# *Meet The Professor*

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

**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

# Commercial Support

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

# Dr Love — Disclosures

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# Dr Hurvitz — Disclosures

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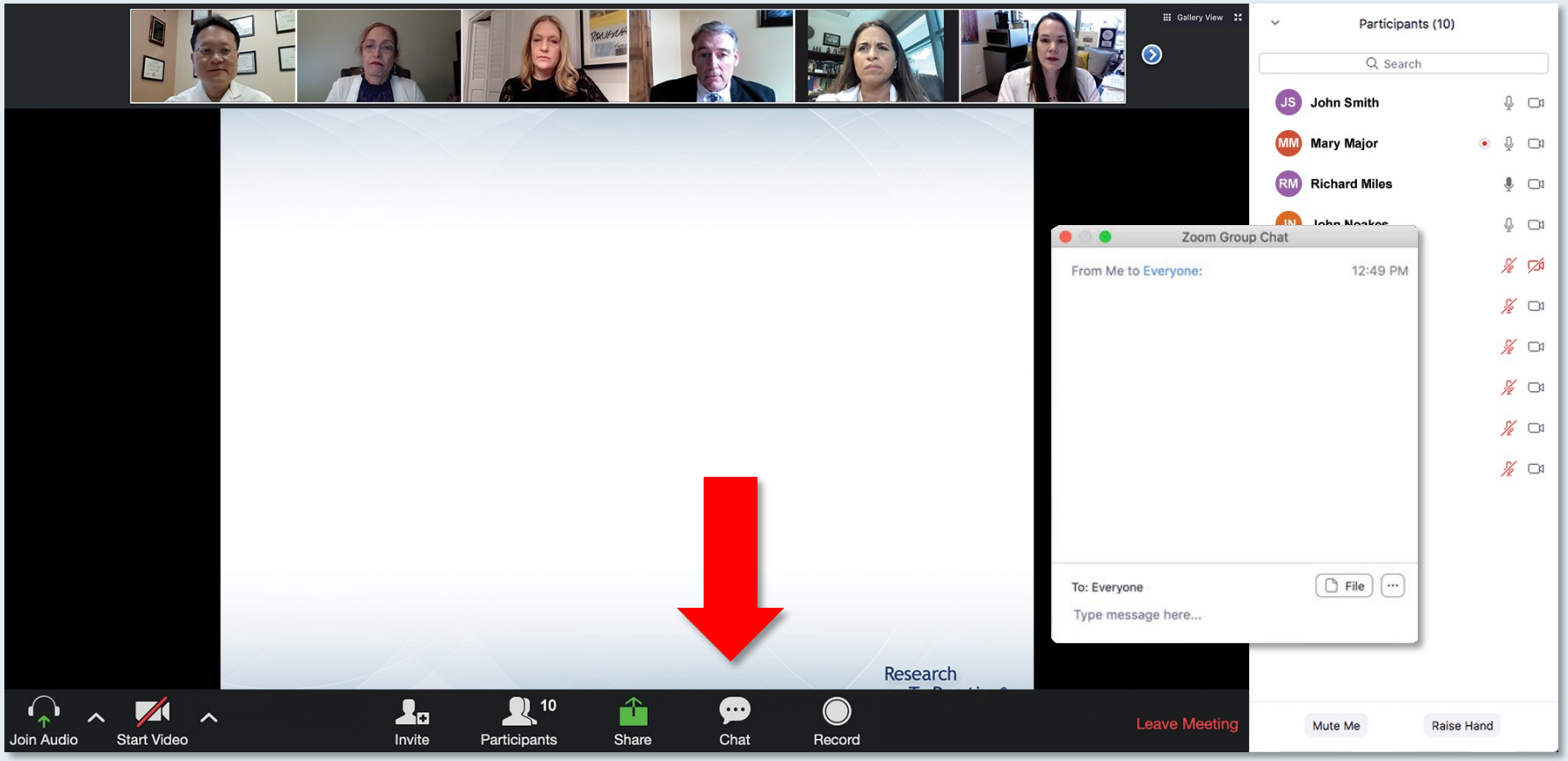
# We Encourage Clinicians in Practice to Submit Questions




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

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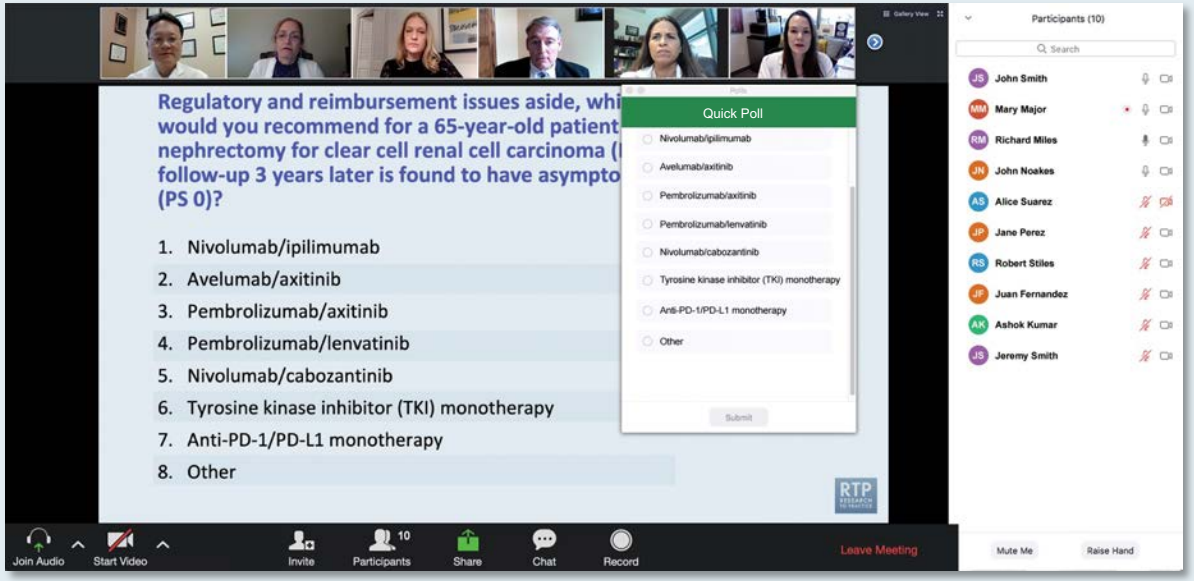
# Familiarizing Yourself with the Zoom Interface

## How to answer survey or poll questions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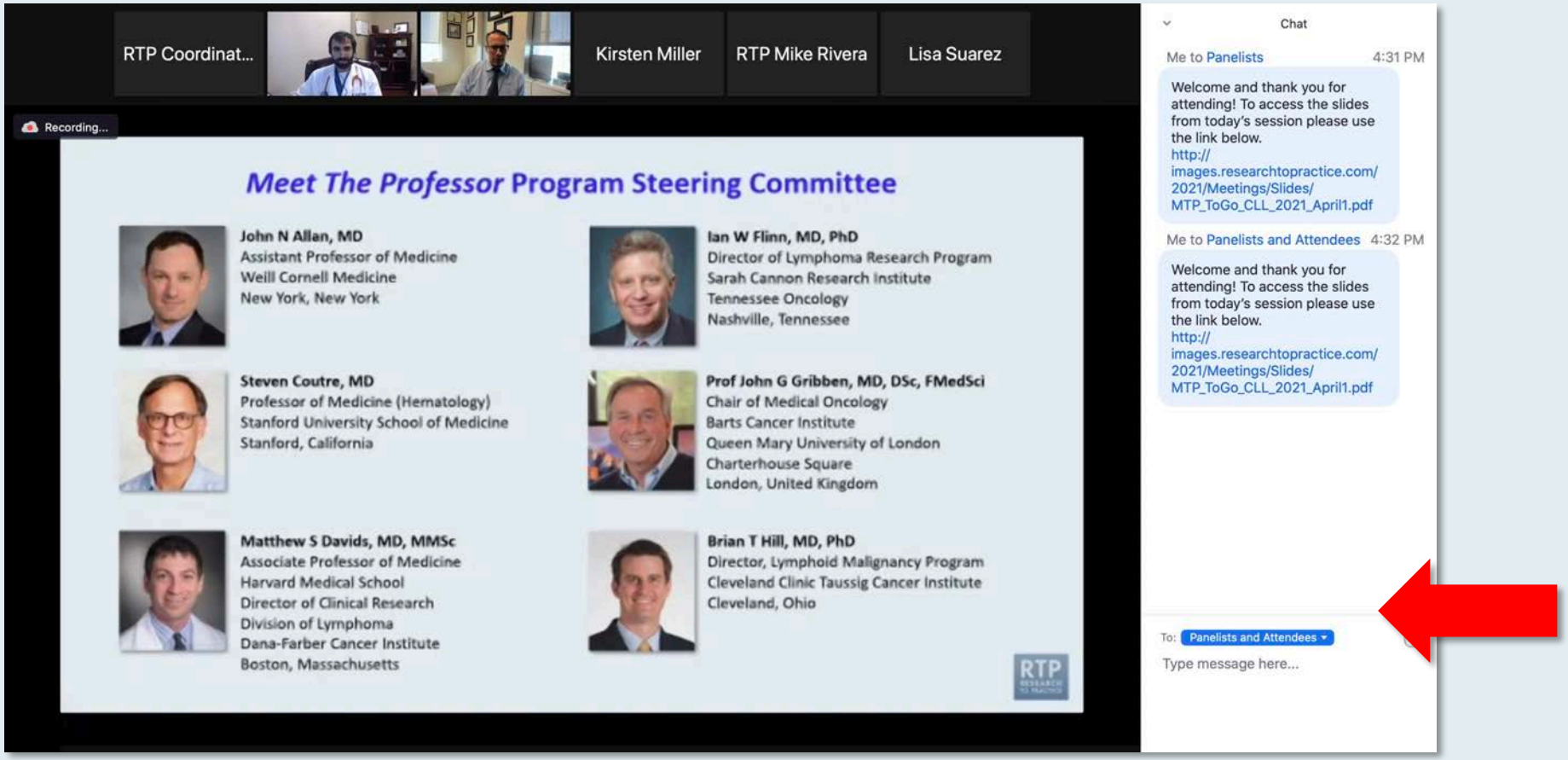


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RTP RESEARCH TO PRACTICE

# Familiarizing Yourself with the Zoom Interface

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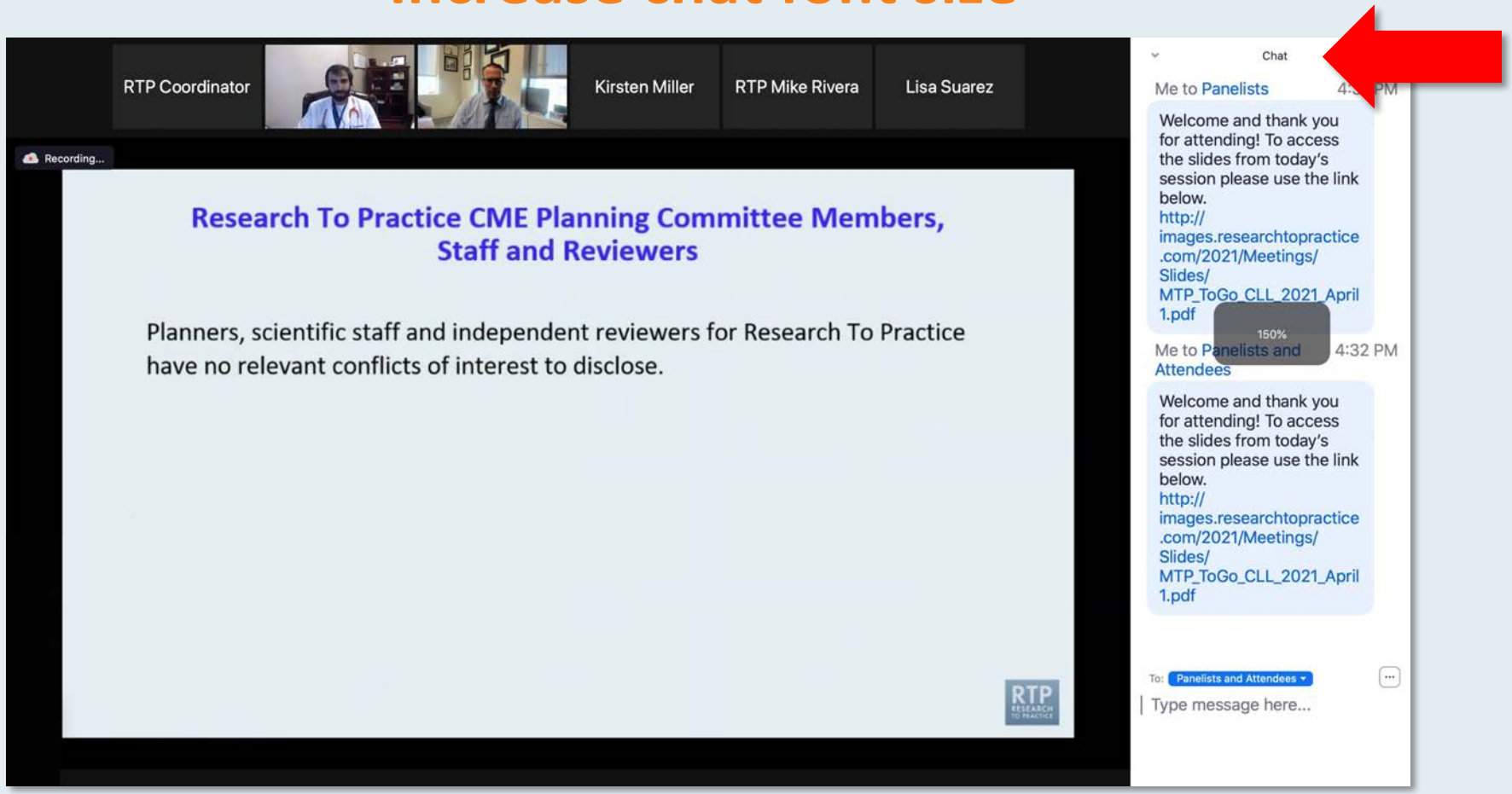


**Press Command (for Mac) or Control (for PC) and the + symbol.**
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# Key Presentations on Breast Cancer from the 2021 ASCO Annual Meeting

DR SARA TOLANEY

DANA-FARBER CANCER INSTITUTE

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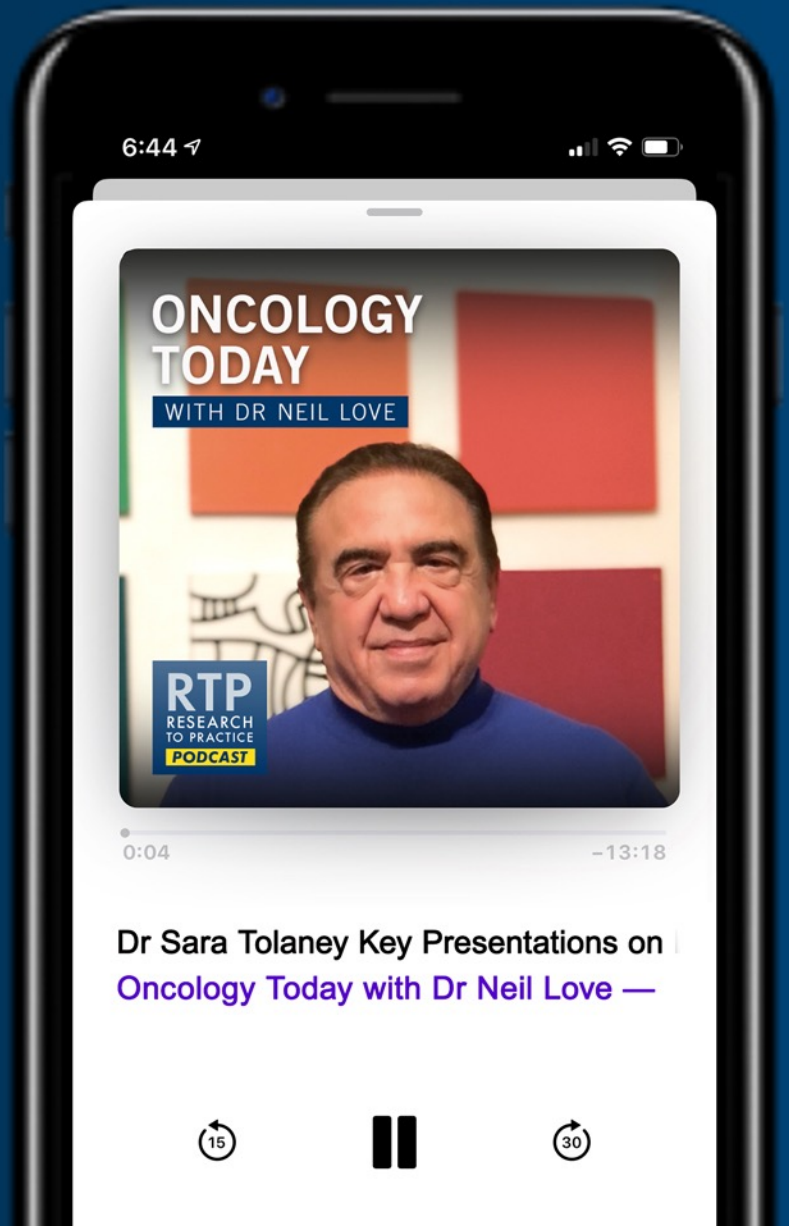

# *Meet The Professor*

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

**Wednesday, August 25, 2021**
**5:00 PM – 6:00 PM ET**

## Faculty

**Wells A Messersmith, MD**

## Moderator

**Neil Love, MD**

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# Summer Oncology Nursing Series

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**Kimberly A Spickes, MNSc, RN, APRN, OCN, ACNP-BC**

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# Data + Perspectives: Clinical Investigators Discuss the Current and Future Management of Chronic Lymphocytic Leukemia

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**Monday, August 30, 2021**
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**Mitchell R Smith, MD, PhD**
**Philip A Thompson, MB, BS**

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**Gilles Salles, MD, PhD**

## Moderator

**Neil Love, MD**

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# *Meet The Professor*

# Immunotherapy and Novel Agents in Gynecologic Cancers

**Wednesday, September 1, 2021**
**5:00 PM – 6:00 PM ET**

## Faculty

**Joyce F Liu, MD, MPH**

## Moderator

**Neil Love, MD**

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**Daniel A Pollyea, MD, MS**
**David Sallman, MD**
**Eunice S Wang, MD**

## Moderator

**Neil Love, MD**

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*Thank you for joining us!*

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

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# *Meet The Professor* 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
The University of Chicago
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

## Moderator

**Neil Love, MD**
Research To Practice
Miami, Florida

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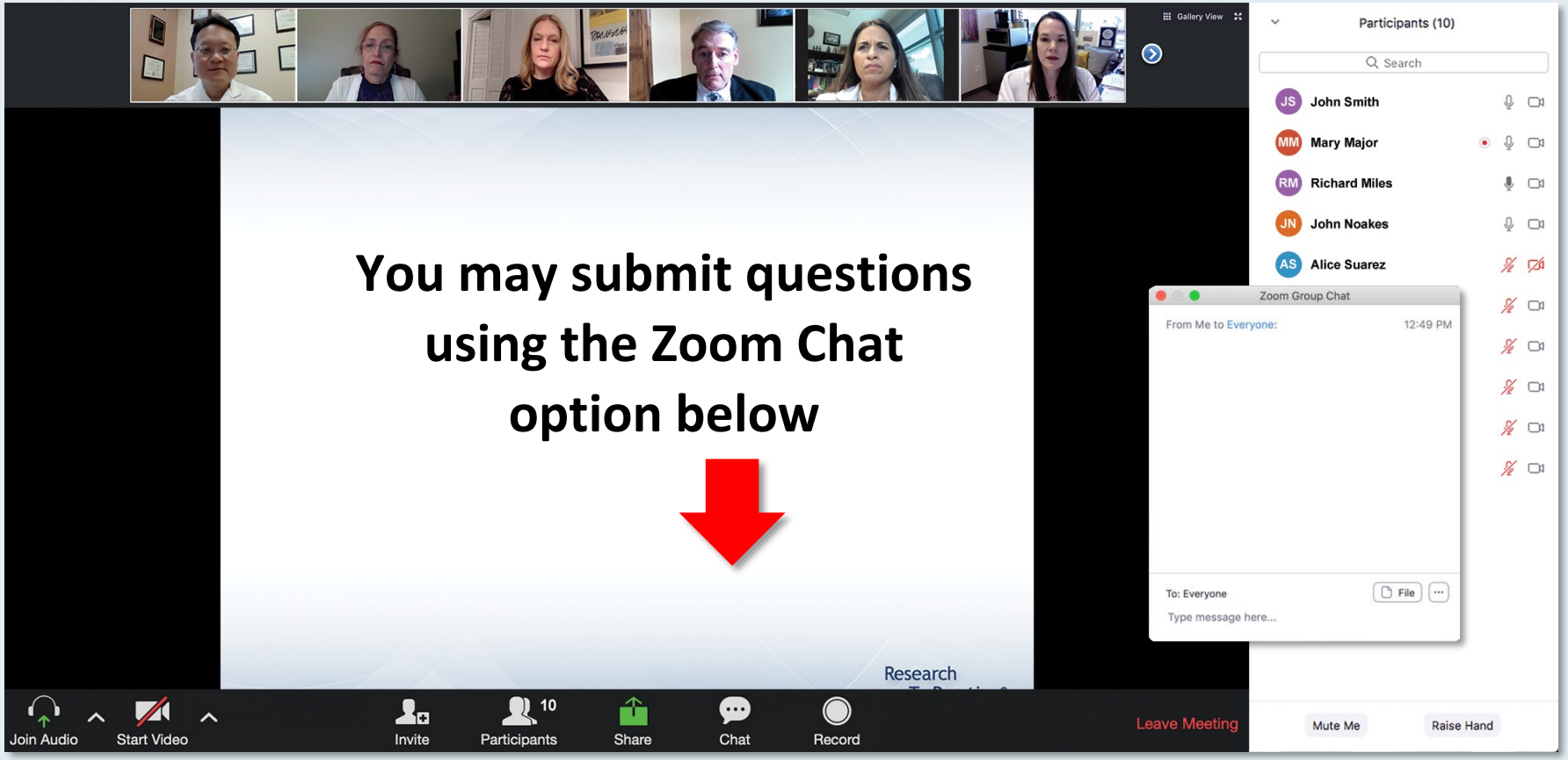


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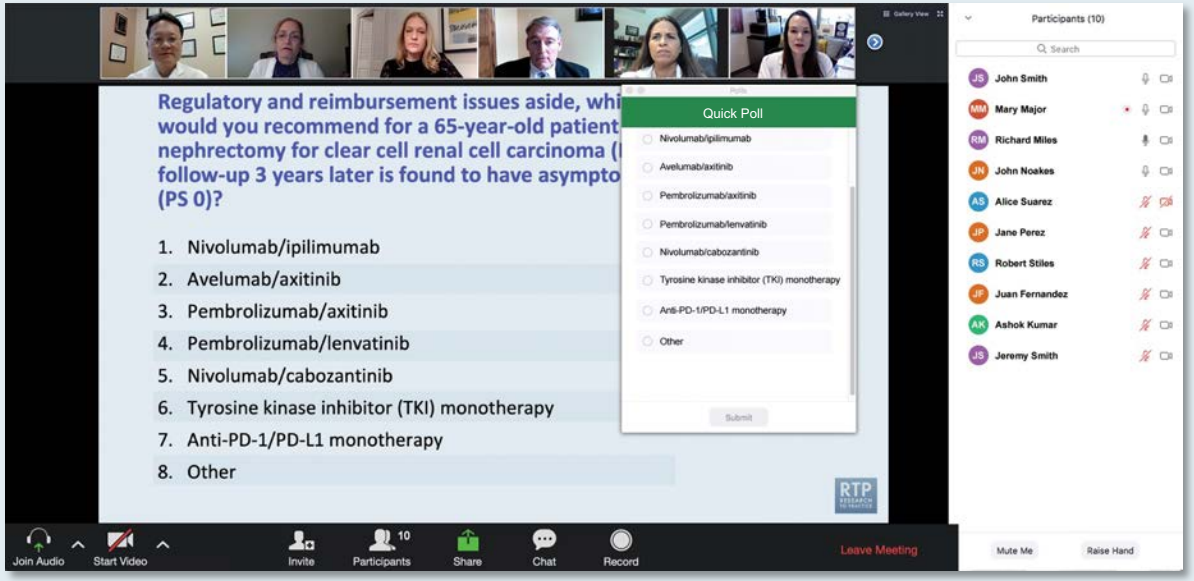


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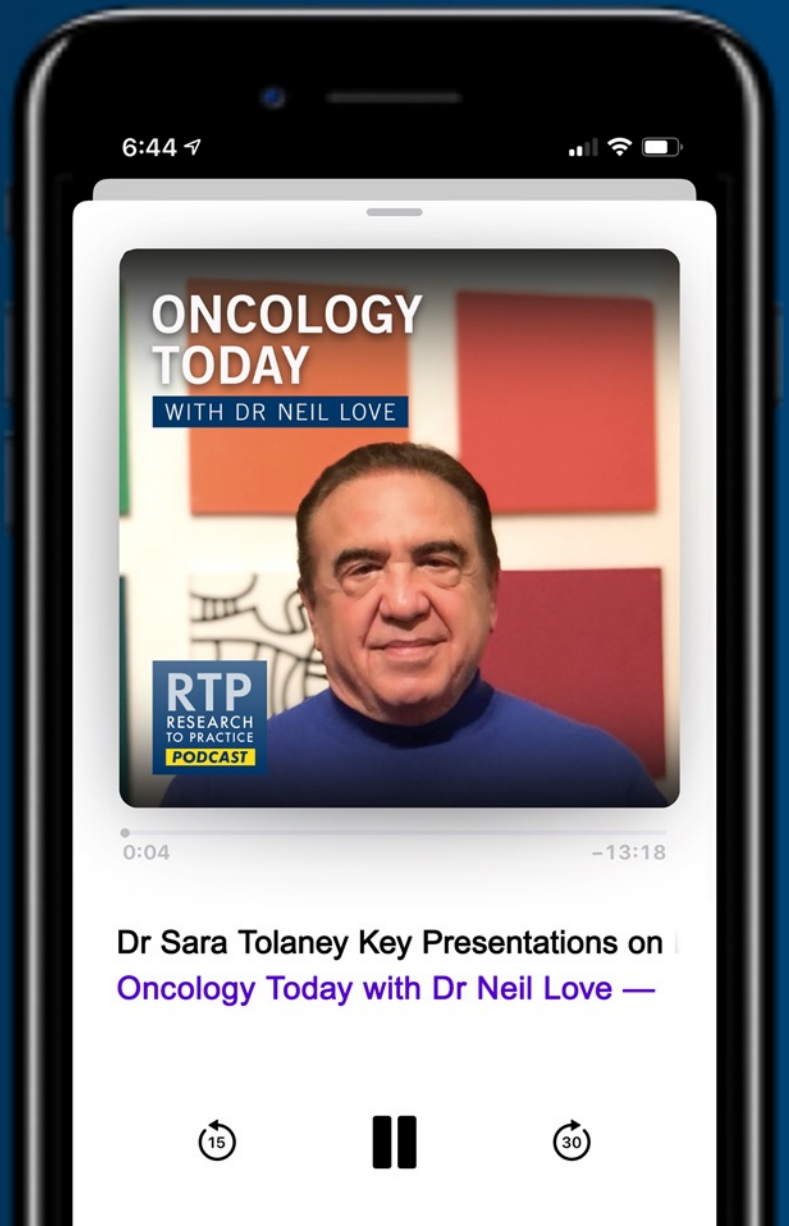

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**Mamta Choksi, MD**
Florida Cancer Specialists and
Research Institute
New Port Richey, Florida

**Ruth O'Regan, MD**
Chair, Department of Medicine
Charles A Dewey Professor of Medicine
University of Rochester
Rochester, New York

**Sulfi Ibrahim, MD**
Hematology/Oncology
Reid Health
Richmond, Indiana

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

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# Meet The Professor with Dr Hurvitz

## MODULE 1: Case Presentation

- Dr Ibrahim: A 41-year-old woman with metastatic triple-negative breast cancer (TNBC)
- Dr Partridge: A 46-year-old woman with oligometastatic TNBC
- Dr O'Regan: A 41-year-old woman with metastatic TNBC and a BRCA2 mutation
- Dr Choksi: A 73-year-old woman with TNBC and suspected bone metastases – MSS, TMB 3 mut/Mb, PD-L1 unknown

## MODULE 2: Beyond the Guidelines

## MODULE 3: Journal Club with Dr Hurvitz

## MODULE 4: Other Key Data Sets

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**A patient with localized triple-negative breast cancer (TNBC) is found to have residual disease after receiving neoadjuvant AC → T. She begins treatment with adjuvant capecitabine and 1 month later is found to have a germline BRCA mutation. Would you offer olaparib?**

1. Yes
2. No

**A patient with localized TNBC is found to have residual disease after neoadjuvant AC → T and receives adjuvant capecitabine. One year after completing adjuvant capecitabine she is found to have a germline BRCA mutation. Would you offer olaparib?**

1. Yes
2. No

# Meet The Professor with Dr Hurvitz

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# Case Presentation – Dr Ibrahim: A 41-year-old woman with metastatic TNBC

**Dr Sulfi Ibrahim**

- Neoadjuvant AC, with shrinkage of mass
- Neoadjuvant paclitaxel, with apparent increase in mass → Surgery
- Patient declines adjuvant capecitabine
- Six months later: Widespread liver and bone metastases with jaundice
  - Biopsy of liver: TNBC
  - PD-L1 testing was positive
- Pembrolizumab/gemcitabine/carboplatin

**Questions**

- Among the two immunotherapy-based regimens approved for patients with triple-negative breast cancer, do you have a preference for one versus the other?

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# Case Presentation – Dr Ibrahim: A 41-year-old woman with metastatic TNBC (continued)

Dr Sulfi Ibrahim

- Neoadjuvant AC, with shrinkage of mass
- Neoadjuvant paclitaxel, with apparent increase in mass → Surgery
- Patient declines adjuvant capecitabine
- Six months later: Widespread liver and bone metastases with jaundice
  - Biopsy of liver: TNBC
  - PD-L1 testing was positive
- Pembrolizumab/gemcitabine/carboplatin
  - ***Response x 6 months before PD, with severe back pain***

**Question**

- ***Do patients with liver metastases receive less benefit from immunotherapy?***
- ***What do we know about CD 274 amplification as a marker of response to immunotherapy?***

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# Case Presentation – Dr Ibrahim: A 41-year-old woman with metastatic TNBC (continued)

Dr Sulfi Ibrahim

- Neoadjuvant AC, with shrinkage of mass
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- Patient declines adjuvant capecitabine
- Six months later: Widespread liver and bone metastases with jaundice
  - Biopsy of liver: TNBC
  - PD-L1 testing was positive
- Pembrolizumab/gemcitabine/carboplatin
  - Response x 6 months before PD, with severe back pain
- ***Sacituzumab govitecan***

**Question**

- ***Would you have recommended another treatment beyond sacituzumab govitecan?***

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# Case Presentation – Dr Partridge: A 46-year-old woman with oligometastatic TNBC

**Dr Ann Partridge**

- 9/2015: Diagnosed with right, Stage II triple-negative IDC
- Dose-dense ACT → Lumpectomy, with residual disease < 0.1-cm, Grade III, with no LVI, SLNB-negative
- RT, with near pCR, followed by observation
- 3/2020: Local recurrence in right internal mammary node, medial chest mass
- 4/2020: Docetaxel/carboplatin and tested positive for PD-L1
- 4/2020: Switched to atezolizumab/*nab* paclitaxel/carboplatin x 6
- 10/2020: Thoracotomy, NED, post-operative RT
- 1/2021: Re-started atezolizumab to complete one full year

**Questions**

- If she presented today, would you include an immune checkpoint inhibitor (ICI) in her neoadjuvant therapy? And then if she had a great response to an ICI would you continue it to complete a full course of up to a year?

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# Case Presentation – Dr O'Regan: A 41-year-old woman with metastatic TNBC and a BRCA2 mutation

**Dr Ruth O'Regan**

- Family history positive for ovarian cancer in paternal grandmother and aunt
- 2020: Diagnosed with triple-negative breast cancer → AC-paclitaxel
- BRCA2 mutation identified → Bilateral mastectomies, with residual disease (ypT2 N0)
- Adjuvant capecitabine (WBC: 40,000 last dose of capecitabine)
- Diagnosed with AML → Induction treatment followed by matched, unrelated donor transplant
- Pulmonary nodules consistent with TNBC

**Question**

- How would you manage a patient like this who's received a large amount of chemotherapy previously?

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# Case Presentation – Dr O'Regan: A 41-year-old woman with metastatic TNBC and a BRCA2 mutation (continued)

Dr Ruth O'Regan

- Family history positive for ovarian cancer in paternal grandmother and aunt
- 2020: Diagnosed with triple-negative breast cancer → AC-paclitaxel
- BRCA2 mutation identified → Bilateral mastectomies, with residual disease (ypT2 N0)
- Adjuvant capecitabine (WBC: 40,000 last dose of capecitabine)
- Diagnosed with AML → Induction treatment followed by matched, unrelated donor transplant
- **Pulmonary nodules consistent with TNBC → Olaparib**

**Questions**

- ***In a patient like this if you gave them a PARP inhibitor what would be your choice in the second-line setting? Would you use just standard chemotherapy, or would you use sacituzumab in a patient like this?***

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# Case Presentation – Dr Choksi: A 73-year-old woman with TNBC and suspected bone metastases – MSS, TMB 3 mut/Mb, PD-L1 unknown

Dr Mamta Choksi

- May 2020: Diagnosed with T2N1/2M0 triple negative breast cancer with inflammatory-like characteristics
- August 2020: AC with dose-dense paclitaxel x 4 cycles completed followed by weekly paclitaxel
- November 2020: CEA rising to 17.3 from 11.4 during treatment
- PET CT shows osseous lesions without FDG activity; bone biopsy is negative for malignancy
- December 2020: Last cycle of weekly paclitaxel completed
- Post chemotherapy: CEA rose to 17.4, residual 2 to 2.5-cm palpable lump in left breast; surgery is scheduled

**Questions**

- If she has residual disease based on the final pathology report, what treatment option would you recommend next?
- What do we know about the use of a checkpoint inhibitor with chemotherapy, especially in those challenging patients with a triple-negative inflammatory breast cancer?

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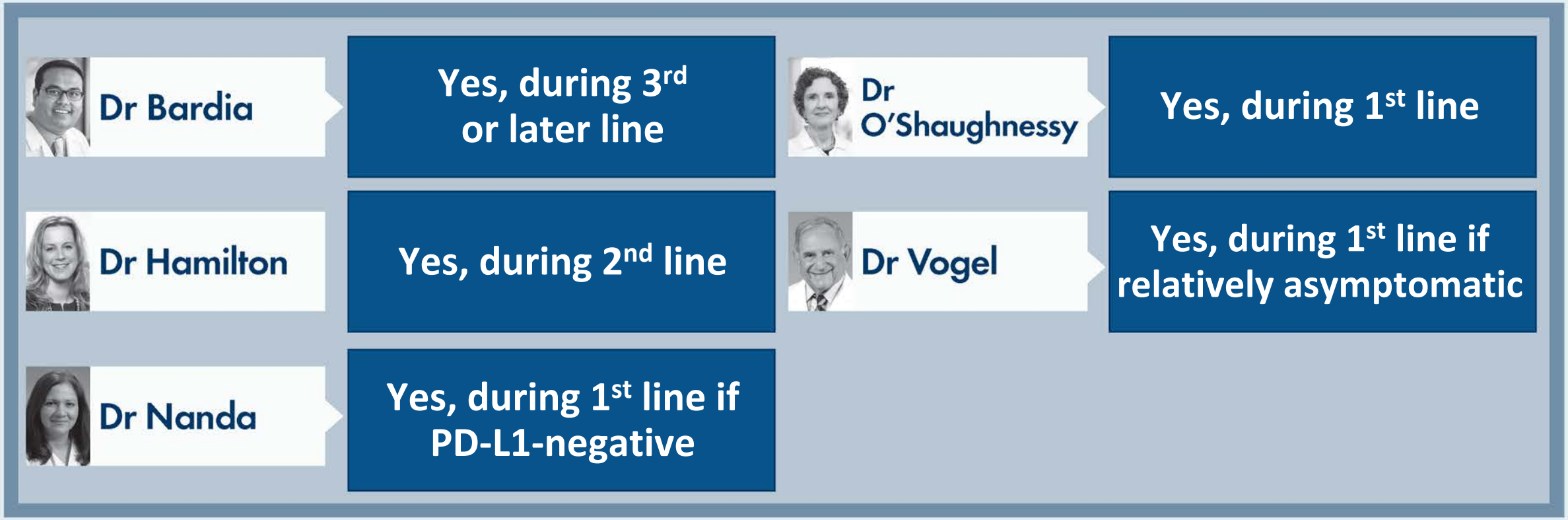
# If a patient with TNBC and a germline BRCA1/2 mutation received olaparib as part of adjuvant therapy on a clinical trial and then developed metastatic disease 3 years later, would you attempt to administer a PARP inhibitor during a subsequent line of treatment?

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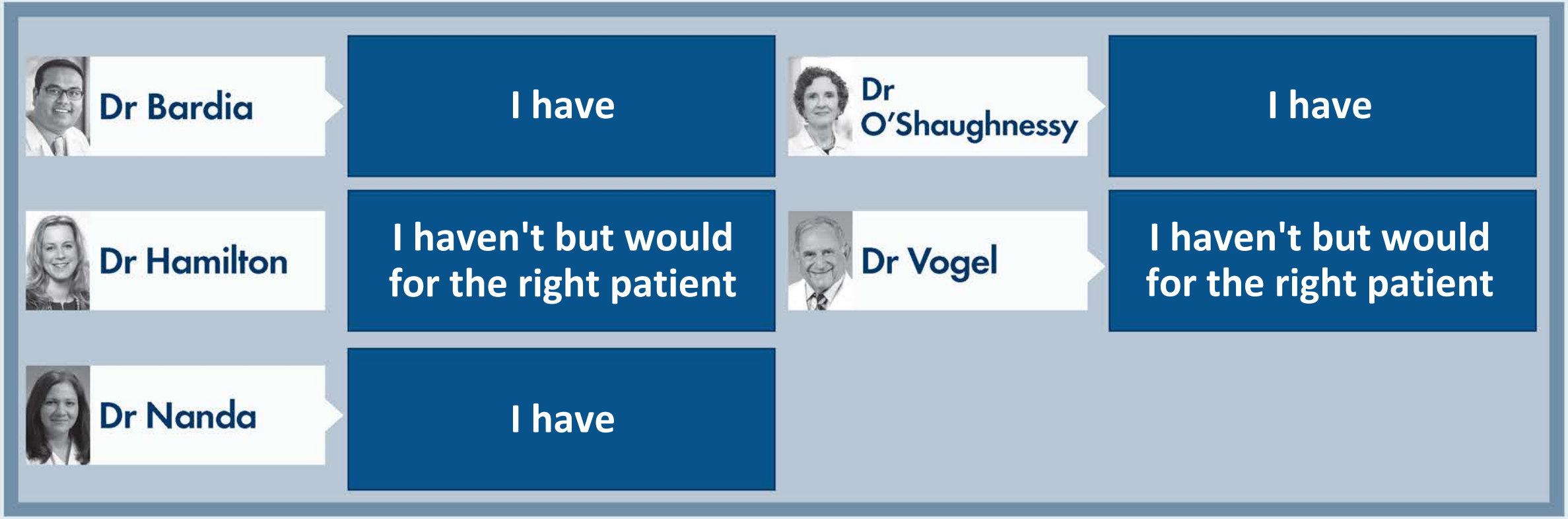
# Regulatory and reimbursement issues aside, have you attempted or would you attempt to access a PARP inhibitor for a patient with metastatic TNBC and a somatic BRCA mutation?

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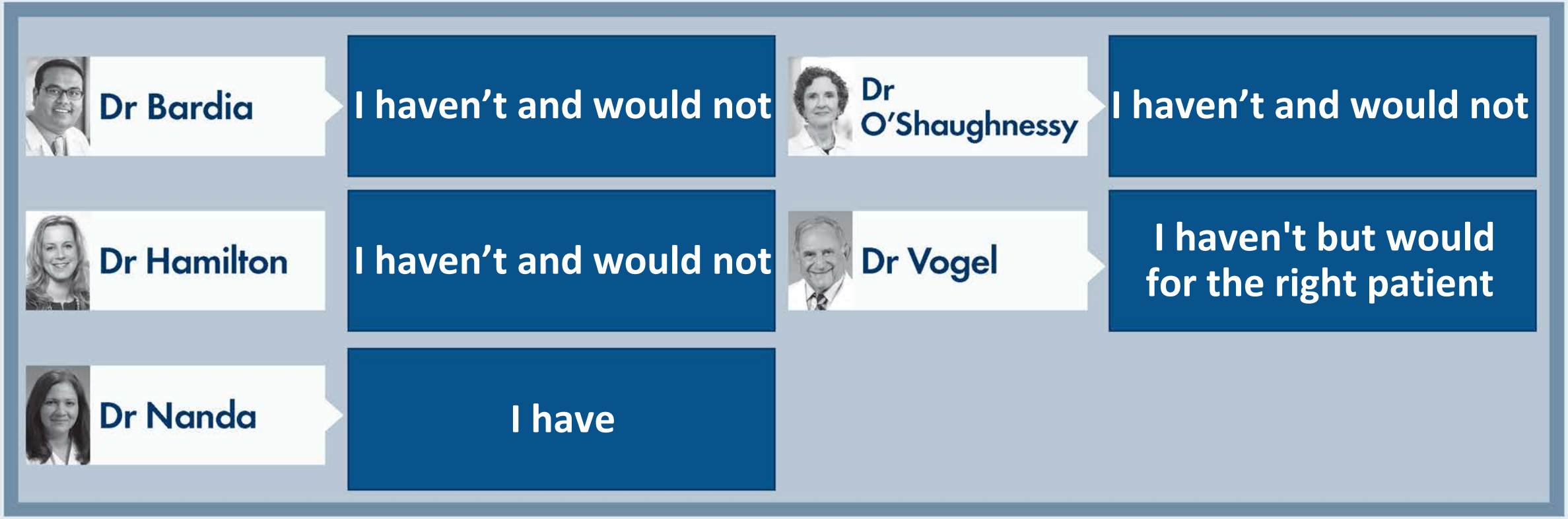
# Regulatory and reimbursement issues aside, have you attempted or would you attempt to access a PARP inhibitor for a patient with metastatic TNBC and a germline ATM mutation?

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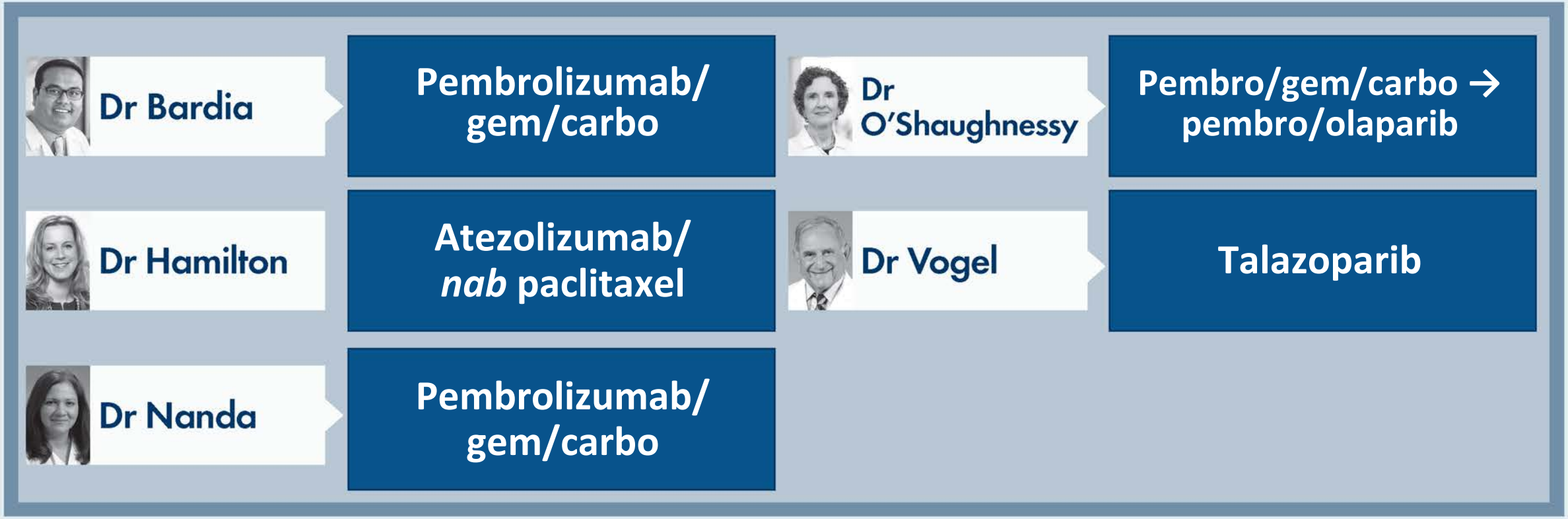
# What would be your preferred treatment approach for a 60-year-old patient with a BRCA germline mutation and de novo metastatic TNBC that is PD-L1-positive?

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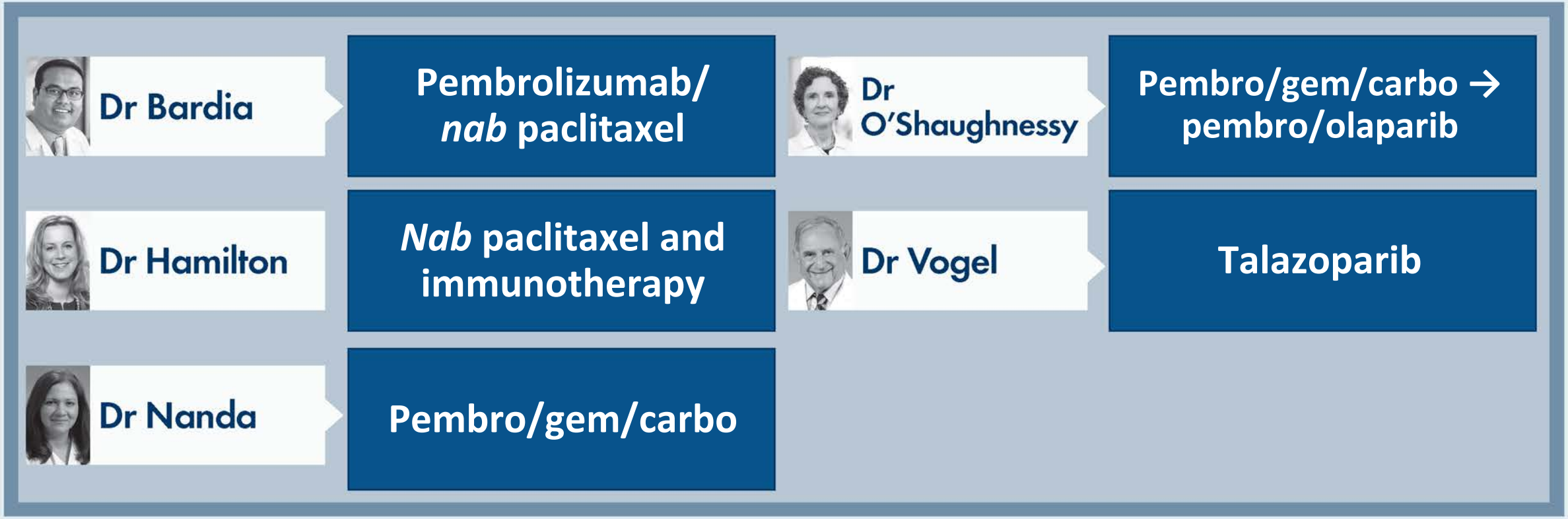
**A 60-year-old woman with TNBC and a germline BRCA1 mutation (PD-L1 CPS >10) receives neoadjuvant carboplatin/paclitaxel/pembrolizumab → AC/ pembrolizumab and achieves a pathologic complete response. Three years after completion of adjuvant pembrolizumab, she develops metastatic TNBC (PD-L1 CPS >10).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




Gem = gemcitabine; carbo = carboplatin

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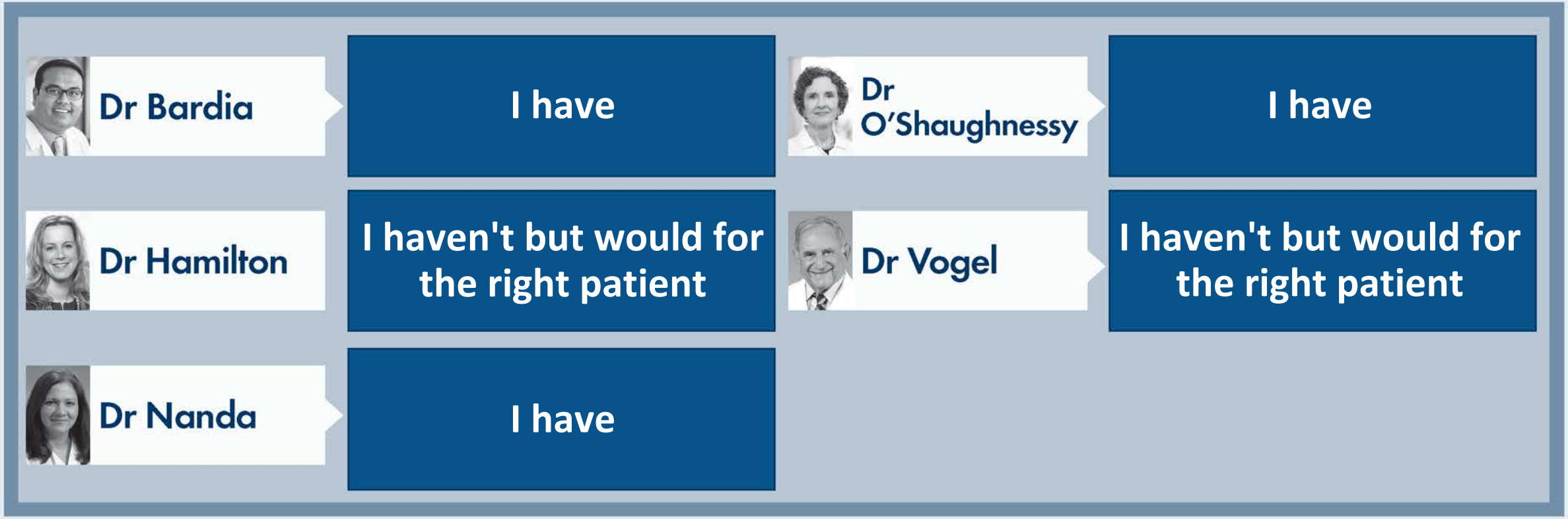
# Regulatory and reimbursement issues aside, have you attempted or would you attempt to access olaparib as part of neoadjuvant therapy for a 45-year-old patient with a germline BRCA2 mutation and a 6-cm TNBC with negative axillary nodes on biopsy (PD-L1 10%)?

| | | | |
|---|---|---|---|
|  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

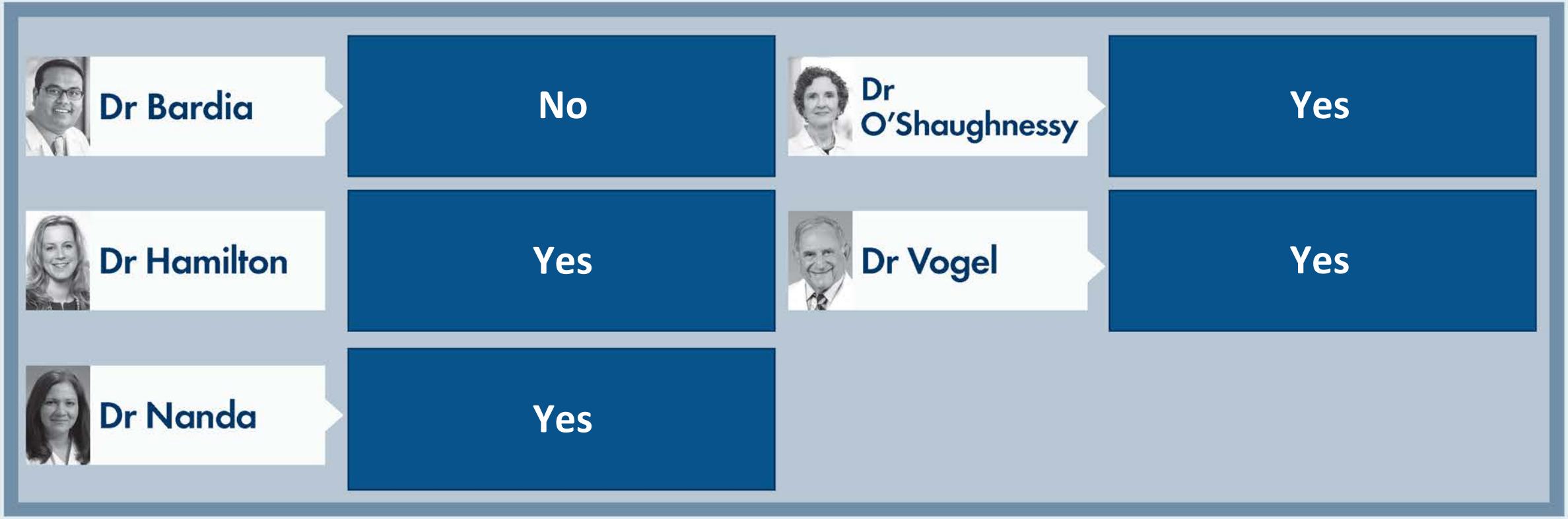
Dr Nanda

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

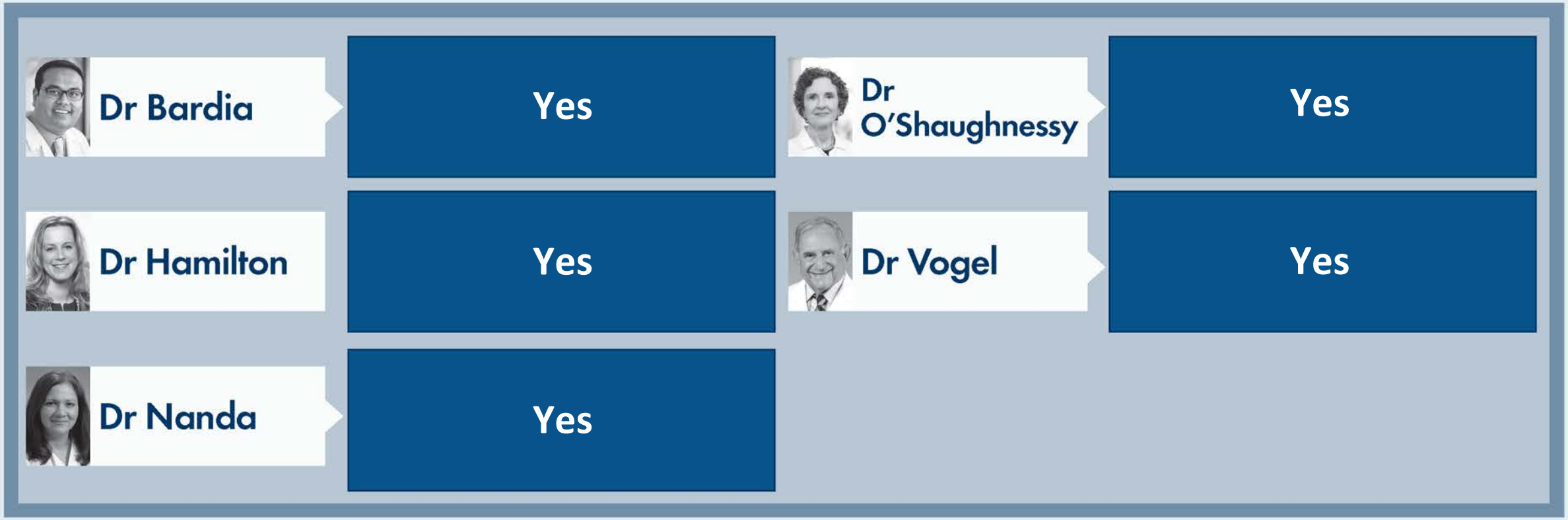
# For a patient with localized TNBC and PD-L1 CPS ≥1, would you generally recommend neoadjuvant chemotherapy/ pembrolizumab → adjuvant pembrolizumab if they had…

## 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?



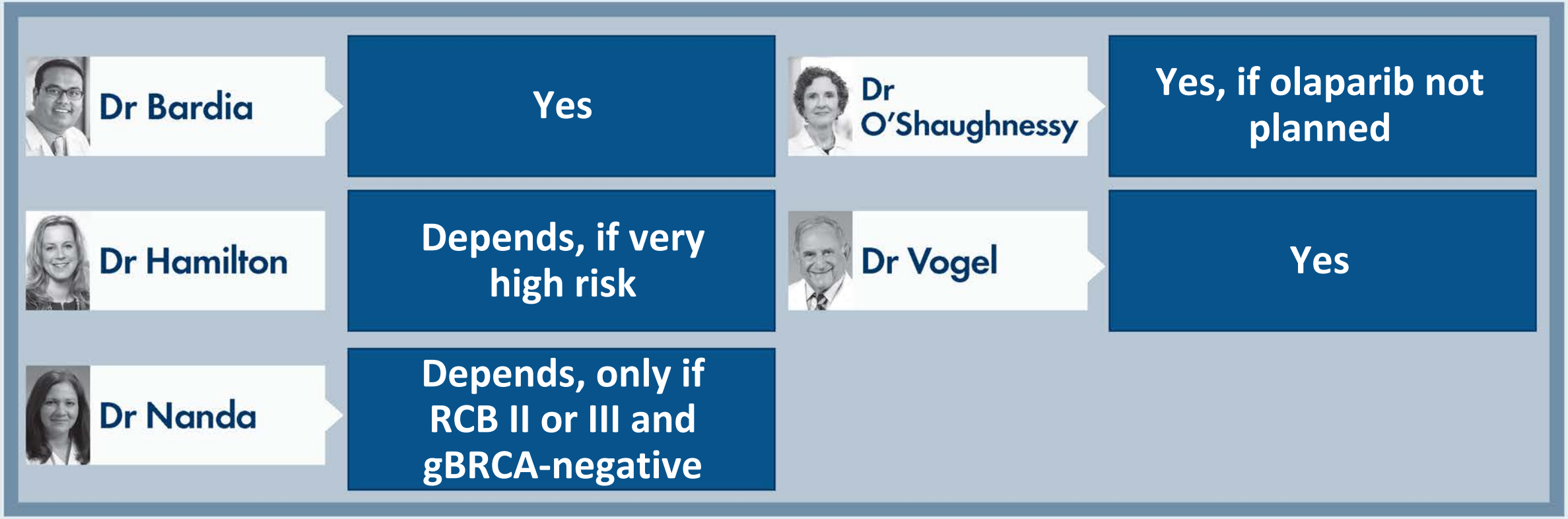

RTP RESEARCH TO PRACTICE

# 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 Hurvitz

## MODULE 1: Case Presentation

- Dr Ibrahim: A 41-year-old woman with metastatic triple-negative breast cancer (TNBC)
- Dr Partridge: A 46-year-old woman with oligometastatic TNBC
- Dr O'Regan: A 41-year-old woman with metastatic TNBC and a BRCA2 mutation
- Dr Choksi: A 73-year-old woman with TNBC and suspected bone metastases – MSS, TMB 3 mut/Mb, PD-L1 unknown

## MODULE 2: Beyond the Guidelines

## MODULE 3: Journal Club with Dr Hurvitz

## MODULE 4: Other Key Data Sets

RTP
RESEARCH
TO PRACTICE

# Journal Club with Dr Hurvitz

- ASCENT: Sacituzumab govitecan for metastatic triple-negative breast cancer (TNBC)
- ASCENT: Outcomes in patients aged ≥65 years
- ASCENT: Assessment of sacituzumab govitecan
- EMBRACA: Characterization of long-term responders after treatment with talazoparib
- EMBRACA: Safety analyses with talazoparib
- EMBRACA: Exploring the impact on efficacy of mutations in non-BRCA DNA damage response (DDR) and non-DDR genes
- EMBRACA: Clinical outcomes in patients with a history of CNS metastases receiving talazoparib
- Innovations in targeted therapy for TNBC
- Do all patients with cancer experience fatigue?
- Oncology team perception and patient experience discordances in TNBC care

*N Engl J Med* 2021;384(16):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*

# 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.

# Assessment of Sacituzumab Govitecan (SG) versus Treatment of Physician's Choice (TPC) Cohort by Agent in the Phase 3 ASCENT Study of Patients (pts) with Metastatic Triple-Negative Breast Cancer (mTNBC)

O'Shaughnessy J et al.

ASCO 2021;Abstract 1077.

# Characterization of Long-Term Responders Following Treatment with Talazoparib (TALA) or Physician's Choice of Chemotherapy (PCT) in the Phase 3 Embraca Trial

Etti J et al.

ASCO 2021;Abstract 1029.

*Oncologist* 2020;25(3):e439-50

The Oncologist®

Breast Cancer

# Talazoparib in Patients with a Germline *BRCA*-Mutated Advanced Breast Cancer: Detailed Safety Analyses from the Phase III EMBRACA Trial

Sara A. Hurvitz,[a] Anthony Gonçalves,[b] Hope S. Rugo,[c] Kyung-Hun Lee,[d] Louis Fehrenbacher,[e] Lida A. Mina,[f] Sami Diab,[g] Joanne L. Blum,[h] Jayeta Chakrabarti,[i] Mohamed Elmeliegy,[j] Liza DeAnnuntis,[k] Eric Gauthier,[l] Akos Czibere,[m] Iulia Cristina Tudor,[l] Ruben G.W. Quek,[l] Jennifer K. Litton,[n] Johannes Ettl[o]

[a]University of California, Los Angeles, Los Angeles, California, USA; [b]Institut Paoli-Calmettes, Marseille, France; [c]UCSF Helen Diller Family Comprehensive Cancer Center, San Francisco, California, USA; [d]Seoul National University Hospital, Seoul, South Korea; [e]Kaiser Permanente, Northern California, Vallejo, California, USA; [f]MD Anderson Cancer Center, Gilbert, Arizona, USA; [g]Rocky Mountain Cancer Centers, Littleton, Colorado, USA; [h]Baylor Sammons Cancer Center, Texas Oncology, U.S. Oncology, Dallas, Texas, USA; [i]Pfizer Ltd, Surrey, United Kingdom; [j]Pfizer, Inc., La Jolla, California, USA; [k]Pfizer Inc., Collegeville, Pennsylvania, USA; [l]Pfizer Inc., San Francisco, California, USA; [m]Pfizer Inc., Cambridge, Massachusetts, USA; [n]The University of Texas MD Anderson Cancer Center, Houston, Texas, USA; [o]Department of Obstetrics and Gynecology, Klinikum rechts der Isar, Technische Universität München, Munich, Germany

*Disclosures of potential conflicts of interest may be found at the end of this article.*

**Key Words.** *BRCA1* • *BRCA2* • Breast cancer • Talazoparib • Chemotherapy

# Exploring Impact of Mutations in Non-BRCA DNA Damage Response (DDR) and Non-DDR Genes on Efficacy in Phase III EMBRACA Study of Talazoparib (TALA) in Patients (pts) with Germline BRCA1/2 Mutated (gBRCAm) HER2-Negative (HER2-) Advanced Breast Cancer (ABC)

Litton JK et al.

ASCO 2020;Abstract 1018.

# Clinical Outcomes in Patients (pts) with a History of Central Nervous System (CNS) Metastases Receiving Talazoparib (TALA) or Physician's Choice of Chemotherapy (PCT) in the Phase 3 EMBRACA Trial

Litton JK et al.

ASCO 2021;Abstract 1090.

REVIEW

*Curr Opin Obstet Gynecol* 2021;33(1):34-47


# Innovations in targeted therapies for triple negative breast cancer

*Kelly E. McCann and Sara A. Hurvitz*

*Cancer* 2021;127(8):1334-44

Original Article

# Do All Patients With Cancer Experience Fatigue? A Longitudinal Study of Fatigue Trajectories in Women With Breast Cancer

Julienne E. Bower, PhD [1,2,3,4]; Patricia A. Ganz, MD [4,5,6]; Michael R. Irwin, MD[2,3]; Steve W. Cole, PhD[2,3,7]; Deborah Garet, MPH[3]; Laura Petersen, MS[4]; Arash Asher, MD[8]; Sara A. Hurvitz, MD[4,7]; and Catherine M. Crespi, PhD[4,9]

# Oncology Team Perception and Patient Experience Discordances in Triple-Negative Breast Cancer (TNBC) Care

Hurvitz SA et al.

ASCO 2021;Abstract e19176.

# Meet The Professor with Dr Hurvitz

## MODULE 1: Case Presentation

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## MODULE 2: Beyond the Guidelines

## MODULE 3: Journal Club with Dr Hurvitz

## MODULE 4: Other Key Data Sets

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

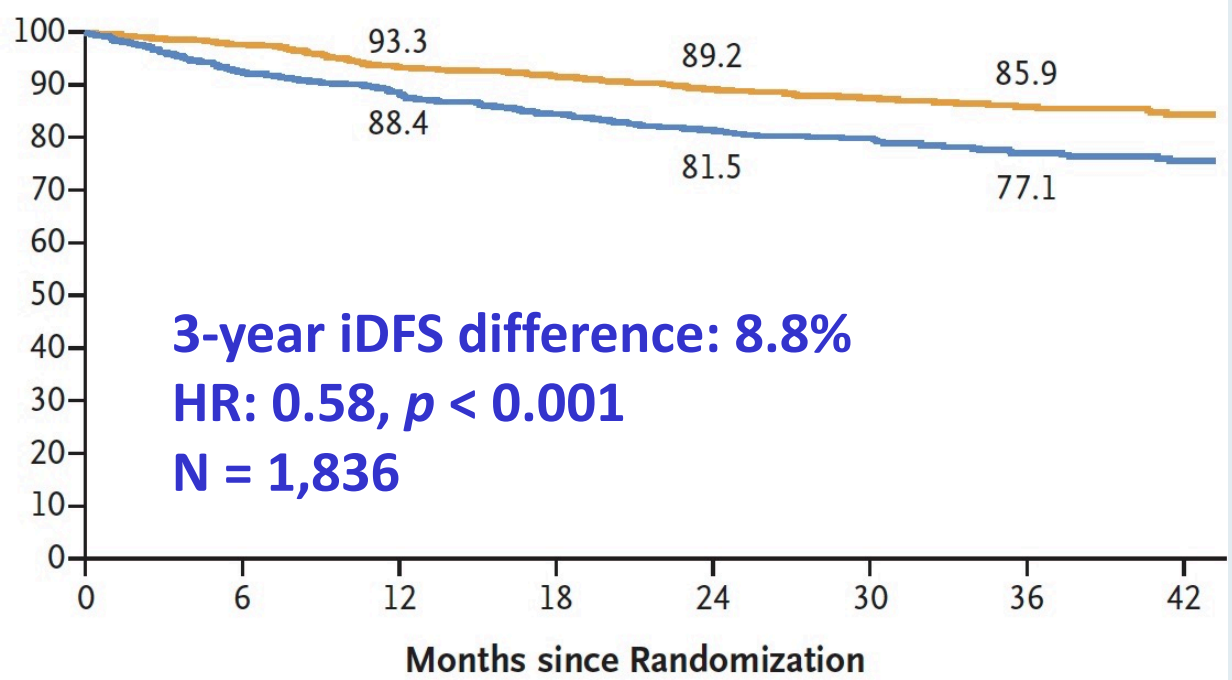
ORIGINAL ARTICLE

# 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*

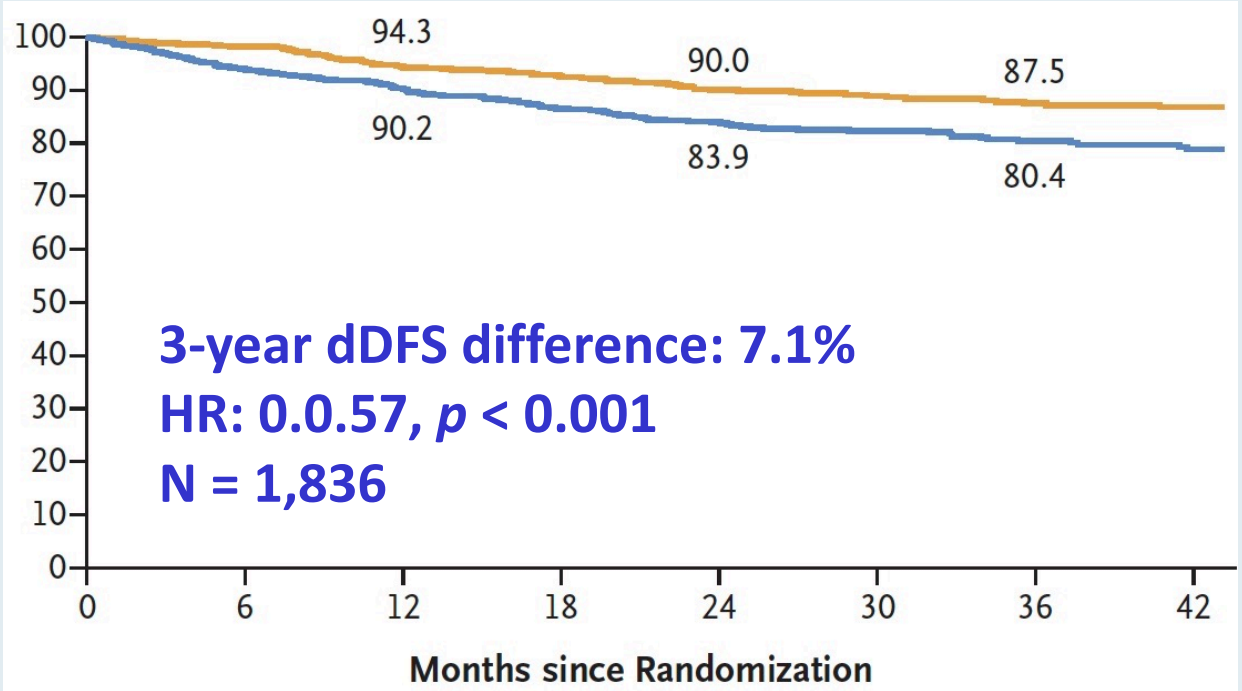
# OlympiA: Invasive and Distant Disease-Free Survival

## Invasive DFS




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

## Distant DFS



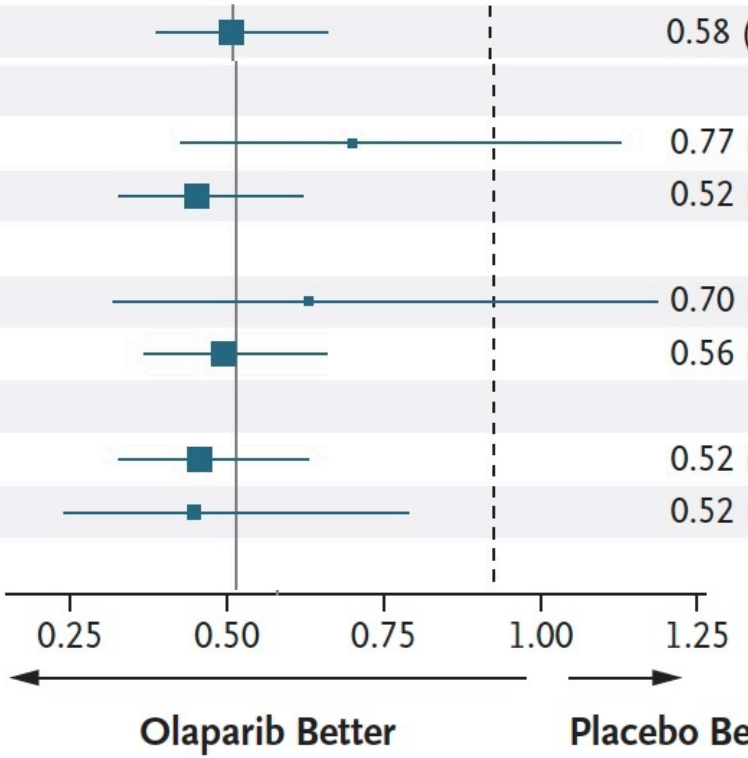

**3-year dDFS difference: 7.1%**
**HR: 0.0.57, $p < 0.001$**
**N = 1,836**

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

RTP RESEARCH TO PRACTICE

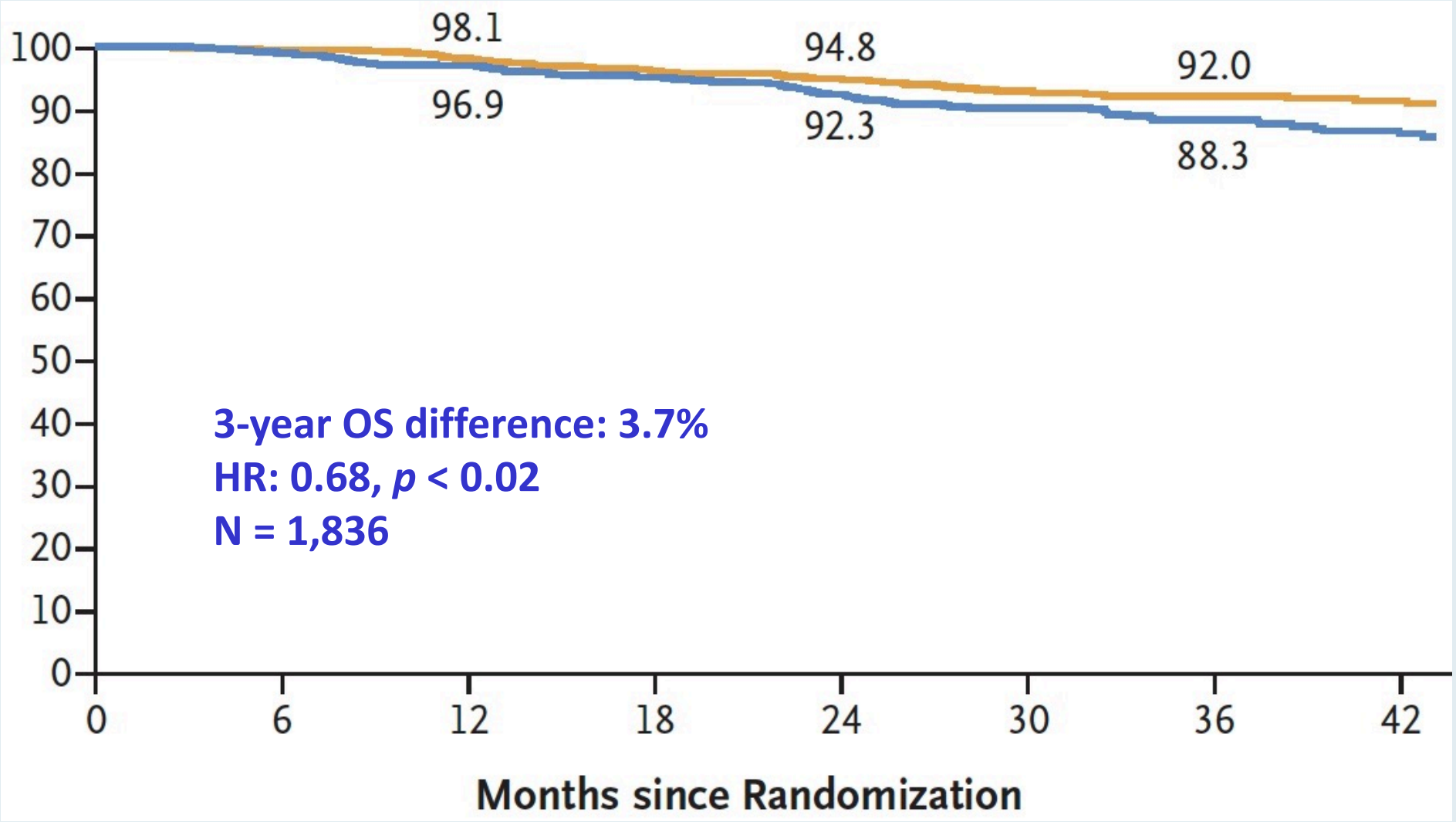
# OlympiA: 3-Year Invasive DFS

| 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

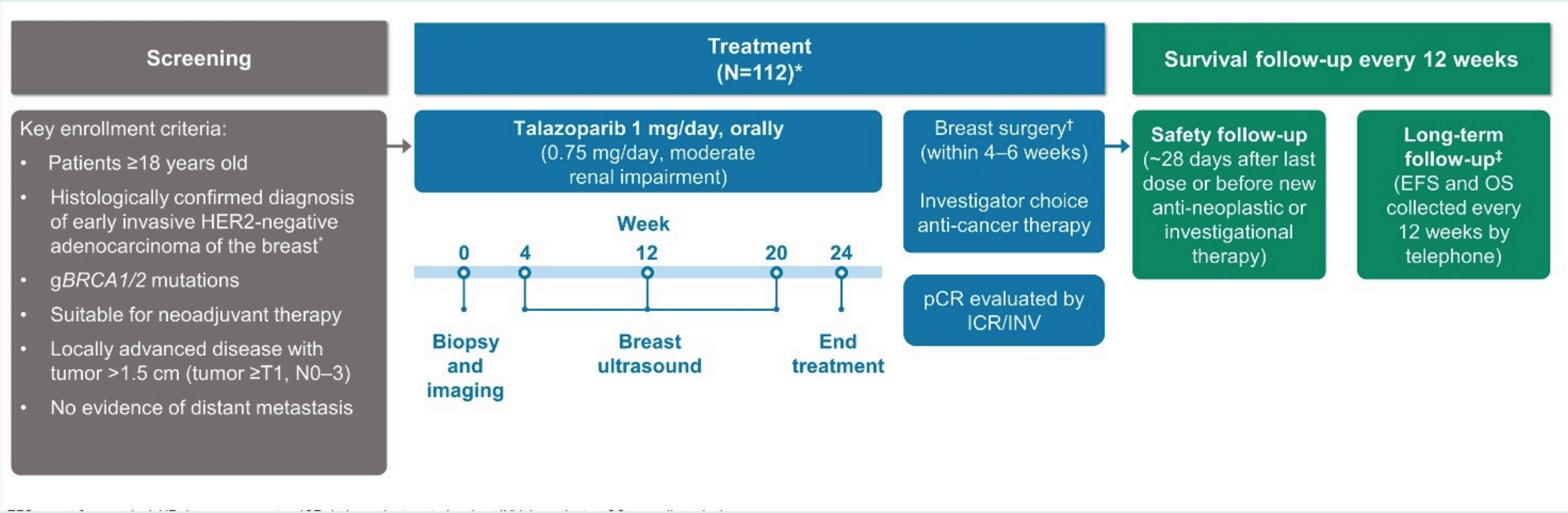
# NEOADJUVANT TALAZOPARIB IN PATIENTS WITH GERMLINE *BRCA1/2* MUTATION-POSITIVE, EARLY HER2-NEGATIVE BREAST CANCER: RESULTS OF A PHASE 2 STUDY

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

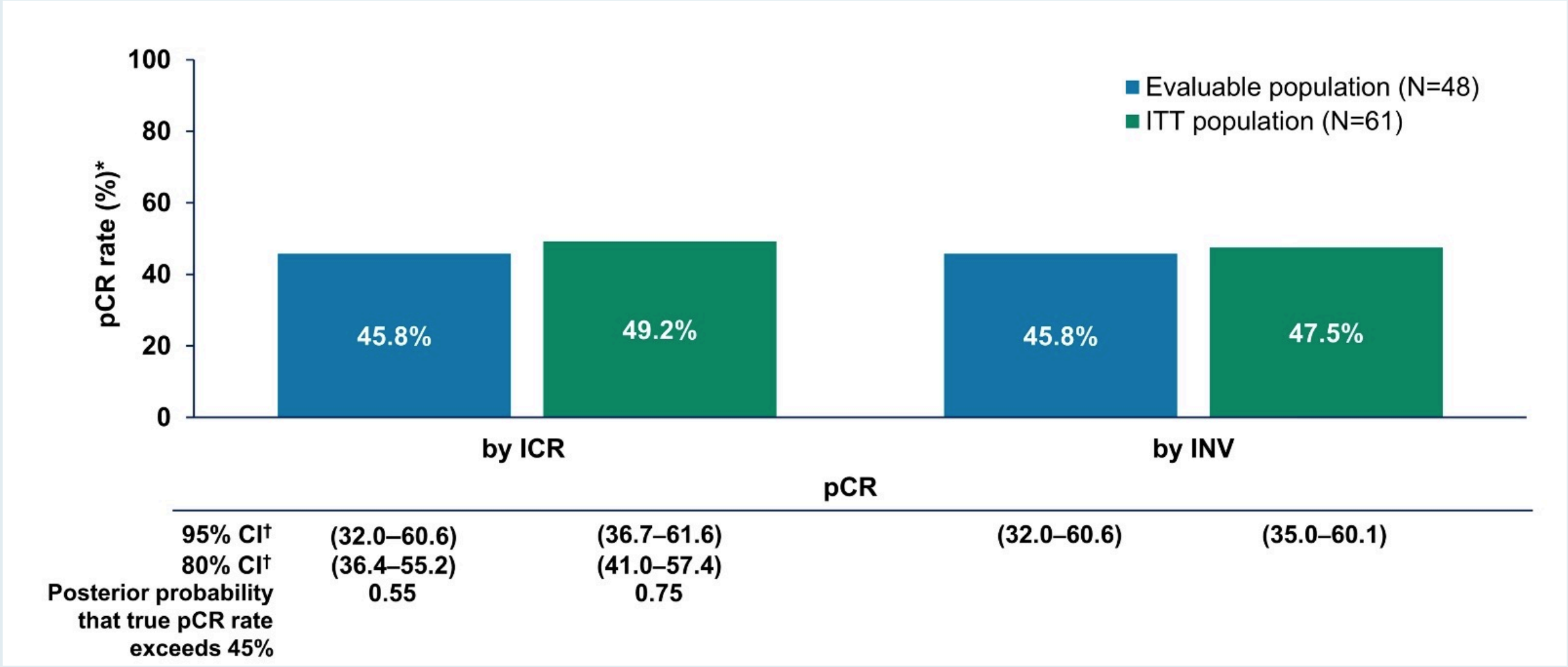
June 6, 2021

# NEOTALA: Multicenter Phase II Study Schema



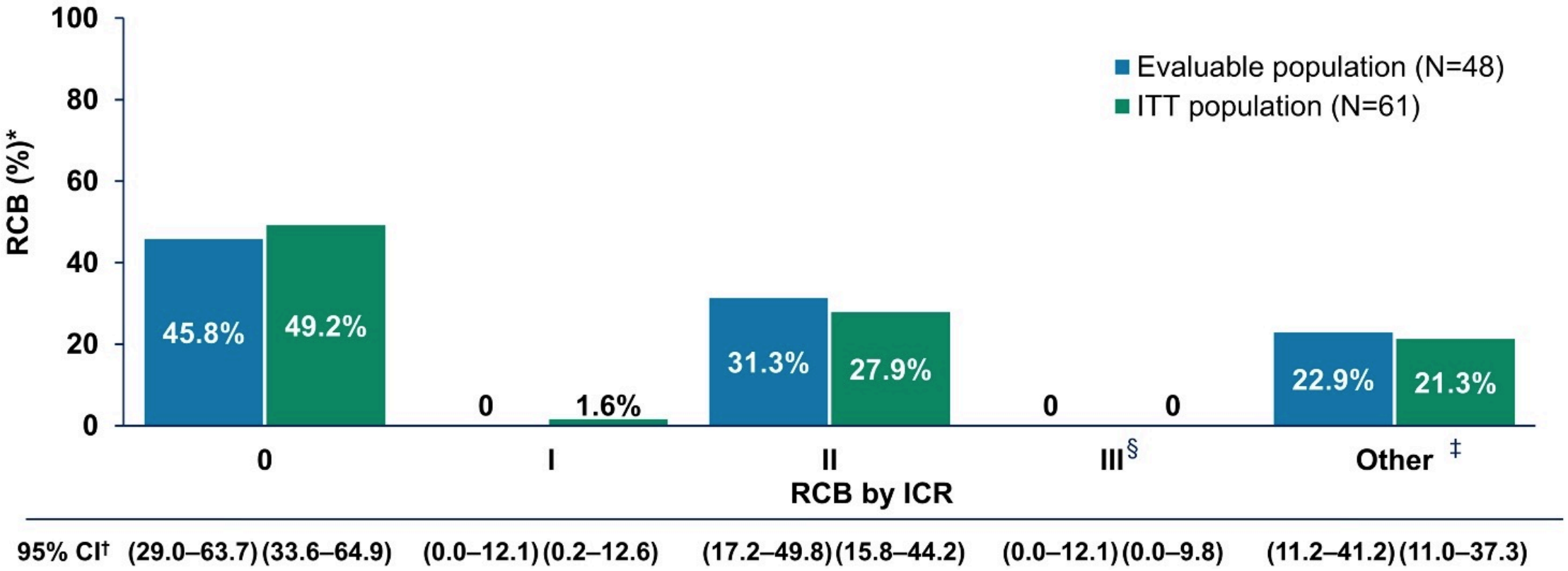

Litton JK et al. ASCO 2021;Abstract 505.

# 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

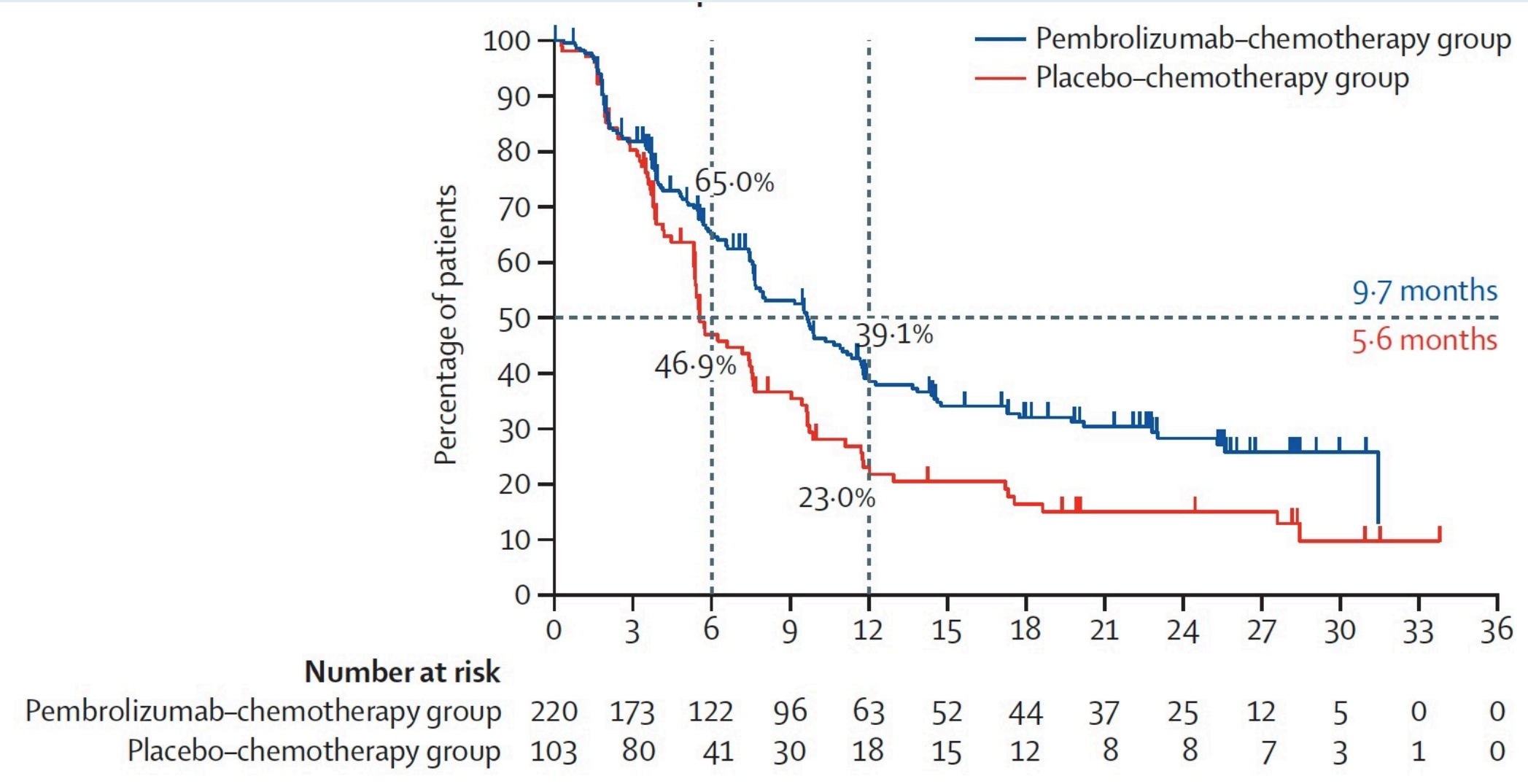
RTP RESEARCH TO PRACTICE

*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.

RTP RESEARCH TO PRACTICE

*Lancet Oncol* 2020;21:44-59

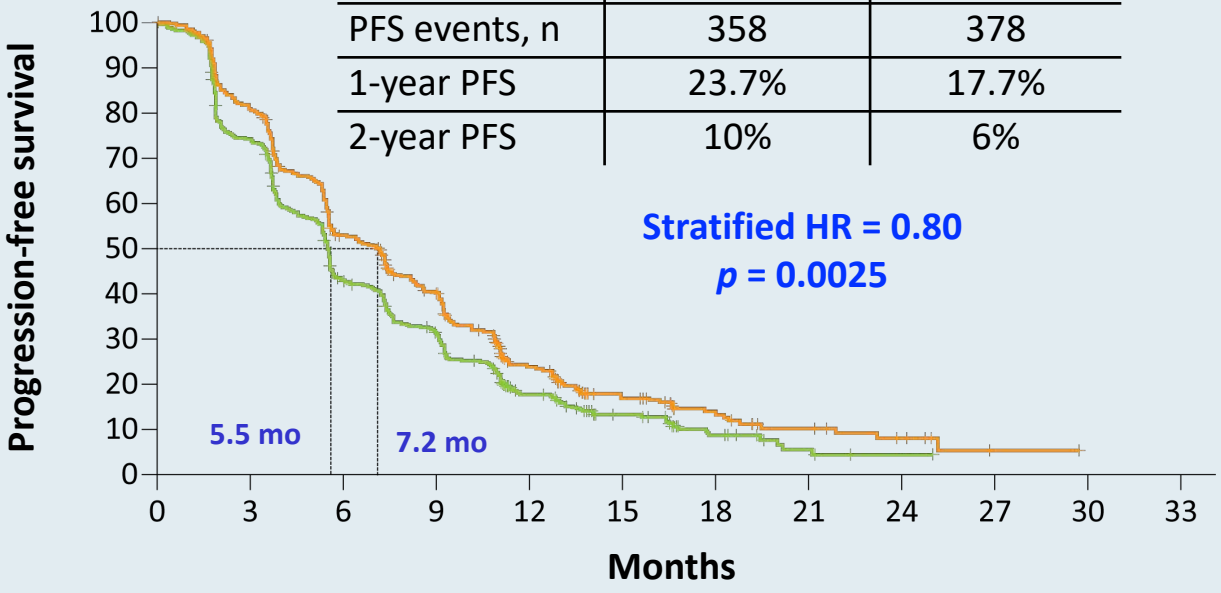
# Atezolizumab plus nab-paclitaxel as first-line treatment for unresectable, locally advanced or metastatic triple-negative breast cancer (IMpassion130): updated efficacy results from a randomised, double-blind, placebo-controlled, phase 3 trial

*Peter Schmid*, Hope S Rugo*, Sylvia Adams, Andreas Schneeweiss, Carlos H Barrios, Hiroji Iwata, Véronique Diéras, Volkmar Henschel, Luciana Molinero, Stephen Y Chui, Vidya Maiya, Amreen Husain, Eric P Winer, Sherene Loi, Leisha A Emens, for the IMpassion130 Investigators†*

# IMpassion130: PFS Results

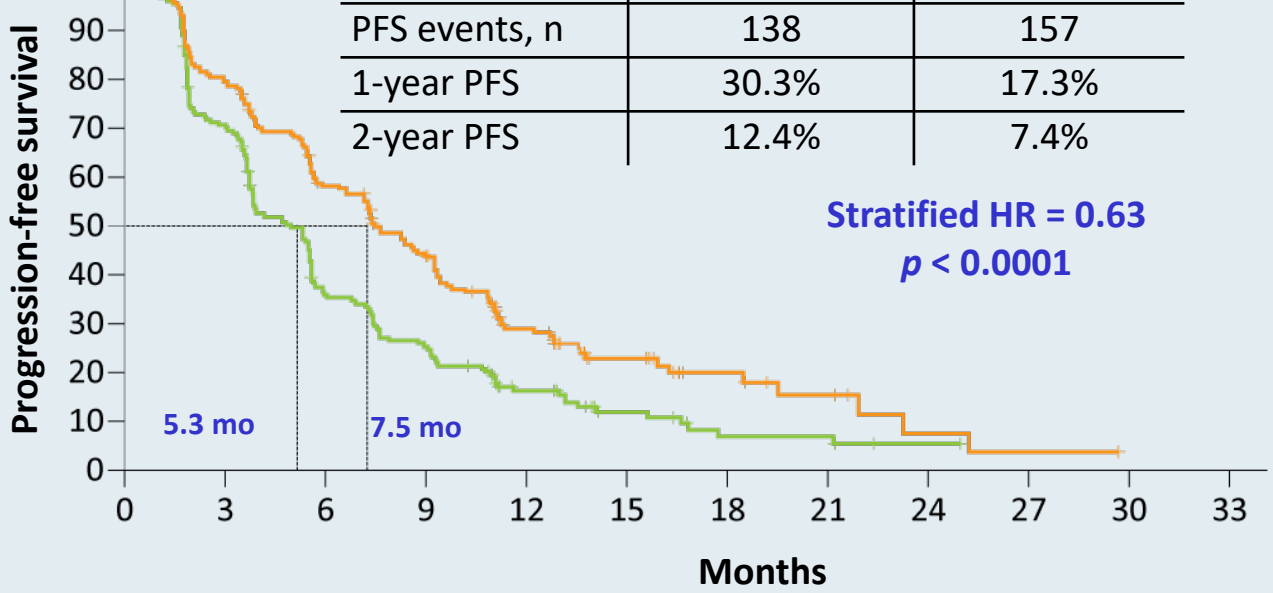
## PFS analysis: ITT population

| | Atezo + *nab*-P (n = 451) | Plac + *nab*-P (n = 451) |
|---|---|---|
| PFS events, n | 358 | 378 |
| 1-year PFS | 23.7% | 17.7% |
| 2-year PFS | 10% | 6% |




## PFS analysis: PD-L1+ population

| | Atezo + *nab*-P (n = 185) | Plac + *nab*-P (n = 184) |
|---|---|---|
| PFS events, n | 138 | 157 |
| 1-year PFS | 30.3% | 17.3% |
| 2-year PFS | 12.4% | 7.4% |

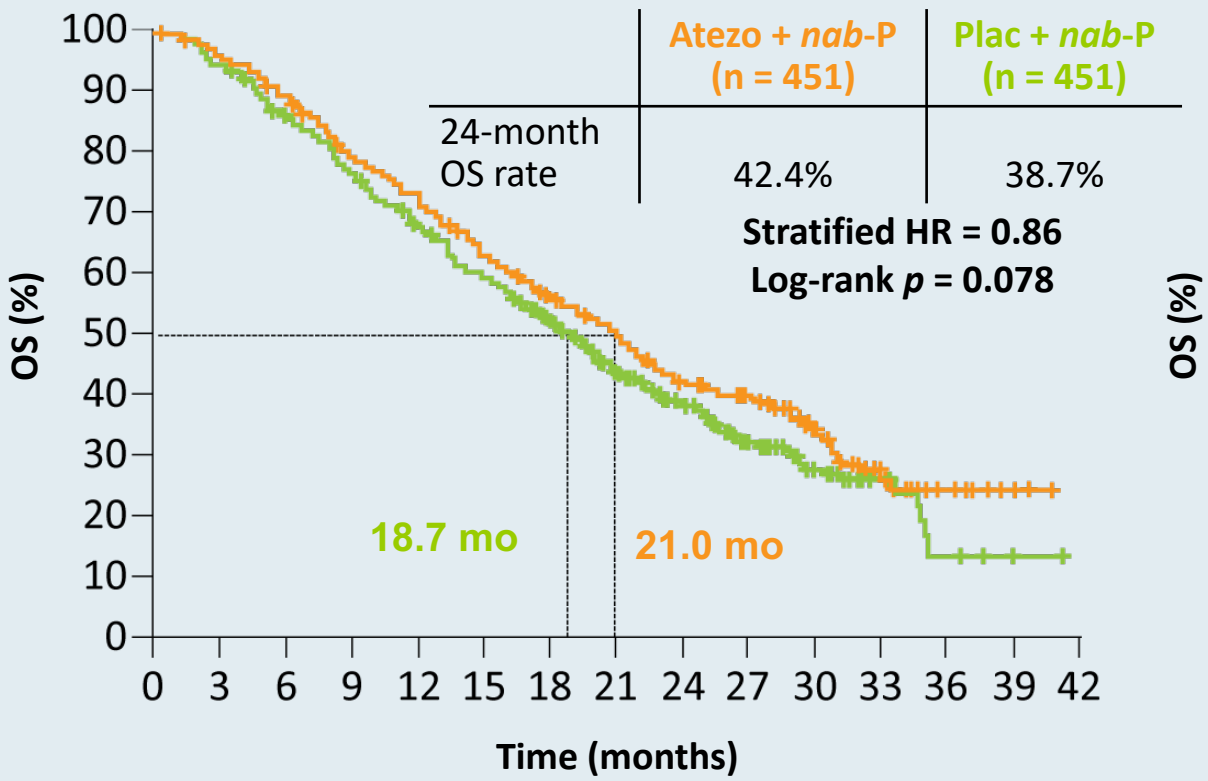



**Second interim analysis median follow-up = 18.5 mo (atezo) vs 17.5 mo (placebo)**

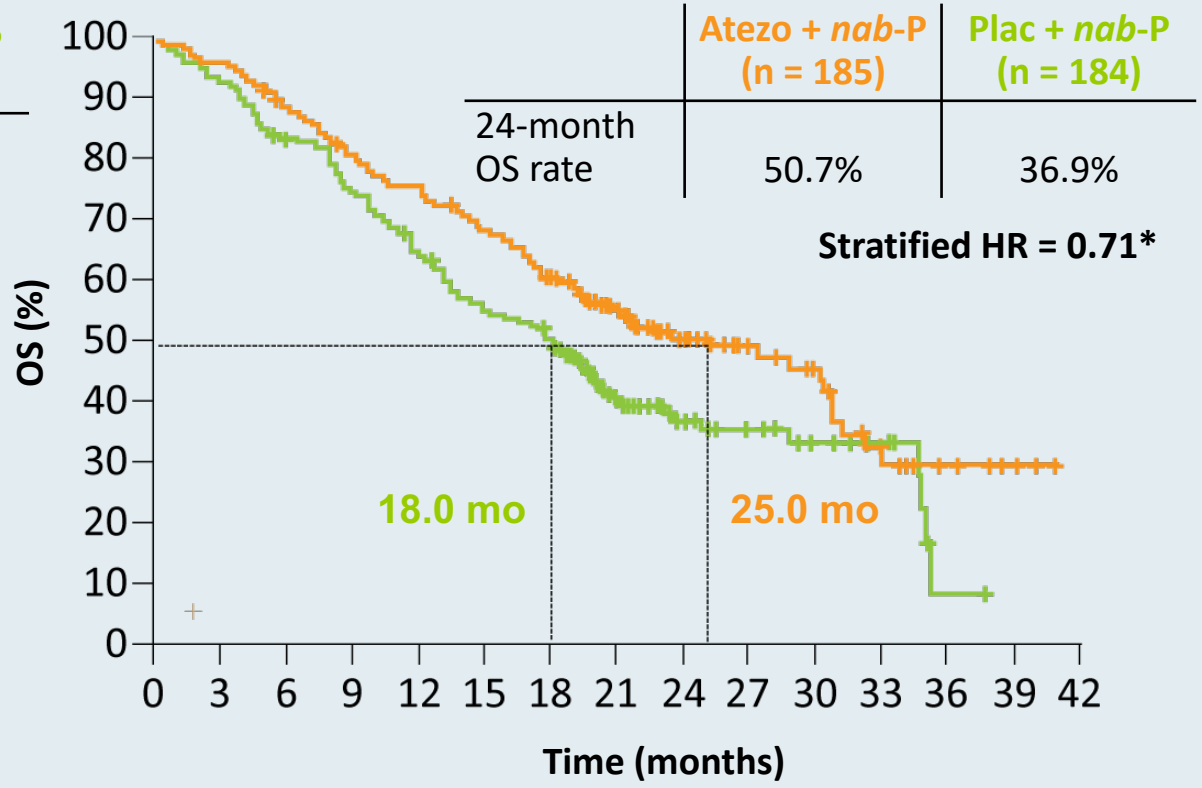
Schmid P et al. *Lancet Oncol* 2020;21(1):44-59.

# IMpassion130: OS Results at Second Interim Analysis

## Second interim analysis of OS: ITT population




## Second interim analysis of OS: PD-L1+ population

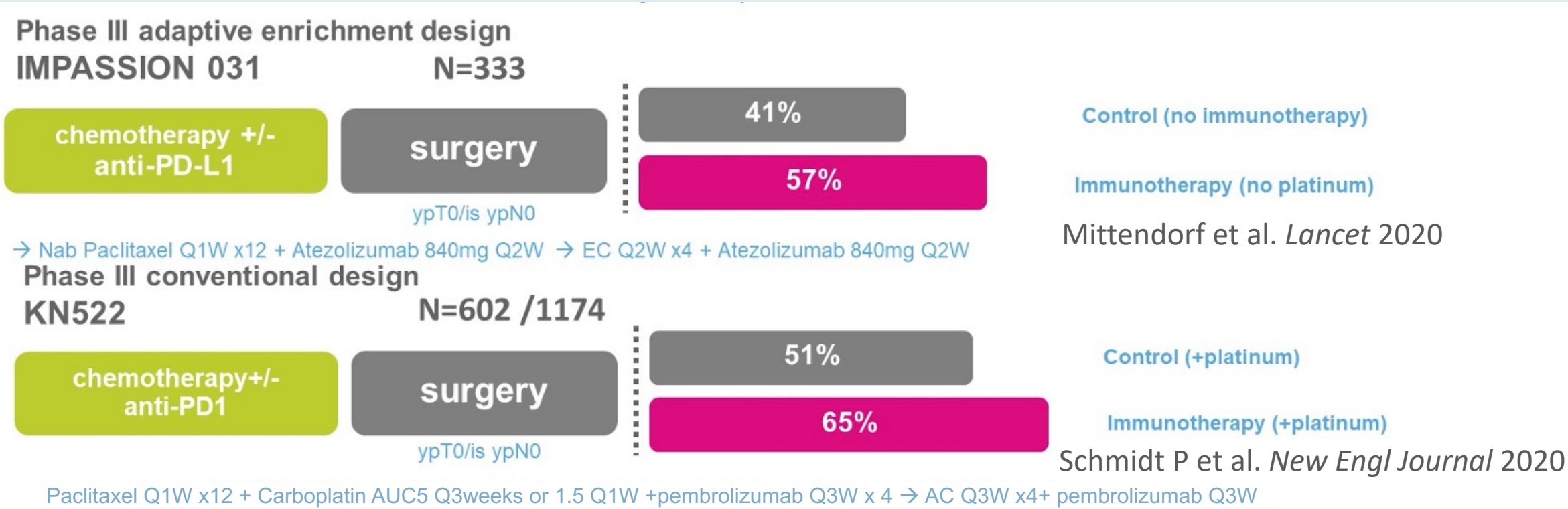



* Not formally tested because of prespecified hierarchical analysis plan

- Median OS (PD-L1-negative population): 19.7 mo (atezo) vs 19.6 mo (placebo); HR = 0.97

Schmid P et al. *Lancet Oncol* 2020;21(1):44-59

# 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

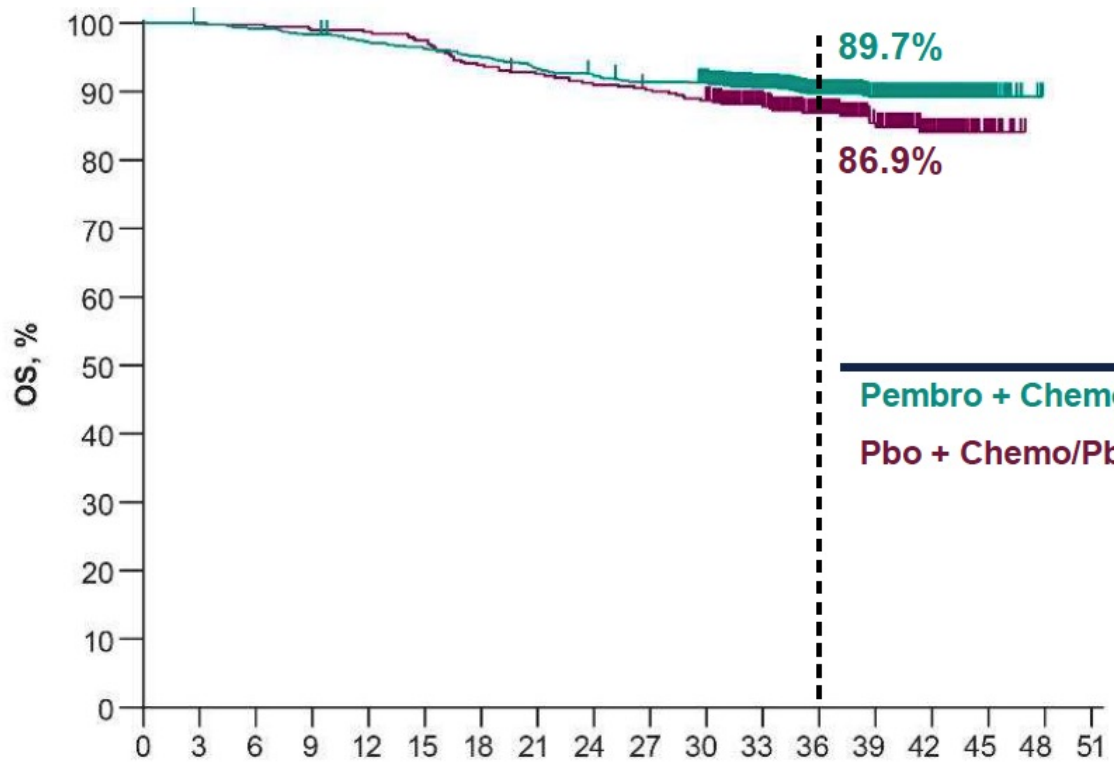
ESMO VIRTUAL PLENARY

# 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

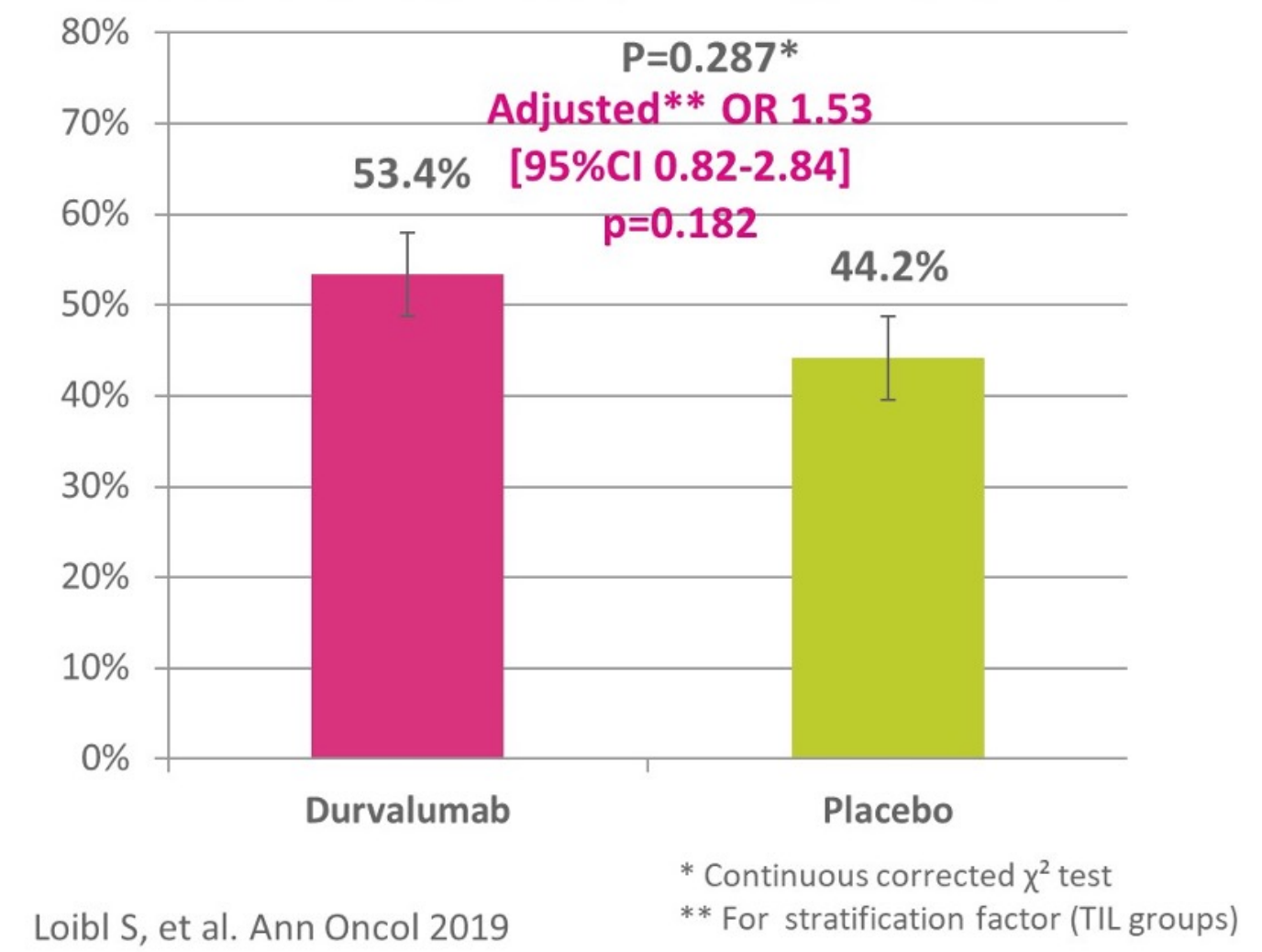
-This is a joint study by GBG and AGO-B-



RTP RESEARCH TO PRACTICE

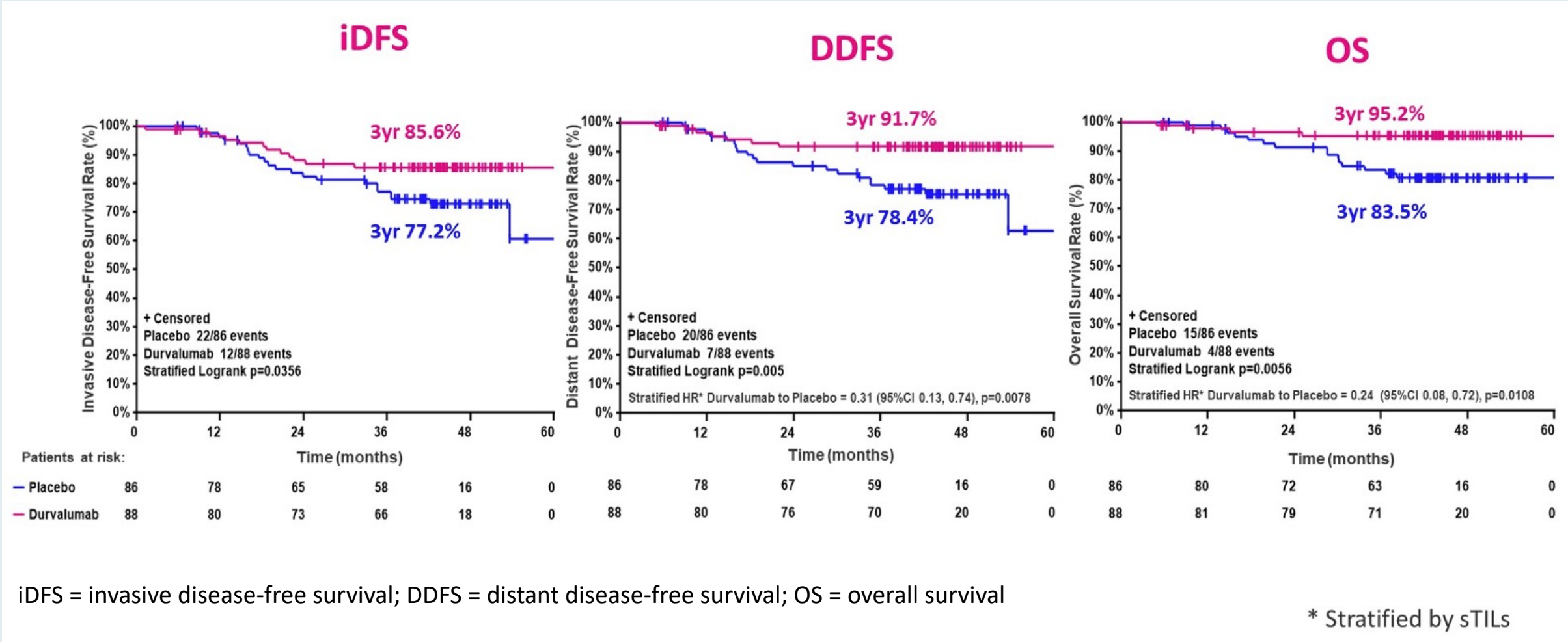
Loibl S et al. ASCO 2021;Abstract 506.

# 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

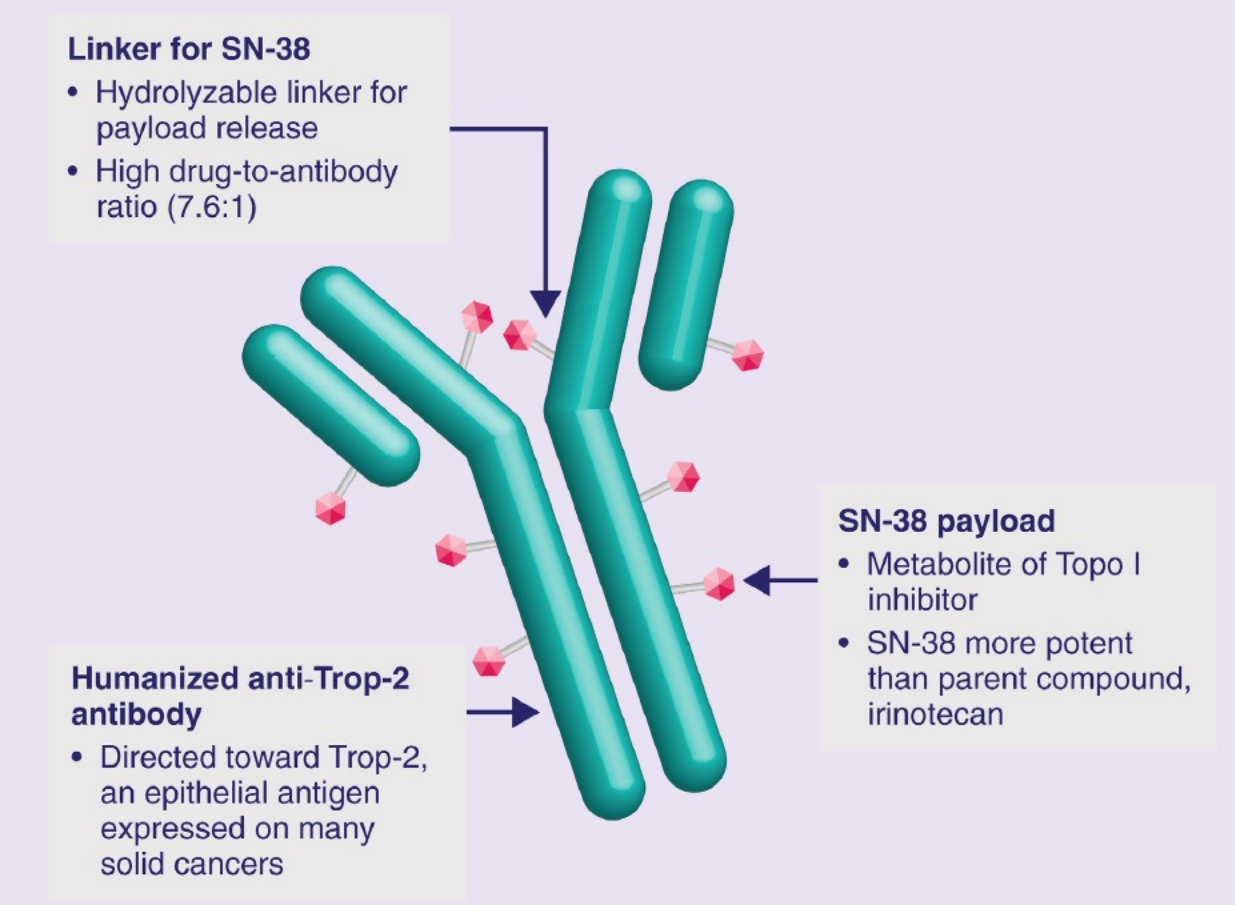
"The Food and Drug Administration granted regular approval to sacituzumab govitecan for patients with unresectable locally advanced or metastatic triple-negative breast cancer (mTNBC) who have received two or more prior systemic therapies, at least one of them for metastatic disease.

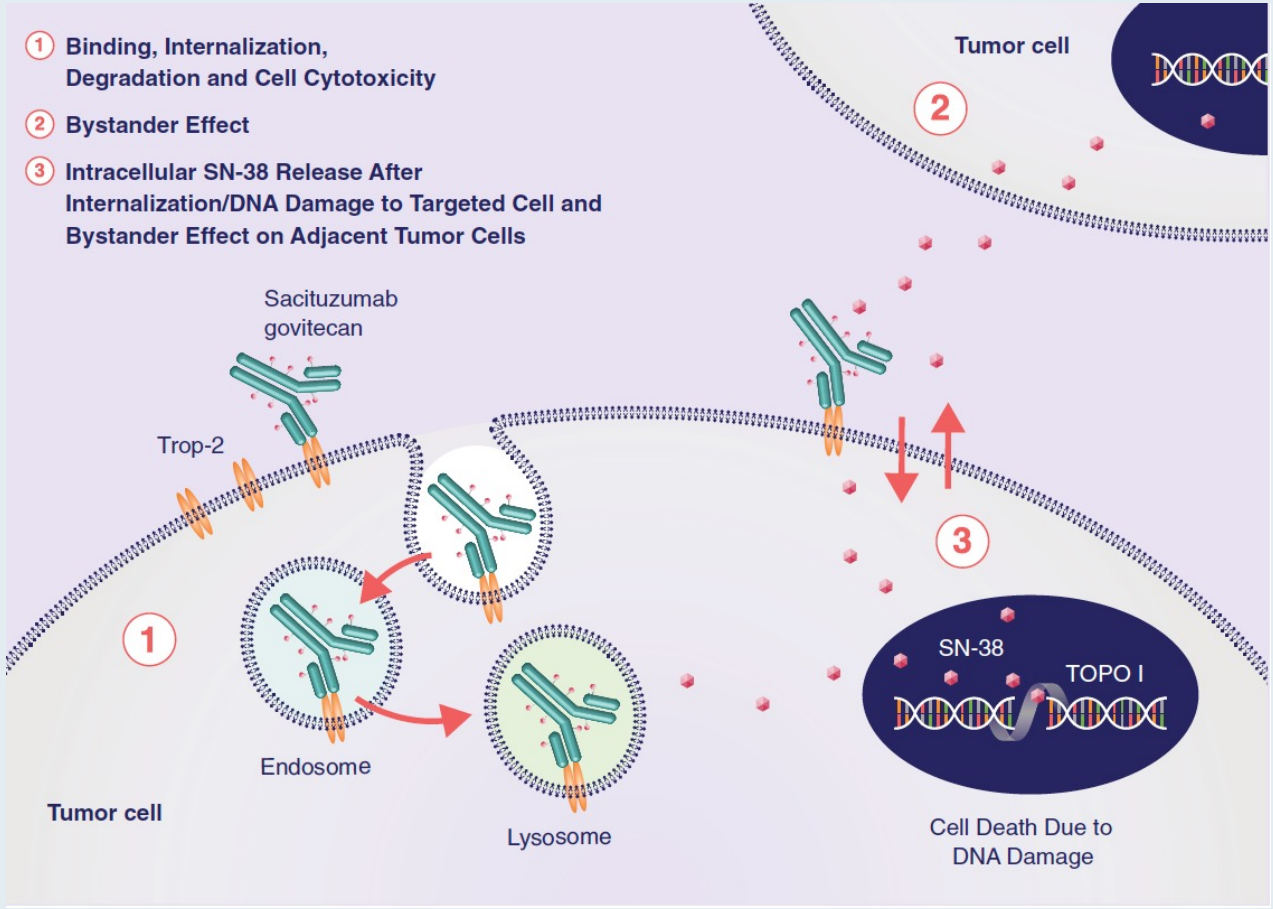
Efficacy and safety were evaluated in a multicenter, open-label, randomized trial (ASCENT; NCT02574455) conducted in 529 patients with unresectable locally advanced or mTNBC who had relapsed after at least two prior chemotherapies, one of which could be in the neoadjuvant or adjuvant setting, if progression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

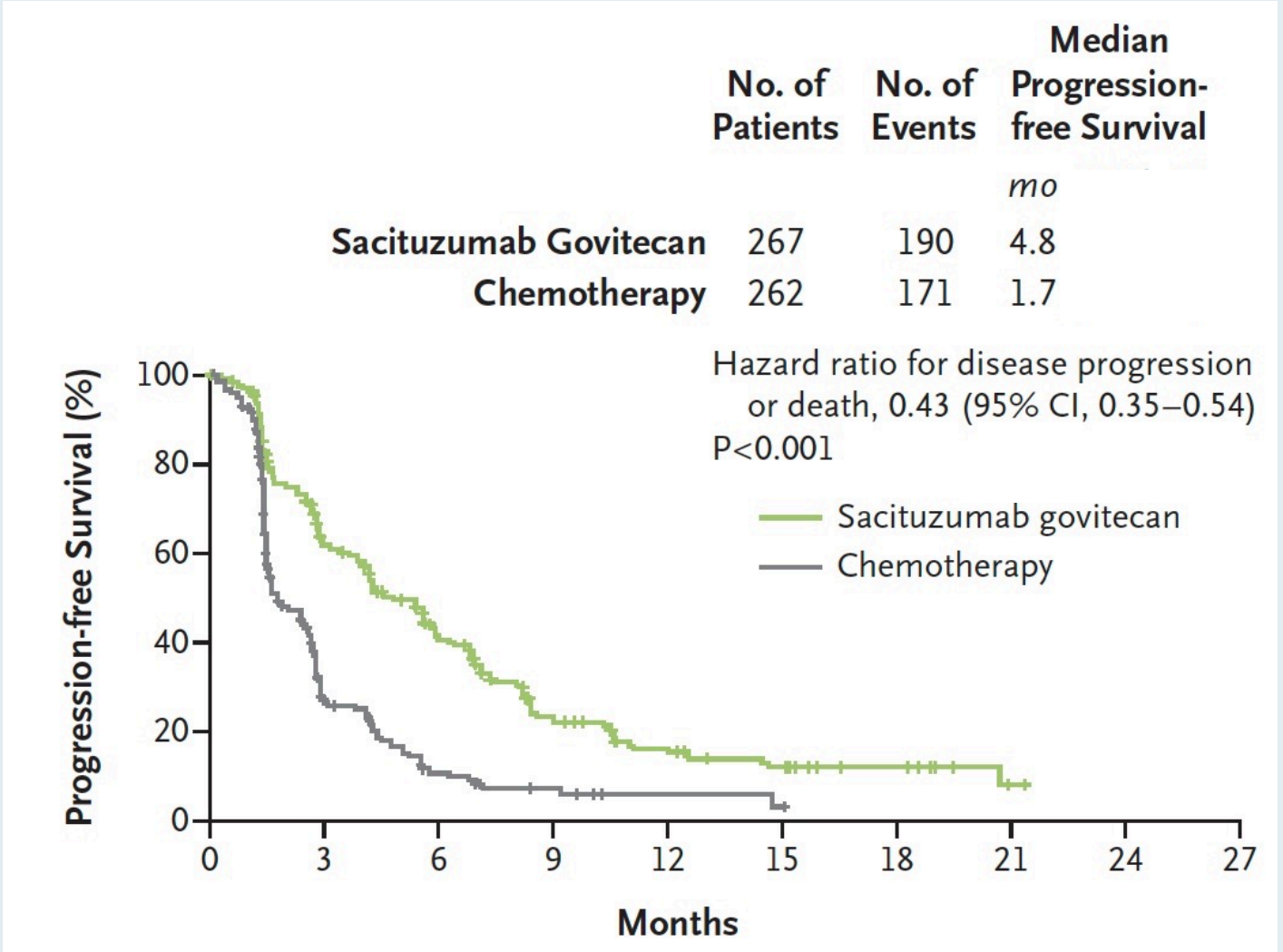
ORIGINAL ARTICLE

# 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)

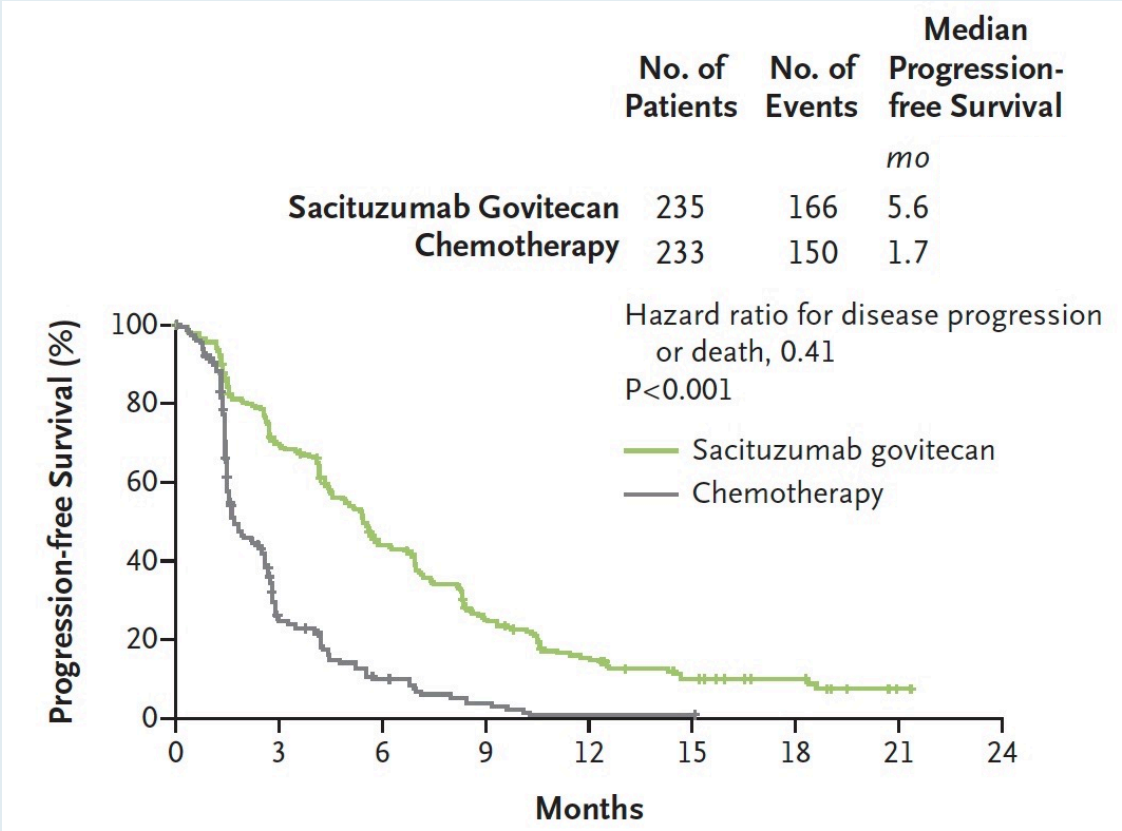
| | No. of Patients | No. of Events | Median Progression-free Survival |
|---|---|---|---|
| | | | *mo* |
| Sacituzumab Govitecan | 267 | 190 | 4.8 |
| Chemotherapy | 262 | 171 | 1.7 |

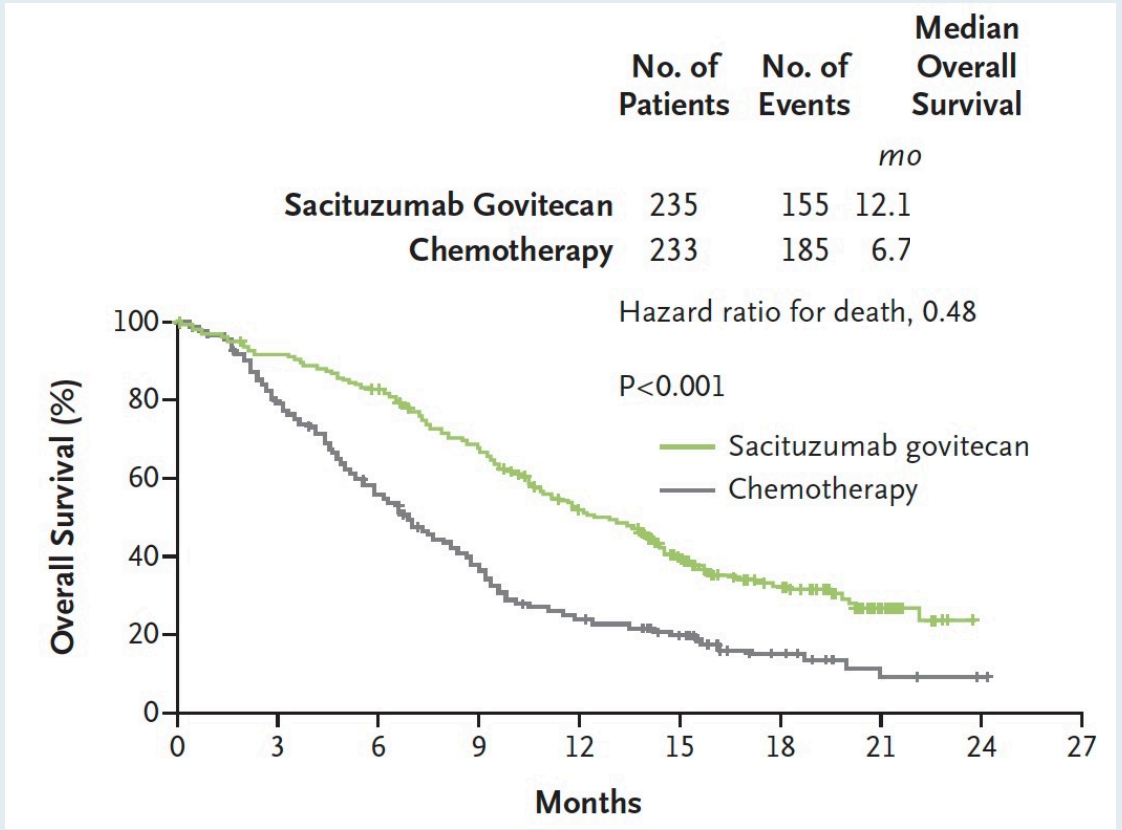



Bardia A et al. *N Engl J Med* 2021;384:1529-41.

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.

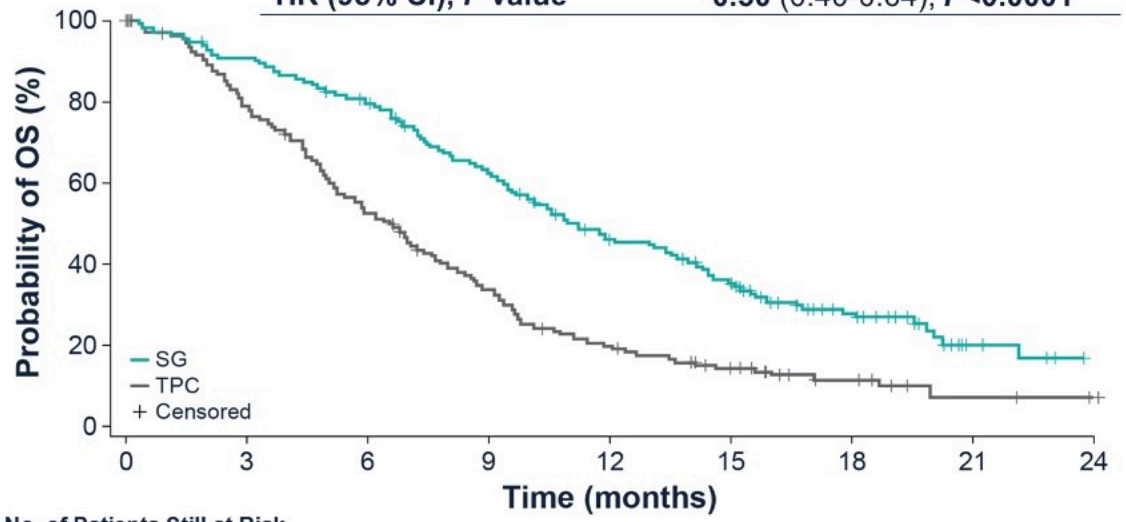
# Outcomes in Patients (pts) Aged ≥65 Years in the Phase 3 ASCENT Study of Sacituzumab Govitecan (SG) in Metastatic Triple-Negative Breast Cancer (mTNBC)

Kalinsky K et al.

ASCO 2021;Abstract 1011.

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

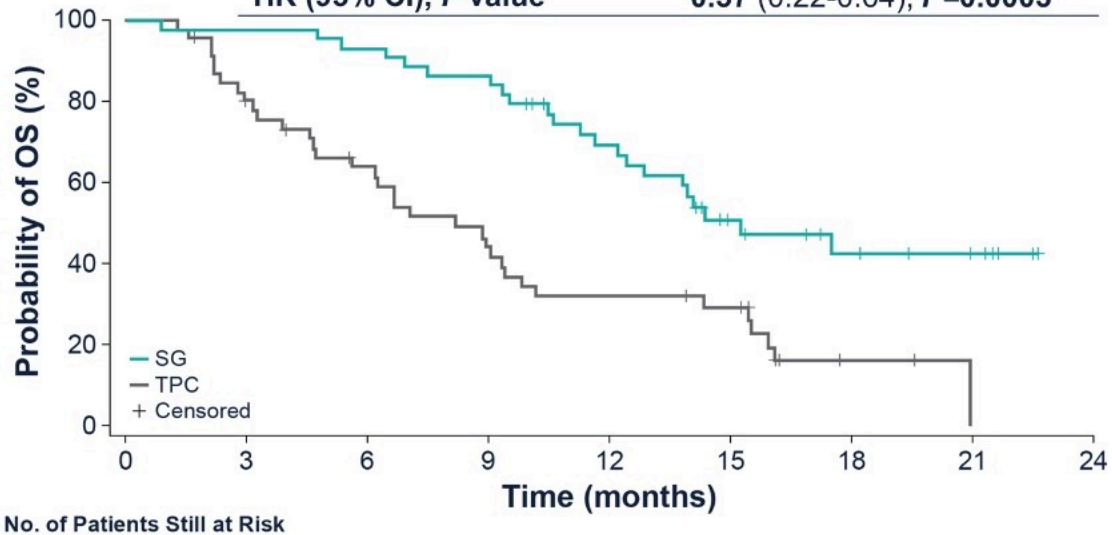
| | <65 y | |
|---|---|---|
| | SG (n=191) | TPC (n=187) |
| No. of events | 133 | 150 |
| Median OS—mo (95% CI) | 11.2 (9.9-13.4) | 6.6 (5.3-7.4) |
| HR (95% CI), *P* value | **0.50** (0.40-0.64), ***P*<0.0001** | |




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.

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

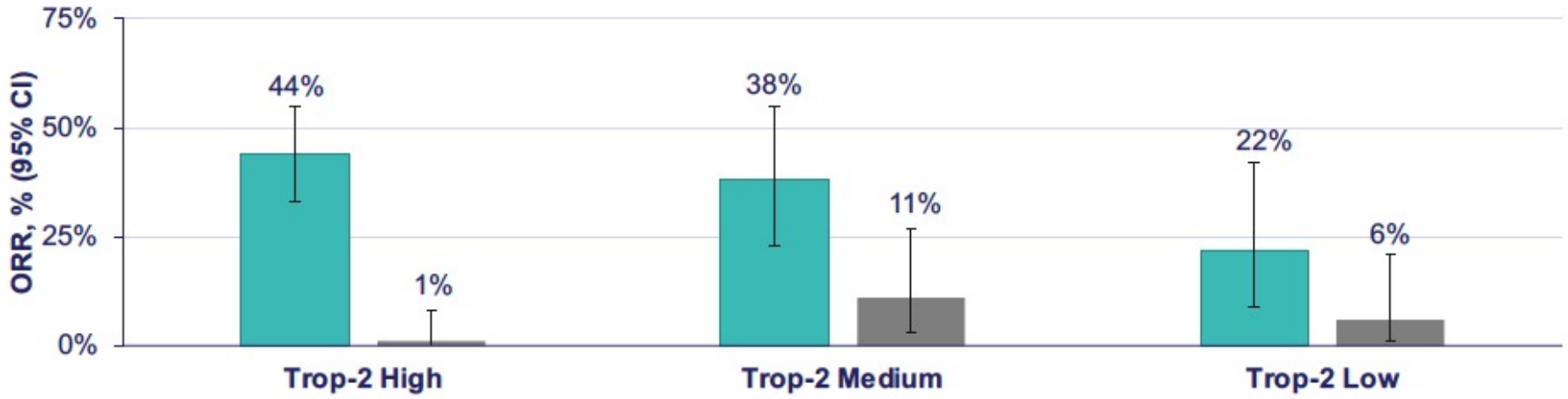

Sara A. Hurvitz,[1] Sara M. Tolaney,[2] Kevin Punie,[3] Delphine Loirat,[4] Mafalda Oliveira,[5] Kevin Kalinsky,[6] Amelia Zelnak,[7] Philippe Aftimos,[8] Florence Dalenc,[9] Sagar Sardesai,[10] Erika Hamilton,[11] Priyanka Sharma,[12] Sabela Recalde,[13] Eva Ciruelos Gil,[14] Tiffany Traina,[15] Joyce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

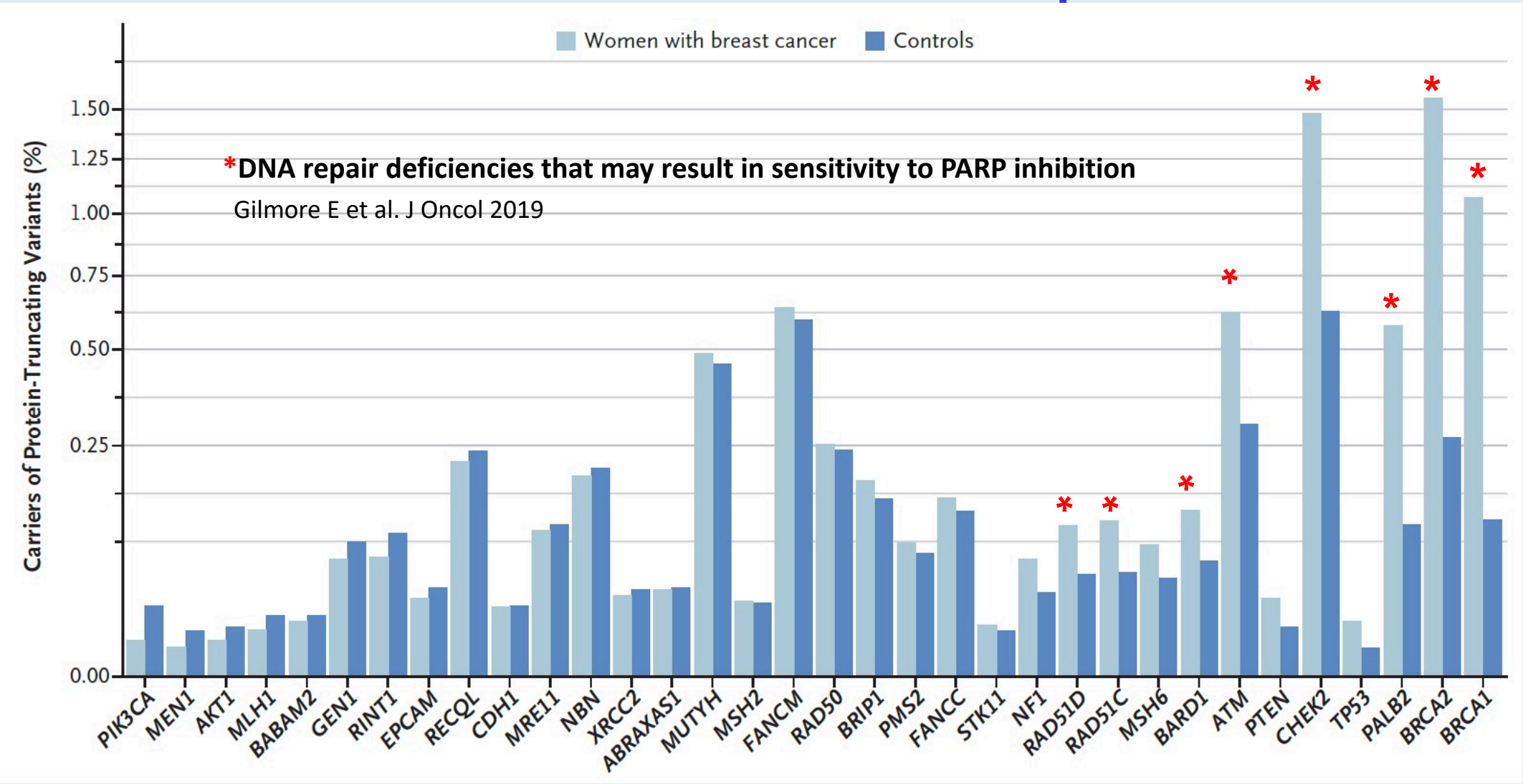
Assessed in the brain metastases-negative population. ORR and PFS are assessed by BICR. Trop-2 expression determined in archival samples by validated immunohistochemistry assay and H-scoring.
BICR, blind independent central review; H-score, histochemical-score; ORR, objective response rate; SG, sacituzumab 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.

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# *Meet The Professor*

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

**Wednesday, August 25, 2021**
**5:00 PM – 6:00 PM ET**

## Faculty

**Wells A Messersmith, 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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