Expert Second Opinion: Investigators Provide Perspectives on the Best-Practice Management of Ovarian Cancer

An Independent CME Symposium During the SGO 2026 Annual Meeting on Women's Cancer®

Sunday, April 12, 2026

1:30 PM – 3:00 PM AST

Faculty

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Gottfried E Konecny, MD

Alexander B Olawaiye, MD

Moderator

Shannon N Westin, MD, MPH, FASCO, FACOG

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Faculty

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Data and Safety Monitoring Boards/Committees	Incyte Corporation
Speakers Bureaus	AstraZeneca Pharmaceuticals LP, Eisai Inc, GSK, MSD

Dr Konecny — Disclosures
Faculty

No relevant financial relationships to disclose.

Dr Olawaiye — Disclosures
Faculty

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Consulting Agreements	Corcept Therapeutics Inc
Speakers Bureaus	Foundation Medicine

Dr Westin — Disclosures
Moderator

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Consulting Clinical Investigator

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Save The Date

Fifth Annual
National General Medical Oncology Summit

A Multitumor CME/MOC-, NCPD- and ACPE-Accredited Educational Conference Developed in Partnership with Florida Cancer Specialists & Research Institute

Friday to Sunday, April 24 to 26, 2026

The Ritz-Carlton Orlando, Grande Lakes | Orlando, Florida

Moderated by Neil Love, MD

Clinicians in the Meeting Room

Please refer to the printed handout provided with your meeting syllabus, and scan the corresponding QR code to

Review and Download Program Slides.

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

Ask a Question: We will aim to address as many questions as possible during the program.

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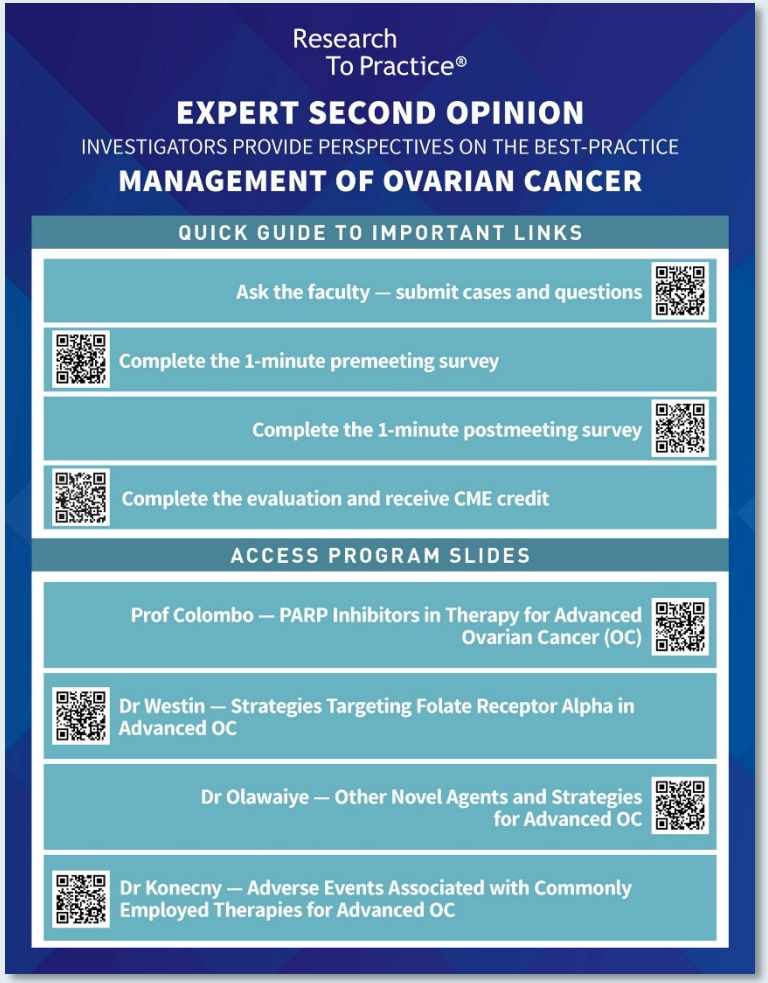

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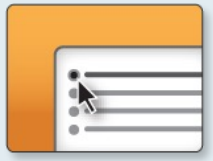
Review Program Slides: A link to the program slides will be posted in the chat room at the start of the program.



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

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About the Enduring Program

- The live meeting is being video and audio recorded.
- The proceedings from today will be edited and developed into an enduring web-based program.
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Second Opinion

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Agenda

Module 1: Current Role of PARP Inhibitors in Advanced Ovarian Cancer (OC) — Prof Colombo

Module 2: Strategies Targeting Folate Receptor Alpha in Advanced OC — Dr Westin

Module 3: Other Novel Agents and Strategies for Advanced OC — Dr Olawaiye

Module 4: Diagnosis and Management of Adverse Events Associated with Commonly Employed Therapies for Advanced OC — Dr Konecny

Agenda

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Current Role of PARP Inhibitors in Advanced Ovarian Cancer (OC)

Nicoletta Colombo
European Institute of Oncology, Milan, Italy

Evolution of First-Line Chemotherapy & Maintenance for advanced ovarian cancer

Chemotherapy (drugs, route of administration, schedule, maintenance), Maintenance, Targeted Therapies

INTRODUCTION OF **TAXANES**
Cisplatin/Paclitaxel
Vs
Cisplatin/Cyclo

WHICH PLATINUM?
GOG158 & AGO OVAR3
Cisplatin
Vs
Carboplatin

ADDING
THIRD DRUGS
Anthracyclins,
Gemcitabine, Topotecan
e.g. GOG 182

DOSE DENSE
PACLITAXEL
JGOG3016, MITO-7,
GOG262, ICON-8;
ICON-8B, EWOC-1

PACLITAXEL MAINTENANCE
GOG 178

BEVACIZUMAB MAINTENANCE
GOG 218, ICON7

PARPi MAINTENANCE +/- Bevacizumab
SOLO2, PAOLA-1, PRIMA

IMMUNOTHERAPY-COMBINATIONS
(CHT/BEV/PARPi)
JAVELIN100, IMAgyn050,
DUO-O, ATHENA COMBO,
KEYLINK 001, FIRST

INTRAPERITONEAL CHEMO / HIPEC?

SWOG9227
GOG-114

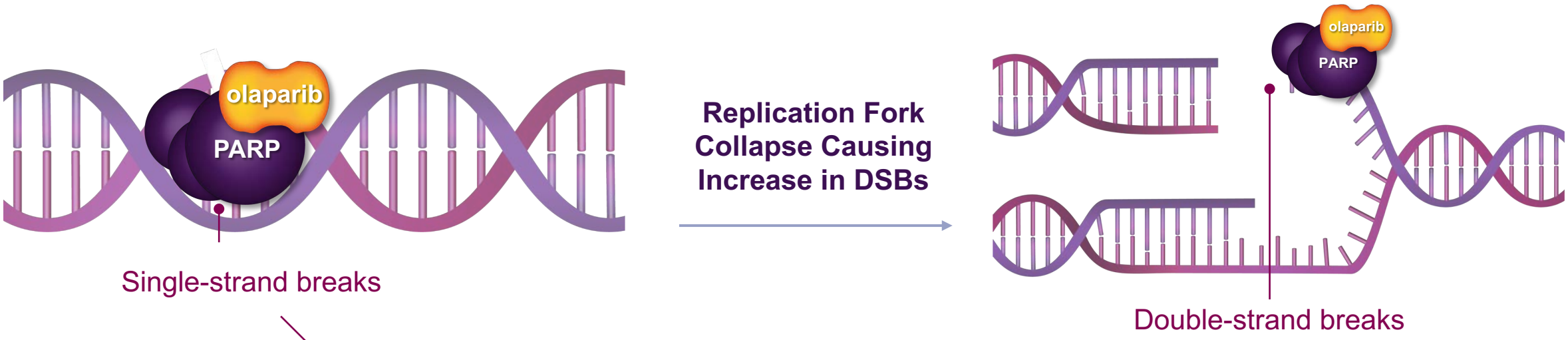
SWOG8501
GOG104

GOG172

GOG252

OVHIPEC-1

PARP-INHIBITION INDUCES INTOLERABLE LEVELS OF DNA-DSBs IN HRR DEFICIENT CELLS – SYNTHETIC LETHALITY



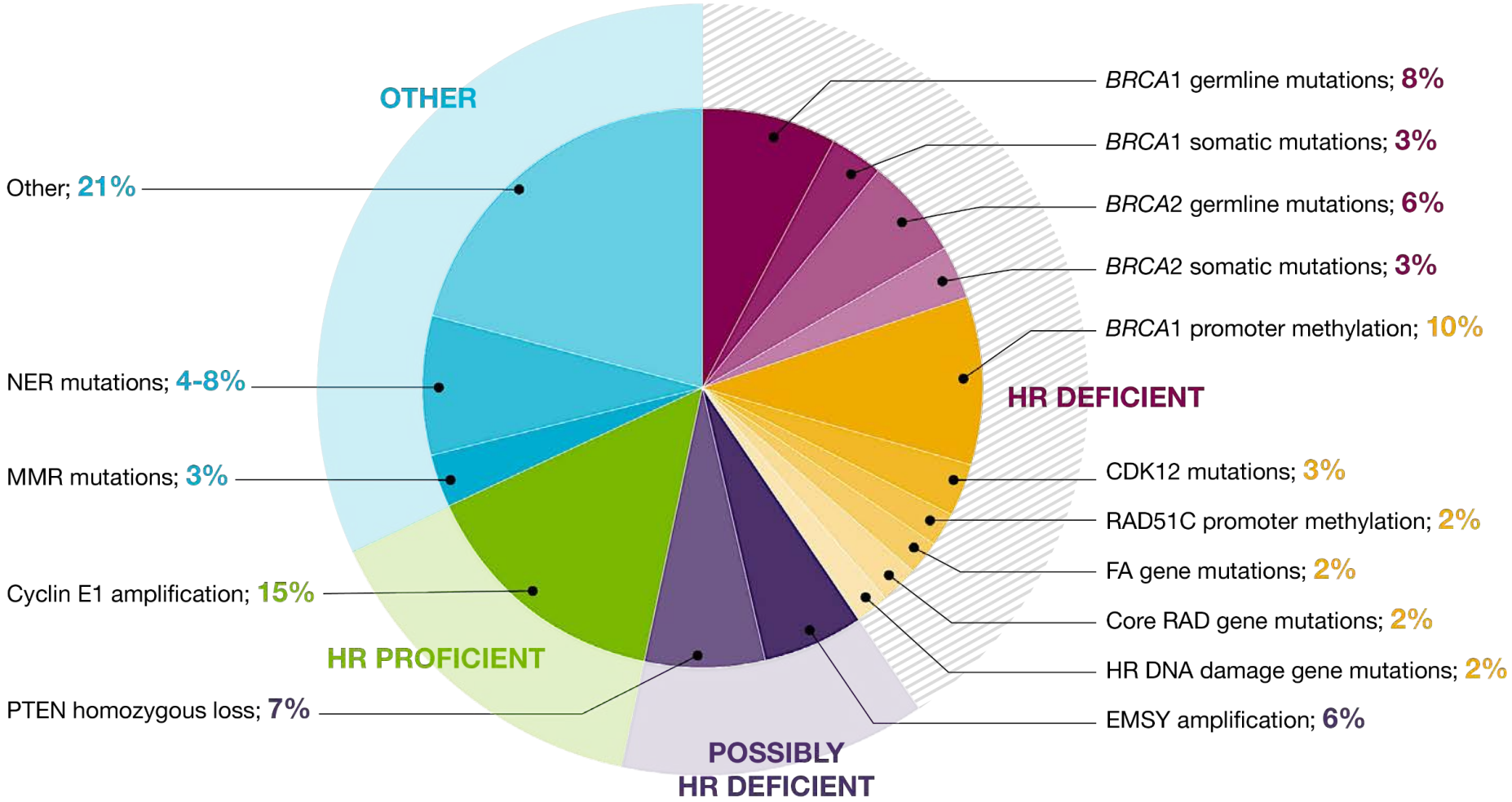
DSB=double-strand breaks;
HR=homologous recombination;
HRD=HR deficient; PARP= poly ADP ribose polymerase .

O'Connor MJ. *Mol Cell*. 2015;60(4):547-560.

HRD IS A PHENOTYPE WITH MANY CAUSES

HRD is present in ~ 50% of HGSOC

HRD as a target



Konstantinopoulos PA, et al. Cancer Discov. 2015;5(11):1137-1154

How to detect HRD?

Types of biomarkers that measure HRD

Look for the *cause* of HRD

***BRCA* test**

HRR gene panel test

Look for the *effect* of HRD

Genomic instability test:

Loss of heterozygosity (LOH)

Telomeric allelic imbalance (TAI)

Large-scale state transitions (LST)

Cause

- Brake failure?
- Distracted driver?
- Traffic light failure?
- Bad weather conditions?
- Driver medical emergency?
- Human error (e.g. speeding)?
- AI error in self-driving vehicle?

Clinically validated methods to detect HRD in newly diagnosed ovarian cancer require *BRCA* mutations testing and scoring of genomic instability

Analysis is performed on DNA isolated from FFPE tumour tissue and assesses two factors to determine HRD status

Testing in newly diagnosed ovarian cancer

Tumour *BRCA* mutation

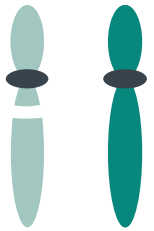
Presence of *BRCA* mutation

Yes

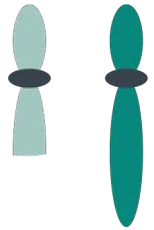
No

Genomic instability

Example: Myriad myChoice® genomic instability

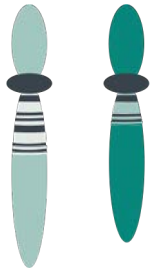


Loss of heterozygosity (LOH)
Presence of a single allele



Telomeric allelic imbalance (TAI)
A discrepancy in the 1:1 allele ratio at the end of the chromosome (telomere)

Score out of 100

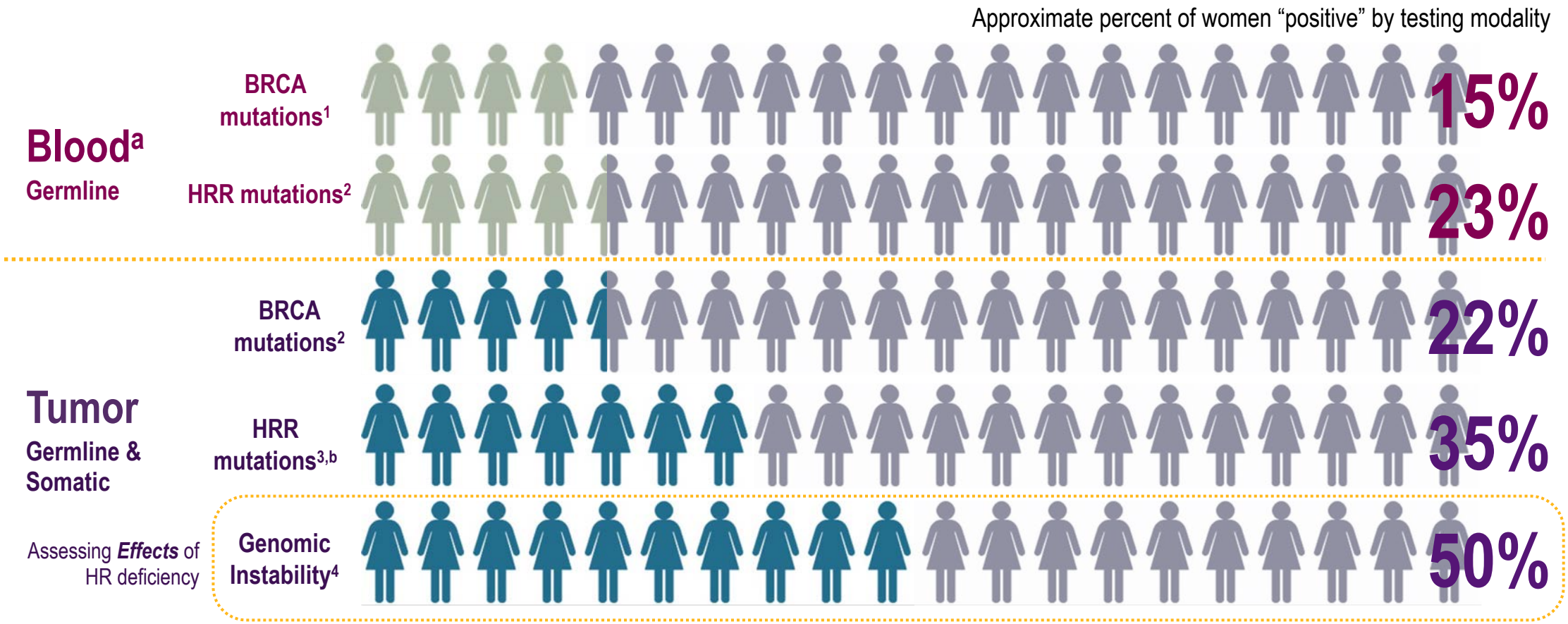


Large-scale state transitions (LST)
Transition points between regions of abnormal and normal DNA or between two different regions of abnormality

BRCA, breast cancer gene; DNA, deoxyribonucleic acid; FFPE, formalin fixed paraffin embedded; HRD, homologous recombination deficiency; LOH, loss of heterozygosity; LST, large-scale state transitions; TAI, telomeric allelic imbalance

Myriad myChoice® HRD Technical Specifications. Available at: https://myriad-web.s3.amazonaws.com/myChoice/downloads/myChoiceHRDTechSpecs.pdf. Accessed 18 August 2020

Patient identification and testing modalities



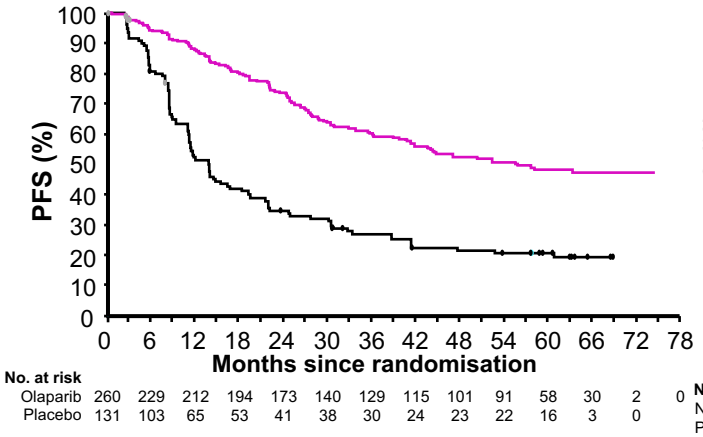
1. Neff RT *et al. Ther Adv Med Oncol*. 2017;9(8):519-31. 2. Pennington KP, *et al. Clin Cancer Res*. 2014;20(3):764-75. 3. Konstantinopoulos PA, *et al. Cancer Discov*. 2015;5(11):1137-54. 4. Cancer Genome Atlas Research Network. *Nature*. 2011;474(7353):609-15.

Why testing for BRCAm and HRD?

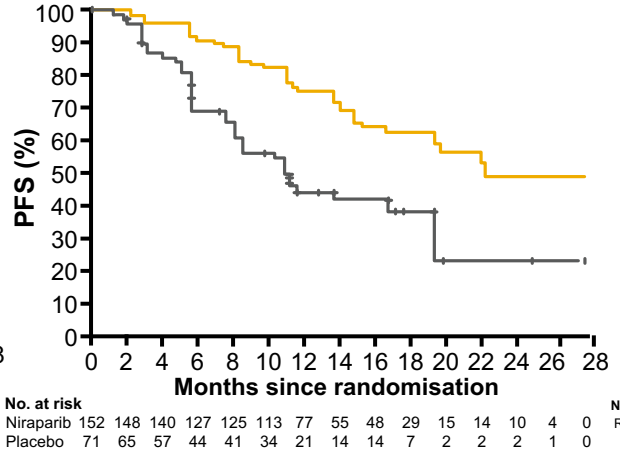
Significant extension in PFS in frontline PARP inhibitor maintenance trials in *BRCA*m ovarian cancer

PARPi monotherapy *versus* watch and wait

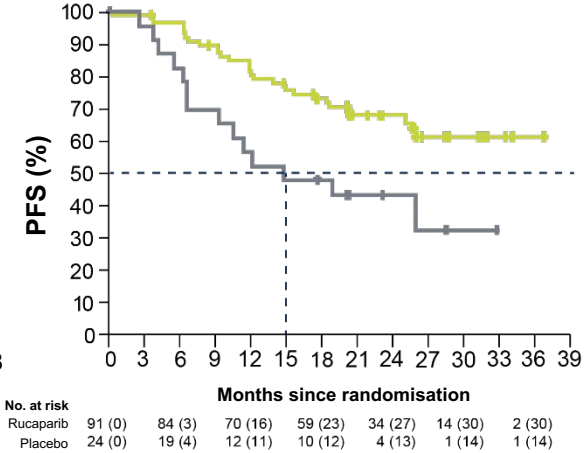
SOLO1[1]



PRIMA[2,3]

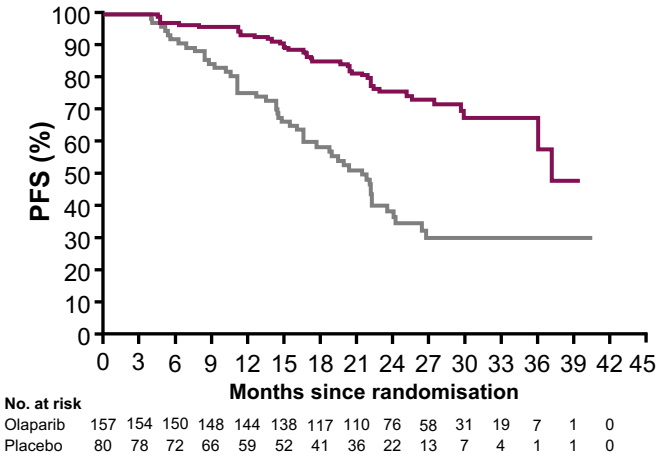


ATHENA-MONO[4]



Olaparib plus bev combination *versus* bev maintenance

PAOLA-1[5]



	Olaparib (n=260)	Placebo (n=131)	Niraparib (n=152)	Placebo (n=71)	Rucaparib (n=91)	Placebo (n=24)	Olaparib + Bev (n=157)	Placebo + Bev (n=80)
Events, n (%)	118 (45)	100 (76)	49 (32.2)	40 (56.3)			41 (26)	49 (61)
Median PFS, months	**56.0**	**13.8**	**22.1**	**10.9**	**NR**	**14.7**	**37.2**	**21.7**
Δ Median PFS	**42.2 months**		**11.2 months**		**N/A**		**15.5 months**	
HR (95% CI)	0.33 (0.25-0.43)		0.40 (0.27-0.62),		0.40 (0.21-0.75),		0.31 (0.20-0.47),	

Please note that head-to-head studies were not conducted between these products. These data are for information purposes only and no comparative claims of non-inferiority or superiority in terms of efficacy or safety are implied or intended

Bev, bevacizumab; *BRCA*, breast cancer susceptibility gene; *BRCA*m, *BRCA* mutated; CI, confidence interval; HR, hazard ratio; N/A, not available; NR, not reached; PARP, poly(ADP-ribose) polymerase; PFS, progression-free survival.

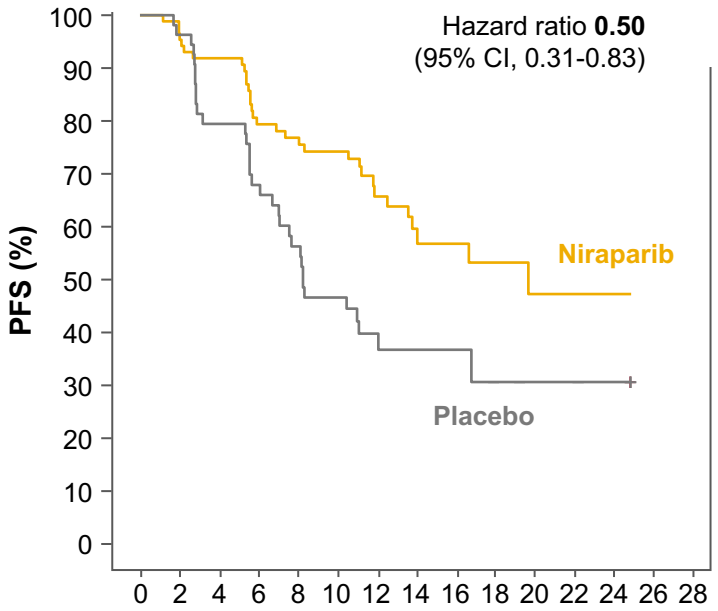
1. Bradley W, et al. Presented at: SGO 2021. Abstract 10520; 2. González-Martín A, et al. *N Engl J Med*. 2019;381(25):2391-2402; 3. González-Martín A, et al. Presented at: ESMO 2019. Presentation 4627; 4. Monk BJ, et al. *J Clin Oncol*. 2022;40(34):3952-3964; 5. Ray-Coquard I, et al. *N Engl J Med*. 2019;381:2416-2428

Exploratory analysis of PFS with PARPi maintenance in patients with *BRCA*wt HRD-positive (high GIS) ovarian cancer

PARPi monotherapy *versus* watch and wait

PRIMA[1]

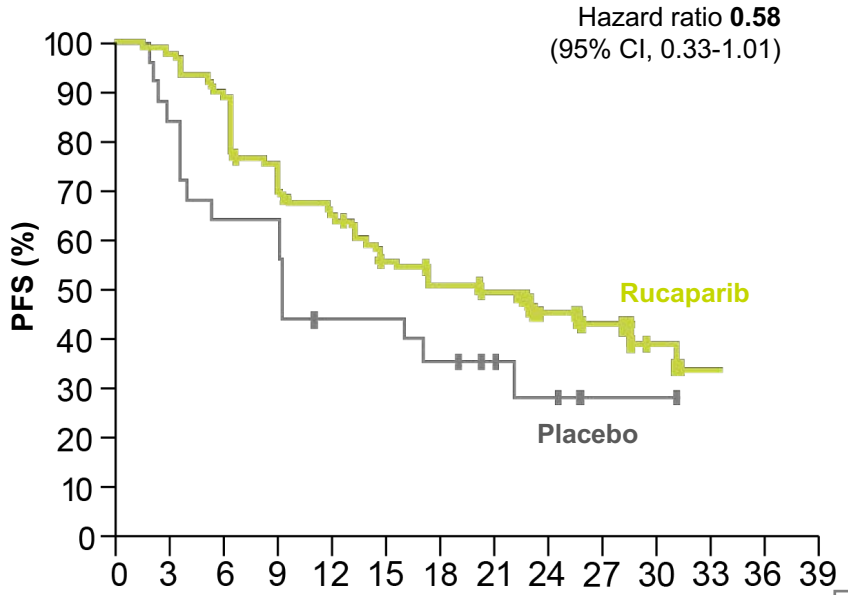
Myriad MyChoice®: HRD positive



No. at risk													
Niraparib	95	83	75	62	59	55	34	21	18	13	7	5	3
Placebo	55	52	42	35	29	23	13	7	7	4	3	3	2

ATHENA-MONO[2]

FoundationOne® CDx: High LOH

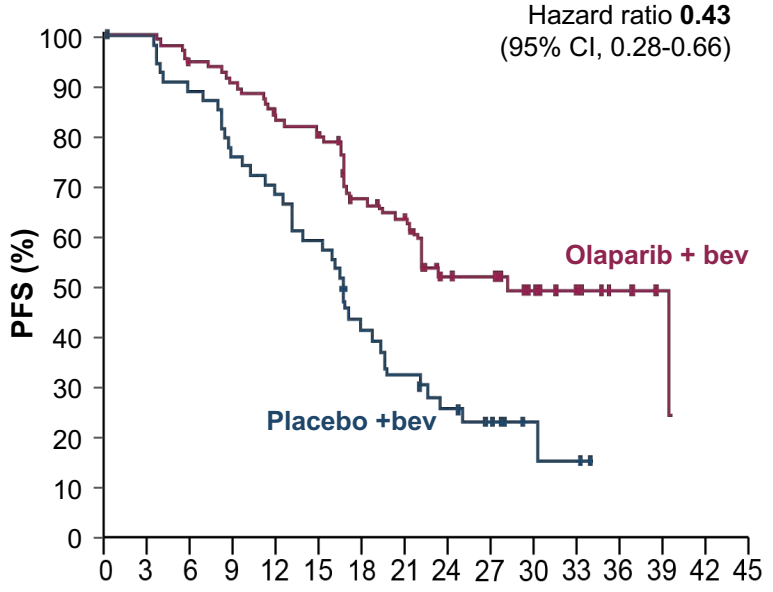


No. at risk							
Rucaparib	94 (0)	81 (9)	57 (30)	41 (43)	25 (47)	8 (49)	4 (50)
Placebo	25 (0)	16 (9)	10 (14)	8 (16)	4 (17)	1 (17)	0 (17)

Olaparib plus bev combination *versus* bev maintenance

PAOLA-1[3]

Myriad MyChoice®: HRD positive



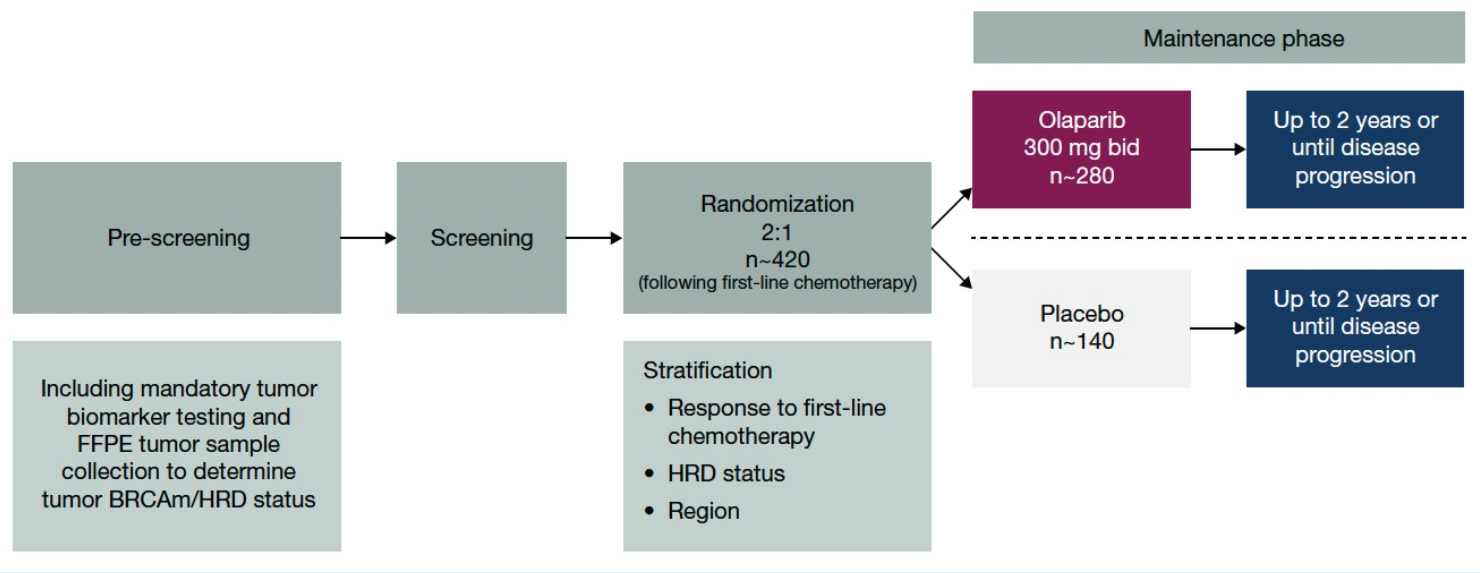
No. At Risk													
Olaparib	97	96	90	86	79	75	54	48	30	29	16	12	4	2	0
Placebo	55	54	48	41	37	32	19	15	11	8	3	2	0		

Please note that head-to-head studies were not conducted between these products. These data are for information purposes only and no comparative claims of non-inferiority or superiority in terms of efficacy or safety are implied or intended

Bev, bevacizumab; *BRCA*, breast cancer susceptibility gene; *BRCA*wt, *BRCA* wild type; CDx, companion diagnostics; CI, confidence interval; GIS, genomic instability score; HR, hazard ratio; HRD, homologous recombination deficiency; LOH, loss of heterozygosity; PARP, poly(ADP-ribose) polymerase; PARPi, PARP inhibitor; PFS, progression-free survival.

1. González-Martín A, et al. *N Engl J Med.* 2019;381(25):2391-2402; 2. Monk BJ, et al. Presented at: SGO 2020. Seminal abstract 31; 3. Ray-Coquard I, et al. *N Engl J Med*. 2019;381:2416-2428.

Olaparib Maintenance Monotherapy for BRCA Wild-Type Advanced Ovarian Cancer: Phase III MONO-OLA1 Study Design



Primary endpoints

- Investigator-assessed PFS by RECIST v1.1 in BRCAwt HRD-positive patients.
- Investigator-assessed PFS by RECIST v1.1 in BRCAwt patients.

Secondary endpoints

- Assessment of the following in BRCAwt HRD-positive and BRCAwt patients:
  - Overall survival (OS)
  - Second PFS
  - Time to first subsequent therapy or death
  - Time to second subsequent therapy or death
  - Time to discontinuation of study intervention or death
  - Time to earliest progression by RECIST v1.1 or cancer antigen 125 or death
  - Health-related quality of life using the European Organisation for Research and Treatment of Cancer (EORTC) QLQ-30 questionnaire and its ovarian-specific module, EORTC QLQ-OV28.
- Assessment of the safety and tolerability of maintenance olaparib

Saevets V et al. SGO 2022;Abstract 334.

One Year of Olaparib or Two? Phase III NRG-GY036 Study Design

FIGO Stage III-IV fallopian tube, ovarian or primary peritoneal cancer with pathogenic BRCA1/2 mutation (germline or somatic) or homologous recombination deficiency (HRD) after response to initial platinum-based chemotherapy

Step 1 Registration
Stratify by:
- BRCA deleterious alterations vs BRCA wt **and** HRD+
- +/- Bevacizumab (physician's choice)
- Response to platinum-based therapy (PR vs CR)

Randomize 1:1

Arm 1
Olaparib 300mg twice daily for **TWO** years
+/- Bevacizumab*

Arm 2
Olaparib 300mg twice daily for **ONE** year
+/- Bevacizumab*

*21-day cycle length. Bevacizumab (reference product or biosimilar) treatment will be stopped at the completion of the first year of treatment in both arms.

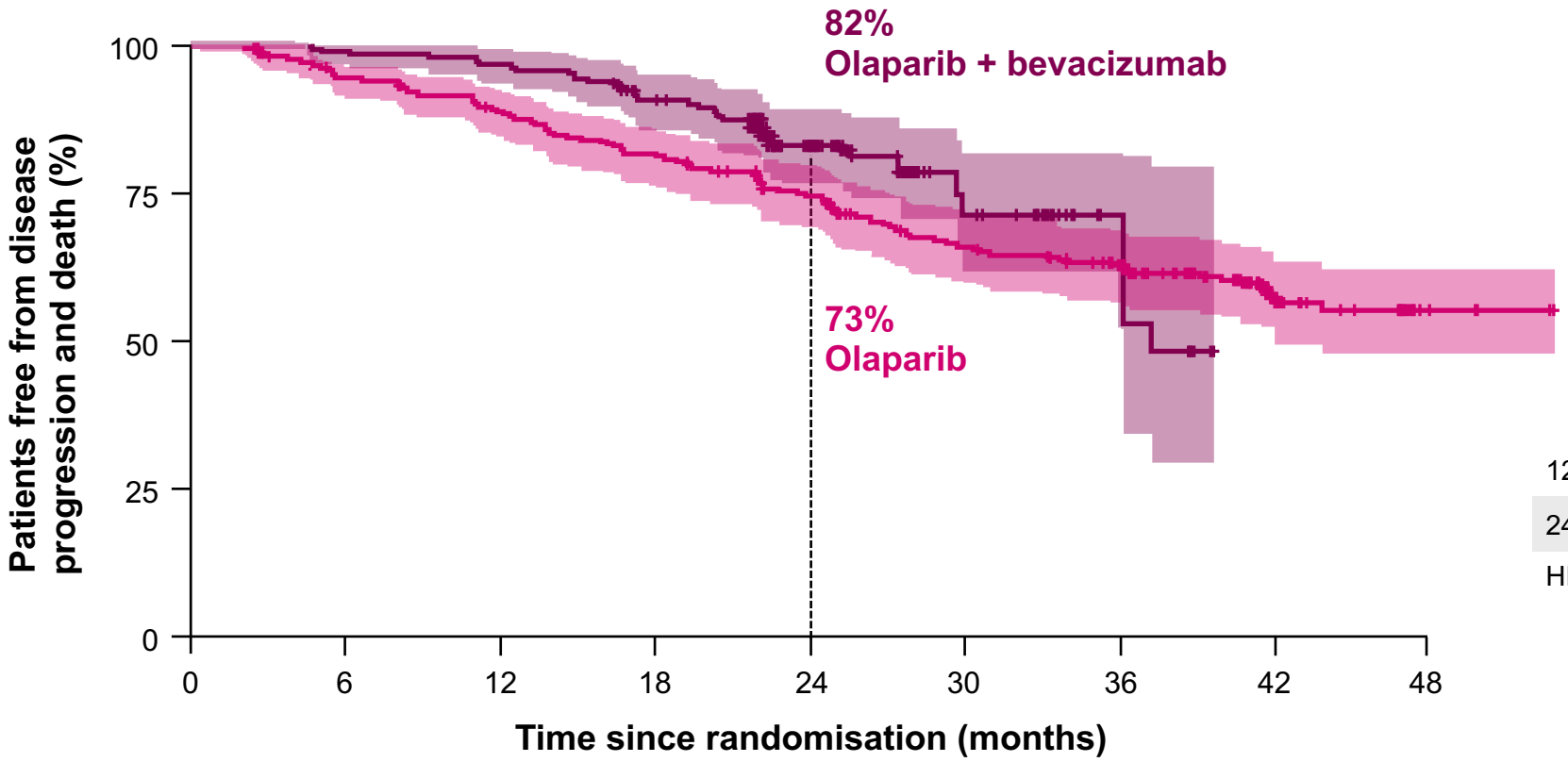
Primary Endpoint: INV-Assessed PFS
Secondary Endpoints: Survival (OS, PFS, PFS2), Toxicity (MDS/AML rates)

wt = wild type; PR = partial response; CR = complete response; INV = investigator; PFS = progression-free survival; OS = overall survival; PFS2 = time to second disease progression or death; MDS = myelodysplastic syndromes; AML = acute myeloid leukemia

www.clinicaltrials.gov. NCT06580314. Accessed April 2026

To Be(v) or not to Be(v)?

A population-adjusted indirect treatment comparison of PAOLA-1 and SOLO1 showed an additive benefit from bevacizumab in BRCAm patients



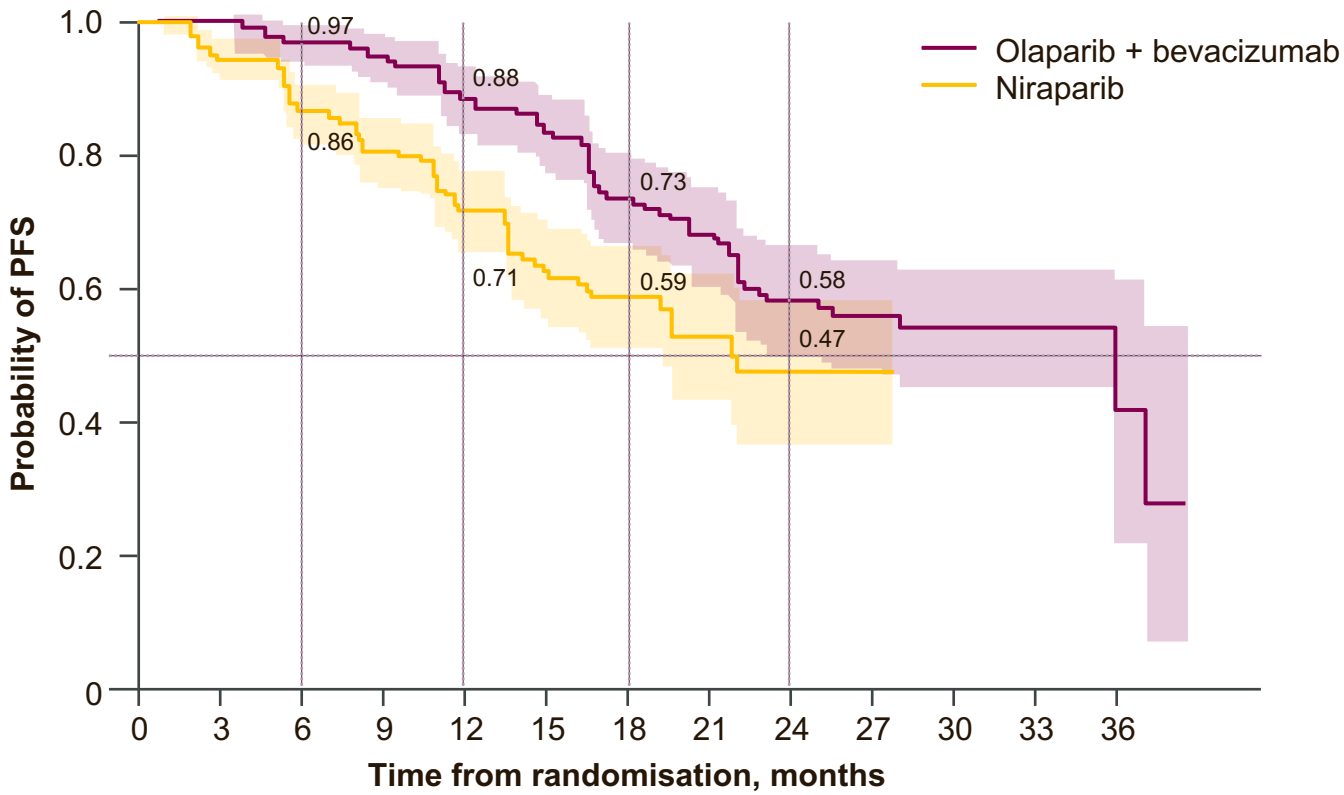
Kaplan-Meier estimate of % of patients progression-free

	PAOLA-1 tumour *BRCA*m	SOLO1
	Olaparib + bevacizumab* n=151	Olaparib n=254
12 months	**96**	**88**
24 months	**82**	**73**
HR (95% CI)	**0.71 (0.45-1.09)†**	

In SOLO1, median follow-up was 40.7 months in the olaparib arm and 41.2 months in the placebo arm. Shaded region represents 95% CI.
In PAOLA-1, median follow-up was 22.7 months in the olaparib + bevacizumab arm and 24.0 months in the placebo + bevacizumab arm.
*These results are based on weighted outcomes after matching tumour location status, ECOG status, FIGO stage, type of surgery (PDS vs IDS), residual disease status after surgery, response to first-line treatment and age to SOLO1. †CIs generated by bootstrapping. *BRCA*, breast cancer susceptibility gene; *BRCA*m, *BRCA* mutation; CI, confidence interval; ECOG, Eastern Cooperative Oncology Group; FIGO, International Federation of Gynecology and Obstetrics; HR, hazard ratio; IDS, interval debulking surgery; PDS, primary debulking surgery.
Vergote I, et al. *Eur J Cancer*. 2021;157:415-423.

Indirect treatment comparison using propensity score weighting showed greater PFS benefit with olaparib + bevacizumab in HRD-positive[a] PAOLA-1 (PRIMA-eligible subset)[b] vs niraparib PRIMA patients

The PAOLA-1 cohort that was eligible for PRIMA was adjusted to match the baseline characteristics of the PRIMA patient population



	PAOLA-1 (PRIMA-eligible subset)[b]	PRIMA
	Olaparib + bevacizumab (ESS=164)	**Niraparib** (n=247)
Median PFS, months	36.0	22.0
PFS rates at 12 months, %	88	71
PFS rates at 24 months, %	58	47

HR 0.57
(95% CI, 0.41–0.79)

PAOLA-1 results based on individual patient data with outcomes weighted after matching FIGO stage, ECOG PS status, age, response to first-line chemotherapy, *BRCA*m status, HRD status, CA-125 levels and use of NACT to the PRIMA baseline characteristics. PRIMA dataset was reconstructed using published PFS curves.[1]

[a]HRD-positive defined as *BRCA*m and/or genomic instability score ≥42 in the Myriad myChoice® CDx assay.[2,3]
[b]Patients with stage IV disease, stage III with residual disease after primary debulking surgery, inoperable stage III disease, or stage III who received NACT.[1]

*BRCA*m, *BRCA* mutated; CA-125, cancer antigen-125; CDx, companion diagnostic; CI, confidence interval; ECOG PS, Eastern Cooperative Oncology Group performance status; ESS, effective sample size; FIGO, International Federation of Gynaecology and Obstetrics; HR, hazard ratio; HRD, homologous recombination deficiency; NACT, neoadjuvant chemotherapy; PFS, progression-free survival.

1. Hettle R, et al. *Ther Adv Med Oncol*. 2021;13:17588359211049639; 2. Ray-Coquard I, et al. *N Engl J Med*. 2019;381:2146–28; 3. González-Martín A, et al. *N Engl J Med.* 2019;381:2391–402.

It is recommended that patients with *BRCA*m or HRD receive maintenance therapy with PARPi

Should we add bevacizumab?

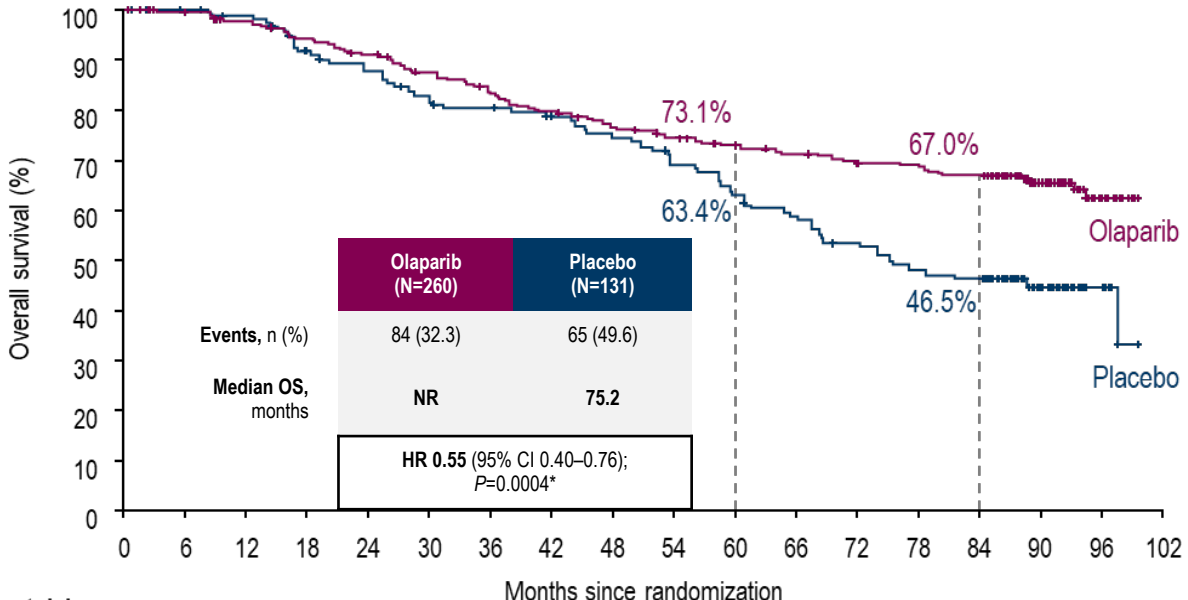
FACTORS TO CONSIDER

- Overall survival data
- Clinical characteristics (stage and residual tumour)
- Response to chemotherapy
- Toxicity and QoL / patient preference

*BRCA*m, *BRCA* mutated; HRD, homologous recombination deficiency; PARPi, poly (ADP-ribose) polymerase inhibitor; QoL, quality of life.

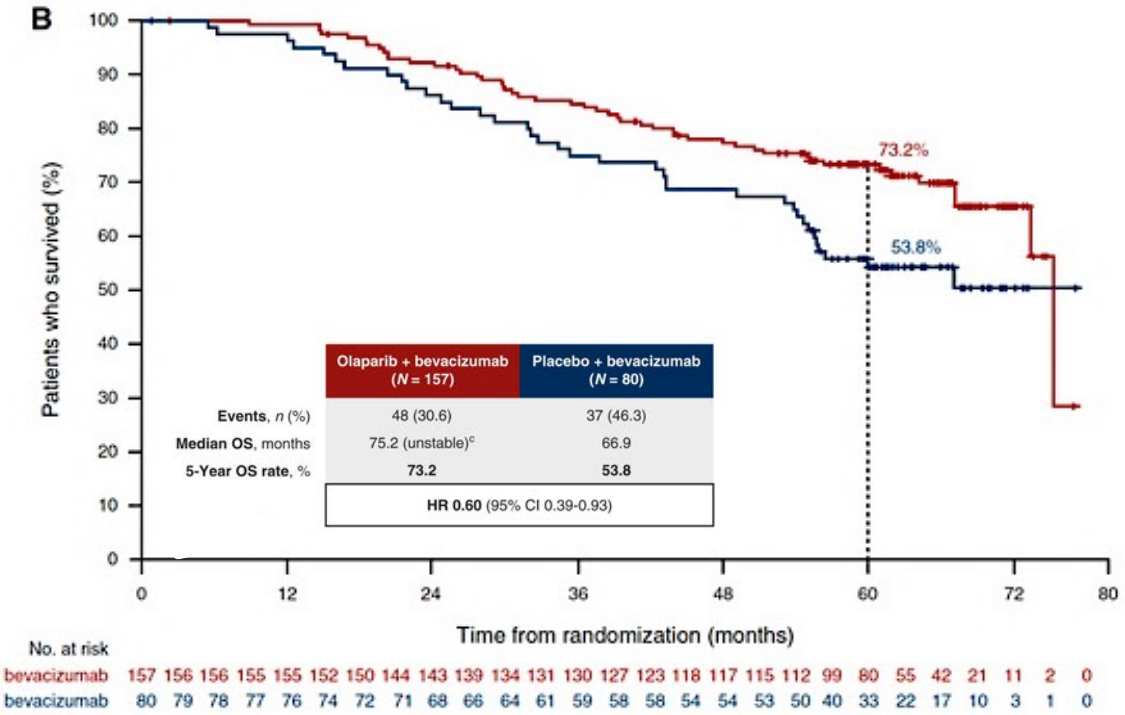
OS data: BRCAm

BRCA+: SOLO-1 Overall Survival



- **Interim OS analysis**
- **HR 0.55 (p=0.0004)**
- **OS delta @ 7J: 21.5%**
  - Not (yet) statistically significant per prespecified significance threshold for interim analysis
- **44% post-study PARPi in Placebo Arm**

BRCAm: PAOLA Overall Survival



	5-yr OS rate (%)
Placebo	53.8%
Olaparib	**73.2%**

HR 0.60 (95% CI, 0.39-0.93)

δ +19.4%

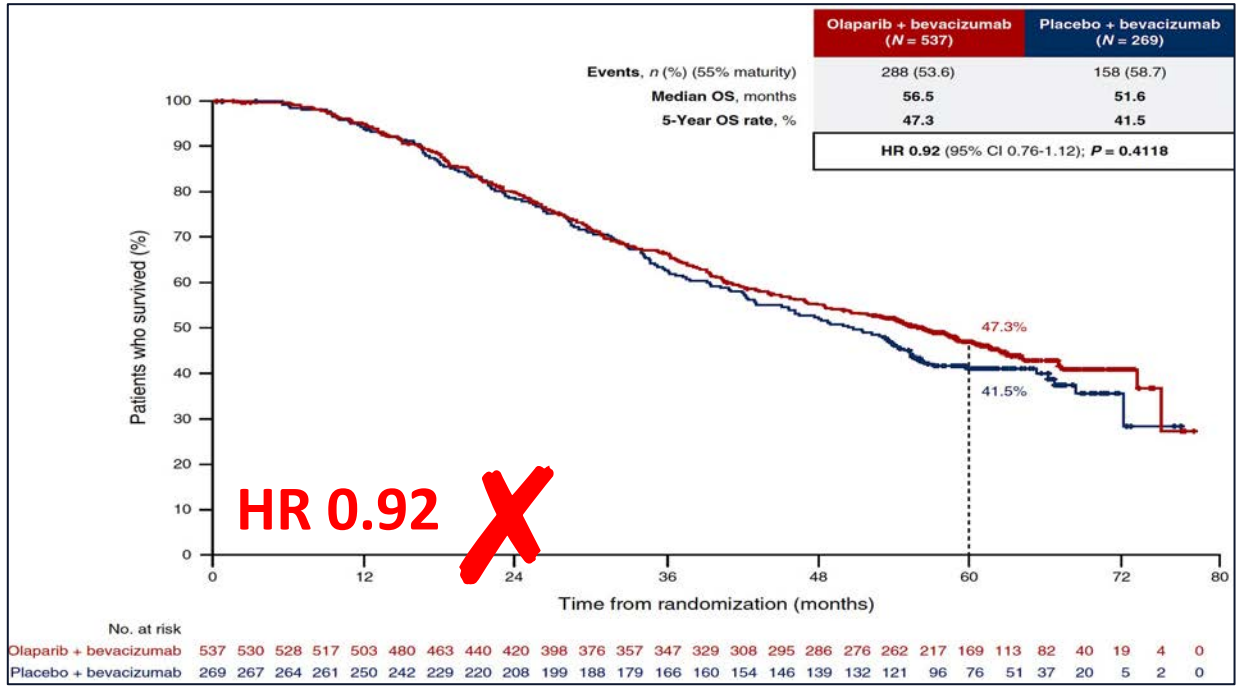
55% post-study PARPi in placebo-arm

Di Silvestro P, et al. J Clin Oncol 2023 *Ray-Coquard I, et al. NEJM 2023*

PAOLA-1:

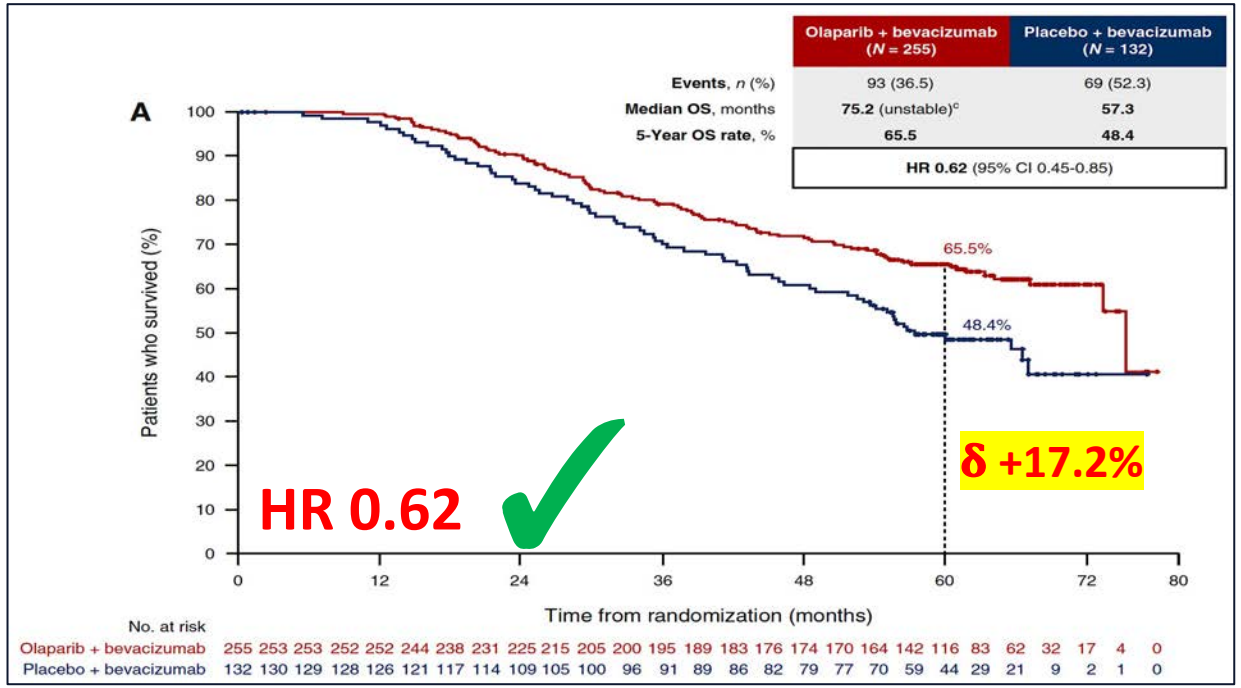
Final Overall Survival

PAOLA-1 (ITT)



Primary analysis population

PAOLA-1 (HRD-positive)



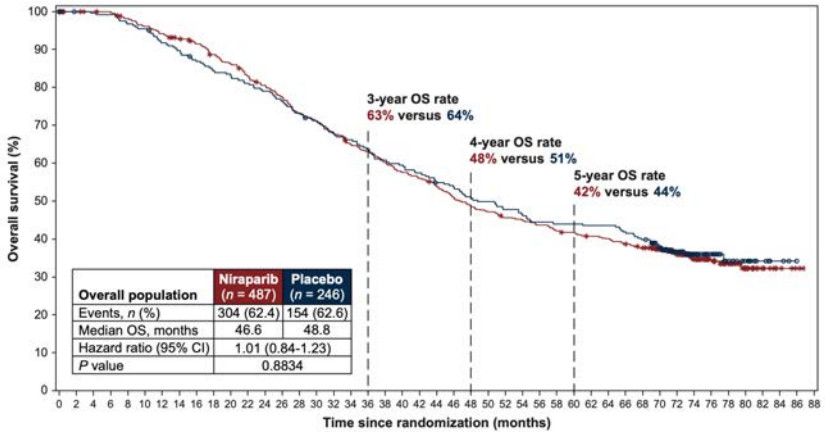
51% post-study PARPi in placebo group

= in-label population

Ray-Coquard et al., Ann Oncol 2023

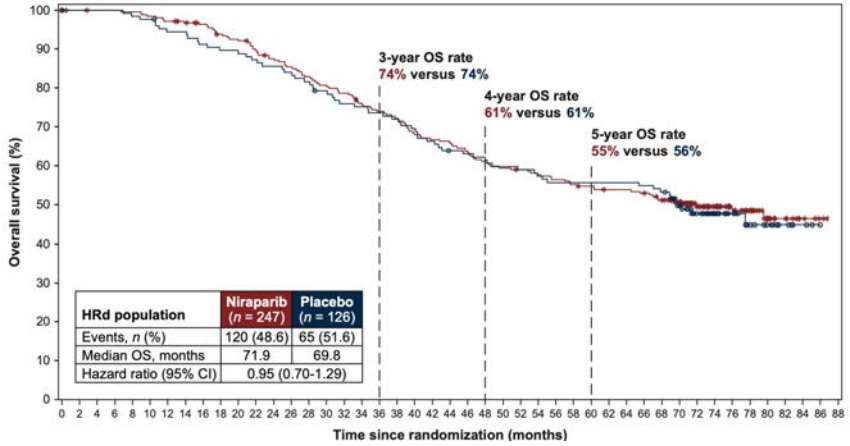
PRIMA: No difference in OS was seen between niraparib and placebo arms in the overall, HRd and HRp populations, BRCAm

Overall Population



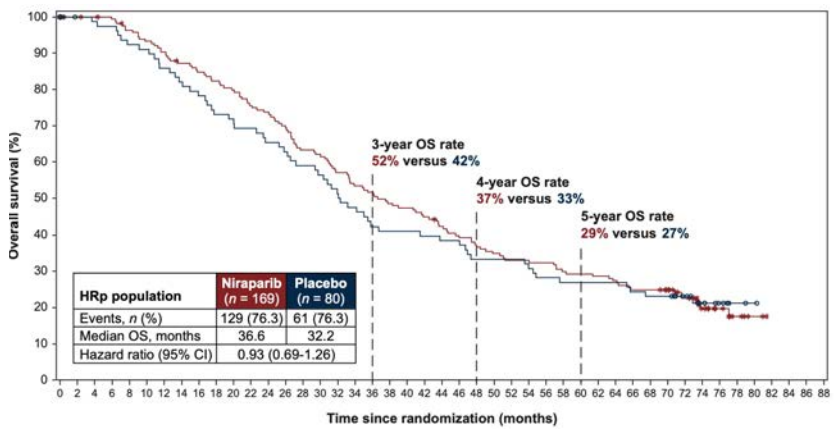
Overall population	Niraparib (*n* = 487)	Placebo (*n* = 246)
Events, *n* (%)	304 (62.4)	154 (62.6)
Median OS, months	46.6	48.8
Hazard ratio (95% CI)	1.01 (0.84-1.23)	
P value	0.8834	

HRd



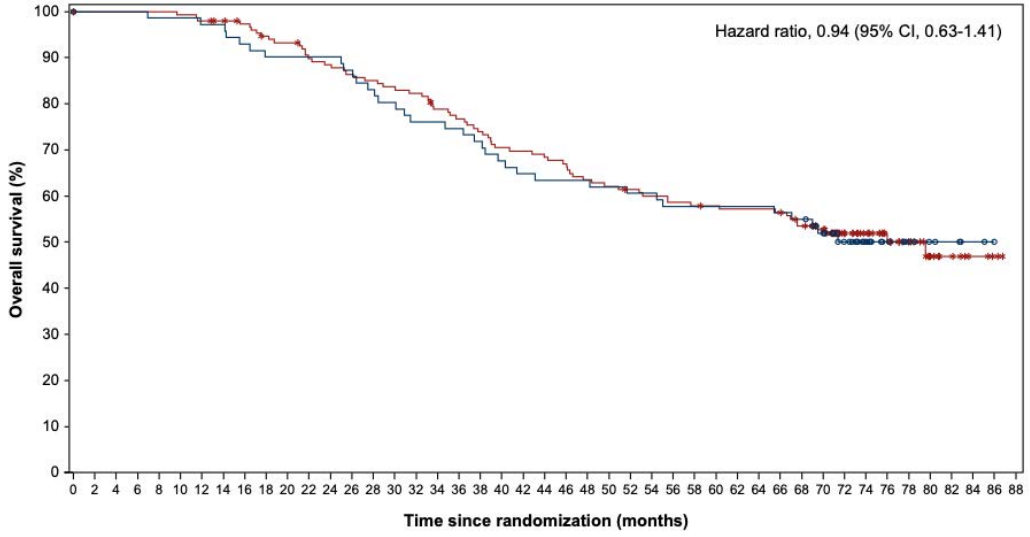
HRd population	Niraparib (*n* = 247)	Placebo (*n* = 126)
Events, *n* (%)	120 (48.6)	65 (51.6)
Median OS, months	71.9	69.8
Hazard ratio (95% CI)	0.95 (0.70-1.29)	

HRp

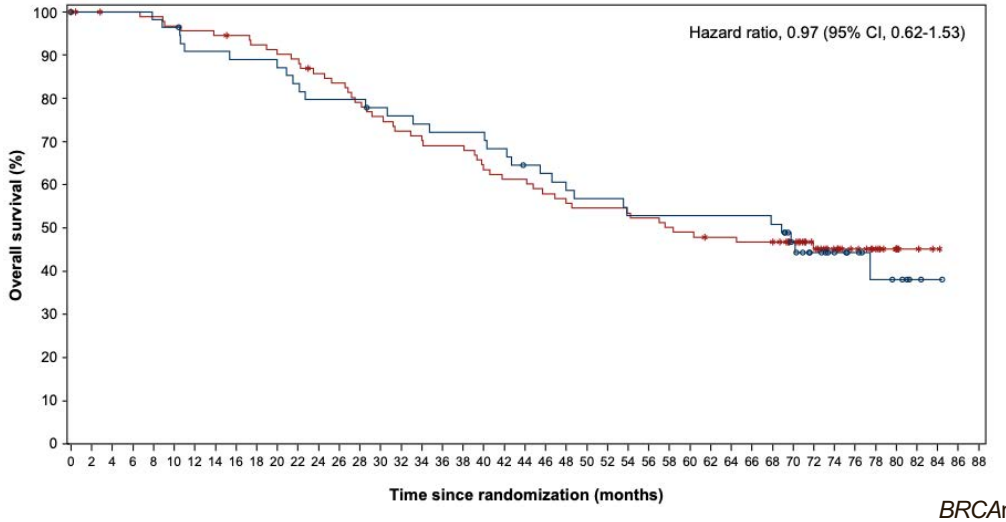


HRp population	Niraparib (*n* = 169)	Placebo (*n* = 80)
Events, *n* (%)	129 (76.3)	61 (76.3)
Median OS, months	36.6	32.2
Hazard ratio (95% CI)	0.93 (0.69-1.26)	

HRd/BRCAm



HRd/BRCAwt



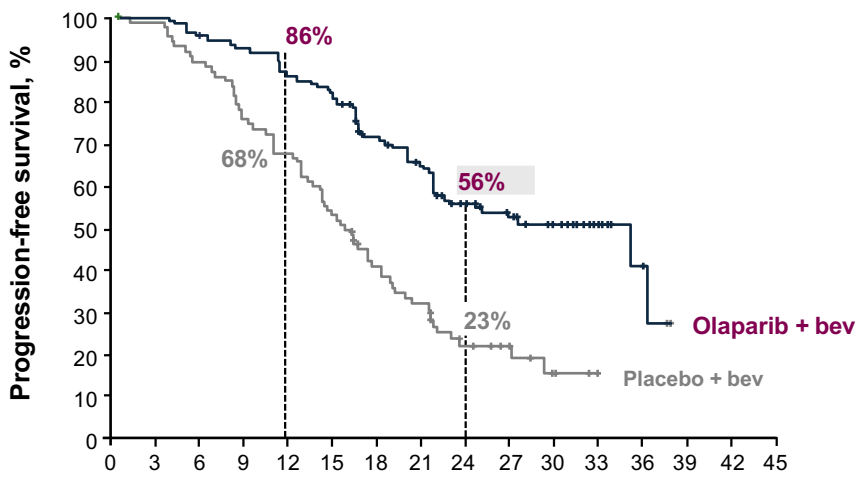
62.5% maturity in overall population.

1. Monk B, et al. *Ann Oncol*. 2024;35(11):981–992.

*BRCA*m, *BRCA* mutated; *BRCA*wt, *BRCA* wild type; CI, confidence interval; HR, hazard ratio; HRd, homologous recombination deficient; HRp, homologous recombination proficient; OS, overall survival.

PAOLA-1: PFS by clinical risk in HRD-positive patients

Higher risk, HRD-positive population

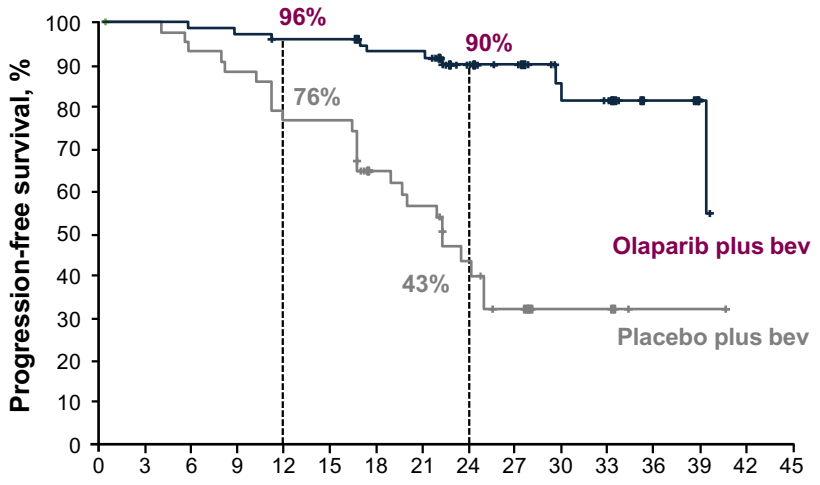


Patients at risk, n:

Olaparib + bev	177	175	166	161	150	140	109	95	63	50	27	15	5	0	0
Placebo + bev	89	86	78	66	59	47	31	24	16	11	5	2	0	0	0

	Olaparib + bev (n=177)	Placebo + bev (n=89)
Events, n (%)	77 (44)	67 (75)
Median PFS, months	**36.0**[a]	**16.0**
	HR 0.39 (95% CI, 0.28–0.54)	

Lower risk, HRD-positive population



Patients at risk, n:

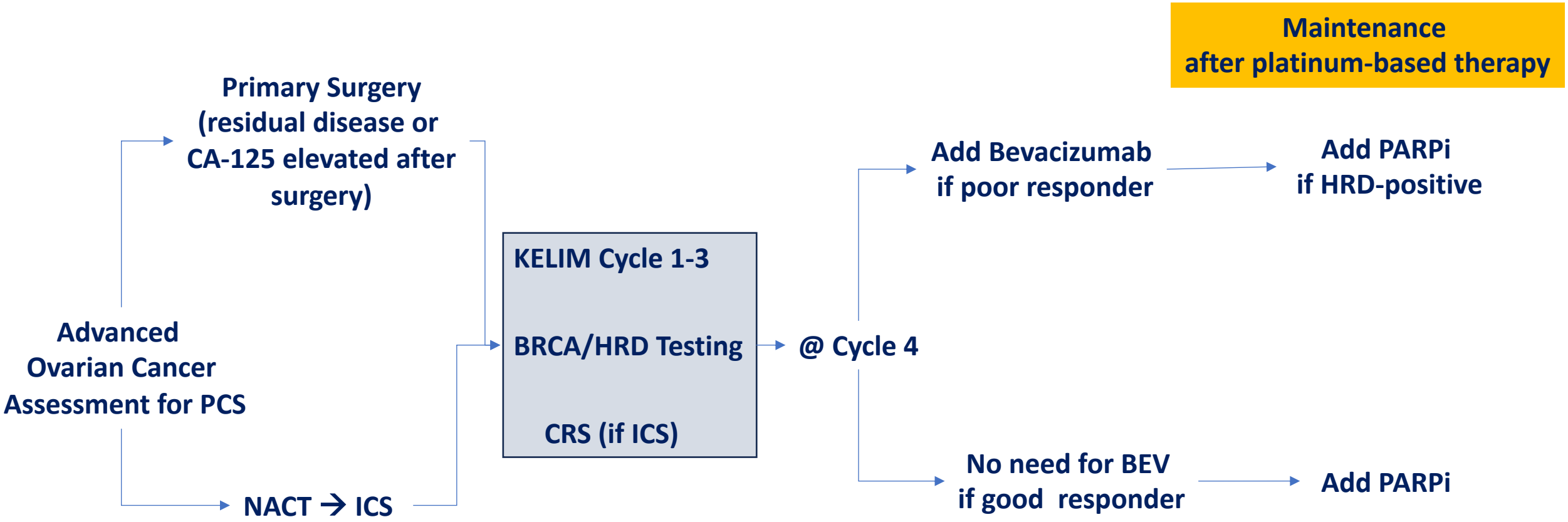
Olaparib + bev	78	77	76	75	73	73	60	60	40	35	19	14	6	3	0
Placebo + bev	43	42	39	37	32	32	23	20	12	7	3	3	1	1	0

	Olaparib + bev (n=78)	Placebo + bev (n=43)
Events, n (%)	10 (13)	25 (58)
Median PFS, months	**NR**	**22.1**
	HR 0.15 (95% CI, 0.07–0.30)	

[a]Unstable median due to lack of events.
bev, bevacizumab; CI, confidence interval; HR, hazard ratio; HRD, homologous recombination deficiency; NR, not reached; PFS, progression-free survival.
Harter P, et al. *Gynecol Oncol*. 2022;164(2):254–264.

To Be(v) or not to Be(v): response to chemotherapy as predictive factor for PARPi

Integrating Molecular Diagnosis & Response to Platinum into Maintenance Therapy Selection



Safety profile across first-line maintenance trials: Summary

	SOLO1[a,1]		PAOLA-1[b,2]		PRIMA[c,3]			ATHENA-MONO[4]	
	Olaparib	Placebo	Olaparib + bev	Bev + placebo	Niraparib (Overall)	Niraparib FSD | ISD	Placebo	Rucaparib	Placebo
N	260	130	535	267	484	313 | 169	244	425	110
Grade ≥3 AEs, %	39.6	20.0	57.0	51.0	73.8	79.0 | 63.9	23.8	60.5	23.6
Thrombocytopenia	0.8	2.0	2.0	<1.0	39.9	49.2 | 22.5	<1	7.1	0.0
Anaemia	21.9	1.5	17.0	<1.0	32.0	36.5 | 23.7	2.0	28.7	0.0
Neutropenia	8.5	4.6	6.0	3.0	21.3	24.8 | 14.8	1.6	14.6	0.9
Hypertension	Not reported	Not reported	19.0	30.0	7.2	8.3 | 5.3	2.0	Not reported	Not reported
AML/MDS, %	1.5	0.8	1.7	2.2	2.3	Not reported	1.6	0.5	0.0

SOLO1 data from 7-year descriptive OS analysis; PAOLA-1 data from primary analysis and final OS analysis (for AML/MDS rates only); PRIMA data from 5-year final OS analysis; ATHENA-MONO from primary analysis.

Please note that head-to-head studies were not conducted between these products. These data are for information purposes only and no comparative claims of non-inferiority or superiority in terms of efficacy or safety are implied or intended. Cross-trial comparisons are not head-to-head studies; varying study designs, methodology and populations limit ability to draw conclusions of comparative efficacy and safety.

[a]Median follow-up of 89 months for olaparib and 87 months for placebo. [b]Median follow-up of 24 months in the olaparib arm and 23 months in the placebo arm. [c]In both arms, median follow-up of 6.2 years.

AE, adverse event; AML, acute myeloid leukaemia; bev, bevacizumab; FSD, fixed starting dose; ISD, individualised starting dose; MDS, myelodysplastic syndrome; OS, overall survival.

1. DiSilvestro P, et al. *J Clin Oncol*. 2023;41(3):609–617; 2. Ray-Coquard I, et al. *N Engl J Med*. 2019;381(25):2416–2428; 3. Monk BJ, et al. *Ann Oncol*. 2024;35(11):981–992;
4. Monk BJ, et al. Presented at: ASCO Annual Meeting; 3–7 June 2022; Chicago, IL, USA [Abstract LBA5500].

Ongoing trials will allow a direct comparison of 1L PARPi with or without bevacizumab

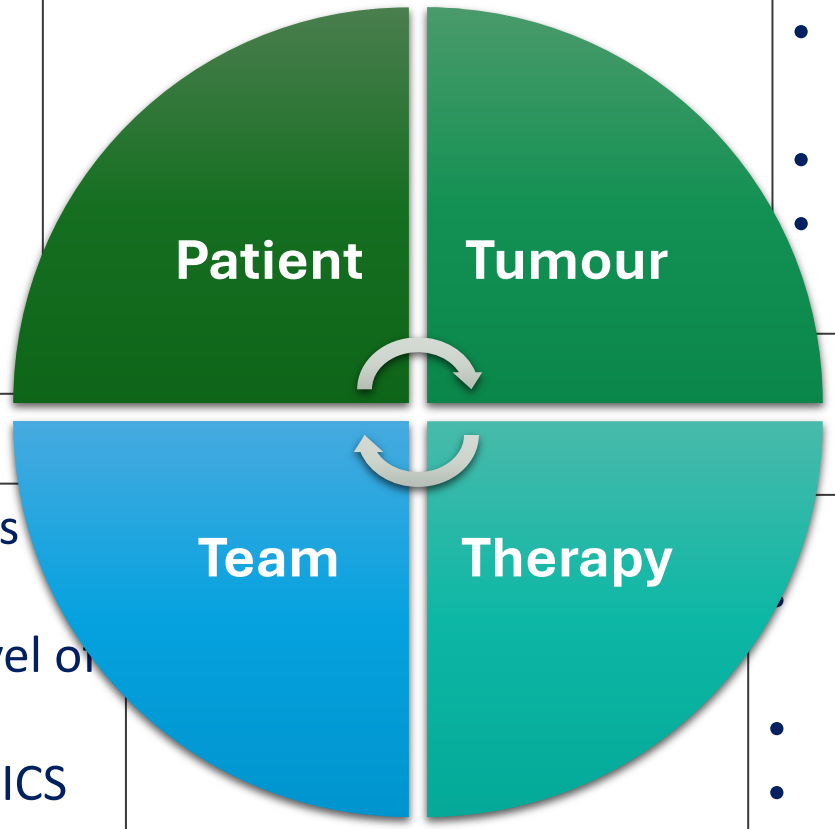
NIRVANA-1[1]	AGO-OVAR 28[2]	MITO25[3]
Niraparib ± bevacizumab as maintenance after complete cytoreduction	Niraparib vs niraparib + bevacizumab as maintenance after platinum + bevacizumab	Chemotherapy ± bevacizumab followed by rucaparib maintenance ± bevacizumab or bevacizumab alone

1. ClinicalTrials.gov. NCT0518398; 2. ClinicalTrials.gov. NCT05009082; 3. ClinicalTrials.gov. NCT03462212. ClinicalTrials.gov website accessed 29 June 2024.

The Complexity of Personalized Therapy: Addressing the Heterogeneity of AOC

- Age
- Performance status (ECOG)
- Co-morbidities
- Expectations
- Desires and own vision of life
- Caregivers' availability and support

- Histology
- BRCA and HRD status
- Other Genomics (CCNE1, RAD51,…)
- Tumour microenvironment
- Mechanisms of resistance to platinum and/or PARPi



- Pre-surgical assessment (CT vs PET vs laparoscopy)
- Skills of the surgical team (level of specialization)
- Residual tumour after PCS or ICS
- Surgical complications

Response to chemo (RECIST)
CA-125 kinetic of elimination (KELIM)
- Bevacizumab and / or PARPi
- Safety & profile of drugs
- Access and reimbursement

1. Caruso G, TomaoF, Parma G, et al. Poly(ADP-ribose)polymeraseinhibitors(PARPi) in ovariancancer:lessonslearnedand future directions.IntJ Gynecol Cancer. 2023;33(4):431–43 2. Mirza MR, Coleman RL, González-Martín A, et al. The forefront of ovarian cancer therapy: update on PARP inhibitors. Ann Oncol. 2020;31(9):1148–59. 3. O'Cearbhaill RE. Using PARP inhibitors in advanced ovarian cancer. Oncology (Williston Park). 2018;32(7):339–43. 4. Havrilesky LJ, Lim S, Ehrisman JA, et al. Patient preferences for maintenance PARP inhibitor therapy in ovarian cancer treatment. Gynecol Oncol. 2020;156(3):561–7.

Take home message

- Maintenance therapy with PARP inhibitors in front line has changed the natural history of patients with HGSOC and GIS+ tumors
- BRCA and HRD Testing is mandatory for patient treatment selection
- Therapeutic management of ovarian cancer in multiple settings has shifted dramatically, with the first-line overall survival data from SOLO-1 and PAOLA-1 raising the hope of a potential cure
- The role of bevacizumab added to PARPi in patients with GIS tumors is still a matter of debate.
  - Clinical characteristics may not play a major role
  - Optimal Response to chemotherapy may favour PARP-i monotherapy
  - KELIM score can help select patients with the greater benefit from bevacizumab but randomized clinical trials are eagerly awaited
- New biomarkers beyond BRCA and GIS (such as ctDNA) are needed to identify patients that will progress on or shortly after PARPi
- Taken together, current evidence highlights the importance of introducing PARPi as early as possible for eligible patients

Second Opinion

Professor Jonathan A Ledermann

Neil Love, MD

RTP
RESEARCH
TO PRACTICE

QUESTIONS FOR THE FACULTY

How do you think through up-front and maintenance therapy for patients with advanced ovarian cancer with somatic/germline BRCA mutations with and without ascites or pleural effusions? Which PARP inhibitor do you prefer, how do you decide on bevacizumab use and how long would you continue maintenance therapy?

How, if at all, does your thinking on these questions differ for patients with BRCA wild-type, HRD-positive disease?

QUESTIONS FOR THE FACULTY

Are there any situations in which you currently offer up-front PARP inhibitor maintenance to your patients with BRCA wild-type, HRD-negative disease?

Do you prefer a particular genetic testing platform? Are some of these more effective than others at detecting somatic/germline BRCA mutations? What about HRD? Have you encountered inconclusive HRD results? How do you approach maintenance therapy for these patients?

QUESTIONS FOR THE FACULTY

How often do you encounter patients with recurrent disease on imaging without CA-125? What role, if any, do you see for ctDNA testing in ovarian cancer?

In which situations, if any, will you rechallenge with a PARP inhibitor for a patient who has received one in the up-front maintenance setting and subsequently experienced disease progression? How does time off treatment factor into your decision? Do you generally use the same or a different PARP inhibitor in this situation?

QUESTIONS FOR THE FACULTY

How do you decide on the use of repeat debulking surgery for patients with recurrent ovarian cancer?

RTP
RESEARCH
TO PRACTICE

Agenda

Module 1: Current Role of PARP Inhibitors in Advanced Ovarian Cancer (OC) — Prof Colombo

Module 2: Strategies Targeting Folate Receptor Alpha in Advanced OC — Dr Westin

Module 3: Other Novel Agents and Strategies for Advanced OC — Dr Olawaiye

Module 4: Diagnosis and Management of Adverse Events Associated with Commonly Employed Therapies for Advanced OC — Dr Konecny

Strategies Targeting Folate Receptor Alpha in Advanced Ovarian Cancer

Shannon N. Westin, MD, MPH

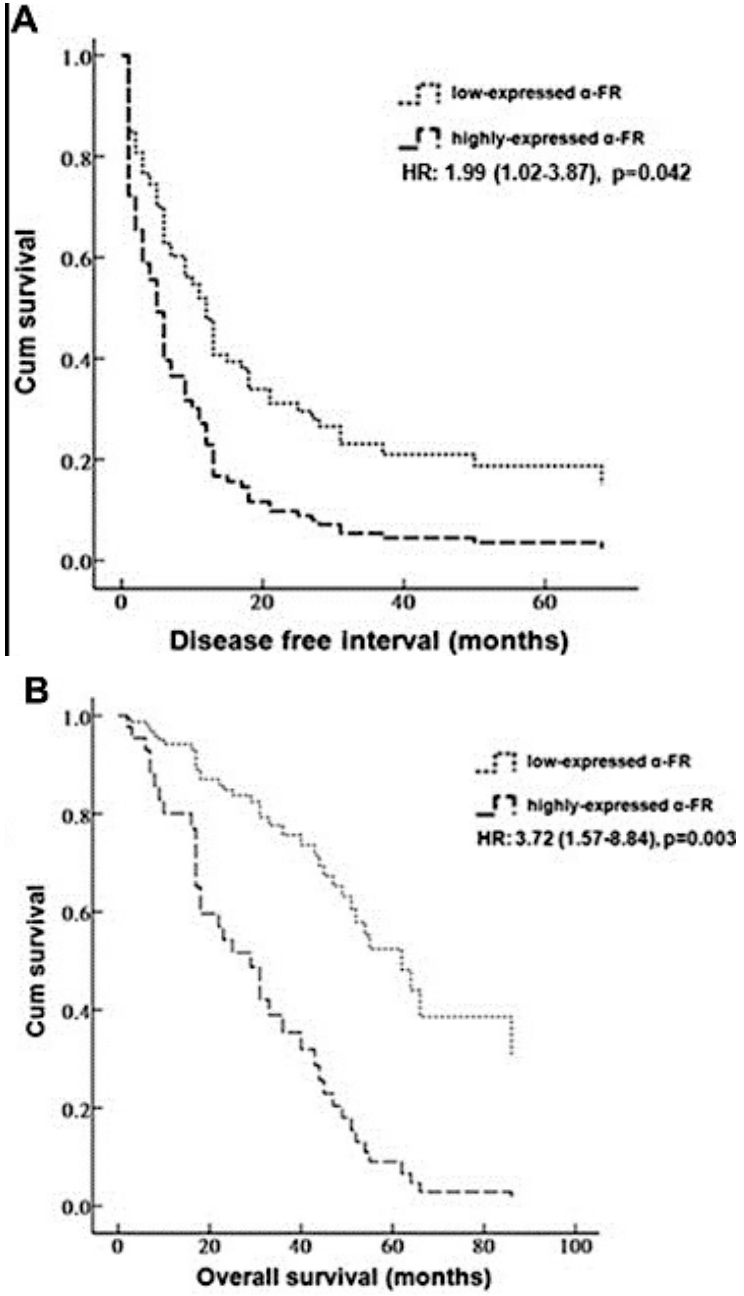
Professor

Department of Gynecologic Oncology and Reproductive Medicine

THE UNIVERSITY OF TEXAS
MD Anderson Cancer Center
Making Cancer History®

Targeting Folate Receptor Alpha

- Cell surface folate receptor - mediates folate transport into epithelial cells.
- FRα expression
  - Limited on normal cells
  - Upregulated on cancers, primarily ovarian, but also endometrial, TNBC
- FRα may be expressed on the alveoli of the lungs and on renal proximal tubules
  - Located on the surface of the cell facing the alveolar and tubular lumen
  - Reduces the exposure of the targets to circulating anti-folate agents
- Expression in ovarian cancer varies by histology (total expression 80-90% all OC)
  - 35-40% with high expression
    - 76% HGS, 50% LGS, 32% Clear cell
- Association with prognosis has been mixed – may be associated with worse outcomes.



Chen Mol Oncol 2012, Kobel Br. J Cancer 2014; Moore KN ESMO. 2019; Oaknin A ASCO 2023

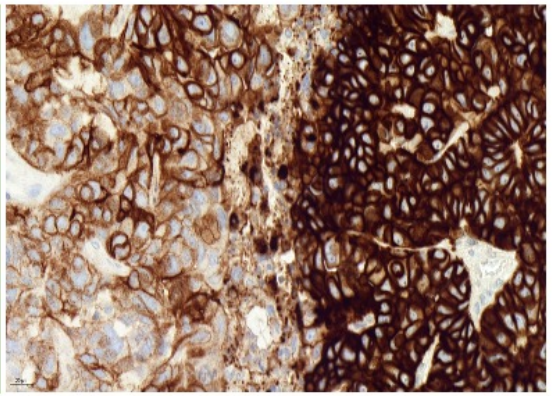
FOLR1 Testing – Assessment of FRα Expression

PS2+ Scoring

Determined by staining intensity and percentage of tumor cells

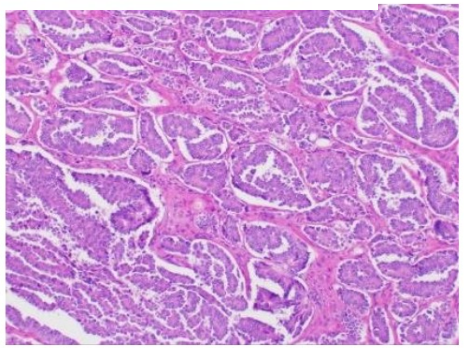
1+ 2+ 3+ intensity

PS2+ Scoring Positive: ≥ 50% tumor cells with ≥ 2+ FRα membrane staining.

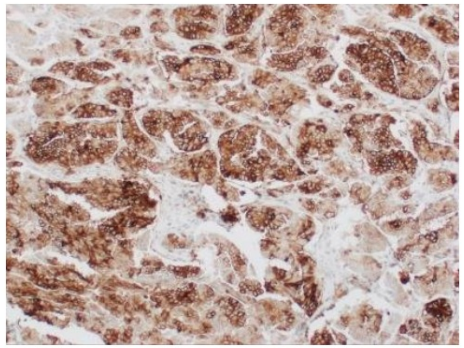


Commercial and institutional options available

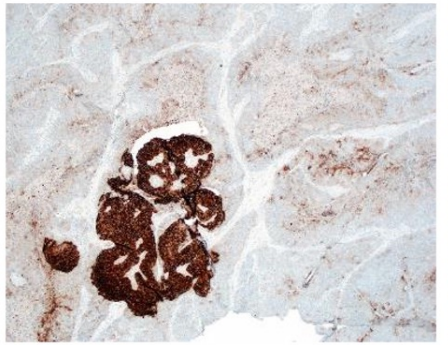
CDx – mirvetuximab sorvtansine at >/= 75%
NCCN – mirvetuximab + bevacizumab at >/= 25%
Future indications for next generation antibody-drug conjugates – potentially at lower expression levels



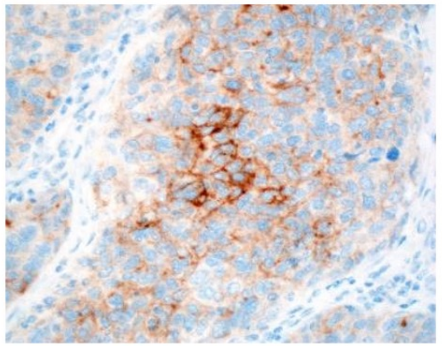
Low Grade Serous



Mod/Strong Membranous Staining



Variable Staining - <75% of cells



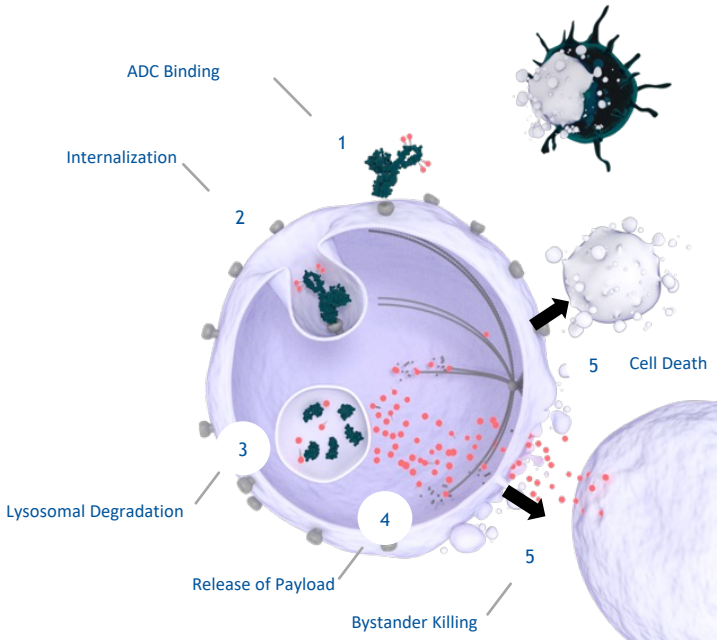
Cytoplasmic Staining

Irrelevant Findings

Moore KN et al. ESMO. 2019; Oaknin A et al. ASCO 2023; Chen YL, et al. *Mol Oncol* 2012, Path slides courtesy of Anais Malpica, MD

Mirvetuximab soravtansine, first FRα-targeted ADC approved for PROC

Antibody-drug conjugate (ADC) comprising an FRα-binding antibody, cleavable linker, and a maytansinoid DM4 payload



FDA grants accelerated approval to mirvetuximab soravtansine-gynx for FRα positive, platinum-resistant epithelial ovarian, fallopian tube, or peritoneal cancer

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

Moore KN et al. *Cancer*. 2017; Matulonis UA et al. *J Clin Oncol*. 2023

Mirvetuximab soravtansine: SORAYA trial (NCT04296890)

Key eligibility criteria

- Platinum-resistant ovarian cancer
- Prior bevacizumab required, prior PARPi allowed
- 1–3 prior lines of therapy
- Patients with *BRCA* mutations allowed
- FRα-positive (≥75% of cells staining positive with ≥2+ staining intensity)

Mirvetuximab soravtansine
(N=106)
6.0 mg/kg adjusted ideal body weight (AIBW) q3w

Primary endpoint

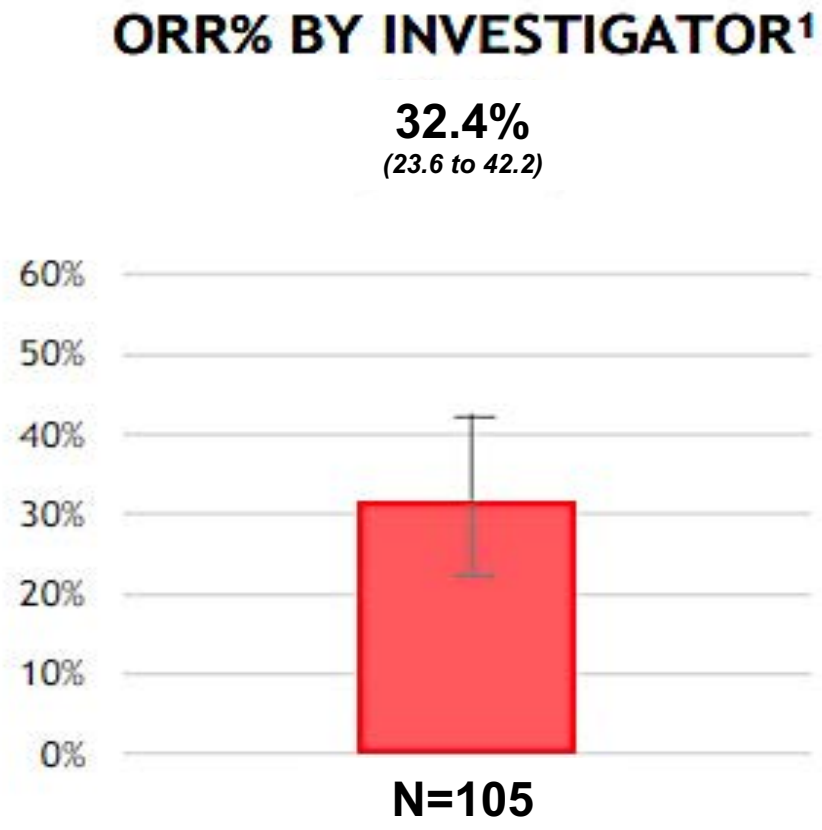
- ORR per Investigator

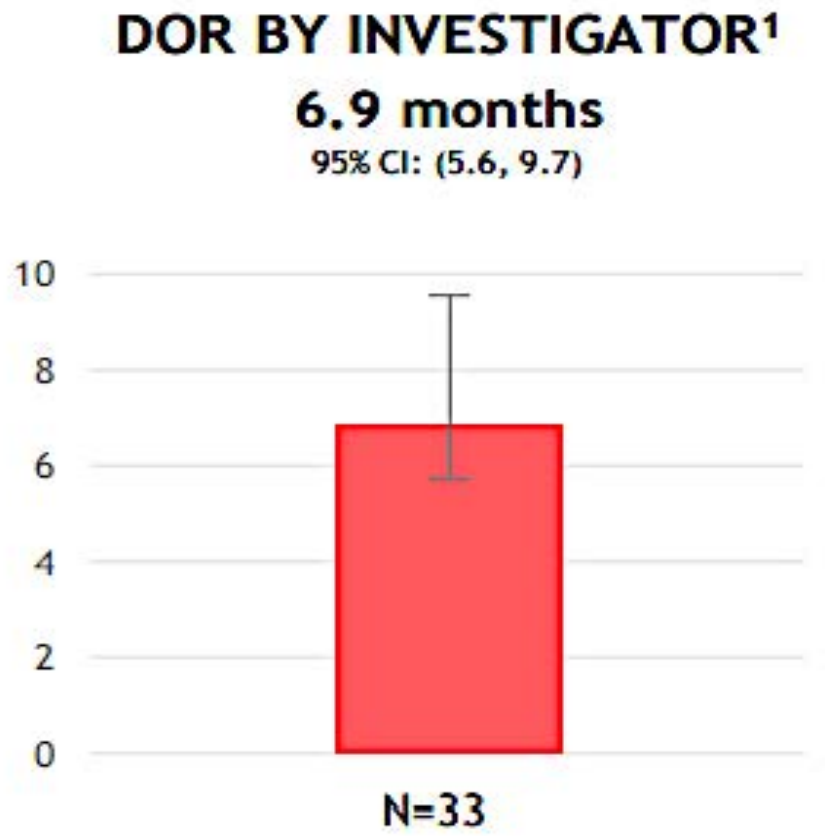
Secondary endpoints

- DOR, PFS, OS, CA-125 response by GCIG criteria, safety

Moore KN et al. *Cancer*. 2017; Matulonis UA et al. *J Clin Oncol*. 2023

Mirvetuximab soravtansine: SORAYA trial (NCT04296890)



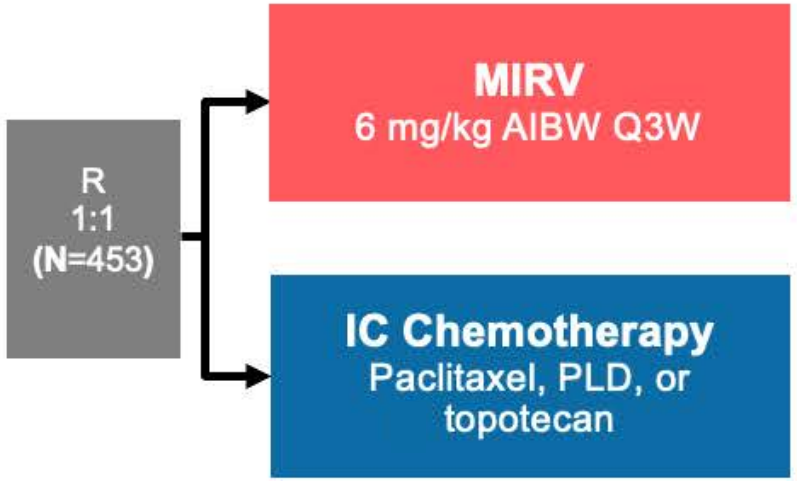


Moore KN et al. *Cancer*. 2017; Matulonis UA et al. *J Clin Oncol*. 2023

MIRASOL (NCT04209855): Randomized, phase 3 study of MIRV vs chemotherapy in FRα-high Platinum–Resistant Ovarian Cancer

Eligible patients:
- PROC (PFI ≤6 mo)
- FRα detected by IHC with PS2+ among ≥75% of viable tumor cells
- High-grade serous histology
- 1–3 prior lines of therapy
- Prior BEV and PARPi allowed
- Participants with *BRCA* mutations allowed

Excluded patients:
- 1º platinum-refractory disease (primary PFI <3 mo)



Stratification:
- IC chemotherapy: paclitaxel, PLD, or topotecan
- Prior lines of therapy: 1 vs 2 vs 3

Primary endpoint[a]:
- PFS by INV (BICR sensitivity analysis)

Select secondary endpoints:
- ORR by INV (BICR sensitivity analysis)
- OS OV28 abdominal/GI subscale[b]
- Safety and tolerability
- DOR
- CA-125 response[c]
- PFS2

ITT population:
- All randomized patients, regardless of receipt of assigned treatment

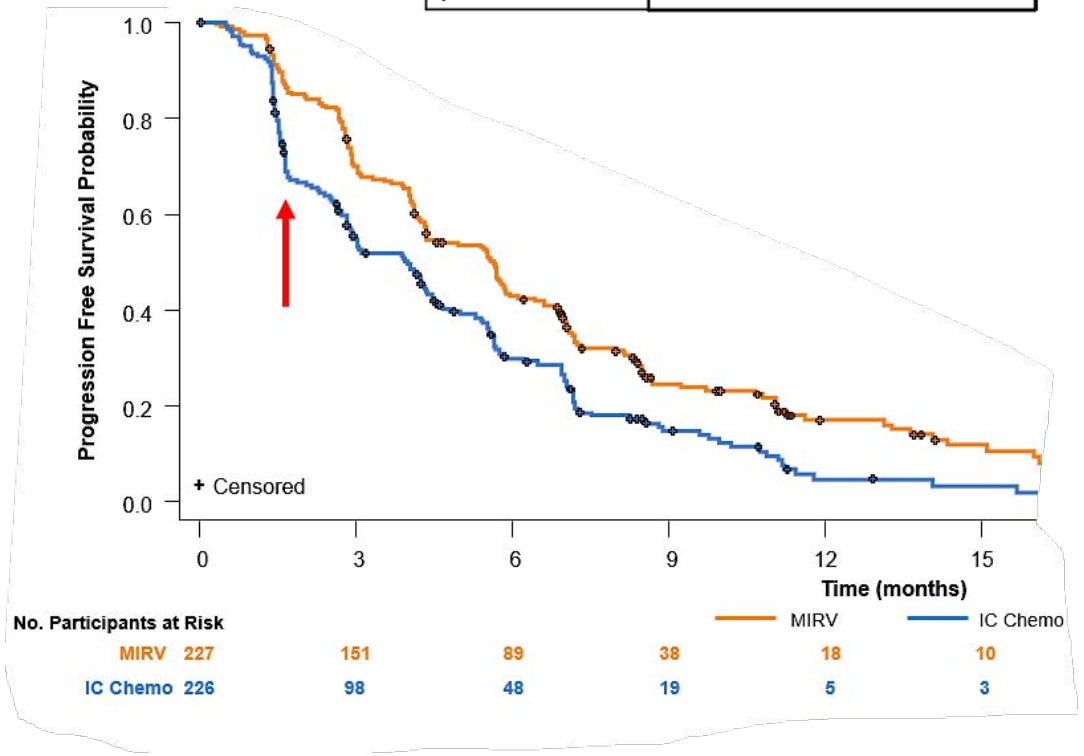
Select exploratory:
- Additional PRO assessments[d]

Safety population:
- All randomized patients who received ≥1 dose of assigned treatment

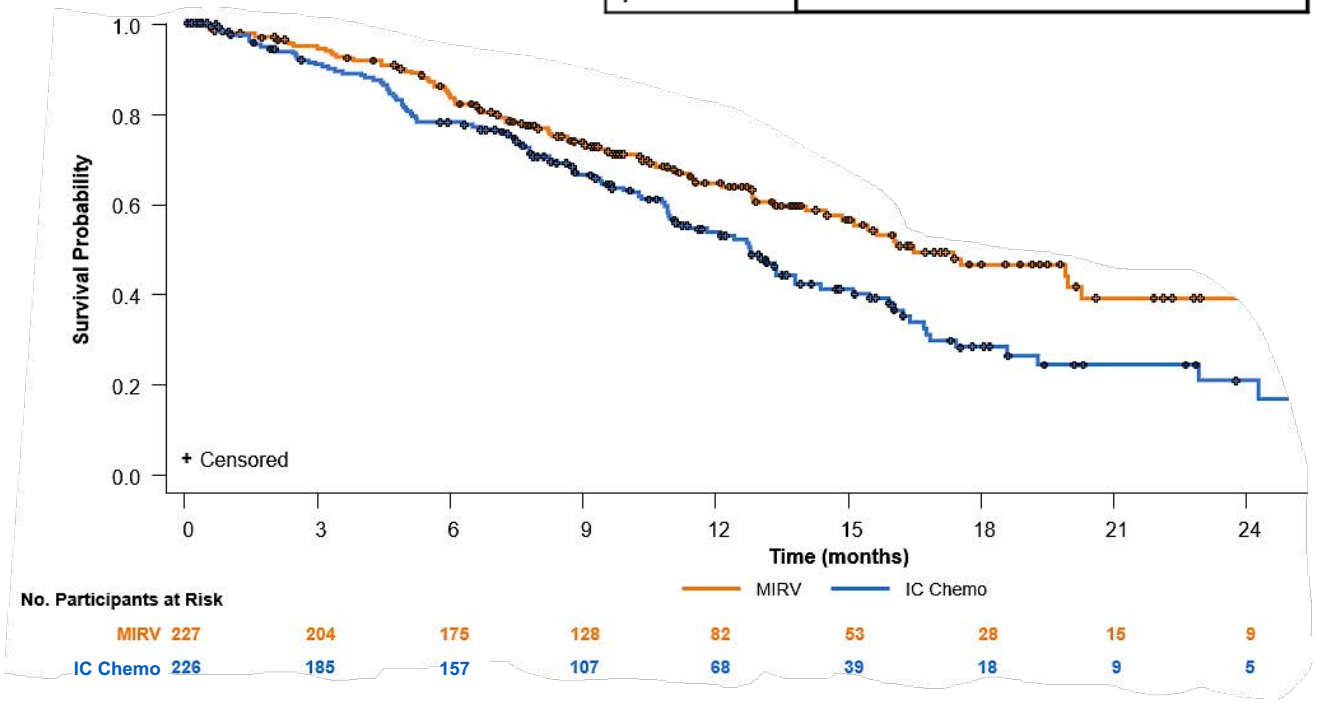
Moore KN, et al. N Engl J Med. 2023;389(23):2162-2174

Confirmation of Superiority – OS Benefit!!!!

	MIRV (n=227)	IC Chemo (n=226)
mPFS (95% CI)	5.62 (4.34, 5.95)	3.98 (2.86, 4.47)
Events, n (%)	176 (77.5)	166 (73.5)
HR (95% CI)	0.65 (0.52, 0.81)	
p-value	<0.0001	

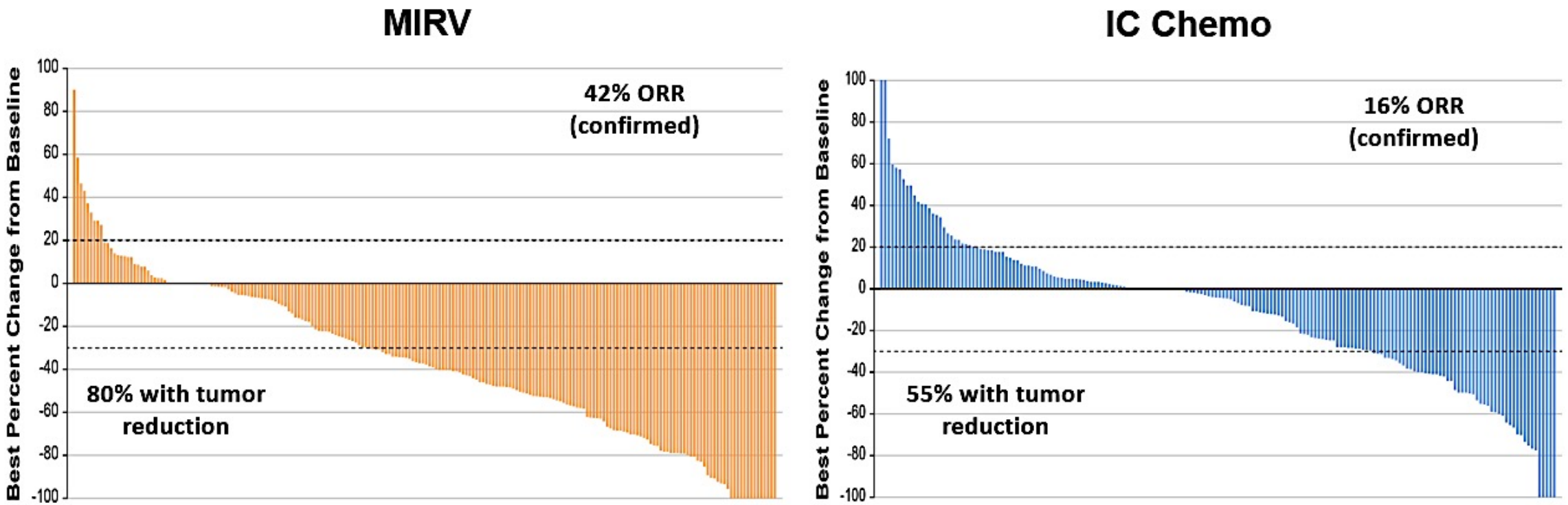


	MIRV (n=227)	IC Chemo (n=226)
mOS (95% CI)	16.46 (14.46, 24.57)	12.75 (10.91, 14.36)
Events, n (%)	90 (39.6)	114 (50.4)
HR (95% CI)	0.67 (0.50, 0.89)	
p-value[a]	0.0046	



Moore et al. ASCO 2023; Moore et al. NEJM 2023

Confirmation of Superiority – ORR and Tumor Reduction

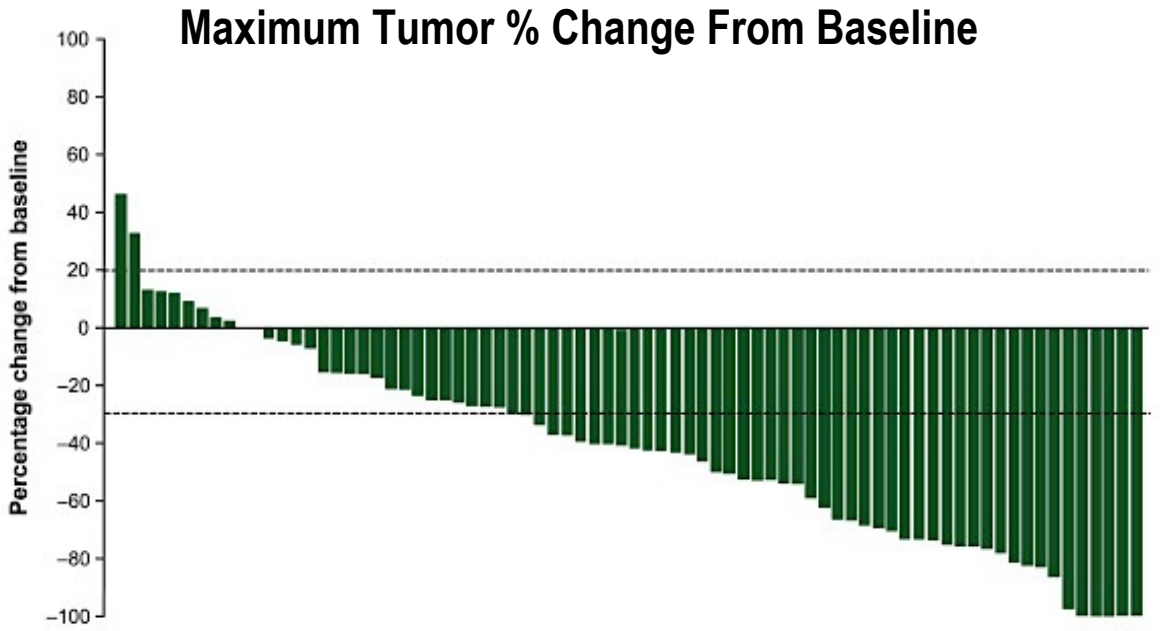


Moore et al. ASCO 2023; Moore et al. NEJM 2023

PICCOLO: Mirvetuximab soravtansine in platinum sensitive ovarian cancer

Characteristics	N=79
Age, median (range), years	66 (41-84)
Race, n (%)	
White	65 (82.3)
Black or African American	4 (5.1)
Asian	1 (1.3)
# prior lines of systemic therapy, n (%)	
1-2[a]	49 (62.0)
≥3	30 (37.9)
Prior exposure to taxanes, n (%), Yes	77 (97.5)
Exposed in multiple lines	20 (25.3)
Prior exposure to PARPi[b],n (%), Yes	64 (81.0)
Progression on PARPi[c]	59 (74.7)
Prior exposure to bev, n (%), Yes	51 (64.6)
Most recent PFI (months)[d], n (%)	
≤12	43 (54.4)
>12	34 (43.0)

Alvarez Secord; Ann Oncol 2025

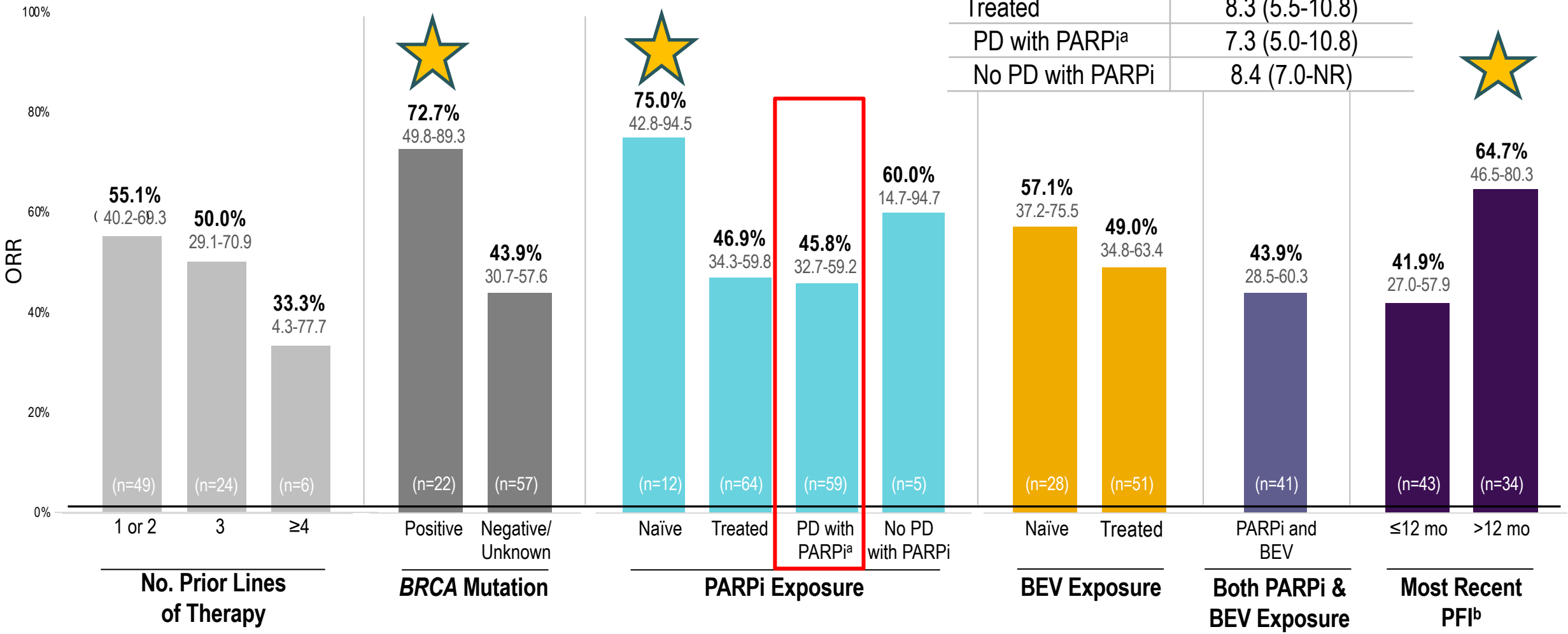


Primary Endpoint	N=79
ORR, n (%)	41 (51.9)
95% CI	40.4-63.3
Best Response, n (%)	
CR	6 (7.6)
PR	35 (44.3)
SD	29 (36.7)
PD	7 (8.9)
Not evaluable	2 (2.5)

Secondary Endpoints	
Median DOR[a]	n=41
Months (95% CI)	8.25 (5.6-10.8)
Median PFS	N=79
Months (95% CI)	6.93 (5.8-9.6)

PICCOLO: Subgroup Analyses

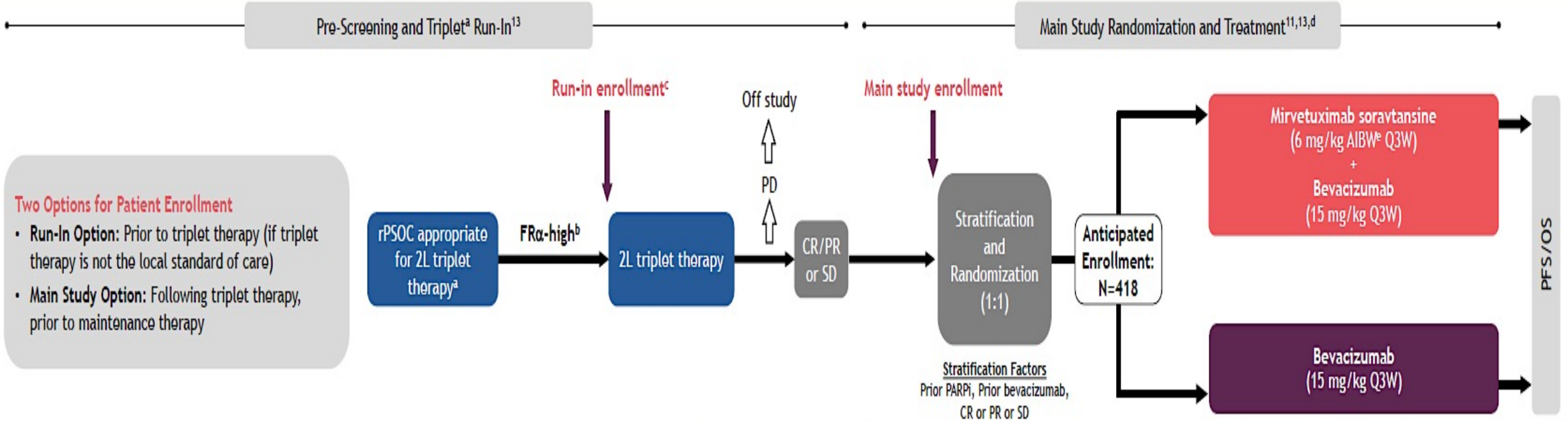
Exposure to PARPis	Median DOR months (95% CI)
Naïve	8.8 (3.5-NR)
Treated	8.3 (5.5-10.8)
PD with PARPi[a]	7.3 (5.0-10.8)
No PD with PARPi	8.4 (7.0-NR)



Alvarez Secord; Ann Oncol 2025

GOG-3078/IMGN853-0421/GLORIOSA

Randomized Phase 3 Trial for Mirvetuximab + Bevacizumab Maintenance in FRα-high Platinum Sensitive Ovarian Cancer (PI: David O'Malley, MD, Co-PI: Tashanna Myers, MD)



[a]Triplet treatment consists of platinum+chemotherapy+bevacizumab for planned 6 cycles (minimum 4 and maximum 8 cycles), including at least 3 cycles of bevacizumab. [b]Pre-screening consent must be obtained for tissue testing for FRα expression by Ventana FOLR1 Assay. [c]FRα-high patients who desire to be treated and followed while on their run-in triplet therapy must sign a run-in consent as part of the main consent form if they meet eligibility criteria as assessed by the investigator. [d]Maintenance treatment must begin ≤12 weeks from last dose of triplet therapy and within 30 days of randomization. Treatment continues until PD, unacceptable toxicity, withdrawal of consent, death, or sponsor study termination. [e]AIBW, also known as AdjBW, is calculated as IBW (kg) + 0.4 (actual weight – IBW). IBW for females is calculated as 0.9*height (cm) – 92.

Key Eligibility Criteria:
- Platinum-sensitive HGS ovarian cancer
- 1 prior platinum treatment
- Prior PARPi required if BRCA+
- CR, PR, or SD after treatment with platinum-based doublet + bevacizumab required

NCT05445778

GOG PARTNERS

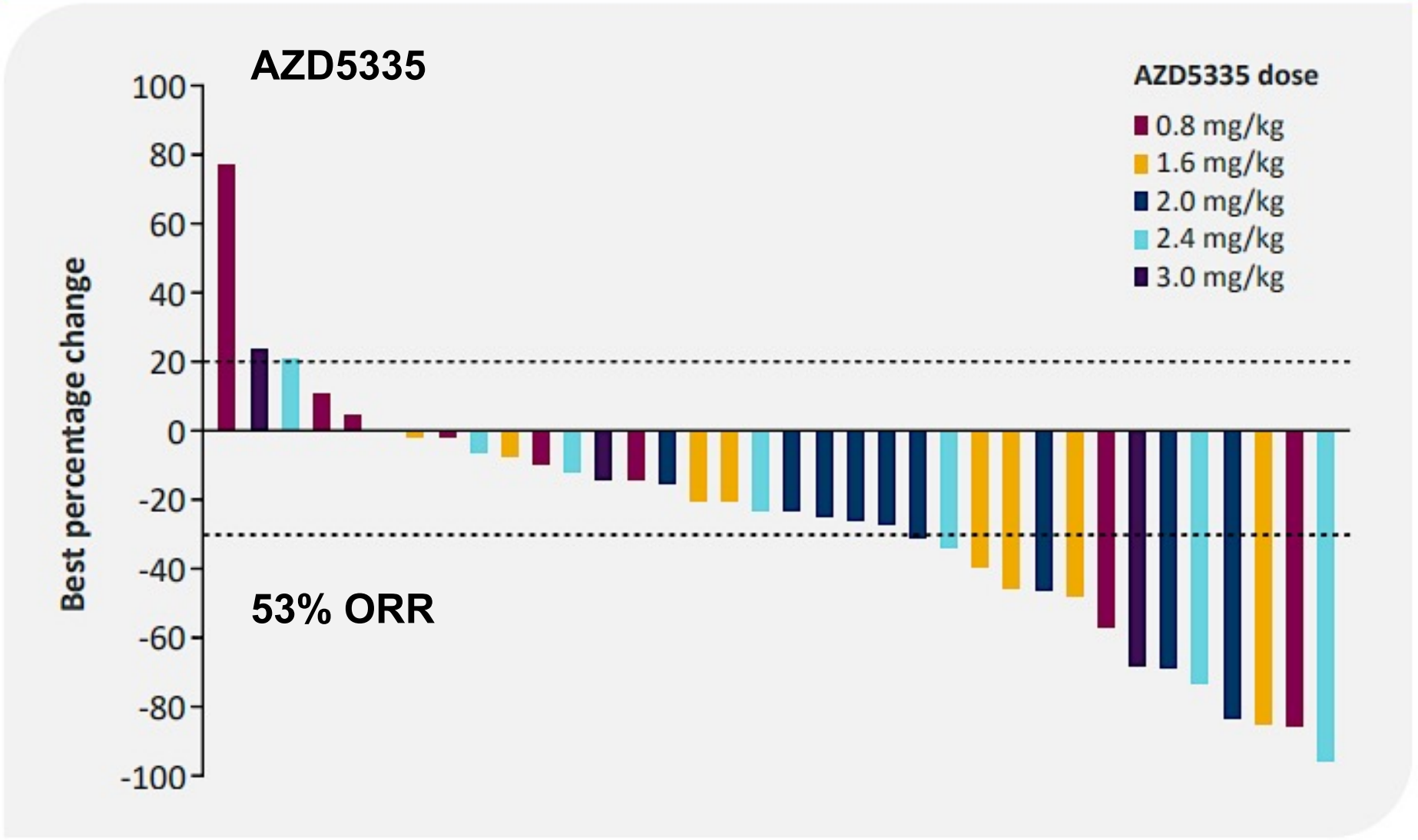
O'Malley. Future Oncology. 2024

The Folate Receptor Alpha Landscape

	Mirvetuximab soravtansine	Sofetabart mipitecan	Rinatabart sesutecan	Torvutatug samrotecan (AZD5335)	Luveltamab Tazevibulin
Payload	DM4	Exatecan	Exatecan	Samrotecan	SC-209 – Hemiasterelin derivative cytotoxic
DAR	4	ND	8	8	4
Linker	Sulfo-SPDB linker	Proprietary	A novel hydrophilic protease-cleavable linker	Novel conjugated linker	Cathepsin B
Trial	MIRASOL	NCT07213804	NCT05579366	NCT 05797168	NCT03748186
ORR	42 vs. 15%	50%ORR 54%(high) 40% (low)	38% ORR 68% (high) 30% (low)	53% ORR 61% (high) 48% (low)	43.8% FRα >25% by TPS (5.2mg/kg) 31.2% (4.3mg/kg)
mPFS	5.62 vs. 3.98 HR = 0.65	NR	NR	NR	FRα > 25% 6.1 (95% CI 4.1- 7.2)
mOS	16.46 vs. 12.75 HR= 0.67	NR	NR	NR	NR

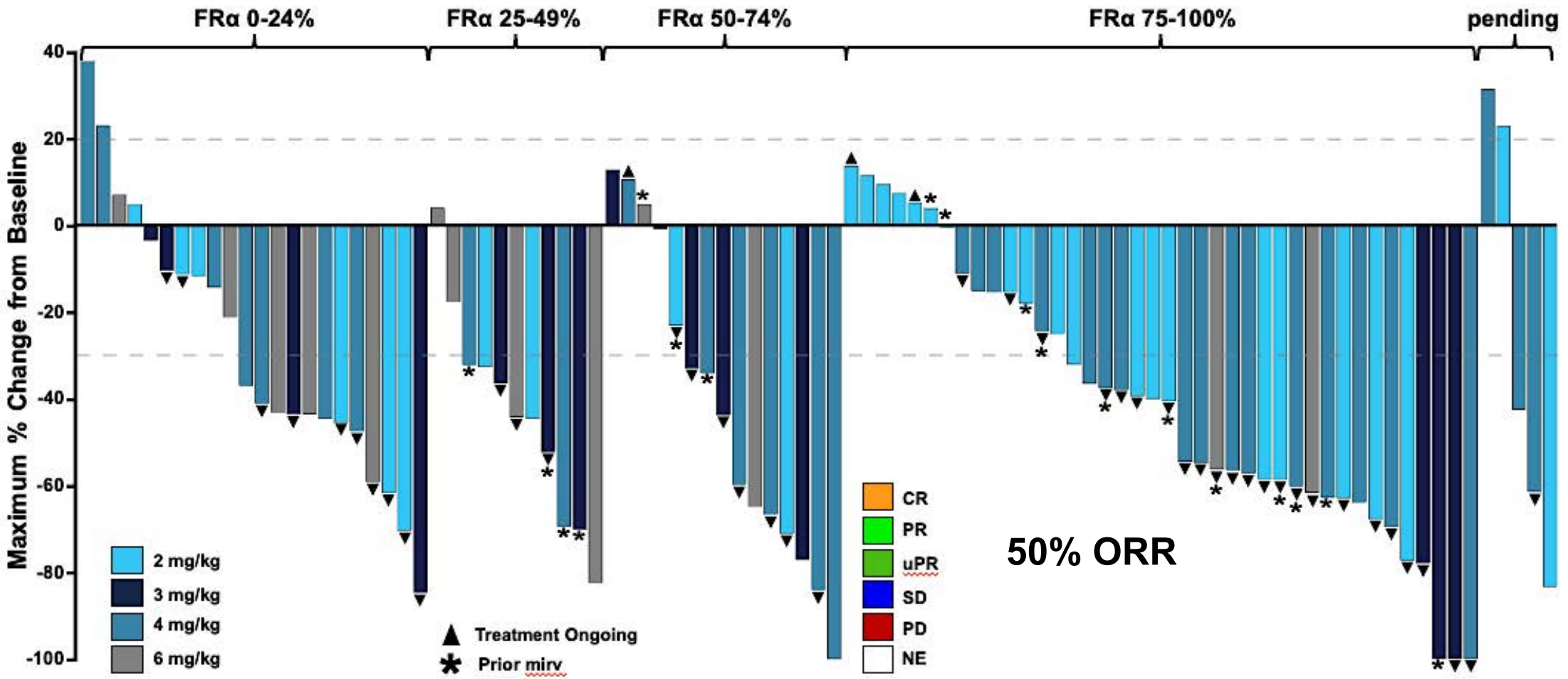
The Data Are Promising (and Consistent!)

Torvutatug samrotecan (AZD5335)



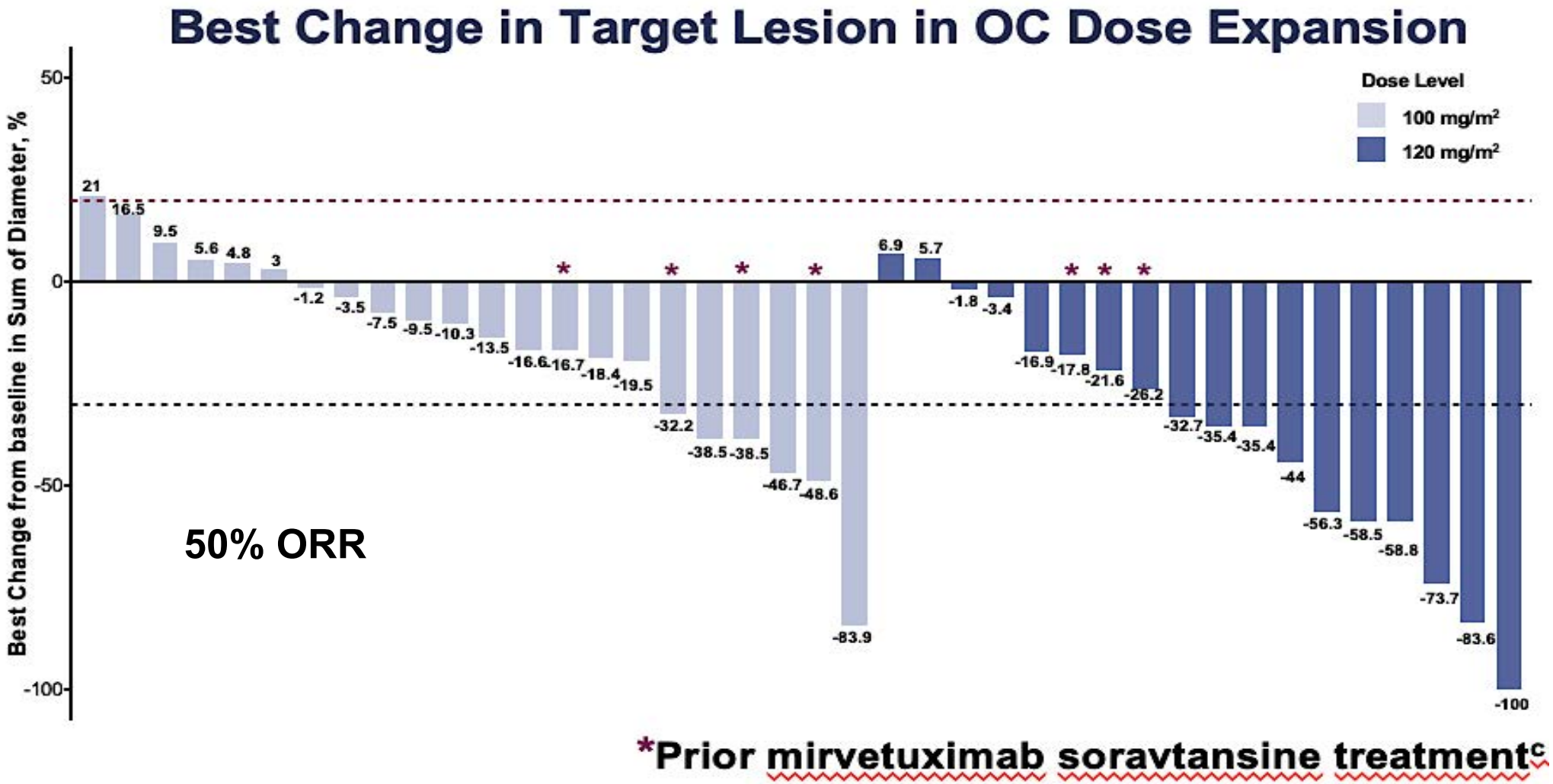
Shapira-Frommer ESMO 2024

Sofetabart mipitecan



Ray-Coquard ESMO 2025

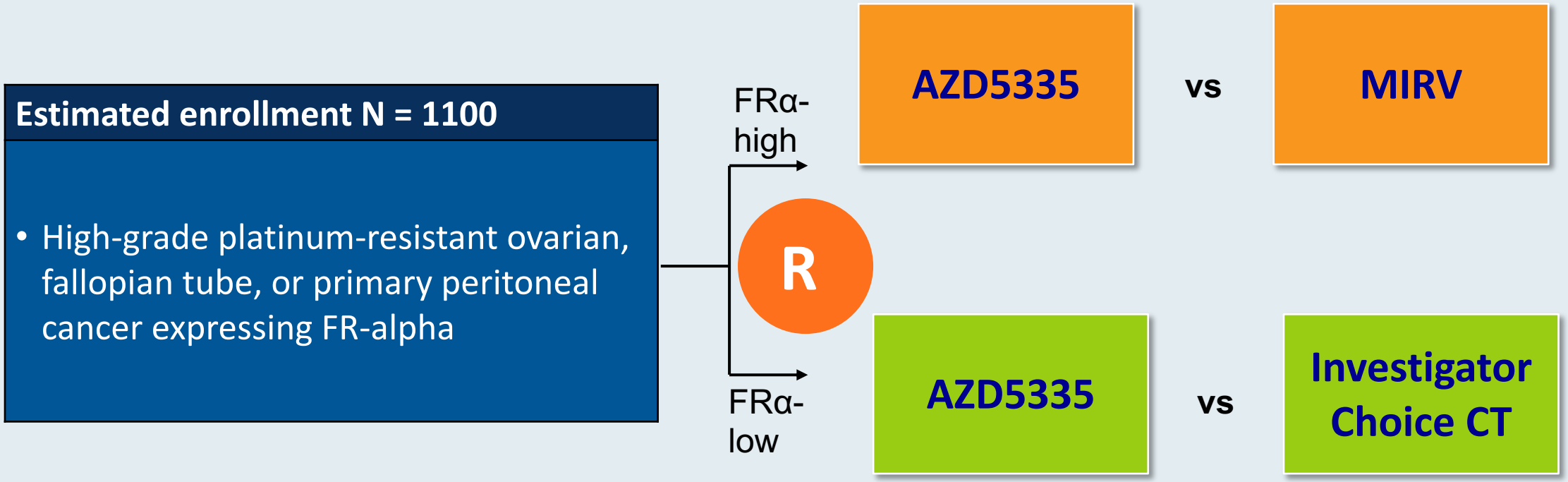
Rinatabart Sesutecan



Lee EK ESMO 2024

Here Come the Phase III Trials!

Phase III TREVI OC 01/GOG 3127/ENGOT ov93 trial

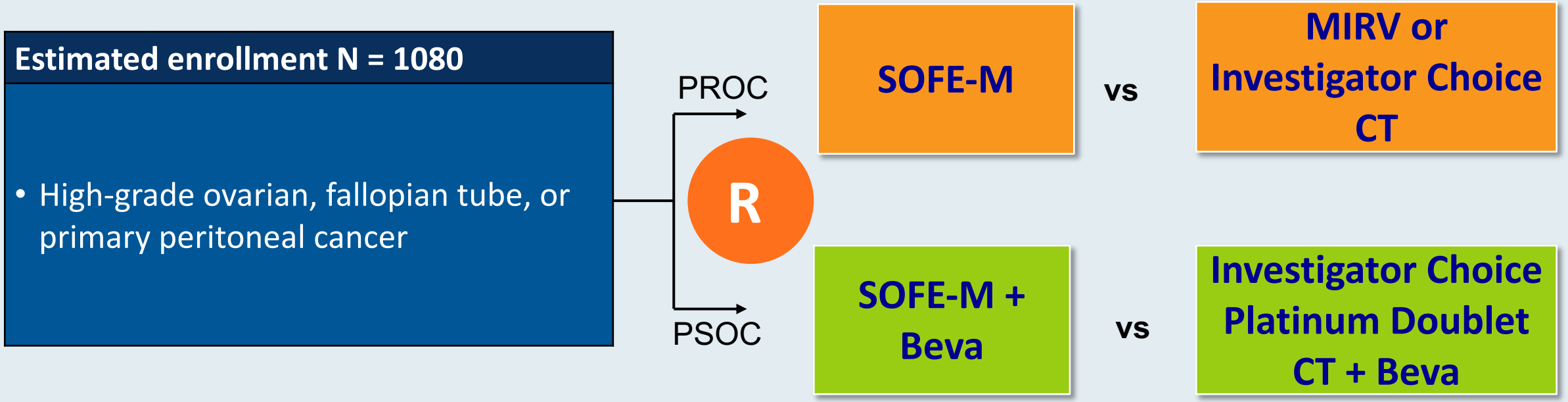


Primary endpoint: Progression-free survival

Secondary endpoint: Overall survival

https://clinicaltrials.gov/ct2/show/NCT07218809. Accessed April 2026.

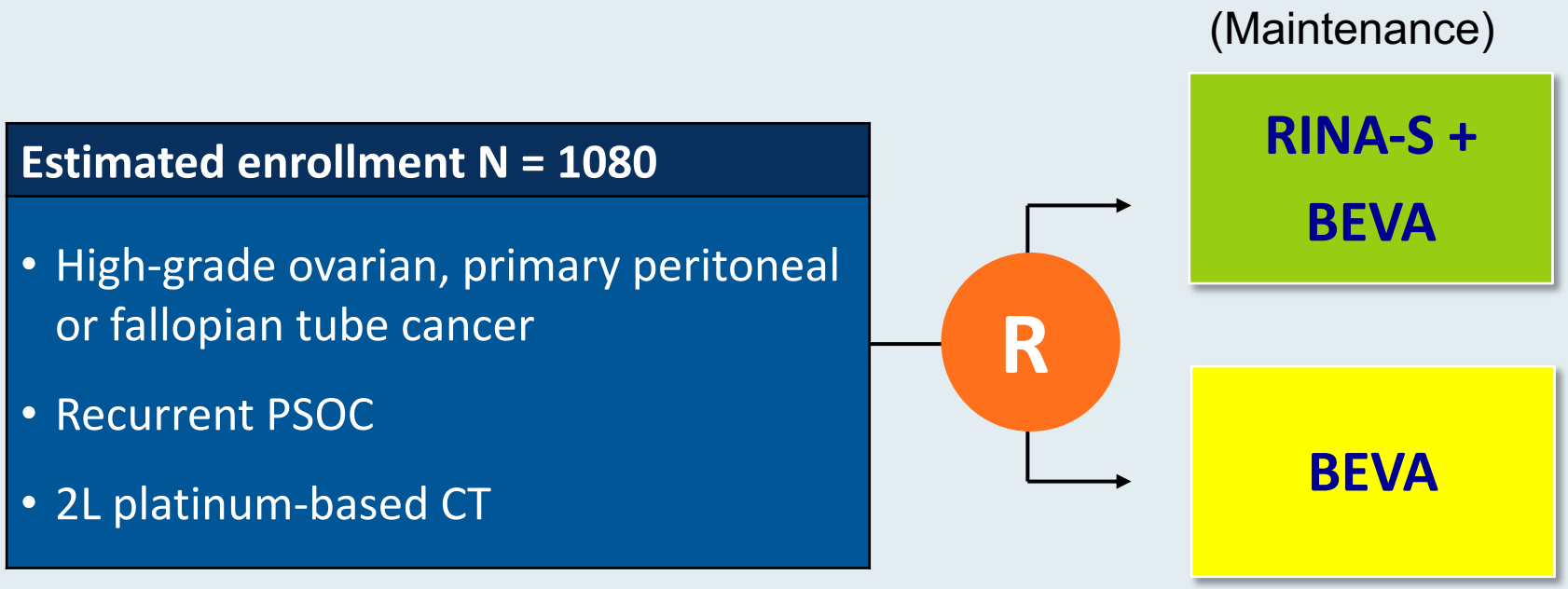
Phase III FRAmework-01



Primary endpoint: Progression-free survival

https://clinicaltrials.gov/ct2/show/NCT07213804. Accessed April 2026.

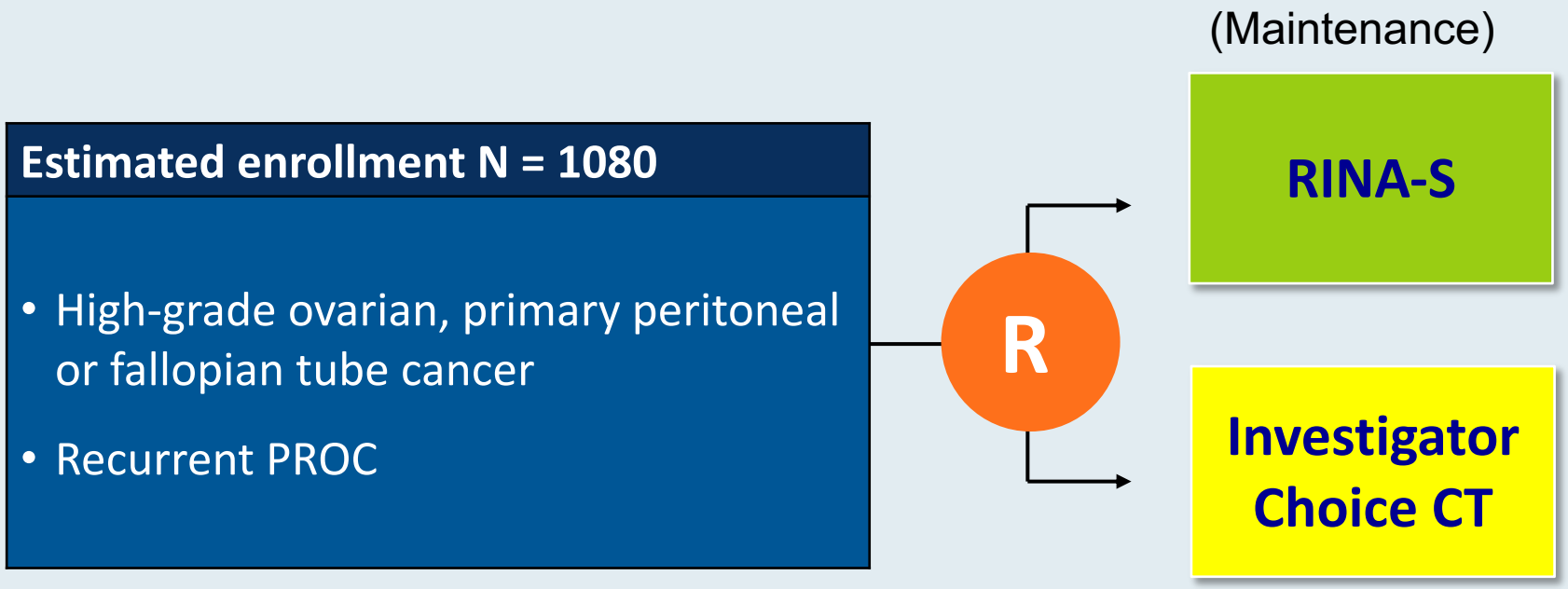
Phase III RAINFOL-04



Primary endpoint: Progression-free survival

https://clinicaltrials.gov/ct2/show/NCT07225270. Accessed April 2026.

Phase III RAINFOL-02



Primary endpoint: Progression-free survival

https://clinicaltrials.gov/ct2/show/NCT06619236. Accessed April 2026.

Second Opinion

Ursula Matulonis, MD

Neil Love, MD

RTP
RESEARCH
TO PRACTICE

QUESTIONS FOR THE FACULTY

How are you currently sequencing mirvetuximab soravtansine for your patients with FRα-positive, platinum-resistant ovarian cancer? Do you always use it as monotherapy, or do you ever combine it with other agents (eg, bevacizumab)?

What is your threshold for FRα positivity for mirvetuximab soravtansine use? Are there any situations in which you would be tempted to try mirvetuximab soravtansine for a patient with low or no FRα expression who has exhausted other treatments? What about for a patient with platinum-sensitive recurrent disease?

QUESTIONS FOR THE FACULTY

How do you generally screen for ocular toxicities in patients receiving mirvetuximab soravtansine? How often do you recommend consultation with an ophthalmologist?

What is your threshold for dose reducing or holding mirvetuximab soravtansine due to ocular toxicities? For Dr Matulonis's patient, would you have reduced the dose of mirvetuximab soravtansine from 6 mg/kg to 5 mg/kg, or would you have continued at 6 mg/kg?

QUESTIONS FOR THE FACULTY

How do you monitor for pneumonitis in patients receiving mirvetuximab soravtansine? How do you manage Grade 1 versus Grade 2 pneumonitis? In which situations will you rechallenge after resolution of symptoms?

QUESTIONS FOR THE FACULTY

Do you believe that any of the FRα-targeted antibody-drug conjugates in development (eg, rinatabart sesutecan, torvutatug samrotecan, sofetabart mipitecan) will have significant activity in patients with disease progression on mirvetuximab soravtansine? Do you believe any of these agents may prove more effective than mirvetuximab soravtansine or that they might have activity in patients with lower levels of FRα expression?

QUESTIONS FOR THE FACULTY

In your view, are any of the investigational FRα-targeting ADCs significantly better tolerated than mirvetuximab soravtansine? Do any of them have significantly less or no ocular toxicities associated with them?

What ongoing clinical trials of FRα-targeted antibody-drug conjugates in development are you most excited about?

Agenda

Module 1: Current Role of PARP Inhibitors in Advanced Ovarian Cancer (OC) — Prof Colombo

Module 2: Strategies Targeting Folate Receptor Alpha in Advanced OC — Dr Westin

Module 3: Other Novel Agents and Strategies for Advanced OC — Dr Olawaiye

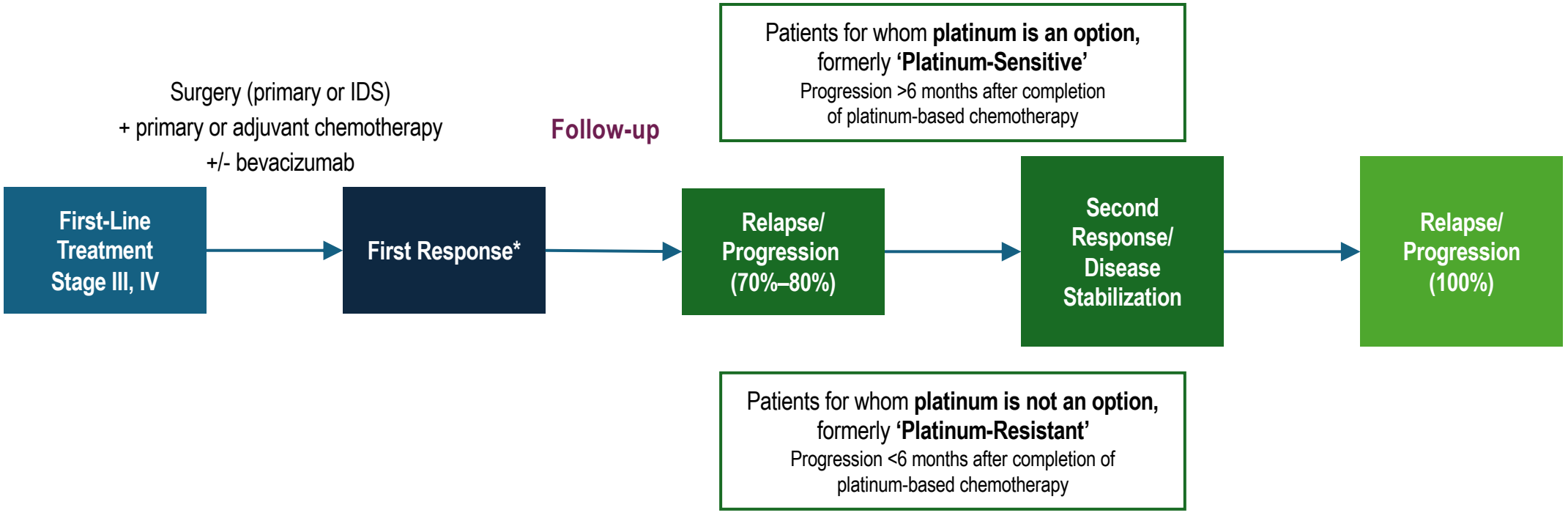
Module 4: Diagnosis and Management of Adverse Events Associated with Commonly Employed Therapies for Advanced OC — Dr Konecny

Other Novel Agents and Strategies for Advanced Ovarian Cancer

Alexander B. Olawaiye, MD
Professor
University of Pittsburgh School of Medicine
Pittsburgh
Pennsylvania, USA

University of Pittsburgh

The Typical Course of Advanced Ovarian Cancer: Almost Ubiquitous Recurrence Following Front Line Chemotherapy



*1. Ledermann JA et al. *Ann Oncol.* 2013;24(Suppl 6):vi24-vi32. 2. Giornelli GH. *Springerplus*. 2016;5(1):1197. 3. Pignata S et al. *Ann Oncol.* 2017;28(suppl_8):viii51-viii56. 4. du Bois A et al. *Cancer*. 2009;115(6):1234-1244.
5. Wilson MK et al. *Ann Oncol*. 2017;28(4):727-732.

University of Pittsburgh

Second-line Platinum Therapy in Patients with Ovarian Cancer Previously Treated with Cisplatin

- Cisplatin-free interval (PFI) of **> 4** months between the completion of their first regimen and the institution of a second cisplatin/carboplatin program

- **31/62 (50% response rate {RR})**
  - PFI = 5 to 12 months, RR= 27%
  - PFI = 13 to 24 months, RR = 33%
  - PFI > 24 months, RR= 59%

"In conclusion, secondary responses to cisplatin/carboplatin-based treatment are common in patients with ovarian cancer who have previously responded to the agents and increase in frequency with greater distance from the initial therapy"

Markman M, et al. *J Clin Oncol.* 1991;Mar;9(3):389-93.

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BERLIN 2025 ESMO congress

Pembrolizumab vs Placebo Plus Weekly Paclitaxel With or Without Bevacizumab for Platinum-Resistant Recurrent Ovarian Cancer: Results from the Randomized, Double-Blind Phase 3 ENGOT-ov65/KEYNOTE-B96 Study

Nicoletta Colombo[1,2], Emese Zsiros[3], Alexandra Sebastianelli[4], Mariusz Bidzinski[5], Carlos Gallardo[6], Emad Matanes[7], Kosei Hasegawa[8], Fatih Kose[9], Manuel Magallanes-Maciel[10], Rebecca Herbertson[11], Sumitra Ananda[12], Judith R. Kroep[13], Andreia Cristina de Melo[14], Philip R Debruyne[15], Jae-Weon Kim[16], Xuan Peng[17], Karin Yamada[17], Agata M. Bogusz[17], Thibault De La Motte Rouge[18], and Xiaohua Wu[19] on behalf of the ENGOT-ov65/KEYNOTE-B96 investigators

[1]Gynecologic Oncology Program, European Institute of Oncology, IRCCS, Milan, Italy; [2]Department of Medicine and Surgery, University of Milan-Bicocca, Italy; [3]Roswell Park Comprehensive Cancer Center, Buffalo, NY, USA; [4]CHU de Québec-Université Laval, Québec, Canada; [5]Narodowy Instytut Onkologii im. Marii Skłodowskiej-Curie, Warsaw, Poland; [6]Bradford Hill Clinical Research Center, Santiago, Chile; [7]Rambam Health Care Campus and Ruth and Bruce Rappaport Faculty of Medicine, Technion, Haifa, Israel; [8]Saitama Medical University International Medical Center, Hidaka, Japan; [9]Başkent University, Ankara, Turkey; [10]Centro Oncologico Internacional, Mexico City, Mexico; [11]University Hospitals Sussex NHS Foundation Trust, West Sussex, United Kingdom; [12]Epworth Healthcare and Peter MacCallum Cancer Centre, Melbourne, Australia; [13]Leiden University Medical Center on behalf of the Dutch Gynecology Oncology Group (DGOG), Leiden, Netherlands; [14]Brazilian National Cancer Institute (INCA), Rio de Janeiro, Brazil; [15]Kortrijk Cancer Centre, AZ Groeninge, Kortrijk, and Belgium and Luxembourg Gynaecological Oncology Group (BGOG), Leuven, Belgium; [16]Seoul National University, Seoul, South Korea; [17]Merck & Co., Inc., Rahway, NJ, USA; [18]Centre Eugene Marquis, Rennes, France; [19]Fudan University Shanghai Cancer Center, Shanghai, China

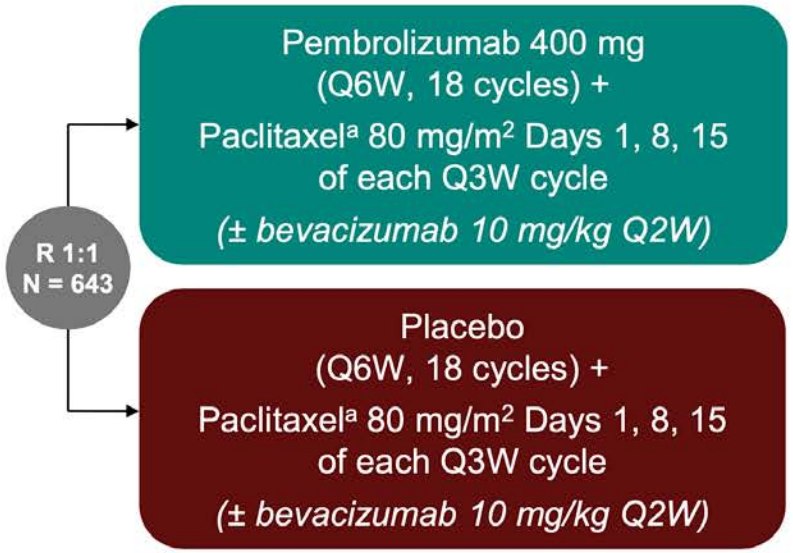
18 October 2025

University of Pittsburgh

ENGOT-ov65/KEYNOTE-B96 Study Design (NCT05116189)

Key Eligibility Criteria

- Histologically confirmed epithelial ovarian, fallopian tube, or primary peritoneal carcinoma
- 1 or 2 prior lines of therapy; at least 1 platinum-based chemotherapy
  - Prior anti-PD-1 or anti-PD-L1, PARPi and bevacizumab permitted
- Radiographic progression within 6 months after the last dose of platinum-based chemotherapy
- ECOG PS 0 or 1



Stratification Factors

- Planned bevacizumab use (yes vs no)
- Region (US vs EU vs ROW)
- PD-L1 CPS (<1 vs 1 to <10 vs ≥10)[b]

Primary Endpoint: PFS per RECIST v1.1 by investigator

Key Secondary: OS

[a]Docetaxel (75 mg/m² Q3W) may be considered in participants with severe hypersensitivity reaction to paclitaxel or an adverse event requiring discontinuation of paclitaxel after consultation with the Sponsor. [b]The combined positive score (CPS) was assessed at a central laboratory using PD-L1 IHC 22C3 pharmDx and defined as the number of PD-L1 CPS ≥1 cells (tumor cells, lymphocytes, macrophages) divided by the total number of tumor cells × 100.

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Colombo N et al. ESMO 2025. LBA3

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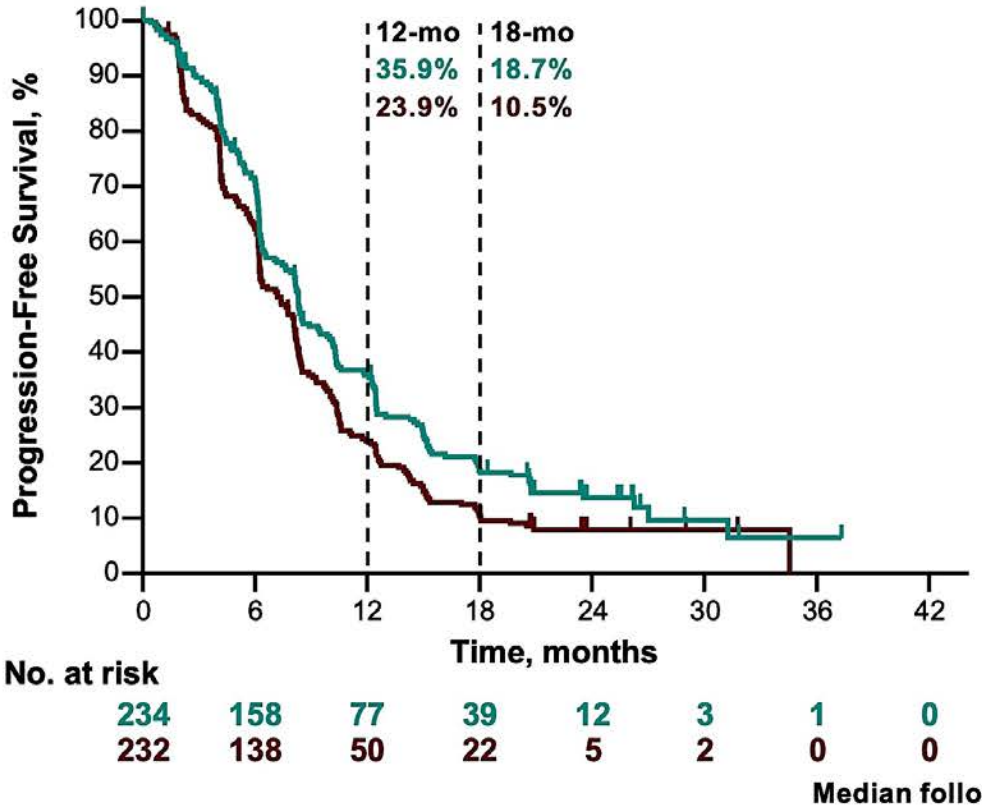
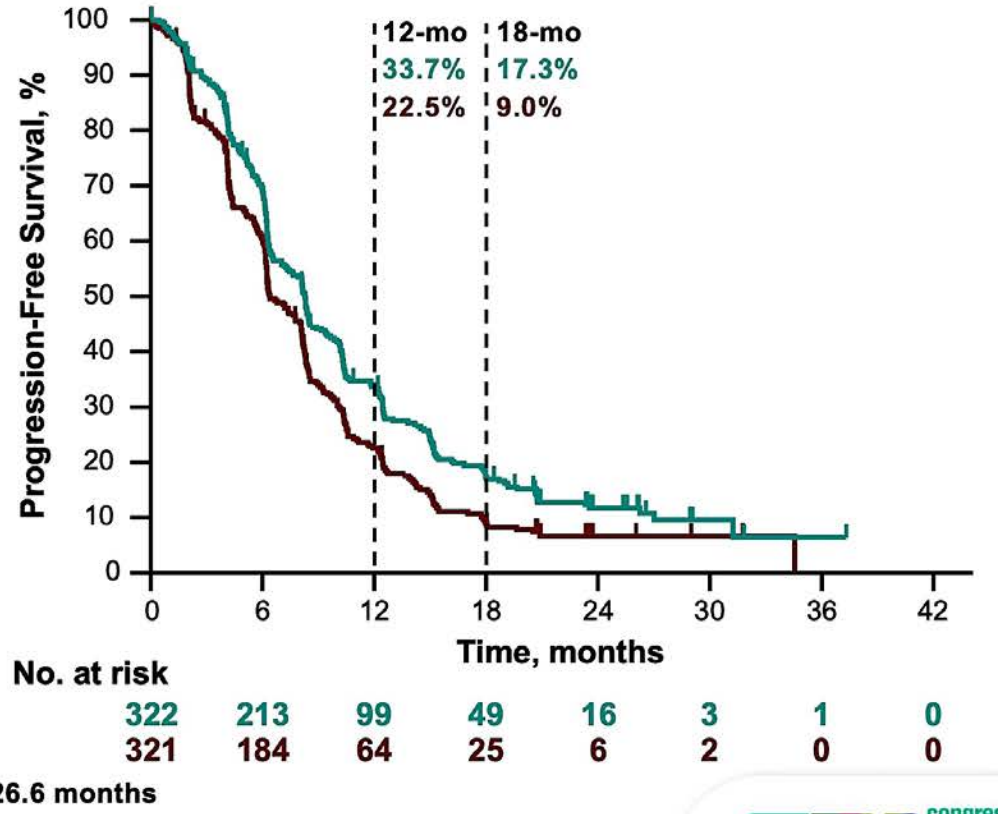
Progression-Free Survival in the CPS ≥1 and ITT Populations at IA2*

CPS ≥1 Population	Median, months	Events	HR (95% CI)
Pembro Arm	8.3	81.6%	0.75[a] (0.61-0.91)
Placebo Arm	7.2	86.6%	



ITT Population	Median, months	Events	HR (95% CI)
Pembro Arm	8.3	83.2%	0.73[a] (0.62-0.86)
Placebo Arm	6.4	87.2%	



Median follow-up: 26.6 months

Response assessed per RECIST v1.1 by investigator review. [a]Hazard ratio (CI) analyzed based on a Cox regression model with treatment as a covariate stratified by the randomization stratification factors. No statistical testing for PFS was done at this analysis because significance was achieved at IA1. Data cutoff date: March 5, 2025.

*IA2 = interim analysis 2

Colombo N et al. ESMO 2025. LBA3

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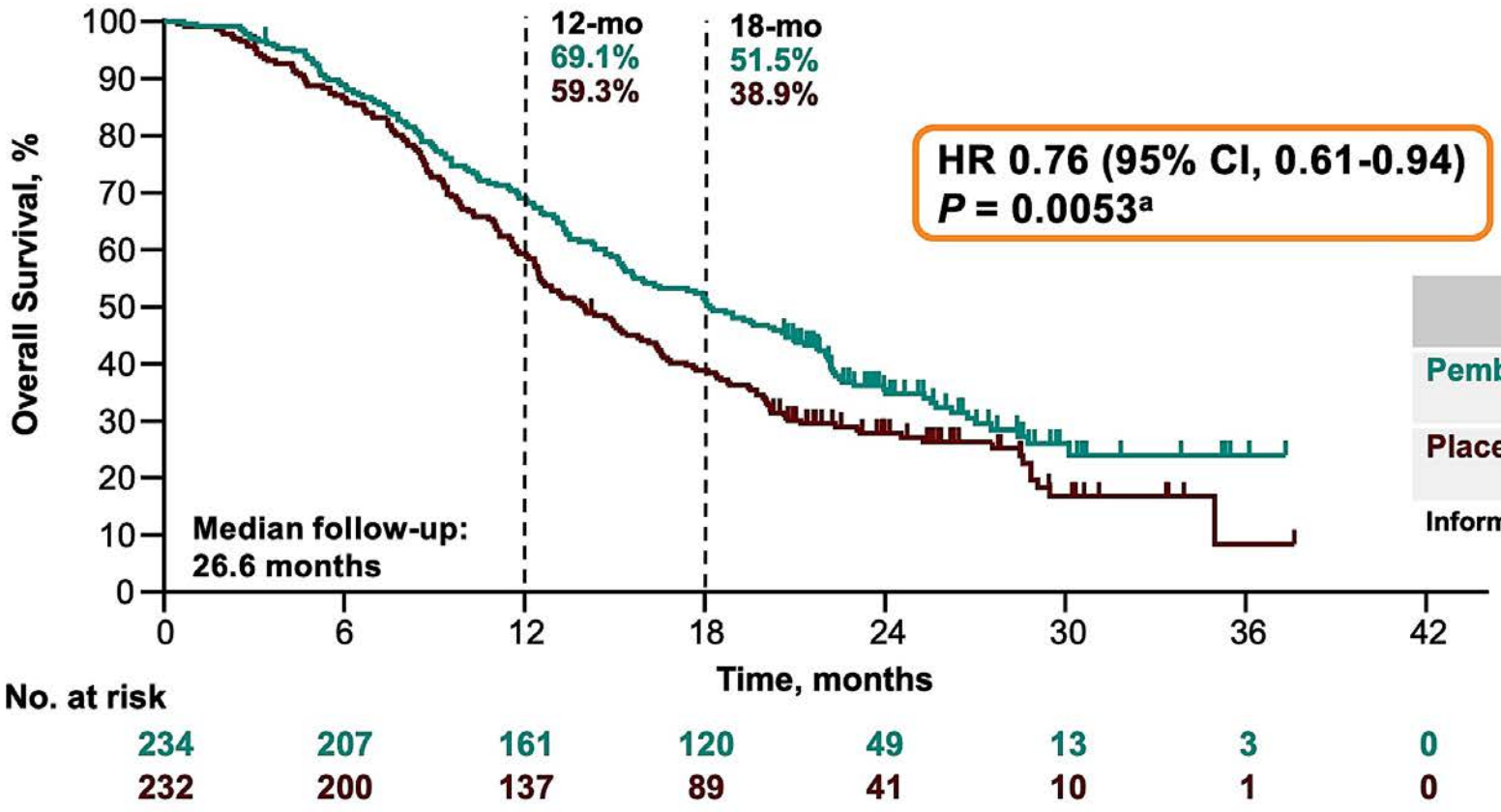
Key Secondary Endpoint: Overall Survival in the CPS ≥1 Population at IA2*



HR 0.76 (95% CI, 0.61-0.94)
***P* = 0.0053[a]**

	Pts w/ Event	Median, mo (95% CI)
Pembro Arm	67.1%	18.2 (15.3-21.0)
Placebo Arm	75.4%	14.0 (12.5-16.1)

Information fraction: 90.0%

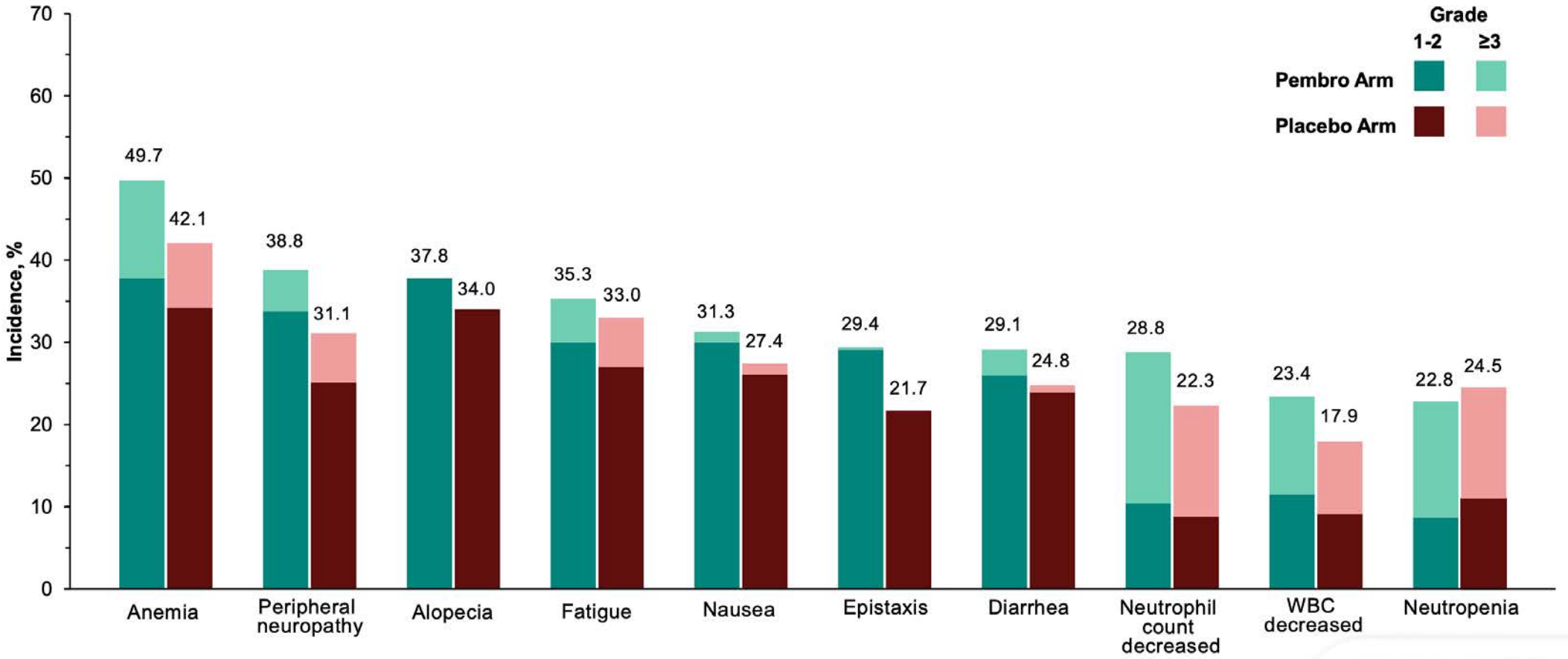
[a]Hazard ratio (CI) analyzed based on a Cox regression model with treatment as a covariate stratified by the randomization stratification factors. The observed p-value crossed the prespecified nominal boundary of 0.0083 at this planned second interim analysis. Data cutoff date: March 5, 2025.

*IA2 = interim analysis 2

Colombo N et al. ESMO 2025. LBA3

University of Pittsburgh

Treatment-Related Adverse Events at IA2*, Incidence ≥20% in Either Arm



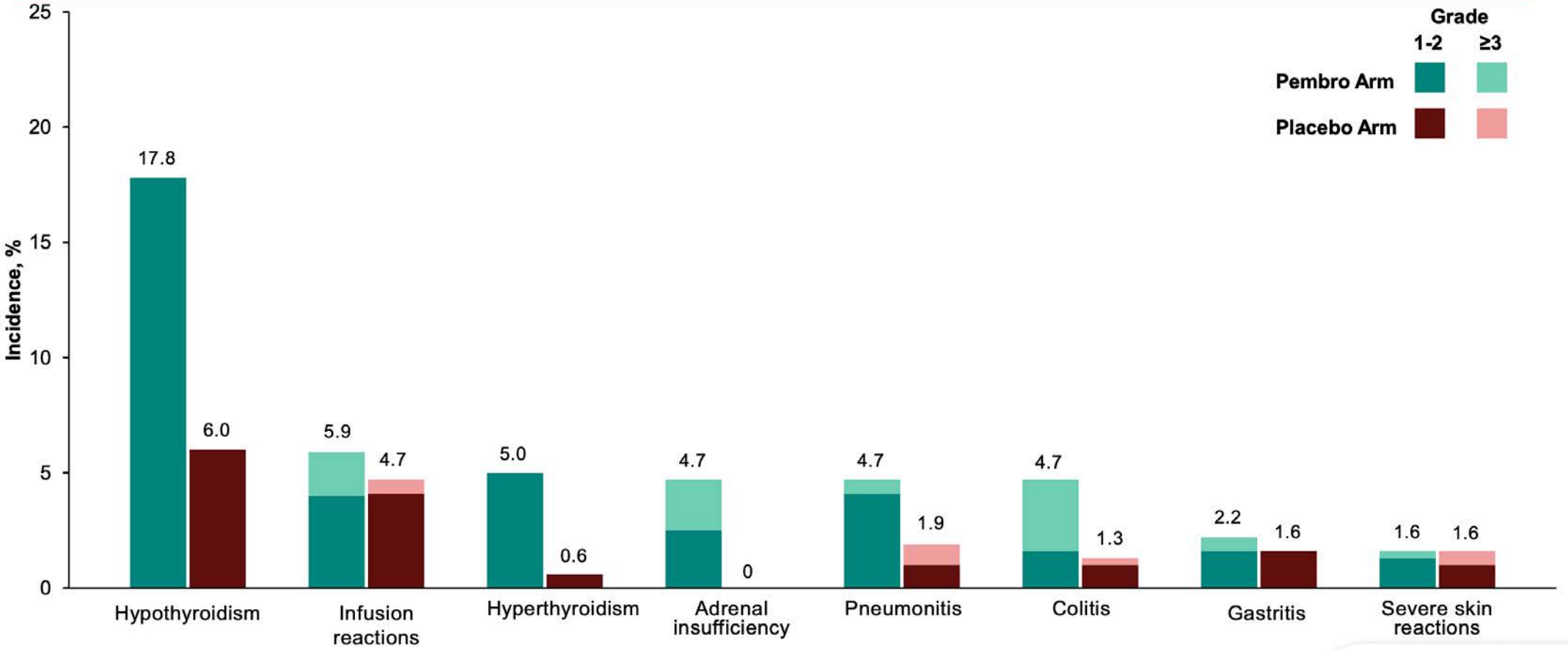
Data cutoff date: March 5, 2025.

*IA2 = interim analysis 2

Colombo N et al. ESMO 2025. LBA3

University of Pittsburgh

Immune-Mediated Adverse Events and Infusion Reactions at IA2*; Incidence ≥5 Participants in Either Arm



Events were based on a list of preferred terms intended to capture the known risks of pembrolizumab and considered regardless of attribution to treatment by the investigator.
Data cutoff date: March 5, 2025.

*IA2 = interim analysis 2

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Colombo N et al. ESMO 2025. LBA3

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FDA approves pembrolizumab with paclitaxel for platinum-resistant epithelial ovarian, fallopian tube, or primary peritoneal carcinoma

"On February 10, 2026, the Food and Drug Administration approved pembrolizumab as well as pembrolizumab and berahyaluronidase alfa-pmph in combination with paclitaxel, with or without bevacizumab, for adult patients with platinum-resistant epithelial ovarian, fallopian tube, or primary peritoneal carcinoma whose tumors express PD-L1 (CPS≥1) as determined by an FDA-authorized test, and who have received one or two prior systemic treatment regimens.

…Efficacy was evaluated in KEYNOTE-B96 (NCT05116189), a multicenter, randomized, double-blind, placebo-controlled trial that enrolled 643 patients with platinum-resistant, epithelial ovarian, fallopian tube, or primary peritoneal carcinoma who received one or two prior lines of systemic therapy for ovarian carcinoma."

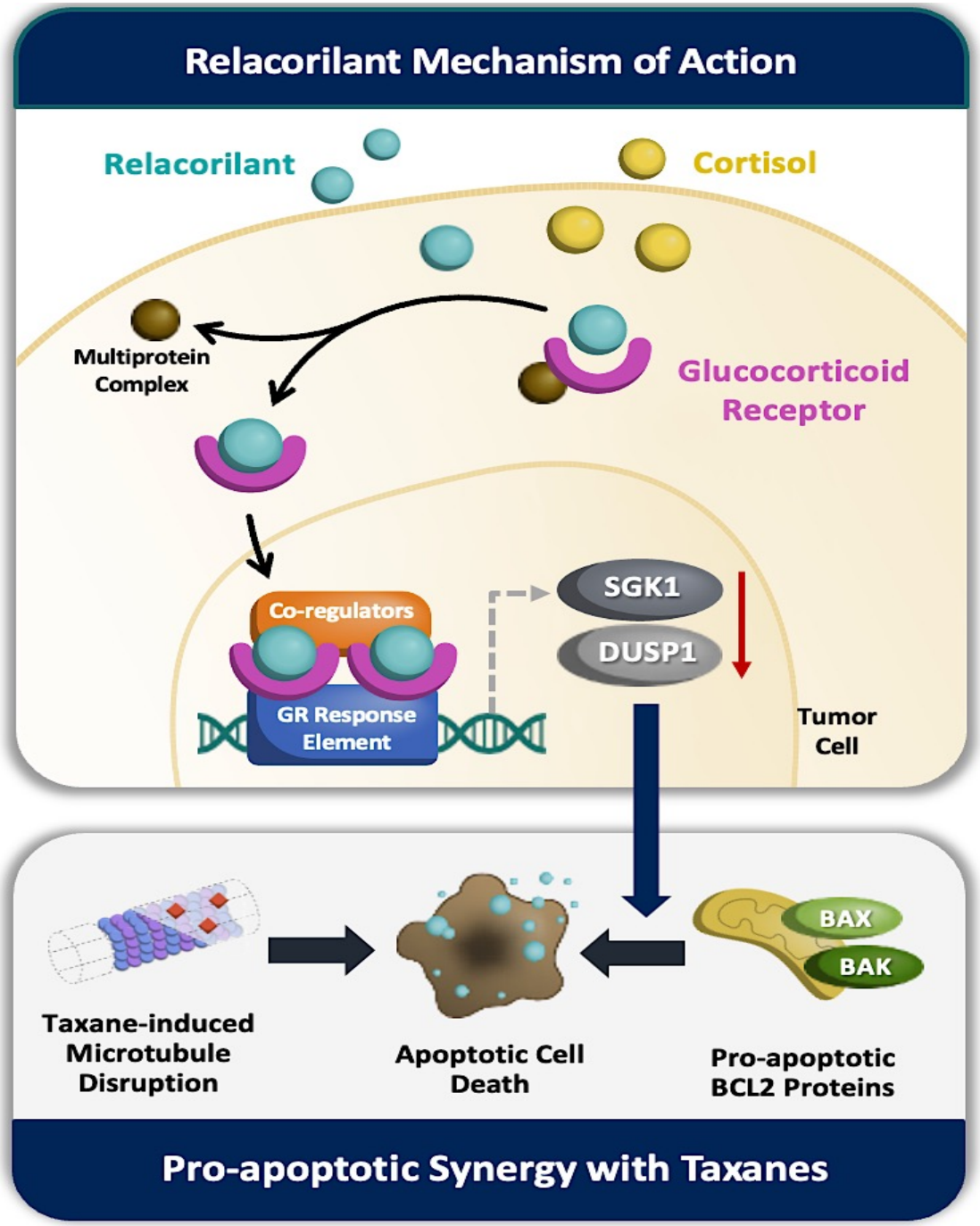
https://www.fda.gov/drugs/resources-information-approved-drugs/fda-approves-pembrolizumab-paclitaxel-platinum-resistant-epithelial-ovarian-fallopian-tube-or

Relacorilant and nab-paclitaxel in patients with platinum-resistant ovarian cancer (ROSELLA): an open-label, randomised, controlled, phase 3 trial

Alexander B Olawaiye, Laurence Gladieff, David M O'Malley, Jae-Weon Kim, Gabriel Garbaos, Vanda Salutari, Lucy Gilbert, Linda Mileshkin, Alix Devaux, Elizabeth Hopp, Yong Jae Lee, Ana Oaknin, Mariana Scaranti, Byoung-Gie Kim, Nicoletta Colombo, Michael E McCollum, Connie Diakos, Andrew Clamp, Aliza L Leiser, Boglárka Balázs, Bradley J Monk, Giuseppa Scandurra, Emily McClung, Emilie Kaczmarek, Brian Slomovitz, Helena De La Cueva, Aknar Freire de Carvalho Calabrich, Chiara Cassani, Benoit You, Toon Van Gorp, Cristina Churruca, Giuseppe Caruso, Shibani Nicum, Andrea Bagaméri, Grazia Artioli, Lubomir Bodnar, Sokbom Kang, Ignace Vergote, Amanda Kesner-Hays, Hristina I Pashova, Sachin G Pai, Iulia Cristina Tudor, Adrian M Jubb, Domenica Lorusso

Olawaiye A et al. Lancet. 2025;405(10496):P2205-2216

University of Pittsburgh



Olawaiye A et al. ASCO 2025

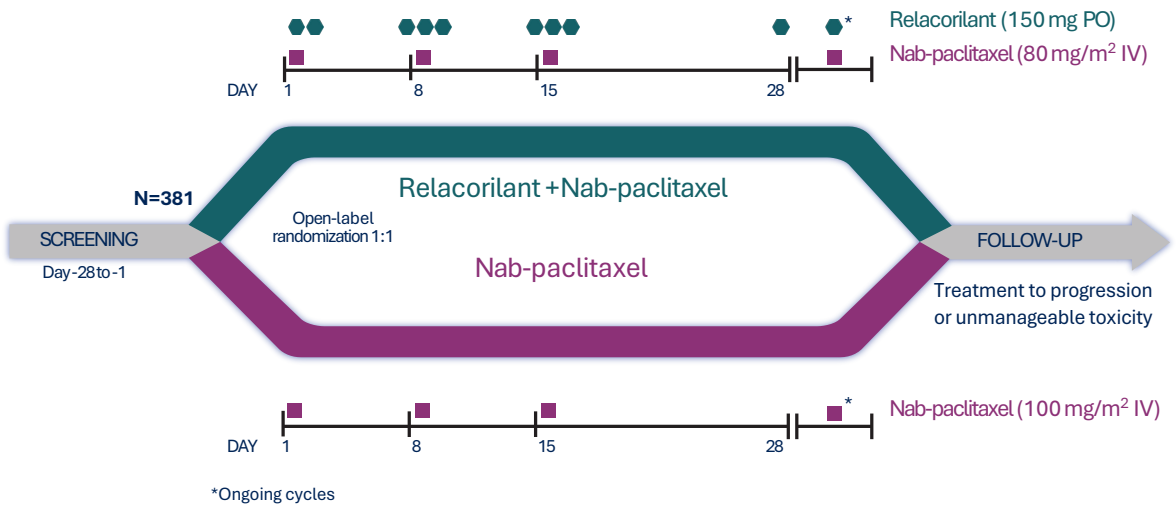
University of Pittsburgh

ROSELLA | Study Schema

Population

- Epithelial ovarian, primary peritoneal or fallopian tube cancer
- ECOG performance status 0 or 1
- Progression <6 months after the last dose of platinum therapy (excluding no response to, or progression in <1 month of primary platinum)
- 1–3 prior lines of therapy
- Prior bevacizumab required

NCT05257408



Stratification Factors

- Prior lines of therapy (1 vs >1)
- Region (North America vs Europe vs Korea, Australia, & Latin America)

Dual Primary Endpoints

- Progression-free survival (PFS) by RECIST v1.1 per blinded independent central review
- Overall survival

Secondary Endpoints

- PFS by RECIST v1.1 per Investigator
- ORR, DoR, CBR (RECIST v1.1)
- Response by CA-125 GCIG criteria
- Combined response (RECIST v1.1 and CA-125 GCIG criteria)
- Safety

First patient enrolled: 5th January 2023
Last patient enrolled: 8th April 2024
Data cutoff: 24th February 2025
Conducted at 117 sites in 14 countries.

CA, cancer antigen; CBR, clinical benefit rate; DoR, duration of response; ECOG, Eastern Cooperative Oncology Group; GCIG, Gynecologic Cancer Intergroup; IV, intravenous; ORR, objective response rate; PFS, progression-free survival; PO, by mouth; RECIST, Response Evaluation Criteria in Solid Tumors.

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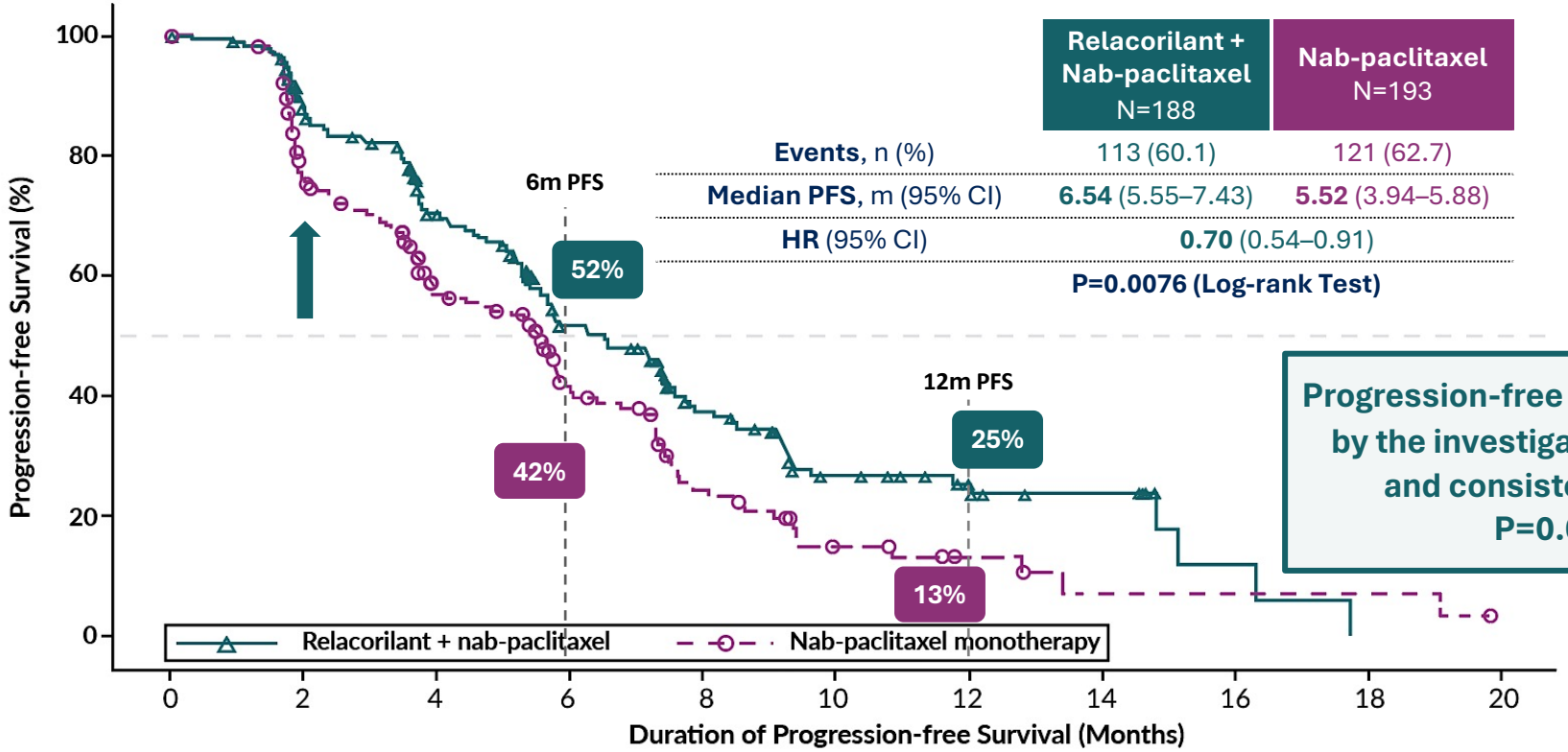
Olawaiye A et al. ASCO 2025

ROSELLA | Relacorilant Significantly Improved Progression-Free Survival Assessed by Blinded Review



	Relacorilant + Nab-paclitaxel N=188	Nab-paclitaxel N=193
Events, n (%)	113 (60.1)	121 (62.7)
Median PFS, m (95% CI)	**6.54** (5.55–7.43)	**5.52** (3.94–5.88)
HR (95% CI)	**0.70** (0.54–0.91)	
	P=0.0076 (Log-rank Test)	

Progression-free survival assessed by the investigator was positive and consistent (HR 0.71, P=0.0030)

No. at risk (events/cumulative events)

Relacorilant + nab-paclitaxel	188 (0/0)	151 (22/22)	109 (29/51)	70 (27/78)	43 (18/96)	24 (11/107)	16 (1/108)	11 (1/109)	2 (2/111)	0 (2/113)	
Nab-paclitaxel monotherapy	193 (0/0)	129 (42/42)	85 (31/73)	47 (20/93)	21 (17/110)	9 (7/117)	5 (1/118)	2 (2/120)	2 (0/120)	2 (0/120)	0 (1/121)

Median follow-up time: 9.0 months; statistical significance threshold: P≤0.04. The Kaplan–Meier method was used to estimate the curves, median estimates and the 95% CIs for progression-free survival in each treatment arm. The HR and the associated 95% CI were estimated using a Cox regression model with treatment group as the main effect and stratification factors at randomization as covariates.
BICR, blinded-independent central review; CI, confidence interval; HR, hazard ratio; m, months; PFS, progression-free survival.

Olawaiye A et al. ASCO 2025

Data cutoff: Feb 24, 2025

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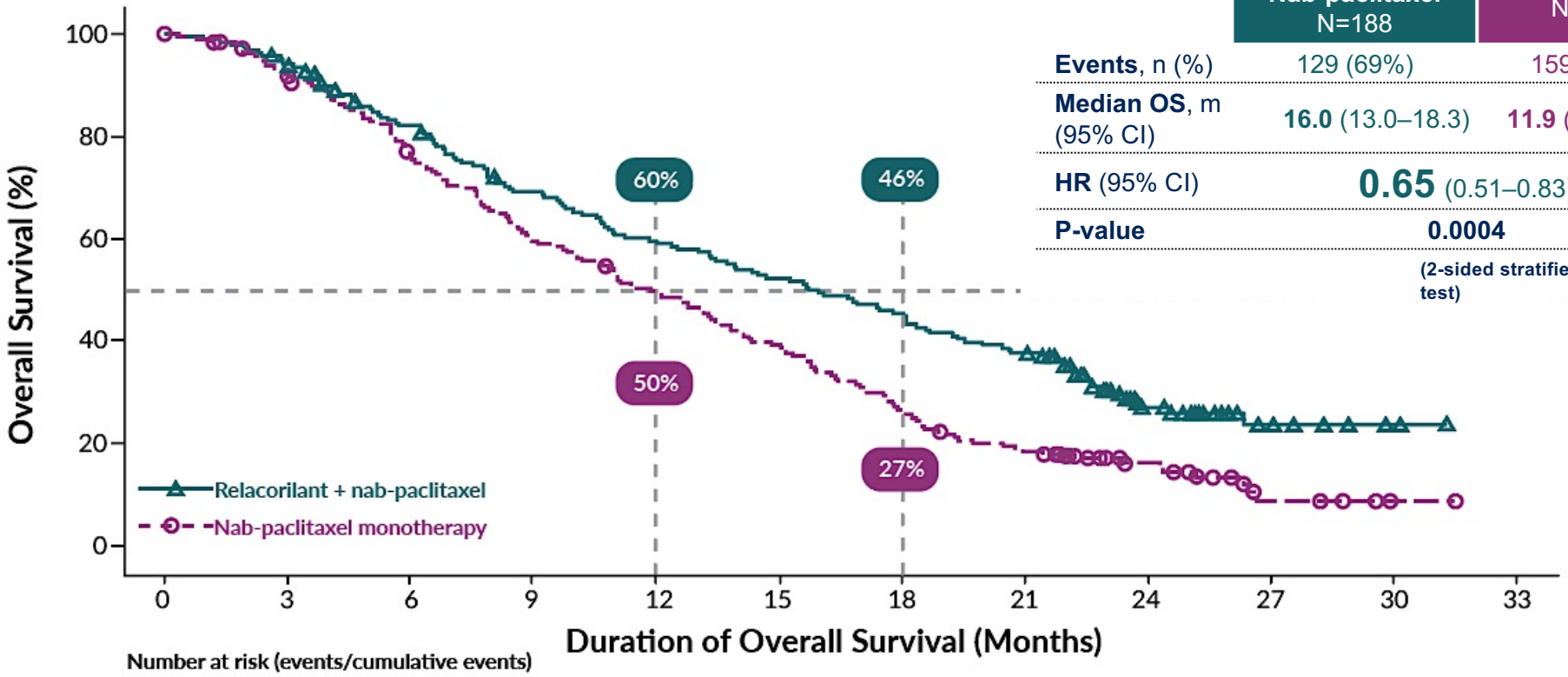
ROSELLA | Relacorilant Significantly Improved Overall Survival at the Final Analysis



	Relacorilant + Nab-paclitaxel N=188	Nab-paclitaxel N=193
Events, n (%)	129 (69%)	159 (82%)
Median OS, m (95% CI)	**16.0** (13.0–18.3)	**11.9** (10.0–13.8)
HR (95% CI)	**0.65** (0.51–0.83)	
P-value	**0.0004** (2-sided stratified log-rank test)	

76% maturity

Number at risk (events/cumulative events)

Relacorilant + nab-paclitaxel	188 (0/0)	176 (11/11)	148 (22/33)	123 (23/56)	106 (17/73)	93 (13/86)	81 (12/98)	67 (14/112)	28 (15/127)	10 (2/129)	3 (0/129)	0 (0/129)
Nab-paclitaxel monotherapy	193 (0/0)	173 (15/15)	142 (28/43)	110 (32/75)	91 (18/93)	72 (19/112)	49 (23/135)	33 (15/150)	18 (3/153)	5 (6/159)	1 (0/159)	0 (0/159)

Median follow-up time: 24.8 months; statistical significance threshold at the final analysis: P≤0.0499. The Kaplan–Meier method was used to estimate the curves, median estimates and the 95% CIs for OS in each treatment arm. The HR and the associated 95% CI were estimated using a Cox regression model with treatment group as the main effect and stratification factors at randomization as covariates.
CI, confidence interval; HR, hazard ratio; m, months; OS, overall survival.

Olawaiye A et al. SGO 2026

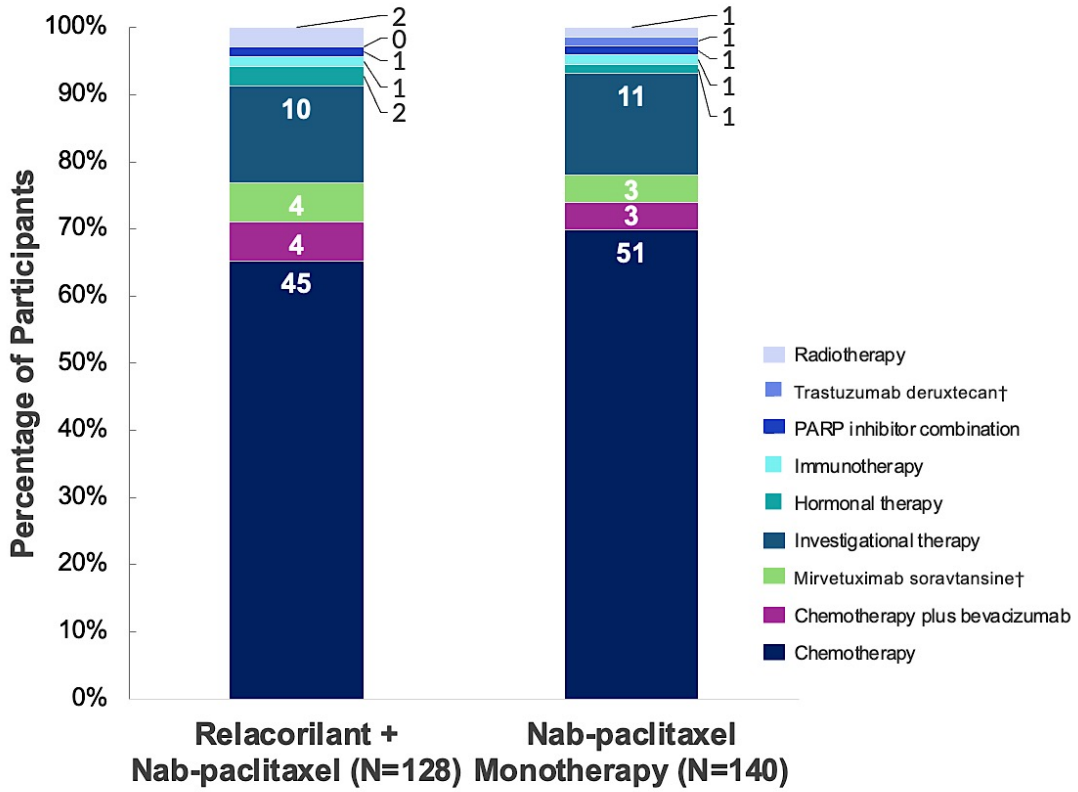
Data cutoff: Jan 8, 2026

University of Pittsburgh

ROSELLA | First and All Subsequent Therapies Were Well Balanced

SGO ANNUAL MEETING ON WOMEN'S CANCER
SAN JUAN, PR
APRIL 10-13, 2026

First Subsequent Anticancer Therapies*



All Subsequent Systemic Anticancer Therapies

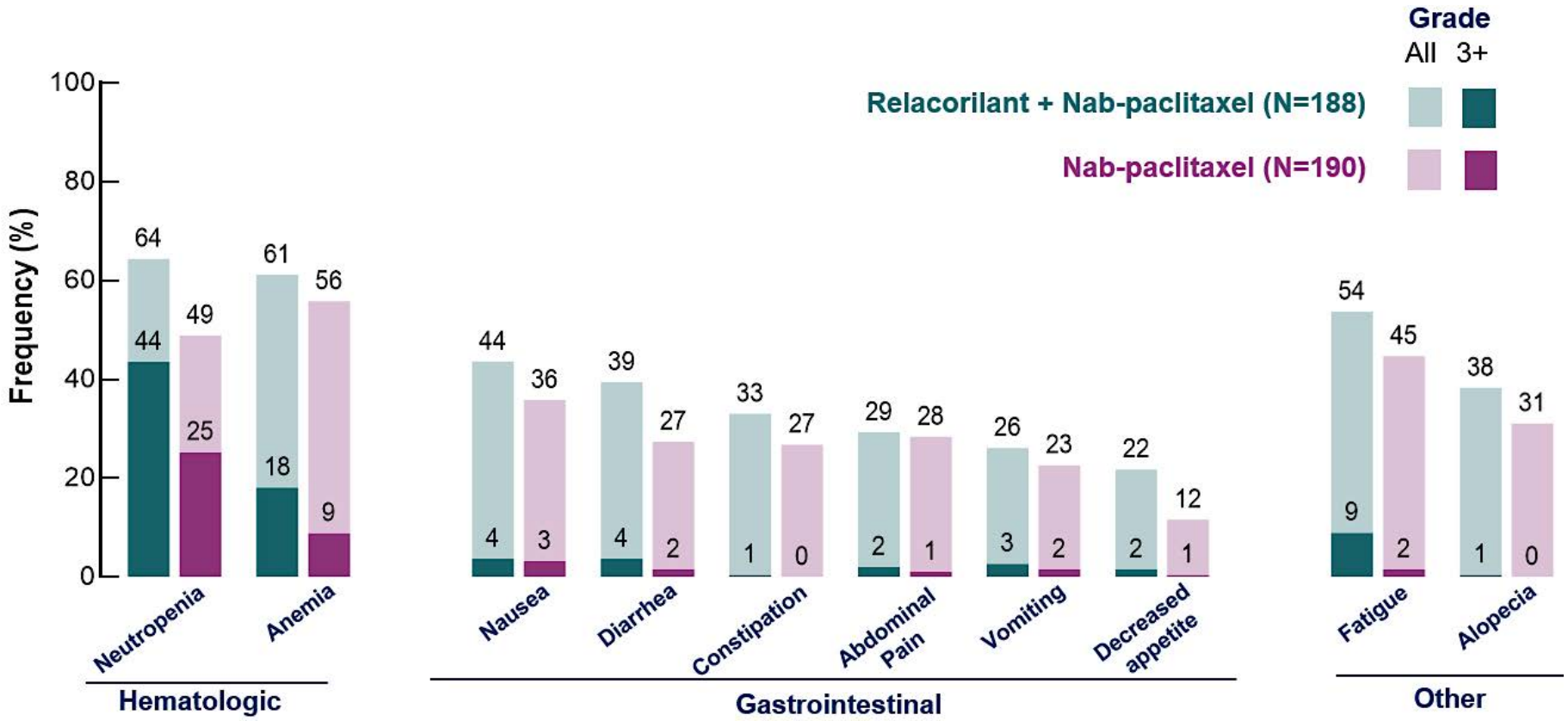
	Relacorilant + Nab-paclitaxel (N=188)	Nab-paclitaxel Monotherapy (N=193)
Patients Receiving Subsequent Systemic Anticancer Therapies, n (%)	127 (67.6)	139 (72.0)
Gemcitabine	66 (35.1)	62 (32.1)
Pegylated Liposomal Doxorubicin	44 (23.4)	40 (20.7)
Investigational Antineoplastic Drugs	27 (14.4)	29 (15.0)
Carboplatin	28 (14.9)	25 (13.0)
Cyclophosphamide	26 (13.8)	23 (11.9)
Topotecan	18 (9.6)	25 (13.0)
Paclitaxel	18 (9.6)	21 (10.9)
Bevacizumab	17 (9.0)	12 (6.2)
Cisplatin	15 (8.0)	8 (4.1)
Mirvetuximab Soravtansine	12 (6.4)	11 (5.7)

*Shown is the first subsequent therapy received by patients who discontinued their assigned trial treatment and received subsequent therapy. Chemotherapy in the first subsequent regimen included both monotherapy and combination regimens. †Monotherapy or combination therapy.
PARP, poly(ADP-ribose) polymerase.

Data cutoff: Jan 8, 2026

University of Pittsburgh

ROSELLA | Common (>20%) Adverse Events



When adjusted for duration of exposure, the incidence rates of neutropenia and anemia were similar between study arms.

Peripheral neuropathy occurred with similar frequency in both arms (19.1% and 17.4%).

5 SAEs of febrile neutropenia: 4 (2.1%) vs 1 (0.5%).* 5 SAEs of sepsis: 3 (1.6%) vs 2 (1.1%).*

Treatment-emergent adverse events that occurred in >20% of patients. Assessed in the safety population of patients who received at least one dose of study drug, N=378. Combined terms are presented for neutropenia (neutropenia, reduced neutrophil count, and febrile neutropenia), anemia (anemia, reduced hemoglobin, and reduced red blood cell count) and fatigue (fatigue and asthenia). SAEs, serious adverse events. *Comparing the relacorilant combination arm to the nab-paclitaxel monotherapy arm, respectively.

FDA approves relacorilant with nab-paclitaxel for platinum-resistant epithelial ovarian, fallopian tube, or primary peritoneal cancer

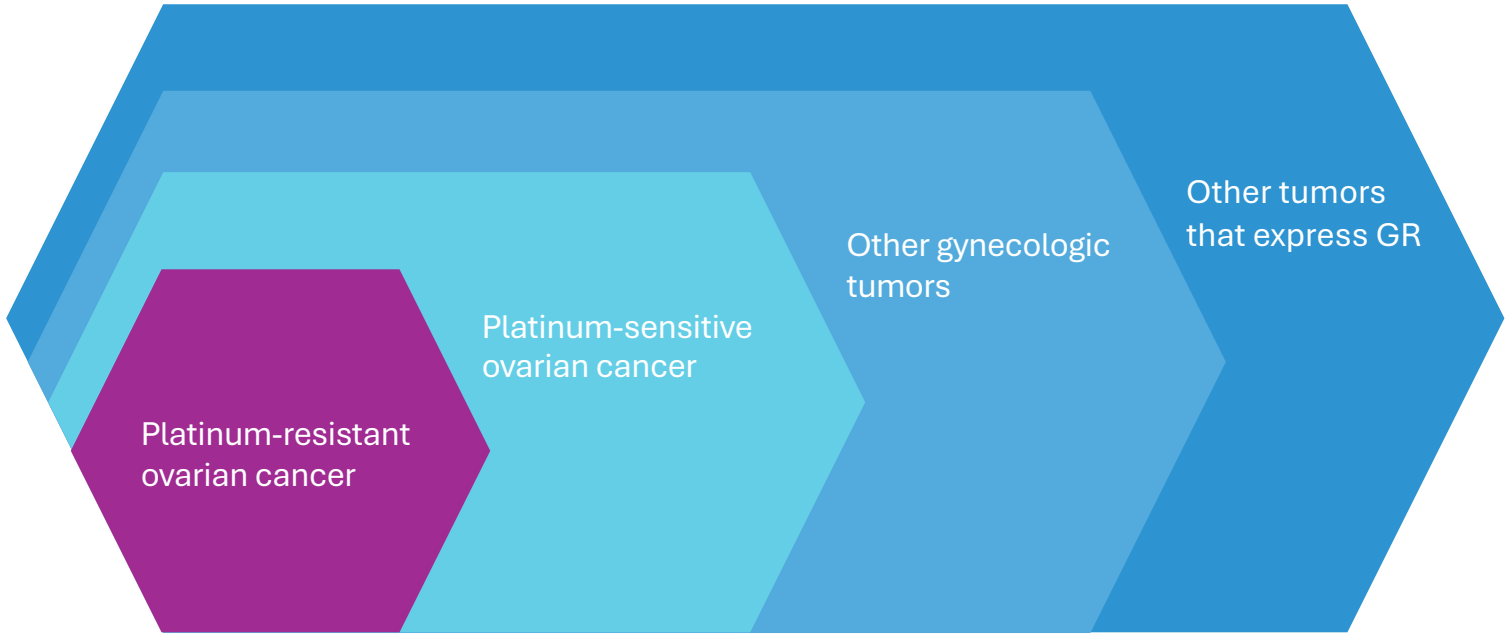
"On March 25, 2026, the Food and Drug Administration approved relacorilant, a glucocorticoid receptor antagonist, in combination with nab-paclitaxel for the treatment of adults with platinum-resistant epithelial ovarian, fallopian tube, or primary peritoneal cancer who have received one to three prior systemic treatment regimens, at least one of which included bevacizumab.

...Efficacy was evaluated in ROSELLA (NCT05257408), a multicenter, open-label, trial in 381 patients with platinum-resistant epithelial ovarian, fallopian tube, or primary peritoneal cancer."

https://www.fda.gov/drugs/resources-information-approved-drugs/fda-approves-relacorilant-nab-paclitaxel-platinum-resistant-epithelial-ovarian-fallopian-tube-or

ROSELLA Results: Support Additional Studies in Combination with Any Cancer Therapy

- **Potential to treat all tumors that express the glucocorticoid receptor**
- **Potential to combine with any chemotherapy**



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Relacorilant in Combination With Chemotherapy: BELLA Arm A Phase 2 Trial in Platinum-Resistant Ovarian Cancer (PROC)

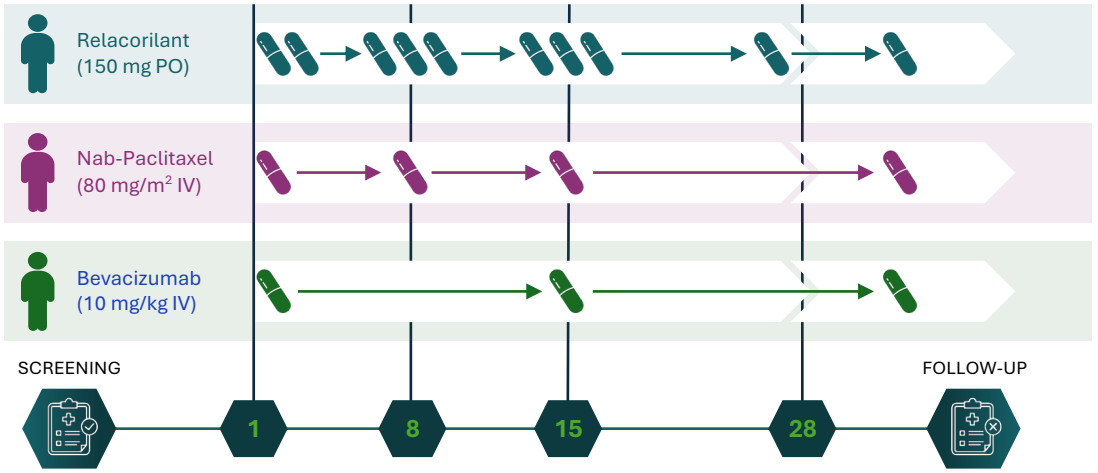
Population

90 patients

- Epithelial ovarian, primary peritoneal, or fallopian tube cancer
- Progression <6 months after the last dose of platinum therapy
- ECOG performance status 0 or 1
- 1 to 3 prior lines of therapy
- Suitable for bevacizumab
- Eligible irrespective of prior bevacizumab

Conducted at 45 sites in the US, EU and Korea

BELLA



Primary Endpoint

- Progression-free survival

Secondary Endpoints

- Overall survival
- ORR, DoR, BOR, CBR
- Safety

~20,000 addressable patients per year in the US[1]

Results expected by year-end 2026

- [1]Decision Resources Group.
- BOR, best overall response; CBR, clinical benefit rate; DoR, duration of response; ECOG, Eastern Cooperative Oncology Group; EU, European Union; IV, intravenous; ORR, objective response rate; PO, by mouth; US, United States.

https://clinicaltrials.gov/study/NCT06906341. Accessed April 2026

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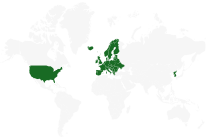
Relacorilant in Combination With Chemotherapy: BELLA Arm B Phase 2 Trial in Platinum-Sensitive Ovarian Cancer (PSOC)

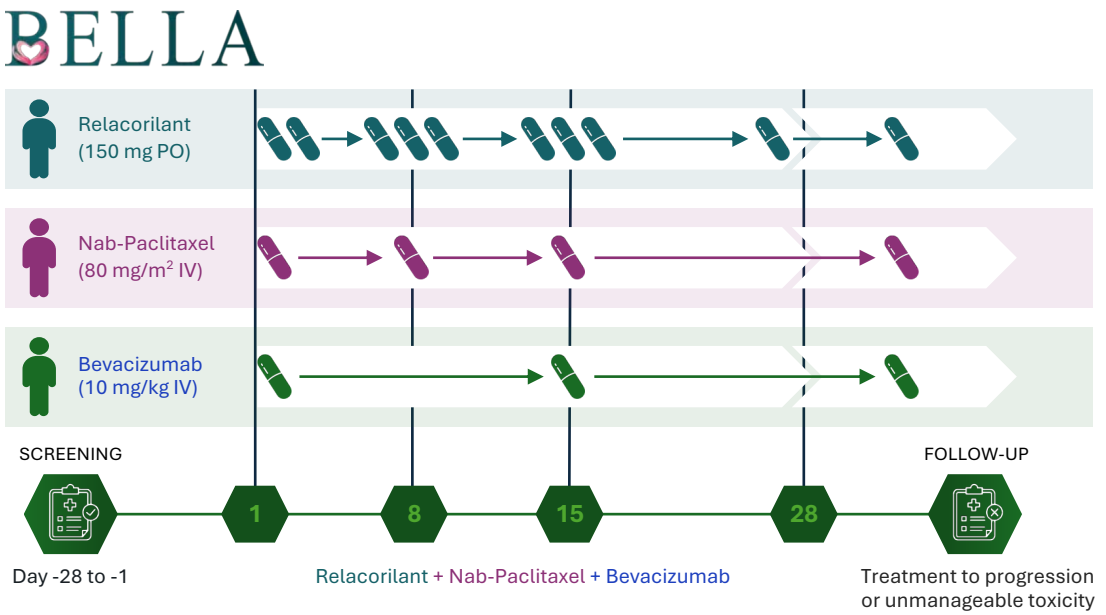
Population

90 patients

- Epithelial ovarian, primary peritoneal, or fallopian tube cancer
- **Platinum-sensitive ovarian cancer with progression while on a PARP inhibitor**
- ECOG performance status 0 or 1
- 1 to 3 prior lines of therapy
- Suitable for bevacizumab



Conducted at 45 sites in the US, EU and Korea



Primary Endpoint

- Progression-free survival

Secondary Endpoints

- Overall survival
- ORR, DoR, BOR, CBR
- Safety

~13,000 addressable patients per year in the US[1]

To begin in coming weeks

- [1]Decision Resources Group.
- BOR, best overall response; CBR, clinical benefit rate; DoR, duration of response; ECOG, Eastern Cooperative Oncology Group; EU, European Union; IV, intravenous; ORR, objective response rate; PARP, poly(adensosine diphosphate-ribose) polymerase; PO, by mouth; US, United States.

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https://clinicaltrials.gov/study/NCT06906341. Accessed April 2026

Conclusions:

- Progress made in the last decade surpasses what was achieved in the previous 4 decades.
- Better understanding re: biology of ovarian cancer
- Expanded systemic therapy options
- Key advances in targeted therapy options
- Immediate future looks promising for our patients

University of Pittsburgh

Second Opinion

Angeles Alvarez Secord, MD, MHSc

Neil Love, MD

RTP
RESEARCH
TO PRACTICE

QUESTIONS FOR THE FACULTY

Now that both are available, how are you sequencing relacorilant/*nab* paclitaxel and pembrolizumab/chemotherapy relative to each other and targeted antibody-drug conjugates (eg, mirvetuximab soravtansine, trastuzumab deruxtecan) for patients eligible to receive those agents?

What has been your experience in terms of the efficacy relacorilant/*nab* paclitaxel? Is there any correlation between the efficacy of relacorilant/*nab* paclitaxel and glucocorticoid receptor (GR) expression levels, and would you use GR expression levels to inform how you sequence this regimen?

QUESTIONS FOR THE FACULTY

How do you approach monitoring of CBCs for patients receiving relacorilant/*nab* paclitaxel? How do you manage neutropenia based on grade?

How do you monitor for adrenal insufficiency in patients receiving relacorilant/*nab* paclitaxel, and what is your threshold for administering glucocorticoid therapy? Do you administer supplemental glucocorticoids for patients who need to undergo surgical procedures? How do you think through the potential use of relacorilant/*nab* paclitaxel for patients who are taking systemic glucocorticoids for other conditions (eg, autoimmune disorders)?

QUESTIONS FOR THE FACULTY

Would you employ relacorilant in combination with any other chemotherapeutic agent beyond *nab* paclitaxel? Do you believe the ROSELLA trial suggests that the use of corticosteroids as a means of preventing adverse events from chemotherapy may have a detrimental effect on tumor response and patient outcomes?

Do you believe that by using pembrolizumab/chemotherapy with or without bevacizumab, you are increasing the likelihood of long-term survival (cure?) in patients with advanced ovarian cancer? How do you decide whether to add bevacizumab or not when using this strategy?

QUESTIONS FOR THE FACULTY

Given the overall survival advantage documented in all comers in KEYNOTE-B96, would you employ pembrolizumab/chemotherapy with or without bevacizumab for a patient with PD-L1-negative disease under any circumstances?

What preexisting autoimmune conditions would cause you to withhold the use of immune checkpoint inhibition for patients with advanced ovarian cancer? Would you consider it for patients with a history of solid organ transplant?

QUESTIONS FOR THE FACULTY

Have you observed patients with MSI-high ovarian cancer?

How have you treated it, and what have you observed in terms of outcomes?

Second Opinion

Professor Jonathan A Ledermann

Neil Love, MD

RTP
RESEARCH
TO PRACTICE

QUESTIONS FOR THE FACULTY

Why do you theorize the KEYNOTE-B96 trial was positive when other immune checkpoint inhibitor studies in ovarian cancer have been less so? To what extent does the use of weekly paclitaxel have an impact?

How often do you encounter patients with ovarian cancer and brain metastases, and how do you manage these cases? What about leptomeningeal disease? What has been your experience in terms of outcomes with these patients?

QUESTIONS FOR THE FACULTY

What degree of CNS activity has been observed with the various systemic therapies available for ovarian cancer?

Agenda

Module 1: Current Role of PARP Inhibitors in Advanced Ovarian Cancer (OC) — Prof Colombo

Module 2: Strategies Targeting Folate Receptor Alpha in Advanced OC — Dr Westin

Module 3: Other Novel Agents and Strategies for Advanced OC — Dr Olawaiye

Module 4: Diagnosis and Management of Adverse Events Associated with Commonly Employed Therapies for Advanced OC — Dr Konecny

Diagnosis and Management of Adverse Events Associated with Commonly Employed Therapies for Advanced Ovarian Cancer

Gottfried E. Konecny M.D.
Professor of Medicine and Ob/Gyn
University of California Los Angeles

UCLA David Geffen School of Medicine

PARP Inhibitors in Ovarian Cancer 2021

	Phase				
BRCA mutated	III	SOLO-1 (olaparib)	SOLO-2 (olaparib)	ARIEL 4 (rucaparib v chemo) SOLO-3 (olaparib vs chemo)	
	II			ARIEL 2 (rucaparib)	
(*BRCAm or HRD)	III	PAOLA-1 (olaparib/bev*)		QUADRA (niraparib*)	QUADRA (niraparib*)
All Comers	III	PRIMA (niraparib) ATHENA-MONO (rucaparib)	Study 19 (olaparib) NOVA (niraparib) ARIEL3 (rucaparib)	AVANOVA2 (niraparib+/-bev)	
	II	OVARIO (niraparib/bev)			

PARP Inhibitors in Ovarian Cancer 2026

	Phase				
BRCA mutated	III	SOLO-1 (olaparib)	SOLO-2 (olaparib)	~~SOLO-3 (olaparib vs chemo)~~	~~ARIEL 4 (rucaparib v chemo)~~
	II			~~ARIEL 2 (rucaparib)~~	
(*BRCAm or HRD)	III	PAOLA-1 (olaparib/bev*)		~~QUADRA (niraparib)~~	~~QUADRA (niraparib)~~
All Comers	III	PRIMA (niraparib) ~~ATHENA-MONO (rucaparib)~~	~~Study 19 (olaparib)~~ ~~NOVA (niraparib)~~ ~~ARIEL3 (rucaparib)~~	~~AVANOVA2 (niraparib+/- bev)~~	
	II	~~OVARIO (niraparib/bev)~~			

PARP Inhibitor Toxicity Profile

Olaparib and Niraparib — Spectrum, Incidence & Severity

Olaparib | **Niraparib**

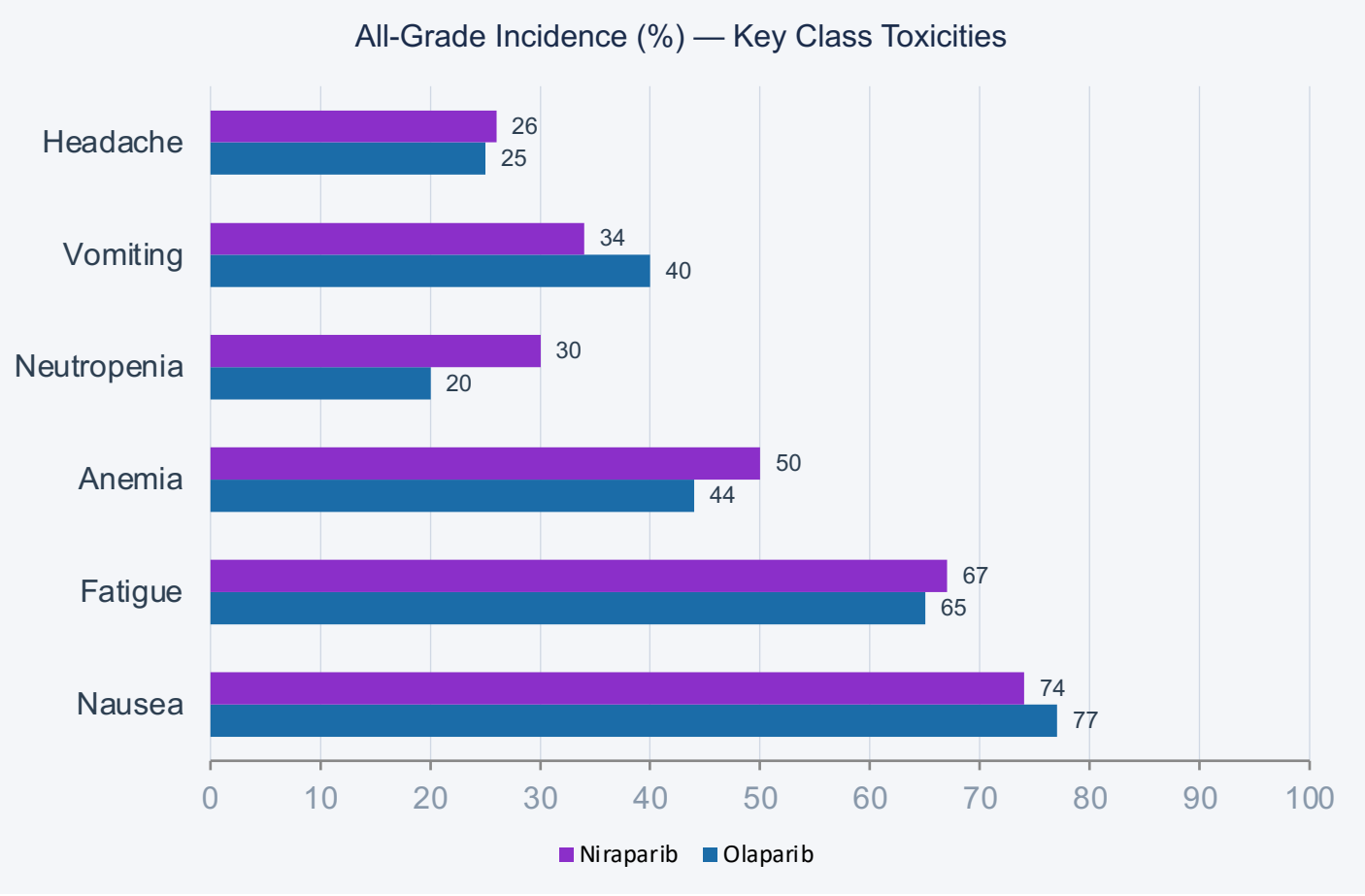
PARP inhibitors trap PARP-1/2 at DNA single-strand breaks, causing replication fork collapse. In BRCA1/2-deficient tumors, defective homologous recombination prevents repair → synthetic lethality.

Toxicity Categories

- **Hematologic** *Most common; dose-limiting*
- **GI / Nausea** *Class effect; manageable*
- **Fatigue** *Class effect; variable*
- **Agent-Specific** *Distinct per drug*
- **Rare / Serious** *MDS/AML, pneumonitis*

Class-Wide Toxicities

Shared adverse effects seen with both olaparib and niraparib



Nausea / Vomiting

G1-2: ~60-70% G3-4: <5%

Prophylactic antiemetics (ondansetron); take with food. Usually peaks in first weeks, attenuates over time.

Fatigue / Asthenia

G1-2: ~55-60% G3-4: 5-10%

Multifactorial. Rule out anemia. Activity pacing; dose reduction for G3.

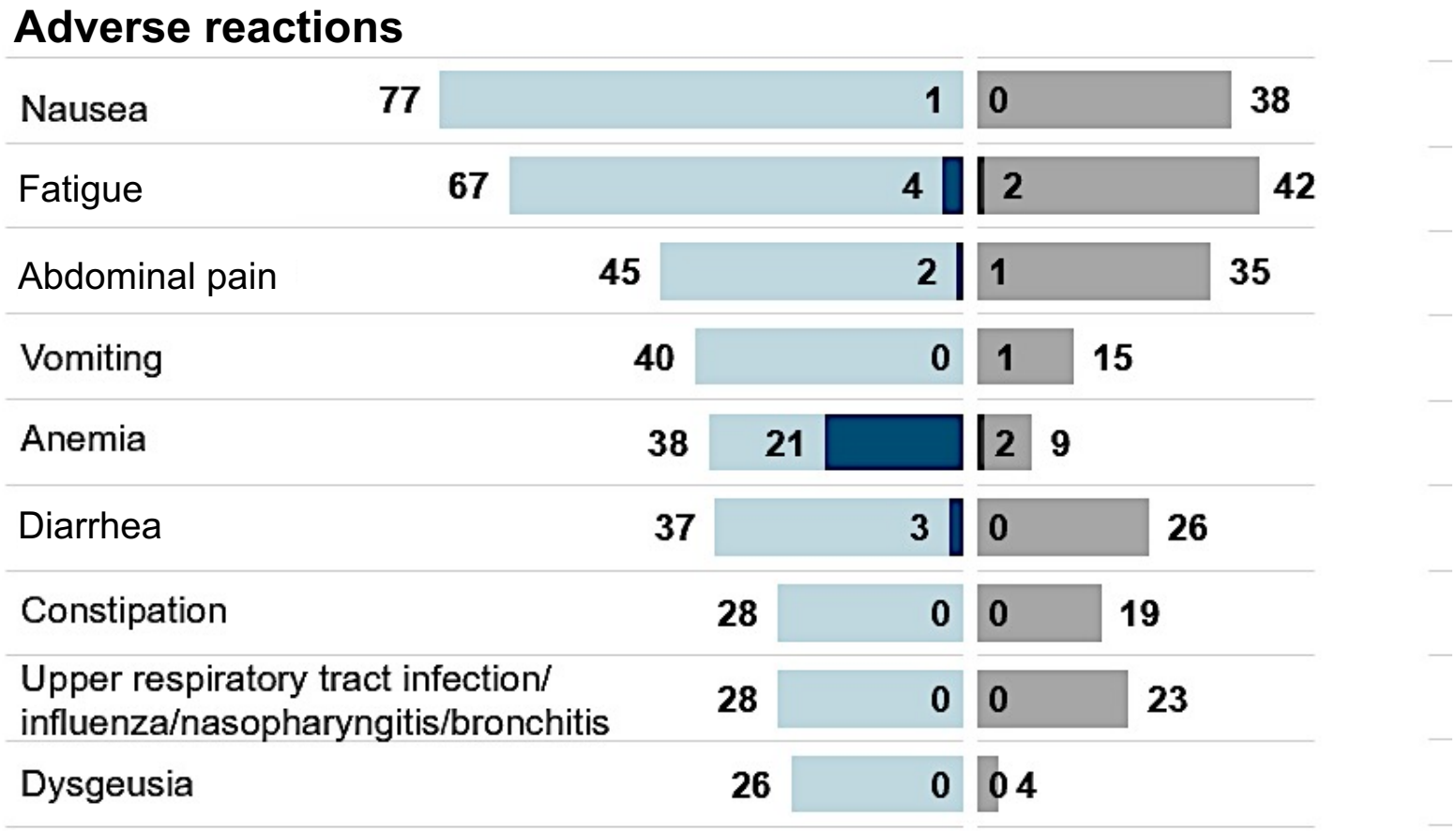
Anemia

G1-2: ~30-35% G3-4: 15-25%

Monitor CBC q4wks × 1yr then monthly. Transfusion or ESA support; hold/reduce for G3-4.

Source: SOLO-1, NOVA, PRIMA trials. Incidence values are approximate all-grade rates.

Adverse Reactions From the Primary Analysis in SOLO-1 Were Mostly Grades 1 and 2



Olaparib prescribing information. 2025.

Agent-Specific & Serious Toxicities

Distinguishing features and clinically important rare adverse events

Olaparib — Agent-Specific

Pneumonitis Rare; hold drug. CT chest. Corticosteroids if confirmed. Can be fatal.	~1%
Elevated Creatinine Non-progressive; monitor renal function. Mechanism unclear.	~20%
Headache Usually G1-2; analgesics PRN. Rarely requires dose modification.	~24%
MDS / AML Serious long-term risk. Monitor CBC; refer hematology if cytopenias persist >4 wks.	~1-1.5%
Embryo-fetal toxicity Teratogenic. Contraception required during + 6 months after treatment.	N/A

Niraparib — Agent-Specific

Thrombocytopenia Most common dose-limiting toxicity. Individualized start dose by weight/platelet count.	~61% (G3-4: ~29%)
Hypertension Monitor BP weekly × 1 month, then regularly. RAAS inhibitors preferred. Dose interrupt for uncontrolled.	~20% (G3: ~9%)
Insomnia / Anxiety Unique to niraparib; thought to relate to monoamine oxidase inhibition (off-target).	~25%
Palpitations / Tachycardia Monitor HR. Usually benign; ECG if sustained. Rarely requires discontinuation.	~10%
MDS / AML Class risk. CBC monitoring per protocol; persistent cytopenias trigger hematology referral.	~1%

MDS/AML in Ovarian Cancer PARPi Maintenance Trials

		PARPi		MDS/AML Events by arm	
Trial	Setting	Agent	Duration	PARPi, n (%)	Comparator, n (%)
SOLO1[4]	1L maint	Olaparib	2 years	3/260 (1.5)	1/130 (0.8)
PRIMA[6]	1L maint	Niraparib	3 years	1/484 (<1)	0/244
PAOLA1[5]	1L maint	Olaparib	2 years	6/535 (1)	1/267 (0.4)
ATHENA MONO[9]	1L maint	Rucaparib	2 years	2/425 (0.5)	0/110
Study19[8]	PS maint	Olaparib	18% >3yrs	2/136 (1.5)	1/129 (<1)
SOLO2[2]	PS maint	Olaparib	mean 29.1 mos	16/195 (8)	4/99 (4)
NOVA[3]	PS maint	Niraparib		13/367 (3.5)	3/179 (1.7)
gBRCAm				9/136 (6.6)	2/65 (3.1)
non-gBRCAm				4/231 (1.7)	1/114 (0.9)
ARIEL3[7]	PS maint	Rucaparib	median 8.3 mos	14/375 (3.8)	6/189 (3.2)
PARPi ≥24m[10]				9/79 (11.4)	
non-gBRCAm				5/245 (2.0)	1/123 (0.8)
gBRCAm				9/130 (6.9)	3/63 (4.8)
PARPi ≥24 mos				7/46 (15.2)	

[2]Poveda A, et al. Lancet Oncol 2021, [3]Matulonis U. et al. SGO 2021, [4]DiSilvestro P, et al. J Clin Oncol 2022, [5]Ray-Coquard I et al. NEJM Dec 2019, [6]Gonzalez-Martin A et al. NEJM 2019, [7]Coleman RL et al. IGCS 2022, [8]Lederman J et al. Lancet 2016 17: 1579-89, [9]Monk B et al. J Clin Oncol 2022, [10]O'Malley et al. Gyn Onc 10/2022

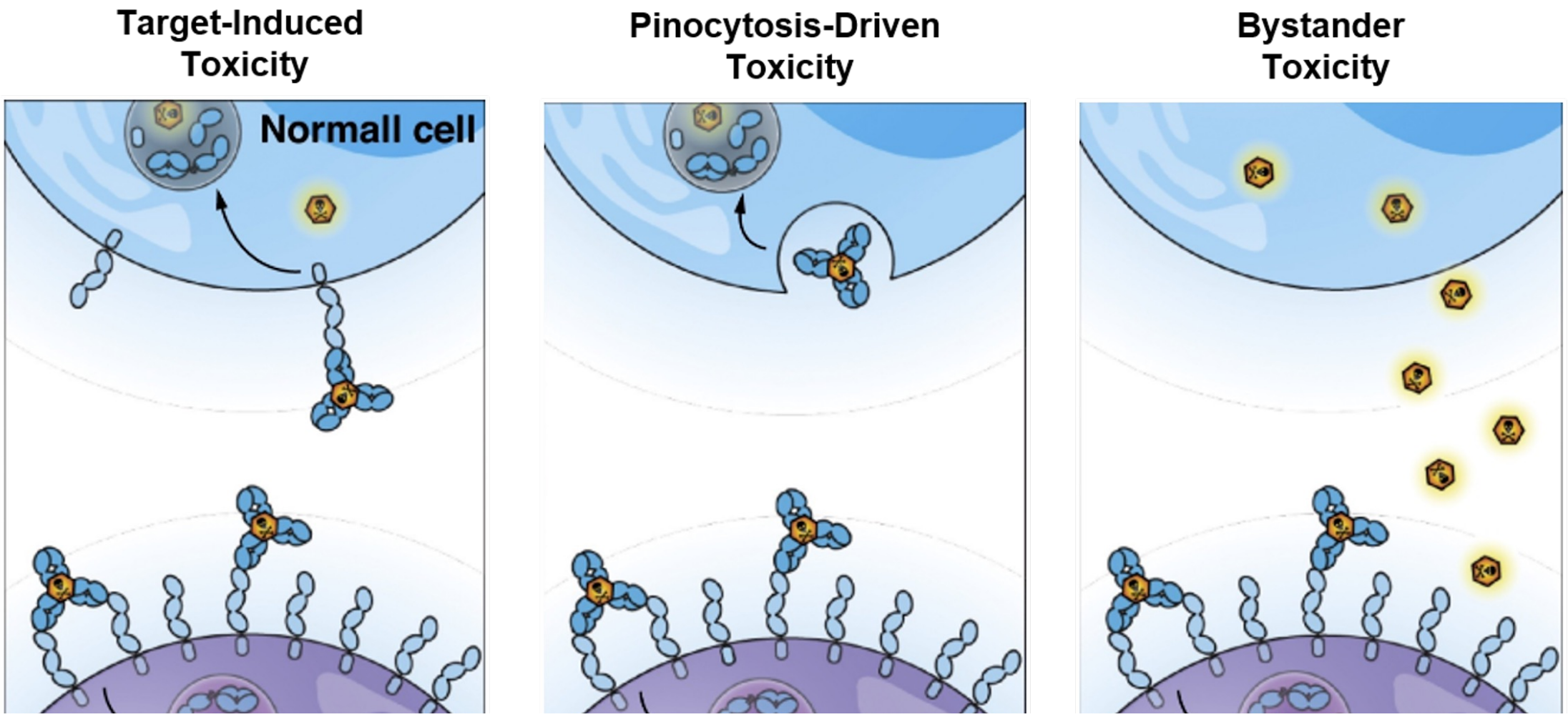
Common toxicities observed with select ADCs
Differentiated Safety Profiles Require Intentional Mitigation

Hematologic	GI	Peripheral neuropathy
Thrombocytopenia	Nausea	Weakness
Neutropenia	Vomiting	Numbness
Anemia	Diarrhea	Pain
Leukopenia	Decreased appetite	
Febrile neutropenia	Constipation	
	Abdominal pain	

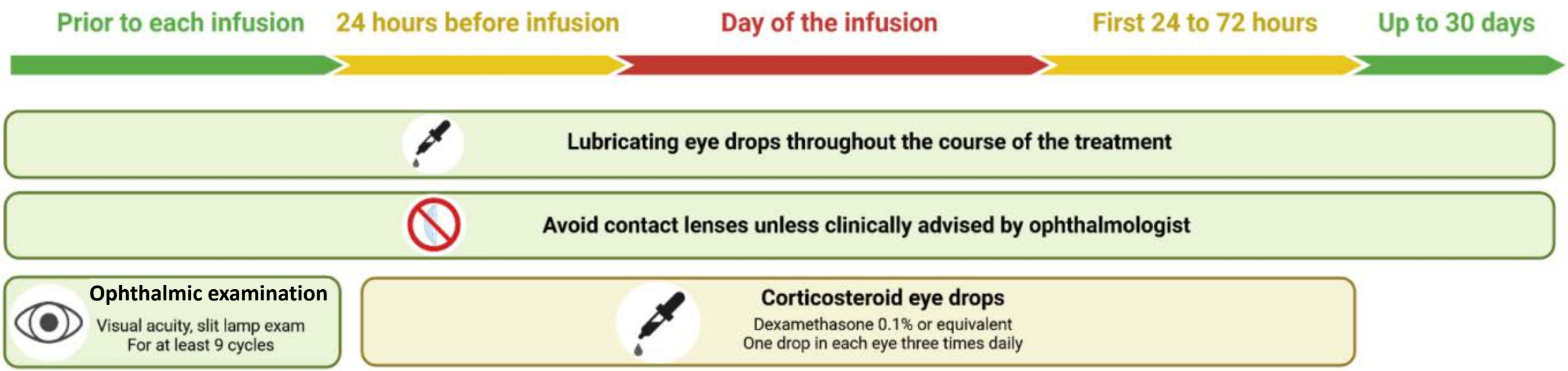
Common toxicities observed with select ADCs
Differentiated Safety Profiles Require Intentional Mitigation

Hematologic	GI	Peripheral neuropathy	Ocular toxicity	Pulmonary toxicity
Thrombocytopenia	Nausea	Weakness	Blurred vision	Inflammation
Neutropenia	Vomiting	Numbness	Dry eye	Fibrosis
Anemia	Diarrhea	Pain	Decreased visual acuity	
Leukopenia	Decreased appetite		Blurred vision	
Febrile neutropenia	Constipation		Conjunctivitis	
	Abdominal pain		Keratopathy	

Mechanisms of Ocular ADC Toxicity



Mitigation of Ocular ADC Toxicity



Ophthalmic examination

Visual acuity, slit lamp exam
Mandatory prior to initiation, every other cycle until cycle 8
Then as clinically indicated

Lubricating eye drops

Throughout the treatment
At least four times daily

Corticosteroid eye drops

Prednisolone 1% or equivalent

Primary prophylaxis

Day prior to infusion until day 4: one drop in each eye, 6 times daily

Days 5 to 8: one drop in each eye, 4 times daily

Avoid contact lenses

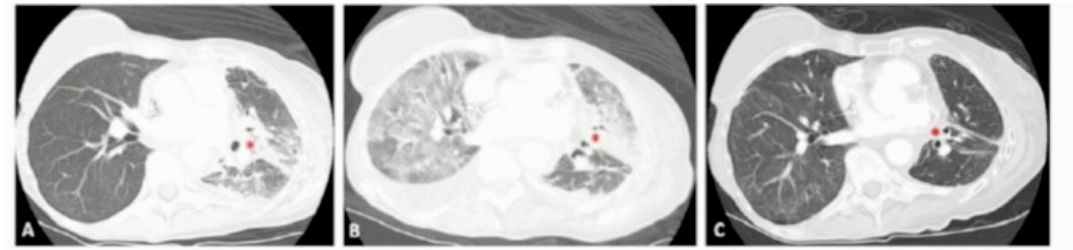
Throughout the treatment

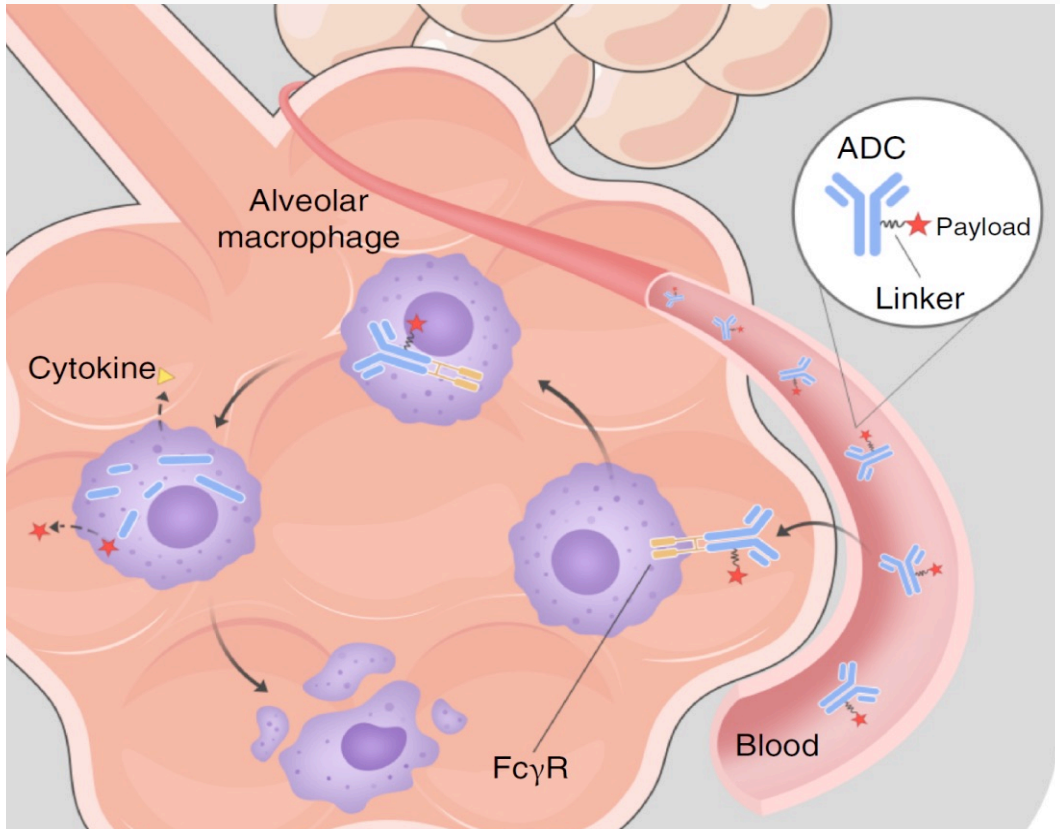
Mechanisms of Pulmonary ADC Toxicity

Can be *on-target* effect

Off-target effect by accumulation of ADC in alveolar macrophages

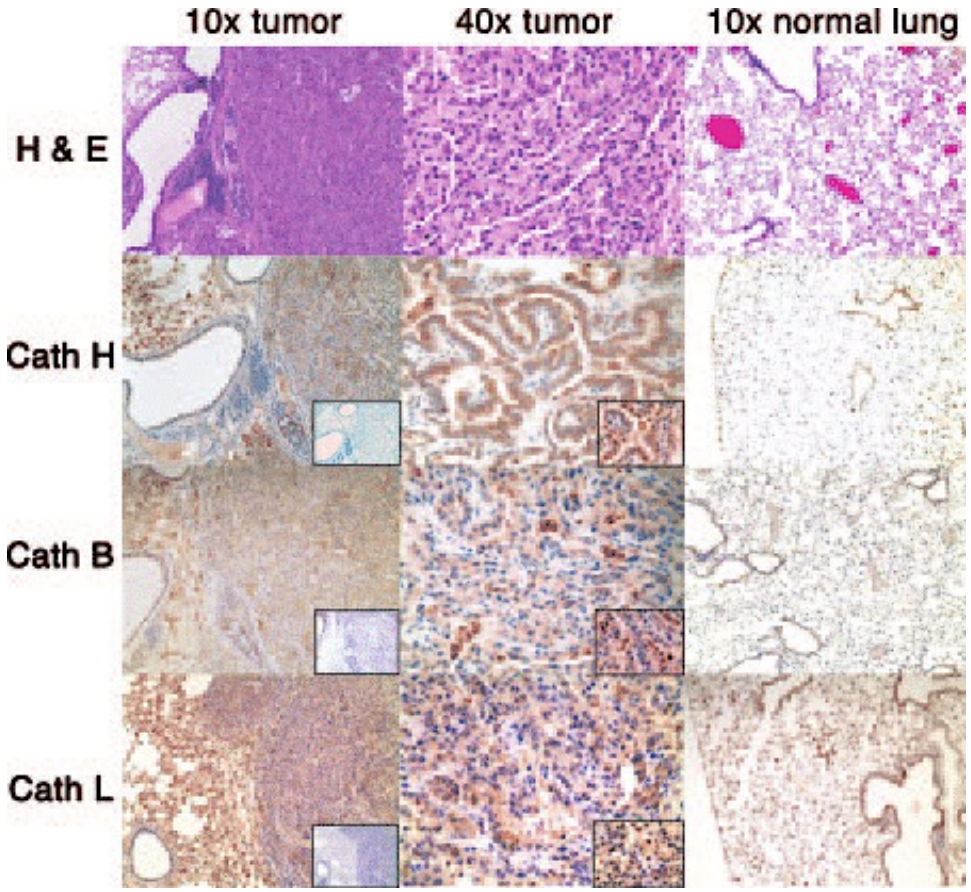
FcγR driven mechanism

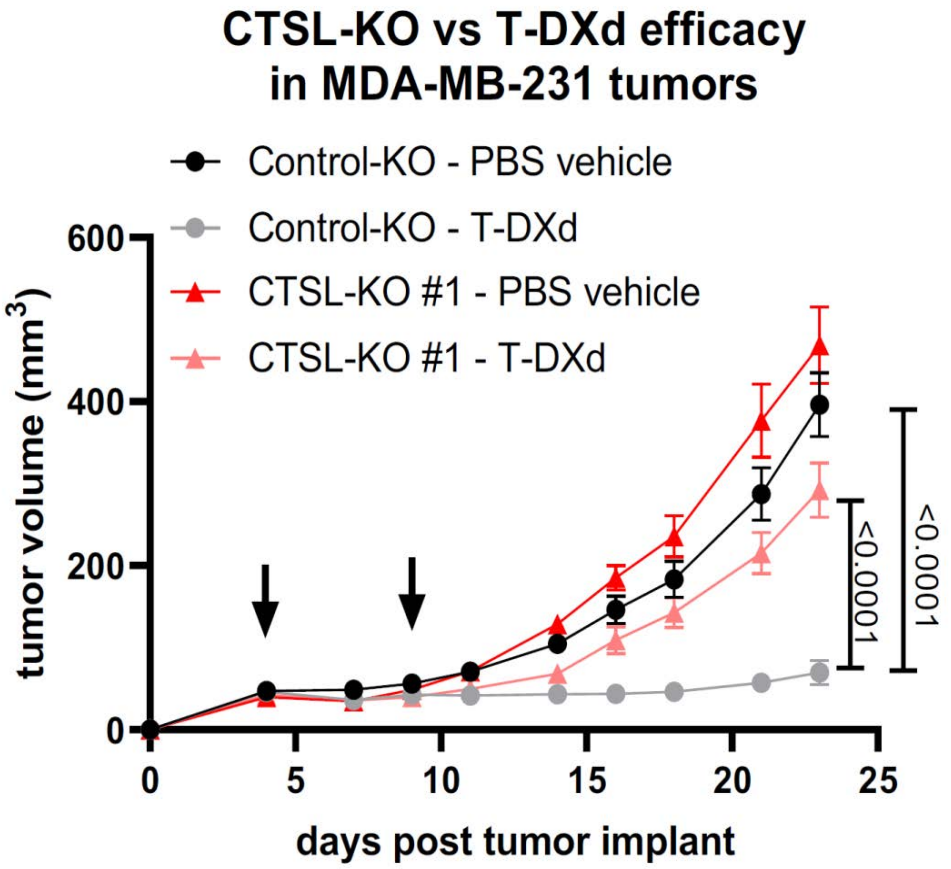




Wei Q, et al. Cancer Res 2025 doi: 10.1158/0008-5472

Extracellular Protease Cathepsins can Cleave ADC Linker Off-target Cytotoxicity



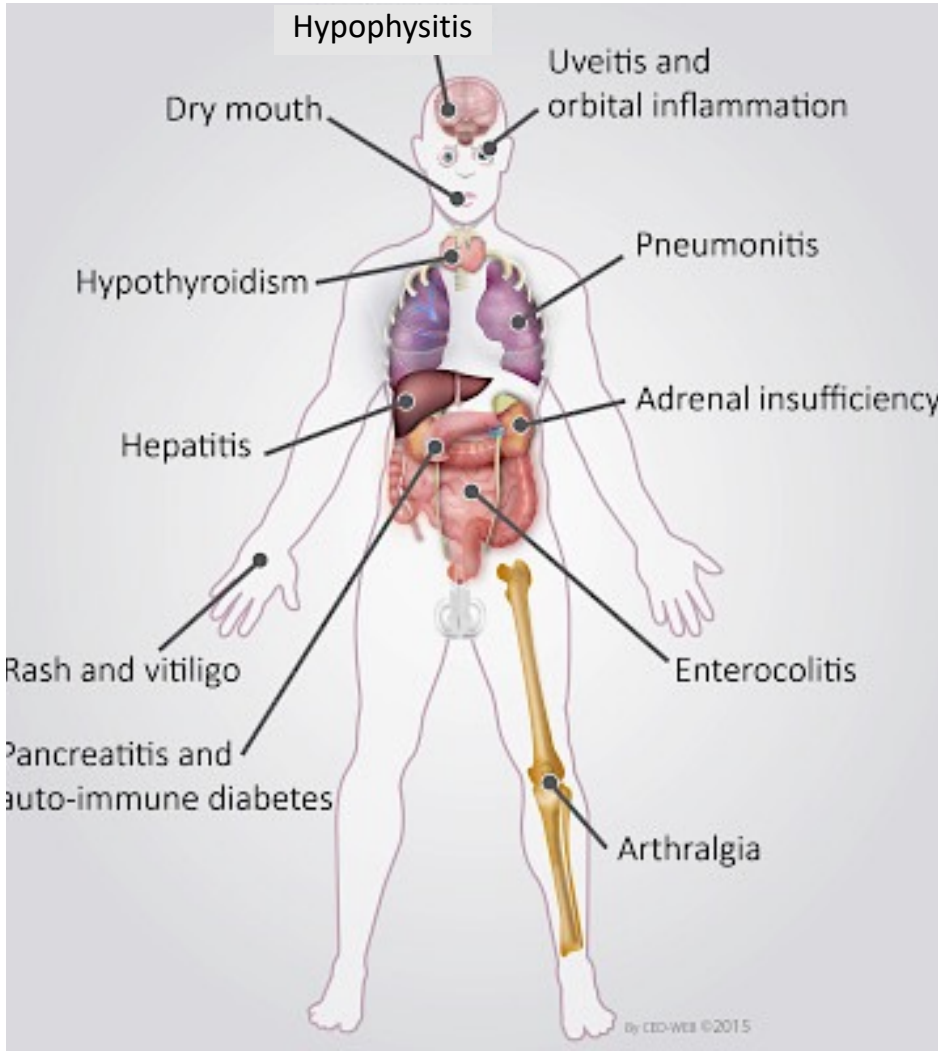


Tsao LC, et al. Nat Commun 2025;16(1):3167

ILD Management

	Trastuzumab deruxtecan	Mirvetuximab soravtansine
Grade 1 (asymptomatic)	**Hold therapy** Consider steroid therapy Resume T-Dxd if ILD resolves completely	**Continue MIRV** with close monitoring
Grade 2	**Permanently discontinue therapy** Steroid therapy	**Hold therapy until ≤ grade 1** (consider MIRV dose level adjustment) Consider steroid therapy
Grade 3	**Permanently discontinue therapy** Steroid therapy (high dose)	**Permanently discontinue therapy** Consider steroid therapy
Grade 4	**Permanently discontinue therapy** Steroid therapy (high dose)	**Permanently discontinue therapy** Consider steroid therapy

What is an Immune Related Side Effect?



- Inflammatory or autoimmune in nature due to proliferation of T cells and proinflammatory cells or release cytokines in organs or normal tissue.
- There is reduction in self tolerance
- **Can target any organ!**

Common Side Effects

Occurring in ≥10% of Patients

PEMBROLIZUMAB

Fatigue
Most frequent; occurs in ~40% of patients. May impact daily function.

Nausea
GI disturbance common early in treatment. Usually manageable.

Diarrhea
Mild-to-moderate loose stools; monitor for immune-related colitis.

Pyrexia
Low-grade fever often signals immune activation; monitor closely.

Pruritus / Rash
Skin reactions in ~20%; can range from mild itch to erythematous rash.

Musculoskeletal Pain
Arthralgia, myalgia, and back pain reported in ~15% of patients.

Rare but Serious Side Effects

PEMBROLIZUMAB

Immune-Related Adverse Events (irAEs) — Requires Prompt Clinical Attention

PULMONARY
Pneumonitis
Immune-mediated lung inflammation (<5%). Can be life-threatening; monitor for cough/dyspnea.

GI
Colitis
Severe immune-related diarrhea/colitis (<2%). May require corticosteroids or treatment discontinuation.

HEPATIC
Hepatitis
Elevated LFTs and immune-mediated hepatitis (<1–2%). Monitor liver enzymes regularly.

ENDOCRINE
Endocrinopathies
Hypophysitis, thyroiditis, adrenal insufficiency. Can be permanent; requires hormone replacement.

RENAL
Nephritis
Immune-mediated kidney injury (<1%). Monitor creatinine; may require steroid therapy.

CARDIAC
Myocarditis
Rare but potentially fatal (<0.1%). Presents with chest pain, arrhythmia, or heart failure.

Treatment of IRAEs: Use of Steroids

- Does not diminish treatment efficacy
- There should be rapid response with steroids in treating IRAEs
- If pt not responding, approx. 3-5 days, consider second immunosuppressant.
- Infliximab 5mg/kg plus high dose steroids with colitis
- Consider Pneumocystis prophylaxis with trimethoprim-sulfamethoxazole, atovaquone, or pentamidine for patients treated with 20 mg of prednisone equivalent daily for 4 weeks or more
- Consider antifungal prophylaxis.
- After a full steroid dose treatment course of generally 2-4 weeks, steroids must be reduced gradually over a period of at least 1 month to avoid recurrence of the IRAE
- Replacement steroid for adrenal insufficiency and hypophysitis are likely lifelong. They will need to be increased if undergoing stress like surgery. Patients can continue immunotherapy if prednisone or equivalent is less than 10 mg a day.

Second Opinion

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