Year in Review: Clinical Investigator Perspectives on the Most Relevant New Datasets and Advances in Oncology

Ovarian Cancer

A CME/MOC-Accredited Live Webinar

Thursday, February 19, 2026
5:00 PM – 6:00 PM ET

Faculty

Nicoletta Colombo, MD
Kathleen N Moore, MD, MS

Moderator

Neil Love, MD

RTP Year in Review 2026

Faculty

Nicoletta Colombo, MD
Director, Gynecologic Oncology Program
European Institute of Oncology IRCCS
Milan, Italy

MODERATOR
Neil Love, MD
Research To Practice
Miami, Florida

Kathleen N Moore, MD, MS
Deputy Director and Director, Phase 1 Clinical Trials
Fred and Pamela Buffett Cancer Center at the University of Nebraska
Omaha, Nebraska

RTP Year in Review 2026

Commercial Support

This activity is supported by educational grants from AstraZeneca Pharmaceuticals LP, Corcept Therapeutics Inc, and Merck.

Dr Love — Disclosures

Dr Love is president and CEO of Research To Practice. Research To Practice receives funds in the form of educational grants to develop CME activities from the following companies: Aadi Bioscience, AbbVie Inc, ADC Therapeutics, Agendia Inc, Alexion Pharmaceuticals, Amgen Inc, Array BioPharma Inc, a subsidiary of Pfizer Inc, Arvinas, Astellas, AstraZeneca Pharmaceuticals LP, Aveo Pharmaceuticals, Bayer HealthCare Pharmaceuticals, BeOne, Biotheranostics, A Hologic Company, Black Diamond Therapeutics Inc, Blueprint Medicines, Boehringer Ingelheim Pharmaceuticals Inc, Bristol Myers Squibb, Celcuity, Clovis Oncology, Coherus BioSciences, Corcept Therapeutics Inc, CTI BioPharma, a Sobi Company, Daiichi Sankyo Inc, Eisai Inc, Elevation Oncology Inc, Exact Sciences Corporation, Exelixis Inc, Genentech, a member of the Roche Group, Genmab US Inc, Geron Corporation, Gilead Sciences Inc, GSK, Helsinn Therapeutics (US) Inc, ImmunoGen Inc, Incyte Corporation, Ipsen Biopharmaceuticals Inc, Jazz Pharmaceuticals Inc, Johnson & Johnson, Karyopharm Therapeutics, Kite, A Gilead Company, Kura Oncology, Legend Biotech, Lilly, MEI Pharma Inc, Merck, Mersana Therapeutics Inc, Mirati Therapeutics Inc, Mural Oncology Inc, Natera Inc, Novartis, Novartis Pharmaceuticals Corporation on behalf of Advanced Accelerator Applications, Novocure Inc, Nuvalent, Nuvation Bio Inc, Pfizer Inc, Pharmacyclics LLC, an AbbVie Company, Puma Biotechnology Inc, Regeneron Pharmaceuticals Inc, Revolution Medicines Inc, Rigel Pharmaceuticals Inc, R-Pharm US, Sanofi, Seagen Inc, Servier Pharmaceuticals LLC, SpringWorks Therapeutics Inc, Stemline Therapeutics Inc, Sumitomo Pharma America, Syndax Pharmaceuticals, Taiho Oncology Inc, Takeda Pharmaceuticals USA Inc, TerSera Therapeutics LLC, and Tesaro, A GSK Company.

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

Dr Moore — Disclosures

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Dr Secord — Disclosures

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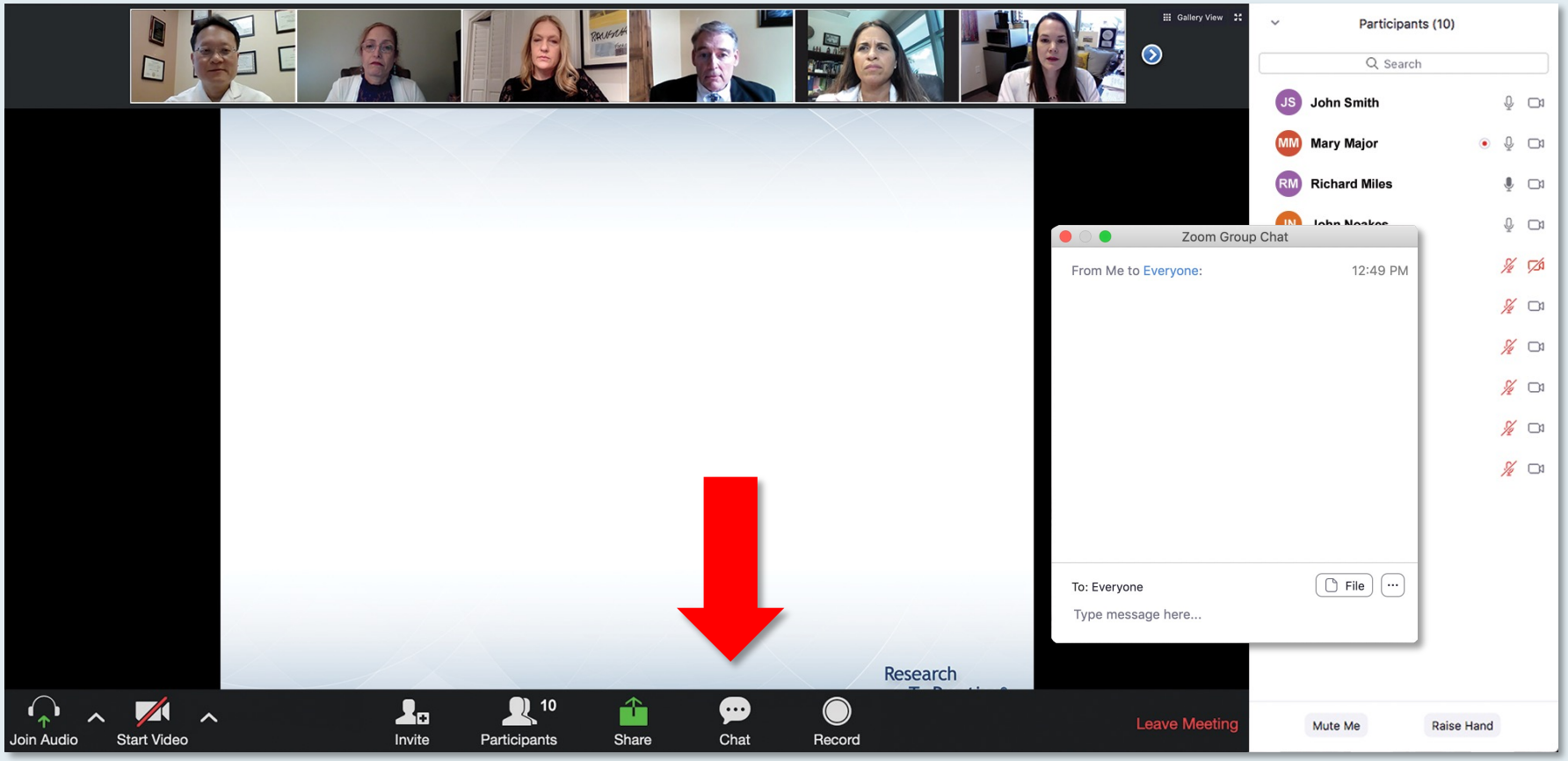
Stock Options/Stock — Public Companies	Stock in Amgen Inc and Johnson & Johnson, divested in June 2024

This educational activity contains discussion of non-FDA-approved uses of agents and regimens. Please refer to official prescribing information for each product for approved indications.

We Encourage Clinicians in Practice to Submit Questions



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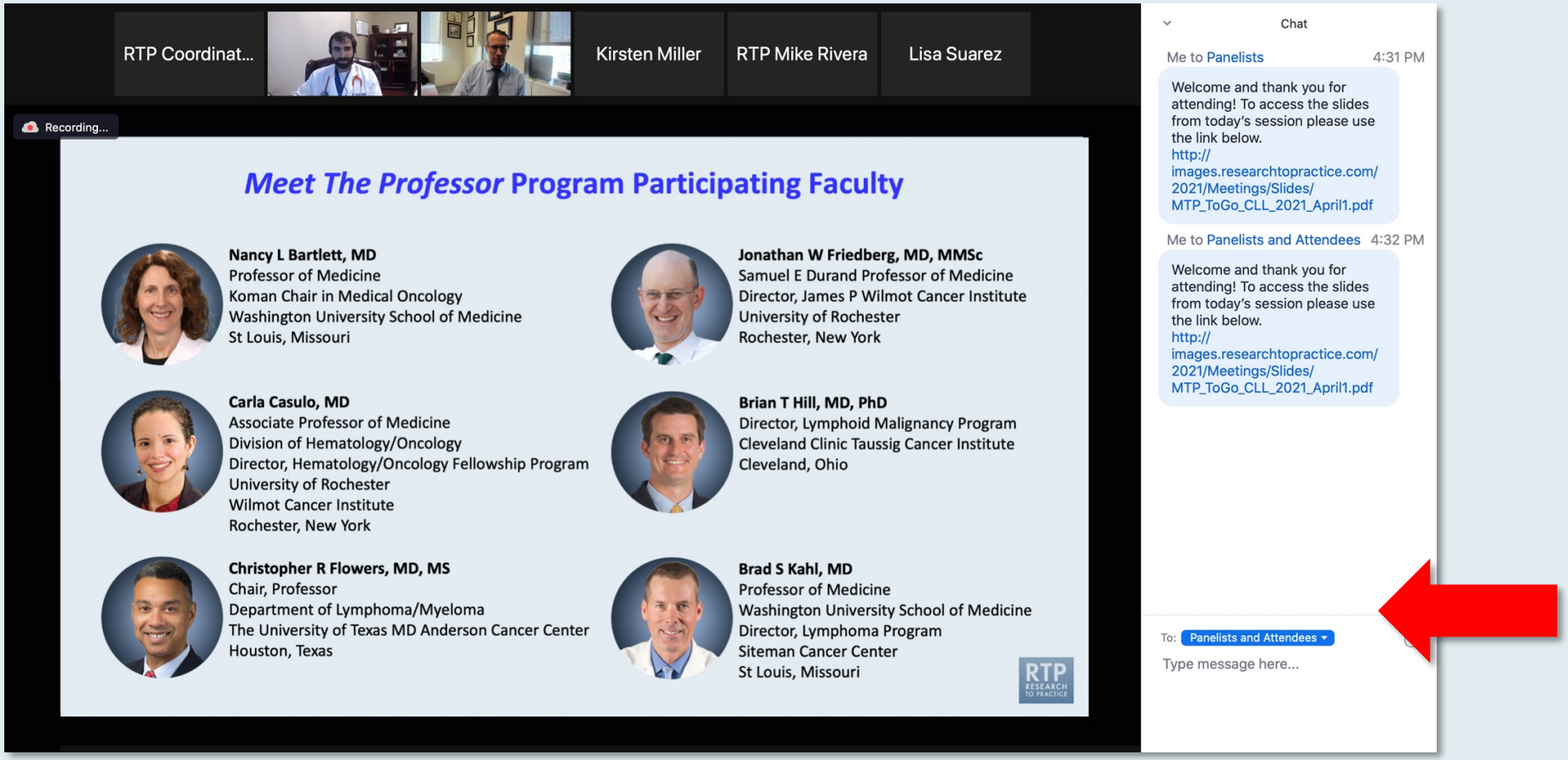

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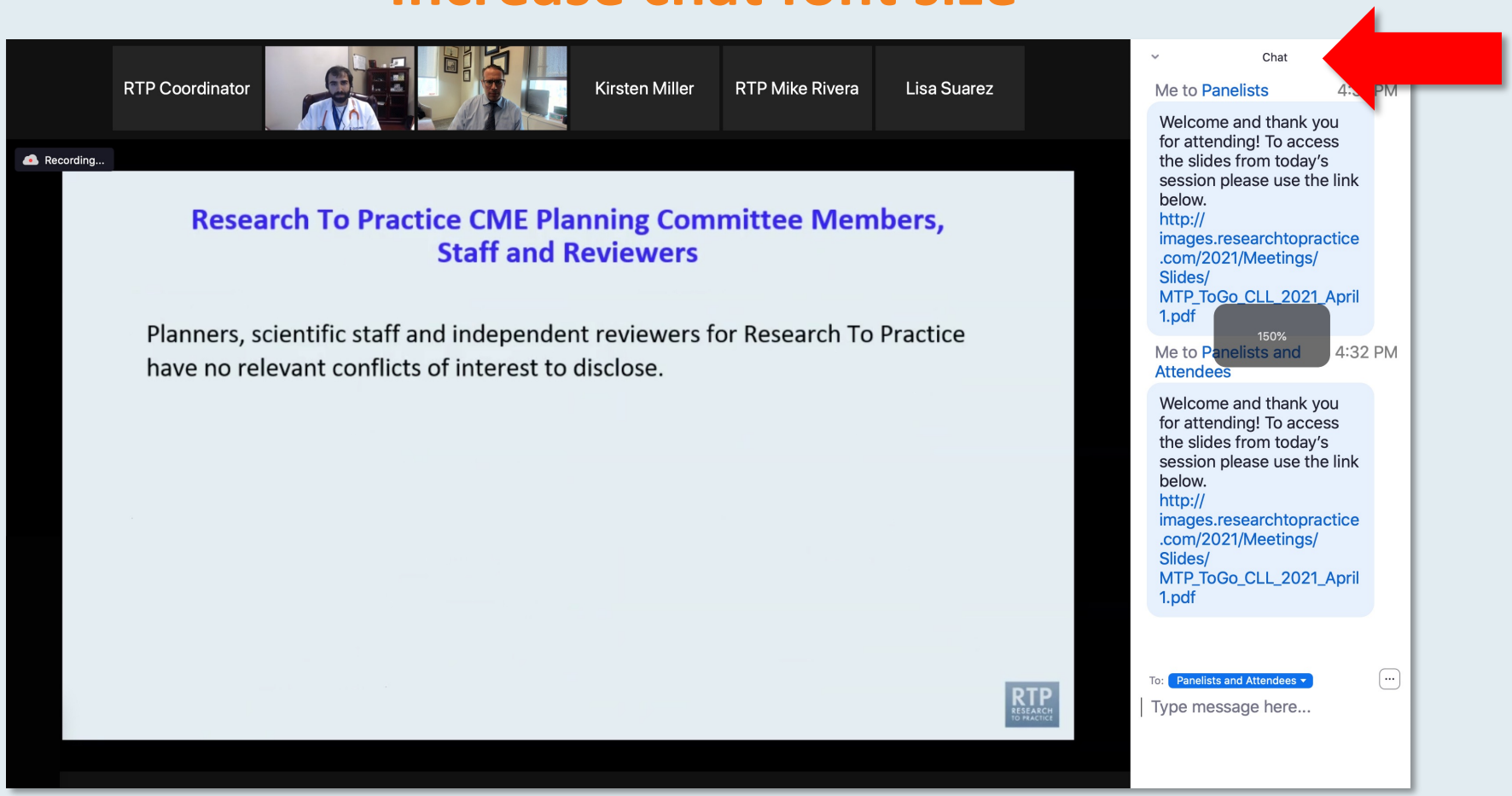

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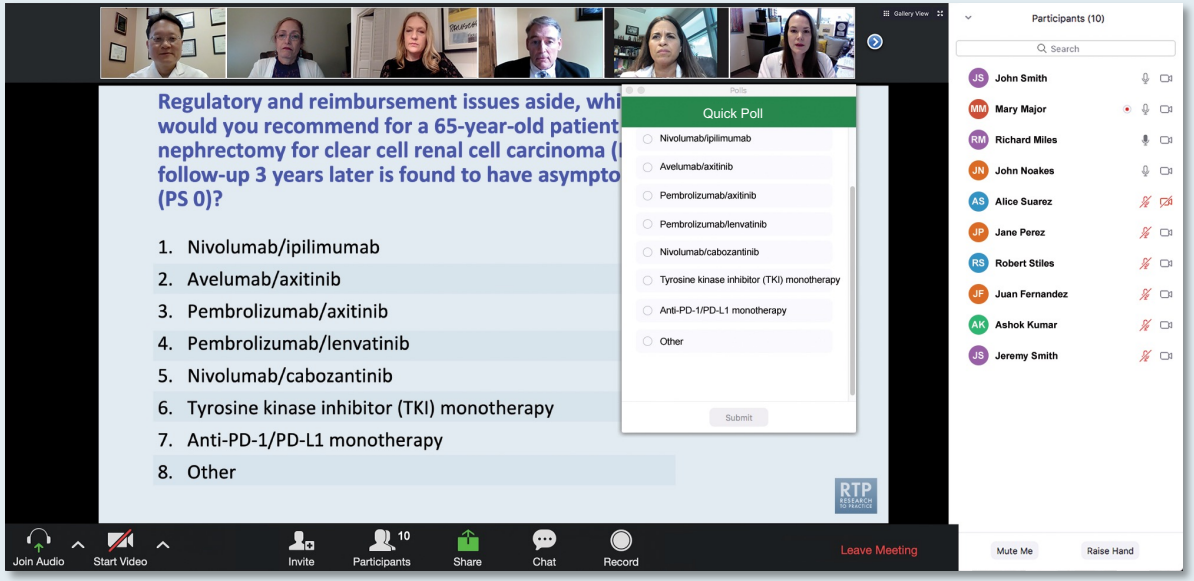

Gynecologic Cancers — Highlights from the 2025 ESMO Annual Meeting

DR RITU SALANI
DAVID GEFFEN SCHOOL OF MEDICINE AT UCLA

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Second Opinion: Integrating Novel Approaches into the Management of Non-Muscle-Invasive and Muscle-Invasive Bladder Cancer

A CME Symposium Held Adjunct to the
2026 ASCO® Genitourinary Cancers Symposium

Thursday, February 26, 2026
7:00 PM – 9:00 PM PT (10:00 PM – 12:00 AM ET)

Faculty

Matthew D Galsky, MD
Shilpa Gupta, MD
Andrea Necchi, MD

Moderator

Terence Friedlander, MD

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Second Opinion: Clinical Investigators Provide Perspectives on the Future Role of AKT Inhibition in the Management of Prostate Cancer

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Professor Karim Fizazi, MD, PhD
Daniel George, MD

Moderator

Elisabeth I Heath, MD

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Year in Review: Clinical Investigator Perspectives on the Most Relevant New Datasets and Advances in Oncology

Bruton Tyrosine Kinase Inhibitors for Chronic Lymphocytic Leukemia

A CME/MOC-Accredited Live Webinar

Wednesday, March 11, 2026

5:00 PM – 6:00 PM ET

Faculty

Jennifer R Brown, MD, PhD

Wojciech Jurczak, MD, PhD

Moderator

Neil Love, MD

RTP Year in Review 2026

What Clinicians Want to Know: First-Line and Maintenance Therapy for Patients with ER-Positive, HER2-Positive Metastatic Breast Cancer

A CME/MOC-Accredited Live Webinar

Wednesday, March 18, 2026

5:00 PM – 6:00 PM ET

Faculty

Virginia F Borges, MD, MMSc

Ian E Krop, MD, PhD

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Optimizing Treatment for Patients with Relapsed/Refractory Chronic Lymphocytic Leukemia

Optimizing the Use of Novel Therapies for Patients with Diffuse Large B-Cell Lymphoma

Optimizing Therapy for Patients with Hormone Receptor-Positive Localized Breast Cancer

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

Friday to Sunday, April 24 to 26, 2026

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

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Year in Review:
Ovarian Cancer

MODULE 1: Promising Novel Agents and Strategies Under Investigation in Ovarian Cancer

- Antibody-drug conjugates
- KEYNOTE-B96 Phase III trial: Pembrolizumab and paclitaxel +/- bevacizumab
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- Mirvetuximab soravtansine
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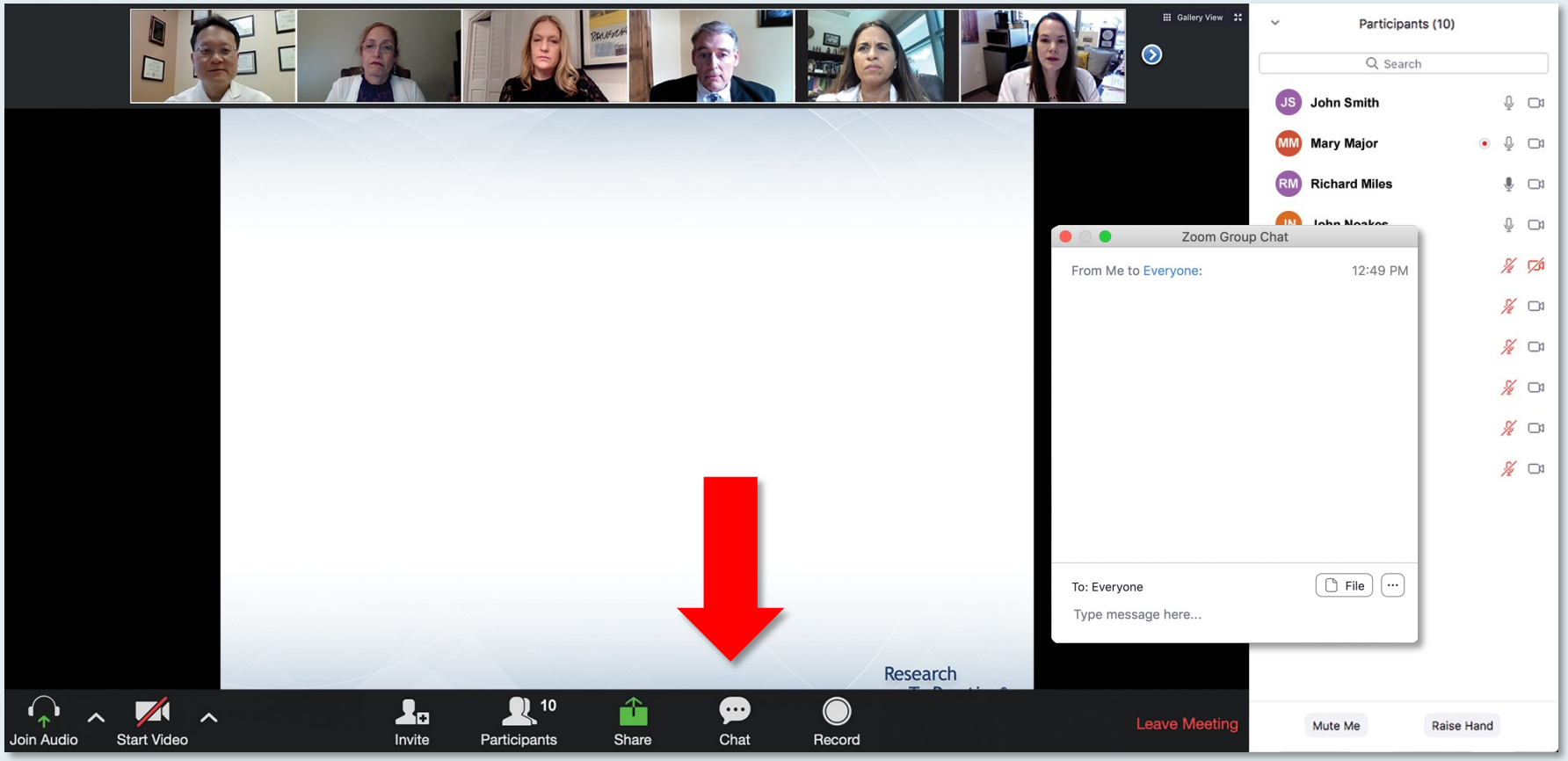

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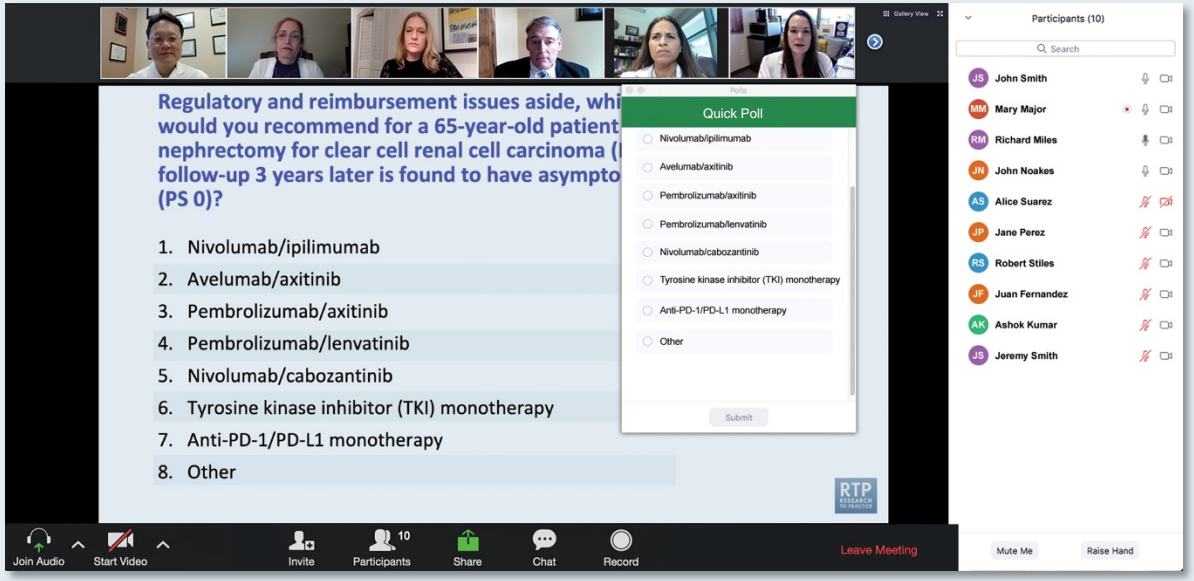

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Current Management of Newly Diagnosed and Relapsed/Refractory Ovarian Cancer

Angeles Alvarez Secord, MD, MHSc
Director, Gynecologic Oncology Clinical Trials
Division of Gynecologic Oncology, Department Ob/Gyn
Duke Cancer Institute

DukeHealth

Promising Novel Agents and Strategies Under Investigation in OC

Nicoletta Colombo, MD
European Institute of Oncology, Milan

Key Datasets

Nicoletta Colombo, MD

- Olawaiye AB et al. **Relacorilant** and ***nab*-paclitaxel** in patients with **platinum-resistant ovarian cancer (ROSELLA):** An **open-label, randomised, controlled, phase 3 trial**. *Lancet* 2025;405(10496):2205-16.
- Lorusso D et al. **ROSELLA (GOG3073, ENGOTov72, APGOT-OV10): Relacorilant + *nab*-paclitaxel** in the **subgroup** of patients with **platinum-resistant ovarian cancer (PROC) previously exposed to a PARP inhibitor**. ESMO 2025;Abstract LBA45.
- Colombo N et al. **Pembrolizumab** vs placebo **plus weekly paclitaxel ± bevacizumab** in **platinum-resistant recurrent ovarian cancer: Results** from the **randomized double-blind phase III ENGOT-ov65/KEYNOTE-B96 study**. ESMO 2025;Abstract LBA3.
- Ray-Coquard IL et al. **Raludotatug deruxtecan (R-DXd)** in patients (pts) with **platinum-resistant ovarian cancer (PROC): Primary analysis** of the **phase II dose-optimization part of REJOICE-Ovarian01**. ESMO 2025;Abstract LBA42.
- Moore KN et al. **Raludotatug deruxtecan (R-DXd) monotherapy** in patients (pts) with **heavily pretreated platinum-sensitive ovarian cancer (PSOC): Subgroup analysis** of a **phase I study**. ESMO Gynaecological Cancers 2025;Abstract 77MO.

Key Datasets

Nicoletta Colombo, MD (continued)

- Lee EK et al. **Rinatabart sesutecan** for patients with **advanced ovarian cancer: Results** from **dose expansion cohort B1 of phase I/II study**. SGO 2025;Abstract 809034.
- Secord A et al. A **phase 3, open-label, randomized** study of **rinatabart sesutecan (Rina-S)** vs investigator's choice (IC) of chemotherapy in patients with **platinum-resistant ovarian cancer (PROC)**. ASCO 2025;Abstract TPS5627.
- Oaknin A et al. **First-in-human study of AZD5335**, a folate receptor α (FRα)-targeted antibody-drug conjugate, in patients with **platinum-resistant recurrent ovarian cancer**. ESMO 2025;Abstract 1065MO.

Key Datasets

Angeles Alvarez Secord, MD, MHSc

- Harter P et al. **Efficacy of subsequent therapies** in patients with **advanced ovarian cancer** who **relapse** after **first-line olaparib maintenance: Results** of the **PAOLA-1/ENGOT-ov25 trial**. *Ann Oncol* 2025 February;36(2):185-96.
- Vergote I et al. **Chemotherapy with or without pembrolizumab** followed by **maintenance with olaparib** RR placebo for **first-line** treatment of **advanced BRCA non-mutated epithelial ovarian cancer: Results** from **the randomized phase 3 ENGOT-OV43/GOG-3036/KEYLYNK-001 study**. ESGO 2025;Abstract 128.
- Hardy-Bessard AC et al. **Dostarlimab and niraparib** in **primary advanced ovarian cancer**. *Ann Oncol* 2025 December;36(12):1503-13.
- Clamp AR et al. **ICON8B**: GCIG phase III randomised trial comparing **first-line weekly dose-dense chemotherapy + bevacizumab** to three-weekly chemotherapy + bevacizumab in high-risk stage III-IV epithelial ovarian cancer (EOC): **Final overall survival (OS) analysis**. ESMO 2025;Abstract 1064O.
- González-Martín A et al. An **open-label, randomized, multicenter, phase III study** of **trastuzumab deruxtecan (T-DXd) with bevacizumab (BEV)** vs BEV monotherapy as **first-line (1L) maintenance therapy in HER2-expressing ovarian cancer: DESTINY-Ovarian01 (DO 01)**. ESMO Gynaecological Cancers 2025;Abstract 127TiP.

Key Datasets

Angeles Alvarez Secord, MD, MHSc (continued)

- Pujade-Lauraine E et al. **Bevacizumab combined with chemotherapy** for **platinum-resistant recurrent** ovarian cancer: The **AURELIA** open-label randomized phase III trial. *J Clin Oncol* 2014;32(13):1302-8.
- Poveda AM et al. Bevacizumab combined with weekly paclitaxel, pegylated liposomal doxorubicin, or topotecan in platinum-resistant recurrent ovarian cancer: **Analysis by chemotherapy cohort** of the randomized phase III **AURELIA** trial. *J Clin Oncol* 2015;33(32):3836-8.
- Van Gorp T et al. **Final overall survival analysis** among patients with **folate receptor alpha-positive, platinum-resistant ovarian cancer** treated with **mirvetuximab soravtansine** versus investigator's choice chemotherapy in **phase II MIRASOL (GOG-3045/ENGOT-ov55) study**. SGO 2025;Abstract 939696.
- Secord AA et al. The efficacy and safety of **mirvetuximab soravtansine** in FRα-positive, third-line and later, recurrent platinum-sensitive ovarian cancer: the single-arm **phase II PICCOLO trial**. *Ann Oncol* 2025;36(3):321-30.
- Secord AA et al. **Final analysis** of the **single-arm phase 2 PICCOLO trial** of **mirvetuximab soravtansine (MIRV)** in **folate receptor alpha (FRα)-positive**, third-line and later, **recurrent platinum-sensitive ovarian cancer (PSOC)**. ESMO Gynaecological Cancers 2025;Abstract 76MO.

Key Datasets

Angeles Alvarez Secord, MD, MHSc (continued)

- Matulonis UA et al. **Safety** and **efficacy** of **mirvetuximab soravtansine**, a folate receptor alpha (FRα)-targeting antibody-drug conjugate (ADC), **in combination with pembrolizumab** in patients with **platinum-resistant ovarian cancer**. *Gynecol Oncol* 2025;200:96-104.
- Makker V et al. **Trastuzumab deruxtecan (T-DXd)** for pretreated patients (pts) with **HER2-expressing solid tumors: DESTINY-PanTumor02 (DP-02) part 1 final analysis**. ESMO 2025;Abstract 957P.
- Banerjee SN et al. **Efficacy and safety** of **avutometinib defactinib** in **recurrent low-grade serous ovarian cancer: Primary analysis of ENGOT-OV60/GOG-3052/RAMP 201**. *J Clin Oncol* 2025;43(25):2782-92.

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Ovarian Cancer

MODULE 1: Promising Novel Agents and Strategies Under Investigation in Ovarian Cancer

- Antibody-drug conjugates
- KEYNOTE-B96 Phase III trial: Pembrolizumab and paclitaxel +/- bevacizumab
- ROSELLA Phase III trial: Relacorilant with *nab* paclitaxel

MODULE 2: Current Management of Newly Diagnosed and Relapsed/Refractory Ovarian Cancer

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Platinum Ineligible Ovarian Cancer

ANTIBODY DRUG CONJUGATED (ADCS)

Mirvetuximab-soravtansine [1]

Trastuzumab-deruxtecan [2]

Raludotatug- Deruxtecan [3]

Rinatabart Sesutecan (Rina-S)[4]

AZD5335 [5]

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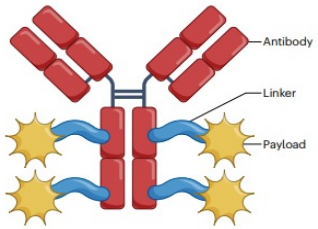
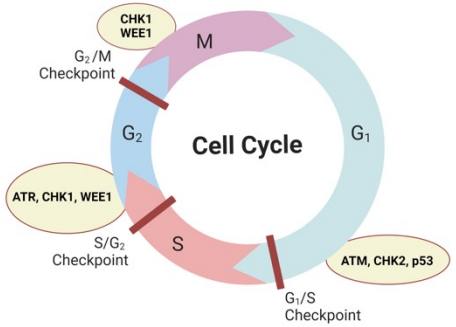


CELL CYCLE REGULATION AND DNA REPAIR

ADAVOSERTIB [8]

azenosertib[9]

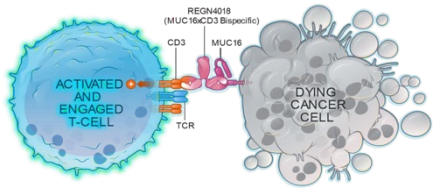
CDK2i [10]



IMMUNOTHERAPY

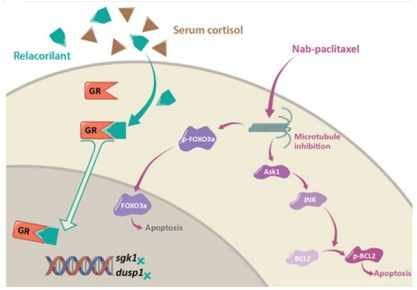
Paclitaxel/pembro [11]

UBAMATAMAB [12]



GLUCOCORTICOID RECEPTOR

RELACORILANT [13]



[1] [NCT04296890 – Soraya] [NCT04209855 – Mirasol]; [2] [NCT04482309]; [3] [NCT04707248]; [4] [NCT06619236]; [5] [NCT05797168] ; [6] [NCT06400472]; [7] [NCT06303505]; [8] [NCT03579316]; [9] [NCT02595892]; [10] [INCB123667]; [11] [NCT05116189]; [12] [NCT03564340] [13] [NCT05257408 – Rosella]; [NCT03776812 – phase II];

Courtesy of Nicoletta Colombo, MD

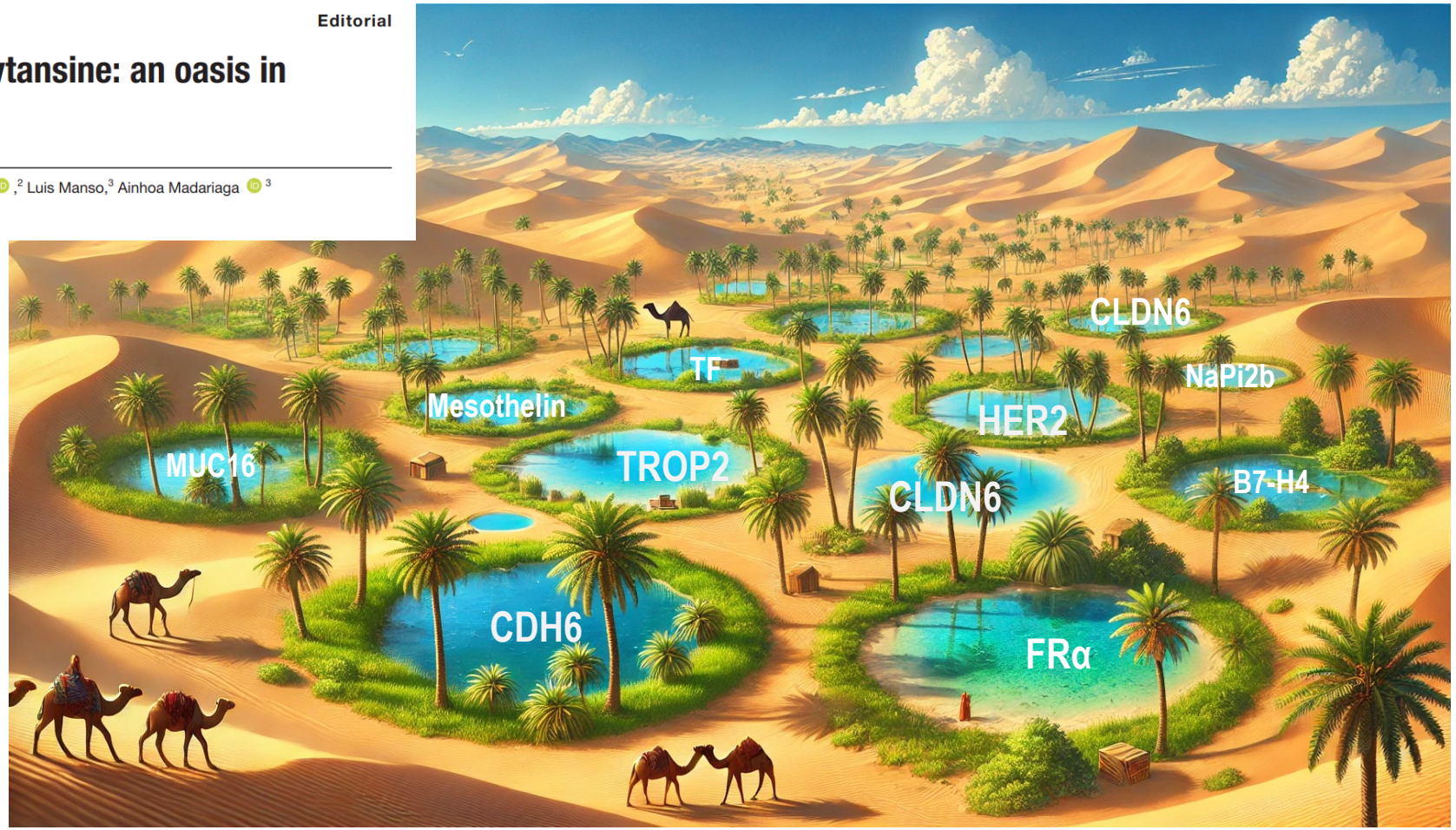
Antibody Drug Conjugates in ovarian cancer

Editorial

Mirvetuximab soravtansine: an oasis in the desert?

Luisa Bonilla [1], Lawrence Kasherman [2], Luis Manso,[3] Ainhoa Madariaga [3]

Future?



With permission of Ainhoa Madariaga

Courtesy of Nicoletta Colombo, MD

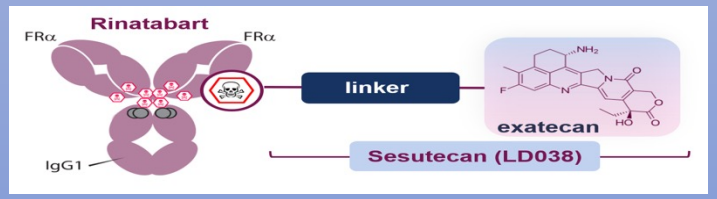
Targeting FRα: RAINFOL-01 Phase 1/2 Study (NCT05579366)

Courtesy of Nicoletta Colombo, MD

Rinatabart sesutecan (Rina-S)

Novel FRα-directed ADC

- Highly hydrophilic linker, sesutecan
- Topoisomerase 1 inhibitor payload



Antitumor Activity

	Rina-S 100 mg/m² (n=22)[a]	Rina-S 120 mg/m² (n=18)[a]
Median on-study follow-up, weeks (range)	46.4 (6.6, 65.3)	48.1 (10.9-65.9)
Confirmed ORR[b], % (95% CI)	22.7 (7.8-45.4)	55.6 (30.8-78.5)
Confirmed response, n (%)		
CR	1 (4.5)	2 (11.1)
PR	4 (18.2)	8 (44.4)
SD	14 (63.6)	6 (33.3)
NE	0	1 (5.6)
Disease control rate, % (95% CI)	86.4 (65.1-97.1)	88.9 (65.3-98.6)

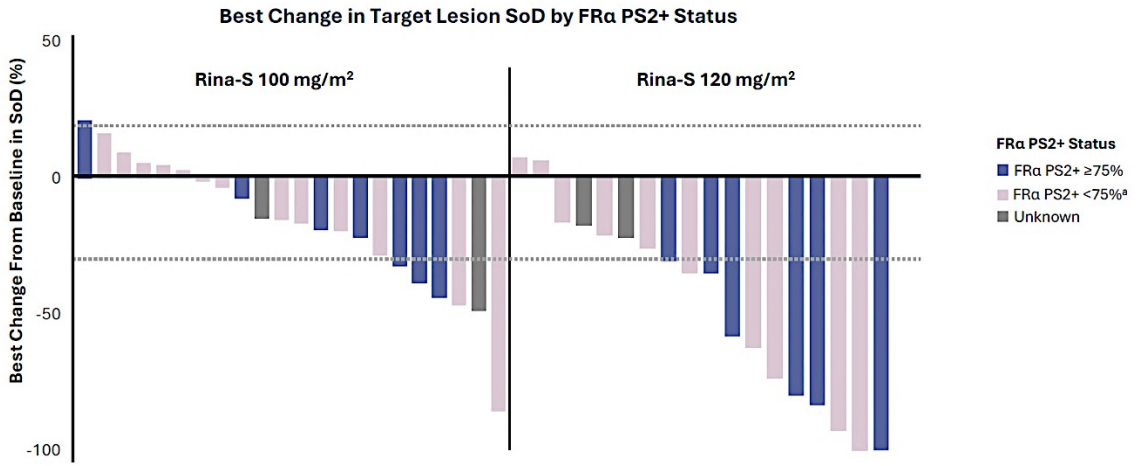
Encouraging confirmed ORR, including deep responses, observed with Rina-S 120 mg/m²

Phase I/II: Part B – Dose expansion
R (1:1): Rina-S 100 or Rina-S 120 mg/m2, q 3w

	Rina-S 100 mg/m² (n=22)	Rina-S 120 mg/m² (n=20)
Median age, years (range)	62.5 (42-82)	64.5 (37-83)
≥65 years, n (%)	10 (45.5)	10 (50.0)
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)	12 (60.0)
Mirvetuximab soravtansine, n (%)	4 (18.2)	4 (20.0)
Platinum sensitivity status, n (%)		
Resistant	21 (96.0)	18 (90.0)
Sensitive	1 (4.5)	2 (10.0)
ECOG PS status, n (%)		
1	15 (68.2)	16 (80.0)
0	7 (31.8)	4 (20.0)

Data cutoff for all presented analyses: January 15th, 2025

Response by FRα Expression

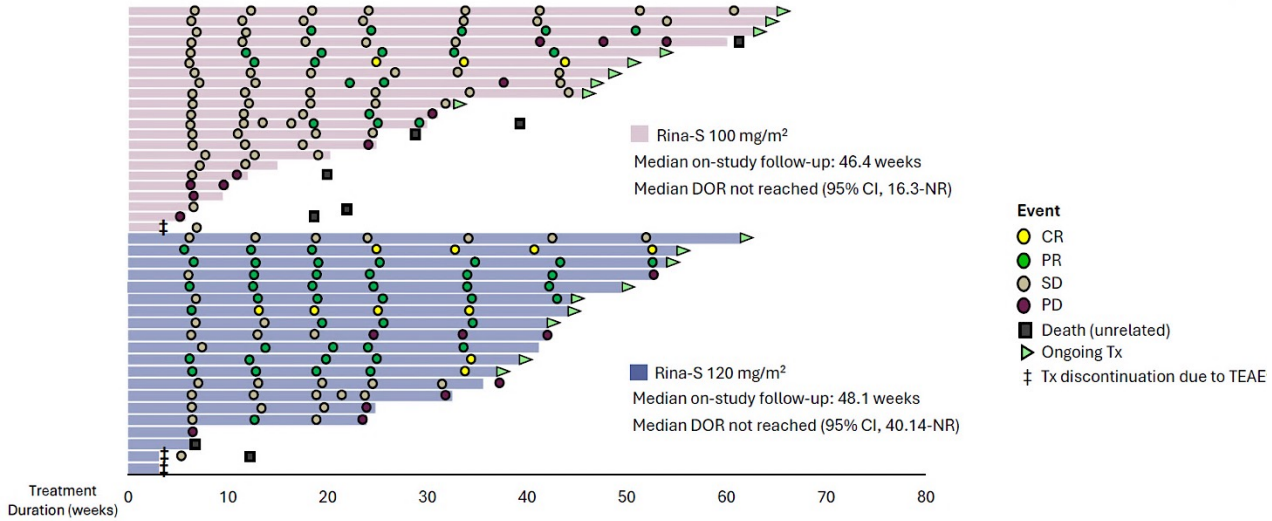


Deep responses observed regardless of FRα expression levels with Rina-S 120 mg/m²

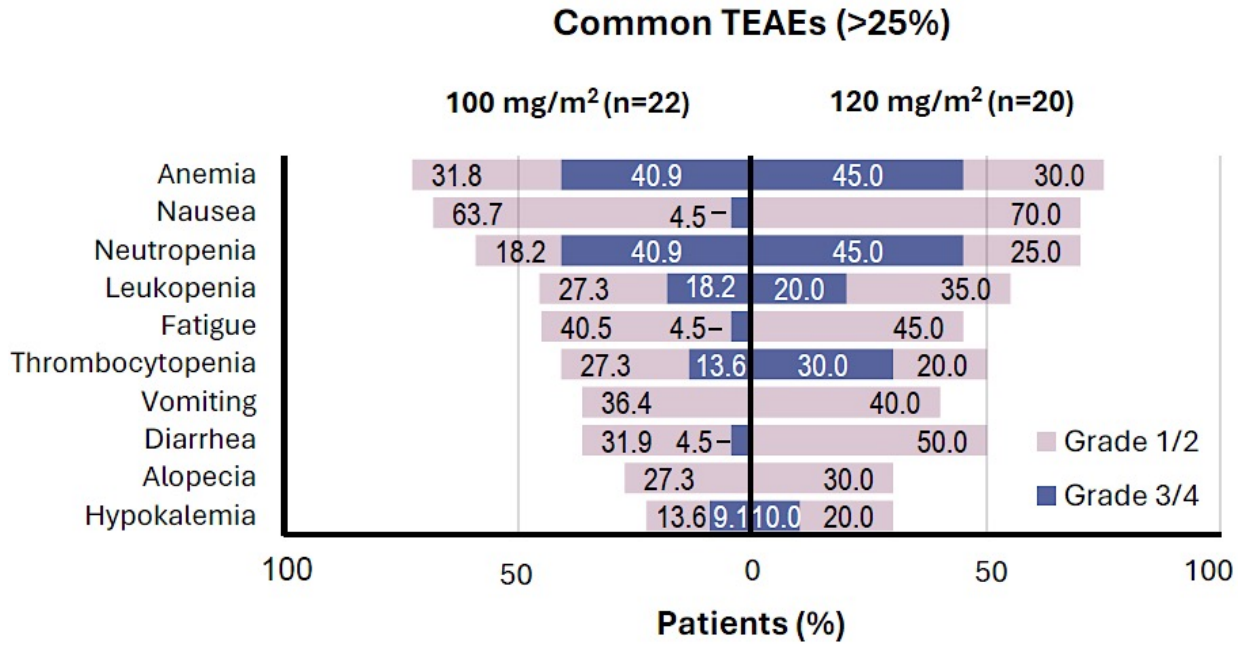
1. https://clinicaltrials.gov/study/NCT05579366. 2. Lee, EK et al. SGO 2025 Abstract #809034

Targeting FRα: RAINFOL-01 Phase 1/2 Study (NCT05579366)

Responses Over Time



Complete responses observed in 4 patients (2 pending confirmation) with Rina-S 120 mg/m²
Most responses with Rina-S 120 mg/m² were early and durable (one PD in responders since prior report[1])



Rina-S was well tolerated with TEAEs of primarily cytopenias and low-grade GI events
No signals of ocular toxicity, neuropathy, or ILD were observed

1. https://clinicaltrials.gov/study/NCT05579366. 2. Lee, EK et al. SGO 2025 Abstract #809034

Courtesy of Nicoletta Colombo, MD

RAINFOL-02: Overview and Study Design

Patients with PROC

Multicenter: 190 sites

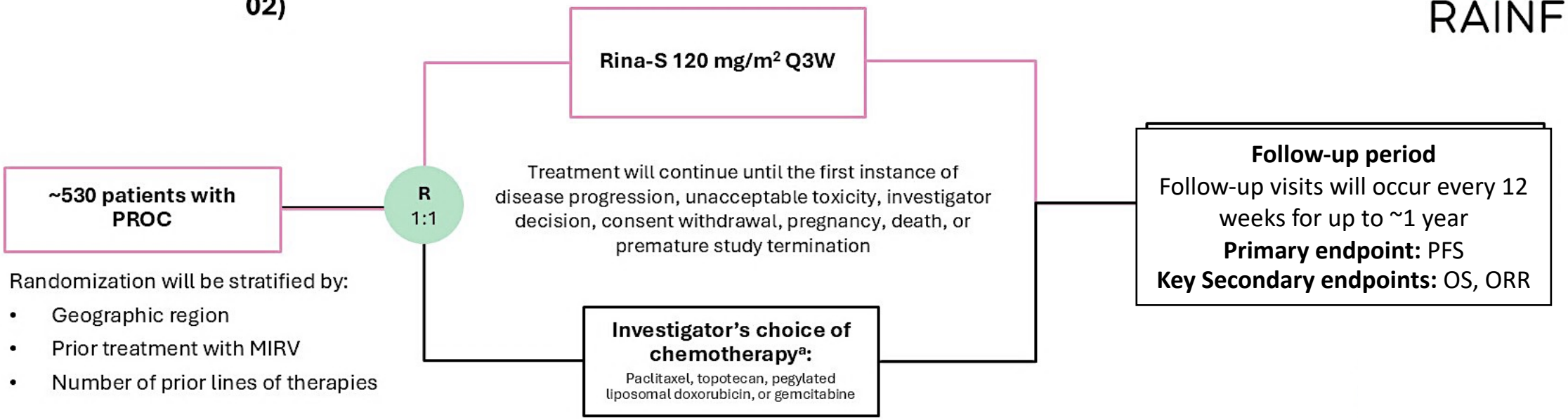
Open-label

International

1° Primary endpoint: PFS

Study Design for the Phase 3 Trial of Rina-S in Patients With PROC (RAINFOL-02)

RAINFOL™



Angeles Alvarez Secord presented at ASCO 2025;Abstract TPS5627

[a]Must be selected prior to randomization.
ORR, overall response rate; OS, overall survival; PFS, progression-free survival; PROC, platinum-resistant ovarian cancer; R, randomization; Rina-S, rinatabart sesutecan; Q3W, once every 3 weeks.

Courtesy of Nicoletta Colombo, MD

AZD5335: An FRα-targeting TOP1i ADC

- FRα is a cell surface protein that binds and internalises folate, a cofactor required for DNA synthesis, cell growth, and proliferation.[1–3]
- FRα is highly expressed in multiple epithelial tumours and a clinically validated ADC target in HGSOC.[2–4]
- AZD5335 is a specific, targeted ADC with a potent TOP1i payload (AZ14170132) that binds to FRα with high affinity.[5]
  - The cleavable peptide linker (mp-PEG8-Val-Ala) is bystander-capable and serum-stable.
  - AZD5335 has an average DAR of 8.

Schematic of AZD5335

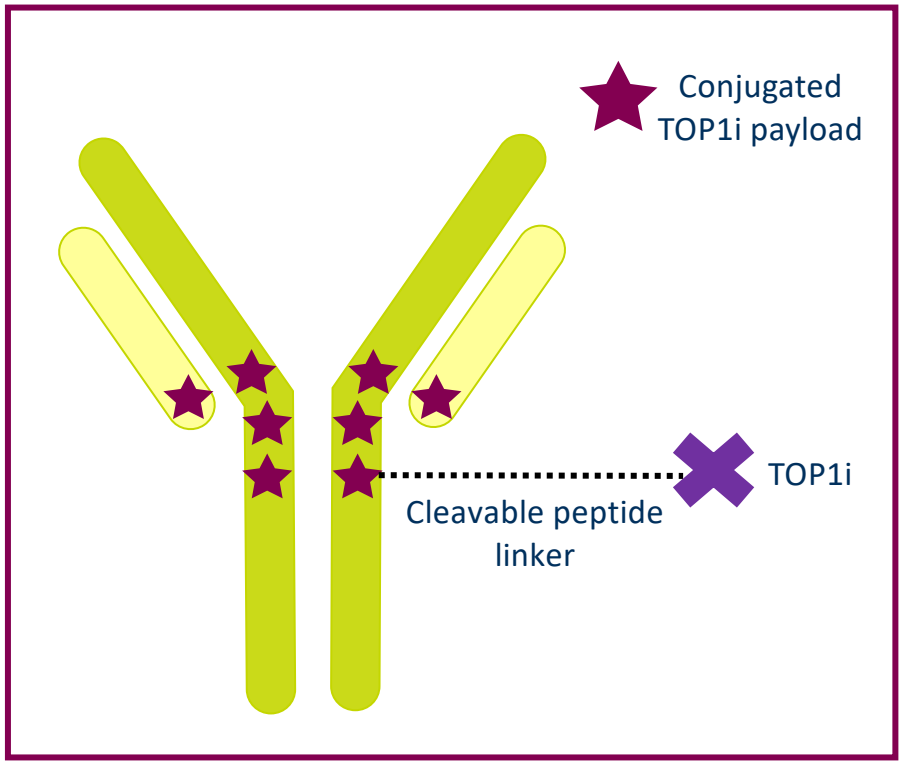


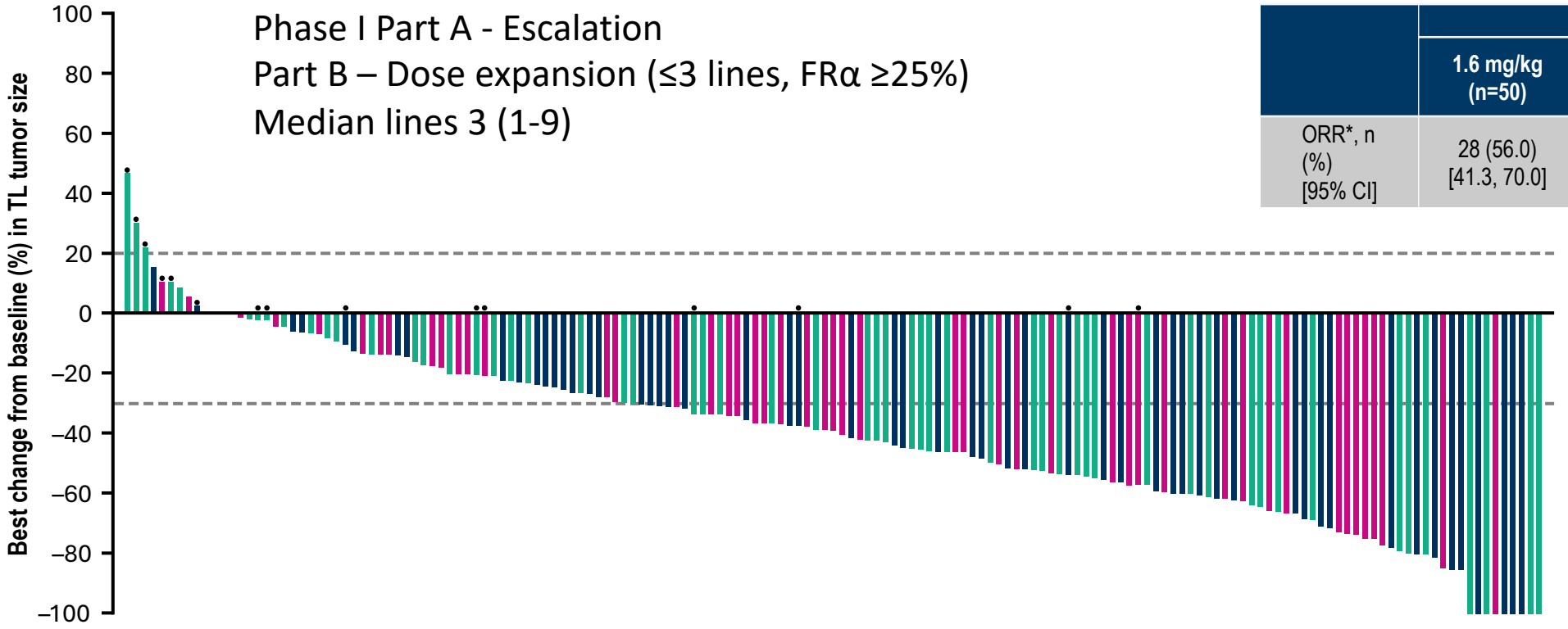
Figure adapted from Gymnopoulos M, et al. Presented at AACR 2023 (LB025).

ADC, antibody-drug conjugate; DAR, drug-to-antibody ratio; FRα, folate receptor α; OC, ovarian cancer; TOP1i, topoisomerase 1 inhibitor

1. Kelemen LE. *Int J Cancer* 2006;119:243–50;
2. Ledermann JA, et al. *Ann Oncol* 2015;26:2034–43;
3. Scaranti M, et al. *Nat Rev Clin Oncol* 2020;17:349–59;
4. Moore KN, et al. *N Engl J Med* 2023;389:2162–74;
5. Gymnopoulos M, et al. Poster presented at AACR 2023 (Abstract LB025).

Courtesy of Nicoletta Colombo, MD

AZD5335 demonstrates efficacy across 1.6–2.4 mg/kg dose range



	Parts A + B1		
	1.6 mg/kg (n=50)	2.0 mg/kg (n=57)	2.4 mg/kg (n=61)
ORR*, n (%) [95% CI]	28 (56.0) [41.3, 70.0]	32 (56.1) [42.4, 69.3]	30 (49.2) [36.1, 62.3]

Oaknin, ESMO 2025

Among patients who received 1.6, 2.0, or 2.4 mg/kg AZD5335 in Parts A + B1, the overall ORR* was 53.6% (95% CI: 45.7, 61.3).

The most common TEAEs across the 1.6–2.4 mg/kg dose range were nausea, fatigue, and neutropenia.

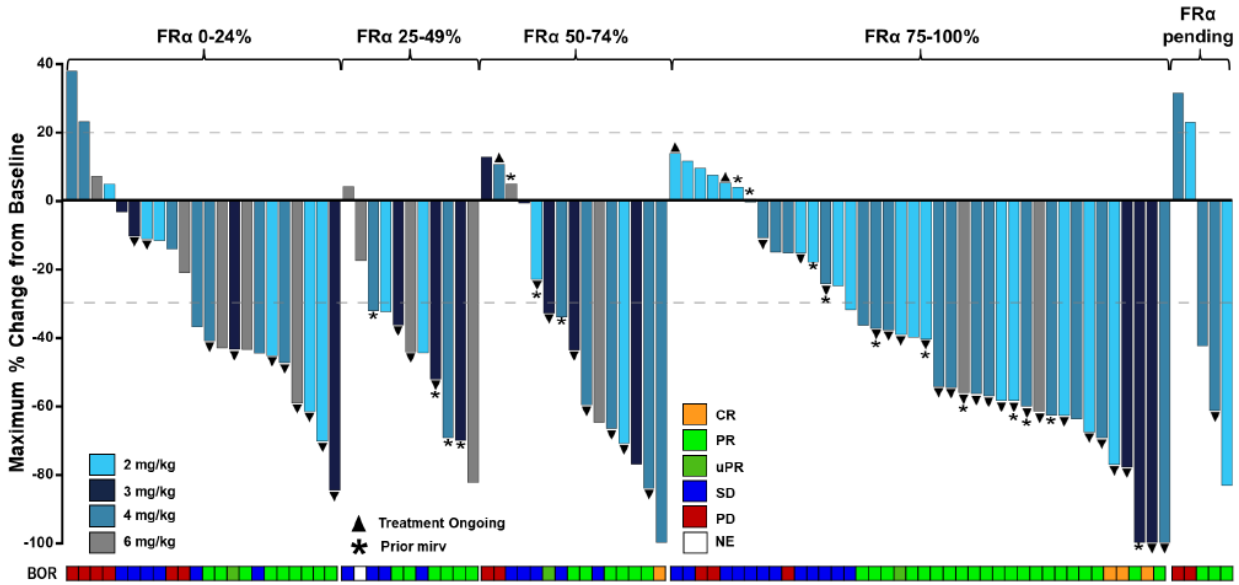
AZD5335 vs. Mirvetuximab Soravtansine in FRα-high and AZD5335 vs. Chemotherapy in FRα-low Platinum-resistant Ovarian Cancer (TREVI-OC-01) ClinicalTrials.gov ID NCT07218809

Courtesy of Nicoletta Colombo, MD

Sofetabart mipitecan (Sofe-M): FRα-binding Ab, cleavable PSAR linker, exatecan topo1i payload, DAR 8

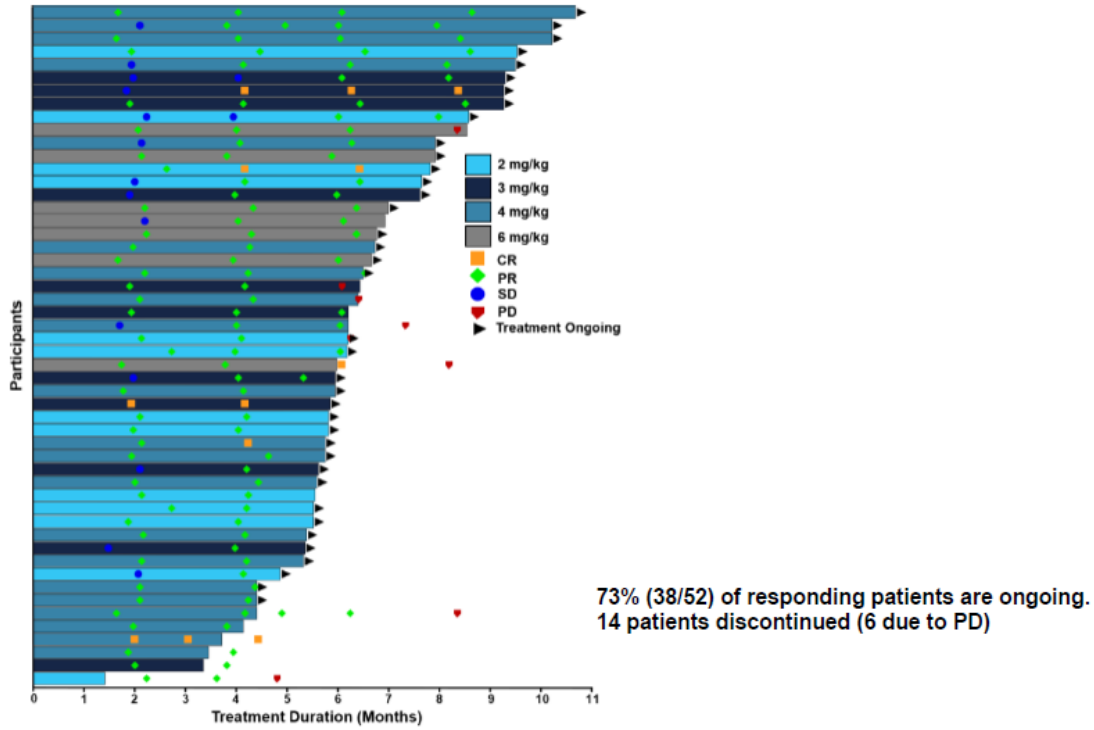
Initial results from a first-in-human phase 1 study of LY4170156 in advanced ovarian cancer and other solid tumors.

Fig 1. Antitumor activity by dose level and FRα expression



Efficacy Evaluable Patients	FRα 0-24% (n=25)	FRα 25-49% (n=12)	FRα 50-74% (n=16)	FRα ≥75% (n=46)	FRα pending (n=5)	Total (N=104)
ORR[a], % (n/N)	40 (10/25)	50 (6/12)	50 (8/16)	54 (25/46)	60 (3/5)	50 (52/104)
CR, n	-	-	1	3	-	4
PR, n	10[b]	6	7[b]	22[b]	3	48[c]
DCR[d], % (n/N)	68 (17/25)	83 (10/12)	81 (13/16)	83 (38/46)	60 (3/5)	78 (81/104)

Fig 2. Treatment Duration in Responders



73% (38/52) of responding patients are ongoing.
14 patients discontinued (6 due to PD)

Most common adverse events: Nausea, fatigue, myelotoxicity

Phase III FRAmework-01 NCT07213804

Ray-Coquard, ESMO 2025

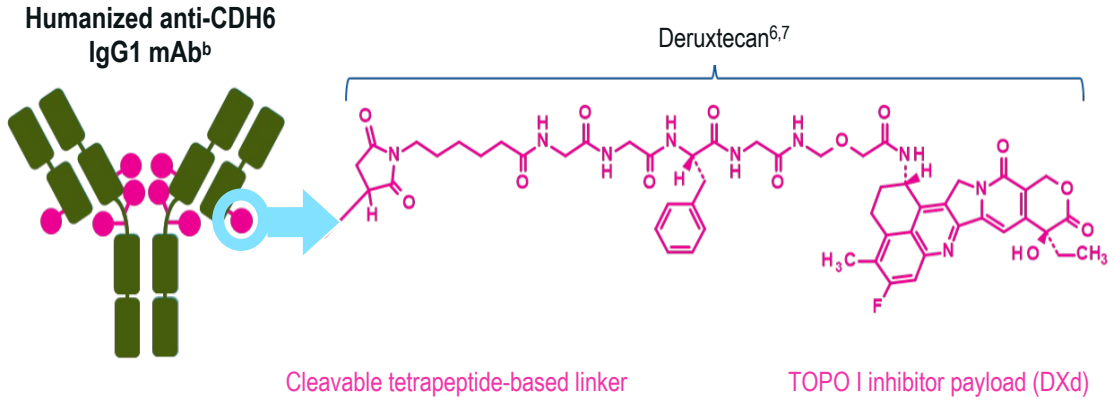
Courtesy of Nicoletta Colombo, MD

Courtesy of Nicoletta Colombo, MD

Targeting Cadherin 6 (CDH6)

- Platinum-resistant OC is associated with poor outcomes;[1,2] standard of care is single-agent non-platinum chemotherapy, which provides only a modest benefit; ORR is 10–15% and median OS is 10–12 months[1]
- Expression of CDH6 is observed in ~65 to 85% of epithelial OC tumors[3–5]
- Raludotatug deruxtecan (R-DXd) is a CDH6-directed ADC comprising a humanized CDH6 IgG1 mAb, covalently linked to a TOPO I inhibitor payload via a tetrapeptide-based cleavable linker[6,7]
- In the ongoing Phase 1 trial (NCT04707248), R-DXd demonstrated a manageable safety profile and promising antitumor activity in 45 patients with heavily pretreated OC (89% had platinum-resistant OC)[8,a]
- R-DXd was administered at 4.8, 5.6, or 6.4 mg/kg IV Q3W. Across doses, 48.6% of patients achieved a confirmed objective response[8]

R-DXd was designed with 7 key attributes:



1	Payload mechanism of action: TOPO I inhibitor[7,c]
2	High potency of payload[6,7,c]
3	High drug-to-antibody ratio of ≈8[6,c]
4	Payload with short systemic half-life[7,c,d]
5	Plasma-stable linker-payload[6,7,c]
6	Tumor-selective cleavable linker[6,7,c]
7	Bystander antitumor effect[6,c]

[a]Defined as TFIp <6 months. [b]Image is for illustrative purposes only; actual drug positions may vary. [b]The clinical relevance of these features is under investigation. [c]Based on animal data.
ADC, antibody–drug conjugate; CDH6, cadherin 6; DXd, exatecan derivative; IgG1, immunoglobulin G1; IV, intravenous; mAb, monoclonal antibody; OC, ovarian cancer; ORR, objective response rate; OS, overall survival; Q3W, every 3 weeks; TFIp, treatment-free interval from last platinum dose; TOPO I, topoisomerase I.

1. González-Martín A, et al. *Ann Oncol.* 2023;34:833–848. 2. Richardson DL, et al. JAMA Oncol. 2023;9:851–859; 3. Bartolomé RA, et al. Mol Oncol. 2021;15:1849–1865; 4. Shintani D, et al. Poster presentation at the European Society for Medical Oncology congress. October 20–24, 2023; Madrid, Spain. Presentation 777P. 5. Suzuki H, et al Poster presentation at the European Society for Medical Oncology congress. October 10–16, 2021; Virtual. Presentation #919. 6. Suzuki H, et al. *Mol Cancer Ther*. 2024;23:257–271. 7. Nakada T, et al. *Chem Pharm Bull (Tokyo)*. 2019;67:173–185. 8. Moore KN, et al. Oral presentation at the Society of Gynecologic Oncology 2024 Annual Meeting on Women's Cancer. March 16–18, 2024; San Diego, CA, USA.

Courtesy of Nicoletta Colombo, MD

REJOICE-Ovarian01 study design

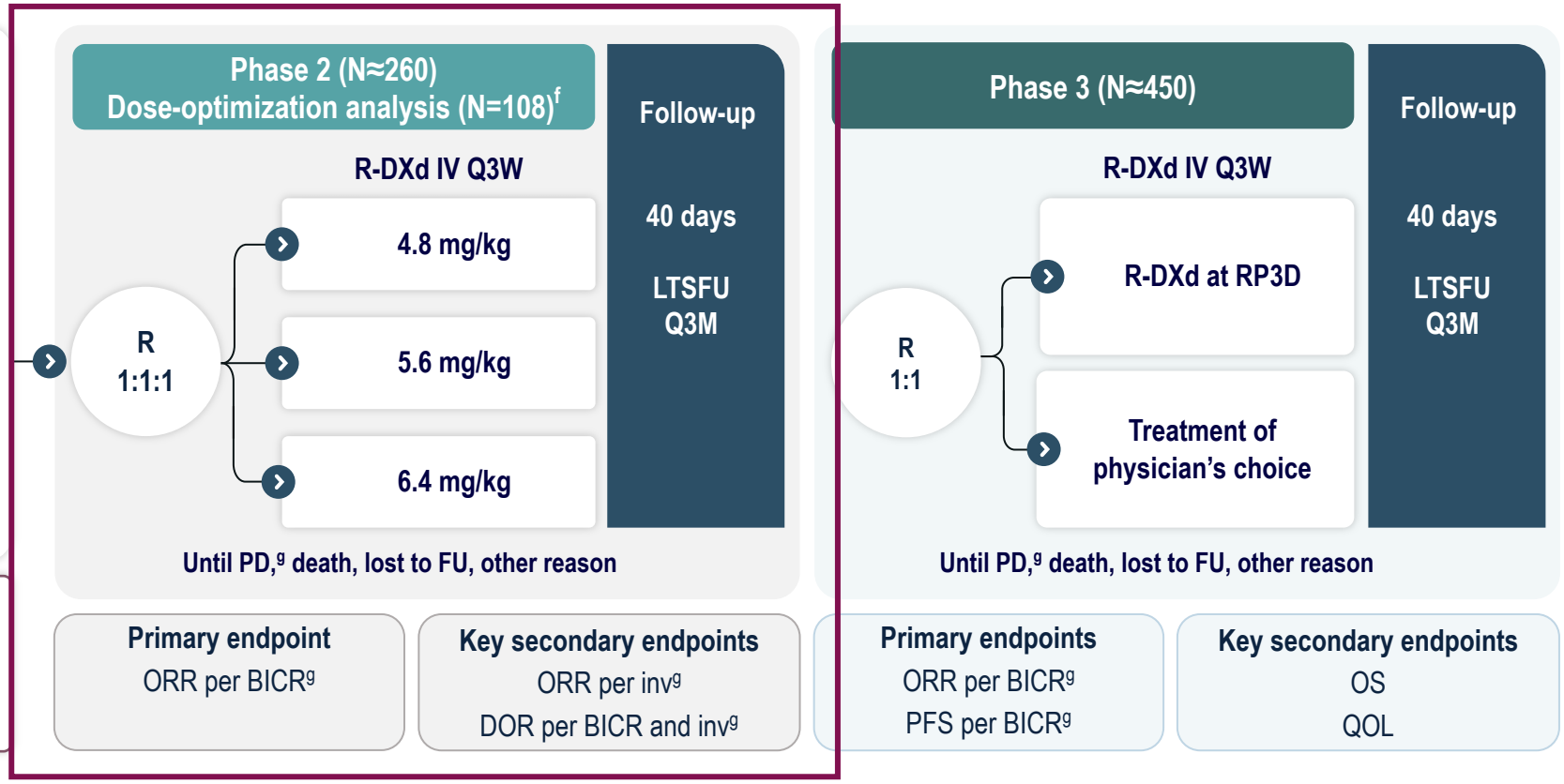
A Phase 2/3 multicenter, randomized study of R-DXd in patients with platinum-resistant, high-grade serous or endometroid ovarian, primary peritoneal, or fallopian tube cancer[1,2]

Key eligibility criteria

- High-grade serous or high-grade endometrioid ovarian, primary peritoneal, or fallopian tube cancer[a]
- 1–3 prior LOT, including bevacizumab[b]
- Platinum-resistant disease[c] (primary platinum-refractory disease is exclusionary)
- Prior mirvetuximab soravtansine[d] (for tumors with high FRα expression)
- ECOG PS 0–1
- No prior CDH6-targeting agents or ADCs with a linked exatecan derivative
- No selection by tumor CDH6 expression

Stratification factors

- Number of prior LOT (1 vs 2–3)
- CDH6 expression (≥75% vs <75%)[e]
- TPC (paclitaxel vs other; Phase 3 only)



Primary endpoint
ORR per BICR[g]

Key secondary endpoints
ORR per inv[g]
DOR per BICR and inv[g]

Primary endpoints
ORR per BICR[g]
PFS per BICR[g]

Key secondary endpoints
OS
QOL

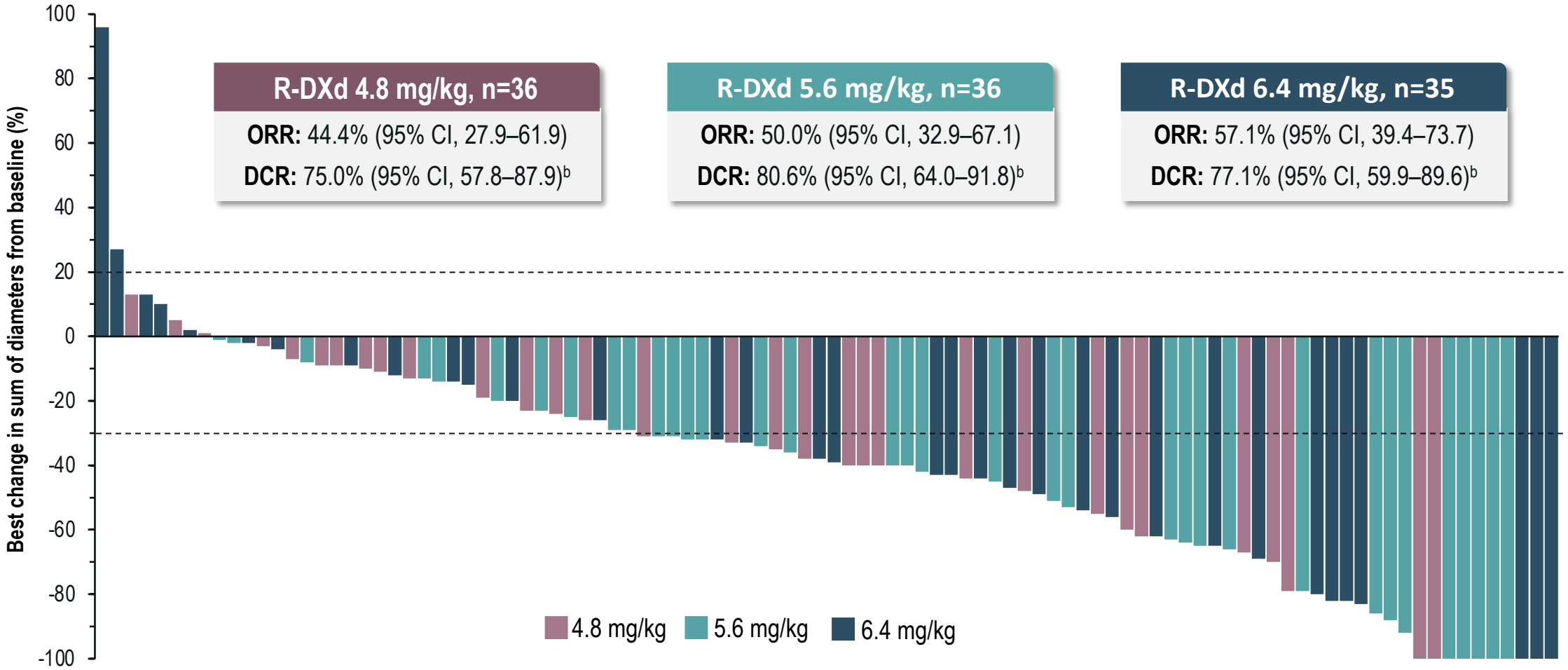
[a]Patients must have ≥1 lesion not previously irradiated and amenable to biopsy; must consent to provide a pretreatment biopsy and, in Phase 2 only, an on-treatment biopsy tissue sample and have ≥1 measurable lesion per RECIST 1.1. [b]Unless ineligible. [c]Defined as 1 line of prior platinum therapy (≥4 cycles with best response of not PD) with radiologically documented progression >90 and ≤180 days following last dose of platinum therapy, or 2–3 lines of prior platinum therapy (≥2 cycles) with radiologically documented progression ≤180 days following the last dose of platinum. [d]Unless ineligible, not approved or not available locally. [e]A stratification cutoff of 75% tumor cell membrane staining at any intensity was selected based on the median observed percentage tumor cell membrane staining (at any intensity) in the Phase 1 study population.[3] [f]Overall, 108 patients were randomized to receive R-DXd. One patient did not receive treatment, so 107 patients were treated and were included in the safety analysis set. [g]Per RECIST 1.1.
ADC, antibody–drug conjugate; BICR, blinded independent central review; CDH6, cadherin 6; DOR, duration of response; ECOG PS, Eastern Cooperative Oncology Group performance status; FRα, folate receptor alpha; FU, follow-up; IV, intravenous; inv, investigator; LOT, lines of therapy; LTSFU, long-term survival follow up; ORR, objective response rate; OS, overall survival; RP3D, recommended phase 3 dose; PD, progressive disease; Q3M, every 3 months; QOL, quality of life; Q3W, every 3 weeks; R, randomization; RECIST 1.1, Response Evaluation Criteria in Solid Tumours version 1.1; TPC, treatment of physician's choice.

1. ClinicalTrials.gov. https://clinicaltrials.gov/study/NCT06161025. Accessed 26 June 2025. 2. Ray-Coquard I, et al. Poster presentation at American Society Clinical Oncology 2024; May 31–June 4; Chicago, IL, USA. Poster TPS5625. 3. Moore KN, et al. Oral presentation at the Society of Gynecologic Oncology 2024 Annual Meeting on Women's Cancer. March 16–18, 2024; San Diego, CA, USA.

Ray-Coquard, ESMO 2025

Courtesy of Nicoletta Colombo, MD

Clinically meaningful tumor responses were seen irrespective of dose[a]



Data cutoff: February 26, 2025. The median follow-up for 4.8-mg/kg, 5.6-mg/kg, and 6.4-mg/kg cohorts was 5.6 months (95% CI, 4.7–6.3), 5.6 months (95% CI, 4.6–5.8), and 5.2 months (95% CI, 4.9–5.8), respectively.

[a]Antitumor response assessed by BICR per RECIST 1.1. Only patients with measurable disease at baseline and ≥1 post-baseline tumor scan, both by BICR, were included in the waterfall plot (n=100). Six patients (R-DXd 4.8 mg/kg [n=5]; 6.4 mg/kg [n=1]) did not have measurable disease at baseline and one patient (R-DXd 5.6 mg/kg) had no adequate post-baseline tumor assessment. [b]DCR is defined as percentage of patients with BOR of CR, PR, or SD (per RECIST 1.1).

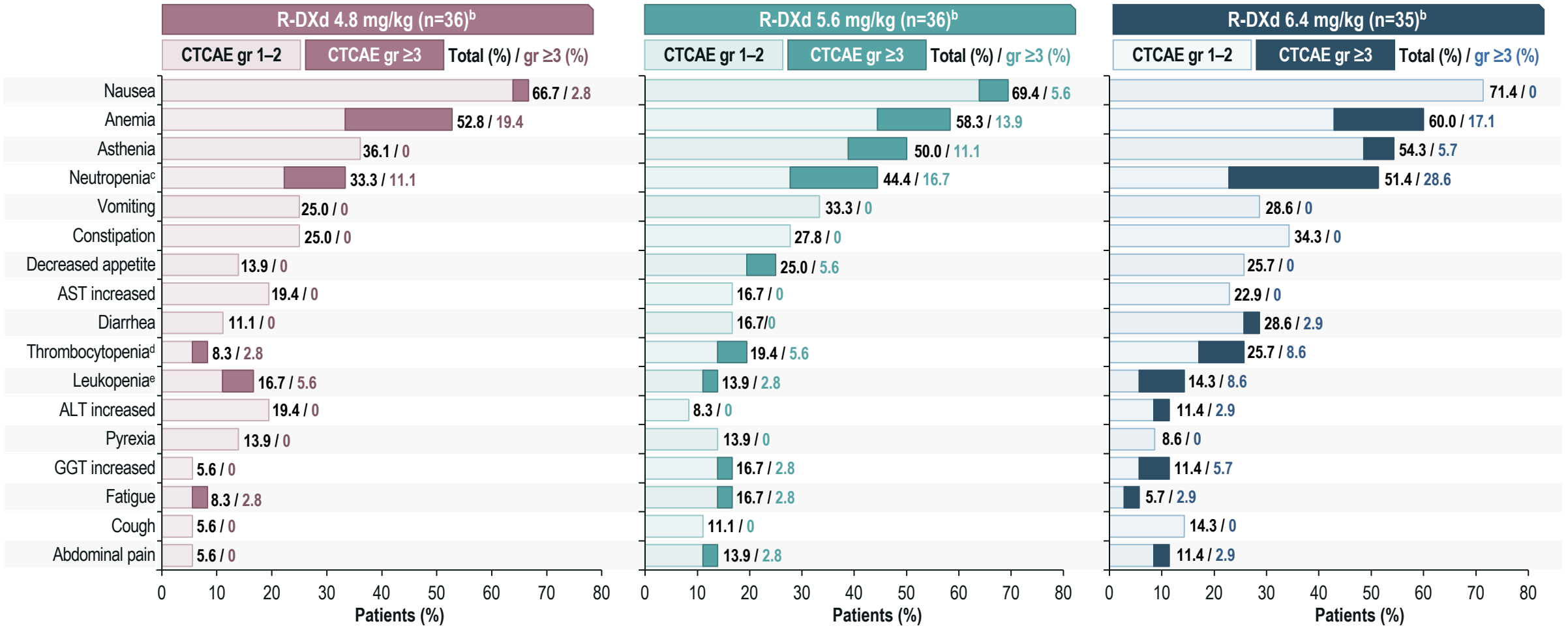
BICR, blinded independent central review; CI, confidence interval; DCR, disease control rate; ORR, objective response rate; RECIST 1.1, Response Evaluation Criteria in Solid Tumours version 1.1.

Ray-Coquard, ESMO 2025

The 5.6-mg/kg dose provided the optimal benefit–risk profile

Most common TEAEs (≥10% of overall population)[a]

Courtesy of Nicoletta Colombo, MD



Nausea, anemia, asthenia and neutropenia were the most common TEAEs across all doses

Data cutoff: February 26, 2025.

[a]TEAEs reported in ≥10% of all patients who received R-DXd 4.8–6.4 mg/kg. Reported safety events are defined by MedDRA preferred terminology. [b]Grade 4 hematologic TEAEs reported at 4.8 mg/kg: neutropenia[c] (n=2), thrombocytopenia[d] (n=1); at 5.6 mg/kg: neutropenia[c] (n=2), thrombocytopenia[d] (n=1), leukopenia[e] (n=1); at 6.4 mg/kg: neutropenia[c] (n=3), thrombocytopenia[d] (n=1), lymphopenia (n=1). No grade 5 hematologic TEAEs were reported at any dose. Grade 3 febrile neutropenia was reported in 2 patients, one each in the R-DXd 5.6 and 6.4 mg/kg cohorts. [c]Neutropenia is defined as the grouped incidence of events reported under the preferred terms '*neutropenia*' and '*neutrophil count decreased*', with a maximum of one event per patient per grouped preferred term. [d]Thrombocytopenia is defined as the grouped incidence of events reported under the preferred terms '*thrombocytopenia*' and '*platelet count decreased*', with a maximum of one event per patient per grouped preferred term. [e]Leukopenia is defined as the preferred term '*white blood cell count decreased.*'

ALT, alanine aminotransferase; AST, aspartate aminotransferase; CTCAE, Common Terminology Criteria for Adverse Events; GGT, gamma-glutamyltransferase; MedDRA, Medical Dictionary for Regulatory Activities; TEAE, treatment-emergent adverse event.

Ray-Coquard, ESMO 2025

REJOICE-Ovarian01: Efficacy of R-DXd in PROC

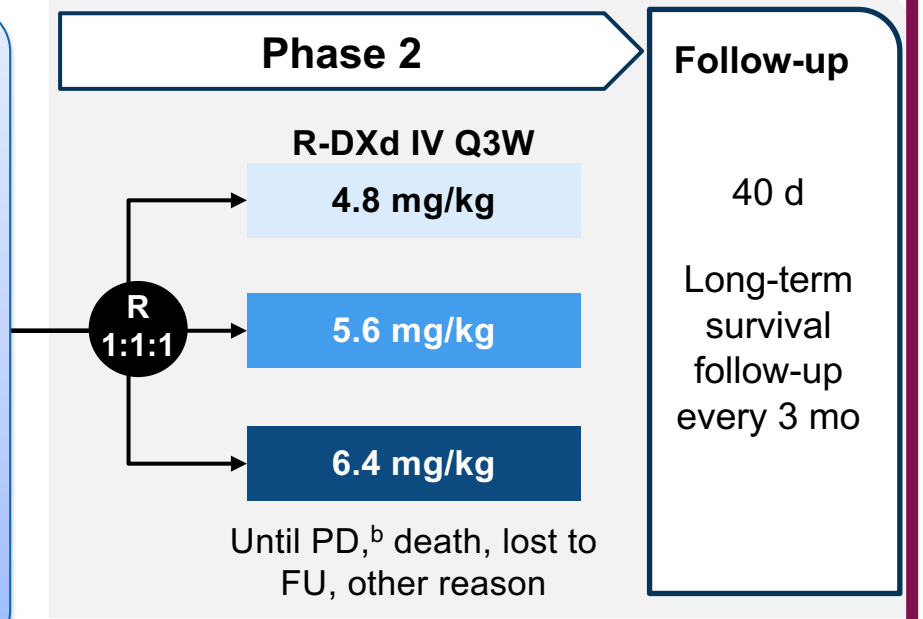
Phase 2/3 REJOICE-Ovarian01/ENGOT-ov77; GOG-3096

Key Eligibility Criteria

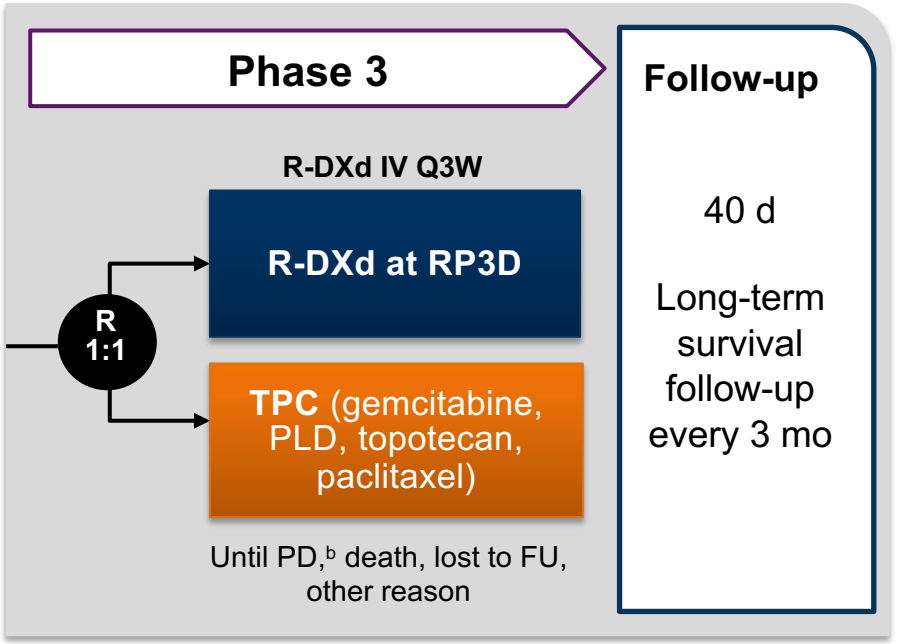
- High-grade serous or endometrioid ovarian, primary peritoneal, or fallopian tube cancer
- 1-3 prior LOT (including bevacizumab)
- Platinum-resistant disease
- Prior MIRV if high FRα[a]
- ECOG PS 0-1
- No prior CDH6-targeting agents or ADCs with linked TOPO I inhibitor
- Patients with primary platinum-refractory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

Stratification

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



- **Primary endpoint:** ORR per BICR[b]
- **Key secondary endpoints:** ORR per investigator,[b] DOR



- **Primary endpoints:** ORR per BICR,[b] PFS per BICR[b]
- **Key secondary endpoints:** OS, QOL

[a] Unless ineligible, not approved, or available locally. [b] Per RECIST v1.1.

1. https://clinicaltrials.gov/study/NCT06161025.

Courtesy of Nicoletta Colombo, MD

Raludotatug Deruxtecan Granted FDA Breakthrough Therapy Designation for CDH6-Expressing Platinum-Resistant Ovarian, Primary Peritoneal or Fallopian Tube Cancers Previously Treated with Bevacizumab

Press Release: September 15, 2025

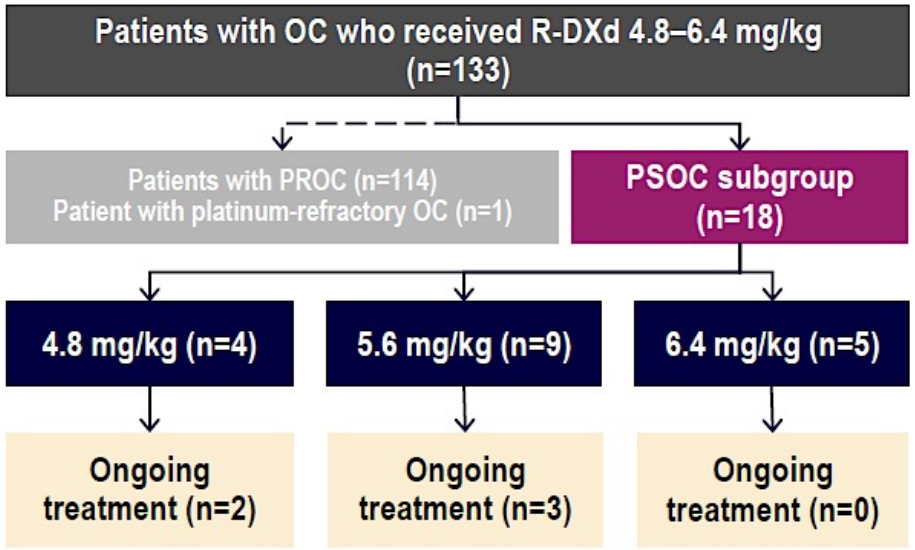
"Raludotatug deruxtecan (R-DXd) has been granted Breakthrough Therapy Designation (BTD) by the U.S. Food and Drug Administration (FDA) for the treatment of adult patients with platinum-resistant epithelial ovarian, primary peritoneal or fallopian tube cancers expressing CDH6 who have received prior treatment with bevacizumab.

The FDA granted this BTD based on data from a phase 1 trial and the ongoing REJOICE-Ovarian01 phase 2/3 trial. A subgroup analysis of the phase 1 trial was presented at the 2023 European Society for Medical Oncology meeting (#ESMO23). Subsequent subgroup analyses of the phase 1 trial were presented at the 2024 Society for Gynecologic Oncology Annual Meeting on Women's Cancer and the 2025 European Society for Medical Oncology Gynaecological Cancers Congress."

https://daiichisankyo.us/press-releases/-/article/raludotatug-deruxtecan-granted-breakthrough-therapy-designation-by-us-fda-for-patients-with-cdh6-expressing-platinum-resistant-ovarian-primary-peritoneal-or-fallopian-tube-cancers-previously-treated-with-bevacizumab

REJOICE-Ovarian01: Efficacy of R-DXd in PSOC

	PSOC subgroup 4.8–6.4 mg/kg[a] n=18
Age, years, median (range)	65 (50–81)
Age ≥65 years, n (%)	9 (50.0)
Country, n (%)	
United States	14 (77.8)
Japan	4 (22.2)
ECOG PS, n (%)	
0	4 (22.2)
1	14 (77.8)
Number of prior systemic regimens, median (range)	4 (2–6)
Received prior bevacizumab treatment, n (%)	14 (77.8)
Received prior PARP inhibitor treatment, n (%)	15 (83.3)
Disease progression on PARP inhibitor,[b] n/N (%)	12/15 (80.0)
Tumor CDH6 membrane positivity,[c] median % (range)	67.5 (20–100)



- In total, 13 patients (72.2%) have discontinued study treatment, including:
  - 9 patients (50.0%) with PD[d]
  - 3 patients (16.7%) with adverse events[e]
  - 1 patient (5.6%) with clinical progression
- The median duration on study treatment was 6.9 months (range, 0.7–12.2)

Data cutoff: January 10, 2025.

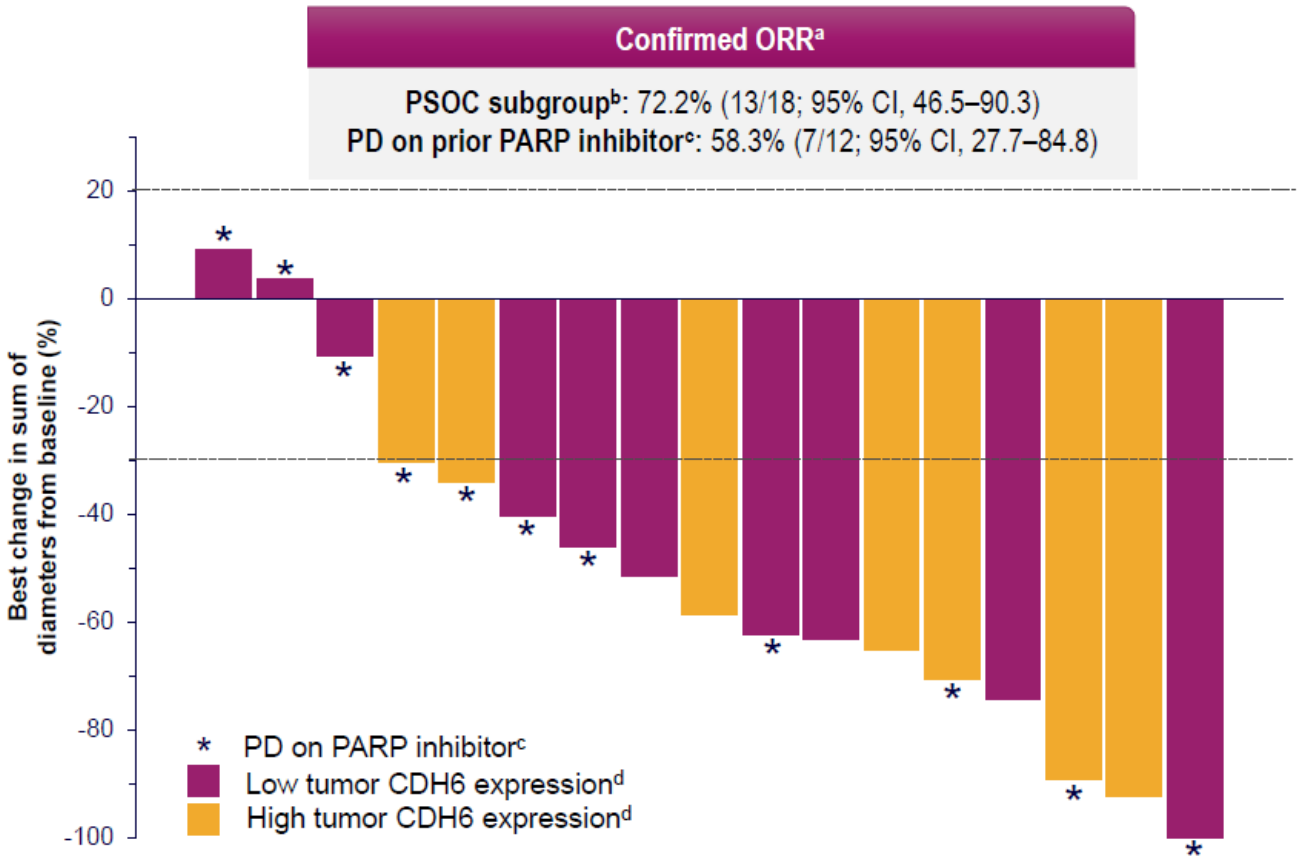
[a]Only patients with PSOC (TFIp ≥6 months) and treated with ≥1 dose of R-DXd 4.8–6.4 mg/kg were included in the PSOC subgroup analysis. [b]PD on or within ≤30 days of prior PARP inhibitor treatment . [c]Total positive staining for CDH6 membrane expression is determined by clinical trial assay for CDH6 (SP450; Roche Diagnostics). [d]Per RECIST 1.1. [e]Discontinuations due to adverse events were due to increased ALT and AST (n=1), cardiac arrest (n=1), and ILD (n=1).

ALT, alanine aminotransferase; AST, aspartate aminotransferase; CDH6, cadherin 6; ECOG PS, Eastern Cooperative Oncology Group performance status; ILD, interstitial lung disease; OC, ovarian cancer; PARP, poly (ADP-ribose) polymerase; PD, progressive disease; PROC, platinum-resistant OC; PSOC, platinum-sensitive OC; RECIST 1.1, Response Evaluation Criteria in Solid Tumours, version 1.1; TFIp, treatment-free interval from last platinum dose.

Kathleen Moore, ESMO GYN 2025

Courtesy of Nicoletta Colombo, MD

REJOICE-Ovarian01: Efficacy of R-DXd in PSOC



	PSOC subgroup 4.8–6.4 mg/kg n=18	PD on PARP inhibitor[c] n=12
Best overall response,[e] n (%)		
CR	0	0
PR	13 (72.2)	7 (58.3)
SD	3 (16.7)	3 (25.0)
PD	1 (5.6)	1 (8.3)
Not evaluable	1 (5.6)	1 (8.3)
Disease control rate,[f] % (95% CI)	88.9 (65.3–98.6)	83.3 (51.6–97.9)
Clinical benefit rate,[g] % (95% CI)	77.8 (52.4–93.6)	66.7 (34.9–90.1)
Median TTR, months, (95% CI)	1.4 (1.2–2.7)	1.4 (1.2–NE)
Median DOR, months, (95% CI)	5.7 (4.2–NE)	5.1 (2.8–NE)
Median follow-up, months (range)	6.9 (1.6–10.5)	6.9 (1.6–6.9)
Median PFS, months, (95% CI)	8.1 (4.1–NE)	7.1 (2.8–NE)
Median follow-up, months (range)	8.3 (0–11.7)	8.3 (0–11.4)

Data cutoff: January 10, 2025.

Only patients with measurable disease at baseline and ≥1 postbaseline tumor scan were included in the waterfall plot. One patient who received R-DXd 6.4 mg/kg had a target lesion at baseline but no postbaseline scan, so was not evaluable.
[a]ORR by investigator is shown. [b]Efficacy-evaluable population (n=18) includes all patients with PSOC who received ≥1 dose of R-DXd and have completed ≥1 postbaseline tumor assessment or discontinued from treatment due to AE, PD, or death prior to the first postbaseline tumor assessment. [c]PD during or ≤30 days following completion of PARP inhibitor treatment. [d]Tumor CDH6 expression is defined as <75% (low) or ≥75% (high); total tumor cells positive for CDH6 membrane staining is determined by clinical trial assay for CDH6 (SP450; Roche Diagnostics). [e]Best overall response of CR or PR (per RECIST 1.1) must be confirmed and maintained ≥28 days. [f]CR + PR + SD (per RECIST 1.1) ≥5 weeks. [g]CR + PR + SD (per RECIST 1.1) ≥180 days.
AE, adverse event; CDH6, cadherin 6; CI, confidence interval; CR, complete response; DOR, duration of response; NE, not estimable; ORR, objective response rate; PARP, poly (ADP-ribose) polymerase; PD, progressive disease; PFS, progression-free survival; PR, partial response; PSOC, platinum-sensitive ovarian cancer; RECIST 1.1, Response Evaluation Criteria in Solid Tumours, version 1.1; SD, stable disease; TTR, time to response.

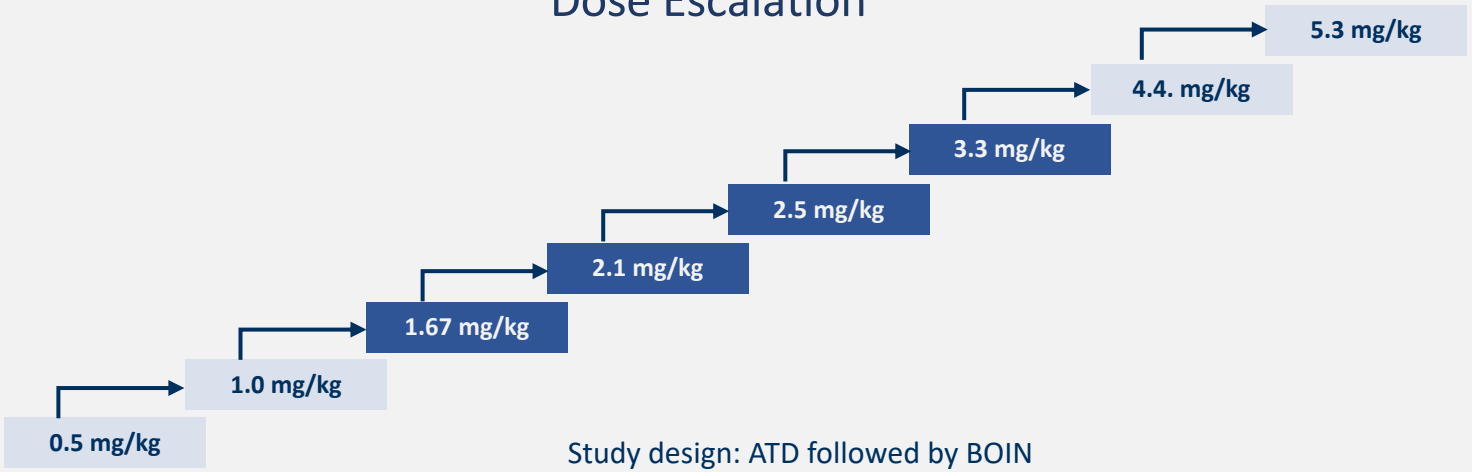
Kathleen Moore, ESMO GYN 2025

Courtesy of Nicoletta Colombo, MD

NAPISTAR 1-01: Study Design

A multicenter, FIH dose escalation and optimization Phase I/IIa Study (NCT06303505), investigating the NaPi2b ADC TUB-040 in PROC*

Phase I
Dose Escalation



Study design: ATD followed by BOIN

Phase IIa
Dose Optimization

- Dose 1
- Dose 2

Key Eligibility Criteria

- Histologically confirmed, platinum resistant, high-grade serous epithelial ovarian, fallopian tube or primary peritoneal cancer
- A maximum of 5 platinum-based and 2 non-platinum prior lines of therapy
- ECOG 0-1
- No prior treatment with an ADC containing a TOPO-I inhibitor payload
- No biomarker selection based on NaPi2b expression

Objectives and Endpoints

- Safety and tolerability
- Determination of MTD
- ORR per RECIST 1.1, DCR, DoR, PFS and OS
- PK parameters of TUB-040
- Immunogenicity
- Quality of life

* NAPISTAR 01-1 also includes an NSCLC arm, which is currently being explored independently from the PROC arm. Cut off: 01 September 2025. ADAs, anti-drug antibodies; ADC=antibody-drug conjugate; ATD, accelerated titration dosing; BOIN, Bayesian optimal interval; DCR, disease control rate; DoR, duration of response; FIH, first-in-human; MTD, maximum tolerated dose; NaPi2b, sodium-dependent phosphate transporter protein 2B; NSCLC, non-small cell lung cancer; ORR, overall response rate; OS, overall survival; PBC, platinum-based chemotherapy; PFS, progression-free survival; PK, pharmacokinetics; PROC, platinum-resistant ovarian cancer.

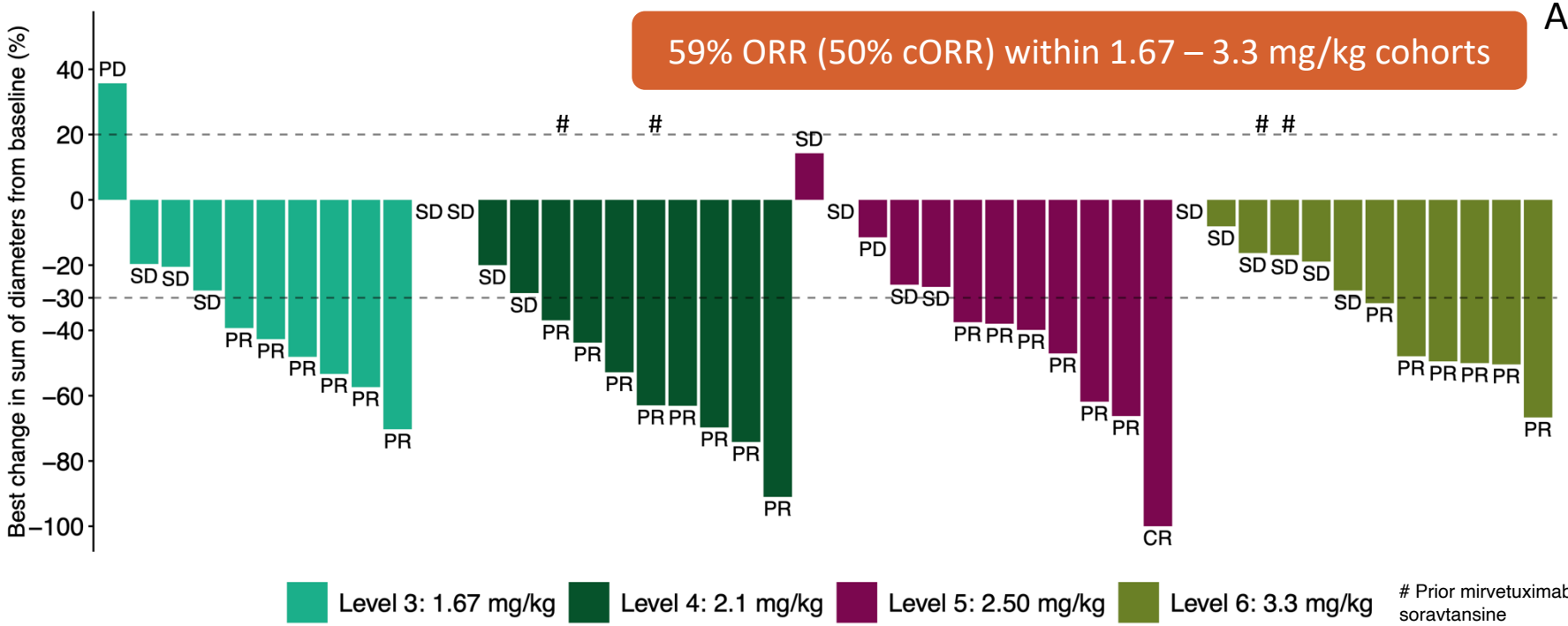
Antonio Gonzalez-Martin, ESMO 2025

Courtesy of Nicoletta Colombo, MD

Efficacy across a wide therapeutic range with complete responses

Antonio Gonzalez-Martin, ESMO 2025

59% ORR (50% cORR) within 1.67 – 3.3 mg/kg cohorts



Across 1.67 – 3.3 mg/kg:

- Onset of activity at low doses
- Complete response observed
- CA125 response rate[4] 81%
- 93% (25/27) of responding patients are ongoing
- 80% (37/46) of patients remain on treatment, indicating durable benefit

Efficacy	Dose Levels					All evaluable patients
	1.67 mg/kg (n=10)	2.1 mg/kg (n=12)	2.5 mg/kg (n=12)	3.3 mg/kg (n=12)	1.67-3.3 mg/kg (n=46)	0.5 – 5.3 mg/kg (n=66)[1]
ORR[2] n (%)	6 (60)	8 (67)	7 (58)	6 (50)[3]	27 (59)	36 (55)
Confirmed ORR, n (%)	4 (40)	7 (58)	7 (58)	5 (42)	23 (50)	26 (39)
DCR n (%)	9 (90)	12 (100)	11 (92)	12 (100)	44 (96)	64 (97)
Confirmed DCR, n (%)	9 (90)	12 (100)	11 (92)	12 (100)	44 (96)	60 (91)
Confirmed CR, n (%)	0	0	1 (8)	0	1 (2)	1 (2)

1. N=66 evaluable patients who had at least 1 RECIST response assessment across doses from 0.5 – 5.3 mg/kg. There were no responses observed at doses below 1.67 mg/kg. 2. Responses of PR/CR per RECIST at a minimum of 1 post-baseline assessment. 3. Efficacy data in patients treated at 3.3 mg/kg continue to mature. 4. CA125 responses determined per GCIG; 34 responders in 42 CA125 evaluable subjects. CR, complete response; DCR, disease control rate; PR, partial response; SD, stable disease. Data Cut off: 01 September 2025.

Courtesy of Nicoletta Colombo, MD

Platinum Ineligible Ovarian Cancer

ANTIBODY DRUG CONJUGATED (ADCS)

Mirvetuximab-soravtansine [1]

Trastuzumab-deruxtecan [2]

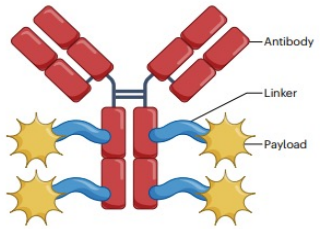
Raludotatug- Deruxtecan [3]

Rinatabart Sesutecan (Rina-S)[4]

AZD5335 [5]

Ly4170156 [6]

NAPISTAR 1-01 [7]

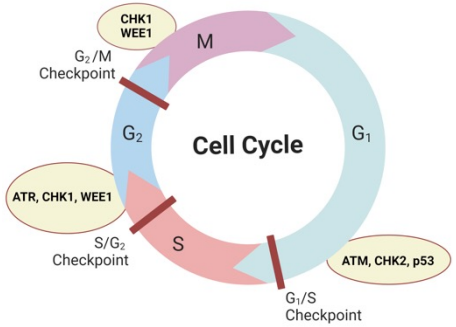


CELL CYCLE REGULATION AND DNA REPAIR

ADAVOSERTIB [8]

azenosertib[9]

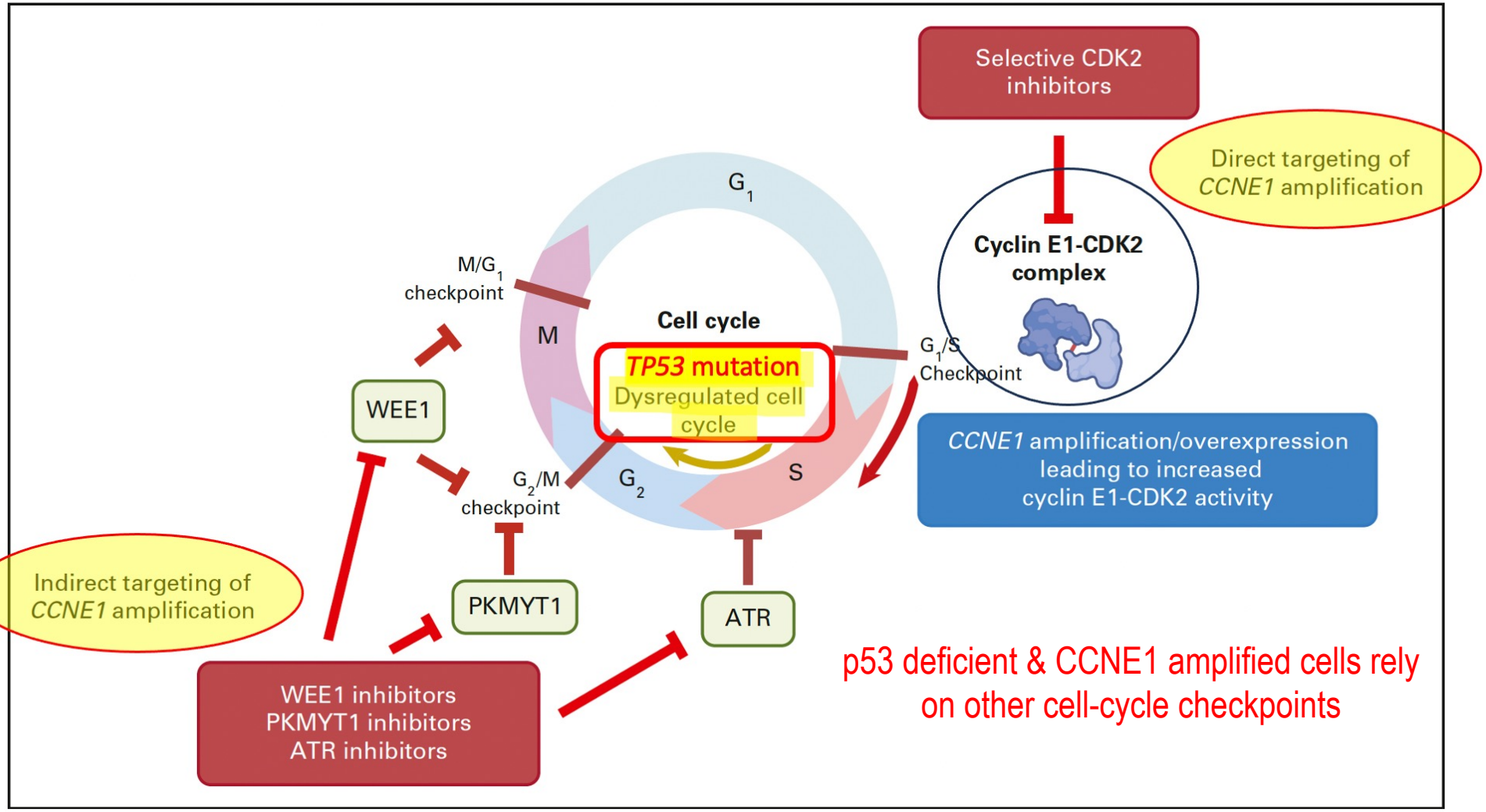
CDK2i [10]



[1] [NCT04296890 – Soraya] [NCT04209855 – Mirasol]; [2] [NCT04482309]; [3] [NCT04707248]; [4] [NCT06619236]; [5] [NCT05797168] ; [6] [NCT06400472]; [7] [NCT06303505]; [8] [NCT03579316]; [9] [NCT02595892]; [10] [INCB123667]; [11] [NCT05116189]; [12] [NCT03564340] [13] [NCT05257408 – Rosella]; [NCT03776812 – phase II];

Courtesy of Nicoletta Colombo, MD

EXPLOITING REPLICATION STRESS IN *CCNE1* AMPLIFIED TUMOURS



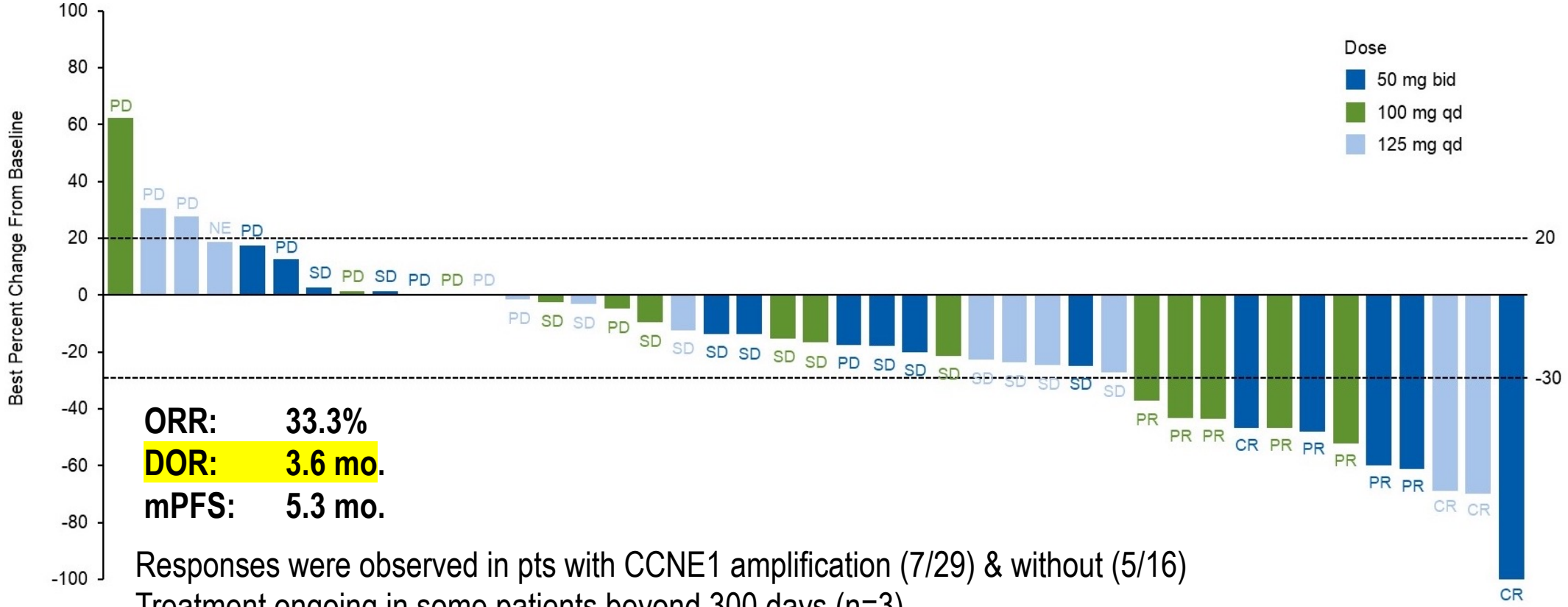
Au-Yeung G etal., JCO 2023

Courtesy of Nicoletta Colombo, MD

DIRECT TARGETING OF CCNE1

CDK2-inhibitors in Platinum Resistant/Refractory Ovarian cancer

INCB123667: Phase 1B, CCNE1 amplified or overexpressed EOC (n=45)



ORR: **33.3%**

DOR: **3.6 mo.**

mPFS: **5.3 mo.**

Responses were observed in pts with CCNE1 amplification (7/29) & without (5/16)

Treatment ongoing in some patients beyond 300 days (n=3)

Good tolerability

Damian S et al., ASCO 2025 abstract #5514

Damian S et al., Journal of Clinical Oncology 2025 Vol. 43 Issue 16_suppl Pages 5514-5514

Courtesy of Nicoletta Colombo, MD

Platinum Ineligible Ovarian Cancer

ANTIBODY DRUG CONJUGATED (ADCS)

Mirvetuximab-soravtansine [1]

Trastuzumab-deruxtecan [2]

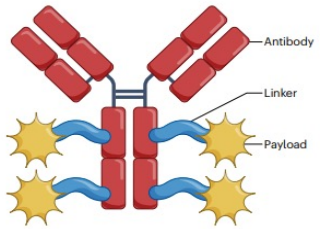
Raludotatug- Deruxtecan [3]

Rinatabart Sesutecan (Rina-S)[4]

AZD5335 [5]

Ly4170156 [6]

NAPISTAR 1-01[7]

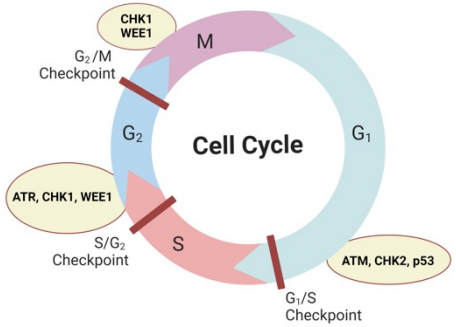


CELL CYCLE REGULATION AND DNA REPAIR

ADAVOSERTIB [8]

azenosertib[9]

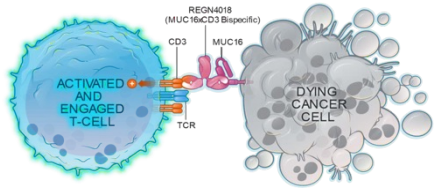
CDK2i [10]



IMMUNOTHERAPY

Paclitaxel/pembro [11]

UBAMATAMAB [12]



[1] [NCT04296890 – Soraya] [NCT04209855 – Mirasol]; [2] [NCT04482309]; [3] [NCT04707248]; [4] [NCT06619236]; [5] [NCT05797168] ; [6] [NCT06400472]; [7] [NCT06303505]; [8] [NCT03579316]; [9] [NCT02595892]; [10] [INCB123667]; [11] [NCT05116189]; [12] [NCT03564340] [13] [NCT05257408 – Rosella]; [NCT03776812 – phase II];

Courtesy of Nicoletta Colombo, MD

Immune Checkpoint Inhibitors In Ovarian Cancer: Phase 3 Evidence

1st-Line				
• JAVELIN-10				X
• IMAgyn050				X
• DUO-O			ARPi	X
• ATHENA Co			ARPi	X
• FIRST			ARPi	?
• KEYLINK 001			ARPi	X
„Platin-sensitiv				
• ATALANTE				X
• ANITA			ARPi	X
„Platin-resistan				
• JAVELIN-200				X
• NRG GY 009				X
• AGO OVAR 2				X
• KEYNOTE-B96	(Pembro)	CHT + IO ± Bev		?

No clinically meaningful activity of Immune Checkpoint Inhibitors

Irrespective of:

- line of treatment
- Combination (Bev & PARPi)

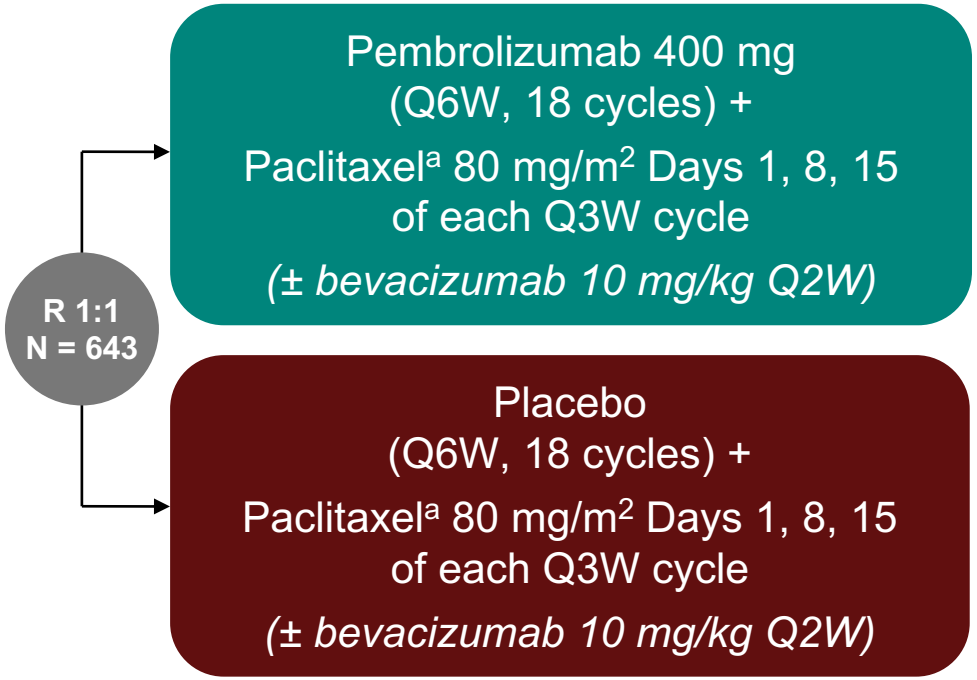
Frederik Marmé

Courtesy of Nicoletta Colombo, MD

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

Key Eligibility Criteria

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



Stratification Factors

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

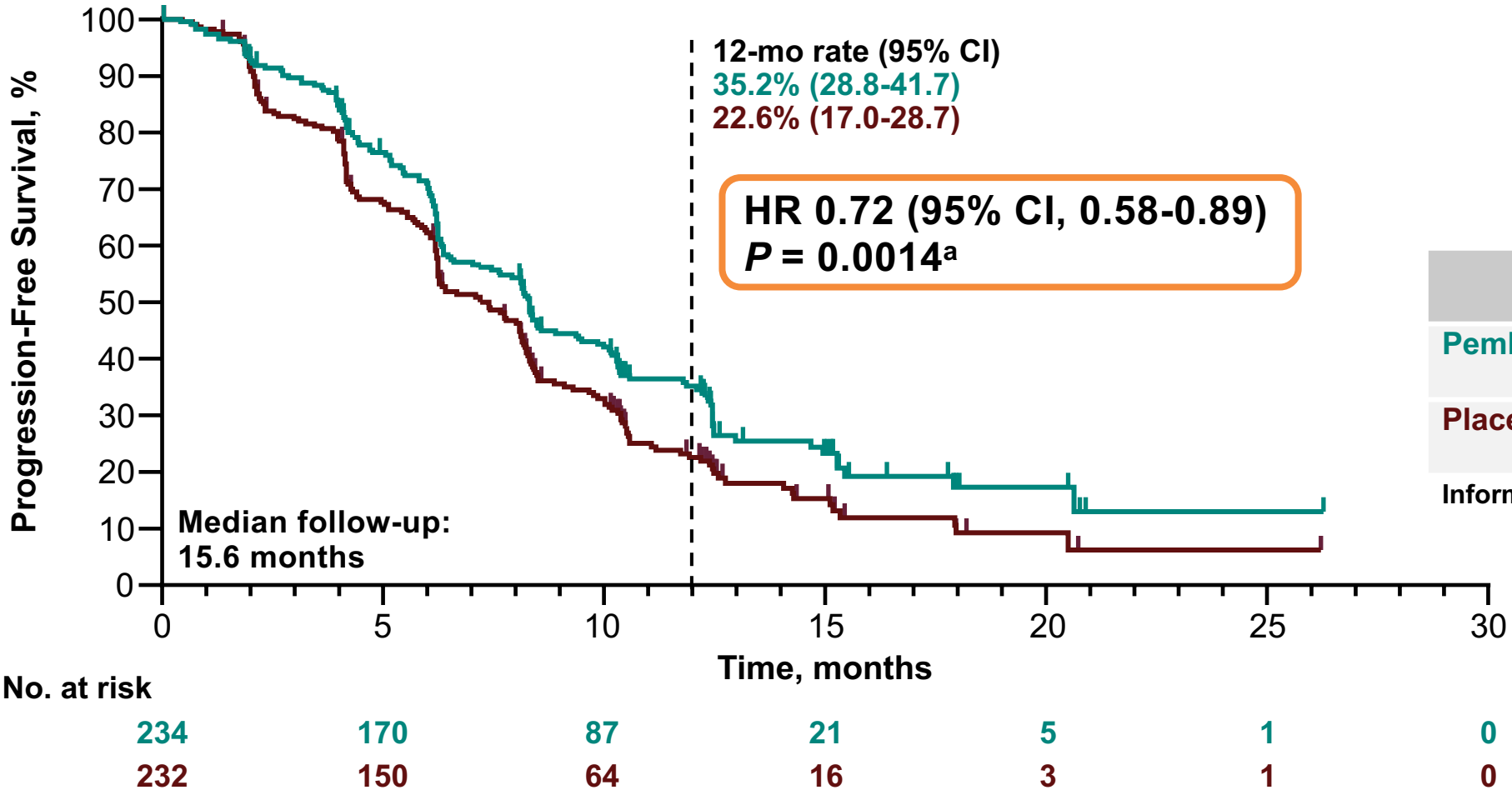
Primary Endpoint: PFS per RECIST v1.1 by investigator

Key Secondary: OS

[a]Docetaxel (75 mg/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.

Courtesy of Nicoletta Colombo, MD

Progression-Free Survival in the CPS ≥1 Population at IA1



	Pts w/ Event	Median, mo (95% CI)
Pembro Arm	69.2%	8.3 (7.0-9.4)
Placebo Arm	77.6%	7.2 (6.2-8.1)

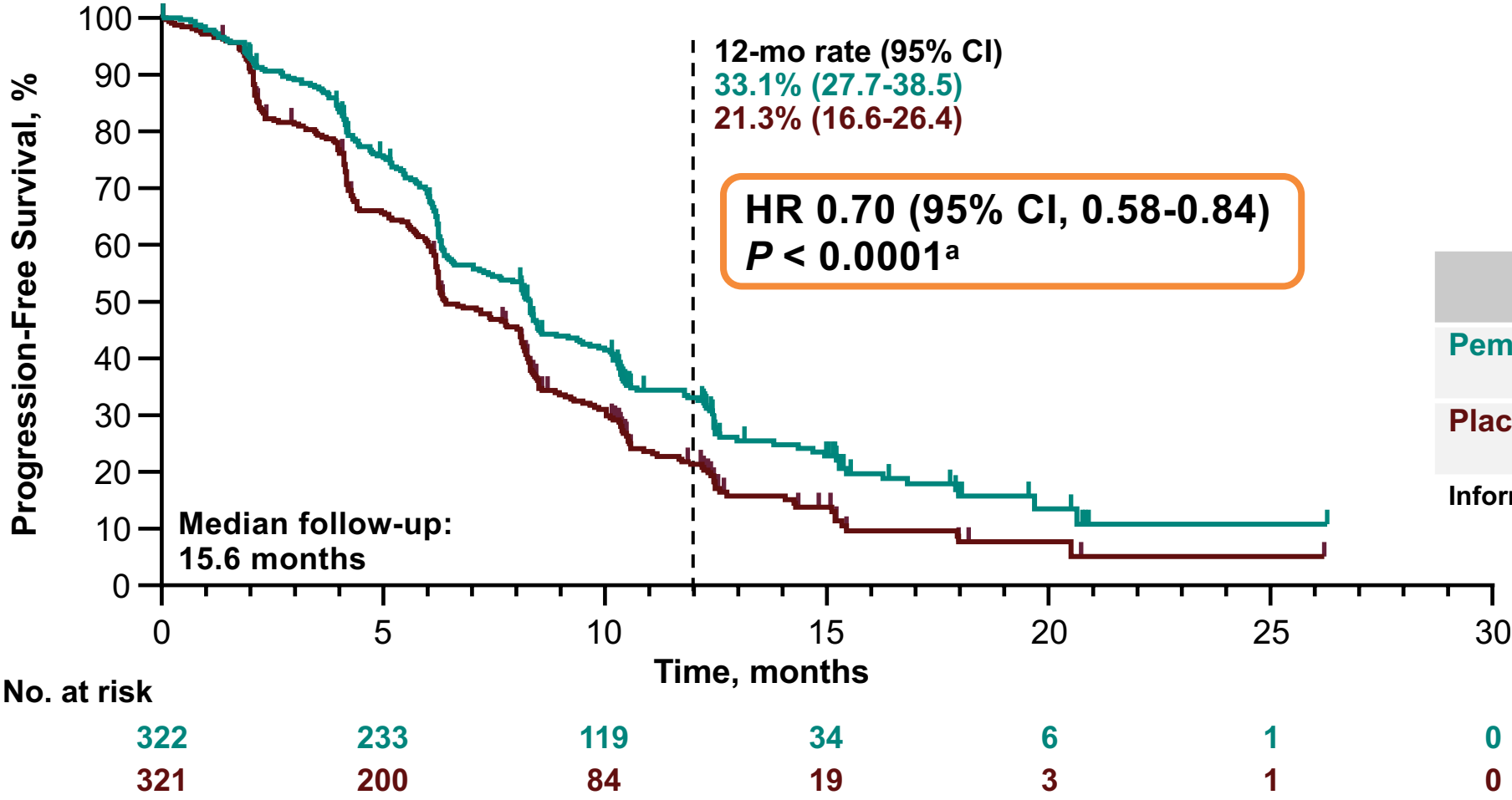
Information fraction: 87.9%

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. The observed p-value crossed the prespecified nominal boundary of 0.0116 at this planned first interim analysis; because the success criterion of the PFS hypothesis was met, no formal testing of PFS will be performed at later analyses. Data cutoff date: April 3, 2024.

Colombo N, ESMO 2025

Courtesy of Nicoletta Colombo, MD

Progression-Free Survival in the ITT Population at IA1



	Pts w/ Event	Median, mo (95% CI)
Pembro Arm	71.7%	8.3 (7.2-8.6)
Placebo Arm	78.8%	6.4 (6.2-8.1)

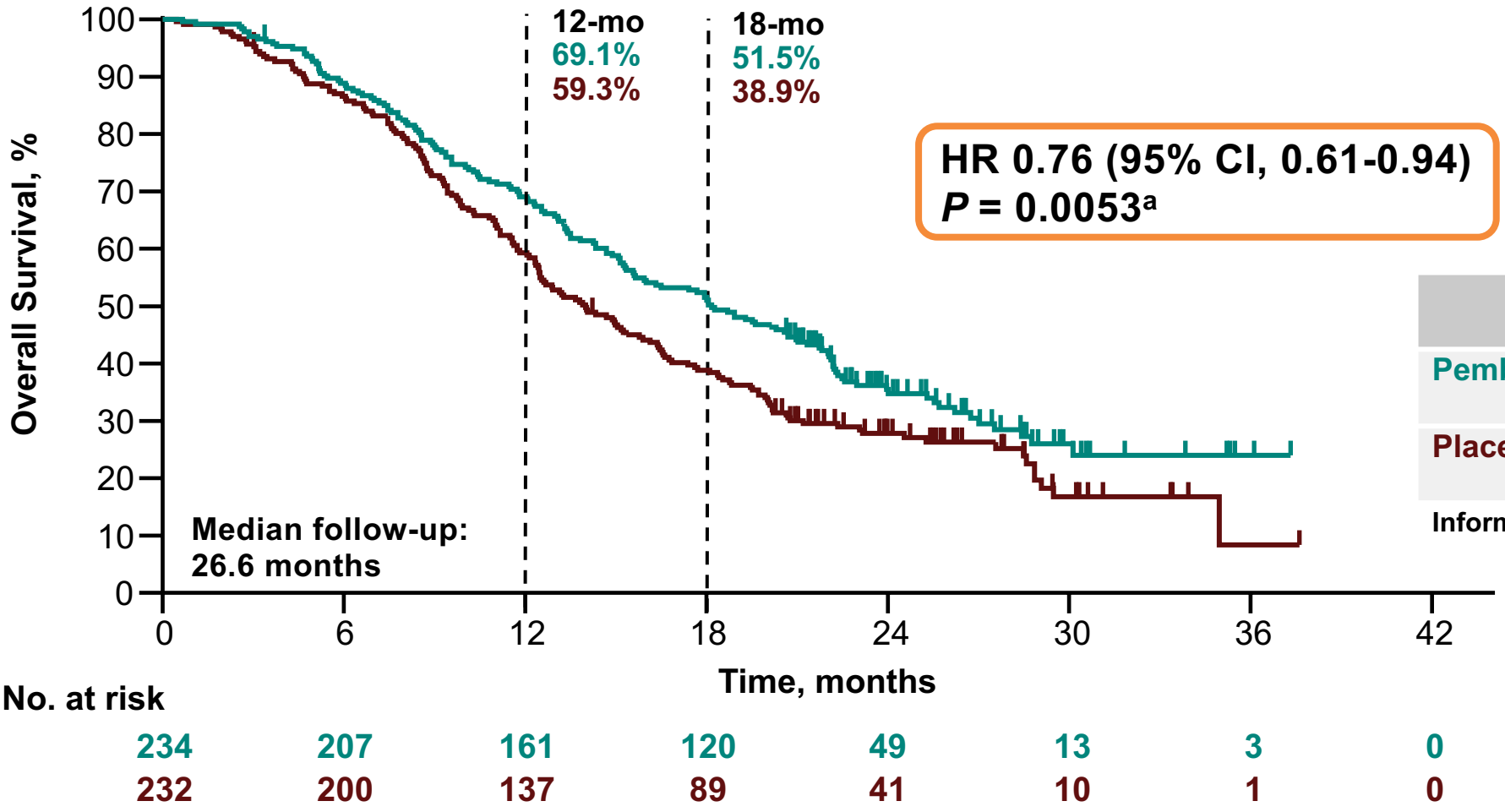
Information fraction: 89.5%

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. The observed p-value crossed the prespecified nominal boundary of 0.0023 at this planned first interim analysis; because the success criterion of the PFS hypothesis was met, no formal testing of PFS will be performed at later analyses. Data cutoff date: April 3, 2024.

Colombo N, ESMO 2025

Courtesy of Nicoletta Colombo, MD

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



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

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

Information fraction: 90.0%

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

Colombo N, ESMO 2025

Courtesy of Nicoletta Colombo, MD

FDA Approves Pembrolizumab with Paclitaxel for Platinum-Resistant Epithelial Ovarian, Fallopian Tube or Primary Peritoneal Carcinoma

Press Release: February 10, 2026

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

FDA also approved the PD-L1 IHC 22C3 pharmDx as a companion diagnostic device to identify patients with epithelial ovarian, fallopian tube, or primary peritoneal carcinoma whose tumors express PD-L1 (CPS≥1) for treatment with pembrolizumab.

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

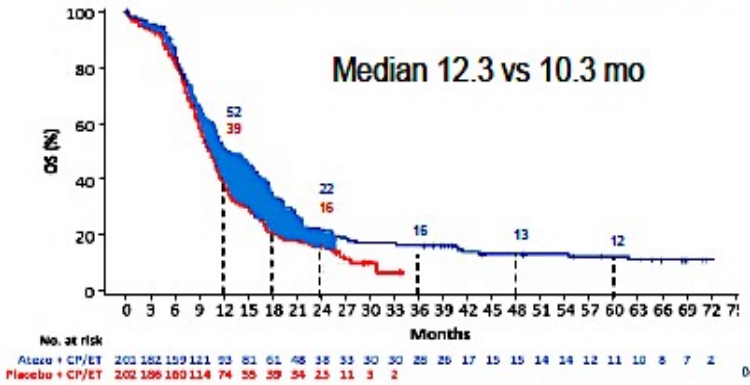
https://www.fda.gov/drugs/resources-information-approved-drugs/fda-approves-pembrolizumab-paclitaxel-platinum-resistant-epithelial-ovarian-fallopian-tube-or

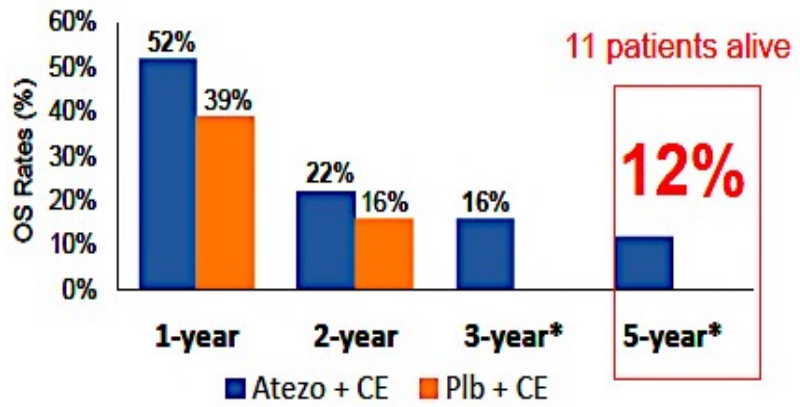

MIAMI
LIV
Wilson

Pivotal Trials of ICIs in ES SCLC – Long term outcome

IMpower133 and IMbrella A

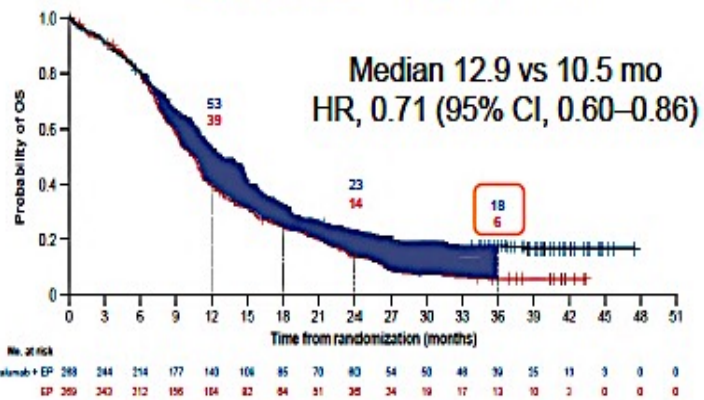
Atezolizumab + CP/ET vs CP/ET + Plb[1-2]

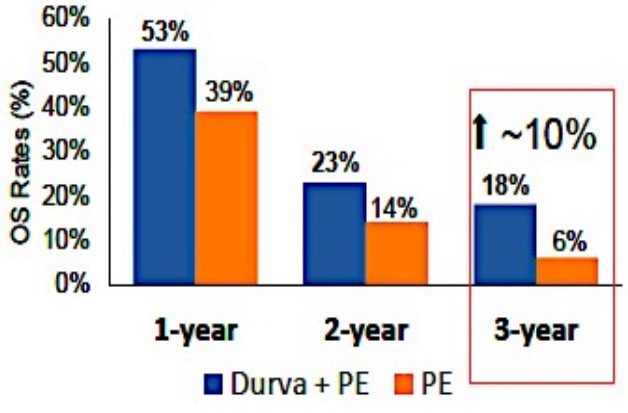




CASPIAN

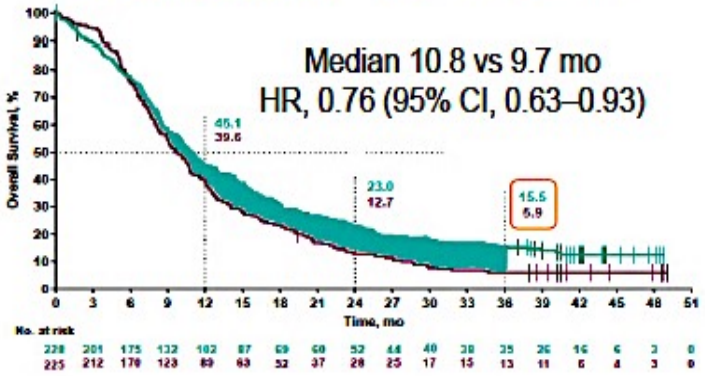
Durvalumab + P/ET vs P/ET[3-4]

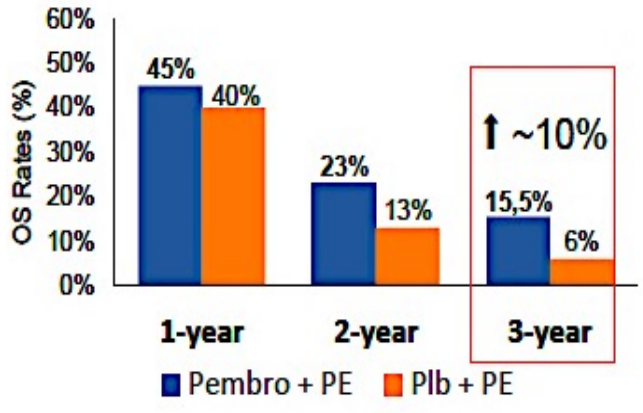




KEYNOTE-604

Pembrolizumab + P/ET vs P/ET + Plb[5-6]





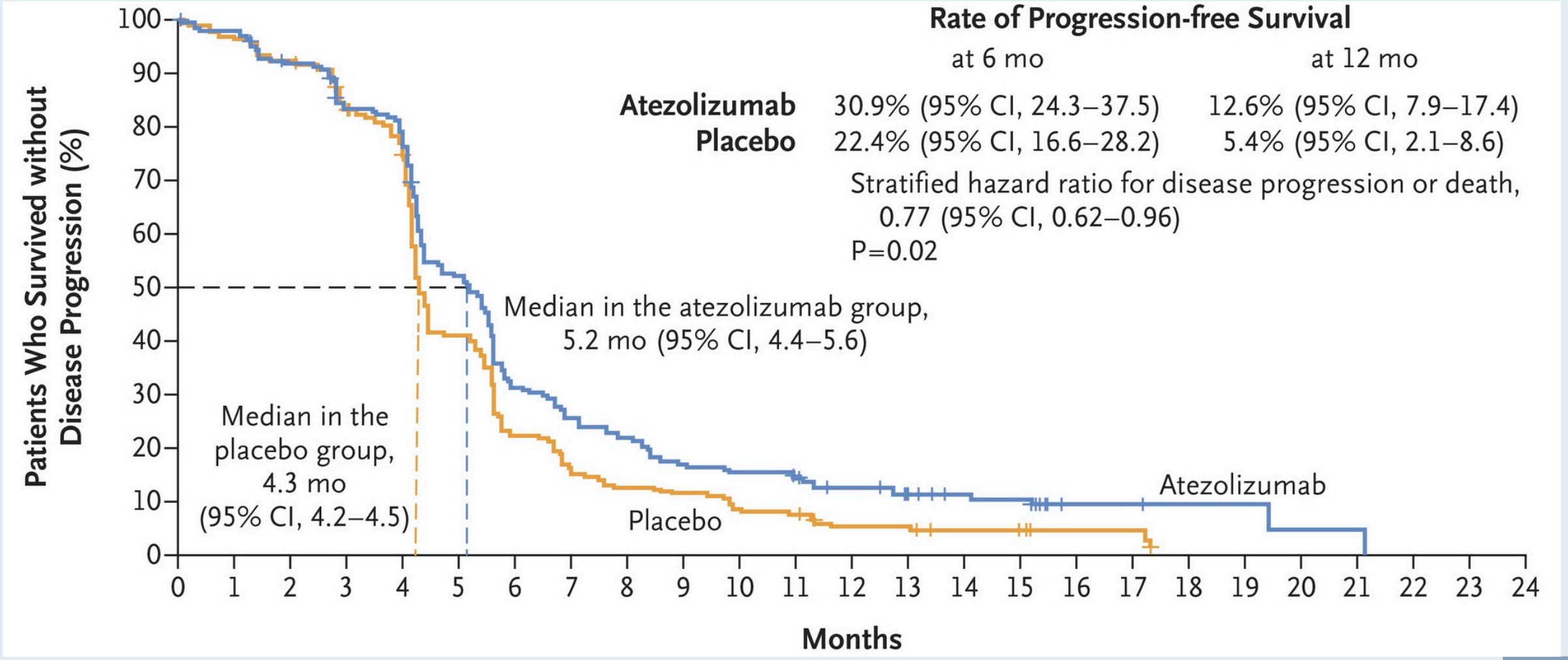
CP, carboplatin; ET, etoposide; P, platinum; Plb, placebo; NE, not estimable. * OS rates at 3-5 years were not estimable in the control arm as rollover to IMbrella A was not permitted.

1.- Horn L, et al. N Engl J Med 2018; 2.- Liu S, et al. OA01.04, WCLC 2023; 3.- Paz-Ares L, et al. Lancet 2019; 4.- Paz-Ares L, et al. ESMO Open 2022; 5.- Rudin CM, et al. J Clin Oncol 2020; 6.- Rudin CM, et al. WCLC 2022

Penn Medicine
Abramson Cancer Center

Courtesy of Corey J Langer, MD

Phase III IMpower133 Trial: Primary Progression-Free Survival with Atezolizumab/Carboplatin/Etoposide (ITT Population)



ITT = intention to treat

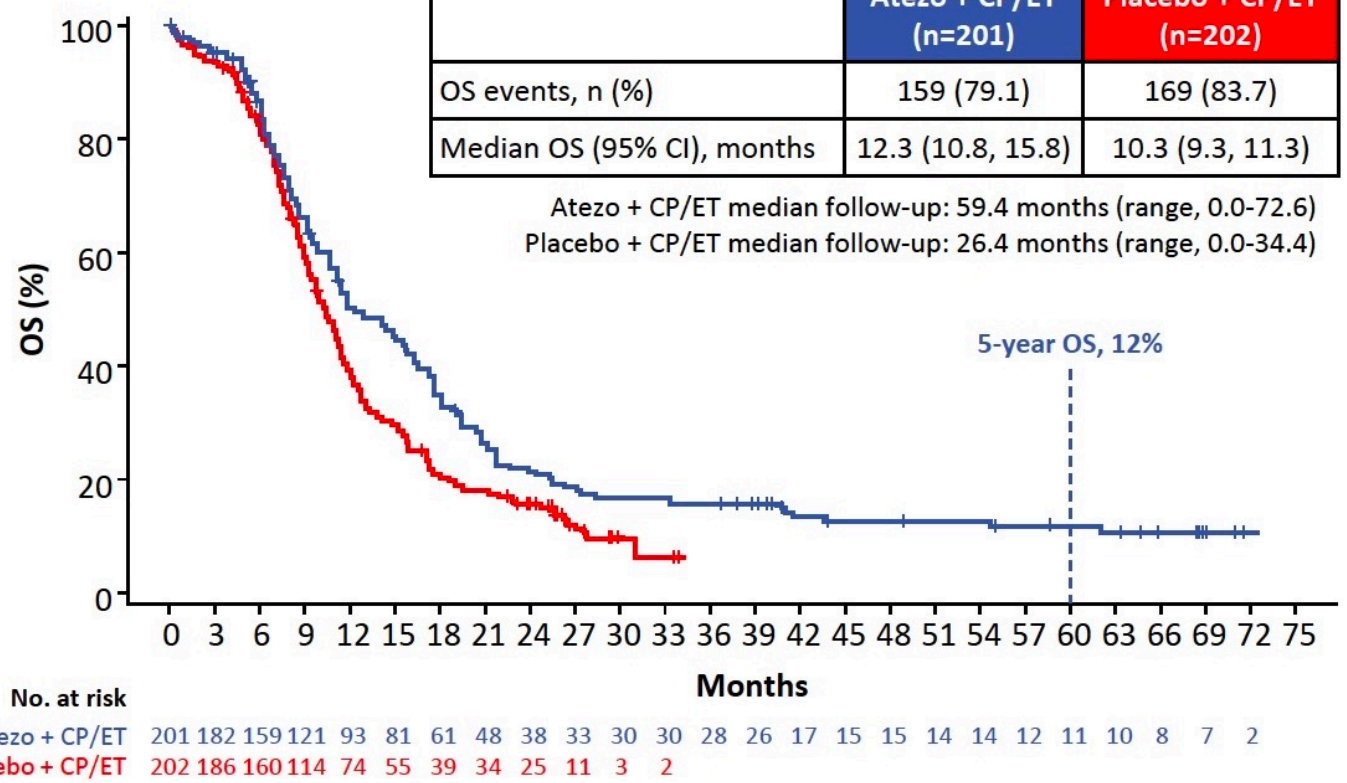
Horn L et al. *N Engl J Med* 2018 December 6;379(23):2220-9.

RTP RESEARCH TO PRACTICE

Merged Analysis of IMpower133 and IMbrella A: Long-Term OS

	Atezo + CP/ET (n=201)	Placebo + CP/ET (n=202)
OS events, n (%)	159 (79.1)	169 (83.7)
Median OS (95% CI), months	12.3 (10.8, 15.8)	10.3 (9.3, 11.3)

Atezo + CP/ET median follow-up: 59.4 months (range, 0.0-72.6)
Placebo + CP/ET median follow-up: 26.4 months (range, 0.0-34.4)



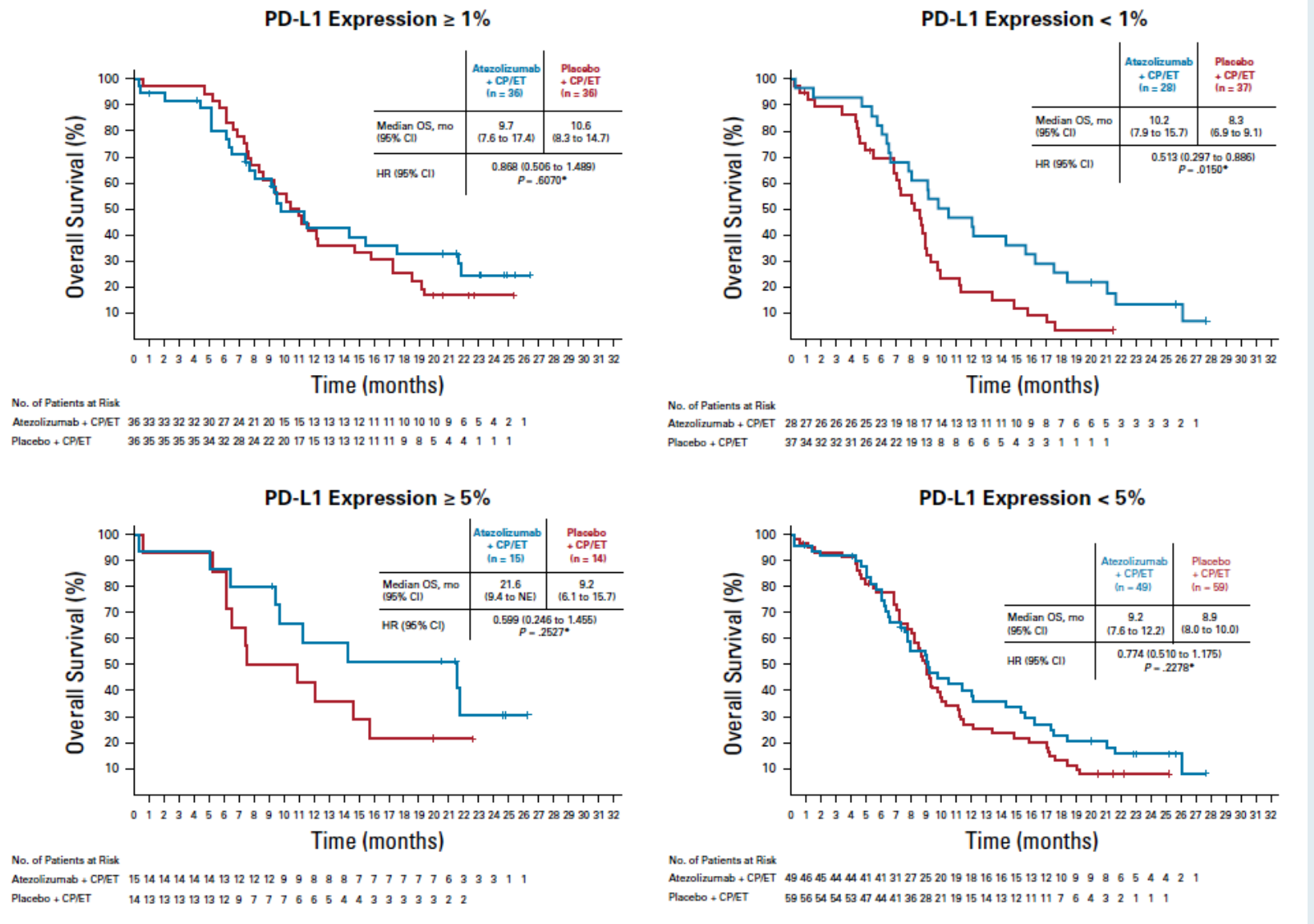
OS rate (95% CI), %	IMpower133 and IMbrella A Atezo + CP/ET (n=201)	IMpower133 only Placebo + CP/ET (n=202)
1-year	52% (45-59)	39% (32-46)
2-year	22% (16-28)	16% (11-21)
3-year	16% (11-21)	NE[a]
4-year	13% (8-18)	NE[a]
5-year	12% (7-17)	NE[a]

Clinical cutoff date: 16 March 2023. NE, not estimable. [a] OS rates were NE in the control arm as rollover to IMbrella A was not permitted.

NE = not evaluable

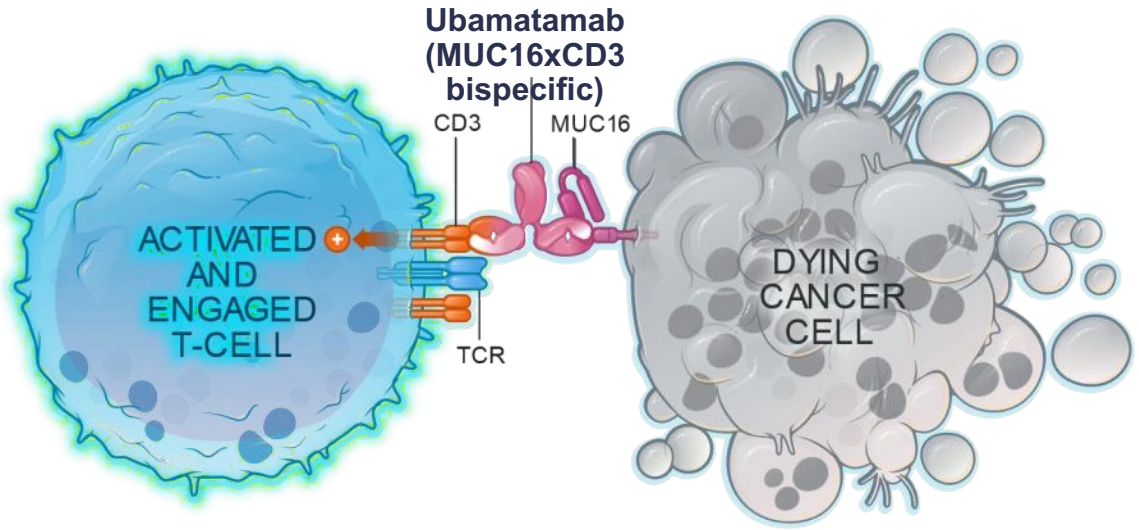
Liu SV et al. WCLC 2023;Abstract OA01.04; Reck M et al. *Lung Cancer* 2024;196:107924.

Phase III IMpower133: OS by PD-L1 Expression with Atezolizumab/Carboplatin/Etoposide



Liu SV et al. *J Clin Oncol* 2021;39:619-30.

T-cell Engagers
Ubamatamab (REGN4018) in Advanced Ovarian Cancer



- 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.

Courtesy of Nicoletta Colombo, MD

Randomised Phase 2 study of ubamatamab ± cemiplimab in patients (pts) with platinum-resistant ovarian cancer (OC)

Figure 2. Comparison of best overall tumour response across treatment Arms A, B and C*

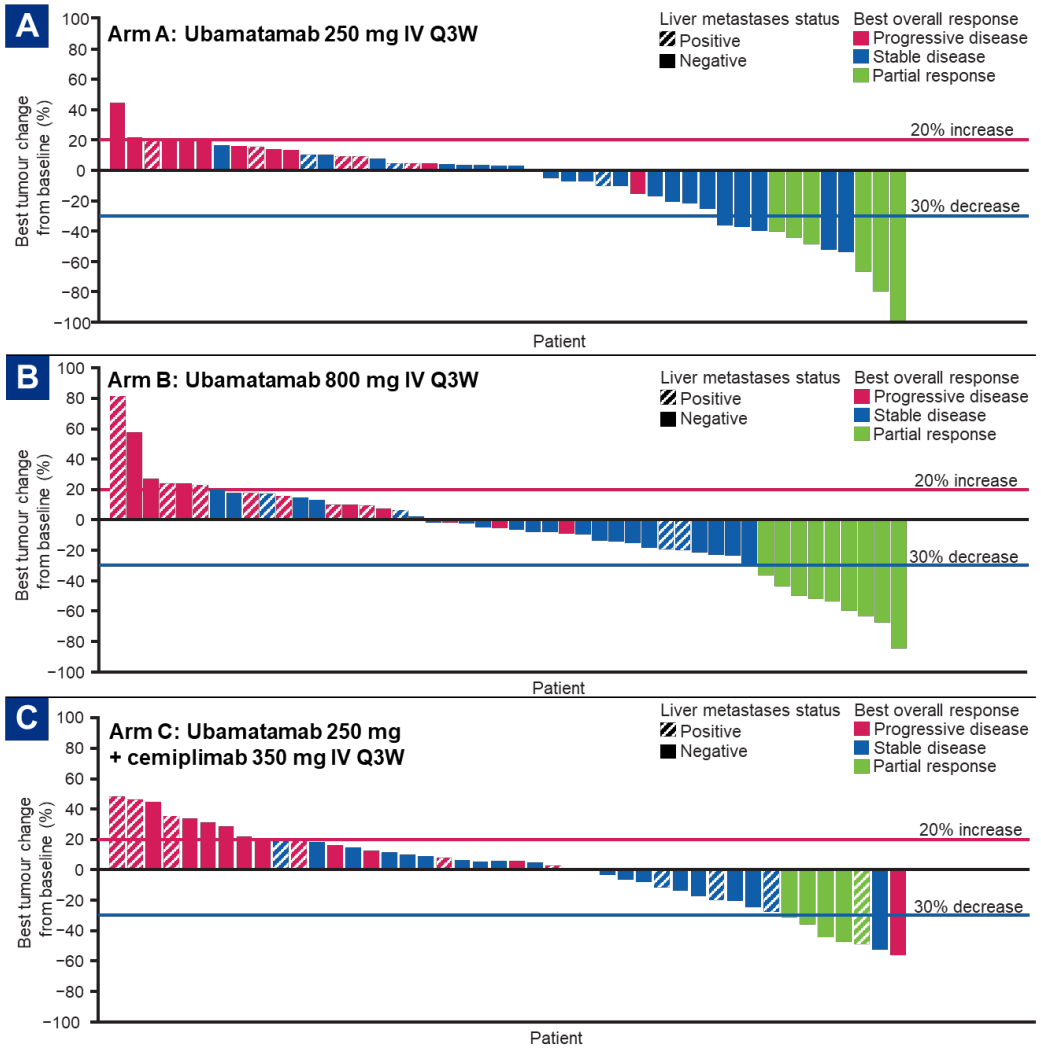
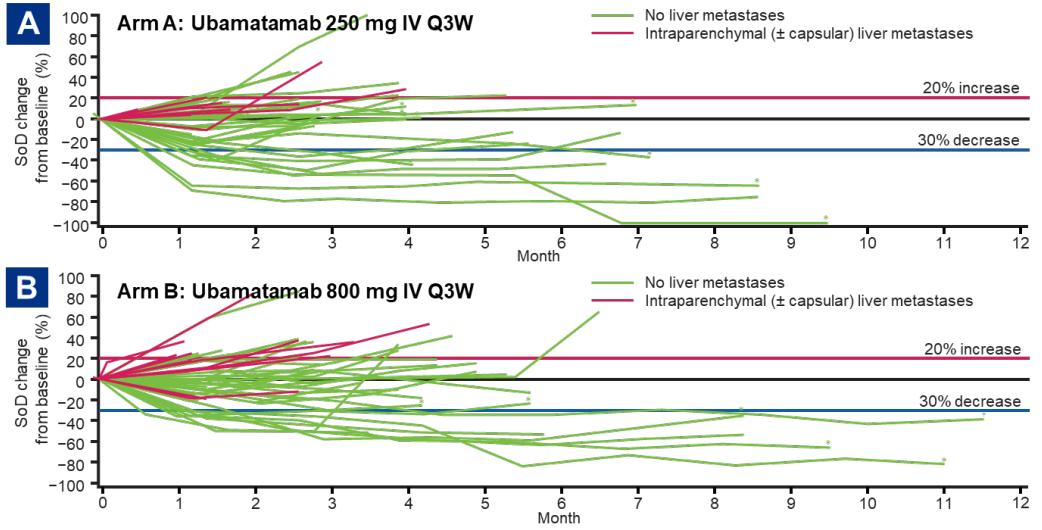


Figure 3. Comparison of DOR spider plots for treatment Arms A and B



	Arm A: Ubamatamab 250 mg IV Q3W n=50	Arm B: Ubamatamab 800 mg IV Q3W n=50
Median DOR (range), months	5.7 (2.8–NE)	10.5 (2.5–NE)

Data cut-off: 15 Jan 2025. *Patient remains on treatment as of data lock; †Patient continued treatment beyond 12 months.
DOR, duration of response; IV, intravenous; NE, not evaluable; Q3W, once every 3 weeks; SoD, sum of diameters.

Jung-Yun Lee, ESMO 2025

Courtesy of Nicoletta Colombo, MD

Platinum Ineligible Ovarian Cancer

ANTIBODY DRUG CONJUGATED (ADCS)

Mirvetuximab-soravtansine [1]

Trastuzumab-deruxtecan [2]

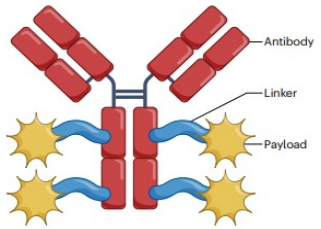
Raludotatug- Deruxtecan [3]

Rinatabart Sesutecan (Rina-S)[4]

AZD5335 [5]

Ly4170156 [6]

NAPISTAR 1-01[7]

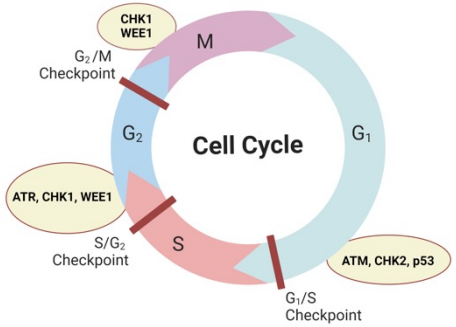


CELL CYCLE REGULATION AND DNA REPAIR

ADAVOSERTIB [8]

azenosertib[9]

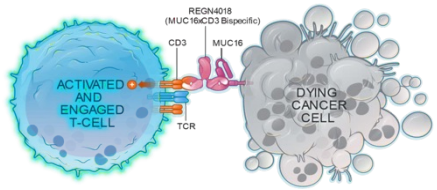
CDK2i [10]



IMMUNOTHERAPY

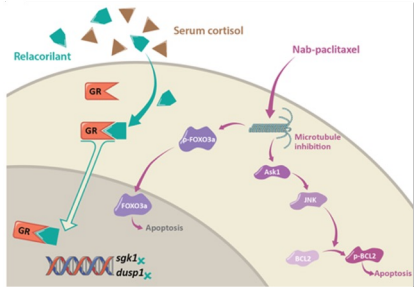
Paclitaxel/pembro [11]

UBAMATAMAB [12]



GLUCOCORTICOID RECEPTOR

RELACORILANT [13]



[1] [NCT04296890 – Soraya] [NCT04209855 – Mirasol]; [2] [NCT04482309]; [3] [NCT04707248]; [4] [NCT06619236]; [5] [NCT05797168] ; [6] [NCT06400472]; [7] [NCT06303505]; [8] [NCT03579316]; [9] [NCT02595892]; [10] [INCB123667]; [11] [NCT05116189]; [12] [NCT03564340] [13] [NCT05257408 – Rosella]; [NCT03776812 – phase II];

Courtesy of Nicoletta Colombo, MD

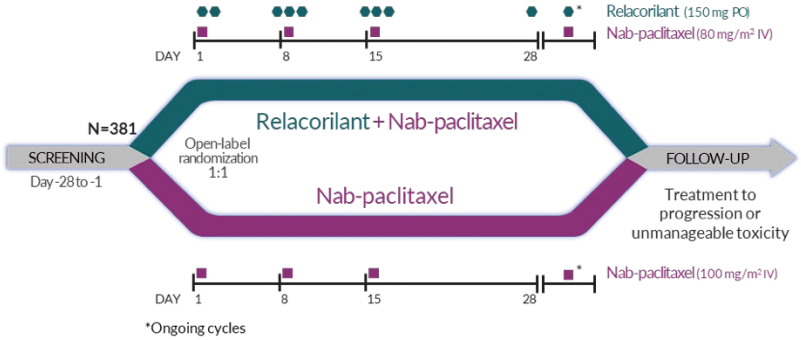
ROSELLA

- Relacorilant is a novel, selective GR antagonist (SGRA) that restores the sensitivity of cancers to cytotoxic chemotherapy[3,5,6]

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
- Must have received prior bevacizumab

NCT05257408



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

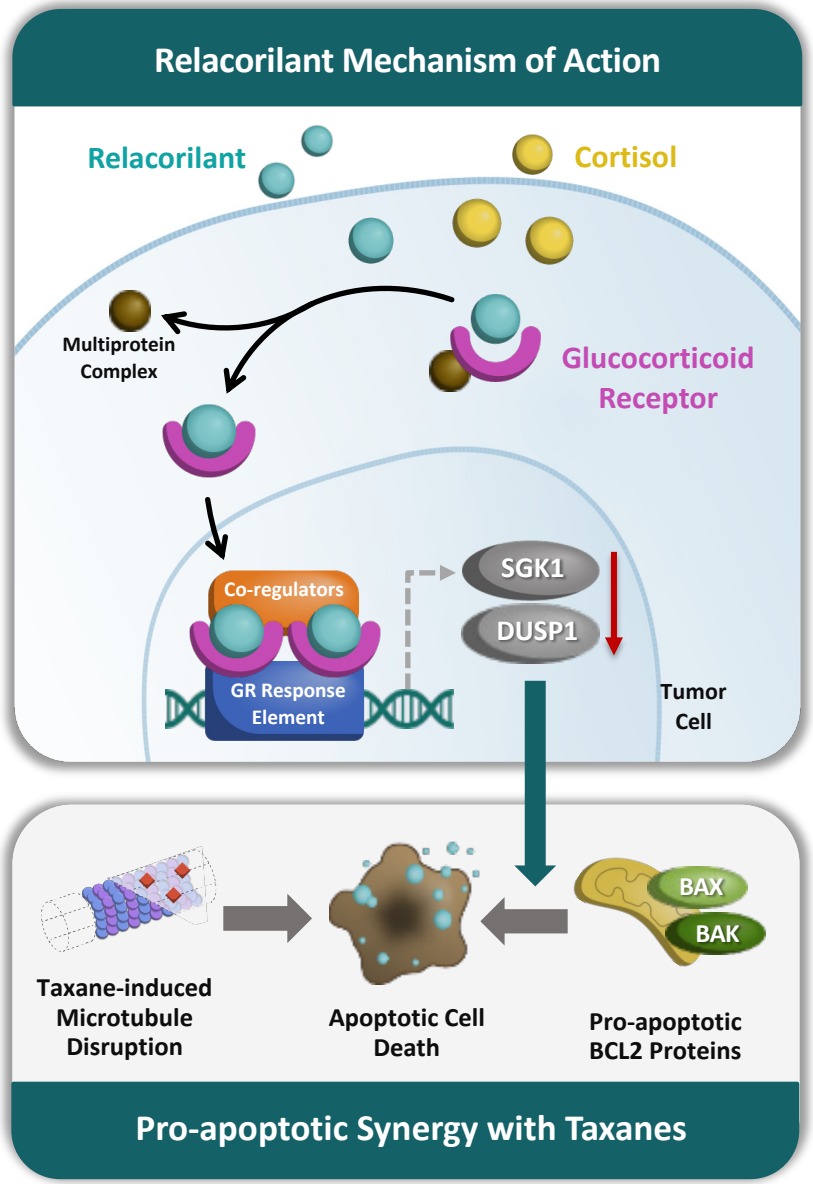
Dual Primary Endpoints

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

Secondary Endpoints

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

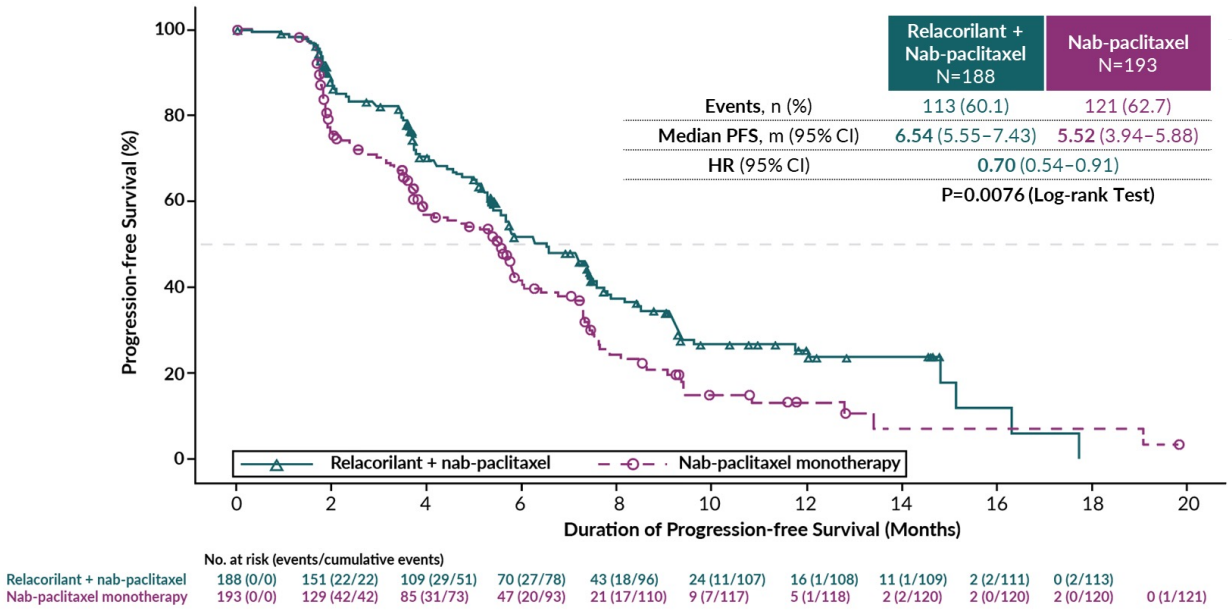
First patient enrolled: 5th January 2023
Last patient enrolled: 8th April 2024
Data cutoff: 24th February 2025
Conducted at 117 sites in 14 countries.



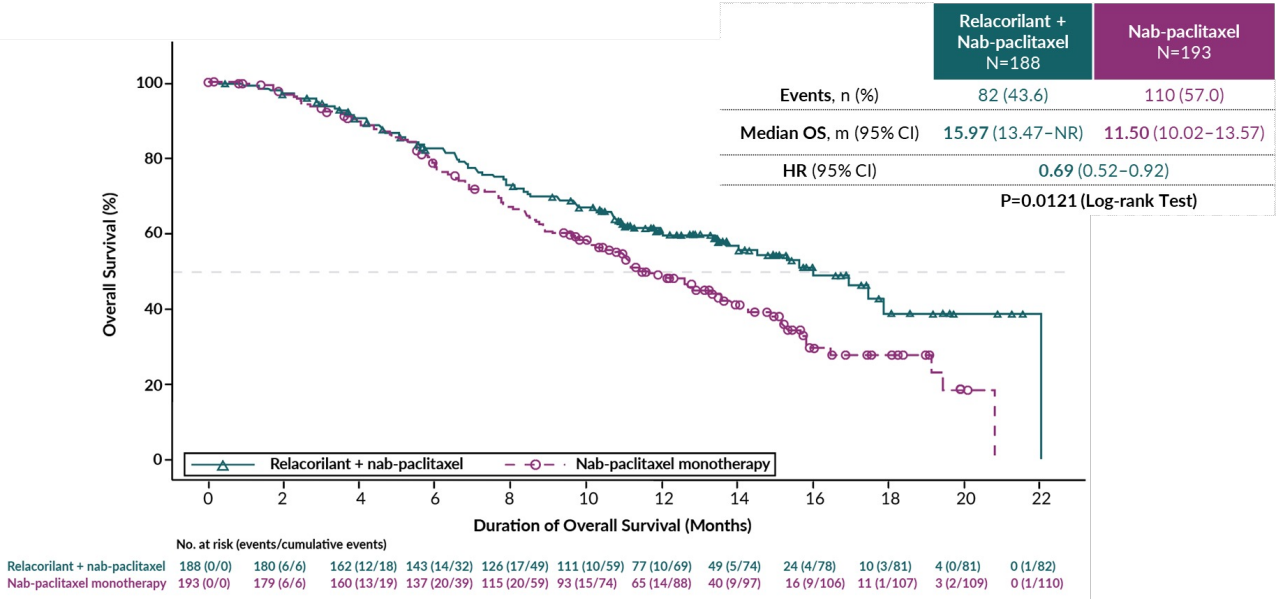
1. Martorana, et al. *Int J Gynecol Cancer*. 2025;35(1):100009. 2. Veneris, et al. *Gynecol Oncol*. 2017;146(1):153-60. 3. Greenstein, et al. *Oncotarget*. 2021;12(13):1243-55. 4. Melhelm, et al. *Clin Cancer Res*. 2009;15(9):3196-3204. 5. Stringer-Reasor, et al. *Gynecol Oncol*. 2015;138(3):656-62. 6. Munster, et al. *Clin Cancer Res*. 2022;28(15):3214-24. 7. Colombo, et al. *J Clin Oncol*. 2023;41(30):4779-89.

Courtesy of Nicoletta Colombo, MD

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



ROSELLA | Relacorilant Improved Overall Survival at this Interim Analysis (not yet significant)



statistical significance threshold at the interim analysis: P≤0.0001

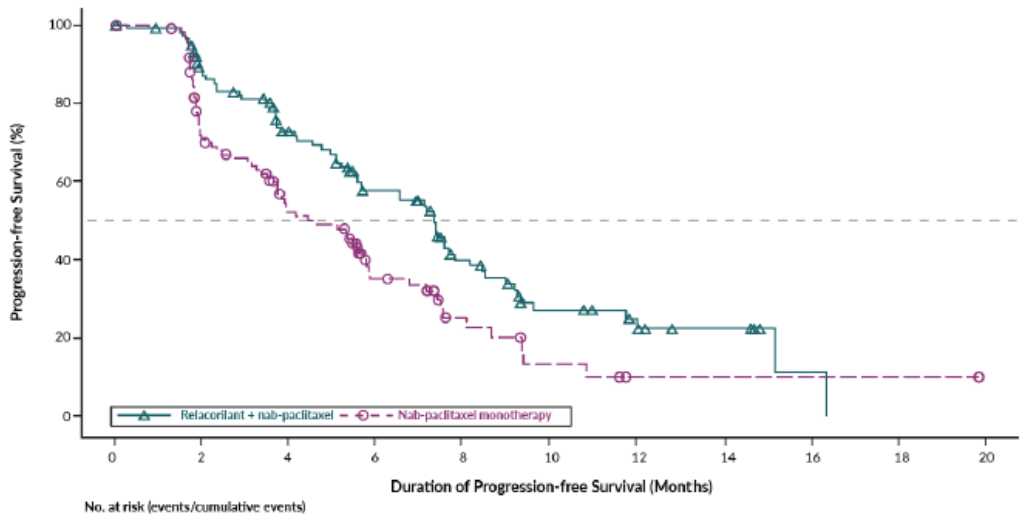
Alexander Olawaiye, ASCO 2025, Lancet 2025

Courtesy of Nicoletta Colombo, MD

ROSELLA | Relacorilant Improved PFS Assessed by BICR in the Subgroup of Patients Who Received Prior PARP Inhibitor Treatment

	Relacorilant + Nab-paclitaxel N=114	Nab-paclitaxel N=120
Events, n (%)	66 (57.9)	72 (60.0)
Median PFS, m (95% CI)	**7.36** (5.59–8.18)	**4.63** (3.55–5.72)
HR (95% CI)	**0.60** (0.42–0.85)	

Nominal P=0.0035 (Log-rank Test)



No. at risk (events/cumulative events)

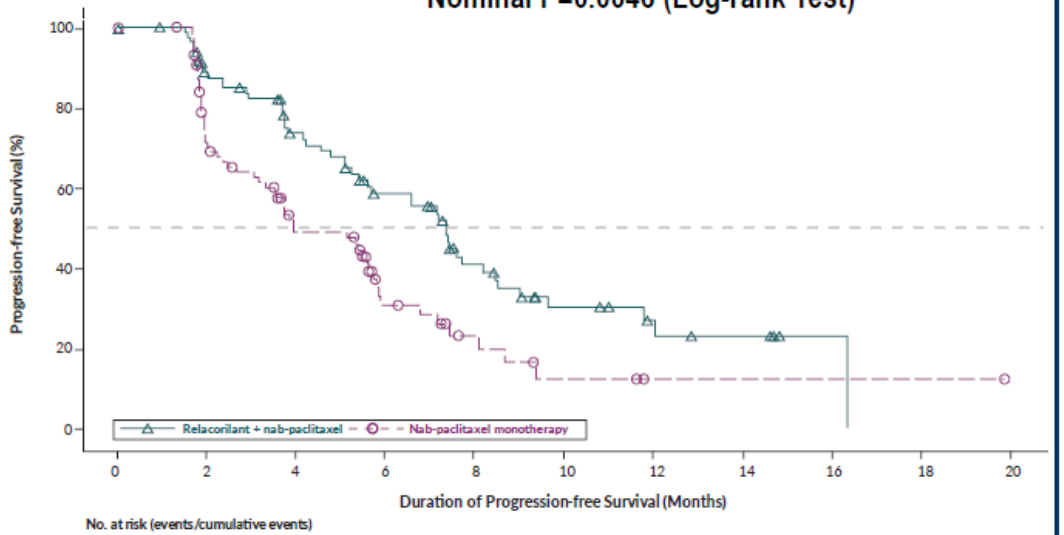
Relacorilant + nab-paclitaxel	114 (0/0)	90 (12/12)	66(16/28)	46 (13/41)	27 (13/54)	15 (8/62)	10(1/63)	6(1/64)	6 (1/65)	0 (1/66)
Nab-paclitaxel monotherapy	120 (0/0)	74 (30/30)	47 (19/49)	22 (13/62)	10 (5/67)	4 (4/71)	1 (1/72)	1 (0/72)	1 (0/72)	1 (0/72)	0 (0/72)

ORR (Investigator): 39.5% (45/114) vs **30.8%** (37/120)

ROSELLA | Relacorilant Improved PFS Assessed by BICR in the Subgroup of Patients Who had Progressed on a PARP Inhibitor

	Relacorilant + Nab-paclitaxel N=86	Nab-paclitaxel N=97
Events, n (%)	48 (55.8)	57 (58.8)
Median PFS, m (95% CI)	**7.36** (5.39–8.44)	**3.94** (3.32–5.72)
HR (95% CI)	**0.56** (0.37–0.84)	

Nominal P=0.0046 (Log-rank Test)



No. at risk (events/cumulative events)

Relacorilant + nab-paclitaxel	86 (0/0)	67 (9/9)	50 (11/20)	36 (10/30)	21 (10/40)	12 (5/45)	7 (1/46)	5 (1/47)	6 (0/47)	0 (1/48)
Nab-paclitaxel monotherapy	97 (0/0)	58 (24/24)	34 (17/41)	14 (10/51)	7 (3/54)	3 (3/57)	1 (0/57)	1 (0/57)	1 (0/57)	1 (0/57)	0 (0/57)

ORR (Investigator): 34.9% (30/86) vs **26.8%** (26/97)

Data cutoff: Feb 24, 2025

Lorusso, ESMO 2025

Courtesy of Nicoletta Colombo, MD

Overall Survival Primary Endpoint Met in Phase III ROSELLA Trial of Relacorilant for Patients with Platinum-Resistant Ovarian Cancer

Press Release: January 22, 2026

"…[The company] today announced that ROSELLA, the company's pivotal Phase 3 trial of relacorilant plus *nab*-paclitaxel to treat patients with platinum-resistant ovarian cancer, met its overall survival (OS) primary endpoint.

- Data demonstrate a 35 percent reduction in the risk of death

- Both dual primary endpoints (progression-free and overall survival) were met, without the need for biomarker selection and without increased safety burden

Relacorilant's New Drug Application (NDA) is under review by the U.S. Food and Drug Administration as a treatment for patients with platinum-resistant ovarian cancer with a Prescription Drug User Fee Act (PDUFA) target action date of July 11, 2026.

Complete results from ROSELLA will be presented at an upcoming medical conference."

https://ir.corcept.com/news-releases/news-release-details/overall-survival-primary-endpoint-met-corcepts-pivotal-phase-3

Year in Review:
Ovarian Cancer

MODULE 1: Promising Novel Agents and Strategies Under Investigation in Ovarian Cancer

- Antibody-drug conjugates
- KEYNOTE-B96 Phase III trial: Pembrolizumab and paclitaxel +/- bevacizumab
- ROSELLA Phase III trial: Relacorilant with *nab* paclitaxel

MODULE 2: Current Management of Newly Diagnosed and Relapsed/Refractory Ovarian Cancer

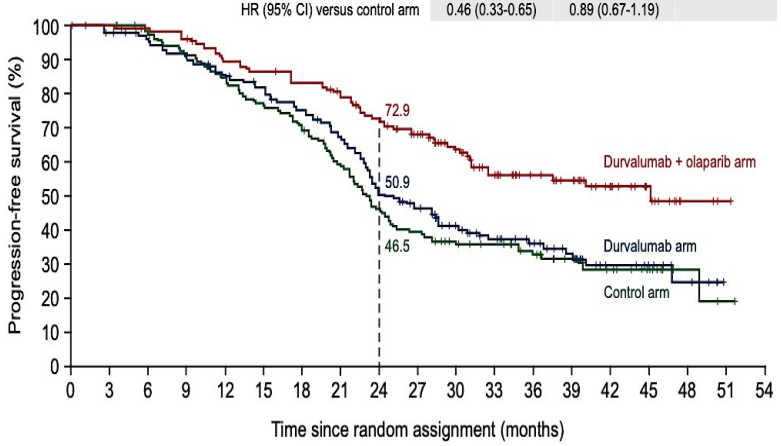
- First-line treatment approaches
- Chemotherapy/bevacizumab for platinum-resistant ovarian cancer
- Mirvetuximab soravtansine
- Trastuzumab deruxtecan

Progression-Free Survival: PARPi and Immunotherapy

DUO-O

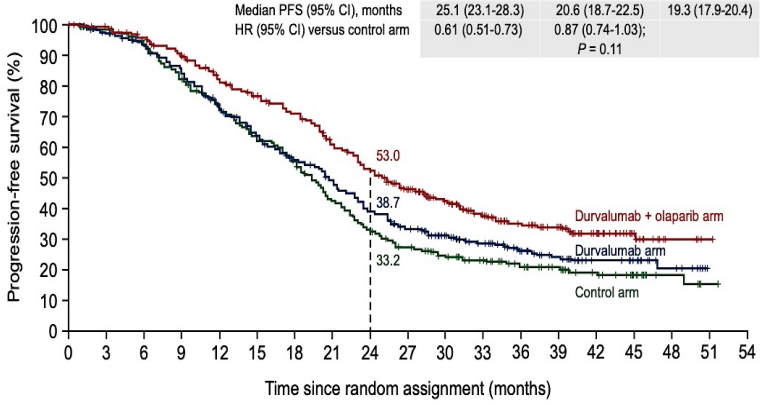
Non-tBRCAm HRD-positive population: Final PFS (DCO: 18 Sept 2023)

	Durvalumab + olaparib arm (*n* = 140)	Durvalumab arm (*n* = 148)	Control arm (*n* = 143)
Events, *n* (%)	57 (40.7)	89 (60.1)	94 (65.7)
Median PFS (95% CI), months	45.1 (31.1-NR)	25.1 (22.9-28.6)	23.3 (21.2-25.0)
HR (95% CI) versus control arm	0.46 (0.33-0.65)	0.89 (0.67-1.19)	



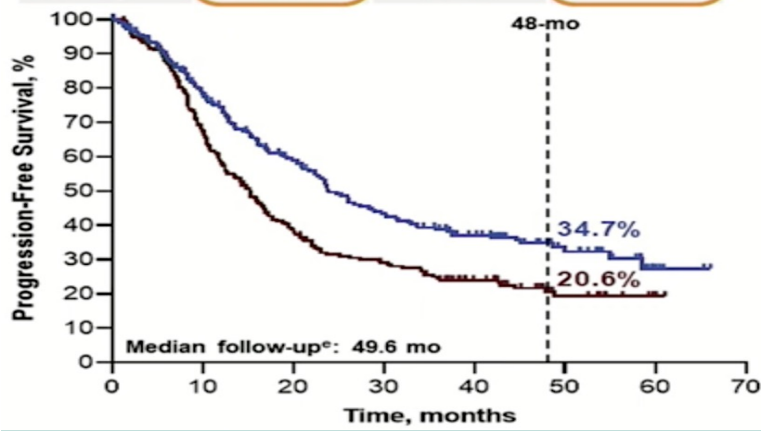
Non-tBRCAm ITT population: Final PFS (DCO: 18 Sept 2023)

	Durvalumab + olaparib arm (*n* = 378)	Durvalumab arm (*n* = 374)	Control arm (*n* = 378)
Events, *n* (%)	221 (58.5)	257 (68.7)	283 (74.9)
Median PFS (95% CI), months	25.1 (23.1-28.3)	20.6 (18.7-22.5)	19.3 (17.9-20.4)
HR (95% CI) versus control arm	0.61 (0.51-0.73)	0.87 (0.74-1.03); *P* = 0.11	

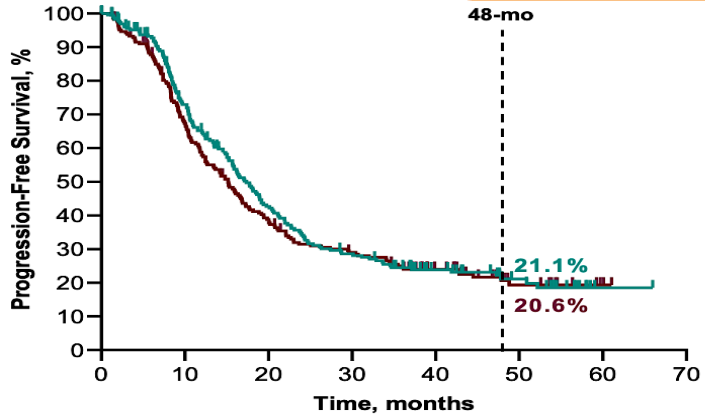


KEYLYNK 001

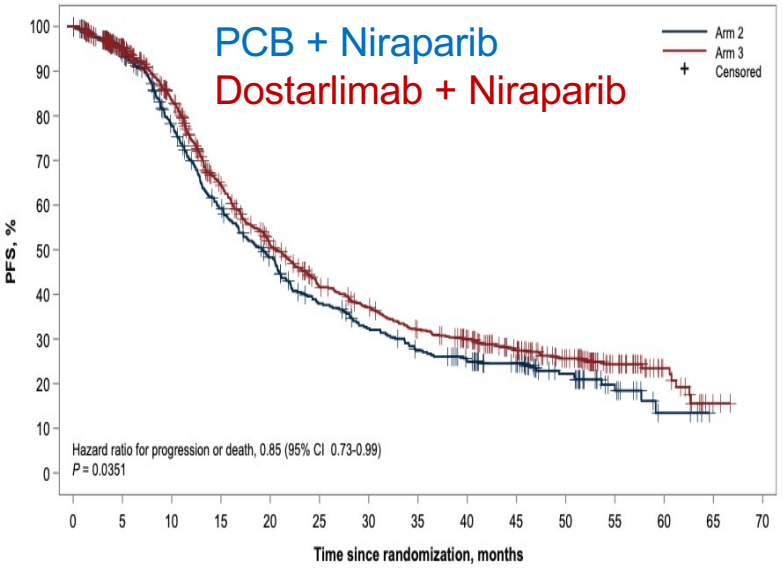
CPS ≥10 Population	FA[b]	Median, months	Events	HR (95% CI)
	P–O Group	23.9	58.5%	0.66[c] (0.53-0.83)
	C Group	15.2	72.4%	



CPS ≥10 Population	Median, months	Events	HR (95% CI)	*P*-value
P Group	17.3	69.6%	0.95[a] (0.77-1.19)	0.3339[b]
C Group	15.2	72.4%		



FIRST



Harter P *Ann Oncol* 2025; Vergote I ESGO 2025; Hardy-Bessard AC *Ann Oncol* 2025

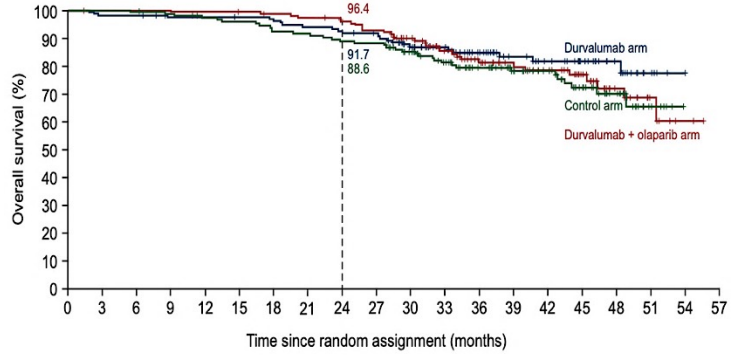
Courtesy of Angeles Alvarez Secord, MD, MHSc

Overall Survival: PARPi and Immunotherapy

DUO-O

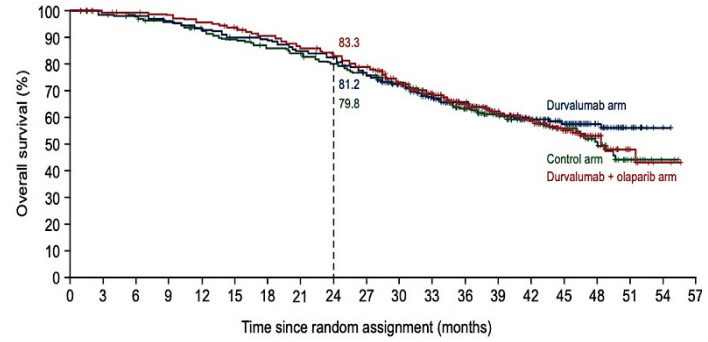
Non-tBRCAm HRD-positive population: Interim OS (DCO: 18 Sept 2023)

	Durvalumab + olaparib arm (*n* = 140)	Durvalumab arm (*n* = 148)	Control arm (*n* = 143)
Events, *n* (%)	30 (21.4)	24 (16.2)	35 (24.5)
Median OS (95% CI), months	NR (NR-NR)	NR (NR-NR)	NR (NR-NR)
HR (95% CI) versus control arm	0.84 (0.51-1.37)	0.69 (0.41-1.15)	

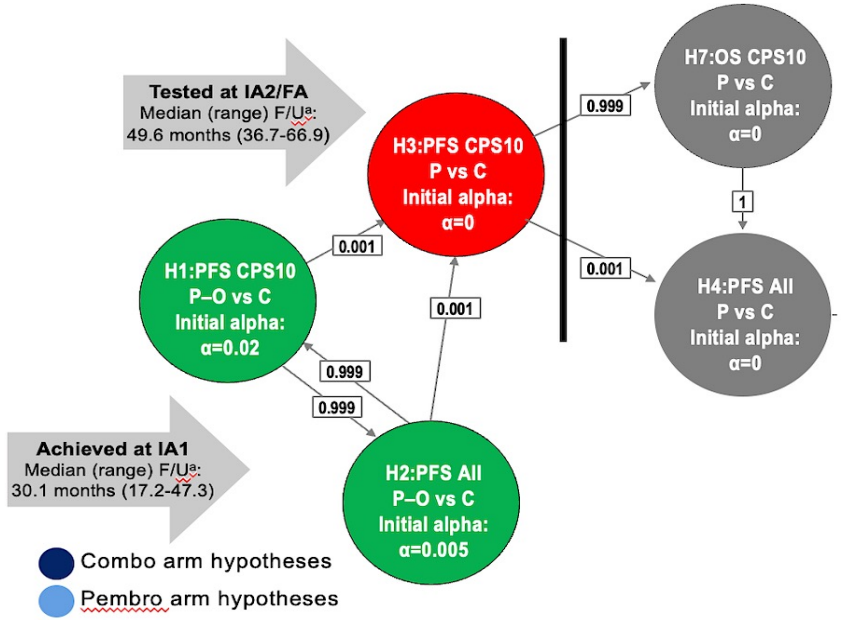


Non-tBRCAm ITT population: Interim OS (DCO: 18 Sept 2023)

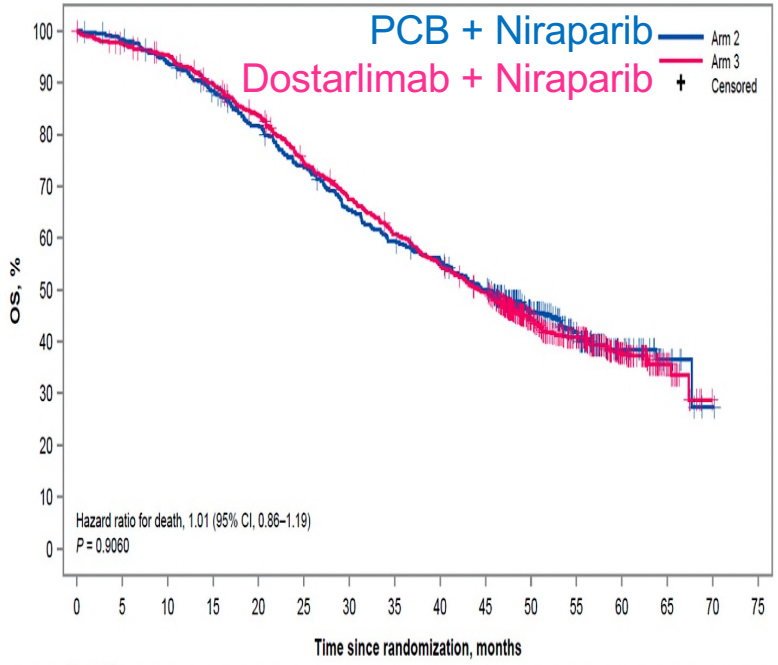
	Durvalumab + olaparib arm (*n* = 378)	Durvalumab arm (*n* = 374)	Control arm (*n* = 378)
Events, *n* (%)	145 (38.4)	137 (36.6)	150 (39.7)
Median OS (95% CI), months	48.5 (43.8-NR)	NR (NR-NR)	48.0 (44.1-NR)
HR (95% CI) versus control arm	0.95 (0.76-1.20); *P* = 0.68	0.92 (0.73-1.16)	



KEYLYNK 001



FIRST

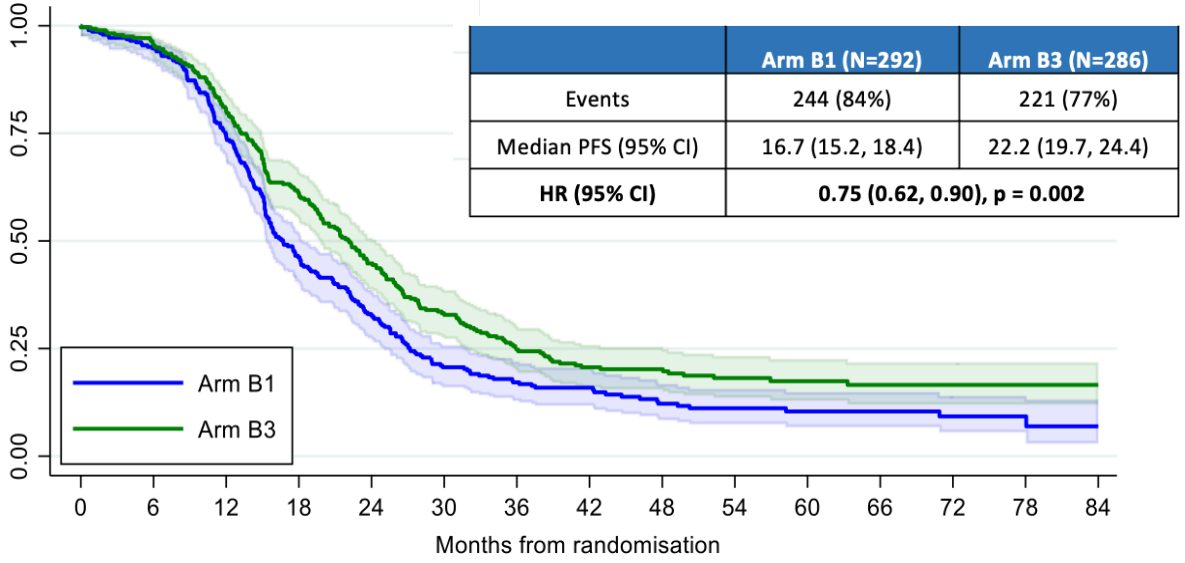


Harter P *Ann Oncol* 2025; Vergote I ESGO 2025;
Hardy-Bessard AC *Ann Oncol* 2025

Courtesy of Angeles Alvarez Secord, MD, MHSc

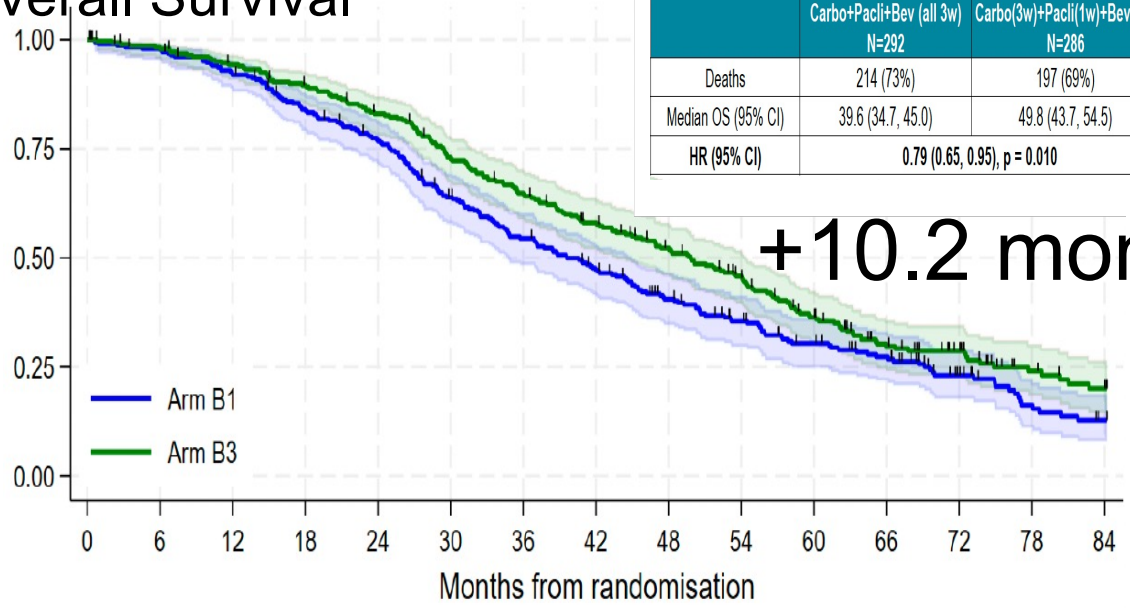
ICON8B: Revisiting Weekly Paclitaxel in Epithelial Ovarian Cancer
Survival outcomes

Progression-free Survival



	Arm B1 (N=292)	Arm B3 (N=286)
Events	244 (84%)	221 (77%)
Median PFS (95% CI)	16.7 (15.2, 18.4)	22.2 (19.7, 24.4)
HR (95% CI)	**0.75 (0.62, 0.90), p = 0.002**	

Overall Survival

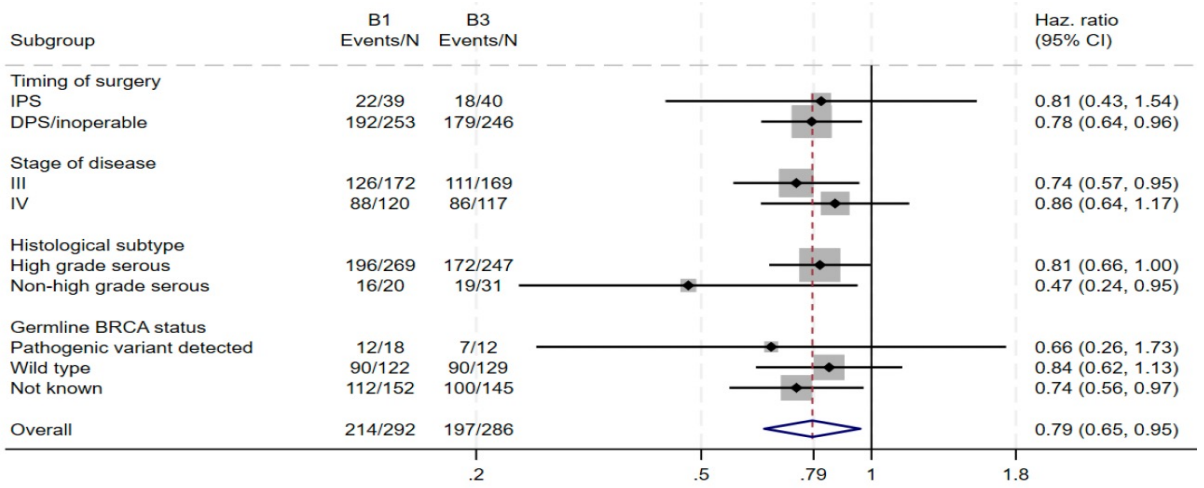


	Arm B1 Carbo+Pacli+Bev (all 3w) N=292	Arm B3 Carbo(3w)+Pacli(1w)+Bev(3w) N=286
Deaths	214 (73%)	197 (69%)
Median OS (95% CI)	39.6 (34.7, 45.0)	49.8 (43.7, 54.5)
HR (95% CI)	**0.79 (0.65, 0.95), p = 0.010**	

+10.2 months

Median FU 72 months

Overall Survival Subgroup Analysis



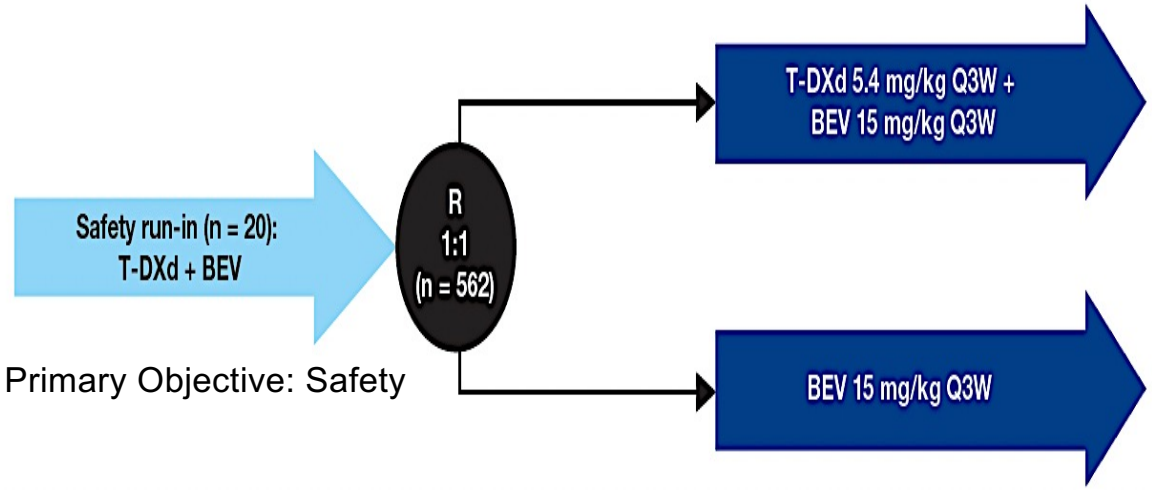
Clamp A ESMO 2025

Courtesy of Angeles Alvarez Secord, MD, MHSc

DESTINY-Ovarian01 (DO-01) Phase 3 Study of trastuzumab deruxtecan (T-DXd) with bevacizumab vs bevacizumab monotherapy 1L maintenance in HER2-expressing ovarian cancer

Patient population

- Adult (≥18 years)
- Histologically confirmed diagnosis of epithelial high-grade ovarian, fallopian tube, or primary peritoneal carcinoma
- Centrally confirmed HER2-expression (IHC 3+/2+/1+)[a]
- FIGO stage III or IV
- No disease progression after 1L therapy[b]
- ECOG PS of 0 or 1
- Received SOC BEV with platinum-based chemotherapy



Primary Objective: Safety

Primary Endpoint: PFS by BICR in HER2 IHC 3+/2+ population

Key Secondary: OS HER2 3+/2+ population

Secondary:
PFS by BICR HER2 3+/2+/1+
OS HER2 3+/2+/1+
PFS and PFS2 HER2 3+/2+ and 3+/2+/1+
ORR and DOR by BICR HER2 3+/2+ and 3+/2+/1+
TFST/TSST HER2 3+/2+ and 3+/2+/1+
Safety & PROs

Exploratory:
CBR by BICR HER2 3+/2+ and 3+/2+/1+
PFS by CA125 HER2 3+/2+ and 3+/2+/1+
HRQoL

Minimum 30% with HER2 IHC 3+
Maximum 15% with HER2 IHC 1+

Stratification Factors:
HER2 expression (3+ vs 2+ vs 1+)
Surgical outcome (No residual vs residual vs no surgery)
Histology (HGSC vs nonserous)

T-DXd for a maximum of 34 cycles and BEV for up to 16 cycles (maximum 22 cycles including concurrent with 1L chemotherapy or until PD, unacceptable toxicity, withdrawal consent or study termination.

González-Martín A ESMO GYN 2025

Courtesy of Angeles Alvarez Secord, MD, MHSc

AURELIA Open-Label Phase III 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]**

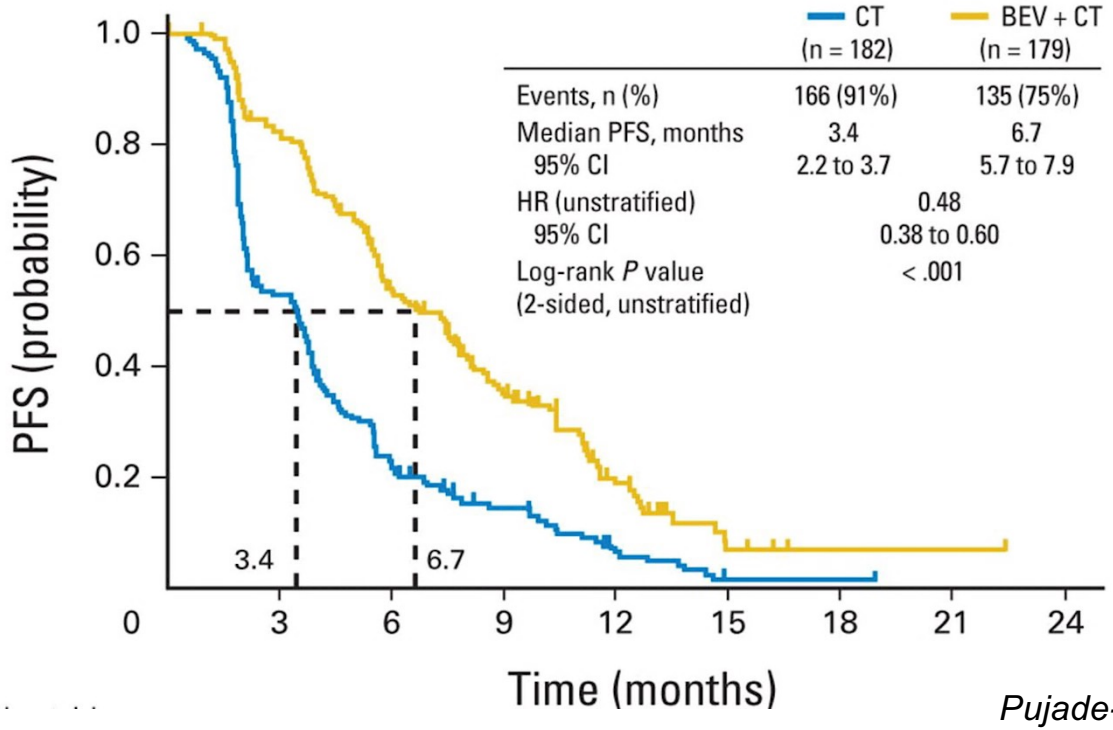
BEV 15 mg/kg q 3 w[b] + chemotherapy → **Treat to PD/toxicity** → **Investigator's choice* (without BEV)**

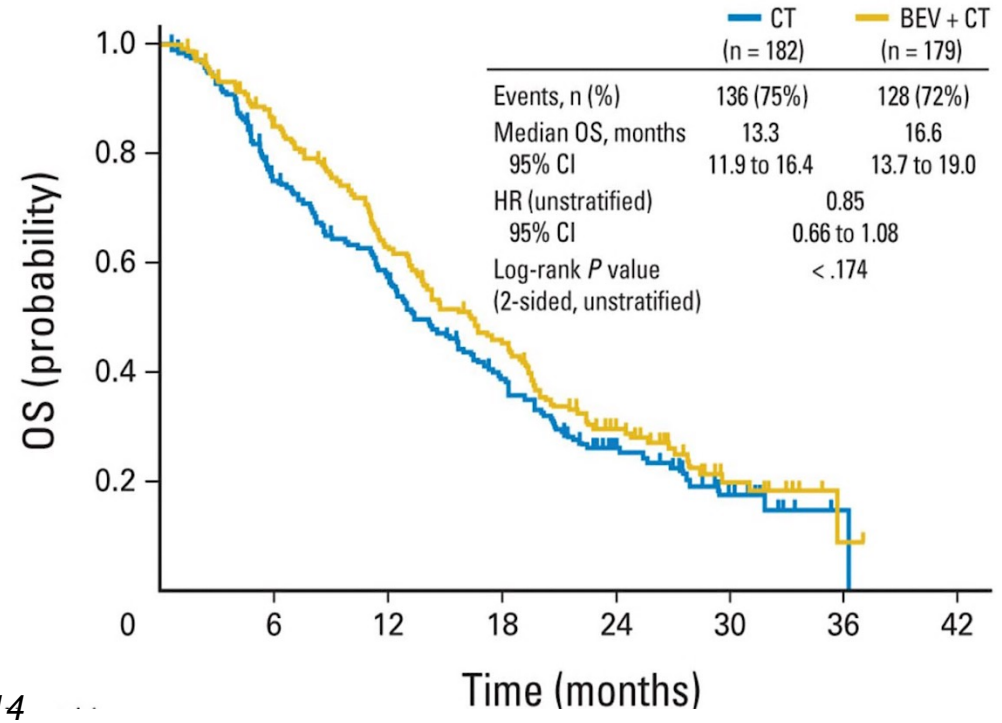
***Chemotherapy options (investigator's choice):**

Paclitaxel 80 mg/m² D1,8,15,22 – q4w

Topotecan 4 mg/m² D1,8,15 – q4w
(or 1.25 mg/m² D1 to 5 – q3w)

PLD 40 mg/m² D1 – q4w

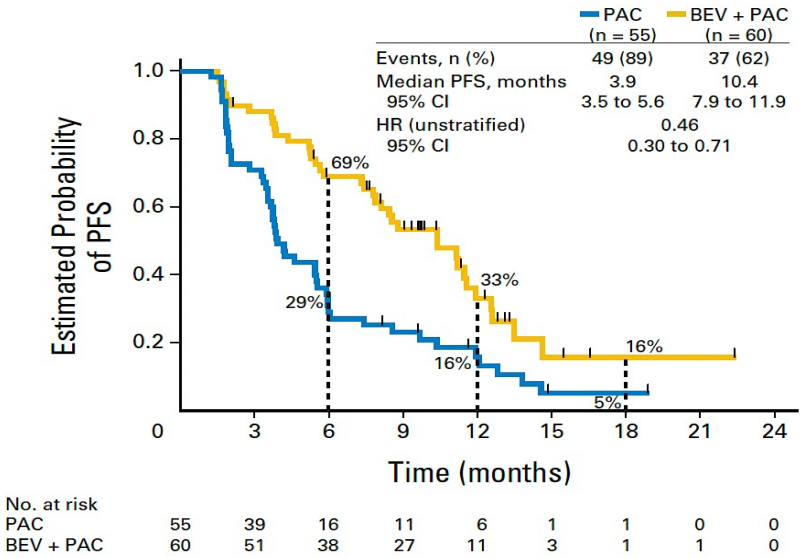


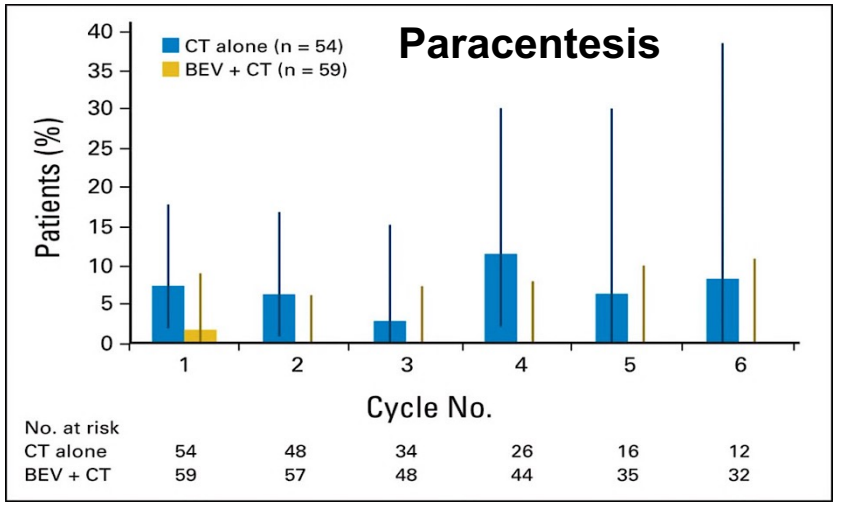


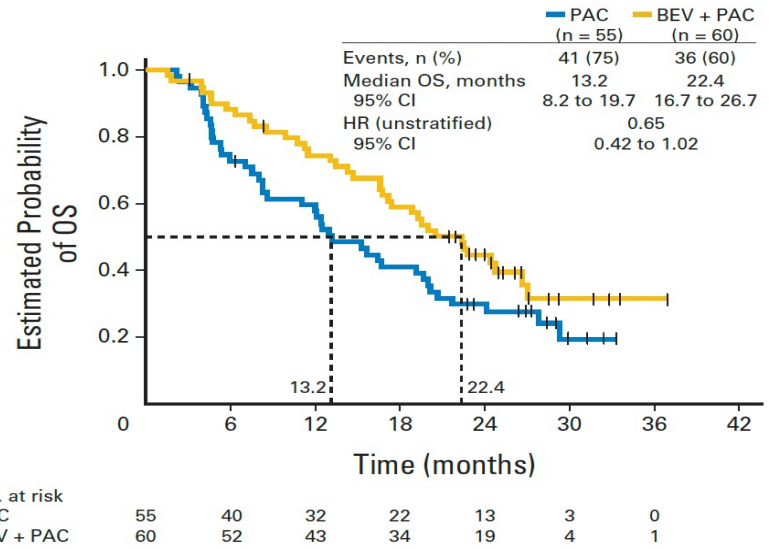
Pujade-Lauraine E JCO 2014

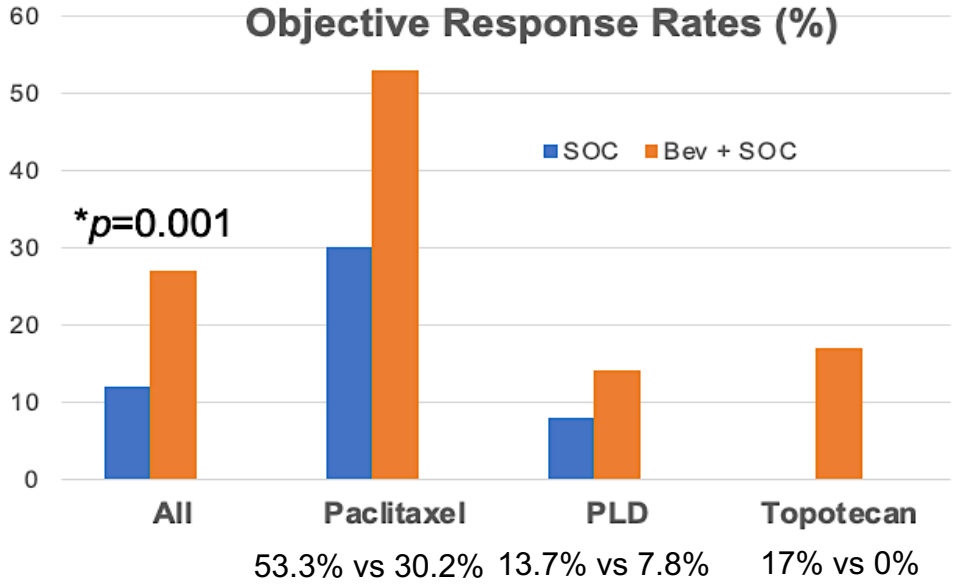
Courtesy of Angeles Alvarez Secord, MD, MHSc

AURELIA Open-Label Phase III Trial









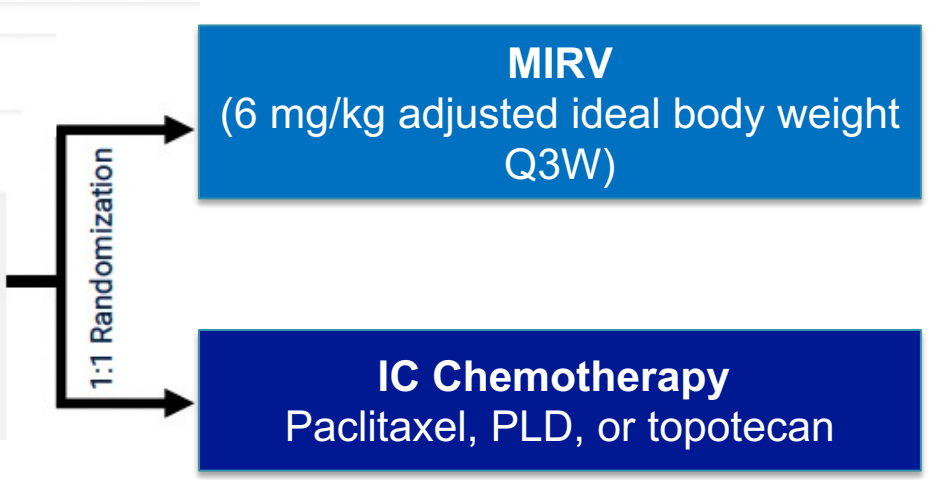
Pujade-Lauraine E *JCO* 2014; Poveda AM *JCO* 2015

Courtesy of Angeles Alvarez Secord, MD, MHSc

MIRASOL (GOG 3045/ENGOT-ov55) Phase 3 study MIRV vs Investigator's Choice Chemotherapy in FRα-Positive, Platinum-Resistant Ovarian Cancer (PROC) : Final Overall Survival Analysis

Patient Population

Key Eligibility
- Platinum-resistant disease (PFI ≤6 mo)
- FRα+ by IHC (≥75% tumor cells with ≥2+ membrane staining)
- High-grade serous
- 1-3 prior lines of therapy
- Prior BEV and PARPi allowed
- 1º platinum-refractory disease excluded (primary PFI <3 mo)



Treatment until progression or unacceptable toxicity

- **Primary Endpoint:** PFS by INV (BICR sensitivity analysis)
- **Key Secondary:**
  ORR by INV
  OS
  PRO (EORTC QLQ-OV28 abdominal/GI subscale)
- **Secondary: S**afety and tolerability, DOR, CA-125 response, and PFS2

Stratification Factors"

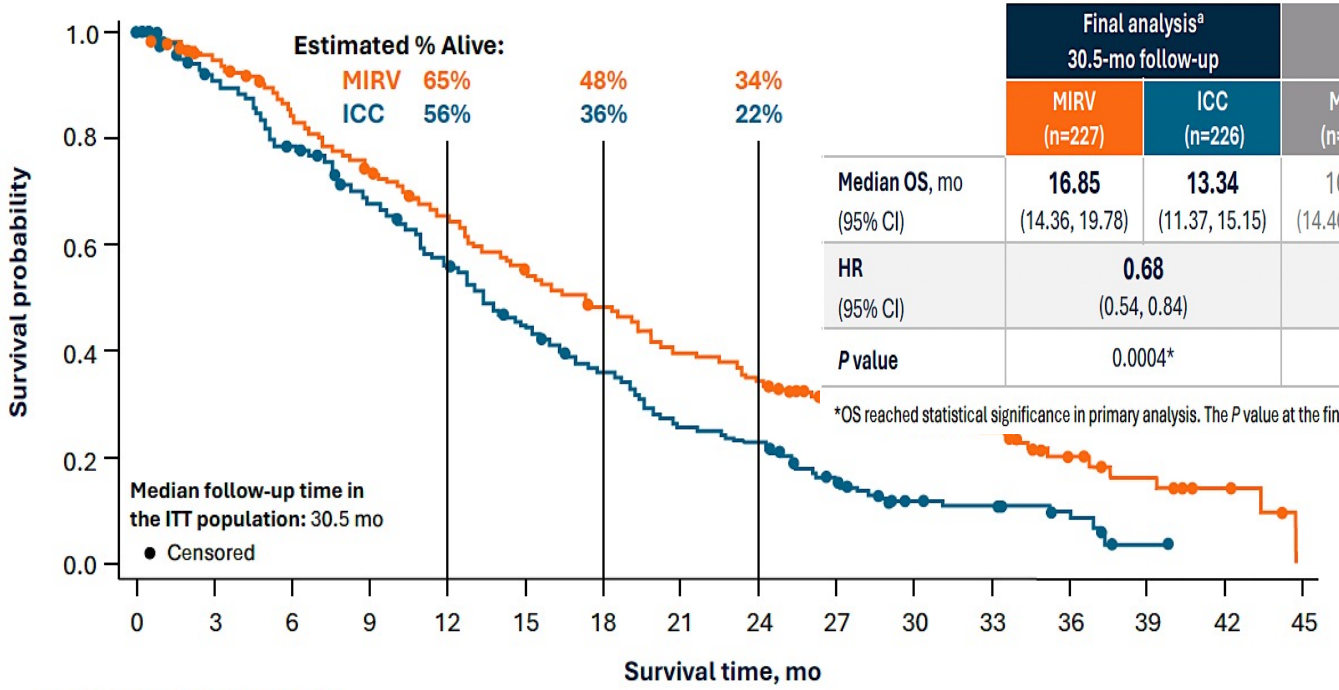
IC chemotherapy: paclitaxel, PLD, or topotecan
Prior lines of therapy: 1 vs 2 vs 3

*Final OS analysis after 300 deaths, if statistical significance at the IA is not reached per the prespecified efficacy stopping boundary

VanGorp T SGO Meeting 2025

Courtesy of Angeles Alvarez Secord, MD, MHSc

MIRASOL Phase III Trial: Platinum Resistant Ovarian Cancer

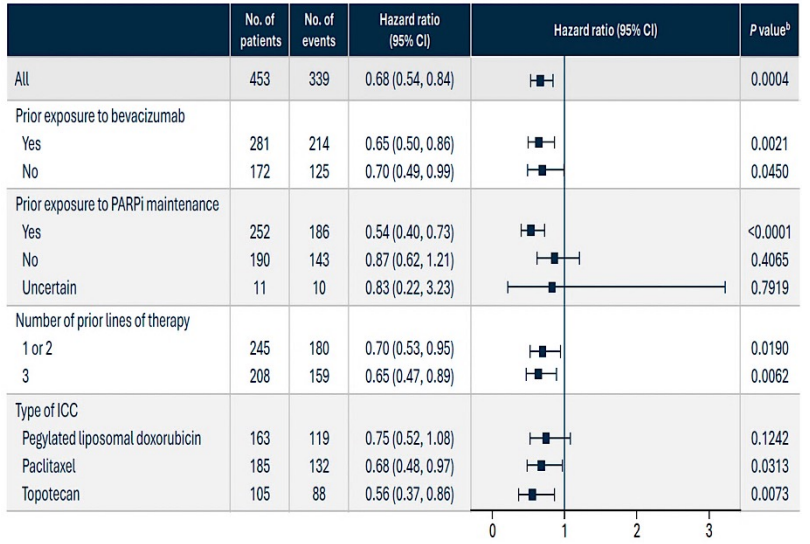


Number of patients at risk:

MIRV	227	204	178	156	135	114	98	80	70	50	33	25	12	8	4	0
ICC	226	186	159	134	110	85	67	48	42	25	13	11	7	1	0	

	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.



	Final analysis[a]	
Endpoints	MIRV (n=227)	ICC (n=226)
ORR by INV, n (%) (95% CI)	**95 (41.9)[c]** (35.4, 48.6)	**36 (15.9)** (11.4, 21.4)
Odds ratio (95% CI)	**3.75** (2.4, 5.85)	
Best overall response, n (%)		
Complete response	**13 (5.7)**	**0**
Partial response	**82 (36.1)**	**36 (15.9)**
Stable disease	87 (38.3)	91 (40.3)
Progressive disease	31 (13.7)	63 (27.9)
Not evaluable	14 (6.2)	36 (15.9)
Median DOR, mo (95% CI)	**6.93** (5.78, 8.84)	**4.44** (4.17, 5.75)
Median PFS2, mo (95% CI)	**11.01** (9.30, 12.02)	**7.59** (6.60, 8.84)

No new safety signals

Most common ≥ G3 in MIRV versus ICC, respectively, were blurred vision (8% vs 0%), keratopathy (10% vs 0%), abdominal pain (3% vs 1%), fatigue (2% vs 5%) and diarrhea (1% vs 1%). Ocular AEs completely or partially resolved in 93% of patients.

VanGorp T SGO Meeting 2025

Courtesy of Angeles Alvarez Secord, MD, MHSc

PICCOLO Phase II Trial: 3L+ Platinum Sensitive Ovarian Cancer

Novel therapies in PSOC are urgently needed:

In a Medidata® pooled clinical trials analysis of patients with 3L+ PSOC, of whom 96.9% had PD on PARPi

- ORR was 16.9%
- median PFS was 6.11 months
- median OS was 19.35 months

Patient Population (N=79)

Key eligibility

- Platinum-sensitive disease (defined as radiographic progression >6 mo from last dose of most recent platinum therapy)
- FRα positivity by IHC (≥75% tumor cells with ≥2+ membrane staining)
- At least 2 prior platinum-containing regimens
- Prior PARPi required if *BRCA*+
- Appropriate for single-agent therapy

Prior BEV not required

→ **MIRV** (6 mg/kg adjusted ideal body weight Q3W)

Treatment until PD, unacceptable toxicity, withdrawal of consent, or death, whichever comes first

- **Primary Endpoint: ORR** by INV
- **Key Secondary:** DOR by INV
- **Secondary:** PFS, OS, Safety

Alvarez Secord A *Ann Oncol* 2025; Coleman RL ASCO 2025

Courtesy of Angeles Alvarez Secord, MD, MHSc

PICCOLO Phase II Trial: 3L+ Platinum Sensitive Ovarian Cancer

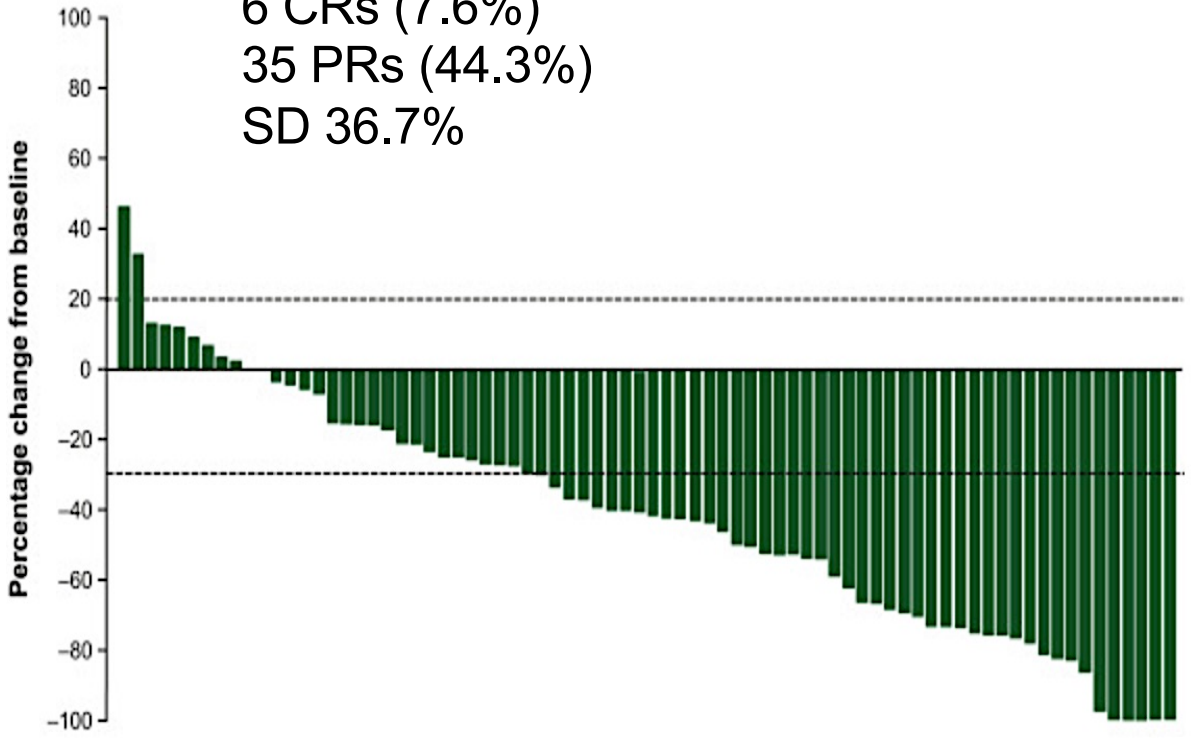
Confirmed inv-assessed ORR:

51.9% (95% CI 40.4%- 63.3%)

6 CRs (7.6%)

35 PRs (44.3%)

SD 36.7%



mDOR = 8.25 months (95% CI 5.55-10.78 months)

mPFS was 6.93 months (95% CI 5.85-9.59 months)

Alvarez Secord A *Ann Oncol* 2025

Subgroup	ORR subgroup, *n*	ORR, *n* (%) [95% CI]
Prior lines of therapy		
1 or 2	49	27 (55.1) [40.2-69.3]
3	24	12 (50.0) [29.1-70.9]
≥4	6	2 (33.3) [4.3-77.7]
Exposure to PARPis		
Yes	64	30 (46.9) [34.3-59.8]
Progression on PARPi[b]	59	27 (45.8) [32.7-59.2]
Without progression on PARPi	5	3 (60.0) [14.7-94.7]
No	12	9 (75.0) [42.8-94.5]
Unknown[c]	3	2 (66.7) [9.4-99.2]
Exposure to bevacizumab		
Yes	51	25 (49.0) [34.8-63.4]
No	28	16 (57.1) [37.2-75.5]
Exposure to both PARPis and bevacizumab	41	18 (43.9) [28.5-60.3]
Exposure to taxanes		
1 line only	57	28 (49.1) [35.6-62.7]
Multiple lines	20	12 (60.0) [36.1-80.9]
BRCA mutation status		
Positive	22	16 (72.7) [49.8-89.3]
Negative/Unknown	57	25 (43.9) [30.7-57.6]
Most recent PFI[d]		
≤12 months	43	18 (41.9) [27.0-57.9]
>12 months	34	22 (64.7) [46.5-80.3]
Missing	2	1 (50.0) [1.3-98.7]

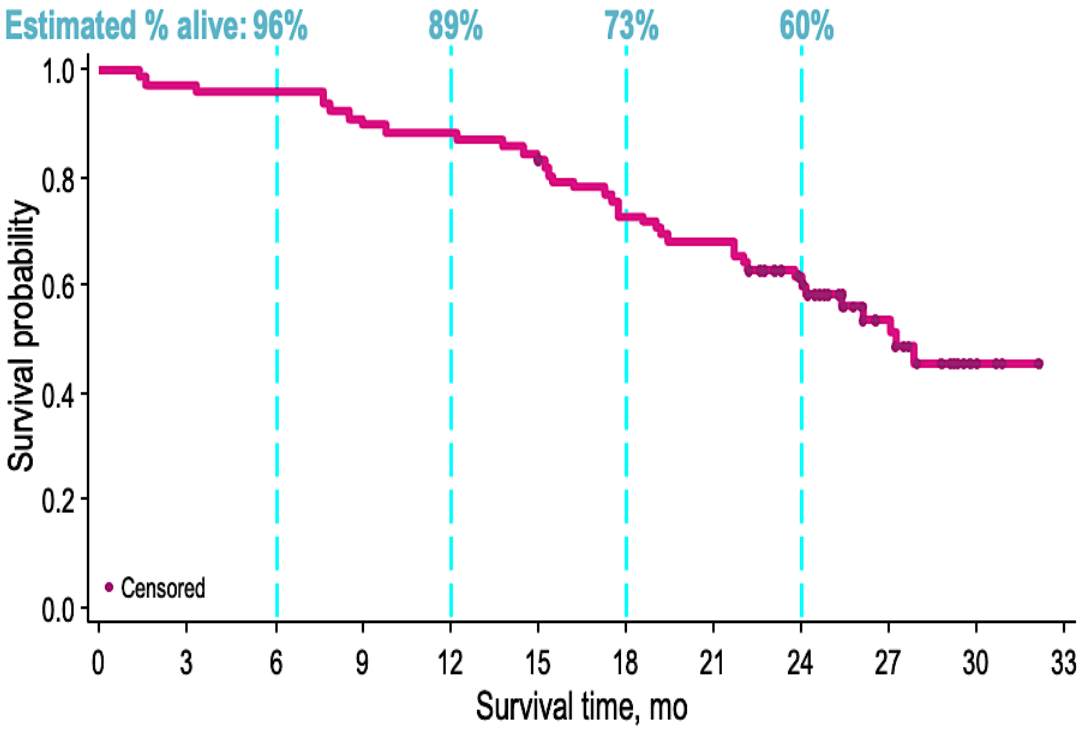
Courtesy of Angeles Alvarez Secord, MD, MHSc

PICCOLO Phase II Trial: 3L+ Platinum Sensitive Ovarian Cancer: Final Analysis

Efficacy summary in overall population and by prior PARPi treatment

Outcome	Overall population (N=79)	PARPi naïve (n=12)	Prior PARPi treatment (n=64)	PD with PARPi (n=59)
ORR, n (%)[a]	41 (51.9)	9 (75.0)	30 (46.9)	27 (45.8)
(95% CI)	(40.4–63.3)	(42.8–94.5)	(34.3–59.8)	(32.7–59.2)
Median DOR, mo[a,b]	8.25	8.77	8.25	7.33
(95% CI)	(5.55–10.78)	(3.52–15.18)	(5.45–10.78)	(5.03–10.78)
Median PFS, mo[a]	6.93	10.02	6.87	6.18
(95% CI)	(5.85–9.59)	(6.87–15.31)	(5.55–8.90)	(5.55–8.41)
Median OS, mo	27.17	27.89	27.17	27.04
(95% CI)	(23.79–NR)	(15.31–NR)	(23.79–NR)	(22.14–NR)

Median OS
27.17 Months (95% CI, 23.79-NR)



77% received subsequent therapy:
47% platinum, 32% gemcitabine, 30% anthracyclines; 28% other chemotherapy; 25% bev; 23% taxanes

Alvarez Secord A *Ann Oncol* 2025; Alvarez Secord A *ESMO-Gyn* 2025;

Courtesy of Angeles Alvarez Secord, MD, MHSc

FORWARD II: Mirvetuximab and Pembrolizumab in Platinum Resistant Ovarian Cancer

Patient Population (N=56)

Key eligibility

- Recurrent EOC/FT/PP Cancer
- Platinum-resistant disease (defined as radiographic progression within 6 mo from last dose of most recent platinum therapy)
- Tumor FRα expression thresholds were ≥25 % (dose escalation cohort) and ≥50 % (dose expansion cohort) of cells with ≥2+ membrane staining intensity.

→ **MIRV** (6 mg/kg adjusted ideal body weight) + Pembrolizumab 200 mg Q3W

- **Primary Endpoint: ORR**
- **Secondary:** DOR, PFS, Safety

Treatment until PD, unacceptable toxicity, withdrawal of consent, or death, whichever comes first. If MIRV was discontinued, participants could continue on pembrolizumab monotherapy for up to 2 years.

Participants grouped by FRα expression

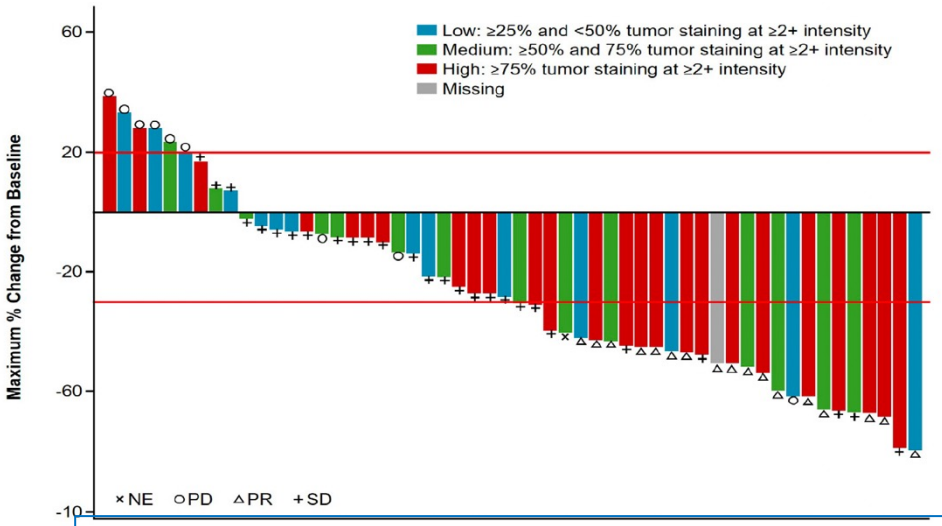
- low, *n* = 14
- medium, *n* = 14
- high, *n* = 26

- 20% had 3 priors, 43 % had ≥4 priors
- 43 % had prior Bev
- 41 % had prior PARPi

Matulonis U *Gynecol Oncol* 2025

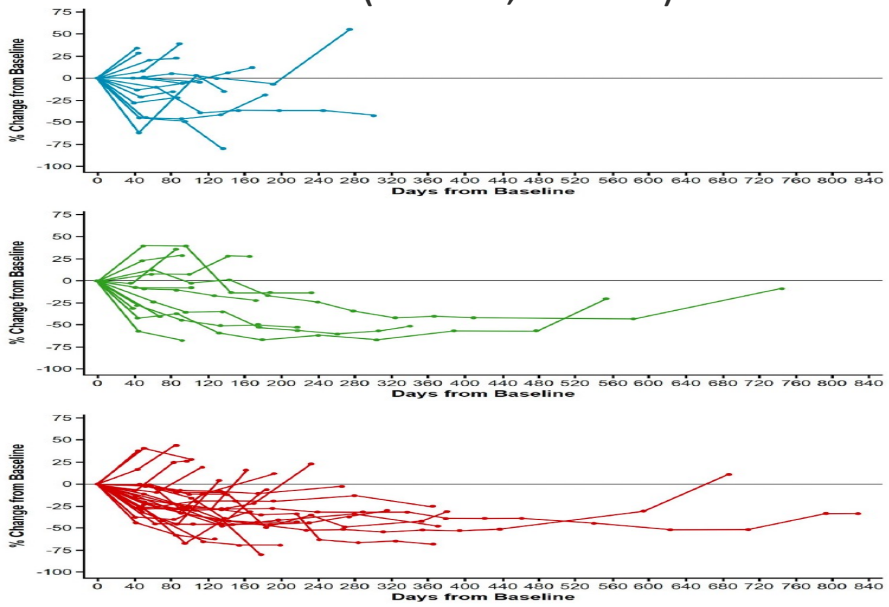
Courtesy of Angeles Alvarez Secord, MD, MHSc

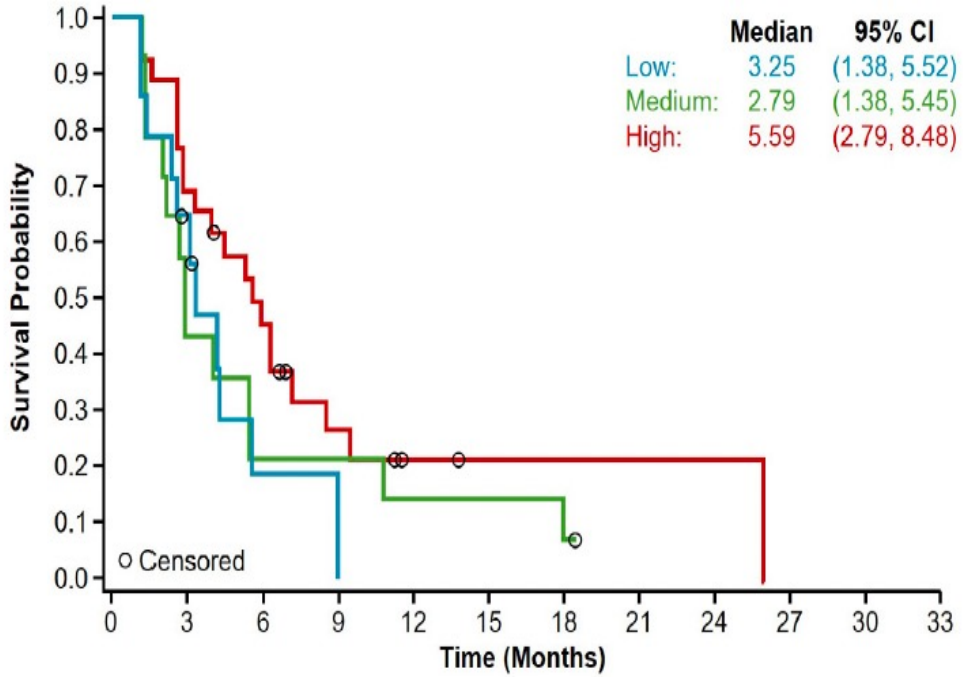
FORWARD II: Mirvetuximab and Pembrolizumab in PROC



N= 55 evaluable
ORR was 31 % (95% CI, 19–45)

Median DOR = 8.0 months (95% CI, 4.2-NR)





Median PFS = 4.2 months (95% CI, 2.8–5.6)

**Treatment-emergent pneumonitis 25 %, G ≥3 in 2 (4 %) participants.

Matulonis U *Gynecol Oncol* 2025

Courtesy of Angeles Alvarez Secord, MD, MHSc

DESTINY-PanTumor02: Phase 2 study of Trastuzumab deruxtecan (T-DXd), HER2-targeted ADC, in advanced HER2 expressing tumors. Part 1 Final Analysis

Study type

Open label, multicenter, multicohort, Phase 2

Treatment

T-DXd 5.4 mg/kg IV Q3W

NCT04482309

Endpoints

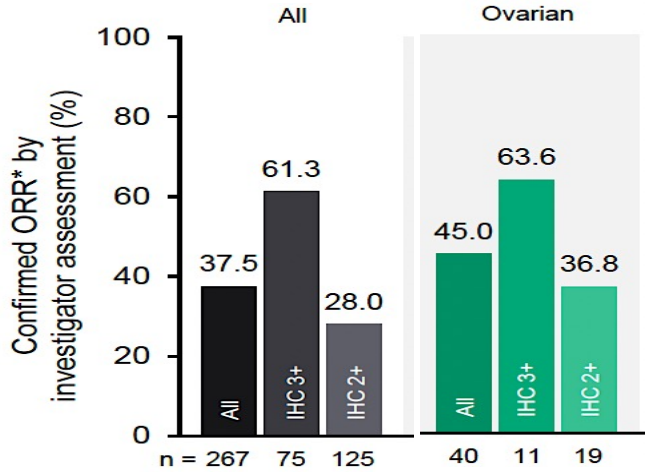
Primary:
- Confirmed ORR*

Secondary:
- DOR*
- DCR*
- PFS*
- OS
- Safety and tolerability

Exploratory:
- Subgroup analyses by HER2 status
- Subgroup analyses by biomarker status

Cohorts

- Endometrial
- Cervical
- Ovarian
- Bladder
- Other tumors†
- Biliary tract
- Pancreatic



Inv-assessed ORRs by central HER2 IHC Status

	All patients	HER2 IHC status by central testing**		HER2 IHC status at enrollment‡	
		IHC 3+	IHC 2+	IHC 3+	IHC 2+
Median PFS* Months	**5.9** (4.0, 8.3) [40]	**12.5** (3.1, NE) [11]	**4.1** (2.3, 12.6) [19]	**12.6** (4.1, NE) [15]	**4.4** (2.3, 7.1) [25]
Median OS* Months	**13.2** (8.0, 17.7) [40]	**20.0** (3.8, NE) [11]	**13.0** (4.7, 21.9) [19]	**20.0** (7.2, NE) [15]	**10.7** (5.9, 14.8) [25]

(95% CI) [n]; ** Based on ASCO/CAP guidelines for HER2 scoring for gastric cancer; ‡ HER2 for enrollment based on local assessment.

Makker V. *ESMO* 2025

Courtesy of Angeles Alvarez Secord, MD, MHSc

DESTINY-PanTumor02: Phase 2 study of Trastuzumab deruxtecan (T-DXd), HER2-targeted ADC, in advanced HER2 expressing tumors. Part 1 Final Analysis

Safety Summary

AE category, n (%)	All patients (N=267)
Any AE	261 (97.8)
Any drug-related AE	226 (84.6)
Grade ≥3	111 (41.6)
Drug-related serious AEs	36 (13.5)
Drug-related AEs associated with dose interruptions	55 (20.6)
Drug-related AEs associated with dose reductions	56 (21.0)
Drug-related AEs associated with discontinuations	27 (10.1)
Drug-related AEs associated with deaths	4 (1.5)
Adjudicated drug-related ILD/pneumonitis	31 (11.6)
Grade ≥3	4 (1.5)

- Drug-related Grade ≥3 AEs occurred in 111 (41.6%) patients
- The most common were neutropenia (11.2%), anemia (10.9%), decreased ANC (8.6%), and fatigue (6.0%)
- Adjudicated drug-related ILD/pneumonitis 11.6% (n=31)
  - Most G1 (n=8, 3.0%) or G2 (n=19, 7.1%)
- Three (1.1%) G5 events reported

Makker V. *ESMO* 2025

Courtesy of Angeles Alvarez Secord, MD, MHSc

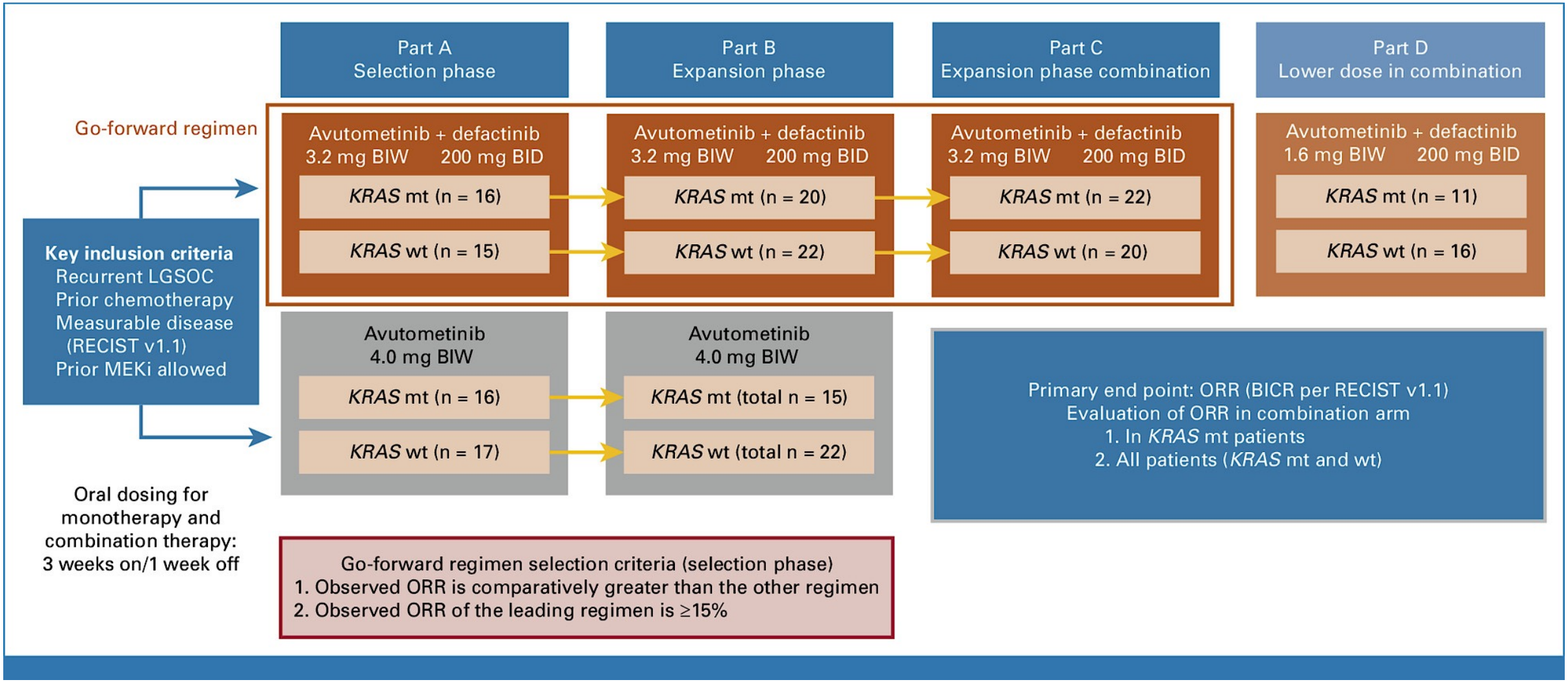
Emerging ADC Therapies: Clinical Characteristics and Efficacy Summary

	T-DXd HER2	R-DXd CDH6	Rina-S FRa	AZD5335 FRa	HS-20089 B7-HR	TUB-040 NaPi2b
Population	EOC	HGSC/HGEC	EOC	EOC	EOC	HGSC
Prior Regimen (1L/2L/3L)	Median 3 (1-12)	9%/39%/51%	Median 3 (1-5)	Median 3 (1-9)	Median 3 (1-9)	Median 4 (1-7)
PFI < 3 mo	--	44%	--	--	46%	--
Prior PARPi	--	70%	64%	63%	73%	--
Prior Bev	--	83%	90%	69%	73%	84%
Prior Mirv	--	3%	19%	4%*	--	13%
ORR (%)	64% 3+/37% 2+	44-57%	23-56%	54%	48%	55%
Median DoR (mo)	11.3	--	NR	--	6.8	--
Median PFS (mo)	12.5 3+/5.9 all	--	--	--	6.4	--
Median OS (mo)	13.2	--	--	--	14.6	--

Meric-Bernstam F *JCO* 2023; Ray-Coquard I ESMO 2025; Lee EK SGO 2025; Oaknin A ESMO 2025; Yuan G ESMO 2025; Gonzalez Martin A ESMO 2025

Courtesy of Angeles Alvarez Secord, MD, MHSc

Efficacy and safety of avutometinib +/- defactinib in recurrent LGSOC: ENGOT-OV60/GOG-3052/RAMP 201

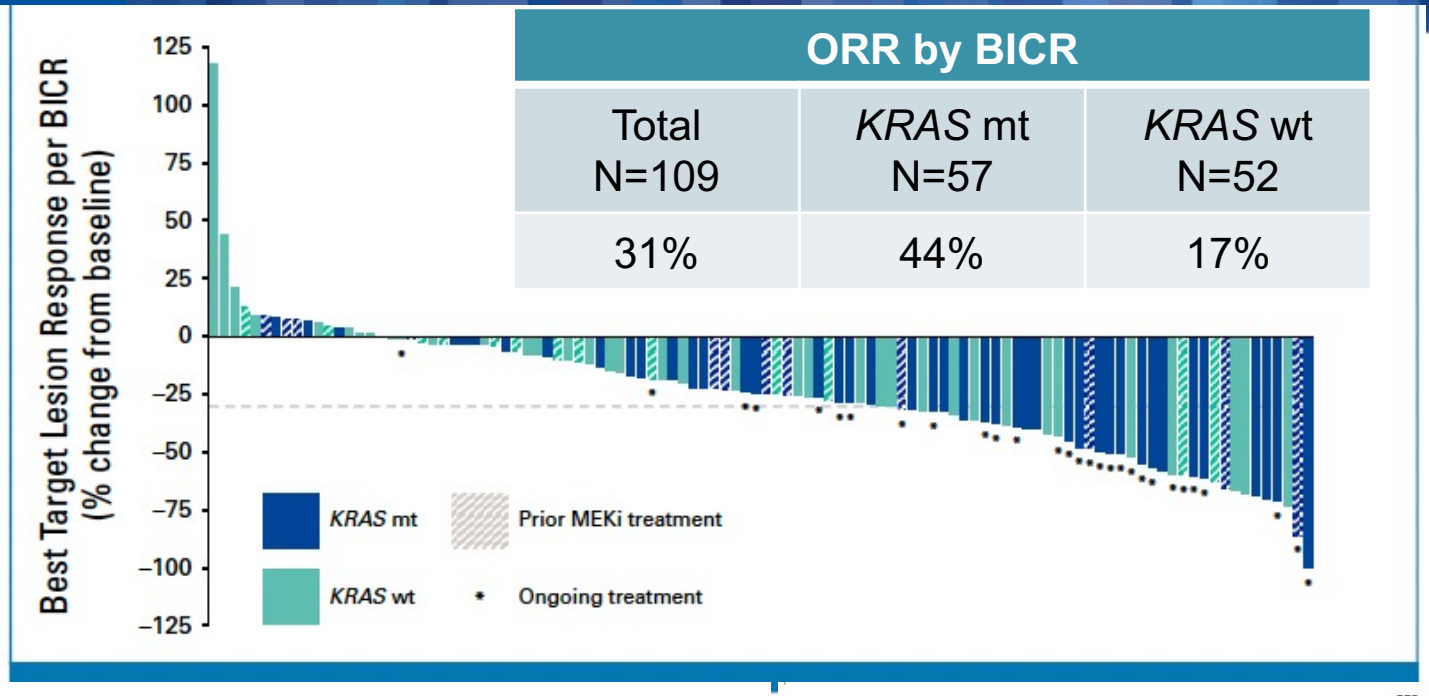


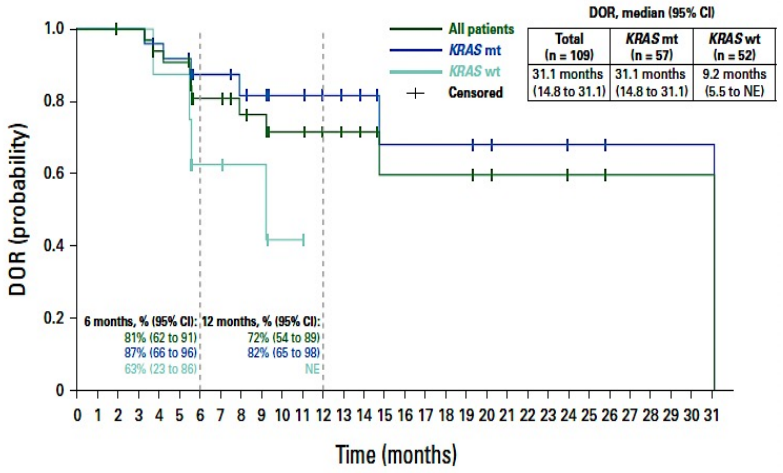
Banerjee SN *J Clin Oncol* 2025

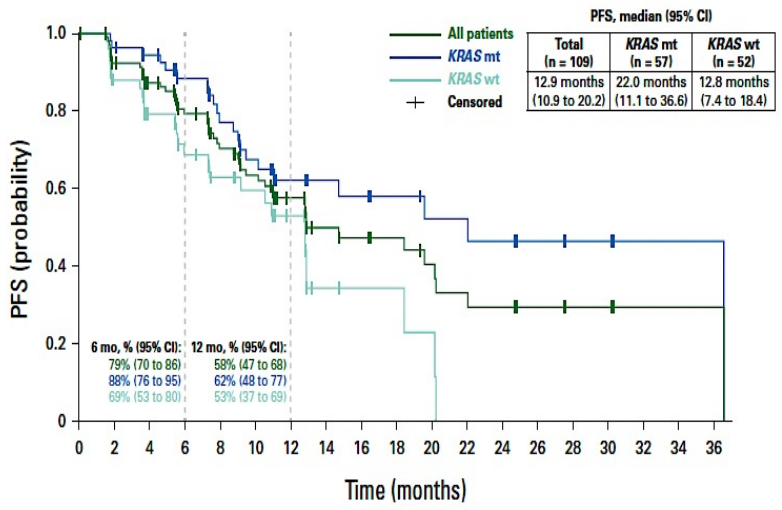
Courtesy of Angeles Alvarez Secord, MD, MHSc

Efficacy and safety of avutometinib +/- defactinib in recurrent LGSOC: ENGOT-OV60/GOG-3052/RAMP 201

ORR by BICR		
Total N=109	*KRAS* mt N=57	*KRAS* wt N=52
31%	44%	17%







Preferred Term	Avutometinib (3.2 mg two times per week) + Defactinib (200 mg two times per day), n = 115	
	All Grades, No. (%)	Grade ≥3,[a] No. (%)
Nonlaboratory AEs		
Nausea	77 (67)	3 (3)
Diarrhea	67 (58)	9 (8)
Edema peripheral	61 (53)	1 (1)
Rash[b]	58 (50)	3 (3)
Fatigue	50 (44)	3 (3)
Vomiting	49 (43)	3 (3)
Vision blurred	47 (41)	0
Dermatitis acneiform	39 (34)	5 (4)
Dry skin	30 (26)	0
Anemia	26 (23)	6 (5)
Stomatitis	18 (16)	3 (3)
Laboratory-related AEs		
Increased blood CPK	69 (60)	28 (24)
Increased blood bilirubin	38 (33)	5 (4)
AST increased	36 (31)	2 (2)
ALT increased	25 (22)	2 (2)

Banerjee SN *J Clin Oncol* 2025

Courtesy of Angeles Alvarez Secord, MD, MHSc

Efficacy and safety of avutometinib +/- defactinib in recurrent LGSOC: ENGOT-OV60/GOG-3052/RAMP 201

May 8, 2025

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

For patients with KRAS-mutated recurrent low-grade serous ovarian cancer who have received prior systemic therapy.

https://www.fda.gov/drugs/resources-information-approved-drugs/fda-grants-accelerated-approval-combination-avutometinib-and-defactinib-kras-mutated-recurrent-low

Courtesy of Angeles Alvarez Secord, MD, MHSc

Second Opinion: Integrating Novel Approaches into the Management of Non-Muscle-Invasive and Muscle-Invasive Bladder Cancer

A CME Symposium Held Adjunct to the
2026 ASCO® Genitourinary Cancers Symposium

Thursday, February 26, 2026
7:00 PM – 9:00 PM PT (10:00 PM – 12:00 AM ET)

Faculty

Matthew D Galsky, MD
Shilpa Gupta, MD
Andrea Necchi, MD

Moderator

Terence Friedlander, MD

RTP
RESEARCH
TO PRACTICE

Thank you for joining us!

Please take a moment to complete the survey currently up on Zoom. Your feedback is very important to us. The survey will remain open for 5 minutes after the meeting ends.

Information on how to obtain CME, ABIM MOC and ABS credit is provided in the Zoom chat room. Attendees will also receive an email in 1 to 3 business days with these instructions.

RTP Year in Review 2026