What Clinicians Want to Know: Addressing Current Questions and Controversies in the Care of Patients with Ovarian Cancer

An Independent CME Symposium During
the 2025 SGO Annual Meeting on Women's Cancer®

Sunday, March 16, 2025
12:30 PM – 2:00 PM PT (3:30 PM – 5:00 PM ET)

Faculty

Kathleen N Moore, MD, MS
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Shannon N Westin, MD, MPH, FASCO, FACOG

Moderator

Angeles Alvarez Secord, MD, MHSc

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Advisory Committees	Aadi Bioscience, AbbVie Inc, AstraZeneca Pharmaceuticals LP, BioNTech SE, Blueprint Medicines, Caris Life Sciences, Corcept Therapeutics, Daiichi Sankyo Inc, Duality Biologics, Eisai Inc, Genentech, a member of the Roche Group, GSK, ImmunoGen Inc, Janssen Biotech Inc, Lilly, Merck, Mersana Therapeutics Inc, Novartis, Regeneron Pharmaceuticals Inc, Schrödinger, Takeda Pharmaceuticals USA Inc, Verastem Inc, Zentalis Pharmaceuticals, Zymeworks Inc
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Dr Salani — Disclosures
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Dr Westin — Disclosures
Faculty

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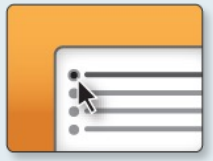
Clinicians in the Meeting Room

Networked iPads are available.

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



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

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

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

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Clinicians Attending via Zoom

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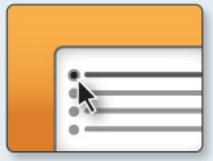

Answer Survey Questions: Complete the pre- and postmeeting surveys.

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

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About the Enduring Program

- The live meeting is being video and audio recorded.
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Agenda

Module 1: Up-Front Treatment for Advanced Ovarian Cancer (OC) — Dr Westin

Module 2: Management of Relapsed/Refractory OC — Dr Secord

Module 3: Novel Investigational Therapies for Advanced OC — Dr Moore

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

Survey of Gynecologic Oncologists and General Medical Oncologists
March 3-5, 2025

Results available on iPads and Zoom chat room

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Up-Front Maintenance in Advanced Ovarian Cancer

Shannon N. Westin, MD, MPH

Professor, Center Medical Director

Gynecologic Oncology and Reproductive Medicine

UT MD Anderson Cancer Center

NCCN Guidelines Version 1.2025
Epithelial Ovarian Cancer/Fallopian Tube Cancer/ Primary Peritoneal Cancer

NCCN Guidelines Index
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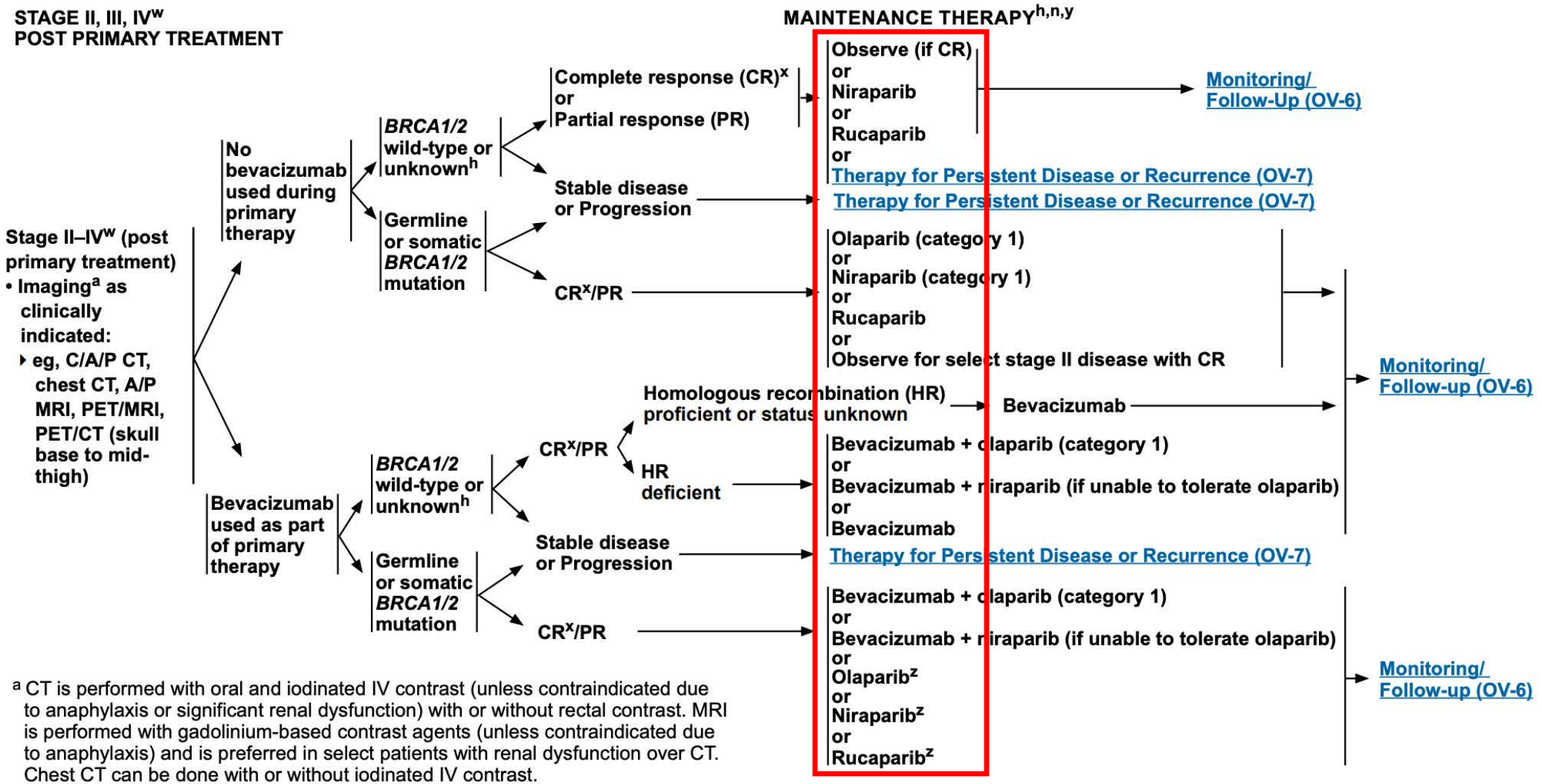
Discussion



[a] CT is performed with oral and iodinated IV contrast (unless contraindicated due to anaphylaxis or significant renal dysfunction) with or without rectal contrast. MRI is performed with gadolinium-based contrast agents (unless contraindicated due to anaphylaxis) and is preferred in select patients with renal dysfunction over CT. Chest CT can be done with or without iodinated IV contrast.

[h] In the absence of a BRCA1/2 mutation, HRD status may provide information on

SOLO-1: Olaparib in *BRCA*m OC

- Newly diagnosed, FIGO stage III–IV, high-grade serous or endometrioid ovarian, primary peritoneal or fallopian tube cancer
- *BRCA*m
- ECOG performance status 0–1
- Cytoreductive surgery[a]
- In clinical complete[b] or partial response after platinum-based chemotherapy

Olaparib 300 mg bid (n=260)

2:1 randomisation stratified by response to platinum-based chemotherapy

Placebo (n=131)

For up to 2 years or until disease progression[c]

Primary endpoint
- PFS (investigator-assessed)

Secondary endpoints
- OS
- TFST
- TSST
- Safety

Primary PFS analysis (DCO: 17 May 2018)

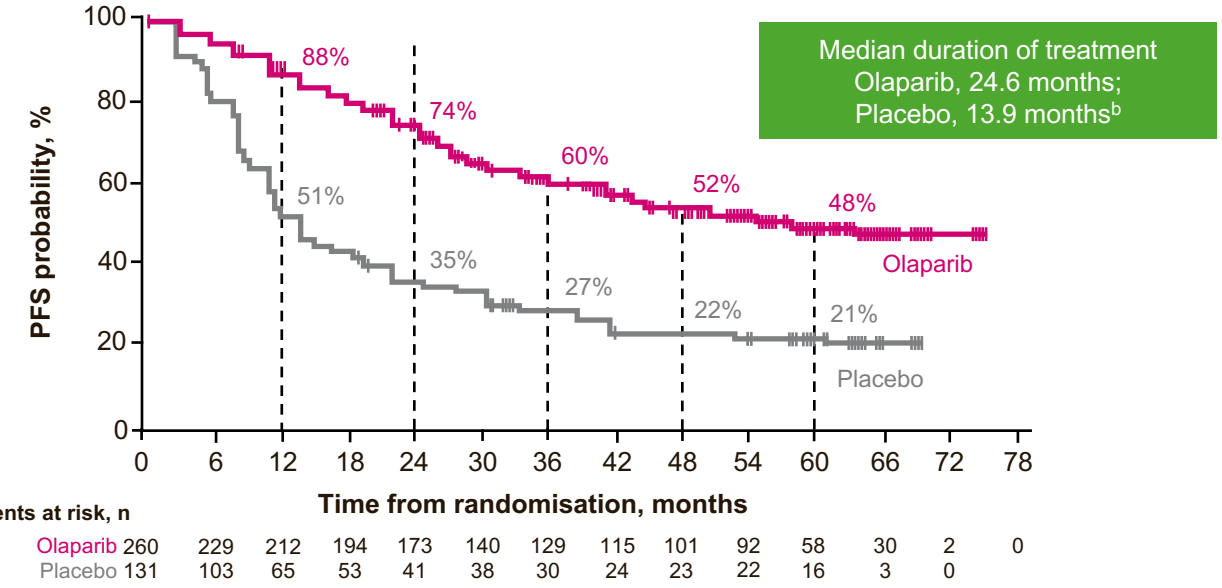
	Olaparib (n=260)	Placebo (n=131)
Events, n (%)	102 (39.2)	96 (73.3)
Median PFS, months	NR	13.8
3-year PFS rate, %	60.4	26.9
HR 0.30 (95% CI, 0.23–0.41)		
P<0.001		

Updated PFS analysis (DCO: 5 March 2020)

	Olaparib (n=260)	Placebo (n=131)
Events, n (%)	118 (45.4)	100 (76.3)
Median PFS, months	56.0	13.8
5-year PFS rate, %	48.3	20.5
HR 0.33 (95% CI, 0.25–0.43)		

Olaparib yielded sustained PFS benefit beyond the end of treatment and improved OS (still immature)

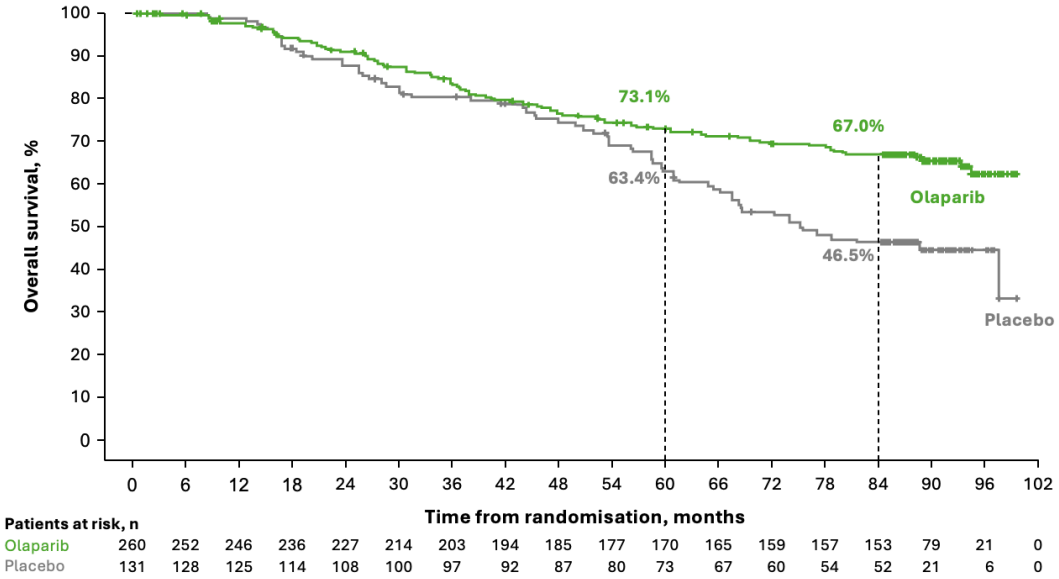
PFS beyond end of treatment



Median duration of treatment
Olaparib, 24.6 months;
Placebo, 13.9 months[b]

	Olaparib (n=260)	Placebo (n=131)
Events, n (%)	118 (45)	100 (76)
Median PFS, months	**56.0**	**13.8**
	HR 0.33 (95% CI, 0.25–0.43)	

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[a]	

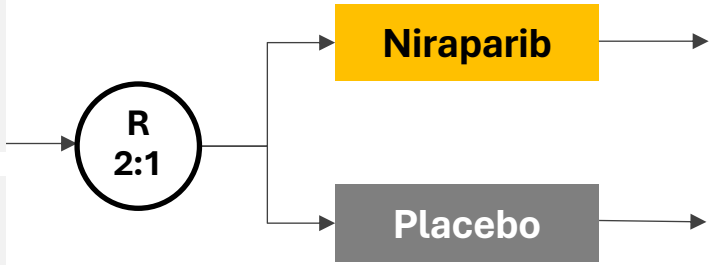
PRIMA: Niraparib in all-comers OC

Eligible patients

- Newly diagnosed HGS/HGE aOC
- CR or PR to 1L PBCT
- Tumour sample for HRD testing

Stratification factors

- Neoadjuvant chemotherapy: yes or no
- Best response to 1L PBCT: CR or PR
- Tumour HRD status: HRd or HRp/HRnd



Patients treated once daily for 36 months or until disease progression

Endpoints

Primary endpoint:
PFS by BICR

Key secondary endpoint:
OS

Secondary endpoints:
PFS2, TFST, PROs, safety

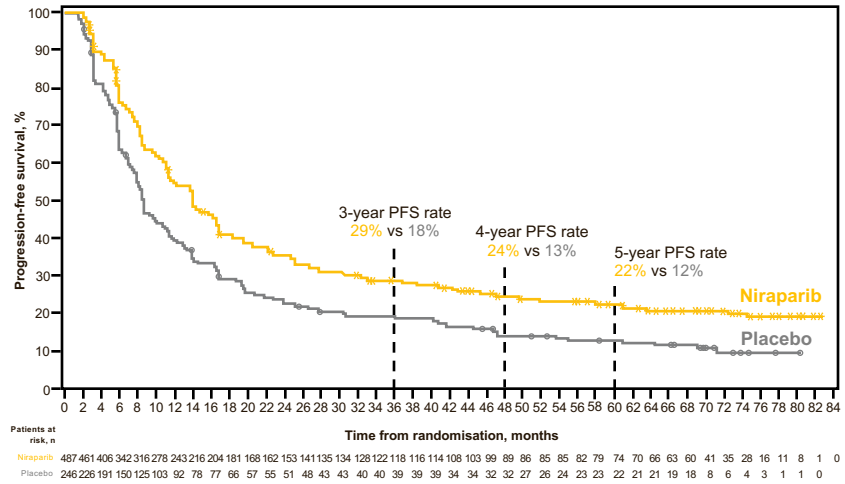
OS testing

- Conducted at ~60% maturity in overall population (≈440 deaths)
- Hierarchical testing: overall then HRd
- 80% power to detect a statistically significant difference if the true hazard ratio was ≤0.75 in overall population

González-Martín A, *N Engl J Med*. 2019

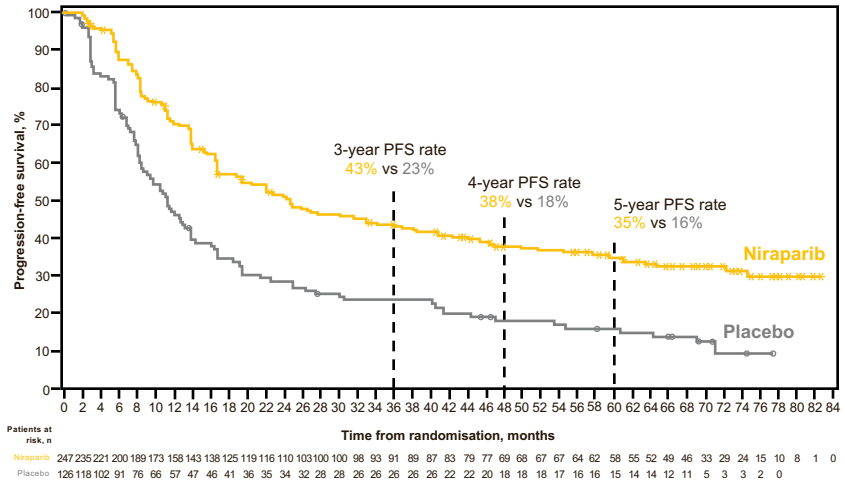
Niraparib yielded long term PFS benefit in the HRd and overall populations

Overall population



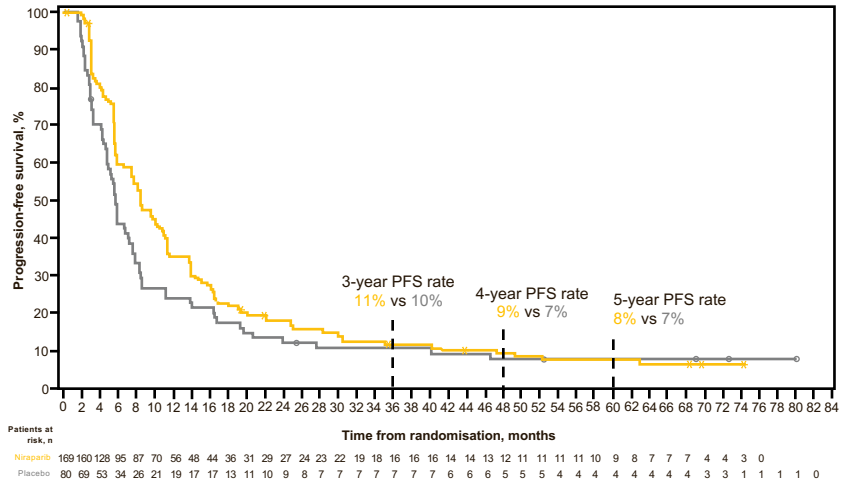
	Niraparib (n=487)	Placebo (n=246)
Events, n (%)	352 (72.3)	209 (85.0)
Median PFS, months	**13.8**	**8.2**
HR 0.66 (95% CI, 0.55–0.78)		

HRd population



	Niraparib (n=247)	Placebo (n=126)
Events, n (%)	150 (60.7)	105 (83.3)
Median PFS, months	**24.5**	**11.2**
HR 0.51 (95% CI, 0.40–0.66)		

HRp population

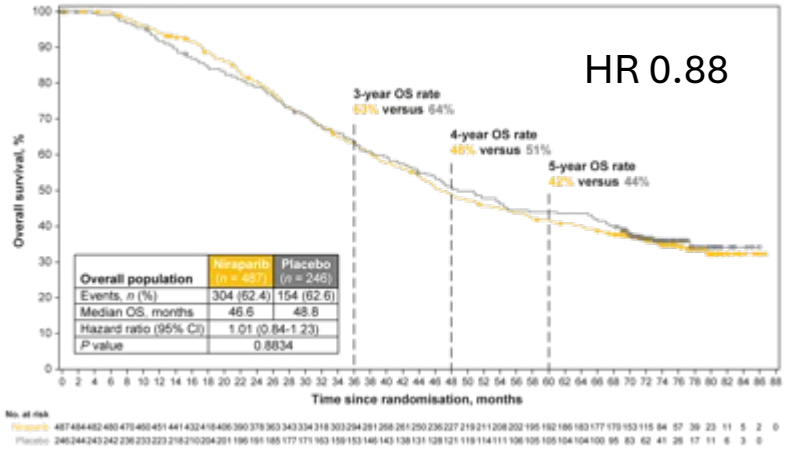


	Niraparib (n=169)	Placebo (n=80)
Events, n (%)	147 (87.0)	71 (88.8)
Median PFS, months	**8.4**	**5.4**
HR 0.67 (95% CI, 0.50–0.89)		

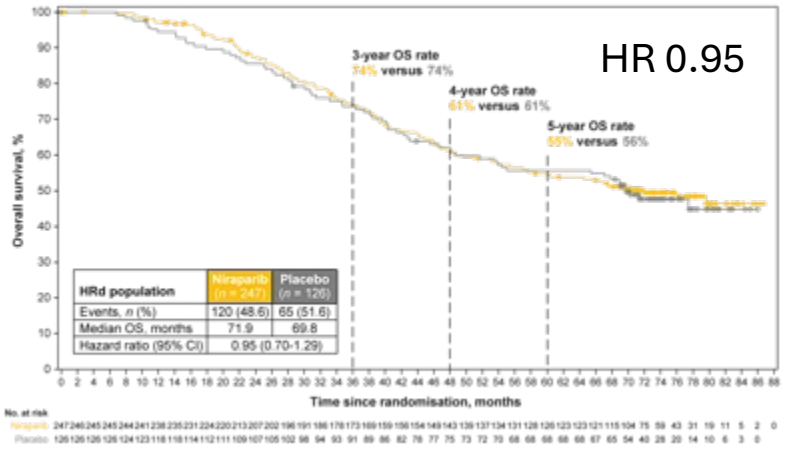
Median duration of follow-up: 73.9 months

No difference in OS in PRIMA across all populations

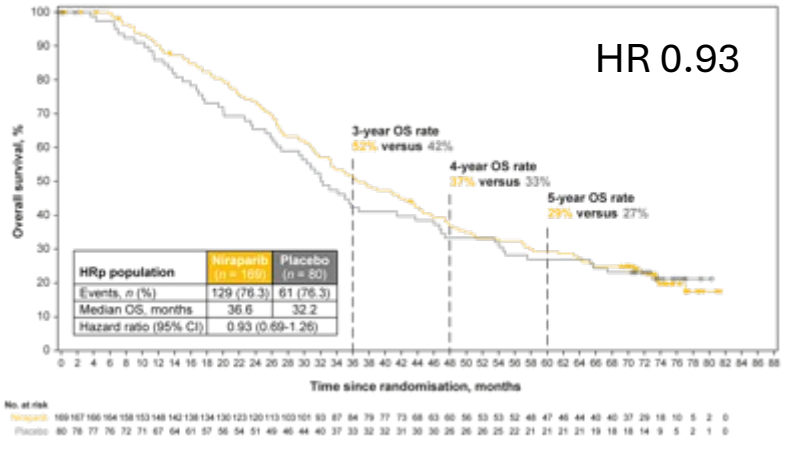
Overall



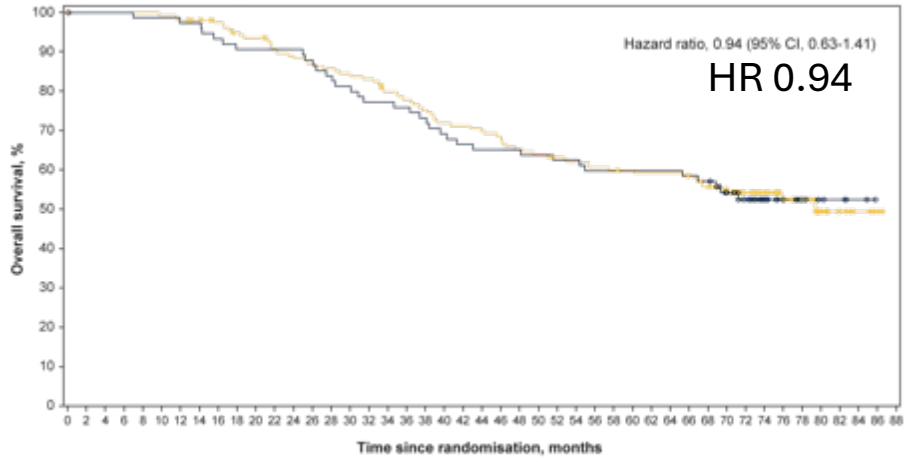
HRd



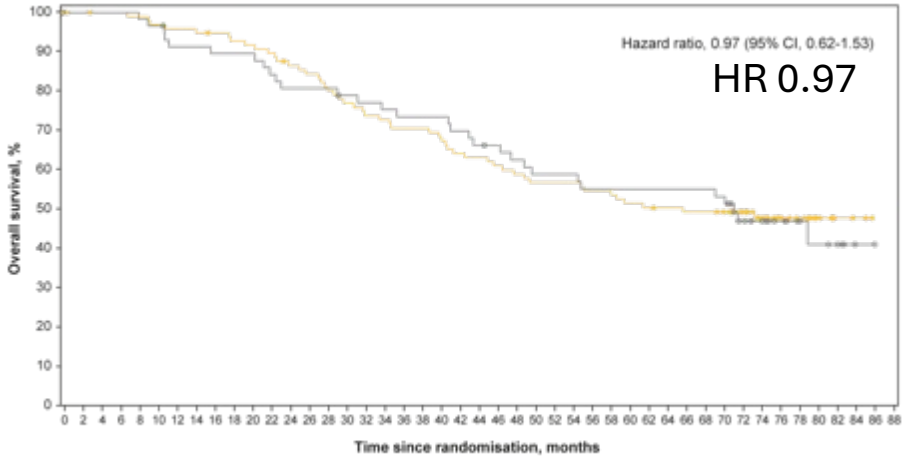
HRp



BRCAm



HRd/BRCAwt



Monk B *Ann Oncol*. 2024

*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: Olaparib and bevacizumab in all comers OC

Patients

- Newly diagnosed, FIGO stage III–IV, high-grade serous or endometrioid ovarian, fallopian tube and/or primary peritoneal cancer

First-line treatment

- Upfront or interval surgery
- Platinum–taxane-based chemotherapy plus ≥2 cycles of bevacizumab

≤9 weeks

NED/CR/PR

Maintenance therapy

Olaparib tablets 300 mg bid × 2 years

+ Bevacizumab[d]

2:1 randomisation stratified by:

- Tumour *BRCA*m status
- First-line treatment outcome

Placebo × 2 years

+ Bevacizumab

Primary endpoint

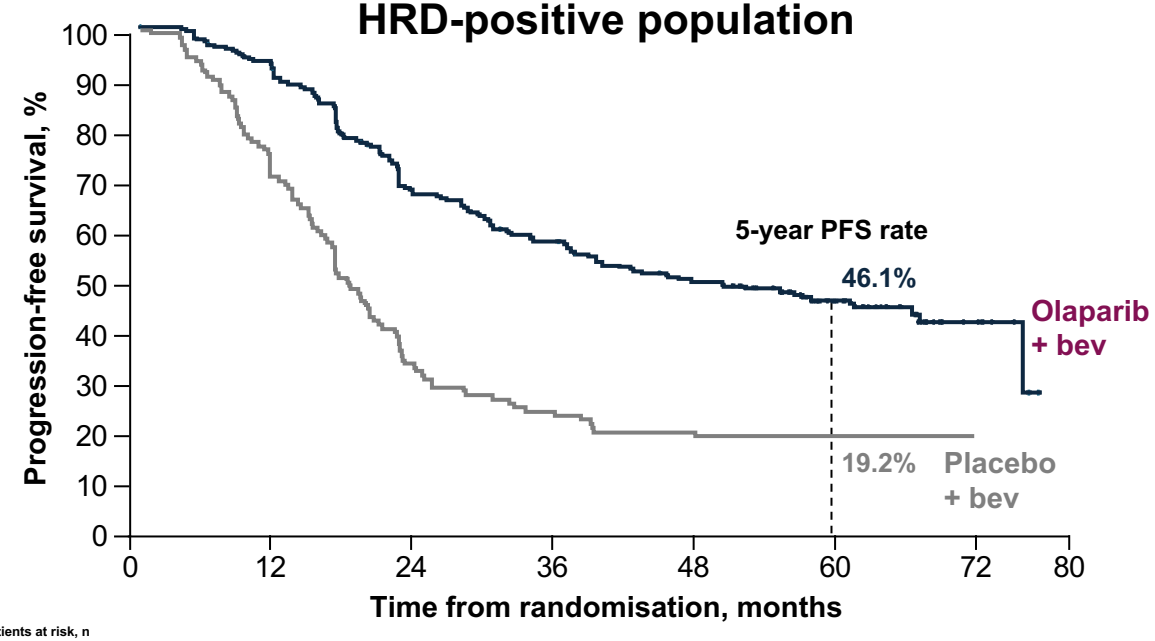
- Investigator-assessed PFS (RECIST v1.1)

Key secondary endpoints

- PFS2
- OS (planned for 3 years after the primary PFS analysis or 60% data maturity)

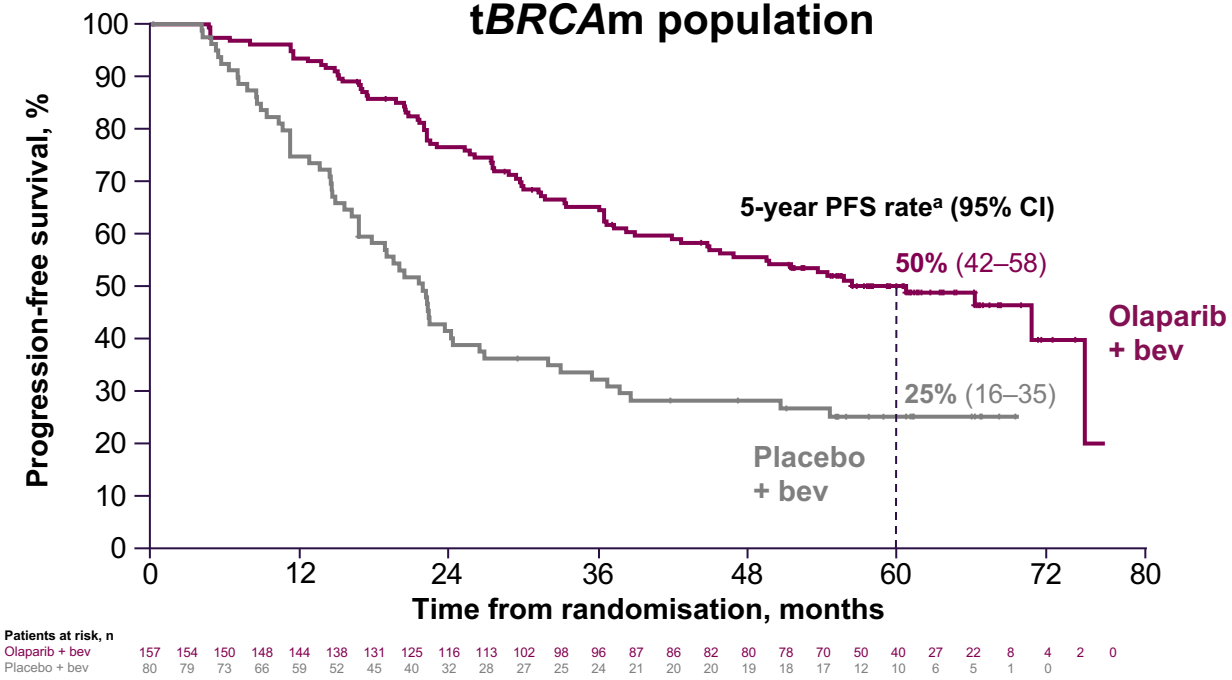
Olaparib + bevacizumab yielded PFS benefit in HRD and t*BRCA*m populations at 5 years

HRD-positive population



	Olaparib + bev (n=255)	Placebo + bev (n=132)
mPFS, months	**46.8**	**17.6**
	HR 0.41 (95% CI, 0.32–0.54)	

t*BRCA*m population

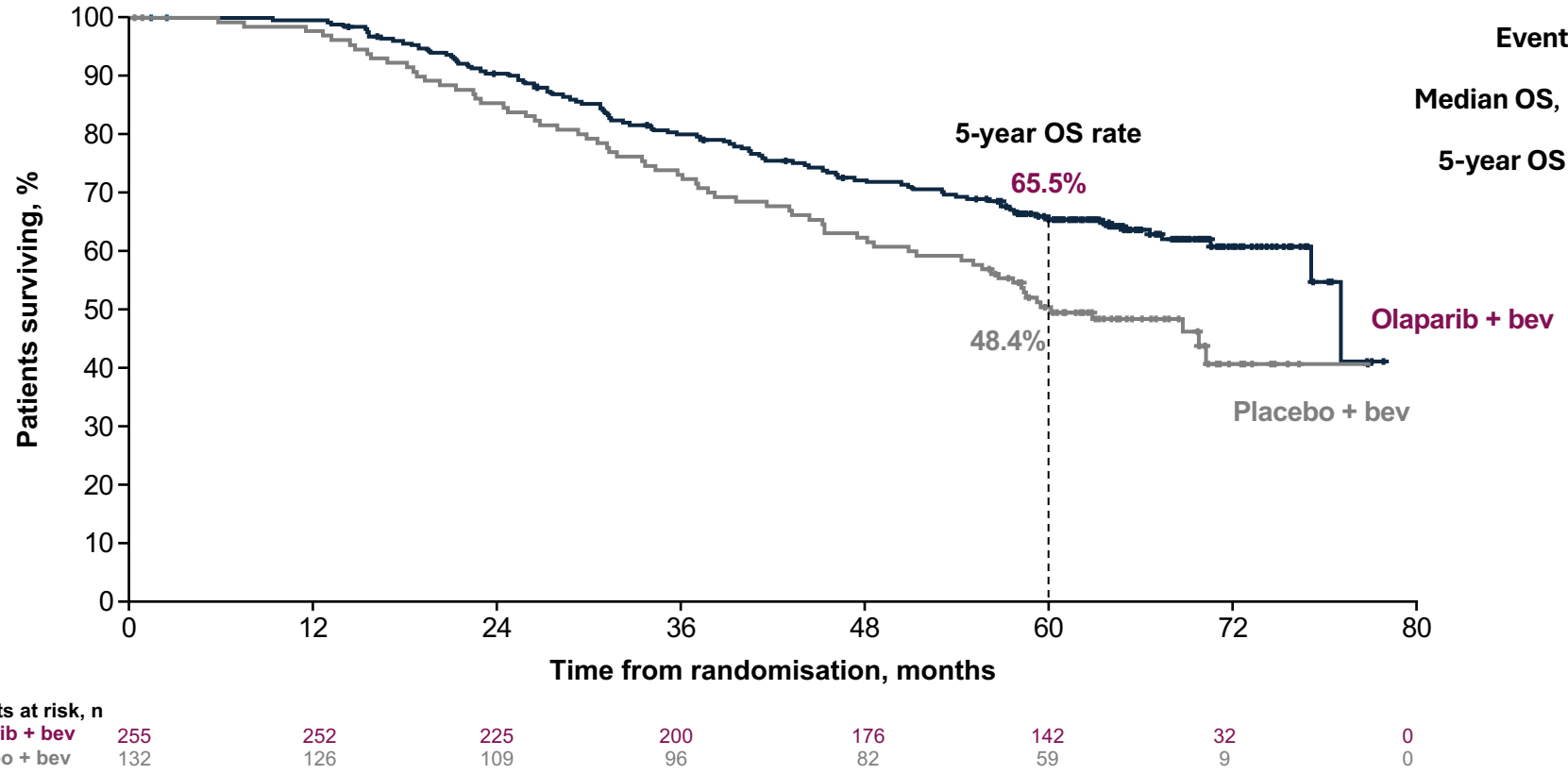


	Olaparib + bev (n=157)	Placebo + bev (n=80)
Events, n (%)	78 (50)	58 (73)
mPFS, months	**60.7**	**21.7**
	HR 0.45 (95% CI, 0.32–0.64)	

Median follow-up 61.7 and 61.9 months in the olaparib + bev and placebo + bev arms, respectively

Maintenance olaparib + bevacizumab yielded OS benefit HRD population

Prespecified exploratory analysis, HRD-positive population



	Olaparib + bev (n=255)	Placebo + bev (n=132)
Events, n (%)	93 (36.5)	69 (52.3)
Median OS, months	**75.2** (unstable)[a]	**57.3**
5-year OS rate, %	**65.5**	**48.4**
HR 0.62 (95% CI, 0.45–0.85)		

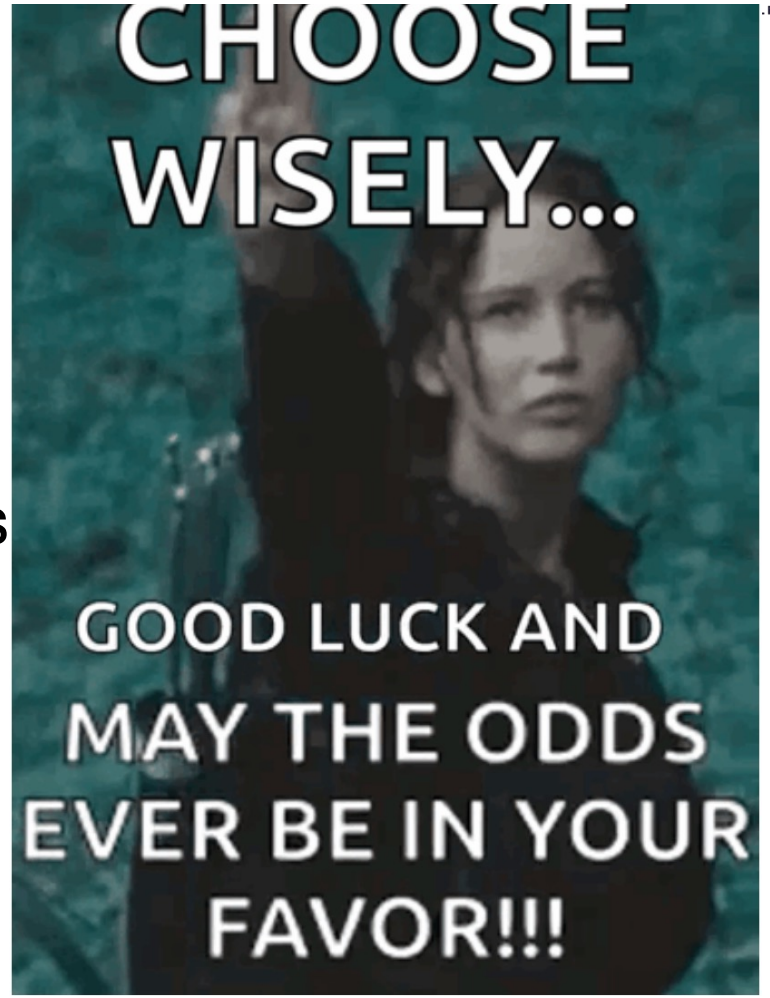
38% reduction in risk of death for olaparib + bevacizumab vs bevacizumab alone

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

Ray-Coquard I *Ann Oncol*. 2023

How do we choose?

- Indication
- Biomarkers – *BRCA*, HRD
  - Overall survival? Long term PFS?
- Use of bevacizumab
- Response to therapy, clinical characteristics
- Toxicities
- Schedule
- Price



Safety profile across first-line maintenance trials

	SOLO-1[a,1]		PAOLA-1[b,2]		PRIMA[c,3]		
	Olaparib	Placebo	Olaparib + bev	Bev + placebo	Niraparib (Overall)	Niraparib FSD | ISD	Placebo
n	260	130	535	267	484	313 | 169	244
Grade ≥3 AEs, %	39.6	20.0	57.0	51.0	73.8	79.0 | 63.9	23.8
Thrombocytopenia	0.8	1.5	2.0	<1.0	39.9	49.2 | 22.5	<1
Anaemia	21.9	1.5	17.0	<1.0	32.0	36.5 | 23.7	2.0
Neutropenia	8.5	4.6	6.0	3.0	21.3	24.8 | 14.8	1.6
Hypertension	NR	NR	19.0	30.0	7.2	8.3 | 5.3	2.0
Fatigue	3.8	1.5	5.0	1.0	2.3	2.2 | 2.4	0.4
Insomnia	0.0	0.0	NR	NR	1.0	1.6 | 0.0	0.4
Nausea	0.8	0.0	2.0	1.0	1.2	1.3 | 1.2	0.8
Diarrhoea	3.1	0.0	2.0	2.0	0.8	0.3 | 1.8	0.4
Constipation	0.0	0.0	0.0	<1.0	0.4	0.3 | 0.6	0.0
AML/MDS, %	1.5	0.8	1.7	2.2	2.3	NR	1.6
New primary malignancies, % Breast Cancer	5.4 3.8	6.2 3.8	4.1[5] 2.1[5]	3.0 1.5	2.5 NR	NR	2.5 NR

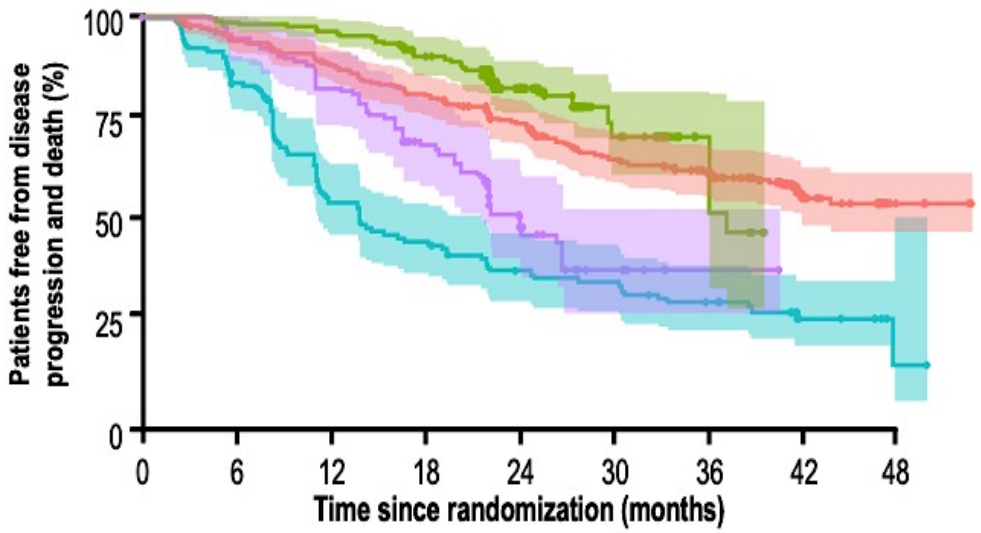
DiSilvestro P *J Clin Oncol*. 2023; Ray-Coquard I, *N Engl J Med*. 2019; Monk BJ, *Ann Oncol*. 2024; Monk BJ, *J Clin Oncol*. 2022; Ray-Coquard I, Ann Oncol 2023

A case of missing arms…Population adjusted – indirect comparisons of PFS to the rescue

SOLO-1 and PAOLA-1

Summary of all Treatment Arms

ison

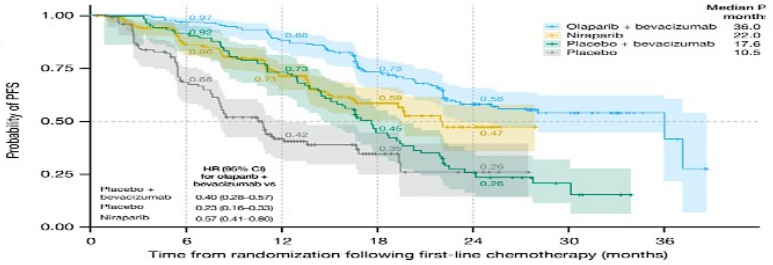


HR 0.23 (95% CI 0.14–0.34)†

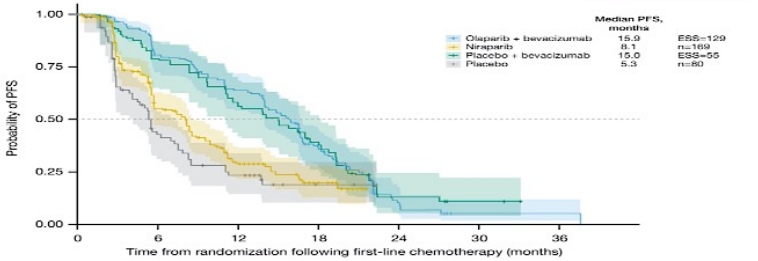
Olaparib plus bevacizumab | Olaparib | Placebo plus bevacizumab | Placebo

PAOLA-1 and PRIMA

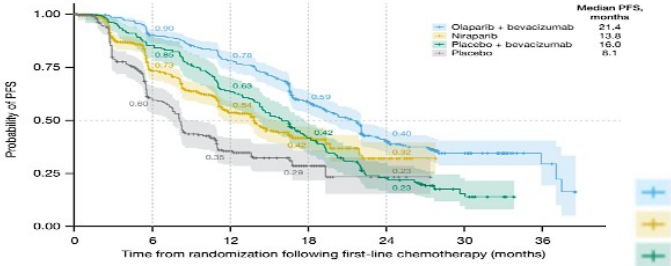
Comparison PFS in HRD patients



Comparison PFS in HRP patients



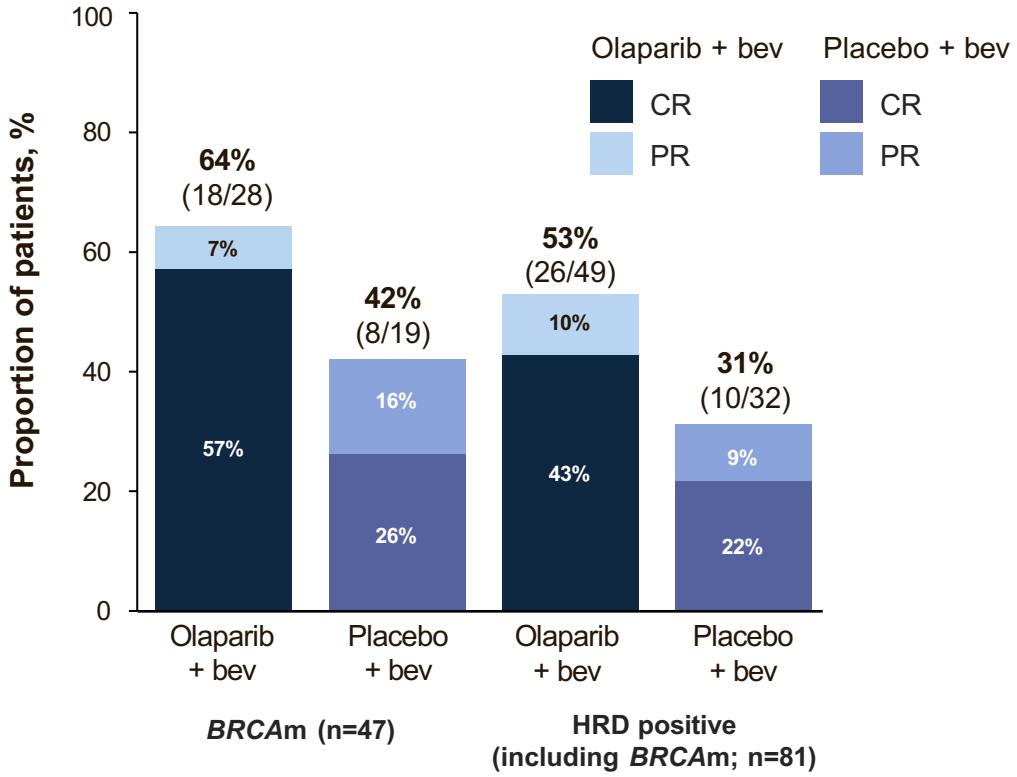
Comparison PFS in biomarker unselected patients



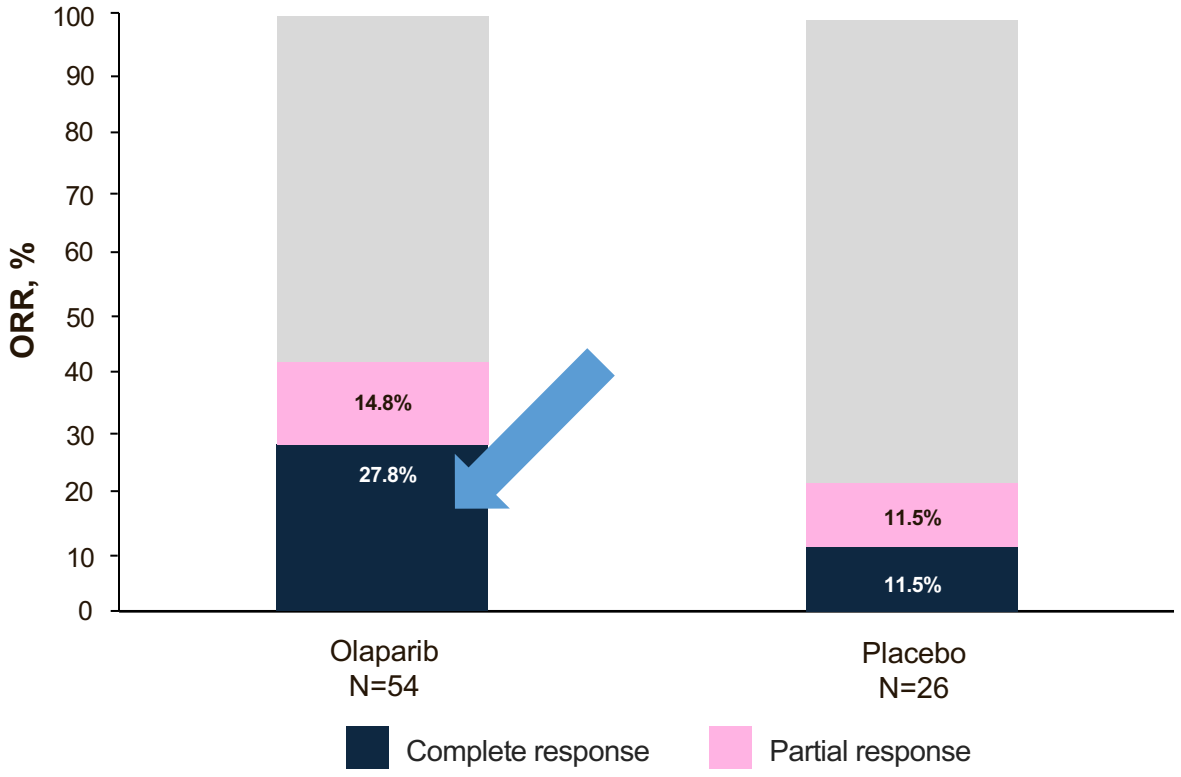
Olaparib + bevacizumab
Niraparib
Placebo + bevacizumab
Placebo

Can the use of bevacizumab improve complete response to therapy?

RECIST and CA-125 response rates by molecular subgroups



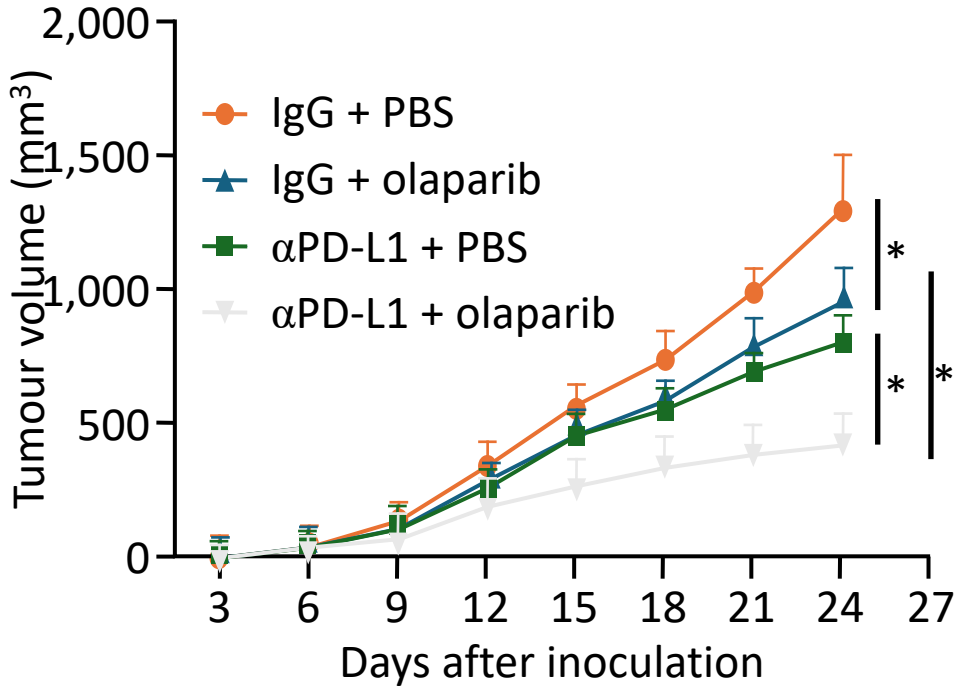
SOLO-1 ORR in patients with evidence of disease achieved a CR with olaparib



Colombo N *Ann Oncol 2020;*
DiSilvestro P*J Clin Oncol*. 2020

Why PARPi and immunotherapy?

- Neoantigen load of HR defective tumors
  - Higher number of TILs
- PARPi:
  - DNA Fragments resulting from PARPi activity Induce a STING Response
  - PARP inhibitor increases peritoneal CD8+ T
- Xenograft models: Synergy between PARP inhibition and checkpoint inhibition

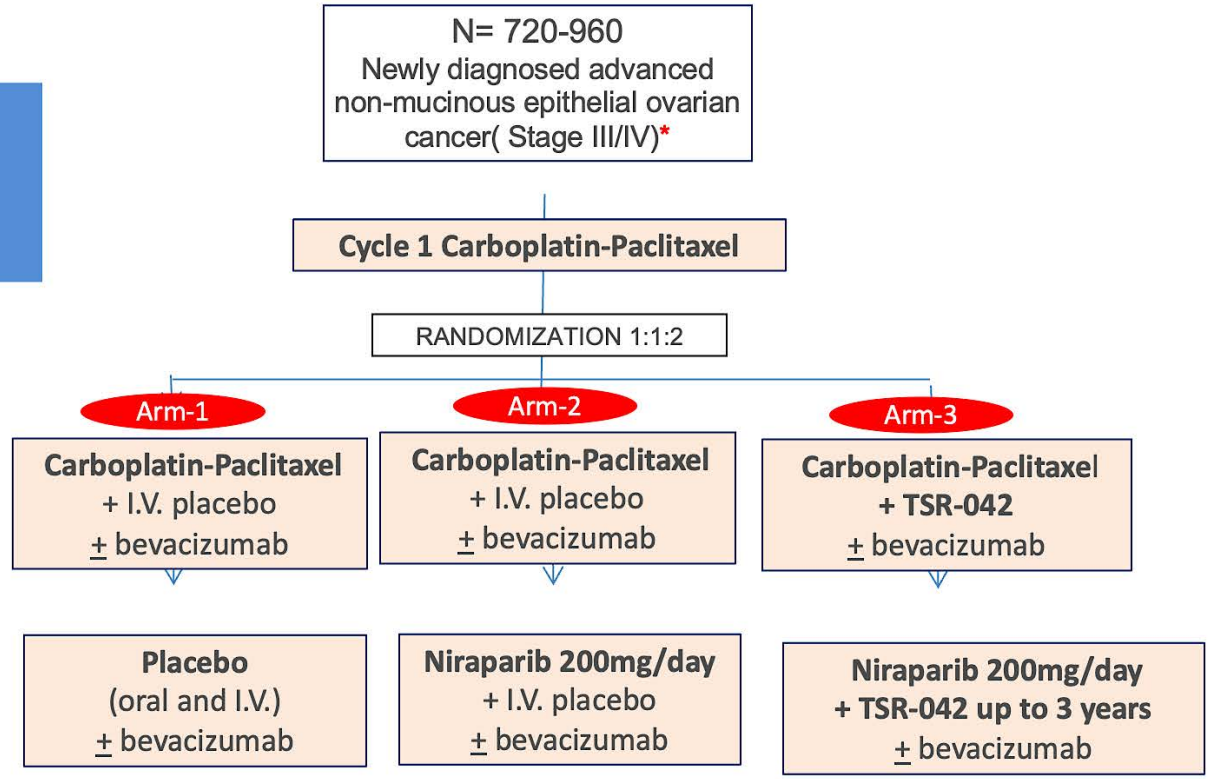


Chen & Mellman. Immunity 2013; Galluzzi Nat Rev Drug Discov 2012; Jiao CCR 2017
Hannani Cancer J 2011; Vanneman and Dranoff. Nat Rev Cancer 2012; Kyle Immunology 2017

FIRST Trial: First-line ovarian cancer treatment with Niraparib plus TSR-042

Primary objective:
PFS by Investigator assessment per RECIST v1.1. PFS based upon blinded independent central review committee (BICR) will be a sensitivity analysis.

Secondary endpoints:
OS
ORR/DOR/DCR
Safety and tolerability of all treatments
Patient-reported outcomes (PROs)
Time to first subsequent therapy (TFST)
Time to second subsequent therap (TSST)
PFS2



Stratification Factors

- Bevacizumab use (investigator choice).
- HRR and BRCA status based on ctDNA with tumor sample as back-up
- Stage III < 1 cm at PDS versus others

*Not eligible: complete surgical resection at primary debulking surgery **and low risk of relapse.**

TSR-042 is an anti-PD-1 immunoglobulin G4 (IgG4) humanized monoclonal antibody (mAb) that binds with high affinity to PD-1

-ClinicalTrials.gov Identifier: NCT03602859

FIRST trial met its primary endpoint of progression free survival in first line advanced ovarian cancer

December 20, 2024

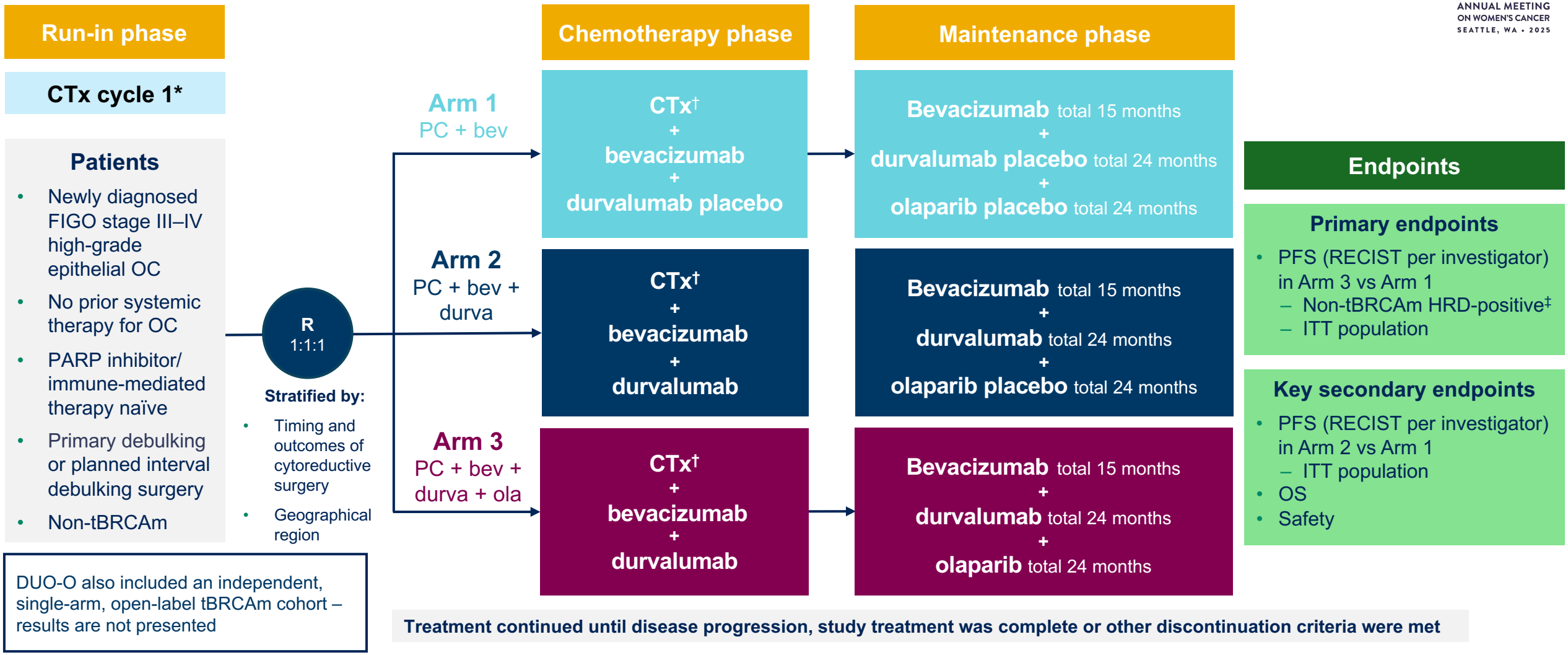
"[The manufacturer] today announced headline results from the FIRST-ENGOT-OV44 phase III trial evaluating niraparib and dostarlimab in first line advanced ovarian cancer. The trial met its primary endpoint of PFS demonstrating a statistically significant difference with the addition of dostarlimab to both standard of care carboplatin-paclitaxel chemotherapy and niraparib maintenance, with or without bevacizumab.

The key secondary endpoint of overall survival did not meet statistical significance. Further analyses are ongoing and data will be shared with health authorities and presented at an upcoming scientific meeting. The safety and tolerability profile was generally consistent with the known safety profiles of the individual agents."

https://www.gsk.com/en-gb/media/press-releases/gsk-announces-first-trial-met-its-primary-endpoint-of-progression-free-survival-in-first-line-advanced-ovarian-cancer/

DUO-O Chemo + Bevacizumab + Durvalumab + Olaparib

SGO ANNUAL MEETING ON WOMEN'S CANCER SEATTLE, WA • 2025



Endpoints

Primary endpoints

- PFS (RECIST per investigator) in Arm 3 vs Arm 1
  - Non-tBRCAm HRD-positive‡
  - ITT population

Key secondary endpoints

- PFS (RECIST per investigator) in Arm 2 vs Arm 1
  - ITT population
- OS
- Safety

DUO-O also included an independent, single-arm, open-label tBRCAm cohort – results are not presented

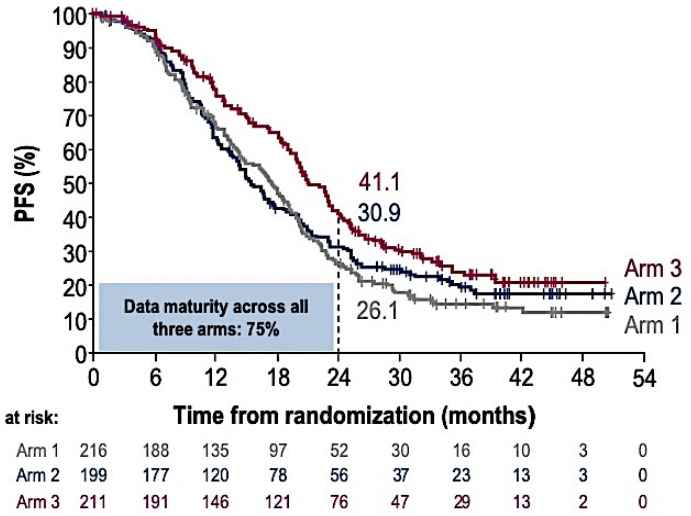
Treatment continued until disease progression, study treatment was complete or other discontinuation criteria were met

Dosing and schedule: bevacizumab (15 mg/kg IV q3w); durvalumab (1120 mg IV q3w); olaparib (300 mg po bid); chemotherapy: paclitaxel 175 mg/m² IV q3w and carboplatin at AUC5 or AUC6 IV q3w. PFS interim analysis DCO: December 5, 2022.
*With or without bevacizumab according to local practice; †Cycles 2–6; ‡Genomic instability score ≥42 assessed prospectively by Myriad MyChoice CDx assay.
AUC, area under the curve; bev, bevacizumab; bid, twice daily; CTx, chemotherapy; DCO, data cutoff; durva, durvalumab; FIGO, International Federation of Gynecology and Obstetrics; HRD, homologous recombination deficiency; ITT, intent-to-treat; IV, intravenous; ola, olaparib; OS, overall survival; PC, paclitaxel/carboplatin; po, by mouth; q3w, every 3 weeks; R, randomization; RECIST, Response Evaluation Criteria for Solid Tumors.

Unstratified subgroup analysis of HRD-negative population

Final PFS (predefined)

	Arm 1 CP + B N=216	Arm 2 CP + B + D N=199	Arm 3 CP + B + D + O N=211
Median follow-up,* mo	31.0	34.1	30.2
Events, n (%)	173 (80)	152 (76)	144 (68)
Median,† mo	17.5	15.4	21.1
HR (95% CI) vs Arm 1‡		**0.92** (0.74–1.14)	**0.68** (0.54–0.85)

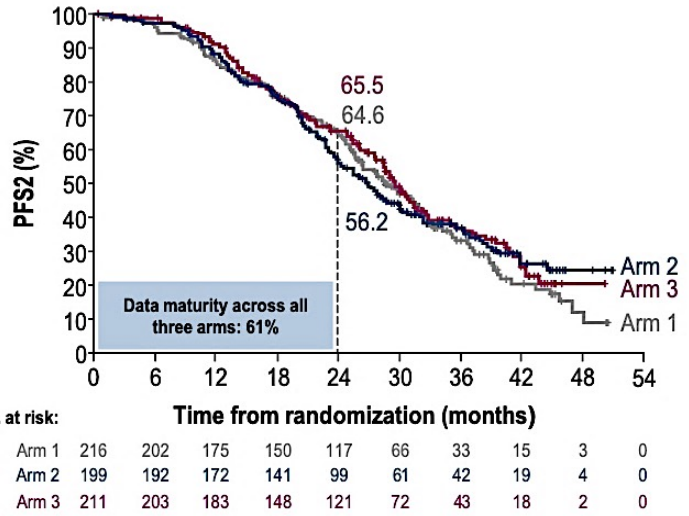


No. at risk:

Arm 1	216	188	135	97	52	30	16	10	3	0	
Arm 2	199	177	120	78	56	37	23	13	3	0	
Arm 3	211	191	146	121	76	47	29	13	2	0	

PFS2 (ad hoc)

	Arm 1 CP + B N=216	Arm 2 CP + B + D N=199	Arm 3 CP + B + D + O N=211
	28.4	33.7	30.2
	133 (62)	124 (62)	124 (59)
	28.6	26.7	29.5
		0.96 (0.75–1.23)	**0.89** (0.70–1.14)

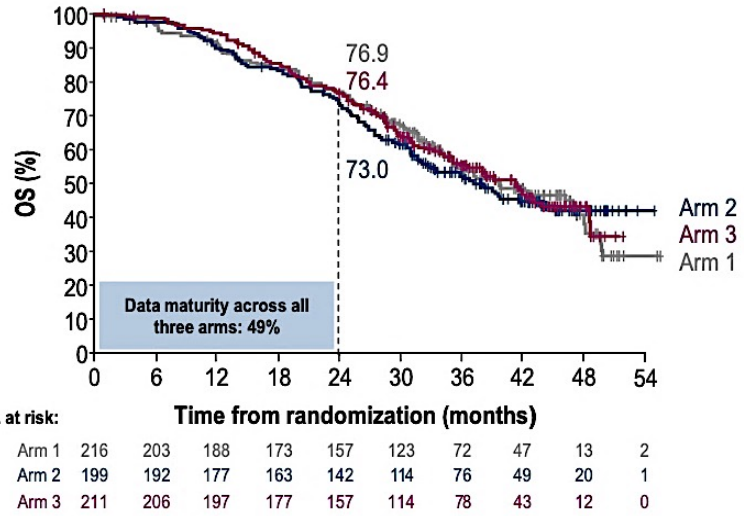


No. at risk:

Arm 1	216	202	175	150	117	66	33	15	3	0	
Arm 2	199	192	172	141	99	61	42	19	4	0	
Arm 3	211	203	183	148	121	72	43	18	2	0	

Interim OS (ad hoc)

	Arm 1 CP + B N=216	Arm 2 CP + B + D N=199	Arm 3 CP + B + D + O N=211
	35.9	41.7	37.2
	103 (48)	103 (52)	101 (48)
	39.6	37.9	41.1
		1.05 (0.80–1.38)	**0.99** (0.76–1.31)



No. at risk:

Arm 1	216	203	188	173	157	123	72	47	13	2	
Arm 2	199	192	177	163	142	114	76	49	20	1	
Arm 3	211	206	197	177	157	114	78	43	12	0	

DCO2 = 18 Sep 2023. *In censored patients; †Medians and rates were estimated by the KM method (medians are unstable in arms with <50% maturity); ‡HRs and CIs were estimated from an unstratified Cox PH model.

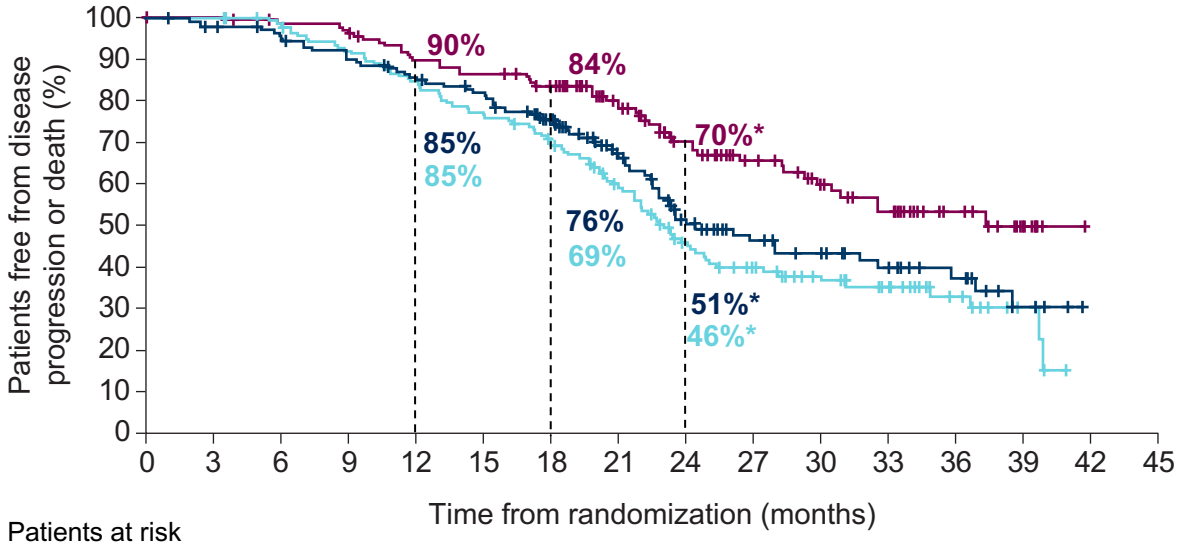
mo, months.

Trillsch F et al, ESMO 2024; Abstract 430.

Durva/Olaparib yielded improved PFS but missing olaparib arm

ANNUAL MEETING ON WOMEN'S CANCER SEATTLE, WA • 2025

Non-tBRCAm HRD-positive

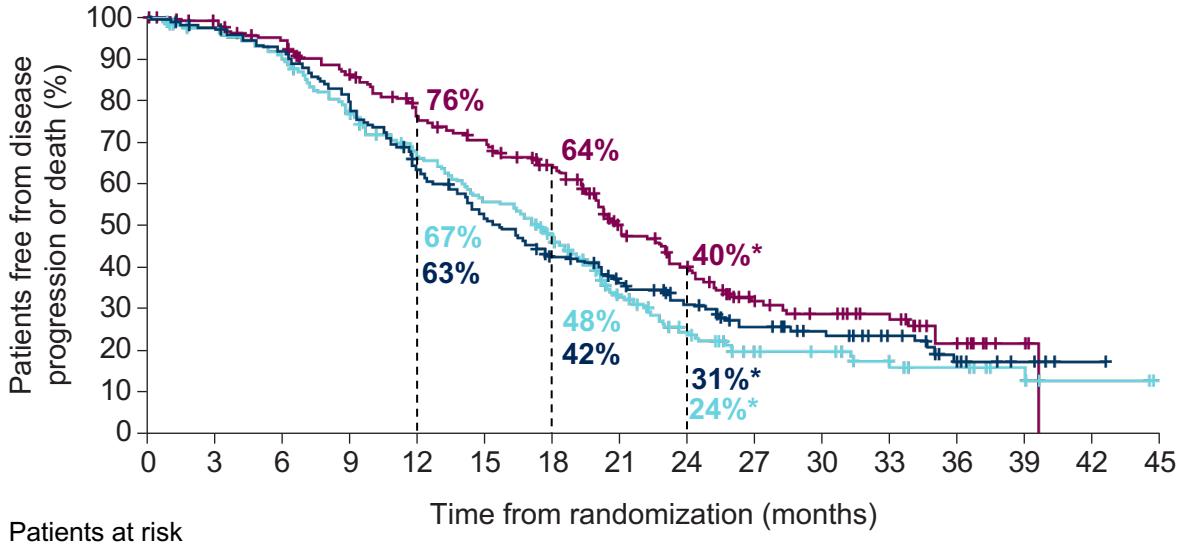


Patients at risk

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

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

HRD-negative



Patients at risk

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

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

- Dr Philipp Harter

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

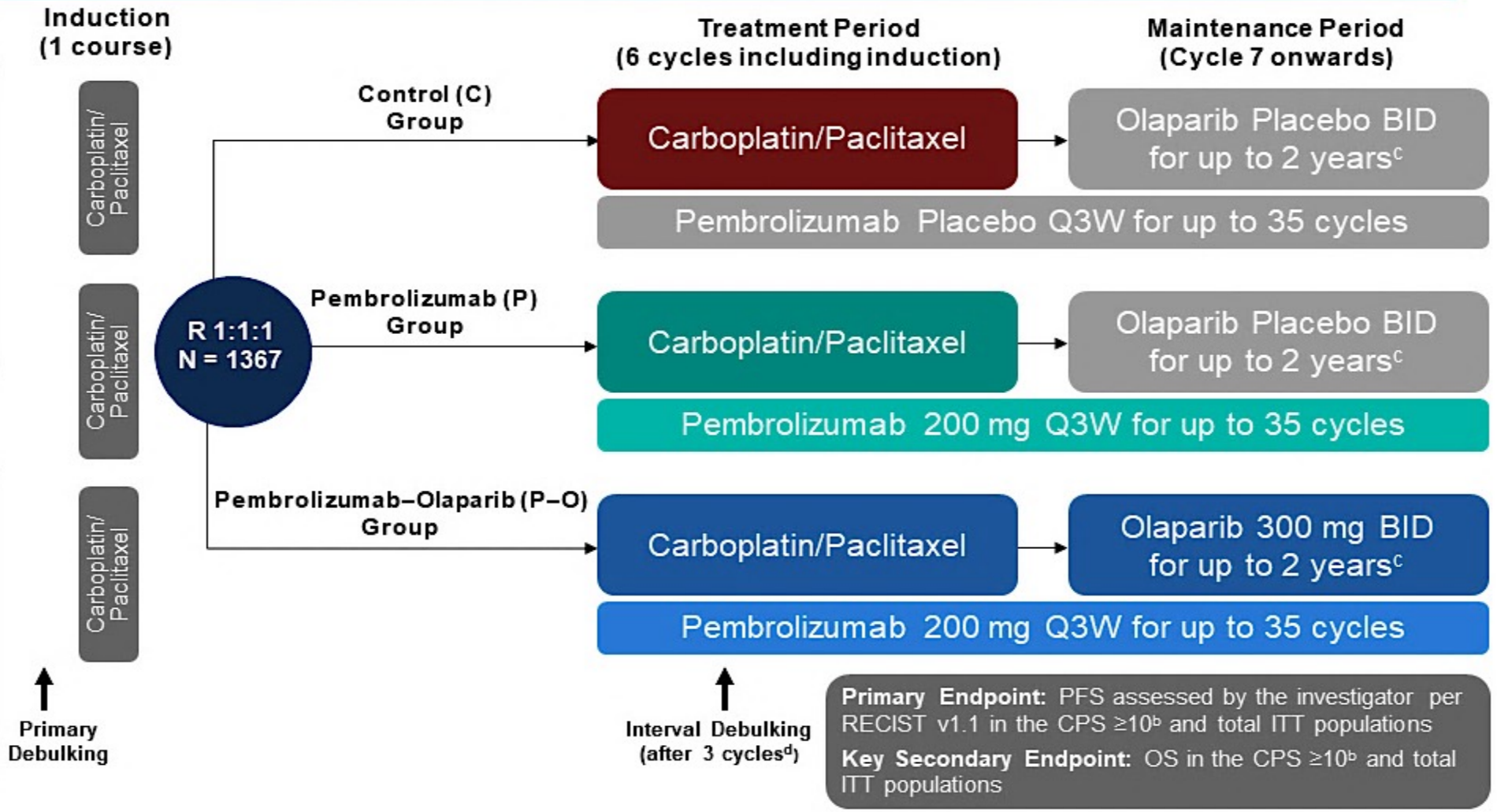
KEYLYNK-001: Chemo + Pembrolizumab + Olaparib

Key Eligibility Criteria

- Advanced (FIGO Stage ≥III) epithelial ovarian cancer
- *BRCA1/2*-nonmutated
- No prior systemic therapy
- Candidate for carboplatin + paclitaxel[a] as adjuvant or neoadjuvant therapy
- Bevacizumab permitted per investigator discretion

Stratification Factors

- PD-L1 expression[b] (CPS ≥10 vs <10)
- Planned bevacizumab use (yes vs no)
- Surgery status (no residual tumor [R0] after primary debulking vs residual tumor [R1] after primary debulking vs planned interval debulking)



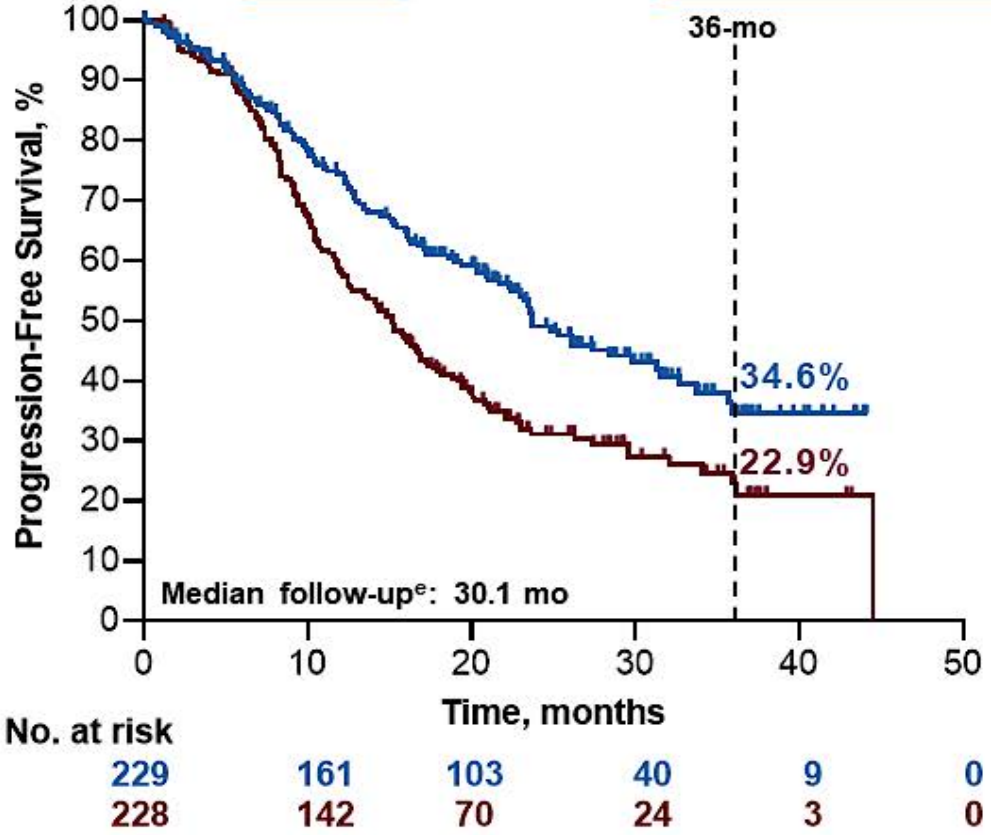
Primary Endpoint: PFS assessed by the investigator per RECIST v1.1 in the CPS ≥10[b] and total ITT populations

Key Secondary Endpoint: OS in the CPS ≥10[b] and total ITT populations

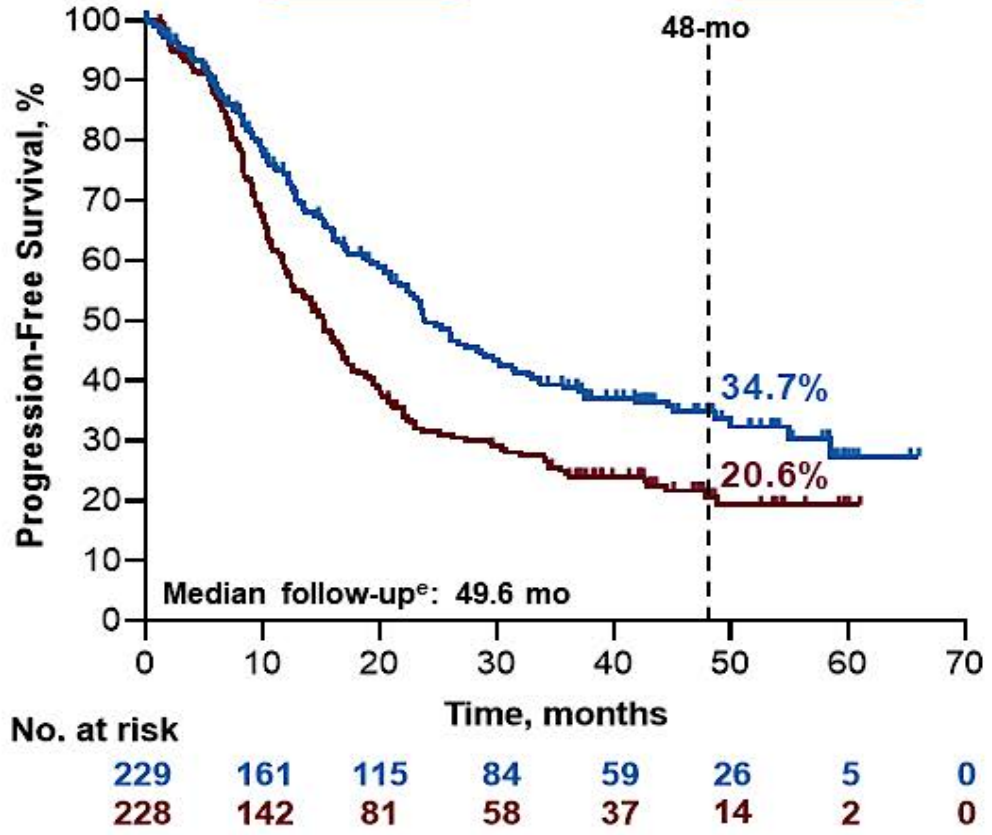
[a]Docetaxel may be considered for participants who experience either a severe hypersensitivity reaction to paclitaxel or an adverse event requiring discontinuation of paclitaxel. [b]Assessed at a central laboratory using PD-L1 IHC 22C3 pharmDx and measured using the combined positive score (CPS; number of PD-L1–positive tumor cells, lymphocytes, and macrophages divided by total number of tumor cells x 100). [c]Only participants with no evidence of disease at start of maintenance and no progression stopped after 2 years. [d]Including induction cycle.

H1: Progression-Free Survival P–O vs C, CPS ≥10 Population at IA1 and FA

IA1[a]	Median, months	Events	HR (95% CI)	*P*-value
P–O Group	23.7	48.9%	0.63[c] (0.49-0.80)	<0.0001[d]
C Group	15.2	66.2%		



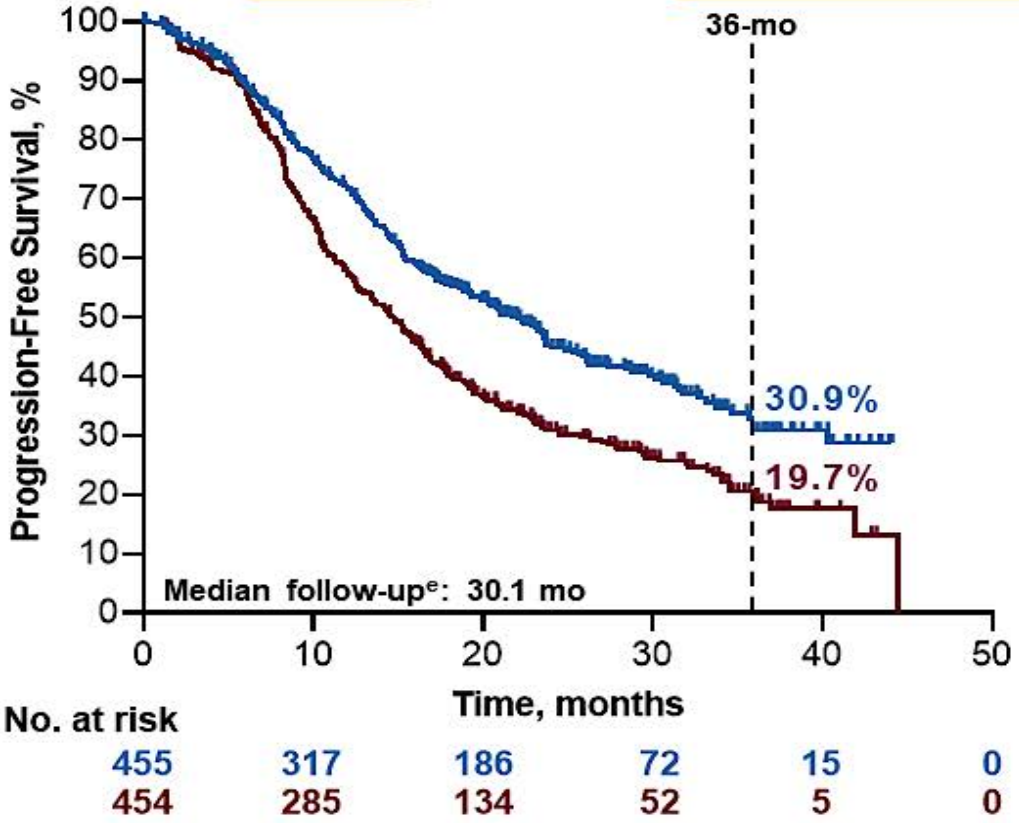
FA[b]	Median, months	Events	HR (95% CI)
P–O Group	23.9	58.5%	0.66[c] (0.53-0.83)
C Group	15.2	72.4%	



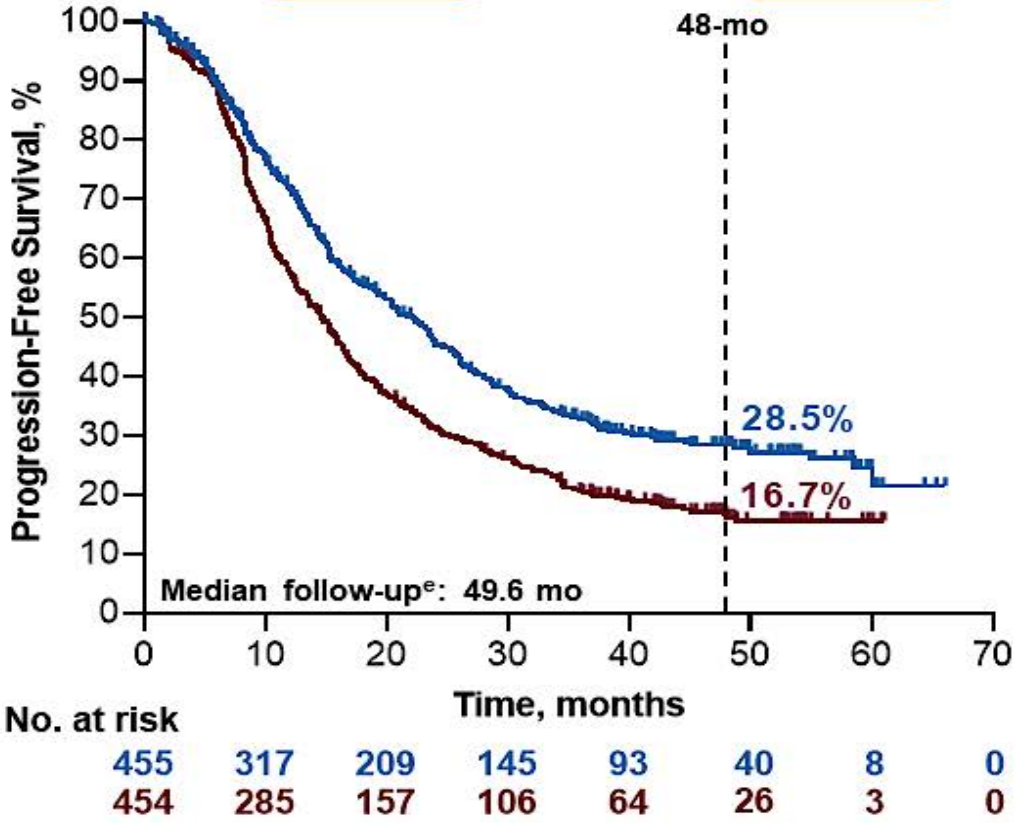
Response assessed per RECIST v1.1 by investigator review. [a]Data cutoff date: January 9, 2023. [b]Data cutoff date: August 26, 2024. [c]Hazard ratio (CI) analyzed based on a Cox regression model with treatment as a covariate stratified by the randomization stratification factors. [d]Prespecified *P*-value boundary met. [e]Defined as the time from randomization to the data cutoff date.

H2: Progression-Free Survival P–O vs C, Total ITT Population at IA1 and FA

IA1[a]	Median, months	Events	HR (95% CI)	*P*-value
P–O Group	22.1	53.0%	0.68[c] (0.58-0.81)	<0.0001[d]
C Group	14.6	69.2%		

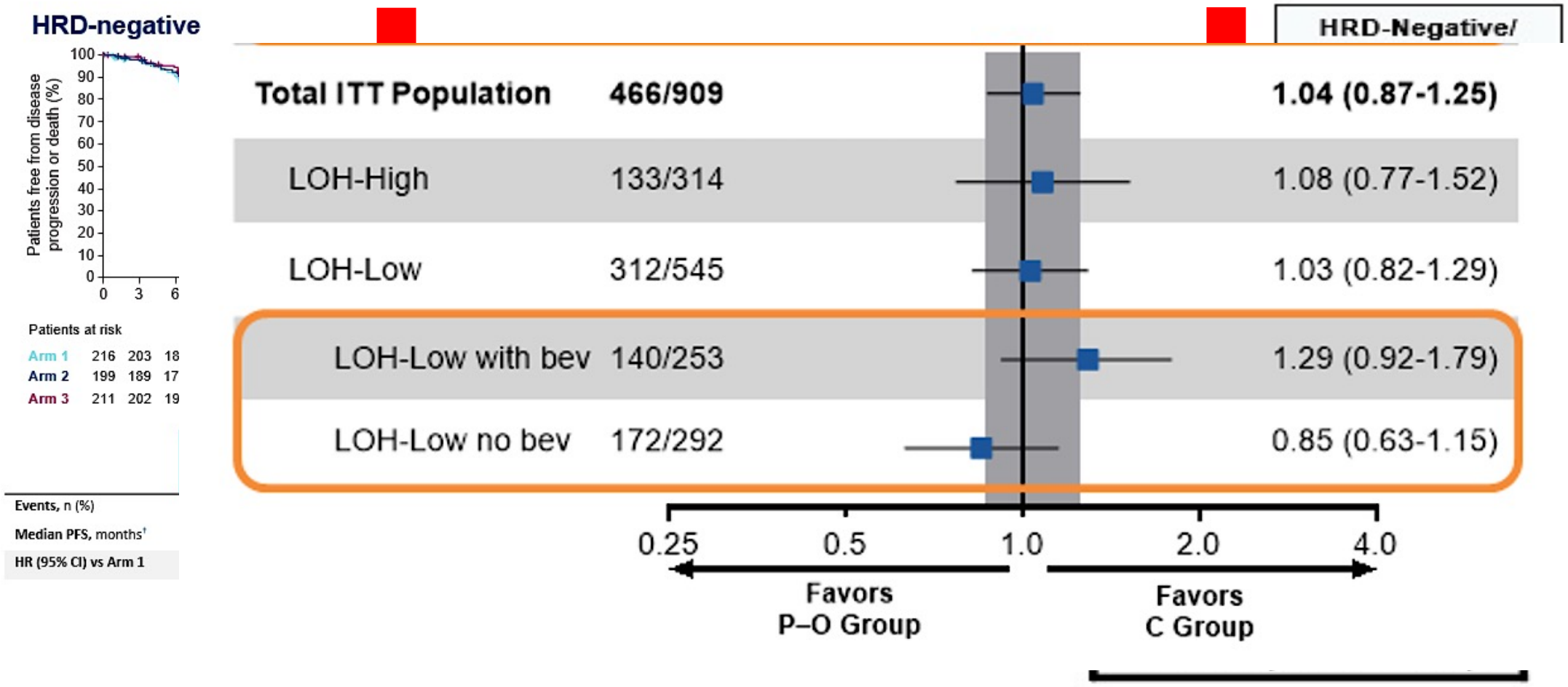


FA[b]	Median, months	Events	HR (95% CI)
P–O Group	22.2	64.0%	0.71[c] (0.61-0.84)
C Group	14.6	77.5%	



Response assessed per RECIST v1.1 by investigator review. [a]Data cutoff date: January 9, 2023. [b]Data cutoff date: August 26, 2024. [c]Hazard ratio (CI) analyzed based on a Cox regression model with treatment as a covariate stratified by the randomization stratification factors. [d]Prespecified *P*-value boundary met. [e]Defined as the time from randomization to the data cutoff date.

DUO-O vs KEYLYNK-001 vs PAOLA-1: PFS in BRCAwt/HRD test neg



Slide modified from K. Moore

Questions from Gynecologic Oncologists and General Medical Oncologists

- **Regulatory/reimbursement issues aside, which patients, if any, would you treat in the primary setting with carboplatin/paclitaxel + PARP + IO + bevacizumab?**
- **How do you sequence your biomarker testing to be logistically/ economically sound? Send germline testing, then HRD, then NGS? Or just NGS directly?**
- **What maintenance approach would you recommend for a patient with a germline PALB2 mutation? Do you treat these as essentially equivalent to BRCA?**

Questions from Gynecologic Oncologists and General Medical Oncologists

- **A 47 yo patient w/ Stage IIIC OC undergoes optimal debulking → carboplatin/paclitaxel x 6. Germline and somatic testing returns negative for BRCA but positive for HRD. Given OS data from PAOLA-1 versus PRIMA, what is the optimal maintenance strategy?**
  - **A) Give her niraparib**
  - **B) Start her on bevacizumab so that you can give her olaparib**
  - **C) Assume that the OS in PAOLA-1 was driven by olaparib and give olaparib alone**
- **How do you incorporate KELIM score into decisions regarding PARP inhibitor maintenance in the up-front setting?**

RTP RESEARCH TO PRACTICE

Questions from Gynecologic Oncologists and General Medical Oncologists

- 49-year-old female with Stage IIIC clear cell ovarian cancer who is BRCA and HRD-negative, completed 6 cycles of chemotherapy plus bevacizumab. What would you recommend as maintenance treatment? Do you recommend PARP in HRD-negative patients? Is there a subset of HRD-negative patients who benefit from PARP maintenance (eg, suboptimal cytoreduction, Stage IV)?
- When should we incorporate bevacizumab as a component of up-front treatment? For patients who receive carboplatin/paclitaxel without bevacizumab, is there any data to support a PARPi + bev as maintenance?

Agenda

Module 1: Up-Front Treatment for Advanced Ovarian Cancer (OC) — Dr Westin

Module 2: Management of Relapsed/Refractory OC — Dr Secord

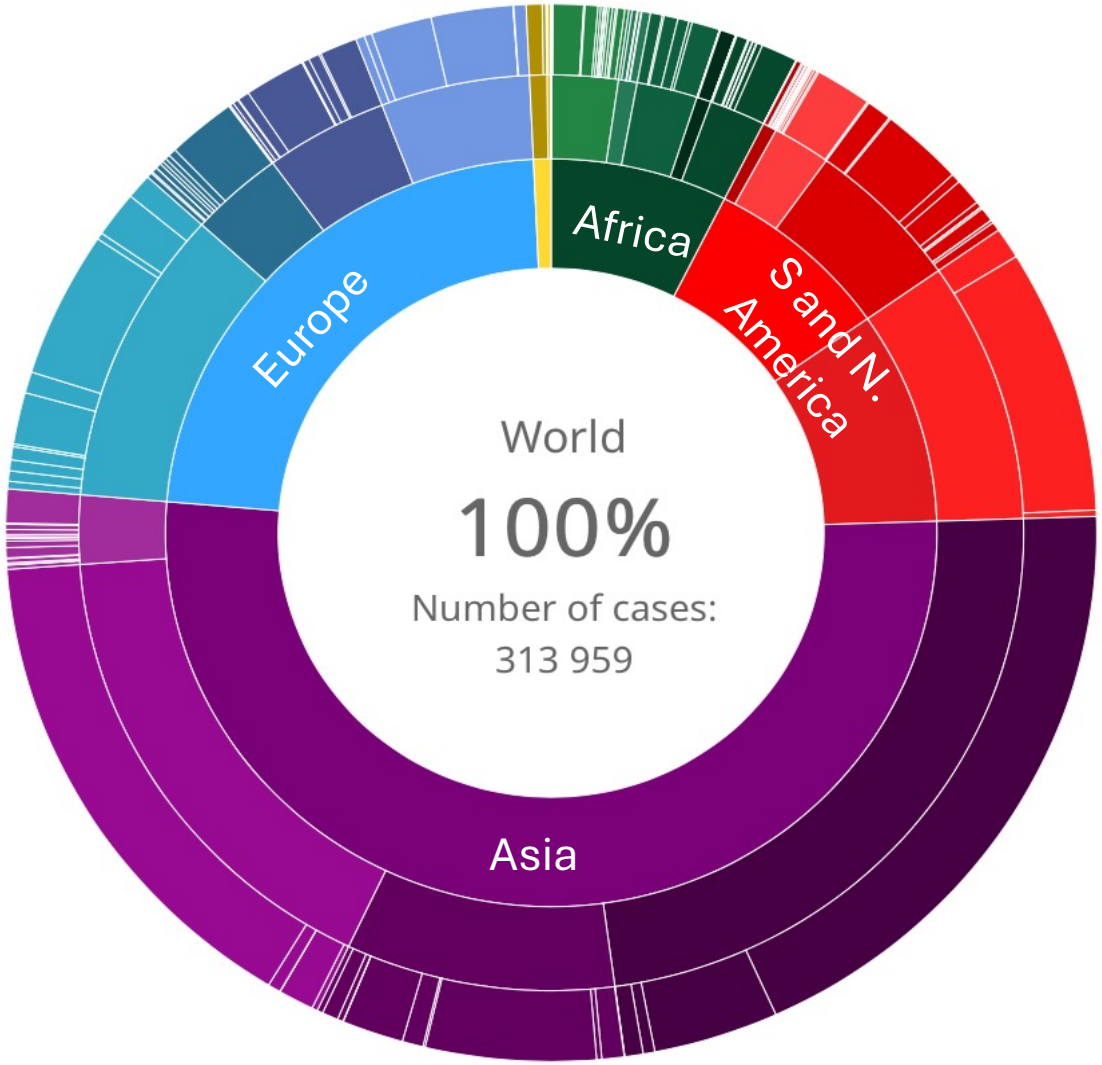
Module 3: Novel Investigational Therapies for Advanced OC — Dr Moore

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

Management of Relapsed/Refractory Epithelial Ovarian Cancer

Angeles Alvarez Secord, MD, MHS
Director of Gyn Onc Clinical Trials
Division of Gynecologic Oncology
Duke Cancer Institute
Department of Obstetrics & Gynecology
Duke University Health System

Objectives – Recurrent Epithelial Ovarian Cancer



- **Describe prevalence and clinical relevance** of *BRCA* alterations, HRD status, FRα-positive expression, and HER2-overexpression in relapsed ovarian cancer
  - Discuss optimal approach to tumor testing
- **Review the clinical utility** of PARP inhibitors, FRα- and HER2- targeting antibody drug conjugates
- **Summarize the current landscape** of clinical trials evaluating FRα- and HER2-targeting ADCs in recurrent epithelial ovarian cancer

Globocan accessed May 2022

The changing landscape in the management of epithelial ovarian cancer over four decades

2003

1990s – The Taxane Era

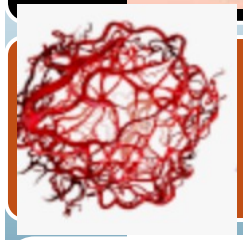
- Taxane platinum chemotherapy improves survival outcomes becomes standard of care.

2006

2000s – IP Therapy

- Intraperitoneal therapy becomes a standard of care; limited due to toxicity and administration challenges

2011



2011 – Antiangiogenic therapy

- Bevacizumab improved PFS versus chemotherapy alone; selective use.

2018

2014-Beyond – The Era of PARP inhibitors and personalized therapy

- 2014 approved for patients with BRCA mutations
- 2018 front-line therapy for patients
- ADC and targeted directed therapies

Olaparib	**SOLO-1** *NCT01844986*	**Niraparib**	**PRIMA** *NCT02655016*	**Olaparib + bevacizumab**	**PAOLA-1** *NCT02477644*	**Rucaparib**	**ATHENA-MONO** *NCT03522246*

McGuire WP, et al. *N Engl J Med* 1996; Armstrong, D, et al. *N Engl J Med* 2006; du Bois A, et al. *J Natl Cancer Inst* 2003; Burger RA, et al. *N Engl J Med* 2011; Perren TJ, et al. *N Engl J Med* 2011; Moore K, et al. *N Engl J Med* 2018; Gonzalez-Martin A *N Engl J Med.* 2019; Ray-Coquard I et al. *N Engl J Med* 2019; Monk JM, et al. *J Clin Oncol* 2022.

Role of IO therapy in front-line epithelial ovarian cancer

FIRST Study Design

20 December 2024

The manufacturer announces FIRST trial met its primary endpoint of progression free survival In first line advanced ovarian cancer

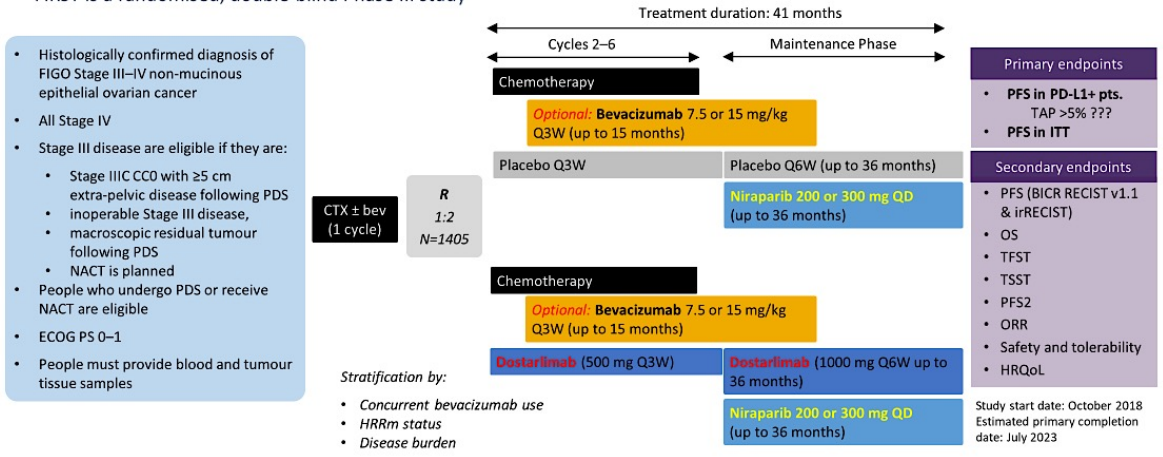
KEYLYNK-001 Study Design | non-BRCAm

The manufacturer announces Phase 3 KEYLYNK-001 Trial Met Primary Endpoint of Progression-Free Survival (PFS) in Patients With Advanced Epithelial Ovarian Cancer

December 9, 2024 6:45 am ET

FIRST Study Design

FIRST is a randomised, double-blind Phase III study

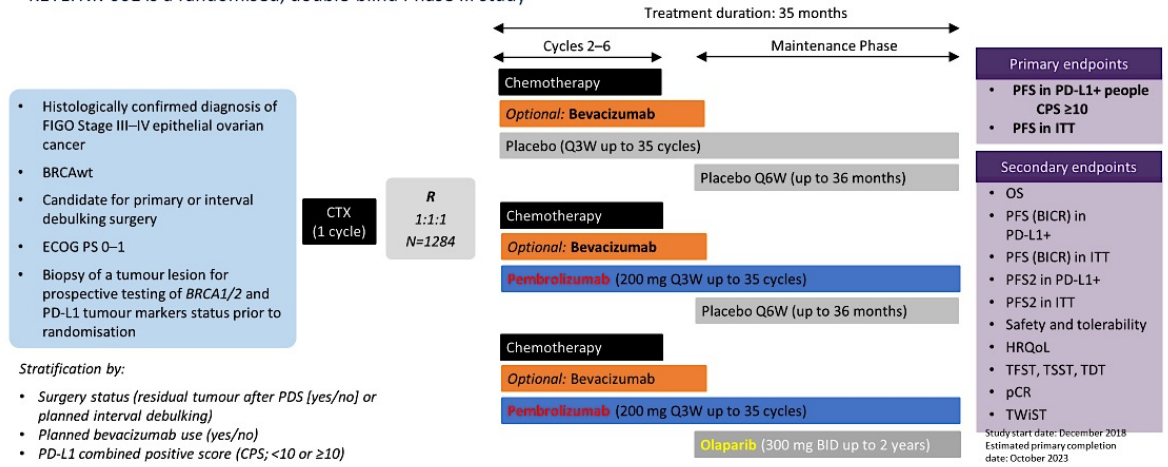


Bev=bevacizumab; BICR=blinded independent central review; CC=complete cytoreductive; CTX=chemotherapy; ECOG PS=Eastern Cooperative Oncology Group performance status; FIGO=International Federation of Gynecology and Obstetrics; HRRm=homologous recombination repair mutation; HRQoL=health-related quality of life; (ir)RECIST=(immune-related) Response Evaluation Criteria in Solid Tumors; ITT=intent-to-treat; NACT=neoadjuvant chemotherapy; ORR=overall response rate; OS=overall survival; PD-L1=programmed death ligand 1; PDS=primary debulking surgery; PFS=progression-free survival; PFS2=time to progression on subsequent therapy; Q3W=every 3 weeks; Q6W=every 6 weeks; QD=once daily; R=randomised; TFST=time to first subsequent therapy; TSST=time to start of second subsequent therapy or death.

1. FIRST. Available at: https://clinicaltrials.gov/ct2/show/NCT03602859. Accessed November 2022.

KEYLYNK-001 Study Design | non-BRCAm

KEYLYNK-001 is a randomised, double-blind Phase III study



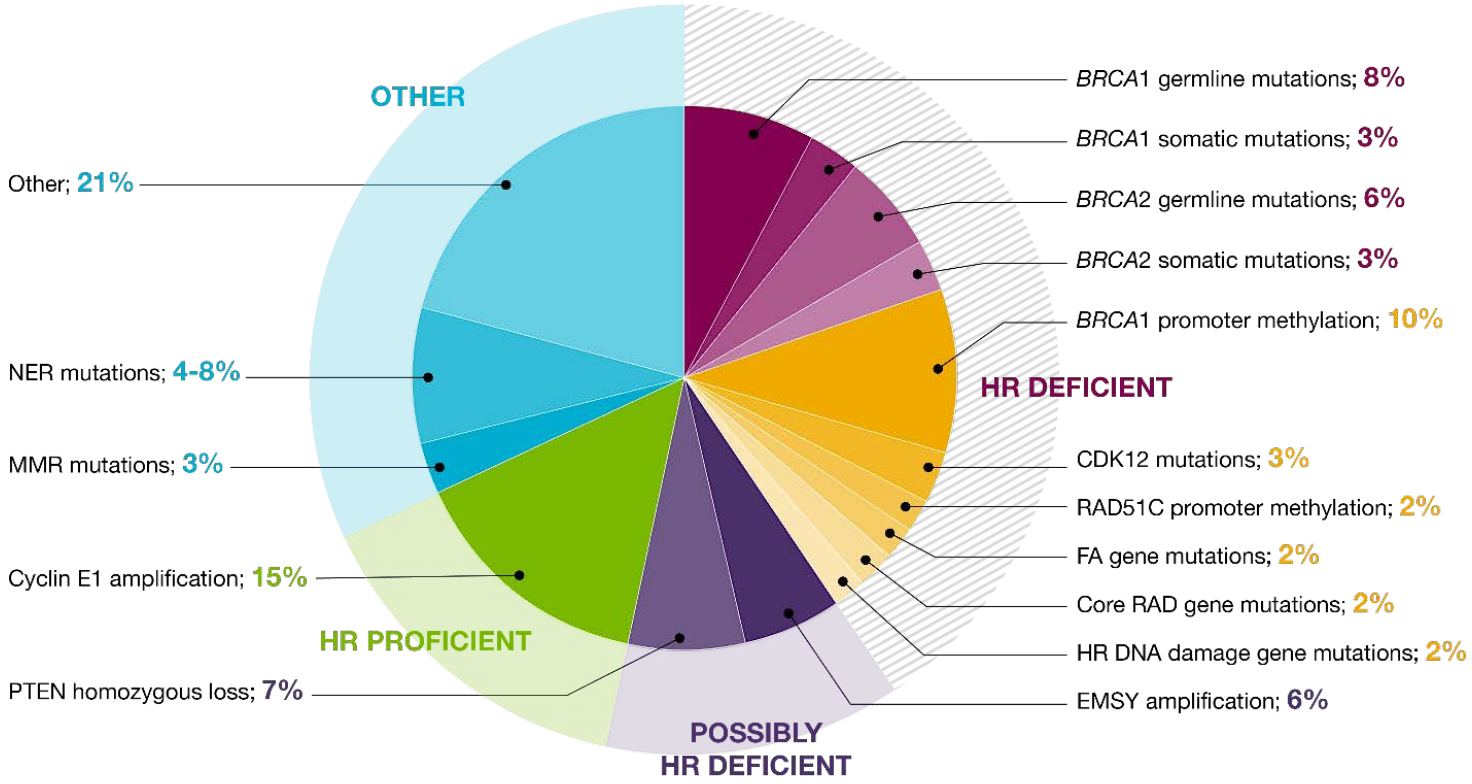
aOC=advanced ovarian cancer; BICR=blinded independent central review; BID=twice daily; BRCAm=BRCA mutated; CPS=combined positive score; CTX=chemotherapy; ECOG PS=Eastern Cooperative Oncology Group performance status; FIGO=International Federation of Gynecology and Obstetrics; HRQoL=health-related quality of life; ITT=intent-to-treat; OS=overall survival; pCR=pathological complete response; PD-L1=programmed death ligand 1; PDS=primary debulking surgery; PFS=progression-free survival; PFS2=time to progression on subsequent therapy; R=randomised; TDT=time to treatment discontinuation; TFST=time to first subsequent therapy; TSST=time to start of second subsequent therapy or death; TWiST=time without symptoms of disease progression or toxicity; Q3W=every 3 weeks; Q6W=every 6 weeks

1. KEYLYNK-001. Available at: https://clinicaltrials.gov/ct2/show/NCT03740165. Accessed November 2022; 2. Fujiwara K, et al. *Ann Oncol*. 2019;30(suppl_9):ix77–ix90.

Recurrent ovarian cancer: The role of biomarkers

Genetic and HRD testing

These defects can be identified using different clinical and molecular biomarkers



Clinical Implications:

Approximately 50% High Grade Epithelial Ovarian Cancers Characterized by HRD

Is this targetable in recurrent epithelial ovarian cancer?

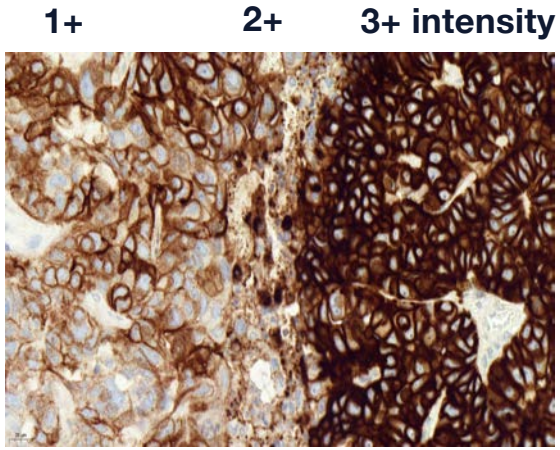
Konstantinopoulos PA, et al. *Cancer Discov*. 2015

Recurrent ovarian cancer: The role of biomarkers FRα Testing

PS2+ Scoring

Determined by staining intensity and percentage of tumor cells staining at 0, 1+, 2+, or 3+

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



Mirv FDA approved treatment for PROC patients whose tumors express ≥75% viable cells 2+ and/or 3+ staining.

10X Scoring

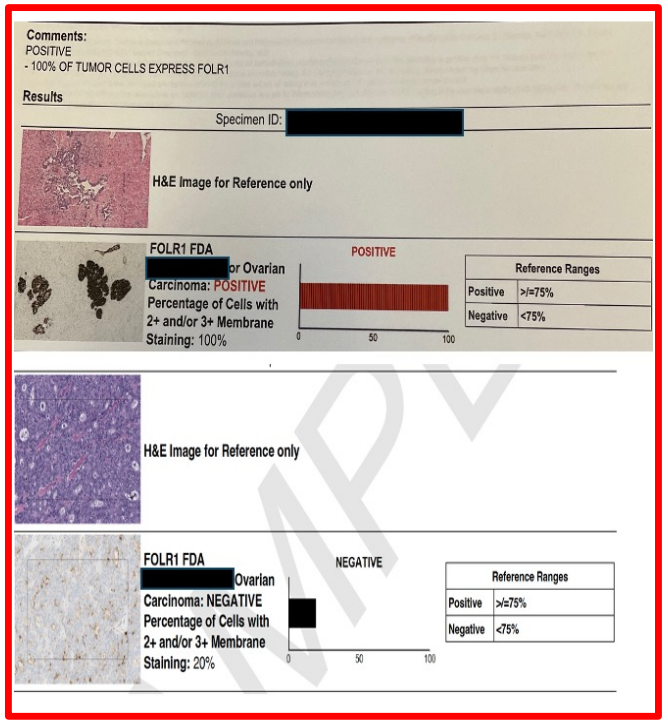
Simplified scoring method based on % cells with membrane staining by ≤10X magnification, without regard to intensity

10X Scoring
Positive: ≥ 50% of tumor cells with FRα membrane staining visible at 10X microscope objective

TPS Scoring

A scoring paradigm based on the % of cells with any intensity expression.

Simple and straightforward interpretation. Does not require differentiation between staining intensity. TPS >25% was selected for further analysis in STRO-002 studies.



FRα expression upregulated in cancers.

- Expressed in ~80-90% of ovarian carcinomas
- ~ 35-40% with high levels of FRα
- FRα expression associated with worse outcomes

Moore KN et al. ESMO. 2019; Oaknin A et al. ASCO 2023; Chen YL, et al. *Mol Oncol* 2012

Recurrent ovarian cancer: The role of biomarkers

HER2 Scoring

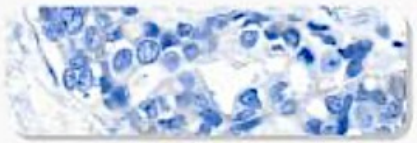
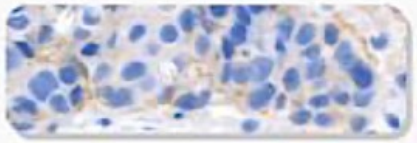
- Highest in mucinous carcinomas (25%); mixed-type carcinomas (11.9%), clear cell carcinomas (4%), serous papillary carcinomas (3%), and endometrioid carcinomas (2.1%); Amplification: 14%.
- HER2 expression associated with worse PFS and OS
- In GOG160, a phase II trial evaluating trastuzumab in patients with recurrent or refractory ovarian cancer had ORR of 7.3 % in patients with HER2 overexpression (n=41)

HER2	Breast (ASCO/CAP 2007)	Breast (ASCO/CAP 2013; 2018*)	Gastric (ASCO/CAP 2016)	Colorectal (HERACLES trial)
IHC 3+	>30% strong, uniform, complete	>10% circumferential, strong, complete	≥10%, strong complete or basolateral/lateral	≥50% strong, complete or basolateral/lateral
FISH amplification	HER2/CEPT17 ratio >2.2 Patients with HER2/CEPT17 ratio 2-2.2 eligible	HER2/CEPT17 ratio ≥2.0 OR ratio <2.0 and HER2 signal ≥6.0/nucleus *(if IHC 2+ or 3+)	HER2/CEPT17 ratio ≥2.0 OR ratio <2.0 and HER2 signal ≥6.0/nucleus	HER2/CEPT17 ratio ≥2.0 in ≥50% of cells

Lassus H et al. *Gynecol Onc* 2004; McCaughan H et al. *J Clin Pathol* 2012; Hale RJ et al. *Int J Gynecol Pathol* 2013; Bellone S et al. *J Clin Pathol* 2003; Ersoy E et al. *Gyn Path* 2022

Standardized pathology report for HER2 testing in compliance with 2023 ASCO/CAP updates and 2023 ESMO consensus statements on HER2-low breast cancer

Spectrum of HER2 positivity according to ASCO/CAP guidelines

	IHC score	HER2 test intepretation	HER2 status
	0	No staining or incomplete and faint/barely perceptible membrane staining ≤10% of tumor cells	Negative
	1+	Incomplete and faint/barely perceptible membrane staining in >10% of tumor cells	Low
	2+	Weak-moderate complete membrane staining in >10% of tumor cells OR intense membrane staining in ≤10% of tumor cells	NO ISH amplification? YES
	3+	Complete and intense membrane staining in >10% of tumor cells	Positive

Ivanova M et al. Virchows Arch. 2023

Recurrent ovarian cancer: Role of HRD, FRα and HER2 Testing

HER2 expression is higher in mucinous and clear cell histologic subtypes

p=0.003

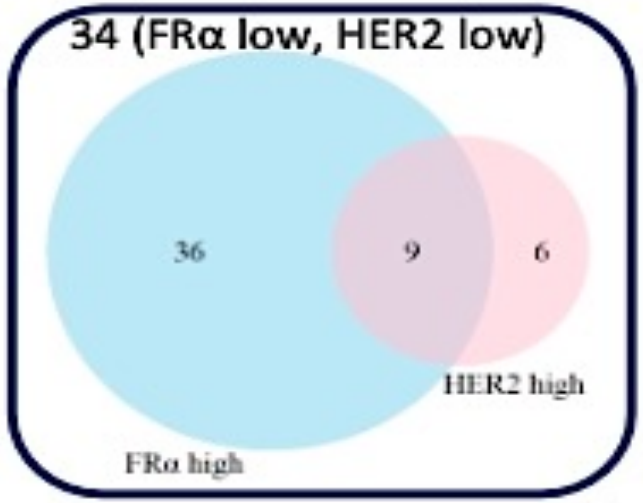
HER2	HGSC	Endometrioid	Clear cell	Mucinous	Others
0	204 (63.0%)	8 (66.7%)	12 (36.4%)	5 (33.3%)	17 (65.4%)
1+	66 (18.3%)	3 (25.0%)	7 (21.2%)	2 (13.3%)	2 (7.7%)
2+	43 (13.4%)	1 (8.3%)	11 (33.3%)	4 (26.7%)	6 (23.1%)
3+	19 (5.3%)	0 (0.0%)	4 (9.1%)	4 (26.7%)	1 (3.8%)
Total	332	12	34	15	26

HER2 expression is higher in patients with *BRCA*m and HRD status in HGSOC and HGEOC

p=0.006

HER2	HRp	BRCAm/HRD
0/1+	55 (94.8%)	115 (79.3%)
2+/3+	3 (5.2%)	30 (20.7%)
Sum	58	145

*FRα high: > 75%
HER2 high: 3+



Lee D, ESMO 2024;Abstract 765P

Recurrent ovarian cancer: Role of HRD, FRα and HER2 Testing

High-Grade Serous and High-Grade Endometrioid

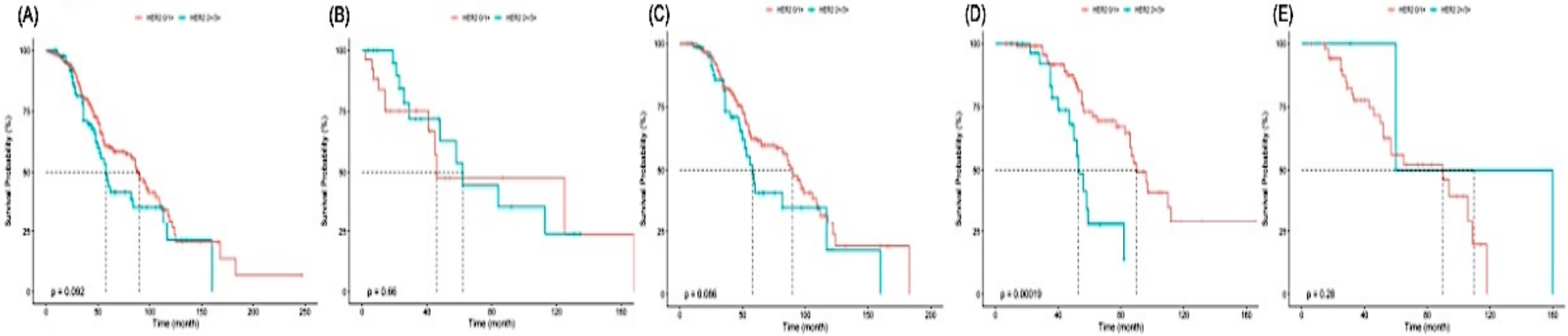
All Histologies

Clear Cell & Mucinous

All Patients

*BRCA*m/HRD status

HRP status



- High HER2 (2-3+) is associated with worse overall survival outcomes in patients with HGSOC and HGEOC characterized by *BRCA*m/HRD status
- Data support targeting HER2 in patients with clear cell/mucinous, and *BRCA*m/HRD+ HGSOC/HGEOC

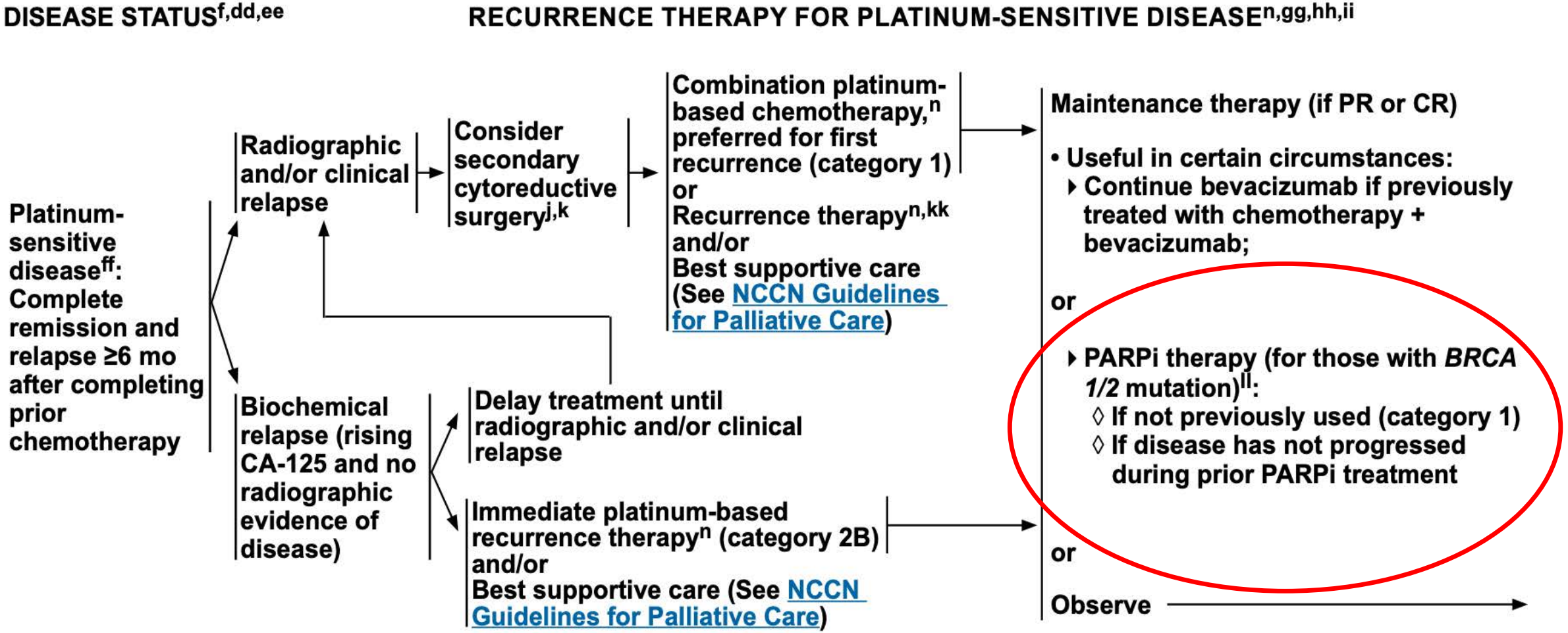
HER2 *2-3+*

HER2 *0-1+*

Lee D, ESMO 2024;Abstract 765P

National Comprehensive Cancer Network®

NCCN Guidelines Version 1.2025
Epithelial Ovarian Cancer/Fallopian Tube Cancer/ Primary Peritoneal Cancer



www.nccn.org accessed March 9, 2025

NCCN Guidelines Version 1.2025
Epithelial Ovarian Cancer/Fallopian Tube Cancer/ Primary Peritoneal Cancer

PRINCIPLES OF SYSTEMIC THERAPY
Acceptable Recurrence Therapies for Epithelial Ovarian (including LCOC)[o]/Fallopian Tube/Primary Peritoneal Cancer

Recurrence Therapy for Platinum-Sensitive Disease[p] (alphabetical order)

Preferred Regimens	Other Recommended Regimens[s]	Useful in Certain Circumstances
Carboplatin/ gemcitabine[14] ± bevacizumab[q,r,15] Carboplatin/liposomal doxorubicin[16] ± bevacizumab[q,17] Carboplatin/paclitaxel[g,18] ± bevacizumab[q,r,19] Cisplatin/gemcitabine[20] Targeted Therapy (single agents) Bevacizumab[q,21,22]	Capecitabine Carboplatin[14] Carboplatin/docetaxel[23,24] Carboplatin/paclitaxel (weekly)[g,25] Cisplatin[18] Cyclophosphamide Doxorubicin Ifosfamide Irinotecan Melphalan Oxaliplatin Paclitaxel Paclitaxel, albumin bound Pemetrexed Vinorelbine Targeted Therapy Niraparib/bevacizumab (category 2B)[q,26] Niraparib (category 3)[t,27] Olaparib (category 3)[u,28] Pazopanib (category 2B)[29] Rucaparib (category 3)[v,30] Hormone Therapy Aromatase inhibitors (anastrozole, exemestane, letrozole) Goserelin acetate Leuprolide acetate Megestrol acetate Tamoxifen[j]	For mucinous carcinoma: • 5-FU/leucovorin/oxaliplatin ± bevacizumab (category 2B for bevacizumab)[q] • Capecitabine/oxaliplatin ± bevacizumab (category 2B for bevacizumab)[q] Carboplatin/paclitaxel (for age >70)[g,w] Carboplatin/paclitaxel, albumin bound (for confirmed taxane hypersensitivity) Irinotecan/cisplatin (for clear cell carcinoma)[31] Targeted Therapy[x] Dabrafenib + trametinib (for *BRAF* V600E-positive tumors)[32] Entrectinib[33] or larotrectinib[34] or repotrectinib[35] (for *NTRK* gene fusion-positive tumors) Fam-trastuzumab deruxtecan-nxki (for HER2-positive tumors [IHC 3+ or 2+])(category 2B)[36] Mirvetuximab soravtansine-gynx[y] (for FRα-expressing tumors [≥75% positive tumor cells])[37] Mirvetuximab soravtansine-gynx/bevacizumab[q] (for FRα-expressing tumors [≥50% positive tumor cells]) (category 2B)[38] Selpercatinib (for *RET* gene fusion-positive tumors)[39] For low-grade serous carcinoma: • Trametinib[40] • Binimetinib (category 2B)[41,42] Hormone Therapy Fulvestrant (for low-grade serous carcinoma) Immunotherapy[x] Dostarlimab-gxly (for dMMR/MSI-H recurrent or advanced tumors)[43] Pembrolizumab (for MSI-H or dMMR solid tumors, or patients with TMB-H tumors ≥10 mutations/megabase)[44]

www.nccn.org accessed March 9, 2025

NCCN Guidelines Version 1.2025
Epithelial Ovarian Cancer/Fallopian Tube Cancer/ Primary Peritoneal Cancer

PRINCIPLES OF SYSTEMIC THERAPY

Recurrence Therapy for Platinum-Resistant Disease (alphabetical order)

Preferred Regimens

Cytotoxic Therapy
- Cyclophosphamide (oral)/ bevacizumab[q,45]
- Docetaxel[46]
- Etoposide (oral)[47]
- Gemcitabine[48,49]
- Liposomal doxorubicin[48,49]
- Liposomal doxorubicin/ bevacizumab[q,50]
- Paclitaxel (weekly)[g,51]
- Paclitaxel (weekly)/ bevacizumab[g,q,50]
- Topotecan[52,53]
- Topotecan/bevacizumab[q,50]

Targeted Therapy (single agents)
- Bevacizumab[q,21,22]
- Mirvetuximab soravtansine-gynx (for FRα-expressing tumors [≥75% positive tumor cells])(category 1)[x,54,55]

Other Recommended Regimens

Cytotoxic Therapy[s]
- Capecitabine
- Carboplatin[*]
- Carboplatin/docetaxel[*]
- Carboplatin/paclitaxel (weekly)[g,*]
- Carboplatin/gemcitabine[14] ± bevacizumab[q,r,15,*]
- Carboplatin/liposomal doxorubicin[16] ± bevacizumab[q,17,*]
- Carboplatin/paclitaxel[g,18] ± bevacizumab[q,r,19,*]
- Cyclophosphamide
- Cyclophosphamide (oral)/pembrolizumab/bevacizumab[57,58]
- Doxorubicin
- Gemcitabine/bevacizumab[59]
- Gemcitabine/cisplatin[20,*]
- Ifosfamide
- Irinotecan
- Ixabepilone/bevacizumab (category 2B)[z,60]
- Melphalan
- Oxaliplatin
- Paclitaxel
- Paclitaxel, albumin bound
- Pemetrexed
- Sorafenib/topotecan[56]
- Vinorelbine

Targeted Therapy (single agents)
- Niraparib (category 3)[t,27]
- Olaparib (category 3)[u,28]
- Pazopanib (category 2B)[29]
- Rucaparib (category 3)[v,30]

Hormone Therapy
- Aromatase inhibitors (anastrozole, exemestane, letrozole)
- Goserelin acetate
- Leuprolide acetate
- Megestrol acetate
- Tamoxifen[j]

Useful in Certain Circumstances

- Carboplatin/paclitaxel (for age >70)[g,w,*]
- Carboplatin/paclitaxel, albumin bound (for confirmed taxane hypersensitivity)[*]

Immunotherapy[x]
- Dostarlimab-gxly (for dMMR/MSI-H recurrent or advanced tumors)[43]
- Pembrolizumab (for patients with MSI-H or dMMR solid tumors, or TMB-H tumors ≥10 mutations/megabase)[44]

Hormone Therapy
- Fulvestrant (for low-grade serous carcinoma)

Targeted Therapy[x]
- Dabrafenib + trametinib (for *BRAF* V600E-positive tumors)[32]
- Entrectinib[33] or larotrectinib[34] or repotrectinib[35] (for *NTRK* gene fusion-positive tumors)
- Fam-trastuzumab deruxtecan-nxki (for HER2-positive tumors [IHC 3+ or 2+])[36]
- Mirvetuximab soravtansine-gynx/bevacizumab (for FRα-expressing tumors [≥25% positive tumor cells])[q,38,61,62]
- Selpercatinib (for *RET* gene fusion-positive tumors)[39]

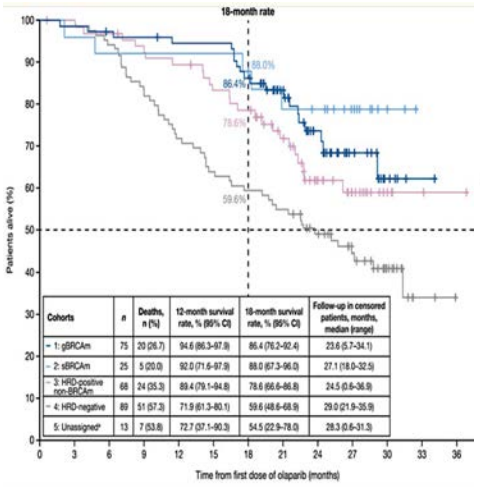
For low-grade serous carcinoma:
- Trametinib[40]
- Binimetinib (category 2B)[41,42]

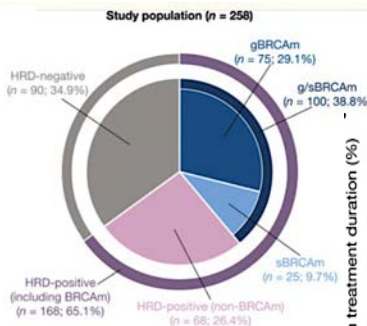
For mucinous carcinoma:
- FOLFIRI ± bevacizumab (category 2B)[63-66]

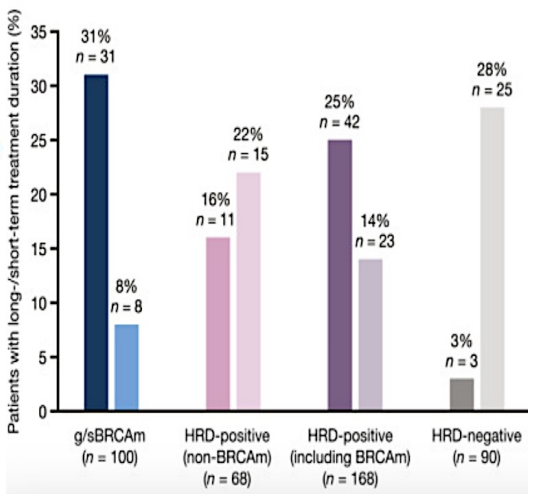
www.nccn.org accessed March 9, 2025

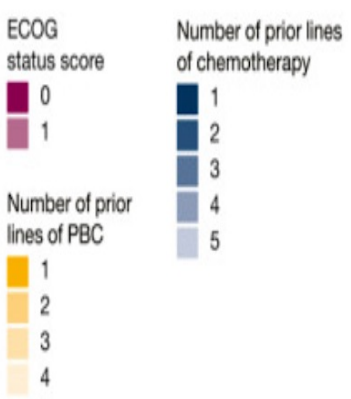
PARP inhibitors in Recurrent Ovarian Cancer

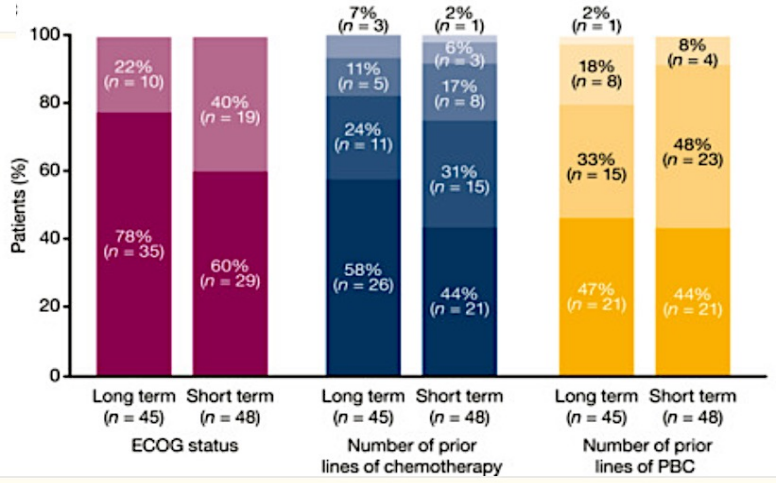
LIGHT Phase II Trial





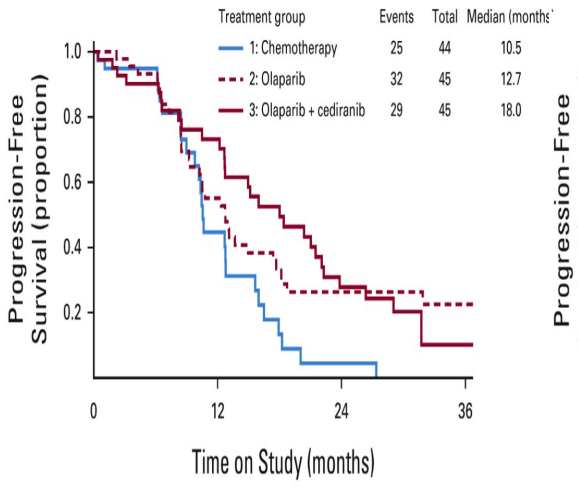




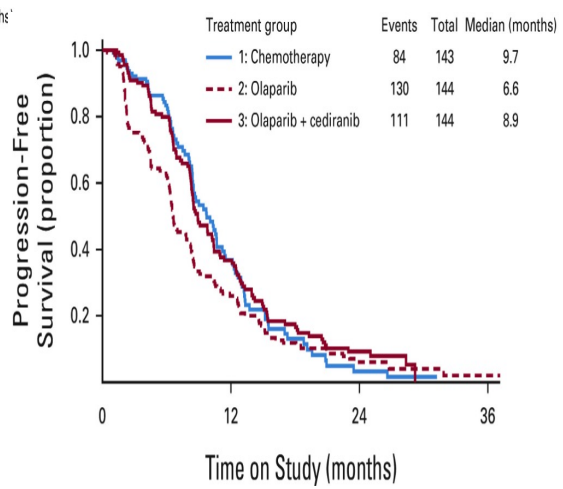


GY004: Olaparib vs Olaparib/Cediranib vs SOC

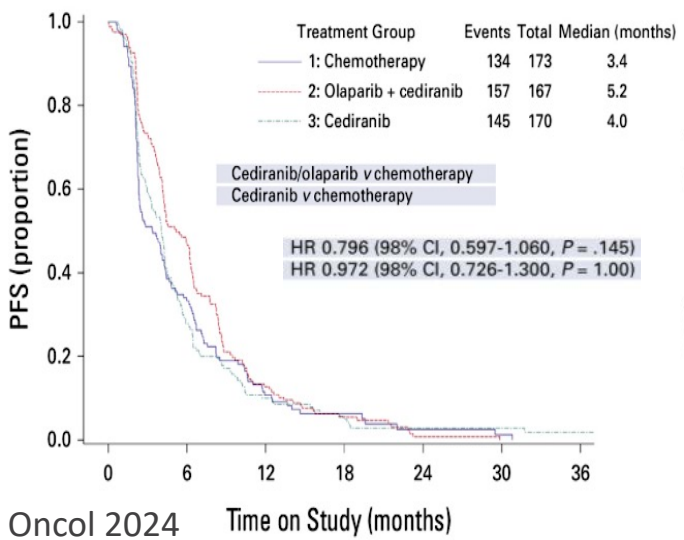
BRCA1/2 mutation

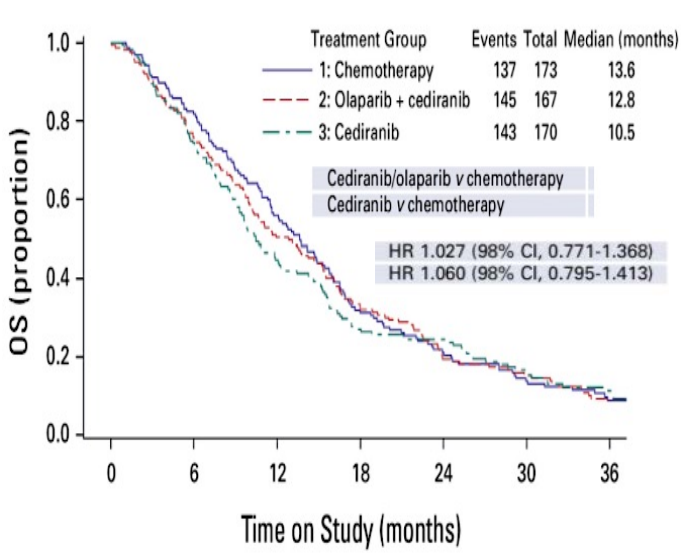


BRCA1/2 no mutation



GY005: Cediranib or Olaparib vs Olaparib/Cediranib vs SOC





Liu YL et al. Cancer 2025; Liu JM et al. J Clin Oncol 2024; Lee J-M et al. J Clin Oncol 2024

Mirvetuximab soravtansine: Targeting Folate Receptor Alpha

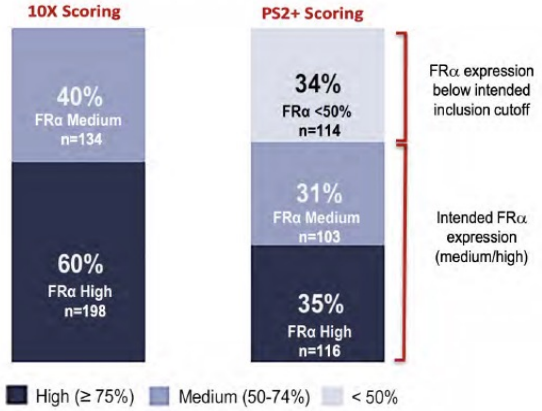
It's a Biomarker story

FORWARD 1

FORWARD I 10X SCORING COMPARED WITH EXPLORATORY PS2+ SCORING

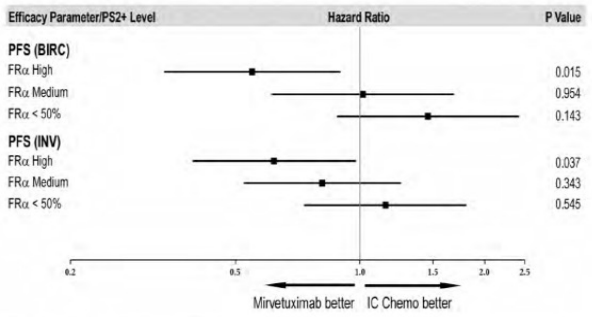
Rescoring of the FORWARD I samples using PS2+ indicates:

- 34% of patients enrolled in FORWARD I had low FRα levels that should have precluded enrollment; and
- the protocol-defined FRα high subset contained patients with a mixture of FRα expression levels



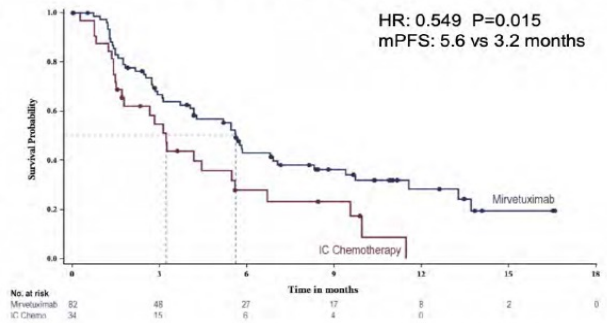
PS2+ RE-SCORING: PFS TRENDS ACROSS SUBGROUPS

PFS Hazard Ratio Plot



P values from unstratified log-rank test

PFS (by BIRC) - FRα High (n=116)

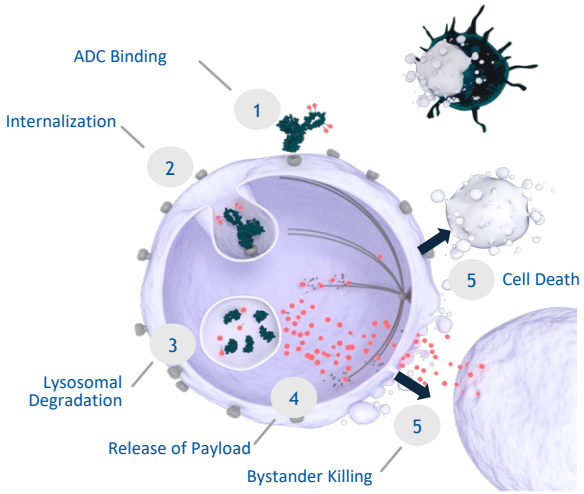


PS2+ RE-SCORING: TRENDS ACROSS SUBGROUPS

Endpoint	FRα < 50% (n=114) (Mirv vs IC Chemo)	FRα Medium (n=103) (Mirv vs IC Chemo)	FRα High (n=116) (Mirv vs IC Chemo)
PFS by BIRC (mo.)	HR: 1.458 (0.878, 2.420) mPFS: 3.8 vs 5.5	HR: 1.015 (0.611, 1.687) mPFS: 4.3 vs 5.6	HR: 0.549 (0.336, 0.897) mPFS: 5.6 vs 3.2
ORR by BIRC 95% CIs	16% vs 16% (8%, 26%) vs (6%, 31%)	28% vs 18% (18%, 40%) vs (7%, 35%)	29% vs 6% (20%, 40%) vs (1%, 20%)
OS (*August 2019*) (mo.)	HR: 0.923 (0.548, 1.554) mOS: 14.0 vs 13.4	HR: 0.936 (0.542, 1.616) mOS: 15.9 vs 20.7	HR: 0.678 (0.410, 1.119) mOS: 16.4 vs 11.4
PFS by INV (mo.)	HR: 1.149 (0.732, 1.803) mPFS: 4.0 vs 4.5	HR: 0.810 (0.523, 1.254) mPFS: 5.1 vs 2.8	HR: 0.619 (0.394, 0.975) mPFS: 5.6 vs 3.7
ORR by INV 95% CIs	18% vs 21% (11%, 29%) vs (10%, 37%)	36% vs 24% (25%, 49%) vs (11%, 41%)	38% vs 9% (27%, 49%) vs (2%, 24%)

Moore, K, ESMO 2019

Mirvetuximab soravtansine, first FRα-targeted ADC approved for PROC



MIRV is an antibody-drug conjugate (ADC) comprising an FRα-binding antibody, cleavable linker, and a maytansinoid DM4 payload[1]

SORAYA (NCT04296890) was a global, single-arm pivotal study evaluating mirvetuximab soravtansine in adult patients with FRα-positive platinum-resistant epithelial ovarian, primary peritoneal, or fallopian tube cancer[2]

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)[2]
6.0 mg/kg adjusted ideal body weight (AIBW) q3w

Primary endpoint

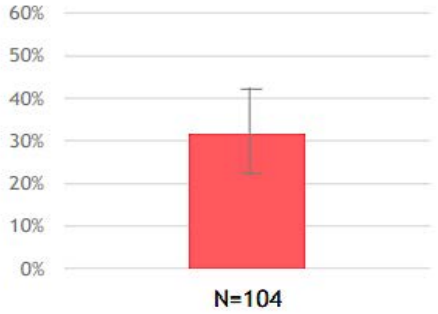
- ORR per Investigator

Secondary endpoints

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

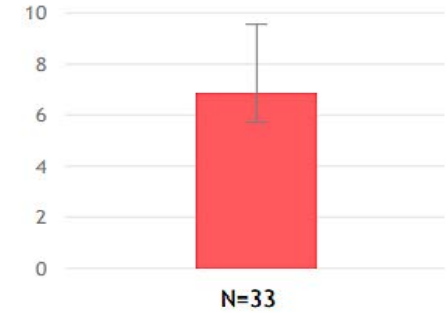
ORR% BY INVESTIGATOR[1]

31.7%
(22.9, 41.6)*



DOR BY INVESTIGATOR[1]

6.9 months
95% CI: (5.6, 9.7)



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

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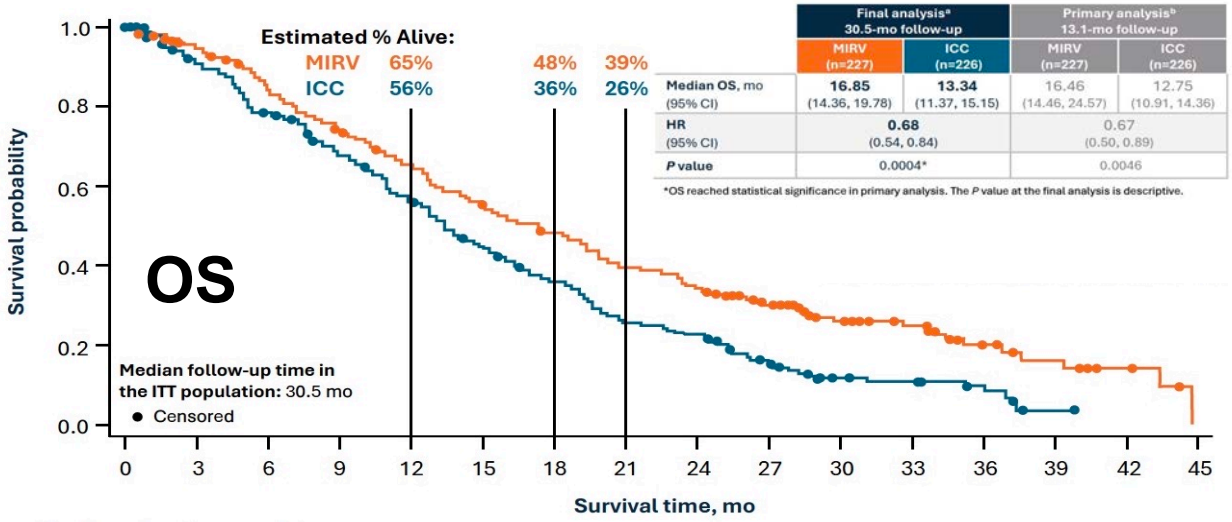
On November 14, 2022, the Food and Drug Administration granted accelerated approval to mirvetuximab soravtansine-gynx [illegible] for adult patients with folate receptor alpha (FRα) positive, platinum-resistant epithelial ovarian, fallopian tube, or primary peritoneal cancer, who have received one to 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.

1. Moore KN et al. *Cancer*. 2017 2. Matulonis UA et al. *J Clin Oncol*. 2023

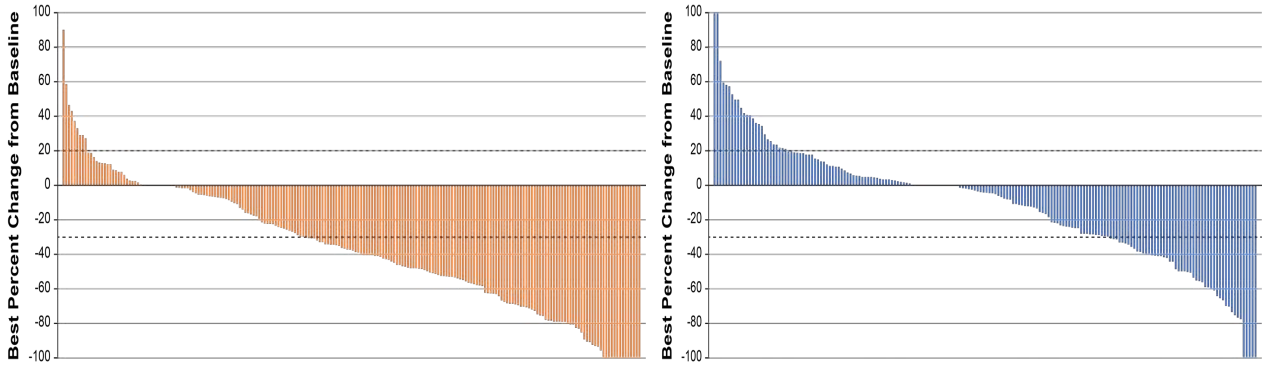
MIRASOL Phase III Trial: Platinum Resistant Ovarian Cancer

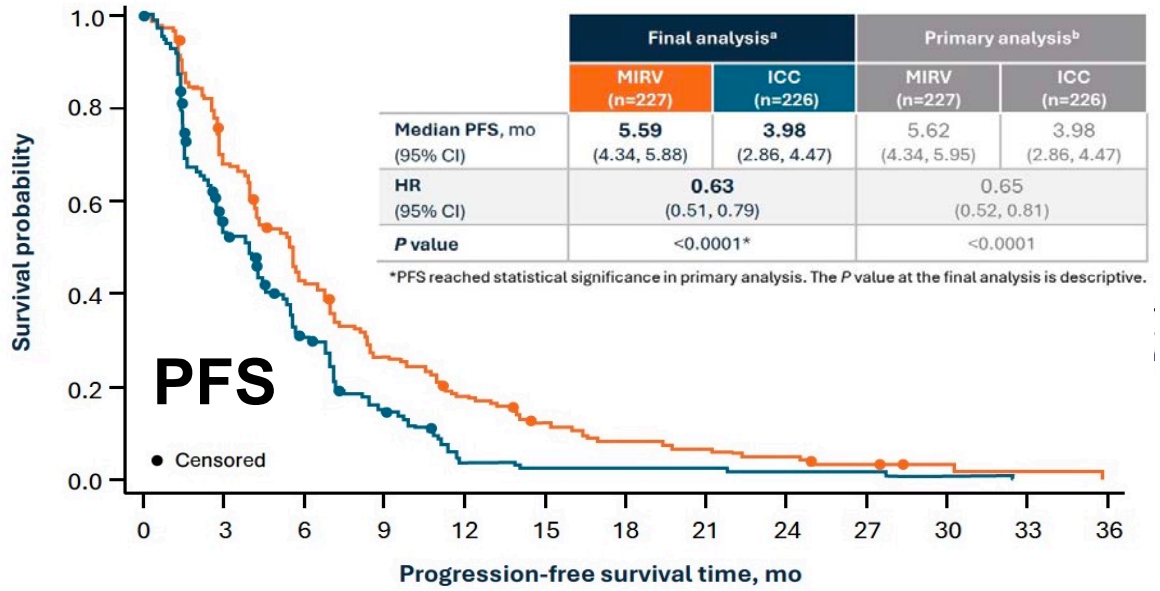


	Final analysis[a] 30.5-mo follow-up		Primary analysis[b] 13.1-mo follow-up	
	MIRV (n=227)	ICC (n=226)	MIRV (n=227)	ICC (n=226)
Median OS, mo (95% CI)	**16.85** (14.36, 19.78)	**13.34** (11.37, 15.15)	16.46 (14.46, 24.57)	12.75 (10.91, 14.36)
HR (95% CI)	**0.68** (0.54, 0.84)		0.67 (0.50, 0.89)	
P value	0.0004*		0.0046	

*OS reached statistical significance in primary analysis. The *P* value at the final analysis is descriptive.

MIRV **IC Chemo**





	Final analysis[a]		Primary analysis[b]	
	MIRV (n=227)	ICC (n=226)	MIRV (n=227)	ICC (n=226)
Median PFS, mo (95% CI)	**5.59** (4.34, 5.88)	**3.98** (2.86, 4.47)	5.62 (4.34, 5.95)	3.98 (2.86, 4.47)
HR (95% CI)	**0.63** (0.51, 0.79)		0.65 (0.52, 0.81)	
P value	<0.0001*		<0.0001	

*PFS reached statistical significance in primary analysis. The *P* value at the final analysis is descriptive.

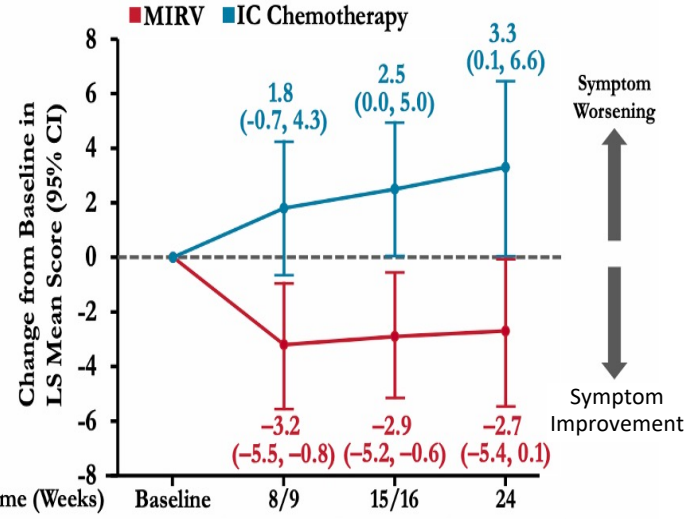
Efficacy Summary

	Final analysis[a]	
Endpoints	**MIRV (n=227)**	**ICC (n=226)**
ORR by INV, n (%) (95% CI)	**95 (41.9)** (35.4, 48.6)	**36 (15.9)** (11.4, 21.4)
Odds ratio (95% CI)	**3.75** (2.4, 5.85)	

Van Gorp T et al. SGO 2025; Konecny GE et al. SGO 2024

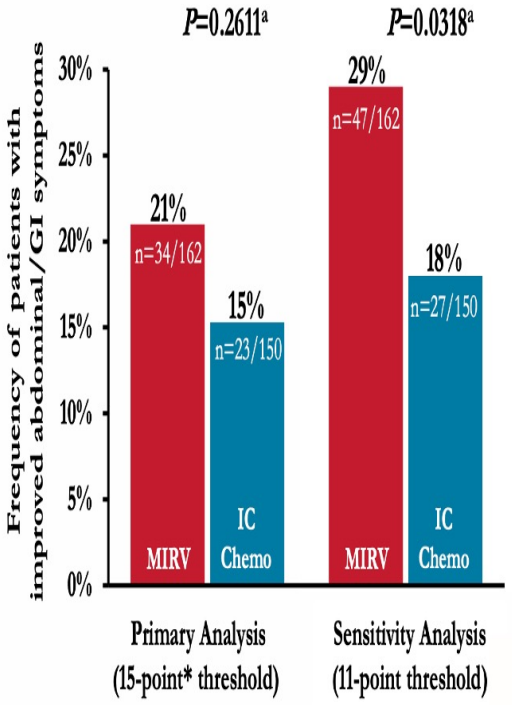
MIRASOL Updates: Quality of Life

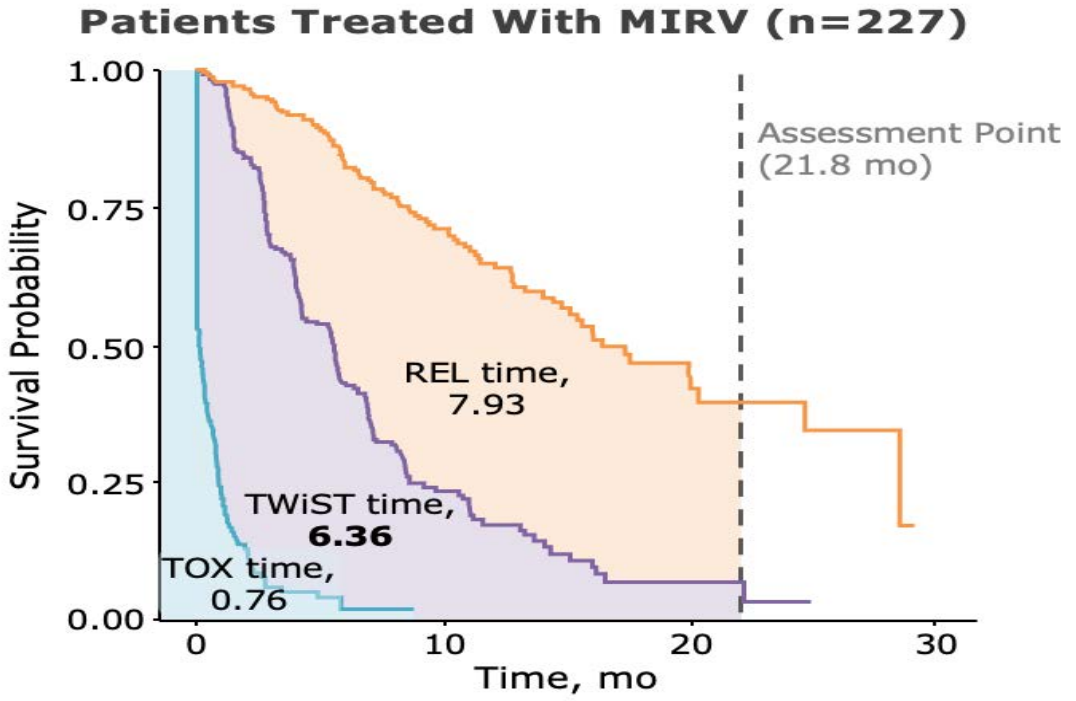
Figure†. Change from baseline in EORTC QLQ-OV28 Abdominal/GI scale – ITT Population

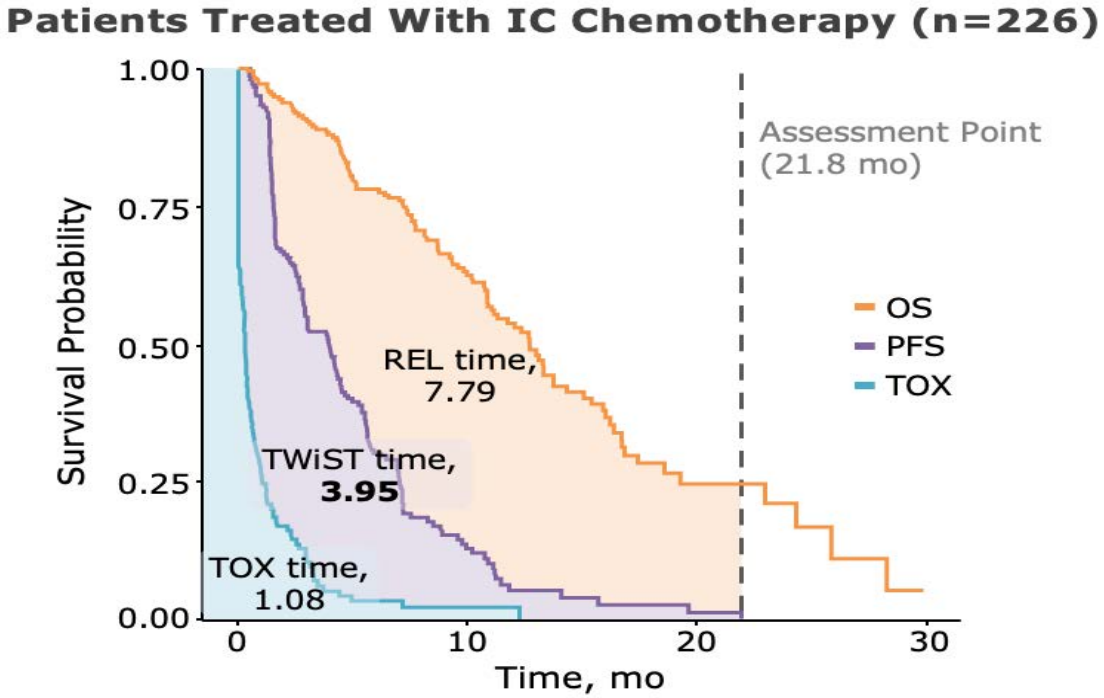


	Baseline	8/9	15/16	24
MIRV, n	185	141	93	53
IC Chemotherapy, n	180	123	54	37
Treatment difference[a]	-	−5.0	−5.4	−6.0
(95% CI)	-	(−8.3, −1.6)	(−8.9, −2.0)	(−10.2, −1.8)
P-value	-	0.0041	0.0020	0.0056

Figure. Responder Analysis for OV28 abdominal/GI symptom subscale scores by treatment group at week 8/9



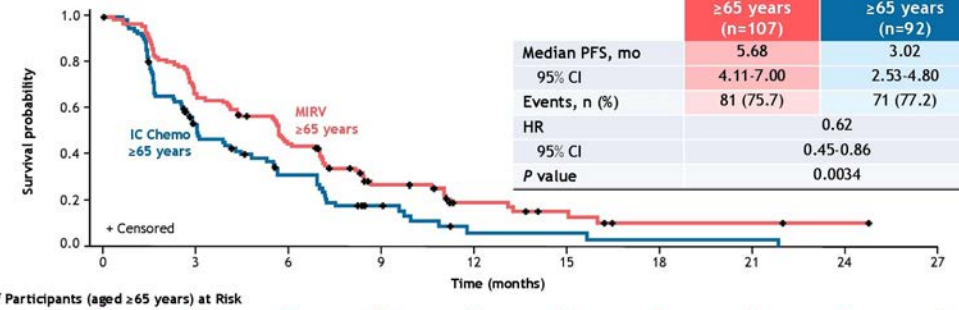




Konecny GE et al. Presented at SGO 2024; Hilpert F et al. Presented at ESGO 2025

MIRASOL ASCO Updates: Older Patients

Figure 1. Post Hoc Progression-Free Survival by Investigator in Older Participants[a] (N=199)



	MIRV ≥65 years (n=107)	IC Chemotherapy ≥65 years (n=92)
Median PFS, mo	5.68	3.02
95% CI	4.11-7.00	2.53-4.80
Events, n (%)	81 (75.7)	71 (77.2)
HR	0.62	
95% CI	0.45-0.86	
P value	0.0034	

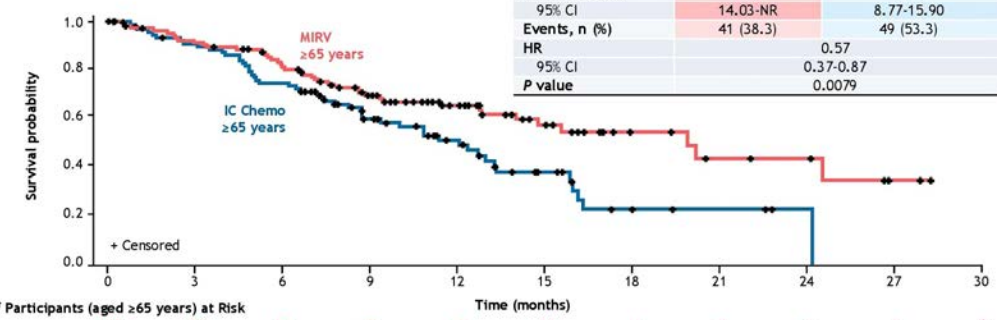
No. of Participants (aged ≥65 years) at Risk

MIRV	107	68	44	20	10	6	2	2	1	0
IC Chemotherapy	92	40	21	9	2	2	1	1	0	

[a]ITT population.

- In older participants, **the HR for PFS was 0.62** (95% CI, 0.45-0.86; nominal *P*=0.0034), **favoring MIRV** over IC chemotherapy

Figure 2. Post Hoc Overall Survival in Older Participants[a] (N=199)



	MIRV ≥65 years (n=107)	IC Chemotherapy ≥65 years (n=92)
Median OS, mo	19.94	12.09
95% CI	14.03-NR	8.77-15.90
Events, n (%)	41 (38.3)	49 (53.3)
HR	0.57	
95% CI	0.37-0.87	
P value	0.0079	

No. of Participants (aged ≥65 years) at Risk

MIRV	107	94	80	58	40	24	11	7	6	2	0
IC Chemotherapy	92	78	64	39	25	13	5	3	1	0	

[a]ITT population.

- In older participants, **the HR for OS was 0.57** (95% CI, 0.37-0.87; nominal *P*=0.0079), **favoring MIRV** over IC chemotherapy

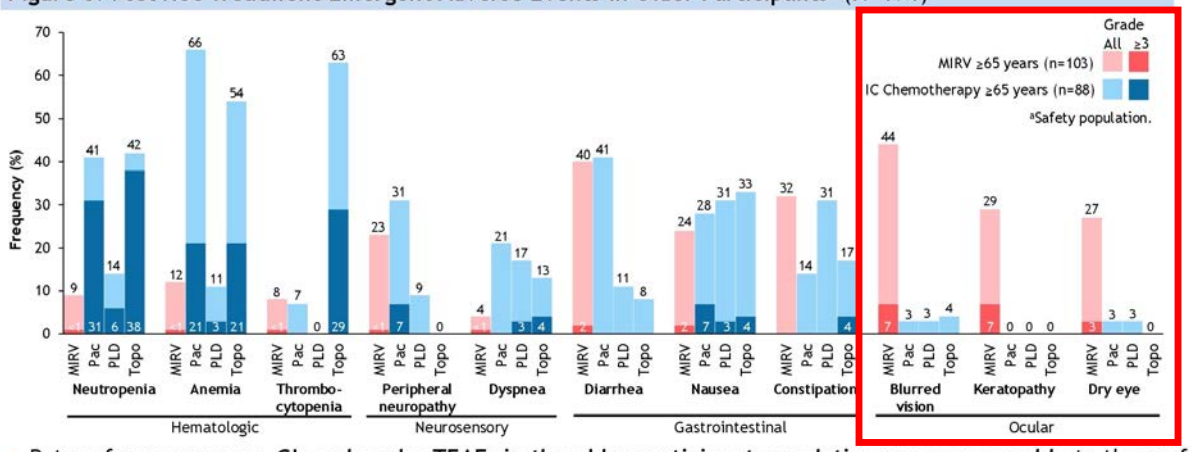
Table 2. Post Hoc Objective Response Rate by Investigator in Older Participants[a] (N=199)

	MIRV ≥65 years (n=107)	IC Chemotherapy ≥65 years (n=92)
ORR by investigator[b]	**39.3%**	**17.4%**
n (95% CI)	42 (30.0-49.2)	16 (10.3-26.7)
Treatment difference, % (95% CI)	21.9 (9.8-33.9)	
Odds ratio (95% CI)	3.07 (1.58-5.96)	
P value	0.0007	
Best overall response, n (%)		
Complete response	7 (6.5%)	0
Partial response	35 (32.7%)	16 (17.4%)
Stable disease[c]	40 (37.4%)	37 (40.2%)
Progressive disease	17 (15.9%)	28 (30.4%)
Not evaluable	8 (7.5%)	11 (12.0%)

[a]ITT population. [b]ORR was calculated as CR plus PR. [c]Stable disease was defined as neither sufficient shrinkage to qualify for partial response nor sufficient increase to qualify for progressive disease.

- **ORR by investigator was 39.3%** (95% CI, 30.0-49.2) for MIRV versus 17.4% (95% CI, 10.3-26.7) for IC chemotherapy among older participants
- The **treatment difference between the ORR in the MIRV and IC chemotherapy arms was 21.9%** (95% CI, 9.8-33.9), with an odds ratio of 3.07 (95% CI, 1.58-5.96) and *P*=0.0007, **favoring MIRV** over IC chemotherapy

Figure 3. Post Hoc Treatment-Emergent Adverse Events in Older Participants[a] (N=191)



- Rates of **neurosensory, GI, and ocular TEAEs in the older participant population were comparable** to those of the full MIRASOL safety population[7]

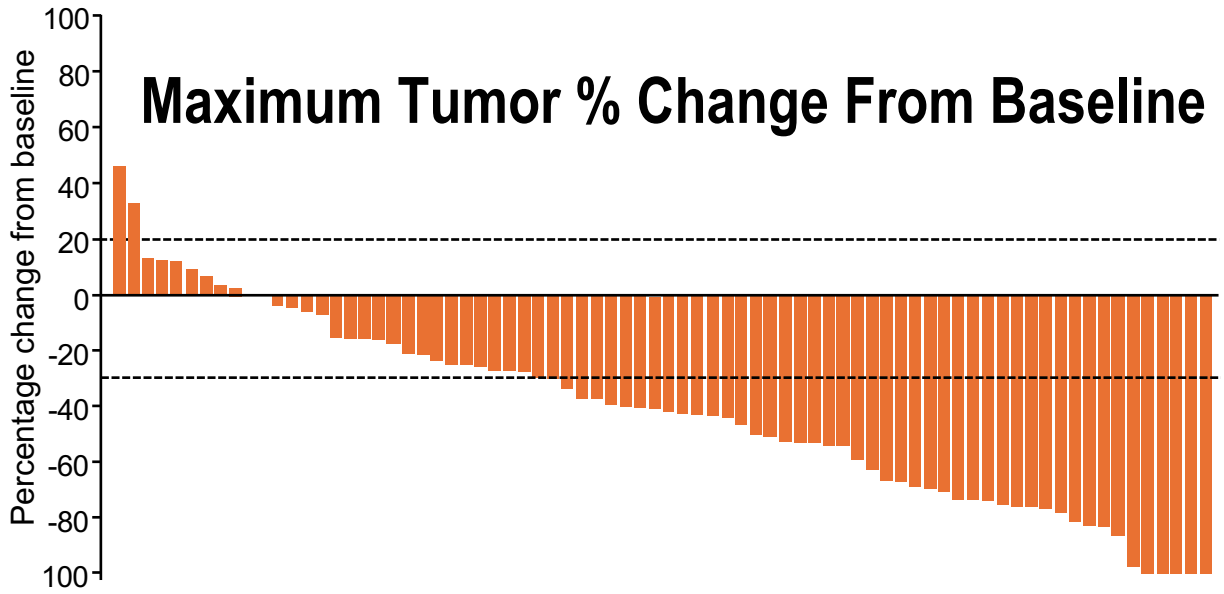
Bello-Roufai et al. ASCO 2024 abstract 5580

PICCOLO: Mirvetuximab soravtansine, targeting FRα for PSOC

Demographics and Investigator-Assessed Efficacy Measures

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)

Characteristics	N=79
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)



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)

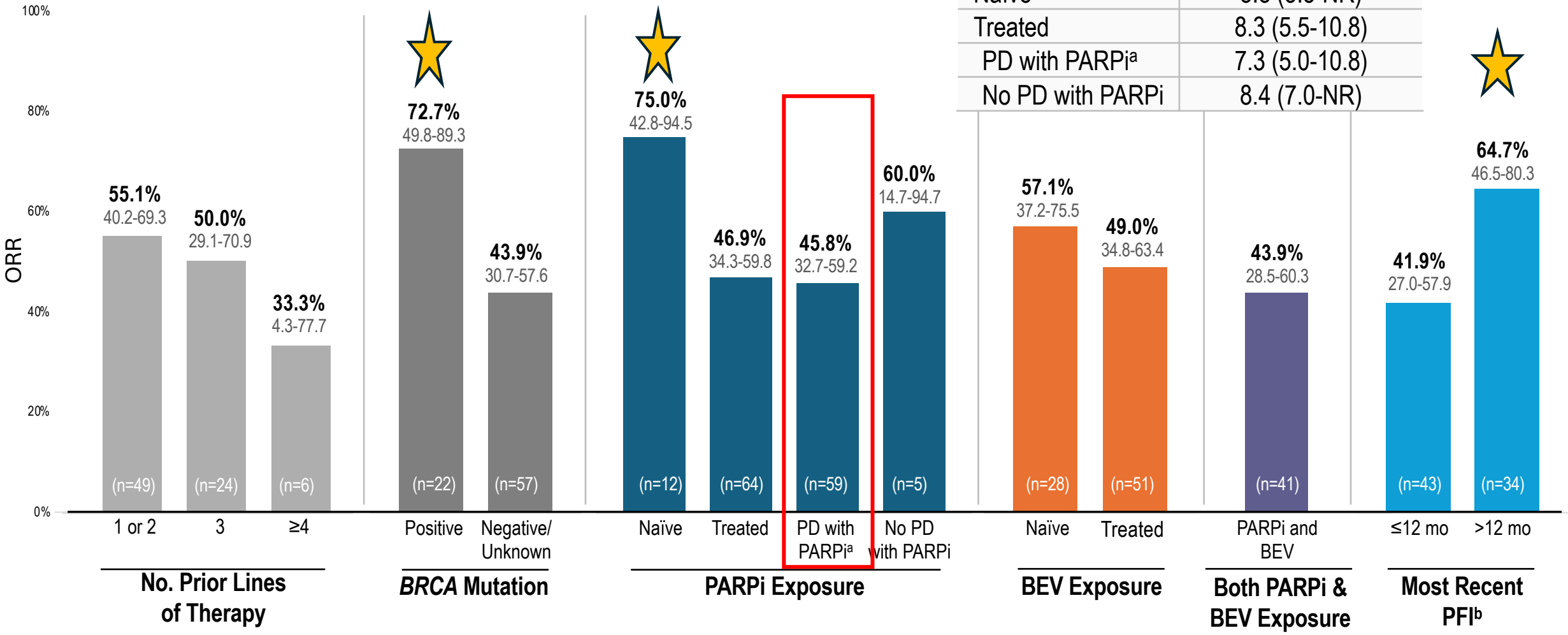
Secondary Endpoints	
Median DOR[a]	n=41
Months (95% CI)	8.25 (5.6-10.8)
Median PFS	N=79
Months (95% CI)	6.93 (5.8-9.6)

Alvarez Secord A et al. Ann Oncol 2025

PICCOLO: ORR by Subgroups

Total population ORR: 51.9% (95% CI, 40.4-63.3)

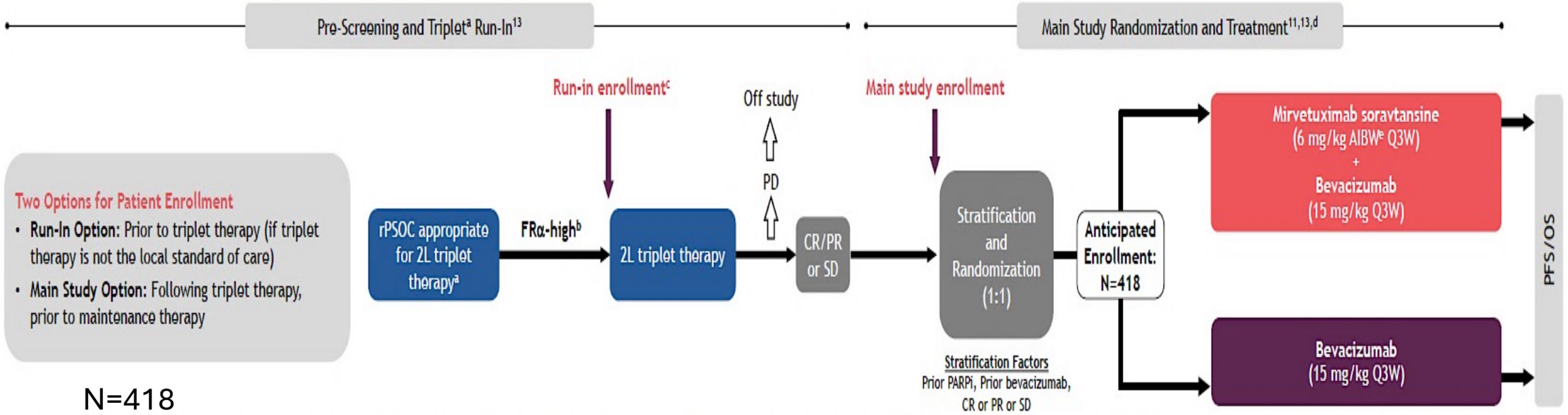
Exposure to PARPis	Median DOR months (95% CI)
Naïve	8.8 (3.5-NR)
Treated	8.3 (5.5-10.8)
PD with PARPi[a]	7.3 (5.0-10.8)
No PD with PARPi	8.4 (7.0-NR)



[a]If the participant had progression of disease within 30 days after the last dosing of a PARPi or progression was listed as the reason for treatment discontinuation of a PARPi, the participant was defined as having progressive disease on prior PARPi and was included in this category. [b]Platinum-free interval is defined as time from last dose of the latest line platinum therapy to the date of disease progression and/or relapse following that line of therapy (time rounded to whole number).

Alvarez Secord A et al. Ann Oncol 2025

GOG-3078 | ENGOT-OV76 | IMGN853-0421 |GLORIOSA



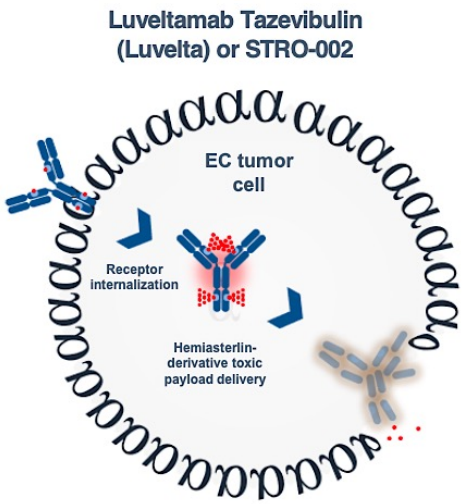
[a]Triplet treatment consists of platinum+chemotherapy+bevacizumab for planned 6 cycles (minimum 4 and maximum 8 cycles), including at least 3 cycles of bevacizumab. [b]Pre-screening consent must be obtained for tissue testing for FRα expression by Ventana FOLR1 Assay. [c]FRα-high patients who desire 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.

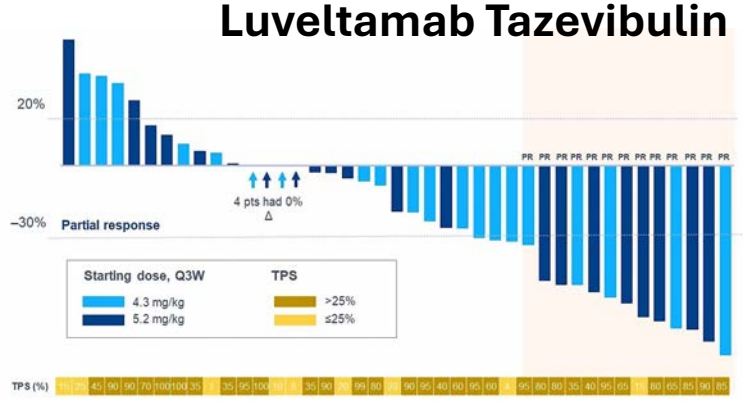
Key Eligibility Criteria:

- 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
- Confirmation of high FRα positivity by IHC using the Ventana FOLR1 CDx Assay
  - High expression = ≥ 75% of viable tumor cells staining at 2+ intensity

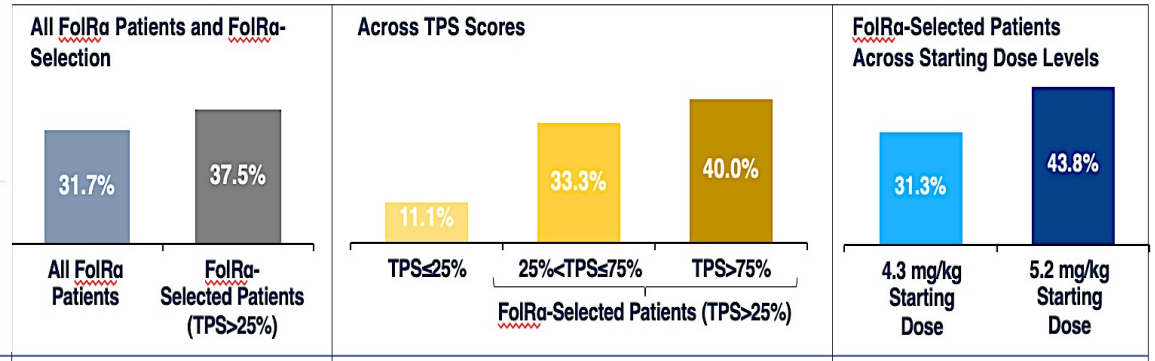
NCT05445778

Luveltamab tazevibulin (STRO-002): Targeting FRα





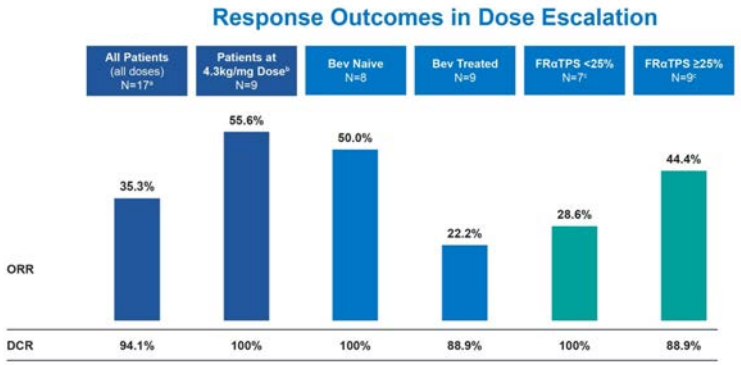
RECIST-Evaluable ORR (%), Median DOR (%), and Median PFS

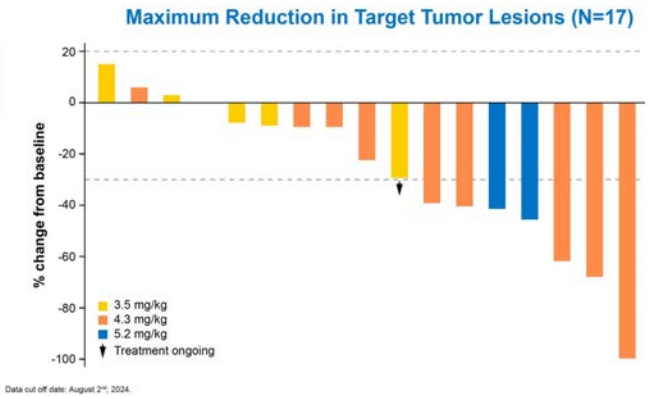


	All FolRα Patients	FolRα-Selected Patients (TPS>25%)	TPS≤25%	25%<TPS≤75%	TPS>75%	4.3 mg/kg Starting Dose	5.2 mg/kg Starting Dose
RECIST-Evaluable Patients	N=41	N=32	N=9	N=12	N=20	N=16	N=16
PR	13	12	1	4	8	5	7
ORR (95%, CI), %	31.7 (18.1, 48.1)	37.5 (21.1, 56.3)	11.1 (0.3, 48.3)	33.3 (10.0, 65.1)	40.0 (19.1, 63.9)	31.3 (11.0, 58.7)	43.8 (19.8, 70.1)
Median DOR (95% CI), mo	5.4 (2.9, 11.0)	5.5 (2.5, 11.0)	2.9	5.6 (2.5, NE)	5.5 (2.4, NE)	13 (4.5, NE)	5.4 (2.4, 6.1)
Patients for median PFS	n=44	n=35	n=9	n=12	n=23	n=19	n=16
Median PFS (95% CI), mo	4.3 (4.0, 6.3)	6.1 (4.1, 7.0)	3.8 (1.3, 4.2)	6.4 (1.4, 10.4)	5.8 (4.0, 6.6)	6.1 (4.0, 8.3)	6.6 (2.9, 7.6)

- Ventana FOLR1 testing
- ORR 31.7% all FolRα +
  - 37.5% TPS>25%
- TPS >25% appears to be the threshold for anti-tumor activity
  - No scoring needed

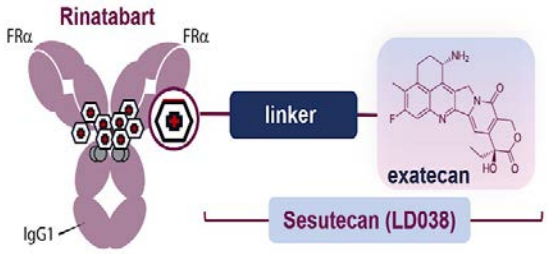
Luveltamab Tazevibulin + Bevacizumab





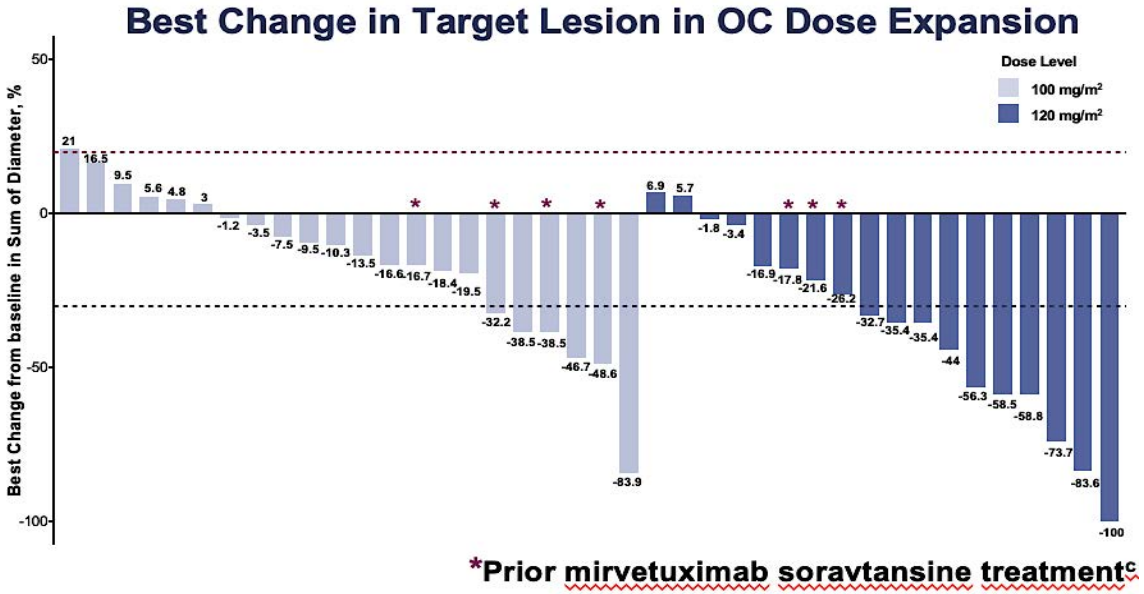
Oaknin A et al. ASCO 2023; Martin LP et al. ESMO 2024

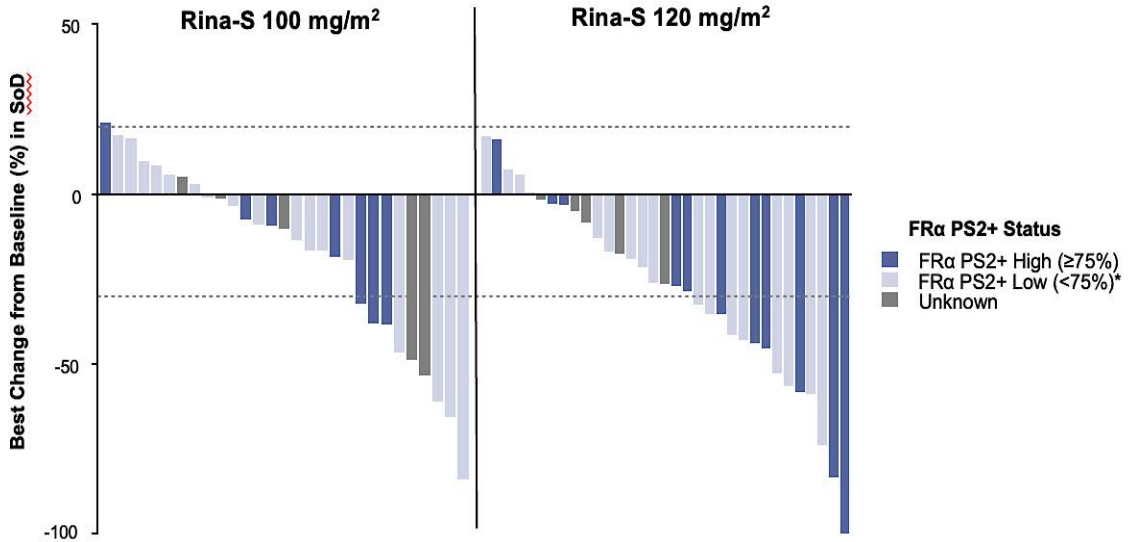
RINA-S: Targeting Folate Receptor Alpha Ovarian Cancer Dose Expansion



OC Dose Expansion	Rina-S 100 mg/m² n = 22[b]	Rina-S 120 mg/m² n = 18[b]
Confirmed ORR,[a,b] % (95% CI)	18.2 (5.2-40.3)	50.0 (26.0-74.0)
Best overall response,[b] n (%)		
CR	0	1 (5.6)
PR	4 (18.2)	8 (44.4)
SD	15 (68.2)	7 (38.9)
PD	3 (13.6)	1 (5.6)
Not evaluable	0	1 (5.6)
DCR, % (95% CI)	86.4 (65.1-97.1)	88.9 (65.3-98.6)
Median DOR (95% CI)	NR (NR-NR)	

Treatment duration, range: 3.0-42.0+ weeks
Median on-study follow-up: 24 weeks

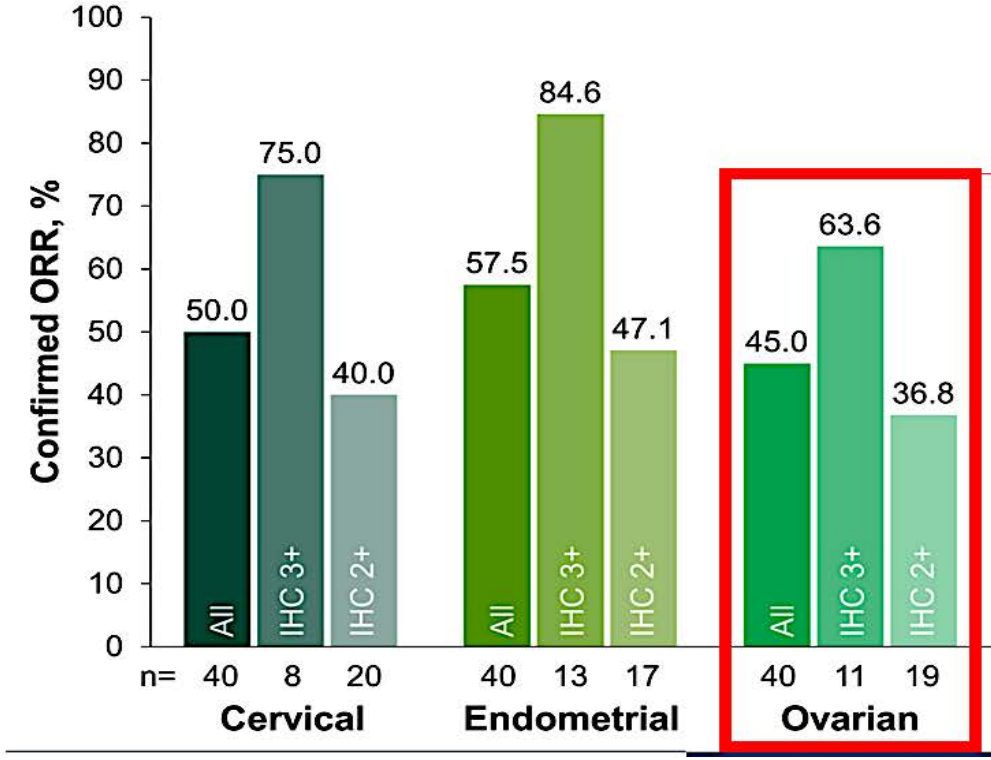




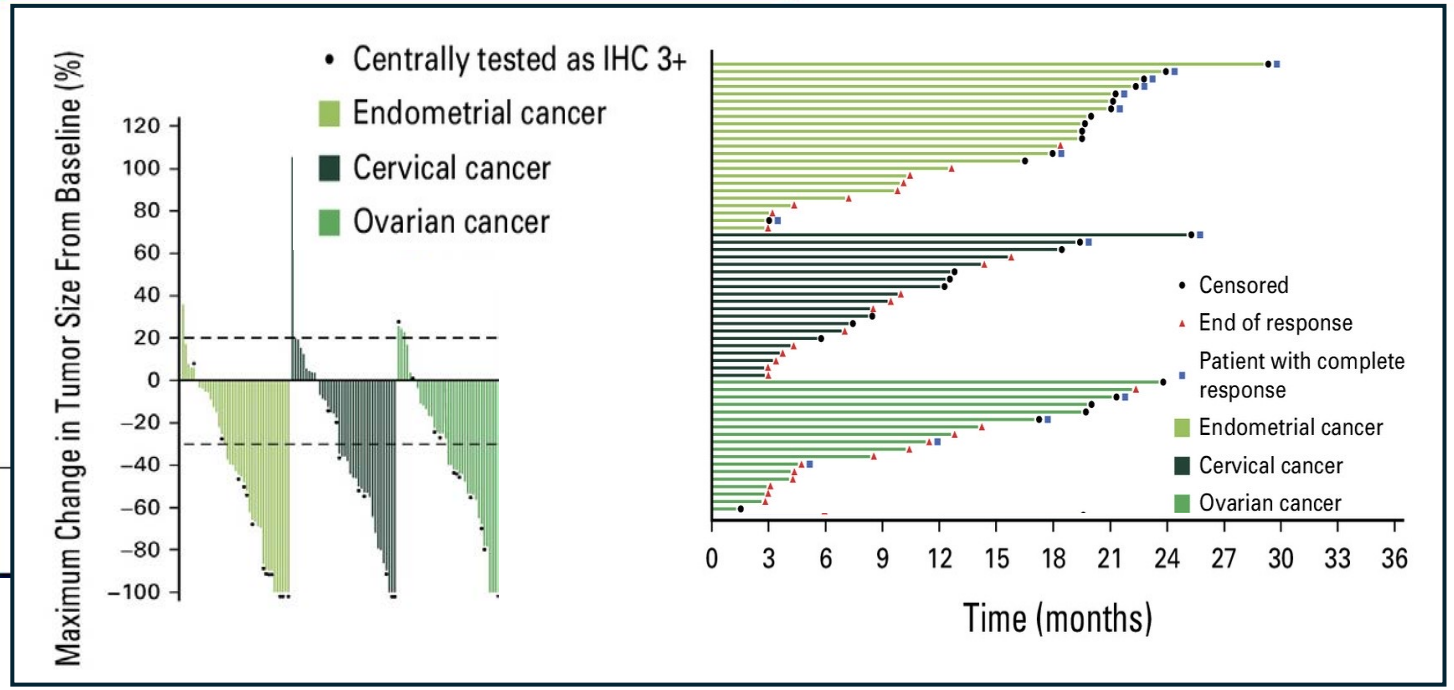
Lee E et al. ESMO 2024

DESTINY-PanTumor02: Trastuzumab deruxtecan, HER2-targeted ADC

Objective Response Rate by HER2 status



Ovarian – 18 responders
- HER2 3+: 7/11 (63.6%)
- HER2 2+: 7/19 (36.8%)
- HER2 1+: 4/10 (40%)



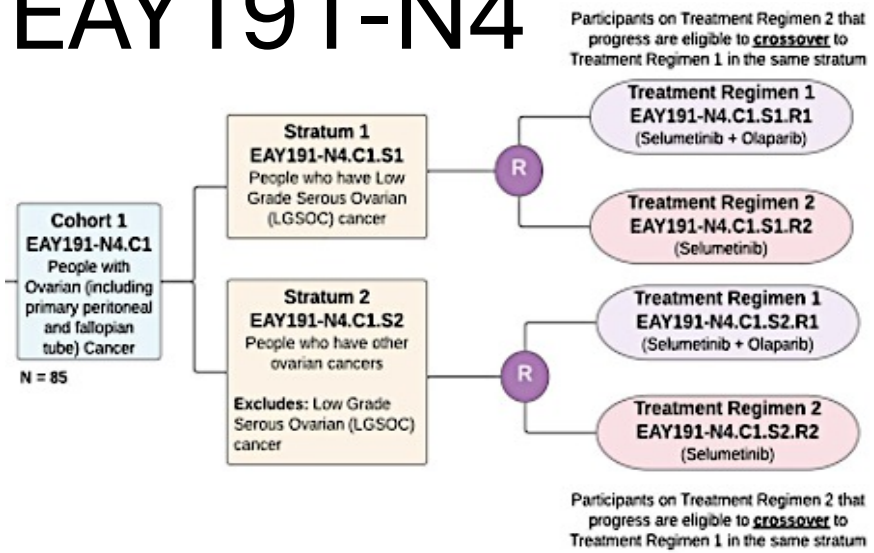
Meric-Bernstam F et al. J Clin Oncol 2024

Targeting FRα and HER2: **Testing is Critical**

- Testing can be done on fresh or archival tissue
  - Start testing patients at diagnosis? Versus recurrence?
  - Testing newly diagnosed patients will determine treatment options at the time of progression to platinum resistance.
  - Tumor heterogeneity
  - Critical decision making
    - Individualized therapy based on biomarkers
    - Clinical Trial options and counseling
    - Sequencing targeted therapies

What to Watch: Clinical Trials

EAY191-N4

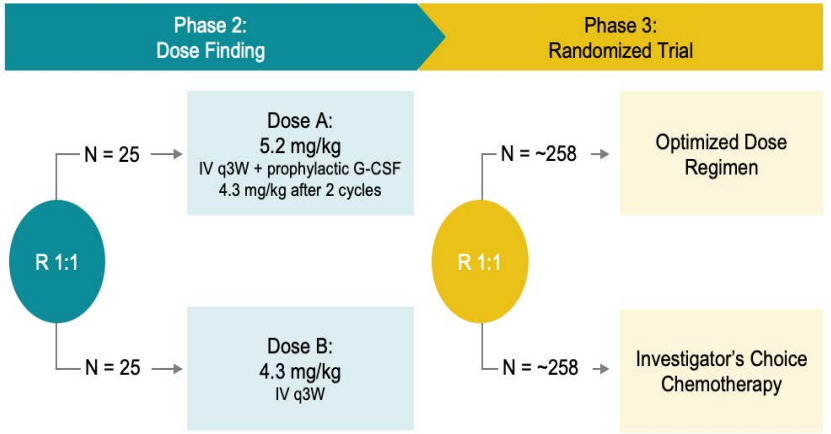


RAS Pathway mutation: *KRAS, NRAS, HRAS, BRAF, MEK1, MEK2, NF1*
Prior PARP allowed if no progression

Study Chair: Shannon Westin, MD, MPH

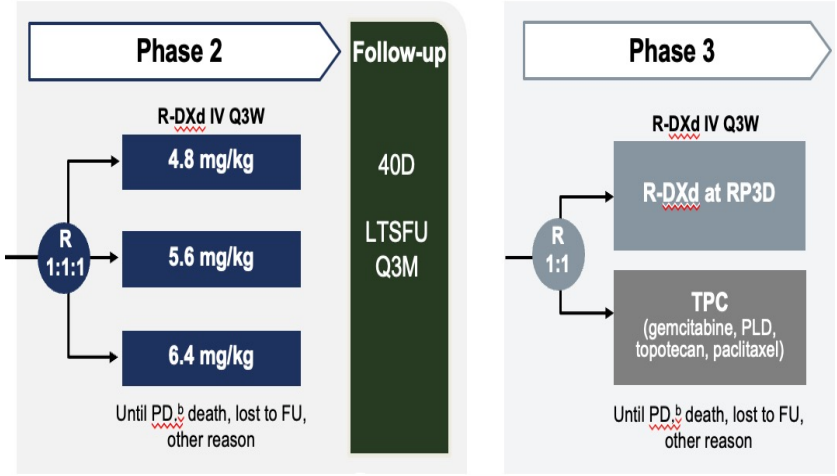
GOG-3086 ReFRame-01
Luveltamab tazevibulin

NCT05870748



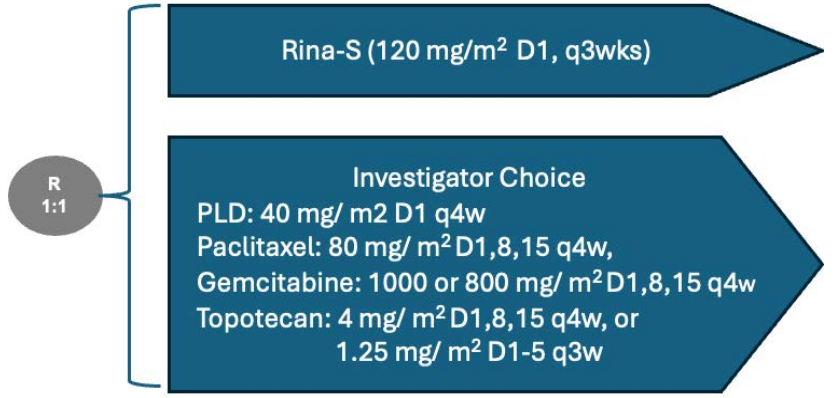
GOG-3096 REJOICE
Raludotatug Deruxtecan (R-DXd)

NCT06161025



GOG-3107 RAINFOL
Rinatabart Sesutecan (Rina-S)

NCT06619236



Questions from Gynecologic Oncologists and General Medical Oncologists

- What are the current indications for PARP in the recurrent setting? In patients with a long DFI after previous PARP (like 4-5 years), should we consider re-treating after second-line chemo?
- How are investigators testing for FRα in patients with relapsed disease? What platform do you use? What is the optimal source material for FRα testing — archival tissue or new biopsy?
- How did the guideline for FRα ≥75% originate? I have had many patients who are in the 60-70% expression range. Is there any indication that they might benefit from mirvetuximab?

Questions from Gynecologic Oncologists and General Medical Oncologists

- In what line do you typically use mirvetuximab? How does this drug compare to other standard treatments in terms of outcomes? Is this now your go-to first therapy after confirmed platinum resistance?
- When do you combine mirvetuximab with bev? If using combination therapy, would you ever try to access mirvetuximab for a patient with lower FRα expression (ie, low and/or medium expressors)?
- Is there a role for mirvetuximab in platinum-sensitive disease? Would this be an option for patients with a history of a hypersensitivity reaction to platinum-based chemo?

Questions from Gynecologic Oncologists and General Medical Oncologists

- 67 y/o patient with OC and gBRCA1, s/p resection, carboplatin/paclitaxel and niraparib maintenance but with disease progression 1 year into maintenance. Two subsequent lines of platinum chemotherapy with responses lasting 10 and 7 months. FRα-positive. What would you recommend next?
- Should HER2 be tested in all patients? Should we test the initial tumor or a new biopsy? How do you test — IHC or NGS?
- If you are looking to start an ADC in a patient with recurrent OC that is both HER2-positive and expresses FRα, would you pick mirvetuximab or T-DXd? And what is the rationale behind your choice?

Agenda

Module 1: Up-Front Treatment for Advanced Ovarian Cancer (OC) — Dr Westin

Module 2: Management of Relapsed/Refractory OC — Dr Secord

Module 3: Novel Investigational Therapies for Advanced OC — Dr Moore

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

Novel Investigational Therapies for Advanced Ovarian Cancer

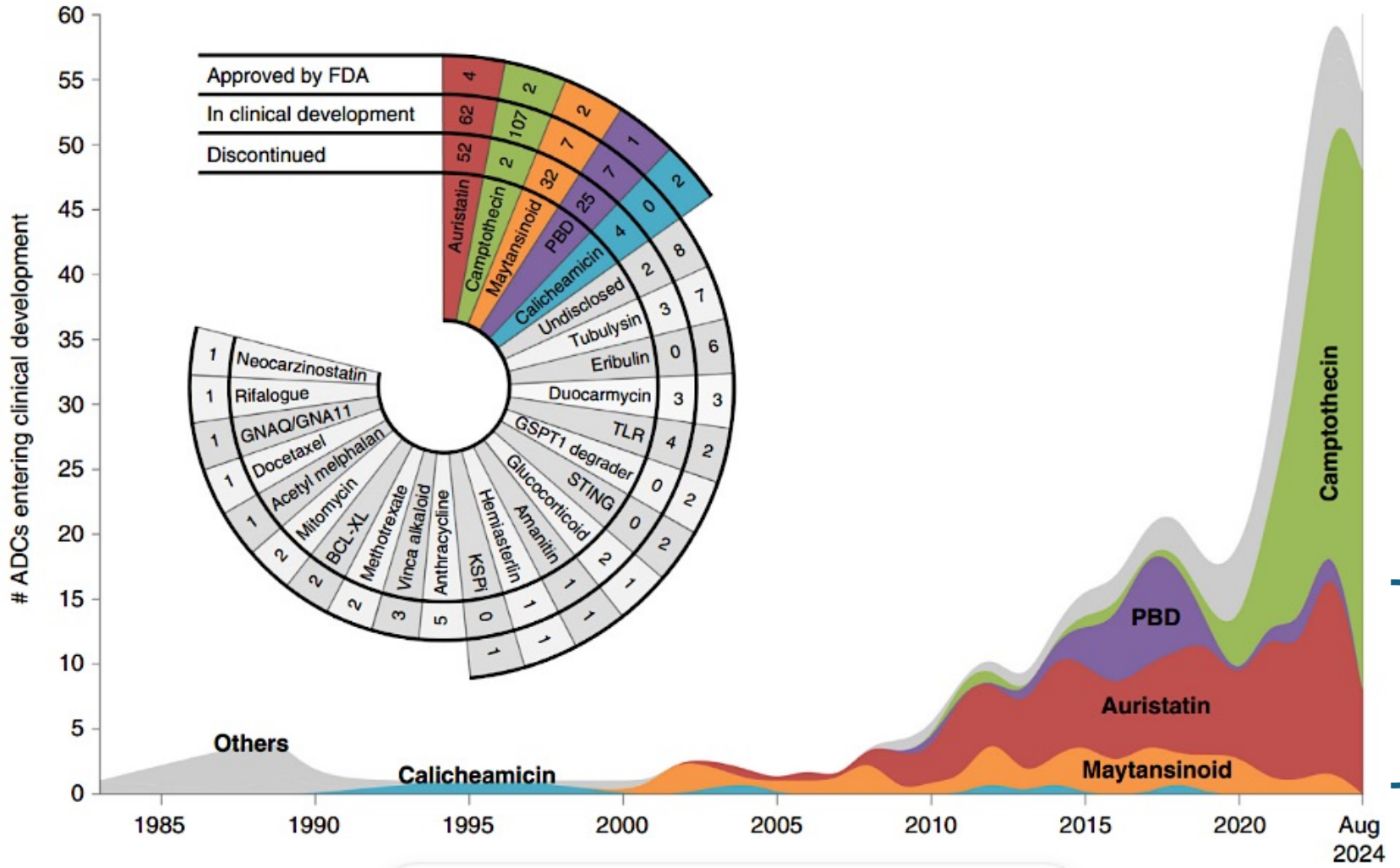
Tumor Associated Antigens Beyond HER2 and FRα and Innovative Approaches to Immunotherapy

Kathleen N. Moore, MD, MS, FASCO
Deputy Director, Stephenson Cancer Center at OU Health
Co-Lead, Cancer Therapeutics Program
Professor, Gynecologic Oncology
ASCO BOD
GOG F BOD

OU Health | Stephenson Cancer Center

@DrKatyMoore

With almost 190 ADCS in development, the opportunity for improving outcomes in ovarian cancer is here



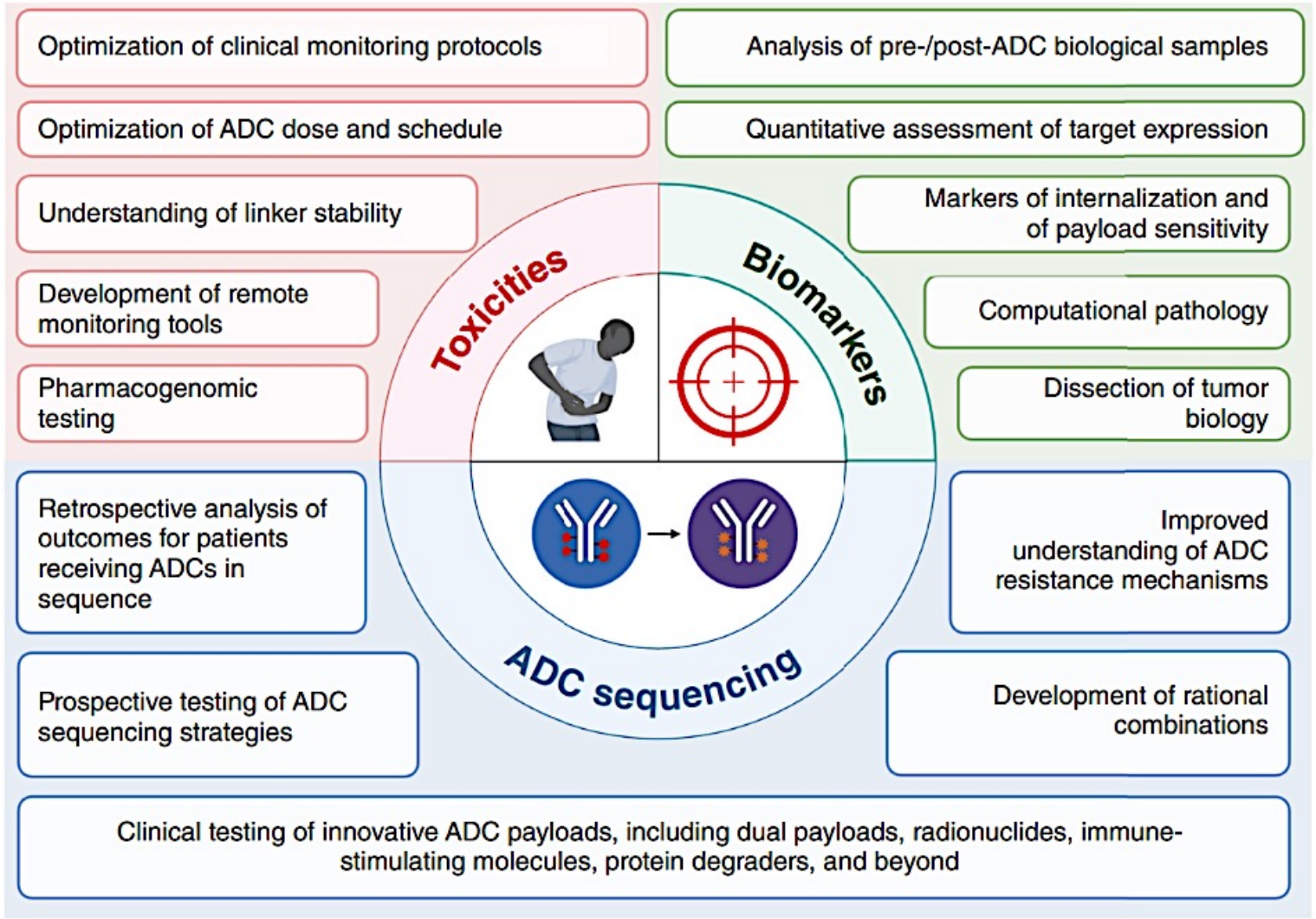
In gynecology, the payloads mainly fall into 2 classes:

Camptothecins

Microtubule Toxins

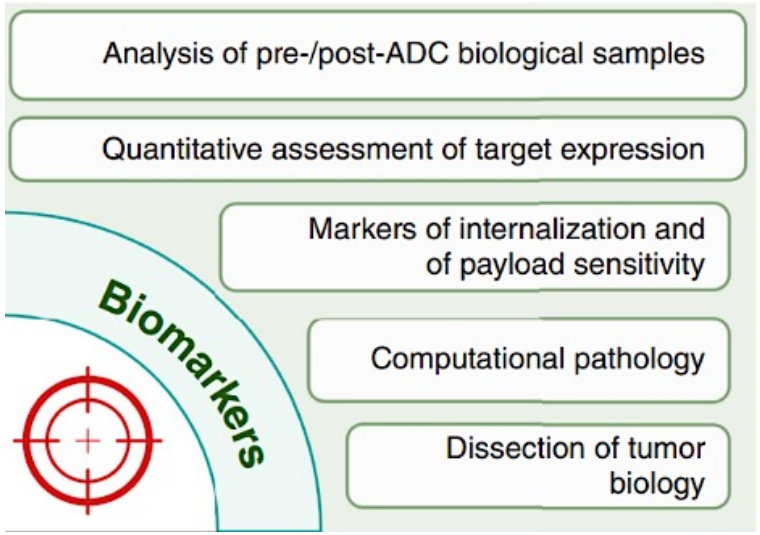
Colombo R et al. Cancer Discovery 2024; 14:2089-108

Opportunities for ADCs across a variety of targets and expanding considerations for the treatment setting demands focus on strategy, safety and sequencing



Colombo R et al. Cancer Discovery 2024; 14:2089-108

Opportunities for ADCs across a variety of targets and expanding considerations for the treatment setting demands focus on strategy, safety and sequencing

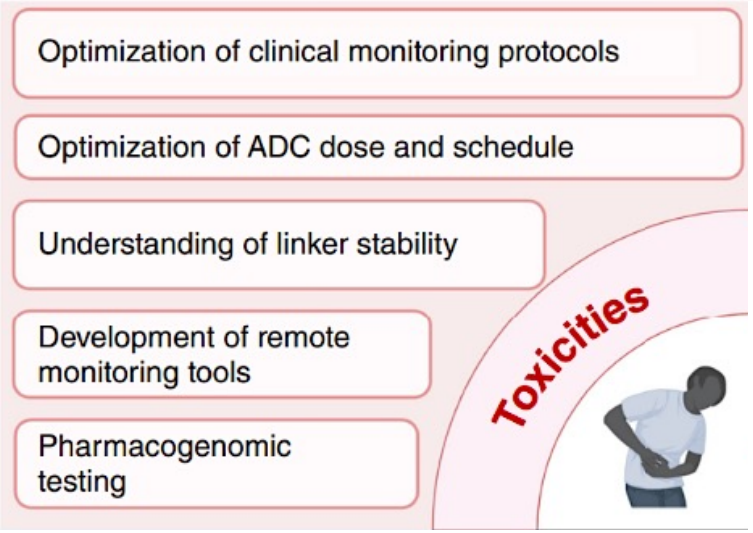


Urgent, unmet needs:

- Validating predictive biomarkers
- Streamlining testing and prioritization of identified targets As is Understanding the temporal and spatial heterogeneity of ADC targets
- Mechanisms of resistance

Colombo R et al. Cancer Discovery 2024; 14:2089-108

Opportunities for ADCs across a variety of targets and expanding considerations for the treatment setting demands focus on strategy, safety and sequencing

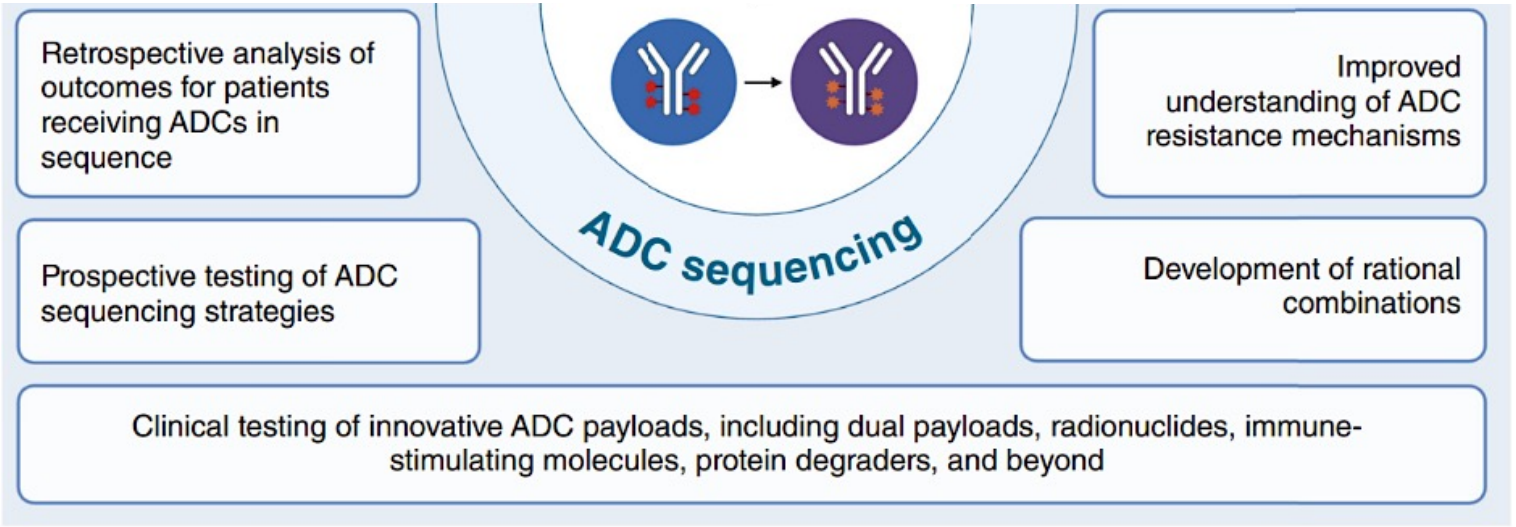


- Dose and Regimen Optimization are Critical (especially if ADCs move into maintenance)
- Patient centered study design to understand acute and chronic toxicities is needed to fully understand sequencing

Colombo R et al. Cancer Discovery 2024; 14:2089-108

Opportunities for ADCs across a variety of targets and expanding considerations for the treatment setting demands focus on strategy, safety and sequencing

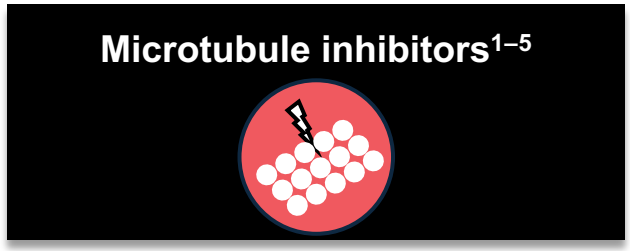
Understanding “IF” and “How” we sequence these agents from both an efficacy and safety standpoint is our next big opportunity to optimize outcomes for our patients



Colombo R et al. Cancer Discovery 2024; 14:2089-108

Assumption: Patients can receive one MTI and one Camptothecin ADC What would this look like?

Two classes of antitumor drugs are commonly used as payloads in ADCs[1]

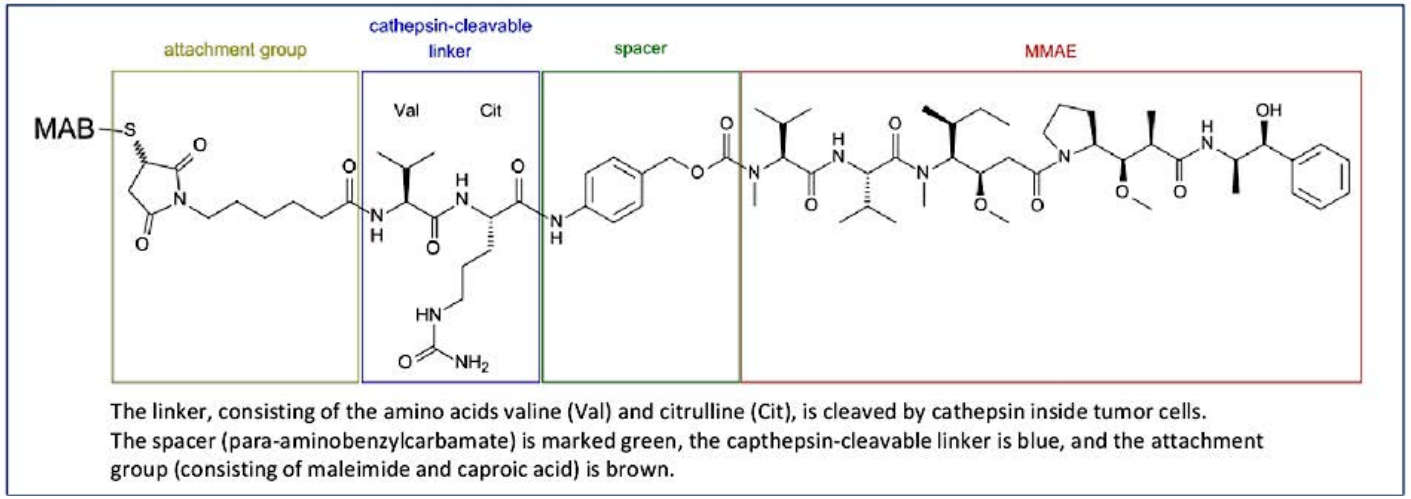


Considerations	Targets rapidly proliferating cells	Agents that may target DNA independent of cell cycle
Classes	• Auristatins (eg, MMAE, MMAF) • Eribulin • Hemiasterlin • Maytansinoids (eg, DM1, DM4) • Tubulysin	• Calicheamicin • Duocarmycin • Pyrrolobenzodiazepine • Topoisomerase inhibitor
Examples	• Mirvetuximab soravtansine • Tisotumab vedotin	• Sacituzumab govitecan • Trastuzumab deruxtecan

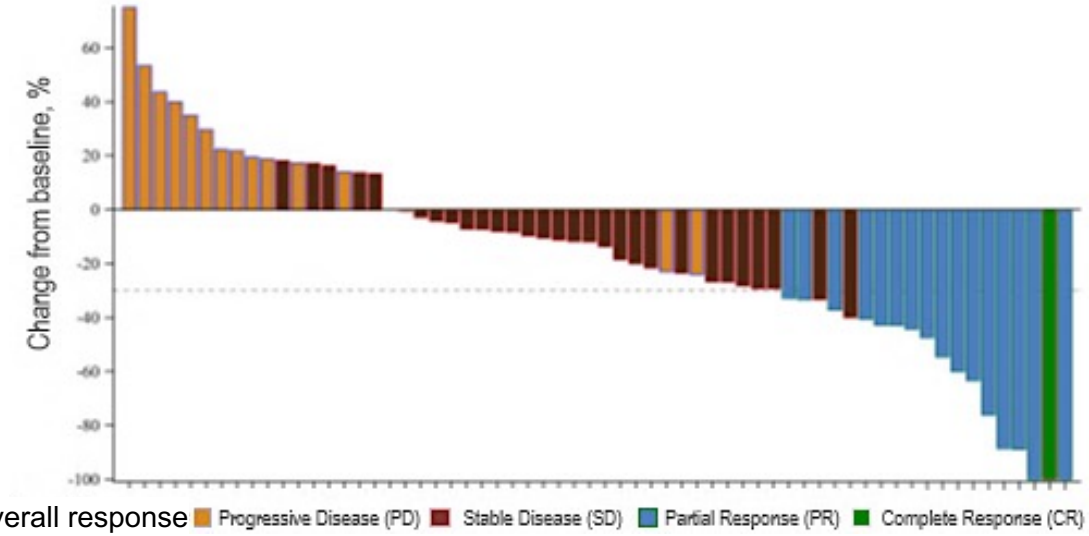
1. Fu Z et al. *Signal Transduct Target Ther*. 2022;7(1):93. 2. Donaghy H et al. *MAbs*. 2016;8(4):659–671. 3. Tang H et al. *Front Pharmacol*. 2019;10:373. 4. Cheng X et al. *Mol Cancer Ther*. 2018;17(2):2665–2675. 5. Chen H et al. *Molecules*. 2017;22(8):1281.

TORL-1-23 is an ADC targeting CLDN6 with a MTI payload
How would this look in clinical practice?

	TORL-1-23[1,2]
Payload	MMAE
DAR	TBD
Linker	Cathepsin hydrolysable dipeptide VC linker
Trial	NCT05103683



The linker, consisting of the amino acids valine (Val) and citrulline (Cit), is cleaved by cathepsin inside tumor cells. The spacer (para-aminobenzylcarbamate) is marked green, the capthepsin-cleavable linker is blue, and the attachment group (consisting of maleimide and caproic acid) is brown.

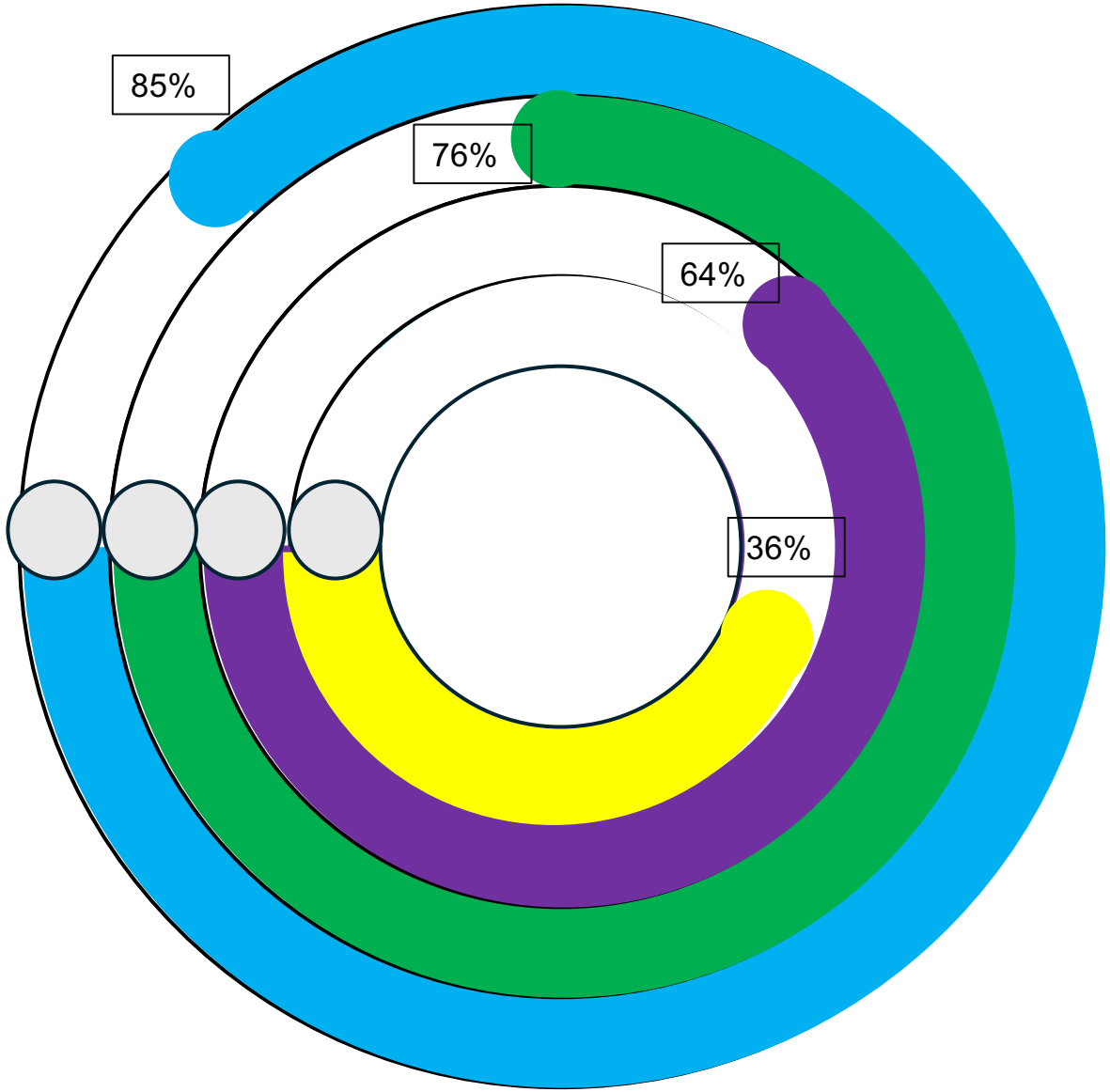


50% at 2.4 mg/kg in CLDN +
42% at 3.0 mg/kg in CLDN +

45% ≥Grade 3 neutropenia –now given with G-CSF…

1. Konecny G et alJ Clin Oncol 41, 2023 (suppl 16; abstr 3082). 2. ClinicalTrials.gov. NCT05103683 Accessed 2024. 1. Konecny G et alJ Clin Oncol 41, 2023 (suppl 16; abstr 3082). 2. ClinicalTrials.gov. NCT05103683 Accessed 2024

Development of additional ADCs with microtubule conjugates creates two categories from which we can choose: FRα and CLDN6



FRα high: 36%

FRα med & high: 64%

FRα positive: 76%

Any CLDN6: 85%

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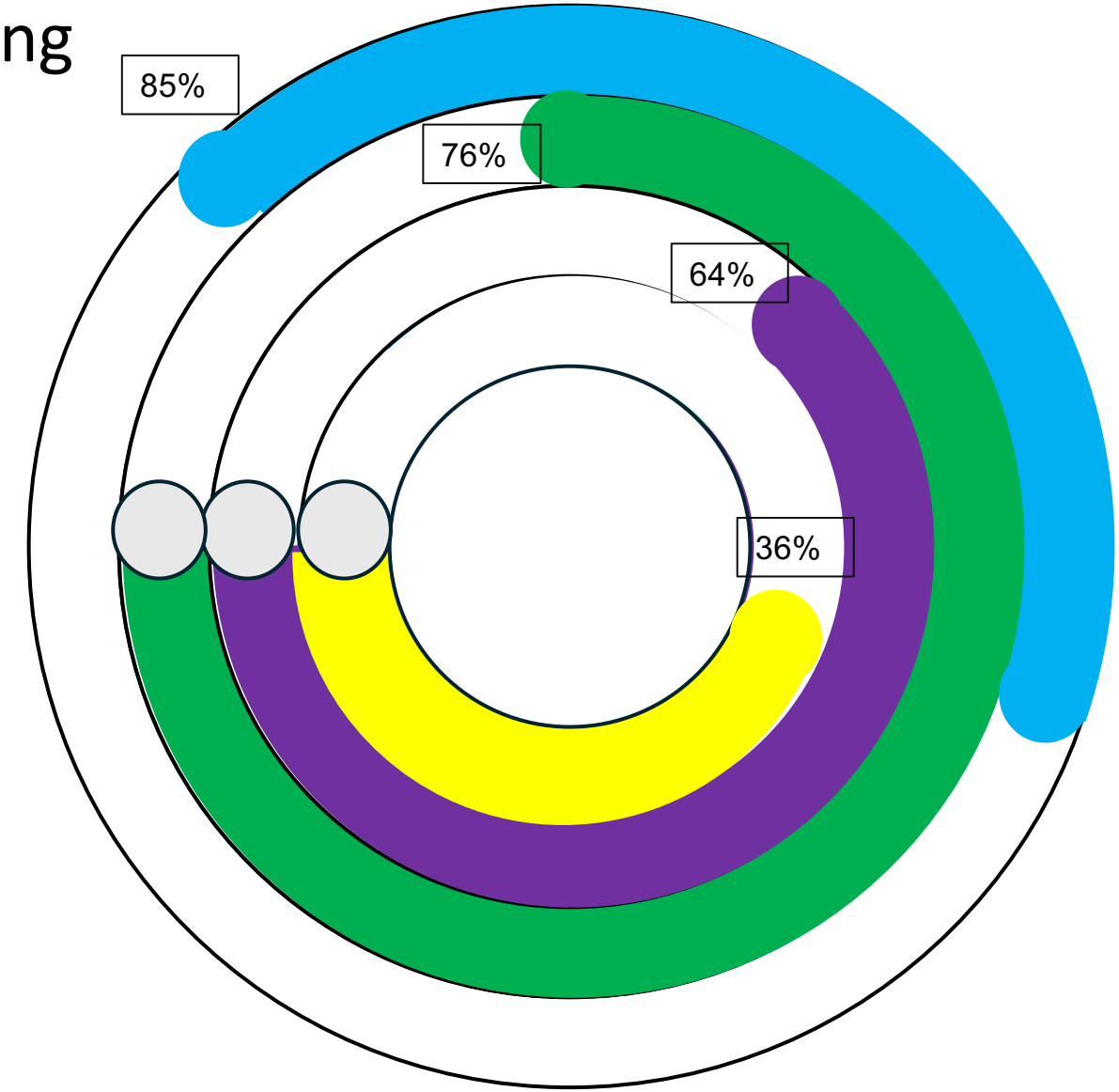
1. Deutschman E, et al. 36th European Congress of Pathology (ECP). 2024; Abs 2093 and poster 2. Lee et al. Annals Oncol Vol 35, Supplement 2 S579, 2024

Which medicine we choose may depend on the overlap or non-overlap of the biomarkers… here FRα high and CLDN6 “+” are basically non overlapping



FRα high: 36%

FRα med & high: 64%

FRα positive: 76%

CLDN6 “+” ?

1. Deutschman E, et al. 36th European Congress of Pathology (ECP). 2024; Abs 2093 and poster 2. Lee et al. Annals Oncol Vol 35, Supplement 2 S579, 2024

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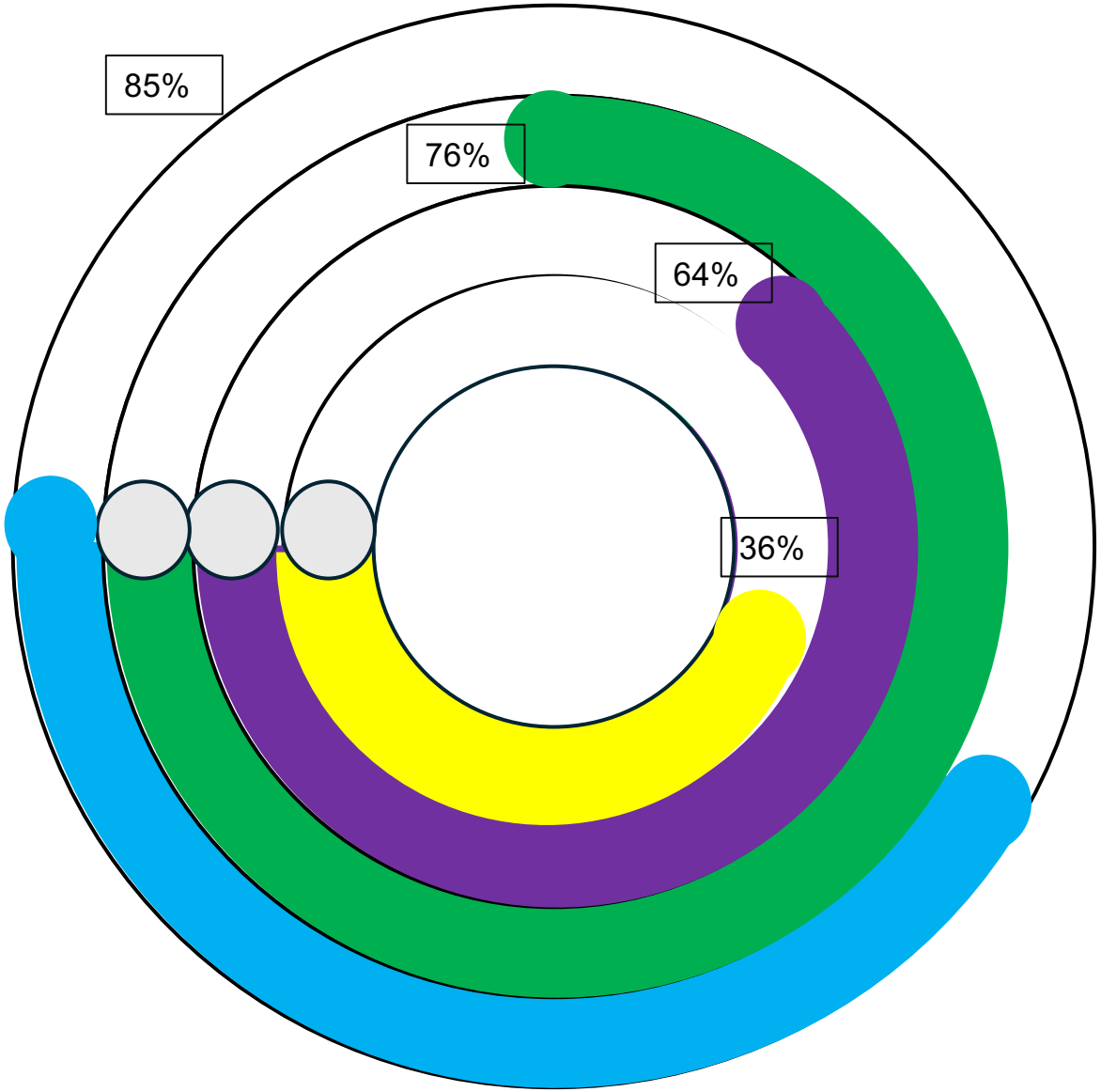
Vs. this scenario where selection of the agent may come down to efficacy, toxicity, shared decision making etc.



FRα high: 36%

FRα med & high: 64%

FRα positive: 76%

CLDN6 “+” ?

1. Deutschman E, et al. 36th European Congress of Pathology (ECP). 2024; Abs 2093 and poster 2. Lee et al. Annals Oncol Vol 35, Supplement 2 S579, 2024

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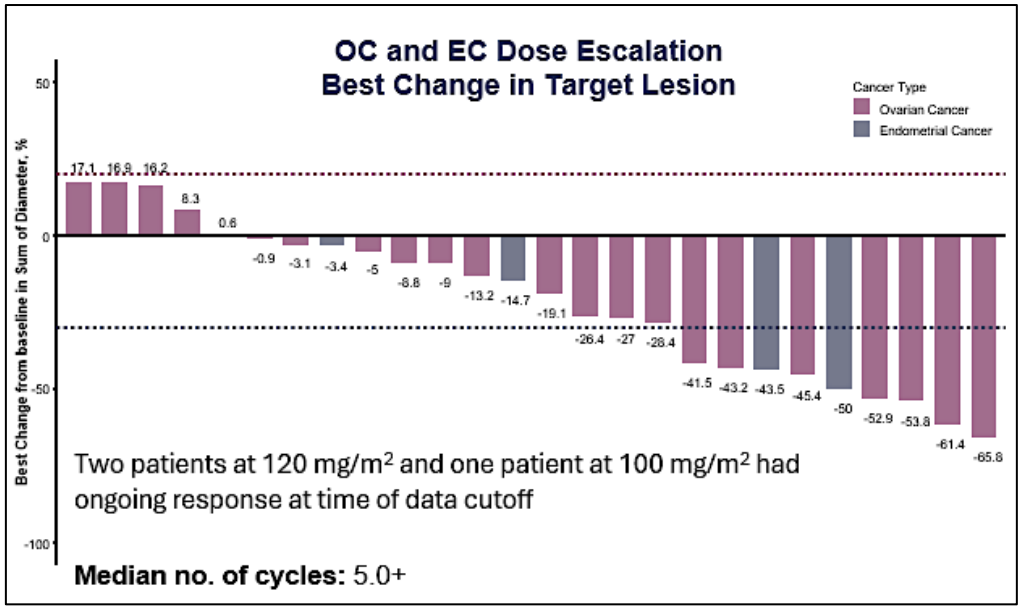
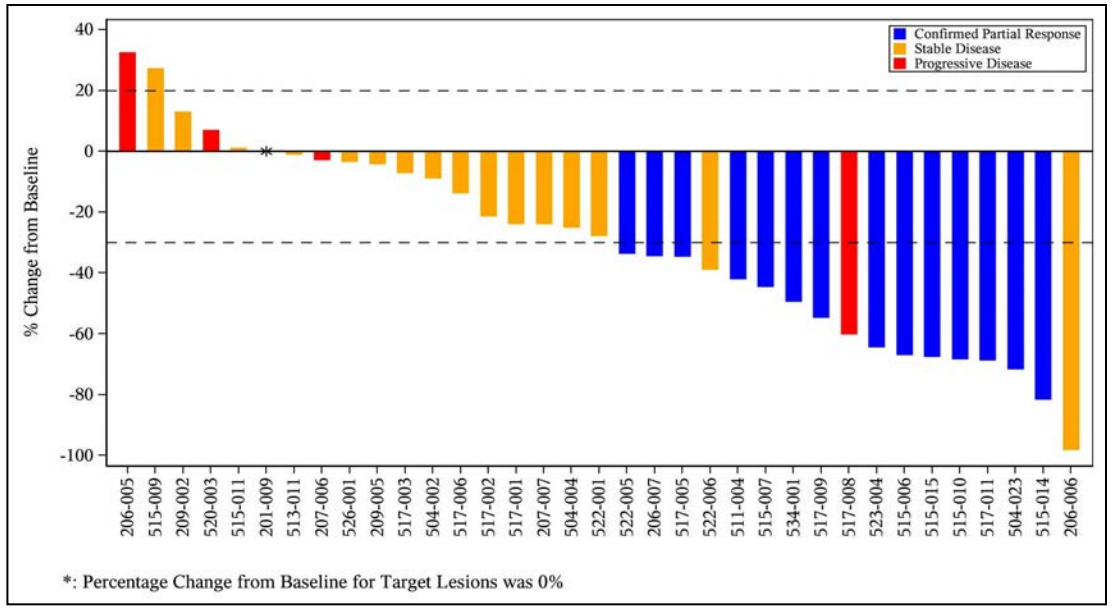
This scenario gets even more complex with camptothecin ADCs

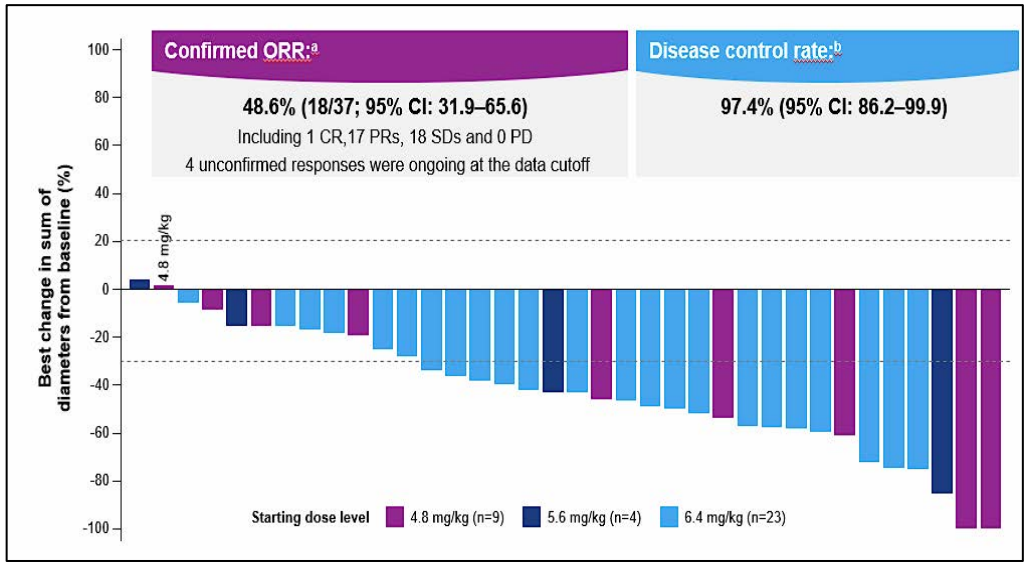
Rinatabart sesutecan



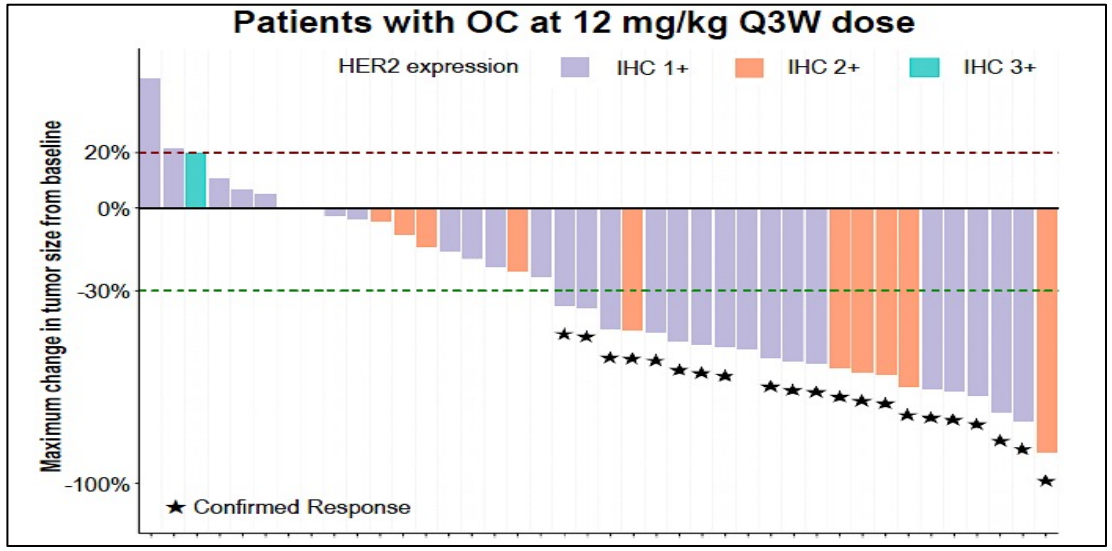
Sacituzumab tirumotecan



Raludotatug deruxtecan



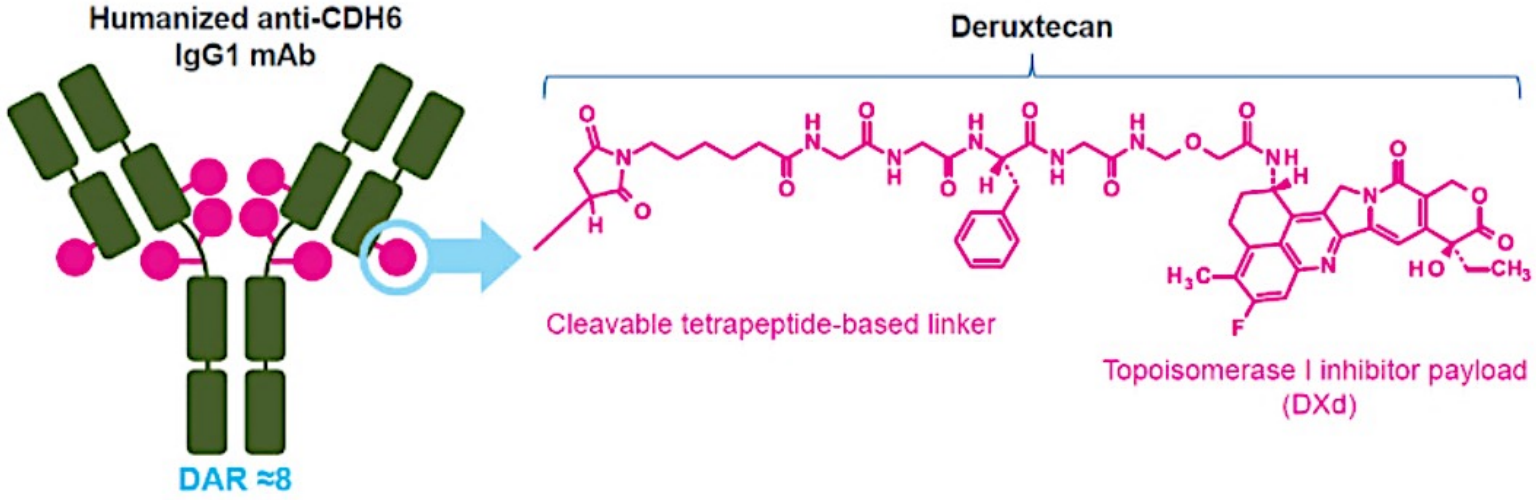
IBI354 (HER2)



Moore K, et al. Presented at European Society for Medical Oncology (ESMO) Annual Meeting; 20-24 October 2023; Madrid, Spain. . Shut J, et al. Presented at European Society for Medical Oncology (ESMO) Annual Meeting; 13-17 September 2024; . Wang D, et al. Presented at European Society for Medical Oncology (ESMO) Annual Meeting; 13-17 September 2024; ; ; Lee E, et al. Presented at European Society for Medical Oncology (ESMO) Annual Meeting; 13-17 September 2024; Barcelona, Spain

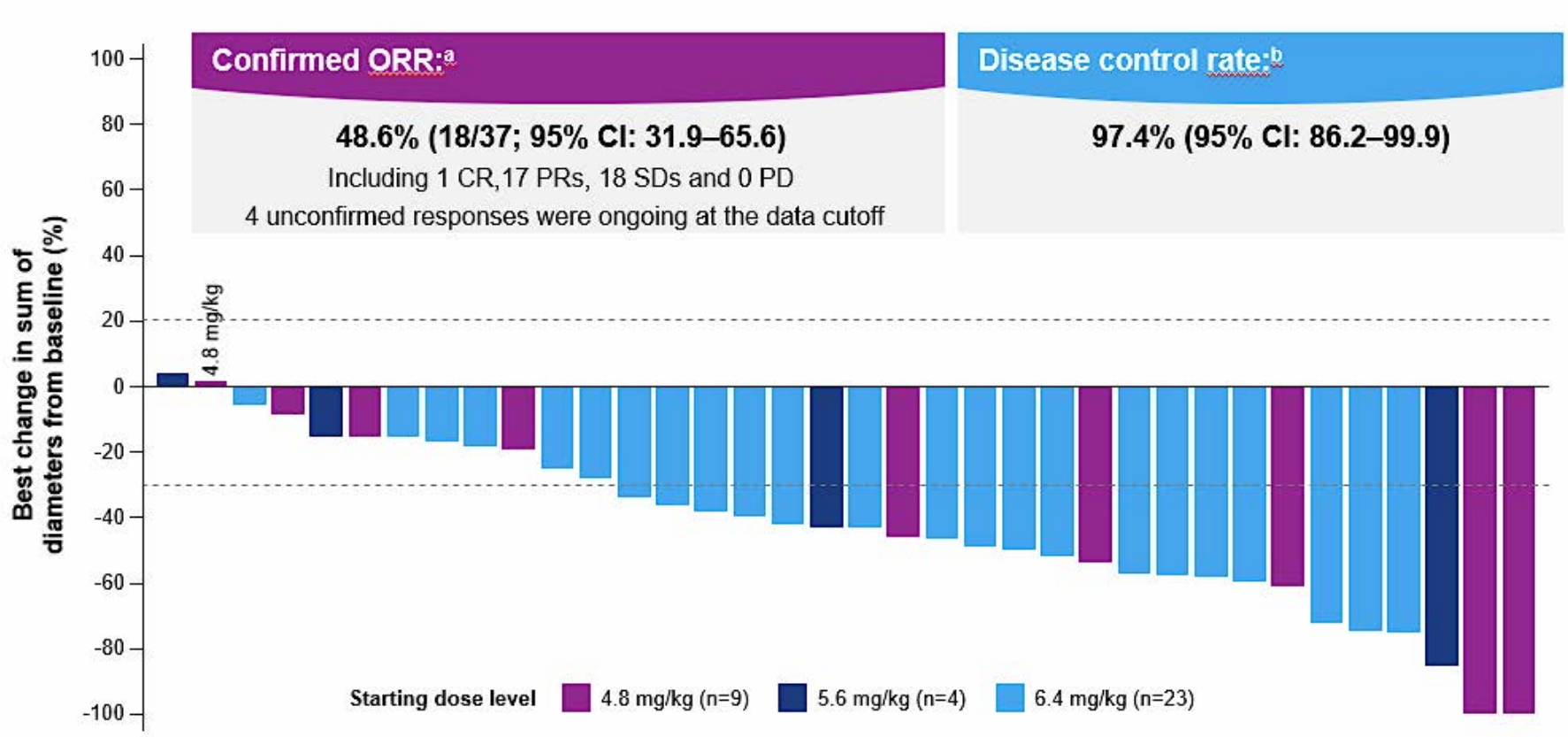
Targeting Cadherin 6 (CDH6): Raludotatug deruxtecan

	Raludotatug deruxtecan (DS-6000)[1,2]
Payload	Topoisomerase 1 inhibitor (DXd)
DAR	8
Linker	Cleavable tetrapeptide based linker
Trial	**NCT04707248**



1. Moore K, et al. Presented at European Society for Medical Oncology (ESMO) Annual Meeting; 20-24 October 2023; Madrid, Spain.;
2. NCT04707248. Accessed from: https://clinicaltrials.gov/study/NCT04707248?cond=NCT04707248&rank=1.

Targeting Cadherin 6 (CDH6): Raludotatug deruxtecan



Median DOR:[a]

11.2 months (95% CI: 3.1–NE)

Median (range) FU: 6.7 months (1.4–16.8)

Median TTR:[a]

5.7 weeks (95% CI: 5.3–11.4)

Median PFS:[b]

8.1 months (95% CI: 5.3–NE)

Median (range) FU: 4.0 months (0–25.1)

Median number of prior systemic therapies = 4 (1-13)

41/60 (68.3%) received prior bevacizumab; 39/60 (65%) received prior PARPi

1. Moore K, et al. Presented at European Society for Medical Oncology (ESMO) Annual Meeting; 20-24 October 2023; Madrid, Spain.;
2. NCT04707248. Accessed from: https://clinicaltrials.gov/study/NCT04707248?cond=NCT04707248&rank=1.

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Raludotatug deruxtecan: Safety

Patients with OVC who received R-DXd at 4.8–8.0 mg/kg

Overview of TEAEs

	n (%) N=60
Any TEAEs	57 (95.0)
TEAE with CTCAE Grade ≥3	31 (51.7)
TEAE associated with drug discontinuation	9 (15.0)
TEAE associated with dose interruption	22 (36.7)
TEAE associated with dose reduction	15 (25.0)
Any treatment-related CTCAE Grade ≥3 TEAE	22 (36.7)
Treatment-related TEAE associated with death	2 (3.3)[a]

- 3.3% (2/60) of patients in the 4.8–8.0 mg/kg cohort experienced Grade 5 ILD; both occurred in the 8.0 mg/kg cohort and were adjudicated as treatment-related
- 8.9% (4/45) of patients in the 4.8–6.4 mg/kg cohort experienced ILD (all Grade 2), of which 2 were adjudicated as treatment-related
- As of October 2022, the 8.0 mg/kg cohort was closed due to a higher incidence of serious and Grade ≥3 TEAEs and lack of a favorable benefit/risk ratio[b]
- Further dose assessment is ongoing at three doses: 4.8, 5.6 and 6.4 mg/kg

Data cutoff: July 14, 2023.

[a]Grade 5 ILD. [b]6/15 (40.0%) patients in the 8.0-mg/kg OVC cohort experienced serious and Grade ≥3 TEAEs.

CTCAE, Common Terminology Criteria for Adverse Events; ILD, interstitial lung disease; OVC, ovarian cancer; TEAE, treatment-emergent adverse event.

Most common (≥10%) treatment-related TEAEs

Preferred term	n (%) N=60	
	All grades	Grade ≥3
Nausea	35 (58.3)	1 (1.7)
Fatigue	27 (45.0)	2 (3.3)
Vomiting	20 (33.3)	1 (1.7)
Anemia	17 (28.3)	11 (18.3)
Decreased neutrophil count	15 (25.0)	7 (11.7)
Diarrhea	16 (26.7)	1 (1.7)
Decreased appetite	15 (25.0)	1 (1.7)
Decreased platelet count	10 (16.7)	3 (5.0)
Alopecia	7 (11.7)	0
Malaise	6 (10.0)	0

MADRID 2023 ESMO congress

Kathleen Moore

Moore K et. al, ESMO 2023; Abstract 745MO.

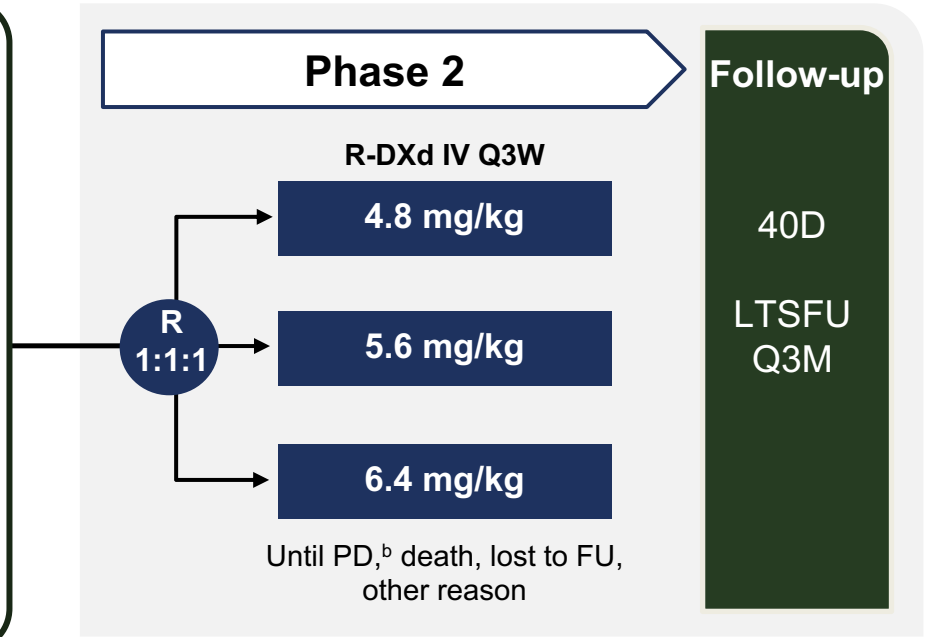
REJOICE-Ovarian01/GOG-3096: Phase 2/3 Randomized Study of R-DXd in Platinum-Resistant EOC

Key eligibility criteria:

- High-grade serous or endometrioid ovarian, primary peritoneal, or fallopian tube cancer
- 1−3 prior LOT (inc. bevacizumab)
- Platinum-resistant disease
- Prior MIRV if high FRα[a]
- ECOG PS 0−1
- No prior CDH6-targeting agents or ADCs with linked TOPO I inhibitor
- Patients with primary platinum-refractory disease are not eligible

Stratification:

- Number of prior LOT (1 vs 2/3)
- CDH6 expression (high vs low)
- TPC (paclitaxel vs others; *Ph 3 only*)

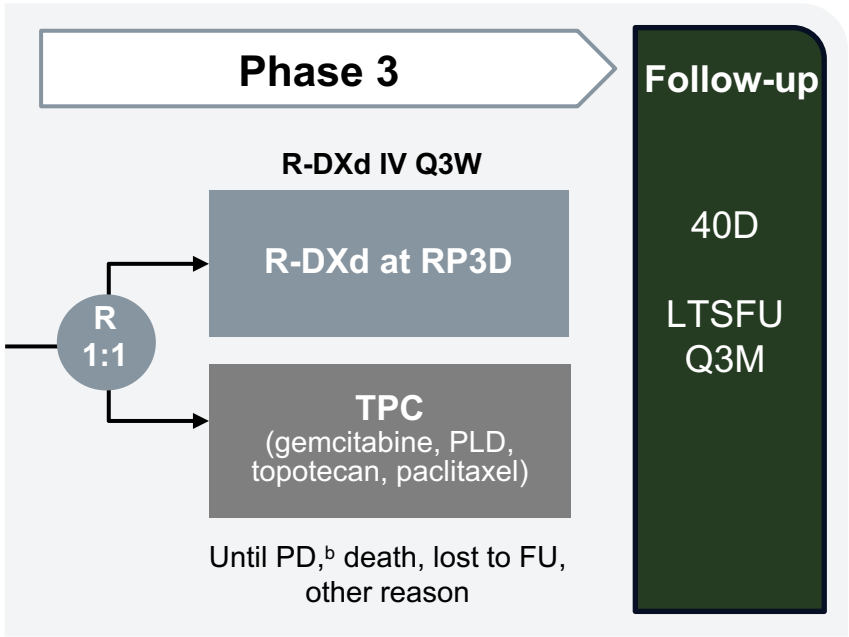


Primary endpoint:

- ORR per BICR[b]

Key secondary endpoints:

- ORR per inv[b]
- DOR



Primary endpoints:

- ORR per BICR[b]
- PFS per BICR[b]

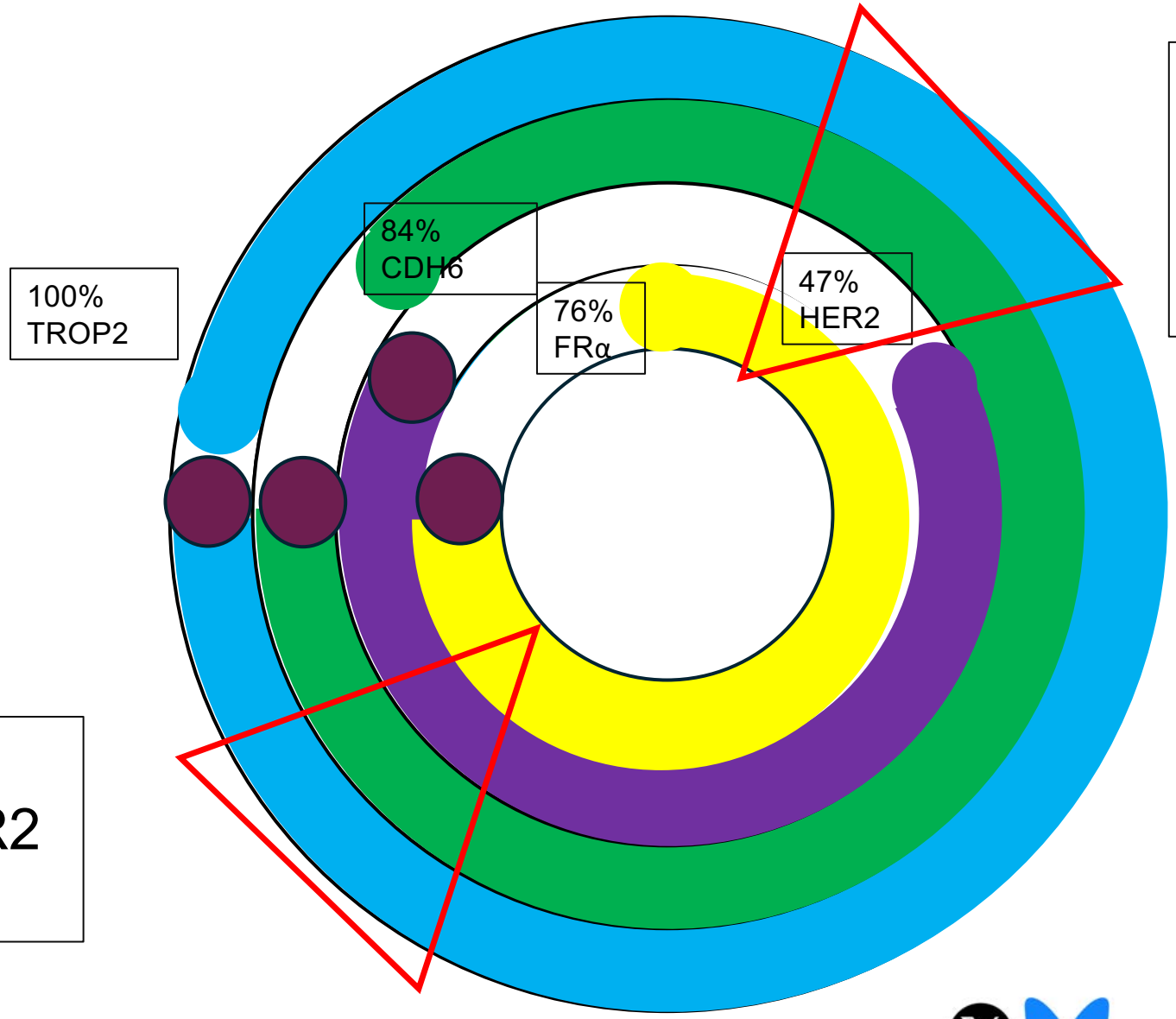
Key secondary endpoints:

- OS
- QOL

NCT06161025

NCT06161025. Accessed from: https://clinicaltrials.gov/study/NCT06161025?term=NCT06161025&rank=1.

Targeting HER2, FRα, CDH6, and TROP2: How do you select an agent?



Vs TROP2 1+, CDH6 3+, HER2 0+ and FRα 3+

TROP2 2+, CDH6 2+, HER2 1+ and FRα 2+

Konecny G, et al. *J Clin Oncol.* 2023;41,S16,Abstract 3082.; NCT05103683 via ClinicalTrials.gov. Accessed 2024.

ADCs for Platinum Sensitive Disease: It's time to Optimize Regimens in OC in a Post PARPi World

	Sacituzumab tirumotecan 5mg/kg D1, D15 N=5 (PSOC)	Datopotamab deruxtecan N=9 (PSOC)	Mirvetuximab soravtansine N=79
Payload	Belotecan derivative Topoisomerase I	Topoisomerase 1- deruxtecan	DM4
DAR	7.4	4	4
Linker	Sulfonyl pyrimidine CL2A-carbonate linker	Cleavable tetrapeptide based linker	Cleavable linker
Trial	NCT06049212	NCT05489211	NCT05041257
ORR	60% (PSOC N=5)	66.7% (PSOC N=9)	51.9% (95%CI 40.4-63.3)
DOR	ND	ND	8.25 (95% CI 5.55-10.78)
mPFS	ND	ND	6.93 (95% CI 5.85-9.59)

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Sequencing of ADCs both in PROC and PSOC space must be considered --- even front line --- Context is important

- Patient Demographics

Variable	Patients (n = 419)
Age (median, ±SD)	54 (± 10.54)
Initial Stage	
I	34 (8.1%)
II	21 (5.0%)
III	166 (39.6%)
IV	197 (47.0%)
Unknown	1 (0.3%)
Histology	
HGSC	332 (79.2%)
Endometrioid	12 (2.9%)
Clear cell	34 (8.1%)
Mucinous	15 (3.6%)
Others*	26 (6.2%)
BRCA status (n=191)	
HRp	54 (27.7%)
BRCAm	76 (38.7%)
BRCAwt HRD	65 (33.5%)

* Others: sarcoma, poorly differentiated carcinoma, etc

- HER2 IHC and BRCA mutation/HRD status in HGSC and high-grade endometrioid carcinoma (p-value 0.005822**)

HER2	HRp	BRCAm/HRD
0/1+	55 (94.8%)	115 (79.3%)
2+/3+	3 (5.2%)	30 (20.7%)
Sum	58	145

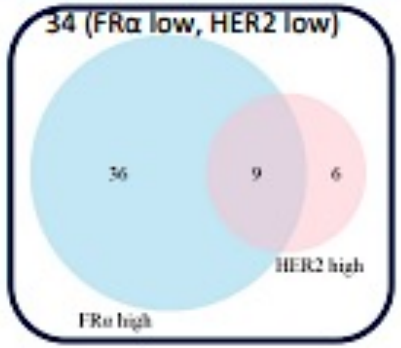
*HRp; Homologous recombination proficiency

- Expression of HER2 IHC according to histology in OC (p-value 0.002794***)

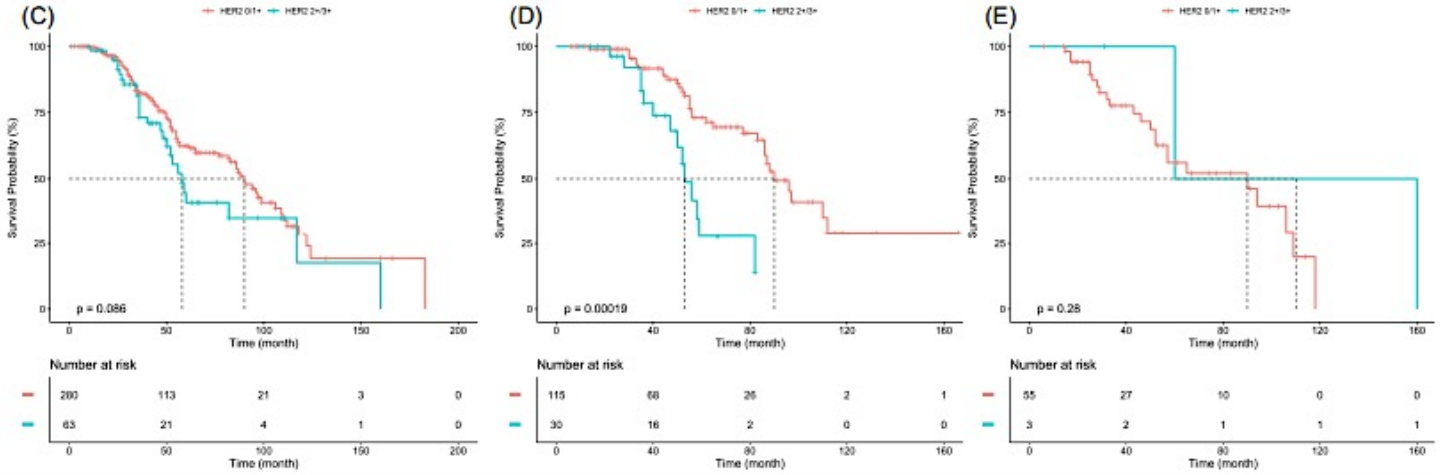
HER2	HGSC	Endometrioid	Clear cell	Mucinous	Others
0	204 (63.0%)	8 (66.7%)	12 (36.4%)	5 (33.3%)	17 (65.4%)
1+	66 (18.3%)	3 (25.0%)	7 (21.2%)	2 (13.3%)	2 (7.7%)
2+	43 (13.4%)	1 (8.3%)	11 (33.3%)	4 (26.7%)	6 (23.1%)
3+	19 (5.3%)	0 (0.0%)	4 (9.1%)	4 (26.7%)	1 (3.8%)
Total	332	12	34	15	26

- HER2 IHC and FRα expression

*FRα high: > 75%
HER2 high: 3+



- Overall survival for patients with HGSC and high-grade endometrioid carcinoma: (C) all patients, (D) those with BRCAm/HRD, and (E) those with HRp.



Lee D et al. ESMO 2024 765P

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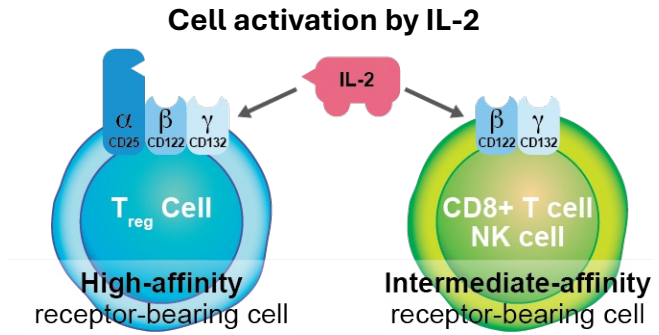
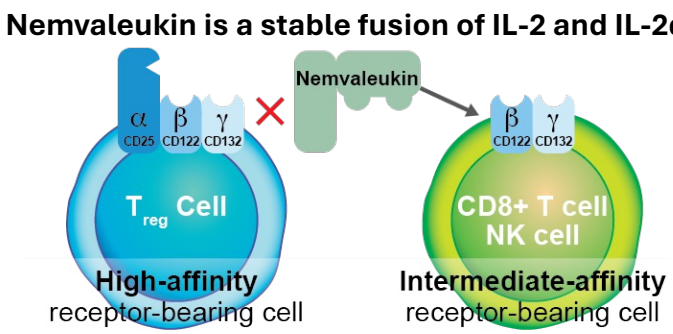
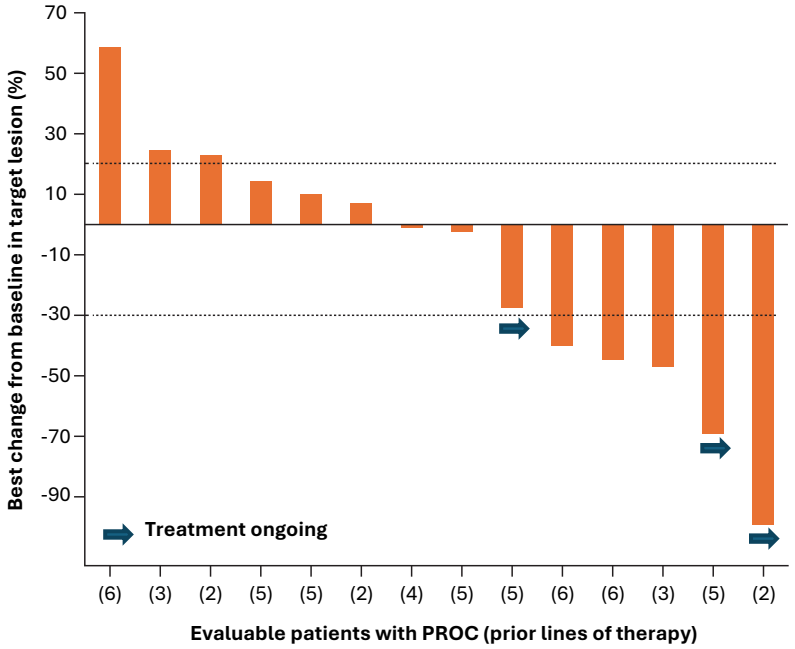
Nemvaleukin alfa: a modified interleukin-2 cytokine



- Preferential activation of high-affinity IL-2R by high-dose IL-2 leads to expansion of T_{regs}, which may counteract antitumor activity as well as stimulate vascular endothelial cells
- Activation of vascular endothelial cells is associated with high incidence of acute toxicities, including capillary leak syndrome



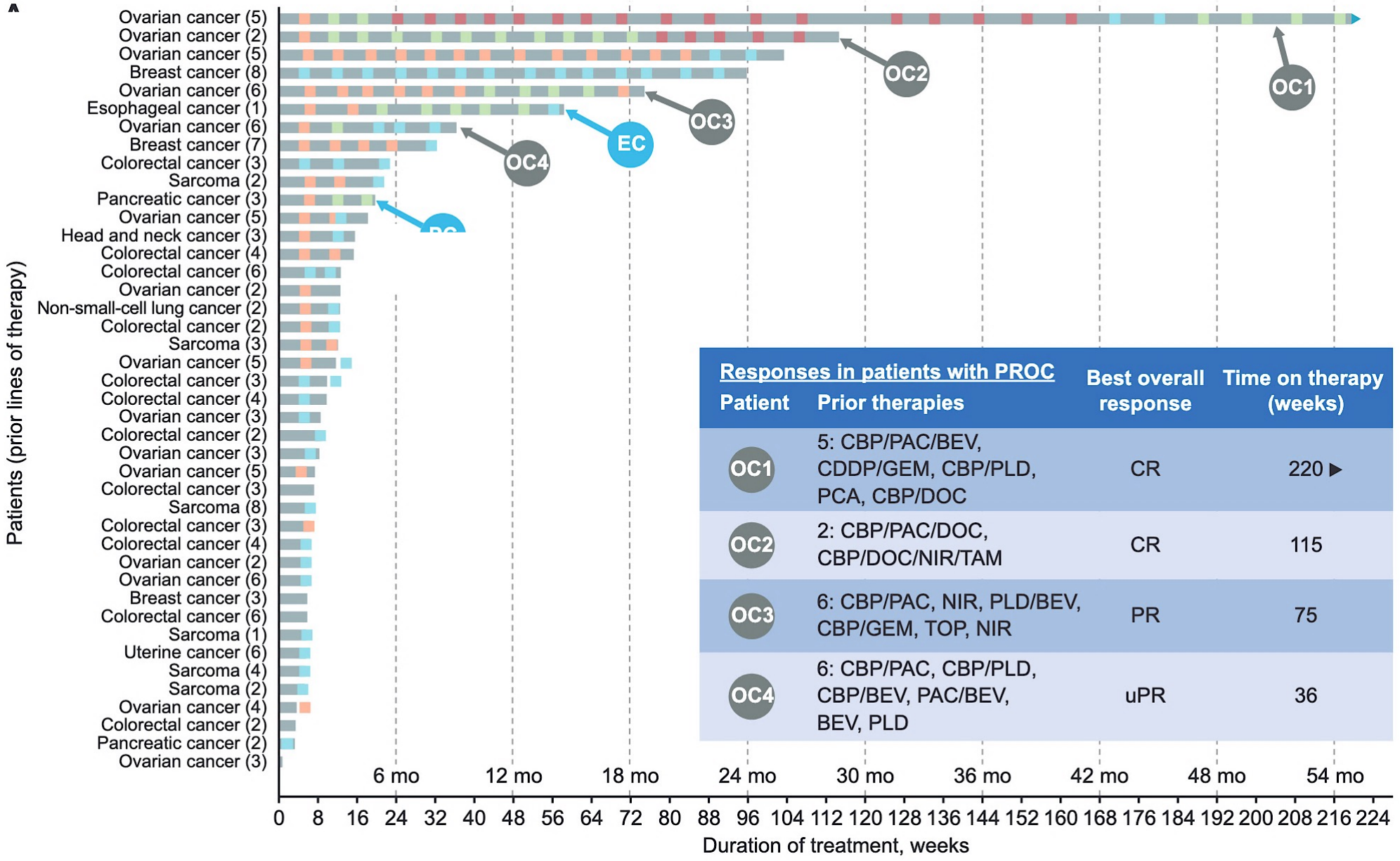
- Stable fusion protein designed to harness the validated IL-2 pathway biology
- Intrinsically active immediately upon systemic entry; does not degrade to native IL-2
- Designed to selectively bind the immediate-affinity IL-2R to:
  - Preferentially activate memory cytotoxic $CD8^+$ T cells and NK cells without expanding $CD4^+$ T_{regs}
  - Mitigate toxicities associated with preferential binding of IL-2 to high-affinity IL-2R



N=14 evaluable patients with PROC who received nemvaleukin 3μg/kg IV + pembrolizumab and ≥ 1 postbaseline scan.

Vaishampayan UN, Muzaffar J, Winer I, et al. *J Immunother Cancer*. 2024;12(11):e010143. Published 2024 Nov 20.

ARTISTRY-1: Summary of responses with nemvaleukin alfa + pembrolizumab

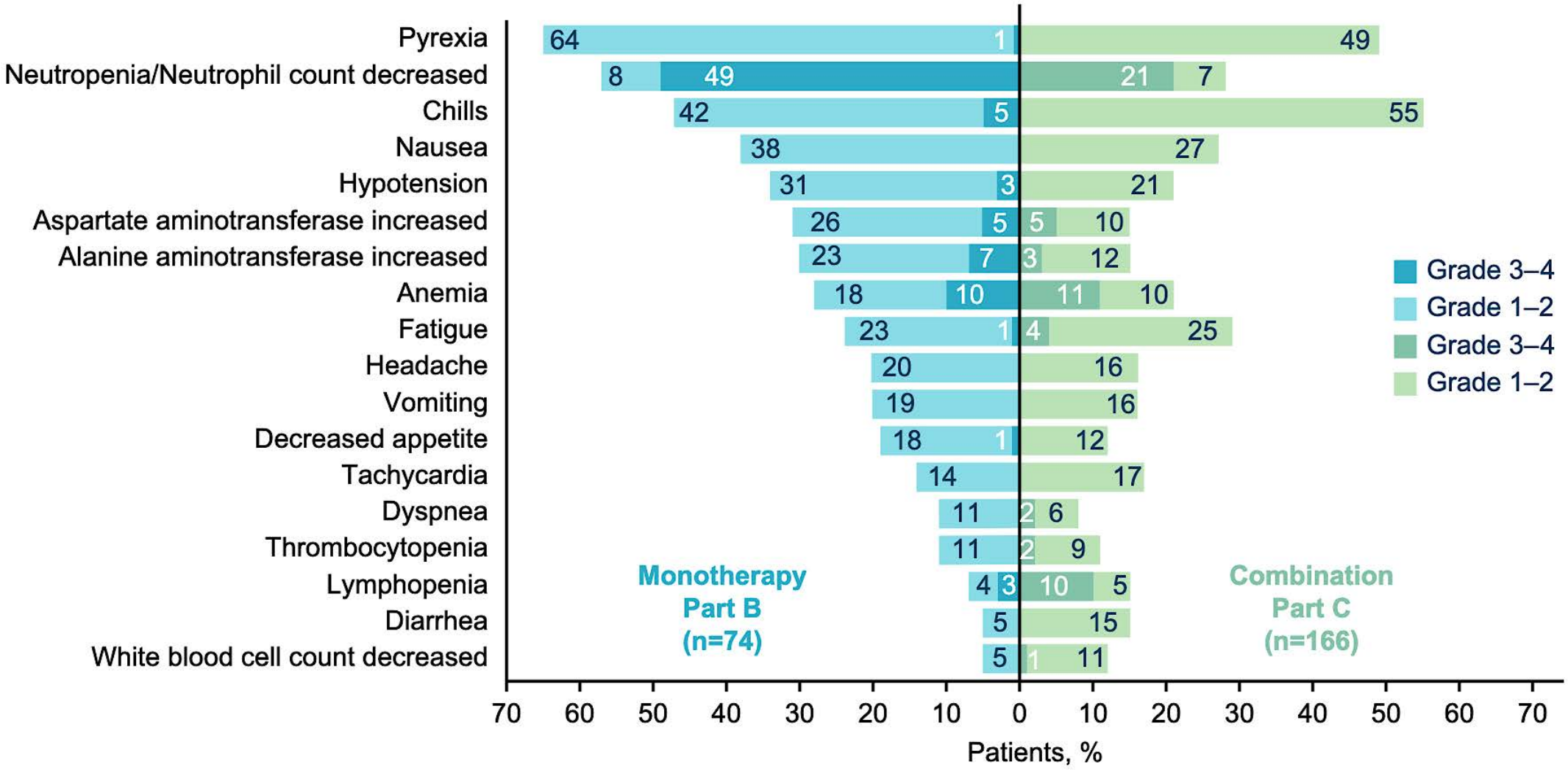


Responses in patients with PROC

Patient	Prior therapies	Best overall response	Time on therapy (weeks)
OC1	5: CBP/PAC/BEV, CDDP/GEM, CBP/PLD, PCA, CBP/DOC	CR	220 ▶
OC2	2: CBP/PAC/DOC, CBP/DOC/NIR/TAM	CR	115
OC3	6: CBP/PAC, NIR, PLD/BEV, CBP/GEM, TOP, NIR	PR	75
OC4	6: CBP/PAC, CBP/PLD, CBP/BEV, PAC/BEV, BEV, PLD	uPR	36

Vaishampayan UN, Muzaffar J, Winer I, et al. *J Immunother Cancer*. 2024;12(11):e010143. Published 2024 Nov 20.

ARTISTRY-1: Safety



Vaishampayan UN, Muzaffar J, Winer I, et al. *J Immunother Cancer*. 2024;12(11):e010143. Published 2024 Nov 20.

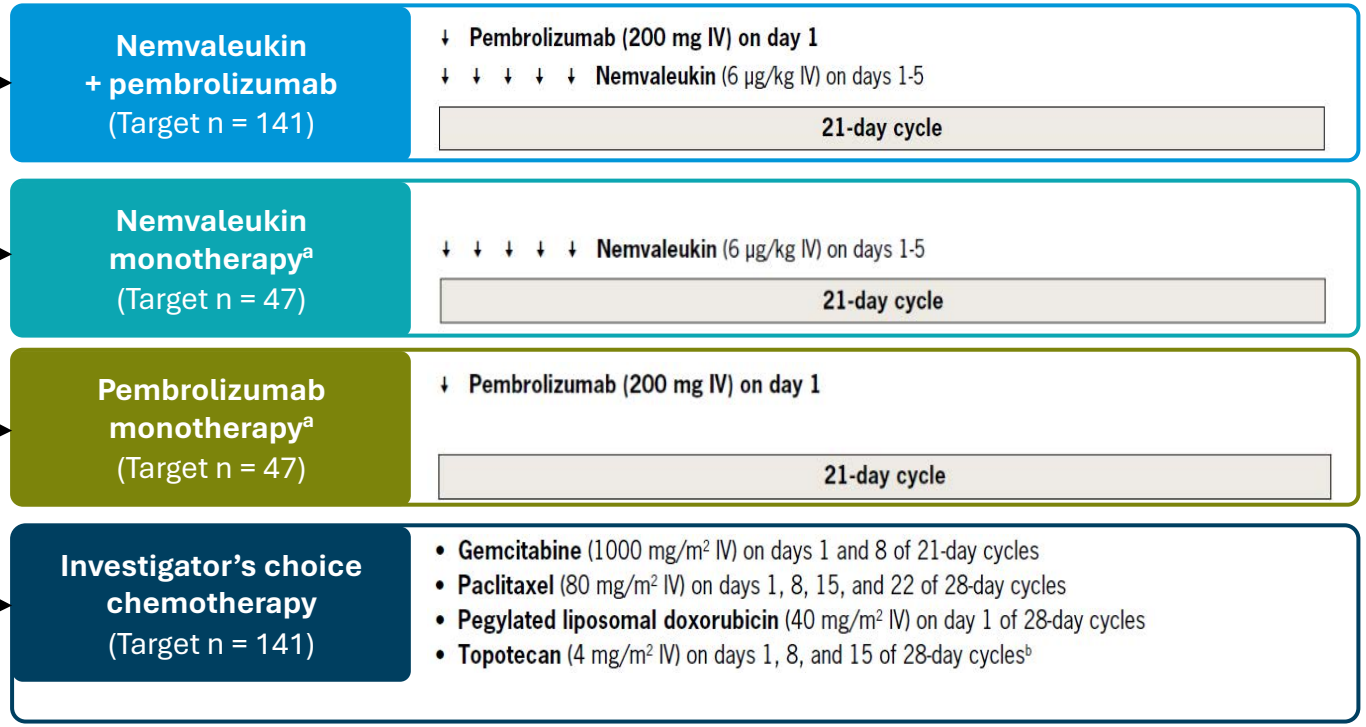
ARTISTRY-7: Phase 3 study of nemvaleukin alfa + pembrolizumab vs chemotherapy in patients with PROC

Key inclusion criteria
- HGSOC
- ≥1 LOT in Pt-sensitive setting
- ≤ 5 prior LOT in Pt-resistant setting
- Prior bev
- Prior PARPi if *BRCA*m

Target
N = 376

Randomization
3:1:1:3

Stratification:
- **PD-(L)1 status**
- **Histology**
- **Chemotherapy**



NCT02839707
- Status: Active, not recruiting
- Actual enrollment: 456 participants
- Estimated primary completion date: December 2025

[a] Futility analyses planned to stop the monotherapy arms earlier. [b] 1.25 mg/m2 on days 1-5 of 21-day cycles is also an option.

1. Herzog TJ et al. ASCO 2022. Abstract TPS5609. 2. ClinicalTrials.gov. NCT02839707. Accessed March 2025.

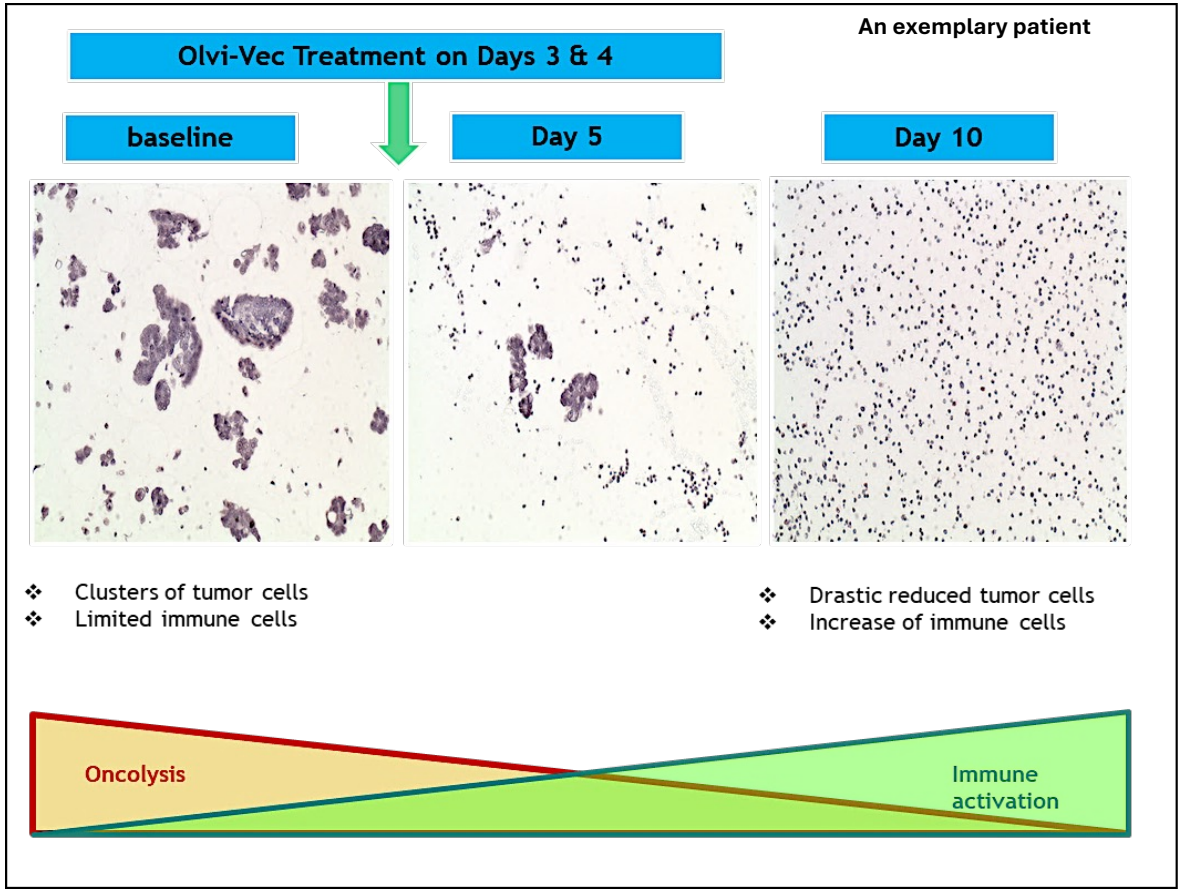
Oncolytic Vaccinia Virus Olvi-Vec (olvimulogene nanivacirepvec)

Olvi-Vec

- Modified oncolytic vaccinia virus (LIVP strain) with mutations that enhance tumor targeting
- AKA: GL-ONC1 and original laboratory name: GLV-1h68

Olvi-Vec converts 'Cold' ovarian cancers to 'Hot'

- Olvi-Vec triggers oncolysis, augmented tumor (neo)antigen presentation, and immunogenic cell death (ICD)
- Enhances tumor-infiltrating lymphocytes (TILs)



Malignant ascites in Phase 1b patient showing tumor cell oncolysis with increasing lymphocyte infiltration

AKA, also known as.

1. Zhang Q et al. *Mol Genet Genomics*. 2009;282(4):417-435. 2. Holloway RW et al. ASCO 2018. Abstract 5577. 3. Holloway RW et al. IGCS 2020. Abstract 1308.

Olvi-Vec VIRO-15 study: ORR,[a] PFS,[a] and OS in platinum-refractory/resistant ovarian cancer

All patients had documented progressive disease at enrollment into VIRO-15 trial.

	ORR by RECIST v1.1[b]	Duration of response, mo	ORR by CA-125	Median PFS, mo	Median OS, mo
All patients (n=27) (95% CI)	**54%** (13[c]/24) (33 – 74)	**7.6** (3.7 – 9.6)	**85%** (22/26) (65 – 96)	**11.0** (6.7 – 13.0)	**15.7** (12.3 – 23.8)
Platinum-resistant (n=14) (95% CI)	**55%** (6[d]/11) (26 – 84)	**7.6** (3.7 – NA)	**85%** (11/13) (55 – 98)	**10.0** (6.4 – NA)	**18.5** (11.3 – 23.8)
Platinum-refractory (n=13) (95% CI)	**54%** (7[e]/13) (27 – 81)	**8.0** (3.7 – NA)	**85%** (11/13) (55 – 98)	**11.4** (4.3 –13.2)	**14.7** (10.8 – 33.6)

[a] Baseline for ORR & PFS evaluation is the timepoint immediately prior to starting post-olvi-vec carboplatin doublet +/- bevacizumab to allow direct comparison to historical data or patients' own previous line of chemotherapy.

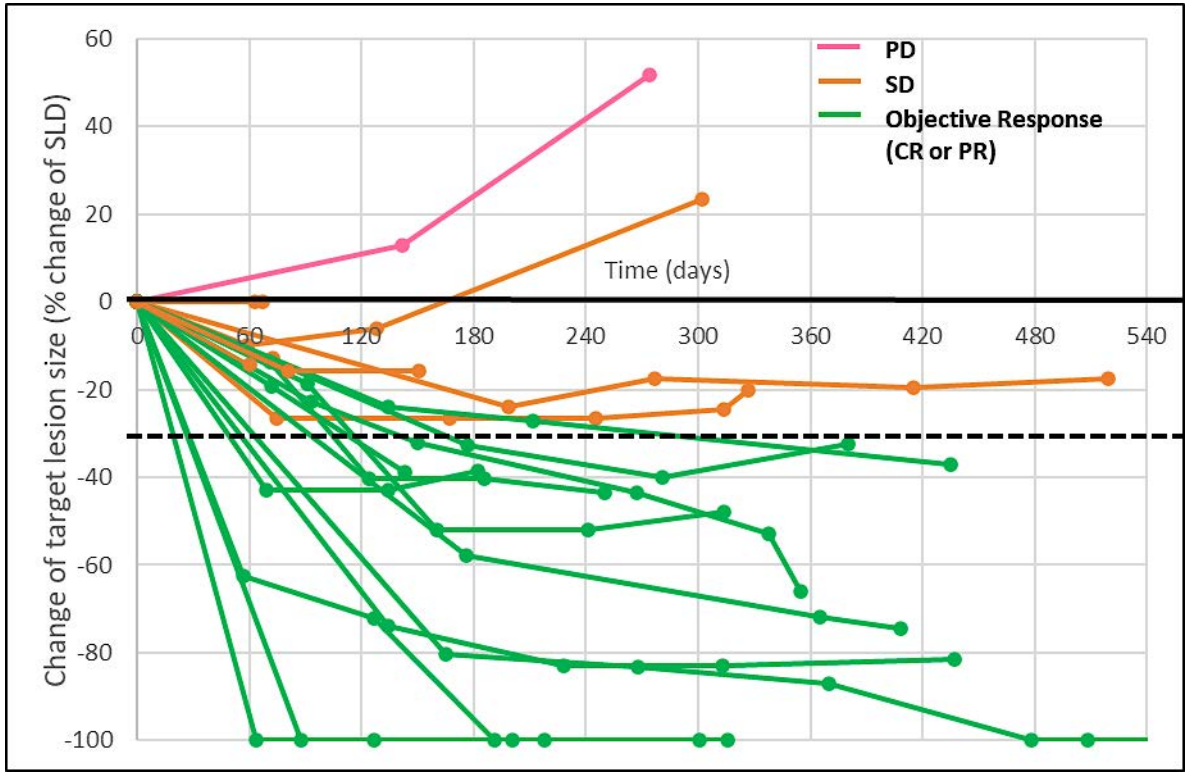
[b] Eligible for evaluation: with at least 1 measurable target lesion at baseline; including 2 patients without post-chemotherapy scan after virotherapy, and therefore are assigned to the 'unevaluable for response' category per RECIST1.1.

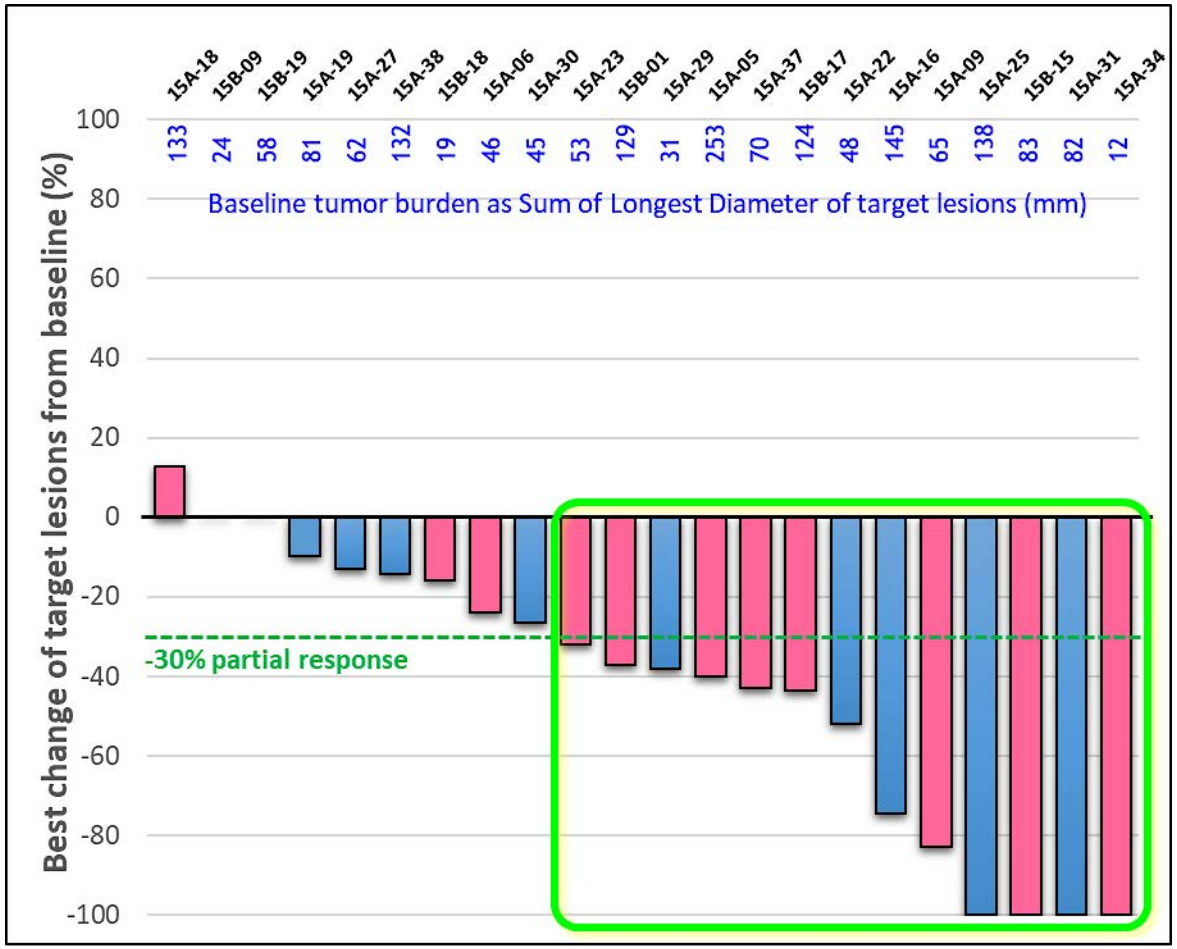
[c] 9 confirmed, 4 unconfirmed. [d] 3 confirmed, 3 unconfirmed. [e] 6 confirmed, 1 unconfirmed.

1. Holloway RW et al. IGCS 2020. Abstract 1308. 2. Holloway RW et al. *Ann Oncol.* 2020;31(suppl_4):S551–S589.

Olvi-Vec VIRO-15 study: ORR by RECIST v1.1

- RECIST v1.1 response = 54% (13/24)
- Disease Control Rate (CR+PR+SD) = 89% (24/27)





4 patients achieved 100% reduction of target lesions (even in a platinum-refractory patient with heavy tumor burden)

CR, complete response; ORR, objective response rate; PR, partial response; RECIST, Response Evaluation Criteria in Solid Tumors; SD, stable disease.

Holloway RW et al. IGCS 2020. Abstract 1308

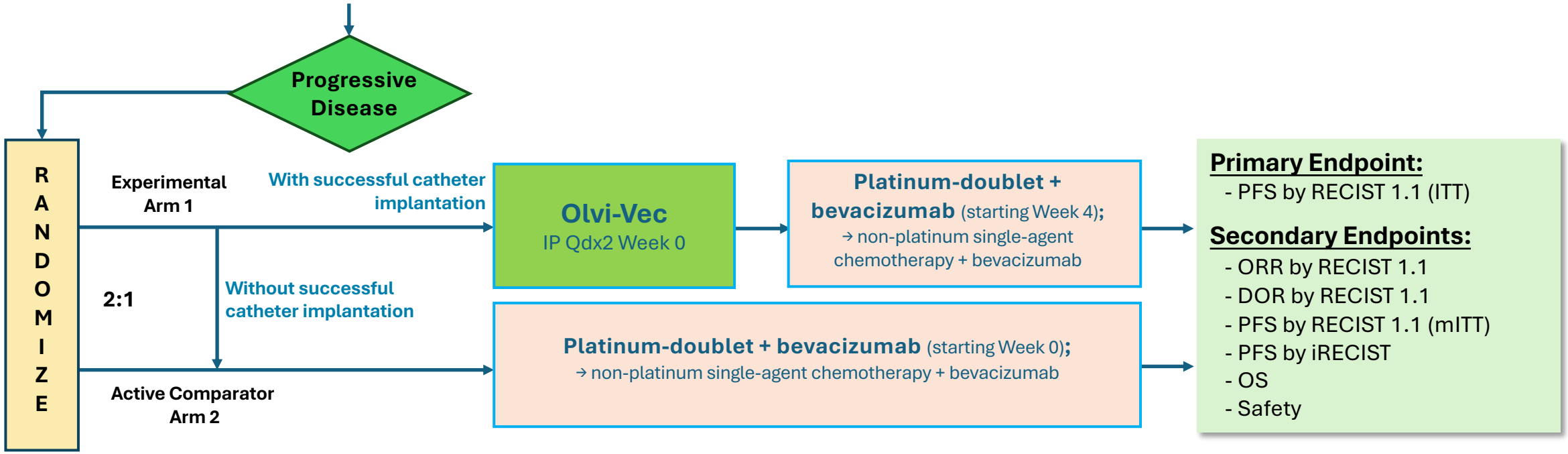
Phase 3 OnPrime/GOG-3076 trial in platinum-refractory/resistant ovarian cancer

Platinum-resistant/refractory ovarian cancer (PRROC)

- Number of prior lines: ≥3
- Had prior bevacizumab or biosimilar
- Platinum-free interval (PFI): 0-1 month or 1-6 months
- Time from last platinum (TFLP) dose: 3-15 months

Stratification at Enrollment Prior to Randomization

- PFI after most recent platinum-based therapy: <1 month vs. 1-6 months
- Baseline germline *BRCA*1/2 mutation status: positive vs. negative



Holloway R et al. IGCS 2022. Abstract TPO26

Questions from Gynecologic Oncologists and General Medical Oncologists

- 68-year-old woman with platinum-resistant relapsed OC. Has progressed on mirvetuximab and most recently on single-agent liposomal doxorubicin. What possible salvage therapies would you recommend if the patient still wants treatment and has an ECOG PS of 1?
- The upcoming treatments for ovarian cancer are so numerous, it is difficult to keep up with the emerging science. What is your 10,000-foot view of the up-and-coming therapies, including at the SGO meeting this year? What clinical trials are you recommending for your own patients?

Questions from Gynecologic Oncologists and General Medical Oncologists

- What is CDH6, and how common is this biomarker in relapsed OC?
- The early reports with CDH6-targeted therapy in OC appear promising. How do response rates with the CDH6-targeted ADC compare to existing ADCs and standard therapies?
- Is there a specific patient subtype that will respond better to treatment with R-DXd? Why does efficacy of this drug seem to be biomarker agnostic?
- Is the side effect profile of R-DXd similar to T-DXd considering that it has the same cytotoxic payload? What are the potential side effects, and how should they be managed? Can R-DXd be used after T-DXd?

Questions from Gynecologic Oncologists and General Medical Oncologists

- How often do you see relapsed OC that has high TMB or MSI-H? Is ICI indicated in these pts? Does single-agent ICI have activity in PROC in patients with borderline PS who still desire some therapy?
- Why haven't we seen the same successes with immunotherapy in OC that our other solid tumor colleagues have? Are there any immunotherapeutic strategies on the horizon that might be more successful than anti-PD-1/PD-L1 antibodies?
- How does nemvaleukin alfa work? What is the efficacy of nemvaleukin alfa in combination with pembrolizumab? Based on early data, is there concern for severe immune adverse effects?

Agenda

Module 1: Up-Front Treatment for Advanced Ovarian Cancer (OC) — Dr Westin

Module 2: Management of Relapsed/Refractory OC — Dr Secord

Module 3: Novel Investigational Therapies for Advanced OC — Dr Moore

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

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

Ritu Salani, M.D., M.B.A.
Professor
Gynecologic Oncologist

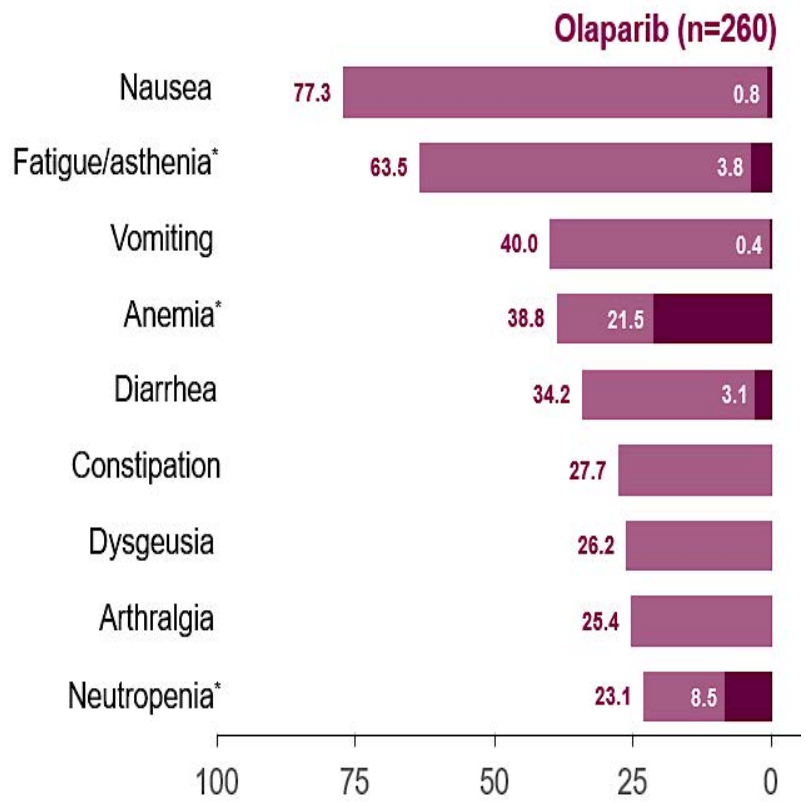
UCLA Health

Objectives

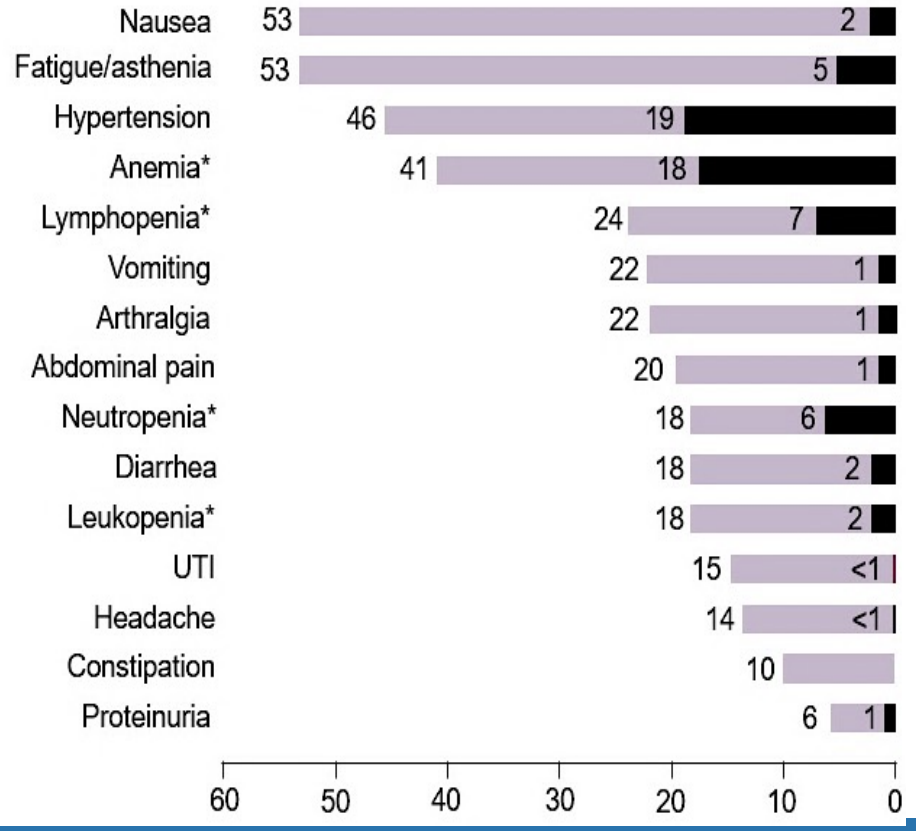
- PARP inhibitors and Mirvetuximab have improved cancer care!
- TOXICITIES
  - Short and long-term side effects
  - Dose modifications
  - Unique side effects
    - Ocular toxicities and management strategies

PARPi: Overall Adverse Events (First Line)

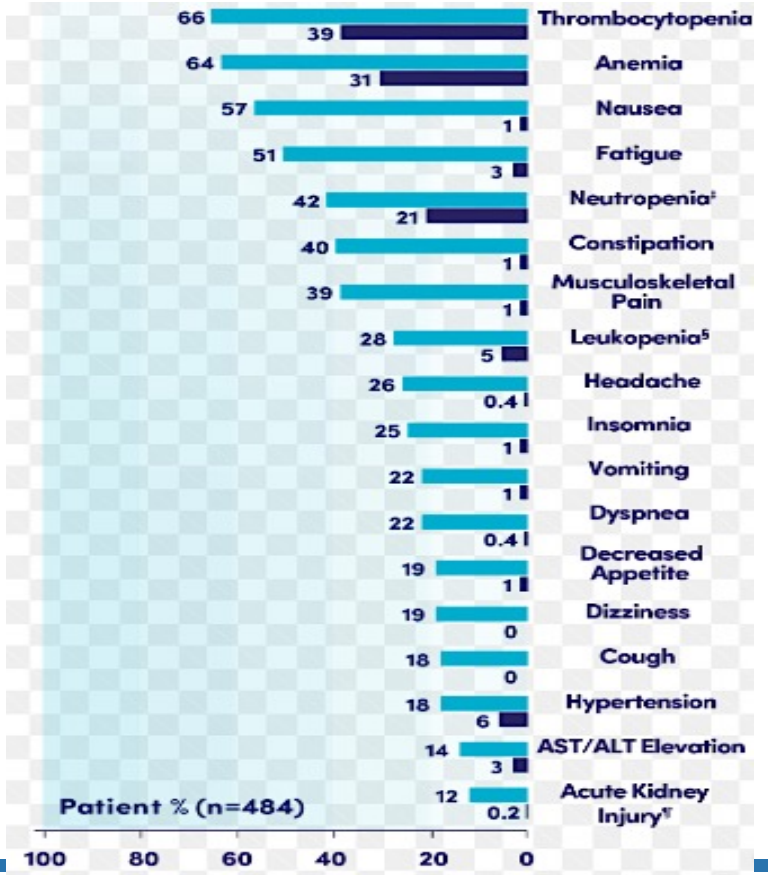
SOLO-1



PAOLA-1



PRIMA



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Moore KN. NEJM 2018; Ray-Coquard I. NEJM 2019. Gonzalez-Martin A. NEJM 2019.

Adverse Events: Gastrointestinal

Toxicity, %	Grade	Olaparib			Rucaparib	Niraparib	
		SOLO-1	SOLO-2	PAOLA-1	ARIEL3	NOVA	PRIMA
Nausea	All Grades	77	76	53	75	74	57
	Grade 3/4	1	3	2	4	3	1
Constipation	All Grades	28	21	10	37	40	39
	Grades 3/4	0	0	0	2	1	<1
Vomiting	All Grades	40	38	22	37	34	22
	Grades 3/4	<1	3	1	4	2	<1
Decreased appetite	All Grades	20	22	NR	23	25	NR
	Grade 3/4	0	0	NR	1	<1	NR
Abdominal pain	All Grades	25	25	19	30	23	22
	Grades 3/4	2	3	1	2	1	1
Diarrhea	All Grades	34	33	18	32	19	NR
	Grades 3/4	3	1	2	1	<1	NR
Dyspepsia	All Grades	17	11	NR	NR	11	NR
	Grade 3/4	0	0	NR	NR	0	NR

Management of Nausea/Vomiting

- Nausea and vomiting
  - Anti-emetics
    - Avoid aprepitant (CYP3Ai)
- Dysgeusia
  - Behavioral modifications
- Dyspepsia
  - PPIs, H2 antagonist

- Patient counseling
  - Symptoms improve with time
  - Niraparib can be taken at night
- Rule out other causes
- Use dose modifications as needed
  - Grade 1 and 2: Dose interruption
  - Grade 3 and recurrent: Dose reduction

Friedlander M. JCO 2016.

Adverse Event: Fatigue

Toxicity, %	Grade	Olaparib			Rucaparib	Niraparib	
		SOLO-1	SOLO-2	PAOLA-1	ARIEL3	NOVA	PRIMA
Fatigue	All Grades	63	66	53	69	59	35
	Grade 3/4	4	4	5	7	8	2

- Rule out other causes
  - Anemia
  - Depression
  - Hypothyroidism
  - Insomnia
- Treatment
  - Non-pharmacologic
    - Behavioral therapy
    - Sleep hygiene
    - Supportive care
    - Exercise
  - Pharmacologic
    - Methylphenidate
    - Grade 1 and 2: Dose interruption
    - Grade 3 and recurrent: Dose reduction

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Pujade-Lauraine E. Lancet Oncol. 2017. Ledermann JA. ESMO 2017. Mirza MR. NEJM 2016. Friedlander M. JCO 2016.

Hematologic Toxicity

Toxicity, %	Grade	Olaparib			Rucaparib	Niraparib	
		SOLO-1[1]	SOLO-2[2]	PAOLA-1[3]	ARIEL3[4]	NOVA[5]	PRIMA[6]
Anemia	All Grades	39	45	41	37	50	63
	Grade 3/4	22	19	17	19	25	31
Thrombocytopenia	All Grades	11	14	8	28	61	46
	Grades 3/4	1	1	2	5	34	29
Neutropenia	All Grades	23	19	18	18	30	26
	Grades 3/4	9	5	6	7	20	13

- Olaparib
  - Monthly labs x 12 months
  - Then every 3 months
- Niraparib
  - Weekly x 4 weeks (stable)
  - Then monthly labs x 12 months
  - Then every 3 months

UCLA Health

Berek JS. Ann Oncol 2018;29(8):1784.
1. Moore K, et al. *N Engl J Med*. 2018;379:2495-2505. 2. Pujade-Lauraine E, et al. *Lancet Oncol*. 2017;18:1274-1284. 3. Ray-Coquard IL, et al. *N Engl J Med*. 2019;381:2416-2428. 4. Ledermann JA, et al. Presented at ESMO 2017 (Abstract LBA40). 5. Mirza MR, et al. *N Engl J Med*. 2016;375:2154-2164. 6. Gonzalez-Martin. *N Engl J Med.* 2019;381:2391.

Anemia

- Core side effect and does not appear to be cumulative
- Management
  - Rule out other causes
  - Transfusion as indicated
  - Dose interruptions up to 28 days (until back to grade 1)
  - Dose reduction (grade 3 or recurrent)
  - Persistent anemia, consider referral to hematology

Friedlander M. JCO 2016.

Hematologic Toxicity

Toxicity, %	Grade	Olaparib			Rucaparib	Niraparib	
		SOLO-1[1]	SOLO-2[2]	PAOLA-1[3]	ARIEL3[4]	NOVA[5]	PRIMA[6]
Thrombocytopenia	All Grades	11	14	8	28	61	46
	Grades 3/4	1	1	2	5	34	29

- Thrombocytopenia
  - Higher rates with niraparib
  - Weekly labs x 4 until stable
- Individualized Starting Dose
  - Starting dose of 200 mg if
    - Weight <77 kg
    - Platelet count <150

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Berek JS. Ann Oncol 2018;29(8):1784.

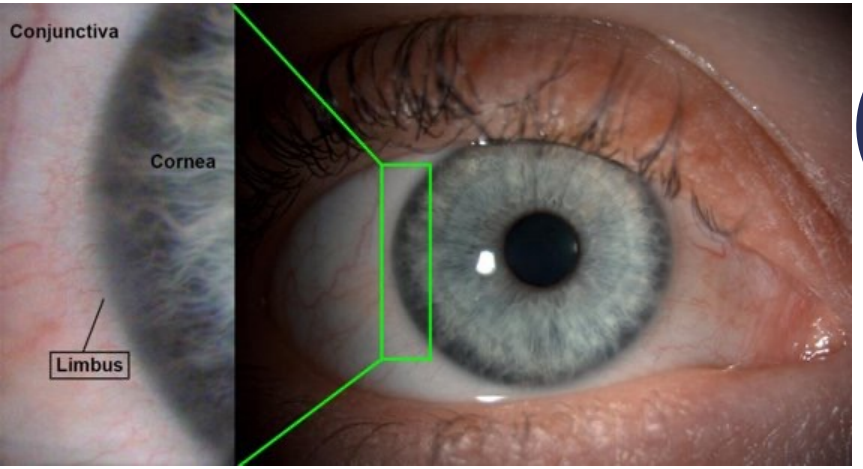
Risk of Myeloid Neoplasms

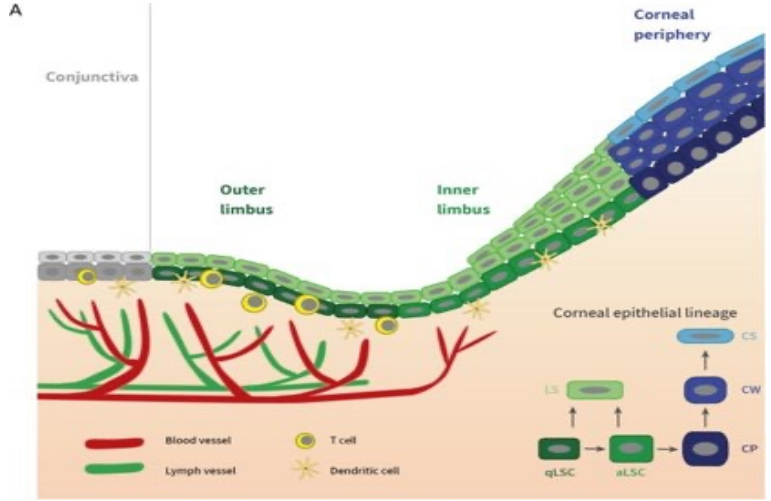
1st Line	Agent	Duration	AML/MDS risk	
			PARPi	Placebo
SOLO-1	Olaparib	2 years	1.5%	0.8%
PAOLA-1	Olaparib	2 years	1.7%	2.2%
PRIMA	Niraparib	3 years	2.3%	1.6%
ATHENA	Rucaparib	2 years	0.98%	0.89
Platinum Sensitive Recurrence				
SOLO-2	Olaparib	Progression or toxicity	8.2%	4%
NOVA *gBRCA* *Non-gBRCA*	Niraparib	Progression or toxicity	 6.6% 1.7%	 3.1% 0.9%
ARIEL3 *>24 months*	Rucaparib	Progression or toxicity	3.7% 11.4%	3.2% 0%

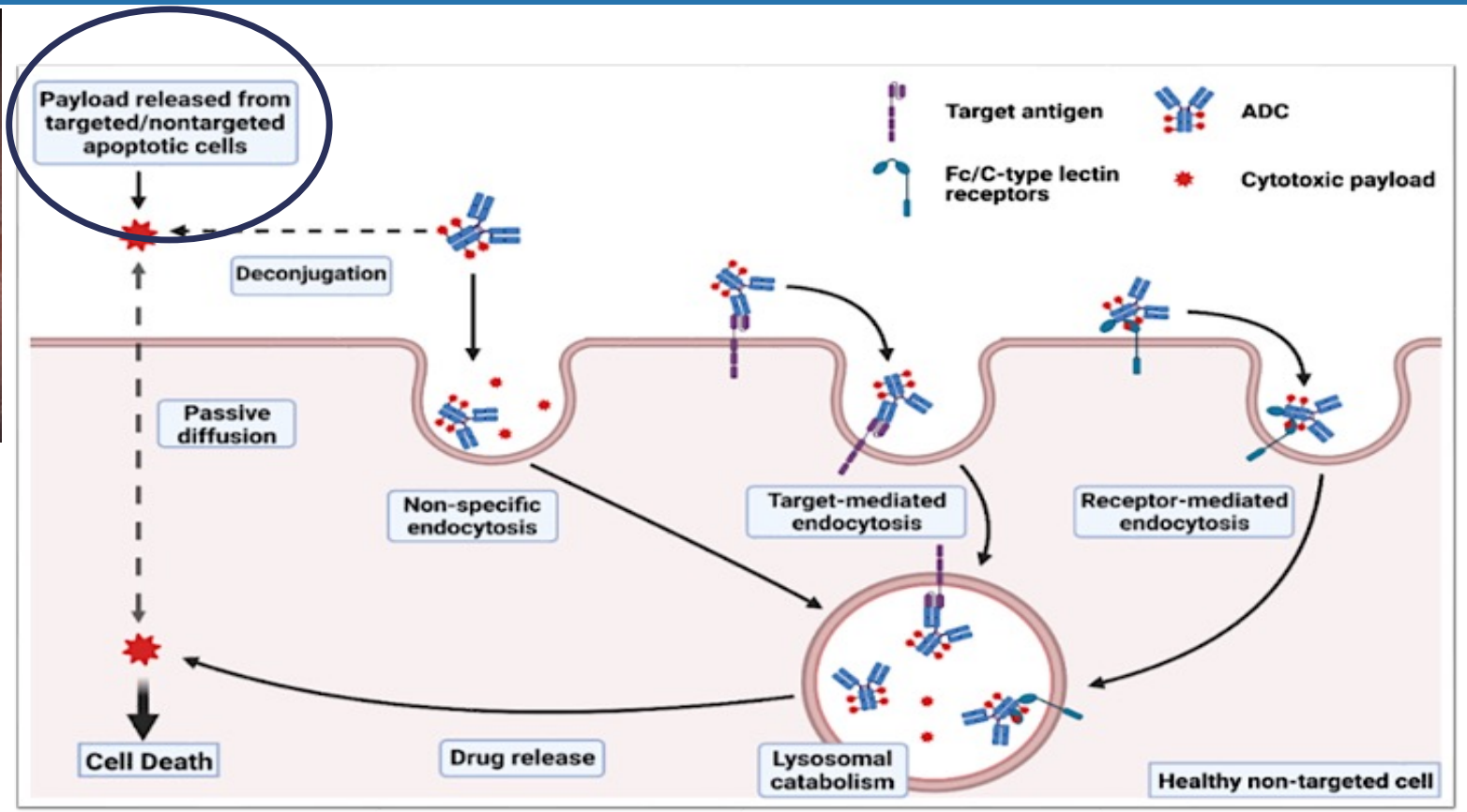
PARP Inhibitor Dose Adjustments

	SOLO-1		PAOLA-1		PRIMA		
	Olaparib (n=260)	Placebo (n=131)	Olaparib + bevacizumab (n=535)	Placebo + bevacizumab (n=269)	Niraparib all patients (n=484)	Niraparib modified dosing (n=169)	Placebo (n=244)
Median treatment duration (months)	24.6	13.9	17.3	15.6	11.0	11.0	NR
AE (%)	98	92	99	96	99	NR	92
Grade ≥3 AE (%)	40	19	57	51	70	76	19
Dose adjustments due to Adverse Events							
Dose interruption (%)	52	17	54	24	80	72	18
Dose reduction (%)	29	3	41	7	71	62	8
Treatment discontinuation (%)	12	3	20	6	12	14	2

Mirvetuximab Soravtansine







Uptake of ADC by endocytosis, particularly by the limbal cells in the cornea

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Ocular Toxicity

Table 3. Adverse Events That Occurred during the Treatment Period in the Safety Population.*

Adverse Event	MIRV (N=218)		Chemotherapy (N=207)	
	Any Grade	Grade ≥3	Any Grade	Grade ≥3
	number of participants (percent)			
Any adverse event	210 (96.3)	91 (41.7)	194 (93.7)	113 (54.6)
Any treatment-related adverse event	188 (86.2)			
Serious adverse event	52 (23.9)			
Serious treatment-related adverse event	20 (9.2)			
Adverse event leading to dose reduction	74 (33.9)			
Adverse event leading to dose delay or hold	117 (53.7)			
Adverse event leading to dose discontinuation	20 (9.2)			
Adverse event leading to death	5 (2.3)			
Treatment-related adverse event leading to death	1 (0.5)			
Adverse events occurring in ≥20% of participants in a trial group				
Blurred vision	89 (40.8)			
Keratopathy	70 (32.1)			
Abdominal pain	66 (30.3)			
Fatigue	66 (30.3)			
Diarrhea	64 (29.4)			
Dry eye	61 (28.0)			
Constipation	59 (27.1)			
Nausea	58 (26.6)	4 (1.8)	60 (29.0)	4 (1.9)
Peripheral neuropathy	47 (21.6)	3 (1.4)	30 (14.5)	4 (1.9)
Neutropenia	24 (11.0)	2 (0.9)	59 (28.5)	36 (17.4)
Anemia	21 (9.6)	2 (0.9)	71 (34.3)	21 (10.1)

* Adverse events were graded according to the National Cancer Institute Common Terminology Criteria for Adverse Events, version 5.0. The relatedness of adverse events to treatment was determined by the investigator.

Visual impairment (49%)
Keratopathy (36%)
Dry eye (26%)
Cataract (15%)
Photophobia (13%)
Eye pain (12%)

TEAEs ≥10%,[c] *n* (%)	All grades	Grade 3	Grade 4	Grade 5
Participants with any TEAE	78 (99)	37 (47)	1 (1)	2 (3)
Blurred vision	50 (63)	8 (10)	0	0
Dry eye	29 (37)	2 (3)	0	0
Nausea	29 (37)	1 (1)	0	0
	26 (33)	3 (4)	0	0
	24 (30)	2 (3)	0	0
	23 (29)	2 (3)	0	0
	22 (28)	3 (4)	0	0
	19 (24)	6 (8)	0	0
	16 (20)	1 (1)	0	0
	16 (20)	0	0	0
	15 (19)	1 (1)	0	0
	14 (18)	0	0	0
	14 (18)	0	0	0
	13 (16)	0	0	0
	13 (16)	0	0	0
	12 (15)	0	0	0
	12 (15)	0	0	0
Neutropenia	11 (14)	1 (1)	1 (1)	0
Abdominal pain	11 (14)	0	0	0
Neurotoxicity	10 (13)	2 (3)	0	0
Dysgeusia	9 (11)	0	0	0
Pneumonitis	8 (10)	2 (3)	0	1 (1)

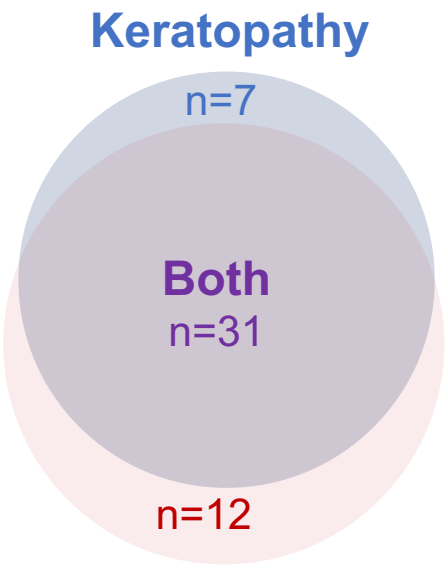
Alvarez Secord A. Annal Oncol 2025;36(3):321. Moore KN. NEJM 2023. Mirvetuximab FDA PI.

Ocular Toxicity: Prevention and Management

- Screening
  - Must undergo baseline ophthalmology exam, then every other cycle x 8
    - Slit lamp, intraocular pressure, and BVCA
  - Symptom review at every visit!
- Mitigation strategies
  - Corticosteroid eye drops (1% prednisolone)
  - Lubricating eye drops
  - Avoid contacts

Ocular Toxicity

- Median time to onset: Cycle 2 (1.5 months)
- Manageable with dose modification
  - 22% required dose delay or reduction
- Reversibility
  - >80% with grade 2-3 events resolved to grade 0-1
  - <1% discontinuation due to ocular events
  - No permanent ocular sequelae
    - Discontinuation advised if grade 4 toxicity



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

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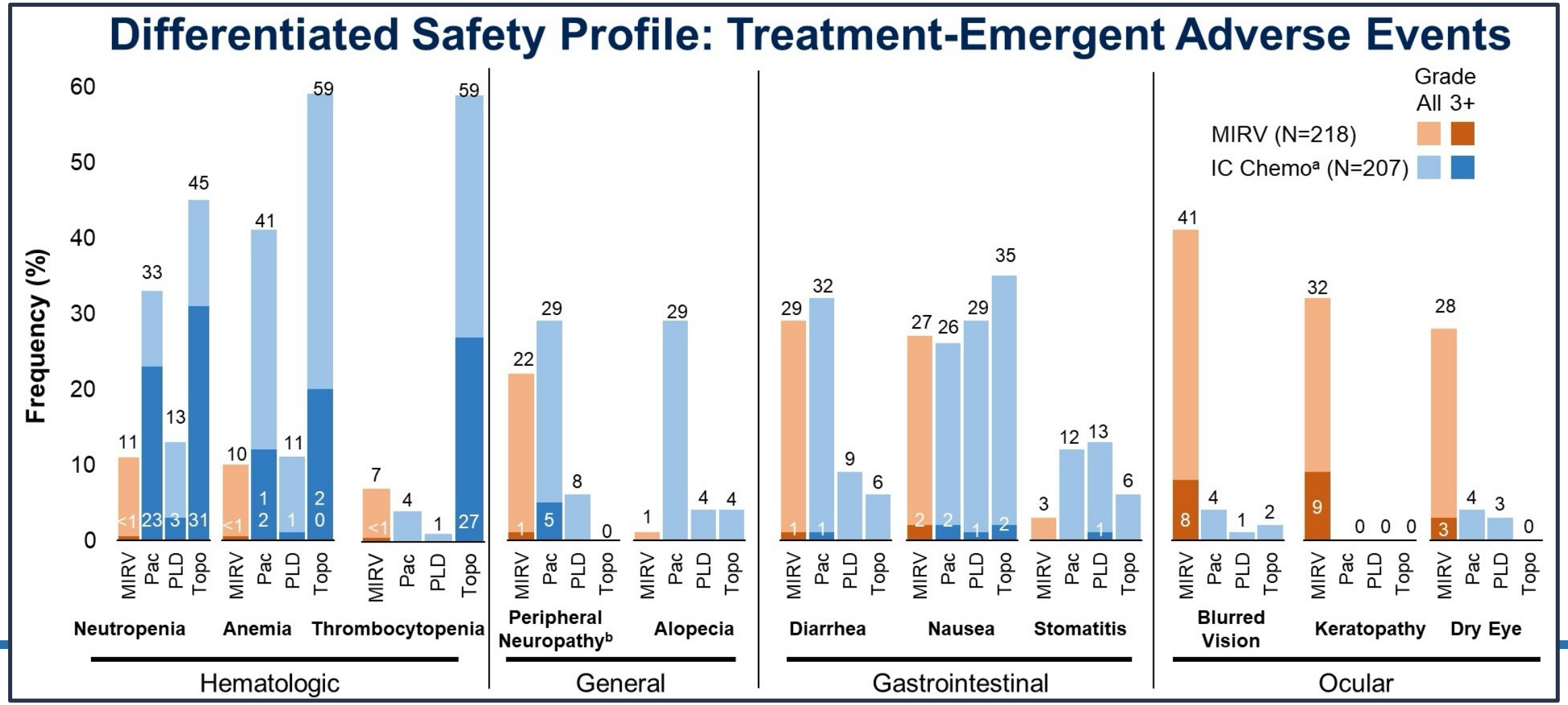
FDA Mirvetuximab PI. Matulonis U. J Clin Oncol 2023.

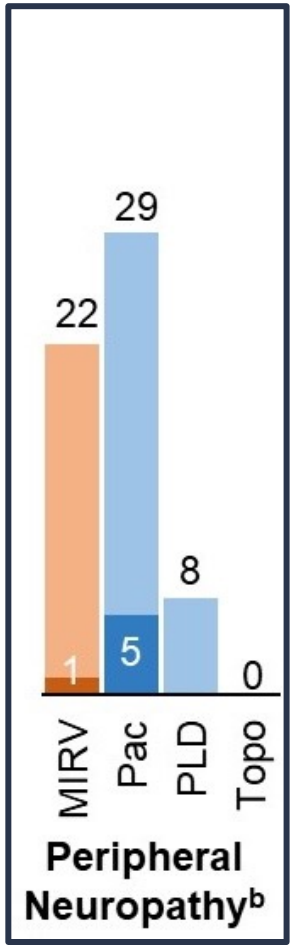
Mirvetuximab Soravtansine: Adverse Events



Moore KN. ASCO 2023;Abstract LBA5507

Peripheral Neuropathy

- Occurred in 36% of patients across trials
  - 2% experienced grade 3
- Median time to onset was 1.3 months
- Management
  - Grade 2: Withhold until grade 1 or less
    - Reduce dose level
  - Grade 3 or 4: Permanently discontinue



FDA Mirvetuximab PI

Infusion Reactions

- ~9% risk of infusion reaction

	Active management	Future management
Grade 1	Maintain infusion rate	
Grade 2	Stop infusion and provide supportive care After recovery, infuse at 50% rate	Premedication
Grade 3 or 4	Stop infusion and supportive treatment	Permanent discontinuation

- Pre-medications
  - Dexamethasone, diphenhydramine, acetaminophen, 5HT3 antagonist

Pneumonitis

- Occurred in 10% of patients
  - ~1% grade 3 and 4
- Monitor patients
  - Hypoxia
  - Cough
  - Dyspnea
  - Interstitial infiltrates on radiologic exams
- Evaluation
  - Rule out other causes
  - Asymptomatic: Routine chest imaging
  - Symptomatic: Immediate chest CT
- Management
  - Grade 1: Monitor
  - Grade 2: Hold until grade 1
    - Restart at same or reduced dose
  - Grade 3 or 4: Permanent discontinuation

Conclusions

- Novel therapies are introducing new opportunities for our patients
  - Improving survival but also introducing toxicities (some also novel!)
- Awareness and counseling of side effects are essential
- Recommended assessments/management
  - Lab monitoring (CBC) for PARP inhibitors (and mirvetuximab)
  - Eye examinations and eye care plan (mirvetuximab)
- Symptom management and dose adjustments are key
  - May allow patients to safely stay on effective treatments

Questions from Gynecologic Oncologists and General Medical Oncologists

- What is the impact of dose reductions on the effectiveness of PARP? At what dose is efficacy compromised? Would you ever preemptively dose reduce PARPi in elderly patients?
- How often do you see peripheral neuropathy with mirvetuximab? How would you manage Grade 2 peripheral neuropathy with mirvetuximab?
- What are the data with regard to AML/MDS with PARP inhibitors? How do expert clinicians counsel patients about the likelihood of secondary malignancies? What figures do they quote?

Questions from Gynecologic Oncologists and General Medical Oncologists

- How frequently should ophthalmic exams be performed for patients receiving mirvetuximab? Now that we have more patients receiving mirvetuximab, do we have enough data to suggest that a slightly less intense ophthalmic evaluation schedule is reasonable, especially in rural areas or if patients remain asymptomatic?
- How frequently should we monitor blood counts with PARP inhibitors? How can we manage myelosuppression with these agents? For patients who do not tolerate one PARPi due to heme toxicity, is there clinical evidence supporting a switch to another?
- For some patients, fatigue with PARPs is a huge QoL factor. What are strategies people have employed to improve fatigue?

Questions from Gynecologic Oncologists and General Medical Oncologists

- How can we tell if a patient using mirvetuximab has just a cough or early pneumonitis? We have seen several cases of severe pneumonitis that started so mild they could easily be mistaken for a cold or allergies. Is chest X-ray sufficient for initial evaluation? Are the monitoring and management algorithms for ILD/pneumonitis with mirvetuximab and T-DXd the same?
- How do you decide based on comorbidities if one PARP maintenance approach is more suitable than the others? How do you approach the use of PARPs for patients with long QT? What about renal impairment?

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

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