Beyond Chemotherapy: Next Generation Ovarian Cancer Therapies Including Antibody-Drug Conjugates, Glucocorticoid Receptors, and Bispecific Antibodies

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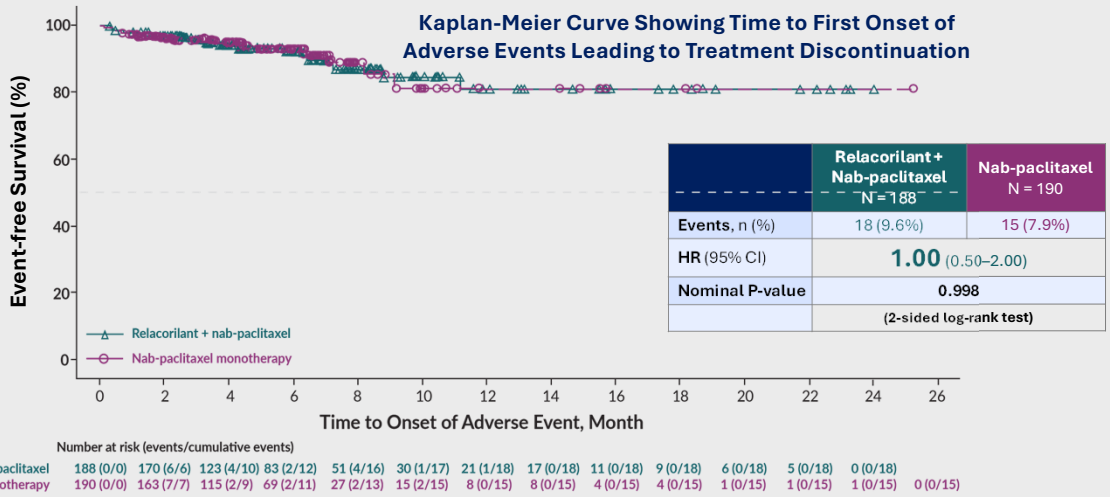
ROSELLA – Treatment Discontinuations Due to Adverse Events Were Infrequent



	Relacorilant + Nab-paclitaxel N = 188	Nab-paclitaxel N = 190
Events, n (%)	18 (9.6%)	15 (7.9%)
HR (95% CI)	**1.00** (0.50–2.00)	
Nominal P-value	0.998	
	(2-sided log-rank test)	

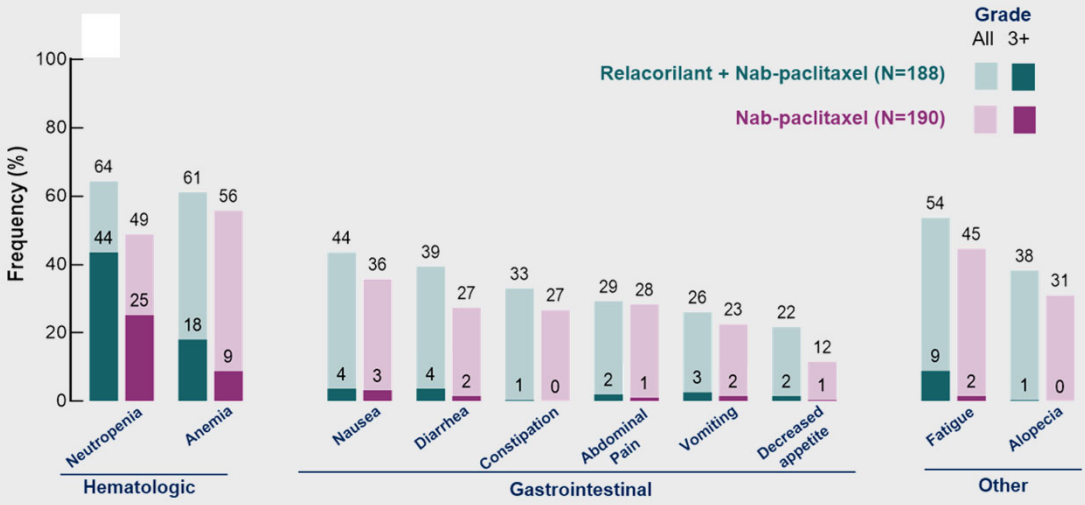
Discontinuations due to AEs were infrequent, well balanced across arms, and occurred in a similar timeframe in both arms

AEs = adverse events.

Alexander Olawaiye. et al. Presented at SGO Meeting, 2026

Data cutoff: Jan 8, 2026

ROSELLA | Common (>20%) Adverse Events



When adjusted for duration of exposure, the incidence rates of neutropenia and anemia were similar between study arms.
Peripheral neuropathy occurred with similar frequency in both arms (19.1% and 17.4%).
5 SAEs of febrile neutropenia: 4 (2.1%) vs 1 (0.5%).* 5 SAEs of sepsis: 3 (1.6%) vs 2 (1.1%).*

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

Alexander Olawaiye. et al. Presented at SGO Meeting, 2026

Data cutoff: Jan 8, 2026

KEYNOTE-B96/ENGOT-ov65: Pembrolizumab + Weekly Paclitaxel ± Bevacizumab vs Placebo

Key Eligibility Criteria

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

R 1:1
N = 643

Pembrolizumab 400 mg (Q6W, 18 cycles) +
Paclitaxel[a] 80 mg/m^2 Days 1, 8, 15 of each Q3W cycle
(± bevacizumab 10 mg/kg Q2W)

Placebo (Q6W, 18 cycles) +
Paclitaxel[a] 80 mg/m^2 Days 1, 8, 15 of each Q3W cycle
(± bevacizumab 10 mg/kg Q2W)

Stratification Factors

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

Primary Endpoint: PFS per RECIST v1.1 by investigator
Key Secondary: OS

ECOG = Eastern Cooperative Oncology Group; PD-1 = programmed cell death 1; PD-L1 = programmed death-ligand 1; PFS = progression-free survival; RECIST = Response Evaluation Criteria in Solid Tumors

[a]Docetaxel (75 mg/m^2 Q3W) may be considered in participants with severe hypersensitivity reaction to paclitaxel or an adverse event requiring discontinuation of paclitaxel after consultation with the Sponsor. [b]The combined positive score (CPS) was assessed at a central laboratory using PD-L1 IHC 22C3 pharmDx and defined as the number of PD-L1 CPS ≥1 cells (tumor cells, lymphocytes, macrophages) divided by the total number of tumor cells × 100.

Monk BJ. et al. Presented at SGO Meeting, 2026

(NCT05116189)

KEYNOTE-B96/ENGOT-ov65

Baseline Characteristics

	Pembro Arm (N = 322)	Placebo Arm (N = 321)
Age, median (range), y	62 (37–85)	61 (37–82)
Race,[a] n (%)		
White	207 (64.3)	217 (67.6)
Asian	72 (22.4)	58 (18.1)
Multiple	12 (3.7)	17 (5.3)
Black or African American	8 (2.5)	6 (1.9)
Hawaiian/Pacific Islander	1 (0.3)	1 (0.3)
PD-L1 CPS, n (%)		
<1	88 (27.3)	89 (27.7)
1 to <10	133 (41.3)	132 (41.1)
≥10	101 (31.4)	100 (31.2)
Stage at diagnosis (FIGO 2014 criteria), n (%)		
IA–IIB	24 (7.4)	26 (8.1)
III–IIIC	183 (56.9)	189 (58.9)
IVA–IVB	115 (35.7)	106 (33.0)

	Pembro Arm (N = 322)	Placebo Arm (N = 321)
ECOG PS 1, n (%)	142 (44.1)	144 (44.9)
High-grade serous histology,[b] n (%)	278 (86.3)	275 (85.7)
Bevacizumab use, n (%)	235 (73.0)	236 (73.5)
Prior lines of therapy,[c] n (%)		
1 line	121 (37.6)	113 (35.2)
2 lines	200 (62.1)	207 (64.5)
Prior anticancer therapy, n (%)		
Anti–PD-1 or PD-L1	7 (2.2)	7 (2.2)
Bevacizumab	149 (46.3)	146 (45.5)
PARP inhibitor	112 (34.8)	123 (38.3)
Platinum-free interval, n (%)		
<3 mo	137 (42.5)	161 (50.2)
≥3 to ≤6 mo	183 (56.8)	155 (48.3)
>6 mo	2 (0.6)	5 (1.6)

CPS – combined positive score; ECOG = Eastern Cooperative Oncology Group; PARP = poly (ADP-ribose) polymerase; PD-1 = programmed cell death 1; PD-L1 = programmed death-ligand 1; PFS = progression-free survival; RECIST = Response Evaluation Criteria in Solid Tumors

[a]44 participants had missing information for race, 22 (6.8%) in the pembro arm and 22 (6.9%) in the placebo arm. [b]Other histology subtypes in the pembro and placebo arms, respectively, were clear cell in 24 (7.5%) and 26 (8.1%), endometrioid in 9 (2.8%) and 4 (1.2%), low-grade serous in 6 (1.9%) and 10 (3.1%), carcinosarcoma in 3 (0.9%) and 5 (1.6%), and other carcinoma in 2 (0.6%) and 1 (0.3%). [c]2 participants had 3 prior lines of therapy, 1 (0.3%) in each treatment arm. Data cutoff date: September 5, 2025.

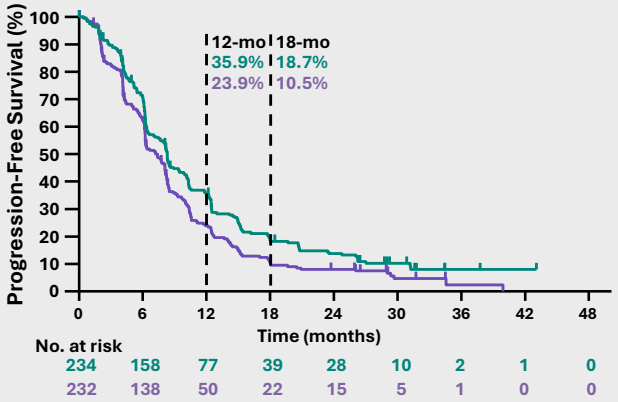
Monk BJ. et al. Presented at SGO Meeting, 2026

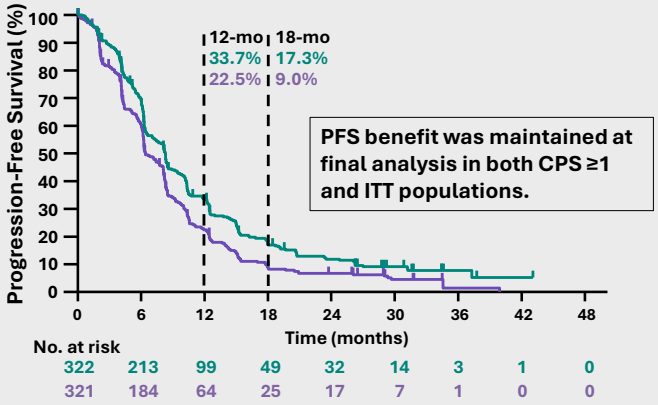
KEYNOTE B96/ENGOT-ov65

PFS in CPS ≥1 and ITT Populations at Final Analysis

CPS ≥1 Population	Events	Median, mo (95% CI)	HR[a] (95% CI)
Pembro Arm	84.6%	8.3 (7.0–9.5)	0.76 (0.62–0.93)
Placebo Arm	88.8%	7.2 (6.2–8.1)	

ITT Population	Events	Median, mo (95% CI)	HR[a] (95% CI)
Pembro Arm	85.7%	8.3 (7.2–8.6)	0.73 (0.62–0.87)
Placebo Arm	89.1%	6.4 (6.2–8.1)	





PFS benefit was maintained at final analysis in both CPS ≥1 and ITT populations.

Median follow-up: 32.7 months

Response assessed per RECIST v1.1 by investigator review.

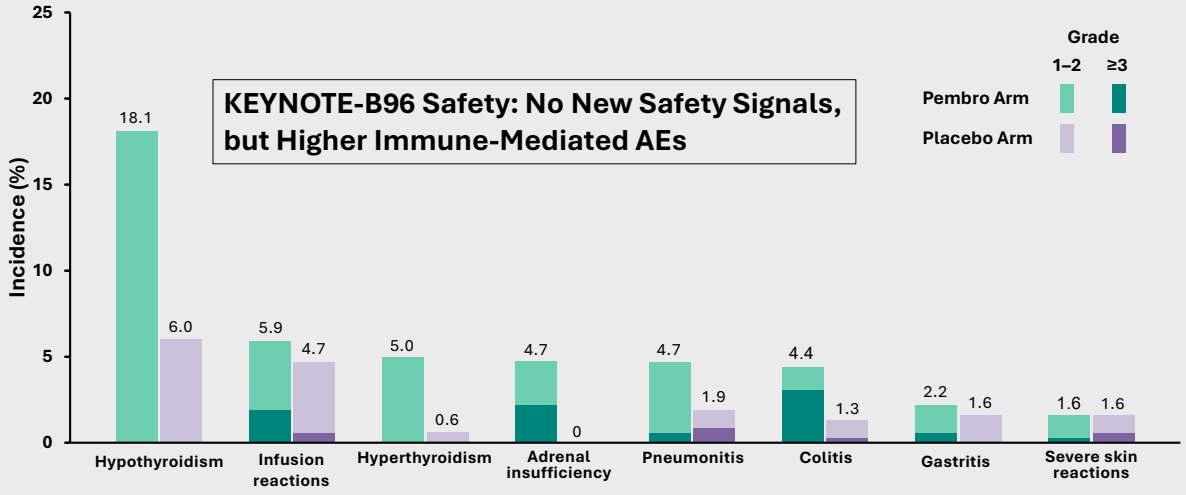
[a]Hazard ratio (CI) analyzed based on a Cox regression model with treatment as a covariate stratified by the randomization stratification factors.

Data cutoff date: September 5, 2025.

Monk BJ. et al. Presented at SGO Meeting, 2026

CI = confidence interval; CPS = combined positive score; HR = hazard ratio; ITT = intention to treat; PFS = progression-free survival; RECIST = Response Evaluation Criteria in Solid Tumors.

Immune-Mediated AEs and Infusion Reactions, Incidence ≥5 Participants in Either Arm*



* Final Analysis

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

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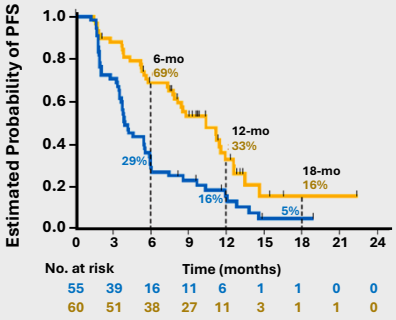
Taxane-based combinations in PROC

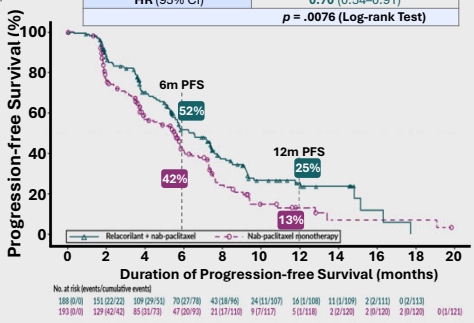
No prior Bev ≤ 2 prior lines

	PAC n = 55	BEV + PAC n = 60
Events, n (%)	49 (89)	37 (62)
Median PFS, m (95% CI)	**3.9** (3.5–5.6)	**10.4** (7.9–11.9)
HR (unstratified) (95% CI)	**0.46** (0.30–0.71)	



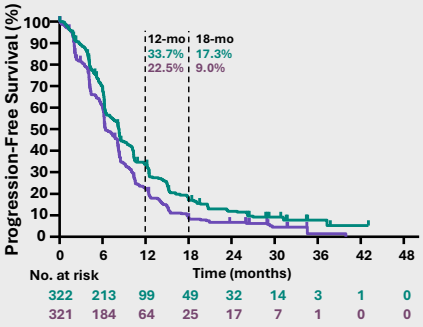
Prior Bev for all ≤ 3 prior lines

	Relacorilant + Nab-paclitaxel N = 188	Nab-paclitaxel N = 193
Events, n (%)	113 (60.1)	121 (62.7)
Median PFS, m (95% CI)	**6.54** (5.55–7.43)	**5.52** (3.94–5.88)
HR (95% CI)	**0.70** (0.54–0.91)	
	***p* = .0076 (Log-rank Test)**	



Prior Bev for 45% patients ≤ 2 prior lines

ITT Population	Events	Median, mo (95% CI)	HR[a] (95% CI)
Pembro Arm	85.7%	8.3 (7.2–8.6)	0.73 (0.62–0.87)
Placebo Arm	89.1%	6.4 (6.2–8.1)	



Which is the best companion for weekly paclitaxel?
How to choose between doublet or triplet?
Which is the best combination if Bevacizumab cannot be used?

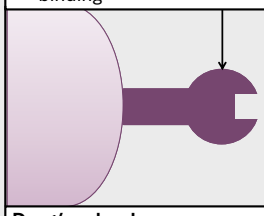
Issue → no validated biomarkers to guide patients' selection

1. Pujade-Lauraine E. et al. J Clin Oncol. 2014;32:1302-1308. 2. Olawaiye A. et al. Presented at SGO Annual Meeting 2026. 3. Monk BJ. et al. Presented at SGO Annual Meeting 2026.

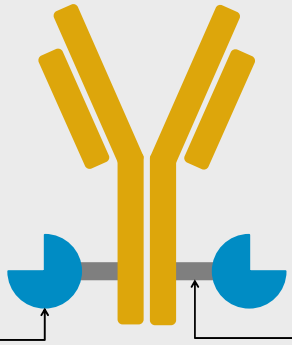
ADCs: A Paradigm Shift in the Treatment of Ovarian Cancer

Understanding their composition and structure

Tumor associated antigen/target
- High homogeneous expression in tumor
- Limited/absent expression in normal tissue
- Limited heterogeneity
- Efficient internalization following ADC binding



Drug/payload
- Highly potent chemotherapy (e.g., microtubule inhibitor, DNA-damaging agents)
- Amenable to linker attachment
- Maximized drug-to-antibody ratio



Antibody
- High affinity and avidity for target antigen
- Long half-life
- Conjugation sites with minimal impact on ADC stability, internalization, and pharmacokinetics (e.g., cysteine, lysine)
- Chimeric or humanized (decreasing immunogenicity)

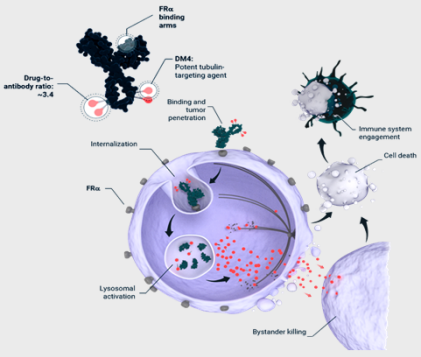
Linker
- Controlled release of payload at the target site:
- Non-cleavable (e.g., lysosomal degradation of mAb)
- Cleavable (e.g., acid/redox/lysosomal sensitive)

Figure adapted from Marks S, Naidoo J.[1]

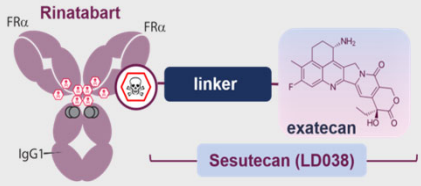
1. Marks S, Naidoo J. *Lung Cancer*. 2022;163:59-68.

FRα: A Biologically Relevant Target in Ovarian Cancer

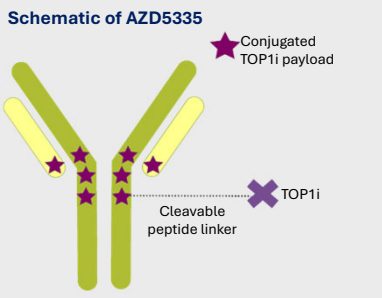
Mirvetuximab soravtansine-gynx
- MIRV is comprised of:
- FRα-binding antibody,
- Cleavable linker
- Anti-Microtubule Payload: Maytansinoid (DM4)



Rinatabart sesutecan* (Rina-S)
- A human monoclonal antibody directed at FRα
- A novel hydrophilic protease-cleavable linker
- DNA-damaging agents: Exatecan, a TOPO 1inh
- Rina-S features a high, homogenous DAR=8



Torvutatug samrotecan* (AZD5335)
- Targeted ADC with a potent TOP1i payload
- The cleavable peptide linker is bystander-capable and serum-stable
- AZD5335 has an average DAR of 8



*Investigational; Not FDA-approved for ovarian cancer

From Ana Oaknin, with permission. Moore K. et al, NEJM, Dec 7;389(23):2162-2174. *Figure adapted from Gymnopoulos M, et al. Presented at AACR 2023 (LB025)*

MIRASOL: FRα-High PROC Treated With Mirvetuximab vs Chemotherapy.

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)

FR detected by IHC with PS2+ intensity among ≥75% of viable tumor cells

High-grade serous histology

1° 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; FR = 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..

Moore K. et al; Presented at ASCO Meeting 2023; Moore KN et al; N Engl J Med 2023; 389:2162-2174

Part C of RAINFOL-01: A Phase 2 Study of Single Agent Rinatabart-Sesutecan* In Patients With PROC

RAINFOL™

Study Design

- This phase 2 multicenter, single-agent study (Part C of RAINFOL™ -01; ClinicalTrials.gov NCT05579366) will enroll ~100 patients with PROC who have received 1-4 prior lines of therapy
- Patients will be treated with Rina-S 120 mg/m^2 Q3W (the recommended phase 2 dose)

RAINFOL™ -01: Phase 2 Trial (Part C) of Rina-S in Patients With PROC

~100 patients with PROC → **Rina-S 120 mg/m^2 Q3W[a]** → **Primary endpoint:** ORR (assessed by blinded independent central review per RECIST v1.1)

Key secondary endpoints: DOR, PFS, OS

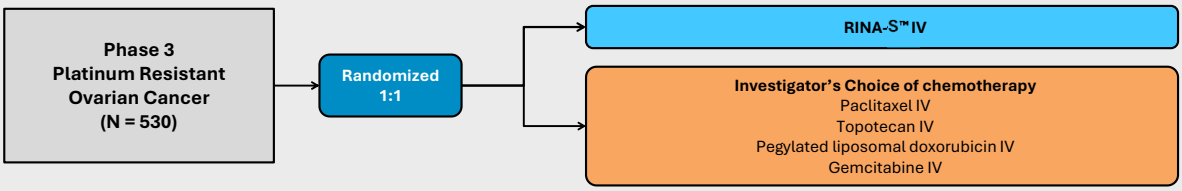
Treatment will continue until the first instance of disease progression, unacceptable toxicity, completion of therapy, investigator decision, withdrawal of consent, study termination, or pregnancy

[a]Recommended phase 2 dose determined in Part B (dose expansion) study. DOR = duration of response; ORR = objective response rate; OS = overall survival; PFS = progression-free survival; PROC = platinum-resistant ovarian cancer; Q3W = once every 3 weeks; RECIST v1.1 = Response Evaluation Criteria in Solid Tumors, version 1.1.

NCT05579366

*Investigational; Not FDA-approved for ovarian cancer

Efficacy of Rina-S* Compared to Treatment of Investigator's Choice in Participants with PROC: ENGOT-OV86/GOG 3107/ RAINFOL-OV2



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

NCT06619236. PI: Angeles Secord

*Investigational; Not FDA-approved for ovarian cancer

Safety Profile of Sofetabart mipitecan*

Treatment-Emergent AEs (≥20%), All Doses and Patients

	2 mg/kg (n = 35)		3 mg/kg (n = 17)		4 mg/kg (n = 39)		6 mg/kg (n = 14)		Total (N = 105)	
Adverse Event, %	Any	G ≥3	Any	G ≥3	Any	G ≥3	Any	G ≥3	Any	G ≥3
Nausea	60	3	47	—	69	—	79	14	64	3
Fatigue[a]	60	3	41	—	46	—	71	7	53	2
Anemia	20	9	41	18	44	31	71	57	39	25
Vomiting	46	3	24	—	33	—	36	7	36	2
Neutropenia[a]	17	6	35	18	41	31	57	57	34	24
Diarrhea	26	-	29	—	44	3	29	—	33	1
Abdominal pain	43	6	6	—	23	—	14	7	26	3
Constipation	34	3	12	—	18	—	29	—	24	1
Decreased appetite	11	—	24	—	31	—	36	—	24	—
Dose reductions due to TEAEs, %	—		24		36		64		26	

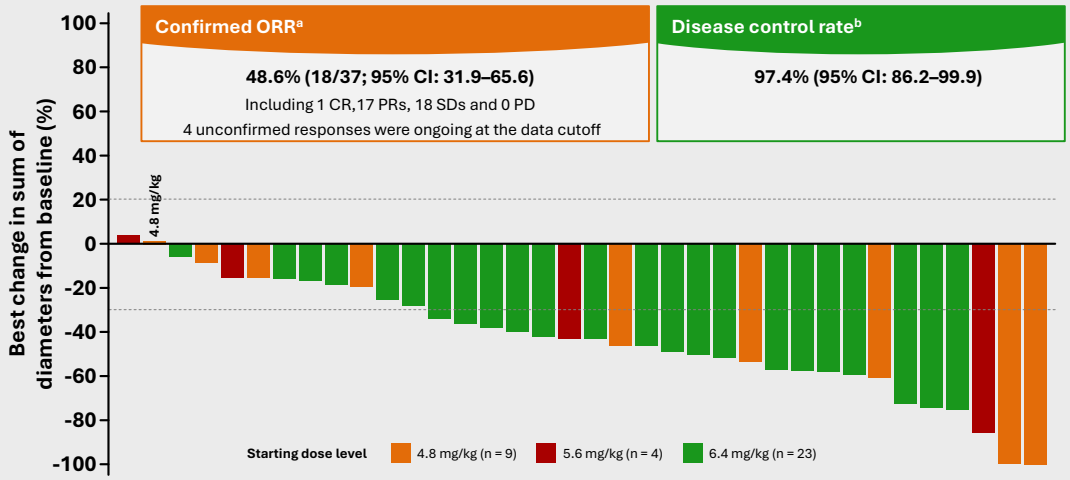
- 50 pts are ongoing, 12 discontinued due to AEs (10 due to related AEs)
- 8% had grade 4 neutropenia, 2% had febrile neutropenia (no prophylactic GCSF used)
- No keratopathy, and low rates of grade 1/2 peripheral neuropathy (3%) and alopecia (10%), were observed

Pothuri B, et al. presented at SGO 2026. Pothuri B, et al. Gynecologic Oncology. 2026 May 1;208:S34-5.

[a]Consolidated terms: fatigue includes fatigue and asthenia; neutropenia includes neutropenia and neutrophil count decreased

*Investigational; Not FDA-approved for ovarian cancer

Preliminary Antitumor Activity of R-DXd* is Promising in Heavily Pretreated Patients with OVC Receiving Doses of 4.8–6.4 mg/kg



Kathleen Moore et al. Presented at ESMO 2023 Madrid; Moore KN, et al. Annals of Oncology. 2023;34:S510.

*Investigational; Not FDA-approved for ovarian cancer

DS6000-109/REJOICE-Ovarian01/ENGOT-ov77/GOG-3096

- Raludotatug Deruxtecan (R-DXd)*, a CDH6-directed Antibody-drug Conjugate, in Subjects with Platinum-resistant, High-grade Ovarian, Primary Peritoneal, or Fallopian Tube Cancers US PI: Debra Richardson, MD

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
- 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*)

Phase 2

R-DXd IV Q3W

R 1:1:1

- 4.8 mg/kg
- 5.6 mg/kg
- 6.4 mg/kg

Ph 2 Extension*: 5.6 mg/kg

Until PD, death, lost to FU, other reason

Follow-up: 40D, LTSFU Q3M

Primary endpoints:
- ORR per BICR

Key secondary endpoints:
- ORR per inv
- DOR

Opening Q4 2025

Phase 3

R-DXd IV Q3W

R 1:1

- R-DXd at RP3D
- TPC (gemcitabine, PLD, topotecan, paclitaxel)

Until PD, death, lost to FU, other reason

Follow-up: 40D, LTSFU Q3M

Primary endpoints:
- ORR per BICR
- PFS per BICR

Key secondary endpoints:
- OS
- QOL

*Phase 2 extension currently enrolling 100 patients at selected dose of 5.6 mg/kg

BTD awarded Sept 15, 2025

BICR = blinded independent central review; BTD = breakthrough therapy designation; FU = follow up; LTSFU = long-term safety follow up; ORR = objective response rate; PD =

*Investigational; Not FDA-approved for ovarian cancer