

Meet The Professor

Management of Ovarian Cancer

Kathleen Moore, MD

The Virginia Kerley Cade Endowed Chair in Cancer Development

Associate Director, Clinical Research

Director, Oklahoma TSET Phase I Program

Stephenson Cancer Center

Associate Professor, Section of Gynecologic Oncology

Director, Gynecologic Oncology Fellowship

Department of Obstetrics and Gynecology

University of Oklahoma Health Sciences Center

Oklahoma City, Oklahoma

Commercial Support

These activities are supported by an educational grant from GlaxoSmithKline.

Dr Love — Disclosures

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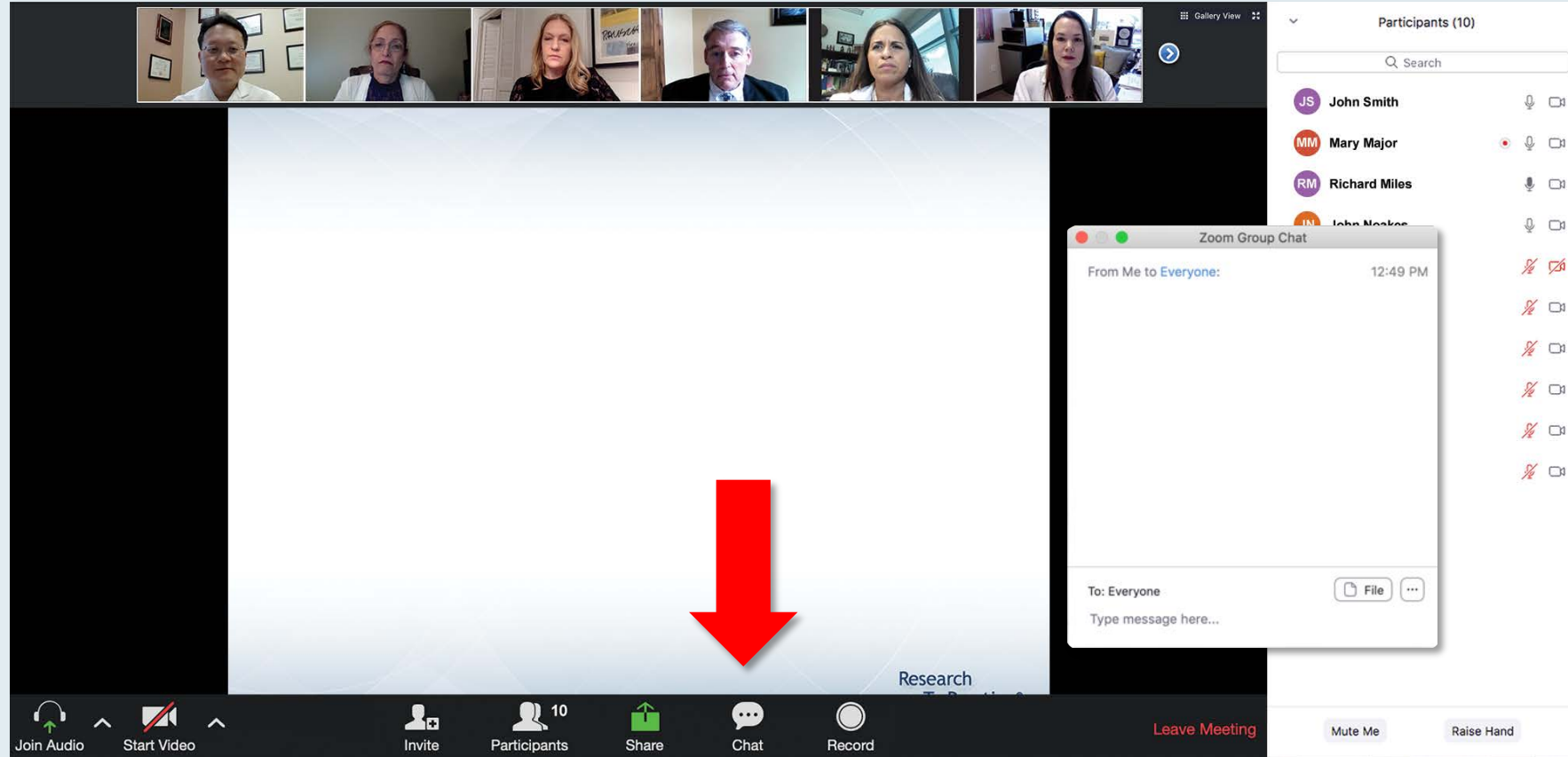
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Dr Moore — Disclosures

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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.

Familiarizing Yourself with the Zoom Interface

How to answer poll questions

The screenshot shows a Zoom meeting interface. At the top, there are six video thumbnails of participants. Below them is a slide with a poll question: "What is your usual treatment recommendation for a patient with MM followed by ASCT and maintenance experiences an asymptomatic relapse?". The slide lists ten options, including combinations of Carfilzomib, Pomalidomide, Elotuzumab, Daratumumab, and Ixazomib with or without dexamethasone. A "Quick Poll" window is overlaid on the slide, showing the same options with radio buttons for selection. The Zoom control bar at the bottom includes icons for Join Audio, Start Video, Invite, Participants (10), Share, Chat, Record, and Leave Meeting. On the right side, there is a "Participants (10)" list with names and icons for audio and video status.

Participants (10)

Search

- JS John Smith
- MM Mary Major
- RM Richard Miles
- JN John Noakes
- AS Alice Suarez
- JP Jane Perez
- RS Robert Stiles
- JF Juan Fernandez
- AK Ashok Kumar
- JS Jeremy Smith

What is your usual treatment recommendation for a patient with MM followed by ASCT and maintenance experiences an asymptomatic relapse?

Quick Poll

- Carfilzomib +/- dexamethasone
- Pomalidomide +/- dexamethasone
- Carfilzomib + pomalidomide +/- dexamethasone
- Elotuzumab + lenalidomide +/- dexamethasone
- Elotuzumab + pomalidomide +/- dexamethasone
- Daratumumab + lenalidomide +/- dexamethasone
- Daratumumab + pomalidomide +/- dexamethasone
- Daratumumab + bortezomib +/- dexamethasone
- Ixazomib + Rd
- Other

Submit

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When a poll question pops up, click your answer choice from the available options. Results will be shown after everyone has answered.

Upcoming Webinars

**Friday, October 16, 2020
11:00 AM – 12:00 PM ET**

Addressing Current Questions and Controversies in the Management of Non-Small Cell Lung Cancer with an EGFR Mutation

Faculty

Roy S Herbst, MD, PhD

Suresh S Ramalingam, MD

Helena Yu, MD

Moderator

Neil Love, MD

**Tuesday, October 20, 2020
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Optimizing the Role of Radiation Oncologists and Other Multidisciplinary Team Members in the Management of Locally Advanced Non-Small Cell Lung Cancer

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**Thursday, October 22, 2020
12:00 PM – 1:00 PM ET**

**Meet The Professor: Management
of Multiple Myeloma**

Faculty

Krina K Patel, MD, MSc

Moderator

Neil Love, MD

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**Current Concepts and Recent
Advances in Oncology:
A Daylong Clinical Summit
Hosted in Partnership with
Florida Cancer Specialists**

Moderator

Neil Love, MD

Thank you for joining us!

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

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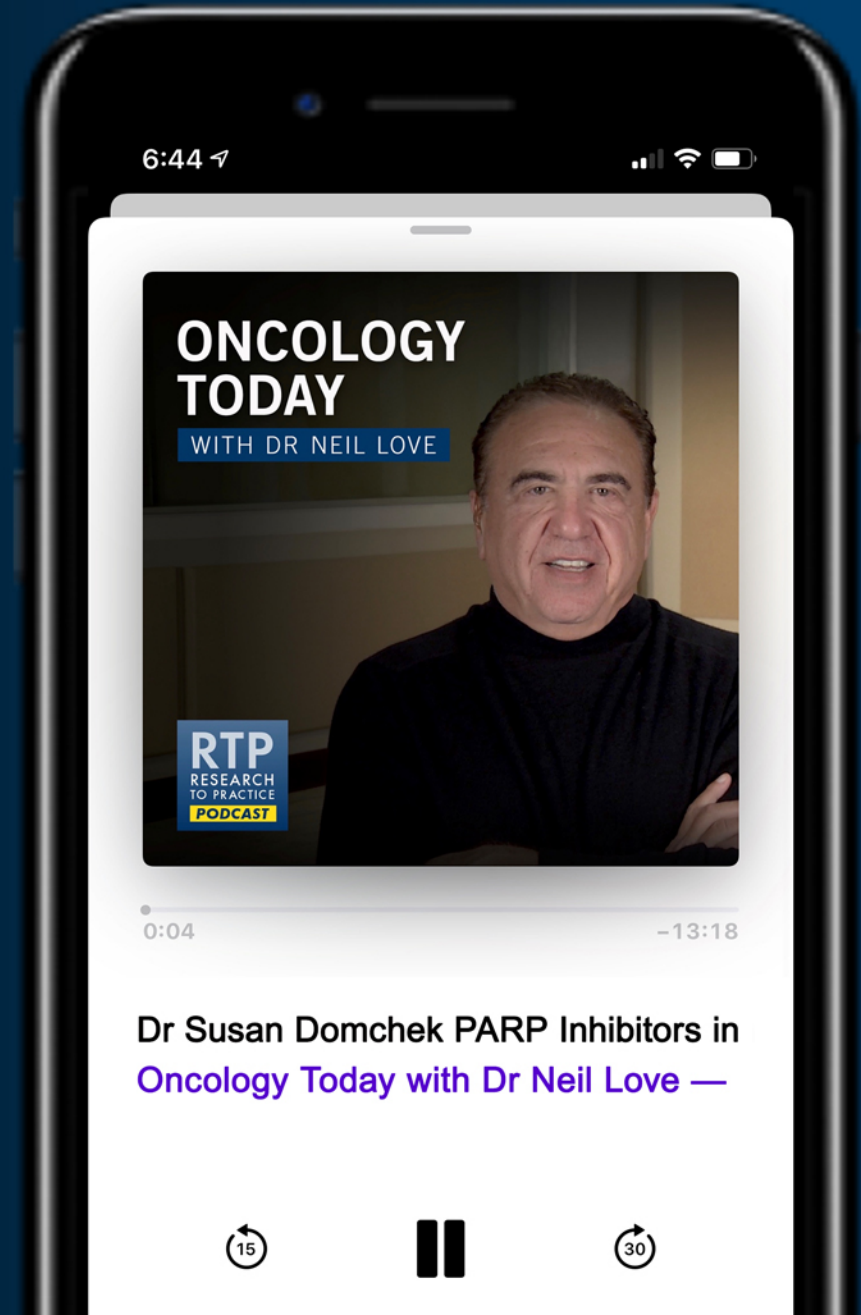
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Oklahoma City, Oklahoma

Meet The Professor Program Participating Faculty



Deborah K Armstrong, MD
Professor of Oncology
Professor of Gynecology and Obstetrics
Skip Viragh Outpatient Cancer Building
Johns Hopkins Sidney Kimmel
Comprehensive Cancer Center
Baltimore, Maryland



Robert L Coleman, MD
Chief Scientific Officer
US Oncology Research
Gynecologic Oncology
McKesson
The Woodlands, Texas



Don S Dizon, MD
Professor of Medicine, Brown University
Director, Women's Cancers and Hematology-
Oncology Outpatient Clinics
Lifespan Cancer Institute
Director, Medical Oncology and the Oncology
Sexual Health Program
Rhode Island Hospital
Providence, Rhode Island



Professor Jonathan A Ledermann
Professor of Medical Oncology
Clinical Director
University College London Cancer
Institute
Director, Cancer Research UK and UCL
Cancer Trials Centre
London, United Kingdom



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

Meet The Professor Program Participating Faculty



Mansoor Raza Mirza, MD

Medical Director, Nordic Society of Gynaecological Oncology
Vice-Chairman, Danish Society of Gynaecologic Oncology
Executive Director, Gynecologic Cancer InterGroup
Chief Oncologist, Department of Oncology
Rigshospitalet, Copenhagen University Hospital
Copenhagen, Denmark



Shannon N Westin, MD, MPH

Associate Professor
Director, Early Drug Development
Department of Gynecologic Oncology and Reproductive Medicine
The University of Texas
MD Anderson Cancer Center
Houston, Texas



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University of Oklahoma Health Sciences Center
Oklahoma City, Oklahoma



Project Chair

Neil Love, MD
Research To Practice
Miami, Florida

We Encourage Clinicians in Practice to Submit Questions

The image shows a Zoom meeting interface. At the top, there is a gallery view of six participants. The main area is a white slide with the text: "You may submit questions using the Zoom Chat option below". A large red arrow points downwards from this text. On the right side, there is a "Participants (10)" list with names and initials: John Smith (JS), Mary Major (MM), Richard Miles (RM), John Noakes (JN), and Alice Suarez (AS). Below the list is a "Zoom Group Chat" window showing a message from "Me to Everyone" at 12:49 PM. The bottom toolbar includes icons for "Join Audio", "Start Video", "Invite", "Participants" (10), "Share", "Chat", "Record", "Leave Meeting", "Mute Me", and "Raise Hand".

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The screenshot displays a Zoom meeting interface. At the top, there are six video thumbnails of participants. Below them, a central slide contains a poll question: "What is your usual treatment recommendation for a patient with MM who has been followed by ASCT for 1-5 years who then experiences an asymptomatic relapse?". The slide lists ten treatment options, with the first six highlighted in blue. A "Quick Poll" dialog box is overlaid on the slide, showing a list of radio button options corresponding to the first six treatment options. The bottom of the slide features the "USF Health Research To Practice" logo. The Zoom control bar at the bottom includes icons for "Join Audio", "Start Video", "Invite", "Participants" (10), "Share", "Chat", "Record", and "Leave Meeting". On the right side, a "Participants (10)" list is visible, showing names and icons for audio and video status.

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What is your usual treatment recommendation for a patient with MM who has been followed by ASCT for 1-5 years who then experiences an asymptomatic relapse?

1. Carfilzomib +/- dexamethasone
2. Pomalidomide +/- dexamethasone
3. Carfilzomib + pomalidomide +/- dexamethasone
4. Elotuzumab + lenalidomide +/- dexamethasone
5. Elotuzumab + pomalidomide +/- dexamethasone
6. Daratumumab + lenalidomide +/- dexamethasone
7. Daratumumab + pomalidomide +/- dexamethasone
8. Daratumumab + bortezomib +/- dexamethasone
9. Ixazomib + Rd
10. Other

Quick Poll

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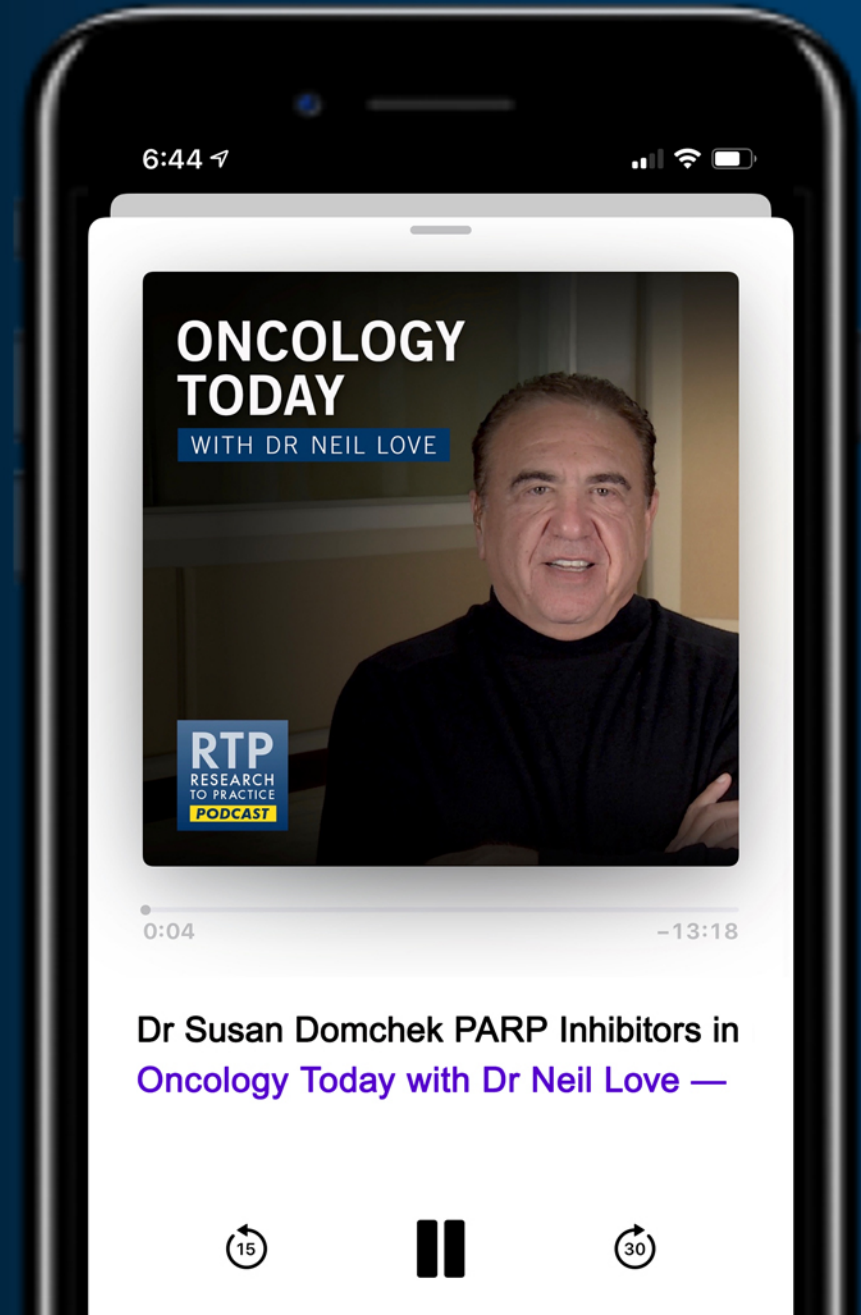
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Johanna Bendell, MD
Axel Grothey, MD
Brad S Kahl, MD
Shaji K Kumar, MD**

**Kathleen Moore, MD
Loretta Nastoupil, MD
William K Oh, MD
David M O'Malley, MD
Robert Z Orlowski, MD, PhD**

**Gregory J Riely, MD, PhD
Hope S Rugo, MD
David R Spigel, MD
Sara M Tolaney, MD, MPH**

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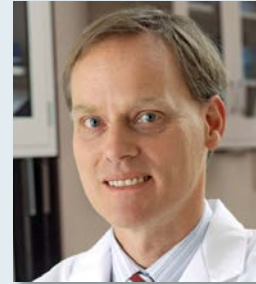


Neil Morganstein, MD
Hematology Oncology
Atlantic Health System
Summit, New Jersey

Dr Neil Morganstein Case Presentations for *Meet The Professor*



John V Heymach, MD, PhD
August 6, 2020



Ola Landgren, MD, PhD
September 21, 2020



Leora Horn, MD, MSc
August 18, 2020



Benjamin Levy, MD
September 29, 2020



Brad S Kahl, MD
August 21, 2020



William G Wierda, MD, PhD
October 2, 2020



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Contents lists available at ScienceDirect

Gynecologic Oncology

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

Meeting Report

The 2020 SGO Annual Meeting Report

Gynecol Oncol 2020;158:12-5

rapid communications

PARP Inhibitors in the Management of Ovarian Cancer: ASCO Guideline



William P. Tew, MD¹; Christina Lacchetti, MHSc²; Annie Ellis^{3,4}; Kathleen Maxian, BSW⁵; Susana Banerjee, PhD⁶; Michael Bookman, MD⁷; Monica Brown Jones, MD⁸; Jung-Min Lee, MD⁹; Stéphanie Lheureux, MD, PhD¹⁰; Joyce F. Liu, MD¹¹; Kathleen N. Moore, MD¹²; Carolyn Muller, MD¹³; Patricia Rodriguez, MD¹⁴; Christine Walsh, MD¹⁵; Shannon N. Westin, MD¹⁶; and Elise C. Kohn, MD⁹

J Clin Oncol 2020;[epub ahead of print].

ASCO Guideline Recommendations

“All patients with newly diagnosed, stage III-IV EOC whose disease is in complete or partial response to first-line, platinum-based chemotherapy with high-grade serous or endometrioid EOC should be offered PARPi maintenance therapy with niraparib.

For patients with germline or somatic pathogenic or likely pathogenic variants in BRCA1 (g/sBRCA1) or BRCA2 (g/sBRCA2) genes should be treated with olaparib.

The addition of olaparib to bevacizumab may be offered to patients with stage III-IV EOC with g/sBRCA1/2 and/or genomic instability and a partial or complete response to chemotherapy plus bevacizumab combination.”

Meet The Professor with Dr Moore

MODULE 1: Cases from Dr Morganstein

- A 71-year-old woman with ovarian cancer and somatic BRCA mutation
- A 54-year-old woman with HRD-positive ovarian cancer
- A 48-year-old woman with ovarian cancer and a BRCA2 mutation
- A 42-year-old woman with ovarian cancer and recurrent ascites

MODULE 2: Journal Club with Dr Moore

- Review of PARP inhibitors for ovarian cancer
- Niraparib in the treatment of ovarian, fallopian tube or primary peritoneal cancer
- SOLO-1 trial 5-year follow-up
- Long-term survival among patients with newly diagnosed ovarian cancer and a BRCA 1/2 mutation
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MODULE 3: Beyond the Guidelines – Clinical Investigator Approaches to Common Clinical Scenarios

MODULE 4: Key Recent Papers

Case Presentation – Dr Morganstein: A 71-year-old woman with ovarian cancer and somatic BRCA mutation



Dr Neil Morganstein

- Diagnosis of stage IIIc ovarian cancer → carboplatin/paclitaxel x 6 cycles → remission
- Germline BRCA mutation testing: negative
- Somatic BRCA mutation testing: positive
- Olaparib maintenance initiated
- Lower extremity edema developed and persisted despite several olaparib dose reductions and treatment delays

Questions

- Have you observed significant edema in the lower extremities with PARP inhibitors?
- What are the differences between PARP inhibitors? Are there class effects or certain effects specific for each PARP inhibitor that we should be aware of?

Case Presentation – Dr Morganstein: A 54-year-old woman with HRD-positive ovarian cancer



Dr Neil Morganstein

- Presented with extensive ovarian cancer with peritoneal disease during COVID pandemic
- Neoadjuvant carboplatin/paclitaxel q3wk → changed to weekly due to poor tolerance
- Debulking surgery → minimal residual disease → HIPEC
- Germline BRCA mutation negative
- HRD positive

Questions

- Would this patient benefit from treatment with a PARP inhibitor?
- What is the role of q3wk versus weekly chemotherapy and of HIPEC?

Case Presentation – Dr Morganstein: A 48-year-old woman with ovarian cancer and a BRCA2 mutation



Dr Neil Morganstein

- Presented with Stage IIIC high-grade serous carcinoma
- Mother died of breast cancer
- Neoadjuvant carboplatin/paclitaxel switched to nab-paclitaxel due to reaction
- TAH/BSO → 3 cycles of IP cisplatin
- BRCA2 mutation; maintenance olaparib

Questions

- How long should the PARP inhibitor be maintained?
- What is the role of HIPEC?

Case Presentation – Dr Morganstein: A 42-year-old woman with ovarian cancer and recurrent ascites



Dr Neil Morganstein

- Initially presented with Stage IIIC high-grade serous carcinoma; BRCA WT
- Mother of 2 young children
- Received multiple lines of treatment for recurrent disease

Questions

- At what point should the palliative specialist become involved?

Above and beyond the practical clinical value of learning about oncology, do you find personal comfort in the process?

1. No
2. Somewhat
3. Quite a bit
4. A great deal

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GYNECOLOGIC CANCER

PARP Inhibitors for Ovarian Cancer: Current Indications, Future Combinations, and Novel Assets in Development to Target DNA Damage Repair

Panagiotis A. Konstantinopoulos, MD¹; Stephanie Lheureux, MD²; and Kathleen N. Moore, MD³

Am Soc Clin Oncol Educ Book 2020;40:1-16

Chronic PARPi exposure: Current challenges and opportunities for combination therapy

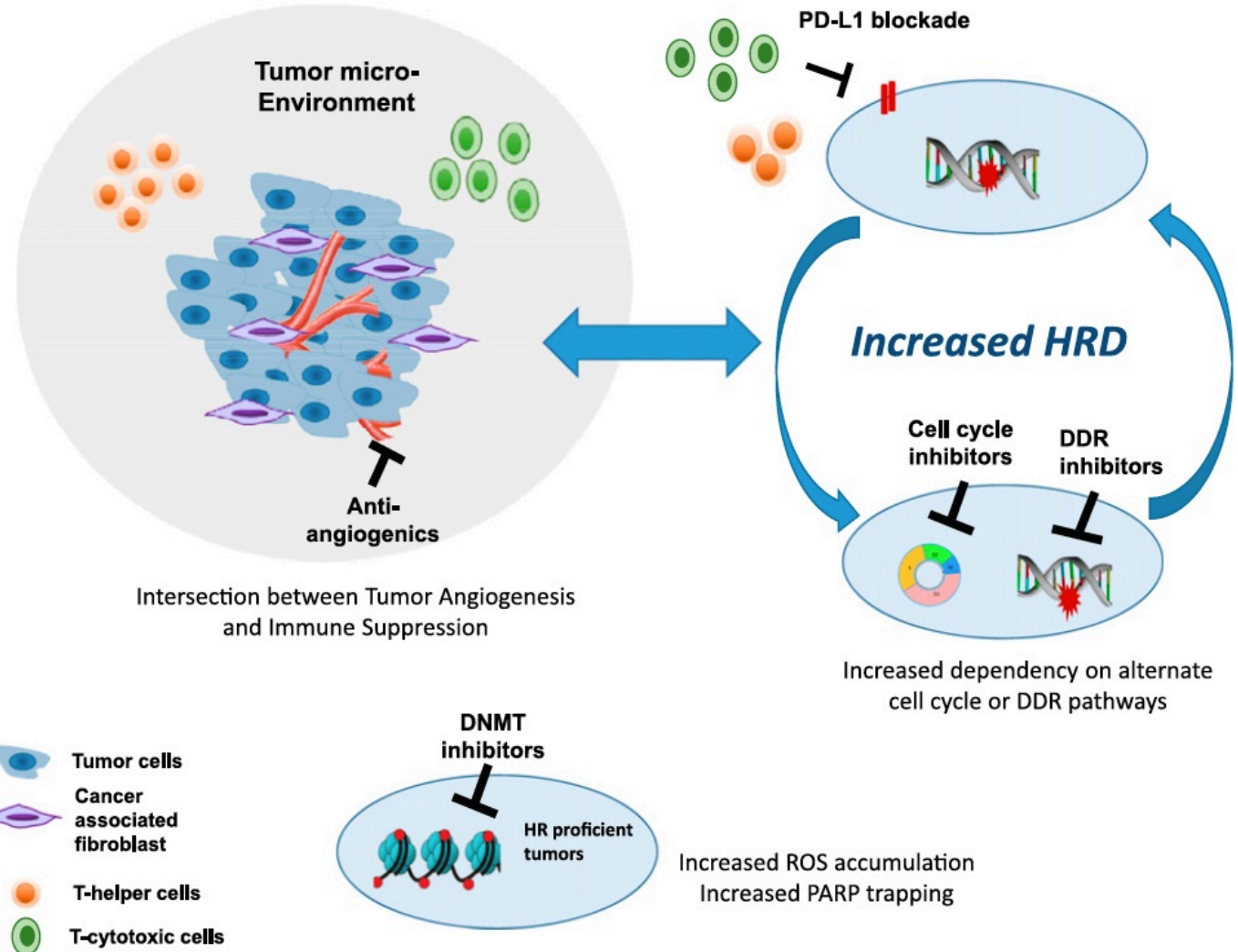
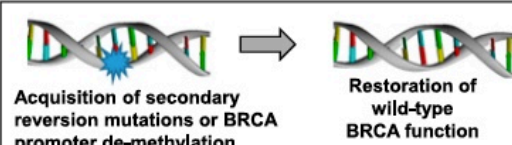
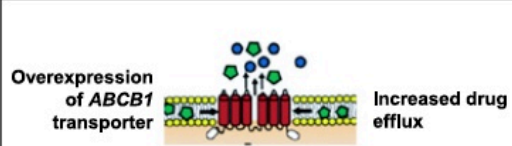
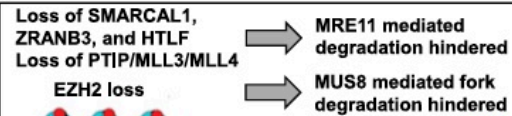
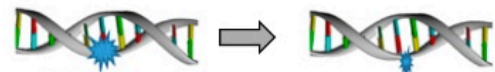
Tackling PARPi Resistance

PARPi Combination Approaches

Development of PARP resistance

Restoration of HRD deficiency

Mechanisms of PARPi resistance



Drug Evaluation

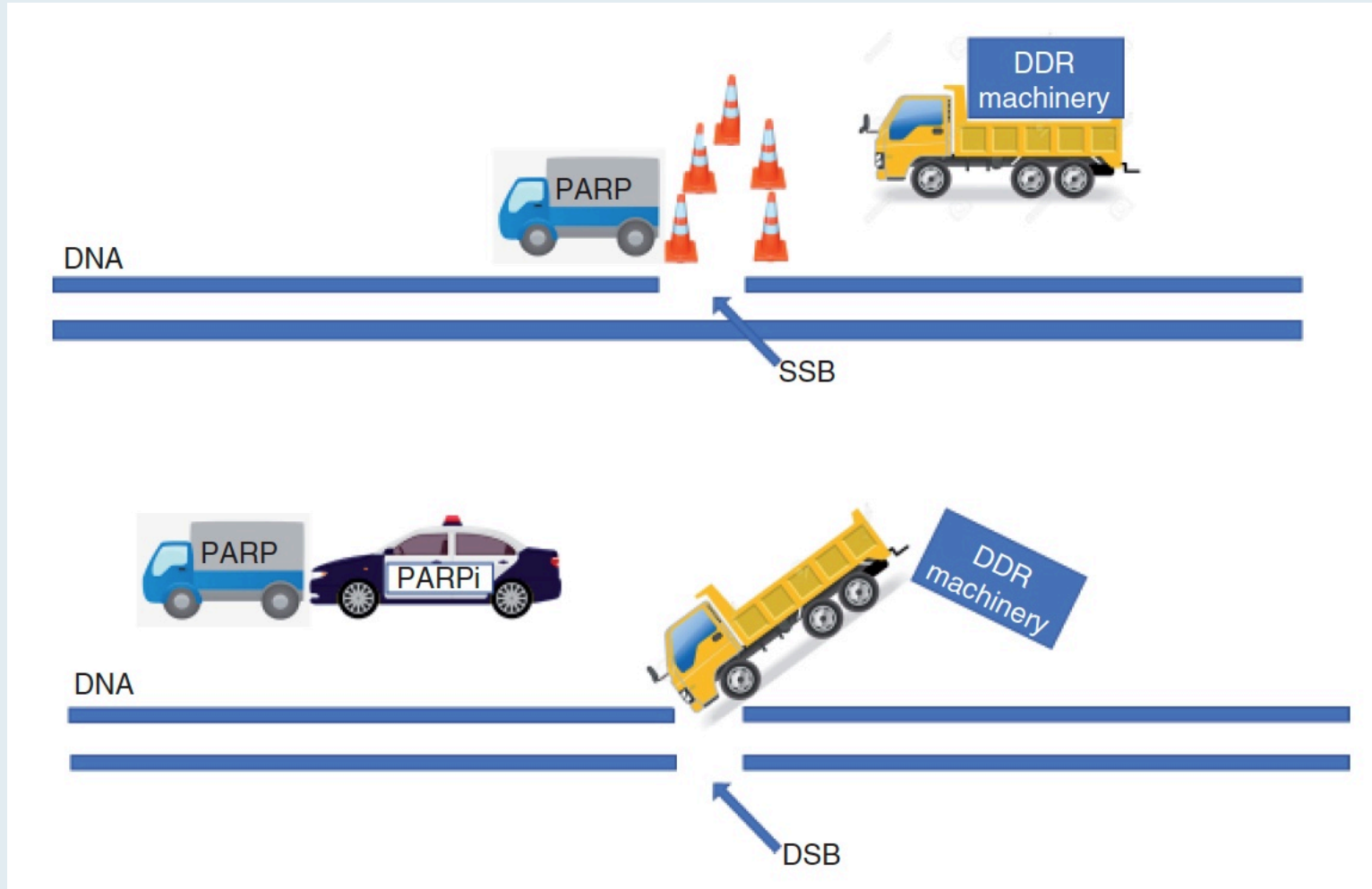
For reprint orders, please contact: reprints@futuremedicine.com

Niraparib in the treatment of previously treated advanced ovarian, fallopian tube or primary peritoneal cancer

BJ Rimel¹, Lauren Dockery², Leslie M Randall³ & Kathleen Moore^{*,4} 

Future Oncol 2020;[Online ahead of print]

Poly(ADP-Ribose) Polymerase Inhibitor Simplified Mechanism of Action



DDR: DNA damage response; DSB: Double-strand break; PARP: Poly(ADP-ribose) polymerase; PARPi: Poly(ADP-ribose) polymerase inhibitor; SSB: Single-strand break.

Maintenance Olaparib for Patients (pts) with Newly Diagnosed, Advanced Ovarian Cancer (OC) and a BRCA Mutation (BRCAm): 5-Year (y) Follow-Up (f/u) from SOLO1

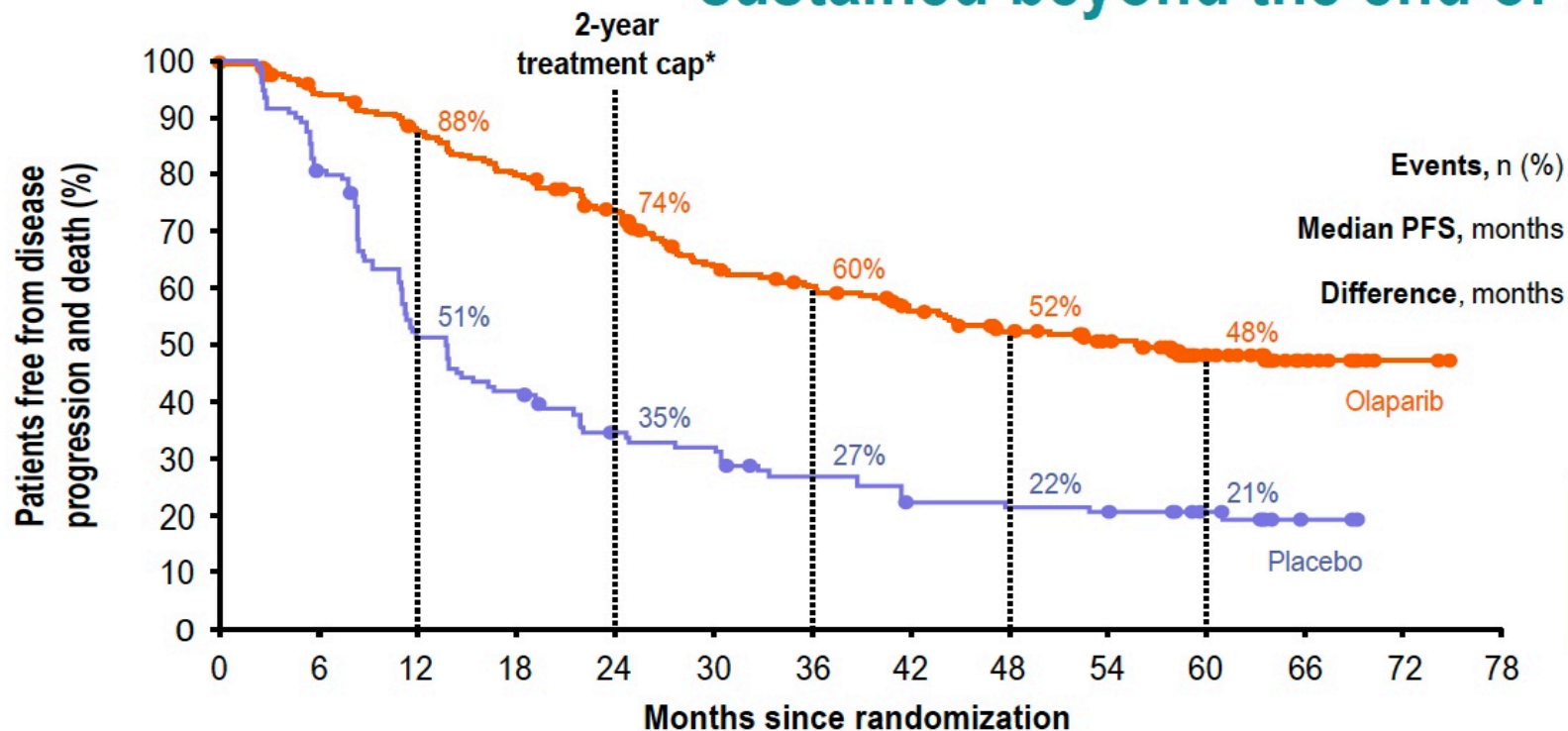
Banerjee S et al.

ESMO 2020;Abstract 811MO.

SOLO-1 Trial 5-Year Follow-Up



PFS benefit of maintenance olaparib was sustained beyond the end of treatment



	Olaparib (N=260)	Placebo (N=131)
Events, n (%)	118 (45)	100 (76)
Median PFS, months	56.0	13.8
Difference, months	42.2	
HR 0.33 (95% CI 0.25–0.43)		

Median treatment duration:
Olaparib, 24.6 months
Placebo[†], 13.9 months

No. at risk

	0	6	12	18	24	30	36	42	48	54	60	66	72	78
Olaparib	260	229	212	194	173	140	129	115	101	91	58	30	2	0
Placebo	131	103	65	53	41	38	30	24	23	22	16	3	0	0

[†]13 patients, all in the olaparib arm, continued study treatment past 2 years; n=130 (safety analysis set)
 Investigator-assessed by modified RECIST v1.1. DCO: 5 March 2020

SOLO-1 Trial 5-Year Follow Up



Secondary efficacy outcomes* support the observed PFS benefit

	Overall		Patients in CR at baseline	
	Olaparib (n=260)	Placebo (n=131)	Olaparib (n=189)	Placebo (n=101)
PFS2				
Events, n (%)	80 (31)	61 (47)	49 (26)	45 (45)
Event free at 5 years, %	64	41	68	44
Median, months	NR	42.1	NR	52.9
	HR 0.46 (95% CI 0.33–0.65)		HR 0.48 (95% CI 0.32–0.71)	
TSST				
Events, n (%)	95 (37)	77 (59)	64 (34)	56 (55)
Event free at 5 years, %	62	36	65	39
Median, months	NR	40.7	NR	47.7
	HR 0.46 (95% CI 0.34–0.63)		HR 0.50 (95% CI 0.35–0.72)	

Safety profile remained consistent with the primary DCO

n (%)	Olaparib (n=260)	Placebo (n=130)
Any AE	256 (98)	120 (92)
Grade ≥3 AE	103 (40)	25 (19)
Serious AE	55 (21)	17 (13)
AE leading to dose interruption	136 (52)	22 (17)
AE leading to dose reduction	75 (29)	4 (3)
AE leading to treatment discontinuation	30 (12)	4 (3)
MDS/AML	3 (1)	0 (0)
New primary malignancy	7 (3)	5 (4)

No additional cases of MDS/AML reported; incidence remained <1.5%
Follow-up for MDS/AML continued until death due to any cause

*Measured from randomization. AE, adverse event; AML, acute myeloid leukaemia; CR, complete response; MDS, myelodysplastic syndrome. DCO: 5 March 2020

Projection of Long-Term Overall Survival Among Patients with Newly Diagnosed Advanced Ovarian Cancer and a BRCA1/2 Mutation

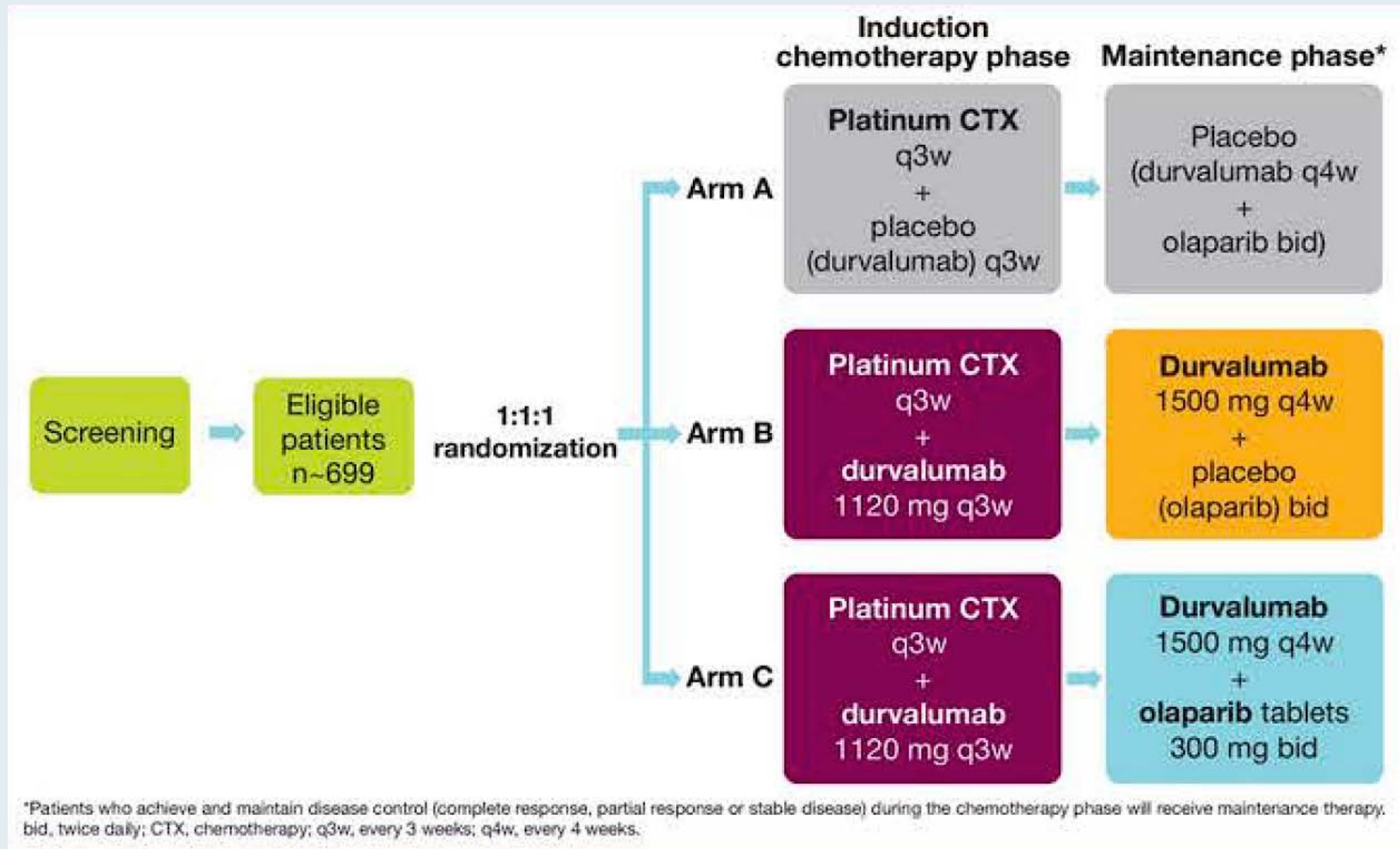
Muston DRG et al.
SGO 2020;Abstract 286.

DUO-E/GOG-3041/ENGOT-EN10: A Randomized Phase III Trial of First-Line Carboplatin (Carb) and Paclitaxel (Pac) in Combination with Durvalumab (Durva), Followed by Maintenance Durva with or without Olaparib (Ola), in Patients (pts) with Newly Diagnosed (nd) Advanced or Recurrent Endometrial Cancer (EC)

Westin SN et al.

ASCO 2020;Abstract TPS6108.

DUO-E/GOG-3041/ENGOT-EN10 Phase III Study Schema



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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

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 Moore

MODULE 1: Cases from Dr Morganstein

- A 71-year-old woman with ovarian cancer and somatic BRCA mutation
- A 54-year-old woman with ovarian cancer and no germline BRCA mutation
- A 48-year-old woman with ovarian cancer and a BRCA2 mutation
- A 42-year-old woman with ovarian cancer and recurrent ascites

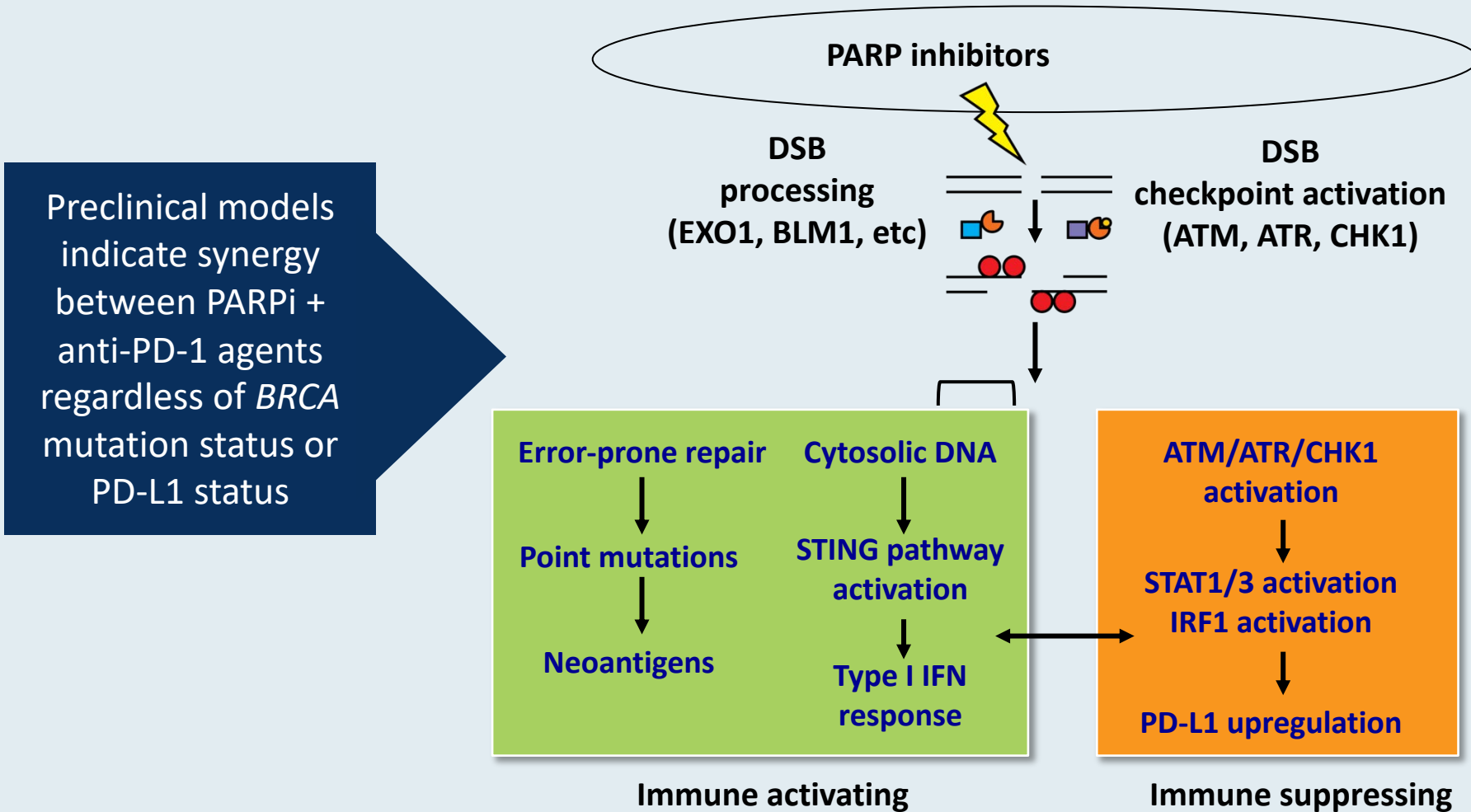
MODULE 2: Journal Club with Dr Moore

- Review of PARP inhibitors for ovarian cancer
- Niraparib in the treatment of ovarian, fallopian tube or primary peritoneal cancer
- SOLO-1 trial 5-year follow-up
- Long-term survival among patients with newly diagnosed ovarian cancer and a BRCA 1/2 mutation
- Ongoing Phase III trial of durvalumab-based first-line therapy and maintenance for newly diagnosed patients

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

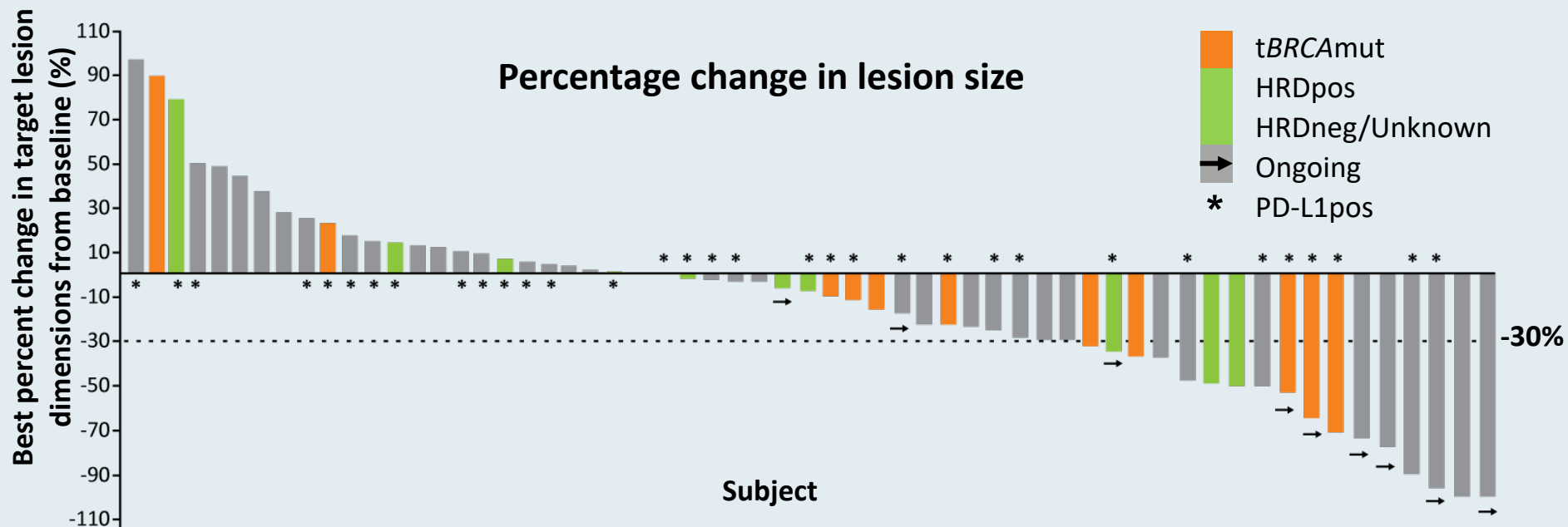
MODULE 4: Key Recent Papers

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



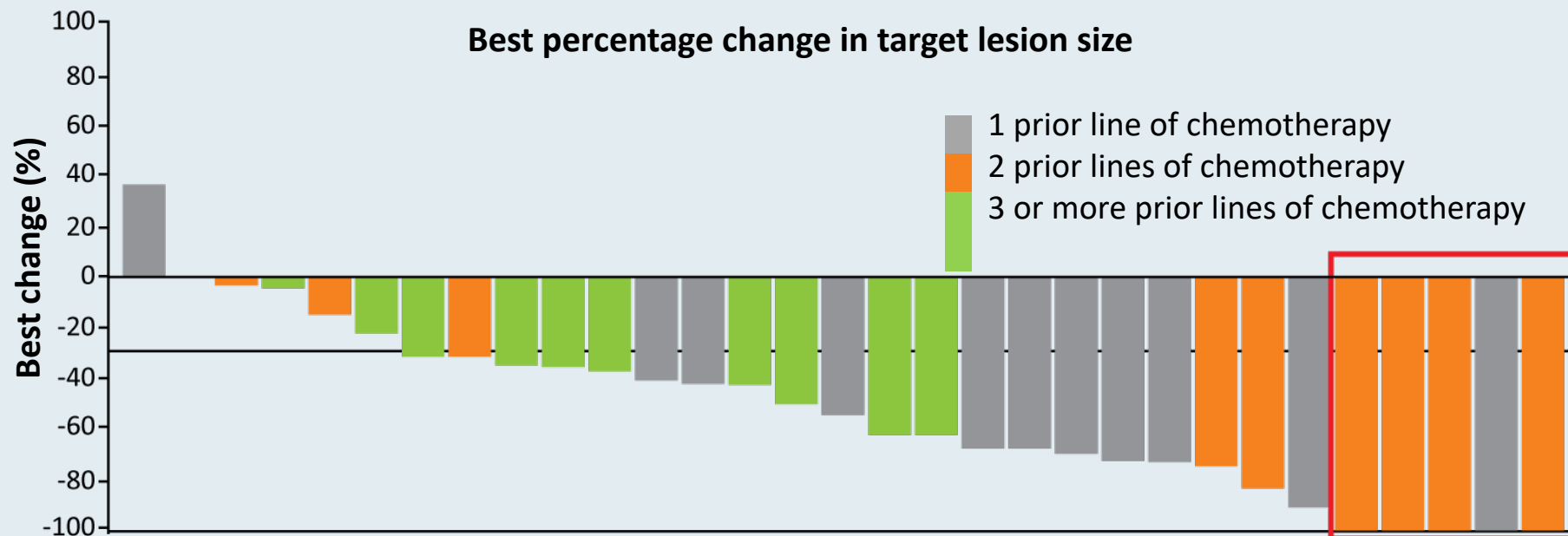
Preclinical data demonstrate synergy with PARPi and anti-PD-1 combinations.

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%)

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%)

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

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	<ul style="list-style-type: none"> • Rucaparib + Nivolumab • Rucaparib + Placebo • Nivolumab + Placebo • Placebo
DUO-O (NCT03737643)	1,056	Maintenance therapy after 1L platinum-based chemo/Bev ± Durvalumab	<ul style="list-style-type: none"> • Bev • Bev + Durvalumab • Bev + Durvalumab + Olaparib
NRG-GY004 (NCT02446600)	549	Recurrent, platinum-sensitive	<ul style="list-style-type: none"> • Platinum-based chemo • Olaparib • Olaparib + Cediranib
ANITA (NCT03598270)	414	Recurrent, platinum-sensitive	<ul style="list-style-type: none"> • Placebo + Platinum-based chemo → Niraparib • ATEZO + Platinum-based chemo → Niraparib + ATEZO

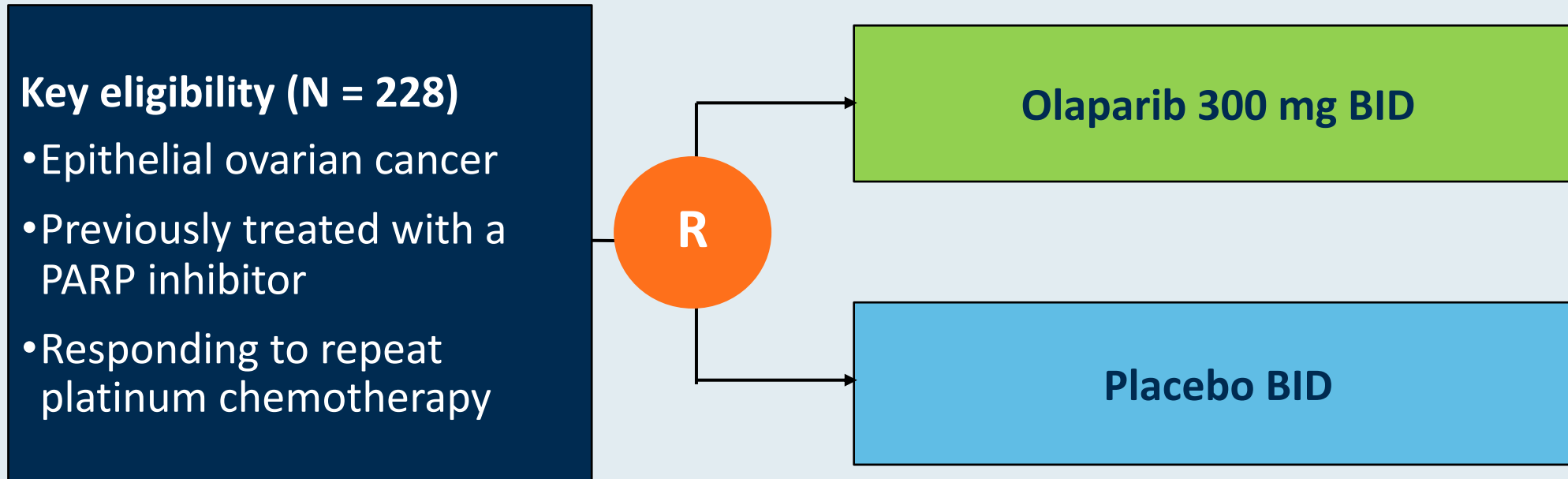
Bev = bevacizumab; ATEZO = atezolizumab

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

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

NCCN¹

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

SGO²

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

ASCO³

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

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

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	<i>BRCA</i> mutation	All comers	All comers	<i>All comers</i>
Treatment Duration	24 months	15 months for Bev 24 months for Olaparib	36 months or until PD	24 months

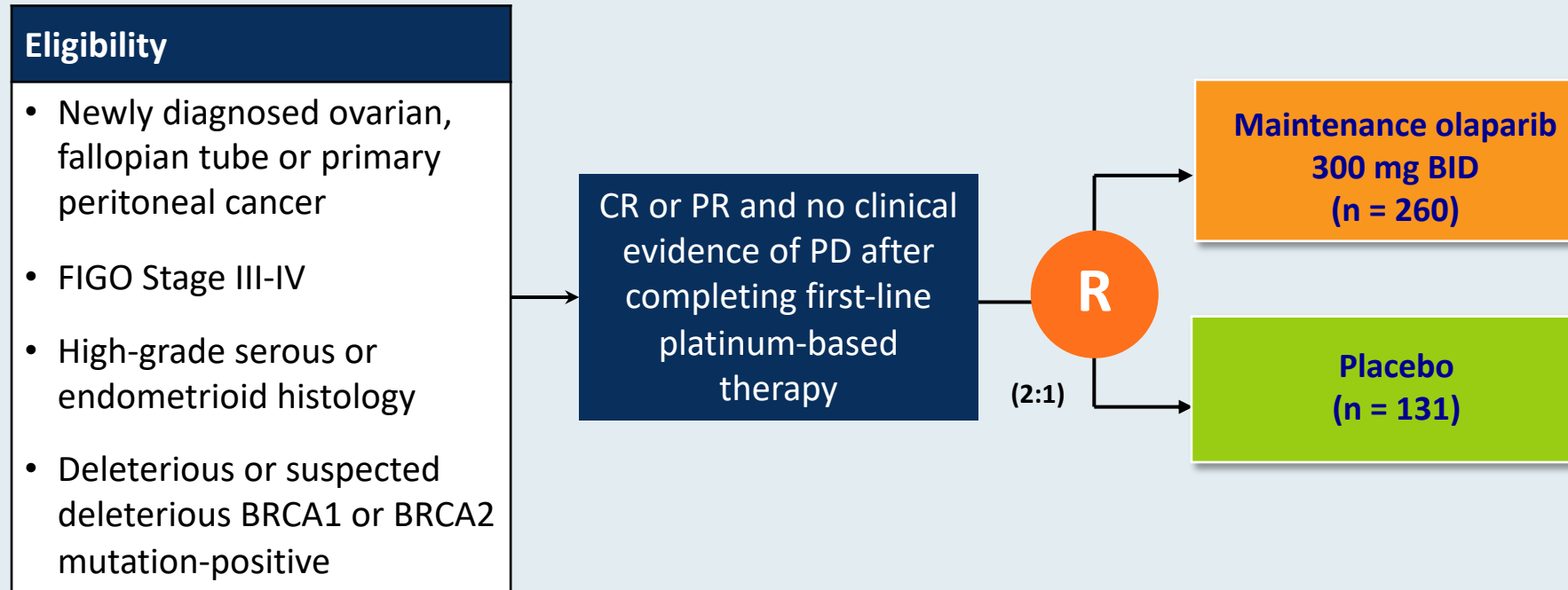
^aResidual disease based on stage was not reported. ^bStage III and IV eligible, but requirements for prior surgery not reported (NR) on clinicaltrials.gov

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

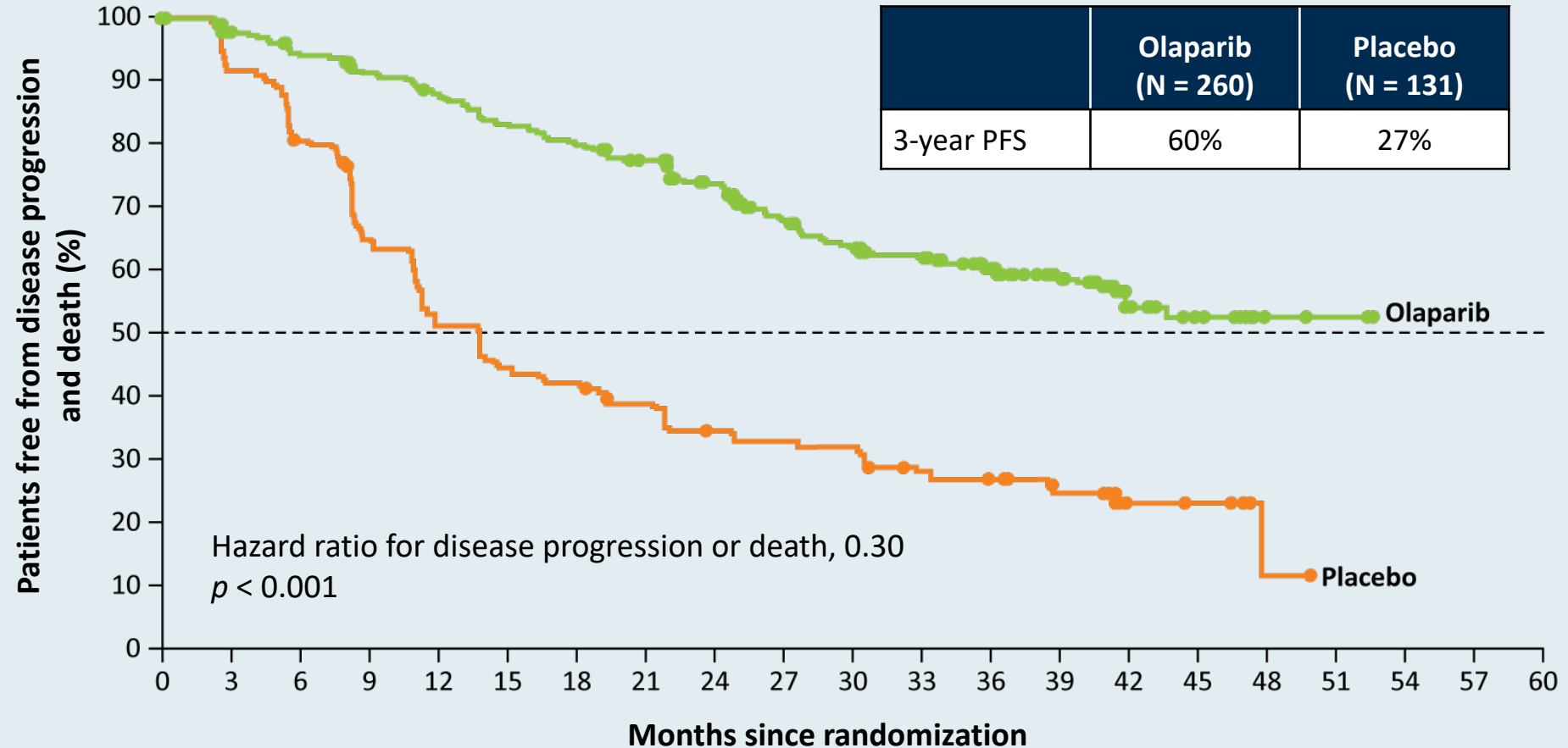
SOLO-1: A Phase III Trial of Maintenance Olaparib in OC with BRCA Mutation

NCT01844986

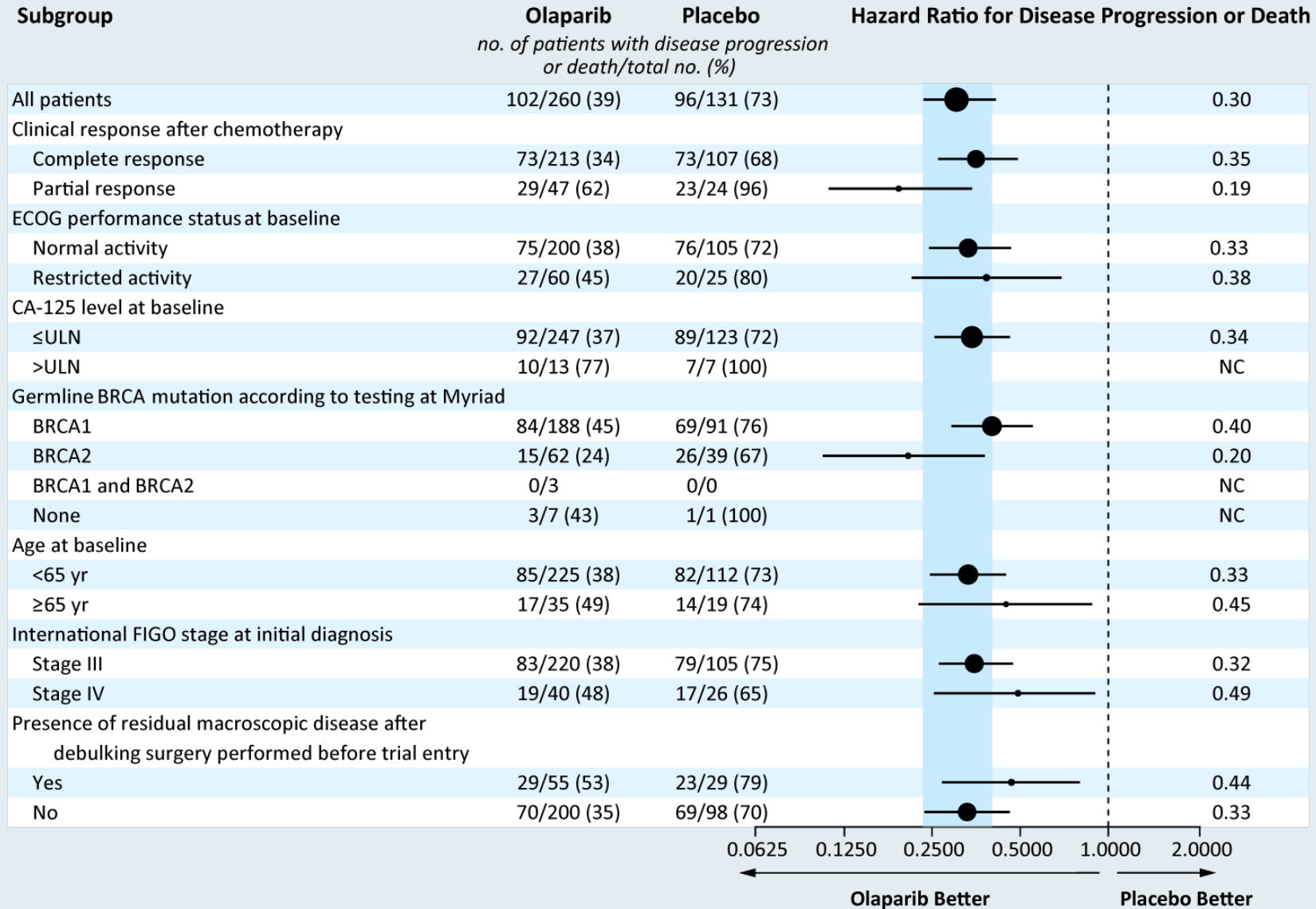


Primary endpoint: Investigator-assessed progression-free survival

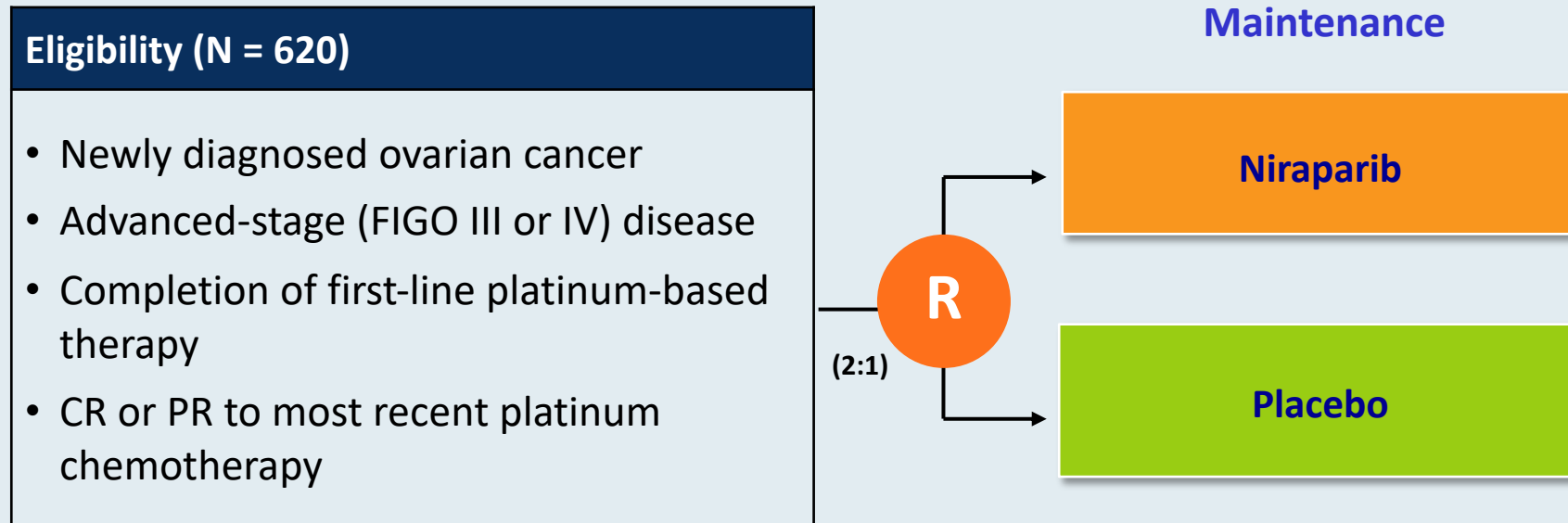
SOLO-1: Primary Endpoint Progression-Free Survival (Investigator Assessed)



SOLO-1: PFS Subgroup Analyses

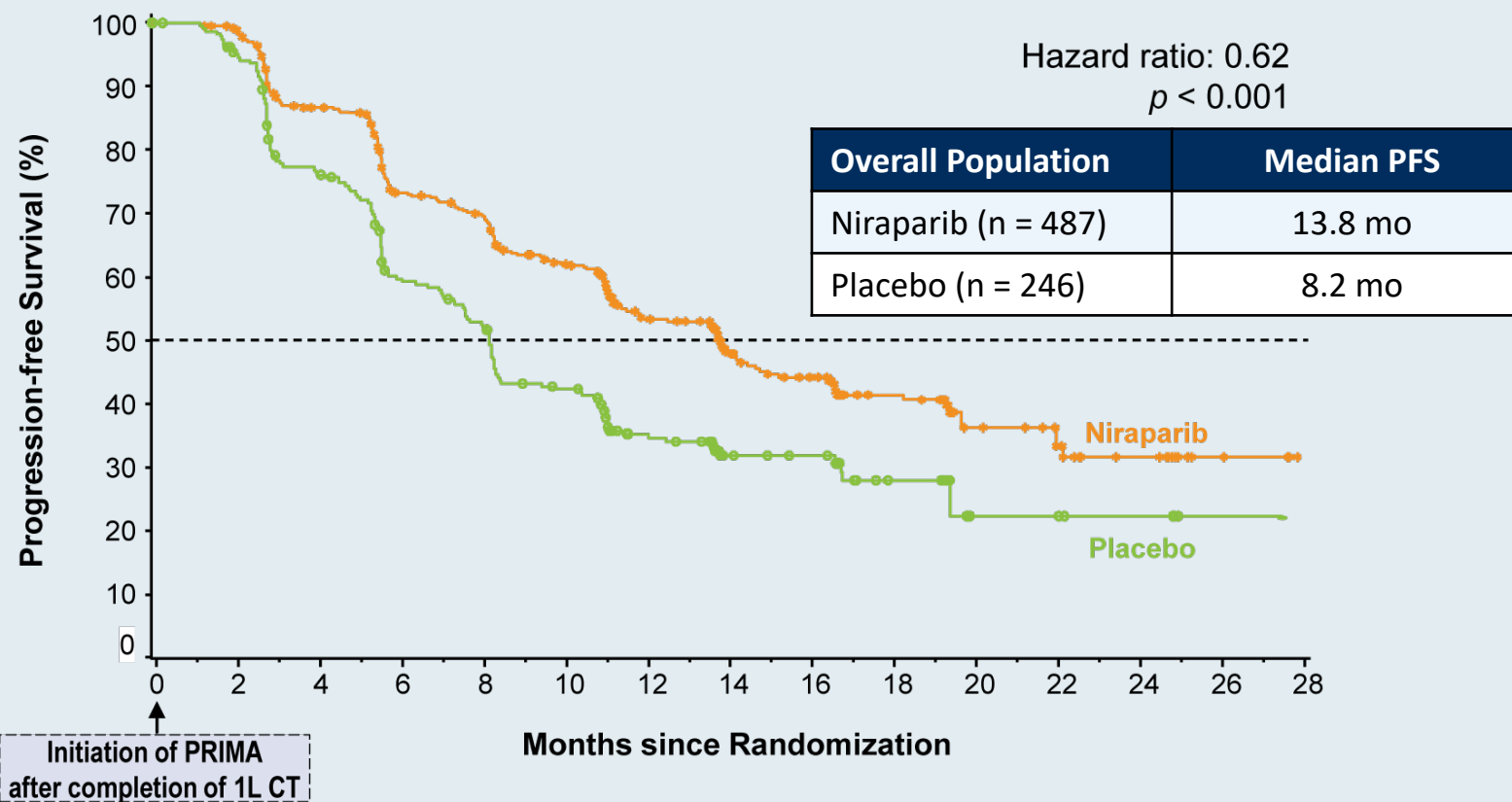


PRIMA Trial: Maintenance Niraparib for Advanced Ovarian Cancer After Response to Front-Line Platinum-Based Chemotherapy



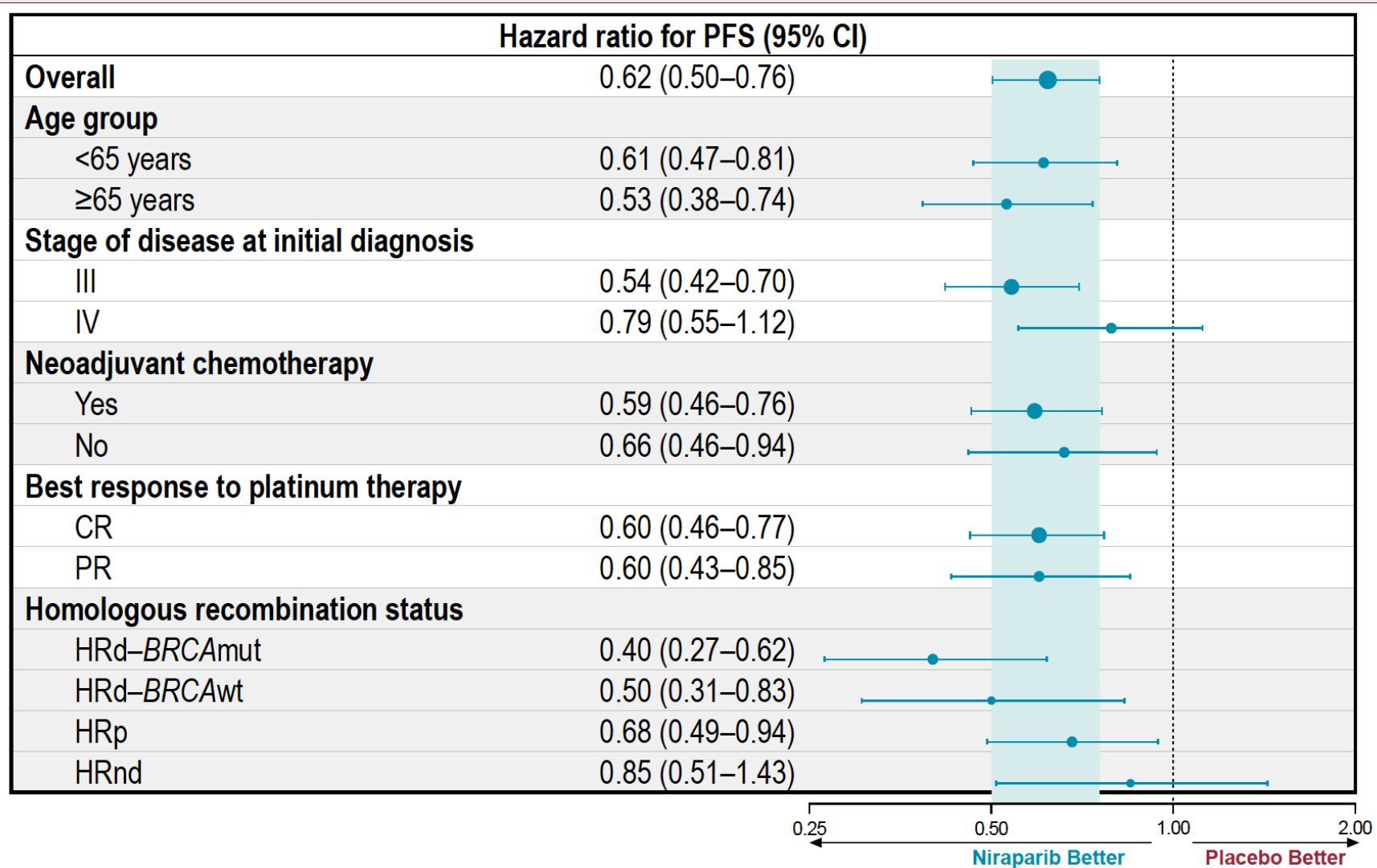
Primary endpoint: Progression-free survival

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.

PRIMA: Progression-Free Survival Subgroup Analysis



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

Press Release – May 28, 2020

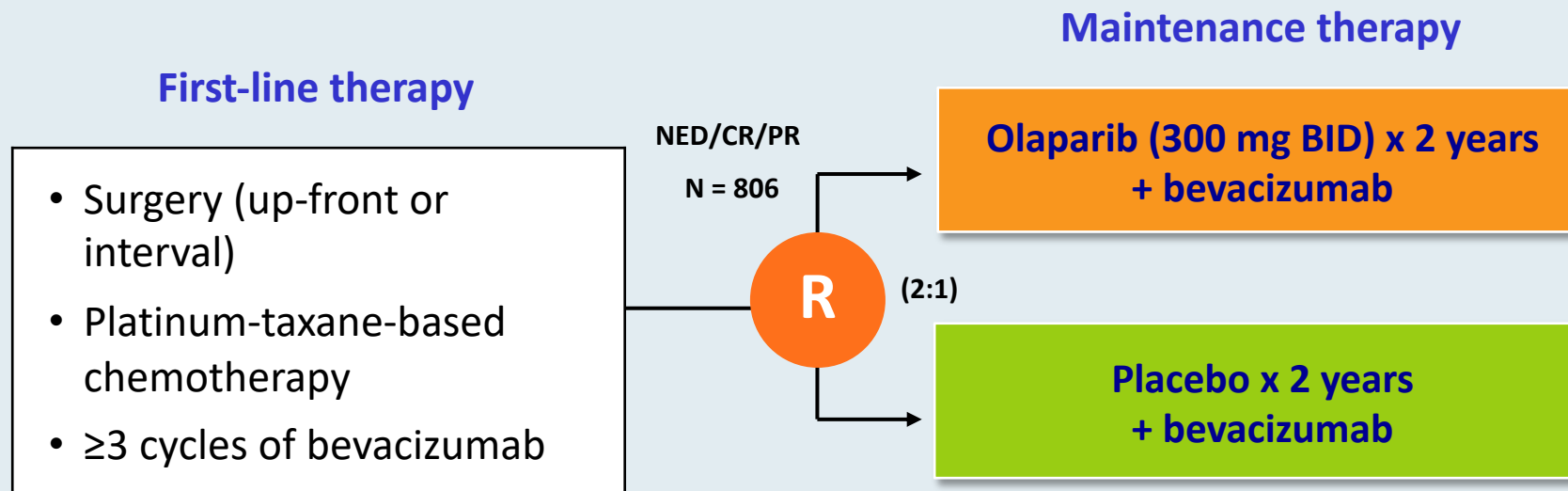
“The Food and Drug Administration expanded the indication of olaparib to include its combination with bevacizumab for first-line maintenance treatment of adult patients with advanced epithelial ovarian, fallopian tube, or primary peritoneal cancer who are in complete or partial response to first-line 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.

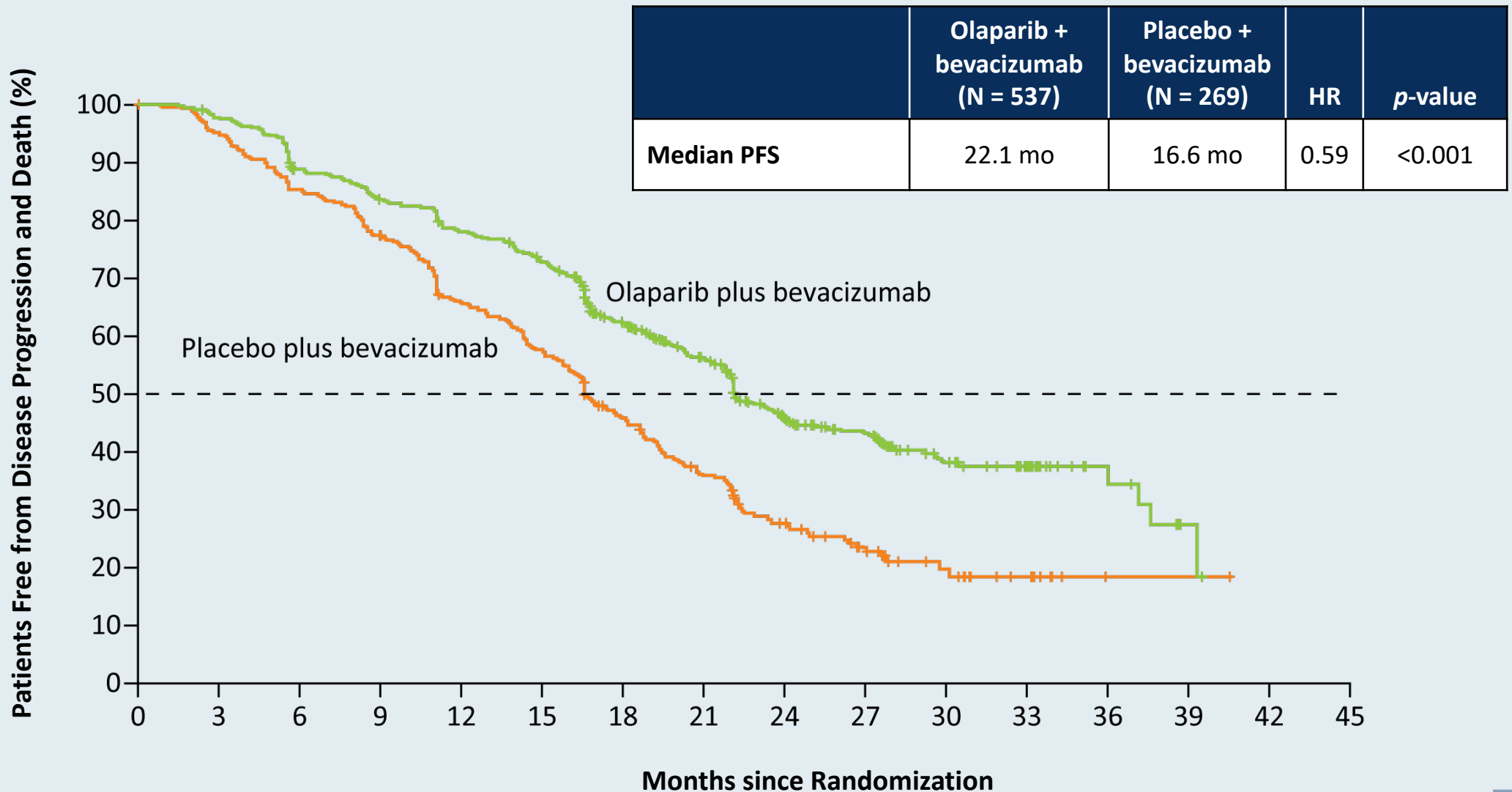
Efficacy of this new indication was investigated in PAOLA-1 (NCT03737643), a randomized, double-blind, placebo-controlled, multi-center trial comparing olaparib with bevacizumab versus placebo plus bevacizumab in patients with advanced high-grade epithelial ovarian cancer, fallopian tube, or primary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

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

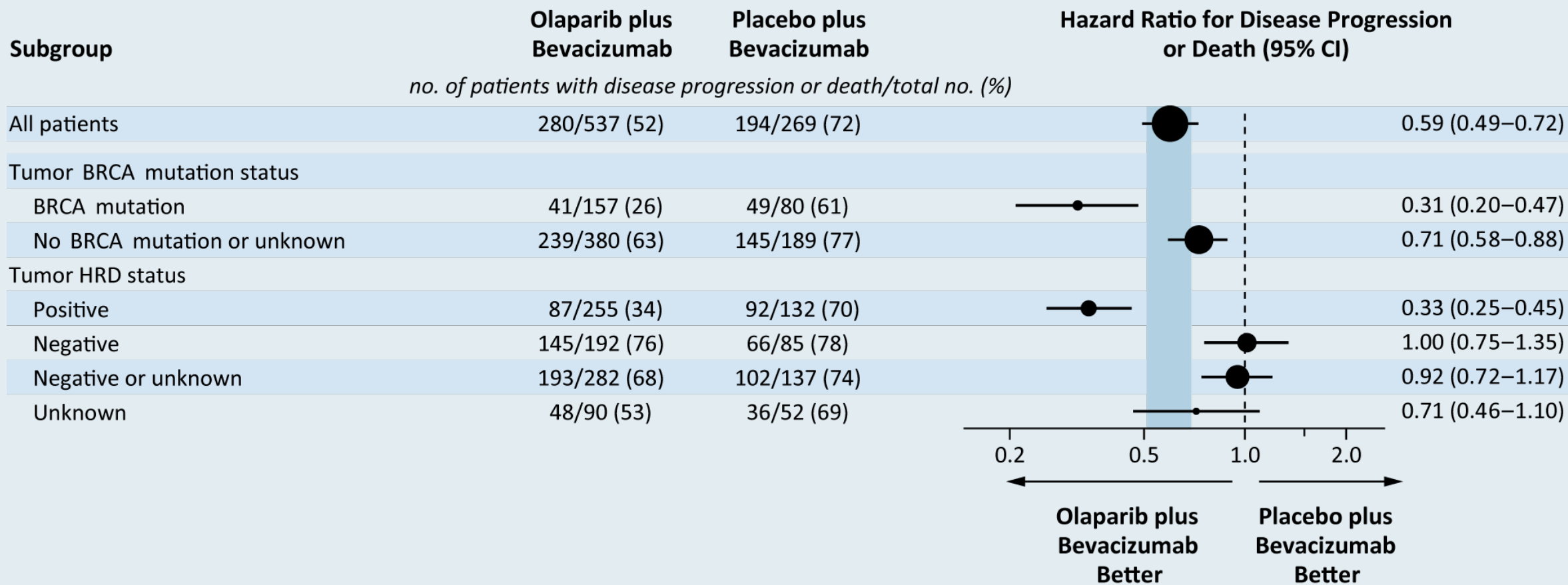
Newly diagnosed FIGO Stage III or IV high-grade serous/endometrioid ovarian, fallopian tube or primary peritoneal cancer



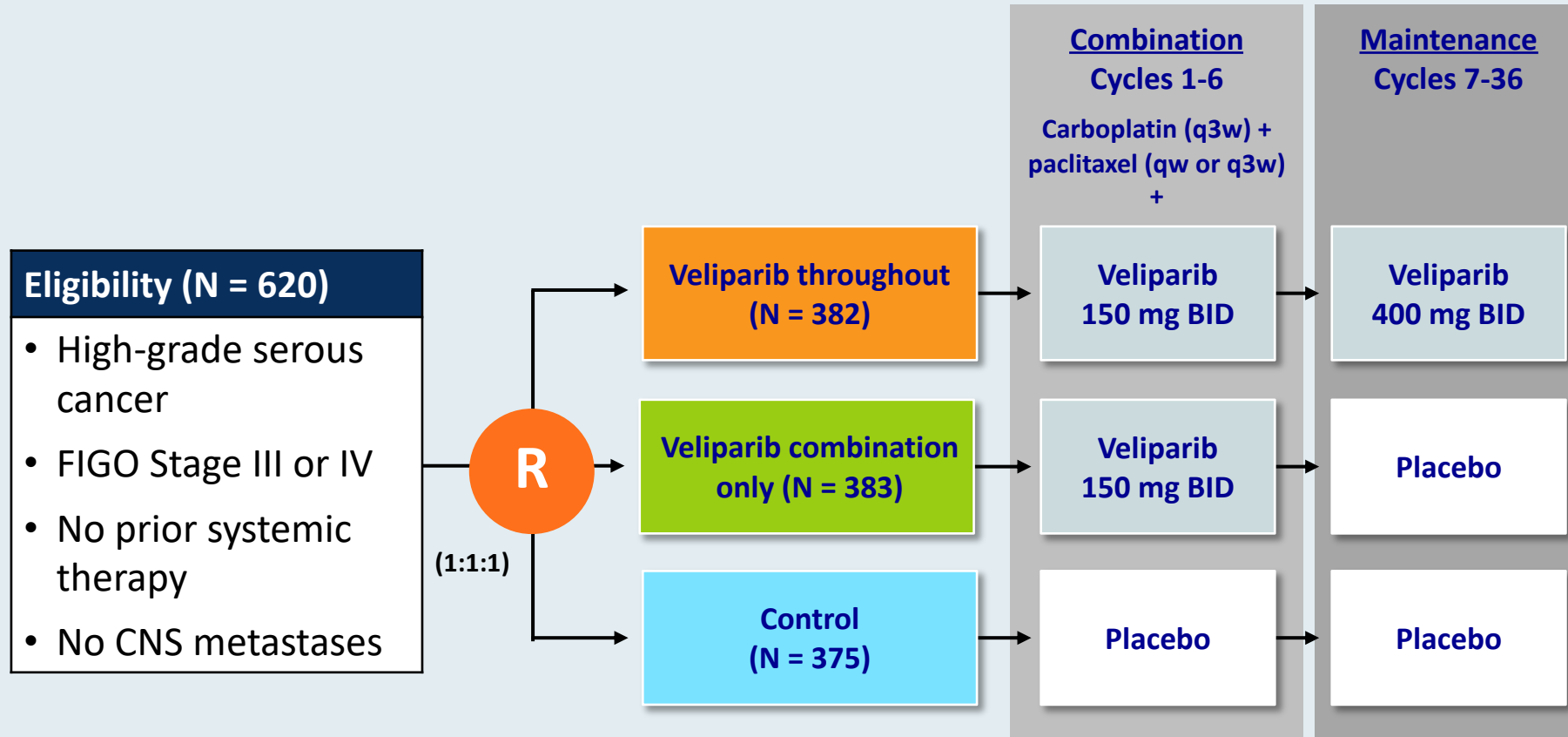
PAOLA-1: Investigator-Assessed PFS (Primary Endpoint)



PAOLA-1: Select Subgroup Analysis of PFS

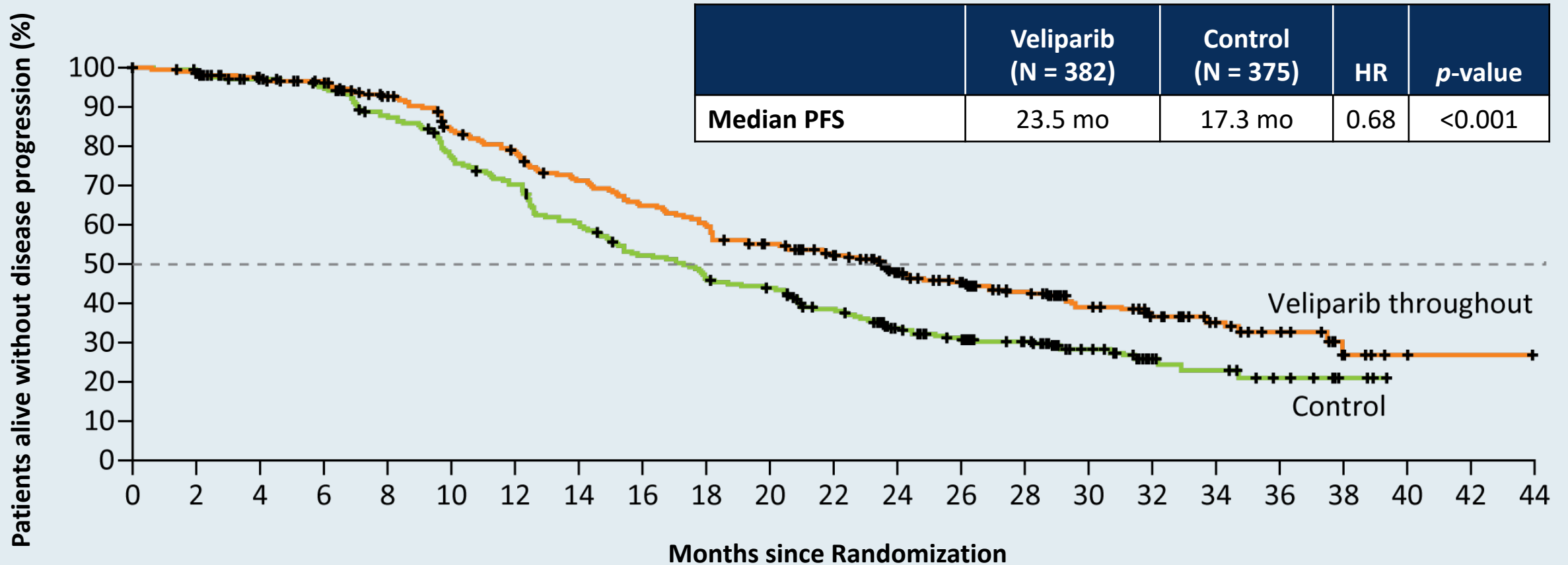


VELIA/GOG-3005: A Phase III Trial of Veliparib with Front-Line Chemotherapy and as Maintenance Therapy for High-Grade Serous Epithelial Ovarian, Fallopian Tube or Primary Peritoneal Cancers



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

VELIA/GOG-3005: Investigator-Assessed PFS



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	<ul style="list-style-type: none"> BRCA mut or wt Stage III or IV Surgery or inoperable 	<ul style="list-style-type: none"> Platinum-based chemo Platinum-based chemo + TSR-042 	<ul style="list-style-type: none"> Niraparib + TSR-042 Niraparib + placebo Placebo + placebo
ATHENA (NCT03522246)	1,012	<ul style="list-style-type: none"> BRCA mut or wt Stage III or IV Prior surgery 	<ul style="list-style-type: none"> Platinum-based chemo 	<ul style="list-style-type: none"> Rucaparib + nivolumab Rucaparib + placebo Placebo + nivolumab Placebo + placebo

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

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

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

	NOVA¹ (Niraparib)	SOLO-2² (Olaparib)	ARIEL3³ (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.

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

	PARPi	Control	HR
NOVA¹ — 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-2² — Olaparib			
gBRCA mutation	19.1 mo	5.5 mo	0.30
ARIEL3³⁻⁴ — 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
<p>Indications:</p> <ul style="list-style-type: none">• 4th-line therapy and beyond• Germline BRCA mutation <p>Dosing:</p> <ul style="list-style-type: none">• 300 mg BID <p>Approved: 12/2014</p>	<p>Indications:</p> <ul style="list-style-type: none">• 3rd-line therapy and beyond• Germline <u>and/or</u> somatic BRCA mutation <p>Dosing:</p> <ul style="list-style-type: none">• 600 mg BID <p>Approved: 12/2016</p>	<p>Indications:</p> <ul style="list-style-type: none">• 4th-line therapy and beyond• HRD-positive <p>Dosing:</p> <ul style="list-style-type: none">• Weight- and platelet count-dependent: 200 or 300 mg QD <p>Approved: 102/2019</p>

Efficacy Summary of PARP Inhibitors for Multiply Relapsed OC

	Objective Response Rate
QUADRA¹ — Niraparib	
HRD-positive	29/189 (15%)
HRD-negative/unknown	8/230 (3%)
BRCA-mutated	18/63 (29%)
SOLO-3² — Olaparib	
gBRCA-mutation	109/151 (72%)
ARIEL2³⁻⁴ — 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.

Addressing Current Questions and Controversies in the Management of Non-Small Cell Lung Cancer with an EGFR Mutation

Friday, October 16, 2020
11:00 AM – 12:00 PM ET

Faculty

Roy S Herbst, MD, PhD
Suresh S Ramalingam, MD
Helena Yu, MD

Moderator

Neil Love, MD

Thank you for joining us!

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