

Meet The Professor

Management of Ovarian Cancer

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

Commercial Support

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Dr Love — Disclosures

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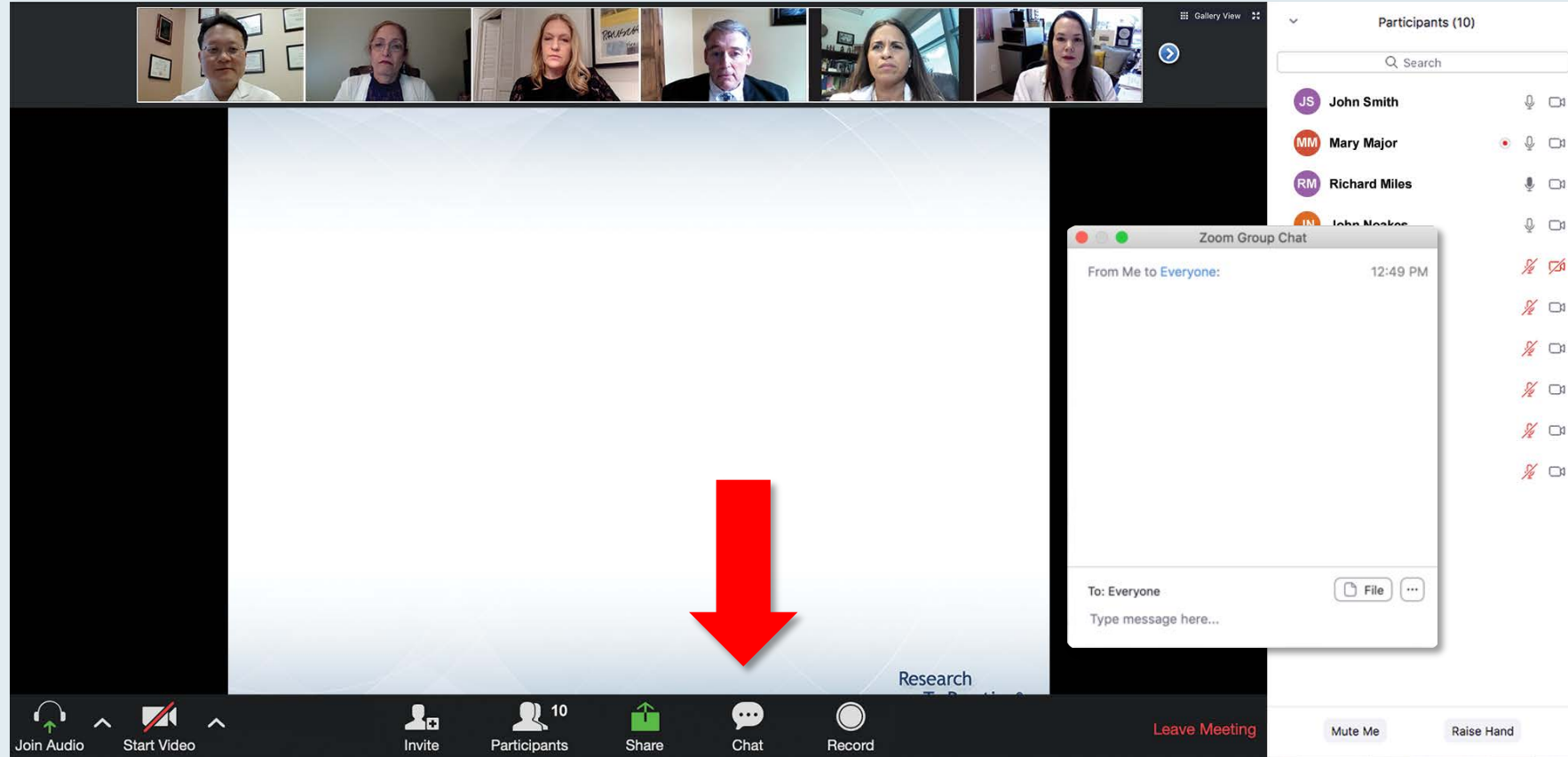
Research To Practice CME Planning Committee Members, Staff and Reviewers

Planners, scientific staff and independent reviewers for Research To Practice have no relevant conflicts of interest to disclose.

Dr Armstrong — Disclosures

| | |
|---|--|
| Advisory Committee | AbbVie Inc, Cue Biopharma, Eisai Inc |
| Contracted Research | Advaxis Inc, AstraZeneca Pharmaceuticals LP, Clovis Oncology, Eisai Inc, Pfizer Inc, Syndax Pharmaceuticals Inc, Tesaro, A GSK Company |
| Data and Safety Monitoring Board/Committee | AstraZeneca Pharmaceuticals LP, DUO-O, DUO-E trials |

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, with the first three highlighted in blue. 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 status icons (mute, video off).

Quick Poll

What is your usual treatment recommendation for a patient with MM followed by ASCT and maintenance 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

Co-provided by **USF Health** Research To Practice®

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

Join Audio Start Video Invite Participants 10 Share Chat Record Leave Meeting Mute Me Raise Hand

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

Upcoming Webinars

**Tuesday, December 1, 2020
5:00 PM – 6:00 PM ET**

**Year in Review: Clinical
Investigators Provide Perspectives
on the Most Relevant New
Publications, Data Sets and
Advances in Oncology
Prostate Cancer**

Faculty

Emmanuel S Antonarakis, MD
Andrew J Armstrong, MD, ScM

Moderator

Neil Love, MD

Friday, December 4, 2020

**Consensus or Controversy?
Investigators Discuss Clinical Practice
Patterns and Available Research Data
Guiding the Management of Hematologic
Cancers**

A 4-Part Friday Satellite Symposia Live Webinar
Series Preceding the 62nd ASH Annual Meeting

Moderator

Neil Love, MD

Thank you for joining us!

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

ONCOLOGY TODAY

COMMENTS ON THE MANAGEMENT OF OVARIAN CANCER DURING THE COVID-19 PANDEMIC

WITH DR NEIL LOVE



DR KATHLEEN MOORE

UNIVERSITY OF OKLAHOMA
HEALTH SCIENCES CENTER



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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



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Don S Dizon, MD
Professor of Medicine, Brown University
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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
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Houston, Texas



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



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".

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 displays a Zoom meeting interface. At the top, there is a gallery view of six participants. The main content area shows 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?". Below the question is a list of ten treatment options, each with a radio button for selection. A "Quick Poll" dialog box is overlaid on the list, showing the selected option: "Carfilzomib +/- dexamethasone". The bottom of the screen shows the Zoom control bar with 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 search and status icons for each participant.

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?

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

Co-provided by USFHealth Research To Practice®

Participants (10)

Search

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Join Audio Start Video Invite Participants 10 Share Chat Record Leave Meeting Mute Me Raise Hand

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

ONCOLOGY TODAY

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WITH DR NEIL LOVE



DR KATHLEEN MOORE
UNIVERSITY OF OKLAHOMA
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**Year in Review: Clinical Investigators Provide
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Data Sets and Advances in Oncology**

Prostate Cancer

**Tuesday, December 1, 2020
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Faculty

**Emmanuel S Antonarakis, MD
Andrew J Armstrong, MD, ScM**

Moderator

Neil Love, MD

Consensus or Controversy? Investigators Discuss Clinical Practice Patterns and Available Research Data Guiding the Management of Hematologic Cancers

A 4-Part Friday Satellite Symposia Live Webinar Series Preceding the 62nd ASH Annual Meeting

Friday, December 4, 2020

Multiple Myeloma

8:30 AM – 10:00 AM Pacific Time
(11:30 AM – 1:00 PM ET)

Chronic Lymphocytic Leukemia

12:00 PM – 1:30 PM Pacific Time
(3:00 PM – 4:30 PM ET)

Acute Myeloid Leukemia

3:00 PM – 4:30 PM Pacific Time
(6:00 PM – 7:30 PM ET)

Hodgkin and Non-Hodgkin Lymphoma

7:00 PM – 8:30 PM Pacific Time
(10:00 PM – 11:30 PM ET)

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Gigi Chen, MD

Diablo Valley Oncology and Hematology Medical Group
Pleasant Hill, California



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

Meet The Professor with Dr Armstrong

MODULE 1: Cases from Drs Chen and Westin

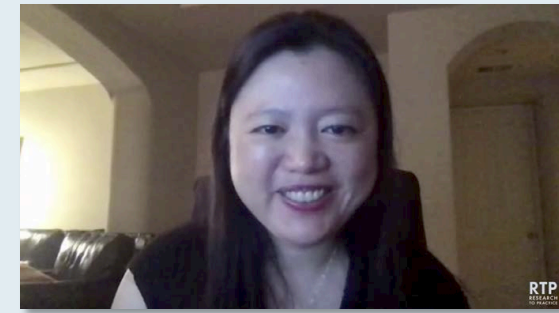
- Dr Chen: A 72-year-old woman with Stage IIIC serous carcinoma of the fallopian tube – Part 1
- Dr Chen: A 72-year-old woman with Stage IIIC serous carcinoma of the fallopian tube – Part 2
- Dr Westin: A 41-year-old woman with Stage IIIC high-grade serous ovarian cancer, somatic BRCA mutation
- Dr Westin: Perspective on Management Strategies to Minimize Nausea Associated with PARP Inhibitors
- Dr Chen: A frail 84-year-old woman with metastatic serous carcinoma

MODULE 2: Journal Club with Dr Armstrong

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

MODULE 4: Key Recent Papers

Case Presentation – Dr Chen: A 72-year-old woman with Stage IIIC serous carcinoma of the fallopian tube – Part 1



Dr Gigi Chen

- 10/2019: Diagnosed with Stage IIIC fallopian tube cancer
- Upfront optimal debulking surgery and IP port
- BRCA wildtype
- FoundationOne® testing: MSS, LOH < 16%, BRAF deletion intron 3, BRIP1 rearrangement, MDM2, MYC amplification, RAD21 and TP53
- IV/IP chemotherapy x 6
 - Persistent anemia with hemoglobin of 9 two months after completion

Questions

- What is the role for IV/IP versus IV chemotherapy?
- In light of her BRCA wildtype status for both somatic and germline and her low LOH, what is the role for PARP inhibitor maintenance therapy? And what would be the best agent for her?

Case Presentation – Dr Chen: A 72-year-old woman with Stage IIIC serous carcinoma of the fallopian tube – Part 2



Dr Gigi Chen

- 10/2019: Diagnosed with Stage IIIC fallopian tube cancer
- Upfront optimal debulking surgery and IP port
- BRCA wildtype
- FoundationOne testing: MSS, LOH < 16%, BRAF deletion intron 3, BRIP1 rearrangement, MDM2, MYC amplification, RAD21 and TP53
- IV/IP chemotherapy x 6
 - Persistent anemia with hemoglobin of 9 two months after completion

Questions

- What is the role for IV/IP versus IV chemotherapy?
- In light of her BRCA wildtype status for both somatic and germline and her low LOH, what is the role for PARP inhibitor maintenance therapy? And what would be the best agent for her?
- **What is the best dose of niraparib to start with, particularly in light of her anemia?**

Case Presentation – Dr Westin: A 41-year-old woman with Stage IIIC HGSOE, somatic BRCA mutation



Dr Shannon Westin

- Stage IIIC HGSOE s/p optimal debulking surgery (R0)
 - Somatic BRCA mutation, germline BRCA wildtype
- Carboplatin/paclitaxel x 6, NED at the completion of treatment, with minimal neuropathy
- Olaparib 300mg PO BID x 9 and ongoing, with mild fatigue
 - Initial N/V for ~ 2 weeks addressed via pre-treatment with anti-5HT3 inhibitor

Initial Imaging: Bilateral Ovarian Masses with Peritoneal Carcinomatosis



Question

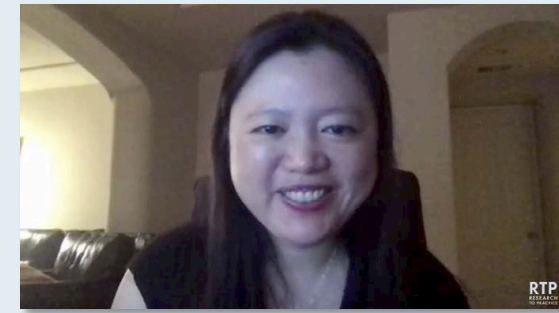
- How do you manage the gastrointestinal side effects associated with PARP inhibitors?

Perspective on Management Strategies to Minimize Nausea Associated with PARP Inhibitors



Dr Shannon Westin

Case Presentation – Dr Chen: A frail 84-year-old woman with metastatic serous carcinoma



Dr Gigi Chen

- PMH: Hypertension, chronic kidney disease (creatinine of 2)
- Exploratory laparotomy, posterior pelvic exenteration with primary end-to-end low rectal anastomosis, pancreatic biopsy, protocol sigmoidoscopy and complete excision of pelvic mass
- 12/2015: High-grade serous carcinoma of the left fallopian tube and pancreas
- 5/2016: GOG-3005 clinical trial of adjuvant carboplatin/paclitaxel +/- veliparib
- BRCA wildtype, HRD-positive
- 7/2017: Recurrent ovarian cancer → Carboplatin/paclitaxel → Maintenance niraparib 100 mg
- Currently, PD in LLL lung, other disease is stable

Questions

- What are the options for oligoprogression, particularly in a frail patient? Is SBRT an option? Single-agent chemotherapy? Switch to a different PARP inhibitor?
- What was the outcome of the GOG-3005 trial with adjuvant carboplatin/paclitaxel +/- veliparib?

Meet The Professor with Dr Armstrong

MODULE 1: Cases from Drs Chen and Westin

MODULE 2: Journal Club with Dr Armstrong

- ASCO guidelines: Germline and somatic testing in epithelial ovarian cancer (OC)
- SGO practice statement: Front-line PARP inhibitor maintenance therapy for OC
- ASCO guidelines: PARP inhibitors in the management of OC
- Role of intraperitoneal therapy in the initial management of OC
- Intravenous or intraperitoneal chemotherapy with veliparib and bevacizumab
- Secondary surgical cytoreduction for recurrent OC
- Dabrafenib/trametinib in patients with BRAF V600E mutations: NCI-MATCH trial
- Patient-centered outcomes in the ARIEL3 trial with maintenance rucaparib
- Anticancer therapy and clinical trial considerations for patients with gynecologic cancer during the COVID-19 pandemic

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

MODULE 4: Key Recent Papers

Germline and Somatic Tumor Testing in Epithelial Ovarian Cancer: ASCO Guideline

Panagiotis A. Konstantinopoulos, MD, PhD¹; Barbara Norquist, MD²; Christina Lacchetti, MHSc³; Deborah Armstrong, MD⁴; Rachel N. Grisham, MD⁵; Paul J. Goodfellow, PhD⁶; Elise C. Kohn, MD⁷; Douglas A. Levine, MD⁸; Joyce F. Liu, MD, MPH¹; Karen H. Lu, MD⁹; Dorinda Sparacio, MS¹⁰; and Christina M. Annunziata, MD, PhD¹¹

J Clin Oncol 2020;38(11):1222-45.

Gynecologic Oncology 159 (2020) 8–12

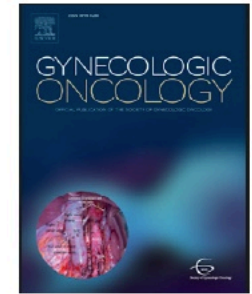


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Gynecologic Oncology

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



Frontline PARP inhibitor maintenance therapy in ovarian cancer: A Society of Gynecologic Oncology practice statement

Bhavana Pothuri *, Roisin O'Cearbhaill, Ramez Eskander, Deborah Armstrong

Dosing, Interactions and Dose Reductions

| | Olaparib | Niraparib | Veliparib |
|---|---|--|--|
| Formulations | 100 mg and 150 mg tablets | 100 mg capsules | 100 mg and 50 mg capsules |
| Interaction with cytochrome (CYP) enzymes | Inhibits CYP3A4 and induces CYP2B6 Avoid Seville oranges and grapefruits | Not significantly metabolized by CYP enzymes | Not significantly metabolized by CYP enzymes |
| Initial dose | 300 mg BID (two 150 mg tablets BID) | 300 mg daily (three 100 mg capsules) | 400 mg BID (four 100 mg capsules BID) |
| 1st dose reduction | 250 mg BID (one 150 mg and one 100 mg tablet BID) | 200 mg daily (two 100 mg capsules) | 300 mg (three 100 mg capsules BID) |
| 2nd dose reduction | 200 mg BID (two 100 mg tablets BID) | 100 mg daily (one 100 mg capsule) | 250 mg (two 100 mg and one 50 mg capsules BID) |

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;38(30):3468-93.

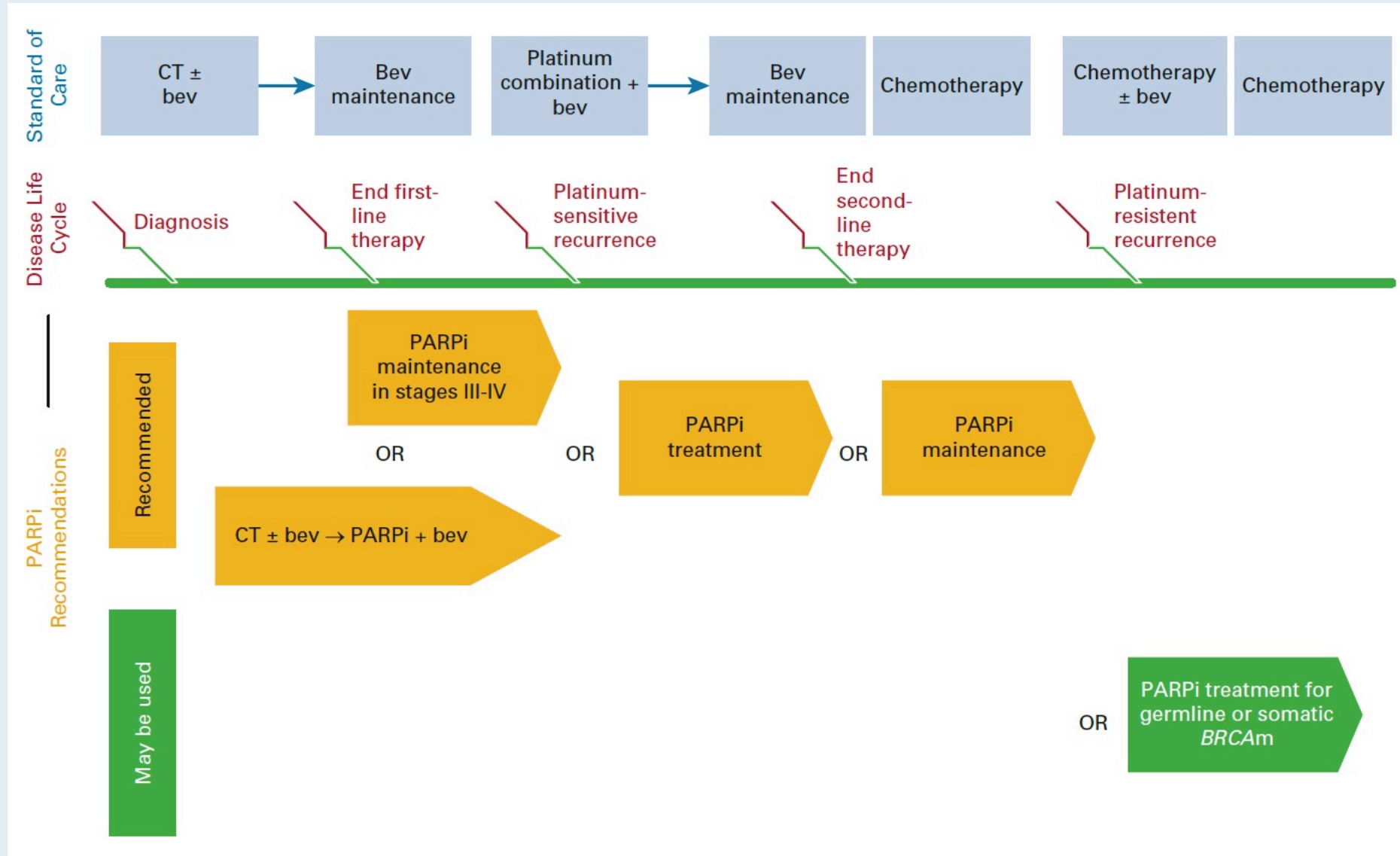
ASCO Guideline Recommendations

“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.”

PARP Inhibitor Use Opportunities for Women Who Are PARPi Naïve



SPECIAL SERIES: ADVANCES IN THE MANAGEMENT OF GYNECOLOGIC CANCERS

comments and controversies

Role of Intraperitoneal Therapy in the Initial Management of Ovarian Cancer

Deborah K. Armstrong, MD,¹ and Joan L. Walker, MD²

J Clin Oncol 2019;37(27):2416-9.

Tolerability and Adverse Events Experienced by Women with Ovarian Cancer Treated with Intravenous or Intraperitoneal Chemotherapy plus Veliparib and Bevacizumab Based on *BRCA* Status

Gillen J et al.

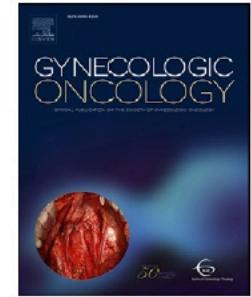
SGO 2020;Abstract 28.



Contents lists available at [ScienceDirect](https://www.sciencedirect.com)

Gynecologic Oncology

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



A phase I study of intravenous or intraperitoneal platinum based chemotherapy in combination with veliparib and bevacizumab in newly diagnosed ovarian, primary peritoneal and fallopian tube cancer

Kathleen N. Moore ^{a,*}, Austin Miller ^b, Katherine M. Bell-McGuinn ^{c,**,1},
Russell J. Schilder ^d, Joan L. Walker ^a, Roisin E. O’Cearbhaill ^c, Saketh R. Guntupalli ^e,
Deborah K. Armstrong ^f, Andrea R. Hagemann ^g, Heidi J. Gray ^h, Linda R. Duska ⁱ,
Cara A. Mathews ^j, Alice Chen ^k, David O’Malley ^l, Sarah Gordon ^m, Paula M. Fracasso ^{i,2},
Carol Aghajanian ^c

The NEW ENGLAND JOURNAL of MEDICINE

N Engl J Med 2019;381(20):1929-39.

ORIGINAL ARTICLE

Secondary Surgical Cytoreduction for Recurrent Ovarian Cancer

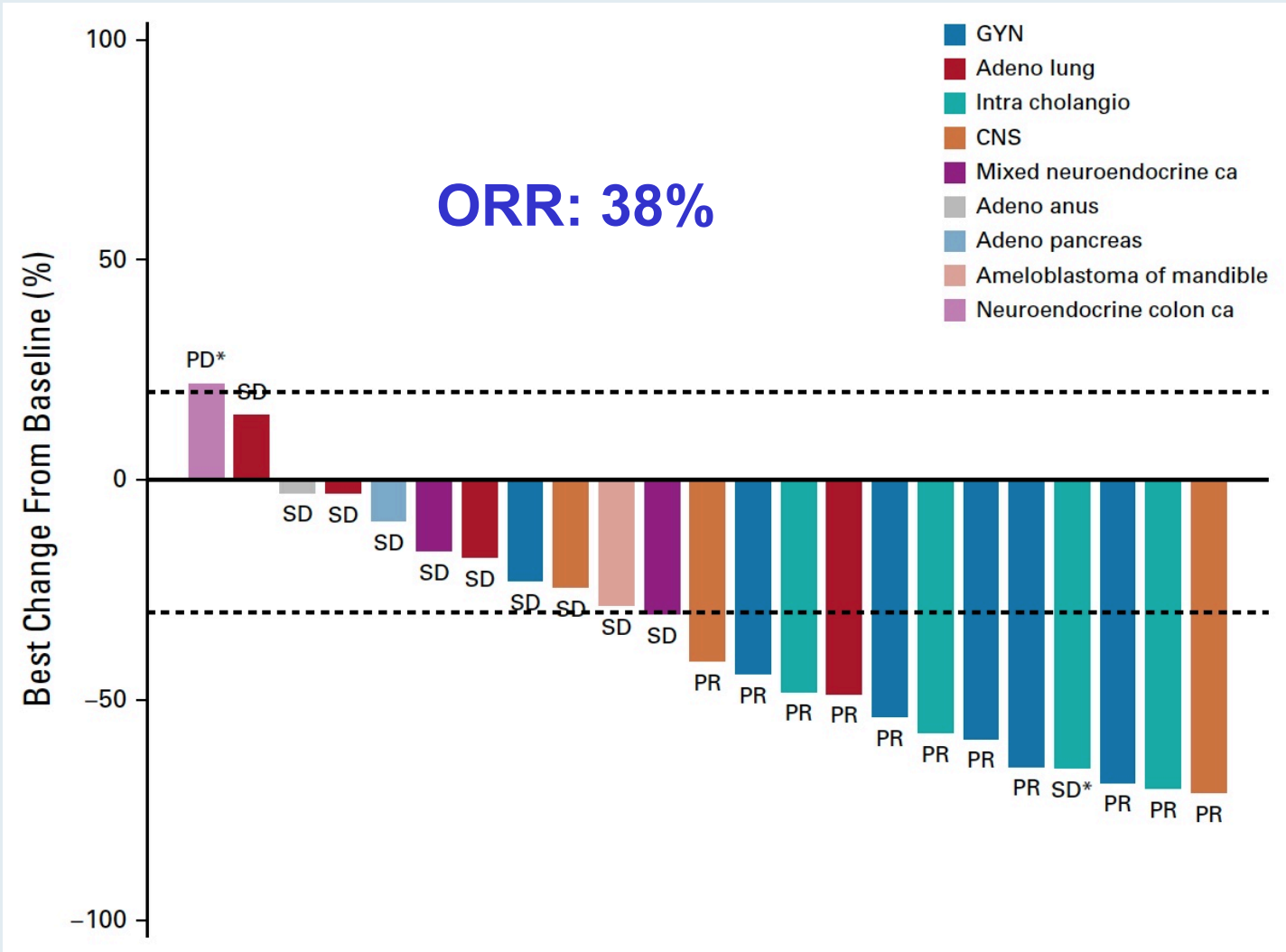
Robert L. Coleman, M.D., Nick M. Spirtos, M.D., Danielle Enserro, Ph.D.,
Thomas J. Herzog, M.D., Paul Sabbatini, M.D., Deborah K. Armstrong, M.D.,
Jae-Weon Kim, M.D., Sang-Yoon Park, M.D., Byoung-Gie Kim, M.D.,
Joo-Hyun Nam, M.D., Keiichi Fujiwara, M.D., Joan L. Walker, M.D.,
Ann C. Casey, M.D., Angeles Alvarez Secord, M.D., Steve Rubin, M.D.,
John K. Chan, M.D., Paul DiSilvestro, M.D., Susan A. Davidson, M.D.,
David E. Cohn, M.D., Krishnansu S. Tewari, M.D., Karen Basen-Engquist, Ph.D.,
Helen Q. Huang, M.S., Mark F. Brady, Ph.D., and Robert S. Mannel, M.D.

Dabrafenib and Trametinib in Patients With Tumors With *BRAF*^{V600E} Mutations: Results of the NCI-MATCH Trial Subprotocol H

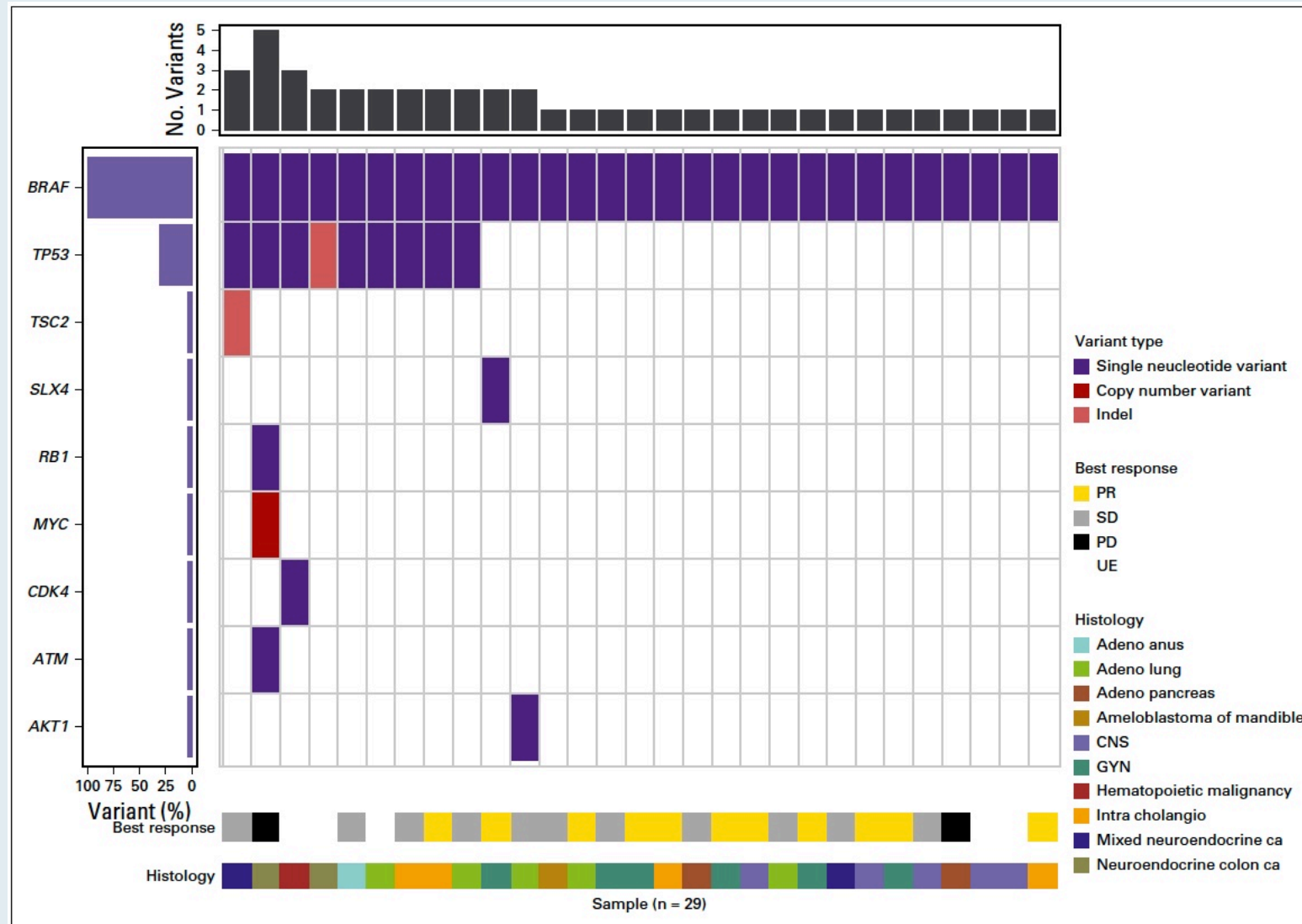
April K. S. Salama, MD¹; Shuli Li, PhD²; Erin R. Macrae, MD³; Jong-In Park, PhD⁴; Edith P. Mitchell, MD⁵; James A. Zwiebel, MD⁶; Helen X. Chen, MD⁷; Robert J. Gray, PhD²; Lisa M. McShane, PhD⁸; Larry V. Rubinstein, PhD⁸; David Patton, MS⁹; P. Mickey Williams, PhD¹⁰; Stanley R. Hamilton, MD¹¹; Deborah K. Armstrong, MD¹²; Barbara A. Conley, MD¹³; Carlos L. Arteaga, MD¹⁴; Lyndsay N. Harris, MD¹³; Peter J. O'Dwyer, MD¹⁵; Alice P. Chen, MD¹³; and Keith T. Flaherty, MD¹⁶

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

Best Percentage Change from Baseline in 23 Patients with Evaluable Measurements



Co-Occurring Genomic Alterations with BRAF V600E Using the Central NCI-MATCH Assay for 29 Patients

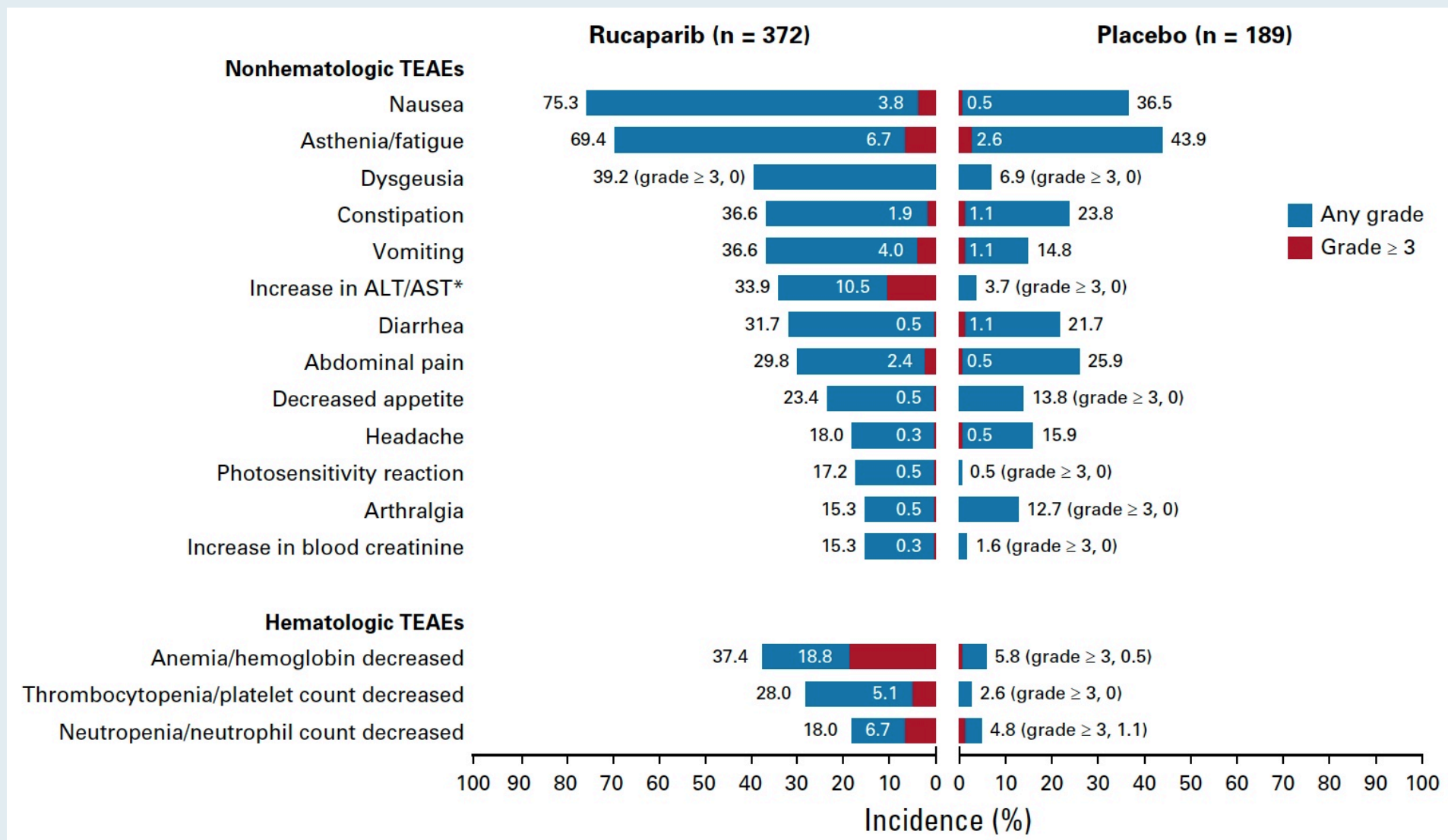


Patient-Centered Outcomes in ARIEL3, a Phase III, Randomized, Placebo-Controlled Trial of Rucaparib Maintenance Treatment in Patients With Recurrent Ovarian Carcinoma

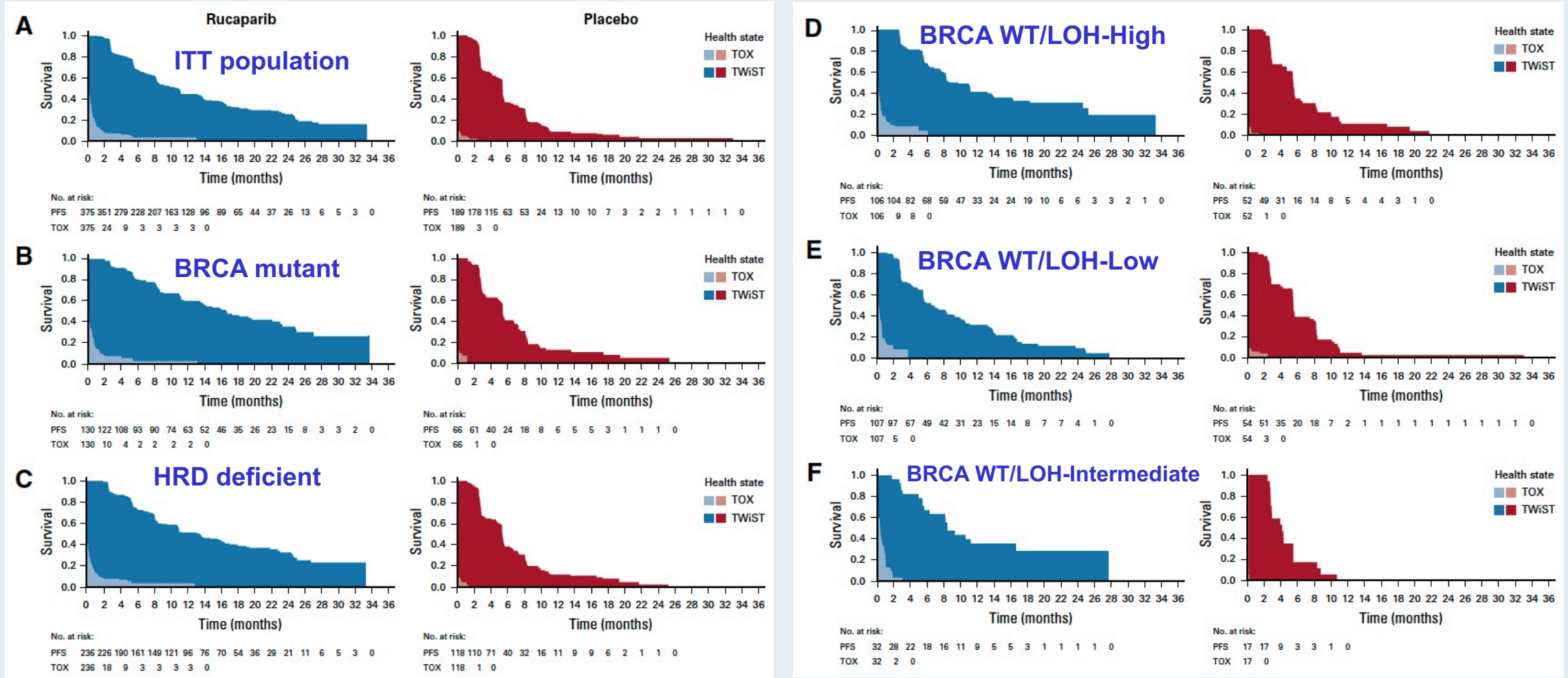
Amit M. Oza, MD¹; Domenica Lorusso, MD²; Carol Aghajanian, MD³; Ana Oaknin, MD, PhD⁴; Andrew Dean, MD⁵; Nicoletta Colombo, MD⁶; Johanne I. Weberpals, MD⁷; Andrew R. Clamp, MD, PhD⁸; Giovanni Scambia, MD²; Alexandra Leary, MD⁹; Robert W. Holloway, MD¹⁰; Margarita Amenedo Gancedo, MD¹¹; Peter C. Fong, MBBS¹²; Jeffrey C. Goh, MBBA¹³; David M. O'Malley, MD¹⁴; Deborah K. Armstrong, MD¹⁵; Susana Banerjee, PhD¹⁶; Jesus García-Donas, MD¹⁷; Elizabeth M. Swisher, MD¹⁸; David Cella, PhD¹⁹; Juliette Meunier, MSc²⁰; Sandra Goble, MS²¹; Terri Cameron, MSc²²; Lara Maloney, BA²¹; Ann-Christin Mörk, PhD²³; Josh Bedel, MSc²⁴; Jonathan A. Ledermann, MD²⁵; and Robert L. Coleman, MD²⁶

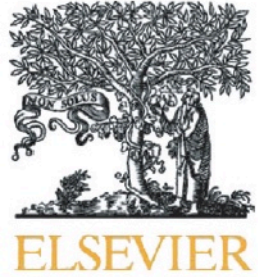
J Clin Oncol 2020;38(30):3494-505.

Most Frequent Treatment-Emergent Adverse Events (TEAEs; Reported in $\geq 35\%$ of Patients) in ARIEL3



Time Without Symptoms or Toxicity (TWiST) Analysis





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Gynecologic Oncology

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



The effect of age on efficacy, safety and patient-centered outcomes with rucaparib: A post hoc exploratory analysis of ARIEL3, a phase 3, randomized, maintenance study in patients with recurrent ovarian carcinoma

Nicoletta Colombo ^{a,*}, Amit M. Oza ^b, Domenica Lorusso ^c, Carol Aghajanian ^d, Ana Oaknin ^e, Andrew Dean ^f, Johanne I. Weberpals ^g, Andrew R. Clamp ^h, Giovanni Scambia ^c, Alexandra Leary ⁱ, Robert W. Holloway ^j, Margarita Amenedo Gancedo ^k, Peter C. Fong ^l, Jeffrey C. Goh ^m, David M. O'Malley ⁿ, Deborah K. Armstrong ^o, Susana Banerjee ^p, Jesus García-Donas ^q, Elizabeth M. Swisher ^r, Juliette Meunier ^s, Terri Cameron ^t, Lara Maloney ^u, Sandra Goble ^v, Josh Bedel ^w, Jonathan A. Ledermann ^x, Robert L. Coleman ^y

Gynecologic Oncology 158 (2020) 16–24

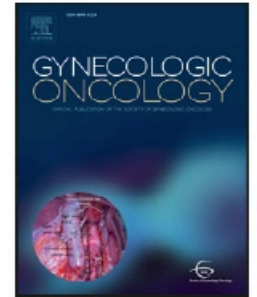


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Clinical Practice Statement

Anti-cancer therapy and clinical trial considerations for gynecologic oncology patients during the COVID-19 pandemic crisis☆

Bhavana Pothuri ^{a,*}, Angeles Alvarez Secord ^b, Deborah K. Armstrong ^c, John Chan ^d, Amanda N. Fader ^c, Warner Huh ^e, Joshua Kesterson ^f, Joyce F. Liu ^g, Kathleen Moore ^h, Shannon N. Westin ⁱ, R. Wendel Naumann ^j

Issues to Deliberate When Starting or Continuing Anticancer Therapy in Patients with Gynecologic Cancers During the COVID-19 Pandemic

| Issue | Consideration |
|---|---|
| What is the goal of treatment for your patient? | <ul style="list-style-type: none">• Are you impacting OS? Cure?• Are you expecting meaningful prolongation of PFS? |

Issues to Deliberate When Starting or Continuing Anticancer Therapy in Patients with Gynecologic Cancers During the COVID-19 Pandemic

| Issue | Consideration |
|---|--|
| What is the health status of your individual patient? | <ul style="list-style-type: none">• Can you assess their overall morbidity and mortality due to cancer? Use of Geriatric Screening G8 for older patients (9) |

Issues to Deliberate When Starting or Continuing Anticancer Therapy in Patients with Gynecologic Cancers During the COVID-19 Pandemic

| Issue | Consideration |
|--|---|
| What is the likelihood of toxicity from anti-cancer treatment? | <ul style="list-style-type: none">• Utilization of CARG toxicity tool to predict grade 3–5 toxicity• http://www.mycarg.org/Chemo_Toxicity_Calculator |

Issues to Deliberate When Starting or Continuing Anticancer Therapy in Patients with Gynecologic Cancers During the COVID-19 Pandemic

| Issue | Consideration |
|--|--|
| Are there alternatives of similar efficacy which minimize toxicity from anti-cancer therapy and/or risk from exposure to the health care system? | <ul style="list-style-type: none">• Oral agents (oral ≠ non-toxic)• Fewer in-person visits• Treatment holidays |

Meet The Professor with Dr Armstrong

MODULE 1: Cases from Drs Chen and Westin









MODULE 2: Journal Club with Dr Armstrong

- ASCO guidelines: Germline and somatic testing in epithelial ovarian cancer (OC)
- SGO practice statement: Front-line PARP inhibitor maintenance therapy for OC
- ASCO guidelines: PARP inhibitors in the management of OC
- Role of intraperitoneal therapy in the initial management of OC
- Intravenous or intraperitoneal chemotherapy with veliparib and bevacizumab
- Secondary surgical cytoreduction for recurrent OC
- Dabrafenib/trametinib in patients with BRAF V600E mutations: NCI-MATCH trial
- Patient-centered outcomes in the ARIEL3 trial with maintenance rucaparib
- Anticancer therapy and clinical trial considerations for patients with gynecologic cancer during the COVID-19 pandemic

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

MODULE 4: Key Recent Papers

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 Armstrong

MODULE 1: Cases from Drs Chen and Westin

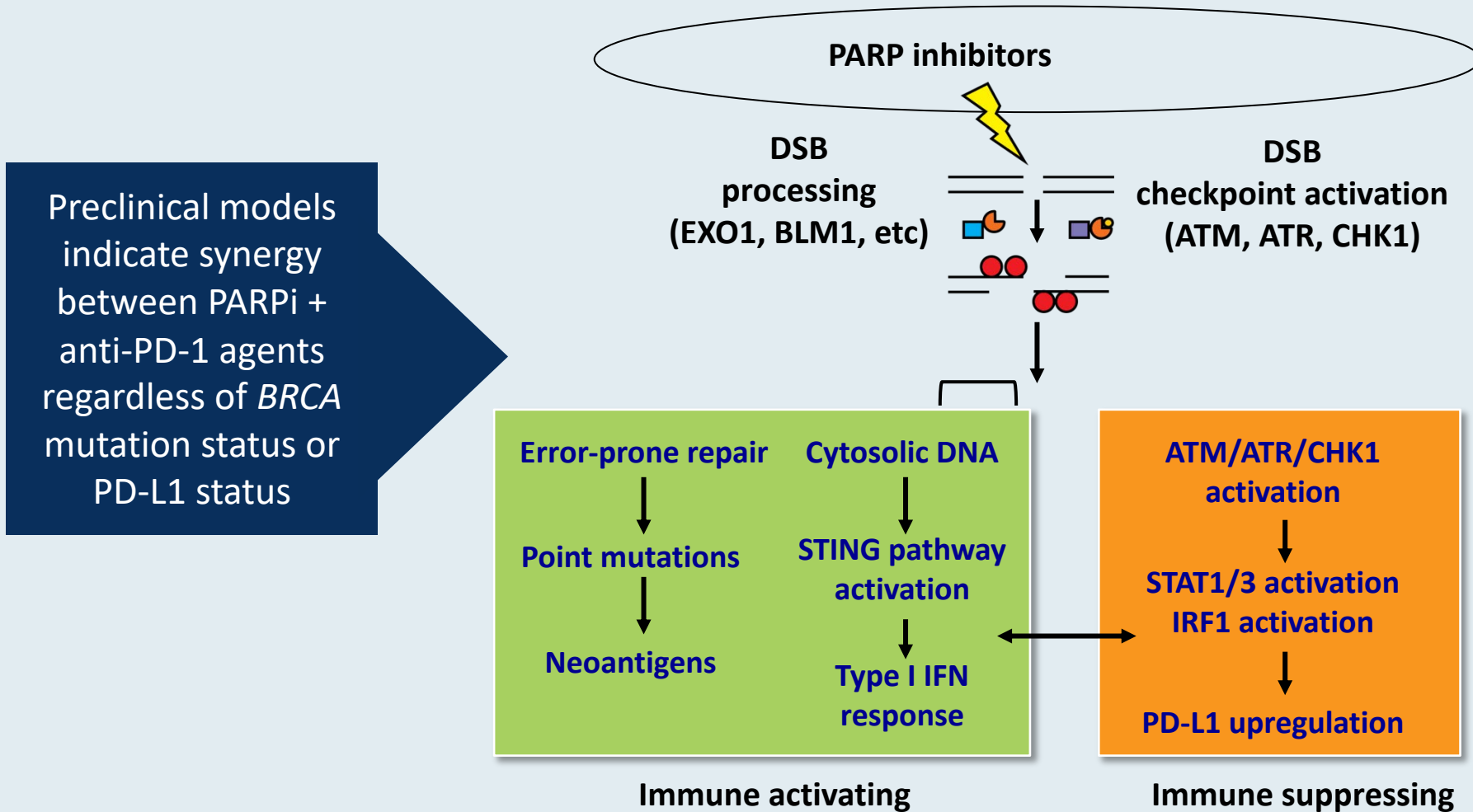
MODULE 2: Journal Club with Dr Armstrong

- ASCO guidelines: Germline and somatic testing in epithelial ovarian cancer (OC)
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MODULE 3: Beyond the Guidelines – Clinical Investigator Approaches to Common Clinical Scenarios

MODULE 4: Key Recent Papers

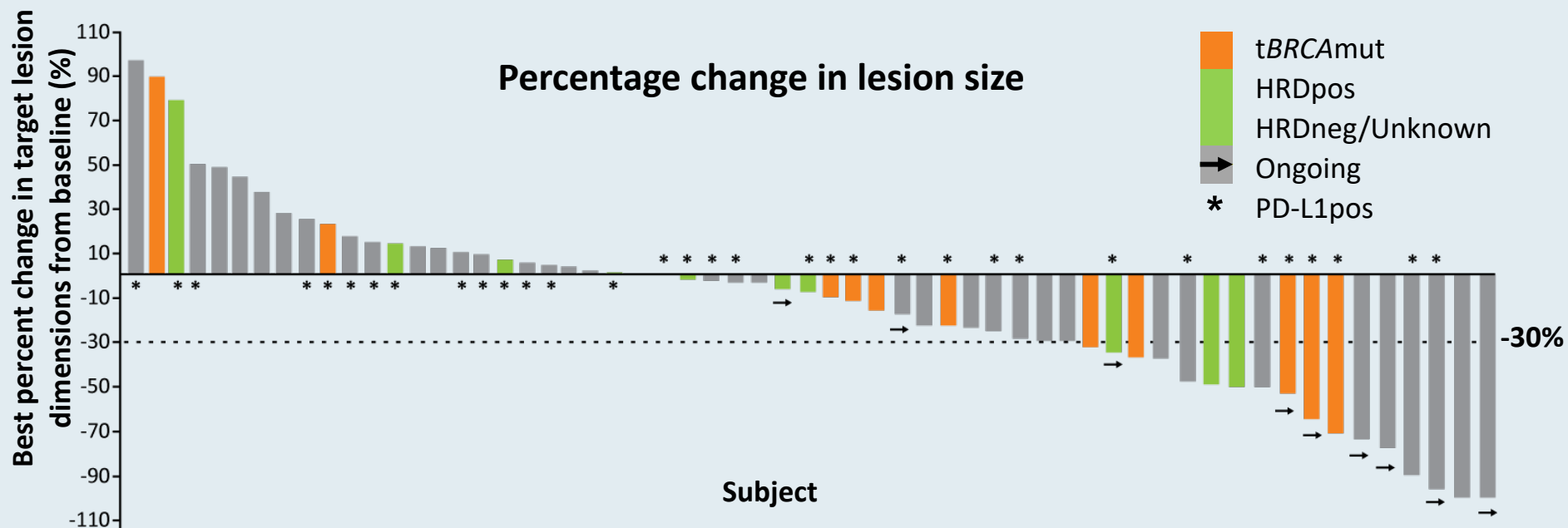
Biologic Rationale for the Combination of a PARP Inhibitor with an Immune Checkpoint Inhibitor



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

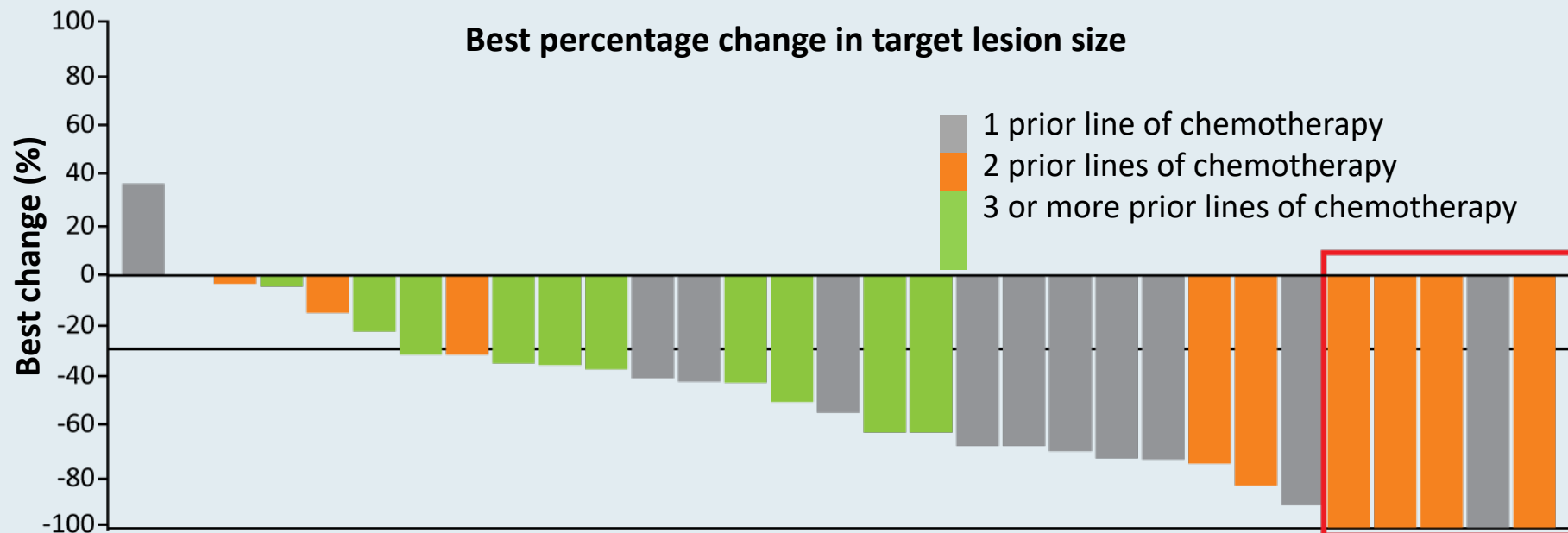
Preclinical data demonstrate synergy with PARPi and anti-PD-1 combinations.

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 |

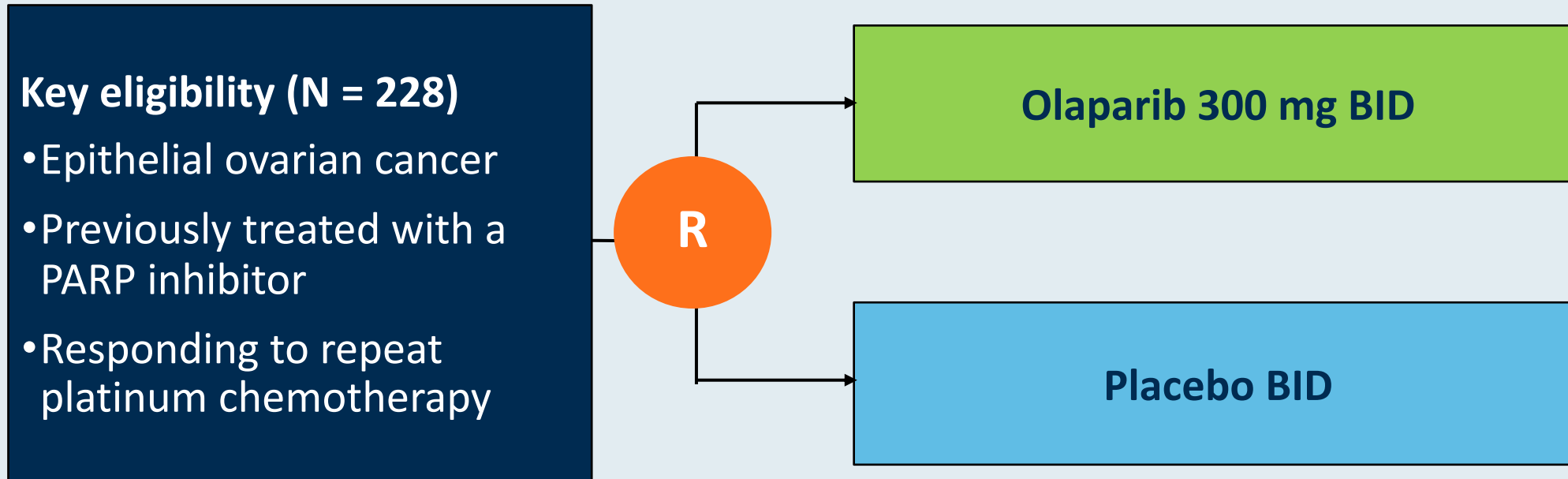
Bev = bevacizumab; ATEZO = atezolizumab

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 |

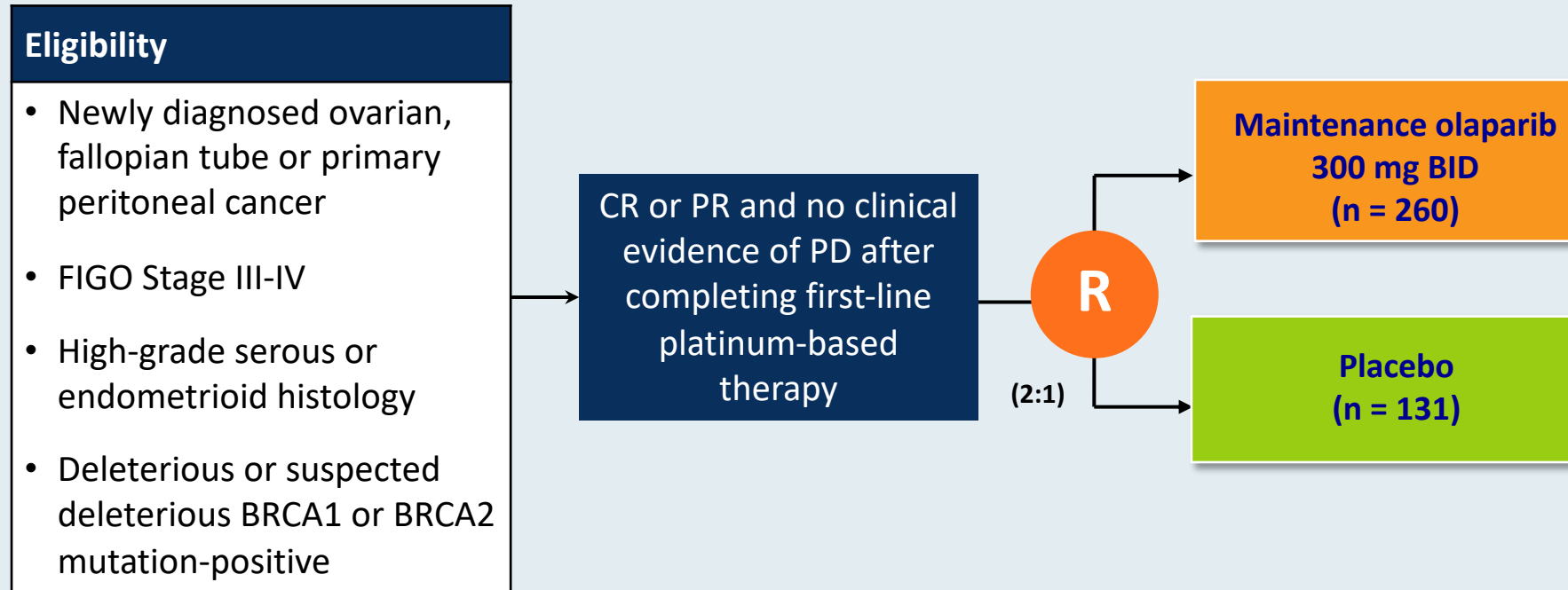
^aResidual disease based on stage was not reported. ^bStage III and IV eligible, but requirements for prior surgery not reported (NR) on clinicaltrials.gov

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

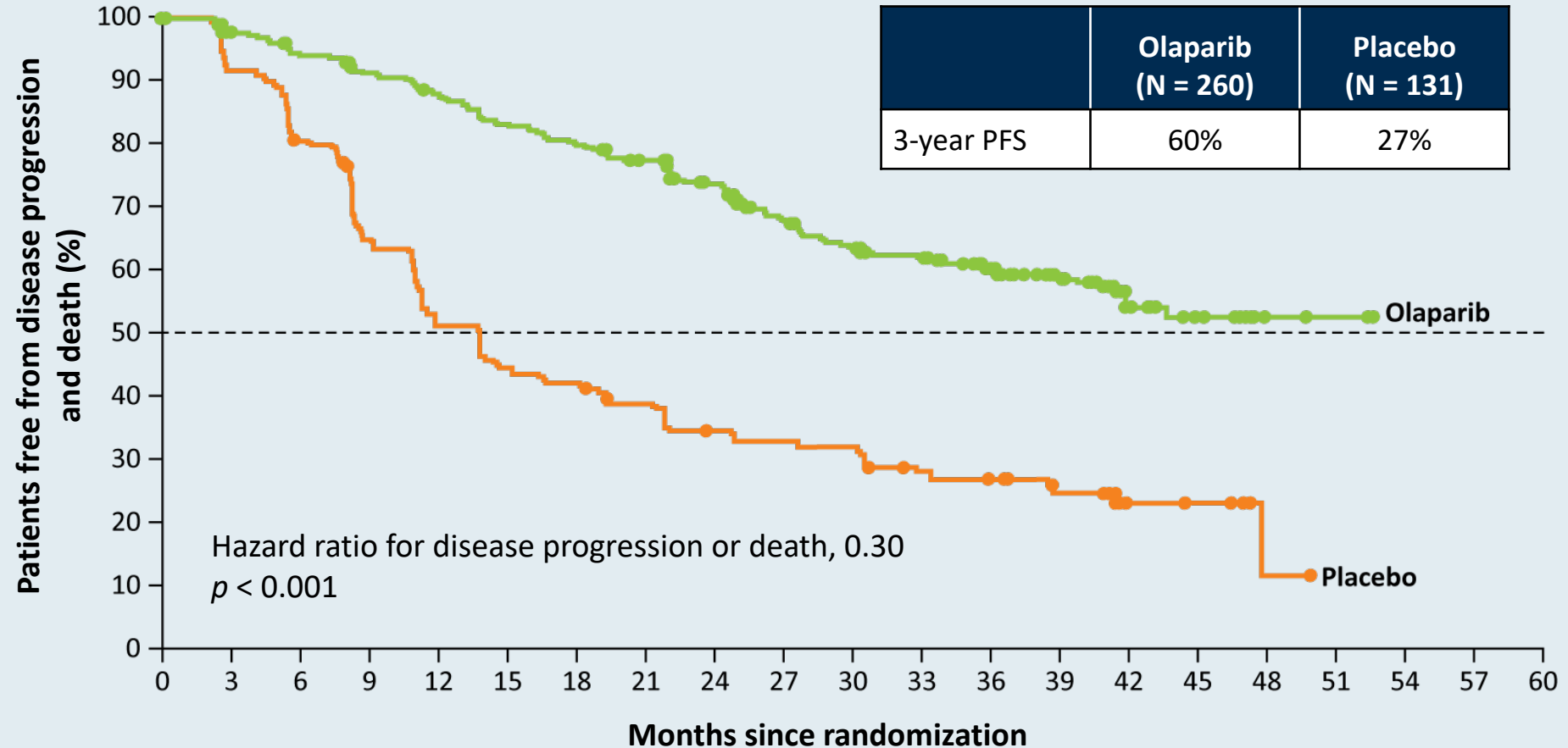
SOLO-1: A Phase III Trial of Maintenance Olaparib in OC with BRCA Mutation

NCT01844986

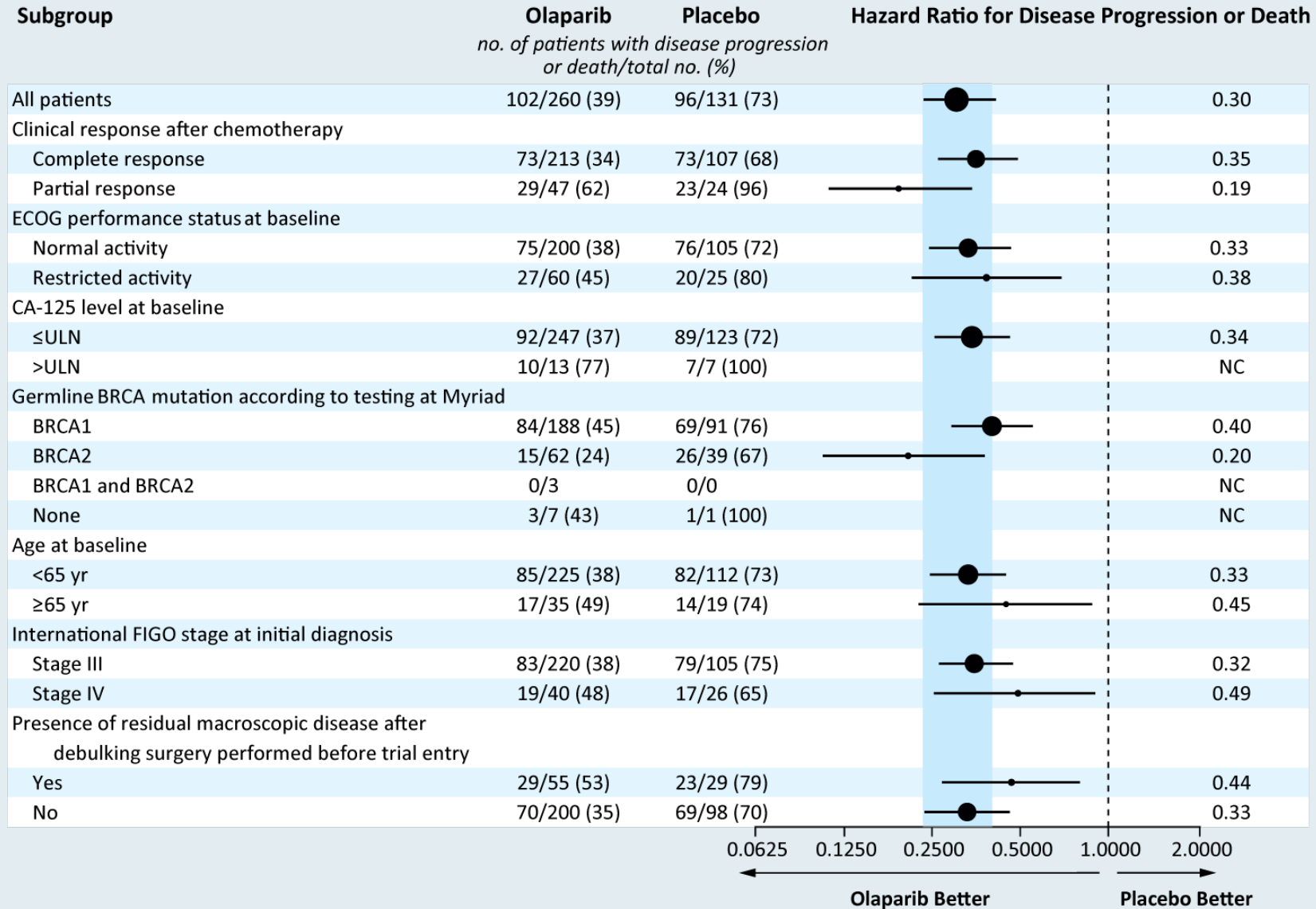


Primary endpoint: Investigator-assessed progression-free survival

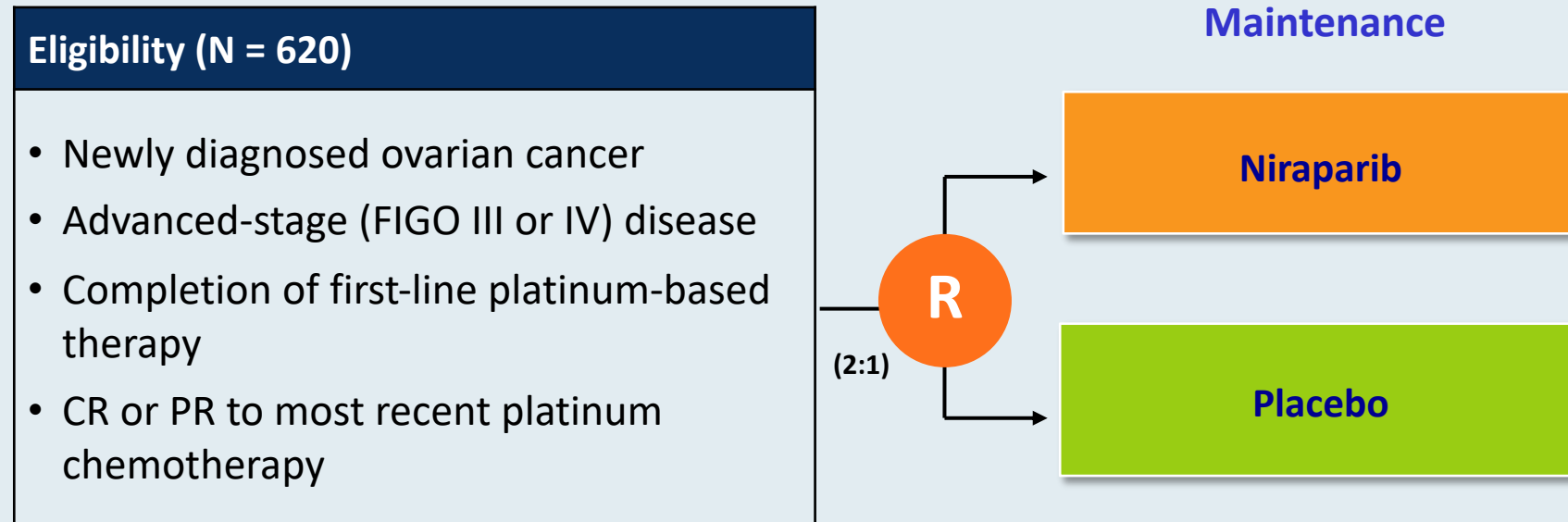
SOLO-1: Primary Endpoint Progression-Free Survival (Investigator Assessed)



SOLO-1: PFS Subgroup Analyses

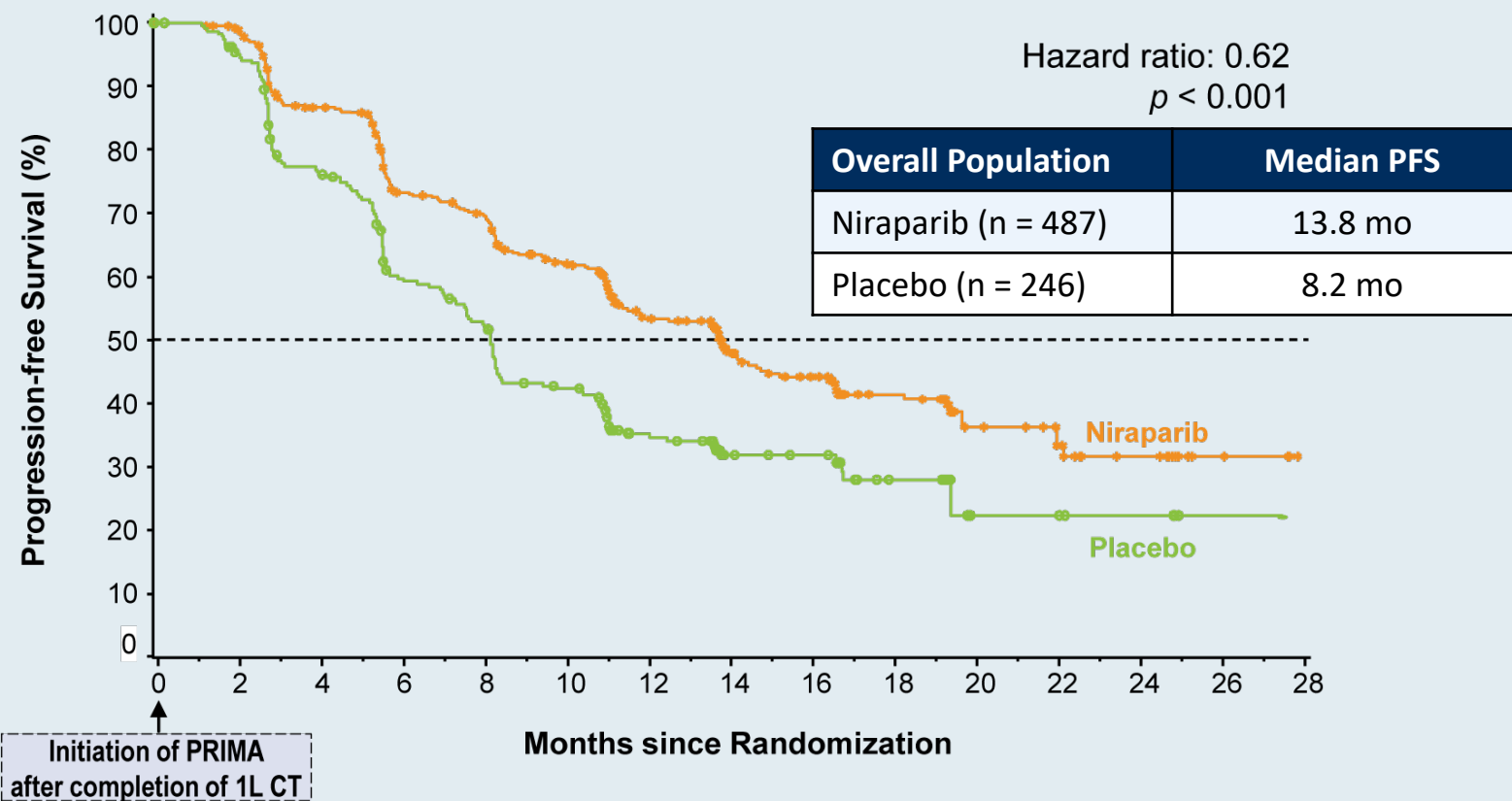


PRIMA Trial: Maintenance Niraparib for Advanced Ovarian Cancer After Response to Front-Line Platinum-Based Chemotherapy



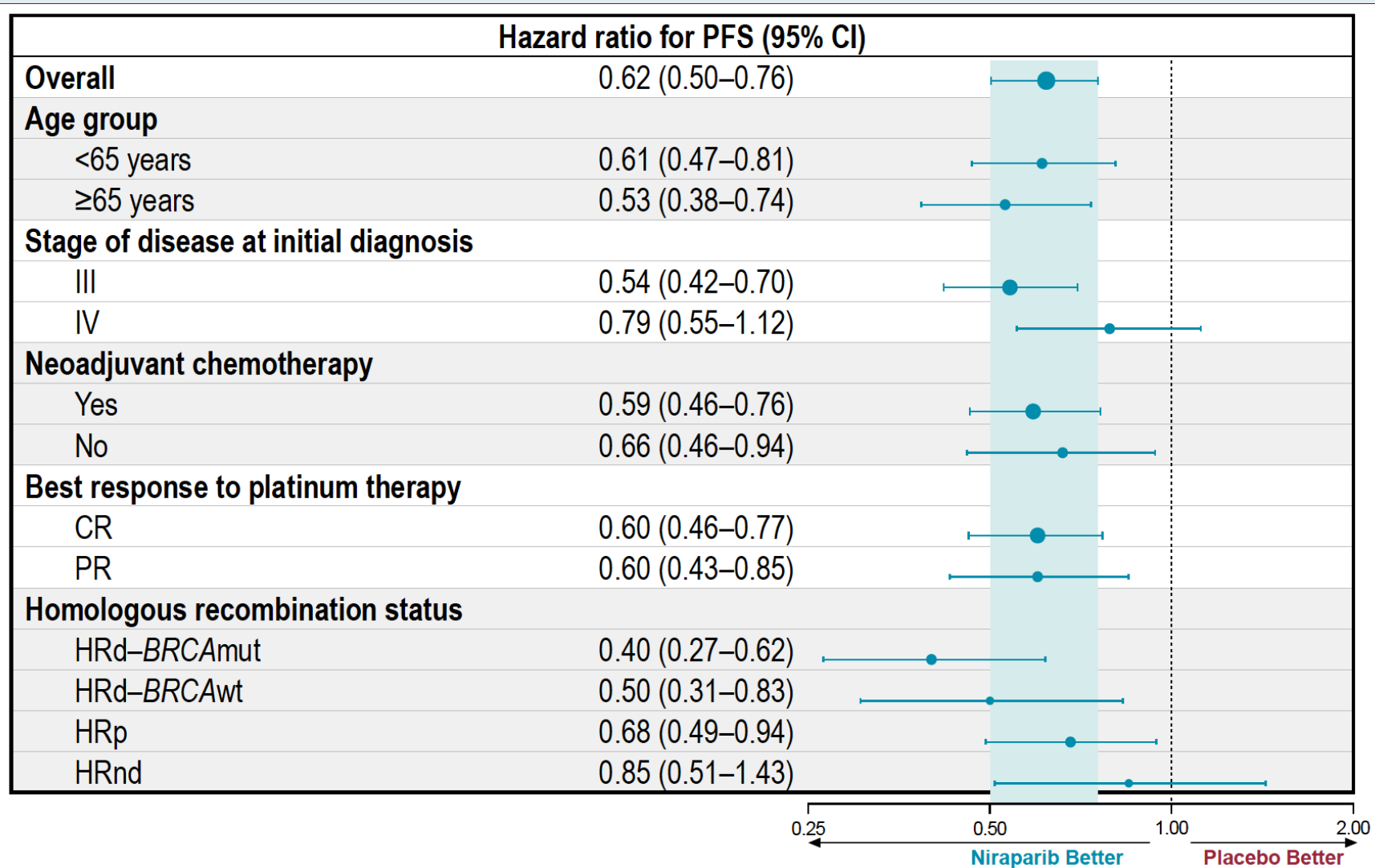
Primary endpoint: Progression-free survival

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

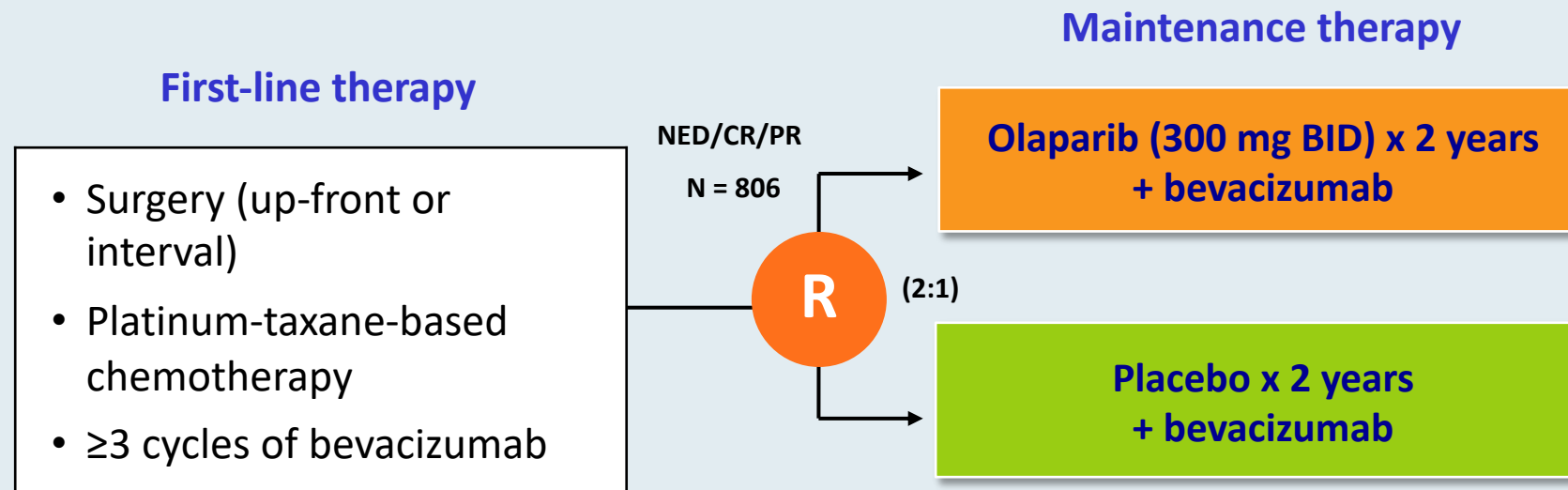
“The Food and Drug Administration expanded the indication of olaparib to include its combination with bevacizumab for first-line maintenance treatment of adult patients with advanced epithelial ovarian, fallopian tube, or primary peritoneal cancer who are in complete or partial response to first-line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

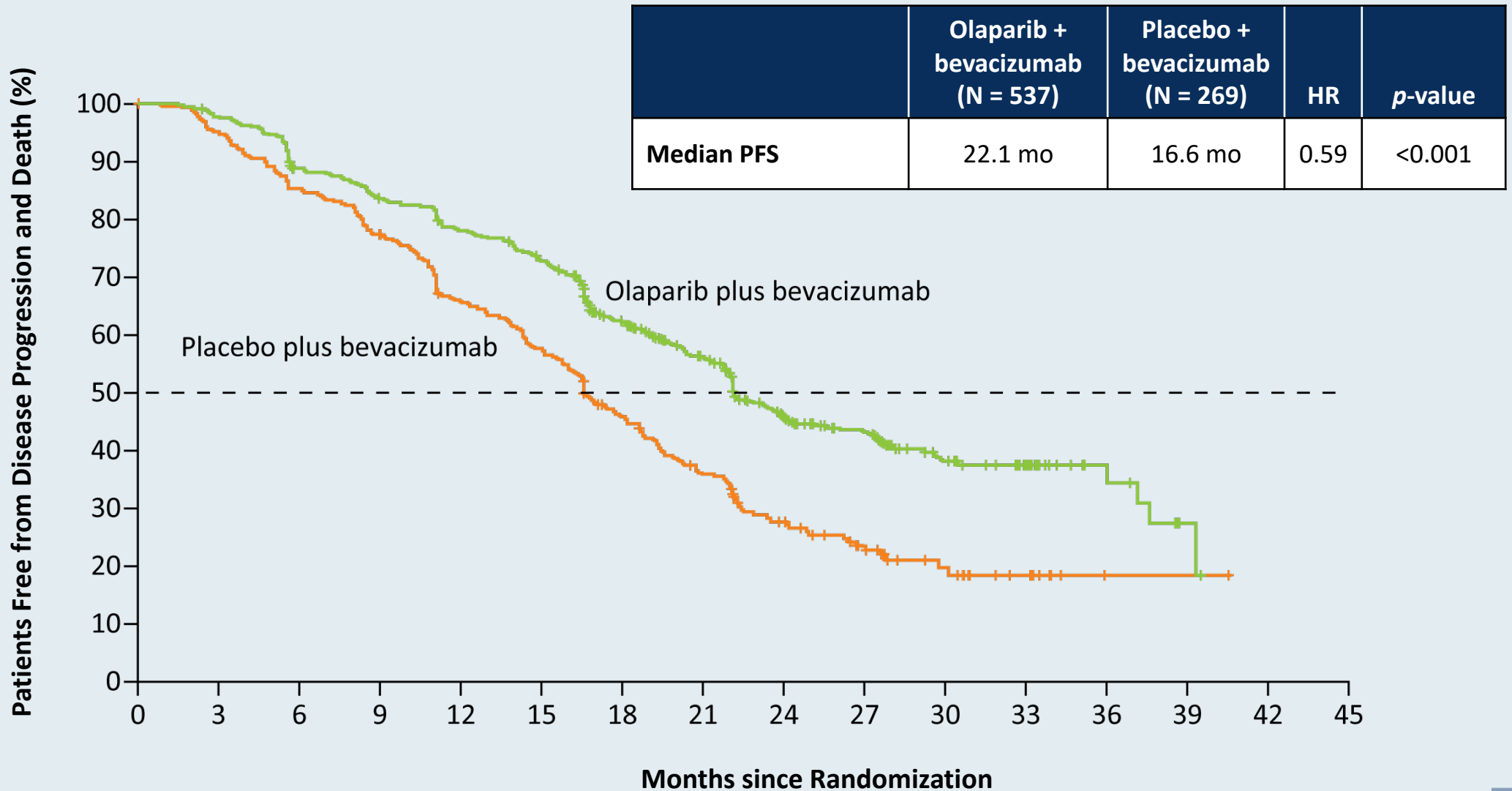
Efficacy of this new indication was investigated in PAOLA-1 (NCT03737643), a randomized, double-blind, placebo-controlled, multi-center trial comparing olaparib with bevacizumab versus placebo plus bevacizumab in patients with advanced high-grade epithelial ovarian cancer, fallopian tube, or primary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

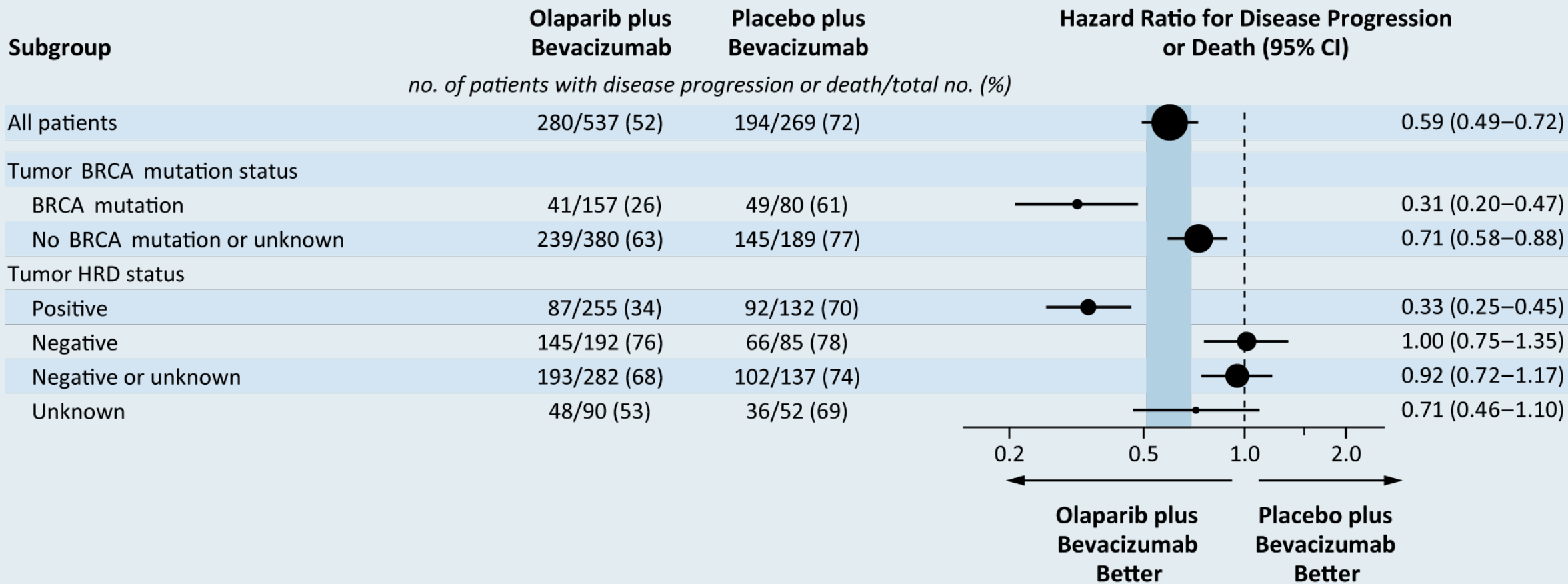
Newly diagnosed FIGO Stage III or IV high-grade serous/endometrioid ovarian, fallopian tube or primary peritoneal cancer



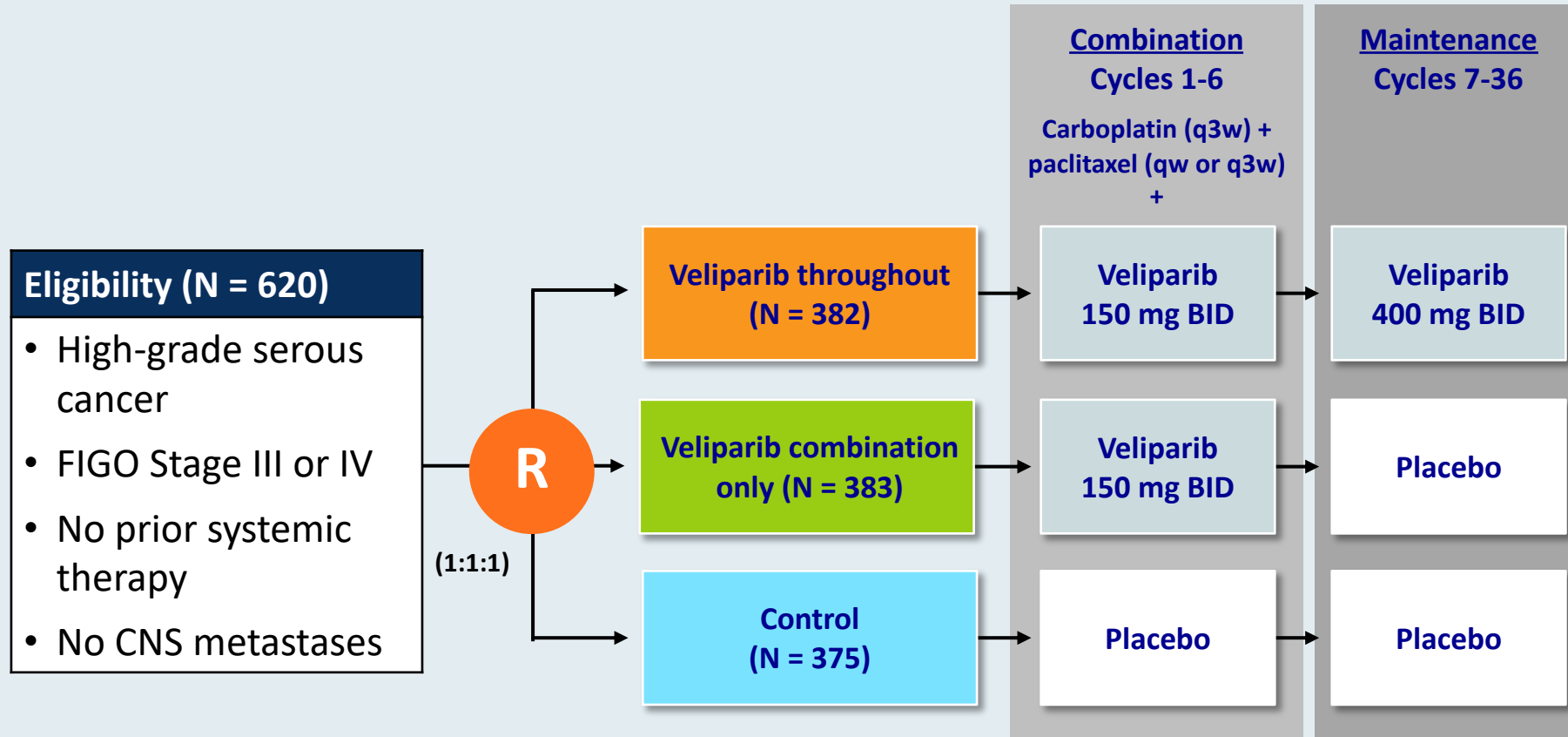
PAOLA-1: Investigator-Assessed PFS (Primary Endpoint)



PAOLA-1: Select Subgroup Analysis of PFS

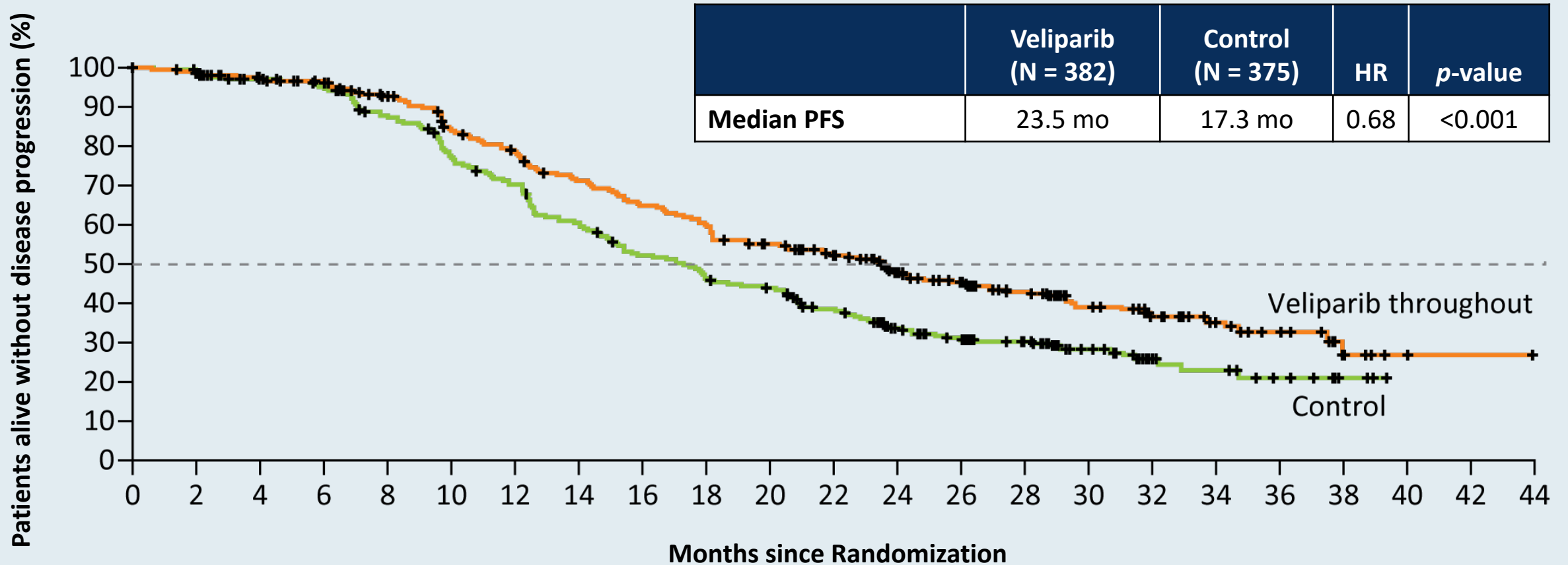


VELIA/GOG-3005: A Phase III Trial of Veliparib with Front-Line Chemotherapy and as Maintenance Therapy for High-Grade Serous Epithelial Ovarian, Fallopian Tube or Primary Peritoneal Cancers



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 | Rucaparib | Olaparib |
|---|--|--|
| <p>Indications:</p> <ul style="list-style-type: none">• Maintenance following response to platinum-based therapy• Irrespective of BRCA status <p>Pivotal study: ENGOT-OV16/NOVA</p> <p>Approved: 3/2017</p> | <p>Indications:</p> <ul style="list-style-type: none">• Maintenance following response to platinum-based therapy• Irrespective of BRCA status <p>Pivotal study: ARIEL3</p> <p>Approved: 4/2018</p> | <p>Indications:</p> <ul style="list-style-type: none">• Maintenance following response to platinum-based therapy• Irrespective of BRCA status <p>Pivotal studies: SOLO-2, Study 19</p> <p>Approved: 8/2017</p> |

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.

**Year in Review: Clinical Investigators Provide
Perspectives on the Most Relevant New Publications,
Data Sets and Advances in Oncology**

Prostate Cancer

**Tuesday, December 1, 2020
5:00 PM – 6:00 PM ET**

Faculty

**Emmanuel S Antonarakis, MD
Andrew J Armstrong, MD, ScM**

Moderator

Neil Love, MD

Thank you for joining us!

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