An Industry Supported Symposium at the SGO Annual Meeting on Women's Cancer 2025

Expanding the Arsenal: Innovative Strategies to Treat Platinum Resistant Ovarian Cancer

Sunday, March 16, 2025 | 7:00 – 8:15 am PT
Seattle, Washington, USA

Objectives

- Explore Recent Advancements in Ovarian Cancer
- Discuss Competitive Landscape
- Understand Treatment Efficacy: Treatment Outcomes
- Engage in Collaborative Dialogue

Agenda

7:00 – 7:05am	**Welcome and Introductions** ***Dr. Thomas J. Herzog***
7:05 – 7:20am	**Understanding the Competitive Landscape of Platinum Resistant Ovarian Cancer (PROC)** ***Dr. Alexander B. Olawaiye***
7:20 – 7:35am	**Evaluating New Opportunities in Ovarian Cancer Beyond ADCs** ***Dr. Nicoletta Colombo***
7:35 – 8:00am	**Future Direction in Ovarian Cancer Care – An Engaging Discussion** ***Dr. Lyndsay Willmott*** ***Moderator Led Panel Discussion Among Experts***
8:00 – 8:10am	**Q&A and Audience Engagement** ***All Faculty – Moderator Led***
8:10 – 8:15am	**Closing Remarks** ***Dr. Thomas J. Herzog***

Moderator | Faculty

Thomas J. Herzog, MD
University of Cincinnati
Cincinnati, OH, USA

Nicoletta Colombo, MD, PhD
Chair, Ovarian Cancer Centre
European Institute of Oncology (IEO)
Milan, Italy

Alexander B. Olawaiye, MD
University of Pittsburgh
Magee-Women's Hospital
Pittsburgh, PA, USA

Lyndsay Willmott, MD
HonorHealth Research
and Innovation Institute
Phoenix, AZ, USA

Disclosures

Speaker Name	Role in Activity	Name of Ineligible Company(ies) and Nature of Financial Relationships
Dr. Thomas J. Herzog	**Moderator**	**Scientific Advisory Boards:** Aadi; AbbVie; AstraZeneca; Caris; Clovis; Corcept; Eisai; Epsilogen; Genmab; Genelux; Genentech; GSK; Merck; Mersana; Pfizer; Sutro
Dr. Nicoletta Colombo	**Speaker**	**Advisor:** AstraZeneca; BioNTech; Eisai; GSK; Immunogen; Mersana; MSD/Merck; Novocure
Dr. Alexander B. Olawaiye	**Speaker**	**Advisory Board:** AstraZeneca; Daiichi Sankyo; GSK; Merck
Dr. Lyndsay Willmott	**Speaker**	**Advisory Board:** Daiichi Sankyo; GSK **Speakers Bureau:** AbbVie; AstraZeneca; GSK; Merck; Pfizer

The GOG Foundation, Inc. Continuing Education

In support of improving patient care, this activity has been planned and implemented by The GOG Foundation, Inc.

Accreditation Statement

The GOG Foundation, Inc. is accredited by the Accreditation Council for Continuing Medical Education (ACCME) to provide Continuing Medical Education for physicians.

AMA PRA Category 1 Credits™

The GOG Foundation, Inc. designates this live activity for a maximum of ***1.25 AMA PRA Category 1 Credits™***.
Physicians should claim only the credit commensurate with the extent of their participation in the activity.

Method of Participation

In accordance with the ACCME Accreditation Criteria, The GOG Foundation, Inc., as the accredited provider of this activity, must ensure that anyone in a position to control the content of the educational activity has disclosed all relevant financial relationships with any ineligible company *(formally known as commercial interests). All Committee/Planning/Faculty members were required to disclose all financial relationships and speakers were required to disclose any financial relationship as it pertains to the content of the presentations. All relevant financial relationships listed for these individuals have been mitigated to ensure a bias-free presentation. Please see the faculty disclosure list for detailed information.

Participants who complete the educational activity, pre-/post-tests, and evaluation, will receive certificate of credit.

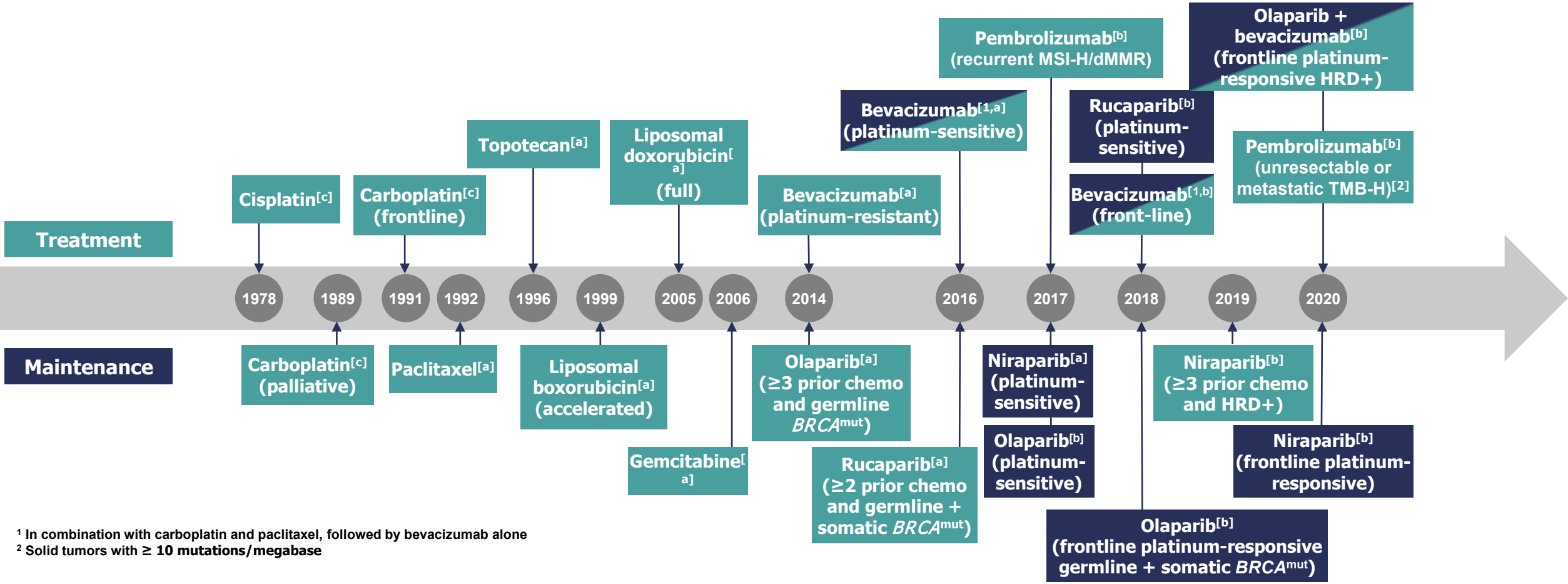
Complete Our Pre-Test

Understanding the Competitive Landscape of PROC

Alexander B. Olawaiye, MD
University of Pittsburgh,
UPMC Magee-Women's Hospital, Pittsburgh, PA

Landmark FDA Approvals in Ovarian Cancer Therapy

Treatments Options and Approaches Have Increased Substantially in the Last Decade[a,b]



[1] In combination with carboplatin and paclitaxel, followed by bevacizumab alone
[2] Solid tumors with ≥ 10 mutations/megabase

BRCA, breast cancer susceptibility gene; chemo, chemotherapy; dMMR, deficient mismatch repair; FDA, US Food and Drug Administration; HRD+, homologous recombination deficiency positive; MSI-H, high microsatellite instability; mut, mutation; TMB-H, tumor mutational burden-high.

a. Drugs@FDA: FDA-approved drugs. https://www.accessdata.fda.gov/scripts/cder/daf/; b. FDA. Hematology/oncology (cancer) approvals & safety notifications. https://www.fda.gov/drugs/resources-information-approved-drugs/hematologyoncology-cancer-approvals-safety-notifications; c. Kelland L. *Nat Rev Cancer.* 2007;7:573-584.

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

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

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

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

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

Responses to Salvage Chemotherapy in OC:
A Critical Need for Precise Definitions of the Treated Population

Secondary Platinum-resistant: Patients who responded to a platinum as primary therapy and did not respond to a second organoplatinum

Potentially* platinum-sensitive:** ***All *patients whose most recent response to an organoplatinum resulted in at least a partial response. This group can be further subdivided into patients with PFI of:*

- *< 6 months*
- *6-12 months*
- *More 12 months*

Markman M, et al. *J Clin Oncol.* 1992;Apr;10(4):513-4.

Platinum Until "Platinum Not an Option:" *Platinum Combinations in PROC*

Trial	Regimen	ORR	PFS/TTP
Nagourney RA[1] (P)	D1 cisplatin (30 mg/m^2) and D1/8 gem (600-750 mg/m^2) on 21-day cycle	8/14 (57%)	6
Penson RT[2] (P)	D1 carbo and D1/8 gem, and iniparib on 21-day cycle	11/45 (26%)	6.8
Nasu H[3] (P)	D1 carbo (AUC4) & D1/8 gem (1000 mg/m^2) & bev on 21-day cycle D1 carbo (AUC4) & D1/8 gem (1000 mg/m^2) on 21-day cycle	12/20 (60%) 2/7 (28%)	8.8 5.6
GOG 126L (P) Brewer CA[4]	D1/8 gem (750 mg/m^2) & D1/8 cis (30 mg/m^2) on 28-day cycle* *Limited to primary platinum resistant	9/57 (16%)	5.4
Walsh CS[5] (P)	D1/8 cis (30 mg/m^2) & D1/8 gem (750 mg/m^2) & D1 pembro on 21-day cycle	11/18 (61%)	5.2
Rose PG[6] (R)	D1/8 cis (30 mg/m^2) & D1/8 gem (750 mg/m^2) on 21-day cycle	13/33 (43%)	6.0
Richardson DL[7] (R)	D1/15 platinum/gem/bev on a 28-day cycle	7/12 (58%)	NR
Havrilesky LJ[8] (P)	D1, 8, 15, paclitaxel (80 mg/m^2) & carbo (AUC 2) on 28-day cycle	3/8 (38%)	3.2
Sharma R[9] (R)	D1, 8, 15, paclitaxel (70 mg/m^2) & carbo (AUC 3) on 28-day cycle	12/20 (60%)	7.9
Tatsuki S[10] (R)	platinum "rechallenge" (paclitaxel; docetaxel; Gem; PLD; CPT-11)	26/47 (55%)	8.5

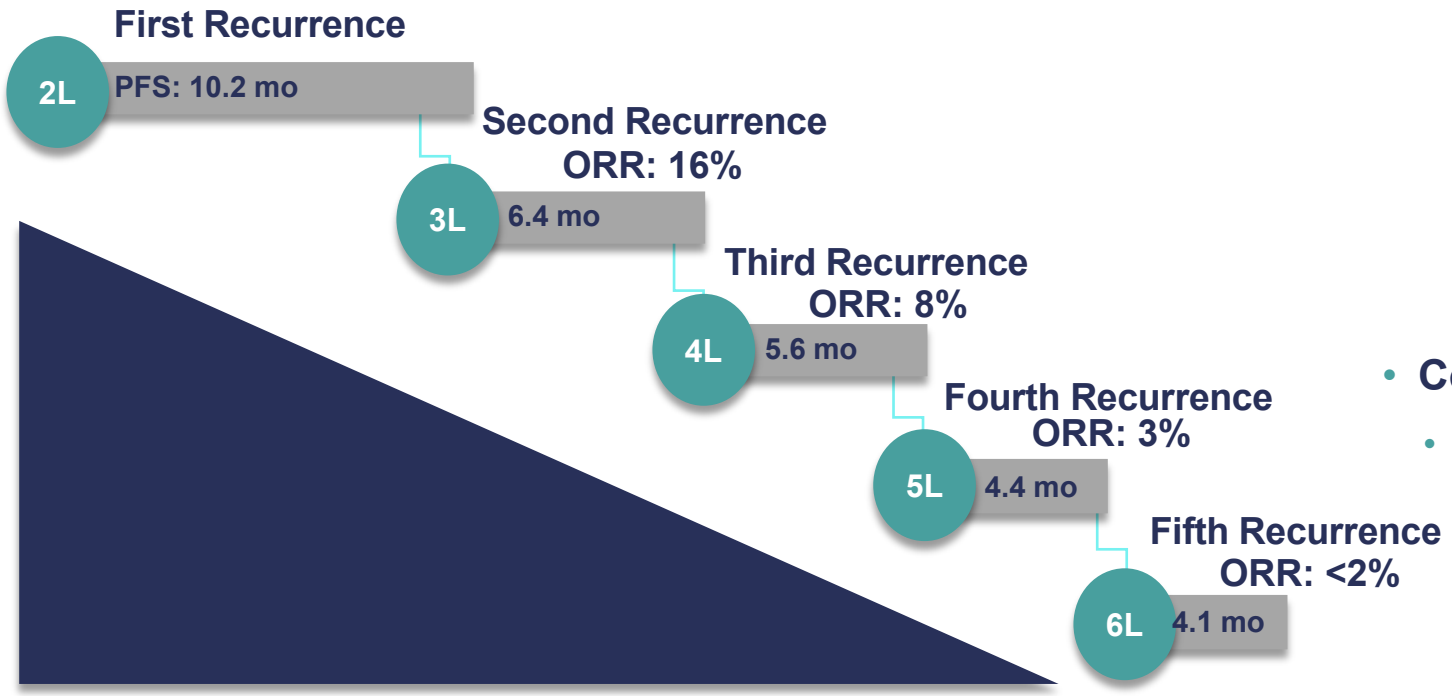
AUC, area under the curve; bev, bevacizumab; cis, cisplatin; carbo, carboplatin; gem, gemcitabine; NR, not reported; ORR, objective response rate; P, prospective; PFS, progression-free survival; PLD, pegylated liposomal doxorubicin; PROC, platinum-resistant ovarian cancer; R, retrospective; TTP, time to progression.

1. Nagourney RA, et al. *Gynecol Oncol*. 2003;88(1):35–39. 2. Penson RT, et al. *Oncologist*. 2023;oyac275. 3. Nasu H, et al. *J Clin Oncol*. 2022;27(4):790–801. 4. Brewer CA, et al. *Gynecol Oncol*. 2006;103(2):446–450. 5. Walsh CS, et al. *PLoS One*. 2021;16(6):e0252665. 6. Rose PG, et al. *Gynecol Oncol*. 2003;88(1):17–21. 7. Richardson DL, et al. *Gynecol Oncol* 2008; 111(3):461–466. 8. Havrilesky LJ, et al. *Gynecol Oncol*. 2003;88(1):51–57. 9. Sharma R, et al. *Br J Cancer*. 2009;100(5):707–712. 10. Tatsuki S, et al. *Anticancer Res*. 2022;42(9):4603–4610.

Platinum Resistant Ovarian Cancer is Now:

"in patients when platinum-based therapy is not an option"

PFS and ORR historically decrease with increasing lines of therapy[1–3]



PROC Re-defined[4]

- **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
    - Experienced a symptomatic relapse soon after the end of the last platinum-based chemotherapy
    - Contraindication to use further platinum-based treatment, such as allergy

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.[2]

L, line of therapy; mo, month;

1. Hanker LC, et al. *Ann Oncol*. 2012;23(10):2605–2612. 2. Pignata S, et al. *Ann Oncol*. 2017;28(suppl 8):viii51–viii56. 3. Griffiths RW, et al. *Int J Gynecol Cancer*. 2011;21(1):58–65. 4. Colombo N et al. *Ann Oncol*. 2019;30(5):672–705.

Patients for Which Platinum Is Not an Option Bevacizumab in Combination With Chemotherapy: AURELIA Trial

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[c]**

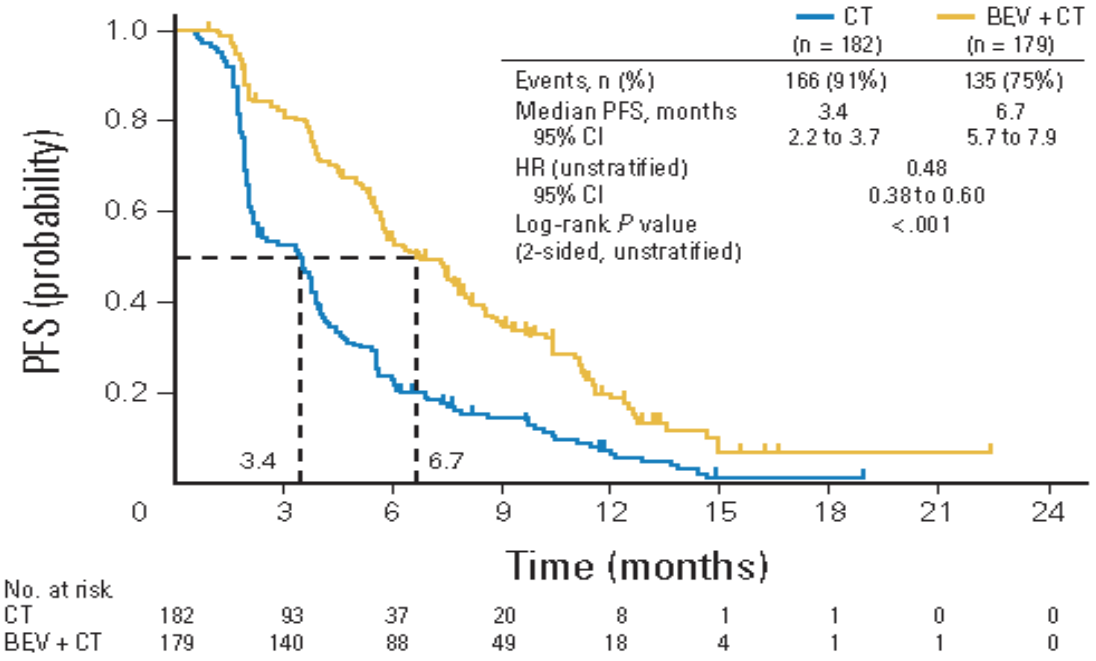
BEV 15 mg/kg q 3 w[b] + chemotherapy → **Treat to PD/toxicity** → **Investigator's choice* (without BEV)**

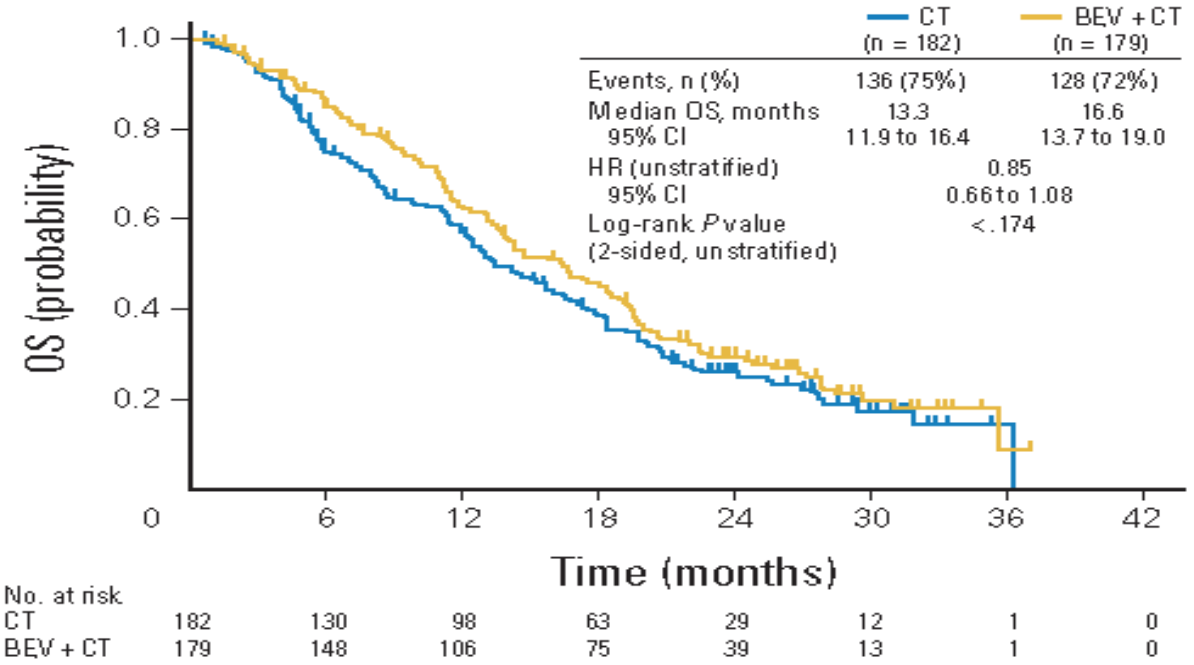
***Chemotherapy options (investigator's choice):**

Paclitaxel 80 mg/m^2 D1,8,15,22 – q4w

Topotecan 4 mg/m^2 D1,8,15 – q4w
(or 1.25 mg/m^2 D1 to 5 – q3w)

PLD 40 mg/m^2 D1 – q4w

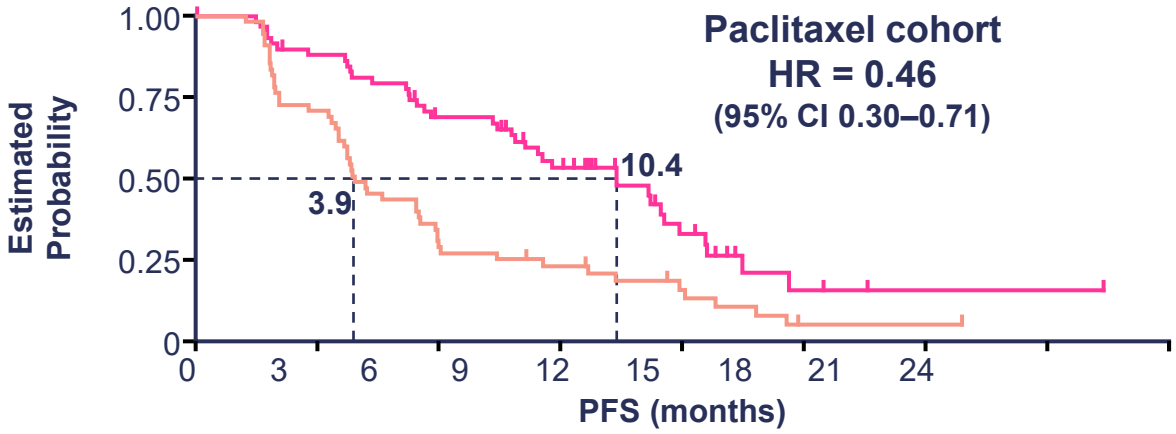


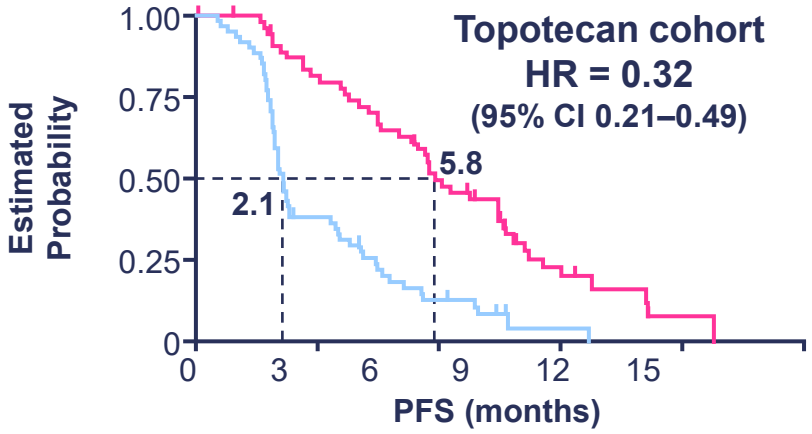


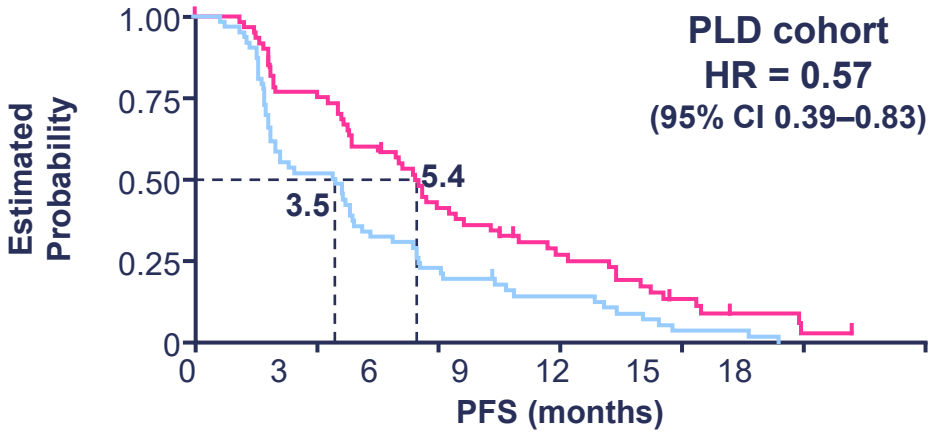
Pujade-Lauraine E, et al. *J Clin Oncol*. 2014;32(13):1302-1308.

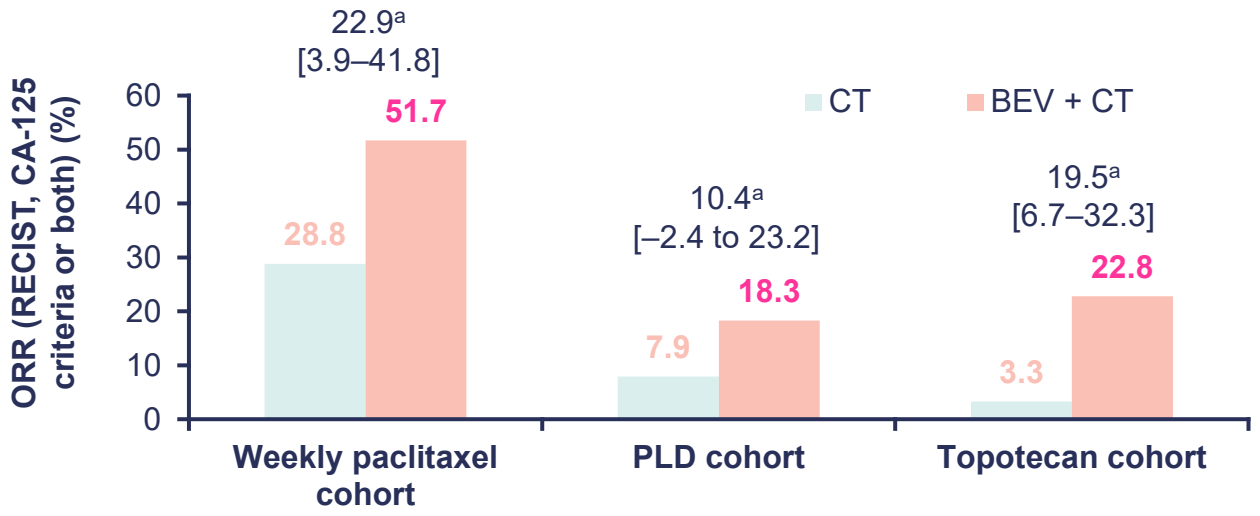
Patients for Which Platinum Is Not an Option

AURELIA trial: Results According to Chemotherapy Cohort







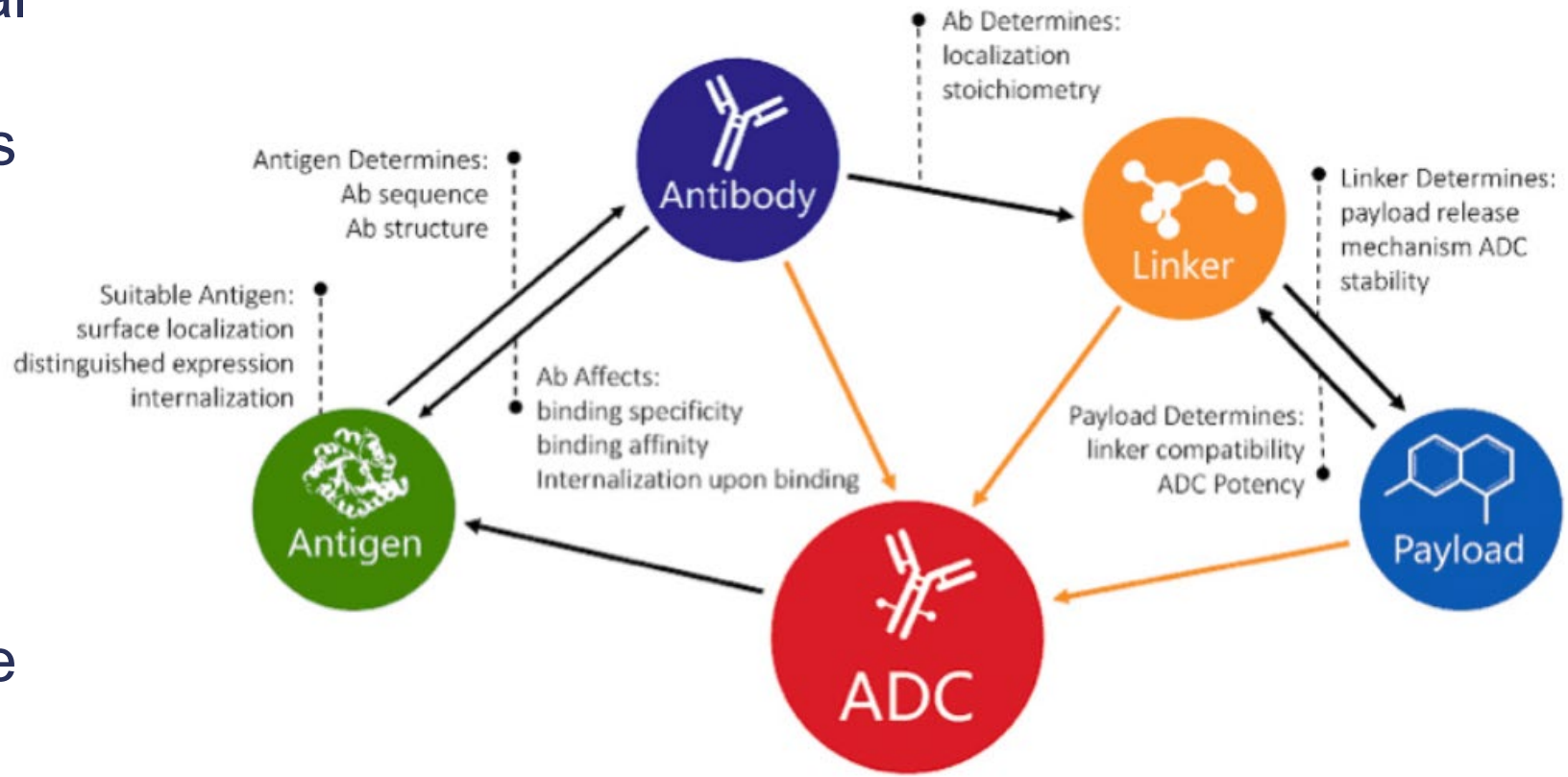


[a]Difference in ORR; 95% CI with Hauck–Anderson continuity correction

Pujade-Lauraine E, et al. *J Clin Oncol*. 2014;32(13):1302-1308.

Antibody Drug Conjugates: A Paradigm Shift

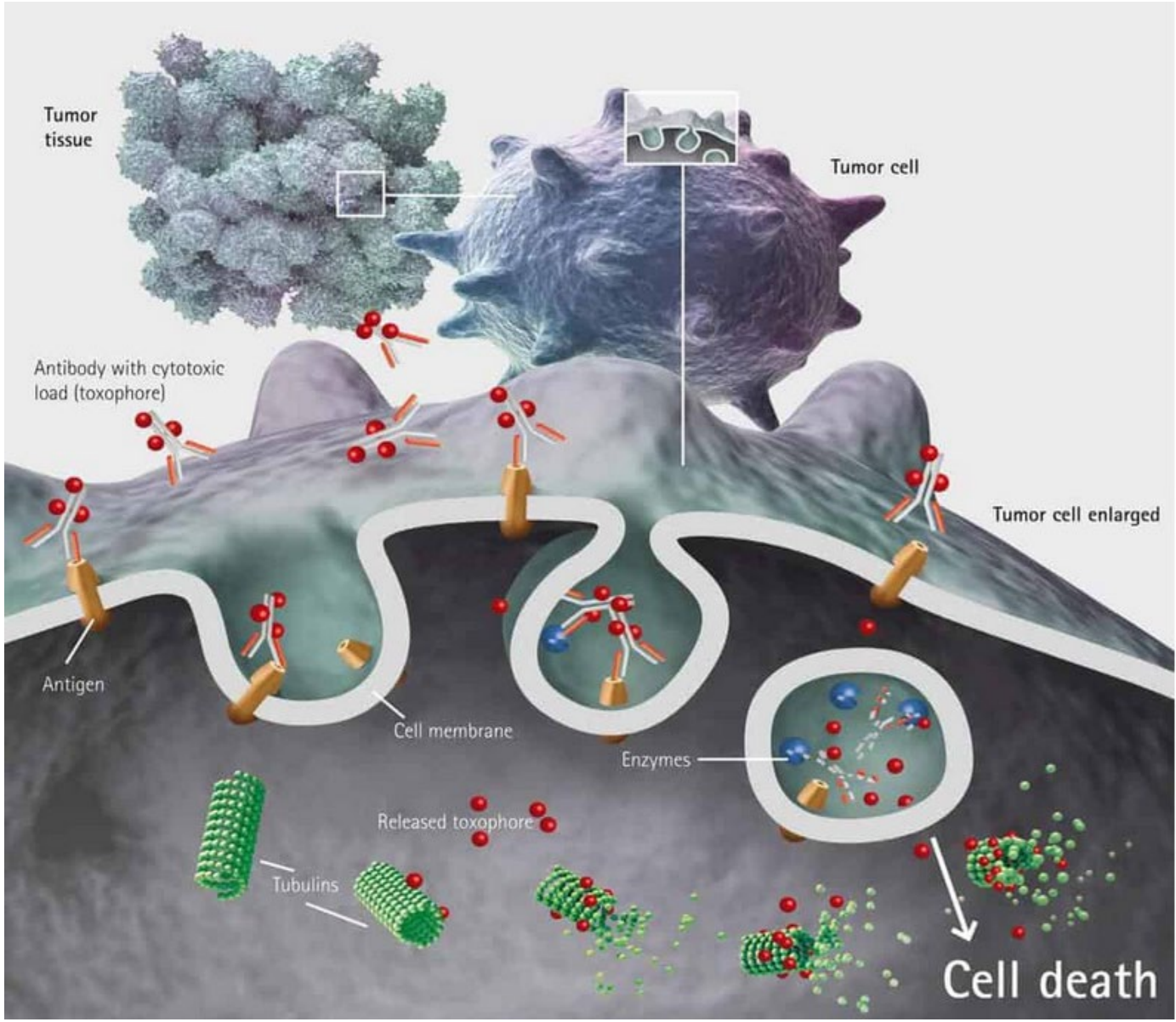
- Highly selective monoclonal antibodies (mAb) tumor associated antigen that has limited, to no exposure, on normal cells
- A potent cytotoxic
- A linker that is stable in circulation, but releases the cytotoxic in the target cell



https://www.adcreview.com/the-review/antibody-drug-conjugate-development/

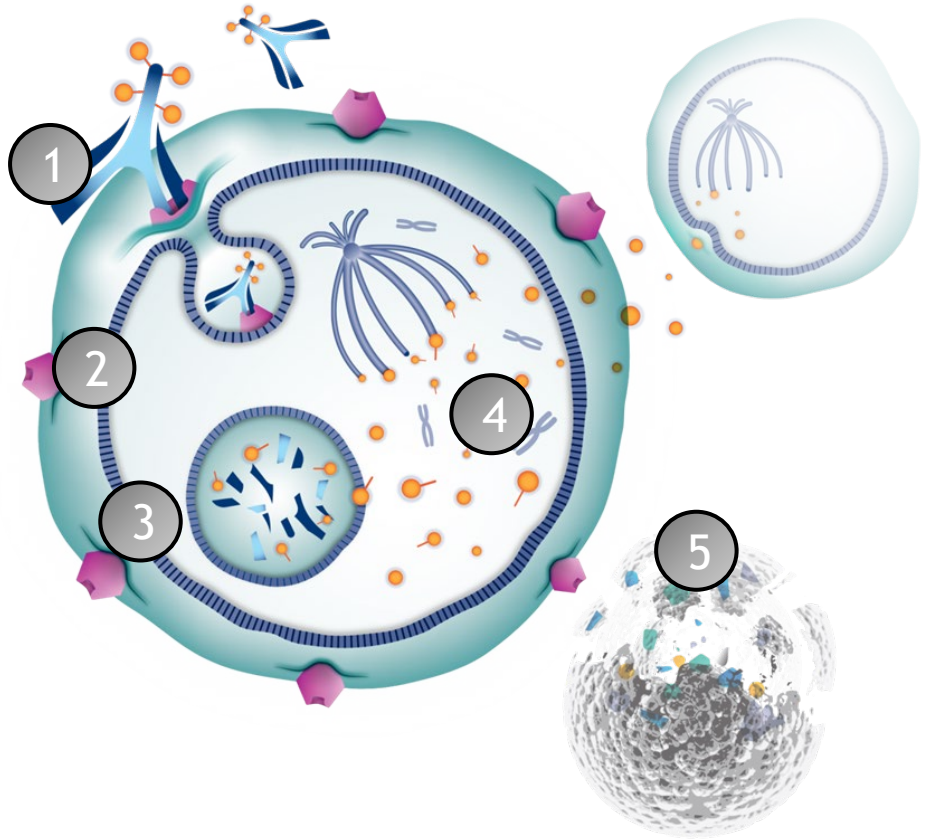
Mechanism of Action:

- ADC localizes to tumor and binds to target antigen
- ADC is internalized
- Internalized vesicles fuse with other vesicles and enter the endosome-lysosome pathway
- Proteases digest the antibody to release the toxins which → apoptosis



https://www.adcreview.com/the-review/antibody-drug-conjugate-development/

Mirvetuximab Soravtansine (MIRV)



- Antibody portion of MIRV binds to FRα found on the surface of epithelial ovarian cancer cells
- MIRV is internalized via endocytosis
- MIRV is degraded within the lysosome to release its cytotoxic payload (DM4)
- DM4 disrupts tubulin resulting in mitotic arrest and apoptosis
- DM4 also diffuses through the lipophilic cell membrane allowing bystander killing on adjacent tumor cells

O'Malley DM & Calo CA. *Curr Oncol Rep*. 2021;23(89). doi: 10.1007/s11912-021-01080-4.

Phase III SORAYA Study of Mirvetuximab Soravtansine: Efficacy Summary

Outcome	Investigator Assessed N=105 (%)	BICR-Assessed N=95 (%)
ORR, n (%) (95% CI)	34 (32.4) (23.6-42.2)	30 (31.6) (22.4-41.9)
Best overall response, n%		
• CR	5 (4.8)	5 (5.3)
• PR	29 (27.6)	25(26.3)
• SD	48 (45.7)	53 (55.8)
• PD	20 (19.0)	8 (8.4)
• Not evaluable	3 (2.9)	4 (4.2)
Median DoR, mo (95% CI)	6.9 (5.6-8.1)	11.7 (5.0-NR)
Median PFS, mo (95% CI)	4.3 (3.7-5.1)	5.5 (3.8-6.9)

- Clinically meaningful activity seen in patients with FRα-high platinum-resistant OC
- Consistent antitumor activity regardless of prior number of therapies, or prior PARPi
  - **ORR if 1-2 lines of therapy:** 35.3% (range: 22.4-49.9)
  - **ORR if 3 lines of therapy:** 30.2% (range: 18.3%-44.3%)
  - **ORR if prior exposure to PARPi (yes vs no):** 38.0% (range: 24.7%-52.8%) vs 27.5% (range: 15.9%-41.7%)
- Overall median DoR and by prior PARPi were comparable between those with 1-2 prior lines vs. 3 prior lines

Matulonis. SGO 2022. Abstr 242.

Phase III SORAYA Study | MIRV | Safety Summary

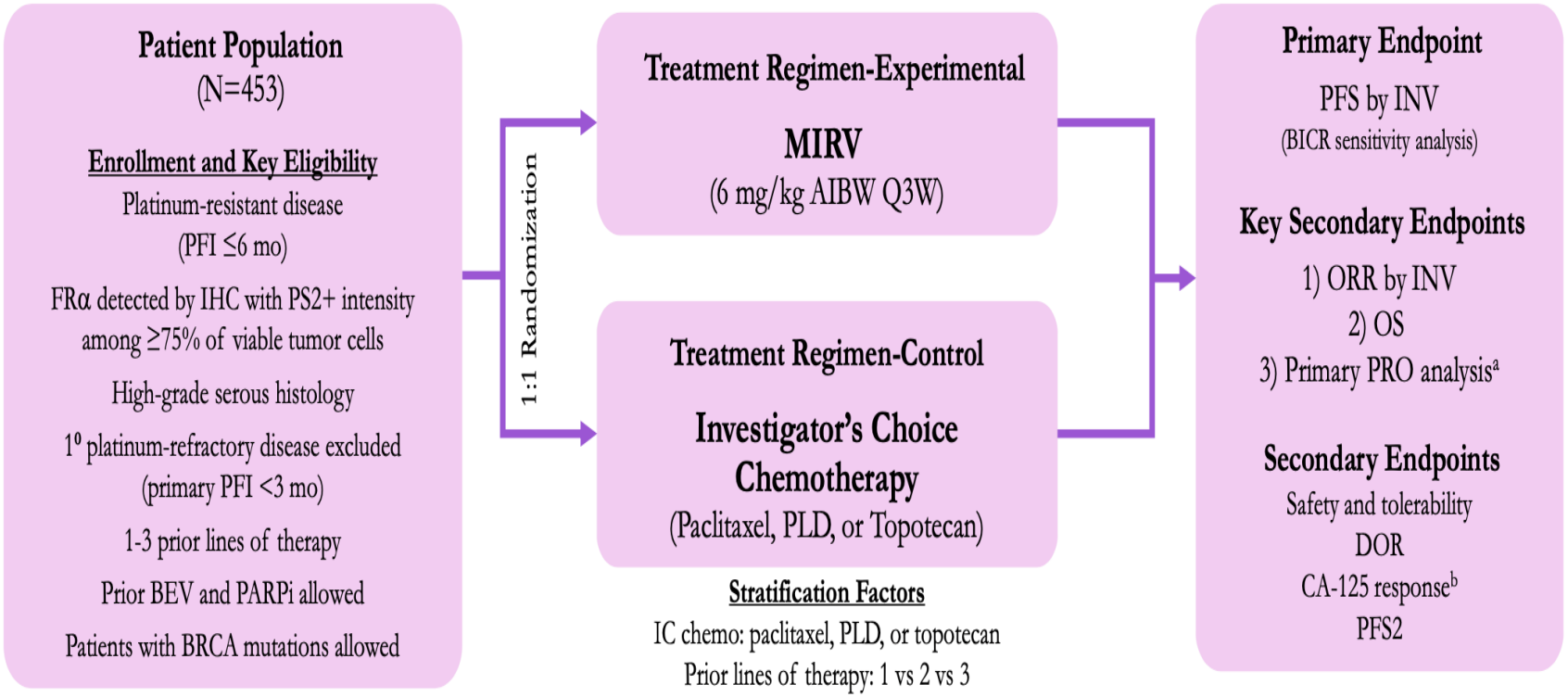
TRAE, n (%)	Any Grade	Grade 3	Grade 4
Pts with any event	91 (86)	29 (27)	1 (1)
Blurred vision	43 (41)	6 (6)	0 (0)
Keratopathy	38 (36)	8 (8)	1 (1)
Nausea	31 (29)	0 (0)	0 (0)
Dry eye	24 (23)	2 (2)	0 (0)
Fatigue	24 (23)	1 (1)	0 (0)
Diarrhea	23 (22)	2 (2)	0 (0)
Asthenia	16 (15)	1 (1)	0 (0)
Photophobia	15 (14)	0 (0)	0 (0)
Peripheral neuropathy	13 (12)	0 (0)	0 (0)
Decreased appetite	13 (12)	1 (1)	0 (0)
Vomiting	12 (11)	0 (0)	0 (0)
Neutropenia	11 (10)	1 (1)	0 (0)

- Most ocular and GI AEs low-grade and reversible
- Grade ≥3 TRAEs: 8%
  - Dose delay: 32%
  - Dose reduction: 19%
  - Discontinuation: 7%
- One death possibly related to study drug
  - Respiratory failure
  - Autopsy: no evidence of drug reaction; lung mets
- No appreciable myelosuppression and limited low-grade neuropathy

Matulonis. SGO 2022. Abstr 242.

MIRASOL Phase III Trial: Platinum Resistant Ovarian Cancer

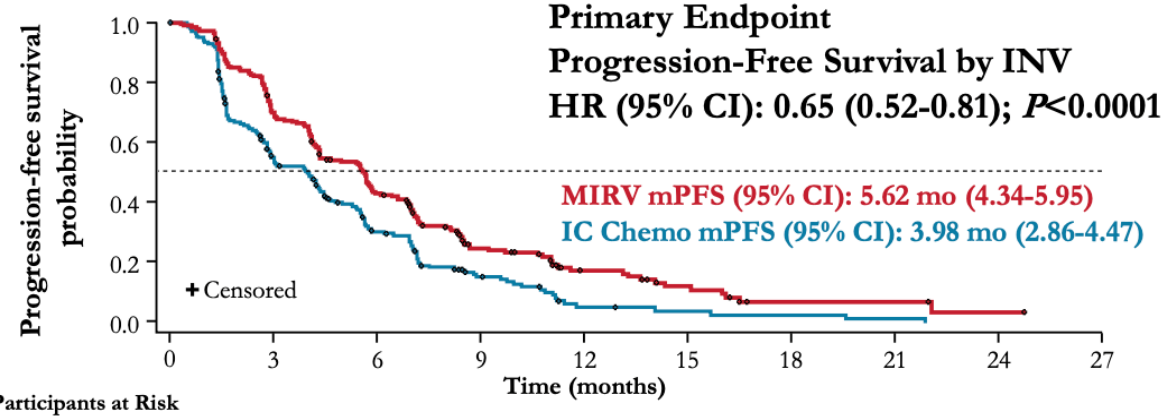
An open-label, phase 3 randomized trial of MIRV vs investigator's choice chemotherapy in patients with FRα-high platinum-resistant ovarian cancer

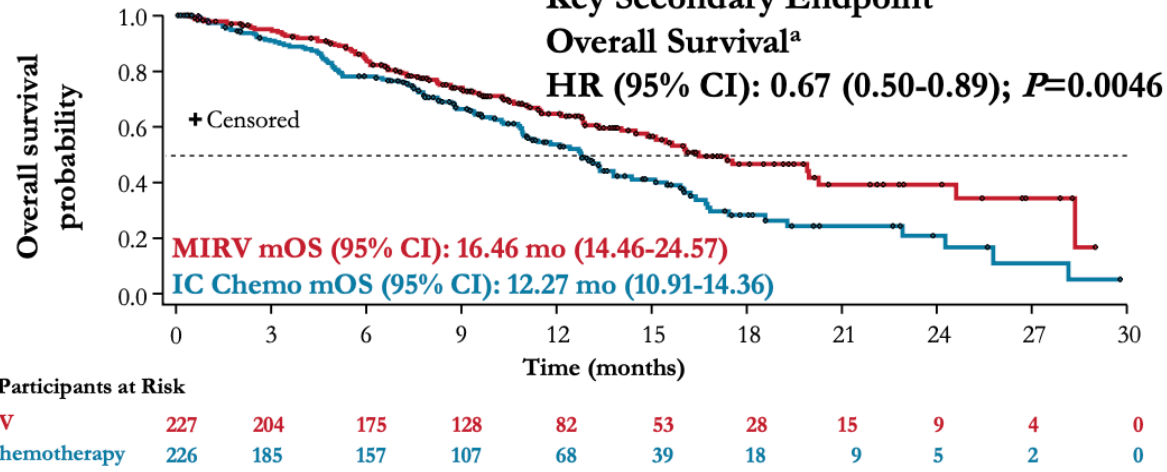


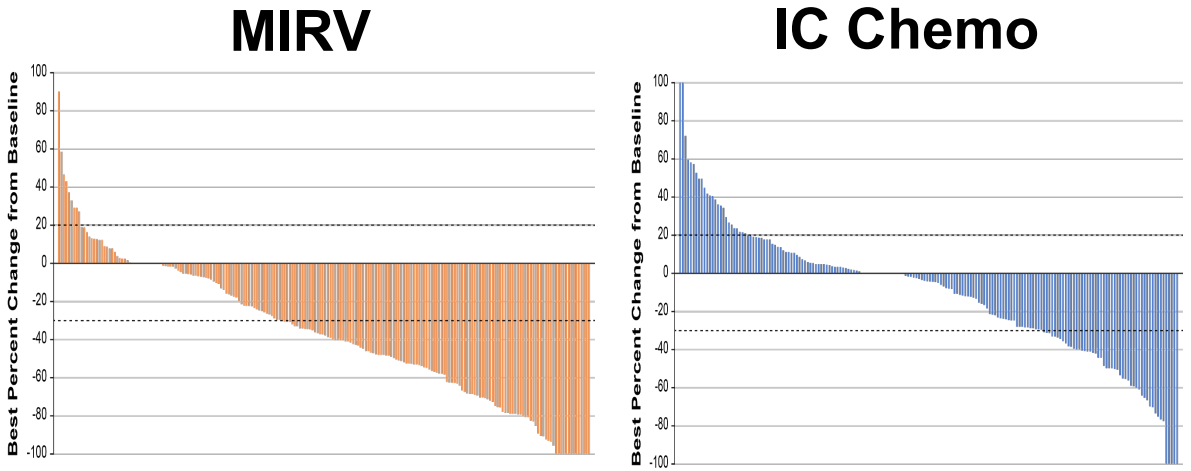
- The primary PRO assessment in MIRASOL (a prespecified key secondary endpoint) evaluated improvements in OV28 Abdominal/GI subscale score from baseline at Week 8/9, with a **conservative improvement threshold** of 15-point[a] decrease
- Anchor-based analyses were performed to further evaluate meaningful change thresholds in abdominal/GI symptoms
- All PROs were assessed at screening and on day 1 of every treatment cycle
  - Upon discontinuation and end of treatment, PRO assessment visit took place within 7 days

Moore KN, et al. *New Engl J Med*. 2023;389:2162-2174. doi:10.1056/NEJMoa2309169.;
Konecny GE, et al. Presented at: Society of Gynecologic Oncology's (SGO) Annual Meeting on Women's Cancer; 18-21 March 2022; Phoenix, AZ USA.

MIRASOL Phase III Trial: PROC *cont.*







Key Secondary Endpoint: Objective Response Rate by INV

	MIRV (n=227)	IC Chemotherapy (n=226)
ORR by INV, (%)[b] n (95% CI)	42.3% 96 (35.8-49.0)	15.9% 36 (11.4-21.4)
ORR Difference (95% CI), 26.4% (18.4-34.4)		
Odds Ratio (95% CI), 3.81 (2.44-5.94)		
P<0.0001		

Moore KN, et al. *New Engl J Med*. 2023;389:2162-2174. doi:10.1056/NEJMoa2309169.; Konecny GE, et al. Presented at: Society of Gynecologic Oncology's (SGO) Annual Meeting on Women's Cancer; 18-21 March 2022; Phoenix, AZ USA.

Plenty of Payloads: Multiple ADCs Are Approved, and Others Are Being Actively Evaluated

ADC	Target	Antibody	Linker	Payload	Regulatory Status
Tisotumab vedotin[1] (TV)	Tissue factor	IgG1-κ	Cleavable	MAME	**Cervical:** Accelerated FDA approval; FDA full approval Apr 29, 2024
Mirvetuximab soravtansine[2] (MIRV)	FRα	IgG1-κ	Cleavable	DM4	**Ovarian:** Accelerated FDA approval; FDA prior full approval Mar 22, 2024
Trastuzumab deruxtecan[3] (T-DXd)	HER2	IgG1	Cleavable	Topoisomerase I inhibitor	**HER2 IHC3+ tumor agnostic:** Accelerated FDA approval Apr 5, 2024

Other transmembrane glycoproteins are highly expressed in gynecologic tumors, often associated with poor prognosis, and under study as ADC targets

TROP2 **B7-H4** **CDH6** **Mesothelin**

1. https://www.fda.gov/drugs/resources-information-approved-drugs/fda-approves-tisotumab-vedotin-tftv-recurrent-or-metastatic-cervical-cancer. 2. https://www.fda.gov/drugs/resources-information-approved-drugs/fda-approves-mirvetuximab-soravtansine-gynx-fra-positive-platinum-resistant-epithelial-ovarian. 3. https://www.fda.gov/drugs/resources-information-approved-drugs/fda-grants-accelerated-approval-fam-trastuzumab-deruxtecan-nxki-unresectable-or-metastatic-her2. 4. Drago JZ, et al. *Nat Rev Clin Oncol.* 2021;18(6):327-344; doi:10.1038/s41571-021-00470-8.

Summary of Additional ADCs in Development: Ovarian

ADC Asset	Target	Dev. Stage	Payload | MOA | DAR	Key Studies / Data	Upcoming Milestones

AZD5335	**FRα**	**PI/II**	**AZ-14170132 | TOP1i | ~8**	Results from PI/II FONTANA (PROC cohort, among patients expressing FRα TPS ≥25% PS1+):
				• ORR (n=38): 34.2% (dose escalation)
				  ○ FRα-high: TPS ≥75% PS2+ (n=13): 46.2%
				  ○ FRα-low: TPS ≥25% PS1+ but outside of TPS ≥75% PS2+ (n=14): 35.7%
					AZ has communicated 2025+ trial readout, timing of module 1 Part B dose optimization data unclear (though dose escalation is still ongoing)

BAT8006	**FRα**	**PII *(not yet recruiting)***	**Exatecan | TOP1i | ~8**	Results from PI NCT05378737 (BAT8006 in PROC) in patients by FRα status: • ORR: All FRα (n=54): 37.0%; FRα<50% (n=21): 33.3%; FRα≥50% (n=33): 39.4%; FRα≥75% (n=15): 46.7%	PI/II PROC trial posted on ct.gov (NCT06545617) is not yet enrolling (n=170, PCD: 3/2026)
Farletuzumab Ecteribulin (FZEC)	**FRα**	**PII**	**Eribulin | TOP1i | ~4**	Results from PII NCT03386942 (FZEC in PROC) in patients with "FRα-positive" PROC (>5% cells stained at 1+, 2+, or 3+ intensity level by IHC): • ORR at 0.9 mg/kg (n=24): 25.0%; 1.2 mg/kg (n=21): 52.4%	Currently being evaluated in a non-registrational PII trial vs. chemo in PROC with US sites (n=90, PCD: 6/2024); future registrational development of FZEC unclear after BMS pulled out of Eisai collaboration in July 2024
TUB-040	**NaPi2b**	**PI/II**	**Exatecan | TOP1i | ~8**	*No OC data available*	Received FDA FTD in PROC; first US patient dosed in PI/IIa NAPISTAR-01 trial in 6/2024 (FIH trial evaluating TUB-040 in PROC and NSCLC)
TORL-1-23	**CLDN6**	**PII (planned)**	**MMAE | MTi | ~4.1**	Results from the PI FIH trial NCT05103683 among CLDN6+ PROC patients • ORR at <2.4 mg/kg: 30% • ORR at 2.4 mg/kg (n=8): 50% • ORR at 3.0 mg/kg (n=12): 42%	ESMO 2024 presenter concluded that a registrational in PII CLDN6+ PROC is planned
BNT325 / DB-1305	**TROP2**	**PI/II**	**P1021 | TOP1i | ~4**	Results from the PI/II FIH trial NCT05438329 (BNT325 monotherapy in n=44 solid tumors, including n=2 OC): • ORR (n=23): 30.4%	FDA FTD for 2-4L PROC (Jan 2024); currently being evaluated in a PI/II trial with OC cohorts (NCT05438329) in monotherapy and combined with BNT327 (PD-L1xVEGF-A bsAb); next trial update expected in 2025
RC88	**MSLN**	**PII**	**MMAE | MTi | ~4**	Among n=31 efficacy-evaluable 2-4L recurrent MSLN IHC1+ and above OC patients receiving RC88 monotherapy at 2.0mg/kg in a PI/II basket trial: • ORR: 45.2% (cORR: 41.9%) • mDOR = 8.02 mo	FDA FTD and IND clearance in PROC; ongoing PII in PROC (NCT06173037) with no ex-China sites currently listed (n=88, PCD: 6/2026)

The results presented in this slide should be interpreted individually and not as a direct comparison between different studies. Each study has unique methodologies, sample sizes, and contexts that may influence the outcomes.

Summary of Additional ADCs in Development: Ovarian *cont.*

AZD5335
- Shapira-Frommer et al., ESMO 754P, 2024 (https://oncologypro.esmo.org/meeting-resources/esmo-congress-2024/initial-results-from-a- first-in-human-study-of-azd5335-a-folate-receptor-a-fra-targeted-antibody-drug-conjugate-in-patients-pts-with-platinum)

BAT8006
- Jia et al., ASCO Abs 5550, 2024 (https://www.bio-thera.com/uploads/allimg/240604/3-240604200942P7.pdf)

FZEC
- Nishio et al., ASCO Abs 5513, 2022 (https://www.eisai.com/news/2022/news202245.html)

TUB-040
- Tubulis June 2024 Press Release (https://tubulis.com/news/tubulis-receives-fda-fast-track-designation-for-antibody-drug-conjugate-candidate- tub-040-in-platinum-resistant-ovarian-cancer/)

TORL-1-23
- Konency et al., ESMO 721MO, 2024 (https://oncologypro.esmo.org/meeting-resources/esmo-congress-2024/phase-i-two-part-multicenter- first-in-human-fih-study-of-torl-1-23-a-novel-claudin-6-cldn6-targeting-antibody-drug-conjugate-adc-in-patien)

BNT325/DB-1305
- Marathe et al., ESMO 689P, 2023 (https://investors.biontech.de/system/files-encrypted/nasdaq_kms/assets/2023/10/26/10-55-13/ESMO%202023_BNTX%20data_external%20slide%20deck.pdf)

RC88
- Liu et al., ASCO Abs 5551, 2024 (https://ascopubs.org/doi/10.1200/JCO.2024.42.16_suppl.5551)

Target	Name	Payload	Payload	DAR	Linker	Development stage
HER2	Trastuzumab deruxtecan	Topo1i	deruxtecan	8	Cleavable	Phase II – FDA acc appr
	DB-1303 (BNT323)	Topo1i	P1003	8	Cleavable	Phase I/IIA – FDA BTD
	Trastuzumab duocarmazine	DNA alkylating	duocarmazine	2.8	Cleavable	Phase II
	Disitamab vedotin (RC48)	Anti-microtubule	MMAE	4	Cleavable	Phase II
FRα	Mirvetuximab soravtansine	Anti-microtubule	DM4	3.5	Cleavable	Phase II
	Luveltamab tazevibulin (STRO-002)	Anti-microtubule	SC209	4	Cleavable	Phase I/IIA
	Rinatabart sesutecan (Rina-S, PRO1184)	Topo1i	exatecan	8	Cleavable	Phase I/II
	IMGN151	Anti-microtubule	DM21	3.5	Cleavable	Phase I
TROP2	Sacituzumab govitecan (IMMU-132)	Topo1i	SN38	7.6	Cleavable	Phase II
	Sacituzumab tirumotecan (MK-2870)	Topo1i	tirumotecan	7.4	Cleavable	Phase III
	Datopotamab deruxtecan (DS-1062)	Topo1i	deruxtecan	4	Cleavable	Phase II
	LCB84	Anti-microtubule	MMAE	4	Cleavable	Phase I/II
B7-H4	SGN-B7H4V	Anti-microtubule	MMAE	4	Cleavable	Phase I
	HS-20089	Topo1i	undisclosed	6	Cleavable	Phase II
	XMT-1660	Anti-microtubule	MMAF	6	Cleavable	Phase I
	AZD8205	Topo1i	AZ14170133	8	Cleavable	Phase I/IIA
B7-H3	Ifinatamab veruxtecan (DS-7300a)	Topo1i	deruxtecan	4	Cleavable	Phase I
TF	Tisotumab vedotin	Anti-microtubule	MMAE	4	Cleavable	Phase II
	XB002	Anti-microtubule	MMAE	3.3	Cleavable	Phase I
AXL	Enapotamab vedotin	Anti-microtubule	MMAE	4	Cleavable	Phase I/II
Claudin6	TORL-1–23	Anti-microtubule	MMAE	?	Cleavable	Phase I

Slide courtesy of Toon van Gorp, MD

GOG Partners Phase 2/3 Portfolio: PROC

	Trial	Phase	Regimen	Prior total lines	Prior total lines for PROC	Tumor Testing/ Prevalence
Taxanes	GOG-3073 (ROSELLA)	3	Nab Paclitaxel+/- relacorliant Completed	3	<3	No
ADCs	GOG-3086 (REFRaME-01)	2/3	Luveltamab tazevibulin (luvelta) versus SOC	1-3	ND	Frα
	GOG-3096 (REJOICE)	2/3	Raludotatug Deruxtecan (R-DXd) versus SOC	1-3	ND	Yes
	GOG-3107 (RAINFOL)	3	(Rina-S) versus SOC	1-5	ND	Yes
IO therapy	GOG-3063 (ARTISTRY 7)	3	Nemvaleukin + pembrolizumab vs Per Completed Nemvaleukin vs Investigator Choice c	Unlimited (prior bev requ)	<6	No
	GOG-3076 (OnPrime)	3	Olvi-Vec followed by platinum doublet + bev vs. IC chemo	≥3	ND	No
	GOG-3081 (PRESERVE-004)	2	ONC-392 (CTL A4) + Pembro in PROC Completed	1-3	ND	No
	GOG-3084 (SURPASS-3)	2	RPh2 of MAGE directed SPEAR T cell Closed	1-4	ND	Yes
Targeting DDR/PARPi resistance	GOG-3066 (DENALI)	2	Durvalumab/Olaparib/Cediranib vs Olaparib/Cediranib vs Durvalumab/cediranib vs Investigator Choice chemotherapy	5 (prior bev req)		No
	GOG-3067 (MAMMOTH)	2	Olaparib + copanlisib vs Investigator Choice chemotherapy (PARPi resistant)	Unlimited (prior bev req)	≤2	No
	GOG-3072 (ZN-c3-002)	2	ZN-c3 (wee-1) as monotx and in combo			+/-
	GOG-3082 (ACR-368-201)	1b/2	ACR-368 (CHK1/2) + gemcitabine in PROC	1-4	ND	Yes

Evaluating New Opportunities in Ovarian Cancer Beyond ADCs

Dr. Nicoletta Colombo

Chair, Ovarian Cancer Centre at European Institute of Oncology (IEO)

Milan, Italy

Platinum Resistant Ovarian Cancer: Current Strategies

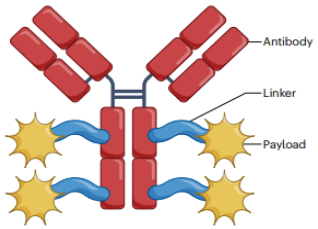
ADCs

MIRVETUXIMAB-SORAVTANSINE [2]

FARLETUZUMAB-ECTERIBULIN [3]

TRASTUZUMAB-DERUXTECAN [4]

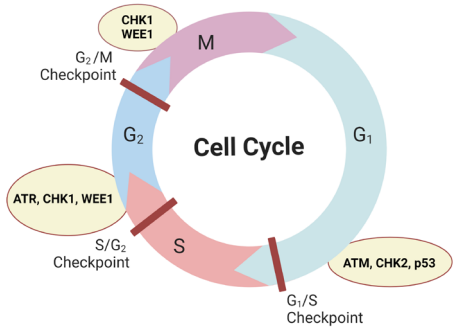
RALUDOTATUG-DERUXTECAN [5]



CELL CYCLE REGULATION AND DNA REPAIR

ADAVOSERTIB [6]

azenosertib[7]

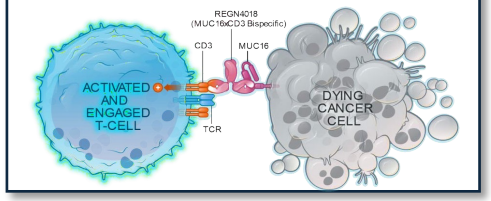


IMMUNOTHERAPY WITH NOVEL AGENTS

NEMVALEUKIN [9]

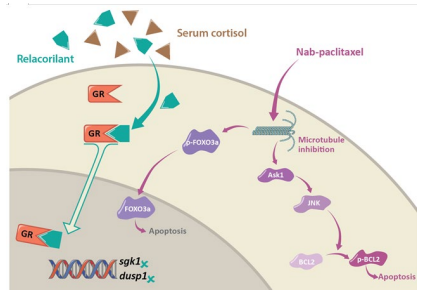
UBAMATAMAB [10]

ADOPTIVE CELL THERAPY



GLUCOCORTICOID RECEPTOR

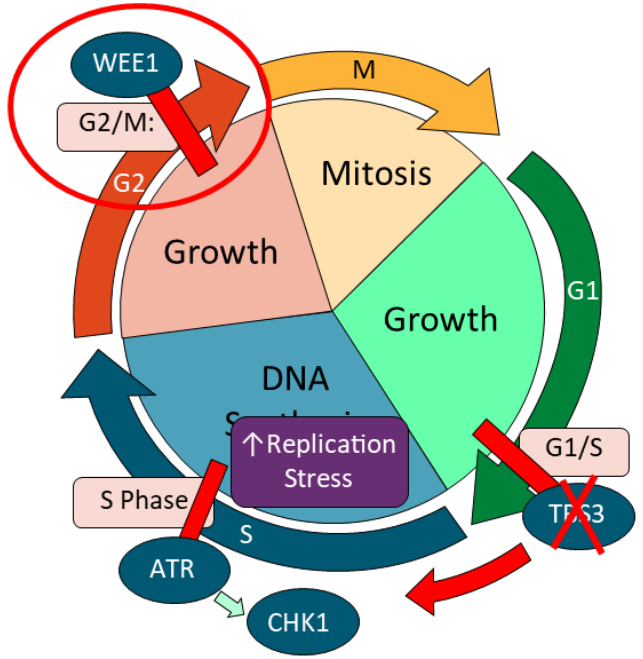
RELACORILANT [1]



[1] [NCT05257408 – Rosella]; [NCT03776812 – phase II]; [2] [NCT04296890 – Soraya] [NCT04209855 – Mirasol]; [3] [NCT05613088]; [4] [NCT04482309]; [5] [NCT04707248]; [6] [NCT03579316]; [7] [NCT02595892]; [8] [NCT04729387]; [9] [NCT05092360]; [10] [NCT03564340]

Targeting G2-M Checkpoint: Adavosertib

- Upon DNA damage, cell cycle checkpoints are activated, forcing cell cycle arrest
  - ✓ Cell cycle arrest allows for appropriate DNA replication by preventing progression to mitosis with damaged DNA
- **WEE1:** key regulator of the intra-S and G2/M cell cycle checkpoint, which is important to induce cell cycle arrest during DNA repair[1,2]
  - ✓ Loss of p53 function, which controls the G1/S cell cycle checkpoint, increases dependence on the G2/M checkpoint
  - ✓ Leads to early entry into S phase
  - ✓ Increases replication stress
- **Adavosertib:** oral small-molecule inhibitor of WEE1 has demonstrated activity alone and in combination with olaparib in PARPi-resistant preclinical models[3]

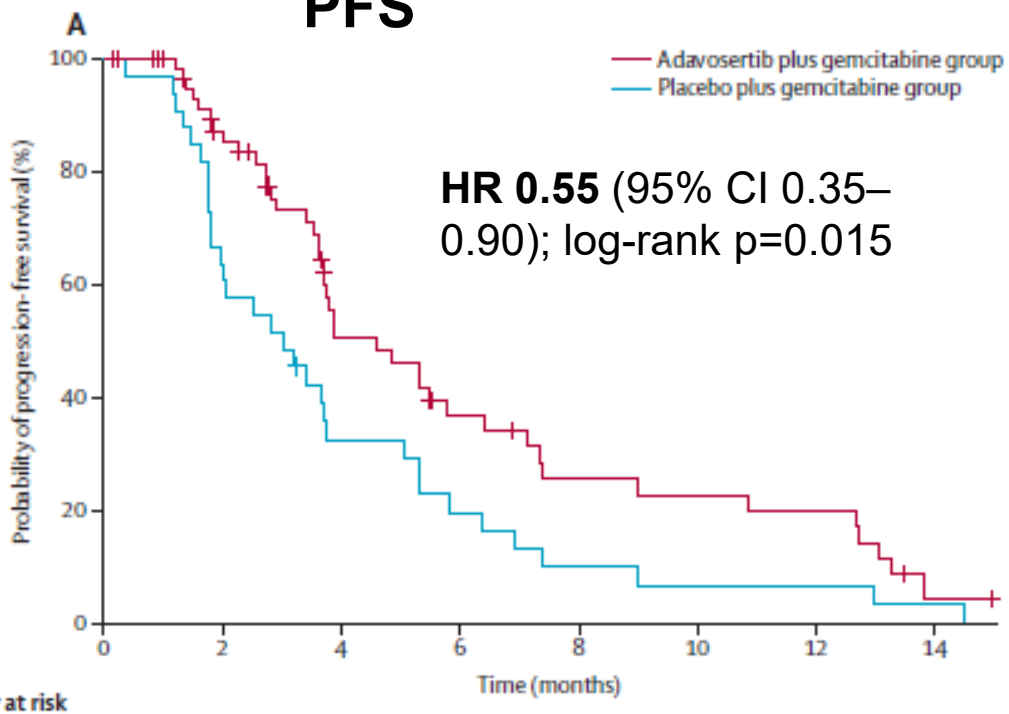


WEE1 inhibition leads to dysregulation of G2M checkpoint and to mitotic catastrophe

1. Ghelli. *J Hematol Oncol.* 2020;13:126. 2. Barnum. *Methods Mol Biol.* 2014; 1170:29. 3. Lallo. *Clin Cancer Res.* 2018;24:5153.

Adavosertib Plus Gemcitabine for Platinum-Resistant or Platinum-Refractory Recurrent Ovarian Cancer: A Double-Blind, Randomised, Placebo-Controlled, Ph2 Trial

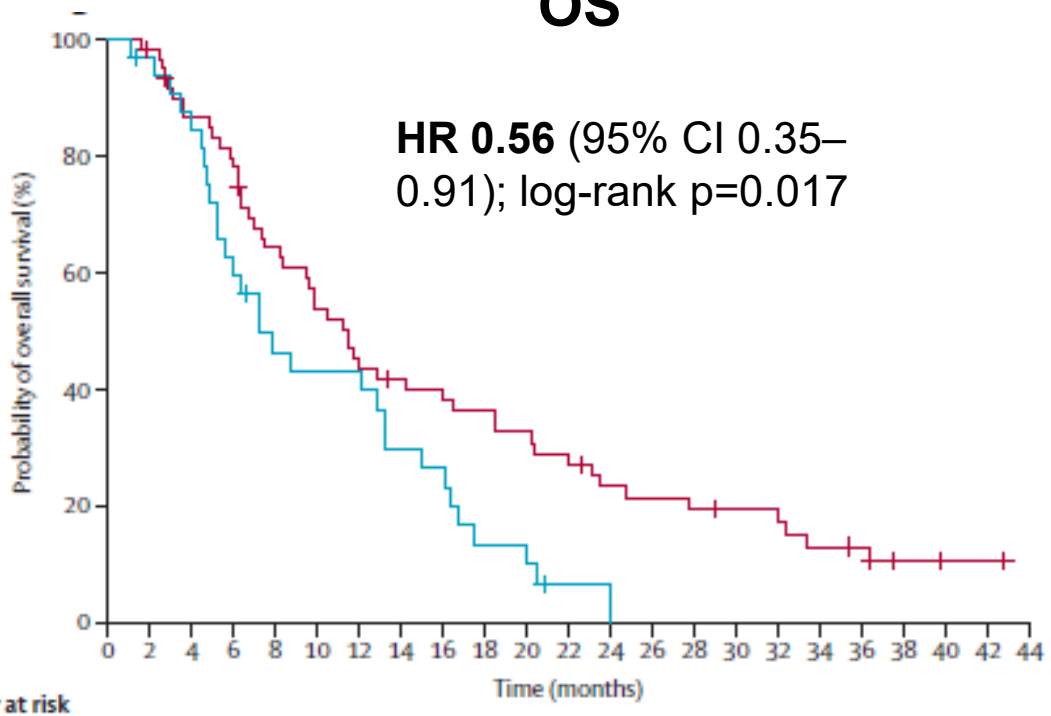
PFS



HR 0.55 (95% CI 0.35–0.90); log-rank p=0.015

Number at risk (number censored)								
Adavosertib plus gemcitabine group	61 (0)	46 (8)	22 (15)	14 (17)	9 (18)	8 (18)	7 (18)	1 (19)
Placebo plus gemcitabine group	33 (0)	21 (0)	10 (1)	6 (1)	3 (1)	2 (1)	2 (1)	1 (1)

OS



HR 0.56 (95% CI 0.35–0.91); log-rank p=0.017

Number at risk number censored)																							
Adavosertib plus gemcitabine group	61 (0)	59 (1)	51 (2)	46 (2)	37 (3)	31 (3)	25 (3)	23 (4)	21 (4)	20 (4)	18 (4)	15 (4)	12 (5)	11 (5)	10 (5)	9 (6)	9 (6)	6 (6)	5 (7)	2 (9)	1 (10)	1 (10)	0 (11)
Placebo plus gemcitabine group	33 (0)	31 (1)	27 (1)	19 (1)	14 (2)	13 (2)	13 (2)	9 (2)	8 (2)	4 (2)	3 (3)	1 (3)	0 (3)	0 (3)	0 (3)	0 (3)	0 (3)	0 (3)	0 (3)	0 (3)	0 (3)	0 (3)	0 (3)

Lheureux S, et al. *Lancet.* 2021;397:281–292

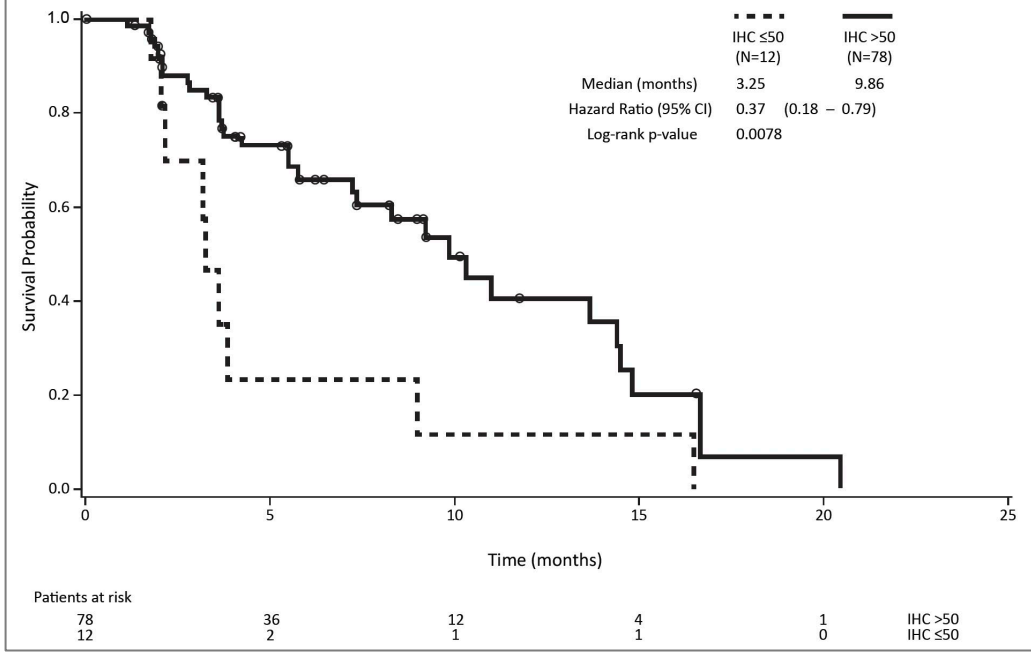
GOG-3072/ZN-c3-002: Azenosertib (ZN-c3) Plus Chemo in PROC

Correlation with CCNE1 expression

Table 4: Objective Responses by Cyclin E1 IHC-Status

Endpoints	Azenosertib + Paclitaxel	Azenosertib + Carboplatin	Azenosertib + Gemcitabine	Azenosertib + PLD	Total
Response Evaluable with IHC (N) *	19	22	13	28	82
Overall Response Rate, n (%)	10 (52.6)	8 (36.4)	5 (38.5)	6 (21.4)	29 (35.4)
Response Evaluable IHC H-Score >50 (N)	19	18	11	22	70
Overall Response Rate, n (%)	10 (52.6)	8 (44.4)	5 (45.5)	5 (22.7)	40 %
Response Evaluable IHC H-Score ≤50 (N)	0	4	2	6	12
Overall Response Rate, n (%)	NA	0	0	1 (16.7)	8 %

Figure 8: Kaplan-Meier Curve of Progression-Free Survival by Cyclin E1 IHC-Status



In collaboration with: GOG FOUNDATION® *Transforming the standard of care™*

Study PI: Premal Thaker, MD
NCT04516447

Immune Checkpoint Inhibitors in Ovarian Cancer: Phase 3 Evidence

1st-Line

- JAVELIN-100 (Avelu
- IMAgyn050 (Atezo
- DUO-O (Durva
- ATHENA Combo (Nivo)
- FIRST (Dosta
- KEYLINK 001 (Pemb

„Platin-sensitive“

- ATALANTE (Atezo
- ANITA (Atezo

„Platin-resistant“

- JAVELIN-200 (Avelu
- NRG GY 009 (Atezo
- AGO OVAR 2.29 (Atezo)

CHT + IO + Bev X

- KEYNOTE-B96 (Pembro) CHT + IO ± Bev ?

No clinically meaningful activity of Immune Checkpoint Inhibitors

Irrespective of:

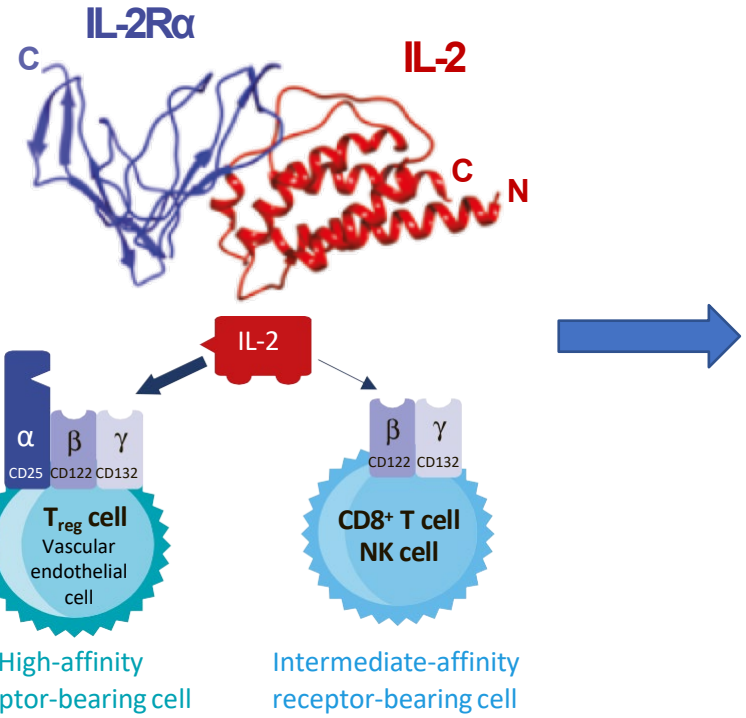
- line of treatment
- Combination (Bev & PARPi)

Data of 3 phase 3 trials still awaited

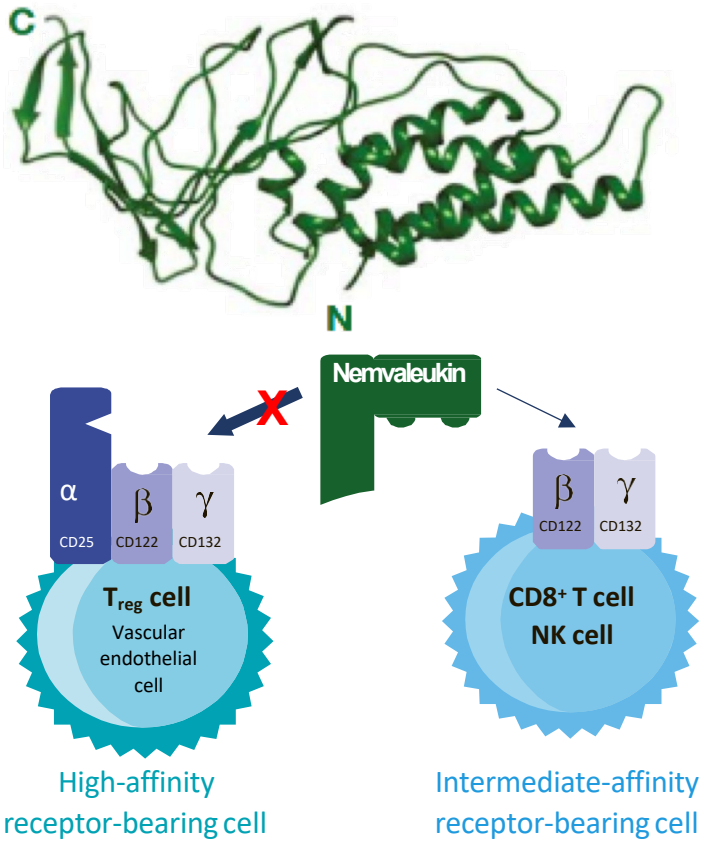
Slide Courtesy of Frederik Marmé

Bogani G, et al. *Gyn Oncol.* 2025;193:30-40. doi:10.1016/j.ygyno.2024.12.011.

Novel Agents: Nemvaleukin Alfa is a Novel, Engineered Cytokine



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

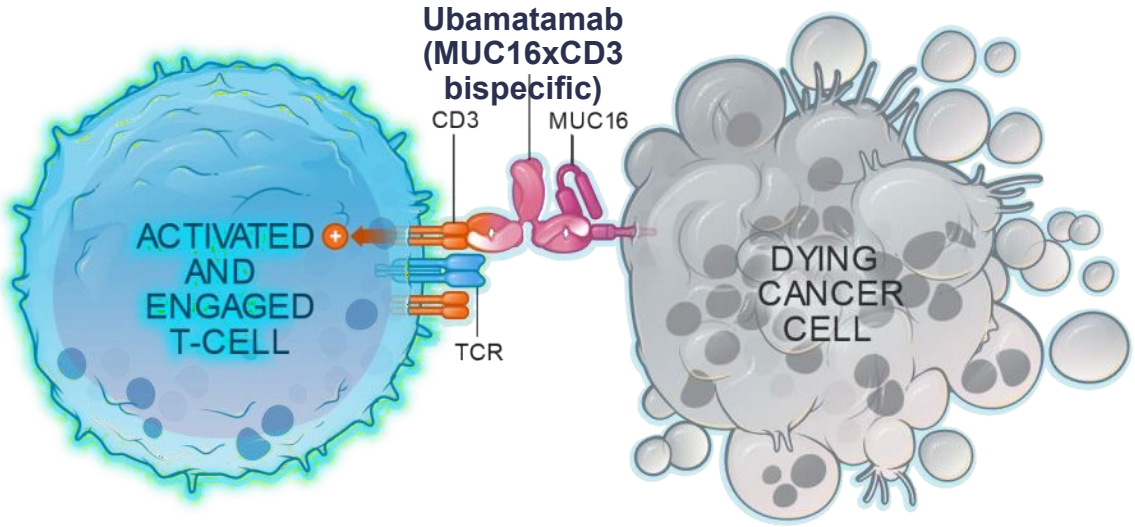


Nemvaleukin

- Stable fusion protein designed to harness the validated IL-2 pathway biology
- Intrinsically active immediately upon systemic entry; does not degrade into native IL-2
- Designed to selectively bind the intermediate-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
- Leads to increases in both peripheral and intratumoral immune effector cells

IL-2, interleukin-2; IL-2R, IL-2 receptor; NK, natural killer; T_{reg}, regulatory T cell. Lopes JE, et al. *J Immunother Cancer*. 2020;8(1):e000673.

Ubamatamab (REGN4018) in Advanced OC

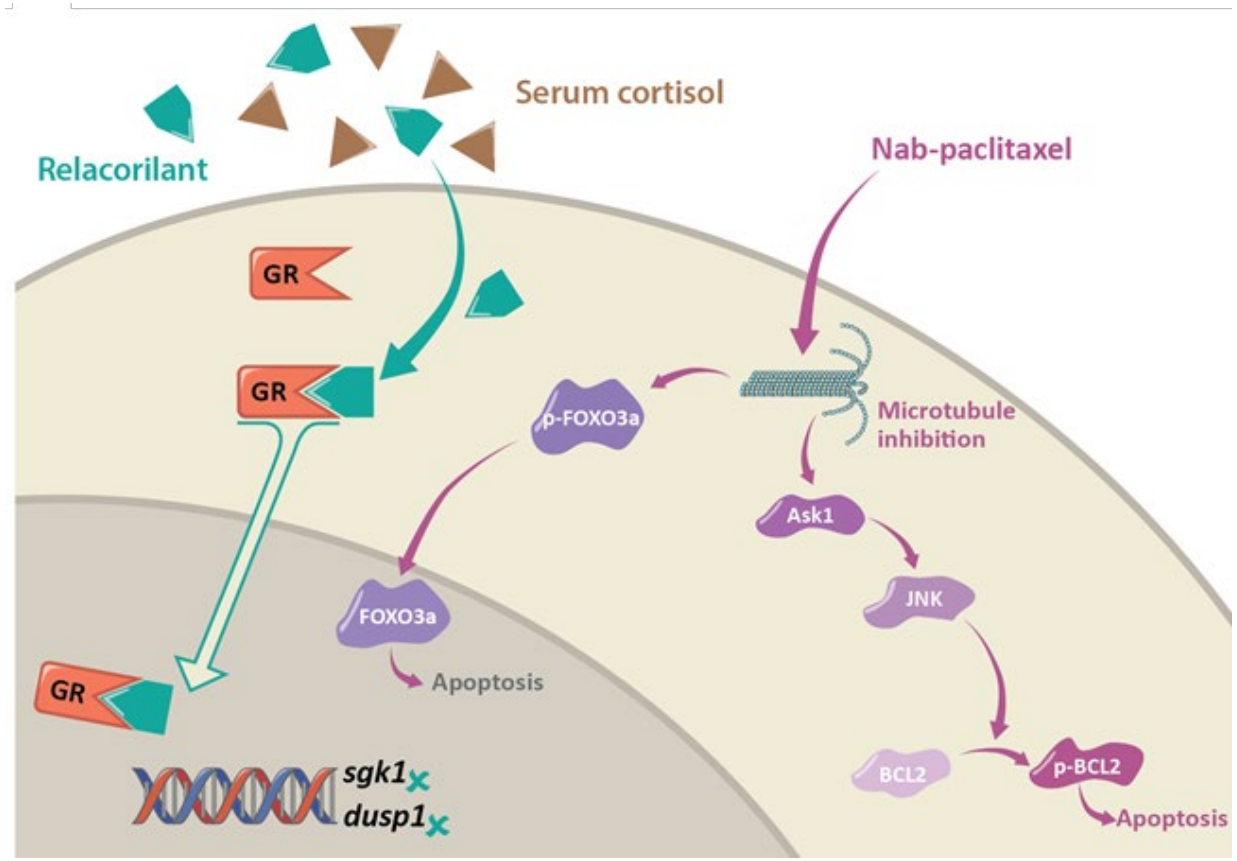


- Ubamatamab is a human bispecific antibody, developed using VelocImmune technology
- Ubamatamab is designed to bridge MUC16 on cancer cells with CD3-expressing T cells to facilitate T-cell activation and cytotoxicity[4]
- In immune-deficient mice, ubamatamab combined with human immune cells led to dose-dependent antitumor activity against intraperitoneal MUC16- expressing ovarian tumour cells and malignant ascites[5,6]

1. National Cancer Institute. Available at: https://seer.cancer.gov/statfacts/html/ovary.html. Accessed January 20, 2022; 2. Siddiqui MK et al. Gynecol Oncol. 2017;146:44–51; 3. Pujade-Lauraine et al. J Clin Oncol. 2014; 13:1302-8; 4. Crawford A et al. Sci Transl Med. 2019;11:1–13; 5. Crawford A et al. Abstract presented at AACR 2018, Chicago, USA; 6. Crawford A et al. Oral presentation at PEGS Boston Summit 2020, Virtual.

Targeting Glucocorticoid Receptor

- **Cortisol** contributes to chemotherapy resistance by suppressing apoptotic pathways that cytotoxic agents, such as **nab-paclitaxel**
  - Cortisol acts by binding to the glucocorticoid receptor (GR)
- **GR** is abundantly expressed in ovarian tumors, and high GR expression is associated poor outcomes[2]
- **GR modulation with relacorilant** inhibits the anti-apoptotic effects of cortisol and enhances the efficacy of cytotoxic agents



[1] Luvero et al. 2014; [2] Veneris et al. 2017; Munster et al. 2019

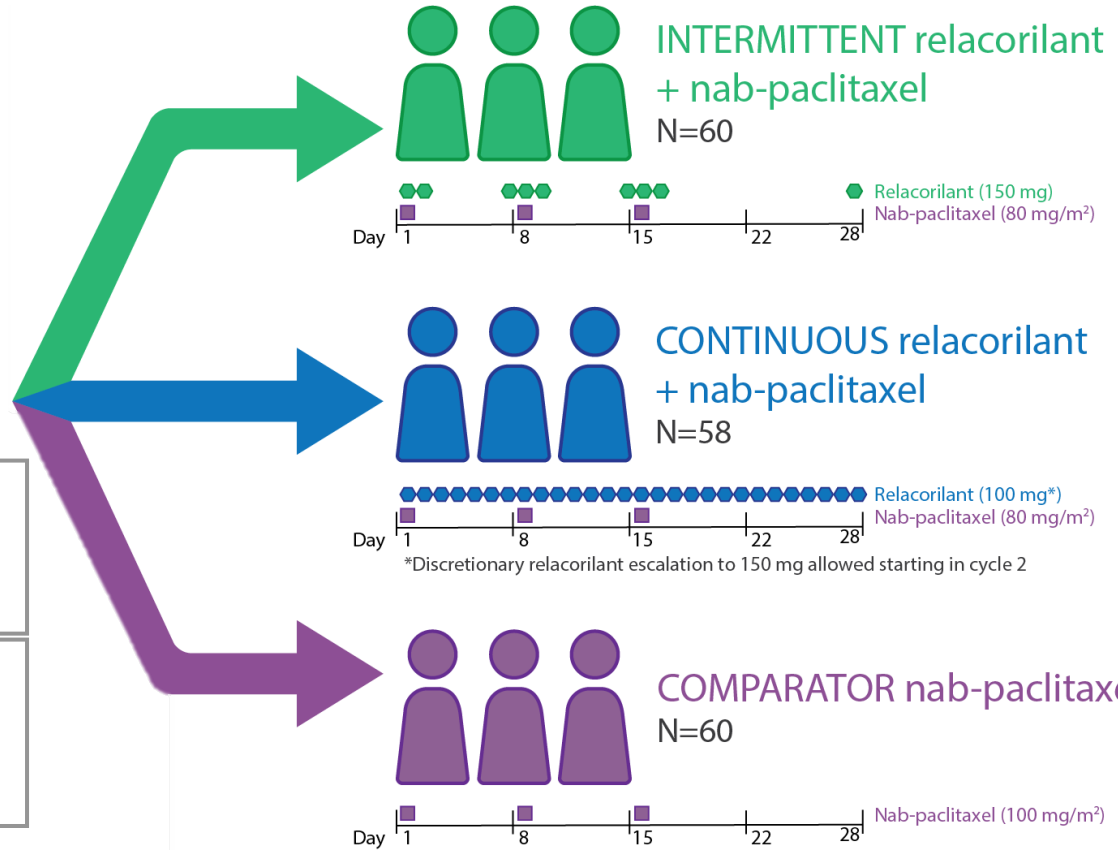
Relacorilant + Nab-Paclitaxel Phase 2 Study Design

Randomized 1:1:1

- Measurable or non-measurable disease by RECIST v1.1
- Up to 4 prior chemotherapeutic regimens

Stratification factors:

- Relapse within 6 months of most recent taxane
- Presence of ascites



Primary endpoint:

- **PFS** by investigator and RECIST v1.1

Secondary endpoints:

- Objective response rate (ORR)
- Duration of response (DoR)
- Overall survival (OS)
- Safety of the relacorilant + nap-paclitaxel combination

Statistical assumptions:

- **CONTINUOUS vs COMPARATOR**: 91 PFS events to detect a HR=0.56 (median PFS increase from 3.8 to 6.8 mo)
- **INTERMITTENT vs COMPARATOR**: 92 PFS events to detect a HR=0.7 (median PFS increase from 3.8 to 5.4 mo)

NCT03776812

Colombo N, *J Clin Oncol*. 2023;
PFS analysis reported at ESMO 2021

Baseline Characteristics

	INTERMITTENT N=60	CONTINUOUS N=58	COMPARATOR N=60	OVERALL N=178
Age, median (range), years	60 (38, 81)	60 (45, 75)	61.5 (41, 81)	61 (38, 81)
Platinum refractory*, no. (%)	23 (38.3%)	20 (34.5%)	22 (36.7%)	65 (36.5%)
Primary platinum refractory, no. (%)	7 (11.7%)	3 (5.2%)	1 (1.7%)	11 (6.2%)
Number of prior therapies, median (range)	2.5 (1, 4)	3 (1, 4)**	3 (1, 4)	3 (1, 4)**
Patients with 4 prior lines of therapy, no. (%)	7 (11.7%)	15 (25.9%)	9 (15.0%)	31 (17.4%)
Prior taxane therapy, no. (%)	59 (98.3%)	58 (100%)	60 (100%)	177 (99.4%)
Prior bevacizumab therapy, no. (%)	31 (51.7%)	37 (63.8%)	37 (61.7%)	105 (59.0%)
Prior PARP therapy, no. (%)	18 (30.0%)	27 (46.6%)	20 (33.3%)	65 (36.5%)
Molecular profiling (available in a subset of the study population only)				
BRCA1(+), n/N (%)	5/42 (11.9%)	4/42 (9.5%)	7/48 (14.6%)	16/132 (12.1%)
BRCA2(+), n/N (%)	1/36 (2.8%)	3/39 (7.7%)	3/39 (7.7%)	7/114 (6.1%)

* Progressing during or within 1 month from last platinum treatment. ** Data entry error resolved for 1 patient after the primary analysis data cutoff date

CONTINUOUS, once-daily relacorilant + nab-paclitaxel; INTERMITTENT, intermittent relacorilant + nab-paclitaxel; COMPARATOR, nab-paclitaxel monotherapy

NCT03776812

Safety of Intermittent Relacorilant + Nab-Paclitaxel Comparable to Nab-Paclitaxel

n, (%)	INTERMITTENT N=60	CONTINUOUS N=57	COMPARATOR N=60
Neutropenia[a]	12 (20.0%)	22 (38.6%)	22 (36.7%)
Grade ≥3	4 (6.7%)	15 (26.3%)	9 (15.0%)
Febrile neutropenia (Grade 3)[b]	0 (0.0%)	0 (0.0%)	1 (1.7%)
Anemia[c]	29 (48.3%)	37 (64.9%)	34 (56.7%)
Grade ≥3	8 (13.3%)	11 (19.3%)	7 (11.7%)
Peripheral neuropathy[d]	22 (36.7%)	31 (54.4%)	21 (35.0%)
Grade ≥3	0 (0.0%)	9 (15.8%)	3 (5.0%)
Fatigue or asthenia	33 (55.0%)	41 (71.9%)	39 (65.0%)
Grade ≥3	7 (11.7%)	5 (8.8%)	1 (1.7%)

[a] Neutropenia, neutrophil count decreased; [b] Secondary to E.coli urinary sepsis in this patient; [c] Anemia, hemoglobin decreased; [d] Neuropathy peripheral, neurotoxicity, peripheral motor neuropathy, peripheral sensorimotor neuropathy, peripheral sensory neuropathy, hypoesthesia.

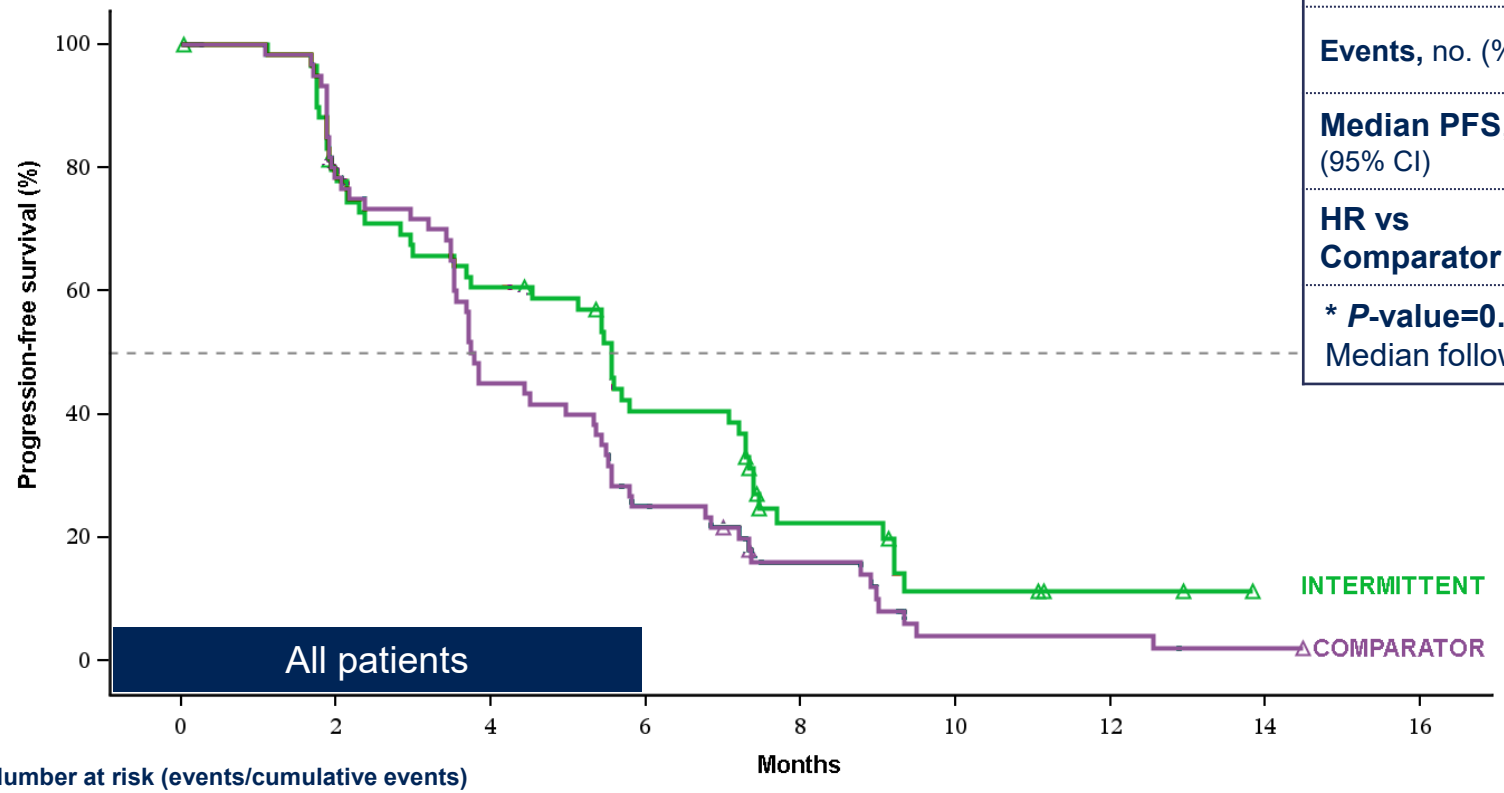
CONTINUOUS, once-daily relacorilant + nab-paclitaxel; INTERMITTENT, intermittent relacorilant + nab-paclitaxel; COMPARATOR, nab-paclitaxel monotherapy; G-CSF, granulocyte-colony stimulating factor

- All relacorilant-treated patients received prophylactic G-CSF to reduce the risk of neutropenia
- 46.7% of patients in the comparator arm received G-CSF per the investigator's standard practice

Data cutoff: March 7, 2022

NCT03776812

Intermittent Relacorilant + Nab-Paclitaxel Improved PFS



	INTERMITTENT* N=60	COMPARATOR N=60
Events, no. (%)	47 (78.3%)	57 (95.0%)
Median PFS, mo (95% CI)	**5.6** (3.7, 7.2)	3.8 (3.5, 5.4)
HR vs Comparator	**0.66** (0.44, 0.98)	N/A

* ***P*-value=0.038 vs. nab-paclitaxel alone**; no multiplicity adjustment

Median follow-up time: 11.1 months

Data cutoff: March 22, 2021

While ORR was similar, **DoR** was **significantly improved in the INTERMITTENT** vs the COMPARATOR arm.

HR 0.36, 95% CI (0.16-0.77), *P*=0.006

Number at risk (events/cumulative events)

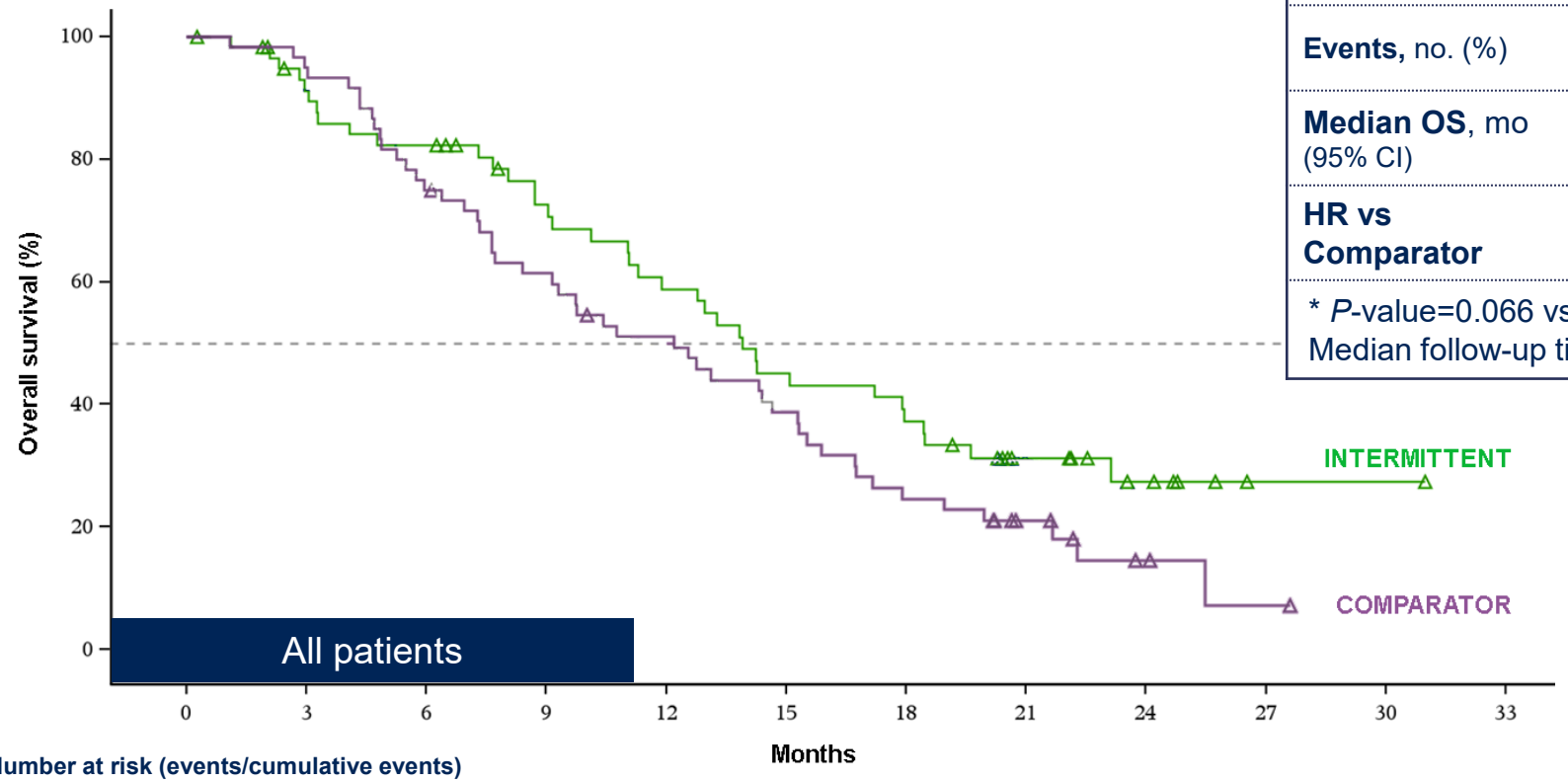
INTERMITTENT	60 (0/0)	46 (12/12)	35 (11/23)	22 (11/34)	9 (9/43)	4 (4/47)	2 (0/47)	0 (0/47)
COMPARATOR	60 (0/0)	47 (13/13)	27 (20/33)	15 (12/45)	8 (5/50)	2 (6/56)	2 (0/56)	1 (1/57)	0 (0/57)

CONTINUOUS, once-daily relacorilant + nab-paclitaxel; INTERMITTENT, intermittent relacorilant + nab-paclitaxel; COMPARATOR, nab-paclitaxel monotherapy

NCT03776812

Dr. Nicoletta Colombo, *J Clin Oncol.* 2023.

Intermittent Relacorilant + Nab-Paclitaxel Improved OS



	INTERMITTENT* N=60	COMPARATOR N=60
Events, no. (%)	37 (61.7%)	49 (81.7%)
Median OS, mo (95% CI)	13.9 (11.1, 18.4)	12.2 (7.7, 15.3)
HR vs Comparator	0.67 (0.43, 1.03)	N/A

* *P*-value=0.066 vs. nab-paclitaxel alone
Median follow-up time: 22.5 months

Data cutoff: March 7, 2022

Number at risk (events/cumulative events)

INTERMITTENT	60 (0/0)	51 (5/5)	46 (5/10)	37 (5/15)	30 (7/22)	23 (7/29)	19 (4/33)	11 (3/36)	6 (1/37)	1 (0/37)	1 (0/37)	0 (0/37)
COMPARATOR	60 (0/0)	57 (3/3)	45 (12/15)	36 (8/23)	29 (6/29)	22 (7/36)	14 (8/44)	8 (2/46)	3 (2/48)	1 (1/49)	0 (0/49)	

In the **INTERMITTENT arm, 27% of patients were still alive at 24 months** compared to **14% in the COMPARATOR arm**.

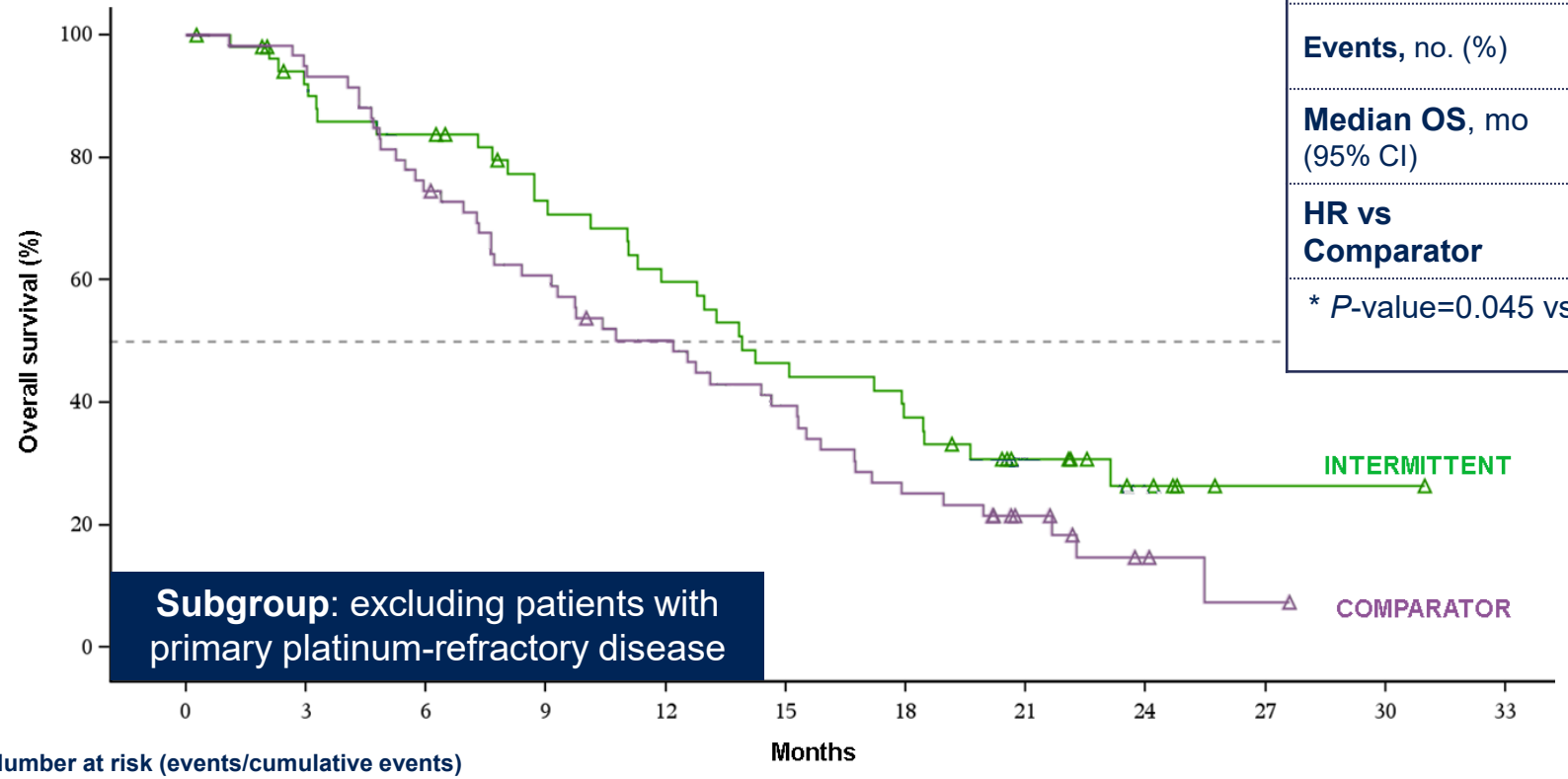
Trend toward **improved OS** consistent at interim and final analyses.

CONTINUOUS, once-daily relacorilant + nab-paclitaxel; INTERMITTENT, intermittent relacorilant + nab-paclitaxel; COMPARATOR, nab-paclitaxel monotherapy

NCT03776812

Dr. Nicoletta Colombo, *J Clin Oncol.* 2023.

Intermittent Relacorilant + Nab-Paclitaxel Improved OS



	INTERMITTENT* N=53	COMPARATOR N=59
Events, no. (%)	33 (62.3%)	48 (81.4%)
Median OS, mo (95% CI)	13.9 (11.1, 18.4)	12.2 (7.7, 15.3)
HR vs Comparator	0.63 (0.39, 0.99)	N/A

* *P*-value=0.045 vs. nab-paclitaxel alone

Data cutoff: March 7, 2022

Number at risk (events/cumulative events)

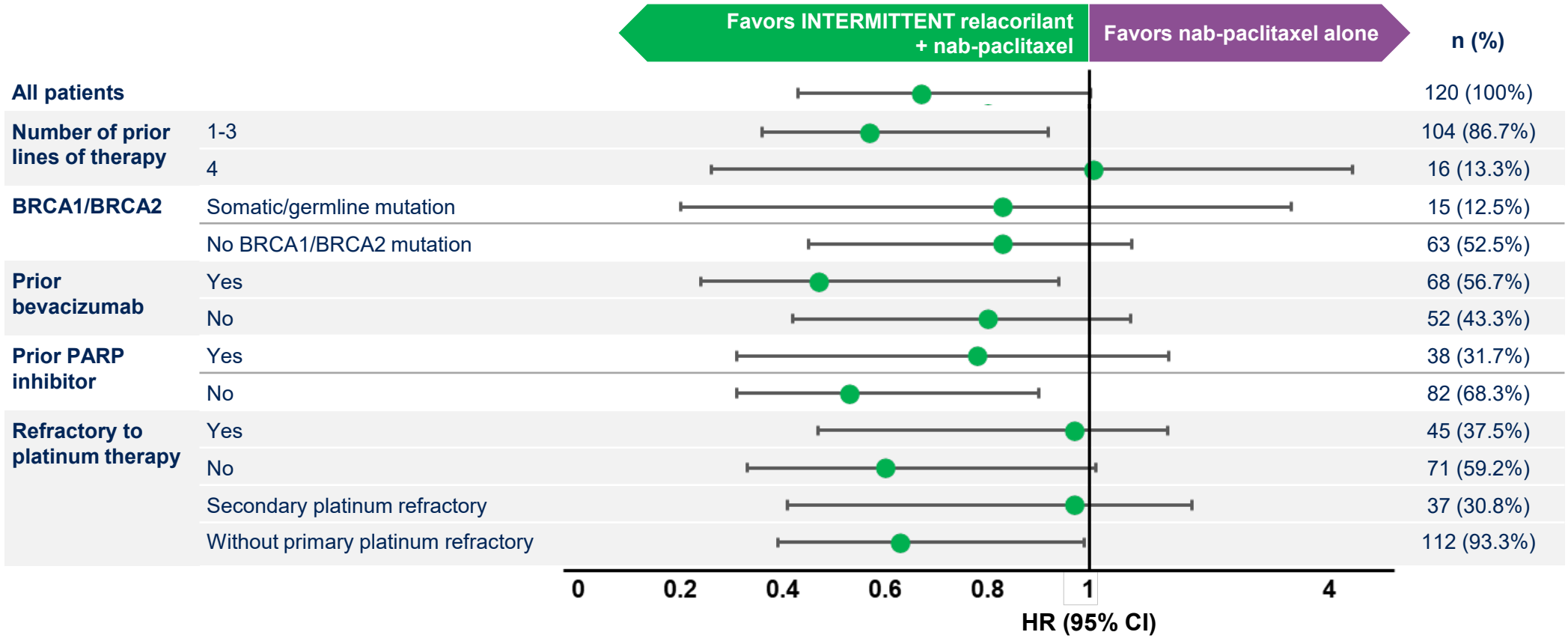
INTERMITTENT	53 (0/0)	45 (4/4)	41 (4/8)	33 (5/13)	27 (6/19)	21 (6/25)	17 (4/29)	10 (3/32)	5 (1/33)	1 (0/33)	1 (0/33)	0 (0/33)
COMPARATOR	59 (0/0)	56 (3/3)	44 (12/15)	35 (8/23)	28 (6/29)	22 (6/35)	14 (8/43)	8 (2/45)	3 (2/47)	1 (1/48)	0 (0/48)	

CONTINUOUS, once-daily relacorilant + nab-paclitaxel; INTERMITTENT, intermittent relacorilant + nab-paclitaxel; COMPARATOR, nab-paclitaxel monotherapy

NCT03776812

Dr. Nicoletta Colombo, *J Clin Oncol.* 2023.

OS in Relevant Subgroups

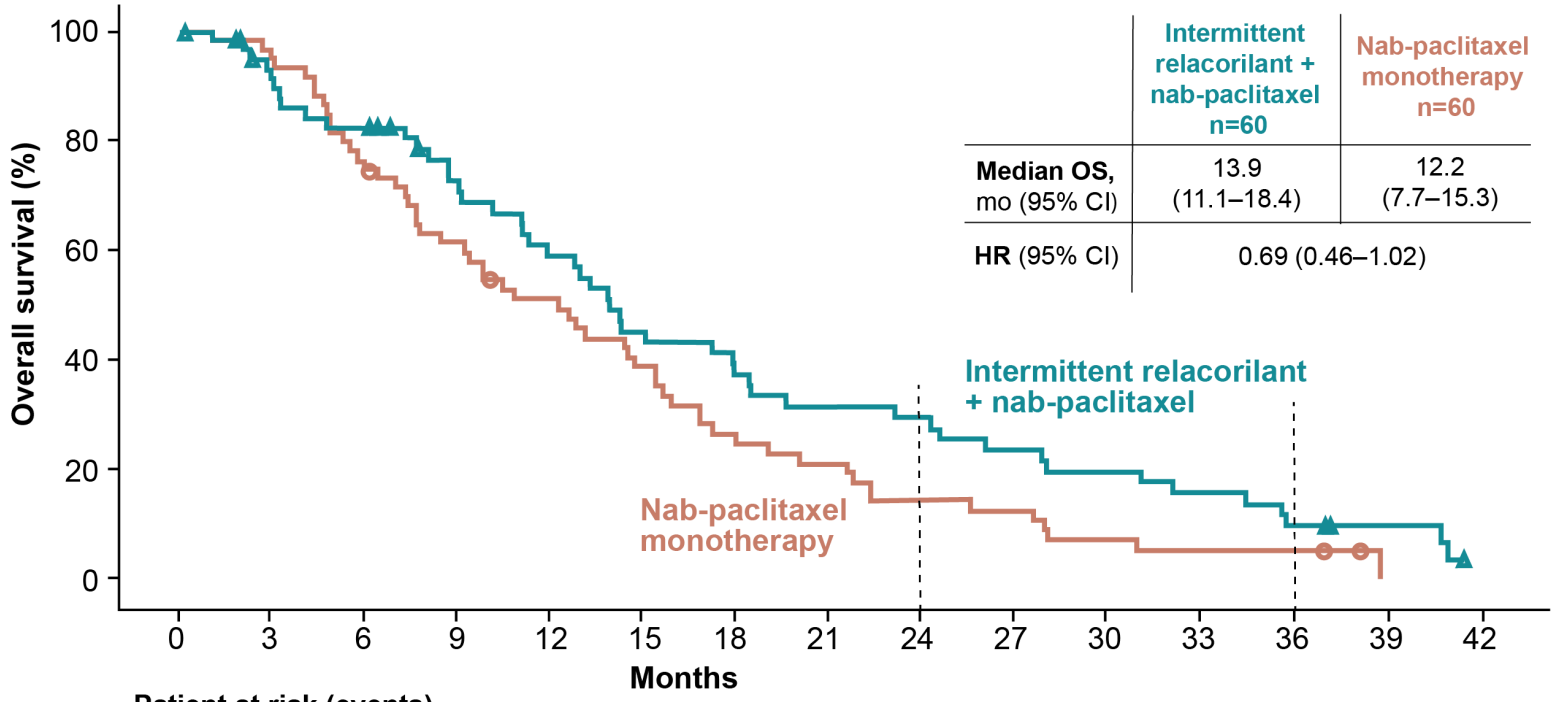


NCT03776812

Dr. Nicoletta Colombo, *J Clin Oncol*. 2023.

OS for Intermittent Relacorilant + Nab-Paclitaxel vs Nab-Paclitaxel Monotherapy at the End-of-Study Analysis

Full Study Population



	Intermittent relacorilant + nab-paclitaxel n=60	Nab-paclitaxel monotherapy n=60
Median OS, mo (95% CI)	13.9 (11.1–18.4)	12.2 (7.7–15.3)
HR (95% CI)	0.69 (0.46–1.02)	

Patient at risk (events)

Intermittent	60 (0)	51 (5)	46 (5)	37 (5)	30 (7)	23 (7)	19 (4)	16 (3)	15 (1)	12 (3)	10 (2)	8 (2)	5 (3)	3 (0)	0 (2)
Nab-paclitaxel	60 (0)	57 (3)	45 (12)	36 (8)	29 (6)	22 (7)	14 (8)	12 (2)	8 (4)	7 (1)	4 (4)	3 (1)	3 (0)	0 (1)	

Kaplan-Meier estimates of OS in intermittent relacorilant + nab-paclitaxel and nab-paclitaxel monotherapy arms:

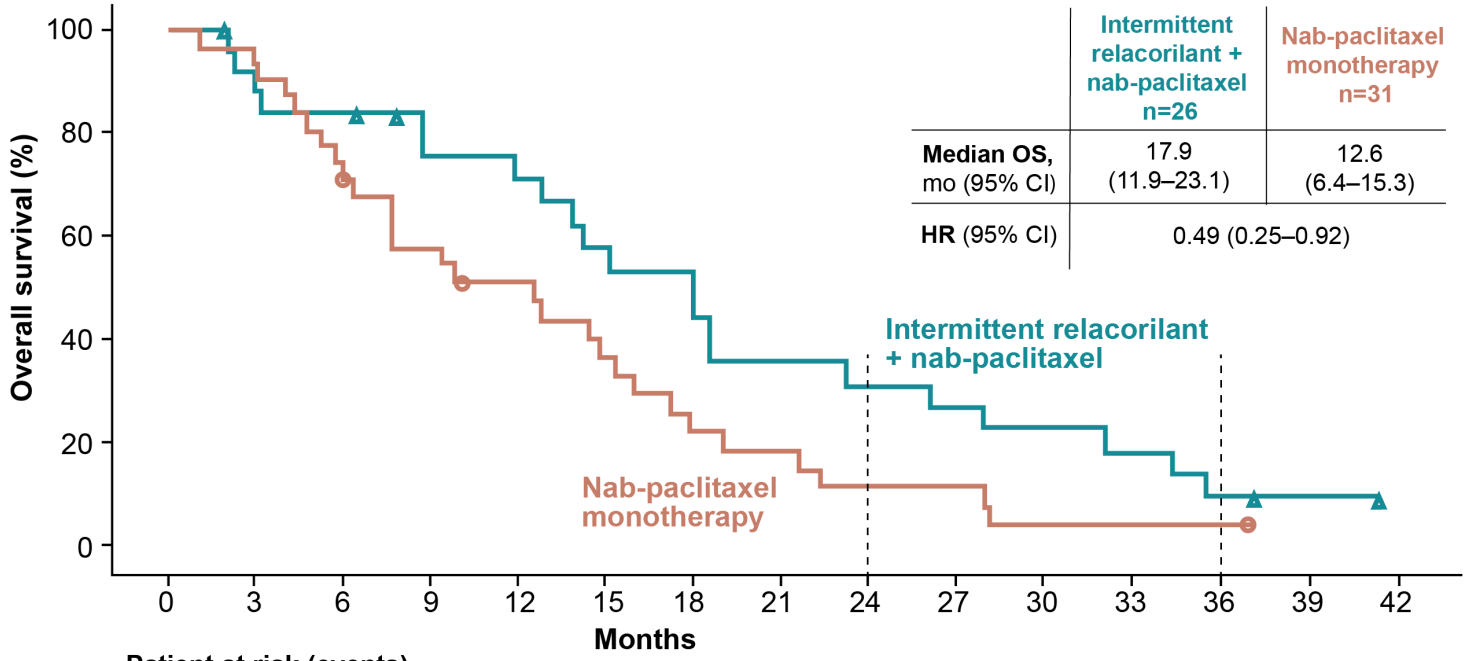
- **At 24 mos:**
  - **29.4%** (95% CI: 17.7–42.1) and **14.1%** (6.6–24.3)
- **At 36 mos:**
  - **9.8%** (3.6–19.7) and **5.3%** (1.4–13.2)

NCT03776812

Dr. Nicoletta Colombo, *SGO 2024*

OS for Intermittent Relacorilant + Nab-Paclitaxel vs Nab-Paclitaxel Monotherapy at the End-of-Study Analysis

Patients with 1–3 Prior Therapies, Including Prior Bevacizumab, Excluding Primary Platinum-Refractory Disease



	Intermittent relacorilant + nab-paclitaxel n=26	Nab-paclitaxel monotherapy n=31
Median OS, mo (95% CI)	17.9 (11.9–23.1)	12.6 (6.4–15.3)
HR (95% CI)	0.49 (0.25–0.92)	

Patient at risk (events)

Intermittent	26 (0)	22 (3)	21 (1)	17 (2)	16 (1)	13 (3)	10 (3)	8 (2)	7 (1)	6 (1)	5 (1)	4 (1)	2 (2)	1 (0)	0 (2)
Nab-paclitaxel	31 (0)	29 (2)	22 (7)	17 (4)	14 (2)	10 (4)	6 (4)	5 (1)	3 (2)	3 (0)	1 (2)	1 (0)	1 (0)	0 (0)	

- In this subgroup, mOS was prolonged by 5 months in intermittent relacorilant + nab-paclitaxel arm vs. nab-paclitaxel monotherapy
- This population is similar to that being enrolled in the phase 3 ROSELLA study

Dr. Nicoletta Colombo, *SGO 2024*

Summary and Conclusions

- **SGRM relacorilant has shown potential in restoring chemosensitivity and enhancing chemotherapy efficacy**
- In randomized, open-label phase 2 study, intermittently dosed relacorilant + nab-paclitaxel improved PFS, DOR, and OS vs. nab-paclitaxel monotherapy
- With additional ~16 mos of follow-up, end-of-study analysis confirmed findings from primary OS analysis:
  - Intermittent relacorilant + nab-paclitaxel improved OS vs. nab-paclitaxel monotherapy (HR: 0.69 [95% CI: 0.46–1.02]; 38 mos follow up), with frequency and nature of AEs similar across study arms
  - Chance of survival at 24 mos doubled for patients receiving relacorilant + nab-paclitaxel vs. nab-paclitaxel monotherapy; this trend continued at 36 mos
  - In subgroup of patients with 1–3 prior therapies, including prior bevacizumab, without primary platinum-refractory disease, median OS was prolonged by 5 mos in intermittent relacorilant + nab-paclitaxel arm (17.9 mos) vs nab-paclitaxel monotherapy (12.6 mos)
- **These promising results have paved the way for currently enrolling phase 3 ROSELLA trial**

ROSELLA | GOG-3073 | ENGOT-ov72
A Phase 3 Randomized, 2-Arm, Open-Label, Multicenter Study

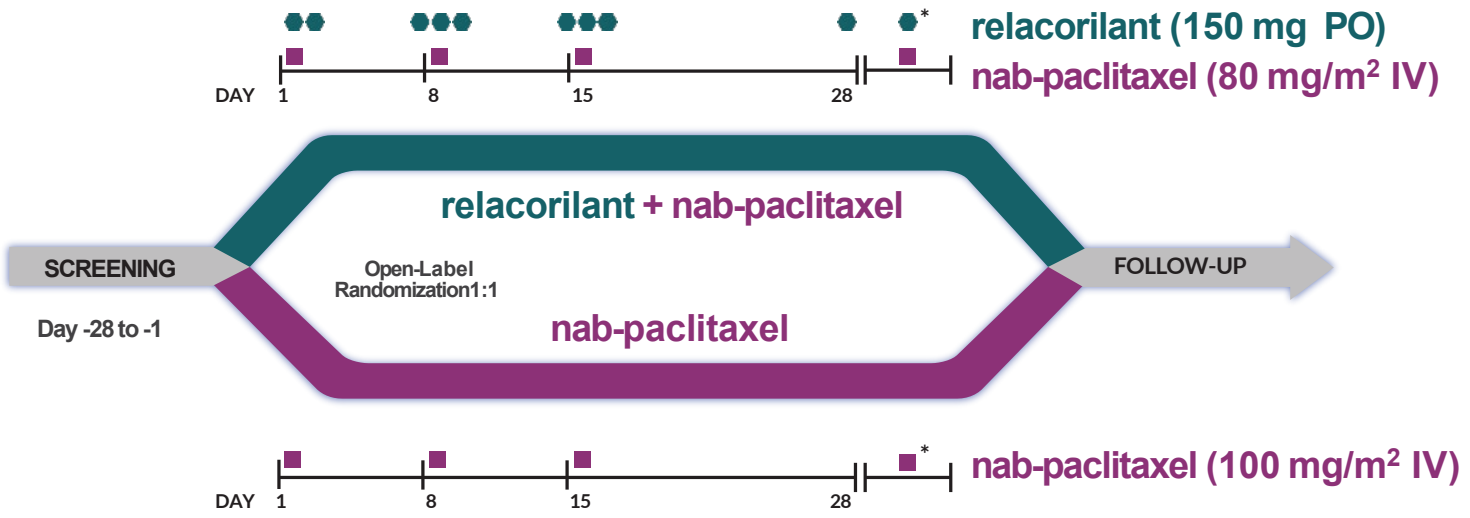
Patient population

- Confirmed high-grade serous epithelial ovarian, primary peritoneal or fallopian tube cancer
- Progression <6 months after last dose of platinum-based therapy *(excludes primary platinum-refractory disease)*
- 1-3 prior lines of systemic anticancer therapy
- Must have received prior bevacizumab

Stratification factors

- Region of the world (North America vs Europe vs Rest of World)
- Prior lines therapy (1 vs >1)

ROSELLA
Relacorilant with nab-paclitaxel in Ovarian Cancer



Endpoints

Primary endpoint

- Progression-free survival by RECIST v1.1 per BICR)

Key secondary/exploratory endpoints

- Overall survival
- Safety
- PROs and QOL

Study Status

- **381** enrolled patients
- Last patient enrolled: **April 8, 2024**

In collaboration with: GOG FOUNDATION® Transforming the standard of care™ | ENGOT European Network of Gynaecological Oncological Trial groups

Study PI: Alexander B. Olawaiye, MD
NCT05257408

*Ongoing cycles

https://clinicaltrials.gov/study/NCT05257408

Relacorilant is an investigational product that has not been approved for any use in any country; its safety and efficacy have not been established.

Future Direction in Ovarian Cancer Care – An Engaging Discussion

Dr. Lyndsay Willmott

HonorHealth Research and Innovation Institute

Phoenix, AZ

Clinical Case

- Patient initially diagnosed at age 62 with stage IIIC high grade serous ovarian cancer
- She was treated with neoadjuvant chemotherapy and enrolled on FIRST (received carboplatin/paclitaxel/bevacizumab) and niraparib/dostarlimab vs. placebo
- Interval debulking to no gross residual
- Completed adjuvant chemotherapy then transitioned to bevacizumab, dostarlimab vs. placebo plus niraparib maintenance

Case courtesy of Dr. Lyndsay Willmott

Clinical Case | *First Recurrence*

- She was without evidence of disease for 14 months following completion of upfront cytotoxic chemotherapy, but then diagnosed with platinum sensitive recurrence
- She received carboplatin/paclitaxel/bevacizumab
- She had evidence of disease recurrence 4 months following completion of cytotoxic chemotherapy

Case courtesy of Dr. Lyndsay Willmott

Your Patient is Plat Sensitive…what to do when she becomes plat resistant?

- Non-Platinum Chemo (PLD, GEM, Topo, Pac) +/- Bev
- Platinum-Based Chemo +/-Bev
- MIRV
- Clinical trials
  - Rosella Trial
  - ADC Trial
- **Other…Come to the microphone!**

Clinical Case | *Second Recurrence*

- Folate receptor alpha upregulated (75%)
- HER2 negative
- Patient started mirvetuximab soravtansine
- She received 7 cycles of therapy, but then showed evidence of disease progression

Case courtesy of Dr. Lyndsay Willmott

Your Patient is Plat Sensitive…what to do when she becomes plat resistant?

- Non-Platinum Chemo (PLD, GEM, Topo, Pac) +/- Bev
- Platinum-Based Chemo +/-Bev
- Hormonal Therapy
- Clinical trials
  - Rosella Trial
  - ADC Trial
- **Other…Come to the microphone!**

Case courtesy of Dr. Lyndsay Willmott

Clinical Case | *Clinical Trial Consideration*

Patient was counseled regarding clinical trial opportunities.

- Opted to enroll on **ROSELLA**
- Important to assess:
  - Assess for concomitant medications, such as…?
    - Corticosteroids
    - CYP3A inducers/inhibitors
  - Performance status
  - Ability to be compliant with an oral regimen?

Case courtesy of Dr. Lyndsay Willmott

Faculty Discussion

Thomas J. Herzog, MD
University of Cincinnati
Cincinnati, OH, USA

Nicoletta Colombo, MD, PhD
Chair, Ovarian Cancer Centre
European Institute of Oncology (IEO)
Milan, Italy

Alexander B. Olawaiye, MD
University of Pittsburgh
Magee-Women's Hospital
Pittsburgh, PA, USA

Lyndsay Willmott, MD
HonorHealth Research
and Innovation Institute
Phoenix, AZ, USA

Q&A and Audience Engagement

Moderator and All Faculty

The GOG Foundation, Inc. Continuing Education

In support of improving patient care, this activity has been planned and implemented by The GOG Foundation, Inc.

Accreditation Statement

The GOG Foundation, Inc. is accredited by the Accreditation Council for Continuing Medical Education (ACCME) to provide Continuing Medical Education for physicians.

AMA PRA Category 1 Credits™

The GOG Foundation, Inc. designates this live activity for a maximum of ***1.25 AMA PRA Category 1 Credits™***.
Physicians should claim only the credit commensurate with the extent of their participation in the activity.

Method of Participation

In accordance with the ACCME Accreditation Criteria, The GOG Foundation, Inc., as the accredited provider of this activity, must ensure that anyone in a position to control the content of the educational activity has disclosed all relevant financial relationships with any ineligible company *(formally known as commercial interests). All Committee/Planning/Faculty members were required to disclose all financial relationships and speakers were required to disclose any financial relationship as it pertains to the content of the presentations. All relevant financial relationships listed for these individuals have been mitigated to ensure a bias-free presentation. Please see the faculty disclosure list for detailed information.

Participants who complete the educational activity, pre-/post-tests, and evaluation, will receive certificate of credit.

Complete Our Pre-Test

SCAN ME

THANK YOU