Data + Perspectives: The Potential Role of TROP2- and CDH6-Directed Antibody-Drug Conjugates in Gynecologic Cancers

An Independent CME Symposium During the SGO 2026 Annual Meeting on Women's Cancer®

Sunday, April 12, 2026

1:30 PM – 3:00 PM AST

Faculty

Ramez N Eskander, MD

Bradley J Monk, MD

Moderator

Kathleen N Moore, MD, MS

RTP RESEARCH TO PRACTICE

Faculty

Ramez N Eskander, MD
Julie St John Endowed Chair
in Gynecologic Oncology
Professor, Department of Obstetrics, Gynecology
and Reproductive Sciences
Clinical Trials Office Medical Director
Fellowship Director – Gynecologic Oncology
UC San Diego Health
Rebecca and John Moores NCI-Designated
Comprehensive Cancer Center
San Diego, California

Bradley J Monk, MD
Medical Director, Late-Phase Research Program
Florida Cancer Specialists & Research Institute
Professor at the University of Central Florida College of Medicine
Vice President and Member, Board of Directors
GOG Foundation
Co-Director, GOG Partners
West Palm Beach, Florida

Moderator

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
RESEARCH
TO PRACTICE

Prof Eskander — Disclosures
Faculty

Advisory Committees and Consulting Agreements	AbbVie Inc, AstraZeneca Pharmaceuticals LP, BeOne, Bristol Myers Squibb, Daiichi Sankyo Inc, Eisai Inc, Foundation Medicine, Gilead Sciences Inc, GSK, ImmunoGen Inc, Loxo Oncology Inc, a wholly owned subsidiary of Eli Lilly & Company, Merck, MSD, Myriad Genetic Laboratories Inc, Natera Inc, Novocure Inc, Pfizer Inc, pharmaand GmbH, PMV Pharma, Regeneron Pharmaceuticals Inc, Tesaro, A GSK Company
Data and Safety Monitoring Boards/Committees	Xencor

RTP
RESEARCH
TO PRACTICE

Dr Monk — Disclosures
Faculty

Consulting Agreements	AbbVie Inc, Alkermes, AstraZeneca Pharmaceuticals LP, BioNTech SE, Corcept Therapeutics Inc, Daiichi Sankyo Inc, Eisai Inc, Genentech, a member of the Roche Group, Genmab US Inc, GSK, ImmunoGen Inc, Incyte Corporation, Karyopharm Therapeutics, Lilly, Merck, Mersana Therapeutics Inc, Mural Oncology Inc, Myriad Genetic Laboratories Inc, Natera Inc, Novartis, Novocure Inc, OncoC4, Panavance Therapeutics, Pfizer Inc, pharmaand GmbH, ProfoundBio, Regeneron Pharmaceuticals Inc, Seagen Inc, Sutro Biopharma, Takeda Pharmaceuticals USA Inc, Tubulis, Verastem Inc, Zai Lab, Zentalis Pharmaceuticals, Zymeworks Inc
Speakers Bureaus	AbbVie Inc, AstraZeneca Pharmaceuticals LP, Daiichi Sankyo Inc, Eisai Inc, GSK, ImmunoGen Inc, Merck, Takeda Pharmaceuticals USA Inc, Zai Lab

Dr Moore — Disclosures
Moderator

Advisory Committees	AstraZeneca Pharmaceuticals LP, Corcept Therapeutics Inc, GSK, Mersana Therapeutics Inc
Consulting Agreements	Aadi Bioscience, AbbVie Inc, AstraZeneca Pharmaceuticals LP, BioNTech SE, Caris Life Sciences, Corcept Therapeutics Inc, Daiichi Sankyo Inc, Duality Biologics, GSK, ImmunoGen Inc, Janssen Biotech Inc, Merck, Regeneron Pharmaceuticals Inc, Schrödinger, Takeda Pharmaceuticals USA Inc, Verastem Inc, Whitehawk Therapeutics, Zentalis Pharmaceuticals, Zymeworks Inc
Contracted Research	Accent Therapeutics, Advaxis Inc, Allarity Therapeutics, AstraZeneca Pharmaceuticals LP, Daiichi Sankyo Inc, GSK, Immunocore, Iovance Biotherapeutics, Regeneron Pharmaceuticals Inc, Schrödinger, Verastem Inc
Data and Safety Monitoring Boards/Committees	Bicycle Therapeutics
Nonrelevant Financial Relationships	ASCO, GOG Partners, NRG Oncology

RTP
RESEARCH
TO PRACTICE

Commercial Support

This activity is supported by educational grants from Daiichi Sankyo Inc, Gilead Sciences Inc, and Merck.

Research To Practice CME Planning Committee Members, Staff and Reviewers

Planners, scientific staff and independent reviewers for Research To Practice have no relevant financial relationships to disclose.

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.

RTP
RESEARCH
TO PRACTICE

Save The Date

Fifth Annual
National General Medical Oncology Summit

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

Moderated by Neil Love, MD

Clinicians in the Meeting Room

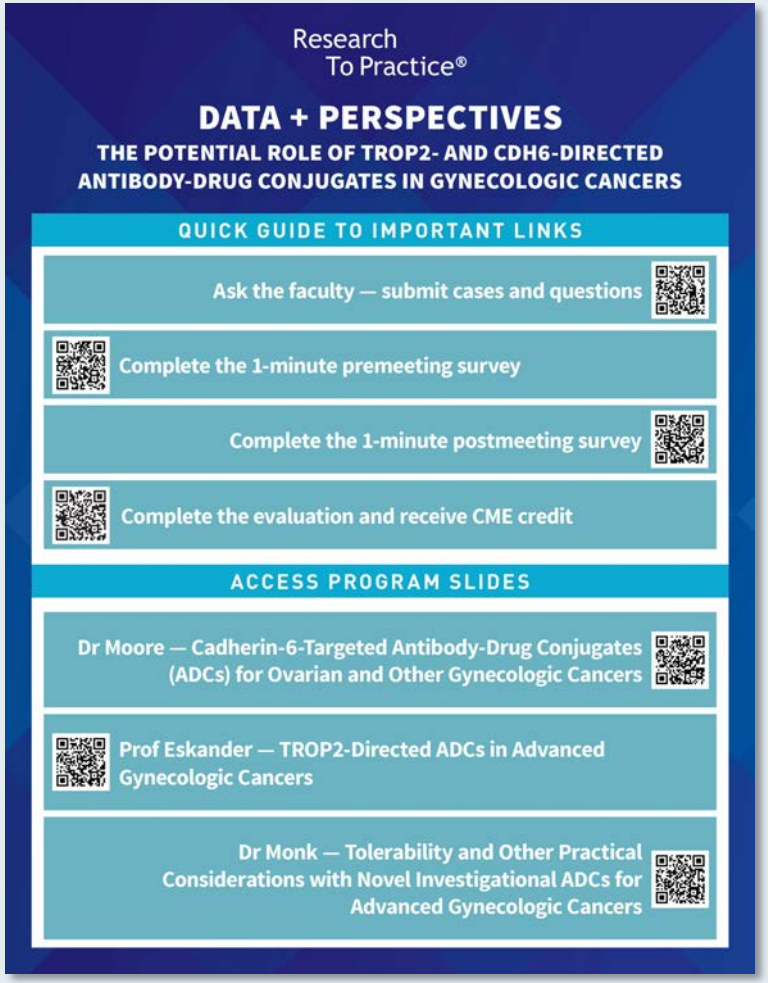
Please refer to the printed handout provided with your meeting syllabus, and scan the corresponding QR code to

Review and Download Program Slides.

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

Ask a Question: We will aim to address as many questions as possible during the program.

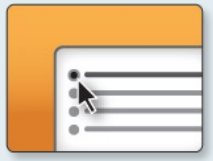
Get CME Credit: Complete the course evaluation.



RTP RESEARCH TO PRACTICE

Clinicians Attending via Zoom

Review Program Slides: A link to the program slides will be posted in the chat room at the start of the program.



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

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

Get CME Credit: A credit link will be provided in the chat room at the conclusion of the program.

RTP
RESEARCH
TO PRACTICE

About the Enduring Program

- The live meeting is being video and audio recorded.
- The proceedings from today will be edited and developed into an enduring web-based program.
  An email will be sent to all attendees when the activity is available.
- To learn more about our education programs, visit our website, **www.ResearchToPractice.com**

RTP RESEARCH TO PRACTICE

Data + Perspectives: The Potential Role of TROP2- and CDH6-Directed Antibody-Drug Conjugates in Gynecologic Cancers

An Independent CME Symposium During the SGO 2026 Annual Meeting on Women's Cancer®

Sunday, April 12, 2026

1:30 PM – 3:00 PM AST

Faculty

Ramez N Eskander, MD

Bradley J Monk, MD

Moderator

Kathleen N Moore, MD, MS

RTP RESEARCH TO PRACTICE

Agenda

Module 1: Advances in Human Cadherin-6-Targeted Antibody-Drug Conjugates (ADCs) in Ovarian and Other Gynecologic Cancers — Dr Moore

Module 2: Leveraging TROP2-Directed ADCs in Advanced Gynecologic Cancers — Prof Eskander

Module 3: Tolerability and Other Practical Considerations with Novel Investigational ADCs in Advanced Gynecologic Cancers — Dr Monk

Agenda

Module 1: Advances in Human Cadherin-6-Targeted Antibody-Drug Conjugates (ADCs) in Ovarian and Other Gynecologic Cancers — Dr Moore

Module 2: Leveraging TROP2-Directed ADCs in Advanced Gynecologic Cancers — Prof Eskander

Module 3: Tolerability and Other Practical Considerations with Novel Investigational ADCs in Advanced Gynecologic Cancers — Dr Monk

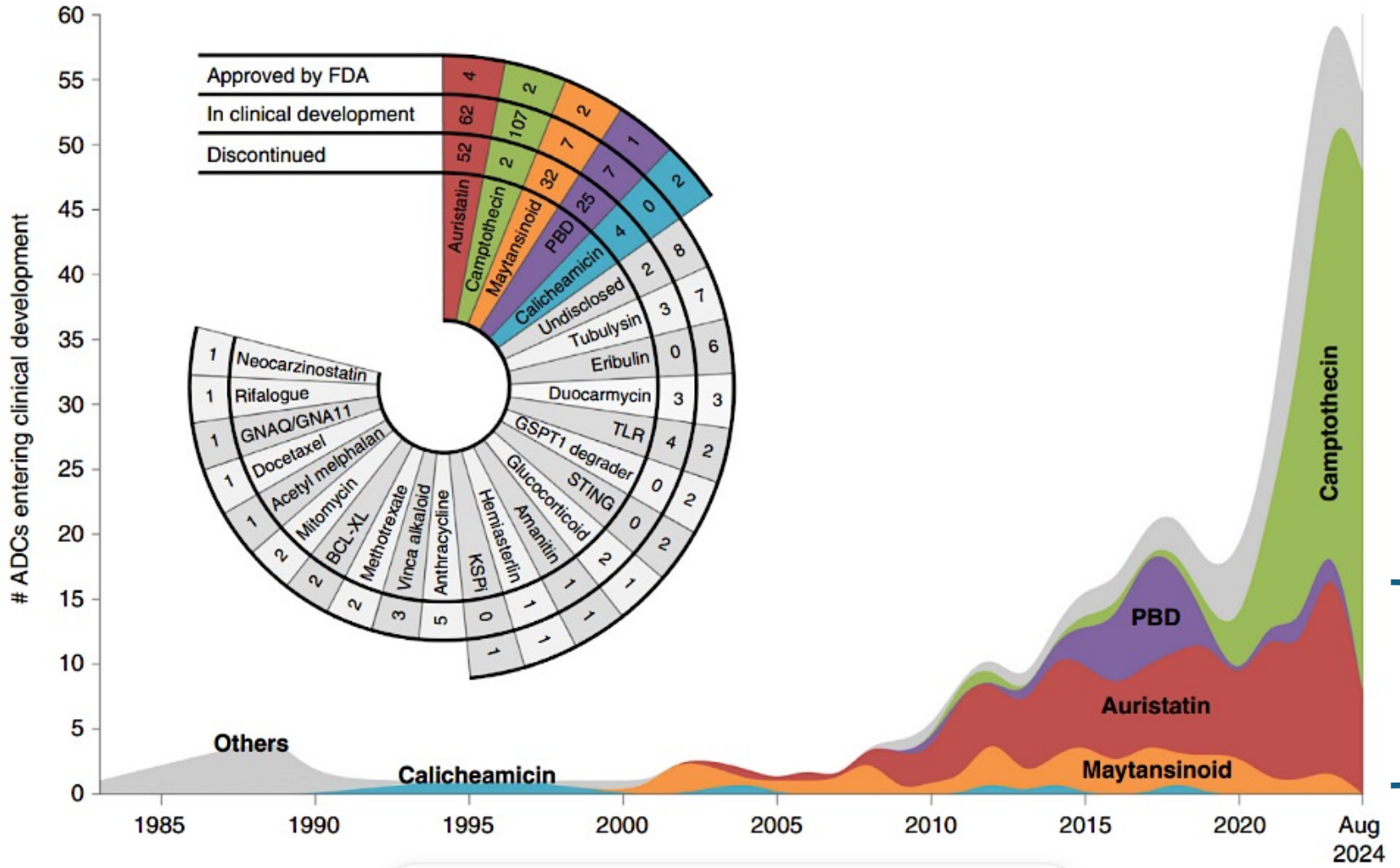
Antibody Drug Conjugate in Ovarian Cancer: Selection, Sequencing and Strategy

Tumor Associated Antigens Including CDH6, TROP2 and FRα

Kathleen N. Moore, MD, MS, FASCO
Deputy Director, Buffett Cancer Center at the University of Nebraska Medical Center
Professor, Gynecologic Oncology
ASCO BOD
GOG F BOD

@DrKatyMoore

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

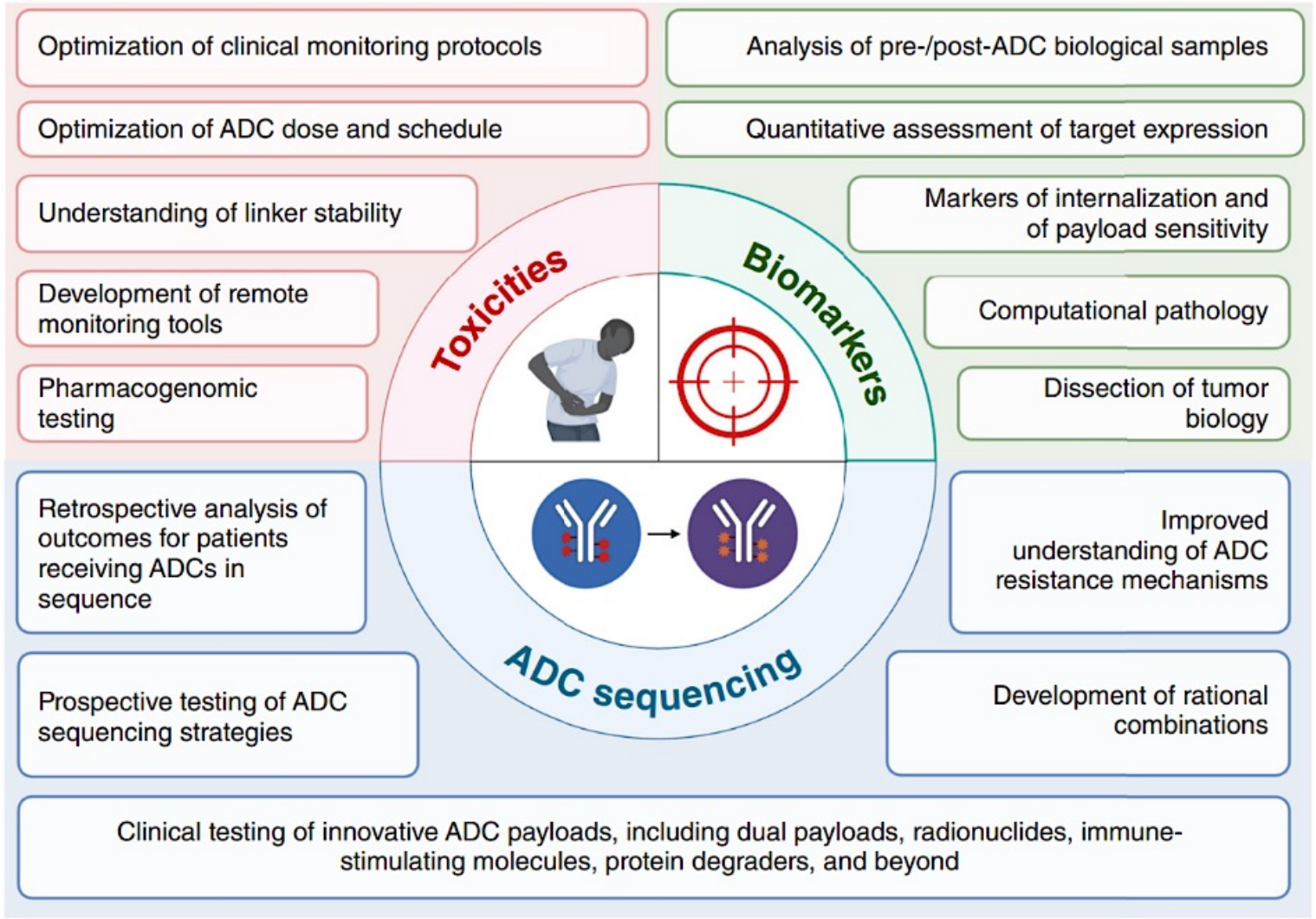


In gynecology, the payloads mainly fall into 2 classes:

- Camptothecins
- Microtubule Toxins

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

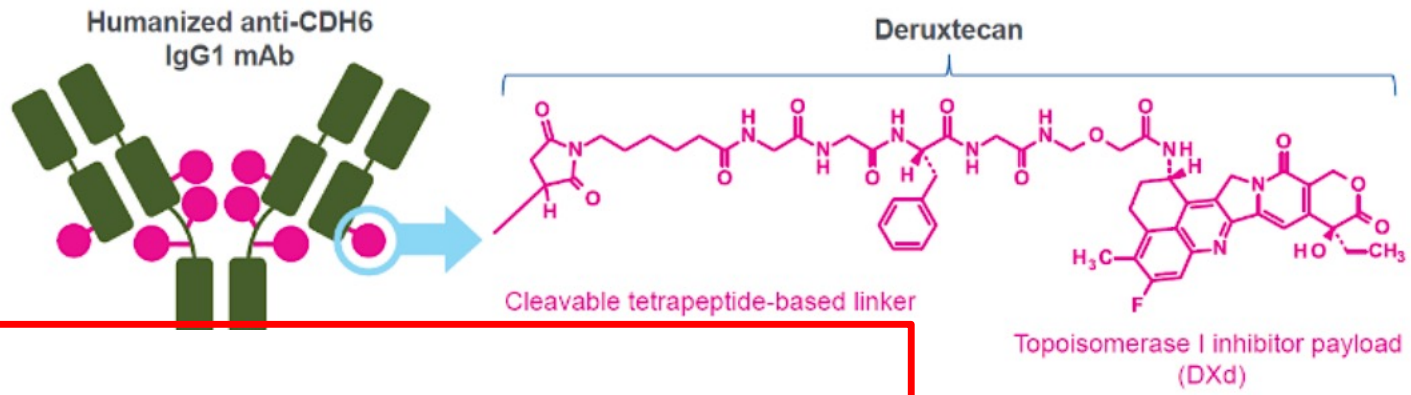
Opportunities for ADCs across a variety of targets and expanding considerations for the treatment setting demands focus on Selection, Sequencing, Safety and Strategy



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

Targeting Cadherin 6 (CDH6): Raludotatug deruxtecan

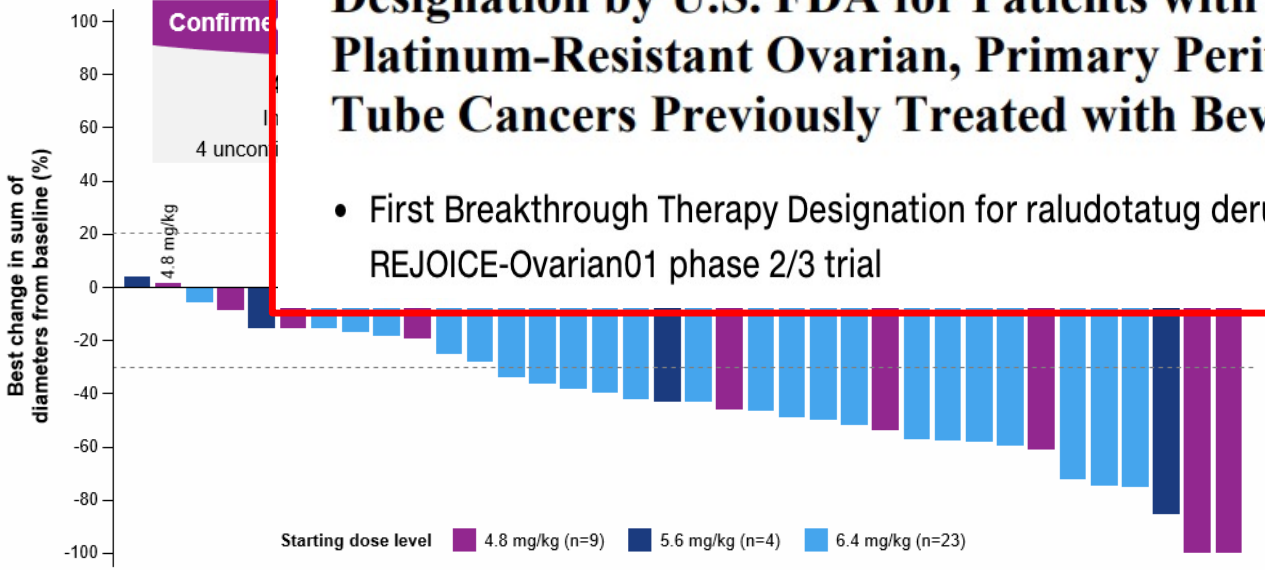
	Raludotatug deruxtecan (DS-6000)[1,2]
Payload	Topoisomerase 1 inhibitor (DXd)
DAR	8
Linker	
Trial	



Press Release

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

- First Breakthrough Therapy Designation for raludotatug deruxtecan based on phase 1 trial and REJOICE-Ovarian01 phase 2/3 trial



(95% CI: 3.1–NE)
6.7 months (1.4–16.8)

5% CI: 5.3–11.4)

Median PFS:[b]

8.1 months (95% CI: 5.3–NE)
Median (range) FU: 4.0 months (0–25.1)

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

@DrKatyMoore

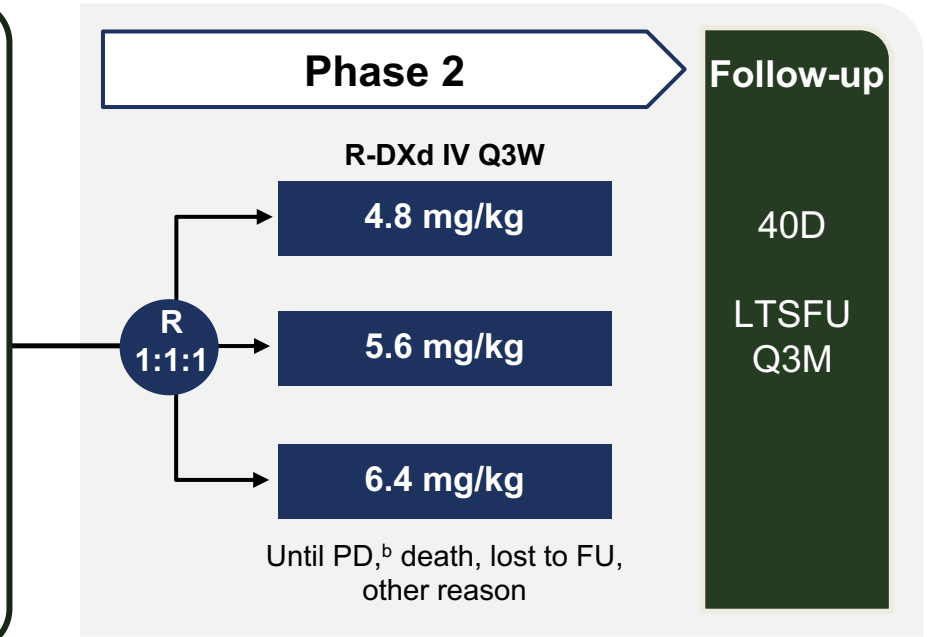
REJOICE-Ovarian01/GOG-3096: Phase 2/3 Randomized Study of R-DXd in Platinum-Resistant EOC

Key eligibility criteria:

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

Stratification:

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

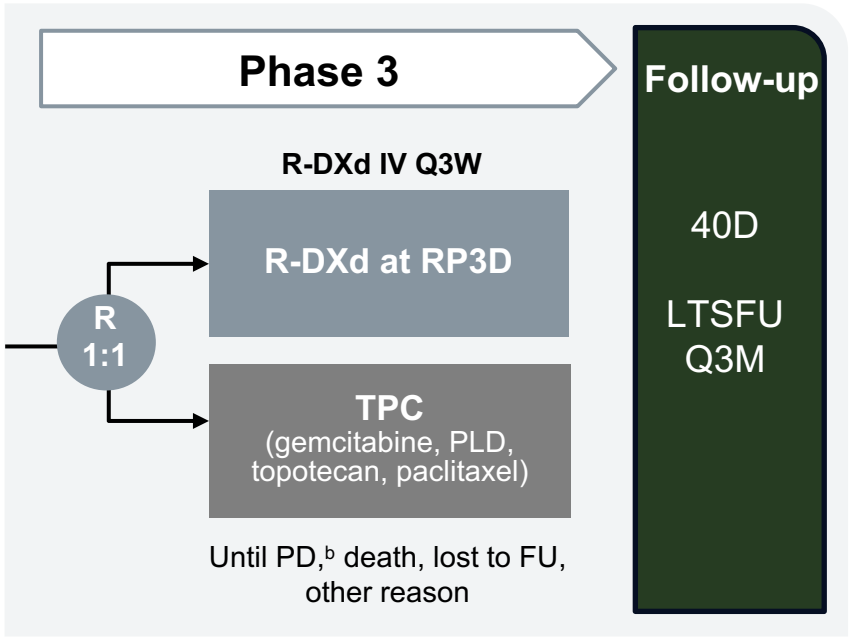


Primary endpoints:

- ORR per BICR[b]

Key secondary endpoints:

- ORR per inv[b]
- DOR



Primary endpoints:

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

Key secondary endpoints:

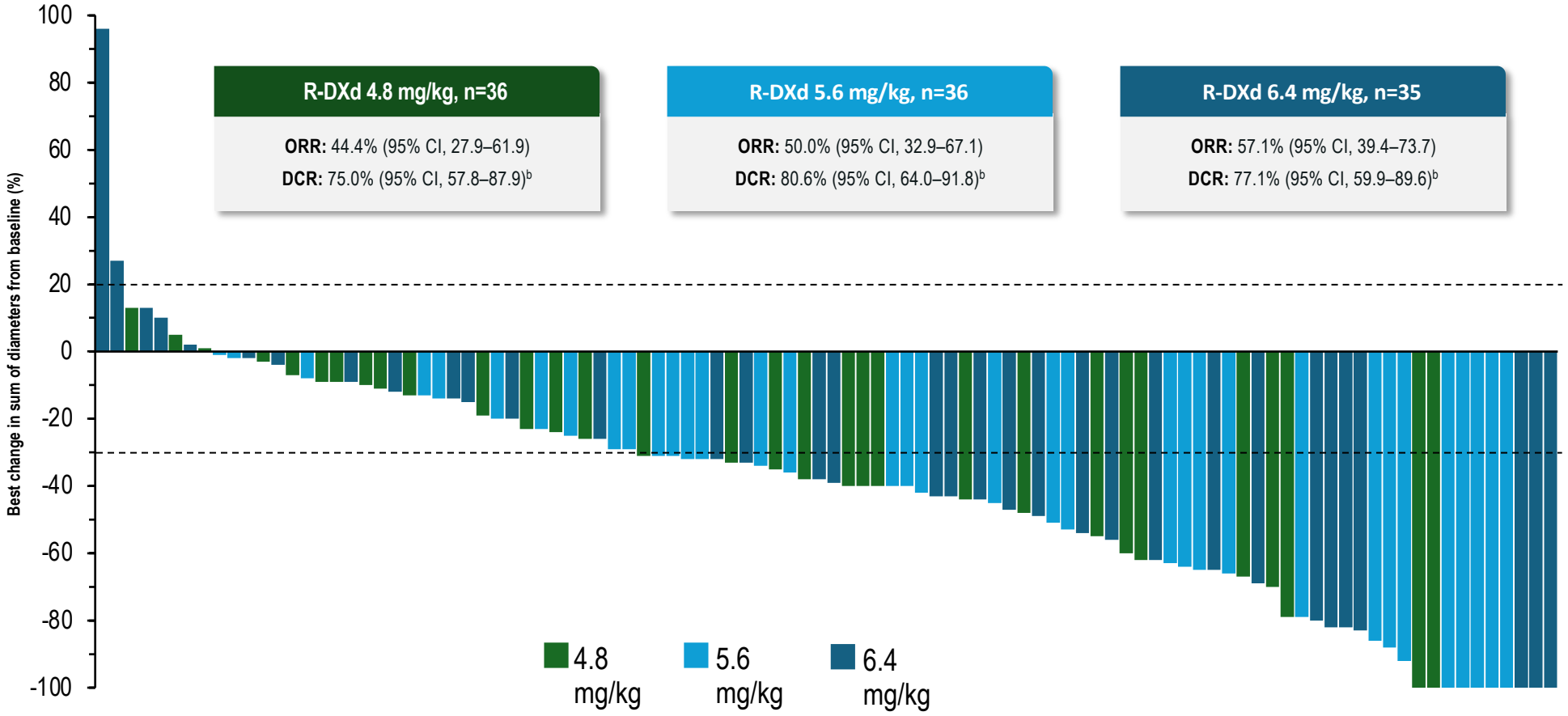
- OS
- QOL

NCT06161025

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

REJOICE 01: Phase 2

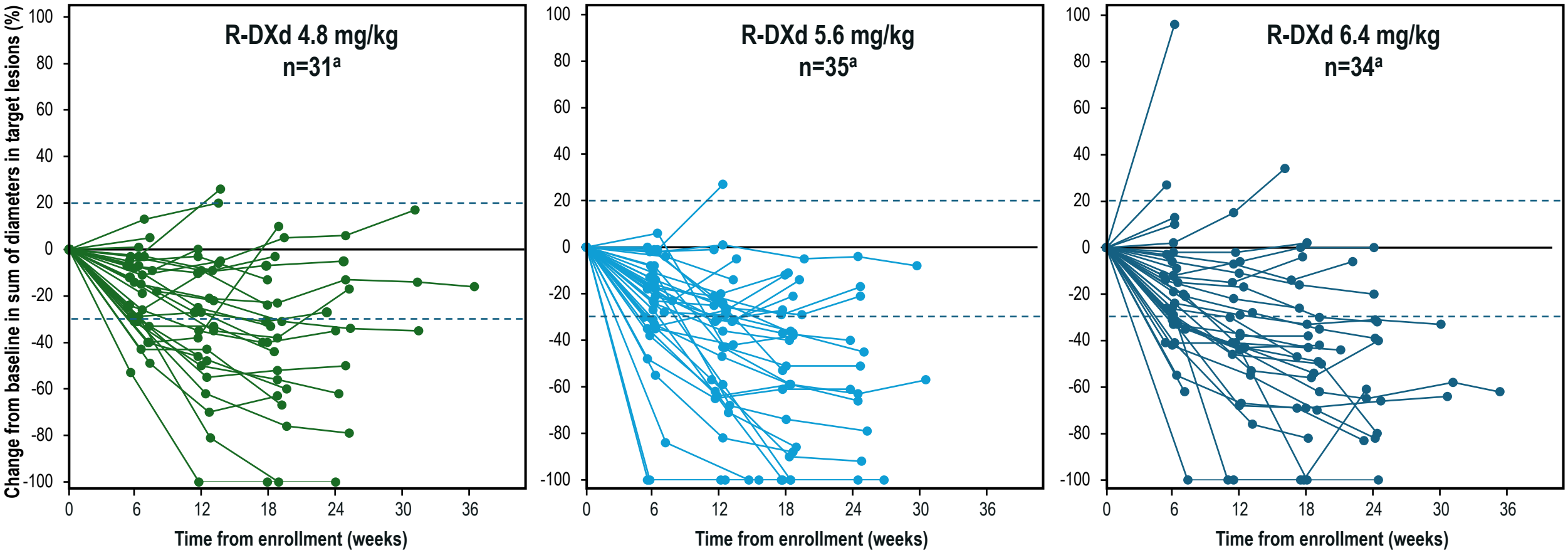
Raludotatug deruxtecan



Ray Couquad et al. ESMO 2025;Abstract LBA42

@DrKatyMoore

R-DXd treatment was associated with rapid responses at all doses



Median TTR:[b] 7.1 weeks (range, 5.4–18.7)

Median TTR:[b] 6.6 weeks (range, 5.1–18.3)

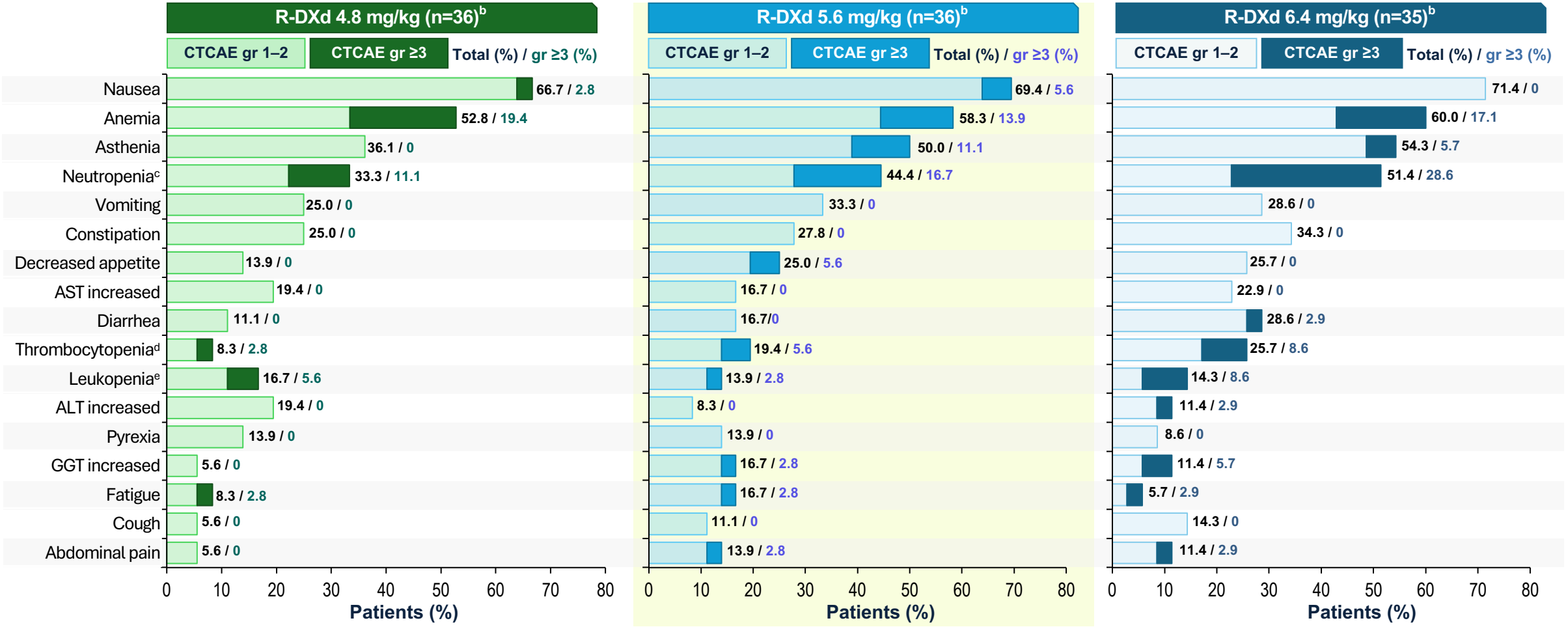
Median TTR:[b] 7.2 weeks (range, 5.3–19.1)

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 spider plots (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]By BICR per RECIST 1.1. Overall median TTR was 7.1 weeks (range, 5.1–19.1).

BICR, blinded independent central review; CI, confidence interval; RECIST 1.1, Response Evaluation Criteria in Solid Tumours, version 1.1; TTR, time to response.

REJOICE-Ovarian01: Most common TEAEs (≥10%)



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

[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 was 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 was 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 was 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.

1. Ray-Coquard I et al. Presented at ESMO Congress 2025; October 17–21, 2025; Berlin, Germany; Oral LBA42

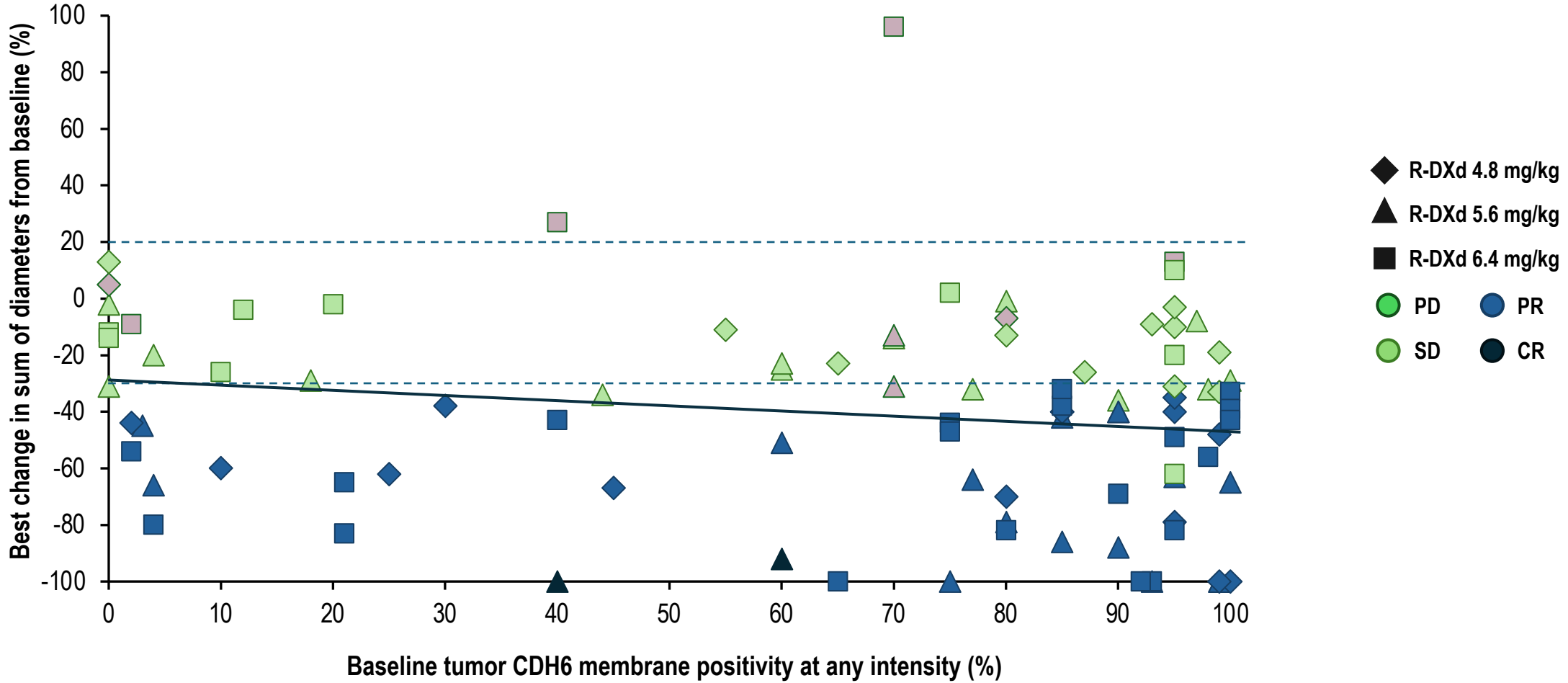
REJOICE-Ovarian01: The 5.6-mg/kg dose provided the optimal benefit-risk profile

	R-DXd 4.8 mg/kg n=36	R-DXd 5.6 mg/kg n=36	R-DXd 6.4 mg/kg n=35	R-DXd 4.8–6.4 mg/kg N=107
Any TEAE, n (%)	35 (97.2)	36 (100)	35 (100)	106 (99.1)
Grade ≥3	16 (44.4)	20 (55.6)	20 (57.1)	56 (52.3)
Any treatment-related TEAE, n (%)	32 (88.9)	34 (94.4)	34 (97.1)	100 (93.5)
Grade ≥3	10 (27.8)	11 (30.6)	17 (48.6)	38 (35.5)
Grade 5	0	0	0	0
Any SAE, n (%)	14 (38.9)	12 (33.3)	14 (40.0)	40 (37.4)
Grade ≥3	13 (36.1)	10 (27.8)	11 (31.4)	34 (31.8)
Grade 5	3 (8.3)[a]	2 (5.6)[b]	1 (2.9)[c]	6 (5.6)
Any treatment-related SAE, n (%)	3 (8.3)	3 (8.3)	7 (20.0)	13 (12.1)
Grade ≥3	3 (8.3)	3 (8.3)	5 (14.3)	11 (10.3)
Grade 5	0	0	0	0
Dose modifications associated with treatment-related TEAEs,[d] n (%)				
Drug discontinuation	3 (8.3)	0	3 (8.6)	6 (5.6)
Dose reduction	5 (13.9)	4 (11.1)	11 (31.4)	20 (18.7)
Dose delay	8 (22.2)	7 (19.4)	10 (28.6)	25 (23.4)
ILD/pneumonitis adjudicated as treatment related,[e] n (%)				
Any grade	1 (2.8)	1 (2.8)	2 (5.7)	4 (3.7)
Grade ≥3	1 (2.8)[f]	0	0	1 (0.9)
Grade 5	0	0	0	0

The safety profile of the 4.8 and 5.6 mg/kg cohorts were similar.
Treatment-related TEAEs occurred more frequently in the 6.4 mg/kg cohort (vs 4.8 and 5.6 mg/kg cohorts)

Reported safety events are defined using MedDRA Preferred Terms and CTCAE criteria.
[a]Grade 5 events were hepatic failure, ovarian cancer, and malignant neoplasm progression. [b]Grade 5 events were ovarian cancer and aspiration. [c]Grade 5 event was influenza infection. [d]Dose modifications associated with treatment-related TEAEs defined as: dose discontinuation, no subsequent administration of R-DXd; dose reduction, R-DXd dose was reduced at next administration; dose delay, study drug was not administered at the next scheduled cycle but was administered at a later date.
[e]ILD/pneumonitis events were adjudicated by an independent ILD adjudication committee. [f]ILD/pneumonitis Grade ≥3 event (adjudicated as treatment related) was grade 3.
CTCAE, Common Terminology Criteria for Adverse Events; ILD, interstitial lung disease; MedDRA, Medical Dictionary for Regulatory Activities; SAE, serious adverse event; TEAE, treatment-emergent adverse event.
1. Ray-Coquard I et al. Presented at ESMO Congress 2025; October 17–21, 2025; Berlin, Germany; Oral LBA42

Clinically meaningful tumor responses were observed across a range of CDH6 expression levels

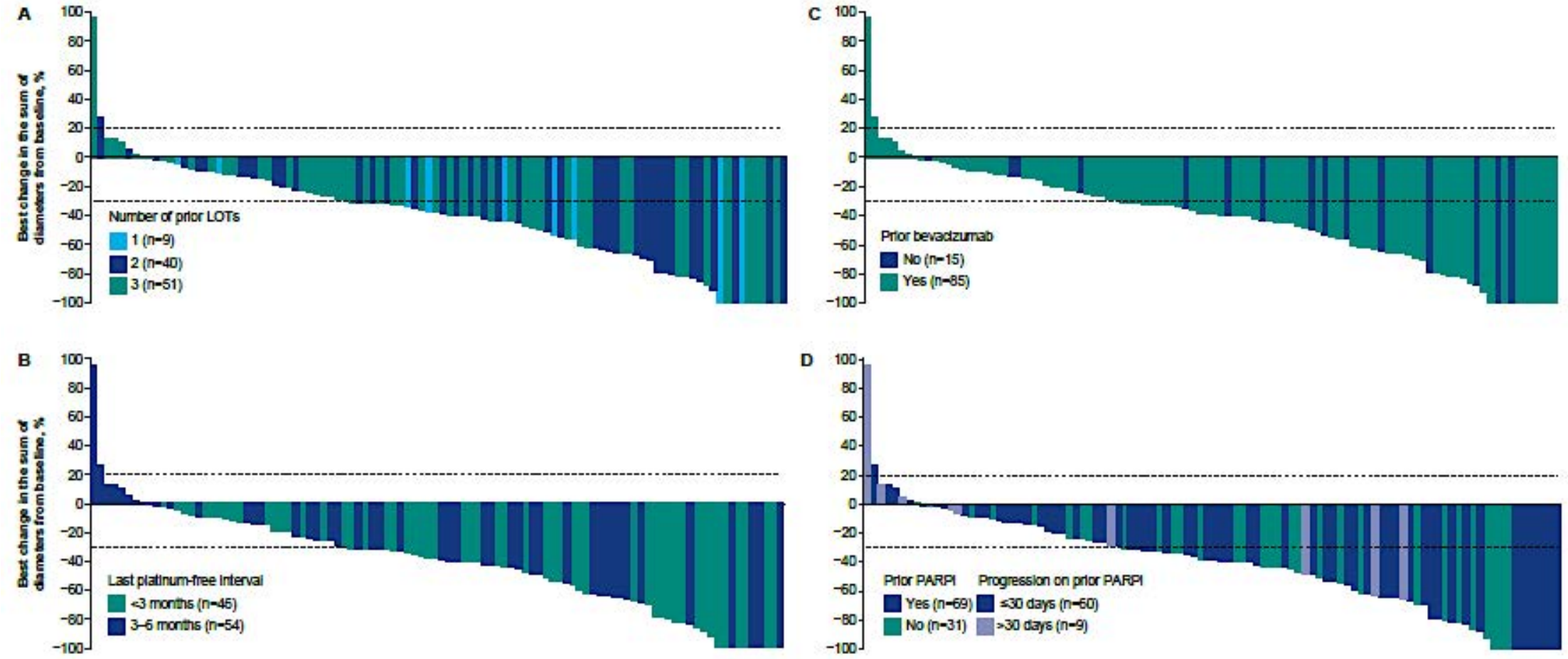


Data cutoff: February 26, 2025. The median follow-up for 4.8-mg/kg, 5.6-mg/kg, and 6.4-mg/kg cohorts was 5.6 months (95% CI, 4.7–6.3), 5.6 months (95% CI, 4.6–5.8), and 5.2 months (95% CI, 4.9–5.8), respectively.

Patients with available baseline tumor CDH6 expression data, who had measurable disease at baseline and ≥1 post-baseline tumor scan (assessed by BICR), were included in the scatter plot (n=94).

Ray Couquad et al. ESMO 2025;Abstract LBA42

Exploratory Analysis of ORR based on LOT & Prior Therapy Demonstrates No Difference



*Only patients with measurable disease at baseline and ≥1 post-baseline tumor scan (both by BICR) were included (n=100). Six patients had no measurable baseline disease, and one had no adequate post-baseline assessment.

Ray Coquard et al. ESGO 2026

Nausea and Vomiting Are Among the Most Common TEAEs Reported In Clinical Trials of R-DXd; Most Events are Grade 1 and 2

	DS6000-A-U101 (Phase 1) (NCT04707248)		REJOICE-Ovarian01 (Phase 2/3) (NCT06161025)		
	Patients with heavily pretreated advanced OC[a] who had received prior platinum and taxane therapy		Patients with PROC[b] who had received 1–3 prior lines of systemic therapy, including bevacizumab (if eligible) and mirvetuximab (unless ineligible, not approved or not available locally)[3]		
TEAE, %	**Total OC cohort 4.8–6.4 mg/kg (N=45)[1]**	**PSOC subgroup 4.8–6.4 mg/kg (n=18)[2,c]**	**4.8 mg/kg (n=36)**	**5.6 mg/kg (n=36)**	**6.4 mg/kg (n=35)**
Nausea, any grade	**57.8**	**50.0**	**66.7**	**69.4**	**71.4**
Grade ≥3	2.2	0	2.8	5.6	0
Vomiting, any grade	**40.0**	**22.2**	**25.0**	**33.0**	**28.6**
Grade ≥3	2.2	0	0	0	0
	Interim analysis Data cutoff: July 14, 2023	Interim subgroup analysis Data cutoff: January 10, 2025	Ph 2 dose-optimization analysis in which patients have completed >18 weeks FU. Data cutoff: Feb 26, 2025 R-DXd 5.6 mg/kg is considered the optimal dose to be further evaluated in the Ph 3 study		

[a]High-grade serous ovarian, primary peritoneal, or fallopian tube cancer. [b]High-grade serous or endometroid ovarian, primary peritoneal, or fallopian tube cancer. [c]Please note that the PSOC subgroup includes patients also captured in the 4.8–6.4 mg/kg cohorts, therefore the cases of nausea and vomiting could represent the same events.
FU, follow-up; OC, ovarian cancer; Ph, Phase; OC, ovarian cancer; PROC, platinum-resistant ovarian cancer; PSOC, platinum-sensitive ovarian cancer; R-DXd, raludotatug deruxtecan; TEAE, treatment-emergent adverse event.

1. Moore K, et al. Presented at SGO Annual Meeting; March 16–18, 2024; San Diego, CA. **2.** Moore K, et al. Presented at ESMO Gynaecolgical Cancers Congress; June 18–20, 2025; Vienna, Austria; Oral 77MO. **3.** Ray-Coquard I, et al. Presented at ESMO Congress 2025; October 17–21, 2025; Berlin, Germany; Oral LBA42.

Diarrhea (Any Grade) Is a Common TEAE Reported In Clinical Trials of R-DXd; Most Events Have Been Grade 1 or 2

	DS6000-A-U101 (Phase 1) (NCT04707248)		REJOICE-Ovarian01 (Phase 2/3) (NCT06161025)		
	Patients with heavily pretreated advanced OC[a] who had received prior platinum and taxane therapy		Patients with PROC[b] who had received 1–3 prior lines of systemic therapy, including bevacizumab (if eligible) and mirvetuximab (unless ineligible, not approved or not available locally)[3]		
TEAE, %	**Total OC cohort 4.8–6.4 mg/kg (N=45)[1]**	**PSOC subgroup 4.8–6.4 mg/kg (n=18)[2,c]**	**4.8 mg/kg (n=36)**	**5.6 mg/kg (n=36)**	**6.4 mg/kg (n=35)**
Diarrhea, any grade	**31.1**	**16.7**	**11.1**	**16.7**	**28.6**
Grade ≥3	0	0	0	0	2.9
	Interim analysis Data cutoff: Jul 14, 2023	Interim subgroup analysis Data cutoff: Jan 10, 2025	Ph 2 dose-optimization analysis in which patients have completed >18 weeks FU. Data cutoff: Feb 26, 2025 R-DXd 5.6 mg/kg is considered the optimal dose to be further evaluated in the Ph 3 study		

[a]High-grade serous ovarian, primary peritoneal, or fallopian tube cancer. [b]High-grade serous or endometroid ovarian, primary peritoneal, or fallopian tube cancer. [c]Please note that the PSOC subgroup includes patients also captured in the 4.8–6.4 mg/kg cohorts, therefore the cases of diarrhea could represent the same events.
FU, follow-up; OC, ovarian cancer; Ph, Phase; PROC, platinum-resistant ovarian cancer; PSOC, platinum-sensitive ovarian cancer; R-DXd, raludotatug deruxtecan; TEAE, treatment-emergent adverse event.
1. Moore K, et al. Presented at SGO Annual Meeting; March 16–18, 2024; San Diego, CA. **2.** Moore K, et al. Presented at ESMO Gynaecolgical Cancers Congress; June 18–20, 2025; Vienna, Austria; Oral 77MO. **3.** Ray-Coquard I, et al. Presented at ESMO Congress; October 17–21, 2025; Berlin, Germany; Oral LBA42.

Hematologic Toxicities Were the Most Common Grade ≥3 TEAEs Reported In Clinical Trials of R-DXd

	DS6000-A-U101 (Phase 1) (NCT04707248)		REJOICE-Ovarian01 (Phase 2/3) (NCT06161025)		
	Patients with heavily pretreated advanced OC[a] who had received prior platinum and taxane therapy		Patients with PROC[b] who had received 1–3 prior lines of systemic therapy, including bevacizumab (if eligible) and mirvetuximab (unless ineligible, not approved or not available locally)[3]		
TEAE, %	**Total OC cohort 4.8–6.4 mg/kg (N=45)[1,c]**	**PSOC subgroup 4.8–6.4 mg/kg (n=18)[2,c,d]**	**4.8 mg/kg (n=36)[e]**	**5.6 mg/kg (n=36)[e]**	**6.4 mg/kg (n=35)[e]**
Anemia, any grade	**26.7**	**38.9**	**52.8**	**58.3**	**60.0**
Grade ≥3	15.6	22.2	19.4	13.9	17.1
Neutrophil count decreased, any grade	**24.4**	**22.2**	**33.3[f]**	**44.4[f]**	**51.4[f]**
Grade ≥3	11.1	16.7	11.1[f]	16.7[f]	28.6[f]
Platelet count decreased, any grade	**13.3**	**16.7**	**8.3[g]**	**19.4[g]**	**25.7[g]**
Grade ≥3	4.4	5.6	2.8[g]	5.6[g]	8.6[g]
	Interim analysis Data cutoff: Jul 14, 2023	Interim subgroup analysis Data cutoff: Jan 10, 2025	Ph 2 dose-optimization analysis in which patients have completed >18 weeks FU. Data cutoff: Feb 26, 2025 R-DXd 5.6 mg/kg is considered the optimal dose to be further evaluated in the Ph 3 study		

[a]High-grade serous ovarian, primary peritoneal, or fallopian tube cancer. [b]High-grade serous or endometroid ovarian, primary peritoneal, or fallopian tube cancer. [c]No treatment-related Grade 5 hematologic TEAEs were reported. [d]Please note that the PSOC subgroup includes patients also captured in the 4.8–6.4 mg/kg cohorts, therefore the cases of hematologic toxicity could represent the same events. [e]Grade 4 hematologic TEAEs reported at 4.8 mg/kg: neutropenia (n=2), thrombocytopenia (n=1); at 5.6 mg/kg: neutropenia (n=2), thrombocytopenia (n=1); at 6.4 mg/kg: neutropenia (n=3), thrombocytopenia (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. [f]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. [g]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.
FU, follow-up; OC, ovarian cancer; Ph, Phase; PROC, platinum-resistant ovarian cancer; PSOC, platinum-sensitive ovarian cancer; R-DXd, raludotatug deruxtecan; TEAE, treatment-emergent adverse event.
1. Moore K, et al. Presented at SGO Annual Meeting; March 16–18, 2024; San Diego, CA. **2.** Moore K, et al. Presented at ESMO Gynaecolgical Cancers Congress; June 18–20, 2025; Vienna, Austria; Oral 77MO. **3.** Ray-Coquard I, et al. Presented at ESMO Congress; October 17–21, 2025; Berlin, Germany; Oral LBA42.

ILD/Pneumonitis Has Been Reported In Clinical Trials of R-DXd

	DS6000-A-U101 (Phase 1) (NCT04707248)		REJOICE-Ovarian01 (Phase 2/3) (NCT06161025)			
	Patients with heavily pretreated advanced OC[a] who had received prior platinum and taxane therapy		Patients with PROC[b] who had received 1–3 prior lines of systemic therapy, including bevacizumab (if eligible) and mirvetuximab (unless ineligible, not approved or not available locally)[3]			
Adjudicated as treatment-related ILD/pneumonitis, n (%)	**Total OC cohort 4.8–6.4 mg/kg (N=45)[1]**	**PSOC subgroup 4.8–6.4 mg/kg (n=18)[2,c]**	**4.8 mg/kg (n=36)**	**5.6 mg/kg (n=36)**	**6.4 mg/kg (n=35)**	**4.8–6.4 mg/kg (N=107)**
Any-grade	**2 (4.4)[d]**	**1 (5.6)[d]**	**1 (2.8)**	**1 (2.8)**	**2 (5.7)**	**4 (3.7)**
Grade ≥3	0	0	1 (2.8)[e]	0	0	1 (0.9)
	Interim analysis Data cutoff: Jul 14, 2023	Interim subgroup analysis Data cutoff: Jan 10, 2025	Ph 2 dose-optimization analysis in which patients have completed >18 weeks FU. Data cutoff: Feb 26, 2025 R-DXd 5.6 mg/kg is considered the optimal dose to be further evaluated in the Ph 3 study			

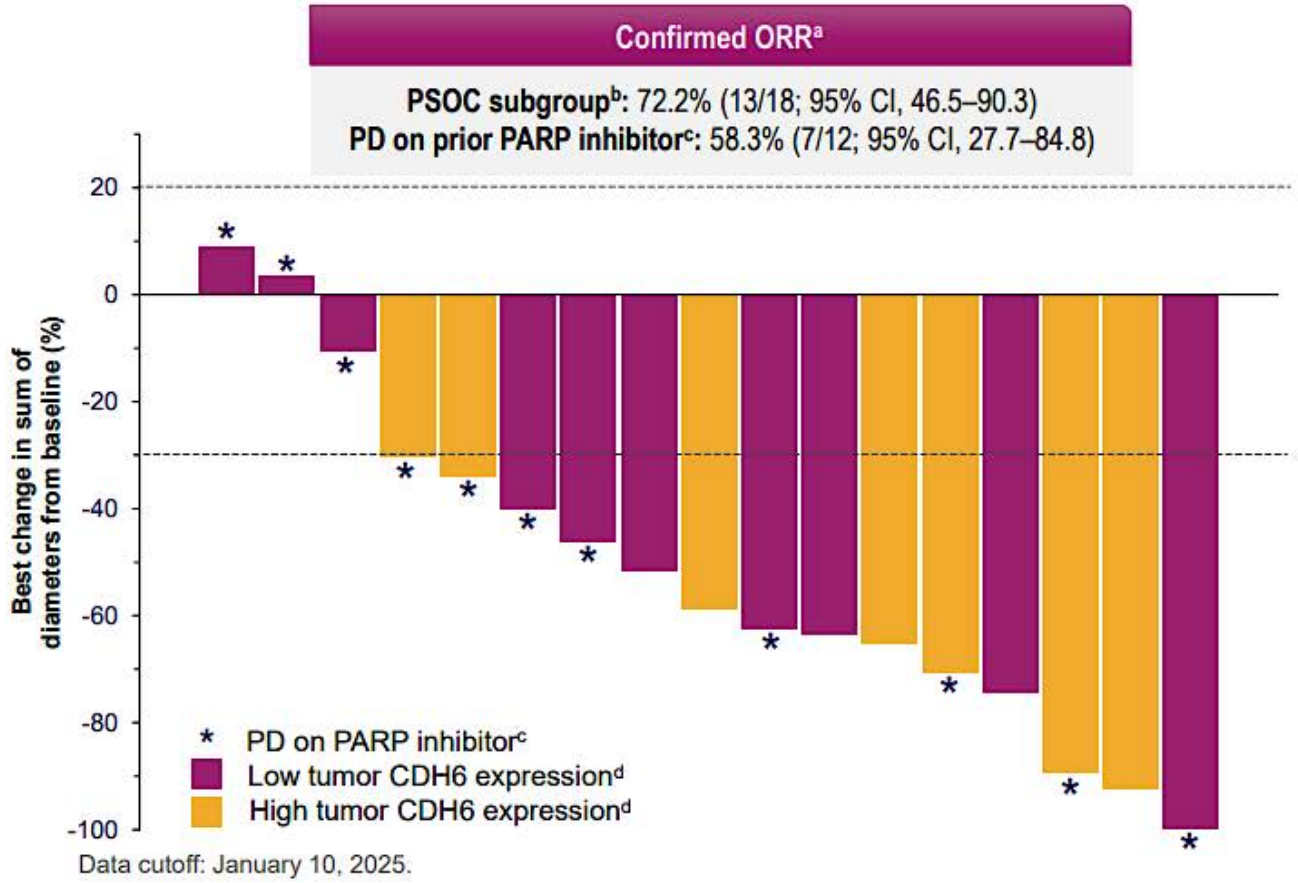
In the Phase 1 study, two Grade 5 drug-related ILD events occurred in the 8.0 mg/kg cohort (n=15), which was closed in October 2022 due to a higher incidence of serious and Grade ≥3 TEAEs, and lack of a favorable benefit–risk ratio[4]

[a]High-grade serous ovarian, primary peritoneal, or fallopian tube cancer. [b]High-grade serous ovarian or endometroid ovarian, primary peritoneal, or fallopian tube cancer. [c]Please note that the platinum-sensitive OC subgroup includes patients also captured in the 4.8–6.4 mg/kg cohorts, therefore the ILD/pneumonitis case could represent the same event; [d]ILD/pneumonitis Grade 2 with starting dose of 6.4 mg/kg. [e]ILD/pneumonitis Grade ≥3 event (adjudicated as treatment related) was CTCAE Grade 3.

CTCAE, Common Terminology Criteria for Adverse Events; FU, follow-up; ILD, interstitial lung disease; OC, ovarian cancer; Ph, Phase; PROC, platinum-resistant ovarian cancer; PSOC, platinum-sensitive ovarian cancer; R-DXd, raludotatug deruxtecan; TEAE, treatment-emergent adverse event.

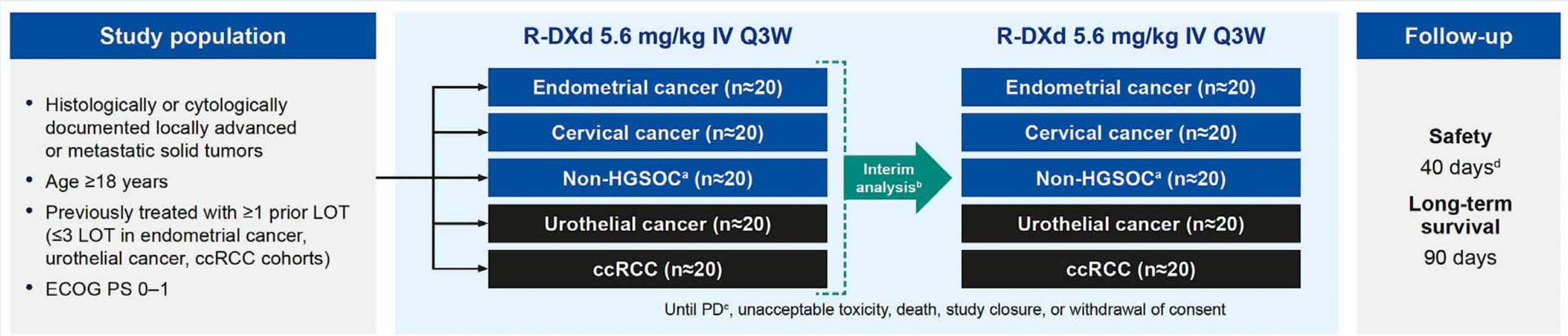
1. Moore K, et al. Presented at SGO Annual Meeting; March 16–18, 2024; San Diego, CA. **2.** Moore K, et al. Presented at ESMO Gynaecolgical Cancers Congress; June 18–20, 2025; Vienna, Austria; Oral 77MO. **3.** Ray-Coquard I, et al. Presented at ESMO Congress; October 17–21, 2025; Berlin, Germany; Oral LBA42. **4.** Moore K, et al. Presented at ESMO Congress 2023; October 20–24, 2023; Madrid, Spain; Abstract 745MO.

Moving ADCs into PSOC: RDXd ESMO Gyne 2025



	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)

Phase II REJOICE-PanTumor01 Study Design



[a]Including clear cell, low-grade endometrioid, low-grade serous, or mucinous OC. [b]Interim nonbinding futility analysis will be performed for each cohort when 20 patients have undergone 12 weeks of follow-up from study-drug initiation or discontinued per protocol. [c]Investigator-assessed per RECIST 1.1. [d]Forty days after the last study-drug administration or 30 days after the last study-drug administration if the patient starts a new anticancer treatment, whichever occurs first.

Primary endpoints: ORR (all except ccRCC cohort), DCR (ccRCC cohort only), Safety
Secondary endpoints: ORR (ccRCC cohort only), DCR (all except ccRCC cohort), PFS, DoR

R-DXd = raludotatug deruxtecan; HGSOC = high-grade serous ovarian cancer; ccRCC = clear cell renal cell carcinoma

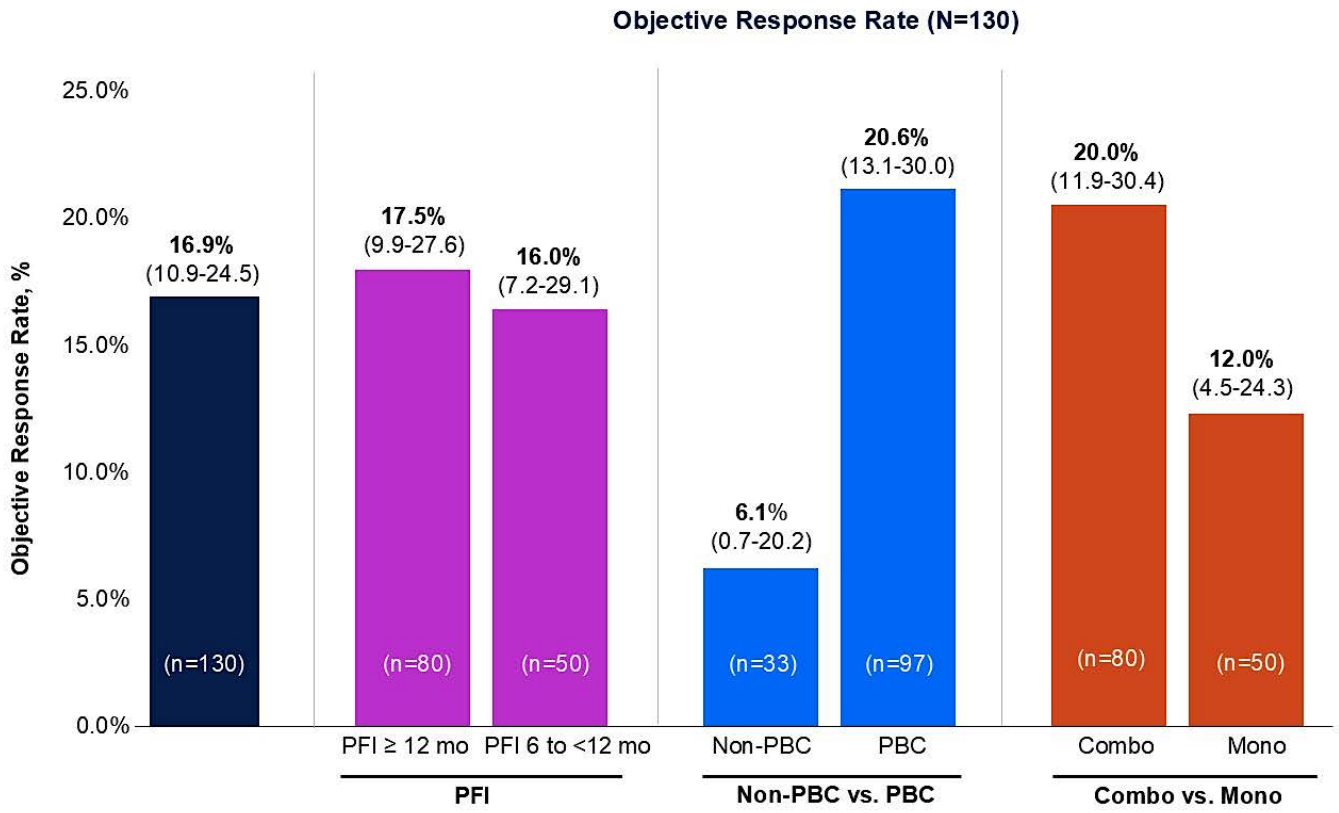
Albiges L et al. ASCO 2025;Abstract TPS3158.

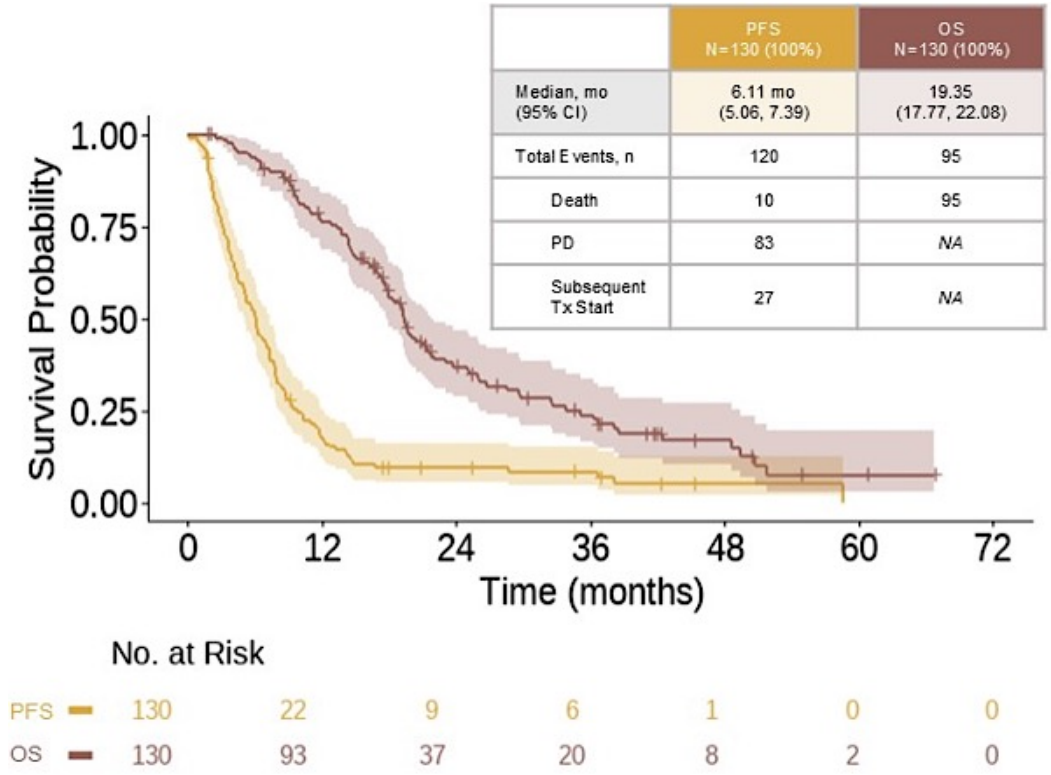
Data for ADCs in PSOC is starting to emerge.....

	Sacituzumab tirumotecan 5mg/kg D1, D15 N=5 (PSOC)	Datopotamab deruxtecan N=9 (PSOC)	Mirvetuximab soravtansine N=79 (PICCOLO)	Raludotatug deruxtecan N=18
Payload	Belotecan derivative Topoisomerase I	Topoisomerase 1- deruxtecan	DM4	Topoisomerase 1 – deruxtecan
DAR	7.4	4	4	8
Linker	Sulfonyl pyrimidine CL2A-carbonate linker	Cleavable tetrapeptide based linker	Cleavable linker	Tetrapeptide-based cleavable linker
Trial	NCT06049212	NCT05489211	NCT05041257	NCT04707248
ORR	60% (PSOC N=5)	66.7% (PSOC N=9)	51.9% (95%CI 40.4-63.3) 45.8% (95% CI 32.7-59.2)	72.2% (9% CI 46.5-90.3) ITT 58.3% (95% CI 27.7-84.8) Post Pi
DOR	ND	ND	8.25 (95% CI 5.55-10.78) ITT 7.33 (95% CI 5.03-10.78) Post Pi	5.7 (4.2-NE) ITT 5.1 (2.8- NE) Post Pi
mPFS	ND	ND	6.93 (95% CI 5.85-9.59) ITT 6.18 (95% CI 5.55-8.41) post Pi	8.1 (4.1-NE) ITT 7.1 (2.8-NE) Post Pi

Wang et al. ESMO 2024, Oaknin A et al. ESMO 2024, Alvarez Secord ESMO Gyne 2025, Moore ESMO Gyne 2025

If progression on PARPi is the new “high risk” marker for poor anticipated response to platinum, what do we know about expectations for platinum in this setting?





	PFS N=130 (100%)	OS N=130 (100%)
Median, mo (95% CI)	6.11 mo (5.06, 7.39)	19.35 (17.77, 22.08)
Total Events, n	120	95
Death	10	95
PD	83	*NA*
Subsequent Tx Start	27	*NA*

ORR is 20% at highest and mPFI is around 6-7 months

Coleman et al. ASCO 2025

GOG FOUNDATION® Transforming the standard of care™

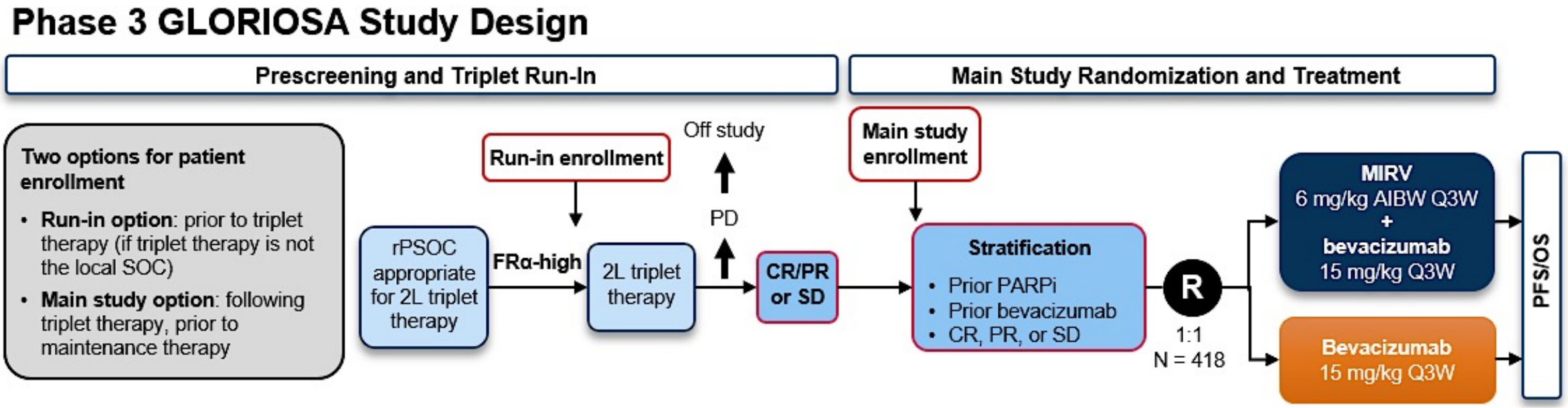
@DrKatyMoore

Data for ADCs in PSOC is starting to emerge….. Will they be better than platinum even in high risk tumors?

	Sacituzumab tirumotecan 5mg/kg D1, D15 N=5 (PSOC)	Datopotamab deruxtecan N=9 (PSOC)	Mirvetuximab soravtansine N=79 (PICCOLO)	Raludotatug deruxtecan N=18	Coleman et al. PSOC post PARPi PD Platinum
Payload	Belotecan derivative Topoisomerase I	Topoisomerase 1-deruxtecan	DM4	Topoisomerase 1 – deruxtecan	Platinum
DAR	7.4	4	4	8	NA
Linker	Sulfonyl pyrimidine CL2A-carbonate linker	Cleavable tetrapeptide based linker	Cleavable linker	Tetrapeptide-based cleavable linker	NA
Trial	NCT06049212	NCT05489211	NCT05041257	NCT04707248	ASCO 2025
ORR	60% (PSOC N=5)	66.7% (PSOC N=9)	51.9% (95%CI 40.4-63.3) 45.8% (95% CI 32.7-59.2)	72.2% (9% CI 46.5-90.3) ITT 58.3% (95% CI 27.7-84.8) Post Pi	20.6%
DOR	ND	ND	8.25 (95% CI 5.55-10.78) ITT 7.33 (95% CI 5.03-10.78) Post Pi	5.7 (4.2-NE) ITT 5.1 (2.8- NE) Post Pi	NR
mPFS	ND	ND	6.93 (95% CI 5.85-9.59) ITT 6.18 (95% CI 5.55-8.41) post Pi	8.1 (4.1-NE) ITT 7.1 (2.8-NE) Post Pi	7.39 (combo data)

Wang et al. ESMO 2024, Oaknin A et al. ESMO 2024, Alvarez Secord ESMO Gyne 2025, Moore ESMO Gyne 2025

Or for those tumors deemed not high risk for platinum failure do we use ADCs as maintenance? Aka GLORIOSA



Conclusions

- In the past 1-2 years we have seen a panoply of new ADCs – many with very promising efficacy signals in patients with limited options. Now the hard work begins
    - Dose Optimization will be key for each disease type and agent - how much and how often to maximize benefit and minimize toxicity
    - Regimen Optimization is upon us – where do we use these assets? All in R/M? or moving up to PSOC, maintenance – what data do we need to get the timing right?
    - Sequencing is a huge opportunity for our patients. The biomarkers have to be evaluated and validated and built into trials.
    - New constructs will have to be evaluated carefully – all comer studies may not give us the information we need to really craft scientifically based directions for drug development with these exciting agents.

Faculty Case Presentations

RTP
RESEARCH
TO PRACTICE

Dr Monk: OC PROC Case

- Every patient should have an opportunity to enroll on an ADC protocol.
  - Numerous clinical trial options:
    - Must account for most active and approved agents in this space:
      - **Weekly paclitaxel**
      - **Bevacizumab**
      - **mirvetuximab soravtansine** if FRα high
      - **Pembrolizumab** if weekly paclitaxel eligible and PD-L1 positive

Dr Monk: OC PROC Case: My Approach

- Outside of a clinical trial, my approach is:
  - Is she appropriate for **weekly taxane**?
    - Does not have grade 2 or worse neuropathy
    - Has not failed weekly paclitaxel in the recurrent setting
    - Accepts the inconvenience and increased toxicity of weekly paclitaxel
    - Line of therapy (B-96 1-2; Rosella 1-3)
    - PD-L1 status
  - Is she appropriate for **bevacizumab**?
    - No contraindications
    - Did not recently progress on bevacizumab
  - Can she tolerate oral anti-cancer therapies?
  - Additional **biomarkers**?
    - FRα and HER2

QUESTIONS FOR THE FACULTY

To what extent does your approach to the selection and sequencing of therapies for patients with platinum-resistant advanced ovarian cancer align with Dr Monk's? Is there anything that you do fundamentally differently or any clinical pearls you would like to add?

Which ongoing clinical trials of novel investigational therapies, including ADCs, are you prioritizing for your patients with platinum-resistant advanced ovarian cancer? To what extent do you think clinical trial participation is potentially advantageous for these patients?

QUESTIONS FOR THE FACULTY

What are the most common barriers to clinical trial participation that you encounter in your patients with ovarian and other gynecologic cancers, and what, if any, measures have you found useful in overcoming them?

RTP
RESEARCH
TO PRACTICE

Prof Eskander: Case Presentation

- 62 yo who presented to an outside hospital with progressive R sided flank pain, abdominal pain, bloating with intermittent nausea and emesis
  - **PMHx**: Low grade stage 1A adenocarcinoma of lung, RA, depression, sleep apnea, obesity, GERD
  - **PSHx**: Tonsillectomy, appendectomy, cervical and lumbar spine fusion, right lung lobectomy
- Imaging at the time of that hospitalization was **notable for widely metastatic disease**, large volume ascites, peritoneal carcinomatosis and concern for small volume malignant pleural effusion
- IR image guided biopsy: **high-grade serous carcinoma of Mullerian origin**
  - Pathology: grade 3 nuclear features, strongly and diffusely positive for CK7 and PAX8
- **Started on NACT with carboplatin and paclitaxel by outside medical oncologist**

Prof Eskander: Case Presentation

- **Treatment (NACT carboplatin and paclitaxel x 3 cycles)**
  - Tolerated her NACT well with excellent clinical, radiographic and biochemical response
- **Interval CRS:** TAH, BSO, with en bloc resection of portion of rectum and sigmoid with primary anastomosis, pan pelvic peritonectomy, omentectomy, R diaphragm peritonectomy**, HIPEC** (cisplatin total dose 188 mg). **R0 surgical resection with no visible residual disease**
- **Surgical pathology:**
  - All resected specimens involved by high grade serous carcinoma – **primary site confirmed to be left fallopian tube**
- **Molecular testing:**
  - **Germline negative; HRD test negative; HER2 1+; FOLR1 80%; PD-L1 CPS score 5;** TP53 mutation p.G154fs; TMB 3 mut/Mb; CCNE1 amplification not detected
- **After interval CRS:**
  - Resumed systemic chemotherapy, with addition of bevacizumab beginning with cycle 5
  - Required 1 level dose reduction of her carboplatin due to thrombocytopenia

UC San Diego
SCHOOL OF MEDICINE

Prof Eskander: Case Presentation

- **Treatment (maintenance bevacizumab)**
  - While on maintenance bevacizumab she began to demonstrate a progressive increase in her CA 125 values
  - Interval CT and PET CT imaging **concerning for peritoneal based disease recurrence and retroperitoneal nodal recurrence, but not amenable to image guided biopsy**
  - Post-op developed multiple large ventral abdominal wall hernias
- Based on imaging, and rising CA 125 she was diagnosed with platinum resistant recurrent high grade serous fallopian tube carcinoma **(platinum free interval of 4 months)**
- **After counseling and discussion the patient was started in single agent mirvetuximab which she started in May 2024**

Prof Eskander: Case Presentation

- **Treatment (single agent mirvetuximab)**
  - She tolerated her treatment reasonably well
  - **Treatment related AEs:**
    - Grade 1 fatigue
    - Grade 1 neuropathy – did have period of grade 2 neuropathy that required dose delay as well as one level dose reduction
    - Intermittent Grade 1 nausea
- She received a total of ~31 cycle of mirvetuximab
- **April 2026 (~24 months of treatment), imaging was notable for disease progression with rising CA 125**

Prof Eskander: Case Presentation

- **Treatment considerations:**
  - Excellent ECOG PS of 1
  - Prior carboplatin + paclitaxel + bevacizumab
  - Prior FRalpha targeting ADC with MMAE payload
  - FOLR1 80% 2+
  - PD-L1 CPS score 5
  - HER2 IHC 1+

- **What next???**

UC San Diego
SCHOOL OF MEDICINE

QUESTIONS FOR THE FACULTY

What would you most likely recommend next for this patient outside of a clinical trial, and what outcomes would you expect? Would you have any hesitation about offering pembrolizumab/chemotherapy to her given her history of rheumatoid arthritis? Given her HER2 IHC score of 1+, would you ever consider treatment with trastuzumab deruxtecan?

What ongoing clinical trials would be a good match for this patient if she were interested in participation?

QUESTIONS FOR THE FACULTY

How do response rates and other efficacy outcomes documented with R-DXd thus far compare to those with currently available therapies that this patient might receive? If R-DXd were available today, where in the therapeutic sequence do you envision it fitting for a patient like this?

How does the rapidity of response with R-DXd compare to conventional chemotherapy and other strategies used in the platinum-resistant setting? For a patient who was in need of symptom relief, would you be comfortable administering R-DXd?

QUESTIONS FOR THE FACULTY

Is there any evidence indicating that multiple ADCs with the same or a similar payload are or are not effective when given in sequence? What about multiple ADCs with the same target? Would the fact that this patient has previously received an ADC with an MMAE payload dissuade you from attempting to administer one like R-DXd with a topoisomerase I inhibitor payload?

Would you be concerned about the potential for ILD with the use of an ADC with a topoisomerase I inhibitor payload such as R-DXd for this patient, given her history of lung cancer/right lung lobectomy?

Agenda

Module 1: Advances in Human Cadherin-6-Targeted Antibody-Drug Conjugates (ADCs) in Ovarian and Other Gynecologic Cancers — Dr Moore

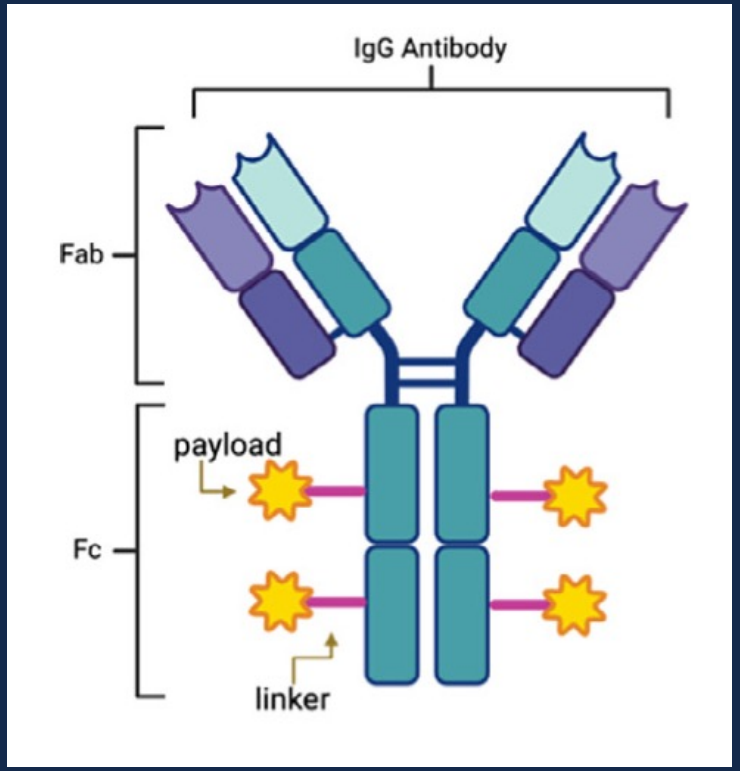
Module 2: Leveraging TROP2-Directed ADCs in Advanced Gynecologic Cancers — Prof Eskander

Module 3: Tolerability and Other Practical Considerations with Novel Investigational ADCs in Advanced Gynecologic Cancers — Dr Monk

UC San Diego
SCHOOL OF MEDICINE

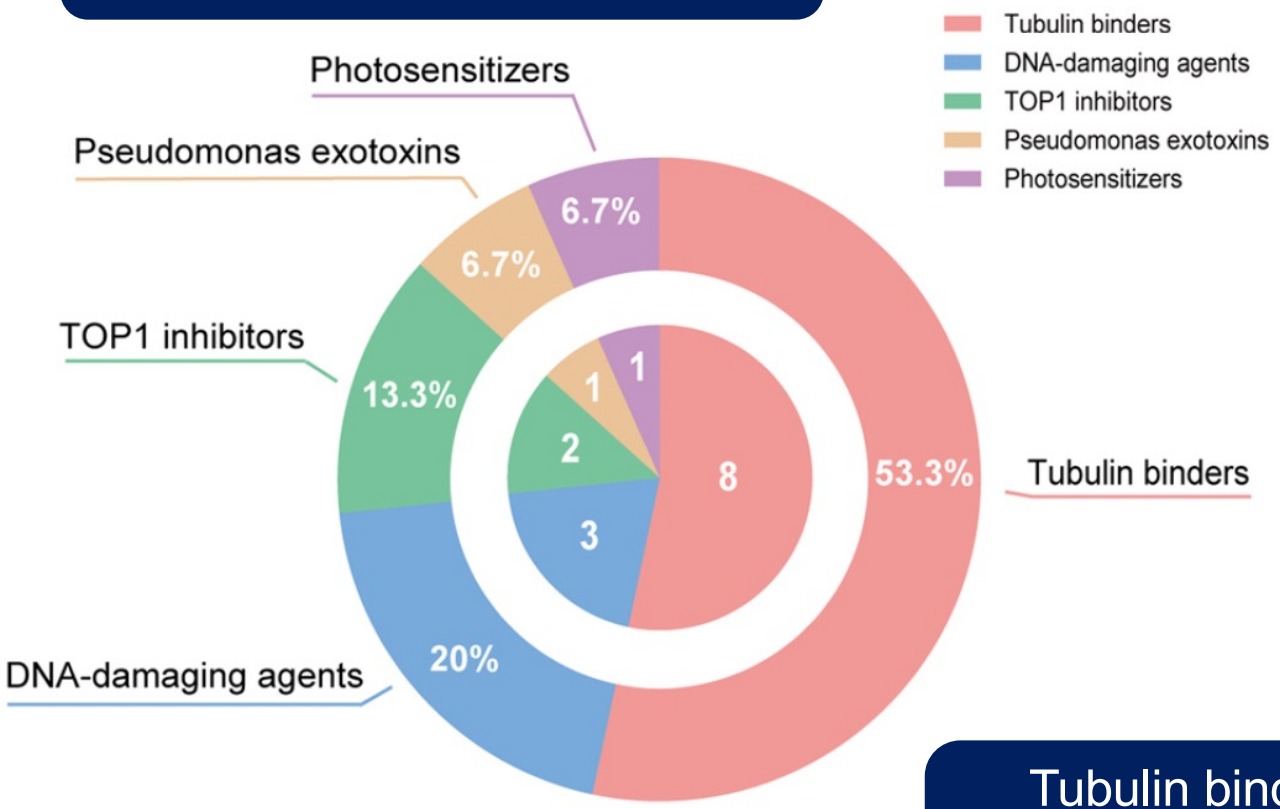
Leveraging TROP2-Directed ADCs in Advanced Gynecologic Cancers

Ramez N. Eskander
Julie St. John Endowed Chair in Gynecologic Oncology
Professor of Obstetrics, Gynecology and Reproductive Sciences
Medical Director, Clinical Trials Office
Fellowship program Director, Gynecologic Oncology
UC San Diego Health
Rebecca & John Moores NCI Designated Comprehensive Cancer Center
La Jolla, CA

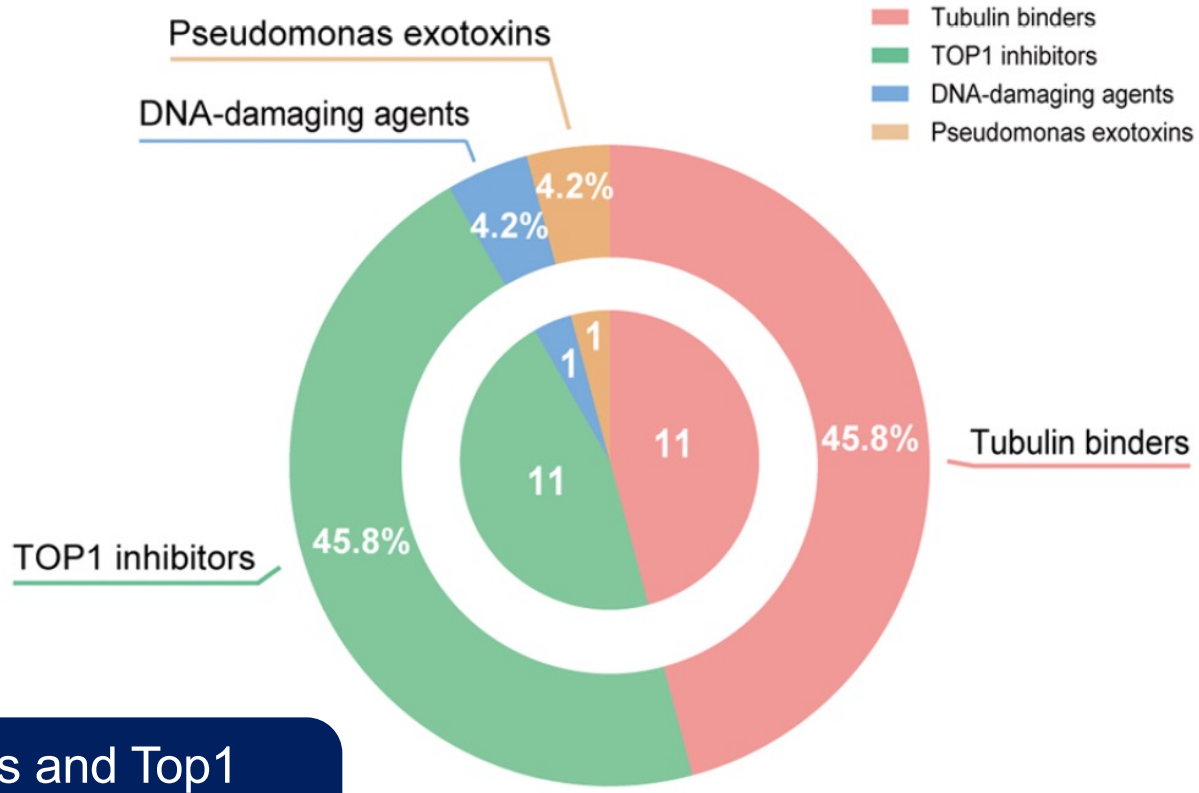


Antibody Drug Conjugates: Over 400 in development…

Marketed ADC Payloads



Ph3 ADC Payloads

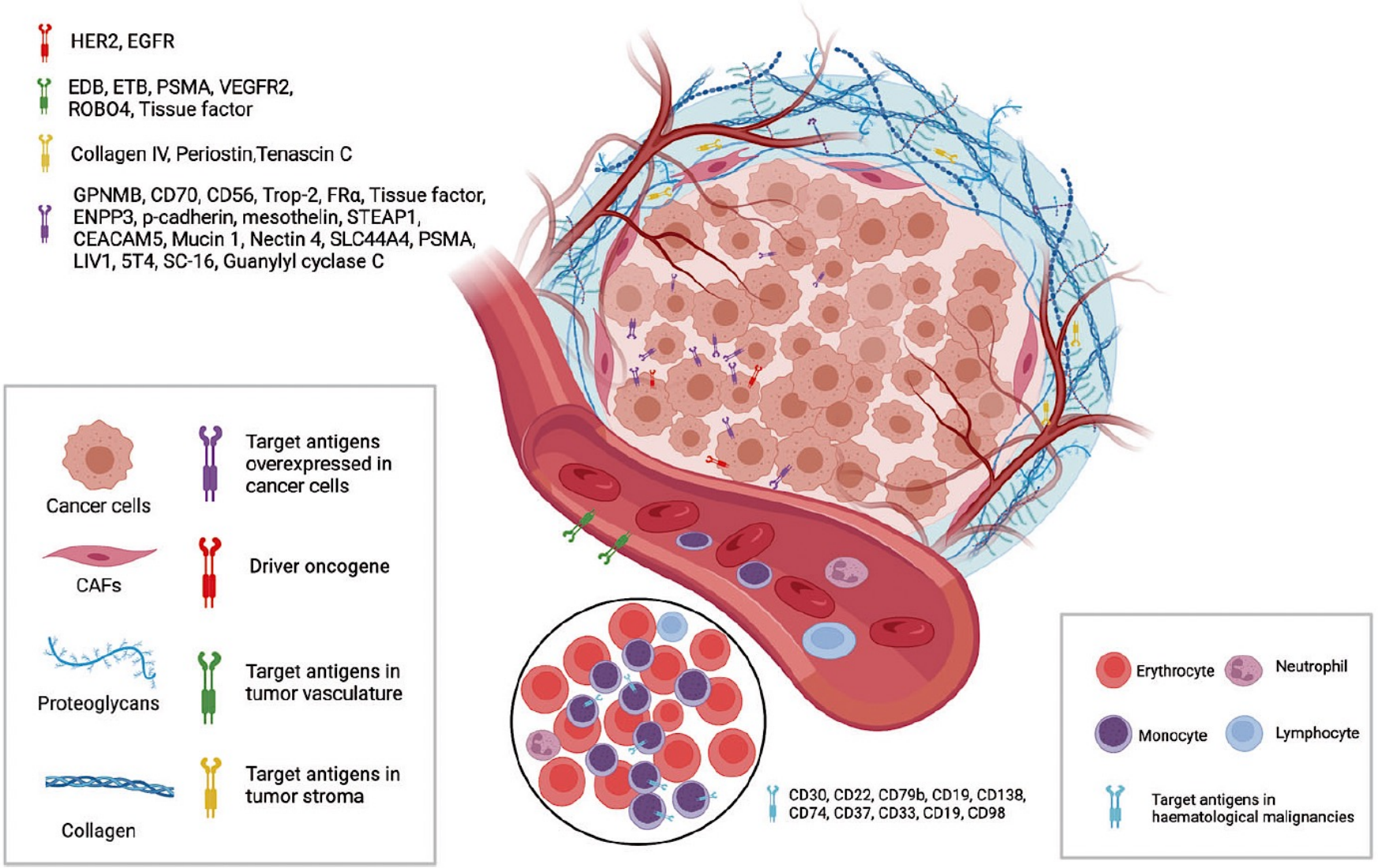


Tubulin binders and Top1 inhibitors are the most prevalent payloads

UC San Diego
SCHOOL OF MEDICINE

Ruan et al. Cancer Communications 2024; Wang et al. Journal of Hematology & Oncology 2025

Antigen Targets: Tumor Cells & Tumor Microenvironment



Fu et al. Signal Transduction and Targeted Therapy. 2022

UC San Diego
SCHOOL OF MEDICINE

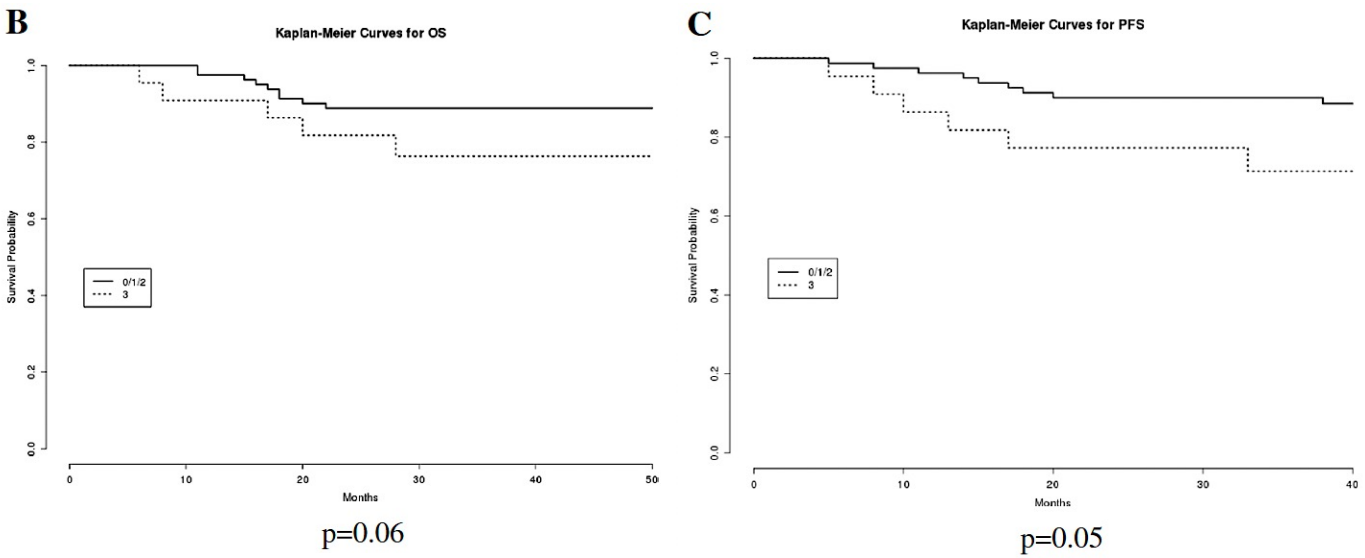
Why TROP2? Biologic Rationale

- TROP2 is a transmembrane glycoprotein (discovered in trophoblasts) overexpressed in many solid tumors including:
  - Endometrial, ovarian and cervical cancer

N=103
OS & PFS by TROP2 expression

- TROP2 expression is associated with:
  - Tumor proliferation
  - Invasion/metastases
  - Negative prognostic indicator

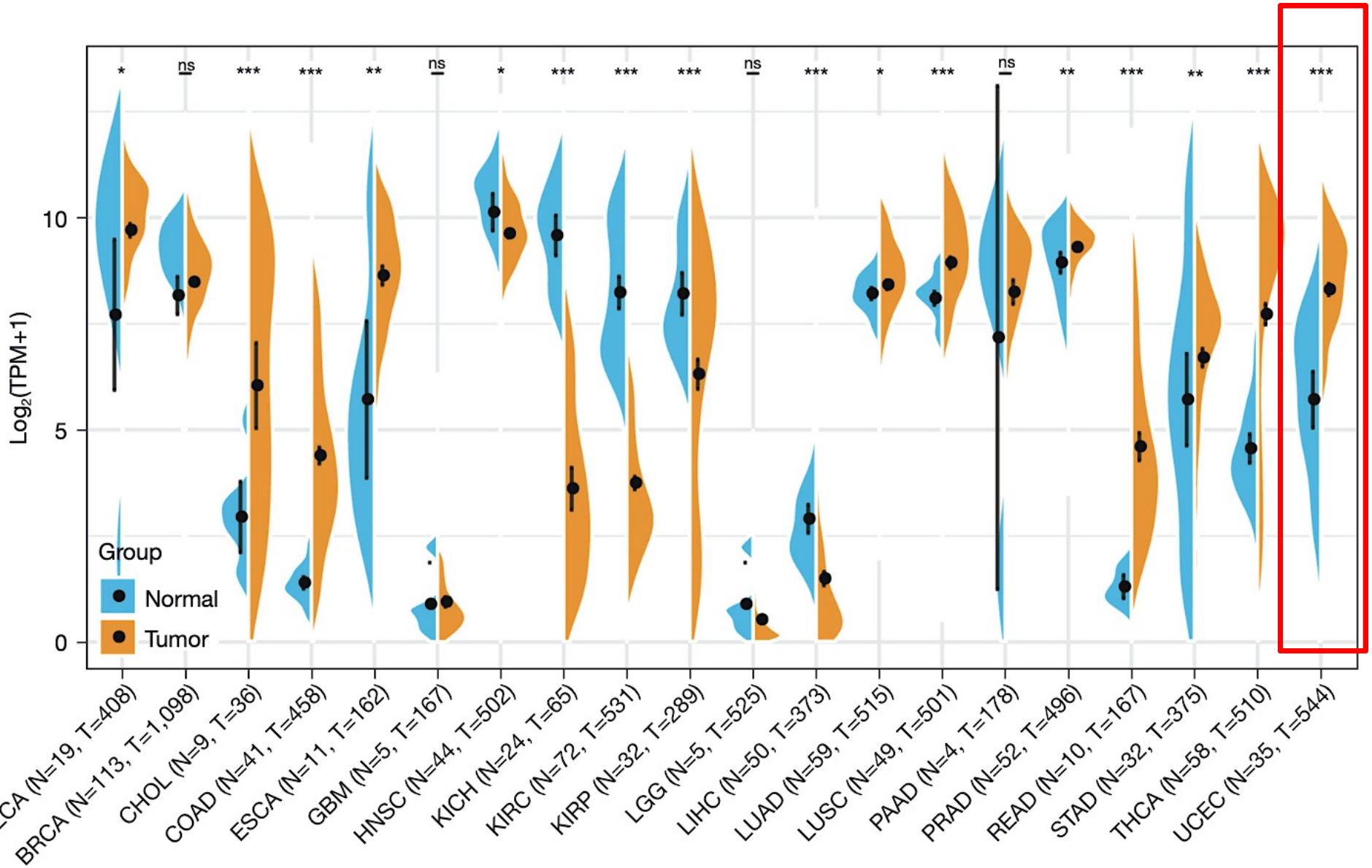
- **Biomarker + Possible functional driver**



UC San Diego
SCHOOL OF MEDICINE

Wen et al. Annals of Translational Medicine. 2022; Bignotti et al. BMC Clinical Pathology 2012

Why TROP2? Biologic Rationale



- TROP2 is expressed in up to 92% of EnCa:
  - 96.2% EEC
  - 95.1% Serous EnCa
  - 35% Carcinosarcoma

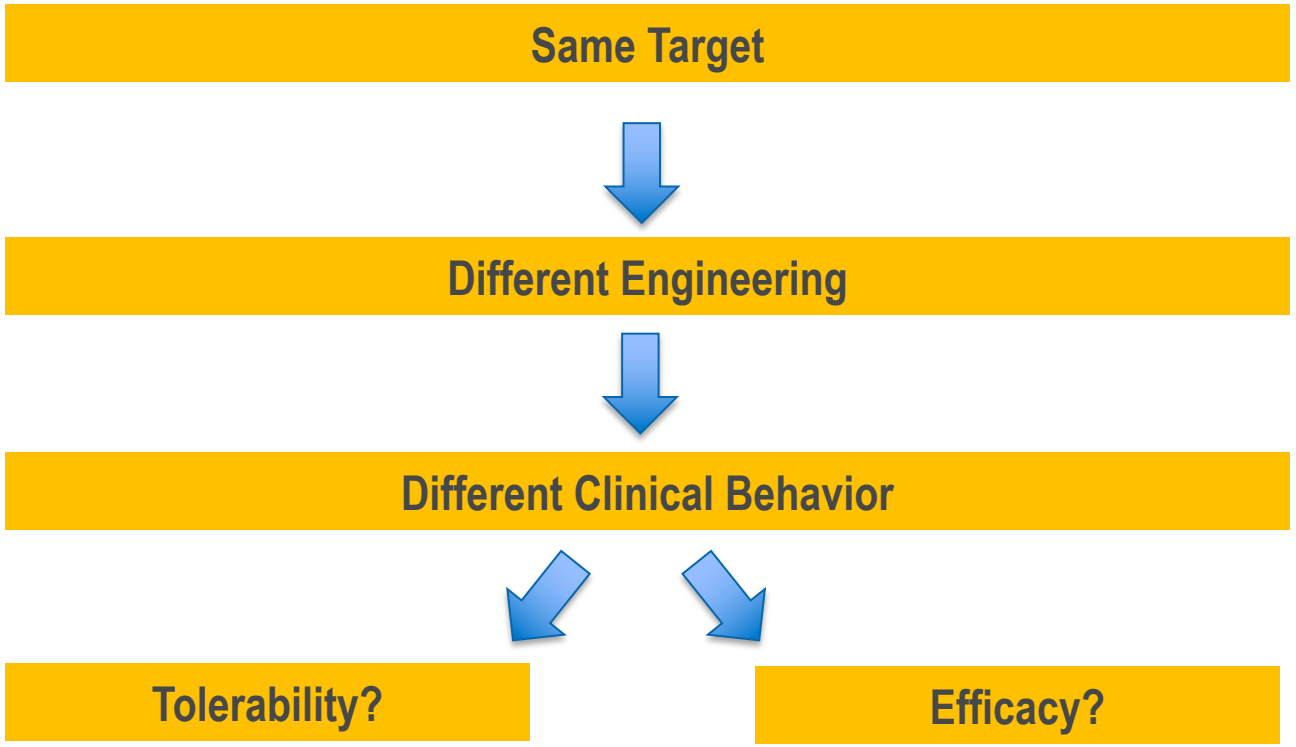
UC San Diego
SCHOOL OF MEDICINE

Wen et al. Annals of Translational Medicine. 2022; Bujnak et al. Gynecologic Oncology 2025

TROP2 ADC Platform and Mechanistic Comparisons

- All current agents in study **share**:
  - Anti-TROP2 monoclonal antibody
  - Cleavable linker
  - Topoisomerase 1 payload

- Key **differences:**
  - Payload type
  - DAR
  - Linker stability
  - Adverse event profile



UC San Diego
SCHOOL OF MEDICINE

TROP2 ADC Platform and Mechanistic Comparisons

Agent/Drug	Payload	Key Features	Common AEs
Sacituzumab Govitecan (SG)	**SN-38** (topoisomerase 1 inhibitor)	**DAR 7.6:1** Bystandard affect Hydrolysable linker	Neutropenia, diarrhea
Datopotamab Deruxtecan (Dato-DXd)	**DXd** (topoisomerase 1 inhibitor)	**DAR 4:1** Lower affinity for target than SG and sac-TMT Tetrapeptide based linker	Stomatitis, ILD
Sacituzumab Tirumotecan (sac-TMT)	**Belotecan-derived** topoisomerase 1 inhibitor	**DAR 7.4:1** Bystandard effect Kthiol linker	Stomatitis, neutropenia

SG + sac-TMT utilize the same humanized TROP2 IgG1 monoclonal antibody hRS7

UC San Diego
SCHOOL OF MEDICINE

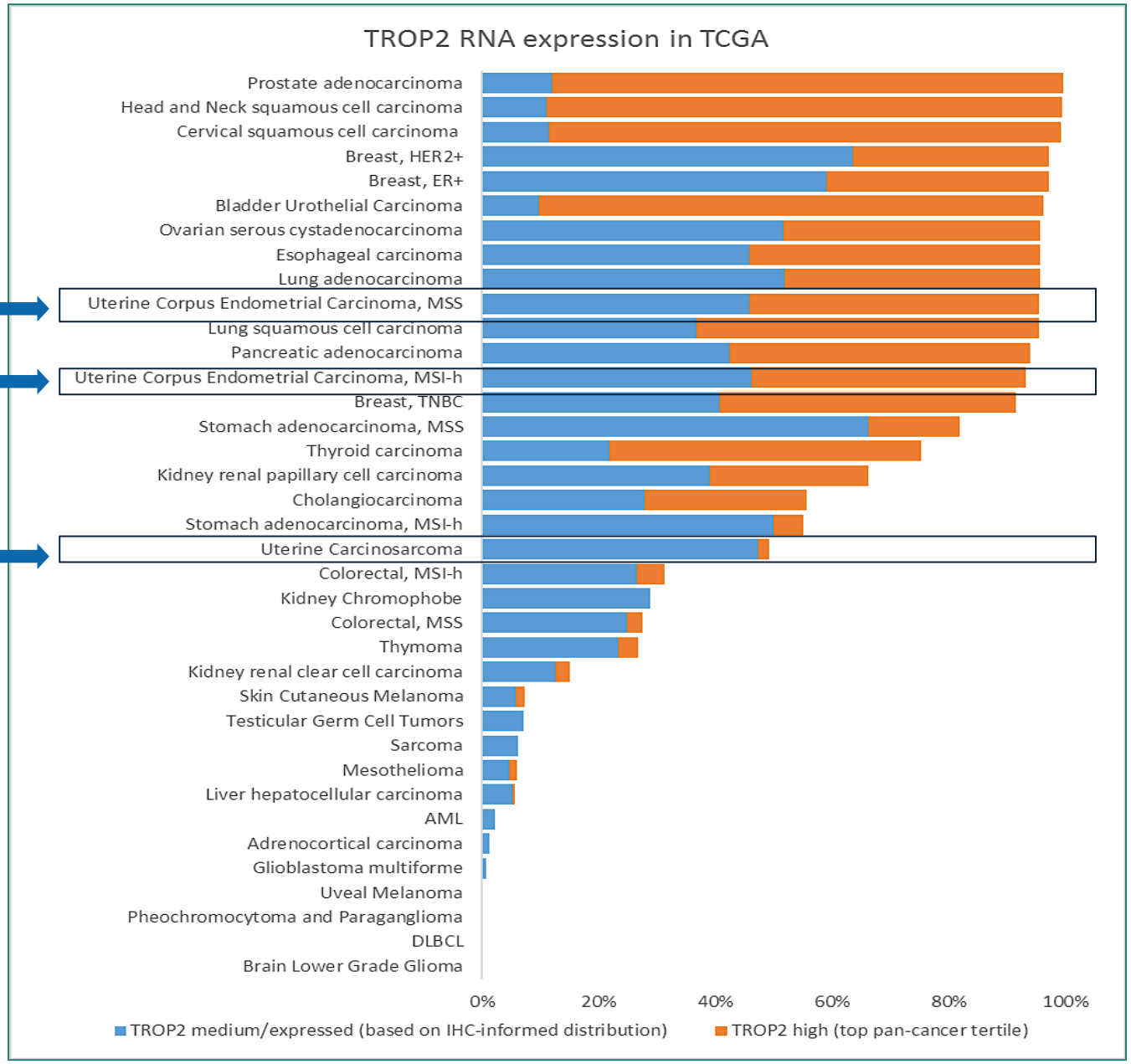
Zhou et al. Cancer Chemotherapy and Pharmacology. 2025

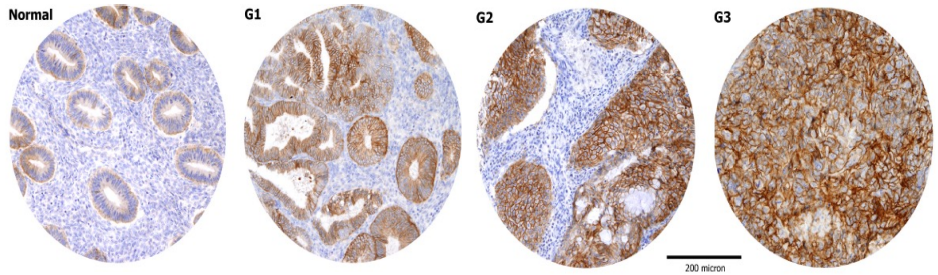
UC San Diego
School of Medicine

TROP2 ADCs in Development

Endometrial Cancer

TROP2 Expression and EnCa





TROP2 Expression in Endometroid Histology is *inversely* correlated with differentiation.

UC San Diego
SCHOOL OF MEDICINE

Preliminary TROP2 ADC Efficacy in EnCa

	Sacituzumab Govitecan (SG) TROPiCS-03	Datopotamab Deruxtecan (Dato-DXd) TROPION-PanTumor03	Sacituzumab Tirumotecan (sac-TMT)
Target	Trop-2	Trop-2	Trop-2
Study Size	N=41	N=40	N=44
Patient Population	- 61% with ≥3 prior lines - 85% prior IO	- 73% with 1 prior line - 22.5% prior IO	- 48% with 1 prior line - 36% prior IO
Region Trial conducted	- United States	- EU (45%) - Asia (45%)	- Almost entirely China
Efficacy	ORR 22%	ORR 27.5%	ORR 27.3% (41.7% H-score>200)
SAEs	- Neutropenia - Diarrhea	- Stomatitis - Anemia - Amylase Increase	- Stomatitis - Anemia - Neutropenia

UC San Diego
SCHOOL OF MEDICINE

Santin A et al J Clin Oncol 2024,A Oaknin et al ESMO 2024, Wang et al. ESMO 2024, Lee et al ESMO 2024; Winer et al ASCO 2025

Phase 3 TROP2 ADC Clinical Trials in Recurrent EnCa

ASCENT-GYN-01/GOG-3104/ENGOT-en26: A Phase 3 Study of SG vs TPC in Patients With Endometrial Cancer Who Have Received Prior Platinum-Based Chemotherapy and Anti-PD-1/PD-L1 Immunotherapy

NCT06486441

Key Eligibility Criteria

- Recurrent or persistent endometrial cancer (endometrial carcinoma or carcinosarcoma)
- Up to 3 prior lines of systemic therapy for endometrial cancer, including systemic platinum-based chemotherapy and anti-PD-1/PD-L1 therapy, either in combination or separately
- Radiologically evaluable disease (either measurable or nonmeasurable) per RECIST v1.1
- ECOG Performance Status of 0-1

N=520

R 1:1

Sacituzumab Govitecan (SG)
10 mg/kg on D1 and 8 of a 21-day cycle

Treatment of Physician's Choice (TPC)
Doxorubicin 60 mg/m^2 on D1 of a 21-day cycle, or Paclitaxel 80 mg/m^2 on D1, 8, and 15 of a 28-day cycle

Treat until disease progression or unacceptable toxicity

Key Endpoints

Primary Endpoints
- PFS by BICR
- OS

Secondary Endpoints
- ORR, DOR, CBR
- PFS by INV
- Safety
- QOL

Trofuse ENGOT-en23/GOG-3095/SAC-TMT: A Phase 3 Study of SG vs TPC in Patients With Endometrial Cancer Who Have Received Prior Platinum-Based Chemotherapy and Anti-PD-1/PD-L1 Immunotherapy

NCT06132958

Key Eligibility Criteria

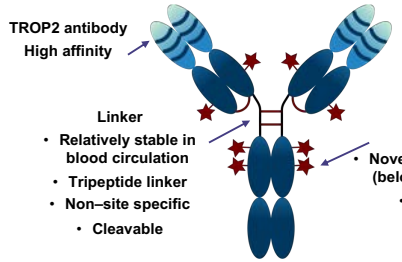
- Histologically confirmed endometrial carcinoma or carcinosarcoma
- Radiographically evaluable disease, either measurable or nonmeasurable per RECIST v1.1 (by BICR)
- Must have received prior platinum-based chemo and anti–PD-1/anti–PD-L1 therapy, either separately or in combination
- No neuroendocrine tumors or endometrial sarcoma, including stromal sarcoma, leiomyosarcoma, adenosarcoma, or other types of pure sarcomas
- Has not received >3 prior lines of therapy for endometrial carcinoma or carcinosarcoma
- Has not had a recurrence of endometrial carcinoma or carcinosarcoma >180 days after completing platinum-based therapy administered in the curative-intent or adjuvant setting without any additional platinum-based therapy received in the metastatic or recurrent setting

TROP2: transmembrane glycoprotein overexpressed by several gynecologic tumor types

R

MK-2870 4 mg/kg IV on day 1 of each 14-day cycle

Doxorubicin 60 mg/m^2 IV on day 1 of each 21-day cycle or Paclitaxel 80 mg/m^2 IV on days 1, 8, and 15 of each 28-day cycle



- **Primary endpoints:** PFS, OS
- **Secondary endpoints:** ORR, DOR, safety, HRQOL

- **MK-2870 employs the same antibody as sacituzumab govitecan**
- **Its linker was designed to have higher stability**
- **Novel TOPO I inhibitor payload (KL610023) is a belotecan derivative/topoisomerase inhibitor that has similar in vitro activity to belotecan and SN-38 (sacituzumab govitecan's payload)**

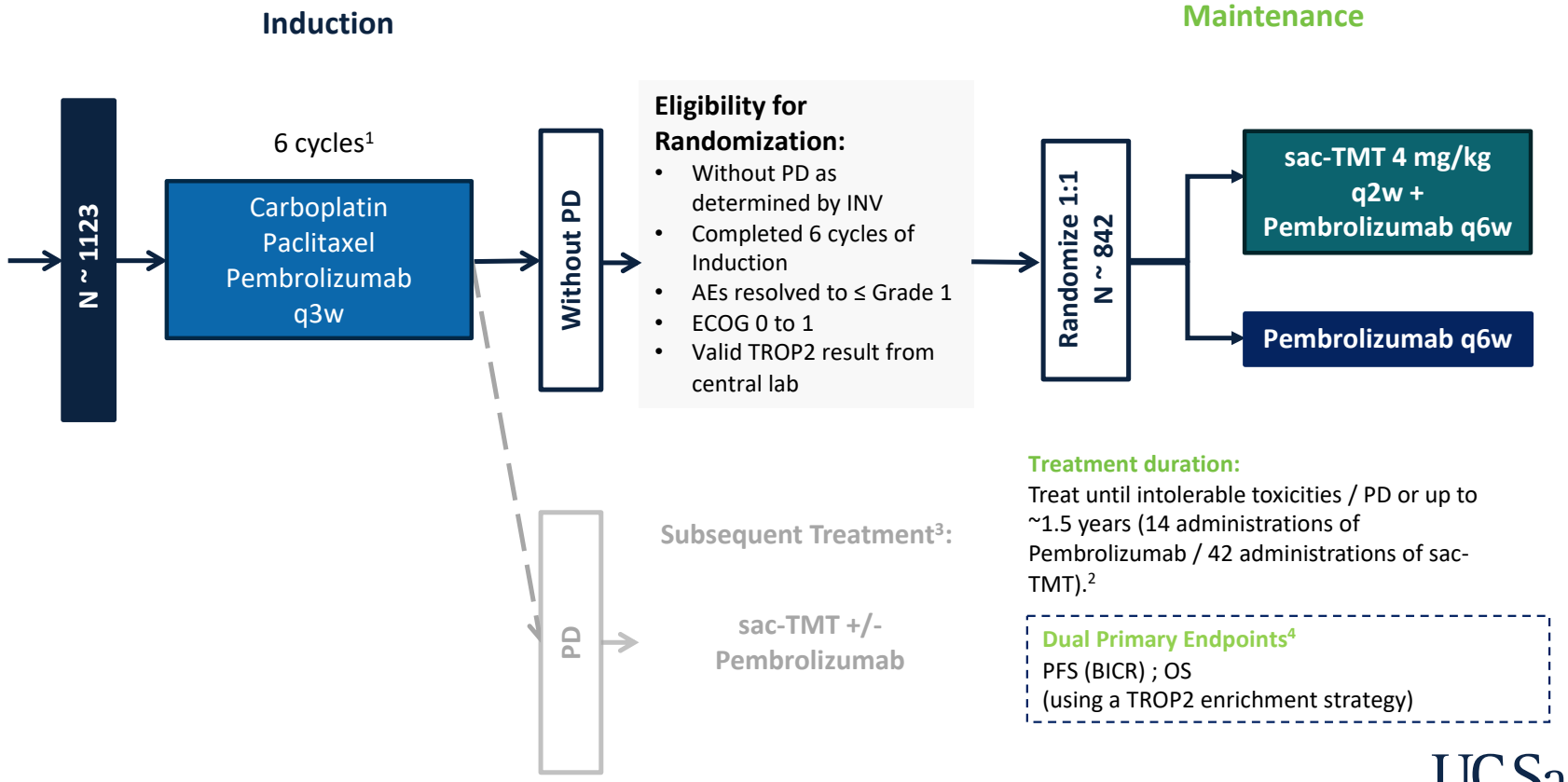
UC San Diego
SCHOOL OF MEDICINE

Phase 3 TROP2 ADC Clinical Trials in Advanced Stage, Metastatic and Recurrent EnCa

MK-2870-033/TroFuse-033/GOG-3119/ENGOT-en29) (TroFuse-033): A Phase 3 Study to Compare Sacituzumab Tirumotecan in Combination With Pembrolizumab Vs Pembrolizumab Alone as Treatment in Participants With pMMR Endometrial Cancer **(NCT06952504)**

Key Eligibility Criteria

- Primary advanced/recurrent endometrial carcinoma
- pMMR
- No prior systemic therapy OR recurred after adjuvant (no PFI required)
- No prior anti-PD-1/PD-L1
- Radiologically apparent disease (measurable for St. III, measurable or non-measurable for St. IV & recurrent disease)
- Available tissue to test for TROP2 / MMR / p53
- ECOG 0 to 1



Treatment duration:
Treat until intolerable toxicities / PD or up to ~1.5 years (14 administrations of Pembrolizumab / 42 administrations of sac-TMT).[2]

Dual Primary Endpoints[4]
PFS (BICR) ; OS
(using a TROP2 enrichment strategy)

[1] If pt. needs more time to recover after 6 cycles of Carboplatin/ Paclitaxel/ Pembrolizumab, two additional cycles of pembrolizumab (cycle 7 + 8) may be administered after sponsor consultation; [2] Pts. with confirmed CR by BICR (following Induction or Maintenance) may discontinue sac-TMT after 6 months of sac-TMT after sponsor consultation; [3]Patients with PD on Induction Treatment will be randomized to sac-TMT vs. sac-TMT + pembrolizumab if eligible per safety criteria outlined in IC/EC; Subsequent Treatment is an exploratory part of the study [4]From start of randomization to Maintenance;

UC San Diego
School of Medicine

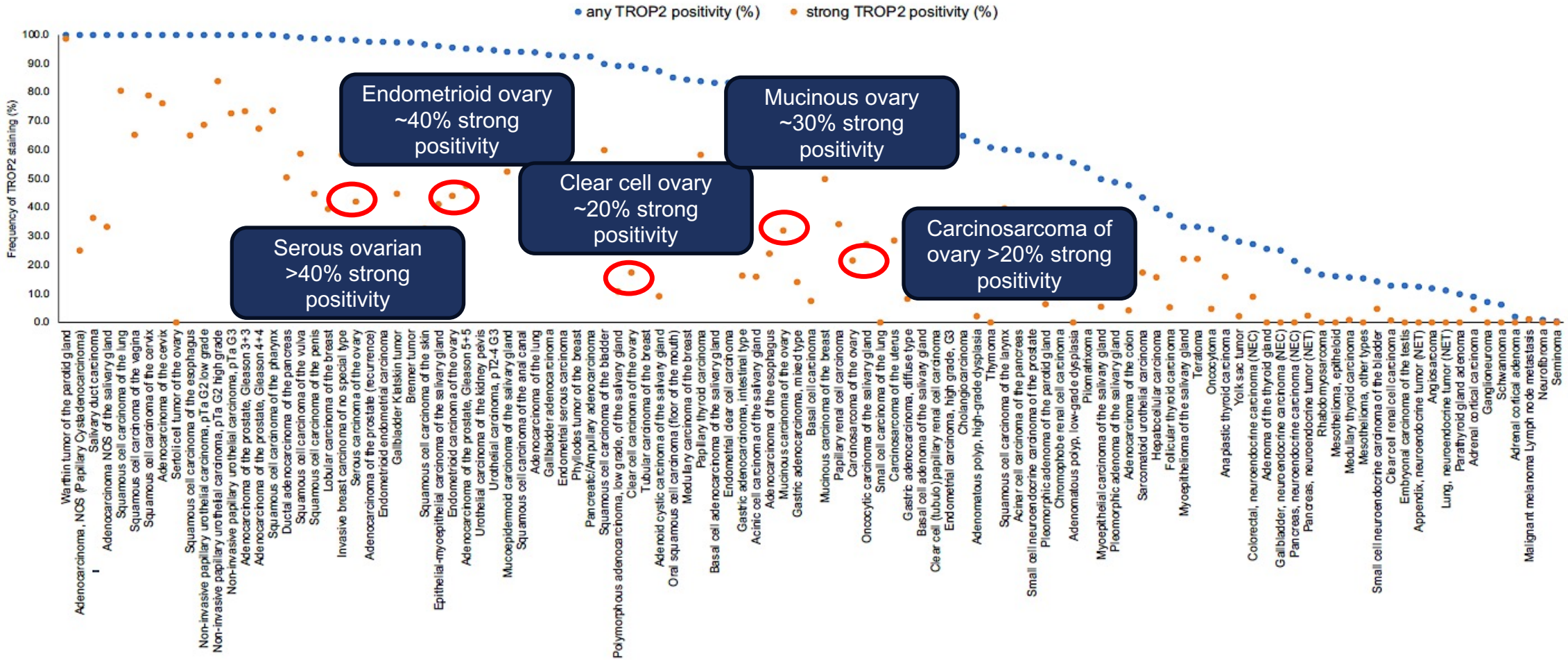
UC San Diego
School of Medicine

TROP2 ADCs in Development

Ovarian Cancer

Is TROP2 a Relevant Target in Ovarian Cancer

Ranking order of TROP2 immuno-staining in cancers. Both the frequency of positive cases (blue dots) and the frequency of strongly positive cases (orange dots) are shown.



Dum D, et al. *Ann Oncol.* (2022);33(suppl_7):S27-S54.

UC San Diego
SCHOOL OF MEDICINE

Preliminary TROP2 ADC Efficacy in OvCa

	Sacituzumab Govitecan (SG)	Datopotamab Deruxtecan (Dato-DXd) TROPION-PanTumor03	Sacituzumab Tirumotecan (sac-TMT)
Study Size	N/A	N=35	N=40
Patient Population		- Median of 2 prior lines of therapy - Range 1-4 - **74% PROS** - **26% PSOC (n-9)**	- All with ≥ 2 prior lines of treatment - 80% with ≥3 prior lines - **87.5% PROC**
Region Trial conducted		- White (63%) - Asia (23%)	- Almost entirely China
Efficacy		**cORR 42.9%** (67% PSOC) - 1 CR and 14 PR - DoR 5.7 months - Median PFS 5.6 months	**ORR 40%** (61.5% H-score>200) - Median PFS 6 months
SAEs		- Stomatitis - Nausea - Alopecia	- Stomatitis - Neutropenia - Anemia

UC San Diego SCHOOL OF MEDICINE

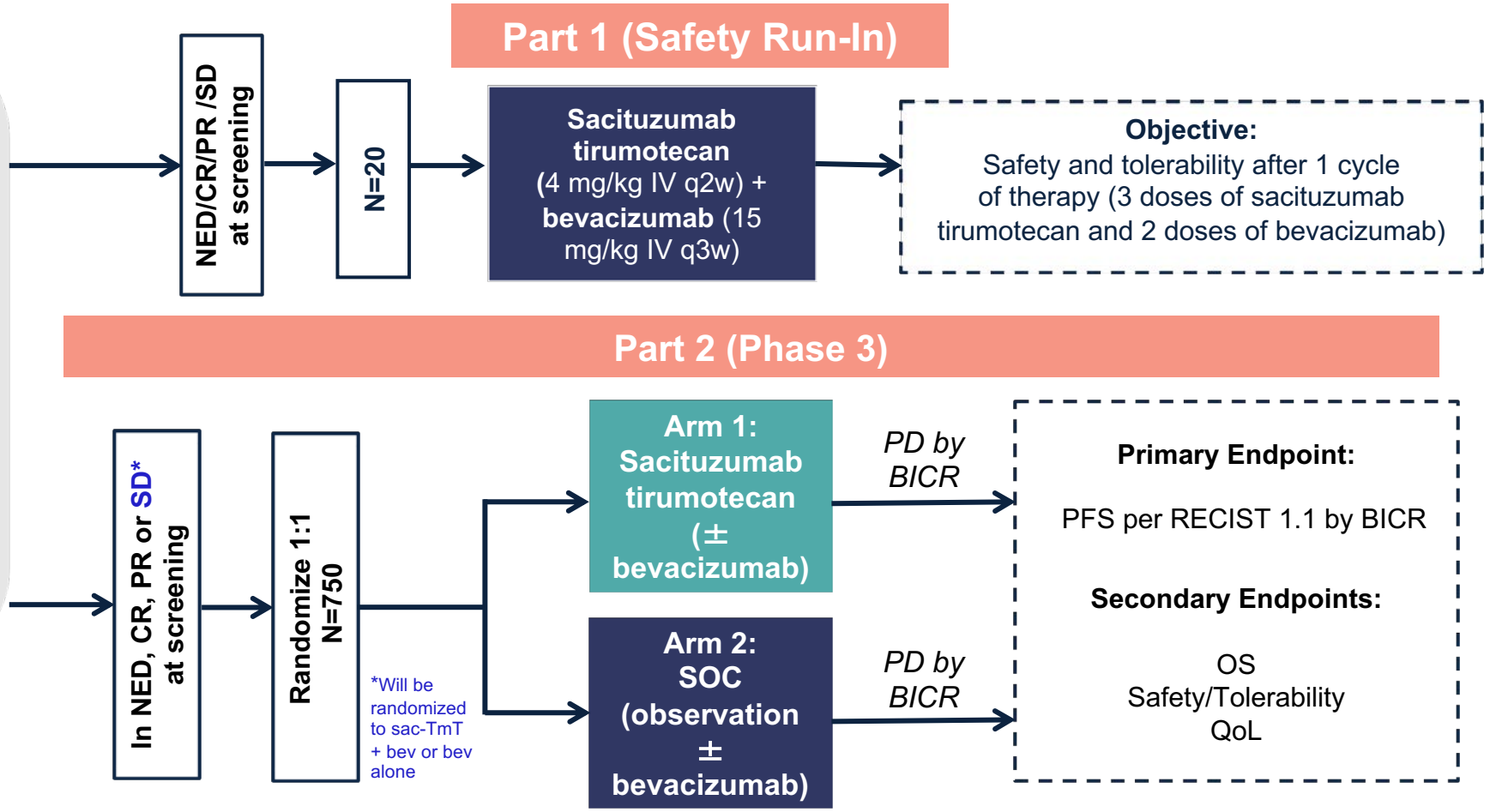
A Oaknin et al ESMO 2024, Wang et al. ESMO 2024, Greenman et al. Gynecol Oncol Rep 2024

Phase 3 TROP2 ADC maintenance trial in PSOC

TroFuse-022/GOG-3101/ENGOT-ov84 (NCT06824467): A Phase 3, Randomized, Open-label, Multicenter Study to Evaluate the Efficacy and Safety of Sacituzumab Tirumotecan Maintenance Treatment With or Without Bevacizumab Versus Standard of Care After Second-line Platinum-based Doublet Chemotherapy in Participants With Platinum-sensitive Recurrent Ovarian Cancer

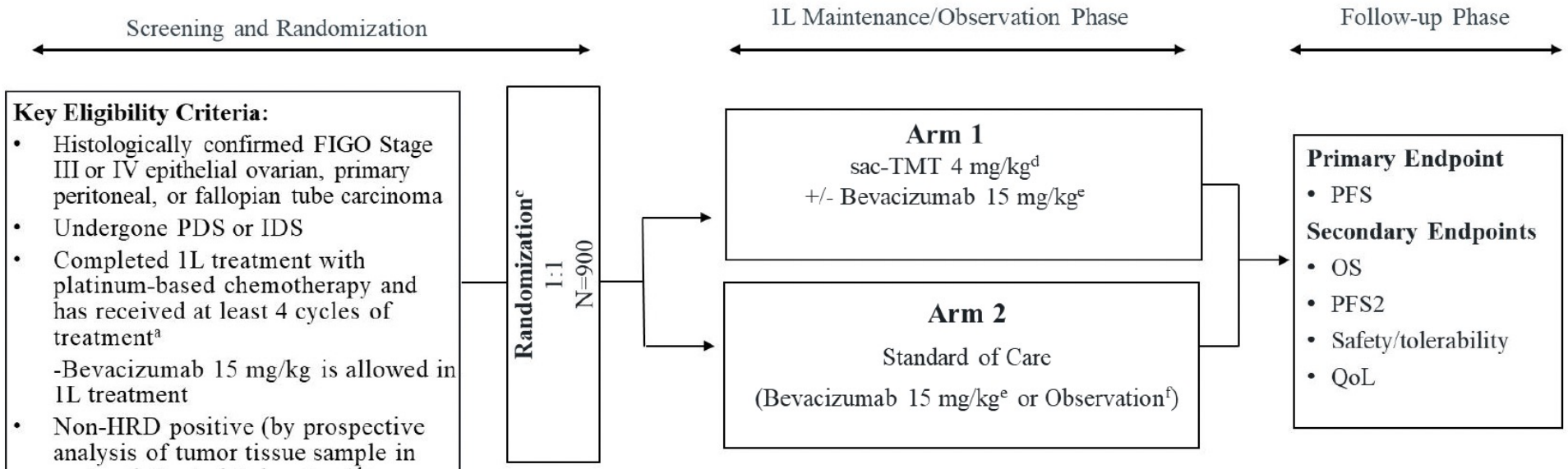
Key eligibility criteria:

- Histologically confirmed epithelial ovarian, fallopian tube, or primary peritoneal cancer
- PSROC with progression >180d after last dose of 1L platinum doublet chemotherapy
- Must have received 6 cycles of 2L carboplatin-based doublet chemotherapy (± bevacizumab)
- Patients with SD must be receiving bevacizumab in combination with chemo and be eligible to continue treatment with bev



Phase 3 TROP2 ADC maintenance trial in Newly Diagnosed OvCa

TroFuse-021/GOG-3102/ENGOT-ov85 (NCT07318558): A clinical trial of sac-TMT in people with non-HRD positive advanced ovarian cancer



UC San Diego
SCHOOL OF MEDICINE

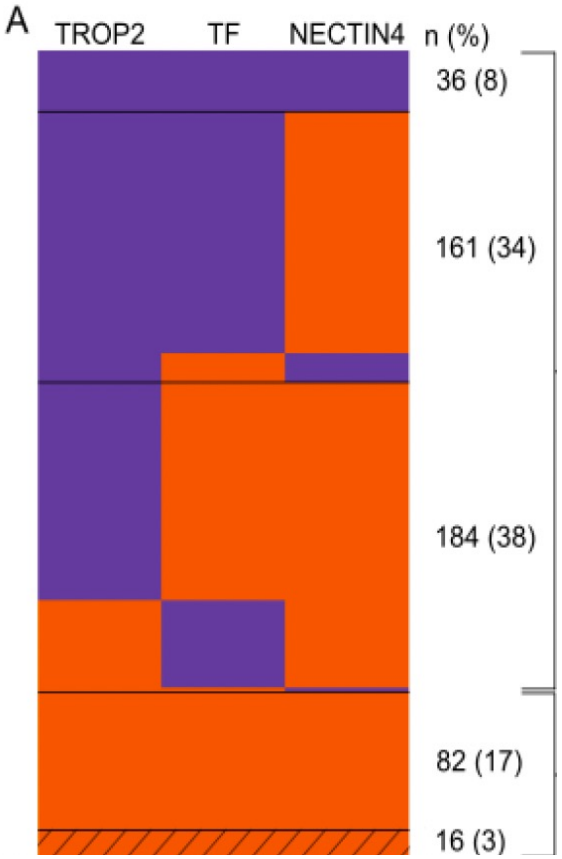
TROP2 ADCs in Development

Cervical Cancer

Target Antigen Expression in Cervical Cancer

TROP2 AND TISSUE FACTOR ARE HIGHLY EXPRESSED IN CERVICAL CANCER

Protein expression	TROP2, n (%)	Tissue Factor, n (%)	NECTIN4, n (%)
n, total	n = 501	n = 500	n = 511
3+	185 (37 %)	144 (29 %)	21 (4 %)
2+	157 (31 %)	97 (19 %)	42 (8 %)
1+	127 (25 %)	159 (32 %)	170 (33 %)
0	32 (7 %)	100 (20 %)	278 (55 %)
High (3+ and 2+)	342 (68 %)	241 (48 %)	63 (12 %)
Low (1+ and 0)	159 (32 %)	259 (52 %)	448 (88 %)



PRIMARY AND MATCHED RECURRENT LESIONS

Level of high (2+, 3+) recurrent lesion expression:

- TROP2: 56%
- Tissue Factor: 46%
- NECTIN4: 35%

Level of concordance (low *versus* high) between primary and matched recurrent lesion:

- TROP2: 15/22 (68%)
- Tissue Factor: 20/22 (91%)
- NECTIN4: 15/22 (68%)

Halle et al. ESMO 2024

UC San Diego SCHOOL OF MEDICINE

Preliminary TROP2 Targeting ADC Efficacy in Cervical Cancer

	N	Trial	Prior Bevacizumab	Prior ICI	ORR	mDOR
SacTMT +pembrolizumab	38	NCT05642780	53%	42%	**58%**	**NR**
Sacituzumab govitecan	18	NCT05838521	61%	78%	**50%**	**9.2 mo**

Considerations:
- **Relative contribution of pembrolizumab?**

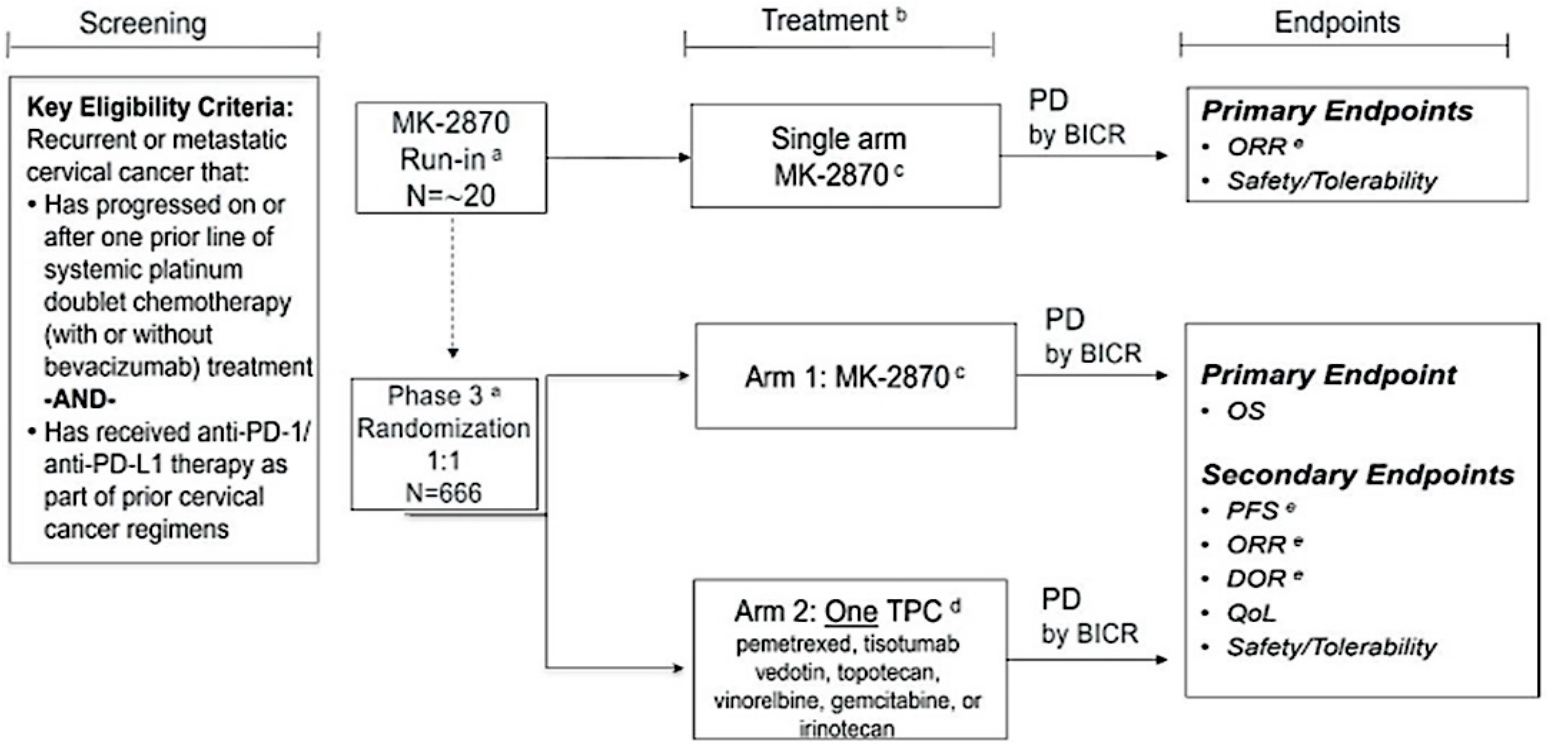
Context - Tisotumab vedotin:
- **ORR 17.8%**
- **Prior Bev: 65% and Prior ICI: 28%**

UC San Diego
SCHOOL OF MEDICINE

Phase 3 TROP2 ADC Trial in Recurrent Cervical Cancer

TroFuse-020/GOG-3101/ENGOT-cx20: A Phase 3 randomized , active-controlled, open-label, multicenter study to compare the efficacy and safety of MK-2870 monotherapy versus treatment of physician choice as second-line treatment for participants with recurrent or metastatic cervical cancer **(NCT06459180).**

Figure 1 Study Design



Stratification – Phase 3 Portion Only:
- Prior use of bevacizumab (yes vs no)
- TROP2 expression (low + medium vs high)
- Selection of TPC (tisotumab vedotin vs other TPC)

UC San Diego
SCHOOL OF MEDICINE

Phase 3 TROP2 ADC Trial in Newly Diagnosed Advanced Stage, Metastatic and Recurrent Cervical Cancer

TroFuse-036/GOG-3123/ENGOT-cx22 (NCT07216703). Part 2

Screening for Enrollment

Key Eligibility Criteria for Enrollment:

- Persistent, recurrent, or newly diagnosed metastatic cervical cancer that is not amenable to curative treatment
- Histologically confirmed diagnosis of squamous cell carcinoma, adenosquamous carcinoma, or adenocarcinoma of cervix
- Measurable disease
- No prior systemic treatment, including prior IO
- Prior radiation + radiosensitizing chemotherapy is allowed
- PD-L1 CPS >1 per Central Laboratory
- ECOG PS 0 to 1
- Excluded if have received prior systemic anticancer therapy other than what is specified in this protocol

Induction (6 x 3-weeks cycles)

Cisplatin 50 mg/m2 or Carboplatin AUC 5 mg/mL/min, Paclitaxel 175 mg/m2, Pembrolizumab 200 mg +/- Bevacizumab 15 mg/kg per investigator Q3W

Randomize

Arm A

Sac-TMT 4 mg/kg Q2W + Pembrolizumab 400 mg Q6W +/- Bevacizumab 15 mg/kg Q3W per investigator

Arm B

Pembrolizumab 400 mg Q6W +/- Bevacizumab 15 mg/kg Q3W per investigator

Sacituzumab Tirumotecan (Sac-TMT) plus Pembrolizumab Maintenance Therapy in Ovarian Cancer: Results from the Phase 2 2870-002/SKB264-II-06 Study

Wu X et al.

SGO 2026.

FOCUSED FORUM IX

MONDAY, APRIL 13, 2026

BALLROOM B

8:38 AM – 8:44 AM CDT

Sacituzumab Tirumotecan (Sac-TMT) plus Pembrolizumab in Participants with Recurrent or Metastatic Cervical Cancer: Results from the Phase 2 2870-002/SKB264-II-06 Study

Wu X et al.

SGO 2026.

SCIENTIFIC PLENARY V

MONDAY, APRIL 13, 2026

EXHIBIT HALL A

10:19 AM – 10:27 AM CDT

Remaining Questions/Considerations….

- Optimal Sequencing
- Duration of Therapy
- TROP2 expression levels
  - Predictive of response and what assay?
- Is ADC after ADC viable in the gynecologic space?
  - Relevance of antigenic target and payload
  - Cross-resistance
- AE education and mitigation strategies
- Novel combinations

UC San Diego
SCHOOL OF MEDICINE

Conclusions

- **TROP2 is a validated and actionable target**
- **ADC design informs efficacy and tolerability**
- **The largest data set, currently, for TROP2 ADCs is in the endometrial cancer space**
  - **2 completed phase 3 trials, in the recurrent setting, with results pending**
- **Promising early signals in ovarian cancer and cervical cancer**
- **Ongoing Phase 3 trials will define the future standard of care**
- **Enroll!**

UC San Diego
SCHOOL OF MEDICINE

Faculty Case Presentations

RTP
RESEARCH
TO PRACTICE

Dr Monk: EC After 1-L Immunotherapy

- 66 year old black American with stage 4B (no residual) uterine serous cancer (pMMR, HER2 1+, TP53 mut, ER -, POLE not tested)
- Treated with carboplatin + paclitaxel + pembrolizumab (KN-868, GY-018) and recurred in the peritoneum 9 months into maintenance.

Is this pt appropriate for a TROP2 targeted ADC?

QUESTIONS FOR THE FACULTY

What would you most likely recommend next for this patient outside of a clinical trial, and what outcomes would you expect? Is this patient an appropriate candidate for a clinical trial of a TROP2-targeted ADC?

QUESTIONS FOR THE FACULTY

Have any of the TROP2-targeted ADCs that have been evaluated in endometrial cancer — sacituzumab govitecan, datopotamab deruxtecan (Dato-DXd) or sacituzumab tirumotecan (sac-TMT) — stood out as relatively efficacious compared to the others? If this patient were interested in a clinical trial of a TROP2-targeted ADC and asked you to estimate the likelihood that she would experience a meaningful response to treatment, how would you respond?

QUESTIONS FOR THE FACULTY

Do you believe TROP2-directed ADCs will eventually have a role in the management of advanced endometrial cancer? If so, where will they most likely fall in the treatment sequence? Do you anticipate that they'll be reserved for later-line use after disease progression on up-front chemoimmunotherapy? Based on the experience in breast cancer, do you think that TROP2-directed ADCs might eventually replace standard chemotherapy as the partner for anti-PD-1/PD-L1 antibodies in the up-front setting?

QUESTIONS FOR THE FACULTY

If multiple TROP2-directed ADCs were to reach the clinic in advanced endometrial cancer, would you attempt to administer more than one of them to the same patient in sequence?

Do you believe TROP2-directed ADCs will eventually have a role in the management of advanced cervical cancer and, if so, in what setting(s)? Given the relatively low response rates with tisotumab vedotin, do you think TROP2-targeted ADCs have the potential to supplant it as second-line therapy?

Dr Moore: Patient presentation

72 year-old female h/o Stage IIIC high grade serous ovarian cancer in 2019

- Treated with NACT with paclitaxel and carboplatin and bevacizumab followed by bevacizumab maintenance x 1 year
- BRCAwt/HRD test +
- Recurred 24 months after last platinum with liver mets
- Carboplatin and PLD x 6 cycles with PR. Maintenance Olaparib x 12 months with PD
- Carboplatin x 4 with PD

Work up

Imaging with liver metastases, no bowel obstruction, no ascites

PS = 1

Biomarkers: *BRCA*wt/HRD+/FRα med/ HER2 2+/ TP53 Y220C/HLA 0201

- SOC: No biomarker linked FDA approved medications
- NCCN: FRα expression links to MIRV + BEV, HER2 2+ links to TDXd
- Trials: TP53 Y220C links to rezatapopt

What additional testing do you order? What are you looking for?

Dr Moore: Patient presentation

72 year-old female h/o Stage IIIC high grade serous ovarian cancer in 2019

- Treated with NACT with paclitaxel and carboplatin and bevacizumab followed by bevacizumab maintenance x 1 year
- BRCAwt/HRD test +
- Recurred 24 months after last platinum with liver mets
- Carboplatin and PLD x 6 cycles with PR. Maintenance Olaparib x 12 months with PD
- Carboplatin x 4 with PD

Work up

Imaging with liver metastases, no bowel obstruction, no ascites

PS = 1

What additional testing do you order? What are you looking for?

Biomarkers: *BRCA*wt/HRD+/FRα med/ HER2 2+/ TP53 Y220C/HLA 0201

- SOC: No biomarker linked FDA approved medications
- NCCN: FRα expression links to MIRV + BEV, HER2 2+ links to TDXd
- Trials: TP53 Y220C links to rezatapopt

What are your considerations for therapy?

- 3 prior lines
- Prior Bevacizumab & PARPi
- Progressed on platinum and on PARPi

QUESTIONS FOR THE FACULTY

Do you believe TROP2-directed ADCs will eventually have a role in the management of advanced ovarian cancer? In your experience, are these agents more or less effective in any particular histologic subtypes (serous, clear cell, mucinous, etc)? Where do you think they are most likely to be used, and how might this vary based on biomarker profile and eligibility for other targeted treatments?

QUESTIONS FOR THE FACULTY

If TROP2-targeted ADCs were to become available in the maintenance setting for patients with newly diagnosed or platinum-sensitive recurrent ovarian cancer, how long do you envision continuing them — until disease progression or unacceptable toxicity or for a finite duration?

If ADCs with four different targets — FRα, HER2, CDH6 and TROP2 — were to eventually become available in advanced ovarian cancer, would you have any hesitation about administering them all in sequence to a patient who was eligible?

QUESTIONS FOR THE FACULTY

Given that sacituzumab govitecan and Dato-DXd are already available in other tumor types, would you try to access either one of them outside of a clinical trial for a patient with advanced endometrial, ovarian or cervical cancer who had exhausted other available therapies? If so, in which specific scenarios would you be most likely to attempt this?

Beyond CDH6 and TROP2, what other novel targets for ADCs are you excited about in advanced gynecologic cancers?

Agenda

Module 1: Advances in Human Cadherin-6-Targeted Antibody-Drug Conjugates (ADCs) in Ovarian and Other Gynecologic Cancers — Dr Moore

Module 2: Leveraging TROP2-Directed ADCs in Advanced Gynecologic Cancers — Prof Eskander

Module 3: Tolerability and Other Practical Considerations with Novel Investigational ADCs in Advanced Gynecologic Cancers — Dr Monk

ADCs in Gynecologic Cancers

HOPE VERSUS HYPE

Bradley J. Monk, MD FACOG FACS

Florida Cancer Specialists and Research Institute
West Palm Beach, FL 33401 USA
Professor at University of Central Florida College of Medicine

Vice President and Member Board of Directors GOG-Foundation
Director GOG-Partners

Biomarker Expression Differences Between HGSC and Non-HGSC

- Preliminary data show expression levels of non-HGSC compared with HGSC.
- Positivity of FRα was defined as expression in ≧75% of the cells.
  For HER2, CDH6, B7-H4, and TROP2, positivity was defined as IHC scores of 2+ or 3+.

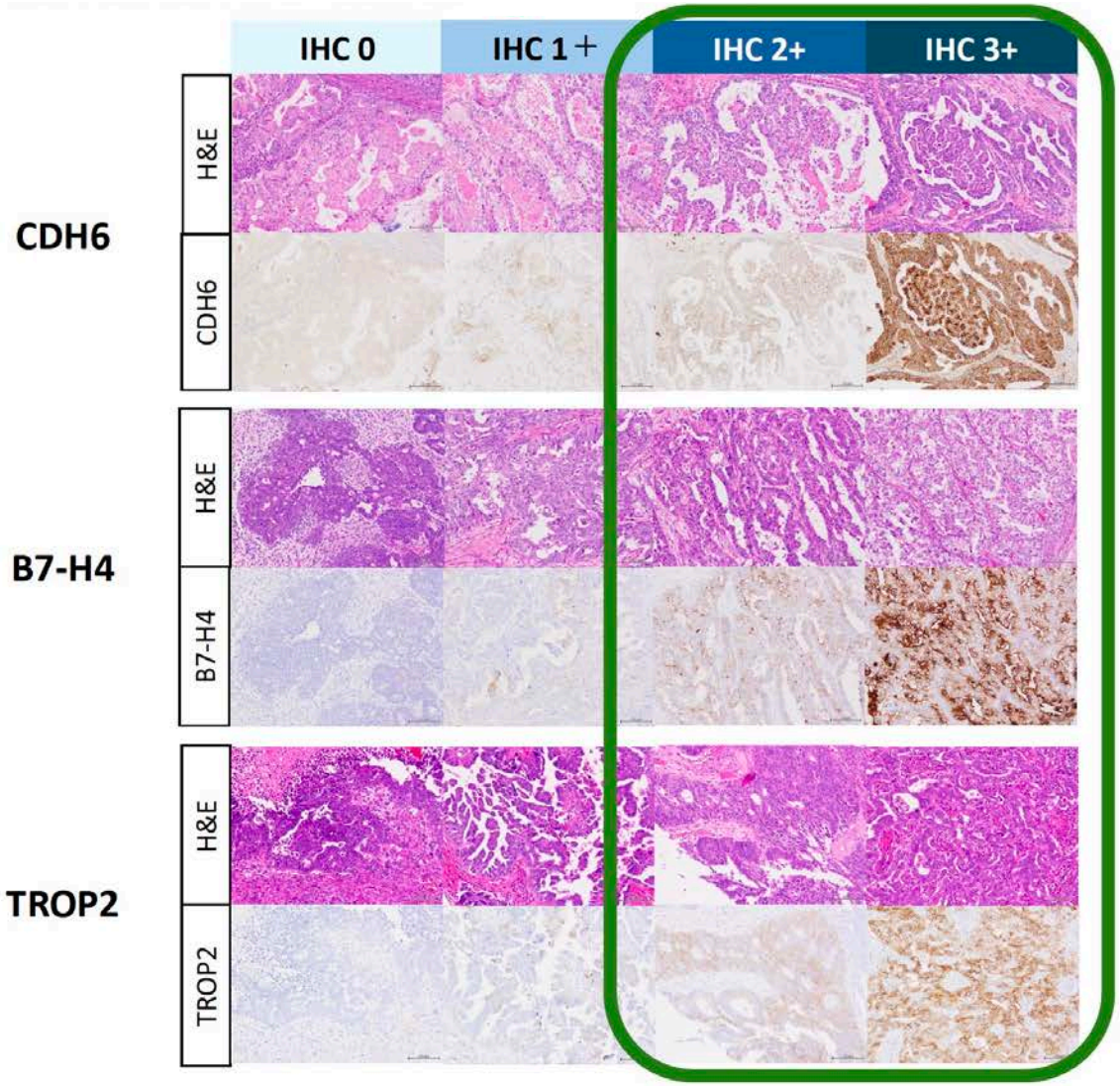
	HGSC		non-HGSC	
	+	%	+	%
FRα	18/80	23%	**5/80**	**6.3%**
HER2	5/80	6.3%	**11/80**	**13.8%**
CDH6	55/80	69%	**25/80**	**32.5%**
B7-H4	43/80	54%	**38/80**	**47.5%**
TROP2	40/80	50%	**33/80**	**41.3%**

- FRα and CDH6 show higher expression in HGSC
- HER2 shows higher expression in non-HGSC.
- TROP2 and B7-H4 are expressed at similar levels in both HGSC and non-HGSC.

HGSC = high-grade serous carcinoma

Hamagawa K et al. ESMO Gyn 2025;Abstract 71O.

CDH6, B7-H4 and TROP2 in High-Grade Serous Carcinoma



- IHC expression was graded using a 4-tier scoring system based on the HER2 scoring criteria for gastric cancer from the ASCO/CAP guidelines.
- Staining scores of 2+ and 3+ were defined as high expression.
- **For CDH6, B7-H4, and TROP2, there is no standardized method to evaluate target expression.**

Defined αs high expression

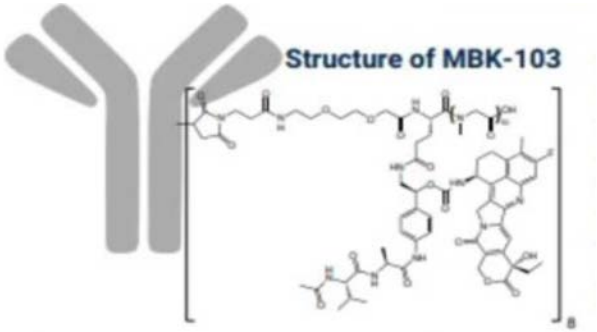
Original magnification x 200, a bar indicates 100μm.

Hamagawa K et al. ESMO Gyn 2025;Abstract 71O.

Targeting the Folate Receptor

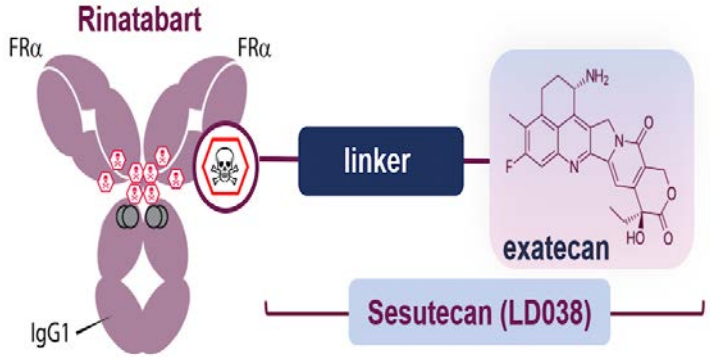
Sofetabart mipitecan * (LY4170156 / MBK-102)

- Fc-silenced FRα IgG1 that binds at low nm affinities
- Polysaccharide hydrophobic linker with a high DAR (8) Cleavable linker
- Proprietary orthogonally embedded dipeptide (VAL-Ala)
- Exatecan payload (topoisomerase inhibitor)



Rinatabart sesutecan (Rina-S)

- A human monoclonal antibody directed at FRα
- A novel hydrophilic protease-cleavable linker
- DNA-damaging agents: Exatecan payload (topoisomerase inhibitor)
- Rina-S features a high, homogenous DAR=8



Torvutatug samrotecan (AZD5335)

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

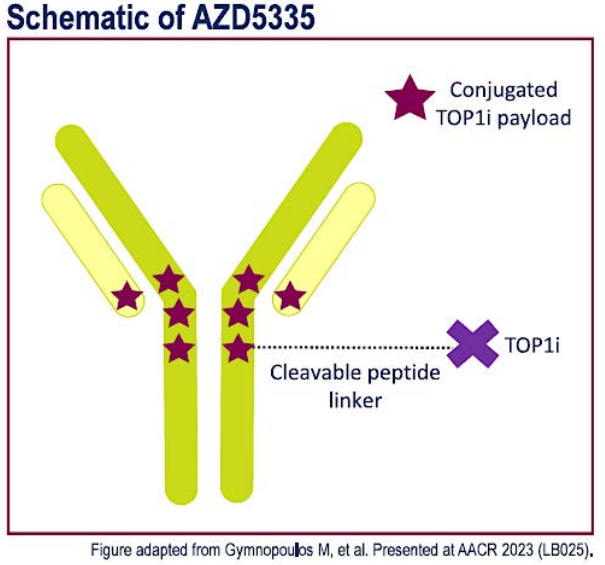


Figure adapted from Gymnopoulos M, et al. Presented at AACR 2023 (LB025).

* Breakthrough Therapy designation for the treatment of certain patients with platinum-resistant ovarian
\# Breakthrough Therapy designation in advanced endometrial cancer

Inferential Cross-trial Comparisons for Anti-FRα ADCs in OC

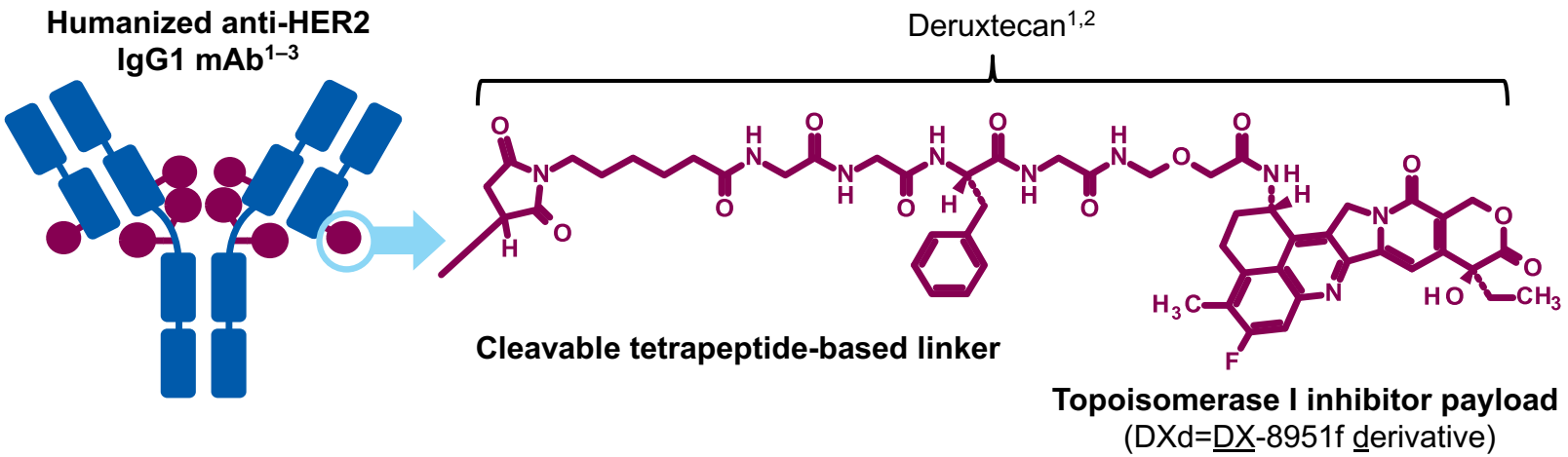
Project	Company	Trial	ORR in all-comers	ORR in FRα ≥75%	ORR in FRα <75%	ORR in FRα <25%
Mirv	AbbVie (ex ImmunoGen)	Mirasol	42% (n=225)	42% (n=225)	Not tested	Not tested
Rina-S	Genmab (ex ProfoundBio)	Rainfol-01	38% (n=40)	68% (n=13)	30% (n=23)	Not split out
Sofe-M	Lilly (ex Mablink)	LOXO-FRA-24001	50% (n=104)	54% (n=46)	45% (n=53)	40% (n=25)
Torvuta-S	AstraZeneca	Fontana	53% (n=168)	61% (n=56)	Not split out	48% (n=61)

Source: OncologyPipeline.

Trastuzumab Deruxtecan (T-DXd): ADC targeting Her2

T-DXd is an ADC with three components:

1. A humanized anti-HER2 IgG1 mAb with the same amino acid sequence as trastuzumab
2. A topoisomerase I inhibitor payload, an exatecan derivative
3. A tetrapeptide-based cleavable linker



Seven Key Attributes[a,1–5]
Payload mechanism of action: topoisomerase I inhibitor
High potency of payload
High drug-to-antibody ratio ≈8
Payload with short systemic half-life
Stable linker payload
Tumor-selective cleavable linker
Bystander antitumor effect

[a]The clinical relevance of these features is under investigation.

ADC, antibody–drug conjugate; HER2, human epidermal growth factor receptor 2; IgG1, immunoglobulin G1; mAb, monoclonal antibody; T-DXd, trastuzumab deruxtecan.

1. Nakada T, et al. *Chem Pharm Bull (Tokyo)*. 2019;67(3):173–185. 2. Ogitani Y, et al. *Clin Cancer Res.* 2016;22(20):5097–5108. 3. Trail PA, et al. *Pharmacol Ther*. 2018;181:126–142.
4. Okamoto H, et al. *Xenobiotica*. 2020;50(10):1242–1250. 5. Nagai Y, et al. *Xenobiotica*. 2019;49(9):1086–1096.

DESTINY-PanTumor02: T-DXd for HER2-expressing solid tumors

A Phase 2, open-label, multicenter study (NCT04482309)

Key eligibility criteria

- Advanced solid tumors not eligible for curative therapy
- Second-line plus patient population
- **HER2 expression (IHC 3+ or 2+)**
  - Local test or central test by HercepTest **if local test not feasible (ASCO/CAP gastric cancer scoring[1])***
  - **Cervical cohort was expanded to include five IHC 1+ patients**
- Prior HER2-targeting therapy allowed
- ECOG/WHO PS 0–1

T-DXd 5.4 mg/kg Q3W

n≈40 per cohort†

Primary endpoint

- Confirmed ORR (investigator)

Secondary endpoints

- DOR, DCR, PFS, OS
- Safety

Exploratory analysis

- Subgroup analyses by HER2 status

Primary analysis DCO:

- June 8, 2023

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

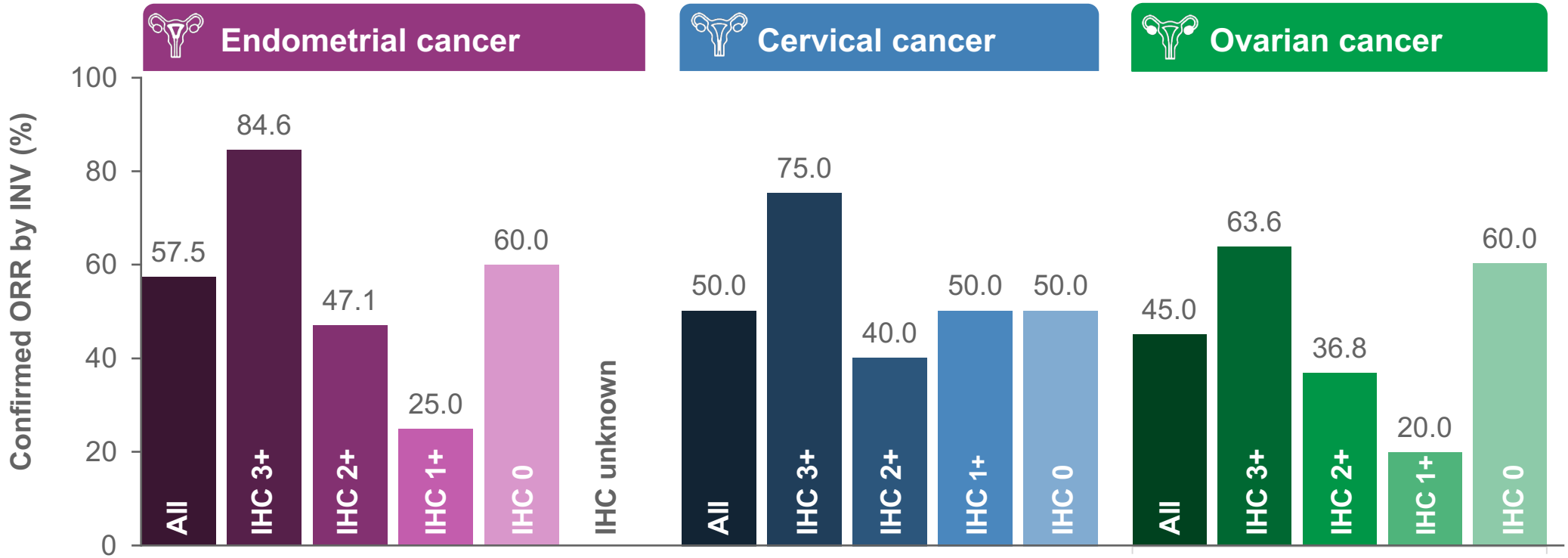
*Patients were eligible for either test. All patients were centrally tested; †planned recruitment; cohorts with no objective responses in the first 15 patients were to be closed; ‡patients with tumors that express HER2, excluding tumors in the tumor-specific cohorts, and breast cancer, non-small cell lung cancer, gastric cancer, and colorectal cancer

ASCO, American Society of Clinical Oncology; CAP, College of American Pathologists; DCO, data cutoff; DCR, disease control rate; DOR, duration of response; ECOG, Eastern Cooperative Oncology Group; HER2, human epidermal growth factor receptor 2; IHC, immunohistochemistry; ORR, objective response rate; OS, overall survival; PFS, progression-free survival; PS, performance status; Q3W, every 3 weeks; T-DXd, trastuzumab deruxtecan; WHO, World Health Organization

1. Hofmann M, et al. *Histopathology*. 2008;52:797–805

Presented by Funda Meric-Bernstam et al at ASCO Meeting 2023 and ESMO 2023; Presented by JungYun Lee et al at IGCS 2023

ORR and DOR (INV)*



	Endometrial cancer						Cervical cancer					Ovarian cancer				
	All	IHC 3+	IHC 2+	IHC 1+	IHC 0	IHC unknown	All	IHC 3+	IHC 2+	IHC 1+	IHC 0	All	IHC 3+	IHC 2+	IHC 1+	IHC 0
Total n in subgroup	40	13	17	4	5	1	40	8	20	8	4	40	11	19	5	5
n of responders	23	11	8	1	3	0	20	6	8	4	2	18	7	7	1	3
Median DOR, months†	**NR**	**NR**	**18.2**	**NR**	**9.9**	**-**	**14.2**	**NR**	**3.8**	**14.2**	**NR**	**11.3**	**22.1**	**11.3**	**8.3**	**4.5**
95% CI‡	9.9, NE	9.6, NE	3.0, NE	-	2.8, NE	-	4.1, NE	9.3, NE	2.8, NE	8.3, NE	6.8, NE	4.1, 22.1	4.2, NE	2.8, NE	-	2.6, NE

HER2 status by central testing

*Similar ORR and DOR results were reported by retrospective independent central review; †median DOR reported for patients with a confirmed and objective response only; ‡CI not shown where n=1 responder

CI, confidence interval; DOR, duration of response; HER2, human epidermal growth factor receptor 2; IHC, immunohistochemistry; INV, investigator; NE, not evaluable; NR, not reached; ORR, objective response rate

Presented by Jung-Yun Lee et al at IGCS 2023

Toxicities Associated with ADCs: Approaches to Monitor and Manage

General principles:

- TRAEs are mostly related to linker-payload and independent of target (e.g. Vedotin and Deruxtecan)
  - Distinct differences between tubulin inhibitor payloads (Peripheral neuropathy) versus topoisomerase inhibitor payloads (Gastrointestinal and Heme)
  - Exception: Some targets have unique expression in normal tissue (TROP2 and oral mucosa)
  - Unique TRAEs include ocular and pneumonitis

TRAEs: Treatment Related Adverse Events

Cross trial comparisons are misleading and inappropriate

AE Profiles of ADCs Using Deruxtecan Linker-Payload

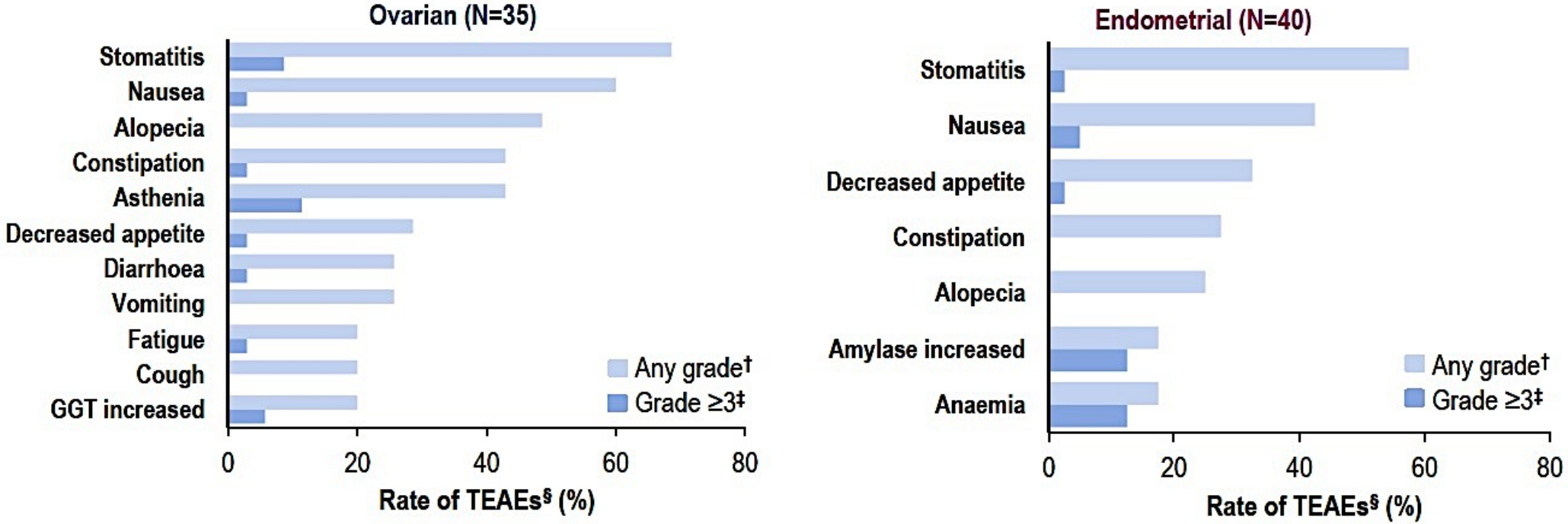
Approved HER2-directed ADC	Common adverse events (any grades)	Common grade ≥3 adverse events
Trastuzumab deruxtecan	GI (nausea, vomiting, diarrhea, constipation) Cytopenia (neutropenia, anemia, leukopenia, thrombocytopenia) Fatigue Alopecia Decreased appetite	Neutropenia Anemia Nausea Leukopenia Lymphopenia Fatigue

ADC = antibody-drug conjugate; AE = adverse event; GI = gastrointestinal.

Adapted from Nguyen TD, et al. *Cancers (Basel).* 2023;15:713.

TROPION-PanTumor03 Trial: Safety Data with Datopotamab Deruxtecan

- The most common TEAEs in both cohorts were stomatitis* and nausea; the majority of cases were grade 1–2
- Adjudicated drug-related ILD* was reported in 1 patient in each cohort; both cases were grade 3
- Ocular surface events* were reported in 40.0% (grade 3: 0%) and 27.5% (grade 3: 5%) of patients in the ovarian and endometrial cohorts, respectively; there were no grade 4 or 5 events



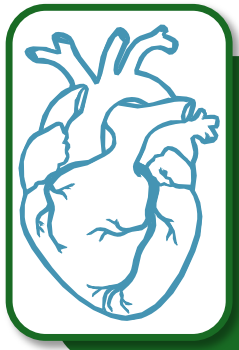
*Adverse events of Special Interest. Ocular surface events and ILD are reported as group terms; †TEAEs that occurred at any grade in ≥20% of patients shown; ‡According to CTCAE v5.0; grade ≥3 AEs that occurred in ≥5 patients included; §Patients with multiple events in the same category are counted only once in that category. Patients with events in more than one category are counted once in each of those categories.
GGT, gamma-glutamyltransferase.

Oaknin A et al. ESMO 2024;Abstract 714MO.

Deruxtecan Linker-Payload Related Adverse Events Management

Anemia/neutropenia/thrombocytopenia

- Dose reductions or delays
- Transfusion
- G-CSF for prevention and/or management of neutropenia

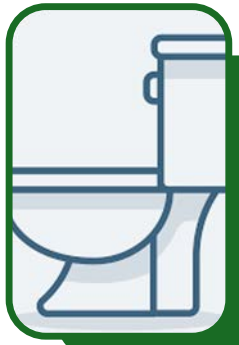


Left ventricular dysfunction

- Only for T-DXd

Nausea/vomiting

- High emetic risk
- Initiate tailored prophylactic antiemetic regimens (3 agents) before T-DXd infusion



Diarrhea

- Infectious workup
- Loperamide/fluid/electrolyte
- Atropine for severe diarrhea with cholinergic syndrome

Fatigue

- Listen/ask/counsel
- Consider holds/reductions
- Rule out other causes
- Encourage exercise/staying active

Alopecia

- Patient counseling/education
- Wig prescription
- Scalp cooling clinical trials ongoing (eg, NCT04986579)

G-CSF = granulocyte colony-stimulating factor; LVEF = left ventricular ejection fraction; RBC = red blood cell; T-DXd = trastuzumab deruxtecan.

Rugo HS, et al. *ESMO Open*. 2022;7:100553. NCCN Guidelines. Antiemesis v2.2024 (https://www.nccn.org/professionals/physician_gls/pdf/antiemesis.pdf). Accessed 11/8/2024.

T-DXd and R-DXd Dose Modifications

- Toxicities treated maximum supportive care (including withholding agent as needed)
- At resolution of toxicity with supportive care, consider continuing the same dose with appropriate supportive care
- Dose modifications as needed

Starting dose	First reduction	Second reduction
T- DXd 5.4 mg/kg	4.4 mg/kg	3.2 mg/kg
R- DXd 6.4 mg/kg	5.6 mg/kg	4.8 mg/kg

- After dose reduction, subsequent cycles should be given at lower dose level unless further dose reduction is required
- Discontinue therapy if unacceptable toxicity occurs after 2 dose reductions

Meric-Bernstam F, et al. *J Clin Oncol*. 2024;42:47-58 including supplementary materials.

Interstitial Lung Disease: Recognition and Management

- **Advise** patients of risks of ILD prior to start of treatment, as well as signs/symptoms of ILD
- **Monitor** for new or worsening cough, dyspnea, or fever

- **Incidental findings on routine scan**
- **Symptomatic findings**

If ILD is suspected…

- Exclude other etiologies, including infectious etiologies
- Initiate evaluation without delay, which may include
  - High-resolution CT
  - Consultation with pulmonologist
  - Blood culture and CBC
  - Additional tests, as clinically indicated

Grade 1 (asymptomatic)

- Hold T-DXd until resolved
- May resume treatment once fully resolved
- Consider starting systemic steroids (eg, 0.5 mg/kg/day of prednisone or equivalent) until improvement, followed by gradual taper over 4 weeks
- If >28 days to resolve, reduce dose by 1 dose level

Grade 2+ (symptomatic)

- Discontinue T-DXd permanently
- Begin steroid treatment (eg, prednisone ≥1 mg/kg daily) with gradual taper

CBC = complete blood (cell) count; CT = computed tomography; ILD = interstitial lung disease; T-DXd = fam-trastuzumab deruxtecan-nxki.

Fam-trastuzumab deruxtecan-nxki (Enhertu®) prescribing information (PI) 2024 (https://daiichisankyo.us/prescribing-information-portlet/getPIContent?productName=Enhertu&inline=true). Accessed 11/8/2024. Swain SM, et al. *Cancer Treat Rev*. 2022;106:102378.

Strategies to Manage ILD/Pneumonitis

Monitor

Suspected ILD

Urge patients to immediately report cough, dyspnea, fever, and/or new or worsening pulmonary symptoms

- Monitor patients for signs/symptoms of ILD
- Promptly investigate evidence of ILD
- Evaluate patients with suspected ILD by radiographic imaging and assess as follows

Confirm

Assessments should include

- High-resolution CT
- Pulmonologist consult; if indicated, ID consult
- Blood culture and CBC; other blood tests as needed
- Consider bronchoscopy and BAL if indicated and feasible
- PFTs and pulse oximetry
- Arterial blood gases, if indicated
- As soon as ILD suspected, collect 1 blood sample for PK assessment, if feasible
- Rule out other causes of ILD (eg, progression, infection, other drugs, radiotherapy)
- All ILD events should be followed until resolution and after drug discontinuation

Manage

- **Grade 1 T-DXd:** Hold until resolved to grade 0; consider corticosteroids (0.5 mg/kg/day prednisolone), then
  - *If resolved ≤28 days from onset:* Maintain dose
  - *If resolved >28 days after onset:* Reduce dose by 1 level
  - *-Taper steroid over at least 4 weeks*
- **Grades 2–4:** Permanently discontinue treatment and promptly initiate systemic corticosteroid treatment (eg, ≥1 mg/kg/day prednisolone or equivalent) for ≥14 days followed by taper for ≥4 weeks

BAL = bronchoalveolar lavage; ID = infectious disease; PFTs = pulmonary function tests; PK = pharmcokinetics.

Ado-trastuzumab emtansine (Kadcyla®) PI 2022 (https://www.kadcyla.com/). Fam-trastuzumab deruxtecan-nxki (Enhertu®) PI 2024 (https://daiichisankyo.us/prescribing-information-portlet/getPIContent?productName=Enhertu& inline=true). URLs accessed 11/8/2024.
Tarantino P, et al. *JAMA Oncol*. 2021;7:1873-1881.

Strategies to Manage Grade 2 to 4 ILD/Pneumonitis

Grade 2

- Promptly start systemic glucocorticoids (eg, ≥1 mg/kg/d prednisone or equivalent) for ≥2 weeks or to complete resolution of clinical and chest CT findings, then gradual taper over ≥4 weeks
- Monitor symptoms closely
- Re-image as indicated
- If clinical or diagnostic observations worsen or do not improve in 5 days
  - Consider increase in steroid dose (eg, 2 mg/kg/day prednisone or equivalent) or switch to intravenous (IV)
  - Reconsider additional workup for alternative etiologies
  - Escalate care as needed

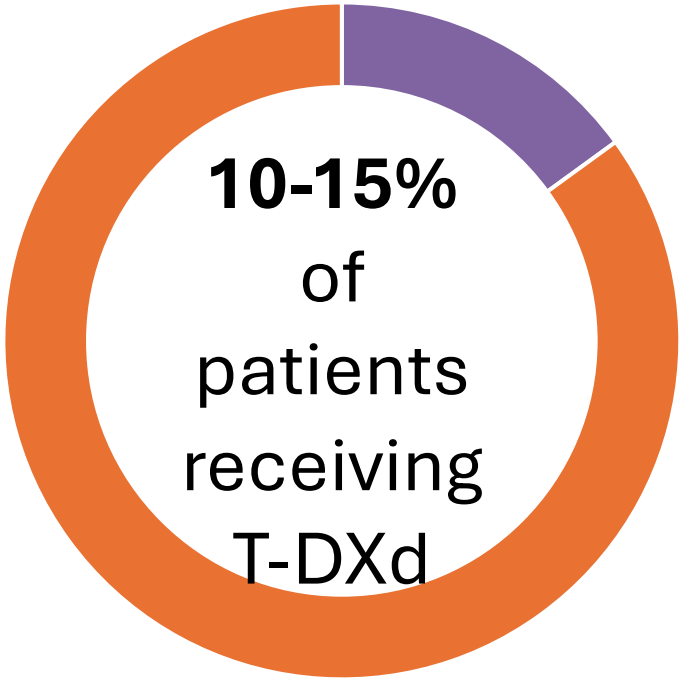
Grade 3 or 4

- Hospitalization required
- Promptly initiate empirical high-dose methylprednisolone IV (eg, 500–1000 mg/day for 3 days), followed by ≥1 mg/kg/ day prednisone (or equivalent) for ≥2 weeks until resolution of clinical and chest CT findings, then gradual taper over ≥4 weeks
- Re-image as clinically indicated
- If still no improvement with 3 to 5 days
  - Reconsider additional workup for alternative etiologies
  - Consider other immunosuppressants and/or treat per local practice

Li BT, et al. *N Engl J Med*. 2022;386:241-251 (Protocol).

ILD/Pneumonitis Associated With T-DXd

Adjudicated drug-related ILD/pneumonitis



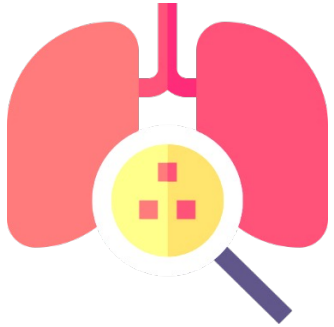
- 87.0% had their first event within 12 months
  - Median: 5.4 months
  - Range: <0.1–46.8 months
- Median time to onset

- Most patients with ILD/pneumonitis experienced low-grade events (grade 1 or 2, 77.4%)
- Overall rate of fatal events: 2.2%

Powell CA, et al. *ESMO Open*. 2022;7:100554.

5 “S” Rules

Screen

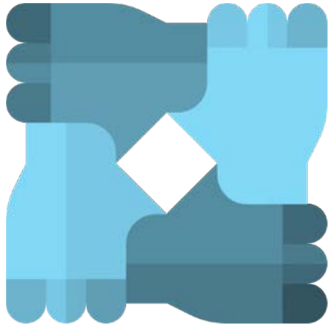


- Careful patient selection before initiating T-DXd to optimize the monitoring strategies based on the baseline risk; screening continues during treatment, with regular assessments to exclude signs/symptoms of ILD
- Increased knowledge is needed on the impact of prior ILD with other treatments (eg, everolimus, CDK4/6 inhibitors)

Scan

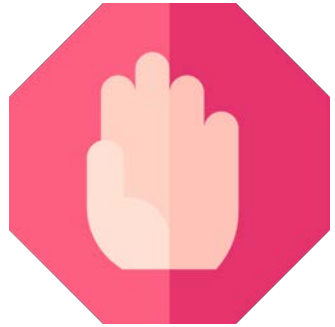
- The fundamental diagnostic tools for ILD remain radiological scans, with preference for high-resolution CT scans of the chest; a baseline scan is recommended, with repeat scans to be performed every 6 to 12 weeks

Synergy



- Minimizing the risk of ILD involves teamwork, which includes educating patients and all the care team, as well as multidisciplinary management once ILD is suspected
  - Improved synergy with pulmonologists during T-DXd treatment is being explored in several studies
  - Evaluate the predictive/ prognostic role of monitoring pulmonary function tests

Suspend treatment



- T-DXd should always be interrupted if ILD is suspected; it can only be restarted in the case of asymptomatic ILD that fully resolves

Steroids

- The mainstay for treating T-DXd–induced ILD remains corticosteroids, with the dose to be adapted to the toxicity grade

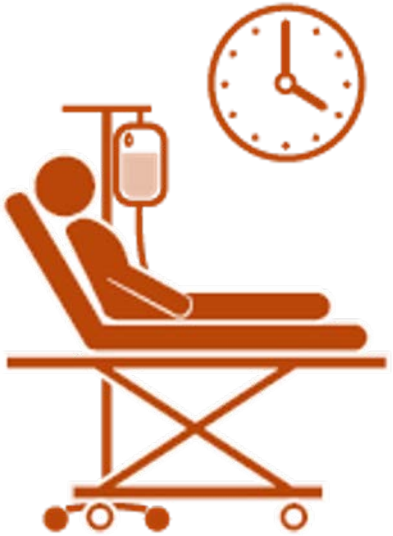
Tarantino P, Tolaney SM. *J Oncol Practice*. 2023;19:526-527.

T-DXd: Infusion-Related Reactions

Infusion-related reactions are a clinically relevant risk that can be effectively managed with proper preparation!

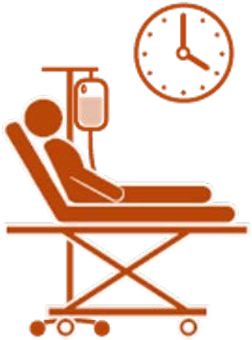
- Prompt recognition and treatment are important for reducing the risk of severe symptoms
  - Signs of T-DXd-related IRRs include fever and chills, N/V, pain, headache, dizziness, dyspnea, and/or hypotension
- Keep resources to treat IRR readily on hand
- Suspected anaphylaxis: Follow local management guidelines (eg, epinephrine (1 mg/mL IM every 5–15 minutes); normal saline (1–2 L at 5–10 ml/kg for first 5 minutes IV); H1/H2 antagonists

Infusion 1
90 minutes



If well tolerated

Subsequent infusions
30 minutes



IRR

Grade 1: ↓ Reduce infusion rate to 50%
Grade 2: ✋ Temporarily stop infusion
Grade 3 or 4: ⬢ Permanently stop

1% to 3% of patients receiving T-DXd experience an IRR with T-DXd 5.4 mg/kg.

Rugo HS, et al. *ESMO Open*. 2022;7:100553. Fam-trastuzumab deruxtecan-nxki (Enhertu®) PI 2024 (https://daiichisankyo.us/prescribing-information-portlet/getPIContent?productName=Enhertu&inline=true). Accessed 11/8/2024.

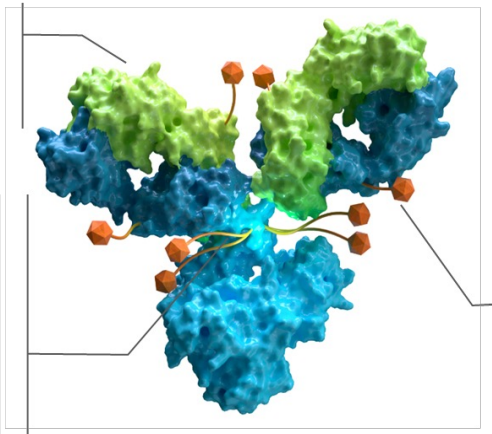
IRR = infusion-related reaction; N/V = nausea and/or vomiting.

Targeting TROP2

Sacituzumab tirumotecan (sac-TMT)

Antibody
- hRS7, a recombinant humanized anti-TROP2 antibody with high affinity

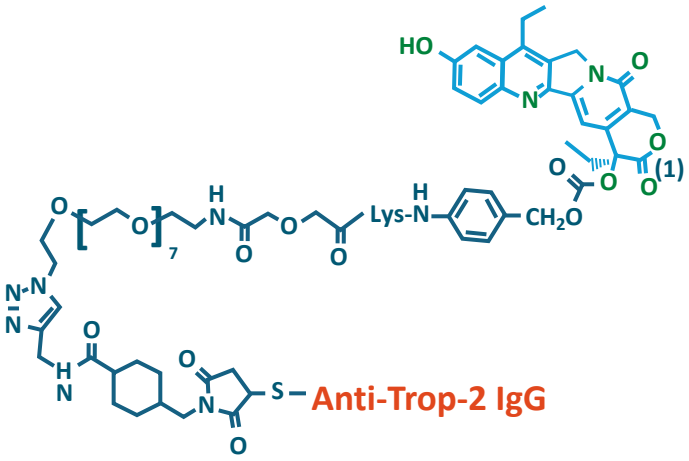
Linker
- **Kthiol conjugation:** irreversible coupling to improve stability of ADC
- **Payload release:** intracellular cleavage and extracellular hydrolysis in TME
- **Balanced stability:** balance between efficacy and safety to expand therapeutic window



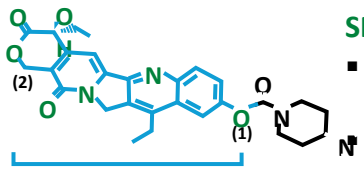
Payload
- **Novel topo I inhibitor** (a belotecan derivative), highly active
- Average **DAR: 7.4** (range: 7–8)
- **Bystander effect**
- Methylsulfonyl derivatization enhances linker stability and toxin permeability

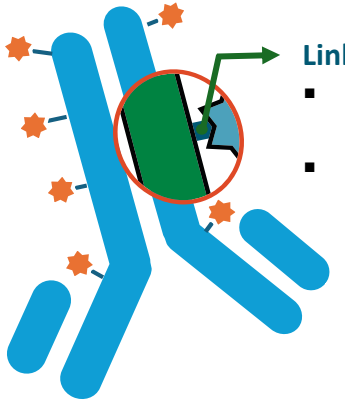
Xu B et al. Presented at: American Society of Clinical Oncology Annual Meeting; 31 May – 4 June 2024; Chicago, IL. Abstract 104

Sacituzumab Govitecan (sac-G)



Irinotecan (Topoisomerase Inhibitor)





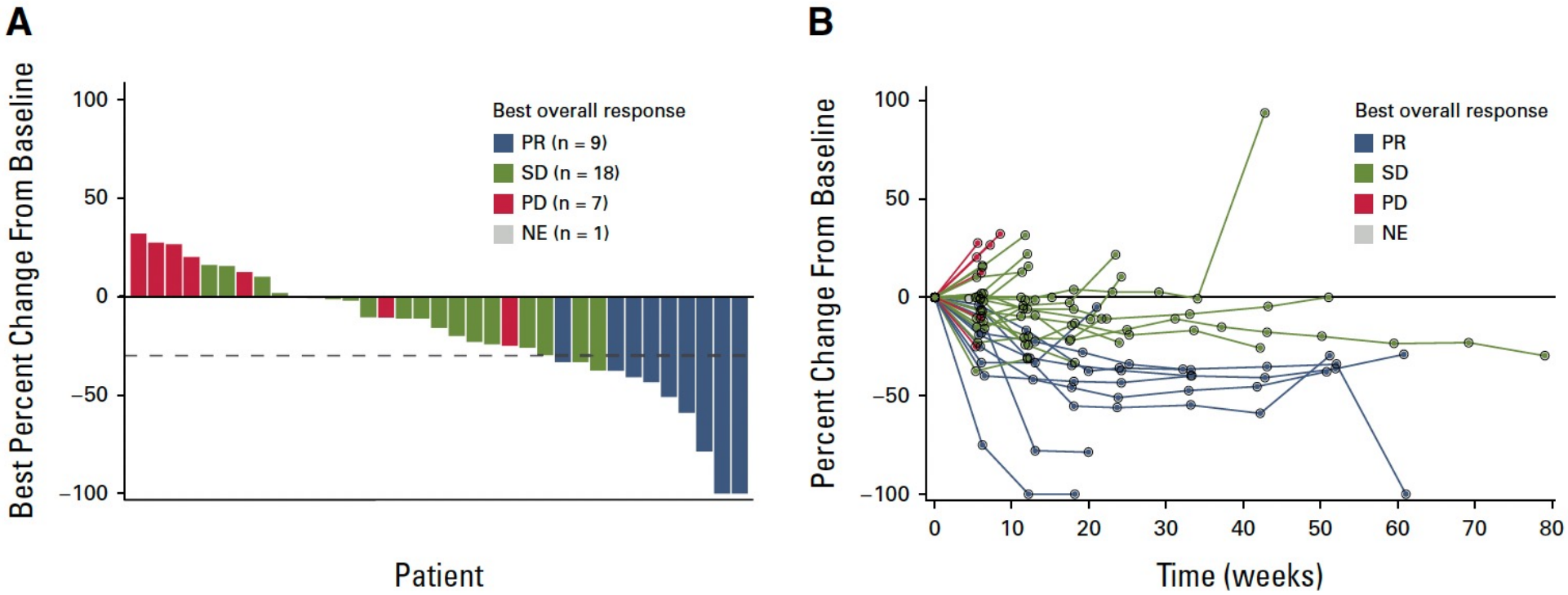
Linker for SN-38
- High drug-to-antibody ratio (7.6:1)
- pH-sensitive linker for rapid release of payload at or inside tumor

SN-38 Payload
- Targets 136-fold more than parent compound irinotecan
- Unique chemistry improves solubility, selectively delivers SN-38 to tumor

Humanized RS7 Antibody
- Targets Trop-2, an antigen expressed in many epithelial cancers, including mTNBC (88%)
- Antibody type: h-IgG1

Khoury. ASCO 2019. Abstr e14651. Bardia. JCO. 2017;35:2141.

Efficacy and Safety of Sacituzumab Govitecan in Patients With Advanced Solid Tumors (TROPiCS-03): Analysis in Patients With Advanced Endometrial Cancer



10 mg/kg of SG via intravenous infusion once on day 1 and day 8 of a 21-day cycle

Not NCCN recommended

Santin AD et al J Clin Oncol . 2024 Oct 10;42(29):3421-3429.

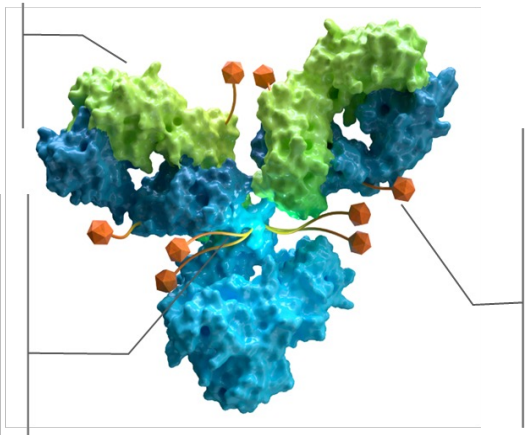
Sacituzumab tirumotecan (sac-TMT)

- Sac-TMT employs the same anti–TROP2 antibody as SG, hRS7[1,2]
- **Linker was designed to have higher stability** than SG[1]
- Novel Topo 1 inhibitor payload (belotecan) with similar activity to SN-38 (the payload for SG) [1]

Components of sac-TMT[2]

Antibody
- hRS7, a recombinant humanized anti-TROP2 antibody with high affinity

Linker
- **Kthiol conjugation:** irreversible coupling to improve stability of ADC
- **Payload release:** intracellular cleavage and extracellular hydrolysis in TME
- **Balanced stability:** balance between efficacy and safety to expand therapeutic window



Payload
- **Novel topo I inhibitor** (a belotecan derivative), highly active
- Average **DAR: 7.4** (range: 7–8)
- **Bystander effect**
- Methylsulfonyl derivatization enhances linker stability and toxin permeability

Figure used with permission from: Xu et al. 2024.

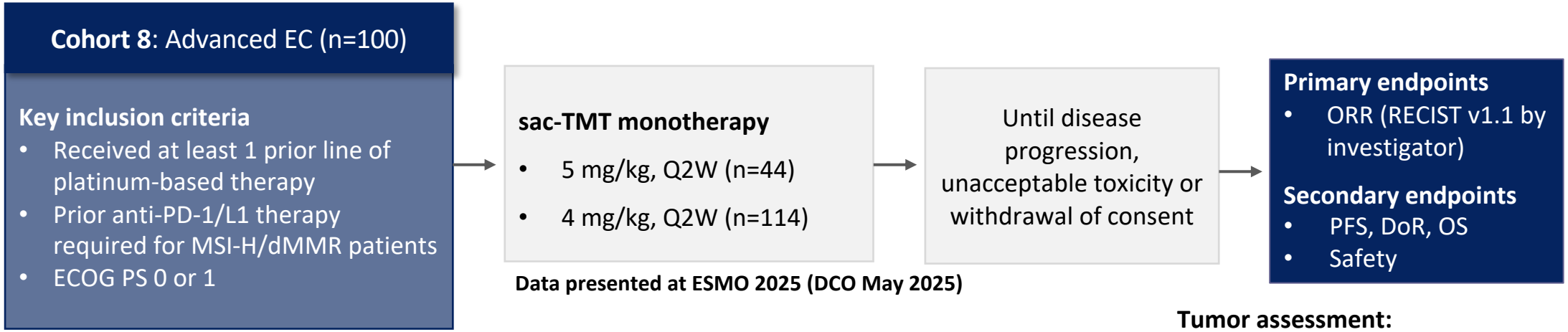
- Sac-TMT is an investigational ADC being evaluated in late-stage clinical trials for various cancers[3–8]
- Sac-TMT showed encouraging antitumor activity and manageable toxicity in phase 1/2 studies of patients with solid tumors,[9,10] and demonstrated statistically significant and clinically meaningful improvements in both PFS and OS vs chemotherapy in the phase 3 OptiTROP-Breast01 study in recurrent or metastatic TNBC[2] and in the phase 3 OptiTROP-Lung04 in EGFRm lung cancer[11]

ADC, antibody–drug conjugate; DAR, drug-to-antibody ratio; OS, overall survival; PFS, progression-free survival; sac-TMT, sacituzumab tirumotecan; SG, sacituzumab govitecan; Topo I, topoisomerase I; TME, tumor microenvironment; TNBC, triple-negative breast cancer;
TROP2, trophoblast cell-surface antigen 2.

1. Cheng Y et al. *Front Oncol.* 2022;12:951589. 2. Xu B et al. Presented at: American Society of Clinical Oncology Annual Meeting; 31 May – 4 June 2024; Chicago, IL. Abstract 104. 3. ClinicalTrials.gov. https://clinicaltrials.gov/study/NCT06074588. Accessed: 5 July 2024. 4. Clinicaltrials.gov. https://clinicaltrials.gov/study/NCT06132958. Accessed: 5 July 2024. 5. Clinicaltrials.gov. https://clinicaltrials.gov/study/NCT06356311. Accessed: 5 July 2024. 6. Clinicaltrials.gov. https://clinicaltrials.gov/study/NCT06312176. Accessed: 5 July 2024. 7. Clinicaltrials.gov. https://clinicaltrials.gov/study/NCT06393374. Accessed: 5 July 2024. 8. Clinicaltrials.gov. https://clinicaltrials.gov/study/NCT06459180. Accessed: 5 July 2024. 9. Yin Y et al. Presented at: San Antonio Breast Cancer Symposium; 5–9 December 2023; San Antonio, TX.
Abstract PSO8-08. 10. Fang W et al. Presented at: American Society of Clinical Oncology Annual Meeting; 2–6 June 2023; Chicago, IL. Abstract 8520. [11] Fang et al NEJM 2025; DOI: 10.1056/NEJMoa2512071

sac-TMT – Basket Study Including EC Cohort

- Preliminary efficacy and safety results for **endometrial cancer** is available from the sac-TMT **Phase 2 basket study** (MK2870-001, NCT04152499).
- In the **EC cohort**, **patients with advanced EC were enrolled:**
  - Initial cohort was treated at **5 mg/kg monotherapy**
  - Additional pts were treated at **4 mg/kg monotherapy**



Data presented at ESMO 2025 (DCO May 2025)

Tumor assessment:

- Once every 8 weeks for the first 12 months, and every 12 weeks thereafter.

ADC, antibody-drug conjugate; dMMR, deficient mismatch repair; DoR, duration of response; EC, endometrial cancer; ECOG PS, Eastern Cooperative Oncology Group performance status; MSI-H, microsatellite instability high; ORR, objective response rate; OS, overall survival; PD-1, programmed cell death protein 1; PD-L1, programmed cell death ligand 1; PFS, progression-free survival; pts, patients; Q2W, every 2 weeks; RECIST, Response Evaluation Criteria in Solid Tumors.

Updated data presented at IGCS (*Wang et al. IGCS 2025*)

TF-033 Population

	Sac-TMT 4 mg/kg n = 114	Sac-TMT 5 mg/kg n = 44	Total N = 158
Confirmed ORR			
ORR,[a] %, 95% CI	30.7 (22.4–40.0)	34.1 (20.5–49.9)	31.6 (24.5–39.5)
Subgroups, responders/ n, % (95% CI)			
Histology			
Endometrioid	23/80, 28.8 (19.2–40.0)	8/26, 30.8 (14.3–51.8)	31/106, 29.2 (20.8–38.9)
Nonendometrioid	12/27, 44.4 (25.5–64.7)	6/15, 40.0 (16.3–67.7)	18/42, 42.9 (27.7–59.0)
Carcinosarcoma	0/7, 0 (0.0–41.0)	1/3, 33.3 (0.8–90.6)	1/10, 10.0 (0.3–44.5)
pMMR carcinoma[b]	22/54, 40.7 (27.6–55.0)	7/17, 41.2 (18.4–67.1)	29/71, 40.8 (29.3–53.2)
Confirmed + unconfirmed ORR, % (95% CI)	35.1 (26.4–44.6)	36.4 (22.4–52.2)	35.4 (28.0–43.4)
pMMR carcinoma[b]	46.3 (32.6–60.4)	47.1 (23.0–72.2)	46.5 (28.7–34.5)
DCR,[c] % (95% CI)	74.6 (65.6–82.3)	75.0 (59.7–86.8)	74.7 (67.2–81.3)
Best overall response,[c] n (%)			
PR	35 (30.7)	15 (34.1)	50 (31.6)
SD	50 (43.9)	18 (40.9)	68 (43.0)
PD	22 (19.3)	10 (22.7)	32 (20.3)
NE	7 (6.1)	1 (2.3)	8 (5.1)
Median DOR,[c] mo (range)	9.3 (2.1+ to 12.0+)	8.7 (3.8 to 17.7)	9.3 (2.1+ to 17.7)

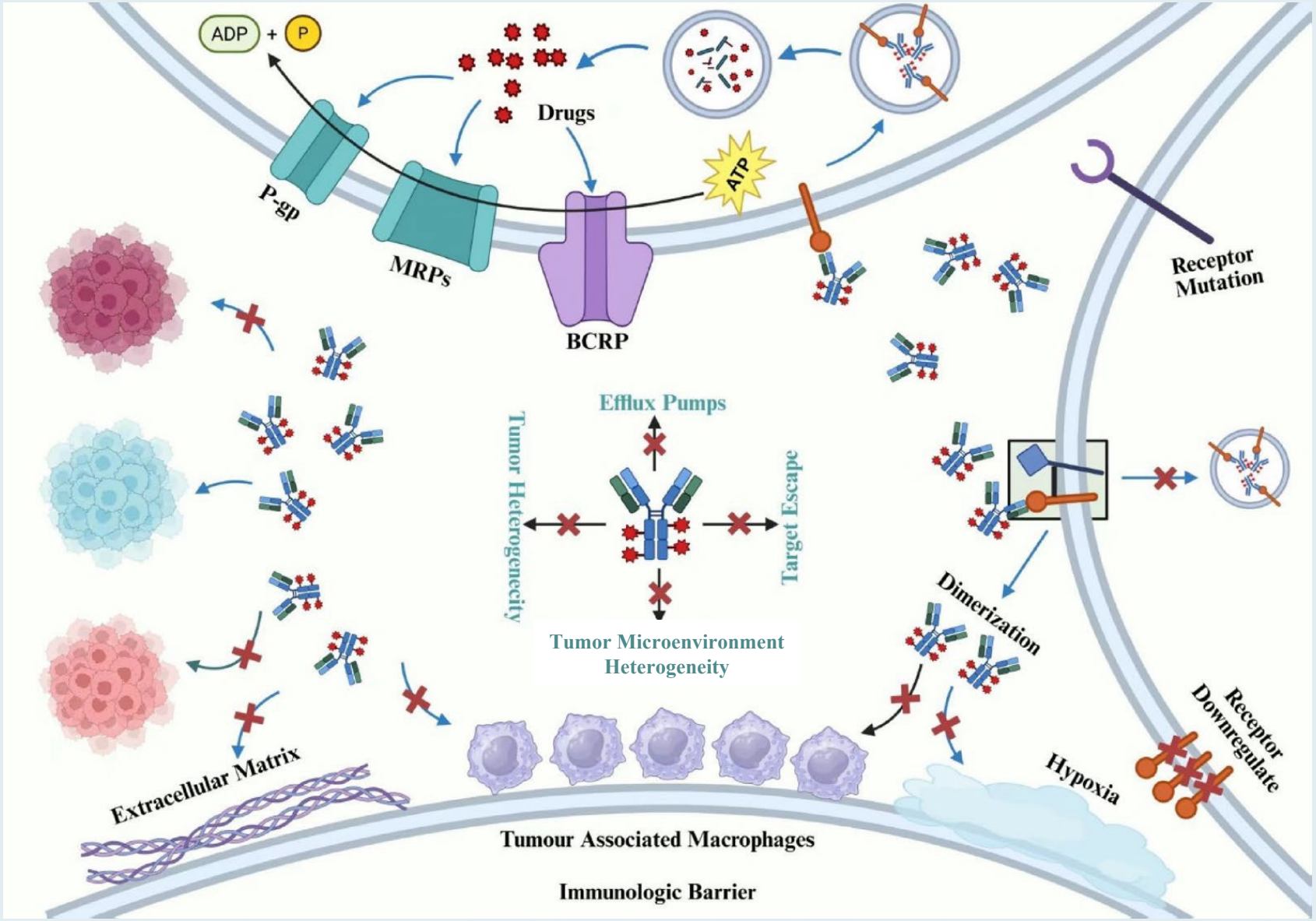
DCR, disease control rate; NE, not evaluable; ORR, objective response rate; PD, progressive disease; PR, partial response; SD, stable disease.
"+" indicates a censored observation.
[a]All responses were PR.
[b]pMMR carcinoma includes participants with endometrioid, nonendometrioid, and other tumors and with ≥1 imaging assessment completed.
[c]Based on confirmed responses.

Treatment-Related AE Summary

	Sac-TMT 4 mg/kg n = 114		Sac-TMT 5 mg/kg n = 44		Total N = 158	
Any treatment-related AE[a]	113 (99.1)		44 (100)		157 (99.4)	
Grade ≥3	59 (51.8)		34 (77.3)		93 (58.9)	
Led to treatment discontinuation	2 (1.8)		1 (2.3)		3 (1.9)	
Led to any dose reduction	28 (24.6)		19 (43.2)		47 (29.7)	
Serious	13 (11.4)		9 (20.5)		22 (13.9)	
Led to death[b]	1 (0.9)		0		1 (0.6)	
Treatment-related[a] AEs occurring in ≥20% of participants in either group	All grade	Grade 3/4	All grade	Grade 3/4	All grade	Grade 3/4
Anemia	90 (78.9)	22 (19.3)	40 (90.9)	13 (29.5)	130 (82.3)	35 (22.2)
White blood cell count decreased	58 (50.9)	17 (14.9)	36 (81.8)	19 (43.2)	94 (59.5)	36 (22.8)
Neutrophil count decreased	60 (52.6)	32 (28.1)	30 (68.2)	19 (43.2)	90 (57.0)	51 (32.3)
Stomatitis	42 (36.8)	3 (2.6)	19 (43.2)	8 (18.2)	61 (38.6)	11 (7.0)
Platelet count decreased	36 (31.6)	2 (1.8)	12 (27.3)	3 (6.8)	48 (30.4)	5 (3.2)
Nausea	34 (29.8)	1 (0.9)	13 (29.5)	0	47 (29.7)	1 (0.6)
Alopecia	29 (25.4)	0	15 (34.1)	0	44 (27.8)	0
Alanine aminotransferase increased	27 (23.7)	1 (0.9)	10 (22.7)	0	37 (23.4)	1 (0.6)
Aspartate aminotransferase increased	22 (19.3)	2 (1.8)	12 (27.3)	0	34 (21.5)	2 (1.3)
Vomiting	17 (14.9)	0	16 (36.4)	0	33 (20.9)	0
Hypokalemia	10 (8.8)	2 (1.8)	9 (20.5)	0	19 (12.0)	2 (1.3)
Hyperglycemia	6 (5.3)	0	9 (20.5)	0	15 (9.5)	0

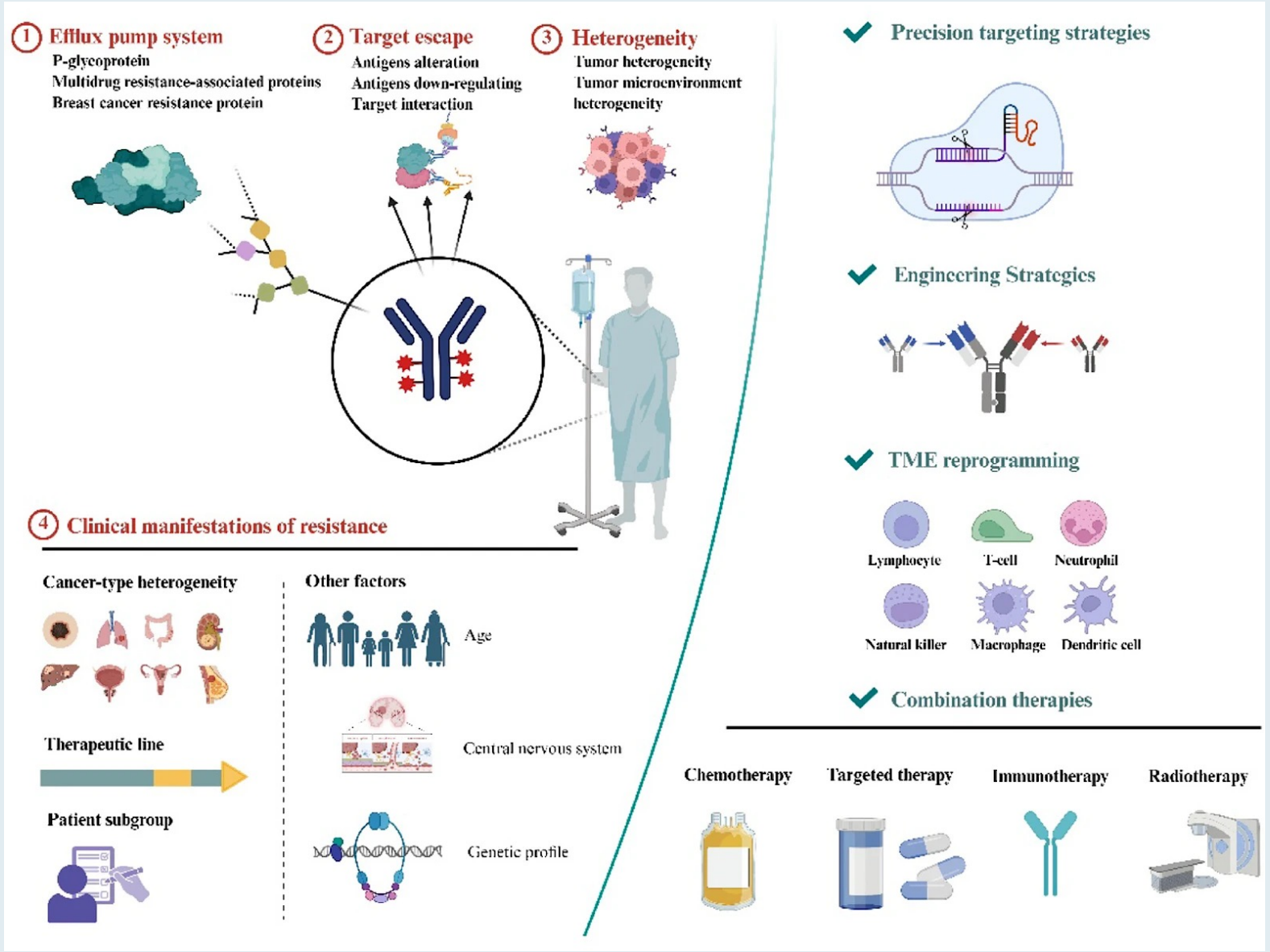
Data are n (%).
[a]Determined by the investigator to be related to the drug.
[b]1 participant in the sac-TMT 4 mg/kg group died due to cardiac failure. The participant had a history of hypertension and presented with hyperlipidemia, palpitations, and dyspnea before the first dose. Echocardiography during screening showed left atrial enlargement. The event could not be ruled out as related to the participant's underlying pre-existing conditions.

Multifaceted Mechanisms of ADC Resistance



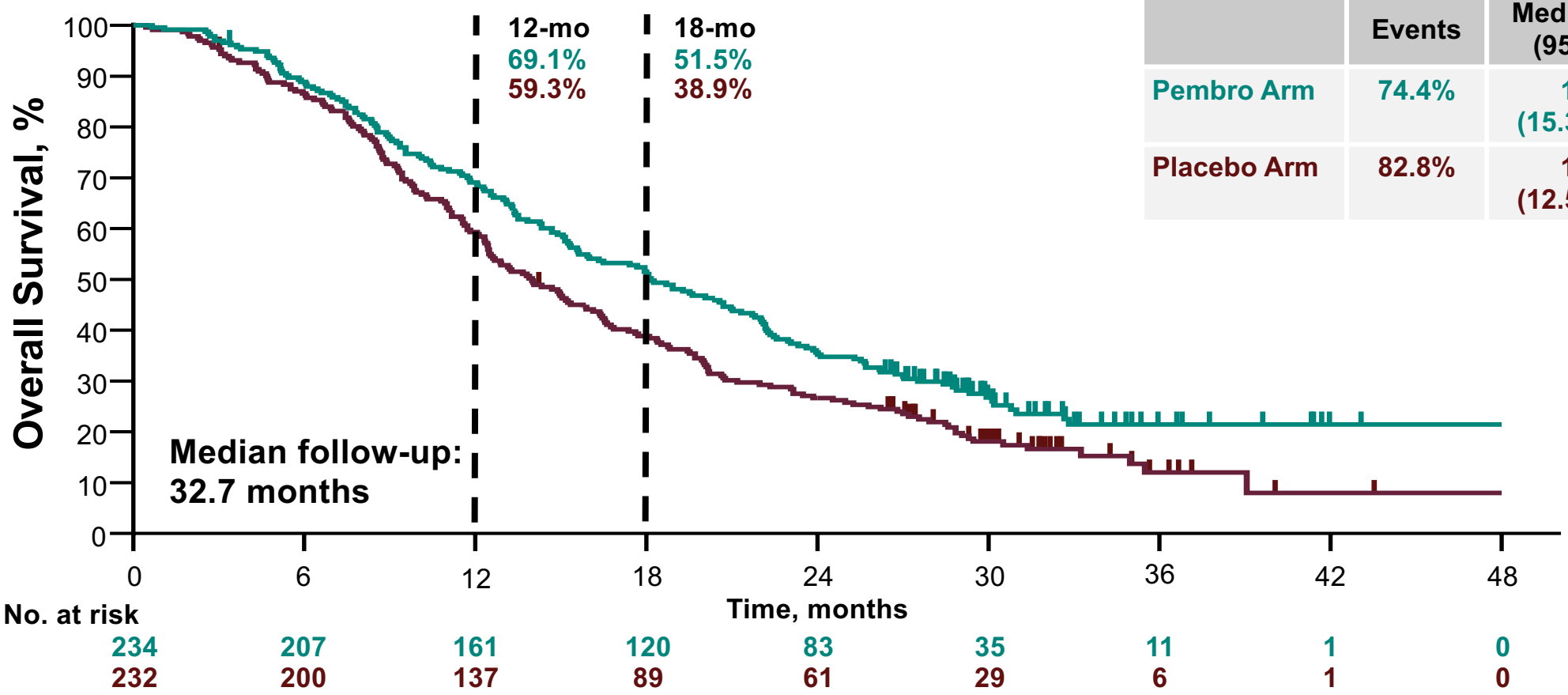
Zhou K et al. *J Hematol Oncol* 2025 November 3;18:96.

Techniques for Overcoming Resistance to ADCs



Zhou K et al. *J Hematol Oncol* 2025 November 3;18:96.

B-96: OS in CPS ≥1 Population at Final Analysis



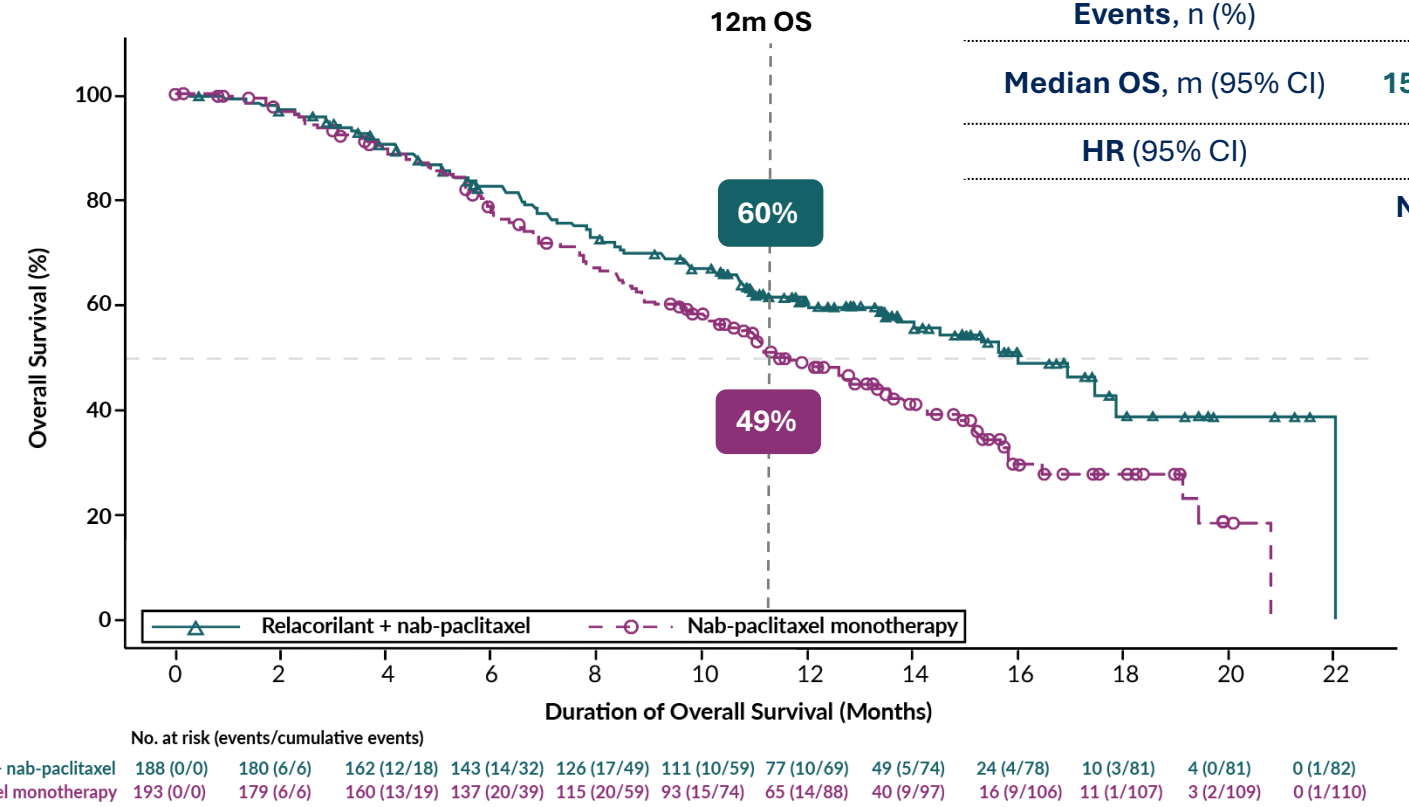
	Events	Median, mo (95% CI)	HR (95% CI)
Pembro Arm	74.4%	18.2 (15.3–21.3)	0.76 (0.62–0.93)
Placebo Arm	82.8%	14.0 (12.5–16.1)	

[a]Hazard ratio (CI) analyzed based on a Cox regression model with treatment as a covariate stratified by the randomization stratification factors. Data cutoff date: September 5, 2025.

ROSELLA | Relacorilant Improved Overall Survival at this Interim Analysis (all comer)

OVERALL SURVIVAL PRIMARY ENDPOINT MET IN CORCEPT'S PIVOTAL PHASE 3 ROSELLA TRIAL OF RELACORILANT IN PATIENTS WITH PLATINUM-RESISTANT OVARIAN CANCER

January 22, 2026 at 8:00 AM EST



No. at risk (events/cumulative events)

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

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

Nominal P=0.0121 (Log-rank Test)

Median follow-up time: 13.9 months; statistical significance threshold at the interim analysis: P≤0.0001; statistical significance threshold at the final analysis: P≤0.0499. The Kaplan–Meier method was used to estimate the curves, median estimates and the 95% confidence intervals (CI) for overall survival in each treatment arm. The HR and the associated 95% CI were estimated using a Cox regression model with treatment group as the main effect and stratification factors at randomization as covariates. CI, confidence interval; HR, hazard ratio; m, months; NR, not reached; OS, overall survival.

Data cutoff: Feb 24, 2025

Alexander Olawaiye et al. Lancet. 2025 Jun 21;405(10496)

Faculty Case Presentations

RTP
RESEARCH
TO PRACTICE

Dr Moore: Patient presentation

75-year-old female h/o Stage IV high grade endometrioid ovarian cancer in 2020

- Treated with NACT paclitaxel and carboplatin x 3, iCRS to NGR and then 3 additional cycles of paclitaxel and carboplatin
- BRCAwt
- Received niraparib maintenance x 1 year with PD.
- Carboplatin and PLD and bevacizumab x 3 cycles with PD.
- Now platinum resistant

Work up

Imaging with peritoneal disease, no bowel obstruction, no ascites, but enlarged lymph nodes in the mediastinum

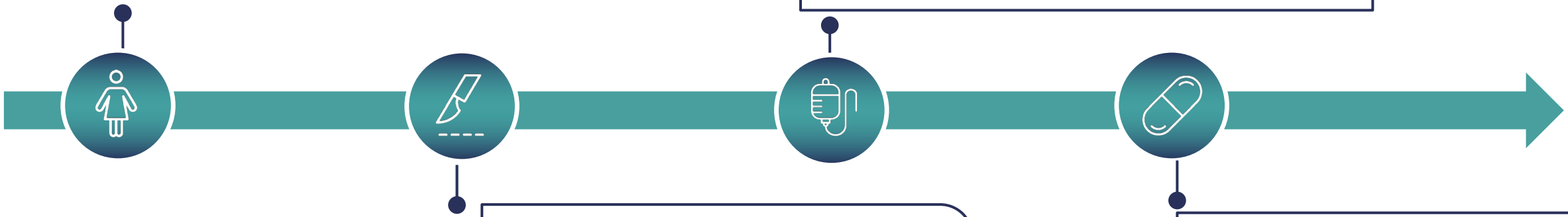
PS = 1

What additional testing do you order? What are you looking for?

Dr Moore: Patient presentation

75-year-old female h/o Stage IV high grade endometrioid ovarian cancer in 2020

- Treated with NACT paclitaxel and carboplatin x 3, iCRS to NGR and then 3 additional cycles of paclitaxel and carboplatin
- BRCAwt
- Received niraparib maintenance x 1 year with PD.
- Carboplatin and PLD and bevacizumab x 3 cycles with PD.
- Now platinum resistant



Work up

Imaging with peritoneal disease, no bowel obstruction, no ascites, but enlarged lymph nodes in the mediastinum

PS = 1

What additional testing do you order? What are you looking for?

Biomarkers: BRCAwt/HRD neg/FRα low

- SOC: no biomarkers currently link to FDA approved therapies
- NCCN: FRα expression links to MIRV + BEV
- Trials: No clear biomarker direction

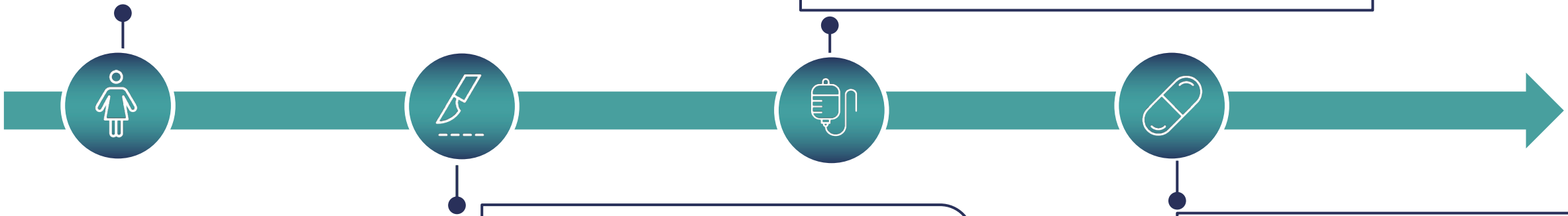
What happened?

- Patient was offered weekly paclitaxel vs a novel ADC
- Selected clinical trial with Raludotatug deruxtecan – has a deep PR after 4 cycles
- Presents for cycle 6 with some ground glass opacities on her chest CT, otherwise feels great

Dr Moore: Patient presentation

75-year-old female h/o Stage IV high grade endometrioid ovarian cancer in 2020

- Treated with NACT paclitaxel and carboplatin x 3, iCRS to NGR and then 3 additional cycles of paclitaxel and carboplatin
- BRCAwt
- Received niraparib maintenance x 1 year with PD.
- Carboplatin and PLD and bevacizumab x 3 cycles with PD.
- Now platinum resistant



Biomarkers: BRCAwt/HRD neg/FRα low

- SOC: no biomarkers currently link to FDA approved therapies
- NCCN: FRα expression links to MIRV + BEV
- Trials: No clear biomarker direction

Work up

Imaging with peritoneal disease, no bowel obstruction, no ascites, but enlarged lymph nodes in the mediastinum

PS = 1

What additional testing do you order? What are you looking for?

What happened?

- Presents for cycle 6 with some ground glass opacities on her chest CT, otherwise feels great
- Seen by pulmonology, steroids started and GGO resolve within 4 weeks
- RDxD restarted at a dose modification and is ongoing at cycle 12 with continued PR

QUESTIONS FOR THE FACULTY

How does the incidence and severity of ILD with R-DXd compare to that with other ADCs employed in gynecologic cancers, particularly trastuzumab deruxtecan?

If R-DXd were to reach the clinic, what screening techniques would you employ for early detection of ILD in patients receiving the drug? How would you manage ILD based on grade, and would this differ at all from the paradigm employed with T-DXd? At what grade of ILD would you permanently discontinue R-DXd?

QUESTIONS FOR THE FACULTY

Is there any reason to believe that ILD would be more likely and/or more severe with one of the novel ADCs — R-DXd or a TROP2-targeted agent — in a patient who had developed this AE on prior T-DXd treatment? What about in a patient who had developed immune-related ILD/pneumonitis on prior immune checkpoint inhibition?

QUESTIONS FOR THE FACULTY

What has been your experience with other toxicity issues with R-DXd? How do you anticipate approaching antiemetic and/or antidiarrheal prophylaxis with this agent? What about monitoring of CBCs and use of growth factors? Have you encountered any AEs with R-DXd that haven't been reported with any of the other ADCs that are currently employed in gynecologic cancers?

QUESTIONS FOR THE FACULTY

How is CDH6 expression measured (ie, what platform is employed and how are various levels of expression categorized)? If R-DXd were available, would you test for CDH6 expression and use the results as the basis for identifying appropriate candidates? How would you respond to the same questions vis-à-vis TROP2 expression and TROP2-targeted ADCs? Is there any practical reason that clinicians in community-based practice should be testing for these proteins now?

Prof Eskander: Case Presentation

- 70 yo otherwise healthy female, who presented with progressive symptoms of abdominal bloating, pain and decreased oral intake as well as postmenopausal vaginal bleeding
- **EMB 12-2023:**
  - High grade mixed carcinoma with predominantly serous (85%) features
  - Molecular testing: TP53mut; pMMR; HER2 IHC 2+; ER/PR negative
- **CT C/A/P 1-5-23:**
  - **Peritoneal carcinomatosis** with small volume **ascites**. Mass-like enlargement of the bilateral adnexa measuring 3.9 cm on the left and 4.7 cm on the right. Endometrial thickening measuring 2.2 cm. **Peritoneal and omental nodularity**. For example, a left anterior omental nodule measures 1.3 cm
  - Subcentimeter but mildly prominent enhancing **anterior pericardiophrenic, pericaval and AP window lymph nodes are suspicious for intrathoracic lymph nodal metastases**
- **Image guided biopsy of intrathoracic lymph nodes confirmed metastatic high grade endometrial carcinoma**

UC San Diego
SCHOOL OF MEDICINE

Prof Eskander: Case Presentation

- In the context of **stage 4B disease**, patient was counseled and started on neoadjuvant systemic therapy
- **Treatment (carboplatin, paclitaxel, pembrolizumab)**
  - **Treated with 3 cycles of neoadjuvant therapy**
  - **CT C/A/P after cycle 3: Decreased conspicuity of peritoneal and omental nodularity**. No enlarging soft tissue nodules. Small volume pelvic ascites has decreased in amount from prior. Persistent endometrial thickening, decreased in thickness from prior. Bilateral adnexal masses have mildly decreased in size noting also changed in morphology and differences in measuring technique. **Resolution of her intrathoracic nodal disease**
- **Interval surgery:**
  - **RATLH, BSO, infra-colic omentectomy**

Prof Eskander: Case Presentation

- **Surgical pathology and molecular testing:**
  - TMB low 5 Muts/Mb
  - MSS
  - PD-L1 negative by TPS score
  - PIK3R1 mutation
  - TP53 mutation
  - PPP2R1A mutation

- **Pathology**
  - Final pathology: **uterine carcinosarcoma (epithelial component predominantly serous with small clear cell features)**. Sigmoid colon epiploic nodule, omentum, and peritoneal noudle all involved by disease

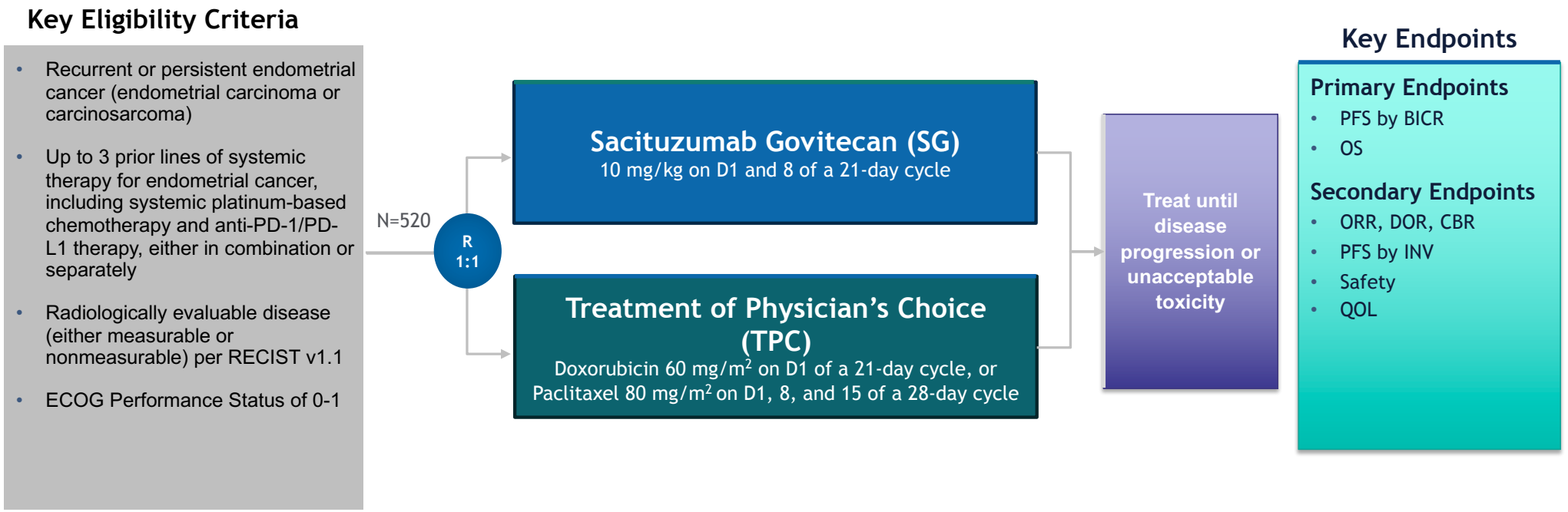
- **Following surgery:**
  - Completed 3 additional cycles of therapy and transitioned onto maintenance pembrolizumab

Prof Eskander: Case Presentation

- **6 months after initiation of maintenance pembrolizumab,** interval imaging was notable for:
  - **CT C/A/P:** Findings concerning for disease progression with **new peritoneal carcinomatosis and serosal deposits** along the distal transverse colon, splenic flexure and omentum abutting the ascending colon as described above. **Additional small volume pelvic ascites and peritoneal enhancement** in the pelvis is also visualized.
  - A few serosal deposits on bowel loops are now visualized for example the subsequently described new peritoneal conglomerate in the left midabdomen measuring up to 3.2 cm on the splenic flexure and other serosal deposits on the distal transverse colon on series 13, image 55
- Image guided biopsy of serosal deposit: **confirmed recurrent metastatic carcinosarcoma**
- **Treatment considerations:**
  - **Excellent ECOG PS of 0**
  - **Prior carboplatin + paclitaxel with prior checkpoint exposure**
  - **HER2 IHC 0+**

Prof Eskander: Case Presentation

- **After counseling and discussion, this patient was interested in enrollment and treatment on a TROP2 ADC phase 3 clinical trial.**
- **ASCENT-GYN-01/GOG-3104: A Randomized, Open-label, Phase 3 Study of Sacituzumab Govitecan Versus Treatment of Physician's Choice in Participants With Endometrial Cancer Who Have Received Prior Platinum-based Chemotherapy and Anti-PD-1/PD-L1 Immunotherapy**



UC San Diego
SCHOOL OF MEDICINE

Prof Eskander: Case Presentation

- **ASCENT-GYN-01/GOG-3104:** A Randomized, Open-label, Phase 3 Study of Sacituzumab Govitecan Versus Treatment of Physician's Choice in Participants With Endometrial Cancer Who Have Received Prior Platinum-based Chemotherapy and Anti-PD-1/PD-L1 Immunotherapy
- **Started on study directed therapy in Feb 2025**
- She remains on treatment, most recently receiving cycle 30, with radiographic imaging showing RECIST v1.1 **complete response (14 months after start of treatment)**
- **On treatment side effects:**
  - Grade 1 fatigue
  - Grade 1 constipation
  - Preserved ECOG PS 0

QUESTIONS FOR THE FACULTY

Thus far, has the tolerability profile of TROP2-targeted ADCs in patients with advanced gynecologic cancers been consistent with what has been observed with these drugs in other tumor types? Globally, would you say that any one of the TROP2-directed ADCs is better tolerated than the others?

QUESTIONS FOR THE FACULTY

How typical or atypical is this patient's experience with sacituzumab govitecan from a tolerability perspective? With proper supportive care, how likely are patients to tolerate this drug without significant issues? What prophylactic measures (eg, antidiarrheals, G-CSF) do you think are most appropriate to mitigate the risk of GI toxicities and cytopenias with sacituzumab govitecan? Do you apply the same approach for Dato-DXd and sac-TMT?

QUESTIONS FOR THE FACULTY

Do you test for homozygous for the UGT1A1*28 allele in your patients about to begin treatment with sacituzumab govitecan? Would you approach AE mitigation, monitoring and/or management any differently in a patient with known reduced UGT1A1 activity?

What is your experience with the tolerability of Dato-DXd and sac-TMT? What prophylactic measures, if any, do you recommend to prevent oral mucositis/stomatitis with these drugs?

QUESTIONS FOR THE FACULTY

How do ocular toxicities in patients receiving Dato-DXd and sac-TMT compare to those with other ADCs used in gynecologic cancers, such as mirvetuximab soravtansine and tisotumab vedotin, in terms of type(s) and severity? How do you generally screen for ocular toxicities in patients receiving Dato-DXd and sac-TMT? How often do you recommend consultation with an ophthalmologist? How are ocular toxicities best managed when they occur? What is your threshold for dose reducing or holding TROP2-targeted ADCs due to ocular toxicities?

QUESTIONS FOR THE FACULTY

How do you monitor for pneumonitis in patients receiving Dato-DXd and sac-TMT? How do you manage Grade 1 versus Grade 2 pneumonitis? In which situations will you rechallenge after resolution of symptoms?

Data + Perspectives: The Potential Role of TROP2- and CDH6-Directed Antibody-Drug Conjugates in Gynecologic Cancers

An Independent CME Symposium During the SGO 2026 Annual Meeting on Women's Cancer®

Sunday, April 12, 2026

1:30 PM – 3:00 PM AST

Faculty

Ramez N Eskander, MD

Bradley J Monk, MD

Moderator

Kathleen N Moore, MD, MS

RTP RESEARCH TO PRACTICE

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

Please complete the postmeeting survey currently available via the corresponding QR code on the printed handout for attendees in the room and on Zoom for those attending virtually. The survey will remain open up to 5 minutes after the meeting ends.

How to Obtain CME Credit

In-person attendees: Please refer to the program syllabus for the CME credit link or QR code. Online/Zoom attendees: The CME credit link is posted in the chat room.

RTP
RESEARCH TO PRACTICE