectable or metastatic TNBC whose tumors express PD-L1 (Combined Positive Score [CPS] ≥10) as determined by an FDA approved test. FDA granted accelerated approval to pembrolizumab for this indication in November 2020.

The following trial was the basis of the neoadjuvant and adjuvant approval, as well as the confirmatory trial for the accelerated approval.

The efficacy of pembrolizumab in combination with neoadjuvant chemotherapy followed by surgery and continued adjuvant treatment with pembrolizumab as a single agent was investigated in KEYNOTE-522 (NCT03036488), a randomized, multicenter, double-blind, placebo-controlled trial conducted in 1174 patients with newly diagnosed previously untreated high-risk early-stage TNBC (tumor size >1 cm but ≤2 cm in diameter with nodal involvement or tumor size >2 cm in diameter regardless of nodal involvement). Patients were enrolled regardless of tumor PD-L1 expression."

www.fda.gov/drugs/resources-information-approved-drugs/fda-approves-pembrolizumab-high-risk-early-stage-triple-negative-breast-cancer?utm_medium=email&utm_source=govdelivery

RTP RESEARCH TO PRACTICE

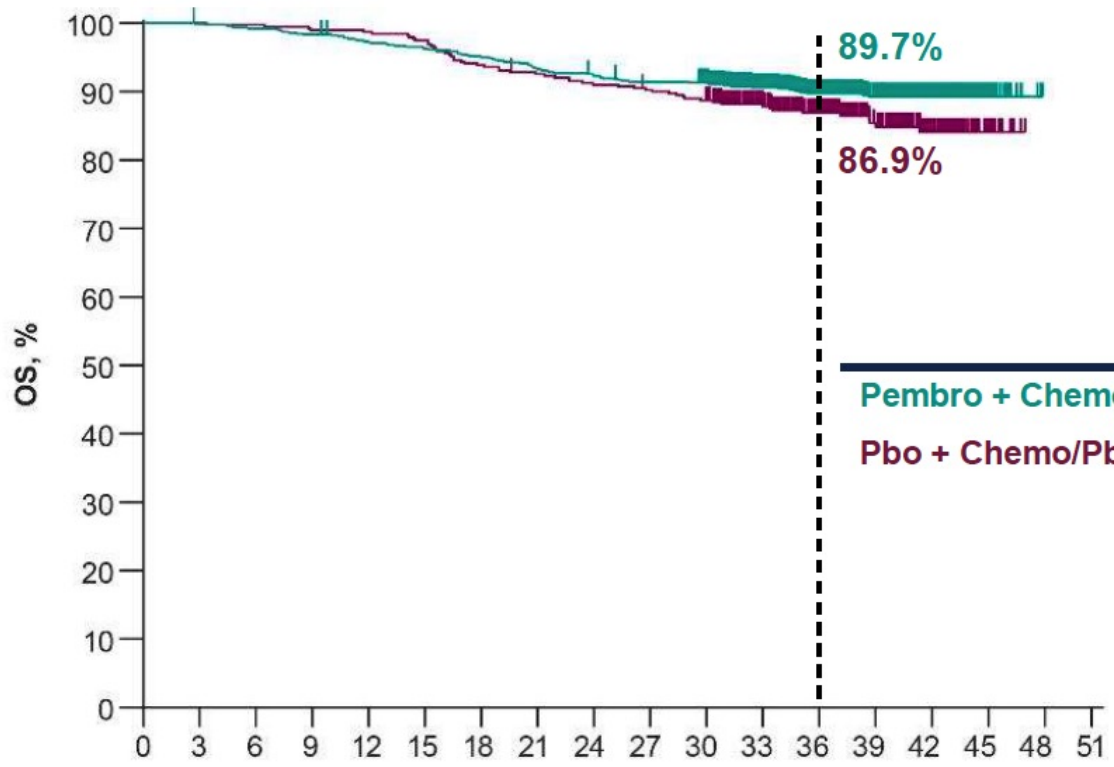
ESMO VIRTUAL PLENARY

KEYNOTE-522: Phase 3 Study of Neoadjuvant Pembrolizumab + Chemotherapy versus Placebo + Chemotherapy, Followed by Adjuvant Pembrolizumab versus Placebo for Early-Stage Triple-Negative Breast Cancer

Peter Schmid[1], Javier Cortes[2], Rebecca Dent[3], Lajos Pusztai[4], Heather McArthur[5], Sherko Kümmel[6], Jonas Bergh[7], Carsten Denkert[8], Yeon Hee Park[9], Rina Hui[10], Nadia Harbeck[11], Masato Takahashi[12], Michael Untch[13], Peter A. Fasching[14], Fatima Cardoso[15], Yu Ding[16], Konstantinos Tryfonidis[17], Gursel Aktan[17], Vassiliki Karantza[17], Joyce O'Shaughnessy[18]

1. Centre for Experimental Cancer Medicine, Barts Cancer Institute, Queen Mary University London, London, UK; 2. International Breast Cancer Center, Quirón Group, Madrid and Barcelona, Spain and Vall d'Hebron Institute of Oncology, Barcelona, Spain; 3. National Cancer Center Singapore, Duke–National University of Singapore Medical School, Singapore; 4. Yale School of Medicine, Yale Cancer Center, New Haven, CT, USA; 5. Breast Oncology, Cedars-Sinai Medical Center, Los Angeles, CA, USA; 6. Breast Unit, Kliniken Essen-Mitte, Essen, Germany; 7. Department of Oncology-Pathology, Karolinska Institutet and Breast Cancer Centre, Cancer theme, Karolinska University Hospital, Solna, Sweden; 8. Institute of Pathology, Philipps-University Marburg and University Hospital Marburg (UKGM), Marburg, Germany; 9. Samsung Medical Center, Sungkyunkwan University School of Medicine, Seoul, Republic of Korea; 10. Westmead Breast Cancer Institute, Westmead Hospital and the University of Sydney, Sydney, NSW, Australia; 11. Breast Center, LMU University Hospital, Munich, Germany; 12. Department of Breast Surgery, Hokkaido Cancer Center, Sapporo, Japan; 13. Breast Cancer Center, Helios Klinikum Berlin-Buch, Berlin, Germany; 14. University Hospital Erlangen, Comprehensive Cancer Center Erlangen-EMN, Erlangen, Germany; 15. Breast Unit, Champalimaud Clinical Center/Champalimaud Foundation, Lisbon, Portugal; 16. Biostatistics, Merck & Co., Inc., Kenilworth, NJ, USA; 17. Merck Research Laboratories, Merck & Co., Inc., Kenilworth, NJ, USA; 18. Baylor University Medical Center, Texas Oncology, US Oncology, Dallas, TX, USA

KEYNOTE-522: Updated OS (Median Follow-Up 39.1 Months)



	Events	HR (95% CI)	*P*-value
Pembro + Chemo/Pembro	10.2%	0.72[a] (0.51-1.02)	0.03214[b]
Pbo + Chemo/Pbo	14.1%		

No. at Risk

Pembro + Chemo/Pembro	784	782	777	770	759	752	742	729	720	712	701	586	461	323	178	30	0	0
Pbo + Chemo/Pbo	390	390	389	386	385	380	366	360	354	350	343	286	223	157	89	17	0	0

[a]Hazard ratio (CI) analyzed based on a Cox regression model with treatment as a covariate stratified by the randomization stratification factors. [b]Prespecified *P*-value boundary of 0.00086 not reached at this analysis.
Data cutoff date: March 23, 2021.

Schmid P et al. ESMO 2021 Virtual Plenary

GBG GERMAN BREAST GROUP

ASCO 2021;Abstract 506

Gepar Nuevo

Durvalumab improves long-term outcome in TNBC: Results from the phase II randomized GeparNUEVO study investigating neoadjuvant durvalumab in addition to an anthracycline/taxane based neoadjuvant chemotherapy in early triple-negative breast cancer (TNBC)

Sibylle Loibl, Andreas Schneeweiss, Jens Huober, Michael Braun, Julia Rey, Jens-Uwe Blohmer, Jenny Furlanetto, Dirk-Michael Zahm, Claus Hanusch, Jörg Thomalla, Christian Jackisch, Peter Staib, Theresa Link, Kerstin Rhiem, Christine Solbach, Peter A Fasching, Nicole Burchardi, Carsten Denkert, Michael Untch

-This is a joint study by GBG and AGO-B-

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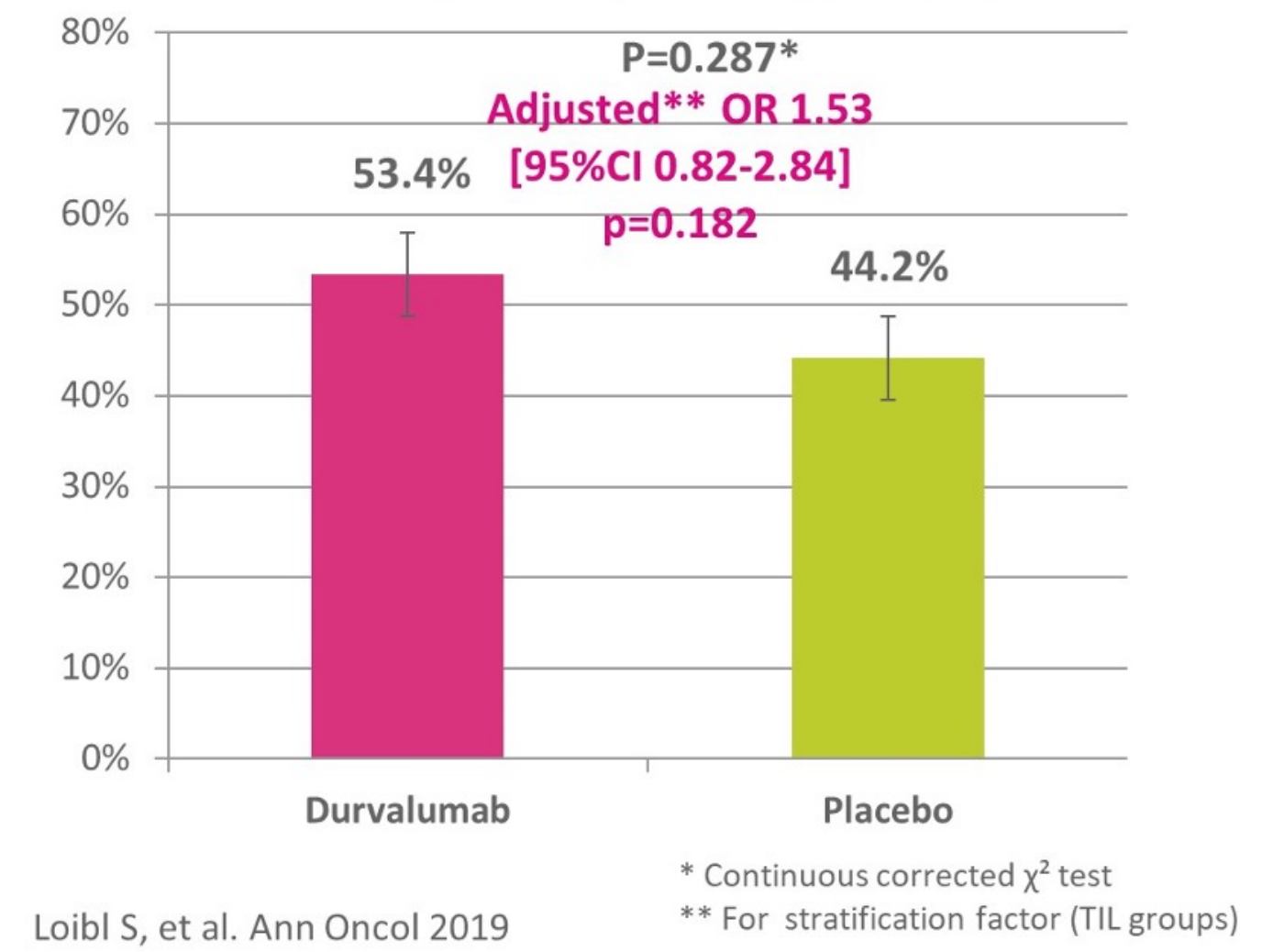
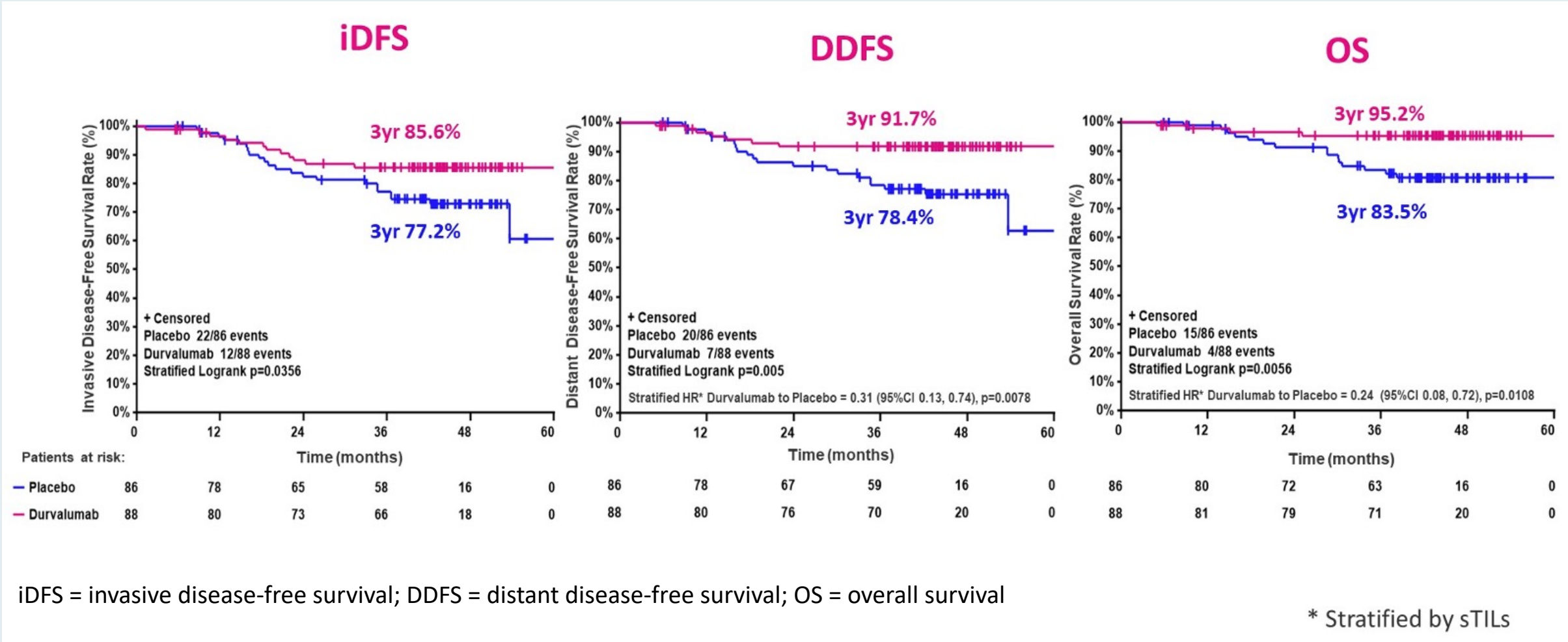
Loibl S et al. ASCO 2021;Abstract 506.

GeparNuevo Primary Endpoint: pCR – ypT0, ypN0



Loibl S, et al. Ann Oncol 2019

GeparNuevo: iDFS, DDFS and OS Between Treatment Arms



iDFS = invasive disease-free survival; DDFS = distant disease-free survival; OS = overall survival

* Stratified by sTILs

Loibl S et al. ASCO 2021;Abstract 506.

FDA Grants Regular Approval to Sacituzumab Govitecan for Triple-Negative Breast Cancer

Press Release: April 7, 2021

"The Food and Drug Administration granted regular approval to sacituzumab govitecan for patients with unresectable locally advanced or metastatic triple-negative breast cancer (mTNBC) who have received two or more prior systemic therapies, at least one of them for metastatic disease.

Efficacy and safety were evaluated in a multicenter, open-label, randomized trial (ASCENT; NCT02574455) conducted in 529 patients with unresectable locally advanced or mTNBC who had relapsed after at least two prior chemotherapies, one of which could be in the neoadjuvant or adjuvant setting, if progression occurred within 12 months. Patients were randomized (1:1) to receive sacituzumab govitecan, 10 mg/kg as an intravenous infusion, on days 1 and 8 of a 21-day (n = 267) cycle or physician's choice of single agent chemotherapy (n = 262)."

https://www.fda.gov/drugs/resources-information-approved-drugs/fda-grants-regular-approval-sacituzumab-govitecan-triple-negative-breast-cancer

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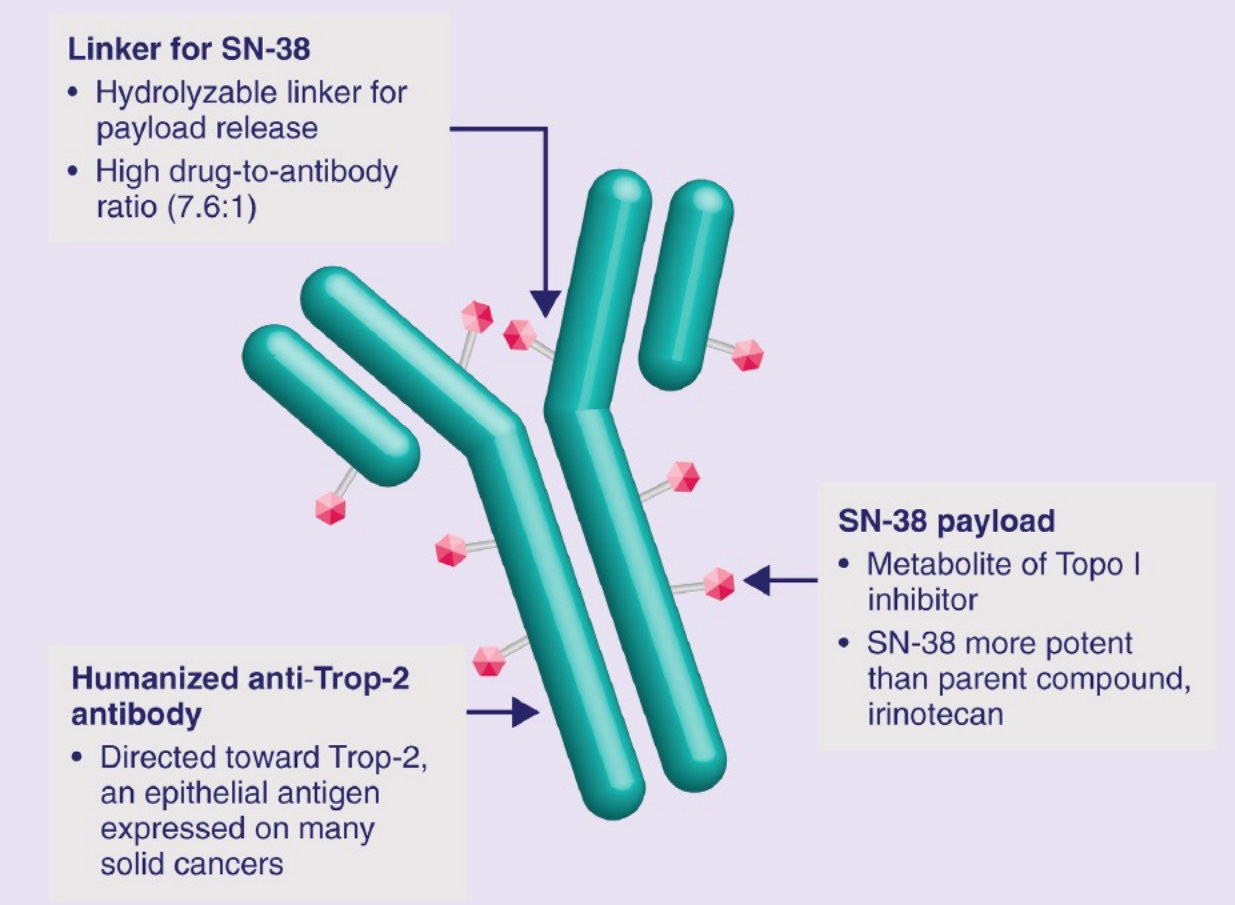
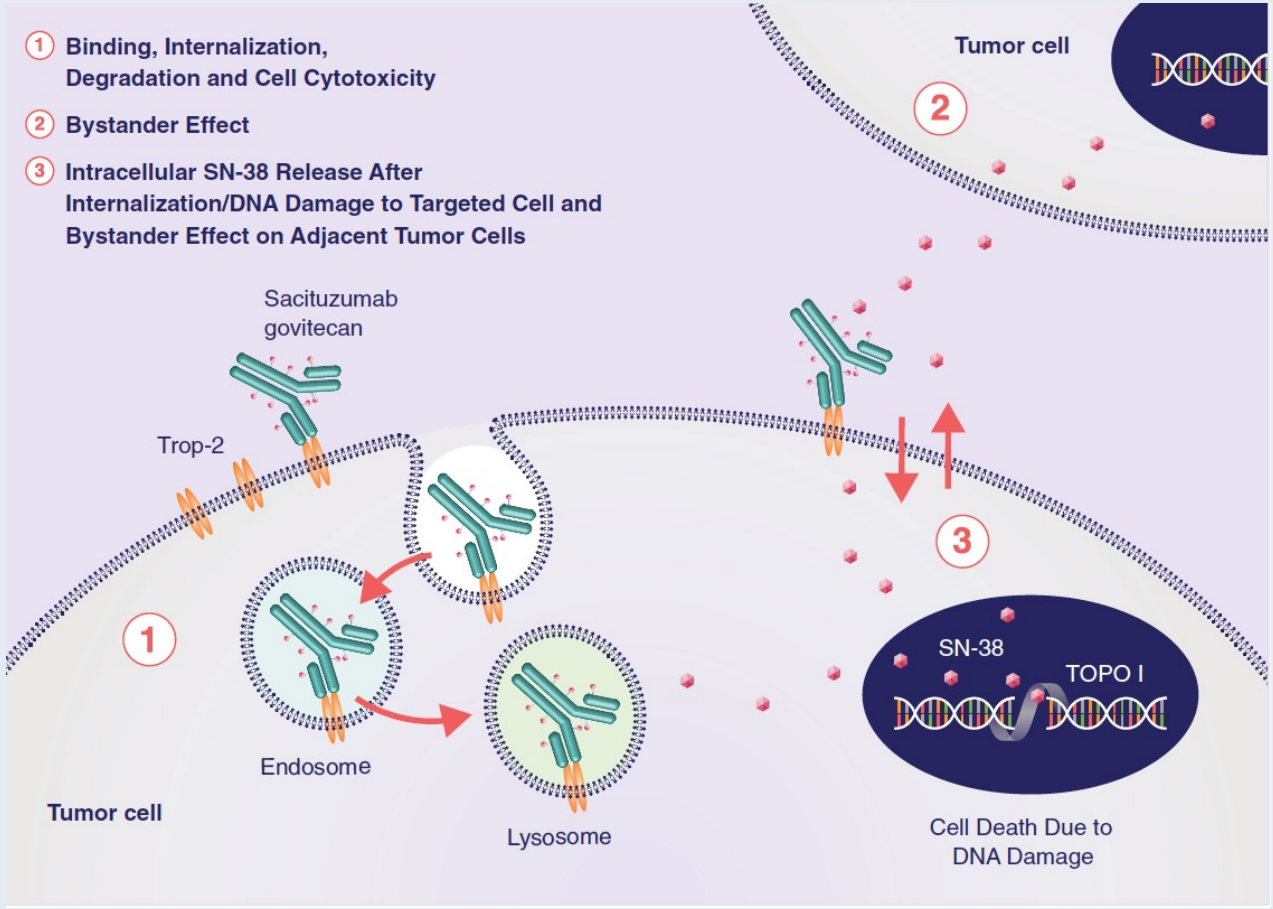
Sacituzumab Govitecan Is a First-in-Class TROP-2-Directed Antibody-Drug Conjugate





Rugo H et al. *Future Oncol* 2020;16(12):705-15.

N Engl J Med 2021;384:1529-41.

The NEW ENGLAND JOURNAL of MEDICINE

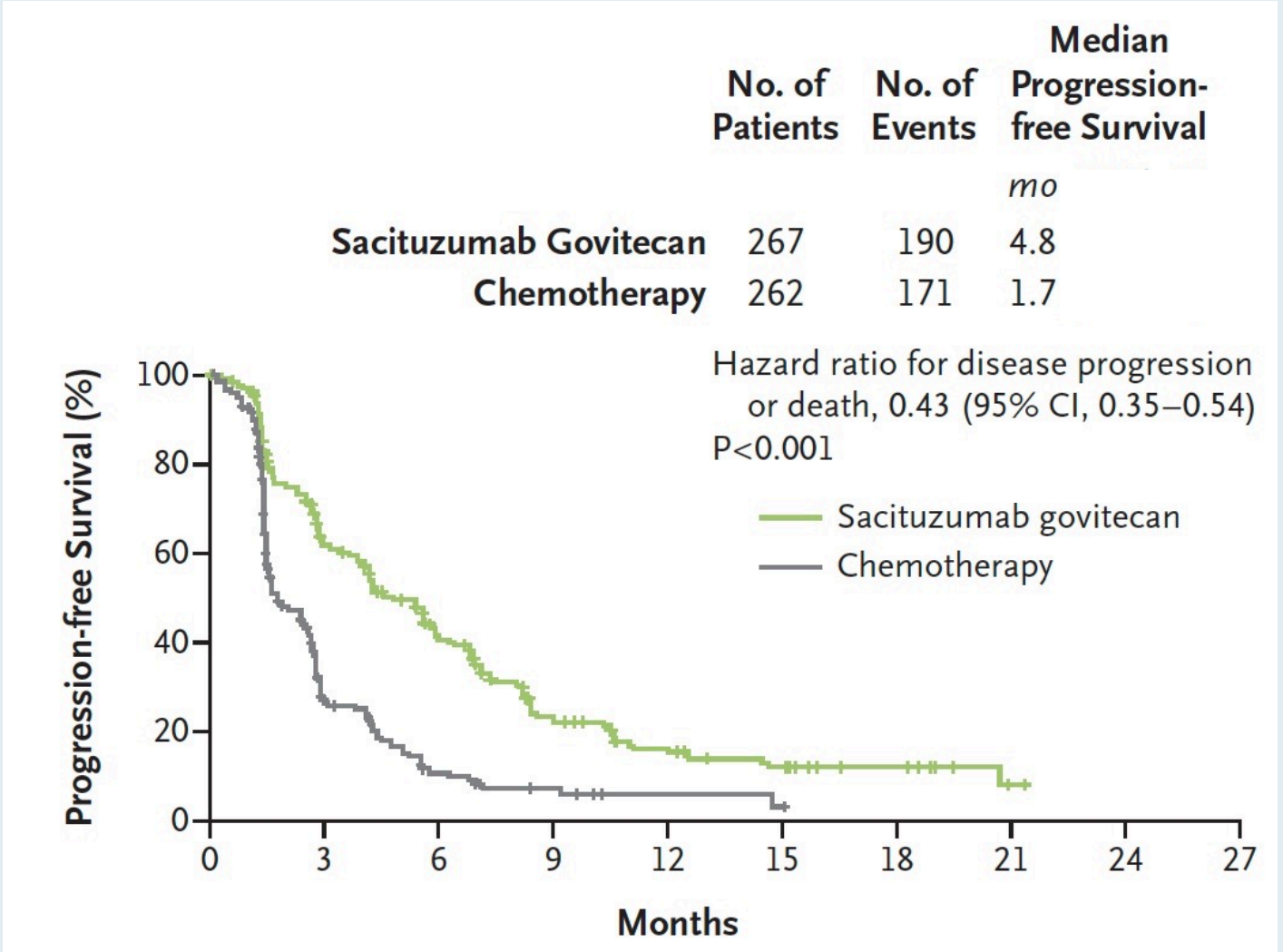
ORIGINAL ARTICLE

Sacituzumab Govitecan in Metastatic Triple-Negative Breast Cancer

A. Bardia, S.A. Hurvitz, S.M. Tolaney, D. Loirat, K. Punie, M. Oliveira, A. Brufsky, S.D. Sardesai, K. Kalinsky, A.B. Zelnak, R. Weaver, T. Traina, F. Dalenc, P. Aftimos, F. Lynce, S. Diab, J. Cortés, J. O'Shaughnessy, V. Diéras, C. Ferrario, P. Schmid, L.A. Carey, L. Gianni, M.J. Piccart, S. Loibl, D.M. Goldenberg, Q. Hong, M.S. Olivo, L.M. Itri, and H.S. Rugo, for the ASCENT Clinical Trial Investigators*

ASCENT: Progression-Free Survival (Overall Population)

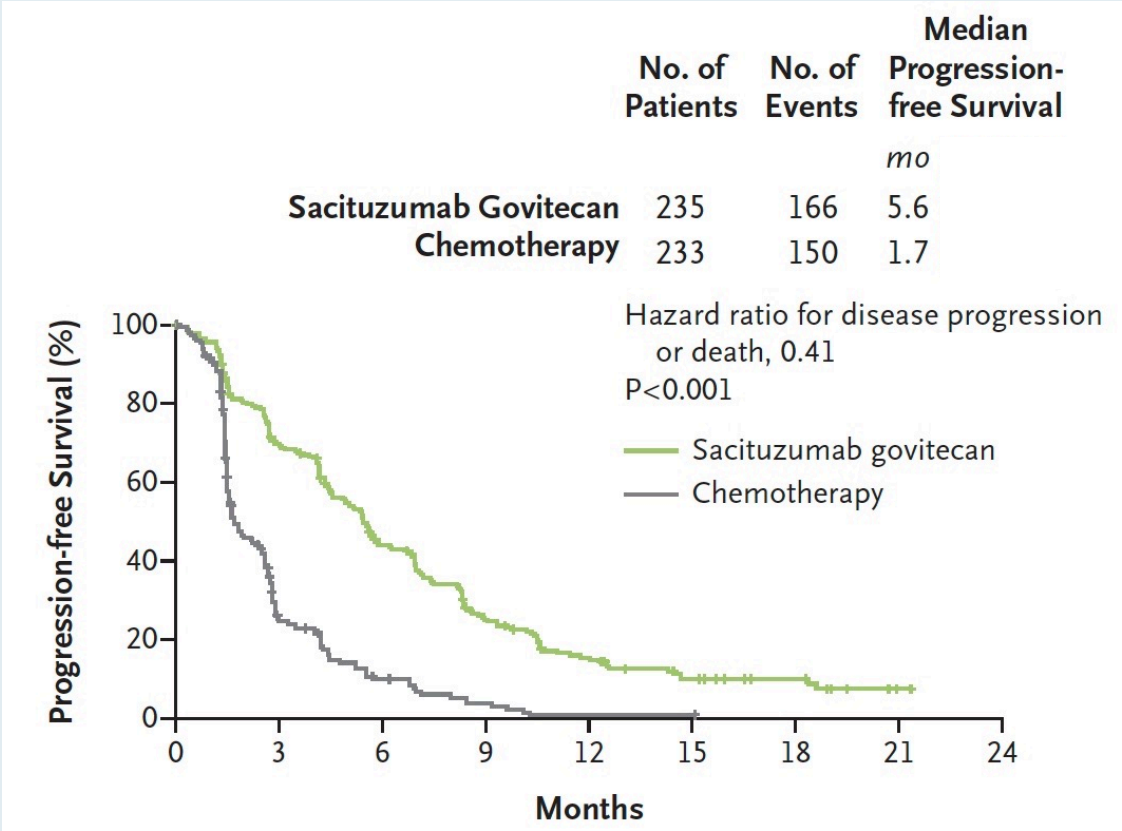
	No. of Patients	No. of Events	Median Progression-free Survival
			mo
Sacituzumab Govitecan	267	190	4.8
Chemotherapy	262	171	1.7

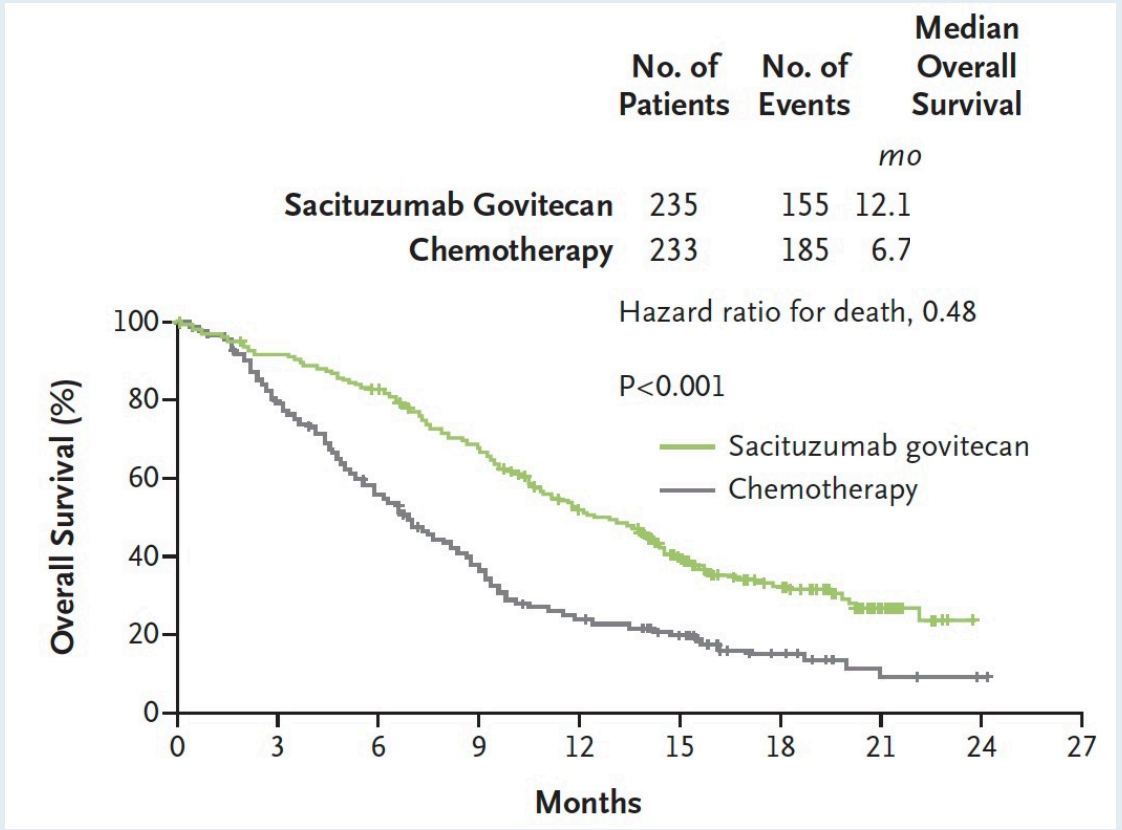


Bardia A et al. *N Engl J Med* 2021;384:1529-41.

RTP RESEARCH TO PRACTICE

ASCENT: PFS and OS among Patients without Brain Metastases





Bardia A et al. *N Engl J Med* 2021;384:1529-41.

RTP RESEARCH TO PRACTICE

ASCENT: Selected Adverse Events

Adverse event	Patients (N = 108)		
	Any grade	Grade 3	Grade 4
Gastrointestinal disorders			
Nausea	67%	6%	0
Diarrhea	62%	8%	0
Vomiting	49%	6%	0
Blood and lymphatic system disorders			
Neutropenia	64%	26%	16%
Anemia	50%	11%	0
Abnormal values			
Decrease white blood cell counts	21%	8%	3%

Bardia A et al. *N Engl J Med* 2021;384:1529-41.

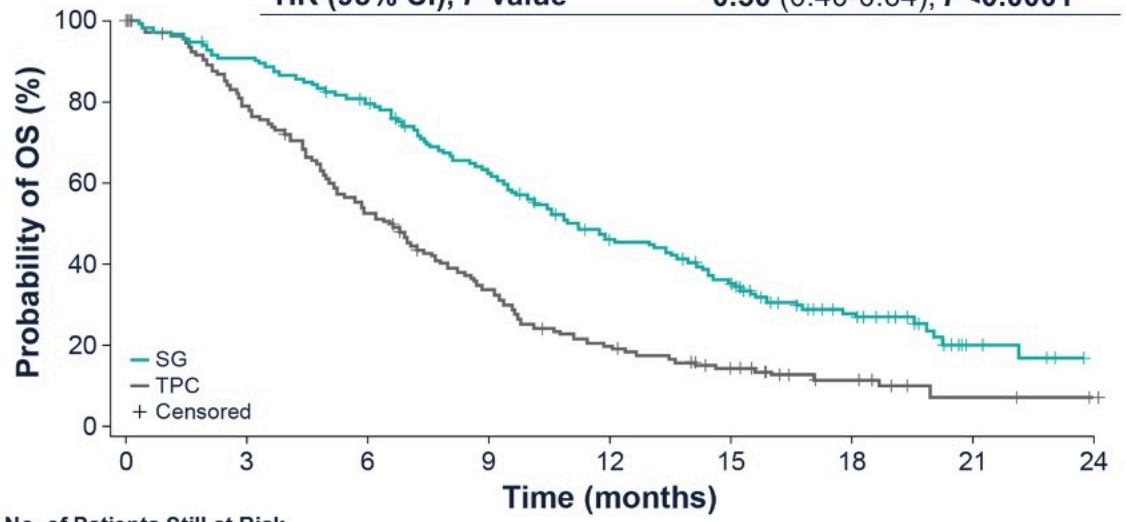
Outcomes in Patients (pts) Aged ≥65 Years in the Phase 3 ASCENT Study of Sacituzumab Govitecan (SG) in Metastatic Triple-Negative Breast Cancer (mTNBC)

Kalinsky K et al.

ASCO 2021;Abstract 1011.

ASCENT: Overall Survival for Young and Older Patients with mTNBC Treated with Sacituzumab Govitecan

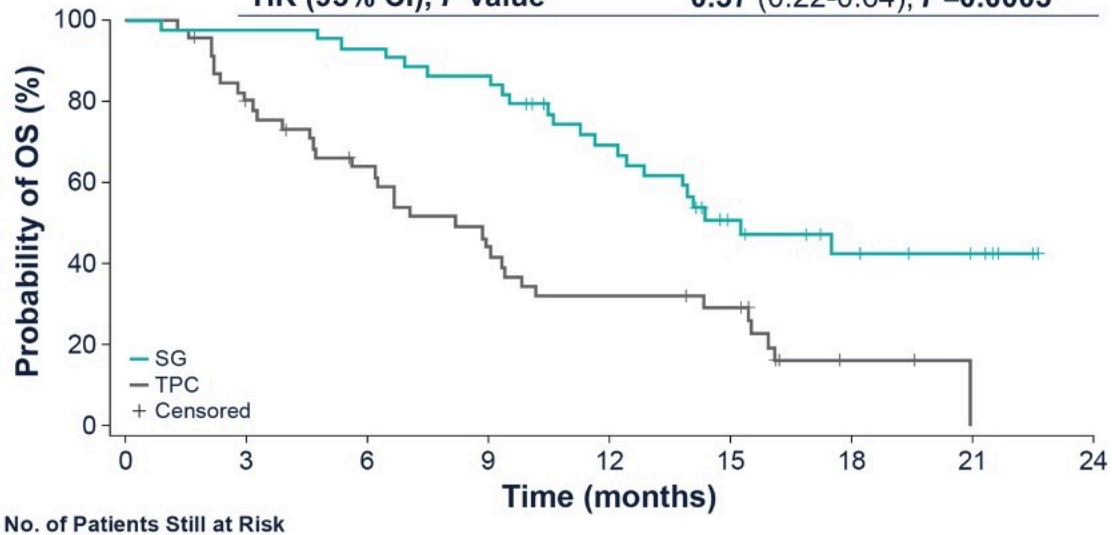
	<65 y	
	SG (n=191)	TPC (n=187)
No. of events	133	150
Median OS—mo (95% CI)	11.2 (9.9-13.4)	6.6 (5.3-7.4)
HR (95% CI), *P* value	**0.50** (0.40-0.64), ***P*<0.0001**	



No. of Patients Still at Risk

SG	191	185	177	171	163	155	149	135	123	115	102	89	80	77	68	56	40	32	28	22	14	7	6	1	0
TPC	187	168	157	138	125	106	91	77	66	56	42	37	32	28	25	19	14	11	9	5	3	3	3	2	1

	≥65 y	
	SG (n=44)	TPC (n=46)
No. of events	22	35
Median OS—mo (95% CI)	15.3 (12.4-NE)	8.2 (5.6-9.8)
HR (95% CI), *P* value	**0.37** (0.22-0.64), ***P*=0.0003**	



No. of Patients Still at Risk

SG	44	43	43	43	43	42	41	39	38	38	33	29	27	24	22	14	12	11	9	8	7	6	2	0
TPC	46	46	43	35	31	28	26	22	21	18	14	13	13	13	12	11	6	3	2	2	1	0	0	0

- In patients aged ≥65 years, improvement in median OS with SG vs TPC treatment was comparable with that of the overall population (12.1 vs 6.7 months)[1]

Kalinsky K et al. ASCO 2021;Abstract 1011.

RTP RESEARCH TO PRACTICE

San Antonio Breast Cancer Symposium 2020;Abstract GS3-06

Biomarker Evaluation in the Phase 3 ASCENT Study of Sacituzumab Govitecan Versus Chemotherapy in Patients With Metastatic Triple-Negative Breast Cancer

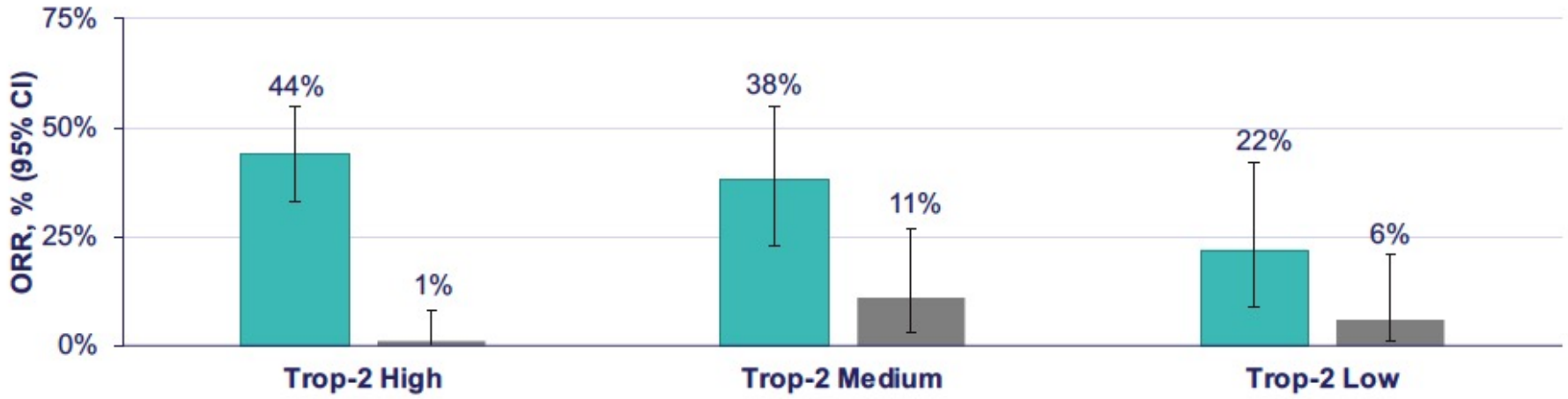
Sara A. Hurvitz,[1] Sara M. Tolaney,[2] Kevin Punie,[3] Delphine Loirat,[4] Mafalda Oliveira,[5] Kevin Kalinsky,[6] Amelia Zelnak,[7] Philippe Aftimos,[8] Florence Dalenc,[9] Sagar Sardesai,[10] Erika Hamilton,[11] Priyanka Sharma,[12] Sabela Recalde,[13] Eva Ciruelos Gil,[14] Tiffany Traina,[15] Joyce O'Shaughnessy,[16] Javier Cortes,[17] Michaela Tsai,[18] Linda Vahdat,[19] Véronique Diéras,[20] Lisa Carey,[21] Hope S. Rugo,[22] David M. Goldenberg,[23] Quan Hong,[23] Martin Olivo,[23] Loretta M. Itri,[23] and Aditya Bardia[24]

[1]Medical Oncology, University of California, Los Angeles, Jonsson Comprehensive Cancer Center, Los Angeles, CA, USA; [2]Dana-Farber Cancer Institute, Boston, MA, USA; [3]Department of General Medical Oncology, University Hospitals Leuven, Leuven, Belgium; [4]Institut Curie, Paris, France; [5]Hospital Universitari Vall d'Hebron, Barcelona, Spain; [6]Winship Cancer Institute, Emory University, Atlanta, GA, USA; [7]Northside Hospital, Atlanta, GA, USA; [8]Institut Jules Bordet, Brussels, Belgium; [9]Institut Claudius Regaud, Toulouse, France; [10]The Ohio State University Wexner Medical Center, Columbus, OH, USA; [11]Sarah Cannon Research Institute/Tennessee Oncology, Nashville, TN, USA; [12]University of Kansas Cancer Center - The Richard and Annette Bloch Cancer Care Pavilion, Kansas City, KS, USA; [13]Institut Catala d'Oncologia Hospitalet, Barcelona, Spain; [14]Hospital Universitario 12 de Octubre, Madrid, Spain; [15]Memorial Sloan Kettering Cancer Center, New York, NY, USA; [16]Texas Oncology - Baylor Charles A. Sammons Cancer Center, Dallas, TX, USA; [17]IOB Institute of Oncology, Quiron Group, Madrid & Barcelona, Spain; [18]VPCI Oncology Research, Minneapolis, MN, USA; [19]Memorial Sloan Kettering Cancer Center, New York, NY, USA; [20]Centre Eugène-Marquis, Rennes, France; [21]University of North Carolina Lineberger Comprehensive Cancer Center, Chapel Hill, NC, USA; [22]University of California San Francisco Comprehensive Cancer Center, San Francisco, CA, USA; [23]Immunomedics, Morris Plains, NJ, USA; and [24]Massachusetts General Hospital, Harvard Medical School, Boston, MA, USA

To obtain presentation, https://bit.ly/2020hurvitzgs3-06

ClinicalTrials.gov Number: NCT02574455

ORR by Trop-2 Expression

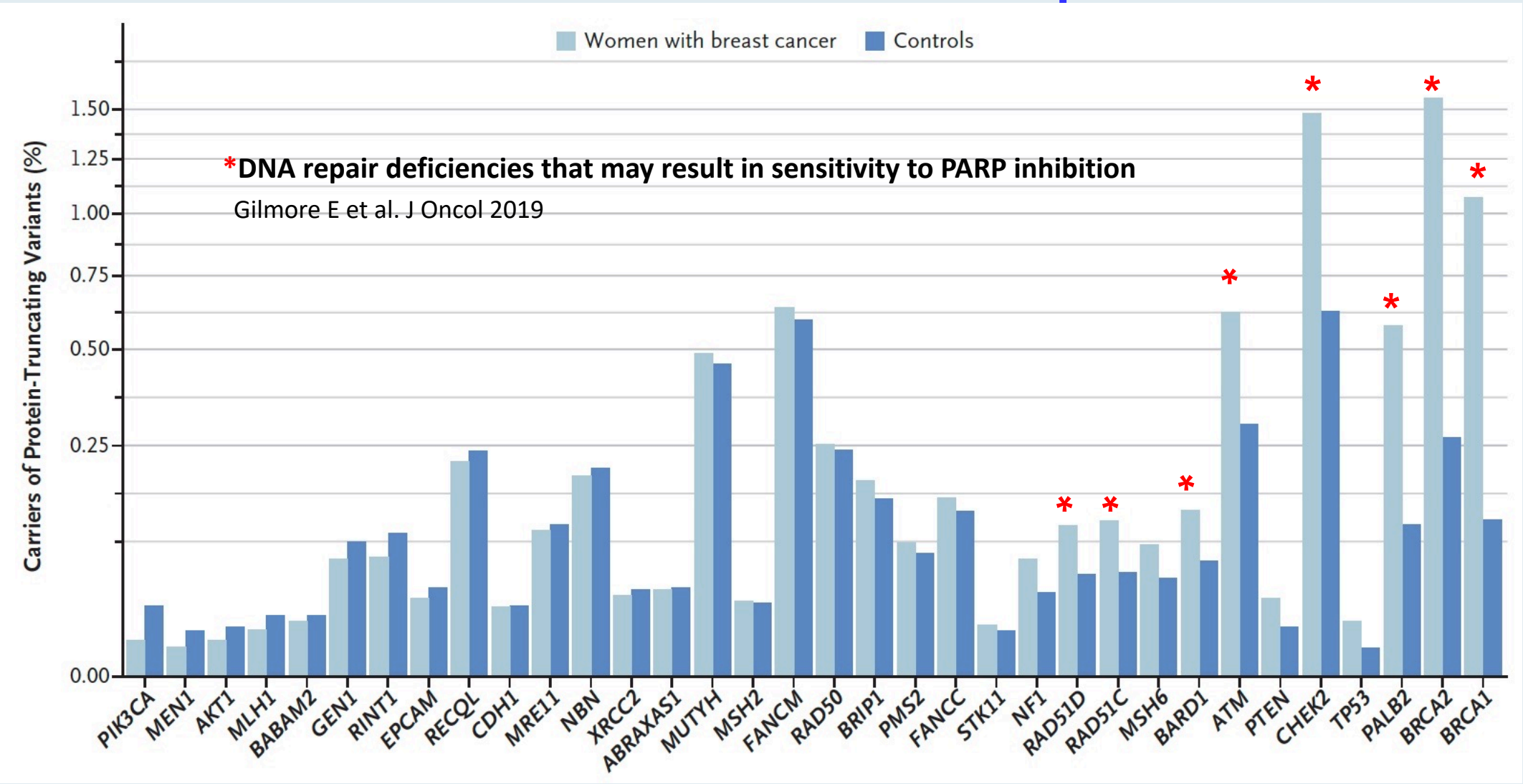


	Trop-2 High H-score: 200-300 (n=157)		Trop-2 Medium H-score: 100-200 (n=74)		Trop-2 Low H-score: <100 (n=59)	
	SG (n=85)	TPC (n=72)	SG (n=39)	TPC (n=35)	SG (n=27)	TPC (n=32)
ORR—% (no.)	44% (37)	1% (1)	38% (15)	11% (4)	22% (6)	6% (2)
95% CI	33-55	0-8	23-55	3-27	9-42	1-21

Assessed in the brain metastases-negative population. ORR and PFS are assessed by BICR. Trop-2 expression determined in archival samples by validated immunohistochemistry assay and H-scoring.
BICR, blind independent central review; H-score, histochemical-score; ORR, objective response rate; SG, sacituzumab govitecan; TPC, treatment of physician's choice; Trop-2, trophoblast cell surface antigen-2.

Hurvitz SA et al. SABCS 2020;Abstract GS3-06.

Gene Mutations Associated with Breast Cancer Risk in Population-Based Studies: Proportion of Carriers among Women with Breast Cancer and Control Groups



Breast Cancer Association Consortium. *N Engl J Med* 2021;384:428-39.

RTP RESEARCH TO PRACTICE

Datopotamab Deruxtecan (Dato-DXd), a TROP2-Directed Antibody-Drug Conjugate (ADC), for Triple-Negative Breast Cancer (TNBC): Preliminary Results from an Ongoing Phase 1 Trial

Bardia A et al.

ESMO Breast 2021;Abstract LBA4.

TROPION-PanTumor01: Datopotamab Deruxtecan for Heavily Pretreated Metastatic TNBC

Efficacy endpoint	Total evaluable in TNBC cohort (N = 21)
ORR	9/21 (43%)
CR/PR (confirmed)	N = 5
CR/PR (pending confirmation)	N = 4
Disease control rate	20/21 (95%)
Disease progression	1/21 (5%)

Bardia A et al. ESMO Breast 2021;Abstract LBA4.

Meet The Professor

Optimizing the Clinical Management of Hodgkin and Non-Hodgkin Lymphomas

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

Faculty

Brad S Kahl, MD

Moderator

Neil Love, MD

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Thank you for joining us!

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

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