ADC's (anticuerpos conjugados a fármacos) en cáncer de ovario

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4ª jornada de actualización en cáncer ginecológico

Bilbao 20/5/2026

Disclousures

GSK, Advisory Board, Personal

Astra-Zeneca, Advisory Board, Personal

Roche, Advisory Board, Personal

pharma&, Advisory Board, Personal

AbbVie, Advisory Board, Personal

GSK, Invited Speaker, Personal

Astra-Zeneca, Invited Speaker, Personal

Roche, Invited Speaker, Personal

MSD, Other, Personal, Congrees fees and travel expenses

GSK, Other, Personal, Congress fees

ADC's: nowaday's oncology revolution

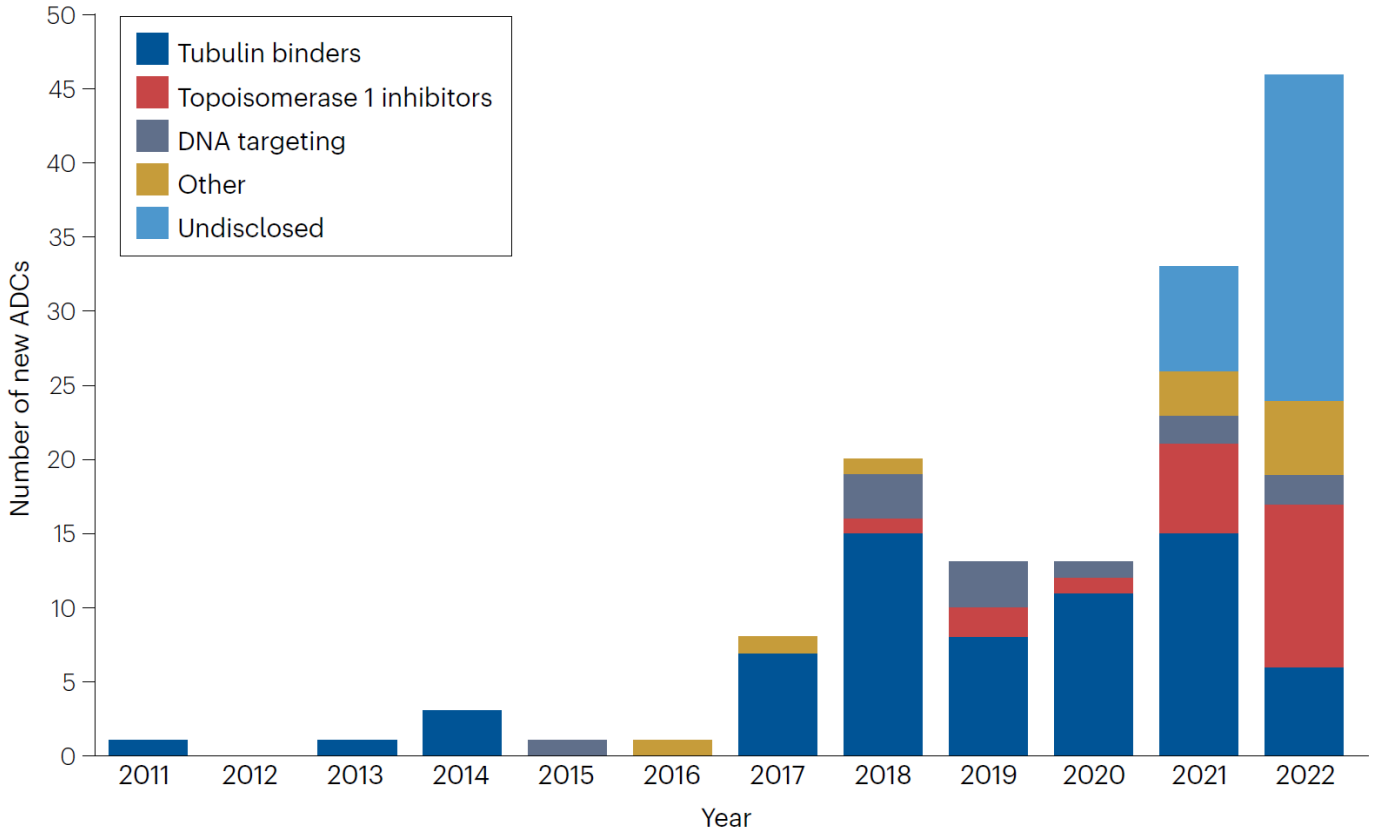
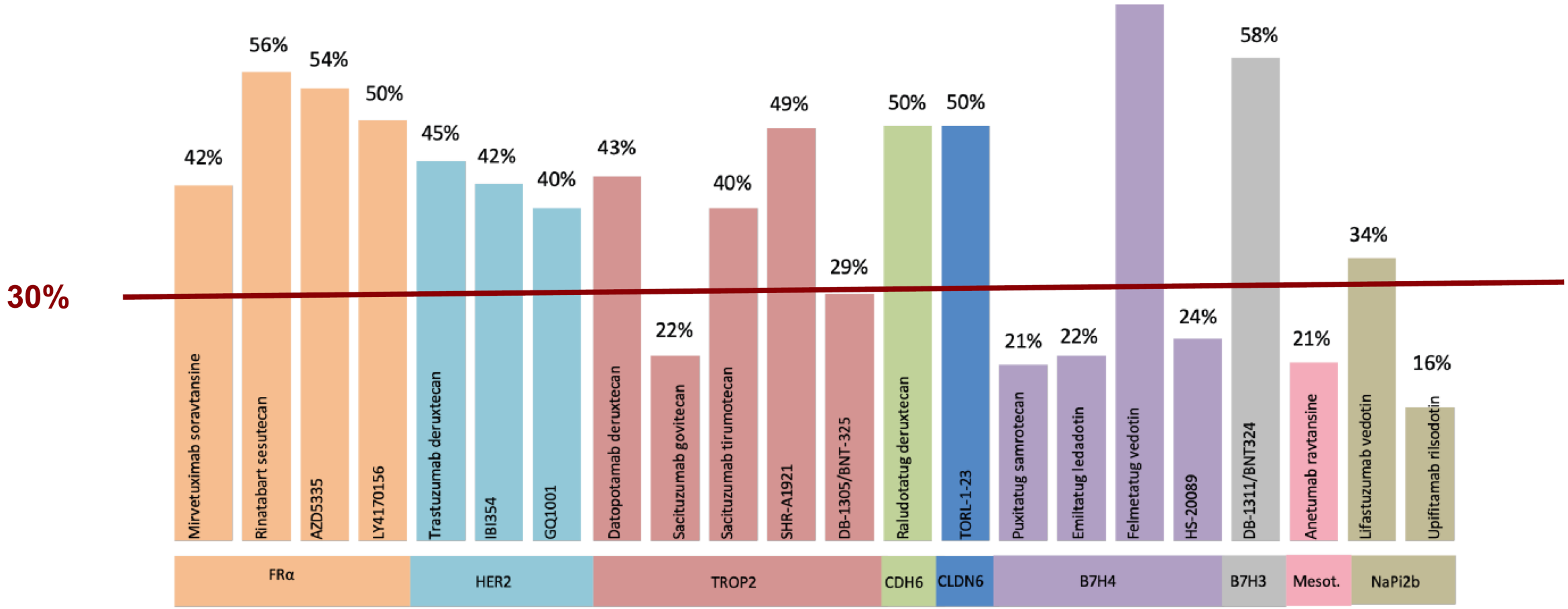


Fig. 4 | Number of new ADCs reaching clinical trials between 2012 and 2022. The number of new ADCs entering clinical evaluation has rapidly increased over the past few years. The fraction of topoisomerase 1 inhibitor-containing ADCs has increased since 2021. There is an increasing fraction of undisclosed payloads (48% in 2022).

>200 nuevos ADC's en desarrollo

Dumontet C, et al Nature reviews drug discovery 2023 https://doi.org/10.1038/s41573-023-00709-2

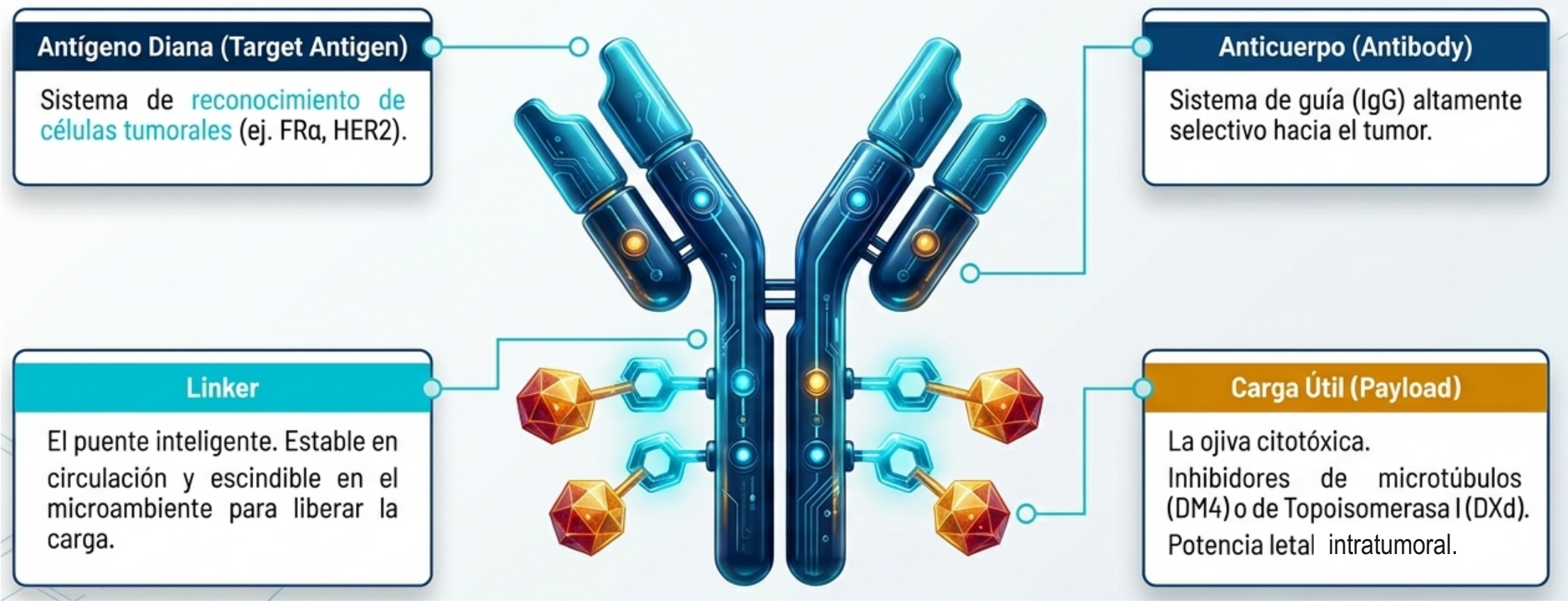
ADCs are the near future of ovarian cancer patients
Efficacy from available data



ADC

- Conceptos básicos ADC’s
- ADC’s aprobados
- ADC’s desarrollo: datos fase 1/2
- Retos futuros
- Conclusiones

Estructura ADC



Mechanism of action & ADC's efficacy and toxicity

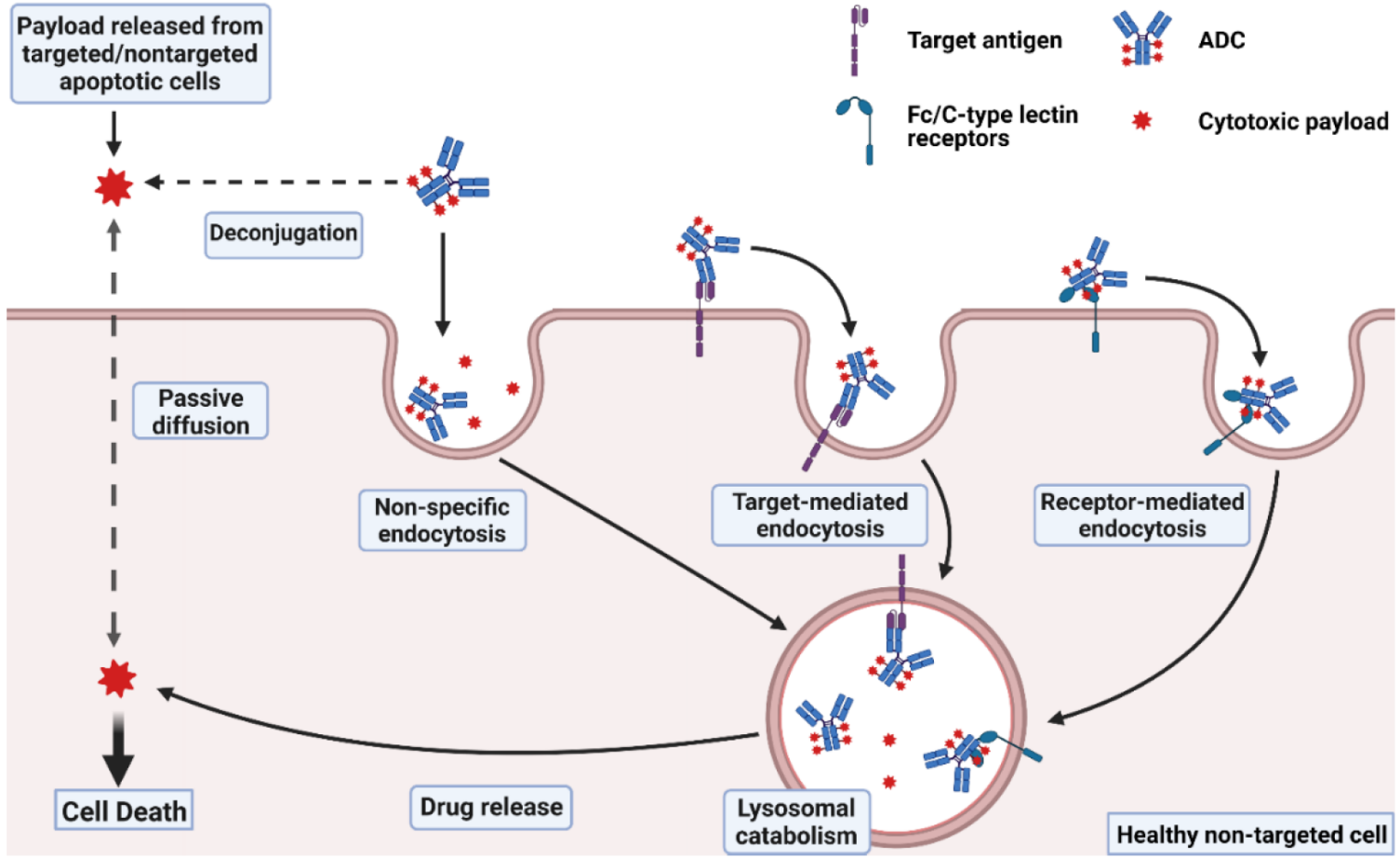
1. Target-independent toxicity: ADC uptake into non-malignant cells

- Nonspecific endocytosis
- Macropinocytosis and micropinocytosis
- Binding to Fc receptors

2.On-target, off-tumour toxicity: target antigen may be expressed on normal cells and contribute to target antigen–dependent uptake of ADCs

Bystander effect (off-target, off-tissue toxicity): membrane-permeable drug payloads diffuse from target cell into neighbouring cells

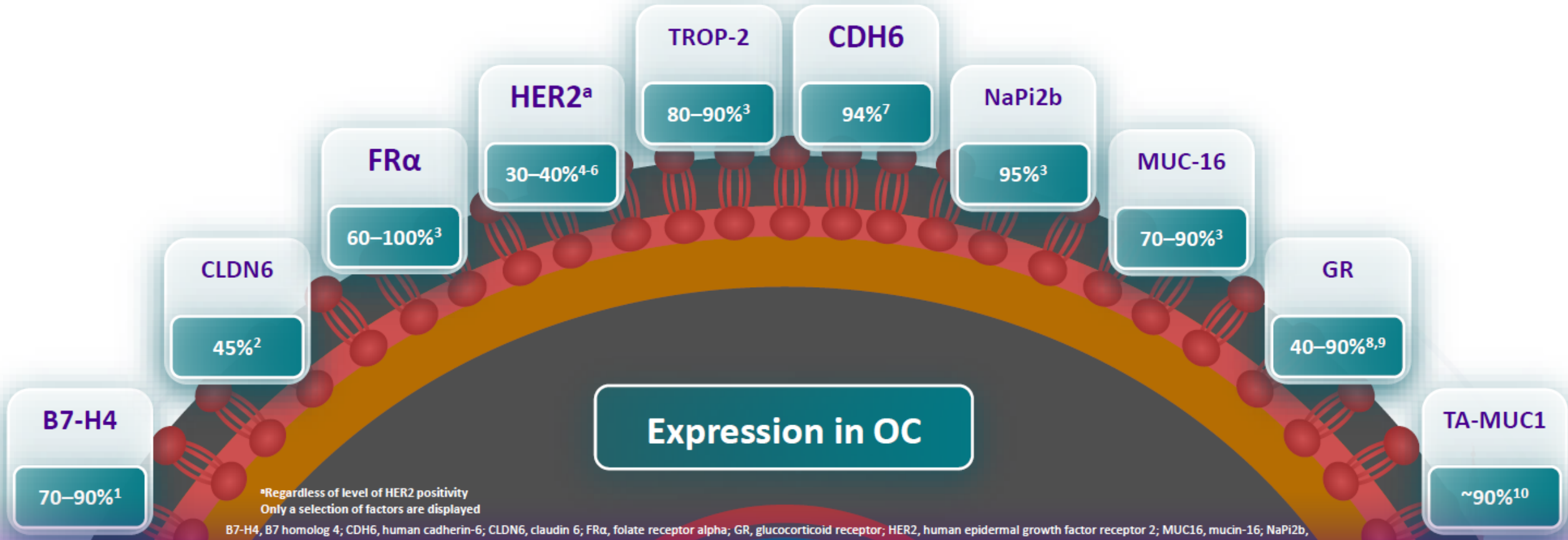
- May be **beneficial** if the neighbouring cell is cancerous, or **detrimental** if neighbouring cell is healthy



Nguyen, T.D, et al. Cancers 2023, 15, 713. https://doi.org/ 10.3390/cancers15030713

ADC, antibody-drug conjugate; FC, fragment crystallizable; MOA, mode of action.

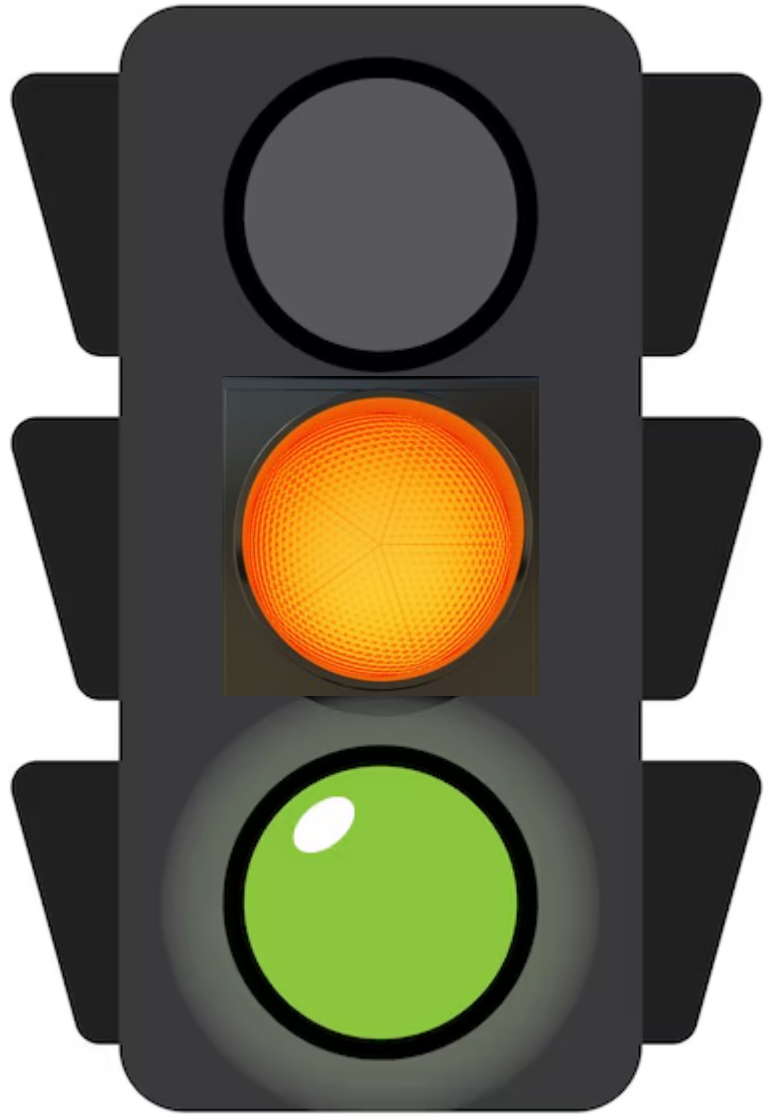
ADC by target in OC



[a]Regardless of level of HER2 positivity
Only a selection of factors are displayed

B7-H4, B7 homolog 4; CDH6, human cadherin-6; CLDN6, claudin 6; FRα, folate receptor alpha; GR, glucocorticoid receptor; HER2, human epidermal growth factor receptor 2; MUC16, mucin-16; NaPi2b, sodium-dependent phosphate transport protein 2B; OC, ovarian cancer; PD-L1, programmed death-ligand 1; PROC, platinum-resistant ovarian cancer; TROP2, trophoblast cell surface antigen 2.

1. Liang L, et al. *Hum Pathol*. 2016;57:1–6; 2. McDermott MSJ, et al. *Clin Cancer Res*. 2023;29(11):2131–2143; 3. Chelariu-Raicu A, et al. *IJGC*. 2023;33(3):420–442; 4. Do-Youn O, et al. Nat Rev Clin Oncol. 2020;17(1):33–48; 5. Pils D, et al. Br J Cancer. 2007;96(3):485–491; 6. Uzunparmak B, et al. Ann Oncol. 2023;34(11):1035–1046; 7. Ray-Coquard I, et al. Presented at ESMO congress, 2025; LBA42; 8. Veneris JT, et al. *Gynecol Oncol*. 2017;146(1):153–160; 9. Galli MC, et al. *Cancer*. 1981;47(6):1297–1302;
10. Takano K, et al. *Mol Cancer Ther*. 2025. Online ahead of print.



Mirvetuximab soravtansine

DM4; cleavable; DAR: 4; bystander

Target: RFalfa

Trial	Citation	Study design and comparison	Population characteristics	Key findings
Mirvetuximab soravtansine (MIRV)				
SORAYA (NCT04296890)	[3]	Phase 2 single-arm study of MIRV	Platinum-resistant epithelial ovarian cancer with high FRα expression[a]	• ORR: 32.4% (95% CI, 23.6 to 42.2) • Median DOR: 6.9 months (95% CI, 5.6 to 9.7). • TRAEs led to dose-reduction in 20% and discontinuation in 9% of participants.
PICCOLO (NCT05041257)	[4]	Phase 2 single-arm study of MIRV	Platinum-sensitive recurrent high-grade epithelial ovarian cancers with high FRα expression[a] as third-line or later therapy	• ORR: 51.9% (95% CI, 40.4 to 63.3) • Median PFS 6.93 months (95% CI, 5.85 to 9.59) • Median DOR: 8.25 months (95% CI, 5.55 to 10.78) • TRAEs led to discontinuation in 16% and death in 3%
MIRASOL (NCT04209855)	[5]	Phase 3 open-label RCT: MIRV vs. chemotherapy	Platinum-resistant high-grade serous ovarian cancer with high FRα expression[a]	• Improved PFS with MIRV at 5.62 months (95% CI: 4.34 to 5.95) vs. 3.98 months (95% CI: 2.86 to 4.47) with chemotherapy • Higher ORR with MIRV than chemotherapy (OR 3.81; 95% CI, 2.44 to 5.94) • Longer OS with MIRV, median 16.46 months, than chemotherapy, median 12.75 months (HR 0.67; 95% CI, 0.50 to 0.89) • Fewer SAEs with MIRV than chemotherapy (23.9% vs. 32.9%)
FORWARD I (NCT02631876)	[6]	Phase 3 open-label RCT: MIRV vs. chemotherapy	Platinum-resistant epithelial ovarian cancer with medium or high FRα expression[b]	• MIRV did not significantly improve PFS in either the ITT or high FRα subgroup analyses • ORR (24% vs. 10%), CA-125 response rate (53% vs. 25%), and patient-reported outcomes (27% vs. 13%) better with MIRV than chemotherapy • Fewer grade 3 or higher TRAEs with MIRV than chemotherapy (4.5% vs. 8.3%)
FORWARD II (NCT02606305) expansion studies	[7,8]	Phase 1b study of MIRV + carboplatin + bevacizumab	Recurrent, platinum-sensitive ovarian cancer with medium or high FRα expression[a]	• ORR: 83%, median DOR 10.9 months • Median PFS: 13.5 months • TRAEs leading to discontinuation: 59%
		Phase 1b/II study of MIRV + bevacizumab	Platinum-resistant epithelial ovarian cancer, primary peritoneal, or fallopian tube cancer with low, medium, or high FRα expression[a]	• ORR: 44%, median DOR 9.7 months, rate increased with increasing FRα expression • Median PFS: 8.2 months • TRAEs leading to discontinuation: 32%

The NEW ENGLAND JOURNAL of MEDICINE

Target: RFalfa

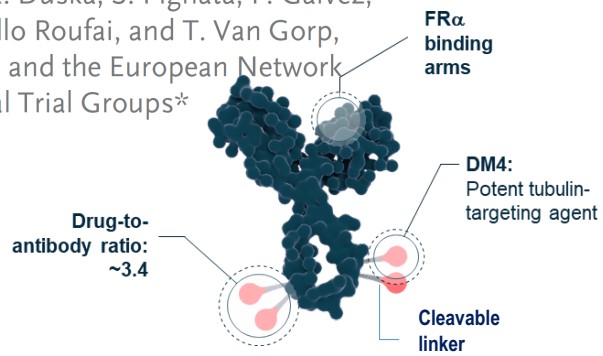
ORIGINAL ARTICLE

Mirvetuximab Soravtansine in FRα-Positive, Platinum-Resistant Ovarian Cancer

K.N. Moore, A. Angelergues, G.E. Konecny, Y. García, S. Banerjee, D. Lorusso, J.-Y. Lee, J.W. Moroney, N. Colombo, A. Roszak, J. Tromp, T. Myers, J.-W. Lee, M. Beiner, C.M. Cosgrove, D. Cibula, L.P. Martin, R. Sabatier, J. Buscema, P. Estévez-García, L. Coffman, S. Nicum, L.R. Duska, S. Pignata, F. Gálvez, Y. Wang, M. Method, A. Berkenblit, D. Bello Roufai, and T. Van Gorp, for Gynecologic Oncology Group Partners and the European Network of Gynaecological Oncological Trial Groups*

EMA APPROVED

FDA APPROVED



Key eligibility[1]

- High-grade PROC, primary peritoneal cancer or fallopian tube cancer (not primary refractory)
- 1–3 prior systemic LOT
- Radiological progression on/after most recent LOT
- High FOLR1 expression
- Measurable disease per RECIST v1.1
- ECOG PS 0–1
- Suitable for single-agent therapy as next LOT
- Adequate organ function
- Stabilized/recovered (Grade 1 or baseline) from prior TRAE

N=453
R 1:1[2]

MIRV 6 mg/kg AIBW Q3W

CT: investigator's choice
- Paclitaxel 80 mg/m² days 1, 8, 15 and 22 Q4W
- Topotecan 4.0 mg/m² days 1, 8 and 15 Q4W **or** 1.25 mg/m² days 1–5 Q3W
- Pegylated liposomal doxorubicin 40 mg/m² Q4W

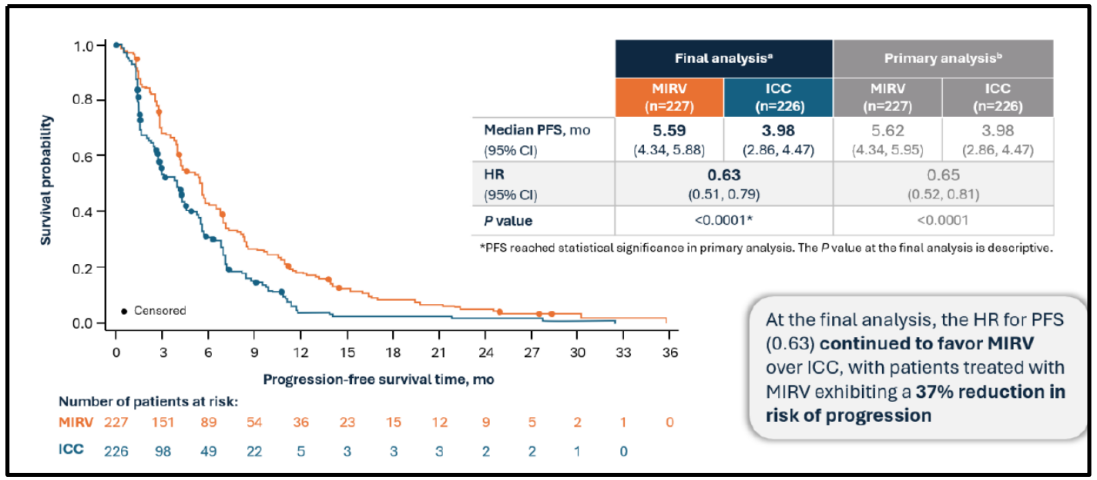
Stratified by:[2]
- Previous LOT
- CT agent

Endpoints[1]

Primary
- PFS per RECIST v1.1

Secondary
- Incidence of TEAEs, ORR, OS, DOR per RECIST v1.1, percentage of participants achieving ≥ 15-point improvement in the abdominal/GI scale of QLQ-OV28 at week 8/9, CA-125-confirmed clinical response per GCIG criteria (%), time to PFS-2

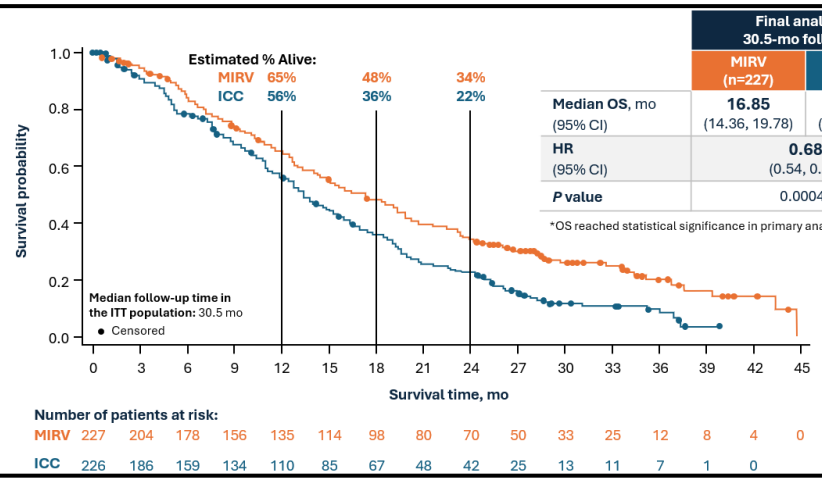
Primary completion: Mar 2023



	Final analysis[a]		Primary analysis[b]	
	MIRV (n=227)	ICC (n=226)	MIRV (n=227)	ICC (n=226)
Median PFS, mo (95% CI)	5.59 (4.34, 5.88)	3.98 (2.86, 4.47)	5.62 (4.34, 5.95)	3.98 (2.86, 4.47)
HR (95% CI)	0.63 (0.51, 0.79)		0.65 (0.52, 0.81)	
P value	<0.0001*		<0.0001	

*PFS reached statistical significance in primary analysis. The *P* value at the final analysis is descriptive.

At the final analysis, the HR for PFS (0.63) **continued to favor MIRV** over ICC, with patients treated with MIRV exhibiting a **37% reduction in risk of progression**



	Final analysis[a] 30.5-mo follow-up		Primary analysis[b] 13.1-mo follow-up	
	MIRV (n=227)	ICC (n=226)	MIRV (n=227)	ICC (n=226)
Median OS, mo (95% CI)	16.85 (14.36, 19.78)	13.34 (11.37, 15.15)	16.46 (14.46, 24.57)	12.75 (10.91, 14.36)
HR (95% CI)	0.68 (0.54, 0.84)		0.67 (0.50, 0.89)	
P value	0.0004*		0.0046	

*OS reached statistical significance in primary analysis. The *P* value at the final analysis is descriptive.

At the final analysis, the HR for OS (0.68) **continued to favor MIRV** over ICC, with patients treated with MIRV exhibiting a **32% reduction in risk of death**

Moore et al, NEJM 2024. Figures excerpt taken from Van Gorp T, et al. Presented at SGO 2025[4]

Trastuzumab deruxtecan:

(Topo1i, DAR: 8, cleavable, bystander)

Destiny panTumour 02

Cohorts (Part 1)

- **Cohort 1**: BTC
- **Cohort 2**: urothelial bladder cancer
- **Cohort 3:** CC
- **Cohort 4**: EC
- **Cohort 5**: OC
- **Cohort 6**: Pancreatic cancer
- **Cohort 7**: Rare tumors

Cohorts (Part 2)

- **Cohort 1**: HER2 IHC 3+ tumors
- **Cohort 2**: HER2 IHC 2+ /ISH+ tumors
- **Cohort 3:** HER2 IHC 2+ or 1+ EC
- **Cohort 4**: HER2 IHC 2+ or 1+ OC
- **Cohort 5**: HER2 IHC 2+ or 1+ CC

Key eligibility: OC[1,2]

- ≥ 18 years
- Metastatic or advanced solid HER2 OC (IHC 2+ or 1+)
- Progressed following prior treatment or have no satisfactory alternative treatment option
- ECOG PS 0–1
- No evidence of current ILD or pneumonitis

Cohort 5: OC (n=40)[2]

Phase 2

T-DXd 5.4 mg/kg IV Q3W

Endpoints[2]

Primary

- ORR (IA)

Secondary

- DOR, DCR, PFS, OS, AEs, PK, immunogenicity

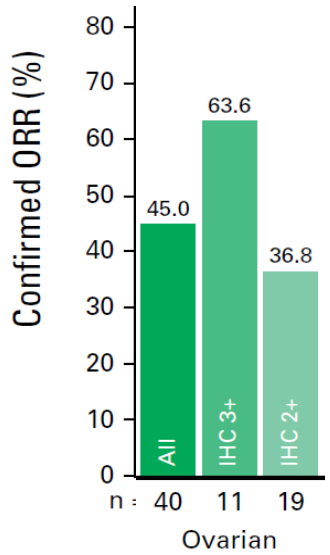
Primary completion: Jul 2027

Meric-Bernstam F, et al JCO 2023 DOI https://doi.org/10.1200/JCO.23.02005

FDA APPROVED

Target: Her-2

ORR: 45.0% (95% CI, n=40 [29.3–61.5])
IHC3+: 63.6% (n=11 [95% CI, 30.8–89.1])
mPFS: 5.9 months (4.0–8.3)
mOS: 13.2 months (8.0–17.7)



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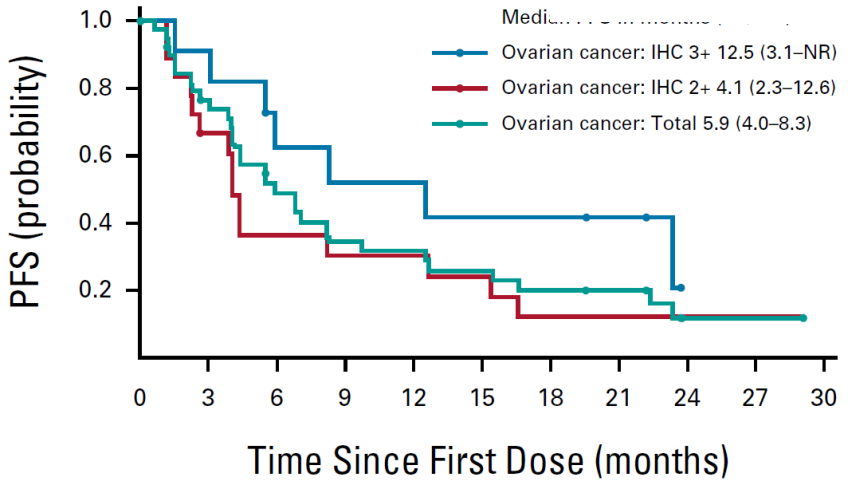


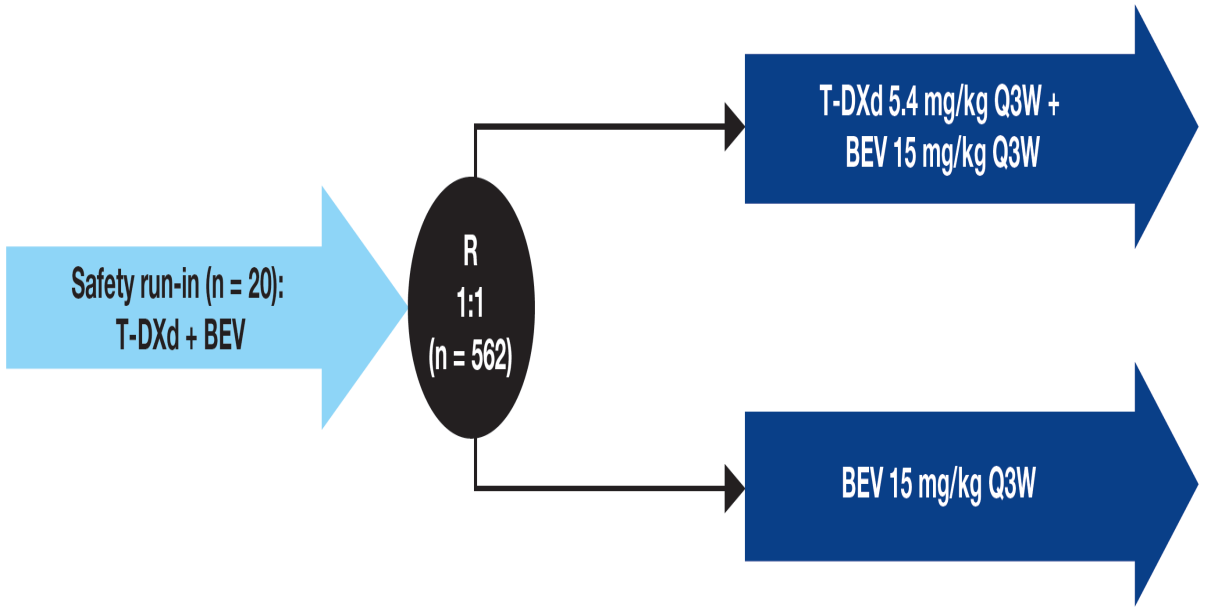
No. at risk:

Ovarian cancer: IHC 3+	11	10	6	5	5	4	4	3	0		
Ovarian cancer: IHC 2+	19	11	6	5	5	4	2	2	1	1	0
Ovarian cancer: Total	40	28	17	12	11	9	7	6	1	1	0

DESTINY-Ovarian01 Study Design (ENGOT-ov89/GEICO144-O/GOG-3112/APGOT-OV13 [NCT06819007])

Patient population

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



- Primary:
  Pfs by ICR in the Her2 IHC 3+/2+ population
- Key secondary:
  OS in the Her2 IHC 3+/2+ population

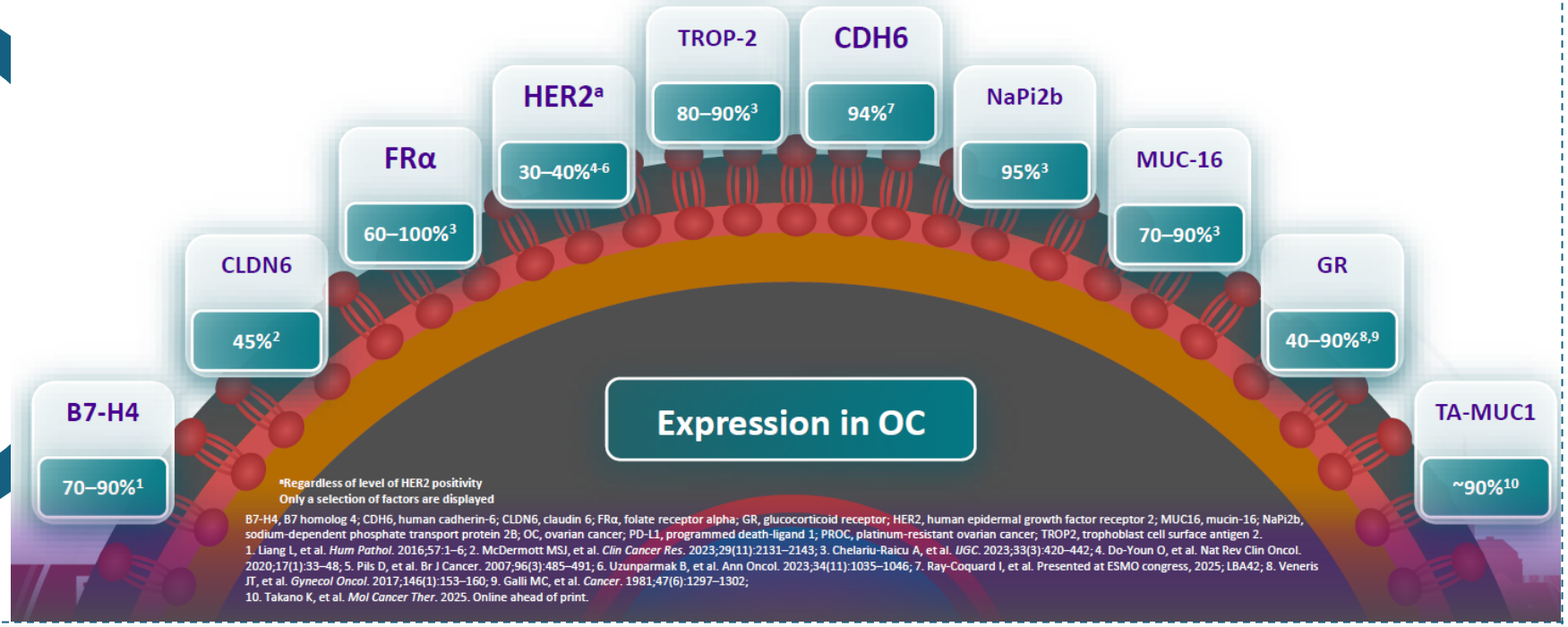
Participants will receive T-DXd for a maximum of 34 cycles and BEV for up to 16 cycles (a maximum of 22 cycles including the doses given in combination with first-line chemotherapy) or until disease progression, unacceptable toxicity, withdrawal of consent, or study termination.

[a]With a minimum of 168 participants (30%) for HER2 IHC 3+ and a maximum of 82 participants (15%) for HER2 IHC 1+.

[b]No disease progression is defined as no residual disease after primary debulking surgery (PDS) or complete response (CR)/partial response (PR)/stable disease (SD) as per response evaluation criteria in solid tumors version 1.1 (RECIST v1.1) assessed by the investigator at the end of front-line chemotherapy (after completion of ≥6 and ≤8 cycles of front-line carboplatin-paclitaxel ± bevacizumab); there should be no clinical evidence of disease progression as per physical examination, imaging, or presence of cancer antigen 125 (CA-125) throughout the patient's front-line treatment and prior to trial randomization.

Antonio González-Martin et al, ESMO Gyn Cancer 2025

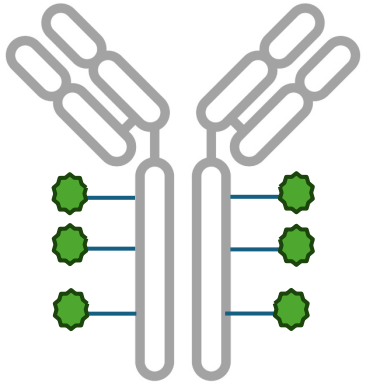
ADC's en Desarrollo: Datos de EC fase I/II



Developmental scenarios for ADC's

PROC

PSOC Maintenance



CT/anti-angiogenic combination

1L maintenance BMK selected

Mirvetuximab soravtansine: PSOC IMNG853-420 fase 2 FOLR1≥ 25%

Target: RFalfa

IMGN853-0420 (NCT05456685) Study Design

A global, single-arm, phase 2 trial of MIRV plus carboplatin in adult patients with FRα-expressing PSOC

SGO ANNUAL MEETING ON WOMEN'S CANCER SAN JUAN, PR APRIL 10-13, 2026

Eligibility

- Platinum-sensitive, high-grade serous EOC[a]
- 1 prior line of platinum-based chemotherapy
- FRα positivity detected by IHC (≥25% tumor cells with ≥2+ membrane intensity)[b]
- Prior PARPi required for patients with somatic and/or germline *BRCA* mutations
- Measurable disease by RECIST v1.1

Overall Study Period

Combination Phase: **MIRV** (6 mg/kg AIBW) + **Carbo** (AUC 5) Q3W for 6–8 cycles

N=125

Patients without PD

Continuation Phase: **MIRV monotherapy** (6 mg/kg AIBW) Q3W

Patients received single-agent MIRV until PD, death, the start of new anticancer therapy, or withdrawal of consent

Primary Endpoint

ORR by INV[c] by the end of 6 combination cycles in a subset of patients from the overall population (ie, patients with ≥25% FRα expression) who had ≥50% FRα expression

Key Secondary Endpoint

ORR by INV[c] by the end of 6 combination cycles in the overall population (ie, patients with ≥25% FRα expression)

Additional Secondary Endpoints

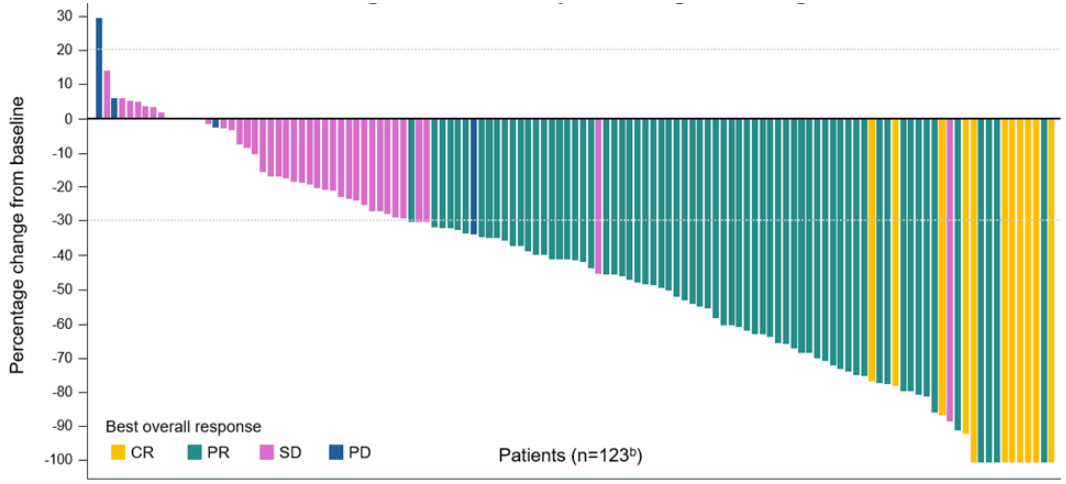
In the overall study period:

- DOR[c]
- PFS[c]
- CA-125 response
- OS
- TEAEs

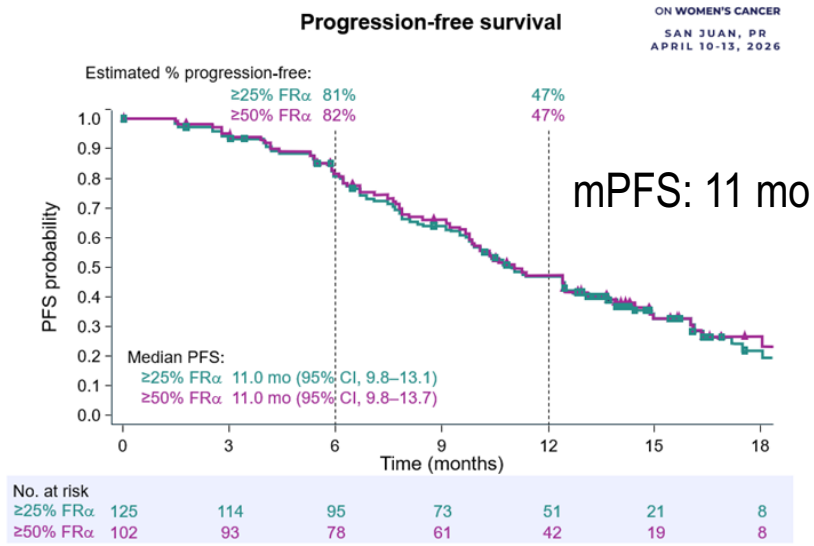
Statistical Testing

- For the primary and key secondary endpoint, a 1-sided binomial test at an alpha level of 0.05 was used to test the null hypothesis that ORR was ≤60% versus an alternative hypothesis that ORR was ≥75%
- The key secondary endpoint was tested if the primary endpoint was statistically significant

[a]EOC includes ovarian, fallopian tube, and pr
[b]Sensitivity analysis by blinded independent c
IHC, immunohistochemistry; INV, investigato
Response Evaluation Criteria in Solid Tumor



	Overall population (≥25% FRα expression)	
	Total (N=125)	≥50% FRα subset (n=102)
By the end of 6 combination cycles		
ORR, % (95% CI)	**62.4 (53.3–70.9)**	**62.7 (52.6–72.1)**
CR, n (%)	11 (8.8)	9 (8.8)
PR, n (%)	67 (53.6)	55 (53.9)
SD, n (%)	41 (32.8)	34 (33.3)
PD, n (%)	4 (3.2)	2 (2.0)
NE, n (%)	0 (0.0)	0 (0.0)
Missing, n (%)	2 (1.6)	2 (2.0)
Overall study (combination + continuation phases)		
ORR, % (95% CI)	**68.0 (59.1–76.1)**	**67.6 (57.7–76.6)**
Median DOR, mo (95% CI)	11.2 (8.6–13.9)	11.2 (8.6–13.9)



mPFS: 11 mo

Konecny GE, SGO 2026

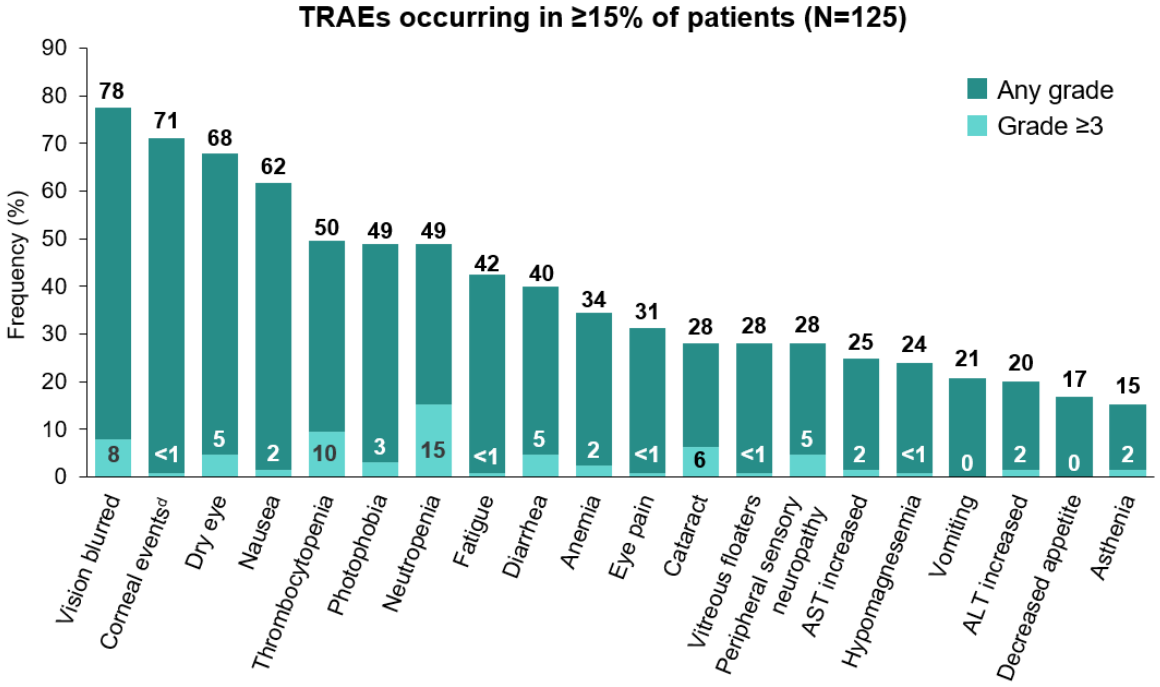
Mirvetuximab soravtansine: PSOC IMNG853-420 fase 2 FOLR1≥ 25%

Target: RFalfa

Safety: Adjudicated Treatment-related Pneumonitis

SGO ANNUAL MEETING ON WOMEN'S CANCER SAN JUAN, PR APRIL 10-13, 2026

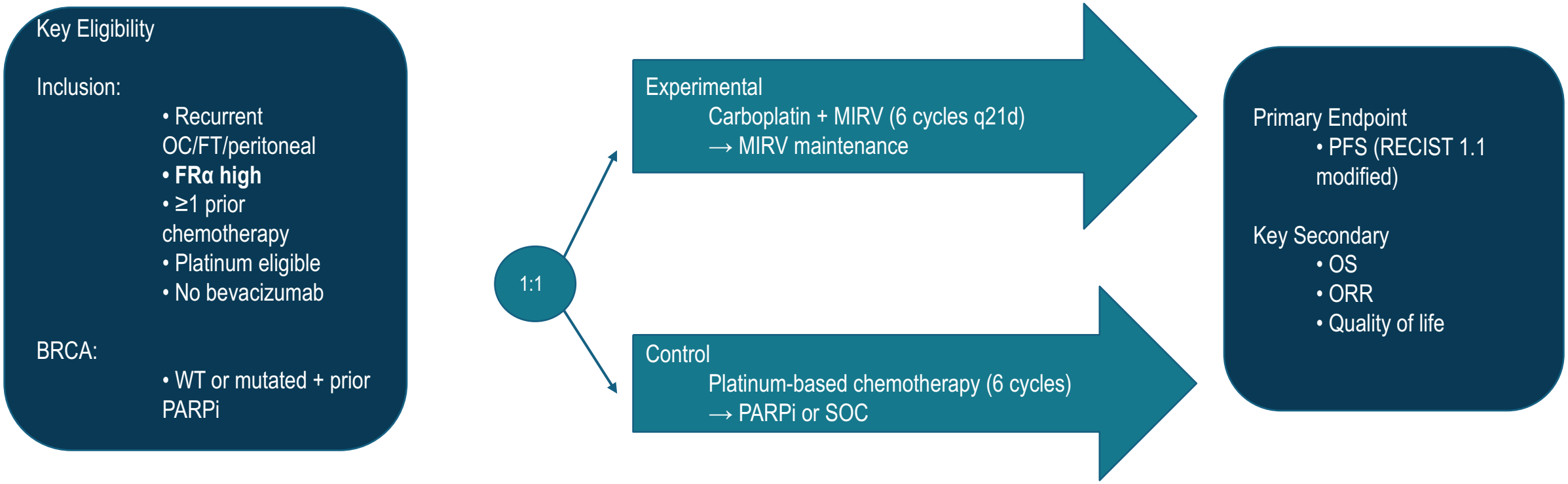
- Investigator-assessed pneumonitis AEs were retrospectively reviewed by an **independent adjudication committee** of ≥6 members, including ≥2 specialists each in radiology, medical oncology, and pulmonology
- **Adjudicated treatment-related pneumonitis occurred in 19 patients (15.2%)**
  - 14 (11.2%) had grade 1-2 events
  - 3 (2.4%) had grade 3–4 events
  - 2 (1.6%) deaths occurred (grade 5); both with underlying cardiopulmonary disorders
- **16/19 patients had a final grade of 1 or better**, including 10 with complete resolution
- 11/19 patients were **retreated with MIRV**
- **Median (range) time to onset was 32.1 (8.6–72.0) weeks**



Konecny GE, SGO 2026

Target: RFalfa

AGO-OVAR2.34 / MIROVA
Randomized Phase II trial in FRα-high recurrent ovarian cancer



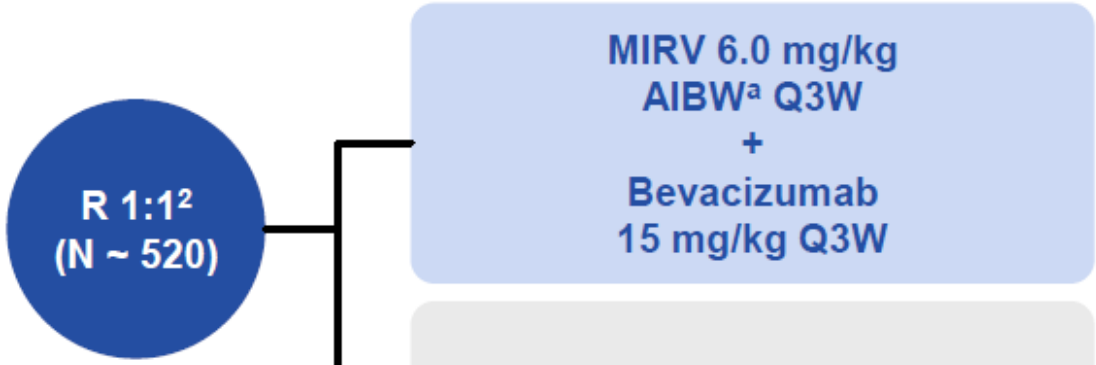
n=136 patients | NCT04274426

GLORIOSA: Phase 3, multicenter, open-label study of mirvetuximab soravtansine (MIRV; FRα ADC) + bevacizumab vs bevacizumab in PSOC with high FRα expression

Target: RFalfa

Key eligibility[1,2]

- High-grade serous epithelial OC, primary peritoneal or fallopian tube cancer
- ECOG PS 0–1
- High FRα expression
- PARPi MT where appropriate
- Relapsed after 1L platinum-based chemotherapy
  - Platinum sensitive (progression > 6 months after last dose)
- Response (CR, PR or SD) to 2L platinum-based doublet plus bevacizumab[2]
- One of the following:
  - Measurable disease per RECIST v1.1 (SD or PR)



Stratified by:[2]

- Prior PARPi
- Prior bevacizumab
- Response to 2L platinum doublet plus bevacizumab (CR, PR or SD)

Endpoints[1]

Primary

- PFS (investigator assessed)

Secondary

- Key:[2] OS, AEs, PFS2, ORR, DOR, DFS, CA-125 response, HRQoL (NFOSI-18 DRS-P subscale)

Primary completion: Mar 2027

Preliminary results Results pending; recruiting NCT05445778

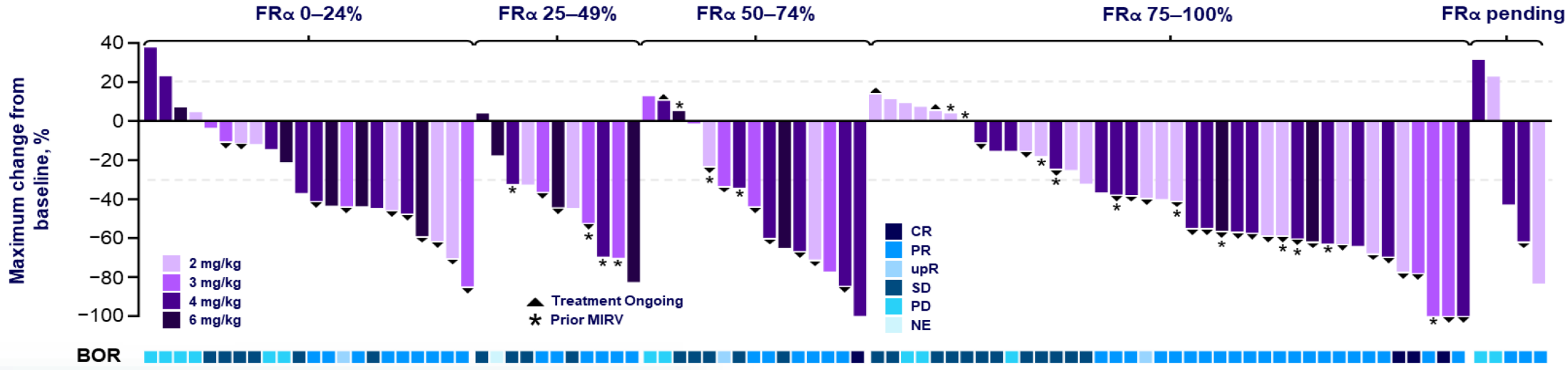
Sofetabart mipitecan: cohort A2 PROC

Topo 1 inh; cleavable; DAR 8

FDA BREAKTHROUGH THERAPY

Target: RFalfa

Antitumour activity by dose level and FRα expression



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

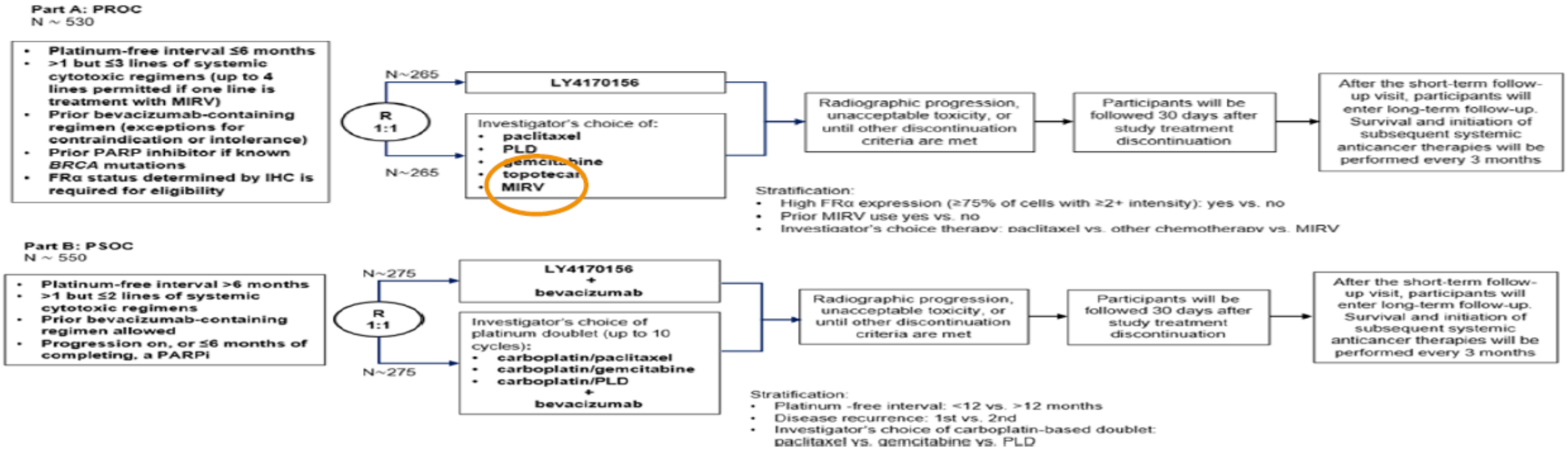
Median 5 L (1-11)
96% PR
Previous lines: 17% mirv/88% bev/ 66% iparp
>60% cORR in prior MIRV and other ADC-exposed patients
Low rates of G1-2 neuropathy (7%), ILD (4%), vision blurred (4%) or alopecia (4%)
Comparable efficacy and safety to the entire PROC population

Ray-Coquard I ESMO 2025; Bavana P, SGO 2026

Target: RFalfa

Framework 01 Sofetabart mipitecan: PSOC & PROC

Main Study Randomization and Treatment



Primary endpoint: PFS

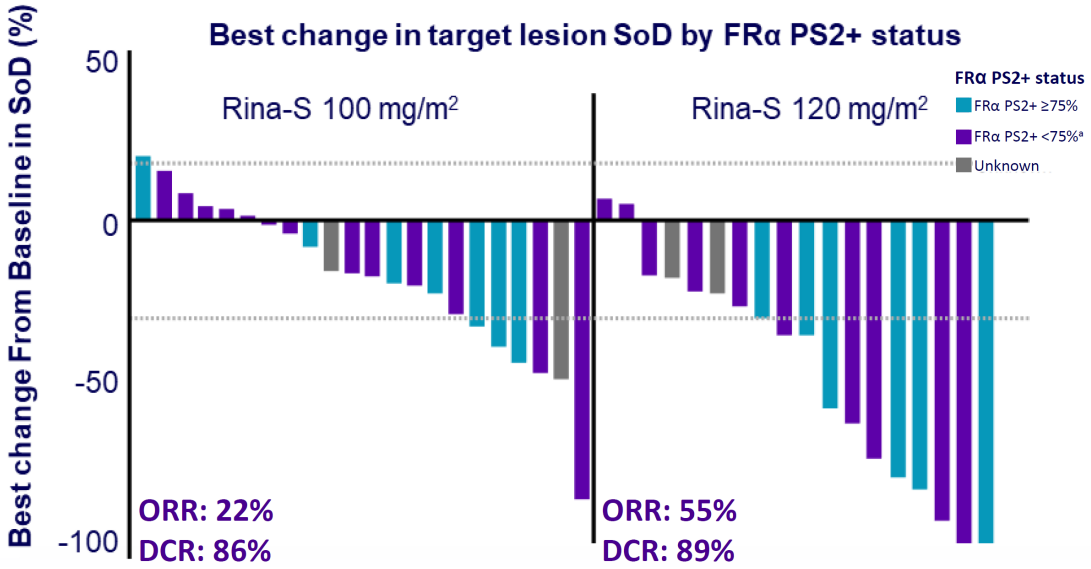
Key secondary endpoint: OS

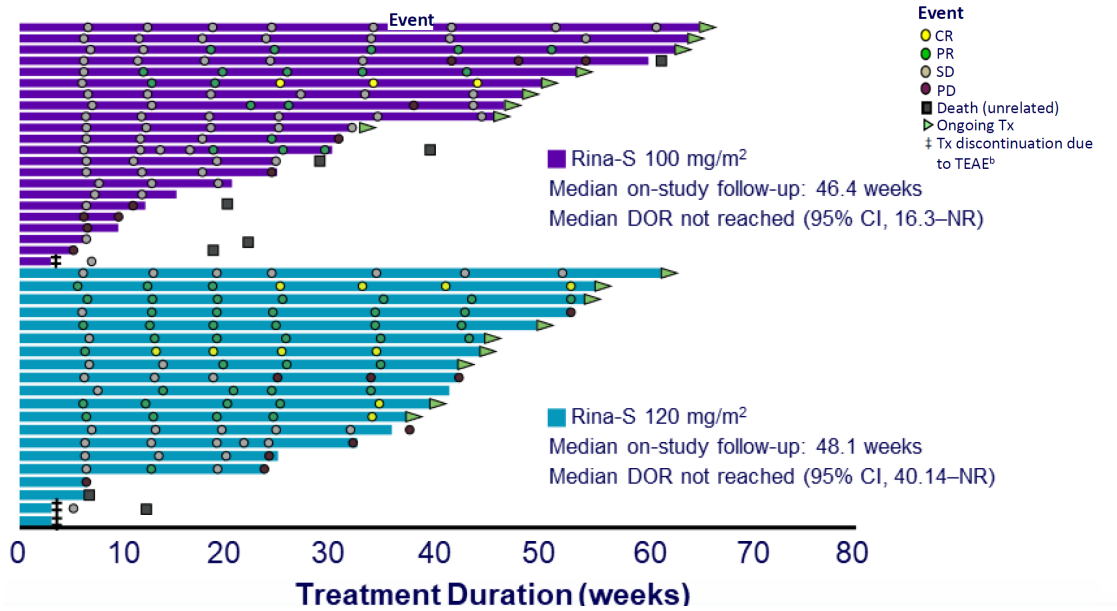
Secondary endpoints: ORR, PRO's, Safety, DOR, CA125 response, PFS2

NCT07213804: RECRUITING

Ritanabart sesutecan (Rina-S): Rainfol 01 fase I
Topo1i, DAR:8 , cleavable, bystander

Target: RFalfa





In this phase I study, there were no reports of ocular toxicity, neuropathy or ILD in those receiving Rina-S

- The most common TEAEs (occurring in >25% of patients) were **anaemia, nausea** and **neutropenia**
- Grade ≥3 TEAEs were reported in **72.7%** and **65.0%** of patients in the 100 mg/kg and 120 mg/kg cohorts, respectively
- TEAEs led to dose reduction in **22.7%** and **25.0%** of patients, and treatment discontinuation in **9.1%** and **5.0%,** in the 100 mg/kg and 120 mg/kg cohorts, respectively
- GCSF was used in **36.4%** and **55.0%** of patients at 100 mg/m^2 and 120 mg/m^2, respectively

Lee EK, et al. SGO 2024

AGO 86 ENGOT-ov86 **RAINFOL-OV2** PRO1184

Target: RFalfa

~530 Subjects (21 months)

Key Eligibility

Inclusion:

- Platinum resistant ovarian cancer
- 1–4 prior therapies

Treatment with all the following:

  - Platinum chemo
  - Bevacizumab (unless contraindication)
  - PARP (if BRCA mutated)
  - Mirvetuximab (if FRα-high)

- ECOG 0 or 1
- RECIST v1.1 measurable
- FRα results must be available
- Enrollment regardless FRα

Exclusion:

- Prior ADC topo 1 inhibitor
- Platinum refractory ≤ 91 days

R 1:1

Rina-S (120 mg/m² D1; q3w)

Investigator Choice
PLD: 40 mg/m² q4w
Paclitaxel: 80 mg/m² D1,8,15 q4w
Gemcitabine: 1000/800 mg/m²
Topotecan regimens

Stratification factors:

- Region (US vs EU vs RoW)
- Prior therapies (1 vs 2 vs 3–4)
- mirv status:

(naive& FRα low vs naive &FR high vs mirv treated)

Primary Endpoint:

- **PFS** per investigator (RECIST v1.1)

Key Secondary:

- Overall Survival
- ORR

Other Secondary:

- Safety and tolerability
- DoR
- CA-125 response
- PFS2
- PROs

NCT 06619236: Active not recruiting

Mocertatug rezetecan (Mo-Rez): Behold1 fase 1

(Topo1i, DAR6, cleavable, bystander)

Target: B7H4

BEHOLD-1:

A 2-part, open-label, global, Phase 1 study with randomized dose optimization

Scan Me

SGO ANNUAL MEETING ON WOMEN'S CANCER SAN JUAN, PR APRIL 10-13, 2026

Eligibility criteria

- Aged ≥18 years
- Histologically confirmed advanced solid tumor
- ECOG PS 0–2
- ≥1 measurable target lesion (RECIST v1.1)
- No prior B7-H4 therapy

Phase 1B only:

- PROC*: 1–3 prior LOT
- EC†: 1–3 prior LOT
- No prior TOPi

Phase 1A: Dose Escalation

Advanced solid tumors

7.2 mg/kg Q3W

5.8 mg/kg Q3W

4.8 mg/kg Q3W

2.8 mg/kg Q3W

Phase 1A: Main findings

- N=44 patients; DCO July 1, 2025
- MTD was not reached
- MAD was determined as 5.8 mg/kg Q3W

Scan QR code for more Phase 1A data

Phase 1B: Dose Expansion/Optimization

PROC

R 1:1:1

2.8 mg/kg Q3W, (n~30–50)

4.8 mg/kg Q3W, (n~30–50)

5.8 mg/kg Q3W, (n~30–50)

Recurrent/advanced EC

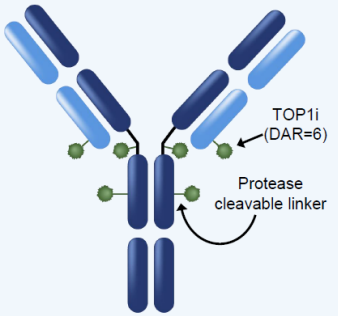
R 1:1

2.8 mg/kg Q3W, (n~30–50)

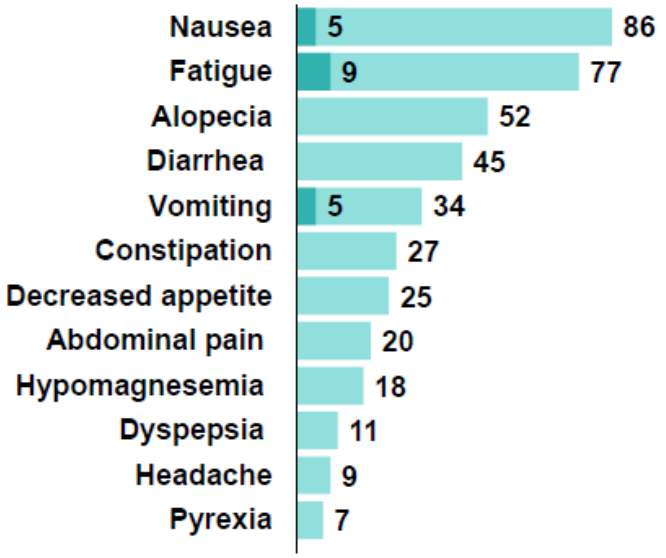
4.8 mg/kg Q3W, (n~30–50)

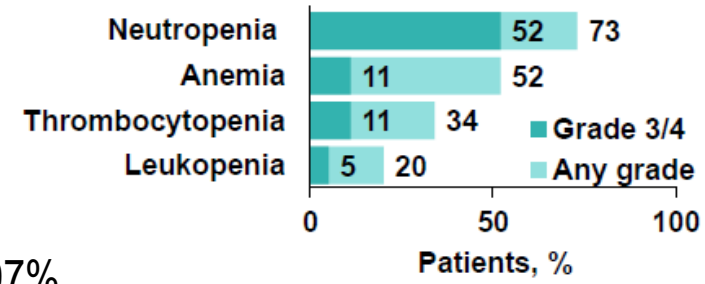
Expansion at recommended dose informed by totality of data

Mocertatug Rezetecan



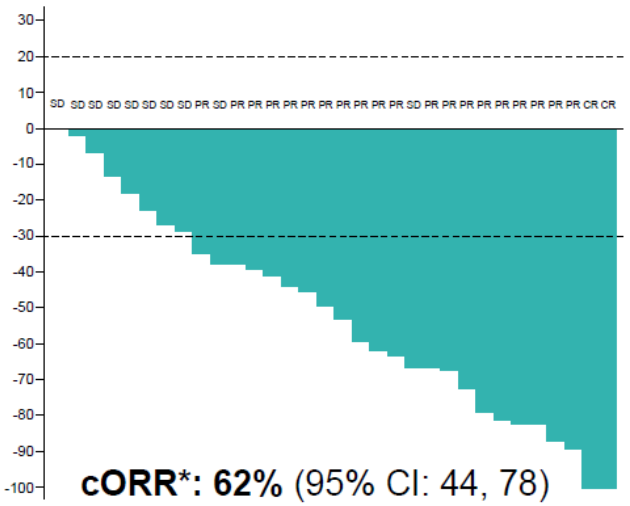
Mo-Rez 5.8 mg/kg (N=44)





BEHOLD-1

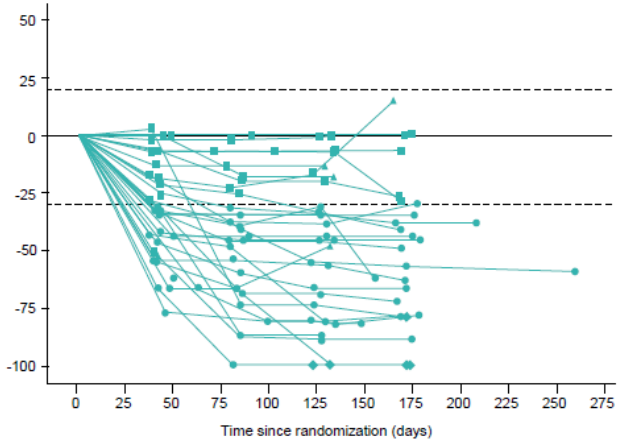
Mo-Rez 5.8 mg/kg (N=34)



cORR*: 62% (95% CI: 44, 78)

Mo-Rez 5.8 mg/kg (N=34)

1.4 months
(1.4, 1.6)



B7H4 + 97%
Follow up: 6,1 m
ILD 3% g1-2 all cohorts

Oaknin et al, SGO 2026

Mocertatug rezetecan (Mo-Rez): PSOC fase 1&2 asian

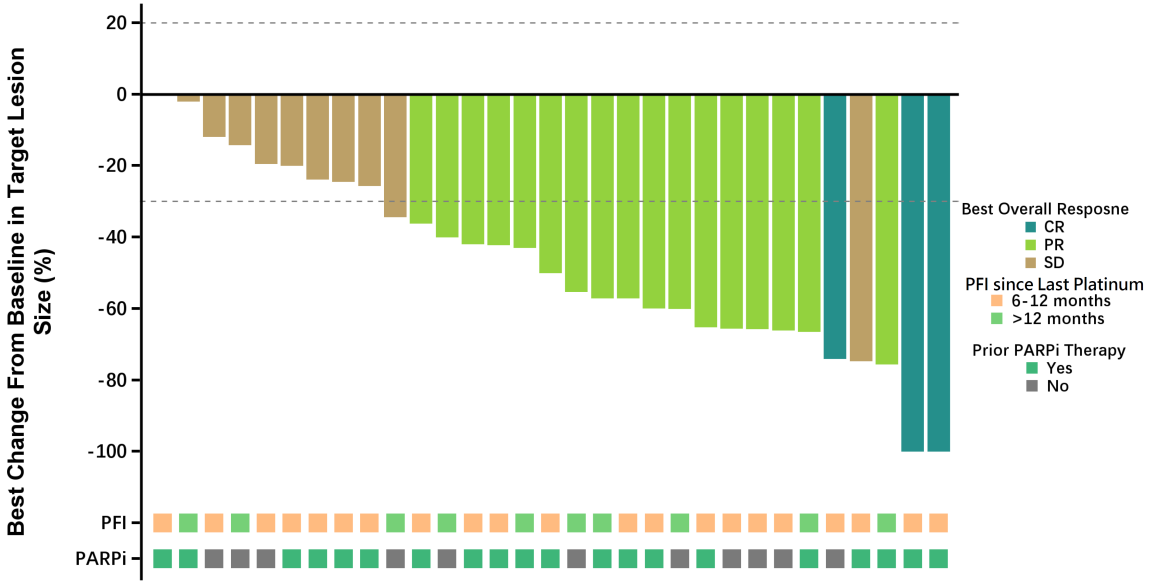
Target: B7H4

Table 2. Efficacy outcomes

	PSOC (N=31)
cORR, % (95% CI)	64.5 (45.4, 80.8)
cCR, n (%)	3 (9.7)
cPR, n (%)	17 (54.8)
mDoR* (mo) (95% CI)	13.8 (8.1, NR)
DCR, % (95% CI)	100.0 (88.8, 100.0)
mPFS (mo) (95% CI)	14.1 (8.6, NR)

*Based on patients with confirmed response.
Event rates of DoR and PFS were 45.0% and 54.8%, respectively.

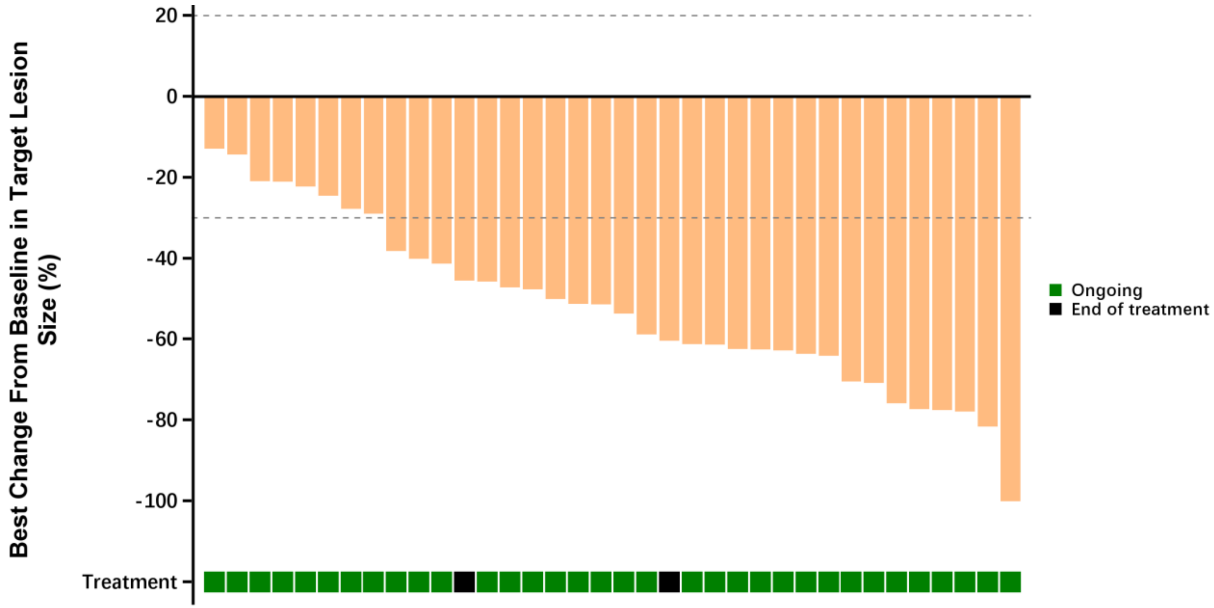
Figure 1. Depth of best response



Wang et al, ESGO 2026

Items	Mo-Rez 4.8 mg/kg + Bevacizumab 15.0 mg/kg (N=36)
ORR, % (95% CI)	72.2 (54.8, 85.8)
CR, n (%)	2 (5.6)
PR, n (%)	24 (66.7)
SD, n (%)	10 (27.8)
PD, n (%)	0
DCR, % (95% CI)	100.0 (90.3, 100.0)

The ORR, CR and PR were all confirmed; DCR=CR+PR+SD



Yuan et al, ESGO 2026

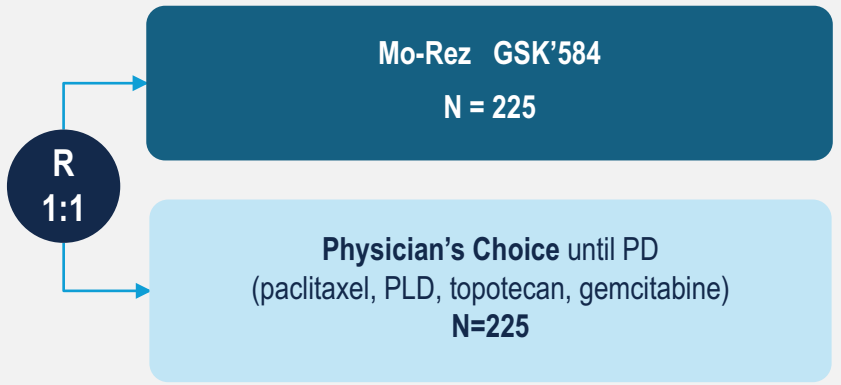
Mo-Rez will be evaluated in global Phase 3 trials at the 5.8 mg/kg Q3W dose

- PROC (BEHOLD-Ovarian01; NCT07286266)
- Advanced/recurrent EC (BEHOLD-Endometrial01; NCT07286331)

Key eligibility

- ≥18 yrs old
- 1-3 prior lines*
- HGS or HGE Platinum-resistant (<6 month after completion of plat-based therapy)
- Prior Mirv, bev, PARPi if candidate and treatment available
- Measurable disease
- FFPE tissue
- Primary platinum refractory excluded
- Prior B7-H4 and topo1i excluded

Intervention[1]



Endpoints

Primary (Dual)

- **PFS (BICR)**
- **OS**

Secondary

- ORR, DOR, PFS (inv)
- ORR, DOR (BICR)
- PFS2
- Safety, Tolerability
- HRQL
- PK/Immunogenicity

1. ClinicalTrials.gov identifier NCT07286266. Available at: https://clinicaltrials.gov/study/NCT07286266

DB-1311/BNT 324: fase I/II PROC/CC

Target: B7H3

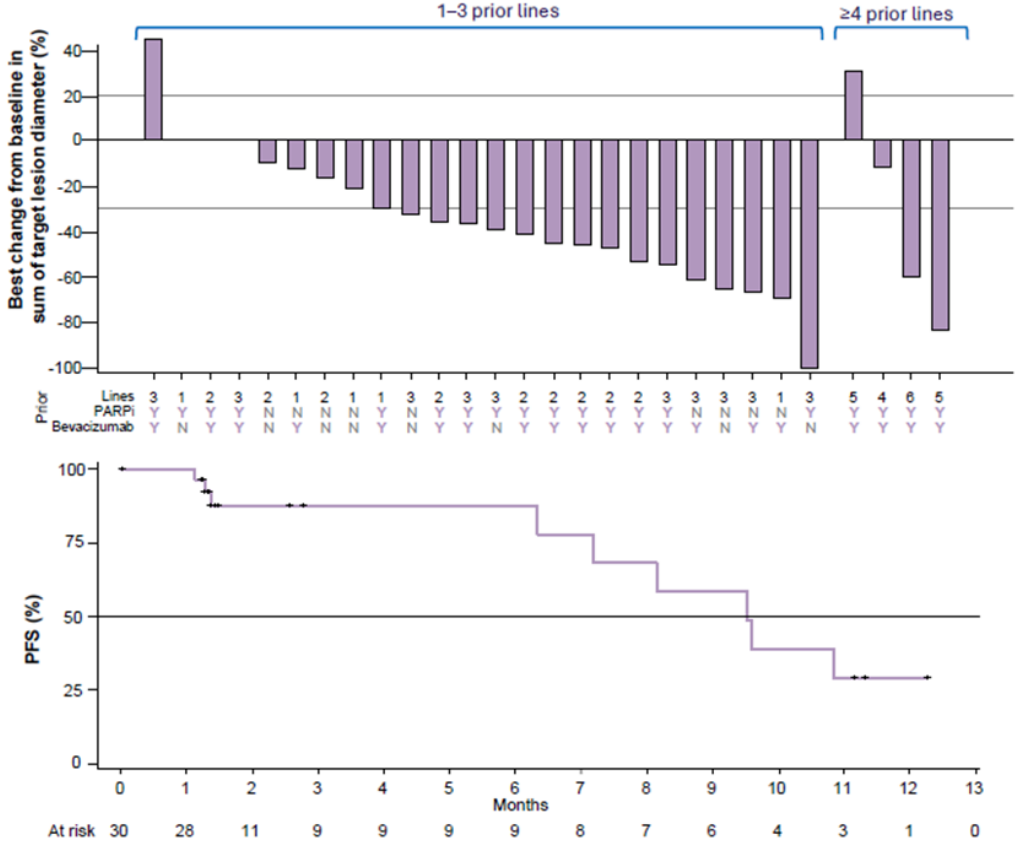
(topo I inh/ cleavable/DAR: 6/bystander effect +)

Efficacy in PROC and prior treatment subgroups

ANNUAL MEETING ON WOMEN'S CANCER
SAN JUAN, PR
APRIL 10-13, 2026

All patients received prior chemotherapy, 70% received prior bevacizumab, 54% received prior PARPi

PROC: ORR 53.3%, DCR 83.3%,
median DoR was 8.0 months, mPFS was 9.5 months



Clinical activity regardless of prior treatment with bevacizumab (ORR 54.5%) or prior PARPi (ORR 57.9%)

PROC	Overall N=30	Prior Bevacizumab n=22	Prior PARPi n=19
BOR, n (%)			
CR	2 (6.7)	0	1 (5.3)
PR	14 (46.7)	12 (54.5)	10 (52.6)
SD	9 (30.0)	5 (22.7)	5 (26.3)
PD	3 (10.0)	3 (13.6)	3 (15.8)
ORR,* % (95% CI)	**53.3** (34.3, 71.7)	**54.5** (32.2, 75.6)	**57.9** (33.5, 79.8)
DCR, % (95% CI)	83.3 (65.3, 94.4)	77.3 (54.6, 92.2)	84.2 (60.4, 96.6)
Median PFS (95% CI), months	**9.5** (6.3, NE)	**9.5** (6.3, NE)	**7.2** (6.3, NE)

Among patients with the longest follow-up, previously presented at ESMO Asia 2025[1] (N=12: median follow-up 12.1 months; median time on treatment 9.0 months; 5/12 patients still on treatment), **ORR was 58.3%, median DoR 8.0 months, median PFS 9.5 months**

28/37 patients remain on treatment. Median follow-up: 2.1 months (range 0.5–14.0). *Unconfirmed ORR is reported, BOR was missing for 2 patients.

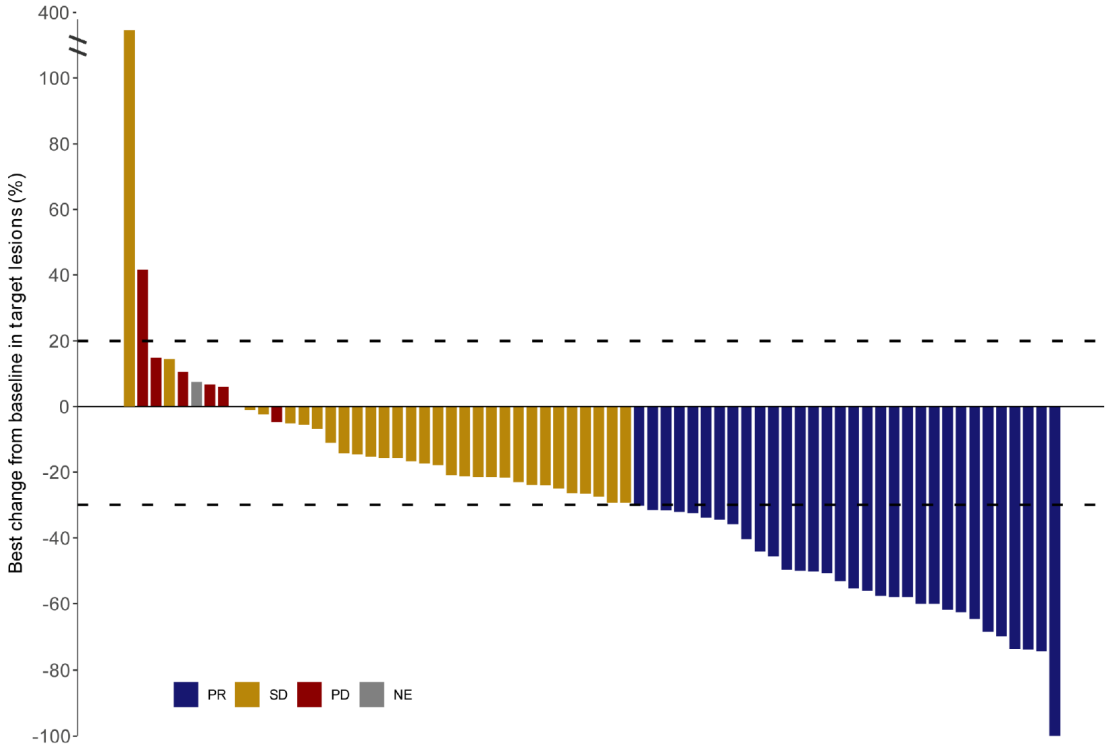
1. Chang C-L, et al. ESMO Asia 2025. #603O. See abbreviations on the last slide.

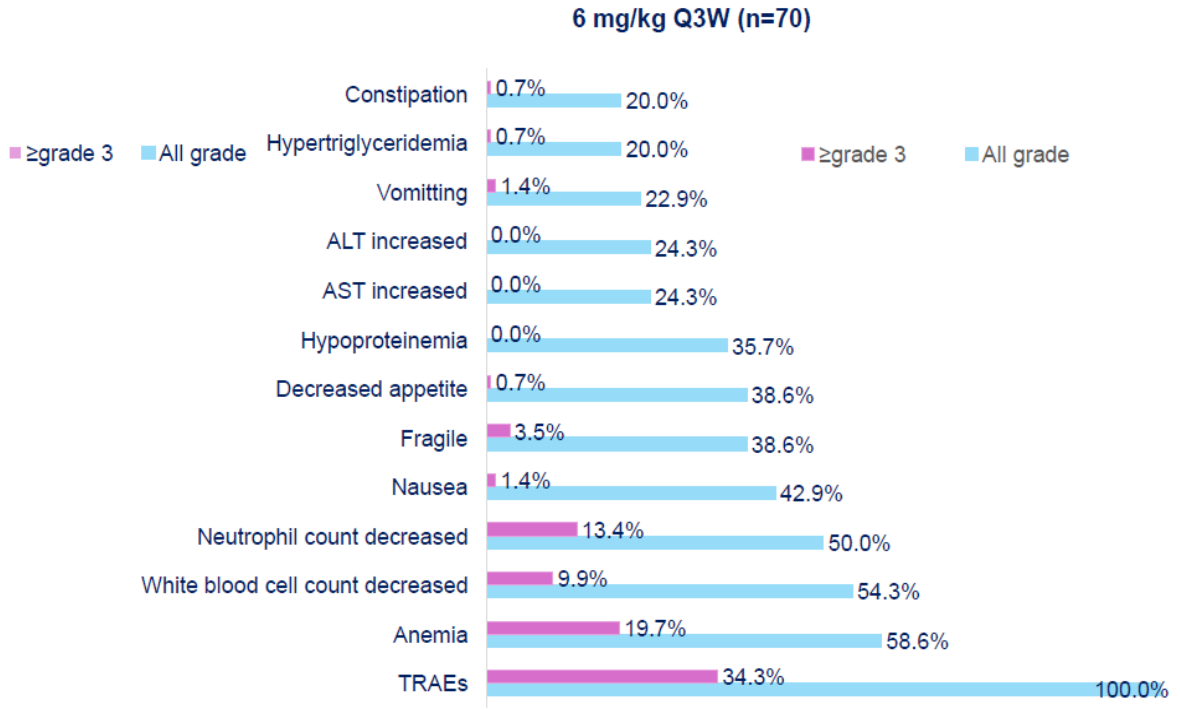
Winer S et al, SGO 2026

Target: B7H3

SYS 6043 (topo I inh/cleavable/DAR: 6/bystander effect +)

- Fase I/II cohortes expansión (CC, EC, OC)
- Dosis optimizada 6 mg/kg
- OC: 91,8% PROC; 67% ≥ 3L; iparp previo: 61,6% ORR 53.1%,DCR 90.6%
- No diferencias por biomarcador
- TRAEs 100% (34,3% ≥ G3; hematological, nausea; general; AST/ALT g1-2).





Zuo J, SGO 2026

Raludotatug deruxtecan (R-DxD): fase 1, first in human
(topo1 inh; cleavable; DAR: 8; bystander)

Target: CDH6

FDA BREAKTHROUGH THERAPY

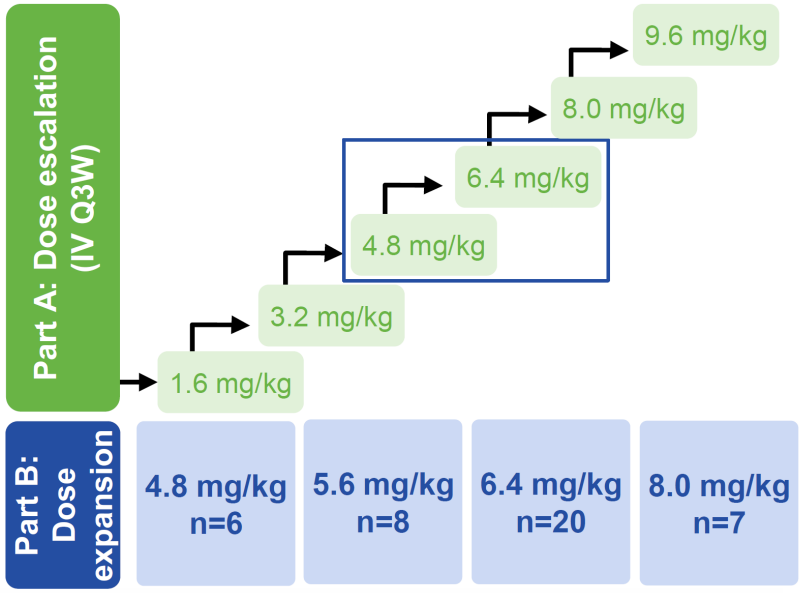
Cohorts[1]

- Advanced RCC
- OC

Key eligibility (OC cohort)[2]

- Advanced/metastatic OC not amenable to SoC therapy
- ECOG-PS 0–1
- Prior taxane and platinum-based CT
- No previous CDH6 targeting agents or ADCs with a linked TOP1i
- Patients were not selected based on tumor CDH6 expression

Subgroup analysis: OC cohort (N=45)[2]

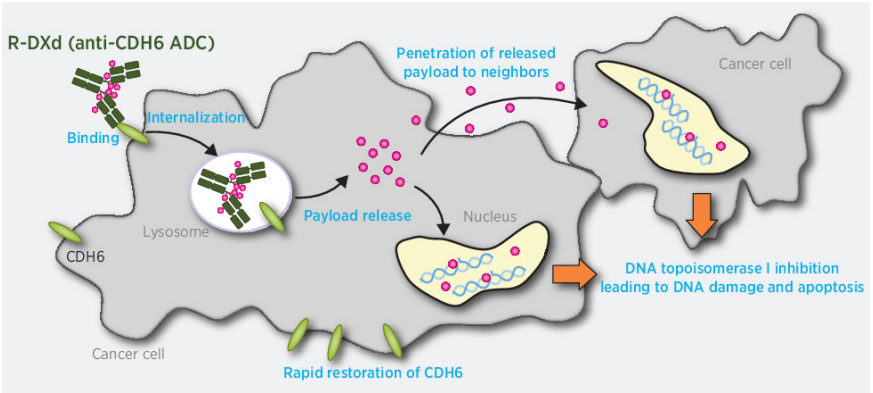


- OC cohort:

ORR: 48,6 %
mPFS: 8,1 m
mDOR: 11,2 m

- Safety

TRAEs grade≥ 3 (44.4%)
  - Anemia: 15,6%;
  - neutropenia 11,1%
  - ILD 2 patients. Grade 2



Endpoints[2]

Primary

- Safety and tolerability, MTD, RDE, ORR per RECIST v1.1 (dose expansion)

Secondary

- PK, ORR per RECIST v1.1 (dose escalation), DOR, DCR, and CBR per RECIST v1.1, immunogenicity

Primary completion: Apr 2026

Moore K, et al. SGO 2024,

R-DxD Rejoice fase 2/3

(topo1 inh; cleavable; DAR: 8; bystander)

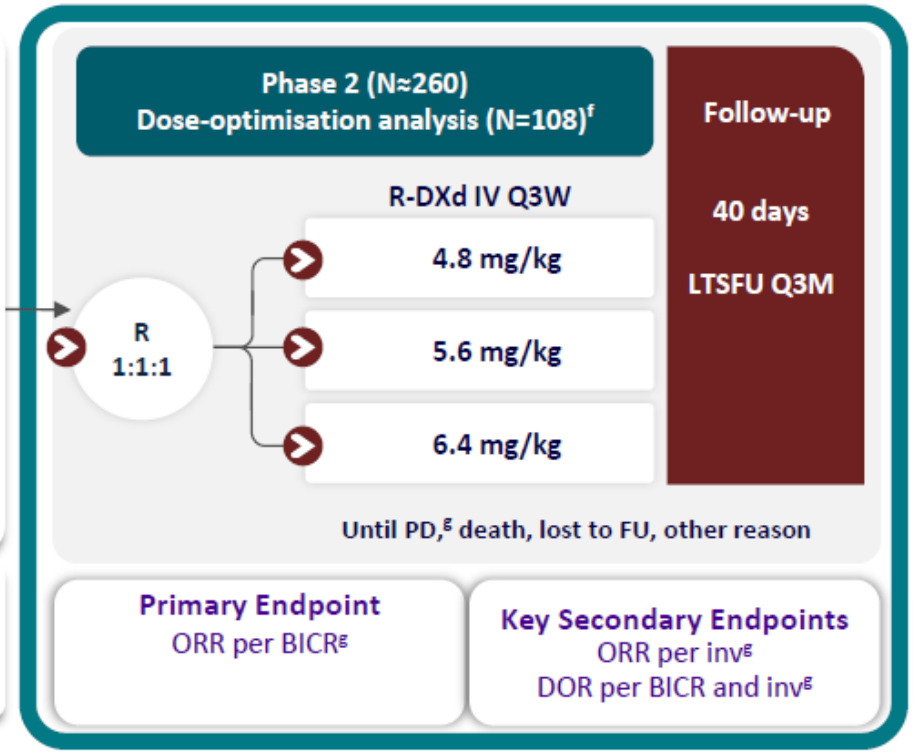
Target: CDH6

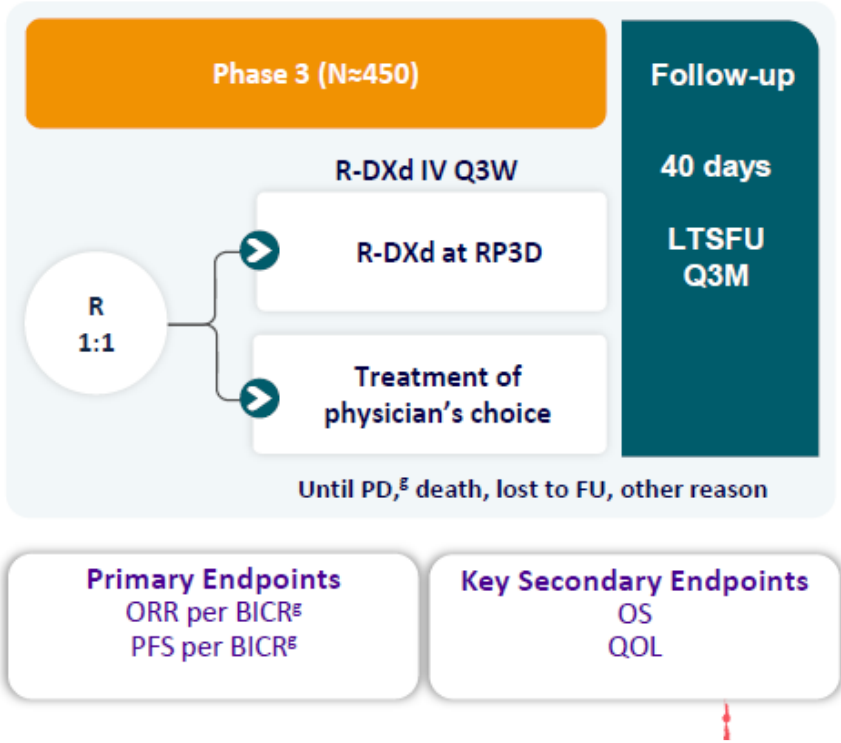
Key Eligibility Criteria

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

Stratification Factors

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

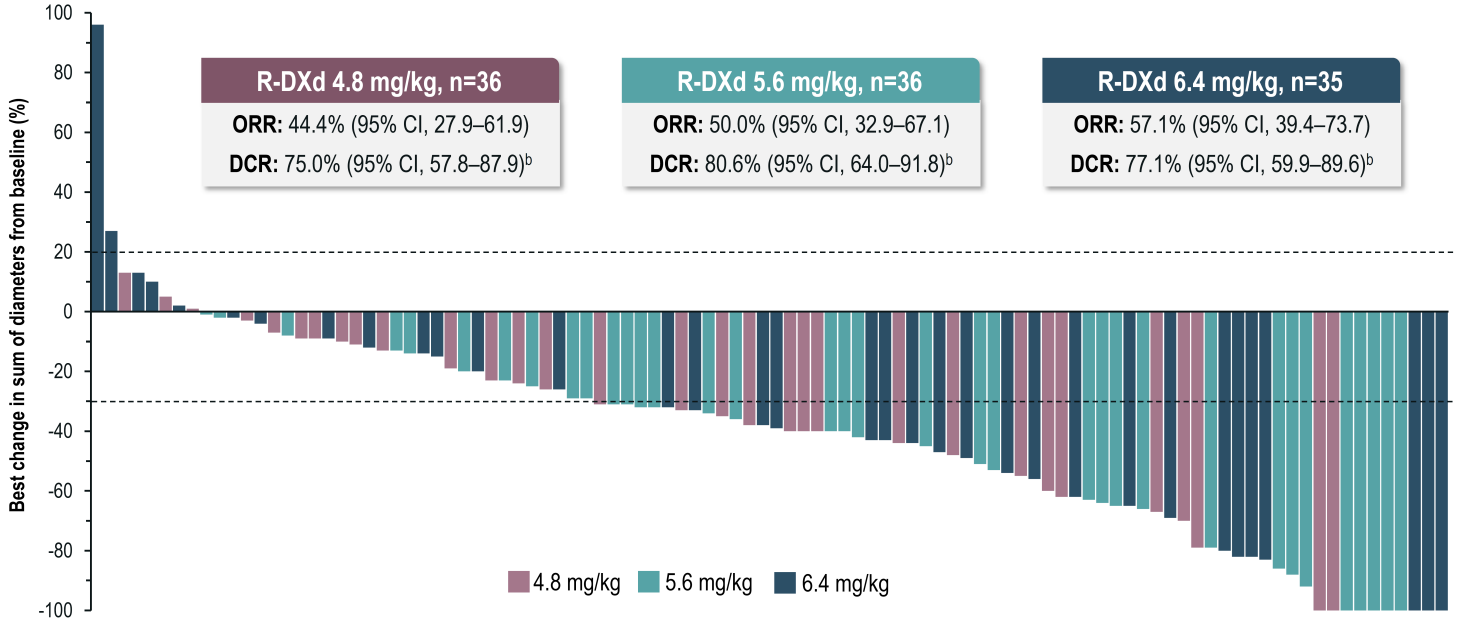


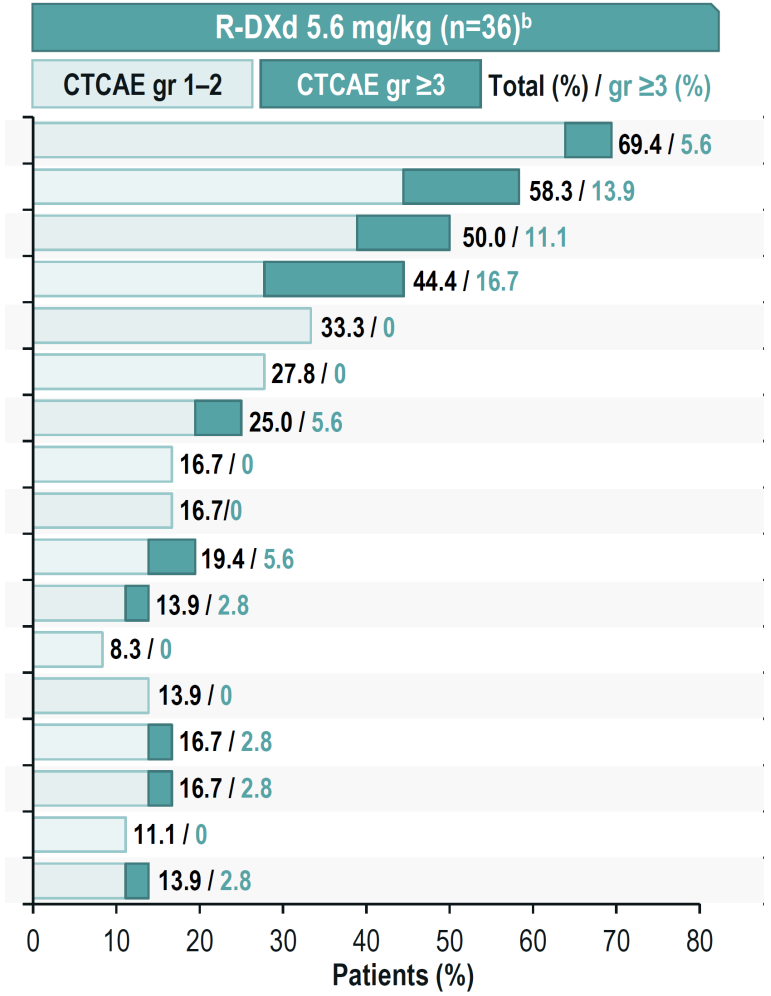


Ray-Coquard I, ESMO 2025

Target: CDH6

Fase 2 optimización dosis





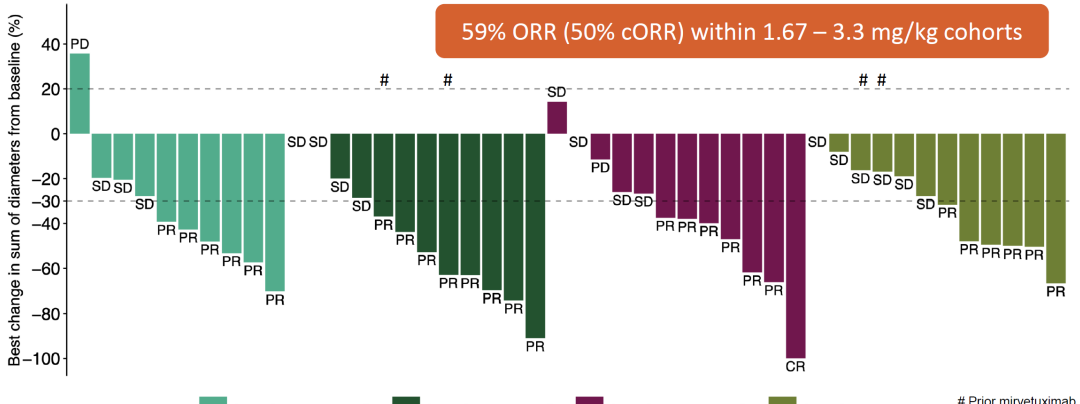
5,6 mg/kg optimized dose
Nausea, anemia, asthenia and neutropenia were the most common TEAEs across all doses

Ray-Coquard I, ESMO 2025

Napistar 1-01: TUB040 fase 1

(TOPO1i; DAR:8 cleavable: bystander)

NaPi2B

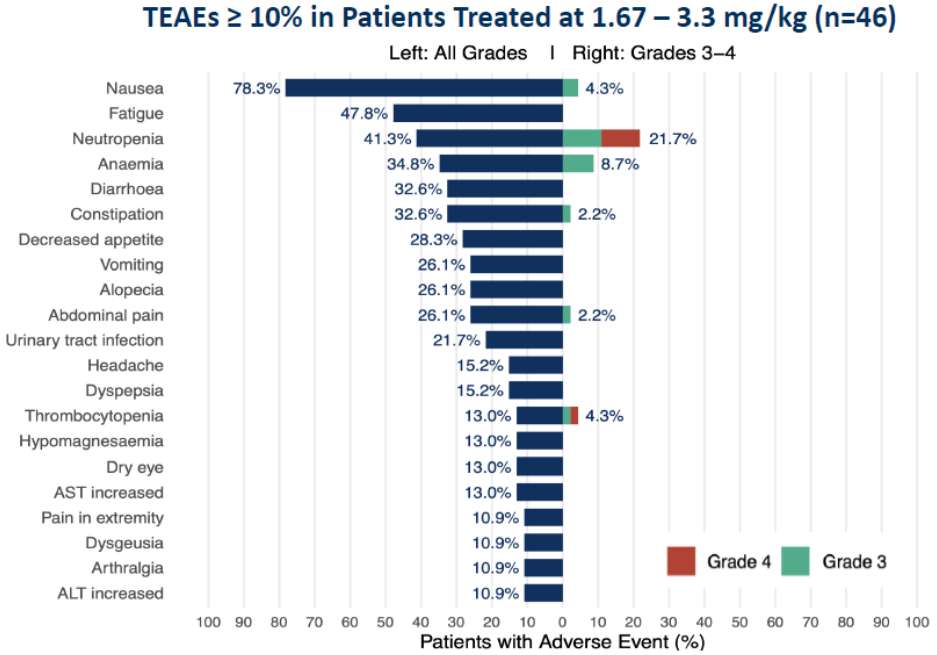


Across 1.67 – 3.3 mg/kg:

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

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

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



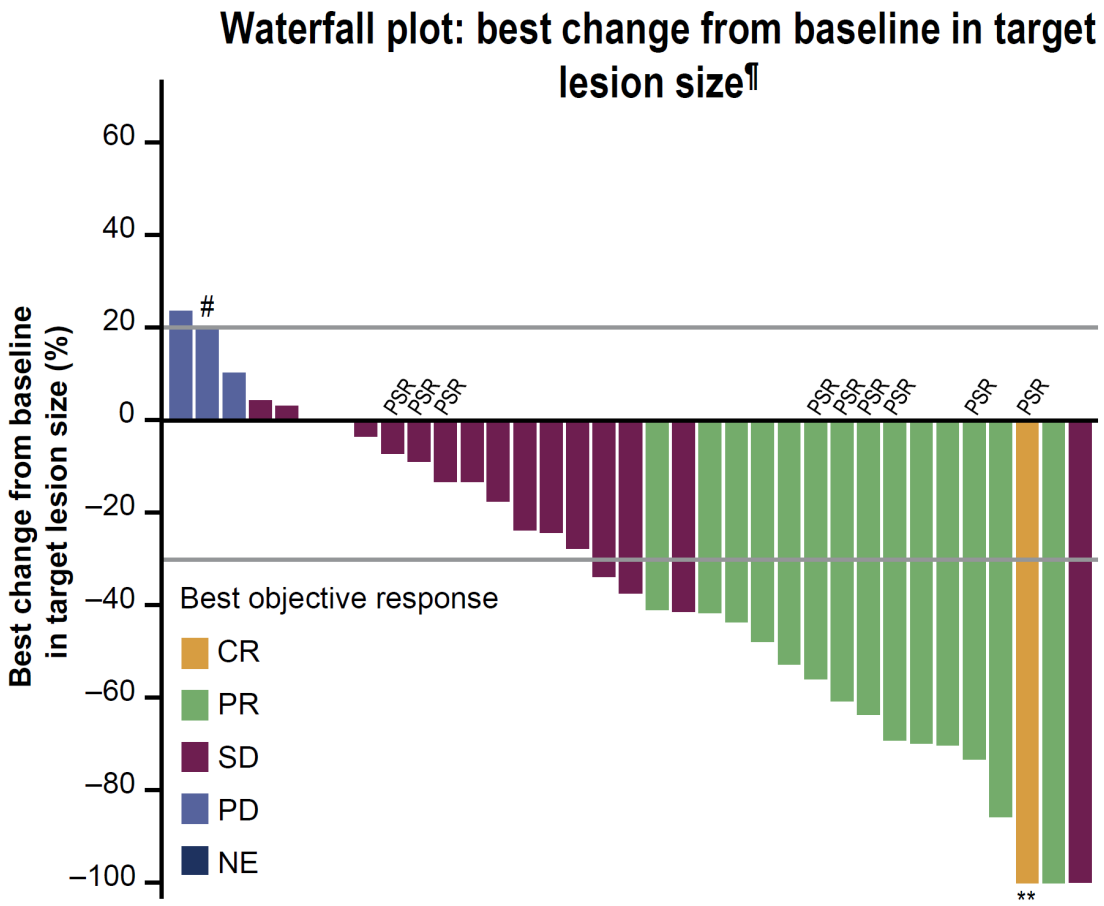
PROC HGSC
50% ORR
TRAEs g3-4: neutropenia
21,7% anemia: 6,7%

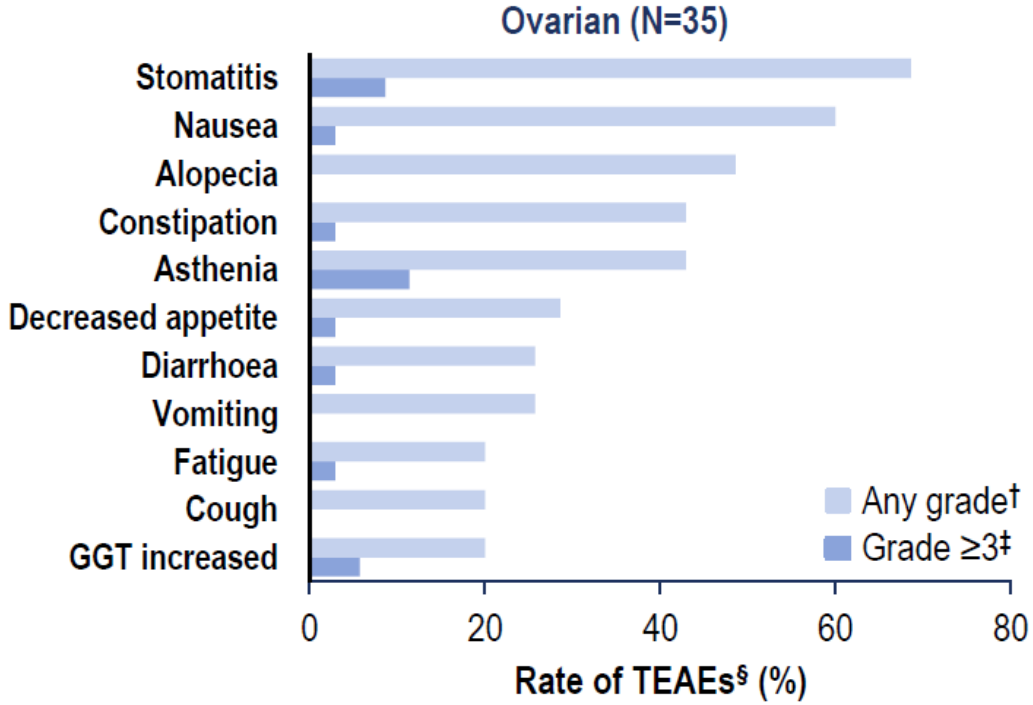
Gonzalez-Martín A et al, ESMO 2025

Trop 2

Datopotamab deruxtecan: TOPO 1i, DAR 4, cleavable, bystander effect
TROPION Pan-tumor 03 PROC fase II

- Análisis intermedio ORR 42,9% (34,6 %PR/66,7 %PS) PFS: 5,6 DOR: 5,6





Ocular Surface events: 40% (g1-2)

TRAEs grade ≥3: 54,3%

1 case ILD grade 3

5,7% discontinuation

Oaknin et al, ESMO 2024

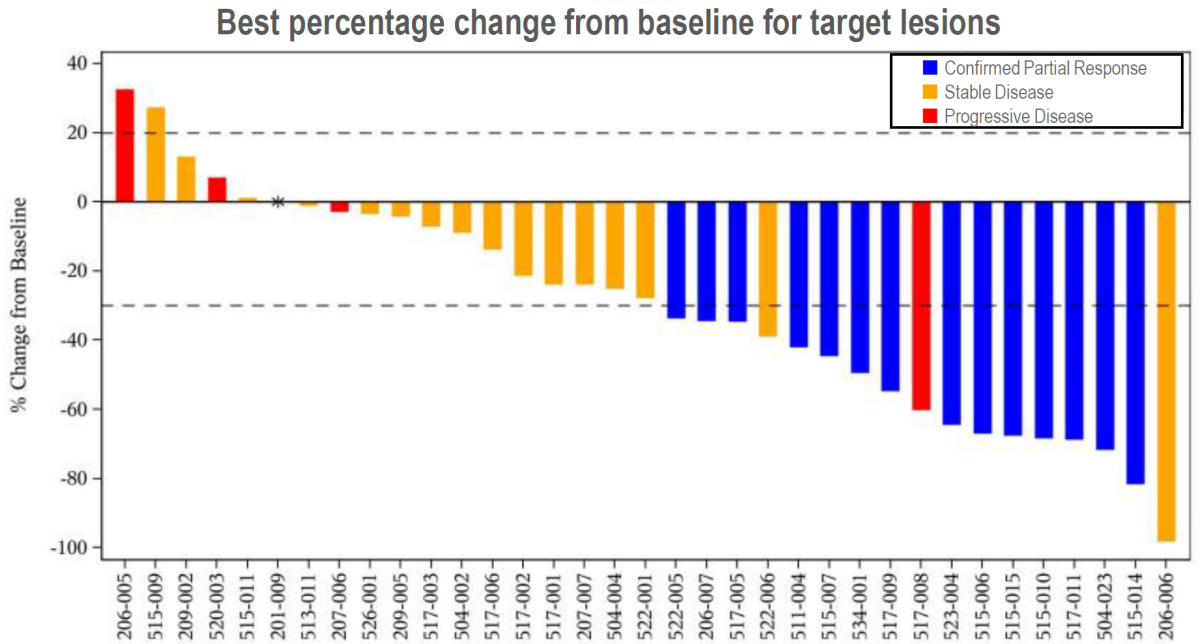
Trop 2

Sacituzumab Timurotecan

(topo1i; DAR: 7,4, cleavable, bystander)

	OC (N = 40)[a]
ORR, % (n/N)	**40.0 (16/40)**
Confirmed ORR	35.0 (14/40)
Subgroups	
TROP2 H-score > 200	61.5 (8/13)
Platinum resistant	37.1 (13/35)
DCR, % (n/N)	**75.0 (30/40)**
PR	40.0 (16/40)
SD	35.0 (14/40)
DoR	
Median (range), months	5.3 (2.1, 24.4+)
PFS	
Median (95% CI), months	6.0 (3.9, 7.3)

a. Responses assessed per RECIST v1.1 by investigator.



TRAEs ≥g 3 67,5%
Discontinuación 12,5%
Tox hematológica y GI, estomatitis ≥g 3 15%
No ILD

Wang D et al, ESMO 2024

Trop 2

Sacituzumab Timurotecan:

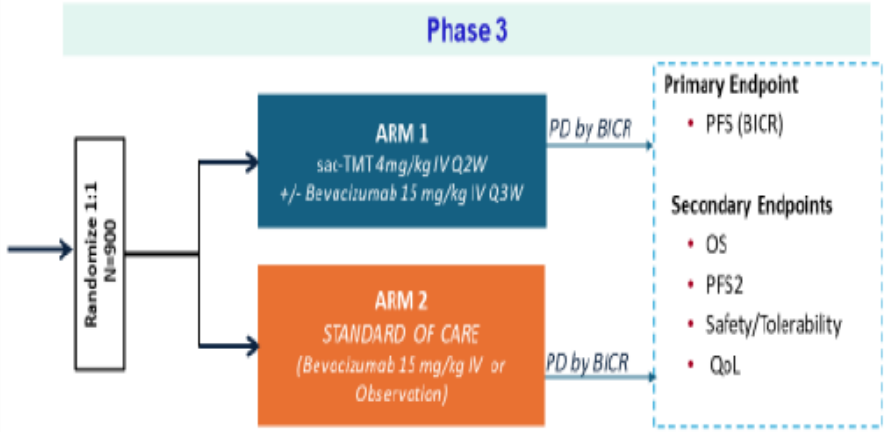
Proprietary

TroFuse-021: Phase 3, Randomized, Open-label Study of Sacituzumab-Tirumotecan(MK-2870)Maintenance Treatment with or without Bevacizumab Versus SOC in Participants With Newly-Diagnosed Advanced non HRD-Positive Ovarian Cancer Following 1L Platinum-based Chemotherapy (ENGOT-ov85/GOG-3102/TroFuse-021)

Clinicaltrials.gov - NCT07318558

Key eligibility criteria:

- Histologically confirmed Epithelial Ovarian Cancer, fallopian tube cancer, or primary peritoneal cancer.
- Undergone PDS or IDS
- Completed 1L treatment with platinum-based chemotherapy with a response of SD, PR or CR per protocol*.
  - Bevacizumab 15 mg/kg is allowed in 1L treatment
- Non HRD positive – Has provided a tumor tissue that is not previously irradiated.
- ECOG PS of 0 or 1



Sacituzumab tirumotecan: 4 mg/kg IV q2w on Days 1, 15, and 29 of every 6-week cycle
Bevacizumab: 15 mg/kg IV q3w on Days 1 and 22 of every 6-week cycle

1L maintenance HRD negative +/- bev

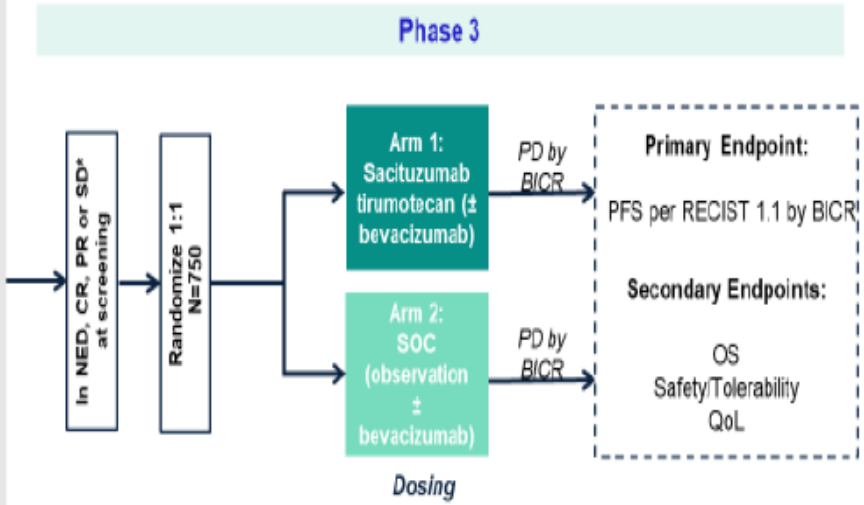
roprietary

TroFuse 022 - A Phase 3, Randomized, Open-label, Multicenter Study to Evaluate the Efficacy and Safety of Sacituzumab Tirumotecan (MK-2870) 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 (ENGOT-ov84/GOG-3103/TroFuse-022)

Clinicaltrials.gov - NCT06824467

Key eligibility criteria:

- Histologically confirmed epithelial ovarian, fallopian tube, or primary peritoneal cancer*
- PSRCC with progression >180d after last dose of 1L platinum doublet chemotherapy
  - Prior bevacizumab use permitted
  - BRCAm/ HRD+ who had CR/PR/NED after 1L must have received PARPi as 1L maintenance
- Must have received 6 cycles of 2L carboplatin-based doublet chemotherapy (+/- bevacizumab)
- Patients with response to 2L of SD must be receiving bevacizumab in combination with chemo and be eligible to continue treatment with bev, will be randomized to sac-TMT + bev or bev alone



Sacituzumab tirumotecan: 4 mg/kg IV q2w on Days 1, 15, and 29 of every 6-week cycle
Bevacizumab: 15 mg/kg IV q3w on Days 1 and 22 of every 6-week cycle

PSOC 2L maintenance+/- bev

Trop 2

DB-1305/BNT325 (TOPO1i, DAR: 4, bystander)

-3 mg/kg N=30
*ORR: 40%
*Estomatitis 66,7%
20% g3-4

Rubinstein M, SGO 2025

We present efficacy and safety data from patients with ovarian cancer treated with DB-1305/BNT325

Key inclusion criteria:
- ≥18 years of age
- ≥1 measurable lesion per RECIST v1.1
- ECOG PS 0–1
- Adequate organ function
- Asymptomatic brain metastases are allowed

For Phase 2a Cohort 3 dose optimization:
- Ovarian cancer, primary peritoneal cancer, or fallopian tube cancer (high-grade serous histology)
- 1–4 prior lines of systemic therapy
- PROC disease

Phase 1:	Dose escalation	2 mg/kg up to 5 mg/kg IV Q3W	(n=18)
Phase 2a Cohort 3 in 2L–5L PROC:	Dose optimization	4 mg/kg/3.5 mg/kg vs 3 mg/kg IV Q3W	(n=40)

Dose optimization started with 4 mg/kg and was changed per SMC guidance to 3.5 mg/kg after 10 patients had received 4 mg/kg

R1 n=20 → 4 mg/kg Q3W / 3 mg/kg Q3W

R2 n=20 → 3.5 mg/kg Q3W / 3 mg/kg Q3W

Until disease progression/ unacceptable toxicity

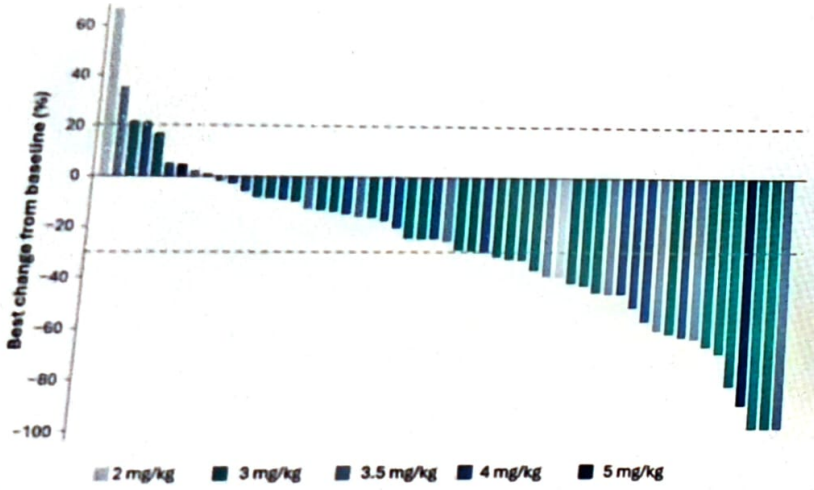
Primary endpoint: Investigator-assessed ORR per RECIST v1.1 and safety

Secondary endpoints: DCR, DOR, PFS, OS

Exposure-response (E-R) relationships for efficacy and safety were performed to support dose identification

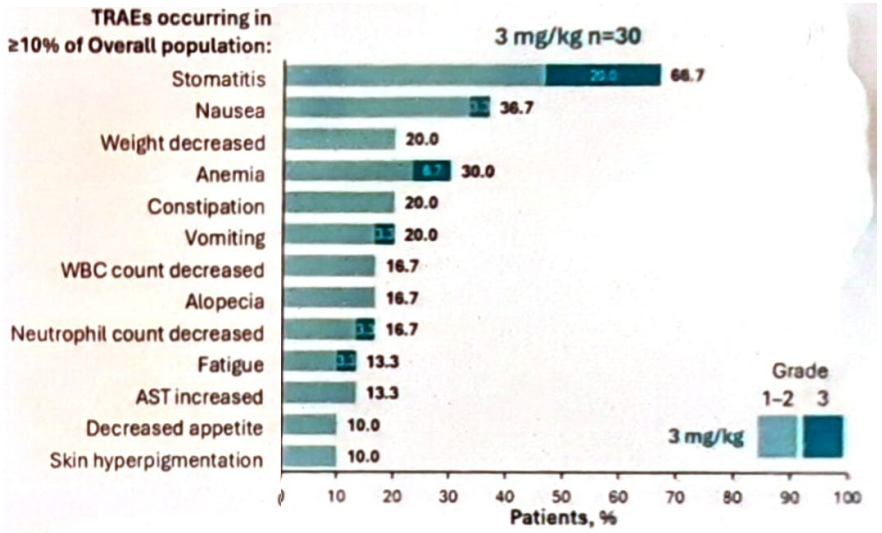
- 58 patients with ovarian cancer received ≥1 dose of DB-1305/BNT325
- 3 mg/kg (n=30) dose identified for further expansion

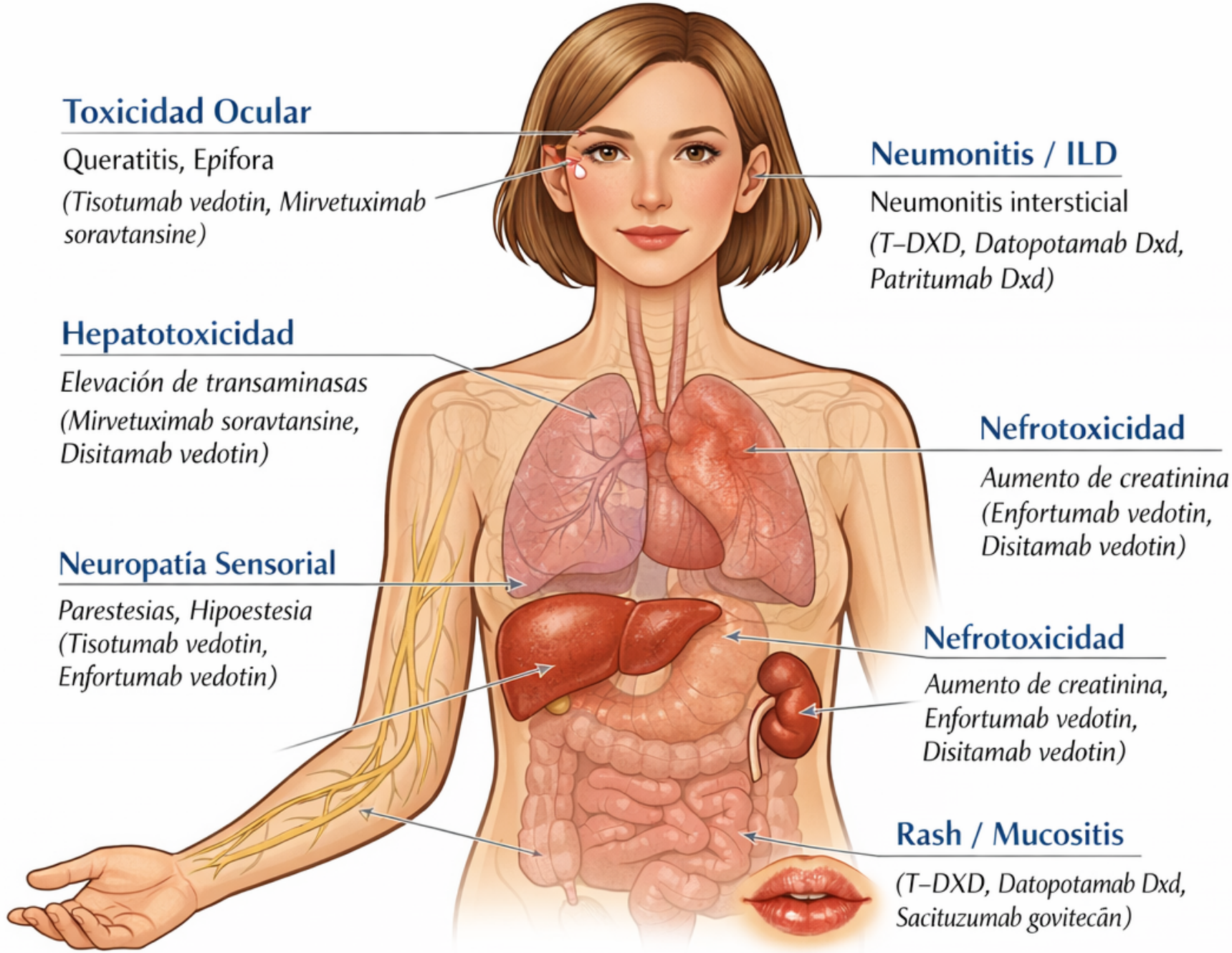
n (%)	TRAE		TRAE leading to		
	Any	Grade ≥3*	Dose reduction	Interruption	Discontinuation
Overall (2–5 mg/kg) (N=58)	57 (98.3)	31 (53.4)	27 (46.6)	13 (22.4)	3 (5.2)
3 mg/kg (n=30)	29 (96.7)	12 (40.0)	8 (26.7)	6 (20.0)	2 (6.7)



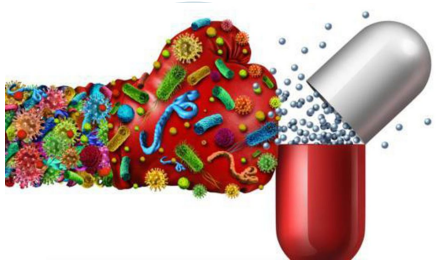
	3 mg/kg (n=30)	3.5 mg/kg (n=10)	4 mg/kg (n=14)	Overall (2–5 mg/kg) (N=58)
BOR,* n (%)				
CR	1 (3.3)	0	0	2 (3.4)
PR	11 (36.7)	5 (50.0)	5 (35.7)	22 (37.9)
SD	12 (40.0)	4 (40.0)	7 (50.0)	24 (41.4)
PD	3 (10.0)	1 (10.0)	1 (7.1)	6 (10.3)
NE	0	0	1 (7.1)	1 (1.7)
ORR, % [95% CI]	**40.0** [22.7, 59.4]	**50.0** [18.7, 81.3]	**35.7** [12.8, 64.9]	**41.4** [28.6, 55.1]
cORR, % [95% CI]	**26.7** [12.3, 45.9]	**40.0** [12.2, 73.8]	**21.4** [4.7, 50.8]	**29.3** [18.1, 42.7]
DCR, % [95% CI]	**80.0** [61.4, 92.3]	**90.0** [55.5, 99.8]	**85.7** [57.2, 98.2]	**82.8** [70.6, 91.4]

- Confirmation of response was pending for 2 patients receiving 3 mg/kg that was confirmed post DCO, leading to a **cORR of 33.3% (3 mg/kg)** and **32.8% (overall)**

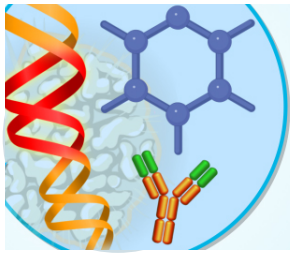



Toxicidad Ocular
Queratitis, Epifora
(Tisotumab vedotin, Mirvetuximab soravtansine)
Neumonitis / ILD
Neumonitis intersticial
(T–DXD, Datopotamab Dxd, Patritumab Dxd)
Hepatotoxicidad
Elevación de transaminasas
(Mirvetuximab soravtansine, Disitamab vedotin)
Nefrotoxicidad
Aumento de creatinina
(Enfortumab vedotin, Disitamab vedotin)
Neuropatía Sensorial
Parestesias, Hipoestesia
(Tisotumab vedotin, Enfortumab vedotin)
Nefrotoxicidad
Aumento de creatinina,
Enfortumab vedotin,
Disitamab vedotin)
Rash / Mucositis
(T–DXD, Datopotamab Dxd, Sacituzumab govitecān)

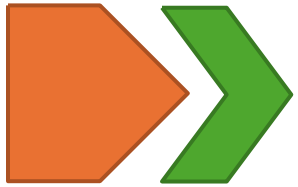
Retos futuros



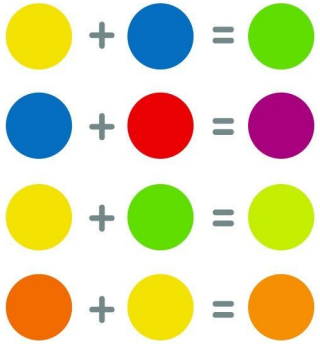
IDENTIFICACIÓN DE MECANISMOS DE RESISTENCIA



DESARROLLO DE BIOMARCADORES PRECISOS



SECUENCIACIÓN OPTIMA DE ADCS



EXPLORAR LAS COMBINACIONES CON Y DE ADC'S

PREDICCIÓN DE RESISTENCIA ADC'S

Conclusiones

- Tratamiento cáncer de ovario con la incorporación de ADC's en rápida evolución→ pendientes de resultados EC fase III consolidados

- **Mirvetuximab soravtansine** primer ADC aprobado EMA en PROC con selección por biomarcador.
  - Incluido en guías clínicas SEOM-GEICO y ESMO

- **T-DxD** con aprobación tumor agnostic FDA IHC 3+

- Nuevos ADC's con diferentes dianas, combinaciones y escenarios y nuevos retos para integrarlos en la práctica clínica

Mila esker
Moltes gràcies
Moitas grazas
Muchas gracias

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