Meet The Professor

Optimizing the Management of Ovarian Cancer

Thursday, September 29, 2022
5:00 PM – 6:00 PM ET

Faculty

Stephanie Lheureux, MD, PhD

Moderator

Neil Love, MD

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Commercial Support

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

Dr Love — Disclosures

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

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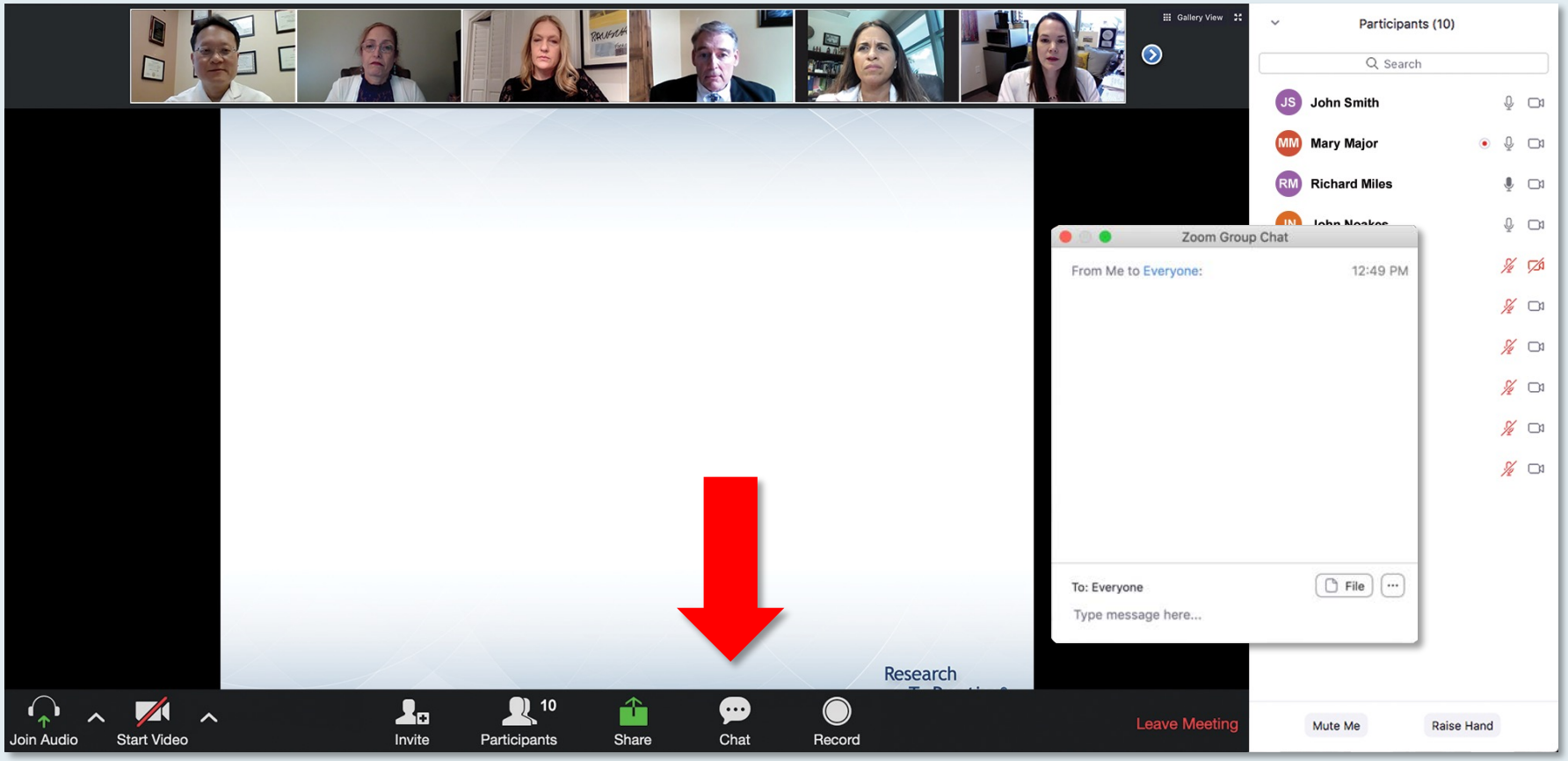
We Encourage Clinicians in Practice to Submit Questions



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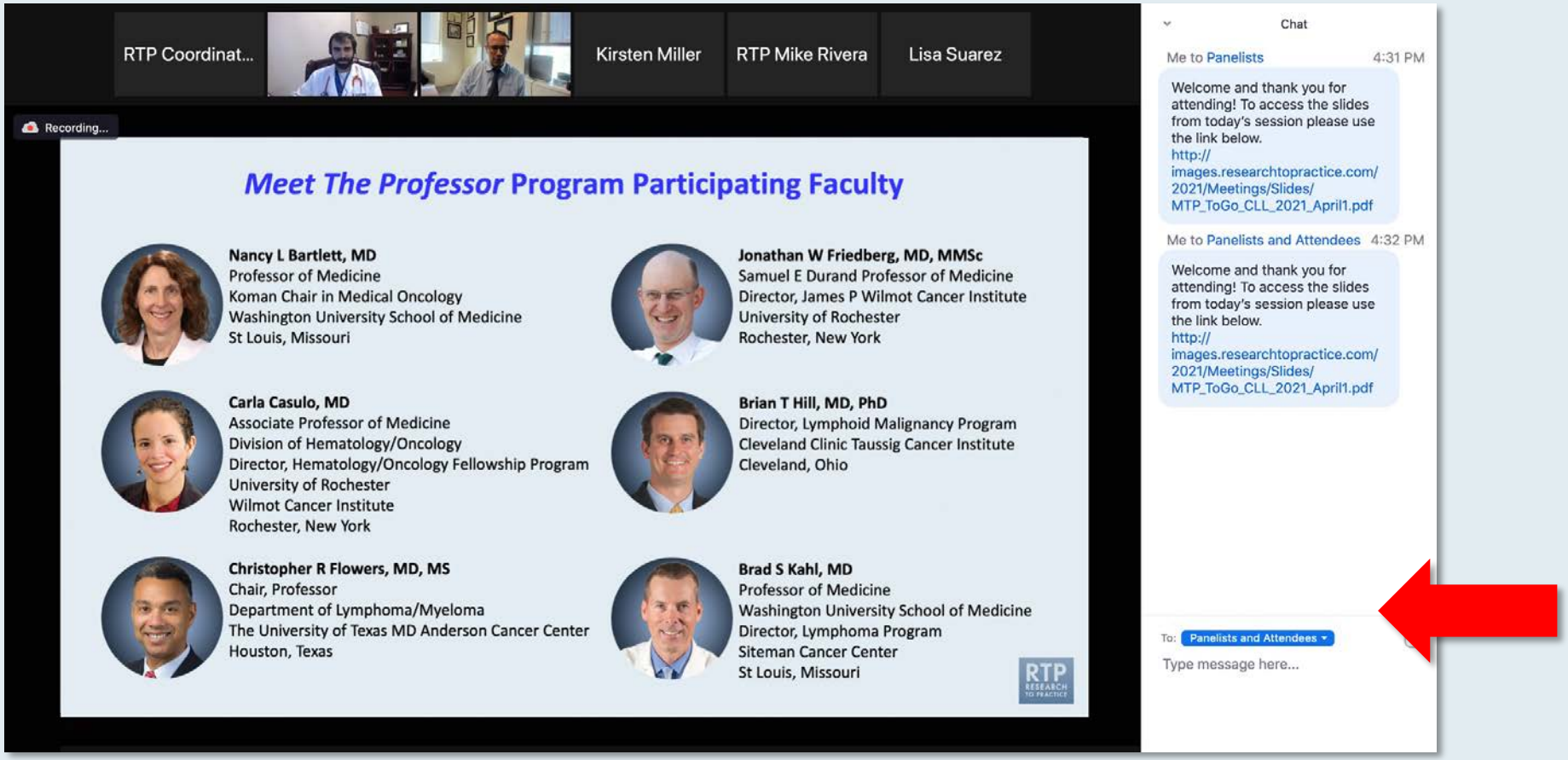
Expand chat submission box



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

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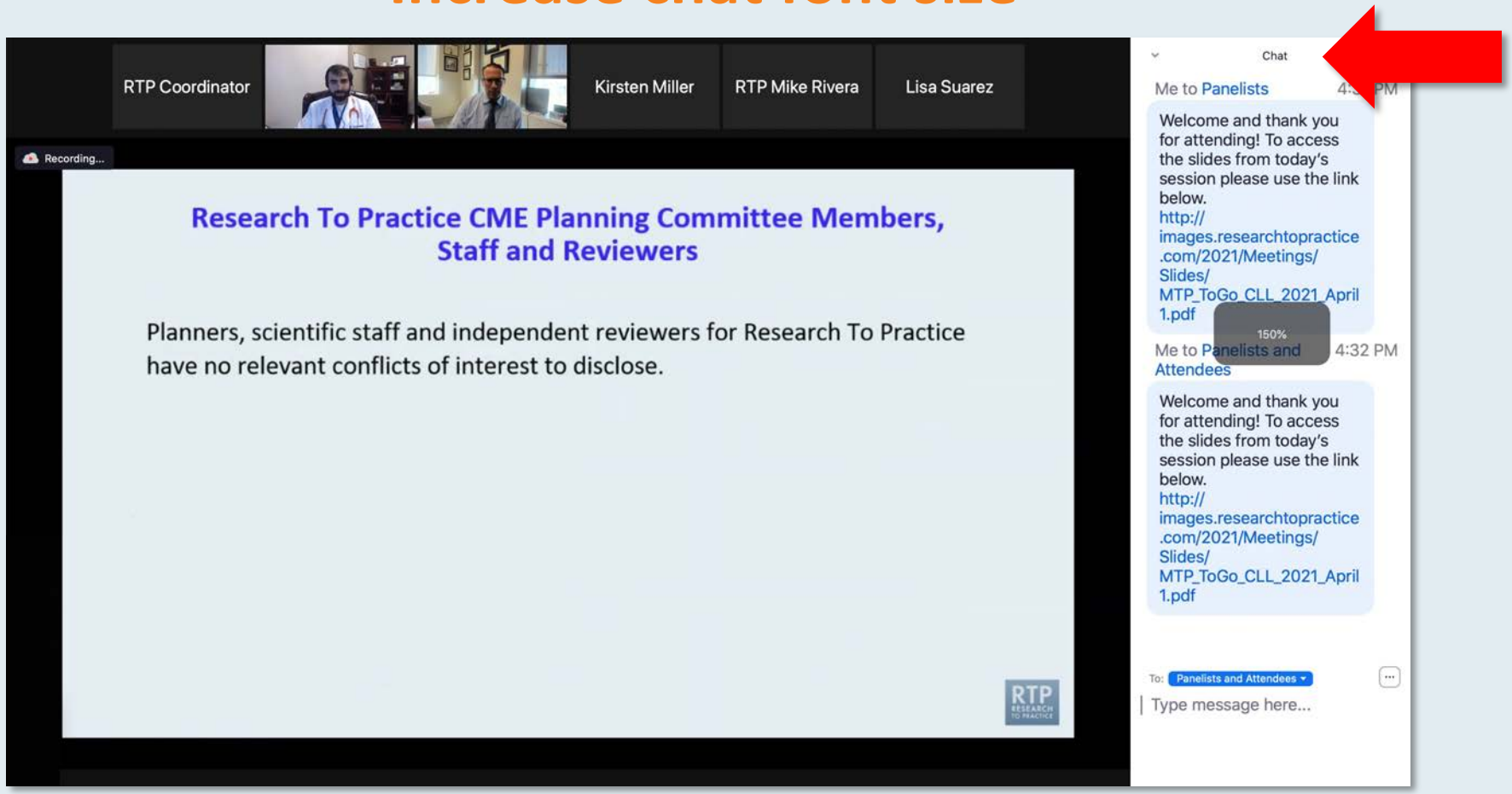
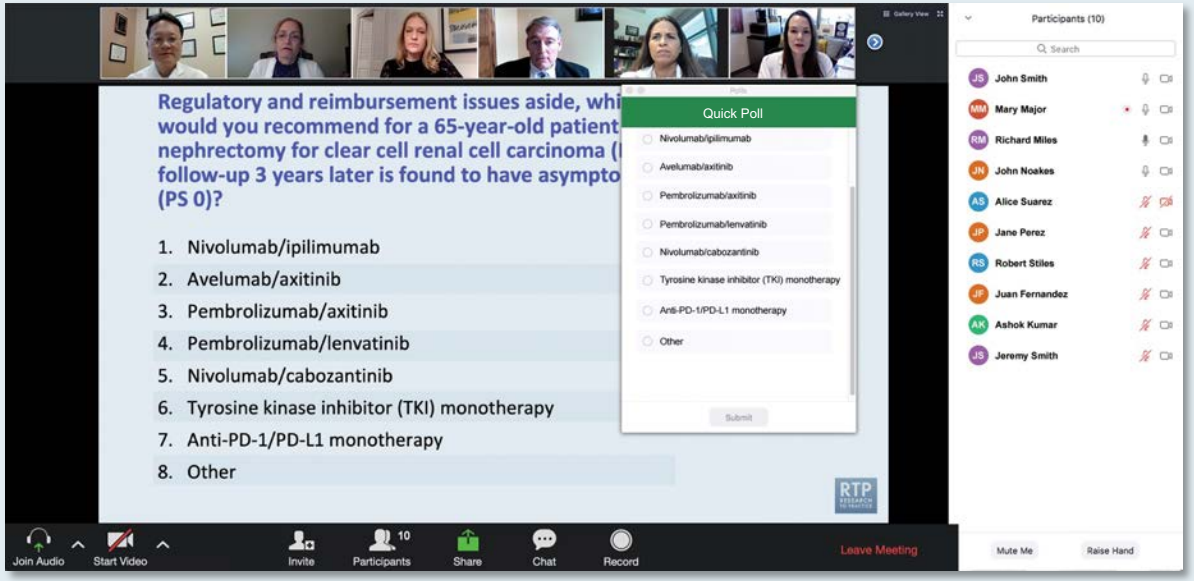
Increase chat font size



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

Clinicians in the Audience, Please Complete the Pre- and Postmeeting Surveys



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William G Wierda, MD, PhD

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The Clinical Implications of Key Recent Data Sets in Oncology: A Daylong Multitumor Educational Symposium in Partnership with Florida Cancer Specialists

Saturday, October 22, 2022

7:30 AM – 5:30 PM ET

JW Marriott Orlando| Orlando, Florida

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Matthew P Goetz, MD
Ian E Krop, MD, PhD
Ann S LaCasce, MD, MMSc
Corey J Langer, MD
Prof Georgina Long, AO, BSc, PhD, MBBS
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Thank you for joining us!

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

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Drug Development Program - Gynecology
Division of Medical Oncology and Hematology
Gynecology Site Lead
Co-Director of the Beyond Chemotherapy Program
Princess Margaret Cancer Centre
Associate Professor
University of Toronto
Toronto, Ontario, Canada

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Meet The Professor Program Participating Faculty

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Associate Clinical Professor of Obstetrics, Gynecology and Reproductive Sciences
UC San Diego Health
La Jolla, California

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Prof Jonathan A Ledermann
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UCL Cancer Institute
London, United Kingdom

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

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Richard T Penson, MD, MRCP
Associate Professor of Medicine
Harvard Medical School
Clinical Director, Medical Gynecologic Oncology
Massachusetts General Hospital
Boston, Massachusetts

MODERATOR
Neil Love, MD
Research To Practice

Shannon N Westin, MD, MPH
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Director, Early Drug Development
Department of Gynecologic Oncology and
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The University of Texas
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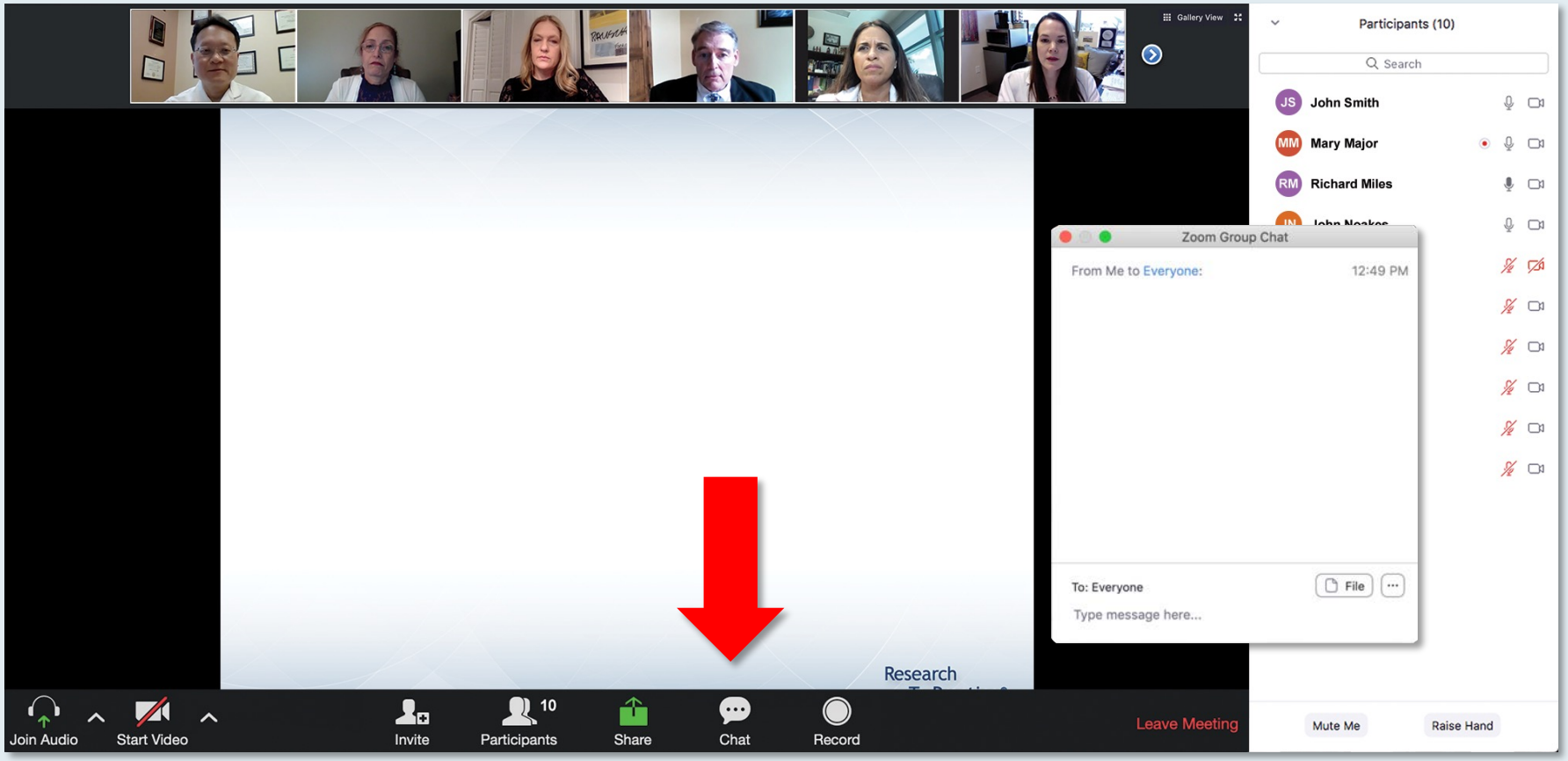

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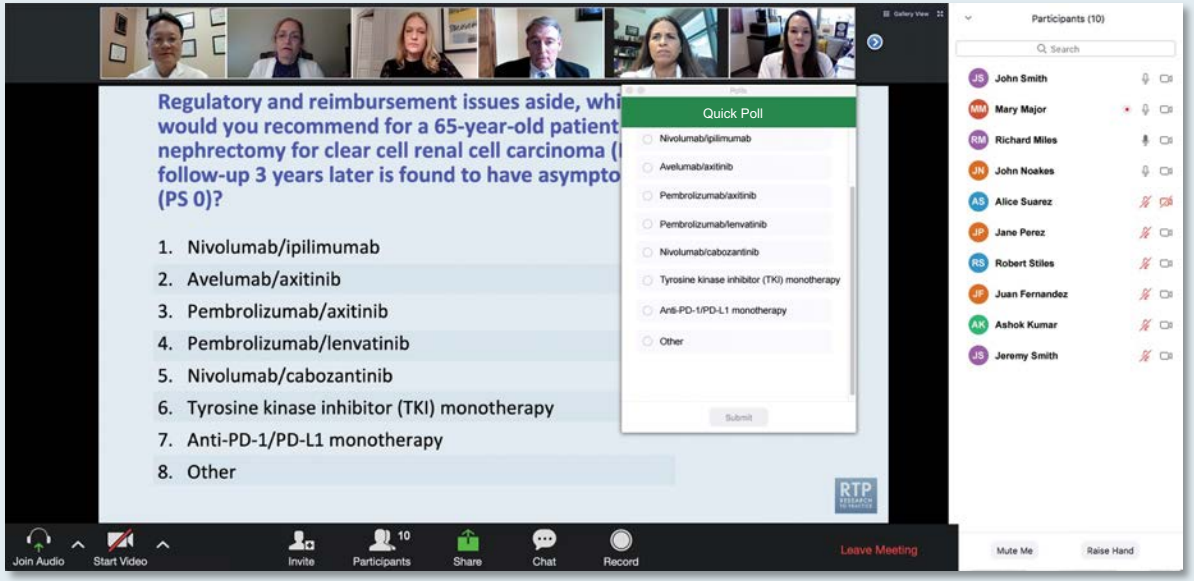

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Dana M Chase, MD
University of Arizona
College of Medicine
Phoenix, Arizona

Kimberly Ku, MD
Oncologist
Bloomington, Illinois

Gigi Chen, MD
John Muir Health
Pleasant Hill, California

Joseph Martins, MD
UT Health Science Center
Tyler, Texas

Karim ElSahwi, MD
Hackensack Meridian Health
Neptune City, New Jersey

Neil Morganstein, MD
Atlantic Health System
Summit, New Jersey

Rahul Gosain, MD
Guthrie Corning Cancer Center
Corning, New York

Erik Rupard, MD
The Reading Hospital
West Reading, Pennsylvania

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Meet The Professor with Dr Lheureux

Prologue: Seminars in Cancer Biology

MODULE 1: Cases

MODULE 2: Faculty Survey

MODULE 3: Journal Club

Appendix

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Meet The Professor with Dr Lheureux

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Appendix

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Semin Cancer Biol 2022 April 5;[Online ahead of print].

Contents lists available at ScienceDirect

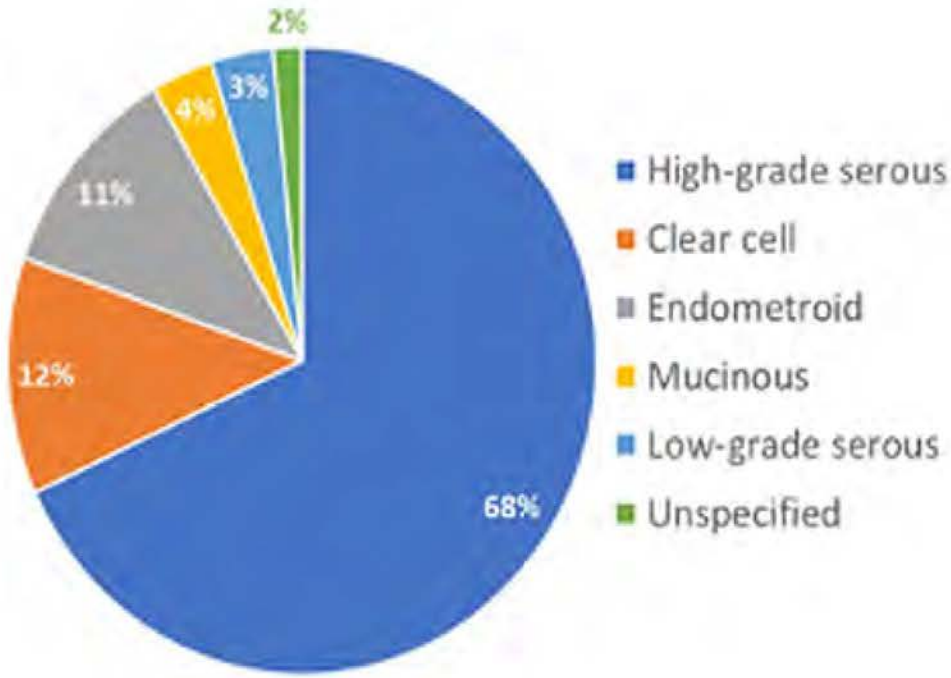
Seminars in Cancer Biology

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

Molecular, cellular and systemic aspects of epithelial ovarian cancer and its tumor microenvironment

Esther Schoutrop [a,1], Lidia Moyano-Galceran [b,1], Stephanie Lheureux [c,d], Jonas Mattsson [a,c,e,f], Kaisa Lehti [b,g], Hanna Dahlstrand [a,h,*,2], Isabelle Magalhaes [a,i,*,2]

Histological Classification of Epithelial Ovarian Cancer



STIC or CIC precursor lesions
Mutations in *TP53* + DNA damage & repair/cell cycle control genes
High chromosomal instability
Typically high FIGO stage (III/IV) at diagnosis
Highly aggressive neoplasms
High mortality rate
Initial chemosensitivity; development of resistance is common

Endometriosis as risk factor
Mutations in *ARID1A*, *PIK3CA*, *HNF1B* and *PTEN*

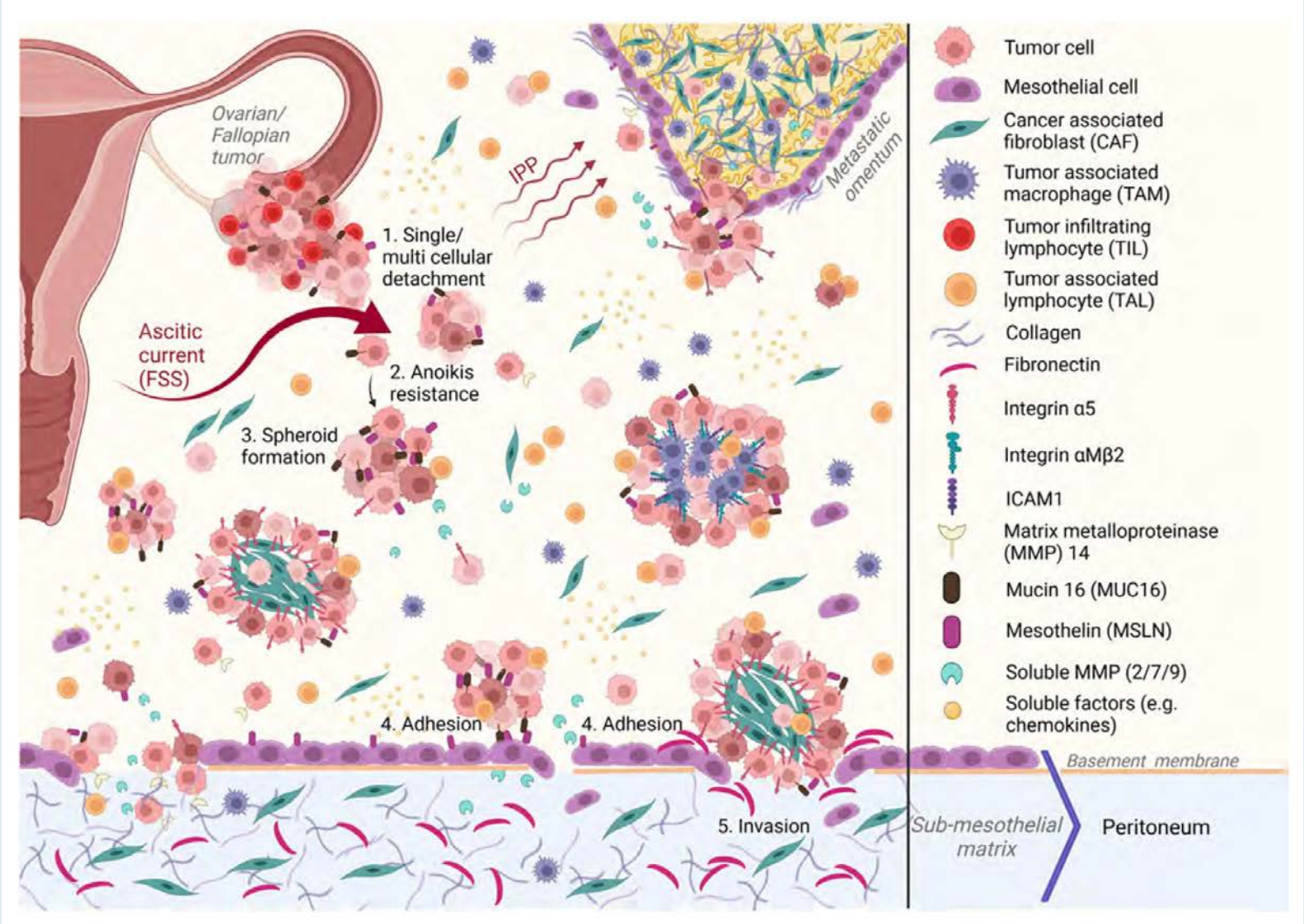
Same as in Clear cell + mutations in DNA mismatch repair genes

Mutations in EERB2 and KRAS/BRAF/MEK pathways

Benign precursor lesions as origin?
Mutations in EERB2 and KRAS/BRAF/MEK pathways
Typically low FIGO stage (I/II) at diagnosis
Low proliferative capacity
Low contribution to OC deaths
Relatively chemoresistant

Schoutrop E et al. *Semin Cancer Biol* 2022 April 5;[Online ahead of print].

Transcoelomic Metastasis of Ovarian Cancer



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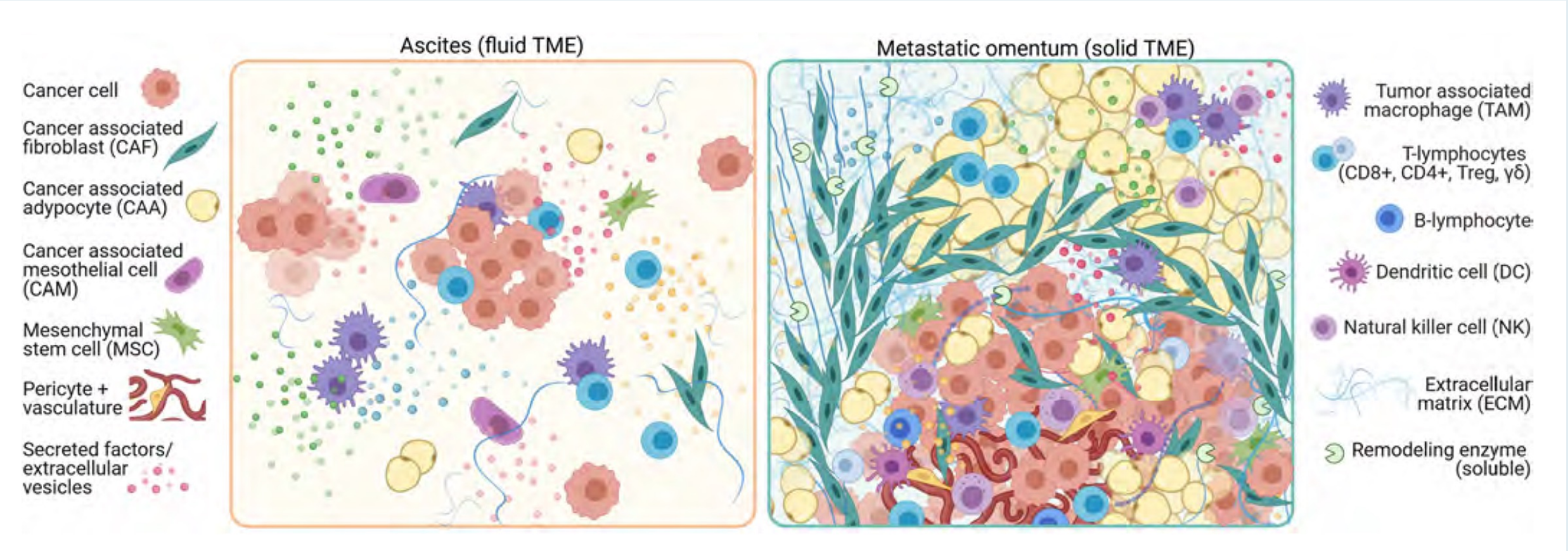

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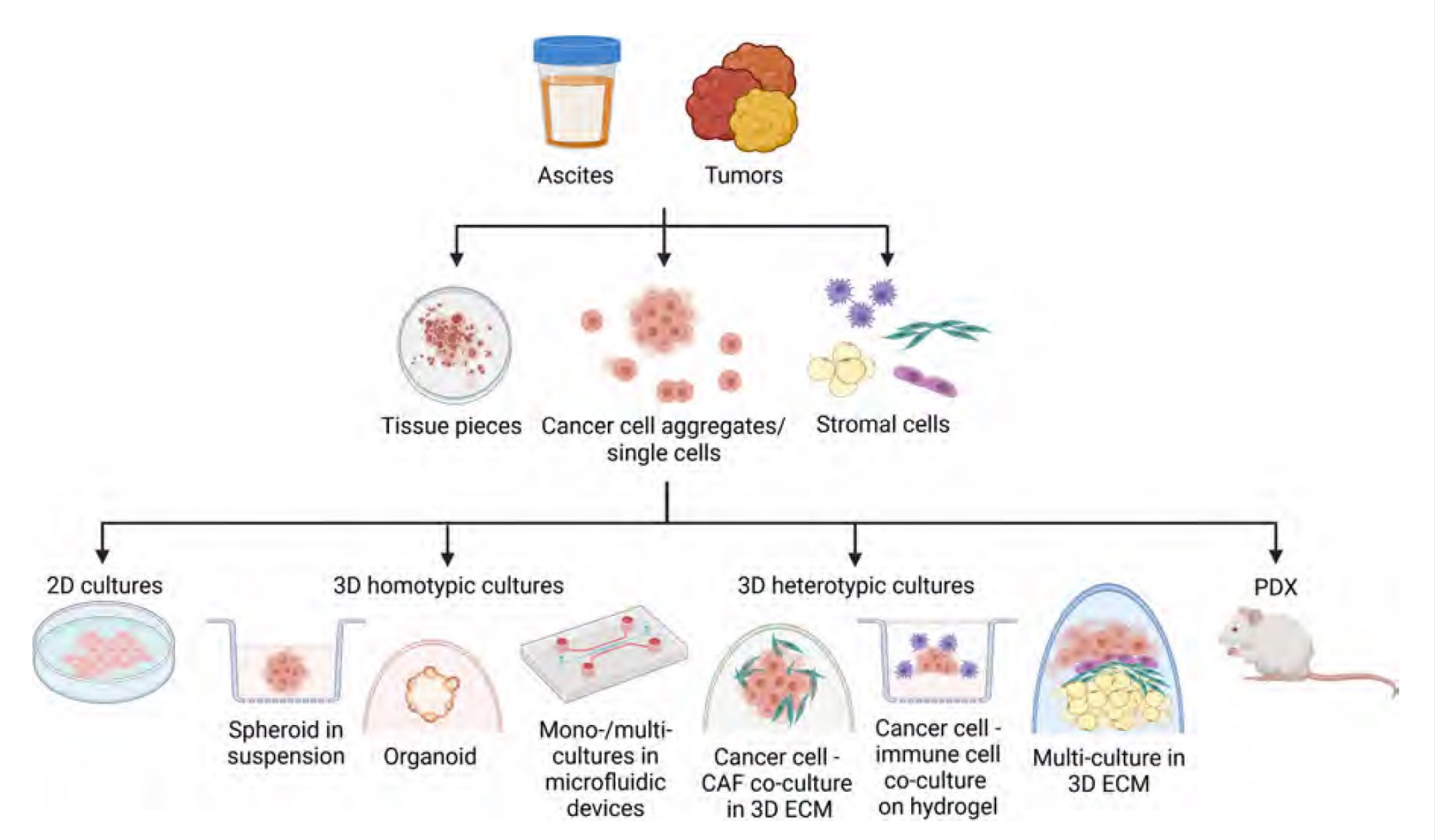
Patient-Derived Models for the Study of Ovarian Cancer



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Meet The Professor with Dr Lheureux

MODULE 1: Cases

- Dr Chase: 55-year-old woman with Stage IVB BRCA WT, HR-proficient primary peritoneal cancer
- Dr ElSahwi: 74-year-old woman with recurrent gBRCA2-mutant, platinum-sensitive peritoneal cancer – Lynch VUS
- Dr Martins: 63-year-old woman with ovarian cancer and prolonged pancytopenia after treatment with a PARP inhibitor
- Dr Morganstein: 64-year-old woman with platinum-resistant recurrence of BRCA WT clear cell ovarian cancer s/p carboplatin/paclitaxel/bevacizumab and maintenance bevacizumab – HRD-negative
- Dr Gosain: 61-year-old woman with multiregimen-recurrent BRCA WT, HRD-negative metastatic ovarian cancer
- Dr Chen: 62-year-old woman with BRCA WT recurrent ovarian cancer who experiences significant anemia and thrombocytopenia on maintenance niraparib
- Dr Chase: 69-year-old woman with recurrent platinum-resistant, BRCA WT, HR-proficient ovarian cancer s/p paclitaxel/tumor treating fields on a clinical trial
- Dr Ku: 57-year-old woman with BRCA2 mutation-positive metastatic ovarian cancer and platinum-resistant recurrence on third-line cisplatin/gemcitabine
- Dr ElSahwi: A 55-year-old woman with BRCA WT, MSS oligometastatic HGSOC
- Dr Rupard: 66-year-old woman with recurrent metastatic BRCA WT ovarian cancer who does not want further RT or chemotherapy

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Case Presentation: 55-year-old woman with Stage IVB BRCA WT, HR-proficient primary peritoneal cancer

Dr Dana Chase (Phoenix, Arizona)

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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/

RTP RESEARCH TO PRACTICE

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

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

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

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

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

June 17, 2022

"In consultation with the FDA, [the manufacturer of rucaparib] recently was advised not to file a supplemental new drug application based on data from a cohort of the Phase III ATHENA study until the study's overall survival data mature.

In the 8-K, [the manufacturer] said the FDA has accepted a request for a pre-NDA meeting and noted that the ATHENA-MONO portion of the Phase III study has met its primary endpoint of progression-free survival compared to placebo. OS is a secondary endpoint for ATHENA-MONO and the data are approximately 25% mature at present. [The manufacturer] said the FDA urged it to hold off filing for supplemental approval until the OS data reach 50% maturity, and indicated an advisory committee review would likely be necessary if the data were filed earlier than that point.

In a statement to *Scrip*, the firm said that although it cannot anticipate the outcome of the pre-NDA meeting, 'we are encouraged that the FDA is willing to have a dialogue.' [They] estimate the ATHENA-MONO OS data will reach 50% maturity in approximately two years."

https://scrip.pharmaintelligence.informa.com/SC146575/Clovis-Withdraws-Rubraca-Ovarian-Cancer-Indication-Due-To-Survival-Imbalance?vid=Pharma

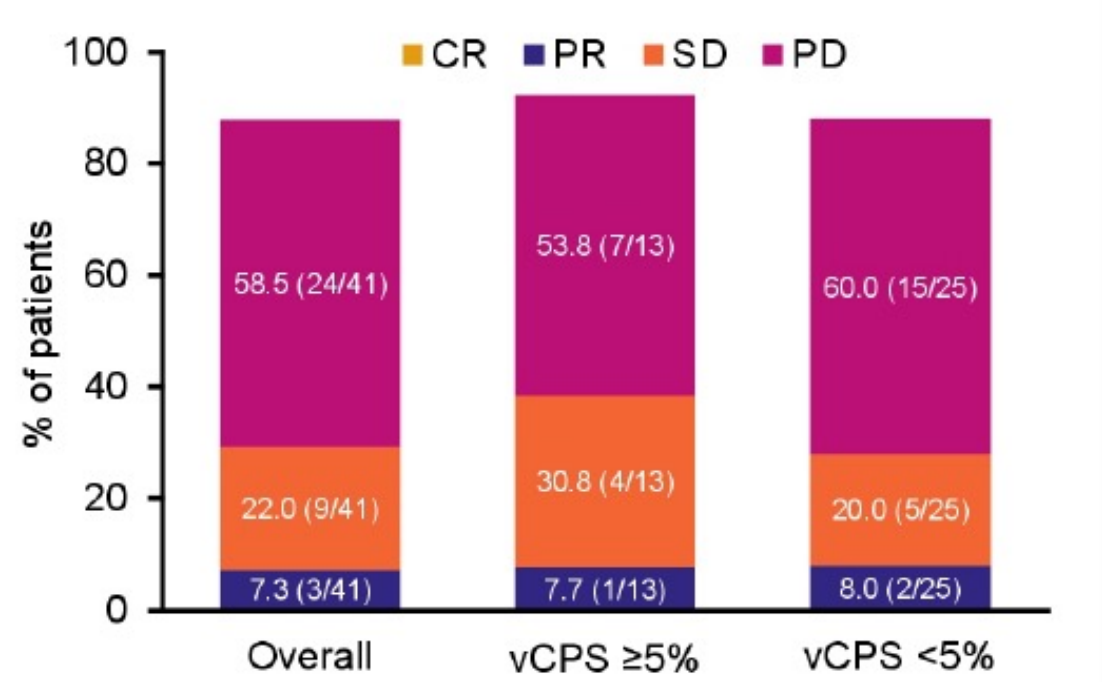
RTP RESEARCH TO PRACTICE

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

Randall LM et al.

ASCO 2022;Abstract 5573.

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



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

Randall LM et al. ASCO 2022;Abstract 5573.

PARIS 2022 ESMO congress

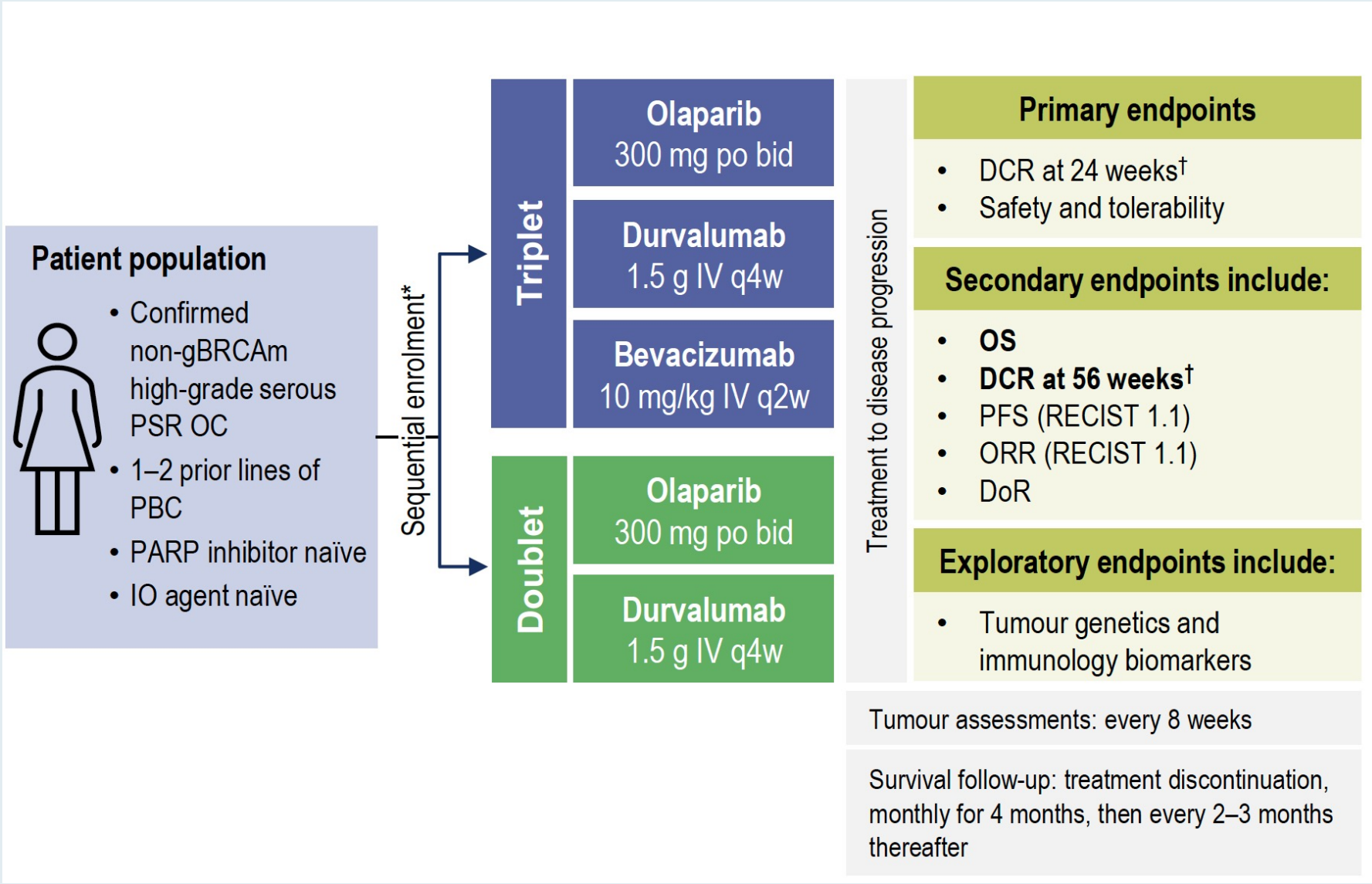
Abstract 529MO

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*]

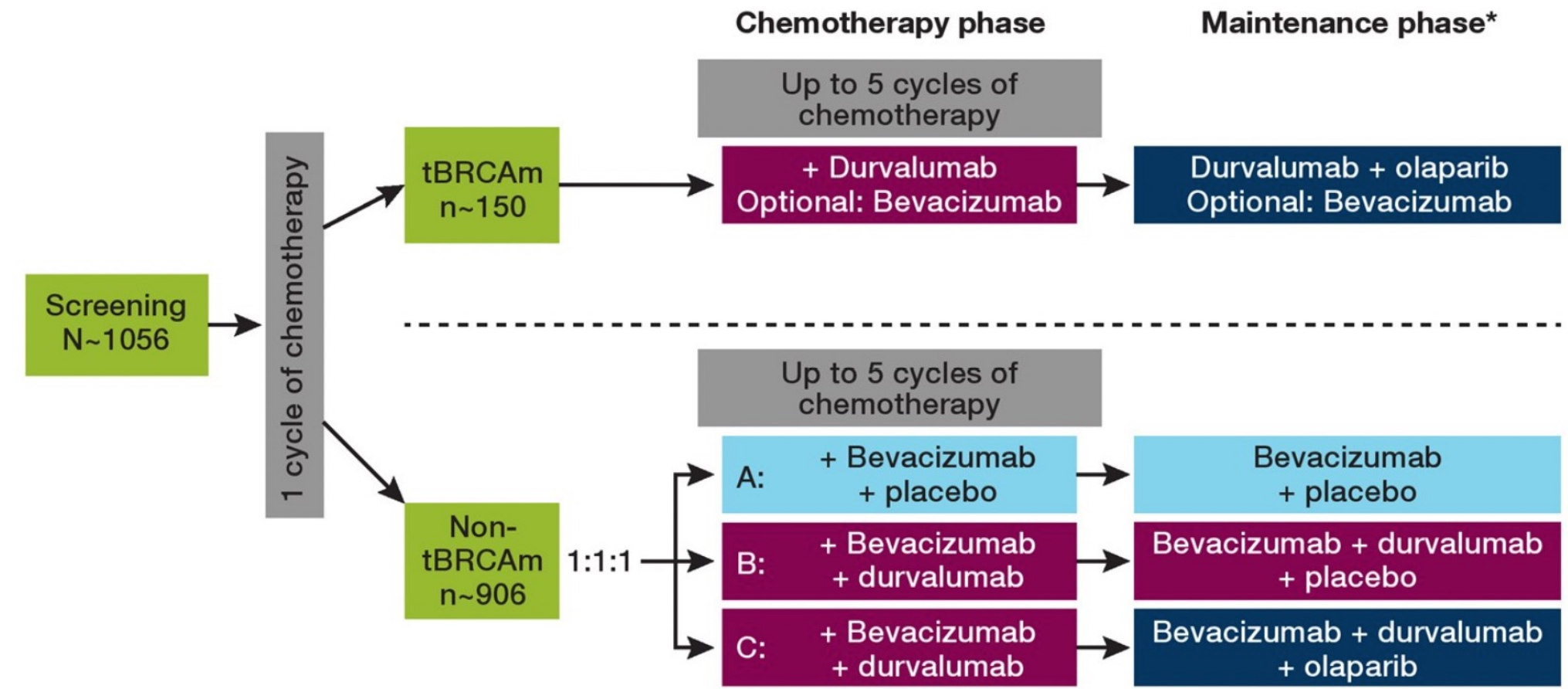
RTP RESEARCH TO PRACTICE

MEDIOLA: Non-gBRCAm Cohorts Study Design



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

DUO-O Study Design in Newly Diagnosed Advanced Ovarian Cancer



Estimated completion date: July 2023

Harter P et al. ASCO 2019;Abstract TPS5598; www.clinicaltrials.gov (NCT03737643) Accessed July 2022.

RTP RESEARCH TO PRACTICE

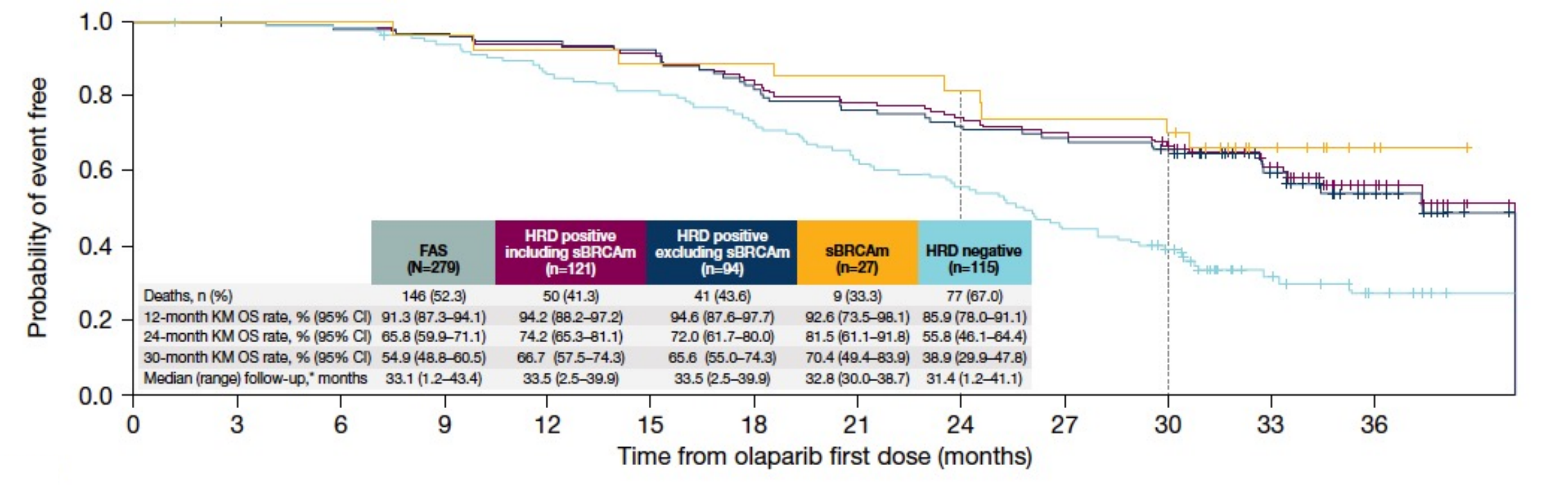
Abstract: 2799
Poster: 531P

ESMO 2022

Maintenance olaparib monotherapy in patients with platinum-sensitive relapsed ovarian cancer without a germline *BRCA1/BRCA2* mutation: final overall survival results from the OPINION trial

Andrés Poveda,[1] Stéphanie Lheureux,[2] Nicoletta Colombo,[3] David Cibula,[4] Mari Elstrand,[5] Johanne Weberpals,[6] Maria Bjurberg,[7] Ana Oaknin,[8] Magdalena Sikorska,[9] Antonio González-Martín,[10] Radoslaw Madry,[11] María Rubio Pérez,[12] Jonathan Ledermann,[13] Ozan Ozgoren,[14] Alan Barnicle,[14] Helen Marshall,[14] Zahid Bashir,[14] Erik Škof[15]

OPINION: Overall Survival



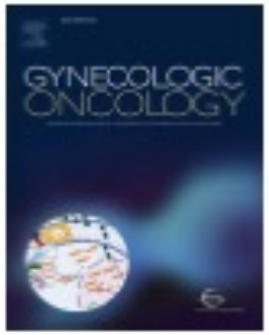
	FAS (N=279)	HRD positive including sBRCAm (n=121)	HRD positive excluding sBRCAm (n=94)	sBRCAm (n=27)	HRD negative (n=115)
Deaths, n (%)	146 (52.3)	50 (41.3)	41 (43.6)	9 (33.3)	77 (67.0)
12-month KM OS rate, % (95% CI)	91.3 (87.3–94.1)	94.2 (88.2–97.2)	94.6 (87.6–97.7)	92.6 (73.5–98.1)	85.9 (78.0–91.1)
24-month KM OS rate, % (95% CI)	65.8 (59.9–71.1)	74.2 (65.3–81.1)	72.0 (61.7–80.0)	81.5 (61.1–91.8)	55.8 (46.1–64.4)
30-month KM OS rate, % (95% CI)	54.9 (48.8–60.5)	66.7 (57.5–74.3)	65.6 (55.0–74.3)	70.4 (49.4–83.9)	38.9 (29.9–47.8)
Median (range) follow-up,* months	33.1 (1.2–43.4)	33.5 (2.5–39.9)	33.5 (2.5–39.9)	32.8 (30.0–38.7)	31.4 (1.2–41.1)

Poveda A et al. ESMO 2022;Abstract 531P.

Contents lists available at ScienceDirect

Gynecologic Oncology

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



Olaparib maintenance monotherapy in platinum-sensitive relapsed ovarian cancer patients without a germline *BRCA1/BRCA2* mutation: OPINION primary analysis

A. Poveda [a,*], S. Lheureux [b], N. Colombo [c], D. Cibula [d], K. Lindemann [e], J. Weberpals [f], M. Bjurberg [g], A. Oaknin [h], M. Sikorska [i], A. González-Martín [j], R. Madry [k], M.J. Rubio Pérez [l], J. Ledermann [m], R. Davidson [n,1], C. Blakeley [n,1,1], J. Bennett [n,1], A. Barnicle [n], E. Škof [o]

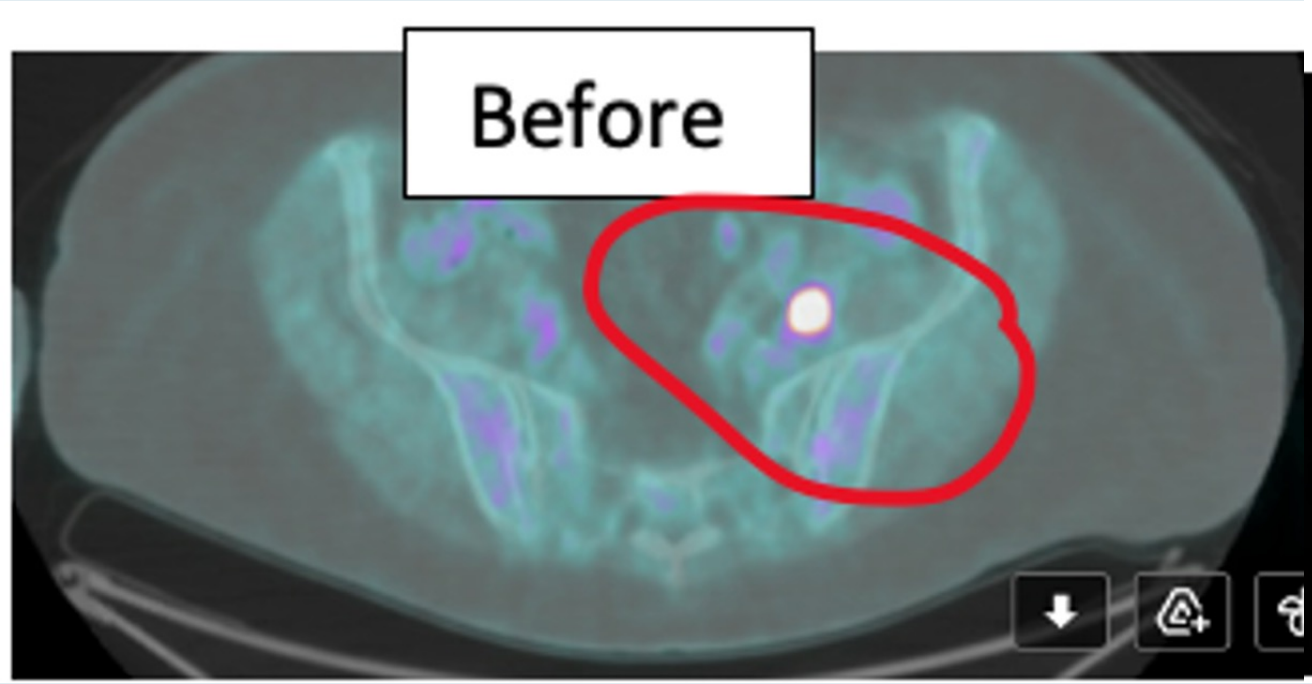
Gynecologic Oncology 2022;164:498-504.

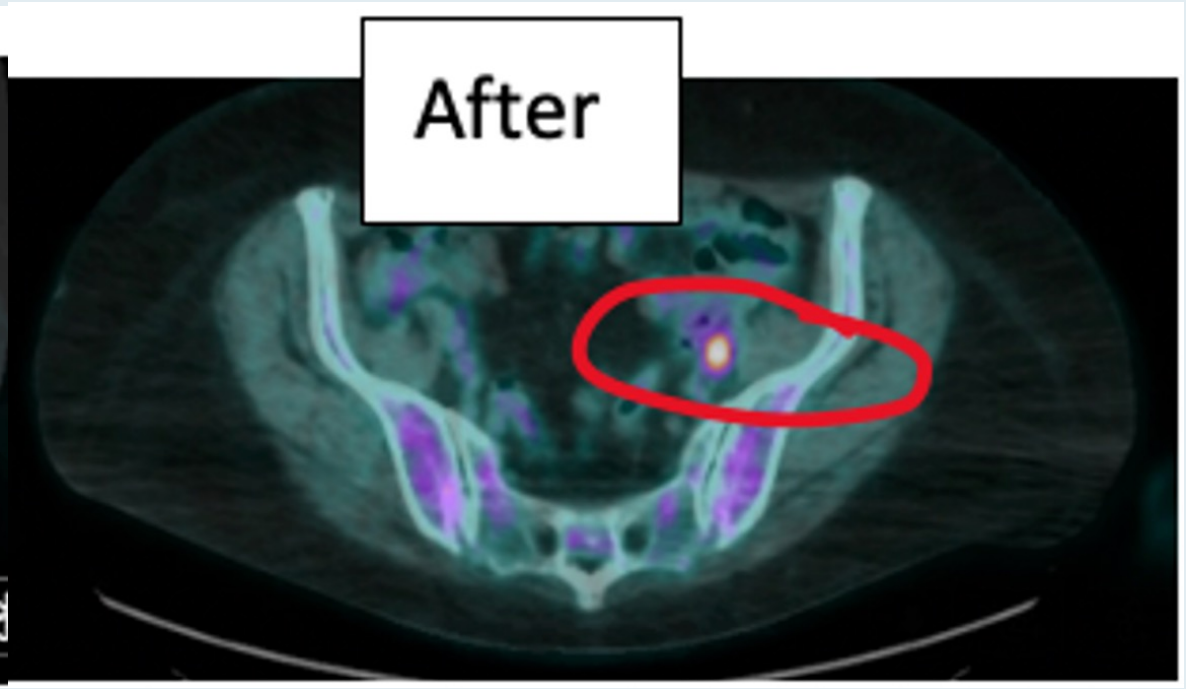
JC JOURNAL CLUB RTP RESEARCH TO PRACTICE

Case Presentation: 74-year-old woman with recurrent gBRCA2-mutant, platinum-sensitive peritoneal cancer – Lynch VUS

Dr Karim ElSahwi (Neptune City, New Jersey)

RTP RESEARCH TO PRACTICE





Component	Ref Range & Units	2 wk ago	1 mo ago	2 mo ago	3 mo ago	4 mo ago	5 mo ago	6 mo ago
CA 125 New Method	<35 U/mL	12	17 CM	18 CM	24 CM	60 ▲ CM	96 ▲ CM	142 ▲ CM

Case Presentation: 63-year-old woman with ovarian cancer and prolonged pancytopenia after treatment with a PARP inhibitor

Dr Joseph Martins (Tyler, Texas)

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Case Presentation: 64-year-old woman with platinum-resistant recurrence of BRCA WT clear cell ovarian cancer s/p carboplatin/paclitaxel/bevacizumab and maintenance bevacizumab – HRD-negative

Dr Neil Morganstein (Summit, New Jersey)

RTP RESEARCH TO PRACTICE

Clin Cancer Res 2022 September 12:[Online ahead of print].

Multi-omics uncovering different faces of Clear-Cell Ovarian Cancer

Stephanie Lheureux

CLINICAL CANCER RESEARCH | TRANSLATIONAL CANCER MECHANISMS AND THERAPY

Molecular Subclasses of Clear Cell Ovarian Carcinoma and Their Impact on Disease Behavior and Outcomes

Kelly L. Bolton[1], Denise Chen[2], Rosario Corona de la Fuente[3], Zhuxuan Fu[4], Rajmohan Murali[5], Martin Köbel[6], Yanis Tazi[5], Julie M. Cunningham[7], Irenaeus C.C. Chan[1], Brian J. Wiley[1], Lea A. Moukarzel[5], Stacey J. Winham[7], Sebastian M. Armasu[7], Jenny Lester[8], Esther Elishaev[4], Angela Laslavic[4], Catherine J. Kennedy[9,10], Anna Piskorz[11], Magdalena Sekowska[11], Alison H. Brand[9,12], Yoke-Eng Chiew[9,10], Paul Pharoah[11], Kevin M. Elias[13], Ronny Drapkin[14], Michael Churchman[15], Charlie Gourley[15], Anna DeFazio[9,10,12,16], Beth Karlan[8], James D. Brenton[11], Britta Weigelt[5], Michael S. Anglesio[17], David Huntsman[17], Simon Gayther[3], Jason Konner[5], Francesmary Modugno[4], Kate Lawrenson[3], Ellen L. Goode[7], and Elli Papaemmanuil[5]

Case Presentation: 61-year-old woman with multiregimen-recurrent BRCA WT, HRD-negative metastatic ovarian cancer

Dr Rahul Gosain (Corning, New York)

RTP
RESEARCH
TO PRACTICE

cancers

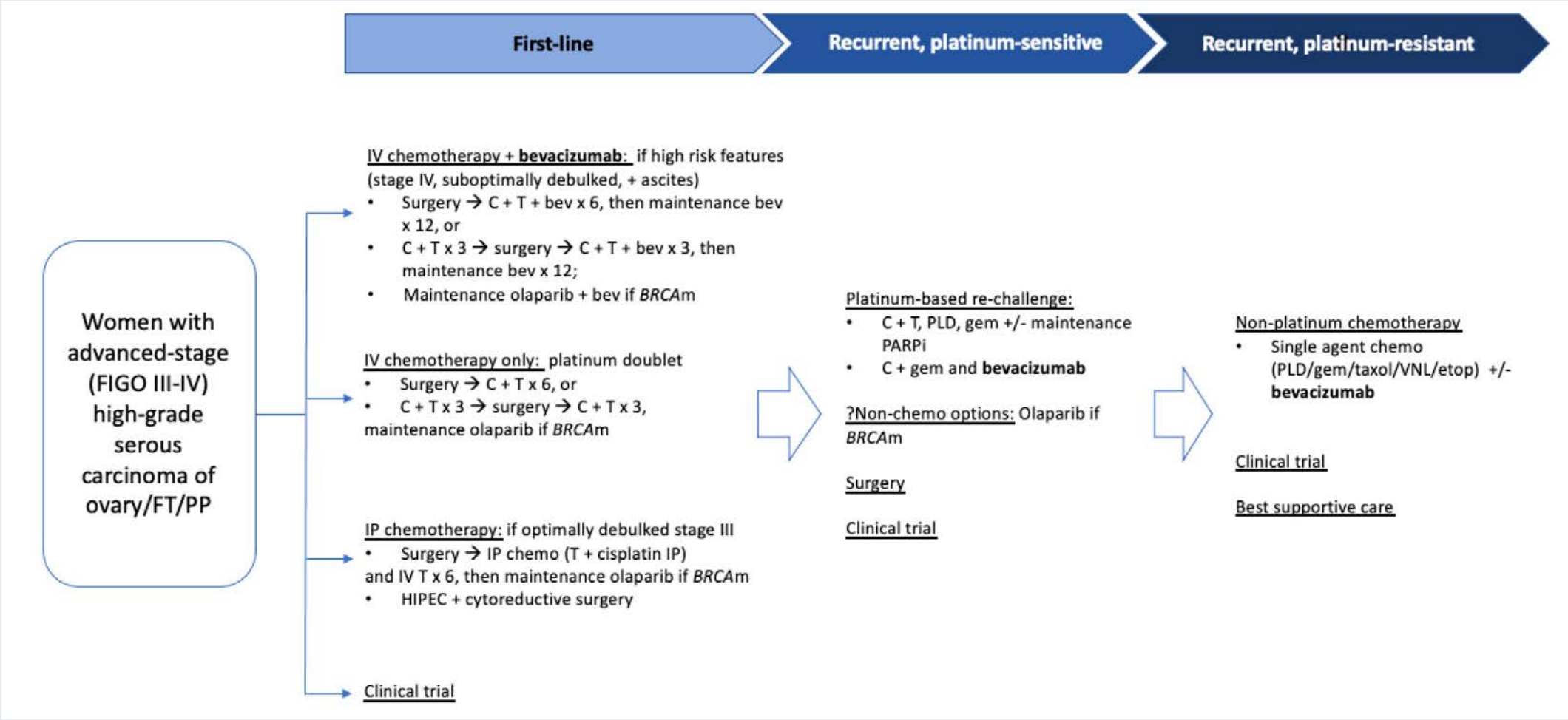
Cancers (Basel) 2022 February 22;14(5):1122.

Review

Angiogenesis: A Pivotal Therapeutic Target in the Drug Development of Gynecologic Cancers

Lawrence Kasherman [1,2,3], Shiru (Lucy) Liu [4], Katherine Karakasis [5] and Stephanie Lheureux [6,*]

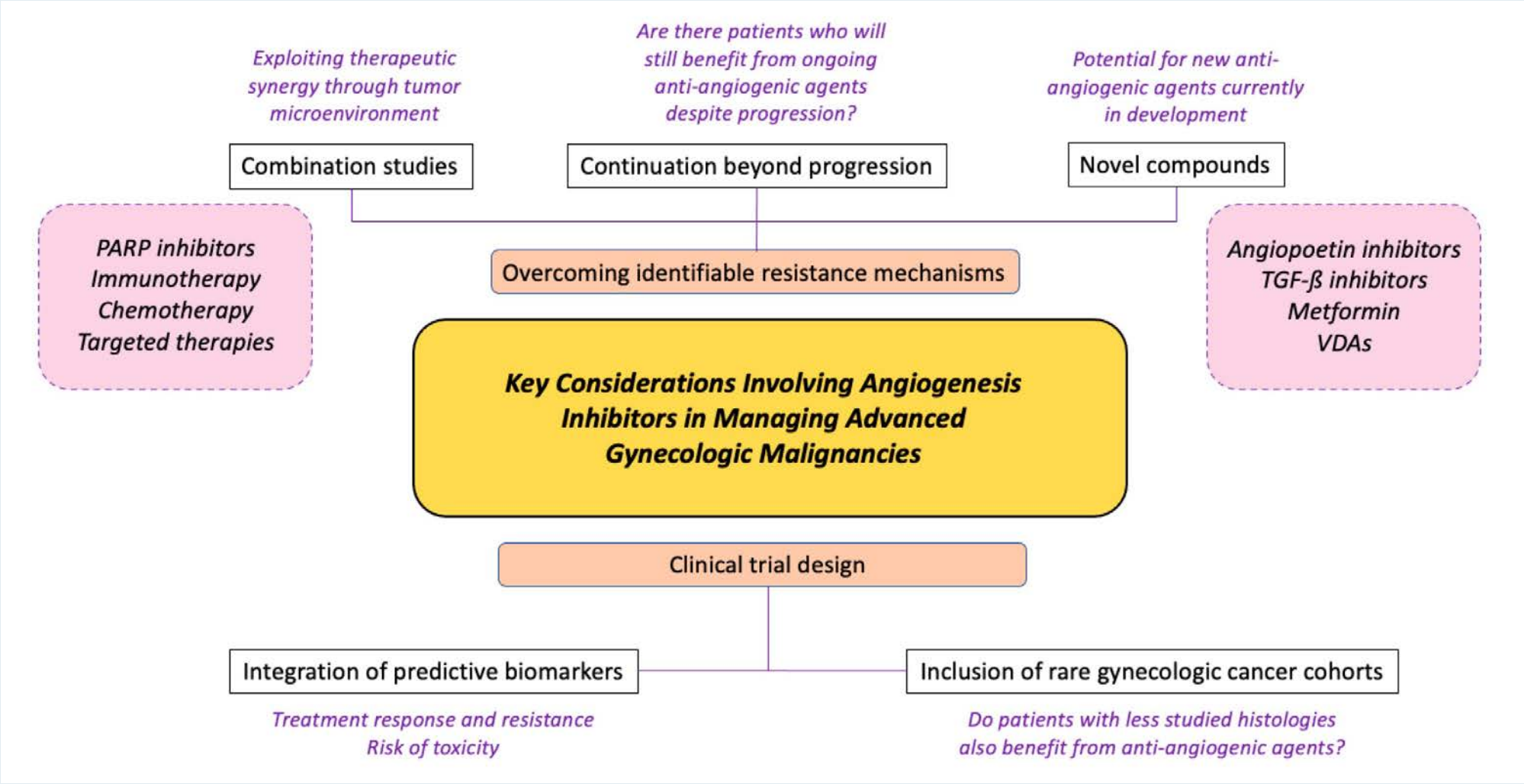
Schematic Diagram of Standard Treatment Algorithm for Advanced-Stage First-Line and Recurrent High-Grade Serous Ovarian, Fallopian Tube or Primary Peritoneal Carcinoma



FT = fallopian tube; PP = primary peritoneum; C = carboplatin; T = paclitaxel; bev = bevacizumab; IP = intraperitoneal; HIPEC = heated intraperitoneal chemotherapy; PLD = pegylated liposomal doxorubicin; gem = gemcitabine; VNL = vinorelbine; etop = etoposide

Kasherman L et al. *Cancers (Basel)* 2022 February 22;14(5):1122.

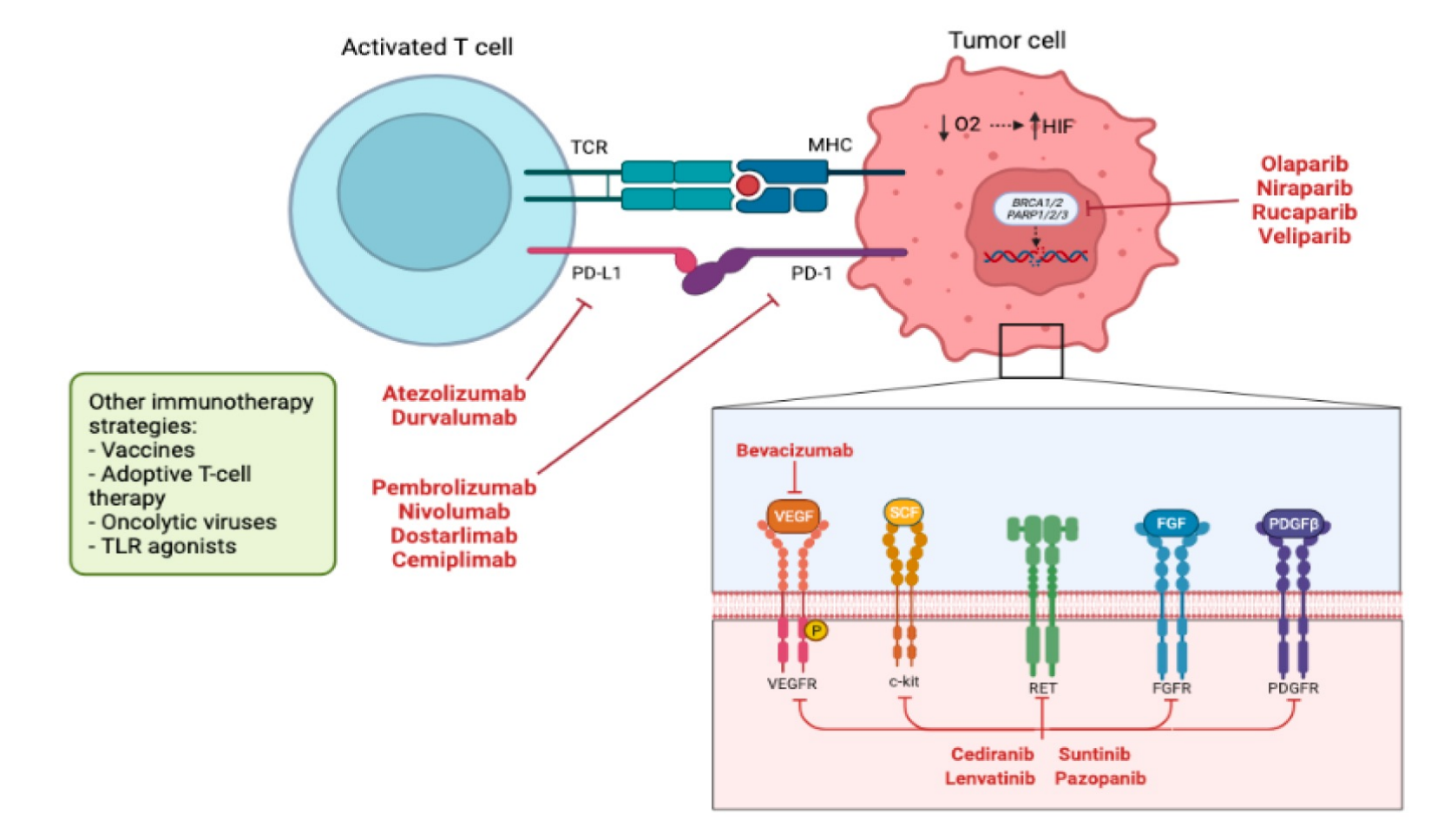
Schema of Key Considerations Involving Angiogenesis Inhibitors for Managing Advanced Gynecologic Cancers



TGF-ß = transforming growth factor-beta; VDAs = vascular disrupting agents

Kasherman L et al. *Cancers (Basel)* 2022 February 22;14(5):1122.

Schematic Diagram of Current Therapeutic Targets in Gynecologic Cancers



TCR = T-cell receptor; MHC = major histocompatibility complex; HIF = hypoxia inducible factor; TLR = toll-like receptor; VEGF = vascular endothelial growth factor; FGF = fibroblast growth factor; PDGF = platelet-derived growth factor

Kasherman L et al. *Cancers (Basel)* 2022 February 22;14(5):1122.

Gynecologic Oncology 161 (2021) 601–612

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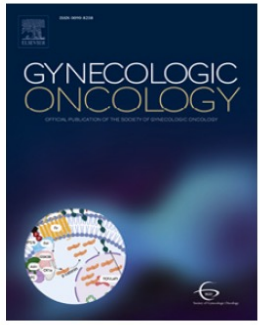
journal homepage: www.elsevier.com/locate/ygyno



Review Article

The use of bevacizumab in the modern era of targeted therapy for ovarian cancer: A systematic review and meta-analysis

Shiru Liu [a,1], Lawrence Kasherman [a], Rouhi Fazelzad [b], Lisa Wang [c], Genevieve Bouchard-Fortier [d], Stephanie Lheureux [a], Monika K. Krzyzanowska [e,*]

Case Presentation: 62-year-old woman with BRCA WT recurrent ovarian cancer who experiences significant anemia and thrombocytopenia on maintenance niraparib

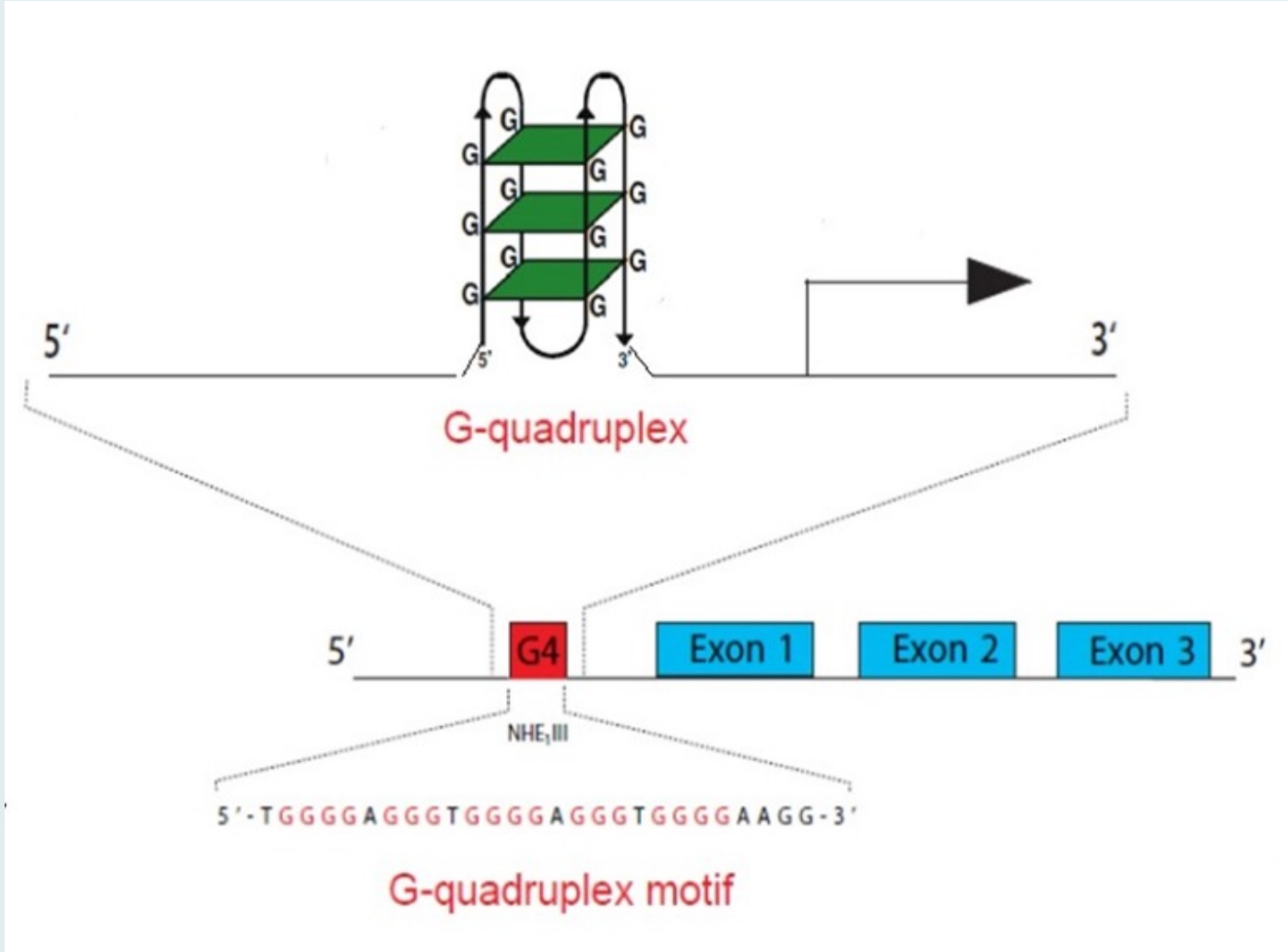
Dr Gigi Chen (Pleasant Hill, California)

OZM-114: Phase Ib Expansion Study of CX-5461 in Patients with Solid Tumors and BRCA2 and/or PALB2 Mutation

Alqaisi H et al.

ASCO 2021;Abstract TPS5621.

G-Quadruplex Stabilizer Selectively Kills HR-Deficient Cancer Cells Through Stabilizing G4 Structures and Inducing Replication-Dependent DNA Damage



Alqaisi H et al. ASCO 2021;Abstract TPS5621.

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

Selle F et al.

ASCO 2022;Abstract 5558.

Case Presentation: 69-year-old woman with recurrent platinum-resistant, BRCA WT, HR-proficient ovarian cancer s/p paclitaxel/tumor treating fields on a clinical trial

Dr Dana Chase (Phoenix, Arizona)

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Seminars in Cancer Biology 77 (2021) 167–181

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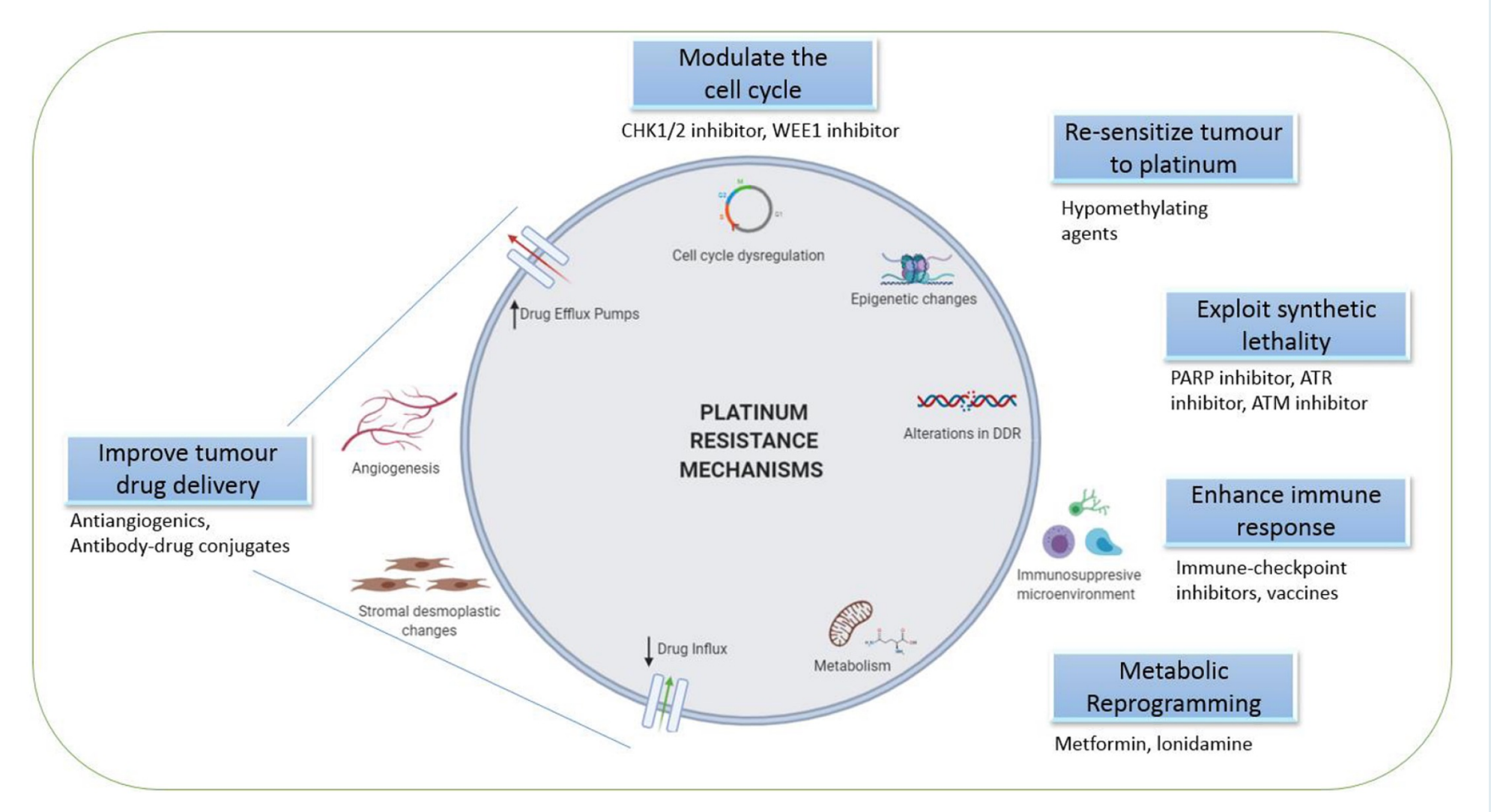
Seminars in Cancer Biology

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

New approaches for targeting platinum-resistant ovarian cancer

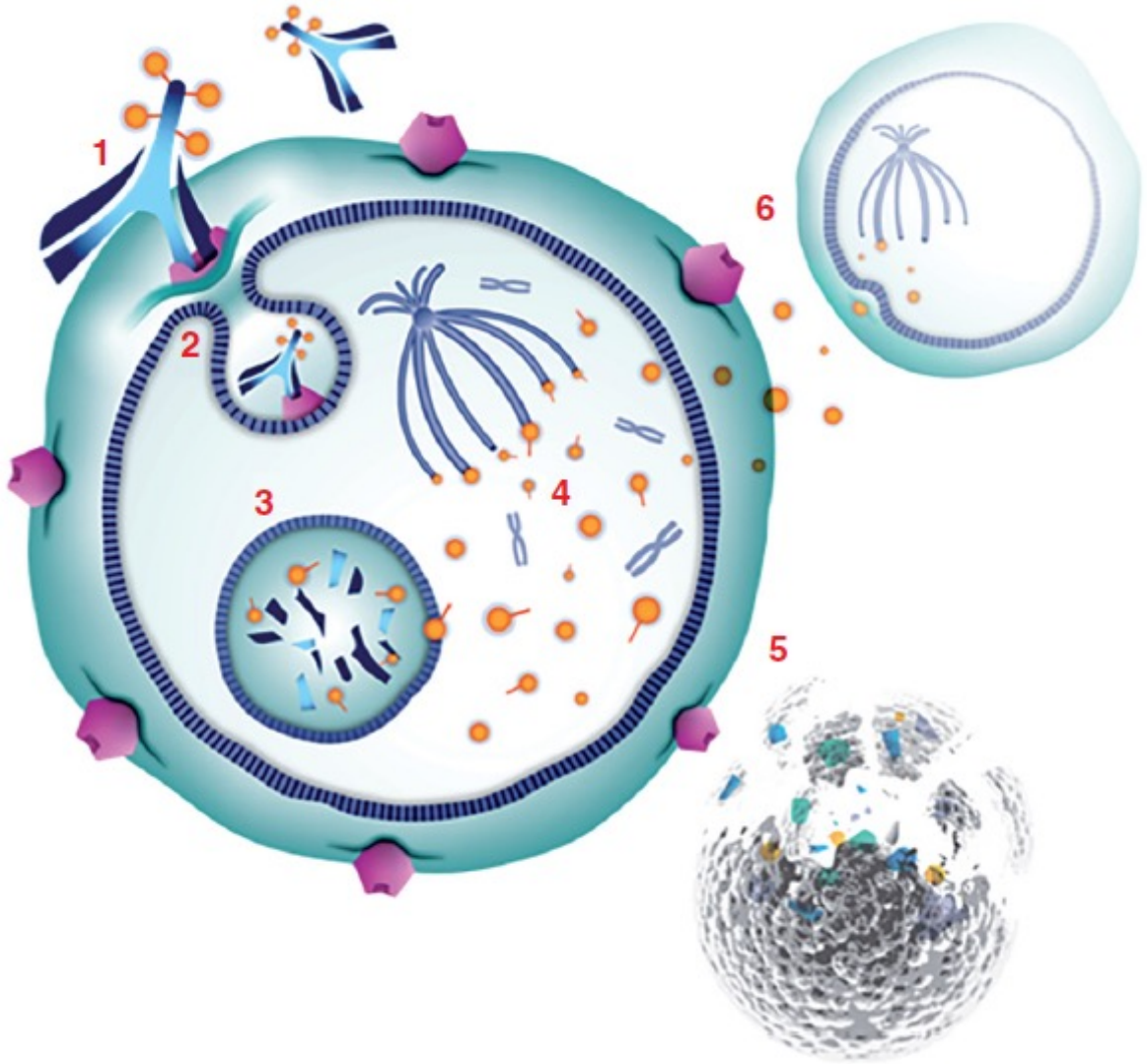
Michelle McMullen [a], Ainhoa Madariaga [a], Stephanie Lheureux [a,b,*]

Combination of Treatment Approaches to Overcome Resistance



McMullen M et al. *Sem Cancer Biol* 2021;77:167-81.

Mirvetuximab Soravtansine: Mechanism of Action



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

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

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

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

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

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

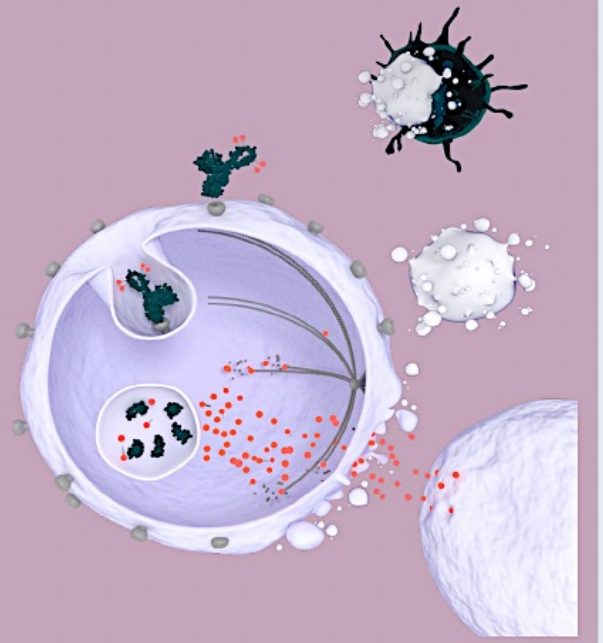
Moore K et al. *Future Oncol* 2018:14(2);123-36.

RTP RESEARCH TO PRACTICE

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

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

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



SORAYA

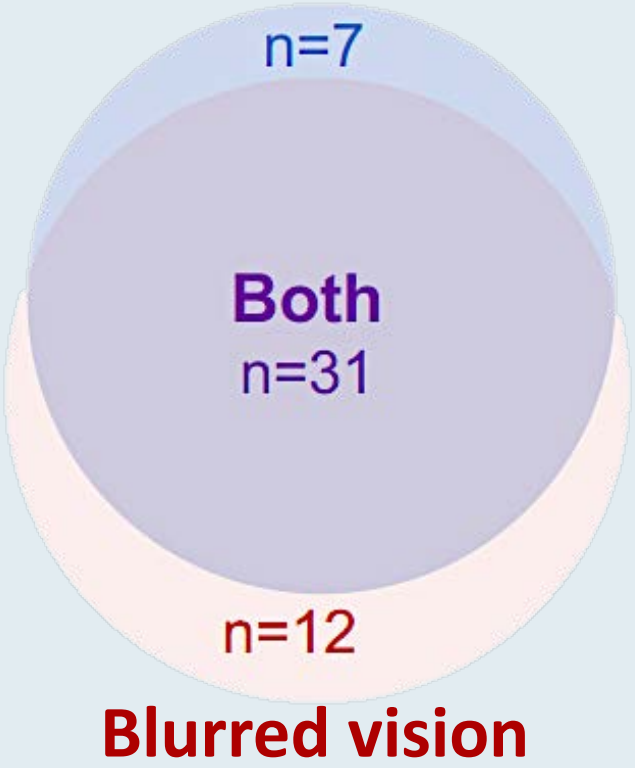
ANNUAL MEETING ON WOMENS' CANCER®
BUILDING BRIDGES // BREAKING BARRIERS
SGO // PHOENIX, ARIZONA // MARCH 18 - 21, 2022

SGO 2022;Abstract LBA4.

Society of Gynecologic Oncology

Unique Events Associated with Mirvetuximab Soravtansine: Keratopathy and Blurred Vision

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



Proactive supportive care
– Lubricating artificial tears
– Corticosteroid eye drops

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

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

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

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

Matulonis UA et al. SGO 2022;Abstract LBA4.

MIRASOL Phase III Study Schema

MIRASOL

Enrollment and Key Eligibility

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

Statistical Assumptions

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

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

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

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

Moore KN et al. SGO 2022;Abstract 297.

PICCOLO Phase II Trial Schema

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.

Evaluation of NaPi2b Expression in a Well-Annotated Longitudinal Tissue Series of Ovarian Serous Carcinomas

Drapkin, Ronny[1]; Jung, Euihye[2]; Bradshaw, Chelsea[3]; DeMars, Leslie[3]; Mosher, Rebecca[3]

[1]Perelman School of Medicine, University of Pennsylvania, Philadelphia, PA; [2]OCRC Tumor BioTrust Collection, University of Pennsylvania, Philadelphia, PA; [3]Mersana Therapeutics, Inc., Cambridge, MA

BACKGROUND

NaPi2b Is a Sodium-Dependent Phosphate Transporter Broadly Expressed in Ovarian Cancer, With Limited Expression in Healthy Tissues[1]

- NaPi2b is a lineage antigen and not an oncogene; its expression remains consistent throughout the course of disease[2]
- It is believed that approximately two-thirds of patients with HGSOC have high NaPi2b expression based on an IHC tumor proportion score (TPS) of at least 75%[3]

Upifitamab Rilsodotin (UpRi) – Investigational First-in-Class NaPi2b-targeting Antibody-Drug Conjugate (ADC) With a Novel Scaffold-Linker-Payload[2-4]

Antibody: Humanized monoclonal anti-SLC34A2 (NaPi2b)

Linker: Fleximer polymer scaffold; cleavable ester linker stable in circulation

Payload: AF-HPA (DolaLock-controlled bystander effect); selectively toxic to rapidly dividing cells

Drug-to-Antibody Ratio (DAR): ~10

UpRi Phase 1b Ovarian Cancer Cohort Study

- Preliminary antitumor activity was reported in the platinum-resistant serous ovarian cancer Phase 1b expansion (EXP) cohort, including patients previously treated with bevacizumab and PARP inhibitors[5]
- Results suggest that clinical benefit may correlate with NaPi2b expression, with higher NaPi2b expression associated with higher likelihood of clinical benefit[5]
- Change in NaPi2b expression over the course of ovarian cancer has not been extensively evaluated; therefore, an analysis was performed to evaluate NaPi2b expression in a longitudinal tissue series

METHODS

- 11 patients with HGSOC had tissue sampled at multiple time points throughout the course of their disease:
  - 5 samples were evaluated at the time of primary debulking surgery and after chemotherapy
  - 2 samples were evaluated prior to chemotherapy, after neoadjuvant chemotherapy, and at the time of disease progression or recurrence
  - 4 samples were evaluated prior to chemotherapy and after neoadjuvant chemotherapy
  - Note that none of these treatments were UpRi
- NaPi2b expression was assessed by IHC by QualTek Molecular Laboratories (Discovery Life Sciences) using the GLP assay employed in the Phase 1b UpRi DES/EXP study (NCT03319628) and a TPS calculated
  - In a retrospective analysis, TPS ≥75% was shown to identify patients with a higher likelihood of response, and thus was determined as the cutoff for "NaPi2b-positive"[6]
- Tumor tissue samples were obtained from the Ovarian Cancer Research Center (OCRC) Tumor BioTrust Collection at the University of Pennsylvania

OCRC Tumor BioTrust Collection

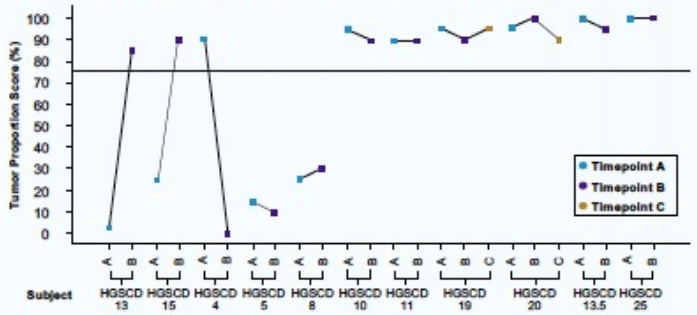
- The OCRC Tumor BioTrust Collection was established in 2007 at the University of Pennsylvania to support cancer research
- The OCRC collects human biospecimens, including cancer tissue, plasma, serum, peripheral blood mononuclear cells, blood, and other biological samples from all cases of patients with ovarian cancer
- Services offered include collection, processing, storage, and distribution of primary and recurrent ovarian tumor samples, and they can work with investigators to prospectively collect specific samples to support their research
- More information can be found at www.med.upenn.edu/OCRCBioTrust

RESULTS

- NaPi2b levels were evaluated by IHC and correlated through the disease course in matched (from the same patient) tissue samples
- 7/11 (64%) had an initial NaPi2b-positive biopsy
  - 6 of these 7 subjects (86%) remained NaPi2b-positive through their matched samples
- 8/11 (73%) maintained NaPi2b status over their treatment course
- 3/11 (27%) had a change in NaPi2b expression status over their treatment course
  - Samples that shifted status had >60% change in intensity

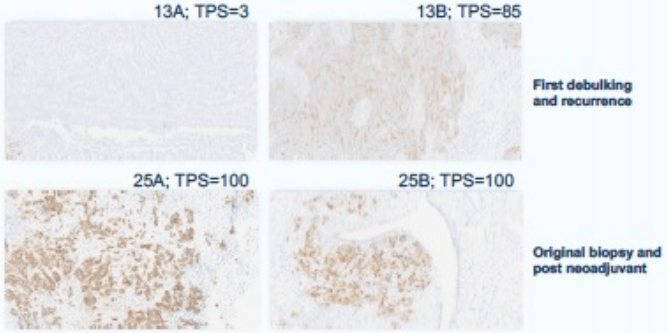
RESULTS

Longitudinal NaPi2b Expression in Matched HGSOC Tissue Samples

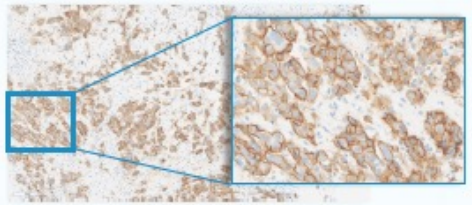


Samples are sequential in time, but "first" may not be from ovary anatomic site.

Representative IHC of Matched HGSOC Tissue Samples



TPS=100 HGSOC Tissue Sample IHC (25A)



CONCLUSIONS

- Approximately two-thirds (64%) of patient tissue sampled for clinical evaluation presented with NaPi2b-positive tumors
- NaPi2b expression status was maintained over the course of treatment in the majority (73%) of evaluated individuals
- NaPi2b appears to remain consistent throughout the course of HGSOC and is a rational target for ongoing clinical trials
- UpRi is being evaluated in platinum-resistant ovarian cancer in the UPLIFT (NCT03319628) study and in platinum-sensitive ovarian cancer in the UP-NEXT (NCT05329545) and UPGRADE (NCT04907968) studies

ACKNOWLEDGMENTS

We would like to thank patients for making this study possible by contributing samples to the Ovarian Cancer Research Center (OCRC) Tumor BioTrust Collection at the University of Pennsylvania. This study is sponsored by Mersana Therapeutics, Inc. IHC analyses were performed by QualTek Molecular Laboratories (Discovery Life Sciences). Editorial support for this poster was provided by BluPrint Oncology.

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1. Lin K et al. *Clin Cancer Res.* 2015;21(22):5139–5150. **2.** Bodyak ND et al. *Mol Cancer Ther.* 2021;20(5):896–905. **3.** Richardson DL et al. SGO Annual Meeting on Women's Cancer 2022; Abstract 585. **4.** Mersana Therapeutics. Accessed July 12, 2022. https://www.mersana.com/pipeline/xmt-1536 **5.** Richardson DL et al. SGO Annual Meeting on Women's Cancer 2022; Abstract 76. **6.** Mersana Therapeutics. Accessed July 12, 2022. https://www.mersana.com/wp-content/uploads/2022/06/MRSN-UpRi-NaPi2b-Diagnostic-Development-Path_FINAL-render.pdf

ADDITIONAL INFORMATION

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Abbreviations: ADC, antibody-drug conjugate; AF-HPA, auristatin F hydroxypropyl amide; DAR, drug-to-antibody ratio; DES, dose escalation; EXP, expansion; GLP, good laboratory practice; HGSOC, high-grade serous ovarian cancer; IHC, immunohistochemistry; NaPi2b, sodium-dependent phosphate transport protein 2B; PARP, poly (ADP-ribose) polymerase; SLC34A2, solute carrier family 34 member 2 gene; TPS, tumor proportion score; UpRi, upifitamab rilsodotin.

Abstract 408

Evaluation of NaPi2b Expression in a Well-Annotated Longitudinal Tissue Series of Ovarian Serous Carcinomas

CONCLUSIONS

- Approximately two-thirds (64%) of patient tissue sampled for clinical evaluation presented with NaPi2b-positive tumors
- NaPi2b expression status was maintained over the course of treatment in the majority (73%) of evaluated individuals
- NaPi2b appears to remain consistent throughout the course of HGSOC and is a rational target for ongoing clinical trials
- UpRi is being evaluated in platinum-resistant ovarian cancer in the UPLIFT (NCT03319628) study and in platinum-sensitive ovarian cancer in the UP-NEXT (NCT05329545) and UPGRADE (NCT04907968) studies

Drapkin R et al. IGCS 2022;Abstract 408.

Comparison of NaPi2b Expression From Paired Tissue Samples in a Clinical Study of Upifitamab Rilsodotin (UpRi; XMT-1536) Supports a Strategy of Testing in Archival Material

Richardson, Debra L[1]; Barve, Minal[2]; Saltos, Andreas[3]; Papadopolous, Kyriakos P[4]; Hays, John L[5]; Tolcher, Anthony[6]; Ellard, Susan[7]; Doroshow, Deborah[8]; Mitchell, Paul[9]; Zarwan, Corrine[10]; Werner, Theresa L[11]; Anderson, Charles[12]; Spira, Alexander I[13]; Mileshkin, Linda[14]; Bradshaw, Chelsea[15]; DeMars, Leslie[15]; Mosher, Rebecca[15]; Hamilton, Erika[16]

[1]Stephenson Cancer Center, University of Oklahoma Health Sciences Center and the Sarah Cannon Research Institute, Oklahoma City, OK; [2]Mary Crowley Cancer Research and Texas Oncology, Dallas, TX; [3]Moffitt Cancer Center, Tampa, FL; [4]START San Antonio, San Antonio, TX; [5]The Ohio State University Wexner Medical Center, Columbus, OH; [6]NEXT Texas Oncology, San Antonio, TX; [7]BC Cancer Agency, University of British Columbia, Vancouver, BC; [8]Icahn School of Medicine at Mount Sinai, New York, NY; [9]Austin Health - Olivia Newton-John Cancer Center, Australia; [10]Lahey Health Cancer Institute, Burlington, MA; [11]Huntsman Cancer Institute, University of Utah, Salt Lake City, UT; [12]Willamette Valley Cancer Institute and Research Center, Eugene, OR; [13]Virginia Cancer Specialists, Fairfax, VA; [14]Peter MacCallum Cancer Centre, Australia; [15]Mersana Therapeutics, Inc., Cambridge, MA; [16]Sarah Cannon Research Institute/Tennessee Oncology, Nashville, TN

BACKGROUND

NaPi2b Is a Sodium-Dependent Phosphate Transporter Broadly Expressed in Ovarian Cancer, With Limited Expression in Healthy Tissues[1]

- It is believed that approximately two-thirds of patients with HGSOC have high NaPi2b expression based on an IHC tumor proportion score (TPS) of at least 75%[2]
- NaPi2b is a lineage antigen and not an oncogene; its expression remains consistent throughout the course of disease[3]

Upifitamab Rilsodotin (UpRi) – Investigational First-in-Class NaPi2b-targeting Antibody-Drug Conjugate (ADC) With a Novel Scaffold-Linker-Payload[2-4]

Antibody: Humanized monoclonal anti-SLC34A2 (NaPi2b)

Linker: Fleximer polymer scaffold; cleavable ester linker stable in circulation

Payload: AF-HPA (DolaLock-controlled bystander effect); selectively toxic to rapidly dividing cells

Drug-to-Antibody Ratio (DAR): ~10

UpRi Phase 1b Ovarian Cancer Cohort Study[5]

- A Phase 1b UpRi single-agent dose escalation (DES) and expansion (EXP) study (NCT03319628) enrolled patients with high-grade, platinum-resistant serous ovarian cancer with 1 to 3 prior lines of therapy, or 4 prior lines of therapy regardless of platinum status
  - Preliminary antitumor activity was reported including patients previously treated with bevacizumab and PARP inhibitors
- The study collected both freshly biopsied and archival tissue samples for retrospective NaPi2b evaluation, if available, but only required a single specimen
- To determine if archival material would be sufficient to classify biomarker status, NaPi2b expression was evaluated in paired freshly biopsied and archival material from patients participating in the UpRi Phase 1b ovarian cancer EXP cohort

METHODS

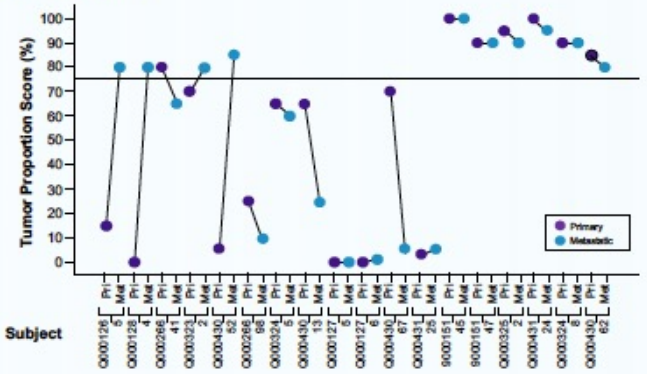
- 2 ovarian cancer sample sets were evaluated for NaPi2b expression using an IHC assay, and a TPS was calculated
  - The first set (18 pairs) was procured from tissue banks, representing synchronous sampling of primary and metastatic lesions to establish a reference NaPi2b heterogeneity rate[a].
  - The second set included matched metachronous samples ("archival" and "fresh") from 56 patients enrolled in the Phase 1b study, sampled prior to UpRi administration
- NaPi2b expression was assessed by QualTek Molecular Laboratories (Discovery Life Sciences) using the GLP assay employed in the Phase 1b UpRi DES/EXP study (NCT03319628)
  - In a retrospective analysis, TPS ≥75% was shown to identify patients with a higher likelihood of response and was thus determined as the cutoff for "NaPi2b-positive"[6]
- Concordance rates and kappa values were calculated

RESULTS

- In the first set of samples, synchronous primary and metastatic lesions from an archival tumor bank showed a concordance rate of 72%
  - 13 of 18 pairs (72%) maintained their NaPi2b status across primary and metastatic tissue samples
  - 7 of the 18 (39%) primary tumor samples were NaPi2b-positive (TPS ≥75%)
  - 10 of the 18 (56%) metastatic tumor samples were NaPi2b-positive (TPS ≥75%)
- In the second set of 56 metachronous samples, high concordance was demonstrated between fresh and archival tissue samples
  - Of 29 patients who were NaPi2b-positive in archival tissue, 22 were NaPi2b-positive in fresh tissue (76% concordance) and 7 were NaPi2b-negative (24%)
  - Of 27 patients who were NaPi2b-negative in archival tissue, 20 were NaPi2b-negative in fresh tissue (74% concordance) and 7 were NaPi2b-positive (26%)

RESULTS (continued)

NaPi2b Status in Primary/Synchronous Metastatic Paired Samples – Sample Set 1 (N=18 pairs)



NaPi2b Status in Fresh vs Archival Samples From Patients Participating in the Phase 1b UpRi Ovarian Cancer Cohort – Sample Set 2 (N=56 pairs), n (%)[b]

- 64% of patients were NaPi2b-positive based on either archival or fresh tissue[c]

	Archival NaPi2b-Positive (TPS ≥75%)	Archival NaPi2b-Negative (TPS <75%)	Total Fresh Samples
Fresh NaPi2b-Positive (TPS ≥75%)	22 (39.3)	7 (12.5)	29 (51.8)
Fresh NaPi2b-Negative (TPS <75%)	7 (12.5)	20 (35.7)	27 (48.2)
Total Archival Samples	29 (51.8)	27 (48.2)	

Kappa 0.5 (0.27, 0.73, moderate agreement).

CONCLUSIONS

- High concordance of NaPi2b status was observed in both synchronous and metachronous samples from the Phase 1b UpRi study
- The high concordance of metachronous samples supports use of archival tissue for NaPi2b biomarker analysis despite intervening lines of therapy
- Fresh or archival tissue samples to evaluate NaPi2b status are requested in the ongoing clinical trials evaluating UpRi therapy in platinum-resistant and platinum-sensitive ovarian cancer
  - UPLIFT (NCT03319628), UP-NEXT (NCT05329545), and UPGRADE (NCT04907968)

ACKNOWLEDGMENTS

We thank the patients, their families, and caregivers for their contribution to this study. This study is sponsored by Mersana Therapeutics, Inc. IHC analyses were performed by QualTek Molecular Laboratories (Discovery Life Sciences). Editorial support for this poster was provided by BluPrint Oncology.

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1. Lin K et al. *Clin Cancer Res*. 2015;21(22):5139–5150. 2. Richardson DL et al. SGO Annual Meeting on Women's Cancer 2022; Abstract 585. 3. Bodyak ND et al. *Mol Cancer Ther*. 2021;20(5):896–905. 4. Mersana Therapeutics. Accessed July 12, 2022. https://www.mersana.com/pipeline/xmt-1536 5. Richardson DL et al. SGO Annual Meeting on Women's Cancer 2022; Abstract 76. 6. Mersana Therapeutics. Accessed July 12, 2022. https://www.mersana.com/wp-content/uploads/2022/06/MRSN-UpRi-NaPi2b-Diagnostic-Development-Path_FINAL-render.pdf

ADDITIONAL INFORMATION

[a] One subject in this set was inadvertently included as 2 separate analysis pairs using different tissue blocks procured from the tissue bank; notably, the 2 primary samples from the subject, annotated as synchronous specimens taken from the ovary, have discordant NaPi2b status. [b] Percent shown as a proportion of total n of 56 paired samples. [c] 36/56 patients were NaPi2b-positive based on both fresh and archival tissue (n=22), fresh tissue alone (n=7), or archival tissue alone (n=7).

Abbreviations: ADC, antibody-drug conjugate; AF-HPA, auristatin F-hydroxypropyl amide; DAR, drug-to-antibody ratio; DES, dose escalation; EXP, expension; GLP, good laboratory practice; HGSOC, high-grade serous ovarian cancer; IHC, immunohistochemistry; Met, metastatic; NaPi2b, sodium-dependent phosphate transport protein 2B; PARP, poly (ADP-ribose) polymerase; Pri, primary; SLC34A2, solute carrier family 34 member 2 gene; TPS, tumor proportion score; UpRi, upifitamab rilsodotin.

IGCS 2022 ANNUAL GLOBAL MEETING NEW YORK CITY

Abstract 425

Comparison of NaPi2b Expression from Paired Tissue Samples in a Clinical Study of Upifitamab Rilsodotin (UpRi) Supports a Strategy of Testing in Archival Material

CONCLUSIONS

- High concordance of NaPi2b status was observed in both synchronous and metachronous samples from the Phase 1b UpRi study
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- Fresh or archival tissue samples to evaluate NaPi2b status are requested in the ongoing clinical trials evaluating UpRi therapy in platinum-resistant and platinum-sensitive ovarian cancer
  - UPLIFT (NCT03319628), UP-NEXT (NCT05329545), and UPGRADE (NCT04907968)

Richardson DL et al. IGCS 2022;Abstract 425.

RTP RESEARCH TO PRACTICE

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

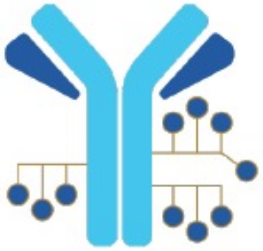
Richardson, Debra[1]; Perez Fidalgo, Jose Alejandro[2]; González Martín, Antonio[3]; Oaknin, Ana[4]; Hamilton, Erika[5]; Hays, John[6]; Pothuri, Bhavana[7]; Papadopoulos, Kyriakos[8]; Taylor, Sara[9]; Huang, Marilyn[10]; Lee, Yeh-Chen[11]; Krivak, Thomas[12]; Moreno Garcia, Victor[13]; Calvo, Emiliano[14]; Randall, Leslie[15]; Starks, David[16]; Ross, Malcom[17]; Duska, Linda[18]; Gao, Bo[19]; Poka, Robert[20]; Putiri, Emily[21]; Barrett, Jamie[21]; DeMars, Leslie[21]; Concin, Nicole[22]

[1]Stephenson Cancer Center, University of Oklahoma Health Sciences Center and the Sarah Cannon Research Institute, Oklahoma City, OK; [2]Hospital Clínico Universitario de Valencia, Valencia, Spain; [3]Clínica Universidad de Navarra, Madrid, Spain; [4]Vall d'Hebron Institute of Oncology, Barcelona, Spain; [5]Sarah Cannon Research Institute/Tennessee Oncology, Nashville, TN; [6]Arthur James Cancer Hospital, Ohio State University, Columbus, OH; [7]Perlmutter Cancer Center, NYU Langone Health, New York, NY; [8]START San Antonio, San Antonio, TX; [9]British Columbia Cancer Agency, British Columbia, Canada; [10]Sylvester Cancer Center, University of Miami, Miami, FL; [11]Prince of Wales, Royal Hospital for Women and Chris O'Brien Lifehouse, Sydney, Australia; [12]Allegheny Health Network, Pittsburgh, PA; [13]University Hospital Foundation Jimenez Diaz, Madrid, Spain; [14]Clara Campal Comprehensive Cancer Center, Madrid, Spain; [15]Virginia Commonwealth University Massey Cancer Center, Richmond, VA; [16]Avera Medical Group Gynecologic Oncology, Sioux Falls, SD; [17]Novant Health, Charlotte, NC; [18]University of Virginia, Department of Obstetrics and Gynecology, Division of Gynecologic Oncology, Charlottesville, VA; [19]Blacktown Road, Blacktown, Australia; [20]University of Debrecen Clinical Center, Debrecen, Hungary; [21]Mersana Therapeutics, Inc, Cambridge, MA; [22]Innsbruck Medical University, Austria; Evangelische Kliniken Essen Mitte, Germany

BACKGROUND

- Effective and well-tolerated treatments for PROC remain a substantial unmet medical need, with SOC single-agent chemotherapy demonstrating response rates of 4–12%, median PFS of 3–4 months, and median OS of <12 months[1–3]
- NaPi2b is a sodium-dependent phosphate transport protein broadly expressed in solid tumors, including high-grade serous epithelial ovarian, fallopian tube, and primary peritoneal cancer, with limited expression in normal tissue[4,5]
- It is believed that approximately two-thirds of patients with HGSOC have high NaPi2b expression based on an IHC tumor proportion score (TPS) of at least 75%[6]
- Upifitamab rilsodotin (UpRi; XMT-1536) is an investigational first-in-class ADC targeting NaPi2b

Upifitamab Rilsodotin (UpRi): Investigational First-in-Class NaPi2b-targeting ADC[5-7]



Antibody: Humanized monoclonal anti-SLC34A2 (NaPi2b)

Linker: Fleximer polymer scaffold; cleavable ester linker stable in circulation

Payload: AF-HPA (DolaLock-controlled bystander effect); selectively toxic to rapidly dividing cells

Drug-to-Antibody Ratio (DAR): ~10

- Preliminary antitumor activity was reported in the PROC Phase 1b expansion cohort, including in patients previously treated with bevacizumab and PARP inhibitors[6]
- Data as of June 2021 demonstrated 34% ORR, 5-month DOR, and 87% DCR in 38 patients with NaPi2b-positive tumors (TPS ≥75%)[6,a]
  - Two patients demonstrated CR following prior treatment with bevacizumab and PARP inhibitors
  - Most frequently reported TRAEs were fatigue, nausea, transient AST increase, thrombocytopenia (transient in nature), and decreased appetite. Most frequently reported grade 3+ TRAEs were fatigue, anemia, transient AST increase, and transient thrombocytopenia
  - No grade ≥3 (severe) TRAEs of neutropenia, peripheral neuropathy, or ocular toxicity occurred
- A post hoc analysis exploring drug exposure across 2 dose groups determined that, at the dose of 36 mg/m^2, UpRi has a more favorable safety profile while maintaining similar efficacy

METHODS

Rationale

- **UPLIFT** was designed as a Phase 2 single-arm registrational trial for PROC as part of the ongoing Phase 1b study
  - Designed to evaluate UpRi's safety and efficacy in PROC
  - Based on preliminary encouraging efficacy and safety data seen in Phase 1
  - Built on Phase 1b data to move directly to pivotal Phase 2

Global
US, Europe, Australia, Canada

UPLIFT

Key Inclusion Criteria
- Platinum-resistant[b] HGSOC[c]
- 1–4 prior lines of therapy
- Prior bevacizumab required if patient received only 1–2 prior lines of therapy
- ECOG PS = 0–1
- Available archived or fresh tissue for retrospective NaPi2b evaluation
- Grade ≤2 peripheral neuropathy

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

UpRi 36 mg/m^2 up to max 80 mg; **IV q4w**

Primary Endpoint
- Investigator-assessed confirmed ORR in NaPi2b-positive (N=~100)

Secondary Endpoints
- Investigator-assessed confirmed ORR in overall population (N=~180-240, including 100 NaPi2b-positive)
- DOR
- Safety

Assessments
- Tumor imaging (MRI or CT) baseline and every 8 weeks
- Response assessed per RECIST v1.1

Statistical Considerations

- Sample size: N=~180-240, including 100 patients with NaPi2b-positive tumors
- NaPi2b cutoff: Pre-defined threshold of TPS ≥75% in retrospectively evaluated tissue specimens
- Power: Sample size of ~100 for NaPi2b-positive expressors provides ≥90% power to rule out the maximum SOC ORR of 12% using a 1-sided 97.5% exact binomial confidence interval

CONCLUSIONS

- UPLIFT will evaluate the efficacy and safety of upifitamab rilsodotin (UpRi) monotherapy in PROC
- UPLIFT will evaluate the relevance of NaPi2b as a biomarker in assessing ORR and DOR in the PROC population
- Tumor samples (fresh or archived) will be collected at enrollment for retrospective tumor tissue evaluation of NaPi2b expression
- Study is being conducted in collaboration with ENGOT (ENGOT-ov67) and GOG (GOG-3048)
- ClinicalTrials.gov registry: NCT03319628

ACKNOWLEDGMENTS

We would like to thank the patients, their families, and the site staff for making this study possible. This study is sponsored by Mersana Therapeutics, Inc. Editorial support for this poster was provided by BluPrint Oncology.

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ADDITIONAL INFORMATION

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For more information on UPLIFT, visit ClinicalTrials.gov page NCT03319628 via QR code provided or contact medicalinformation@mersana.com

[a]TPS as determined by an IHC method. [b]Platinum-resistant is defined as disease that has progressed within 6 months of last dose of platinum. [c]HGSOC, including fallopian tube and primary peritoneal cancer.

Abbreviations: ADC, antibody-drug conjugate; AF-HPA, auristatin F-hydroxypropylamide; AST, aspartate aminotransferase; CR, complete response; CT, computed tomography; DAR, drug-to-antibody ratio; DCR, disease control rate; DOR, duration of response; ECOG, Eastern Cooperative Oncology Group; ENGOT, European Network for Gynecological Oncological Trial groups; GOG, Gynecologic Oncology Group; HGSOC, high-grade serous ovarian cancer; IHC, immunohistochemistry; IV, intravenous; MRI, magnetic resonance imaging; NaPi2b, sodium-dependent phosphate transport protein 2B; ORR, objective response rate; OS, overall survival; PARP, poly (ADP-ribose) polymerase; PFS, progression-free survival; PROC, platinum-resistant ovarian cancer; PS, performance status; q4w, every 4 weeks; RECIST, Response Evaluation Criteria in Solid Tumors; SLC34A2, solute carrier family 34 member 2 gene; SOC, standard of care; TPS, tumor proportion score; TRAE, treatment-related adverse event; UpRi, upifitamab rilsodotin.

IGCS 2022 ANNUAL GLOBAL MEETING NYC NEW YORK CITY

TiP Abstract 426

UPLIFT (ENGOT-ov67/GOG-3048): A Pivotal Cohort of the XMT-1536-1 Trial of Upifitamab Rilsodotin, an NaPi2b-Directed Antibody-Drug Conjugate, for Platinum-Resistant Ovarian Cancer (PROC)

CONCLUSIONS

- UPLIFT will evaluate the efficacy and safety of upifitamab rilsodotin (UpRi) monotherapy in PROC
- UPLIFT will evaluate the relevance of NaPi2b as a biomarker in assessing ORR and DOR in the PROC population
- Tumor samples (fresh or archived) will be collected at enrollment for retrospective tumor tissue evaluation of NaPi2b expression
- Study is being conducted in collaboration with ENGOT (ENGOT-ov67) and GOG (GOG-3048)
- ClinicalTrials.gov registry: NCT03319628

Richardson D et al. IGCS 2022;Abstract TIP426.

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

Richardson, Debra L[1]; Harter, Philip[2]; O'Malley, David M[3]; González-Martín, Antonio[4]; Herzog, Thomas J[5]; Rogalski, Caroline[6]; Burger, Robert A[6]; Mirza, Mansoor R[7]

[1]Stephenson Cancer Center, University of Oklahoma Health Sciences Center, Oklahoma City, OK; [2]Kliniken Essen-Mitte, Essen, Germany; [3]The Ohio State University College of Medicine, Columbus, OH; [4]Clinica Universidad de Navarra, Spain; [5]University of Cincinnati Cancer Center, Cincinnati, OH; [6]Mersana Therapeutics, Inc., Cambridge, MA; [7]Rigshospitalet, Copenhagen University Hospital, Denmark

BACKGROUND

Unmet Medical Need in Platinum-Sensitive Recurrent High-Grade Serous Ovarian Cancer (HGSOC)

- Standard of care for patients with platinum-sensitive recurrent HGSOC consists of platinum-based doublet chemotherapy, with or without bevacizumab, followed by bevacizumab monotherapy or PARPi maintenance[1]
- Recent changes in the treatment landscape with the use of PARP inhibitors in patients with platinum-sensitive recurrent ovarian cancer, and more recently in frontline setting, have created a new unmet need for patients who exhaust these options earlier in their disease course, either because they take them in combination or sequentially[2–4]
- In addition, many patients are not appropriate candidates for these agents due to tolerability concerns, particularly in patients with comorbidities
- PARPi maintenance is not indicated for patients who achieve only stable disease after platinum therapy

NaPi2b Is a Sodium-Dependent Phosphate Transporter Broadly Expressed in Ovarian Cancer With Limited Expression in Healthy Tissues[5]

- It is believed that approximately two-thirds of patients with HGSOC have high NaPi2b expression based on an IHC tumor proportion score (TPS) of at least 75%[6]
- NaPi2b is a lineage antigen and not an oncogene; its expression remains consistent throughout the course of disease[7]

Upifitamab Rilsodotin (UpRi) – Investigational First-in-Class NaPi2b-targeting ADC With a Novel Scaffold-Linker-Payload[6–8]

Antibody: Humanized monoclonal anti-SLC34A2 (NaPi2b)

Linker: Fleximer polymer scaffold; cleavable ester linker stable in circulation

Payload: AF-HPA (DolaLock-controlled bystander effect); selectively toxic to rapidly dividing cells

Drug-to-Antibody Ratio (DAR): ~10

METHODS

Study Design and Eligibility

- **UP-NEXT** is a global Phase 3, double-blind, randomized, placebo-controlled study of UpRi monotherapy maintenance in patients with NaPi2b-positive platinum-sensitive recurrent ovarian cancer

Key Enrollment Criteria

- Patients with platinum-sensitive recurrent HGSOC[a]
- 2–4 prior platinum-containing chemotherapy regimens[b]
- Best response to last line of treatment: NED, CR, PR, or SD[c]
- ECOG PS = 0–1
- NaPi2b-positive (TPS ≥75%) tumor (archival or fresh biopsy)
- Prior PARPi required for patients with known deleterious *BRCA* mutations
- Patients who received bevacizumab in combination with their last platinum-containing regimen are excluded

UP-NEXT

N=350 Randomized 2:1

- **UpRi 30 mg/m² (capped at BSA 2.2 m²) IV q4w**
- **Placebo q4w**

All patients continue until PD or unacceptable AE, or up to 18 months

Primary Endpoint
- PFS by BICR

Secondary Endpoints
- PFS by investigator
- ORR by investigator
- OS
- Safety

Study Locations

CONCLUSIONS

- Upifitamab rilsodotin (UpRi) is an investigational first-in-class NaPi2b-targeting ADC with a novel scaffold-linker-payload that is designed with high DAR and a controlled bystander effect
- UP-NEXT is a global Phase 3 study of UpRi monotherapy maintenance in patients with NaPi2b-positive platinum-sensitive recurrent ovarian cancer
- Primary endpoint is PFS by BICR. Secondary endpoints include PFS by investigator, ORR by investigator, OS, and safety
- Trial is currently open for enrollment and is being conducted in collaboration with GOG (GOG-3049) and ENGOT (ENGOT-ov71-NSGO-CTU)
- ClinicalTrials.gov registry: NCT05329545

ACKNOWLEDGMENTS

We would like to thank the patients, their families, and the site staff for making this study possible.

This study is sponsored by Mersana Therapeutics, Inc.

Editorial support for this poster was provided by BluPrint Oncology.

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For more information on UP-NEXT, visit ClinicalTrials.gov page NCT05329545 via QR code provided or contact medicalinformation@mersana.com

[a] HGSOC, including fallopian tube and primary peritoneal cancer. [b] Carboplatin or cisplatin ± paclitaxel, docetaxel, pegylated liposomal doxorubicin, or gemcitabine. [c] For SD, no increase in disease confirmed by central review of imaging and absence of CA-125 rise >15% in 7 days prior to first dose.

ADC, antibody-drug conjugate; AE, adverse event; AF-HPA, auristatin F-hydroxypropylamide; BICR, blinded independent central review; *BRCA*, BRCA DNA repair associated gene; BSA, body surface area; CA, cancer antigen; CR, complete response; DAR, drug-to-antibody ratio; ECOG, Eastern Cooperative Oncology Group; ENGOT, European Network of Gynaecological Oncological Trial groups; GOG, GOG Foundation; HGSOC, high-grade serous ovarian cancer; HR, hazard ratio; IHC, immunohistochemistry; IV, intravenous; NaPi2b, sodium-dependent phosphate transport protein 2B; NED, no evidence of disease; ORR, objective response rate; OS, overall survival; PARP, poly (ADP-ribose) polymerase; PARPi, PARP inhibitor; PD, progressive disease; PFS, progression-free survival; PR, partial response; PS, performance status; q4w, every 4 weeks; SLC34A2, solute carrier family 34 member 2 gene; SD, stable disease; TPS, tumor proportion score; UpRi, upifitamab rilsodotin.

IGCS 2022 ANNUAL GLOBAL MEETING NYC NEW YORK CITY

TiP Abstract 453

UP-NEXT (GOG-3049/ENGOT-ov71-NSGO-CTU): A Study of Upifitamab Rilsodotin for Platinum-Sensitive Recurrent Ovarian Cancer

CONCLUSIONS

- Upifitamab rilsodotin (UpRi) is an investigational first-in-class NaPi2b-targeting ADC with a novel scaffold-linker-payload that is designed with high DAR and a controlled bystander effect
- UP-NEXT is a global Phase 3 study of UpRi monotherapy maintenance in patients with NaPi2b-positive platinum-sensitive recurrent ovarian cancer
- Primary endpoint is PFS by BICR. Secondary endpoints include PFS by investigator, ORR by investigator, OS, and safety
- Trial is currently open for enrollment and is being conducted in collaboration with GOG (GOG-3049) and ENGOT (ENGOT-ov71-NSGO-CTU)
- ClinicalTrials.gov registry: NCT05329545

DAR = drug-to-antibody ratio

Richardson DL et al. IGCS 2022;Abstract TIP453.

UPGRADE: Phase 1 Combination Trial of the NaPi2b-directed Antibody-Drug Conjugate (ADC) Upifitamab Rilsodotin (UpRi; XMT-1536) in Patients With Ovarian Cancer

Hays, John[1]; Werner, Theresa L[2]; Lakhani, Nehal[3]; Edenfield, Jeffrey[4]; Friedman, Claire[5]; Taylor, Sarah E[6]; Duska, Linda[7]; Buscema, Joseph[8]; Carrington, Cassandra[9]; Keeton, Erika[9]; Burger, Robert[9]; Anderson, Charles[10]

[1]Arthur James Cancer Hospital, Ohio State University, Columbus, OH; [2]Huntsman Cancer Institute, University of Utah, Salt Lake City, UT; [3]START Midwest, Grand Rapids, MI; [4]Prisma Health Cancer Institute, Greenville, SC; [5]Memorial Sloan Kettering Cancer Center, New York, NY; [6]University of Pittsburgh Medical Center, Pittsburgh, PA; [7]University of Virginia, Charlottesville, VA; [8]Arizona Oncology, Tucson, AZ; [9]Mersana Therapeutics, Inc., Cambridge, MA; [10]Willamette Valley Cancer Institute and Research Center, Eugene, OR

BACKGROUND

Unmet Need for Platinum-Sensitive Recurrent HGSOC[1–3]

- Standard of care for patients with newly diagnosed and platinum-sensitive recurrent HGSOC consists of platinum-based chemotherapy with or without bevacizumab, often followed by bevacizumab and/or PARP inhibitor maintenance therapy
- Although platinum-containing combination therapies offer improvement in outcomes over single-agent platinum therapy, this improvement is associated with additional toxicity, with response rates diminishing through subsequent therapies
  - Paclitaxel is associated with high incidence of TRAEs, including hypersensitivity reactions, hematologic toxicity (neutropenia), alopecia, peripheral neuropathy, and myalgia or arthralgia
  - Bevacizumab has been shown to cause additional AEs including hypertension, proteinuria, GI events (perforations, abscesses, and fistulas), thromboembolism, high-grade pain, and wound disruption
- Dose-limiting toxicities, such as thrombocytopenia and neutropenia, limit duration of platinum-based therapy (usually 6 cycles) in the recurrent disease setting
- Poor response rates beyond first line indicate that there is a clear need for effective therapies in the treatment of platinum-sensitive recurrent OC

Upifitamab Rilsodotin (UpRi): Investigational First-in-Class NaPi2b-targeting ADC[4,5]

- **NaPi2b** is a sodium-dependent phosphate transport protein broadly expressed in solid tumors, including high-grade serous epithelial ovarian, fallopian tube, and primary peritoneal cancer, with limited expression in normal tissue
- It is believed that approximately two-thirds of patients with HGSOC have high NaPi2b expression based on an IHC tumor proportion score (TPS) of at least 75%
- Based on the encouraging single-agent safety and efficacy data, we hypothesize that UpRi in combination with other therapies can provide additional clinical benefit and improved tolerability over current standard of care

Antibody: Humanized monoclonal anti-SLC34A2 (NaPi2b)

Linker: Fleximer polymer scaffold; cleavable ester linker stable in circulation

Payload: AF-HPA (DolaLock-controlled bystander effect); selectively toxic to rapidly dividing cells

Drug-to-Antibody Ratio (DAR): ~10

There Is Rationale for Combination Therapy With Carboplatin[3,6,7]

- To address this unmet medical need, novel platinum-based combinations must be developed that:
  - Can be continued as maintenance treatment following completion of platinum-based chemotherapy
  - Specifically contain targeted agents with favorable therapeutic index and lack appreciable overlapping toxicity with carboplatin
  - Have non-overlapping mechanisms of action with other agents typically combined with carboplatin
- ADCs, such as UpRi, may represent a promising strategy in combination with carboplatin to optimize therapeutic index for patients

METHODS

Study Design and Eligibility

UPGRADE-A is a cohort under the UPGRADE umbrella study evaluating UpRi in combination with other therapies (NCT04907968), specifically a Phase 1 dose escalation and expansion study evaluating UpRi in combination with carboplatin in patients with platinum-sensitive* recurrent OC who have received 1–2 prior lines of therapy. Patients are not selected for NaPi2b expression. The trial is currently enrolling patients. Additional combination cohorts will be added.

Key Enrollment Criteria

- Recurrent, platinum-sensitive* high-grade serous ovarian cancer, including fallopian tube or primary peritoneal cancer
- 1–2 prior platinum-based regimens
- Tissue (fresh or archival) will be collected for retrospective assessment of NaPi2b expression
- RECIST v1.1 measurable disease
- ECOG PS = 0–1

Dose Escalation (BOIN Design; N=18)

UpRi (3 dose levels) + carbo AUC 5 q4w × 6 → UpRi q4w until PD or unacceptable AE

Primary Endpoint
- MTD for UpRi with carboplatin AUC 5

Secondary Endpoints
- AEs, PK for UpRi, PK for carboplatin, immunogenicity for UpRi, ORR, PFS, OS

Dose Expansion (N=30)

UpRi MTD + carbo AUC 5 q4w × 6 → UpRi q4w until PD or unacceptable AE

Primary Endpoint
- Feasibility

Secondary Endpoints
- AEs, PK for UpRi, PK for carboplatin, immunogenicity for UpRi, ORR, PFS, OS, efficacy by NaPi2b expression

*Patients with platinum-sensitive disease are defined as having achieved either a partial or complete response to 4 or more cycles in their last platinum-containing regimen and their disease progressing more than 6 months after completion of the last dose of platinum-containing therapy.

Statistical Considerations

Dose escalation

- Bayesian optimal interval (BOIN) design will be used to determine the MTD among the 3 dose levels to be evaluated in this study
- If additional dose levels/schemes are planned to be evaluated, then the maximum sample size will be increased by 6 patients for every dose level/scheme planned to be evaluated

Dose expansion

- Primary objective of expansion cohort is to determine feasibility at MTD determined by ≥60% of participants completing at least 4 cycles of UpRi/carboplatin combination without discontinuing treatment earlier for reasons other than disease progression
- Secondary objectives include assessing correlation of tumor expression of NaPi2b and objective tumor response

CONCLUSIONS

- Upifitamab rilsodotin (UpRi) is an investigational first-in-class ADC targeting the sodium-dependent phosphate transport protein NaPi2b
- Based on available emerging data, we hypothesize that UpRi in combination with other therapies may provide additional clinical benefit and improved tolerability over current standard of care
- UPGRADE-A is a cohort under the umbrella study, UPGRADE, evaluating UpRi in combination with carboplatin in patients with platinum-sensitive (progressing >6 months after completion of last dose of platinum) recurrent OC who have received 1–2 prior lines of therapy
- Primary objectives for the dose escalation and expansion cohorts are to identify the MTD and to assess the feasibility of the combination. Secondary endpoints include safety and tolerability, PK, and preliminary anti-neoplastic activity
- Enrollment to the dose escalation cohort is underway
- ClinicalTrials.gov registry: NCT04907968

ACKNOWLEDGMENTS

We would like to thank the patients, their families, and the site staff for making this study possible.

This study is sponsored by Mersana Therapeutics, Inc.

Editorial support for this poster was provided by BluPrint Oncology.

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1. NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) for Ovarian Cancer V.3.2022. Published July 25, 2022. Accessed August 18, 2022. https://www.nccn.org/professionals/physician_gls/pdf/ovarian.pdf **2.** Herzog TJ. *Clin Cancer Res*. 2004;10(22):7439–7449. **3.** Slaughter KLL et al. *Gynecol Oncol*. 2016;142(2):225–230. **4.** Lin K et al. *Clin Cancer Res*. 2015;21(22):5139–5150. **5.** Richardson DL et al. SGO Annual Meeting on Women's Cancer 2022; Abstract 76. **6.** Ray-Coquard I et al. *Cancer Treat Rev*. 2020;90:102107. **7.** Vasan N et al. *Nature*. 2019;575(7782):299–309.

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Abbreviations: ADC, antibody-drug conjugate; AE, adverse event; AF-HPA, auristatin F-hydroxypropylamide; AUC, area under the curve; BOIN, Bayesian optimal interval; carbo, carboplatin; DAR, drug-to-antibody ratio; ECOG, Eastern Cooperative Oncology Group; GI, gastrointestinal; HGSOC, high-grade serous ovarian cancer; MTD, maximum tolerated dose; NaPi2b, sodium-dependent phosphate transport protein 2B; OC, ovarian cancer; ORR, objective response rate; OS, overall survival; PARP, Poly (ADP-ribose) polymerase; PD, progressive disease; PFS, progression-free survival; PK, pharmacokinetics; PS, performance status; q4w, every 4 weeks; RECIST, Response Evaluation Criteria in Solid Tumors; SLC34A2, solute carrier family 34 member 2 gene; TPS, tumor proportion score; TRAE, treatment-related adverse event; UpRi, upifitamab rilsodotin.

TiP Abstract 446

UPGRADE: A Phase I Combination Trial of Upifitamab Rilsodotin for Patients with Ovarian Cancer

CONCLUSIONS

- Upifitamab rilsodotin (UpRi) is an investigational first-in-class ADC targeting the sodium-dependent phosphate transport protein NaPi2b
- Based on available emerging data, we hypothesize that UpRi in combination with other therapies may provide additional clinical benefit and improved tolerability over current standard of care
- UPGRADE-A is a cohort under the umbrella study, UPGRADE, evaluating UpRi in combination with carboplatin in patients with platinum-sensitive (progressing >6 months after completion of last dose of platinum) recurrent OC who have received 1–2 prior lines of therapy
- Primary objectives for the dose escalation and expansion cohorts are to identify the MTD and to assess the feasibility of the combination. Secondary endpoints include safety and tolerability, PK, and preliminary anti-neoplastic activity
- Enrollment to the dose escalation cohort is underway
- ClinicalTrials.gov registry: NCT04907968

Hays J et al. IGCS 2022;Abstract TIP446.

Case Presentation: 57-year-old woman with BRCA2 mutation-positive metastatic ovarian cancer and platinum-resistant recurrence on third-line cisplatin/gemcitabine

Dr Kimberly Ku (Bloomington, Illinois)

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RESEARCH
TO PRACTICE

Case Presentation: A 55-year-old woman with BRCA WT, MSS oligometastatic HGSOC

Dr Karim ElSahwi (Neptune City, New Jersey)

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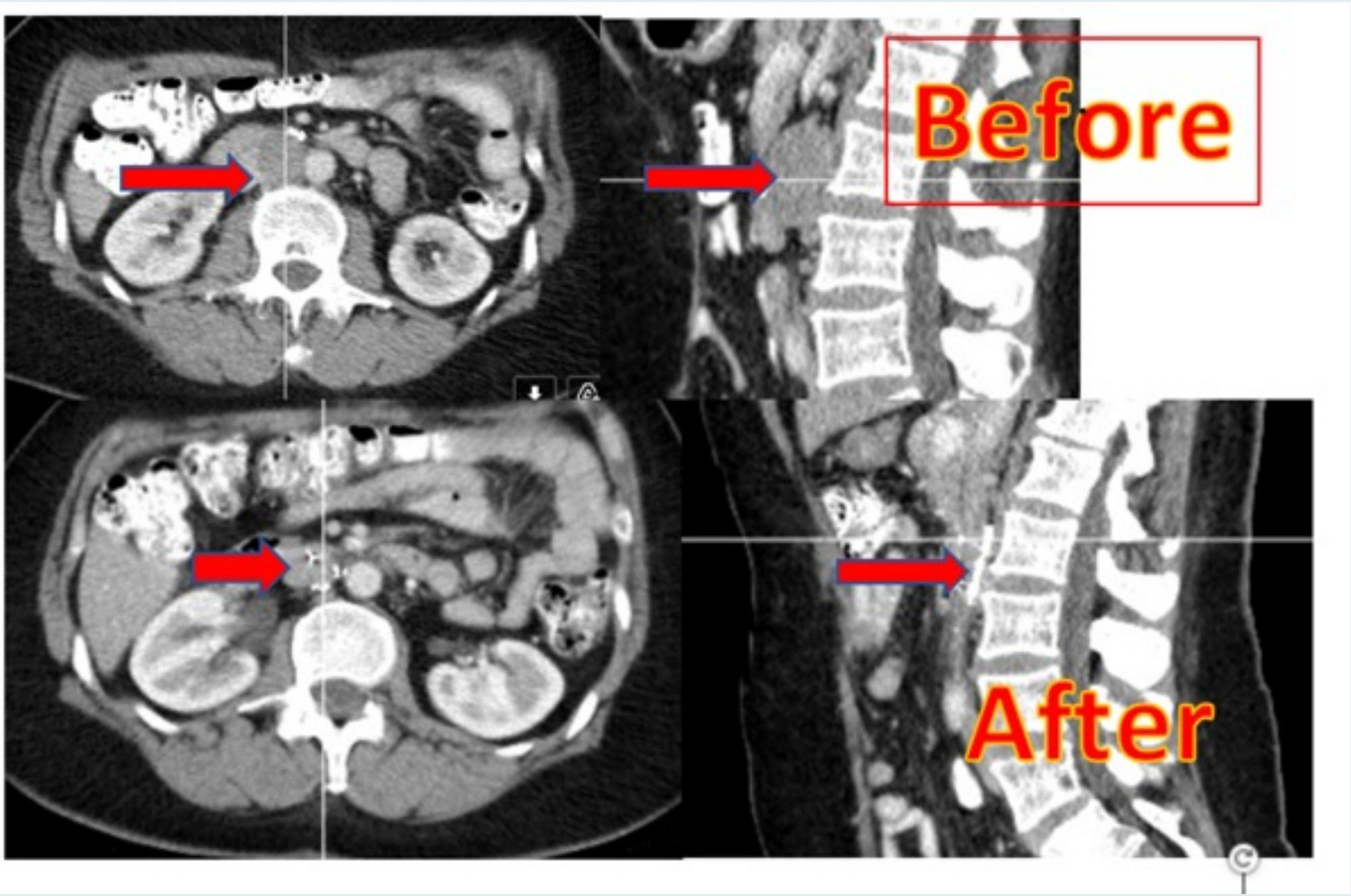
Before
After

Case Presentation: 66-year-old woman with recurrent metastatic BRCA WT ovarian cancer who does not want further RT or chemotherapy

Dr Erik Rupard (West Reading, Pennsylvania)

RTP
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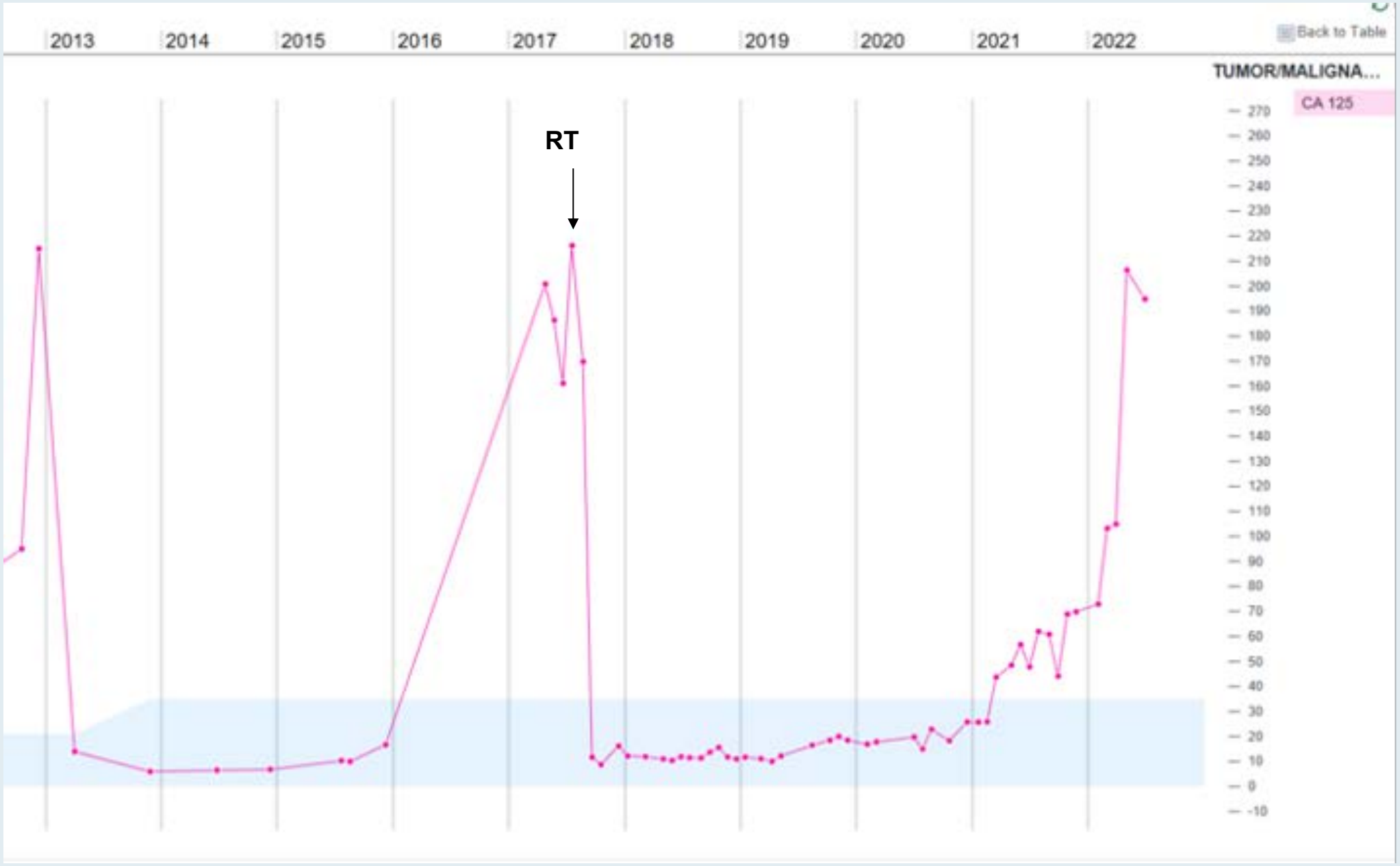
TO PRACTICE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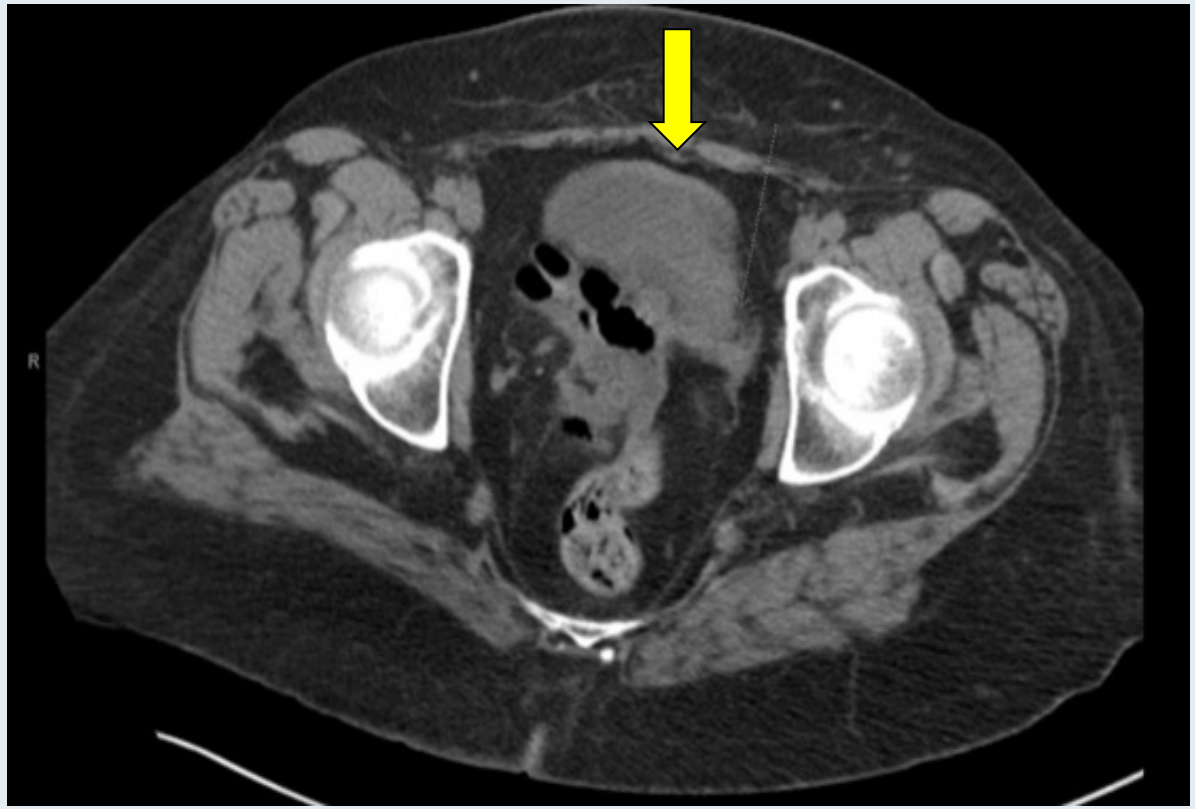
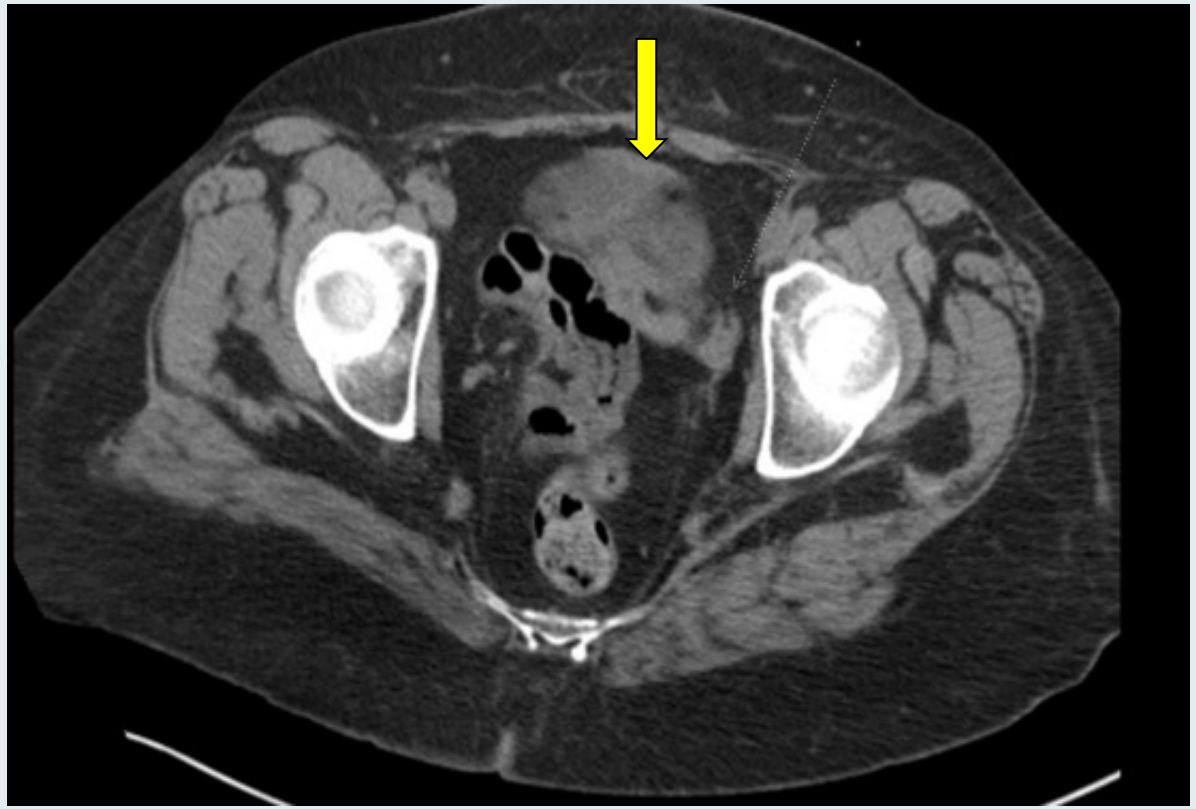
New left hydronephrosis and hydroureter. Unchanged wall thickening along the distal left ureter and adjacent mass-like density concerning for residual disease, now probably causing obstruction





Meet The Professor with Dr Lheureux

Prologue: Seminars in Cancer Biology

MODULE 1: Cases

MODULE 2: Faculty Survey

MODULE 3: Journal Club

Appendix

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

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

RTP RESEARCH TO PRACTICE

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

 Dr Eskander	Niraparib	 Dr Matulonis	None Bevacizumab
 Prof Ledermann	Bevacizumab	 Dr Penson	Niraparib
 Dr Lheureux	Niraparib	 Dr Westin	Niraparib

RTP
RESEARCH
TO PRACTICE

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

 Dr Eskander	Olaparib	 Dr Matulonis	Niraparib
 Prof Ledermann	None	 Dr Penson	Olaparib
 Dr Lheureux	Niraparib	 Dr Westin	Olaparib

RTP RESEARCH TO PRACTICE

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

 Dr Eskander	Olaparib	 Dr Matulonis	Olaparib
 Prof Ledermann	Olaparib	 Dr Penson	Olaparib
 Dr Lheureux	Olaparib	 Dr Westin	Olaparib

RTP RESEARCH TO PRACTICE

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

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

RTP RESEARCH TO PRACTICE

Meet The Professor with Dr Lheureux

Prologue: Seminars in Cancer Biology

MODULE 1: Cases

MODULE 2: Faculty Survey

MODULE 3: Journal Club

Appendix

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Gynecologic Oncology Reports 36 (2021) 100729

Contents lists available at ScienceDirect

Gynecologic Oncology Reports

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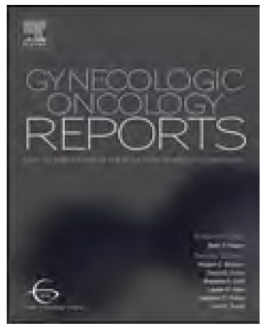


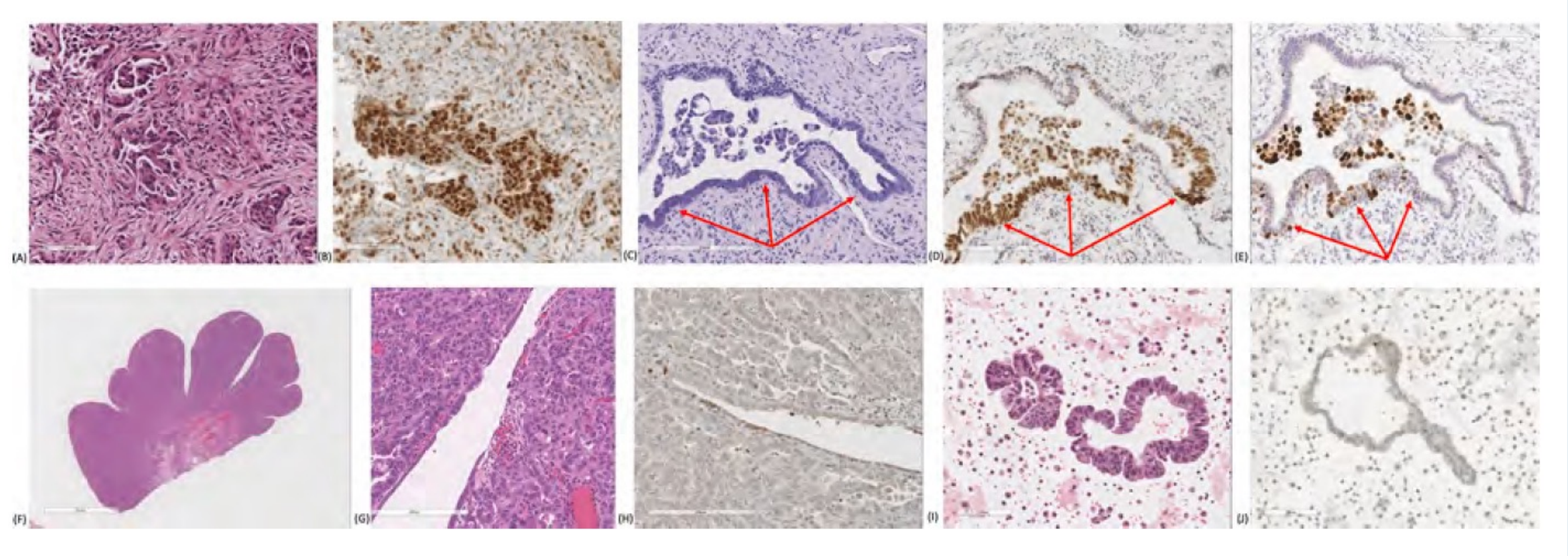
Case report

Can *TP53* variant negative be high-grade serous ovarian carcinoma? A case series

Lawrence Kasherman [a,1], Swati Garg [a,1], Nairi Tchrakian [b], Blaise Clarke [b], Katherine Karakasis [a], Raymond H. Kim [a,c], Tracy L. Stockley [b,d,e], Neesha Dhani [a], Amit M. Oza [a], Stephanie Lheureux [a,*]

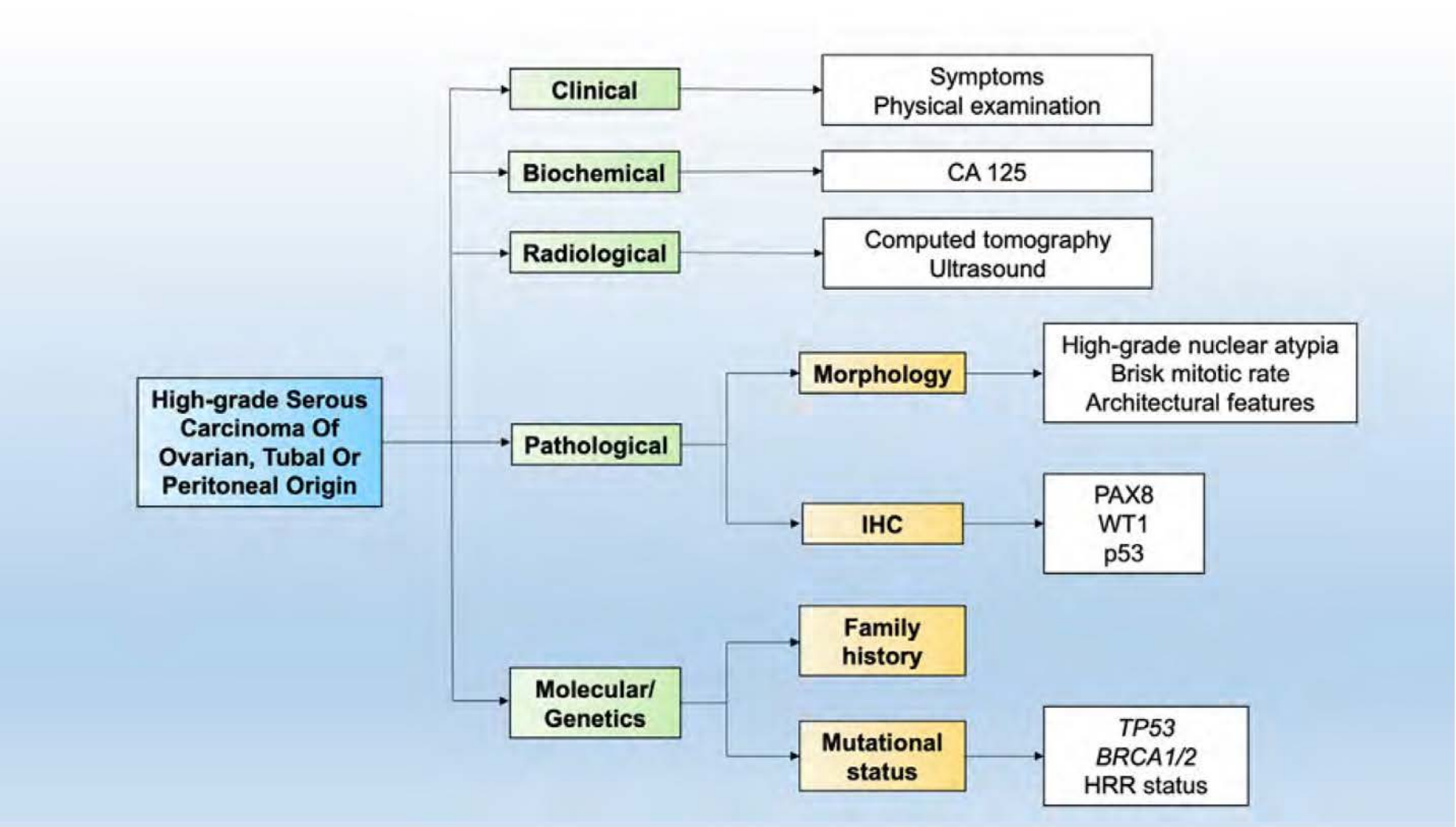
Case 1 (A-E): High-power H&E image of invasive high-grade serous carcinoma in patient 1 showing typical morphologic features of slit-like spaces, high-grade cytologic atypia and brisk mitotic activity (2A) with corresponding mutant overexpression of p53 immunohistochemistry

Case 2 (F-H): Low-power H&E image of the fimbriated end of the fallopian tube in case 2 distended by invasive high-grade serous carcinoma



Kasherman L et al. *Gynecol Oncol* 2021;36:100729.

Schema for Diagnostic Considerations Required for Accurate Diagnosis of High-Grade Serous Ovarian Carcinoma



Kasherman L et al. *Gynecol Oncol* 2021;36:100729.

A Randomized Phase III Trial of Durvalumab with Chemotherapy and Bevacizumab, Followed by Maintenance Durvalumab, Bevacizumab and Olaparib in Newly Diagnosed Advanced Ovarian Cancer (DUO-O): Updated Trial Endpoint and Inclusion of China Cohort

Okamoto A et al.

SGO 2022;Abstract 329.

The Oncologist, 2022, **27**, e393–e401
https://doi.org/10.1093/oncolo/oyac039
Advance access publication 6 April 2022
Original Article

OXFORD

"Game Changer": Health Professionals' Views on the Clinical Utility of Circulating Tumor DNA Testing in Hereditary Cancer Syndrome Management

Salma Shickh[1,2,‡], Leslie E. Oldfield[3,‡], Marc Clausen[1], Chloe Mighton[1,2], Agnes Sebastian[1,2], Alessia Calvo[1,4], Nancy N. Baxter[1,5,6], Lesa Dawson[7,8], Lynette S. Penney[9], William Foulkes[10,11], Mark Basik[10,11], Sophie Sun[12,13], Kasmintan A. Schrader[12,13], Dean A. Regier[12,13], Aly Karsan[12,13], Aaron Pollett[14], Trevor J. Pugh[3,15], Raymond H. Kim[2,3,14,16], Yvonne Bombard[1,2,15,*], on behalf of the CHARM Consortium[**]

The Modeled CA-125 Elimination Rate Constant K (KELIM) Score as a Predictor of Treatment Response in Patients with Advanced High Grade Serous Ovarian Cancer

Piedimonte S et al.

SGO 2022;Abstract 190.

Pharmacokinetic and Pharmacodynamic Analysis of Adavosertib in Advanced Ovarian Cancer

Oza AM et al.

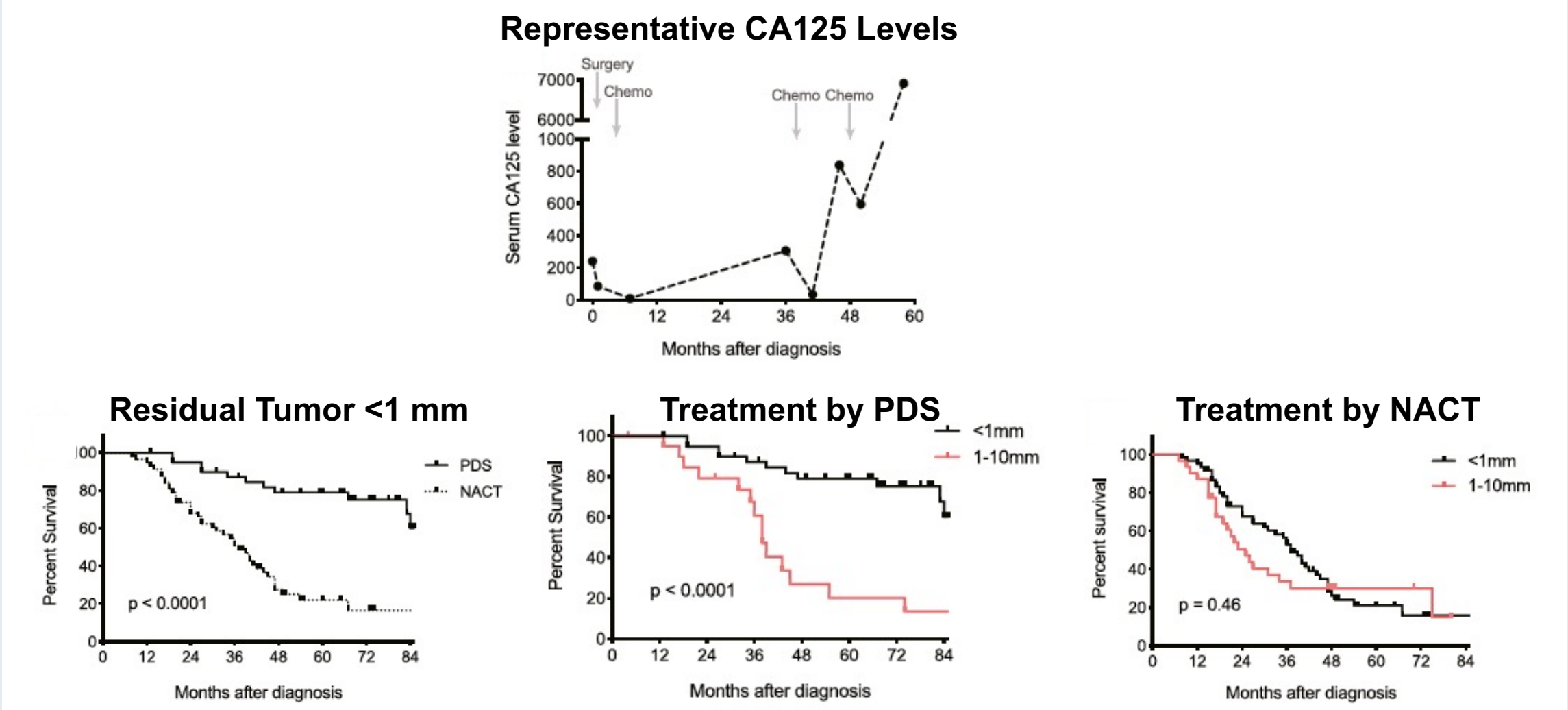
ASCO 2022;Abstract 5579.

Computational modeling of ovarian cancer dynamics suggests optimal strategies for therapy and screening

Shengqing Gu[a,b,1], Stephanie Lheureux[a,c], Azin Sayad[a], Paulina Cybulska[a,d], Liat Hogen[a,d], Iryna Vyarvelska[a,d,2], Dongsheng Tu[e], Wendy R. Parulekar[e], Matthew Nankivell[f], Sean Kehoe[g], Dennis S. Chi[h,i], Douglas A. Levine[j], Marcus Q. Bernardini[a,d], Barry Rosen[a,d,3], Amit Oza[a,c], Myles Brown[k,l,4], and Benjamin G. Neel[a,b,4,5]

Proc Natl Acad Sci U S A 2021 June 22;118(25):e2026663118.

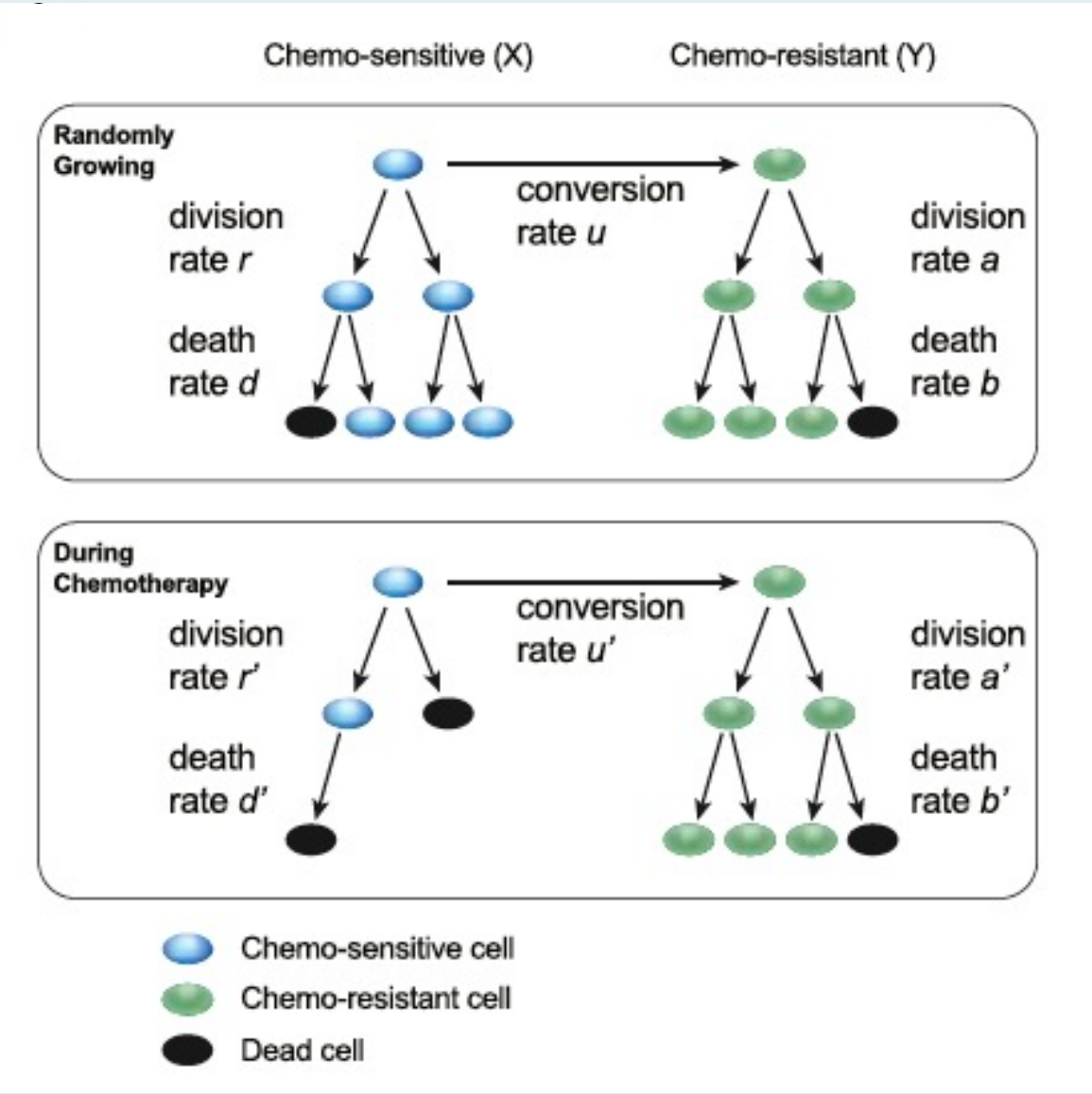
Mathematical Framework of HGSC Clinical Course



HGSC = high-grade serous tubo-ovarian carcinoma; PDS = primary debulking surgery; NACT = neoadjuvant chemotherapy

Gu S et al. *Proc Natl Acad Sci USA* 2021 June 22;118(25):e2026663118 .

Mathematical Framework for Modeling HGSC Progression

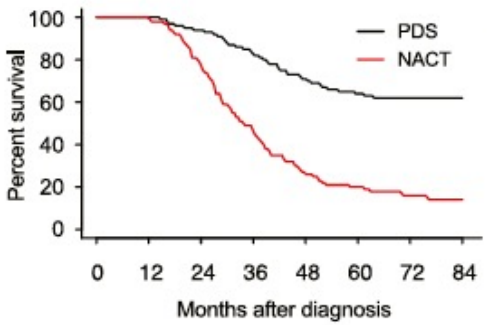


Gu S et al. *Proc Natl Acad Sci USA* 2021 June 22;118(25):e2026663118 .

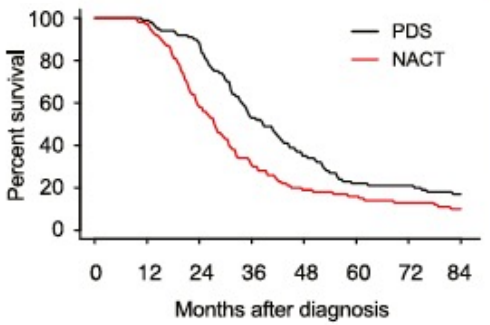
Predicted Outcome for Patients Undergoing PDS or NACT with the Same Initial Tumor Burden

Predicted Survival PDS or NACT

<1-mm residual tumor

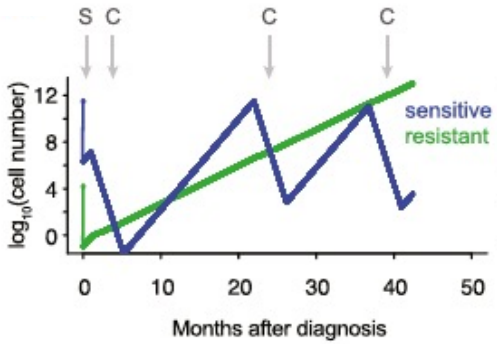


1- to 10-mm residual tumor

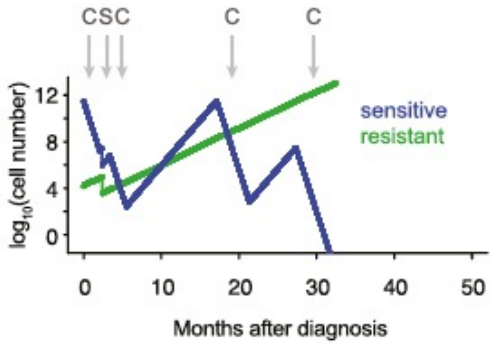


Progression Dynamics Chemosensitive or Chemoresistant

PDS

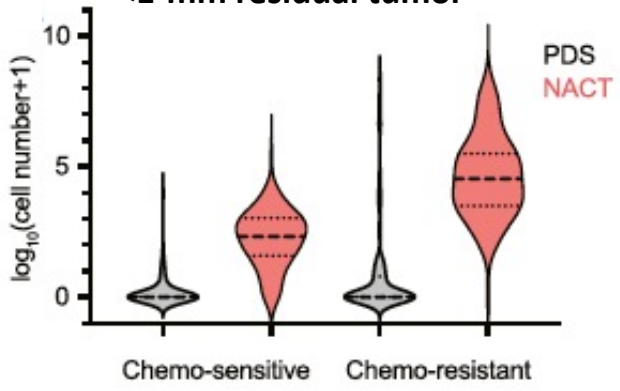


NACT

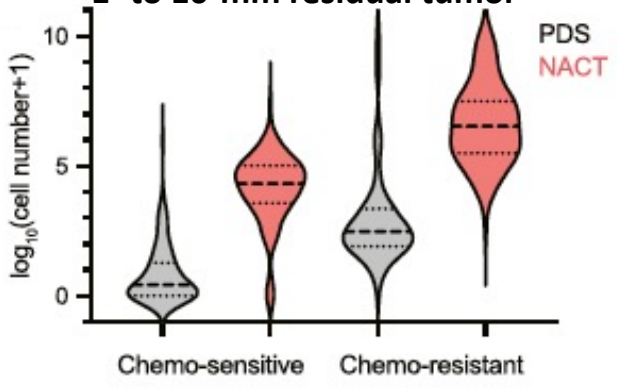


Cell Distribution by Residual Tumor

<1-mm residual tumor

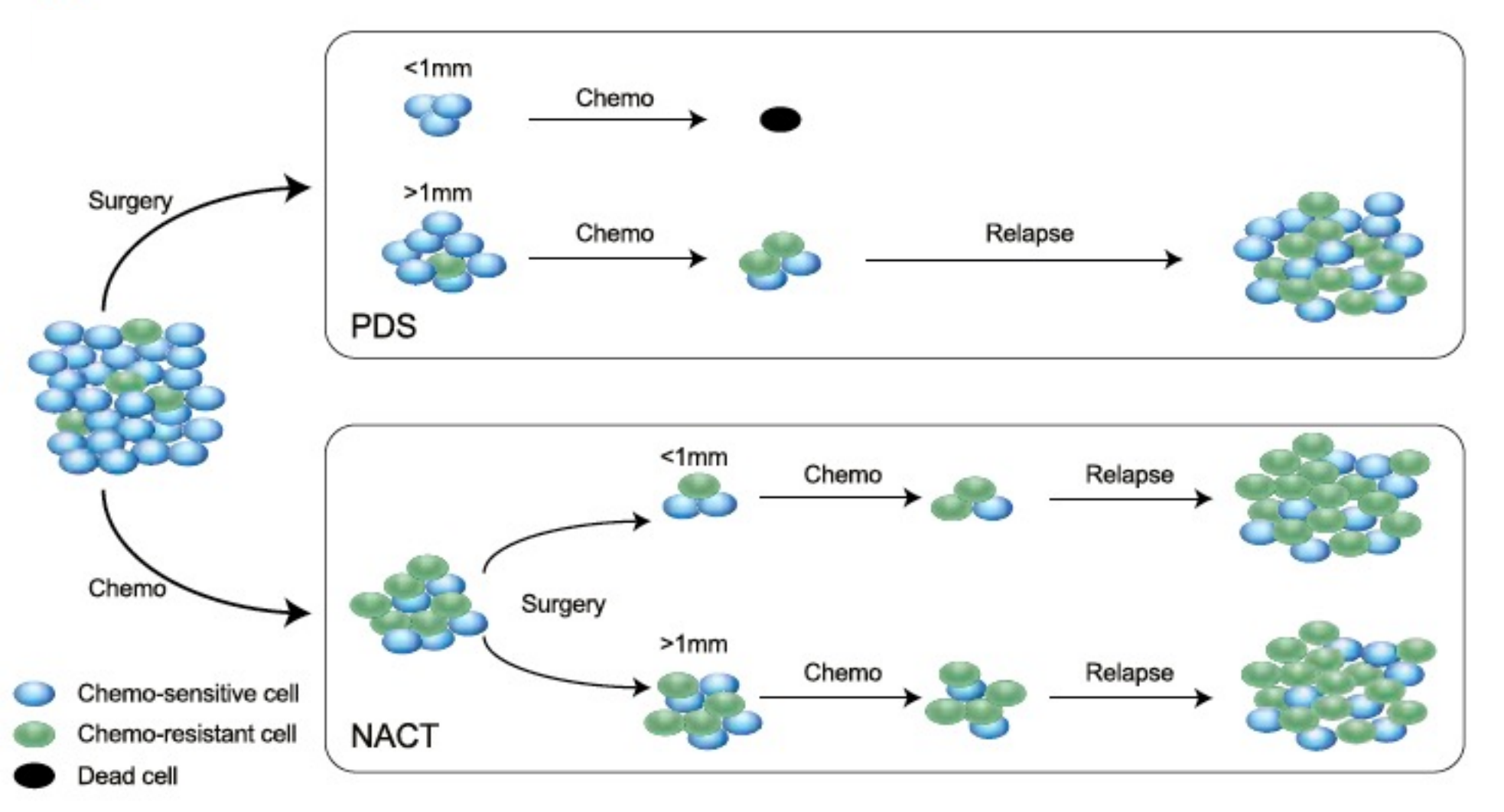


1- to 10-mm residual tumor



Gu S et al. *Proc Natl Acad Sci USA* 2021 June 22;118(25):e2026663118 .

HGSC Clinical Course Following PDS or NACT Treatment

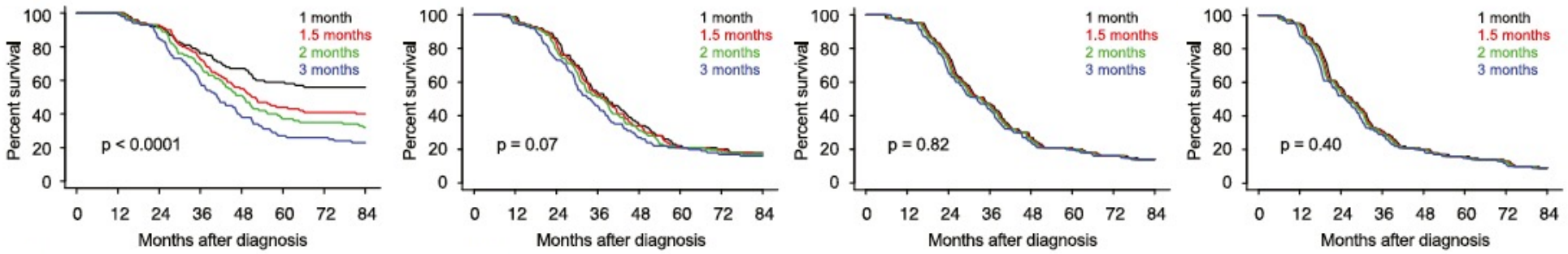


Gu S et al. *Proc Natl Acad Sci USA* 2021 June 22;118(25):e2026663118 .

Predicted Outcome for PDS and NACT Patients with the Same Initial Tumor Burden

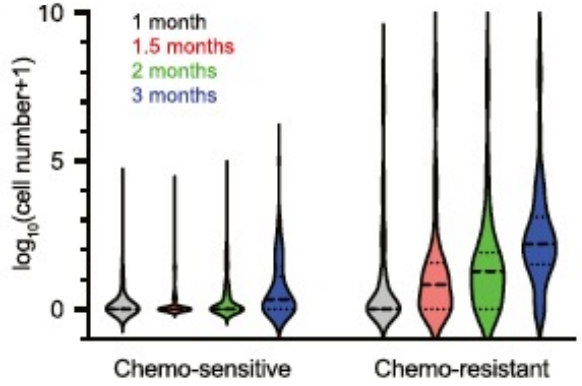
Delay Between Debulking Surgery and Adjuvant Chemotherapy **Progression Dynamics Chemosensitive or Chemoresistant**

PDS <1-mm residual tumor **PDS 1- to 10-mm residual tumor** **NACT <1-mm residual tumor** **NACT 1- to 10-mm residual tumor**



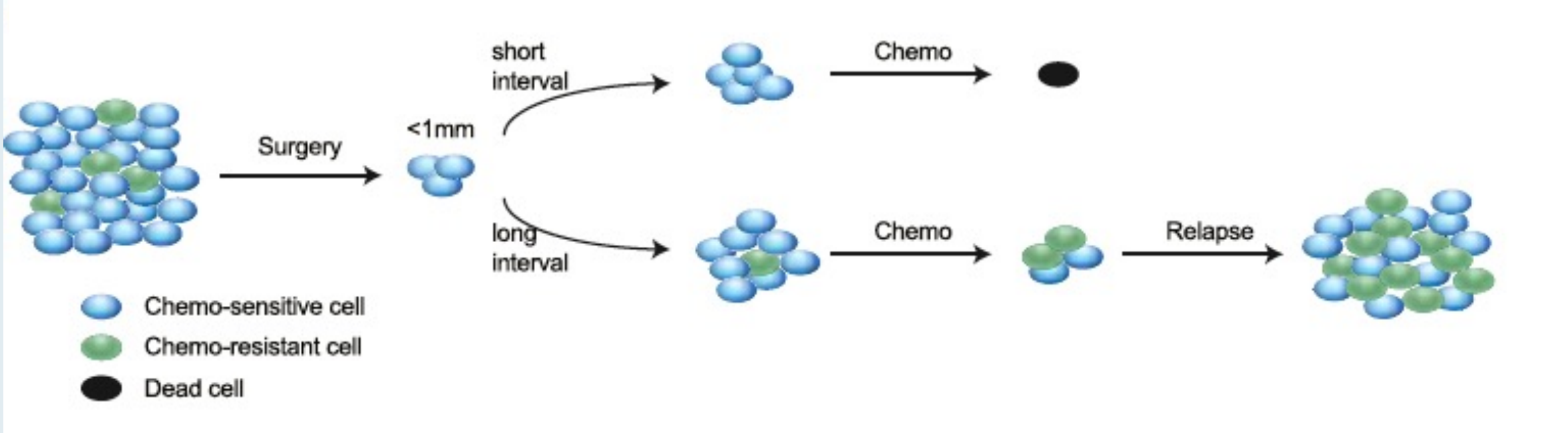
Cell Distribution After PDS <1-mm Residual Tumor

Delay between debulking surgery and adjuvant chemotherapy



Gu S et al. *Proc Natl Acad Sci USA* 2021 June 22;118(25):e2026663118 .

Predicted HGSC Clinical Course Following PDS (<1-mm Residual Tumor) with Standard or Delayed Adjuvant Chemotherapy



Gu S et al. *Proc Natl Acad Sci USA* 2021 June 22;118(25):e2026663118 .

Curr Oncol 2022 August 22;29(8):5988-6009.

Current Oncology

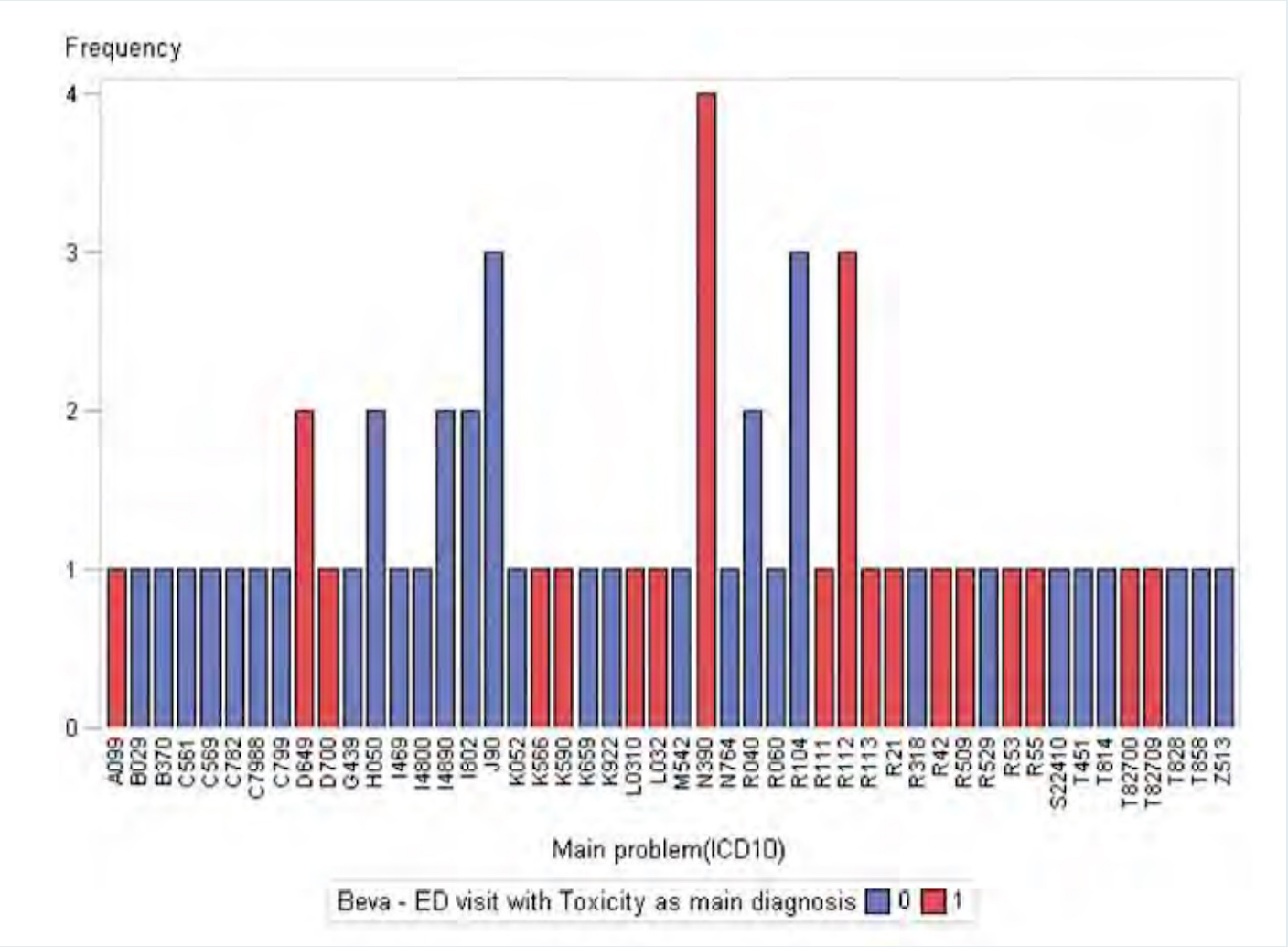
MDPI

Article

Patterns of First-Line Systemic Therapy Delivery and Outcomes in Advanced Epithelial Ovarian Cancer in Ontario

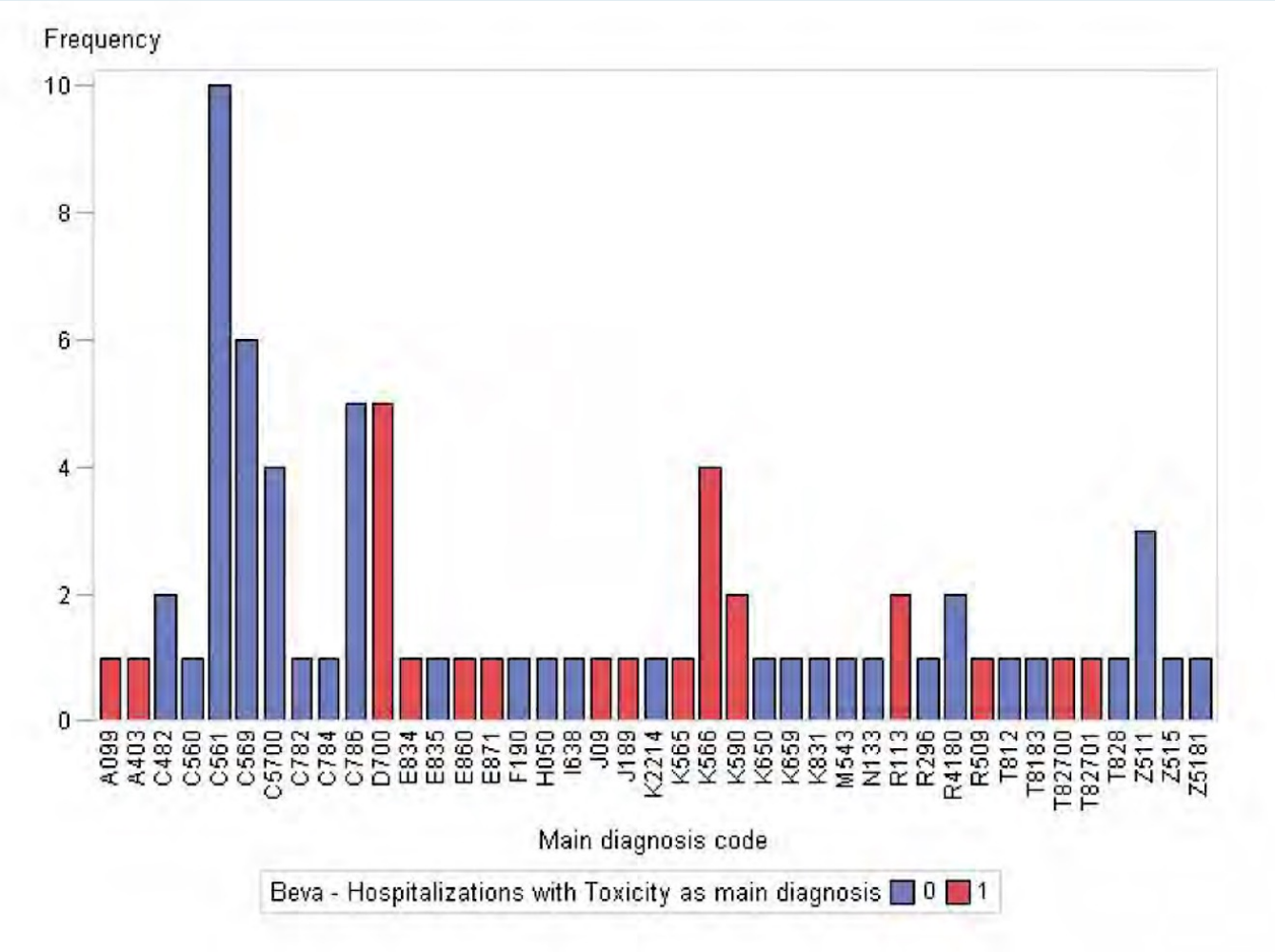
Shiru L. Liu [1,2], Wing C. Chan [3], Geneviève Bouchard-Fortier [4,5], Stephanie Lheureux [6], Sarah E. Ferguson [4,5] and Monika K. Krzyzanowska [1,3,6,*]

ICD-10 Codes of ED Admission Diagnosis During Systemic Treatment for Patients Receiving Bevacizumab Combination in First-Line Setting



Liu SL et al. *Curr Oncol* 2022 August 22;29(8):5988-6009.

ICD-10 Codes for Hospital Admission Diagnoses During Systemic Treatment for Patients Receiving Bevacizumab Combination in First-Line Setting



Liu SL et al. *Curr Oncol* 2022 August 22;29(8):5988-6009.

Meet The Professor with Dr Lheureux

Prologue: Seminars in Cancer Biology

MODULE 1: Cases

MODULE 2: Faculty Survey

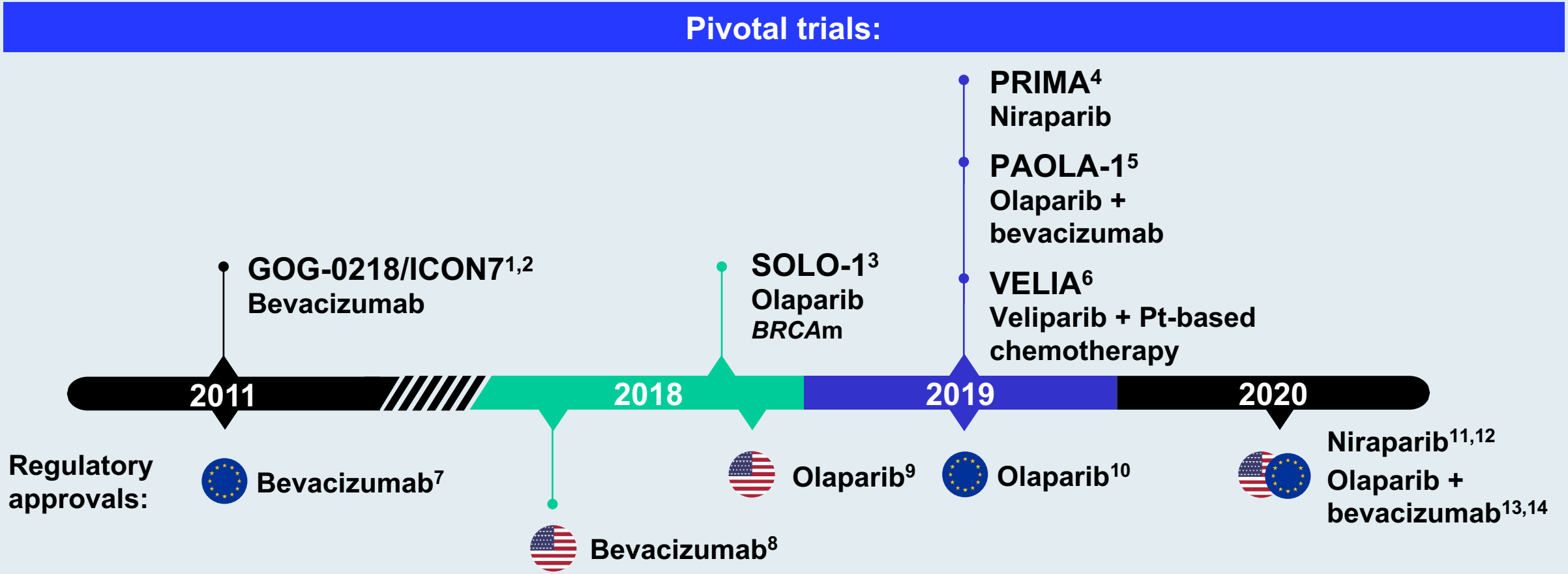
MODULE 3: Journal Club

Appendix

RTP
RESEARCH
TO PRACTICE

Optimal Biomarker Evaluation and Front-Line Management

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



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

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

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

Courtesy of Kathleen Moore, MD

RTP RESEARCH TO PRACTICE

Phase III First-Line PARP Inhibitor Maintenance Trials

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

bev = bevacizumab; PD = disease progression

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

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

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

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

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

Society of Gynecologic Oncology

SGO 2022;Abstract 40.

RTP RESEARCH TO PRACTICE

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

All patients underwent tissue testing for HRd at enrollment

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

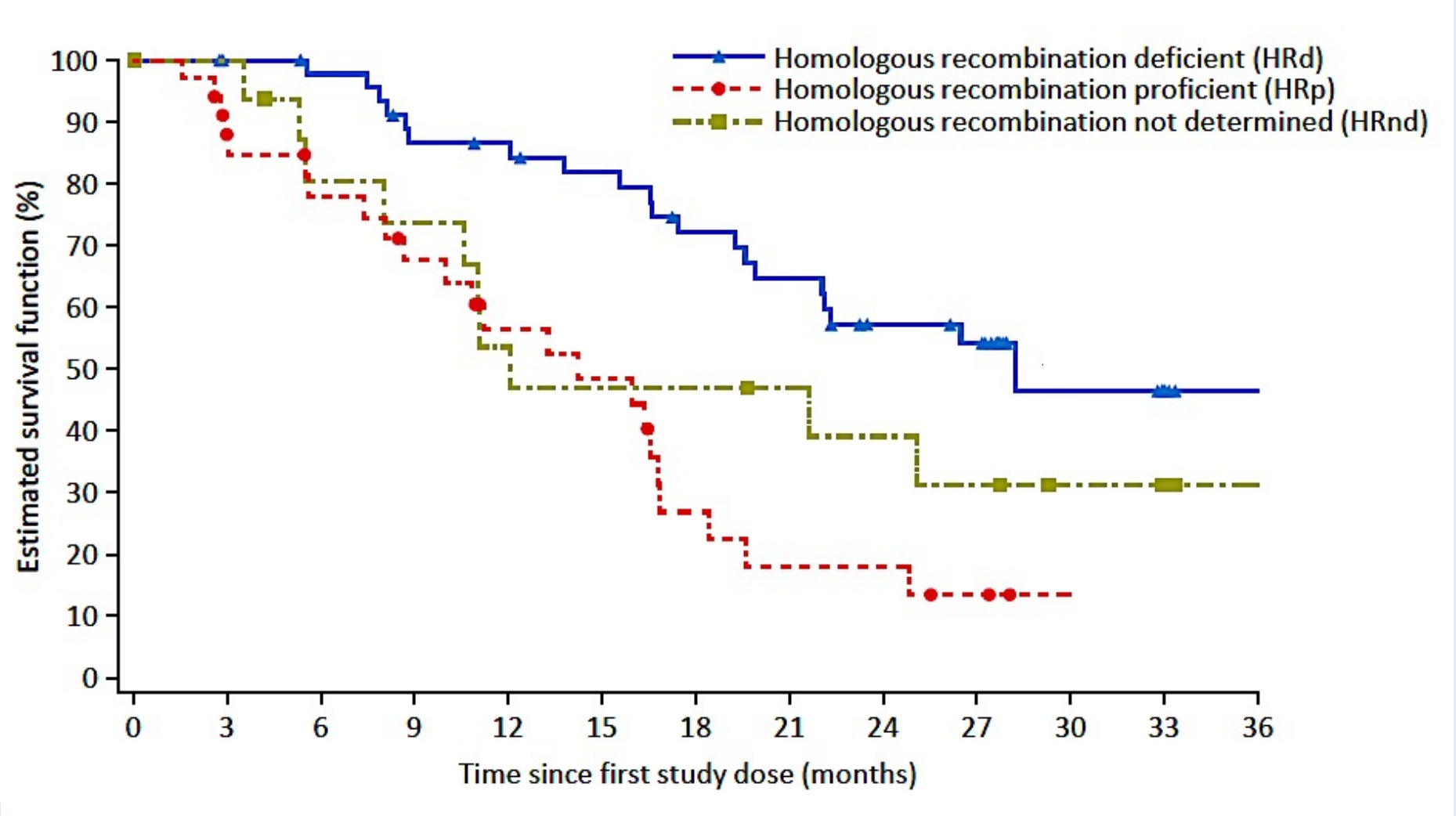
Starting niraparib dose, n (%)	N=105
200 mg (<77 kg and/or platelet count <150,000/µL)	82 (78)
300 mg (all others)	23 (22)

Endpoint assessment

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

Hardesty et al. SGO 2022;Abstract 40.

OVARIO: PFS by Homologous Recombination Deficiency Status



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

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

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

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

Hardesty et al. SGO 2022;Abstract 40.

OVARIO: Treatment-Related Adverse Events (TRAEs)

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

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

Hardesty et al. SGO 2022;Abstract 40.

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

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

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

SGO 2022;Abstract LBA5.

PRIME: Study Design

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

Schema

Eligible Patients

- Age ≥18 years
- FIGO stage III/IV ovarian cancer
- High-grade serous or endometroid tumor[a]
- Receipt of primary or interval cytoreductive surgery, irrespective of postoperative residual disease status
- CR/PR to 1L Pt-based chemotherapy

Stratified randomization

- Status of g*BRCA* mutations (g*BRCA*mut/non-g*BRCA*mut)
- Tumor HRD status[b] (positive/negative)
- Receipt of neoadjuvant chemotherapy (Y/N)
- Response to 1L Pt-based chemotherapy (CR/PR)

2:1 Randomization

- **Niraparib***
- **Placebo***

36 months or until disease progression or unacceptable toxicity

*Individualised starting dose (ISD) was adopted in **ALL** patients: *starting dose of 200 mg administered orally, once daily, but 300 mg for patients with body weight ≥77 kg AND platelet count ≥150,000/μL*

Primary Endpoint

- **PFS by BICR in the ITT population**

Secondary Endpoints

- OS and TFST in the ITT population
- PFS and OS in the HRD subgroup[c]
- Safety

Li et al. SGO 2022;Abstract LBA5.

PRIME: Demographics and Baseline Characteristics

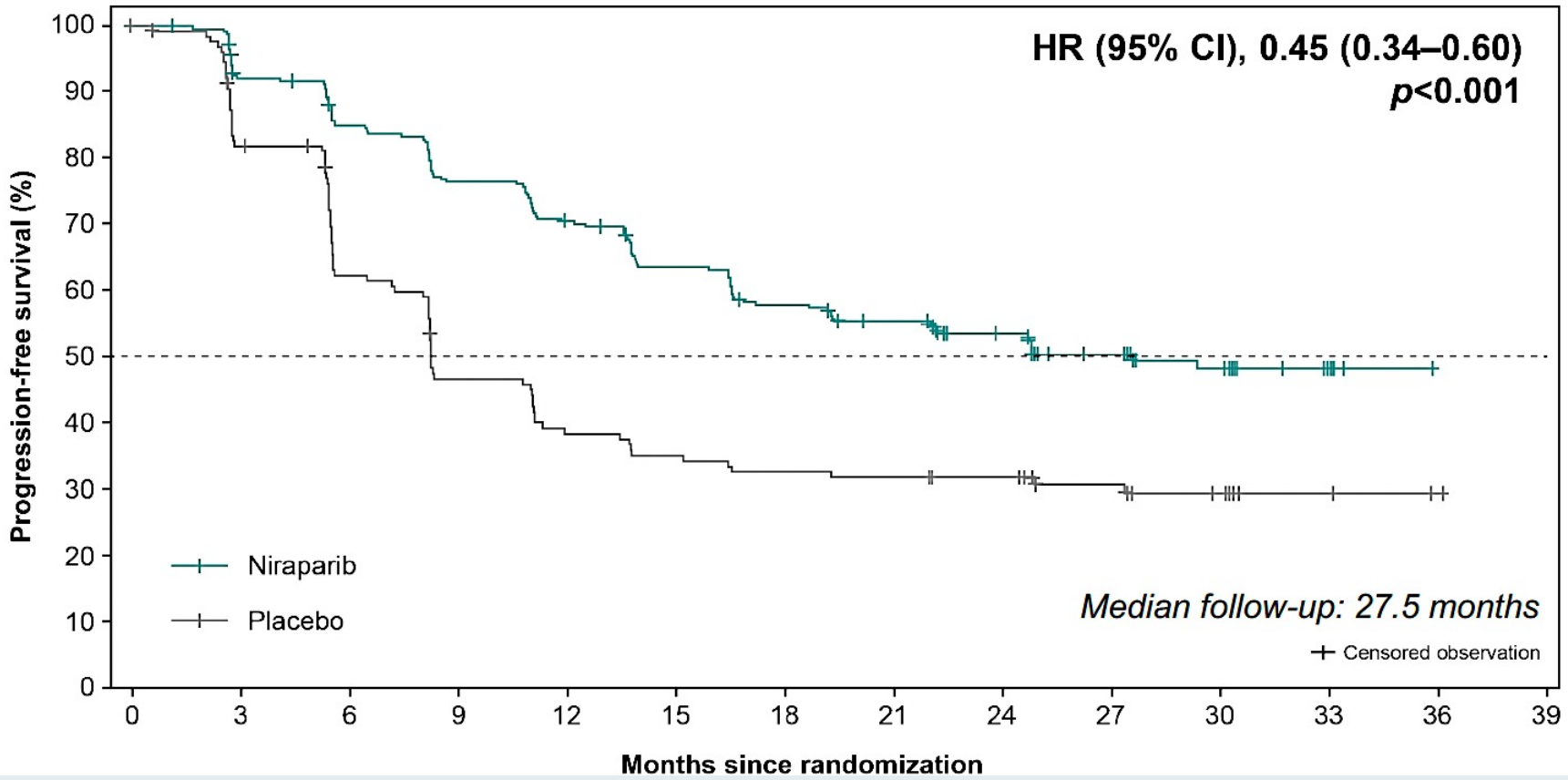
Characteristic	Niraparib (N=255)	Placebo (N=129)
Median age (range), years	53.0 (32–77)	54.0 (33–77)
Median weight (range), kg	59.0 (39.5–100.0)	57.0 (37.0–97.0)
ECOG performance status, n (%)		
0	98 (38.4)	52 (40.3)
1	157 (61.6)	77 (59.7)
FIGO stage, n (%)		
III	182 (71.4)	94 (72.9)
IV	73 (28.6)	35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

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

- The niraparib and placebo groups were well-balanced.

Li et al. SGO 2022;Abstract LBA5.

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



16.5 months longer median PFS with niraparib versus placebo

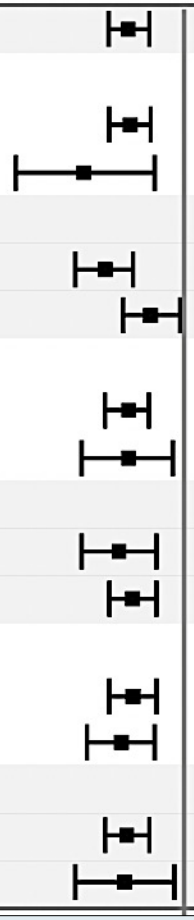
	Niraparib (N=255)	Placebo (N=129)
PFS (54.4% data maturity)		
Events, n (%)	123 (48.2)	86 (66.7)
mPFS (95% CI), months	24.8 (19.2–NE)	8.3 (7.3–11.1)
Patients without PD or death (%)		
24 months	52.6	30.4

Li et al. SGO 2022;Abstract LBA5.

RTP RESEARCH TO PRACTICE

PRIME: PFS Benefit in Prespecified Subgroups

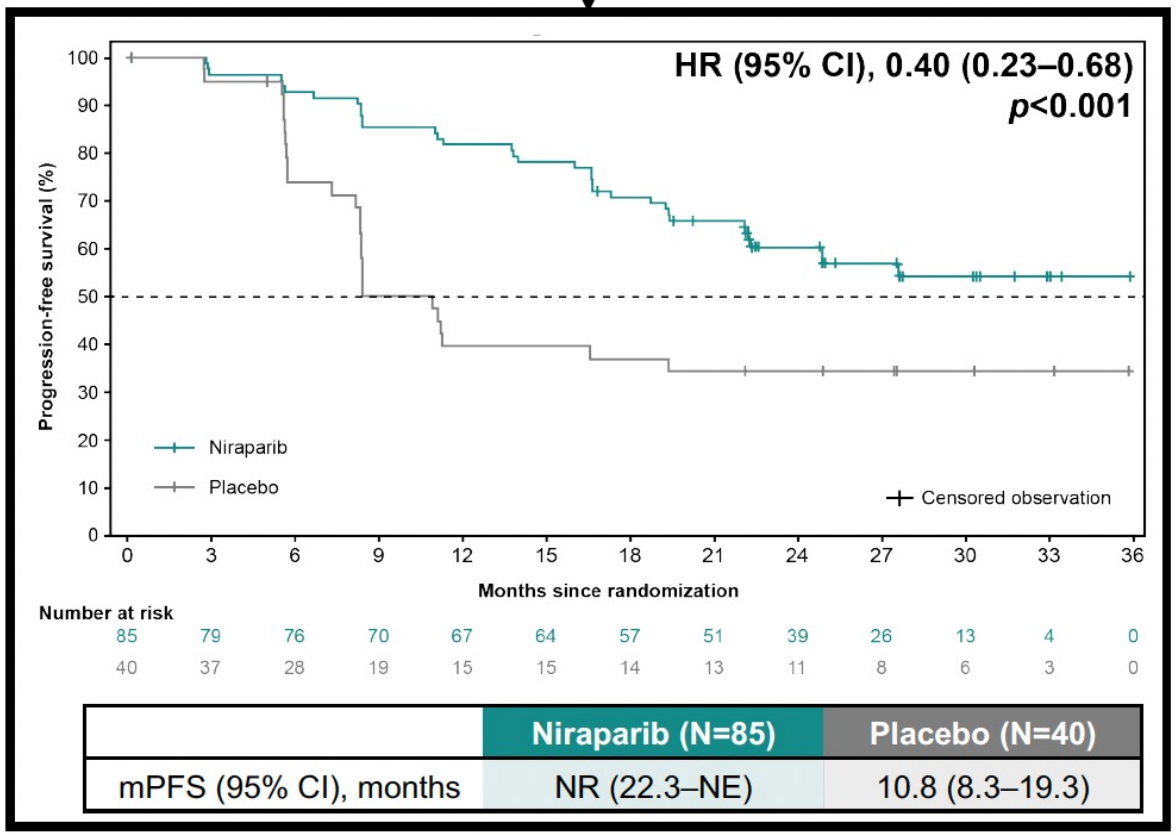
Subgroup	Events/patients (%)		Hazard ratio for PFS (95% CI)
	Niraparib	Placebo	
Overall	123/255 (48.2)	86/129 (66.7)	0.45 (0.34–0.60)
Age			
<65 years	108/229 (47.2)	73/114 (64.0)	0.47 (0.34–0.63)
≥65 years	15/26 (57.7)	13/15 (86.7)	0.24 (0.09–0.66)
Neoadjuvant chemotherapy			
Yes	62/121 (51.2)	46/59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



Li et al. SGO 2022;Abstract LBA5.

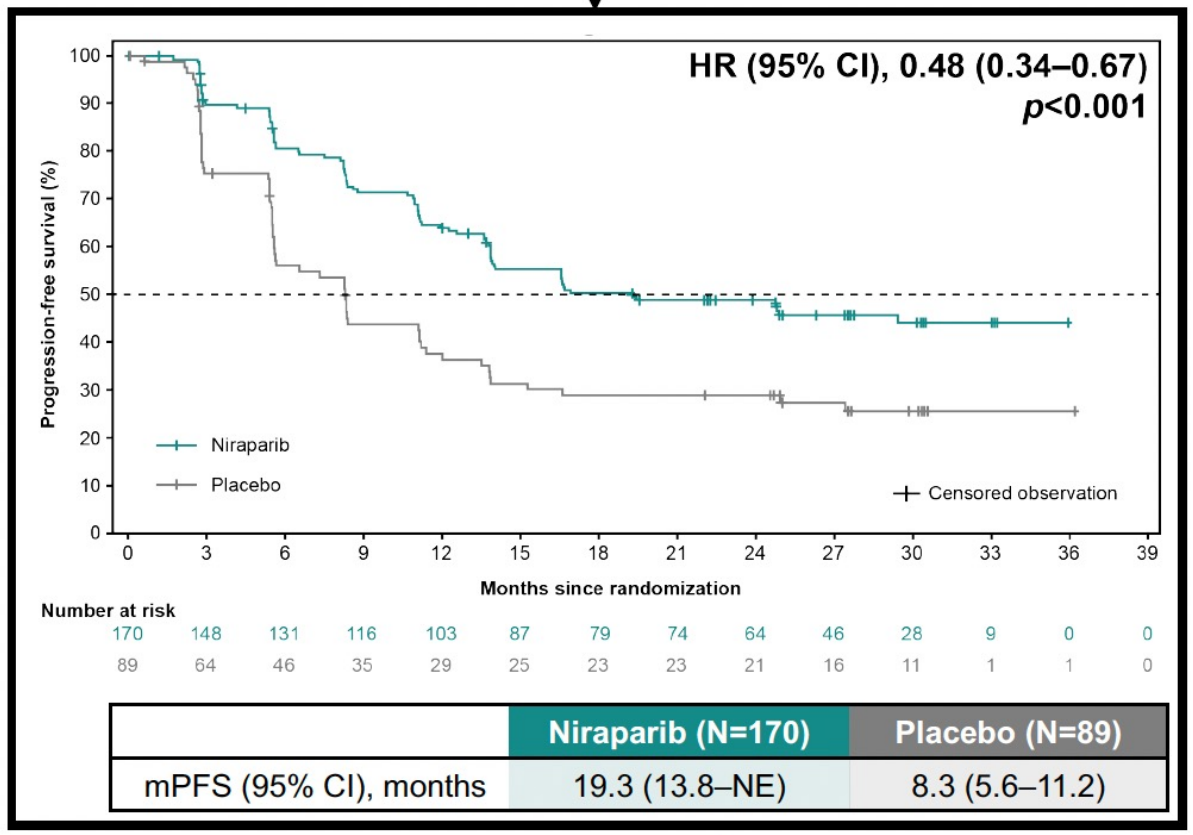
PRIME: PFS Benefit by Germline BRCA Mutation Status

g*BRCA*mut



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

Non-g*BRCA*mut



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

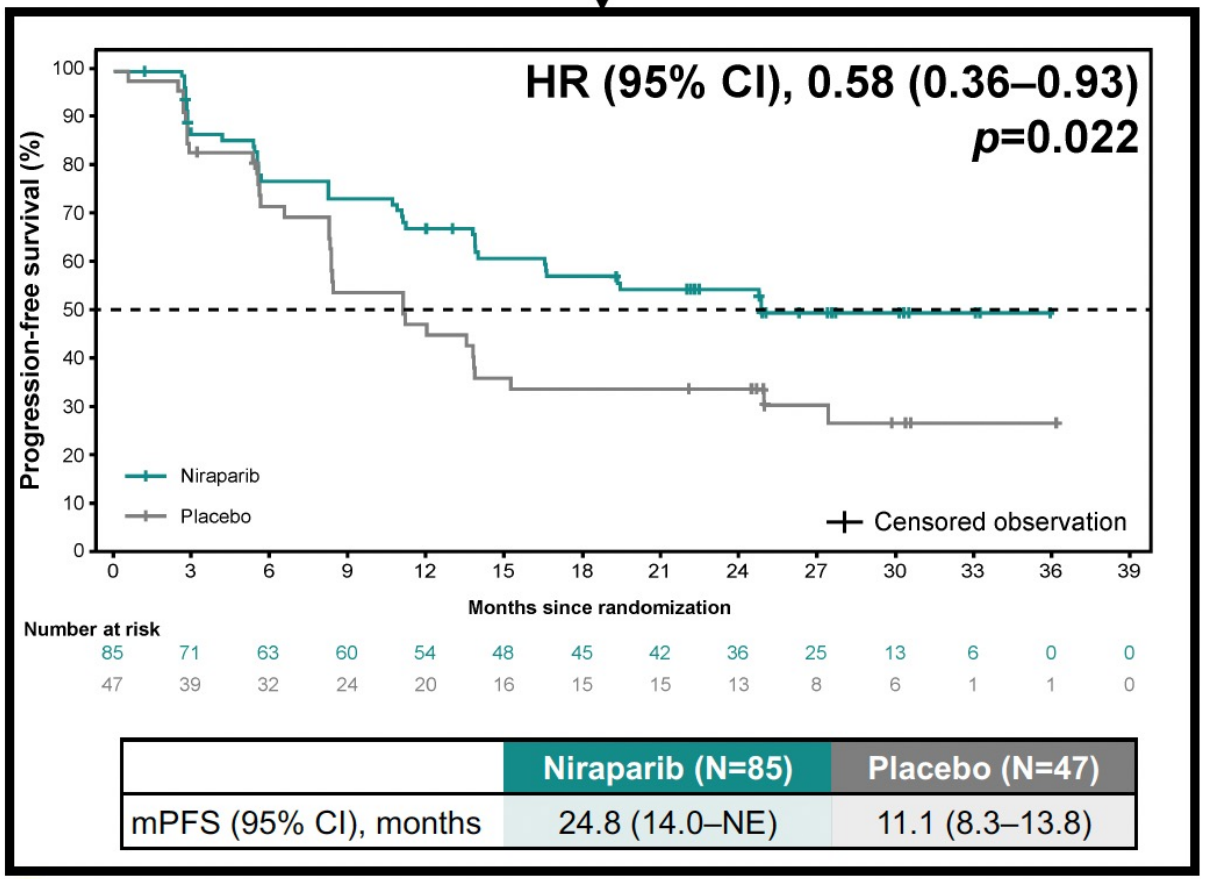
- Median PFS has not been yet reached for the g*BRCA*mut population.
- The benefit of niraparib in the non-g*BRCA*mut population is confirmed.

Li et al. SGO 2022;Abstract LBA5.

RTP RESEARCH TO PRACTICE

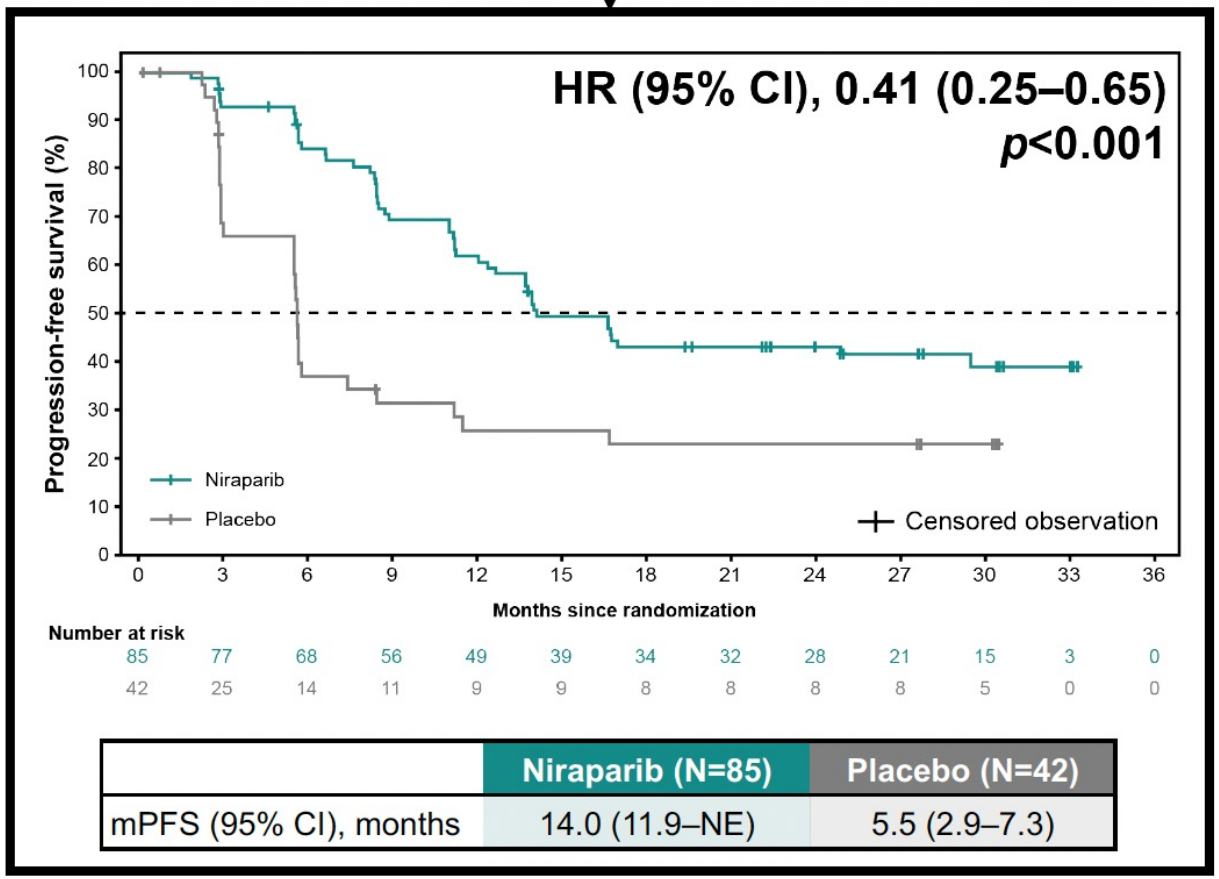
PRIME: PFS Benefit in Non-gBRCAmut Subgroups

Non-g*BRCA*mut/HRd



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

Non-g*BRCA*mut/HRp



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

Li et al. SGO 2022;Abstract LBA5.

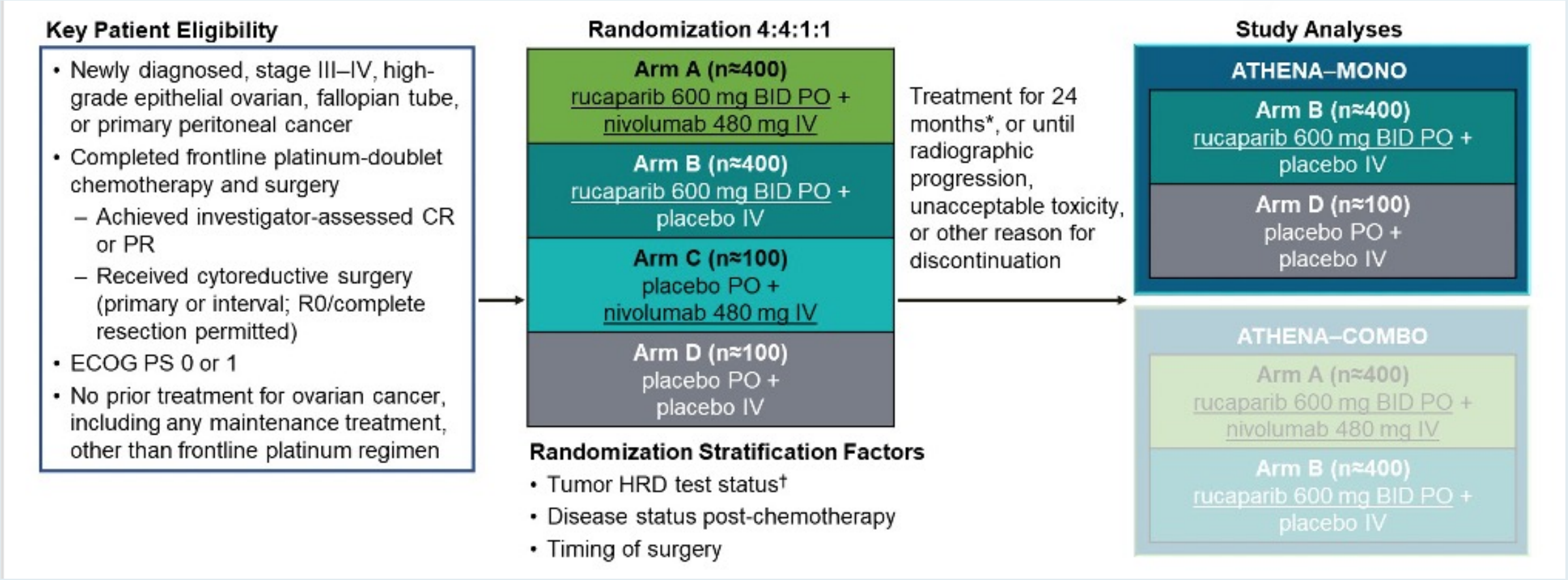
RTP RESEARCH TO PRACTICE

PRIME 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)

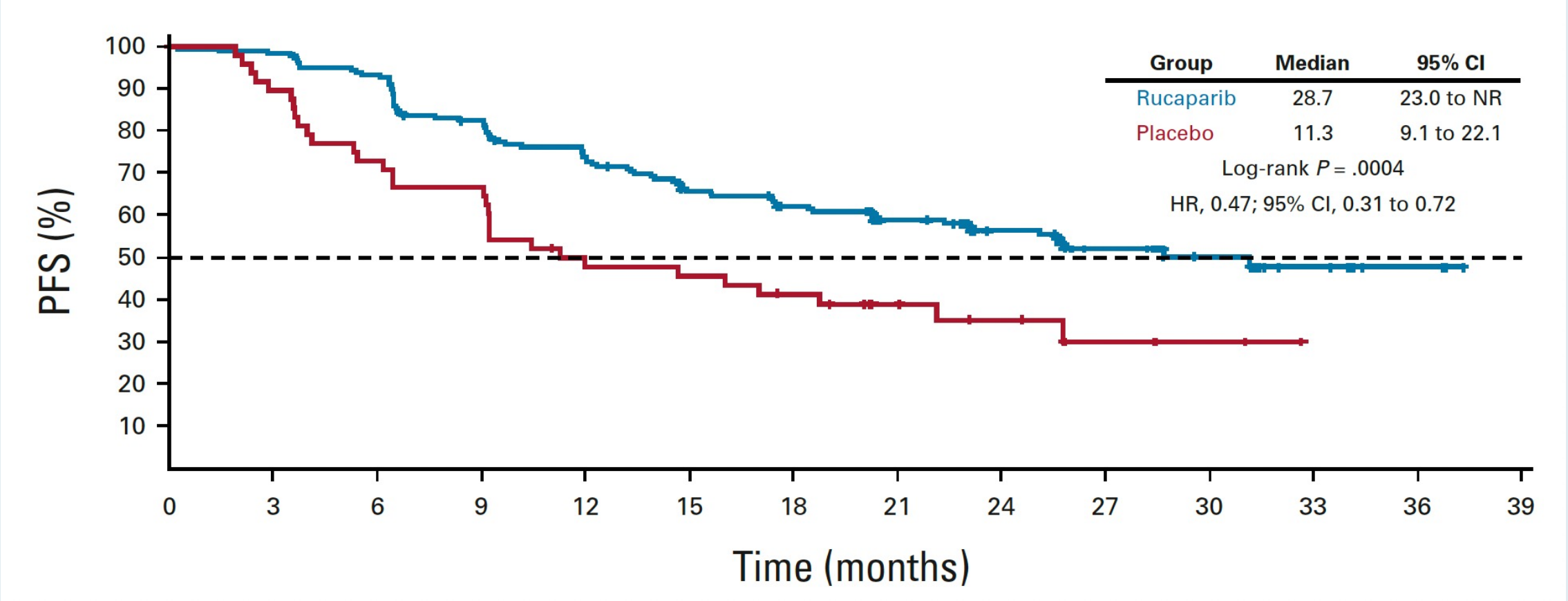
Li et al. SGO 2022;Abstract LBA5.

ATHENA-MONO Study Schema



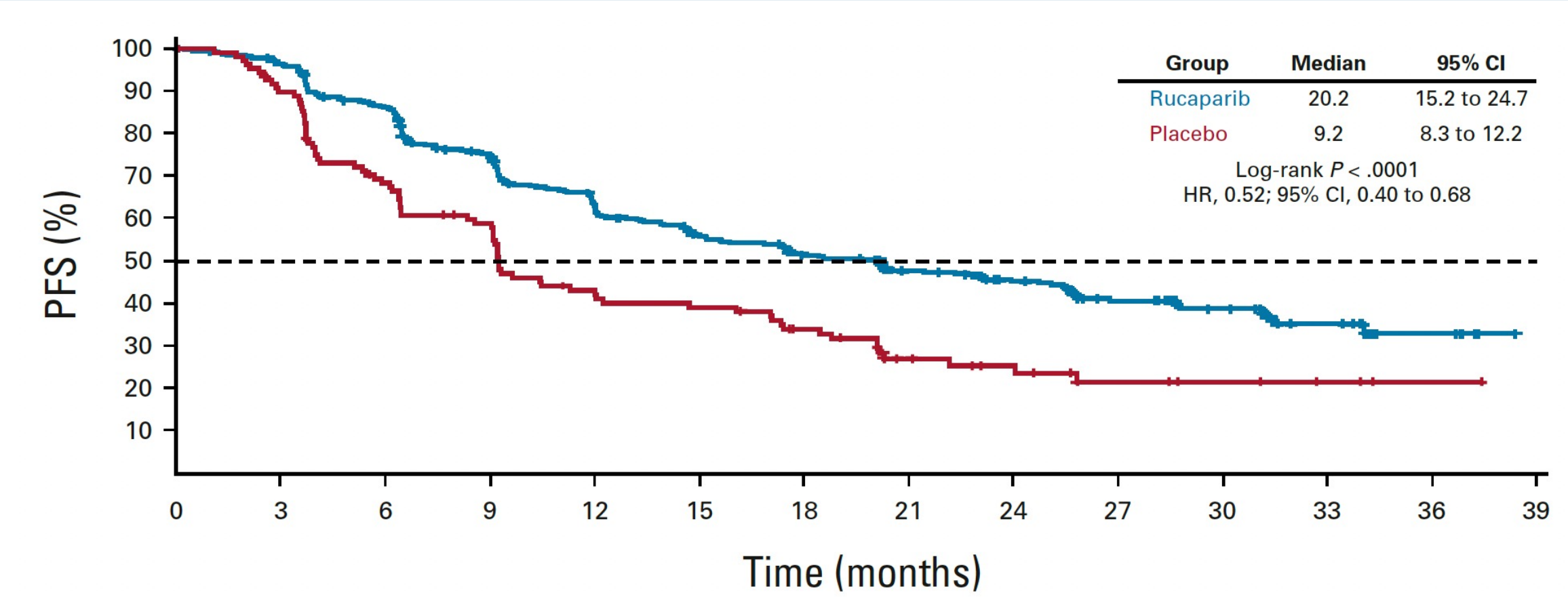
Monk BJ et al. ASCO 2022;Abstract LBA5500.

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



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

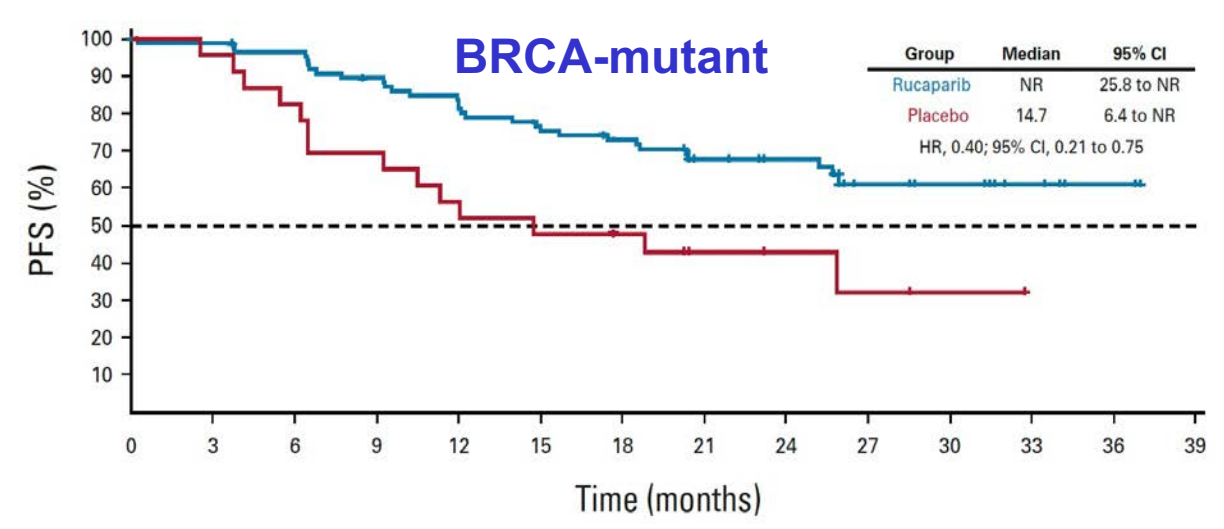
ATHENA-MONO: Investigator-Assessed PFS in the ITT Population (N = 538)

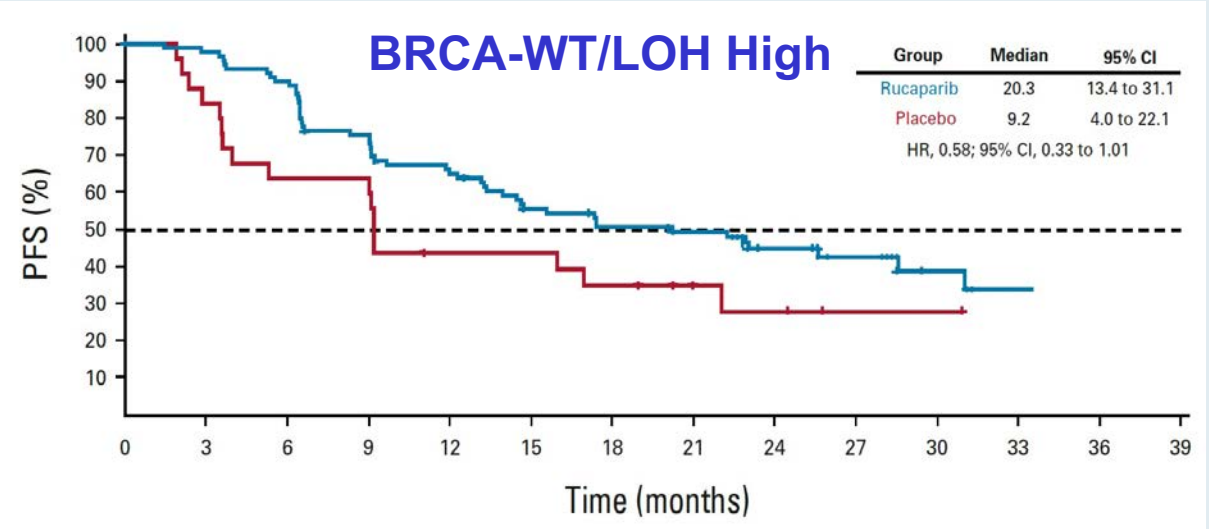


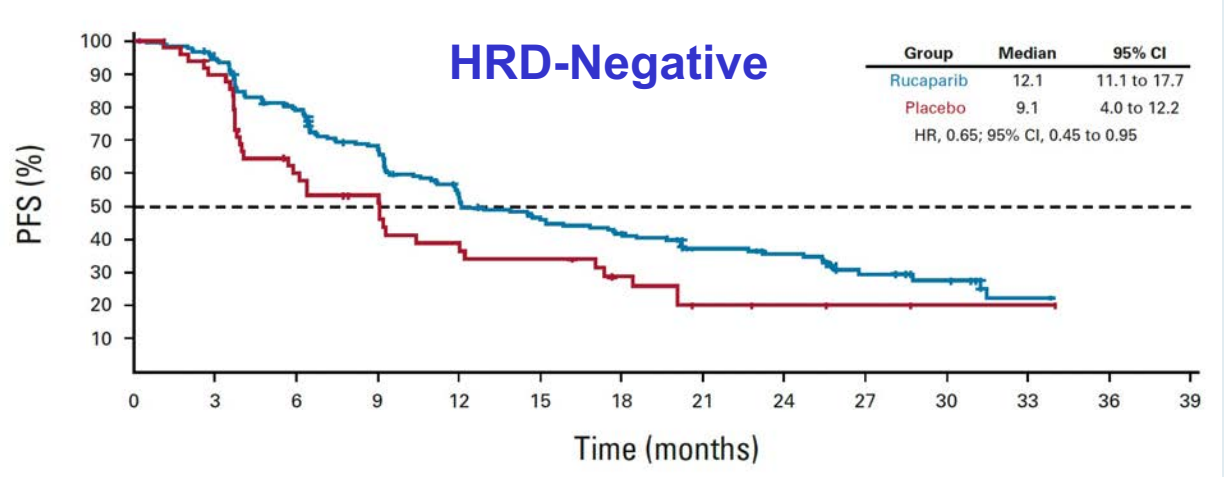
Monk BJ et al. *J Clin Oncol* 2022;[Online ahead of print].

RTP RESEARCH TO PRACTICE

ATHENA-MONO: Investigator-Assessed PFS







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

ATHENA-MONO: Investigator-Confirmed ORR

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

ORR = objective response rate

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

ATHENA-MONO: Common Treatment-Emergent Adverse Events

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

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

Applications Submitted to FDA and EMA for Maintenance Rucaparib for Advanced Ovarian Cancer

Press Release: September 14, 2022

A supplemental new drug application has been submitted to the FDA and a Type II variation to the European Medicines Agency for rucaparib as first-line maintenance treatment for advanced ovarian cancer regardless of biomarker status and after response to first-line platinum-based chemotherapy.

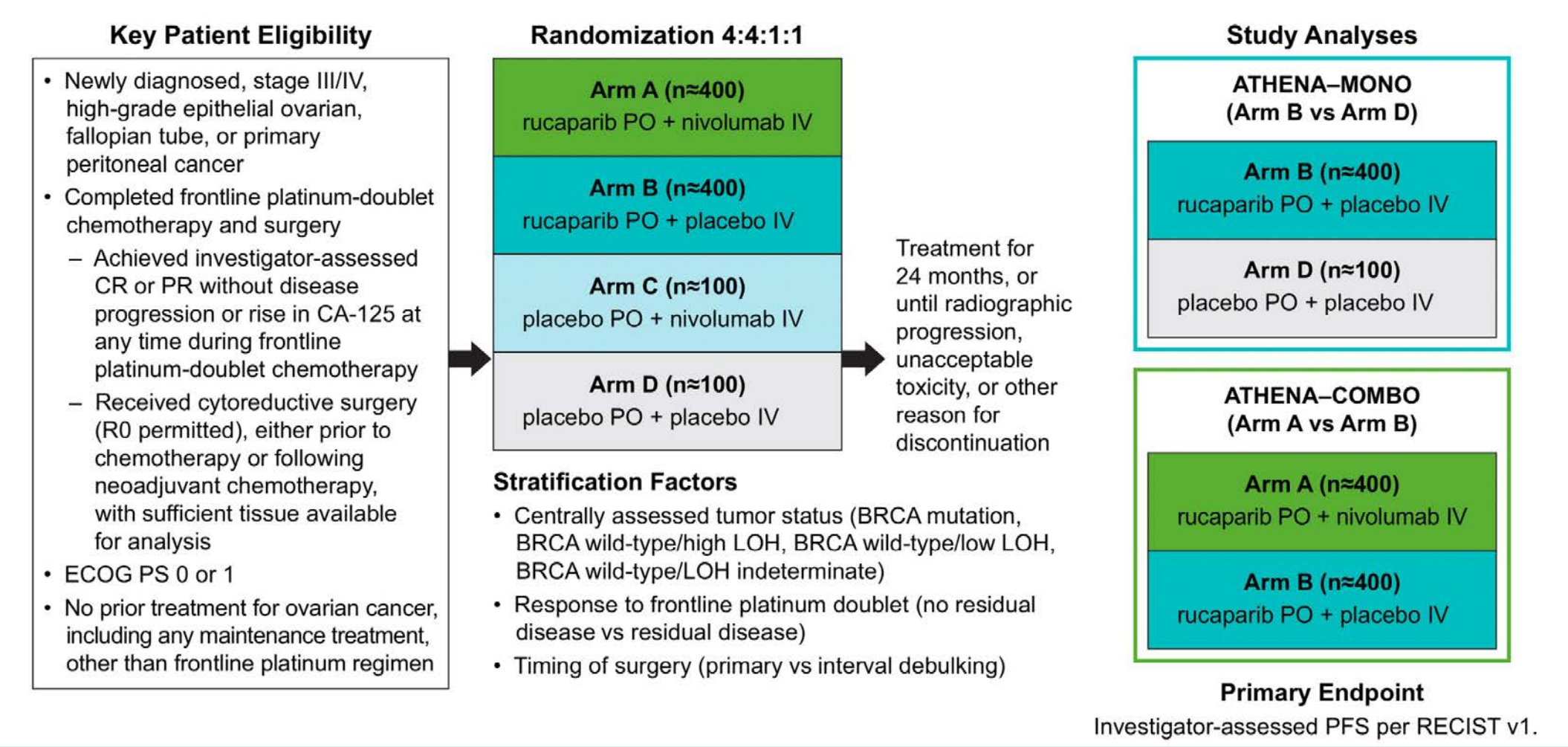
Results from the Phase III ATHENA-MONO trial led to the submission, the results of which were presented at the 2022 ASCO Annual Meeting. In the intent-to-treat (ITT) population, the median progression-free survival (PFS) in the rucaparib group was 20.2 months versus 9.2 months in the placebo arm (HR 0.52, log-rank $p < 0.0001$). Median PFS by blinded independent central radiology review (BICR) was 25.9 months in the rucaparib arm and 9.1 months in the placebo arm (HR 0.47, log-rank $p < 0.0001$).

For patients in the homologous recombination deficiency (HRD) group, the investigator-assessed median PFS was 28.7 months in the rucaparib group vs 11.3 months in the placebo group (HR 0.47, $p = 0.0004$). Additionally, the median PFS by BICR was not reached in the rucaparib group compared to 9.9 months in the placebo group (HR 0.44, $p = 0.0004$).

https://www.cancernetwork.com/view/applications-submitted-to-fda-and-ema-for-maintenance-rucaparib-in-advanced-ovarian-cancer?utm_source=sfmc&utm_medium=email&utm_campaign=09222022_CN_GSK-22-OND0513_Jemperli%20eNL&eKey=cmthZGVybWFuQHJlc2VhcmNodG9wcmFjdGljZS5jb20=

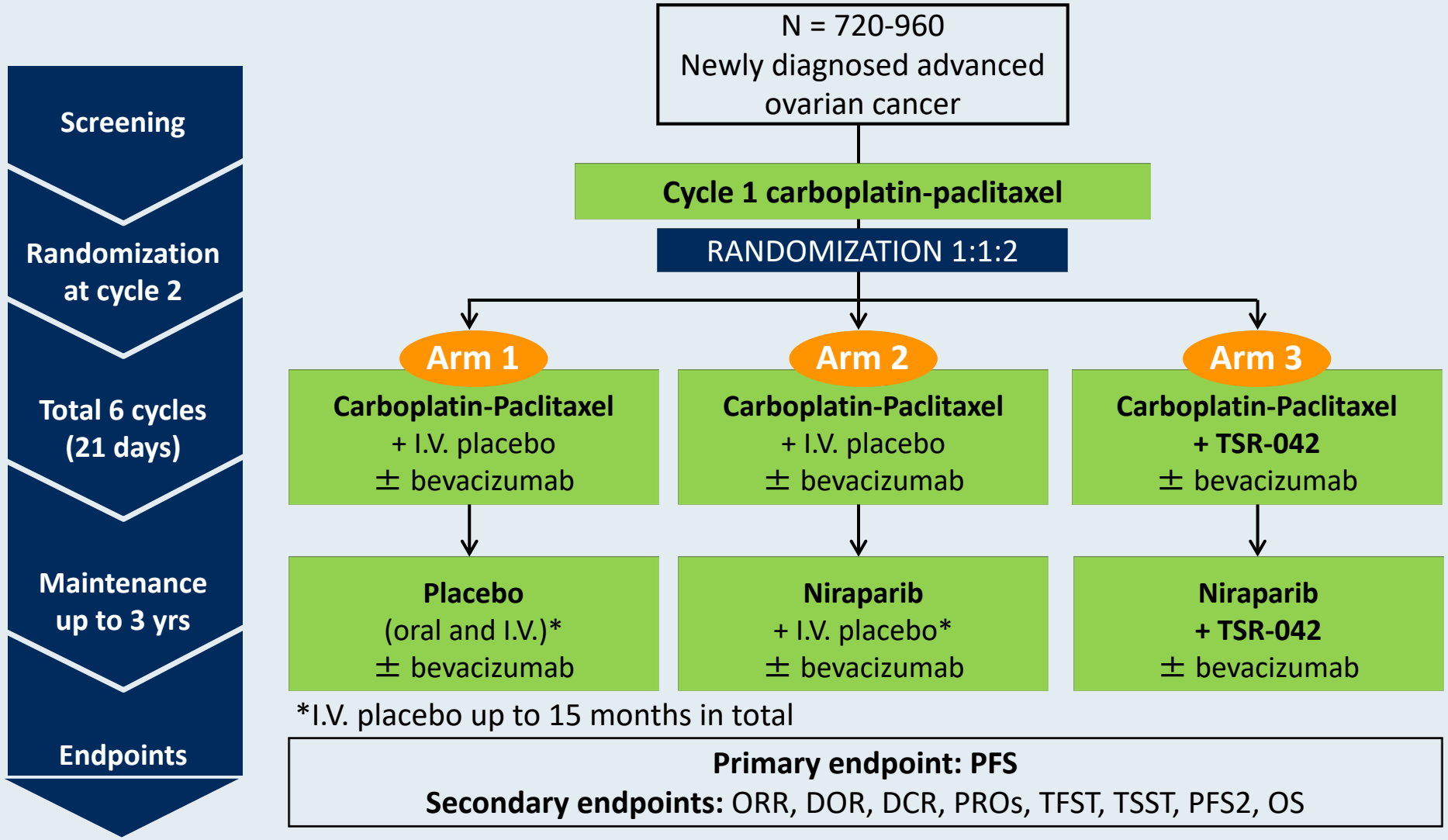
RTP RESEARCH TO PRACTICE

ATHENA-MONO and ATHENA-COMBO Study Design



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

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



www.clinicaltrials.gov/ct2/show/NCT03602859

Courtesy of Ursula Matulonis, MD

Current Treatment Paradigm for Recurrent Disease

Ongoing Research with PARP Inhibitors for Newly Diagnosed and Relapsed Disease

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/

RTP RESEARCH TO PRACTICE

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

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

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

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

	PARPi	Control	HR
NOVA[1-2] — niraparib			
gBRCA mutation	21.0 mo	5.5 mo	0.27
No gBRCA mutation, HRD+	12.9 mo	3.8 mo	0.38
No gBRCA mutation	9.3 mo	3.9 mo	0.45
SOLO-2[3-4] — olaparib			
gBRCA mutation	19.1 mo	5.5 mo	0.30
Overall survival	51.7 mo	38.8 mo	0.74
ARIEL3[5-6] — rucaparib			
ITT (all comers)	10.8 mo	5.4 mo	0.36
g or sBRCA mutation	16.6 mo	5.4 mo	0.23
HRD+	13.6 mo	5.4 mo	0.32
$BRCA^{WT}$/high LOH	13.6 mo	5.4 mo	0.32
$BRCA^{WT}$/low LOH	6.7 mo	5.4 mo	0.58

[1] Mirza MR et al. *N Engl J Med* 2016;375(22):2154-64; [2] Del Campo JM et al. *J Clin Oncol* 2019;37(32):2968-73. [3] Poveda A et al. *Lancet Oncol* 2021;22(5):620-31. [4] Pujade-Lauraine E et al. *Lancet* 2017;18(9):1274-84; [5] Coleman RL et al. *Lancet* 2017;390(10106):1949-61; [6] Ledermann JA et al. *Lancet Oncol* 2020;21(5):710-22.

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

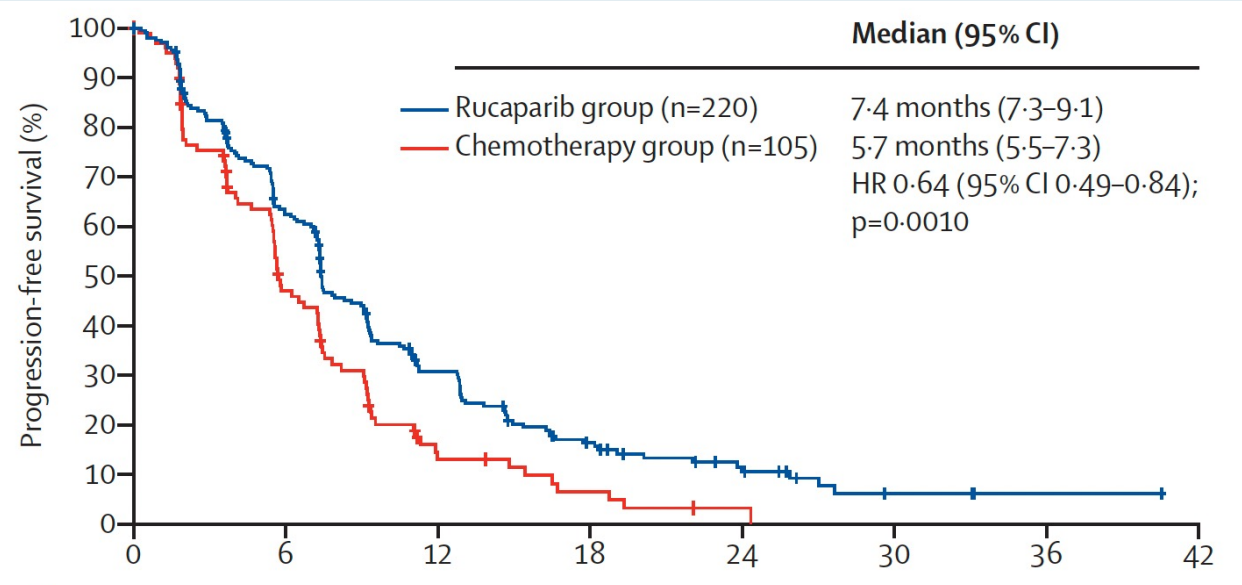
Articles

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

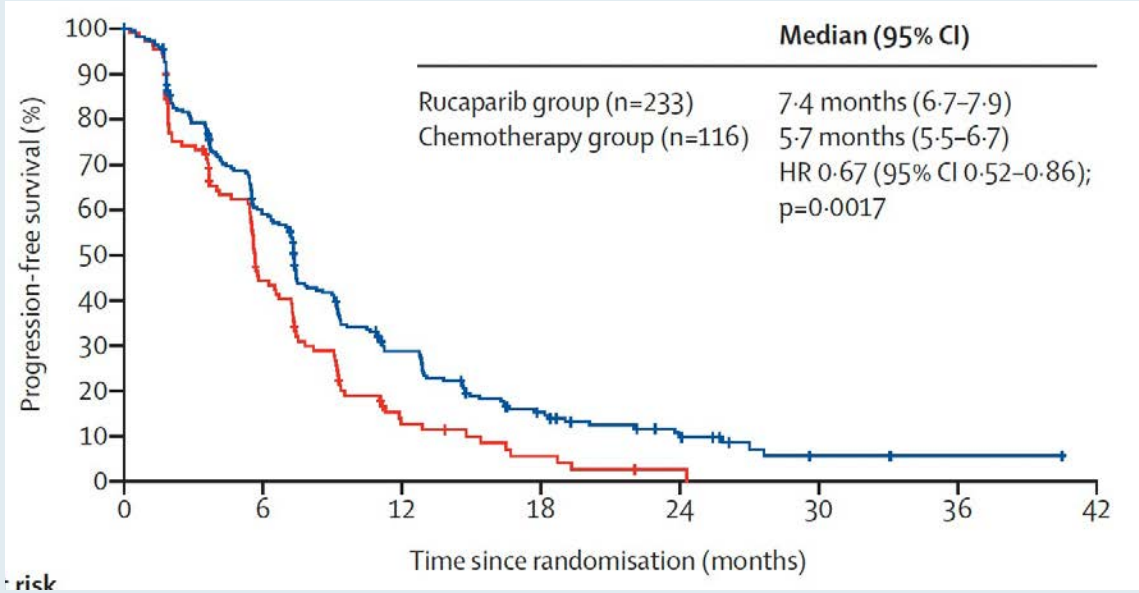
Rebecca Kristeleit, Alla Lisyanskaya, Alexander Fedenko, Mikhail Dvorkin, Andreia Cristina de Melo, Yaroslav Shparyk, Irina Rakhmatullina, Igor Bondarenko, Nicoletta Colombo, Valentyn Svintsitskiy, Luciano Biela, Marina Nechaeva, Domenica Lorusso, Giovanni Scambia, David Cibula, Róbert Póka, Ana Oaknin,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

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

Efficacy population (BRCA1 or BRCA2 mutations with reversion mutations)



Intent to treat population



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

RTP RESEARCH TO PRACTICE

ARIEL4: Overall Response Rate and Duration of Response

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

ORR = overall response rate; DoR = duration of response

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

PARIS 2022 ESMO congress

Abstract 518O

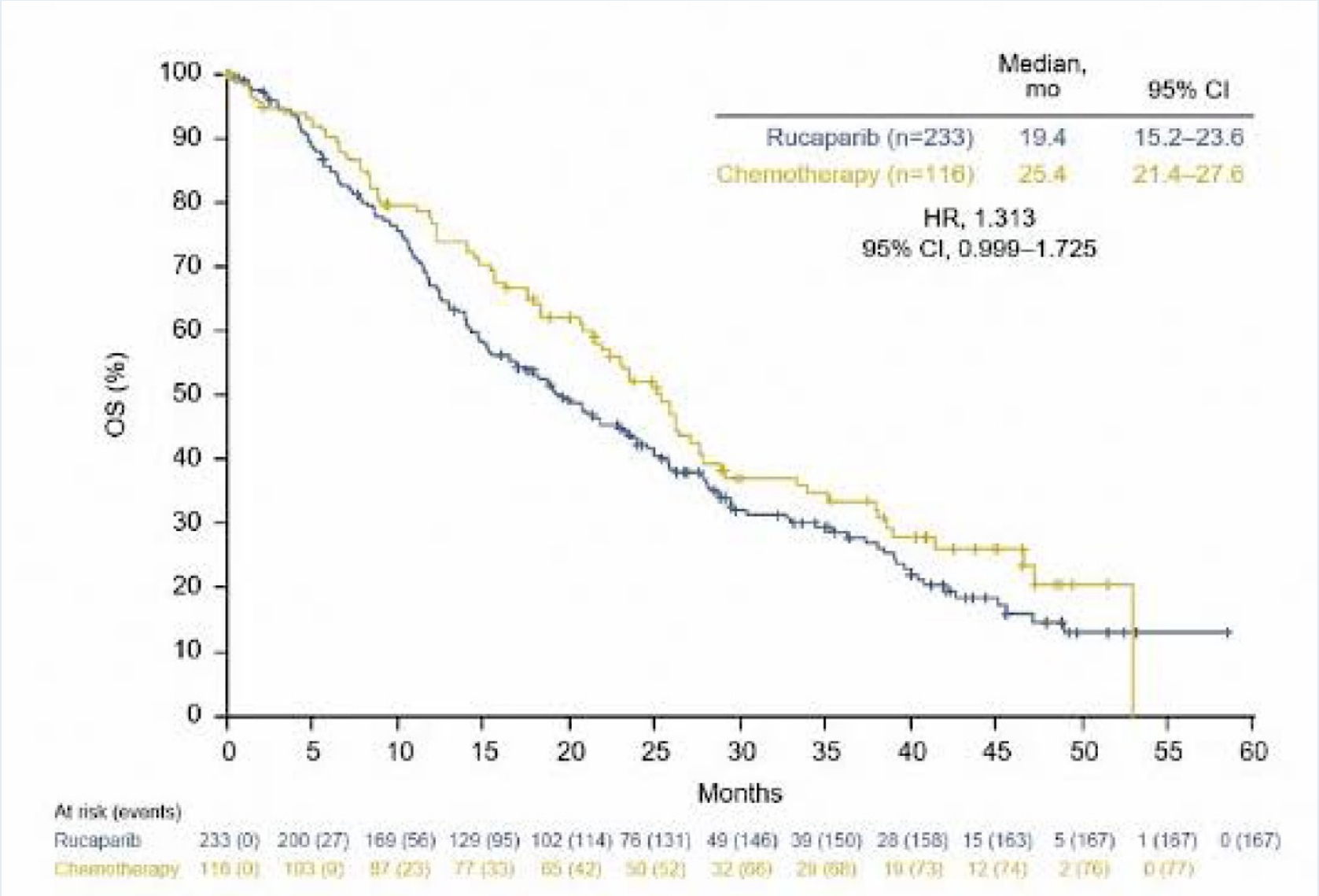
Overall Survival Results From ARIEL4: A Phase 3 Study Assessing Rucaparib vs Chemotherapy in Patients With Advanced, Relapsed Ovarian Carcinoma and a Deleterious *BRCA1/2* Mutation

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 Mańkowiak-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

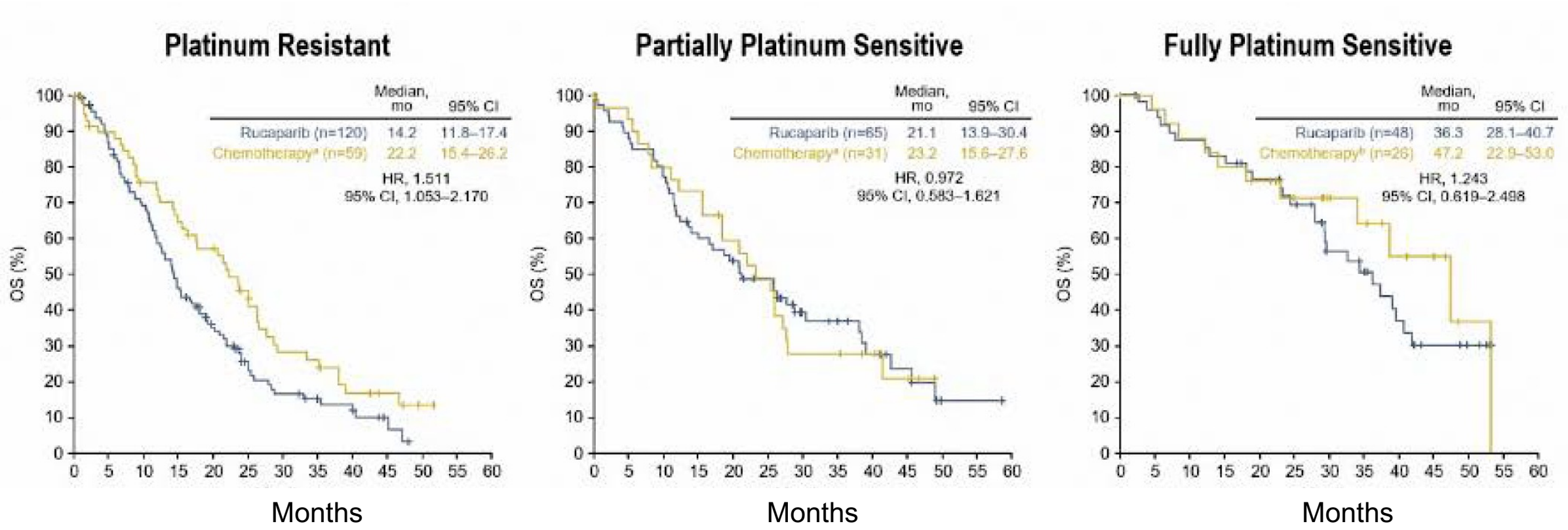
RTP RESEARCH TO PRACTICE

ARIEL4: Overall Survival



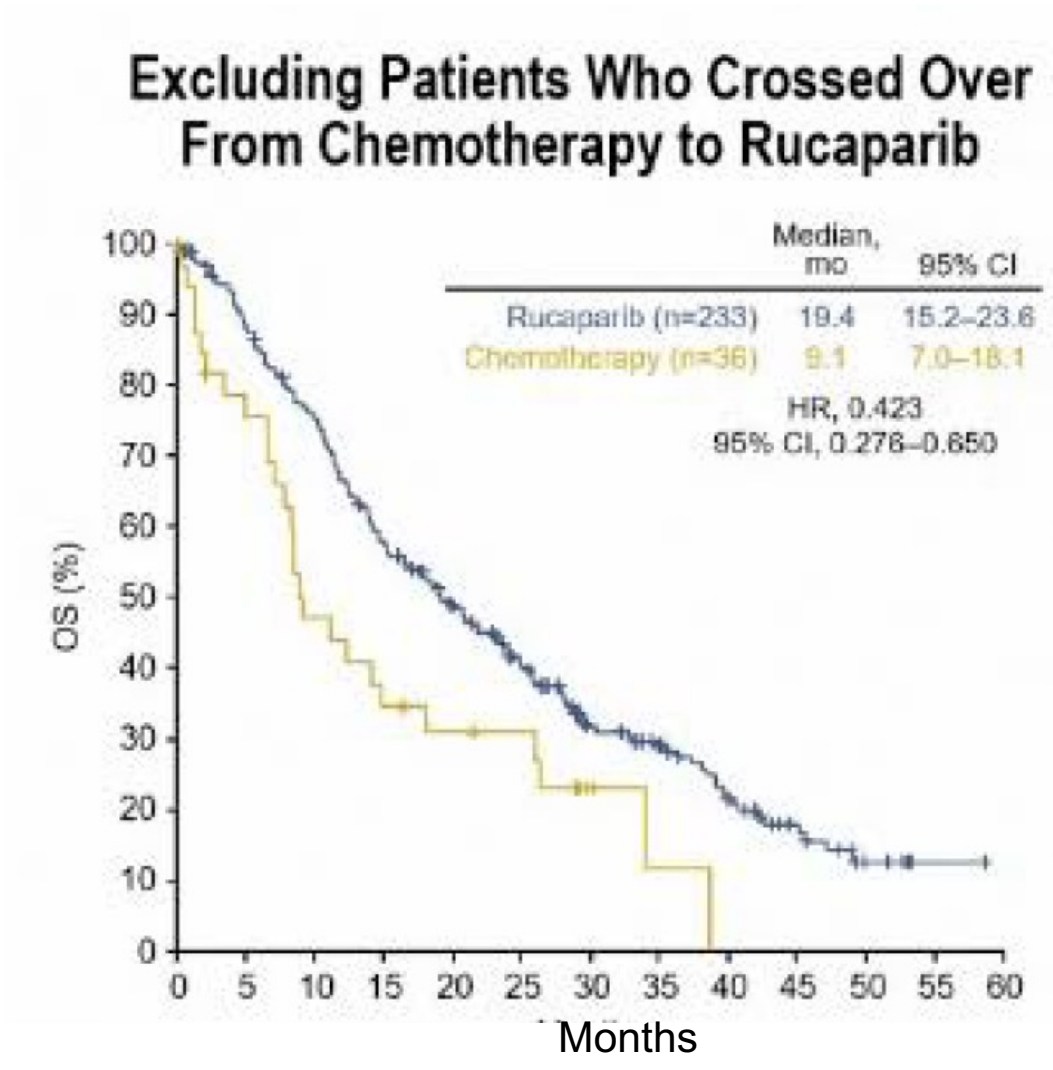
Oza AM et al. ESMO 2022;Abstract 518O.

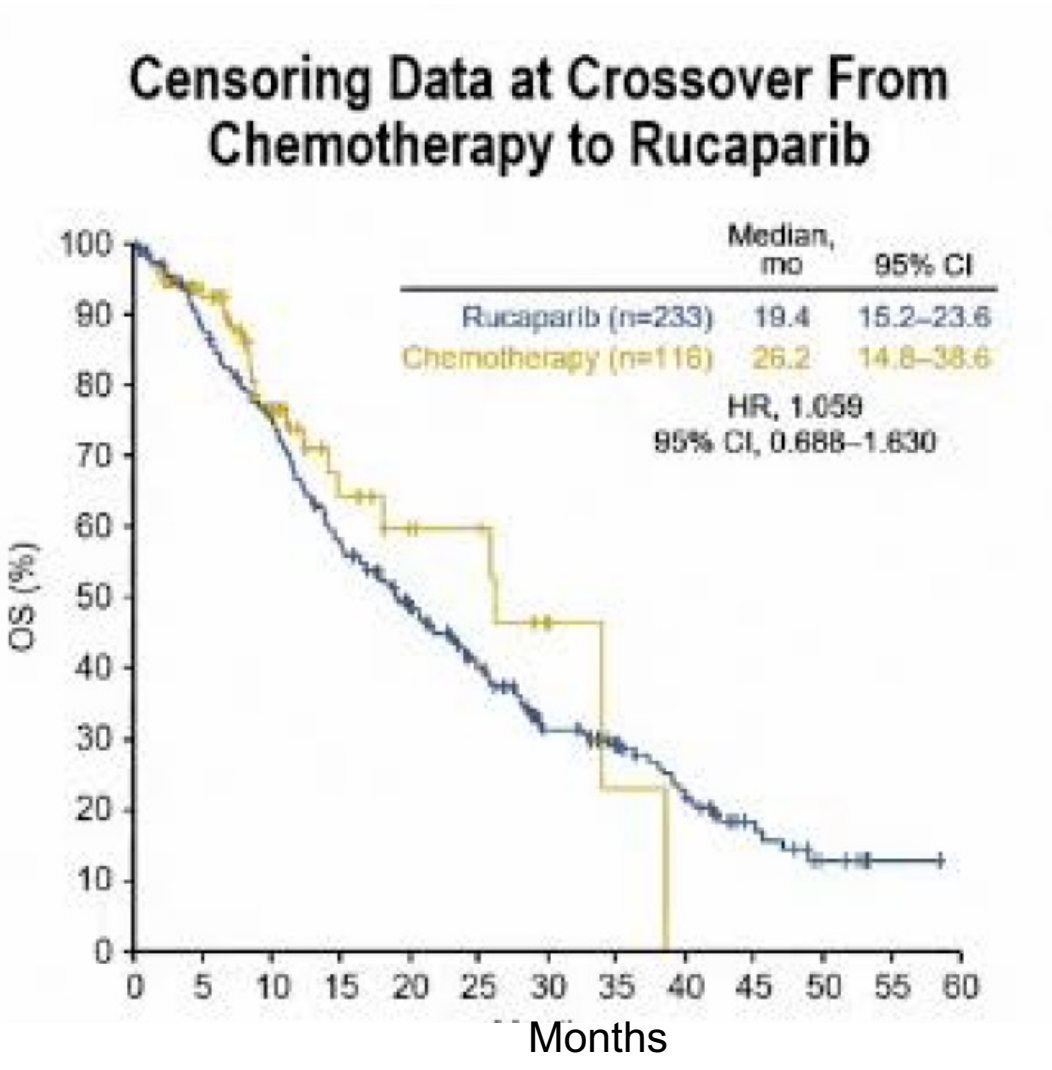
ARIEL4: Overall Survival by Platinum Status



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

ARIEL4: Overall Survival (ITT) Adjustments for Crossover





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

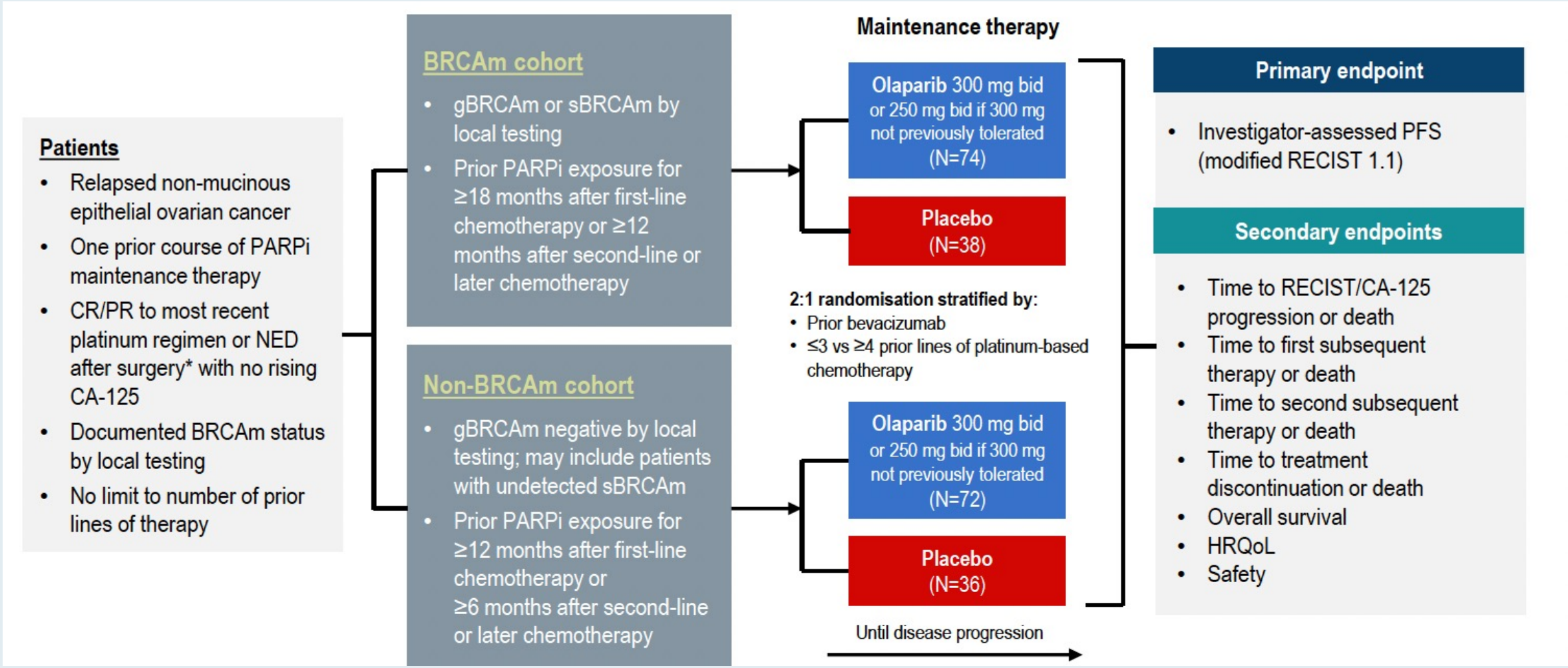
2021 ESMO congress

Abstract LBA33

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

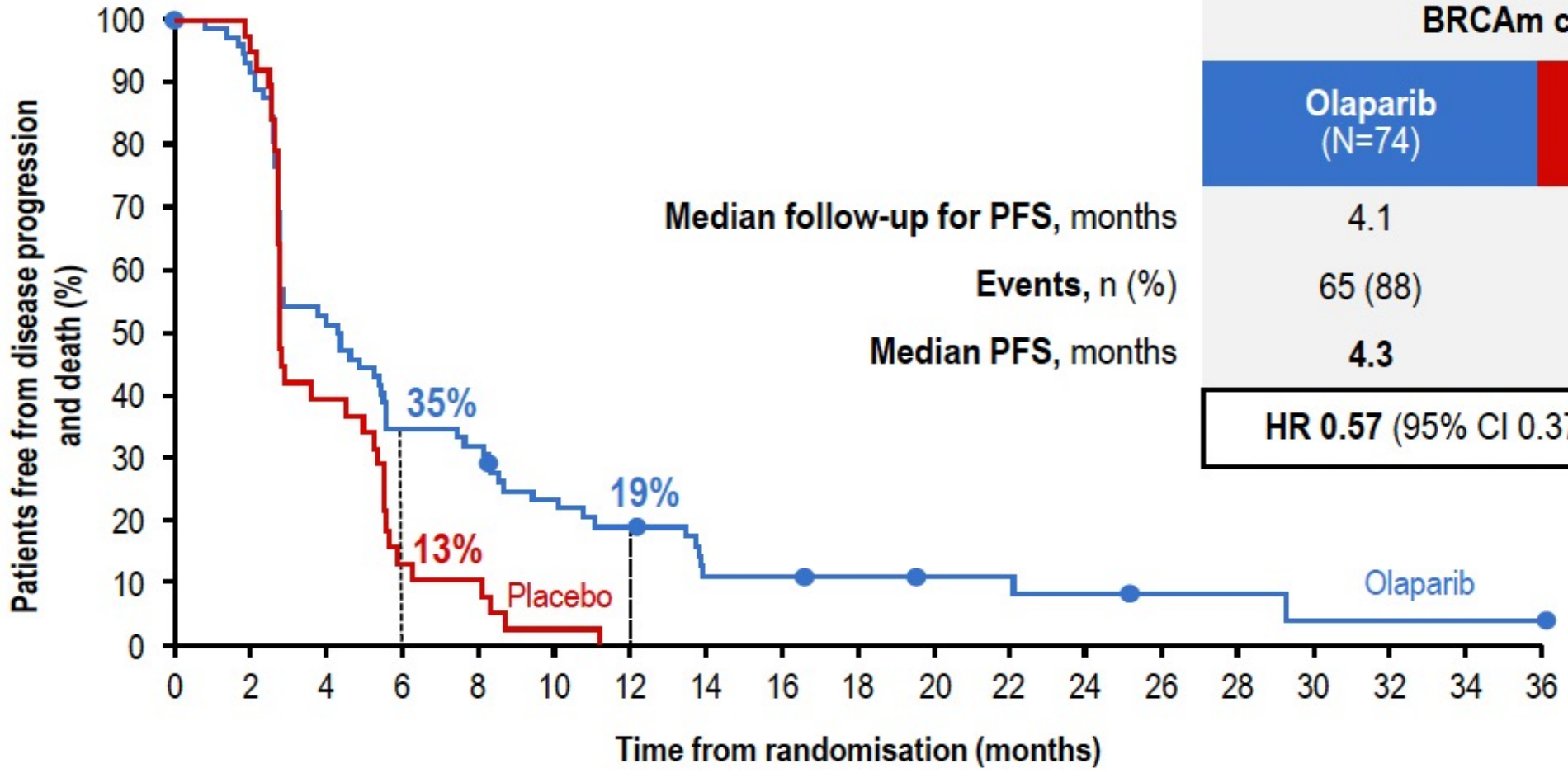
Eric Pujade-Lauraine,[1] Frédéric Selle,[2] Giovanni Scambia,[3] Bernard Asselain,[4] Frederik Marmé,[5] Kristina Lindemann,[6] Nicoletta Colombo,[7] Radoslaw Madry,[8] Rosalind Glasspool,[9] Coraline Dubot,[10] Ana Oaknin,[11] Claudio Zamagni,[12] Florian Heitz,[13] Laurence Gladieff,[14] Maria Jesús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

OReO Phase IIIB Study Schema



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

OReO: Progression-Free Survival in the BRCAm Cohort

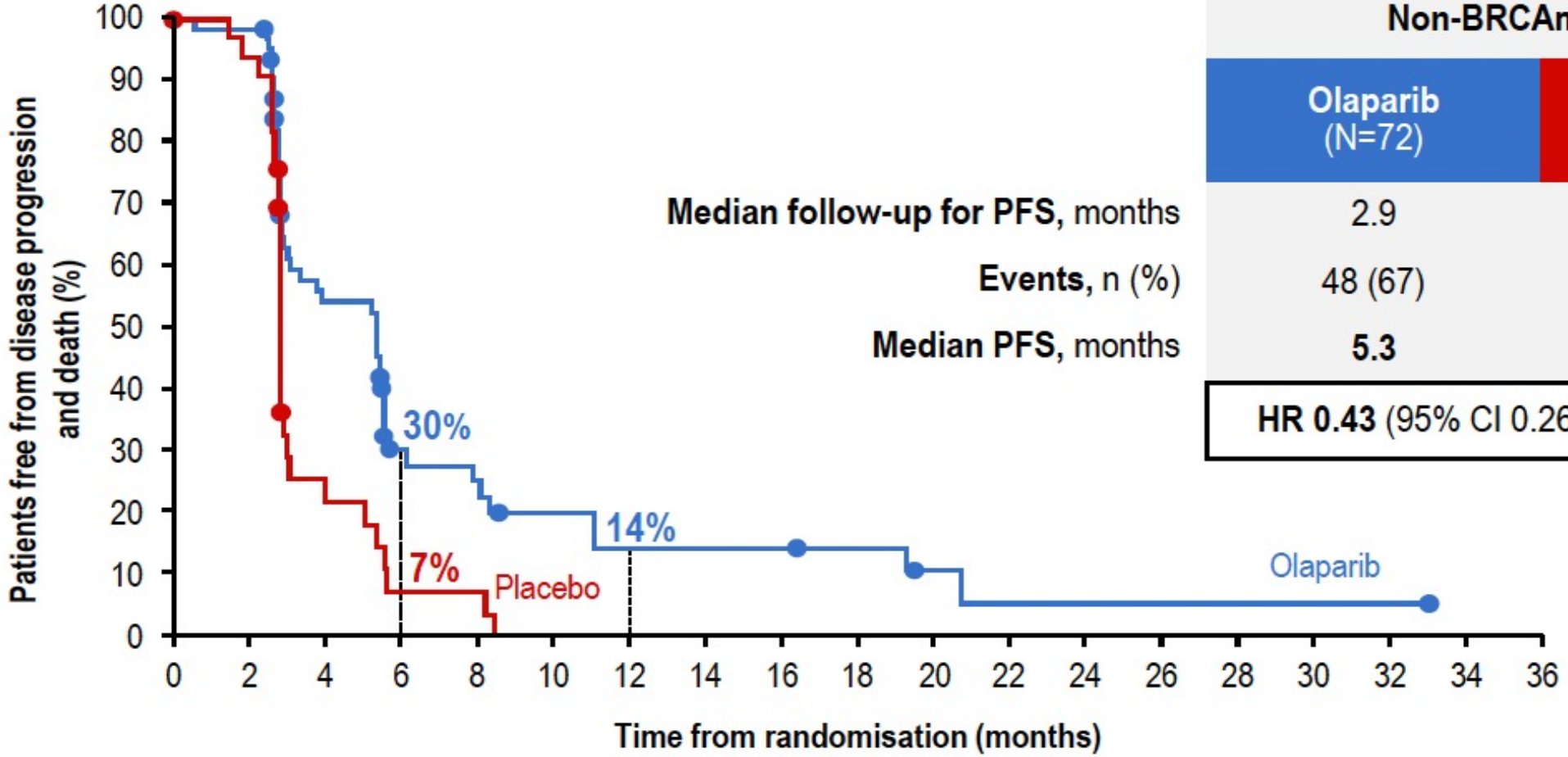


BRCAm cohort	Olaparib (N=74)	Placebo (N=38)
Median follow-up for PFS, months	4.1	2.8
Events, n (%)	65 (88)	38 (100)
Median PFS, months	**4.3**	**2.8**

HR 0.57 (95% CI 0.37–0.87); *P*=0.022

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

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

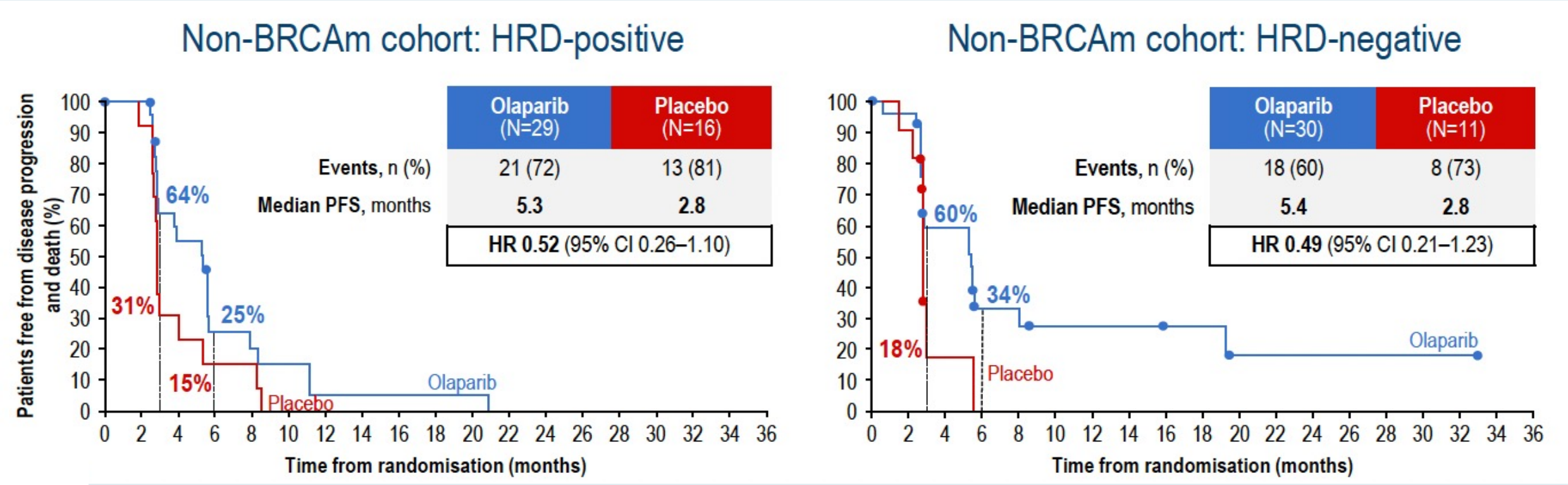


Non-BRCAm cohort	Olaparib (N=72)	Placebo (N=36)
Median follow-up for PFS, months	2.9	2.8
Events, n (%)	48 (67)	30 (83)
Median PFS, months	**5.3**	**2.8**

HR 0.43 (95% CI 0.26–0.71); *P*=0.0023

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

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



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

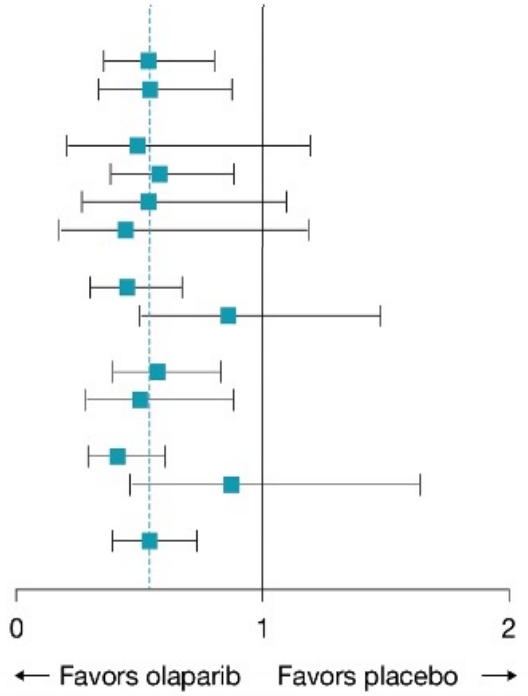
OReO/ENGOT Ov-38 Trial: Impact of Maintenance Olaparib Rechallenge According to Ovarian Cancer Patient Prognosis — An Exploratory Joint Analysis of the BRCA and Non-BRCA Cohorts

Selle F et al.

ASCO 2022;Abstract 5558.

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

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



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

Selle F et al. ASCO 2022;Abstract 5558.

RTP RESEARCH TO PRACTICE

Research

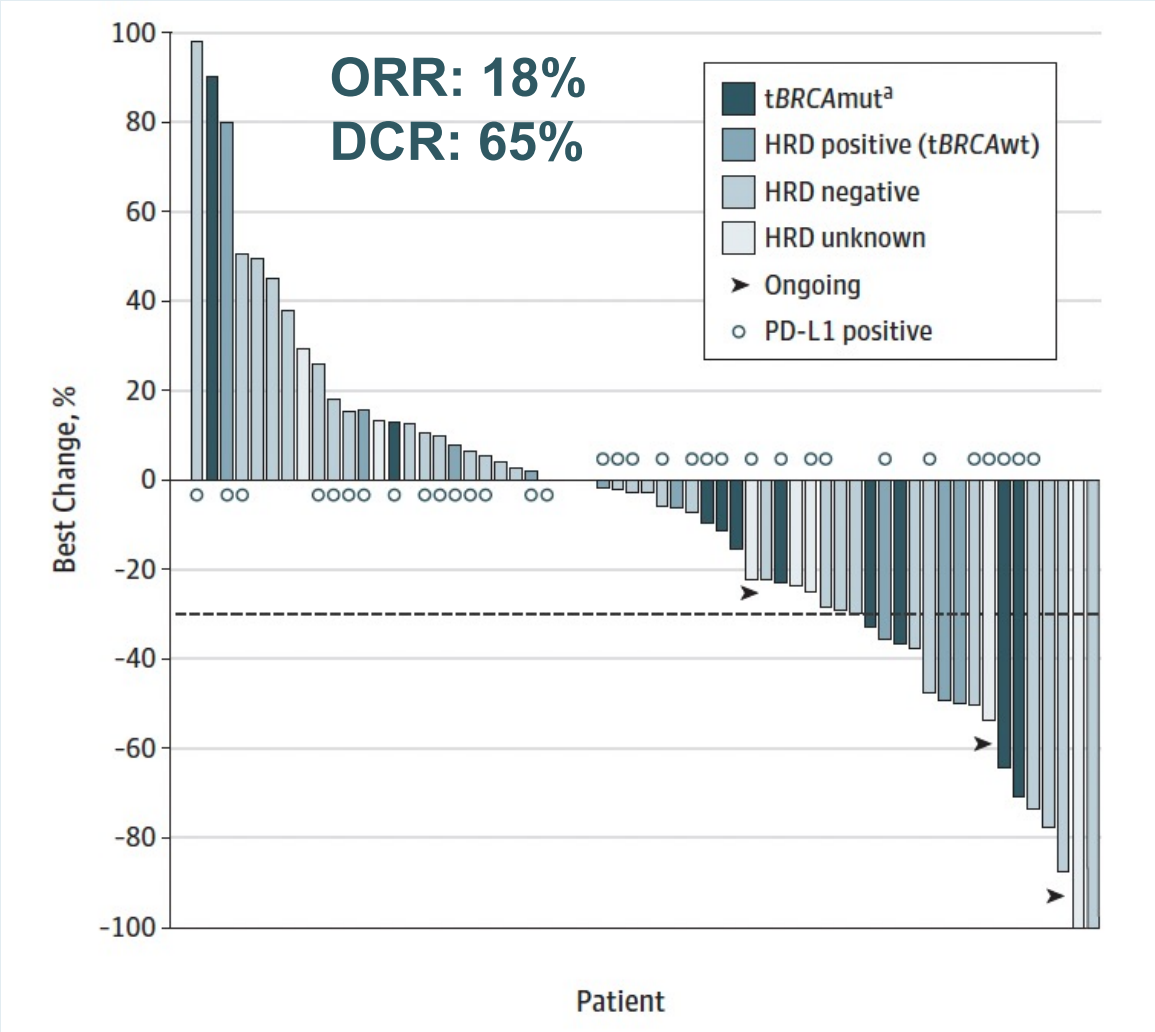
JAMA Oncol 2019;5(8):1141-9.

JAMA Oncology | Original Investigation

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

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

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



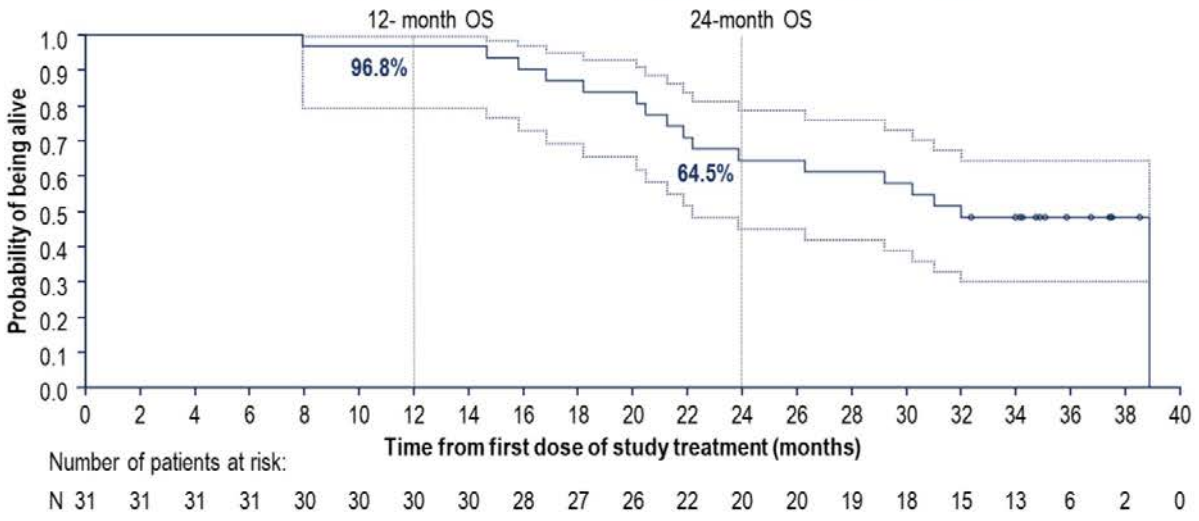
ORR = overall response rate; DCR = disease control rate

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

RTP RESEARCH TO PRACTICE

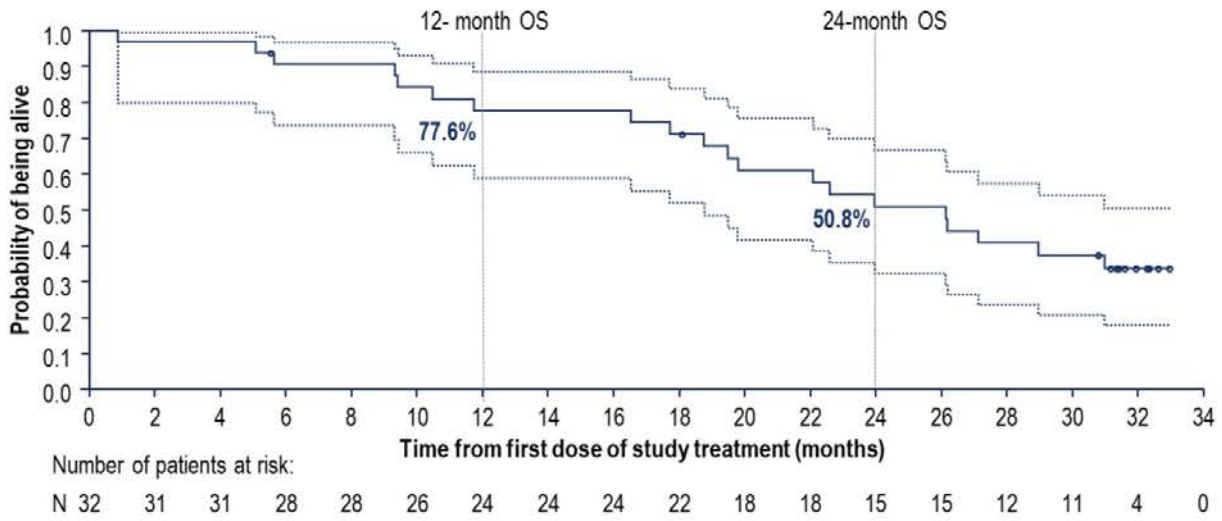
MEDIOLA Final Analysis: Median OS and 56-Week DCR

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



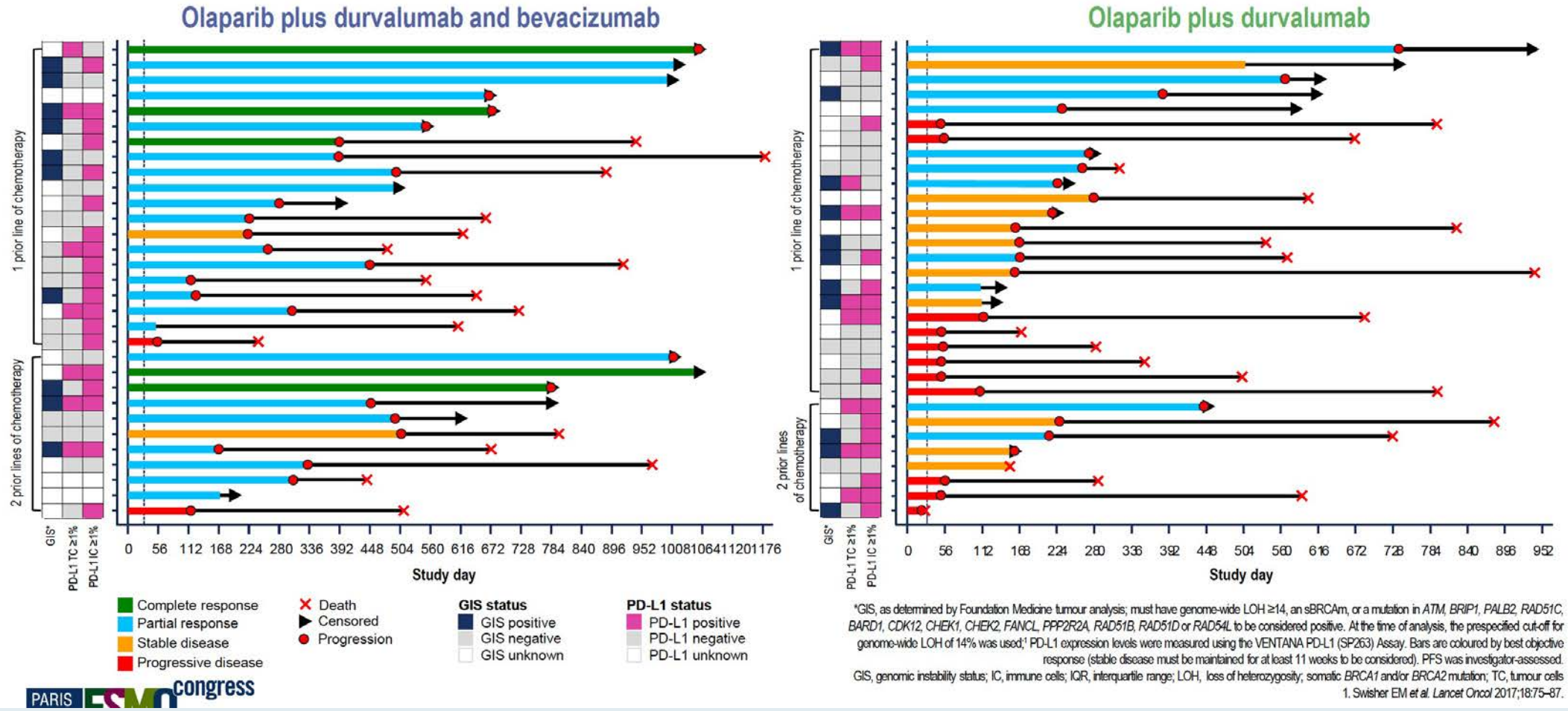
	Olaparib plus durvalumab
Median follow-up for OS, months	23.2
Events, n	20
Median OS (95% CI), months	**26.1 (18.7–NC)**
56-week DCR (90% CI), %	9.4 (2.6–22.5)

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

RTP RESEARCH TO PRACTICE

MEDIOLA Final Analysis: Individual Patient Outcomes of Response, OS and PFS by Line of Therapy, Genomic Instability Status and PD-L1 Status

- Small event numbers and unknown biomarker status limit interpretation based on GIS and PD-L1 status; further investigation is warranted



*GIS, as determined by Foundation Medicine tumour analysis; must have genome-wide LOH ≥14, an sBRCAm, or a mutation in *ATM, BRIP1, PALB2, RAD51C, BARD1, CDK12, CHEK1, CHEK2, FANCL, PPP2R2A, RAD51B, RAD51D* or *RAD54L* to be considered positive. At the time of analysis, the prespecified cut-off for genome-wide LOH of 14% was used;[1] PD-L1 expression levels were measured using the VENTANA PD-L1 (SP263) Assay. Bars are coloured by best objective response (stable disease must be maintained for at least 11 weeks to be considered). PFS was investigator-assessed.

GIS, genomic instability status; IC, immune cells; IQR, interquartile range; LOH, loss of heterozygosity; somatic *BRCA1* and/or *BRCA2* mutation; TC, tumour cells

1. Swisher EM *et al. Lancet Oncol* 2017;18:75–87.

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

MEDIOLA Final Analysis: Safety Profiles

	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.

MEDIOLA Final Analysis: Conclusions

- Olaparib plus durvalumab and bevacizumab demonstrated encouraging clinical activity in women with non-gBRCAm PSR OC
  - Median OS: 31.9 months (26.1 months in doublet cohort)
  - 56-week DCR: 38.7% (9.4% in doublet cohort)
- Findings warrant further investigation of the triplet combination as a non-chemotherapy treatment for non-gBRCAm ovarian cancer
- Previous exploratory analyses showed a high ORR in the triplet cohort and suggested that this was not driven by differences in GIS.[1] Review of PFS and OS outcomes did not identify any clear relationship based on GIS or PD-L1 in this limited dataset. Further investigations are warranted
- The safety profile of olaparib plus durvalumab, with or without bevacizumab, was consistent with that expected for the single agents and no new safety signals emerged with longer follow-up
- Olaparib plus durvalumab and bevacizumab is under investigation as first-line maintenance treatment in patients with non-BRCAm advanced ovarian cancer in the Phase III DUO-O/ENGOT-ov46/GOG-3025 study (NCT03737643)

PSR = platinum-sensitive relapsed

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

BARCELONA 2019 ESMO congress

Poster board number: 1190PD

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

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

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

esmo.org

MEDIOLA mBRCA Cohort Study Schema

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

N=34*

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

Olaparib monotherapy 300 mg bid PO for 4 weeks

then

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

Treatment until disease progression or intolerable toxicity

Primary endpoints

- Disease control rate at 12 weeks
- Safety and tolerability

Secondary endpoints

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

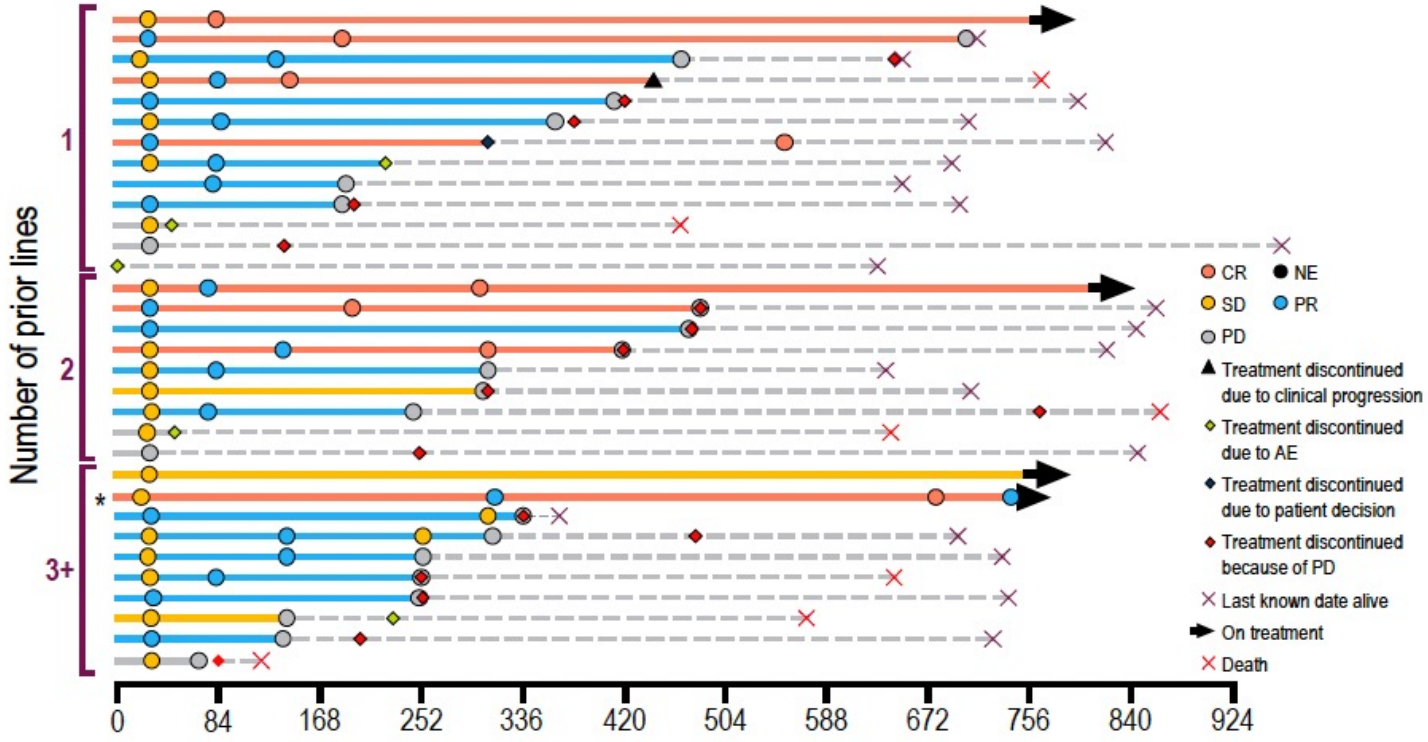
Drew Y et al. ESMO 2019;Abstract 1190PD.

MEDIOLA mBRCA Cohort: Efficacy

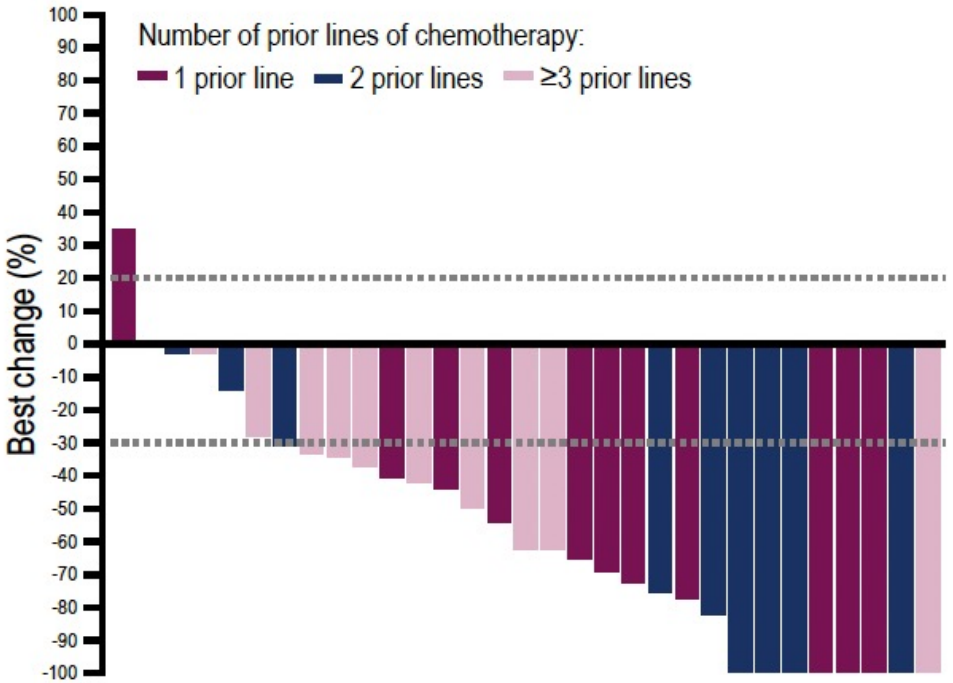
- DCR at 12 weeks: 81.3% (90% CI 66.3, 91.5)
- DCR at 28 weeks: 65.6% (90% CI 49.6, 79.4)
- Unconfirmed ORR: 71.9% (95% CI 53.3, 86.3)
- mPFS: 11.1 months (95% CI 8.2, 15.6)

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

Time to progression or treatment discontinuation



Best percentage change in target lesion size†



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

RTP RESEARCH TO PRACTICE

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

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

Randall LM et al. ASCO 2022;Abstract 5573.

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

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

Poster #23

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

SGO 2021 VIRTUAL ANNUAL MEETING ON WOMEN'S CANCER®

Abstract 10415

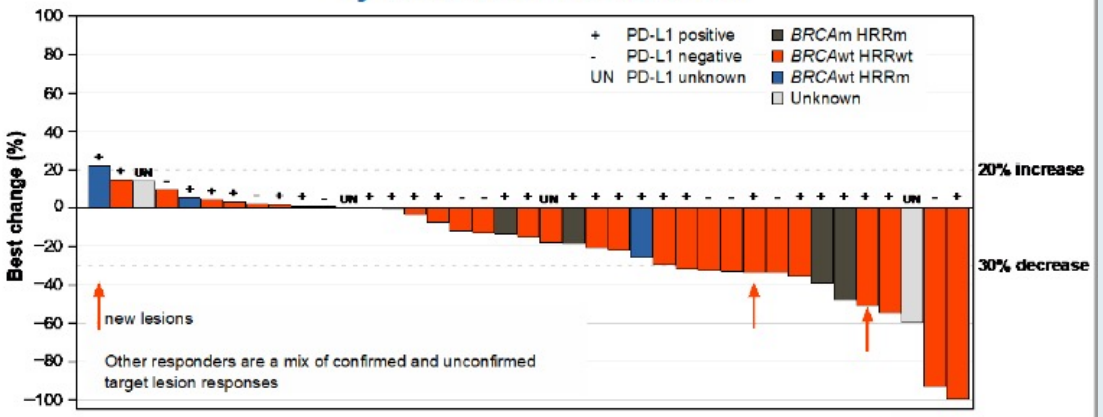
SGO Society of Gynecologic Oncology

Antitumor Activity

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

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

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



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

SGO 2021 VIRTUAL ANNUAL MEETING ON WOMEN'S CANCER®

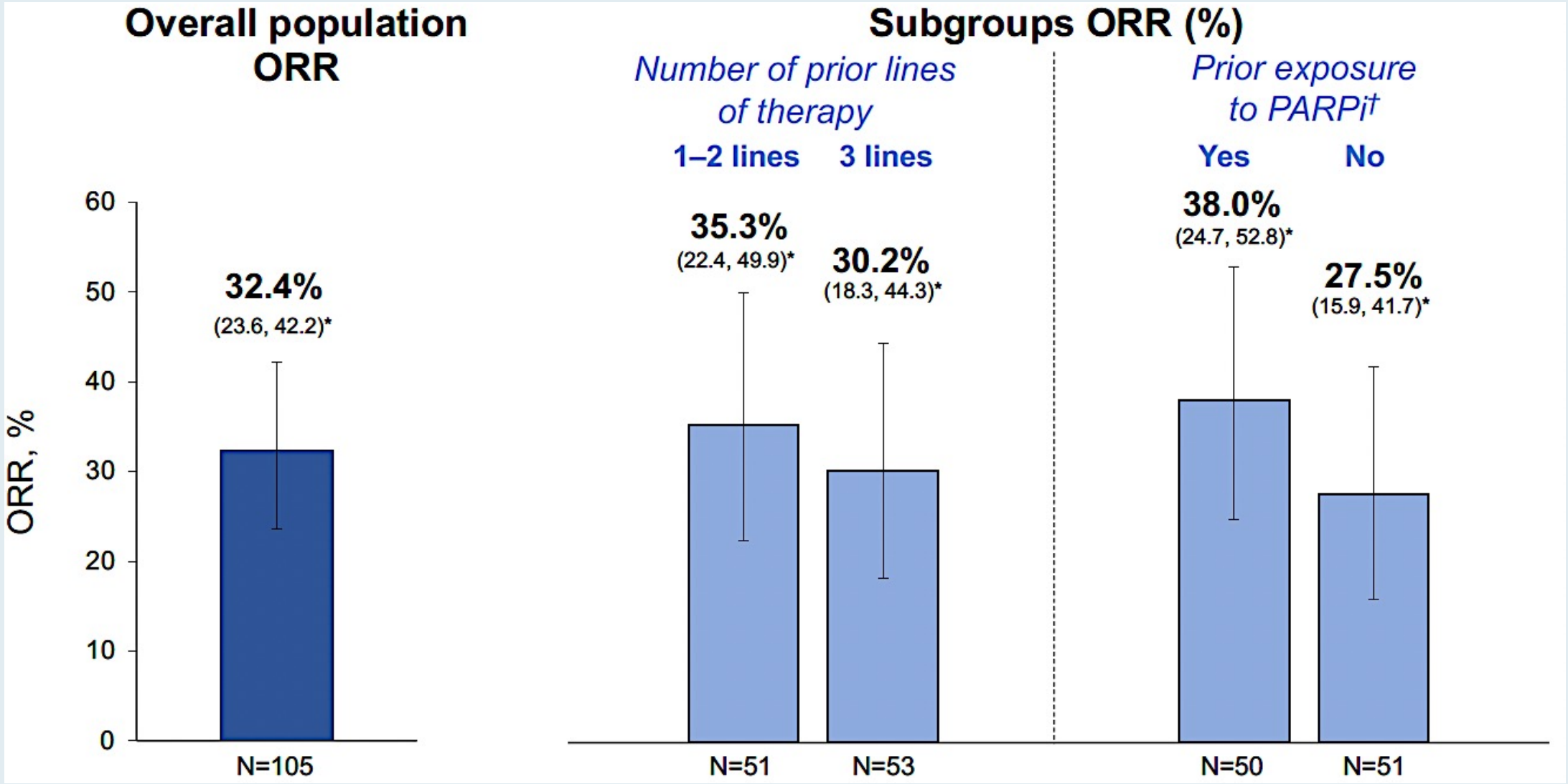
Society of Gynecologic Oncology

Liu JF et al. SGO 2021;Abstract 10415.

RTP RESEARCH TO PRACTICE

Novel Investigational Agents and Strategies

SORAYA: Investigator-Assessed Objective Response Rate by Prior Therapy



Matulonis UA et al. SGO 2022;Abstract LBA4.

RTP RESEARCH TO PRACTICE

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

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

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

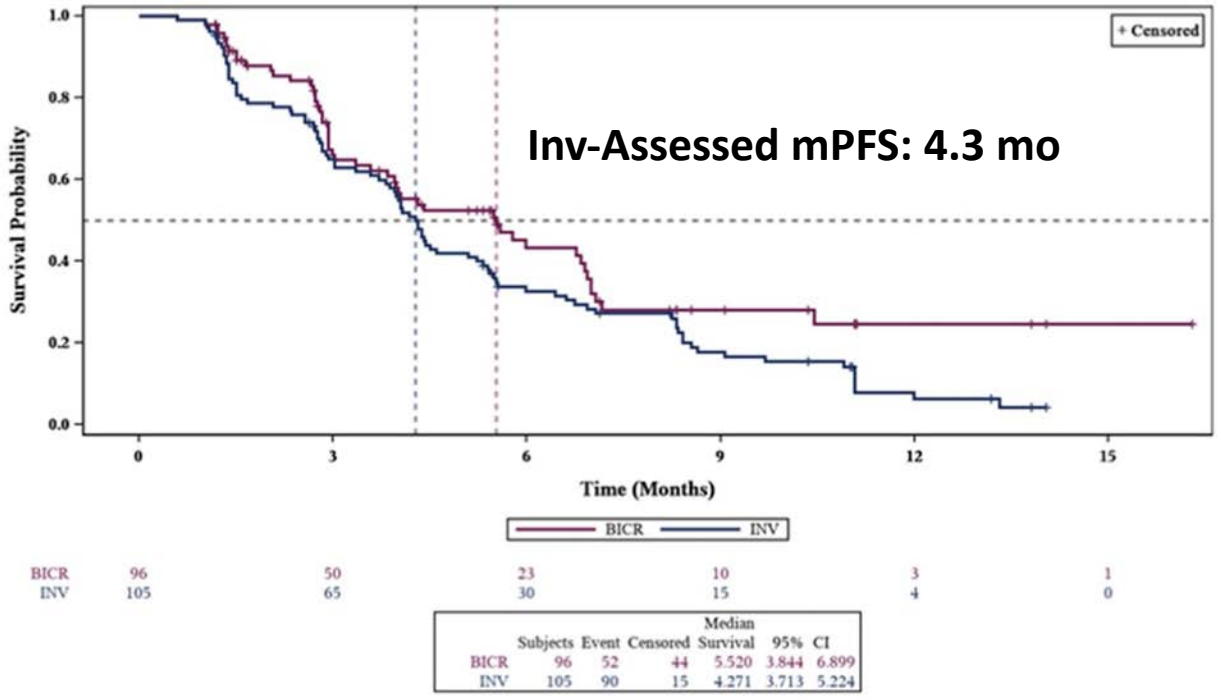
Matulonis UA et al. SGO 2022;Abstract LBA4.

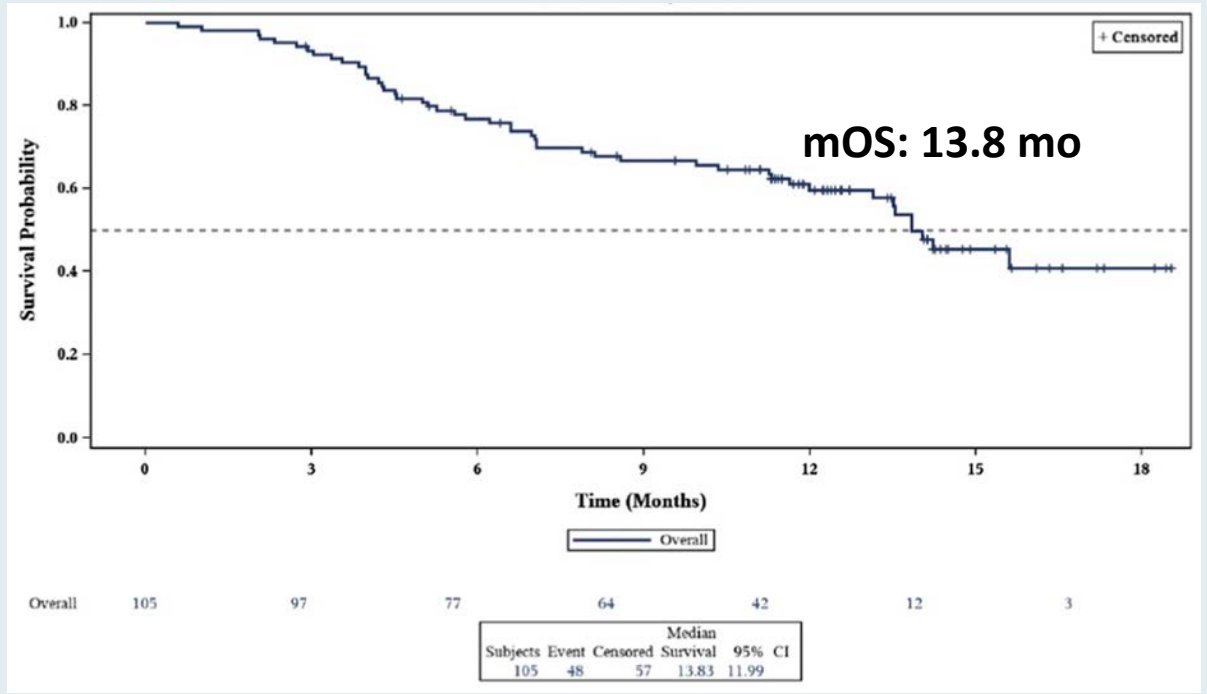
Mirvetuximab Soravtansine (MIRV) in Patients with Platinum-Resistant Ovarian Cancer with High Folate Receptor Alpha (FRα) Expression: Characterization of Antitumor Activity in the SORAYA Study

Matulonis UA et al.

ASCO 2022;Abstract 5512.

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





Matulonis UA et al. ASCO 2022;Abstract 5512.

RTP RESEARCH TO PRACTICE

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

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

Matulonis UA et al. ASCO 2022;Abstract 5512.

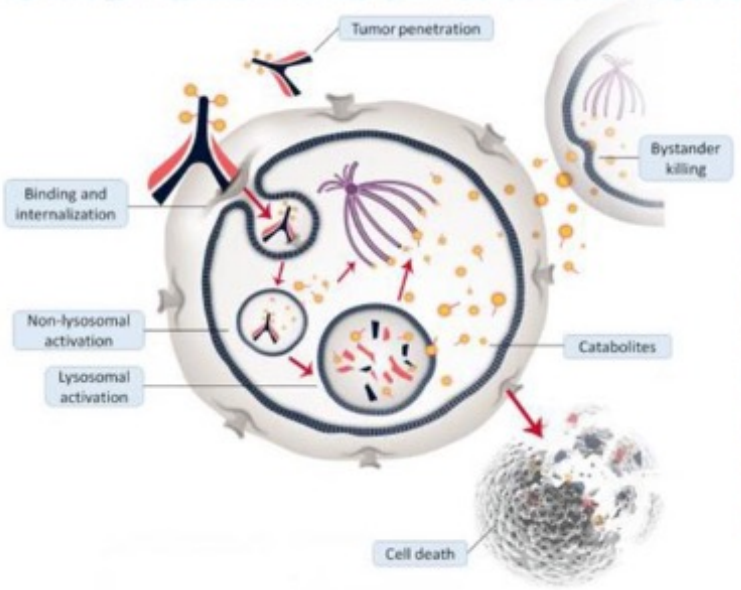
2021 ASCO ANNUAL MEETING

Abstract 5504

Mirvetuximab Soravtansine, a folate receptor alpha-targeting antibody drug conjugate, in combination with bevacizumab in patients with platinum-agnostic ovarian cancer: final analysis

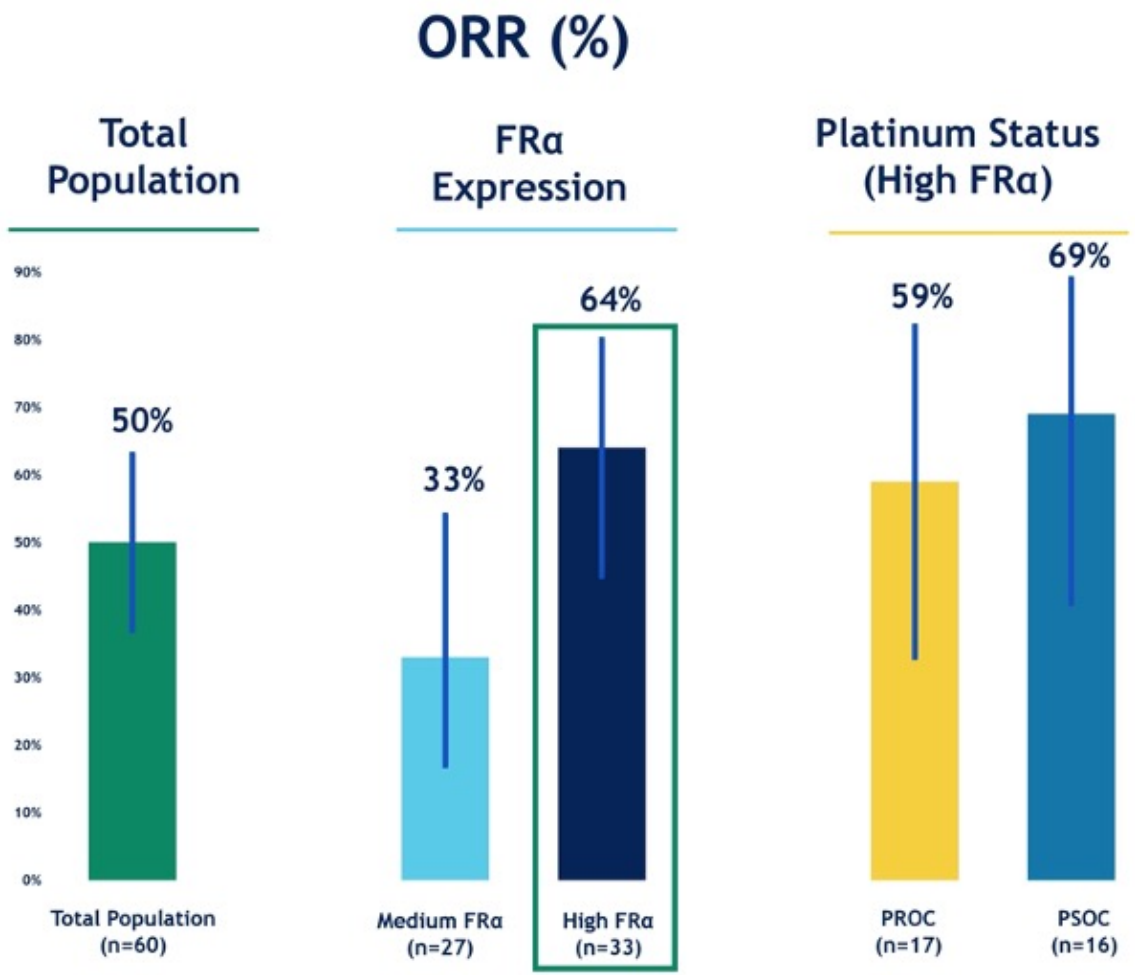
David M. O'Malley[1], Ana Oaknin[2], Ursula A. Matulonis[3], Gina M. Mantia-Smaldone[4], Peter Lim[5], Cesar Castro[6], Diane Provencher[7], Sanaz Memarzadeh[8], Patrick Zweidler-McKay[9], Jiuzhou Wang[9], Brooke Esteves[9], Kathleen N. Moore[10] Lucy Gilbert[11]

[1]Ohio State University, Columbus, OH; [2]Vall D´Hebron University Hospital, Vall D'Hebron Institute of Oncology (VHIO), Barcelona, Spain; [3]Dana Farber Cancer Institute, Boston, MA; [4]Fox Chase Cancer Center, Philadelphia, PA; [5]The Center of Hope Renown Regional Medical Center, Reno, NV; [6]Massachusetts General Hospital, Boston, MA; [7]Institute du Cancer de Montreal, Montreal, Canada; [8]Ronald Reagan UCLA Medical Center UCLA Medical Center, Santa Monica; [9]ImmunoGen, Inc., Waltham, MA; [10]University of Oklahoma Health Sciences Center, Oklahoma City, OK/Sarah Cannon Research Institute, Nashville, TN; [11]McGill University Health Center-RI, Montreal, Canada



RTP RESEARCH TO PRACTICE

Confirmed ORR by FRα Expression and Platinum Status

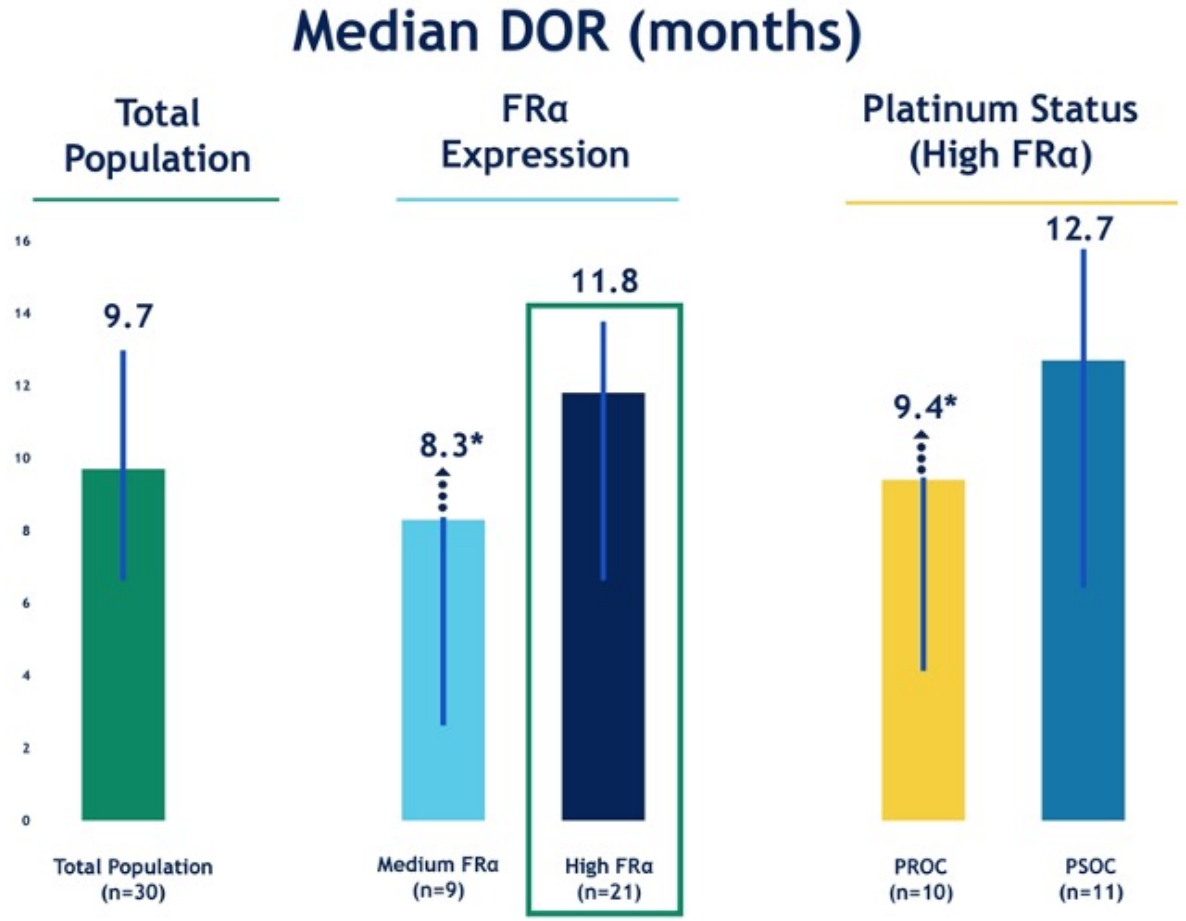


- **50% ORR** (30/60) for overall cohort
- **64% ORR** (21/33) in high FRα tumors
  - **59% ORR** (10/17) in PROC subset
  - **69% ORR** (11/16) in PSOC subset

ORR = overall response rate; PROC = platinum-resistant ovarian cancer; PSOC = platinum-sensitive ovarian cancer

O'Malley DM et al. ASCO 2021;Abstract 5504.

Median Duration of Response (mDOR) by FRα Expression and Platinum Status



- **9.7 mo mDOR** for overall cohort
- **11.8 mo mDOR** in high FRα tumors
  - **9.4 mo mDOR** in PROC subset
  - **12.7 mo mDOR** in PSOC subset

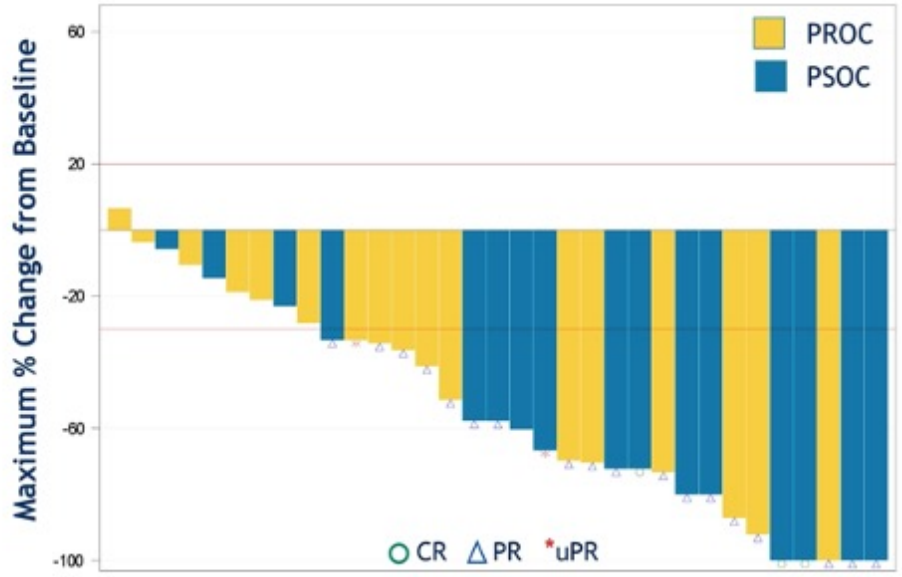
*Upper limit of 95% confidence interval not reached

O'Malley DM et al. ASCO 2021;Abstract 5504.

RTP RESEARCH TO PRACTICE

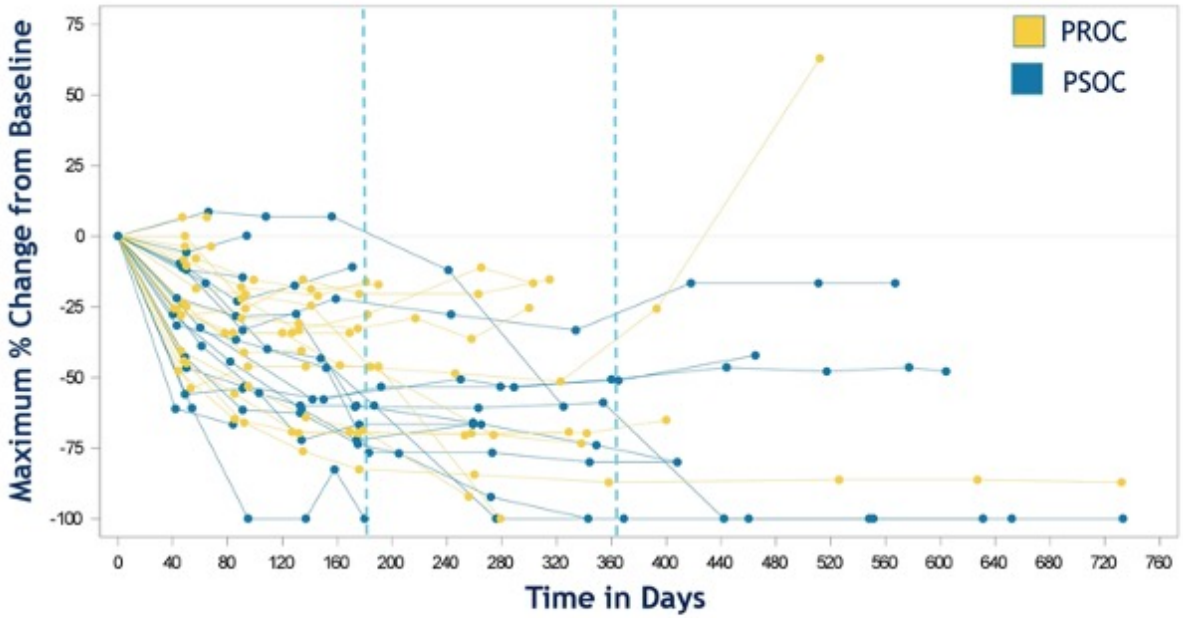
High FRα Tumors Showed a Deep Response and Durable Benefit

Maximum % Change from Baseline



- **97% (32/33)** of patients demonstrated tumor burden reduction

Percent Change and Duration from Baseline



- Rapid tumor shrinkage, with early responses
- Durable benefit in both PSOC and PROC

O'Malley DM et al. ASCO 2021;Abstract 5504.

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]

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Abstract 76

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SGO 2022;Abstract 76.

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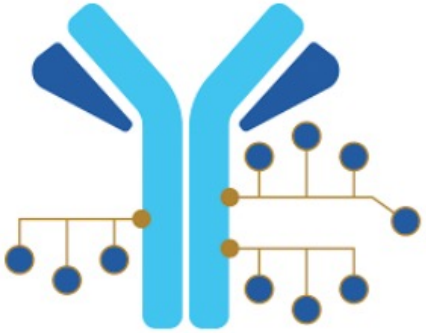
Upifitamab Rilsodotin (UpRi): First-in-Class ADC Targeting NaPi2b



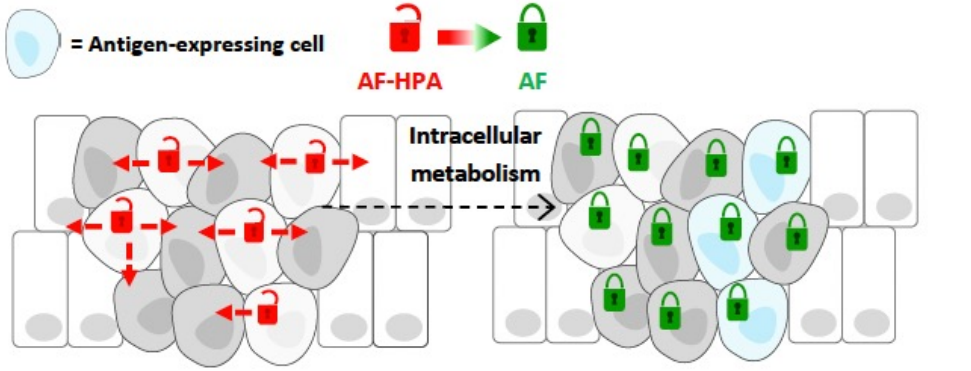
UpRi

Antibody: Humanized monoclonal anti-NaPi2b[1]

Linker: Polymer scaffold; cleavable ester linker[2]

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

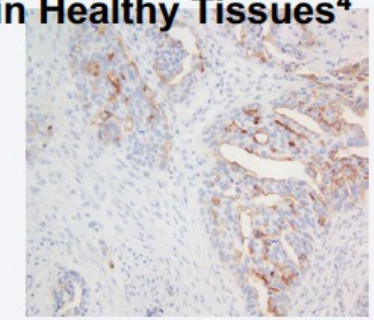
Drug-to-Antibody Ratio: ~10



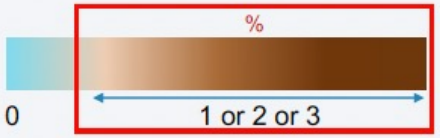
Upon ADC internalization into tumor cells and efficient release of payload, AF-HPA payload is metabolized to AF that remains highly potent but loses the ability to cross the cell membrane, locking it in the tumor, controlling the bystander effect, and consequently limiting impact on adjacent healthy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

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

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



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



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UpRi Phase Ib Study Schema

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

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

UpRi IV Q4W until disease progression or unacceptable toxicity

36 mg/m² cohort initiated in August 2019

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

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

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

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

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

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

Dose Group 36 (33–38 mg/m²) (n=29)

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

+

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

Dose Group 43 (>38–43 mg/m²) (n=66)

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

+

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

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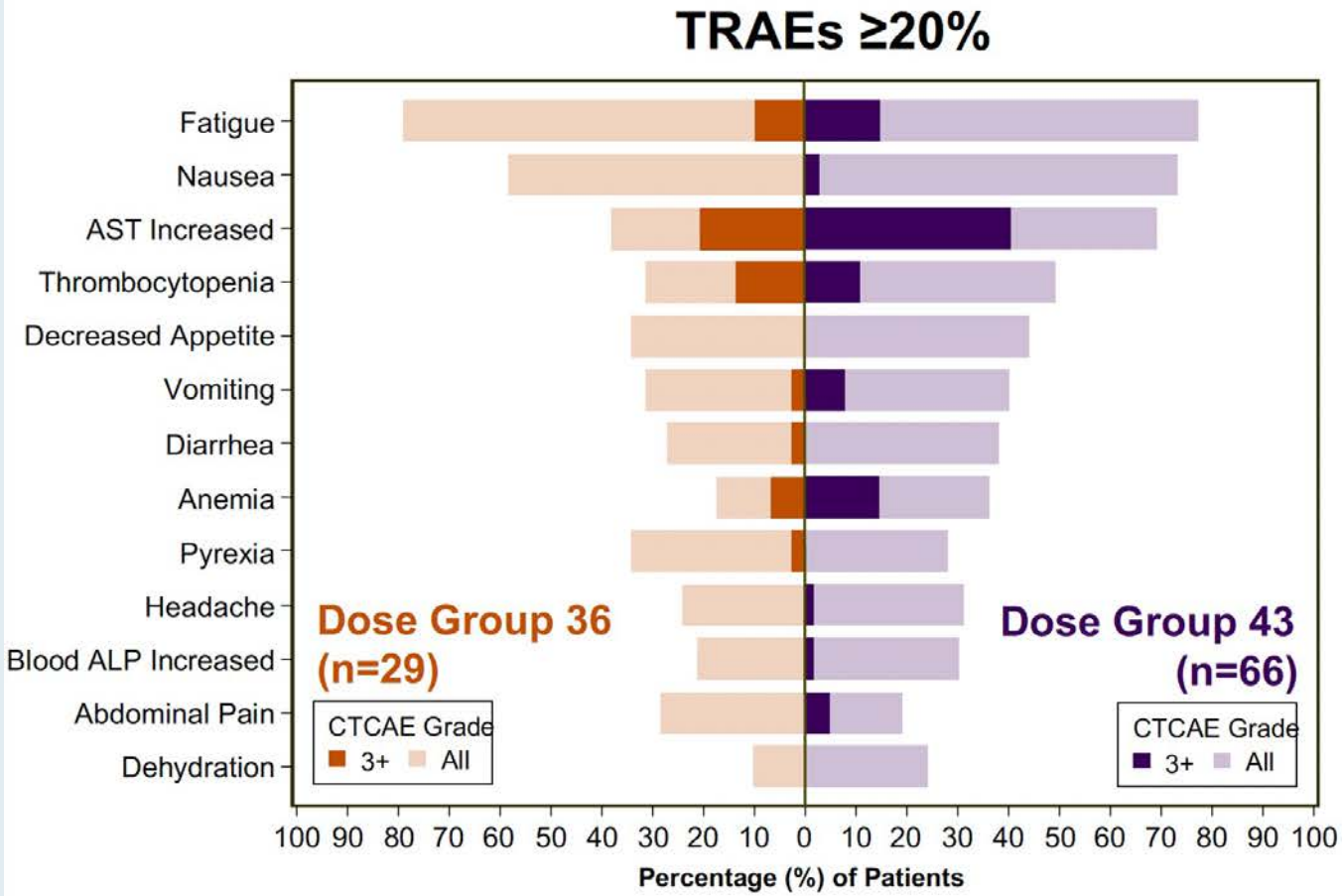
TRAEs by UpRi Dose Group

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



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

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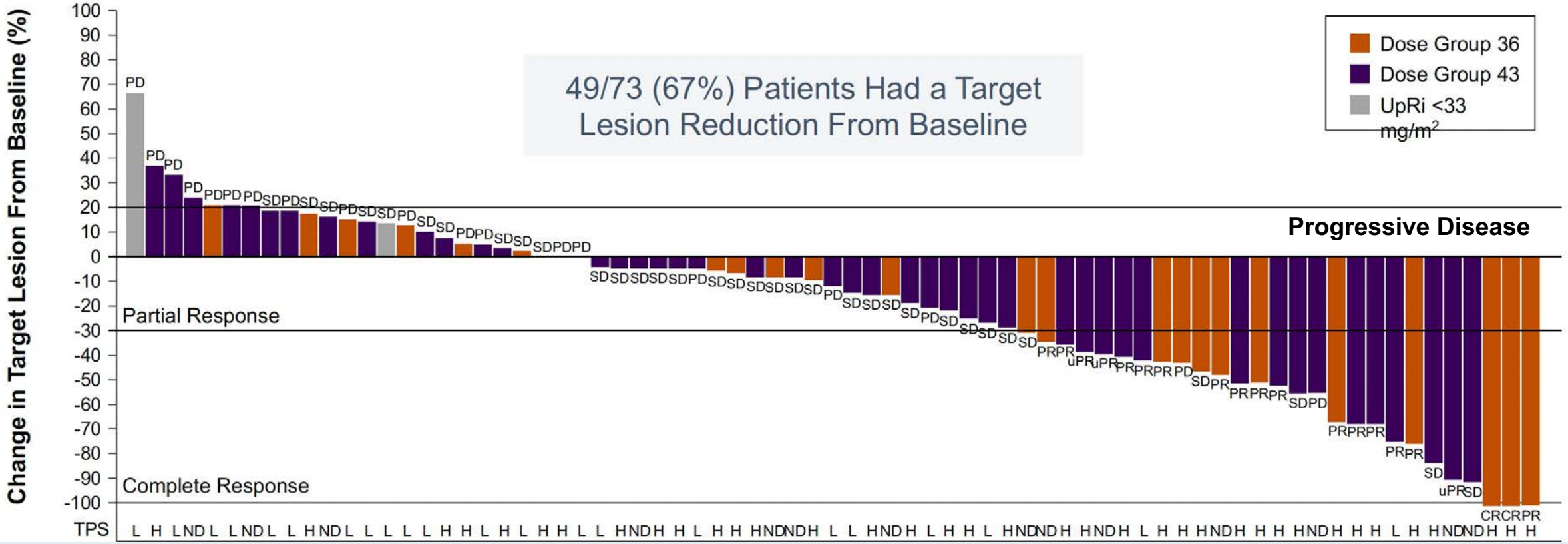
Best Response by UpRi Dose Group

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



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

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

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

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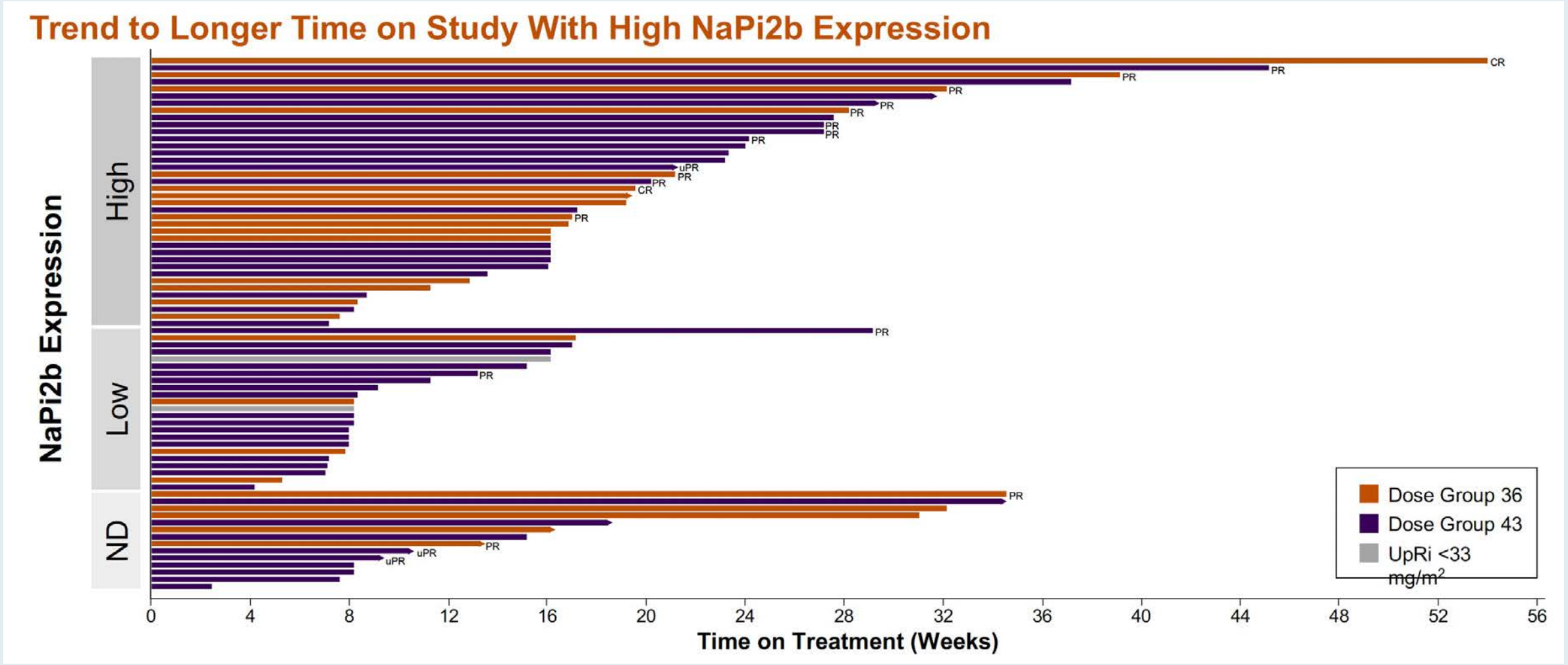
Time on UpRi Study in Evaluable Patients



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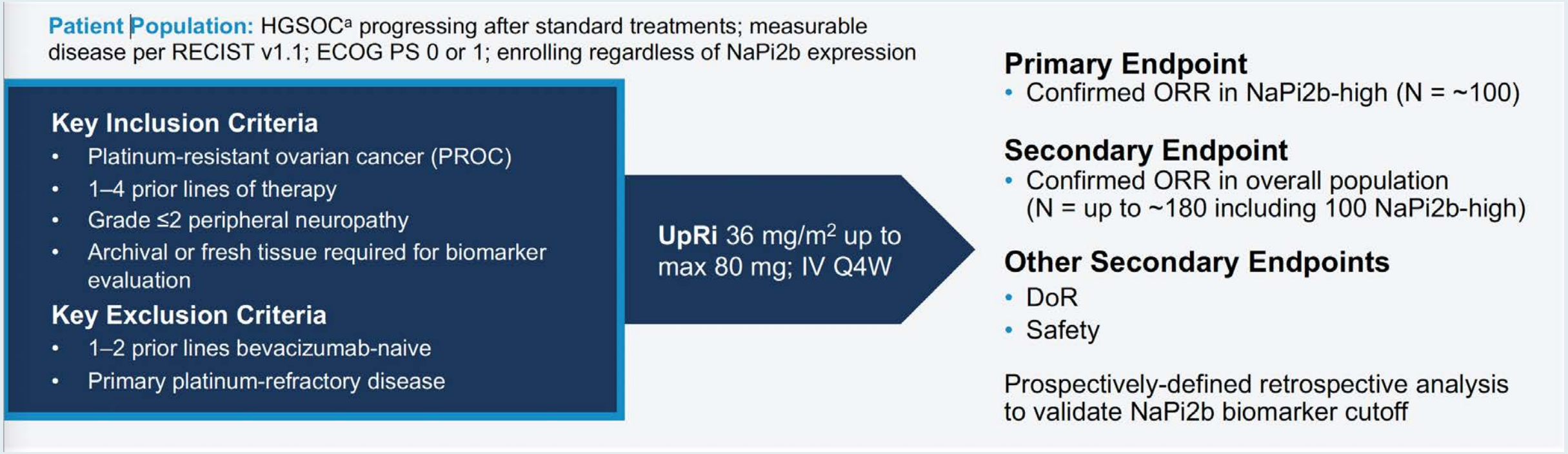
Ongoing UPLIFT (ENGOT-OV67/GOG-3048) Study Schema



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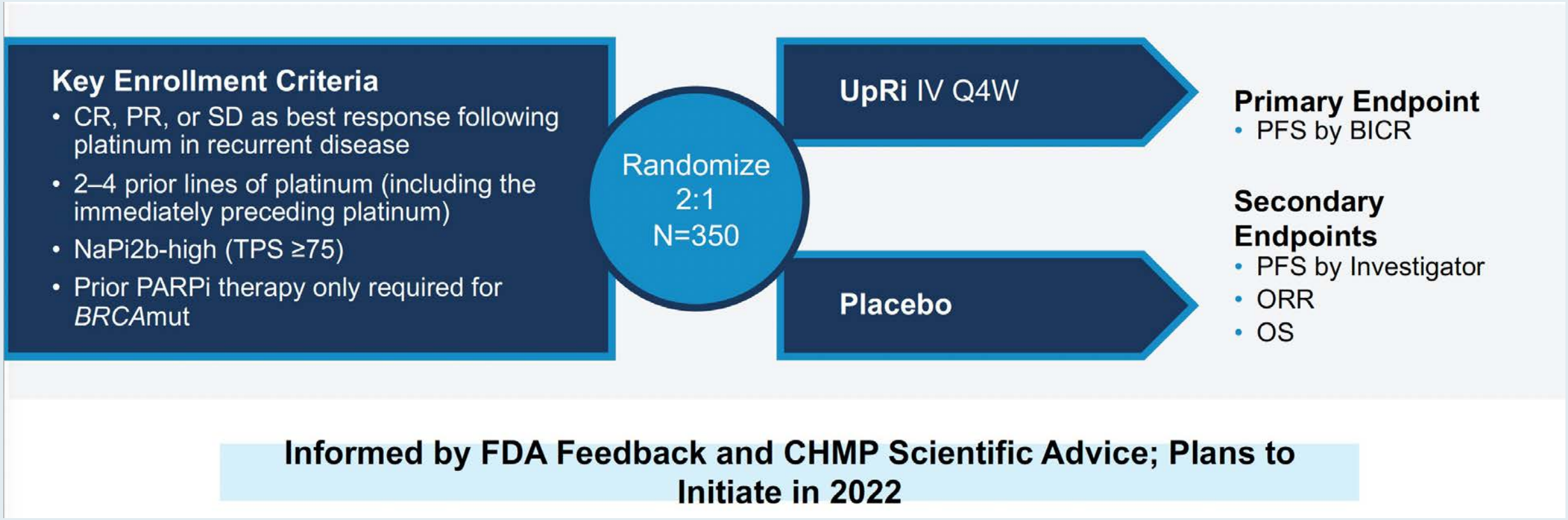
Ongoing UP-NEXT Phase III (ENGOT-OV71-NSGO-CTU/GOG-3049) Study Schema



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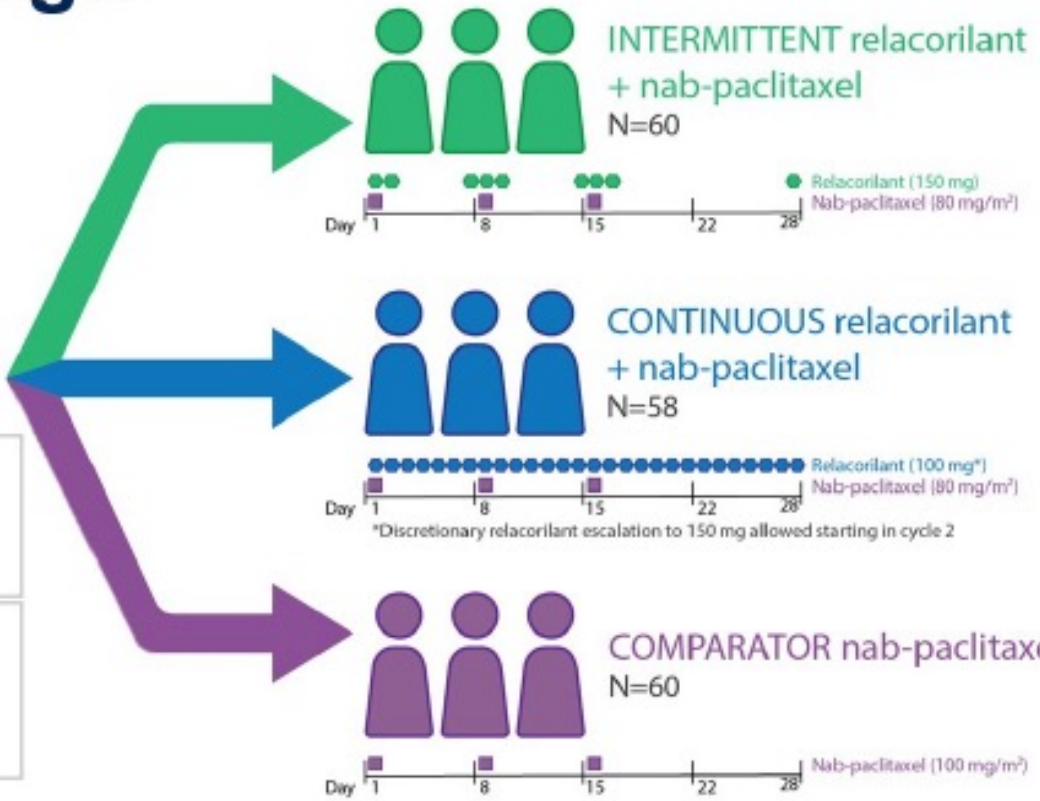
Relacorilant + Nab-paclitaxel Phase 2 Study Design

Randomized 1:1:1

- Measurable or non-measurable disease by RECIST v1.1
- Up to 4 prior chemotherapeutic regimens

Stratification factors:

- Relapse within 6 months of most recent taxane
- Presence of ascites



Primary endpoint:

- Progression-free survival (PFS) by investigator and RECIST v1.1

Secondary endpoints:

- Objective response rate (ORR)
- Duration of response (DoR)
- Overall survival (OS)
- Safety of the relacorilant + nab-paclitaxel combination

Statistical assumptions:

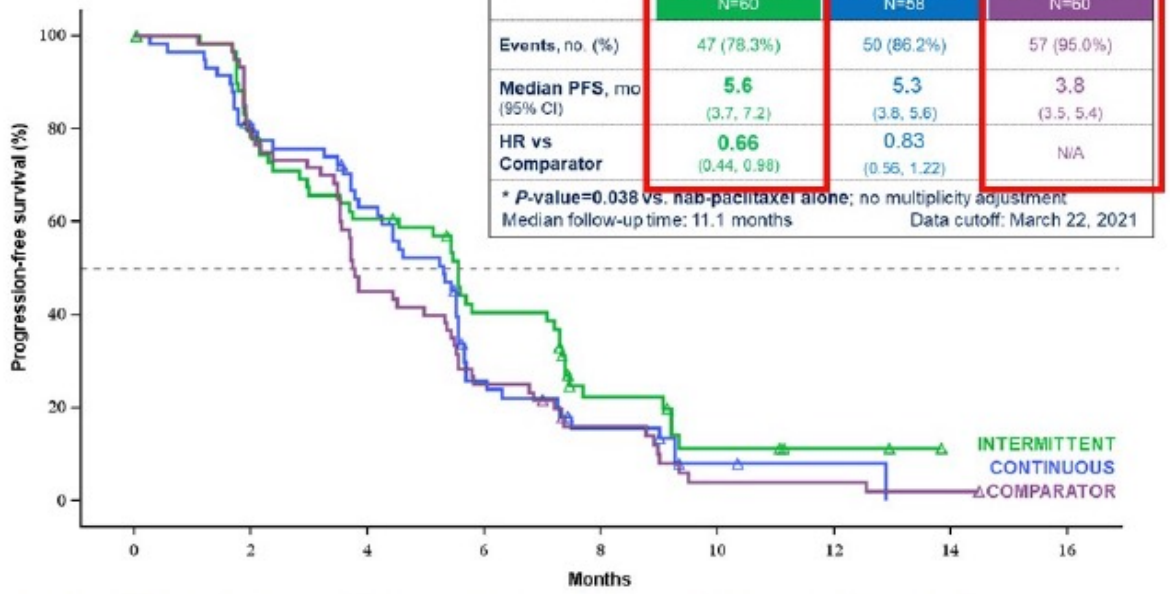
- **CONTINUOUS vs COMPARATOR**: 91 PFS events to detect a HR=0.56 (median PFS increase from 3.8 to 6.8 mo)
- **INTERMITTENT vs COMPARATOR**: 92 PFS events to detect a HR=0.7 (median PFS increase from 3.8 to 5.4 mo)

PFS analysis reported at ESMO 2021

Colombo N et al. ASCO 2022;Abstract LBA5503; Liu N. ASCO 2022;Highlights of the Day: Gynecologic Cancers.

Investigator assessed PFS and OS of relacorilant + nab-paclitaxel

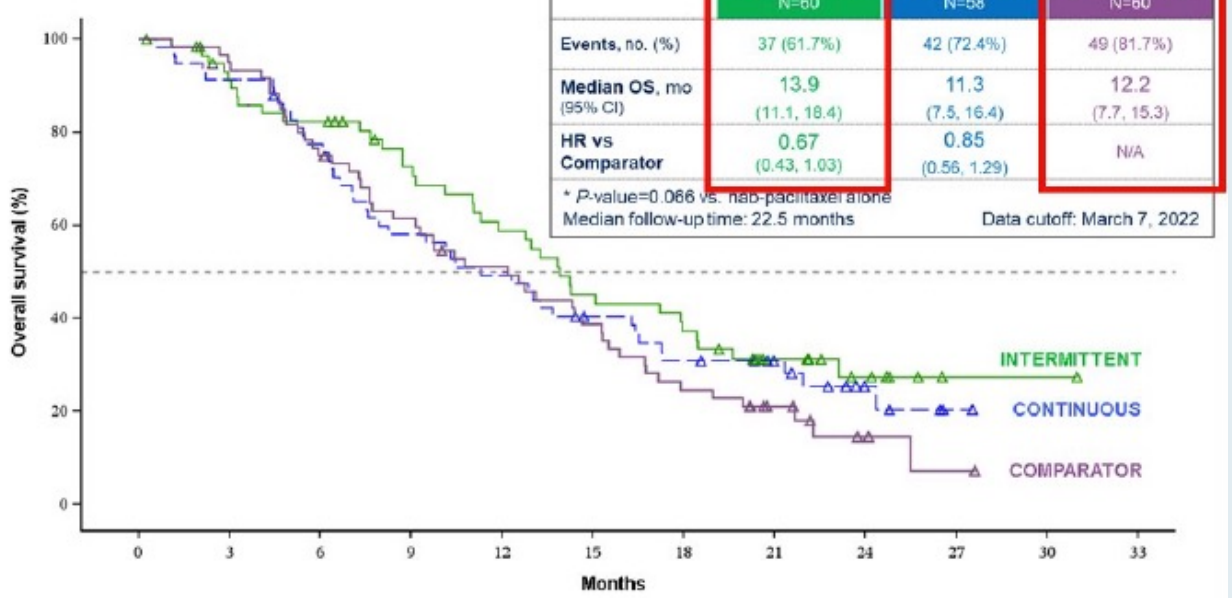
Progression free survival



	INTERMITTENT* N=60	CONTINUOUS N=58	COMPARATOR N=60
Events, no. (%)	47 (78.3%)	50 (86.2%)	57 (95.0%)
Median PFS, mo (95% CI)	5.6 (3.7, 7.2)	5.3 (3.8, 5.6)	3.8 (3.5, 5.4)
HR vs Comparator	0.66 (0.44, 0.98)	0.83 (0.56, 1.22)	N/A

* *P*-value=0.038 vs. nab-paclitaxel alone; no multiplicity adjustment
Median follow-up time: 11.1 months
Data cutoff: March 22, 2021

Overall survival



	INTERMITTENT* N=60	CONTINUOUS N=58	COMPARATOR N=60
Events, no. (%)	37 (61.7%)	42 (72.4%)	49 (81.7%)
Median OS, mo (95% CI)	13.9 (11.1, 18.4)	11.3 (7.5, 16.4)	12.2 (7.7, 15.3)
HR vs Comparator	0.67 (0.43, 1.03)	0.85 (0.56, 1.29)	N/A

* *P*-value=0.066 vs. nab-paclitaxel alone
Median follow-up time: 22.5 months
Data cutoff: March 7, 2022

Colombo N et al. ASCO 2022;Abstract LBA5503; Liu N. ASCO 2022;Highlights of the Day: Gynecologic Cancers.

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Optimizing the Management of HER2-Positive Breast Cancer

Tuesday, October 4, 2022
5:00 PM – 6:00 PM ET

Faculty

Nancy U Lin, MD

Moderator

Neil Love, MD

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