Breakfast with the Investigators: Ovarian Cancer

A CME Symposium Held in Conjunction with the 2023 ASCO® Annual Meeting

Sunday, June 4, 2023

6:45 AM – 7:45 AM CT

Faculty

Philipp Harter, MD, PhD

David M O'Malley, MD

Shannon N Westin, MD, MPH

Moderator

Neil Love, MD

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Faculty

Philipp Harter, MD, PhD
Gynecologic Oncologist
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Evang Kliniken Essen-Mitte
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Professor
Division Director, Gynecologic Oncology
The Ohio State University and The James Cancer Center
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Moderator

Neil Love, MD
Research To Practice
Miami, Florida

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Dr Harter — Disclosures

Advisory Committee	AstraZeneca Pharmaceuticals LP, Clovis Oncology, Eisai Inc, GSK, ImmunoGen Inc, Merck Sharp & Dohme LLC, Mersana Therapeutics Inc, Miltenyi Biotec, Novartis, Roche Laboratories Inc
Consulting Agreement	Exscientia
Contracted Research	AstraZeneca Pharmaceuticals LP, Clovis Oncology, Genmab US Inc, GSK, ImmunoGen Inc, Novartis, Roche Laboratories Inc, Seagen Inc
Travel Support	AstraZeneca Pharmaceuticals LP

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Dr O'Malley — Disclosures

Advisory Committee and Consulting Agreements (Personal Fees)	AbbVie Inc, Adaptimmune, Agenus Inc, Arcus Biosciences, Arquer Diagnostics, AstraZeneca Pharmaceuticals LP, Atossa Therapeutics, Cardiff Oncology, Celcuity, Clovis Oncology, Corcept Therapeutics, Duality Biologics, Eisai Inc, Elevar Therapeutics, Exelixis Inc, F Hoffmann-La Roche Ltd, Genelux Corporation, Genentech, a member of the Roche Group, GSK, ImmunoGen Inc, Imvax Inc, InterVenn Biosciences, InxMed, Iovance Biotherapeutics, Janssen Biotech Inc, Jazz Pharmaceuticals Inc, Laekna Therapeutics, Leap Therapeutics Inc, Luzsana Biotechnology, Merck, Merck Sharp & Dohme LLC, Mersana Therapeutics Inc, Myriad Genetic Laboratories Inc, Novartis, Novocure Inc, OncoC4, Onconova Therapeutics Inc, R-Pharm, Regeneron Pharmaceuticals Inc, Replimune, Roche Diagnostics, Seagen Inc, Sorrento Therapeutics, Sumitomo Dainippon Pharma Oncology Inc, Sutro Biopharma, Tarveda Therapeutics, Toray Industries Inc, Trillium Therapeutics Inc, Umoja Biopharma, VBL Therapeutics, Verastem Inc, Vincerx Pharma, Xencor, Zentalis Pharmaceuticals
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Nonrelevant Financial Relationship	GOG Foundation Inc, Ludwig Institute for Cancer Research Ltd, National Cancer Institute, NRG Oncology, RTOG, SWOG

Dr Westin — Disclosures

Consulting Agreements	AstraZeneca Pharmaceuticals LP, Caris Life Sciences, Clovis Oncology, Eisai Inc, EQRx, Genentech, a member of the Roche Group, Gilead Sciences Inc, GSK, ImmunoGen Inc, Lilly, Merck, Mereo BioPharma, Mersana Therapeutics Inc, NGM Biopharmaceuticals, Nuvectis Pharma Inc, Seagen Inc, Verastem Inc, Vincerx Pharma, Zentalis Pharmaceuticals, ZielBio
Contracted Research	AstraZeneca Pharmaceuticals LP, Avenge Bio, Bayer HealthCare Pharmaceuticals, Bio-Path Holdings, Clovis Oncology, Genentech, a member of the Roche Group, GSK, Mereo BioPharma, Novartis, Zentalis Pharmaceuticals

Commercial Support

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

Research To Practice CME Planning Committee Members, Staff and Reviewers

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

Friday June 2	**Gastroesophageal Cancers** 11:45 AM – 12:45 PM CT (12:45 PM – 1:45 PM ET)
	Non-Small Cell Lung Cancer 6:30 PM – 9:00 PM CT (7:30 PM – 10:00 PM ET)
Saturday June 3	**Hepatobiliary Cancers** 6:45 AM – 7:45 AM CT (7:45 AM – 8:45 AM ET)
	Prostate Cancer 7:00 PM – 9:00 PM CT (8:00 PM – 10:00 PM ET)
Sunday June 4	**Ovarian Cancer** 6:45 AM – 7:45 AM CT (7:45 AM – 8:45 AM ET)
	Lymphoma, Chronic Lymphocytic Leukemia and Multiple Myeloma 7:00 PM – 9:30 PM CT (8:00 PM – 10:30 PM ET)
Monday June 5	**Urothelial Bladder Cancer** 6:45 AM – 7:45 AM CT (7:45 AM – 8:45 AM ET)
	Breast Cancer 7:00 PM – 9:30 PM CT (8:00 PM – 10:30 PM ET)
Tuesday June 6	**Renal Cell Carcinoma (Webinar)** 7:00 AM – 8:00 AM CT (8:00 AM – 9:00 AM ET)

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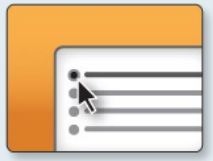
Clinicians in the Meeting Room

Networked iPads are available.

Review Program Slides: Tap the Program Slides button to review speaker presentations and other program content.



Answer Survey Questions: Complete the pre- and postmeeting surveys.

Ask a Question: Tap Ask a Question to submit a challenging case or question for discussion. We will aim to address as many questions as possible during the program.

Complete Your Evaluation: Tap the CME Evaluation button to complete your evaluation electronically to receive credit for your participation.

For assistance, please raise your hand. Devices will be collected at the conclusion of the activity.

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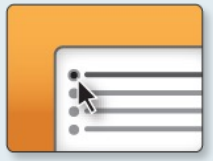
Clinicians Attending via Zoom

Review Program Slides: A link to the program slides will be posted in the chat room at the start of the program.



Answer Survey Questions: Complete the pre- and postmeeting surveys.

Ask a Question: Submit a challenging case or question for discussion using the Zoom chat room.

Get CME Credit: A CME credit link will be provided in the chat room at the conclusion of the program.

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PREMEETING SURVEY – Available Now

Clinicians in Attendance: If you have not already done so, please take a moment to complete the premeeting survey on the iPads for attendees in the room and on Zoom for those attending virtually. Your input on this survey will be integral to the program today.

A postmeeting survey will be posted toward the end of the session.

Thank you for your input.

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About the Enduring Program

- The live meeting is being video and audio recorded.
- The proceedings from today will be edited and developed into an enduring web-based video/PowerPoint program.
  An email will be sent to all attendees when the activity is available.
- To learn more about our education programs, visit our website, **www.ResearchToPractice.com**

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Agenda

Module 1 – Up-Front Treatment for Advanced Ovarian Cancer (OC)

- Front-line maintenance therapy for patients with advanced ovarian cancer
- Adverse events associated with PARP inhibitors and implications for therapeutic selection
- Other considerations for patients with advanced ovarian cancer and germline BRCA mutations: Management of the breast, role of genetic counseling, etc

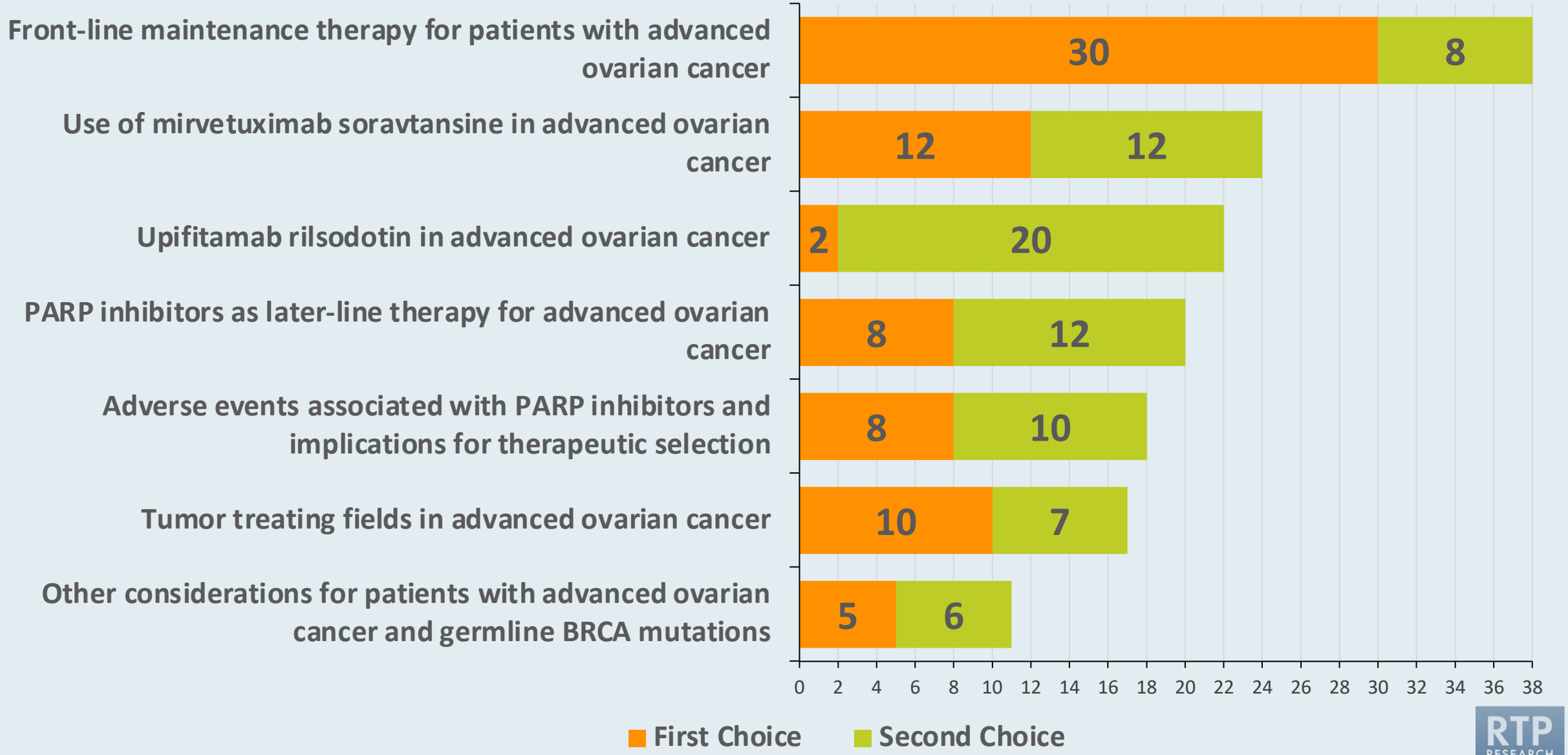
Module 2 – The Evolving Management Paradigm for Relapsed/Refractory OC

- PARP inhibitors as later-line therapy for advanced ovarian cancer
- Use of mirvetuximab soravtansine in advanced ovarian cancer

Module 3 – Novel Agents and Strategies Under Investigation for Advanced OC

- Upifitamab rilsodotin in advanced ovarian cancer
- Tumor treating fields in advanced ovarian cancer

Topics of Interest for Future CME Programs



Survey of US-based general medical oncologists, May 2023. N = 75

Agenda

Module 1 – Up-Front Treatment for Advanced Ovarian Cancer (OC)

- Front-line maintenance therapy for patients with advanced ovarian cancer
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- Upifitamab rilsodotin in advanced ovarian cancer
- Tumor treating fields in advanced ovarian cancer

How comfortable/familiar are you with the published data sets, available guidelines, investigator perspectives and ongoing research studies pertaining to front-line maintenance therapy for patients with advanced ovarian cancer?

57% feel well informed

Survey of US-based general medical oncologists, May 2023. N = 75

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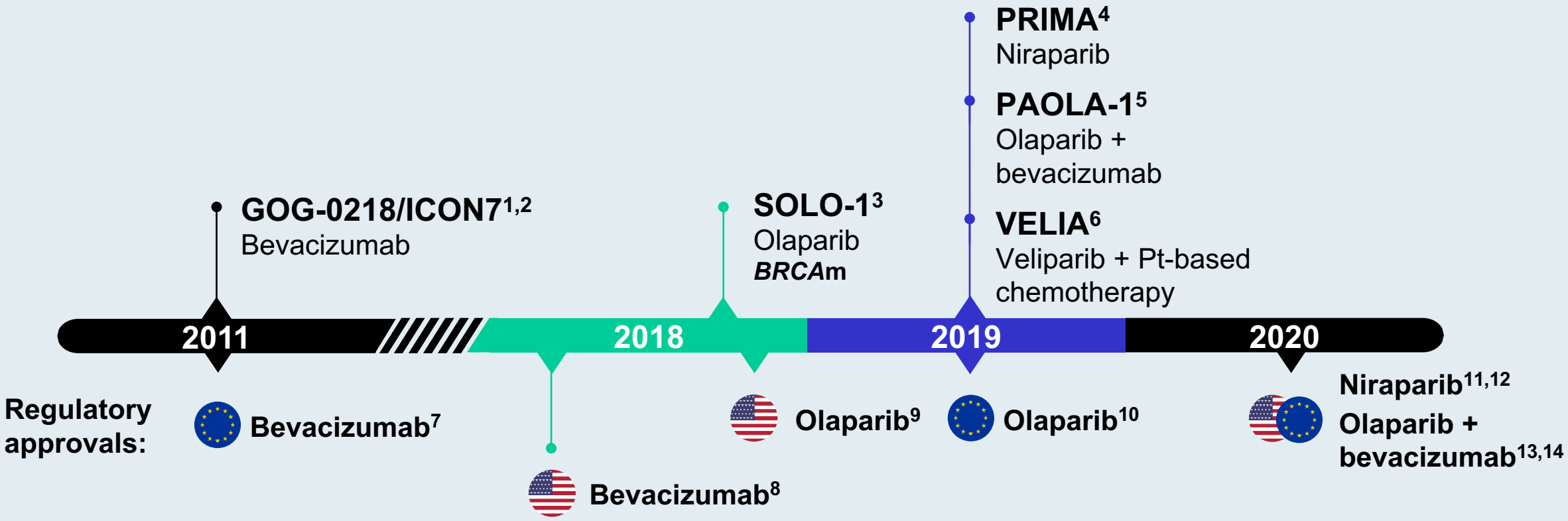
Front-line maintenance therapy for patients with advanced ovarian cancer

- DiSilvestro P et al. **Overall survival with maintenance olaparib at a 7-year follow-up in patients with newly diagnosed advanced ovarian cancer and a BRCA mutation: The SOLO1/GOG 3004 trial.** *J Clin Oncol* 2023;41(3):609-17.
- Ray-Conquard I et al. **Final overall survival results from the phase III PAOLA-1/ENGOT-ov25 trial evaluating maintenance olaparib plus bevacizumab in patients with newly diagnosed advanced ovarian cancer.** ESMO 2022;Abstract LBA29.
- Hardesty MM et al. **OVARIO phase II trial of combination niraparib plus bevacizumab maintenance therapy in advanced ovarian cancer following first-line platinum-based chemotherapy with bevacizumab.** *Gynecol Oncol* 2022;166(2):219-29.
- Gonzalez Martin AJ et al. **PRIMA/ENGOT-OV26/GOG-3012 study: Updated long-term PFS and safety.** ESMO 2022;Abstract 530P.
- Monk BJ et al. **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).** *J Clin Oncol* 2022;40(34):3952-64.

Front-line maintenance therapy for patients with advanced ovarian cancer

- Harter P et al. **Durvalumab with paclitaxel/carboplatin (PC) and bevacizumab (bev), followed by maintenance durvalumab, bev, and olaparib in patients (pts) with newly diagnosed advanced ovarian cancer (AOC) without a tumor BRCA1/2 mutation (non-tBRCAm): Results from the randomized, placebo (pbo)-controlled Phase III DUO-O trial.** ASCO 2023;Abstract LBA5506.

Pivotal Trials and Regulatory Milestones in 1L Maintenance Therapy of Advanced Ovarian Cancer



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

1. Burger RA et al. *N Engl J Med* 2011;365:2473. **2.** Perren TJ et al. *N Engl J Med* 2011;365:2484. **3.** Moore K et al. *N Engl J Med* 2018;379:2495. **4.** González-Martín A et al. *N Engl J Med*. 2019;381:239. **5.** Ray-Coquard I et al. *N Engl J Med* 2019;381:2416. **6.** Coleman RL et al. *N Engl J Med* 2019;381:2403. **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.** FDA. Published December 26, 2018. Accessed June 7, 2021. **10.** EMA. Published April 26, 2019. Accessed June 7, 2021. **11.** GSK. Published April 29, 2020. Accessed June 7, 2021. **12.** GSK. Published October 29, 2020. Accessed June 7, 2021. **13.** FDA. Published May 11, 2020. Accessed June 7, 2021. **14.** EMA. Published September 17, 2020. Accessed June 7, 2021.

Content Courtesy of Kathleen Moore, MD

Ovarian cancer 1L PARPi maintenance trials: design and populations

Trial	PARP inhibitor	Duration	BRCA status	R0 at PDS allowed	% PDS	CR/PR to platinum
SOLO1[1,2]	Olaparib	2 years	*BRCA*mt only	Yes	62.9	Yes
PRIMA[3]	Niraparib	3 years	All comers	No if Stage III	33	Yes
PRIME[4]	Niraparib	3 years	All comers	Yes	53.1	Yes
PAOLA1[5]	Olaparib (w/bevacizumab)	2 years	All comers	Yes	50.7	Yes
VELIA[6]	Veliparib (w/chemo)	36 total cycles	All comers	Yes	67.5	No (tx starts with chemo)
ATHENA-MONO[7]	Rucaparib	2 years	All comers	Yes	48.9	Yes

[1]Moore et al., *N Engl J Med* 2018; [2]Banerjee et al., 2020 ESMO Congress; [3]Gonzalez-Martin et al., *N Engl J Med* 2019; [4]Li et al., 2022 SGO Annual Meeting; [5]Ray-Coquard et al., *N Engl J Med* 2019; [6]Coleman et al., *N Engl J Med* 2019; [7]Monk et al., 2022 ASCO Annual Meeting

Liu N. ASCO 2022;Highlights of the Day: Gynecologic Cancers.

Trials of 1L PARPi maintenance in ovarian cancer

Trial	PARP inhibitor	Duration	All comers	BRCAmt	BRCAwt overall	BRCAwt – HRD	BRCAwt – HRP	HRD assay
ATHENA-MONO[1]	Rucaparib	2 years	**HR 0.52** 20.2 vs 9.2 mos	**HR 0.40** NR vs 14.7 mos	--	**HR 0.58** 95%CI 0.33-1.01 20.3 vs 9.2 mos	**HR 0.65** 95%CI 0.45-0.95 12.1 vs 9.1 mos	Foundation One CDx
SOLO1[2,3]	Olaparib	2 years	--	**HR 0.33** 56.0 vs 13.8 mos	--	--	--	--
PRIMA[4]	Niraparib	3 years	**HR 0.62** 13.8 vs 8.2 mos	**HR 0.40** 22.1 vs 10.9 mos	--	**HR 0.50** 19.6 vs 8.2 mos	**HR 0.68** 8.1 vs 5.4 mos	Myriad MyChoice
PRIME[5]	Niraparib	3 years	**HR 0.45** 24.8 vs 8.3 mos	**HR 0.40** NR vs 10.8 mos	**HR 0.48*** 19.3 vs 8.3 mos	**HR 0.58** 24.8 vs 11.1 mos	**HR 0.41** 14.0 vs 5.5 mos	Not published
PAOLA1[6]	Olaparib (w/bevacizumab)	2 years	**HR 0.59** 22.1 vs 16.6 mos	**HR 0.31** 37.2 vs 21.7 mos	**HR 0.71** 18.9 vs 16.0 mos	**HR 0.43** 28.1 vs 16.6 mos	**HR 0.92 (NS)** 18.9 vs 16.0 mos	Myriad MyChoice
VELIA[7]	Veliparib (w/chemo)	36 total cycles	**HR 0.68** 23.5 vs 17.3 mos	**HR 0.44** 34.7 vs 22.0 mos	**HR 0.80** 18.2 vs 15.1 mos	**HR 0.74 (NS)** 15.0 vs 11.5 mos	**HR 0.81 (NS)** 18.2 vs 15.1 mos	Myriad MyChoice

*does not exclude pts with sBRCAmt tumors

[1]Monk et al., 2022 ASCO Annual Meeting; [2]Moore et al., *N Engl J Med* 2018; [3]Banerjee et al., 2020 ESMO Congress; [4]Gonzalez-Martin et al., *N Engl J Med* 2019; [5]Li et al., 2022 SGO Annual Meeting; [6]Ray-Coquard et al., *N Engl J Med* 2019; [7]Coleman et al., *N Engl J Med* 2019

Liu N. ASCO 2022;Highlights of the Day: Gynecologic Cancers.

original reports

Overall Survival With Maintenance Olaparib at a 7-Year Follow-Up in Patients With Newly Diagnosed Advanced Ovarian Cancer and a BRCA Mutation: The SOLO1/GOG 3004 Trial

Paul DiSilvestro, MD[1]; Susana Banerjee, MD, PhD[2]; Nicoletta Colombo, MD, PhD[3]; Giovanni Scambia, MD[4]; Byoung-Gie Kim, MD, PhD[5]; Ana Oaknin, MD, PhD[6]; Michael Friedlander, MD[7]; Alla Lisyanskaya, MD[8]; Anne Floquet, MD[9,10]; Alexandra Leary, MD[10,11]; Gabe S. Sonke, MD, PhD[12]; Charlie Gourley, MD, PhD[13]; Amit Oza, MD[14]; Antonio González-Martín, MD, PhD[15,16]; Carol Aghajanian, MD[17]; William Bradley, MD[18]; Cara Mathews, MD[1]; Joyce Liu, MD[19]; John McNamara, MSc[20]; Elizabeth S. Lowe, MD[21]; Mei-Lin Ah-See, MB BChir, MD[22]; and Kathleen N. Moore, MD[23]; on behalf of the SOLO1 Investigators

J Clin Oncol 2023;41:609-17.

PRIMA/ENGOT-OV26/GOG-3012 Study: Updated Long-term PFS and Safety

Antonio González-Martín,[1] Bhavana Pothuri,[2] Ignace Vergote,[3] Whitney Graybill,[4] Mansoor R. Mirza,[5] Colleen C. McCormick,[6] Domenica Lorusso,[7] Gilles Freyer,[8] Floor Backes,[9] Klaus Baumann,[10] Andrés Redondo,[11] Richard G. Moore,[12] Christof Vulsteke,[13] Roisin E. O'Cearbhaill,[14] Izabela A. Malinowska,[15] Luda Shtessel,[15] Natalie Compton,[15] Bradley J. Monk[16]

[1]Medical Oncology Department, Clínica Universidad de Navarra, Madrid, Program in Solid Tumours, CIMA, Pamplona, and Grupo Español de Investigación en Cáncer de Ovario (GEICO), Madrid, Spain; [2]Gynecologic Oncology Group (GOG), Department of Obstetrics/Gynecology, Perlmutter Cancer Center, NYU Langone Health, New York, NY, USA; [3]Belgium and Luxembourg Gynaecological Oncology Group (BGOG), Department of Gynaecology and Obstetrics, Division of Gynaecologic Oncology, University Hospitals Leuven, Leuven Cancer Institute, Leuven, Belgium; [4]GOG, Gynecologic Oncology, Medical University of South Carolina, Charleston, SC, USA; [5]NSGO, Rigshospitalet–Copenhagen University Hospital, Copenhagen, Denmark; [6]GOG, Legacy Medical Group Gynecologic Oncology, Portland, OR, USA; [7]Multicentre Italian Trials in Ovarian Cancer and Gynecologic Malignancies (MITO), Fondazione Policlinico Gemelli IRCCS and Catholic University of Sacred Heart, Rome, Italy; [8]Groupe d'Investigateurs Nationaux pour l'Etude des Cancers Ovariens (GINECO), HCL Cancer Institute Department of Medical Oncology, Lyon University, Lyon, France; [9]Division of Gynecologic Oncology, Ohio State University, Columbus, OH, USA; [10]Arbeitsgemeinschaft Gynäkologische Onkologie (AGO), Department of Gynecology and Obstetrics, Klinikum der Stadt Ludwigshafen, Ludwigshafen, Germany; [11]GEICO, Hospital Universitario La Paz-IdiPAZ, Madrid, Spain; [12]US Oncology Research, Division of Gynecologic Oncology, Wilmot Cancer Institute, Department of Obstetrics and Gynecology, University of Rochester, Rochester, NY, USA; [13]BGOG, Department of Medical Oncology and Hematology, AZ Maria Middelares, Gent, and Department of Molecular Imaging, Pathology, Radiotherapy & Oncology, Center for Oncological Research, Antwerp University, Antwerp, Belgium; [14]GOG, Gynecologic Medical Oncology, Memorial Sloan Kettering Cancer Center, and Department of Medicine, Weill Cornell Medical College, New York, NY, USA; [15]GSK, Middlesex, UK; [16]HonorHealth Research Institute, University of Arizona College of Medicine, Phoenix Creighton University, Phoenix, AZ, USA

IGCS 2022;Abstract S005/1753.

SEPT 29 - OCT 1
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PARIS 2022 ESMO congress

Abstract LBA29

Final overall survival results from the Phase III PAOLA-1/ENGOT-ov25 trial evaluating maintenance olaparib plus bevacizumab in patients with newly diagnosed advanced ovarian cancer

Isabelle Ray-Coquard,[1] Alexandra Leary,[2] Sandro Pignata,[3] Claire Cropet,[4] Antonio González-Martín,[5] Gerhard Bogner,[6] Hiroyuki Yoshida,[7] Ignace Vergote,[8] Nicoletta Colombo,[9] Johanna Mäenpää,[10] Frédéric Selle,[11] Barbara Schmalfeldt,[12] Giovanni Scambia,[13] Eva Maria Guerra Alia,[14] Claudia Lefeuvre-Plesse,[15] Antje Belau,[16] Alain Lortholary,[17] Martina Gropp-Meier,[18] Eric Pujade-Lauraine,[19] Philipp Harter[20]

[1]Centre Léon BERARD, Lyon, and GINECO, France; [2]Institut Gustave Roussy, Villejuif, and GINECO, France; [3]Istituto Nazionale Tumori 'Fondazione G Pascale', IRCCS, Napoli, and MITO, Italy; [4]Centre Léon BERARD, Lyon,, France; [5]Clínica Universidad de Navarra, Madrid, and GEICO, Spain; [6]Paracelsus Medical University Salzburg, Salzburg, and AGO Au, Austria; [7]Saitama Medical University International Medical Center, Saitama, and GOTIC, Japan; [8]Leuven Cancer Institute, Leuven, and BGOG, Belgium; [9]European Institute of Oncology, Milan, and MANGO, Italy; [10]Tampere University and University Hospital, Tampere, and NSGO, Finland; [11]Groupe Hospitalier Diaconesses Croix Saint-Simon, Paris, and GINECO, France; [12]Universitätsklinikum Hamburg-Eppendorf, Hamburg, and AGO, Germany; [13]Università Cattolica del Sacro Cuore di Roma, Rome, and MITO, Italy; [14]Hospital Universitario Ramón y Cajal, Madrid, and GEICO, Spain; [15]Centre Eugène Marquis, Rennes, and GINECO, France; [16]Universitätsmedizin Greifswald, Frauenklinik & Frauenarztpraxis, Greifswald, and AGO, Germany; [17]Hopital privé du Confluent, Nantes, and GINECO, France; [18]Onkologie Ravensburg, Ravensburg, and AGO, Germany; [19]ARCAGY Research, Paris, France; [20]Kliniken Essen-Mitte, Essen, and AGO, Germany

ClinicalTrials.gov identifier: NCT02477644 | This study was sponsored by ARCAGY Research.

RTP RESEARCH TO PRACTICE

ATHENA–MONO (GOG-3020/ENGOT-ov45): A Randomized, Double-blind, Phase 3 Trial Evaluating Rucaparib Monotherapy Vs Placebo As Maintenance Treatment Following Response To First-line Platinum-based Chemotherapy In Ovarian Cancer

Bradley J. Monk, on behalf of the ATHENA–MONO investigators

GOG Foundation, HonorHealth Research Institute, University of Arizona College of Medicine, Creighton University School of Medicine, Phoenix, AZ, USA

Originally presented at the 2022 ASCO Annual Meeting, 3-7 June 2022:
Bradley J. Monk, Christine Parkinson, Myong Cheol Lim, David M. O'Malley, Ana Oaknin, Michelle K. Wilson, Robert L. Coleman, Domenica Lorusso, Amit Oza, Sharad Ghamande, Athina Christopoulou, Emily Prendergast, Fuat Demirkiran, Ramey D. Littell, Anita Chudecka-Glaz, Mark A. Morgan, Sandra Goble, Stephanie Hume, Keiichi Fujiwara, Rebecca S. Kristeleit.
J Clin Oncol. 40, 2022 (suppl 17; abstr LBA5500).

IGCS 2022;Abstract S001/1608.

SEPT 29 - OCT 1 IGCS 2022 NYC NEW YORK CITY ANNUAL GLOBAL MEETING

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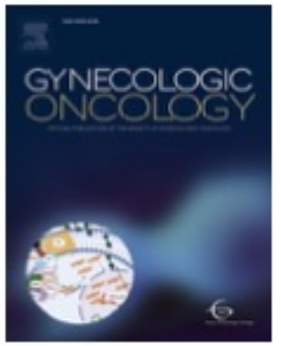
Contents lists available at ScienceDirect

Gynecologic Oncology

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

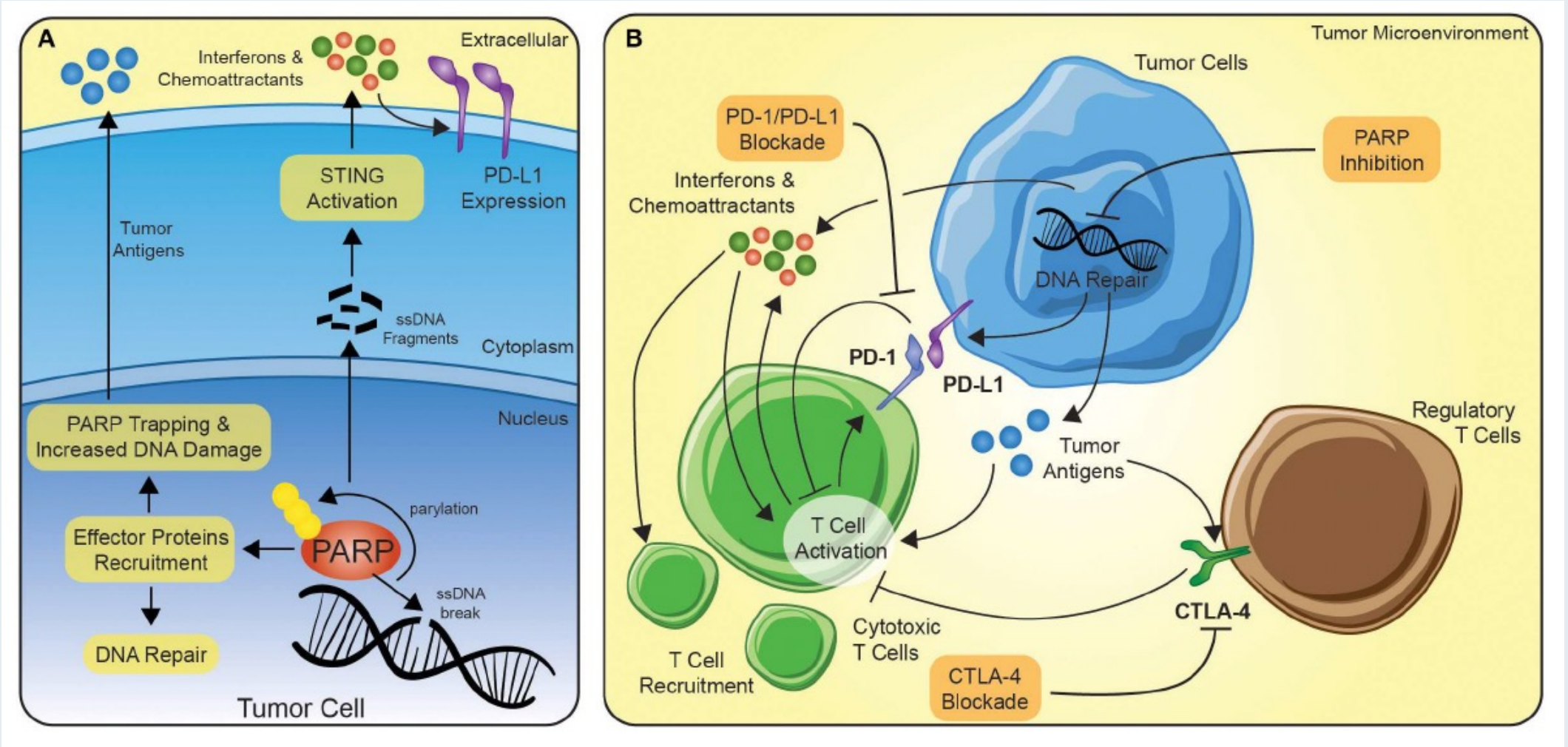


Gynecol Oncol 2022 Aug;166(2)219-229

OVARIO phase II trial of combination niraparib plus bevacizumab maintenance therapy in advanced ovarian cancer following first-line platinum-based chemotherapy with bevacizumab

Melissa M. Hardesty [a,*], Thomas C. Krivak [b], Gail S. Wright [c], Erika Hamilton [d], Evelyn L. Fleming [e], Jimmy Belotte [f], Erika K. Keeton [g], Ping Wang [f], Divya Gupta [f], Aine Clements [h], Heidi J. Gray [i], Gottfried E. Konecny [j], Richard G. Moore [k], Debra L. Richardson [l]

The Potential Synergy Between PARP Inhibition and Immune Checkpoint Blockade



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

Olaparib and durvalumab combination improved progression-free survival in newly diagnosed patients with advanced ovarian cancer without tumor BRCA mutations in DUO-O Phase III trial

Press Release: April 5, 2023

"Positive high-level results from a planned interim analysis of the DUO-O Phase III trial showed treatment with a combination of olaparib, durvalumab, chemotherapy and bevacizumab demonstrated a statistically significant and clinically meaningful improvement in progression-free survival (PFS) versus chemotherapy plus bevacizumab (control arm) in newly diagnosed patients with advanced high-grade epithelial ovarian cancer without tumor BRCA mutations. Patients were treated with durvalumab in combination with chemotherapy and bevacizumab followed by durvalumab, olaparib and bevacizumab as maintenance therapy.

In an additional arm, durvalumab, chemotherapy plus bevacizumab showed a numerical improvement in PFS versus the control arm but did not reach statistical significance at this interim analysis. At the time of this planned interim analysis, the overall survival (OS) and other secondary endpoints are immature and will be formally assessed at a subsequent analysis."

https://www.astrazeneca.com/media-centre/press-releases/2023/lynparza-imfinzi-met-endpoint-in-ovarian-cancer.html

2023 ASCO ANNUAL MEETING

Durvalumab with paclitaxel/carboplatin and bevacizumab followed by maintenance durvalumab, bevacizumab and olaparib in patients with newly diagnosed advanced ovarian cancer without a tumor *BRCA1/BRCA2* mutation: results from the randomized, placebo-controlled Phase III DUO-O/ENGOT-ov46/AGO-OVAR 23/GOG-3025 trial

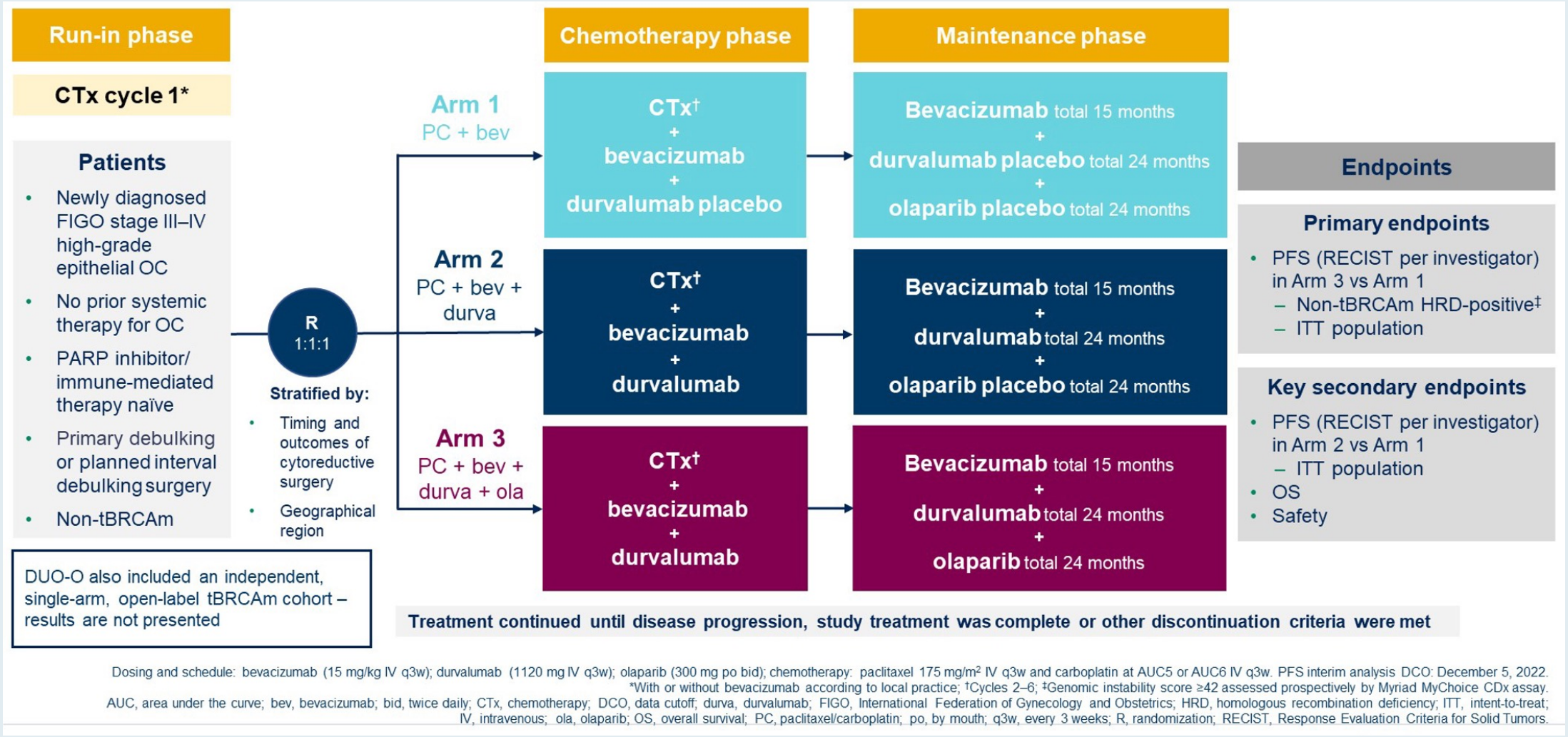
Philipp Harter,[1] Fabian Trillsch,[2] Aikou Okamoto,[3] Alexander Reuss,[4] Jae-Weon Kim,[5] Maria Jesús Rubio-Pérez,[6] Mehmet Ali Vardar,[7] Giovanni Scambia,[8] Olivier Trédan,[9] Gitte-Bettina Nyvang,[10] Nicoletta Colombo,[11] Anita Chudecka-Głaz,[12] Christoph Grimm,[13] Stephanie Lheureux,[14] Els Van Nieuwenhuysen,[15] Florian Heitz,[16] Robert M. Wenham,[17] Kimio Ushijima,[18] Emily Day,[19] Carol Aghajanian[20]

[1]Kliniken Essen-Mitte, Essen, and AGO, Germany; [2]University Hospital, LMU Munich, Munich, and AGO, Germany; [3]The Jikei University School of Medicine, Tokyo, and JGOG, Japan; [4]Coordinating Center for Clinical Trials of the Philipps-University of Marburg, Marburg, and ENGOT, Germany; [5] Seoul National University Hospital, Seoul, and KGOG, South Korea; [6]Reina Sofia University Hospital, Cordoba, and GEICO, Spain; [7]Medical Faculty, University of Cukurova, and Balcalı Hospital, Adana, and TRSGO, Turkey; [8]Fondazione Policlinico Universitario A. Gemelli IRCCS, Rome, and MITO, Italy; [9]Centre Léon Bérard, Centre de Recherche en Cancérologie de Lyon, Lyon, and GINECO, France; [10] Odense Universitetshospital, Odense, and NSGO, Denmark; [11]University of Milan-Bicocca and Istituto Europeo di Oncologia IRCCS, Milan, and MANGO, Italy; [12]SPSK Nr 2, Pomeranian Medical University, Szczecin, and PGOG, Poland; [13]Gynecologic Cancer Unit, Medical University Vienna, and AGO-Au, Austria; [14]Princess Margaret Hospital, Toronto, ON, and PMHC, Canada; [15]UZ Leuven, Leuven, and BGOG, Belgium, [16]Ev. Kliniken Essen-Mitte, Essen, and Charité Campus Virchow-Klinikum, Charité – Universitätsmedizin Berlin, corporate member of Freie Universität Berlin, Humboldt-Universität zu Berlin, Berlin Institute of Health, Berlin, and AGO, Germany; [17]Moffitt Cancer Center, Tampa, FL, and GOG-F, USA; [18]Kurume University School of Medicine, Kurume, and JGOG, Japan; [19]Oncology Biometrics, AstraZeneca, Cambridge, UK; [20]Memorial Sloan Kettering Cancer Center, New York, NY, and GOG-F, USA

ClinicalTrials.gov identifier: NCT03737643
This study was sponsored by AstraZeneca

Harter P et. al, ASCO 2023; Abstract LBA5506.

DUO-O: Study Design



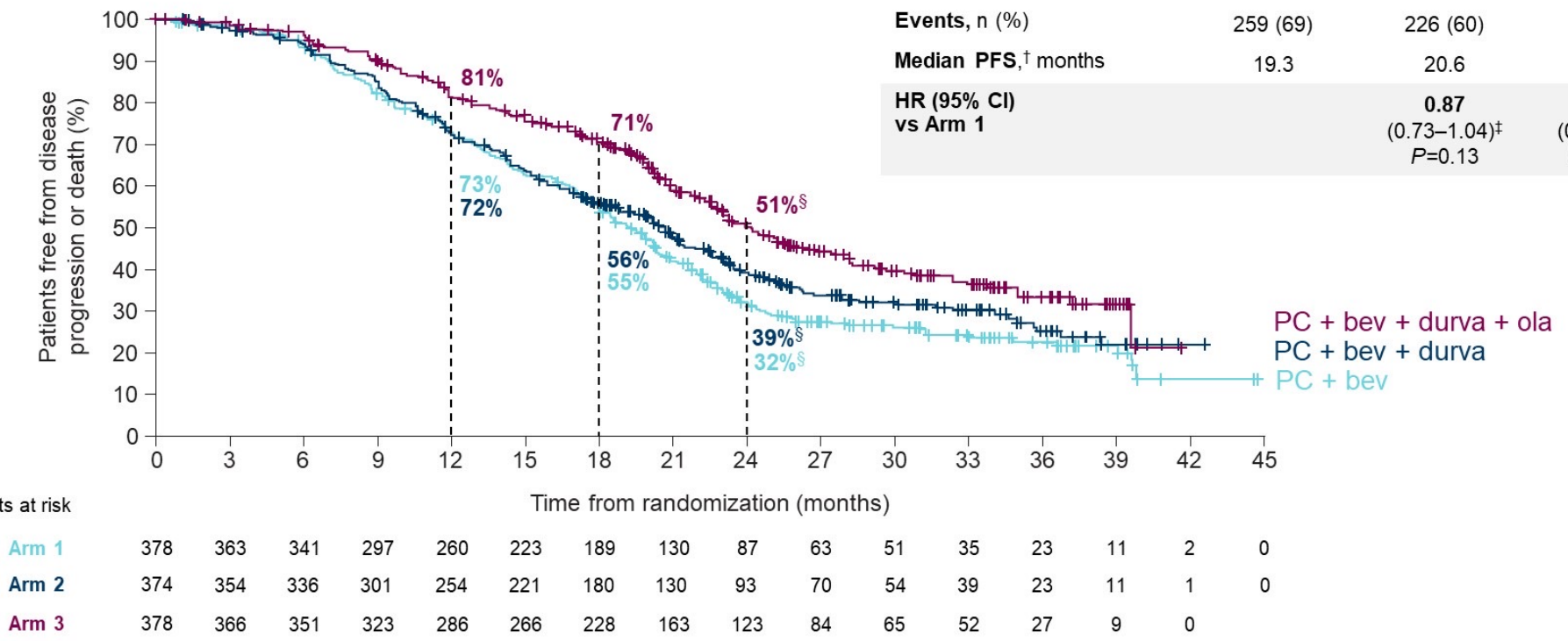
Dosing and schedule: bevacizumab (15 mg/kg IV q3w); durvalumab (1120 mg IV q3w); olaparib (300 mg po bid); chemotherapy: paclitaxel 175 mg/m^2 IV q3w and carboplatin at AUC5 or AUC6 IV q3w. PFS interim analysis DCO: December 5, 2022.
*With or without bevacizumab according to local practice; †Cycles 2–6; ‡Genomic instability score ≥42 assessed prospectively by Myriad MyChoice CDx assay.
AUC, area under the curve; bev, bevacizumab; bid, twice daily; CTx, chemotherapy; DCO, data cutoff; durva, durvalumab; FIGO, International Federation of Gynecology and Obstetrics; HRD, homologous recombination deficiency; ITT, intent-to-treat; IV, intravenous; ola, olaparib; OS, overall survival; PC, paclitaxel/carboplatin; po, by mouth; q3w, every 3 weeks; R, randomization; RECIST, Response Evaluation Criteria for Solid Tumors.

Harter P et. al, ASCO 2023; Abstract LBA5506.

RTP RESEARCH TO PRACTICE

DUO-O: PFS in the ITT Population

	Arm 1 PC + bev N=378	Arm 2 PC + bev + durva N=374	Arm 3 PC + bev + durva + ola N=378
Median follow-up,* months	25.5	23.1	23.3
Events, n (%)	259 (69)	226 (60)	193 (51)
Median PFS,† months	19.3	20.6	24.2
HR (95% CI) vs Arm 1		**0.87** (0.73–1.04)‡ *P*=0.13	**0.63** (0.52–0.76)‡ *P*<0.0001



Patients at risk

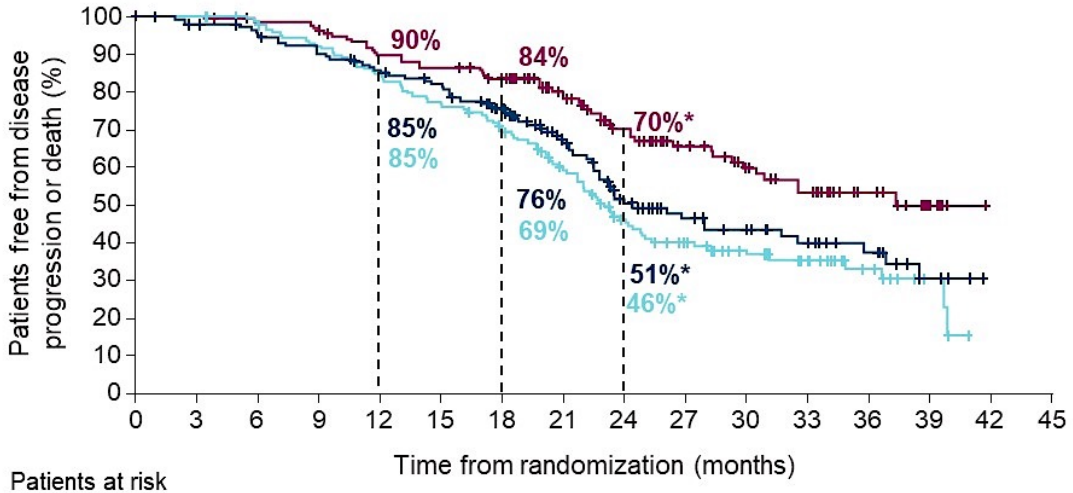
Arm 1	378	363	341	297	260	223	189	130	87	63	51	35	23	11	2	0
Arm 2	374	354	336	301	254	221	180	130	93	70	54	39	23	11	1	0
Arm 3	378	366	351	323	286	266	228	163	123	84	65	52	27	9	0	

*In censored patients; †Medians and rates were estimated by KM method; ‡HR and CI were estimated from a stratified Cox proportional hazards model. Model stratified by timing and outcome of cytoreductive surgery and geographical region. *P* value from a stratified log rank text; §24-month PFS rates unstable.

Harter P et. al, ASCO 2023; Abstract LBA5506.

DUO-O: Subgroup analysis of PFS by HRD status

HRD-positive

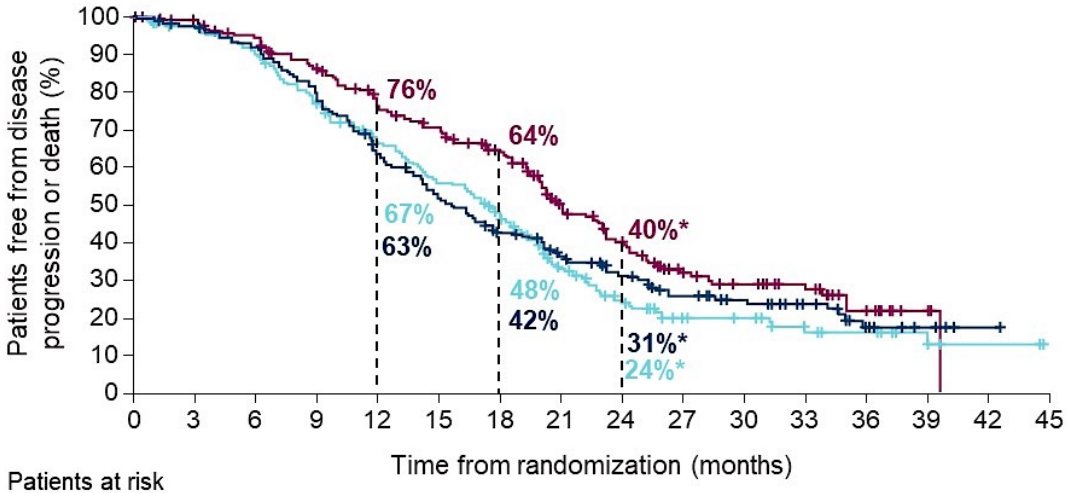


Patients at risk

Arm 1	143	141	136	126	116	105	93	73	52	41	31	22	13	6	0
Arm 2	148	142	137	128	118	112	94	66	45	34	28	21	15	7	0
Arm 3	140	138	135	131	120	116	107	84	63	49	39	32	17	6	0

	Arm 1 PC + bev N=143	Arm 2 PC + bev + durva N=148	Arm 3 PC + bev + durva + ola N=140
Events, n (%)	86 (60)	69 (47)	49 (35)
Median PFS, months†	23.0	24.4‡	37.3‡
HR (95% CI) vs Arm 1		**0.82** (0.60–1.12)§	**0.51** (0.36–0.72)§

HRD-negative



Patients at risk

Arm 1	216	203	188	159	135	112	92	55	34	21	19	12	9	5	2	0
Arm 2	199	189	177	153	120	97	76	59	45	33	25	17	8	4	1	0
Arm 3	211	202	190	169	145	132	111	75	57	33	26	20	10	3	0	

	Arm 1 PC + bev N=216	Arm 2 PC + bev + durva N=199	Arm 3 PC + bev + durva + ola N=211
Events, n (%)	157 (73)	142 (71)	127 (60)
Median PFS, months†	17.4	15.4	20.9
HR (95% CI) vs Arm 1		**0.94** (0.75–1.18)§	**0.68** (0.54–0.86)§

*24-month PFS rates unstable; †Medians and rates were estimated by KM method; ‡Median PFS in HRD-positive subgroup Arm 3 and Arm 2 unstable; §HR and CI were estimated from an unstratified Cox proportional hazards model.

Harter P et. al, ASCO 2023; Abstract LBA5506.

DUO-O: Safety Summary

AEs, n (%)	Overall (chemotherapy phase + maintenance phase)			Maintenance phase		
	Arm 1 PC + bev N=376	Arm 2 PC + bev + durva N=373	Arm 3 PC + bev + durva + ola N=378	Arm 1 PC + bev N=331	Arm 2 PC + bev + durva N=323	Arm 3 PC + bev + durva + ola N=336
Any-grade AE	373 (99)	371 (99)	375 (99)	308 (93)	303 (94)	328 (98)
Grade ≥3 AE	231 (61)	245 (66)	269 (71)	88 (27)	113 (35)	164 (49)
AE with outcome of death	4 (1)	9 (2)	6 (2)	2 (1)	3 (1)	4 (1)
Serious AE (including outcome of death)	128 (34)	161 (43)	148 (39)	50 (15)	91 (28)	83 (25)
AE of special interest to olaparib						
MDS/AML*	1 (<1)	0	2 (1)	1 (<1)	0	1 (<1)
New primary malignancies*	1 (<1)	1 (<1)	4 (1)	1 (<1)	1 (<1)	3 (1)
Pneumonitis	3 (1)	5 (1)	7 (2)	1 (<1)	3 (1)	6 (2)
Any immune-mediated AEs†	132 (35)	209 (56)	200 (53)	94 (28)	139 (43)	141 (42)
AEs leading to dose modification‡,§	272 (72)	299 (80)	323 (85)	163 (49)	182 (56)	254 (76)
AEs leading to discontinuation‡	77 (20)	98 (26)	131 (35)	44 (13)	54 (17)	88 (26)
AEs leading to discontinuation of PC/bevacizumab	57 (15)	59 (16)	70 (19)	27 (8)	24 (7)	35 (10)
AEs leading to discontinuation of durvalumab/placebo	24 (6)	62 (17)	65 (17)	14 (4)	39 (12)	40 (12)
AEs leading to discontinuation of olaparib/placebo	15 (4)	19 (5)	62 (16)	14 (4)	19 (6)	61 (18)

Includes AEs with onset or worsening on or after the date of first dose of durvalumab/placebo or olaparib/placebo (overall) or first dose of olaparib/placebo (maintenance phase) until initiation of the first subsequent anticancer therapy following last dose of study treatment or until the end of the safety follow-up period.
*Includes events from first dose of durvalumab/olaparib/placebo until end of study; †Investigator-assessed; ‡Based on action taken on AE CRF for at least one treatment. For durvalumab/placebo, dose modification includes skipped or delayed doses, or interruption of the infusion; §Either dose reduction or dose interruption. AE, adverse event; AML, acute myeloid leukemia; CRF, case report form; MDS, myelodysplastic syndrome.

Harter P et. al, ASCO 2023; Abstract LBA5506.

DUO-O: Any AE with frequency of ≥20%

AEs	Overall (chemotherapy phase + maintenance phase)			Maintenance phase		
	Arm 1 PC + bev N=376	Arm 2 PC + bev + durva N=373	Arm 3 PC + bev + durva + ola N=378	Arm 1 PC + bev N=331	Arm 2 PC + bev + durva N=323	Arm 3 PC + bev + durva + ola N=336
Nausea, %	31	30	57	15	17	52
Anemia,† %	29	32	55	5	10	41
Neutropenia,† %	44	45	51	8	8	23
Fatigue/asthenia,† %	40	38	49	19	20	32
Arthralgia, %	33	32	34	29	28	27
Constipation, %	26	25	30	11	10	15
Diarrhea, %	29	30	30	21	21	22
Thrombocytopenia,† %	19	20	28	3	5	17
Hypertension, %	34	30	26	24	18	14
Vomiting, %	16	16	26	10	11	22
Leukopenia,† %	18	18	24	5	4	13
Headache, %	21	20	22	19	16	18
Abdominal pain, %	18	22	21	12	15	13
Hypothyroidism, %	7	21	20	6	14	15
Myalgia, %	20	22	18	13	12	9

Includes AEs with onset or worsening on or after the date of first dose of durvalumab/placebo or olaparib/placebo (overall) or first dose of olaparib/placebo (maintenance phase) until initiation of the first subsequent anticancer therapy following last dose of study treatment or until the end the safety follow-up period. *AEs of any grade with overall incidence of ≥20% in any arm and associated incidence in the maintenance phase, excluding alopecia; †Grouped-term.

Harter P et. al, ASCO 2023; Abstract LBA5506.

RTP RESEARCH TO PRACTICE

Questions from General Medical Oncologists

- **"ONE STOP" NGS (for HRD, etc) AND germline at the same time UPFRONT: How to do it? Tempus is enough? To add Myriad? Routine assessment?**
- **In different genetic groups, ie, germline vs somatic BRCA vs HRD vs WT, do you change maintenance option PARPi and/or bev?**
- **Choice of one PARPi over another and recommended duration**
- **In germline BRCA+ disease, is olap + bev better than olap alone in maintenance?**
- **Bevacizumab as maintenance vs bevacizumab with PARP. Is it best to use all your treatment options at once, or keep PARP inhibitor for second line?**
- **Synergy with PARP/IO combination therapy?**

Survey of US-based general medical oncologists, May 2023. N = 75

Questions from General Medical Oncologists (Continued)

- **I have a 40-year-old patient with Stage IC BRCA2-positive ovarian cancer. She was very eager to do PARP maintenance. Any data in this population?**
- **I have a patient who was on PARP (olaparib) for 3 yrs (did not want come off after 2). Developed mild form of MDS so stopped. Now progressing in a few months on Plat/Pac/Bev…in future is it safe to reuse if needed (since MDS was mild) and no further progression in the future?**
- **Should PALB2 patients be treated like BRCA mutation-positive patients? In the metastatic and adjuvant setting?**

Survey of US-based general medical oncologists, May 2023. N = 75

Agenda

Module 1 – Up-Front Treatment for Advanced Ovarian Cancer (OC)

- Front-line maintenance therapy for patients with advanced ovarian cancer
- Adverse events associated with PARP inhibitors and implications for therapeutic selection
- Other considerations for patients with advanced ovarian cancer and germline BRCA mutations: Management of the breast, role of genetic counseling, etc

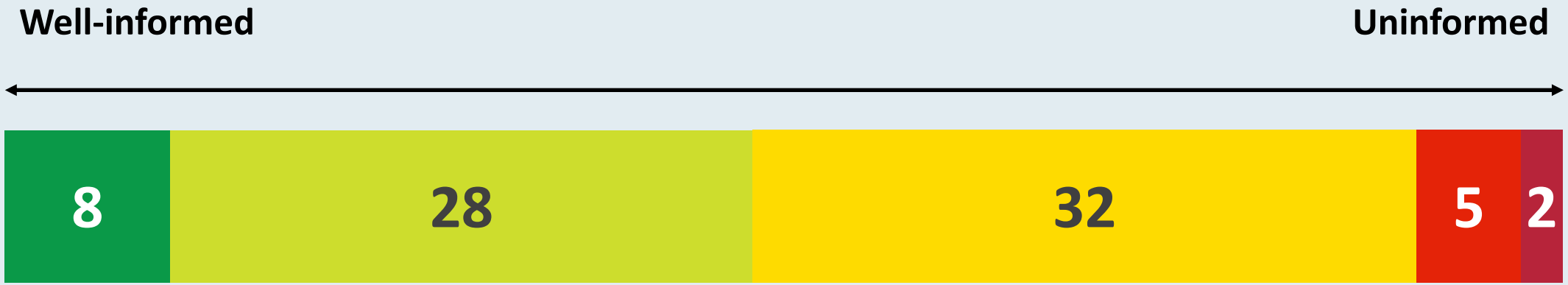
Module 2 – The Evolving Management Paradigm for Relapsed/Refractory OC

- PARP inhibitors as later-line therapy for advanced ovarian cancer
- Use of mirvetuximab soravtansine in advanced ovarian cancer

Module 3 – Novel Agents and Strategies Under Investigation for Advanced OC

- Upifitamab rilsodotin in advanced ovarian cancer
- Tumor treating fields in advanced ovarian cancer

How comfortable/familiar are you with the published data sets, available guidelines, investigator perspectives and ongoing research studies pertaining to adverse events associated with PARP inhibitors and implications for therapeutic selection?



48% feel well informed

Survey of US-based general medical oncologists, May 2023. N = 75

RTP RESEARCH TO PRACTICE

Questions from General Medical Oncologists

- **What is the most common treatment-associated toxicity that leads to the need for a dose reduction?**
- **How do you manage PARP inhibitors in pts with baseline cytopenias?**
- **How often have you seen secondary hematologic malignancies? Any predictors for their occurrence?**
- **Incidence of anemia secondary to PARPi and role of ESAs?**
- **Role of prophylactic antiemetics?**

Survey of US-based general medical oncologists, May 2023. N = 75

Questions from General Medical Oncologists (Continued)

- **I had a BRCA+ patient who within a week became completely pancytopenic (ANC 0, required pRBC and platelet transfusion) on PARP inhibitor (but could already see her CA-125 going down so I suspect she was responding). Would you rechallenge lower dose or not even rechallenge given extreme drop in counts?**
- **If the pt has severe GI side effects with 1 PARP, any role to switch to another one?**
- **I have a 54-year-old ovarian ca patient with BRCA-positive. She has been on olaparib for >3 years as first-line maintenance. I know data is only for 2 years, but she refuses to stop. What is the recommendation?**
- **Concurrent Stage 3 colon cancer and Stage 3 ovarian cancer. How would you select adj therapy? Which do you prioritize treatment for? How long after the colon ca surgery would you give FOLFOX if they could complete carbo/paclitaxel?**

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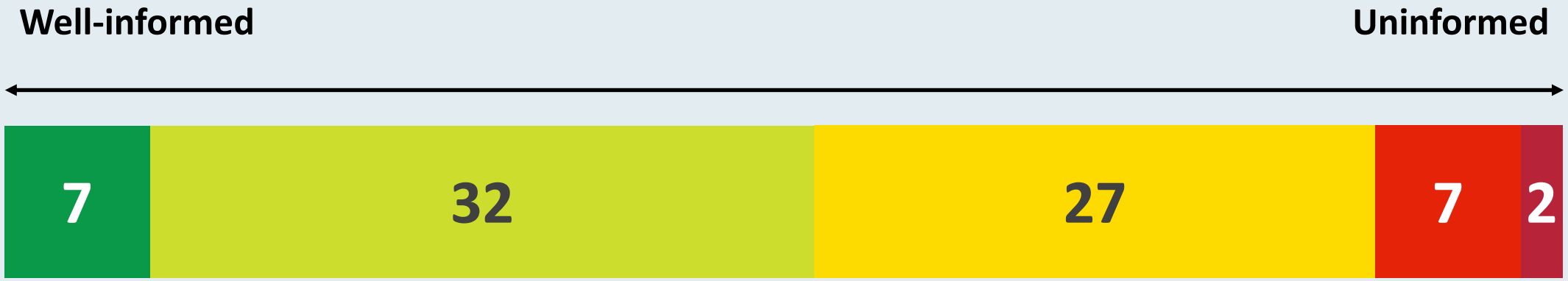
How comfortable/familiar are you with the published data sets, available guidelines, investigator perspectives and ongoing research studies pertaining to other considerations for patients with advanced ovarian cancer and germline BRCA mutations (management of the breast, role of genetic counseling, et cetera)?



52% feel well informed

Survey of US-based general medical oncologists, May 2023. N = 75

RTP RESEARCH TO PRACTICE

Questions from General Medical Oncologists

- **If the patient has a BRCA1 or 2 mutation with advanced ovarian cancer, how is breast management preferably handled? Screening mammograms/breast MRI, mastectomies or observation?**
- **Would the reuse of PARP be indicated if used front line?**
- **Do PARPi work in any cancer harboring a BRCA mutation?**
- **Are somatic mutations similar to germline in response?**
- **Lack of access to genetic counselors in the community setting**
- **What is the maximal age you recommend patients keep ovaries if BRCA1 mutated and desiring fertility preservation?**

Survey of US-based general medical oncologists, May 2023. N = 75

Questions from General Medical Oncologists (Continued)

- **I have a patient with a deleterious BRCA2 mutation and breast cancer unwilling to proceed with prophylactic oophorectomy as she's still interested in childbearing. Is there any role for screening for ovarian cancer in cases such as these?**

Survey of US-based general medical oncologists, May 2023. N = 75

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How comfortable/familiar are you with the published data sets, available guidelines, investigator perspectives and ongoing research studies pertaining to PARP inhibitors as later-line therapy for advanced ovarian cancer?

45% feel well informed

Survey of US-based general medical oncologists, May 2023. N = 75

RTP RESEARCH TO PRACTICE

PARP inhibitors as later-line therapy for advanced ovarian cancer

- Matulonis UA et al. **Final overall survival and long-term safety in the ENGOT-OV16/NOVA phase 3 trial of niraparib in patients with recurrent ovarian cancer.** SGO 2023;Abstract 214.
- Coleman R et al. **Overall survival results from ARIEL3: A phase 3, randomized, double-blind study of rucaparib vs placebo following response to platinum-based chemotherapy for recurrent ovarian carcinoma.** IGCS 2022;Abstract O003.
- Oza AM et al. **Overall survival results from ARIEL4: A phase III study assessing rucaparib vs chemotherapy in patients with advanced, relapsed ovarian carcinoma and a deleterious BRCA1/2 mutation.** ESMO 2022;Abstract 518O.
- Penson R et al. **Final overall survival results from SOLO3: Phase III trial assessing olaparib monotherapy versus non-platinum chemotherapy in heavily pretreated patients with germline BRCA1 - and/or BRCA2-mutated platinum-sensitive relapsed ovarian cancer.** SGO 2022;Abstract 26.
- Selle F et al. **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.** ASCO 2022;Abstract 5558.

ASCO 2022

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.

Abstract 5558

Frederic Selle, Bernard Asselain, François Montestruc, Fernando Bazan, Beatriz Pardo, Vanda Salutari, Frederik Marmé, Anja Ør Knudsen, Alessandra Bologna, Radoslaw Madry, Rosalind Glasspool, Stéphanie Henry, Jacob Korach, Stephanie Lheureux, Bob Shaw, Ana Santaballa, Raffaella Cioffi, Ulrich Canzler, Alain Lortholary, Eric Pujade-Lauraine

Voluntary Withdrawals of Late-Line Indications of PARP Inhibitors

Niraparib – September 14, 2022

The indication for niraparib has been voluntarily withdrawn for the treatment of advanced ovarian, fallopian tube or primary peritoneal cancer in adult patients who have received 3 or more prior chemotherapy regimens and whose cancer is associated with homologous recombination deficiency status. The decision was made in consultation with the US FDA and based on a totality of information from PARP inhibitors for ovarian cancer in the late line treatment setting.

Olaparib – August 26, 2022

The indication for olaparib has been voluntarily withdrawn for the treatment of deleterious or suspected deleterious gBRCAm advanced ovarian cancer in adult patients who have received 3 or more prior lines of chemotherapy. The decision was made in consultation with the US FDA after a recent subgroup analysis indicated a potential detrimental effect on overall survival for olaparib compared to the chemotherapy control arm in the subgroup of patients who had received 3 or more prior lines of chemotherapy in the randomized Phase III study SOLO-3.

Rucaparib – June 10, 2022

The indication for rucaparib has been voluntarily withdrawn for the treatment of BRCA-mutated ovarian cancer after 2 or more chemotherapies. The withdrawal is based on discussions with the US FDA following submission of overall survival data from the ARIEL4 trial, which demonstrated an increased risk of death in participants with BRCA-mutated ovarian cancer treated with rucaparib after 2 or more therapies.

https://medinfo.gsk.com/5f95dbd7-245e-4e65-9f36-1a99e28e5bba/57e2a3fa-7b9b-432f-a220-5976a509b534/57e2a3fa-7b9b-432f-a220-5976a509b534_viewable_rendition__v.pdf?medcommid=REF--ALL-004447; https://www.lynparzahcp.com/content/dam/physician-services/us/590-lynparza-hcp-branded/hcp-global/pdf/solo3-dhcp-final-signed.pdf; https://www.hayesinc.com/news/market-withdrawal-rubraca-for-third-line-ovarian-cancer-indication/

Questions from General Medical Oncologists

- **How do you choose between olaparib, rucaparib and niraparib in a platinum-sensitive recurrence?**
- **What is the utility in adding immunotherapy to PARP inhibitors in late-line setting? Especially if the PD-L1 results are high**
- **67 yo female with Stage 4 high-grade serous ovarian cancer treated with carbo/paclitaxel + bev up front followed by bev maintenance, progressed 7 months after chemo, treated with carbo/paclitaxel again and progressed after 4 months. What would be my next line of therapy for BRCA-negative patients?**

Survey of US-based general medical oncologists, May 2023. N = 75

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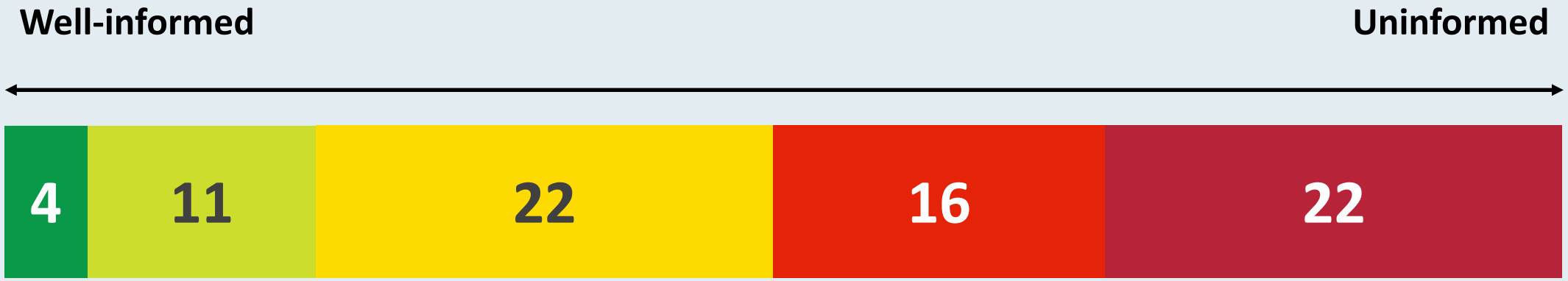
How comfortable/familiar are you with the published data sets, available guidelines, investigator perspectives and ongoing research studies pertaining to the use of mirvetuximab soravtansine in advanced ovarian cancer?



20% feel well informed

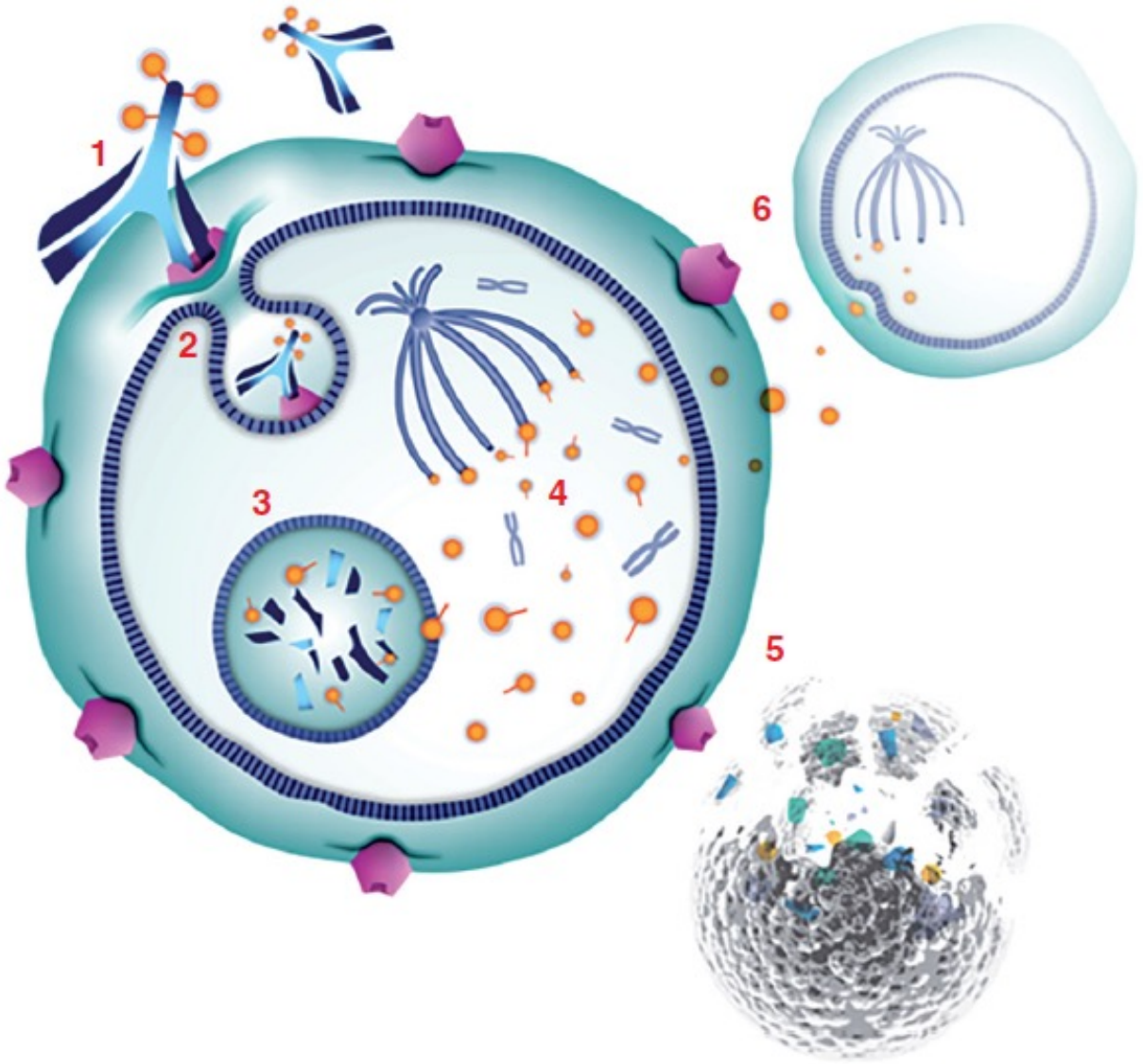
Survey of US-based general medical oncologists, May 2023. N = 75

RTP RESEARCH TO PRACTICE

Use of mirvetuximab soravtansine in advanced ovarian cancer

- Matulonis UA et al. **Efficacy and safety of mirvetuzimab soravtansine in patients with platinum-resistant ovarian cancer with high folate receptor alpha expression: Results from the SORAYA study.** *J Clin Oncol* 2023;41(13):2436-45.
- Moore KN et al. **Phase III MIRASOL (GOG 3045/ENGOT-ov55) study: Initial report of mirvetuximab soravtansine vs investigator's choice of chemotherapy in platinum-resistant, advanced high-grade epithelial ovarian, primary peritoneal, or fallopian tube cancers with high folate receptor-alpha expression.** ASCO 2023;Abstract LBA5507.

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

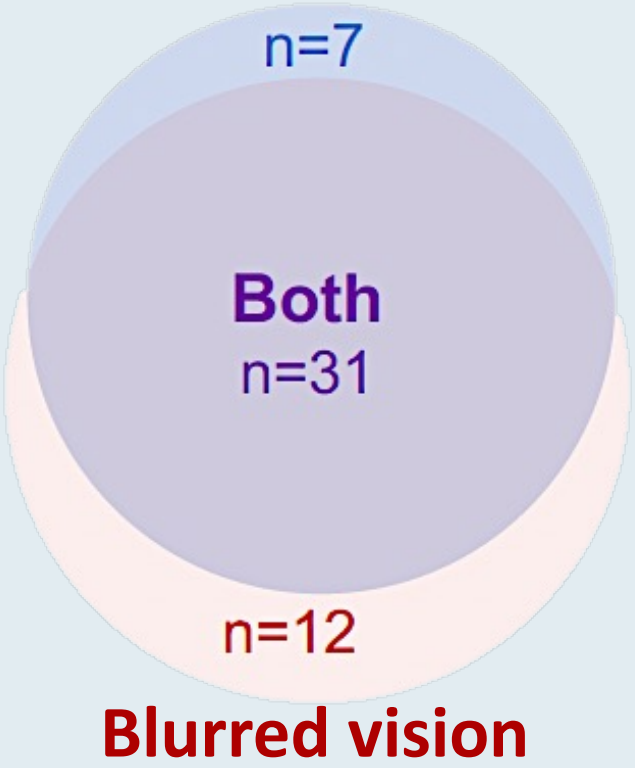
(6) Active metabolites can also diffuse into neighboring cells and induce further cell death — in other words, bystander killing

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

RTP RESEARCH TO PRACTICE

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 patients with grade 2–3 events had resolved to grade 0–1
  – 9 patients still receiving MIRV 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 et al. SGO 2022;Abstract LBA4.

Phase III MIRASOL (GOG 3045/ENGOT-ov55) Study: Initial Report of Mirvetuximab Soravtansine vs Investigator's Choice of Chemotherapy in Platinum-Resistant, Advanced High-Grade Epithelial Ovarian, Primary Peritoneal, or Fallopian Tube Cancers with High Folate Receptor-Alpha Expression

Moore KN et al.

ASCO 2023;Abstract LBA5507.
Sunday, June 4th, 7:30 AM CDT

Questions from General Medical Oncologists

- **Is folate receptor testing included in the standard molecular panel, or is it a separate test?**
- **The best way to manage ocular toxicity is…?**
- **How was the quality of life of patients in this trial, as this was a very heavily pretreated population?**
- **I had a patient with what I thought was Grade 1 pneumonitis from mirvetuximab and pulmonologist thought was disease in the lung. Area was difficult to biopsy due to location/distribution. We are getting PET, but are there radiographic tips to delineate this?**
- **I have several patients with folate receptor alpha expression who are hesitant to receive the drug because of what they've read**

Survey of US-based general medical oncologists, May 2023. N = 75

Questions from General Medical Oncologists (Continued)

- **Does it work in "ovarian visceral crisis" when you need a rapid response and assuming eligible based on testing?**
- **A patient with metastatic ovarian cancer has progressed on 3rd-line therapy. We are considering use of mirvetuximab, but we cannot get an ophthalmologist appointment for 3 months. A local optometrist is not familiar with this drug but is willing to research and see the patient. Would you proceed with this support?**

Survey of US-based general medical oncologists, May 2023. N = 75

Agenda

Module 1 – Up-Front Treatment for Advanced Ovarian Cancer (OC)

- Front-line maintenance therapy for patients with advanced ovarian cancer
- Adverse events associated with PARP inhibitors and implications for therapeutic selection
- Other considerations for patients with advanced ovarian cancer and germline BRCA mutations: Management of the breast, role of genetic counseling, etc

Module 2 – The Evolving Management Paradigm for Relapsed/Refractory OC

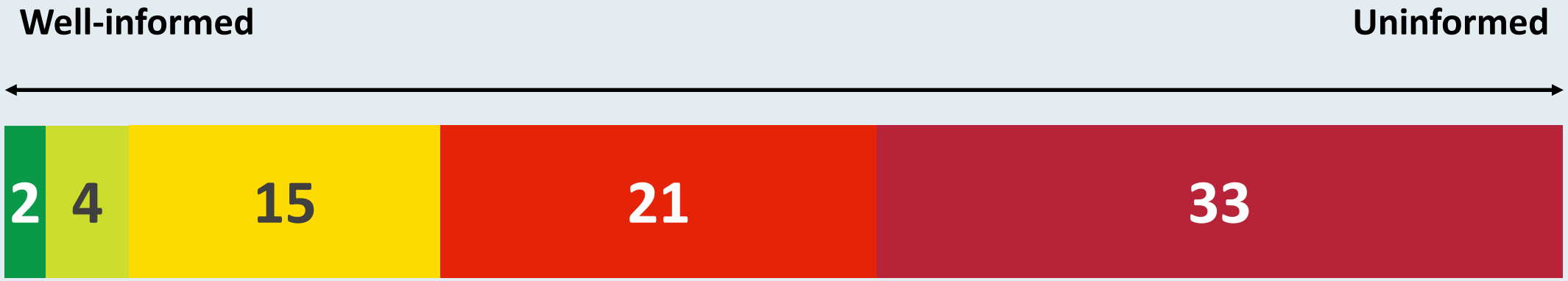
- PARP inhibitors as later-line therapy for advanced ovarian cancer
- Use of mirvetuximab soravtansine in advanced ovarian cancer

Module 3 – Novel Agents and Strategies Under Investigation for Advanced OC

- Upifitamab rilsodotin in advanced ovarian cancer
- Tumor treating fields in advanced ovarian cancer

RTP RESEARCH TO PRACTICE

How comfortable/familiar are you with the published data sets, investigator perspectives and ongoing research studies pertaining to upifitamab rilsodotin in advanced ovarian cancer?



8% feel well informed

Survey of US-based general medical oncologists, May 2023. N = 75

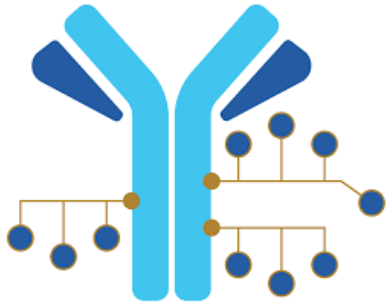
RTP RESEARCH TO PRACTICE

Upifitamab rilsodotin in advanced ovarian cancer

- Richardson DL et al. **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.** SGO 2022;Abstract 76.
- Richardson DL et al. **UPLIFT (ENGOT-ov67/GOG-3048): A pivotal cohort of the XMT-1536-1 trial of upifitamab rilsodotin (XMT-1536; UpRi), a NaPi2b-directed antibody-drug conjugate (ADC), in platinum-resistant ovarian cancer**. IGCS 2022;Abstract TiP426.
- Richardson DL et al. **UP-NEXT (GOG-3049/ENGOT-ov71-NSGO-CTU): A study of upifitamab rilsodotin (UpRi), a NaPi2b-directed antibody-drug conjugate (ADC) in platinum-sensitive recurrent ovarian cancer.** IGCS 2022;Abstract TiP453.
- Hays J et al. **UPGRADE: Phase 1 combination trial of the NaPi2b-directed antibody-drug conjugate (ADC) upifitamab rilsodotin (UpRi; XMT-1536) in patients with ovarian cancer.** IGCS 2022;Abstract TiP446.

-

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



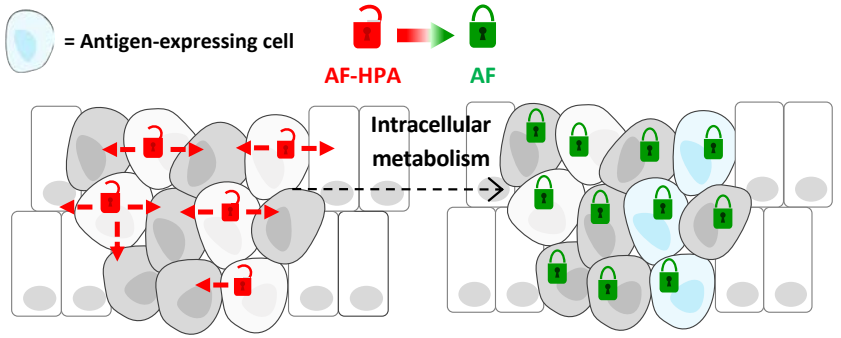
UpRi

Antibody: Humanized monoclonal anti-NaPi2b[1]

Linker: Polymer scaffold; cleavable ester linker[2]

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

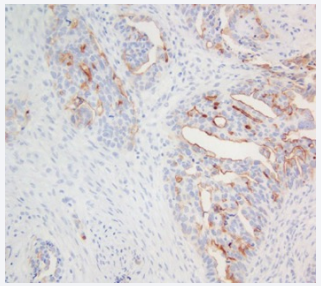
Drug-to-Antibody Ratio: ~10



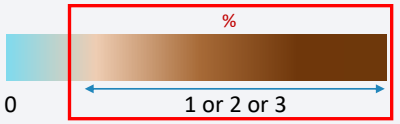
Upon ADC internalization into tumor cells and efficient release of payload, AF-HPA payload is metabolized to AF that remains highly potent but loses the ability to cross the cell membrane, locking it in the tumor, controlling the bystander effect, and consequently limiting impact on adjacent healthy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



ADC, antibody drug conjugate; AF, Auristatin F; AF-HPA, auristatin F-hydroxypropylamide; IHC, immunohistochemistry; NaPi2b, sodium-dependent phosphate transport protein 2B; TPS, tumor proportion score; UpRi, upifitamab rilsodotin.

1. Bodyak ND et al. *Mol Cancer Ther.* 2021;20(5):885–895. 2. Mersana. Data on File. 2022. 3. Tolcher AW et al. ASCO Annual Meeting 2019; Abstract 3010.
4. Lin K et al. *Clin Cancer Res*. 2015;21(22):5139–5150.

Richardson DL et al. SGO 2022;Abstract 76.

UpRi Phase 1b Study — Ovarian Cancer Expansion Cohort Study Design

Study Closed for Enrollment

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)

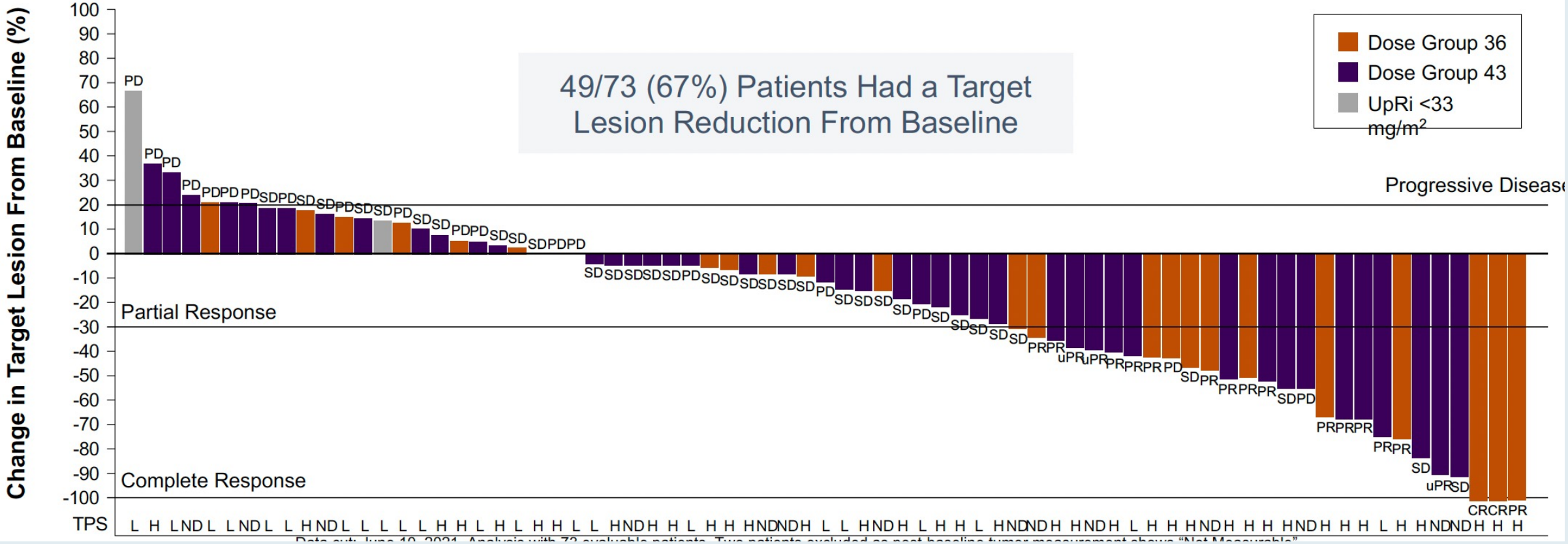
Assessment: Tumor imaging (MRI or CT) at baseline and every 2nd cycle; response assessed per RECIST v1.1

Richardson DL et al. SGO 2022;Abstract 76.

RTP RESEARCH TO PRACTICE

Best Response by UpRi Dose Group

Similar Tumor Reduction in Both Dose Groups: Two-thirds of Patients Had Reductions in Target Tumor Lesions by RECIST 1.1



Richardson DL et al. SGO 2022;Abstract 76.

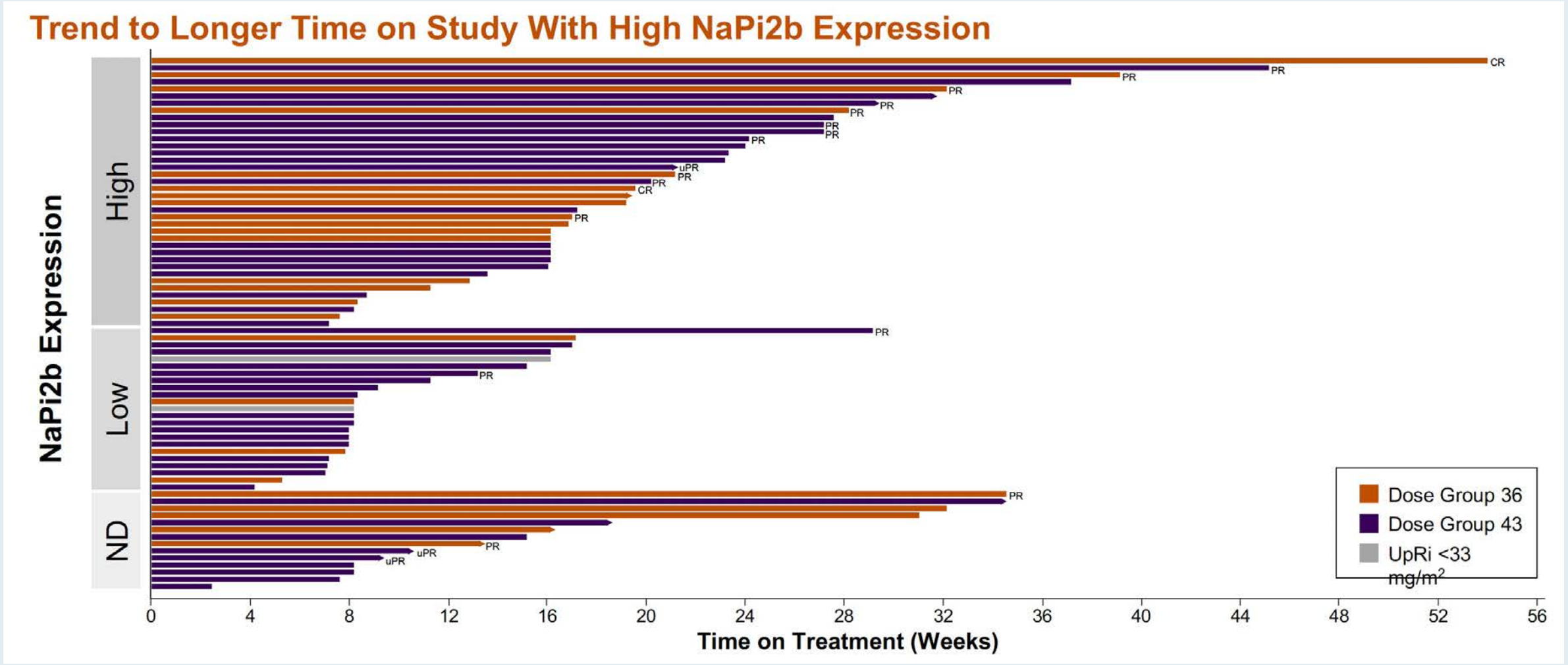
Confirmed ORR by UpRi Dose Group, NaPi2b Level and Duration of Response

		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.

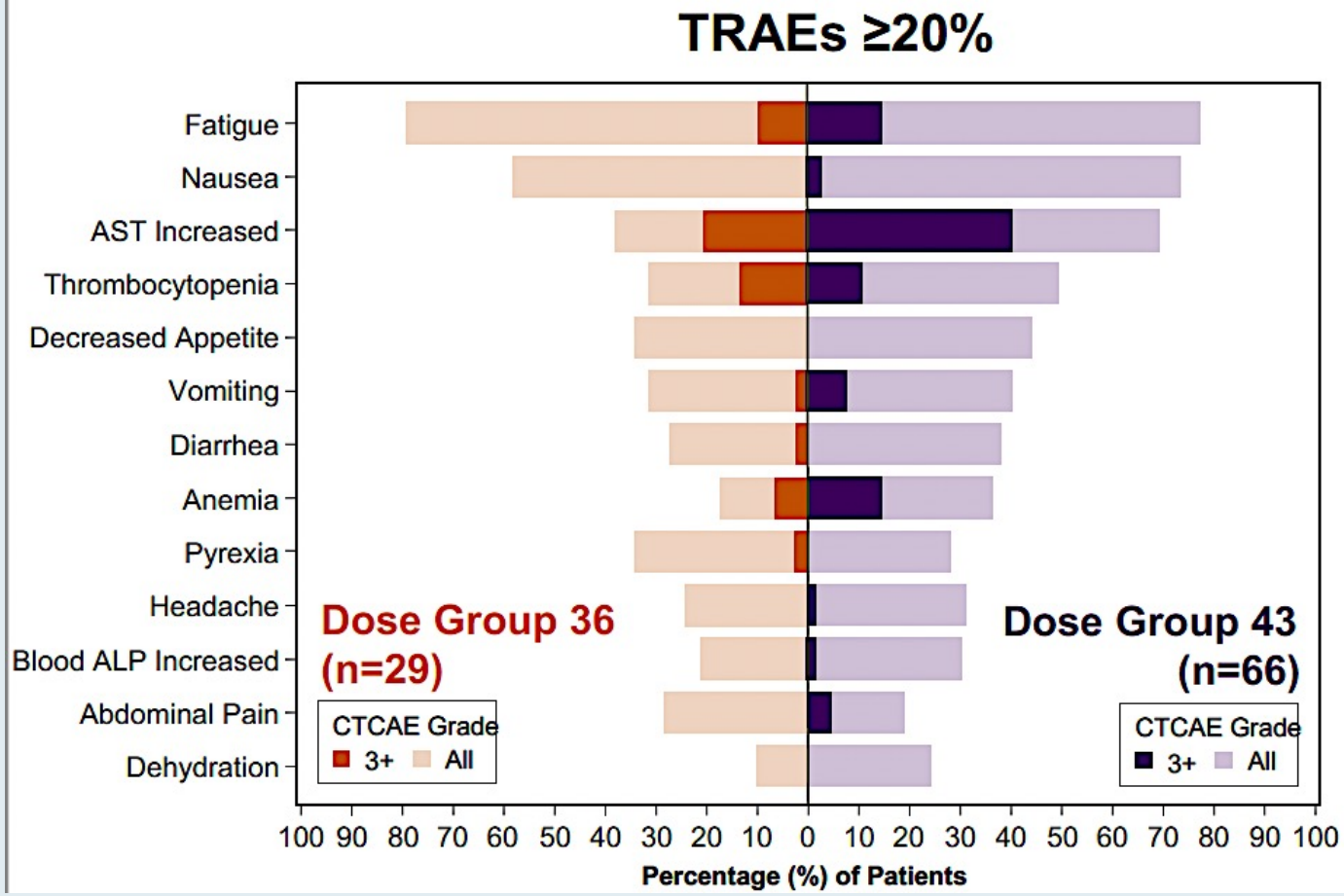
Time on UpRi Study in Evaluable Patients



Richardson DL et al. SGO 2022;Abstract 76.

UpRi Phase 1b Trial: Treatment-Related AEs 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.

RTP RESEARCH TO PRACTICE

Questions from General Medical Oncologists

- **What is the mechanism of action of this medication?**
- **What is the incidence of NaPi2b-positive tumors in high-grade serous ovarian cancers? Does this increase or decrease with treatment courses?**
- **What factors impact your decision to offer this agent?**
- **How do you select based on biomarker?**
- **If this is an antibody-drug conjugate, why are clinical trials combining it with platinum chemo? Does it sensitize cancer for the drug? Or vice versa? I believe NaPi2B is IHC testing. How do we get pathologists to test for this before using up all the tissue?**

Survey of US-based general medical oncologists, May 2023. N = 75

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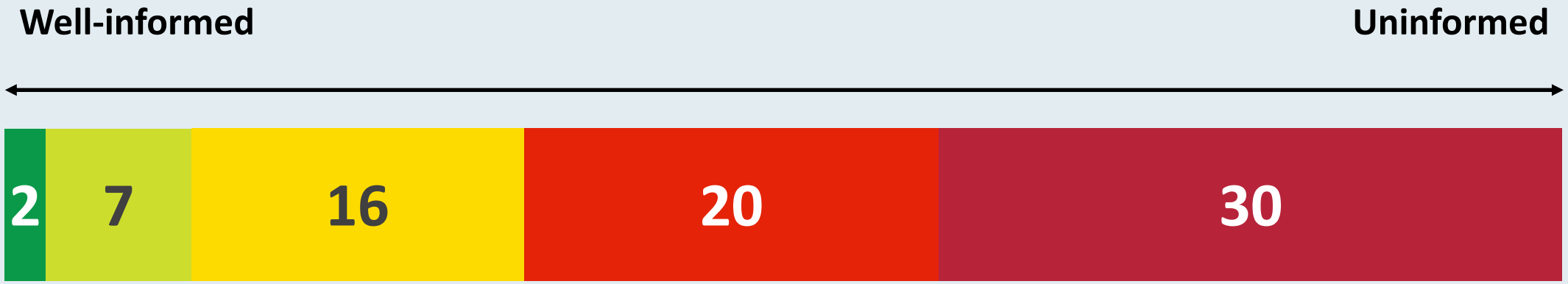
RTP RESEARCH TO PRACTICE

How comfortable/familiar are you with the published data sets, investigator perspectives and ongoing research studies pertaining to tumor treating fields in advanced ovarian cancer?



12% feel well informed

Survey of US-based general medical oncologists, May 2023. N = 75

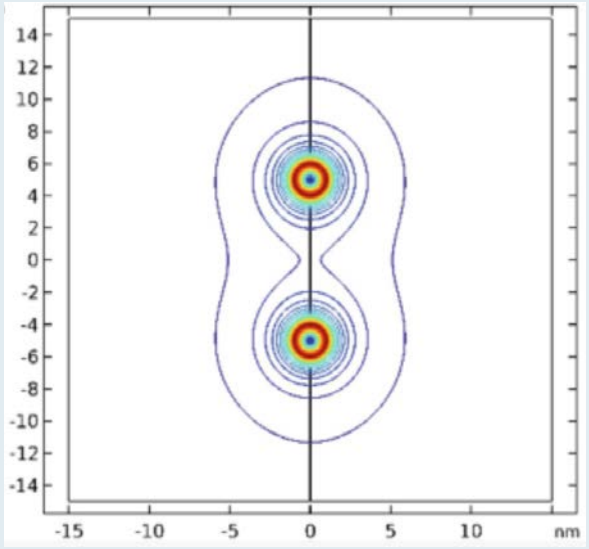
RTP RESEARCH TO PRACTICE

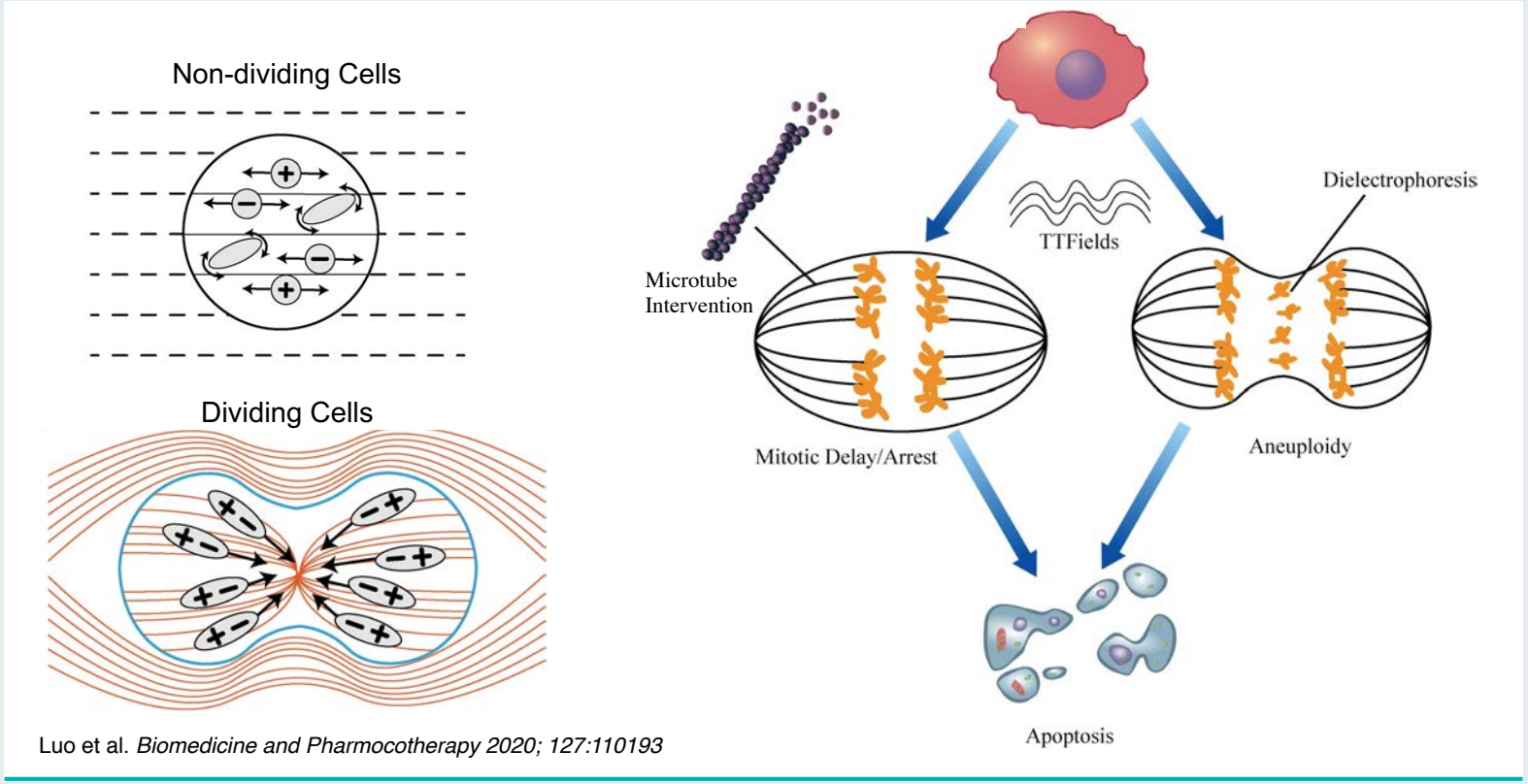
Tumor treating fields in advanced ovarian cancer

- Vergote I et al. **Tumor treating fields in combination with paclitaxel in recurrent ovarian carcinoma: Results of the INNOVATE pilot study.** *Gynecol Oncol* 2018;150(3):471-7.
- Vergote I et al. **Phase 3 trial of tumor treating fields concomitant with weekly paclitaxel for platinum-resistant ovarian cancer: ENGOT-ov50/GOG-329/INNOVATE-3.** IGCS 2020;Abstract 358.

Tumor Treating Fields (TTFields)

Dividing Cell under TTFields
Selective Electric Field Sensitivity





Luo et al. *Biomedicine and Pharmocotherapy 2020; 127:110193*

Luo C et al. *Biomed Pharmacother* 2020;127:110193.

RTP RESEARCH TO PRACTICE

TTFields Mechanism of Action

TTFields therapy mechanism of action

1

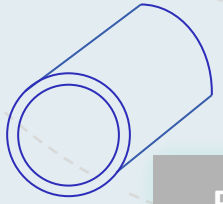
DDR DOWNREGULATION

R-loop formation disruption
Red. replication fork speed
Chromatid aberrations
Downregulation of the FA-BRCA pathway

2

INTERFERENCE IN CELL MOBILITY AND MIGRATION

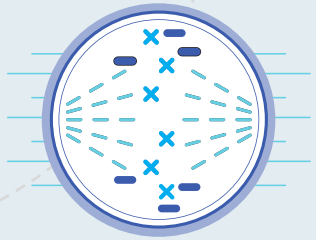
Actin bundling and formation of focal adhesions
Loss of cytoskeletal directionality



3

PERMEABILITY

Tight junction protein delocalisation in endothelial cells



4

DISRUPTION OF MITOSIS

Diminished microtubule abundance
Red. mitotic spindle assembly
Septin disruption and cytoplasmic blebbing
Organelle migration to cleavage furrow

5

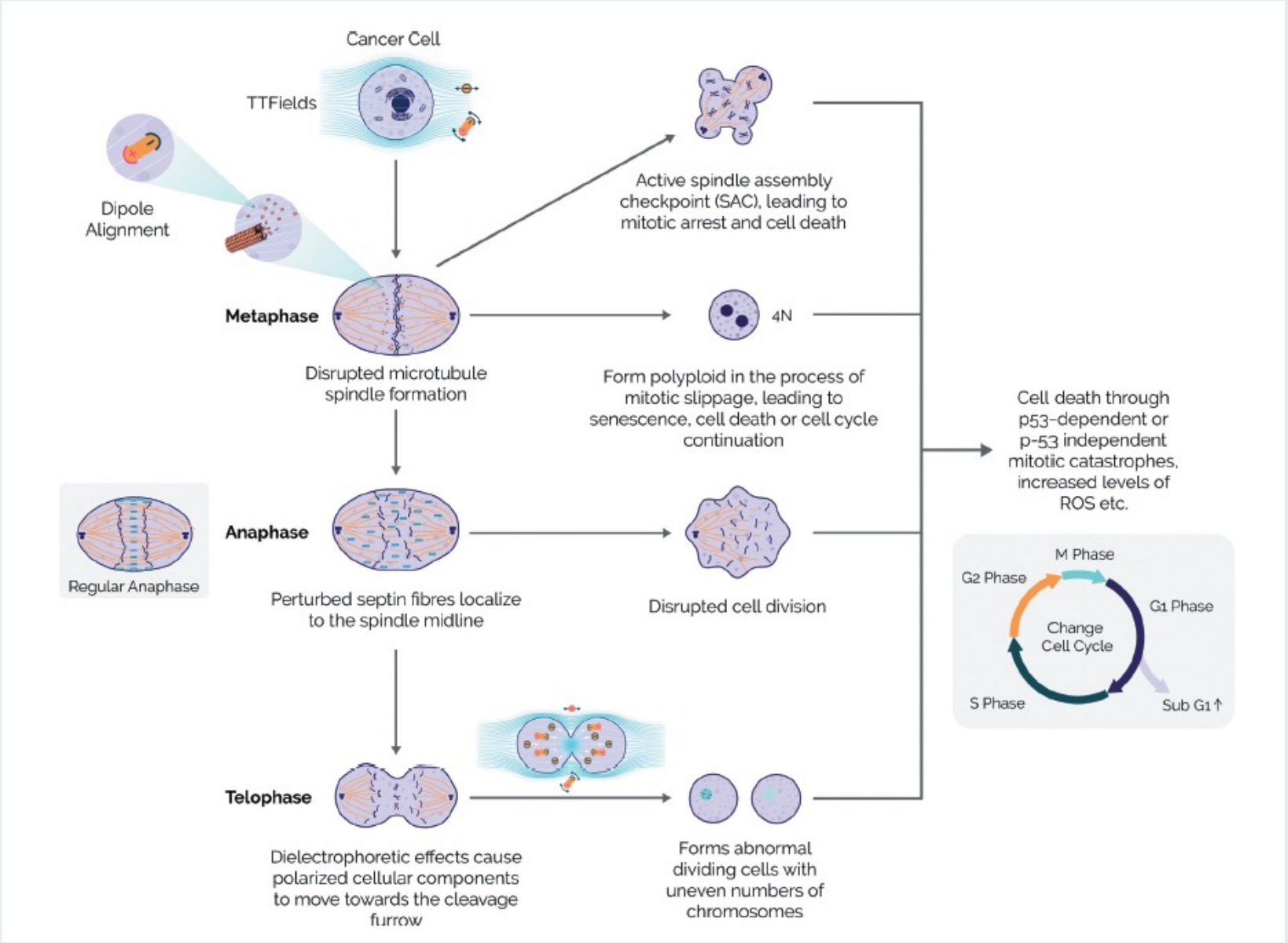
ENHANCEMENT OF ANTITUMOR IMMUNITY

Activation of immunogenic cell death
Recruitment and infiltration of tumor leukocytes
Activation of downstream adaptive immunity

Kirson ED, et al. *Cancer Res* 2004;64(9):3288-95;
Mun EJ, et al. *Clin Cancer Res* 2018;24(2):266-75.

Courtesy of Richard T Penson, MD

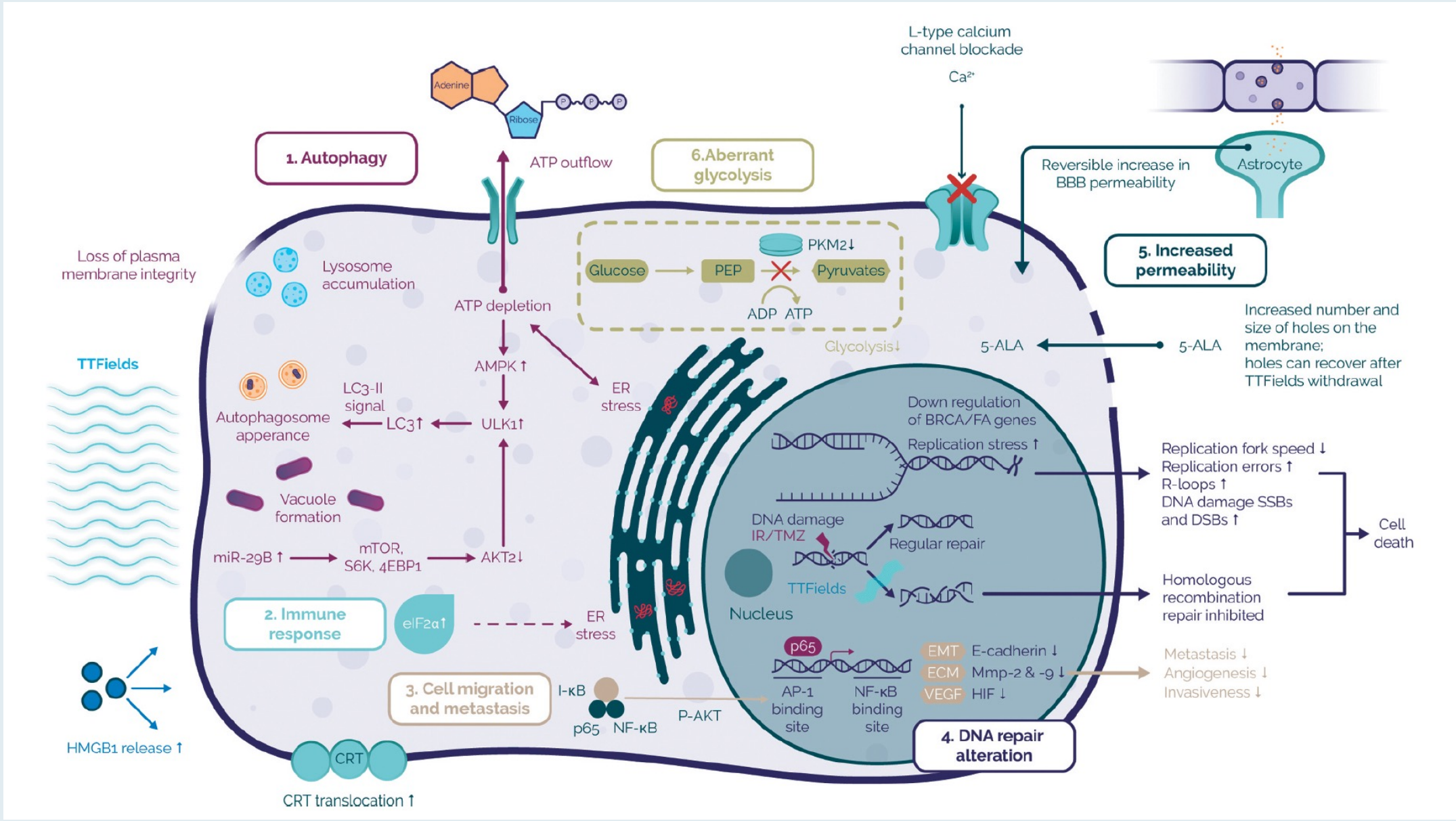
TTFields Effects on the Cell Cycle



Hong P et al. *Expert Rev Mol Diagn* 2022;22(1):19-28.

RTP RESEARCH TO PRACTICE

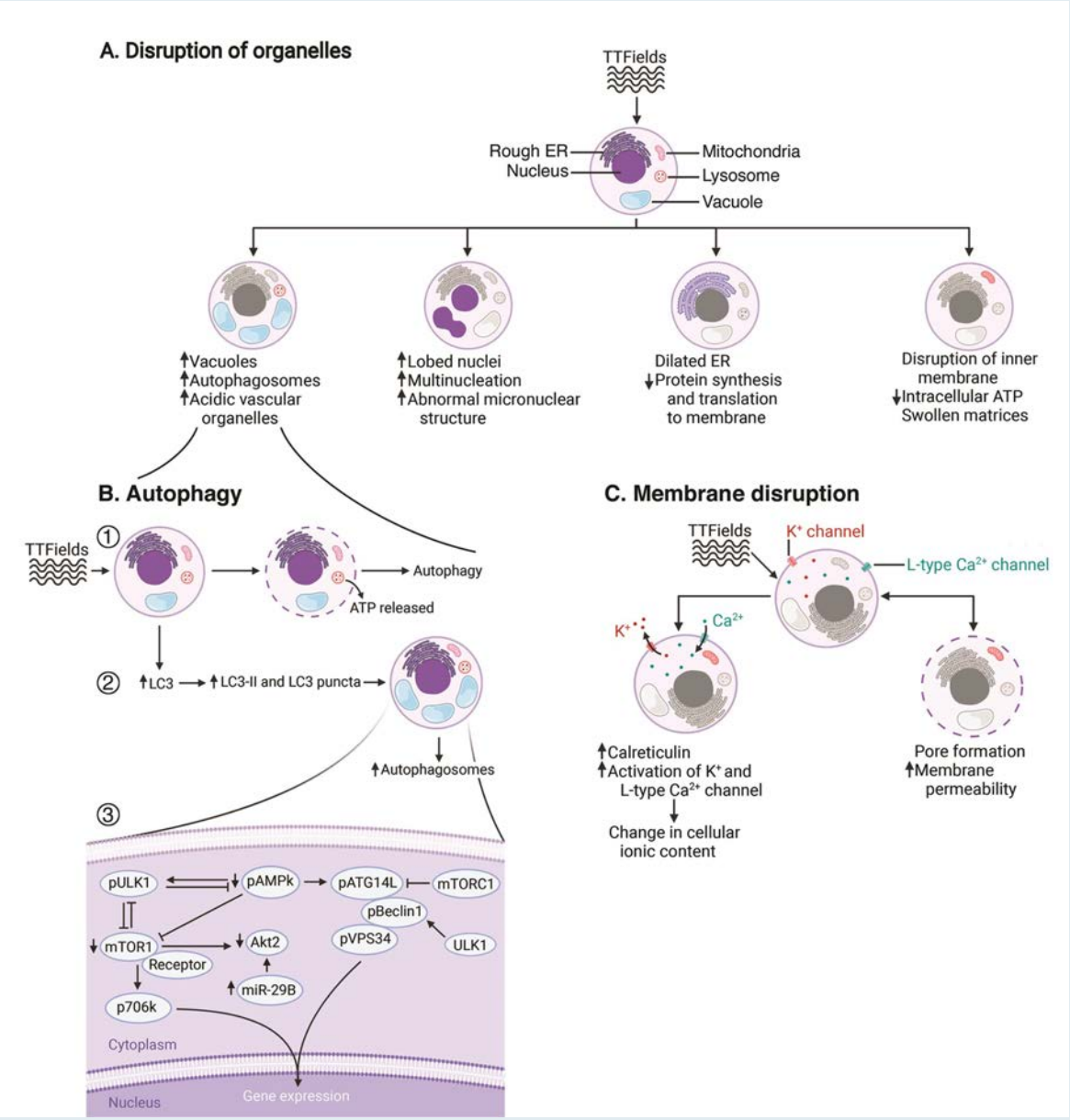
TTFields Antitumor Effects



Hong P et al. *Expert Rev Mol Diagn* 2022;22(1):19-28.

RTP RESEARCH TO PRACTICE

Effects of TTFields on Cell Structure



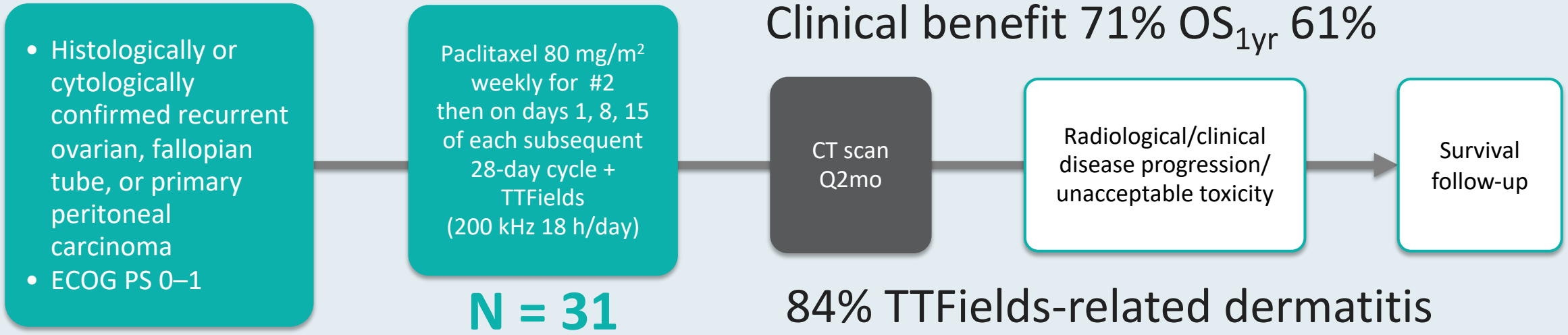
Shams S et al. *J Mol Cell Biol* 2022;14(8):mjac047.

NovoTTF-100L™(O) System: A Portable Medical Device That Allows Normal Daily Activities

Vergote I et al. *Gynecol Oncol* 2018;150(3):471-7.

RTP RESEARCH TO PRACTICE

INNOVATE: Phase 2 Trial Design



Start date: September 2014
Primary completion date: December 2016
Study sites: 5 (Europe)

Primary endpoints:
- AE severity and frequency, No. prematurely DCing TTFields due to skin toxicity

Secondary endpoints:
- PFS, OS, OS_{1yr}, ORR and DOR, CA-125 response and DOR, TTFields usage

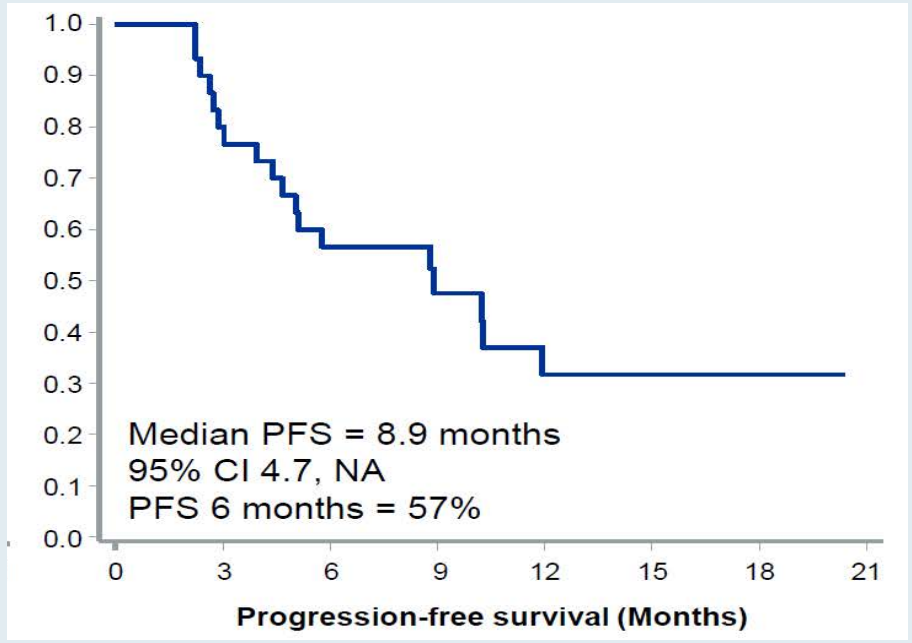
Vergote I et al. *Gynecol Oncol* 2018;150(3):471-7.

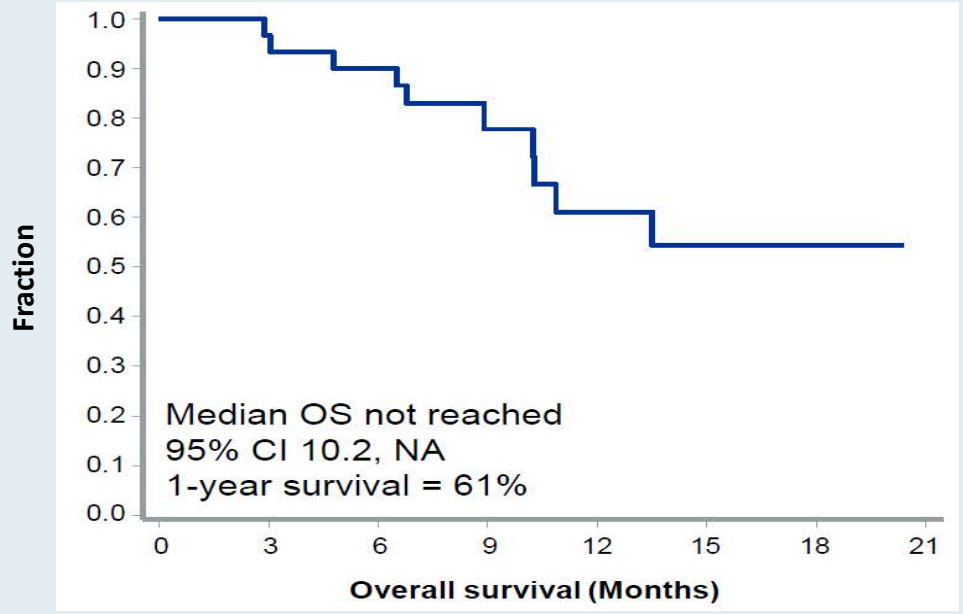
Courtesy of Richard T Penson, MD

RTP RESEARCH TO PRACTICE

INNOVATE: TTFields + Paclitaxel

Outcomes (PROC)	TTFields + paclitaxel (n = 31)
Median OS in months (95% CI)	NR
Survival rates, % (95% CI) 6 months 12 months	 90 (72-97) 61 (37-78)
Median PFS in months (95% CI)	8.9 (4.7-NA)
PFS rates, % (95% CI) 6 months	 57 (37-72)
Best response in patients w/ available radiologic data,* n (%) CR PR SD PD CBR	28 (90%) 0 (0) 7 (25%) 13 (46%) 8 (29%) 20 (71%)





Vergote I et al. *Gynecol Oncol* 2018;150(3):471-7.

RTP RESEARCH TO PRACTICE

INNOVATE: Select Adverse Events

Adverse event	TTFields + paclitaxel (N = 31)	
	Grade 1-2	Grade 3-4
Skin irritation	26 (84%)	2 (6%)
Abdominal pain	13 (42%)	0
Constipation	8 (26%)	0
Diarrhea	15 (48%)	2 (6%)
Nausea	13 (42%)	0
Vomiting	7 (23%)	0
Fatigue	10 (32%)	0
Edema	14 (45%)	0
Dysgeusia	8 (26%)	0
Neuropathy	14 (45%)	0

Vergote I et al. *Gynecol Oncol* 2018;150(3):471-7.

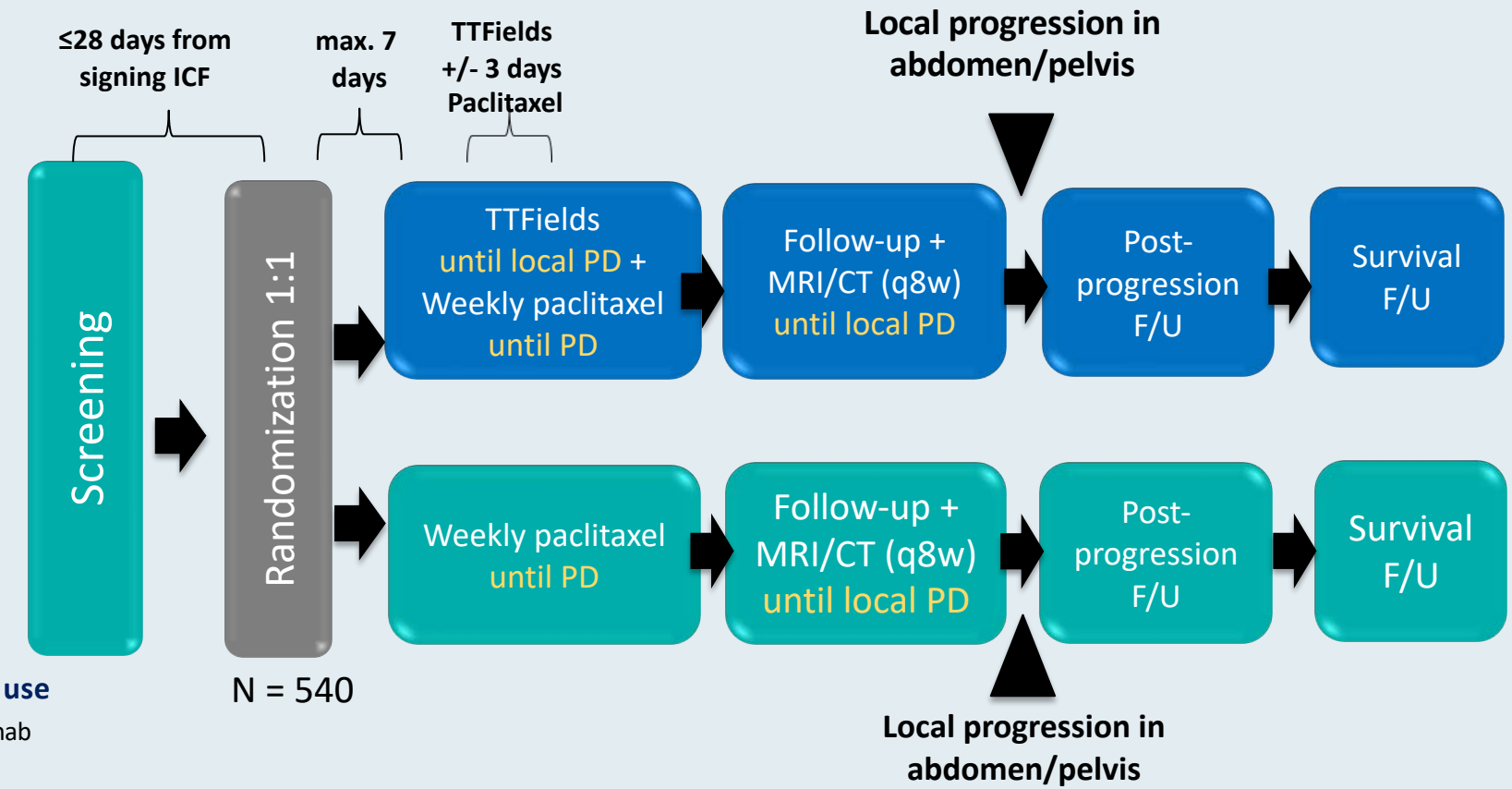
INNOVATE-3 (ENGOT-OV50/GOG-3029) (TTFields, 200 kHz)

Enrollment target (n = 540)

Number of sites (n = 110)

- ENGOT enrollment began March 2019
- GOG enrollment began February 2020

Enrollment closed October 2020



Stratification

- **Prior therapy**
  - no prior systemic therapy following PROC
  - one prior line
  - two prior lines
- **Prior bevacizumab use**
  - prior bevacizumab use
  - no prior bevacizumab
- **BRCA status**
  - mutated BRCA
  - wild type BRCA/ unknown

Primary completion: September 2023

https://clinicaltrials.gov/ct2/show/NCT03940196

RTP RESEARCH TO PRACTICE

Questions from General Medical Oncologists

- **Does this require the patient to wear an attached device for several hours each day?**
- **I know nothing about this topic — a general overview of the data and indications for use would be helpful.**
- **When do you consider this? Ideal candidate? Is ascites an impediment?**
- **What is the incidence of dermatologic toxicity and how do you manage it?**
- **Which pts to use on**
- **Thinking of my experience with using this technique for GBM, where compliance is an issue: What is the adherence of patients to TTF?**

Survey of US-based general medical oncologists, May 2023. N = 75

Impediments you have encountered in delivering high-quality care to patients with ovarian cancer

- **Oral drugs. High co-pays cause delays in starting therapy**
- **A review of the management of carboplatin hypersensitivity reactions and expert approach to this situation would be helpful.**
- **I have a lot of discussions with patients about CA-125 rising and minimal or some progression on imaging, but patient is feeling fine and hesitant to do therapy. When to continue to monitor or step in and resume treatment. This seems to be a common dilemma when trying to figure out the best path for patients.**

Survey of US-based general medical oncologists, May 2023. N = 75

RTP RESEARCH TO PRACTICE

APPENDIX

ASCO 2023 Ovarian Orals

RTP
RESEARCH
TO PRACTICE

Randomized Controlled Phase III Trial of Weekly Paclitaxel ± Ofranergene Obadenovec (VB-111) for Platinum-Resistant Ovarian Cancer (OVAL Study/GOG 3018)

Arend RC et al.

ASCO 2023;Abstract 5505.
Saturday, June 3rd, 5:00 PM CDT

Luveltamab Tazevibulin (STRO-002), an Anti-Folate Receptor Alpha (Folrα) Antibody Drug Conjugate (ADC), Safety and Efficacy in a Broad Distribution of Folrα Expression in Patients with Recurrent Epithelial Ovarian Cancer (OC): Update of STRO-002-GM1 Phase 1 Dose Expansion Cohort

Oaknin A et al.

ASCO 2023;Abstract 5508.

Saturday, June 3rd, 5:24 PM CDT

Neoadjuvant Therapy for Newly Diagnosed Advanced OC

Effectiveness and Safety of Niraparib as Neoadjuvant Therapy in Advanced Ovarian Cancer with Homologous Recombination Deficiency: a Prospective, Multicenter, Exploratory, Phase 2, Single-arm Study（NANT）

Yang Yu[1,2#], Wei Zhang[1,2#], Ronghua Liu[1,2#], Wanying Shan[1,2#], Huayi Li, Jiahao Liu[1,2], Cui Feng[1,2], Yi Huang[3], Bairong Xia[4], Ge Lou[5], Shanyang He[6], Yu Xia[1,2], Siyuan Wang[1,2], Tian Fang[1,2], Zhi Wang[1,2], Rong Liu[1,2], Danhui Weng[1,2], Youguo Chen[7], Kun Song[8], Ke Wang[9], Ping Wang[10], Shuzhong Yao[11], Jundong Li[12], Li Wang[13], Qingshui Li[14], Jinjin Yu[15], Li Hong[16*], Ding Ma[1,2*], Qinglei Gao[1,2*]

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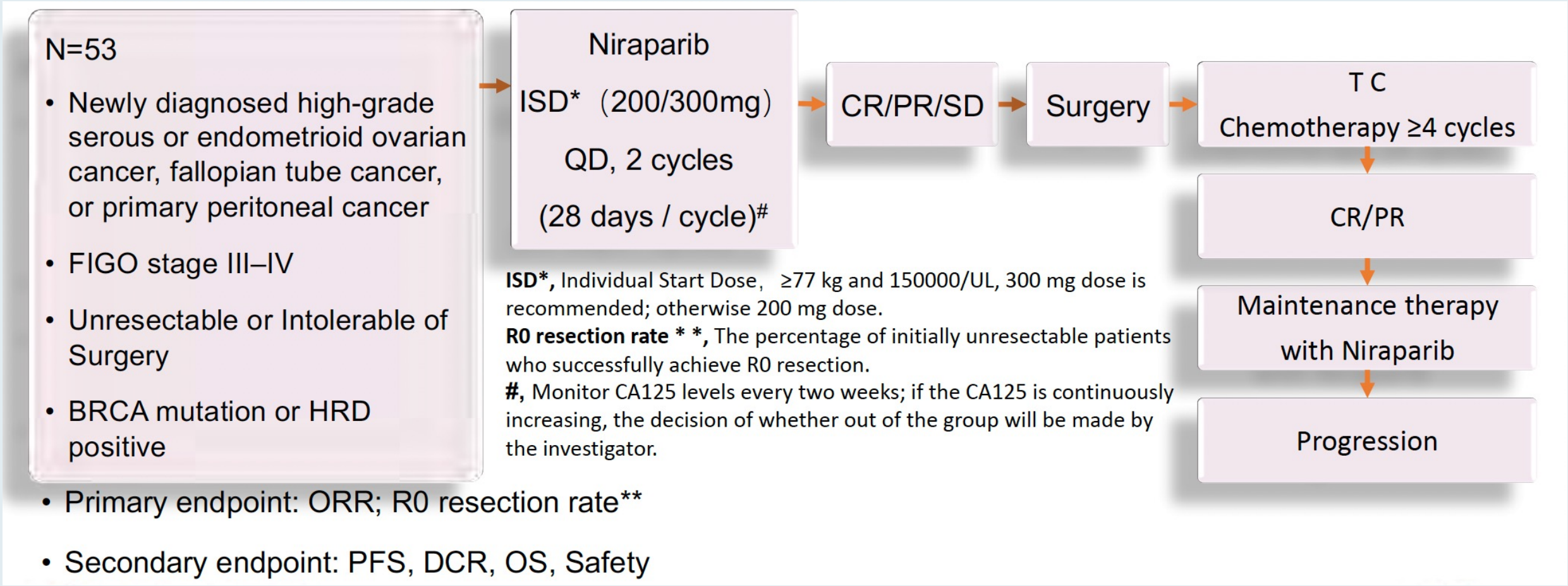
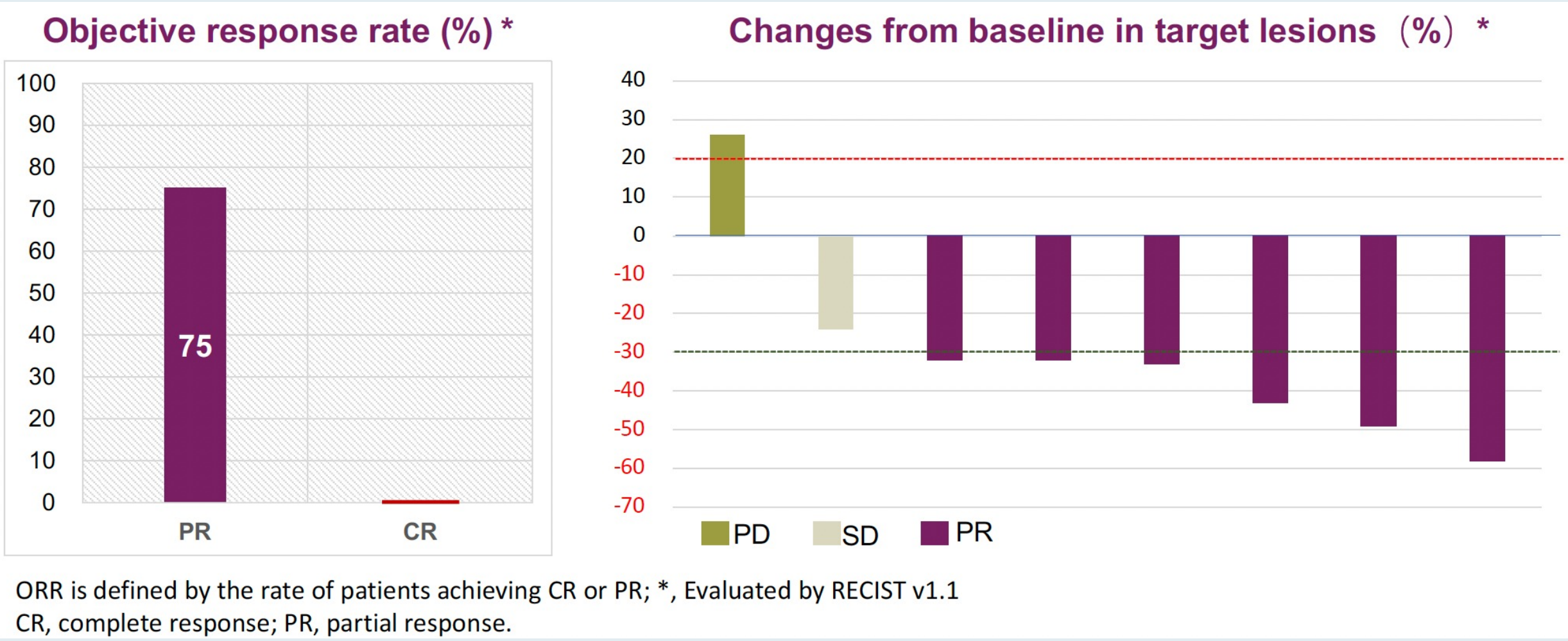
SGO 2022;Abstract 39.

NANT: Phase II Trial of Neoadjuvant Niraparib in Chinese Patients with BRCA mutation or HRD-Positive Advanced Ovarian Cancer



Yu Y et al. SGO 2022;Abstract 39.

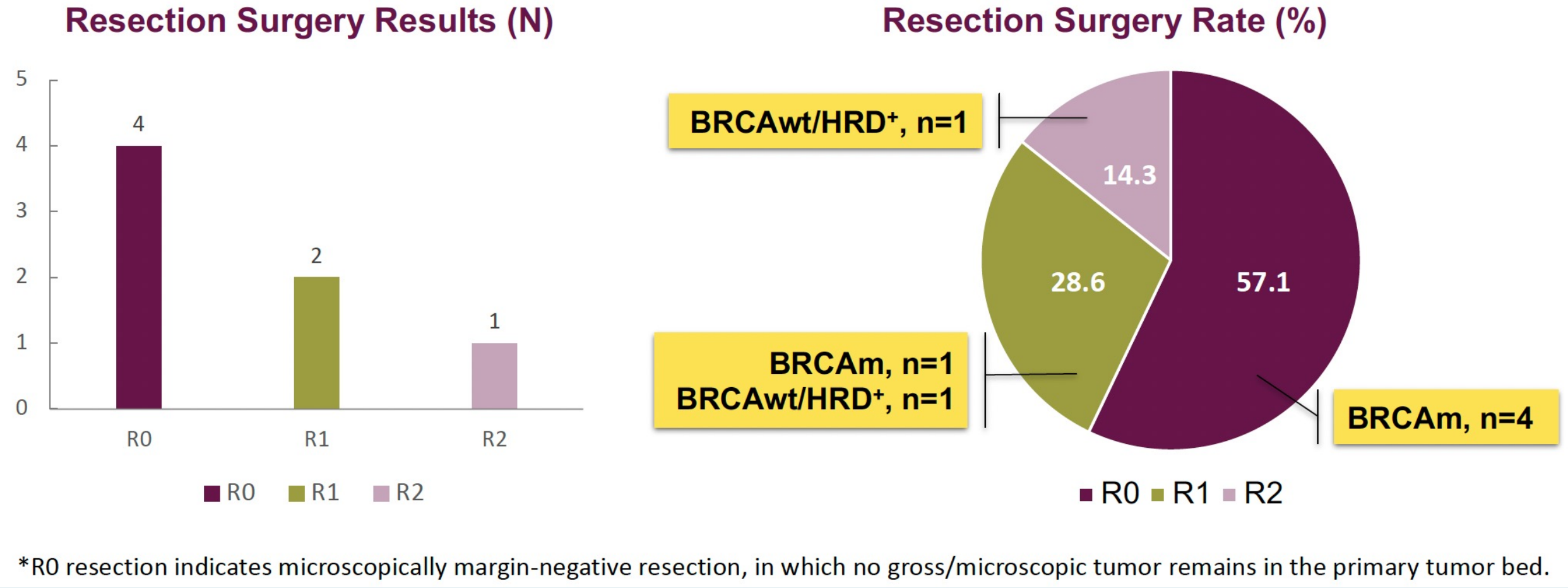
NANT: ORR by Investigator after Niraparib Neoadjuvant Therapy



ORR is defined by the rate of patients achieving CR or PR; *, Evaluated by RECIST v1.1
CR, complete response; PR, partial response.

Yu Y et al. SGO 2022;Abstract 39.

NANT: R0 Resection Rate after Niraparib Neoadjuvant Therapy



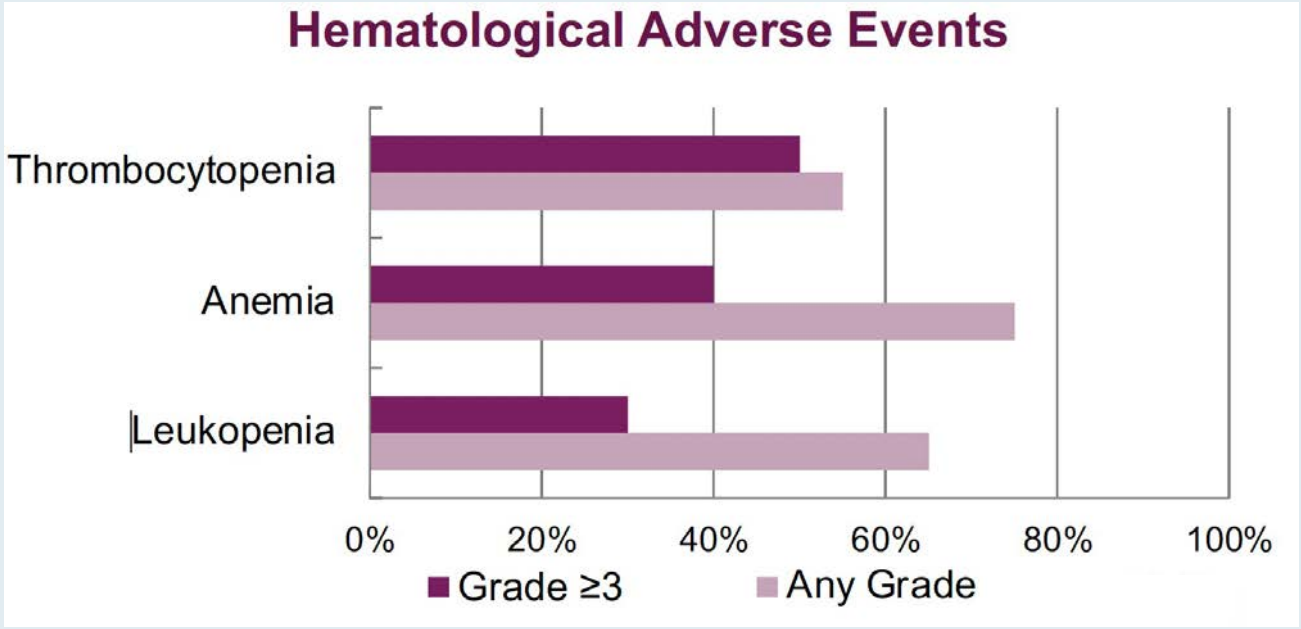
*R0 resection indicates microscopically margin-negative resection, in which no gross/microscopic tumor remains in the primary tumor bed.

Yu Y et al. SGO 2022;Abstract 39.

NANT: Treatment-Emergent Adverse Events and Hematologic Adverse Events with Niraparib

Treatment Emergent Adverse Events

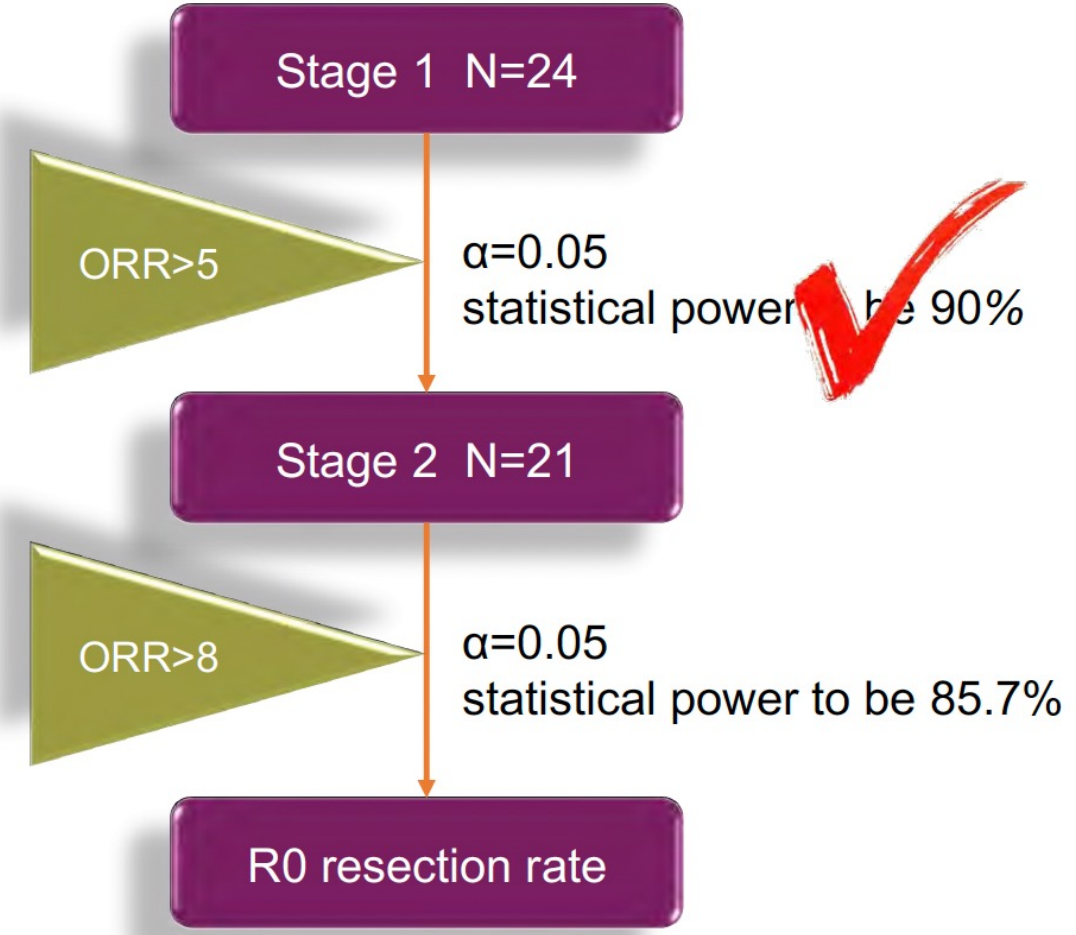
Adverse Events	N (%)
All TEAE	16 (80)
Grade ≥3	13 (65)
Dose reduction	1 (5)
Treatment interruption	12 (60)
Treatment discontinuation	2 (10)
Leading to death	0 (0)



Yu Y et al. SGO 2022;Abstract 39.

NANT: Conclusions

- Neoadjuvant Niraparib monotherapy shows efficacy and tolerable toxicity in BRCA mutation/HRD positive patients with advanced unresectable ovarian cancer.
- The current phase 2 trial has completed stage 1 of Simon's design, and further updated data will be reported after completion of the trial.



Yu Y et al. SGO 2022;Abstract 39.

Final primary analysis in the original cohort of KGOG3046/TRU-D: a phase II study of durvalumab and tremelimumab with front-line neoadjuvant chemotherapy in patients with advanced-stage ovarian cancer

Jung-Yun Lee[1], Junsik Park[1,2], Myong Cheol Lim[3], Byoung-Gie Kim[4], Jae-Weon Kim[5], So Jin Shin[6], Sunghoon Kim[1], Chel Hun Choi[4], Hee Seung Kim[5], and Sang Yoon Park[3] on behalf of KGOG investigators

[1]Yonsei University College of Medicine, Korea, [2]Severance Biomedical Science Institute, Yonsei University College of Medicine, Korea, [3]National Cancer Center, Korea, [4]Sungkyunkwan University, Korea, [5]Seoul National University College of Medicine, Korea, [6]Keimyung University Dongsan Medical Center, Korea

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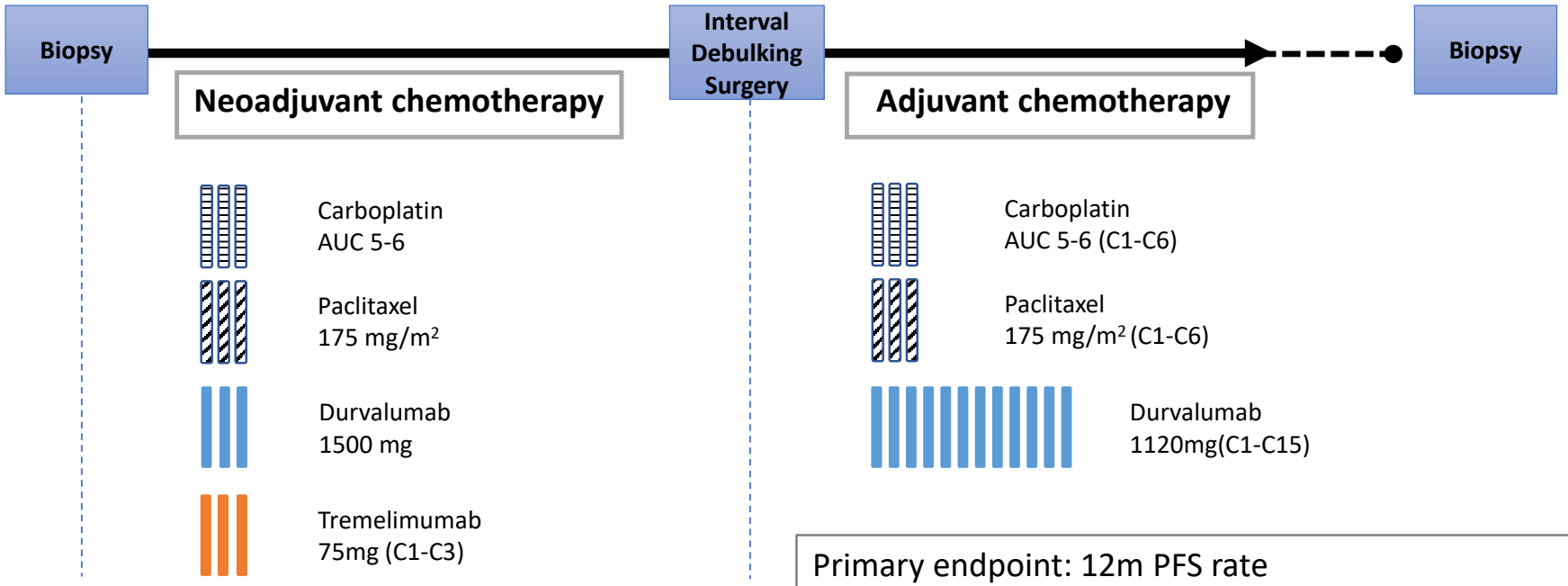
KGOG3046 Phase II Study Design



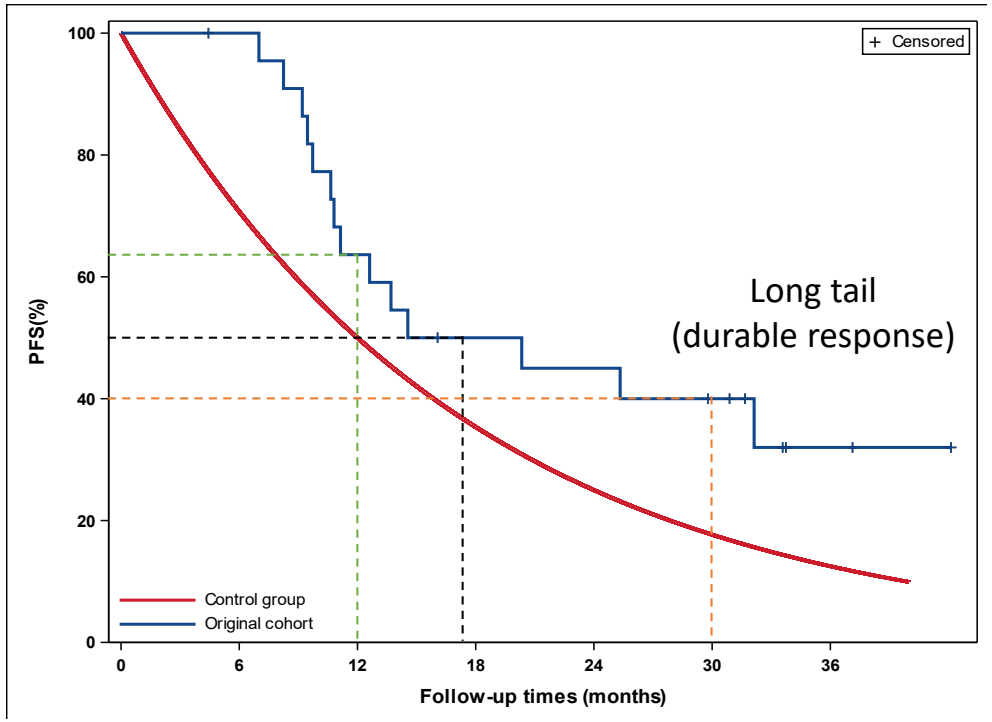
Primary endpoint: 12m PFS rate
Secondary endpoint: PFS, OS, duration of response, pCR rate after NAC, CRS after NAC, R0 rate at IDS, Safety

- Stage IIIC/IV EOC, not eligible for PDS
- Planned enrollment n=24, Safety run-in done after first 7 patients were enrolled

Lee J-Y et al. SGO 2023;Abstract 217.

KGOG3046: 12-month PFS Rate

- One sample log rank test
  - 12-month PFS rate: 63.6% (*P*=0.093)
  - **30-month PFS rate: 40.0% (*P*=0.021)**
- Median follow-up
  - 29.2 months (4.5-42.2)
- Median PFS: 17.5 months
- Historical control (Assumed median PFS was 12 mon and the time has an exponential distribution)



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Lee J-Y et al. SGO 2023;Abstract 217.

RTP RESEARCH TO PRACTICE

KGOG3046: Treatment-Related Adverse Events

	Patients (n=23)	
Events	**Any grade**	**Grade 3-4**
Rash	**16(69.6)**	**3(13.0)**
Neutrophil count decreased	**12(52.2)**	**9(39.1)**
Anemia	9(39.1)	2(8.7)
Aspartate aminotransferase increased	8(34.8)	3(13.0)
Pruritus	8(34.8)	0(0.0)
Alanine aminotransferase increased	7(30.4)	2(8.7)
Amylase increased	5(21.7)	1(4.3)
Pyrexia	5(21.7)	0(0.0)
Febrile neutropenia	4(17.4)	3(13.0)
Feeding disorder	4(17.4)	0(0.0)
Hypothyroidism	4(17.4)	0(0.0)
Lipase increased	4(17.4)	1(4.3)
Neuropathy peripheral	4(17.4)	0(0.0)
Constipation	3(13.0)	0(0.0)
Peripheral sensory neuropathy	3(13.0)	0(0.0)
Thyroiditis	3(13.0)	0(0.0)
Decreased appetite	2(8.7)	0(0.0)
Dyspepsia	2(8.7)	0(0.0)
Hepatitis	2(8.7)	2(8.7)
Hypoalbuminaemia	2(8.7)	0(0.0)
Platelet count decreased	2(8.7)	1(4.3)
Stomatitis	2(8.7)	0(0.0)
Urticaria	2(8.7)	1(4.3)
White blood cell count decreased	2(8.7)	2(8.7)
Pneumonitis	1(4.3)	1(4.3)
Gamma-glutamyltransferase increased	1(4.3)	1(4.3)
Hyponatremia	1(4.3)	1(4.3)
Hypotension	1(4.3)	1(4.3)
Ileal perforation	1(4.3)	1(4.3)
Renal failure	1(4.3)	1(4.3)

Lee J-Y et al. SGO 2023;Abstract 217.

Maintenance Therapy in First Line

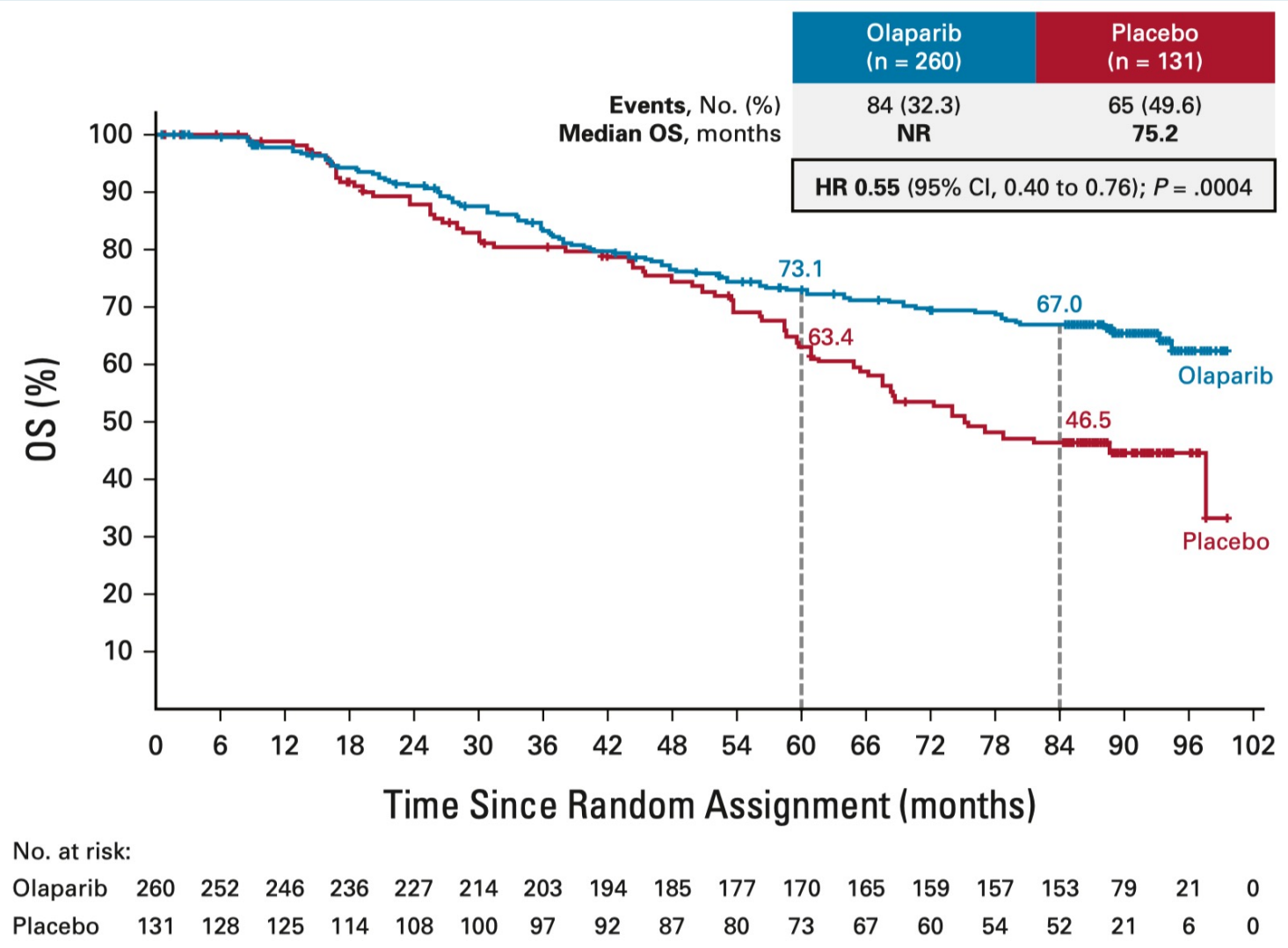
Phase III First-Line PARP Inhibitor Maintenance Trials

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 vs 14 months HR: 0.33	22.1 vs 16.6 months HR: 0.59	22.1 vs 10.9 months HR 0.40	23.5 vs 17.3 months HR: 0.68

PD = disease progression; PFS = progression-free survival

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

SOLO-1: 7-Year Overall Survival



DiSilvestro P et al. *J Clin Oncol* 2023;41:609-17

Overall survival at 7-year follow-up in patients with newly diagnosed advanced ovarian cancer and a BRCA mutation who received maintenance olaparib in the SOLO1/GOG 3004 trial

Paul DiSilvestro,[1] Susana Banerjee,[2] Nicoletta Colombo,[3] Giovanni Scambia,[4] Byoung-Gie Kim,[5] Ana Oaknin,[6] Michael Friedlander,[7] Alla Lisyanskaya,[8] Anne Floquet,[9] Alexandra Leary,[10] Gabe S Sonke,[11] Charlie Gourley,[12] Amit Oza,[13] Antonio González-Martín,[14] Carol Aghajanian,[15] William Bradley,[16] Cara Mathews,[1] John McNamara,[17] Elizabeth S Lowe,[18] Kathleen N Moore[19]

[1]Women & Infants Hospital, Providence, RI, USA; [2]The Royal Marsden NHS Foundation Trust and Institute of Cancer Research, London, UK; [3]University of Milan-Bicocca and Istituto Europeo di Oncologia, Milan, Italy; [4]Università Cattolica del Sacro Cuore-Fondazione Policlinico A. Gemelli, IRCCS, Rome, Italy; [5]Samsung Medical Center, Sungkyunkwan University School of Medicine, Seoul, Korea; [6]Vall d'Hebron University Hospital, Vall d'Hebron Institute of Oncology (VHIO), Barcelona, Spain; [7]University of New South Wales Clinical School, Prince of Wales Hospital, Randwick, NSW, Australia; [8]St Petersburg City Oncology Dispensary, St Petersburg, Russia; [9]Institut Bergonié, Comprehensive Cancer Centre, Bordeaux, and Groupe d'Investigateurs Nationaux pour l'Etude des Cancers Ovariens, France; [10]Institut Gustave-Roussy, Villejuif, and Groupe d'Investigateurs Nationaux pour l'Etude des Cancers Ovariens, France; [11]The Netherlands Cancer Institute, Amsterdam, The Netherlands; [12]Cancer Research UK Edinburgh Centre, University of Edinburgh, Edinburgh, UK; [13]Princess Margaret Cancer Centre, Toronto, ON, Canada; [14]Clínica Universidad de Navarra, Madrid, Spain; [15]Memorial Sloan Kettering Cancer Center, New York, NY, USA; [16]Froedtert and the Medical College of Wisconsin, Milwaukee, WI, USA; [17]Biostatistics, Oncology Biometrics, Oncology R&D, AstraZeneca, Cambridge, UK; [18]Global Medicines Development, Oncology, AstraZeneca, Gaithersburg, MD, USA; [19]Stephenson Oklahoma Cancer Center, Oklahoma City, OK, USA

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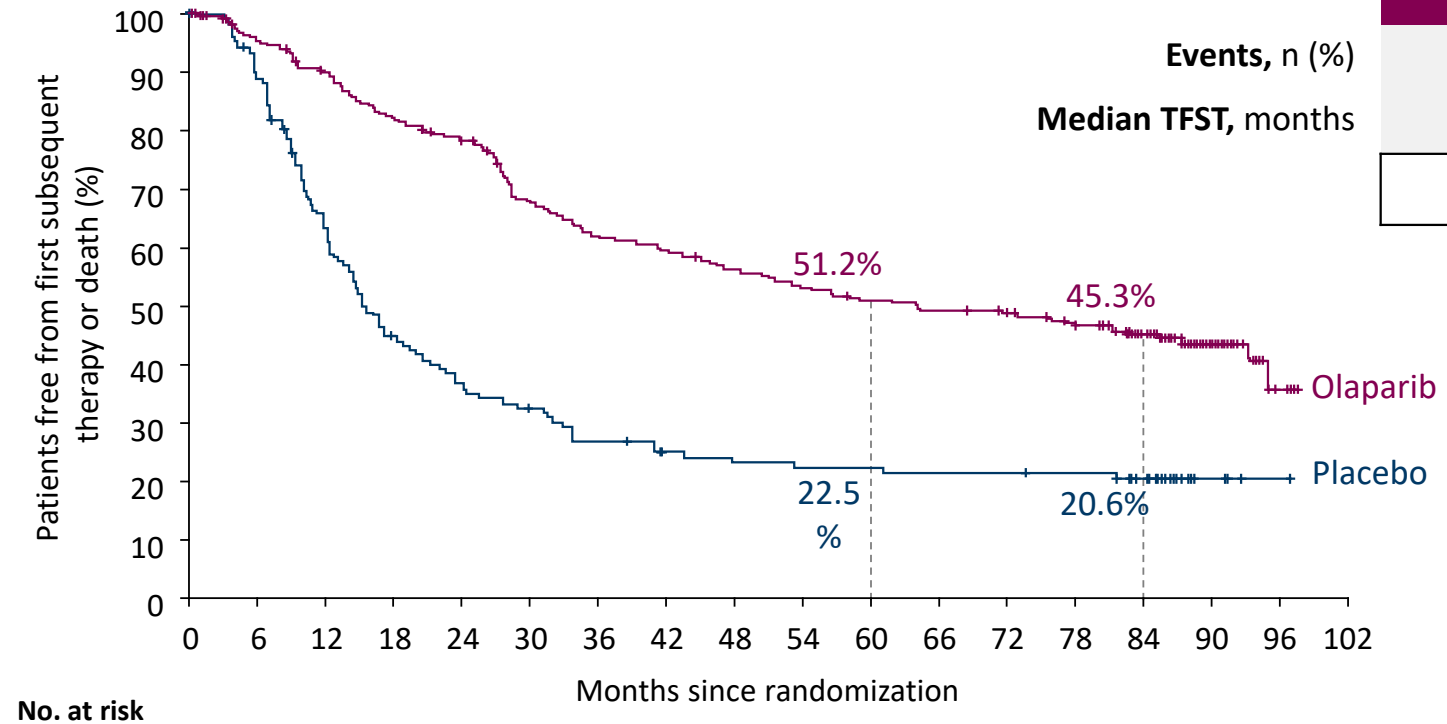
Conducted in partnership with the Gynecologic Oncology Group (GOG 3004)
ClinicalTrials.gov identifier: NCT01844986. This study was sponsored by AstraZeneca and is part of an alliance between AstraZeneca and Merck Sharp & Dohme LLC, a subsidiary of Merck & Co., Inc., Rahway, NJ, USA

DiSilvestro P *et al. J Clin Oncol* 2023;41:609–17

RTP RESEARCH TO PRACTICE

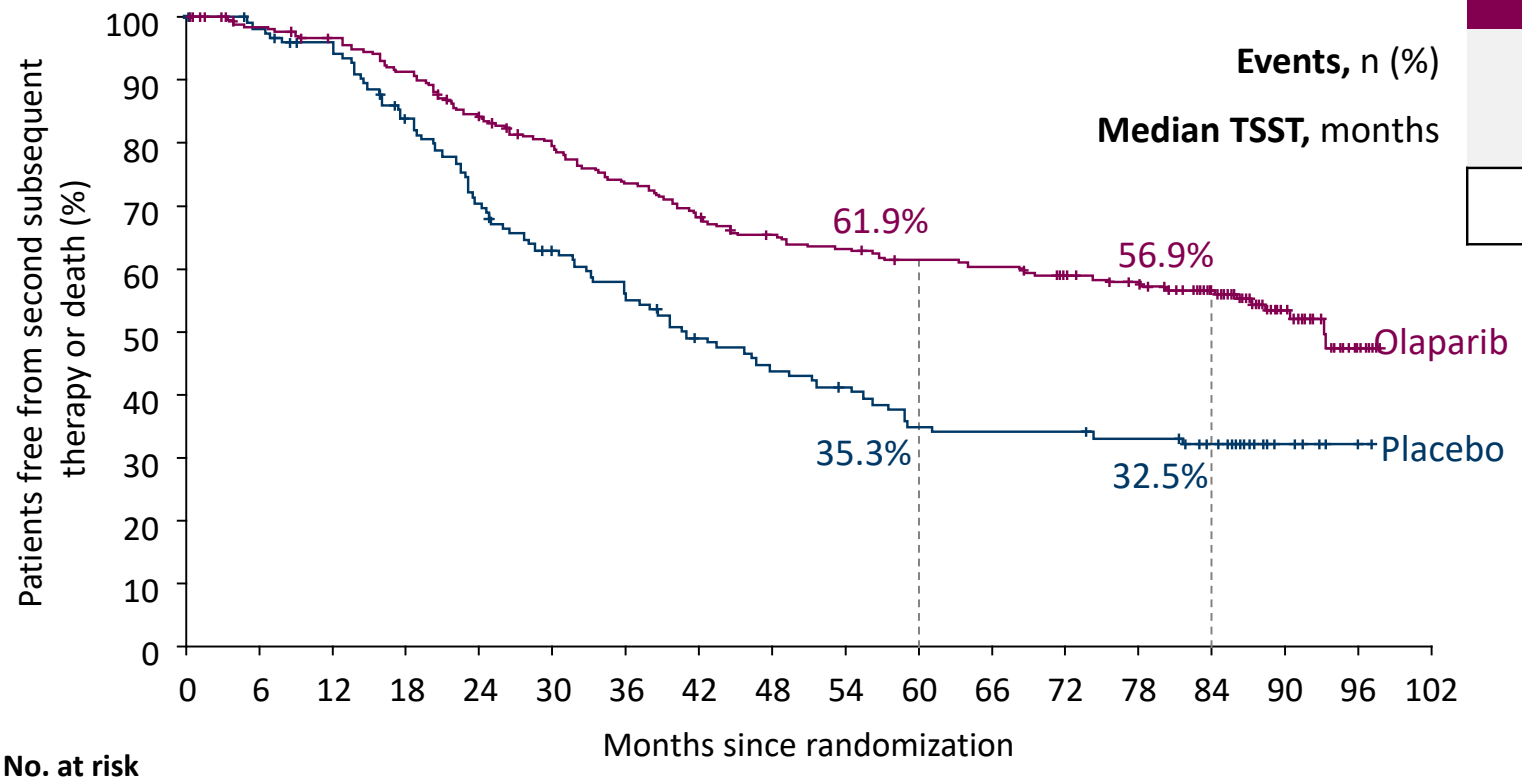
SOLO-1: Time from First Subsequent Therapy or Death



	Olaparib (N=260)	Placebo (N=131)
Events, n (%)	135 (51.9)	98 (74.8)
Median TFST, months	**64.0**	**15.1**
HR 0.37 (95% CI 0.28–0.48)		

DiSilvestro P et al. SGO 2023;Abstract 215.

SOLO-1: Time from Second Subsequent Therapy or Death



	Olaparib (N=260)	Placebo (N=131)
Events, n (%)	110 (42.3)	80 (61.1)
Median TSST, months	**93.2**	**40.7**
HR 0.50 (95% CI 0.37–0.67)		

DiSilvestro P et al. SGO 2023;Abstract 215.

RTP RESEARCH TO PRACTICE

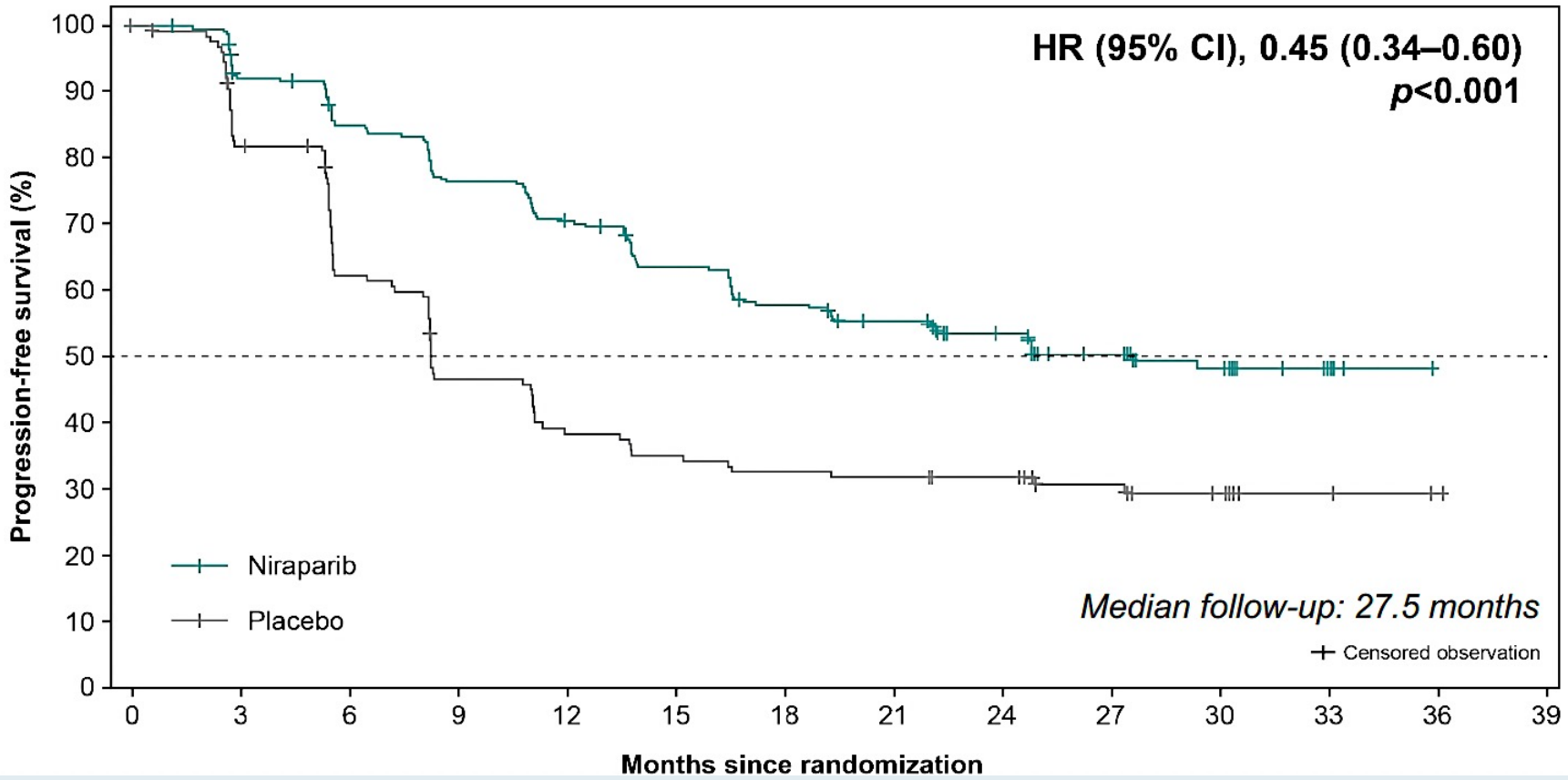
Efficacy and Safety of Niraparib as Maintenance Treatment in Patients with Newly Diagnosed Advanced Ovarian Cancer Using an Individualized Starting Dose (PRIME Study): A Randomized, Double-blind, Placebo-controlled, Phase 3 Trial

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



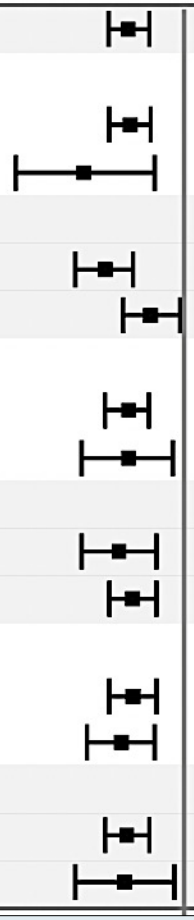
16.5 months longer median PFS with niraparib versus placebo

	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 N et al. SGO 2022;Abstract LBA5.

PRIME: PFS Benefit in Prespecified Subgroups

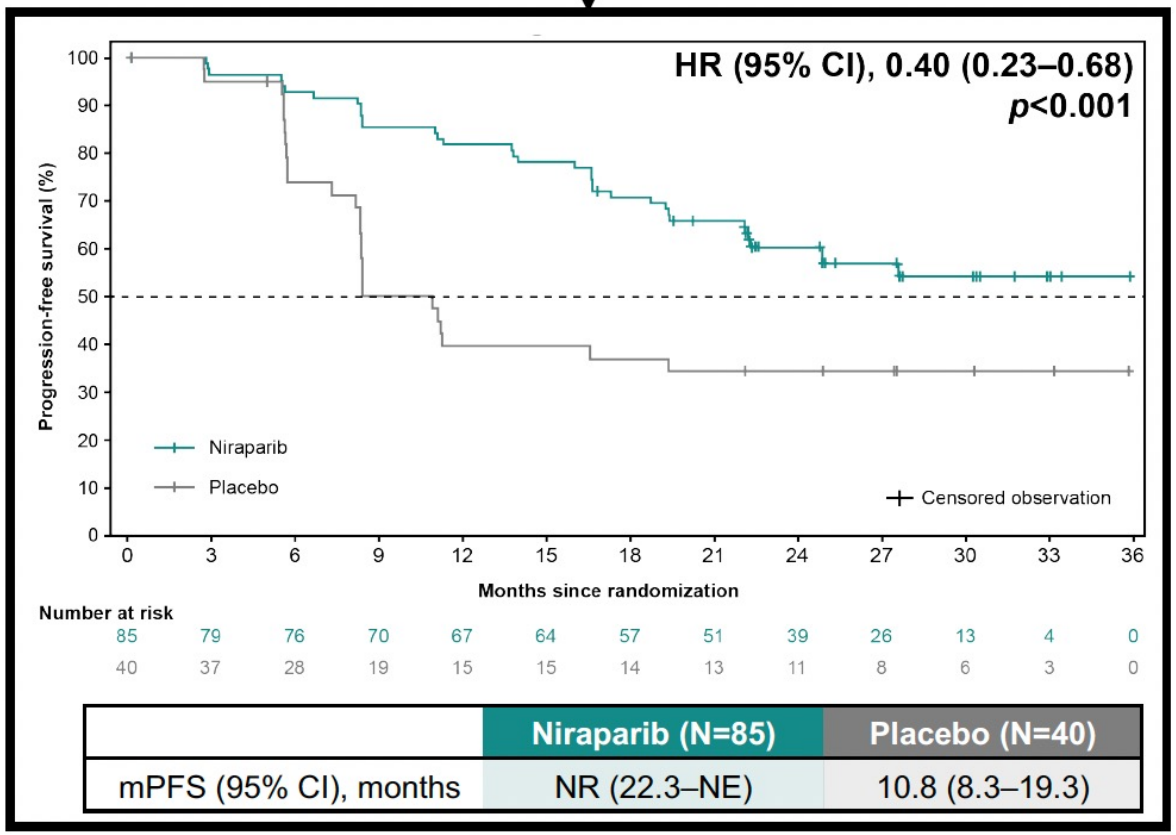
Subgroup	Events/patients (%)		Hazard ratio for PFS (95% CI)
	Niraparib	Placebo	
Overall	123/255 (48.2)	86/129 (66.7)	0.45 (0.34–0.60)
Age			
<65 years	108/229 (47.2)	73/114 (64.0)	0.47 (0.34–0.63)
≥65 years	15/26 (57.7)	13/15 (86.7)	0.24 (0.09–0.66)
Neoadjuvant chemotherapy			
Yes	62/121 (51.2)	46/59 (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 N et al. SGO 2022;Abstract LBA5.

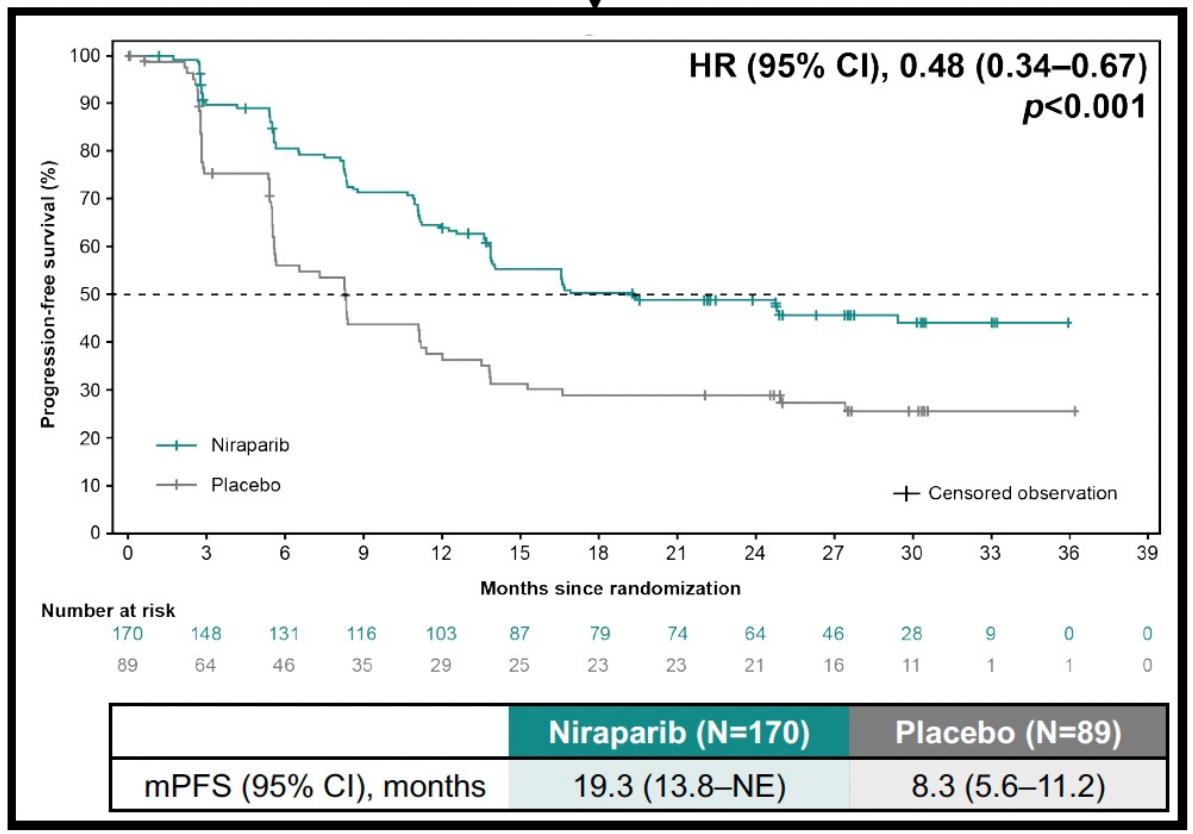
PRIME: PFS Benefit by g*BRCA*mut Status

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)

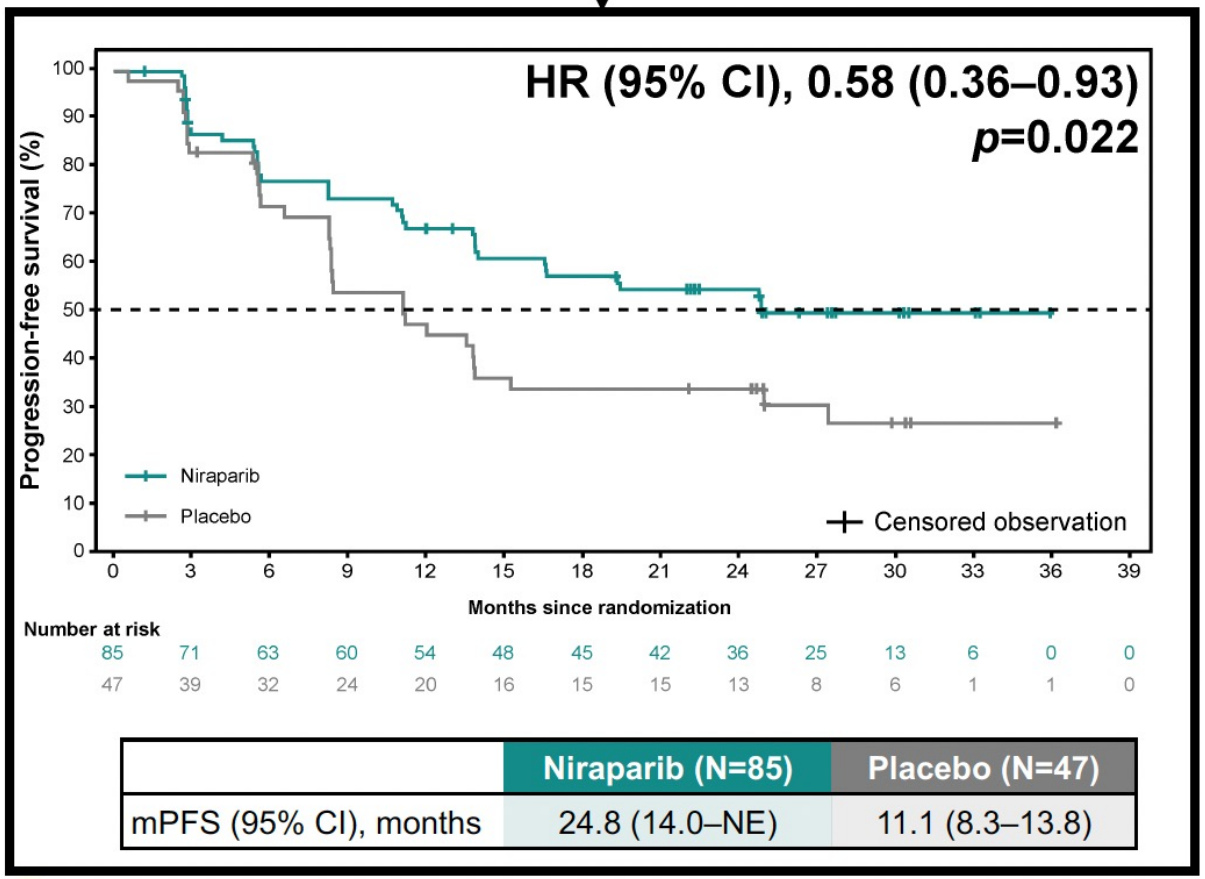
- Median PFS has not been yet reached for the g*BRCA*mut population.
- The benefit of niraparib in the non-g*BRCA*mut population is confirmed.

Li N et al. SGO 2022;Abstract LBA5.

RTP RESEARCH TO PRACTICE

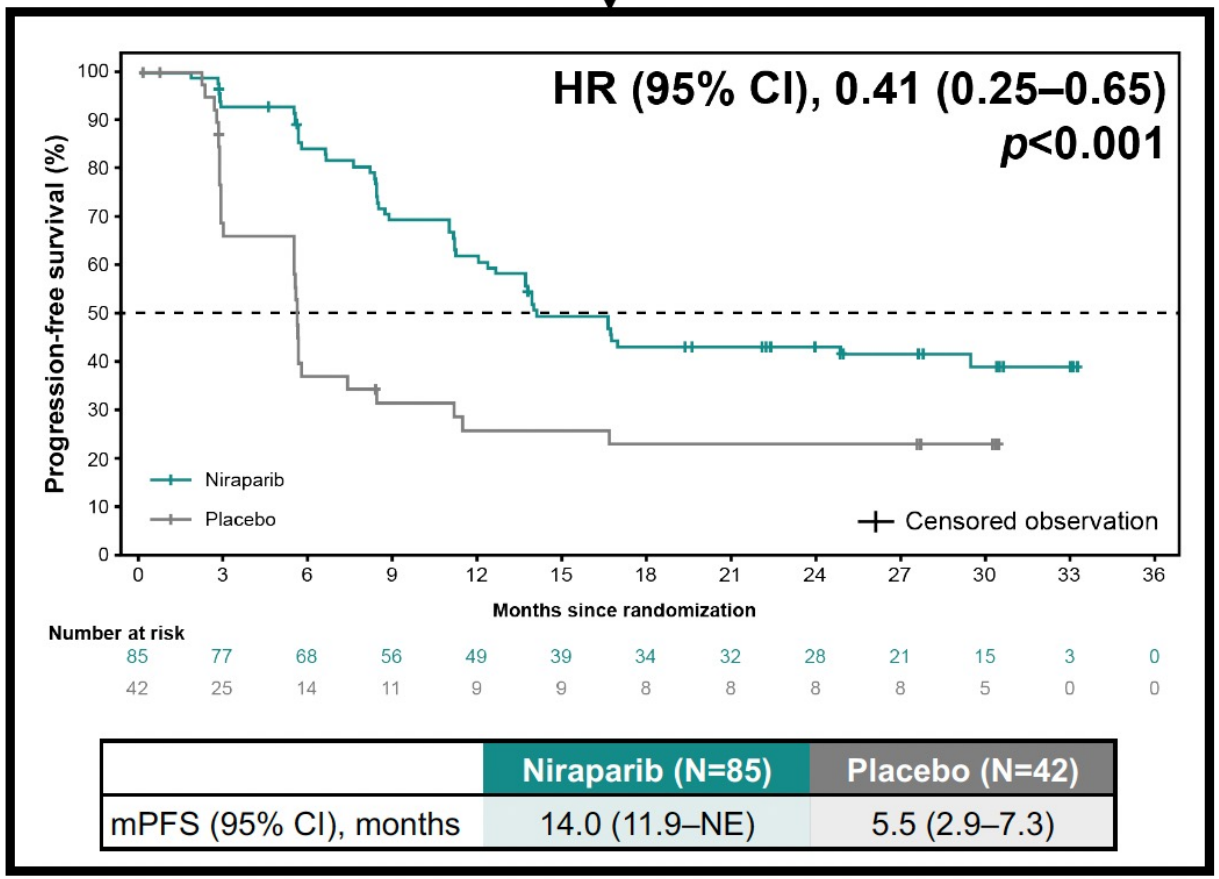
PRIME: PFS Benefit by HRD status in non-g*BRCA*mut Subgroup

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 N et al. SGO 2022;Abstract LBA5.

RTP RESEARCH TO PRACTICE

PRIME and PRIMA Trials: Safety Overview

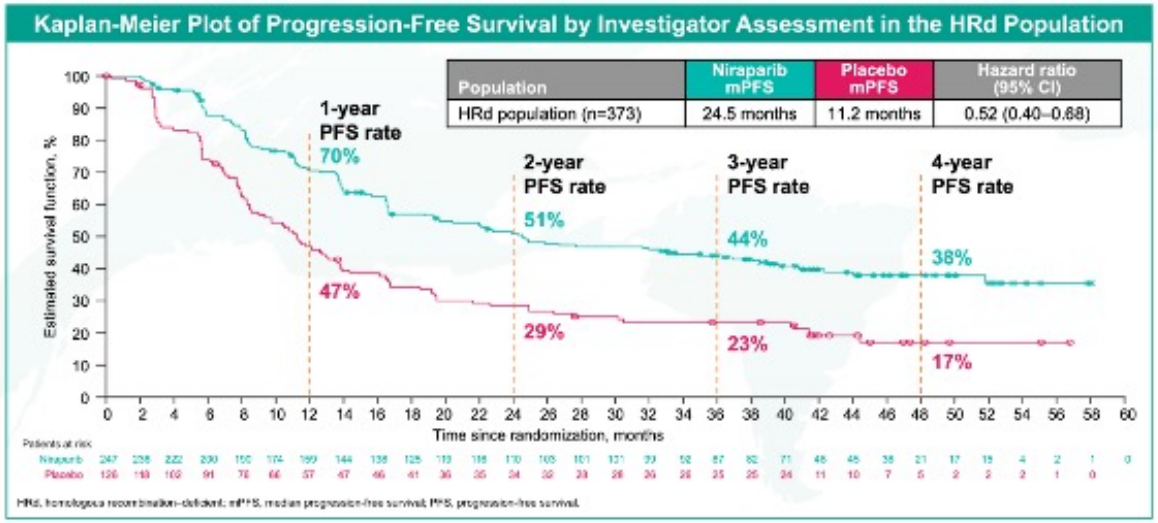
TEAEs, n (%)	PRIME		PRIMA[1]	
	Niraparib (N=255)	Placebo (N=129)	Niraparib (N=484)	Placebo (N=244)
Any TEAEs	253 (99.2)	121 (93.8)	478 (98.8)	224 (91.8)
Treatment-related	249 (97.6)	111 (86.0)	466 (96.3)	168 (68.9)
Grade≥3 TEAEs	139 (54.5)	23 (17.8)	341 (70.5)	46 (18.9)
Treatment-related	125 (49.0)	9 (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 N et al. SGO 2022;Abstract LBA5.

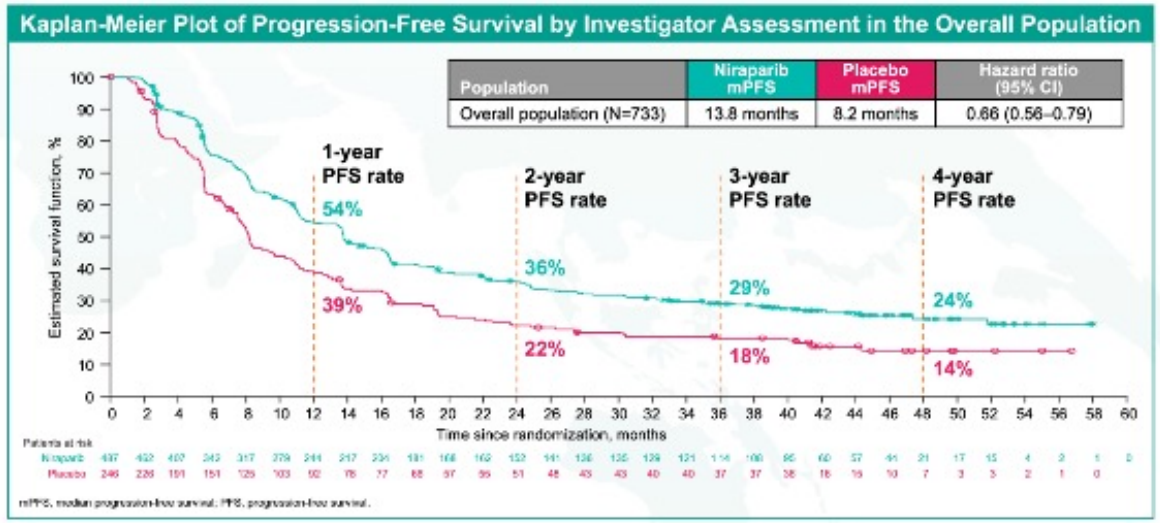
PRIMA: Updated Long-Term PFS (Investigator-Assessed)

November 17, 2021, Clinical Cutoff Date

Kaplan-Meier Plot of Progression-Free Survival by Investigator Assessment in the HRd Population



Kaplan-Meier Plot of Progression-Free Survival by Investigator Assessment in the Overall Population



- At the time of the updated clinical cutoff date, 16.3% and 11.1% of patients were receiving niraparib or placebo, respectively
- Niraparib treatment significantly extended IA PFS compared with placebo in both the HRd and overall populations
- Updated long-term IA PFS results were also consistent with BICR PFS results from the primary analysis
- OS remains immature at 41.2% for the overall population

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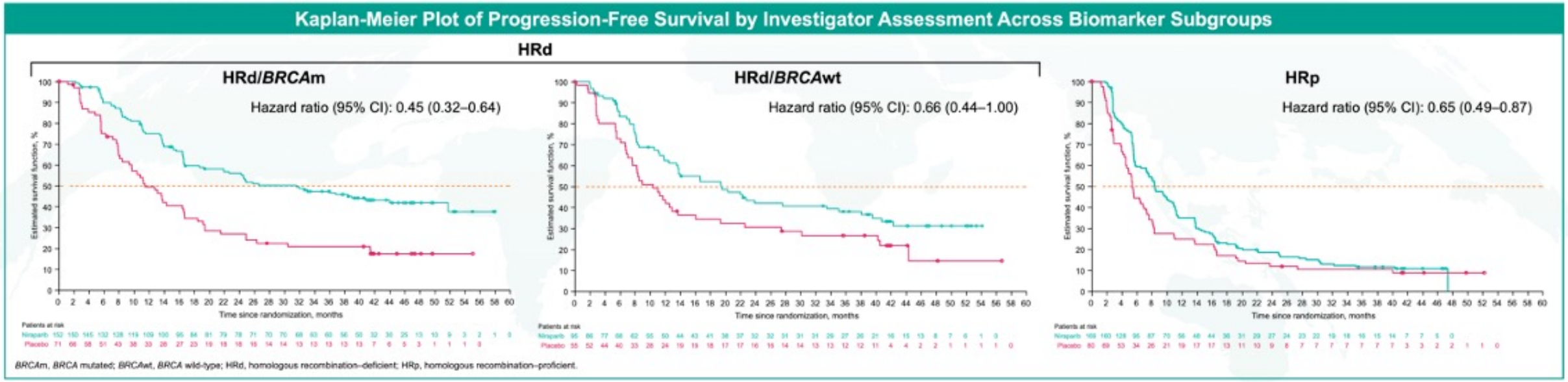
BICR, blinded independent central review; HRd, homologous recombination–deficient; IA, investigator assessed; mPFS, median progression-free survival; OS, overall survival; PFS, progression-free survival.

González-Martín A et al. IGCS 2022;Abstract S005/1753.

RTP RESEARCH TO PRACTICE

PRIMA: PFS Across Biomarker Subgroups (Investigator-Assessed)

November 17, 2021, Clinical Cutoff Date



- Niraparib treatment increased PFS duration compared with placebo treatment across biomarker subgroups
- The greatest treatment benefit was seen in patients with HRd tumors that were *BRCA*m

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González-Martín A et al. IGCS 2022;Abstract S005/1753.

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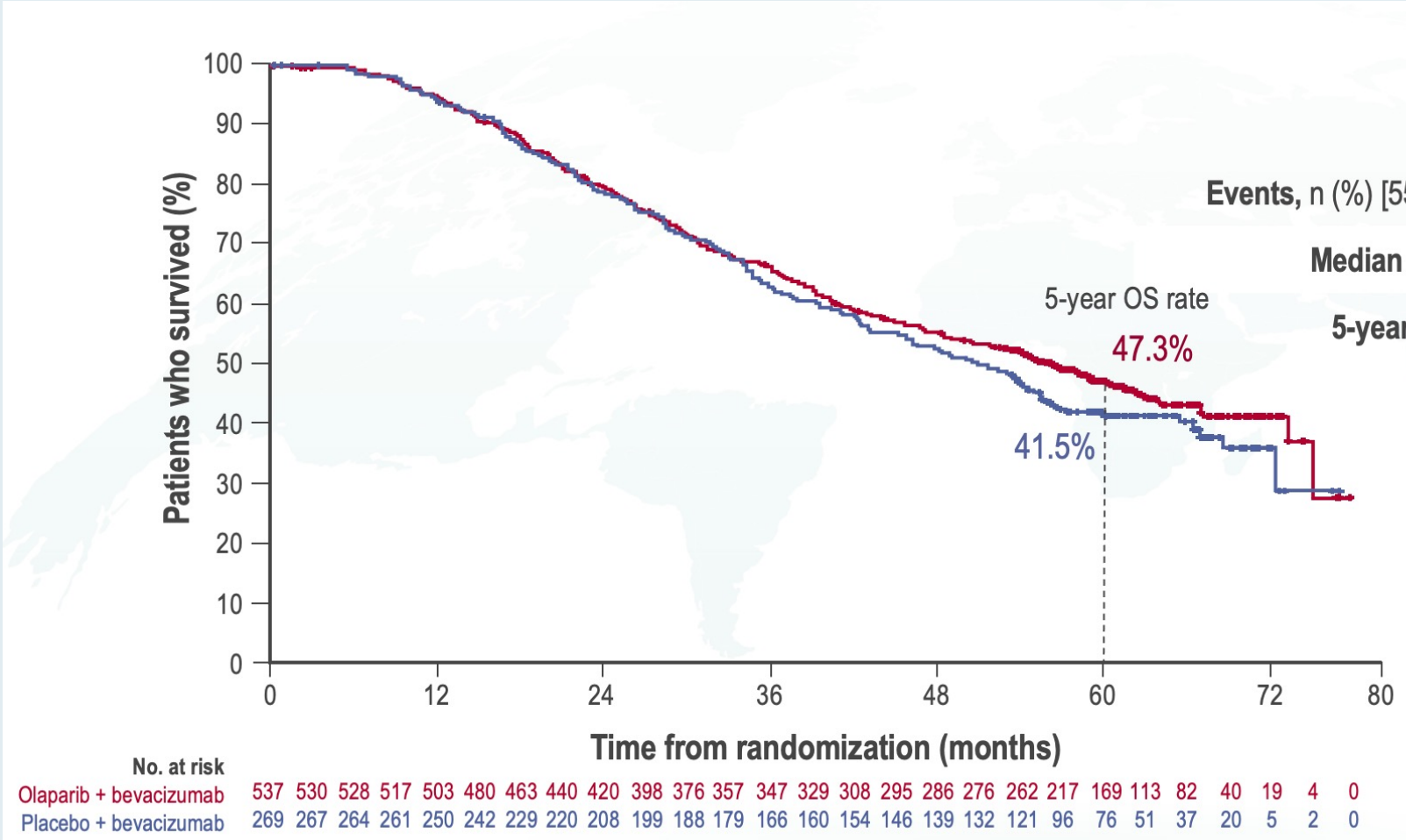
PAOLA-1: Overall Survival (ITT Population)



	Olaparib + bevacizumab (N=537)	Placebo + bevacizumab (N=269)
Events, n (%) [55% maturity]	288 (53.6)	158 (58.7)
Median OS, months	**56.5**	**51.6**
5-year OS rate, %	**47.3**	**41.5**

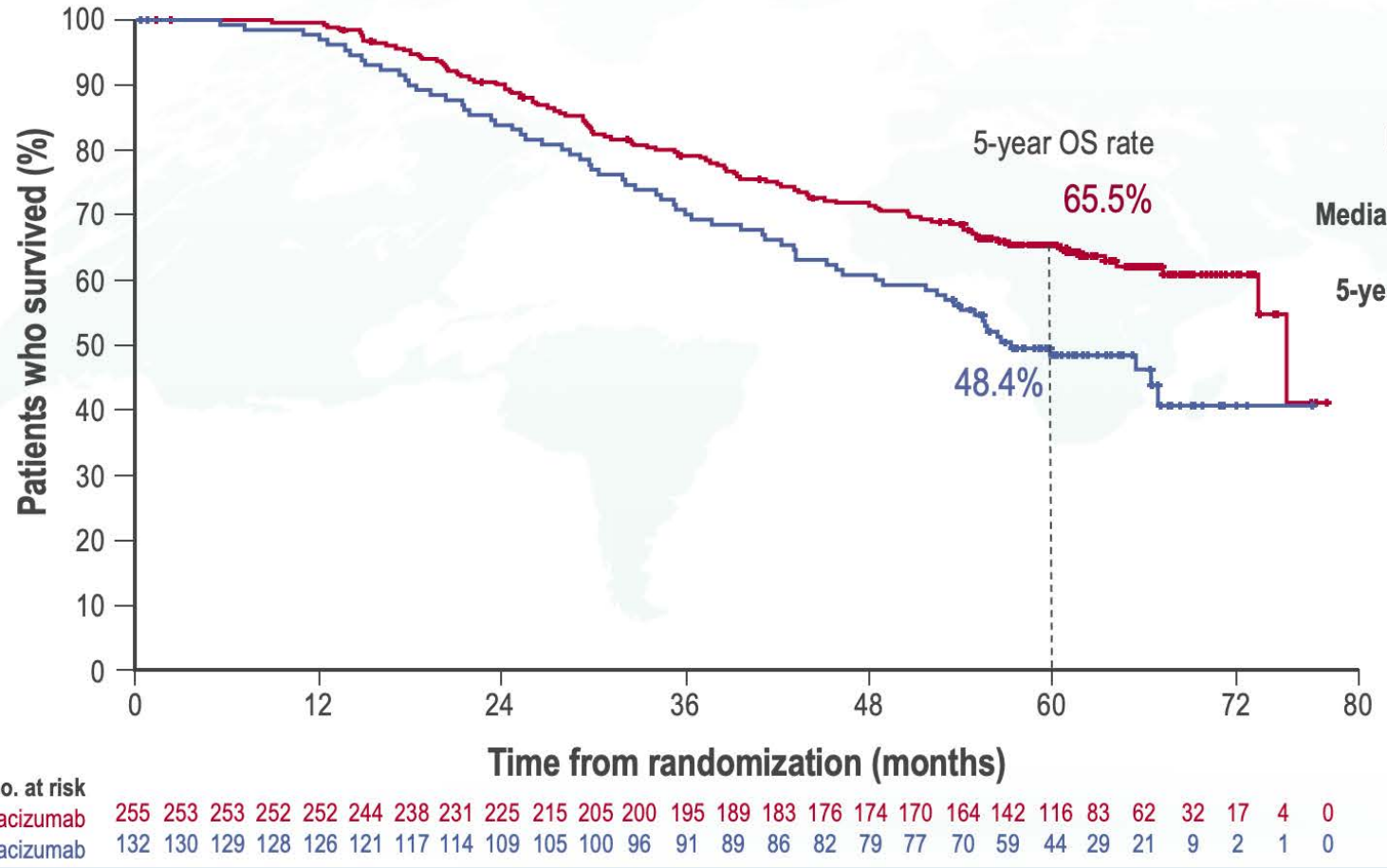
HR 0.92 (95% CI 0.76–1.12);
***P*=0.4118**

Patients receiving a PARP inhibitor during any subsequent treatment
Olaparib + bevacizumab: **19.6%** (105/537)
Placebo + bevacizumab: **45.7%** (123/269)

Median time from first cycle of chemotherapy to randomization = 6 months

Ray-Coquard I et al. ESMO 2022;Abstract LBA29.

PAOLA-1: Overall Survival in the Homologous Repair Deficiency (HRD)-Positive Subgroup



	Olaparib + bevacizumab (N=255)	Placebo + bevacizumab (N=132)
Events, n (%)	93 (36.5)	69 (52.3)
Median OS, months	**75.2** (unstable)*	**57.3**
5-year OS rate, %	**65.5**	**48.4**

HR 0.62 (95% CI 0.45–0.85)

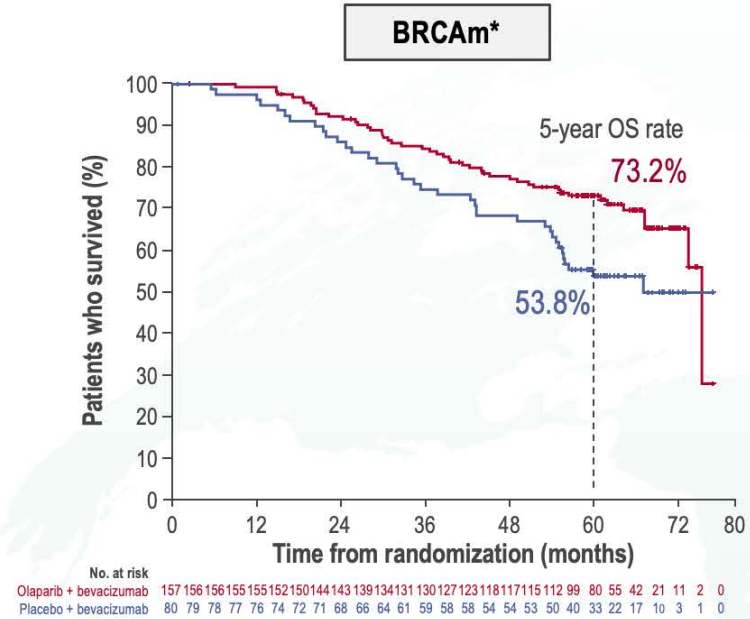
38% reduction in risk of death for olaparib + bevacizumab vs bevacizumab alone

Patients receiving a PARP inhibitor during any subsequent treatment
Olaparib + bevacizumab: **17.3%** (44/255)
Placebo + bevacizumab: **50.8%** (67/132)

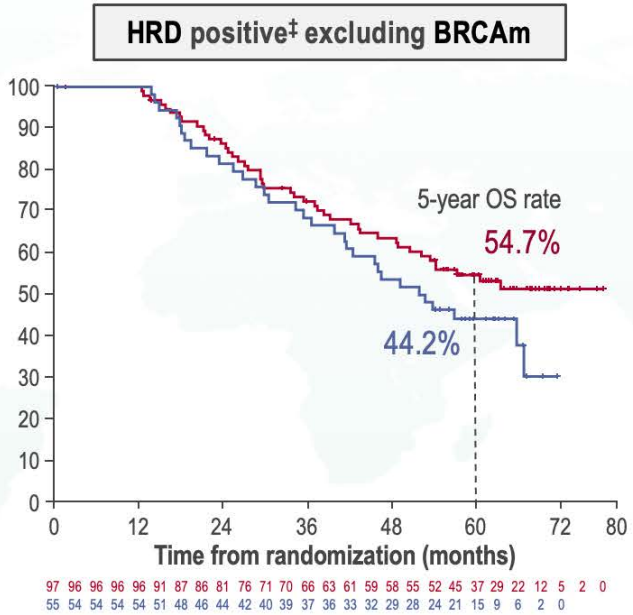
Ray-Coquard I et al. ESMO 2022;Abstract LBA29.

RTP RESEARCH TO PRACTICE

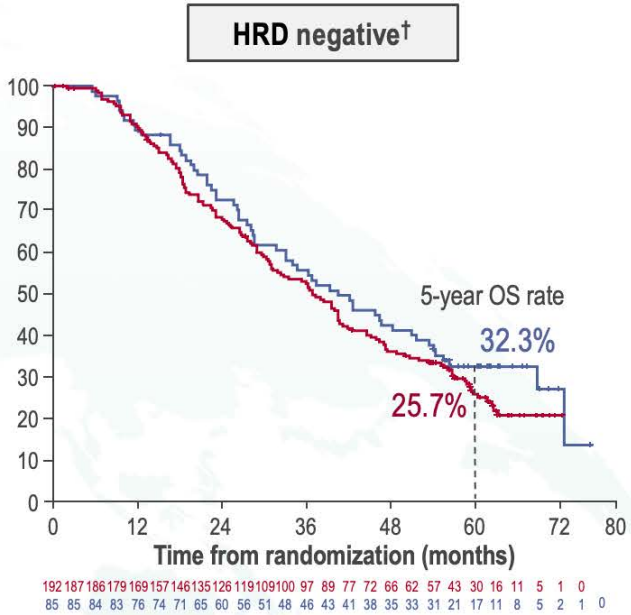
PAOLA-1: Overall Survival Subgroup Analysis by BRCA Mutation and HRD Status



	Olaparib + bevacizumab (N=157)	Placebo + bevacizumab (N=80)
Events, n (%)	48 (30.6)	37 (46.3)
Median OS, months	75.2 (unstable)†	66.9
5-year OS rate, %	**73.2**	**53.8**
PARPi as subsequent treatment, n (%)	38 (24.2)	44 (55.0)
	HR 0.60 (95% CI 0.39–0.93)	



	Olaparib + bevacizumab (N=97)	Placebo + bevacizumab (N=55)
	44 (45.4)	32 (58.2)
	NR	52.0
	54.7	**44.2**
	9 (9.3)	23 (41.8)
	HR 0.71 (95% CI 0.45–1.13)	



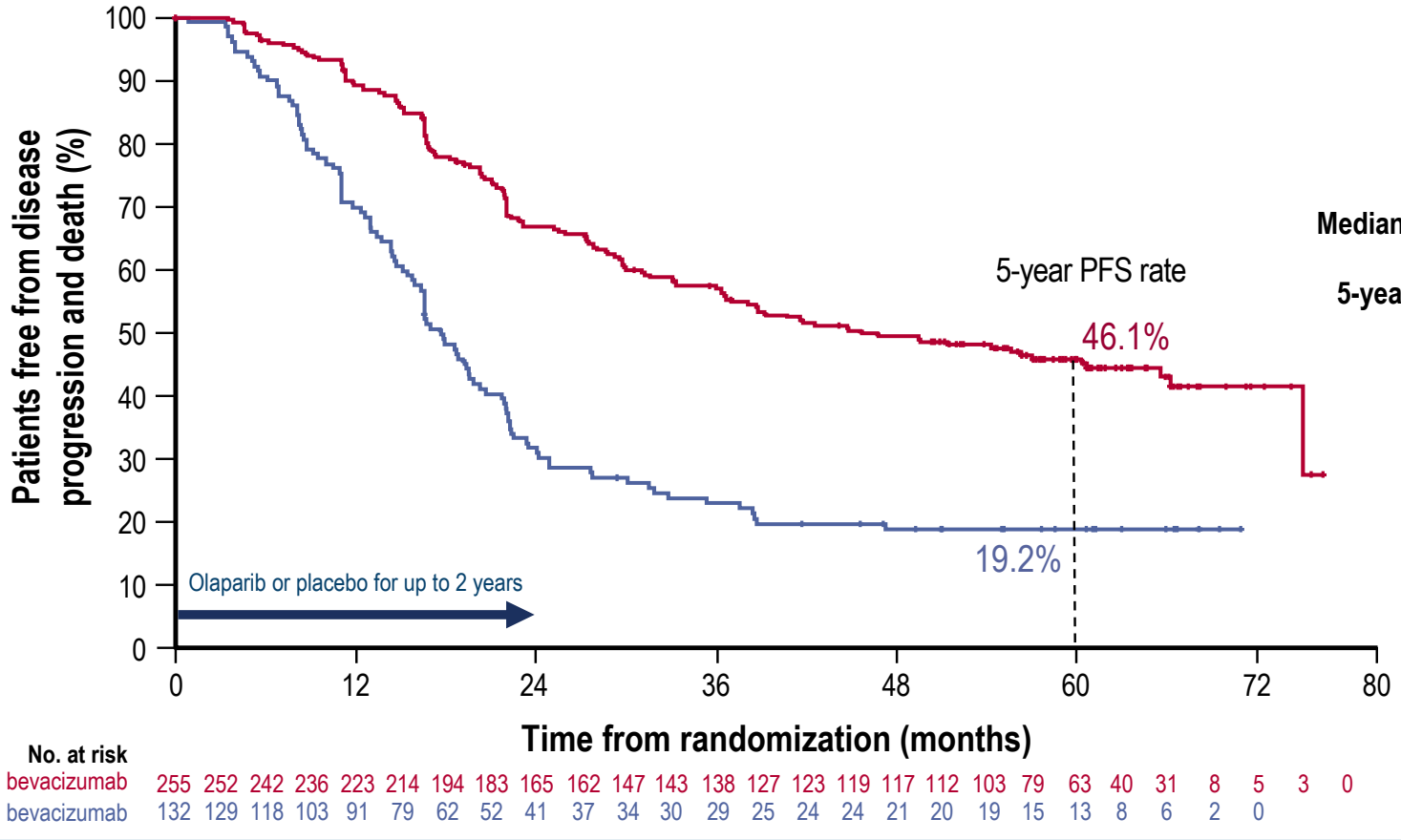
	Olaparib + bevacizumab (N=192)	Placebo + bevacizumab (N=85)
	140 (72.9)	58 (68.2)
	36.8	40.4
	25.7	**32.3**
	46 (24.0)	34 (40.0)
	HR 1.19 (95% CI 0.88–1.63)	

*By central labs; †Unstable median; <50% data maturity; ‡By Myriad myChoice HRD Plus. NR, not reported.

Ray-Coquard I et al. ESMO 2022;Abstract LBA29.

RTP RESEARCH TO PRACTICE

PAOLA-1: Updated Progression-Free Survival in the Homologous Recombination Deficient Population by Investigator Assessment



	Olaparib + bevacizumab (N=255)	Placebo + bevacizumab (N=132)
Events, n (%)	136 (53.3)	104 (78.8)
Median PFS, months	**46.8**	**17.6**
5-year PFS rate, %	**46.1**	**19.2**

HR 0.41 (95% CI 0.32–0.54)

59% reduction in risk of disease progression or death for olaparib + bevacizumab vs bevacizumab alone

Ray-Coquard I et al. ESMO 2022;Abstract LBA29.

RTP RESEARCH TO PRACTICE

PAOLA-1: Updated Adverse Events of Special Interest

	Primary PFS analysis (DCO: 22 March 2019)		Final PFS2 analysis (DCO: 22 March 2020)		Final OS analysis (DCO: 22 March 2022)	
	Olaparib + bevacizumab (N=535)	Placebo + bevacizumab (N=267)	Olaparib + bevacizumab (N=535)	Placebo + bevacizumab (N=267)	Olaparib + bevacizumab (N=535)	Placebo + bevacizumab (N=267)
MDS/AML/AA, n (%)	6 (1.1)	1 (0.4)	7 (1.3)	4 (1.5)	9 (1.7)	6 (2.2)
New primary malignancies, n (%)*	7 (1.3)	3 (1.1)	13 (2.4)	5 (1.9)	22 (4.1)	8 (3.0)
Pneumonitis/ILD/bronchiolitis, n (%)†	6 (1.1)	0 (0.0)	6 (1.1)	0 (0.0)	7 (1.3)	2 (0.7)

- All patients had discontinued treatment at PFS2 DCO

AA, aplastic anemia; AML, acute myeloid leukemia; ILD, interstitial lung disease; MDS, myelodysplastic syndrome

Ray-Coquard I et al. ESMO 2022;Abstract LBA29.

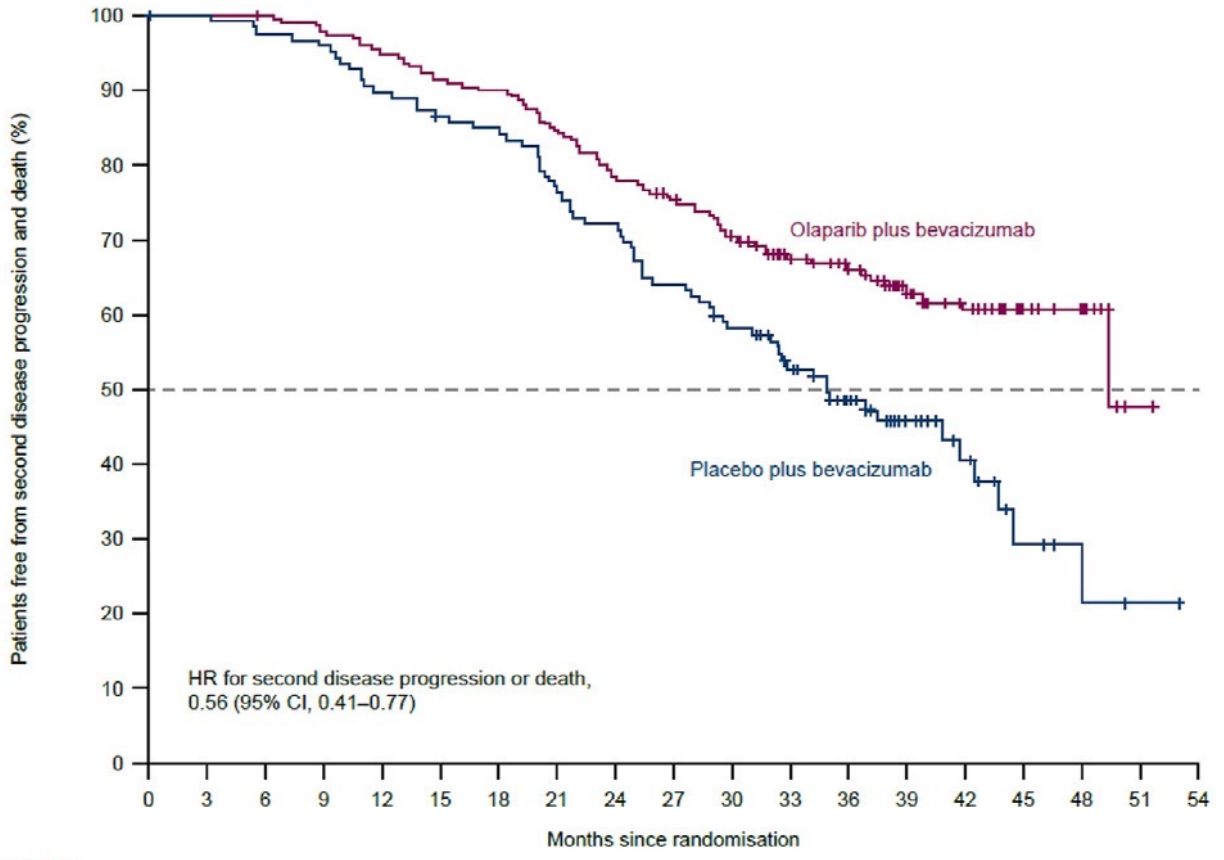
Eur J Cancer 2022 October;174:221-31.

Maintenance olaparib plus bevacizumab in patients with newly diagnosed advanced high-grade ovarian cancer: Main analysis of second progression-free survival in the phase III PAOLA-1/ENGOT-ov25 trial

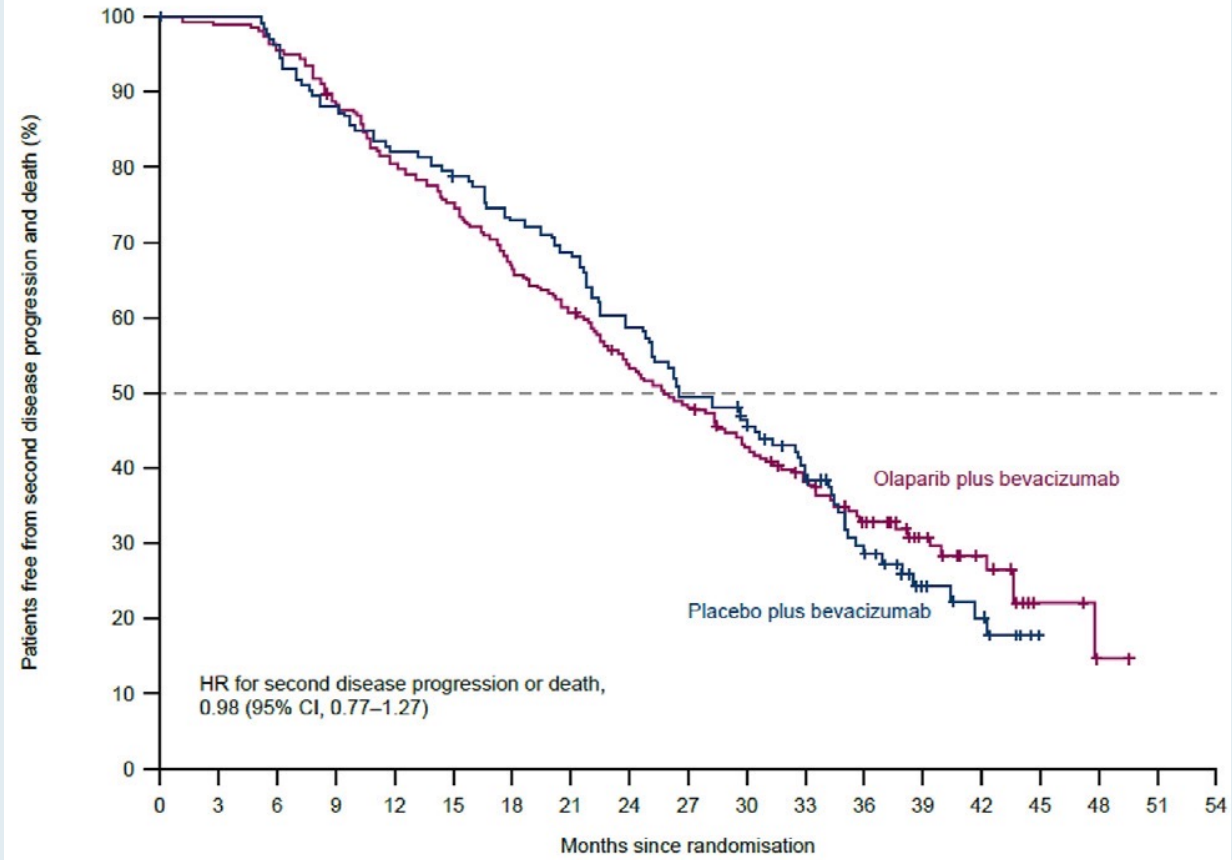
Antonio González-Martín [a,*,1], Christophe Desauw [b], Florian Heitz [c], Claire Cropet [d], Piera Gargiulo [e], Regina Berger [f], Hiroyuki Ochi [g], Ignace Vergote [h], Nicoletta Colombo [i], Mansoor R. Mirza [j], Youssef Tazi [k], Ulrich Canzler [l], Claudio Zamagni [m], Eva M. Guerra-Alia [n], Charles B. Levaché [o], Frederik Marmé [p], Fernando Bazan [q], Nikolaus de Gregorio [r], Nadine Dohollou [s], Peter A. Fasching [t], Giovanni Scambia [u], María J. Rubio-Pérez [v], Tsveta Milenkova [w], Cristina Costan [x], Patricia Pautier [y], Isabelle Ray-Coquard [z] on behalf of the PAOLA1/ENGOT-ov25 investigators

PAOLA-1: PFS2 by Investigator Assessment in Patients with HRD+ and HRD- Tumors

HRD+



HRD- or unknown

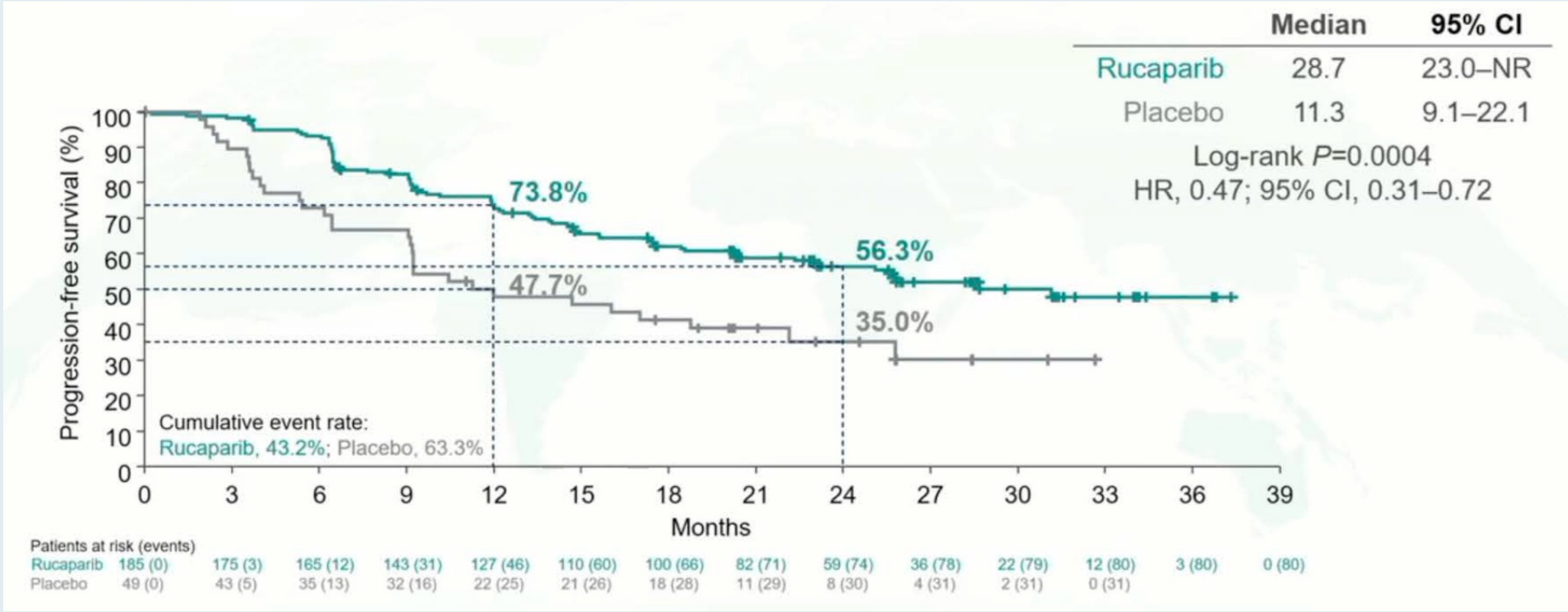


HRD = homologous recombination deficiency

González-Martín A et al. *Eur J Cancer* 2022;174:221-31.

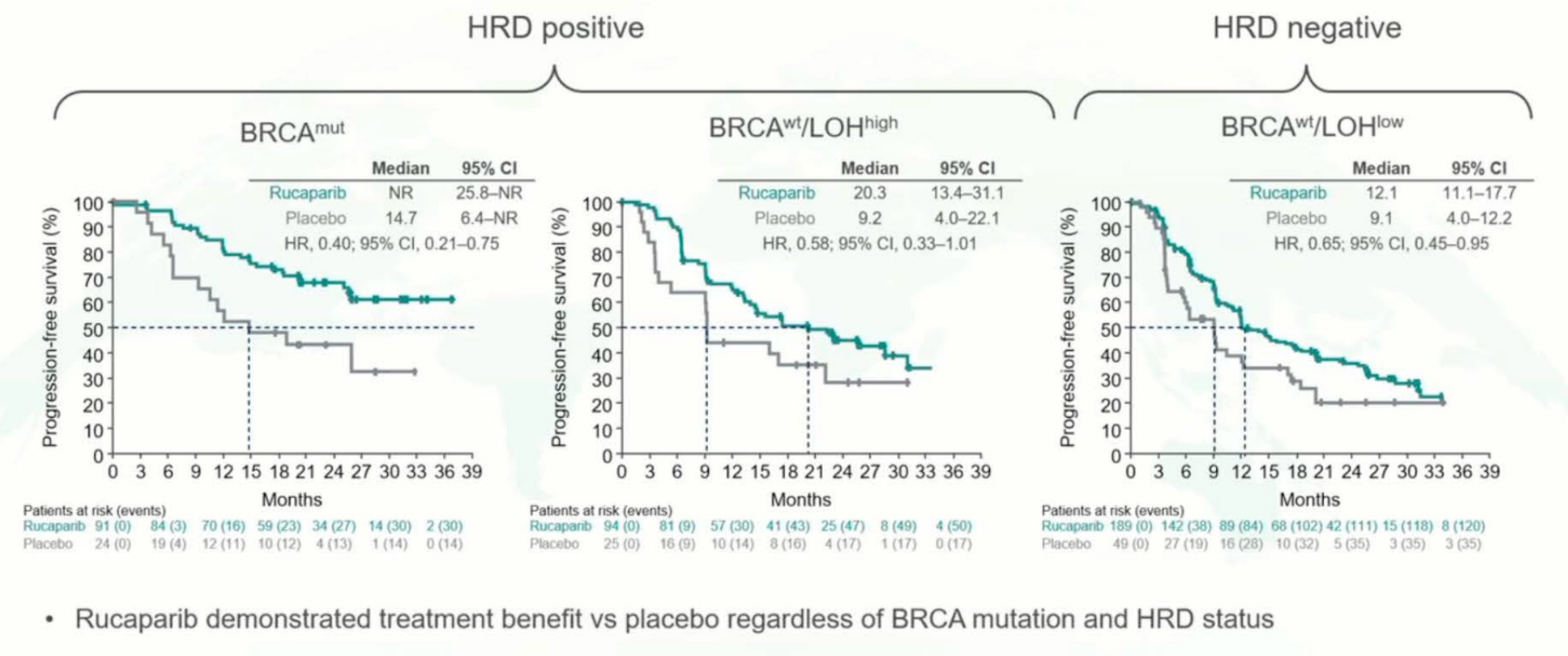
RTP RESEARCH TO PRACTICE

ATHENA-MONO Primary Endpoint: Investigator-Assessed PFS in the HRD Population



Monk BJ et al. IGCS 2022;Abstract S001/1608; Monk B et al. *JCO* 2022;40(34):3952-64.

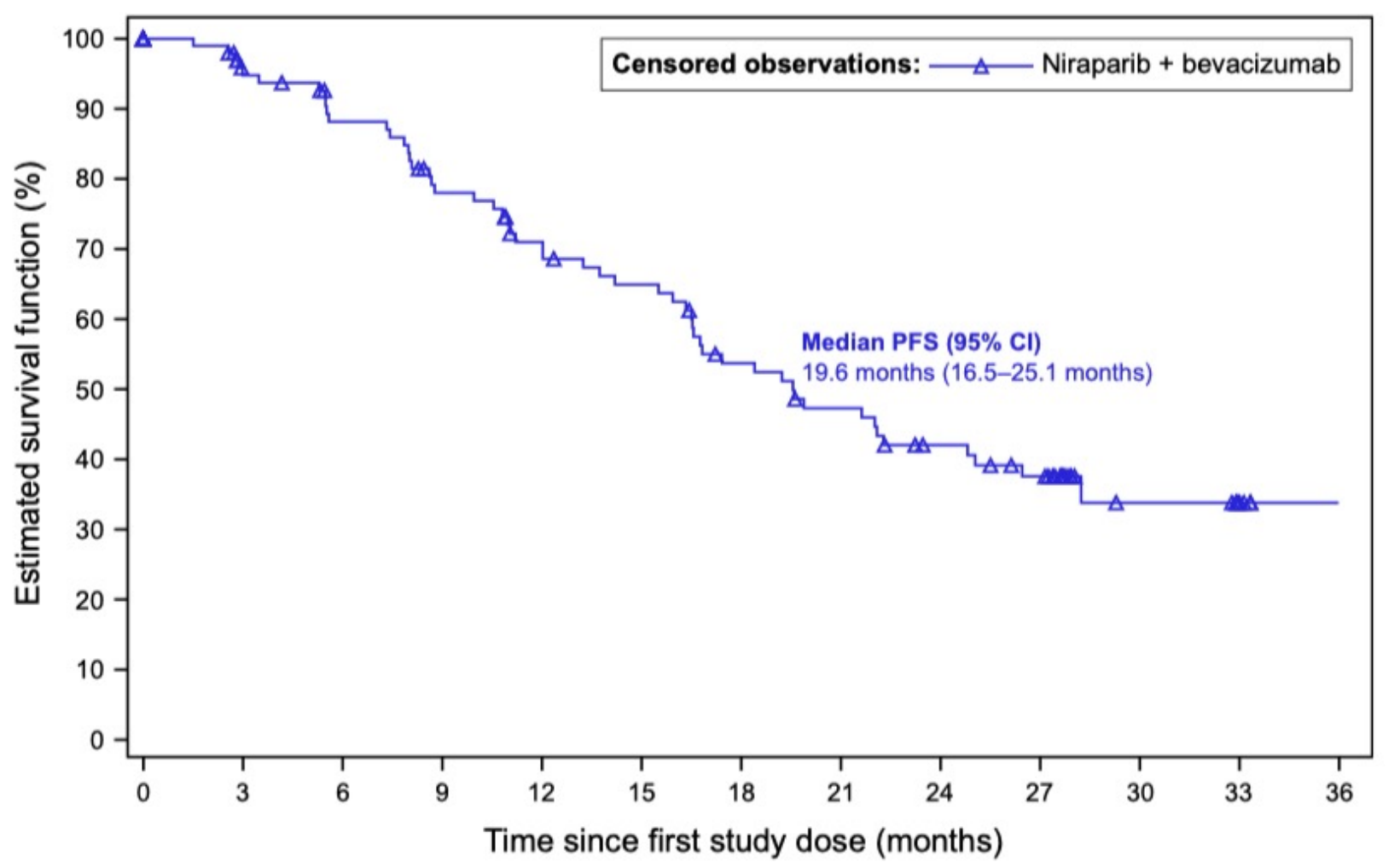
ATHENA-MONO: Investigator-Assessed PFS in Exploratory Subgroups



- Rucaparib demonstrated treatment benefit vs placebo regardless of BRCA mutation and HRD status

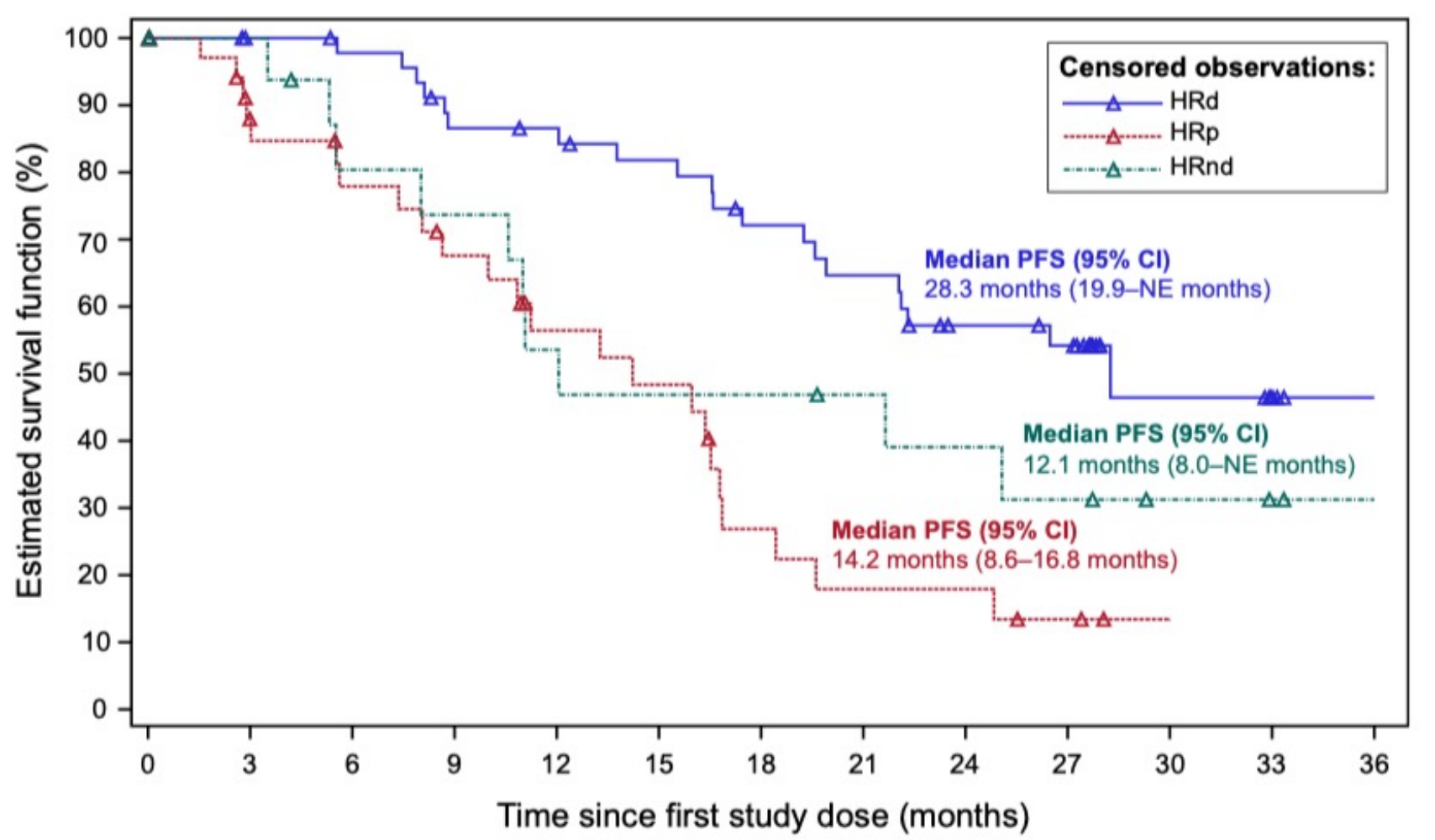
Monk BJ et al. IGCS 2022;Abstract S001/1608; Monk B et al. *JCO* 2022;40(34):3952-64.

OVARIO: Investigator-Assessed Progression-Free Survival in the Overall Population



Hardesty MM et al. *Gynecol Oncol* 2022;166(2):219-29.

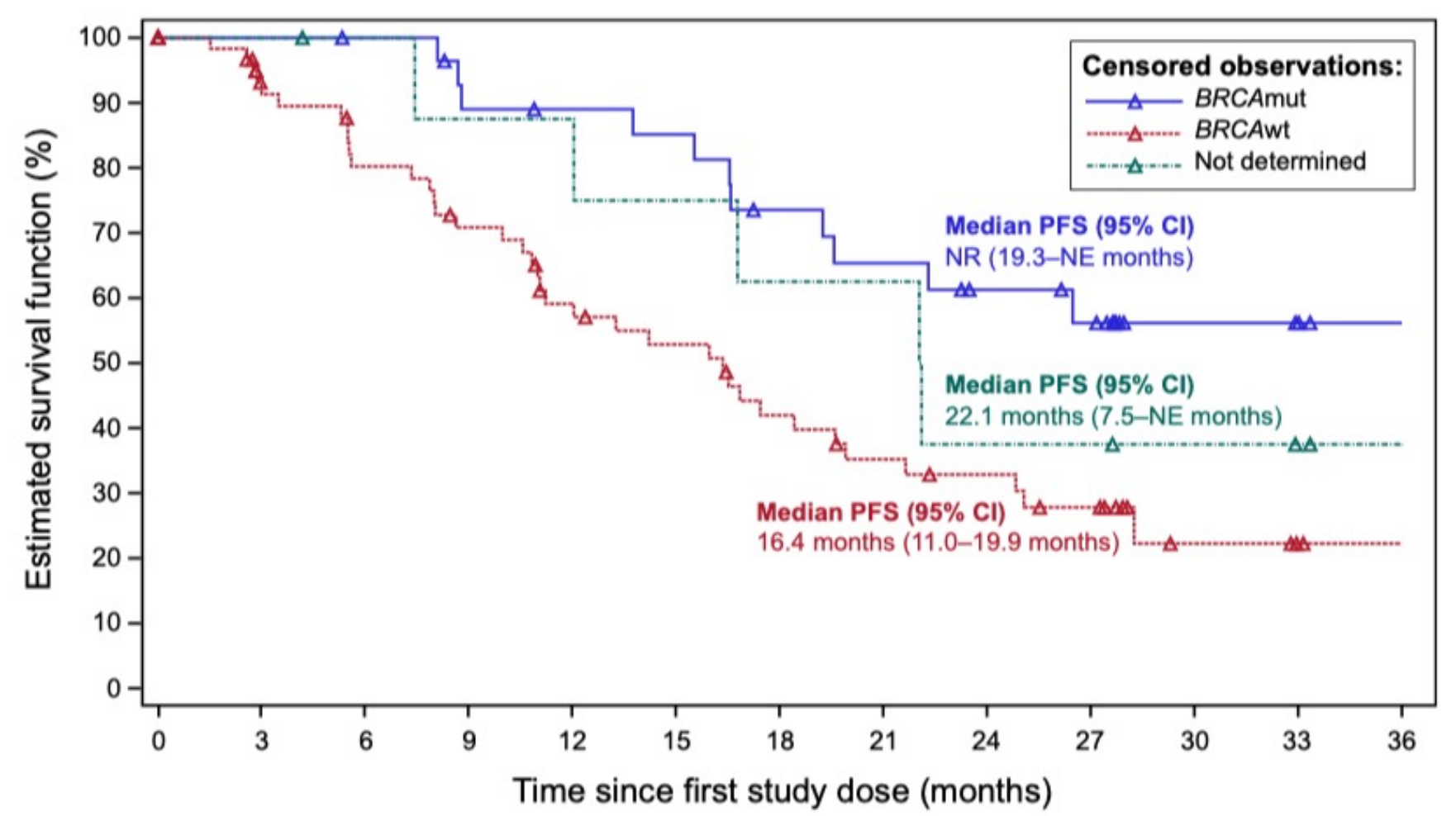
OVARIO: Investigator-Assessed Progression-Free Survival by Homologous Repair Deficiency (HRD) Status



Hardesty MM et al. *Gynecol Oncol* 2022;166(2):219-29.

RTP RESEARCH TO PRACTICE

OVARIO: Investigator-Assessed Progression-Free Survival by BRCA Mutation Status



Hardesty MM et al. *Gynecol Oncol* 2022;166(2):219-29.

RTP RESEARCH TO PRACTICE

OVARIO: Treatment-Related Adverse Effects Summary

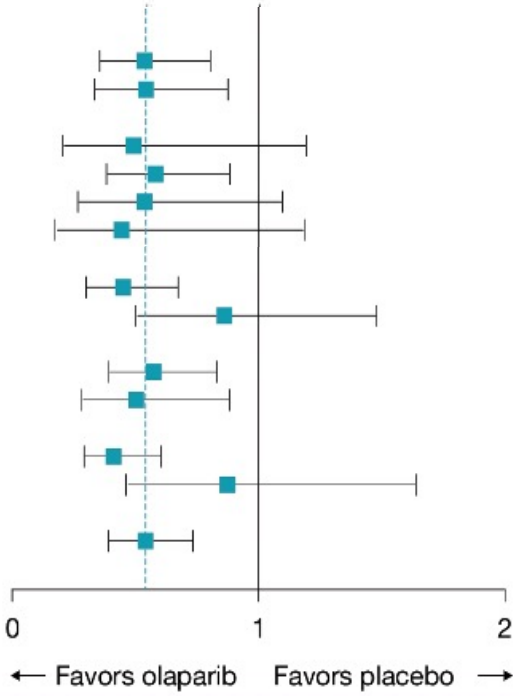
Parameter, n (%)	Overall $N = 105$
Any TRAE	105 (100.0)
Niraparib related	104 (99.0)
Bevacizumab related	96 (91.4)
Any grade ≥ 3 TRAE	84 (80.0)
Niraparib related	81 (77.1)
Bevacizumab related	54 (51.4)
Any serious TRAE	21 (20.0)
Niraparib related	19 (18.1)
Bevacizumab related	7 (6.7)
Any TRAE leading to discontinuation of any study treatment	42 (40.0)
Discontinuation of niraparib	29 (27.6)
Discontinuation of bevacizumab	27 (25.7)
Any TRAE leading to study treatment interruption	93 (88.6)
Niraparib interruption	91 (86.7)
Niraparib dose reduction	78 (74.3)
Bevacizumab interruption	2 (1.9)
Bevacizumab infusion delay	51 (48.6)
Any TEAE leading to death	0

Hardesty MM et al. *Gynecol Oncol* 2022;166(2):219-29.

Maintenance Re-Challenge

OReO: Post-hoc Analysis of Investigator-Assessed 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.

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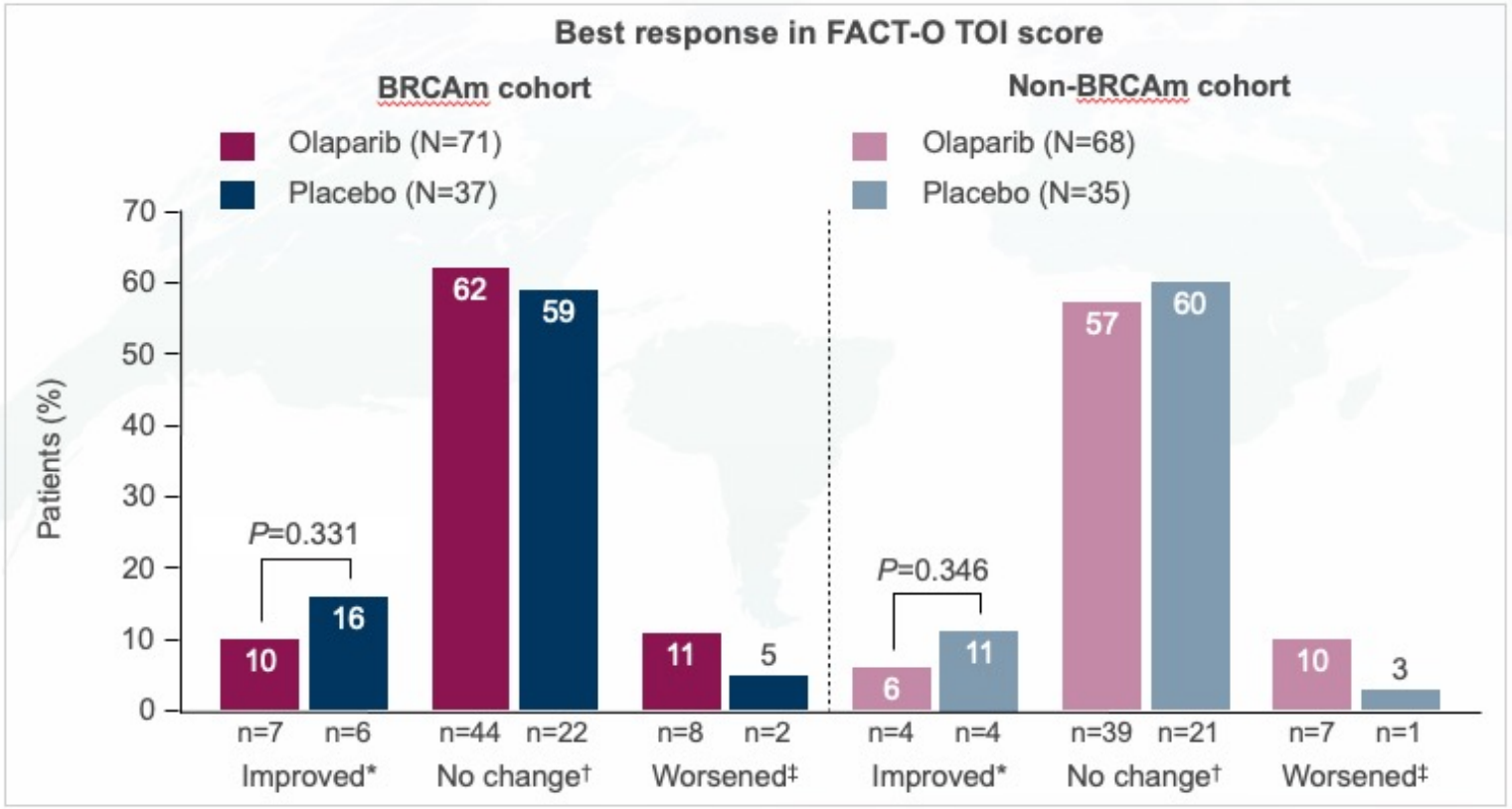
OReO: Proportion of Patients Reporting Best Response of No Change in FACT-O TOI Score



Deterioration§ in TOI score

- Few patients in the olaparib maintenance rechallenge and placebo arms met the criteria for a deterioration in TOI scores during the study
  - BRCAm cohort: 10 (14%) and 4 (11%), respectively
  - Non-BRCAm cohort: 10 (15%) and 2 (6%), respectively

Analyzed in all randomized patients with baseline assessment. The proportion with a best overall response of 'improved' (against any other non-missing response) were compared using the Cochran-Mantel-Haenszel test to account for the randomization stratification factors unless data for fewer than 20 patients was available in a cohort at that timepoint.
P value calculated for the improvement rate (percentage of all analyzed patients with a best overall score response of 'improved'), accounting for the randomization stratification factors of use of prior bevacizumab and the number of lines of prior PBC. *Improved: two visit responses of 'improved' at a minimum of 28 days apart without an intervening visit response of 'worsened'; †No change: two visit responses of either 'no change' or 'improved' and 'no change' at a minimum of 28 days apart without an intervening visit response of 'worsened'; ‡Worsened: a visit response of 'worsened' without a response of 'improved' or 'no change' within 28 days; §Deterioration: ≥10-point decrease from baseline with another ≥10-point decrease from baseline a minimum of 28 days apart and without an intervening improvement or subsequent missing data.

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FACT-O = Functional Assessment of Cancer Therapy – Ovarian; TOI = trial outcome index

Redondo A et al. IGCS 2022;Abstract O025/522.

RTP RESEARCH TO PRACTICE

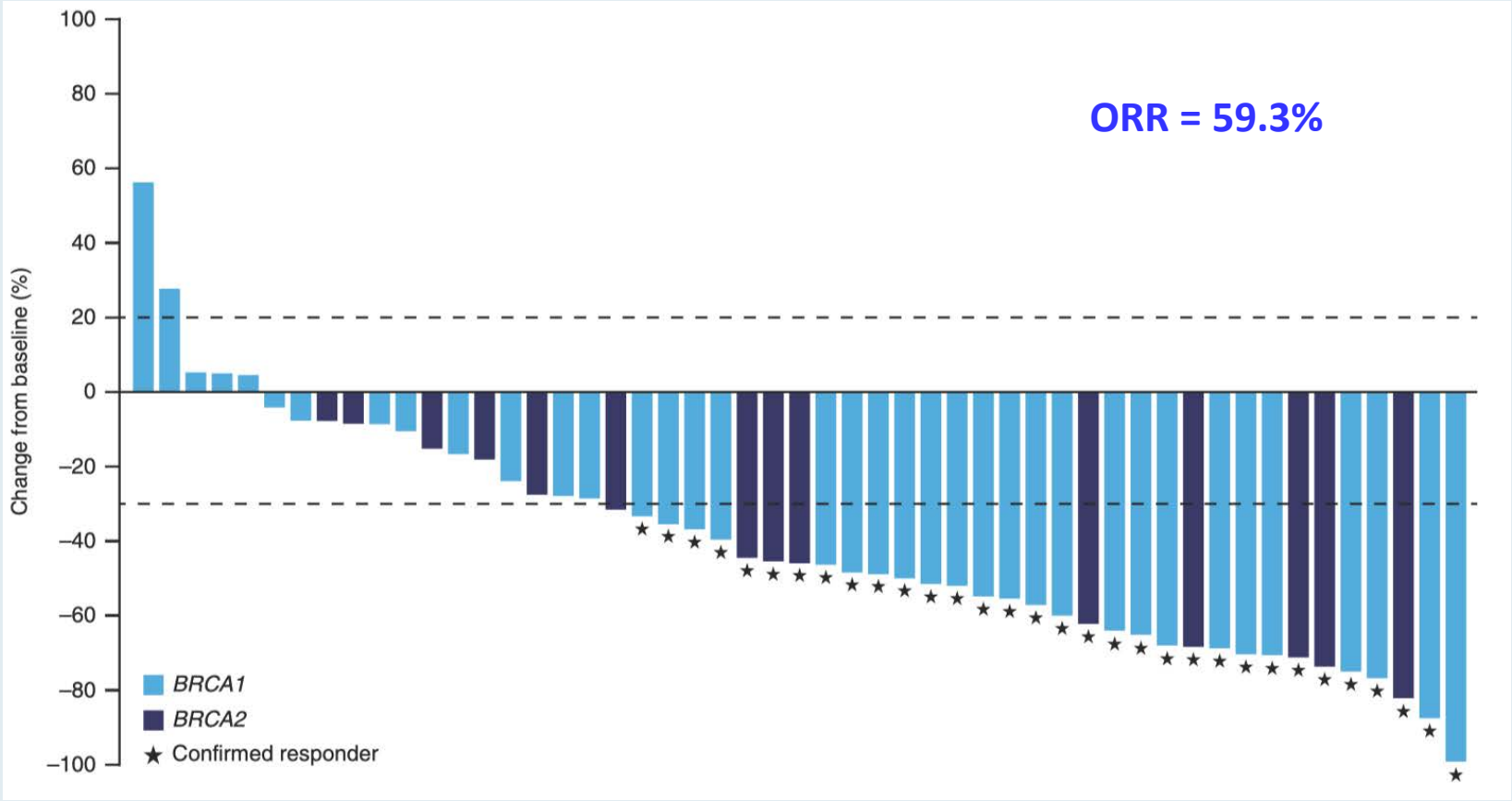
Platinum-Resistant Recurrent or Multiregimen-Recurrent Disease

Clinical Studies *Br J Cancer* January 2023;128(2):255-65.

Efficacy and safety of rucaparib treatment in patients with BRCA-mutated, relapsed ovarian cancer: final results from Study 10

Rebecca S. Kristeleit[1,18]✉, Yvette Drew[2,19], Amit M. Oza[3], Susan M. Domchek[4], Susana Banerjee[5], Rosalind M. Glasspool[6,7], Judith Balmaña[8], Lee-may Chen[9], Manish R. Patel[10], Howard A. Burris[11], Tamar Safra[12], Jennifer Borrow[13], Kevin K. Lin[14], Sandra Goble[15], Lara Maloney[16] and Ronnie Shapira-Frommer[17]

Study 10: Best Overall Change in Target Lesions



Kristeleit RS et al. *Br J Cancer* 2023;128(2):255-65.

Overall Survival Results From the Phase 3 ARIEL4 Study of Rucaparib vs Chemotherapy in Patients With Advanced, Relapsed Ovarian Carcinoma and a Deleterious *BRCA1/2* Mutation

Amit M. Oza,[1] Alla Lisyanskaya,[2] Alexander Fedenko,[3] Andreia Cristina de Melo,[4] Yaroslav Shparyk,[5] Igor Bondarenko,[6] Nicoletta Colombo,[7] Domenica Lorusso,[8] David Cibula,[9] Róbert Póka,[10] Ana Oaknin,[11] Tamar Safra,[12] Beata Maćkowiak-Matejczyk,[13] Ling Ma,[14] Daleen Thomas,[15] Kevin K. Lin,[15] Karen McLachlan,[15] Sandra Goble,[15] Rebecca Kristeleit[16]

[1]Princess Margaret Cancer Centre, University Health Network, Toronto, ON, Canada; [2]Saint Petersburg City Oncological Dispensary, Saint Petersburg, Russia; [3]N.N. Blokhin Russian Cancer Research Center, Moscow, Russia; [4]Instituto Nacional de Câncer - Hospital do Câncer II, Rio de Janeiro, Brazil; [5]Lviv Regional Oncology Dispensary, Lviv, Ukraine; [6]Dnipropetrovsk Medical Academy, Dnipro, Ukraine; [7]University of Milan-Bicocca and European Institute of Oncology (IEO) IRCCS, Milan, Italy; [8]Fondazione Policlinico Universitario Gemelli IRCCS and Catholic University of Sacred Heart, Rome, Italy; [9]First Faculty of Medicine, Charles University and General University Hospital, Prague, Czech Republic; [10]Clinical Center, University of Debrecen, Debrecen, Hungary; [11]Vall d'Hebron Institute of Oncology (VHIO), Hospital Universitari Vall d'Hebron, Vall d'Hebron Barcelona Hospital Campus, Barcelona, Spain; [12]Tel Aviv Medical Center and Sackler Faculty of Medicine, Tel Aviv University, Tel Aviv, Israel; [13]Białostockie Centrum Onkologii im. Marii Skłodowskiej-Curie, Białostockie, Poland; [14]Rocky Mountain Cancer Centers, Lakewood, CO, USA; [15]Clovis Oncology, Inc., Boulder, CO, USA; [16]Guy's and St Thomas' NHS Foundation Trust, Great Maze Pond, London, UK

IGCS 2022;Abstract S004/461.

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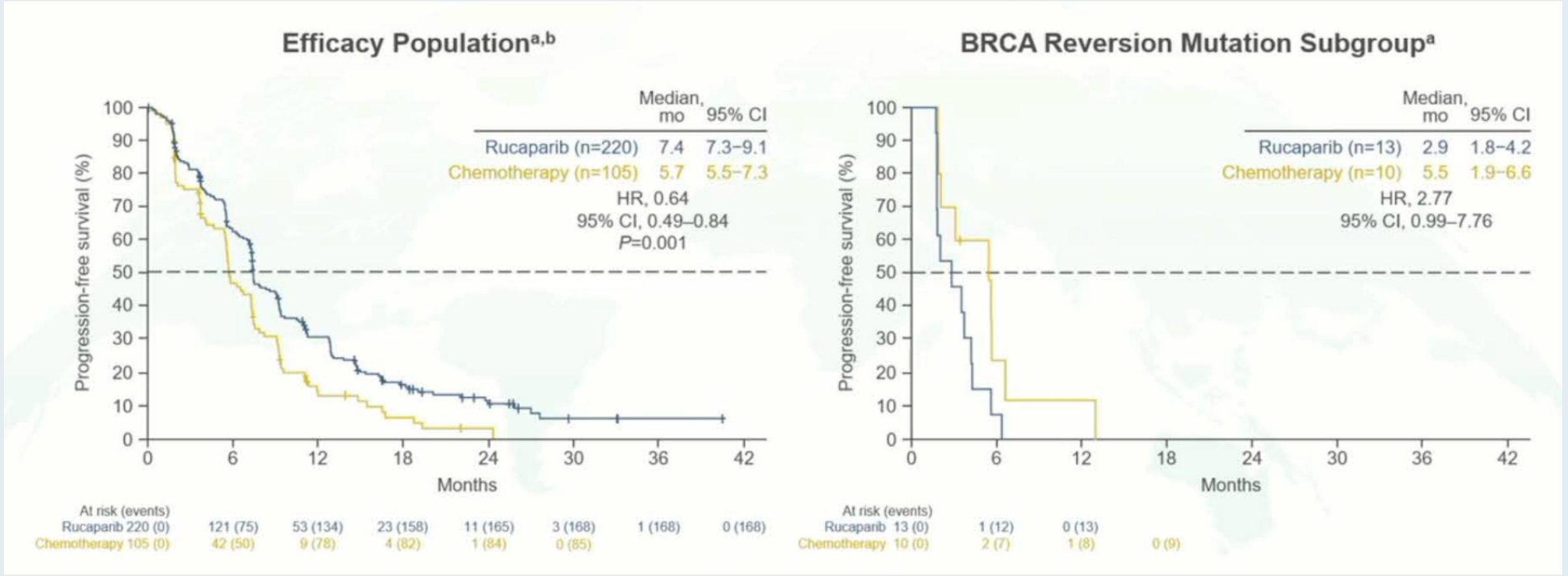
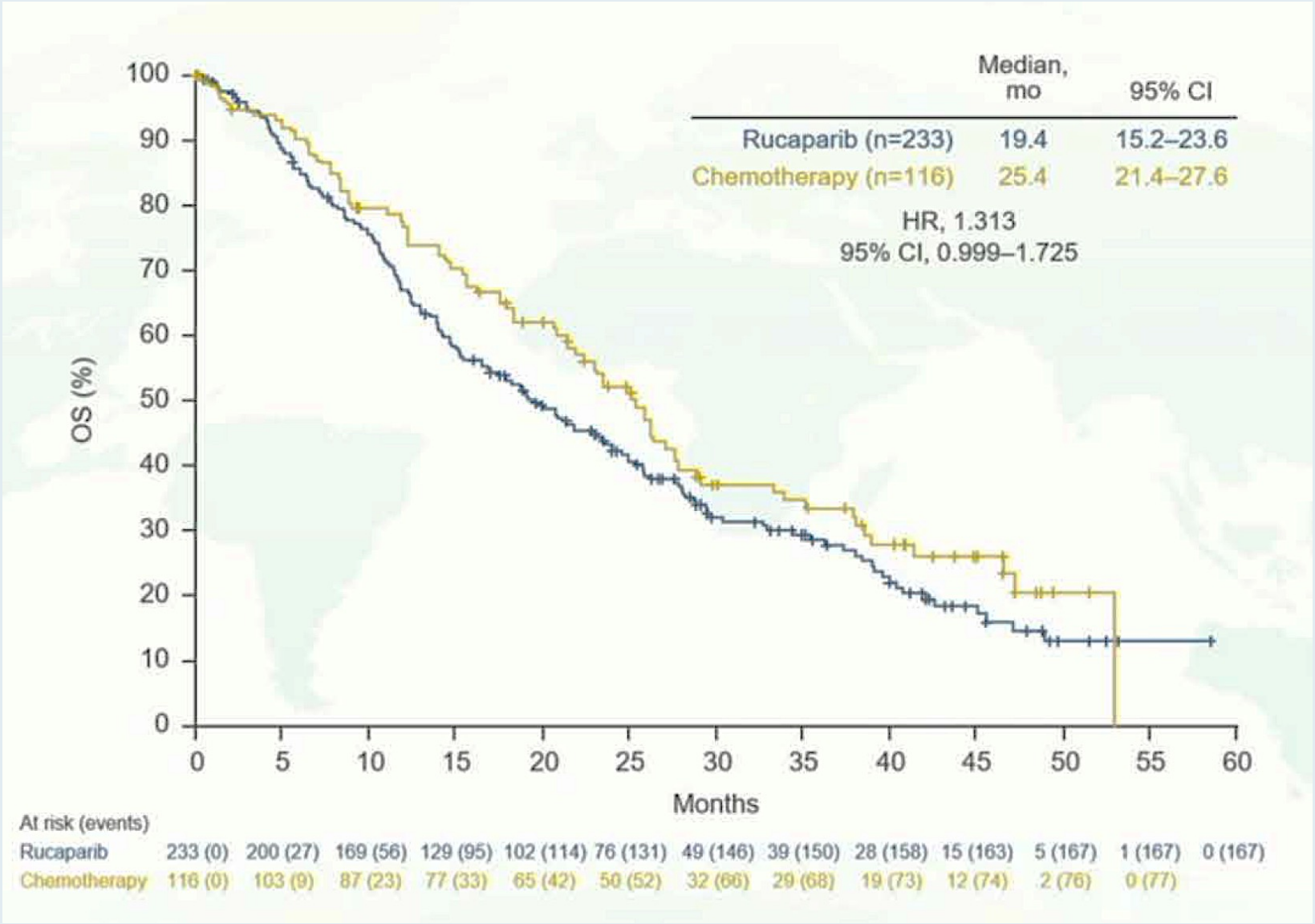
ARIEL4: Investigator-Assessed PFS



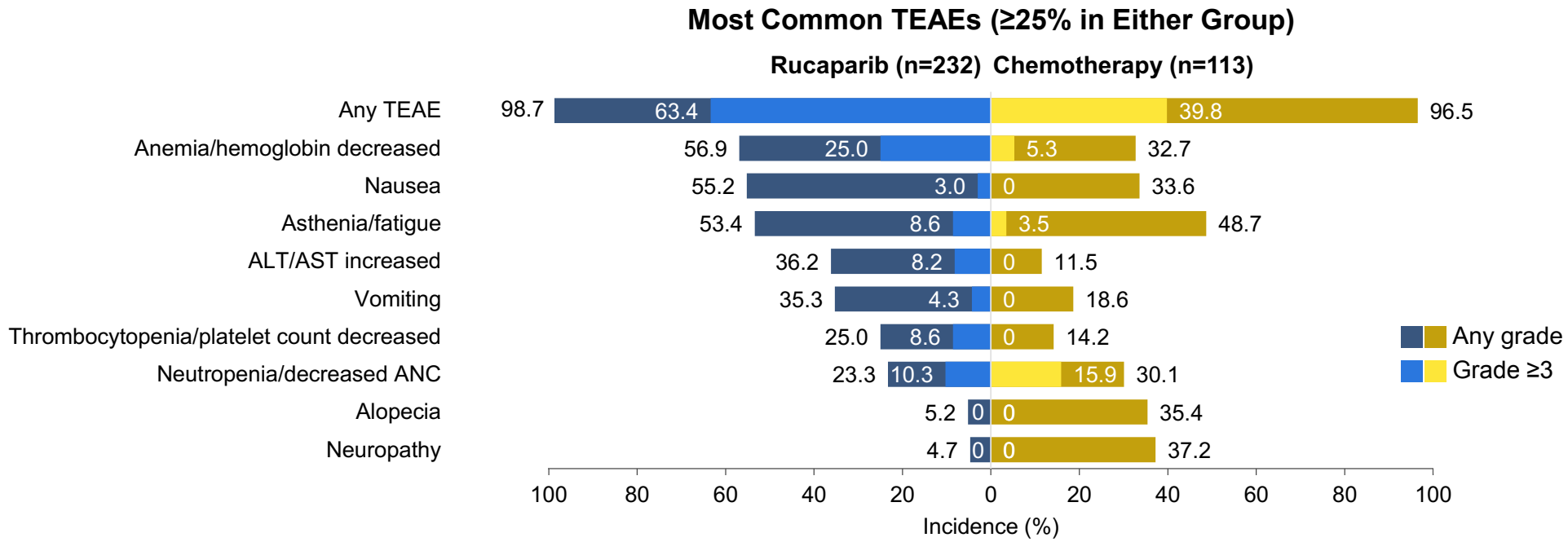
Oza AM et al. IGCS 2022;Abstract S004/461.

ARIEL4: Overall Survival (ITT)



Oza AM et al. IGCS 2022;Abstract S004/461.

ARIEL4: Treatment-Emergent Adverse Events in ≥25% of Patients



- MDS/AML was reported in 7 (3.0%) patients initially randomised to rucaparib (reported during long-term follow-up in 4 cases). No cases were reported among patients initially randomised to chemotherapy

Oza AM et al. ESMO 2022;Abstract 518O.

Scan for slides

Final Overall Survival and Long-Term Safety in the ENGOT-OV16/NOVA Phase 3 Trial of Niraparib in Patients with Recurrent Ovarian Cancer

Ursula A. Matulonis,[1] Jørn Herrstedt,[2] Amit Oza,[3] Sven Mahner,[4] Andrés Redondo,[5] Dominique Berton,[6] Jonathan S. Berek,[7] Charlotte A. Hasland,[8] Frederik Marme,[9] Antonio González-Martín,[10] Stephanie Becourt,[11] Anna V. Tinker,[12] Jonathan Ledermann,[13] Benedict Benigno,[14] Gabriel Lindahl,[15] Nicoletta Colombo,[16] Izabela A. Malinowska,[17] Wenlei Liu,[17] Michael H. A. Schmitz,[18] Bradley J. Monk,[19] Mansoor R. Mirza[20]

[1]Division of Gynecologic Oncology, Dana-Farber Cancer Institute and Harvard Medical School, Boston, MA, USA; [2]Department of Clinical Oncology and Palliative Care, Zealand University Hospital Roskilde and Næstved University of Copenhagen, Copenhagen, Denmark; [3]Division of Medical Oncology and Hematology, Cancer Clinical Research Unit at Princess Margaret Cancer Centre, Ontario, Toronto, Canada; [4]Department of Obstetrics and Gynecology, University Hospital LMU Munich, Germany; [5]Hospital Universitario La Paz – IdiPAZ, Madrid, Spain; [6]GINECO & Institut de Cancerologie de l'Ouest, Centre René Gauducheau, Saint-Herblain, France; [7]Stanford Women's Cancer Center, Stanford Cancer Institute, Stanford, CA, USA; [8]Department of Oncology, Aalborg University Hospital, Aalborg, Denmark; [9]Medical Faculty Mannheim, Heidelberg University, University Hospital Mannheim, Germany; [10]Medical Oncology Department, Clínica Universidad de Navarra, Madrid, Program in Solid Tumours, CIMA, Pamplona, and Grupo Español de Investigación en Cáncer de Ovario (GEICO), Pamplona, Spain; [11]Department of Gynecological Oncology, Oscar Lambert Center, Lille Cedex, France; [12]BC Cancer – Vancouver, Department of Medicine, University of British Columbia, Vancouver, Canada; [13]Department of Oncology, UCL Cancer Institute and UCL Hospitals, London, UK; [14]Ovarian Cancer Institute, University Gynecologic Oncology, Atlanta, GA, USA; [15]Gynecology Section, Department of Oncology, University Hospital Linköping, Linköping, Sweden; [16]Department of Medicine and Surgery, University of Milano-Bicocca, Gynecology Oncology Program European Institute of Oncology, Milan, Italy; [17]GSK, Waltham, MA, USA; [18]GSK, Baar, Switzerland; [19]Division of Gynecologic Oncology, HonorHealth Research Institute, University of Arizona College of Medicine, Creighton University School of Medicine, Phoenix, AZ, USA; [20]Department of Oncology, Rigshospitalet, Copenhagen University Hospital, Copenhagen, and Nordic Society of Gynaecological Oncology-Clinical Trial Unit, Copenhagen, Denmark.

SGO ANNUAL MEETING ON WOMEN'S CANCER TAMPA, FL • 2023 PATIENTS • PURPOSE • PROGRESS

Abstract 214

Presented by Dr. Ursula A. Matulonis

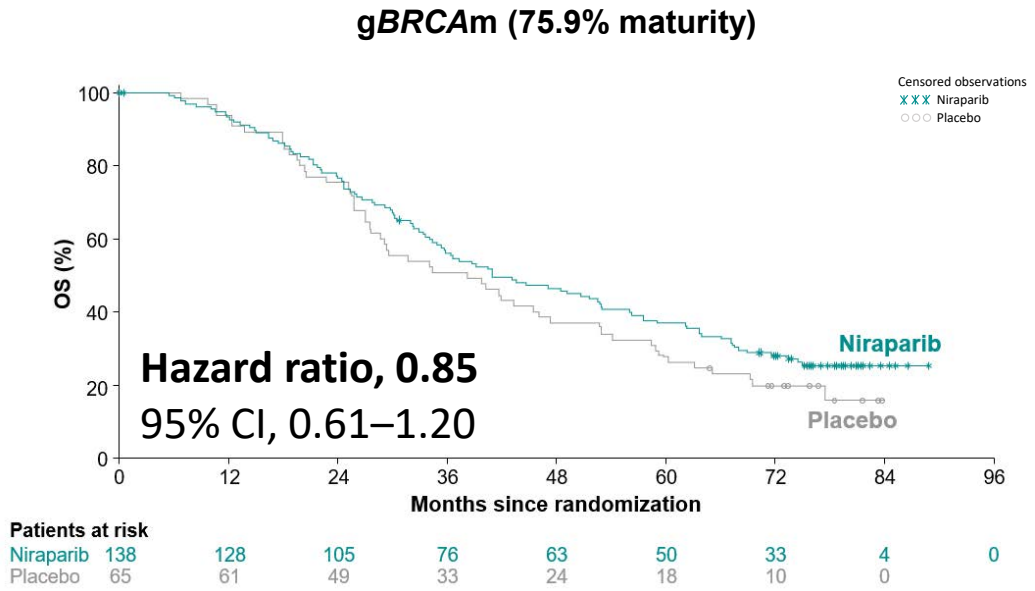
NSGO-CTU Nordic Society of Gynaecological Oncology - Clinical Trial Unit

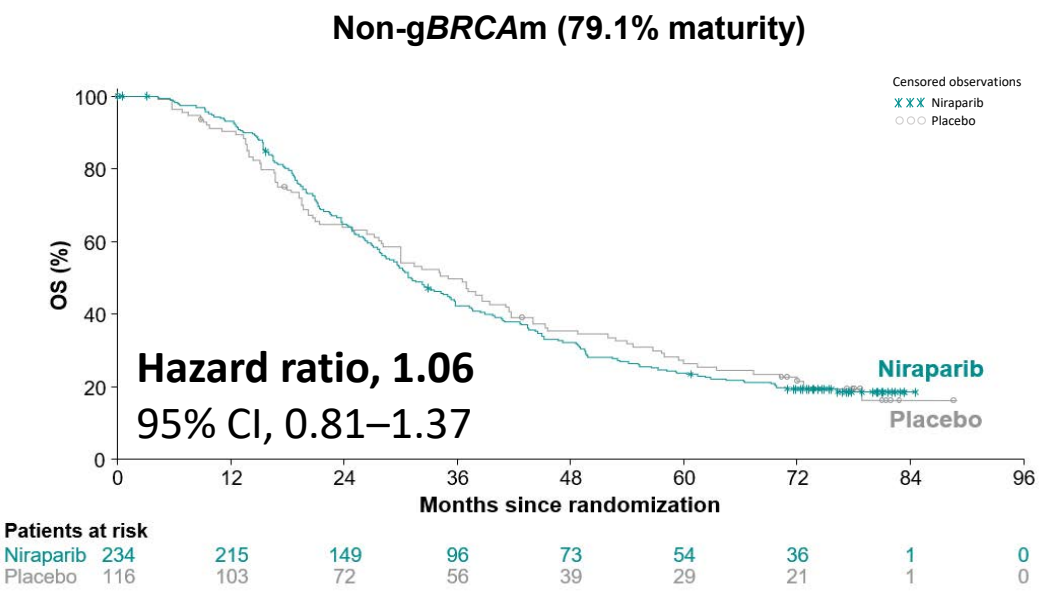
ENGOT European Network of Gynaecological Oncological Trial groups

RTP RESEARCH TO PRACTICE

NOVA: Final OS for gBRCAm and Non-gBRCAm Cohorts

- Overall OS maturity was 77.9%

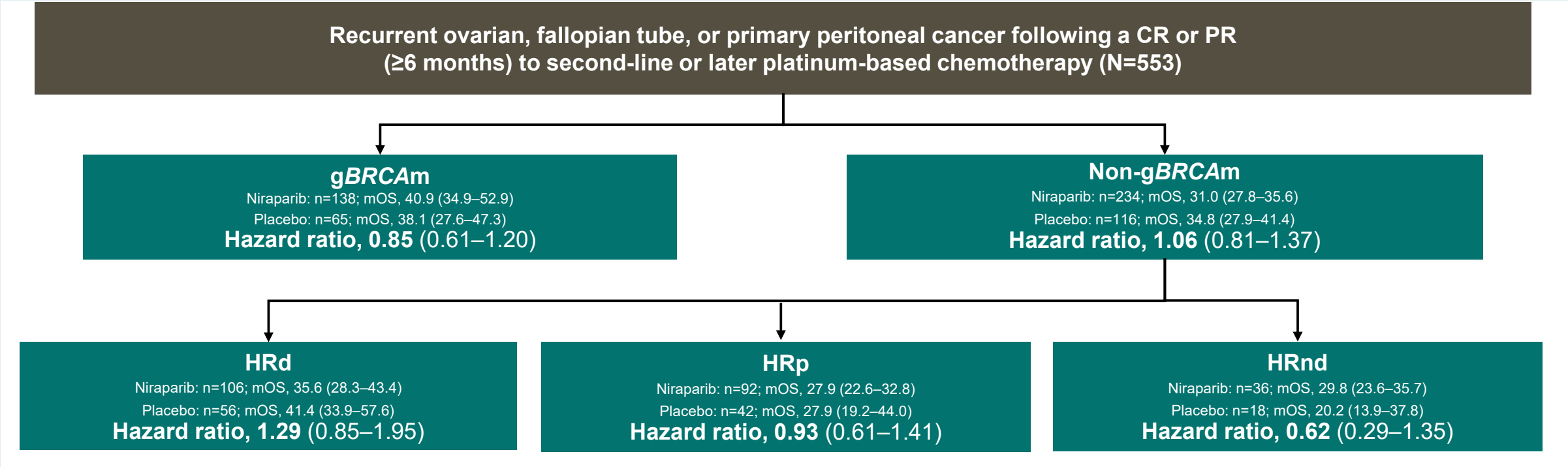




Matulonis UA et al. SGO 2023;Abstract 214.

RTP RESEARCH TO PRACTICE

NOVA: Final OS by HRD Subgroup in the Non-gBRCAm Cohort



Matulonis UA et al. SGO 2023;Abstract 214.

NOVA: Overall Safety Profile

- The safety profile of niraparib in the ENGOT-OV16/NOVA study was consistent with that observed in previous data readouts.[1,2] No new safety signals were detected
- The incidence of grade ≥3 adverse events (including thrombocytopenia, anemia, neutropenia, hypertension, fatigue, and GI disorders) was consistent with that observed in previous data readouts[1,2]

Overall population, n (%)	**Niraparib** (n=367)	**Placebo** (n=179)
Any TEAE	367 (100.0)	172 (96.1)
Any TRAE	359 (97.8)	126 (70.4)
Any TEAE with CTCAE toxicity grade ≥3	281 (76.6)	43 (24.0)
Any TRAE with CTCAE toxicity grade ≥3	244 (66.5)	10 (5.6)
Any serious TEAE	127 (34.6)	29 (16.2)
Any serious TRAE	74 (20.2)	4 (2.2)
Any TEAE leading to dose interruption	255 (69.5)	27 (15.1)
Any TEAE leading to dose reduction	254 (69.2)	9 (5.0)
Any TEAE leading to treatment discontinuation	67 (18.3)	4 (2.2)
Any TEAE leading to death	5 (1.4)	2 (1.1)

Matulonis UA et al. SGO 2023;Abstract 214.

NOVA: Incidence of MDS/AML

- As of the 31 Mar 2021 data cutoff, 3.8% of patients (14/367) who received niraparib and 1.7% of patients (3/179) who received placebo developed MDS/AML
- One additional case was reported in the g*BRCA*m cohort since the 01 October 2020 data cutoff

Incidence of MDS/AML based on final DCO of 31 Mar 2021

Niraparib	Placebo
Overall	
(n=367)	(n=179)
14 (3.8)	3 (1.7)
g*BRCA*m	
(n=136)	(n=65)
10 (7.4)	2 (3.1)
non-g*BRCA*m	
(n=231)	(n=114)
4 (1.7)	1 (0.9)

Matulonis UA et al. SGO 2023;Abstract 214.

Investigational Agents and Strategies:
PARP Inhibitors + Immune checkpoint inhibitors

PARIS 2022 ESMO congress

Abstract 529MO

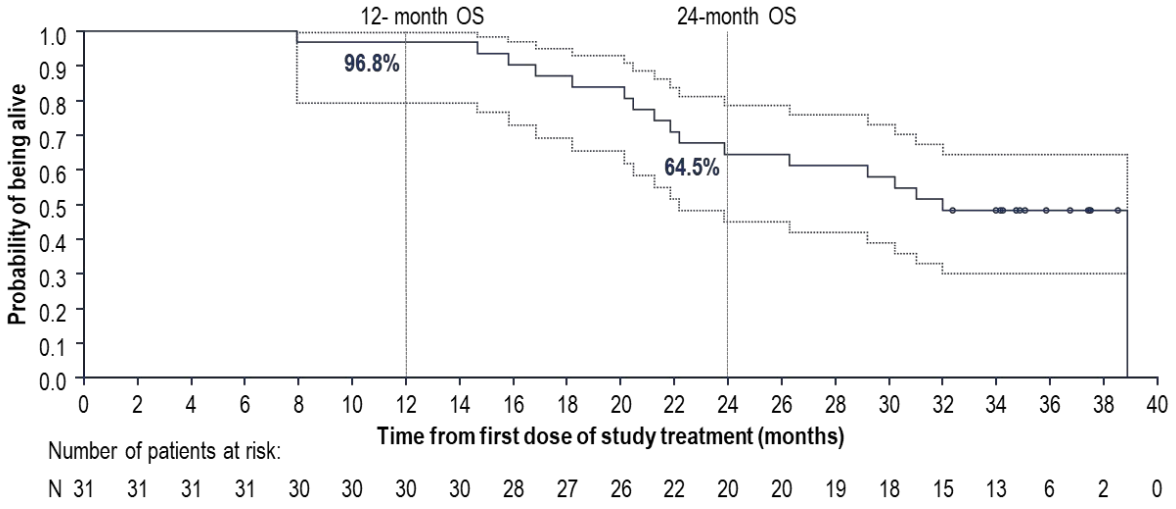
Phase II study of olaparib plus durvalumab with or without bevacizumab (MEDIOLA): final analysis of overall survival in patients with non-germline BRCA-mutated platinum-sensitive relapsed ovarian cancer

Susana Banerjee,[1] Martina Imbimbo,[2] Patricia Roxburgh,[3] Jae-Weon Kim,[4] Min Hwan Kim,[5] Ruth Plummer,[6] Salomon M. Stemmer,[7] Benoit You,[8] Michelle Ferguson,[9] Richard T. Penson,[10] David M. O'Malley,[11] Kassondra Meyer,[12] Haiyan Gao,[13] Helen K. Angell,[14] Ana T. Nunes,[15] Susan Domchek,[16] Yvette Drew[6*]

RTP RESEARCH TO PRACTICE

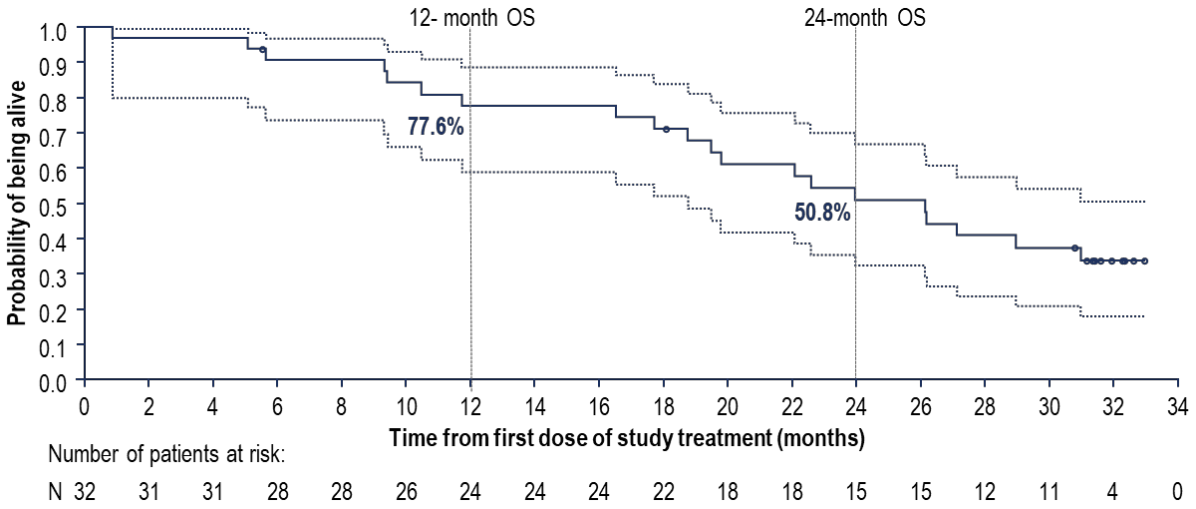
MEDIOLA Final Analysis: Median Overall Survival and 56-Week Disease Control Rate

Olaparib plus durvalumab and bevacizumab



	Olaparib plus durvalumab and bevacizumab
Median follow-up for OS, months	31.9
Events, n	17
Median OS (95% CI), months	**31.9 (22.1–NC)**
56-week DCR (90% CI), %	38.7 (24.1–55.0)

Olaparib plus durvalumab



	Olaparib plus durvalumab
Median follow-up for OS, months	23.2
Events, n	20
Median OS (95% CI), months	**26.1 (18.7–NC)**
56-week DCR (90% CI), %	9.4 (2.6–22.5)

Banerjee S et al. ESMO 2022;Abstract 529MO.

MEDIOLA: Adverse Events

	Olaparib plus durvalumab and bevacizumab N=31	Olaparib plus durvalumab N=32
Patients with any AE, n %	31 (100)	32 (100)
Patients with any Grade ≥3 AE, n (%)	19 (61.3)	21 (65.6)
Patients with any serious AE, n (%)	6 (19.4)	8 (25.0)
Patients with AEs leading to deaths,* n (%)	0	1 (3.1)
Patients with AEs leading to discontinuation of **any** study treatment,†,‡ n (%)	10 (32.3)	1 (3.1)
Olaparib‡	4 (12.9)	1 (3.1)
Durvalumab‡	5 (16.1)	1 (3.1)
Bevacizumab‡	9 (29.0)	–

	Olaparib plus durvalumab and bevacizumab N=31	Olaparib plus durvalumab N=32
Grade ≥3 AEs in ≥2 patients in any cohort, n (%)		
Anaemia	6 (19.4)	7 (21.9)
Hypertension	5 (16.1)	1 (3.1)
Fatigue	2 (6.5)	2 (6.3)
Lipase increased	2 (6.5)	2 (6.3)
Febrile neutropenia	2 (6.5)	1 (3.1)
Neutropenia	1 (3.2)	2 (6.3)
White blood cell count decreased	2 (6.5)	0

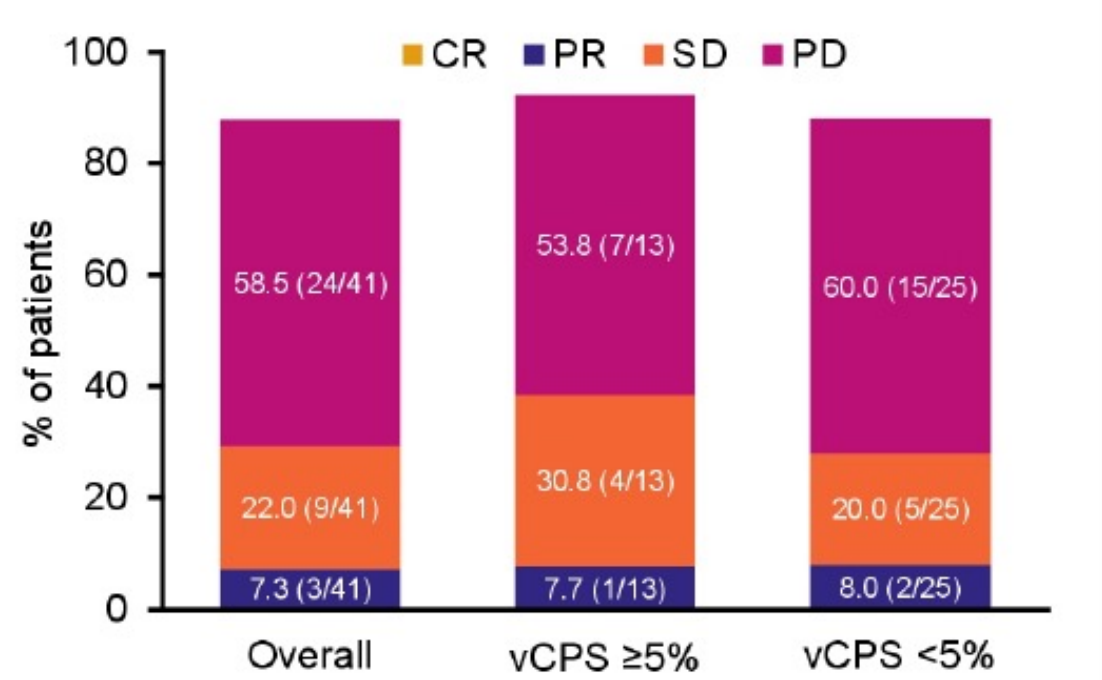
Banerjee S et al. ESMO 2022;Abstract 529MO.

MOONSTONE/GOG-3032: Interim analysis of a phase 2 study of niraparib + dostarlimab in patients (pts) with platinum-resistant ovarian cancer (PROC).

ASCO 2022;Abstract 5573.

Leslie M. Randall, David M. O'Malley, Bradley J. Monk, Robert L. Coleman, Stephanie Gaillard, Sarah F. Adams, Linda R. Duska, Fabio Cappuccini, Heather Dalton, Robert W. Holloway, Marilyn Huang, Hye Sook Chon, Noelle Gillette Cloven, Adam ElNaggar, Roisin Eilish O'Cearbhaill, Steven E. Waggoner, Zebin Wang, Eric Zhi, Vivek Samnotra, Panagiotis A. Konstantinopoulos

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.

MOONSTONE UPDATE

"PROC remains difficult to treat; the ORR observed with niraparib + dostarlimab did not reach the threshold for 2nd-stage accrual in this cohort of pts with PROC, no known *BRCA*m, and prior bevacizumab treatment. PD-L1 status did not predict response; HRD testing is in process. Although DCR was 29%, futility was declared based on low ORR. The safety of the combination was similar to the safety profile of each monotherapy."

Randall LM et al. ASCO 2022;Abstract 5573.

Investigational Agents and Strategies:
Mirvetuximab Soravtansine

FDA Grants Accelerated Approval for Mirvetuximab Soravtansine for FRα Positive, Platinum-Resistant Epithelial Ovarian, Fallopian Tube, or Peritoneal Cancer

Press Release: November 14, 2022

On November 14, 2022, the Food and Drug Administration granted accelerated approval to mirvetuximab soravtansine-gynx for adult patients with folate receptor alpha (FRα) positive, platinum-resistant epithelial ovarian, fallopian tube, or primary peritoneal cancer, who have received one to three prior systemic treatment regimens. Mirvetuximab soravtansine-gynx is a folate receptor alpha directed antibody and microtubule inhibitor conjugate. Patients are selected for therapy based on an FDA approved test.

Today, the FDA also approved the VENTANA FOLR1 (FOLR-2.1) RxDx Assay as a companion diagnostic device to select patients for the above indication.

Efficacy was evaluated in Study 0417 (NCT04296890), a single-arm trial of 106 patients with FRα positive, platinum-resistant epithelial ovarian, fallopian tube, or primary peritoneal cancer. Patients were permitted to receive up to three prior lines of systemic therapy. All patients were required to have received bevacizumab. The trial enrolled patients whose tumors were positive for FRα expression as determined by the above assay. Patients were excluded if they had corneal disorders, ocular conditions requiring ongoing treatment, Grade >1 peripheral neuropathy, or noninfectious interstitial lung disease.

https://www.fda.gov/drugs/resources-information-approved-drugs/fda-grants-accelerated-approval-mirvetuximab-soravtansine-gynx-fra-positive-platinum-resistant

RTP RESEARCH TO PRACTICE

original reports

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, MD[1]; Domenica Lorusso, MD, PhD[2]; Ana Oaknin, MD, PhD[3]; Sandro Pignata, MD, PhD[4]; Andrew Dean, MBChB, MRCP, FRACP[5]; Hannelore Denys, MD, PhD[6]; Nicoletta Colombo, MD, PhD[7,8]; Toon Van Gorp, MD, PhD[9]; Jason A. Konner, MD[10]; Margarita Romeo Marin, MD, PhD[11]; Philipp Harter, MD, PhD[12]; Conleth G. Murphy, MD[13]; Jiuzhou Wang, PhD[14]; Elizabeth Noble, BS[14]; Brooke Esteves, BSN[14]; Michael Method, MD, MPH, MBA[14]; and Robert L. Coleman, MD[15]

J Clin Oncol 2023 May;41(13):2436-45.

RTP RESEARCH TO PRACTICE

SORAYA: ORR and Subgroup Analysis in the Efficacy Evaluable Population

ORR	Investigator-Assessed	BICR-Assessed
No. of efficacy evaluable patients	n = 105	n = 96
ORR, No. (%) [95% CI][a]	34 (32.4) [23.6 to 42.2]	29 (30.2) [21.3 to 40.4]
Best overall response, No. (%)		
CR	5 (4.8)	6 (6.3)
PR	29 (27.6)	23 (24.0)
SD	48 (45.7)	54 (56.3)
PD	20 (19.0)	9 (9.4)
NE	3 (2.9)	4 (4.2)
Tumor reduction, No. (%)	75 (71.4)	ND
Disease control rate, No. (%)	54 (51.4)	ND
CA-125 response[b]	n = 86	
No. (%) [95% CI]	40 (46.5) [35.7 to 57.6]	ND
ORR subgroup analysis		
Prior lines of therapy, No. (%) [95% CI][a]		
1 or 2	n = 51	n = 46
	18 (35.3) [22.4 to 49.9]	15 (32.6) [19.5 to 48.0]
3	n = 53	n = 49
	16 (30.2) [18.3 to 44.3]	14 (28.6) [16.6 to 43.3]
Prior exposure to PARPi, No. (%) [95% CI][a,c]		
Yes	n = 50	n = 47
	19 (38.0) [24.7 to 52.8]	14 (29.8) [17.3 to 44.9]
No	n = 51	n = 46
	14 (27.5) [15.9 to 41.7]	15 (32.6) [19.5 to 48.0]

Matulonis UA et al. *J Clin Oncol* 2023;41(13):2436-45.

RTP RESEARCH TO PRACTICE

Mirvetuximab Soravtansine (MIRV) in Patients with Platinum-Resistant Ovarian Cancer with High Folate Receptor Alpha (FRα) Expression: Evaluation of Sequence of Therapy on Anti-Tumor Activity in the SORAYA Study

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

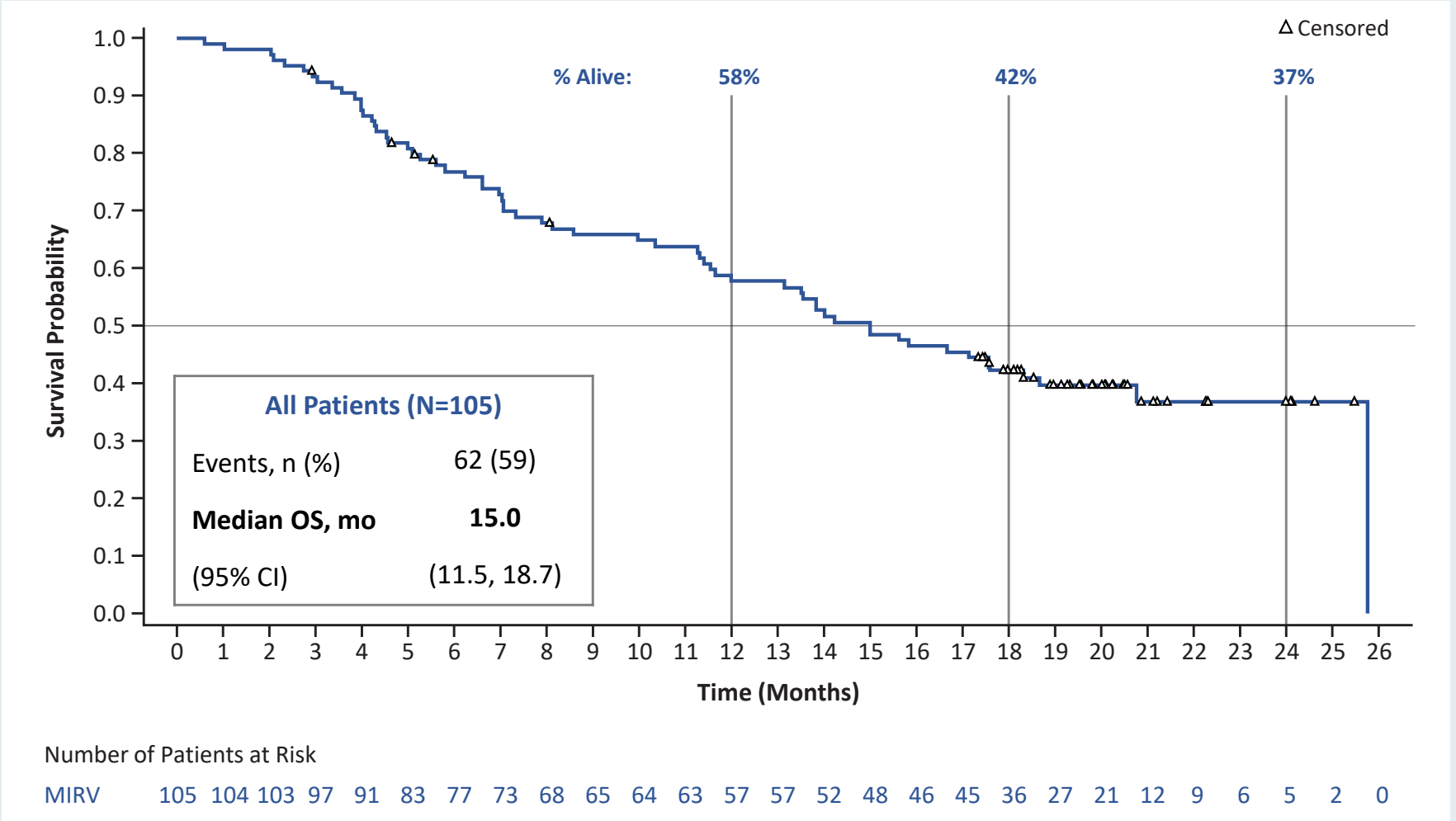
[1]US Oncology Research, Texas Oncology, The Woodlands, TX, USA; [2]Gynaecologic Cancer Programme, Vall d'Hebron Institute of Oncology (VHIO), Hospital Universitari Vall d'Hebron, Vall d'Hebron Barcelona Hospital Campus, Barcelona, Spain; [3]Istituto Nazionale Tumori di Napoli Fondazione G Pascale IRCCS,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

SORAYA

SGO ANNUAL MEETING ON WOMEN'S CANCER TAMPA, FL • 2023 PATIENTS • PURPOSE • PROGRESS

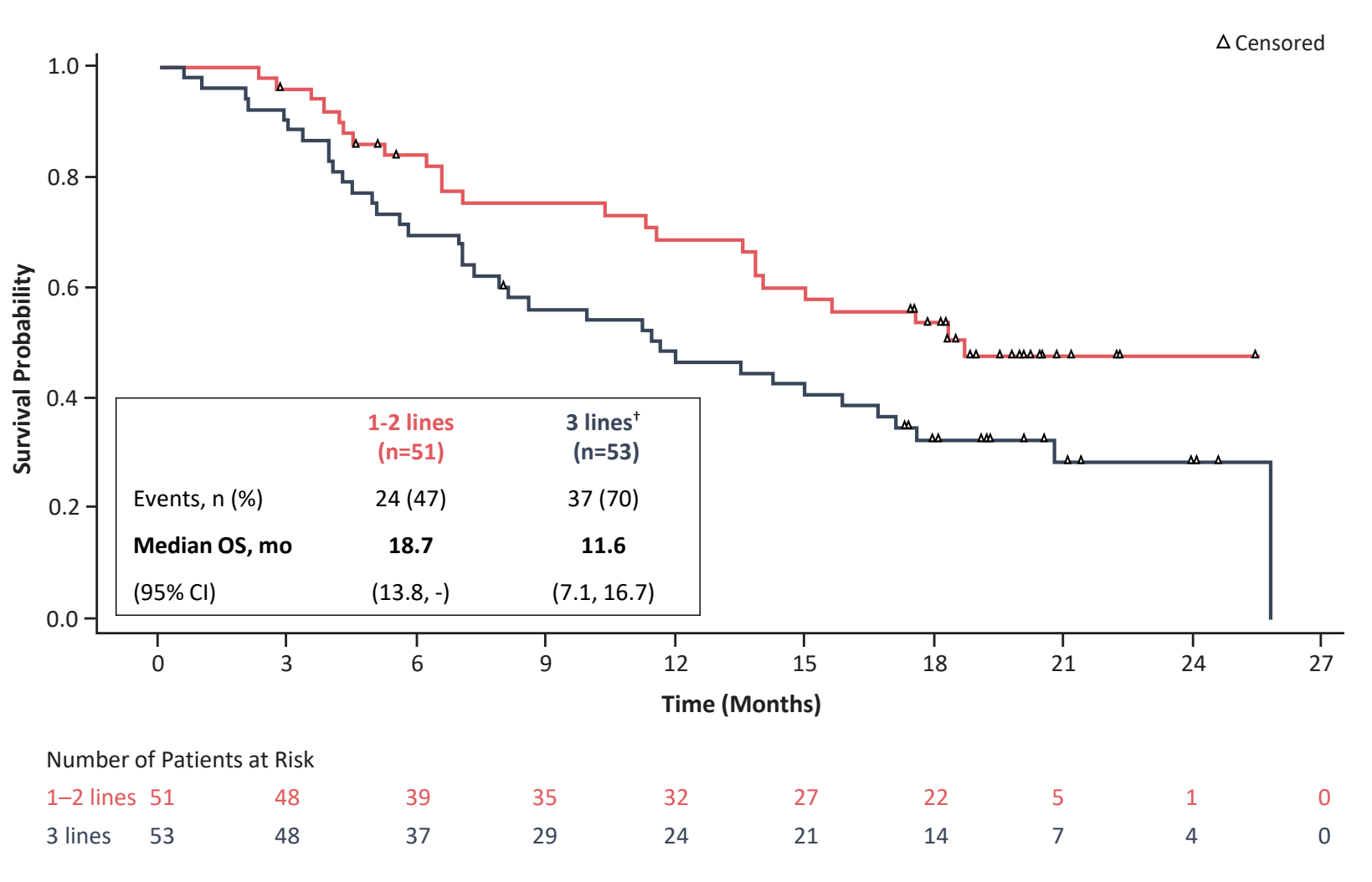
Abstract 139

SORAYA: Final Overall Survival by Investigator in Efficacy Evaluable Population



Coleman RL et al. SGO 2023;Abstract 139.

SORAYA: Final Overall Survival by Number of Prior Lines of Therapy



Coleman RL et al. SGO 2023;Abstract 139.

RTP RESEARCH TO PRACTICE

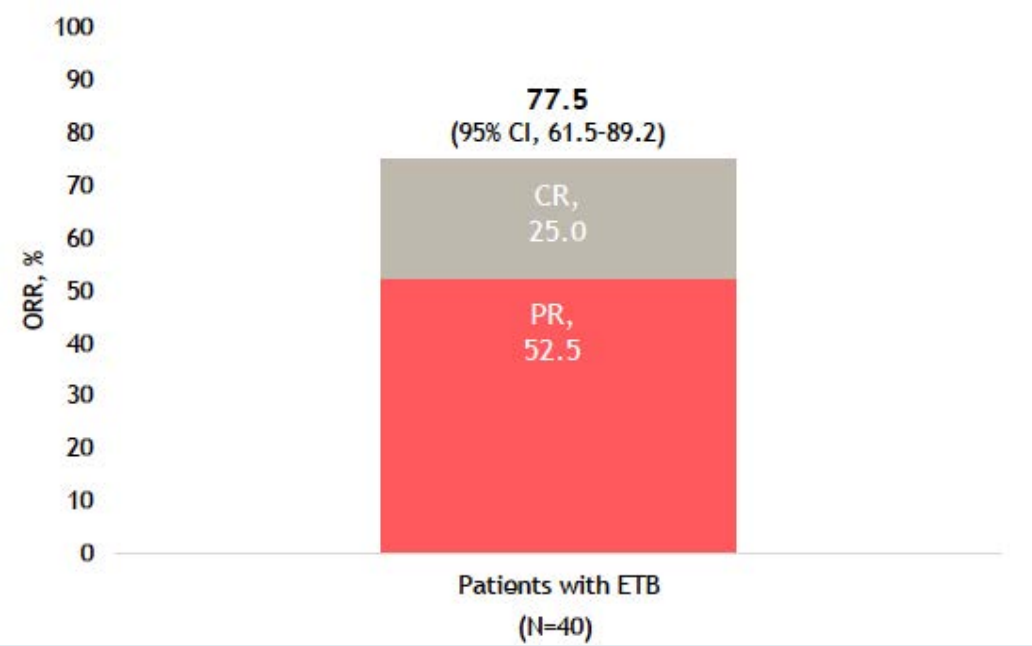
Characterization of Extended Treatment Benefit from Three Phase I and III Clinical Trials Examining Patients with Folate Receptor Alpha-Positive Recurrent Ovarian Cancer Treated with Single-Agent Mirvetuximab Soravtansine

Oaknin A et al.

ESGO 2022;Abstract 2022-RA-660-ESGO.

Efficacy and Safety Summary of Mirvetuximab Soravtansine (MIRV) from a Pooled Analysis of Three Clinical Trials

- Retrospective pooled analysis of 40 patients who achieved extended treatment benefit (ETB), defined as patients with progression-free survival >12 months per investigator assessment, with MIRV monotherapy in the IMGN853-0401 (Phase I), FORWARD I (Phase III) and SORAYA (Phase III) clinical trials



- Median DOR for patients with ETB was 22.1 months
- Median PFS for patients with ETB was 17.0 months

ORR = overall response rate; CR = complete response; PR = partial response

- The most common treatment-related adverse events included blurred vision (60%), fatigue (50%) and nausea (50%)
- Peripheral neuropathy: 35% (no Grade 3+ events); pneumonitis: 20% (no Grade 3+ events); keratopathy: 40% (Grade 3 event in 1 patient that resolved within 20 days)

Oaknin A et al. ESGO 2022;Abstract 2022-RA-660-ESGO.

SORAYA: Treatment-Related Adverse Events in ≥20%

TRAE, n (%)[a]	MIRV 6 mg/kg + BEV 15 mg/kg (N=126)		
	All grades	Grade 3	Grade 4
Diarrhea	74 (59)	2 (2)	0 (0)
Blurred vision	71 (56)	1 (1)	0 (0)
Fatigue	64 (51)	5 (4)	0 (0)
Nausea	64 (51)	1 (1)	0 (0)
Peripheral neuropathy[b]	50 (40)	1 (1)	0 (0)
Keratopathy[c]	43 (34)	0 (0)	0 (0)
Decreased appetite	38 (30)	0 (0)	0 (0)
Dry eye	38 (30)	3 (2)	0 (0)
Hypertension	38 (30)	20 (16)	0 (0)
Thrombocytopenia	35 (28)	4 (3)	1 (1)
AST increased	33 (26)	6 (5)	0 (0)
Headache	33 (26)	0 (0)	0 (0)
Vomiting	33 (26)	1 (1)	0 (0)
ALT increased	29 (23)	6 (5)	0 (0)

- Most TRAEs were low grade; GI, ocular, and fatigue were the most common
- 48% of patients experienced grade ≥3 events; the most common was hypertension (16%)
- Due to treatment-emergent AEs, 30% discontinued MIRV and 37% discontinued BEV
  - 4 patients (3%) discontinued MIRV due to blurred vision
- Patients received a median of 8 cycles of MIRV+ BEV (range 1–35 cycles)
- One patient had a death that was deemed related to a study treatment (intestinal perforation possibly related to BEV)

[a]Related to any study drug (either MIRV or BEV). [b]Peripheral neuropathy includes TRAEs with the following preferred terms: neuropathy peripheral, peripheral sensory neuropathy, peripheral motor neuropathy, paraesthesia, hypoaesthesia. [c]Keratopathy includes TRAES with the following preferred terms: corneal cyst, corneal disorder, corneal epithelial microcysts, keratitis, keratopathy, limbal stem cell deficiency, corneal opacity, corneal erosion, corneal pigmentation, corneal deposits, keratitis interstitial, punctate keratitis, corneal epithelium defect

Coleman R et al. IGCS 2022;Abstract O028 / #376 .

Ongoing Trials with Mirvetuximab Soravtansine in Ovarian Cancer

MIRVETUXIMAB PSOC MONOTHERAPY[1]

64% ORR

FRα-HIGH RECURRENT
N= 11

- Potential for a clinically meaningful benefit in FRα-high recurrent platinum-sensitive ovarian cancer
  - 64% ORR (7/11); 2 CRs and 5 PRs

PICCOLO

- Single-arm Phase 2 trial for mirvetuximab in FRα-high patients with platinum-sensitive ovarian cancer
- Now enrolling
- Potential for label expansion in 2024

MIRVETUXIMAB + BEVACIZUMAB[2,3]

64% ORR

FRα-HIGH RECURRENT
N= 33

- Compelling activity in FRα-high recurrent ovarian cancer, regardless of platinum status
  - 59% ORR (10/17), 9.4 month mDOR, 9.7 month mPFS in the platinum-resistant subgroup
  - 69% ORR (11/16), 12.7 month mDOR, 13.3 month mPFS in the platinum-sensitive subgroup

GLORIOSA

- Randomized Phase 3 trial for mirvetuximab + bevacizumab maintenance in FRα-high platinum-sensitive ovarian cancer
- Aligned with FDA on trial design

MIRVETUXIMAB + CARBOPLATIN[4]

80% ORR

FRα-MED and -HIGH
N= 10

- Highly active in recurrent platinum-sensitive ovarian cancer with mDOR of 24 months
- Supporting ongoing ISTs in recurrent platinum-sensitive ovarian cancer: ~70 patient neo-adjuvant study initiated in H1 2021; and a randomized Phase 2 ~140 patient study

TRIAL 420

- Single-arm Phase 2 trial for mirvetuximab + carboplatin followed by mirvetuximab continuation in FRα-low, medium, and high patients with platinum-sensitive ovarian cancer

[1]Immunogen internal data. [2] Gilbert L et al. ASCO 2020. [3] O'Malley D et al. ASCO 2021. [4] Gynecologic Oncology 2018;151:46-52.

PICCOLO Phase II Trial Schema

PICCOLO

Enrollment and Key Eligibility

- Platinum-sensitive disease (PFI >6 mo)
- At least 2 prior lines of platinum-based therapy
  - Patients with documented platinum allergy require only 1 prior line of platinum
- FRα-high by IHC scoring (≥75% PS2+)
- Appropriate for single agent therapy as next line of therapy as determined by investigator

Statistical Assumptions

- N=75
- Null hypothesis: ORR is ≤ 28% tested using an optimal Simon's two-stage design w/o pause in enrollment

→

Mirvetuximab Soravtansine

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

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

A Targeted Approach: IMGN853-0420 (NCT05456685)

An open-label, phase 2 trial of MIRV + carboplatin followed by MIRV continuation in FRα-low, -medium, and -high patients with platinum-sensitive ovarian cancer

Actively Enrolling

420 Patient Population
(N≈114)

Enrollment and Key Eligibility

Platinum-sensitive disease
(defined as radiographic progression >6 months from last dose of most recent platinum therapy)

FRα detected by IHC with PS2+ intensity among ≥25% of viable tumor cells

1 prior platinum treatment

Prior PARPi required if BRCA+

Treatment Regimen

MIRV
(6 mg/kg AIBW Q3W)
+
Carboplatin
(AUC 5 Q3W)

6 cycles[a]

CR, PR, SD

Treatment Regimen: Continuation[b]

MIRV
(6 mg/kg AIBW Q3W)

Primary Endpoint

ORR by INV

Secondary Endpoints

DOR
Safety and tolerability
PFS
OS
CA-125 response by GCIG criteria
Sensitivity analysis[c]

https://clinicaltrials.gov/ct2/show/NCT05456685

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GLORIOSA Phase III Trial Schema

An open-label, phase 3 trial for MIRV + BEV maintenance in FRα-high patients with platinum-sensitive ovarian cancer

Actively Enrolling

GLORIOSA Patient Population (N≈418)

Enrollment and Key Eligibility

Platinum-sensitive disease
(defined as progression >6 months from last dose of primary platinum therapy)

FRα detected by IHC with PS2+ intensity among ≥75% of viable tumor cells

1 prior systemic treatment

CR, PR, or SD after treatment with platinum-based doublet + BEV

Prior PARPi required if BRCA+

2L Treatment

Platinum-based doublet + BEV

CR, PR, or SD

1:1 Randomization

Treatment Regimen[a] Experimental

MIRV
(6 mg/kg AIBW Q3W)
+
BEV
(15 mg/kg Q3W)

Treatment Regimen[a] Control

BEV
(15 mg/kg Q3W)

Stratification Factors
Prior PARPi,
Prior BEV, CR or PR or SD

Primary Endpoint

PFS

Key Secondary Endpoint

OS

Other Secondary Endpoints

Safety and tolerability
PFS2
ORR
DOR
DFS
CA-125 response by GCIG criteria
PROs[b]

https://clinicaltrials.gov/ct2/show/NCT05445778.

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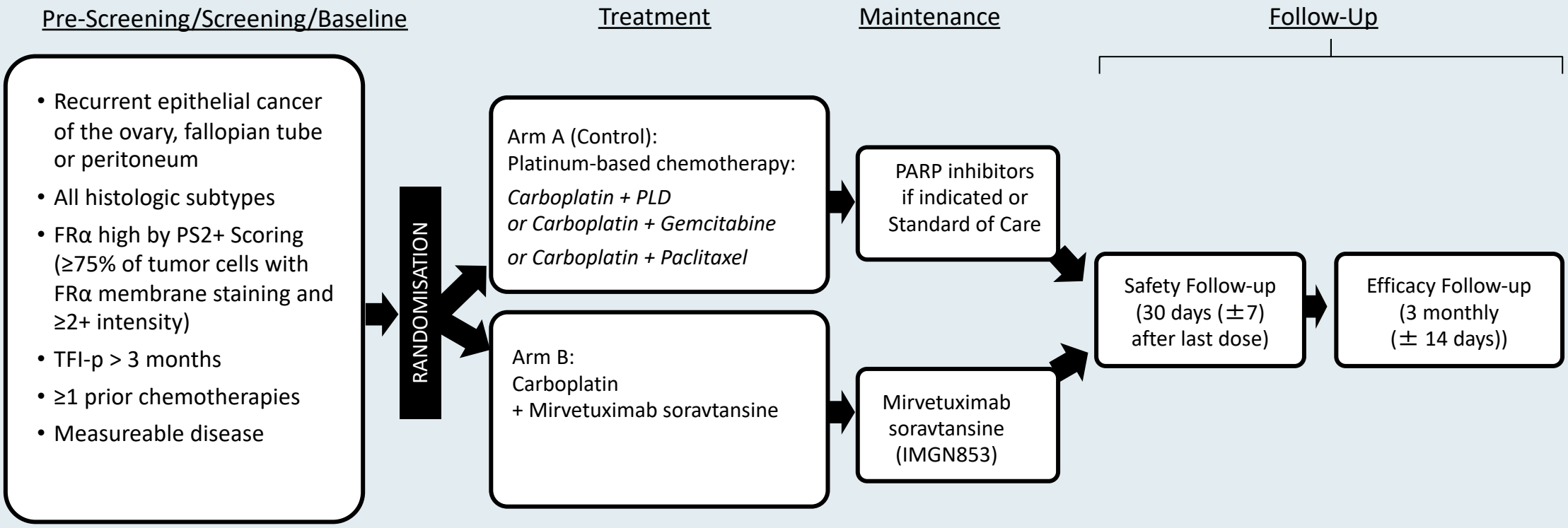
AGO-OVAR 2.34/MIROVA Randomized Phase II Study Design

Study Design



Recruitment Duration: approximately 18 months
Total Study Duration: approximately 5.5 years
Recruitment Start: September 2021

Trillsch F et al. ESGO 2022;Abstract 2022-RA-835-ESGO.

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Investigational Agents and Strategies:
Upifitamab Rilsodotin (UpRI)

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

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

SGO 2022;Abstract 76.

Society of Gynecologic Oncology

Ongoing UPLIFT (ENGOT-ov67 / GOG-3048)
UpRi Single-Arm Registrational Trial in Platinum-Resistant Ovarian Cancer

Patient Population: HGSOC[a] progressing after standard treatments; measurable disease per RECIST v1.1; ECOG PS 0 or 1; enrolling regardless of NaPi2b expression

Key Inclusion Criteria
- Platinum-resistant ovarian cancer (PROC)
- 1–4 prior lines of therapy
- Grade ≤2 peripheral neuropathy
- Archival or fresh tissue required for biomarker evaluation

Key Exclusion Criteria
- 1–2 prior lines bevacizumab-naive
- Primary platinum-refractory disease

UpRi 36 mg/m^2 up to max 80 mg; IV Q4W

Primary Endpoint
- Confirmed ORR in NaPi2b-high (N = ~100)

Secondary Endpoint
- Confirmed ORR in overall population (N = up to ~180 including 100 NaPi2b-high)

Other Secondary Endpoints
- DoR
- Safety

Prospectively-defined retrospective analysis to validate NaPi2b biomarker cutoff

NCT03319628: Trial Completed Enrollment

Topline data expected mid-2023

Richardson DL et al. SGO 2022;Abstract 76.

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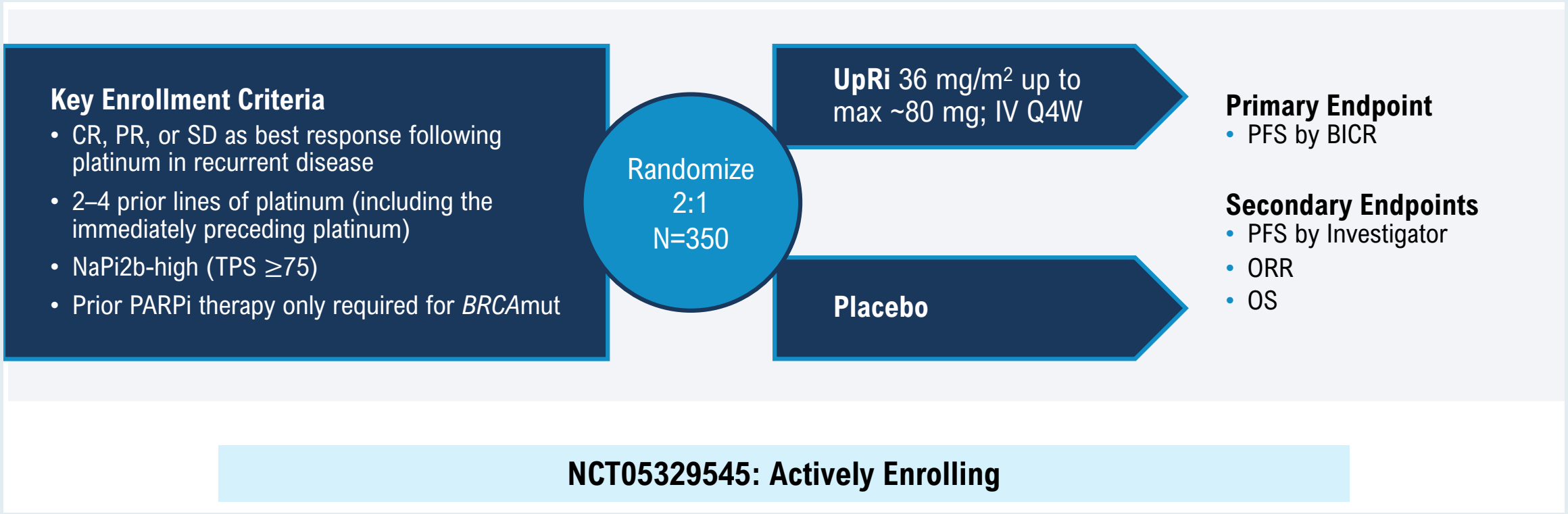
Ongoing UP-NEXT (GOG-3049 / ENGOT-OV71-NSGO-CTU) Phase 3 Study of UpRi Monotherapy Maintenance vs Placebo in Recurrent Platinum-Sensitive Ovarian Cancer



Richardson DL et al. SGO 2022;Abstract 76.

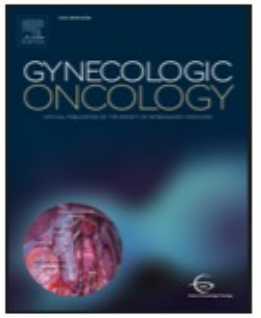
Investigational Agents and Strategies:
Tumor Treating Fields

Gynecologic Oncology 150 (2018) 471–477

Contents lists available at ScienceDirect

Gynecologic Oncology

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



Tumor Treating Fields in combination with paclitaxel in recurrent ovarian carcinoma: Results of the INNOVATE pilot study

Ignace Vergote [a,*], Roger von Moos [b], Luis Manso [c], Els Van Nieuwenhuysen [a], Nicole Concin [a], Cristiana Sessa [d]

[a] University Hospitals Leuven, Leuven Cancer Institute, Leuven, Belgium
[b] Kantonsspital Graubünden, Chur, Switzerland
[c] Hospital Universitario 12 de Octubre, Madrid, Spain
[d] Oncology Institute of Southern, Switzerland, Bellinzona

Breakfast with the Investigators: Ovarian Cancer

A CME Symposium Held in Conjunction with the 2023 ASCO® Annual Meeting

Sunday, June 4, 2023

6:45 AM – 7:45 AM CT

Faculty

Philipp Harter, MD, PhD

David M O'Malley, MD

Shannon N Westin, MD, MPH

Moderator

Neil Love, MD

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POSTMEETING SURVEY – Available Now

Clinicians in Attendance: The postmeeting survey is now available on the iPads for attendees in the room and on Zoom for those attending virtually. We appreciate your completing this survey before the end of the program.

Thank you for your input.

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Meet The Professors Live: Clinical Investigators Provide Perspectives on Actual Cases of Patients with Lymphoma, Chronic Lymphocytic Leukemia and Multiple Myeloma

A CME Symposium Held in Conjunction with the 2023 ASCO® Annual Meeting

Sunday, June 4, 2023

7:00 PM – 9:30 PM CT

Faculty

John N Allan, MD
Shaji K Kumar, MD
Ann S LaCasce, MD, MMSc
Sagar Lonial, MD
Loretta J Nastoupil, MD
Susan O'Brien, MD

Moderator

Neil Love, MD

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Thank you for joining us!
Your feedback is very important to us.

Please complete the survey currently up on the iPads for attendees in the room and on Zoom for those attending virtually. The survey will remain open up to 5 minutes after the meeting ends.

How to Obtain CME Credit

In-person attendees: Please refer to the program syllabus for the CME credit link or QR code. You may also use the iPads available in the meeting room to complete the course evaluation.

Online/Zoom attendees: The CME credit link is posted in the chat room.

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