Updates on Gynecologic Cancer - Ovarian cancer

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DECLARATION OF INTERESTS

Nothing to declare

Contents

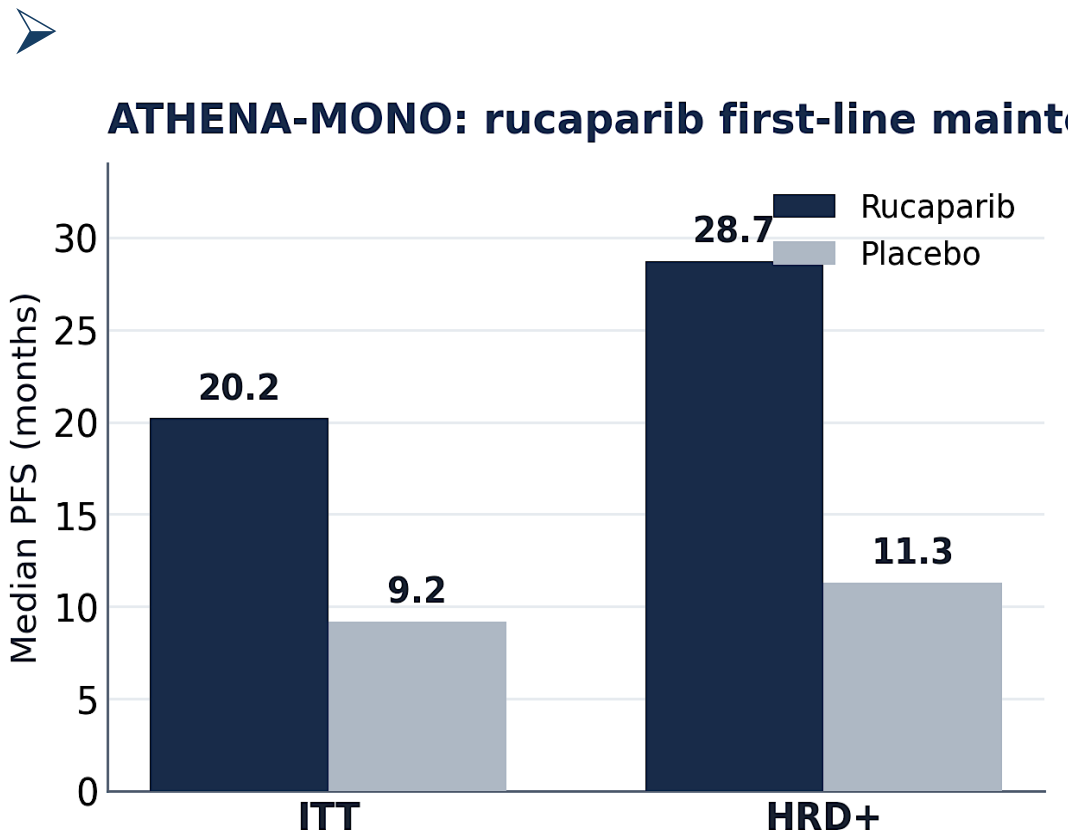
- Maintenance therapy
  - Rucaparib (ATHENA-MONO)
- Platinum-sensitive recurrence
- Platinum-resistant recurrence
  - Mirvetuximab soravtansine (MIRASOL)
  - Other ADCs
  - Albumin-bound paclitaxel/Relacorilant (ROSELLA)
  - Weekly paclitaxel/Pembrolizumab+/-Bevz (KEYNOTE-B96)
- Monitoring
  - ctDNA

First-line maintenance therapy

- Olaparib (SOLO-1)
- Niraparib (PRIMA)
- Olaparib+Bevacizumab (PAOLA-1)

- Rucaparib (ATHENA-MONO) – updated in 2026 ESMO clinical practice guideline

Rucaparib (ATHENA-MONO)



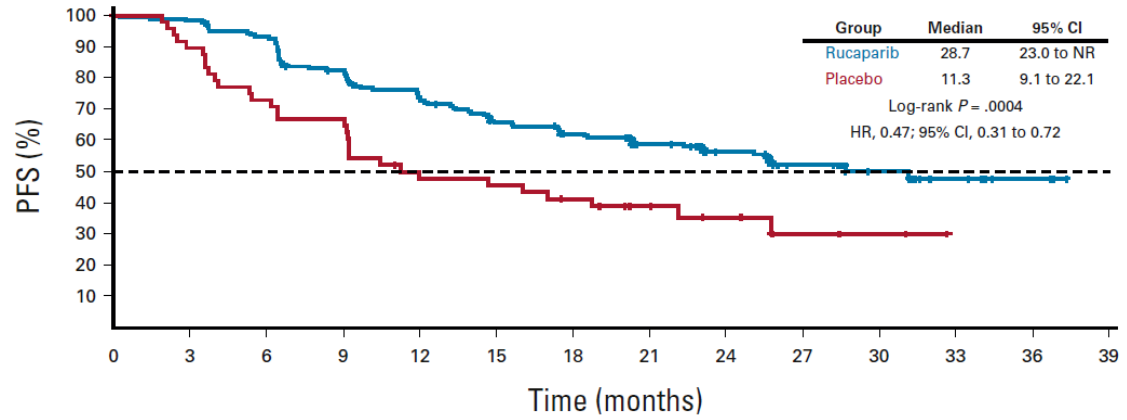
ITT HR 0.52 · HRD+ HR 0.47 (0.31–0.72)

- **All-comers:** rucaparib ×2 years vs placebo after response to platinum
- **ITT PFS:** 20.2 vs 9.2 months (HR 0.52)
- **HRD-positive PFS:** 28.7 vs 11.3 months (HR 0.47, 95% CI 0.31–0.72)
- **HRD-negative:** more modest benefit, consistent with the HR gradient

Monk et al. J Clin Oncol 2022; 5-yr interim update Ann Oncol 2025. ATHENA-MONO/GOG-3020/ENGOT-ov45.

Rucaparib (ATHENA-MONO)

A

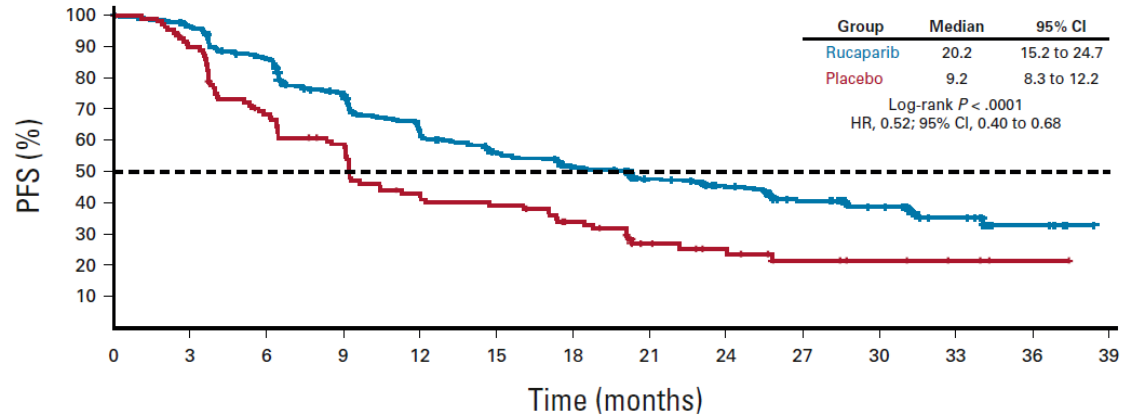


No. at risk (events):

Rucaparib	185 (0)	175 (3)	165 (12)	143 (31)	127 (46)	110 (60)	100 (66)	82 (71)	59 (74)	36 (78)	22 (79)	12 (80)	3 (80)	0 (80)
Placebo	49 (0)	43 (5)	35 (13)	32 (16)	22 (25)	21 (26)	18 (28)	11 (29)	8 (30)	4 (31)	2 (31)	0 (31)		

HRD+
- median PFS: 28.7mo vs. 11.3mo
  (p=0.0004, HR 0.47 (0.31-0.72)

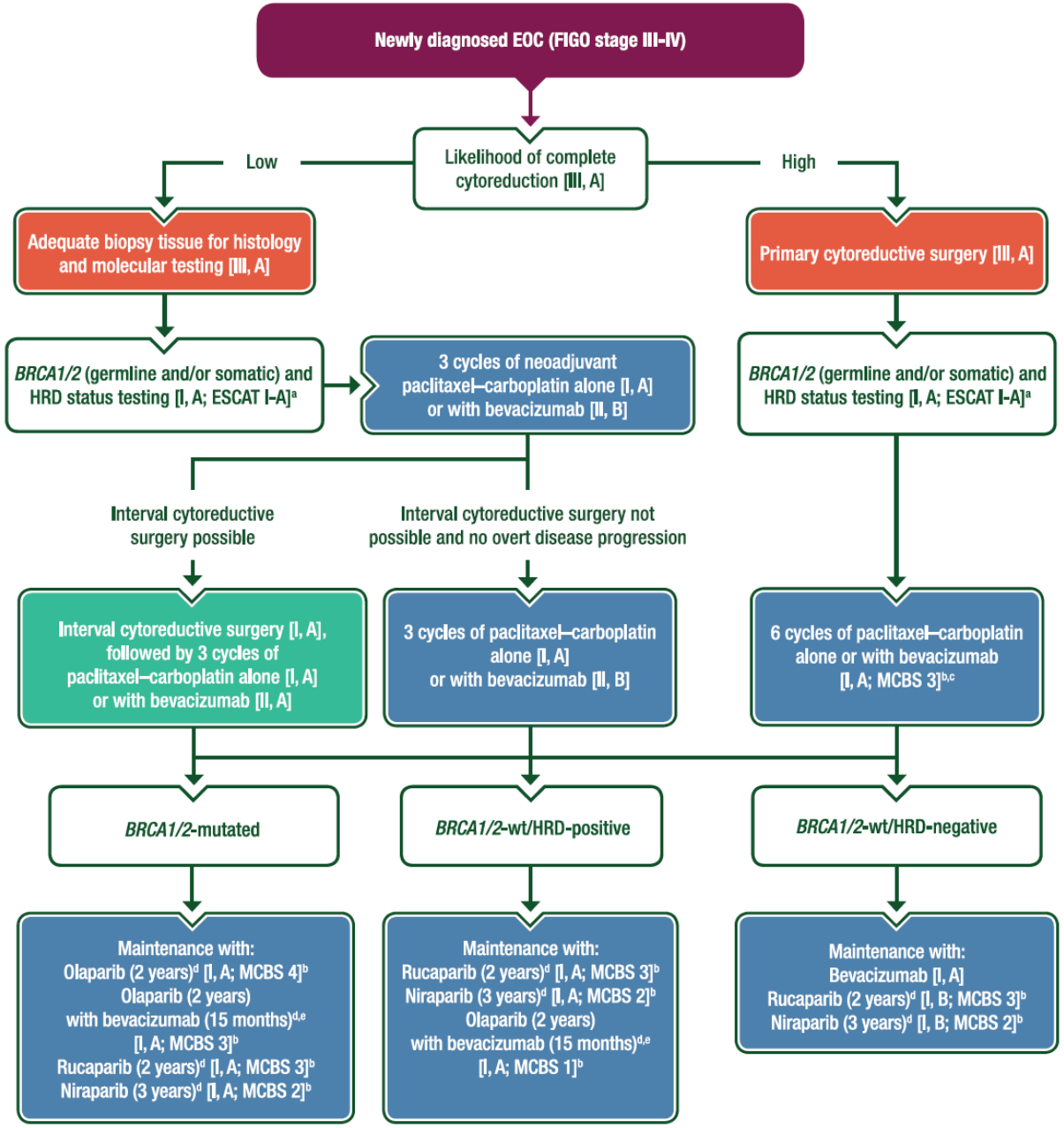
B



No. at risk (events):

Rucaparib	427 (0)	398 (15)	351 (57)	298 (101)	245 (149)	213 (176)	190 (193)	151 (207)	114 (214)	67 (224)	42 (226)	23 (229)	7 (230)	0 (230)
Placebo	111 (0)	97 (11)	72 (34)	60 (44)	42 (61)	39 (64)	31 (69)	18 (75)	14 (76)	8 (78)	5 (78)	3 (78)	1 (78)	0 (78)

ITT
- median PFS: 20.2mo vs. 9.2mo
  (p<0.0001, HR 0.52 (0.40-0.68)


Newly diagnosed EOC (FIGO stage III–IV)
Likelihood of complete cytoreduction [III, A]
Low
High
Adequate biopsy tissue for histology and molecular testing [III, A]
Primary cytoreductive surgery [III, A]
BRCA1/2 (germline and/or somatic) and HRD status testing [I, A; ESCAT I-A][a]
3 cycles of neoadjuvant paclitaxel–carboplatin alone [I, A] or with bevacizumab [II, B]
BRCA1/2 (germline and/or somatic) and HRD status testing [I, A; ESCAT I-A][a]
Interval cytoreductive surgery possible
Interval cytoreductive surgery not possible and no overt disease progression
Interval cytoreductive surgery [I, A], followed by 3 cycles of paclitaxel–carboplatin alone [I, A] or with bevacizumab [II, A]
3 cycles of paclitaxel–carboplatin alone [I, A] or with bevacizumab [II, B]
6 cycles of paclitaxel–carboplatin alone or with bevacizumab [I, A; MCBS 3][b,c]
BRCA1/2-mutated
BRCA1/2-wt/HRD-positive
BRCA1/2-wt/HRD-negative
Maintenance with:
Olaparib (2 years)[d] [I, A; MCBS 4][b]
Olaparib (2 years) with bevacizumab (15 months)[d,e] [I, A; MCBS 3][b]
Rucaparib (2 years)[d] [I, A; MCBS 3][b]
Niraparib (3 years)[d] [I, A; MCBS 2][b]
Maintenance with:
Rucaparib (2 years)[d] [I, A; MCBS 3][b]
Niraparib (3 years)[d] [I, A; MCBS 2][b]
Olaparib (2 years) with bevacizumab (15 months)[d,e] [I, A; MCBS 1][b]
Maintenance with:
Bevacizumab [I, A]
Rucaparib (2 years)[d] [I, B; MCBS 3][b]
Niraparib (3 years)[d] [I, B; MCBS 2][b]

Platinum-sensitive recurrence (PSOC)

- Platinum-based combination CTx +/- Bevacizumab

- Second-line maintenance with PARPi
  - Narrowed PARPi indications (FDA) d/t no significant OS improvements
  - Use of PARPi in post recurrence setting is restricted to *BRCA1/2* mutated EOC.

Regimen	Dose/Administration	Maintenance Setting	Duration
Niraparib monotherapy[2,3]	• 300 mg PO once daily (or an initial dose of 200 mg once daily for patients with a baseline body weight of <77 kg, and/or a platelet count of <150,000/mm^3	Post-primary chemotherapy	• Up to 36 Months unless disease progression or unacceptable toxicity[b]
		Post-recurrence chemotherapy[a]	• Until disease progression or unacceptable toxicity[c]
Olaparib monotherapy[4-6]	• 300 mg PO twice daily	Post-primary chemotherapy	• Up to 2 Years unless disease progression or unacceptable toxicity[b]
		Post-recurrence chemotherapy[a]	• Until disease progression or unacceptable toxicity[c]
Rucaparib monotherapy[7,8]	• 600 mg PO twice daily	Post-primary chemotherapy	• Up to 2 Years unless disease progression or unacceptable toxicity[b]
		Post-recurrence chemotherapy[a]	• Until disease progression or unacceptable toxicity[c]
Olaparib + Bevacizumab[9]	• Olaparib 300 mg PO twice daily • Bevacizumab 15 mg/kg IV every 21 days	Post-primary chemotherapy + Bevacizumab	• Olaparib: Up to 2 Years unless disease progression or unacceptable toxicity • Bevacizumab: Up to 15 Months (total including chemotherapy) unless disease progression or unacceptable toxicity
Niraparib + Bevacizumab[10]	• Niraparib: 300 mg PO once daily (or 200 mg once daily for patients with a baseline body weight of <77 kg, and/or a platelet count of <150,000/mm^3) • Bevacizumab: 15 mg/kg IV every 21 Days	Post-primary chemotherapy + Bevacizumab	• Niraparib: Up to 3 Years unless disease progression or unacceptable toxicity • Bevacizumab: Up to 15 Months (total including chemotherapy) unless disease progression or unacceptable toxicity

[a] Use of PARPi maintenance in post recurrence setting is restricted to *BRCA1/2* mutated setting
[b] In studies, treatment was continued for those whose disease was not in CR at 2 years (olaparib, rucaparib) or 3 years (niraparib).
[c] Clinical trials in the recurrent setting included PARPi maintenance until progression. However, exposure to prolonged PARPi maintenance >2 years in the recurrent setting may increase risk of MDS/AML development.

Platinum-resistant recurrence (PROC)

- Mirvetuximab soravtansine (MIRASOL)
- Other ADCs
- Albumin-bound palictaxel/Relacorilant (ROSELLA)
- Weekly palictaxel/Pembrolizumab+/-Bevz (KEYNOTE-B96)

Platinum-resistant recurrence (PROC)

National Comprehensive Cancer Network®

NCCN Guidelines Version 4.2026
Ovarian Cancer/Fallopian Tube Cancer/Primary Peritoneal Cancer

NCCN Guidelines Index
Table of Contents
Discussion

PRINCIPLES OF SYSTEMIC THERAPY
Acceptable Recurrence Therapies for Epithelial Ovarian (including LCOC)[p]/Fallopian Tube/Primary Peritoneal Cancer

Recurrence Therapy for Platinum-Resistant Disease (alphabetical order)

Preferred	Other Recommended	Useful in Certain Circumstances
Cytotoxic Therapy • Albumin-bound Paclitaxel/ Relacorilant[x,y,44] • Docetaxel[45] • Gemcitabine[46,47] • Liposomal Doxorubicin[46,47] • Liposomal Doxorubicin + Bevacizumab[r,48] • Paclitaxel (Weekly)[h,49] • Paclitaxel (Weekly) + Bevacizumab[h,r,48] • Oral Cyclophosphamide + Bevacizumab[r,50] • Topotecan[51,52] • Topotecan + Bevacizumab[r,48] **Targeted Therapy (single agents)** • Mirvetuximab soravtansine-gynx (for FRα-expressing tumors [≥75% positive tumor cells])(category 1)[v,53,54]	**Cytotoxic Therapy**[t] • Albumin-bound Paclitaxel • Capecitabine • Carboplatin[z] • Carboplatin/Docetaxel[z] • Carboplatin/Paclitaxel (Weekly)[h,z] • Carboplatin/Gemcitabine[15] ± Bevacizumab[r,s,z,16] • Carboplatin/Liposomal Doxorubicin[17] ± Bevacizumab[r,z,18] • Carboplatin/Paclitaxel[h,19] ± Bevacizumab[r,s,z,20] • Cisplatin/Gemcitabine[z,21] • Cyclophosphamide • Doxorubicin • Gemcitabine + Bevacizumab[r,55] • Ifosfamide/Mesna • Irinotecan • Ixabepilone + Bevacizumab (category 2B)[r,aa,56] • Oral Cyclophosphamide + Pembrolizumab + Bevacizumab[r,57,58] • Oral Etoposide[59] • Oxaliplatin • Paclitaxel • Pemetrexed • Sorafenib/Topotecan[60] • Vinorelbine **Targeted Therapy (single agents)** • Bevacizumab[r,25,26] • Pazopanib (category 2B)[28] **Hormone Therapy** • Aromatase inhibitors (Anastrozole, Exemestane, Letrozole) • Goserelin acetate • Leuprolide acetate • Megestrol acetate • Tamoxifen[k]	• Albumin-bound Paclitaxel/Carboplatin (for confirmed taxane hypersensitivity)[z] • Carboplatin/Paclitaxel (for age >70)[h,u,z] **Immunotherapy**[v] • Dostarlimab-gxly (for dMMR/MSI-H recurrent or advanced tumors)[42] • Paclitaxel + Pembrolizumab ± Bevacizumab (for PD-L1-positive tumors [CPS≥1])[h,r,s,bb,61] • Pembrolizumab (for patients with MSI-H or dMMR solid tumors, or TMB-H tumors ≥10 mutations/megabase)[43] • For clear-cell carcinoma ▸ Ipilimumab + Nivolumab[62,63] **Hormone Therapy** • Fulvestrant (for low-grade serous carcinoma) **Targeted Therapy**[v] • Dabrafenib/Trametinib (for *BRAF* V600E positive tumors)[30] • Entrectinib[31] or Larotrectinib[32] or Repotrectinib[33] (for *NTRK1/2/3* gene fusion-positive tumors) • Fam-trastuzumab deruxtecan-nxki (for HER2-positive tumors [IHC 3+ or 2+])[34] • Mirvetuximab soravtansine-gynx + Bevacizumab (for FRα-expressing tumors [≥25% positive tumor cells])[r,36,64,65] • Selpercatinib (for *RET* gene fusion-positive tumors)[37] • For low-grade serous carcinoma: ▸ Avutometinib/Defactinib (for *KRAS*-mutated tumors)[38] ▸ Trametinib[39] ▸ Binimetinib (category 2B)[40,41] • For mucinous carcinoma: ▸ FOLFIRI ± Bevacizumab[r] (category 2B)[66-69]

대한부인종양학회 Korean Society of Gynecologic Oncology

Platinum-resistant recurrence (PROC)

Mirvetuximab soravtansine (MIRASOL)

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

Platinum-resistant recurrence (PROC)

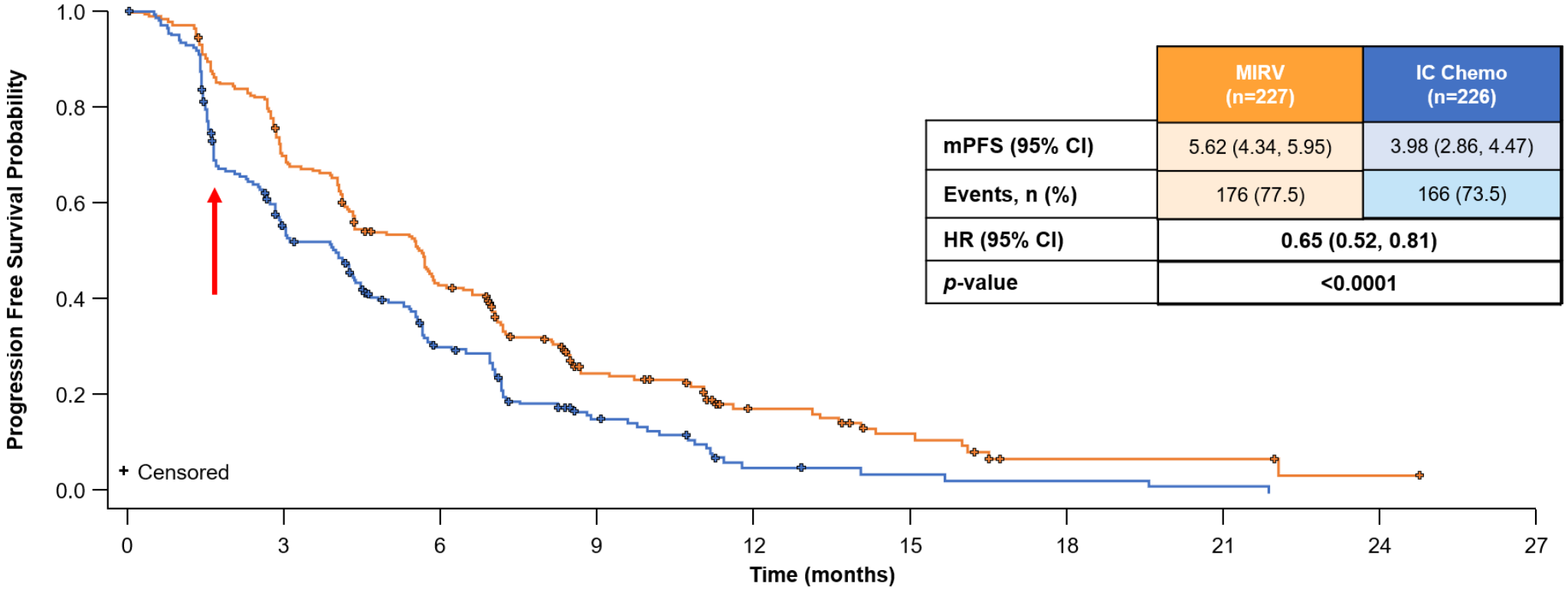
- Mirvetuximab soravtansine (MIRASOL)

Table 2. Investigator-Assessed Objective Response and Other Secondary Efficacy End Points (Intention-to-Treat Population).

End Point	MIRV (N=227)	Chemotherapy (N=226)	Treatment Difference	Odds Ratio or Hazard Ratio*
			percentage points	
Key secondary end point				
Investigator-assessed objective response†				
Participants with response — no.	96	36		
% (95% CI)	42.3 (35.8–49.0)	15.9 (11.4–21.4)	26.4 (18.4–34.4)	3.81 (2.44–5.94)‡
Best overall response — no. (%)				
Complete response	12 (5.3)	0		
Partial response	84 (37.0)	36 (15.9)		
Stable disease§	86 (37.9)	91 (40.3)		
Progressive disease	31 (13.7)	62 (27.4)		
Not evaluable	14 (6.2)	37 (16.4)		
Other secondary end points				
Median duration of response (95% CI) — mo¶	6.77 (5.62–8.31)	4.47 (4.17–5.82)		0.62 (0.40–0.97)
CA-125 response‖				
Participants with response — no./total no. of evaluable participants	105/181	47/155		
% (95% CI)	58.0 (50.5–65.3)	30.3 (23.2–38.2)	27.7 (17.5–37.9)	

Platinum-resistant recurrence (PROC)

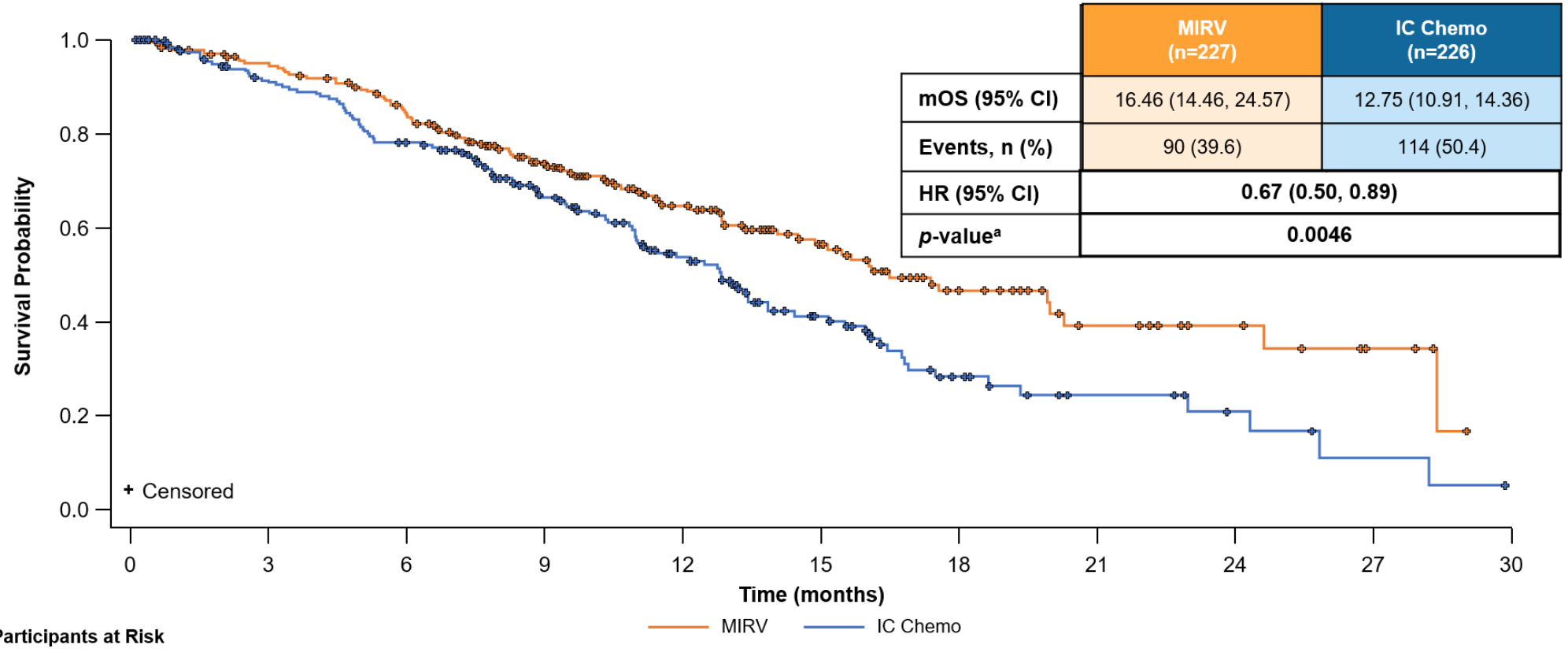
- Mirvetuximab soravtansine (MIRASOL)
  - Primary Endpoint: Progression-Free Survival by Investigator



	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	

Platinum-resistant recurrence (PROC)

- Mirvetuximab soravtansine (MIRASOL)
  - 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	

No. Participants at Risk

MIRV	227	204	175	128	82	53	28	15	9	4	0
IC Chemo	226	185	157	107	68	39	18	9	5	2	0

VENTANA FOLR1 (FOLR1-2.1) RxDx Assay — PS2+ 판독법

판독 원칙

- **Membrane 염색만 정량 평가** (세포질 염색은 참고용으로만 기록)
- Viable 종양세포에서 **염색강도**를 1+ / 2+ / 3+로 구분
- 각 강도별 염색 종양세포의 비율(%)을 산정
- PS2+ score = **'≥2+ 강도'로 염색된 종양세포의 비율(%)**

임상적으로 '고발현(high)' 기준인 PS2+ ≥75%가 Elahere 투여 적응증 컷오프입니다.

FRα 발현 구간 분류

구간	PS2+ 비율	임상적 의미
음성	< 25%	MIRV 적응증 아님
Low	25 – 49%	MIRV 적응증 아님
Medium	50 – 74%	임상시험 맥락에서 탐색
High	≥ 75%	MIRV(Elahere) 승인 대상

판독 시 유의: 종양 내 이질성(heterogeneity)이 있는 경우 대표성 있는 여러 절편 평가를 고려하고, 평가 종양세포 수는 통상 100개 이상을 권장합니다.

Clinical Diagnosis Positive

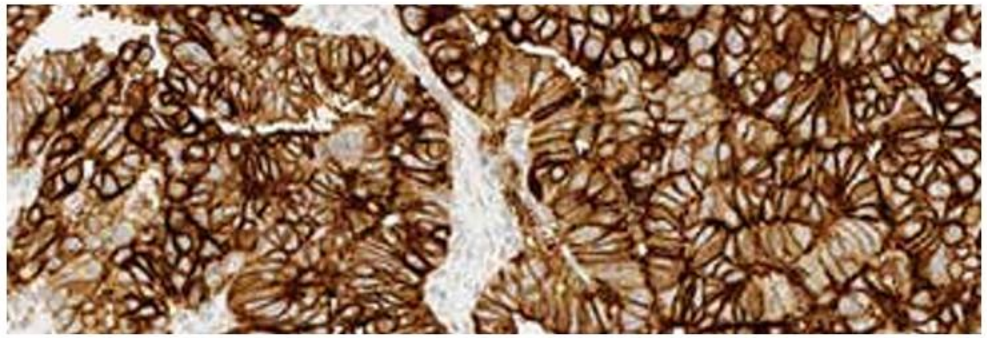


Figure 1: Positive case by VENTANA FOLR1 (FOLR1-2. 1) RxDx Assay with 98% moderate and strong membrane staining

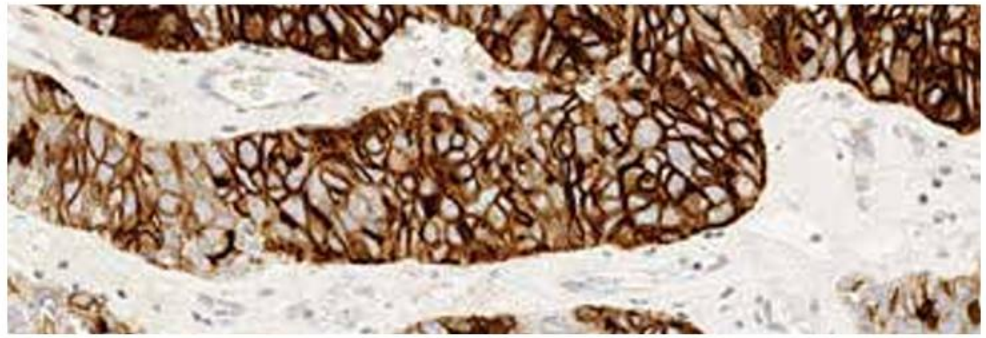


Figure 2: Positive case by VENTANA FOLR1 (FOLR1-2.1) RxDx Assay with 95% moderate and strong membrane staining

Clinical Diagnosis Negative

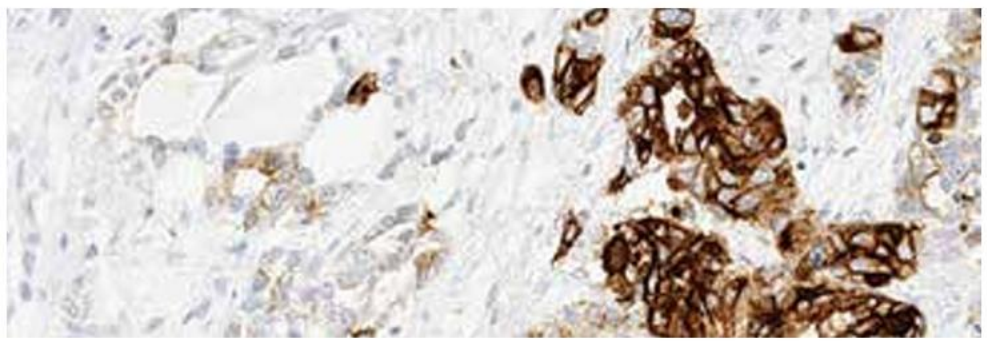


Figure 3: Negative case by VENTANA FOLR1 (FOLR1-2.1) RxDx Assay staining with 20% moderate and strong membrane staining

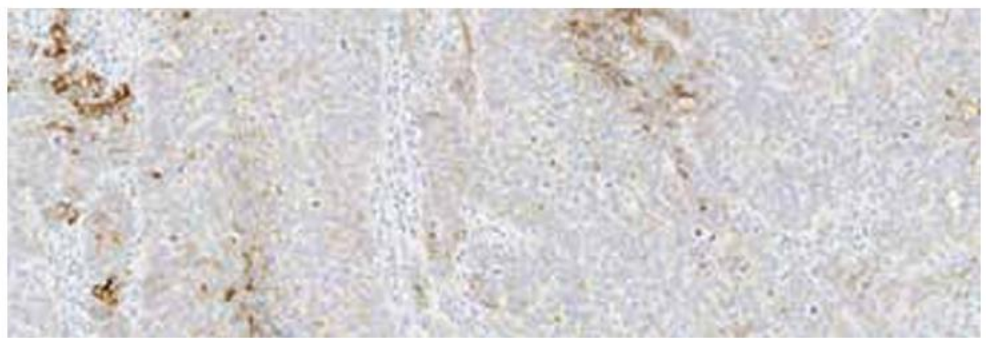
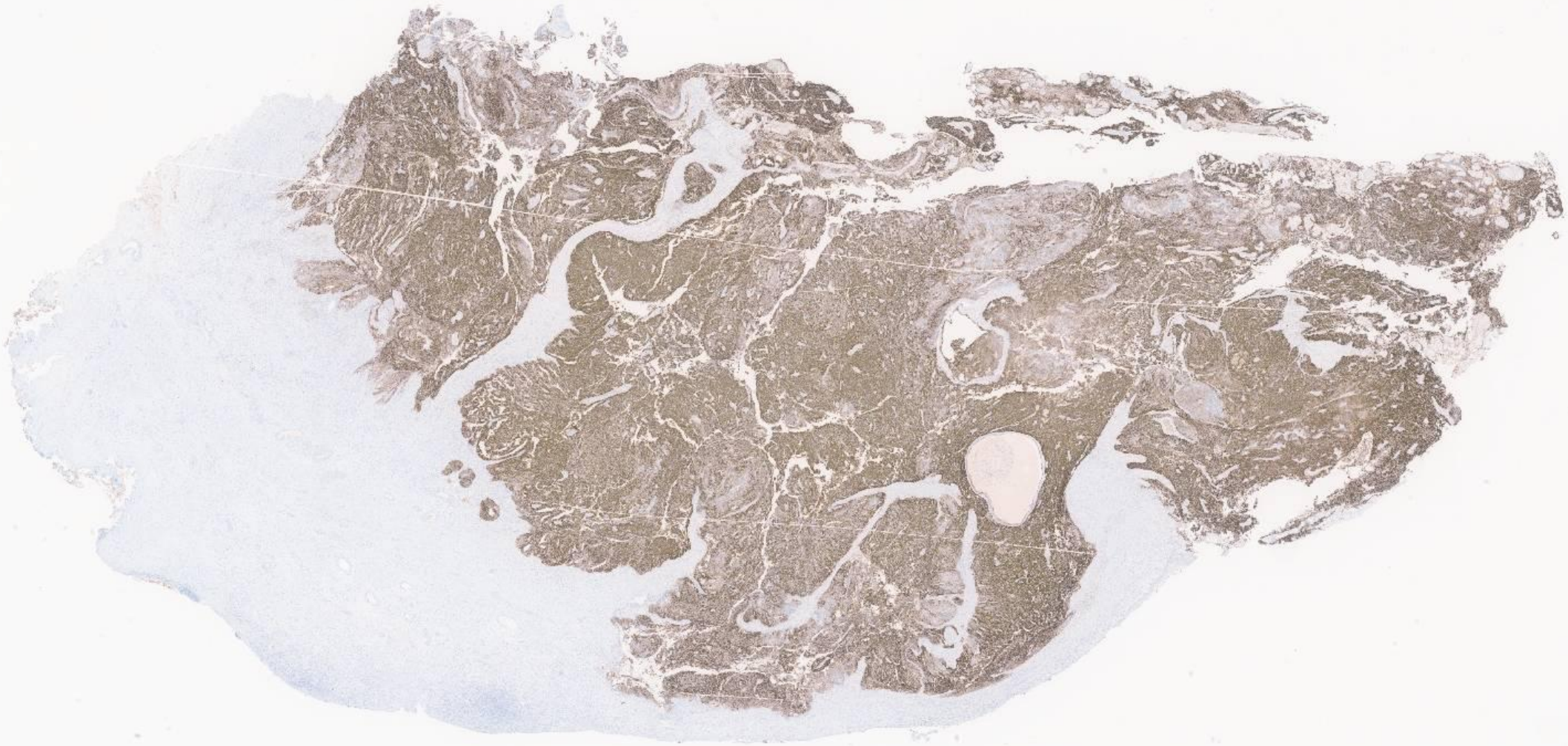
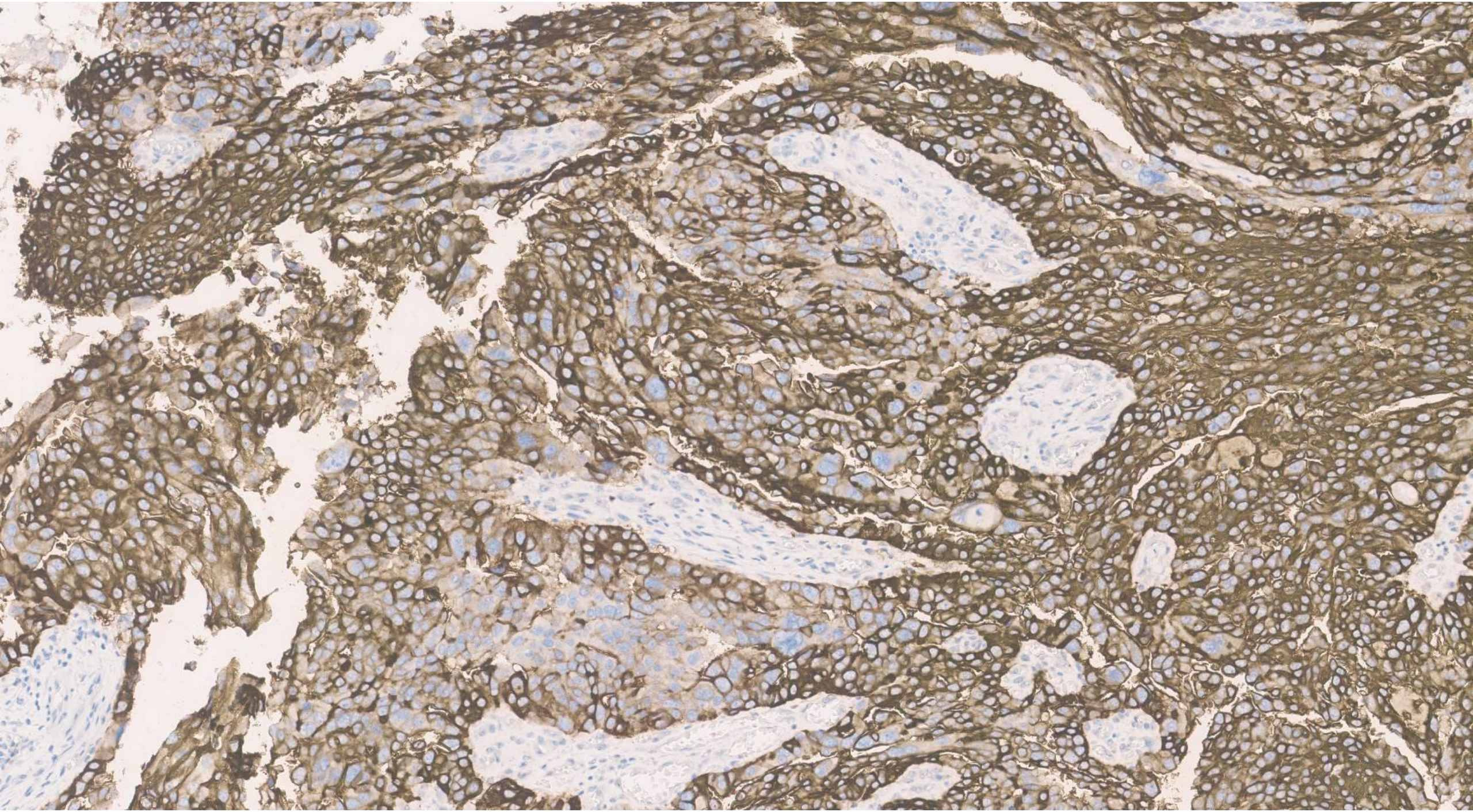
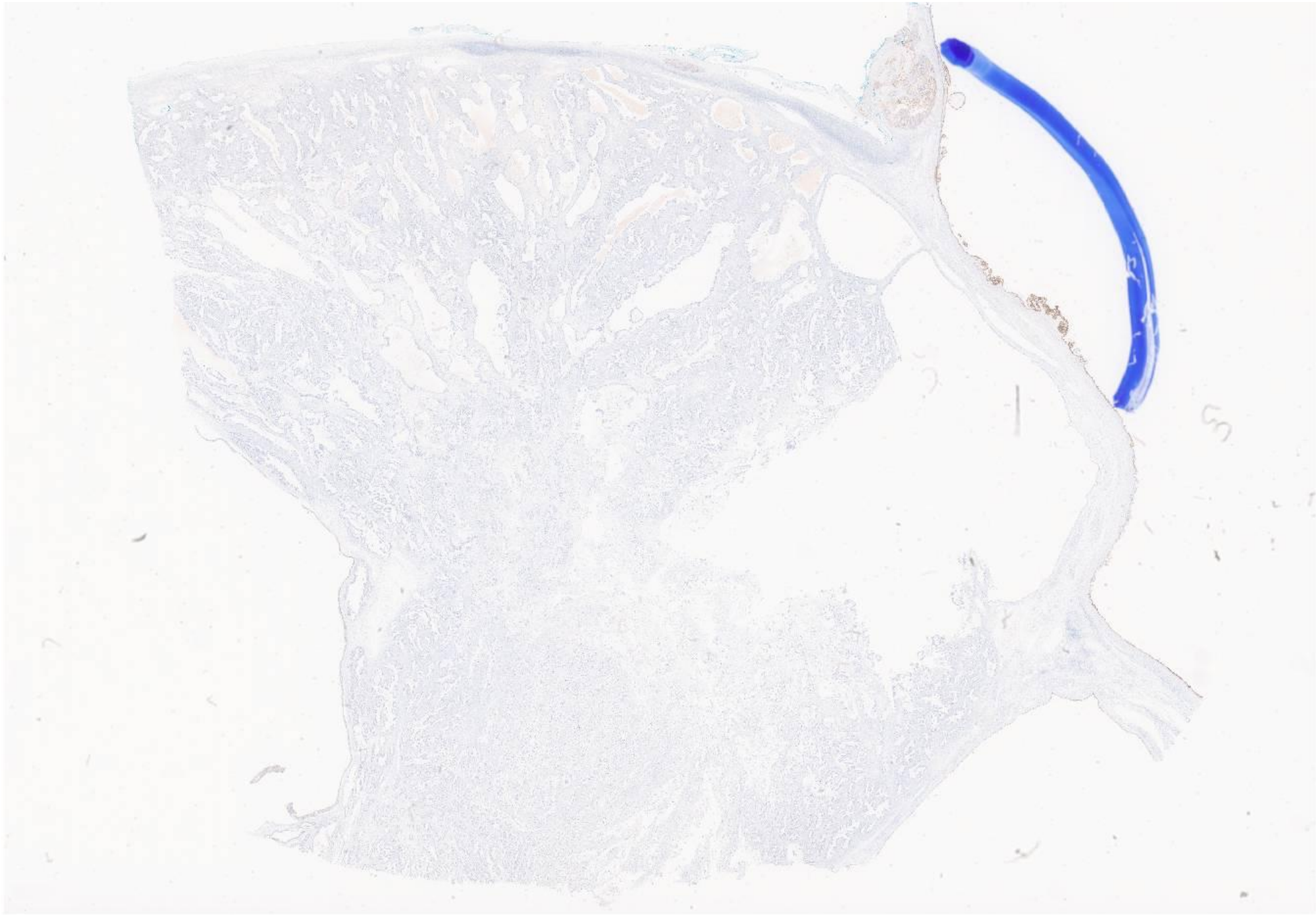
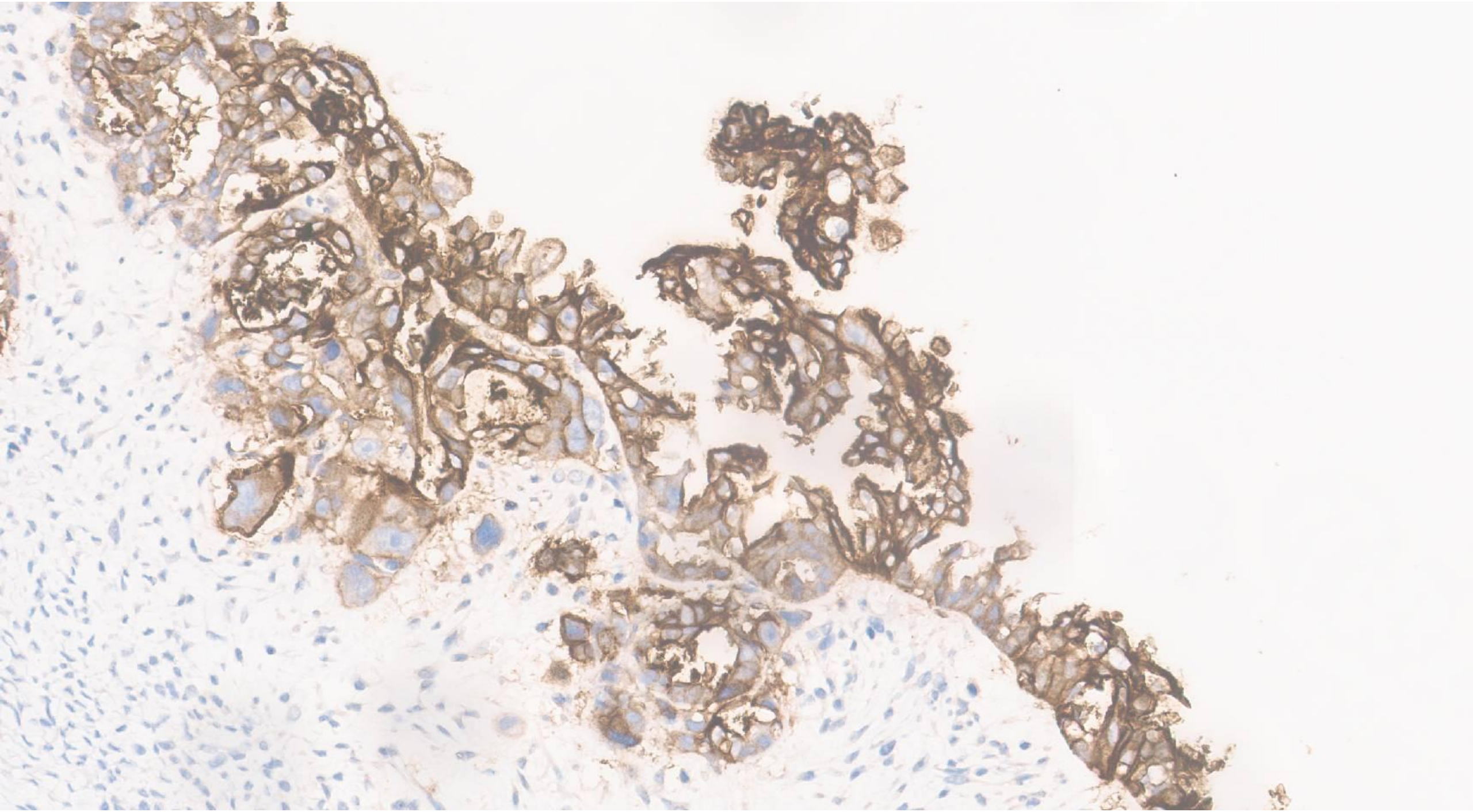


Figure 4: Negative case by VENTANA FOLR1 (FOLR1-2.1) RxDx Assay staining with 7% moderate and strong membrane staining



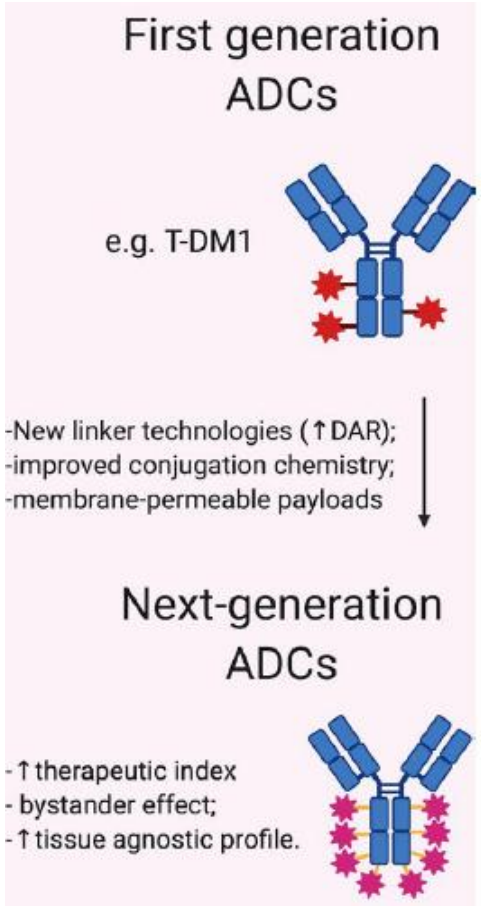


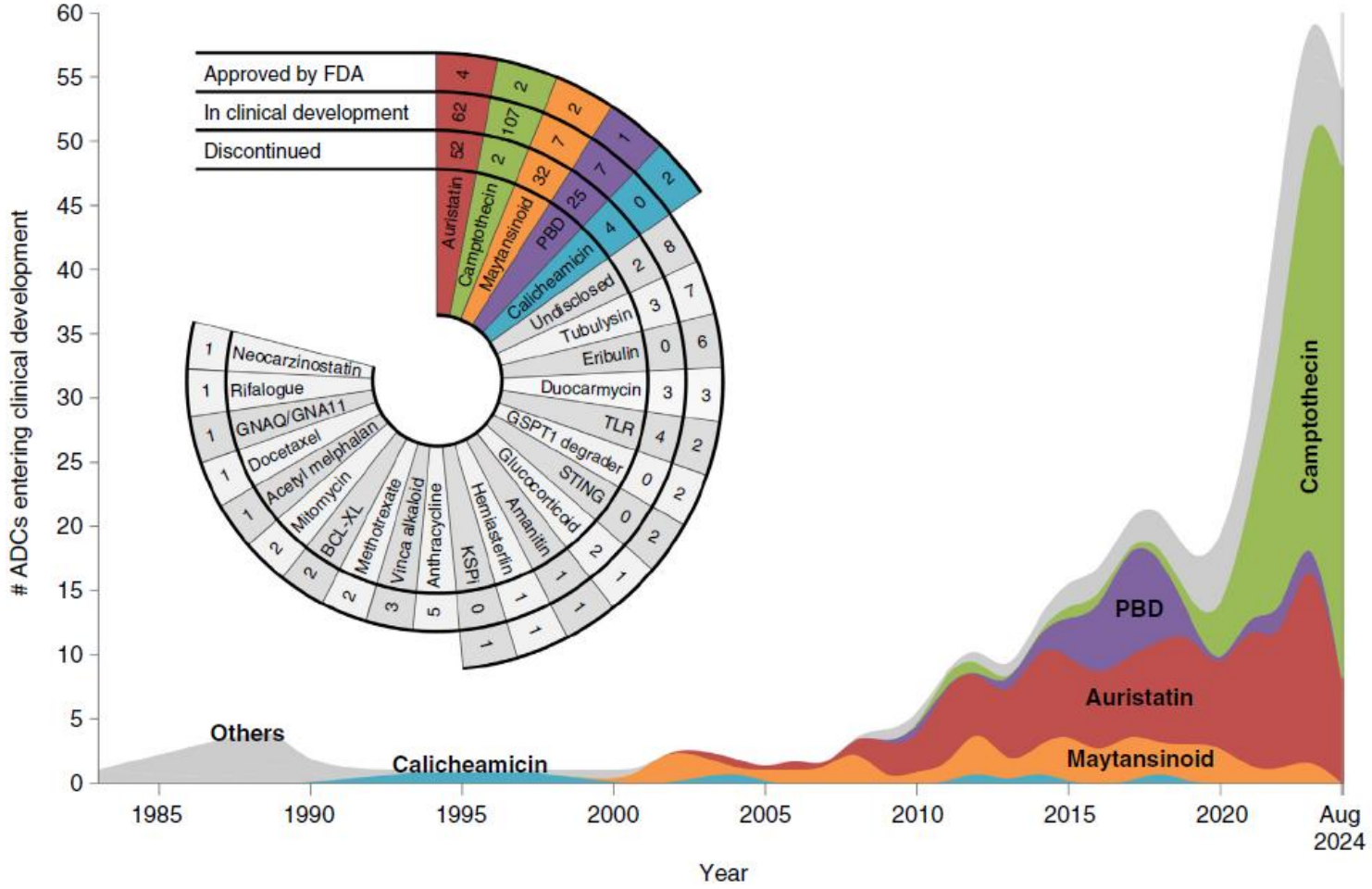




Antibody-Drug Conjugate (ADC)

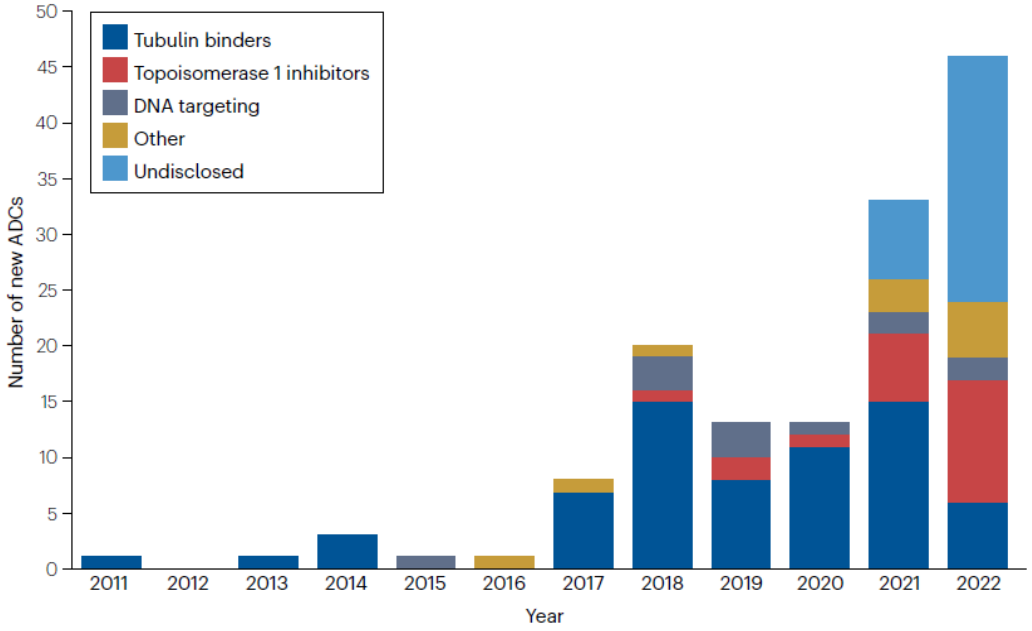
Development of ADCs

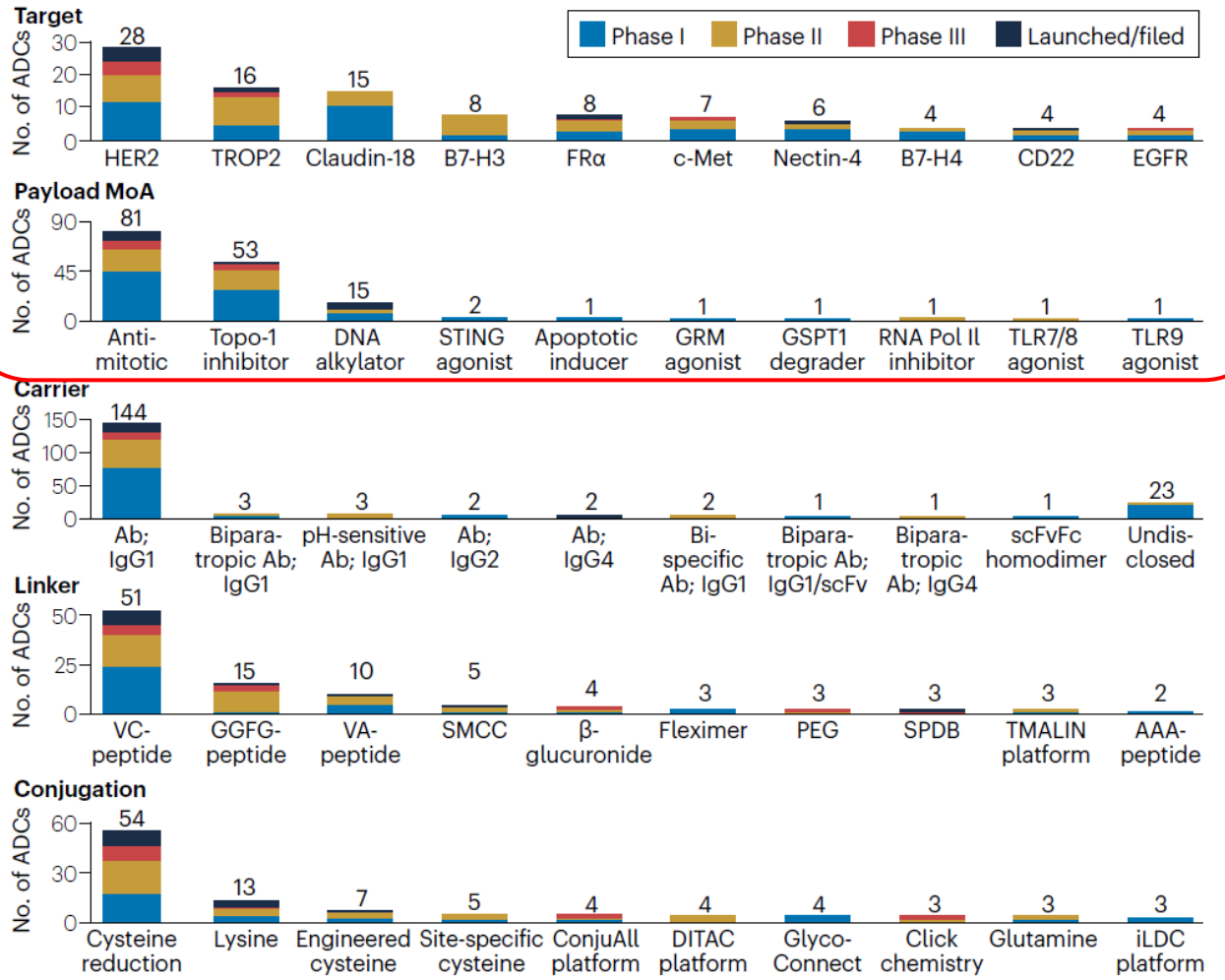




Tarantino P et al., CA Cancer J Clin 2022;72:165-182.
Colombo R et al., Cancer Discov 2024;14:2089-2108.

Antibody-Drug Conjugate (ADC)
- Current landscape



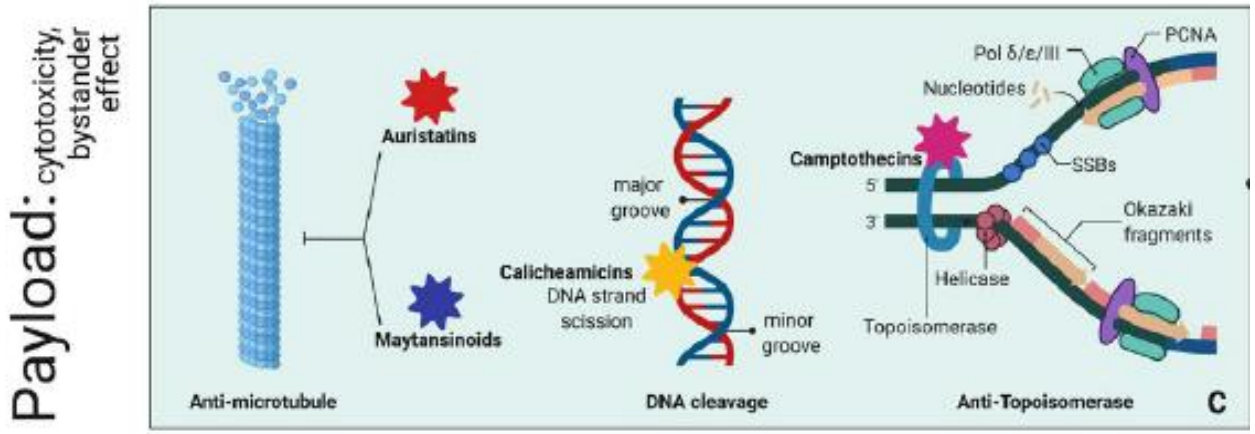


Nat Rev Drug Discov 2023;22:641, Nat Rev Drug Discov 2024;23:577

Antibody-Drug Conjugate (ADC)

3 major payload classes

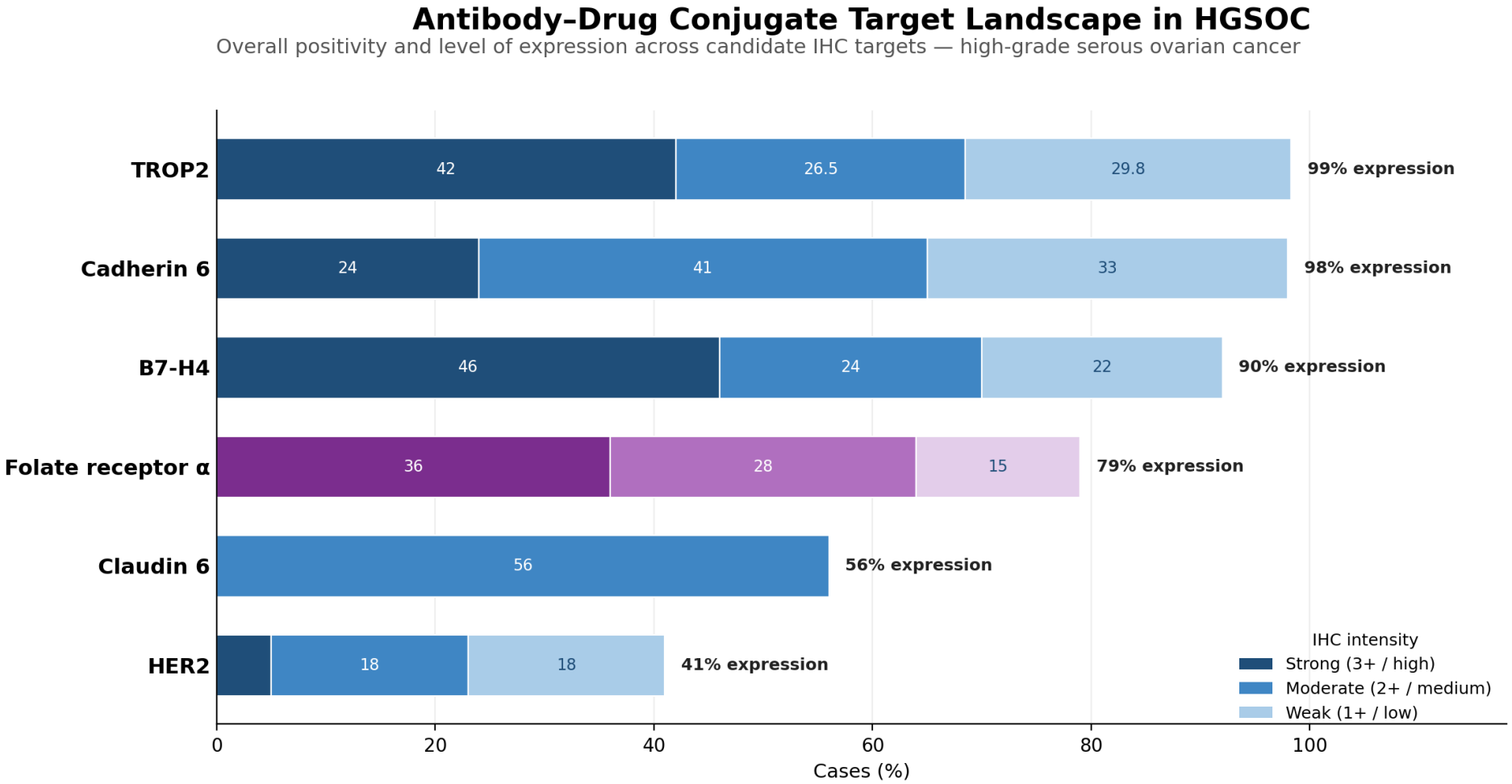
- **Microtubule inhibitors**
  - Auristatin : MMAE (vedotin), MMAF
  - Maytansinoid : DM1, **DM4 (soravtansine)**.
- **DNA-damaging agents** (DNA-targeting agents)
  - Calicheamicin, PBD dimers, duocarmycins.
- **Topoisomerase I inhibitors**
  - **DXd**
  - SN-38 (active metabolite of irinotecan)
  - Other camptothecin derivatives



➡ ADC (targeted chemotherapy) is still Chemotherapy !

Nat Rev Drug Discov 2023;22:641, Nat Rev Drug Discov 2024;23:577

Antibody-Drug Conjugate (ADC)

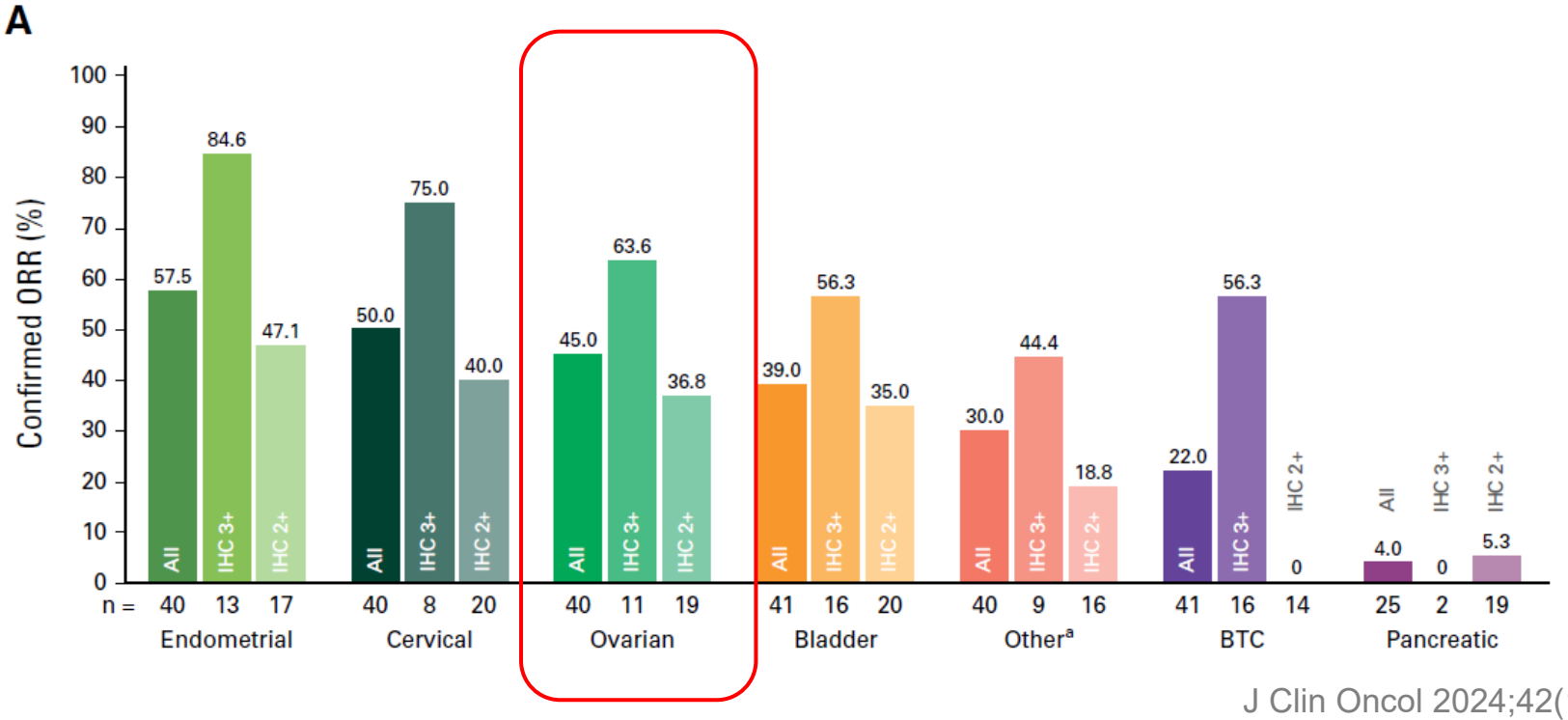


Bars stacked by IHC intensity; total expression labeled at right. FRα four-tier intensity (high 36% / medium 28% / low 15% / negative 21%) — 21% negative, so 79% express. Claudin 6 reported as total expression without a full intensity split.

Leung et al. J Gynecol Oncl 2025; Deutschman E, et al. *Arch Pathol Lab Med*. 2025;149:930-937; Hamagawa K et al. ESMO Gyne 2025; Ettorre VM et al. Int J Gynecol Cancer 2025; Dum D et al. Pathobiology 2022; Liang L et al. Hum Pathol. 2017

Platinum-resistant recurrence (PROC)

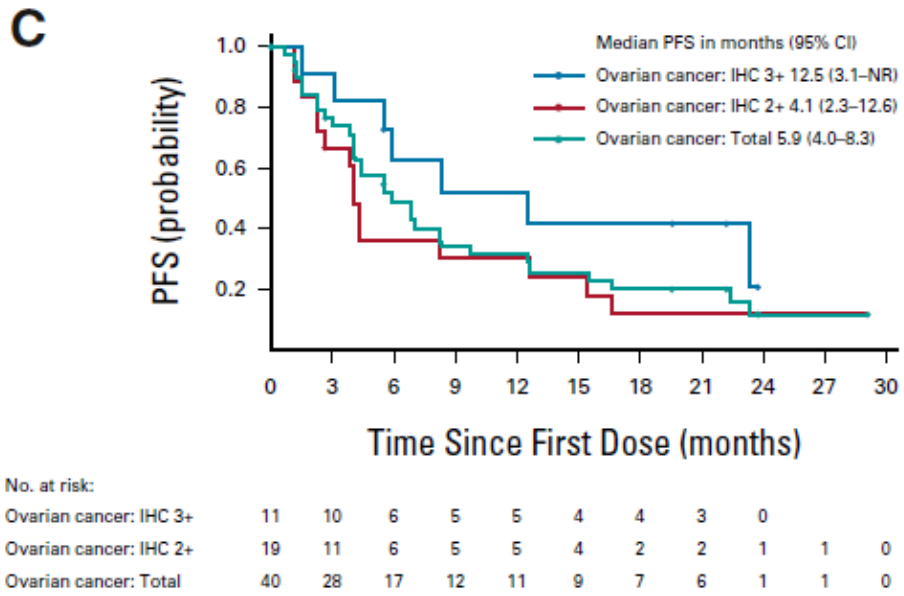
- Trastuzumab deruxtecan (DESTINY-PanTumor2)
  - Open-label phase II study with T-DXd (5.4 mg/kg q 3wks)
  - HER2-expressing (IHC 3+/2+) locally advanced or metastatic disease after ≥1 systemic treatment or without alternative treatments

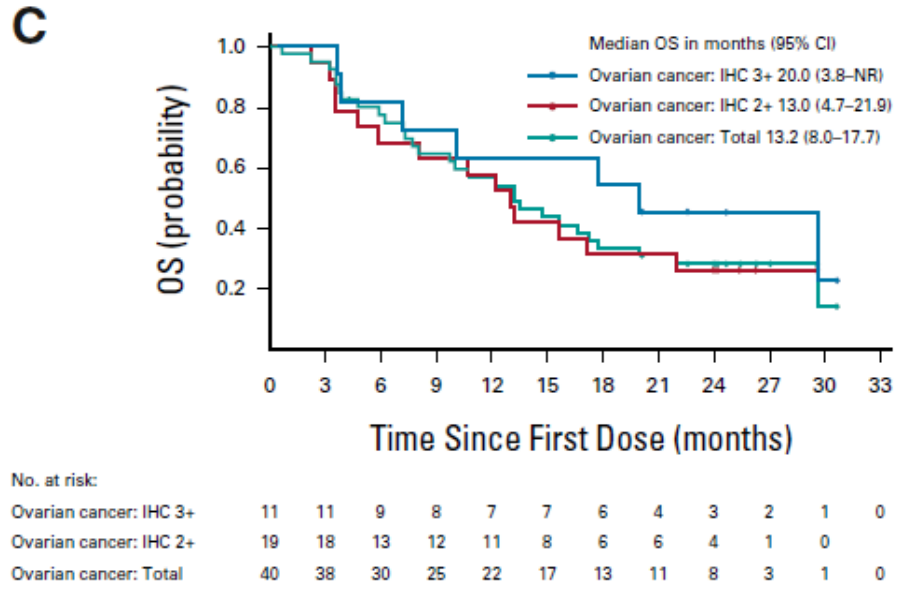


J Clin Oncol 2024;42(1):47-58

Platinum-resistant recurrence (PROC)

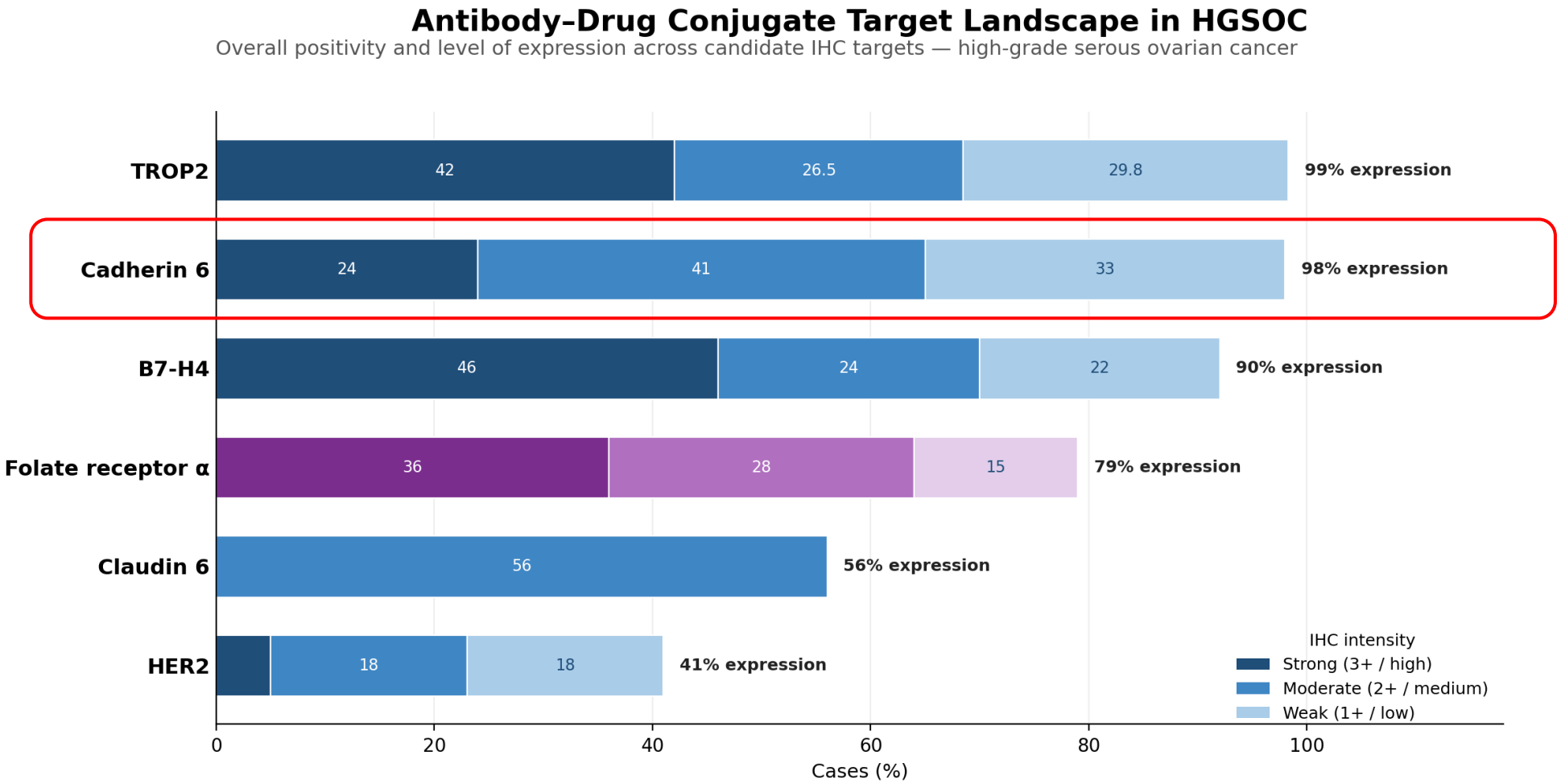
- Trastuzumab deruxtecan (DESTINY-PanTumor2)





J Clin Oncol 2024;42(1):47-58

Antibody-Drug Conjugate (ADC)



Bars stacked by IHC intensity; total expression labeled at right. FRα four-tier intensity (high 36% / medium 28% / low 15% / negative 21%) — 21% negative, so 79% express.
Claudin 6 reported as total expression without a full intensity split.

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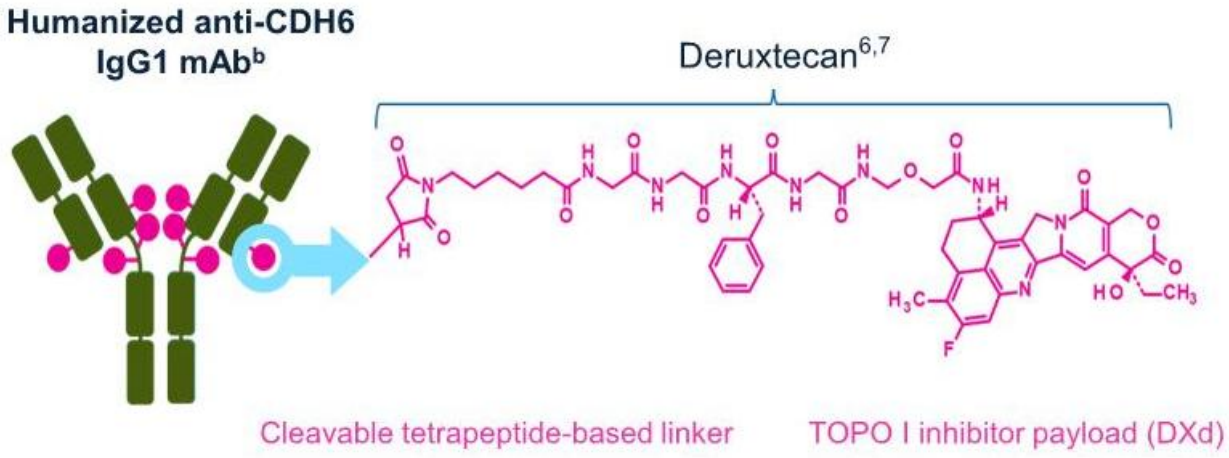
Platinum-resistant recurrence (PROC)

- Raludotatug deruxtecan (R-DXd)
  - CDH6(Cadherin 6)-directed ADC

    (CDH6: calcium-dependent cell adhesion glycoprotein, a mediator of cell-cell adhesion
  - Covalently linked to TOPO I inhibitor payload

    (Drug-to-antibody ratio ≈ 8)



Platinum-resistant recurrence (PROC)

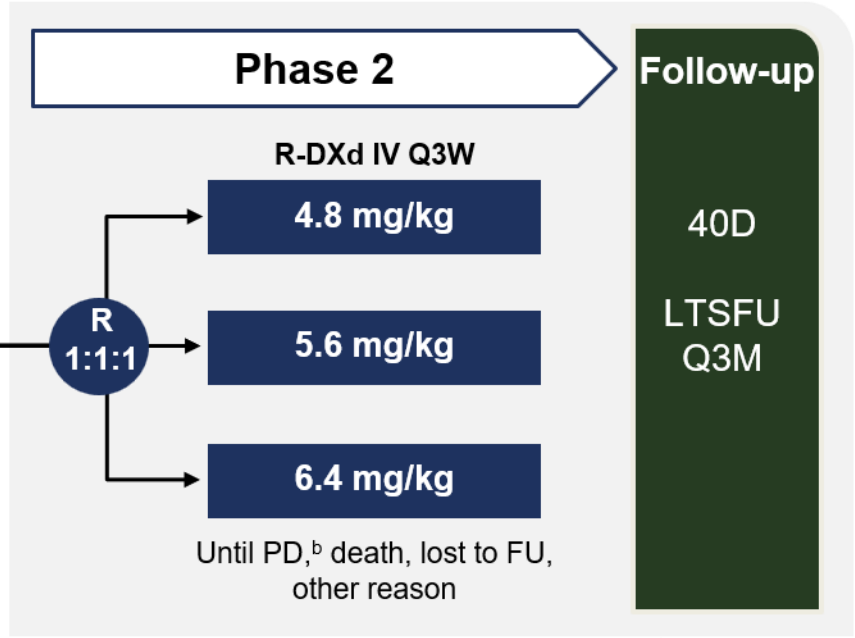
REJOICE-Ovarian01, phase 2/3

Key eligibility criteria:

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

Stratification:

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

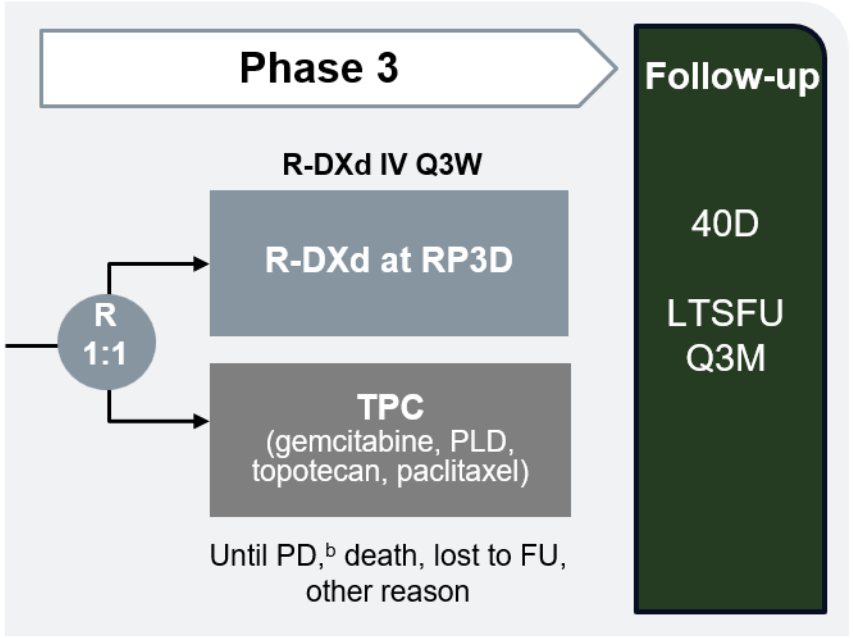


Primary endpoints:

- ORR per BICR[b]

Key secondary endpoints:

- ORR per inv[b]
- DOR



Primary endpoints:

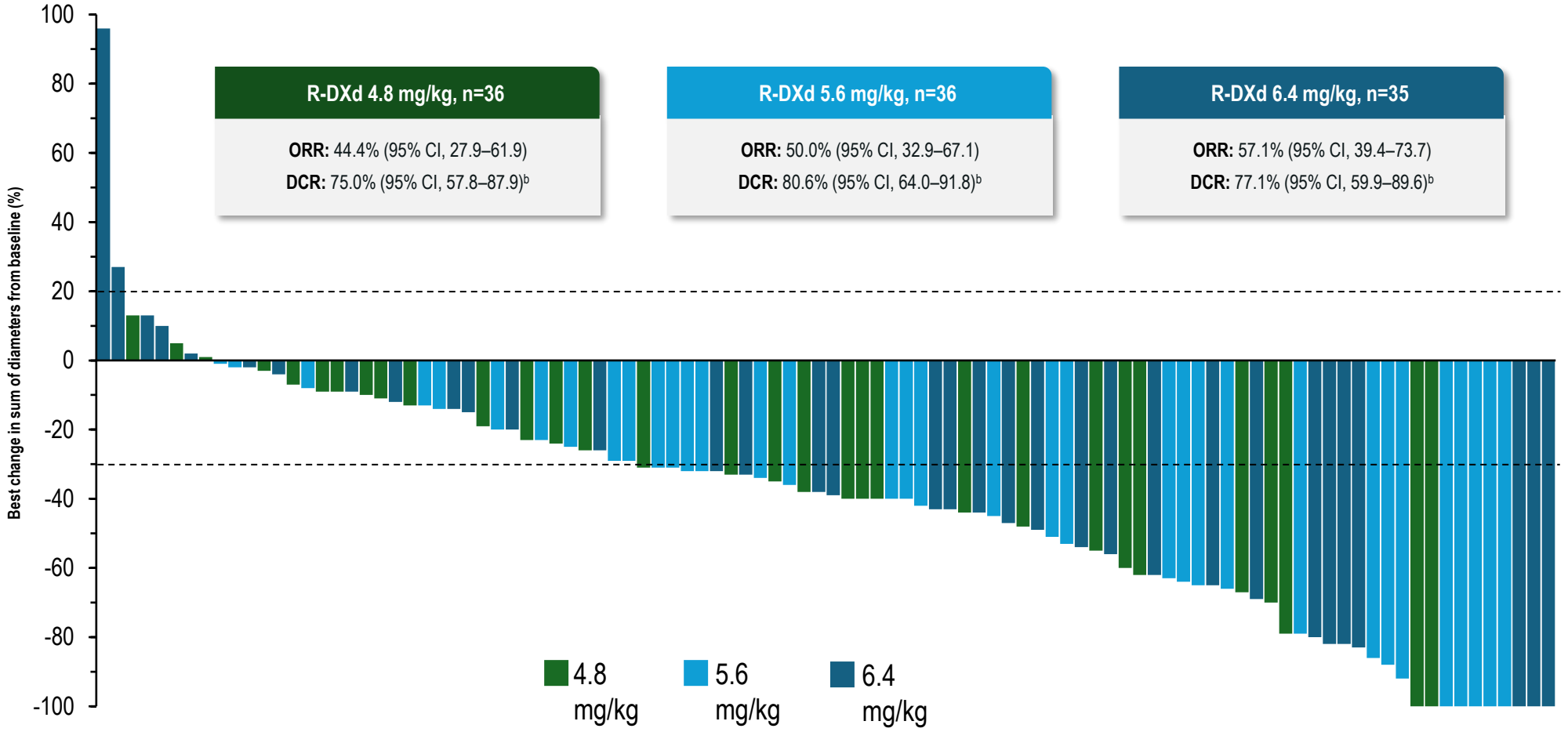
- ORR per BICR[b]
- PFS per BICR[b]

Key secondary endpoints:

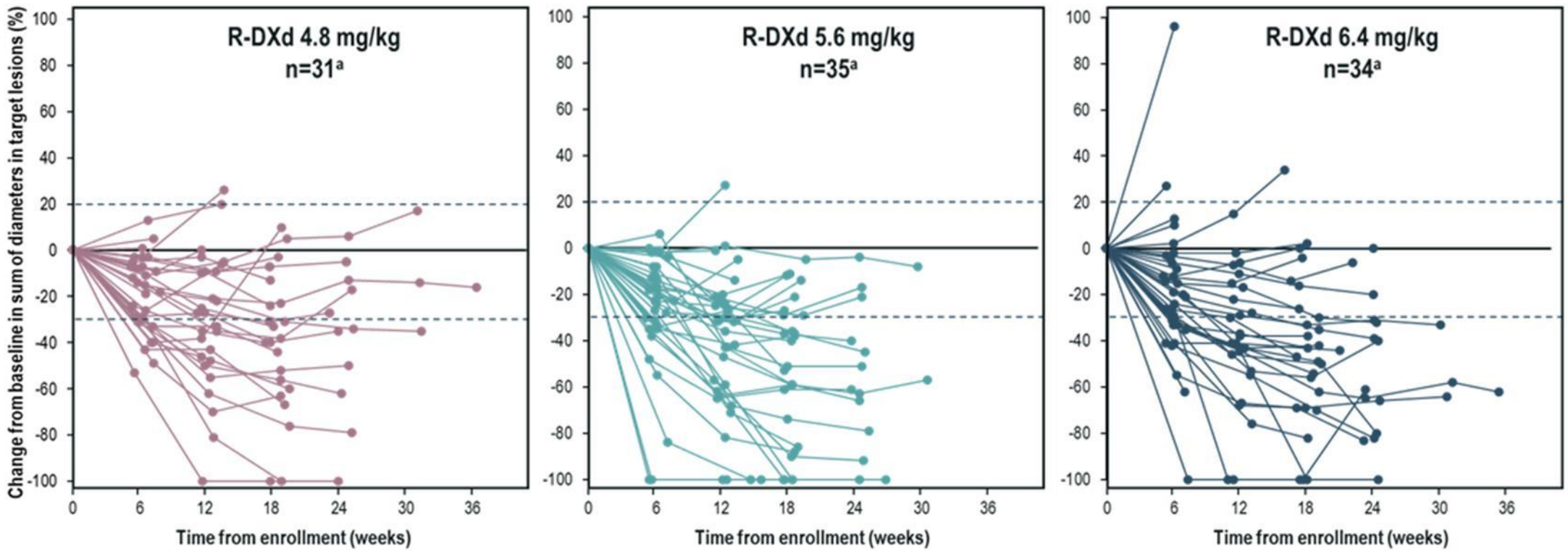
- OS
- QOL

Platinum-resistant recurrence (PROC)

REJOICE 01: Phase 2



R-DXd Treatment Was Associated With Rapid Responses at All Doses



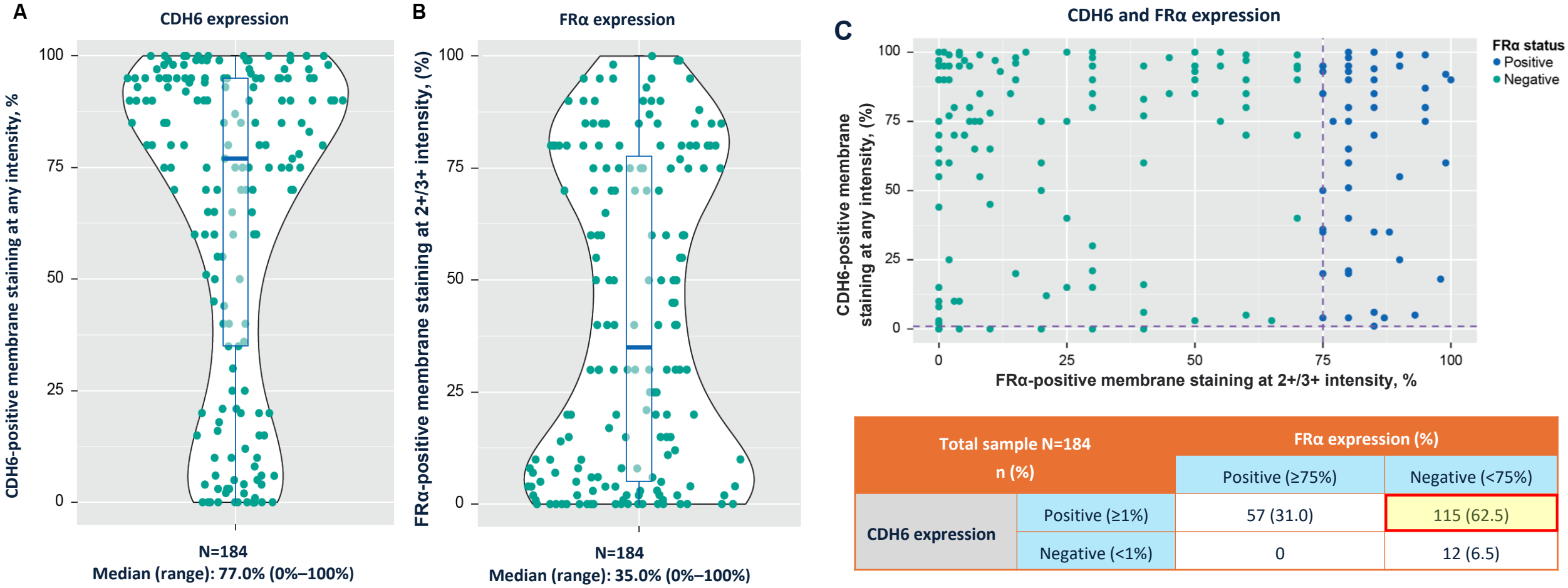
Data cutoff: February 26, 2025. The median follow-up for 4.8-mg/kg, 5.6-mg/kg, and 6.4-mg/kg cohorts was 5.6 months (95% CI, 4.7–6.3), 5.6 months (95% CI, 4.6–5.8), and 5.2 months (95% CI, 4.9–5.8), respectively.

[a]Antitumor response assessed by BICR per RECIST 1.1. Only patients with measurable disease at baseline and ≥1 post-baseline tumor scan, both by BICR, were included in the spider plots (n=100). Six patients (R-DXd 4.8 mg/kg [n=5]; 6.4 mg/kg [n=1]) did not have measurable disease at baseline and one patient (R-DXd 5.6 mg/kg) had no adequate post-baseline tumor assessment. [b]By BICR per RECIST 1.1. Overall median TTR was 7.1 weeks (range, 5.1–19.1).

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

- **Distribution of CDH6 (A) and FRα (B) expression and their association (C) in platinum-resistant OC tumors**

Figure 1

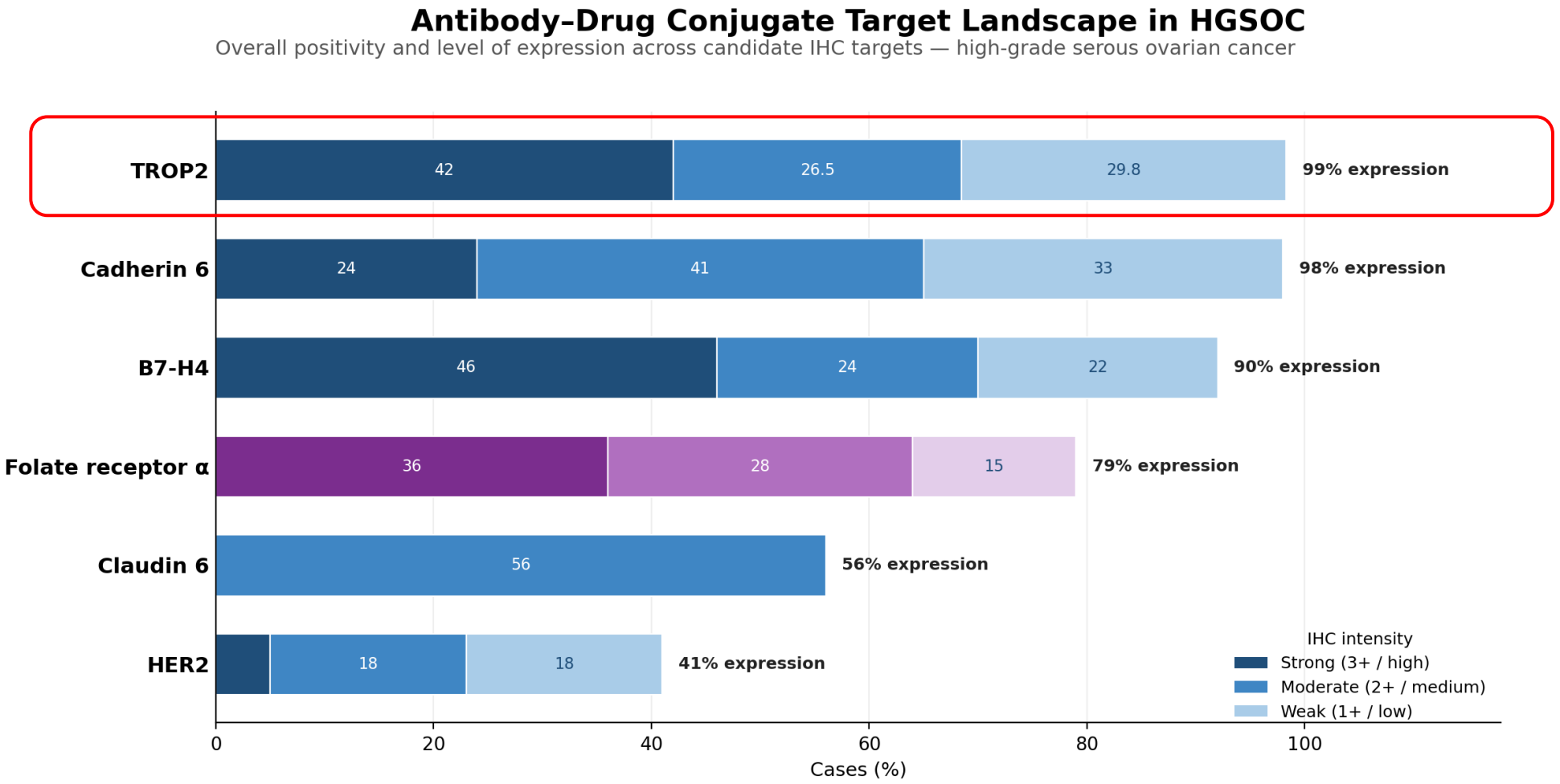


Total sample N=184 n (%)		FRα expression (%)	
		Positive (≥75%)	Negative (<75%)
CDH6 expression	Positive (≥1%)	57 (31.0)	115 (62.5)
	Negative (<1%)	0	12 (6.5)

CDH6, cadherin-6; FRα, folate receptor alpha; OC, ovarian cancer.

Moore K et al. Presented at: Society of Gynecologic Oncology Annual Meeting on Women's Cancer; April 10-13, 2026; San Juan, PR, USA. Abstract 1591.

Antibody-Drug Conjugate (ADC)



Bars stacked by IHC intensity; total expression labeled at right. FRα four-tier intensity (high 36% / medium 28% / low 15% / negative 21%) — 21% negative, so 79% express. Claudin 6 reported as total expression without a full intensity split.

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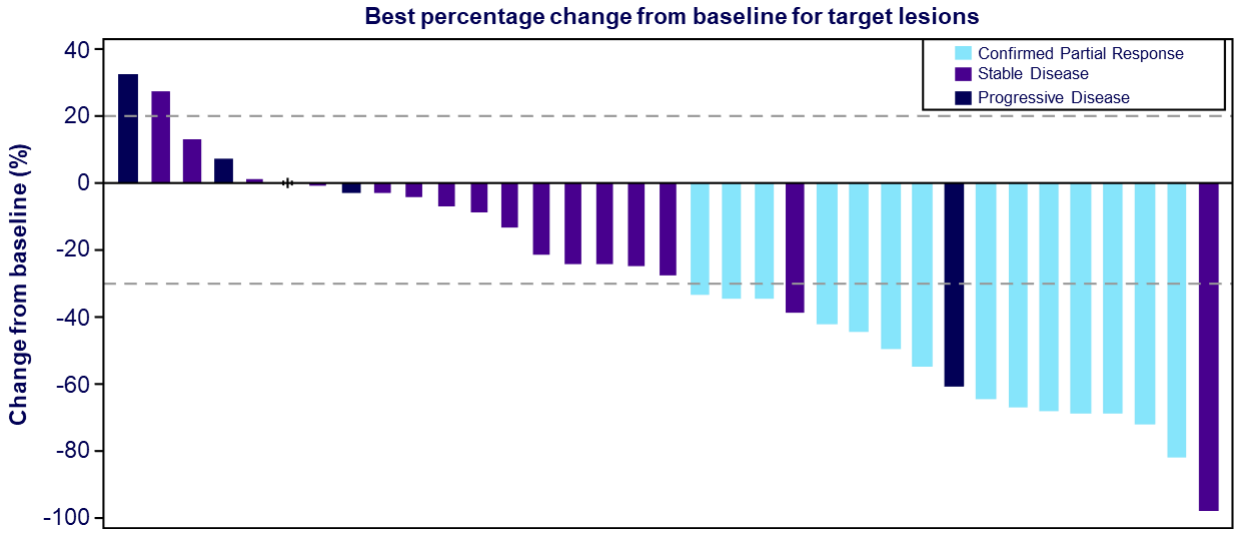
Platinum-resistant recurrence (PROC)

Sacituzumab tirumotecan (Sac-TMT)

- Anti-TROP2 ADC, conjugated to a TOPO I inhibitor payload (DAR ≈ 7.4)

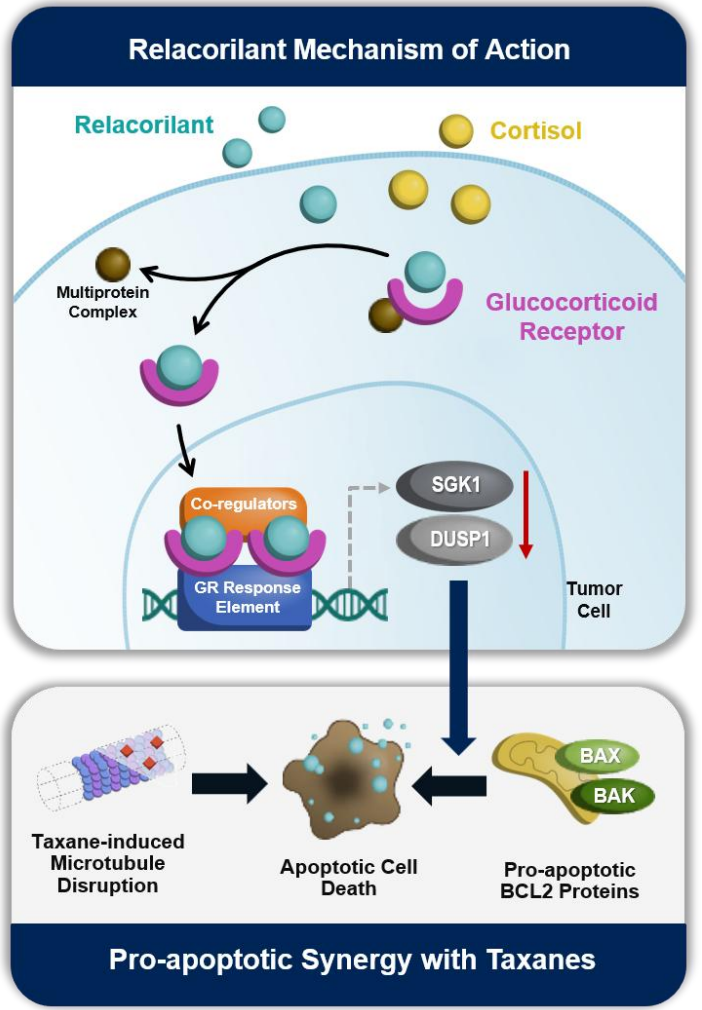
	OC (N=40)*
ORR, % (n/N)	**40.0** (16/40)
Confirmed ORR	**35.0** (14/40)
TROP2 H-score >200	**61.5** (8/13)
Platinum-resistant	**37.1** (13/35)
DCR, % (n/N)	**75.0** (30/40)
PR	**40.0** (16/40)
SD	**35.0** (14/40)
DOR, % (n/N)	
Median (range), months	**5.3** (2.1, 24.4+)
PFS	
Median (95% CI), months	**6.0**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

*Responses assessed per RECIST v1.1 by investigator



Platinum-resistant recurrence (PROC)

- GR antagonist Relacorilant + nab-Paclitaxel (ROSELLA)
  - Glucocorticoid receptor (GR), a marker of poor prognosis in EOC
  - GR signaling reduces sensitivity to chemotherapy
  - Relacorilant
    : a selective GR antagonist that restores the chemosensitivity

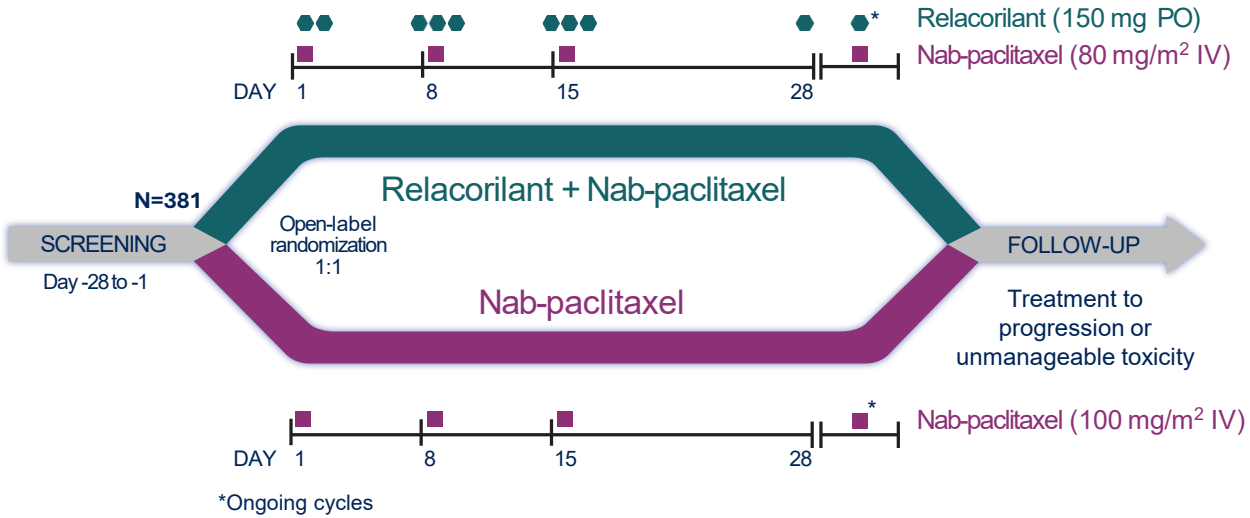


ROSELLA | Study Schema

Population

- Epithelial ovarian, primary peritoneal, or fallopian tube cancer
- ECOG performance status 0 or 1
- Progression <6 months after the last dose of platinum therapy (excluding no response to, or progression in <1 month of primary platinum)
- **1–3 prior lines** of therapy
- Prior bevacizumab required

NCT05257408



Stratification Factors

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

Dual Primary Endpoints

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

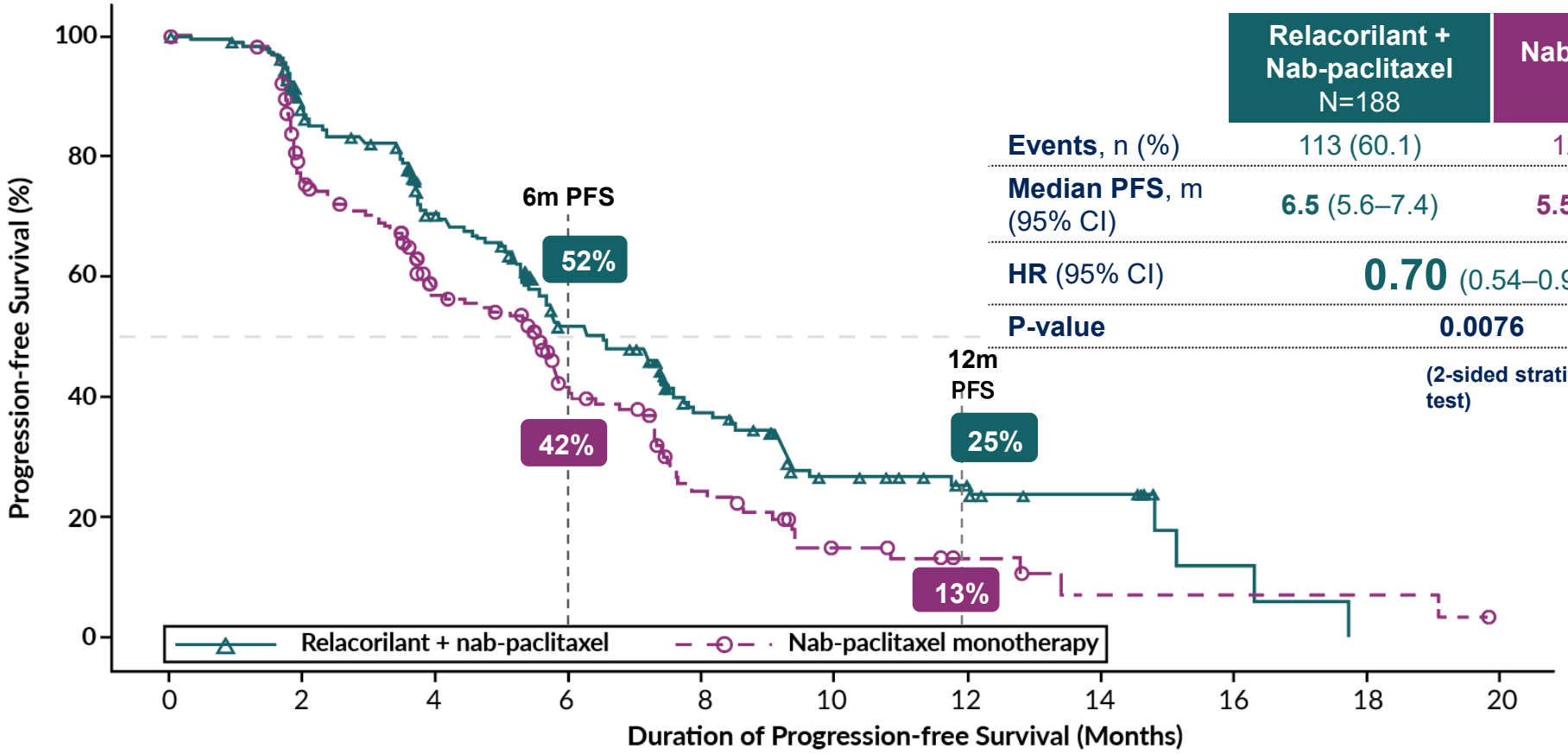
Secondary Endpoints

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

First patient enrolled: Jan 5, 2023
Last patient enrolled: Apr 8, 2024
Primary results data cutoff: Feb 24, 2025
Final OS data cutoff: Jan 8, 2026
Conducted at 117 sites in 14 countries.

CA, cancer antigen; CBR, clinical benefit rate; DoR, duration of response; ECOG, Eastern Cooperative Oncology Group; GCIG, Gynecologic Cancer Intergroup; IV, intravenous; ORR, objective response rate; PO, by mouth; RECIST, Response Evaluation Criteria in Solid Tumors.

ROSELLA | Progression-Free Survival – BICR (Primary Analysis)



	Relacorilant + Nab-paclitaxel N=188	Nab-paclitaxel N=193
Events, n (%)	113 (60.1)	121 (62.7)
Median PFS, m (95% CI)	**6.5** (5.6–7.4)	**5.5** (3.9–5.9)
HR (95% CI)	**0.70** (0.54–0.91)	
P-value	**0.0076**	

(2-sided stratified log-rank test)

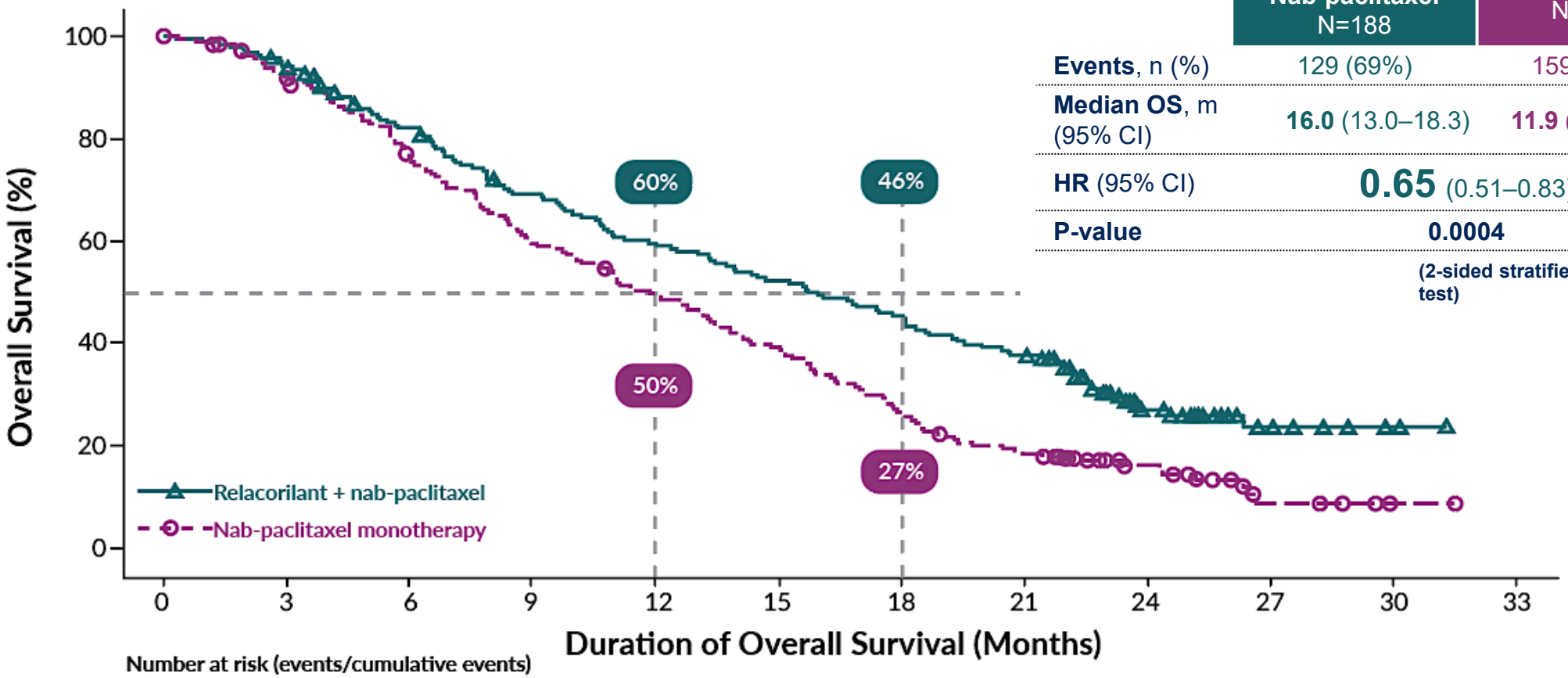
No. at risk (events/cumulative events)

Relacorilant + nab-paclitaxel	188 (0/0)	151 (22/22)	109 (29/51)	70 (27/78)	43 (18/96)	24 (11/107)	16 (1/108)	11 (1/109)	2 (2/111)	0 (2/113)
Nab-paclitaxel monotherapy	193 (0/0)	129 (42/42)	85 (31/73)	47 (20/93)	21 (17/110)	9 (7/117)	5 (1/118)	2 (2/120)	2 (0/120)	0 (2/120)	0 (1/121)

Median follow-up time: 9.0 months; statistical significance threshold: P≤0.04. The Kaplan–Meier method was used to estimate the curves, median estimates and the 95% CIs for progression-free survival in each treatment arm. The HR and the associated 95% CI were estimated using a Cox regression model with treatment group as the main effect and stratification factors at randomization as covariates.
CI, confidence interval; HR, hazard ratio; m, months; PFS, progression-free survival.

Data cutoff: Feb 24, 2025

ROSELLA | Overall Survival - 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

Pembrolizumab vs Placebo Plus Weekly Paclitaxel ± Bevacizumab in Platinum-Resistant Recurrent Ovarian Cancer: Final Analysis Results from the Randomized Double-Blind Phase 3 ENGOT-ov65/KEYNOTE-B96 Study

Nicoletta Colombo[1], Emese Zsiros[2], Alexandra Sebastianelli[3], Radoslaw Madry[4], Carolina Ibañez[5], Jacob Korach[6], Kosei Hasegawa[7], Fatih Kose[8], Roberto Iván Romero Díaz[9], Emma Hudson[10], Jeffrey C. Goh[11], Ingrid Boere[12], Andreia Cristina de Melo[13], Hannelore Denys[14], Jae-Weon Kim[15], Thomas Jemielita[16], Karin Yamada[16], Agata M. Bogusz[16], Thibault De La Motte Rouge[17], Xiaohua Wu[18] and on behalf of the ENGOT-ov65/KEYNOTE-B96 investigators

[1]Gynecologic Oncology Program, European Institute of Oncology, IRCCS, Milan, Italy; [2]Roswell Park Comprehensive Cancer Center, Buffalo, NY, USA; [3]CHU de Québec-Université Laval, Québec, Canada; [4]Department of Gynecologic Oncology, Medical University Karol Marcinkowski, Poznań, Poland; [5]Hematology and Oncology Department, Pontificia Universidad Católica de Chile, Santiago, Chile; [6]Gynecologic Oncology Department, Sheba Medical Center Tel Aviv University, Tel Aviv, Israel; [7]Saitama Medical University International Medical Center, Hidaka, Japan; [8]Başkent University, Ankara, Turkey; [9]Centro de Investigacion Clinica de Oaxaca, Oaxaca de Juarez, Mexico; [10]Velindre Cancer Centre, Cardiff, United Kingdom; [11]Gallipoli Medical Research Ltd-GMRF CTU, Greenslopes Private Hospital, Brisbane, Queensland, Australia; [12]Erasmus MC Cancer Institute – Department of Medical Oncology, Rotterdam, Netherlands; [13]Brazilian National Cancer Institute (INCA), Rio de Janeiro, Brazil; [14]UZ Gent-Medical Oncology, Gent, Belgium; [15]Seoul National University, Seoul, South Korea; [16]Merck & Co., Inc., Rahway, NJ, USA; [17]Centre Eugene Marquis, Rennes, France; [18]Fudan University Shanghai Cancer Center, Shanghai, China

Platinum-resistant recurrence (PROC)

- Weekly paclitaxel + Pembrolizumab +/- Bevacizumab (KEYNOTE-B96)

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/m^2 Days 1, 8, 15 of each Q3W cycle *(± bevacizumab 10 mg/kg Q2W)*

Placebo (Q6W, 18 cycles) + Paclitaxel[a] 80 mg/m^2 Days 1, 8, 15 of each Q3W cycle *(± bevacizumab 10 mg/kg Q2W)*

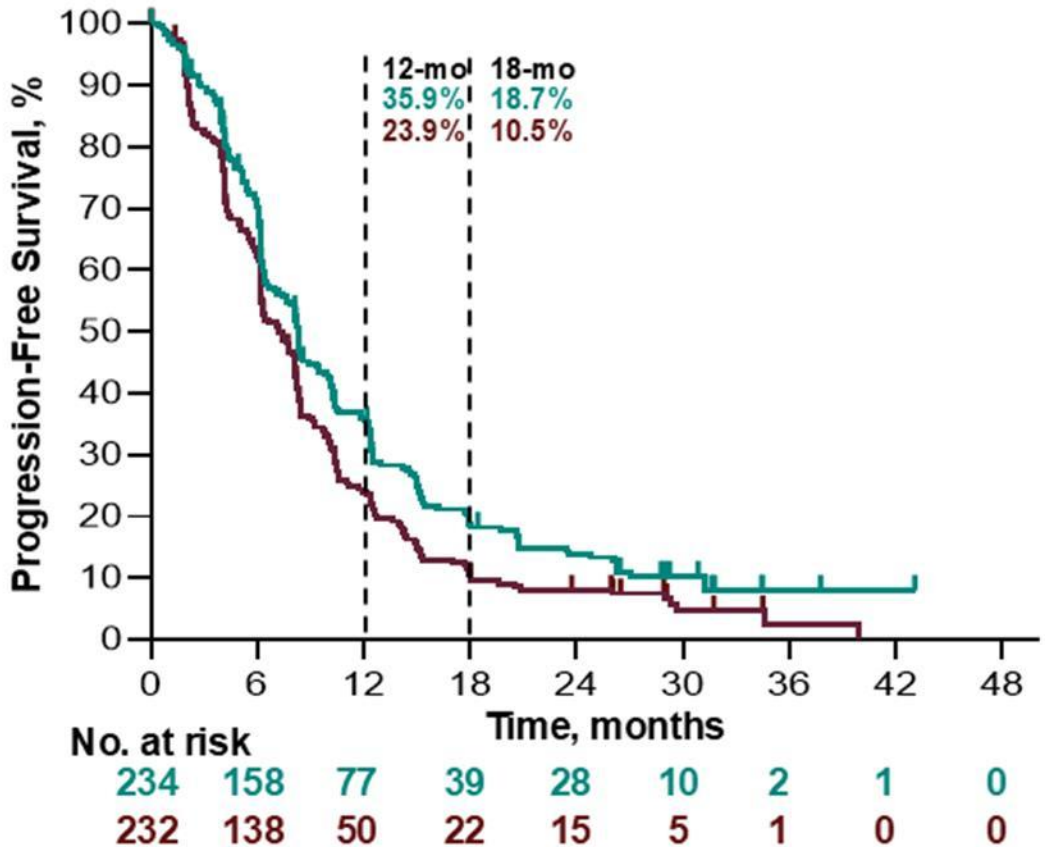
Primary Endpoint: PFS per RECIST v1.1 by investigator

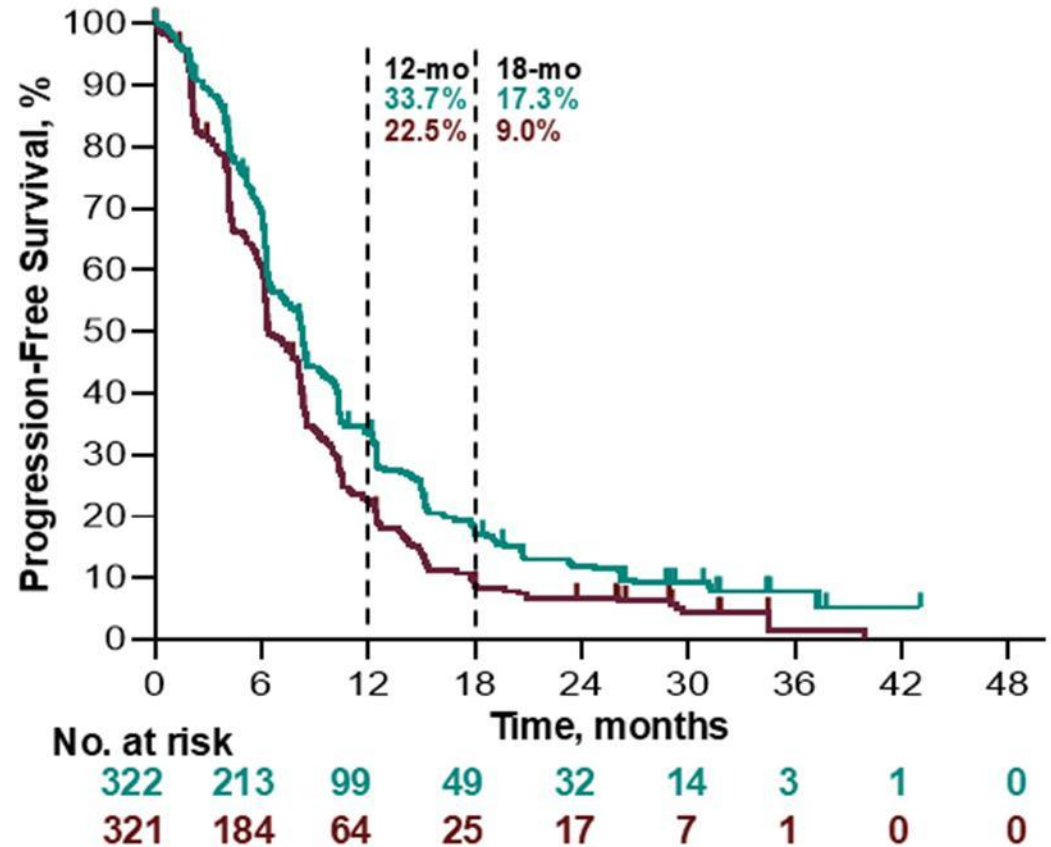
Key Secondary: OS

Clinically Meaningful PFS in CPS ≥1 and ITT Populations at FA

CPS ≥1 Population	Events	Median, mo (95% CI)	HR[a] (95% CI)
Pembro Arm	84.6%	8.3 (7.0-9.5)	0.76 (0.62-0.93)
Placebo Arm	88.8%	7.2 (6.2-8.1)	

ITT Population	Events	Median, mo (95% CI)	HR[a] (95% CI)
Pembro Arm	85.7%	8.3 (7.2-8.6)	0.73 (0.62-0.87)
Placebo Arm	89.1%	6.4 (6.2-8.1)	

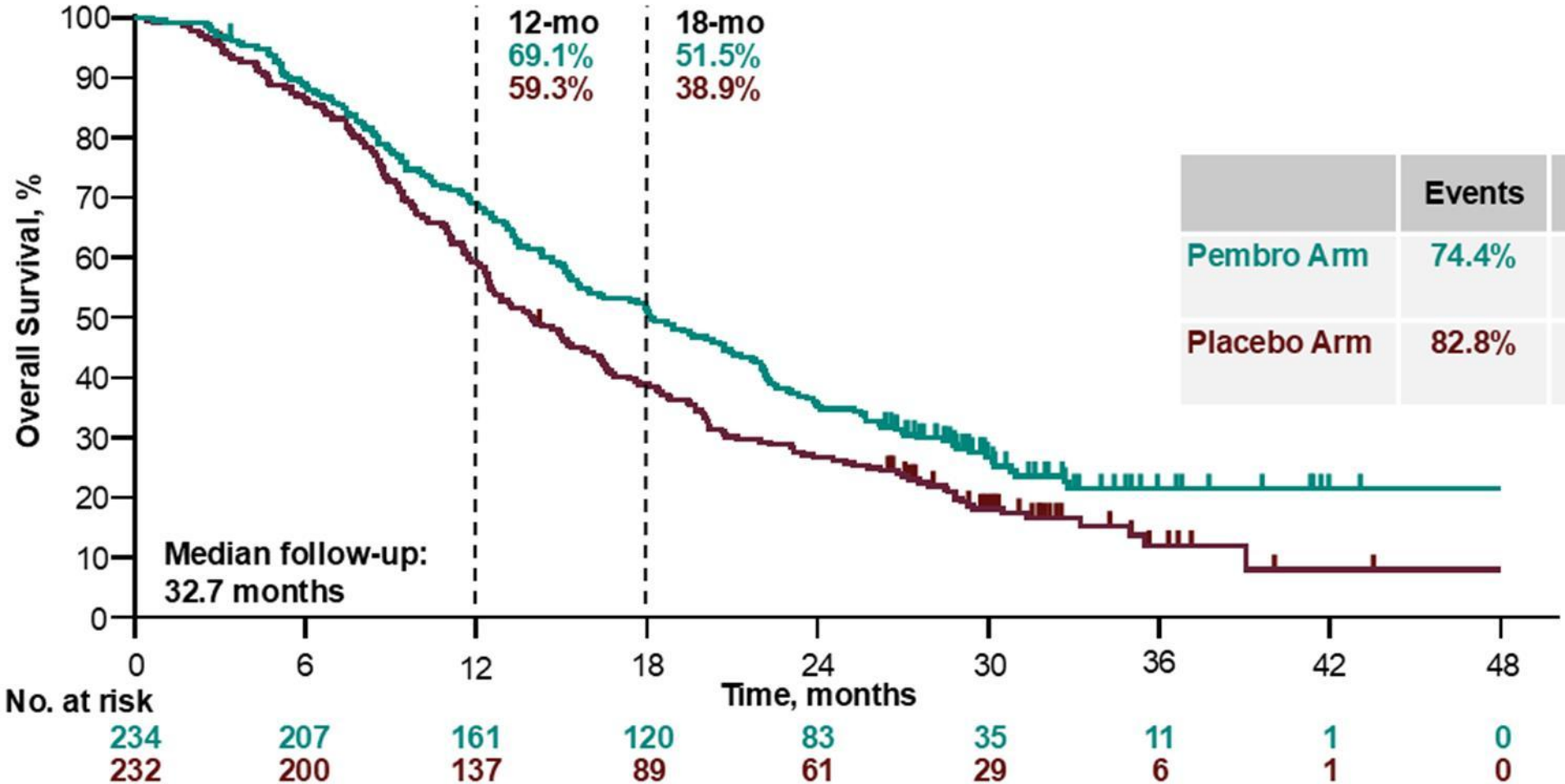




Median follow-up: 32.7 months

Response assessed per RECIST v1.1 by investigator review. [a]Hazard ratio (CI) analyzed based on a Cox regression model with treatment as a covariate stratified by the randomization stratification factors.
Data cutoff date: September 5, 2025.

Clinically Meaningful OS in CPS ≥1 Population at FA

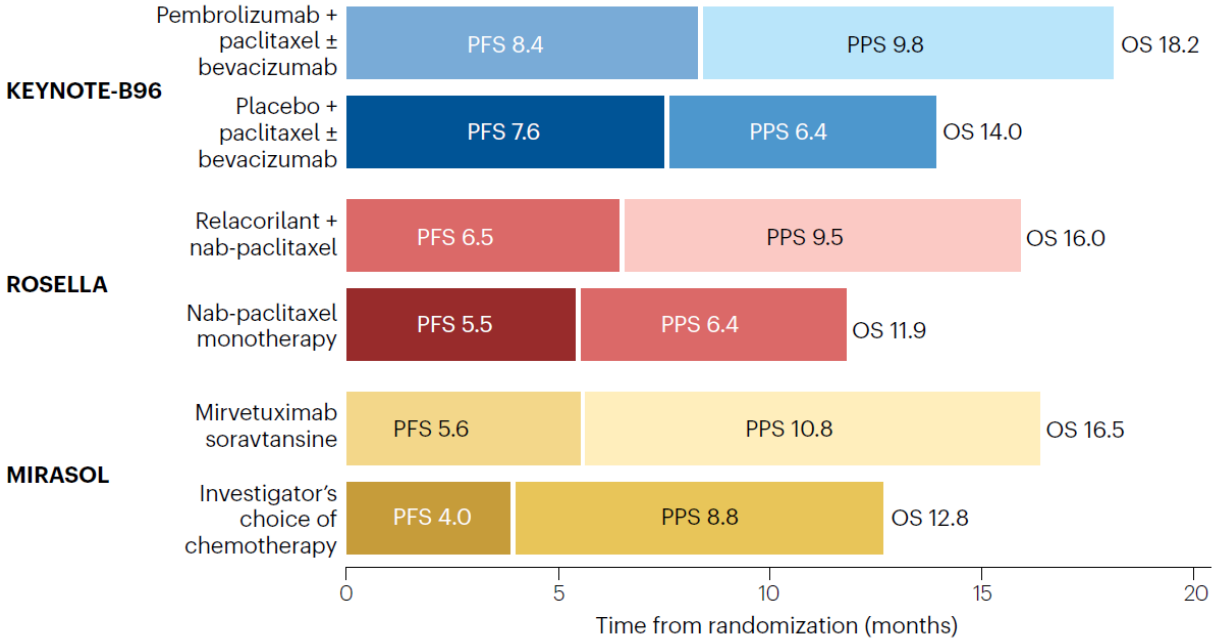


	Events	Median, mo (95% CI)	HR[a] (95% CI)
Pembro Arm	74.4%	18.2 (15.3-21.3)	0.76 (0.62-0.93)
Placebo Arm	82.8%	14.0 (12.5-16.1)	

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

Platinum-resistant recurrence (PROC)

- Meaningful OS improvements after AURELIA (2014)
  - MIRASOL (anti-FRα ADC), ROSELLA (GR antanogist/nab-paclitaxel), KEYNOTE-B96 (paclitaxel+/-bevz/IO drug)
  - OS gains despite modest PFS improvemens
    - Suggesting effects beyond tumor response alone
    - Increase in post-progression survival (PPS)



Nat Rev Clin Oncol 2026;23:566-568.

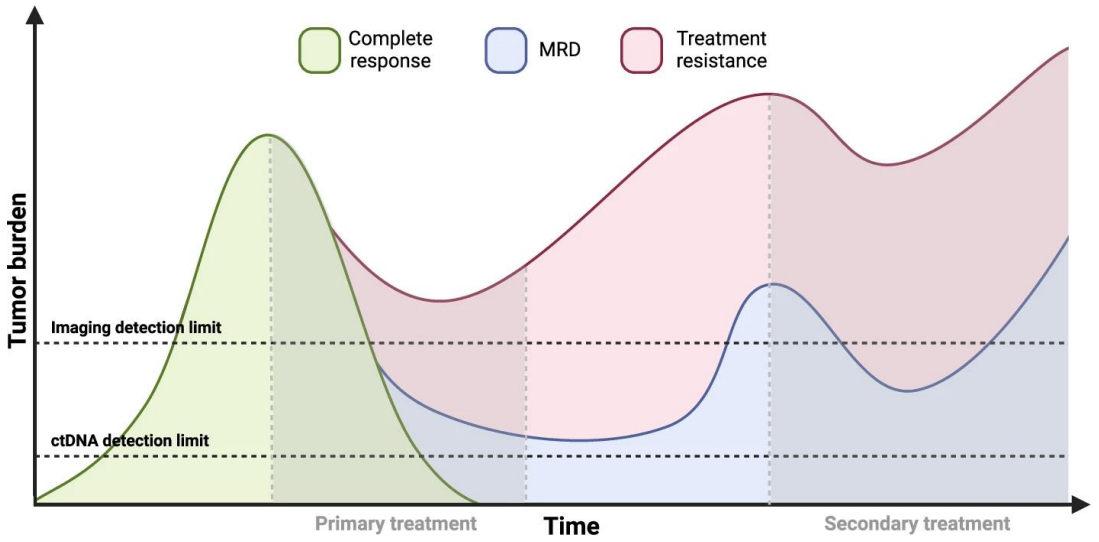
Platinum-resistant recurrence (PROC)

- Considerations in selection and sequencing of PROC Tx
  - Complicated OS analysis
    - Loger PPS, uncontrolled post-progression Tx, changing control arms (new agents after cl inical trials initiate)
  - Cumulative toxicity
    - Peripheral neuropathy (weekly nab-paclitaxel/Relacorilant, weekly paclitaxel/pembro)
  - Resistance mechanisms
    - Similar MoA between previous CTx and ADC payload (e.g. TOPO I, microtubule inhibitors)
  - Patient preferences (cost…)

Nat Rev Clin Oncol 2026;23:566-568.

Surveillance

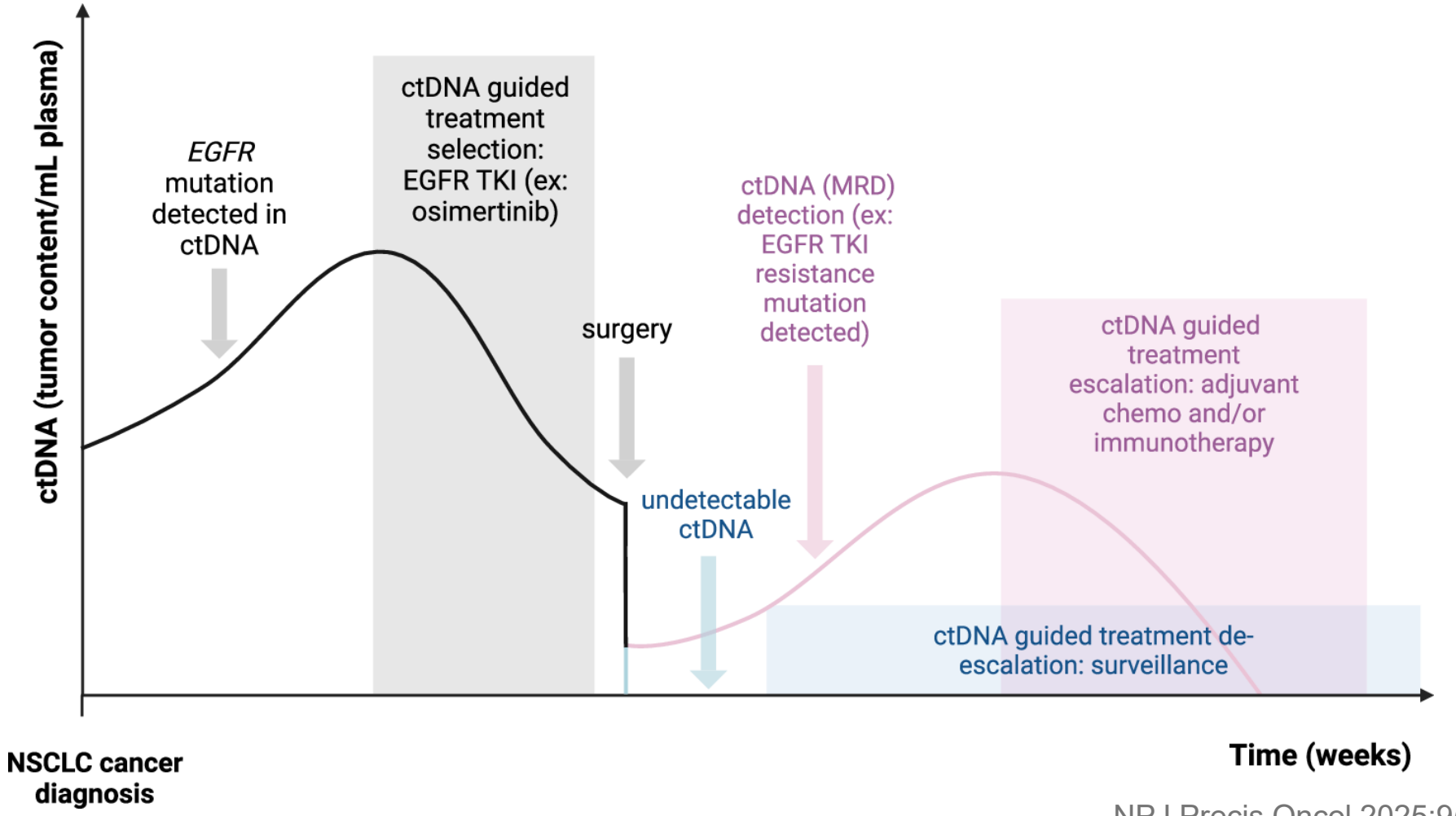
- Circulating tumor DNA (ctDNA) – Liquid biopsy
  - Cell-free DNA from cancer cells
  - Clinical use
    - Response monitoring
    - Surveillance of recurrence (MRD)
    - Molecular profiling : overcoming tumor heterogeneity



NPJ Precis Oncol 2025;9(1):84

Surveillance

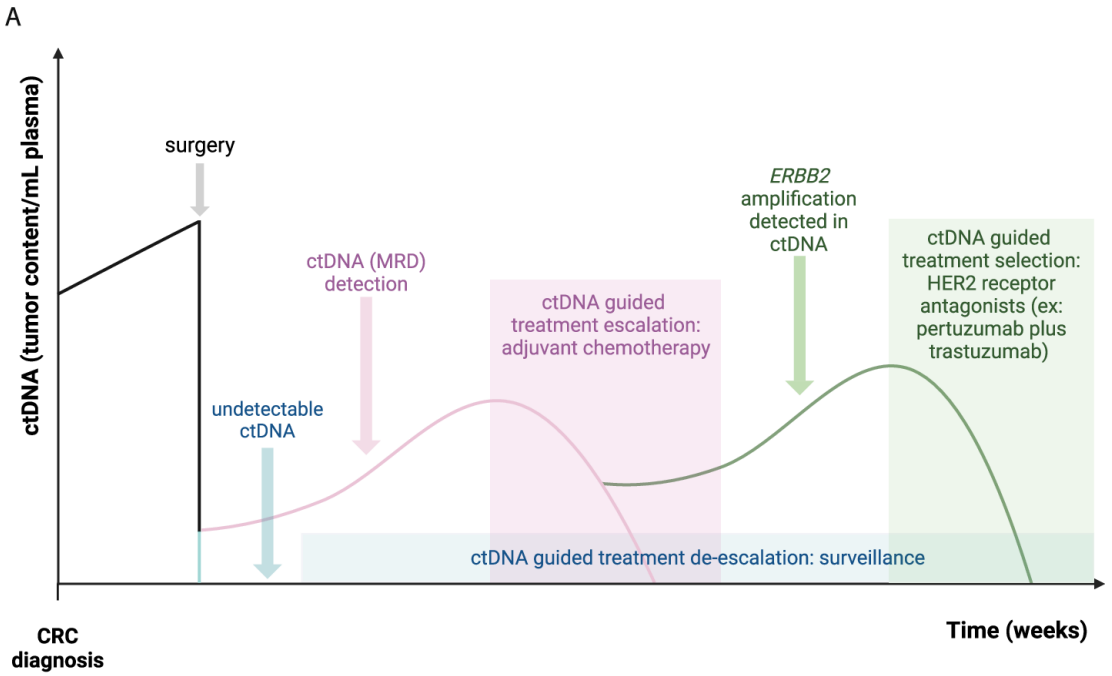
- Circulating tumor DNA (ctDNA) application in NSCLC

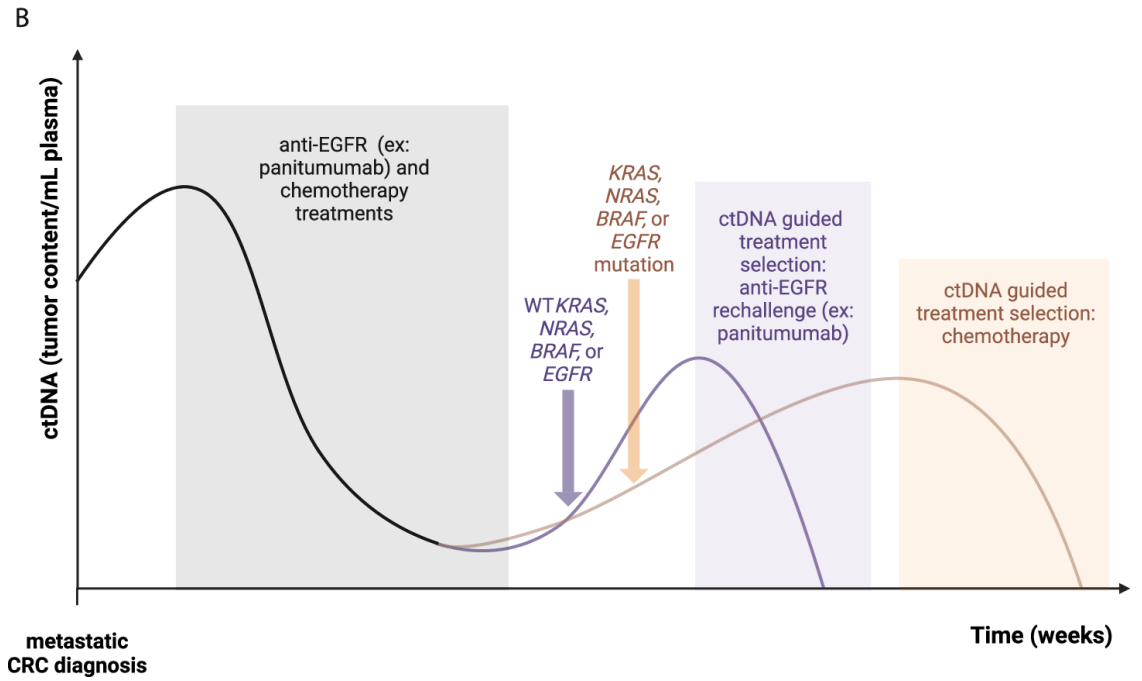


NPJ Precis Oncol 2025;9(1):84

Surveillance

Circulating tumor DNA (ctDNA) application in CRC





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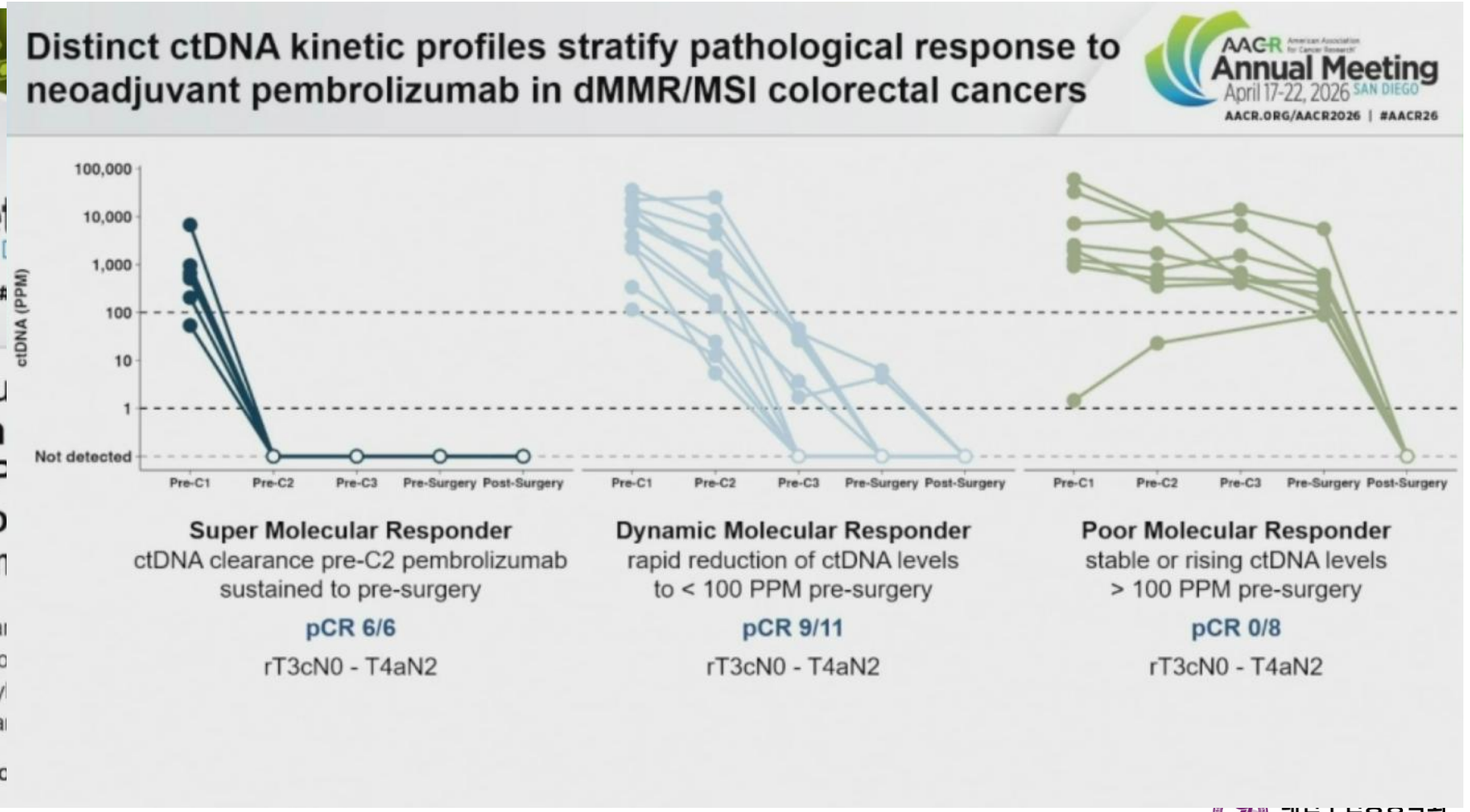
Surveillance

- Circulating tumor DNA (ctDNA)



Surveillance

- Circulating tumor DNA in EOC (2026 ASCO, poster #5562)
  - 89 EOC patients, plasma ctDNA collected in association with debulking surgery
  - Positive correlation with CA125 level (Spearman r = 0.25; p = 0.017)
  - High ctDNA level was associated with worse OS (p=0.0036, HR 3.48 (1.50-8.06))

  - Limitation: Short FU period, lact of standardization of ctDNA assays, no clinical trials to show survival benefit with ctDNA assay over CA125
  - Optimal debulking status and CA125: still standard prognostic biomarkers

Korean Society of
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2026년
대한부인종양학회 하계학술대회
제20차 젊은의사 워크숍
제9차 분과전문의 연수강좌
제1차 부인종양간호사 연수강좌
& 카데바 워크숍

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