Meet The Professor
Management of Ovarian Cancer

Ursula Matulonis, MD
Chief, Division of Gynecologic Oncology
Brock-Wilson Family Chair
Dana-Farber Cancer Institute
Professor of Medicine
Harvard Medical School
Boston, Massachusetts

Commercial Support

These activities are supported by an educational grant from GlaxoSmithKline.

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Dr Love — Disclosures

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Dr Matulonis — Disclosures

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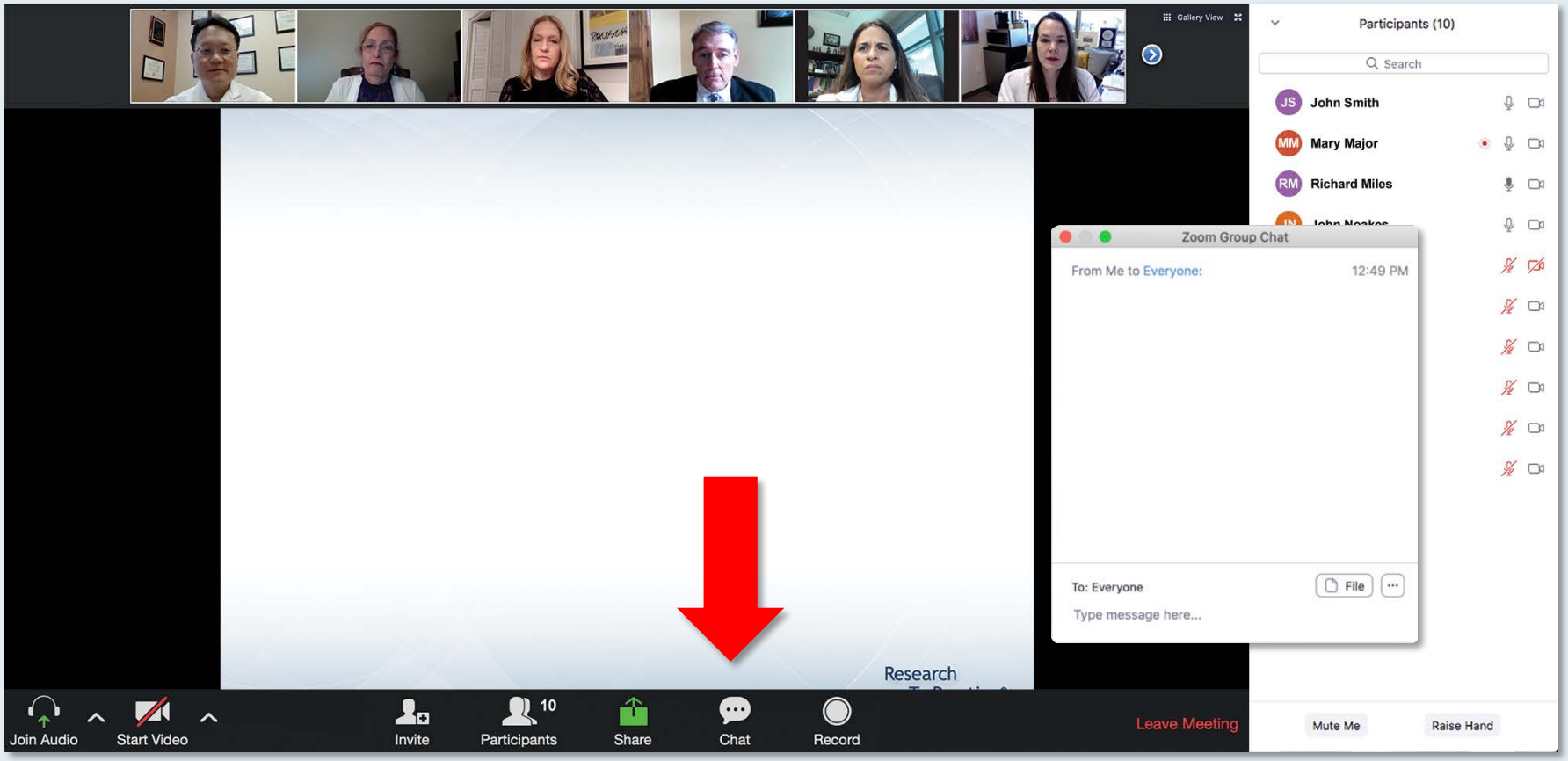
We Encourage Clinicians in Practice to Submit Questions



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Familiarizing Yourself with the Zoom Interface

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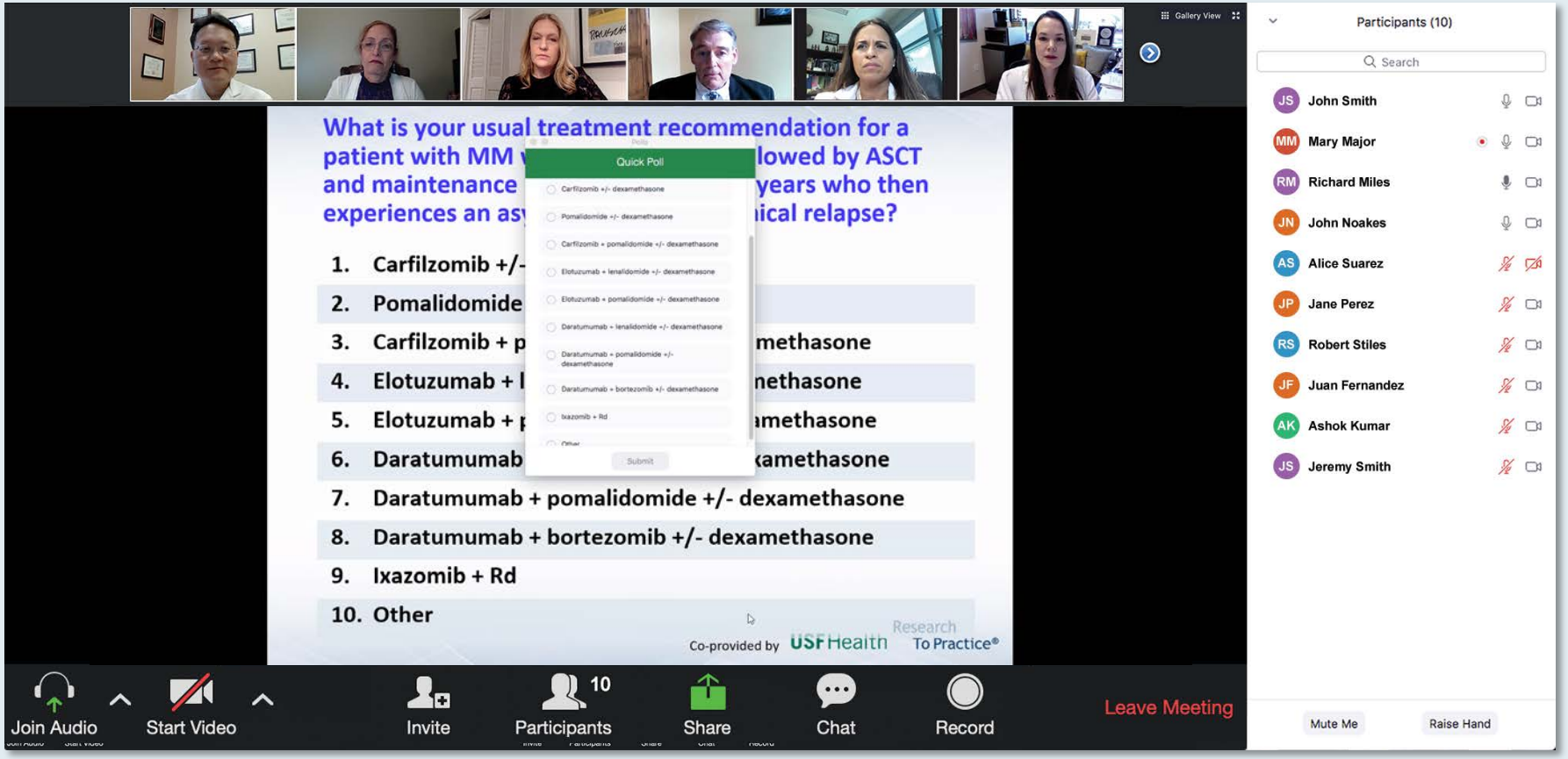

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Upcoming Live Webinars

Friday, October 2, 2020
12:00 PM – 1:00 PM ET

Meet The Professor: Management of Chronic Lymphocytic Leukemia

Faculty
William G Wierda, MD, PhD

Moderator
Neil Love, MD

Monday, October 5, 2020
12:00 PM – 1:00 PM ET

Meet The Professor: Management of Lung Cancer

Faculty
Professor Tony SK Mok, MD

Moderator
Neil Love, MD

Upcoming Live Webinars

Wednesday, October 7, 2020
12:00 PM – 1:00 PM ET

Meet The Professor: Management of Chronic Lymphocytic Leukemia

Faculty
Mitchell R Smith, MD, PhD

Moderator
Neil Love, MD

Thursday, October 8, 2020
12:00 PM – 1:00 PM ET

Meet The Professor: Management of Gynecologic Cancers

Faculty
Brian M Slomovitz, MD

Moderator
Neil Love, MD

Thank you for joining us!

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

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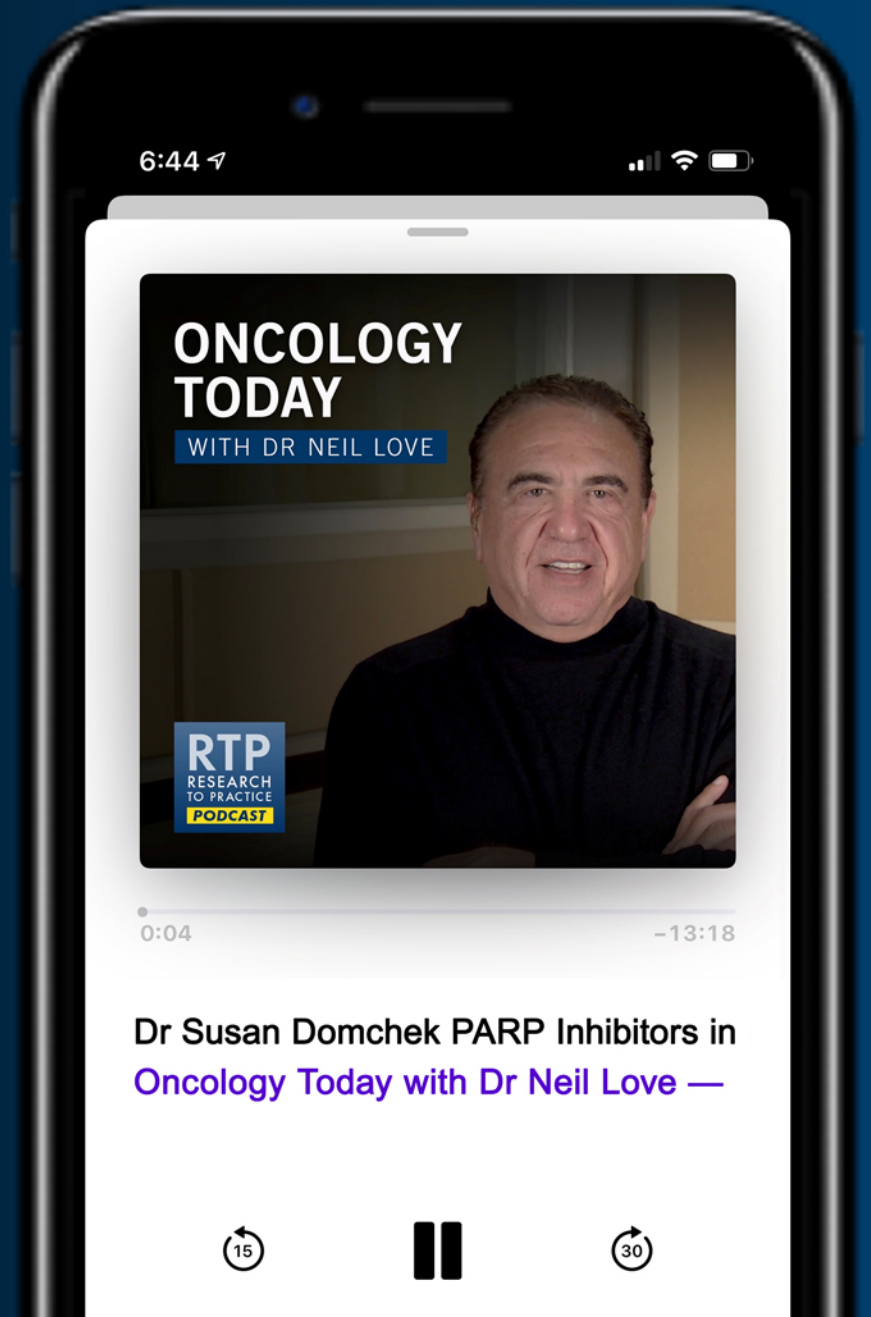

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Boston, Massachusetts

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Professor of Gynecology and Obstetrics
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Comprehensive Cancer Center
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Director, Medical Oncology and the Oncology Sexual Health Program
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University College London Cancer Institute
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Meet The Professor Program Participating Faculty

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Vice-Chairman, Danish Society of Gynaecologic Oncology
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Stephenson Cancer Center
Associate Professor, Section of Gynecologic Oncology
Director, Gynecologic Oncology Fellowship
Department of Obstetrics and Gynecology
University of Oklahoma Health Sciences Center
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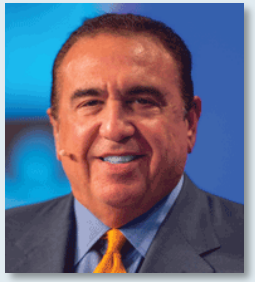

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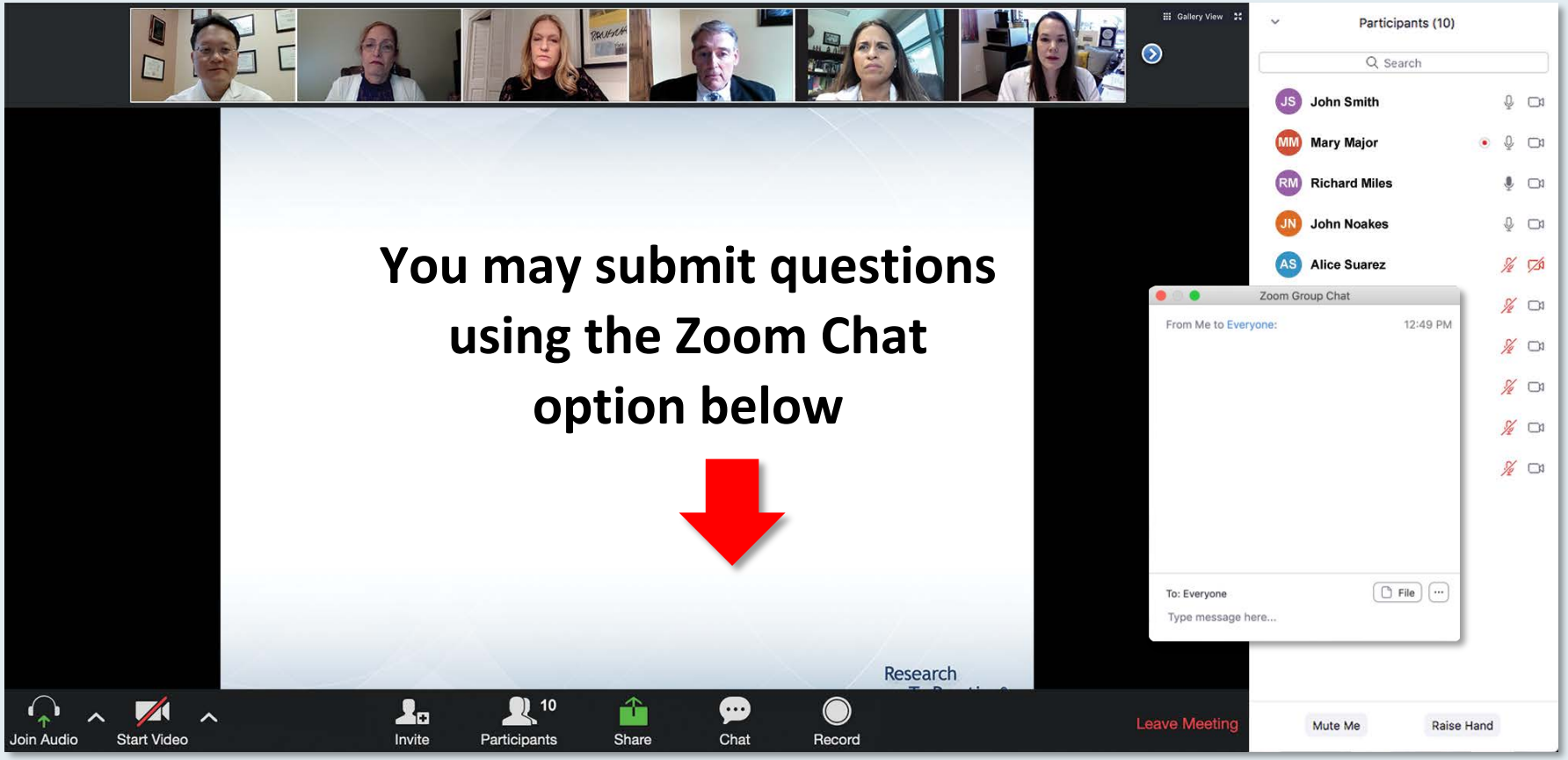

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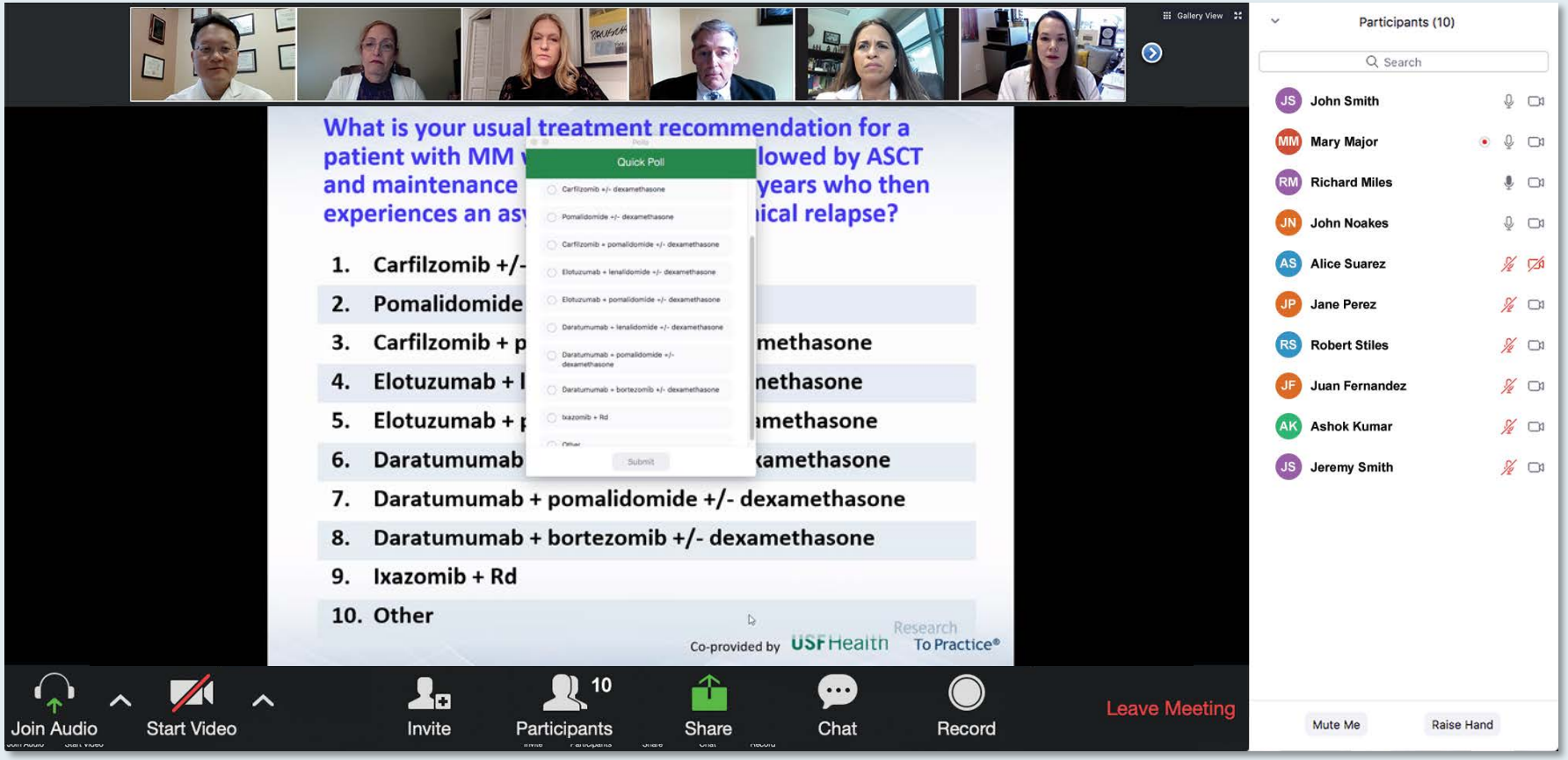

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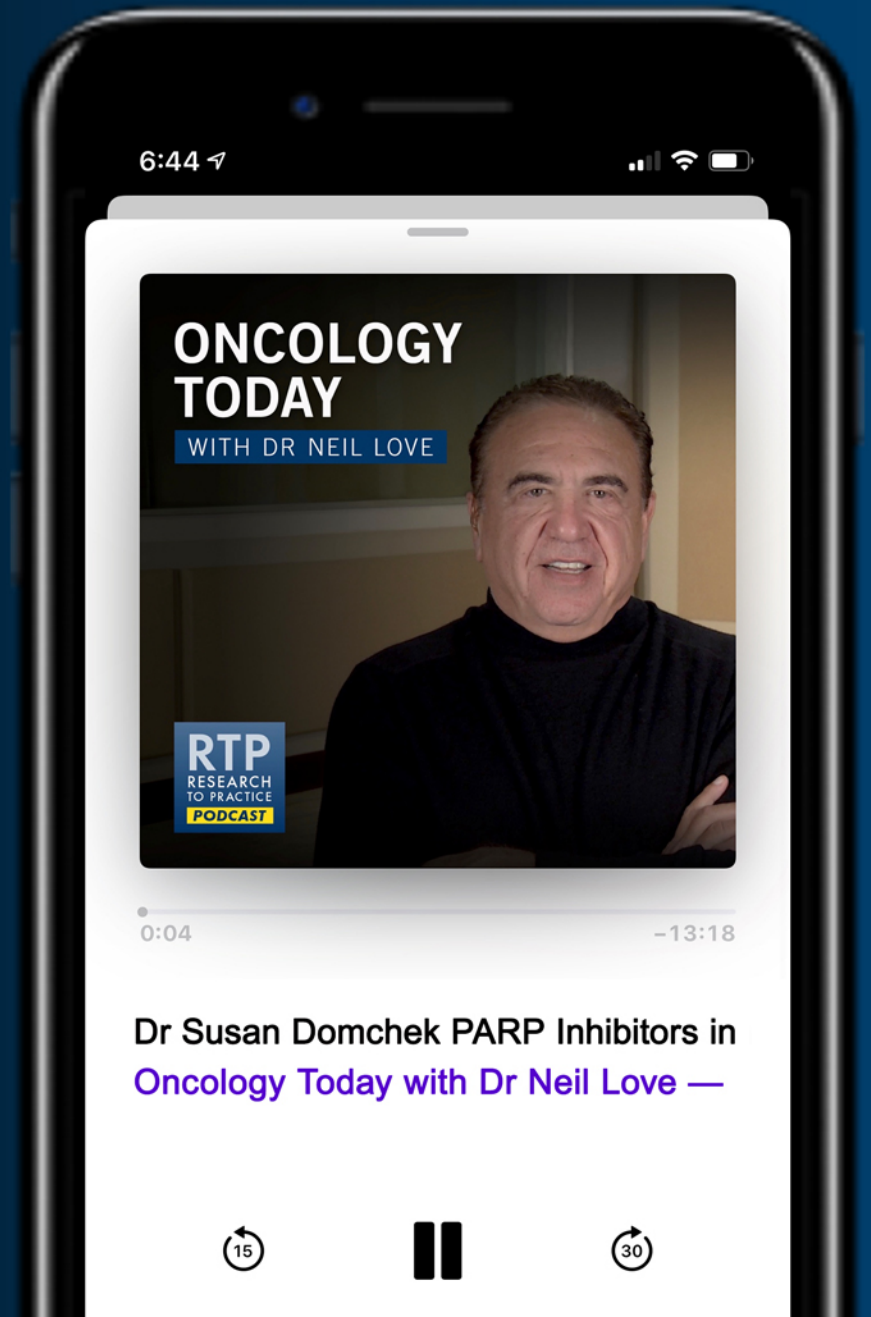

Meet The Professor

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Chief Oncologist, Department of Oncology
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Copenhagen, Denmark

Meet The Professor with Dr Matulonis

MODULE 1: Cases from Dr Mirza

- Questions and Comments: BRCA testing
- A 53-year-old woman with Stage IIIC high-grade serous ovarian cancer (HGSOC) – BRCA mutation
- A 53-year-old woman with Stage IIIC HGSOC – BRCA wild type, HR proficient
- A 53-year-old woman with Stage IIIC HGSOC – BRCA wild type, HR deficient
- Questions and Comments: Management of PARPi-associated low-grade nausea
- Questions and Comments: Niraparib dosing
- Questions and Comments: Management of PARPi-associated hypertension
- A 65-year-old woman with relapsed ovarian cancer – BRCA wild type, HR status unknown
- Questions and Comments: Defining platinum sensitivity

MODULE 2: Journal Club with Dr Matulonis

- ASCO guidelines: PARP inhibitors in the management of ovarian cancer
- ESMO 2020: IMagyn050 Phase III trial of bevacizumab-containing therapy with or without atezolizumab
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- PARP inhibitor resistance mechanisms and post-progression combination therapies
- Single-cell landscape of HGSOC

MODULE 3: Beyond the Guidelines – Clinical Investigator Approaches to Common Clinical Scenarios

MODULE 4: Key Recent Papers

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rapid communications

PARP Inhibitors in the Management of Ovarian Cancer: ASCO Guideline

William P. Tew, MD[1]; Christina Lacchetti, MHSc[2]; Annie Ellis[3,4]; Kathleen Maxian, BSW[5]; Susana Banerjee, PhD[6]; Michael Bookman, MD[7]; Monica Brown Jones, MD[8]; Jung-Min Lee, MD[9]; Stéphanie Lheureux, MD, PhD[10]; Joyce F. Liu, MD[11]; Kathleen N. Moore, MD[12]; Carolyn Muller, MD[13]; Patricia Rodriguez, MD[14]; Christine Walsh, MD[15]; Shannon N. Westin, MD[16]; and Elise C. Kohn, MD[9]

Journal of Clinical Oncology 2020;[Online ahead of print]

Questions and Comments: BRCA testing

Dr Mansoor Raza Mirza

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Case Presentation – Dr Mirza: A 53-year-old woman with Stage IIIC HGSOC – BRCA mutation

Dr Mansoor Raza Mirza

- Stage IIIC HGSOC – BRCA mutation
- Upfront surgery not possible
- Neoadjuvant carboplatin/paclitaxel x 3
- Interval debulking surgery: R=0

Questions

- What treatment would you recommend?
  - Carboplatin-paclitaxel x 3 followed by maintenance niraparib for 36mo
  - Carboplatin/paclitaxel x 3 followed by maintenance olaparib for 24mo
  - Carboplatin/paclitaxel-bevacizumab x 3 followed by maintenance bevacizumab + olaparib

Case Presentation – Dr Mirza: A 53-year-old woman with Stage IIIC HGSOC – BRCA wild type, HR proficient

Dr Mansoor Raza Mirza

- Stage IIIC HGSOC – BRCA wildtype, HR proficient
- Upfront surgery not possible
- Neoadjuvant carboplatin/paclitaxel x 3
- Interval debulking surgery: R=0

Questions

- What treatment would you recommend?
  - Carboplatin/paclitaxel x 3 followed by maintenance niraparib x 36 months
  - Carboplatin/paclitaxel/bevacizumab x 3 followed by maintenance bevacizumab

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Case Presentation – Dr Mirza: A 53-year-old woman with Stage IIIC HGSOC – BRCA wild type, HR deficient

Dr Mansoor Raza Mirza

- Stage IIIC HGSOC – BRCA wildtype, HR deficient
- Upfront surgery not possible
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Questions

- What treatment would you recommend?
  - Carboplatin-paclitaxel x 3 followed by maintenance niraparib for 36mo
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Questions and Comments: Management of PARPi-associated low-grade nausea

Dr Mansoor Raza Mirza

Questions and Comments: Niraparib dosing

Dr Mansoor Raza Mirza

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Questions and Comments: Management of PARPi-associated hypertension

Dr Mansoor Raza Mirza

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Case Presentation – Dr Mirza: A 65-year-old woman with relapsed ovarian cancer – BRCA wild type, HR status unknown

Dr Mansoor Raza Mirza

- Stage IIIC HGSOC – BRCA wildtype, HRD status unknown
- Upfront surgery not possible
- Neoadjuvant carboplatin/paclitaxel x 3
- Interval debulking surgery: R=0
- Carboplatin/paclitaxel x 3
- Relapse after platinum-free interval of 18 months (not eligible for surgery)

Questions

- What are the treatment options, and which treatment would you recommend?

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Questions and Comments: Defining platinum sensitivity

Dr Mansoor Raza Mirza

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Primary Results from IMagyn050/GOG 3015/ ENGOT-OV39, a Double-Blind Placebo (Pbo)-Controlled Randomized Phase III Trial of Bevacizumab (Bev)-Containing Therapy +/- Atezolizumab (Atezo) for Newly Diagnosed Stage III/IV Ovarian Cancer (OC)

Moore K et al.

ESMO 2020;Abstract LBA31.

Contents lists available at ScienceDirect

Gynecologic Oncology

journal homepage: www.elsevier.com/locate/ygyno

Invited Review

Homologous recombination deficiency real-time clinical assays, ready or not?

Katherine Fuh [a,*], Mary Mullen [a], Barbara Blachut [a], Elizabeth Stover [b,c], Panagiotis Konstantinopoulos [b,c], Joyce Liu [b,c], Ursala Matulonis [b,c], Dineo Khabele [a], Nima Mosammaparast [d], Alessandro Vindigni [e]

Gynecol Oncol 2020;[Online ahead of print]

cancers

MDPI

Review

PARP Inhibitor Resistance Mechanisms and Implications for Post-Progression Combination Therapies

Elizabeth K. Lee [1] and Ursula A. Matulonis [1,2,*]

Cancers (Basel) 2020;12(8):2054

nature medicine

LETTERS

https://doi.org/10.1038/s41591-020-0926-0

Check for updates

A single-cell landscape of high-grade serous ovarian cancer

Benjamin Izar[1,2,3,4,5,14,15], Itay Tirosh[6,15], Elizabeth H. Stover[1,15], Isaac Wakiro[1], Michael S. Cuoco[3], Idan Alter[6], Christopher Rodman[3], Rachel Leeson[1], Mei-Ju Su[1,5], Parin Shah[1], Marcin Iwanicki[7], Sarah R. Walker[8], Abhay Kanodia[1], Johannes C. Melms[1], Shaolin Mei[5], Jia-Ren Lin[5], Caroline B. M. Porter[3], Michal Slyper[3], Julia Waldman[3], Livnat Jerby-Arnon[3], Orr Ashenberg[3], Titus J. Brinker[9], Caitlin Mills[5], Meri Rogava[5], Sébastien Vigneau[1,2], Peter K. Sorger[5], Levi A. Garraway[10], Panagiotis A. Konstantinopoulos[1], Joyce F. Liu[1], Ursula Matulonis[1], Bruce E. Johnson[1,2], Orit Rozenblatt-Rosen[3], Asaf Rotem[1,2,3,16] and Aviv Regev[3,11,12,13,16] ✉

Nat Med 2020;26(8):1271-9

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In general, what is the optimal approach to mutation testing for possible use of a PARP inhibitor for a patient with newly diagnosed ovarian cancer? Do you routinely assess homologous recombination deficiency (HRD) status in your patients with advanced ovarian cancer?

	Optimal approach to mutation testing	Routinely assess HRD status
 DEBORAH K ARMSTRONG, MD	Multigene germline and somatic/NGS	No
 ROBERT L COLEMAN, MD	Multigene germline and somatic/NGS	Yes
 DON S DIZON, MD	Germline BRCA; if negative, multigene somatic (eg, NGS)	Yes
 PROFESSOR JONATHAN A LEDERMANN	Multigene germline and somatic/NGS	No
 URSULA MATULONIS, MD	Multigene germline and somatic/NGS	No
 MANSOOR RAZA MIRZA, MD	Multigene germline and somatic/NGS	No
 KATHLEEN MOORE, MD	Multigene germline and somatic/NGS	Yes
 SHANNON N WESTIN, MD, MPH	Germline BRCA; if negative, multigene somatic (eg, NGS)	Yes

NGS = next-generation sequencing

A 60-year-old woman with Stage IIIC ovarian cancer and a germline BRCA mutation is s/p optimal debulking surgery with a normal CA-125 level. Regulatory and reimbursement issues aside, what would you recommend as postoperative systemic therapy?

 DEBORAH K ARMSTRONG, MD	Carboplatin/paclitaxel → olaparib
 ROBERT L COLEMAN, MD	Carboplatin/paclitaxel + bevacizumab → bevacizumab + olaparib
 DON S DIZON, MD	Carboplatin/paclitaxel → olaparib
 PROFESSOR JONATHAN A LEDERMANN	Carboplatin/paclitaxel → olaparib
 URSULA MATULONIS, MD	Carboplatin/paclitaxel → olaparib
 MANSOOR RAZA MIRZA, MD	Carboplatin/paclitaxel → niraparib
 KATHLEEN MOORE, MD	Carboplatin/paclitaxel + bevacizumab → bevacizumab + olaparib
 SHANNON N WESTIN, MD, MPH	Carboplatin/paclitaxel → olaparib or niraparib

A 60-year-old woman with Stage IIIC ovarian cancer and a somatic BRCA mutation is s/p suboptimal debulking surgery with an elevated CA-125 level. Regulatory and reimbursement issues aside, what would you recommend as postoperative systemic therapy?

 DEBORAH K ARMSTRONG, MD	Carboplatin/paclitaxel → olaparib
 ROBERT L COLEMAN, MD	Carboplatin/paclitaxel + bevacizumab → bevacizumab + niraparib
 DON S DIZON, MD	Carboplatin/paclitaxel + bevacizumab → bevacizumab + olaparib
 PROFESSOR JONATHAN A LEDERMANN	Carboplatin/paclitaxel + bevacizumab → bevacizumab + olaparib
 URSULA MATULONIS, MD	Carboplatin/paclitaxel → olaparib
 MANSOOR RAZA MIRZA, MD	Carboplatin/paclitaxel + bevacizumab → bevacizumab + olaparib
 KATHLEEN MOORE, MD	Carboplatin/paclitaxel + bevacizumab → bevacizumab + olaparib
 SHANNON N WESTIN, MD, MPH	Carboplatin/paclitaxel + bevacizumab → bevacizumab + olaparib

A 60-year-old woman with Stage IIIC ovarian cancer and a germline BRCA mutation is status post (s/p) suboptimal debulking surgery with an elevated CA-125 level. Regulatory and reimbursement issues aside, what would you recommend as postoperative systemic therapy?

 DEBORAH K ARMSTRONG, MD	Carboplatin/paclitaxel → olaparib
 ROBERT L COLEMAN, MD	Carboplatin/paclitaxel + bevacizumab → bevacizumab + olaparib
 DON S DIZON, MD	Carboplatin/paclitaxel + bevacizumab → bevacizumab + olaparib
 PROFESSOR JONATHAN A LEDERMANN	Carboplatin/paclitaxel + bevacizumab → bevacizumab + olaparib
 URSULA MATULONIS, MD	Carboplatin/paclitaxel → olaparib
 MANSOOR RAZA MIRZA, MD	Carboplatin/paclitaxel + bevacizumab → bevacizumab + olaparib
 KATHLEEN MOORE, MD	Carboplatin/paclitaxel + bevacizumab → bevacizumab + olaparib
 SHANNON N WESTIN, MD, MPH	Carboplatin/paclitaxel + bevacizumab → bevacizumab + olaparib

A 60-year-old woman with Stage IIIC fallopian tube cancer (BRCA wild type, HRD-negative) is s/p optimal debulking surgery. Regulatory and reimbursement issues aside, what would you recommend as postoperative systemic therapy?

1. Carboplatin/paclitaxel
2. Carboplatin/paclitaxel → olaparib
3. Carboplatin/paclitaxel → niraparib
4. Carboplatin/paclitaxel + bev → olaparib
5. Carboplatin/paclitaxel + bev → niraparib
6. Carboplatin/paclitaxel + bev → bev/olaparib
7. Carboplatin/paclitaxel + bev → bev/niraparib
8. Other

A 60-year-old woman with Stage IIIC ovarian cancer (BRCA wild type, HRD-negative) is s/p optimal debulking surgery with a normal CA-125 level. Regulatory and reimbursement issues aside, what would you recommend as postoperative systemic therapy?

 DEBORAH K ARMSTRONG, MD	Carboplatin/paclitaxel OR carboplatin/paclitaxel → niraparib
 ROBERT L COLEMAN, MD	Carboplatin/paclitaxel + bevacizumab → bevacizumab
 DON S DIZON, MD	Carboplatin/paclitaxel → niraparib
 PROFESSOR JONATHAN A LEDERMANN	Carboplatin/paclitaxel
 URSULA MATULONIS, MD	Discuss several options with patient
 MANSOOR RAZA MIRZA, MD	Carboplatin/paclitaxel → niraparib
 KATHLEEN MOORE, MD	Carboplatin/paclitaxel + bevacizumab → bevacizumab
 SHANNON N WESTIN, MD, MPH	Carboplatin/paclitaxel OR carboplatin/paclitaxel → niraparib

A 60-year-old woman with Stage IIIC ovarian cancer (BRCA wild type) is s/p suboptimal debulking surgery with an elevated CA-125 level. Regulatory and reimbursement issues aside, what would you recommend as postoperative systemic therapy if her disease was…

	HRD-positive	HRD-negative
 DEBORAH K ARMSTRONG, MD	Carbo/pac → niraparib	Carbo/pac OR carbo/pac → niraparib
 ROBERT L COLEMAN, MD	Carbo/pac + bev → bev + olaparib	Carbo/pac + bev → bev
 DON S DIZON, MD	Carbo/pac + bev → bev + olaparib	Carbo/pac + bev → niraparib
 PROFESSOR JONATHAN A LEDERMANN	Carbo/pac + bev → bev + olaparib	Carbo/pac + bev → bev
 URSULA MATULONIS, MD	Discuss several options with patient	Discuss several options with patient
 MANSOOR RAZA MIRZA, MD	Carbo/pac + bev → bev + olaparib	Carbo/pac → niraparib
 KATHLEEN MOORE, MD	Carbo/pac + bev → bev + olaparib	Carbo/pac + bev → bev
 SHANNON N WESTIN, MD, MPH	Carbo/pac + bev → bev + olaparib	Carbo/pac + bev → bev

Carbo/pac = carboplatin/paclitaxel; bev = bevacizumab

A 60-year-old woman with Stage IIIC ovarian cancer and a germline BRCA mutation undergoes suboptimal debulking surgery and receives carboplatin/paclitaxel followed by olaparib. For how long would you typically continue the olaparib if the patient is tolerating it well?

 DEBORAH K ARMSTRONG, MD	2 years (depends on disease status at completion of chemotherapy)
 ROBERT L COLEMAN, MD	2 years
 DON S DIZON, MD	Indefinitely
 PROFESSOR JONATHAN A LEDERMANN	2 years
 URSULA MATULONIS, MD	2 years
 MANSOOR RAZA MIRZA, MD	2 years
 KATHLEEN MOORE, MD	2 years
 SHANNON N WESTIN, MD, MPH	2 years

A 60-year-old woman with Stage IIIC ovarian cancer (BRCA wild type, HRD-positive) undergoes suboptimal debulking surgery and receives carboplatin/paclitaxel followed by niraparib. For how long would you typically continue the niraparib if the patient is tolerating it well?

 DEBORAH K ARMSTRONG, MD	3 years
 ROBERT L COLEMAN, MD	3 years
 DON S DIZON, MD	Indefinitely
 PROFESSOR JONATHAN A LEDERMANN	3 years
 URSULA MATULONIS, MD	3 years
 MANSOOR RAZA MIRZA, MD	3 years
 KATHLEEN MOORE, MD	3 years
 SHANNON N WESTIN, MD, MPH	3 years

Regulatory and reimbursement issues aside, which starting dose of niraparib would you use for a 125-lb patient with advanced ovarian cancer and a platelet count of 200,000 after a response to front-line platinum-based chemotherapy?

1. 300 mg daily
2. 200 mg daily
3. 100 mg daily
4. Other

RTP
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TO PRACTICE

What starting dose of niraparib would you use for a 125-lb patient with advanced ovarian cancer after response to front-line platinum-based chemotherapy with a platelet count of 200,000 for whom you are about to initiate maintenance niraparib?

 DEBORAH K ARMSTRONG, MD	200 mg daily
 ROBERT L COLEMAN, MD	200 mg daily
 DON S DIZON, MD	300 mg daily
 PROFESSOR JONATHAN A LEDERMANN	200 mg daily
 URSULA MATULONIS, MD	200 mg daily
 MANSOOR RAZA MIRZA, MD	200 mg daily
 KATHLEEN MOORE, MD	200 mg daily
 SHANNON N WESTIN, MD, MPH	200 mg daily

A woman in her mid-60s with recurrent high-grade serous ovarian cancer begins rucaparib monotherapy (600 mg BID). Within a few weeks her serum creatinine increases from 0.86 mg/dL to 1.6 mg/dL. What would be the optimal management approach?

 DEBORAH K ARMSTRONG, MD	Continue rucaparib at same dose
 ROBERT L COLEMAN, MD	Continue rucaparib at the same dose
 DON S DIZON, MD	Hold rucaparib until creatinine returns to normal, then restart at reduced dose
 PROFESSOR JONATHAN A LEDERMANN	Hold rucaparib until creatinine returns to normal, then restart at the same dose
 URSULA MATULONIS, MD	Continue rucaparib at the same dose
 MANSOOR RAZA MIRZA, MD	Hold rucaparib until creatinine returns to normal, then restart at the same dose
 KATHLEEN MOORE, MD	Continue rucaparib at the same dose
 SHANNON N WESTIN, MD, MPH	Continue rucaparib at the same dose

In general, what is your approach to antiemetic therapy for a patient with ovarian cancer who is starting treatment on a PARP inhibitor? Does your approach to antiemetic therapy differ according to which PARP inhibitor is administered?

	Antiemetic approach	Differ by PARPi?
 DEBORAH K ARMSTRONG, MD	Recommend antiemetic if pt has nausea	No
 ROBERT L COLEMAN, MD	Recommend antiemetic if pt has nausea	No
 DON S DIZON, MD	Prophylactic antiemetic prior to PARPi	No
 PROFESSOR JONATHAN A LEDERMANN	Recommend antiemetic if pt has nausea	No
 URSULA MATULONIS, MD	Recommend antiemetic if pt has nausea	Yes (cautious use of ondansetron w/niraparib as niraparib may also cause constipation)
 MANSOOR RAZA MIRZA, MD	Reduce PARPi dose if pt has nausea	No
 KATHLEEN MOORE, MD	Prophylactic antiemetic prior to PARPi for the first 2 months	No
 SHANNON N WESTIN, MD, MPH	Recommend antiemetic if pt has nausea	No

According to your clinical experience, do PARP inhibitors cause insomnia?

 DEBORAH K ARMSTRONG, MD	No
 ROBERT L COLEMAN, MD	Yes
 DON S DIZON, MD	No
 PROFESSOR JONATHAN A LEDERMANN	Yes
 URSULA MATULONIS, MD	Yes
 MANSOOR RAZA MIRZA, MD	No
 KATHLEEN MOORE, MD	Yes
 SHANNON N WESTIN, MD, MPH	Yes

A 70-year-old woman with advanced ovarian cancer and a germline BRCA mutation undergoes debulking surgery followed by chemotherapy with carboplatin/paclitaxel and experiences disease relapse 1 year later. Which treatment would you likely recommend?

 DEBORAH K ARMSTRONG, MD	Carboplatin/PLD → maintenance olaparib
 ROBERT L COLEMAN, MD	Carboplatin/PLD → maintenance rucaparib
 DON S DIZON, MD	Carboplatin/pac → maintenance olaparib
 PROFESSOR JONATHAN A LEDERMANN	Carboplatin/PLD → maintenance olaparib
 URSULA MATULONIS, MD	Carboplatin/PLD → maintenance olaparib
 MANSOOR RAZA MIRZA, MD	Carboplatin/PLD → maintenance niraparib
 KATHLEEN MOORE, MD	Carboplatin/PLD → maintenance olaparib
 SHANNON N WESTIN, MD, MPH	Carboplatin/pac + bevacizumab → maintenance olaparib

PLD = pegylated liposomal doxorubicin

A 70-year-old woman with advanced ovarian cancer (BRCA wild type, HRD-negative) undergoes debulking surgery followed by chemotherapy with carboplatin/paclitaxel and experiences disease relapse 1 year later. Which treatment would you likely recommend?

 DEBORAH K ARMSTRONG, MD	Carboplatin/PLD → maintenance rucaparib
 ROBERT L COLEMAN, MD	Carboplatin/PLD + bevacizumab → maintenance bevacizumab
 DON S DIZON, MD	Carboplatin/paclitaxel → maintenance niraparib
 PROFESSOR JONATHAN A LEDERMANN	Carboplatin/PLD → maintenance rucaparib
 URSULA MATULONIS, MD	Carboplatin/PLD → maintenance olaparib or niraparib
 MANSOOR RAZA MIRZA, MD	Carboplatin/PLD → maintenance niraparib
 KATHLEEN MOORE, MD	Carboplatin/PLD + bevacizumab → maintenance bevacizumab
 SHANNON N WESTIN, MD, MPH	Carboplatin/PLD + bevacizumab → maintenance bevacizumab

PARPi = PARP inhibitor

A 70-year-old woman with advanced ovarian cancer and a germline BRCA mutation undergoes debulking surgery, then receives carboplatin/paclitaxel/bevacizumab followed by maintenance therapy with a PARP inhibitor for 2 years and experiences disease relapse 1 year later. Which treatment would you likely recommend?

 DEBORAH K ARMSTRONG, MD	Carboplatin/PLD → maintenance rucaparib
 ROBERT L COLEMAN, MD	Carboplatin/PLD → maintenance rucaparib
 DON S DIZON, MD	Carboplatin/paclitaxel → alternate PARPi than previously received
 PROFESSOR JONATHAN A LEDERMANN	Carboplatin/PLD
 URSULA MATULONIS, MD	Carboplatin/PLD → maintenance olaparib considered if platinum sensitive
 MANSOOR RAZA MIRZA, MD	Carboplatin/PLD + bev → maintenance bev
 KATHLEEN MOORE, MD	Carboplatin/PLD → maintenance niraparib
 SHANNON N WESTIN, MD, MPH	Carboplatin/PLD → maintenance olaparib

PARPi = PARP inhibitor

A 70-year-old woman with advanced ovarian cancer (BRCA wild type, HRD-negative) undergoes debulking surgery, then receives carboplatin/paclitaxel/ bevacizumab followed by maintenance therapy with a PARP inhibitor for 2 years and experiences disease relapse 1 year later. Which treatment would you likely recommend?

 DEBORAH K ARMSTRONG, MD	Gemcitabine/cisplatin → maintenance rucaparib
 ROBERT L COLEMAN, MD	Carboplatin/PLD + bevacizumab → maintenance bevacizumab
 DON S DIZON, MD	Carboplatin/paclitaxel
 PROFESSOR JONATHAN A LEDERMANN	Carboplatin/PLD + bevacizumab → maintenance bevacizumab
 URSULA MATULONIS, MD	Carboplatin/PLD → maintenance olaparib
 MANSOOR RAZA MIRZA, MD	Carboplatin/PLD + bev → maintenance bev
 KATHLEEN MOORE, MD	Carboplatin/PLD + bevacizumab → maintenance bevacizumab
 SHANNON N WESTIN, MD, MPH	Carboplatin/PLD + bevacizumab → maintenance bevacizumab

A 70-year-old woman with advanced ovarian cancer (BRCA wild type, HRD-positive) undergoes debulking surgery, then receives carboplatin/paclitaxel/bevacizumab followed by maintenance therapy with a PARP inhibitor for 2 years and experiences disease relapse 1 year later. Which treatment would you likely recommend?

 DEBORAH K ARMSTRONG, MD	Carboplatin/PLD
 ROBERT L COLEMAN, MD	Carboplatin/PLD → maintenance rucaparib
 DON S DIZON, MD	Carboplatin/paclitaxel → alternate PARPi than previously received
 PROFESSOR JONATHAN A LEDERMANN	Carboplatin/PLD
 URSULA MATULONIS, MD	Carboplatin/PLD → maintenance olaparib considered if platinum sensitive
 MANSOOR RAZA MIRZA, MD	Carboplatin/PLD + bev → maintenance bev
 KATHLEEN MOORE, MD	Carboplatin/PLD → maintenance olaparib
 SHANNON N WESTIN, MD, MPH	Carbo/pac → maintenance niraparib *OR* Carbo/PLD → maintenance niraparib

Outside of a clinical trial, have you used or would you use a second PARP inhibitor or continue the same PARP inhibitor for a patient with ovarian cancer who experienced disease progression on a PARP inhibitor?

 DEBORAH K ARMSTRONG, MD	I have
 ROBERT L COLEMAN, MD	I have but would not again
 DON S DIZON, MD	I have
 PROFESSOR JONATHAN A LEDERMANN	I have
 URSULA MATULONIS, MD	I have
 MANSOOR RAZA MIRZA, MD	I have not and would not
 KATHLEEN MOORE, MD	I have
 SHANNON N WESTIN, MD, MPH	I have

Meet The Professor with Dr Matulonis

MODULE 1: Cases from Dr Mirza

- Questions and Comments: BRCA testing
- A 53-year-old woman with Stage IIIC high-grade serous ovarian cancer (HGSOC) – BRCA mutation
- A 53-year-old woman with Stage IIIC HGSOC – BRCA wild type, HR proficient
- A 53-year-old woman with Stage IIIC HGSOC – BRCA wild type, HR deficient
- Questions and Comments: Management of PARPi-associated low-grade nausea
- Questions and Comments: Niraparib dosing
- Questions and Comments: Management of PARPi-associated hypertension
- A 65-year-old woman with relapsed ovarian cancer – BRCA wild type, HR status unknown
- Questions and Comments: Defining platinum sensitivity

MODULE 2: Journal Club with Dr Matulonis

- ASCO guidelines: PARP inhibitors in the management of ovarian cancer
- ESMO 2020: IMagyn050 Phase III trial of bevacizumab-containing therapy with or without atezolizumab
- Homologous recombination deficiency real-time clinical assays, ready or not?
- PARP inhibitor resistance mechanisms and post-progression combination therapies
- Single-cell landscape of HGSOC

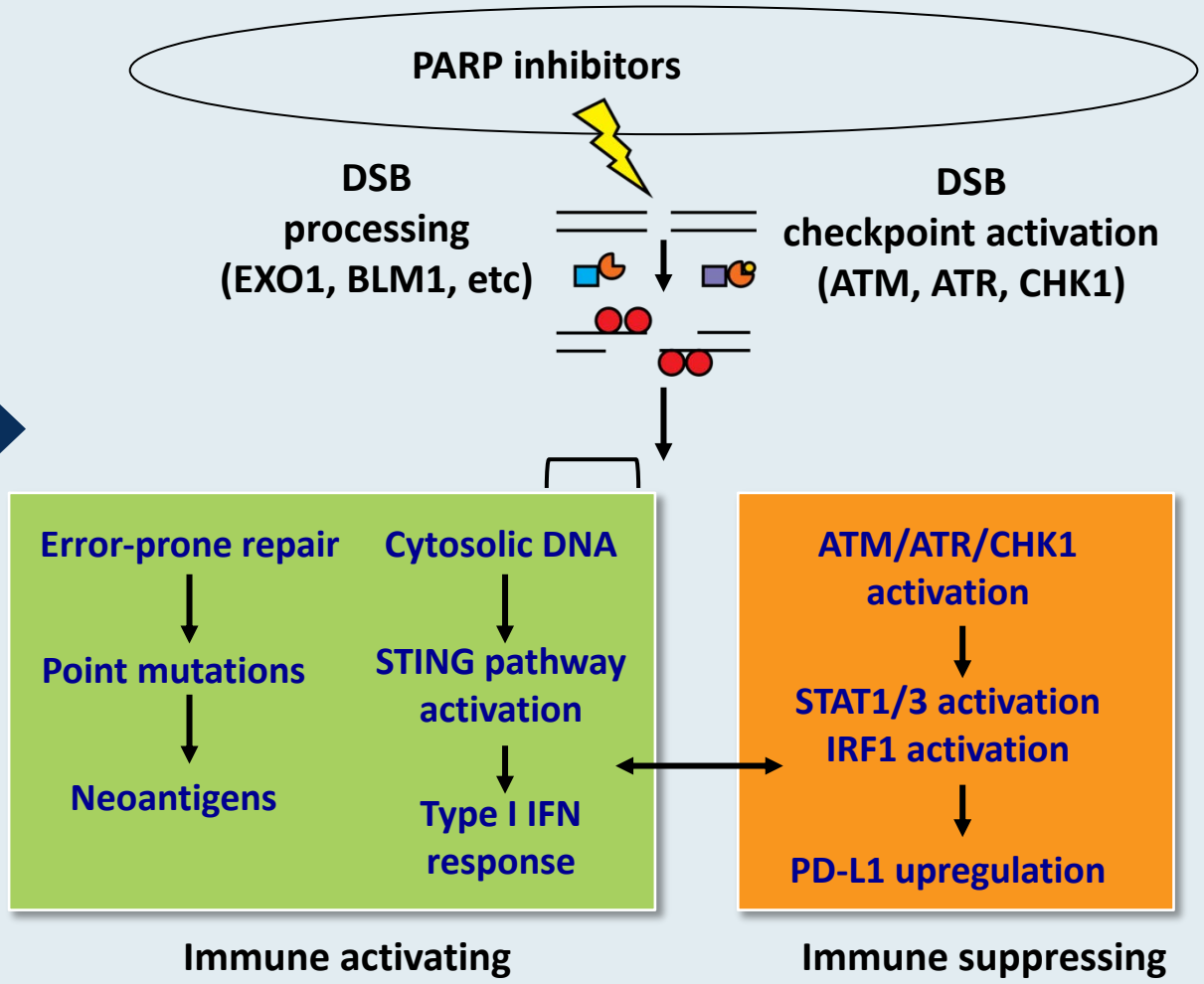
MODULE 3: Beyond the Guidelines – Clinical Investigator Approaches to Common Clinical Scenarios

MODULE 4: Key Recent Papers

RTP RESEARCH TO PRACTICE

Biologic Rationale for the Combination of a PARP Inhibitor with an Immune Checkpoint Inhibitor

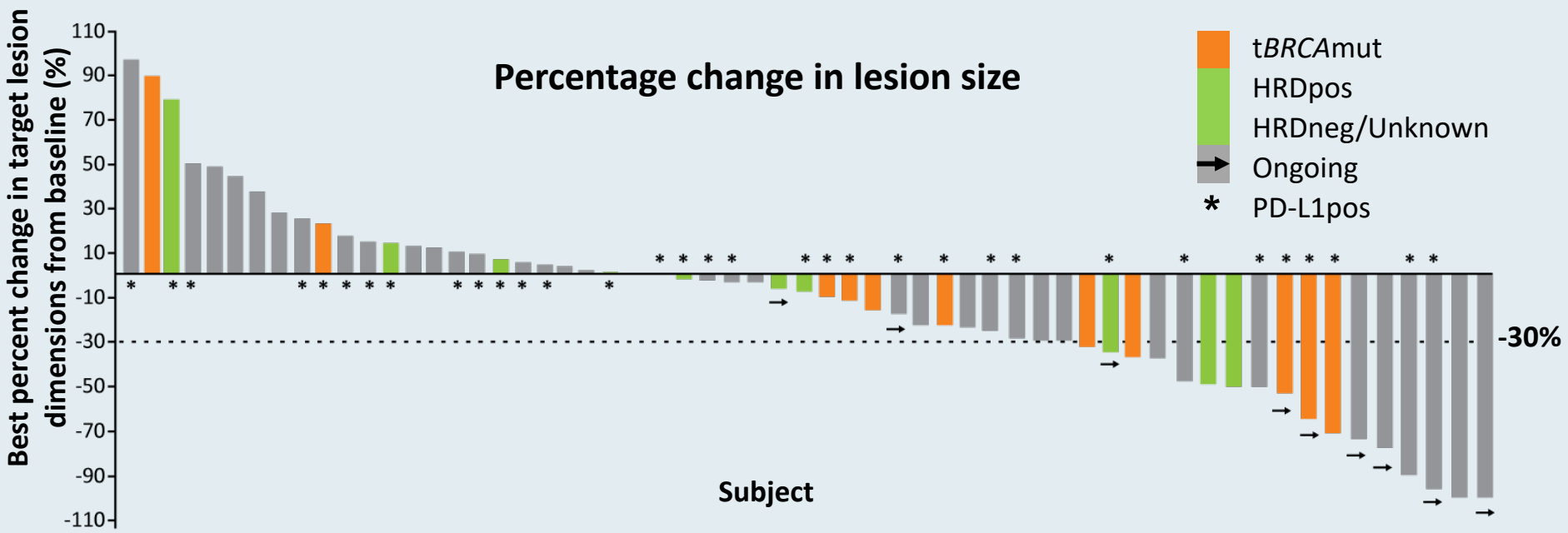
Preclinical models indicate synergy between PARPi + anti-PD-1 agents regardless of *BRCA* mutation status or PD-L1 status



Preclinical data demonstrate synergy with PARPi and anti-PD-1 combinations.

Konstantinopoulos P et al. ASCO 2018;Abstract 106.

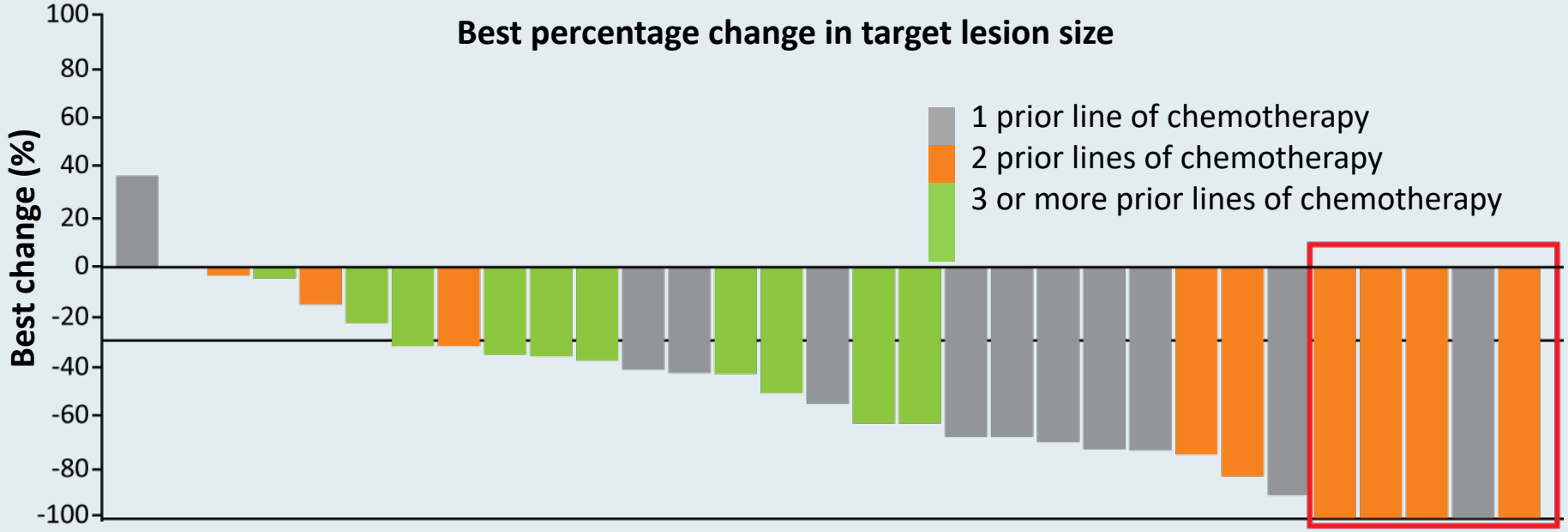
TOPACIO (KEYNOTE-162): A Phase I/II Study of Niraparib with Pembrolizumab in Recurrent, Platinum-Resistant OC



Response	All patients	tBRCAmut	HRD-pos	tBRCAwt	HRD-neg
ORR	11/47 (23%)	2/8 (25%)	4/16 (25%)	9/37 (24%)	7/26 (27%)
DCR	30/47 (64%)	5/8 (63%)	11/16 (69%)	24/37 (65%)	15/26 (58%)

Konstantinopoulos P et al. ASCO 2018;Abstract 106.

MEDIOLA: A Phase I/II Study of Olaparib and Durvalumab in Recurrent, Platinum-Sensitive OC with gBRCA Mutation

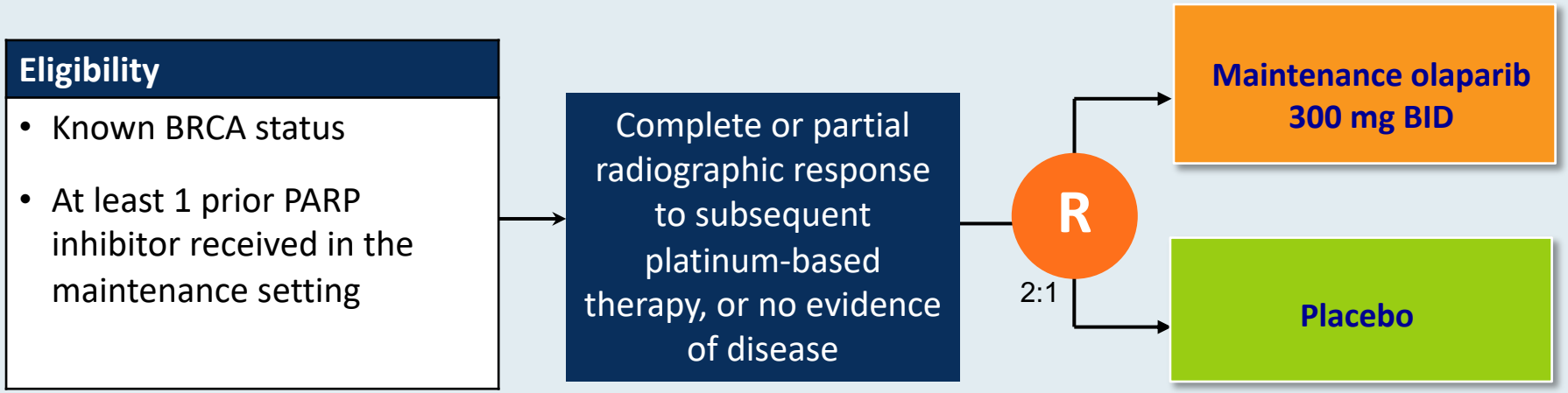


	Second line	Third line	Fourth line	All lines
ORR	10/13 (77%)	6/9 (67%)	7/10 (70%)	23/32 (72%)

Drew Y et al. SGO 2018;Abstract LBA4.

OReO/ENGOT Ov-38: A Phase IIIb Trial of Olaparib Maintenance Retreatment in Patients with EOC Previously Treated with a PARP Inhibitor and Responding to Repeat Platinum Chemotherapy

NCT03106987



Primary endpoint: Investigator-assessed progression-free survival

www.clinicaltrials.gov; Accessed August 2020.

Select Ongoing or Planned Phase III Trials of PARP Inhibitors in Combination Therapy

Trial name (Trial identifier)	N	Setting	Treatment arms
ATHENA (NCT03522246)	1,012	Maintenance therapy after 1L platinum-based chemo	• **Rucaparib** + Nivolumab • **Rucaparib** + Placebo • Nivolumab + Placebo • Placebo
DUO-O (NCT03737643)	1,056	Maintenance therapy after 1L platinum-based chemo/Bev ± Durvalumab	• Bev • Bev + Durvalumab • Bev + Durvalumab + **Olaparib**
NRG-GY004 (NCT02446600)	549	Recurrent, platinum-sensitive	• Platinum-based chemo • **Olaparib** • **Olaparib** + Cediranib
ANITA (NCT03598270)	414	Recurrent, platinum-sensitive	• Placebo + Platinum-based chemo → **Niraparib** • ATEZO + Platinum-based chemo → **Niraparib** + ATEZO

Bev = bevacizumab; ATEZO = atezolizumab

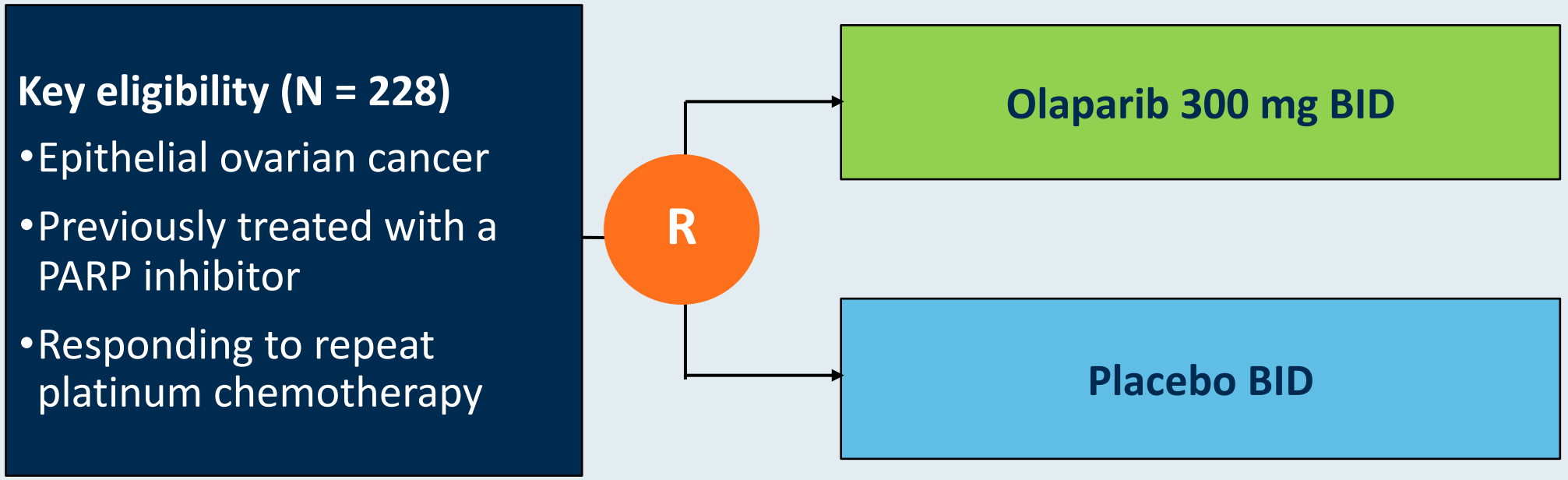
www.clinicaltrials.gov. Accessed December 2018.

The Incidence of Myelodysplastic Syndrome in Patients Receiving Poly-ADP Ribose Polymerase Inhibitors for Treatment of Solid Tumors: A Meta-analysis

Nitecki R et al.

ASCO 2020;Abstract 3641.

OReO/ENGOT Ov-38 Phase III Study Design



Primary endpoint: Progression-free survival

Clinicaltrials.gov, Accessed September 10, 2020 (NCT03106987)

BRCA1/2 Mutations in Ovarian Cancer: Who Should Be Tested?

NCCN[1]

Genetic counseling and testing should be considered for women with a history of ovarian carcinoma, fallopian tube or primary peritoneal cancer

SGO[2]

Women diagnosed with epithelial ovarian, tubal and peritoneal cancers should receive genetic counseling and be offered genetic testing even in the absence of family history

ASCO[3]

Genetic counseling and testing should be considered for women with epithelial ovarian, fallopian tube or primary peritoneal cancer even in the absence of family history

NCCN = National Comprehensive Cancer Network; SGO = Society of Gynecologic Oncology;
ASCO = American Society of Clinical Oncology

1. NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) for Genetic/Familial High-Risk Assessment: Breast and Ovarian V2.2019.

2. Lancaster JM et al. *Gynecol Oncol* 2015;136(1):3-7.

3. Lu KH et al. *J Clin Oncol* 2014;32(8):833-40.

Multigene Panel Testing

Advantages

- More “diagnoses”
- More cost effective
- More time efficient
- Higher mutational detection rate
- Efficient use of single specimen
- Decrease in testing fatigue for patients and providers

Disadvantages

- Cancer risk and management options often not well defined for low- and moderate-penetrance genes
- High uncertain variant rate
- Longer turnaround time
- Panels may include genes that patients don’t want to test for
- Unexpected findings such as “off-phenotypic-target” gene mutation
- Increased prevalence of VUS

Lynce F, Isaacs C. *ASCO Educational Book* 2016:72-8.

Current FDA-Approved and Investigational PARP Inhibitors: Differences

PARP inhibitor	IC_{50}	PARP trapping potency	PARPi target selectivity (strength of binding)	Half life	Dose
Olaparib	6 nM	1	Potent PARP1 inhibitor, less selective	11.9 hours	400 mg BID
Rucaparib	21 nM	1	Potent PARP1 inhibitor, less selective	18 hours	600 mg BID
Niraparib	60 nM	~2	Selective inhibitor of PARP1 and 2	36 hours	300 mg qd
Veliparib	30 nM	<0.2	Potent PARP1 inhibitor, less selective	5 hours	400 mg BID
Talazoparib	4 nM	~100	Potent PARP1 inhibitor, less selective	50 hours	1 mg qd

Lim JSJ, Tan DSP. *Cancers* 2017;9(8):pii:E109.

RTP RESEARCH TO PRACTICE

Phase III First-Line Maintenance Trials

Study Design	SOLO-1 (N=451)	PAOLA-1 (N=612)	PRIMA (N=620)	VELIA (N=1140)
Treatment arms vs placebo	**Olaparib (n=260)**	**Bevacizumab ± Olaparib**	**Niraparib**	**Veliparib**
Patient Population	*BRCA* mutation	All comers	All comers	*All comers*
Treatment Duration	24 months	15 months for Bev 24 months for Olaparib	36 months or until PD	24 months

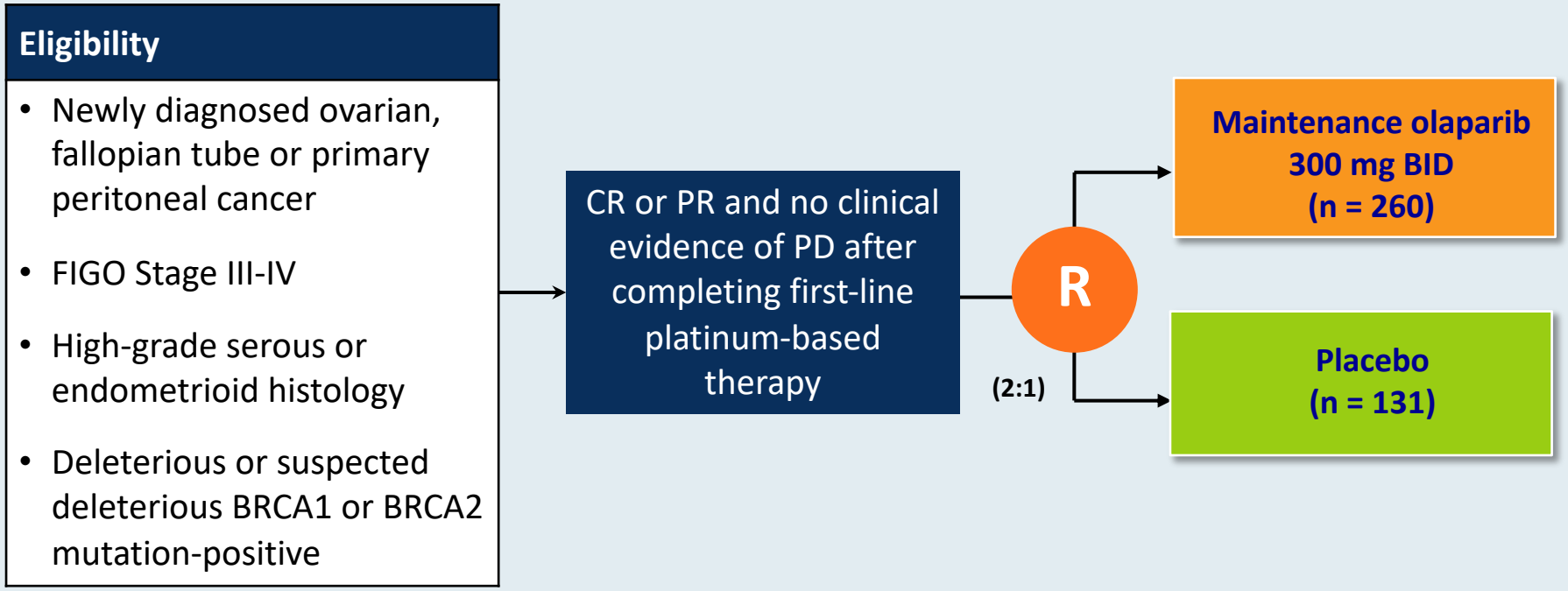
[a]Residual disease based on stage was not reported. [b]Stage III and IV eligible, but requirements for prior surgery not reported (NR) on clinicaltrials.gov

Burger RA, *N Engl J Med* 2011; Norquist B *Clin Cancer Res* 2018*; Bevacizumab* prescribing information; Moore K, NEJM 2018; Gonzalez-Martin NEJM 2019; Ray-Coquard NEJM 2019; Coleman NEJM 2019

Courtesy of Shannon N Westin, MD, MPH

SOLO-1: A Phase III Trial of Maintenance Olaparib in OC with BRCA Mutation

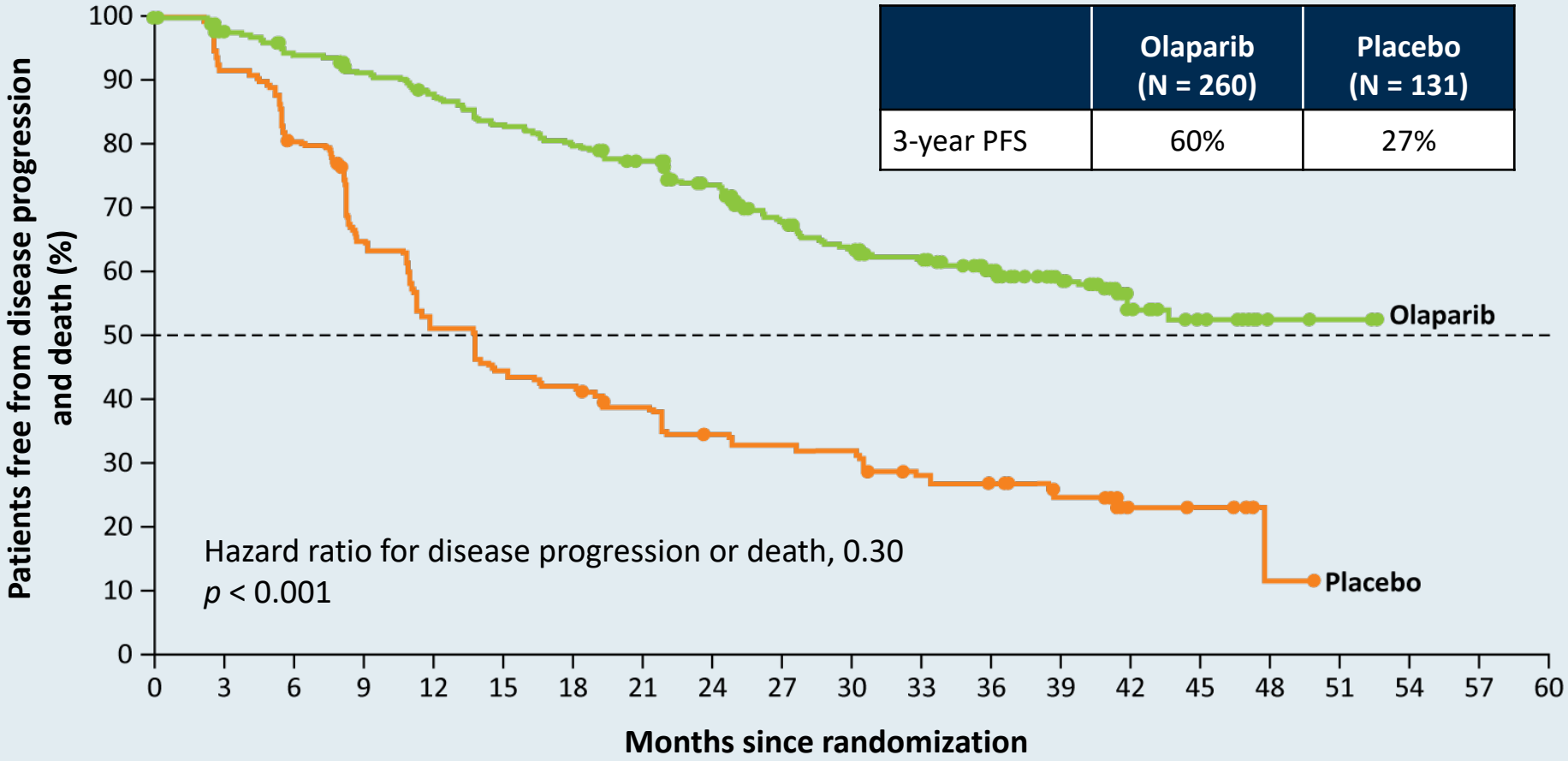
NCT01844986



Primary endpoint: Investigator-assessed progression-free survival

www.clinicaltrials.gov; Moore KN et al. ASCO 2014;Abstract TPS5616; Moore K et al. *N Engl J Med* 2018;[Online ahead of print].

SOLO-1: Primary Endpoint Progression-Free Survival (Investigator Assessed)

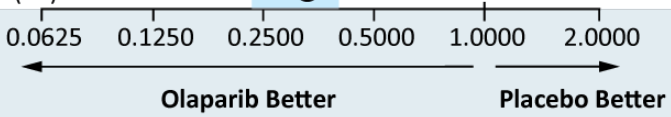


	Olaparib (N = 260)	Placebo (N = 131)
3-year PFS	60%	27%

Moore K et al. *N Engl J Med* 2018;[Online ahead of print].

SOLO-1: PFS Subgroup Analyses

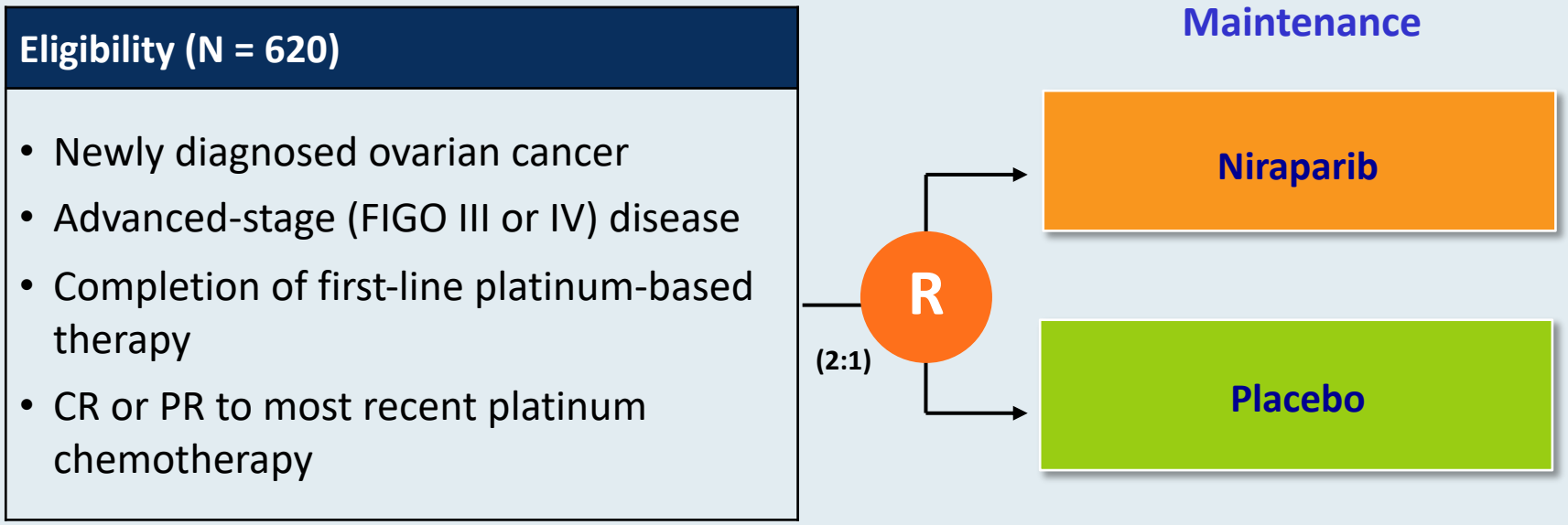
Subgroup	Olaparib	Placebo	Hazard Ratio for Disease Progression or Death
	no. of patients with disease progression or death/total no. (%)		
All patients	102/260 (39)	96/131 (73)	0.30
Clinical response after chemotherapy			
Complete response	73/213 (34)	73/107 (68)	0.35
Partial response	29/47 (62)	23/24 (96)	0.19
ECOG performance status at baseline			
Normal activity	75/200 (38)	76/105 (72)	0.33
Restricted activity	27/60 (45)	20/25 (80)	0.38
CA-125 level at baseline			
≤ULN	92/247 (37)	89/123 (72)	0.34
>ULN	10/13 (77)	7/7 (100)	NC
Germline BRCA mutation according to testing at Myriad			
BRCA1	84/188 (45)	69/91 (76)	0.40
BRCA2	15/62 (24)	26/39 (67)	0.20
BRCA1 and BRCA2	0/3	0/0	NC
None	3/7 (43)	1/1 (100)	NC
Age at baseline			
<65 yr	85/225 (38)	82/112 (73)	0.33
≥65 yr	17/35 (49)	14/19 (74)	0.45
International FIGO stage at initial diagnosis			
Stage III	83/220 (38)	79/105 (75)	0.32
Stage IV	19/40 (48)	17/26 (65)	0.49
Presence of residual macroscopic disease after debulking surgery performed before trial entry			
Yes	29/55 (53)	23/29 (79)	0.44
No	70/200 (35)	69/98 (70)	0.33



Moore K et al. *N Engl J Med* 2018;[Online ahead of print].

RTP RESEARCH TO PRACTICE

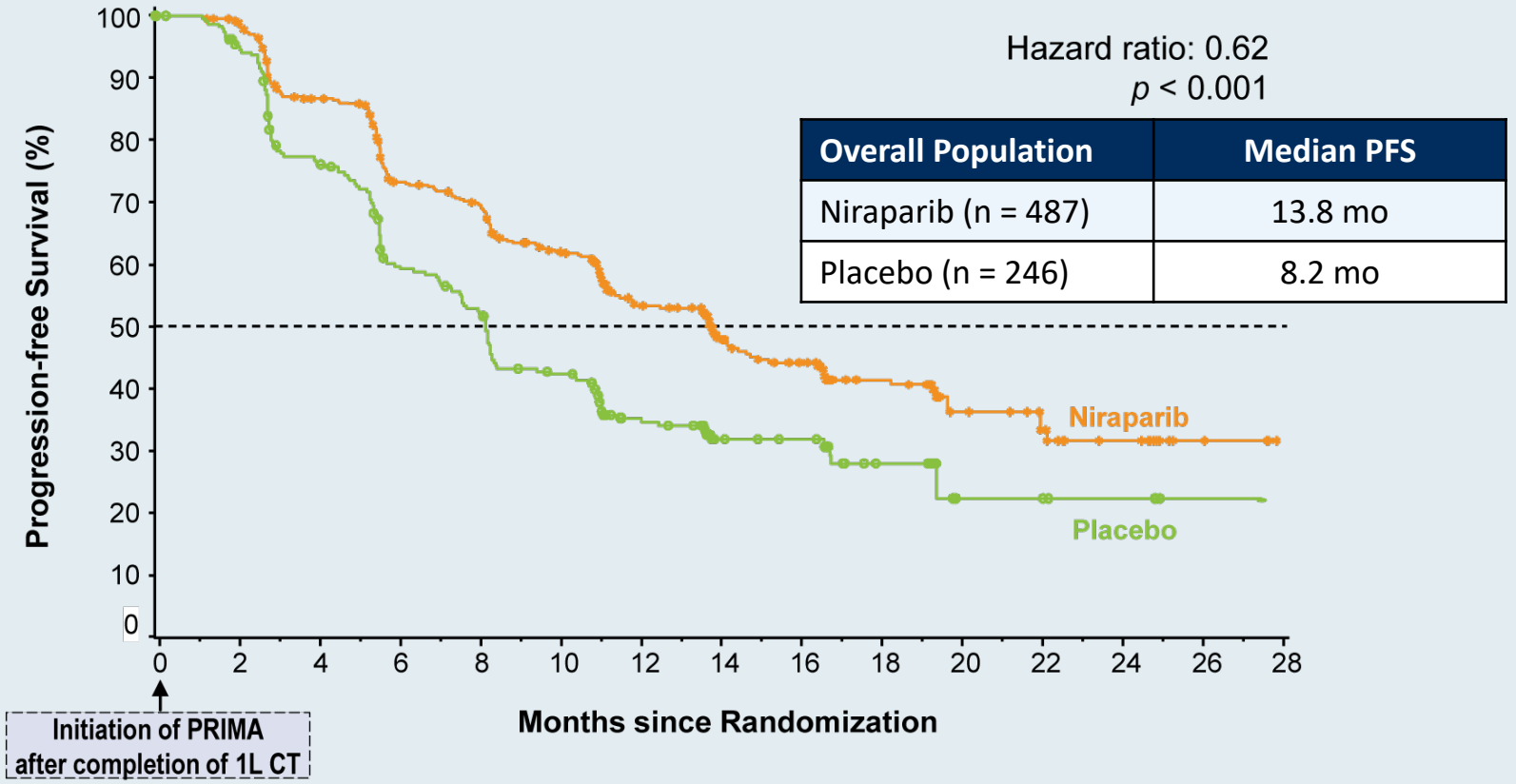
PRIMA Trial: Maintenance Niraparib for Advanced Ovarian Cancer After Response to Front-Line Platinum-Based Chemotherapy



Primary endpoint: Progression-free survival

Gonzalez-Martin A et al. ESMO 2018;Abstract 941PD.

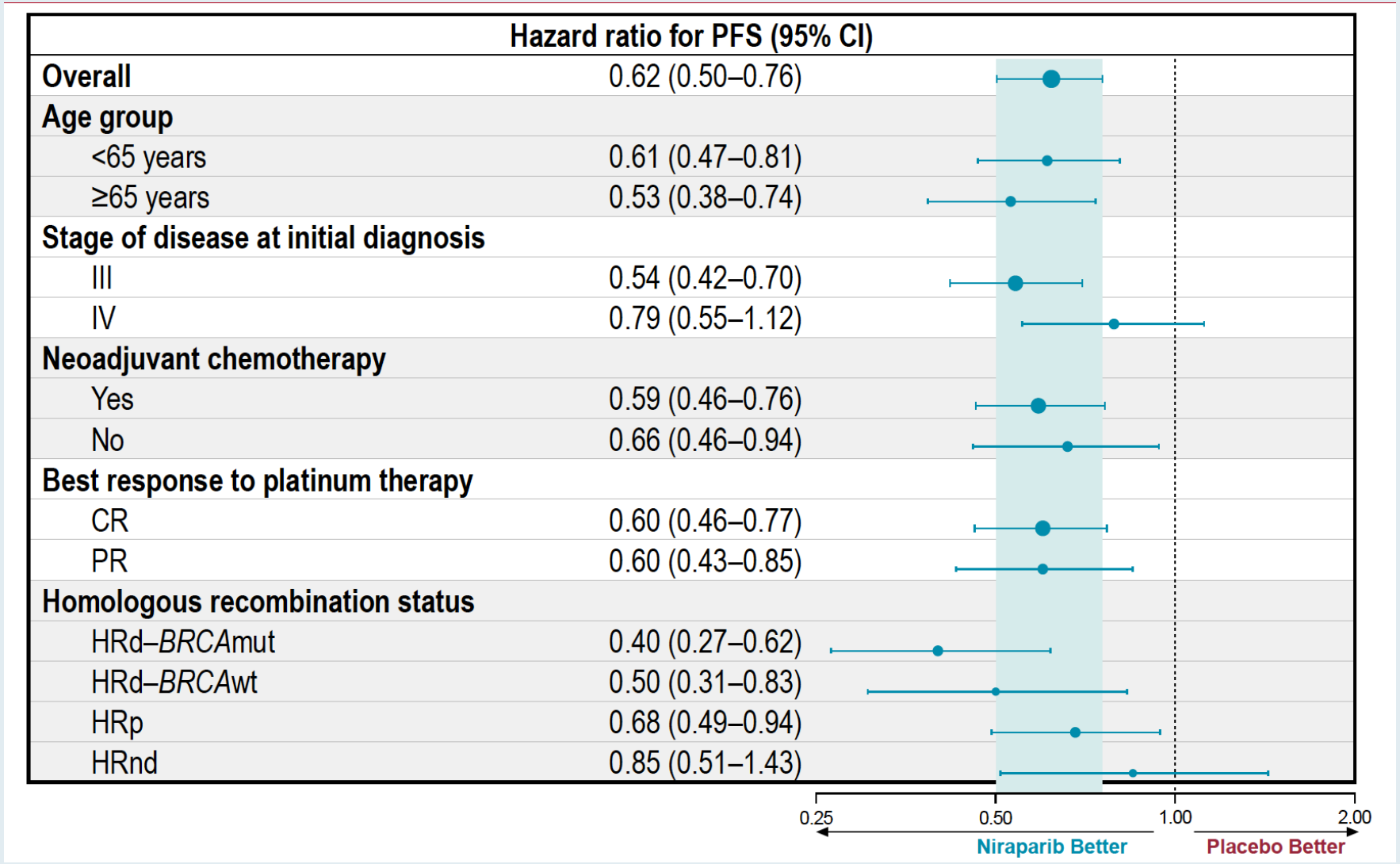
PRIMA Primary Endpoint: Progression-Free Survival



- Median PFS in the HR-deficient population was 21.9 mo for niraparib and 10.4 mo for placebo (HR 0.43, $p < 0.001$).
- No new safety signals were identified for niraparib.

Gonzalez-Martin A et al. ESMO 2019;Abstract LBA1.

PRIMA: Progression-Free Survival Subgroup Analysis



Gonzalez-Martin A et al. ESMO 2019;Abstract LBA1.

FDA approves olaparib plus bevacizumab as maintenance treatment for ovarian, fallopian tube, or primary peritoneal cancers

Press Release – May 28, 2020

"The Food and Drug Administration expanded the indication of olaparib to include its combination with bevacizumab for first-line maintenance treatment of adult patients with advanced epithelial ovarian, fallopian tube, or primary peritoneal cancer who are in complete or partial response to first-line platinum-based chemotherapy and whose cancer is associated with homologous recombination deficiency positive status defined by either a deleterious or suspected deleterious *BRCA* mutation, and/or genomic instability.

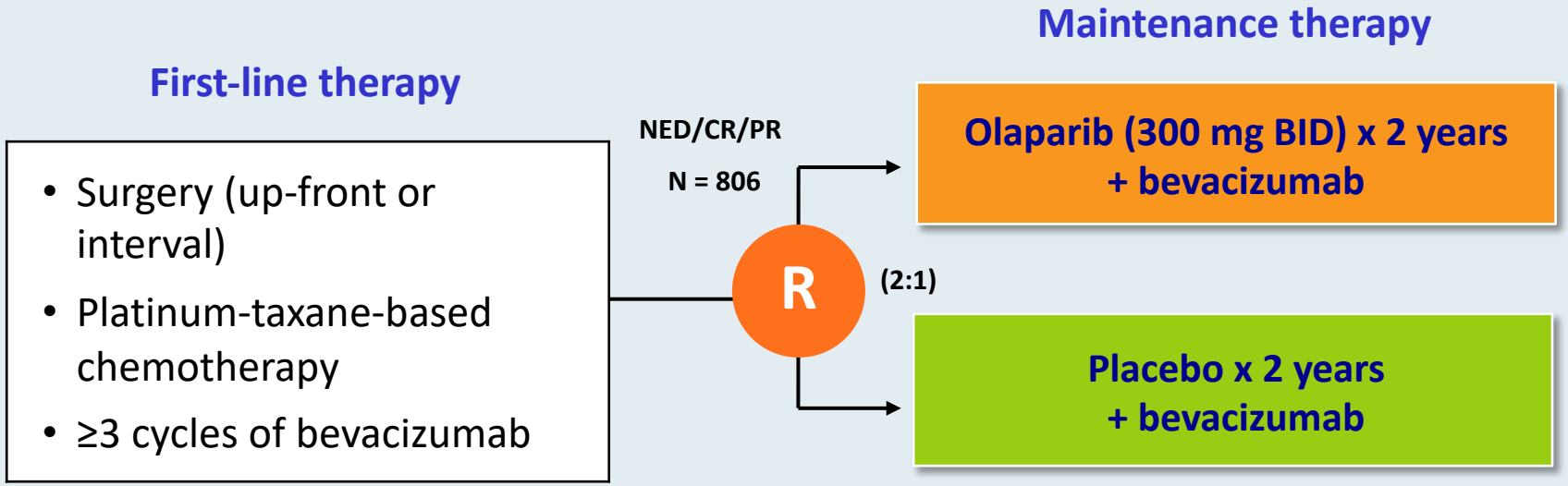
FDA also approved the Myriad myChoice® CDx (Myriad Genetic Laboratories, Inc.) as a companion diagnostic for olaparib.

Efficacy of this new indication was investigated in PAOLA-1 (NCT03737643), a randomized, double-blind, placebo-controlled, multi-center trial comparing olaparib with bevacizumab versus placebo plus bevacizumab in patients with advanced high-grade epithelial ovarian cancer, fallopian tube, or primary peritoneal cancer following first-line platinum-based chemotherapy and bevacizumab."

https://www.fda.gov/drugs/drug-approvals-and-databases/fda-approves-olaparib-plus-bevacizumab-maintenance-treatment-ovarian-fallopian-tube-or-primary

PAOLA-1 Trial: Maintenance Olaparib with Bevacizumab for Advanced Ovarian Cancer After Response to Front-Line Platinum-Based Chemotherapy and Bevacizumab

Newly diagnosed FIGO Stage III or IV high-grade serous/endometrioid ovarian, fallopian tube or primary peritoneal cancer

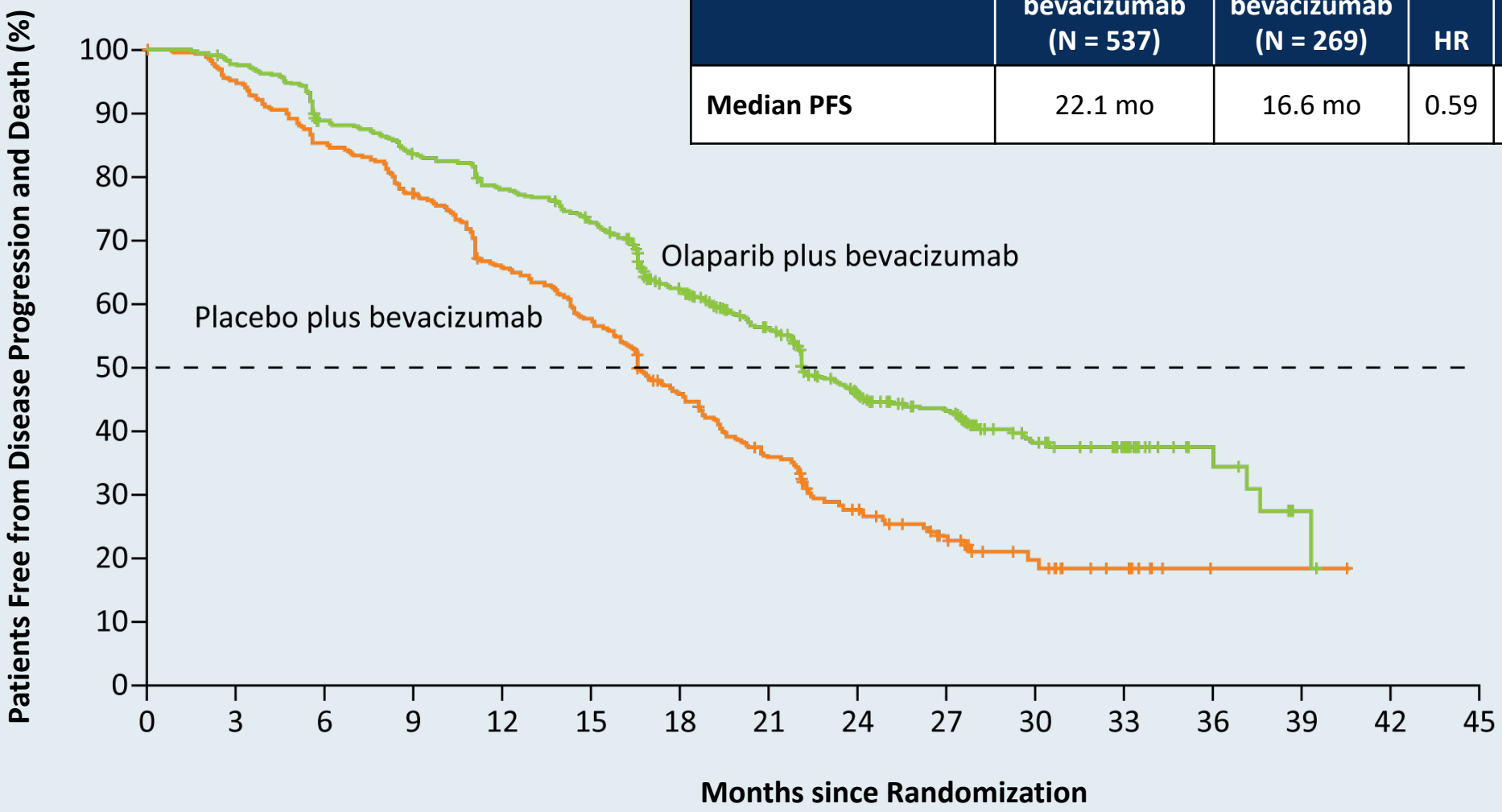


Ray-Coquard I et al. ESMO 2019;Abstract LBA2.

RTP RESEARCH TO PRACTICE

PAOLA-1: Investigator-Assessed PFS (Primary Endpoint)

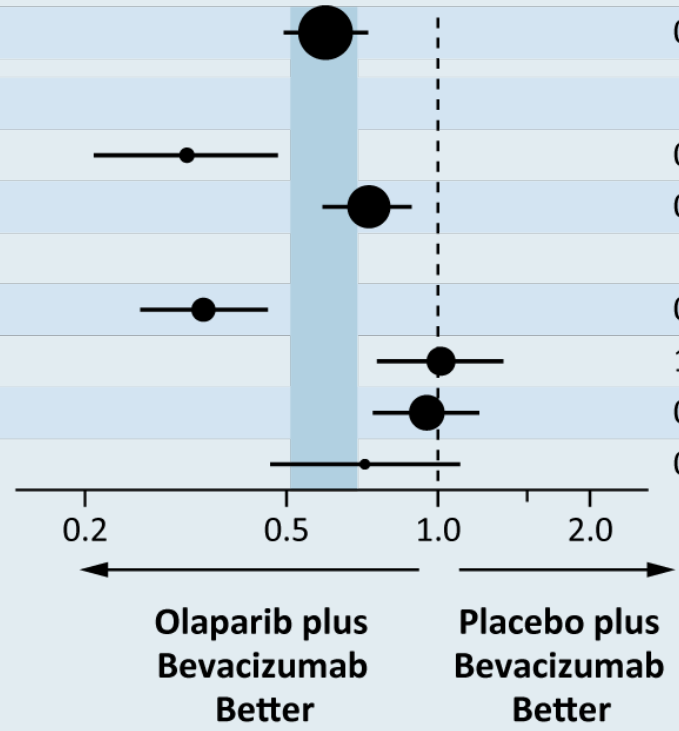
	Olaparib + bevacizumab (N = 537)	Placebo + bevacizumab (N = 269)	HR	*p*-value
Median PFS	22.1 mo	16.6 mo	0.59	<0.001



Ray-Coquard I et al. *NEJM* 2019;381:2416-28.

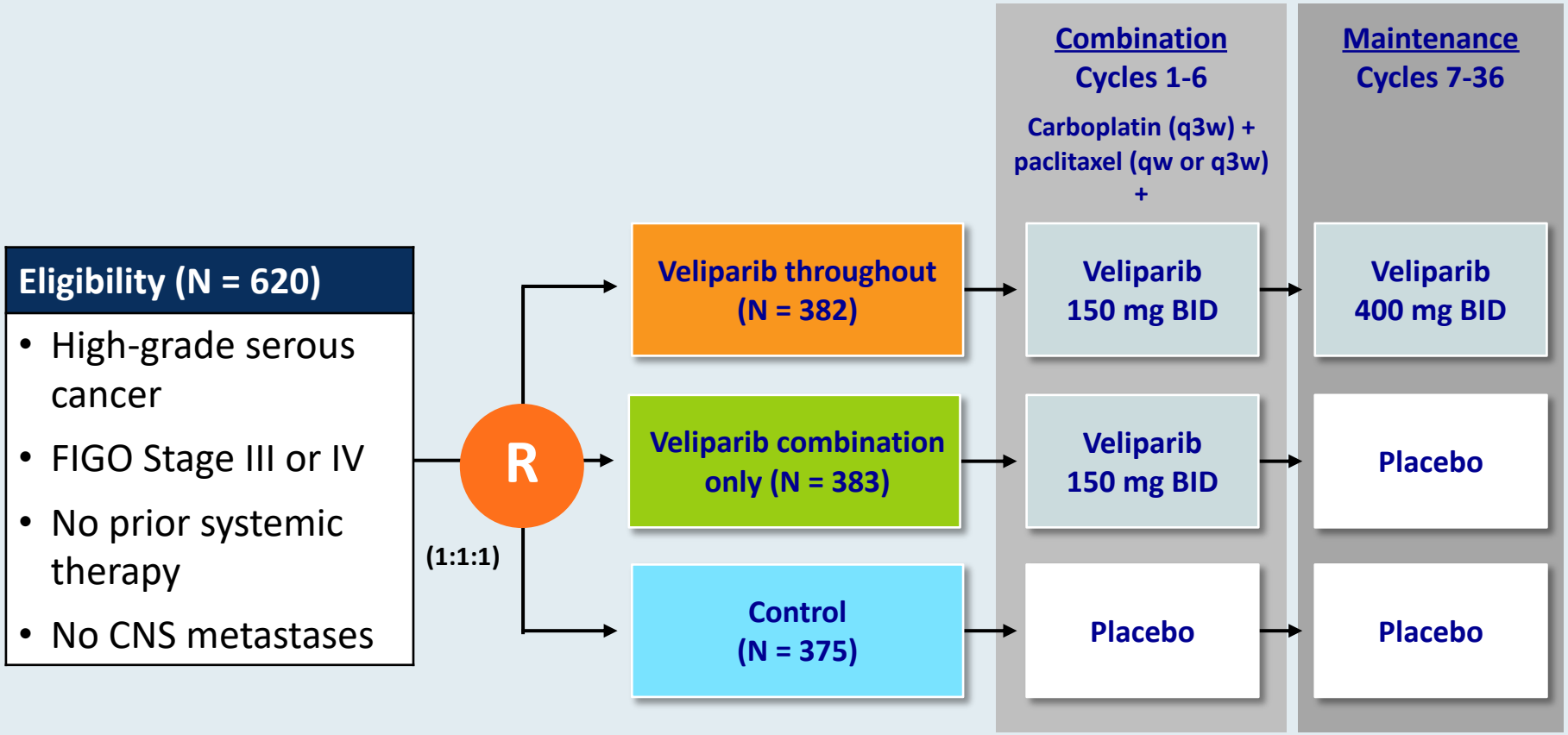
PAOLA-1: Select Subgroup Analysis of PFS

Subgroup	Olaparib plus Bevacizumab	Placebo plus Bevacizumab	Hazard Ratio for Disease Progression or Death (95% CI)
	no. of patients with disease progression or death/total no. (%)		
All patients	280/537 (52)	194/269 (72)	0.59 (0.49–0.72)
Tumor BRCA mutation status			
BRCA mutation	41/157 (26)	49/80 (61)	0.31 (0.20–0.47)
No BRCA mutation or unknown	239/380 (63)	145/189 (77)	0.71 (0.58–0.88)
Tumor HRD status			
Positive	87/255 (34)	92/132 (70)	0.33 (0.25–0.45)
Negative	145/192 (76)	66/85 (78)	1.00 (0.75–1.35)
Negative or unknown	193/282 (68)	102/137 (74)	0.92 (0.72–1.17)
Unknown	48/90 (53)	36/52 (69)	0.71 (0.46–1.10)



Ray-Coquard I et al. *NEJM* 2019;381:2416-28.

VELIA/GOG-3005: A Phase III Trial of Veliparib with Front-Line Chemotherapy and as Maintenance Therapy for High-Grade Serous Epithelial Ovarian, Fallopian Tube or Primary Peritoneal Cancers

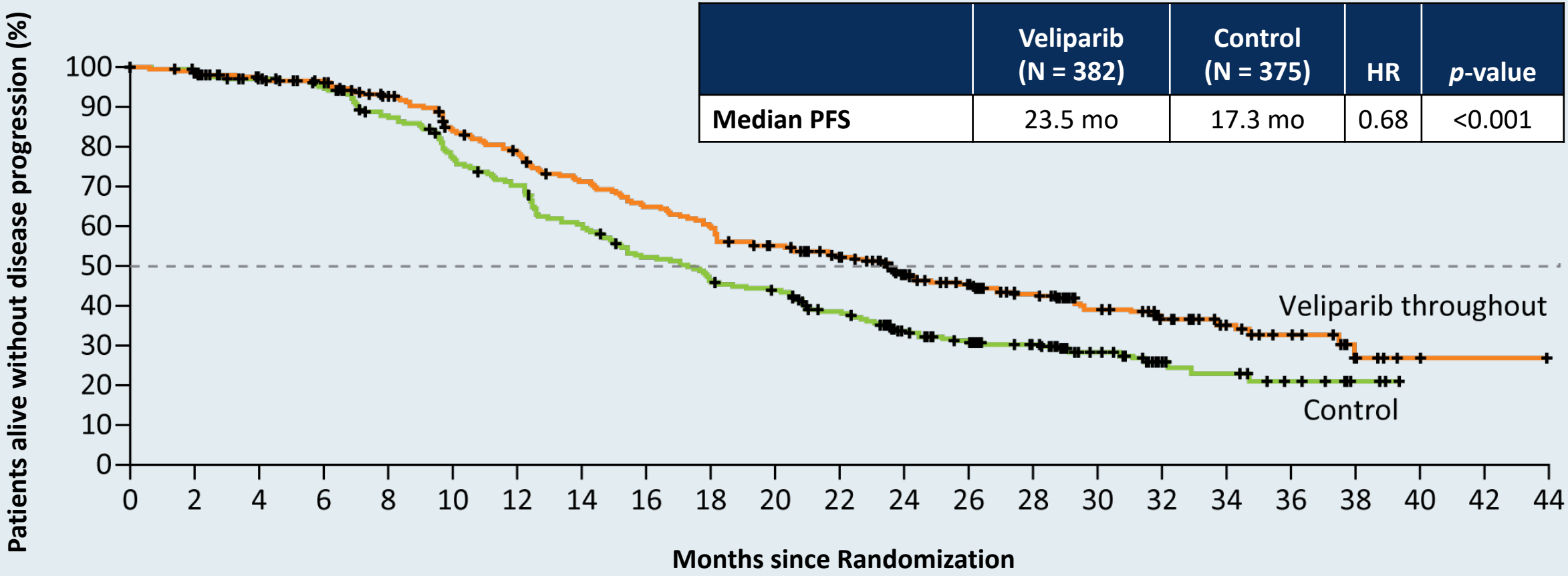


Primary endpoint: Progression-free survival for "veliparib throughout" versus control

Coleman RL et al. ESMO 2019;Abstract LBA3.

VELIA/GOG-3005: Investigator-Assessed PFS

	Veliparib (N = 382)	Control (N = 375)	HR	*p*-value
Median PFS	23.5 mo	17.3 mo	0.68	<0.001

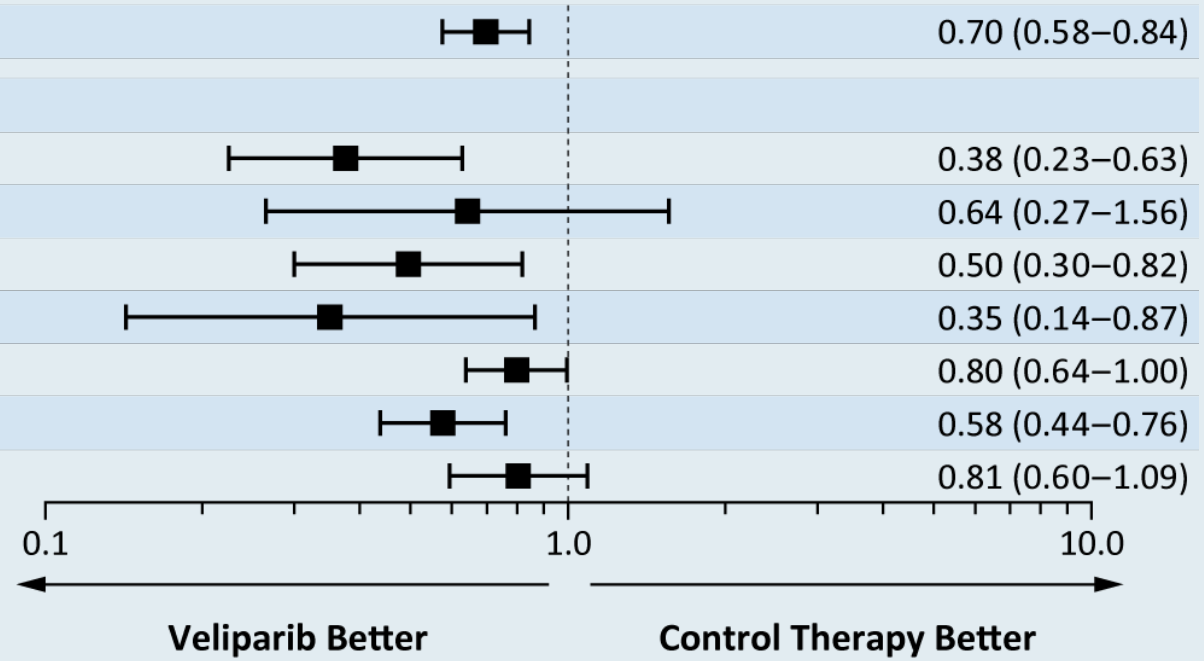


Coleman RL et al. *N Engl J Med* 2019;381:2403-15.

RTP RESEARCH TO PRACTICE

VELIA/GOG-3005: Select Subgroup Analyses of PFS

Subgroup	Veliparib	Control
	no. of patients with events/total no.	
All patients	191/382	237/375
Mutation status		
BRCA1	26/78	36/59
BRCA2	8/30	13/31
Germline BRCA	27/80	36/63
Tissue-based BRCA	7/28	15/29
Nonmutated BRCA	142/245	171/254
HRD-positive	87/214	124/207
HRD-negative	80/125	89/124



Coleman RL et al. *N Engl J Med* 2019;381:2403-15.

RTP RESEARCH TO PRACTICE

VELIA/GOG-3005: Integration of Veliparib with Front-Line Chemotherapy and Maintenance in Women with High-Grade Serous Carcinoma of Ovarian, Fallopian Tube, or Primary Peritoneal Origin

Coleman RL et al.

SGO 2020;Abstract 36.

Ongoing Phase III Clinical Trials of PARP Inhibitors as Maintenance After First-Line Therapy

Trial name (trial identifier)	N	Eligibility	First-line treatment	Maintenance treatment arms
FIRST (NCT03602859)	960	• BRCA mut or wt • Stage III or IV • Surgery or inoperable	• Platinum-based chemo • Platinum-based chemo + TSR-042	• Niraparib + TSR-042 • Niraparib + placebo • Placebo + placebo
ATHENA (NCT03522246)	1,012	• BRCA mut or wt • Stage III or IV • Prior surgery	• Platinum-based chemo	• Rucaparib + nivolumab • Rucaparib + placebo • Placebo + nivolumab • Placebo + placebo

www.clinicaltrials.gov. Accessed December 2018.

RTP RESEARCH TO PRACTICE

Adverse Events: Class Effects and Specific Drug Differences

	Notes	Olaparib	Niraparib	Rucaparib	Talazoparib	Veliparib
Fatigue	50%-70%, mainly Gr1-2	✓	✓	✓	✓	✓
Hematologic AEs						
Anemia	40%-60%	✓	✓	✓	✓	✓ --
Thrombocytopenia	Niraparib dose adjustment, based on platelet counts	✓	✓ ++	✓	✓	✓
Neutropenia	~20%	✓	✓	✓	✓	✓
Gastrointestinal AEs						
Nausea/vomiting	Moderately emetic >30%	✓	✓	✓	✓	✓
Diarrhea	~33%	✓	✓	✓	✓	✓
Laboratory abnormalities						
ALT/AST elevation	5%-10% olaparib, niraparib; 34% rucaparib	✓ --	✓ --	✓ ++	✓ ++	?
Creatinine elevation	10%-12%	✓	✓	✓	NR	NR

NR = not reported

Olaparib PI, rev 5/2020; Niraparib PI, rev 4/2020; Rucaparib PI, rev 5/2020; Talazoparib PI, rev 3/2020;
Madariaga A et al. *Int J Gyn Cancer* 2020 April 9;[Online ahead of print]; Litton JK et al. *NEJM* 2018;379:753-63.

Adverse Events: Class Effects and Specific Drug Differences

	Notes	Olaparib	Niraparib	Rucaparib	Talazoparib	Veliparib
Respiratory disorders						
Dyspnea +/- cough	10%-20%, usually Gr 1-2	✓	✓	✓	✓	NR
Nasopharyngitis	~10%	✓	✓	✓	✓	NR
Nervous system and psychiatric disorders						
Insomnia/headache	10%-25%, usually Gr 1-2	✓	✓	✓	✓	✓
Dermatologic toxicity						
Rash, photosensitivity		<1%	✓	✓++	NR	NR
Cardiovascular toxicity						
Hypertension, tachycardia, palpitation		1%	✓++	NR	NR	NR
Rare AEs						
MDS/AML	~1% of pts	✓	✓	✓	✓	✓

NR = not reported

Olaparib PI, rev 5/2020; Niraparib PI, rev 4/2020; Rucaparib PI, rev 5/2020; Talazoparib PI, rev 3/2020; Madariaga A et al. *Int J Gyn Cancer* 2020 April 9;[Online ahead of print]; Litton JK et al. *NEJM* 2018;379:753-63.

Dose Adjustments for Adverse Events

Olaparib dose reductions	Dose (tablet)
Starting dose	• 300 mg BID
First dose reduction	• 250 mg BID
Second dose reduction	• 200 mg BID

Niraparib dose reductions	Dose
Starting dose	• 300 mg daily
First dose reduction	• 200 mg daily
Second dose reduction	• 100 mg daily

Rucaparib dose reductions	Dose
Starting dose	• 600 mg twice daily
First dose reduction	• 500 mg twice daily
Second dose reduction	• 400 mg twice daily
Third dose reduction	• 300 mg twice daily

Courtesy, Shannon N Westin, MD, MPH

FDA Prescribing Information.

Determinants of Platinum Sensitivity and Resistance

- Distribution of platinum in the tumor cell
- Cellular metabolism of platinum agents
- Expression levels of epithelial-mesenchymal transition (EMT)-related transcription factors
- PARP1 expression level
- BRCA1/2 mutational status
- Hyperexpression or polymorphism of ERCC1
- Mutational status of homologous recombination (HR) pathway genes

Colombo PE et al. *Crit Rev Oncol Hematol* 2014;89(2):207-16.

FDA-Approved PARP Inhibitors as Maintenance Therapy for Recurrent, Platinum-Sensitive Disease

Niraparib

Indications:
- Maintenance following response to platinum-based therapy
- Irrespective of BRCA status

Pivotal study: ENGOT-OV16/NOVA

Approved: 3/2017

Rucaparib

Indications:
- Maintenance following response to platinum-based therapy
- Irrespective of BRCA status

Pivotal study: ARIEL3

Approved: 4/2018

Olaparib

Indications:
- Maintenance following response to platinum-based therapy
- Irrespective of BRCA status

Pivotal studies: SOLO-2, Study 19

Approved: 8/2017

Niraparib FDA insert, revised 3/2017; Rucaparib FDA insert, revised 4/2018; Olaparib FDA insert, revised 1/2018; Pujade-Lauraine E et al. *Lancet* 2017;18(9):1274-84; Mirza MR et al. *N Engl J Med* 2016;375(22):2154-64; Coleman RL et al. *Lancet* 2017;390(10106):1949-61; Ledermann J et al. *N Engl J Med* 2012;366:1382-92.

Eligibility and Dosing in Pivotal Studies of PARP Inhibitors for Recurrent, Platinum-Sensitive OC

	NOVA[1] (Niraparib)	SOLO-2[2] (Olaparib)	ARIEL3[3] (Rucaparib)
BRCA status	With or without gBRCA mutation	gBRCA mutation (Study 19: +/- gBRCA mutation)	With or without gBRCA mutation
HRD testing	Yes	No	Yes
Tumor assessment schedule	Every 8 wk to C14 → every 12 wk	Every 12 wk until wk 72 → every 24 wk	Every 8 wk to C14 → every 12 wk
Dosing/formulation	300 mg qd	300 mg BID	600 mg BID
No. of prior lines of chemo	2 or more	2 or more	2 or more

[1] Mirza MR et al. *N Engl J Med* 2016;375(22):2154-64; [2] Pujade-Lauraine E et al. *Lancet* 2017;18(9):1274-84; [3] Coleman RL et al. *Lancet* 2017;390(10106):1949-61.

RTP RESEARCH TO PRACTICE

Efficacy Summary of PARP Inhibitors for Recurrent, Platinum-Sensitive OC

	PARPi	Control	HR
NOVA[1] — Niraparib			
gBRCA mutation	21.0 mo	5.5 mo	0.27
No gBRCA mutation, HRD+	12.9 mo	3.8 mo	0.38
No gBRCA mutation	9.3 mo	3.9 mo	0.45
SOLO-2[2] — Olaparib			
gBRCA mutation	19.1 mo	5.5 mo	0.30
ARIEL3[3-4] — Rucaparib			
ITT (All comers)	10.8 mo	5.4 mo	0.36
g or sBRCA mutation	16.6 mo	5.4 mo	0.23
HRD+	13.6 mo	5.4 mo	0.32
$BRCA^{WT}$/High LOH	13.6 mo	5.4 mo	0.32
$BRCA^{WT}$/Low LOH	6.7 mo	5.4 mo	0.58

[1] Mirza MR et al. *N Engl J Med* 2016;375(22):2154-64; [2] Pujade-Lauraine E et al. *Lancet* 2017;18(9):1274-84; [3] Coleman RL et al. *Lancet* 2017;390(10106):1949-61; [4] Ledermann JA et al. *Lancet Oncol* 2020;21(5):710-722.

FDA-Approved PARP Inhibitors as Monotherapy for Multiply Relapsed Disease

Olaparib	Rucaparib	Niraparib
Indications: • 4th-line therapy and beyond • Germline BRCA mutation **Dosing:** • 300 mg BID **Approved: 12/2014**	**Indications:** • 3rd-line therapy and beyond • Germline and/or somatic BRCA mutation **Dosing:** • 600 mg BID **Approved: 12/2016**	**Indications:** • 4th-line therapy and beyond • HRD-positive **Dosing:** • Weight- and platelet count-dependent: 200 or 300 mg QD **Approved: 102/2019**

Olaparib prescribing information, revised 12/2018; Rucaparib prescribing information, revised 4/2018; Niraparib prescribing information, revised 04/2020

Efficacy Summary of PARP Inhibitors for Multiply Relapsed OC

	Objective Response Rate
QUADRA[1] — Niraparib	
HRD-positive	29/189 (15%)
HRD-negative/unknown	8/230 (3%)
BRCA-mutated	18/63 (29%)
SOLO-3[2] — Olaparib	
gBRCA-mutation	109/151 (72%)
ARIEL2[3-4] — Rucaparib	
g or sBRCA mutation	57/106 (54%)

[1] Moore KN et al. *Lancet Oncol* 2019;20(5):636-648; [2] Penson RT et al. ASCO 2019;Abstract 5506;
[3] Oza AM et al. *Gynecol Oncol* 2017;147:267-75.

Meet The Professor

Management of Chronic Lymphocytic Leukemia

Friday, October 2, 2020
12:00 PM – 1:00 PM ET

Faculty

William G Wierda, 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 days.