Consensus or Controversy? Current and Future Management of Ovarian Cancer

A CME/MOC-Accredited Virtual Event

Thursday, November 3, 2022
5:00 PM – 6:00 PM ET

Faculty

Ursula Matulonis, MD
Debra L Richardson, MD

Moderator

Neil Love, MD

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Faculty

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

Debra L Richardson, MD
Associate Professor
Section Chief, Division of Gynecologic Oncology
Stephenson Cancer Center
University of Oklahoma Health Sciences Center
Oklahoma City, Oklahoma

MODERATOR
Neil Love, MD
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Commercial Support

This activity is supported by educational grants from ImmunoGen Inc, Mersana Therapeutics Inc, and Novocure Inc.

Dr Love — Disclosures

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Dr Matulonis — Disclosures

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Steering Committee	Karyopharm Therapeutics (SIENDO trial), Tesaro, A GSK Company (OVARIO trial)

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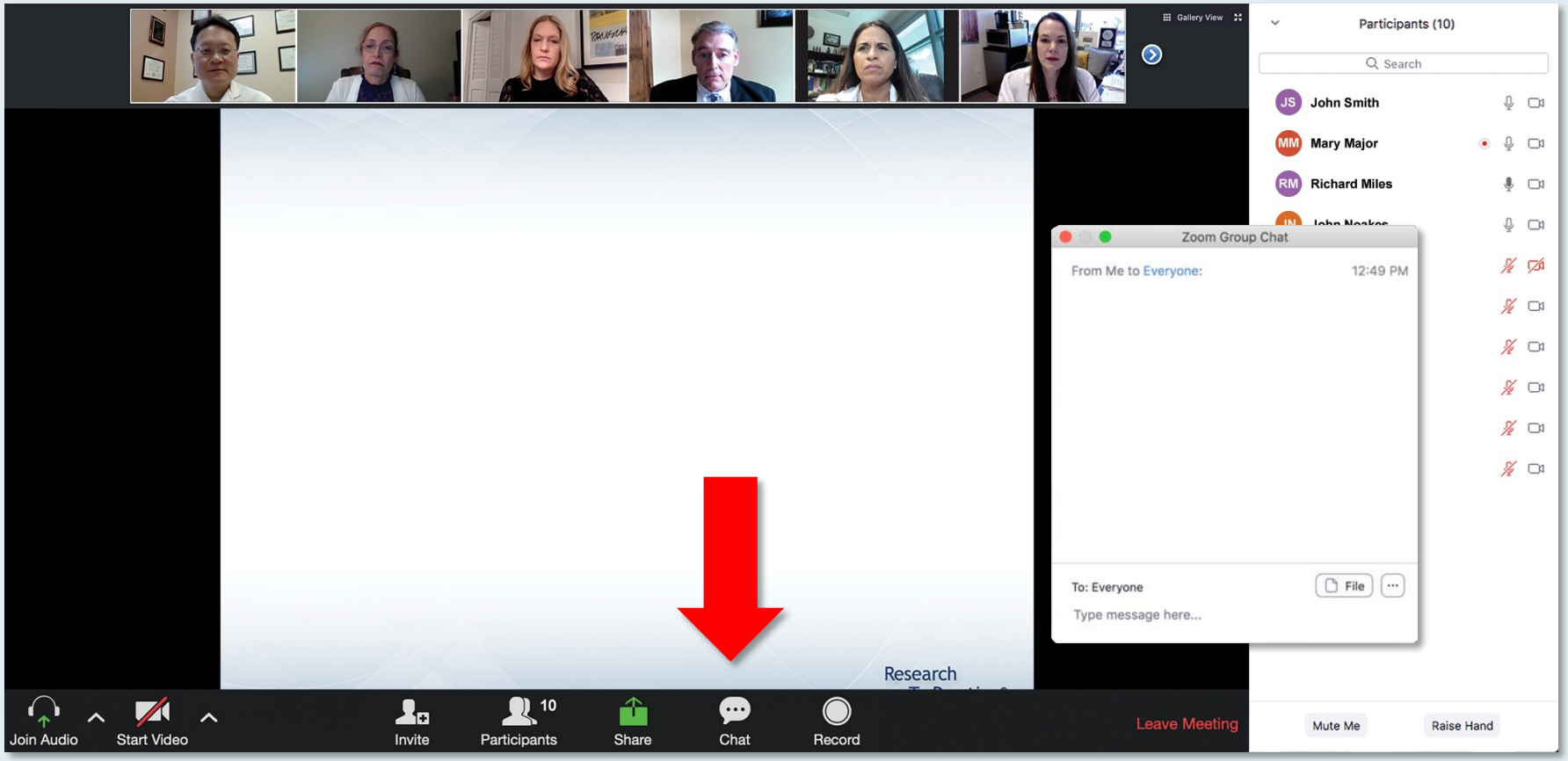

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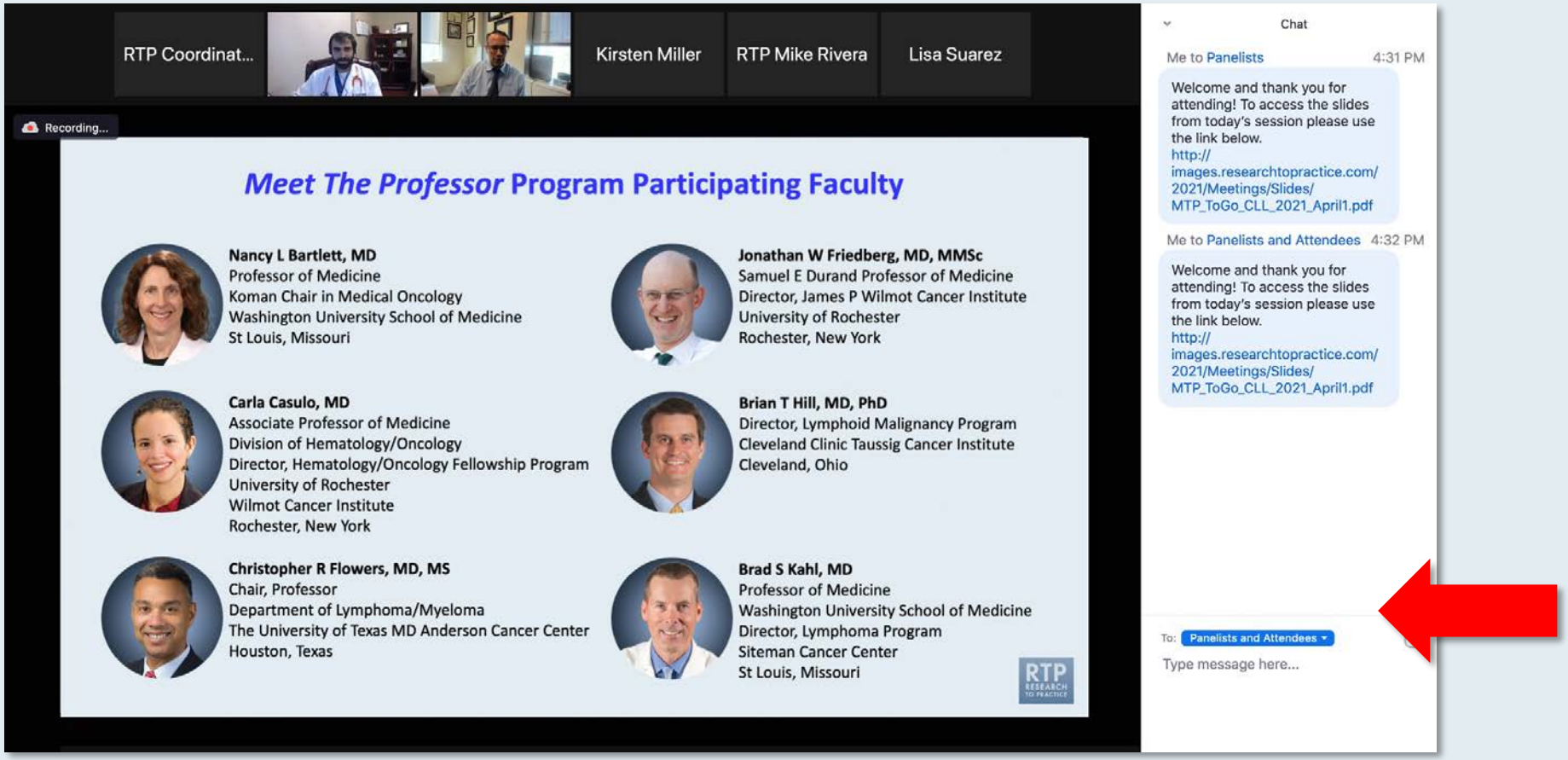
Familiarizing Yourself with the Zoom Interface

Expand chat submission box



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

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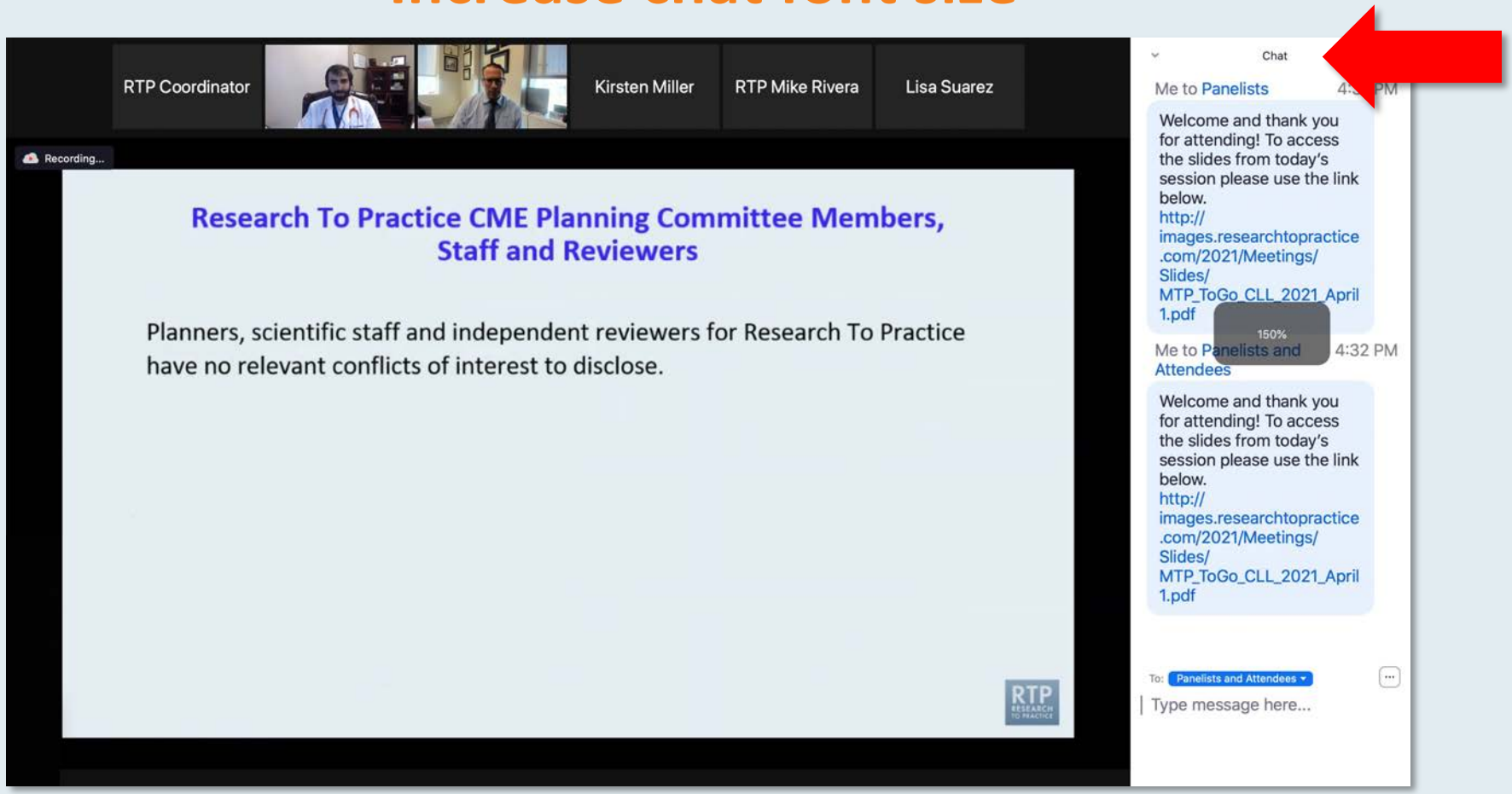
Increase chat font size



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

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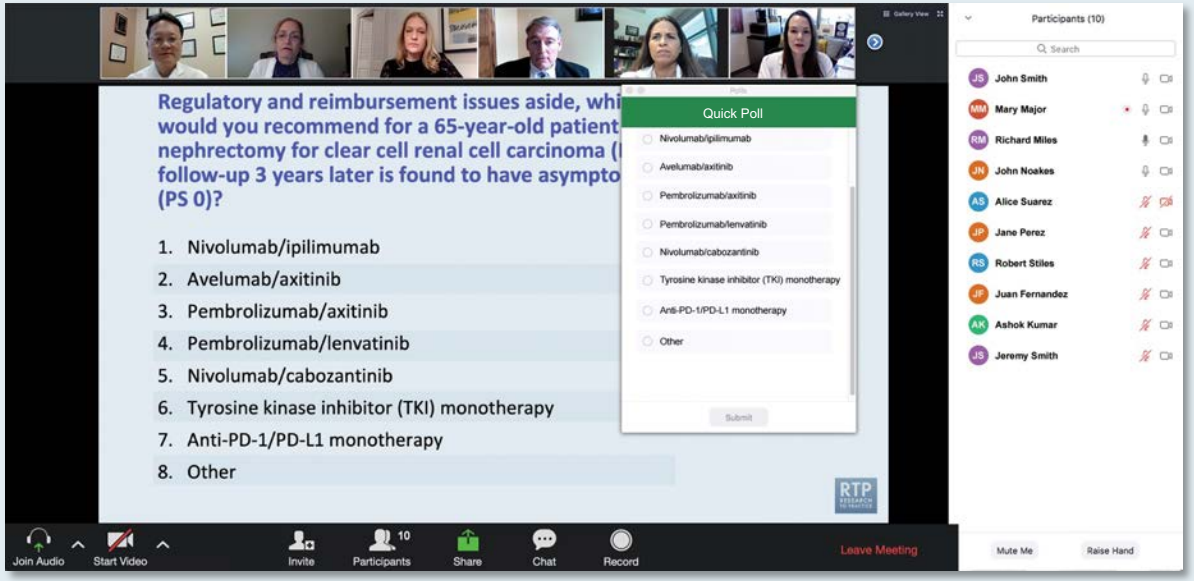

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ONCOLOGY TODAY

WITH DR NEIL LOVE

Ocular Toxicities in Patients Receiving Anticancer Therapy

DR ASIM FAROOQ

THE UNIVERSITY OF CHICAGO MEDICAL CENTER

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Meet The Professor

Optimizing the Management of HER2-Positive Breast Cancer

Tuesday, November 8, 2022
5:00 PM – 6:00 PM ET

Faculty

Lisa A Carey, MD, ScM

Moderator

Neil Love, MD

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Meet The Professor
Optimizing the Management of Multiple Myeloma

Tuesday, November 15, 2022
5:00 PM – 6:00 PM ET

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Paul G Richardson, MD

Moderator

Neil Love, MD

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What Clinicians Want to Know: Addressing Current Questions and Controversies in the Management of HER2-Positive Breast Cancer

Part 1 of a 2-Part CME Satellite Symposium Series Held in Conjunction with the 2022 San Antonio Breast Cancer Symposium®

Wednesday, December 7, 2022

7:15 PM – 9:15 PM CT (8:15 PM – 10:15 PM ET)

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Ian E Krop, MD, PhD

Shanu Modi, MD

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Addressing Current Questions and Controversies in the Management of Chronic Lymphocytic Leukemia — What Clinicians Want to Know

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Friday, December 9, 2022
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Sagar Lonial, MD
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Neil Love, MD

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Thank you for joining us!

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

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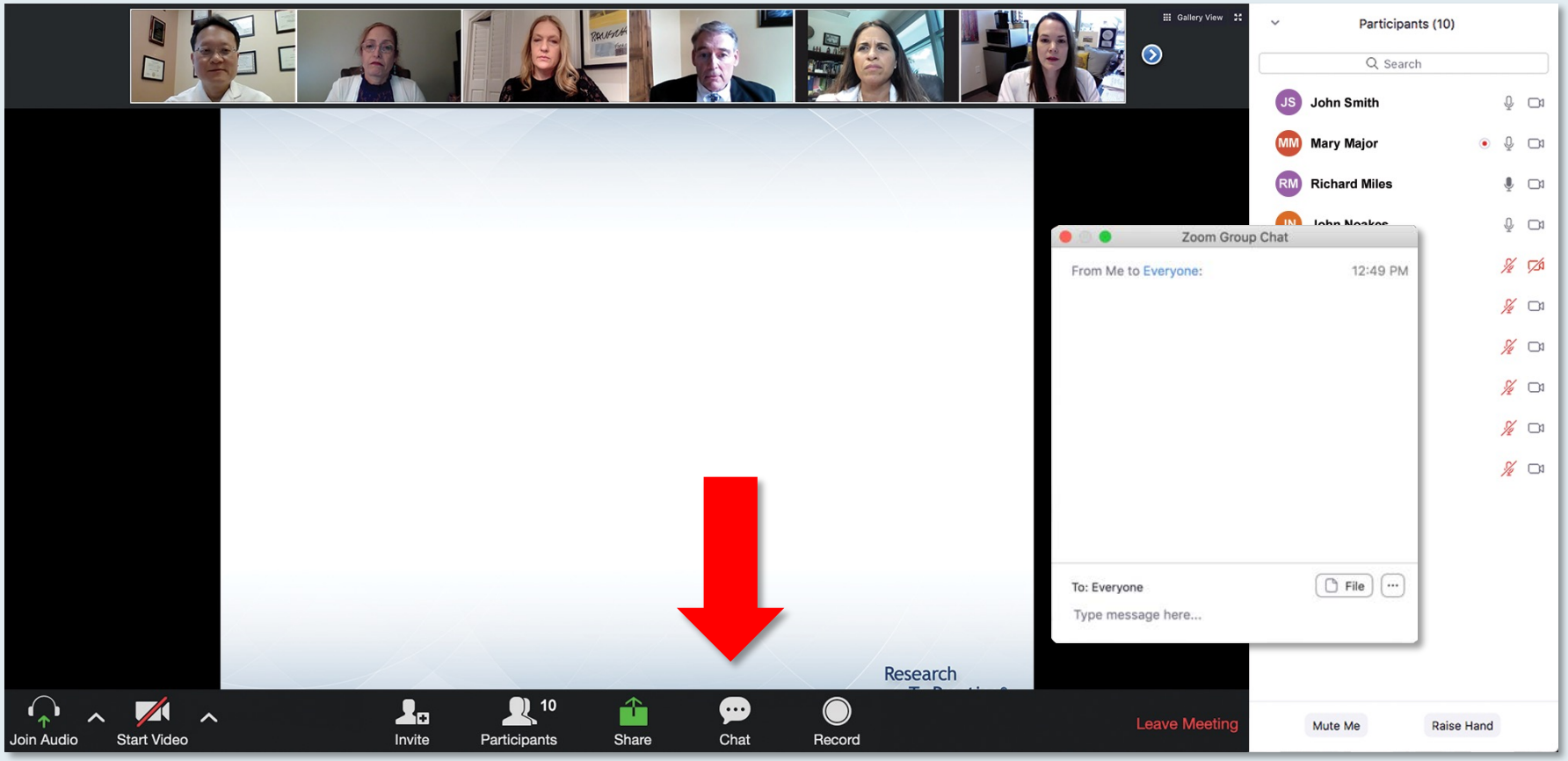

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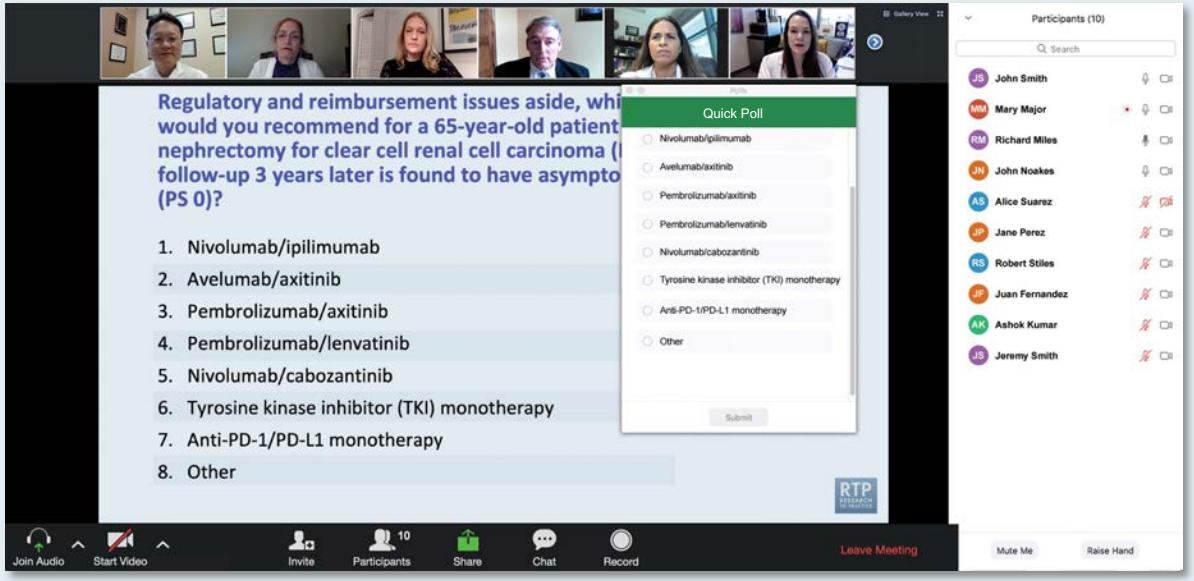

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PROLOGUE: Antibody-Drug Conjugates Across Oncology

MODULE 1: Antibody-Drug Conjugates in Ovarian Cancer

- Mirvetuximab Soravtansine
- Upifitamab Rilsodotin

MODULE 2: Tumor Treating Fields

MODULE 3: PARP Inhibitor Update

Appendix

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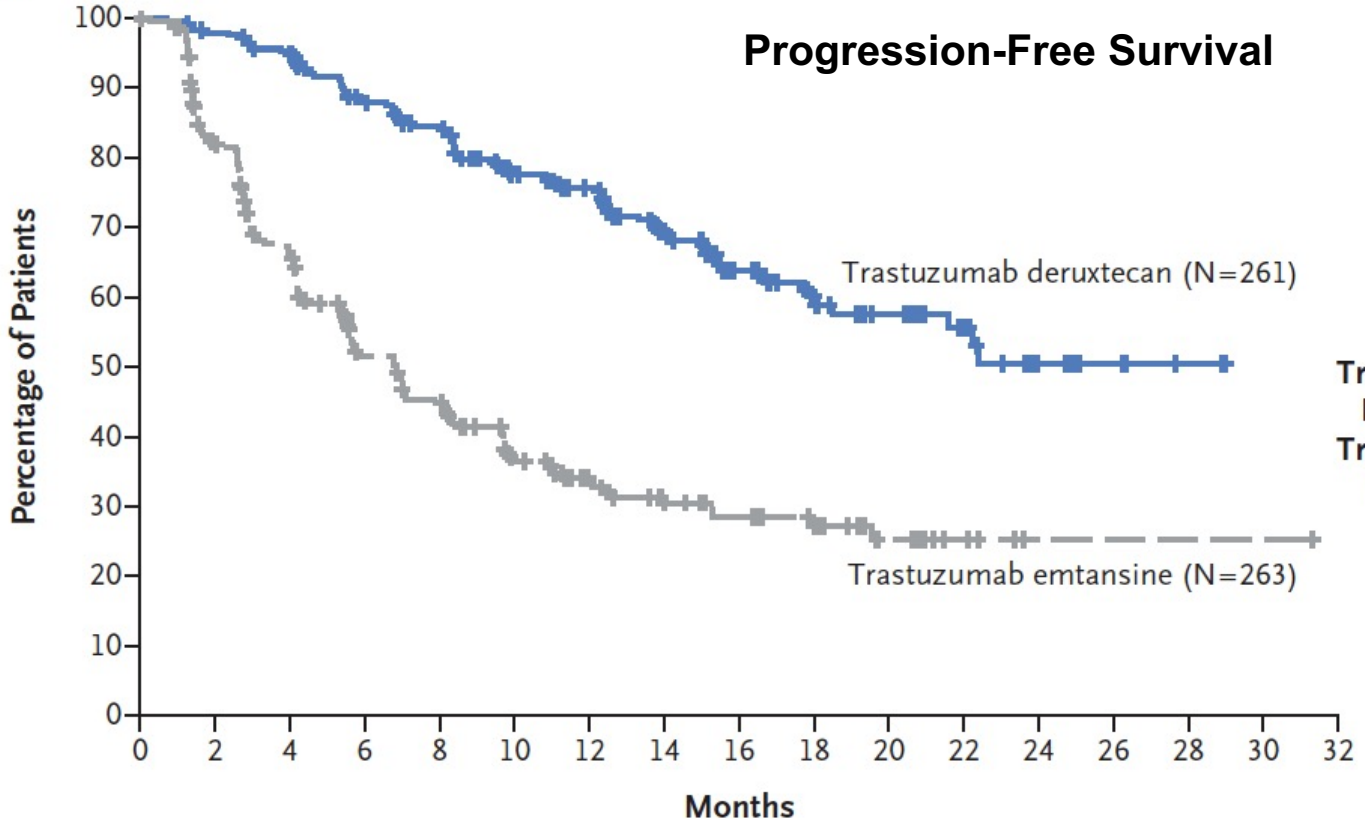
DESTINY-Breast03: Trastuzumab Deruxtecan for HER2-Positive Metastatic Breast Cancer Previously Treated with Trastuzumab and a Taxane

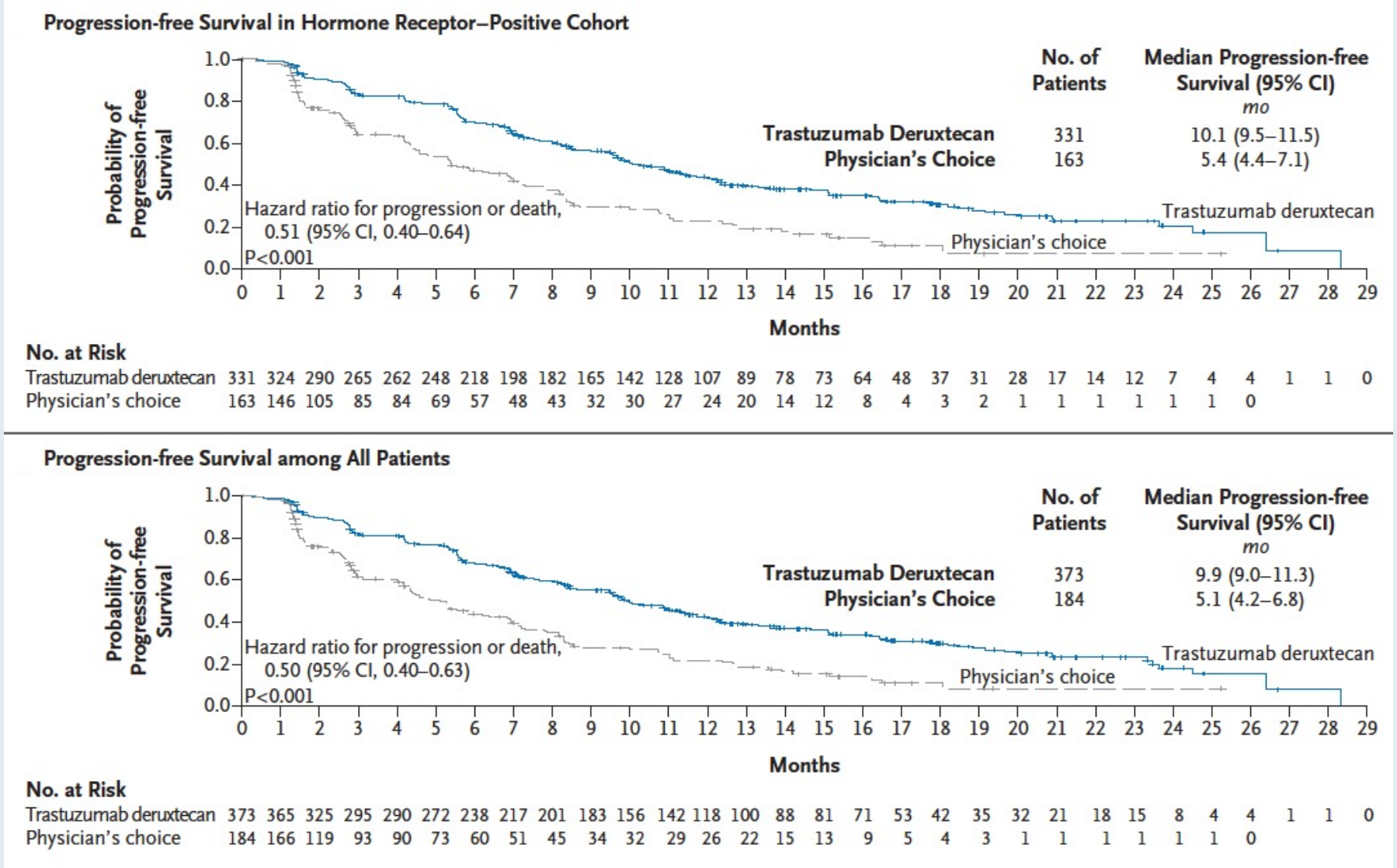


	Median Progression-free Survival (95% CI)	12-Mo Progression-free Survival (95% CI)
	mo	%
Trastuzumab Deruxtecan	NR (18.5–NE)	75.8 (69.8–80.7)
Trastuzumab Emtansine	6.8 (5.6–8.2)	34.1 (27.7–40.5)

Hazard ratio for disease progression or death, 0.28 (95% CI, 0.22–0.37)
P<0.001

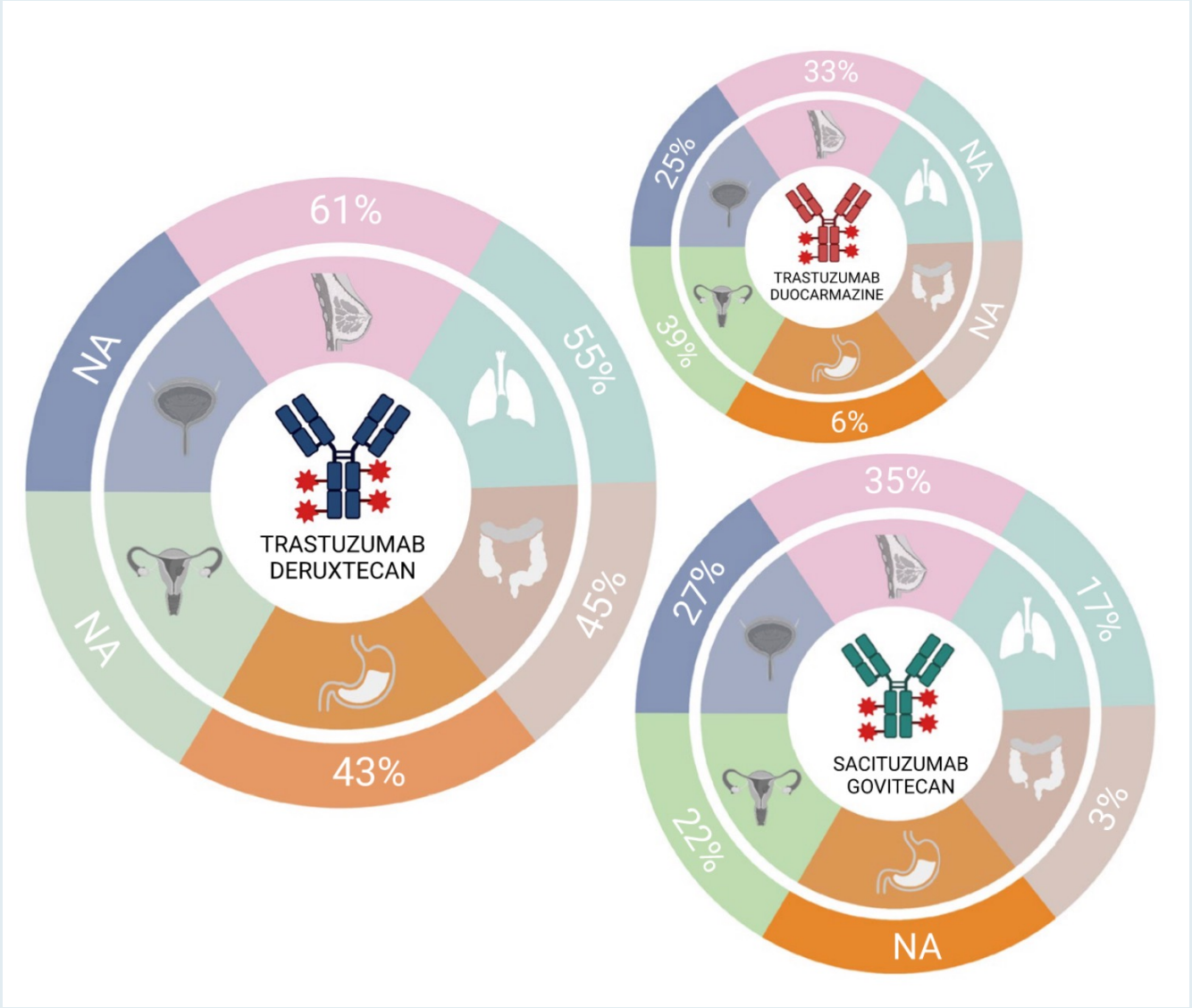
Cortés J et al. *N Engl J Med* 2022;386(12):1143-54.

DESTINY-Breast04: Trastuzumab Deruxtecan in Previously Treated HER2-Low Advanced Breast Cancer



Modi S et al. *N Engl J Med* 2022;387(1):9-20; ASCO 2022;Abstract LBA3.

Emerging Activity of Selected Novel Antibody-Drug Conjugates (ADCs) for Multiple Cancer Types



Tarantino P et al. *CA Cancer J Clin* 2022;72(2):165-82.

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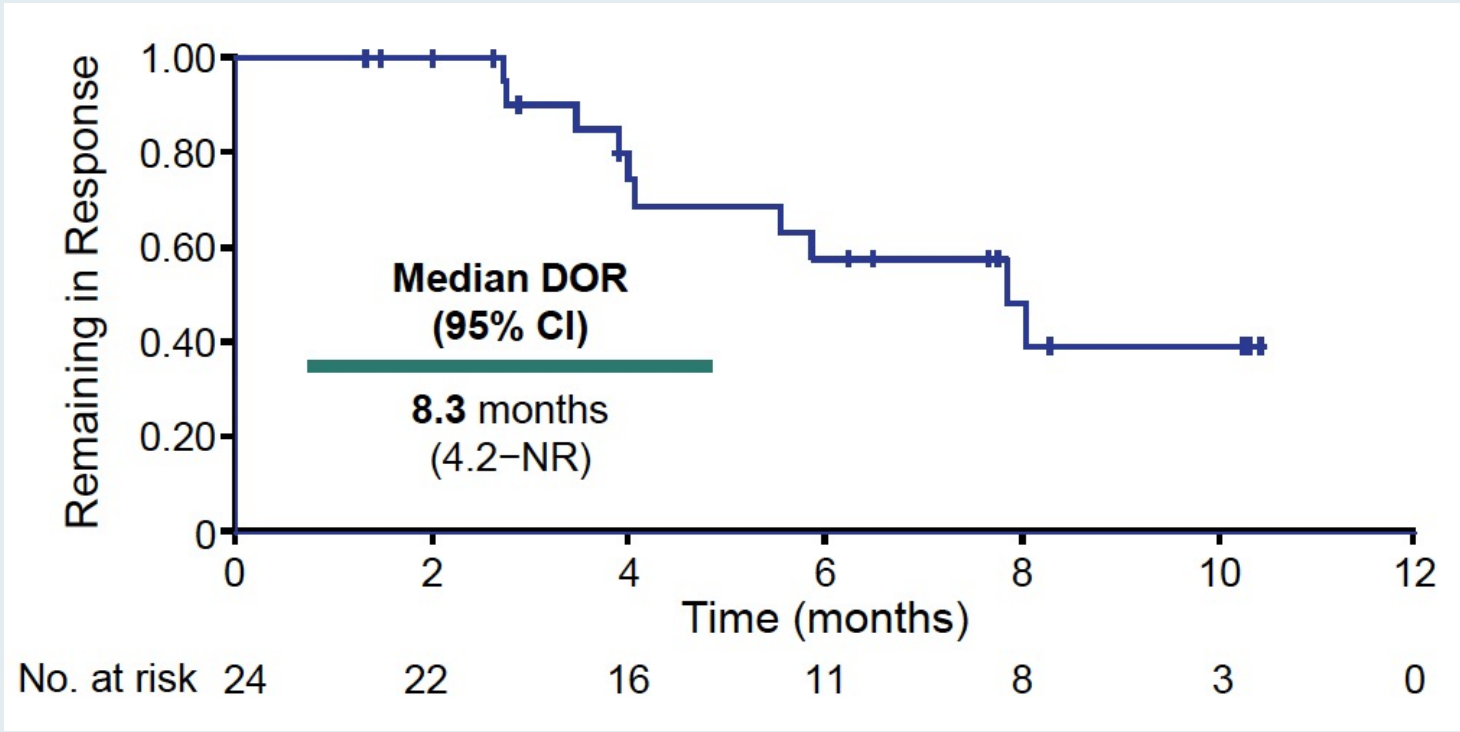
innovaTV 204: Tisotumab Vedotin for Previously Treated Recurrent or Metastatic Cervical Cancer

Clinical Variable	N = 101
Confirmed ORR	24%
CR	7%
PR	17%
SD	49%
PD	24%
Not evaluable	4%

Duration of Response



Coleman RL et al. ESMO 2020;Abstract LBA32.

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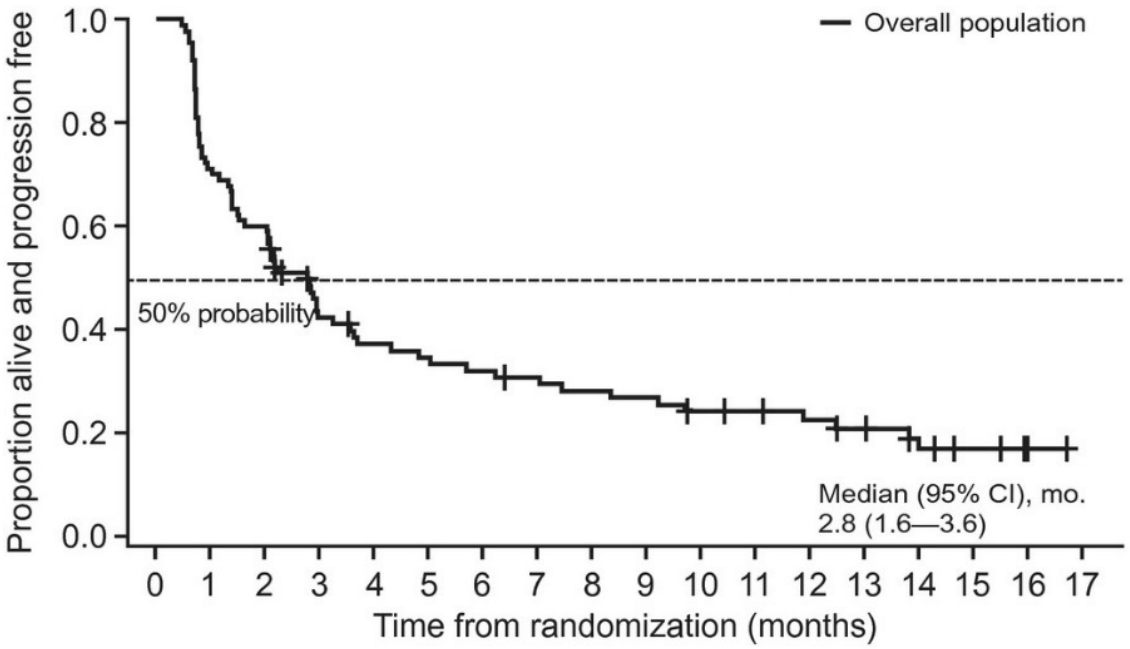
DREAMM-2: Single-Agent Belantamab Mafodotin for Relapsed or Refractory Multiple Myeloma

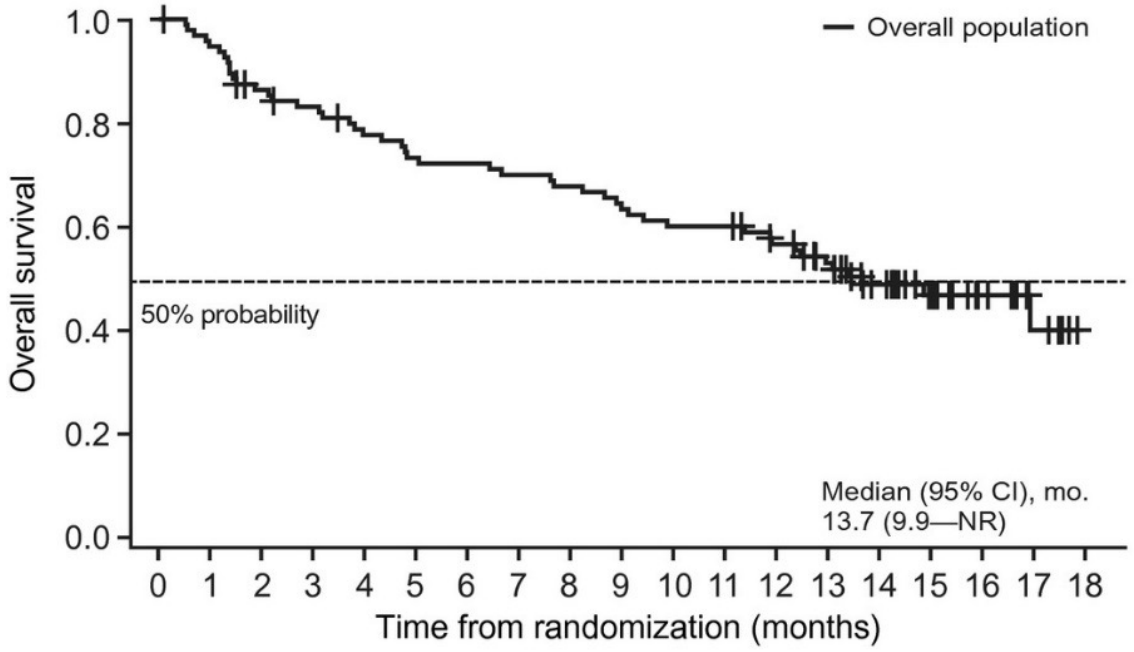
Progression-Free Survival



Number at risk (Number of events)

97	64	54	34	29	27	25	23	21	20	17	16	14	12	8	4	2	0
(0)	(26)	(36)	(51)	(55)	(57)	(59)	(60)	(62)	(63)	(65)	(65)	(66)	(67)	(69)	(69)	(68)	(69)

Overall Survival



Number at risk (Number of events)

97	91	81	77	71	67	66	64	62	59	55	55	49	43	31	22	13	6	0
(0)	(5)	(13)	(16)	(21)	(25)	(26)	(28)	(30)	(33)	(37)	(37)	(39)	(42)	(45)	(46)	(46)	(47)	(47)

Expected median OS in triple-class refractory myeloma: 8.6 months

Lonial S et al. *Cancer* 2021;127(22):4198-212.

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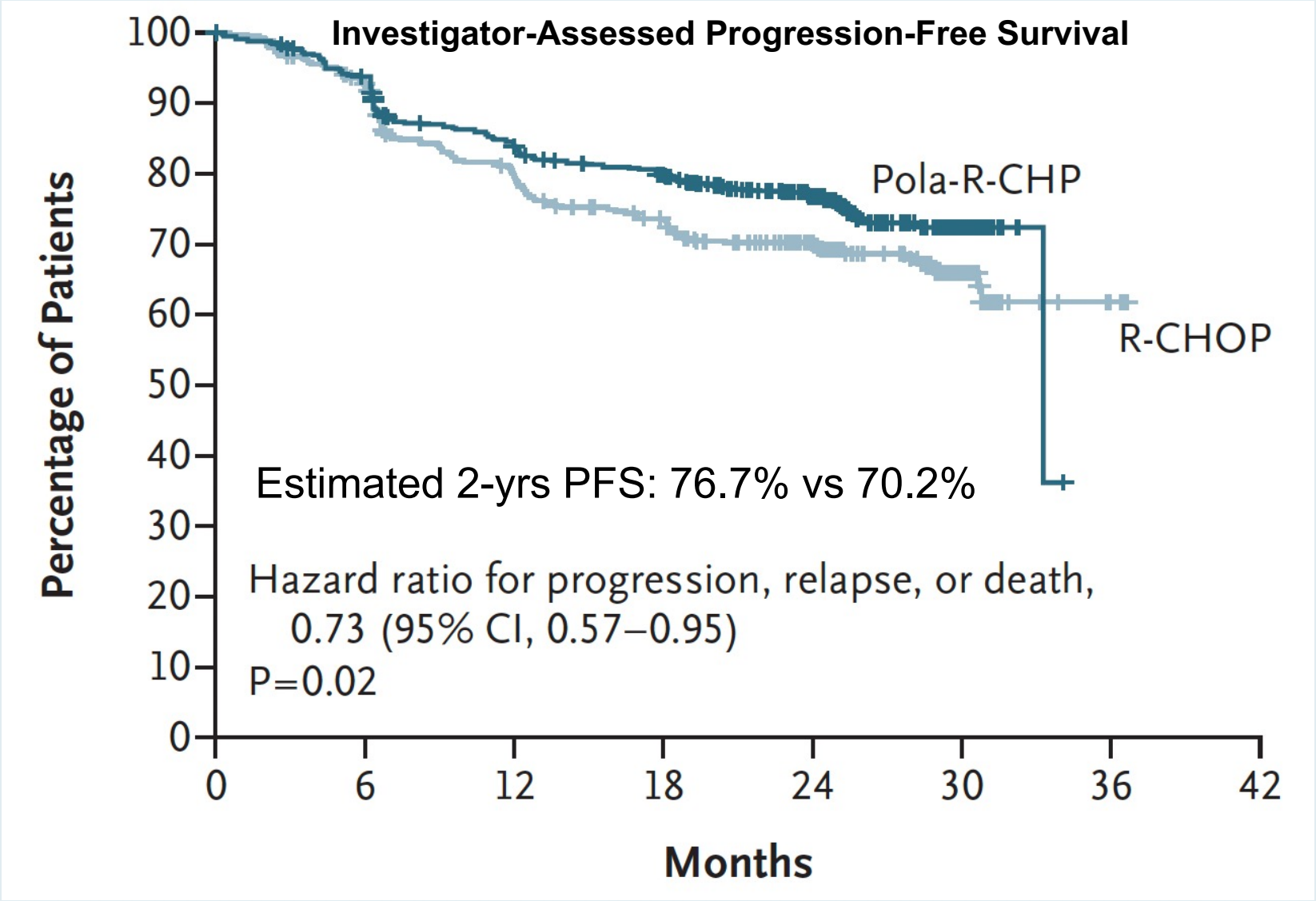
POLARIX: Polatuzumab Vedotin/R-CHP for Previously Untreated Diffuse Large B-Cell Lymphoma



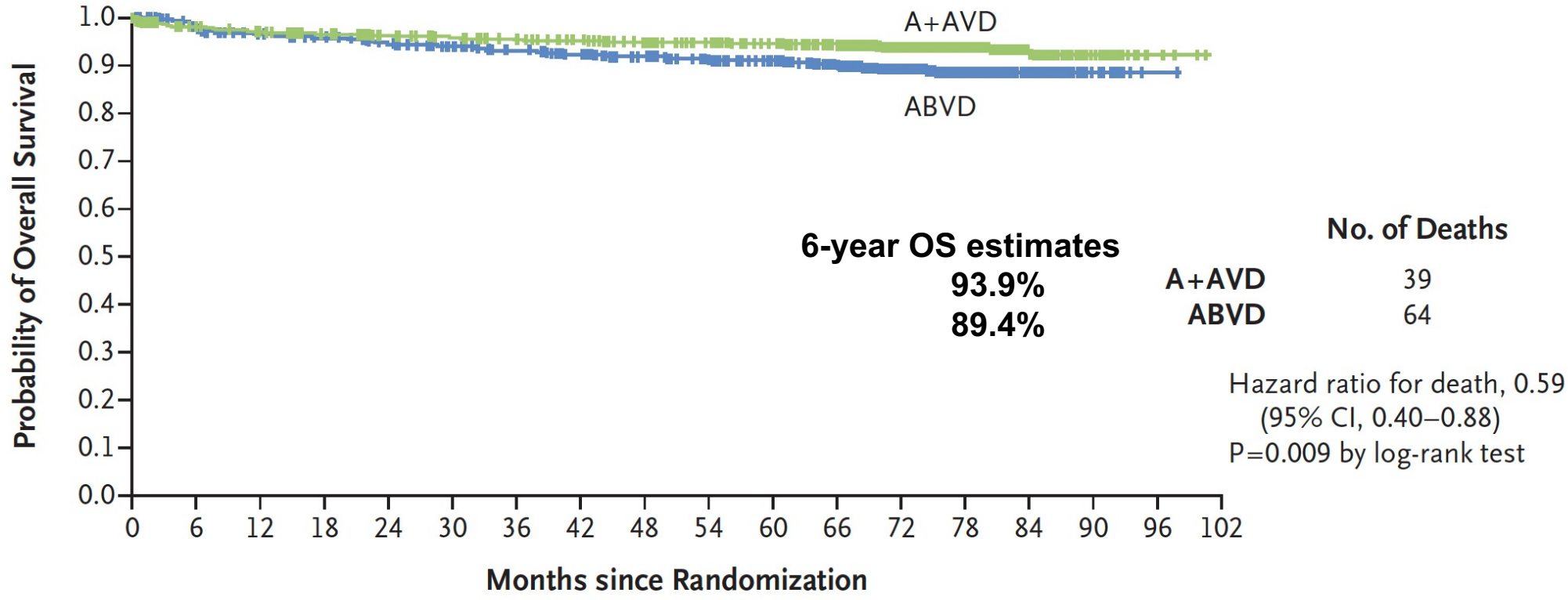
Tilly H et al. *N Engl J Med* 2022;386(4):351-63.

LOTIS-2: Response and Survival with Loncastuximab Tesirine for R/R DLBCL

Response	As-treated population (N = 145)
Overall response rate	70/145 (48.3%)
Complete response rate	35/145 (24.1%)
Complete response	35 (24%)
Partial response	35 (24%)
Stable disease	22 (15%)
Progressive disease	30 (21%)
Not evaluable	23 (16%)
Survival	**As-treated population (N = 145)**
Median progression-free survival	4.9 months
Median overall survival	9.9 months

Caimi PF et al. *Lancet Oncol* 2021;22(6):790-800.

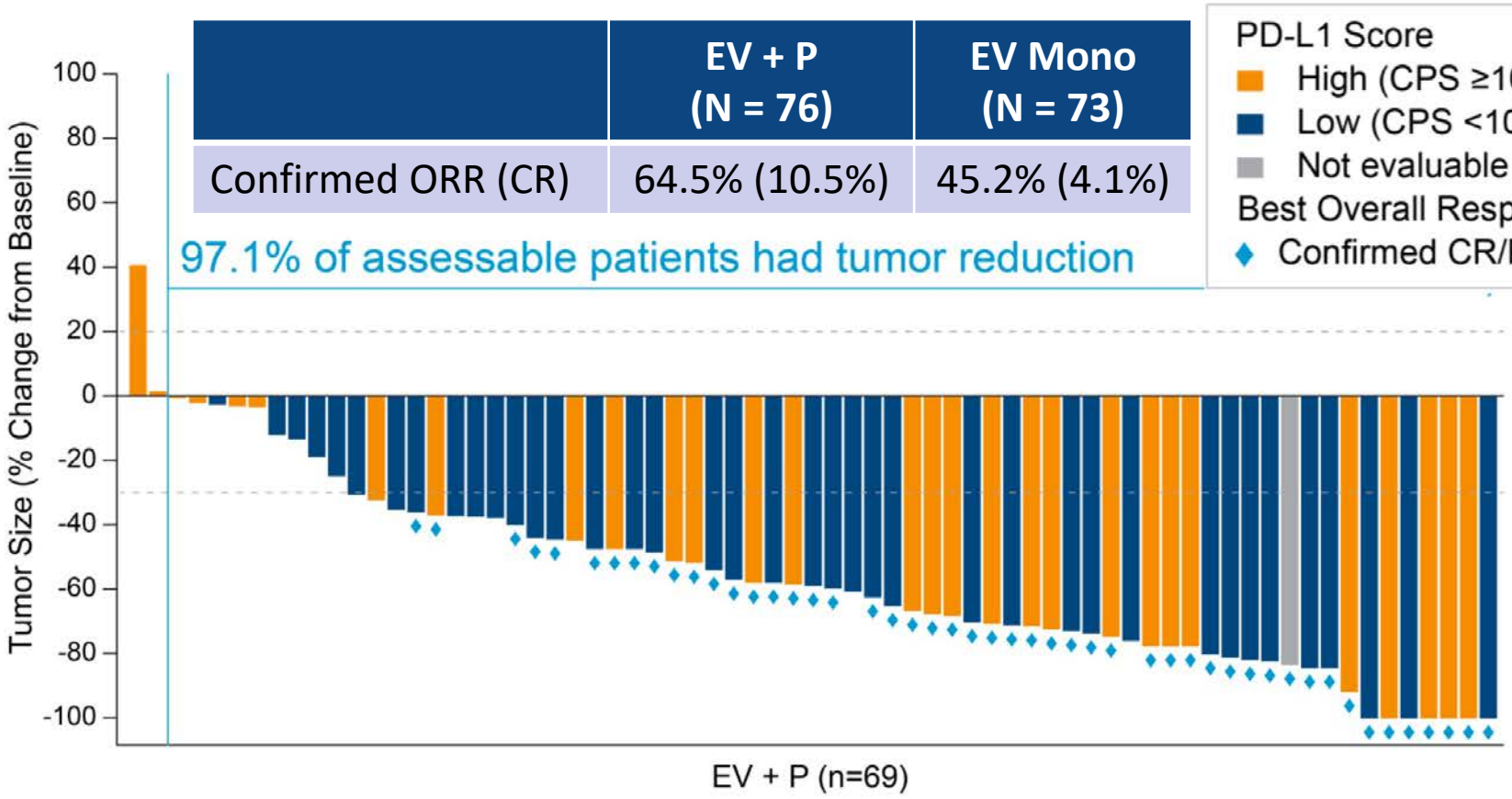
ECHELON-1: Brentuximab Vedotin and Chemotherapy for Stage III or IV Hodgkin Lymphoma



Ansell SM et al. *N Engl J Med* 2022;387(4):310-20.

EV-103 Cohort K: Enfortumab Vedotin as Monotherapy or in Combination with Pembrolizumab for Previously Untreated Locally Advanced or Metastatic Urothelial Cancer

	EV + P (N = 76)	EV Mono (N = 73)
Confirmed ORR (CR)	64.5% (10.5%)	45.2% (4.1%)

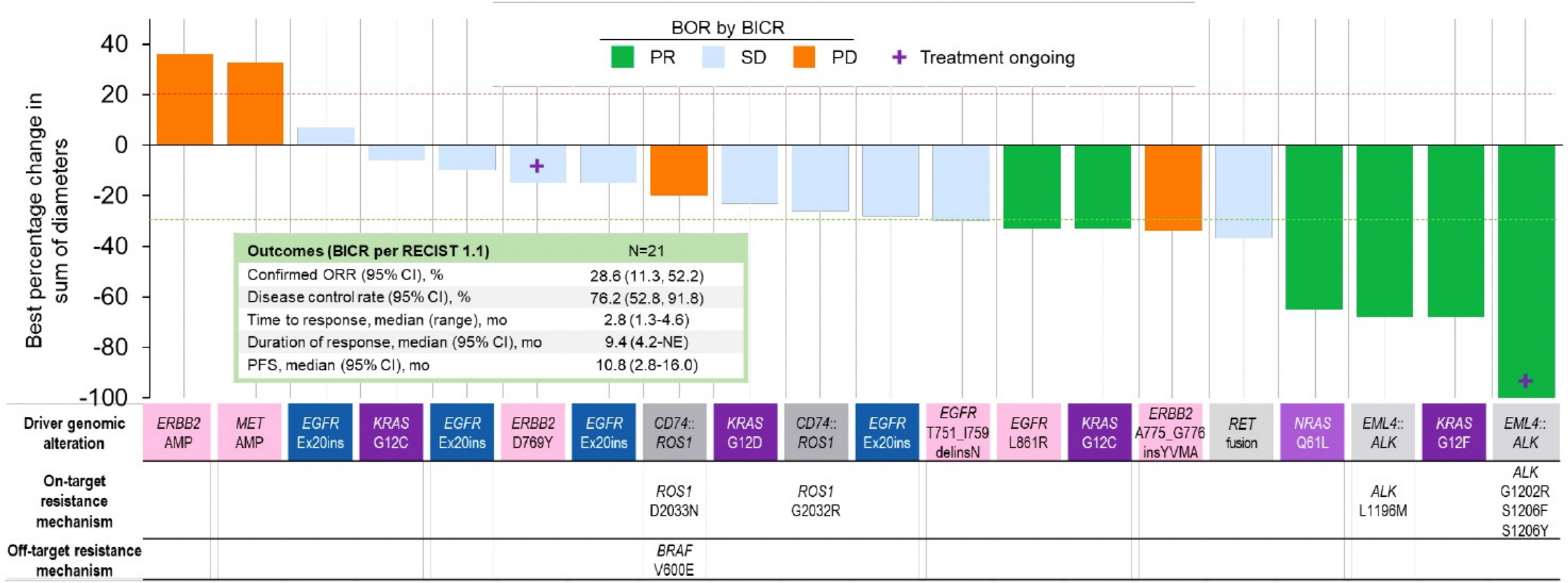


- Activity seen regardless of PD-L1 status
  - 27/44 (61.4%) cORR in CPS<10
  - 21/31 (67.7%) cORR in CPS≥10

BICR: Blinded Independent Central Review; CPS: Combined Positive Score; CR: Complete Response; PD-L1: Programmed Death-Ligand 1 PR: Partial Response

Rosenberg JE et al. ESMO 2022;Abstract LBA73.

U31402-A-U102 (Cohort 2): Patritumab deruxtrecan Activity in Patients with Identified Driver Genomic Alterations



Steuer CE et al. ASCO 2022;Abstract 9017.

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MODULE 3: PARP Inhibitor Update

Appendix

RTP RESEARCH TO PRACTICE

Case Presentation: Dr Ursula Matulonis

68 yo diagnosed with advanced stage IIIC high grade fallopian tube cancer after noting several weeks of vaginal bleeding and spotting. The patient underwent optimal cytoreductive surgery and also had IP port placed. She started chemotherapy and received one cycle of intraperitoneal chemotherapy, which she tolerated poorly and **then completed the six cycles with intravenous carboplatin and paclitaxel chemotherapy.**

She was found to have a germline PMS2 mutation. She started **oral niraparib (tx 1 maintenance) in June 2017 and this was used as primary maintenance.** She started 100 milligrams per day, briefly increasing to 200 milligrams a day, but developed significant tachycardia and hypertension requiring cardiology consult and oral medications for blood pressure control. 3 months later after completion of carboplatin and paclitaxel and start of niraparib, her CA-125 rose from 25 at the completion of chemotherapy to 352. CT scan showed small volume ascites and peritoneal carcinomatosis.

Case Presentation: Dr Ursula Matulonis (continued)

She started **bevacizumab and pegylated liposomal doxorubicin (#2)** and received three treatments of PLD, but developed significant skin toxicities and mouth sores. She discontinued this treatment after 3 treatments, and her CA125 continued to rise despite treatment to 580.

The patient then started **carboplatin and gemcitabine (tx #3) and received six cycles.** Her CA-125 dropped to a nadir of 206 after 3 cycles, but then rose during the latter 3 cycles of carbo/gem.

Patient started on **mirvetuximab (tx #4)** and stayed on treatment for 11 months before cancer progression. Best response was stable disease and -20% reduction by RECIST v1.1.

Toxicities experienced included grade 1 corneal microcysts, grade 1 blurred vision, grade 1 nausea.

Dana-Farber
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Mirvetuximab soravtansine

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SORAYA

- Treatment options for platinum resistant ovarian cancer (PROC) are limited, consisting primarily of single-agent chemotherapy, and the majority of patients will have received prior bevacizumab (BEV)[1,2]
  - Single-agent chemotherapy has limited activity (ORR, 4%–13%) along with considerable toxicity[3-6]
- FRα, also known as folate receptor 1 (FOLR1), has limited expression on normal tissues but is elevated in most ovarian cancers, which makes FRα an attractive target for the development of novel therapies[7,8]
- Single agent MTD of mirvetuximab[9] = 6 mg/kg calculated by Adjusted Ideal Body weight
- SORAYA is a global, single-arm, phase 3 study that evaluated MIRV for the treatment of PROC in patients with high FRα expression who received 1 to 3 prior therapies, including required prior BEV[10,11]

MIRV is the first biomarker-directed agent demonstrating antitumor activity in patients with folate receptor alpha (FRα)-high platinum-resistant ovarian cancer (PROC)[9,10]

1. Indini A, et al. *Cancers (Basel)*. 2021;13(7):1663. 2. McClung EC, Wenham RM. *Int J Womens Health*. 2016;8:59-75. 3. Pujade-Lauraine E, et al. *J Clin Oncol*. 2014;32(13):1302-1308. 4. Gaillard S, et al. *Gynecol Oncol*. 2021;163(2):237-245. 5 Hamanishi J, et al. *J Clin Oncol*. 2021;39(33):3671-3681. 6. Pujade-Lauraine E, et al. *Lancet Oncol*. 2021;22(7):1034-1046. 7. Birrer MJ, et al. *Oncologist*. 2019;24(4):425-429. 8. Zamarin D, et al. *J Immunother Cancer*. 2020;8(1):e000829. doi:10.1136/jitc-2020-000829. 9. Moore et al, Cancer 2017 10. Matulonis UA, et al. ASCO 2022, 11. Matulonis UA, et al. SGO 2022 Annual Meeting on Women's Cancer.

Mirvetuximab Ocular toxicities

--Occur because of off-target effects on the cornea, with primary involvement of the corneal epithelium which leads to blurred vision and can be associated with microcystic keratopathy.

--Corneal damage begins peripherally after mirvetuximab reaches the cornea via the vascularized limbal region.

--Internalization and accumulation of DM4 occurs into transient amplifying cells. These damaged progenitor cells then migrate centripetally and are sufficient to account for the development of microcystic deposits seen in patients.

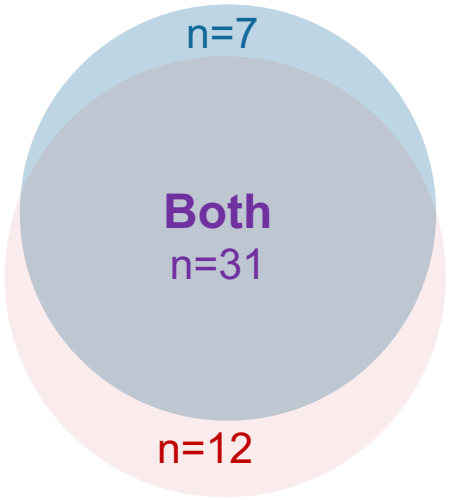
--Ocular steroids can slow down the proliferation of limbal stem cells, potentially leading to a lower sensitivity to the damaging effects of chemotherapeutics, including the DM4 payload present in mirvetuximab soravtansine.

--Ocular steroids also may lead to thinning of the corneal epithelium which can facilitate shedding of corneal microcysts induced by exposure to the ADC.

Matulonis et al, CCR 2018, Zhao et al, Cancer Research 2018, Gan et al, Neuro Onc 2018

Unique Events Specific to MIRV: Keratopathy and Blurred Vision

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



- **Proactive supportive care**
  - Lubricating artificial tears
  - Corticosteroid eye drops
- **Predictable**
  - Median time to onset: cycle 2 (~1.5 months)
- **Manageable with dose modifications, if needed**
  - 22% of patients (23/106) had dose delay and/or reduction
- **Reversible**
  - At data cutoff: >80% of patients with grade 2–3 events had resolved to grade 0–1
    - 9 patients still receiving MIRV or being followed up for resolution
- **<1% discontinuation due to ocular events**
  - 1 of 106 patients discontinued due to grade 4 keratopathy,† which resolved within 15 days

The grouped preferred term “Keratopathy” includes the following preferred terms: “corneal cyst,” “corneal disorder,” “corneal epithelial microcysts,” “keratitis,” “keratopathy,” “limbal stem cell deficiency,” “corneal opacity,” “corneal erosion,” “corneal pigmentation,” “corneal deposits,” “keratitis interstitial,” “punctate keratitis,” and “corneal epithelial defect.” †One patient experiencing a grade 4 event recorded as keratopathy was based upon the visual acuity evaluation of one eye (20/200). This patient had confirmed grade 2 corneal changes, and both the visual acuity and these corneal changes resolved completely (grade 0) in 15 days by ophthalmic exam.

Matulonis et al, SGO 2022, ASCO 2022, IGCS 2022

Conclusions

MIRV demonstrates clinically meaningful antitumor activity in patients with FRα-high platinum-resistant ovarian cancer

- **ORR: 32.4%** investigator-assessed, including 5 complete responses
- **Median DOR: 6.9 months**
- Consistent antitumor activity regardless of prior number of therapies or prior PARPi

The safety and tolerability profile of MIRV in SORAYA is consistent with that observed in previous studies

- Low-grade, reversible ocular and GI events, manageable with supportive care
- No appreciable myelosuppression and limited low-grade neuropathy
- 7 patients (7%) discontinued treatment due to TRAEs
  - Only 1 patient discontinued due to ocular event

These results position MIRV to become a practice-changing, biomarker-driven standard of care treatment option for patients with FRα-positive platinum-resistant ovarian cancer

Single agent mirvetuximab dose and mirvetuximab combinations

1) Phase Ib of carboplatin and mirvetuximab[1]:

Table 2
Summary of dose escalation.

Mirvetuximab soravtansine dose	Carboplatin dose	No. of patients	Treatment-related SAEs and DLTs
5 mg/kg	AUC4	4	None
5 mg/kg	AUC5	4	None
6 mg/kg	AUC5	10	SAE: Diarrhea (grade 3) DLT: Vasculitis (grade 3)

Table 4
Summary of efficacy measures.

Endpoint	$n = 17$
ORR (confirmed)	71%
95% CI	(44, 90)
Median PFS (months)	15
95% CI	(9.9, −)
Median DOR (months)	NR
95%CI	(5.7, −)

ORR, objective response rate; PFS, progression-free survival; DOR, duration of response; NR, not reached.

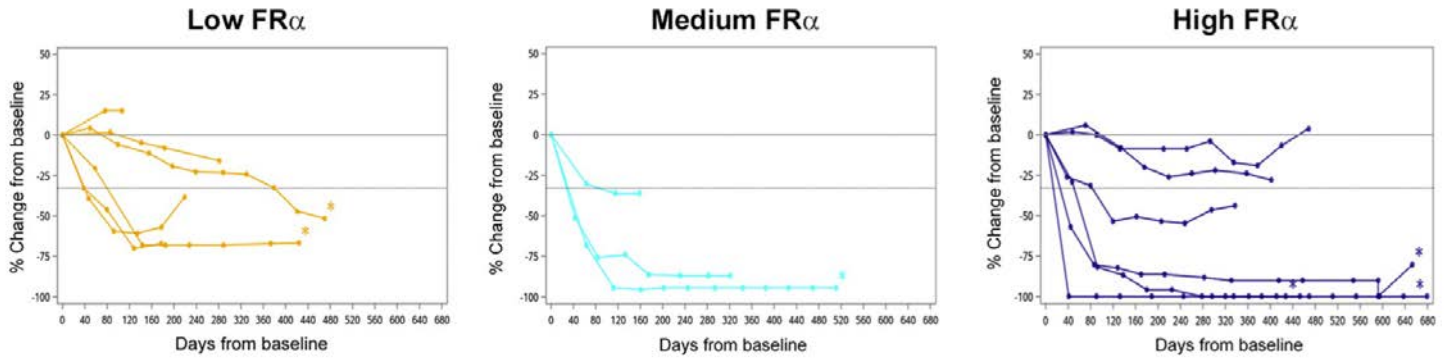


Fig. 1. Percent tumor change in target lesions by FRα expression. Data are presented from 15 patients as individuals with non-measurable disease were enrolled in the study. Asterix denotes patients still on study at time of final analyses. Dotted line in plots corresponds to 30% decrease in tumor size.

2) carboplatin and bevacizumab[2]

[1]Moore et al, Gyn Onc 2018
[2]O'Malley et al, IGCS 2022

Study Design: Mirvetuximab and Bevacizumab

As part of the phase 1b/2 FORWARD II study (NCT02606305), MIRV combined with BEV was evaluated in patients with recurrent FRα-expressing[a] ovarian cancer[1,2]

Objective: Evaluate the efficacy and safety of MIRV+BEV in recurrent FRα-expressing epithelial ovarian cancer (EOC)[1,2,b]

Patient population: Patients with FRα-expressing EOC who were eligible for non-platinum therapy[1]

- FRα expression was assessed using immunohistochemistry PS2+ scoring, scored as the percent of viable tumor cells staining with ≥2+ intensity
  - FRα Low: ≥25% to 49%
  - FRα Medium: 50% to 74%
  - FRα High: ≥75%
- Platinum status was stratified by platinum-free interval (PFI) as PFI > 6 months or PFI ≤ 6 months
- BEV treatment status was defined as BEV-naïve or BEV-treated (defined as having received BEV in any line of therapy)

Treatment schedule: MIRV 6 mg/kg, adjusted ideal body weight[c] + BEV 15 mg/kg intravenously on day 1 of a 3-week cycle[1]

Primary endpoint: Confirmed ORR by RECIST v1.1[2]

Secondary endpoints: DOR, PFS, safety[2]

References: 1. O'Malley DM, et al. Slides presented at: SGO Annual Meeting; March 18-21, 2022; Phoenix, AZ. **2.** ClinicalTrials.gov identifier: NCT02606305. Updated December 17, 2021. Accessed August 11, 2022. https://www.clinicaltrials.gov/ct2/show/NCT02606305

Conclusions

MIRV+BEV demonstrated antitumor activity in patients with recurrent FRα-expressing ovarian cancer

- In the overall population, treatment with MIRV+BEV resulted in confirmed ORR of 44%
- The median duration of these responses was 11.8 months
- Overall, MIRV+BEV led to a median PFS of 8.2 months

•Durable antitumor activity was seen across all levels of FRα expression, in patients that were BEV naïve and pre-treated, and regardless of platinum-free interval

The safety profile of MIRV+BEV reflects the safety profile of each drug as a monotherapy; the most common TRAEs were diarrhea, blurred vision, and fatigue

These data provide evidence to support MIRV+BEV as an efficacious combination choice for patients with FRα-expressing ovarian cancer who are eligible for treatment with BEV

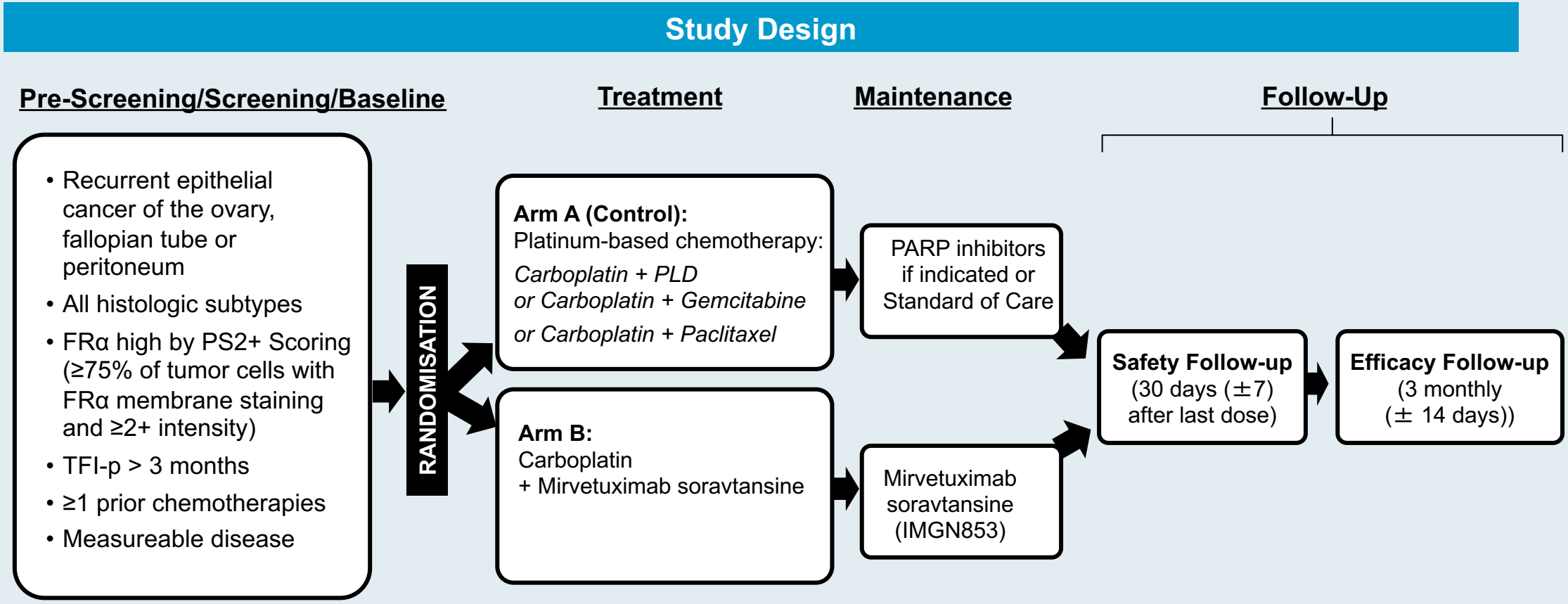
A randomized phase 3 trial (GLORIOSA) is planned to evaluate the efficacy and safety of MIRV+BEV in the maintenance setting for the treatment of patients with FRα-high platinum-sensitive ovarian cancer[1]

Ongoing Trials of Mirvetuximab

Trial	NCT#	Accrual and key eligibility
A Study of Mirvetuximab Soravtansine vs. Investigator's Choice of Chemotherapy in Platinum-Resistant, Advanced High-Grade Epithelial Ovarian, Primary Peritoneal, or Fallopian Tube Cancers With High Folate Receptor-Alpha Expression (MIRASOL)	NCT04209855	n=430 Primary endpoint: PFS as assessed by investigator up to 3 prior lines of treatment
Study of Carboplatin and Mirvetuximab Soravtansine in First-Line Treatment of Patients Receiving Neoadjuvant Chemotherapy With Advanced-Stage Ovarian, Fallopian Tube or Primary Peritoneal Cancer	NCT04606914	n=70 Primary Endpoint: PFS, ORR
Mirvetuximab Soravtansine Monotherapy in Platinum-Sensitive Epithelial, Peritoneal, and Fallopian Tube Cancers (PICCOLO)	NCT05041257	n=75 Primary endpoint: Investigator-assessed ORR Patients must have received at least 2 prior systemic lines of platinum therapy; Patients may have received up to but no more than 1 prior independent non-platinum cytotoxic therapy
Mirvetuximab Soravtansine With Bevacizumab Versus Bevacizumab as Maintenance in Platinum-sensitive Ovarian, Fallopian Tube, or Peritoneal Cancer (GLORIOSA)	NCT05445778	n=418 Primary endpoint: PFS as assessed by investigator. Patients must have relapsed after 1 line (first line) of platinum-based chemotherapy and have platinum-sensitive disease
Mirvetuximab soravtansine with Carboplatin in Second-line Treatment of FRα Expressing, Platinum-sensitive Epithelial Ovarian Cancer followed by Mirvetuximab maintenance	NCT05456685	n=114 Primary endpoint: ORR by investigator FRα positivity of ≥ 25% of tumor staining at ≥ 2+ intensity, and patients must have relapsed after 1 prior line of platinum-based chemotherapy.

Additional Data:
Mirvetuximab Soravtansine

AGO-OVAR 2.34/MIROVA Randomized Phase II Study Design



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

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

RTP RESEARCH TO PRACTICE

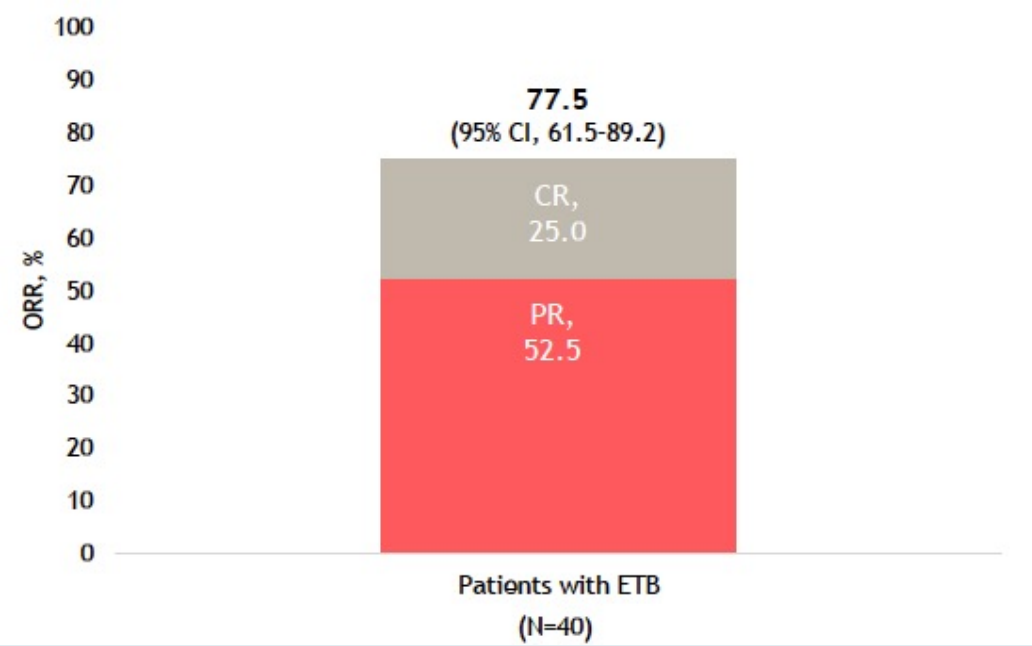
Characterization of Extended Treatment Benefit from Three Phase I and III Clinical Trials Examining Patients with Folate Receptor Alpha-Positive Recurrent Ovarian Cancer Treated with Single-Agent Mirvetuximab Soravtansine

Oaknin A et al.

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

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

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



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

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

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

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

ETB Analysis: Conclusions

- In a pooled analysis of 466 patients, MIRV monotherapy showed ETB in 40 patients (9%)
  - Most patients with ETB had stage III EOC (83%), 1 prior line of therapy (55%), prior bevacizumab exposure (60%), and prior PARPi exposure (53%)
  - ETB occurred in patients with a wide range of FRα expression but did so predominantly among those with high FRα expression
  - ETB was observed among patients with CR, PR, and SD; ETB was not restricted to patients demonstrating CR
- In patients with ETB, the overall adverse event profile is consistent with the previously reported ISS of 464 patients,[17] with no new safety signals identified
  - Adverse events were primarily low-grade gastrointestinal and ocular events that generally resolved with supportive care or, if needed, dose modifications
- The safety profile of MIRV in these patients suggests minimal cumulative toxicity
- The efficacy and safety outcomes in patients with long-term use supports MIRV's potential to become a new standard of care for FRα-expressing ovarian cancer

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

Agenda

PROLOGUE: Antibody-Drug Conjugates Across Oncology

MODULE 1: Antibody-Drug Conjugates in Ovarian Cancer

- Mirvetuximab Soravtansine
- **Upifitamab Rilsodotin**

MODULE 2: Tumor Treating Fields

MODULE 3: PARP Inhibitor Update

Appendix

RTP RESEARCH TO PRACTICE

Case Presentation: Dr Debra Richardson

- 72yo BRCAwt with PROC, CDKN2A- melanoma/pancreatic syndrome germline mutation
- Treatment history
  - 3 cycles NACT, then interval debulking to 1mm gross residual, then 3 cycles adjuvant carboplatin and paclitaxel and bevacizumab. CA125 9852 baseline, CA125 65 completion of chemotherapy, CT NED
  - Maintenance bevacizumab x7 cycles, dc'd for arthralgias
  - CA125 rising, CT with measurable disease 14 month PFI
  - Carboplatin and liposomal doxorubicin x 10 cycles- SD best response. PD with malignant SBO. CA125 1446. CT with carcinomatosis

Case Presentation: Dr Debra Richardson (continued)

- Opted for trial with XMT-1536 (Upifitimab rilsodotin)
- Received 16 cycles
- Best response SD, CA125 baseline 1446, rose to 4631 C2D1, nadired at 234, gradually rose to 2309. PD per RECIST
- Dose reduced twice.
  - C2D1 from 43mg/m2 to 36mg/m2.
    - AE: abdominal pain, nausea, fatigue, fever
  - C7D1 to 20mg/m2
    - Proteinuria grade 2
- Bucket list trip to Spain
- AWD

Research To Practice

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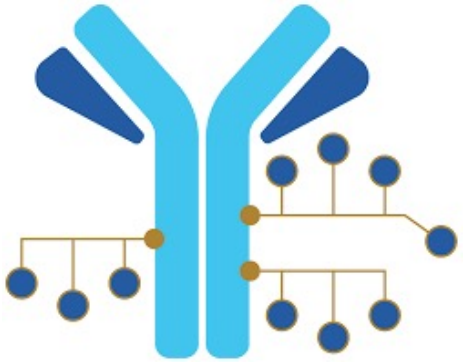
November 3, 2022

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



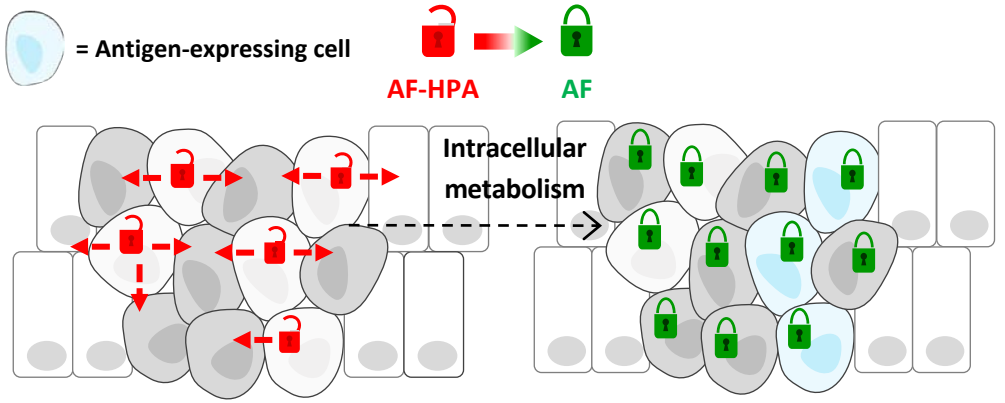
UpRi

Antibody: Humanized monoclonal anti-NaPi2b[1]

Linker: Polymer scaffold; cleavable ester linker[2]

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

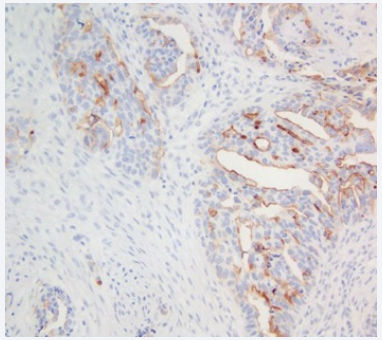
Drug-to-Antibody Ratio: ~10



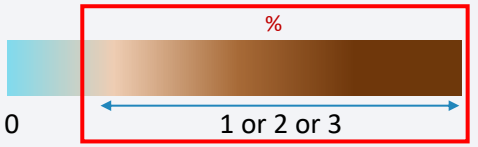
Upon ADC internalization into tumor cells and efficient release of payload, AF-HPA payload is metabolized to AF that remains highly potent but loses the ability to cross the cell membrane, locking it in the tumor, controlling the bystander effect, and consequently limiting impact on adjacent healthy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

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

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



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



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

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

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

Study Closed for Enrollment

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

Ovarian Cancer Cohort

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

UpRi IV Q4W until disease progression or unacceptable toxicity

36 mg/m^2 cohort initiated in August 2019

43 mg/m^2 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

[a] HGSOC including fallopian tube and primary peritoneal cancer.

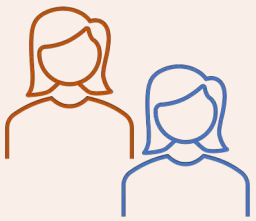
CT, computed tomography; DCR, disease control rate; DoR, duration of response; ECOG, Eastern Cooperative Oncology Group; HGSOC, high-grade serous ovarian cancer; IHC, immunohistochemistry; IV, intravenous; MRI, magnetic resonance imaging; MTD, maximum tolerated dose; NaPi2b, sodium-dependent phosphate transport protein 2B; ORR, overall response rate; PS, performance score; Q4W, every 4 weeks; RECIST, Response Evaluation Criteria in Solid Tumors; RP2D, recommended phase 2 dose; UpRi, upifitamab rilsodotin.

1. Tolcher AW et al. ASCO Annual Meeting 2019; Abstract 3010. 2. Richardson DL et al. SGO Annual Meeting 2020; LBA8. 3. Hamilton E et al. ESMO Virtual Congress 2020; Abstract 2365.

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/m^2) (n=29)

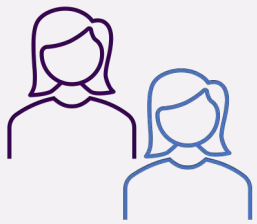


12 patients at **36 mg/m^2** starting dose (all BSA levels)

+

17 patients at ~80 mg starting dose with BSA ≥1.8 who received an actual dose of **33 to 38 mg/m^2**

Dose Group 43 (>38–43 mg/m^2) (n=66)



39 patients at **43 mg/m^2** starting dose with BSA <1.8

+

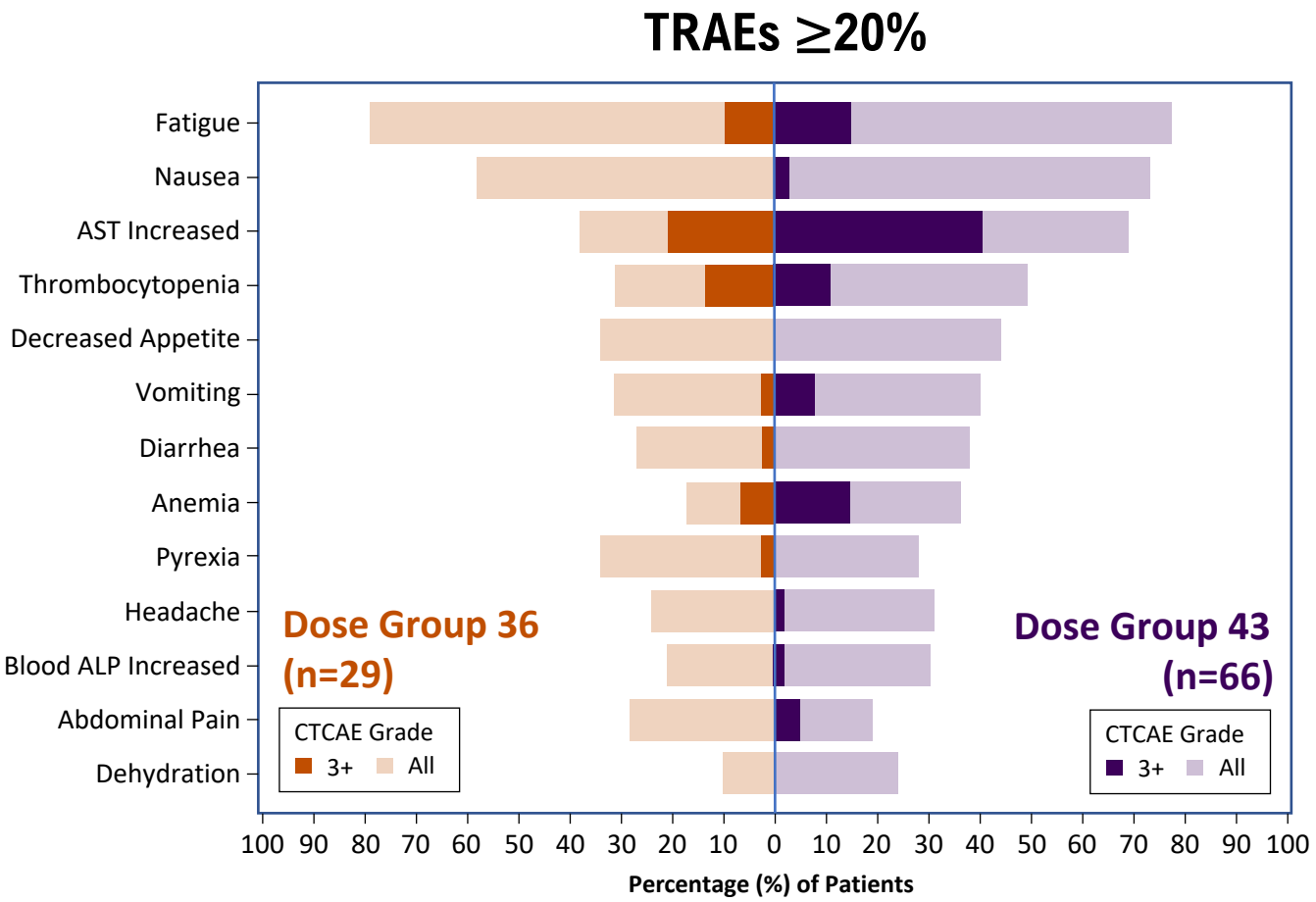
27 patients at ~80 mg starting dose with BSA ≥1.8 who received an actual dose of **>38 mg/m^2**

[a] Two patients received <30 mg/m^2 and therefore were not included in either dose group.

BSA, body surface area; ORR, overall response rate; PROC, platinum-resistant ovarian cancer; UpRi, upifitamab rilsodotin.

Treatment-Related AEs by UpRi Dose Group

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



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

Data cut: June 10, 2021. Analysis with 95 patients. Two patients received <30 mg/m^2 and therefore were not included in either dose group.

[a] Dose Group 36 pneumonitis: Grade 1–2 (n=2), Grade 3+ (n=0); Dose Group 43 pneumonitis: Grade 1–2 (n=5), Grade 3+ (n=4).

AE, adverse event; ALP, alkaline phosphatase; AST, aspartate aminotransferase; CTCAE, Common Terminology Criteria for Adverse Events; SAE, serious adverse event; TRAE, treatment-related adverse event; UpRi, upifitamab rilsodotin.

Dose Modification by UpRi Dose Group

Dose Group 36 Had Fewer Treatment-Related Dose Modifications and Treatment Discontinuations Compared to Dose Group 43

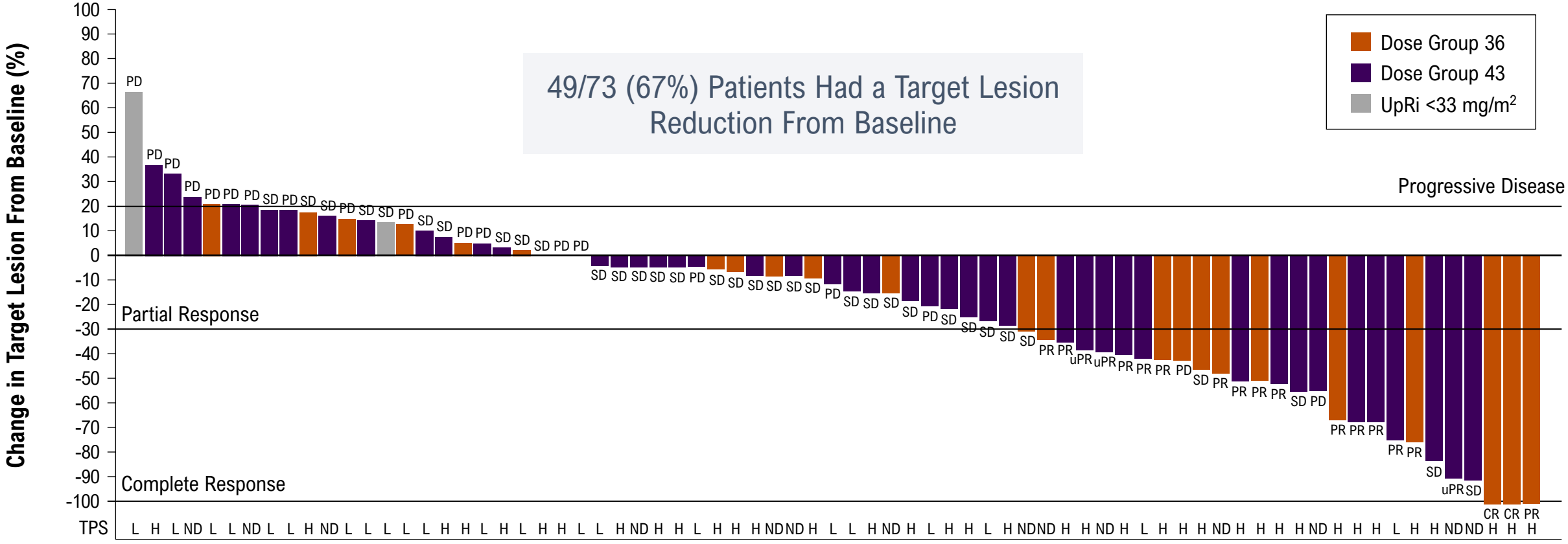
	Dose Group 36 (n=29)	Dose Group 43 (n=66)
Any Dose Modification d/t TRAE (Reduction, Delay, Discontinuation), n (%)	**10 (34)**	**32 (48)**
Dose Reduction d/t TRAE, n (%)	6 (21)	20 (30)
Dose Delay d/t TRAE, n (%)	4 (14)	12 (18)
Dose Discontinuation d/t TRAE, n (%)	2 (7)	8 (12)

Data cut: June 10, 2021. Analysis with 95 patients. Two patients received <30 mg/m^2 and therefore were not included in either dose group.

d/t, due to; TRAE, treatment-related adverse event; UpRi, upifitamab rilsodotin.

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



Data cut: June 10, 2021. Analysis with 73 evaluable patients. Two patients excluded as post-baseline tumor measurement shows “Not Measurable”, yet “PD” was assigned by investigator in response dataset. There were 22 unevaluable patients: 4 in Dose Group 36, 2 patient withdrawals (1 enrolled in hospice), 2 patient deaths; 18 in Dose Group 43, 5 patient withdrawals, 1 clinical progression, 3 due to adverse events, 8 deaths, 1 had not reached first scan.

CR, complete response; H, high; L, low; ND, not yet determined; PD, progressive disease; PR, partial response; RECIST, Response Evaluation Criteria in Solid Tumors; SD, stable disease; TPS, tumor proportion score; uPR, unconfirmed partial response; UpRi, upifitamab rilsodotin.

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

44% ORR in Dose Group 36 for Patients With NaPi2b-High Ovarian Cancer

		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

Data cut: June 10, 2021. Two patients received <30 mg/m^2 and therefore were not included in either dose group. All responses are confirmed. There were 75 evaluable patients. There were 22 unevaluable patients: 4 in Dose Group 36, 2 patient withdrawals (1 enrolled in hospice), 2 patient deaths; 18 in Dose Group 43, 5 patient withdrawals, 1 clinical progression, 3 due to adverse events, 8 deaths, 1 had not reached first scan. Of 4 unevaluable patients in Dose Group 36, 2 were NaPi2b-high; of 18 unevaluable in Dose Group 43, 10 were NaPi2b-high.

CR, complete response; DCR, disease control rate; DoR, duration of response; NaPi2b, sodium-dependent phosphate transport protein 2B; ORR, overall response rate; PR, partial response; TPS, tumor proportion score; UpRi, upifitamab rilsodotin.

UPLIFT (ENGOT-ov67 / GOG-3048)

UpRi Single-Arm Registrational Trial in Platinum-Resistant Ovarian Cancer

Global
US, Europe, Australia, Canada

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

Key Inclusion Criteria

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

Key Exclusion Criteria

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

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

Primary Endpoint

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

Secondary Endpoint

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

Other Secondary Endpoints

- DoR
- Safety

Prospectively-defined retrospective analysis to validate NaPi2b biomarker cutoff

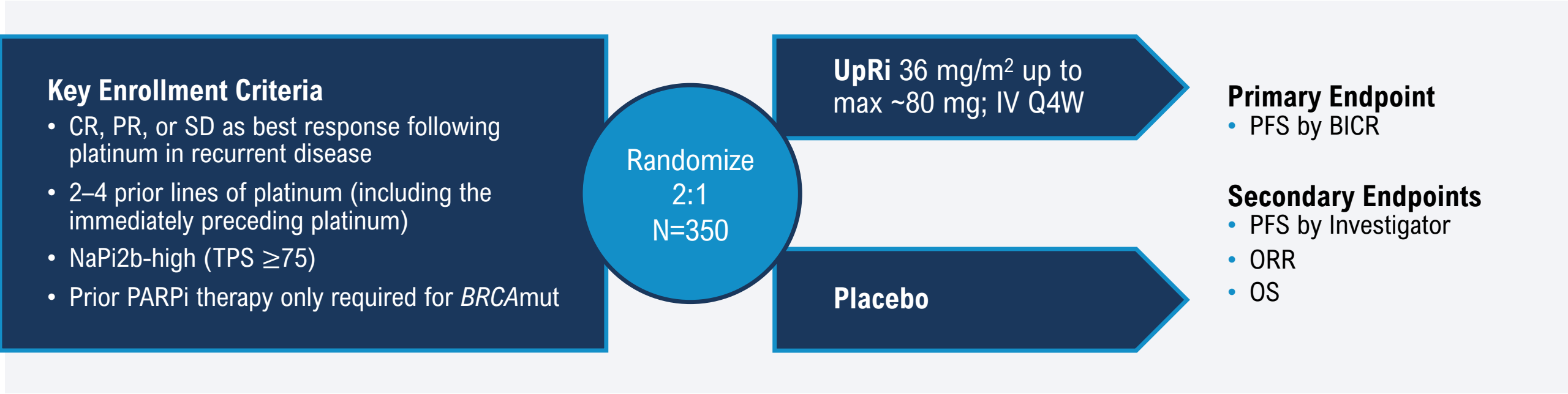
NCT03319628: Trial Completed Enrollment

[a] HGSOC including fallopian tube and primary peritoneal cancer.

HGSOC, high-grade serous ovarian cancer; IV, intravenous; DoR, duration of response; ECOG, Eastern Cooperative Oncology Group; FPD, first patient dosed; NaPi2b, sodium-dependent phosphate transport protein 2B; ORR, overall response rate, PROC, platinum-resistant ovarian cancer; PS, performance score; Q4W, every 4 weeks; RECIST, Response Evaluation Criteria in Solid Tumors; UpRi, upifitamab rilsodotin.

UP-NEXT (GOG-3049 / ENGOT-OV71-NSGO-CTU)

Phase 3 Study of UpRi Monotherapy Maintenance vs Placebo in Recurrent Platinum-Sensitive Ovarian Cancer



NCT05329545: Actively Enrolling

BICR, blinded independent central review; *BRCA*mut, breast cancer susceptibility gene mutated; CHMP, Committee for Medicinal Products for Human Use; CR, complete response; FDA, Food and Drug Administration; IV, intravenous; NaPi2b, sodium-dependent phosphate transport protein 2B; ORR, overall response rate; OS, overall survival; PARPi, poly (ADP-ribose) polymerase inhibitor; PFS, progression-free survival; PR, partial response; Q4W, every 4 weeks; SD, stable disease; TPS, tumor proportion score; UpRi, upifitamab rilsodotin.

Additional Data: Upifitamab Rilsodotin

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 DL et al.

IGCS 2022;Abstract 425.

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TO PRACTICE

Conclusions

- High concordance of NaPi2b status observed in both synchronous and metachronous samples from the Phase Ib UpRi study
- The high concordance of metachronous samples supports the 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 for platinum-resistant and platinum-sensitive ovarian cancer

Richardson DL et al. IGCS 2022;Abstract 425.

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

Ronny D et al.

IGCS 2022;Abstract 408.

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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 high-grade serous ovarian cancer and is a rational target for ongoing clinical trials

Ronny D et al. IGCS 2022;Abstract 408.

Agenda

PROLOGUE: Antibody-Drug Conjugates Across Oncology

MODULE 1: Antibody-Drug Conjugates in Ovarian Cancer

- Mirvetuximab Soravtansine
- Upifitamab Rilsodotin

MODULE 2: Tumor Treating Fields

MODULE 3: PARP Inhibitor Update

Appendix

Research To Practice

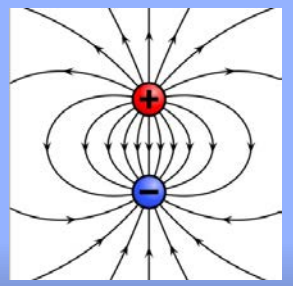
Debra L Richardson, MD
Associate Professor and Section Chief
Gynecologic Oncology
November 3, 2022

TTFields Disrupt Localization and Orientation of Polar Molecules and Organelles

Forces Are Exerted on Cell Components During Cell Division

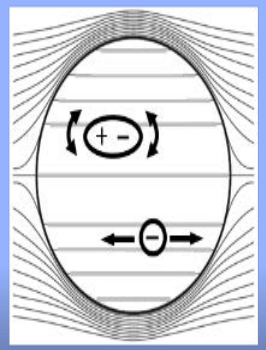
The 3 main types of cytoskeletal filaments in eukaryotic cells are microfilaments, microtubules, and intermediate filaments

physical dipole of electric charges

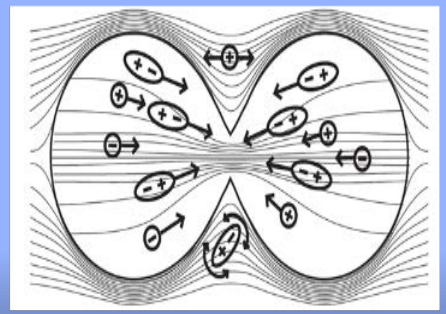


The electric dipole moment is the measure of the electrical polarity of a system of charges

Uniform electric field leads to **dipole alignment**



Nonuniform electric field leads to **dielectrophoresis**



Adapted from Gutin PH et al. 2012

Tubulin and Septin are two examples of polar molecules with very high dipole moments. In the presence of TTFields, the electric field exerted on the cancer cell "disrupts or perturbs" the function of Tubulin and Septin during mitosis

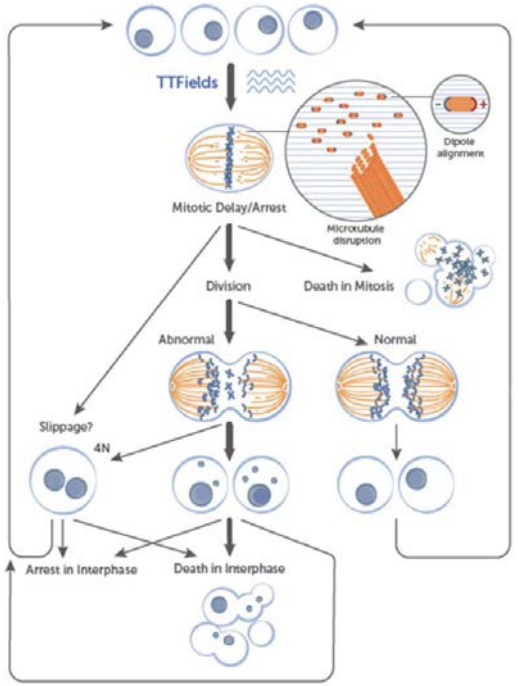
1. Kirson ED et al. *Cancer Res*. 2004;64(9):3288-3295. 2. Kirson ED et al. *Proc Natl Acad Sci U S A*. 2007;104(24):10152-10157.
3. Gera N et al. *PLoS One*. 2015;26;10(5):e0125269. 4. Giladi M et al. *Sci Rep*. 2015;5:18046.

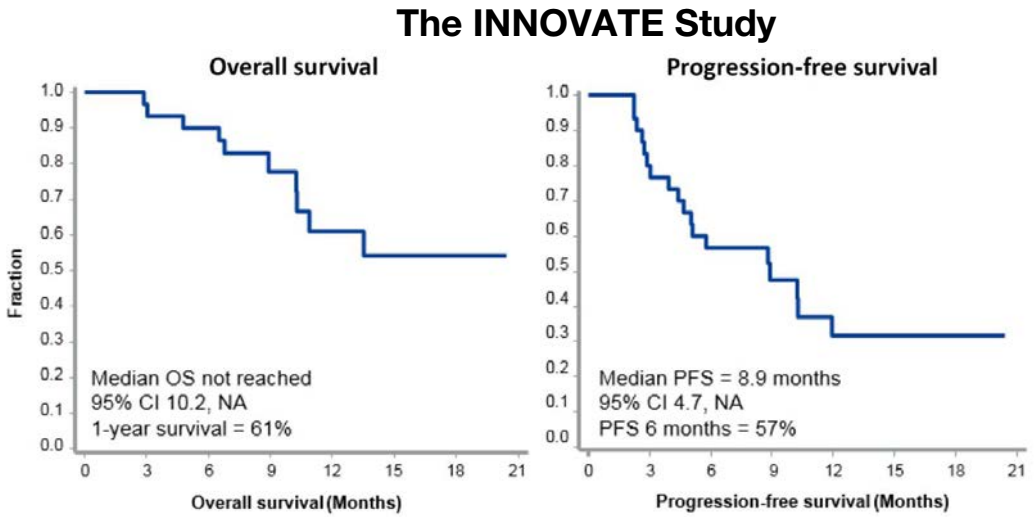
GOG-3029/INNOVATE-3: MOA and Rationale

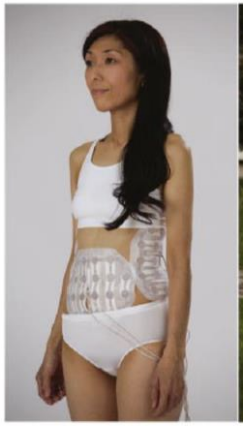
- Tumor Treating Fields (TTFields)
- FDA approvals in GBM in recurrent and primary therapy with standard chemotherapy
- Recent FDA approval in primary treatment of malignant pleural mesothelioma

Tumor Treating Fields Device

- **Electric fields exert forces on charged tubulin proteins, disrupting formation of the mitotic spindle**







Vergote I., et al., *Gynecologic Oncology,* 2018; Giladi M., et al. *Scientific Reports*, 2015; Gera N, et al. *PLoS ONE*. 2015;10(5):e0125269. doi:10.1371/journal.pone.0125269.

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

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

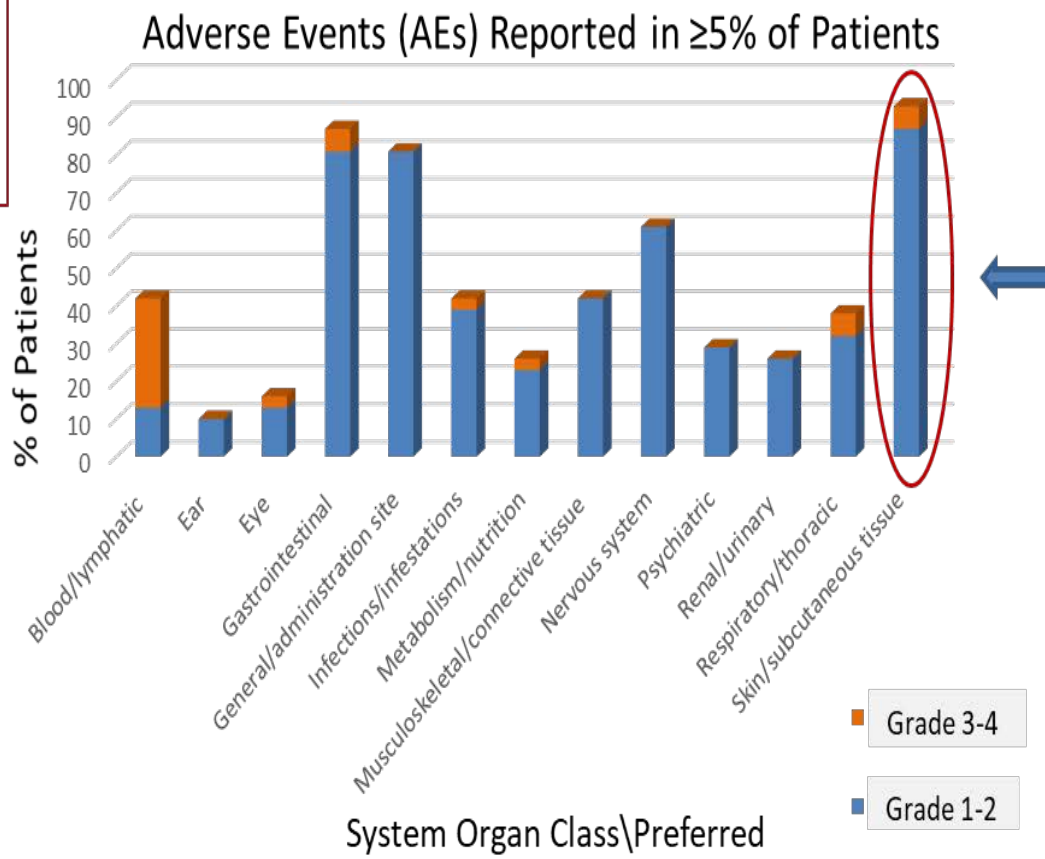
RTP RESEARCH TO PRACTICE

Adverse Events Associated with TTFields + Weekly Paclitaxel in PROC (Pilot Data)

INNOVATE Pilot Study:

- TTFields + Paclitaxel (N = 31)
- Grade 1-2 AE skin issues related to TTFields = 87% , N=28
- Grade 3-4 AE skin issues related to TTFields = 6% , N=2

Number of patients with ≥ 1 AE
Grade 1-2 : 14 (45%)
Grade 3-4: 17 (55%)



Grade 1-2 skin irritation was observed in 87% of patients related to TTFields

Vergote et al. 2018. Tumor Treating Fields in combination with paclitaxel in recurrent ovarian carcinoma: Results of the INNOVATE pilot study

ENGOT-ov50/ GOG-3029/ INNOVATE-3 (EF-28)
Study Design

Enrollment target (n=540)

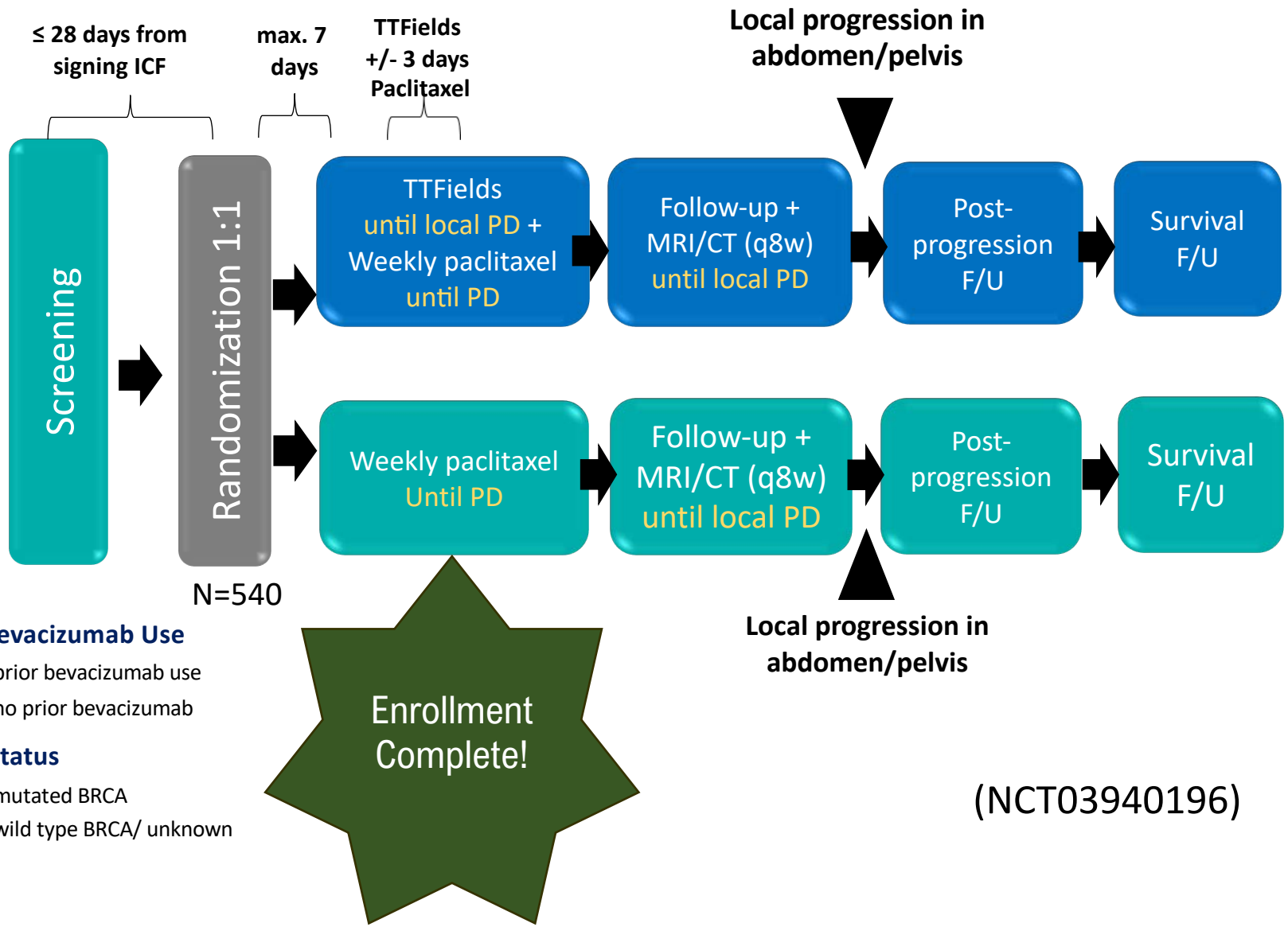
- ENGOT (60%)
- GOG (40%)
- HR estimate (<0.75)

Number of sites (n=110)

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

Stratification

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



(NCT03940196)

Additional Data:
Tumor Treating Fields

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Taylor & Francis
Taylor & Francis Group

Expert Review of Molecular Diagnostics

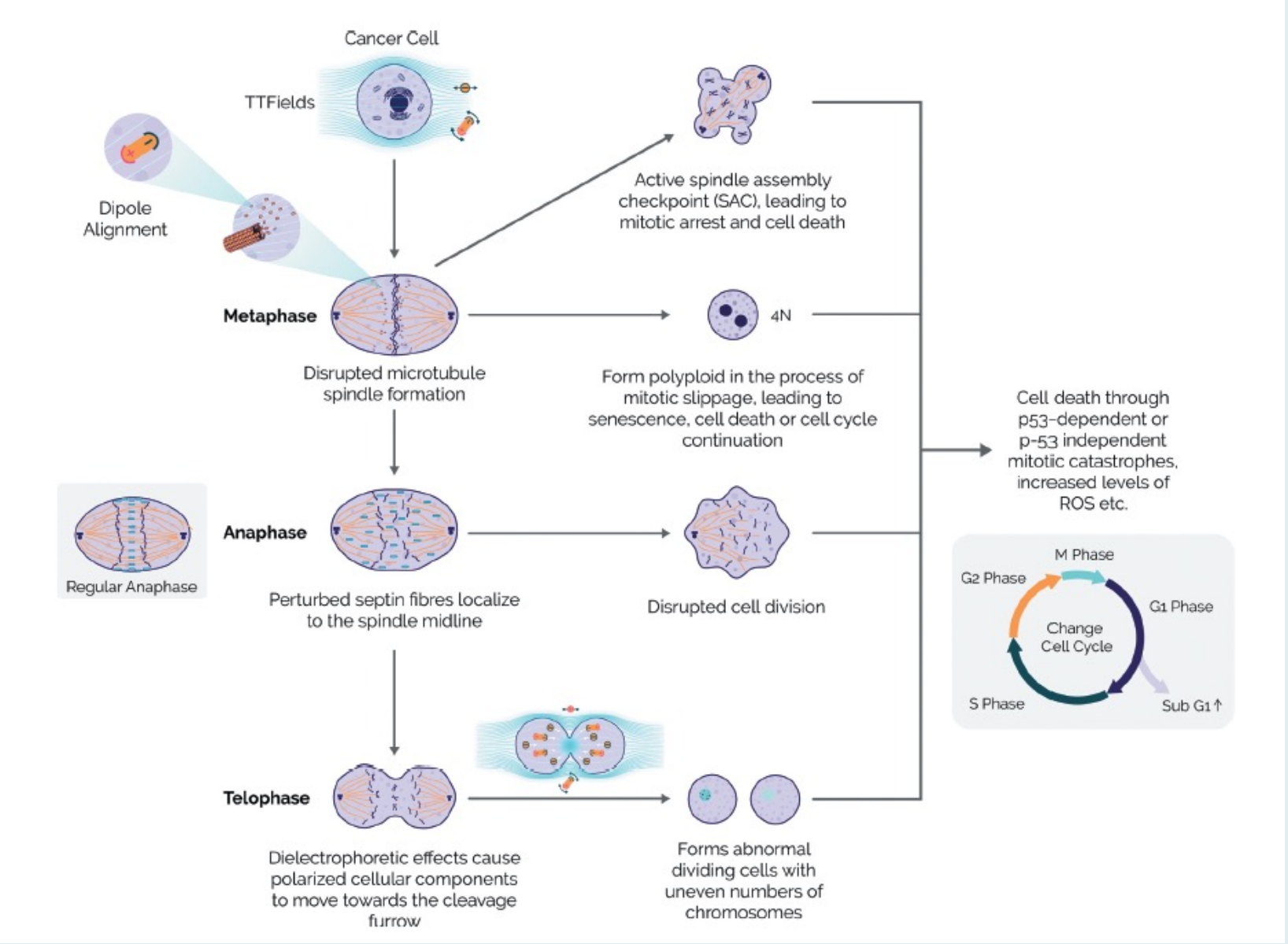
ISSN: (Print) (Online) Journal homepage: https://www.tandfonline.com/loi/iero20

Tumor treating fields: a comprehensive overview of the underlying molecular mechanism

Pengjie Hong, Nijiati Kudulaiti, Shuai Wu, Jingtao Nie & Dongxiao Zhuang

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

Tumor Treating Fields (TTFields) Effects on the Cell Cycle



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

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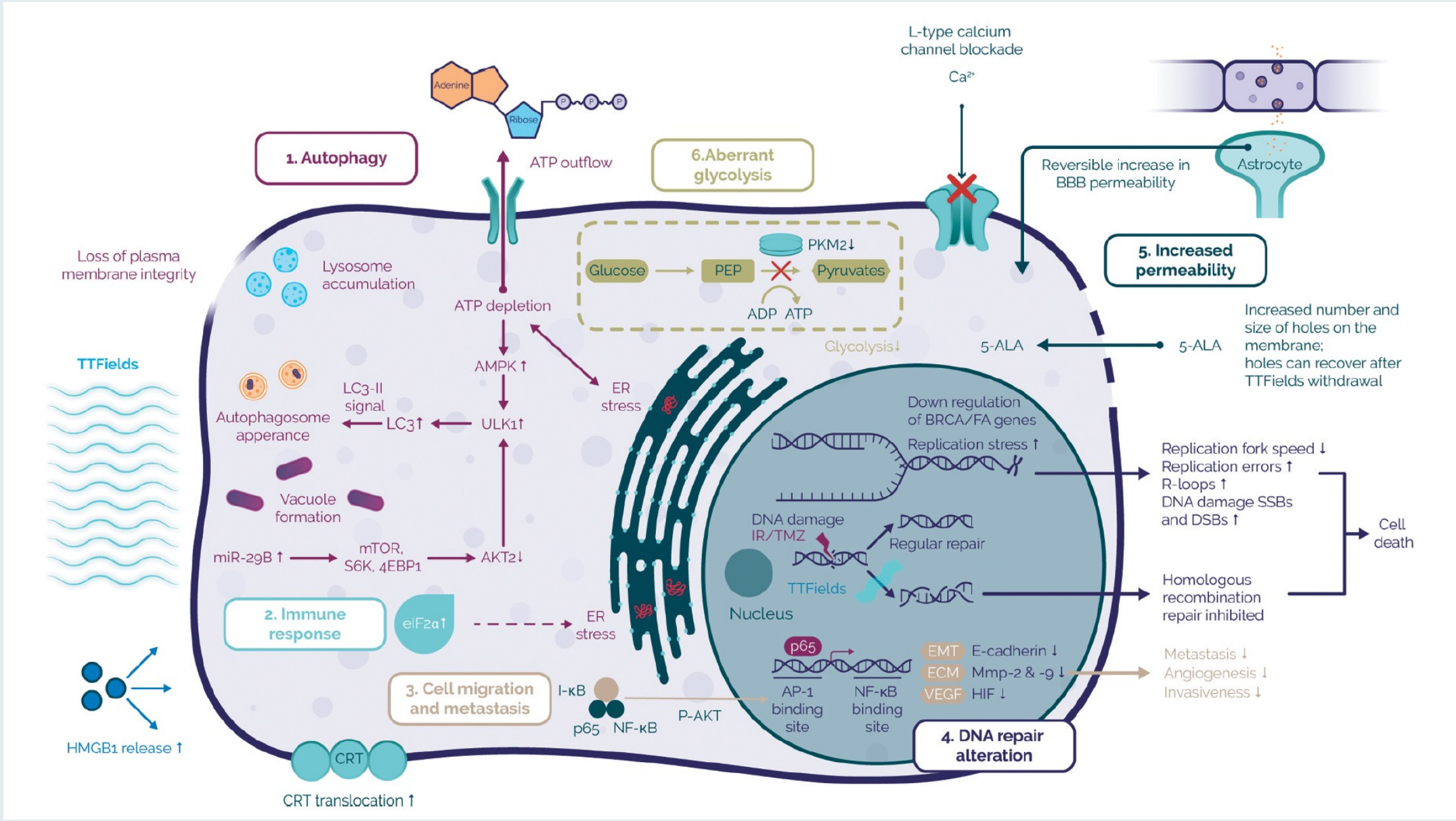
TTFields Antitumor Effects



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

Review *J Mol Cell Bio* 2022;August 15.

Anti-cancer mechanisms of action of therapeutic alternating electric fields (tumor treating fields [TTFields])

Shadi Shams[1] and Chirag B. Patel[2,3,4,*]

[1] Rowan University School of Osteopathic Medicine, Glassboro, NJ 08028, USA

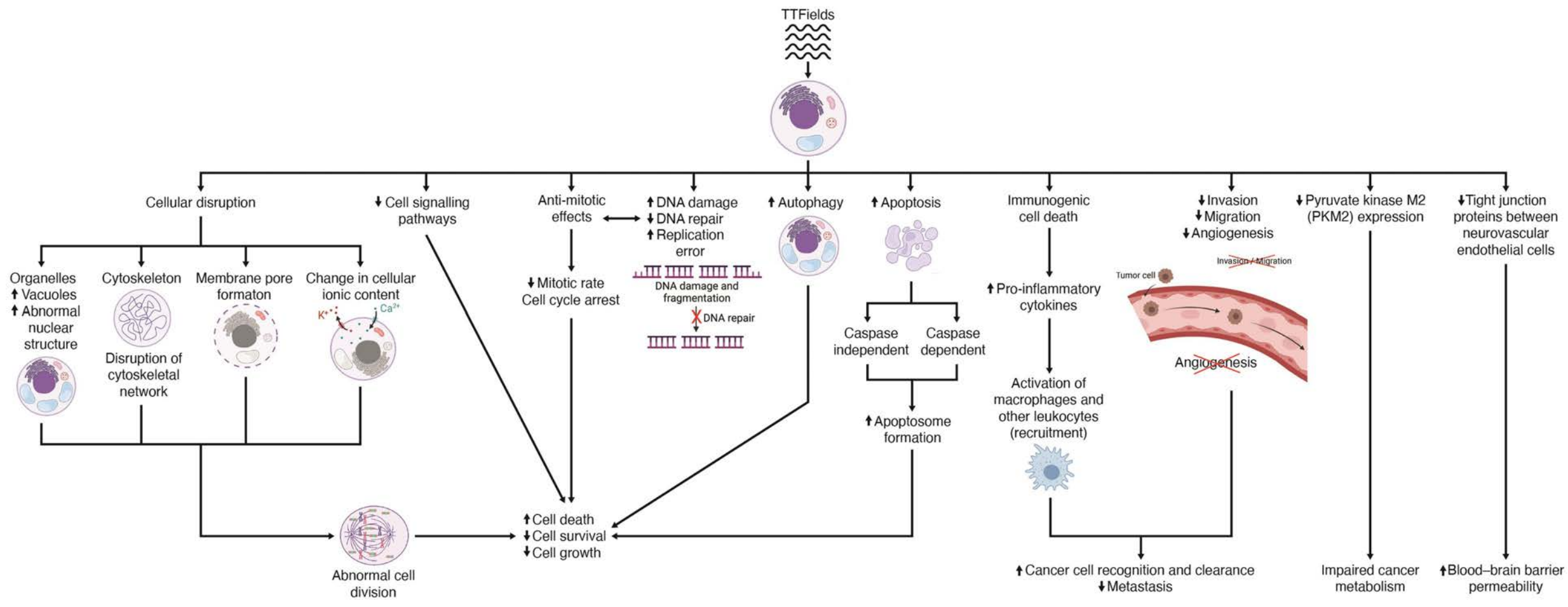
[2] Department of Neuro-Oncology, The University of Texas MD Anderson Cancer Center, Houston, TX 77030, USA

[3] Neuroscience Graduate Program, The University of Texas MD Anderson Cancer Center UTHealth Graduate School of Biomedical Sciences, Houston, TX 77030, USA

[4] Cancer Biology Program, The University of Texas MD Anderson Cancer Center UTHealth Graduate School of Biomedical Sciences, Houston, TX 77030, USA

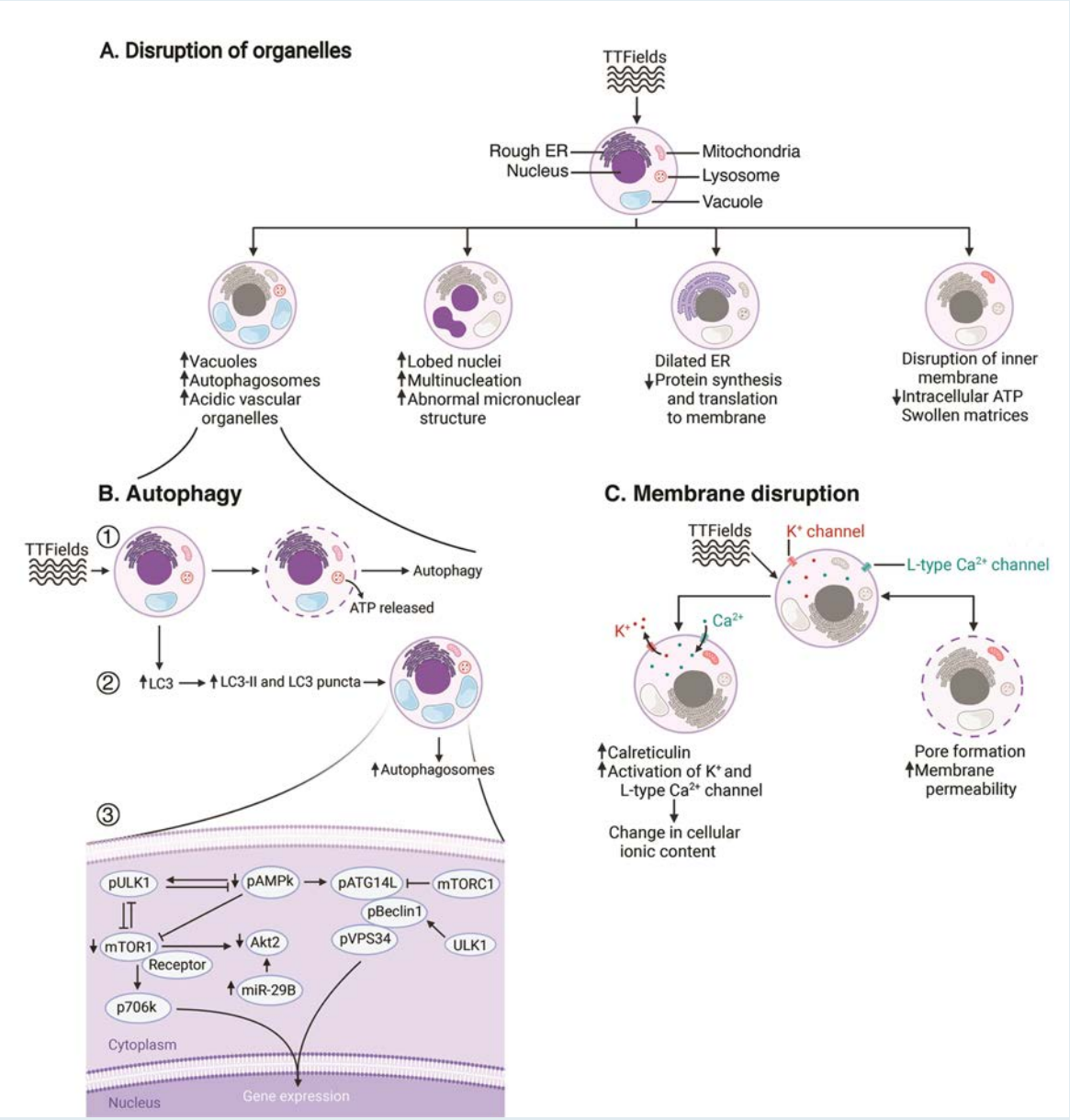
* Correspondence to: Chirag B. Patel, E-mail: cbpatel@mdanderson.org

Overview of the Mechanisms of Action of TTFields



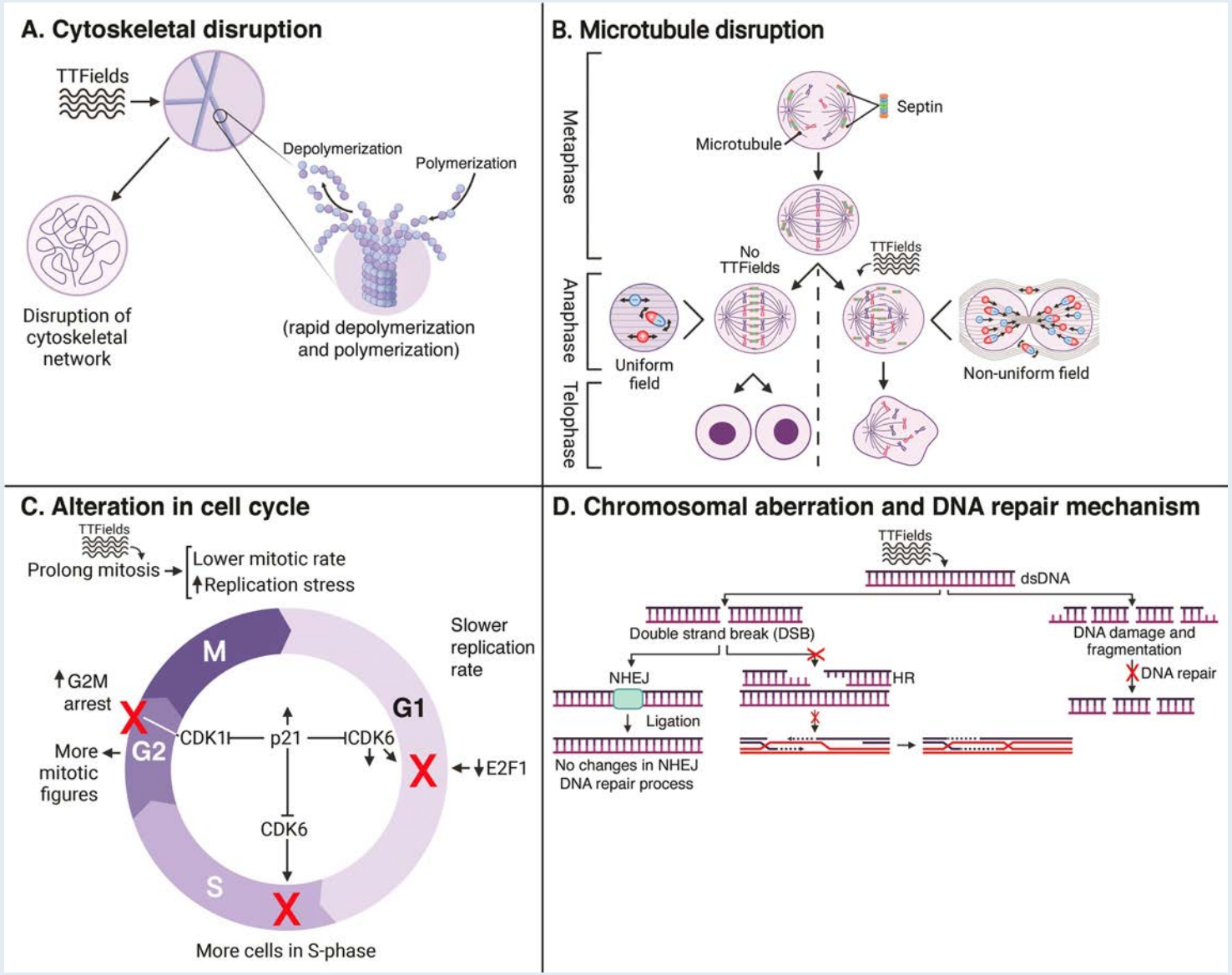
Shams S et al. *J Mol Cell Biol* 2022 August 15;[Online ahead of print].

Effects of TTFields on Cell Structure



Shams S et al. *J Mol Cell Biol* 2022 August 15;[Online ahead of print].

Effects of TTFields on Cell Cycle



Shams S et al. *J Mol Cell Biol* 2022 August 15;[Online ahead of print].

Agenda

PROLOGUE: Antibody-Drug Conjugates Across Oncology

MODULE 1: Antibody-Drug Conjugates in Ovarian Cancer

- Mirvetuximab Soravtansine
- Upifitamab Rilsodotin

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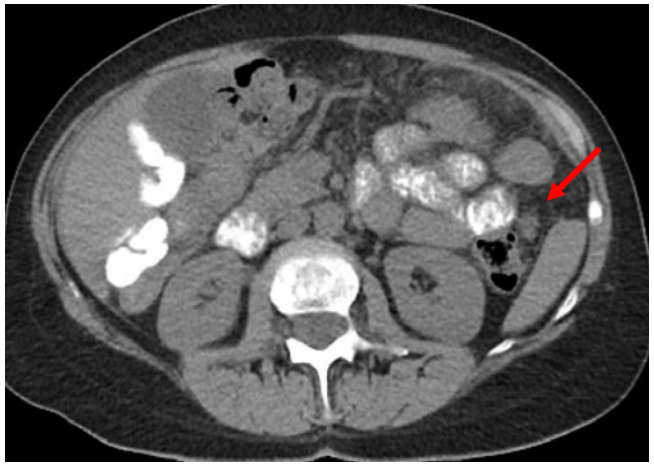
Appendix

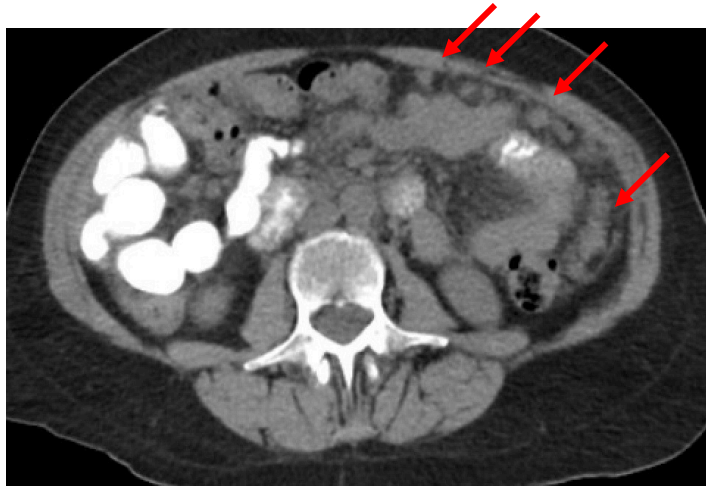
RTP RESEARCH TO PRACTICE

Case Presentation: Dr Ursula Matulonis

61 WF who presented with abdominal pain x 5-6 months.

CT showed the following:





Laparoscope done, and upfront surgery was deemed not possible.

Case Presentation: Dr Ursula Matulonis (continued)

Omental biopsy done c/w high grade serous cancer.
She underwent **neoadjuvant carboplatin, paclitaxel IV** with interval cytoreductive surgery after 3 cycles
Stage IIIC fallopian tube cancer and she underwent an R0 resection. Completed more 3 cycles post surgery. Cycle 5 delayed ~2 weeks because of an SBO admission, and **she completed 6 cycles of carboplatin/paclitaxel**.
Germline and somatic genetic testing negative, and Myriad HRD test "positive."

Started niraparib 200 mg (tx 1 maintenance), and plts dropped to 118K from 290K 3 weeks after starting, niraparib stopped and restarted 3 weeks later at 100 mg.

She is NED, remains on niraparib 100 mg/d and is scheduled to complete 3 years of niraparib in Feb 2023.

Case Presentation: Dr Debra Richardson

- 34yo G2P2 BRCA1m
- Presented with abdominal pain and 9cm adnexal mass on CT A/P
- CA125 351
- Family history of ovarian and pancreatic cancer
- Underwent diagnostic laparoscopy- findings were right pelvic mass and a 1cm diaphragm implant. RSO, diaphragm biopsy. Frozen section consistent with high grade serous carcinoma of both
- Converted to ex lap, TAH, LSO, omentectomy, appendectomy, resection of all gross disease

Case Presentation: Dr Debra Richardson (continued)

- Stage IIIb HGS FTC, postop CA125 18.6
- Received 6 cycles of IP cisplatin and paclitaxel
- CT scan NED at completion of therapy, CA125 8.5
- Started on olaparib maintenance 5 weeks after chemotherapy completed
- Side effects: Nausea, GERD, fatigue
- Completed 2 years of olaparib
- Remains NED 18 months since completing olaparib, 42 months since completing chemo. CA125 <6

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 germline BRCA-mutated 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

Discussion Question

A patient with ovarian cancer (OC) with extensive intra-abdominal disease (clinical Stage IIIC) responds well to neoadjuvant carboplatin/paclitaxel/bevacizumab and proceeds to R0 resection. Regulations and reimbursement aside, what is your preferred maintenance therapy if genetic testing reveals a germline BRCA mutation?

- None
- Bevacizumab
- Niraparib
- Olaparib
- Rucaparib
- Olaparib/bevacizumab
- Niraparib/bevacizumab
- Rucaparib/bevacizumab
- I’m not sure

Discussion Question

A patient with Stage IIIC OC undergoes R0 resection and receives adjuvant carboplatin/paclitaxel with a good response. Regulations and reimbursement aside, what are you most likely to recommend as maintenance therapy if genetic testing reveals BRCA wild type, HR proficiency (eg, LOH low)?

- None
- Bevacizumab
- Niraparib
- Olaparib
- Rucaparib
- Olaparib/bevacizumab
- Niraparib/bevacizumab
- Rucaparib/bevacizumab
- I'm not sure

RTP RESEARCH TO PRACTICE

Discussion Question

A patient with Stage IIIC OC undergoes R0 resection and receives adjuvant carboplatin/paclitaxel with a good response. Regulations and reimbursement aside, what are you most likely to recommend as maintenance therapy if genetic testing reveals a germline PALB2 mutation?

- None
- Bevacizumab
- Niraparib
- Olaparib
- Rucaparib
- Olaparib/bevacizumab
- Niraparib/bevacizumab
- Rucaparib/bevacizumab
- I'm not sure

RTP RESEARCH TO PRACTICE

Discussion Question

A patient with Stage IIIC OC undergoes R0 resection and receives adjuvant carboplatin/paclitaxel with a good response. Regulations and reimbursement aside, what are you most likely to recommend as maintenance therapy if genetic testing reveals BRCA wild type, HR deficiency (eg, LOH high)?

- None
- Bevacizumab
- Niraparib
- Olaparib
- Rucaparib
- Olaparib/bevacizumab
- Niraparib/bevacizumab
- Rucaparib/bevacizumab
- I'm not sure

Discussion Question

Have you used or would you use a PARP inhibitor for a patient who had previously received a PARP inhibitor?

- I have and have seen at least 1 patient respond
- I have
- I have not and would not
- I have not but would in the right situation
- I'm not sure

RTP RESEARCH TO PRACTICE

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Appendix

RTP RESEARCH TO PRACTICE

Mirvetuximab Soravtansine

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Dana-Farber
Cancer Institute

Mirvetuximab soravtansine

Ursula Matulonis, M.D.
Chief, Division of Gynecologic Oncology
Brock Wilson Family Chair
Dana-Farber Cancer Institute
Professor of Medicine
Harvard Medical School
Boston, MA

Pre-clinical testing of mirvetuximab soravtansine

Mirvetuximab soravtansine is an antibody-drug conjugate (ADC) comprised of an FRα-binding antibody, cleavable linker, and a maytansinoid DM4 payload, a potent tubulin-targeting agent[1]

Mirvetuximab preclinical development: the sulfo-SPDB- linked conjugate IMGN853 was the most active *in vivo* using DM4[1]; also tested in several cell lines:

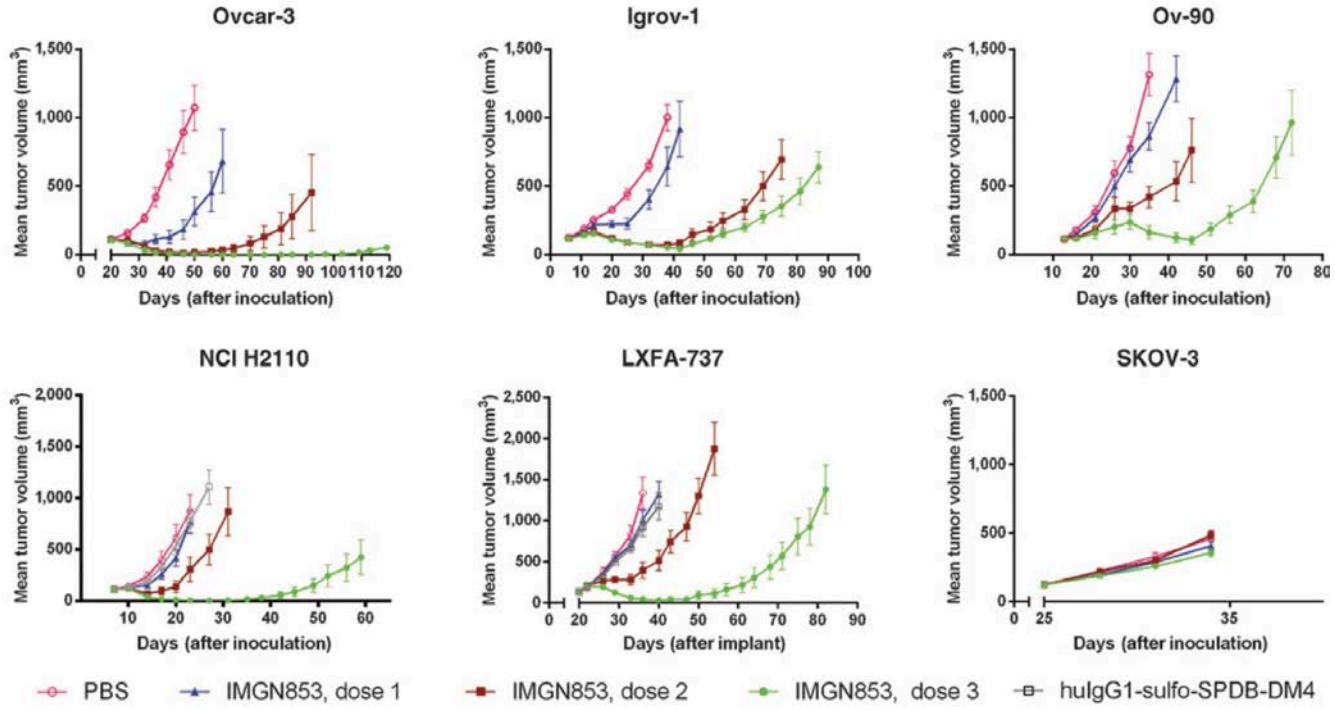

Figure 3.

Mechanism of Action: Mirvetuximab binds to FRα on the cell surface with high affinity, is internalized, degraded in the lysosomes, and active DM4 metabolites are released. These DM4 metabolites induce cell-cycle arrest and cell death. These metabolites can diffuse into proximal tumor cells and induce killing due to bystander cytotoxic activity[2]

[1]Ab et al, Mol Cancer Therapeutics, 2015, [2]Kovtun et al, Cancer Research 2006

SORAYA

- Treatment options for platinum resistant ovarian cancer (PROC) are limited, consisting primarily of single-agent chemotherapy, and the majority of patients will have received prior bevacizumab (BEV)[1,2]
  - Single-agent chemotherapy has limited activity (ORR, 4%–13%) along with considerable toxicity[3-6]
- FRα, also known as folate receptor 1 (FOLR1), has limited expression on normal tissues but is elevated in most ovarian cancers, which makes FRα an attractive target for the development of novel therapies[7,8]
- Single agent MTD of mirvetuximab[9] = 6 mg/kg calculated by Adjusted Ideal Body weight
- SORAYA is a global, single-arm, phase 3 study that evaluated MIRV for the treatment of PROC in patients with high FRα expression who received 1 to 3 prior therapies, including required prior BEV[10,11]

MIRV is the first biomarker-directed agent demonstrating antitumor activity in patients with folate receptor alpha (FRα)-high platinum-resistant ovarian cancer (PROC)[9,10]

1. Indini A, et al. *Cancers (Basel)*. 2021;13(7):1663. 2. McClung EC, Wenham RM. *Int J Womens Health*. 2016;8:59-75. 3. Pujade-Lauraine E, et al. *J Clin Oncol*. 2014;32(13):1302-1308. 4. Gaillard S, et al. *Gynecol Oncol*. 2021;163(2):237-245. 5 Hamanishi J, et al. *J Clin Oncol*. 2021;39(33):3671-3681. 6. Pujade-Lauraine E, et al. *Lancet Oncol*. 2021;22(7):1034-1046. 7. Birrer MJ, et al. *Oncologist*. 2019;24(4):425-429. 8. Zamarin D, et al. *J Immunother Cancer*. 2020;8(1):e000829. doi:10.1136/jitc-2020-000829. 9. Moore et al, Cancer 2017 10. Matulonis UA, et al. ASCO 2022, 11. Matulonis UA, et al. SGO 2022 Annual Meeting on Women's Cancer.

SORAYA: Study Design and Patient Population

Objective: Evaluate efficacy and safety of MIRV in patients with FRα-high platinum-resistant ovarian cancer

Primary endpoint: Confirmed ORR by investigator

ORR by blinded independent central review for sensitivity analysis

Key secondary endpoint: Duration of response

Patient population

Platinum-resistant ovarian cancer (recurrence within 6 months after last platinum dose) treated with 1 to 3 prior regimens

–Primary platinum-refractory disease* was excluded

High-grade serous histology

All enrolled received prior bevacizumab; prior PARP inhibitor was allowed

Tumor demonstrated FRα-high membrane staining with IHC PS2+ scoring

–**≥75%** of cells staining positive with **≥2+** staining intensity

Treatment schedule

- Patients received MIRV 6 mg/kg, adjusted ideal body weight, IV once every 3 weeks

Sample size calculation: 105 patients

- 110 patients planned to result in approximately 105 efficacy-evaluable patients
- 90% power to detect a difference in ORR of 24% vs 12% using a 1-sided binomial test and a 1-sided α level of 0.025
- 12% was chosen as the ORR to rule out based on the ORR for single-agent chemotherapy reported in prior trials of platinum-resistant ovarian cancer, which ranges from 4% to 13%[1-4]

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*Defined as disease that did not respond to first-line platinum therapy or progressed within 3 months of the last dose.

FRα, folate receptor alpha; IHC, immunohistochemistry; IV, intravenous; MIRV, mirvetuximab soravtansine; ORR, confirmed objective response rate; PARP, poly ADP-ribose polymerase; PS2+, sum of staining of 2+ and 3+ intensity.

1. Pujade-Lauraine E, et al. *J Clin Oncol*. 2014;32(13):1302-1308. 2. Gaillard S, et al. *Gynecol Oncol*. 2021;163(2):237-245. 3. Moore KN, et al. *Ann Oncol*. 2021;32(6):757-765. 4. Pujade-Lauraine E, et al. *Lancet Oncol*. 2021;22(7):1034-1046.

Baseline Demographics and Clinical Characteristics

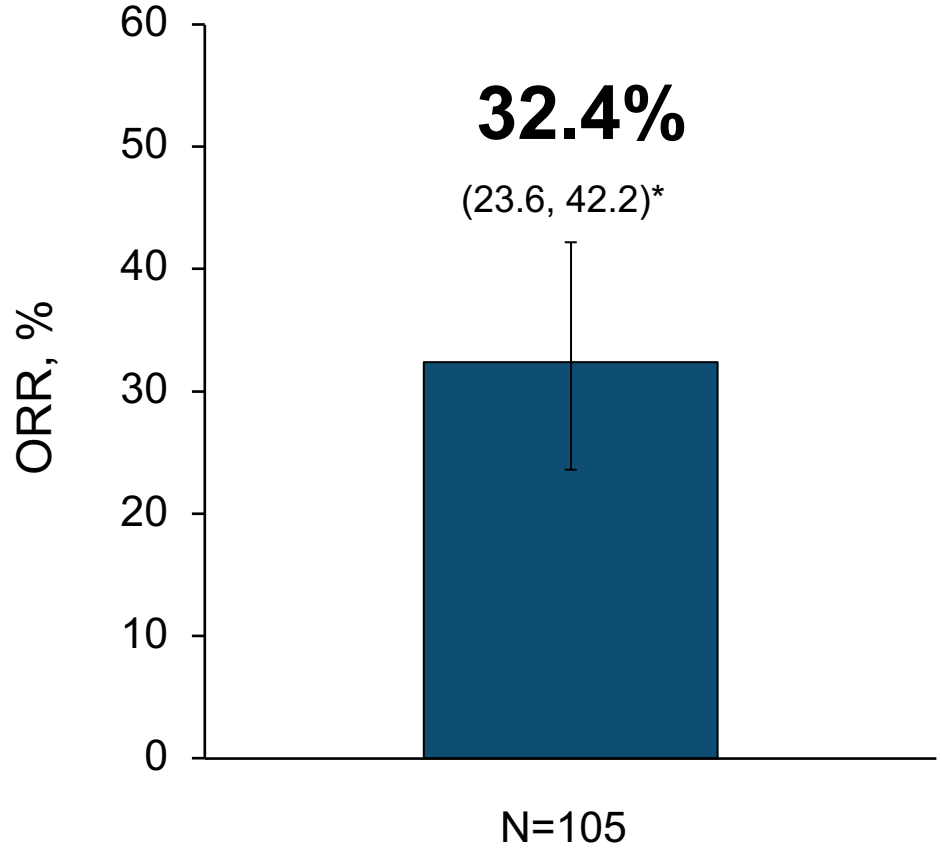
Characteristics		All patients (N=106)
Age, median (range)	Age in years	62 (35–85)
Primary cancer diagnosis, n (%)[a]	Epithelial ovarian cancer Fallopian tube cancer Primary peritoneal cancer	85 (80) 8 (8) 12 (11)
Stage at initial diagnosis, n (%)[b]	I–II III **IV**	2 (2) 63 (59) **40 (38)**
ECOG PS, n (%)	0 1	60 (57) 46 (43)
***BRCA* mutation, n (%)**	Yes No/unknown	21 (20) 85 (80)
No. of prior systemic therapies (%)	1 2 **3[c]**	10 (9) 41 (39) **55 (52)**
Prior exposure, n (%)	**Bevacizumab** **PARPi** Taxanes	**106 (100)** **51 (48)** 105 (99)
Primary platinum-free interval, n (%)	3–12 mo[d] >12 mo	63 (59) 43 (41)
Platinum-free interval, n (%)	**0–3 mo** 3– >6 mo	**39 (37)** 67 (63)

Analysis Population

- **Efficacy-evaluable population:** 105 patients who had measurable disease at baseline by investigator assessment per RECIST v1.1
- **Safety population:** 106 patients who received ≥1 dose of MIRV

Matulonis et al, SGO 2022, ASCO 2022, IGCS 2022

Investigator-Assessed Objective Response Rate in Overall Efficacy Evaluable Population

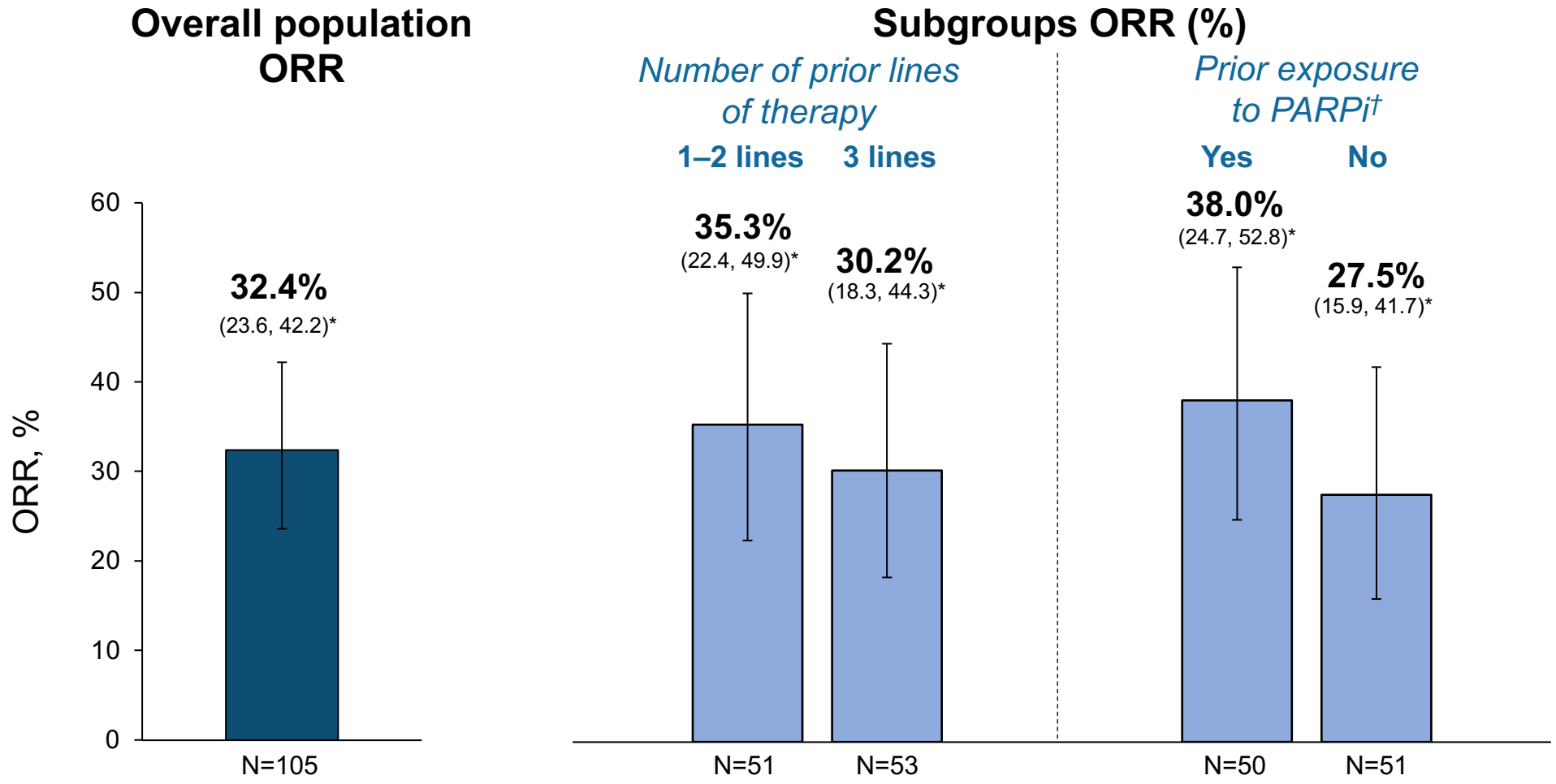


34 responders

- 5 complete responses
- 29 partial responses

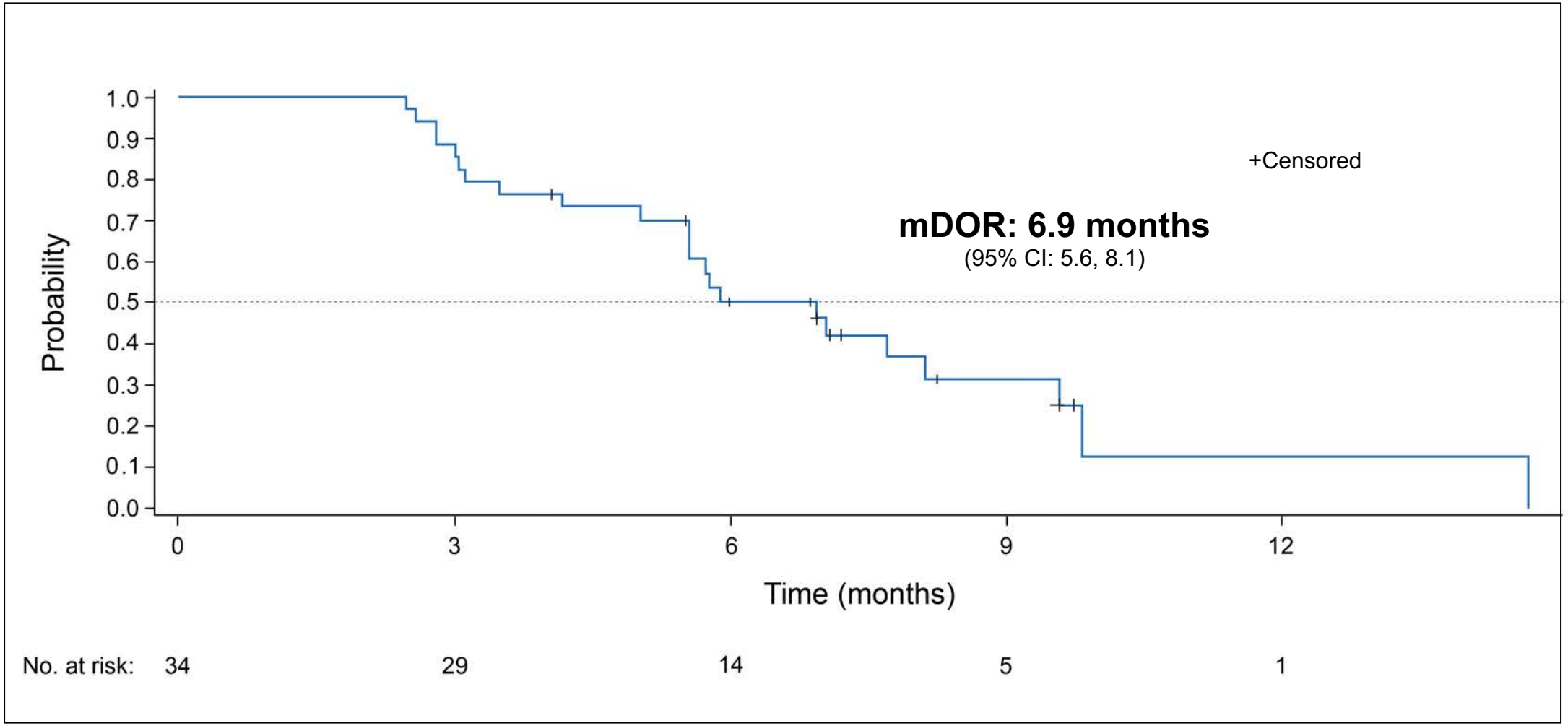
Matulonis et al, SGO 2022, ASCO 2022, IGCS 2022

Investigator-Assessed Objective Response Rate by Prior Therapy



Matulonis et al, SGO 2022, ASCO 2022, IGCS 2022

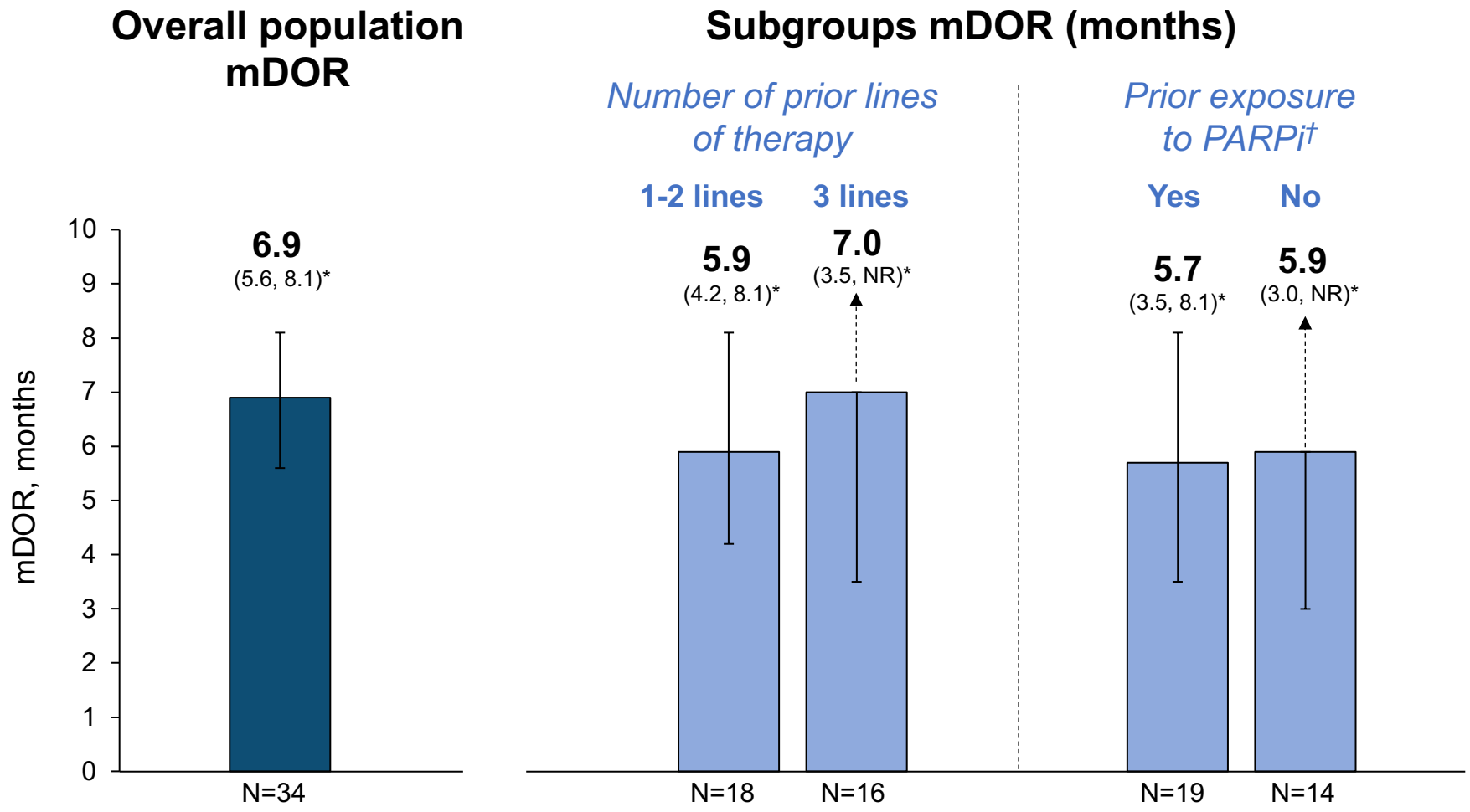
Investigator-Assessed Duration of Response



Data cutoff: March 3, 2022.
CI, confidence interval; mDOR, median duration of response.

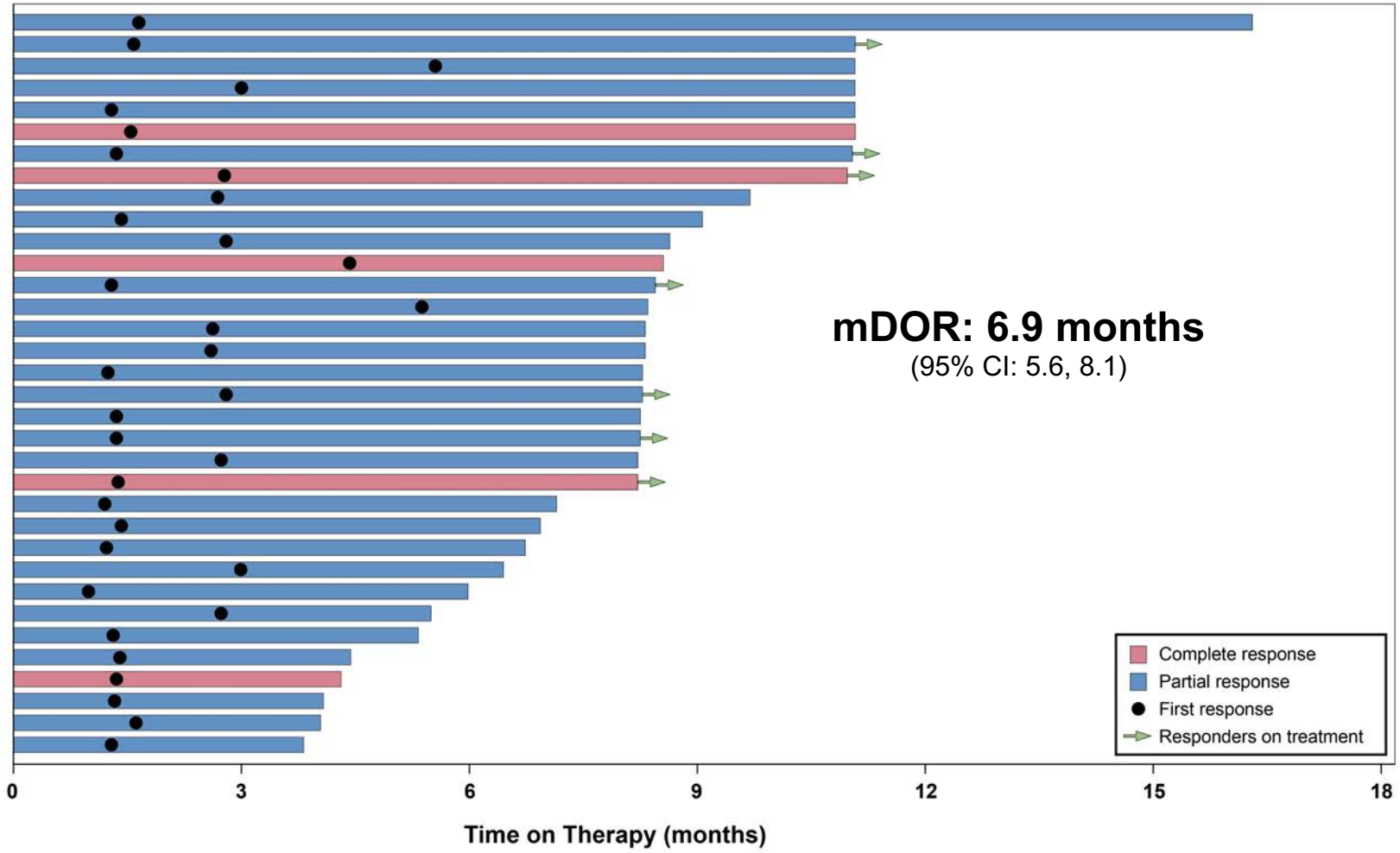
Matulonis et al, SGO 2022, ASCO 2022, IGCS 2022

Investigator-Assessed Duration of Response by Prior Therapy



Matulonis et al, SGO 2022, ASCO 2022, IGCS 2022

Investigator-Assessed Duration of Response for Patients With Complete and Partial Responses



Data cutoff: March 3, 2022.
CI, confidence interval; mDOR, median duration of response.

Matulonis et al, SGO 2022, ASCO 2022, IGCS 2022

Efficacy Endpoints Assessed by Investigator and BICR

Endpoints	Investigator-Assessed (N=105)	BICR-Assessed (N=95)
ORR, n (%)	**34 (32.4)**	**30 (31.6)**
95% CI	[23.6, 42.2]	[22.4, 41.9]
Best overall response, n (%)		
Complete response	**5 (4.8)**	**5 (5.3)**
Partial response	29 (27.6)	25 (26.3)
Stable disease	48 (45.7)	53 (55.8)
Progressive disease	20 (19.0)	8 (8.4)
Not evaluable	3 (2.9)	4 (4.2)
mDOR, months	**6.9**	**11.7**
95% CI	[5.6, 8.1]	[5.0, NR]
mPFS, months	**4.3**	**5.5**
95% CI	[3.7, 5.1]	[3.8, 6.9]

Matulonis et al, SGO 2022, ASCO 2022, IGCS 2022

Treatment-Related Adverse Events

Treatment-Related Adverse Events (≥10%) (N=106)

TRAEs, n (%)	All grades	Grade 3	Grade 4
Blurred vision	43 (41)	6 (6)	0
Keratopathy[a]	31 (29)	8 (8)	1 (1)
Nausea	31 (29)	0	0
Dry eye	26 (25)	2 (2)	0
Fatigue	25 (24)	1 (1)	0
Diarrhea	23 (22)	2 (2)	0
Asthenia	16 (15)	1 (1)	0
Photophobia	14 (13)	0	0
Peripheral neuropathy	14 (13)	0	0
Decreased appetite	14 (13)	1 (1)	0
Neutropenia	14 (13)	2 (2)	0
Vomiting	12 (11)	0	0

- Adverse events were primarily low-grade, reversible ocular and gastrointestinal events
- Serious (grade ≥3) TRAEs occurred in 9% of patients
- TRAEs led to dose delays in 33% of patients and dose reductions in 20% of patients
- Ten patients (9%) discontinued treatment due to TRAEs
  - One patient discontinued due to an ocular TRAE
- One death was recorded as possibly related to study drug
  - Respiratory failure (autopsy found lung metastases and no evidence of drug reaction)

[a]The grouped preferred term "Keratopathy" includes the following preferred terms: corneal cyst, corneal disorder, corneal epithelial microcysts, keratitis, keratopathy, limbal stem cell deficiency, corneal opacity, corneal erosion, corneal pigmentation, corneal deposits, keratitis interstitial, and punctate keratitis.Data cutoff: April 29, 2022.

Mirvetuximab Ocular toxicities

--Occur because of off-target effects on the cornea, with primary involvement of the corneal epithelium which leads to blurred vision and can be associated with microcystic keratopathy.

--Corneal damage begins peripherally after mirvetuximab reaches the cornea via the vascularized limbal region.

--Internalization and accumulation of DM4 occurs into transient amplifying cells. These damaged progenitor cells then migrate centripetally and are sufficient to account for the development of microcystic deposits seen in patients.

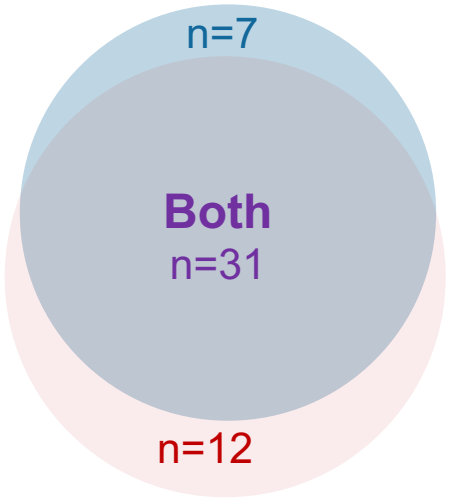
--Ocular steroids can slow down the proliferation of limbal stem cells, potentially leading to a lower sensitivity to the damaging effects of chemotherapeutics, including the DM4 payload present in mirvetuximab soravtansine.

--Ocular steroids also may lead to thinning of the corneal epithelium which can facilitate shedding of corneal microcysts induced by exposure to the ADC.

Matulonis et al, CCR 2018, Zhao et al, Cancer Research 2018, Gan et al, Neuro Onc 2018

Unique Events Specific to MIRV: Keratopathy and Blurred Vision

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



- **Proactive supportive care**
  - Lubricating artificial tears
  - Corticosteroid eye drops
- **Predictable**
  - Median time to onset: cycle 2 (~1.5 months)
- **Manageable with dose modifications, if needed**
  - 22% of patients (23/106) had dose delay and/or reduction
- **Reversible**
  - At data cutoff: >80% of patients with grade 2–3 events had resolved to grade 0–1
    - 9 patients still receiving MIRV or being followed up for resolution
- **<1% discontinuation due to ocular events**
  - 1 of 106 patients discontinued due to grade 4 keratopathy,† which resolved within 15 days

The grouped preferred term “Keratopathy” includes the following preferred terms: “corneal cyst,” “corneal disorder,” “corneal epithelial microcysts,” “keratitis,” “keratopathy,” “limbal stem cell deficiency,” “corneal opacity,” “corneal erosion,” “corneal pigmentation,” “corneal deposits,” “keratitis interstitial,” “punctate keratitis,” and “corneal epithelial defect.” †One patient experiencing a grade 4 event recorded as keratopathy was based upon the visual acuity evaluation of one eye (20/200). This patient had confirmed grade 2 corneal changes, and both the visual acuity and these corneal changes resolved completely (grade 0) in 15 days by ophthalmic exam.

Matulonis et al, SGO 2022, ASCO 2022, IGCS 2022

Conclusions

MIRV demonstrates clinically meaningful antitumor activity in patients with FRα-high platinum-resistant ovarian cancer

- **ORR: 32.4%** investigator-assessed, including 5 complete responses
- **Median DOR: 6.9 months**
- Consistent antitumor activity regardless of prior number of therapies or prior PARPi

The safety and tolerability profile of MIRV in SORAYA is consistent with that observed in previous studies

- Low-grade, reversible ocular and GI events, manageable with supportive care
- No appreciable myelosuppression and limited low-grade neuropathy
- 7 patients (7%) discontinued treatment due to TRAEs
  - Only 1 patient discontinued due to ocular event

These results position MIRV to become a practice-changing, biomarker-driven standard of care treatment option for patients with FRα-positive platinum-resistant ovarian cancer

Single agent mirvetuximab dose and mirvetuximab combinations

1) Phase Ib of carboplatin and mirvetuximab[1]:

Table 2
Summary of dose escalation.

Mirvetuximab soravtansine dose	Carboplatin dose	No. of patients	Treatment-related SAEs and DLTs
5 mg/kg	AUC4	4	None
5 mg/kg	AUC5	4	None
6 mg/kg	AUC5	10	SAE: Diarrhea (grade 3) DLT: Vasculitis (grade 3)

Table 4
Summary of efficacy measures.

Endpoint	$n = 17$
ORR (confirmed)	71%
95% CI	(44, 90)
Median PFS (months)	15
95% CI	(9.9, −)
Median DOR (months)	NR
95%CI	(5.7, −)

ORR, objective response rate; PFS, progression-free survival; DOR, duration of response; NR, not reached.

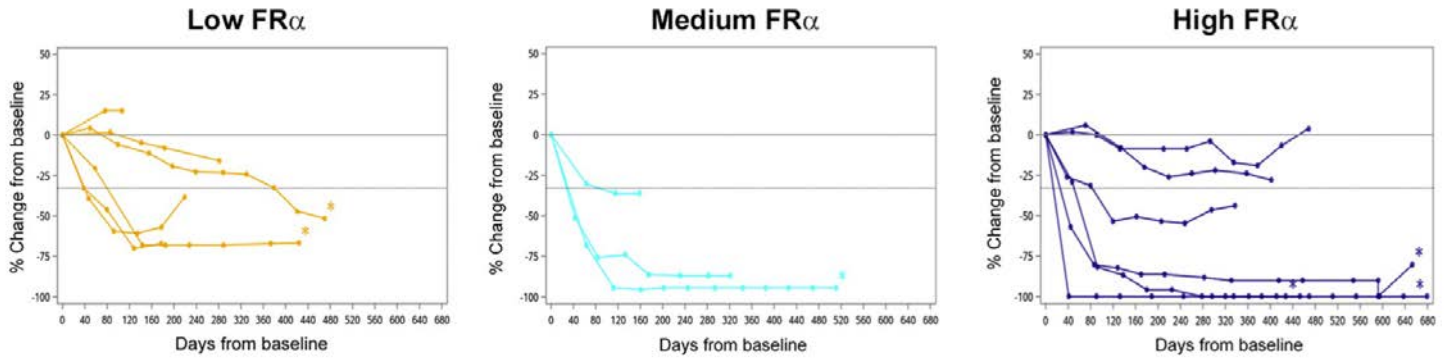


Fig. 1. Percent tumor change in target lesions by FRα expression. Data are presented from 15 patients as individuals with non-measurable disease were enrolled in the study. Asterix denotes patients still on study at time of final analyses. Dotted line in plots corresponds to 30% decrease in tumor size.

2) carboplatin and bevacizumab[2]

[1]Moore et al, Gyn Onc 2018
[2]O'Malley et al, IGCS 2022

Study Design: Mirvetuximab and Bevacizumab

As part of the phase 1b/2 FORWARD II study (NCT02606305), MIRV combined with BEV was evaluated in patients with recurrent FRα-expressing[a] ovarian cancer[1,2]

Objective: Evaluate the efficacy and safety of MIRV+BEV in recurrent FRα-expressing epithelial ovarian cancer (EOC)[1,2,b]

Patient population: Patients with FRα-expressing EOC who were eligible for non-platinum therapy[1]

- FRα expression was assessed using immunohistochemistry PS2+ scoring, scored as the percent of viable tumor cells staining with ≥2+ intensity
  - FRα Low: ≥25% to 49%
  - FRα Medium: 50% to 74%
  - FRα High: ≥75%
- Platinum status was stratified by platinum-free interval (PFI) as PFI > 6 months or PFI ≤ 6 months
- BEV treatment status was defined as BEV-naïve or BEV-treated (defined as having received BEV in any line of therapy)

Treatment schedule: MIRV 6 mg/kg, adjusted ideal body weight[c] + BEV 15 mg/kg intravenously on day 1 of a 3-week cycle[1]

Primary endpoint: Confirmed ORR by RECIST v1.1[2]

Secondary endpoints: DOR, PFS, safety[2]

References: 1. O'Malley DM, et al. Slides presented at: SGO Annual Meeting; March 18-21, 2022; Phoenix, AZ. **2.** ClinicalTrials.gov identifier: NCT02606305. Updated December 17, 2021. Accessed August 11, 2022. https://www.clinicaltrials.gov/ct2/show/NCT02606305

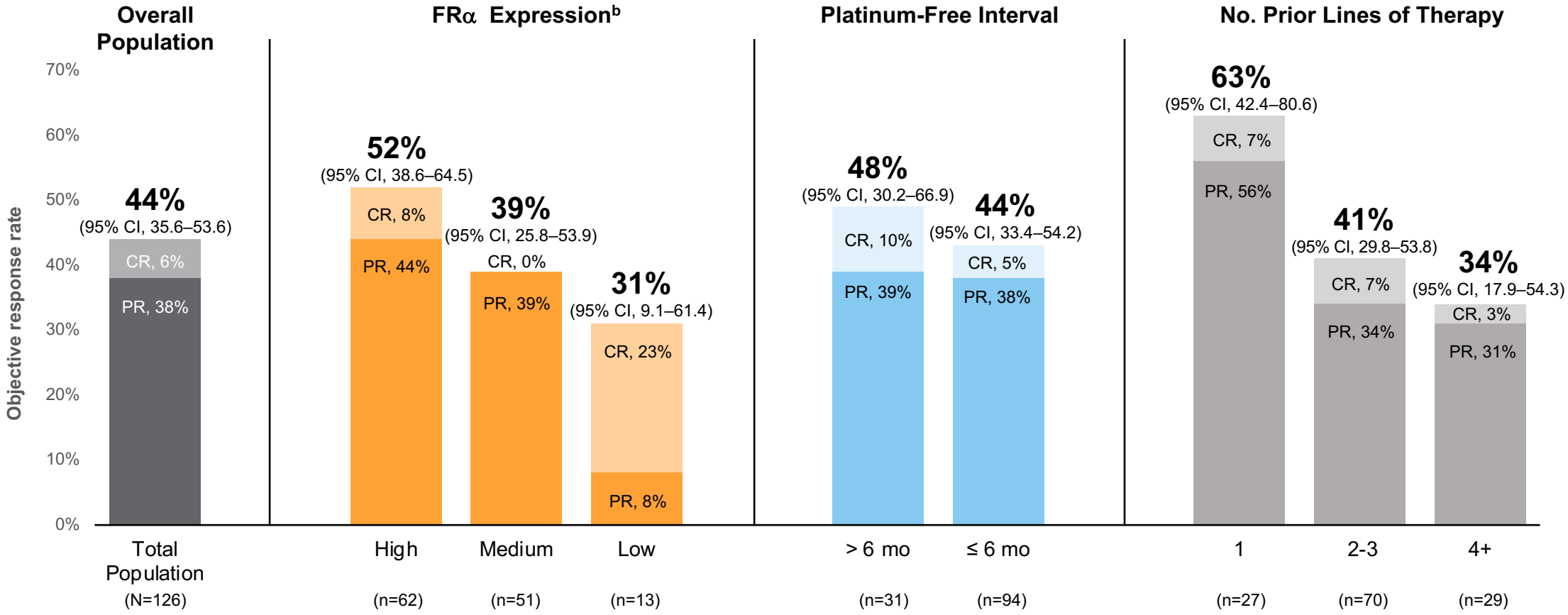
Baseline Demographics and Clinical Characteristics

Characteristic		MIRV+BEV (N=126)
Age, median (range)	Age in years	62 (39–83)
Primary cancer diagnosis, n (%)[a]	Epithelial ovarian Primary peritoneal Fallopian tube	93 (74) 27 (21) 5 (4)
FRα expression, n (%)[b]	High Medium Low	62 (49) 51 (40) 13 (10)
No. prior lines of systemic therapy, n (%)	1 2 **3** **≥4** Median (range)	27 (21) 41 (33) **29 (23)** **29 (23)** 2 (1–4)
Prior exposure, n (%)	**Bevacizumab** PARPi	**66 (52)** 34 (27)
Platinum-free interval, n (%)[c,d]	**≤6 months** >6–12 months >12 months	**94 (75)** 23 (18) 8 (6)
ECOG performance status	0 1	82 (65) 44 (35)

- 46% had ≥3 prior lines of therapy
- 52% had received prior BEV
- 75% had a most recent platinum-free interval of ≤6 months

O'Malley et al, IGCS mtg, 2022

ORR[a] in Subgroups by FRα Expression, Platinum-Free Interval, and Lines of Therapy



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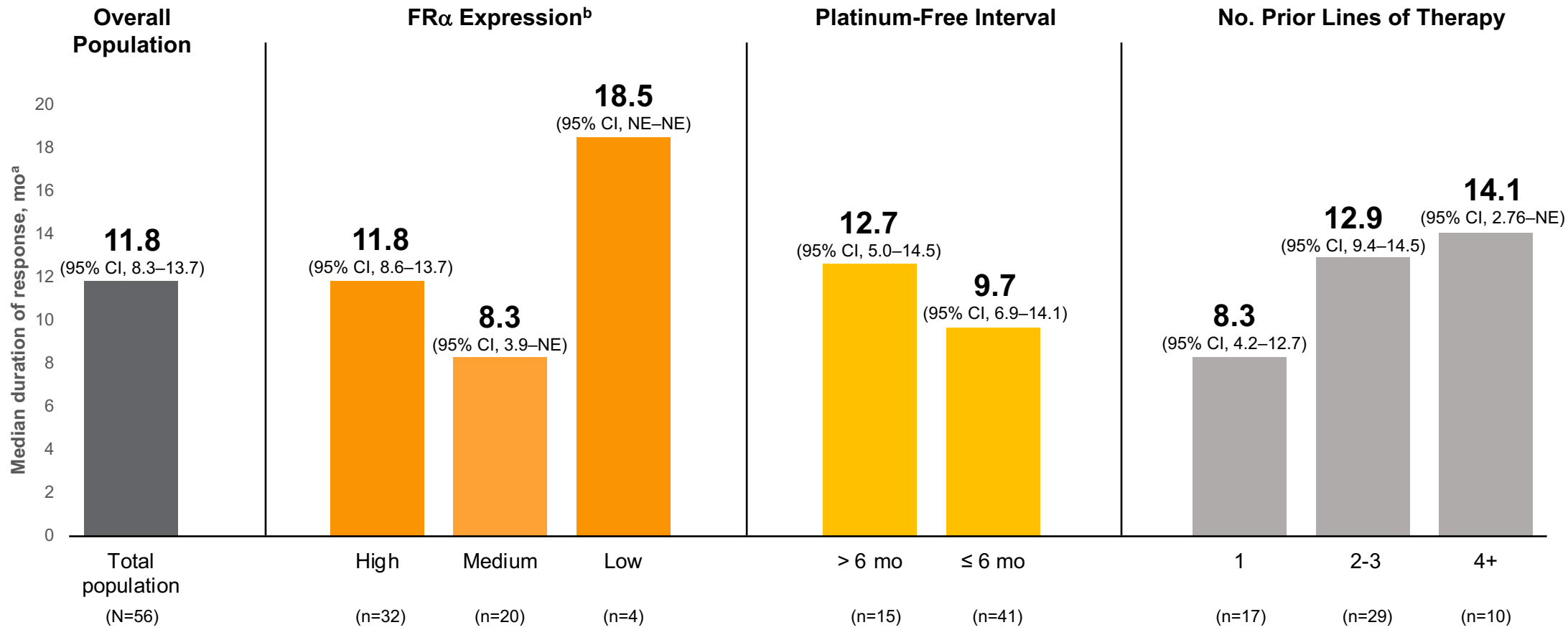
CR, complete response; FRα, folate receptor alpha; ORR, objective response rate; PR, partial response; mo, months.
[a]Investigator assessed. [b]Low, 25% to 49%; medium, 50% to 74%; high ≥75% of tumor cells with ≥2+ staining intensity.
Data cutoff: June 21, 2021.

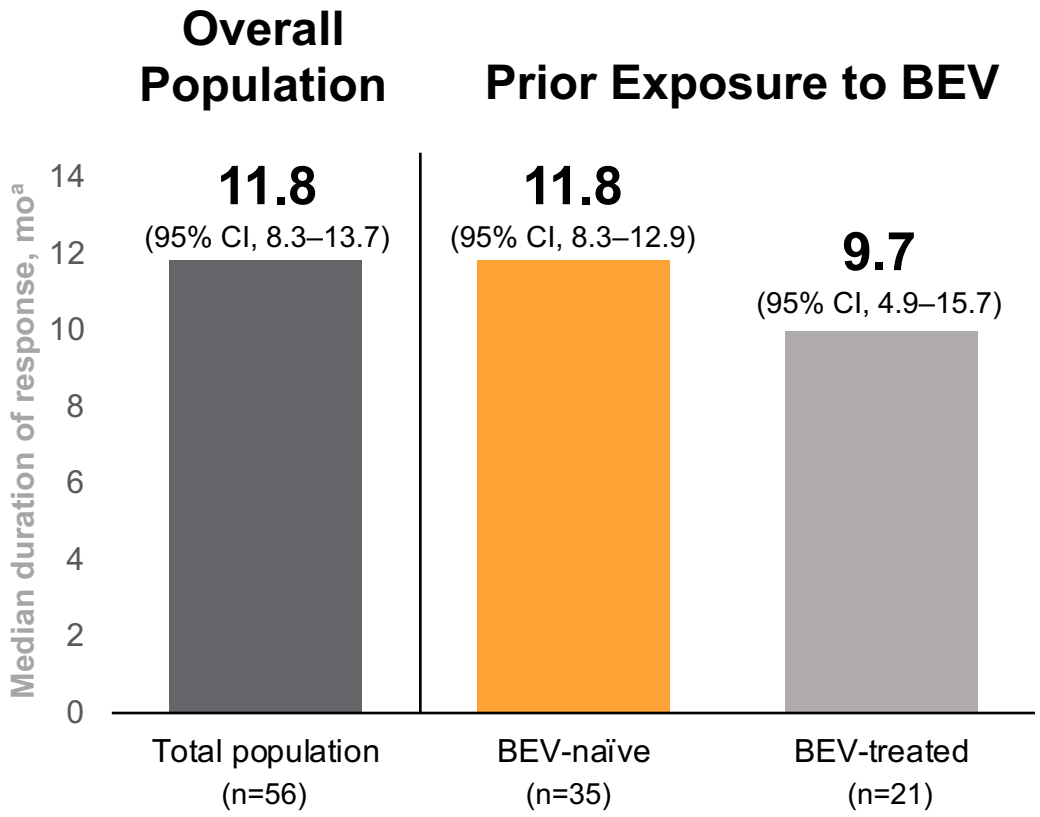
O'Malley et al, IGCS mtg, 2022

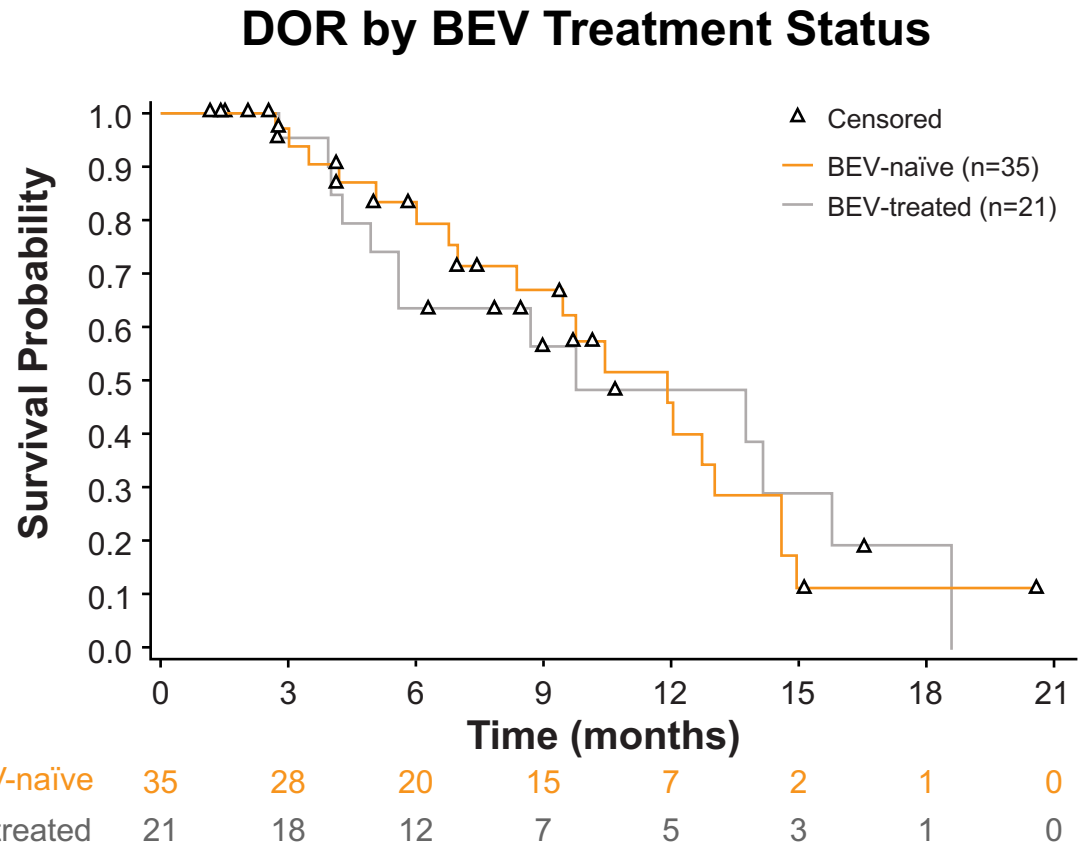
Median DOR[a] in Responders: Subgroups by FRα Expression, Platinum Status, and Lines of Therapy



O'Malley et al, IGCS mtg, 2022

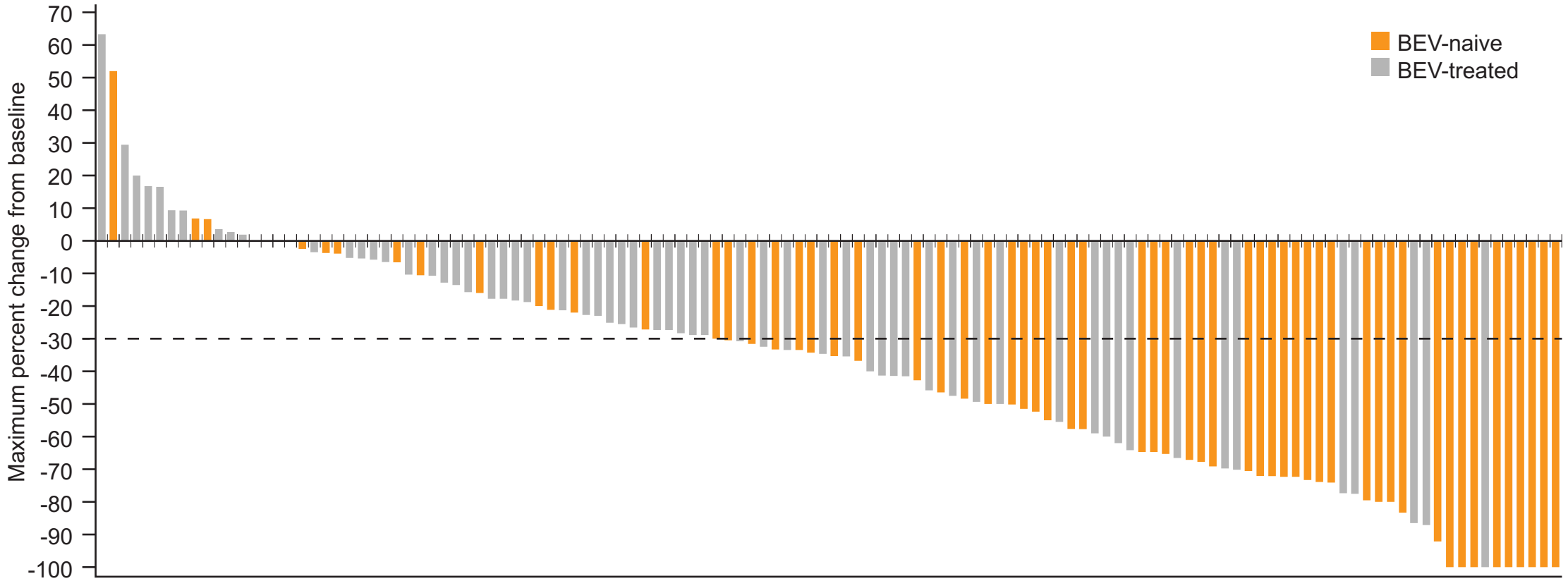
Median DOR[a] in Responders: Overall Population and by BEV Treatment Status Subgroups





O'Malley et al, IGCS mtg, 2022

Best Tumor Response per RECIST by BEV Treatment Status Subgroups



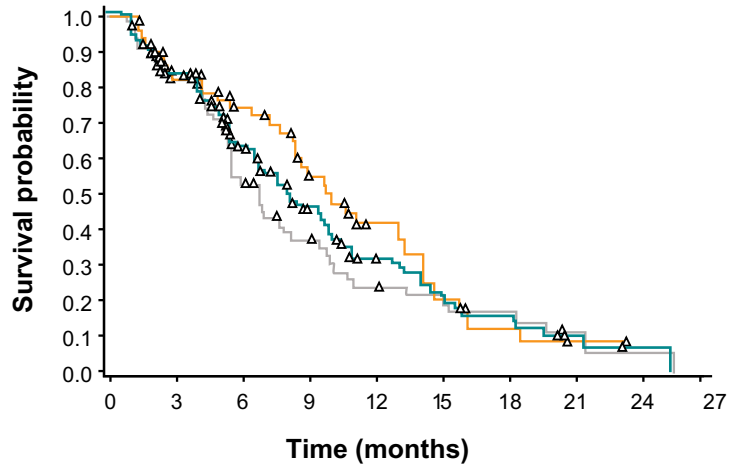
O'Malley et al, IGCS mtg, 2022

Median PFS[a] in the Overall Population and in Subgroups

△ Censored

Overall Population and BEV Exposure

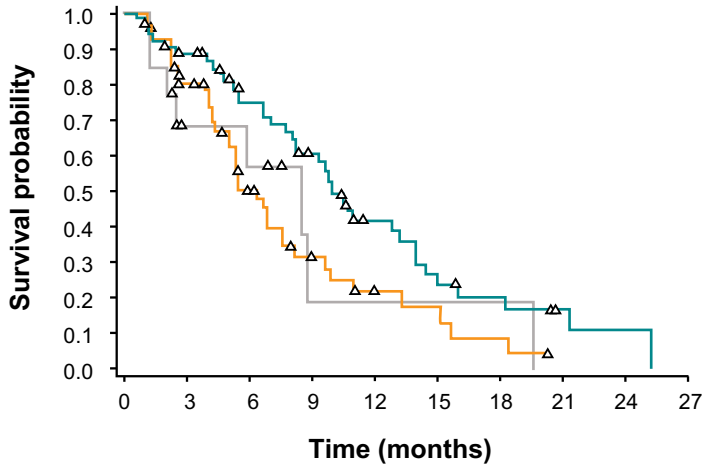
	Overall	BEV-naïve	BEV-treated
mPFS, mo[a]	8.2	9.7	6.8
(95% CI)	(6.8–9.9)	(8.2–13.2)	(5.5–8.2)



Total population	126	93	62	39	21	14	9	3	1	0
BEV-naïve	60	41	33	21	10	5	3	1	0	0
BEV-treated	66	52	29	18	11	9	6	2	1	0

FRα Expression[b]

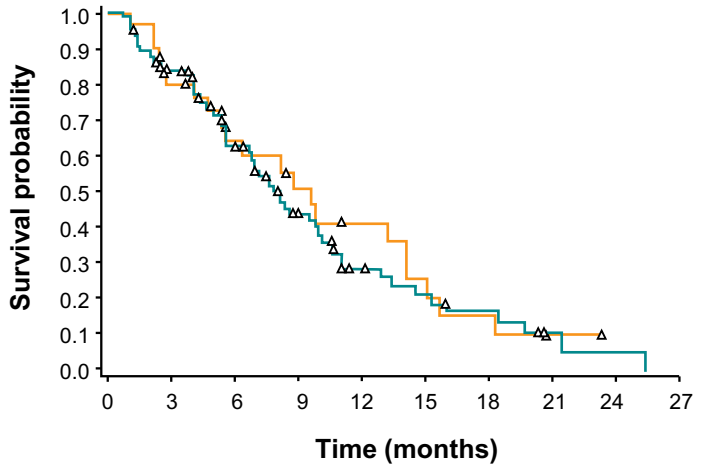
	High	Medium	Low
mPFS, mo[a]	10.1	6.3	8.6
(95% CI)	(8.2–13.2)	(5.1–7.7)	(2.1–NE)



High	62	49	36	27	14	9	6	3	1	0
Medium	51	38	21	11	6	4	2	0	0	0
Low	13	6	5	1	1	1	1	0	0	0

Platinum-Free Interval

	> 6 mo	≤ 6 mo
mPFS, mo[a]	9.6	8.2
(95% CI)	(5.4–14.1)	(6.8–10.0)



> 6 mo	31	22	15	11	8	5	3	1	0	0
≤ 6 mo	94	70	47	28	13	9	6	2	1	0

BEV, bevacizumab; FRα, folate receptor alpha; mPFS, median progression-free survival; mo, months NE, not estimable; PD, progressive disease; PFS, progression-free survival. [a]PFS (a secondary end point) was defined as the time from the date of first dose until the date of PD or death from any cause, whichever occurred first. [b]Low, 25% to 49%; medium, 50% to 74%; high ≥75% of tumor cells with ≥2+ staining intensity.
Data cutoff: June 21, 2021.

O'Malley et al, IGCS mtg, 2022

Treatment-Related Adverse Events ≥20%

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

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

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

Conclusions

MIRV+BEV demonstrated antitumor activity in patients with recurrent FRα-expressing ovarian cancer

- In the overall population, treatment with MIRV+BEV resulted in confirmed ORR of 44%
- The median duration of these responses was 11.8 months
- Overall, MIRV+BEV led to a median PFS of 8.2 months

•Durable antitumor activity was seen across all levels of FRα expression, in patients that were BEV naïve and pre-treated, and regardless of platinum-free interval

The safety profile of MIRV+BEV reflects the safety profile of each drug as a monotherapy; the most common TRAEs were diarrhea, blurred vision, and fatigue

These data provide evidence to support MIRV+BEV as an efficacious combination choice for patients with FRα-expressing ovarian cancer who are eligible for treatment with BEV

A randomized phase 3 trial (GLORIOSA) is planned to evaluate the efficacy and safety of MIRV+BEV in the maintenance setting for the treatment of patients with FRα-high platinum-sensitive ovarian cancer[1]

Ongoing Trials of Mirvetuximab

Trial	NCT#	Accrual and key eligibility
A Study of Mirvetuximab Soravtansine vs. Investigator's Choice of Chemotherapy in Platinum-Resistant, Advanced High-Grade Epithelial Ovarian, Primary Peritoneal, or Fallopian Tube Cancers With High Folate Receptor-Alpha Expression (MIRASOL)	NCT04209855	n=430 Primary endpoint: PFS as assessed by investigator up to 3 prior lines of treatment
Study of Carboplatin and Mirvetuximab Soravtansine in First-Line Treatment of Patients Receiving Neoadjuvant Chemotherapy With Advanced-Stage Ovarian, Fallopian Tube or Primary Peritoneal Cancer	NCT04606914	n=70 Primary Endpoint: PFS, ORR
Mirvetuximab Soravtansine Monotherapy in Platinum-Sensitive Epithelial, Peritoneal, and Fallopian Tube Cancers (PICCOLO)	NCT05041257	n=75 Primary endpoint: Investigator-assessed ORR Patients must have received at least 2 prior systemic lines of platinum therapy; Patients may have received up to but no more than 1 prior independent non-platinum cytotoxic therapy
Mirvetuximab Soravtansine With Bevacizumab Versus Bevacizumab as Maintenance in Platinum-sensitive Ovarian, Fallopian Tube, or Peritoneal Cancer (GLORIOSA)	NCT05445778	n=418 Primary endpoint: PFS as assessed by investigator. Patients must have relapsed after 1 line (first line) of platinum-based chemotherapy and have platinum-sensitive disease
Mirvetuximab soravtansine with Carboplatin in Second-line Treatment of FRα Expressing, Platinum-sensitive Epithelial Ovarian Cancer followed by Mirvetuximab maintenance	NCT05456685	n=114 Primary endpoint: ORR by investigator FRα positivity of ≥ 25% of tumor staining at ≥ 2+ intensity, and patients must have relapsed after 1 prior line of platinum-based chemotherapy.

Tumor Treating Fields (TTFields)

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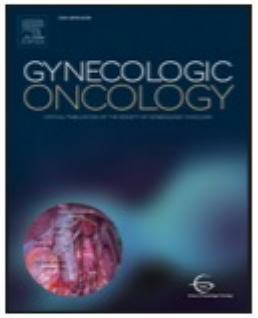
journal homepage: www.elsevier.com/locate/ygyno



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

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

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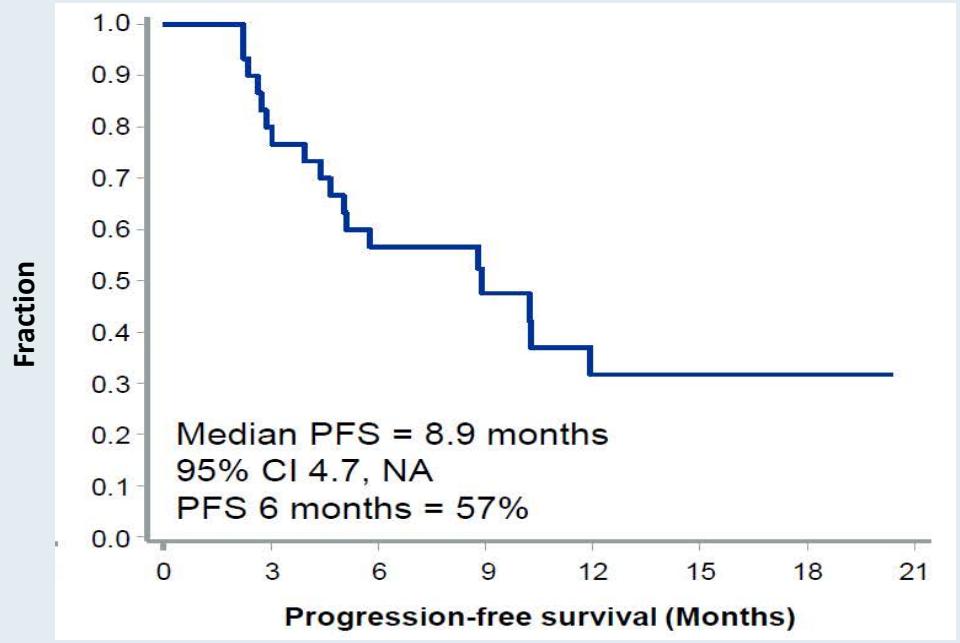
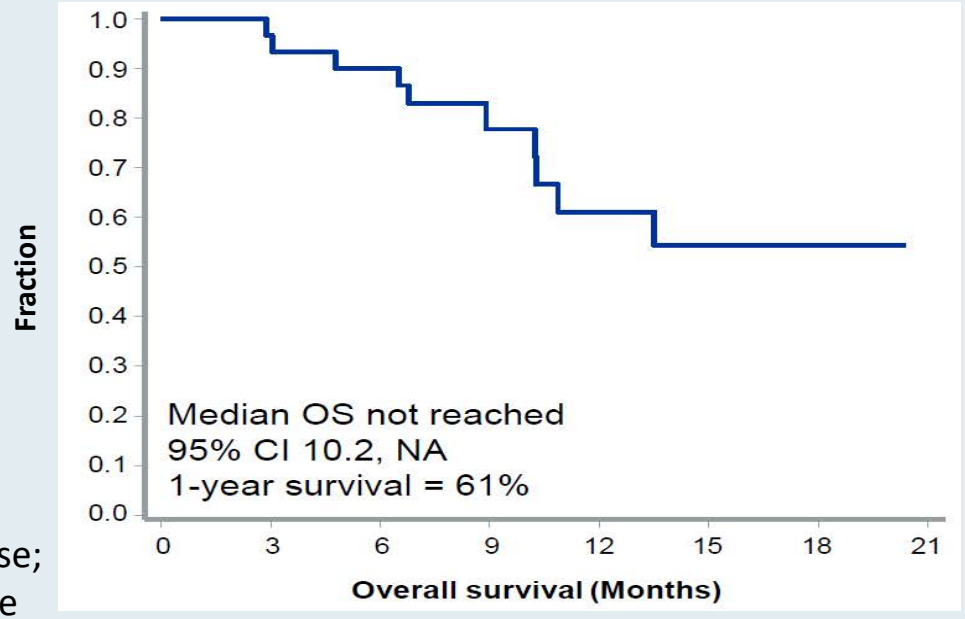
[b] Kantonsspital Graubünden, Chur, Switzerland
[c] Hospital Universitario 12 de Octubre, Madrid, Spain
[d] Oncology Institute of Southern, Switzerland, Bellinzona

INNOVATE: TTFields and Paclitaxel

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

PROs = patient-reported outcomes; OS = overall survival; PFS = progression-free survival; CR = complete response; PR = partial response; SD = stable disease; PD = progressive disease; CBR = clinical benefit rate





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

RTP RESEARCH TO PRACTICE

INNOVATE: Select Adverse Events

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

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

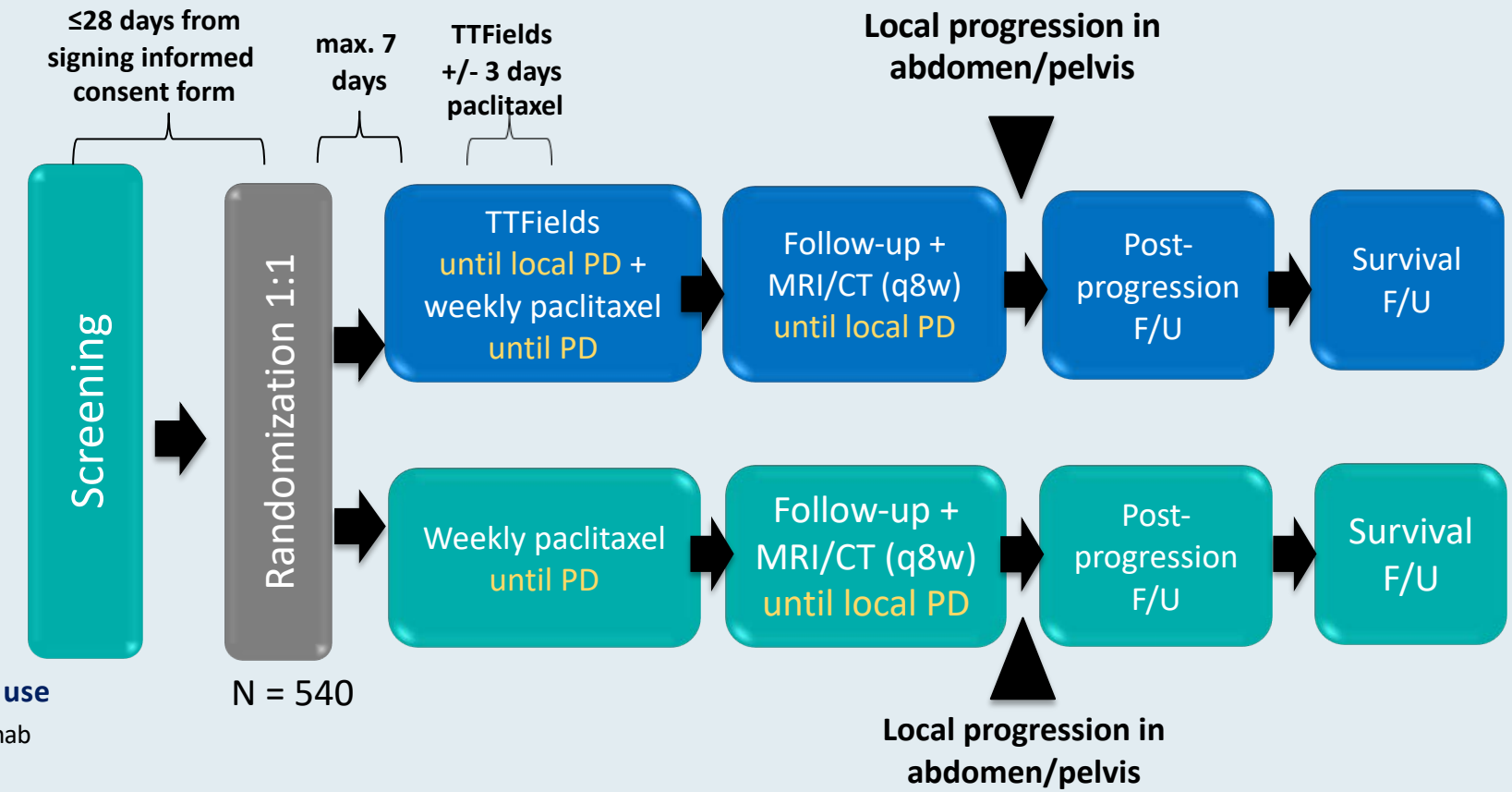
INNOVATE-3 (ENGOT-OV50/GOG-3029): TTFields, 200 kHz

Enrollment target (n = 540)

Number of sites (n = 110)

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

Enrollment closed October 2020



Stratification

- **Prior therapy**
  - No prior systemic therapy after platinum-resistant ovarian cancer
  - One prior line
  - Two prior lines
- **Prior bevacizumab use**
  - Prior bevacizumab use
  - No prior bevacizumab
- **BRCA status**
  - Mutated BRCA
  - Wild-type BRCA/ unknown

www.clinicaltrials.gov. NCT03940196. Accessed November 2022.

RTP RESEARCH TO PRACTICE

Recommendation Announced to Continue the Phase III Pivotal INNOVATE-3 Study of Tumor Treating Fields for Ovarian Cancer

Press Release: March 23, 2022

The results of a prespecified interim analysis for the Phase III pivotal INNOVATE-3 study evaluating the safety and efficacy of tumor treating fields together with paclitaxel for the treatment of platinum-resistant ovarian cancer were announced today.

An independent data monitoring committee (DMC) reviewed the safety data for all platinum-resistant ovarian cancer patients enrolled on the trial. In addition, an analysis of overall survival was performed on the first 540 patients randomized. The interim analysis did not indicate a need to increase the sample size and the DMC recommended that the study should continue to final analysis as planned.

www.yahoo.com/now/novocure-announces-favorable-recommendation-continue-120000088.html

PARP Inhibitor Maintenance Therapy in the First Line

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.

Overall Survival at 7-year Follow-up in Patients with Newly Diagnosed Advanced Ovarian Cancer and a BRCA Mutation Who Received Maintenance Olaparib in the SOLO1/GOG 3004 Trial

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

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

Conducted in partnership with the Gynecologic Oncology Group (GOG 3004)
ClinicalTrials.gov identifier: NCT01844986.

IGCS 2022;Abstract S003/1610.

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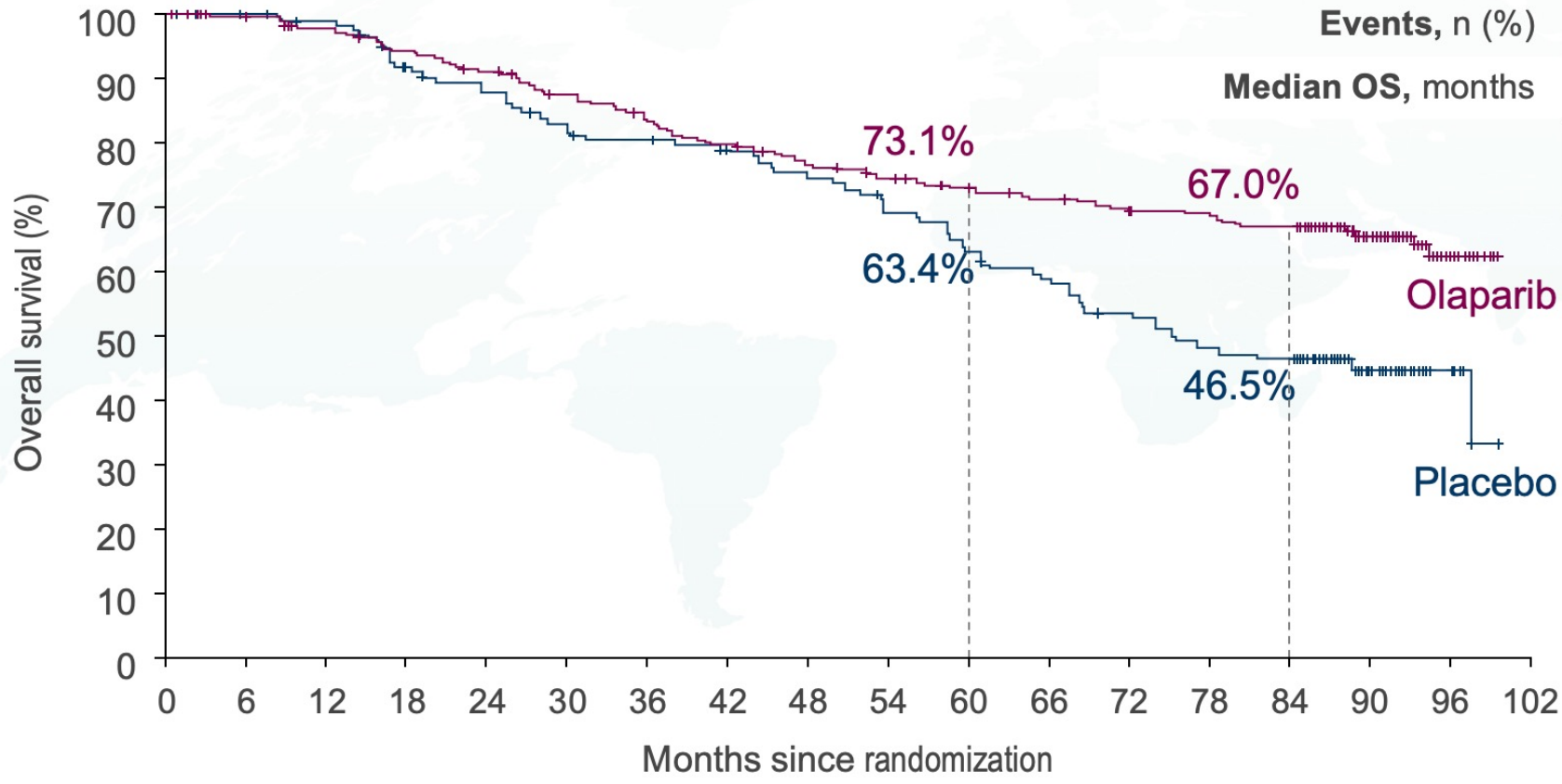
RESEARCH TO PRACTICE

SOLO-1: Overall Survival



	Olaparib (N=260)	Placebo (N=131)
Events, n (%)	84 (32.3)	65 (49.6)
Median OS, months	**NR**	**75.2**

HR 0.55 (95% CI 0.40–0.76); *P*=0.0004*

44.3% of patients in the placebo group received subsequent PARP inhibitor therapy, compared with 14.6% of patients in the olaparib group

DiSilvestro P et al. IGCS 2022;Abstract S003/1610.

RTP RESEARCH TO PRACTICE

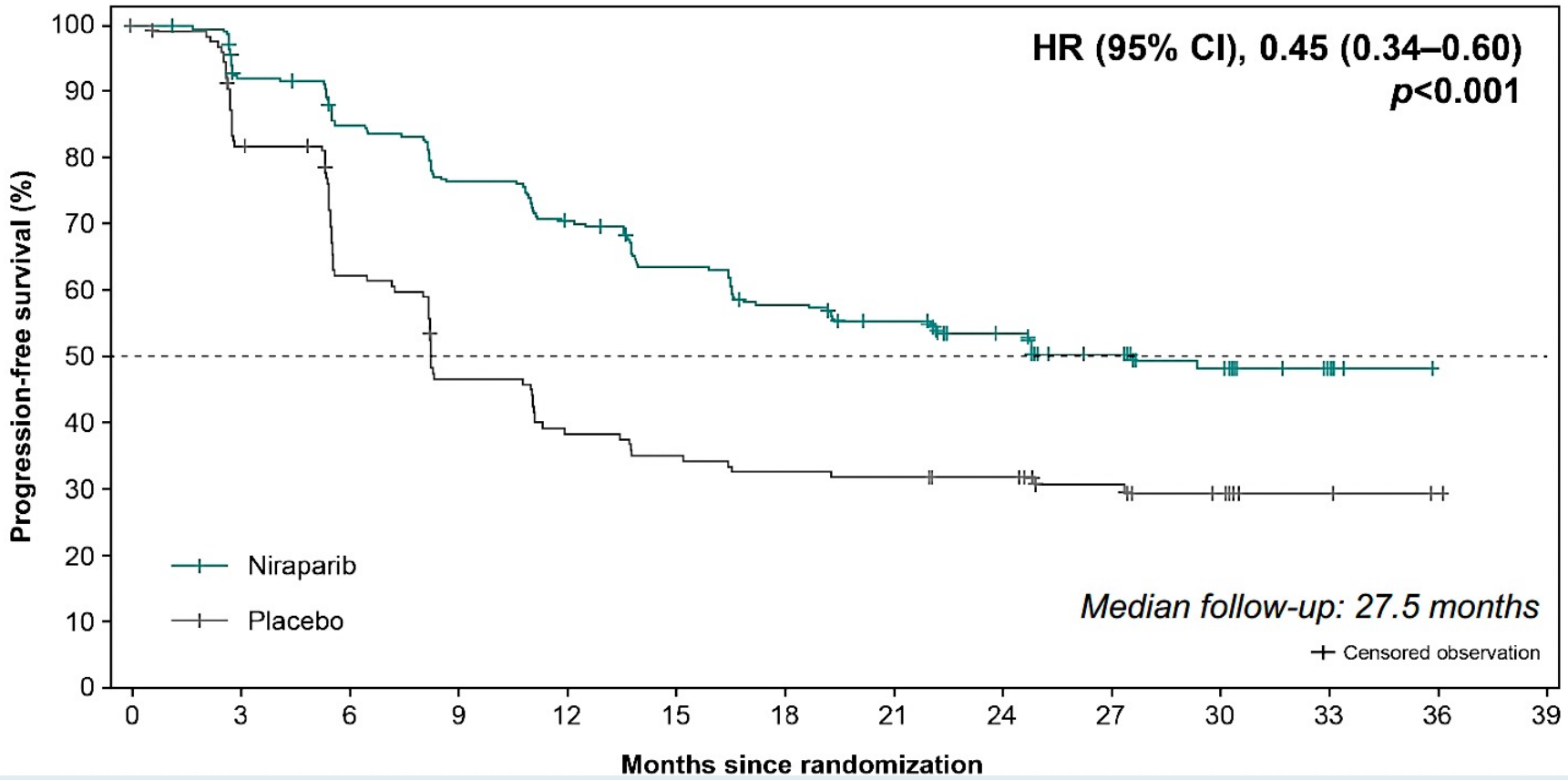
Efficacy and Safety of Niraparib as Maintenance Treatment in Patients with Newly Diagnosed Advanced Ovarian Cancer Using an Individualized Starting Dose (PRIME Study): A Randomized, Double-blind, Placebo-controlled, Phase 3 Trial

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

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

SGO 2022;Abstract LBA5.

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



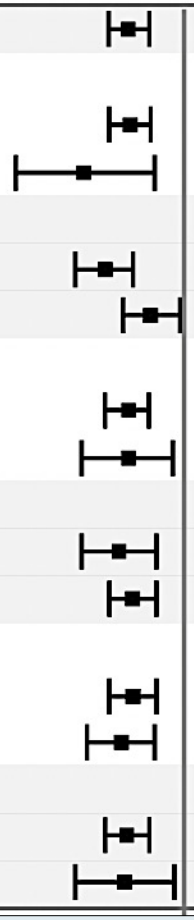
16.5 months longer median PFS with niraparib versus placebo

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

Li N et al. SGO 2022;Abstract LBA5.

PRIME: PFS Benefit in Prespecified Subgroups

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



Li N et al. SGO 2022;Abstract LBA5.

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

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

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

IGCS 2022;Abstract S005/1753.

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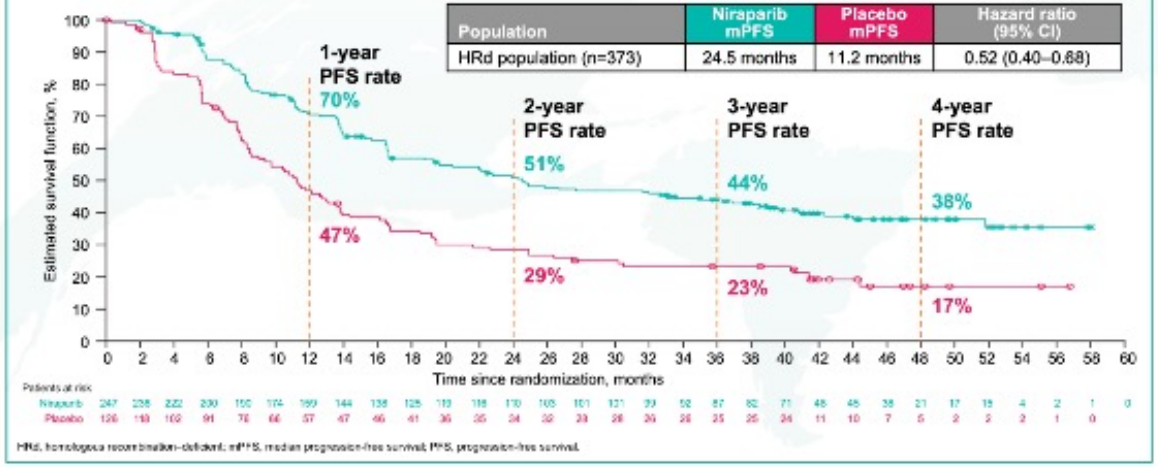
RTP RESEARCH TO PRACTICE

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

November 17, 2021, Clinical Cutoff Date

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

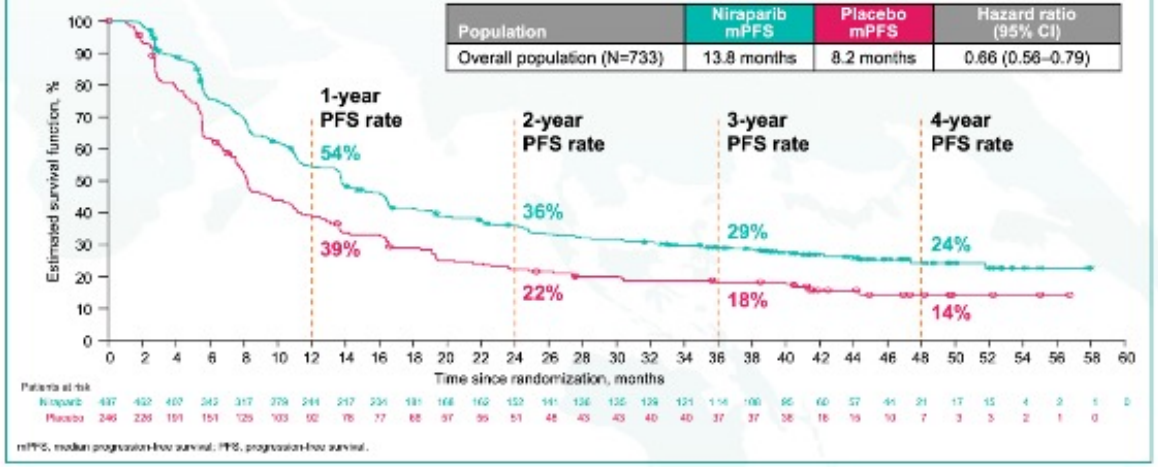
Population	Niraparib mPFS	Placebo mPFS	Hazard ratio (95% CI)
HRd population (n=373)	24.5 months	11.2 months	0.52 (0.40–0.68)



HRd, homologous recombination–deficient; mPFS, median progression-free survival; PFS, progression-free survival.

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

Population	Niraparib mPFS	Placebo mPFS	Hazard ratio (95% CI)
Overall population (N=733)	13.8 months	8.2 months	0.66 (0.56–0.79)



mPFS, median progression-free survival; PFS, progression-free survival.

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

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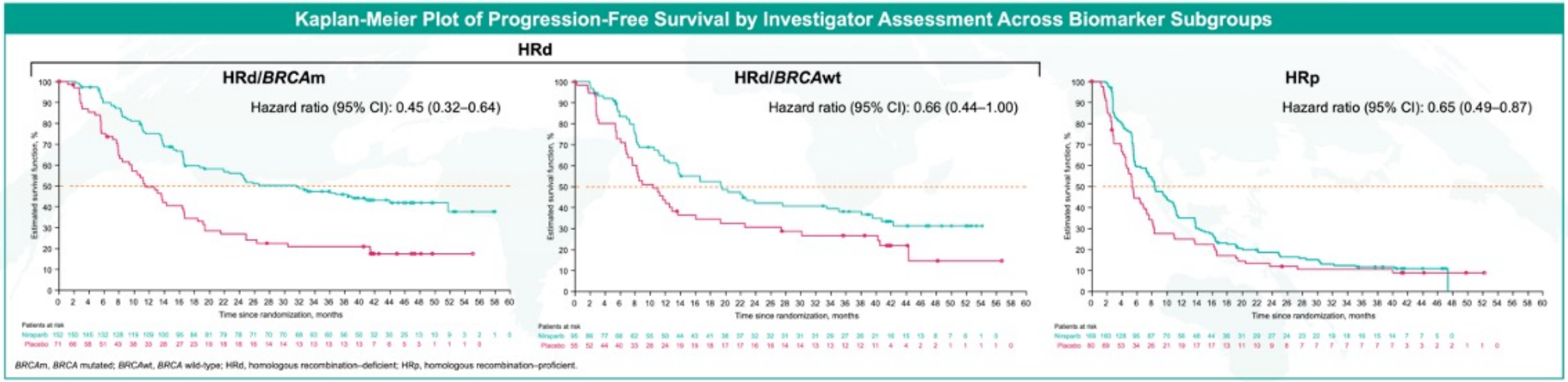
BICR, blinded independent central review; HRd, homologous recombination–deficient; IA, investigator assessed; mPFS, median progression-free survival; OS, overall survival; PFS, progression-free survival.

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

RTP RESEARCH TO PRACTICE

PRIMA: PFS Across Biomarker Subgroups (Investigator-Assessed)

November 17, 2021, Clinical Cutoff Date



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

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

RTP RESEARCH TO PRACTICE

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

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

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

IGCS 2022;Abstract S002/1609.

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

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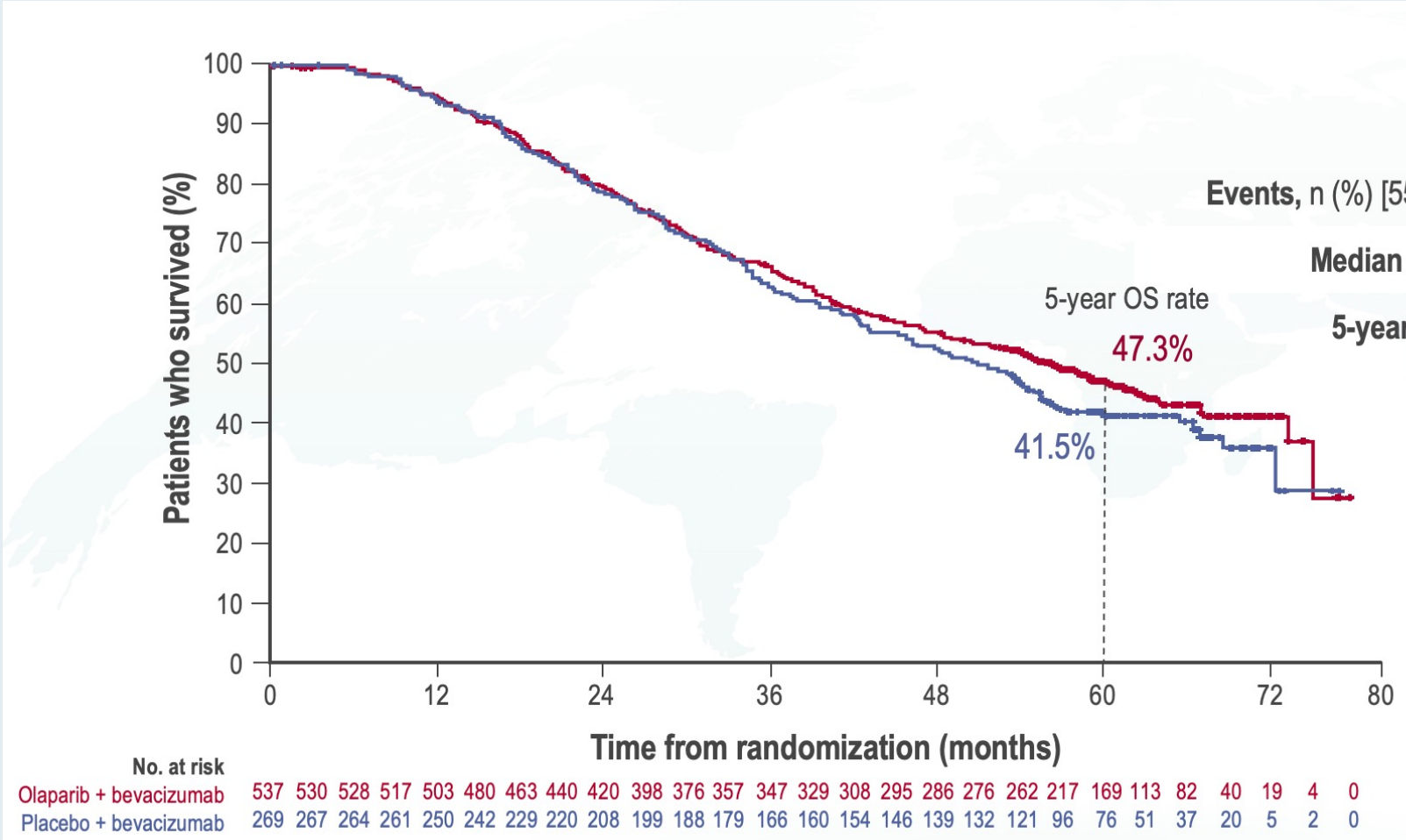
RTP RESEARCH TO PRACTICE

PAOLA-1: Overall Survival (ITT Population)



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

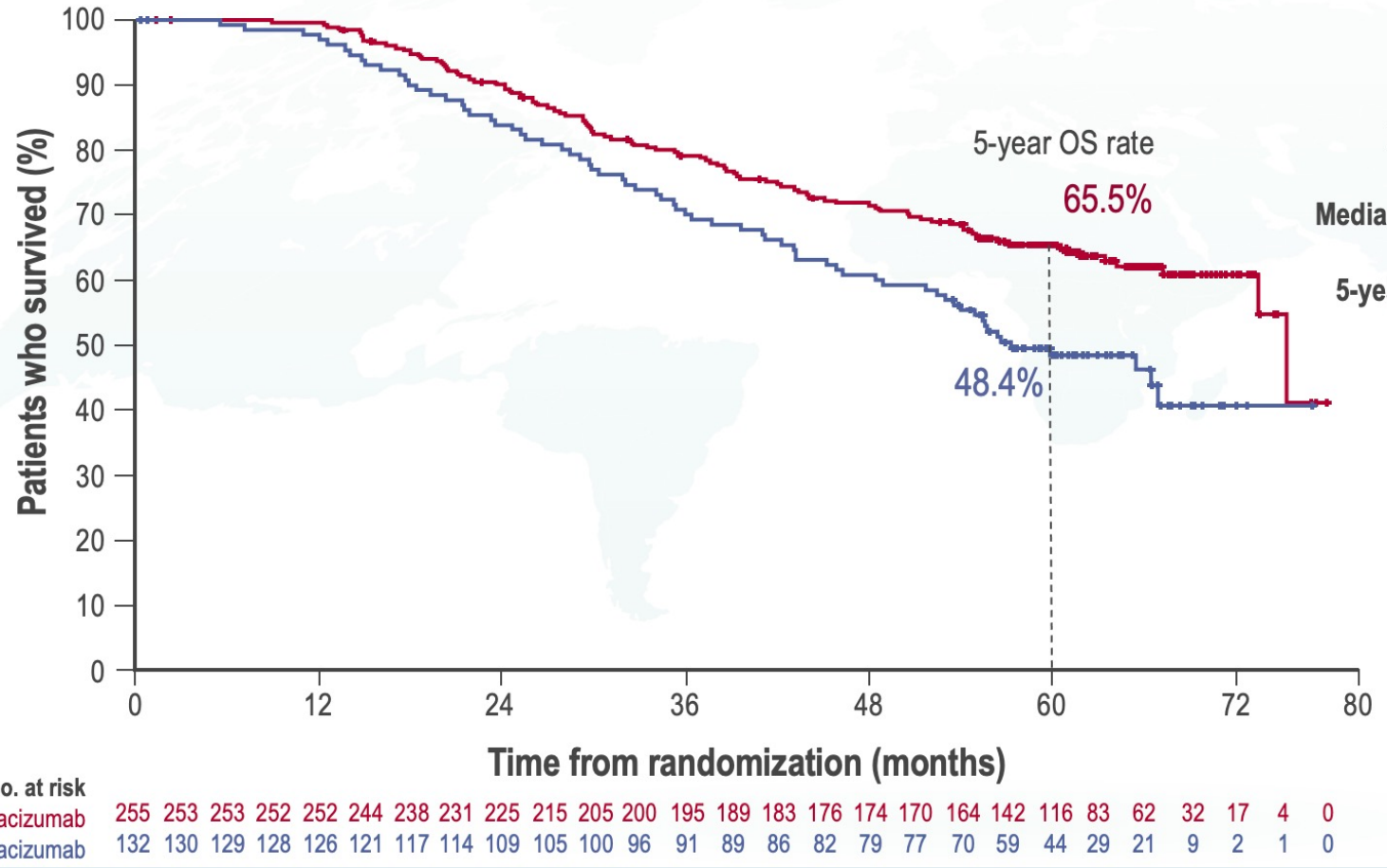
HR 0.92 (95% CI 0.76–1.12);
***P*=0.4118**

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

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

Ray-Coquard I et al. IGCS 2022;Abstract S002/1609.

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



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

HR 0.62 (95% CI 0.45–0.85)

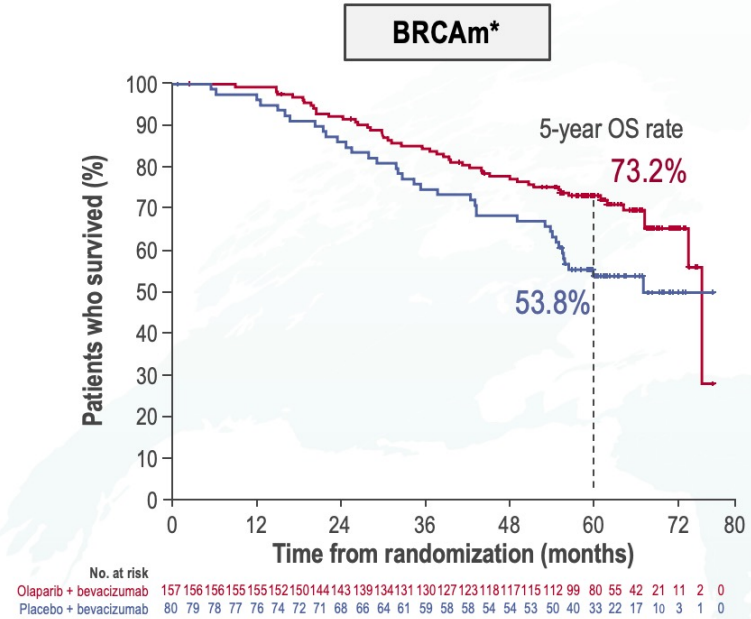
38% reduction in risk of death for olaparib + bevacizumab vs bevacizumab alone

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

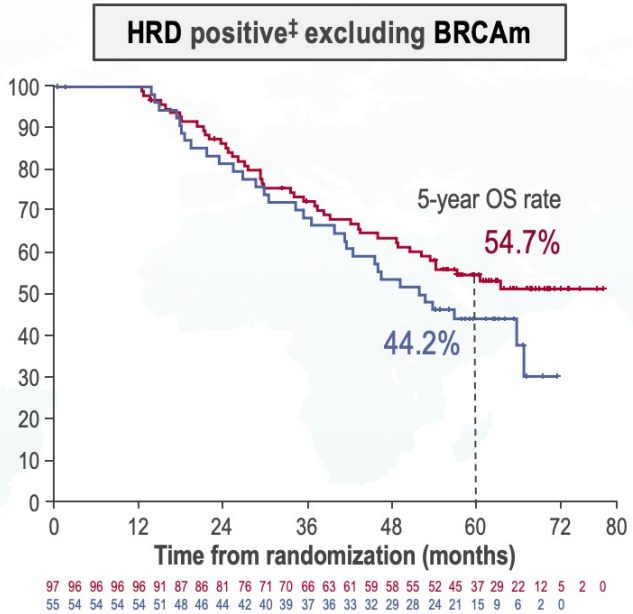
Ray-Coquard I et al. IGCS 2022;Abstract S002/1609.

RTP RESEARCH TO PRACTICE

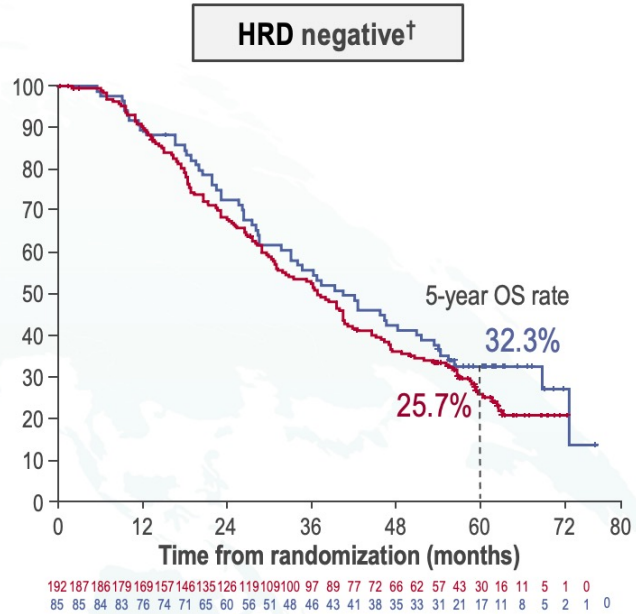
PAOLA-1: Overall Survival Subgroup Analysis by BRCA Mutation and HRD Status



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



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



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

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

Ray-Coquard I et al. IGCS 2022;Abstract S002/1609.

RTP RESEARCH TO PRACTICE

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

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

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

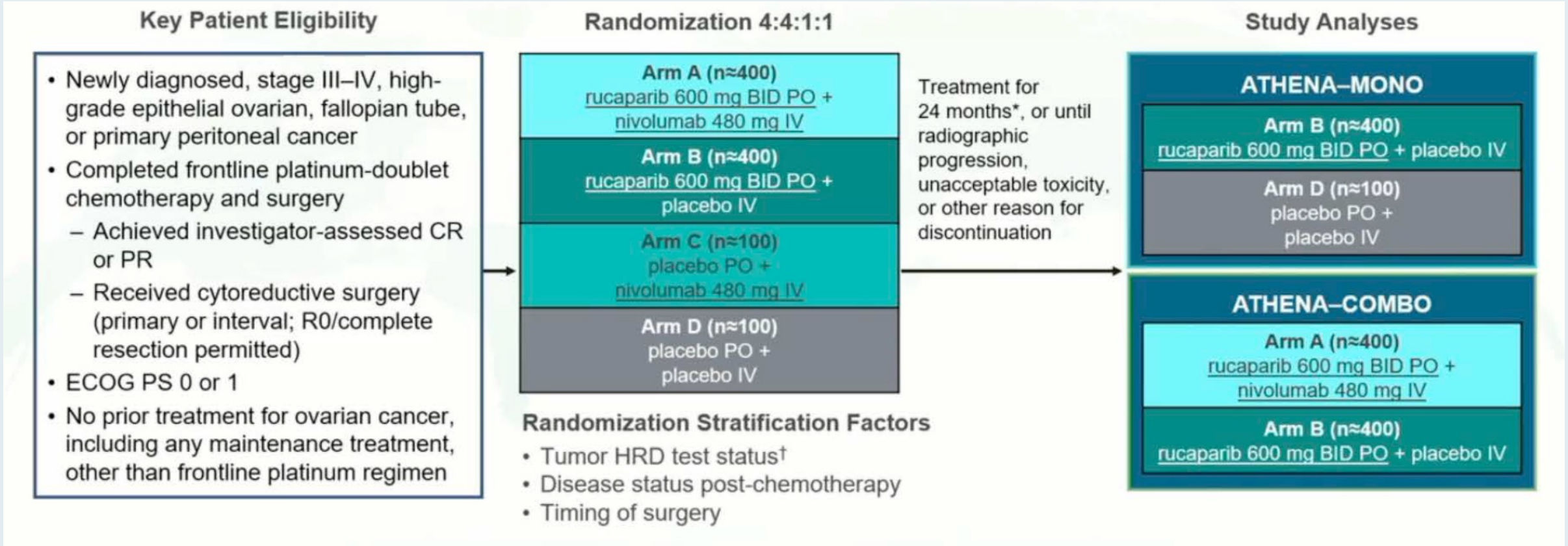
Originally presented at the 2022 ASCO Annual Meeting, 3-7 June 2022:
Bradley J. Monk, Christine Parkinson, Myong Cheol Lim, David M. O'Malley, Ana Oaknin, Michelle K. Wilson, Robert L. Coleman, Domenica Lorusso, Amit Oza, Sharad Ghamande, Athina Christopoulou, Emily Prendergast, Fuat Demirkiran, Ramey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

IGCS 2022;Abstract S001/1608.

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

RTP RESEARCH TO PRACTICE

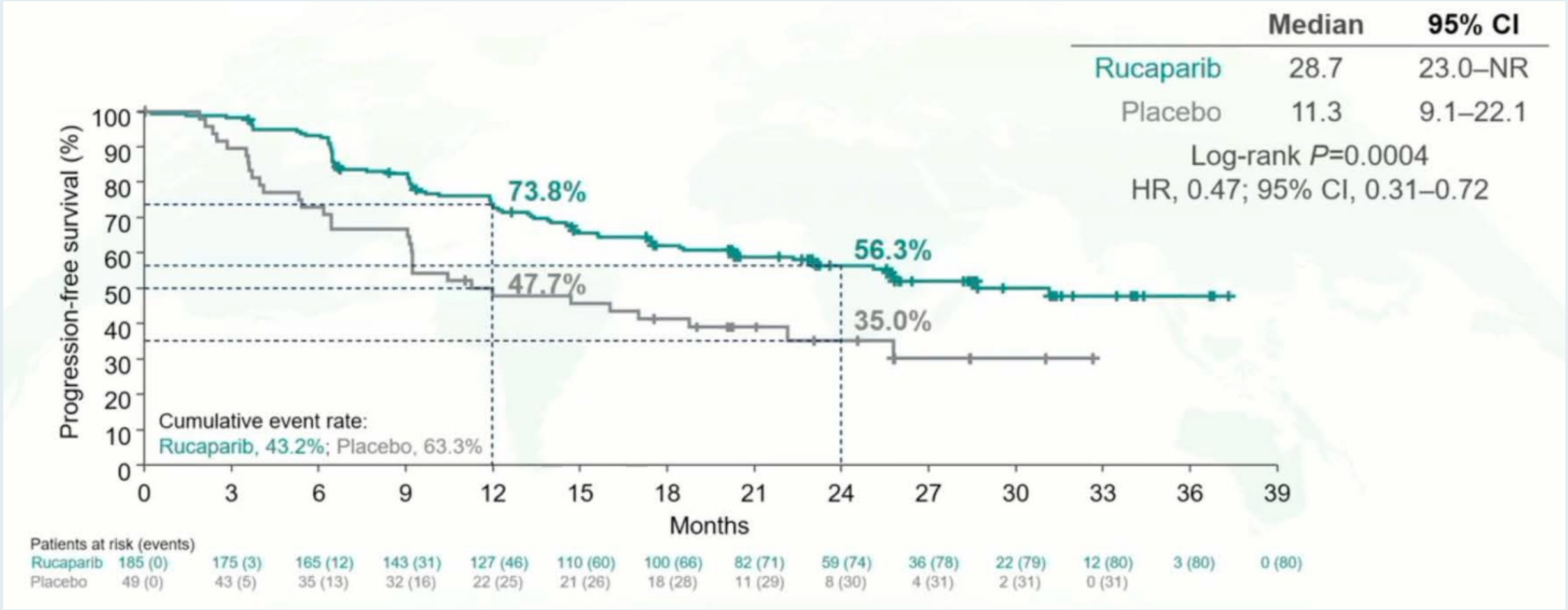
ATHENA-MONO Study Design



Monk BJ et al. IGCS 2022;Abstract S001/1608.

RTP RESEARCH TO PRACTICE

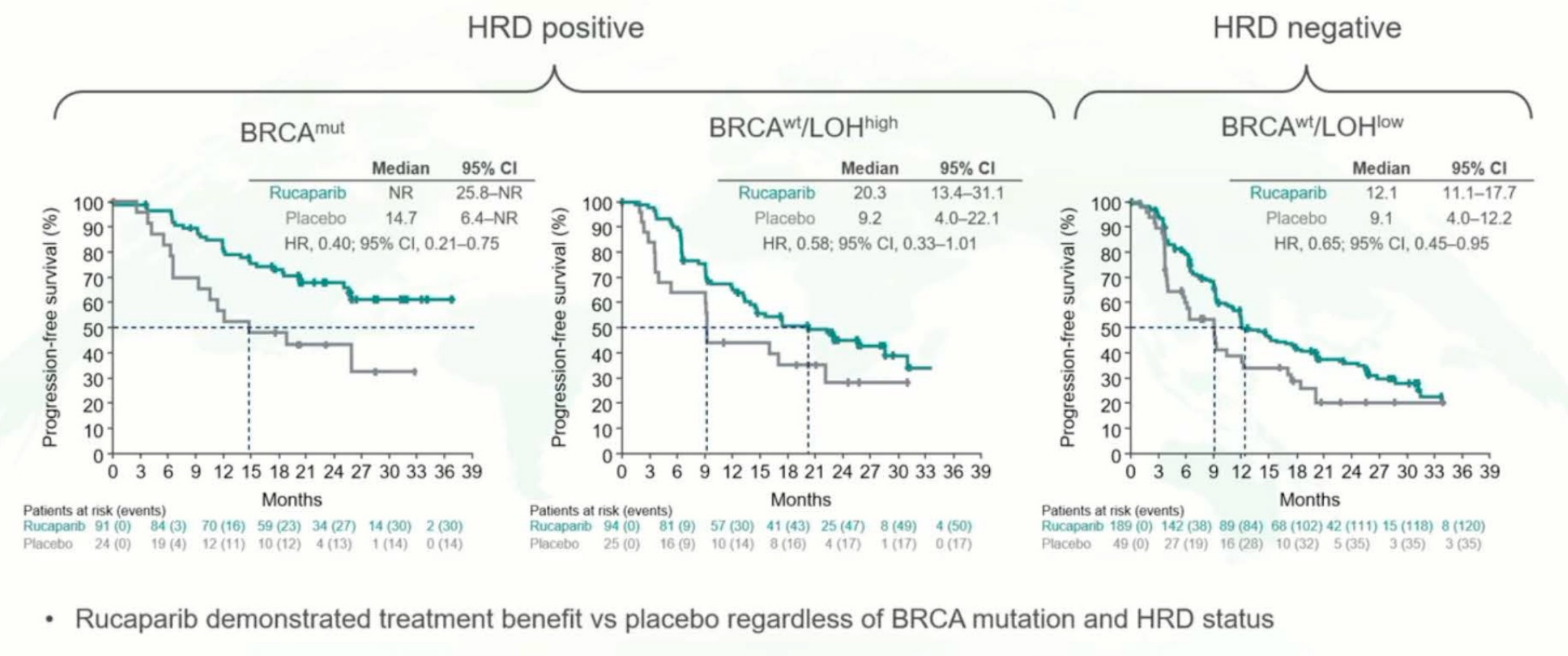
ATHENA-MONO Primary Endpoint: Investigator-Assessed PFS in the HRD Population



Monk BJ et al. IGCS 2022;Abstract S001/1608.

RTP RESEARCH TO PRACTICE

ATHENA-MONO: Investigator-Assessed PFS in Exploratory Subgroups



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

Monk BJ et al. IGCS 2022;Abstract S001/1608.

RTP RESEARCH TO PRACTICE

Efficacy Analysis By Disease Risk Subgroup For The Phase 3 ATHENA–MONO Study (GOG-3020/ENGOT-ov45) Evaluating Rucaparib Maintenance Treatment In Patients With Newly Diagnosed Ovarian Cancer

David M. O'Malley,[1] Athina Christopoulou,[2] Myong Cheol Lim,[3] John P. Diaz,[4] Fuat Demirkiran,[5] Michelle Wilson,[6] Andrea Jewell,[7] Vít Drochýtek,[8] Paul Bessette,[9] Robert T. Morris,[10] Toon Van Gorp,[11] Linda Van Le,[12] Gabriel Lindahl,[13] Ramez N. Eskander,[14] Dearbhaile C. Collins,[15] Sandra Goble,[16] Stephanie Hume,[16] Keiichi Fujiwara,[17] Bradley J. Monk,[18] Rebecca Kristeleit[19]

[1]The Ohio State University, James Cancer Center, Columbus, OH, USA; [2]Saint Andrew General Hospital, Patras, Greece; [3]National Cancer Center Korea, Goyang-si,Gyeonggi-do, Republic of Korea; [4]Miami Cancer Institute, Miami, FL, USA; [5]Istanbul University-Cerrahpaşa, Istanbul, Turkey; [6]Auckland City Hospital, Auckland, New Zealand; [7]University of Kansas Medical Center, Kansas City, KS, USA; [8]Faculty Hospital Kralovske Vinohrady; Charles University, Prague, Czech Republic; [9]University of Sherbrooke, Sherbrooke, Quebec, Canada; [10]Wayne State University Karmanos Cancer Institute, Detroit, MI, USA; [11]University Hospital Leuven, Leuven Cancer Institute, Leuven, Belgium; [12]University of North Carolina Lineberger Comprehensive Cancer Center, Chapel Hill, NC, USA; [13]Nordic Society of Gynaecological Oncology, Copenhagen, Denmark; Linköping University, Linköping, Sweden; [14]University of California San Diego, La Jolla, CA, USA;[15]Cancer Trials Ireland, Dublin, Ireland; Cork University Hospital, Cork, Ireland; [16]Clovis Oncology, Inc., Boulder, CO, USA; [17]Saitama Medical University International Medical Center, Hidaka, Saitama, Japan; [18]GOG Foundation, HonorHealth Research Institute, University of Arizona College of Medicine, Creighton University School of Medicine, Phoenix, AZ, USA; [19]Guy's and St Thomas' NHS Foundation Trust, London, UK

IGCS 2022;Abstract O026/560.

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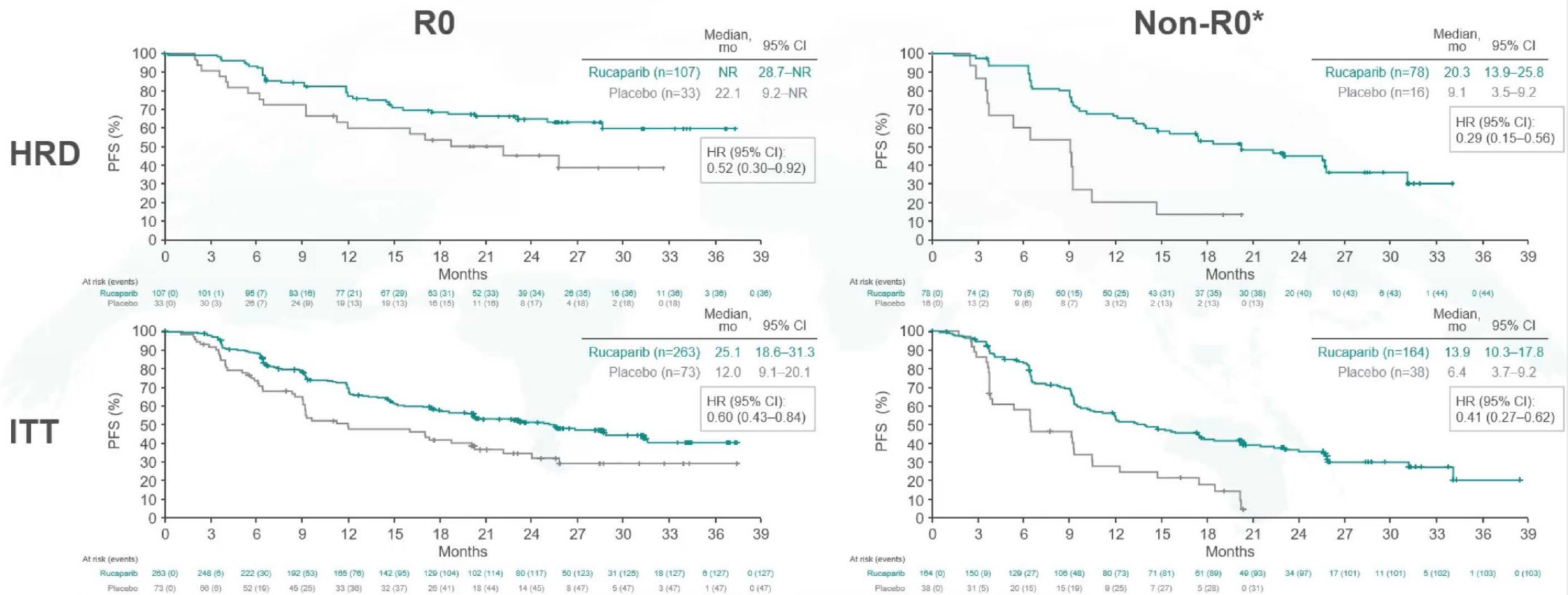
ATHENA-MONO: PFS by Surgical Outcome



Data cutoff: March 23, 2022. *Includes microscopic residual (<1 cm) and macroscopic residual (≥1 cm) disease.
No difference in treatment effect across subgroups based on Cox proportional model including interaction between subgroup and treatment effect in the ITT population.
CI, confidence interval; HR, hazard ratio; HRD, homologous recombination deficiency; ITT, intent-to-treat; NR, not reached; PFS, progression-free survival.

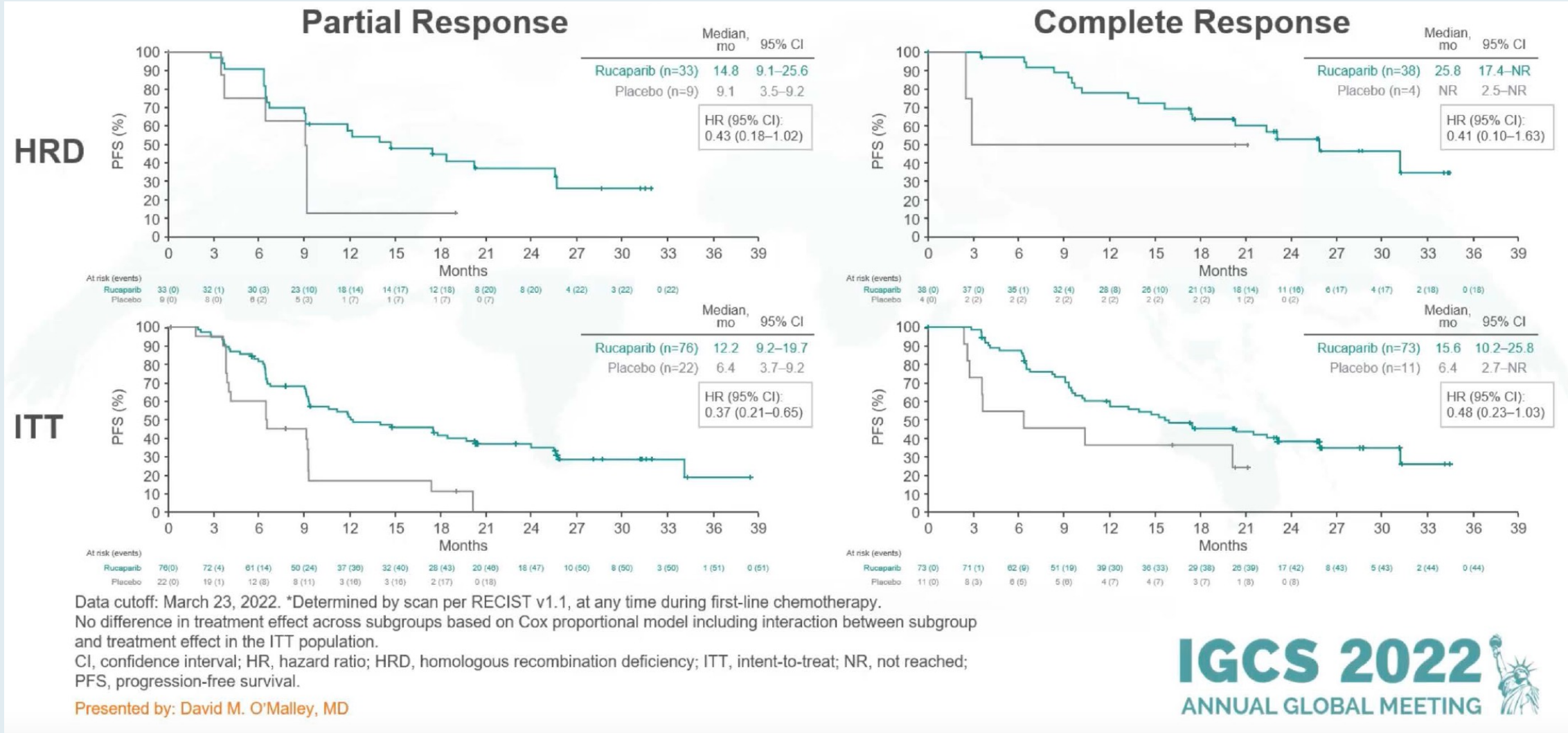
Presented by: David M. O'Malley, MD

IGCS 2022 ANNUAL GLOBAL MEETING

O'Malley DM et al. IGCS 2022;Abstract O026/560.

RTP RESEARCH TO PRACTICE

ATHENA-MONO: PFS by First-Line Chemotherapy Response



Data cutoff: March 23, 2022. *Determined by scan per RECIST v1.1, at any time during first-line chemotherapy.
No difference in treatment effect across subgroups based on Cox proportional model including interaction between subgroup and treatment effect in the ITT population.
CI, confidence interval; HR, hazard ratio; HRD, homologous recombination deficiency; ITT, intent-to-treat; NR, not reached; PFS, progression-free survival.

Presented by: David M. O'Malley, MD

IGCS 2022 ANNUAL GLOBAL MEETING

O'Malley DM et al. IGCS 2022;Abstract O026/560.

RTP RESEARCH TO PRACTICE

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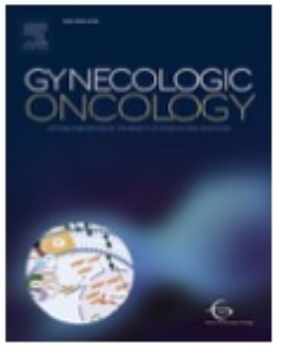
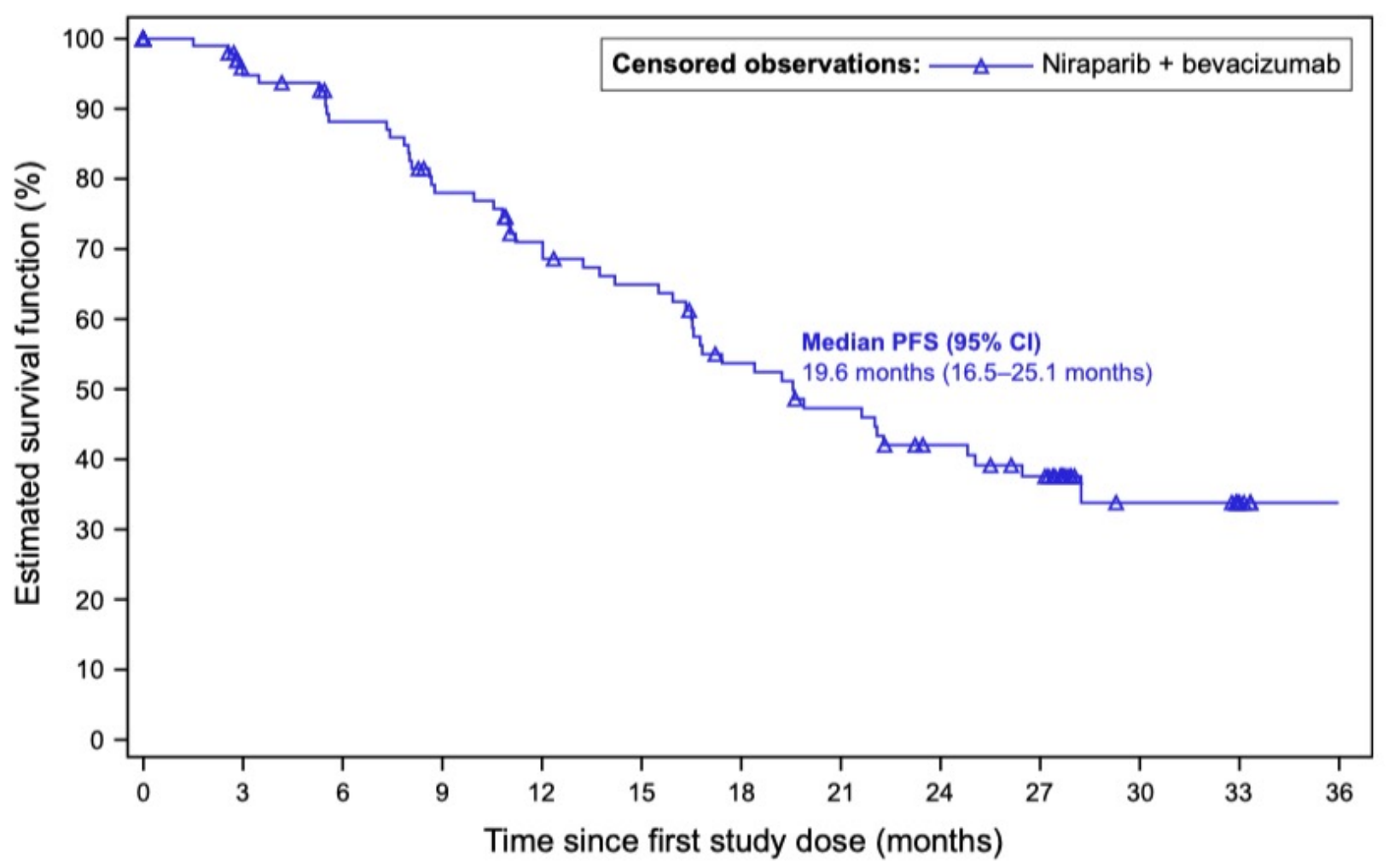


Gynecol Oncol 2022 Aug;166(2):219-29.

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

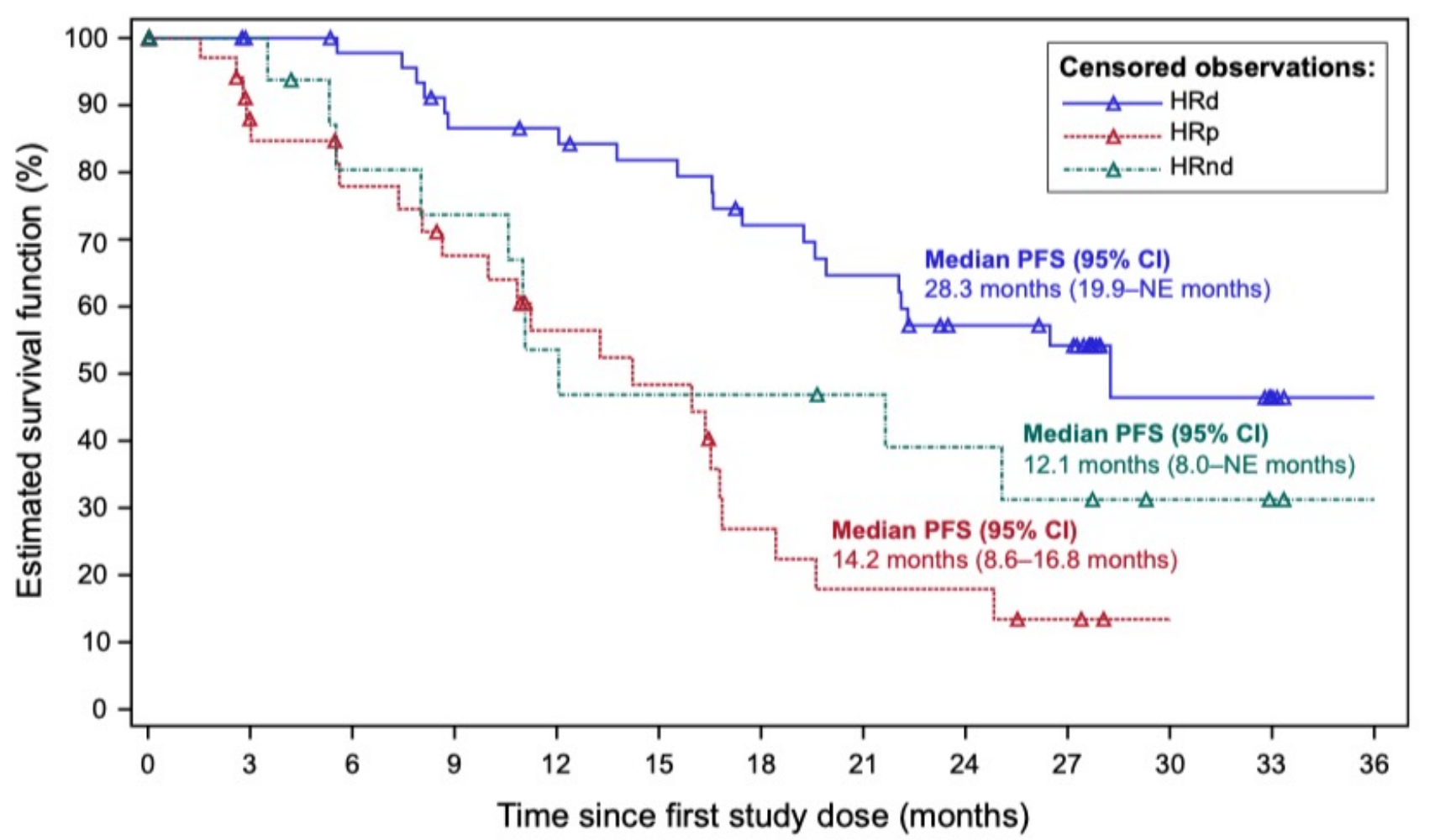
Melissa M. Hardesty [a,*], Thomas C. Krivak [b], Gail S. Wright [c], Erika Hamilton [d], Evelyn L. Fleming [e], Jimmy Belotte [f], Erika K. Keeton [g], Ping Wang [f], Divya Gupta [f], Aine Clements [h], Heidi J. Gray [i], Gottfried E. Konecny [j], Richard G. Moore [k], Debra L. Richardson [l]

OVARIO: Investigator-Assessed PFS in the Overall Population



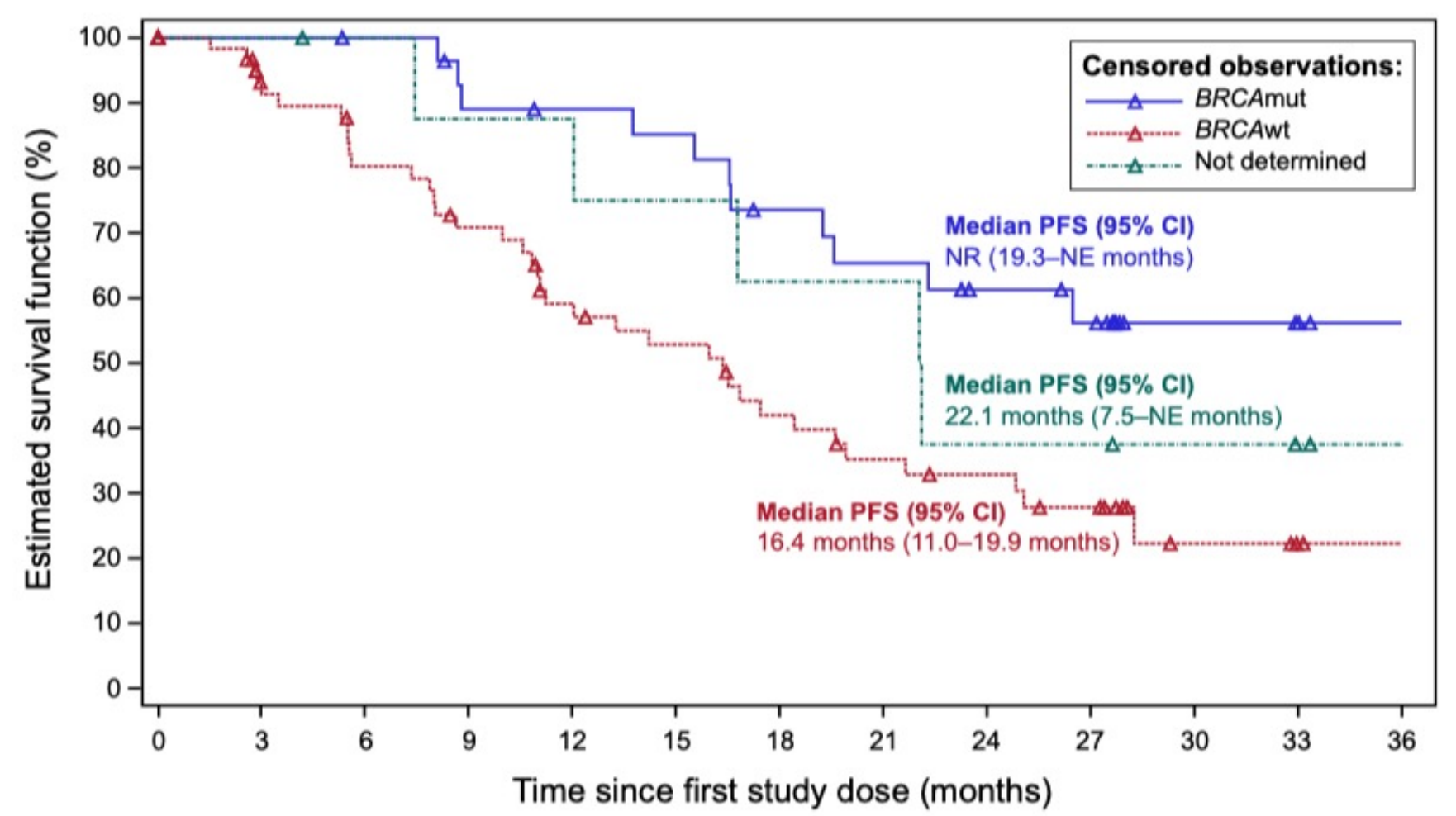
Hardesty MM et al. *Gynecol Oncol* 2022;166(2):219-29.

OVARIO: Investigator-Assessed PFS by HRD Status



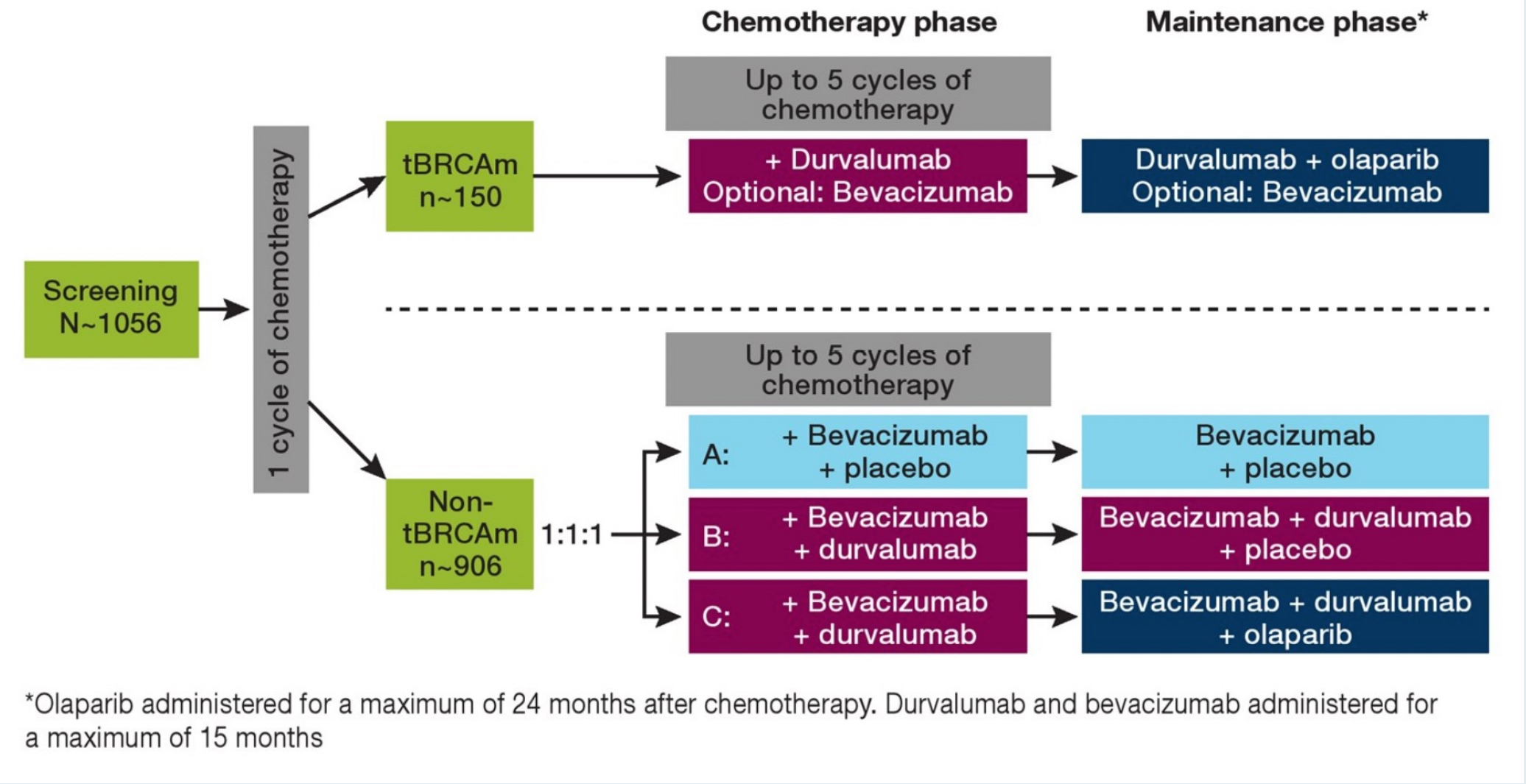
Hardesty MM et al. *Gynecol Oncol* 2022;166(2):219-29.

OVARIO: Investigator-Assessed PFS by BRCA Mutation Status



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

DUO-O Study Design in Newly Diagnosed Advanced Ovarian Cancer

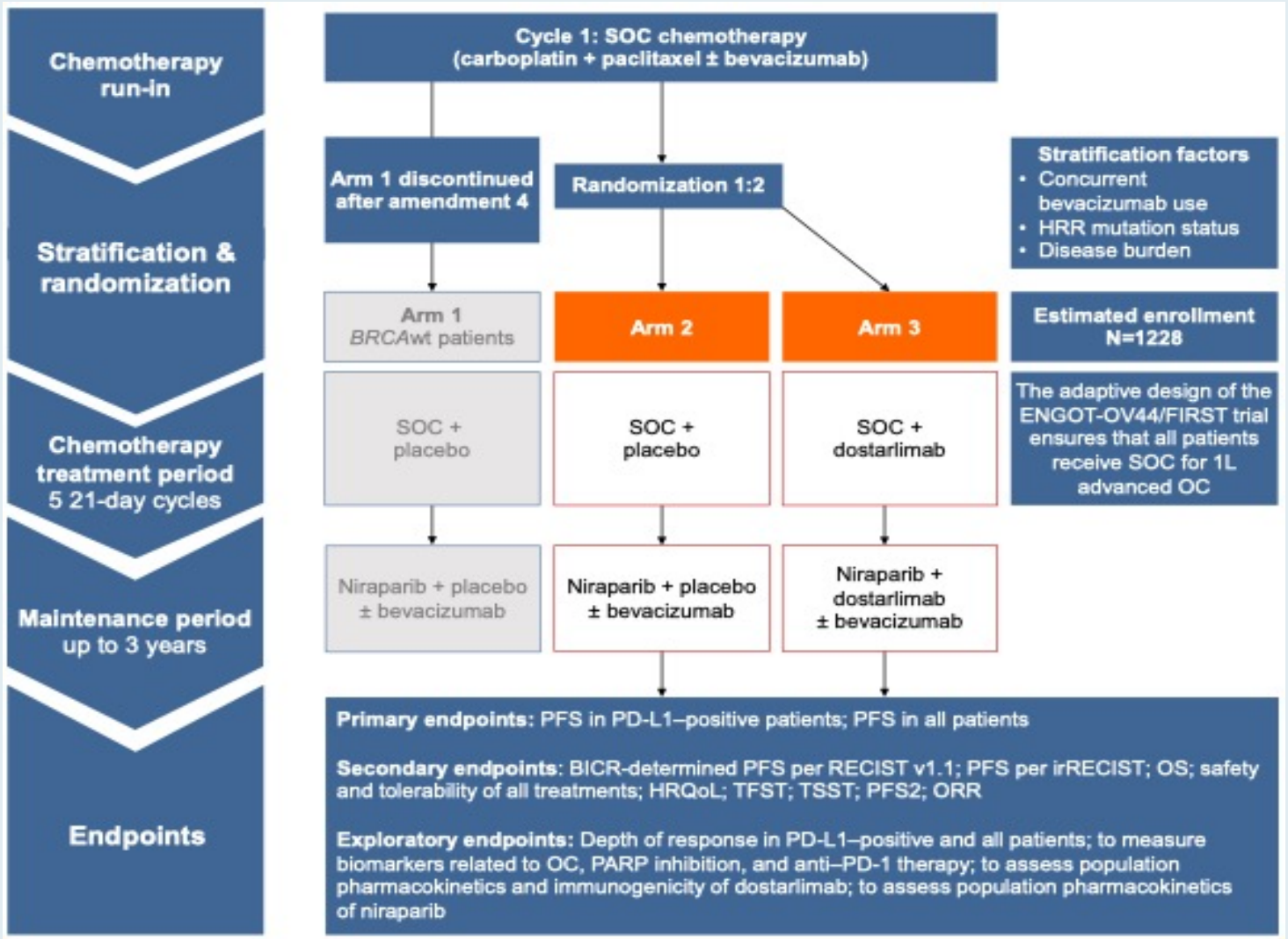


*Olaparib administered for a maximum of 24 months after chemotherapy. Durvalumab and bevacizumab administered for a maximum of 15 months

Estimated completion date: July 2023

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

FIRST/ENGOT-OV44: Phase III Trial of Dostarlimab for Newly Diagnosed Ovarian Cancer



SOC = standard of care; HRR = homologous recombination repair; OC = ovarian cancer; BICR = blind independent central review; PFS = progression-free survival; OS = overall survival; HRQoL = health-related quality of life; TFST = time to first subsequent therapy; TSST = time to second subsequent therapy; PFS2 = progression-free survival with first subsequent therapy; ORR = objective response rate

Hardy-Bessard A-C et al. ASCO 2020;Abstract 272.

RTP RESEARCH TO PRACTICE

PARP Inhibitor Rechallenge

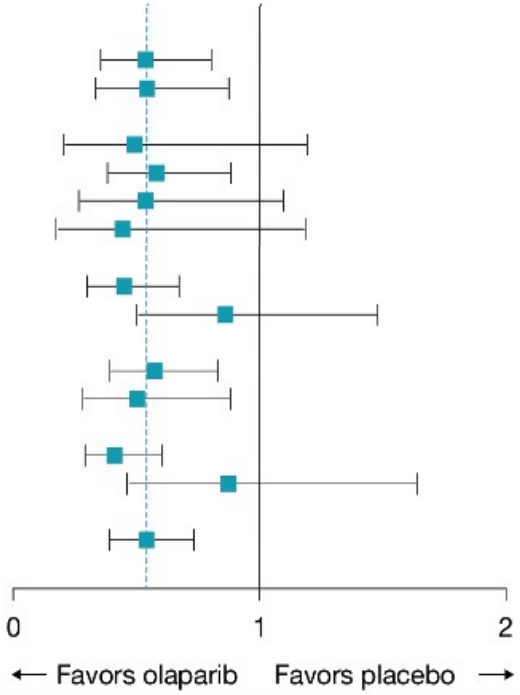
OReO/ENGOT Ov-38 trial: Impact of maintenance olaparib rechallenge according to ovarian cancer patient prognosis—An exploratory joint analysis of the BRCA and non-BRCA cohorts.

ASCO 2022;Abstract 5558.

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

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

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



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

Selle F et al. ASCO 2022;Abstract 5558.

RTP RESEARCH TO PRACTICE

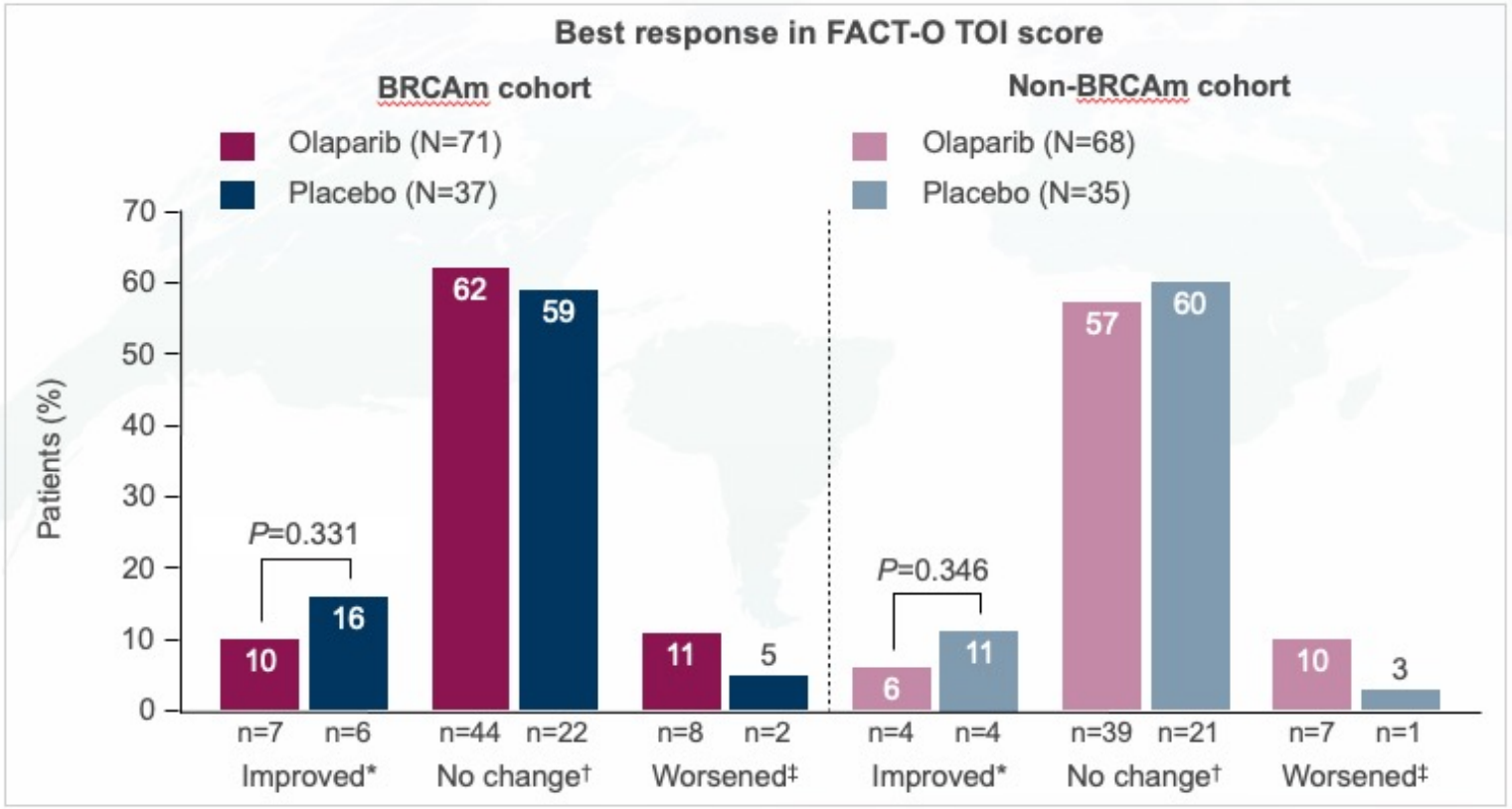
Maintenance olaparib rechallenge in patients with ovarian cancer previously treated with a PARP inhibitor: patient-reported outcomes from the Phase IIIb OReO/ENGOT-ov38 trial

Andrés Redondo,[1] Philippe Follana,[2] Giovanni Scambia,[3] Bernard Asselain,[4] Frederik Marmé,[5] Mansoor R. Mirza,[6] Maria Elena Laudani,[7] Radosław Madry,[8] Rosalind Glasspool,[9] Benoit You,[10] María Jesús Rubio-Perez,[11] Claudio Zamagni,[12] Ahmed El-Balat,[13] Anne Claire Hardy-Bessard,[14] Ana Oaknin,[15] Graziana Ronzino,[16] Bob Shaw,[17] Hitomi Nakamura,[17] Dominique Berton,[18] Eric Pujade-Lauraine[19]

[1]La Paz University Hospital, Madrid, Spain, and GEICO; [2]Centre Antoine Lacassagne, Nice, France, and GINECO; [3]Fondazione Policlinico Universitario A. Gemelli, IRCCS, UOC Ginecologia Oncologica, Dipartimento per la Salute della Donna e del Bambino e della Salute Pubblica, Rome, Italy, and MITO; [4]ARCAGY-GINECO, Paris, France, and GINECO; [5]University Hospital Mannheim, Medical Faculty Mannheim, Heidelberg University, Mannheim, Germany, and AGO; [6]Rigshospitalet, Copenhagen, Denmark, and NSGO; [7]Department of Gynecology and Obstetrics, Sant'Anna Hospital, University of Turin, Turin, Italy, and MITO; [8]Department of Oncological Gynecology Poznan University of Medical Sciences, Poznan, Poland, and PGOG; [9]Beatson West of Scotland Cancer Centre and Institute of Cancer Sciences, University of Glasgow, Glasgow, UK, and SGCTG and NCRI; [10]HCL - Centre Hospitalier Lyon Sud, Lyon, France, and GINECO; [11]Reina Sofia University Hospital, Cordoba, Spain, and GEICO; [12]IRCCS Azienda Ospedaliero-universitaria di Bologna, Bologna, Italy, and MITO; [13]Klinikum der Johann Wolfgang Goethe-Universität, Frankfurt, Germany and AGO; [14]Centre CARIO – HPCA, Plérin, France, and GINECO; [15]Gynaecologic Cancer Programme, Vall d'Hebron Institute of Oncology (VHIO), Hospital Universitari Vall d'Hebron, Vall d'Hebron Barcelona Hospital Campus, Barcelona, Spain, and GEICO; [16]Medical Oncology Unit, Vito Fazzi Hospital, Lecce, Italy, and MITO; [17]Oncology R&D, AstraZeneca, Cambridge, UK; [18]Institut de Cancérologie de l'Ouest, Saint-Herblain, France, and GINECO; [19]ARCAGY-GINECO, Paris, France, and GINECO

IGCS 2022;Abstract O025/522.

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



Deterioration§ in TOI score

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

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

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

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

RTP RESEARCH TO PRACTICE

PARP Inhibitors in Platinum-Sensitive Recurrent OC

RTP
RESEARCH
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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 germline BRCA (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 cycle 14 → every 12 wk	Every 12 wk until wk 72 → every 24 wk	Every 8 wk to cycle 14 → 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
gBRCA 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

sBRCA = somatic BRCA; $BRCA^{WT}$ = wild-type BRCA; LOH = loss of heterozygosity

[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 Oncol* 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.

Overall Survival Results From ARIEL3: A Phase 3 Randomized, Double-blind Study of Rucaparib vs Placebo Following Response to Platinum-Based Chemotherapy for Recurrent Ovarian Carcinoma

Robert L. Coleman,[1*] Amit M. Oza,[2] Domenica Lorusso,[3] Carol Aghajanian,[4] Ana Oaknin,[5] Andrew Dean,[6] Nicoletta Colombo,[7] Johanne I. Weberpals,[8] Andrew R. Clamp,[9] Giovanni Scambia,[10] Alexandra Leary,[11] Robert W. Holloway,[12] Margarita Amenedo Gancedo,[13] Peter C. Fong,[14] Jeffrey C. Goh,[15] David M. O'Malley,[16] Sandra Goble,[17] Lara Maloney,[17] Jonathan A. Ledermann[18]

[1]The University of Texas MD Anderson Cancer Center, Houston, TX, USA; [2]Princess Margaret Cancer Centre, University Health Network, Toronto, ON, Canada; [3]MITO and Gynecologic Oncology Unit, Fondazione IRCCS Istituto Nazionale dei Tumori, Milan, Italy; [4]Memorial Sloan Kettering Cancer Center, New York, NY, USA; [5]Gynaecologic Cancer Programme, Vall d'Hebron Institute of Oncology (VHIO), Hospital Universitari Vall d'Hebron, Vall d'Hebron Barcelona Hospital Campus, Barcelona, Spain; [6]St John of God Subiaco Hospital, Subiaco, WA, Australia; [7]European Institute of Oncology and University of Milan-Bicocca, Milan, Italy; [8]Ottawa Hospital Research Institute, Ottawa, ON, Canada; [9]The Christie NHS Foundation Trust and University of Manchester, Manchester, UK; [10]Fondazione Policlinico Universitario A. Gemelli IRCCS and Scientific Directorate, Rome, Italy; [11]Gustave Roussy Cancer Center, INSERM U981, and Groupe d'Investigateurs Nationaux pour l'Etude des Cancers Ovariens (GINECO), Villejuif, France; [12]Florida Hospital Cancer Institute, Orlando, FL, USA; [13]Oncology Center of Galicia, La Coruña, Spain; [14]Auckland City Hospital, Grafton, Auckland, New Zealand; [15]Cancer Care Services, Royal Brisbane and Women's Hospital, Herston, QLD, Australia, and University of Queensland, St Lucia, QLD, Australia; [16]The Ohio State University, James Cancer Center, Columbus, OH, USA; [17]Clovis Oncology, Inc., Boulder, CO, USA; [18]UCL Cancer Institute, University College London and UCL Hospitals, London, UK

*Affiliation where the work was conducted; current affiliation: US Oncology Research, The Woodlands, TX, USA

IGCS 2022;Abstract O003/557.

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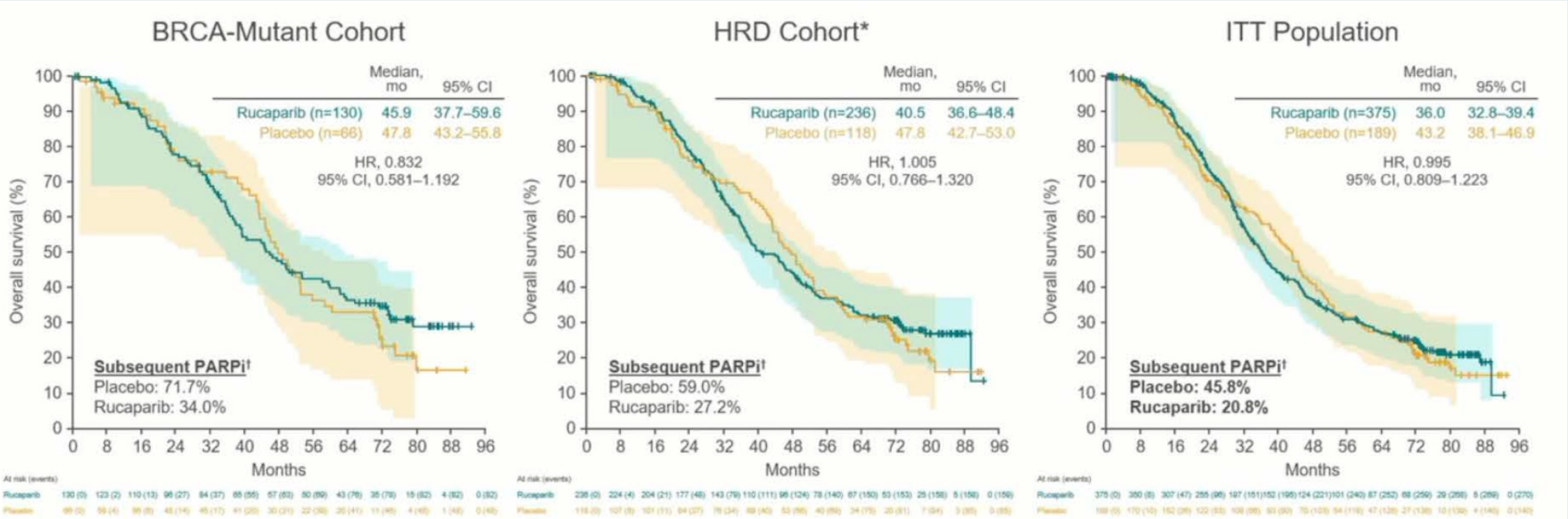
ARIEL3: Final Overall Survival



- Nearly half (45.8%) of patients randomized to the placebo group received subsequent PARP inhibitor therapy

Data cutoff date: April 4, 2022.

*Includes BRCA-mutant and BRCA–wild-type/LOH-high groups. †Patients receiving a PARP inhibitor during any subsequent treatment.
BRCA, *BRCA1* and *BRCA2*; CI, confidence interval; HR, hazard ratio; HRD, homologous recombination deficiency; ITT, intent-to-treat; LOH, loss of heterozygosity; mo, months; OS, overall survival; PARPi, poly(ADP-ribose) polymerase inhibitor.

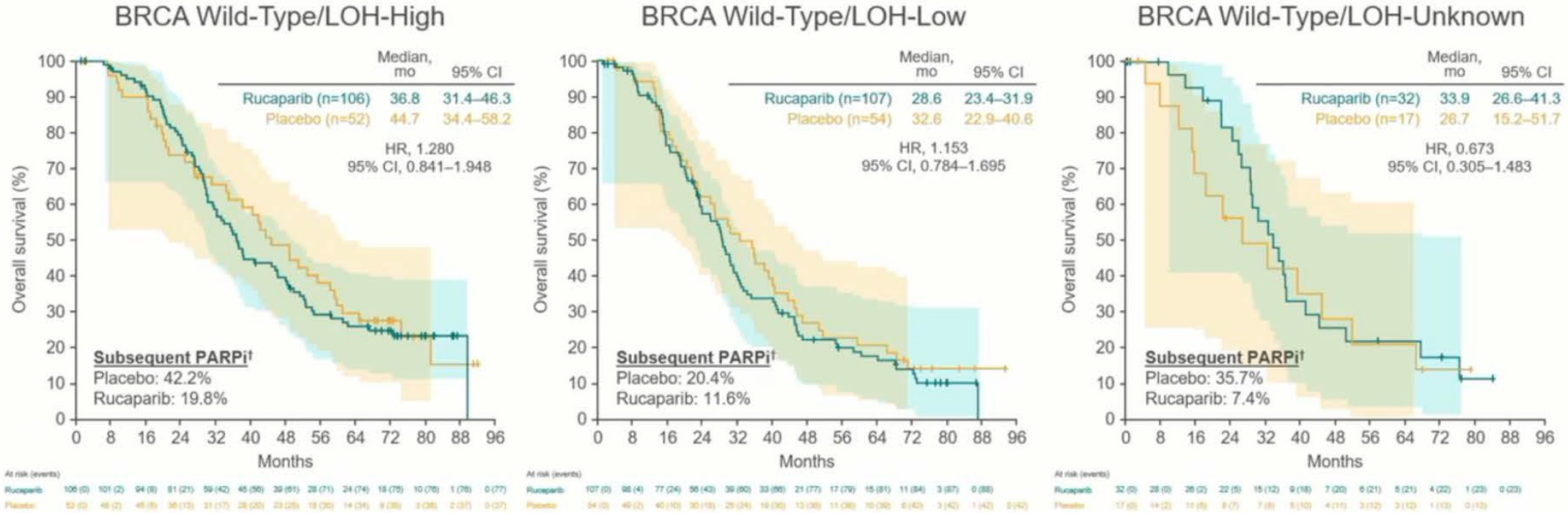
Presented by: Robert L. Coleman, MD, FACOG, FACS

IGCS 2022 ANNUAL GLOBAL MEETING

Coleman RL et al. IGCS 2022;Abstract O003/557.

RTP RESEARCH TO PRACTICE

ARIEL3: Final Overall Survival in BRCA Wild-Type Non-nested Cohorts



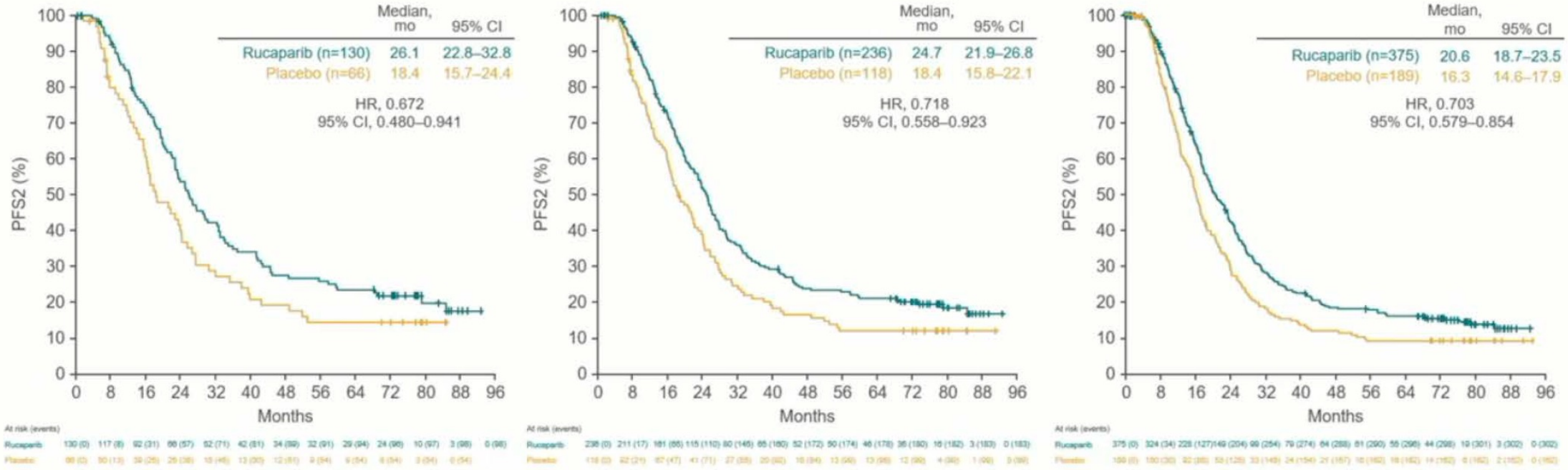
Data cutoff date: April 4, 2022.
†Patients receiving a PARP inhibitor during any subsequent treatment.
BRCA, *BRCA1* and *BRCA2*; CI, confidence interval; HR, hazard ratio; LOH, loss of heterozygosity; mo, months; OS, overall survival. PARPi, poly(ADP-ribose) polymerase inhibitor.
Presented by: Robert L. Coleman, MD, FACOG, FACS

IGCS 2022
ANNUAL GLOBAL MEETING

Coleman RL et al. IGCS 2022;Abstract O003/557.

RTP RESEARCH TO PRACTICE

ARIEL3: PFS2 Post-Progression Outcomes (Nested Cohorts)



Data cutoff date: April 4, 2022.
*Includes BRCA-mutant and BRCA-wildtype/LOH-high groups.
BRCA, *BRCA1* and *BRCA2*; CI, confidence interval; HR, hazard ratio; HRD, homologous recombination deficiency; ITT, intent-to-treat; LOH, loss of heterozygosity; mo, months; PFS2, progression-free survival on the subsequent line of therapy.

Presented by: Robert L. Coleman, MD, FACOG, FACS

IGCS 2022 ANNUAL GLOBAL MEETING

Coleman RL et al. IGCS 2022;Abstract O003/557.

RTP RESEARCH TO PRACTICE

Overall survival by number of prior lines of chemotherapy in patients with BRCA-mutated platinum-sensitive relapsed ovarian cancer receiving olaparib treatment or non-platinum chemotherapy in SOLO3

Charles A. Leath III,[1] Giovanni Scambia,[2] Ricardo Villalobos Valencia,[3] Nicoletta Colombo,[4] David Cibula,[5] Mariusz Bidziński,[6] Jae-Weon Kim,[7] Joo Hyun Nam,[8] Radoslaw Madry,[9] Carlos Hernandez,[10] Paulo Mora,[11] Sang Young Ryu,[12] Mei-Lin Ah-See,[13] Elizabeth S. Lowe,[14] Natalia Lukashchuk,[15] Dave Carter,[16] Richard T. Penson[17]

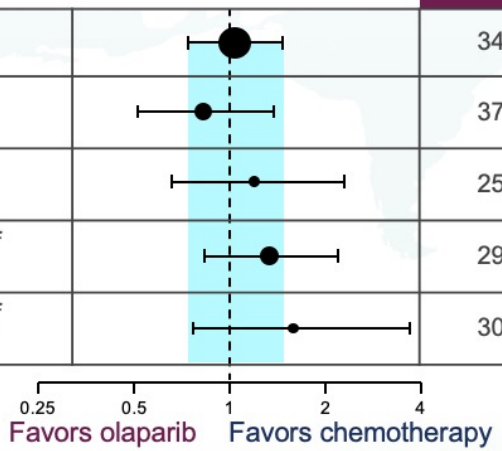
[1]Division of Gynecologic Oncology, O'Neal Comprehensive Cancer Center, University of Alabama, Birmingham, AL, USA; [2]Division of Gynecologic Oncology, Università Cattolica del Sacro Cuore-Fondazione Policlinico A. Gemelli, IRCCS, Rome, Italy; [3]Department of Medical Oncology, Centro Medico Dalinde, Mexico City, Mexico; [4]Division of Gynecologic Oncology, University of Milan-Bicocca and IEO European Institute of Oncology IRCCS, Milan, Italy; [5]Gynecologic Oncology Center, Department of Obstetrics and Gynecology, First Faculty of Medicine, Charles University and General University, Prague, Czech Republic; [6]Department of Gynecologic Oncology, Maria Sklodowska-Curie National Research Institute of Oncology, Warsaw, Poland; [7]Department of Obstetrics and Gynecology, Seoul National University Hospital, Seoul, South Korea; [8]Department of Obstetrics and Gynecology, Asan Medical Center, Seoul, South Korea; [9]Department of Gynecological Oncology, Medical University K. Marcinkowski and the Clinical Hospital of the Transfiguration, Poznań, Poland; [10]Oaxaca Site Management Organization, Oaxaca de Juarez, Mexico; [11]Instituto COI de Educação e Pesquisa, Rio de Janeiro, Brazil; [12]Department of Obstetrics and Gynecology, Korea Institute of Radiological and Medical Sciences, Seoul, South Korea; [13]Oncology R&D, Late-stage Development, AstraZeneca, Cambridge, UK; [14]Global Medicines Development, Oncology, AstraZeneca, Gaithersburg, MD, USA; [15]Translational Medicine, Oncology R&D, AstraZeneca, Cambridge, UK; [16]Biostatistics, Oncology Biometrics, Oncology R&D, AstraZeneca, Cambridge, UK; [17]Division of Hematology and Oncology, Harvard Medical School, Massachusetts General Hospital, Boston, MA, USA

IGCS 2022;Abstract LB001/1731.

SOLO-3: Summary of Efficacy by Lines of Prior Chemotherapy for Patients with gBRCAm, Platinum-Sensitive Recurrent OC

2 prior lines of chemotherapy	Favorable OS and PFS with olaparib vs chemotherapy supported by ORR
≥3 prior lines of chemotherapy	PFS and ORR numerically favored olaparib vs chemotherapy; however, OS favored chemotherapy vs olaparib

	OS				PFS			ORR	
		Median OS, months			Median PFS, months			ORR,† %	
Subgroup	HR (95% CI)*	Olaparib	Chemo-therapy	HR (95% CI)	Olaparib	Chemo-therapy	HR (95% CI)	Olaparib	Chemo-therapy
All patients		34.9	32.9	**1.07** (0.76–1.49)	13.4	9.2	**0.62** (0.43–0.91)	72.2	51.4
2 prior lines of chemotherapy		37.9	28.8	**0.83** (0.51–1.38)	16.4	9.0	**0.46** (0.29–0.75)	85.5	60.5
3 prior lines of chemotherapy		25.2	32.9	**1.20** (0.66–2.29)	11.1	7.4	**0.43** (0.24–0.80)	67.6	31.8
≥3 prior lines of chemotherapy		29.9	39.4	**1.33** (0.84–2.18)	9.4	9.2	**0.87** (0.55–1.45)	58.7	41.2
≥4 prior lines of chemotherapy		30.2	43.2	**1.58** (0.77–3.69)	7.4	NC	**2.92** (1.17–9.78)	50.0	58.3



OS DCO: April 16, 2021. PFS and ORR DCO: October 10, 2018.
*The analysis in all patients was performed using a stratified log-rank test with factors as recorded in Interactive Voice Response System for time to disease progression after the end of last PBC (6–12 months vs > 12 months) in the full analysis set. The analysis in the prior line of chemotherapy subgroups was performed using a single Cox proportional hazards model containing the treatment term, the subgroup covariate of interest and the treatment by subgroup interaction for each subgroup. Size of circle is proportional to the number of events. Blue band represents the 95% CI for the overall (all patients) HR;
†Unconfirmed ORR is based on BICR in the measurable disease population.
NC, not calculable.

IGCS 2022 ANNUAL GLOBAL MEETING

Leath C et al. IGCS 2022;Abstract LB001/1731.

RTP RESEARCH TO PRACTICE

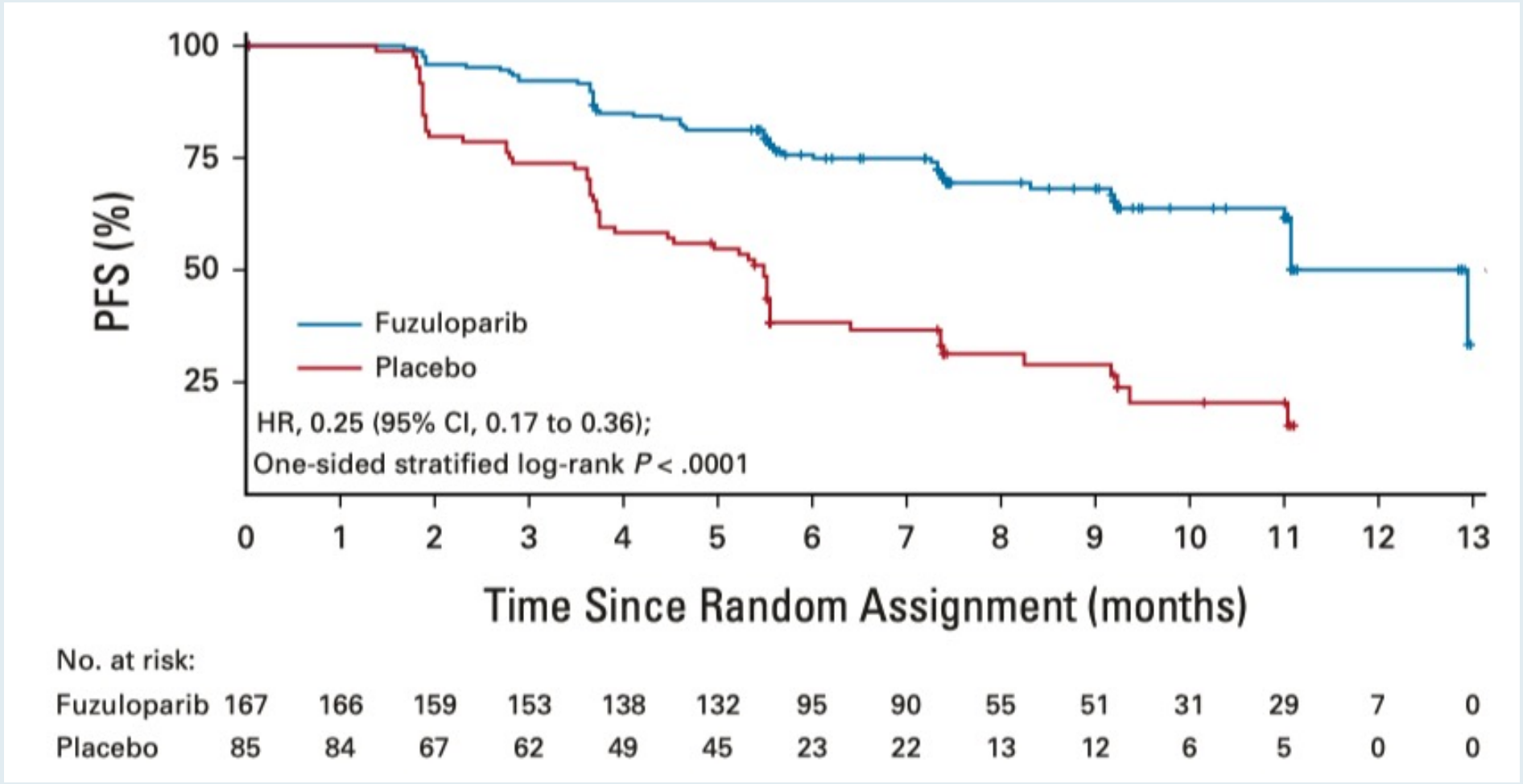
J Clin Oncol 2022 August;40(22):2436-46.

original reports

Fuzuloparib Maintenance Therapy in Patients With Platinum-Sensitive, Recurrent Ovarian Carcinoma (FZOCUS-2): A Multicenter, Randomized, Double-Blind, Placebo-Controlled, Phase III Trial

Ning Li, MD[1]; Youzhong Zhang, PhD[2]; Jing Wang, MD[3]; Jianqing Zhu, MD[4]; Li Wang, MB[5]; Xiaohua Wu, MD[6]; Desheng Yao, PhD[7]; Qiang Wu, PhD[8]; Jihong Liu, PhD[9]; Junying Tang, PhD[10]; Rutie Yin, PhD[11]; Ge Lou, PhD[12]; Ruifang An, MD[13]; Guonan Zhang, MB[14]; Xiaoping Xia, MM[15]; Qingshui Li, MD[16]; Yaping Zhu, PhD[17]; Hong Zheng, PhD[18]; Xinfeng Yang, AC[19]; Yuanjing Hu, PhD[20]; Xin Zhang, PhD[21]; Min Hao, PhD[22]; Yi Huang, MM[23]; Zhongqiu Lin, PhD[24]; Dong Wang, BS[25]; Xiaoqing Guo, PhD[26]; Shuzhong Yao, PhD[27]; Xiaoyun Wan, PhD[28]; Huaijun Zhou, PhD[29]; Liangqing Yao, PhD[30]; Xielan Yang, MM[31]; Heng Cui, MD[32]; Yuanguang Meng, PhD[33]; Songling Zhang, PhD[34]; Jing Qu, MM[35]; Ben Zhang, MS[35]; Jianjun Zou, PhD[35]; and Lingying Wu, MD, PhD[1]

FZOCUS-2: Progression-Free Survival for All Patients (by Blinded Independent Central Review)

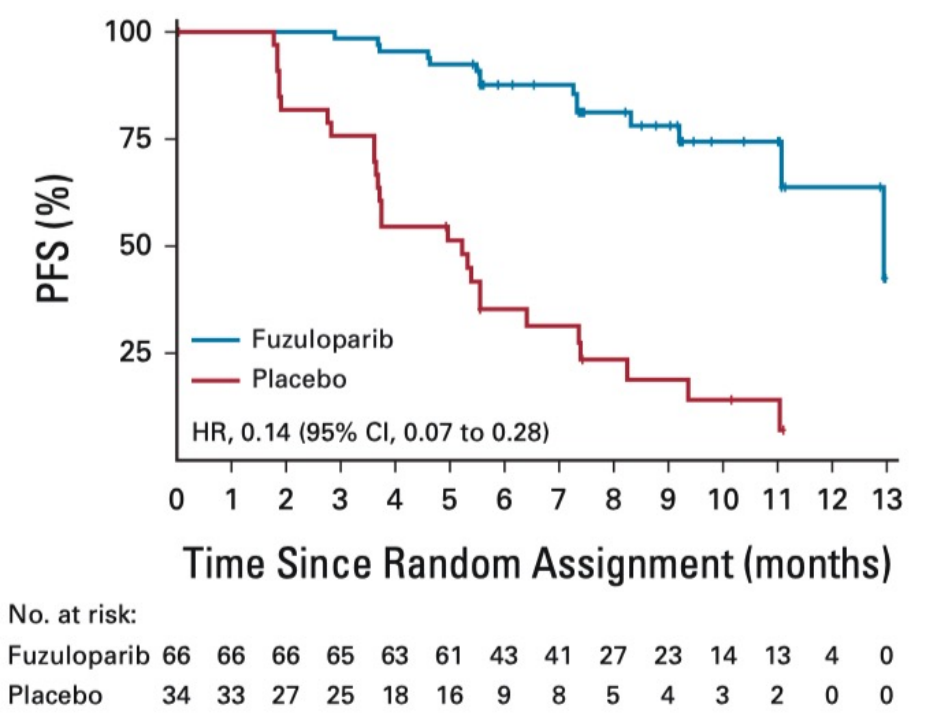


Li N et al. *J Clin Oncol* 2022;40(22):2436-46.

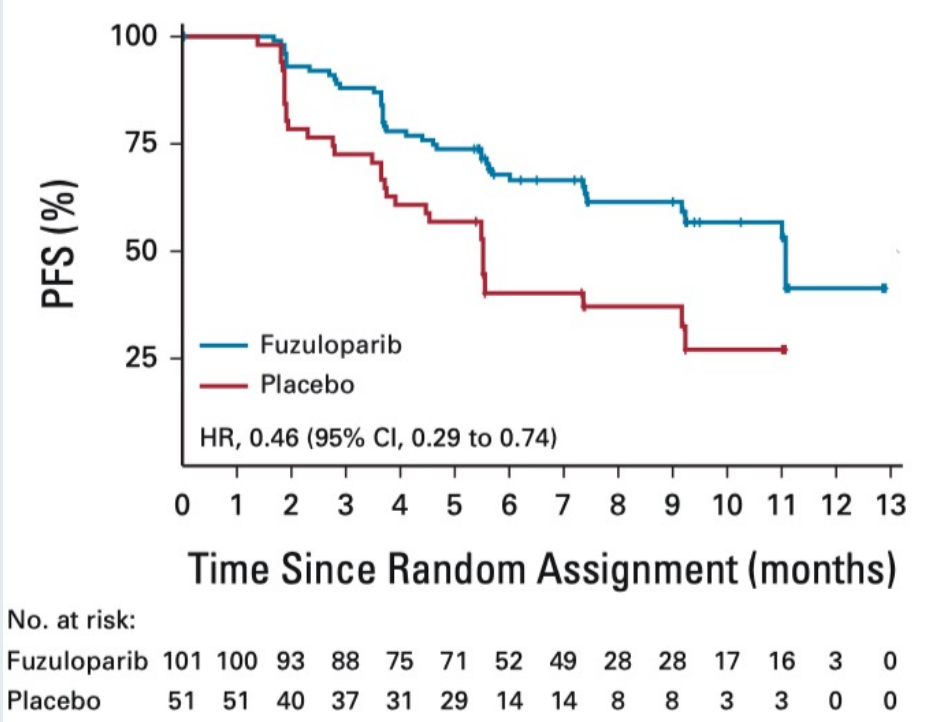
RTP RESEARCH TO PRACTICE

FZOCUS-2: Progression-Free Survival for Patients with or without Germline BRCA1/2 Mutations

With gBRCA1/2m



Without gBRCA1/2m



Li N et al. *J Clin Oncol* 2022;40(22):2436-46.

RTP RESEARCH TO PRACTICE

PARP Inhibitors in Platinum-Resistant Recurrent or Multiregimen-Recurrent Disease

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

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

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

IGCS 2022;Abstract S004/461.

SEPT 29 - OCT 1
IGCS 2022
NYC
NEW YORK CITY
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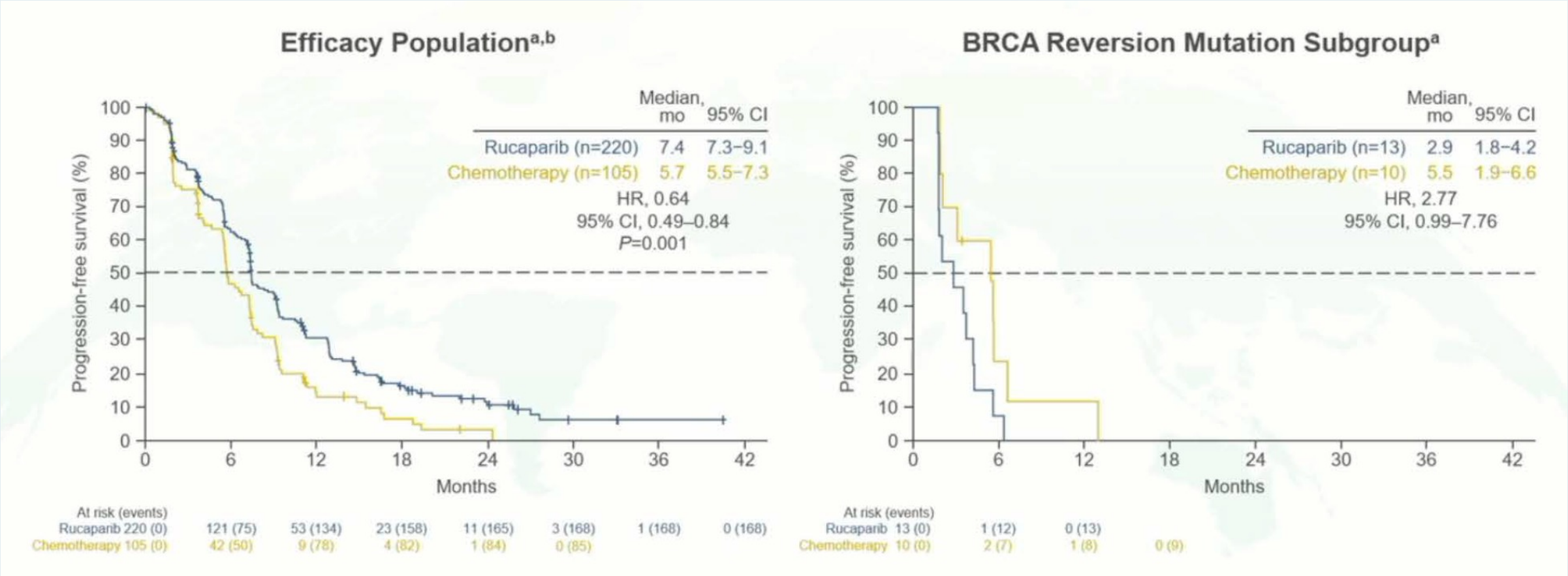
RESEARCH
TO PRACTICE

ARIEL4: Investigator-Assessed PFS



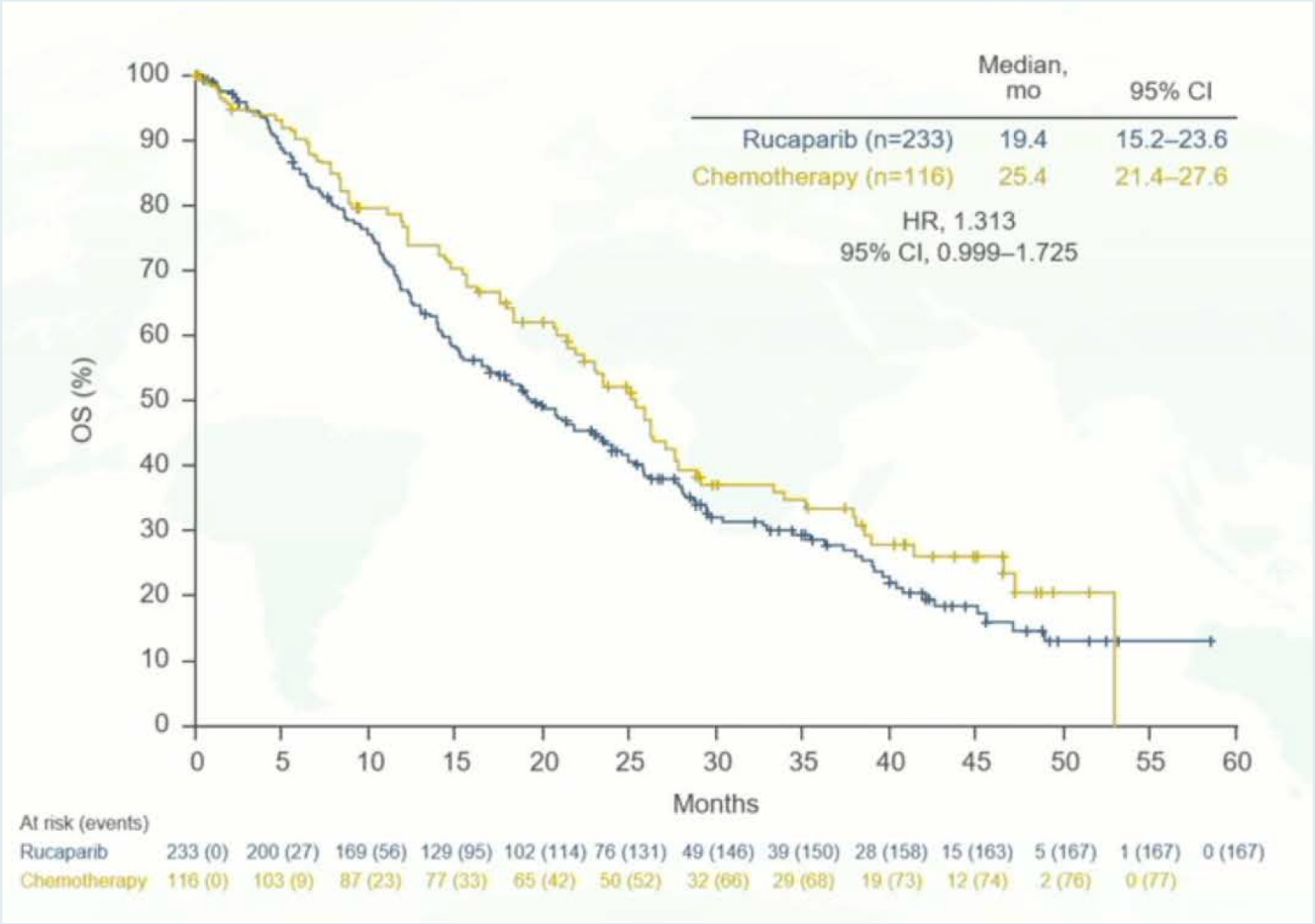
Oza AM et al. IGCS 2022;Abstract S004/461.

ARIEL4: Crossover and Subsequent Treatments

	Platinum Resistant		Partially Platinum Sensitive		Fully Platinum Sensitive	
	Rucaparib (n=120)	Chemotherapy (n=59)	Rucaparib (n=65)	Chemotherapy (n=31)	Rucaparib (n=48)	Chemotherapy (n=26)
Median duration of randomized treatment, mo (range)[a]	5.6 (0–44)	4.4 (0–25)	7.6 (0–60)	4.5 (0–11)	13.7 (0–53)	3.4 (1–8)
Subsequent anticancer treatment reported, n (%)						
Yes	69 (57.5)	45 (76.3)	40 (61.5)	26 (83.9)	26 (54.2)	22 (84.6)
No	51 (42.5)	14 (23.7)	25 (38.5)	5 (16.1)	22 (45.8)	4 (15.4)
Type of first subsequent treatment, n (%)						
Crossover rucaparib	NA	41 (91.1)	NA	25 (96.2)	NA	14 (63.6)
Other PARPi	1 (1.4)	0	0	0	1 (3.8)	4 (18.2)
Platinum-based chemotherapy	29 (42.0)	1 (2.2)	27 (67.5)	1 (3.8)	20 (76.9)	2 (9.1)
Nonplatinum-based chemotherapy	36 (52.2)	2 (4.4)	11 (27.5)	0	5 (19.2)	1 (4.5)
Other[b]	3 (4.3)	1 (2.2)	2 (5.0)	0	0	1 (4.5)
Median duration of crossover rucaparib, mo (range)	NA	9.4 (2–39)	NA	9.7 (0–36)	NA	9.9 (1–37)
<6 months, n (%)		14 (34.1)		7 (28.0)		2 (14.3)
≥6 months, n (%)		27 (65.9)		18 (72.0)		12 (85.7)

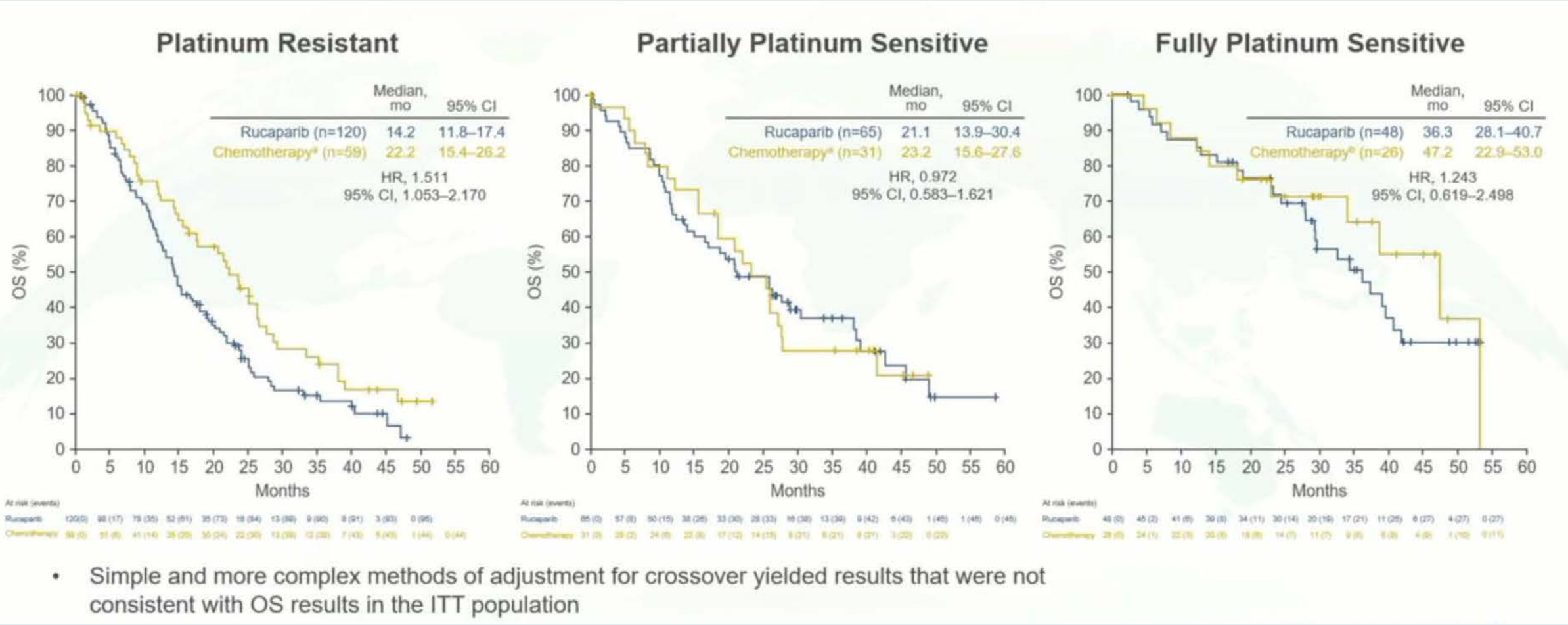
Oza AM et al. IGCS 2022;Abstract S004/461.

ARIEL4: Overall Survival (ITT)



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

ARIEL4: Overall Survival (Platinum Status Subgroups)



- Simple and more complex methods of adjustment for crossover yielded results that were not consistent with OS results in the ITT population

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

ARIEL4: Conclusions

- In ARIEL4, rucaparib significantly improved PFS versus chemotherapy in the ITT population
- OS favored those randomized to chemotherapy vs rucaparib in the ITT population
  - OS was similar between treatment groups amongst patients with platinum-sensitive disease; the difference in OS in the ITT population was driven by the platinum-resistant subgroup
  - OS was confounded by the high rate of crossover from chemotherapy to rucaparib; 90% of patients received rucaparib after randomization or crossover
  - Additionally, 98/233 (42.1%) of patients in the rucaparib arm did not receive subsequent anticancer treatment
- PFS2 was similar between treatment groups in the platinum-resistant subgroup, and favored rucaparib in the platinum-sensitive subgroup
- Safety data were consistent with previous reports
- Further work is ongoing to understand the biological basis of resistance and the optimal sequence of therapy

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

Investigational Agents and Strategies — *PARP Inhibitors + Immune Checkpoint Inhibitors*

PARIS 2022 ESMO congress

Abstract 529MO

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

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

[1]Gynaecology Unit, The Royal Marsden NHS Foundation Trust and Institute of Cancer Research, London, UK; [2]Immuno-oncology Service, Department of Oncology, Lausanne University Hospital, University of Lausanne, Lausanne, Switzerland; [3]Medical Oncology, Beatson West of Scotland Cancer Centre, and Institute of Cancer Sciences, University of Glasgow, Glasgow, UK; [4]Department of Obstetrics and Gynecology, Seoul National University Hospital, Seoul, Republic of Korea; [5]Department of Internal Medicine, Division of Medical Oncology, Yonsei Cancer Centre, Yonsei University College of Medicine, Seoul, Republic of Korea, [6]Translational and Clinical Research Institute, Northern Centre for Cancer Care, Newcastle upon Tyne Hospitals NHS Foundation Trust, and Newcastle University, Newcastle upon Tyne, UK; [7]Davidoff Centre, Rabin Medical Center-Beilinson Campus, Petach Tikva and Felsenstein Medical Research Centre, Sackler Faculty of Medicine, Tel-Aviv University, Tel-Aviv, Israel; [8]Service d'Oncologie Médicale, Institut de Cancérologie des Hospices Civils de Lyon (IC-HCL), CITOHL, GINECO, Univ Lyon, Université Claude Bernard Lyon 1, Lyon, France; [9]Department of Oncology, Ninewells Hospital, NHS Tayside, Dundee, UK; [10]Division of Hematology Oncology, Massachusetts General Hospital, Boston, MA, USA; [11]Division of Gynecology Oncology, The Ohio State University James Comprehensive Cancer Center, Columbus, OH, USA; [12]Late Development Oncology, Oncology R&D, AstraZeneca, Gaithersburg, MD, USA; [13]AstraZeneca, Cambridge, UK†; [14]Translational Medicine, Oncology R&D, AstraZeneca, Cambridge, UK; [15]AstraZeneca, Gaithersburg, MD, USA†; [16]Basser Center for BRCA, University of Pennsylvania, Philadelphia, PA, USA

**Current affiliation: BC Cancer Centre, Vancouver, British Columbia, Canada*
†At the time of analysis

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

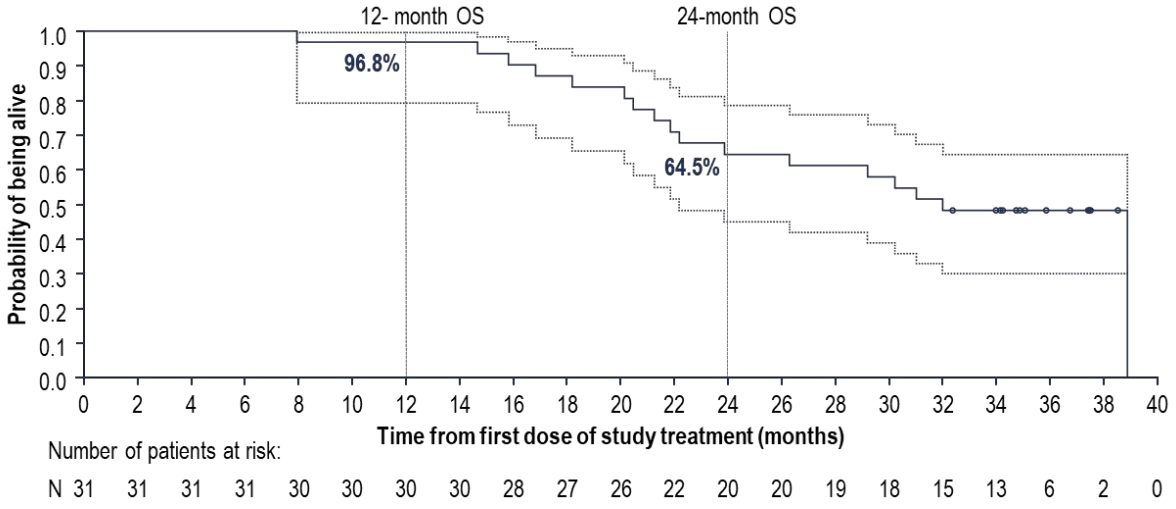
Scan for:

- **Plain-language infographic**
- **Slides**

RTP RESEARCH TO PRACTICE

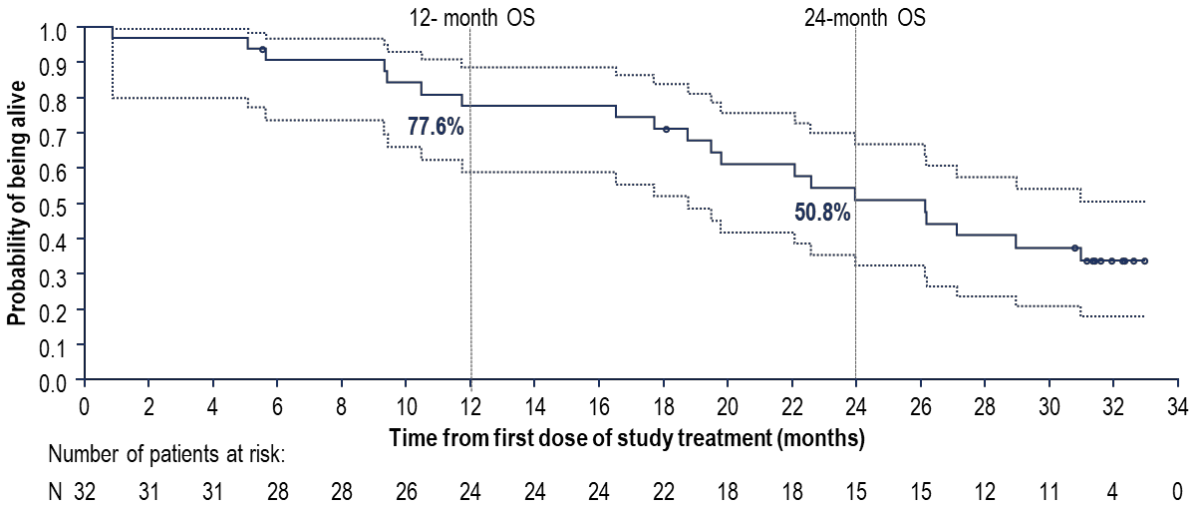
MEDIOLA: Median Overall Survival and 56-Week Disease Control Rate

Olaparib plus durvalumab and bevacizumab



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

Olaparib plus durvalumab



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

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

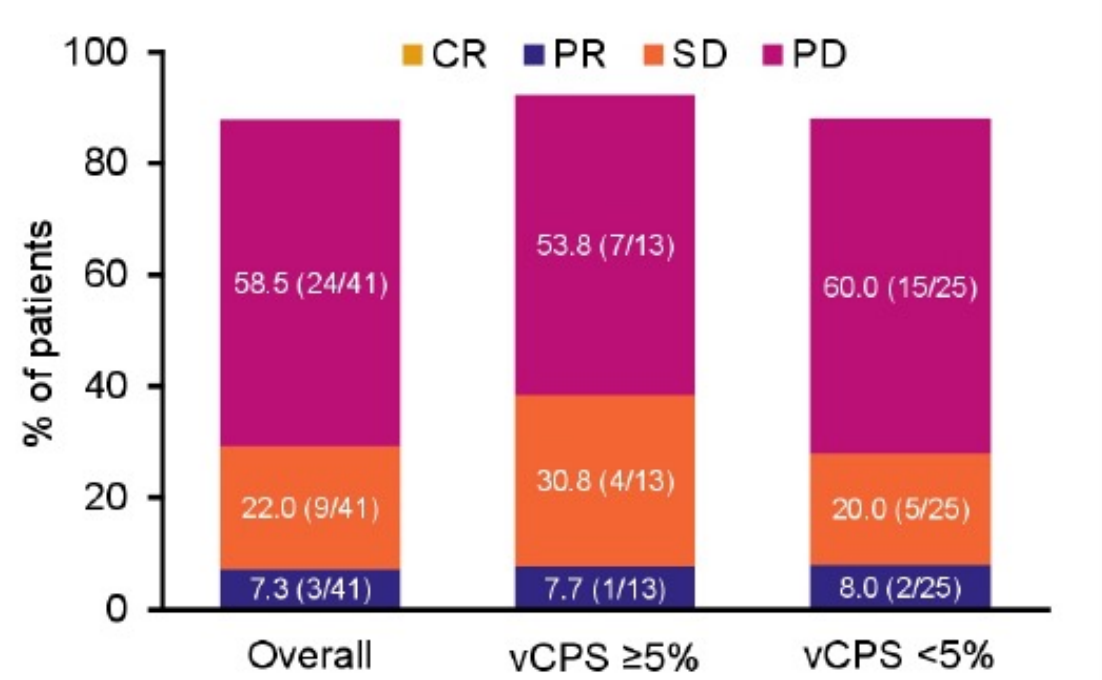
RTP RESEARCH TO PRACTICE

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

ASCO 2022;Abstract 5573.

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

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



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

Randall LM et al. ASCO 2022;Abstract 5573.

Meet The Professor

Optimizing the Management of HER2-Positive Breast Cancer

Tuesday, November 8, 2022
5:00 PM – 6:00 PM ET

Faculty

Lisa A Carey, MD, ScM

Moderator

Neil Love, MD

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Thank you for joining us!

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

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