An Educational Symposium at the FSGO 2026 Annual Meeting

Future of ADCs: Accelerating Progress in Ovarian and Endometrial Cancer

Sunday
June 14, 2026
8:00 am – 8:50 am ET
Long Boat Key, Florida

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Future of ADCs: Accelerating Progress in Ovarian and Endometrial Cancer
Educational Symposium
Sunday, July 14, 2026 | Long Boat Key, FL

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Faculty Disclosures

LAST NAME	FIRST NAME	Individual's Role(s) in Activity	Name of Ineligible Company(s)	Nature of Relevant Financial Relationship(s)
Planning Disclosures				
Jordan, MD	Scott	**Moderator**	AbbVie; AstraZeneca; Corcept; GenMab; GSK; Merck; Pfizer; Caris; Natera	Consultant
Speaker Disclosures				
Indermauer, MD	Megan	**Speaker**	AstraZeneca	Speaker's Bureau
Martino, MD	Marty	**Speaker**	Intuitive; JNJ Medtech; Medtronic; CMR	Patient Safety Consultant
Engbert	Holley	**Staff**	Nothing to disclose	
Rush	Heather	**Staff**	Nothing to disclose	
Shumaker	Kara	**Reviewer/Staff**	Nothing to disclose	
Small, MPH	Michelle N	**Reviewer/Staff**	Nothing to disclose	
Alvarez Secord, MD	Angeles	**Reviewer/Edu-Chair**	AbbVie; Aravive; AstraZeneca; Daiichi Sankyo; Ellipses Pharma; Genmab; GSK; Immunogen; Karyopharm; Merck; Mersana; Myriad; Oncoquest/Canaria Bio; Oncoquest; Roche/Genentech; TORL Biotherapeutics; Zentalis; Foundation Medicine; Gilead; Histosonics; Medtronic; Porject Nana; Up to Date; SGO; FWC; GOG Foundation; Amgen; Johnson & Johnson	Research funds to Institution (AbbVie; Aravive; AstraZeneca; Daiichi Sankyo; Ellipses Pharma; Genmab; GSK; Immunogen; Karyopharm; Merck; Mersana; Myriad; Oncoquest/Canaria Bio; Oncoquest; Roche/Genentech; TORL Biotherapeutics; Zentalis) Honorarium (Merck; GSK) Advisory Board with Honoraria (AbbVie; AstraZeneca; Daiichi Sankyo; Foundation Medicine; GSK; Genmab; Gilead; Histosonics; Medtronic; Merck) Medical Advisory Board (Porject Nana) Steering Committee Uncomp. (Oncoquest; Genmab) Royalties (Up to Date) Board of Directors (SGO; FWC; GOG Foundation) Stock-Divested in June 2024 (Amgen; Johnson & Johnson)
Duska, MD	Linda	**Edu-Co-Chair/ Reviewer**	Merck; Corcept	Honoraria (Merck) Speakers Bureau (Corcept) Research Funding (Merck)
Blank, MD	Stephanie	**Reviewer**	American Board of Obstetrics and Gynecology; Merck; AstraZeneca; GlaxoSmithKline; Pfizer; Seattle Genetics/Astellas; Acrivon; Zentalis; NX Development Corp.	Leadership (American Board of Obstetrics and Gynecology) Research Funding (Merck; AstraZeneca; GlaxoSmithKline; Pfizer; Seattle Genetics/Astellas; Acrivon; Zentalis; NX Development Corp.)
Gien, MD	Lilian	**Reviewer**	Glaxo Smith Kline; Merck; Abbvie; AstraZeneca	Speaker Honoraria (Glaxo Smith Kline; Merck) Advisory Board (Abbvie; AstraZeneca)
Mutch, MD	David	**Reviewer**	Nothing to disclose	
Zweizig, MD	Susan	**Reviewer**	Nothing to disclose	

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

Thank You

GSK

For Supporting This Activity
With An Independent Medical Education Grant

Welcome and The Urgent Push to Improve Ovarian & Endometrial Outcomes

Scott Jordan, MD

Broward Health

Moderator

Scott Jordan, MD
Broward Health

Faculty

Marty Martino, MD
Ascension Florida

Megan Indermaur, MD
Women’s Care Florida

Learning Objectives

By the end of this session, participants will be able to:

1. Differentiate the design components of ADCs (targets, payloads, and linkers) and describe how antigen density, internalization, and bystander effects impact efficacy, safety, and sequencing in ovarian and endometrial cancers.
2. Assess key and emerging clinical data to identify current leaders and anticipate agents likely to set new standards of care.
3. Utilize biomarker-driven methods (FRα, HER2/HER3, TROP2, B7-H4, CDH6, NaPi2b) for selecting patients and planning therapy.
4. Implement strategies for sequencing ADCs with existing regimens and managing key toxicities such as ocular events and interstitial lung disease.
5. Identify suitable clinical trial opportunities and advise eligible patients on participation.

Agenda

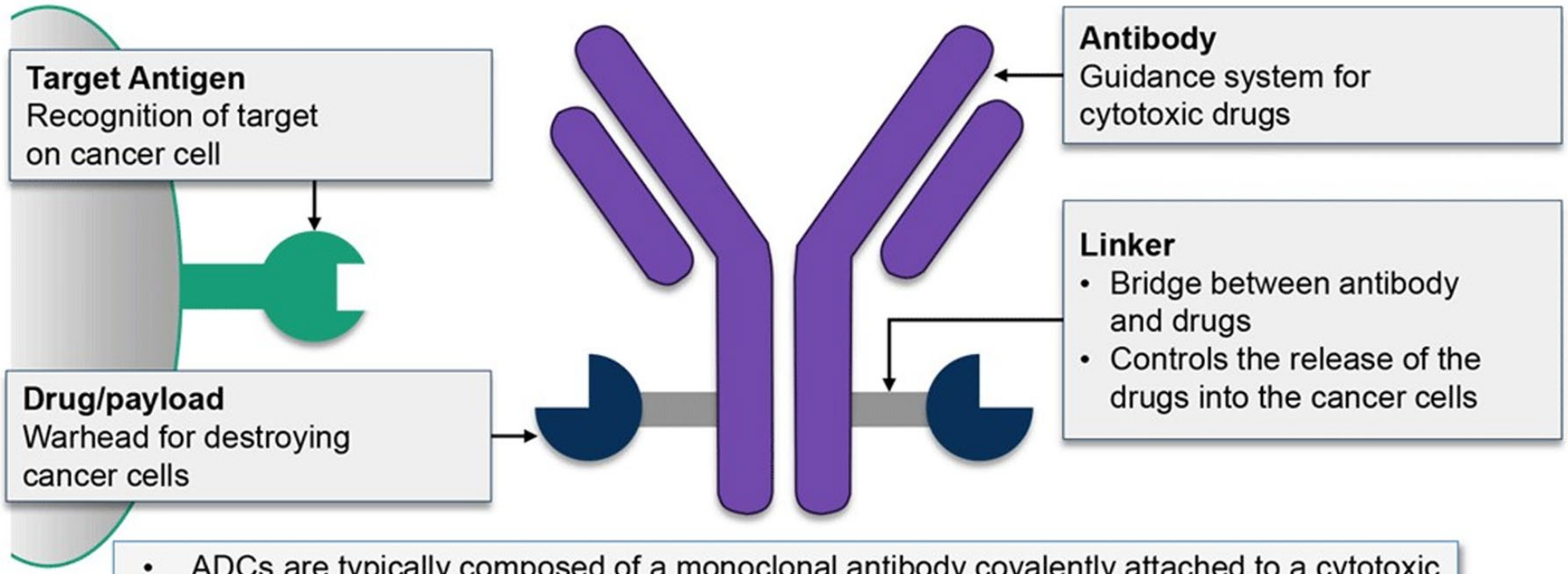
3 minutes	**Welcome and The Urgent Push to Improve Ovarian & Endometrial Outcomes** Scott Jordan, MD
10 minutes	**ADCs in Gynecologic Cancers: Current Landscape and Clinical Impact** Dr. Megan Indermaur
12 minutes	**What Actually Matters Clinically: Understanding the Science: Targets, Payloads, and Linkers** Dr. Martin Martino
10 minutes	**A Conversation: Integrating Disease Management: Sequencing, Selection, and Safety** All Faculty
12 minutes	**Panel Discussion: Who Leads the Next Wave** All Faculty
3 minutes	**Audience Q&A and Closing Remarks** All Faculty

ADCs in Gynecologic Cancers: Current Landscape and Clinical Impact

Megan Indermaur, MD

Women's Care Florida

ADCs – Basic Concept



- ADCs are typically composed of a monoclonal antibody covalently attached to a cytotoxic drug via a chemical linker
- ADCs combine both the advantages of highly specific targeting ability and highly potent killing effect to achieve accurate and efficient elimination of cancer cells

ADC, antibody–drug conjugate.

1. Marks S, et al. Lung Cancer. 2022; 163: 59-68

Why ADCs in Gynecologic Cander

High Expression of targetable antigens

Folate receptor Alpha (Frα)
Tissue Factor (TF)
HER2
TROP2
B7-H4

Need for effective therapies in recurrent disease

Potential to improve efficacy while limiting systemic toxicity

Expanding biomarker-driven treatment options

Bujnak A, et al. Gynecologic Oncology, 2025; 195, 180-191.

FDA-Approved ADCs in Ovarian and Endometrial Cancer

ADC	Target	Payload	Regulatory Status	Setting
Mirvetuximab soravtansine (MIRV)	FRα	DM4	**FRα-positive ovarian** -2024 FDA approval	2L+
Trastuzumab deruxtecan (T-DXd)	HER2	Topoisomerase I inhibitor	**HER2 IHC 3+ tumors** (cervical, endometrial, ovarian) -2024 FDA Accelerated Approval	2L+

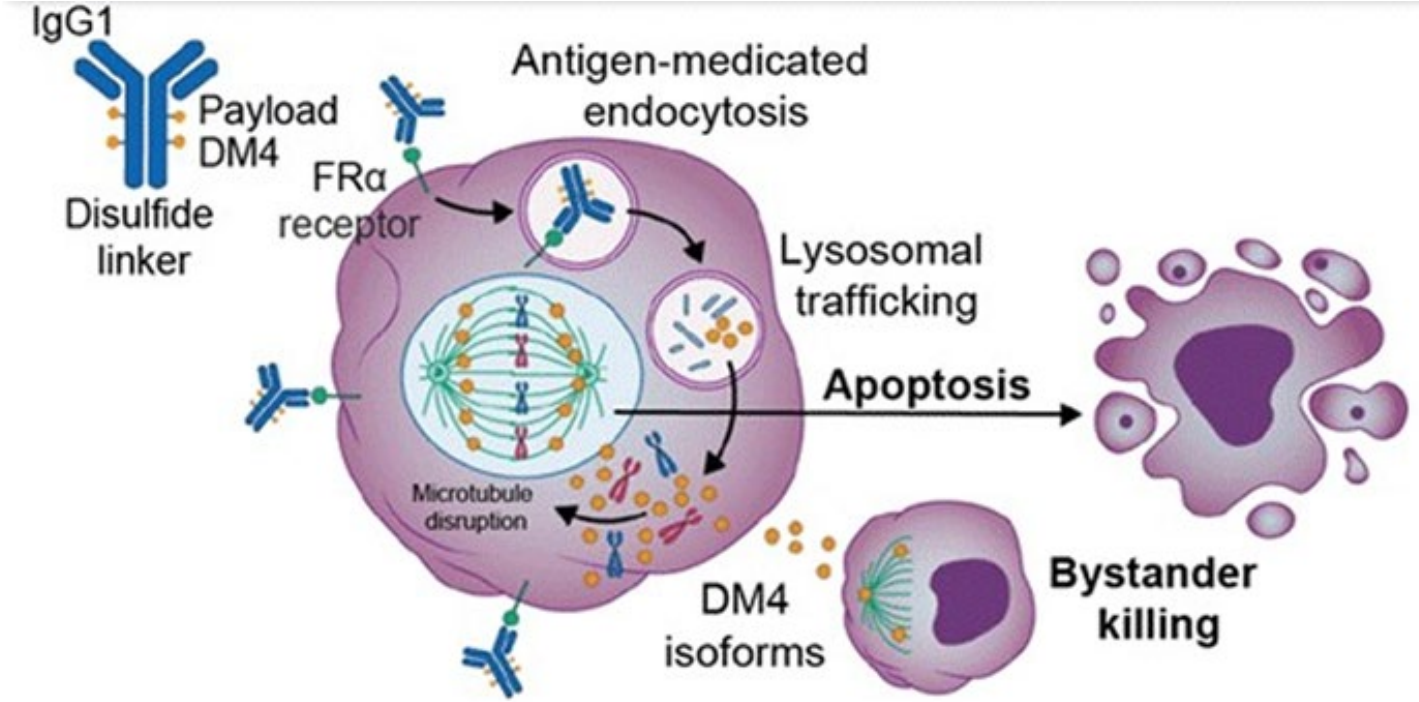
ADC, antibody–drug conjugate; FRα, folate receptor alpha; HER2, human epidermal growth factor receptor 2; IHC, immunohistochemistry.

Moore KN et al. N Engl J Med. 2023;389:2165–2177; FDA. Mirvetuximab Soravtansine Prescribing Information. 2024; FDA. Trastuzumab Deruxtecan Prescribing Information. 2024; Meric-Bernstam F et al. J Clin Oncol. 2024.

Targeting FRα Expression in Epithelial Ovarian Cancer

Prevalence & Epidemiology

- 35-40% of platinum-resistant high grade ovarian cancer patients express high levels of FRα



ADC, antibody–drug conjugate; FRα, folate receptor alpha; DM4, maytansinoid microtubule inhibitor.

1. Bax HJ et al. BR J Cancer. 2023; 128: 342-353;

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

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

Patient Population
(N=453)

Enrollment and Key Eligibility

Platinum-resistant disease (PFI ≤6 mo)

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

High-grade serous histology

1º platinum-refractory disease excluded (primary PFI <3 mo)

1-3 prior lines of therapy

Prior BEV and PARPi allowed

Patients with BRCA mutations allowed

1:1 Randomization

Treatment Regimen-Experimental

MIRV
(6 mg/kg AIBW Q3W)

Treatment Regimen-Control

Investigator's Choice Chemotherapy
(Paclitaxel, PLD, or Topotecan)

Stratification Factors

IC chemo: paclitaxel, PLD, or topotecan

Prior lines of therapy: 1 vs 2 vs 3

Primary Endpoint

PFS by INV
(BICR sensitivity analysis)

Key Secondary Endpoints

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

Secondary Endpoints

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

AIBW, adjusted ideal body weight; BEV; bevacizumab; BICR, blinded independent central review; BRCA, BReast CAncer gene; CA-125, cancer antigen 125; chemo, chemotherapy; DOR, duration of response; FRα, folate receptor alpha; IC, investigator's choice; IHC, immunohistochemistry; INV, investigator; MIRV, mirvetuximab soravtansine; ORR, objective response rate; OS, overall survival; PARPi, poly (ADP-ribose) polymerase inhibitors; PFI, platinum-free interval; PFS, progression-free survival; PFS2, time from randomization until second disease progression; PLD, pegylated liposomal doxorubicin; PROs, patient-reported outcomes; PS2+, positive staining intensity ≥2; Q3W, every 3 weeks.

[a]PROs will be measured using the European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire, 28-item Ovarian Cancer Module (OV28) study instrument.

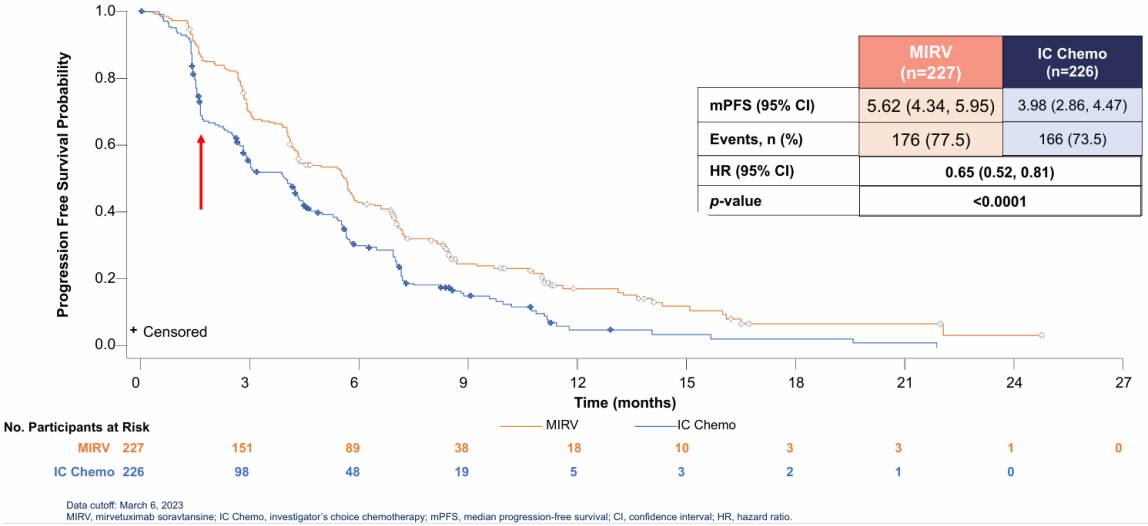
[b]Gynecological Cancer InterGroup (GCIG) criteria.

1. ClinicalTrials.gov identifier: NCT04209855. Updated June 16, 2022. Accessed October 5, 2022. https://clinicaltrials.gov/ct2/show/NCT04209855

2. Moore K, et al. Presented at: 2020 American Society of Clinical Oncology Annual Meeting; May 29-31, 2020; Virtual. Abstract TPS6103.

Slide adapted from Moore K, et al.

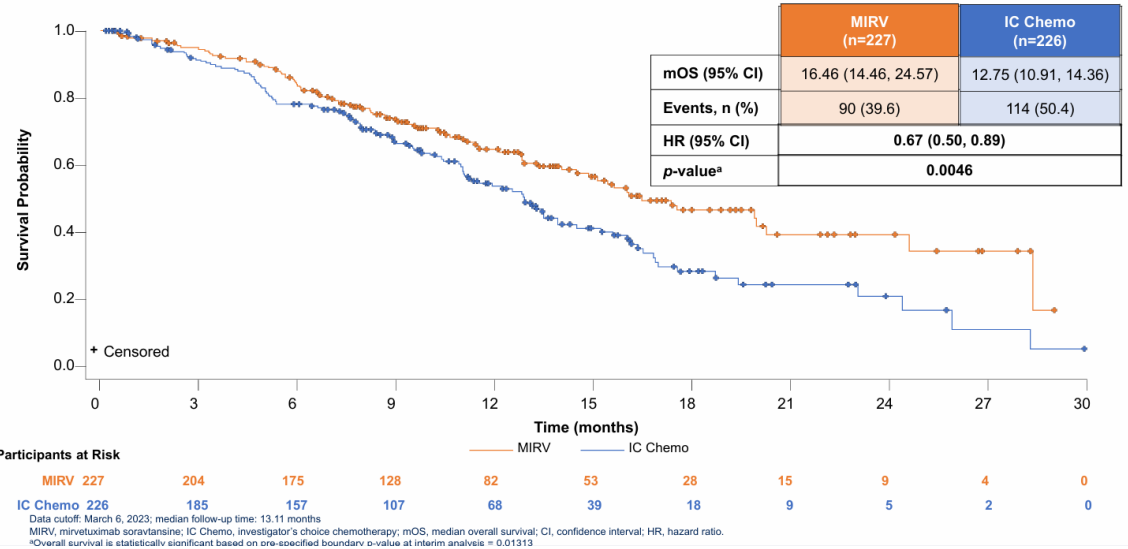
Primary Endpoint: Progression-Free Survival by Investigator



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

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

Overall Survival



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

Data cutoff: March 6, 2023; median follow-up time: 13.11 months
MIRV, mirvetuximab soravtansine; IC Chemo, investigator's choice chemotherapy; mOS, median overall survival; CI, confidence interval; HR, hazard ratio.
[a]Overall survival is statistically significant based on pre-specified boundary p-value at interim analysis = 0.01313

Overall Response Rate by Investigator (N=453)

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

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

CI = confidence interval, HR = hazard ratio, IC = investigator's choice, MIRV = mirvetuximab soravtansine, OR = odds ratio, ORR = objective response rate, OS = overall survival, PFS = progression-free survival, PR = partial response, CR = complete response, SD = stable disease, PD = progressive disease

Moore KN et al. N Engl J Med. 2023;389(23):2162–2174.

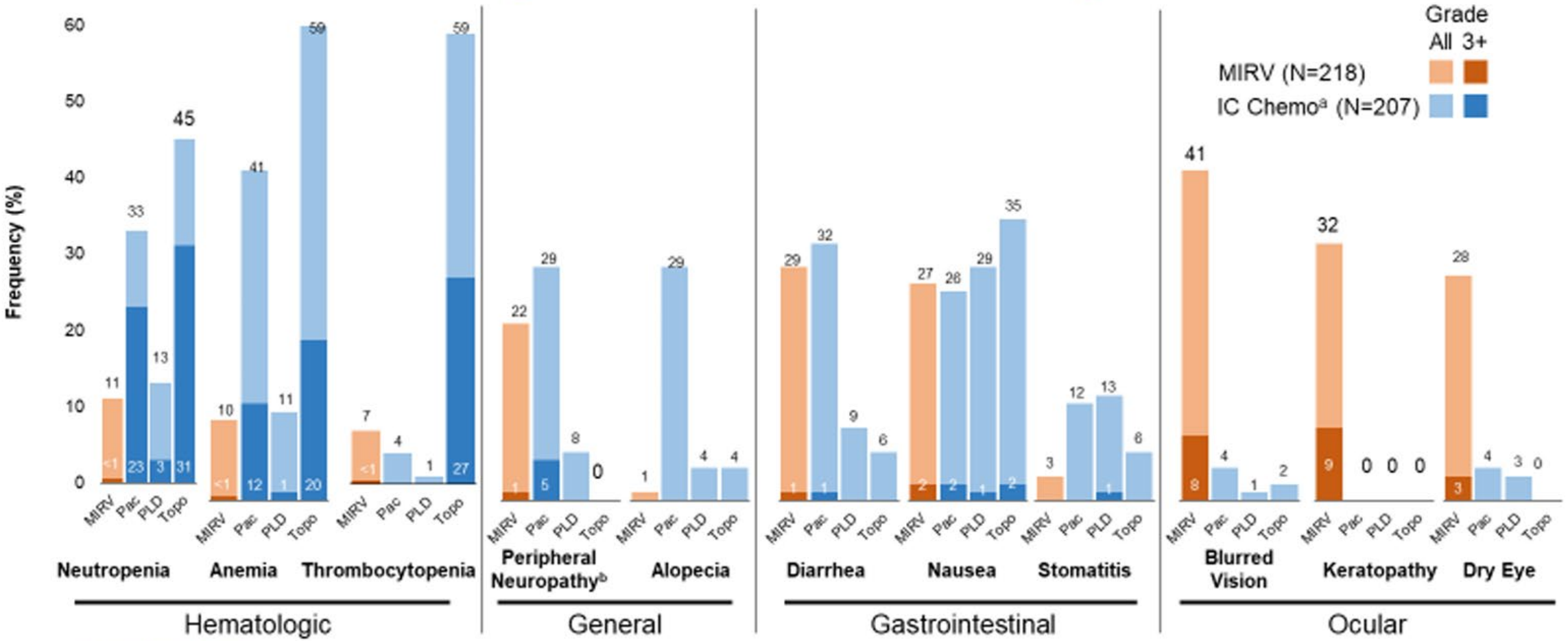
Safety Summary (N=425)

MIRV has a tolerable safety profile compared with IC Chemo

	MIRV (n=218)	IC Chemo (n=207)
Any TEAE, n (%)	210 (96)	194 (94)
Grade 3+ TEAEs, n (%)	91 (42)	112 (54)
SAEs, n (%)	52 (24)	68 (33)
Deaths on study drug or within 30 days of last dose, n (%)	5 (2)	5 (2)
Dose reductions due to TEAEs, n (%)	74 (34)	50 (24)
Dose delays due to TEAEs, n (%)	117 (54)	111 (54)
Discontinuations due to TEAEs, n (%)	20 (9)	33 (16)

Data cutoff: March 6, 2023
The safety population comprises all patients who received at least one dose of MIRV or IC Chemo
TEAEs, treatment-emergent adverse events; SAEs, serious adverse events; MIRV, mirvetuximab soravtansine; IC, investigator's choice chemotherapy.

Differentiated Safety Profile: Treatment-Emergent Adverse Events



Data cutoff: March 6, 2023

MIRV, mirvetuximab soravtansine; IC Chemo: investigator's choice chemotherapy; Pac, paclitaxel; PLD, pegylated liposomal doxorubicin; Topo, topotecan.

[a]Pac n=82 (39%), PLD n=76 (37%), Topo n=49 (24%). [b]Grade 2+ peripheral neuropathy events were observed in 12% and 16% of patients that received MIRV or paclitaxel, respectively.

Guideline Recommendations for FRα-Targeted Treatment in Women with Ovarian Cancer

Acceptable Recurrence Therapies for Epithelial Ovarian (Including LCOC)/Fallopian Tube/Primary Peritoneal Cancer	
Recurrence Therapy for Platinum-Resistant Disease (Alphabetical Order)	
Preferred Regimens: Targeted Therapy (Single Agents)	**Useful in Certain Circumstances: Targeted Therapy**
Bevacizumab – Category 2A	Mirvetuximab soravtansine-gynx/bevacizumab (for FRα-expressing tumors [**≥25%** positive tumor cells]) – Category 2A
Mirvetuximab soravtansine-gynx (for FRα-expressing tumors [**≥75%** positive tumor cells]) – Category 1	

- **Validated molecular testing** should be performed in a **CLIA-approved facility** using the **most recent available tumor tissue**
- Tumor molecular analysis is recommended to include, at a minimum, tests to identify potential benefit from targeted therapeutics that have tumor-specific or tumor-agnostic benefit including FRα, if prior testing did not include these markers
- More comprehensive testing may be particularly important in LCOC with limited approved therapeutic options

CLIA, Clinical Laboratory Improvement Amendments; FRα, folate receptor alpha; LCOC, less common ovarian cancers.

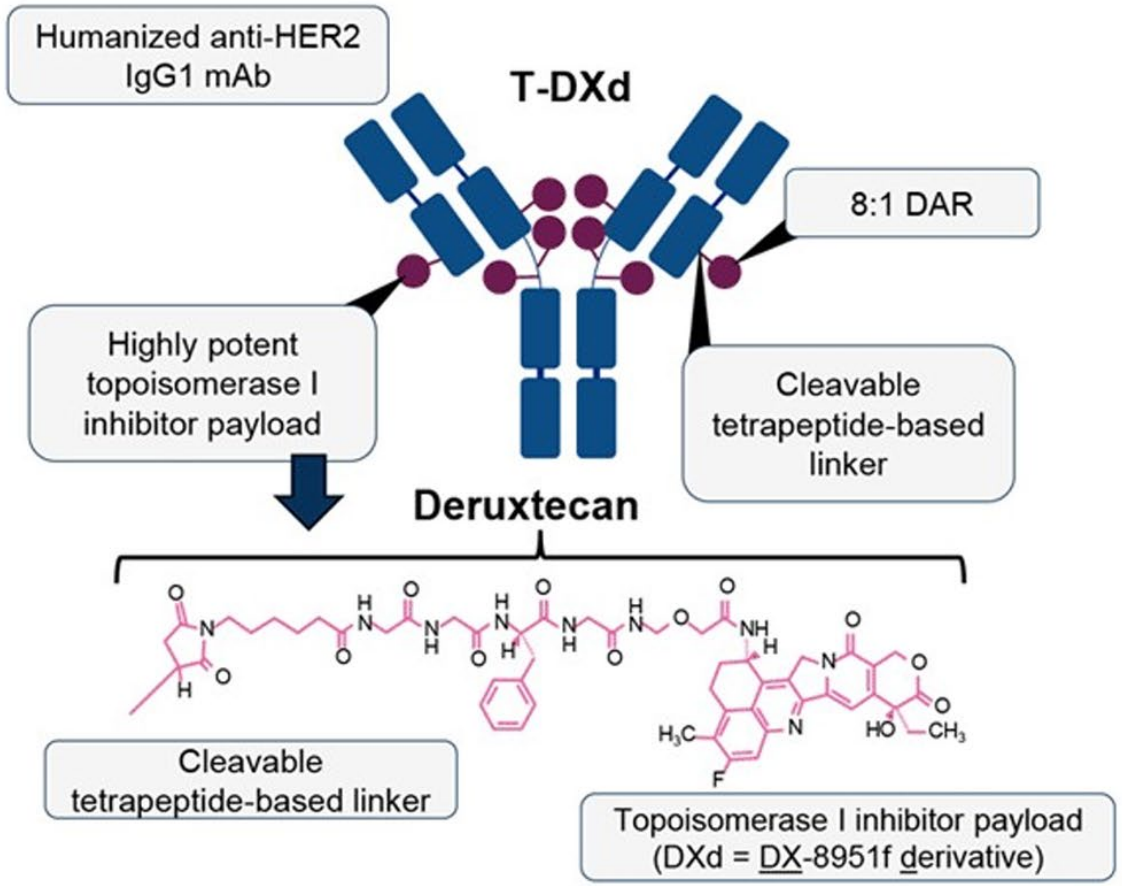
NCCN Guidelines® for Ovarian Cancer Including Fallopian Tube Cancer and Primary Peritoneal Cancer. V4.2026. [Accessed June 12 2026].

Guideline Recommendations for FRα-Targeted Treatment in Women with Ovarian Cancer

Acceptable Recurrence Therapies for Epithelial Ovarian (Including LCOC)/Fallopian Tube/Primary Peritoneal Cancer
Recurrence Therapy for Platinum-Sensitive Disease: Useful in Certain Circumstances
Mirvetuximab soravtansine-gynx (for FRα-expressing tumors [**≥75%** positive tumor cells]) – Category 2A
Mirvetuximab soravtansine-gynx/bevacizumab (for FRα-expressing tumors [**≥50%** positive tumor cells]) – Category 2B

NCCN Guidelines® for Ovarian Cancer Including Fallopian Tube Cancer and Primary Peritoneal Cancer. V4.2026. [Accessed June 12 2026].

Targeting HER2 in Ovarian & Endometrial Cancer



Trastuzumab Deruxtecan (T-DXd)

Payload MOA: topoisomerase I inhibitor
High potency of payload

DAR ~8
Payload with short systemic half-life

Tumor-selective cleavable linker
Bystander antitumor effect

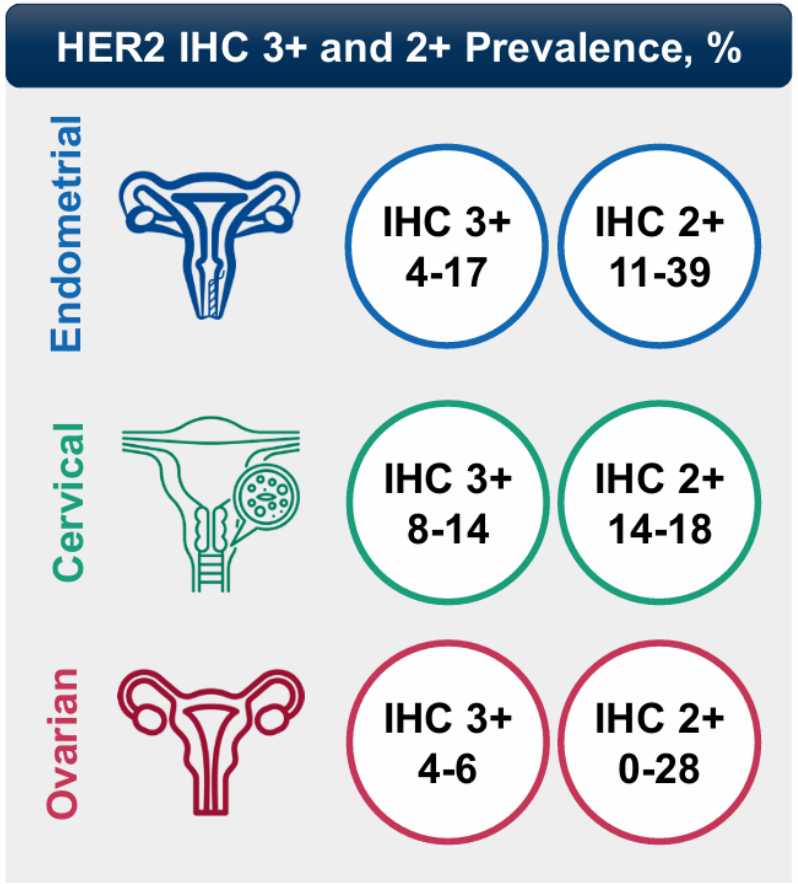
1. Nakada T et al. *Chem Pharm Bull (Tokyo)*. 2019;67:173-185. 2. Ogitani Y et al. *Clin Cancer Res*. 2016;22:5097-5108.
3. Trail PA et al. *Pharmacol Ther*. 2018;181:126-142. 4. Okamoto H et al. *Xenabiotica*. 2020;50:1242-1250. 5. Nagi Y et al. *Xenobiotica*. 2019;49:1086-1096.

DAR, drug-to-antibody ratio; HER2, human epidermal growth factor receptor 2; IgG1, immunoglobulin G1; mAb, monoclonal antibody; MOA, mechanism of action

Background of HER2 in Gynecologic Cancers

HER2

- **Transmembrane tyrosine kinase receptor overexpressed in various malignancies, including cervical, endometrial, and ovarian cancer**
- Tumors with increased protein expression and gene amplification tend to be more likely to be resistant to conventional chemotherapy
- HER2 amplification reported to be associated with poorer prognosis
- HER2 testing should be considered for all recurrent gynecologic cancers



1. Makker V et al. ESMO 2025. Abstract 957P. D. Makker V et al. SGO 2026

Phase 2 DESTINY-PanTumor02

Key Eligibility Criteria

- Advanced solid tumors not eligible for curative therapy
- 2L+ 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)[a]
- Prior HER2-targeting therapy allowed
- ECOG/WHO PS 0-1

→ **T-DXd** 5.4 mg/kg Q3W

40 per cohort[b]

- **Endometrial cancer**
- **Cervical cancer**
- **Ovarian cancer**
- Bladder cancer
- Other tumors
- Biliary tract cancer
- Pancreatic cancer

- **Primary endpoint:** confirmed ORR (investigator)
- **Secondary endpoints:** DOR, DCR, PFS, OS, safety
- **Exploratory analysis:** subgroup analysis by HER2 status

Baseline Characteristics

- 267 patients received treatment; 202 (75.7%) based on local HER2 testing
  - 111 (41.6%) patients were IHC 3+ based on HER2 test (local or central) at enrollment; primary efficacy analysis (all patients)
  - 75 (28.1%) patients were IHC 3+ on central testing; sensitivity analysis on efficacy endpoints (subgroup analyses)

- Gastric HER2 scoring method
- Did NOT use FISH, even for 2+

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, FISH, fluorescence in situ hybridization.

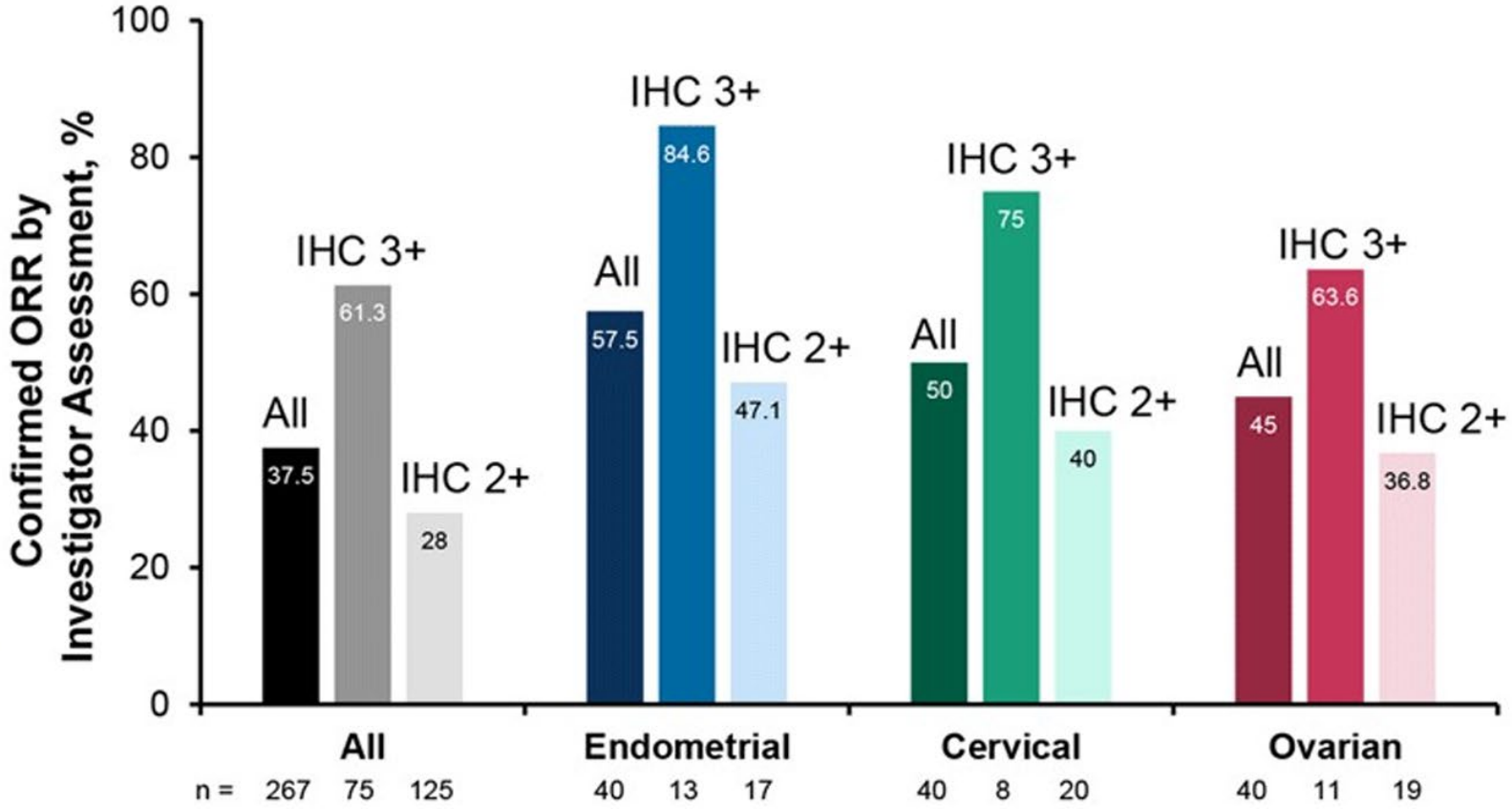
Primary analysis data cutoff: June 8, 2023; median follow-up: 12.75 mo.

[a] Patients were eligible for either test. All patients were centrally confirmed. [b] Planned recruitment, cohorts with no objective responses in the first 15 patients were to be closed.

1. https://clinicaltrials.gov/study/NCT04482309. 2. Hofmann M et al. *Histopathology*. 2008;52:797-805. 3. Meric-Bernstam F et al. ESMO 2023. Abstract LBA34.
4. Meric-Bernstam F et al. *J Clin Oncol*. 2024;42:47-58.

Response with T-DXd Observed Across Gynecologic Cancers

Consistent with the primary and post-hoc analyses, T-DXd continued to show durable and clinically meaningful antitumor activity in patients with HER2-expressing tumors (IHC 3+/2+), irrespective of whether HER2 IHC status was determined by central or local testing

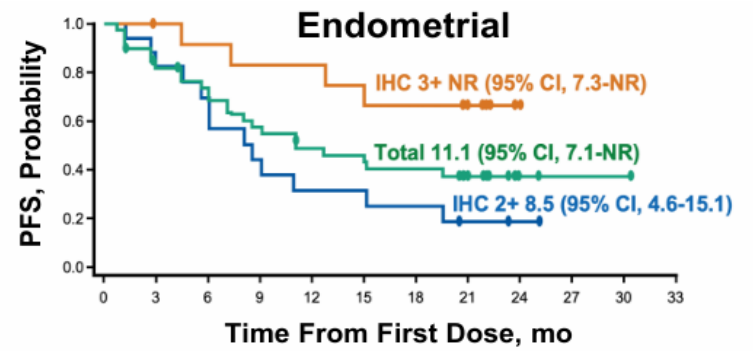


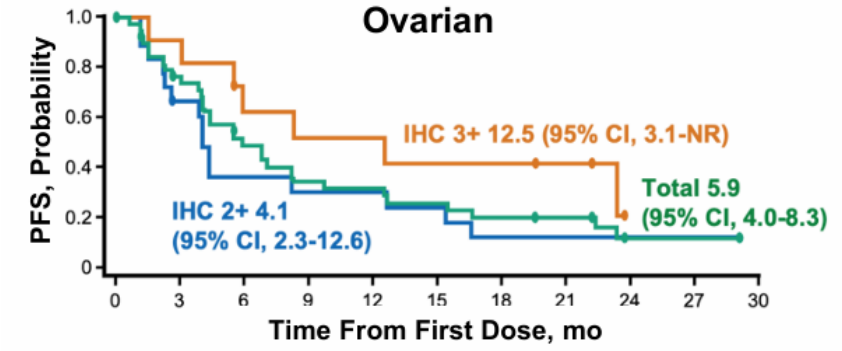
Median follow-up:13.0 mo.

1. Meric-Bernstam F et al. *J Clin Oncol*. 2024;42:47-58. 2. Oaknin A et al. *Adv Ther*. 2024;41:4125-4139. 3 Makker V et al. ESMO 2025 Abstract 957P.

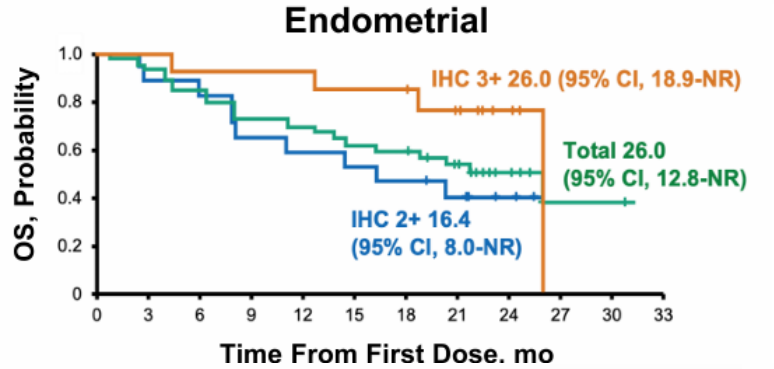
Destiny-PanTumor02 Final Analysis: T-DXd Clinical Antitumor Activity in HER2 Expressing Tumors

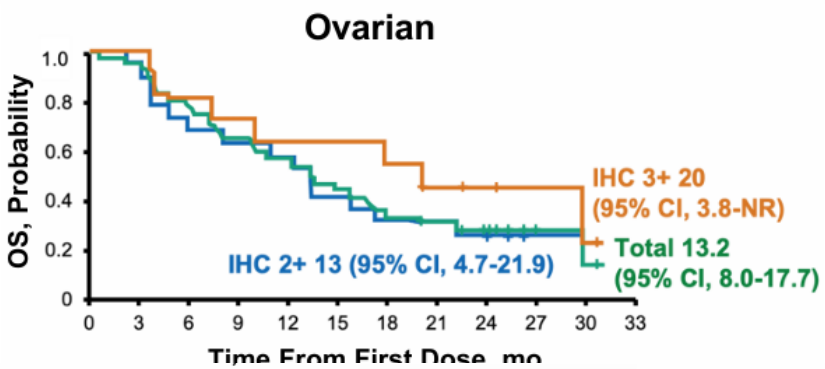
PFS





OS





HER2 IHC 3+
HER2 IHC 2+
Total

Final Analysis confirmed:
Longer INV-assessed mPFS and mOS was observed in patients with HER2 IHC 3+ tumors vs those with IHC 2+ tumors by central testing and according to the HER2 test result used for enrollment

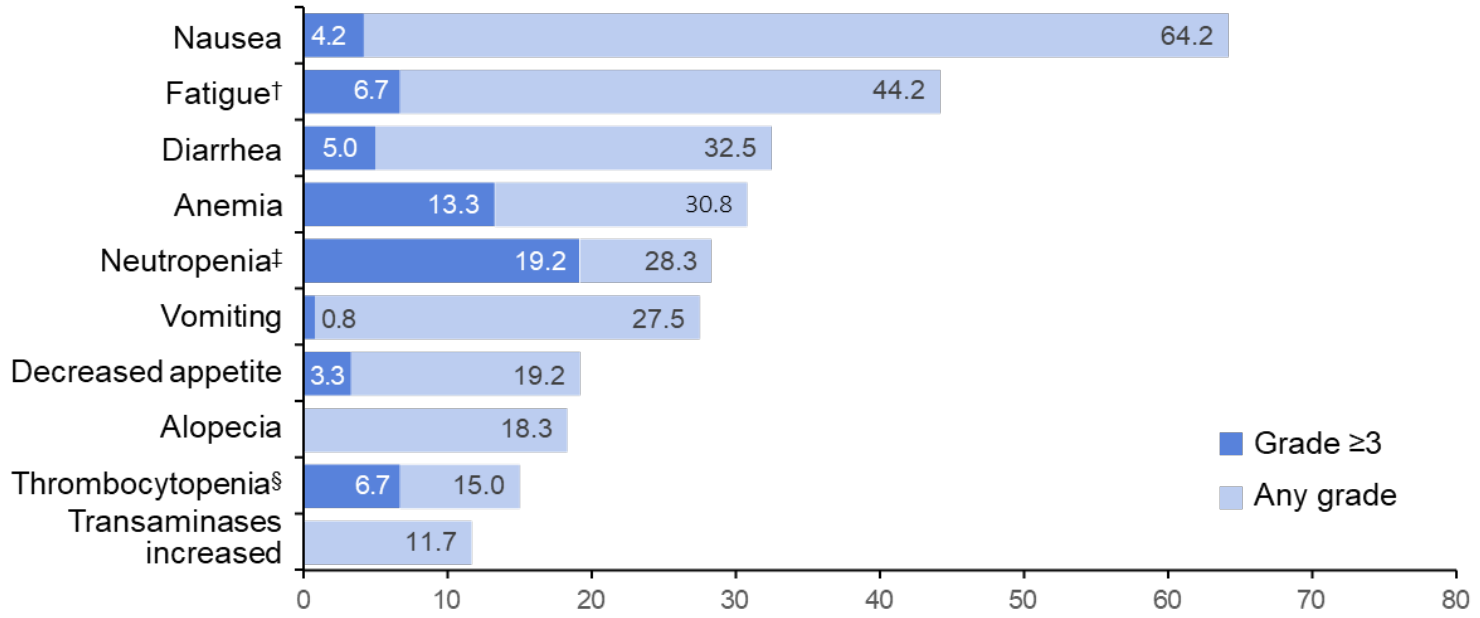
1. Meric-Bernstam F et al. *J Clin Oncol*. 2024;42:47-58. 2. Oaknin A et al. *Adv Ther*. 2024;41:4125-4139. 3. Makker V et al. ESMO 2025. Abstract 957P.
4. Makker V et al. SGO 2026.

CI, confidence interval; HER2, human epidermal growth factor receptor 2; IHC, immunohistochemistry; INV, investigator; mOS, median overall survival; mPFS, median progression-free survival; NR, not reached; OS, overall survival; PFS, progression-free survival; T-DXd, trastuzumab deruxtecan.

Safety Summary: Gynecological Cohorts

n (%)	Gynecological cohorts N=120
Any drug-related TEAEs	106 (88.3)
Drug-related TEAEs Grade ≥3	54 (45.0)
Serious drug-related TEAEs	18 (15.0)
Drug-related TEAEs associated with dose discontinuations	7 (5.8)
Drug-related TEAEs associated with dose interruptions	24 (20.0)
Drug-related TEAEs associated with dose reductions	35 (29.2)
Drug-related TEAEs associated with deaths	2 (1.7)*

Most common drug-related TEAEs (>10%) in gynecological cohorts



ILD/pneumonitis adjudicated as T-DXd related¶, n (%)	Grade 1	Grade 2	Grade 3	Grade 4	Grade 5	Any grade
Gynecological cohorts N=120	4 (3.3)	8 (6.7)	0	0	1 (0.8)	13 (10.8)

Analyses were performed in patients who received ≥1 dose of T-DXd (N=120); median total treatment duration was 9.0, 6.0, and 5.9 months in the endometrial, cervical, and ovarian cohorts, respectively
*Included pneumonia (n=1) and organizing pneumonia (n=1); †category includes the preferred terms fatigue, asthenia, and malaise; ‡category includes the preferred terms neutrophil count decreased and neutropenia; §category includes the preferred terms platelet count decreased and thrombocytopenia; ¶all ILD/pneumonitis cases were reviewed by an Adjudication Committee ILD, interstitial lung disease; T-DXd, trastuzumab deruxtecan; TEAE, treatment-emergent adverse event

Lee JY, et al. Presented at IGCS Annual Meeting 2023 (Abstract #1550); published in Int J Gynecol Cancer. 2023;33(Suppl 4):A6–A7. Figure adapted from Lee JY, et al.

Safety Summary: Special Interest

ILD/pneumonitis adjudicated as T-DXd–related

n (%)	Grade 1	Grade 2	Grade 3	Grade 4	Grade 5	Any grade
All patients (N=267)	6 (2.2)	12 (4.5)	1 (0.4)	0	1 (0.4)	20 (7.5)

Left ventricular dysfunction[a]

n (%)	Grade 1	Grade 2	Grade 3	Grade 4	Grade 5	Any grade
Ejection fraction decreased						
All patients (N=267)	1 (0.4)	4 (1.5)	1 (0.4)	0	0	7 (2.6)[b]
Cardiac failure						
All patients (N=267)	0	0	1 (0.4)	0	0	1 (0.4)

Analyses were performed in patients who received ≥1 dose of T-DXd (n=267).
[a]Left ventricular dysfunction was reported in a total of 12 (4.5%) patients, of which 8 (3.0%) were considered possibly T-DXd–related. [b]One patient had unknown grade of ejection fraction decrease.
ILD, interstitial lung disease; T-DXd, trastuzumab deruxtecan.

Lee JY, et al. Presented at IGCS Annual Meeting 2023 (Abstract #1550); published in Int J Gynecol Cancer. 2023;33(Suppl 4):A6–A7. Figure adapted from Lee JY, et al.

T-DXd: Tumor-Agnostic Approval

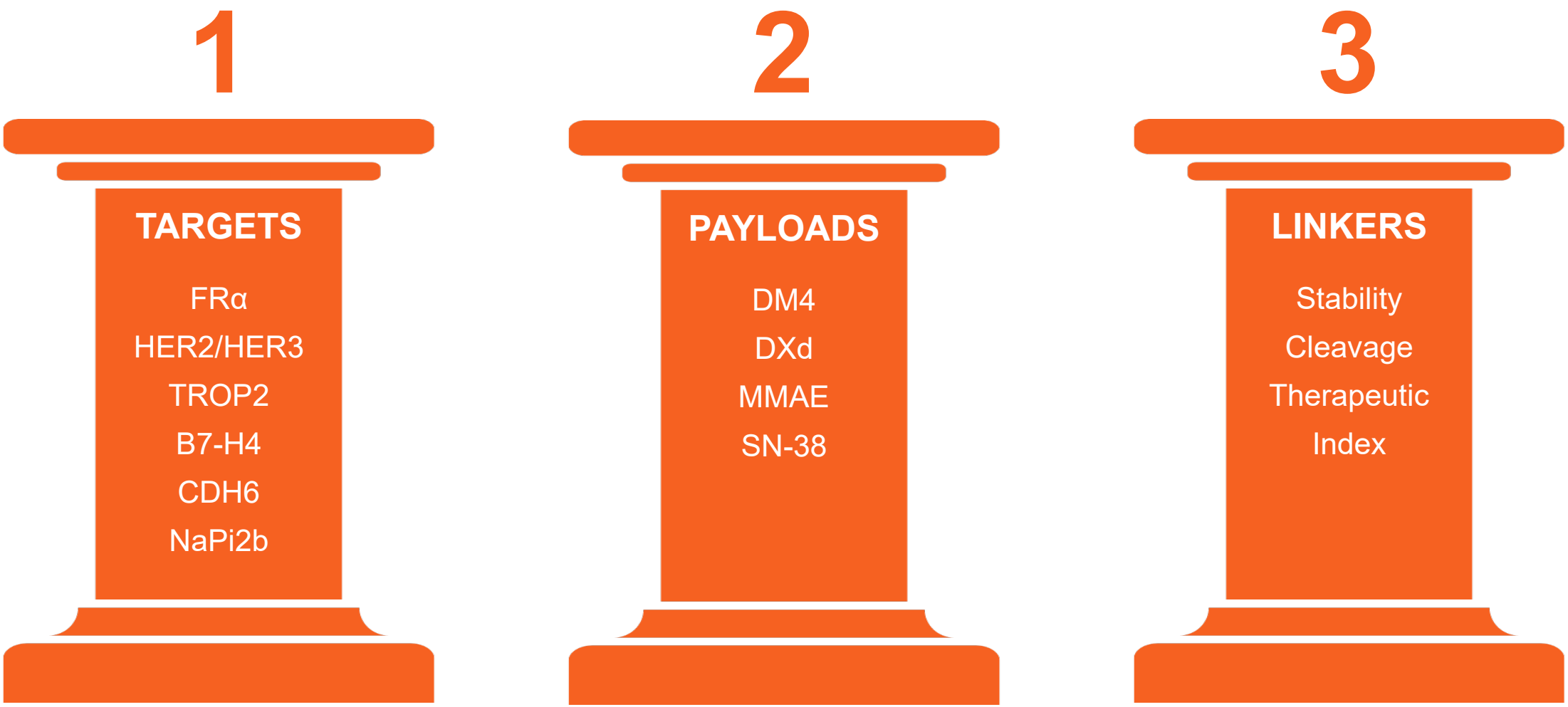
Updated NCCN Guidelines for Ovarian, Uterine, and Cervical Cancers
2L+ therapy: T-DXd for HER2+ tumors (IHC 3+ or 2+)

ADCs in Gynecologic Cancers: Current Landscape and Clinical Impact

Marty Martino, MD

Ascension Florida

Roadmap: The Three Pillars of ADC Function



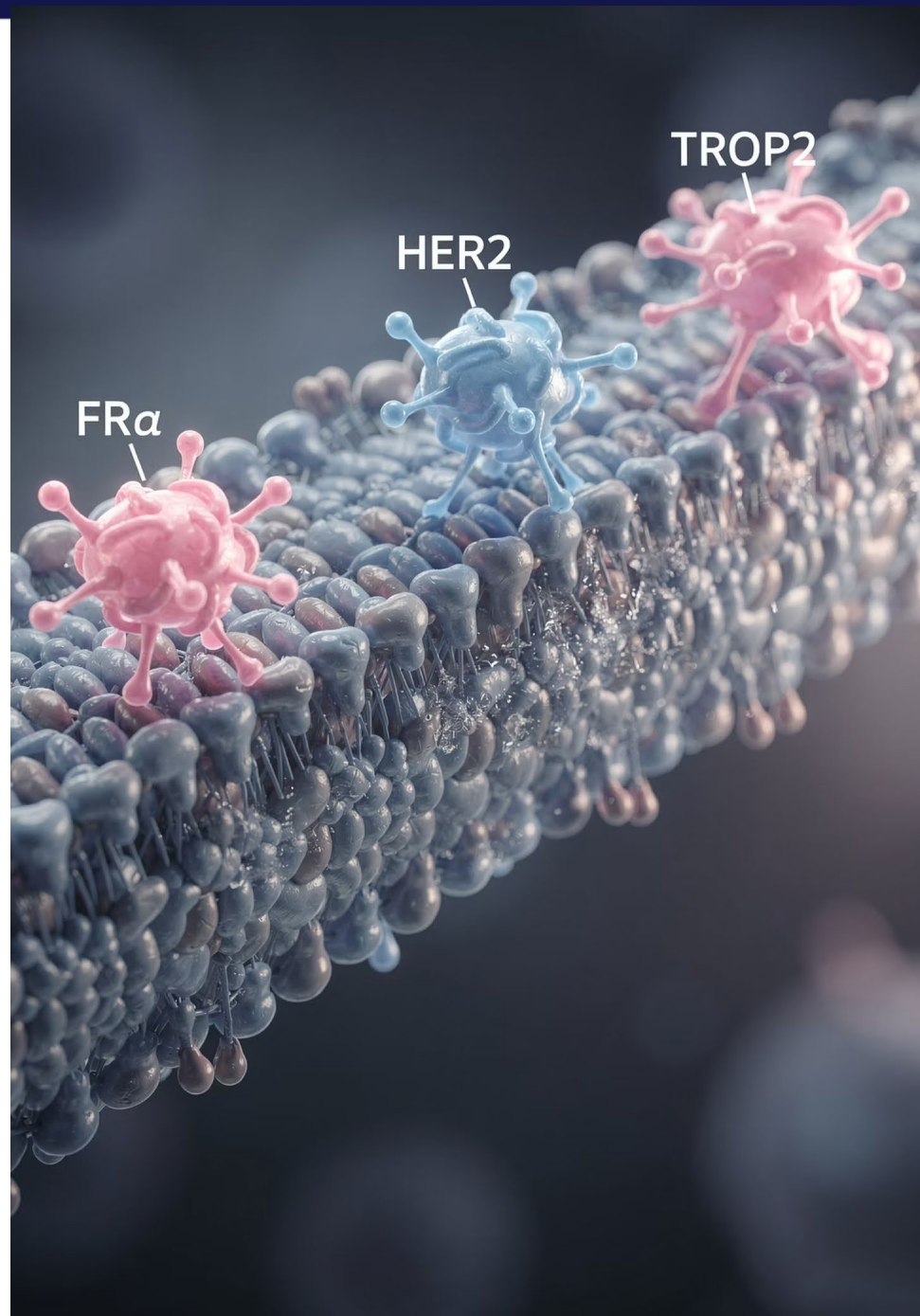
Each pillar shapes efficacy, toxicity, and resistance.

Beck A et al. Nat Rev Drug Discov. 2017;16:315–337.

Target Landscape in Gynecologic Cancers

No single target is universal; select by histology and biomarker profile.

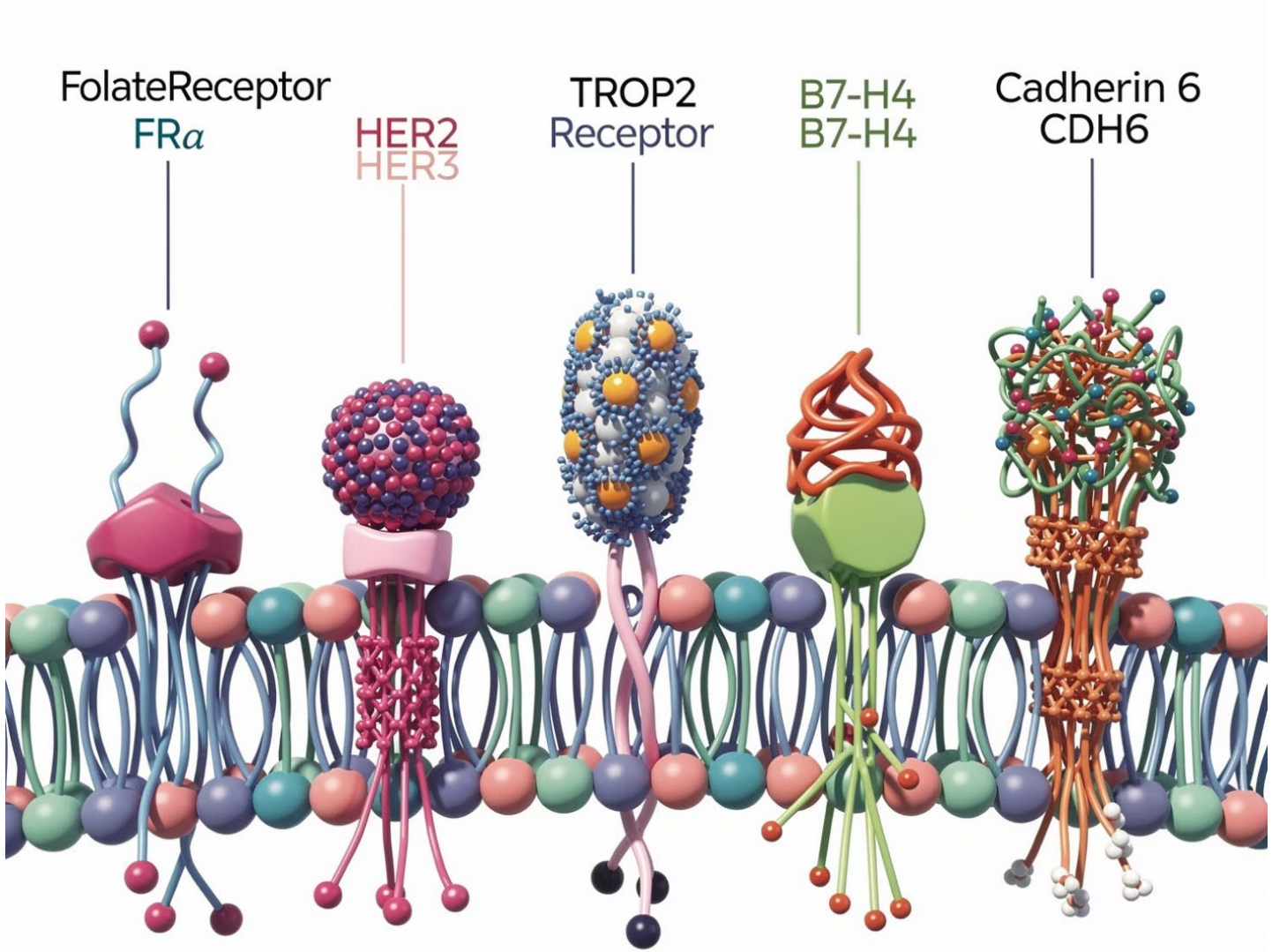
High Selectivity	FRα, NaPi2b — restricted normal tissue expression
Broad Expression	TROP2, HER2, B7-H4 — across multiple histologies
Emerging Targets	CDH6, HER3 — early data in clear cell, endometrial



B7-H4, B7 homolog 4; CDH6, cadherin-6; FRα, folate receptor alpha; HER2, human epidermal growth factor receptor 2; HER3, human epidermal growth factor receptor 3; NaPi2b, sodium-dependent phosphate transport protein 2B; TROP2, trophoblast cell-surface antigen 2.

Barquin A, et al. Cancer. 2026;e70417; Bujnak A, et al. Gynecologic Oncology, 2025; 195, 180-191

Target Deep Dive: Expression Profiles



Clinical Implications

FRα: most tumor-selective.

TROP2/B7-H4: broad coverage.

HER3/CDH6: emerging options.

Barquin A, et al. Cancer. 2026;e70417; Bujnak A, et al. Gynecologic Oncology, 2025; 195, 180-191

Targets — Advantages & Limitations

Choosing the Right Target: What the Data Tell Us

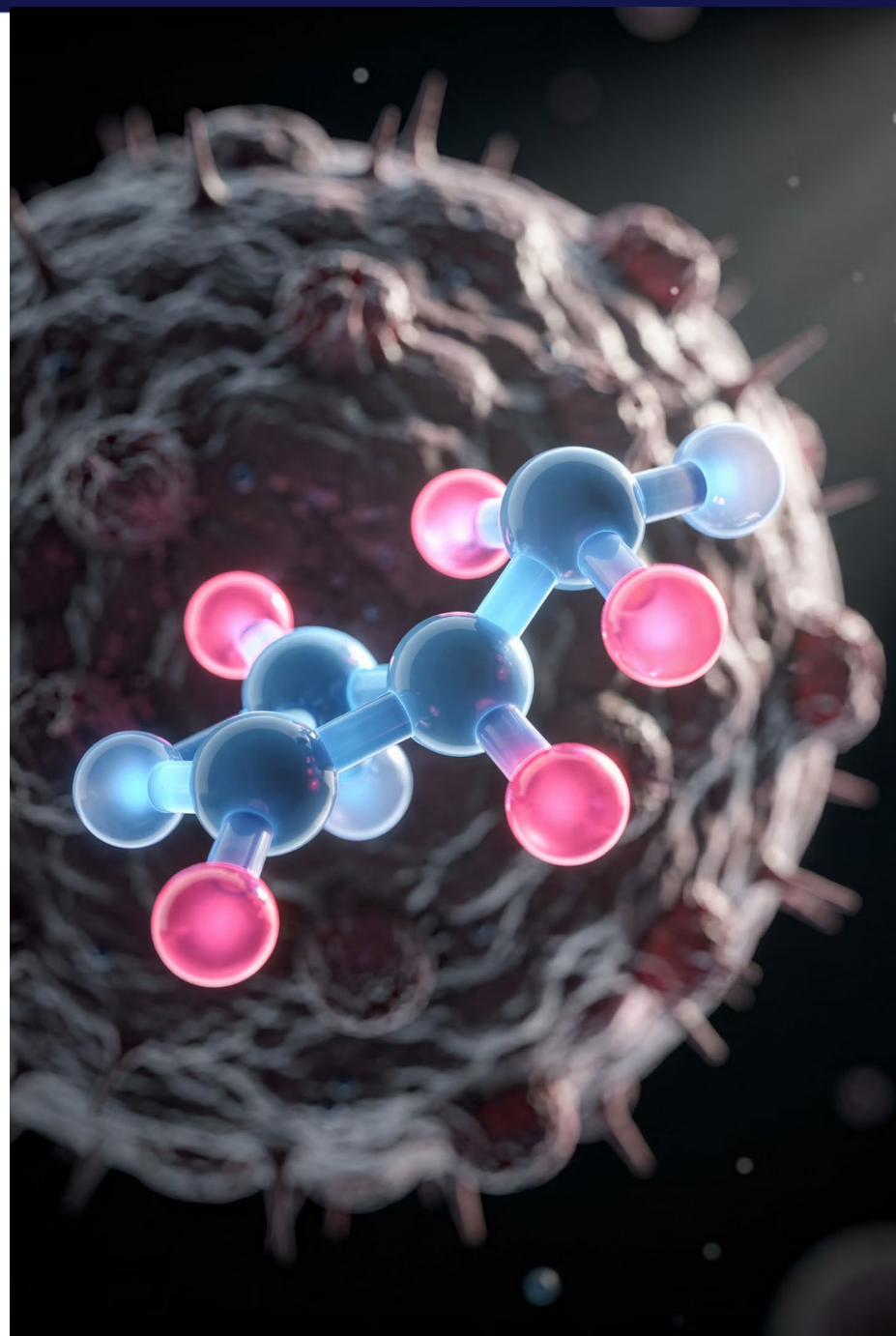
FRα	Advantage: High selectivity; validated PS2+ scoring. Limit: Drops in platinum-resistant disease.
TROP2	Advantage: Strong in cervical and endometrial cancer. Limit: Lung/GI expression raises toxicity risk.
HER2 / HER3	Advantage: Broadly actionable in endometrial, cervical, serous. Limit: Resistance overlap; low expression remains difficult.
B7-H4 / CDH6 / NaPi2b	Advantage: High ovarian/endometrial expression; limited target overlap. Limit: Early data; no approved agents.

Barquin A, et al. Cancer. 2026;e70417; Bujnak A, et al. Gynecologic Oncology, 2025; 195, 180-191

Payload Chemistry: The Warhead Defines The Weapon

Payload choice drives:

- Potency
- Cell-Kill Mechanism
- Tolerability
- Bystander Effect



Beck A et al. Nat Rev Drug Discov. 2017;16:315–337.

Payloads

DM4 · DXd · MMAE · SN-38 — Key Distinctions

DM4 (maytansinoid)	**Microtubule inhibitor:** High potency; modest bystander effect.
MMAE (auristatin)	**Microtubule inhibitor:** Cell-permeable; potent bystander effect.
DXd (camptothecin)	**Topo I inhibitor:** Membrane-permeable; strong bystander effect.
SN-38 (irinotecan metabolite)	**Topo I inhibitor:** Lower potency; high DAR; moderate bystander effect.

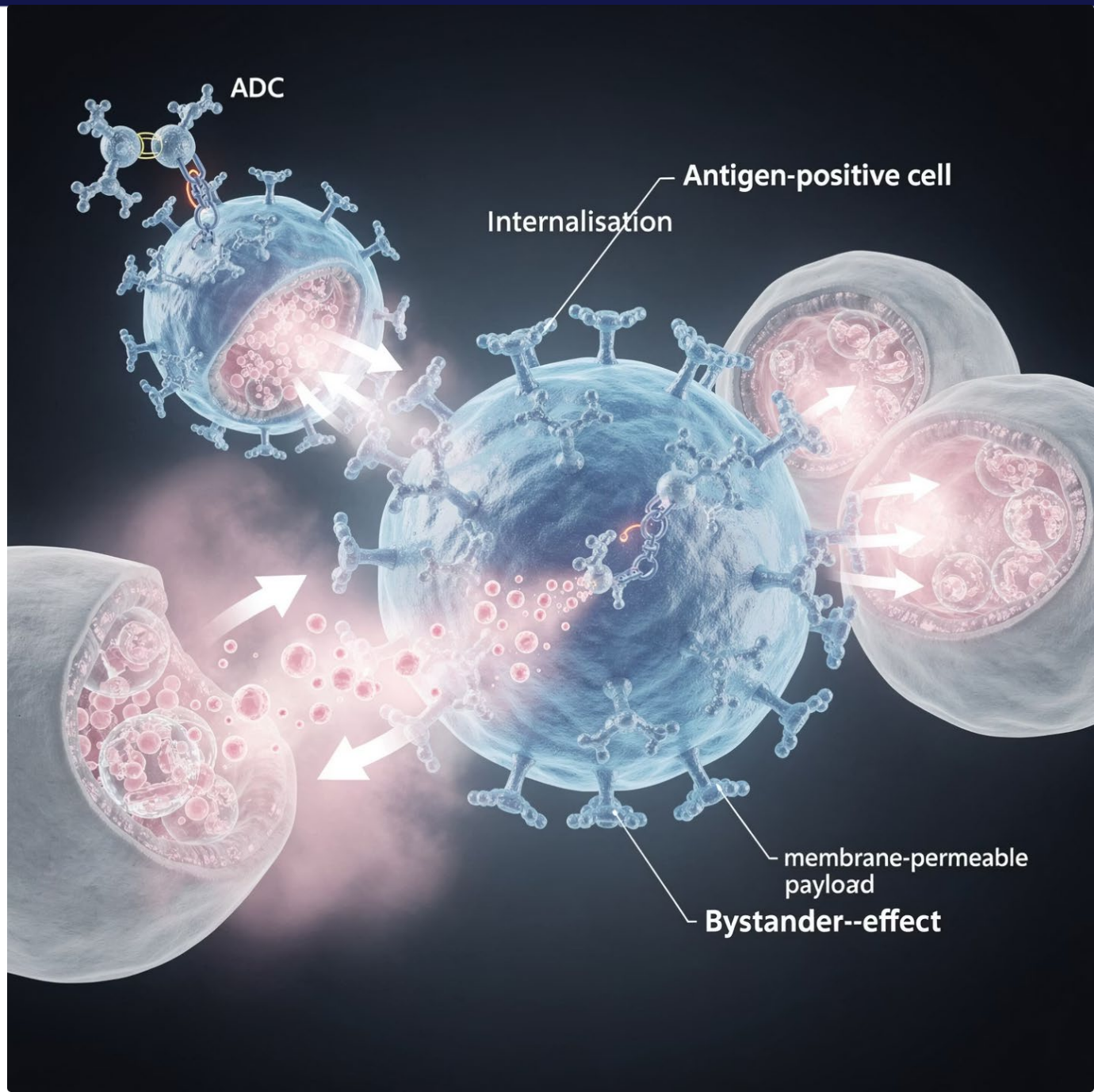
Bystander Effect

Why Membrane Permeability Changes Everything

Clinical Relevance

Heterogeneous tumors.

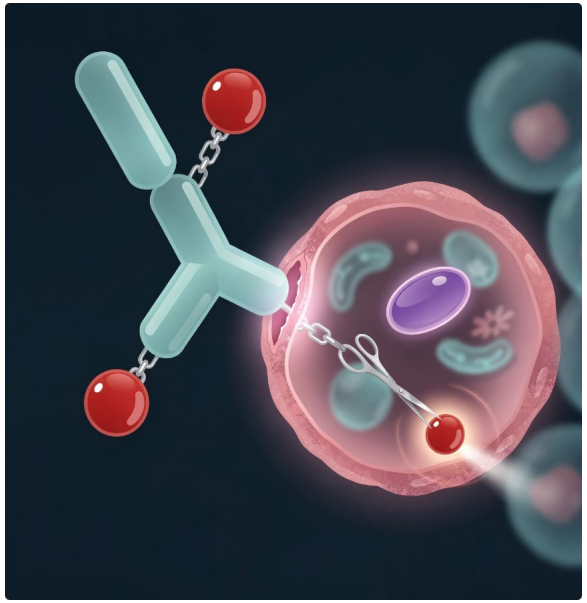
Permeable payloads reach neighbors.



Wang Y, et al. Crit Rev Oncol Hematol. 2025;216:104979.

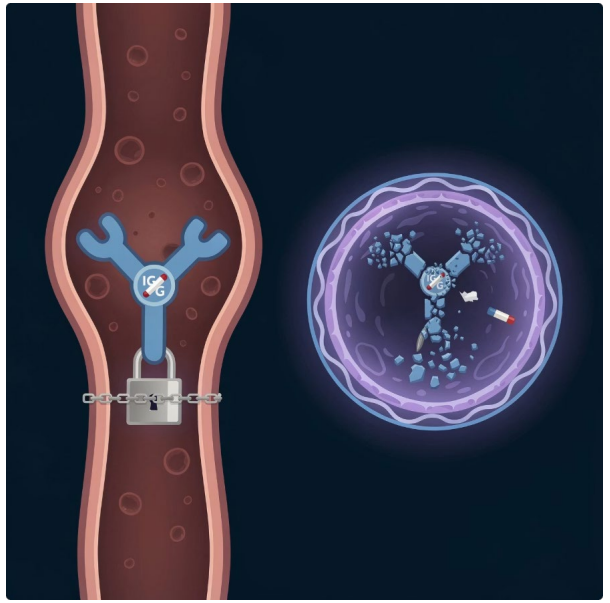
Linker Biology

Stability, Cleavage, and the Therapeutic Window



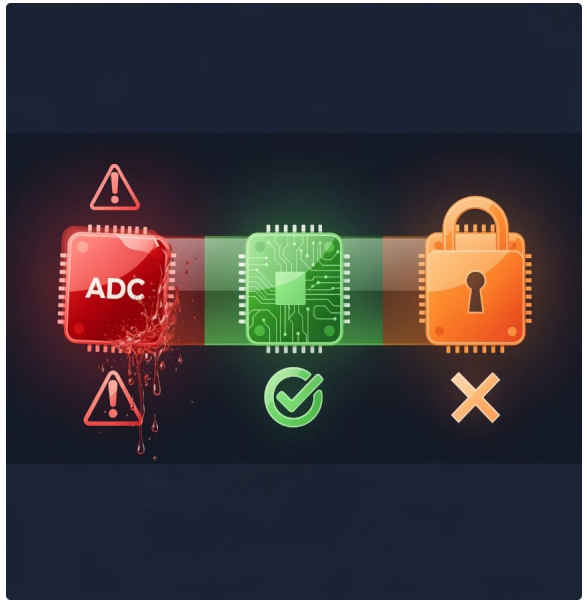
Cleavable Linkers

Cleaved intracellularly; can enable bystander effect.



Non-Cleavable Linkers

More stable in circulation; release requires degradation.



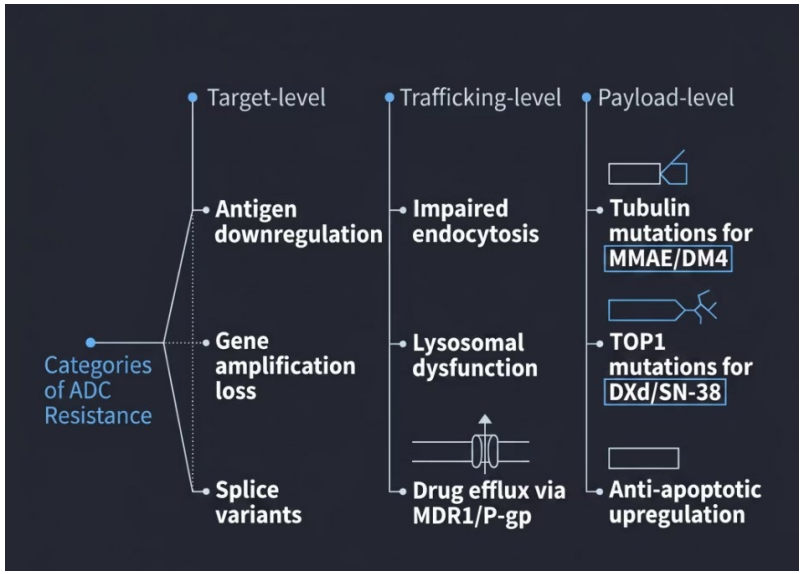
Stability vs. Efficacy

Find the balance between toxicity and tumor kill.

Fu Z, et al. Signal Transduct Target Ther. 2022;7(1):93; Su Z, et al. Acta Pharm Sin B. 2021;11(12):3889-3907.

Linker Biology

How Tumors Escape ADC Therapy

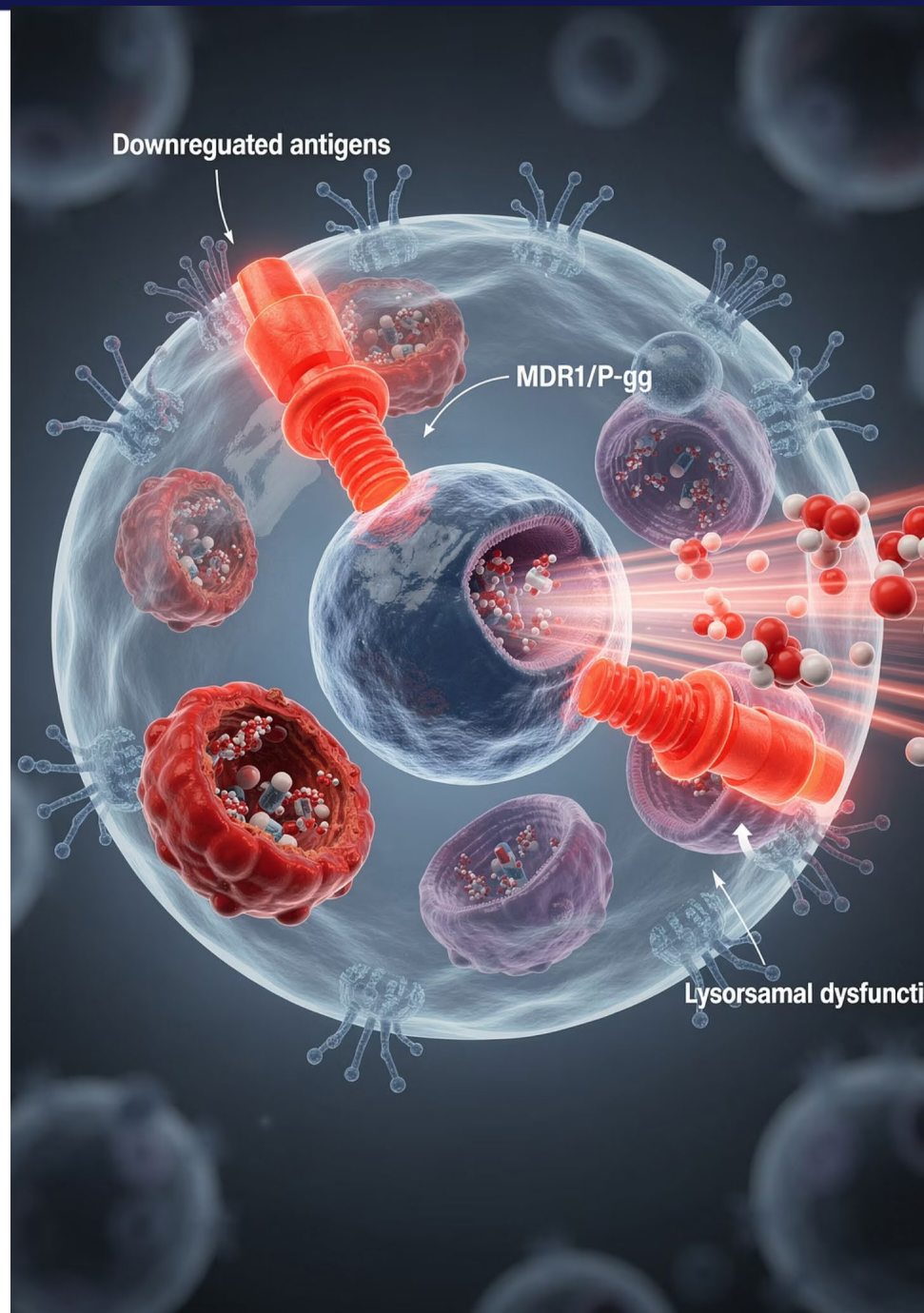


Translational Implications

Target loss is the most documented mechanism; re-biopsy and serial biomarker monitoring are key.

MDR1/P-gp efflux hits MMAE/DM4 most; DXd may retain activity in heavily pretreated disease.

Combo approaches: efflux inhibition or ADC + PARP inhibitor.



Linker Biology

Managing ADC-Related Toxicities

Proactive monitoring and timely intervention are crucial for patient safety.

Ocular Toxicity (Tisotumab)

- **Watch for:** Conjunctivitis, keratitis, dry eyes, vision changes.
- **Management:** Prophylactic eye drops, ophthalmology consult, dose modification.

ILD / Pneumonitis (DXd-based)

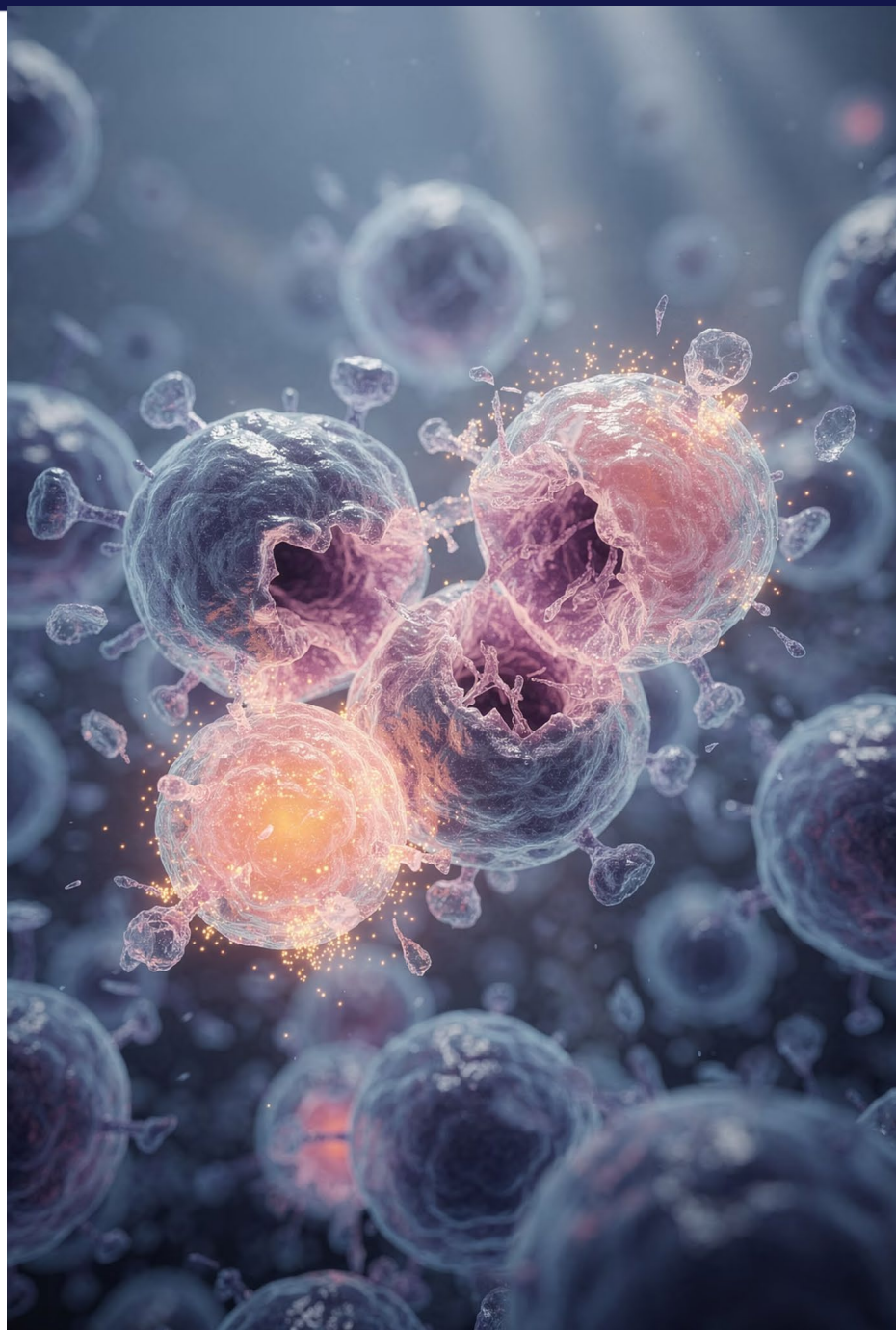
- **Watch for:** Cough, dyspnea, fever, new pulmonary infiltrates.
- **Management:** High-dose corticosteroids, oxygen, permanent ADC discontinuation.

Peripheral Neuropathy (MMAE)

- **Watch for:** Numbness, tingling, pain, motor weakness (G1-2).
- **Management:** Dose reduction/hold, gabapentin for symptoms, PT.

Hematologic Toxicity

- **Watch for:** Neutropenia, anemia, thrombocytopenia (G3-4).
- **Management:** G-CSF support, transfusions, dose modifications.



Synthesis

Connecting Target, Payload, and Linker to Clinical Outcomes

ADC	Target	Payload	Linker	Clinical Signal
Mirvetuximab	FRα	DM4	SPDB	OS benefit
Trastuzumab deruxtecan	HER2/HER3	DXd	Tetrapeptide	HER2-low activity
Tisotumab vedotin	Tissue factor	MMAE	Val-cit	Cervical cancer
Sacituzumab govitecan	TROP2	SN-38	pH-cleavable	High DAR
Upifitamab rilsodotin	TROP2	DM21	Cleavable	Phase II

DAR, drug-to-antibody ratio; DM4, maytansinoid microtubule inhibitor; DXd, exatecan derivative; FRα, folate receptor alpha; HER2, human epidermal growth factor receptor 2; MMAE, monomethyl auristatin E; SN-38, 7-ethyl-10-hydroxycamptothecin; TROP2, trophoblast cell-surface antigen 2.

Moore KN et al. N Engl J Med. 2023;389:2162–2174;; Meric-Bernstam F et al. J Clin Oncol. 2024;42:47–58; Coleman RL et al. Lancet. 2021 22;609-619; Vergote I, et al. N Engl J Med. 2024;391(1):44-55; Santin AD, et al. J Clin Oncol. 2024;42(29):3421-3429.

Clinical Landscape

Key ADC Trials in Gynecologic Oncology

Trial	ADC / Target	Indication	Status
MIRASOL	Mirvetuximab / FRα	Ovarian cancer	Approved
DESTINY-PanTumor02	T-DXd / HER2/HER3	Gynecologic cancers	Positive data
innovaTV 204/301	Tisotumab / Tissue factor	Cervical cancer	Approved
EVOKE-01	Sacituzumab / TROP2	Endometrial cancer	Phase III
Emerging	NaPi2b / B7-H4	Ovarian/ Endometrial	Early phase

Future Directions: Next-Gen ADCs & Emerging Strategies

Pushing the boundaries of targeted therapy in gynecologic oncology.

Bispecific ADCs

Enhanced targeting specificity for complex tumor microenvironments.

Higher DAR Constructs

Increased drug delivery and potency with optimized drug-antibody ratios.

ADC + Immunotherapy

Synergistic anti-tumor effects by combining targeted delivery with immune activation.

ADC + PARP Inhibitors

Strategies to overcome DNA repair resistance, especially in ovarian cancer.

Novel Payloads

Exploring new mechanisms like Topoisomerase II and RNA polymerase inhibitors.

Key Takeaways for Clinical Practice

1. **Targets Are Not Equal**
   Match ADC to histology and biomarker strategy.

2. **Payload Drives Toxicity Profile**
   Payload class predicts key toxicities.

3. **Linker Chemistry Shapes Bystander Effect**
   Cleavable linkers enable bystander killing; non-cleavable linkers do not.

4. **Resistance Is Multimodal**
   Consider antigen loss, efflux, and payload mutations.

A Conversation: Integrating Disease Management: Sequencing, Selection, and Safety

All Faculty

Case 1

- 65 yo with sBRCA1 mutated high grade serous ovarian ca
- Completed upfront treatment in 2023, maintenance: bevacizumab x 1 year, Olaparib x 20 months
- 2025, widespread carcinomatosis. Treated with Carbo/PLD/Bev
  - Progressed after 4 cycles
- 5 cm mesenteric mass biopsied
  - FOLR1 40%
  - HER2 2+
  - PDL1 pos

Case 1 *(continued)*

- 5 cm mesenteric mass biopsied
  - FOLR1 40%
  - HER2 2+
  - PDL1 pos
- No trials available at your institution, and patient does not want to transfer out
- Treatment options?
  - Efficacy concerns?
  - Toxicity concerns?
  - Sequencing concerns?

ROSELLA: Relacorilant + Nab-Paclitaxel vs Nab-Paclitaxel monotherapy in patients With PROC1,2

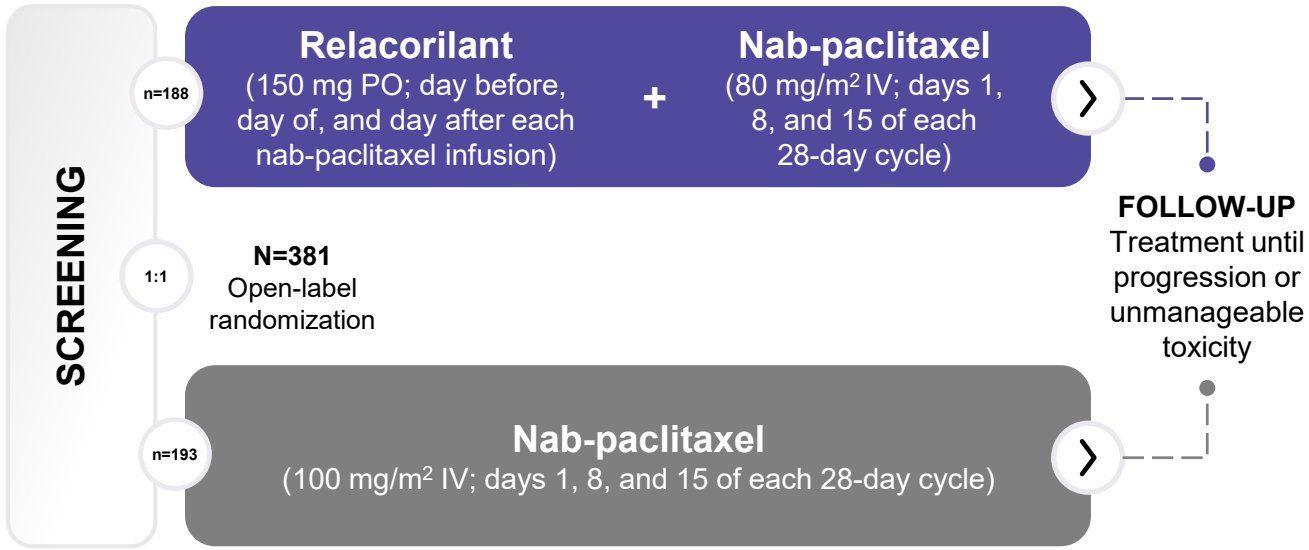
- The efficacy of Relacorilant was evaluated in ROSELLA (NCT05257408), a phase 3, multicenter, open-label, active-controlled, randomized trial in patients (intent-to-treat population N=381) with platinum-resistant epithelial ovarian, fallopian tube, or primary peritoneal cancer

Key Eligibility Criteria

- Platinum-resistant disease: PFI >1 month and <6 months
- ECOG PS 0 or 1
- 1 to 3 prior lines of therapy
- Prior bevacizumab
- Excluded chronic, systemic corticosteroids

Stratification Factors

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



The 80 mg/m² dose of nab-paclitaxel, in combination with Relacorilant (a CYP3A4 inhibitor), provided exposure comparable to the 100 mg/m² monotherapy dose in the Phase 2 study.[1,3]

Dual Primary Endpoints

- OS[a]
- PFS by RECIST BICR[b]

Select Secondary Endpoints

- ORR
- CBR at 24 weeks
- Safety

Conducted at 117 sites in 14 countries

Fully enrolled in 15 months

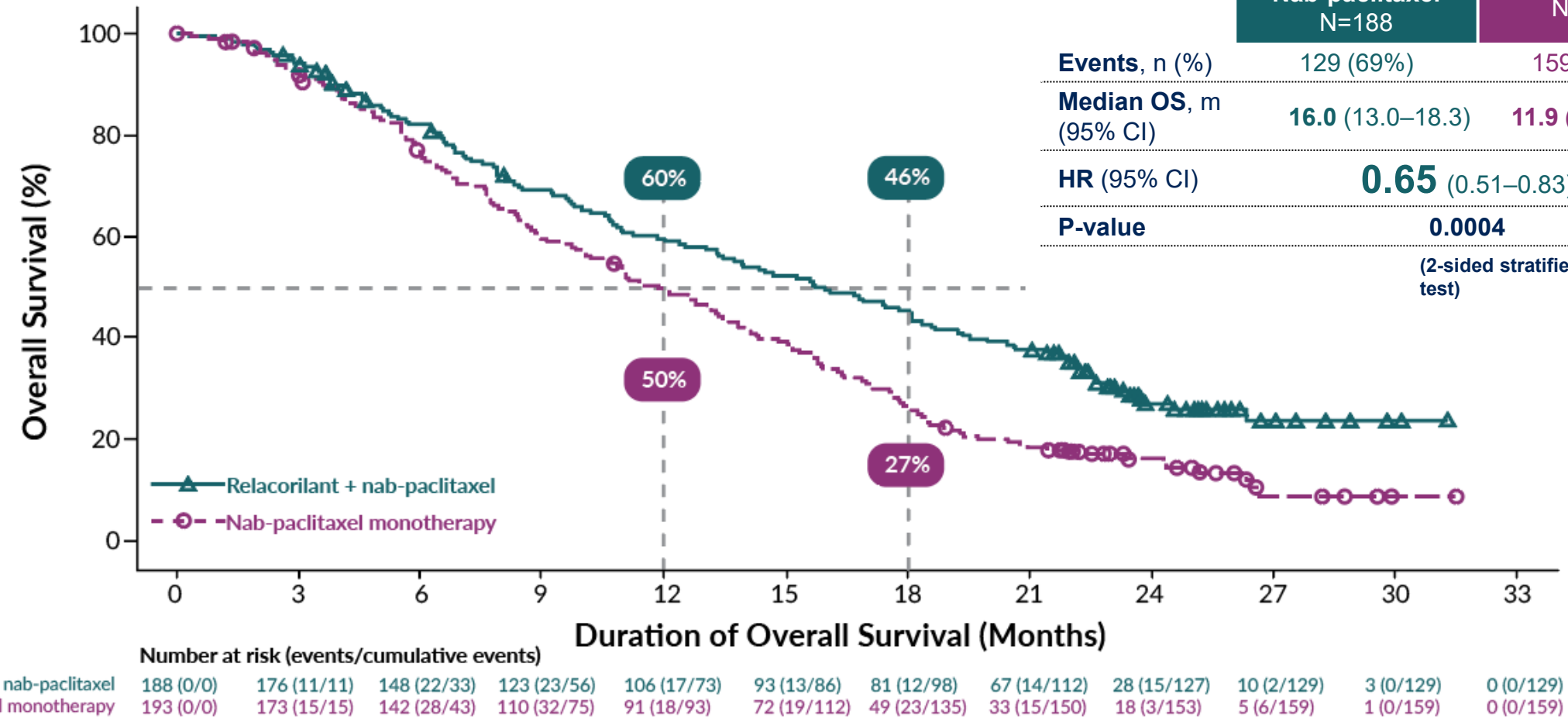
Data cutoff: January 8, 2026.

[a]Defined as the time from randomization to death; [b]Defined as the time from randomization until first documented progressive disease by RECIST v1.1 per BICR, or death, whichever occurred first.

BICR, blinded independent central review; CBR, clinical benefit rate; ECOG, Eastern Cooperative Oncology Group; IV, intravenous; ORR, objective response rate; OS, overall survival; PFI, platinum-free interval; PFS, progression-free survival; PO, by mouth; PS, performance status; RECIST, Response Evaluation Criteria in Solid Tumors.

1. Relacorilant. Prescribing information. Corcept Therapeutics Incorporated; 2026; 2. Olawaiye AB, et al. Lancet. 2025;405(10496):2205-2216; 3. Colombo N, et al. J Clin Oncol. 2023;41(30):4779-4789. ClinicalTrials.gov, NCT05257408; ClinicalTrials.gov identifier: NCT03776812

ROSELLA | Relacorilant Improved Overall Survival at the Final Analysis



	Relacorilant + Nab-paclitaxel N=188	Nab-paclitaxel N=193
Events, n (%)	129 (69%)	159 (82%)
Median OS, m (95% CI)	**16.0** (13.0–18.3)	**11.9** (10.0–13.8)
HR (95% CI)	**0.65** (0.51–0.83)	
P-value	**0.0004**	

(2-sided stratified log-rank test)

76% maturity

Number at risk (events/cumulative events)

Relacorilant + nab-paclitaxel	188 (0/0)	176 (11/11)	148 (22/33)	123 (23/56)	106 (17/73)	93 (13/86)	81 (12/98)	67 (14/112)	28 (15/127)	10 (2/129)	3 (0/129)	0 (0/129)
Nab-paclitaxel monotherapy	193 (0/0)	173 (15/15)	142 (28/43)	110 (32/75)	91 (18/93)	72 (19/112)	49 (23/135)	33 (15/150)	18 (3/153)	5 (6/159)	1 (0/159)	0 (0/159)

Median follow-up time: 24.8 months; 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% CIs for OS 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; OS, overall survival.

Data cutoff: Jan 8, 2026

Olawaiye AB, et al. Presented at SGO Annual Meeting 2026 (Abstract LBA01). Figure adapted from Olawaiye AB, et al. ClinicalTrials.gov, NCT05257408

Combining Pembrolizumab Plus Weekly Paclitaxel +/- Bevacizumab for Platinum-Resistant Recurrent Ovarian Cancer

ENGOT-ov65/KEYNOTE-B96 Study Design

Key Eligibility Criteria

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

Stratification Factors

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

R 1:1
N = 643

Pembrolizumab 400 mg (Q6W, 18 cycles) +
Paclitaxel[a] 80 mg/m² Days 1, 8, 15 of each Q3W cycle
(± bevacizumab 10 mg/kg Q2W)

Placebo (Q6W, 18 cycles) +
Paclitaxel[a] 80 mg/m² Days 1, 8, 15 of each Q3W cycle
(± bevacizumab 10 mg/kg Q2W)

Primary Endpoint: PFS per RECIST v1.1 by investigator

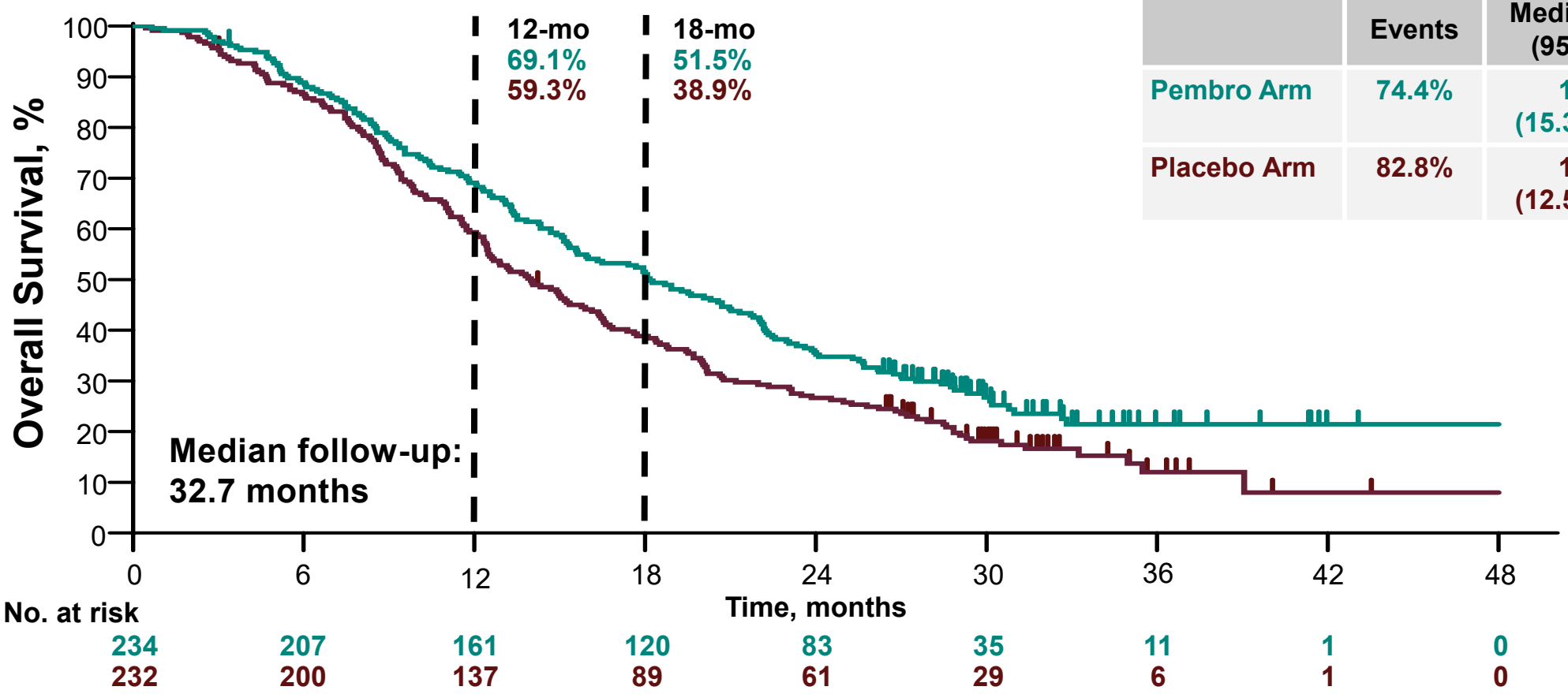
Key Secondary: OS

aDocetaxel (75 mg/m2 Q3W) may be considered in participants with severe hypersensitivity reaction to paclitaxel or an adverse event requiring discontinuation of paclitaxel after consultation with the Sponsor.
bThe combined positive score (CPS) was assessed at a central laboratory using PD-L1 IHC 22C3 pharmDx and defined as the number of PD-L1 CPS ≥1 cells (tumor cells, lymphocytes, macrophages) divided by the total number of tumor cells × 100.
Abbreviations: CPS, combined positive score; ECOG, Eastern Cooperative Oncology Group; OS, overall survival; PARPi, poly(ADP-ribose) polymerase inhibitor; PD-1, programmed cell death protein 1; PD-L1, programmed death ligand 1; PFS, progression-free survival; Q2W, every 2 weeks; Q3W, every 3 weeks; Q6W, every 6 weeks; RECIST, Response Evaluation Criteria in Solid Tumors.

Monk BJ, et al. Presented at SGO Annual Meeting 2026. Figure adapted from Monk BJ, et al. ClinicalTrials.gov, NCT05116189; Colombo N, et al. Lancet. 2026;407(10538):1525-1537

KEYNOTE B96

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. The observed p-value crossed the prespecified nominal boundary of 0.0242 at this planned final analysis. Data cutoff date: September 5, 2025.*

Monk BJ, et al. Presented at SGO Annual Meeting 2026. Figure adapted from Monk BJ, et al. ClinicalTrials.gov, NCT05116189; Colombo N, et al. Lancet. 2026;407(10538):1525-1537.

Case 1 *(continued)*

- Available markers:
  - FOLR1 40%
  - HER2 2+
  - PDL1 pos

- Patient started on weekly nab-pac/relacorilant
- Progression after 6 cycles
- Considerations for next line? She's now willing to transfer out for trial
  - Standard of care options
  - Which novel therapeutics are you most excited about?
    - What would change if she were FOLR1 10%, HER2 1+?

Inferential cross-trial comparisons for Anti-FRα ADCs in OC

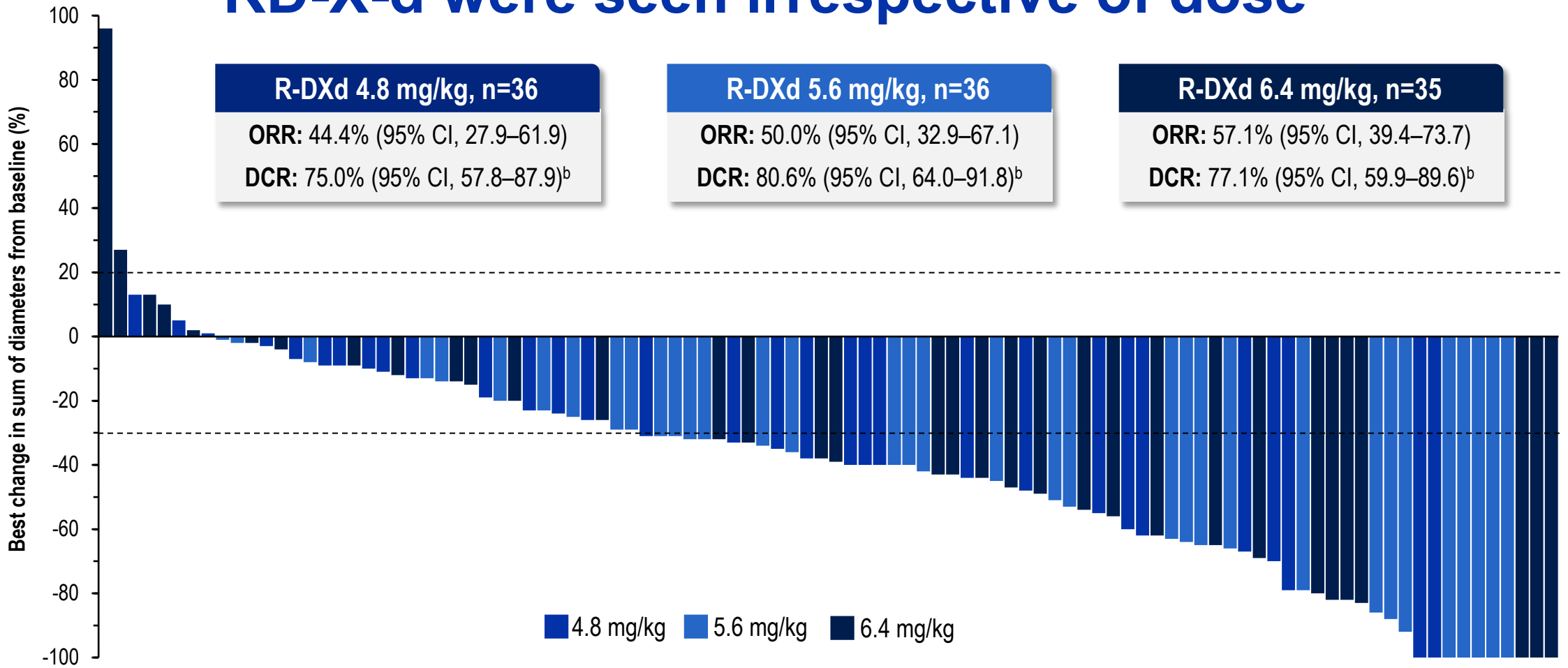
Project	Company	Trial	ORR in all-comers	ORR in FRα ≥75%	ORR in FRα <75%	ORR in FRα <25%
Mirv	AbbVie (ex ImmunoGen)	Mirasol	42% (n=225)	42% (n=225)	Not tested	Not tested
Rina-S	Genmab (ex ProfoundBio)	Rainfol-01	38% (n=40)	68% (n=13)	30% (n=23)	Not split out
Sofe-M	Lilly (ex Mablink)	LOXO-FRA-24001	50% (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.

ADC, antibody-drug conjugate; FRα, folate receptor alpha; MIRV, mirvetuximab soravtansine; Rina-S, rinatabart sesutecan; Sofe-M, sofituzumab mipitecan ; Torvuta-S, torudotatug deruxtecan; OC, ovarian cancer; ORR, objective response rate.

Moore KN et al. N Engl J Med. 2023;389:2162–2174 (NCT04209855); Ray-Coquard IL, et al. Presented at: ESMO Congress 2025. Abstract 809P. NCT06400472; Oaknin A, et al. Presented at ESMO Congress 2025. Abstract #1065MO (NCT05797168).

Targeting CDH6: Tumor responses to RD-X-d were seen irrespective of dose[a]



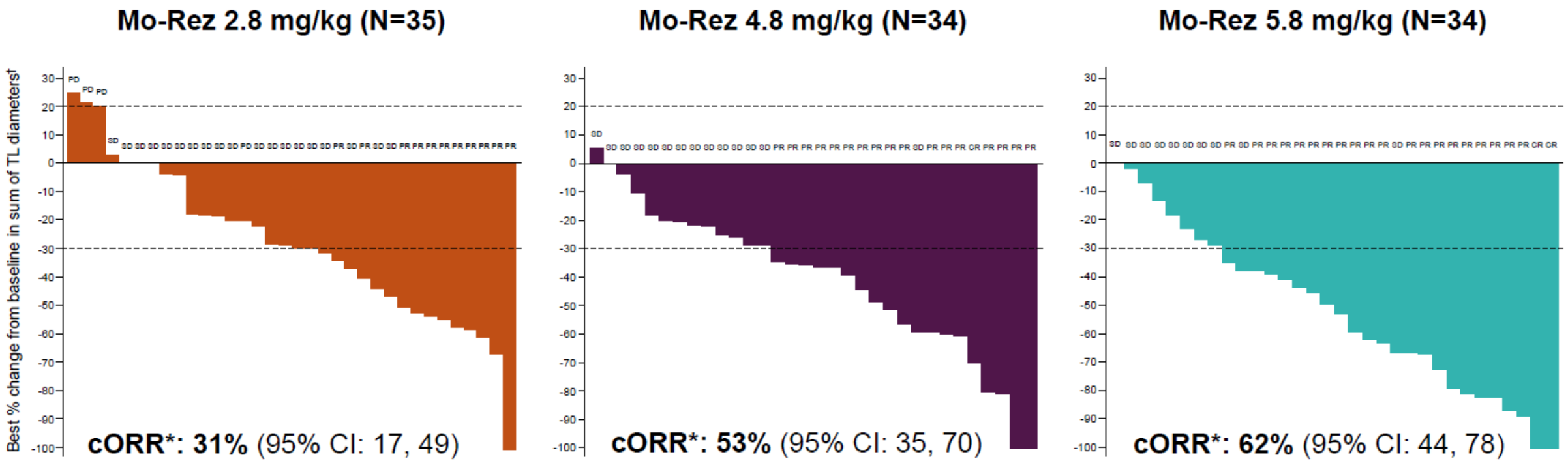
Data cutoff: February 26, 2025. The median follow-up for 4.8-mg/kg, 5.6-mg/kg, and 6.4-mg/kg cohorts was 5.6 months (95% CI, 4.7–6.3), 5.6 months (95% CI, 4.6–5.8), and 5.2 months (95% CI, 4.9–5.8), respectively.

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

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

Ray Coquard I. et al. Presented at ESMO 2025; (presentation #LBA42) (NCT06161025); *Figure adapted from Ray Coquard I et al.*

Targeting B7-H4—Mocertatug Rezetecan (PROC)



Responses were observed across a range of B7-H4 expression levels

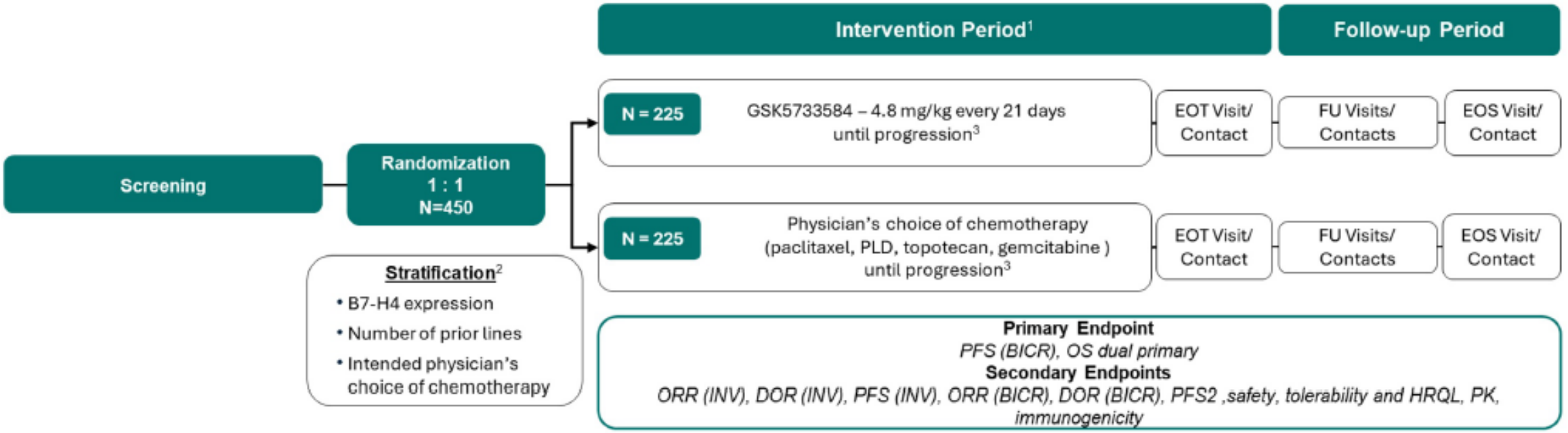
Oaknin, A. et al., presented at SGO 2026 (NCT06431594)

Median (IQR) follow-up was 6.1 (4.7, 6.8) months for the overall cohort (N=131)

BEHOLD-1

Efficacy population: N=103.
*Confirmed ORR reported in all randomized patients who had the opportunity for ≥18 weeks of follow-up;†waterfall plots show confirmed best overall response for patients with at least one post-baseline tumor assessment.
B7-H4, B7 homolog 4 protein; c, confirmed; CI, confidence interval; CR, complete response; Mo-Rez, mocertatug rezetecan; ORR, objective response rate; PD, progressive disease; PR, partial response; PROC, platinum-resistant ovarian cancer; Q3W, every 3 weeksSD, stable disease; TL, target lesion.

GOG-3132/BEHOLD-Ovarian01



B7-H4 = B7 homolog 4 protein; BICR = blinded independent central review; DOR = duration of response; EOS = end of study; EOT = end of treatment; FU = follow-up; HRQL = Health-related quality of life; INV = investigator; N = number of participants; ORR = objective response rate; OS = overall survival; PD = progressive disease; PFS = progression-free survival; PFS2 = time from randomization to objective progression on first subsequent anticancer therapy or death from any cause; PK = pharmacokinetic(s); PLD = pegylated liposomal doxorubicin; RECIST 1.1 = Response Evaluation Criteria in Solid Tumors, version 1.1; VoP = verification of progression.

[1] Participants should continue study intervention until disease progression per RECIST 1.1 (by investigator assessment), unacceptable toxicity, participant withdrawal, investigator's decision, loss to follow-up or death. Participants that are clinically stable at the time of investigator-assessed PD per RECIST 1.1 may continue treatment until PD is verified by BICR, whenever clinically feasible.

[2] B7-H4 expression (centrally assessed): Not evaluable or <25%, ≥25% to <50% and ≥50%; number of prior lines: 1 vs. 2/3/4; physician's choice chemotherapy: paclitaxel vs. others.

[3] Upon sponsor's approval, participants may continue to receive study intervention after PD per RECIST 1.1 (by investigator or BICR VoP) if the participant is clinically stable and the investigator deems that the participant is deriving clinical benefit from the treatment.

NCT07286266

Case 2

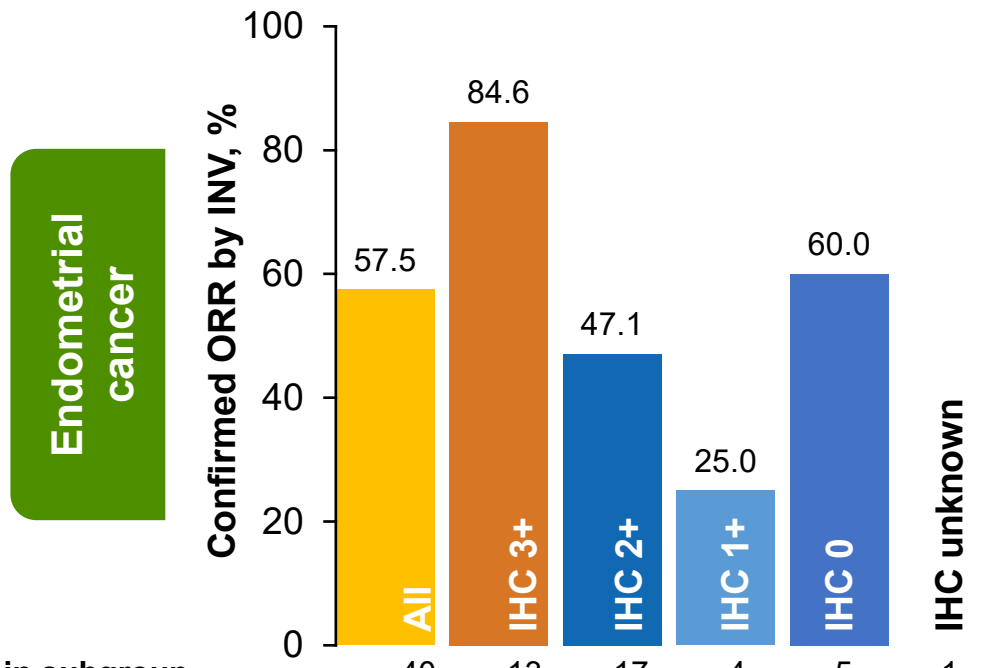
- 55 yo with Stage IVB uterine carcinosarcoma, no gross residual disease after upfront surgical debulking
  - pMMR, HER2 2+ FISH neg, p53mut, ER/PR neg
- 6 cycles 1L Carbo/paclitaxel/dostarlimab
- After 11 months disease free on dostarlimab maintenance, presents to ER with partial small bowel obstruction due to carcinomatosis and loculated ascites

Case 2 *(continued)*

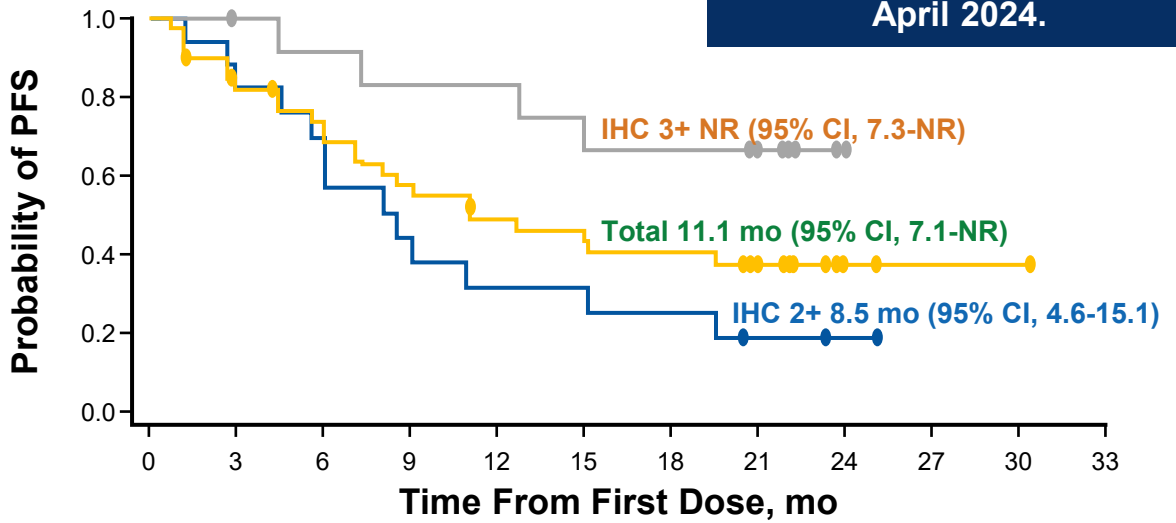
- Biomarkers: pMMR, HER2 2+ FISH neg, p53mut, ER/PR neg
- Treatment options
  - What are your considerations when selecting next line of therapy?
  - Do you have resistance concerns?
- Clinical trial options
  - What agents are you most excited about in this space?
  - Toxicity concerns?
  - Sequencing concerns

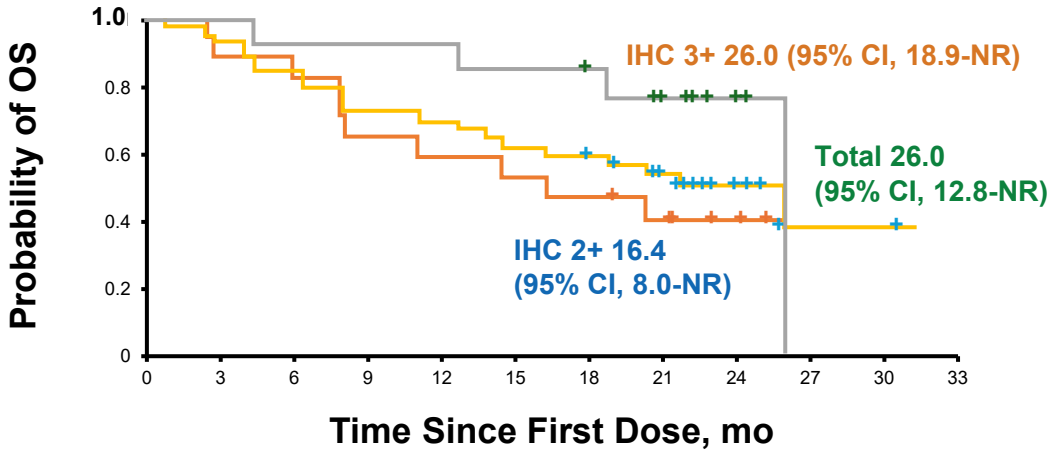
T-DXd: Efficacy by HER2 Status[1-3]

FDA granted accelerated approval to trastuzumab deruxtecan for unresectable or metastatic 3+HER2-positive solid tumors in April 2024.



	All	IHC 3+	IHC 2+	IHC 1+	IHC 0	IHC unknown
Total n in subgroup	40	13	17	4	5	1
n of responders	23	11	8	1	3	0
Median DOR, months[c]	**NR**	**NR**	**18.2**	**NR**	**9.9**	**-**
95% CI[d]	9.9, NE	9.6, NE	3.0, NE	-	2.8, NE	-





[a] HER2 status by central testing. [b] Similar ORR and DOR results were reported by retrospective independent central review. [c] Median DOR reported for patients with a confirmed an objective response only. [d] 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; NR, not reached; ORR, objective response rate; OS, overall survival; PFS, progression-free survival; T-DXd, trastuzumab deruxtecan.

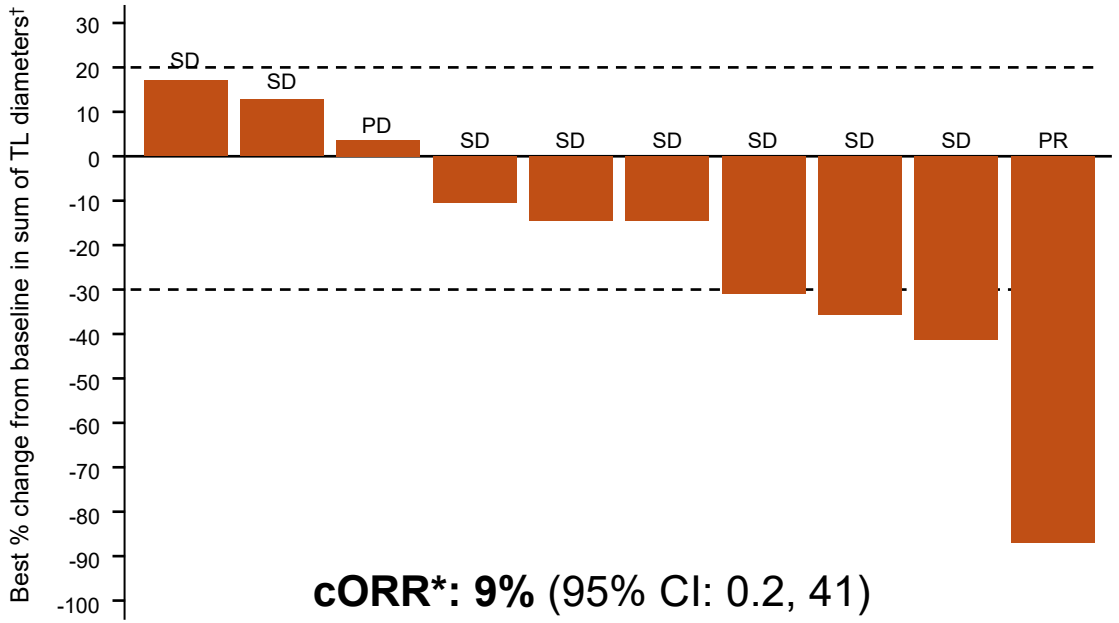
1. Lee J et al. Int J Gynecol Cancer. 2023;33:A6-A7. 2. Meric-Bernstam F et al. ESMO 2023. Abstract LBA34.
3. Meric-Bernstam F et al. J Clin Oncol. 2024;42:47-58.

Phase 1B Efficacy: EC

Confirmed ORR was 67% (n=8/12) in patients with EC at the 4.8 mg/kg Q3W dose

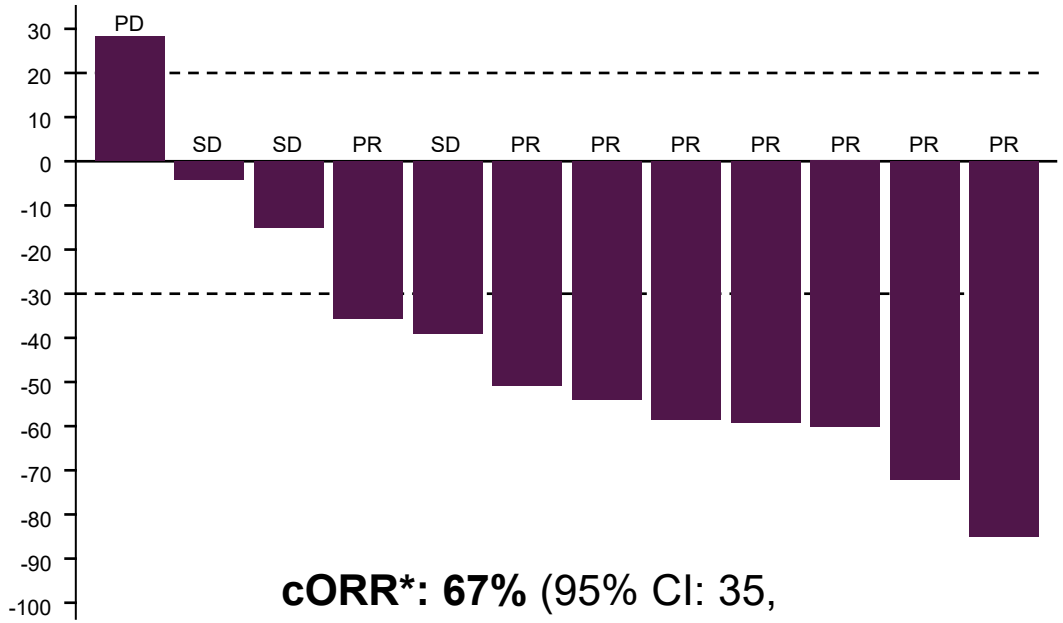
Scan Me

Mo-Rez 2.8 mg/kg (N=11)



cORR*: 9% (95% CI: 0.2, 41)

Mo-Rez 4.8 mg/kg (N=12)



cORR*: 67% (95% CI: 35, 90)

Responses were observed across a range of B7-H4 expression levels

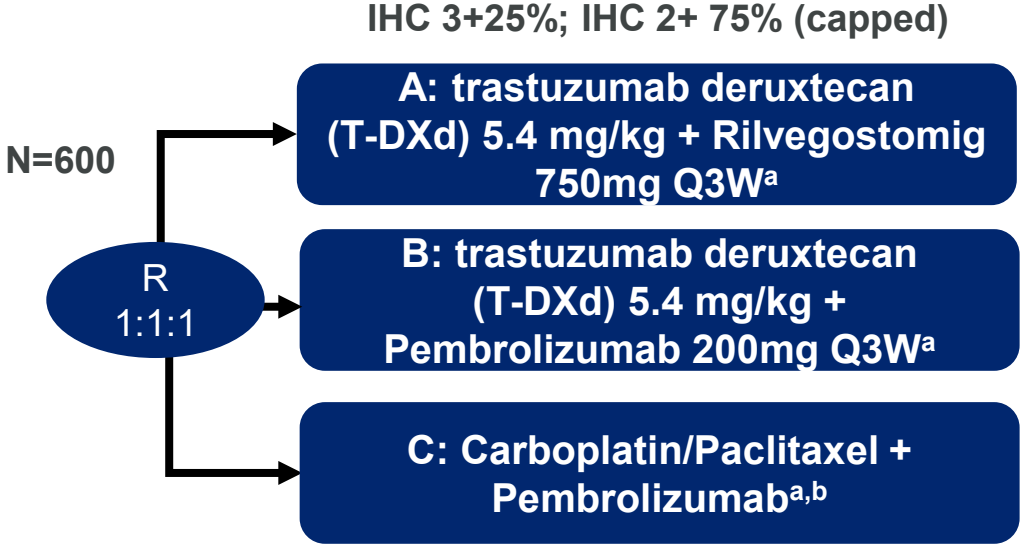
Median (IQR) follow-up was 4.0 (1.7, 5.8) months for the overall cohort (N=49)

BEHOLD-1

DESTINY-Endometrial01/ GOG-3098/ ENGOT-EN24: A Phase III Study of Trastuzumab Deruxtecan Plus Rilvegostomig or Pembrolizumab as First-Line Treatment of HER2-Expressing (IHC 3+/2+), Mismatch Repair Proficient (pMMR) Endometrial Cancer

Patient Population

- HER2 expressing (IHC 3+/2+) EC by central test
- pMMR EC by central test
- Stage III, Stage IV, or recurrent, histologically-confirmed endometrial cancer
- Stage III must have measurable disease
- Any histological subtype except for sarcomas
- May have received 1 prior line of adjuvant/ neoadjuvant chemotherapy (chemotherapy and/ or chemoradiation) if recurrence ≥ 6 months after last dose of chemo
- No prior exposure to ADCs or ICIs
- ECOG PS 0 or 1



Stratification factors:
- HER2 IHC 3+ vs 2+
- PD-L1 TAP ≥1% vs TAP <1%
- Asia vs Non-Asia

Endpoints

Primary:
- PFS (BICR) in ITT

Secondary:
- OS (key secondary endpoint)
- PFS (Investigator)
- ORR
- PFS2
- HRQoL

[a] Treatment will continue until objective disease progression according to RECIST v1.1 as assessed by the Investigator and confirmed by BICR or until other discontinuation criteria is met, whichever occurs first.
[b] Carboplatin AUC5, paclitaxel 175 mg/m2, and pembrolizumab 200 mg IV once Q3W x 6 cycles*, followed by maintenance with pembrolizumab 400 mg IV Q6W. Treatment with pembrolizumab will continue for up to 20 total cycles (approximately 24 months, accounting for combination and maintenance phases) or until other discontinuation criteria is met, whichever occurs first.
* At the discretion of the treating Investigator, participants may continue to receive carboplatin, paclitaxel and pembrolizumab Q3W for up to 10 cycles.
Slomovitz BM, et al. Ann Oncol. 2025;36(suppl 2):S791-S792.
ADC, antibody–drug conjugate; BICR, blinded independent central review; ECOG, Eastern Cooperative Oncology Group; EC, endometrial cancer; HER2, human epidermal growth factor receptor 2; HRQoL, health-related quality of life; ICI, immune checkpoint inhibitor; IHC, immunohistochemistry; ITT, intention-to-treat; ORR, objective response rate; OS, overall survival; PD-L1, programmed death-ligand 1; PFS, progression-free survival; PFS2, progression-free survival 2; pMMR, mismatch repair–proficient; Q3W, every 3 weeks; TAP, tumor area positivity.

NCT06989112

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NSGO-CTU Nordic Society of Gynaecological Oncology - Clinical Trial Unit

TroFuse-033: Ph3, Randomized, Open-label, 1L sac-TMT Maintenance in TROP2 all-comer pMMR Endometrial Cancer (NCT06952504)

Participants:
- 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 Stage III or measurable/non-measurable Stage IV)
- Available tissue to test for TROP2 / MMR / p53
- ECOG 0 to 1

Induction

N ~ 1123

6 cycles[1]

Carboplatin
Paclitaxel
Pembrolizumab
q3w

Without PD

Eligibility for Randomization:
- Without PD as determined by INV
- Completed 6 cycles of Induction
- AEs resolved to ≤ Grade 1
- ECOG 0 to 1
- Valid TROP2 result from central lab

Maintenance

Randomize 1:1
N ~ 842

sac-TMT 4 mg/kg q2w + Pembrolizumab q6w

Pembrolizumab q6w

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

PD

Subsequent Treatment[3]:

sac-TMT +/- Pembrolizumab

Dual Primary Endpoints
(using a TROP2 enrichment strategy)

- PFS (BICR)
- OS

[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

BICR = blinded independent central review, ECOG = Eastern Cooperative Oncology Group, INV = investigator, MMR = mismatch repair, PD = progressive disease, PFI = platinum-free interval, pMMR = proficient mismatch repair, TROP2 = trophoblast cell-surface antigen 2

Eminowicz G, et al. International Journal of Gynecological Cancer, 2026, 36(2), Supp 1, 204392.

Additional Considerations

- In real world, community practice, what do you see as the biggest barriers to adoption of novel therapeutics in Gyn Oncology?

- As new treatments have become available, have you experienced institutional/insurance constraints to use?

Panel Discussion: Who Leads the Next Wave

All Faculty

Audience Q&A and Closing Remarks

All Faculty

Thank You

GSK

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