Great Debates
Solid Tumors

2025

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Miami

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Beyond Platinum: Emerging Treatment Paradigms for Recurrent Ovarian Cancer

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Disclosures

- **Linda R. Duska, MD, MPH:** Advisory Board—Daiichi Sankyo, SGO; Financial or Material Support—Advance Medical, ASCO, British Journal of Obstetrics and Gynaecology, CEA Group, Clinical Care Options, UpToDate, Wiley

- **Leslie M. Randall, MD, MAS, FACS:** Advisory Board—AbbVie, AstraZeneca, GSK, Merck, Natera, Pfizer; Consultant—AbbVie, AstraZeneca, Curio Science, Genmab, GSK, Merck, Pfizer; Grant/Research Support—AstraZeneca, GSK, Merck; Speaker's Bureau—Curio Science, Genmab, Pfizer

Learning Objectives

- Summarize the mechanisms underlying platinum resistance and their impact on therapeutic response
- Evaluate emerging therapeutic strategies and investigational targets for PROC, including GR antagonism
- Apply key considerations in patient-centered care, including treatment sequencing and toxicity management, in the evolving therapeutic landscape

PROC = platinum-resistant ovarian cancer; GR = glucocorticoid receptor.

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Background and Definitions

Moving beyond the Platinum-Sensitive/Resistant Paradigm

Emerging new multiplex classification system

Histology

- HGSC/ endometrioid
- Other, specify

Molecular signature

- BRCA mutation
- BRCA-like
- Other, specify

Treatment-free interval

- <3 months
- 3-12 months
- >12 months

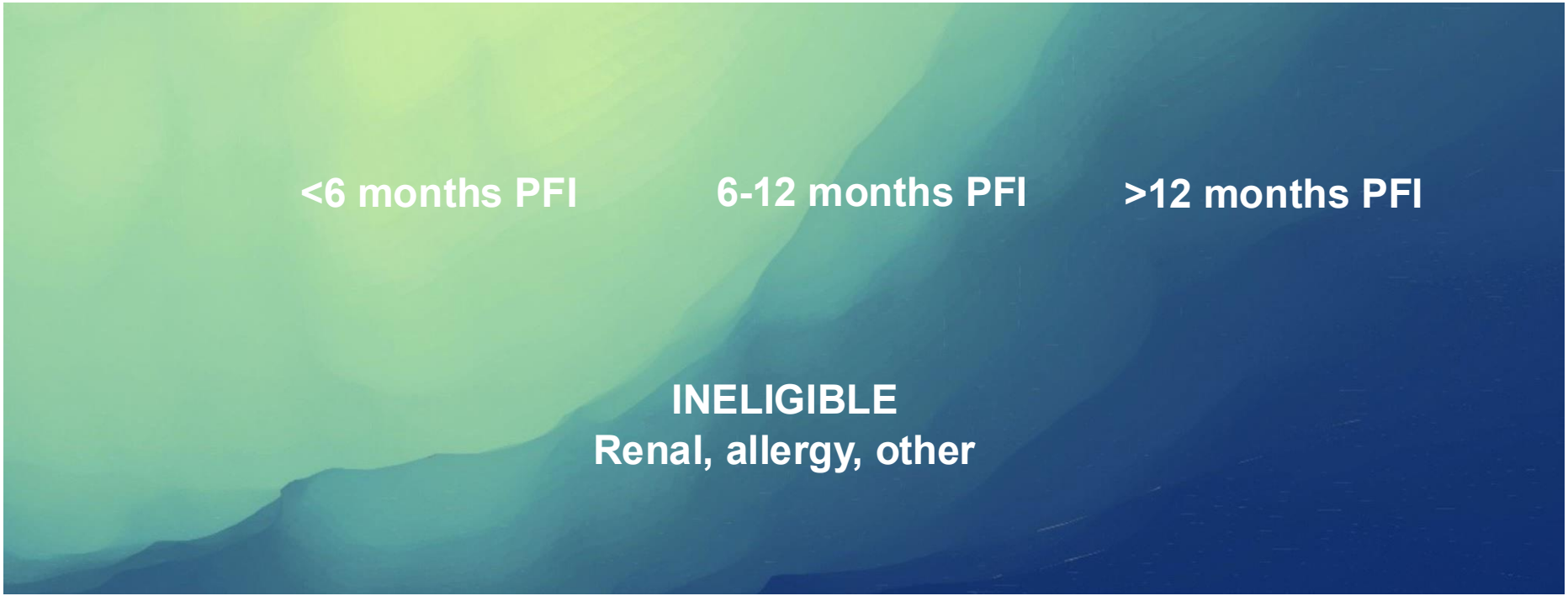
Number of prior chemotherapy regimens

- 3 or fewer
- >3
- Prior bev or PARP

HGSC = high-grade serous carcinoma; bev = bevacizumab; PARP = poly (ADP-ribose) polymerase.

Alvarez RD, et al. *Gynecol Oncol*. 2016;141(3):405-409.

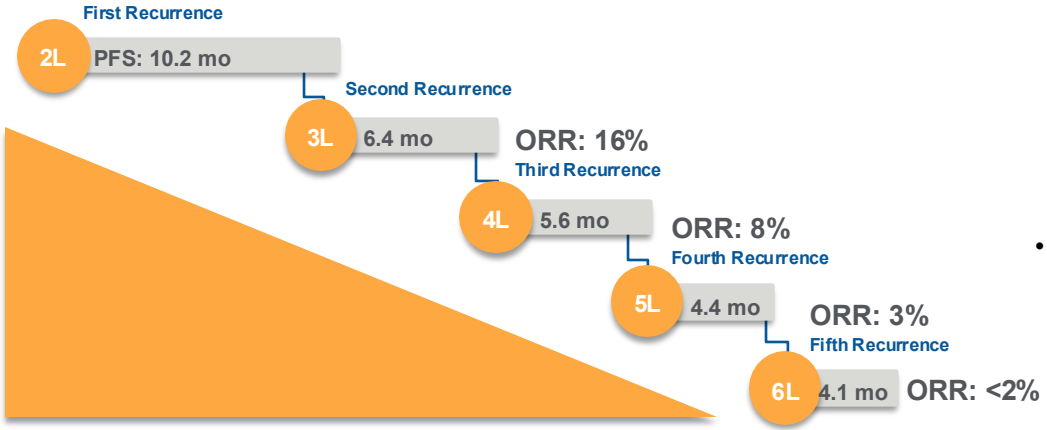
Platinum-Resistant Recurrent Ovarian, Tubal, and Peritoneal Cancer: A Spectrum



PFI = platinum-free interval.

Platinum-Resistant Ovarian Cancer Is Now: "In Patients When Platinum-Based Therapy Is Not an Option/Ineligible"

PFS and ORR historically decrease with increasing lines of therapy[a]



PROC Redefined

- Historically (regulatory standard)
  - Platinum-free interval (PFI)
    - Refractory: Progression (persistence) on primary therapy
    - Primary resistance: Progressed within 6 months of completing primary platinum-based therapy
    - Acquired (secondary) resistance: Progressed on or within 6 months of completing platinum-based therapy after 2nd line or more of therapy
    - Regulatory agencies do NOT differentiate primary vs acquired resistance
- Contemporary (clinical standard)
  - Platinum-based therapy is no longer an option
    - Patients who have progressed while receiving platinum-based chemotherapy
    - Patients who experienced a symptomatic relapse soon after the end of the last platinum-based chemotherapy
    - Contraindication to use further platinum-based treatment, such as allergy

[a]Representative graphic (not to scale) showing mPFS ranges after treatment with various chemotherapy regimens. mPFS estimates predate the routine use of maintenance therapy in clinical practice.
2L = second line; mo = month; mPFS = median progression-free survival; ORR = overall/objective response rate.
Hanker LC, et al. *Ann Oncol*. 2012;23(10):2605-2612. Pignata S, et al. *Ann Oncol*. 2017;28(Suppl 8):viii51-viii56. Griffiths RW, et al. *Int J Gynecol Cancer*. 2011;21(1):58-65. Colombo N, et al. *Ann Oncol*. 2019;30(5):672-705.

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Contemporary PROC Phase 3 Randomized Trials: Single-Agent Chemotherapy Results

Study	Study population	Chemotherapy arm	ORR, %	mPFS, mo	mOS, mo
JAVELIN Ovarian 200 (n=190)	≤3 priors, 75% PROC and 25% platinum refractory (28% prior bev)	PLD	**4**	3.5	15.7
FORWARD I re-read (n=61)	PROC 1-3 priors high FRα (33% prior bev)	Paclitaxel or PLD or topotecan	**6**	3.2	12
CORAIL (n=199)	PROC ≤3 priors (46% prior bev)	PLD or topotecan	**12**	3.6	11
NINJA (n=159)	PROC 77% >2 prior	Gemcitabine or PLD	**13**	3.8	12.1
AURELIA (n=182)	PROC ≤2 priors; 25% platinum refractory (8% prior bev)	Paclitaxel or PLD or topotecan	**13**	3.4	13.3

Direct cross-study comparison of results from independently conducted clinical trials is not intended on this slide.

FRα = folate receptor alpha; PLD = pegylated liposomal doxorubicin; mOS = median overall survival.

Pujade-Lauraine E, et al. *Lancet Oncol*. 2021;22(7):1034-1046. Moore KN, et al. *Ann Oncol*. 2019;30(Suppl 5):V403. Gaillard SL, et al. Presented at: European Society for Medical Oncology (ESMO) Congress; October 19-23, 2018; Munich, Germany. Abstract 932O. Omatsu K, et al. *Ann Oncol*. 2020;31(Suppl 4):S611. Pujade-Lauraine E, et al. *J Clin Oncol*. 2014;32(13):1302-1308.

Traditional 1L PROC Option: Bevacizumab in Combination with Chemotherapy: AURELIA Trial

AURELIA/Nov 14, 2014

AURELIA:
Bevacizumab
FDA-approved
PROC
Nov 14, 2014

Platinum-resistant OC

- ≤2 prior anticancer regimens
- No history of bowel obstruction/abdominal fistula, or clinical/radiological evidence of rectosigmoid involvement

R

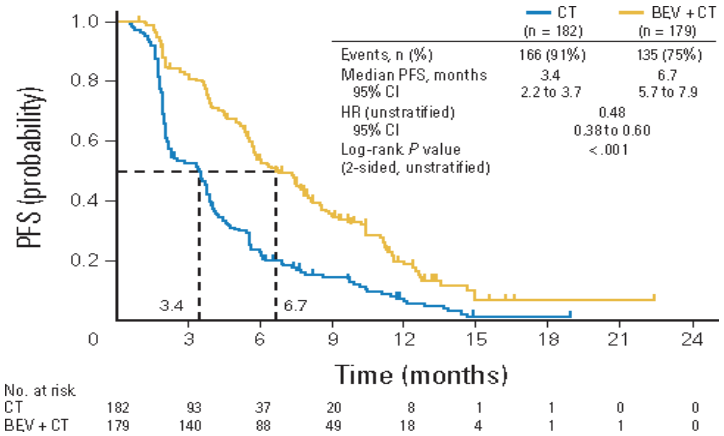
- Chemotherapy → Treat to PD/toxicity → Optional BEV monotherapy
- BEV 15 mg/kg q 3 w + chemotherapy → Treat to PD/toxicity → Investigator's choice* (without BEV)

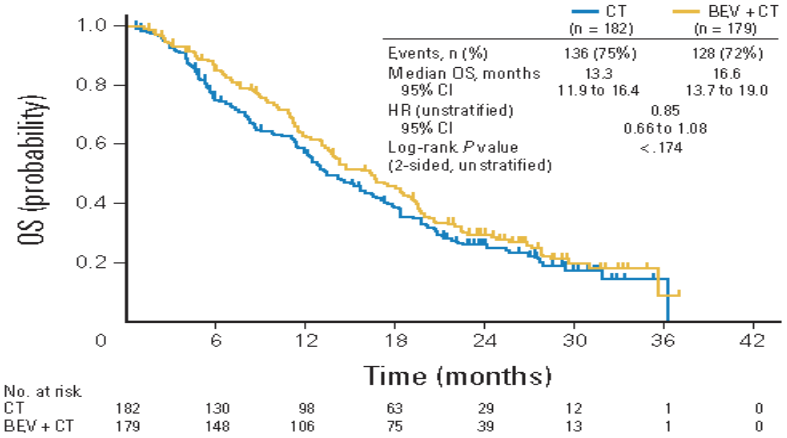
***Chemotherapy options (investigator's choice):**

Paclitaxel 80 mg/m² days 1, 8, 15, & 22 q 4 w

Topotecan 4 mg/m² days 1, 8, & 15 q 4 w
(or 1.25 mg/m², days 1–5 q 3 w)

PLD 40 mg/m² day 1 q 4 w





FDA = US Food and Drug Administration; PD = progressive disease; CT = chemotherapy.
Pujade-Lauraine E, et al. *J Clin Oncol*. 2014;32(13):1302-1308.

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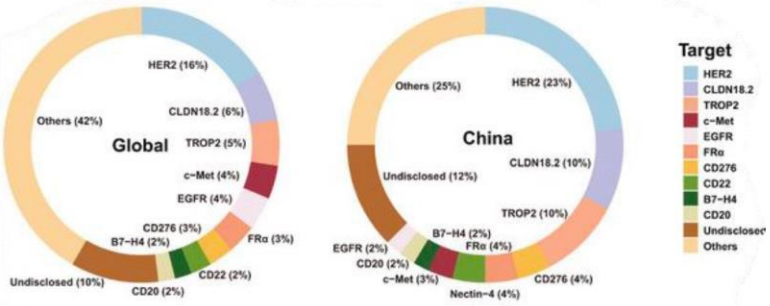
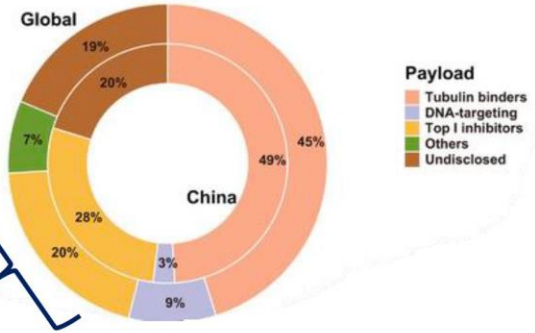
Development of ADCs in PROC

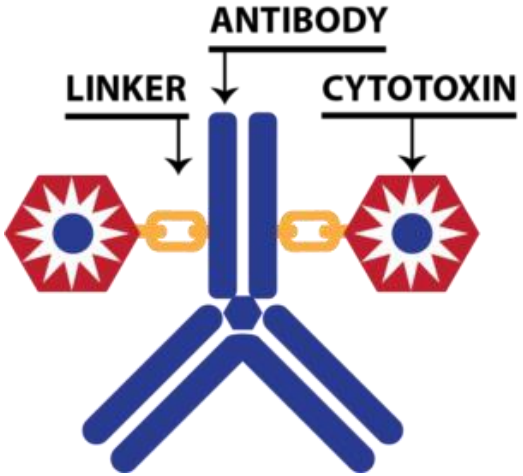
Approximately 190 ADCs in Development!

Diversity of targets continues to increase



And while anti-tubulins still comprise the majority of ADCs, anti-camptothecins are on the rise





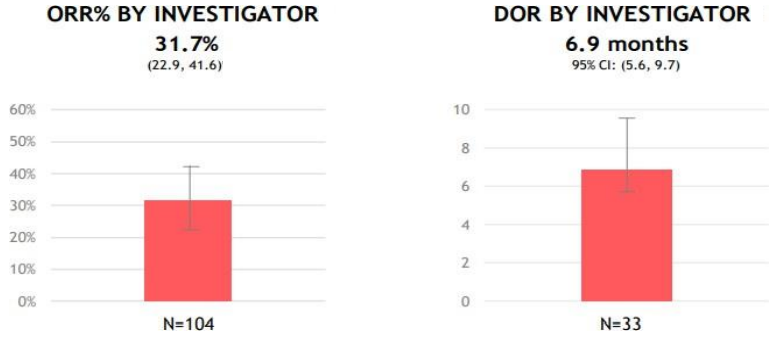
1. Highly selective monoclonal antibody targeted to tumor-associated antigen w/ restricted expression on normal cells
2. Potent cytotoxic agent induces target cell death post-internalization and is released
3. Stable linker in circulation, but releases the cytotoxic agent in target cells

ADC = antibody-drug conjugate.

Ruan DY, et al. *Cancer Commun*. 2024;44(1):3-22. NJ Bio [www.njbio.com]. Last updated June 30, 2025. https://njbio.com/antibody-drug-conjugates.

Mirvetuximab Soravtansine: SORAYA Phase 2 Trial

SORAYA key efficacy endpoints



	Mirvetuximab soravtansine (n=104)
Confirmed ORR, n (%) [95% CI][a]	31.7
	[22.9, 41.6]
Complete response, %	4.8
Partial response, %	26.9
mDOR, months [95% CI]	6.9
	[5.6, 9.7]

November 2022

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

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

[a]Data shown from SORAYA safety population are derived from a separate data cutoff of April 29, 2022.
mDOR = median duration of response; TRAE = treatment-related adverse event.

Mirvetuximab soravtansine-gynx prescribing information (PI). Drugs@FDA: FDA-Approved Drugs. Last updated March 22, 2024. https://www.accessdata.fda.gov/drugsatfda_docs/label/2024/761310Origs005lbl.pdf. US Food and Drug Administration (FDA) [www.fda.gov]. Last updated November 14, 2022. https://www.fda.gov/drugs/resources-information-approved-drugs/fda-grants-accelerated-approval-mirvetuximab-soravtansine-gynx-fra-positive-platinum-resistant. Moore KN, et al. *J Clin Oncol*. 2022;40(Suppl 16):5574.

MIRASOL Confirmatory Trial: Fr Alpha High (>75%, PS2+)

Mirvetuximab FDA-approved Fr alpha high PROC March 2024

MIRASOL (NCT04209855) – Study Design[1,2]

An open-label, phase 3 randomized trial of MIRV vs investigator's choice chemotherapy in patients with FRα-high platinum-resistant ovarian cancer

Patient Population
(N=453)

Enrollment and Key Eligibility
Platinum-resistant disease
(PFI ≤6 mo)
FRα detected by IHC with PS2+ intensity among ≥75% of viable tumor cells
High-grade serous histology
1º platinum-refractory disease excluded (primary PFI <3 mo)
1-3 prior lines of therapy
Prior BEV and PARPi allowed
Patients with BRCA mutations allowed

1:1 Randomization

Treatment Regimen-Experimental
MIRV
(6 mg/kg AIBW Q3W)

Treatment Regimen-Control
Investigator's Choice Chemotherapy
(Paclitaxel, PLD, or Topotecan)

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

Primary Endpoint
PFS by INV
(BICR sensitivity analysis)

Key Secondary Endpoints
1) ORR by INV
2) OS
3) PROs[a]

Secondary Endpoints
Safety and tolerability
DOR
CA-125 response[b]
PFS2

AIBW, adjusted ideal body weight; BEV, bevacizumab; BICR, blinded independent central review; BRCA, BReast CAncer gene; CA-125, cancer antigen 125; chemo, chemotherapy; DOR, duration of response; FRα, folate receptor alpha; IC, investigator's choice; IHC, immunohistochemistry; INV, investigator; MIRV, mirvetuximab soravtansine; ORR, objective response rate; OS, overall survival; PARPi, poly (ADP-ribose) polymerase inhibitors; PFI, platinum-free interval; PFS, progression-free survival; PFS2, time from randomization until second disease progression; PLD, pegylated liposomal doxorubicin; PROs, patient-reported outcomes; PS2+, positive staining intensity ≥2; Q3W, every 3 weeks.
[a]PROs will be measured using the European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire, 28-item Ovarian Cancer Module (OV28) study instrument.
[b]Gynecological Cancer InterGroup (GCIG) criteria.

1. ClinicalTrials.gov identifier: NCT04209855. Updated June 16, 2022. Accessed October 5, 2022. https://clinicaltrials.gov/ct2/show/NCT04209855
2. Moore K, et al. Presented at: 2020 American Society of Clinical Oncology Annual Meeting, May 29-31, 2020; Virtual. Abstract TPS6103.

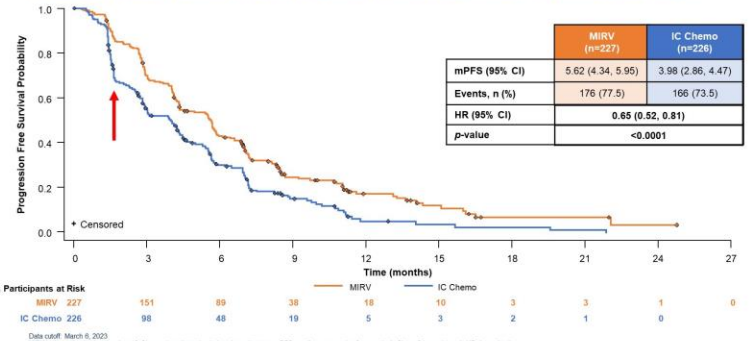
Overall Response Rate by Investigator (N=453)

	MIRV (n=227)	IC Chemo (n=226)
ORR **n, 95% CI**	**42%** 96, (35.8, 49.0)	**16%** 36, (11.4, 21.4)
Best overall response, n (%)		
CR	12 (5%)	0
PR	84 (37%)	36 (16%)
SD	86 (38%)	91 (40%)
PD	31 (14%)	62 (27%)
Not evaluable	14 (6%)	37 (16%)

ORR Difference 26.4% (18.4, 34.4)
OR 3.81 (2.44, 5.94)
***p*<0.0001**

Data cutoff: March 6, 2023
MIRV, mirvetuximab soravtansine; IC chemo, investigator's choice chemotherapy; ORR, objective response rate; CI, confidence interval; CR, complete response; PR, partial response; SD, stable disease; PD, progressive disease; OR, odds ratio.

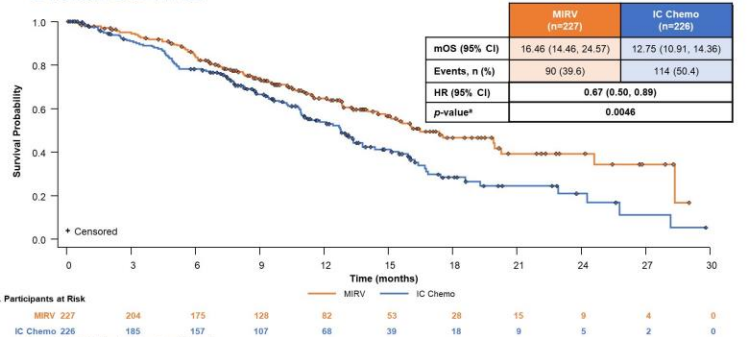
Primary Endpoint: Progression-Free Survival by Investigator



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

Data cutoff: March 6, 2023
MIRV, mirvetuximab soravtansine; IC Chemo, investigator's choice chemotherapy; mPFS, median progression-free survival; CI, confidence interval; HR, hazard ratio.

Overall Survival



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

Data cutoff: March 6, 2023; median follow-up time: 13.11 months
MIRV, mirvetuximab soravtansine; IC Chemo, investigator's choice chemotherapy; mOS, median overall survival; CI, confidence interval; HR, hazard ratio.
[a]Overall survival is statistically significant based on pre-specified boundary p-value at interim analysis = 0.0133.

IHC = immunohistochemistry; PARPi = PARP inhibitor; AIBW = adjusted ideal body weight; PLD = pegylated liposomal doxorubicin; IC = induction chemotherapy; INV = investigator; BICR = blinded independent central review; PRO = patient-reported outcome.
Moore KN, et al. *J Clin Oncol*. 2022;40(Suppl 16):5574.

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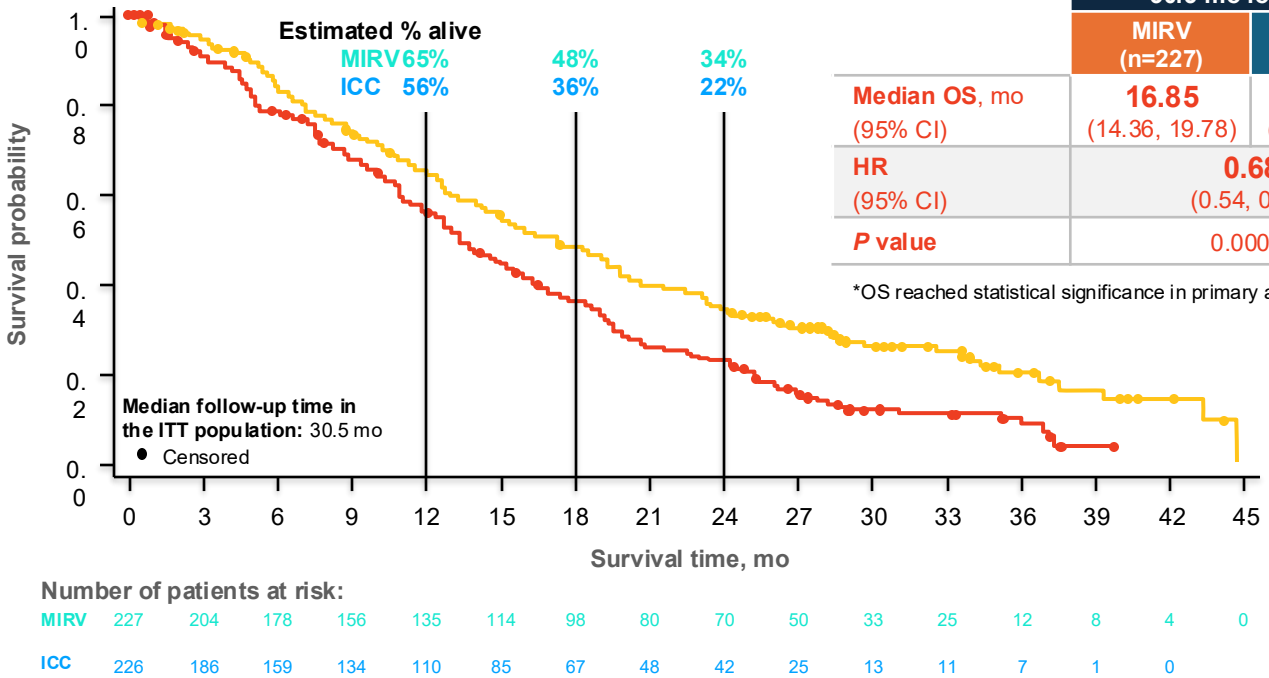
MIRASOL Final Overall Survival



	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	

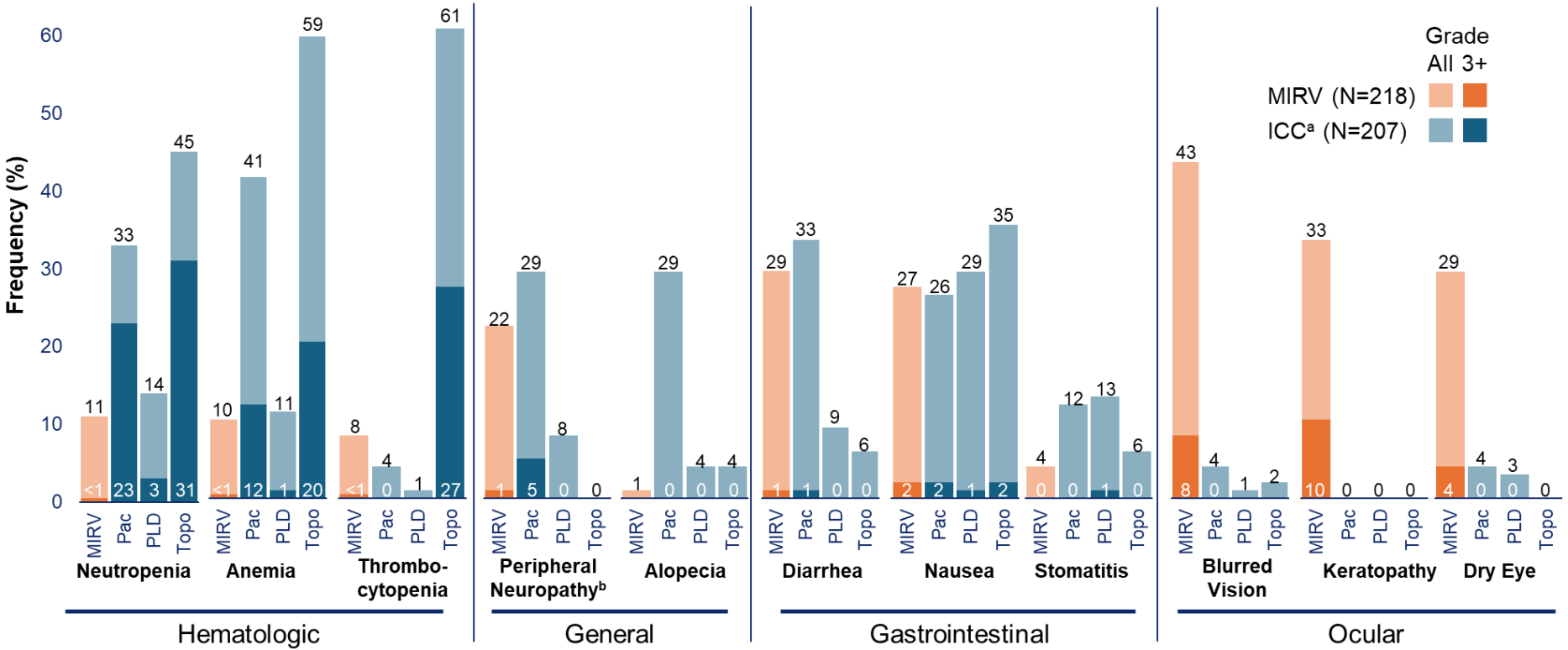
*OS reached statistical significance in primary analysis. The *P*-value at the final analysis is descriptive.

At the final analysis, the HR for OS (0.68) **continued to favor MIRV** over ICC, with patients treated with MIRV exhibiting a **32% reduction in risk of death**

ICC = investigator's choice chemotherapy; ITT = intent-to-treat.
[a]Data cutoff: September 26, 2024; [b]Data cutoff: March 6, 2023.

Van Gorp T, et al. Presented at: Society of Gynecologic Oncology (SGO) Annual Meeting on Women's Cancer; March 14-17, 2025; Seattle, WA. Abstract 939696. Moore KN, et al. *N Engl J Med*. 2023;389(23):2162-2174.

MIRASOL Treatment-Emergent Adverse Events: No New Safety Signals at Final Analysis



Data cutoff: September 26, 2024

[a]Pac, n=82 (40%); PLD, n=76 (37%); Topo, n=49 (24%); [b]Grade 2+ peripheral neuropathy events were observed in 12%, 16%, and 3% of patients that received MIRV, PAC, or PLD, respectively.

Van Gorp T, et al. Presented at: SGO Annual Meeting on Women's Cancer; March 14-17, 2025; Seattle, WA. Abstract 939696.

Mitigation Strategies for Ocular AEs from Mirv

PROACTIVE MEASURES

EYE EXAMS

- Complete 1 eye exam prior to treatment initiation
- Every other cycle (~6 weeks) for the first 8 cycles, and as clinically indicated
- New or worsening patient-reported ocular signs/symptoms
- Eye care provider to contact oncologist with any AEs

CONTACT LENSES

- Avoid unless medically necessary

LUBRICATING EYE DROPS[a]

- QID and PRN administration

CORTICOSTEROID EYE DROPS

- Initial/renewal prescriptions after slit lamp examination
- 1 drop in each eye 6 times per day starting the day prior to mirv infusion until day 4 of each cycle
- 1 drop in each eye, four times per day on days 5-8 of each cycle

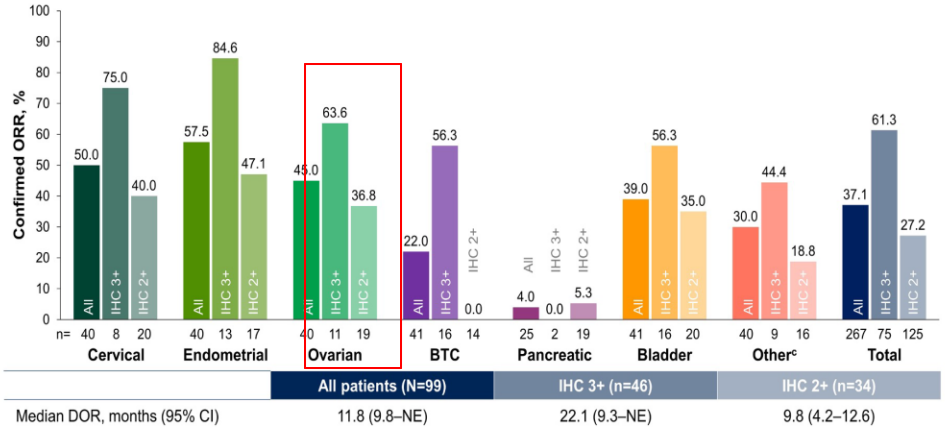
[a]Preservative-free drops recommended for patients with sensitive eyes.

Mirvetuximab soravtansine-gynx PI. Drugs@FDA: FDA-Approved Drugs. Last updated March 22, 2024. https://www.accessdata.fda.gov/drugsatfda_docs/label/2024/761310Origs005lbl.pdf.

Targeting HER2: Trastuzumab Deruxtecan (T-DXd): DESTINY-PanTumor02

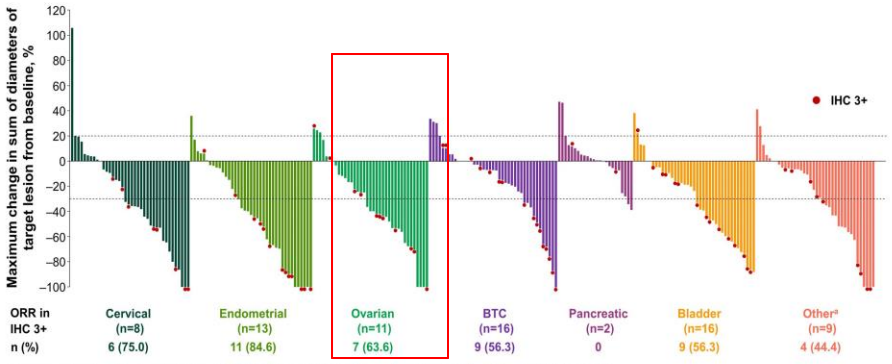
T-DXd FDA approved 3+ HER2 + solid tumors April 2024

Objective Response Rate by HER2 status



	All patients (N=99)	IHC 3+ (n=46)	IHC 2+ (n=34)
Median DOR, months (95% CI)	11.8 (9.8–NE)	22.1 (9.3–NE)	9.8 (4.2–12.6)

Best Percentage Change in Target Lesion From Baseline



Analyses were performed in patients who received ≥1 dose of T-DXd (n=267). Analysis of ORR in IHC 3+ was performed in patients with centrally confirmed HER2 status (n=75).
[a]Responses in extramammary Paget's disease, head and neck cancer, oropharyngeal neoplasm, and salivary gland cancer.
BTC, biliary tract cancer; IHC, immunohistochemistry; ORR, objective response rate.

Meric-Bernstam F, et al. *J Clin Oncol*. 2023;41(Suppl 17):LBA3000.

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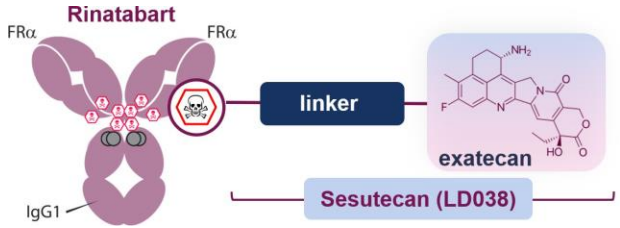
HERE Is Where SOC Ends for Patients with PROC!

- Platinum-containing regimens until platinum no longer an option, progression on platinum, or TFI <6 months
- AURELIA for any biomarker
- Mirvetuximab for FRA >75%
- TDxd for HER2 gastric scoring (3+ label, 2+/3+ NCCN)

- After this – clinical trial
  - TDxd might make pt ineligible for current ADC trials due to topoisomerase class payload (and moving to earlier line)
  - Supportive care key to ensure future inclusion by ECOG

Phase 1/2 Study of Rinatabart in OC



Patient Demographics and Disease Characteristics in OC Dose Expansion

OC Dose Expansion	Rina-S 100 mg/m² n = 22	Rina-S 120 mg/m² n = 20
Age, median (range), years	62.5 (42-82)	64.5 (37-83)
Prior lines of therapy, median (range)	3 (1-5)	3 (1-4)
Bevacizumab, n (%)	20 (90.9)	18 (90.0)
PARPi, n (%)	15 (68.2)	13 (65.0)
Mirvetuximab soravtansine, n (%)	4 (18.2)	4 (20.0)
Platinum sensitivity status, n (%)		
Resistant	20 (90.9)	19 (95.0)
Sensitive	2 (9.1)	1 (5.0)

DCO: July 28, 2024

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

Best Change in Target Lesion in OC Dose Expansion

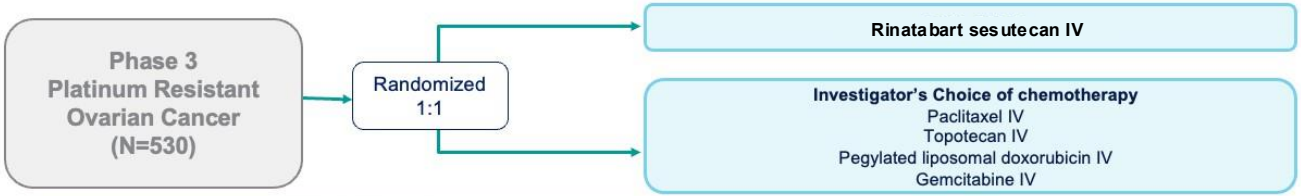
*Prior mirvetuximab soravtansine treatment[c]

Median no. of cycles: 6.5 (100 mg/m²) and 7.0+ (120 mg/m²)

[a]Based on investigator assessment; [b]Response-evaluable population; [c]One patient in the 120 mg/m² cohort with prior mirvetuximab soravtansine was not response-evaluable.
DCO = data cutoff; DCR = disease control rate.
Lee EK, et al. *Ann Oncol.* 2024;35(Suppl 2):S550.

RainFoI: Rinatabart Sesutecan Randomized Phase III Platinum Resistant Ovary Cancer

GCT1184-02 / ENGOT-OV86 / GOG 3107 | Rinatabart Sesutecan in PROC



Evaluation of Study Objectives*

Primary Outcome Measure

- Progression-Free Survival

Secondary Outcome Measures

- Overall Survival
- Objective Response Rate
- Duration of Response
- CA-125 response by GCIG criteria
- Adverse Events
- GHS/QoI (EORTC-QLQ-C30)

Key Inclusion Criteria*

- Histologically or cytologically confirmed high grade serous or endometrioid epithelial ovarian cancer, primary peritoneal cancer, or fallopian tube cancer
- Prior treatment with the following:
  - Platinum-based therapy
  - Bevacizumab (unless contraindicated)
  - PARP inhibitor (if known BRCA mutation)
  - Mirvetuximab (if positive FRα expression and available in the region)
- Platinum-resistant disease
- No prior ADC therapy containing a topoisomerase 1 inhibitor
- No known active central nervous system metastases or carcinomatous meningitis

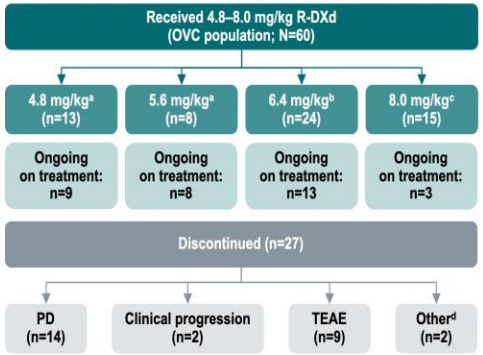
*Not comprehensive.
ADC, anti-drug conjugate; CA, cancer antigen; EORTC-QLQ-C30, European Organization for Research and Treatment of Cancer Quality of Life Core 30 questionnaire; FRα, folate receptor alpha; GCIG, Gynecologic Cancer Intergroup; GHS/QoI; Global Health Status/Quality of Life; IV, intravenous; PROC, Platinum Resistant Ovarian Cancer
https://clinicaltrials.gov/study/NCT06619236

ClinicalTrials.gov [www.clinicaltrials.gov]. Last updated September 4, 2025. https://clinicaltrials.gov/study/NCT06619236.

Raludotatug Deruxtecan (R-DXd; DS-6000) Monotherapy in Patients with Previously Treated Ovarian Cancer (OVC): Subgroup Analysis of a First-in-Human Phase 1 Study

Baseline demographics and disease characteristics

Data cutoff: July 14, 2023



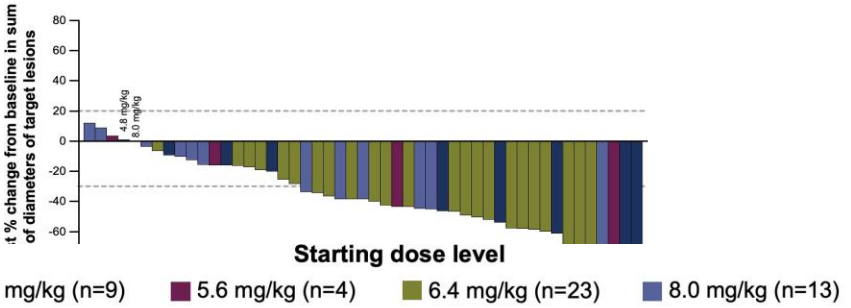
	OVC (4.8–8.0 mg/kg) N=60
Age, median years (range)	66 (42–82)
ECOG PS, n (%)	
0	22 (36.7)
1	38 (63.3)
Platinum-resistant disease[e], n (%)	55 (91.7)
Number of prior systemic regimens, median (range)	4 (1–13)
Received prior systemic therapy, n (%)	
Bevacizumab	41 (68.3)
PARP inhibitor	39 (65.0)
Baseline tumor CDH6 expression H-score, median (range)	125 (0–250)

- Median treatment duration: 18 weeks (range: 3–115)
- 12 (20%) patients received treatment for ≥6 months
- 3 (5%) patients received treatment for ≥18 months

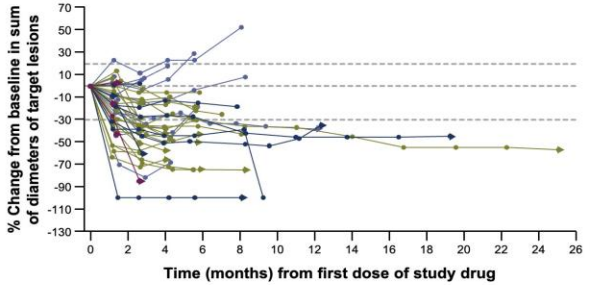
[a]Enrollment ongoing. [b]Enrollment completed. [c]As of October 2022, the patients who were still receiving R-DXd at 8.0 mg/kg were dose-reduced to receive R-DXd 6.4 mg/kg. [d]Death (n=1) and informed consent withdrawn (n=1). [e]Defined as tumor progression during or within 6 months after completion of prior platinum therapy. Five patients had tumor progression 6 months after platinum therapy.

CDH6, cadherin 6; ECOG PS, Eastern Cooperative Oncology Group performance status; OVC, ovarian cancer; PARP, poly adenosine diphosphate-ribose polymerase; PD, progressive disease; TEAE, treatment-emergent adverse event.

- **Confirmed ORR: 46%** in the 4.8–8.0 mg/kg OVC cohort (23/50; 95% CI: 32–61); one CR and 22 PRs
  - 4 unconfirmed responses were ongoing at data cutoff
- **Disease control rate[a]: 98%**



- Median time to response: 6 weeks (95% CI: 5–11)
- Median **DOR[b]: 11.2 months** (95% CI: 3.0–NE)
- Median **PFS[c]: 7.9 months** (95% CI: 4.4–12.4)



Moore KN, et al. Presented at: European Society for Medical Oncology (ESMO) Congress; October 20-24, 2023; Madrid, Spain. Abstract 745MO.

TROP2 ADCs in Ovary Cancer

	Sacituzumab tirumotecan (MK-2870) 5mg/kg D1, D15 N=35 (PROC)	Datopotamab deruxtecan N=26 (PROC)	SHR A1921[2] Q 21 day dosing 3.0mg/kg (N=26) Day 1, 8 2.0mg/kg (N=20)
Payload	Belotecan derivative Topoisomerase I	Topoisomerase 1- deruxtecan	Topoisomerase 1 (proprietary SHR9265)
DAR	7.4	4	4
Linker	Sulfonyl pyrimidine CL2A-carbonate linker	Cleavable tetrapeptide based linker	Cleavable linker
Trial	NCT06049212	NCT05489211	NCT05765032
Prior PARPi	NR	51.4%	65.4% 50.0%
Prior Bev	NR	71.4%	76% 60.0%
ORR (PROC)	37.1% (PROC)	34.6% (95% CI 17.2- 55.7)	42.3% (95% CI 23.4-63.1) 58.8% (95% CI 32.9-81.6)
DOR (PROC)	5.3 months (2.1, 24.4+)	5.6 months (2.9-NC)	9.9 months (4.5-NC) 6.3 months (3.0-NC)
mPFS	6.0 months (95% CI 3.9-7.3) (inclusive of PSOC)	5.6 months (inclusive of PSOC)	7.9 (4.2-NR) 6.9 (4.2- 9.6)

PSOC = platinum-sensitive ovarian cancer.

Wang D, et al. Presented at: ESMO Congress; September 13-17, 2024; Barcelona, Spain. Abstract 715MO. Oaknin A, et al. Presented at: ESMO Congress; September 13-17, 2024; Barcelona, Spain. He N, et al. Presented at: American Association for Cancer Research (AACR) Annual Meeting; April 14-19, 2023; Orlando, Florida. Abstract LB030.

Great Debates
Solid Tumors

Non-ADC Development

Is IO Still a Possibility in the PROC Setting?

Phase 3 KEYNOTE-B96 Trial Met Primary Endpoint of Progression-Free Survival (PFS) in Patients With Platinum-Resistant Recurrent Ovarian Cancer Whose Tumors Expressed PD-L1 and in All Comers

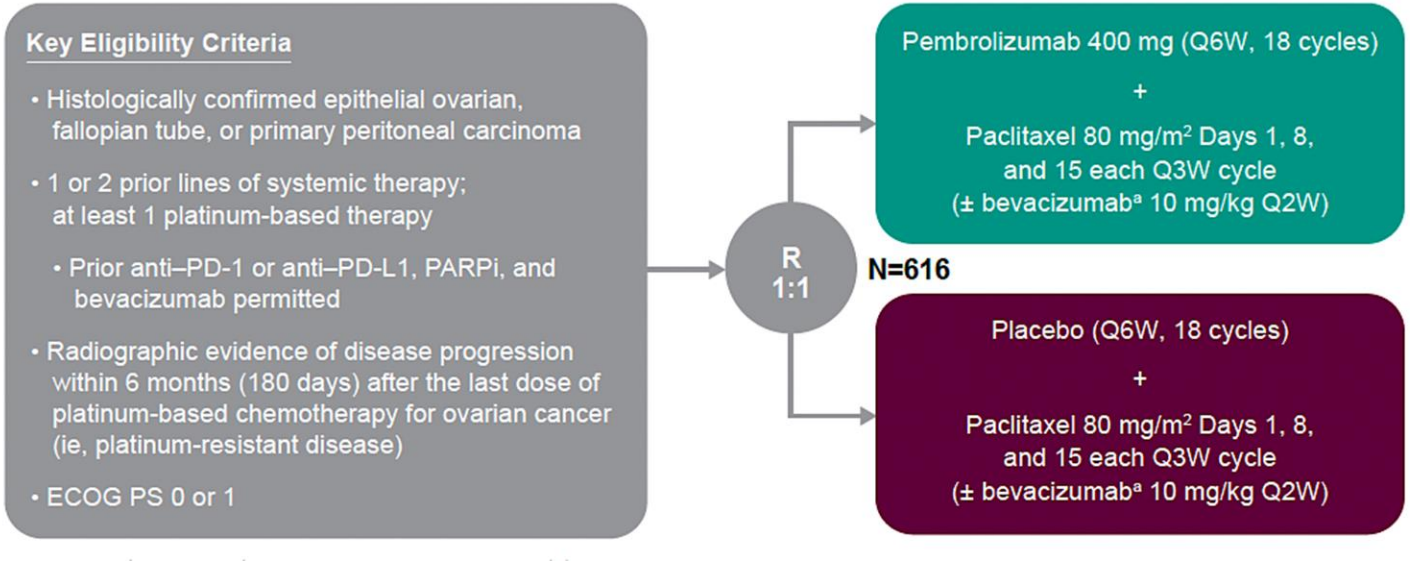
IO = immuno-oncology.

Colombo N. Presented at: European Society of Gynaecological Oncology (ESGO) Congress; October 27-30; Berlin, Germany. Yahoo!Finance [finance.yahoo.com]. Last updated May 15, 2025. https://finance.yahoo.com/news/merck-announces-phase-3-keynote-104500071.html.

ENGOT-ov65/KEYNOTE-B96

Phase 3, Randomized, Double-Blind Study of Pembrolizumab vs Placebo Plus Paclitaxel with Optional Bevacizumab for Platinum-Resistant Recurrent Ovarian Cancer

A road for IO in PROC?



Primary endpoint

- Inv-assessed PFS

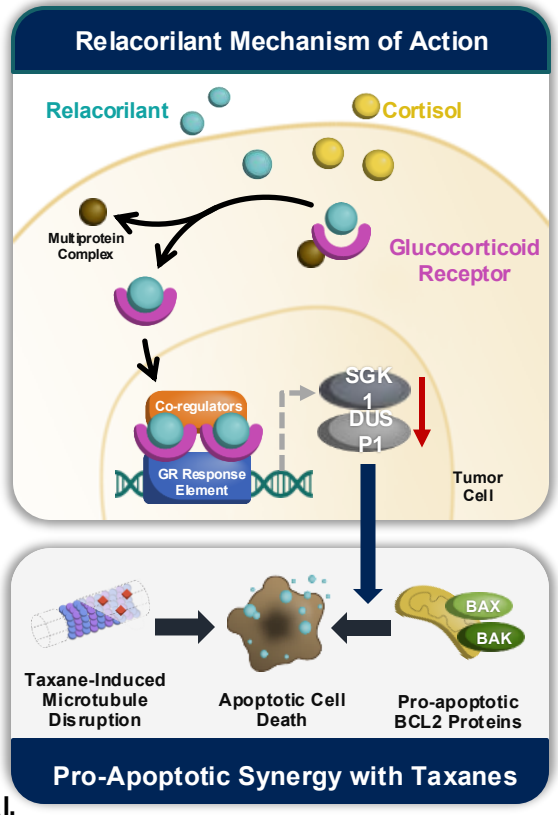
Anticipated at upcoming scientific meeting

Colombo N, et al. *Int J Gynecol Cancer*. 2022;32(Suppl 2):A251.

ROSELLA | GOG-3073 Background

A Phase 3 Study of Relacorilant in Combination with Nab-Paclitaxel vs Nab-Paclitaxel Monotherapy in Advanced, Platinum-Resistant, High-Grade Epithelial Ovarian, Primary Peritoneal, or Fallopian-Tube Cancer

- Patients with platinum-resistant ovarian cancer have an overall survival of ~1 year and need new treatments
- Ovarian cancers express the glucocorticoid receptor (GR), a marker of poor prognosis
- GR signaling reduces sensitivity to chemotherapy
- Relacorilant is a novel, selective GR antagonist (SGRA) that restores the sensitivity of cancers to cytotoxic chemotherapy



nab = nanoparticle albumin-bound.

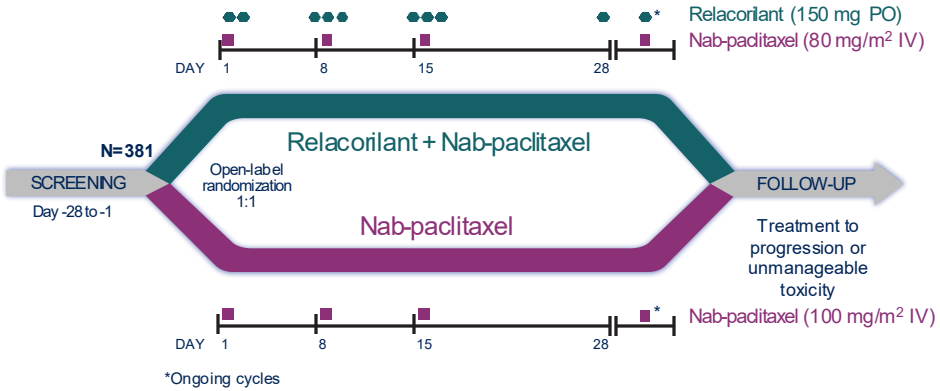
Martorana F, et al. *Int J Gynecol Cancer*. 2025;35(1):100009. Veneris JT, et al. *Gynecol Oncol*. 2017;146(1):153-160. Greenstein AE, Hunt HJ. *Oncotarget*. 2021;12(13):1243-1255. Melhem A, et al. *Clin Cancer Res*. 2009;15(9):3196-3204. Stringer-Reasor EM, et al. *Gynecol Oncol*. 2015;138(3):656-662. Munster PM, et al. *Clin Cancer Res*. 2022;28(15):3214-3224. Colombo N, et al. *J Clin Oncol*. 2023;41(30):4779-4789. Olawaiye A, et al. *J Clin Oncol*. 2025;43(Suppl 17):LBA5507.

ROSELLA | Study Schema

Population

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

NCT05257408



Stratification factors

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

Dual Primary Endpoints

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

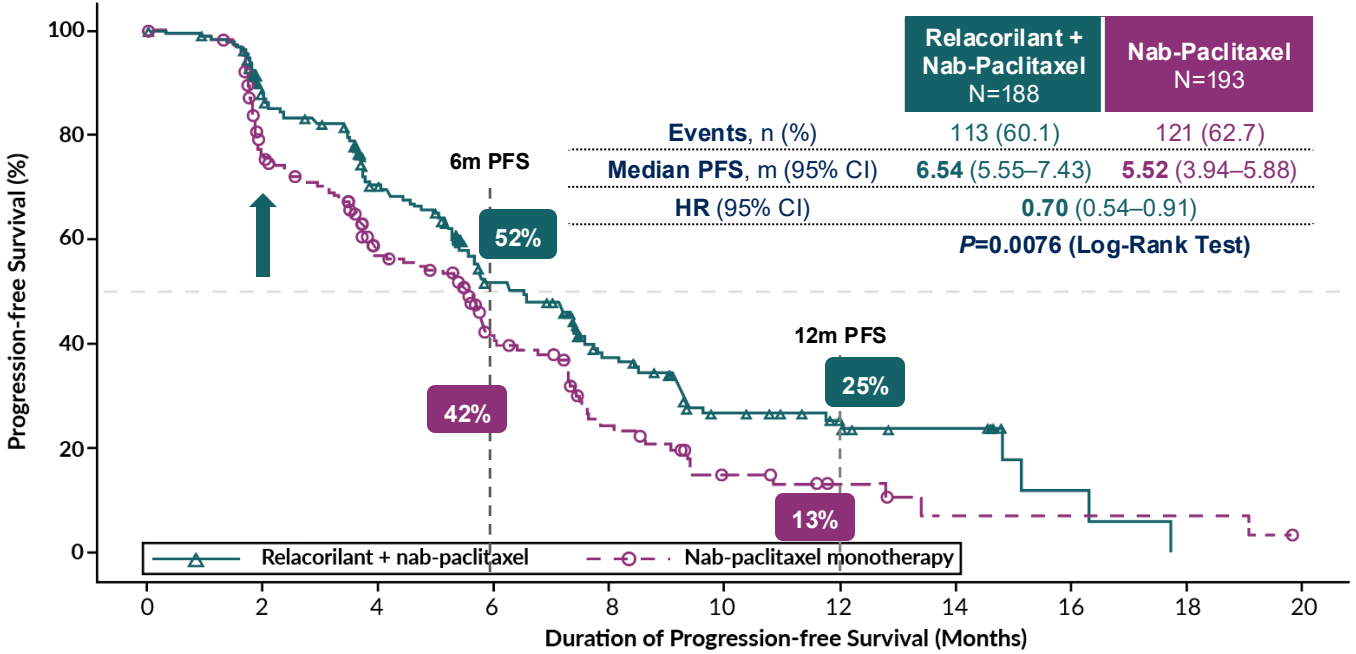
Secondary Endpoints

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

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

Additional study identifiers: APGOT-Ov10, LACOG-0223, and ANZGOG-2221/2023.
CA = cancer antigen; CBR = clinical benefit rate; RECIST = Response Evaluation Criteria in Solid Tumors.
Olawaiye A, et al. *J Clin Oncol*. 2025;43(Suppl 17):LBA5507.

ROSELLA | Progression-Free Survival by BICR

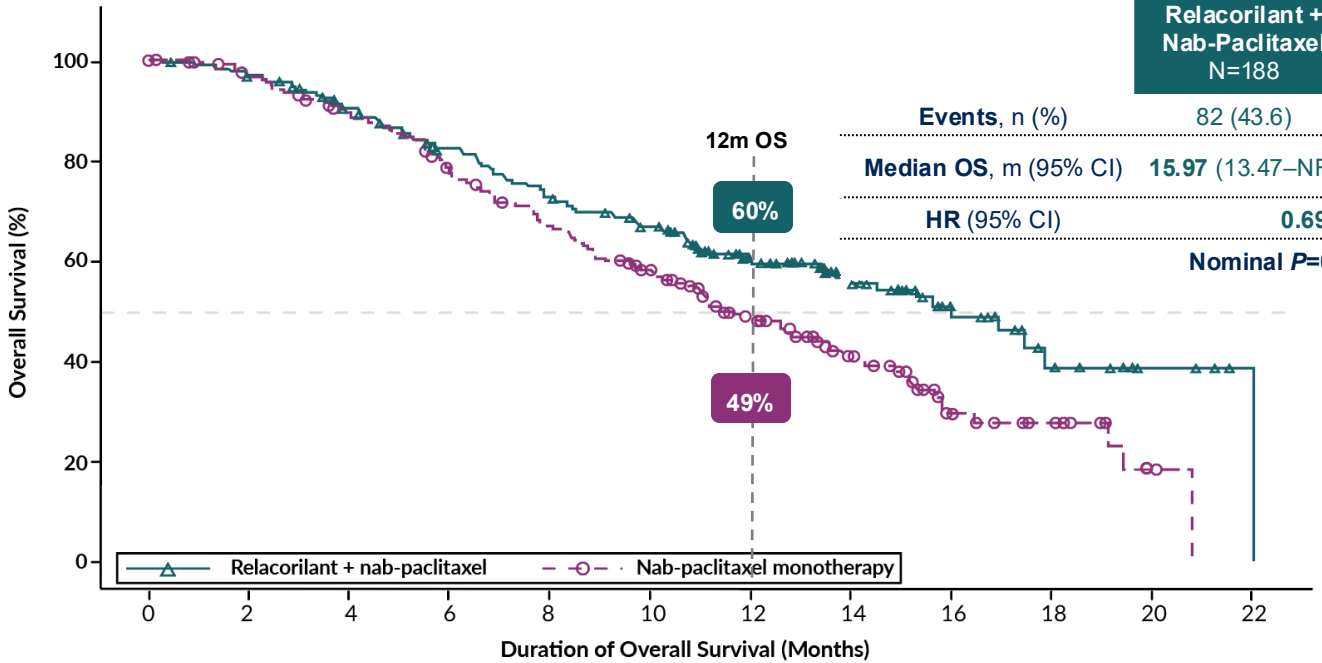


Data cutoff: Feb 24, 2025

Median follow-up time: 9.0 months; statistical significance threshold: *P*≤0.04. The Kaplan-Meier method was used to estimate the curves, median estimates, and the 95% confidence intervals (CIs) for progression-free survival in each treatment arm. The HR and the associated 95% CI were estimated using a Cox regression model with treatment group as the main effect and stratification factors at randomization as covariates. Olawaiye A, et al. *J Clin Oncol*. 2025;43(Suppl 17):LBA5507.

Great Debates Solid Tumors

ROSELLA | Interim Analysis for Overall Survival



	Relacorilant + Nab-Paclitaxel N=188	Nab-Paclitaxel N=193
Events, n (%)	82 (43.6)	110 (57.0)
Median OS, m (95% CI)	**15.97** (13.47–NR)	**11.50** (10.02–13.57)
HR (95% CI)	**0.69** (0.52–0.92)	

Nominal *P*=0.0121 (Log-Rank Test)

No. at risk (events/cumulative events)

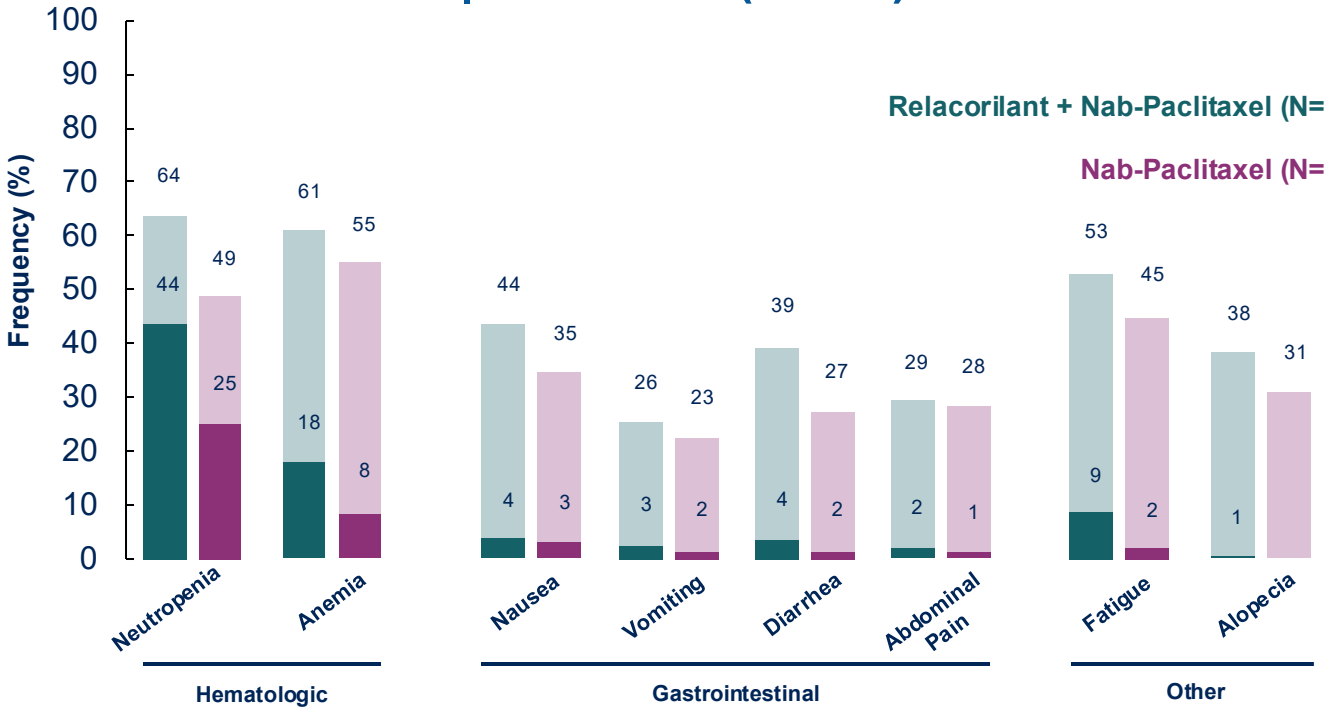
Relacorilant + nab-paclitaxel	188 (0/0)	180 (6/6)	162 (12/18)	143 (14/32)	126 (17/49)	111 (10/59)	77 (10/69)	49 (5/74)	24 (4/78)	10 (3/81)	4 (0/81)	0 (1/82)
Nab-paclitaxel monotherapy	193 (0/0)	179 (6/6)	160 (13/19)	137 (20/39)	115 (20/59)	93 (15/74)	65 (14/88)	40 (9/97)	16 (9/106)	11 (1/107)	3 (2/109)	0 (1/110)

Data cutoff: Feb 24, 2025

Median follow-up time: 13.9 months; statistical significance threshold at the interim analysis: *P*≤0.0001; statistical significance threshold at the final analysis: *P*≤0.0499. The Kaplan-Meier method was used to estimate the curves, median estimates, and the 95% confidence intervals (CIs) for overall survival in each treatment arm. The HR and the associated 95% CI were estimated using a Cox regression model with treatment group as the main effect and stratification factors at randomization as covariates.

Olawaiye A, et al. *J Clin Oncol*. 2025;43(Suppl 17):LBA5507.

ROSELLA | Common (>20%) Adverse Events



Data cutoff: Feb 24, 2025

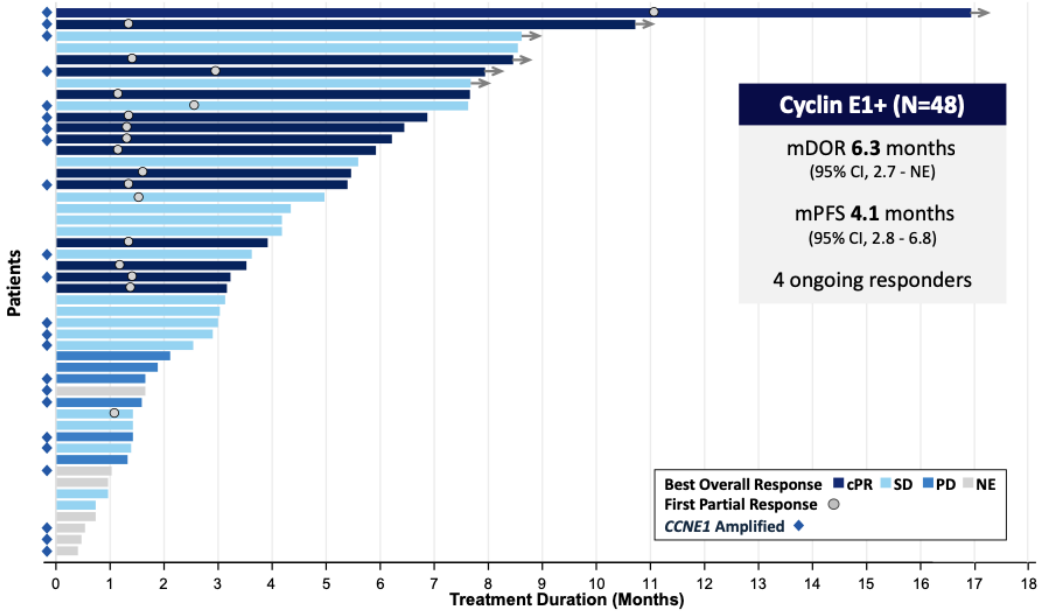
5 SAEs of febrile neutropenia were reported, 4 (2.1%) with relacorilant + nab-paclitaxel and 1 (0.5%) with nab-paclitaxel monotherapy
5 SAEs of sepsis were reported, 3 (1.6%) with relacorilant + nab-paclitaxel and 2 (1.1%) with nab-paclitaxel monotherapy

TEAEs that occurred in >20% of patients. Assessed in the safety population of patients who received at least one dose of study drug, N=378. Combined terms are presented for neutropenia (neutropenia, reduced neutrophil count, and febrile neutropenia), anemia (anemia, reduced hemoglobin, and reduced red blood cell count), and fatigue (fatigue and asthenia).
SAE = serious adverse event; TEAE = treatment-emergent adverse event.
Olawaiye A, et al. *J Clin Oncol*. 2025;43(Suppl 17):LBA5507.

Great Debates Solid Tumors

Cyclin E1 Sensitizes Cells to WEE1 and Other Cell Cycle Inhibition

DENALI Part 1b: Duration of Response in Cyclin E1 IHC+ Ovarian Cancer

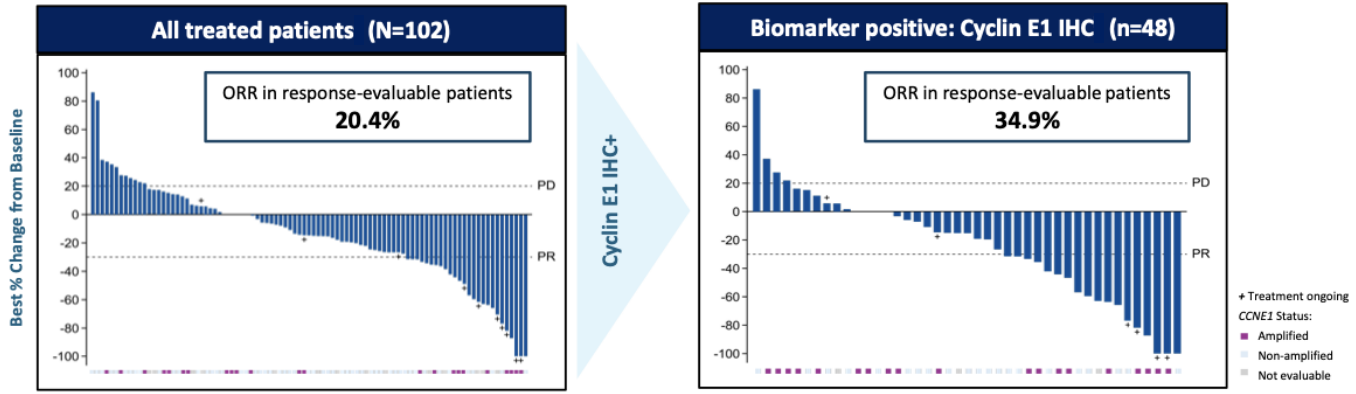


Simpkins F, et al. Presented at: SGO Annual Meeting on Women's Cancer; March 14-17, 2025; Seattle, Washington.

Great Debates Solid Tumors

Cyclin E1 Sensitizes Cells to WEE1 and Other Cell Cycle Inhibition

Cyclin E1+ by IHC is a Biomarker Predicting Response to Azenosertib



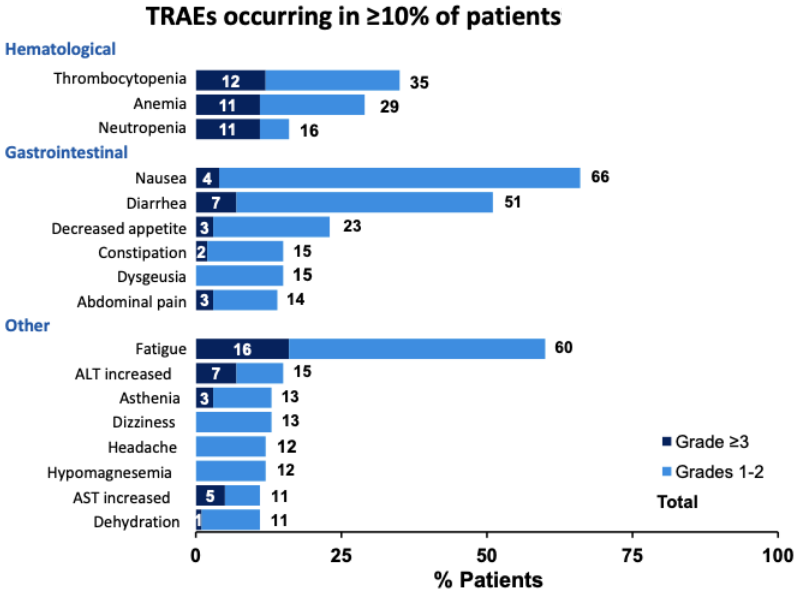
	All treated patients (N=102)	Cyclin E1 IHC+ (n=48)
ORR in response-evaluable patients, % (n/N; 95% CI)	20.4 (19/93; 12.8-30.1)	34.9 (15/43; 21.0-50.9)
ORR, ITT % (n/N; 95% CI)	18.6 (19/102; 11.6-27.6)	31.3 (15/48; 18.7-46.3)

Simpkins F, et al. Presented at: SGO Annual Meeting on Women's Cancer; March 14-17, 2025; Seattle, Washington.

Great Debates Solid Tumors

Cyclin E1 Sensitizes Cells to WEE1 and Other Cell Cycle Inhibition

DENALI Part 1b: Safety and Tolerability Summary



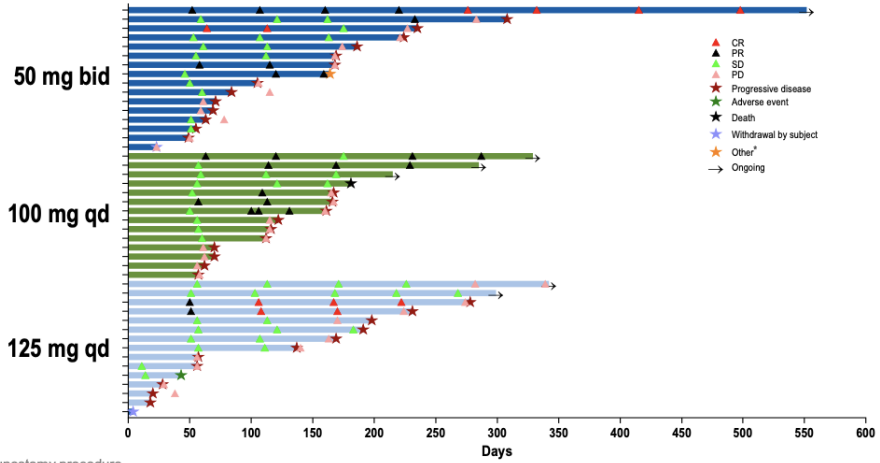
TRAEs, n (%)	
Leading to dose reduction	44 (43.1)
Leading to dose interruption	59 (57.8)
Leading to discontinuation	22 (21.6)
Leading to death	2 (2.0)
Serious TRAEs	22 (21.6)

Simpkins F, et al. Presented at: SGO Annual Meeting on Women's Cancer; March 14-17, 2025; Seattle, Washington.

Cyclin E1 Sensitizes Cells to Other Cell Cycle Inhibition: INCB123667 – Selective CDK2 Inhibitor

Duration of Treatment and Response

- Median duration of treatment (range) was 4.5 (0.1-18.1) months
- Median time to response (range) was 2.1 (1.6-7.7) months



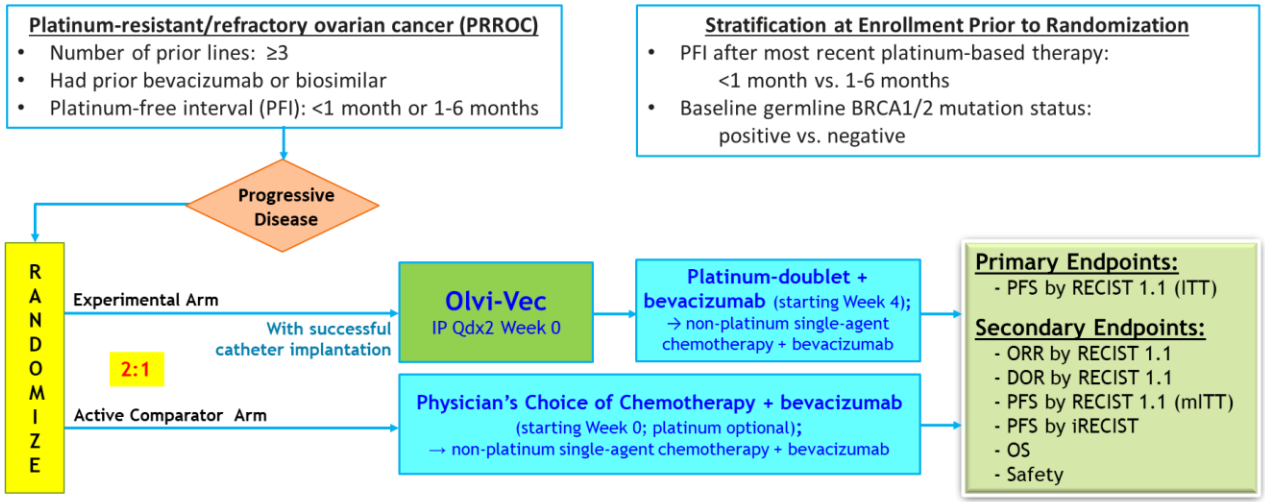
*Sponsor decision after jejunostomy procedure.
bid, twice daily; CR, complete response; PD, progressive disease; PR, partial response; qd, daily; SD, stable disease.

Lorusso D, et al. Presented at: ASCO Annual Meeting; May 30-June 3, 2025; Chicago, Illinois.

GOG-3076/Olvi-Vec-022/OnPrime

A Randomized Phase 3 Study Assessing the Efficacy and Safety of Olvi-Vec followed by Platinum-Doublet Chemotherapy and Bevacizumab Compared with Physician's Choice of Chemotherapy and Bevacizumab in Women with Platinum-Resistant/Refractory Ovarian Cancer (PRROC)

(NPI: Robert Holloway, MD; Co-NPIs: Premal Thaker, MD, Ramez Eskander, MD, Erin Crane, MD)



- Olvimulogene nanivacirepvec: oncolytic vaccinia virus-based immunotherapy
- Virus-mediated immune activation
- Re-sensitization of tumor cells to chemotherapy
- No maximal limit on the number of prior lines
- Temporary intraperitoneal dialysis catheter can be placed either through laparoscopy or interventional radiology (requires backup surgical option available if IR placement fails)
- Institutional BioSafety Committee, BSL-1 practice, -70C ± 10 freezer required

Olvi-Vec = oovimulogene nanivacirepvec (o-v).
ClinicalTrials.gov [www.clinicaltrials.gov]. Last updated August 26, 2025. https://clinicaltrials.gov/study/NCT05281471.

Great Debates
Solid Tumors

Rare Histologies

Ovarian Clear Cell-Standard: Addition of Bevacizumab 1L – Retrospective Data in Rare Histology

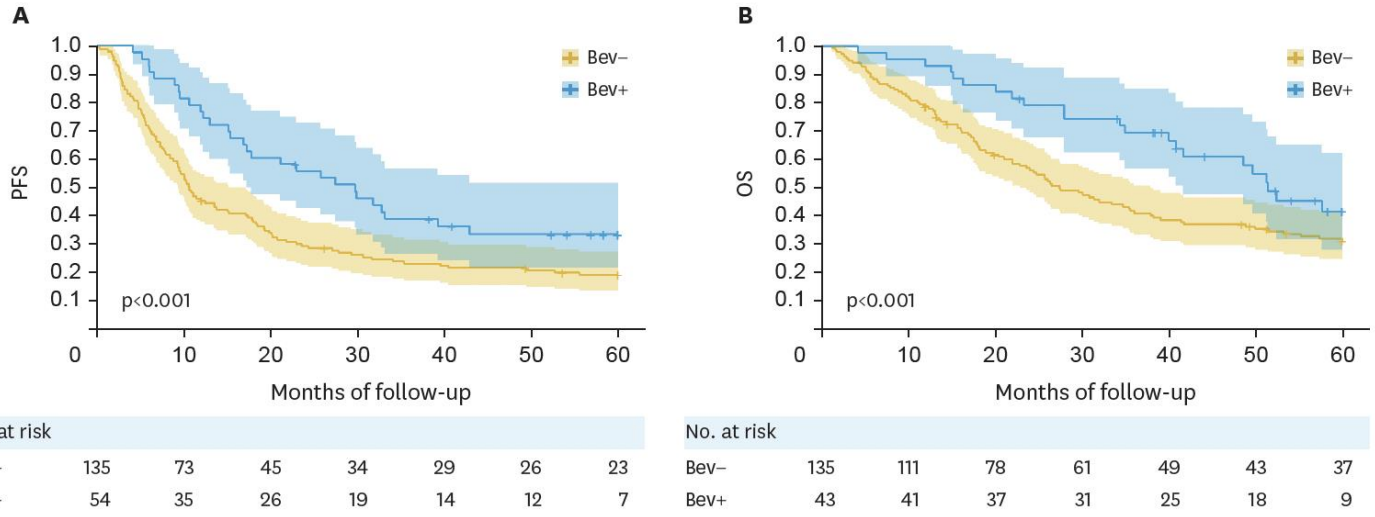
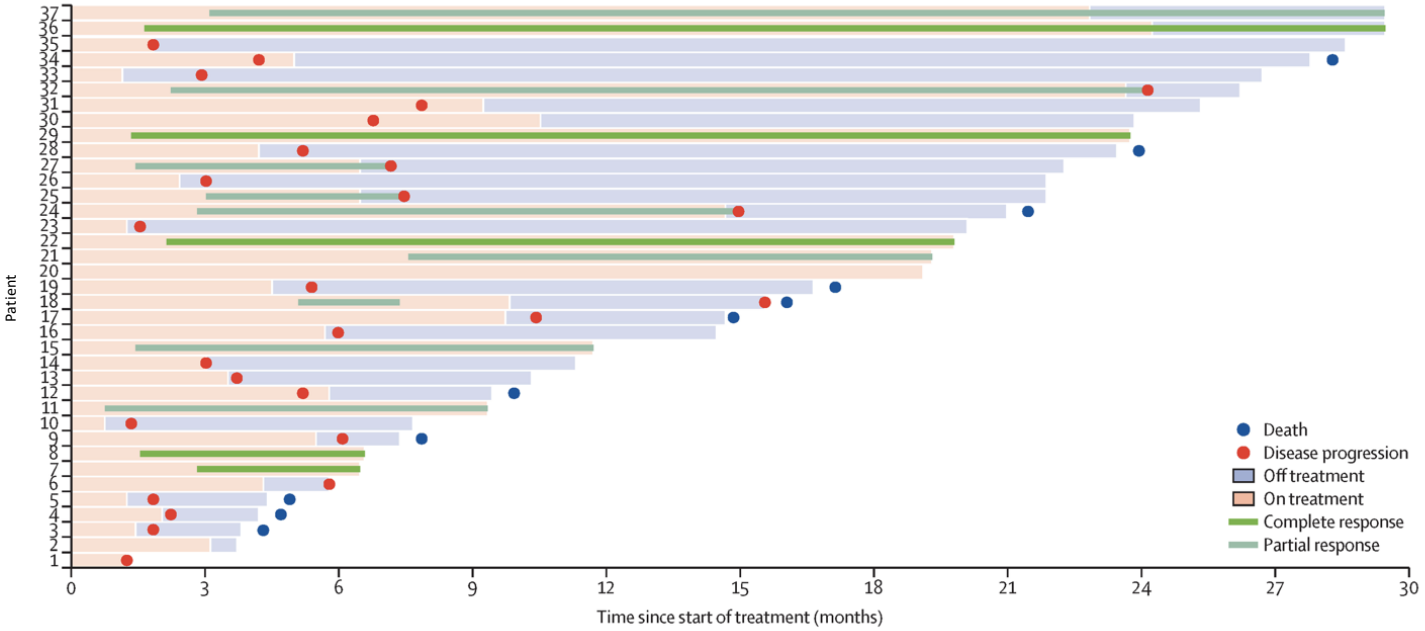


Fig. 3. Survival curves according to bevacizumab use.
(A) PFS and (B) OS.
Bev+, bevacizumab-treated; Bev–, non-bevacizumab-treated; OS, overall survival; PFS, progression-free survival.

Tate S, et al. *J Gynecol Oncol*. 2025;36(5):e80.

Great Debates Solid Tumors

Sintilimab Combined with Bevacizumab in Relapsed or Persistent Ovarian Clear Cell Carcinoma (INOVA): A Multicenter, Single-Arm, Phase 2 Trial

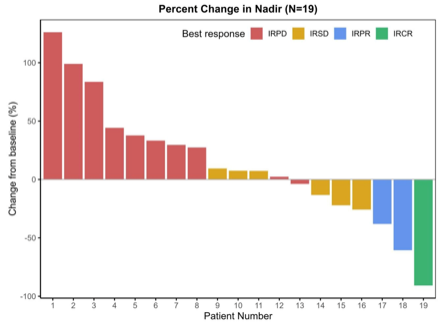


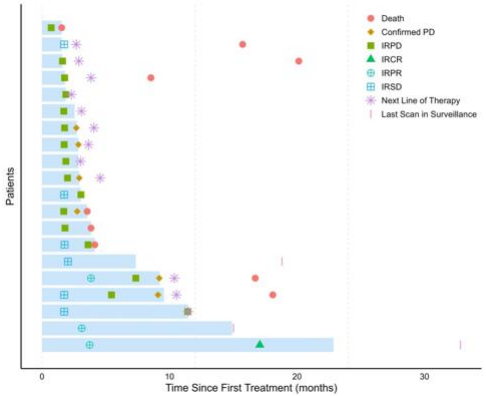
Peng Z, et al. *Lancet Oncol*. 2024;25(10):1288-1297.

Great Debates Solid Tumors

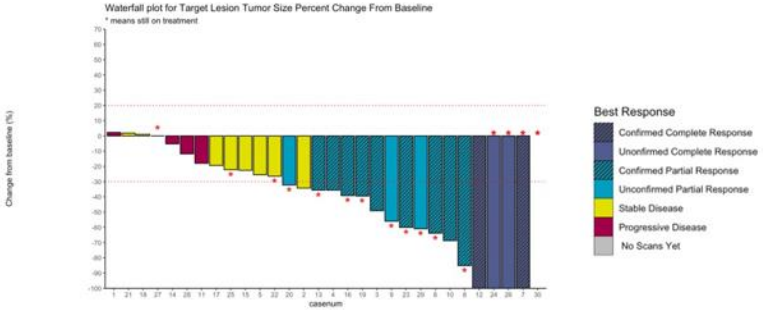
Additional Development in Ovarian Clear Cell Carcinoma

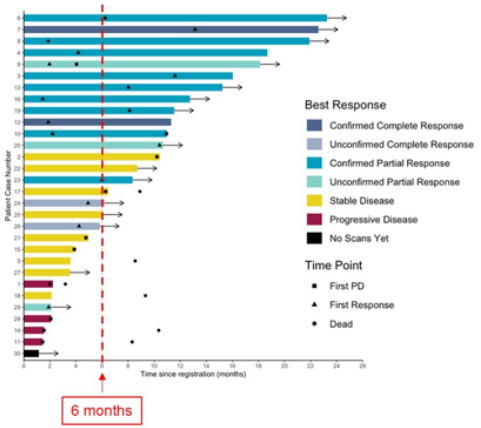
Etigilimab + Nivolumab in OCCC
ORR 15% / CBR 30%





Pembrolizumab + Lenvatinib in OCCC
ORR 36.7%





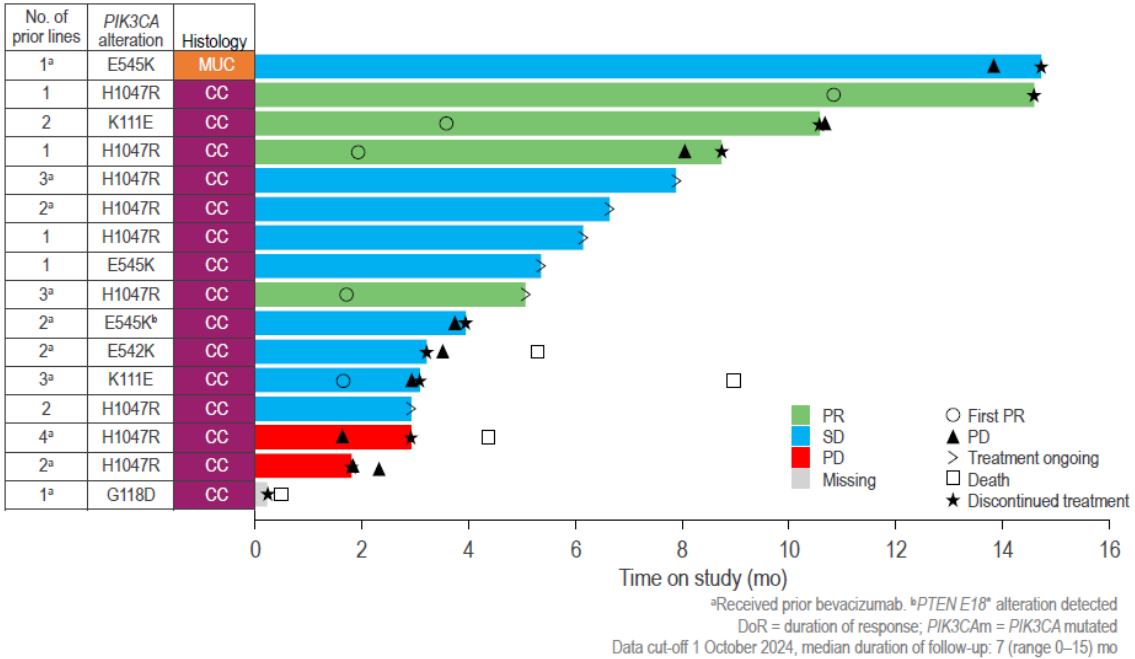
Used with permission from Dr. Katy Moore.
Son J, et al. Presented at: ASCO Annual Meeting; May 30-June 3, 2025; Chicago, Illinois.
Lee JY, et al. Presented at: ASCO Annual Meeting; May 30-June 3, 2025; Chicago, Illinois

Great Debates Solid Tumors

Ovarian Clear Cell Carcinoma: Inavolisib + Palbociclib in PIK3CAm (BOUQUET Trial)

- 94% CC, 75% 1–2 prior lines, 63% prior bevacizumab
- Median treatment duration: 5.2 mo inavolisib, 5.1 mo palbociclib
  - 6 patients still on treatment

Endpoint (95% CI)	n=16
cORR	25% (7–52)
Median DoR, mo	6.6 (6.1–NE)
DCR	63% (35–85)
Median PFS, mo	8.0 (3.5–NE)
6-mo PFS rate	63% (39–86)



[a]Received prior bevacizumab. [b]*PTEN E18** alteration detected
DoR = duration of response; *PIK3CAm* = *PIK3CA* mutated
Data cut-off 1 October 2024, median duration of follow-up: 7 (range 0–15) mo

Used with permission from Dr. Katy Moore.
Ray-Coquard IL, et al. Presented at: ESMO Gynaecological Cancers Congress; June 19-21, 2025; Vienna, Austria.

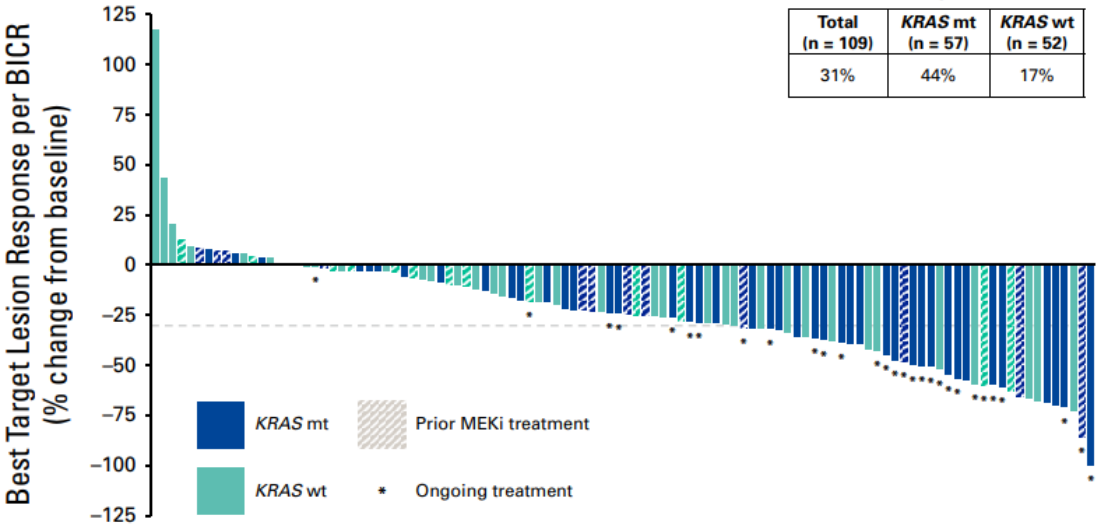
Great Debates Solid Tumors

LGSOC: Avutometinib + Defactinib – RAMP 201

FDA grants accelerated approval to the combination of avutometinib and defactinib for KRAS-mutated recurrent low-grade serous ovarian cancer

ORR by BICR

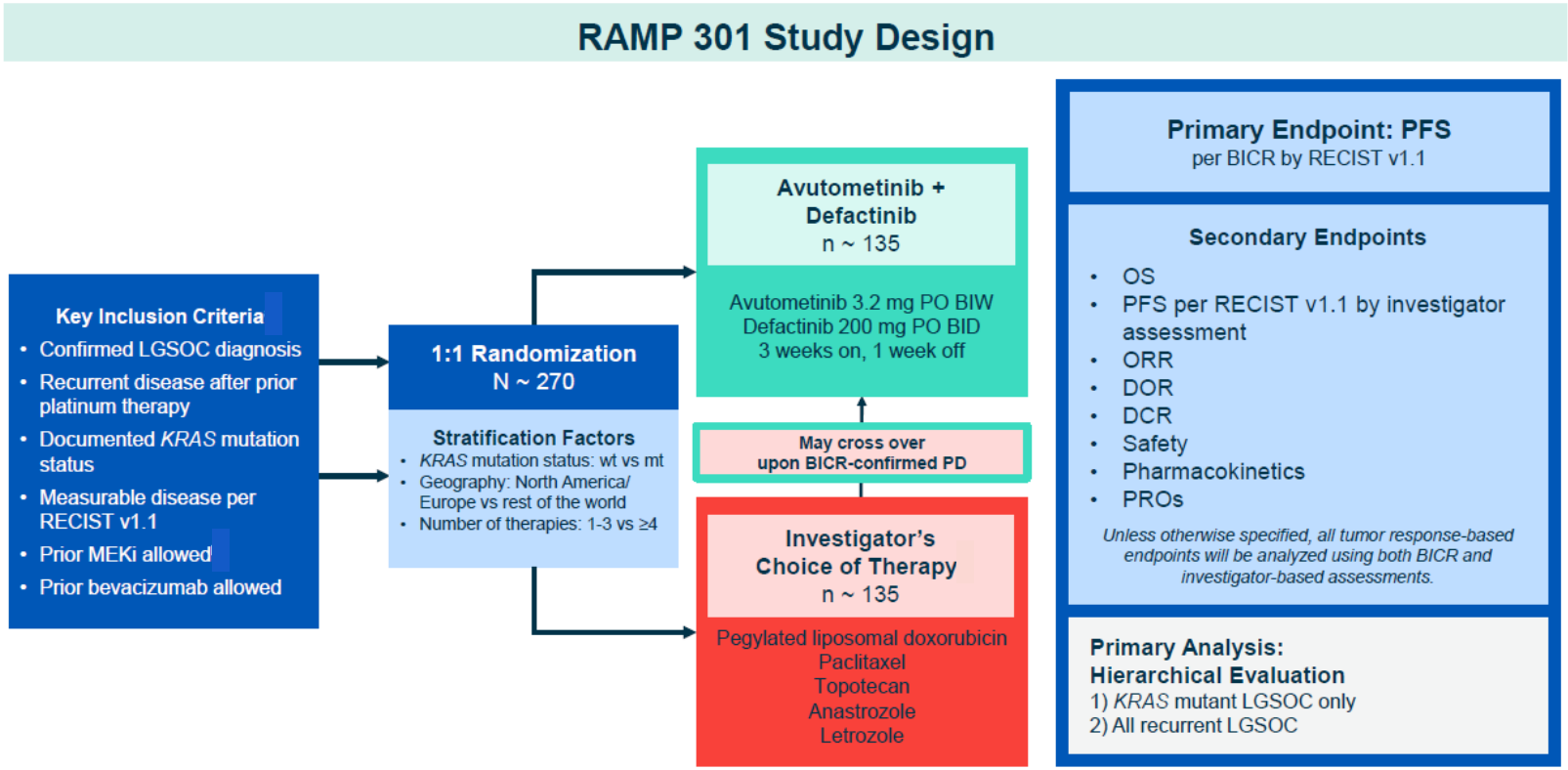
Total (n = 109)	*KRAS* mt (n = 57)	*KRAS* wt (n = 52)
31%	44%	17%



Used with permission from Dr. Katy Moore.

Banerjee SN, et al. *J Clin Oncol*. 2025;43(25):2782-2792. FDA. May 8, 2025. https://www.fda.gov/drugs/resources-information-approved-drugs/fda-grants-accelerated-approval-combination-avutometinib-and-defactinib-kras-mutated-recurrent-low.

LGSOC: Avutometinib + Defactinib – RAMP 301



Used with permission from Dr. Katy Moore.
Grisham RN, et al. Presented at: SGO Annual Meeting on Women's Cancer; March 14-17, 2025; Seattle, Washington. (TIPs)

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Key Learning Points

- SOC options for PROC remain limited
- Significant OS gains have been achieved with
  - Mirvetuximab for select patients (FRA >75%) (available)
  - Relacorilant for all-comers receiving weekly paclitaxel (not yet available/PDUFA 7/11/2026)
- Clinical trials remain priority to test the many agents in the pipeline
- Additional pragmatic/real-world studies will be necessary to investigate sequencing and patient preferences regarding multiple options
- Supportive care more important than ever as patients can have longer and meaningful survival with preserved quality of life

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Thank You!