Meet The Professor
Optimizing the Management of Ovarian Cancer

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

Commercial Support

This activity is supported by educational grants from AstraZeneca Pharmaceuticals LP, GlaxoSmithKline, Merck, and Mersana Therapeutics Inc.

Dr Love — Disclosures

Dr Love is president and CEO of Research To Practice. Research To Practice receives funds in the form of educational grants to develop CME activities from the following companies: AbbVie Inc, Adaptive Biotechnologies Corporation, ADC Therapeutics, Agios Pharmaceuticals Inc, Alexion Pharmaceuticals, Amgen Inc, Array BioPharma Inc, a subsidiary of Pfizer Inc, Astellas, AstraZeneca Pharmaceuticals LP, Aveo Pharmaceuticals, Bayer HealthCare Pharmaceuticals, BeiGene Ltd, BeyondSpring Pharmaceuticals Inc, Blueprint Medicines, Boehringer Ingelheim Pharmaceuticals Inc, Bristol-Myers Squibb Company, Celgene Corporation, Clovis Oncology, Coherus BioSciences, CTI BioPharma Corp, Daiichi Sankyo Inc, Eisai Inc, Elevation Oncology Inc, EMD Serono Inc, Epizyme Inc, Exact Sciences Corporation, the parent company of GHI, Exelixis Inc, Five Prime Therapeutics Inc, Foundation Medicine, G1 Therapeutics Inc, Genentech, a member of the Roche Group, Genmab, Gilead Sciences Inc, GlaxoSmithKline, Grail Inc, Halozyme Inc, Helsinn Healthcare SA, ImmunoGen Inc, Incyte Corporation, Ipsen Biopharmaceuticals Inc, Janssen Biotech Inc, administered by Janssen Scientific Affairs LLC, Jazz Pharmaceuticals Inc, Karyopharm Therapeutics, Kite, A Gilead Company, Lilly, Loxo Oncology Inc, a wholly owned subsidiary of Eli Lilly & Company, Merck, Mersana Therapeutics Inc, Natera Inc, Novartis, Novartis Pharmaceuticals Corporation on behalf of Advanced Accelerator Applications, Novocure Inc, Oncopeptides, Pfizer Inc, Pharmacyclics LLC, an AbbVie Company, Puma Biotechnology Inc, Regeneron Pharmaceuticals Inc, Sanofi Genzyme, Seagen Inc, Servier Pharmaceuticals LLC, Sumitomo Dainippon Pharma Oncology Inc, Taiho Oncology Inc, Takeda Pharmaceuticals USA Inc, Tesaro, A GSK Company, TG Therapeutics Inc, Turning Point Therapeutics Inc, Verastem Inc and Zymeworks Inc.

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Dr Westin — Disclosures

Consulting Agreements	Agenus Inc, AstraZeneca Pharmaceuticals LP, Clovis Oncology, Eisai Inc, EQRx, GlaxoSmithKline, ImmunoGen Inc, Merck, Mereo BioPharma, Mersana Therapeutics Inc, Seagen Inc, Vincerx Pharma, Zentalis Pharmaceuticals
Contracted Research	AstraZeneca Pharmaceuticals LP, Bayer HealthCare Pharmaceuticals, Bio-Path Holdings Inc, Clovis Oncology, Cotinga Pharmaceuticals Inc, GlaxoSmithKline, Mereo BioPharma, OncXerna Therapeutics Inc, Zentalis Pharmaceuticals

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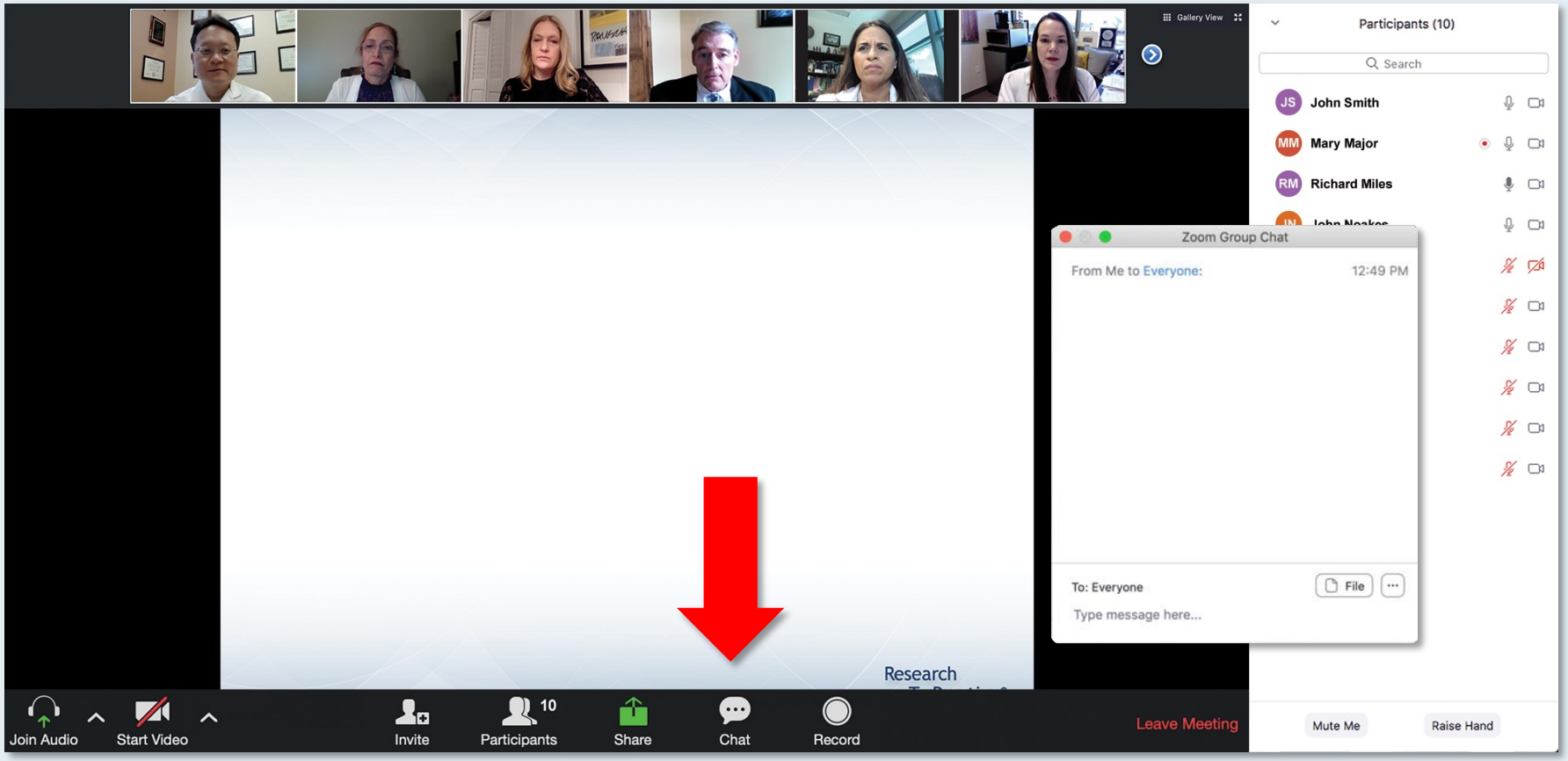
We Encourage Clinicians in Practice to Submit Questions



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

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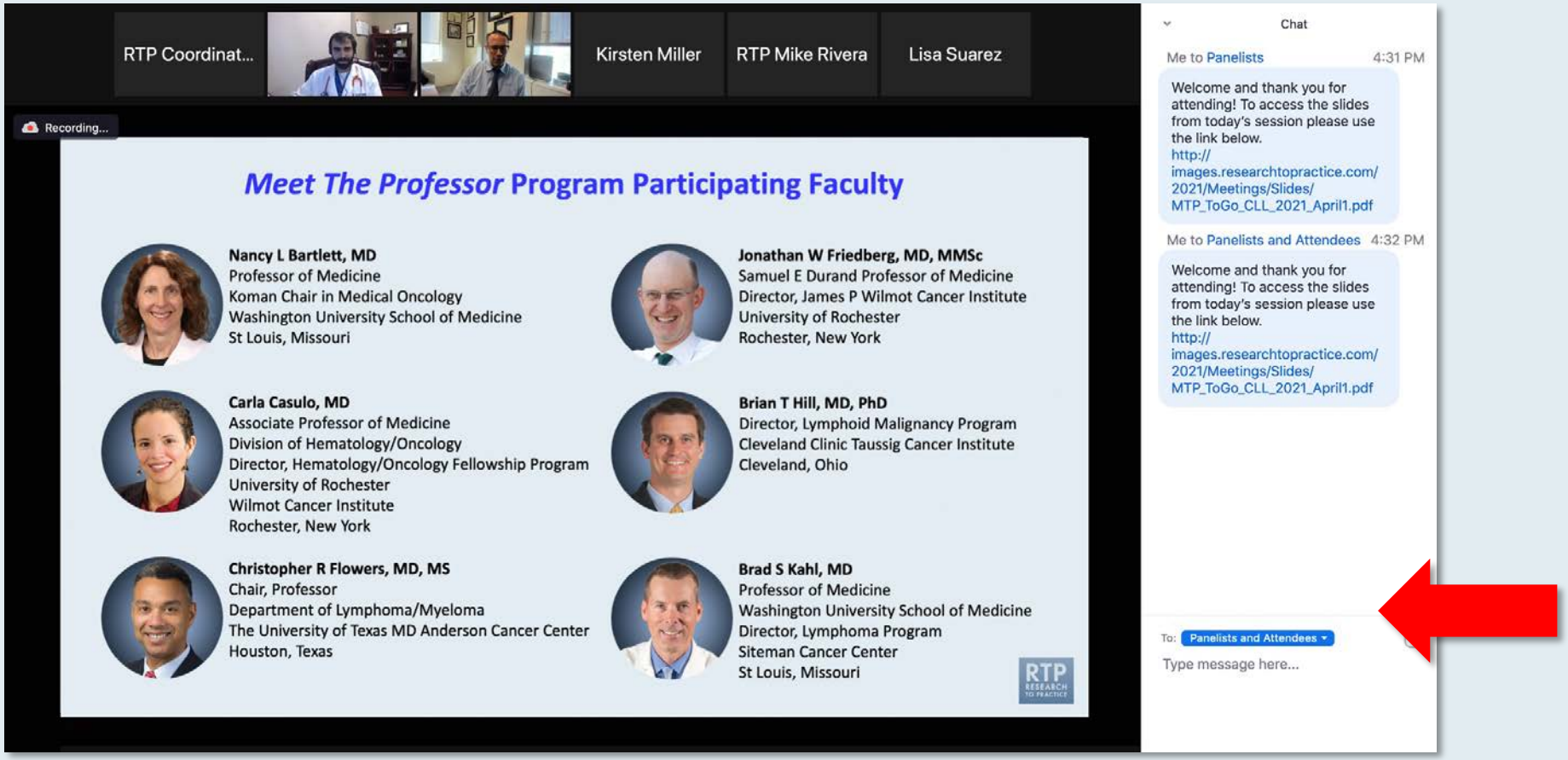
Familiarizing Yourself with the Zoom Interface

Expand chat submission box



Drag the white line above the submission box up to create more space for your message.

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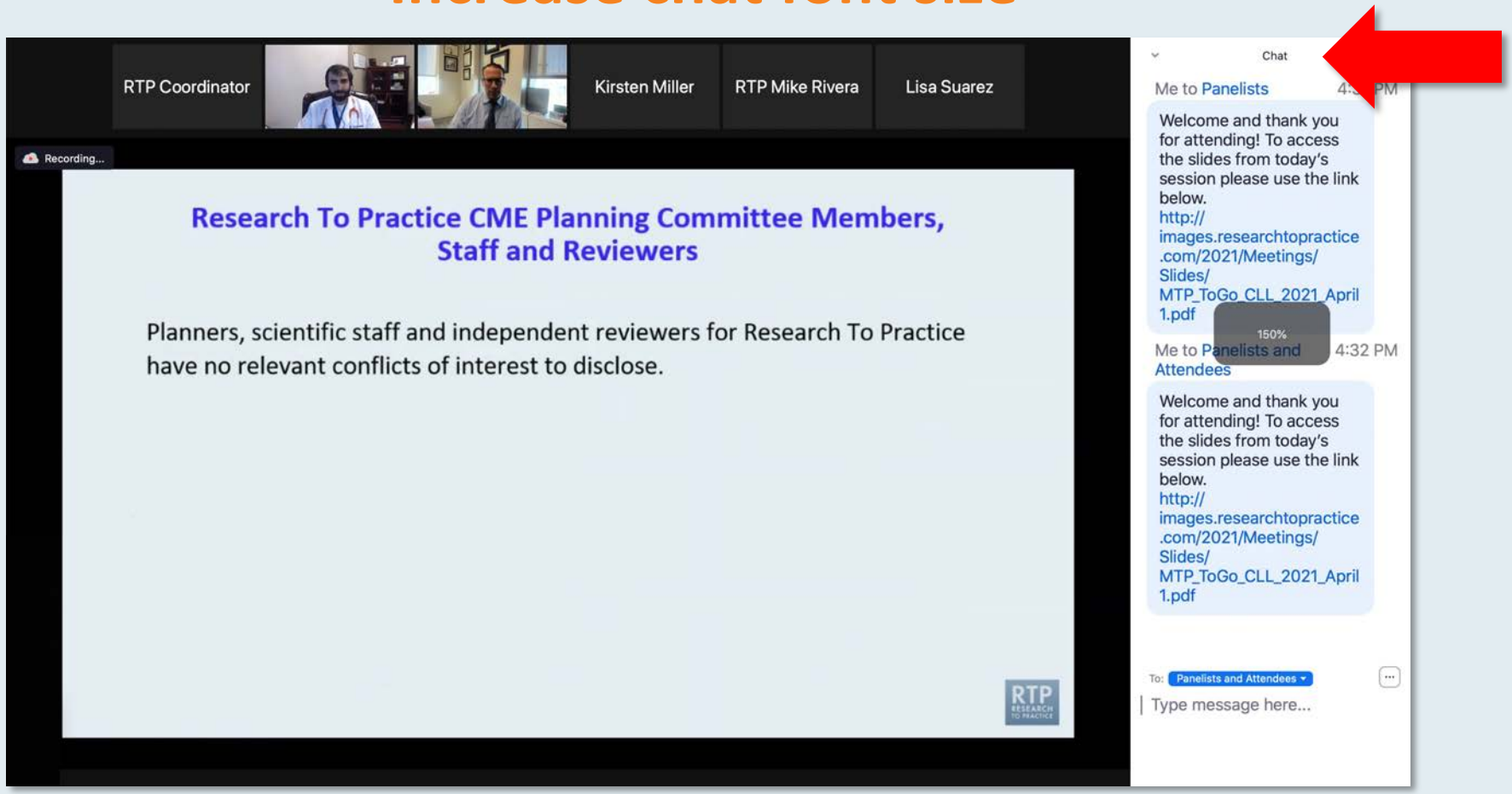
Familiarizing Yourself with the Zoom Interface

Increase chat font size



Press Command (for Mac) or Control (for PC) and the + symbol.
You may do this as many times as you need for readability.

ONCOLOGY TODAY

WITH DR NEIL LOVE

Updates on Ovarian Cancer from SGO 2022

DR DAVID O'MALLEY

THE OHIO STATE UNIVERSITY AND
THE JAMES CANCER CENTER

Listen on Apple Podcasts

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Meet The Professor

Optimizing the Management of Gastroesophageal Cancers

Wednesday, June 22, 2022
5:00 PM – 6:00 PM ET

Faculty

Eric Van Cutsem, MD, PhD

Moderator

Neil Love, MD

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PARP Inhibition in the Management of Prostate Cancer — Where We Are and Where We're Headed

Thursday, June 23, 2022
5:00 PM – 6:00 PM ET

Faculty

Johann S de Bono, MB ChB, MSc, PhD, FMedSci
Fred Saad, MD

Moderator

Neil Love, MD

RTP RESEARCH TO PRACTICE

Meet The Professor

Optimizing the Management of Chronic Myeloid Leukemia

Tuesday, June 28, 2022
5:00 PM – 6:00 PM ET

Faculty

Jorge E Cortes, MD

Moderator

Neil Love, MD

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Meet The Professor

Current and Future Management of Non-Small Cell Lung Cancer with an EGFR Mutation

Thursday, June 30, 2022
5:00 PM – 6:00 PM ET

Faculty

Joel W Neal, MD, PhD

Moderator

Neil Love, MD

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Meet The Professor

Optimizing the Management of Ovarian Cancer

Wednesday, July 6, 2022
5:00 PM – 6:00 PM ET

Faculty

Ursula Matulonis, MD

Moderator

Neil Love, MD

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Meet The Professor

Optimizing the Management of Hepatobiliary Cancers

Thursday, July 7, 2022
5:00 PM – 6:00 PM ET

Faculty

Ghassan Abou-Alfa, MD, MBA

Moderator

Neil Love, MD

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Thank you for joining us!

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

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MD Anderson Cancer Center
Houston, Texas

Meet The Professor Program Participating Faculty

Prof Jonathan A Ledermann
Professor of Medical Oncology
UCL Cancer Institute
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

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Gynecology Site Lead
Co-Director of the Beyond Chemotherapy Program
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Richard T Penson, MD, MRCP
Associate Professor of Medicine
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Clinical Director, Medical Gynecologic Oncology
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Meet The Professor Program Participating Faculty

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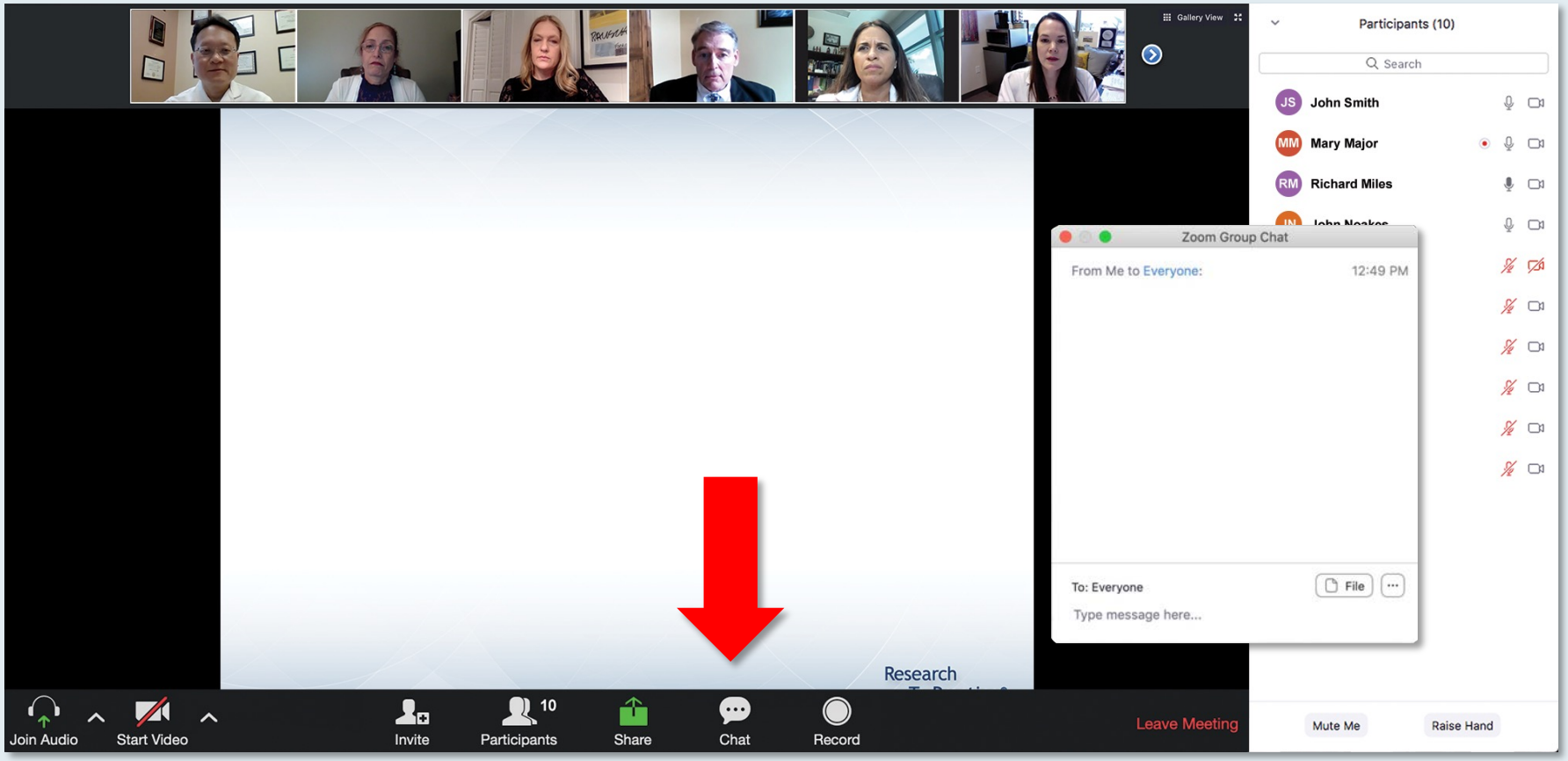

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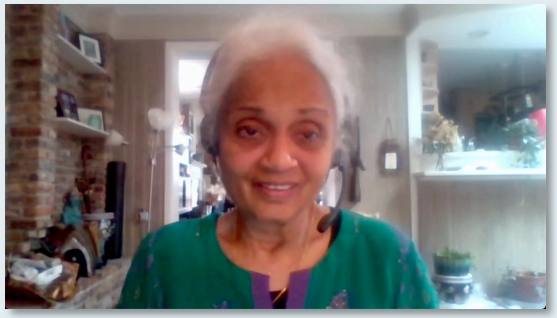
Syed M Ahmed, MD, PhD
Advocate Medical Group
Libertyville, Illinois



Rajalaxmi McKenna, MD
Southwest Medical Consultants SC
Willowbrook, Illinois

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John Muir Health
Pleasant Hill, California

Syed Farhan Zafar, MD
Florida Cancer Specialists
Fort Myers, Florida

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Meet The Professor with Dr Westin

Introduction

MODULE 1: Case Presentations – Part 1

- Dr Chen: A 58-year-old woman with Stage IIIC high-grade serous carcinoma and a gBRCA2 mutation
- Dr Ahmed: A 66-year-old woman with Stage IIIA BRCA1/2 wild-type, high-grade serous ovarian adenocarcinoma
- Dr Zafar: A 61-year-old woman with metastatic MSS ovarian carcinoma – gBRCA1 mutation
- Dr McKenna: A 60-year-old woman with multiregimen-recurrent advanced ovarian cancer – gBRCA1 mutation

MODULE 2: Journal Club with Dr Westin – Part 1

MODULE 3: Case Presentations – Part 2

- Dr Ahmed: A 51-year-old woman with metastatic hepatoid carcinoma of the ovary with an FGFR fusion
- Dr McKenna: A 92-year-old woman with Stage IIIC/IV papillary ovarian cancer and concurrent chronic lymphocytic leukemia
- Dr Zafar: A 46-year-old woman with metastatic BRCA1/2 wild-type, clear cell ovarian cancer – MSI-high, TMB 43 mut/Mb, PD-L1 15%
- Dr Chen: A 60-year-old woman with multiregimen-recurrent BRCA1/2 wild-type ovarian cancer

MODULE 4: Journal Club with Dr Westin – Part 2

MODULE 5: Appendix of Key Publications

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Meet The Professor with Dr Westin

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MODULE 4: Journal Club with Dr Westin – Part 2

MODULE 5: Appendix of Key Publications

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#84

Final Overall Survival Results from BELLINI, a Phase 3 Study of Venetoclax or Placebo in Combination With Bortezomib and Dexamethasone in Relapsed/Refractory Multiple Myeloma

ASH 2021;Abstract 84.

Shaji K. Kumar,[1] Simon J. Harrison,[2] Michele Cavo,[3] Javier de la Rubia,[4] Rakesh Popat,[5] Cristina Gasparetto,[6] Vania Hungria,[7] Hans Salwender,[8] Kenshi Suzuki,[9] Inho Kim,[10] Maika Onishi,[11] Grace Ku,[11] Rajvineeth Pothacamury,[12] Vasudha Sehgal,[12] Abdullah Masud,[12] Jeremy A. Ross,[12] Edyta Dobkowska,[13] and Philippe Moreau[14]

[1]Mayo Clinic, Rochester, MN, USA; [2]Peter MacCallum Cancer Centre and Royal Melbourne Hospital, Melbourne, Victoria, Australia; [3]IRCCS Azienda Ospedaliero-Universitaria di Bologna, Seragnoli Institute of Hematology, Bologna University School of Medicine, Bologna, Italy; [4]Hematology Service Hospital La Fe and School of Medicine and Dentistry, Catholic University of Valencia, Valencia, Spain; [5]University College Hospitals, London, United Kingdom; [6]Duke University Medical Center, Durham, NC, USA; [7]Clinica São Germano, São Paulo, Brazil; [8]Asklepios Tumorzentrum Hamburg, AK Altona and AK St Georg, Hamburg, Germany; [9]Japanese Red Cross Medical Center, Tokyo, Japan; [10]Seoul National University, Seoul, South Korea; [11]Genentech, Inc, South San Francisco, CA, USA; [12]AbbVie, Inc, North Chicago, IL, USA; [13]Pharmacyclics Switzerland GmbH, An AbbVie Company, Schaffhausen, Switzerland; [14]University Hospital, Nantes, France

American Society of Hematology Annual Meeting, December 11–14, 2021, Atlanta, Georgia

BELLINI: Progression-Free Survival and Overall Survival in All Patients and Key Biomarker Subgroups

	N	Ven + Bd	Pbo + Bd	HR (95% CI)
Median PFS, mo				
All pts	291	23.4	11.4	0.58 (0.43–0.78)
Pts with t(11;14)	35	36.8	9.3	0.12 (0.03–0.44)
Pts with *BCL2*^{high}	98	30.1	9.9	0.37 (0.21–0.64)
Pts with t(11;14), *BCL2*^{high}	114	34.3	9.9	0.32 (0.20–0.53)
Pts with non-t(11;14), *BCL2*^{low}	164	15.3	12.2	0.76 (0.51–1.13)
Median OS, mo				
All pts	291	NR	NR	1.19 (0.80–1.77)
Pts with t(11;14)	35	NR	NR	0.61 (0.16–2.32)
Pts with *BCL2*^{high}	98	NR	NR	0.70 (0.32–1.51)
Pts with t(11;14), *BCL2*^{high}	114	NR	NR	0.82 (0.40–1.70)
Pts with non-t(11;14), *BCL2*^{low}	164	46.4	NR	1.34 (0.81–2.20)

B, bortezomib; d, dexamethasone; HR, hazard ratio; NR, not reached; OS, overall survival; Pbo, placebo; PFS, progression-free survival; pts, patients; Ven, venetoclax.

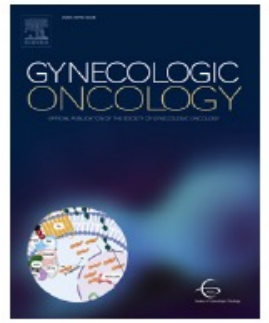
Kumar SK et al. ASH 2021;Abstract 84.

Gynecologic Oncology 166 (2022) 18–24

Contents lists available at ScienceDirect

Gynecologic Oncology

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



State of the Science

State of the science: Contemporary front-line treatment of advanced ovarian cancer

Phase III First-Line PARP Inhibitor Maintenance Trials

Study design	SOLO-1[1] (N = 391)	PAOLA-1[2] (N = 612)	PRIMA[3] (N = 620)	VELIA[4] (N = 1,140)
Treatment arms vs placebo	**Olaparib (n=260)**	**Bevacizumab ± olaparib**	**Niraparib**	**Veliparib**
Patient population	*BRCA* mutation	All comers	All comers	All comers
Treatment duration	24 months	15 months for bev 24 months for olaparib	36 months or until PD	24 months
Median PFS	56 mo vs 14 mo HR: 0.33	22.1 mo vs 16.6 mo HR: 0.59	22.1 mo vs 10.9 mo HR 0.40	23.5 mo vs 17.3 mo HR: 0.68

bev = bevacizumab; PD = disease progression

[1] Banerjee et al. *Lancet Oncol* 2021;22(12):1721-31; [2] Ray-Coquard et al. SGO 2020;Abstract 33; [3] González-Martín A et al. ASCO 2021;Abstract 5518; [4] Aghajanian C et al. *Gyn Oncol* 2021;162(2):375-81.

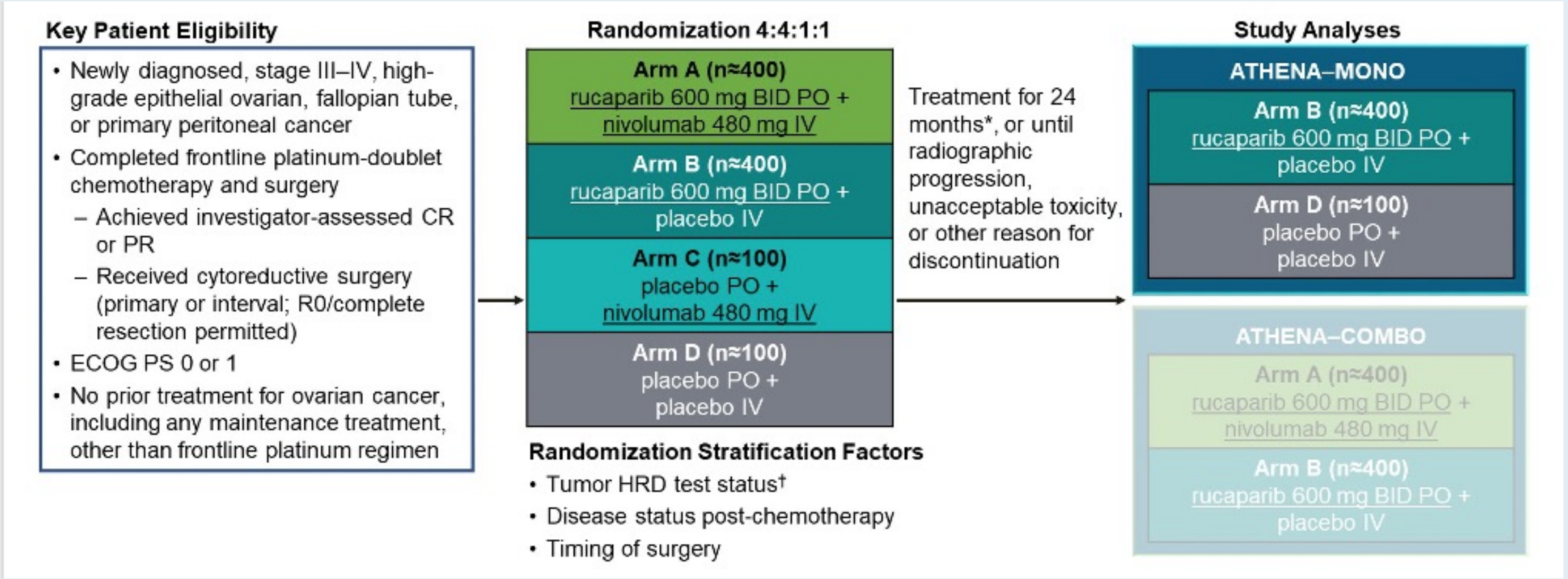
original reports

A Randomized, Phase III Trial to Evaluate Rucaparib Monotherapy as Maintenance Treatment in Patients With Newly Diagnosed Ovarian Cancer (ATHENA–MONO/GOG-3020/ENGOT-ov45)

Bradley J. Monk, MD[1]; Christine Parkinson, MD[2]; Myong Cheol Lim, MD, PhD[3]; David M. O'Malley, MD[4]; Ana Oaknin, MD, PhD[5]; Michelle K. Wilson, MD[6]; Robert L. Coleman, MD[7]; Domenica Lorusso, MD, PhD[8]; Paul Bessette, MD[9]; Sharad Ghamande, MD[10]; Athina Christopoulou, MD, PhD[11]; Diane Provencher, MD[12]; Emily Prendergast, MD[13]; Fuat Demirkiran, MD[14]; Olga Mikheeva, MD[15]; Oladapo Yeku, MD, PhD[16]; Anita Chudecka-Glaz, MD, PhD[17]; Michael Schenker, MD, PhD[18]; Ramey D. Littell, MD[19]; Tamar Safra, MD[20]; Hung-Hsueh Chou, MD[21,22]; Mark A. Morgan, MD[23]; Vít Drochýtek, MD[24]; Joyce N. Barlin, MD[25]; Toon Van Gorp, MD[26]; Fred Ueland, MD[27]; Gabriel Lindahl, MD[28,29]; Charles Anderson, MD[30]; Dearbhaile C. Collins, MBBCh, MA, PhD[31]; Kathleen Moore, MD[32]; Frederik Marme, MD, PhD[33]; Shannon N. Westin, MD, MPH[34]; Iain A. McNeish, MD, PhD[35]; Danny Shih, BA[36]; Kevin K. Lin, PhD[37]; Sandra Goble, MS[38]; Stephanie Hume, PhD[39]; Keiichi Fujiwara, MD, PhD[40]; and Rebecca S. Kristeleit, MD, PhD[41]

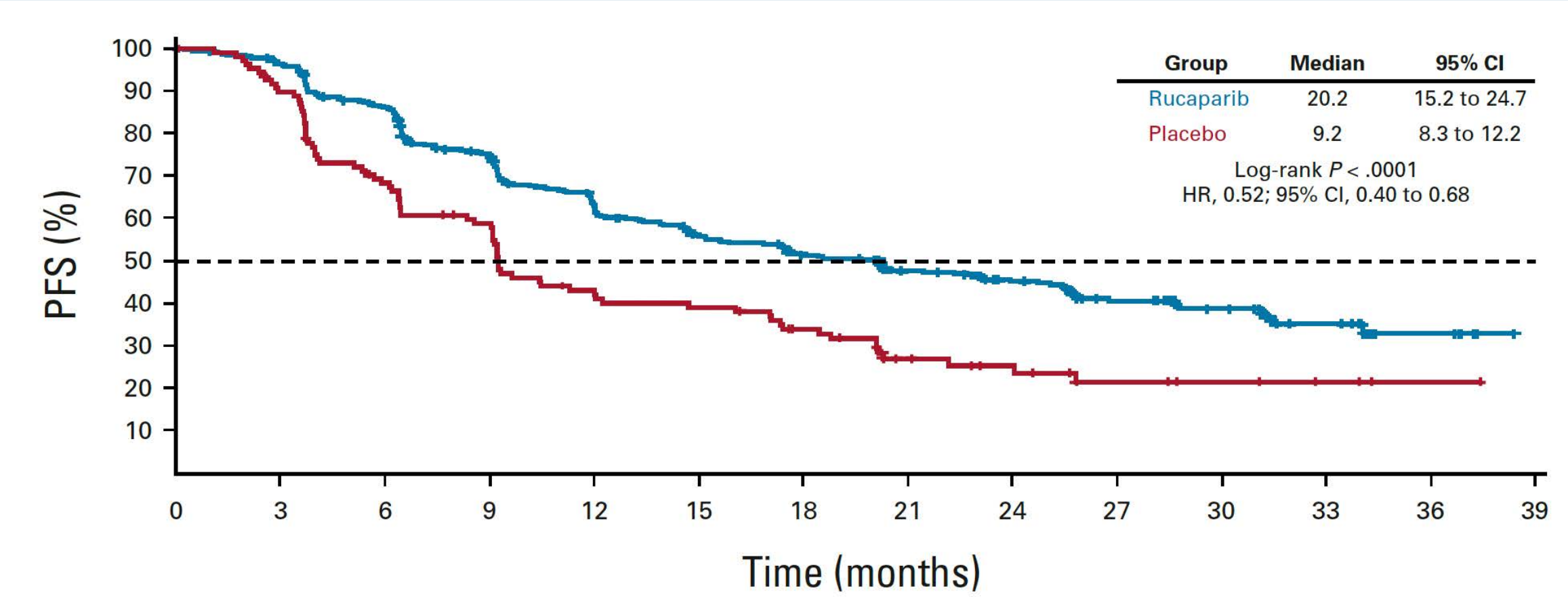
J Clin Oncol 2022;[Online ahead of print].

ATHENA-MONO Study Schema



Monk BJ et al. ASCO 2022;Abstract LBA5500.

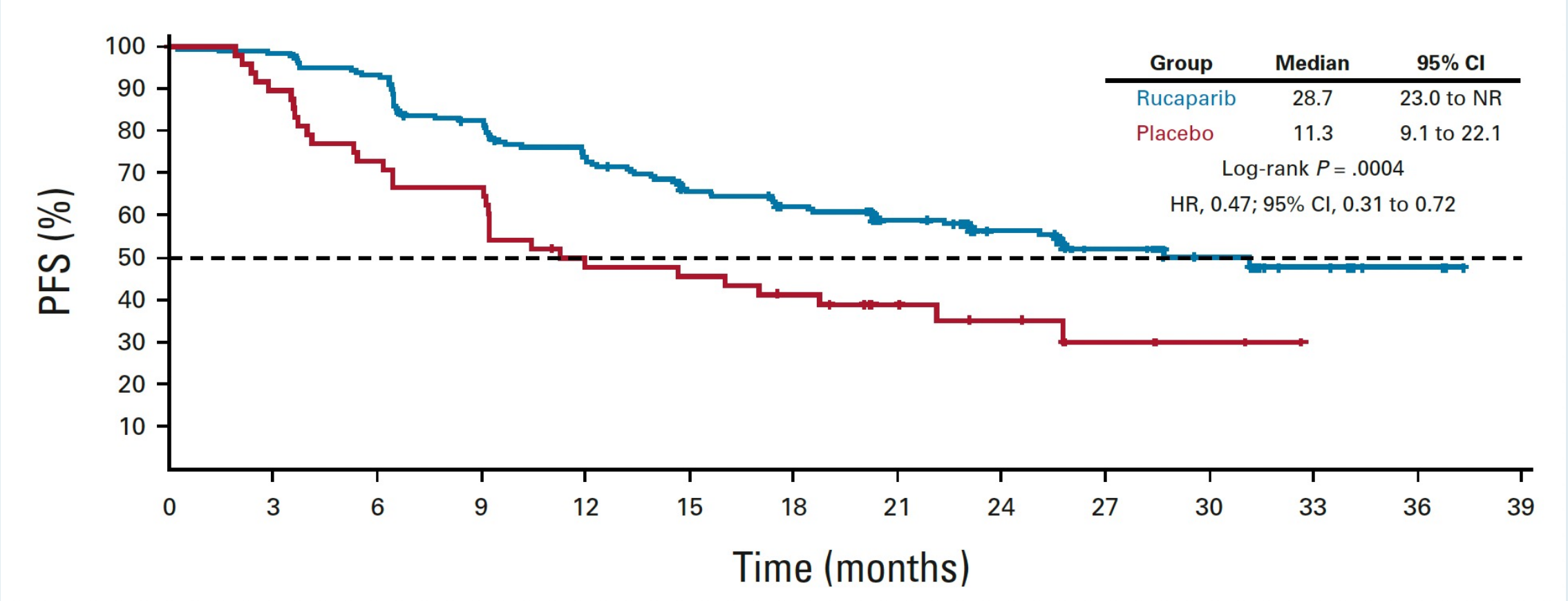
ATHENA-MONO Investigator-Assessed PFS in the ITT Population (N = 538)



ITT = intent to treat

Monk BJ et al. *J Clin Oncol* 2022;[Online ahead of print].

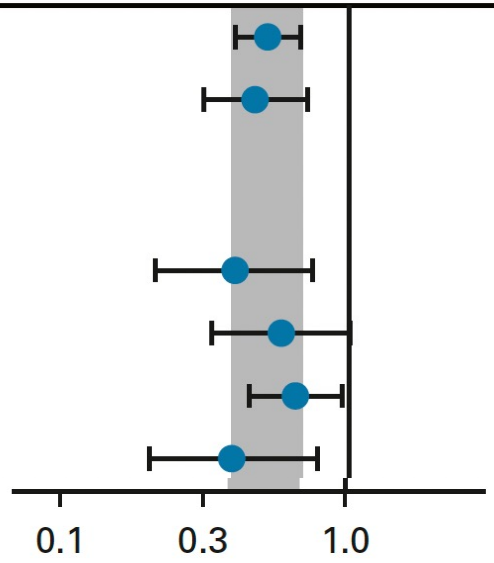
ATHENA-MONO Investigator-Assessed Progression-Free Survival (PFS) in the Homologous Recombination Deficiency Population (N = 234)



Monk BJ et al. *J Clin Oncol* 2022;[Online ahead of print].

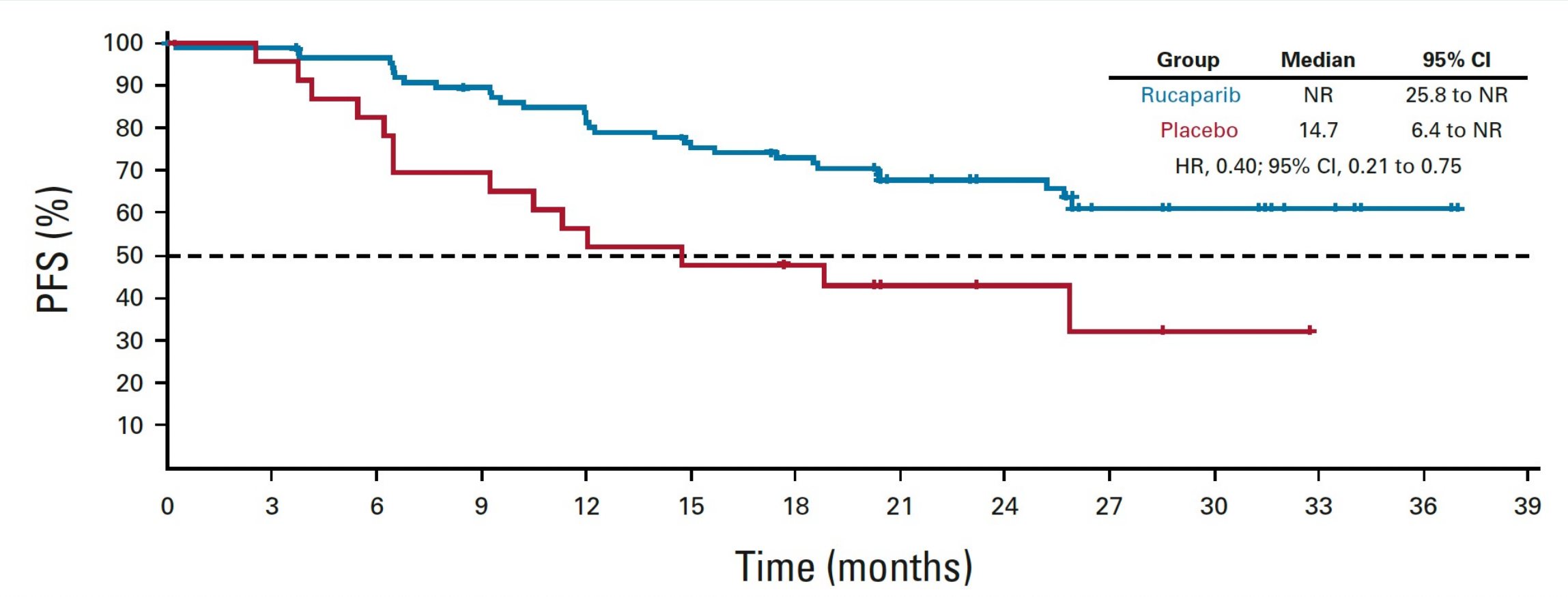
ATHENA-MONO Investigator-Assessed PFS in HRD Subgroups in the ITT Population

Subgroup	Rucaparib (events/patients in subgroup)	Placebo (events/patients in subgroup)	HR (95% CI)
ITT population	230/427	78/111	0.52 (0.40 to 0.68)
HRD population	80/185	31/49	0.47 (0.31 to 0.72)
Randomization stratification factors			
HRD test status			
BRCA mutation	30/91	14/24	0.40 (0.21 to 0.75)
BRCA wild-type/LOH high	50/94	17/25	0.58 (0.33 to 1.01)
BRCA wild-type/LOH low	120/189	35/49	0.65 (0.45 to 0.95)
BRCA wild-type/LOH indeterminate	30/53	12/13	0.39 (0.20 to 0.78)



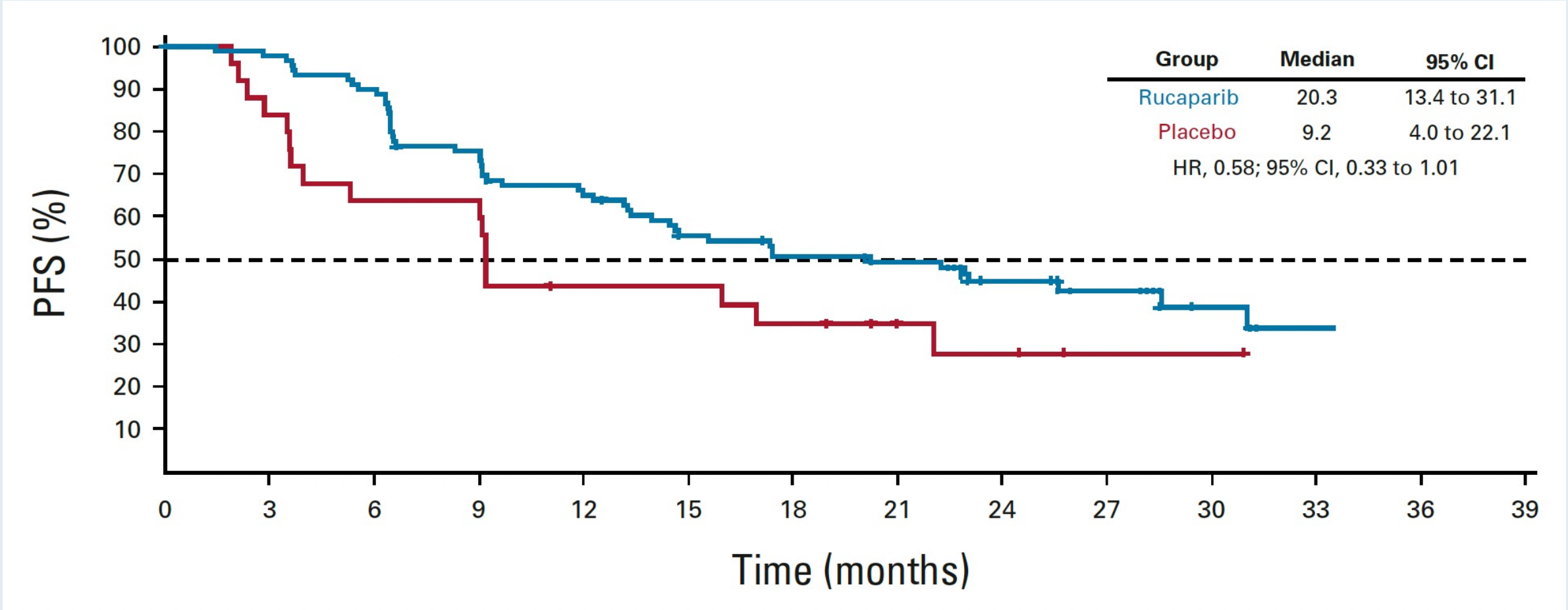
Monk BJ et al. *J Clin Oncol* 2022;[Online ahead of print].

ATHENA-MONO Investigator-Assessed PFS for Patients with BRCA Tumor Mutations



Monk BJ et al. *J Clin Oncol* 2022;[Online ahead of print].

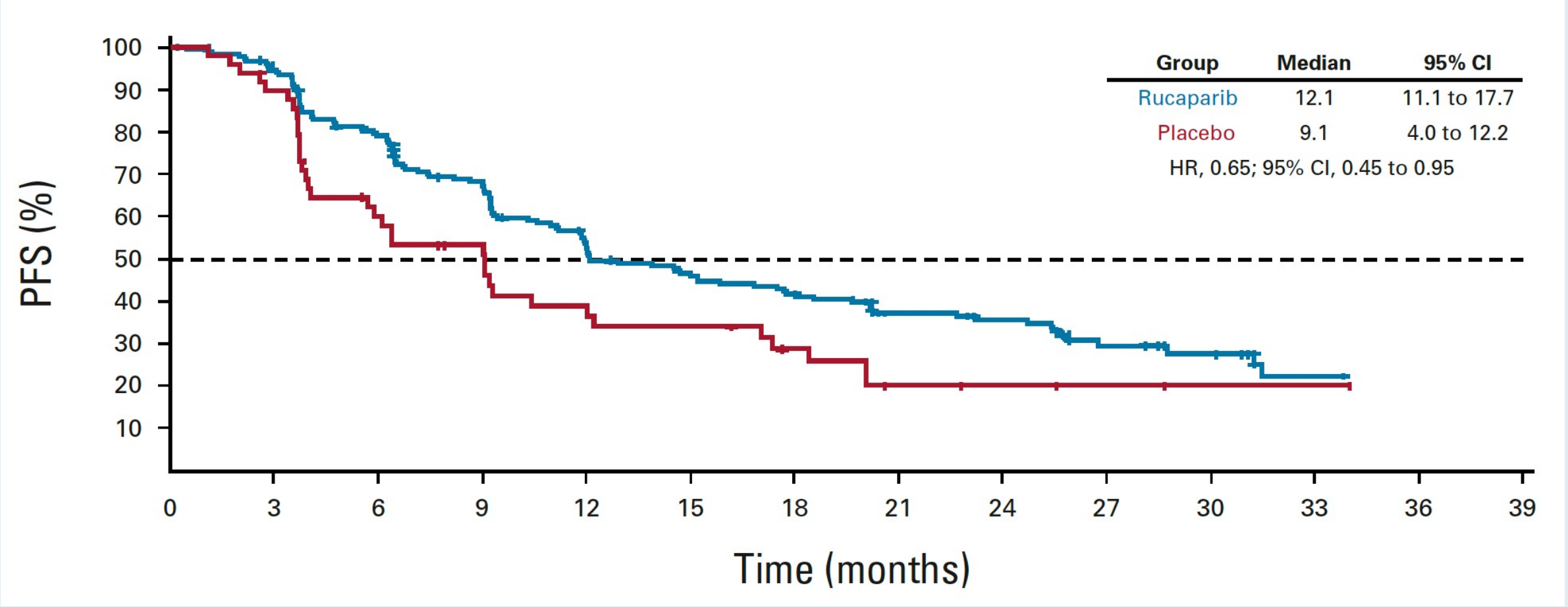
ATHENA-MONO Investigator-Assessed PFS for Patients with BRCA Wild-Type/LOH-High Tumors



Monk BJ et al. *J Clin Oncol* 2022;[Online ahead of print].

RTP RESEARCH TO PRACTICE

ATHENA-MONO Investigator-Assessed PFS for Patients in the HRD-Negative Subgroup (BRCA Wild Type, LOH Low)



Monk BJ et al. *J Clin Oncol* 2022;[Online ahead of print].

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FDA Advises Manufacturer Not to Submit First-Line Maintenance sNDA Until OS Survival from the ATHENA-MONO Trial Are More Mature

Clovis 2022 Q1 Earnings Report

"We are currently evaluating the timing of our planned sNDA and Type II variation submissions. As suggested by the recent Oncologic Drugs Advisory Committee ("ODAC") involving PI3K inhibitors, and our recent discussions with the FDA on May 3 and 4, 2022, the FDA is placing increasing emphasis on overall survival ("OS") in oncology trials.

Despite the fact that the ATHENA-MONO trial met its primary endpoint, and OS is a secondary endpoint, the FDA advised us that we should not submit the first line maintenance sNDA until OS data from the ATHENA-MONO trial are as much as 50% mature, and if we do choose to submit prior to that, we should expect the FDA to require a discussion at an ODAC meeting in connection with its review of such sNDA submission. This recommendation by the FDA was also influenced by their interpretation of the ARIEL4 survival data.

Currently, the OS data are approximately 25% mature and our initial estimates suggest we would reach 50% maturity in approximately 2 years."

https://ir.clovisoncology.com/investors-and-news/financial-information/quarterly-results/default.aspx

SCENARIO 1

A patient presenting with ovarian cancer with extensive intra-abdominal disease (clinical Stage IIIC) receives neoadjuvant carboplatin/paclitaxel/bevacizumab with good response and proceeds to surgery with R0 resection. Regulatory and reimbursement issues aside, what would you most likely recommend as maintenance therapy if genetic testing revealed the following results:

SCENARIO 2

A patient presenting with Stage IIIC ovarian cancer undergoes R0 resection and receives adjuvant carboplatin/paclitaxel with good response. Regulatory and reimbursement issues aside, what would you most likely recommend as maintenance therapy if genetic testing revealed the following results:

RTP RESEARCH TO PRACTICE

Genetic Testing Results

- Germline BRCA mutation
- Somatic BRCA mutation
- Germline PALB2 mutation
- BRCA wild type, HR deficient (eg, LOH high)
- BRCA wild type, HR proficient (eg, LOH low)

Options for Maintenance Therapy

- None
- Bevacizumab
- Niraparib
- Olaparib
- Rucaparib
- Olaparib/bevacizumab
- Niraparib/bevacizumab
- Rucaparib/bevacizumab
- Other

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 and no relevant family history?

1. Germline BRCA; if negative, multigene somatic (eg, NGS)
2. Multigene germline and somatic/NGS
3. Germline BRCA
4. Multigene somatic/NGS
5. Multigene germline panel

NGS = next-generation sequencing

RTP RESEARCH TO PRACTICE

A patient presenting with ovarian cancer with extensive intra-abdominal disease (clinical Stage IIIC) receives neoadjuvant carboplatin/paclitaxel/bevacizumab with good response and proceeds to surgery with R0 resection. Regulatory and reimbursement issues aside, what would you most likely recommend as maintenance therapy if genetic testing revealed a germline BRCA mutation?

1. None
2. Bevacizumab
3. Niraparib
4. Olaparib
5. Rucaparib
6. Olaparib/bevacizumab
7. Niraparib/bevacizumab
8. Rucaparib/bevacizumab
9. Other

RTP RESEARCH TO PRACTICE

A patient presenting with ovarian cancer with extensive intra-abdominal disease (clinical Stage IIIC) receives neoadjuvant carboplatin/paclitaxel/ bevacizumab with good response and proceeds to surgery with R0 resection. Regulatory and reimbursement issues aside, what would you most likely recommend as maintenance therapy if genetic testing revealed a germline BRCA mutation?

Dr Eskander

Olaparib/bevacizumab

Dr Penson

Olaparib

Prof Ledermann

Olaparib/bevacizumab

Dr Westin

Olaparib/bevacizumab

Dr Matulonis

Olaparib/bevacizumab

RTP RESEARCH TO PRACTICE

The patient in the previous scenario comes to you for a second opinion after her primary oncologist has recommended niraparib/bevacizumab as maintenance therapy. Regulatory and reimbursement issues aside, how would you respond?

1. I agree with the recommendation
2. I disagree with the recommendation
3. I believe it is acceptable, but it is not my treatment of choice

Phase 2 OVARIO Study of Niraparib + Bevacizumab Therapy in Advanced Ovarian Cancer Following Frontline Platinum-Based Chemotherapy with Bevacizumab

Melissa M. Hardesty,[1] Thomas Krivak,[2] Gail S. Wright,[3] Erika Hamilton,[4] Evelyn L. Fleming,[5] Jimmy Belotte,[6] Erika Keeton,[6] Ping Wang,[6] Aine Clements,[7] Heidi J. Gray,[8] Gottfried E. Konecny,[9] Richard G. Moore,[10] Debra L. Richardson[11]

[1]Alaska Women's Cancer Care, Anchorage, AK, USA; [2]Division of Gynecologic Oncology, Department of Obstetrics and Gynecology, The Western Pennsylvania Hospital, Pittsburgh, PA, USA; [3]Florida Cancer Specialists and Research Institute, New Port Richey, FL, USA; [4]Sarah Cannon Research Institute; Tennessee Oncology, Nashville, TN, USA; [5]Division of Gynecologic Oncology, Norris Cotton Cancer Center, Dartmouth-Hitchcock Medical Center, Lebanon, NH, USA; [6]GlaxoSmithKline, Waltham, MA, USA; [7]Department of Gynecologic Oncology, Riverside Methodist Hospital, Columbus, OH, USA; [8]Division of Gynecologic Oncology, Department of Obstetrics and Gynecology, University of Washington, Seattle, WA, USA; [9]University of California Los Angeles, Los Angeles, CA, USA; [10]Division of Gynecologic Oncology, Department of Obstetrics and Gynecology, Wilmot Cancer Institute, University of Rochester Medical Center, Rochester, NY, USA; [11]Division of Gynecologic Oncology, Stephenson Cancer Center, University of Oklahoma Health Sciences Center, Oklahoma City, OK, USA

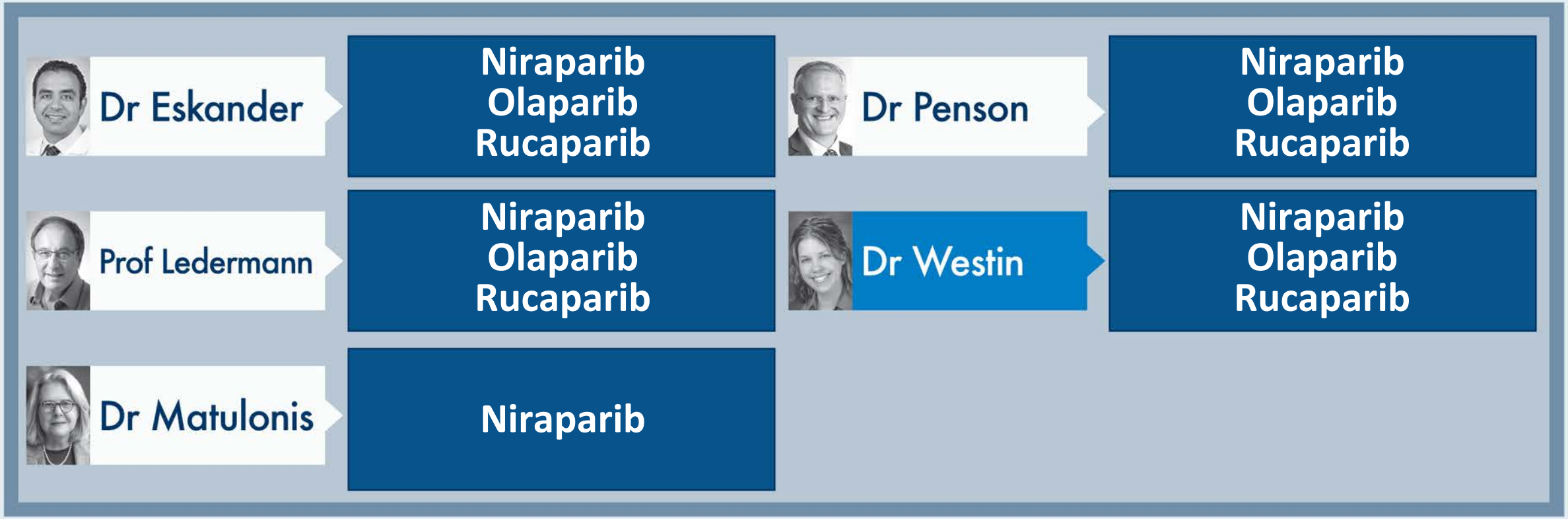
ANNUAL MEETING ON WOMENS' CANCER®
BUILDING BRIDGES // BREAKING BARRIERS
SGO // PHOENIX, ARIZONA // MARCH 19 - 21, 2022

Society of Gynecologic Oncology

SGO 2022;Abstract 40.

RTP RESEARCH TO PRACTICE

A patient presenting with ovarian cancer and a germline BRCA mutation with extensive intra-abdominal disease (clinical Stage IIIC) receives neoadjuvant carboplatin/paclitaxel/bevacizumab with good response and proceeds to surgery with R0 resection. Beyond your preferred approach, which other approaches to maintenance therapy do you believe are acceptable in this situation?



RTP RESEARCH TO PRACTICE

A patient presenting with Stage IIIC ovarian cancer undergoes R0 resection and receives adjuvant carboplatin/paclitaxel with good response. Regulatory and reimbursement issues aside, what would you most likely recommend as maintenance therapy if genetic testing revealed BRCA wild type, HR proficient (eg, LOH low)?

1. None
2. Bevacizumab
3. Niraparib
4. Olaparib
5. Rucaparib
6. Olaparib/bevacizumab
7. Niraparib/bevacizumab
8. Rucaparib/bevacizumab
9. Other

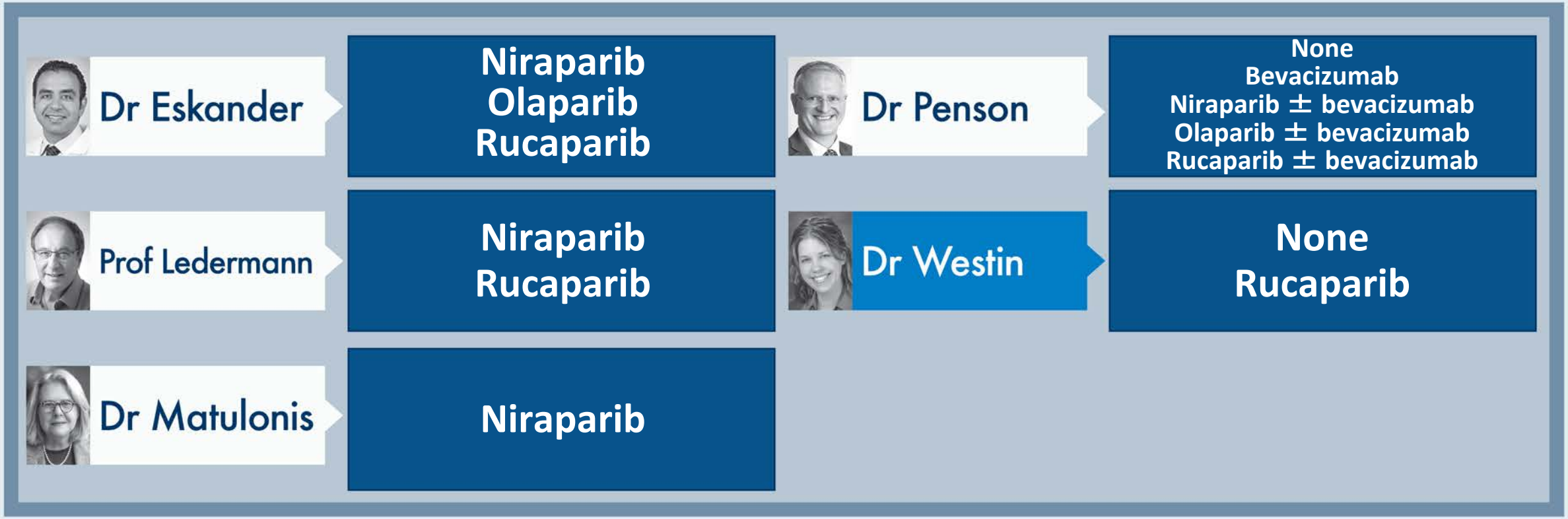
A patient presenting with Stage IIIC ovarian cancer undergoes R0 resection and receives adjuvant carboplatin/paclitaxel with good response. Regulatory and reimbursement issues aside, what would you most likely recommend as maintenance therapy if genetic testing revealed BRCA wild type, HR proficient (eg, LOH low)?

The patient in the previous scenario comes to you for a second opinion after her primary oncologist has recommended rucaparib as maintenance therapy. Regulatory and reimbursement issues aside, how would you respond?

1. I agree with the recommendation
2. I disagree with the recommendation
3. I believe it is acceptable, but it is not my treatment of choice

RTP
RESEARCH
TO PRACTICE

A patient presenting with Stage IIIC ovarian cancer, BRCA wild type, HR proficient (eg, LOH low), undergoes R0 resection and receives adjuvant carboplatin/paclitaxel with good response. Beyond your preferred approach, which other approaches to maintenance therapy do you believe are acceptable in this situation?



A patient presenting with Stage IIIC ovarian cancer undergoes R0 resection and receives adjuvant carboplatin/paclitaxel with good response. Regulatory and reimbursement issues aside, what would you most likely recommend as maintenance therapy if genetic testing revealed a germline PALB2 mutation?

RTP RESEARCH TO PRACTICE

A patient presenting with Stage IIIC ovarian cancer undergoes R0 resection and receives adjuvant carboplatin/paclitaxel with good response. Regulatory and reimbursement issues aside, what would you most likely recommend as maintenance therapy if genetic testing revealed a somatic BRCA mutation?

A patient presenting with Stage IIIC ovarian cancer undergoes R0 resection and receives adjuvant carboplatin/paclitaxel with good response. Regulatory and reimbursement issues aside, what would you most likely recommend as maintenance therapy if genetic testing revealed BRCA wild type, HR deficient (eg, LOH high)?

 Dr Eskander	Niraparib	 Dr Penson	Niraparib
 Prof Ledermann	Olaparib/bevacizumab	 Dr Westin	Niraparib
 Dr Matulonis	Niraparib		

RTP RESEARCH TO PRACTICE

Meet The Professor with Dr Westin

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MODULE 1: Case Presentations – Part 1

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- Dr Chen: A 60-year-old woman with multiregimen-recurrent BRCA1/2 wild-type ovarian cancer

MODULE 4: Journal Club with Dr Westin – Part 2

MODULE 5: Appendix of Key Publications

RTP RESEARCH TO PRACTICE

Case Presentation: A 58-year-old woman with Stage IIIC high-grade serous carcinoma and a germline BRCA2 (gBRCA2) mutation

Dr Gigi Chen (Pleasant Hill, California)

RTP
RESEARCH
TO PRACTICE

Case Presentation: A 66-year-old woman with Stage IIIA BRCA1/2 wild-type, high-grade serous ovarian adenocarcinoma

Dr Syed Ahmed (Libertyville, Illinois)

RTP
RESEARCH
TO PRACTICE

Case Presentation: A 61-year-old woman with metastatic MSS ovarian carcinoma – gBRCA1 mutation

Dr Syed Zafar (Fort Myers, Florida)

RTP
RESEARCH
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Case Presentation: A 60-year-old woman with multiregimen-recurrent advanced ovarian cancer – gBRCA1 mutation

Dr Rajalaxmi McKenna (Willowbrook, Illinois)

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RTP RESEARCH TO PRACTICE

Curr Opin Obstet Gynecol. 2021 February 01; 33(1): 19–25.

Current and future landscape of PARPi resistance

Emily Hinchcliff, MD MPH[1], Anca Chelariu-Raicu, MD[2], Shannon N. Westin, MD MPH[1]

REVIEW ARTICLE

The Clinical Challenges, Trials, and Errors of Combatting Poly(ADP-Ribose) Polymerase Inhibitors Resistance

Melissa M. Pham, MD, Emily Hinchcliff, MD, MPH,† Monica Avila, MD, MPH,* and Shannon N. Westin, MD, MPH**

***Cancer J* 2021;27(6):491-500.**

JC JOURNAL CLUB RTP RESEARCH TO PRACTICE

Correlation of HRD Status with Clinical and Survival Outcomes in Patients with Advanced-Stage Ovarian Cancer

Sims TT et al.

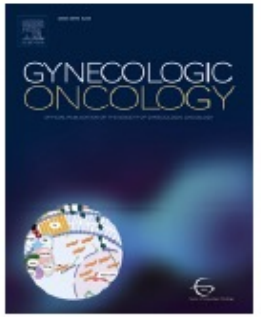
ASCO 2022;Abstract 5568.

Gynecologic Oncology 162 (2021) 482–495

Contents lists available at ScienceDirect

Gynecologic Oncology

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

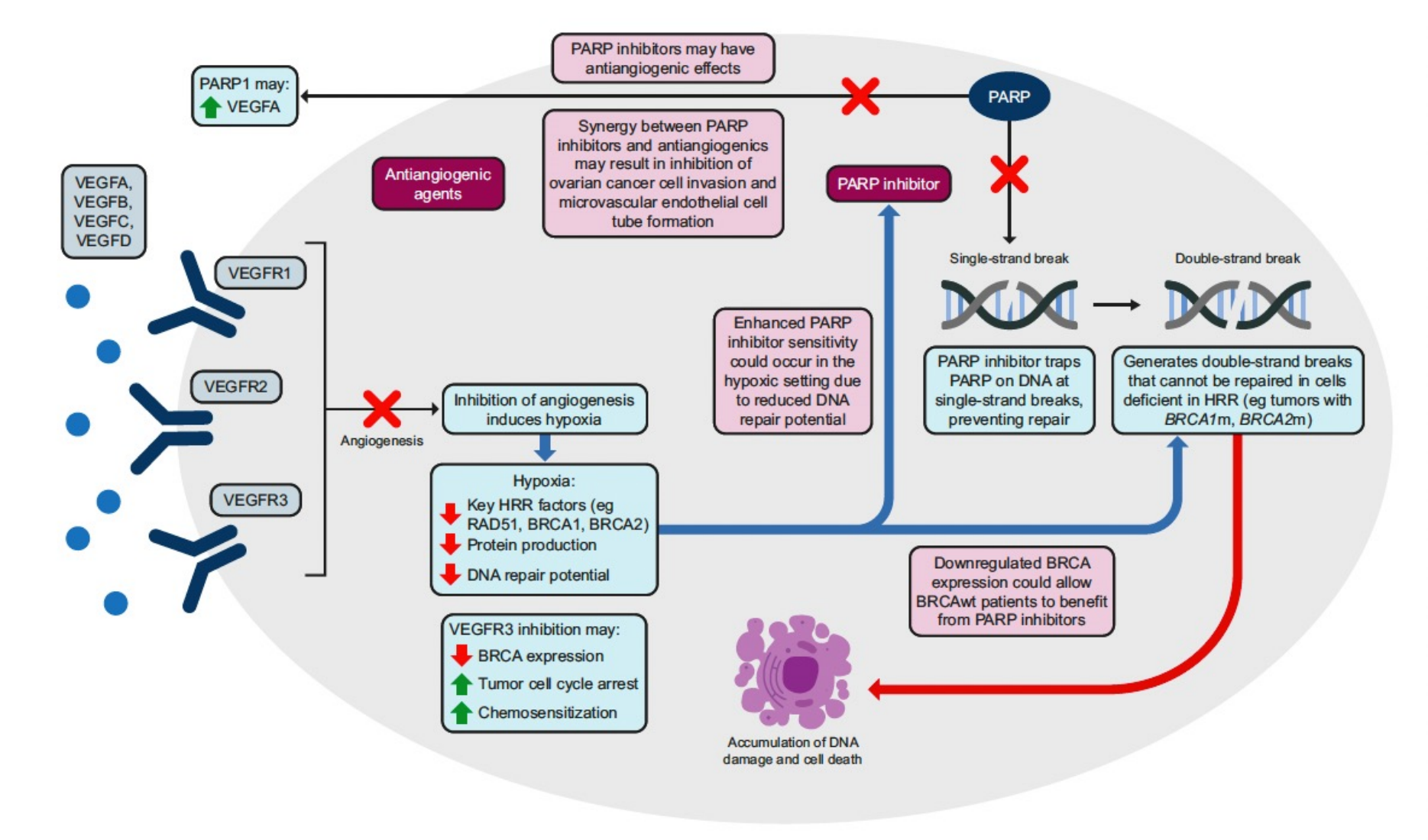


Review Article

Rationale for combination PARP inhibitor and antiangiogenic treatment in advanced epithelial ovarian cancer: A review

Angeles Alvarez Secord [a,*], David M. O'Malley [b], Anil K. Sood [c], Shannon N. Westin [c], Joyce F. Liu [d]

Potential Mechanisms of PARP Inhibitor and Anti-angiogenic Combination Treatment



Secord AA et al. *Gyn Oncol* 2021;162:482-95.

Journal of Cancer Research and Clinical Oncology (2021) 147:3545–3555
https://doi.org/10.1007/s00432-021-03778-1

ORIGINAL ARTICLE – CANCER RESEARCH

Immune microenvironment composition in high-grade serous ovarian cancers based on *BRCA* mutational status

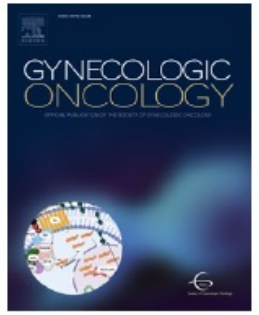
Sara Corvigno[1] · Jared K. Burks[2] · Wei Hu[1] · Yanping Zhong[3,4] · Nicholas B. Jennings[1] · Nicole D. Fleming[1] · Shannon N. Westin[1] · Bryan Fellman[5] · Jinsong Liu[3] · Anil K. Sood[1,6]

Gynecologic Oncology 162 (2021) 65–71

Contents lists available at ScienceDirect

Gynecologic Oncology

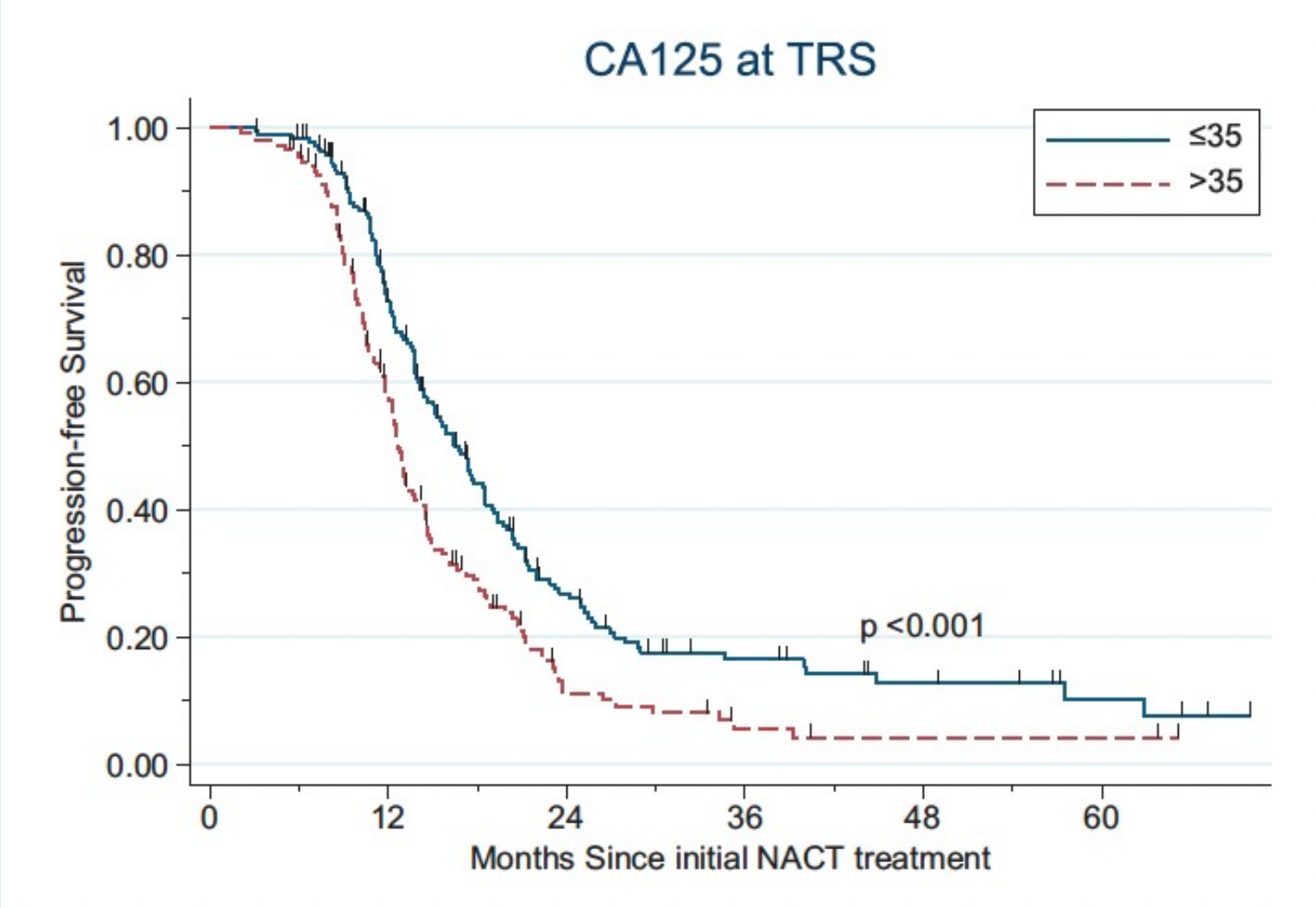
journal homepage: www.elsevier.com/locate/ygyno



Factors associated with response to neoadjuvant chemotherapy in advanced stage ovarian cancer

Nicole D. Fleming [a,*], Shannon N. Westin [a], J. Alejandro Rauh-Hain [a], Pamela T. Soliman [a], Bryan M. Fellman [b], Robert L. Coleman [c], Larissa A. Meyer [a], Aaron Shafer [a], Lauren P. Cobb [a], Amir Jazaeri [a], Karen H. Lu [a], Anil K. Sood [a]

Progression-Free Survival by Normalization of CA-125 at Interval Tumor Reductive Surgery (TRS)

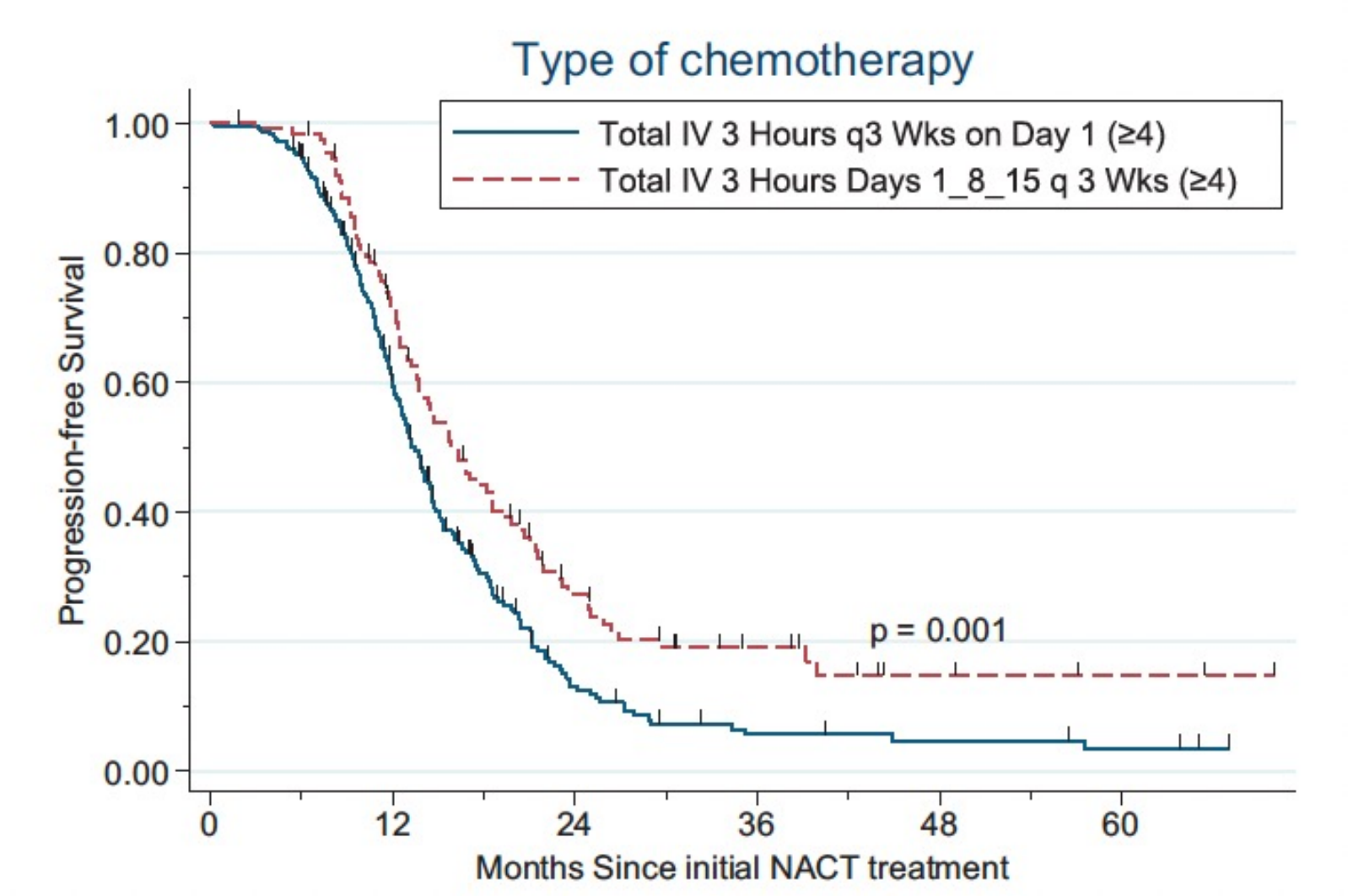


NACT = neoadjuvant chemotherapy

Fleming ND et al. *Gyn Oncol* 2021;162:65-71.

RTP RESEARCH TO PRACTICE

Progression-Free Survival by Type of Chemotherapy Dosing



Fleming ND et al. *Gyn Oncol* 2021;162:65-71.

RTP RESEARCH TO PRACTICE

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MODULE 4: Journal Club with Dr Westin – Part 2

MODULE 5: Appendix of Key Publications

RTP RESEARCH TO PRACTICE

Case Presentation: A 51-year-old woman with metastatic hepatoid carcinoma of the ovary with an FGFR fusion

Dr Syed Ahmed (Libertyville, Illinois)

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Case Presentation: A 92-year-old woman with Stage IIIC/IV papillary ovarian cancer and concurrent chronic lymphocytic leukemia

Dr Rajalaxmi McKenna (Willowbrook, Illinois)

RTP RESEARCH TO PRACTICE

Case Presentation: A 46-year-old woman with metastatic BRCA1/2 wild-type, clear cell ovarian cancer – MSI-high, TMB 43 mut/Mb, PD-L1 15%

Dr Syed Zafar (Fort Myers, Florida)

RTP
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TO PRACTICE

Case Presentation: A 60-year-old woman with multiregimen-recurrent BRCA1/2 wild-type ovarian cancer

Dr Gigi Chen (Pleasant Hill, California)

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Gynecologic Oncology 163 (2021) 217–219

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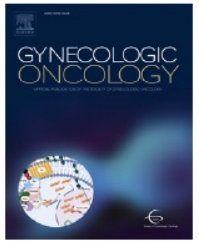
journal homepage: www.elsevier.com/locate/ygyno



Editorial

Next generation sequencing for gynecologic malignancy: Promise and potential pitfalls

Emily M. Hinchcliff

Northwestern University Feinberg School of Medicine, Division of Gynecologic Oncology, Department of Obstetrics and Gynecology, Chicago, IL, United States

Robert H Lurie Comprehensive Cancer Center, Northwestern University, Chicago, IL, United States

Shannon N. Westin

Department of Gynecologic Oncology and Reproductive Medicine, University of Texas MD Anderson Cancer Center, Houston, TX, United States

*Corresponding author at: Department of Gynecologic Oncology and Reproductive Medicine, University of Texas M.D. Anderson Cancer Center, 1155 Herman Pressler Blvd., Unit 1362, Houston, TX 77030, United States

Gynecologic Oncology 163 (2021) 220–228

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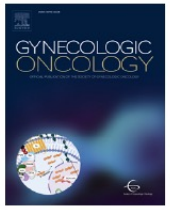

Outcomes after targeted treatment based on somatic tumor genetic testing for women with gynecologic cancers

Sahana Somasegar [a,*], Claire Hoppenot [a], Kristine Kuchta [b], Annette Sereika [c], Janardan Khandekar [c], Gustavo Rodriguez [d], Elena Moore [d], Jean Hurteau [d,e], Tilley Jenkins Vogel [d]

Gynecologic Oncology 165 (2022) 560–567

Contents lists available at ScienceDirect

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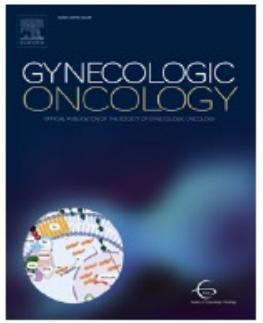

The genomic landscape of low-grade serous ovarian/peritoneal carcinoma and its impact on clinical outcomes

David M. Gershenson [a,*], Charlotte C. Sun [a], Shannon N. Westin [a], Mostafa Eyada [a,b], Lauren P. Cobb [a], Lisa C. Nathan [a], Anil K. Sood [a], Anais Malpica [c], Robert T. Hillman [a,d,e], Kwong K. Wong [a]

Int J Gynecol Cancer. 2021 January; 31(1): 92–97. doi:10.1136/ijgc-2020-001718.

Correlation of surgeon radiology assessment with laparoscopic disease site scoring in patients with advanced ovarian cancer

Nicole D. Fleming[1], Shannon N. Westin[1], Larissa A. Meyer[1], Aaron Shafer[1], J. Alejandro Rauh-Hain[1], Michaela Onstad[1], Lauren Cobb[1], Michael Bevers[1], Bryan M. Fellman[2], Jennifer K. Burzawa[3], Priya Bhosale[4], Behrouz Zand[1], Amir A. Jazaeri[1], Charles Levenback[1], Robert L. Coleman[1], Pamela T. Soliman[1], Anil K. Sood[1]

Gynecologic Oncology 166 (2022) 50–56

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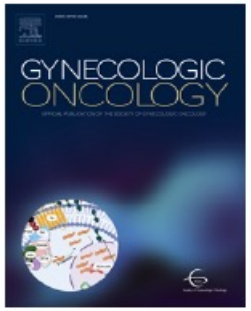
journal homepage: www.elsevier.com/locate/ygyno



Research Paper

Frailty repels the knife: The impact of frailty index on surgical intervention and outcomes☆

Katelyn F. Handley [a,b,c], Anil K. Sood [a], Graziela Zibetti Dal Molin [d], Shannon N. Westin [a], Larissa A. Meyer [a], Bryan Fellman [e], Pamela T. Soliman [a], Robert L. Coleman [f], Nicole D. Fleming [a,*]

Identifying Disparities in Gynecologic Cancer: Results and Analysis from a Patient Preference Survey

Chapman-Davis E et al.

ASCO 2022;Abstract 5561.

Meet The Professor with Dr Westin

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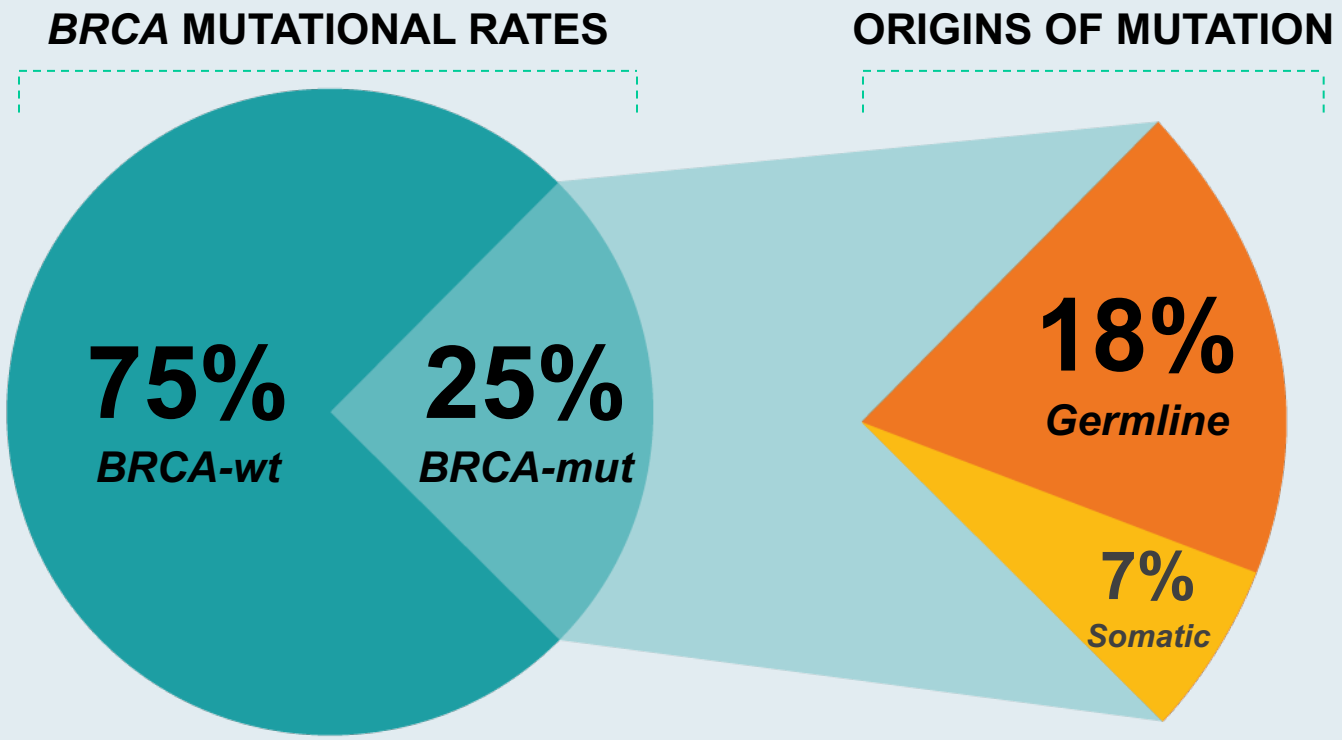
MODULE 5: Appendix of Key Publications

RTP RESEARCH TO PRACTICE

Optimal Biomarker Evaluation and Front-Line Management

An Estimated 25% of Newly Diagnosed Ovarian Cancers Harbor BRCA1/2 Mutations



An estimated 1 in 4 women with EOC will have a *BRCA*-positive tumor result
Tumor testing detects more patients with *BRCA* mutations than blood/saliva tests that do not look at tumor DNA

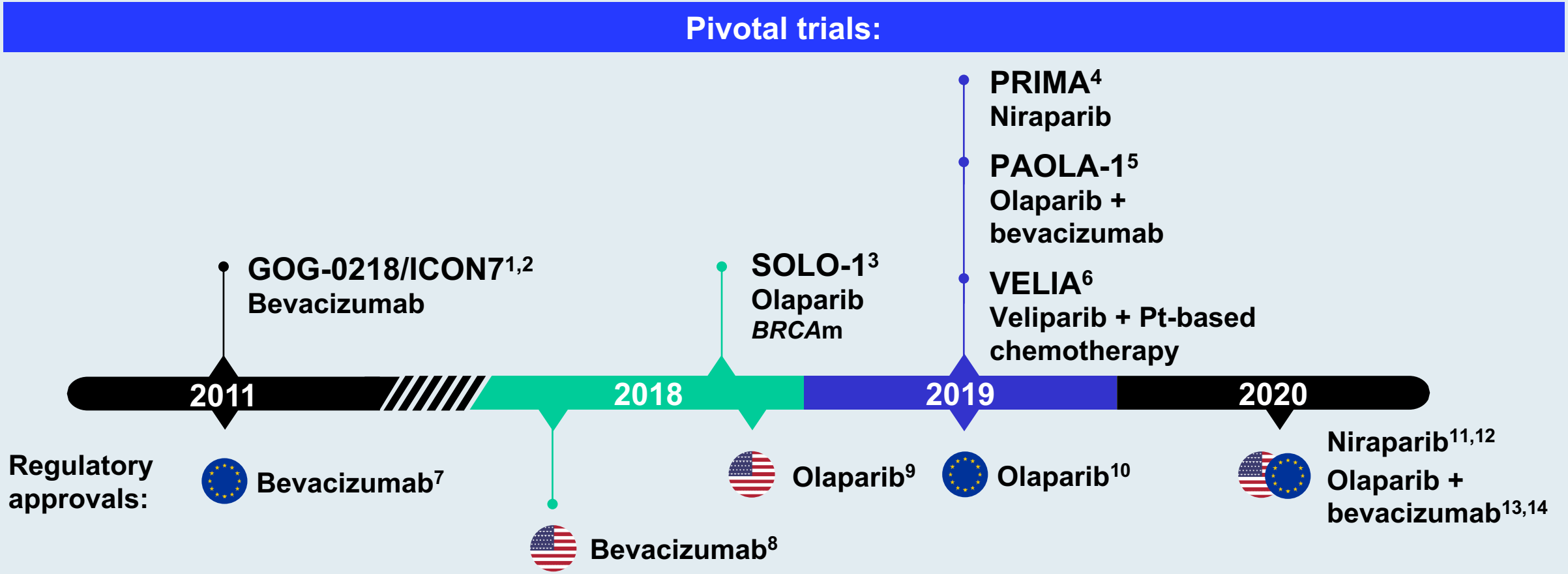
EOC = epithelial ovarian cancer; mut = mutation; wt = wild type

Pennington et al. *Clin Cancer Res* 2014;20(3):764-75.

Courtesy of Kathleen Moore, MD

RTP RESEARCH TO PRACTICE

Pivotal Trials and Regulatory Milestones in First-Line Maintenance Therapy for Advanced Ovarian Cancer



Dates shown indicate the year of the publication of the pivotal studies and regulatory approvals for these compounds.

*BRCA*m, breast cancer gene mutant; GOG, Gynecologic Oncology Group; Pt, platinum.

1. Burger RA et al. *N Engl J Med*. 2011;365(26):2473-2483. 2. Perren TJ et al. *N Engl J Med*. 2011;365(26):2484-2496. 3. Moore K et al. *N Engl J Med*. 2018;379(26):2495-2505. 4. González-Martín A et al. *N Engl J Med*. 2019;381(25):2391-2402. . Ray-Coquard I et al. *N Engl J Med*. 2019;381(25):2416-2428. 6. Coleman RL et al. *N Engl J Med*. 2019;381(25):2403-2415. 7. European Medicines Agency. Published September 22, 2011. Accessed June 7, 2021. 8. F. Hoffmann-La Roche Ltd. Published June 13, 2018. Accessed June 7, 2021. 9. US Food and Drug Administration. Published December 26, 2018. Accessed June 7, 2021. 10. European Medicines Agency. Published April 26, 2019. Accessed June 7, 2021. 11. GlaxoSmithKline. Published April 29, 2020. Accessed June 7, 2021. 12. GlaxoSmithKline. Published October 29, 2020. Accessed June 7, 2021. 13. US Food and Drug Administration. Published May 11, 2020. Accessed June 7, 2021. 14. European Medicines Agency. Published September 17, 2020. Accessed June 7, 2021.

Courtesy of Kathleen Moore, MD

Phase III First-Line PARP Inhibitor Maintenance Trials

Study design	SOLO-1[1] (N = 391)	PAOLA-1[2] (N = 612)	PRIMA[3] (N = 620)	VELIA[4] (N = 1,140)
Treatment arms vs placebo	**Olaparib (n=260)**	**Bevacizumab ± olaparib**	**Niraparib**	**Veliparib**
Patient population	*BRCA* mutation	All comers	All comers	All comers
Treatment duration	24 mo	15 mo for bev 24 mo for olaparib	36 mo or until PD	24 mo
Median PFS	56 mo vs 14 mo HR: 0.33	22.1 mo vs 16.6 mo HR: 0.59	22.1 mo vs 10.9 mo HR 0.40	23.5 mo vs 17.3 mo HR: 0.68

bev = bevacizumab; PD = disease progression

[1] Banerjee et al. *Lancet Oncol* 2021;22(12):1721-31; [2] Ray-Coquard et al. SGO 2020;Abstract 33; [3] González-Martín A et al. ASCO 2021;Abstract 5518; [4] Aghajanian C et al. *Gyn Oncol* 2021;162(2):375-81.

Phase 2 OVARIO Study of Niraparib + Bevacizumab Therapy in Advanced Ovarian Cancer Following Frontline Platinum-Based Chemotherapy with Bevacizumab

Melissa M. Hardesty,[1] Thomas Krivak,[2] Gail S. Wright,[3] Erika Hamilton,[4] Evelyn L. Fleming,[5] Jimmy Belotte,[6] Erika Keeton,[6] Ping Wang,[6] Aine Clements,[7] Heidi J. Gray,[8] Gottfried E. Konecny,[9] Richard G. Moore,[10] Debra L. Richardson[11]

[1]Alaska Women's Cancer Care, Anchorage, AK, USA; [2]Division of Gynecologic Oncology, Department of Obstetrics and Gynecology, The Western Pennsylvania Hospital, Pittsburgh, PA, USA; [3]Florida Cancer Specialists and Research Institute, New Port Richey, FL, USA; [4]Sarah Cannon Research Institute; Tennessee Oncology, Nashville, TN, USA; [5]Division of Gynecologic Oncology, Norris Cotton Cancer Center, Dartmouth-Hitchcock Medical Center, Lebanon, NH, USA; [6]GlaxoSmithKline, Waltham, MA, USA; [7]Department of Gynecologic Oncology, Riverside Methodist Hospital, Columbus, OH, USA; [8]Division of Gynecologic Oncology, Department of Obstetrics and Gynecology, University of Washington, Seattle, WA, USA; [9]University of California Los Angeles, Los Angeles, CA, USA; [10]Division of Gynecologic Oncology, Department of Obstetrics and Gynecology, Wilmot Cancer Institute, University of Rochester Medical Center, Rochester, NY, USA; [11]Division of Gynecologic Oncology, Stephenson Cancer Center, University of Oklahoma Health Sciences Center, Oklahoma City, OK, USA

ANNUAL MEETING ON WOMENS' CANCER®
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SGO // PHOENIX, ARIZONA // MARCH 19 - 21, 2022

Society of Gynecologic Oncology

SGO 2022;Abstract 40.

RTP RESEARCH TO PRACTICE

Patients with newly diagnosed high-grade serous or endometrioid stage IIIB to IV epithelial ovarian, fallopian tube, or peritoneal cancer who achieved a CR, PR, or NED result after front-line platinum-based chemotherapy + bevacizumab

All patients underwent tissue testing for HRd at enrollment

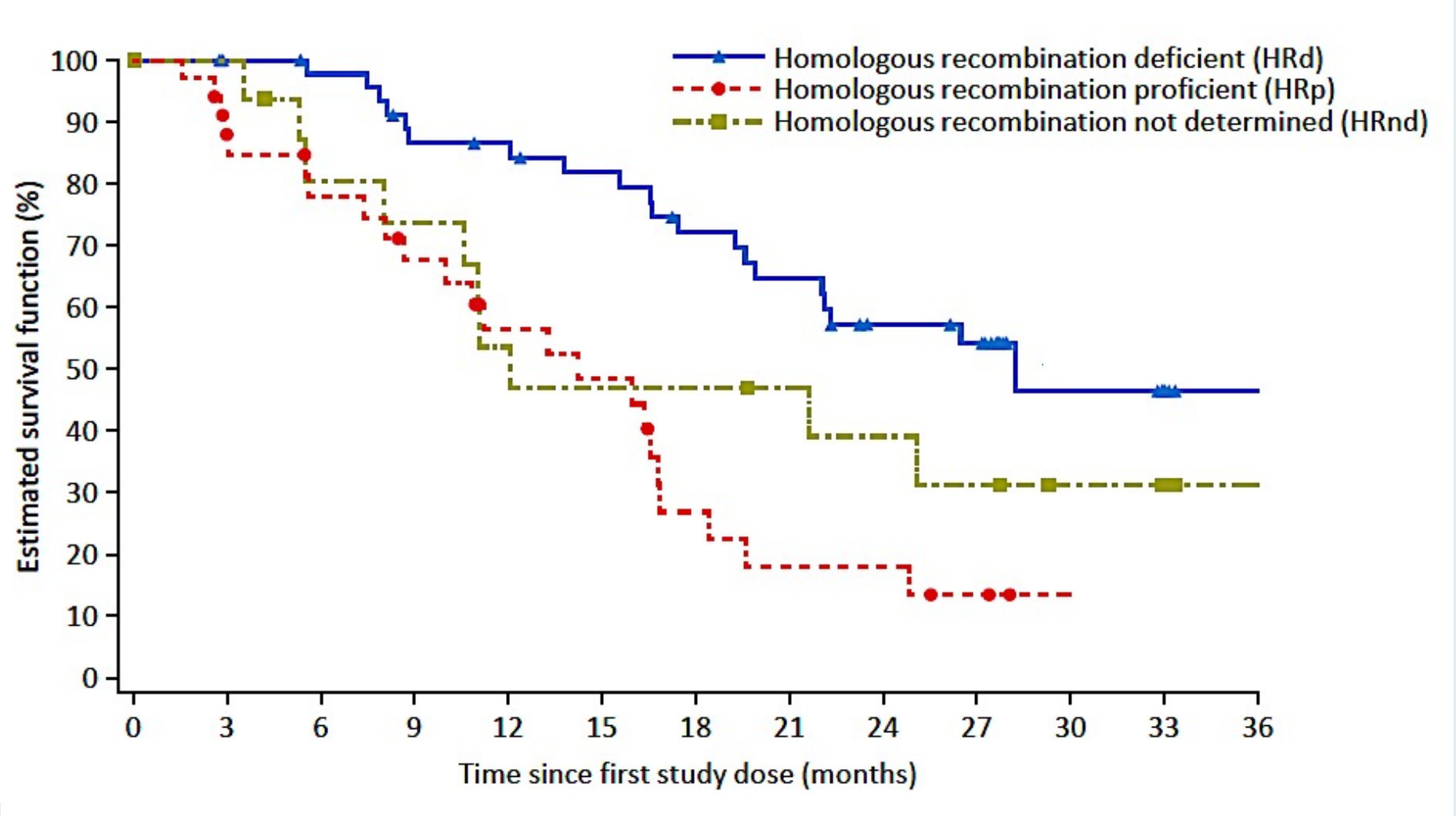
Niraparib (200 or 300 mg QD) + bevacizumab (15 mg/kg Q3W)

Starting niraparib dose, n (%)	N=105
200 mg (<77 kg and/or platelet count <150,000/µL)	82 (78)
300 mg (all others)	23 (22)

Endpoint assessment	
Primary endpoint	• PFS rate at 18 months (PFS18)
Secondary endpoints	• PFS • Overall survival • RECIST or CA-125 PFS • Time to first subsequent therapy • Time to second subsequent therapy • Safety and tolerability • Patient-reported outcome
Exploratory endpoints	• PFS rate at 6 months (PFS6) and 12 months (PFS12)
Statistical analysis plan	• Efficacy: PFS18 and PFS24 will be estimated by frequency analysis, with corresponding 95% exact CI will be reported • The time to event endpoints (PFS, TFST, TSST) will be analyzed using Kaplan-Meier methodology • Progression will be assessed by RECIST v1.1 per investigator

Hardesty et al. SGO 2022;Abstract 40.

OVARIO: PFS by Homologous Recombination Deficiency Status



Overall (n = 105)	
18-mo PFS rate	62
24-mo PFS rate	53

HRd (n = 49)	
18-mo PFS rate	76
24-mo PFS rate	63

HRp (n = 38)	
18-mo PFS rate	47
24-mo PFS rate	42

HRnd (n = 18)	
18-mo PFS rate	56
24-mo PFS rate	50

Hardesty et al. SGO 2022;Abstract 40.

RTP RESEARCH TO PRACTICE

OVARIO: Treatment Related Adverse Events (TRAEs)

Parameter, n (%)	N=105		
	Related to nira or bev	Related to nira	Related to bev
Any TRAE	105 (100)	104 (99)	96 (91)
Any Grade ≥3 TRAE	84 (80)	81 (77)	54 (51)
Any serious TRAE	21 (20)	19 (18)	7 (7)
TRAE leading to treatment discontinuation	42 (40)	32 (30)	23 (22)
TRAE leading to dose reduction	78 (74)	77 (73)	27 (26)
TRAE leading to treatment interruption	93 (88)	90 (86)	58 (55)

TRAEs in ≥20% of patients (N=105) Related to niraparib or bevacizumab		
Preferred term, n (%)	Any Grade	Grade ≥3
Thrombocytopenia[a]	74 (70)	41 (39)
Fatigue	60 (57)	9 (9)
Anemia[b]	55 (52)	36 (34)
Nausea	55 (52)	1 (1)
Hypertension[c]	53 (50)	28 (27)
Proteinuria	41 (39)	5 (5)
Headache	32 (30)	6 (6)
Neutropenia[d]	28 (27)	13 (12)
Leukopenia[e]	24 (23)	0

Hardesty et al. SGO 2022;Abstract 40.

Efficacy and Safety of Niraparib as Maintenance Treatment in Patients with Newly Diagnosed Advanced Ovarian Cancer Using an Individualized Starting Dose (PRIME Study): A Randomized, Double-blind, Placebo-controlled, Phase 3 Trial

Ning Li*, Jianqing Zhu, Rutie Yin, Jing Wang, Lingya Pan, Beihua Kong, Hong Zheng, Jihong Liu, Xiaohua Wu, Li Wang, Yi Huang, Ke Wang, Dongling Zou, Hongqin Zhao, Chunyan Wang, Weiguo Lu, An Lin, Ge Lou, Guiling Li, Pengpeng Qu, Hongying Yang, Xiaoa Zhen, Wenzhao Hang, Jianmei Hou, Lingying Wu*

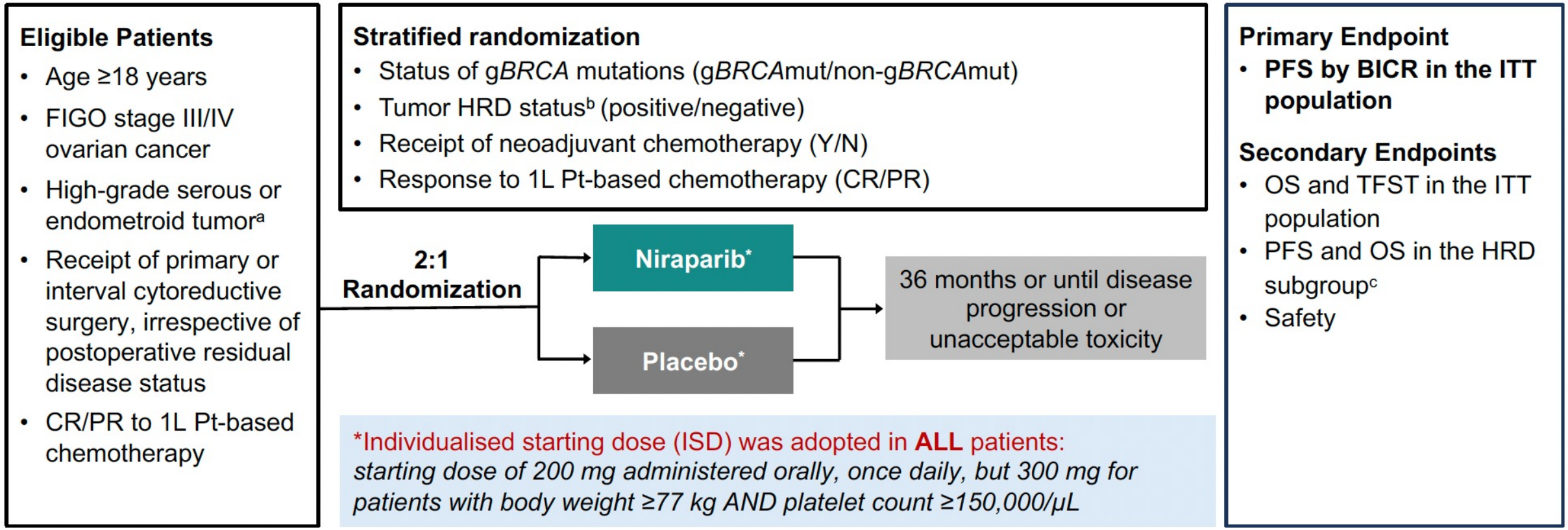
* National Cancer Center/National Clinical Research Center for Cancer/Cancer Hospital, Chinese Academy of Medical Sciences and Peking Union Medical College, Beijing, China

SGO 2022;Abstract LBA5.

PRIME: Study Design

PRIME is a randomized, double-blind, placebo-controlled phase III trial (NCT03709316).

Schema



Li et al. SGO 2022;Abstract LBA5.

PRIME: Demographics and Baseline Characteristics

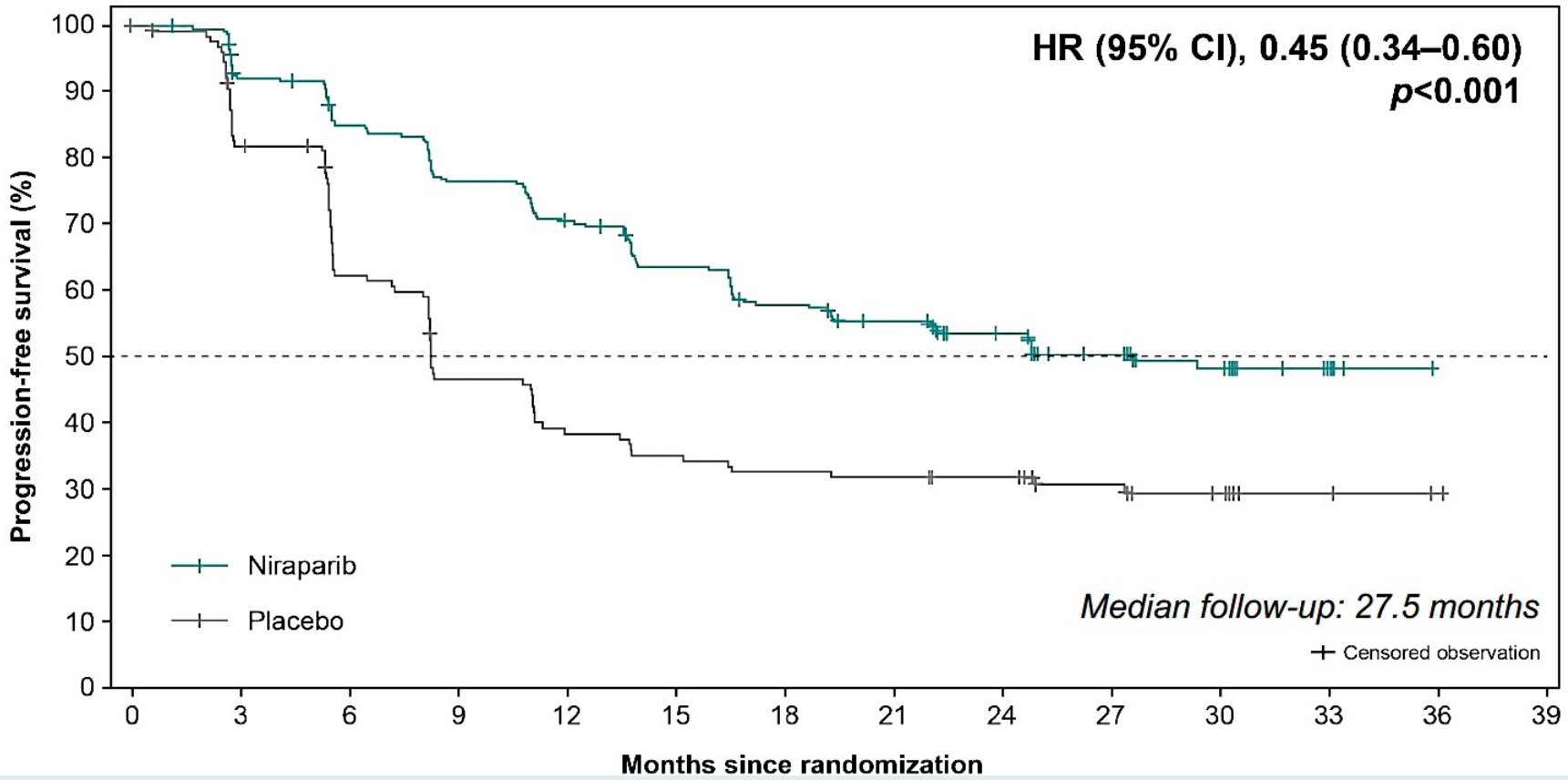
Characteristic	Niraparib (N=255)	Placebo (N=129)
Median age (range), years	53.0 (32–77)	54.0 (33–77)
Median weight (range), kg	59.0 (39.5–100.0)	57.0 (37.0–97.0)
ECOG performance status, n (%)		
0	98 (38.4)	52 (40.3)
1	157 (61.6)	77 (59.7)
FIGO stage, n (%)		
III	182 (71.4)	94 (72.9)
IV	73 (28.6)	35 (27.1)
Primary tumor location, n (%)		
Ovary	229 (89.8)	117 (90.7)
Fallopian tube	19 (7.5)	9 (7.0)
Peritoneum	7 (2.7)	3 (2.3)
Histologic subtype, n (%)		
Serous ovarian cancer	253 (99.2)	128 (99.2)
Endometrioid carcinoma	2 (0.8)	0
Other	0	1 (0.8)

Characteristic	Niraparib (N=255)	Placebo (N=129)
Neoadjuvant chemotherapy, n (%)		
Yes	121 (47.5)	59 (45.7)
No	134 (52.5)	70 (54.3)
Response to Pt-based CT, n (%)		
CR	212 (83.1)	103 (79.8)
PR	43 (16.9)	26 (20.2)
g*BRCA* mutation status, n (%)		
g*BRCA*mut	85 (33.3)	40 (31.0)
Non-g*BRCA*mut	170 (66.7)	89 (69.0)
Homologous recombination[a], n (%)		
Deficient	170 (66.7)	87 (67.4)
Proficient	85 (33.3)	42 (32.6)
Postoperative residual disease status, n (%)		
Optimal (R0/R1)	193 (75.7)	105 (81.4)
Suboptimal (R2) or missing	52 (24.3)	24 (18.6)

- The niraparib and placebo groups were well-balanced.

Li et al. SGO 2022;Abstract LBA5.

PRIME: PFS (by Blinded Independent Central Review) in the ITT Population



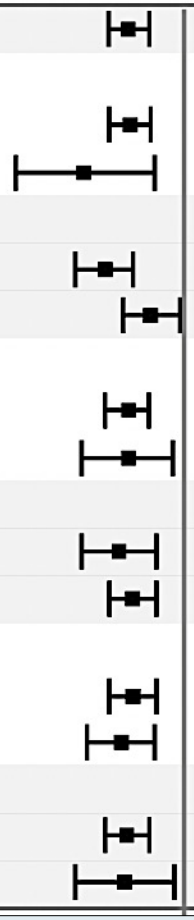
16.5 months longer median PFS with niraparib versus placebo

	Niraparib (N=255)	Placebo (N=129)
PFS (54.4% data maturity)		
Events, n (%)	123 (48.2)	86 (66.7)
mPFS (95% CI), months	24.8 (19.2–NE)	8.3 (7.3–11.1)
Patients without PD or death (%)		
24 months	52.6	30.4

Li et al. SGO 2022;Abstract LBA5.

PRIME: PFS Benefit in Prespecified Subgroups

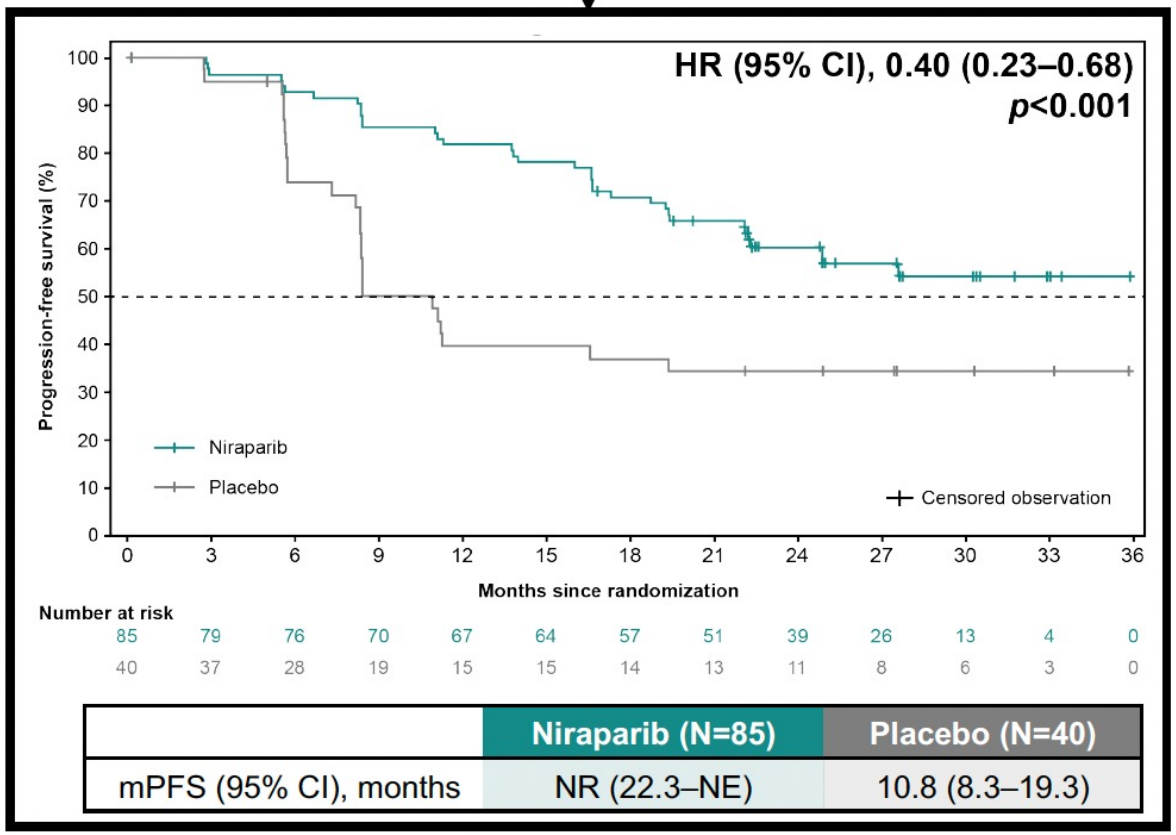
Subgroup	Events/patients (%)		Hazard ratio for PFS (95% CI)
	Niraparib	Placebo	
Overall	123/255 (48.2)	86/129 (66.7)	0.45 (0.34–0.60)
Age			
<65 years	108/229 (47.2)	73/114 (64.0)	0.47 (0.34–0.63)
≥65 years	15/26 (57.7)	13/15 (86.7)	0.24 (0.09–0.66)
Neoadjuvant chemotherapy			
Yes	62/121 (51.2)	46/59 (78.0)	0.32 (0.21–0.48)
No	61/134 (45.5)	40/70 (57.1)	0.63 (0.42–0.94)
Response to Pt-based chemotherapy			
Complete response	98/212 (46.2)	66/103 (64.1)	0.45 (0.32–0.61)
Partial response	25/43 (58.1)	20/26 (76.9)	0.45 (0.23–0.86)
***gBRCA* mutation status**			
*gBRCA*mut	35/85 (41.2)	25/40 (62.5)	0.40 (0.23–0.68)
Non-g*BRCA*mut	88/170 (51.8)	61/89 (68.5)	0.48 (0.34–0.67)
Homologous recombination			
Deficient	75/170 (44.1)	57/87 (65.5)	0.48 (0.34–0.68)
Proficient	48/85 (56.5)	29/42 (69.0)	0.41 (0.25–0.65)
Postoperative residual disease status			
Optimal	94/193 (48.7)	71/105 (67.6)	0.44 (0.32–0.61)
Suboptimal or missing	29/62 (46.8)	15/24 (62.5)	0.43 (0.21–0.87)



Li et al. SGO 2022;Abstract LBA5.

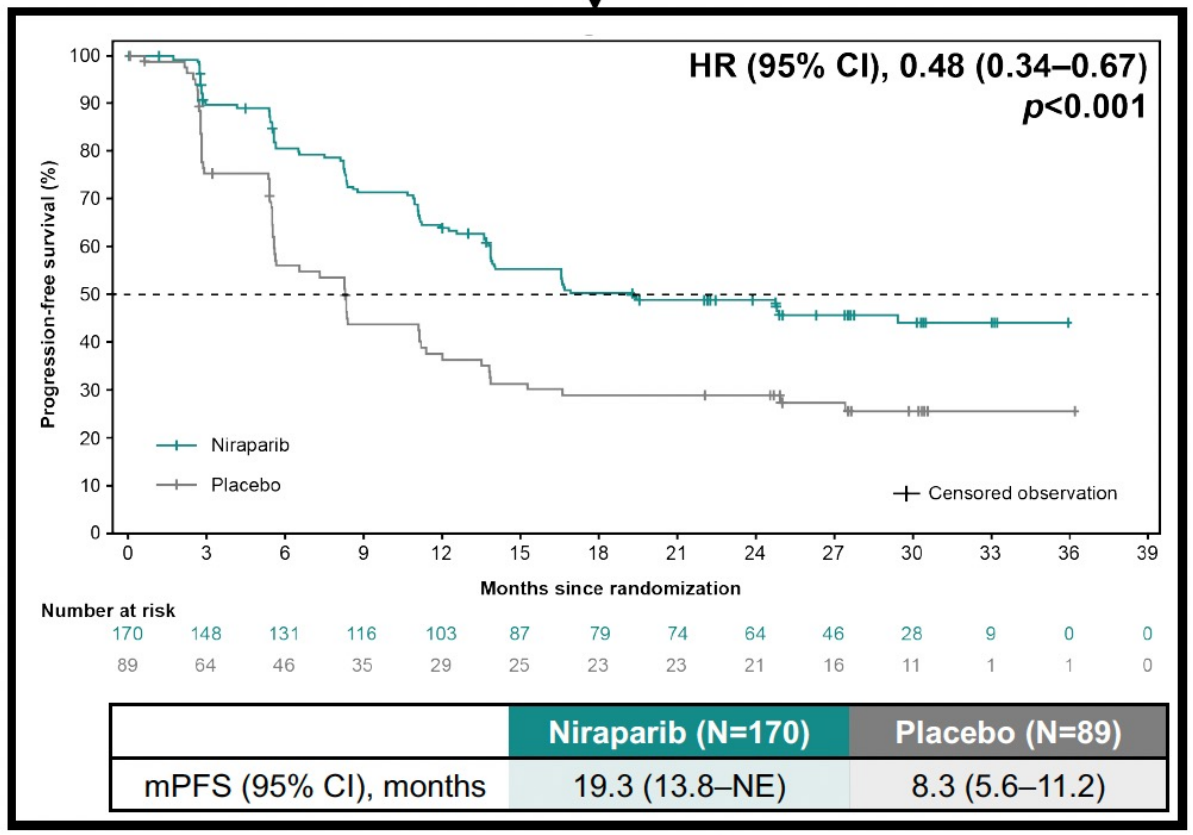
PRIME: PFS Benefit by g*BRCA*mut Status

g*BRCA*mut



	Niraparib (N=85)	Placebo (N=40)
mPFS (95% CI), months	NR (22.3–NE)	10.8 (8.3–19.3)

Non-g*BRCA*mut



	Niraparib (N=170)	Placebo (N=89)
mPFS (95% CI), months	19.3 (13.8–NE)	8.3 (5.6–11.2)

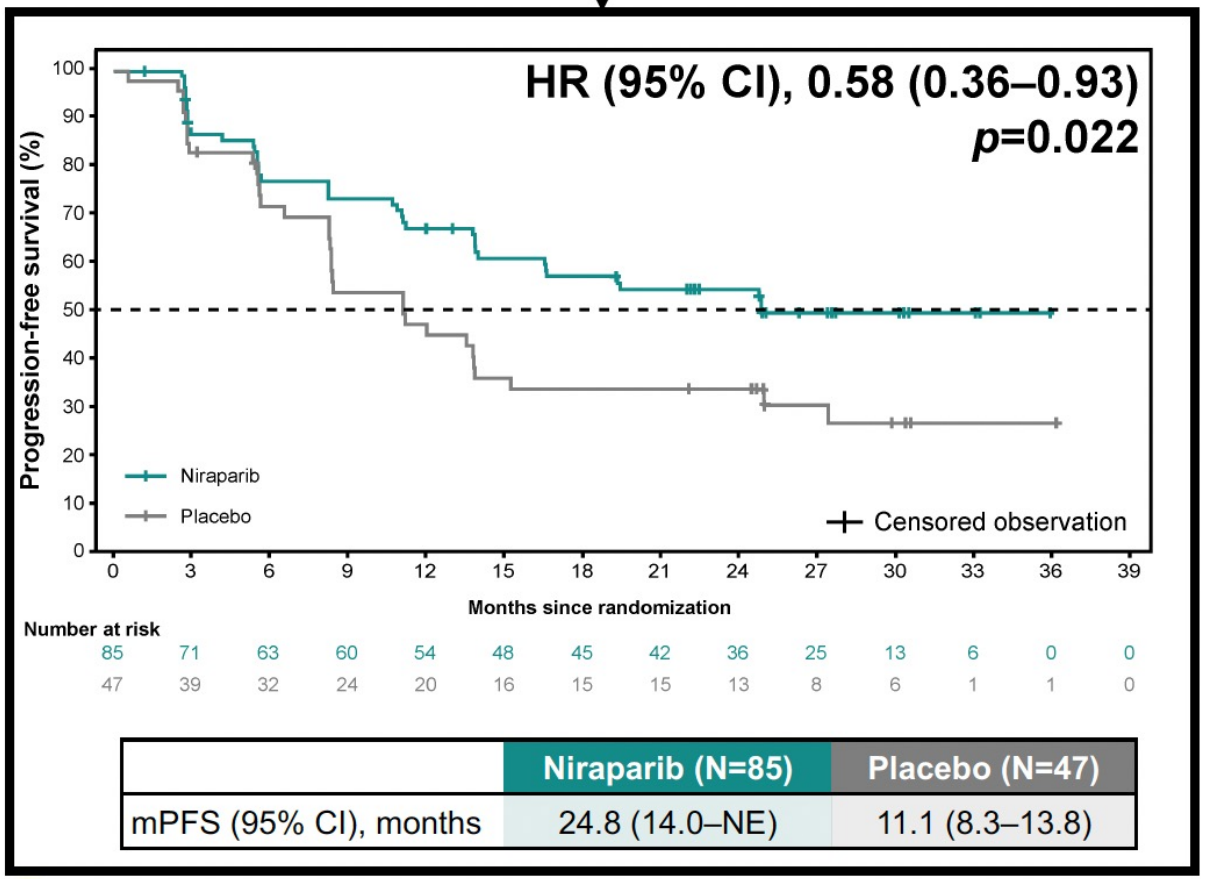
- Median PFS has not been yet reached for the g*BRCA*mut population.
- The benefit of niraparib in the non-g*BRCA*mut population is confirmed.

Li et al. SGO 2022;Abstract LBA5.

RTP RESEARCH TO PRACTICE

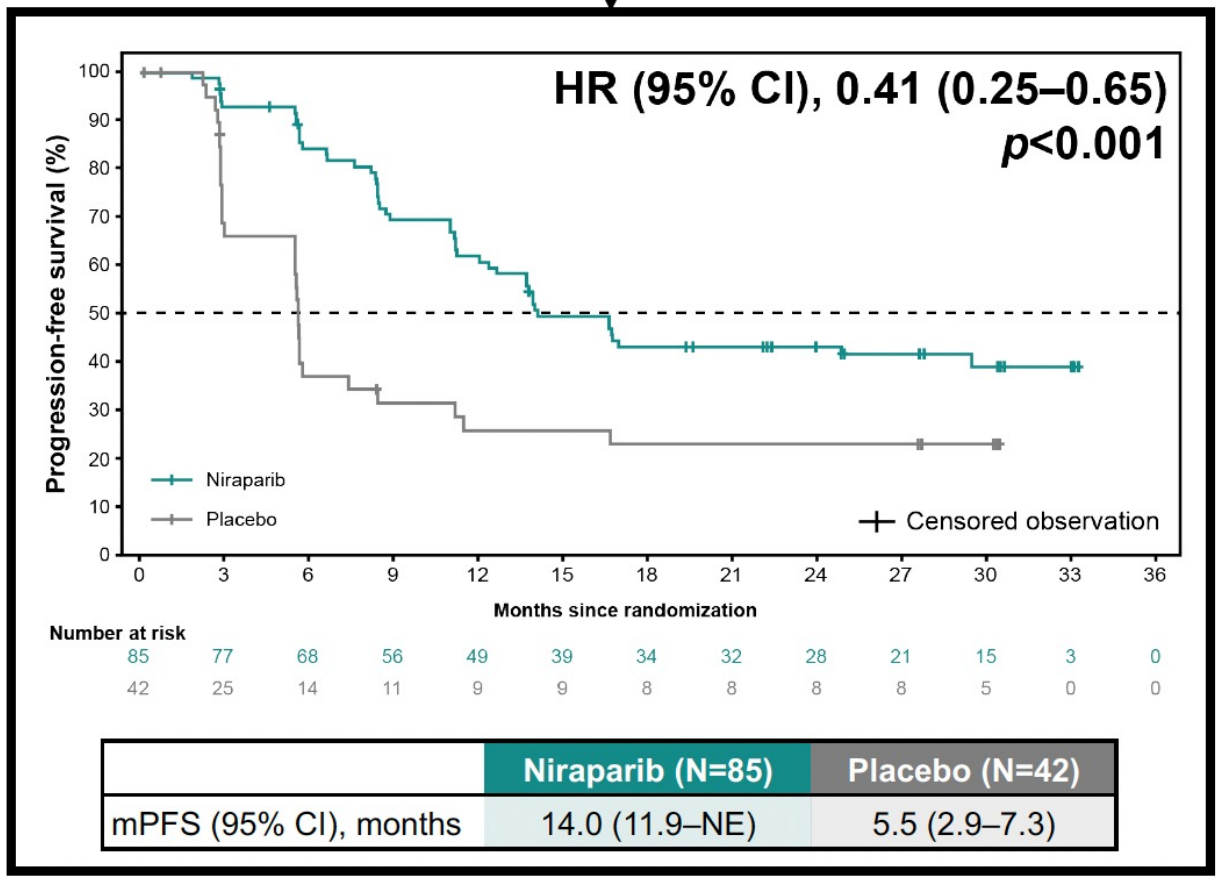
PRIME: PFS Benefit in non-g*BRCA*mut Subgroups

Non-g*BRCA*mut/HRd



	Niraparib (N=85)	Placebo (N=47)
mPFS (95% CI), months	24.8 (14.0–NE)	11.1 (8.3–13.8)

Non-g*BRCA*mut/HRp



	Niraparib (N=85)	Placebo (N=42)
mPFS (95% CI), months	14.0 (11.9–NE)	5.5 (2.9–7.3)

Li et al. SGO 2022;Abstract LBA5.

RTP RESEARCH TO PRACTICE

PRIME: Safety Overview (and PRIMA)

TEAEs, n (%)	PRIME		PRIMA[1]	
	Niraparib (N=255)	Placebo (N=129)	Niraparib (N=484)	Placebo (N=244)
Any TEAEs	253 (99.2)	121 (93.8)	478 (98.8)	224 (91.8)
Treatment-related	249 (97.6)	111 (86.0)	466 (96.3)	168 (68.9)
Grade≥3 TEAEs	139 (54.5)	23 (17.8)	341 (70.5)	46 (18.9)
Treatment-related	125 (49.0)	9 (7.0)	316 (65.3)	16 (6.6)
Serious TEAEs	48 (18.8)	11 (8.5)	156 (32.2)	32 (13.1)
Treatment-related	38 (14.9)	5 (3.9)	118 (24.4)	6 (2.5)
TEAEs leading to treatment interruption	160 (62.7)	25 (19.4)	385 (79.5)	44 (18.0)
TEAEs leading to dose reduction[b]	103 (40.4)	8 (6.2)	343 (70.9)	20 (8.2)
TEAEs leading to discontinuation	17 (6.7)	7 (5.4)	58 (12.0)	6 (2.5)
TEAEs leading to death	1 (0.4)	0	2 (0.4)	1 (0.4)

Li et al. SGO 2022;Abstract LBA5.

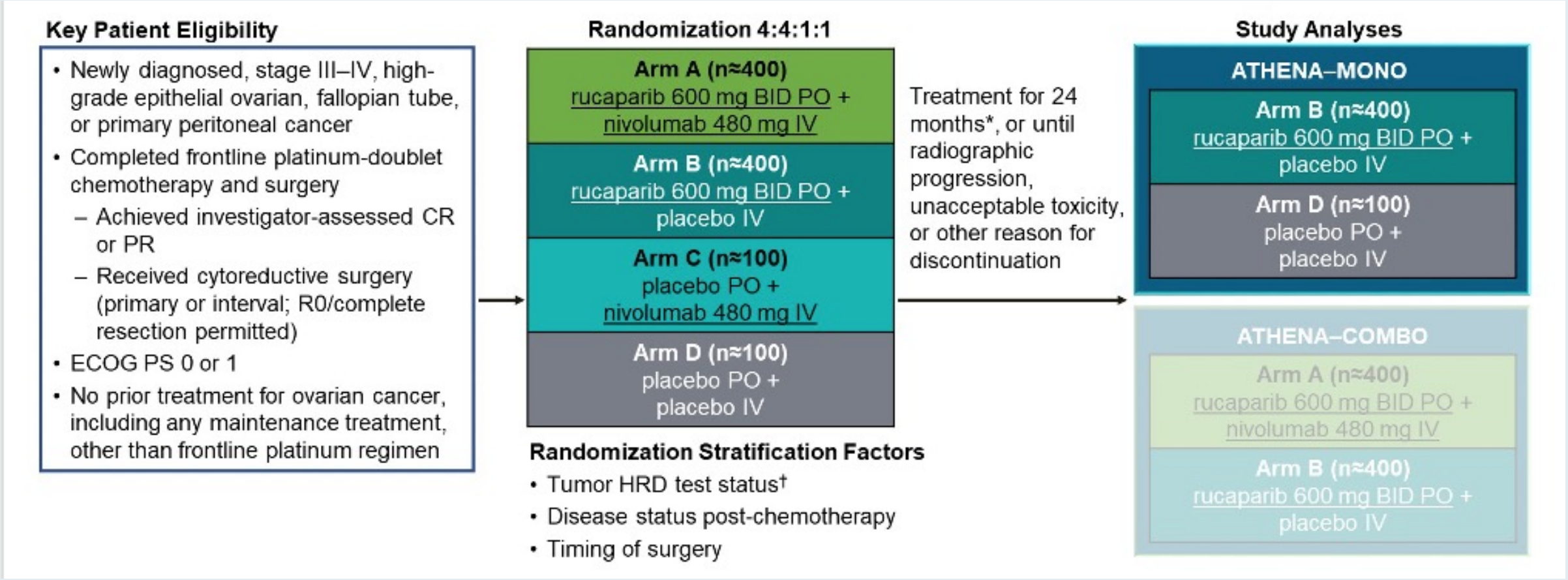
original reports

A Randomized, Phase III Trial to Evaluate Rucaparib Monotherapy as Maintenance Treatment in Patients With Newly Diagnosed Ovarian Cancer (ATHENA–MONO/GOG-3020/ENGOT-ov45)

Bradley J. Monk, MD[1]; Christine Parkinson, MD[2]; Myong Cheol Lim, MD, PhD[3]; David M. O'Malley, MD[4]; Ana Oaknin, MD, PhD[5]; Michelle K. Wilson, MD[6]; Robert L. Coleman, MD[7]; Domenica Lorusso, MD, PhD[8]; Paul Bessette, MD[9]; Sharad Ghamande, MD[10]; Athina Christopoulou, MD, PhD[11]; Diane Provencher, MD[12]; Emily Prendergast, MD[13]; Fuat Demirkiran, MD[14]; Olga Mikheeva, MD[15]; Oladapo Yeku, MD, PhD[16]; Anita Chudecka-Glaz, MD, PhD[17]; Michael Schenker, MD, PhD[18]; Ramey D. Littell, MD[19]; Tamar Safra, MD[20]; Hung-Hsueh Chou, MD[21,22]; Mark A. Morgan, MD[23]; Vít Drochýtek, MD[24]; Joyce N. Barlin, MD[25]; Toon Van Gorp, MD[26]; Fred Ueland, MD[27]; Gabriel Lindahl, MD[28,29]; Charles Anderson, MD[30]; Dearbhaile C. Collins, MBBCh, MA, PhD[31]; Kathleen Moore, MD[32]; Frederik Marme, MD, PhD[33]; Shannon N. Westin, MD, MPH[34]; Iain A. McNeish, MD, PhD[35]; Danny Shih, BA[36]; Kevin K. Lin, PhD[37]; Sandra Goble, MS[38]; Stephanie Hume, PhD[39]; Keiichi Fujiwara, MD, PhD[40]; and Rebecca S. Kristeleit, MD, PhD[41]

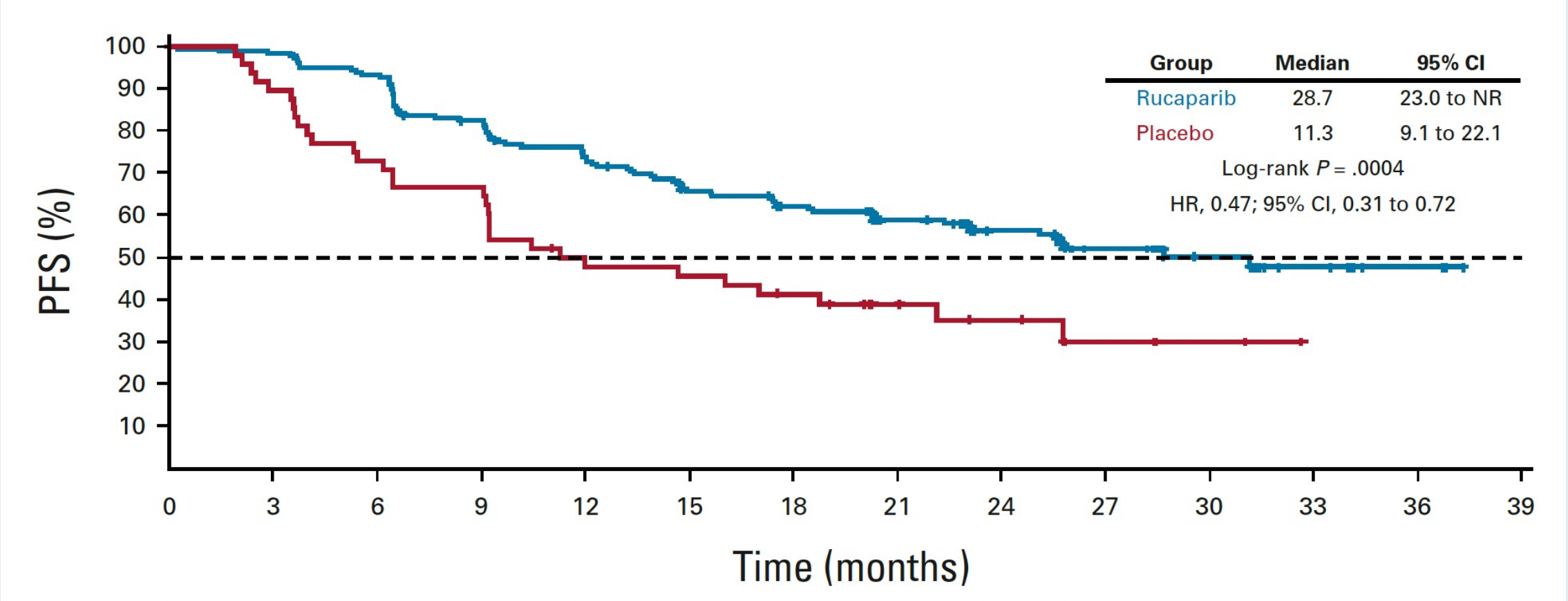
J Clin Oncol 2022;[Online ahead of print].

ATHENA-MONO Study Schema



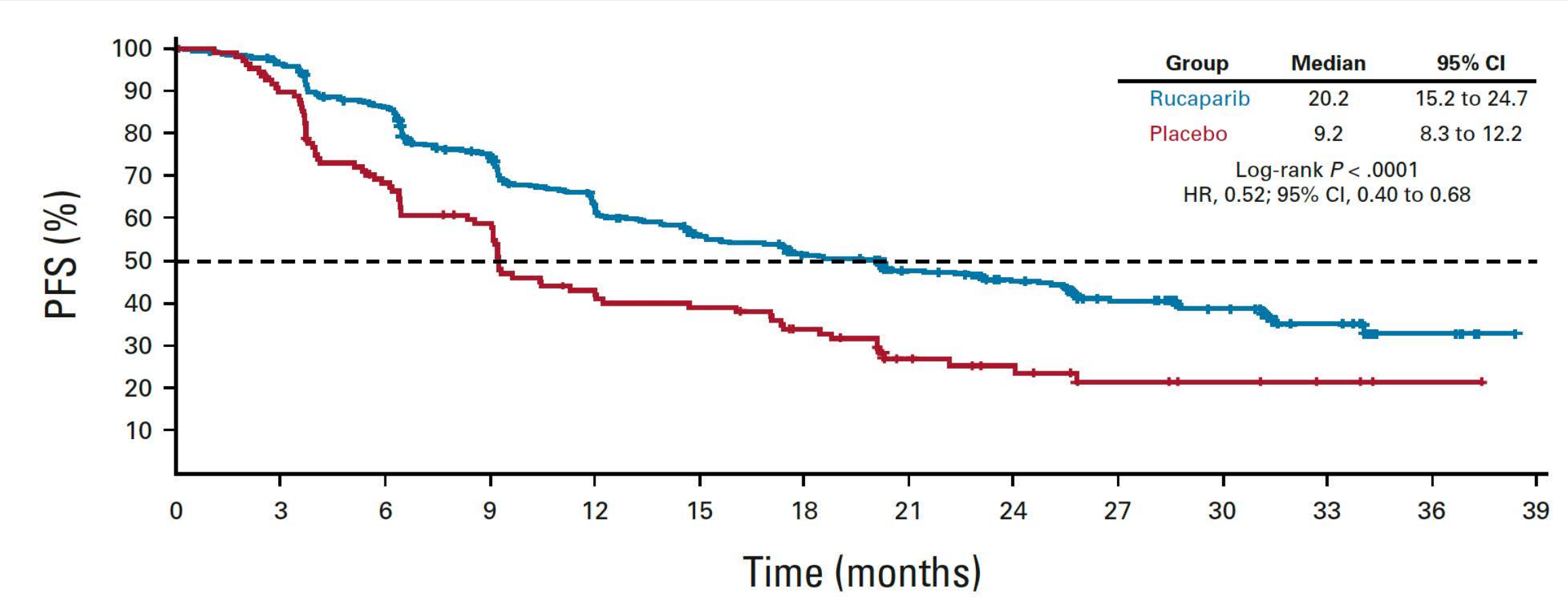
Monk BJ et al. ASCO 2022;Abstract LBA5500.

ATHENA-MONO: Investigator-Assessed PFS in the HRD Population (N = 234)



Monk BJ et al. *J Clin Oncol* 2022;[Online ahead of print].

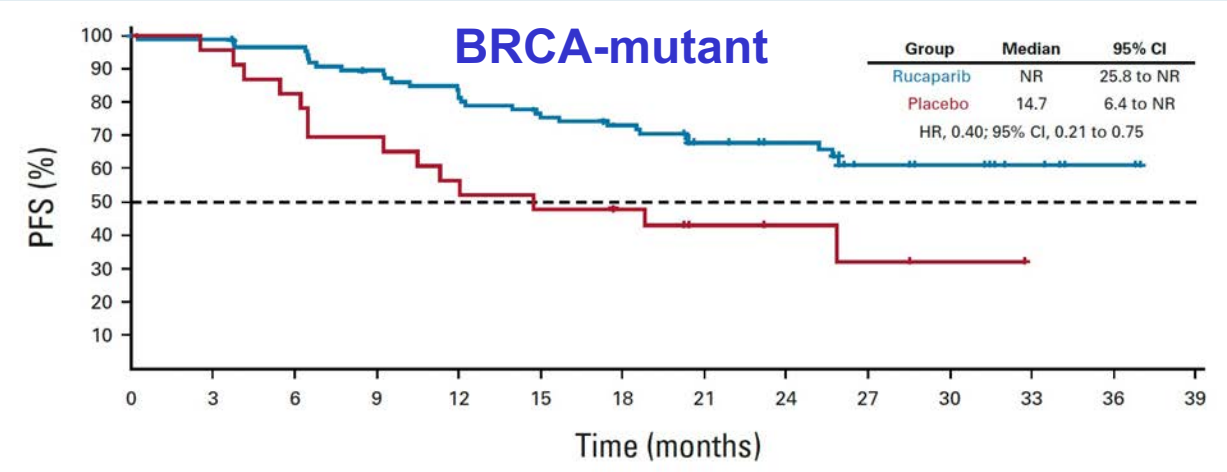
ATHENA-MONO: Investigator-Assessed PFS in the ITT Population (N = 538)

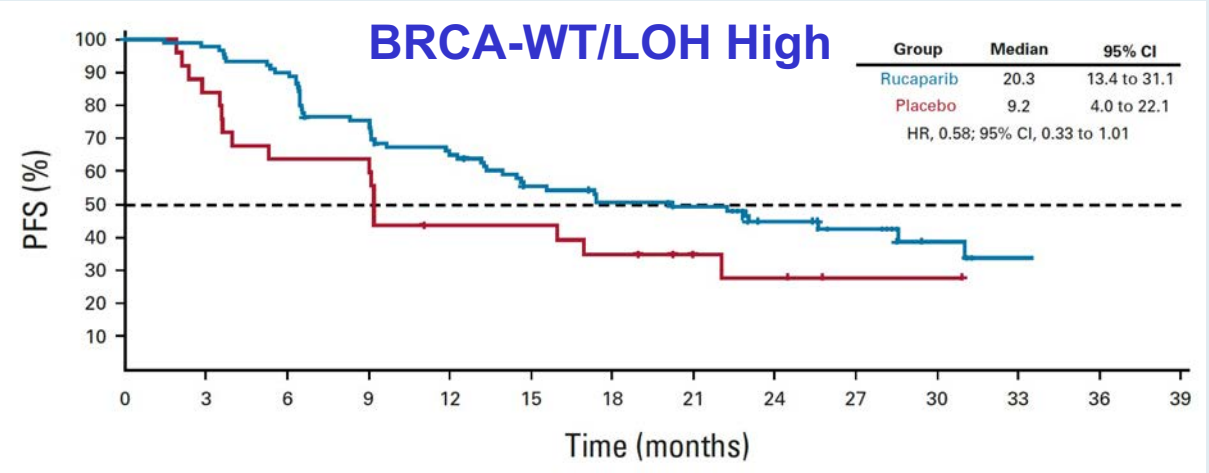


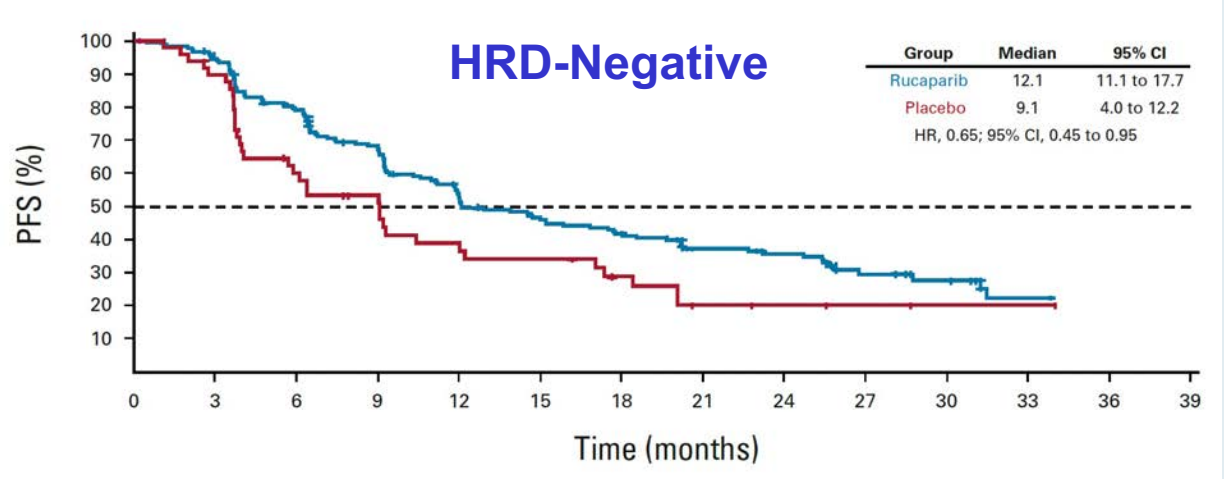
Monk BJ et al. *J Clin Oncol* 2022;[Online ahead of print].

RTP RESEARCH TO PRACTICE

ATHENA-MONO: Investigator-Assessed PFS







Monk BJ et al. *J Clin Oncol* 2022;[Online ahead of print].

ATHENA-MONO: Investigator-Confirmed ORR

	HRD Population		ITT Population	
Response	**Rucaparib (n = 17)**	**Placebo (n = 5)**	**Rucaparib (n = 41)**	**Placebo (n = 11)**
Confirmed ORR per RECIST				
No.	10	1	20	1
% (95% CI)	58.8 (32.9 to 81.6)	20.0 (0.5 to 71.6)	48.8 (32.9 to 64.9)	9.1 (0.2 to 41.3)
CR, No. (%)	0	0	1 (2.4)	0
PR, No. (%)	10 (58.8)	1 (20.0)	19 (46.3)	1 (9.1)
Stable disease, No. (%)	6 (35.3)	2 (40.0)	10 (24.4)	4 (36.4)
Progressive disease, No. (%)	1 (5.9)	2 (40.0)	10 (24.4)	6 (54.5)
Not evaluable, No. (%)	0	0	1 (2.4)	0

ORR = objective response rate

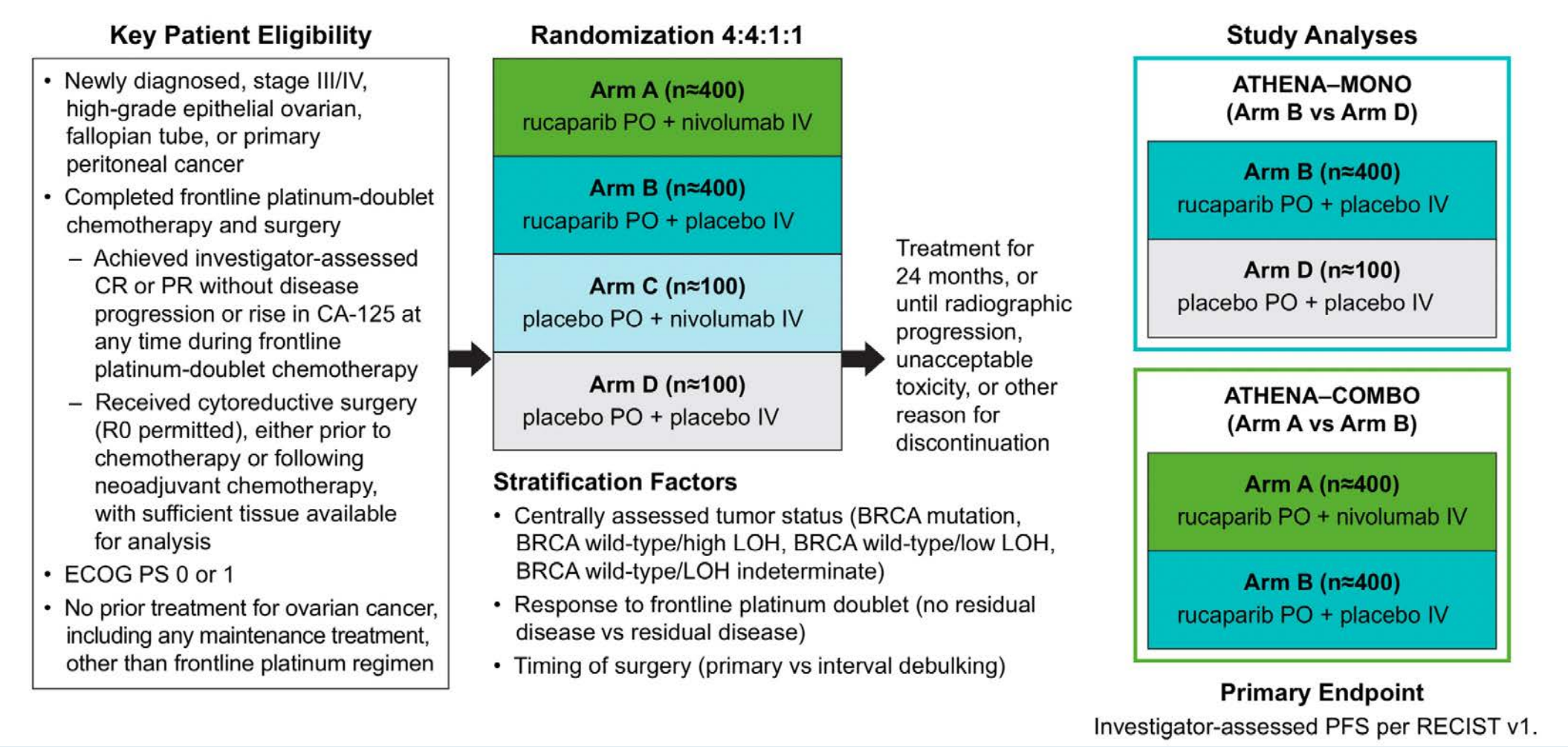
Monk BJ et al. *J Clin Oncol* 2022;[Online ahead of print].

ATHENA-MONO: Common Treatment-Emergent Adverse Events

	Rucaparib (n = 425)		Placebo (n = 110)	
TEAE	**Any Grade**	**Grade ≥ 3**	**Any Grade**	**Grade ≥ 3**
At least one TEAE, No. (%)	411 (96.7)	257 (60.5)	102 (92.7)	25 (22.7)
Nausea	239 (56.2)	8 (1.9)	33 (30.0)	0
Asthenia/fatigue	237 (55.8)	21 (4.9)	41 (37.3)	1 (0.9)
Anemia/decreased hemoglobin	198 (46.6)	122 (28.7)	10 (9.1)	0
Increased ALT/AST	181 (42.6)	45 (10.6)	9 (8.2)	1 (0.9)
Neutropenia/neutrophil count decreased	118 (27.8)	62 (14.6)	8 (7.3)	1 (0.9)
Abdominal pain	106 (24.9)	2 (0.5)	31 (28.2)	2 (1.8)
Diarrhea	102 (24.0)	6 (1.4)	23 (20.9)	1 (0.9)
Thrombocytopenia/platelet count decreased	101 (23.8)	30 (7.1)	1 (0.9)	0
Vomiting	100 (23.5)	6 (1.4)	13 (11.8)	0
Dysgeusia	90 (21.2)	1 (0.2)	6 (5.5)	0
Arthralgia	86 (20.2)	1 (0.2)	25 (22.7)	0
Headache	85 (20.0)	2 (0.5)	16 (14.5)	0

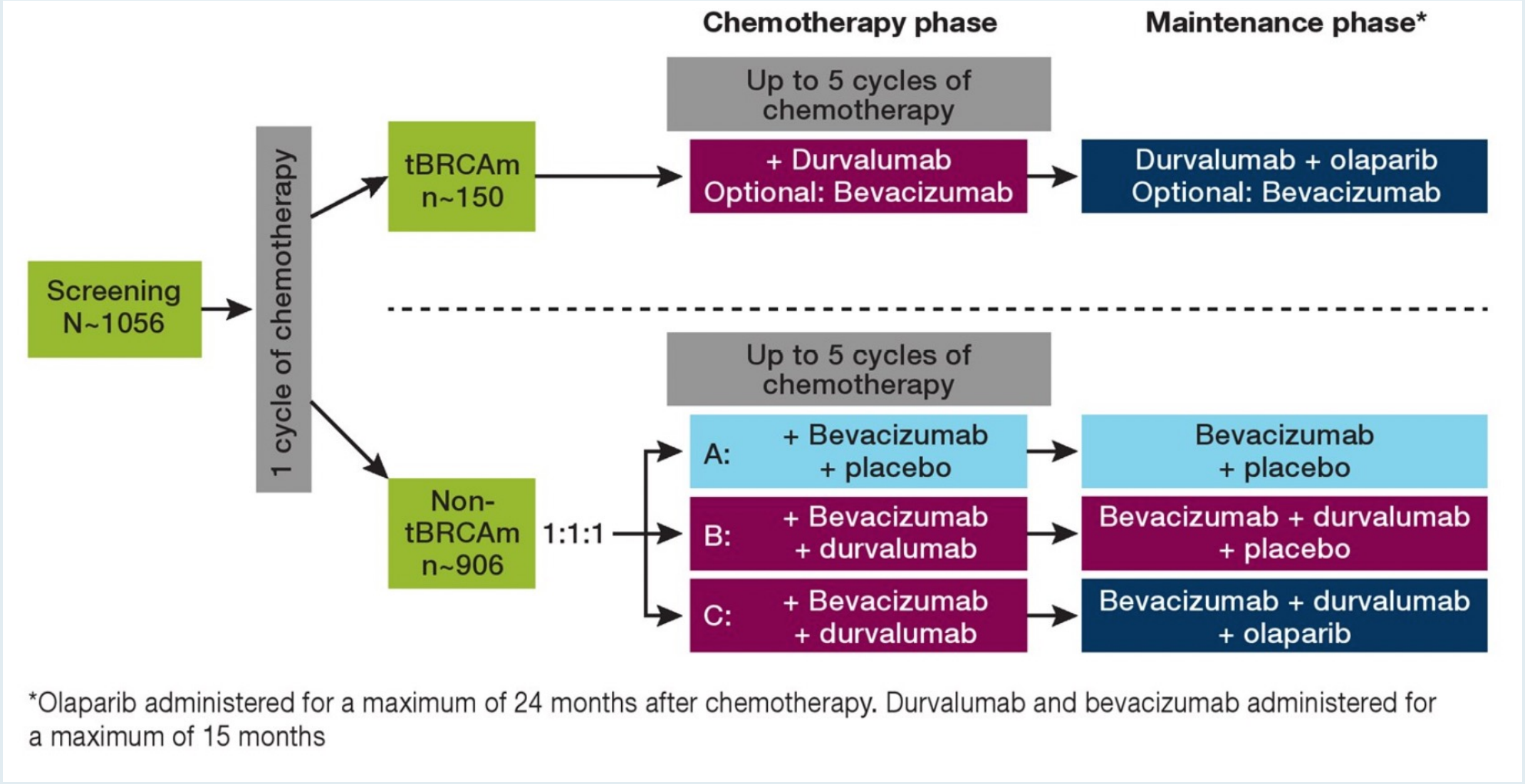
Monk BJ et al. *J Clin Oncol* 2022;[Online ahead of print].

ATHENA-MONO and ATHENA-COMBO Study Design



Monk BJ et al. *Int J Gynecol Cancer* 2021;31(12):1589-94.

DUO-O Study Design in Newly Diagnosed Advanced Ovarian Cancer

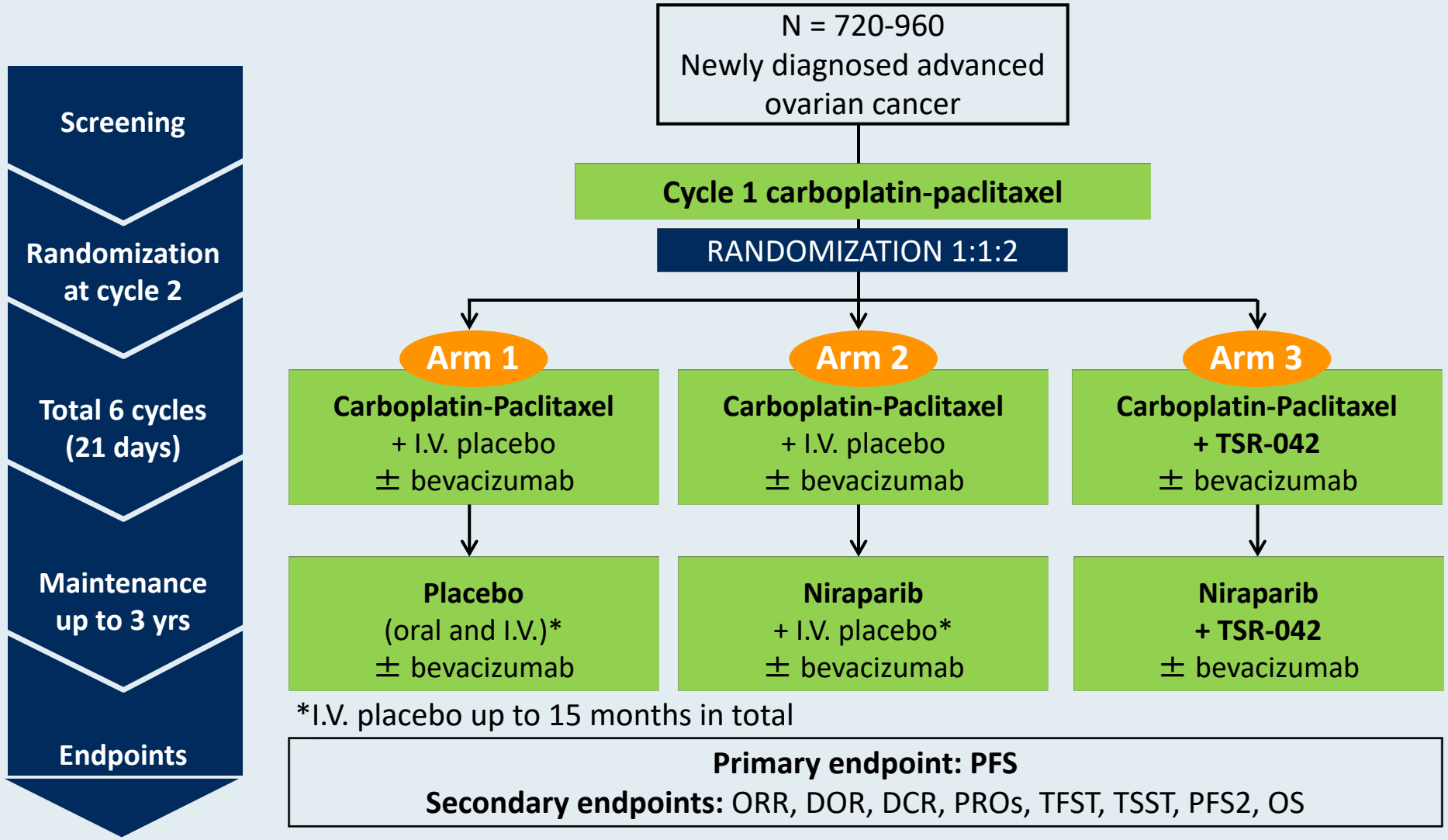


*Olaparib administered for a maximum of 24 months after chemotherapy. Durvalumab and bevacizumab administered for a maximum of 15 months

Harter P et al. ASCO 2019;Abstract TPS5598.

RTP RESEARCH TO PRACTICE

FIRST Phase III Trial of Dostarlimab (TSR-042) for Newly Diagnosed Ovarian Cancer



www.clinicaltrials.gov/ct2/show/NCT03602859

Courtesy of Ursula Matulonis, MD

Current Treatment Paradigm for Recurrent Disease

Ongoing Research with PARP Inhibitors for Newly Diagnosed and Relapsed Disease

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

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

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

Progression-Free Survival with PARP Inhibitors for Recurrent, Platinum-Sensitive Ovarian Cancer

	PARPi	Control	HR
NOVA[1-2] — niraparib			
gBRCA mutation	21.0 mo	5.5 mo	0.27
No gBRCA mutation, HRD+	12.9 mo	3.8 mo	0.38
No gBRCA mutation	9.3 mo	3.9 mo	0.45
SOLO-2[3-4] — olaparib			
gBRCA mutation	19.1 mo	5.5 mo	0.30
Overall survival	51.7 mo	38.8 mo	0.74
ARIEL3[5-6] — 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]Del Campo JM et al. *J Clin Oncol* 2019;37(32):2968-73. [3]Poveda A et al. *Lancet Oncol* 2021;22(5):620-31. [4]Pujade-Lauraine E et al. *Lancet* 2017;18(9):1274-84; [5] Coleman RL et al. *Lancet* 2017;390(10106):1949-61; [6]Ledermann JA et al. *Lancet Oncol* 2020;21(5):710-722.

Lancet Oncol 2022;23(4):465-78.

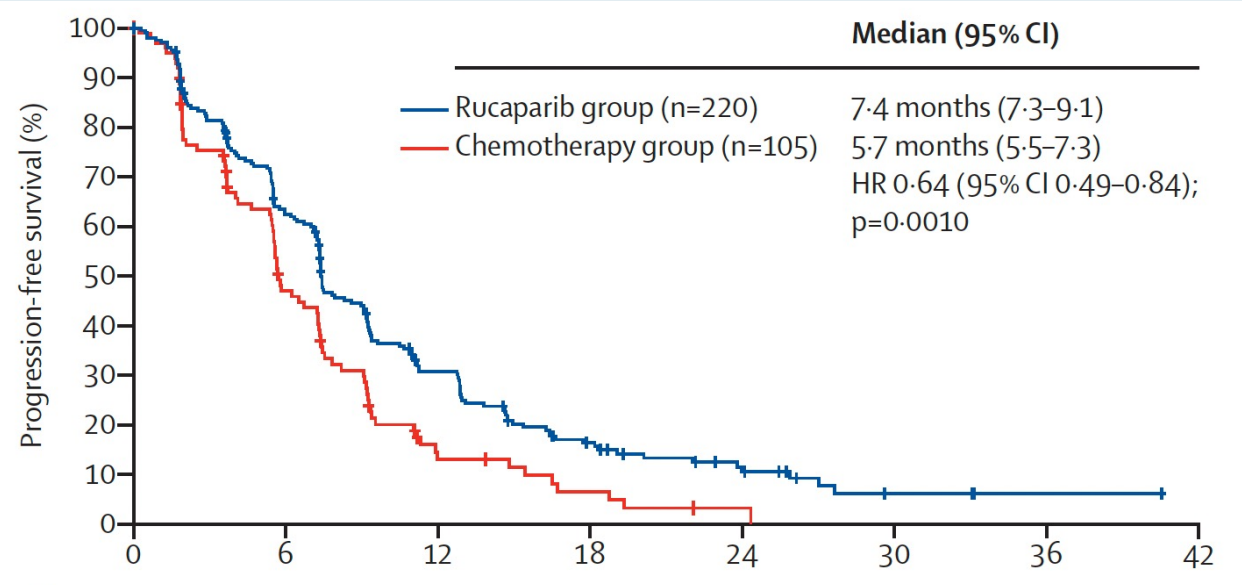
Articles

Rucaparib versus standard-of-care chemotherapy in patients with relapsed ovarian cancer and a deleterious *BRCA1* or *BRCA2* mutation (ARIEL4): an international, open-label, randomised, phase 3 trial

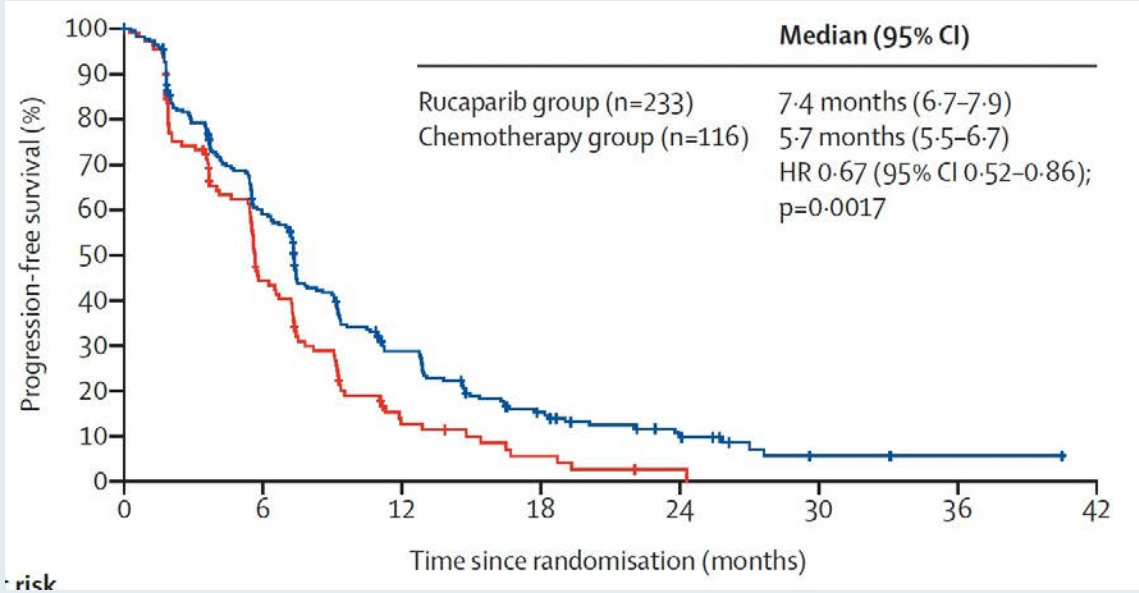
Rebecca Kristeleit, Alla Lisyanskaya, Alexander Fedenko, Mikhail Dvorkin, Andreia Cristina de Melo, Yaroslav Shparyk, Irina Rakhmatullina, Igor Bondarenko, Nicoletta Colombo, Valentyn Svintsitskiy, Luciano Biela, Marina Nechaeva, Domenica Lorusso, Giovanni Scambia, David Cibula, Róbert Póka, Ana Oaknin, Tamar Safra, Beata Mackowiak-Matejczyk, Ling Ma, Daleen Thomas, Kevin K Lin, Karen McLachlan, Sandra Goble, Amit M Oza

ARIEL4: Progression-Free Survival in the Efficacy and ITT Populations

Efficacy population (BRCA1 or BRCA2 mutations with reversion mutations)



Intent to treat population



Kristeleit et al. *Lancet Oncol* 2022;23(4):465-78.

RTP RESEARCH TO PRACTICE

ARIEL4: Overall Response Rate and Duration of Response

Endpoint	Efficacy population			ITT population		
	Rucaparib (n = 220)	Chemotherapy (n = 105)	*p*-value	Rucaparib (n = 233)	Chemotherapy (n = 116)	*p*-value
ORR	40%	32%	0.13	38%	30%	0.13
DoR, median	9.4 mo	7.2 mo	—	9.4 mo	7.2 mo	—

ORR = overall response rate; DoR = duration of response

Kristeleit et al. *Lancet Oncol* 2022;23(4):465-78.

2021 ESMO congress

Abstract LBA33

ENGOT European Network of Gynaecological Oncological Trial groups

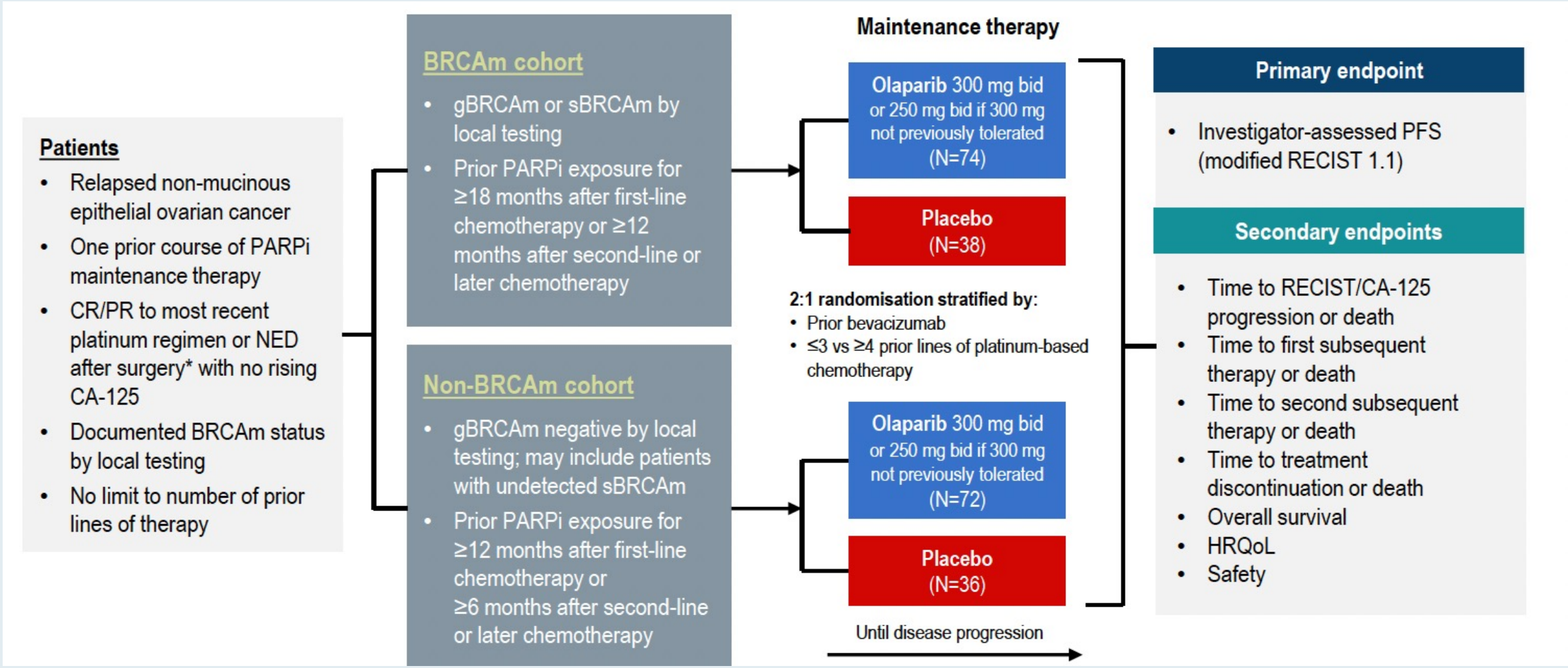
GINECO

Maintenance olaparib rechallenge in patients with ovarian carcinoma previously treated with a PARP inhibitor: Phase IIIb OReO/ENGOT Ov-38 trial

Eric Pujade-Lauraine,[1] Frédéric Selle,[2] Giovanni Scambia,[3] Bernard Asselain,[4] Frederik Marmé,[5] Kristina Lindemann,[6] Nicoletta Colombo,[7] Radoslaw Madry,[8] Rosalind Glasspool,[9] Coraline Dubot,[10] Ana Oaknin,[11] Claudio Zamagni,[12] Florian Heitz,[13] Laurence Gladieff,[14] Maria Jesús Rubio-Pérez,[15] Paolo Scollo,[16] Christopher Blakeley,[17] Bob Shaw,[17] Isabelle Ray-Coquard,[18] Andrés Redondo[19]

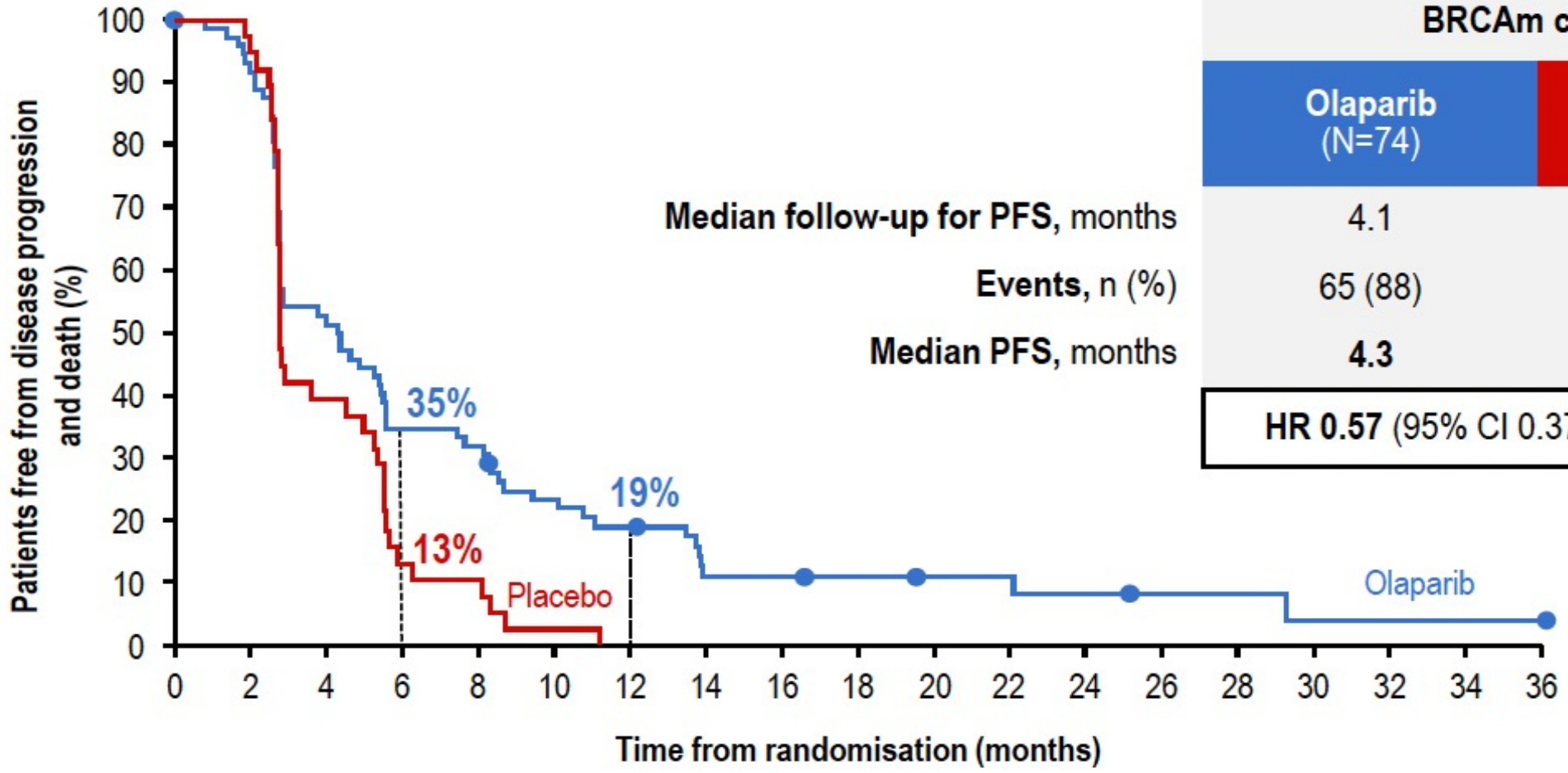
RTP RESEARCH TO PRACTICE

OReO Phase IIIB Study Schema



Pujade-Lauraine E et al. ESMO 2021;Abstract LBA33.

OReO: Progression-Free Survival in the BRCAm Cohort

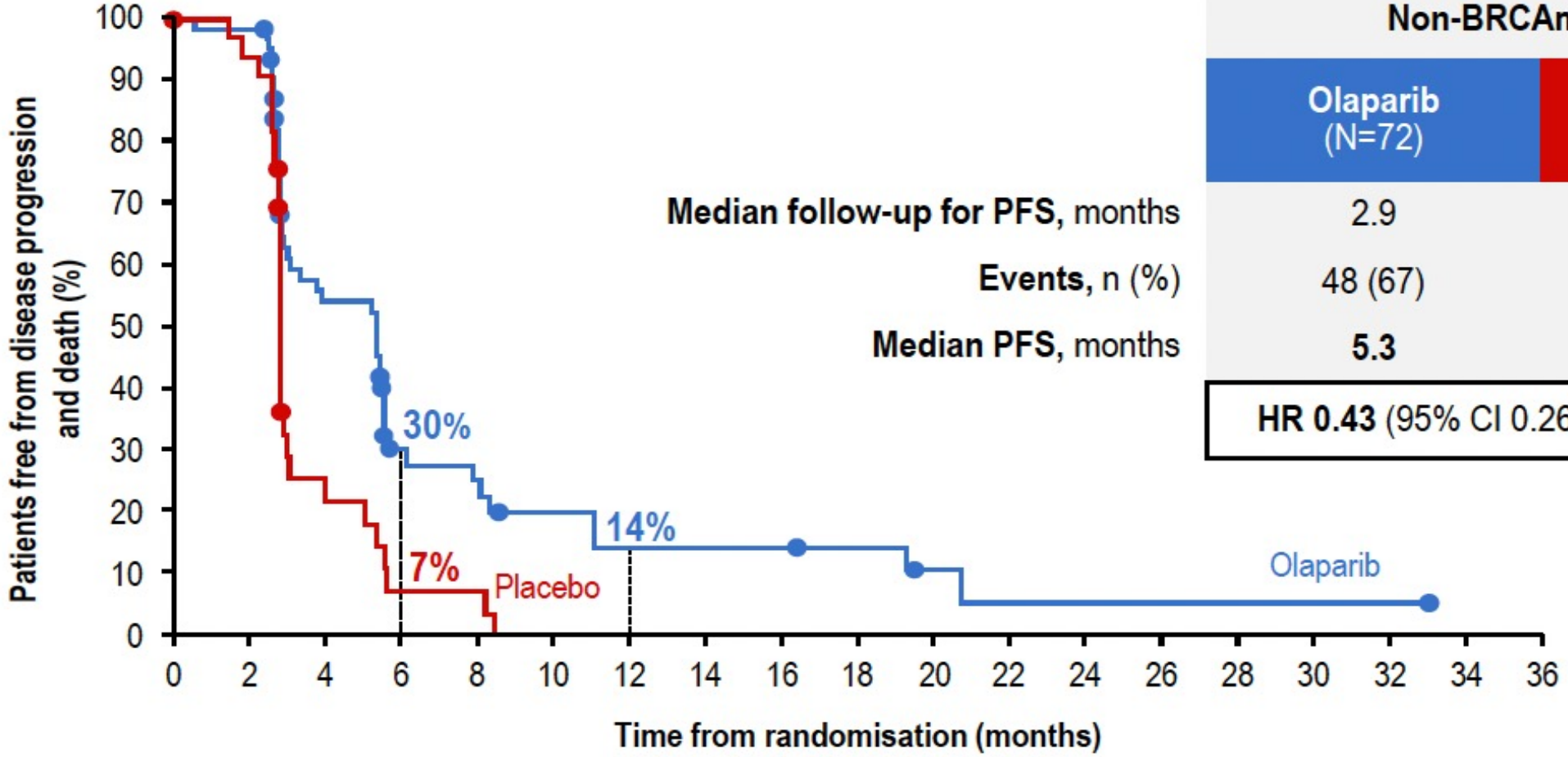


BRCAm cohort	Olaparib (N=74)	Placebo (N=38)
Median follow-up for PFS, months	4.1	2.8
Events, n (%)	65 (88)	38 (100)
Median PFS, months	**4.3**	**2.8**

HR 0.57 (95% CI 0.37–0.87); *P*=0.022

Pujade-Lauraine E et al. ESMO 2021;Abstract LBA33.

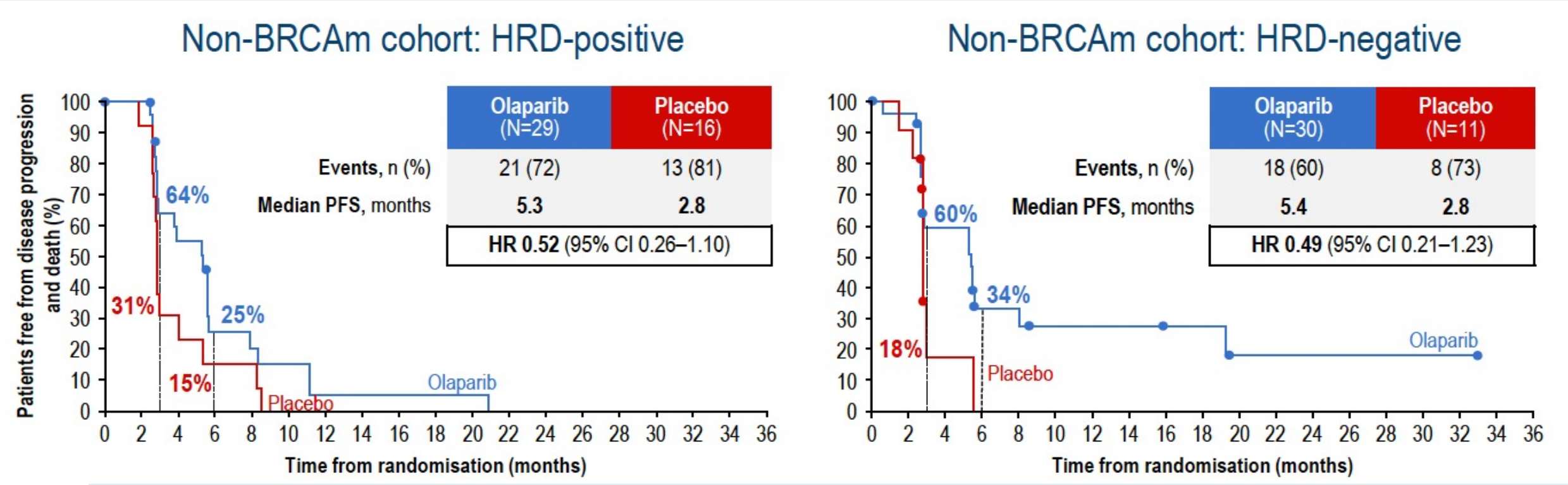
OReO: Progression-Free Survival in the Non-BRCAm Cohort



	Non-BRCAm cohort	
	Olaparib (N=72)	Placebo (N=36)
Median follow-up for PFS, months	2.9	2.8
Events, n (%)	48 (67)	30 (83)
Median PFS, months	**5.3**	**2.8**
HR 0.43 (95% CI 0.26–0.71); *P*=0.0023		

Pujade-Lauraine E et al. ESMO 2021;Abstract LBA33.

OReO: Progression-Free Survival in the Non-BRCAm Cohort by Homologous Recombination Deficiency (HRD) Status



Pujade-Lauraine E et al. ESMO 2021;Abstract LBA33.

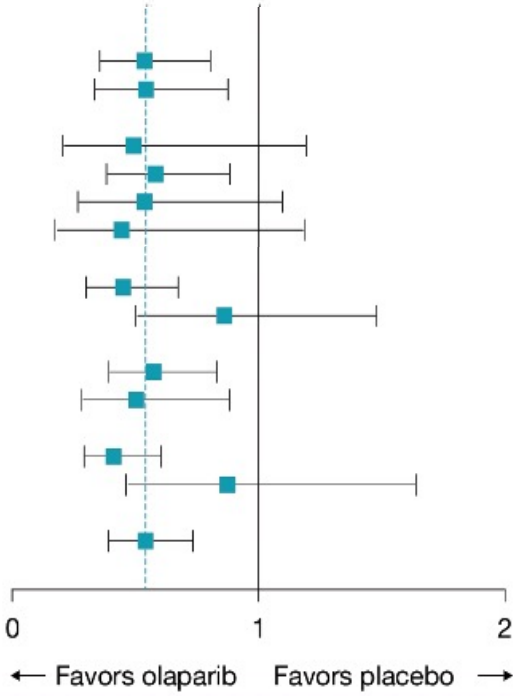
OReO/ENGOT Ov-38 Trial: Impact of Maintenance Olaparib Rechallenge According to Ovarian Cancer Patient Prognosis — An Exploratory Joint Analysis of the BRCA and Non-BRCA Cohorts

Selle F et al.

ASCO 2022;Abstract 5558.

OReO: Post-hoc Analysis of Progression-Free Survival According to Patient Characteristics and Prognostic Factors

Subgroup	Events/N olaparib	Events/N placebo	Hazard ratio (95% CI)	Interaction
Age				0.89
<65	66/84	40/43	0.53 (0.35–0.80)	
≥65	47/62	28/31	0.54 (0.33–0.87)	
Genomic BRCAm and HRD status				0.93
BRCAwt HRD negative	18/31	8/11	0.49 (0.20–1.19)	
BRCAm	65/74	38/38	0.58 (0.38–0.88)	
BRCAwt HRD positive	21/28	13/16	0.53 (0.26–1.09)	
BRCAwt HRD unknown	9/13	9/9	0.44 (0.17–1.18)	
CA-125				0.19
<35	79/104	43/48	0.45 (0.30–0.67)	
≥35	31/39	24/25	0.86 (0.50–1.48)	
ECOG performance status				0.59
0	84/108	44/47	0.57 (0.39–0.83)	
1	29/38	24/27	0.50 (0.28–0.88)	
Visceral site of metastatic disease				0.07
N	71/99	55/60	0.41 (0.29–0.60)	
Y	42/47	13/14	0.87 (0.46–1.64)	
All patients	113/146	68/74	0.54 (0.39–0.73)	



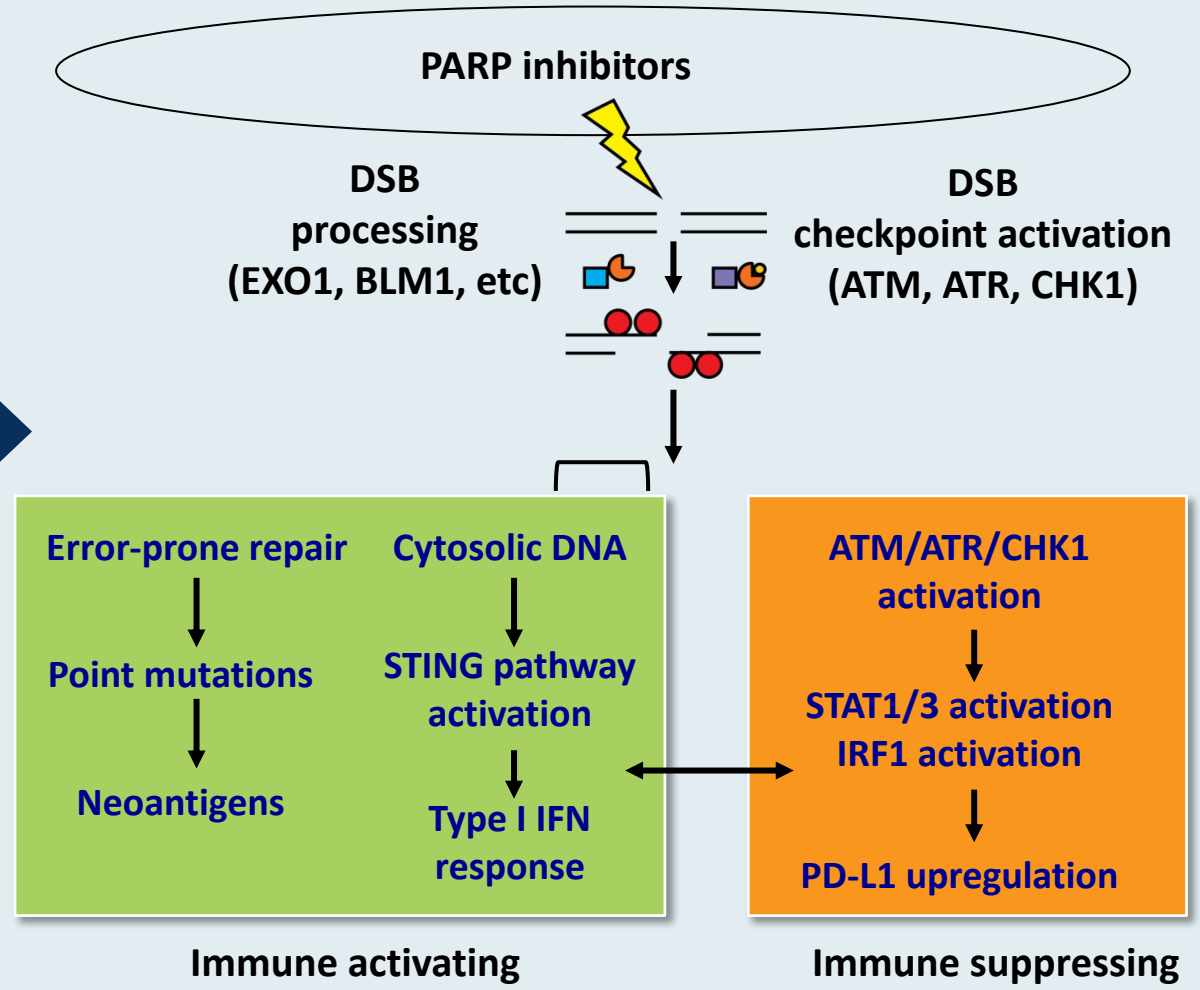
- Olaparib rechallenge was effective regardless of prognostic subgroup
- CA-125 levels and the presence of visceral disease at baseline were the best predictors of patient outcome

Selle F et al. ASCO 2022;Abstract 5558.

RTP RESEARCH TO PRACTICE

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

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

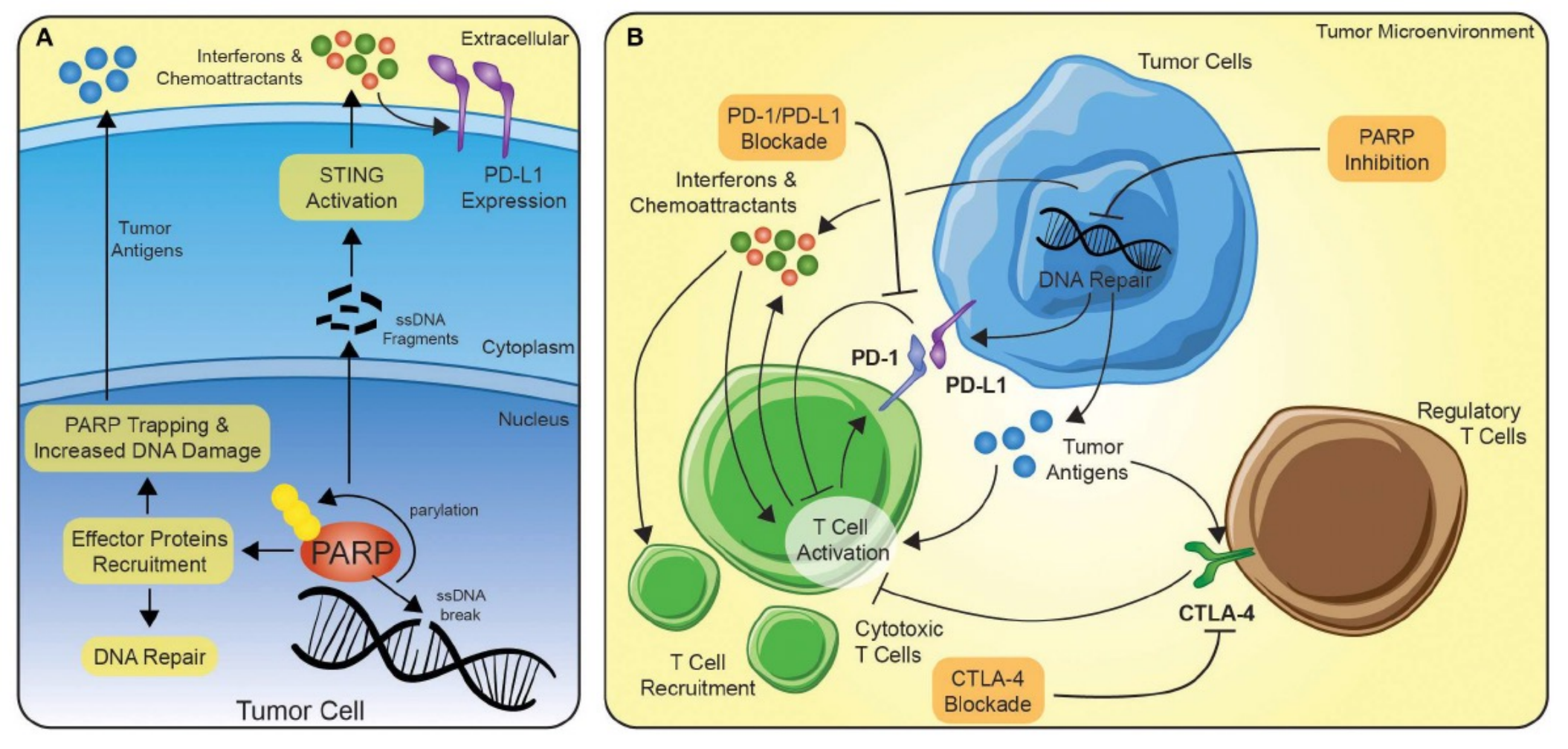


Preclinical data demonstrate synergy with PARPi and anti-PD-1 combinations.

Konstantinopoulos P et al. ASCO 2018;Abstract 106.

RTP RESEARCH TO PRACTICE

Potential Synergy Between PARP Inhibition and Immune Checkpoint Blockade



Vikas P et al. *Front Oncol* 2020;10:570.

Research

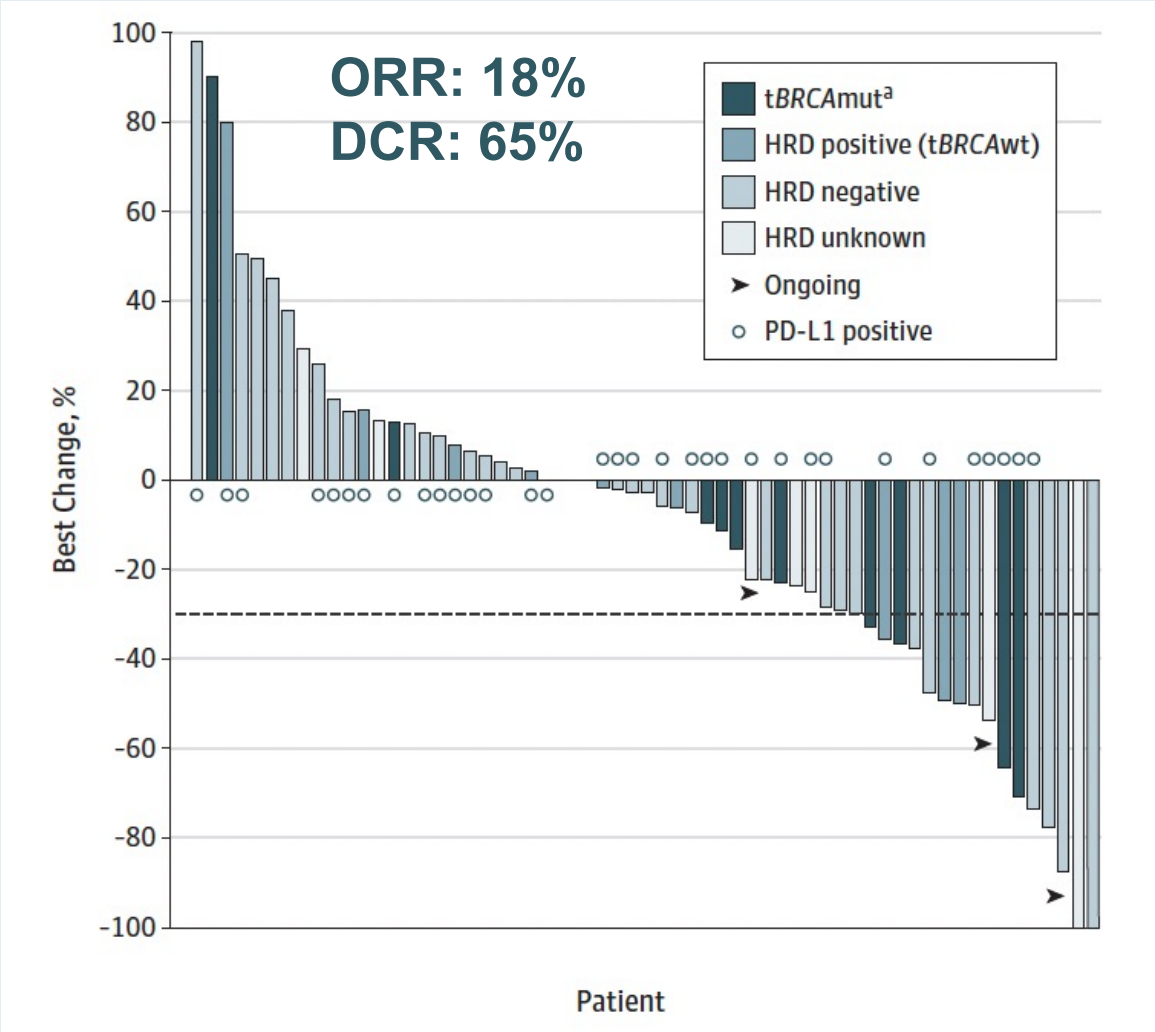
JAMA Oncol 2019;5(8):1141-9.

JAMA Oncology | Original Investigation

Single-Arm Phases 1 and 2 Trial of Niraparib in Combination With Pembrolizumab in Patients With Recurrent Platinum-Resistant Ovarian Carcinoma

Panagiotis A. Konstantinopoulos, MD, PhD; Steven Waggoner, MD; Gregory A. Vidal, MD; Monica Mita, MD; John W. Moroney, MD; Robert Holloway, MD; Linda Van Le, MD; Jasgit C. Sachdev, MD; Eloise Chapman-Davis, MD; Gerardo Colon-Otero, MD; Richard T. Penson, MD; Ursula A. Matulonis, MD; Young Bae Kim, MD; Kathleen N. Moore, MD; Elizabeth M. Swisher, MD; Anniina Färkkilä, MD; Alan D'Andrea, MD; Erica Stringer-Reasor, MD; Jing Wang, PhD; Nathan Buerstatte, MPH; Sujata Arora, MS; Julie R. Graham, PhD; Dmitri Bobilev, MD; Bruce J. Dezube, MD; Pamela Munster, MD

TOPACIO/KEYNOTE-162: Antitumor Activity of Niraparib in Combination with Pembrolizumab



ORR = overall response rate; DCR = disease control rate

Konstantinopoulos PA et al. *JAMA Oncol* 2019;5(8):1141-9.

RTP RESEARCH TO PRACTICE

VIRTUAL 2020 ESMO congress

Abstract 814MO.

Phase II study of olaparib plus durvalumab and bevacizumab (MEDIOLA): initial results in patients with non-germline BRCA-mutated platinum sensitive relapsed ovarian cancer

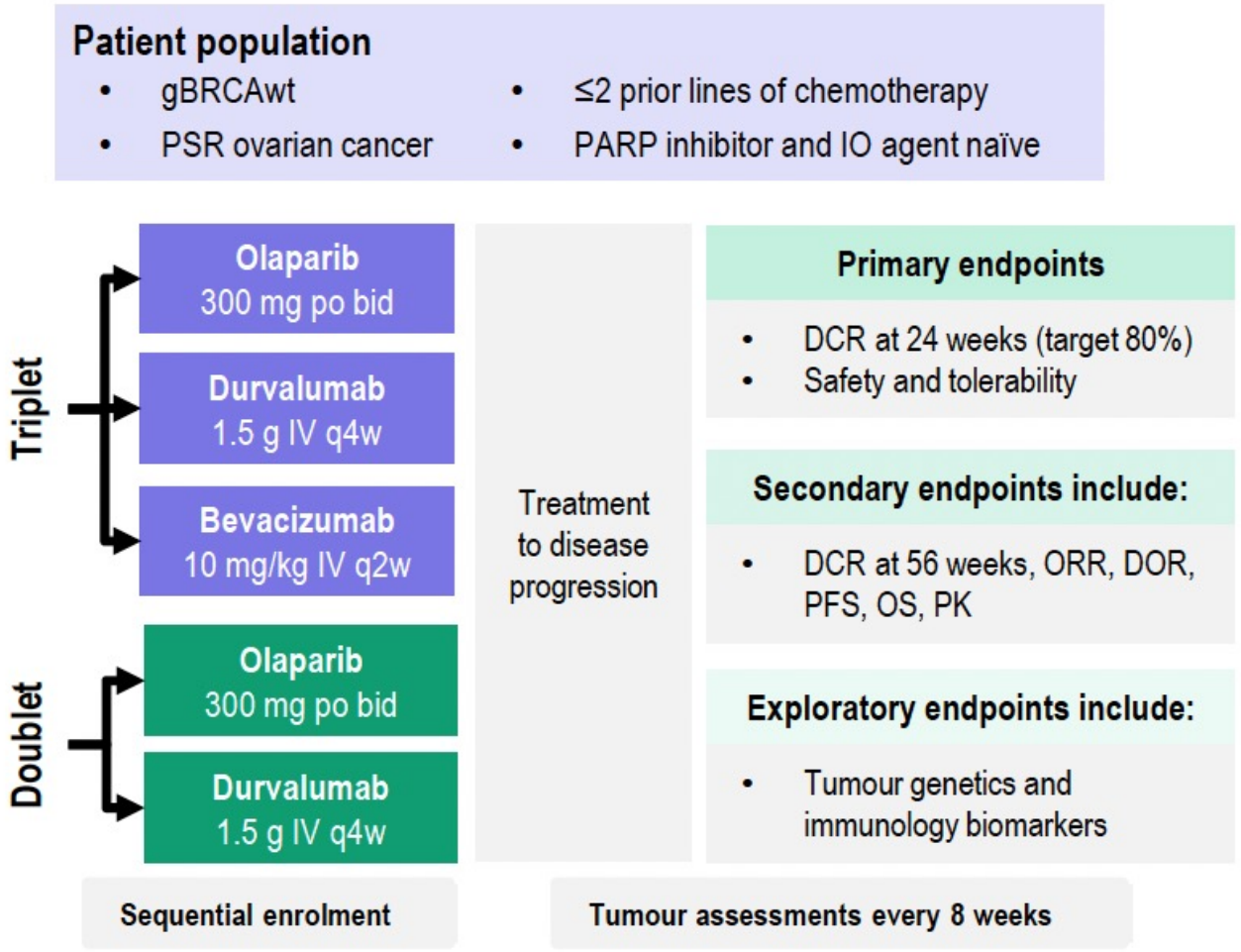
Yvette Drew,[1] Richard Penson,[2] David M O'Malley,[3] Jae-Weon Kim,[4] Stefan Zimmermann,[5] Patricia Roxburgh,[6] Joohyuk Sohn,[7] Salomon M Stemmer,[8] Sara Bastian,[9] Michelle Ferguson,[10] Benoit You,[11] Susan Domchek,[12] Haiyan Gao,[13] Helen K Angell,[13] Kassondra Meyer,[14] Laura Opincar,[14] Lone Ottesen,[13] Susana Banerjee[15]

[1]Northern Centre for Cancer Care, Newcastle upon Tyne Hospitals NHS Foundation Trust, and Newcastle University, Newcastle upon Tyne, UK; [2]Massachusetts General Hospital, Boston, MA, USA; [3]The Ohio State University – James Comprehensive Cancer Center, Columbus, OH, USA; [4]Seoul National University Hospital, Seoul, Republic of Korea; [5]Lausanne University Hospital, University of Lausanne, Lausanne, Switzerland; [6]Beatson West of Scotland Cancer Centre, and Institute of Cancer Sciences, University of Glasgow, Glasgow, UK, [7]Yonsei Cancer Centre, Yonsei University, Sinchon-dong, Republic of Korea; [8]Rabin Medical Center-Beilinson Campus, Petach Tikva and Tel-Aviv University, Tel-Aviv, Israel; [9]Kantonsspital Graubuenden, Chur, Switzerland; [10]NHS Tayside, Dundee, UK; [11]Institut de Cancérologie des Hospices Civils de Lyon, CITOHL, GINECO, Université Claude Bernard Lyon 1, Lyon, France; [12]Basser Center for BRCA University of Pennsylvania, Philadelphia, PA, USA; [13]AstraZeneca, Cambridge, UK; [14]AstraZeneca, Gaithersburg, MD, USA; [15]The Royal Marsden NHS Foundation Trust and Institute of Cancer Research, London, UK

ClinicalTrials.gov identifier: NCT02734004
This study was sponsored by AstraZeneca

RTP RESEARCH TO PRACTICE

MEDIOLA gBRCA Wild Type Study Schema

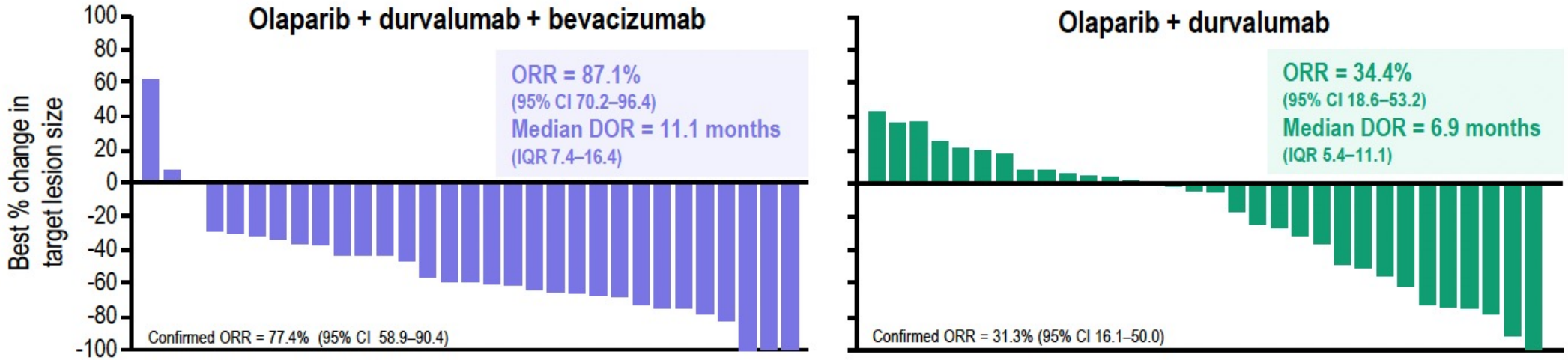


	Olap + durva + bev (N=31)	Olap + durva (N=32)
Median age, years	64.0	68.5
Age group (years), n (%)		
<50	3 (9.7)	4 (12.5)
≥50–<65	14 (45.2)	8 (25.0)
≥65	14 (45.2)	20 (62.5)
Race, n (%)		
White	20 (64.5)	24 (75.0)
Asian	10 (32.3)	3 (9.4)
Other	1 (3.2)	5 (15.6)
Platinum sensitivity, n (%)		
>6–12 months	18 (58.1)	14 (43.8)
>12 months	13 (41.9)	18 (56.3)
Number of prior lines of chemotherapy, n (%)		
1 prior line	20 (64.5)	23 (71.9)
2 prior lines	11 (35.5)	9 (28.1)
Enrolment completed	January 2019	February 2019
Patients on study treatment at DCO, n (%) (13 February 2020)		
Olap; durva; bev	13 (41.9); 13 (41.9); 12 (38.7)	7 (21.9); 6 (18.8); NA

Drew Y et al. ESMO 2020;Abstract 814MO.

RTP RESEARCH TO PRACTICE

MEDIOLA gBRCA Wild Type: Antitumor Activity



Genomic instability status* subgroup	Olaparib + durvalumab + bevacizumab		Olaparib + durvalumab	
	ORR (95% CI), %	n/N patients	ORR (95% CI), %	n/N patients
GIS-positive	100.0 (69.2–100.0)	10/10	50.0 (18.7–81.3)	5/10
GIS-negative	75.0 (34.9–96.8)	6/8	16.7 (0.4–64.1)	1/6
GIS-unknown	84.6 (54.6–98.1)	11/13	31.3 (11.0–58.7)	5/16

*GIS, as determined by Foundation Medicine tumour analysis; must have genome-wide LOH ≥14, a somatic *BRCA1* and/or *BRCA2* mutation, or a mutation in *ATM*, *BRIP1*, *PALB2*, *RAD51C*, *BARD1*, *CDK12*, *CHEK1*, *CHEK2*, *FANCL*, *PPP2R2A*, *RAD51B*, *RAD51D* or *RAD54L* to be considered positive. At the time of the DCO, the prespecified cut-off for genome-wide LOH of 14% was used[1]; GIS, genomic instability status; IQR, interquartile range; LOH, loss of heterozygosity. [1]Swisher *et al. Lancet Oncol* 2017;18:75–87

Drew Y et al. ESMO 2020;Abstract 814MO.

RTP RESEARCH TO PRACTICE

BARCELONA 2019 ESMO congress

Poster board number: 1190PD

Phase II study of olaparib + durvalumab (MEDIOLA): Updated results in the germline BRCA-mutated platinum-sensitive relapsed ovarian cancer cohort

Yvette Drew,[1] Bella Kaufman,[2] Susana Banerjee,[3] Alain Lortholary,[4] Sook Hee Hong,[5] Yeon Hee Park,[6] Stefan Zimmermann,[7] Patricia Roxburgh,[8] Michelle Ferguson,[9] Ricardo H Alvarez,[10] Susan Domchek,[11] Christopher Gresty,[12] Helen K Angell,[12] Vidalba Rocher Ros,[13] Kassondra Meyer,[13] Mark Lanasa,[13] Pia Herbolsheimer,[13] Maja de Jonge[14]

[1]Northern Centre for Cancer Care, Newcastle upon Tyne Hospitals NHS Foundation Trust Newcastle upon Tyne, UK; [2]Chaim Sheba Medical Center, Tel Hashomer, Israel; [3]The Royal Marsden Hospital, London, UK; [4]Centre Catherine de Sienne, Nantes, France; [5]Seoul St Mary's Hospital, Catholic University of Korea, Seoul, South Korea; [6]Samsung Medical Center, Seoul, Republic of Korea; [7]Lausanne University Hospital, University of Lausanne, Lausanne, Switzerland; [8]University of Glasgow and Beatson West of Scotland Cancer Centre, Glasgow, UK; [9]NHS Tayside, Dundee, UK; [10]Cancer Treatment Centers of America-Atlanta and Augusta University, Augusta, GA, USA; [11]Basser Center for BRCA University of Pennsylvania, Philadelphia, PA, USA; [12]AstraZeneca, Cambridge, UK; [13]AstraZeneca, Gaithersburg, MD, USA and [14]Erasmus MC Daniel den Hoed Cancer Center, Rotterdam, Netherlands

esmo.org

MEDIOLA mBRCA Cohort Study Schema

- MEDIOLA is a multi-cohort, Phase I/II study
- The design of the BRCAm ovarian cohort is presented below; other ovarian cancer cohorts are ongoing

N=34*

- Platinum-sensitive relapsed ovarian cancer†
- Germline mutation in *BRCA1* or *BRCA2*
- ≥1 previous platinum-based therapy
- PARP inhibitor and immunotherapy naïve

Olaparib monotherapy 300 mg bid PO for 4 weeks

then

Olaparib 300 mg bid PO plus **durvalumab** IV 1.5 g every 4 weeks

Treatment until disease progression or intolerable toxicity

Primary endpoints

- Disease control rate at 12 weeks
- Safety and tolerability

Secondary endpoints

- Disease control rate at 28 weeks
- Objective response rate
- Duration of response
- Progression-free survival
- Overall survival
- PD-L1 expression in tumour samples

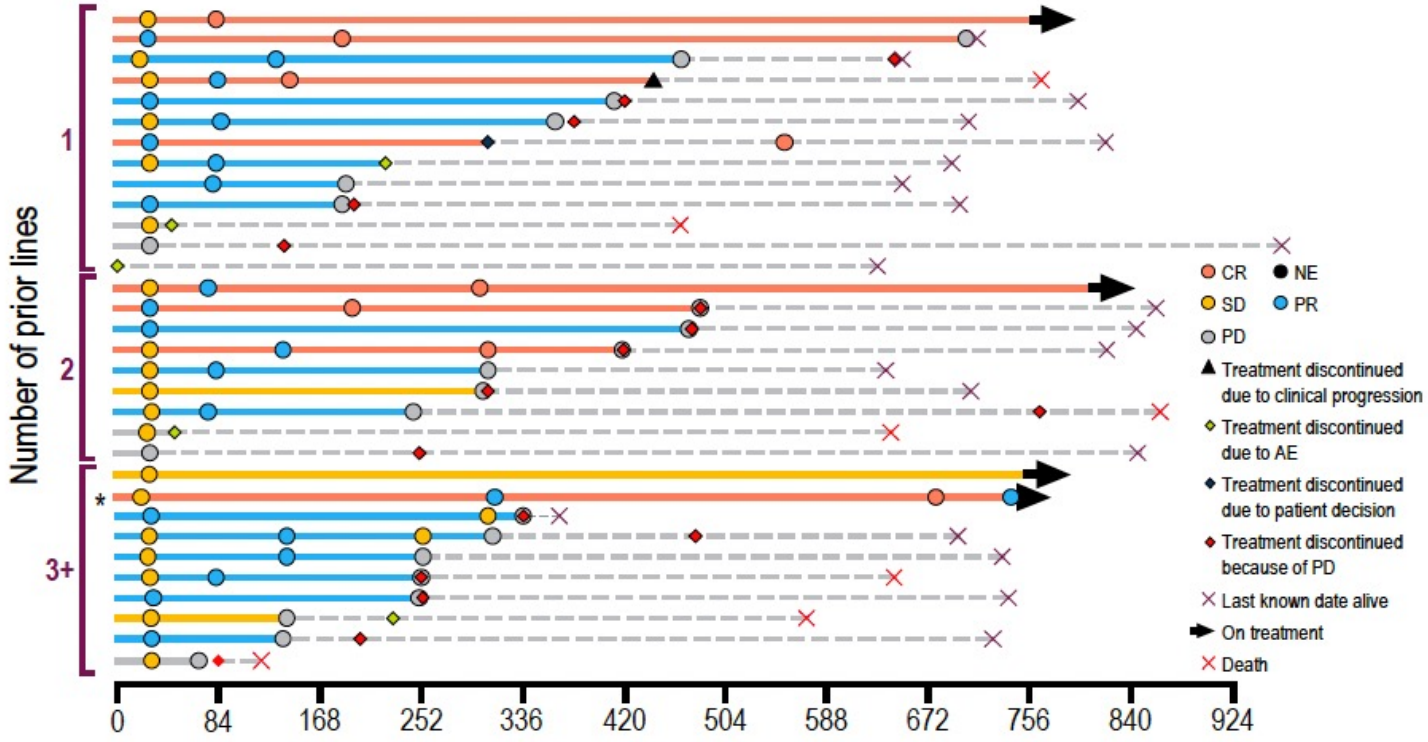
Drew Y et al. ESMO 2019;Abstract 1190PD.

MEDIOLA mBRCA Cohort: Efficacy

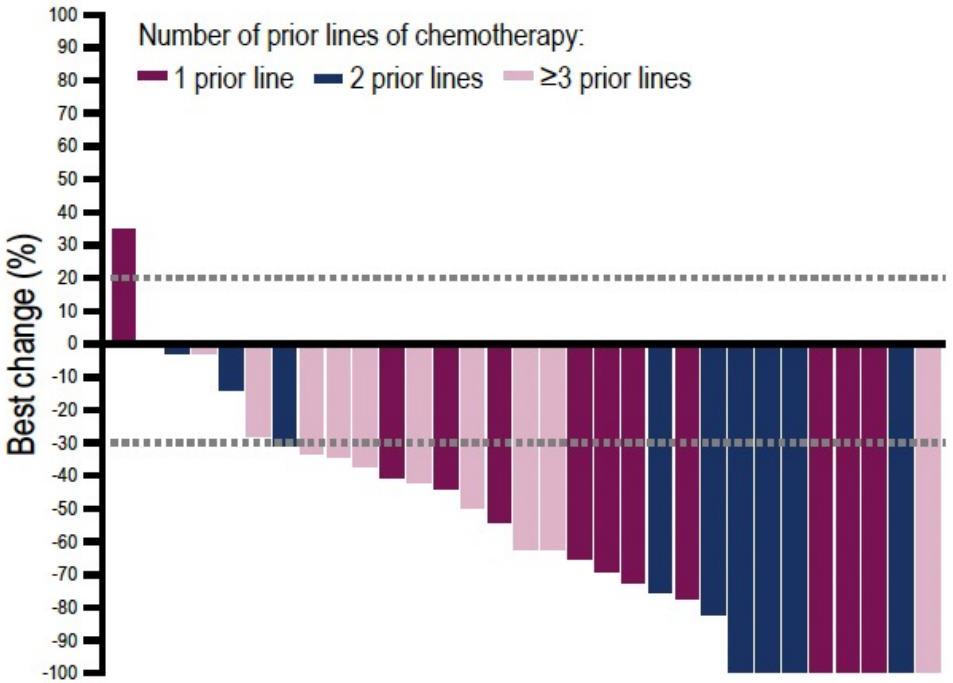
- DCR at 12 weeks: 81.3% (90% CI 66.3, 91.5)
- DCR at 28 weeks: 65.6% (90% CI 49.6, 79.4)
- Unconfirmed ORR: 71.9% (95% CI 53.3, 86.3)
- mPFS: 11.1 months (95% CI 8.2, 15.6)

Greater clinical activity was seen in earlier- versus later-line patients

Time to progression or treatment discontinuation



Best percentage change in target lesion size†



Drew Y et al. ESMO 2019;Abstract 1190PD.

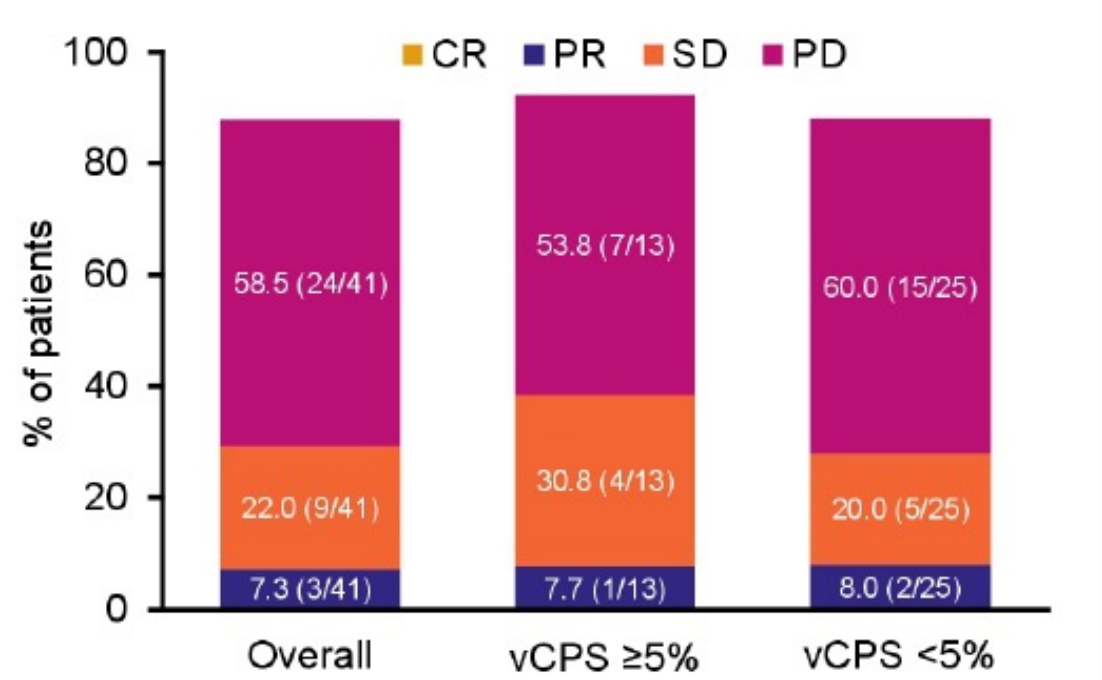
RTP RESEARCH TO PRACTICE

MOONSTONE/GOG-3032: Interim Analysis of a Phase 2 Study of Niraparib + Dostarlimab in Patients (pts) with Platinum-Resistant Ovarian Cancer (PROC)

Randall LM et al.

ASCO 2022;Abstract 5573.

MOONSTONE: Efficacy Summary of Niraparib with Dostarlimab for Platinum-Resistant Ovarian Cancer



Efficacy, n (%) [95% CI]*	Overall N=41	PD-L1 status	
		vCPS ≥5% n=13	vCPS <5% n=25
ORR (CR + PR)	3 (7.3) [1.5–19.9]	1 (7.7) [0.2–36.0]	2 (8.0) [1.0–26.0]
DCR (CR + PR + SD)	12 (29.3) [16.1–45.5]	5 (38.5) [13.9–68.4]	7 (28.0) [12.1–49.4]
Median PFS, months (95% CI)	2.1 (2.0–2.2)	2.2 (1.6–not evaluable)	2.1 (1.8–2.2)

Randall LM et al. ASCO 2022;Abstract 5573.

MOONSTONE: Select Treatment-Related Adverse Events in >10% of Patients

Adverse event n (%)	Related to either niraparib or dostarlimab	Related to niraparib	Related to dostarlimab
Nausea	23 (56.1)	21 (51.2)	11 (26.8)
Fatigue	14 (34.1)	13 (31.7)	13 (31.7)
Vomiting	13 (31.7)	13 (31.7)	7 (17.1)
Anemia	13 (31.7)	13 (31.7)	7 (17.1)
Platelet count decreased	11 (26.8)	11 (26.8)	0 (0)
Thrombocytopenia	8 (19.5)	8 (19.5)	0 (0)

Randall LM et al. ASCO 2022;Abstract 5573.

An Open-Label Phase 2 Study of Dostarlimab, Bevacizumab, and Niraparib Combination in Patients with Platinum-Resistant Ovarian Cancer: Cohort A of the OPAL Trial

Joyce F. Liu,[1] Stéphanie Gaillard,[2] Andrea E. Wahner Hendrickson,[3] John W. Moroney,[4] Oladapo Yeku,[5] Elisabeth Diver,[6] Camille Gunderson,[7] Rebecca Arend,[8] Elena Ratner,[9] Vivek Samnotra,[10] Divya Gupta,[10] Lena Evilevitch,[10] Zebin Wang,[10] Ping Wang,[10] Joseph Tang,[10] Emeline Bacqué,[10] Xiaohong Liu,[10] Gottfried E. Konecny[11]

Poster #23

[1]Dana-Farber Cancer Institute, Boston, MA, USA; [2]Sidney Kimmel Comprehensive Cancer Center at Johns Hopkins, Baltimore, MD, USA; [3]Mayo Clinic Rochester, Rochester, NY, USA; [4]University of Chicago Medicine Comprehensive Cancer Center, Chicago, IL, USA; [5]Massachusetts General Cancer Center, Boston, MA, USA; [6]Stanford Women's Cancer Center, Palo Alto, CA, USA; [7]University of Oklahoma Stephenson Cancer Center, Oklahoma City, OK, USA; [8]The University of Alabama at Birmingham, UAB Comprehensive Cancer Center, Birmingham, AL, USA; [9]Yale University, New Haven, CT, USA; [10]GlaxoSmithKline, Waltham, MA, USA; [11]Ronald Reagan UCLA Medical Center, Los Angeles, CA, USA.

SGO 2021 VIRTUAL ANNUAL MEETING ON WOMEN'S CANCER®

Abstract 10415

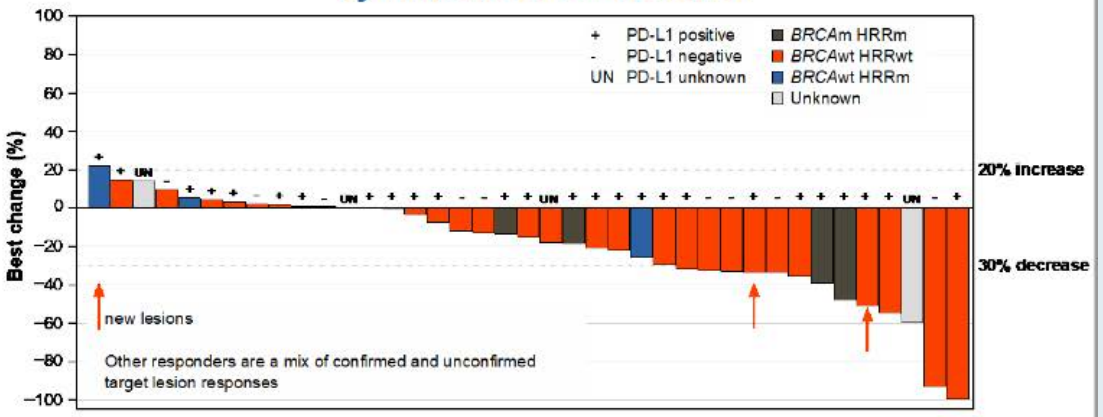
SGO Society of Gynecologic Oncology

Antitumor Activity

- Antitumor activity was assessed in the response-evaluable population (n=39)
  - 2 patients in the safety population did not have a postbaseline scan and were excluded from the response-evaluable population
- Response data required that patients with a best response of complete response or partial response had a confirmation scan ≥4 weeks after the first scan in which a response was observed

Antitumor Activity per RECIST v1.1	
Variable, n (%)	**Response-evaluable population (n=39)**
Complete response	0
Partial response	7 (17.9)
Stable disease	23 (59.0)
Progressive disease	8 (20.5)
Inconclusive	1 (2.6)
ORR (90% CI), %	17.9 (8.7–31.1)
DCR (90% CI), %	76.9 (63.2–87.4)

Best Percent Change from Baseline Sum of Target Lesions by HRR and PD-L1 Status



*BRCA*m, *BRCA* mutation; *BRCA*wt, *BRCA* wild type; HRRm, homologous recombination repair mutation; HRRwt, homologous recombination repair wild type; PD-L1, programmed death ligand 1.

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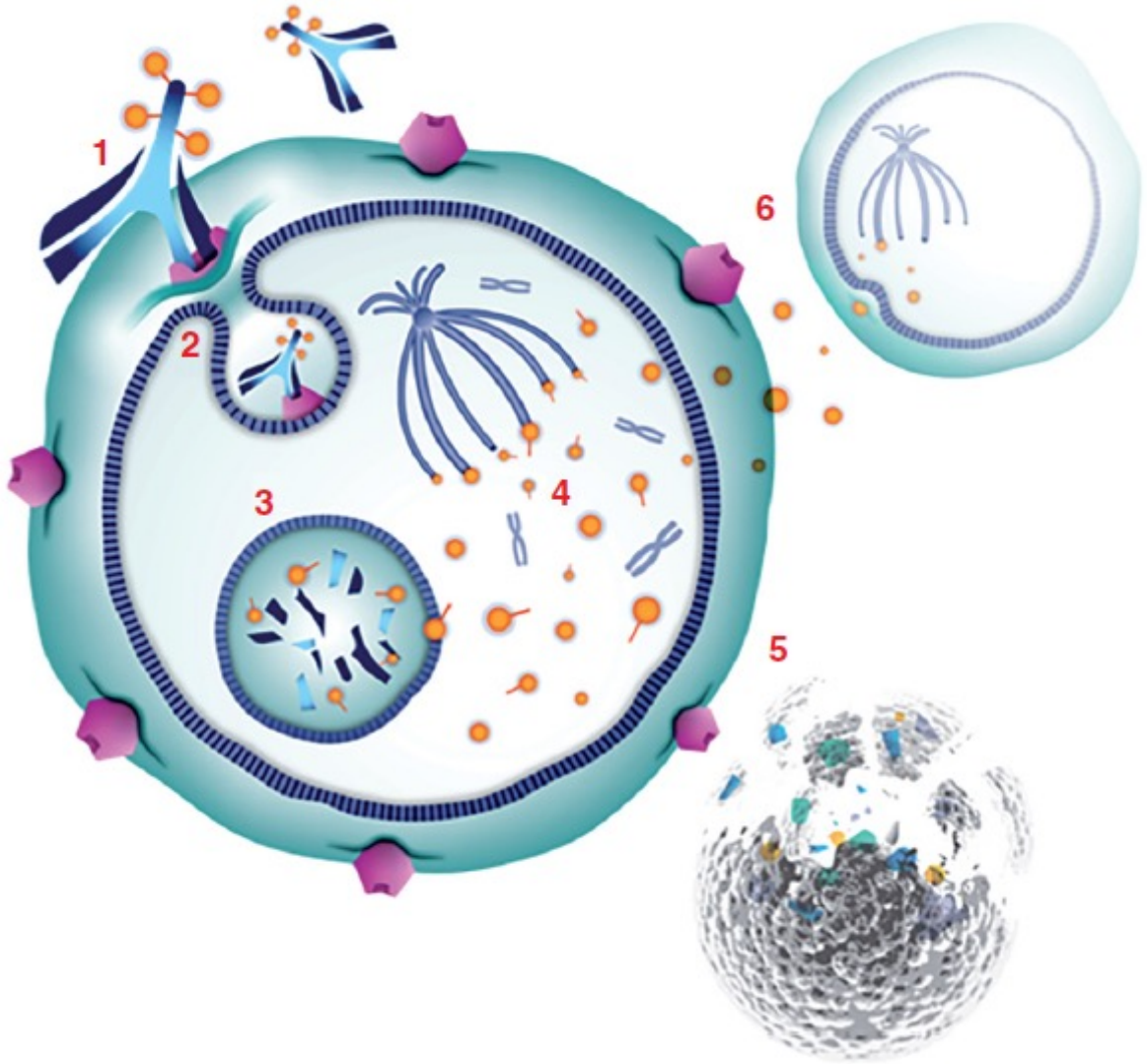
Liu JF et al. SGO 2021;Abstract 10415.

RTP RESEARCH TO PRACTICE

Novel Investigational Agents and Strategies

Mirvetuximab Soravtansine: Mechanism of Action



(1) Mirvetuximab soravtansine binds with high affinity to FRα expressed on the tumor cell surface

(2) The antibody-drug conjugate (ADC)/receptor complex becomes internalized via antigen-mediated endocytosis

(3) Lysosomal processing releases active DM4 catabolites from the ADC molecule

(4) These maytansinoid derivatives inhibit tubulin polymerization and microtubule assembly

(5) The potent antimitotic effects result in cell-cycle arrest and apoptosis

(6) Active metabolites can also diffuse into neighboring cells and induce further cell death — in other words, bystander killing

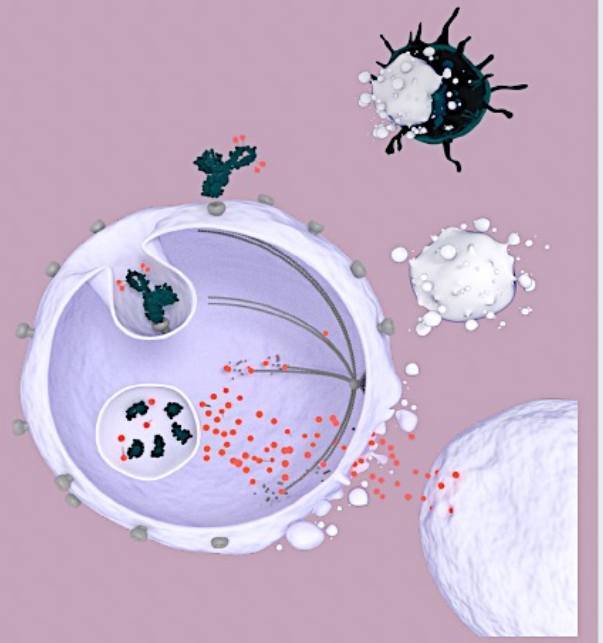
Moore K et al. *Future Oncol* 2018:14(2);123-36.

RTP RESEARCH TO PRACTICE

Efficacy and Safety of Mirvetuximab Soravtansine in Patients With Platinum-Resistant Ovarian Cancer With High Folate Receptor Alpha Expression: Results From the SORAYA Study

Ursula A. Matulonis,[1] Domenica Lorusso,[2] Ana Oaknin,[3] Sandro Pignata,[4] Hannelore Denys,[5] Nicoletta Colombo,[6] Toon Van Gorp,[7] Jason A. Konner,[8] Margarita Romeo Marin,[9] Philipp Harter,[10] Conleth G. Murphy,[11] Jiuzhou Wang,[12] Elizabeth Noble,[12] Brooke Esteves,[12] Michael Method,[12] Robert L. Coleman[13]

[1]Dana-Farber Cancer Institute, Boston, MA, USA; [2]Fondazione Policlinico Universitario A. Gemelli, IRCCS and Catholic University of Sacred Heart, Rome, Italy; [3]Gynaecologic Cancer Programme, Vall d'Hebron Institute of Oncology (VHIO), Hospital Universitari Vall d'Hebron, Vall d'Hebron Barcelona Hospital Campus, Barcelona, Spain; [4]Istituto Nazionale Tumori di Napoli Fondazione G Pascale IRCCS, Naples, Italy; [5]Ghent University Hospital, Ghent, Belgium; [6]European Institute of Oncology IRCCS, Milan, Italy and University of Milan-Bicocca, Milan, Italy; [7]University Hospital Leuven, Leuven Cancer Institute, Leuven, Belgium; [8]Memorial Sloan Kettering Cancer Center, New York, NY, USA; [9]Institut Català d'Oncologia, Badalona, Spain; [10]Ev. Kliniken Essen-Mitte, Essen, Germany; [11]Bon Secours Hospital and Cancer Trials, Cork, Ireland; [12]ImmunoGen, Inc., Waltham, MA, USA; [13]US Oncology Research, Texas Oncology, The Woodlands, TX, USA



SORAYA

ANNUAL MEETING ON WOMENS' CANCER®
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SGO // PHOENIX, ARIZONA // MARCH 18 - 21, 2022

SGO 2022;Abstract LBA4.

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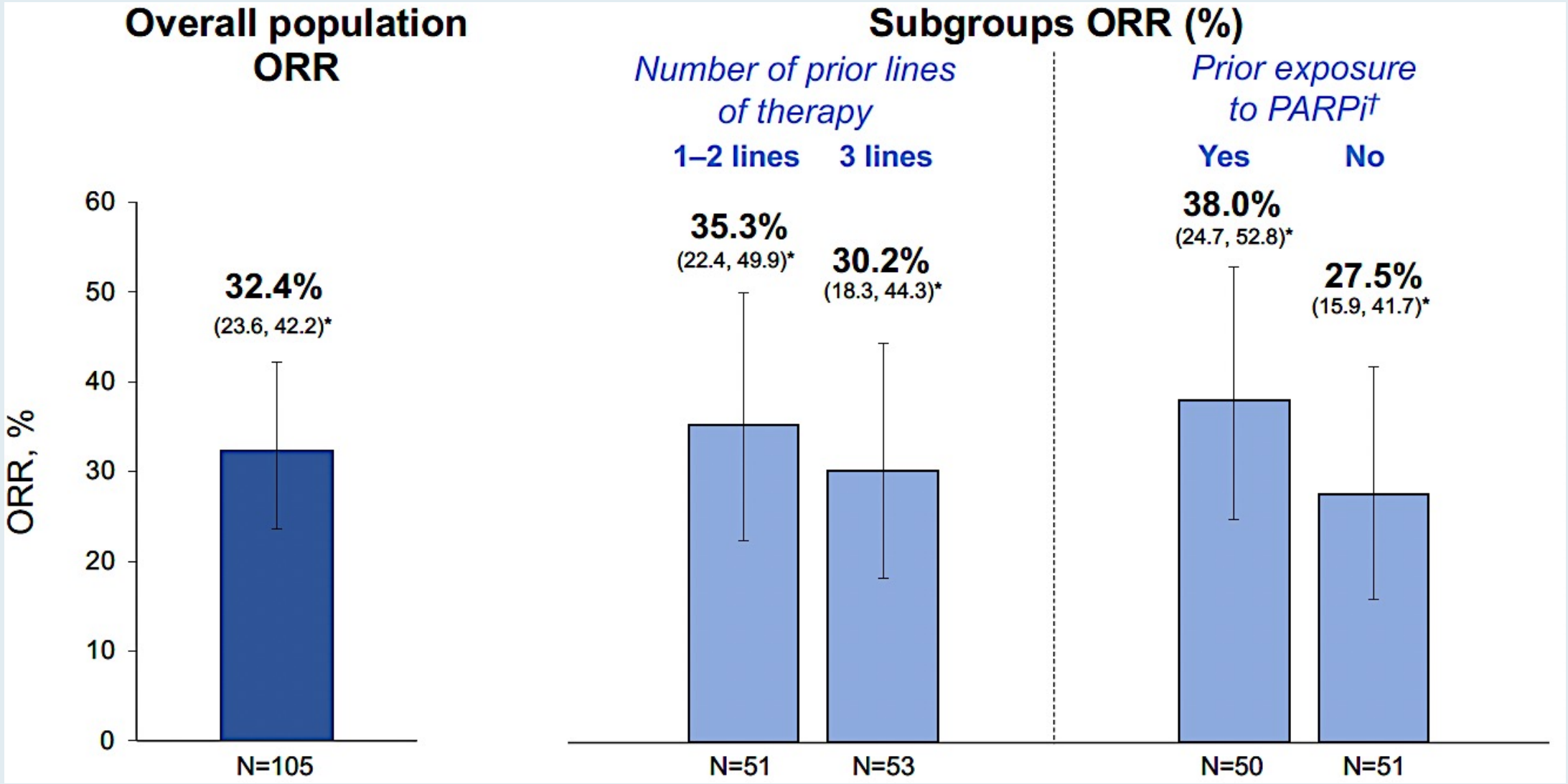
SORAYA: Investigator-Assessed Objective Response Rate by Prior Therapy



Matulonis UA et al. SGO 2022;Abstract LBA4.

RTP RESEARCH TO PRACTICE

SORAYA: Treatment-Related Adverse Events (≥10%)

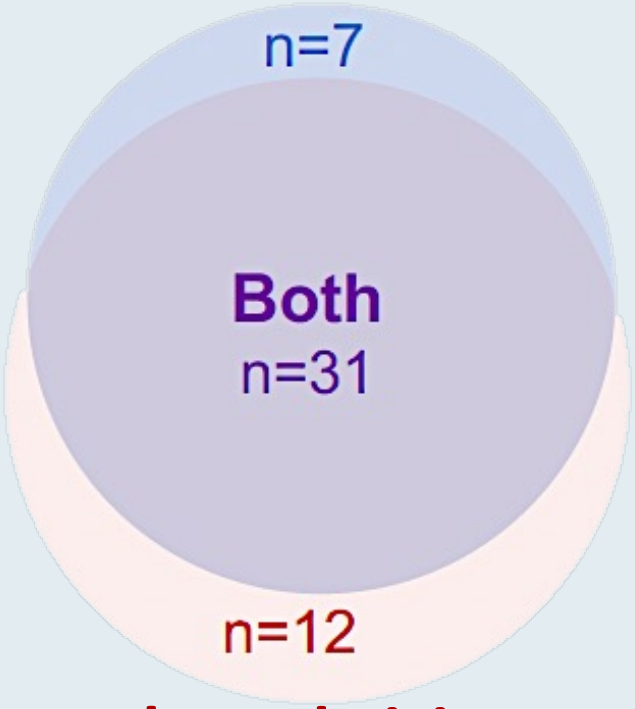
TRAEs, n (%)	All Grades	Grade 3	Grade 4
Patients with any event	91 (86)	29 (27)	1 (1)
Blurred vision	43 (41)	6 (6)	0 (0)
Keratopathy*†	38 (36)	8 (8)	1 (1)
Nausea	31 (29)	0 (0)	0 (0)
Dry eye	24 (23)	2 (2)	0 (0)
Fatigue	24 (23)	1 (1)	0 (0)
Diarrhea	23 (22)	2 (2)	0 (0)
Asthenia	16 (15)	1 (1)	0 (0)
Photophobia	15 (14)	0 (0)	0 (0)
Peripheral neuropathy	13 (12)	0 (0)	0 (0)
Decreased appetite	13 (12)	1 (1)	0 (0)
Vomiting	12 (11)	0 (0)	0 (0)
Neutropenia	11 (10)	1 (1)	0 (0)

- Most adverse events (AEs) were low-grade, reversible ocular and GI events
- Serious Grade ≥3 treatment-related AEs (TRAEs) were reported in 8% of patients
- TRAEs led to dose delay in 32% and dose reduction in 19%
- 7 patients (7%) discontinued treatment due to TRAEs
- 1 death was recorded as possibly related to study drug
  - Respiratory failure
  - Autopsy: No evidence of drug reaction; lung metastases

Matulonis UA et al. SGO 2022;Abstract LBA4.

Unique Events Associated with Mirvetuximab Soravtansine: Keratopathy and Blurred Vision

Events developed in 50/106 (47%) patients: mostly low grade



Proactive supportive care
– Lubricating artificial tears
– Corticosteroid eye drops

Predictable
– Median time to onset: cycle 2 (~1.5 months)

Manageable with dose modifications, if needed
– 22% of patients (23/106) had dose delay and/or reduction

Reversible
– At data cutoff: >80% of Grade 2-3 events had resolved to Grade 0-1
  – 9 patients still receiving mirvetuximab soravtansine or being followed up for resolution

<1% discontinuation due to ocular events
– 1 of 106 patients discontinued due to Grade 4 keratopathy, which resolved within 15 days

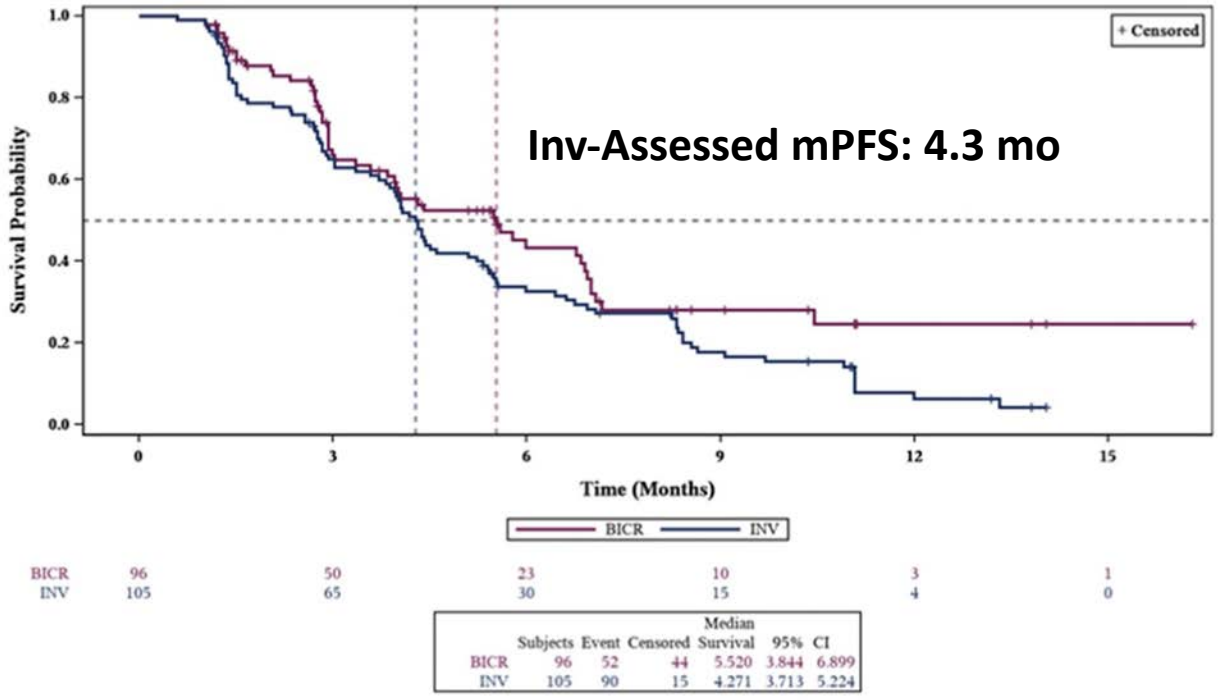
Matulonis UA et al. SGO 2022;Abstract LBA4.

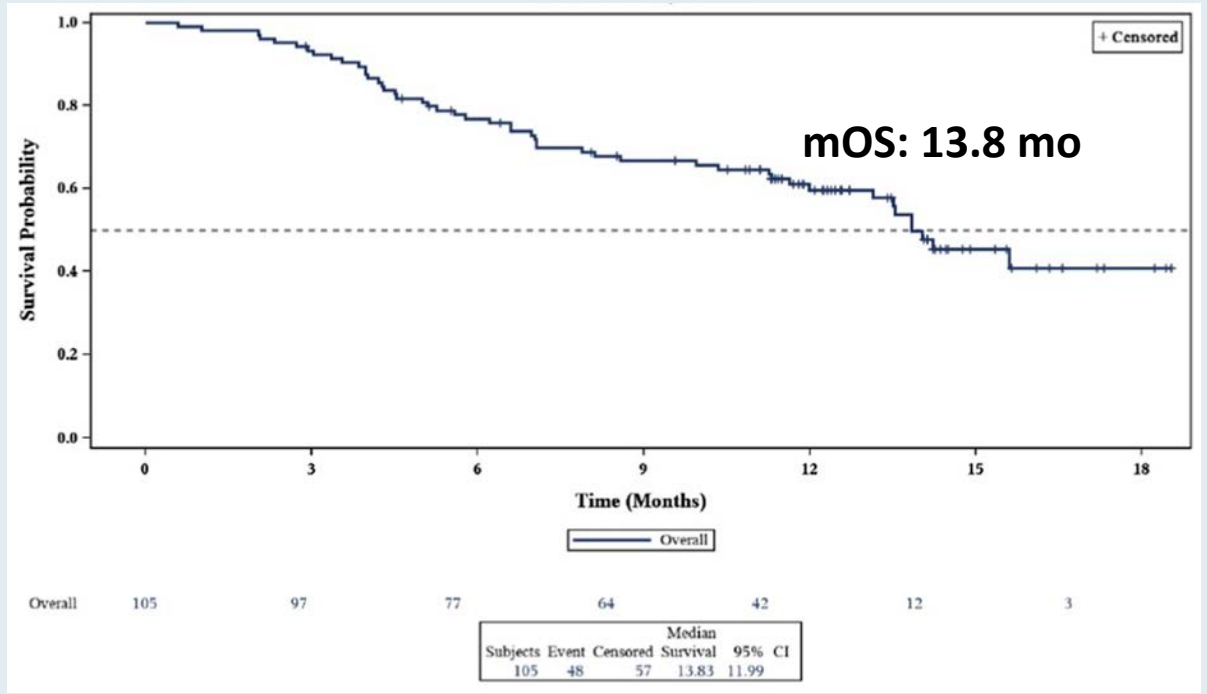
Mirvetuximab Soravtansine (MIRV) in Patients with Platinum-Resistant Ovarian Cancer with High Folate Receptor Alpha (FRα) Expression: Characterization of Antitumor Activity in the SORAYA Study

Matulonis UA et al.

ASCO 2022;Abstract 5512.

SORAYA: Overall Response Rate in the BRCA Mutation-Positive Subgroup





Matulonis UA et al. ASCO 2022;Abstract 5512.

RTP RESEARCH TO PRACTICE

SORAYA: Overall Response Rate in the BRCA Mutation-Positive Subgroups

	BRCAmt with prior PARPi (n=16)	*BRCAmt* without prior PARPi (n=4)
Responders, n	6	3
ORR	38%	75%

Matulonis UA et al. ASCO 2022;Abstract 5512.

MIRASOL Phase III Study Schema

MIRASOL

Enrollment and Key Eligibility

- Platinum-resistant disease (PFI ≤ 6 mo)
  - 1° platinum refractory disease excluded (primary PFI < 3 mo)
- Prior bevacizumab and PARPi allowed
- 1-3 prior lines of therapy
- Patients with BRCA mutations allowed
- FRα-high by PS2+ scoring (≥75% PS2+)

Statistical Assumptions

- 430 patients/ 330 events for PFS by INV
- α=0.05 (two-sided)
- Power=90%; HR=0.7; control arm mPFS 3.5 mo

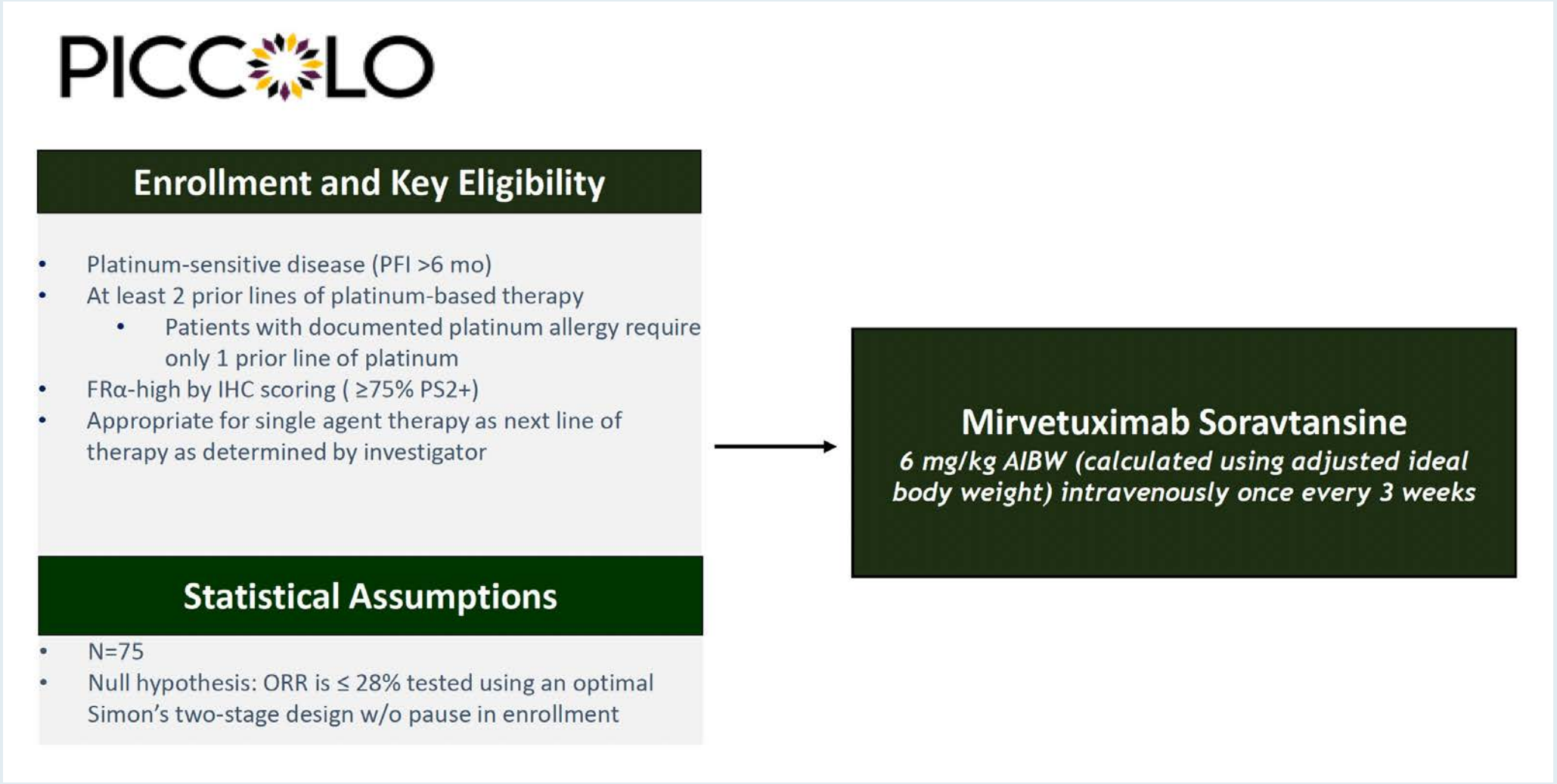
Mirvetuximab Soravtansine
6 mg/kg AIBW (calculated using adjusted ideal body weight) intravenously once every 3 weeks

1:1 Randomization
STRATIFICATION FACTORS
Investigator's Choice (IC) Chemotherapy
(Paclitaxel, PLD, Topotecan)
Prior Therapies
(1 vs 2 vs 3)

Investigator's Choice (IC) Chemotherapy
Paclitaxel, PLD,† or Topotecan
Paclitaxel: 80 mg/m2 weekly; PLD: 40 mg/m² every 4 weeks;
Topotecan: 4 mg/m² on days 1, 8, and 15 every four weeks;
or 1.25 mg/m² on days 1-5 every 3 weeks

Moore KN et al. SGO 2022;Abstract 297.

PICCOLO Phase II Trial Schema



Alvarez Secord A et al. SGO 2022;Abstract 300.

Updated Results From the Phase 1b Expansion Study of Upifitamab Rilsodotin (UpRi; XMT-1536), a NaPi2b-directed Dolaflexin Antibody Drug Conjugate (ADC) in Ovarian Cancer

Richardson, Debra L[1]; Hamilton, Erika P[2]; Barve, Minal[3]; Anderson, Charles K[4]; Taylor, Sara K[5]; Lakhani, Nehal[6]; Buscema, Joseph[7]; Tolcher, Anthony W[8]; Zarwan, Corrine[9]; Werner, Theresa L[10]; Hays, John L[11]; Richards, Paul[12]; Arend, Rebecca[13]; Edenfield, Jeffery[14]; Putiri, Emily[15]; Bernardo, Patricia[15]; Burger, Robert A[15]; Matulonis, Ursula A[16]

[1]Stephenson Cancer Center, University of Oklahoma Health Sciences Center and the Sarah Cannon Research Institute, Oklahoma City, OK; [2]Sarah Cannon Research Institute/Tennessee Oncology, Nashville, TN; [3]Mary Crowley Cancer Research, Dallas, TX; [4]Willamette Valley Cancer Institute and Research Center, Eugene, OR; [5]BC Cancer - Kelowna, Kelowna BC, Canada; [6]START Midwest, Grand Rapids, MI; [7]Arizona Oncology, Tucson, AZ; [8]NEXT Oncology, San Antonio, TX; [9]Lahey Clinic, Burlington, MA; [10]Huntsman Cancer Institute, University of Utah, Salt Lake City, UT; [11]Arthur James Cancer Hospital, Ohio State University, Columbus, OH; [12]US Oncology, Oncology and Hematology Assoc. of Southwest VA, Salem, VA; [13]University of Alabama at Birmingham, Birmingham, AL; [14]Prisma Health Cancer Institute, Greenville, SC; [15]Mersana Therapeutics, Inc, Cambridge, MA; [16]Dana-Farber Cancer Institute, Boston, MA

Abstract 76

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SGO 2022;Abstract 76.

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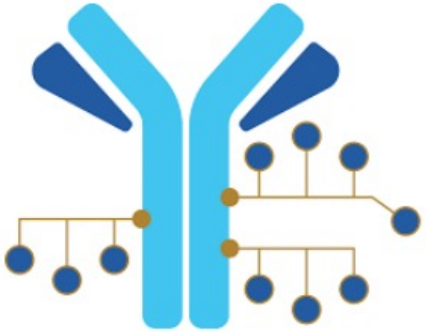
Upifitamab Rilsodotin (UpRi): First-in-Class ADC Targeting NaPi2b



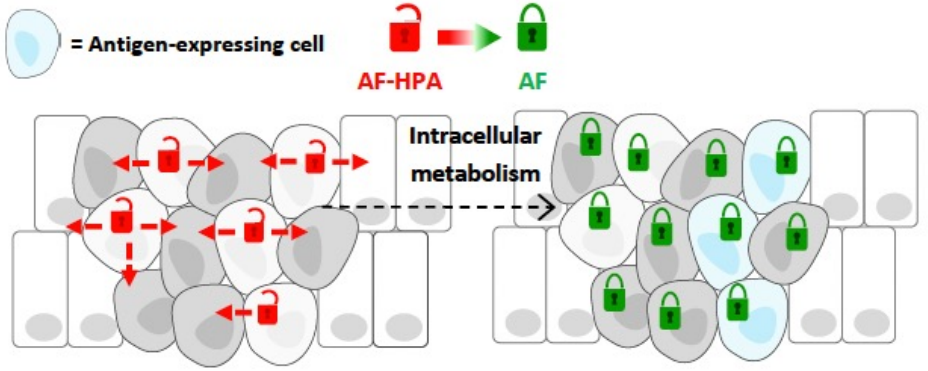
UpRi

Antibody: Humanized monoclonal anti-NaPi2b[1]

Linker: Polymer scaffold; cleavable ester linker[2]

Payload: AF-HPA (DolaLock-controlled bystander effect)[1]

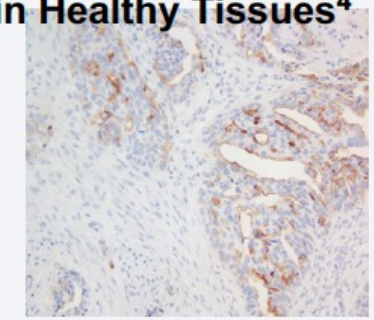
Drug-to-Antibody Ratio: ~10



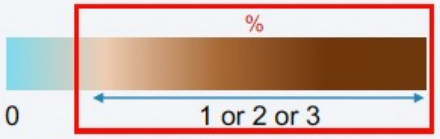
Upon ADC internalization into tumor cells and efficient release of payload, AF-HPA payload is metabolized to AF that remains highly potent but loses the ability to cross the cell membrane, locking it in the tumor, controlling the bystander effect, and consequently limiting impact on adjacent healthy cells[2,3]

NaPi2b Is a Sodium-Dependent Phosphate Transporter Broadly Expressed in Ovarian Cancer With Limited Expression in Healthy Tissues[4]

- NaPi2b expressed by tumor cells in two-thirds of patients with high-grade serous ovarian cancer[2]
- NaPi2b is a lineage antigen (not an oncogene)[1]



NaPi2b IHC assay in development *– an optimal diagnostic assay would be robust, predictive, reproducible, easily able to distinguish a wide range of expression using* ***TPS scoring method***[2]



Richardson DL et al. SGO 2022;Abstract 76.

RTP RESEARCH TO PRACTICE

UpRi Phase Ib Study Schema

Patient Population: HGSOC[a] progressing after standard treatments; measurable disease per RECIST v1.1; ECOG PS 0 or 1

Ovarian Cancer Cohort
- 1–3 prior lines in platinum-resistant
- 4 prior lines regardless of platinum status
- High-grade serous histology
- Archived tumor and fresh biopsy (if medically feasible) for NaPi2b
- Exclusion: Primary platinum-refractory disease

UpRi IV Q4W until disease progression or unacceptable toxicity

36 mg/m² cohort initiated in August 2019

43 mg/m² to a max of ~80 mg cohort initiated in December 2019

Primary Objectives
- Evaluate safety and tolerability of MTD or RP2D
- Assess preliminary efficacy (ORR, DCR)

Secondary Objectives
- Association of tumor NaPi2b expression and objective tumor response using an IHC assay with a broad dynamic range to distinguish tumors with high and low NaPi2b expression
- Further assessment of preliminary anti-neoplastic activity (DoR)

Assessment: Tumor imaging (MRI or CT) at baseline and every 2nd cycle; response assessed per RECIST v1.1

Richardson DL et al. SGO 2022;Abstract 76.

Expansion Cohort Experience Across a Range of Doses Allowed for Further Optimization of UpRi Profile

Updated Analysis of Phase 1b PROC Expansion Cohort to Evaluate Safety and ORR Based on UpRi Dose Levels[a]

Dose Group 36 (33–38 mg/m²) (n=29)

12 patients at **36 mg/m²** starting dose (all BSA levels)

+

17 patients at ~80 mg starting dose with BSA ≥1.8 who received an actual dose of **33 to 38 mg/m²**

Dose Group 43 (>38–43 mg/m²) (n=66)

39 patients at **43 mg/m²** starting dose with BSA <1.8

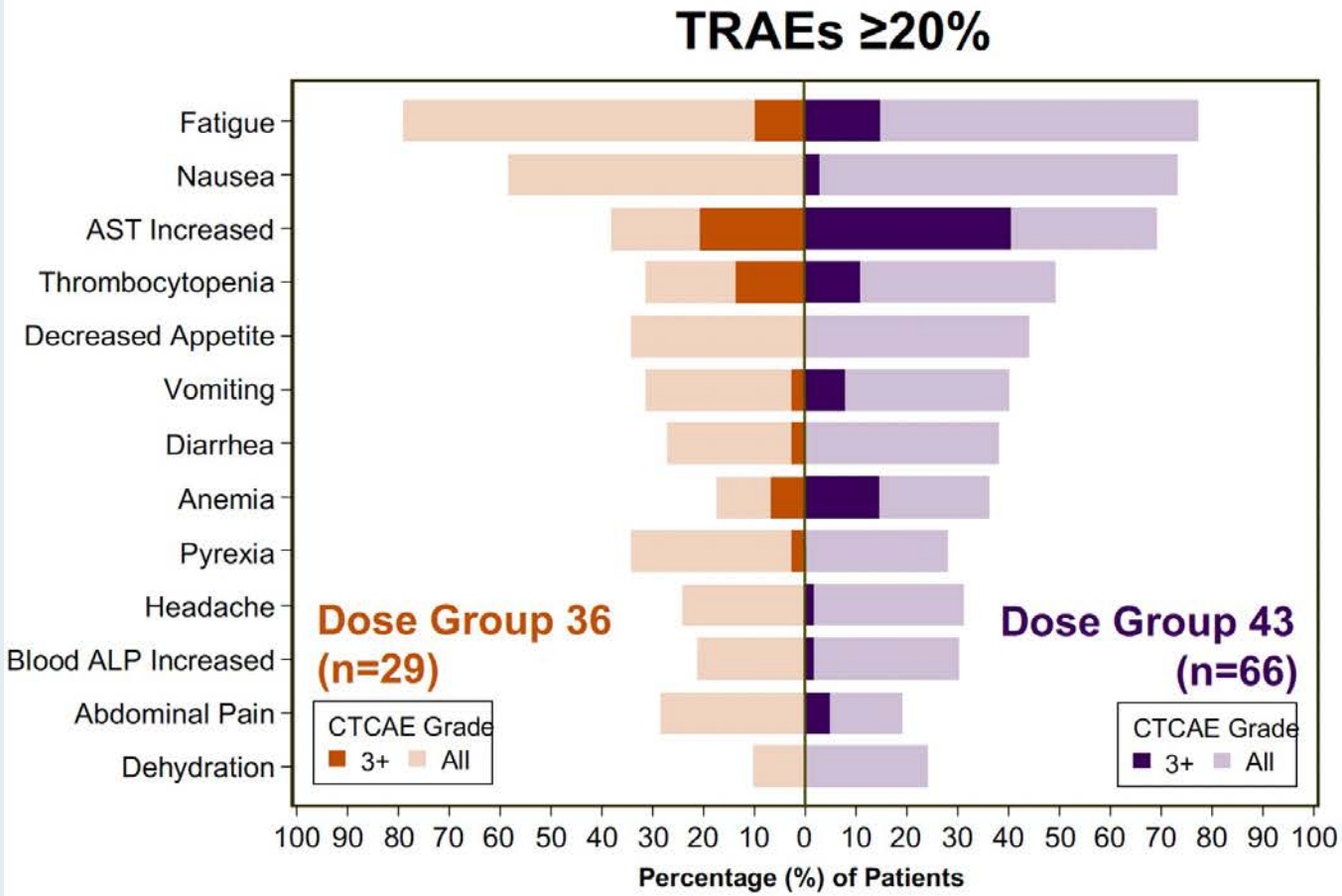
+

27 patients at ~80 mg starting dose with BSA ≥1.8 who received an actual dose of **>38 mg/m²**

Richardson DL et al. SGO 2022;Abstract 76.

TRAEs by UpRi Dose Group

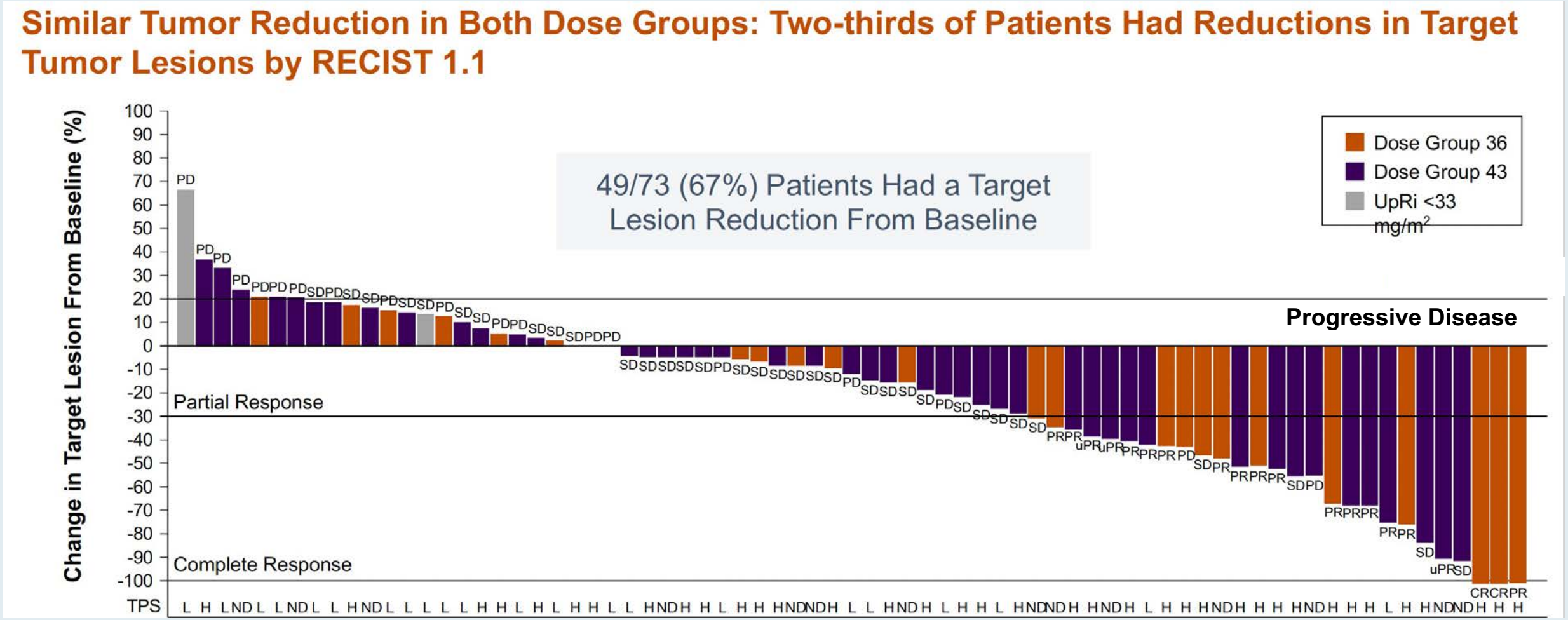
Dose Group 36 Had a More Favorable Safety Profile Compared to Dose Group 43



- No severe ocular toxicity, neutropenia, or peripheral neuropathy in either dose group
- 4 (14%) patients had treatment-related SAEs in Dose Group 36 vs 18 (27%) in Dose Group 43
- Lower frequencies and lower grade pneumonitis occurred in Dose Group 36 (with no Grade 3+) vs Dose Group 43[a]

Richardson DL et al. SGO 2022;Abstract 76.

Best Response by UpRi Dose Group



Richardson DL et al. SGO 2022;Abstract 76.

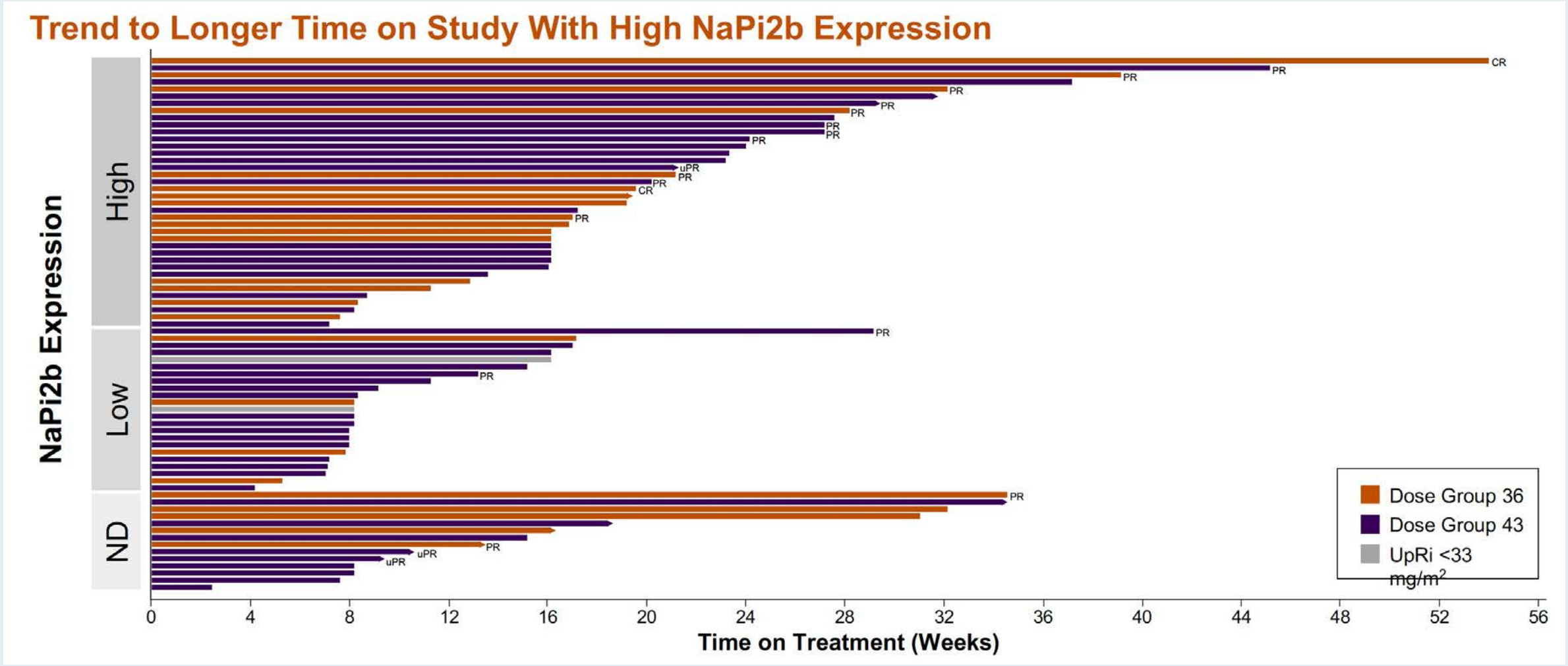
Confirmed ORR by UpRiDose Group and NaPi2b Level and Duration of Response (DoR)

		All Dose Levels	Dose Group 36	Dose Group 43
NaPi2b-High (TPS ≥75)	N	38	16	22
	ORR, n (%)	**13 (34)**	**7 (44)**	**6 (27)**
	CR, n (%)	2 (5)	2 (13)	0
	PR, n (%)	11 (29)	5 (31)	6 (27)
	DCR, n (%)	33 (87)	12 (75)	21 (95)
All NaPi2b Levels	N	75	25	48
	ORR, n (%)	**17 (23)**	**9 (36)**	**8 (17)**
	CR, n (%)	2 (3)	2 (8)	0
	PR, n (%)	15 (20)	7 (28)	8 (17)
	DCR, n (%)	54 (72)	18 (72)	35 (73)

- **Median DoR in patients (all dose levels) with NaPi2b-high ovarian cancer (n=13): 5 months**
- No obvious difference in median DoR observed between Dose Groups 36 and 43

Richardson DL et al. SGO 2022;Abstract 76.

Time on UpRi Study in Evaluable Patients



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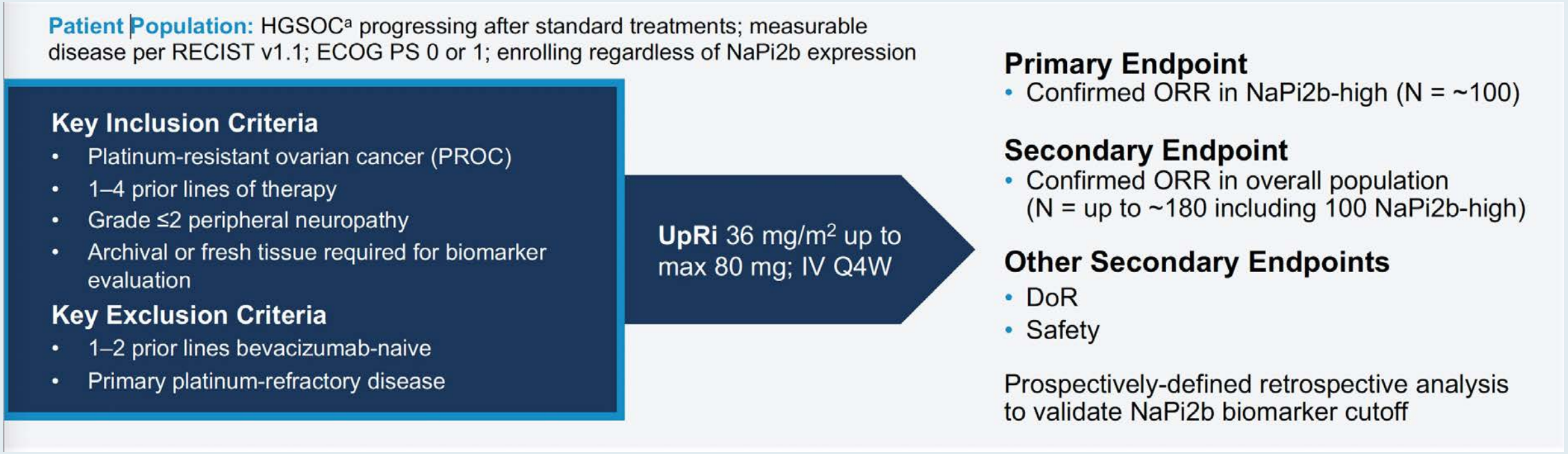
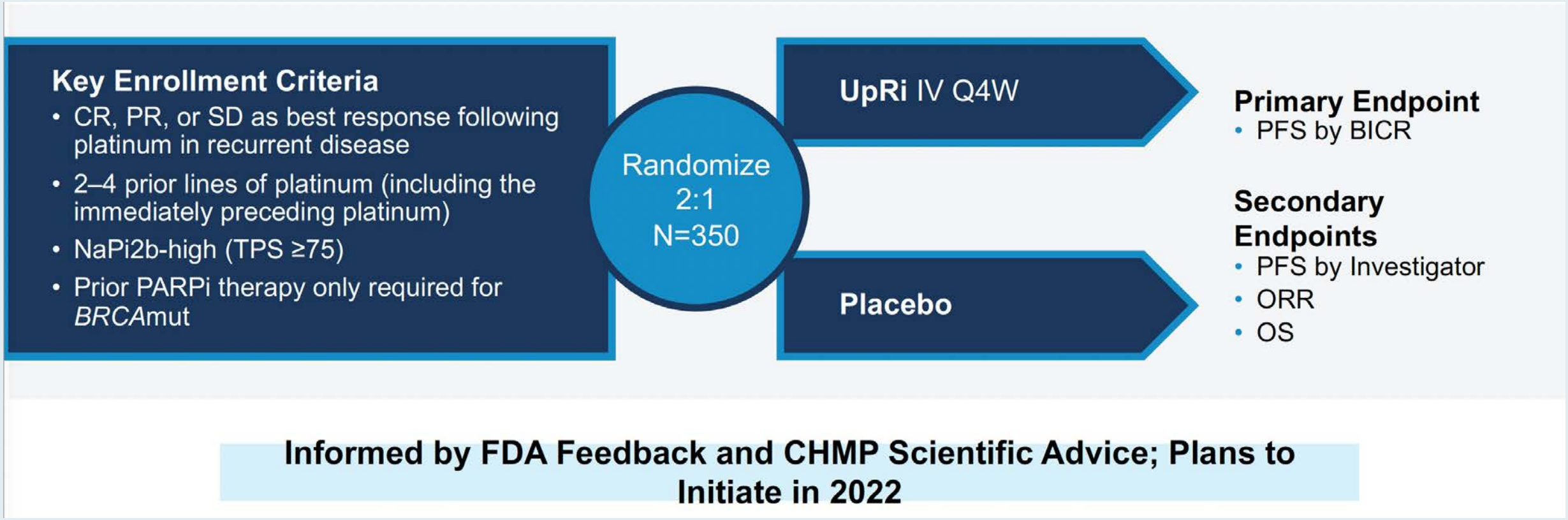
Ongoing UPLIFT (ENGOT-OV67/GOG-3048) Study Schema



Richardson DL et al. SGO 2022;Abstract 76.

Ongoing UP-NEXT Phase III (ENGOT-OV71-NSGO-CTU/GOG-3049) Study Schema



Richardson DL et al. SGO 2022;Abstract 76.

Meet The Professor

Optimizing the Management of Gastroesophageal Cancers

Wednesday, June 22, 2022
5:00 PM – 6:00 PM ET

Faculty

Eric Van Cutsem, MD, PhD

Moderator

Neil Love, MD

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Thank you for joining us!

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

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