Meet The Professor

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

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Director, Breast Cancer Research Program
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Attending Physician
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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, Genmab, 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, Natera Inc, 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 Pharmaceuticals USA Inc, Tesaro, A GSK Company, TG Therapeutics Inc, Turning Point Therapeutics Inc and Verastem Inc.

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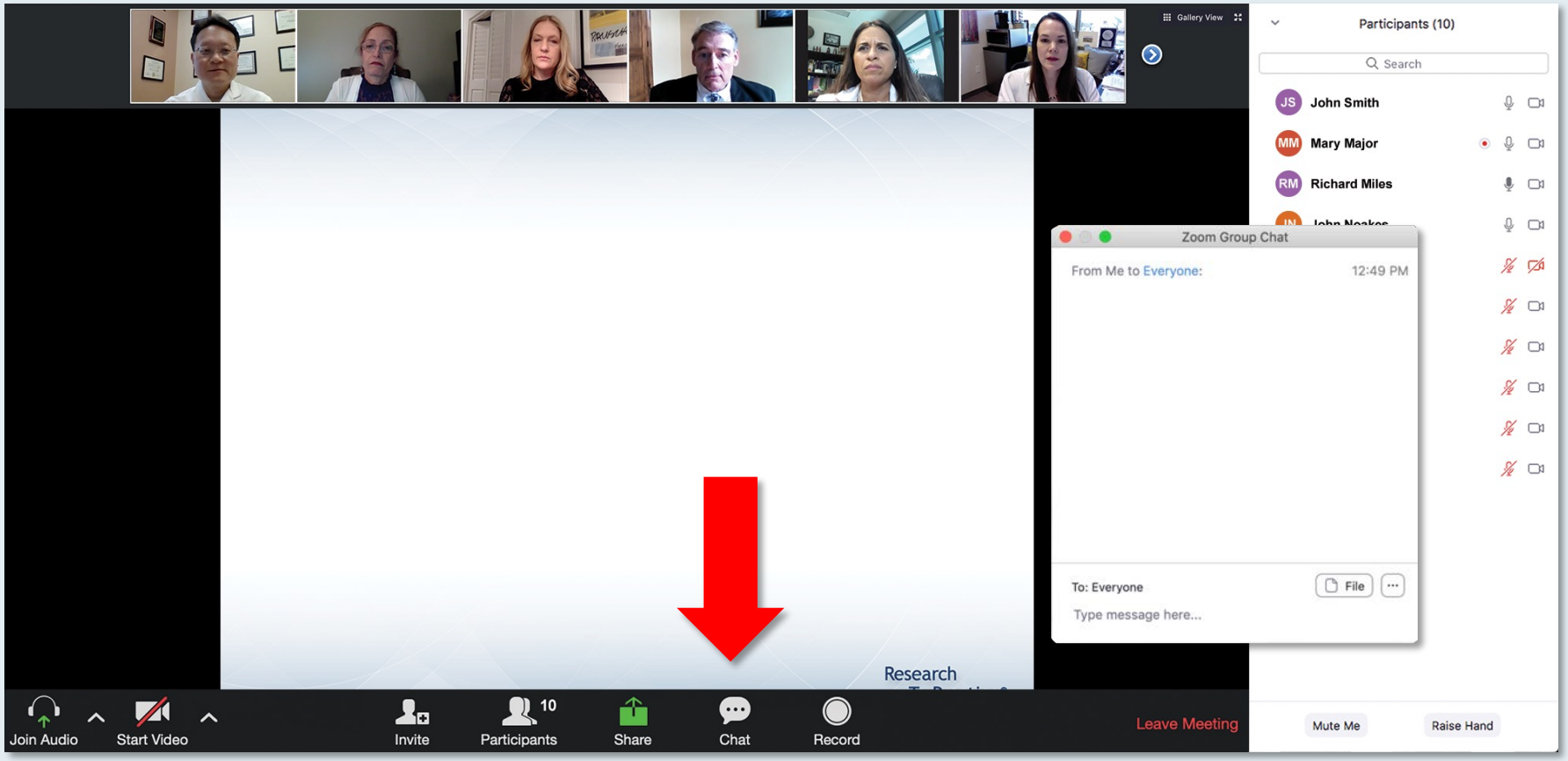
Dr Bardia — Disclosures

Consulting Agreements	AstraZeneca Pharmaceuticals LP, bioTheranostics Inc, Daiichi Sankyo Inc, Foundation Medicine, Genentech, a member of the Roche Group, Immunomedics Inc, Lilly, Merck, Novartis, Pfizer Inc, Phillips HealthCare Services Ltd, Puma Biotechnology Inc, Radius Health Inc, Sanofi Genzyme, Taiho Oncology Inc
Contracted Research	AstraZeneca Pharmaceuticals LP, Daiichi Sankyo Inc, Genentech, a member of the Roche Group, Immunomedics Inc, Merck, Novartis, Pfizer Inc, Radius Health Inc, Sanofi Genzyme

We Encourage Clinicians in Practice to Submit Questions



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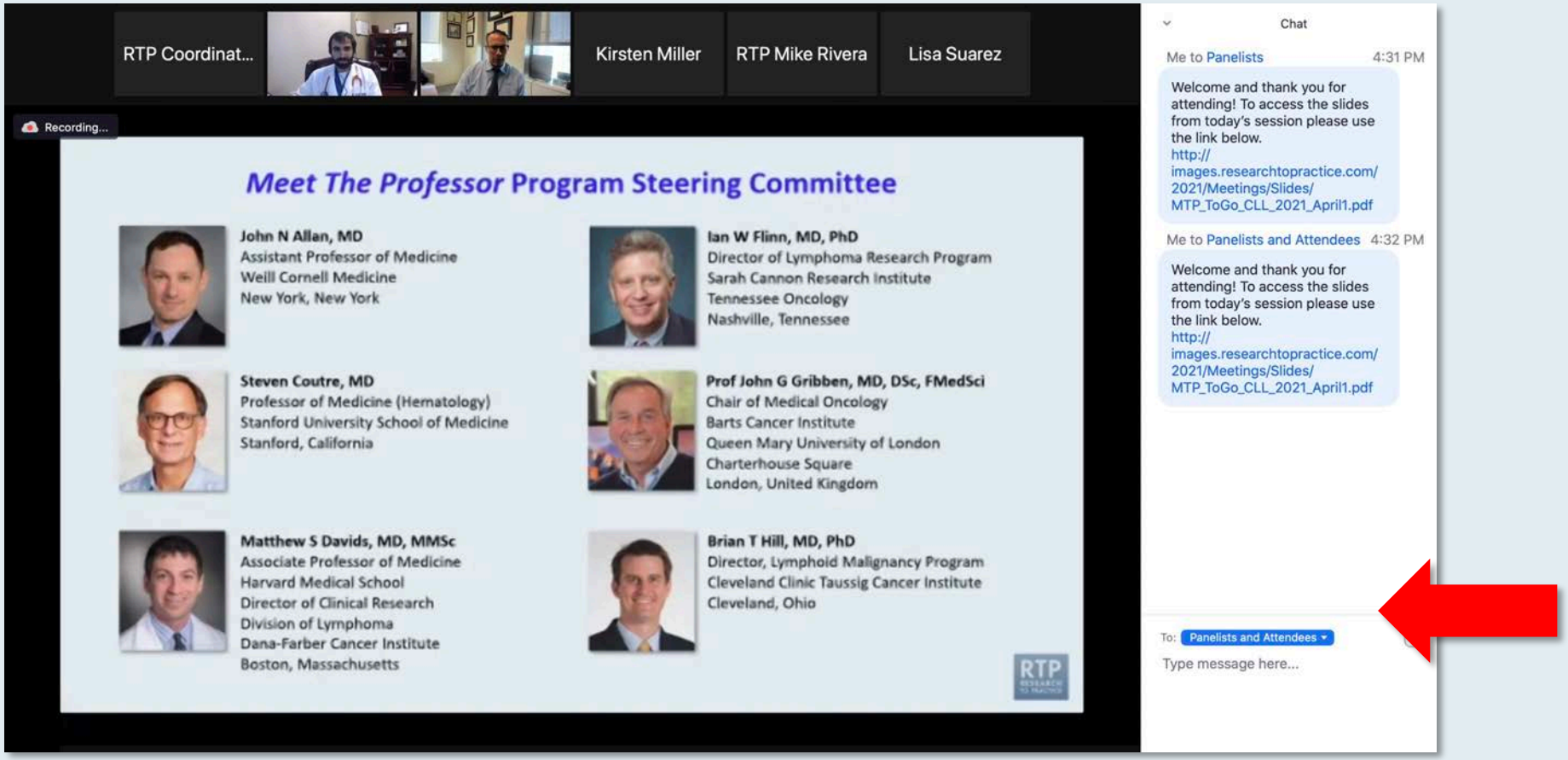

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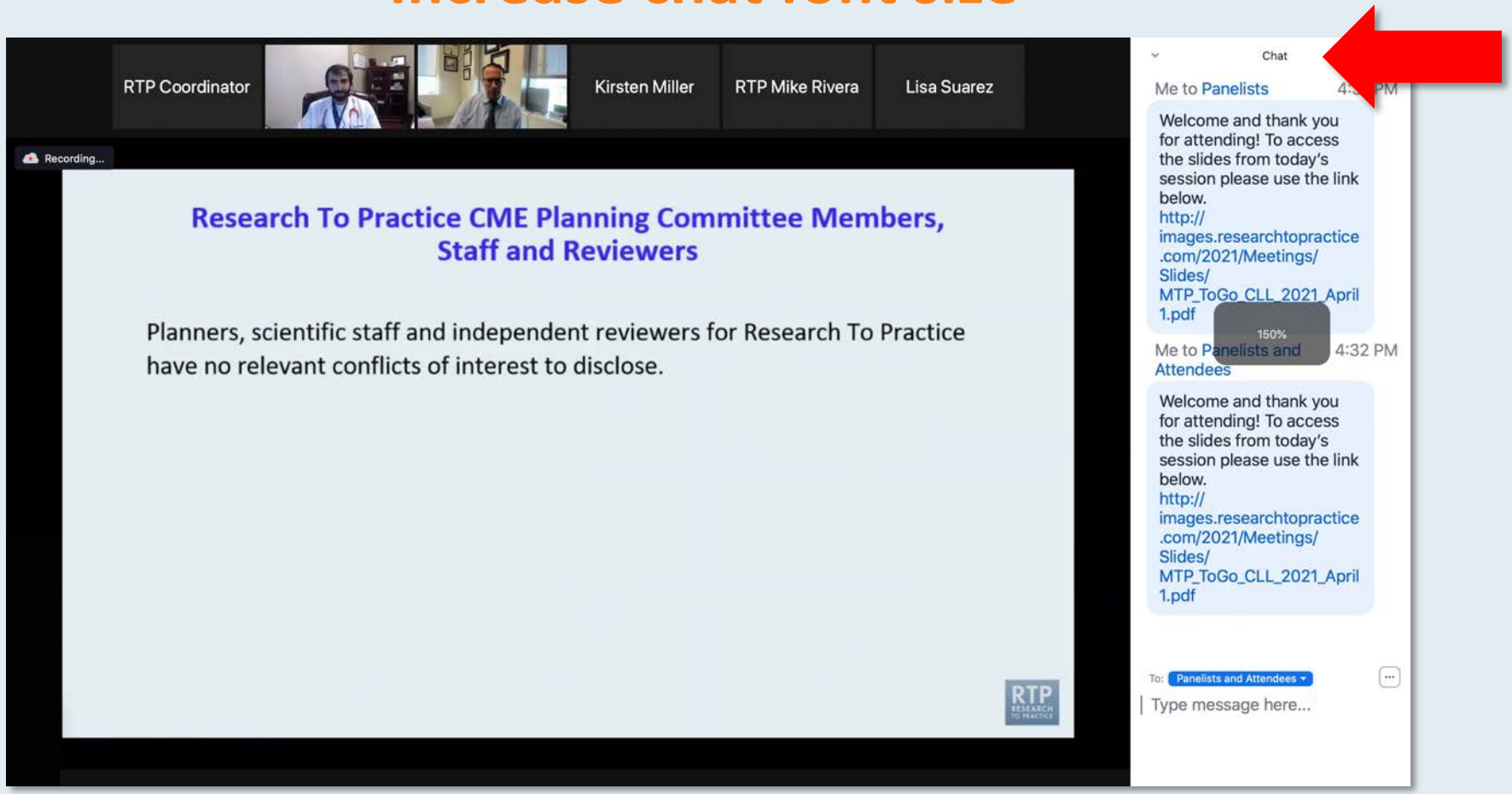

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You may do this as many times as you need for readability.

ONCOLOGY TODAY

WITH DR NEIL LOVE

Management of HER2-Low Breast Cancer

DR IAN KROP

DANA-FARBER CANCER INSTITUTE

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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

Neeraj Agarwal, MD
Tanios Bekaii-Saab, MD
Kristen K Ciombor, MD, MSCI
Brad S Kahl, MD
Mark Levis, MD, PhD
Ann Partridge, MD, MPH
Mark D Pegram, MD
Daniel P Petrylak, MD
Noopur Raje, MD
David Sallman, MD
Lecia V Sequist, MD, MPH
David R Spigel, MD
Saad Zafar Usmani, MD, MBA
Andrew D Zelenetz, MD, PhD

Moderator

Neil Love, MD

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Virtual Molecular Tumor Board: Optimizing Biomarker-Based Decision-Making for Patients with Non-Small Cell Lung Cancer with EGFR Mutations or with Other Oncogene-Addicted Lung Cancers

A 2-Part CME/MOC-Accredited Webinar Series

Role of Genomic Profiling for Patients with Non-Small Cell Lung Cancer (NSCLC) and the Optimal Application of Available Testing Platforms

Tuesday, October 26, 2021
5:00 PM – 6:00 PM ET

Guest Speaker
Joel W Neal, MD, PhD

New and Important Developments in the Management of NSCLC with EGFR Mutations or Other Novel Targets

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

Guest Speaker
Helena Yu, MD

Faculty

Marc Ladanyi, MD
Andrew J McKenzie, PhD

Moderator

Neil Love, MD

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Meet The Professor

Optimizing the Clinical Management of Hodgkin and Non-Hodgkin Lymphomas

Wednesday, October 27, 2021
5:00 PM – 6:00 PM ET

Faculty

Jonathan W Friedberg, MD, MMSc

Moderator

Neil Love, MD

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Meet The Professor

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

Thursday, October 28, 2021
5:00 PM – 6:00 PM ET

Faculty

Matthew P Goetz, MD

Moderator

Neil Love, MD

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Meet The Professor

Management of BRAF-Mutant Melanoma

Monday, November 1, 2021
5:00 PM – 6:00 PM ET

Faculty

Prof Georgina Long, AO, BSc, PhD, MBBS

Moderator

Neil Love, MD

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Meet The Professor

Optimizing the Selection and Sequencing of Therapy for Patients with Urothelial Bladder Carcinoma

Tuesday, November 2, 2021
5:00 PM – 6:00 PM ET

Faculty

Andrea Apolo, MD

Moderator

Neil Love, MD

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Meet The Professor

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

Wednesday, November 3, 2021
5:00 PM – 6:00 PM ET

Faculty

Adam M Brufsky, MD, 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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Associate Professor
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Co-Director, Santa Monica-UCLA Outpatient Oncology Practice
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Rita Nanda, MD
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Meet The Professor Program Participating Faculty

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Celebrating Women Chair in Breast Cancer Research
Baylor University Medical Center
Director, Breast Cancer Research Program
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US Oncology
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Breast Medical Oncology
Baptist Health South Florida
Miami Cancer Institute
Plantation, Florida

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

Moderator
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Research To Practice
Miami, Florida

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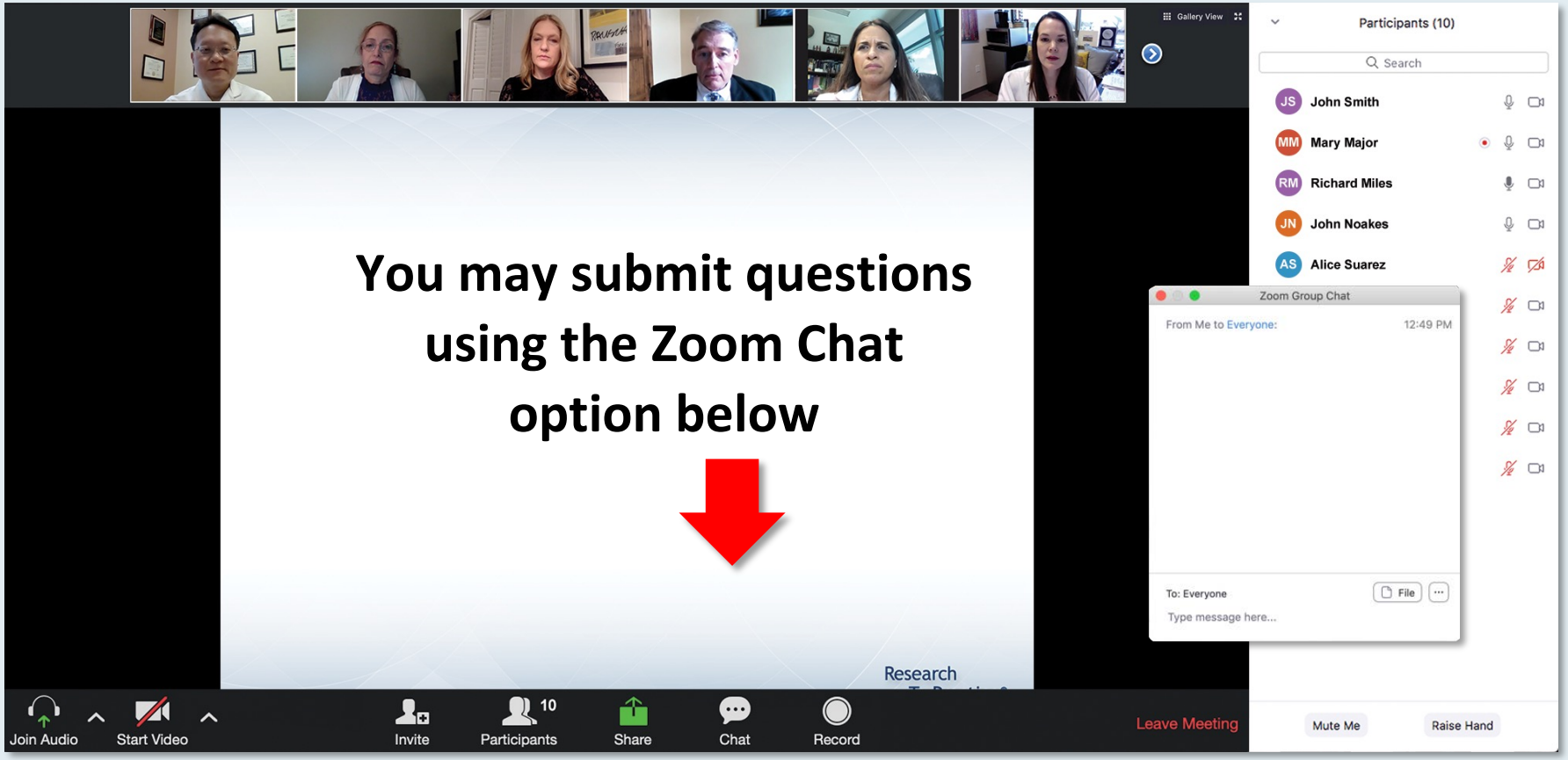

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RTP RESEARCH TO PRACTICE

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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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Florida Cancer Specialists and
Research Institute
New Port Richey, Florida

Kapisthalam (KS) Kumar, MD
Physician Partner
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Breast Medical Oncologist
Assistant Professor
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Charlotte, North Carolina

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Co-Leader, Breast Cancer Program
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University of Miami
Miami, Florida

Nikesh Jasani, MD
Texas Oncology-Cypress
Houston, Texas

Debra Patt, MD, PhD, MBA
Executive Vice President, Policy and
Strategic Initiatives
Texas Oncology
Austin, Texas

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Meet The Professor with Dr Bardia

MODULE 1: Introduction

MODULE 2: Case Presentations

- Dr Patt: A 40-year-old woman with localized triple-negative breast cancer (TNBC)
- Dr Jasani: A 60-year-old Jehovah's Witness with metastatic TNBC – PD-L1 >1%
- Dr Heeke: A 61-year-old woman with metastatic TNBC – HRD-positive, TP53 and RB1 mutations
- Dr Mahtani: A 55-year-old woman with metastatic TNBC – PD-L1 5%
- Dr Choksi: A 73-year-old woman with microsatellite stable TNBC and suspected bone metastases
- Dr Kumar: A 53-year-old Jehovah's Witness with localized TNBC

MODULE 3: Beyond the Guidelines

MODULE 4: Journal Club with Dr Bardia

MODULE 5: Other Key Data Sets

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REVIEW

Novel Agents for Metastatic Triple-Negative Breast Cancer: Finding the Positive in the Negative

Neelima Vidula, MD[1]; Leif W. Ellisen, MD[1]; and Aditya Bardia, MD[1]

J Natl Compr Canc Netw 2020;1-9.

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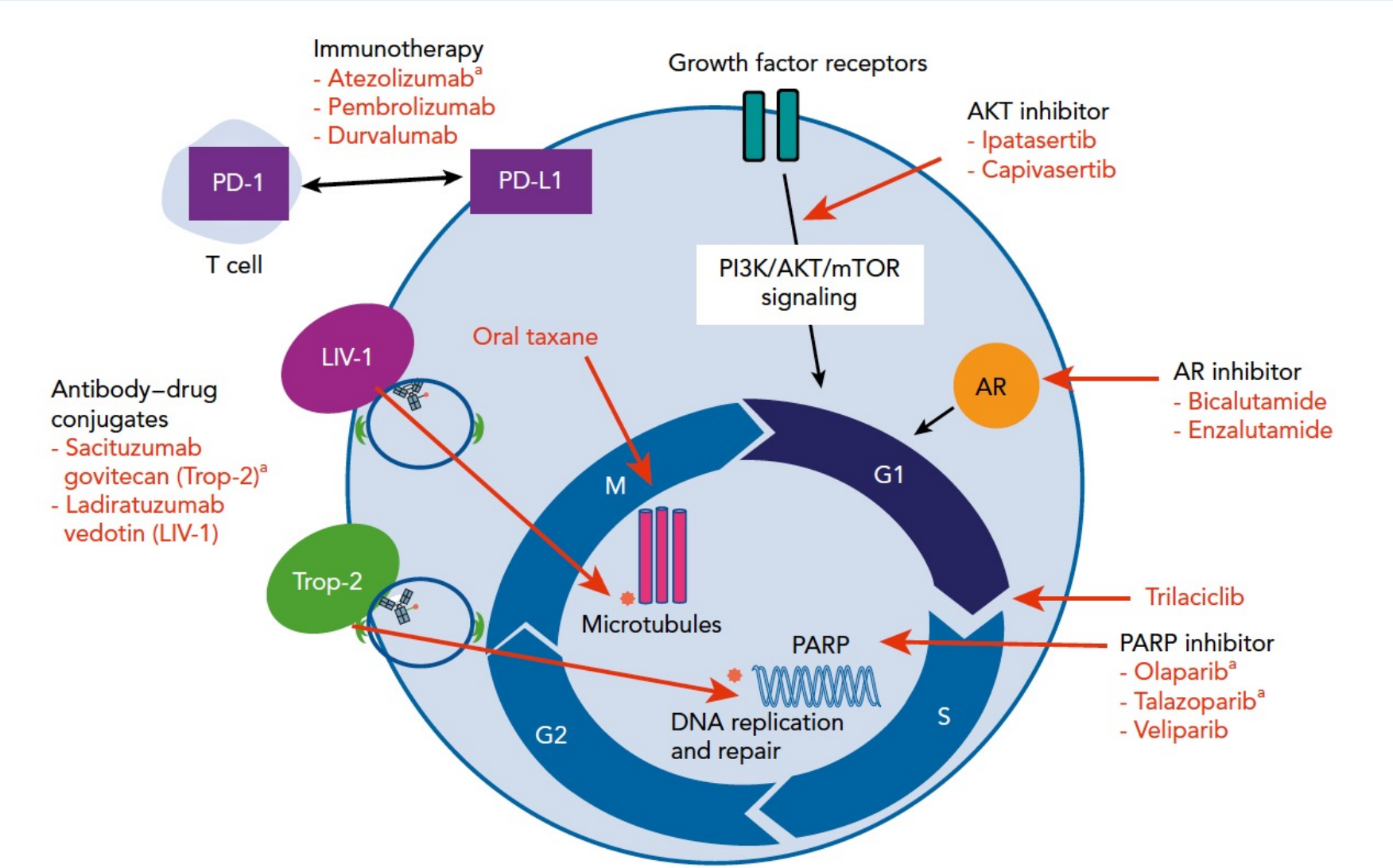
Novel Targets for Therapeutic Intervention in Triple-Negative Breast Cancer



Vidula N et al. *J Natl Compr Canc Netw* 2020;1-9.

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Case Presentation – Dr Patt: A 40-year-old woman with localized TNBC

Dr Debra Patt

- March 2021: normal screening mammogram
- Patient self-palpated firmness in upper outer quadrant of right breast
- May 2021: additional imaging by contrast-enhanced mammography and ultrasound show a 5-cm abnormality and axillary lymphadenopathy
- Biopsy: invasive TNBC

Questions

- Are there optimal breast imaging strategies when mammography is normal to identify potential disease?
- What is the optimal approach for neoadjuvant therapy for patients with localized TNBC?
- What is the role of genetic testing and what implications can that information have for potential therapeutic options in the adjuvant setting?

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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 Heeke: A 61-year-old woman with metastatic TNBC – HRD-positive, TP53 and RB1 mutations

Dr Arielle Heeke

- Initially diagnosed with Stage IIIA TNBC and treated with neoadjuvant ddAC followed by carboplatin/paclitaxel → surgery → adjuvant capecitabine due to residual disease (RCB3)
- Experienced swelling and pain in the affected breast and biopsy confirmed inflammatory recurrence of TNBC
- Staging and biopsy revealed small-volume metastatic disease in the lungs
- Molecular profiling: HRD-positive with LOH 43.5%, TP53 and RB1 mutations
- Atezolizumab/*nab* paclitaxel → PD
- Currently receiving pembrolizumab/carboplatin/gemcitabine with some areas showing PD

Question

- What is the role of PARP inhibitors for patients that don't have an actionable mutation?

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Case Presentation – Dr Mahtani: A 55-year-old woman with metastatic TNBC – PD-L1 5%

Dr Reshma Mahtani

- Diagnosed with metastatic TNBC at another institution
- Genetic testing was negative; PD-L1 5%
- Atezolizumab/*nab* paclitaxel with strong hypersensitivity reaction → atezolizumab discontinued, *nab* paclitaxel continued until disease progression in breast, nodes and bones
- Seen as a second opinion and given palliative radiation to the breast
- Screened for precision medicine trials, such as MATCH and TAPUR, but was not a candidate
- Discussed re-challenging with pembrolizumab and gemcitabine/carboplatin

Question

- Would you feel comfortable re-challenging this patient given her prior strong infusion reaction?

Case Presentation – Dr Mahtani: A 55-year-old woman with metastatic TNBC – PD-L1 5% (continued)

Dr Reshma Mahtani

- Diagnosed with metastatic TNBC at another institution
- Genetic testing was negative; PD-L1 5%
- Atezolizumab/*nab* paclitaxel with strong hypersensitivity reaction → atezolizumab discontinued, *nab* paclitaxel continued until disease progression in breast, nodes and bones
- Seen as a second opinion and screened for precision medicine trials, such as MATCH and TAPUR, but was not a candidate
- ***Pembrolizumab and gemcitabine/carboplatin x 2 doses and tolerating well with some improvement of tumor nodules***

Case Presentation – Dr Choksi: A 73-year-old woman with microsatellite stable 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?

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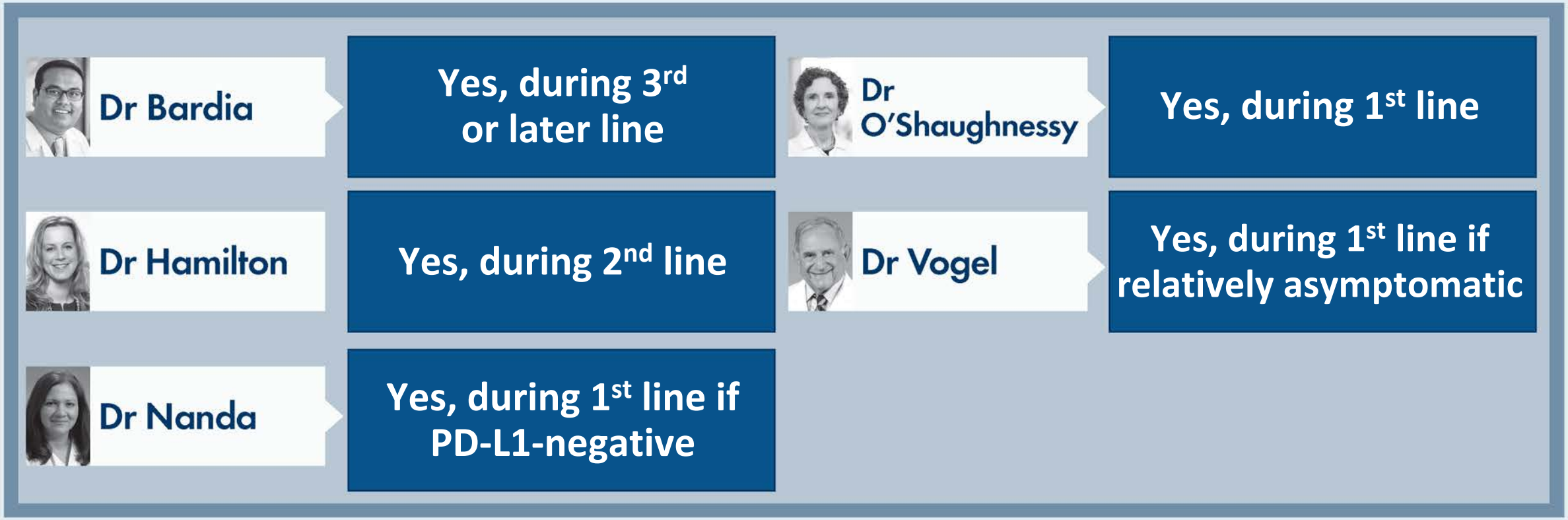
If a patient with TNBC and a germline BRCA1/2 mutation received olaparib as part of adjuvant therapy on a clinical trial and then developed metastatic disease 3 years later, would you attempt to administer a PARP inhibitor during a subsequent line of treatment?



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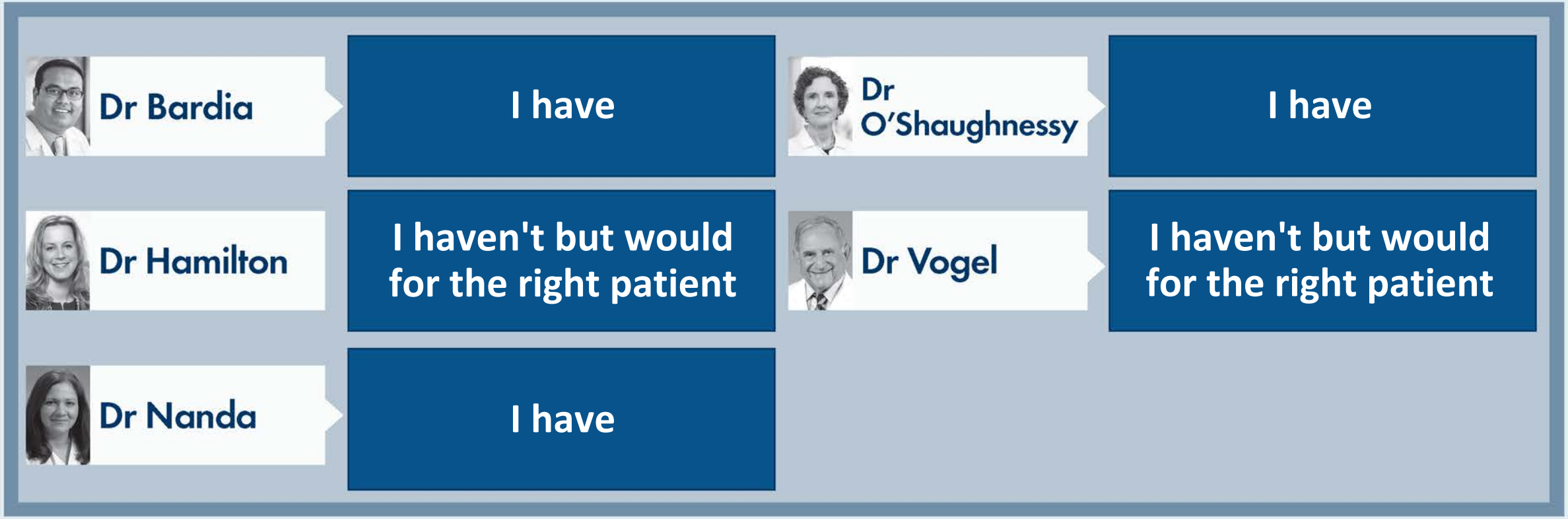
Regulatory and reimbursement issues aside, have you attempted or would you attempt to access a PARP inhibitor for a patient with metastatic TNBC and a somatic BRCA mutation?

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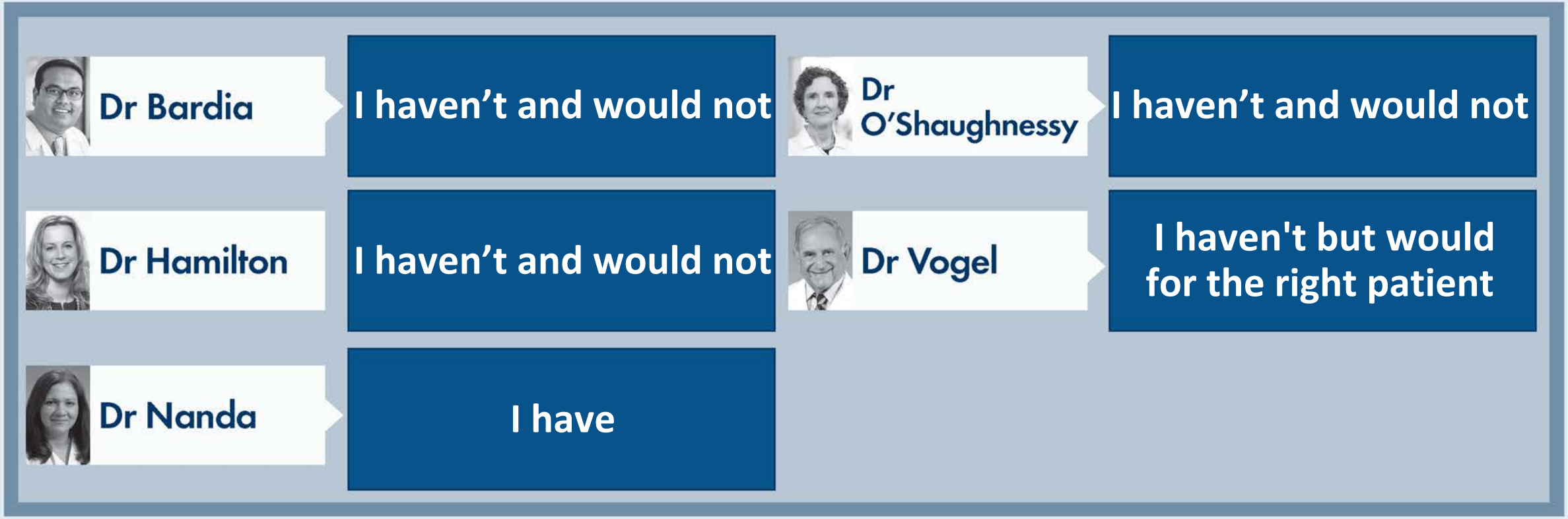
Regulatory and reimbursement issues aside, have you attempted or would you attempt to access a PARP inhibitor for a patient with metastatic TNBC and a germline ATM mutation?



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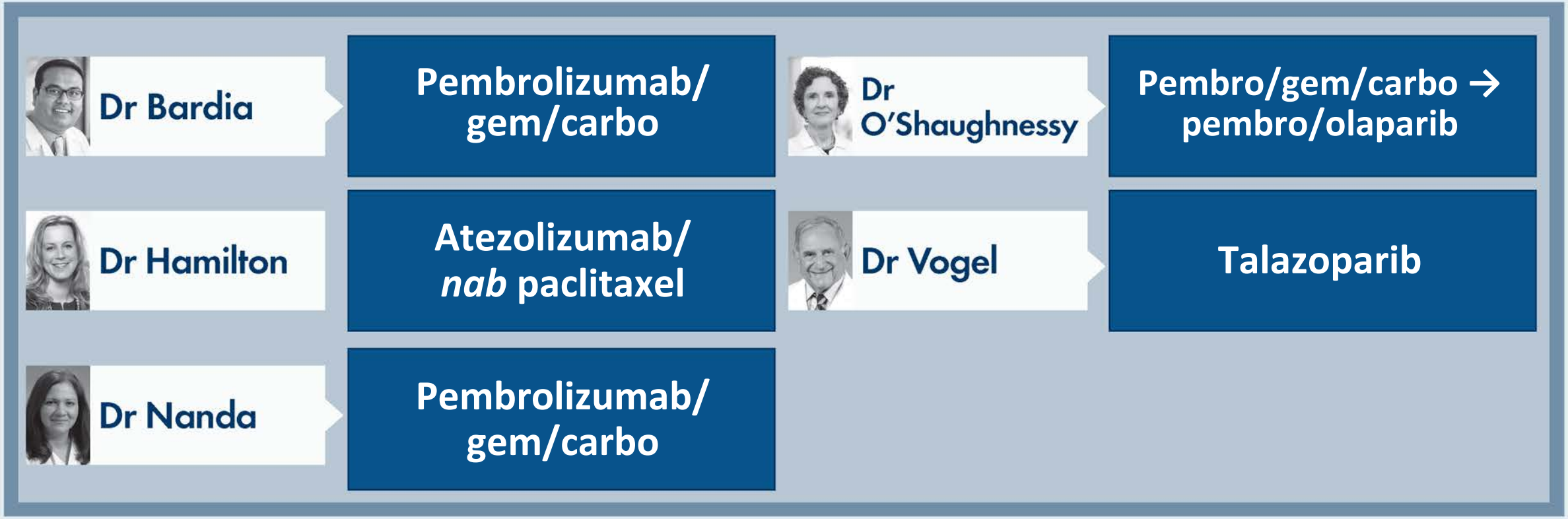
What would be your preferred treatment approach for a 60-year-old patient with a BRCA germline mutation and de novo metastatic TNBC that is PD-L1-positive?



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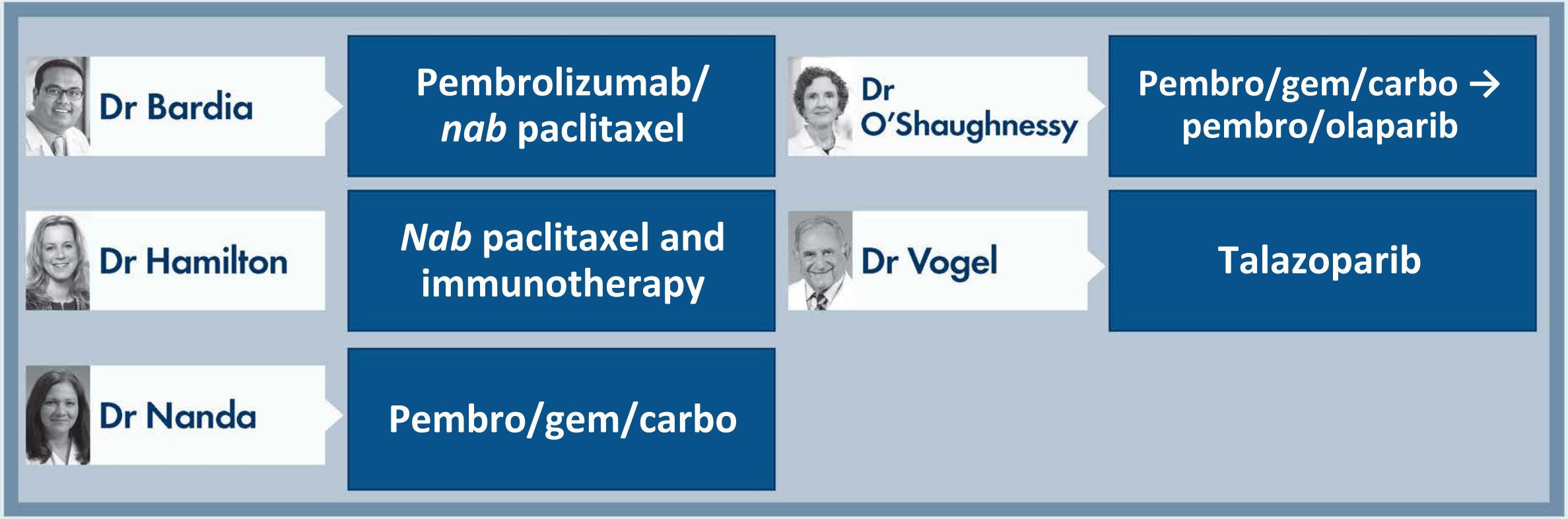
A 60-year-old woman with TNBC and a germline BRCA1 mutation (PD-L1 CPS >10) receives neoadjuvant carboplatin/paclitaxel/pembrolizumab → AC/ pembrolizumab and achieves a pathologic complete response. Three years after completion of adjuvant pembrolizumab, she develops metastatic TNBC (PD-L1 CPS >10).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



Gem = gemcitabine; carbo = carboplatin

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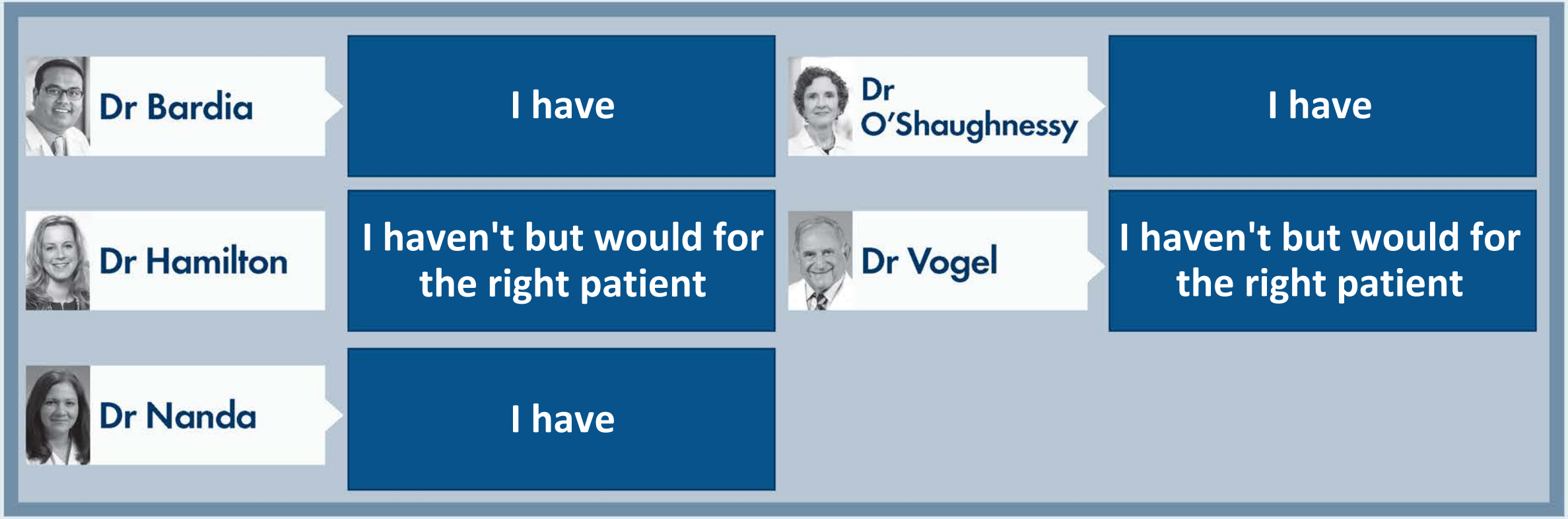
Regulatory and reimbursement issues aside, have you attempted or would you attempt to access olaparib as part of neoadjuvant therapy for a 45-year-old patient with a germline BRCA2 mutation and a 6-cm TNBC with negative axillary nodes on biopsy (PD-L1 10%)?

 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

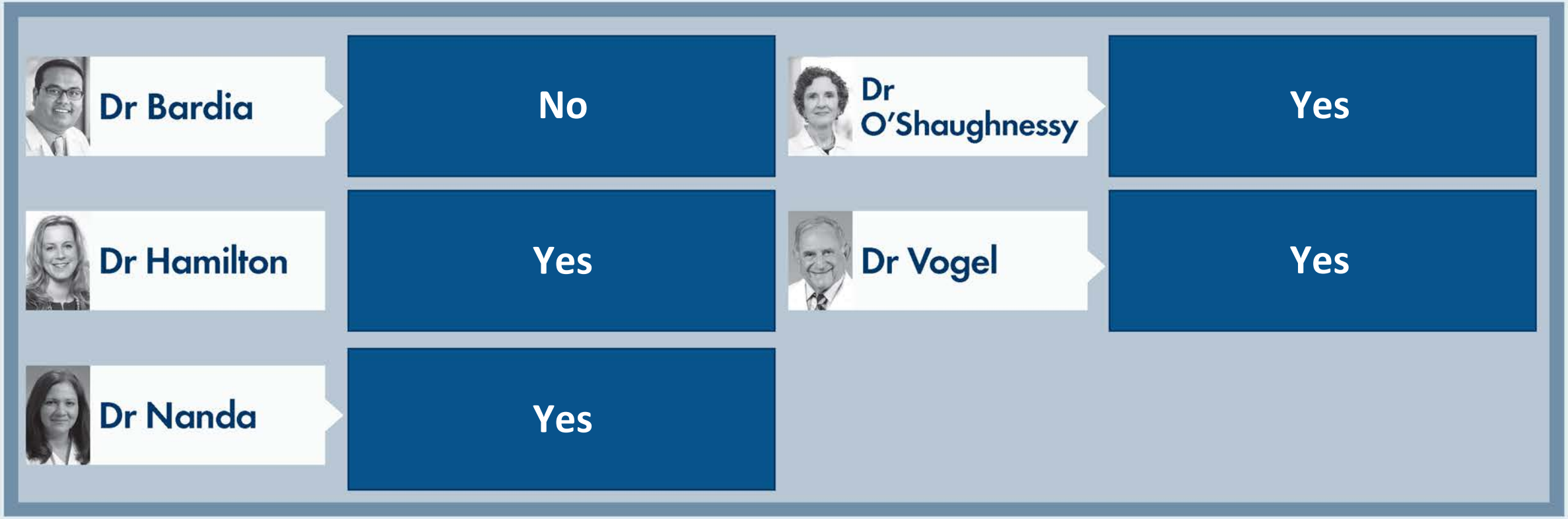
Dr Nanda

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

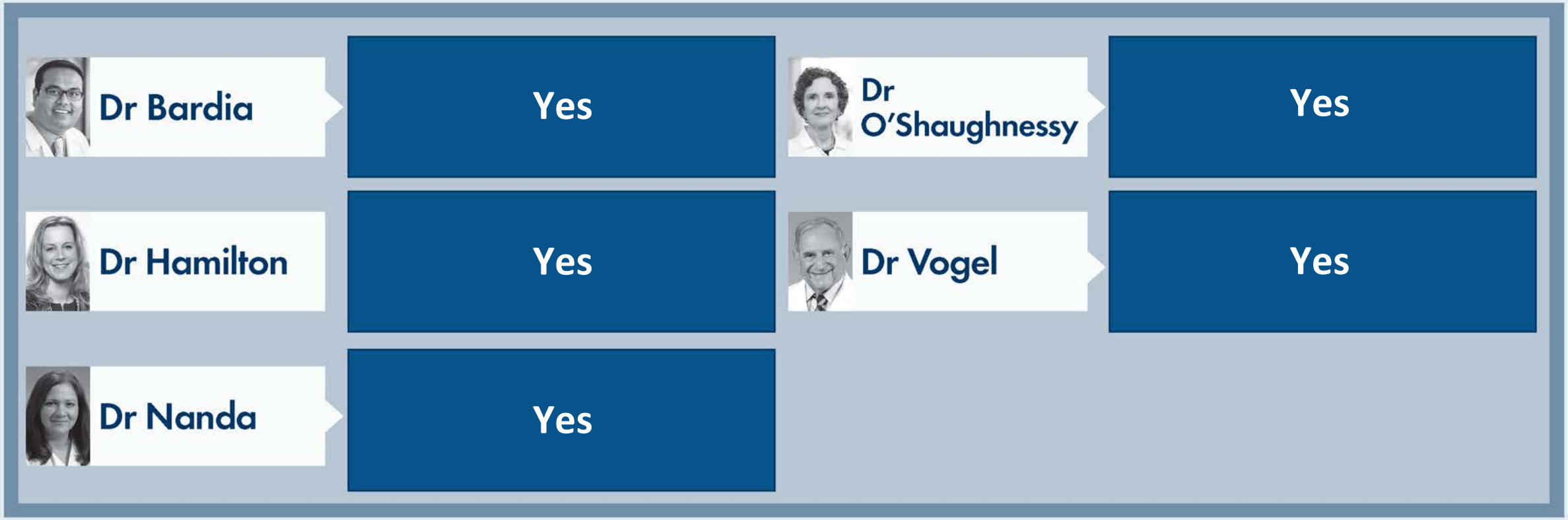
For a patient with localized TNBC and PD-L1 CPS ≥1, would you generally recommend neoadjuvant chemotherapy/ pembrolizumab → adjuvant pembrolizumab if they had…

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?



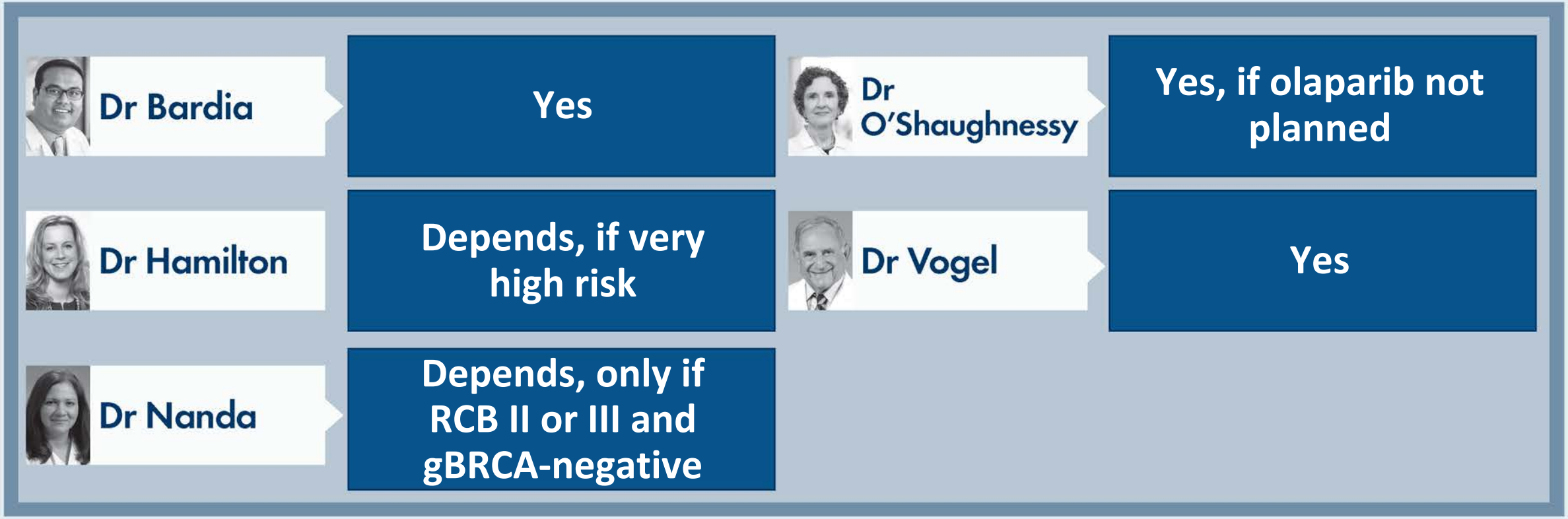
RTP RESEARCH TO PRACTICE

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 Dr Bardia

MODULE 1: Introduction

MODULE 2: Case Presentations

- Dr Patt: A 40-year-old woman with localized TNBC
- Dr Jasani: A 60-year-old Jehovah's Witness with metastatic TNBC – PD-L1 >1%
- Dr Heeke: A 61-year-old woman with metastatic TNBC – HRD-positive, TP53 and RB1 mutations
- Dr Mahtani: A 55-year-old woman with metastatic TNBC – PD-L1 5%
- Dr Choksi: A 73-year-old woman with microsatellite stable TNBC and suspected bone metastases
- Dr Kumar: A 53-year-old Jehovah's Witness with localized TNBC

MODULE 3: Beyond the Guidelines

MODULE 4: Journal Club with Dr Bardia

MODULE 5: Other Key Data Sets

RTP
RESEARCH
TO PRACTICE

Journal Club with Dr Bardia

- Krop I et al. **GS1-05 datopotamab deruxtecan in advanced/metastatic HER2- breast cancer: Results from the phase 1 TROPION-PanTumor01 study**. SABCS 2021;Abstract GS1-05.
- Vidula N et al. **Phase II study of a PARP inhibitor in metastatic breast cancer with somatic BRCA1/2mutations identified by cell-free DNA: Genotyping based clinical trial**. SABCS 2021;Abstract OT2-24-03.
- Beyerlin K et al. **The adjuvant use of capecitabine for residual disease following pre-operative chemotherapy for breast cancer: Challenges applying CREATE-X to a US population**. *J Oncol Pharm Pract* 2020:[Online ahead of print].
- Spring LM et al. **Sacituzumab govitecan for metastatic triple-negative breast cancer: Clinical overview and management of potential toxicities**. *Oncologist* 2021;26(10):827-34.
- Bardia A et al. **Sacituzumab govitecan in metastatic breast cancer. Reply.** *N Engl J Med* 2021;385(3):e12.
- Spring LM et al. **Phase 2 study of response-guided neoadjuvant sacituzumab govitecan (IMMU-132) in patients with localized triple-negative breast cancer (NeoSTAR).** SABCS 2020;Abstract OT-03-06.

RTP RESEARCH TO PRACTICE

Journal Club with Dr Bardia

- Spring LM et al. **Case 22-2020: A 62-year-old woman with early breast cancer during the Covid-19 pandemic.** *N Engl J Med* 2020;383(3):262-72.
- Reynolds KL et al. **The art of oncology: COVID-19 era**. *Oncologist* 2020;25(11):997-1000g.
- Zubiri L et al. **Temporal trends in inpatient oncology census before and during the COVID-19 pandemic and rates of nosocomial COVID-19 among patients with cancer at a large academic center.** *Oncologist* 2021;26(8):e1427-33.
- Jacob S et al. **The use of serial circulating tumor DNA to detect resistance alterations in progressive metastatic breast cancer**. *Clin Cancer Res* 2021;27(5):1361-70.
- Vidula N et al. **Phase II multicenter study of talazoparib for somatic BRCA1/2 mutant metastatic breast cancer**. ASCO 2021;Abstract TPS1110.
- Vidula N et al. **Clinical application of liquid biopsies to detect somatic BRCA1/2 mutations and guide potential therapeutic intervention for patients with metastatic breast cancer.** *Oncotarget* 2021;12(2):63-5.

RTP
RESEARCH
TO PRACTICE

Journal Club with Dr Bardia

- Rugo H et al. **KEYLYNK-009: A phase 2/3, open-label, randomized study of pembrolizumab plus olaparib vs pembrolizumab plus chemotherapy after induction with first-line pembrolizumab plus chemotherapy in patients with locally recurrent inoperable or metastatic triple-negative breast cancer (TNBC).** SABCS 2020;Abstract OT-30-01.
- Dai C et al. **Molecular alterations in the androgen receptor and associated clinical outcomes in hormone receptor-positive/HER2- metastatic breast cancer.** SABCS 2020;Abstract PS17-02.
- Vidula N et al. **Microsatellite instability high (MSI-H) detection utilizing targeted plasma based genotyping in metastatic breast cancer.** SABCS 2020;Abstract PS18-18.
- Isakoff SJ et al. **Feasibility of integrating the Outcomes4Me smartphone navigation application into the care of breast cancer patients (FIONA).** ASCO 2021;Abstract 1570.

RTP
RESEARCH
TO PRACTICE

Meet The Professor with Dr Bardia

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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.

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

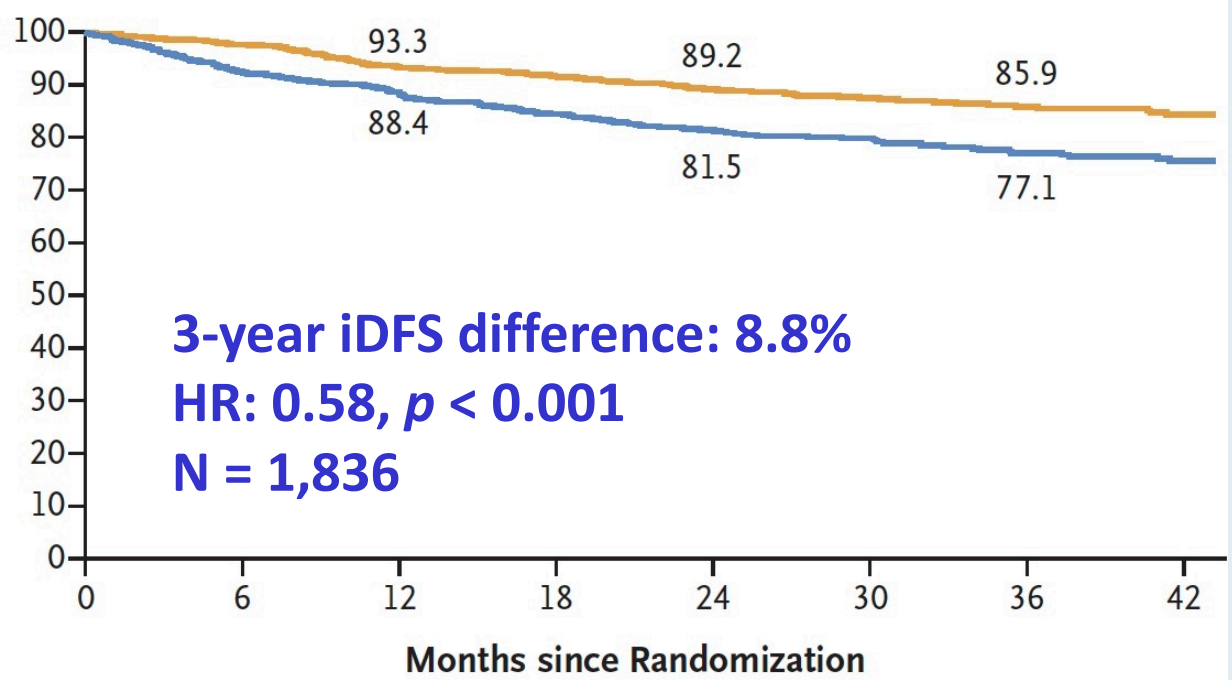
ORIGINAL ARTICLE

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*

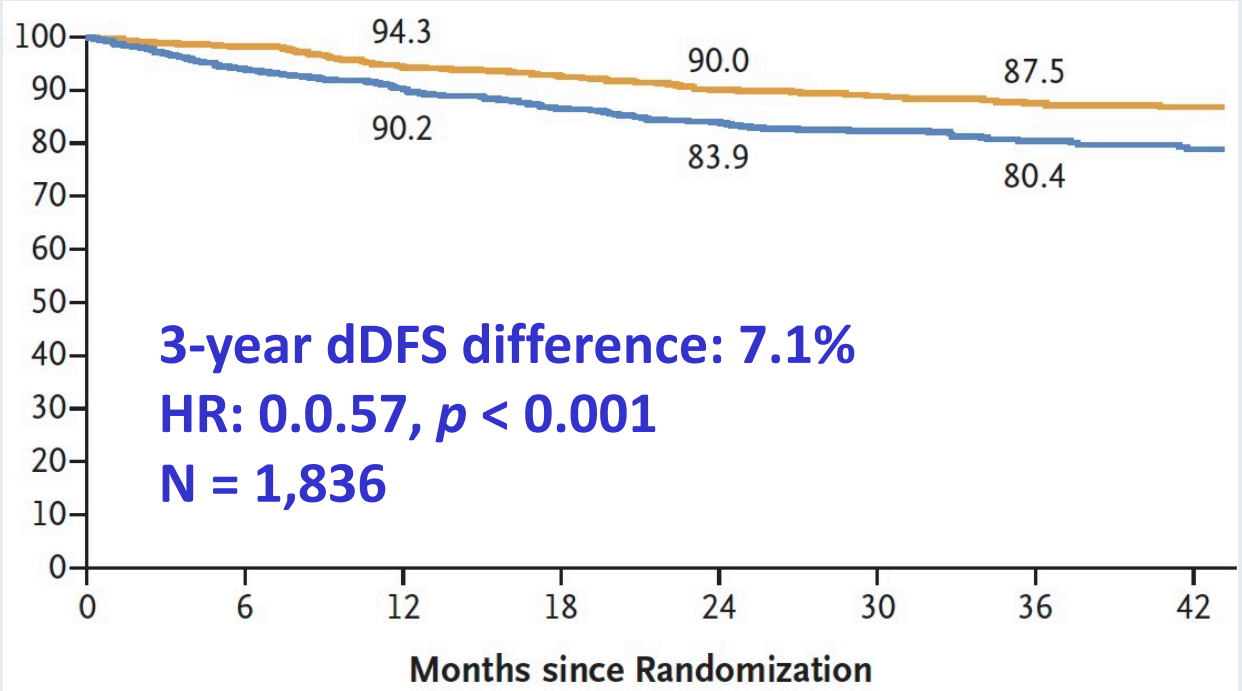
OlympiA: Invasive and Distant Disease-Free Survival

Invasive DFS



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

Distant DFS



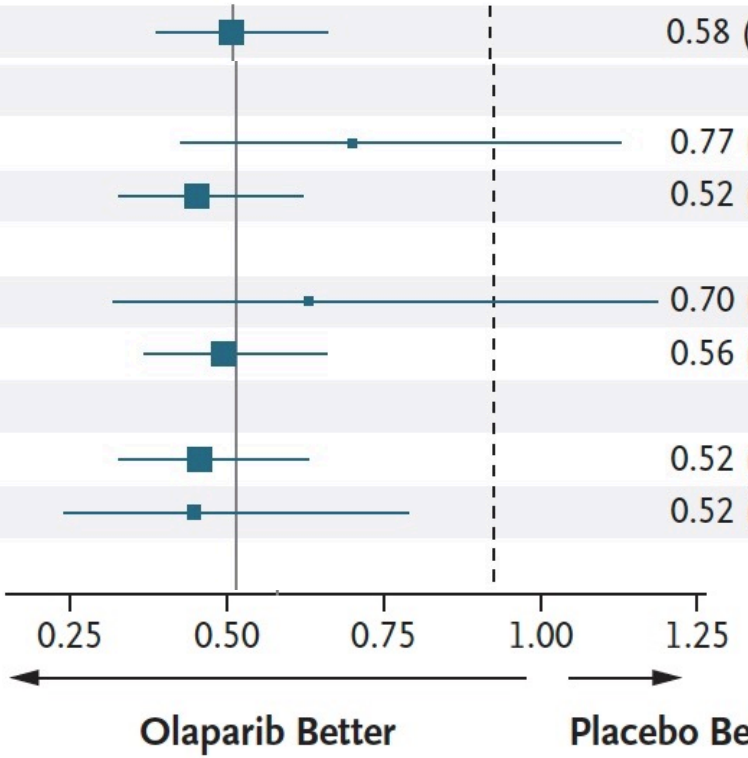
3-year dDFS difference: 7.1%
HR: 0.0.57, $p < 0.001$
N = 1,836

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

RTP RESEARCH TO PRACTICE

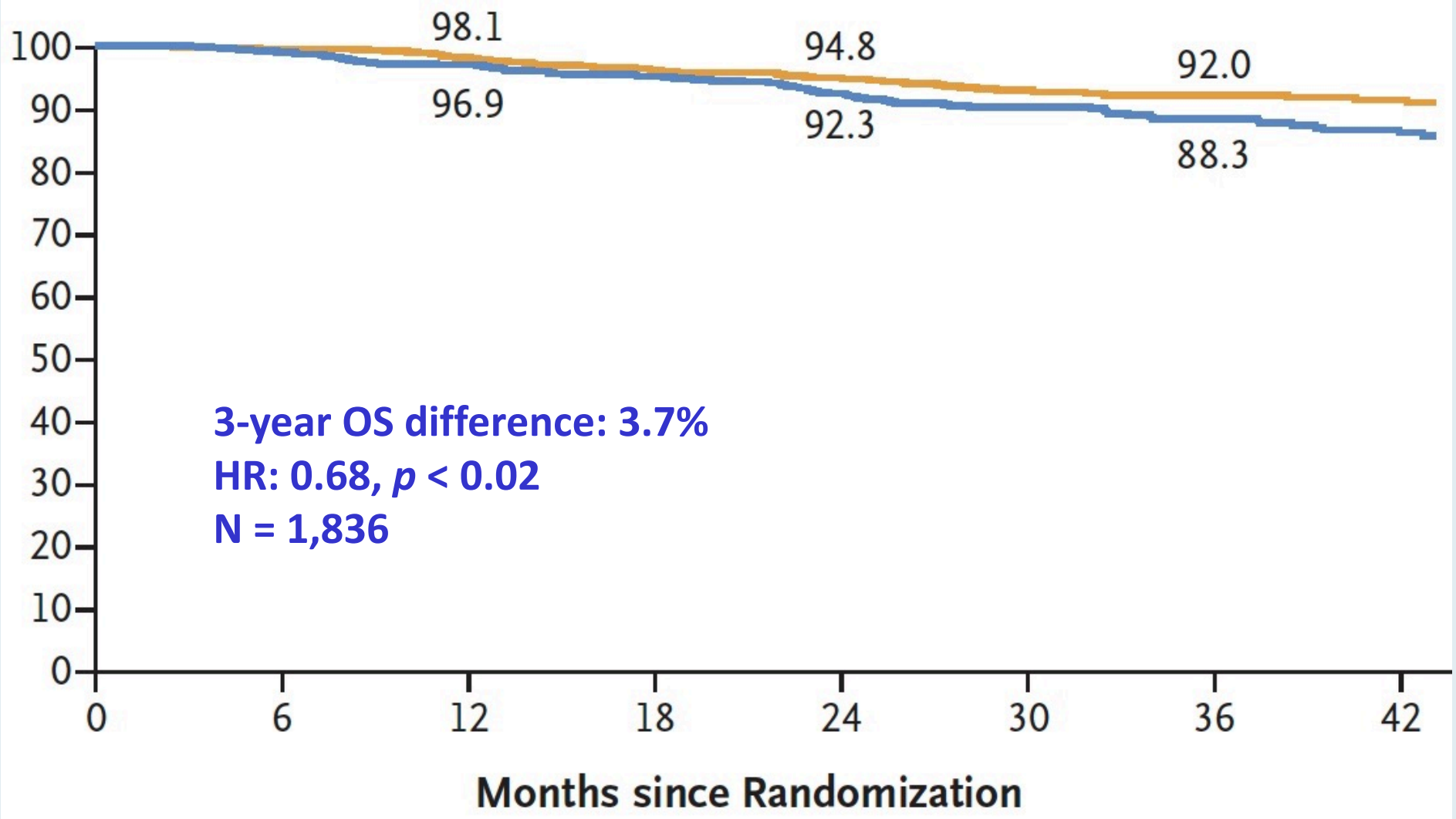
OlympiA: 3-Year Invasive DFS

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.

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

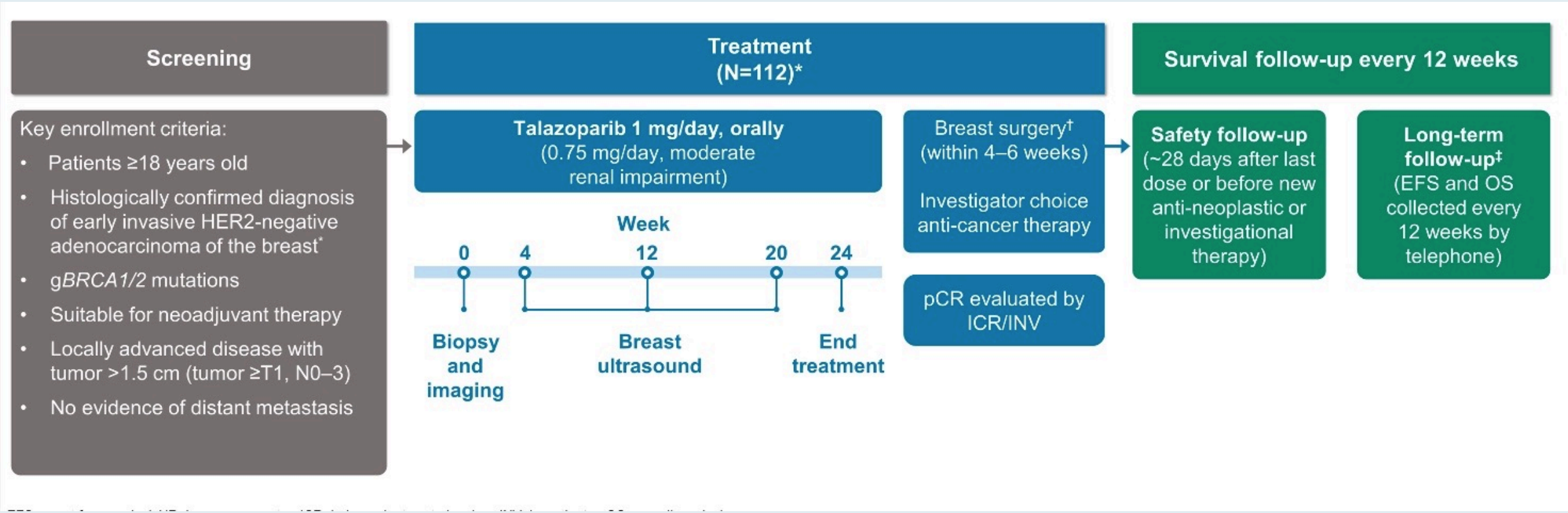
NEOADJUVANT TALAZOPARIB IN PATIENTS WITH GERMLINE *BRCA1/2* MUTATION-POSITIVE, EARLY HER2-NEGATIVE BREAST CANCER: RESULTS OF A PHASE 2 STUDY

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

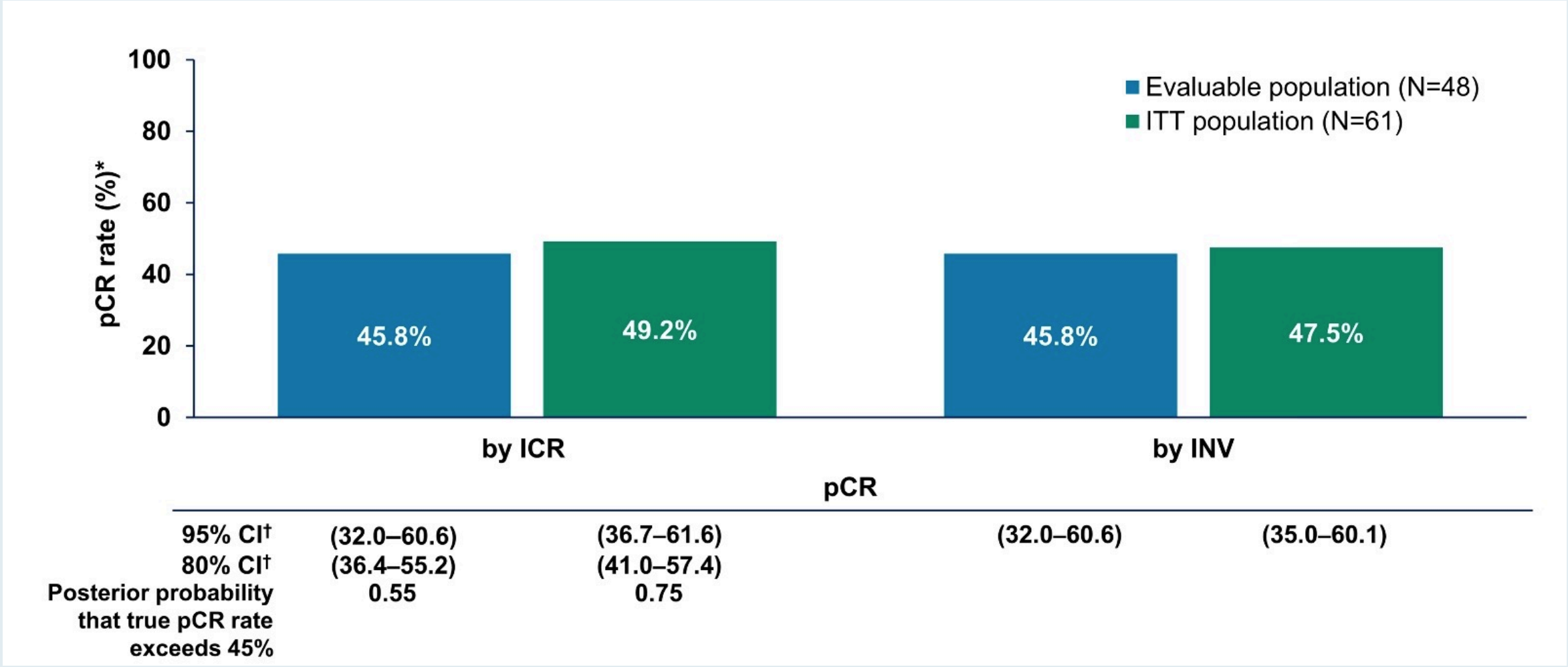
June 6, 2021

NEOTALA: Multicenter Phase II Study Schema



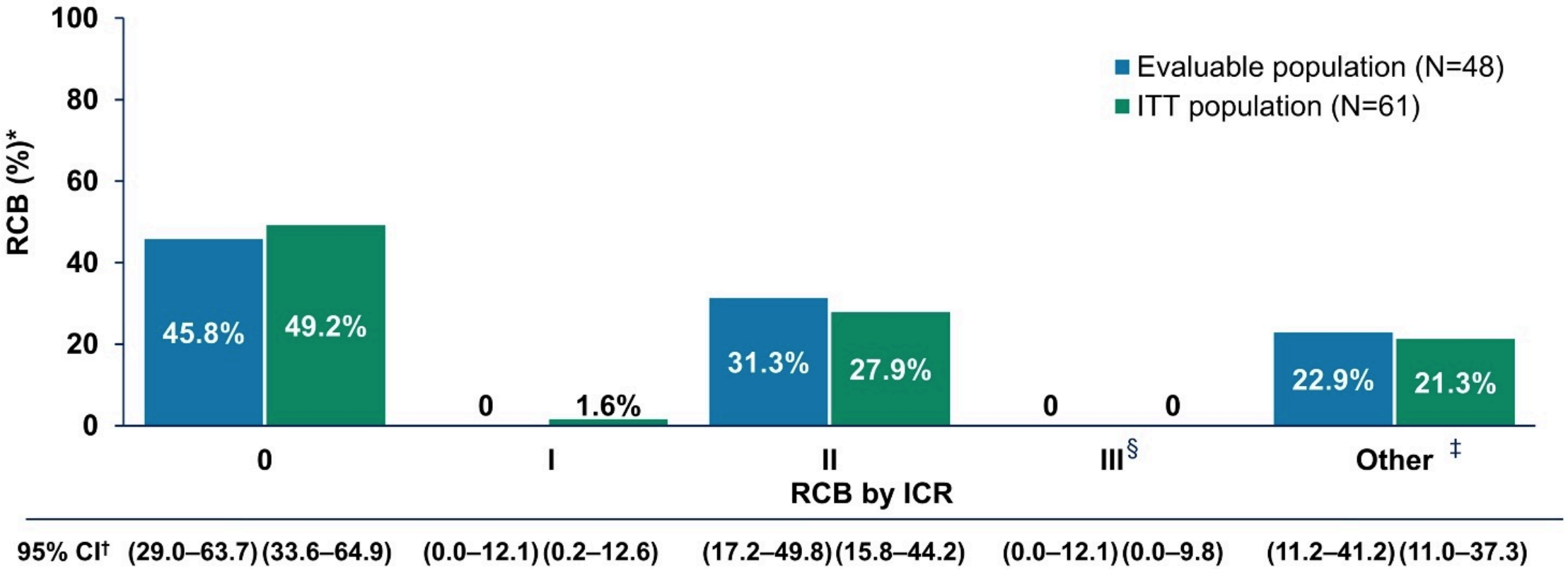
Litton JK et al. ASCO 2021;Abstract 505.

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

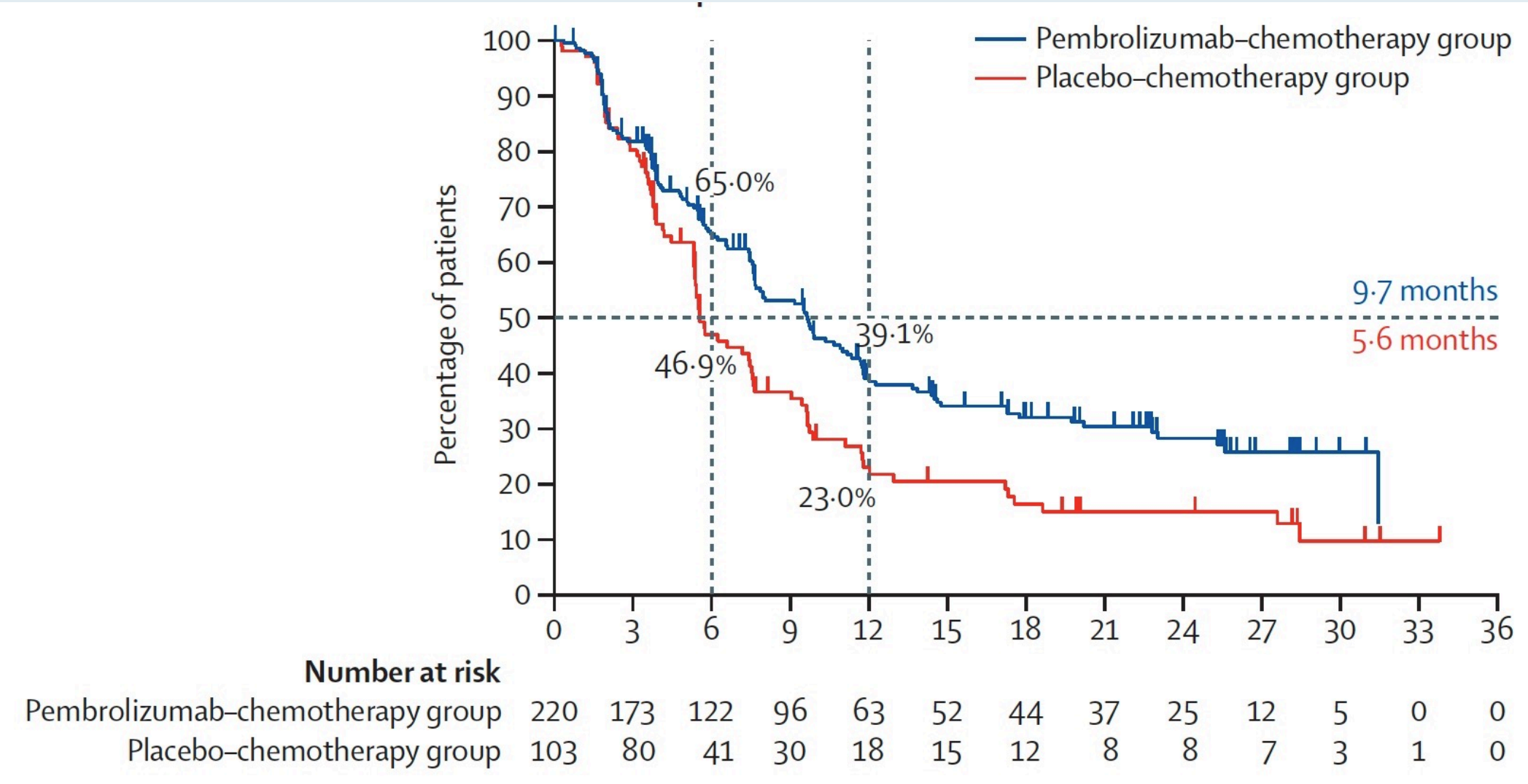
RTP RESEARCH TO PRACTICE

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

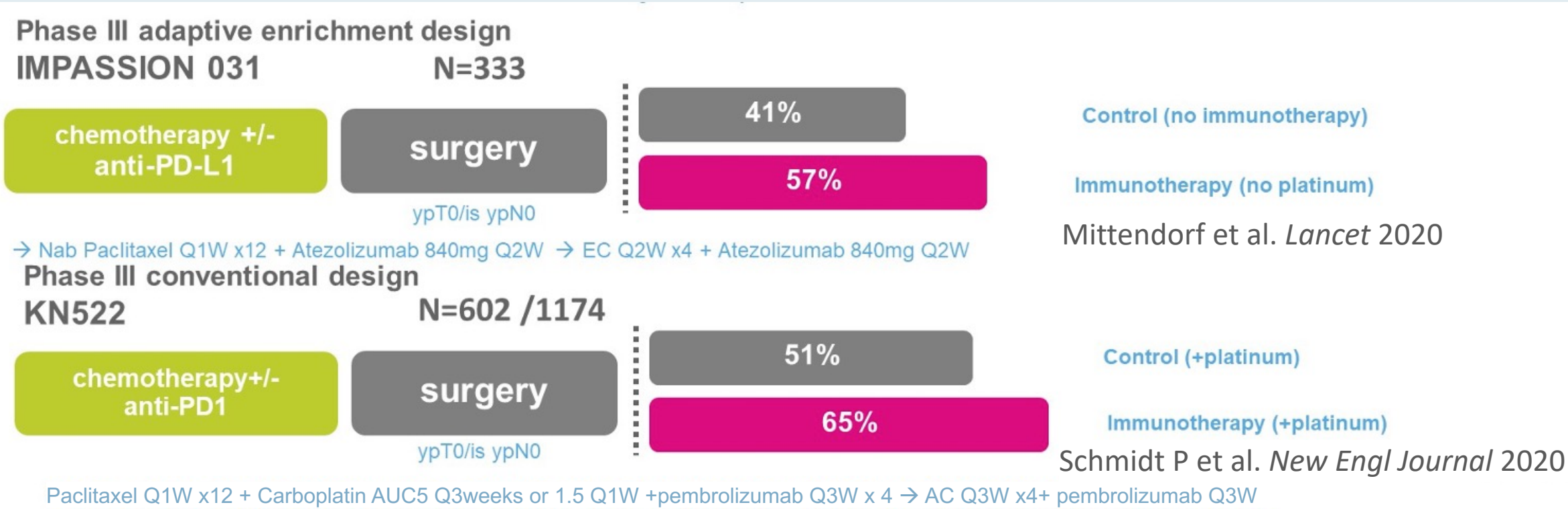
Press Release – August 27, 2021

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

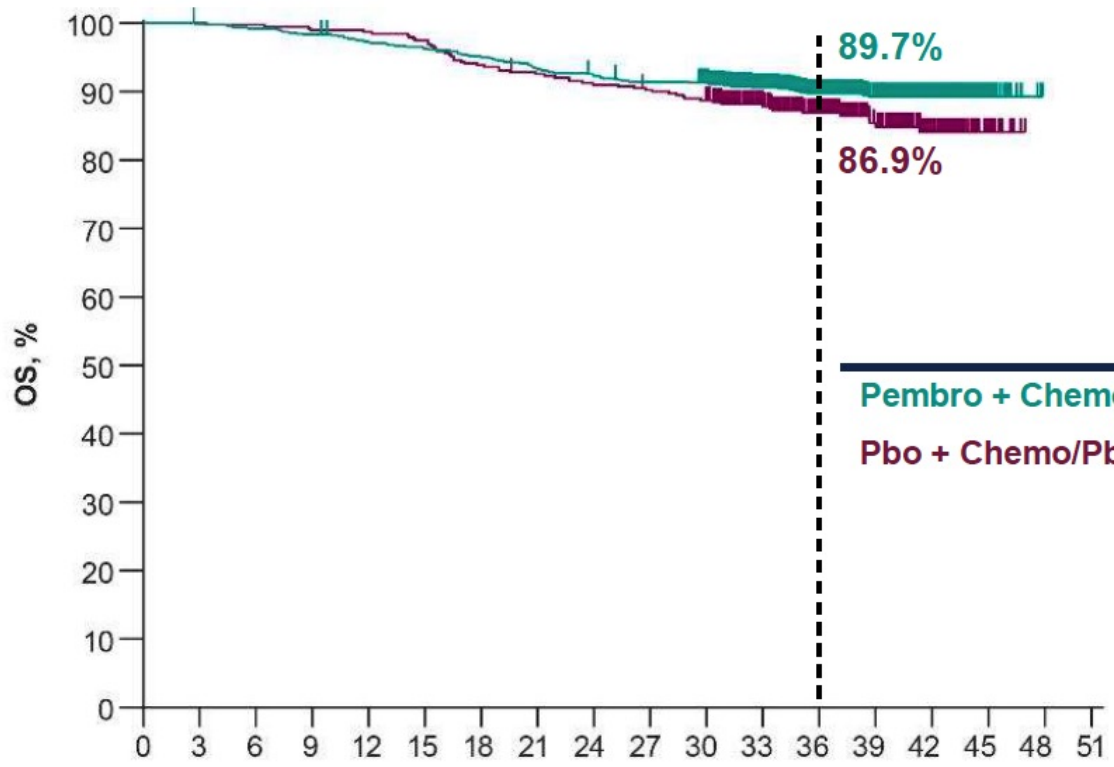
ESMO VIRTUAL PLENARY

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)

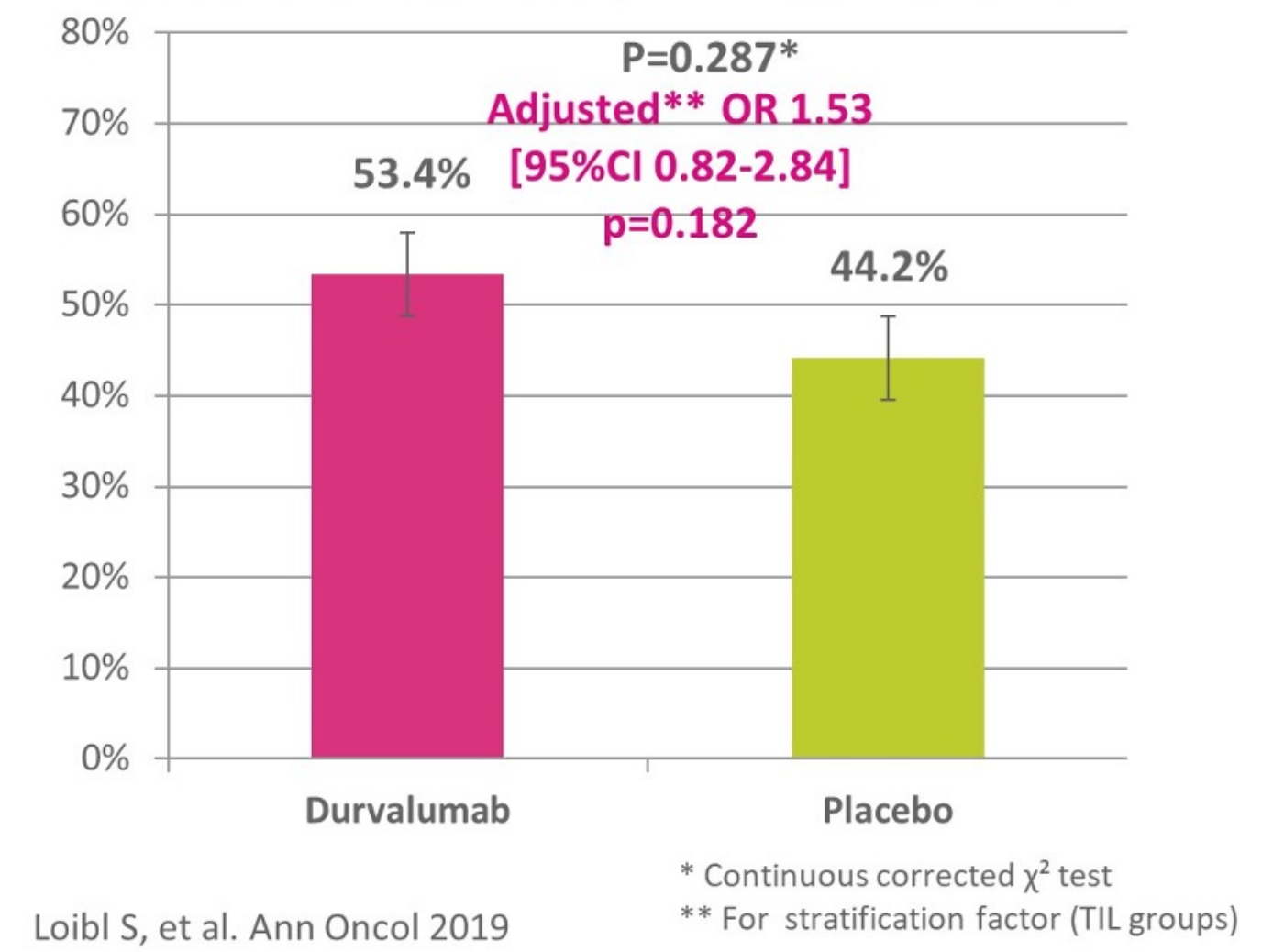
Sibylle Loibl, Andreas Schneeweiss, Jens Huober, Michael Braun, Julia Rey, Jens-Uwe Blohmer, Jenny Furlanetto, Dirk-Michael Zahm, Claus Hanusch, Jörg Thomalla, Christian Jackisch, Peter Staib, Theresa Link, Kerstin Rhiem, Christine Solbach, Peter A Fasching, Nicole Burchardi, Carsten Denkert, Michael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

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

RTP RESEARCH TO PRACTICE

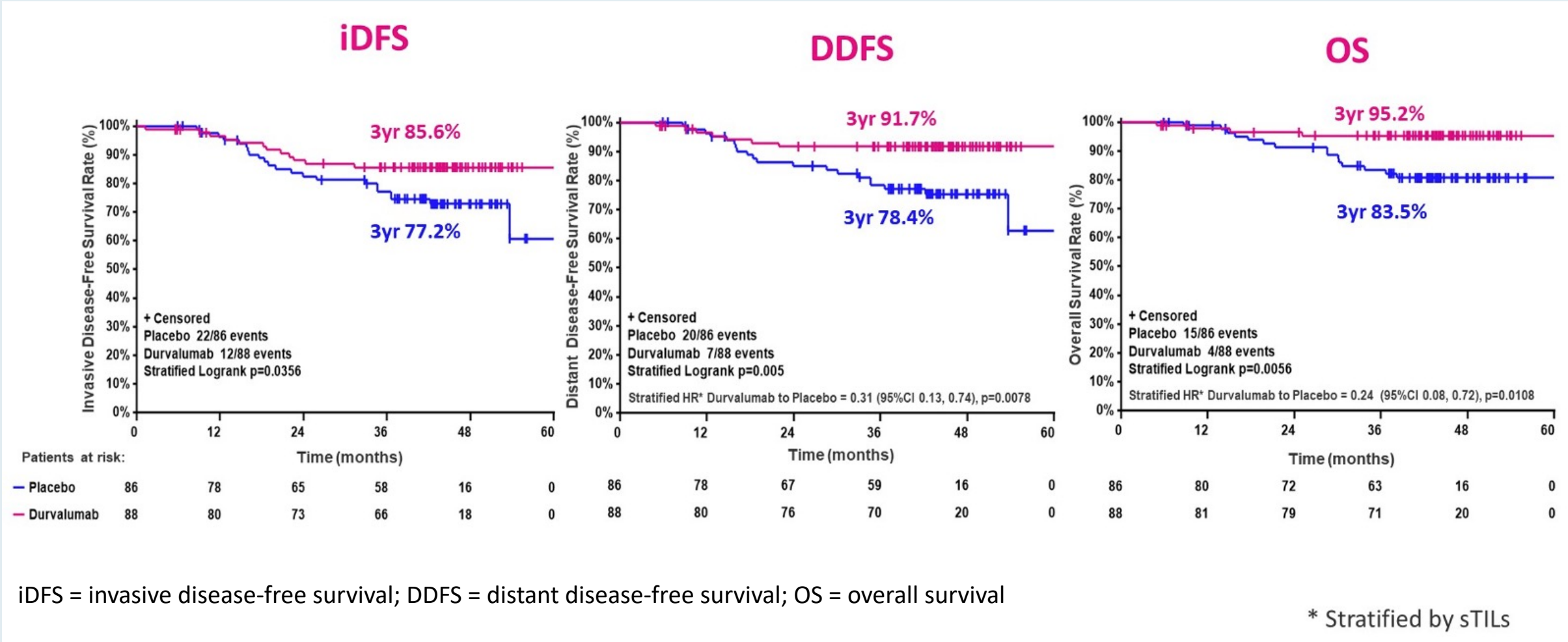
Loibl S et al. ASCO 2021;Abstract 506.

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

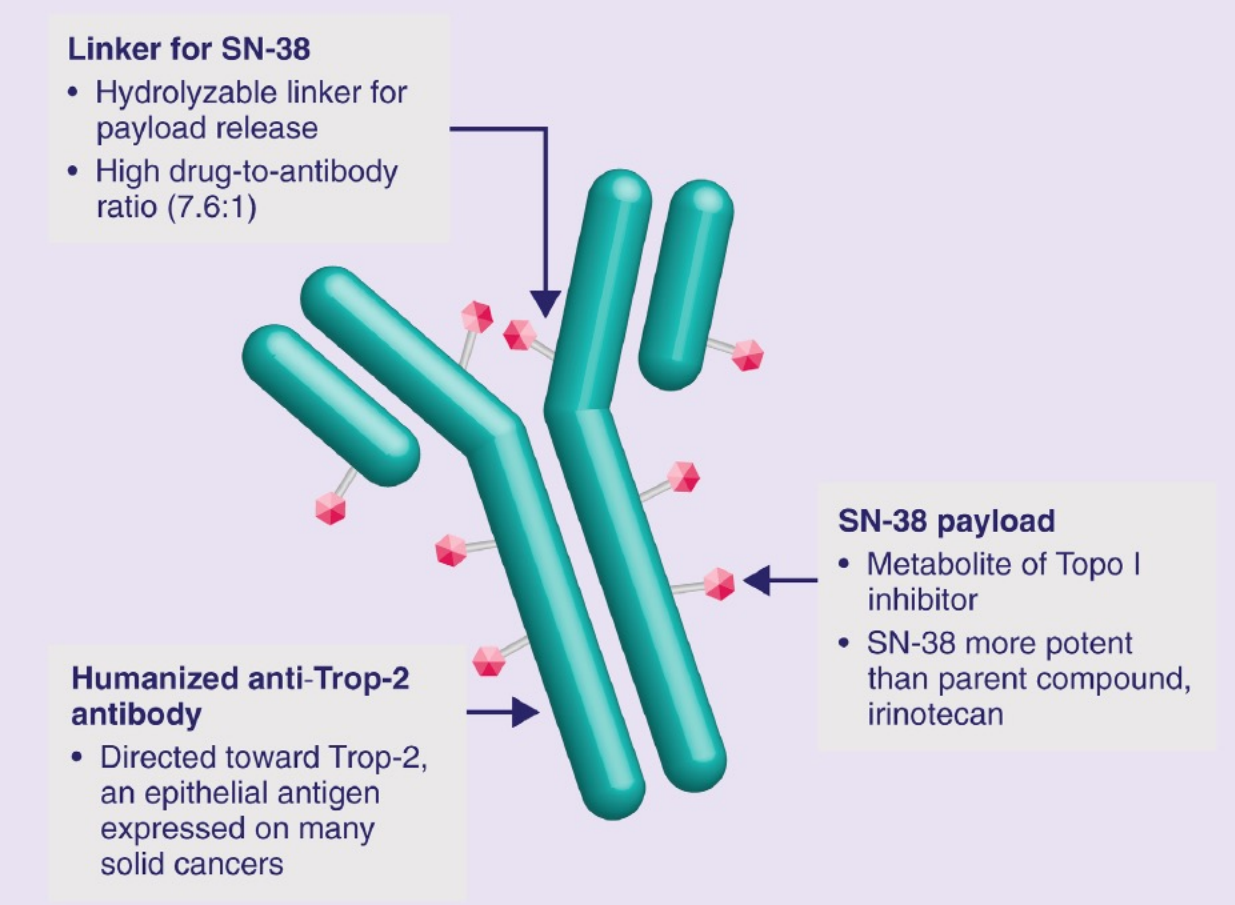
"The Food and Drug Administration granted regular approval to sacituzumab govitecan for patients with unresectable locally advanced or metastatic triple-negative breast cancer (mTNBC) who have received two or more prior systemic therapies, at least one of them for metastatic disease.

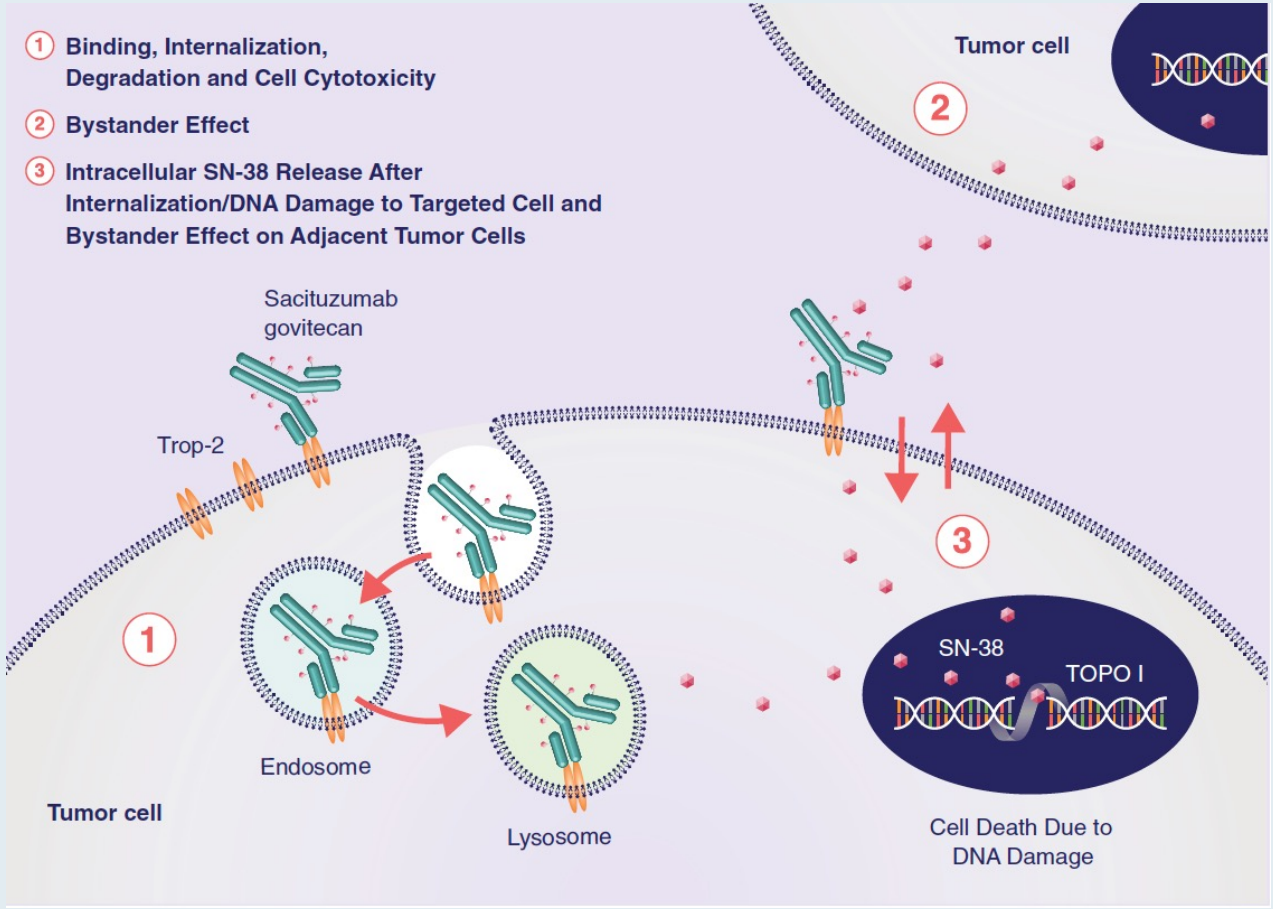
Efficacy and safety were evaluated in a multicenter, open-label, randomized trial (ASCENT; NCT02574455) conducted in 529 patients with unresectable locally advanced or mTNBC who had relapsed after at least two prior chemotherapies, one of which could be in the neoadjuvant or adjuvant setting, if progression 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

RTP RESEARCH TO PRACTICE

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

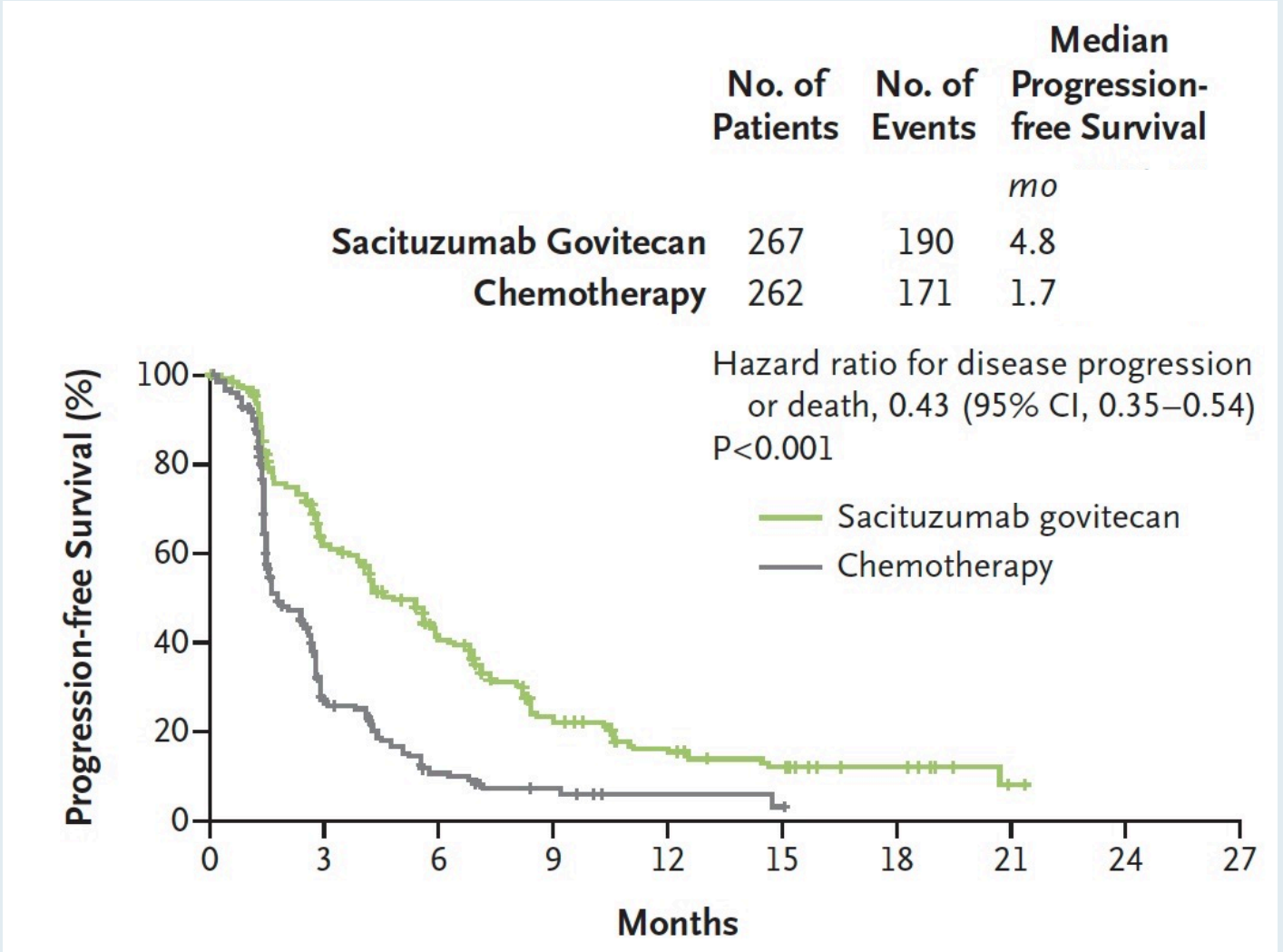
ORIGINAL ARTICLE

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)

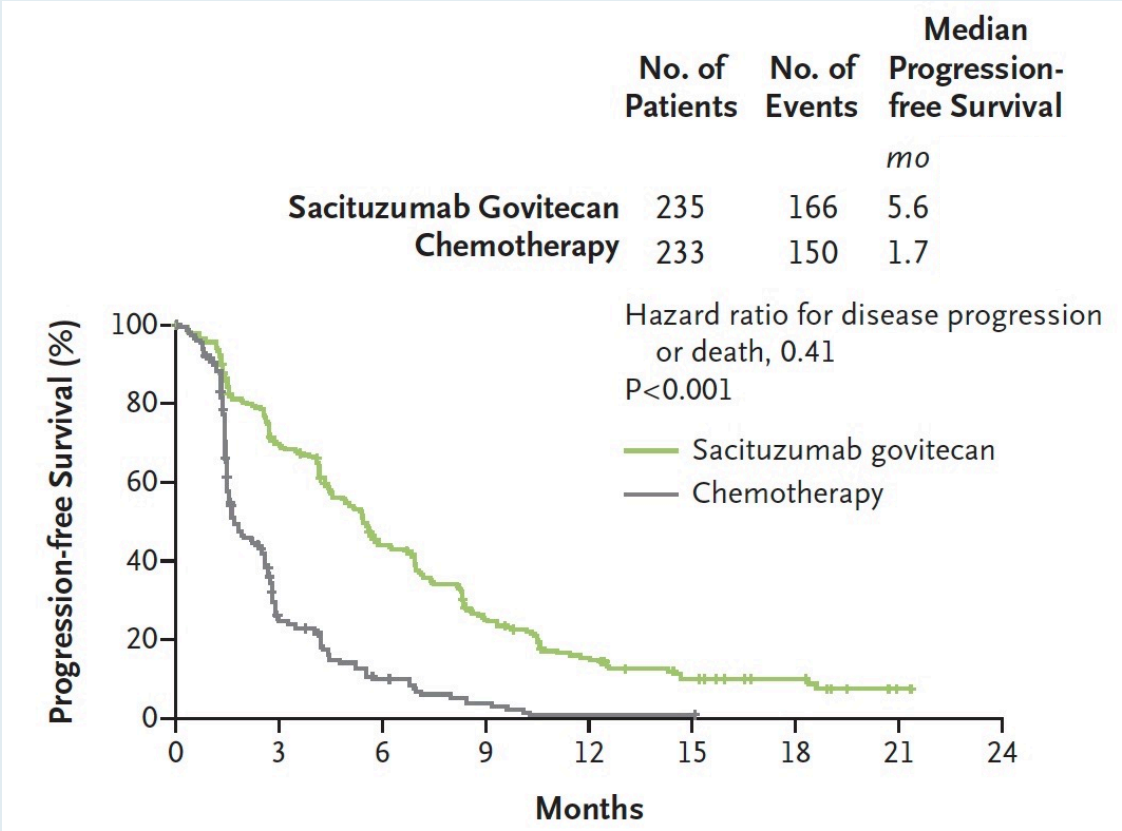
	No. of Patients	No. of Events	Median Progression-free Survival
			mo
Sacituzumab Govitecan	267	190	4.8
Chemotherapy	262	171	1.7

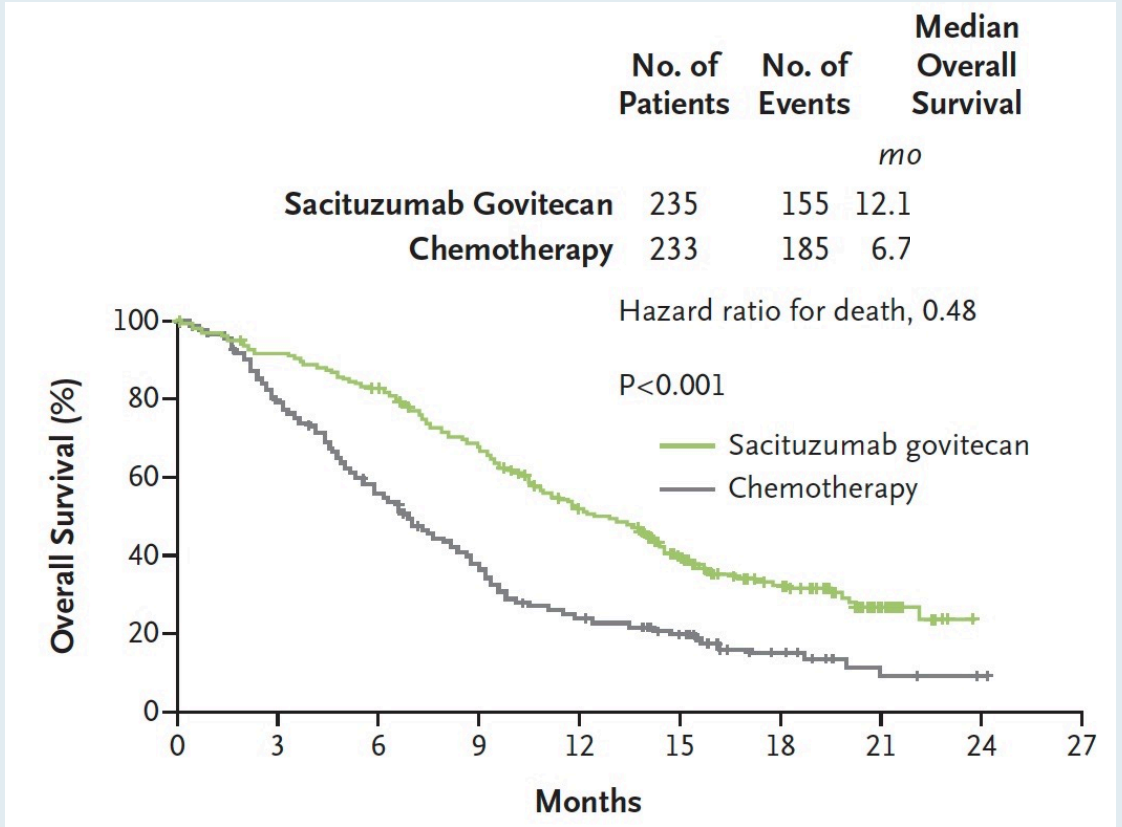


Bardia A et al. *N Engl J Med* 2021;384:1529-41.

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.

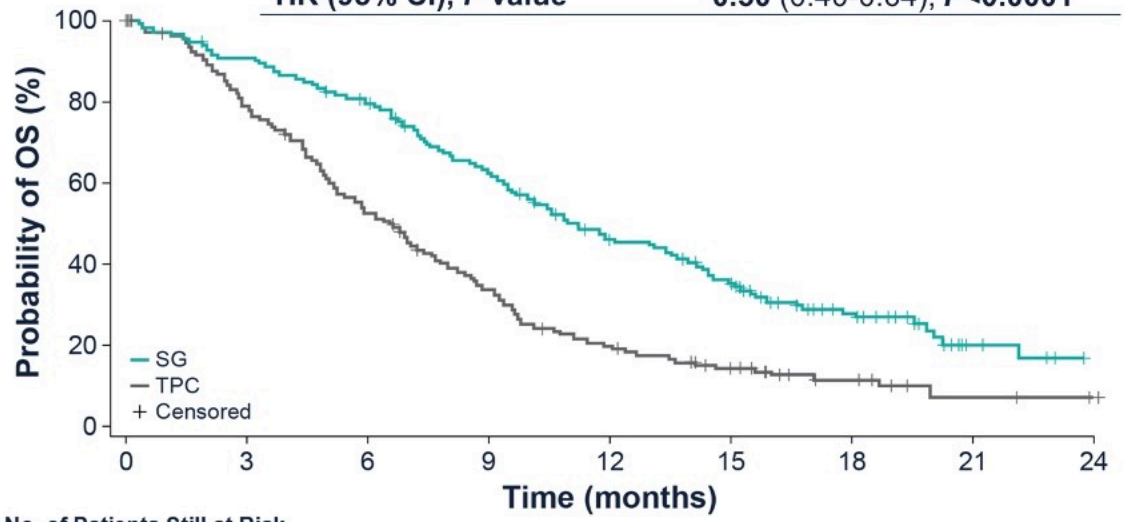
Outcomes in Patients (pts) Aged ≥65 Years in the Phase 3 ASCENT Study of Sacituzumab Govitecan (SG) in Metastatic Triple-Negative Breast Cancer (mTNBC)

Kalinsky K et al.

ASCO 2021;Abstract 1011.

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

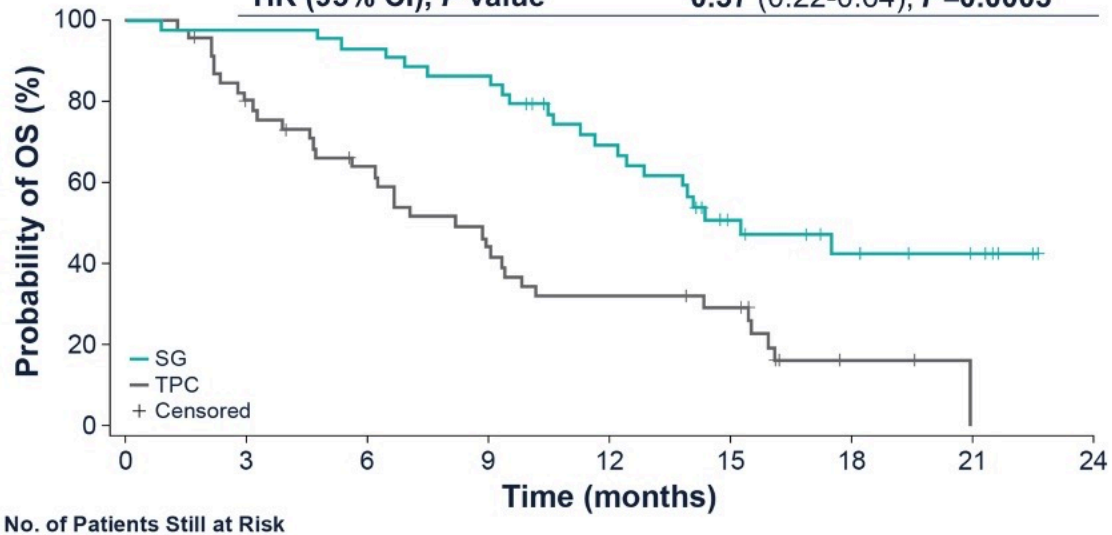
	<65 y	
	SG (n=191)	TPC (n=187)
No. of events	133	150
Median OS—mo (95% CI)	11.2 (9.9-13.4)	6.6 (5.3-7.4)
HR (95% CI), *P* value	**0.50** (0.40-0.64), ***P*<0.0001**	



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.

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

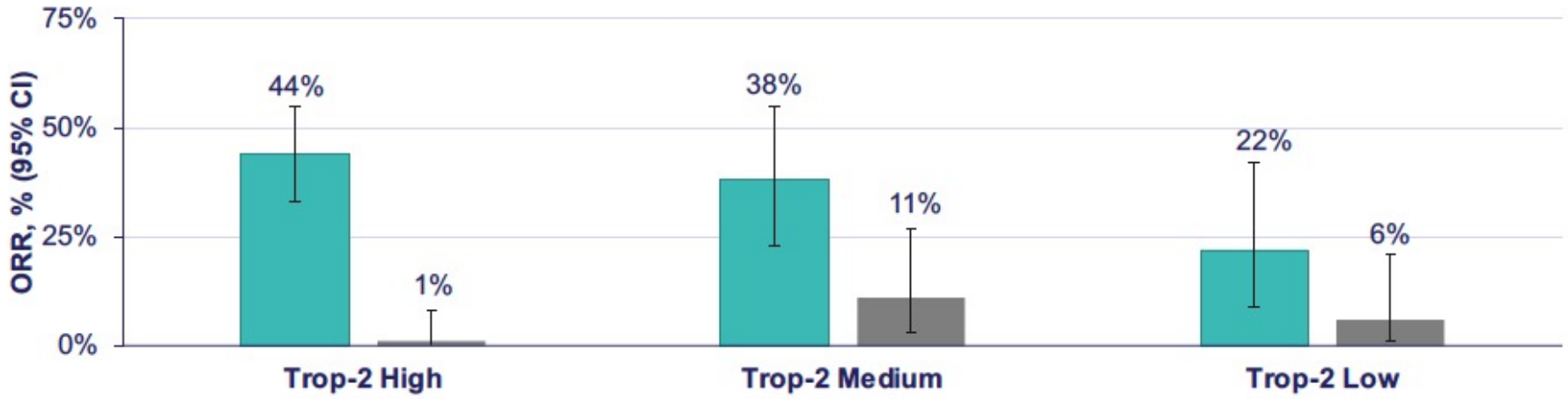
Sara A. Hurvitz,[1] Sara M. Tolaney,[2] Kevin Punie,[3] Delphine Loirat,[4] Mafalda Oliveira,[5] Kevin Kalinsky,[6] Amelia Zelnak,[7] Philippe Aftimos,[8] Florence Dalenc,[9] Sagar Sardesai,[10] Erika Hamilton,[11] Priyanka Sharma,[12] Sabela Recalde,[13] Eva Ciruelos Gil,[14] Tiffany Traina,[15] Joyce 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

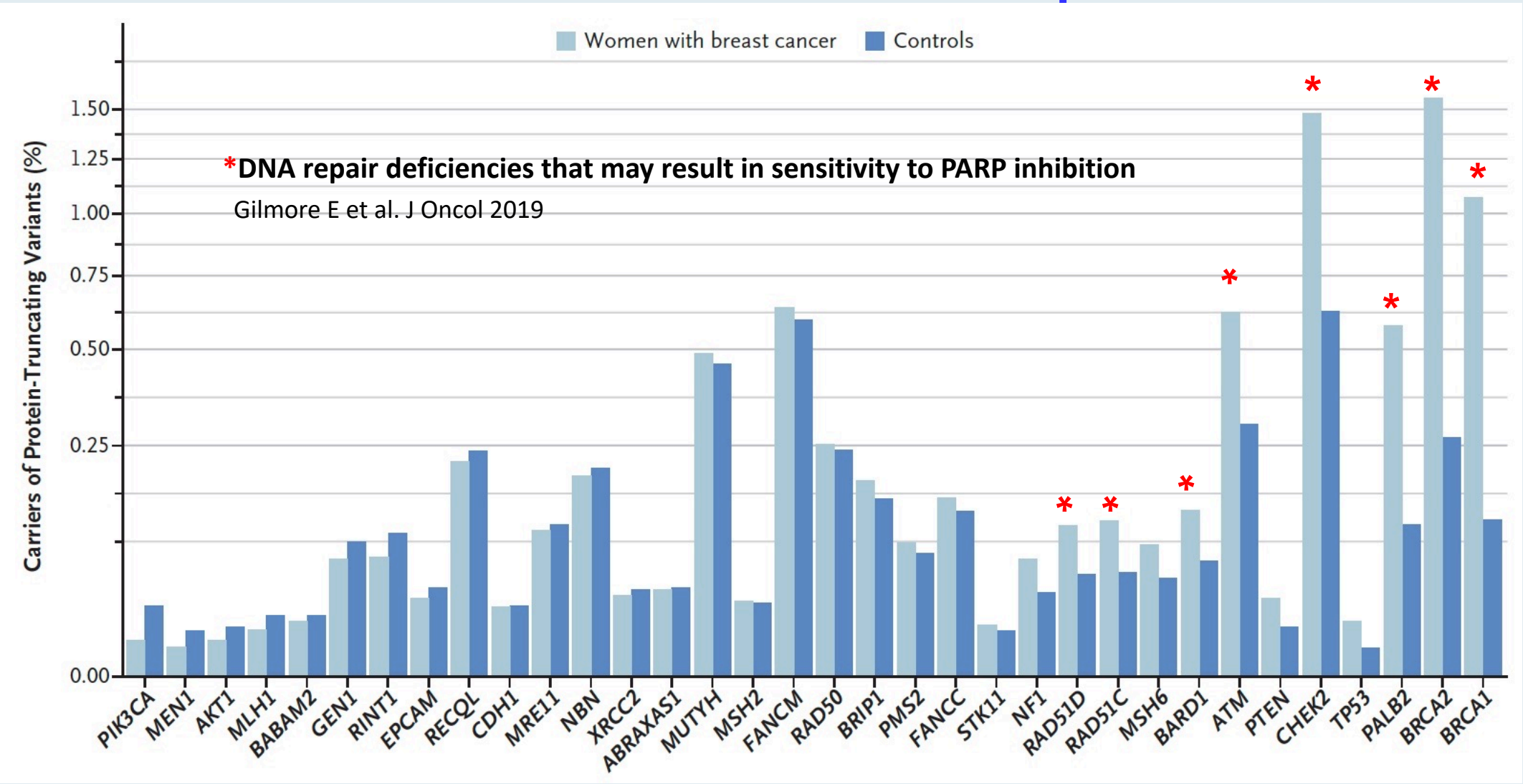


	Trop-2 High H-score: 200-300 (n=157)		Trop-2 Medium H-score: 100-200 (n=74)		Trop-2 Low H-score: <100 (n=59)	
	SG (n=85)	TPC (n=72)	SG (n=39)	TPC (n=35)	SG (n=27)	TPC (n=32)
ORR—% (no.)	44% (37)	1% (1)	38% (15)	11% (4)	22% (6)	6% (2)
95% CI	33-55	0-8	23-55	3-27	9-42	1-21

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.

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

Neeraj Agarwal, MD
Tanios Bekaii-Saab, MD
Kristen K Ciombor, MD, MSCI
Brad S Kahl, MD
Mark Levis, MD, PhD
Ann Partridge, MD, MPH
Mark D Pegram, MD
Daniel P Petrylak, MD
Noopur Raje, MD
David Sallman, MD
Lecia V Sequist, MD, MPH
David R Spigel, MD
Saad Zafar Usmani, MD, MBA
Andrew D Zelenetz, MD, 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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