

Integrating New Advances into the Care of Patients with Cancer

**A Multitumor Symposium in Partnership
with the American Oncology Network**

CME/MOC, NCPD and ACPE Accredited

**Saturday, November 8, 2025
10:00 AM – 3:00 PM CT**

Agenda

Module 1 — Lung Cancer: *Drs Gainor, Langer and Shields*

Module 2 — Chronic Lymphocytic Leukemia: *Dr Rogers*

Module 3 — Ovarian Cancer: *Dr Konecny*

Module 4 — Gastroesophageal Cancers: *Dr Shah*

Ovarian Cancer Faculty



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MODERATOR

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Chief Medical Officer
American Oncology Network
Hot Springs, Arkansas

Dr Konecny — Disclosures

No relevant conflicts of interest to disclose.

Dr Divers — Disclosures

Advisory Committees	Daiichi Sankyo Inc
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Snapshot of AON Practice Ovarian Cancer

BRCA1/2 mutation

57

Snapshot of AON Practice Ovarian Cancer — PARP Inhibitors

Olaparib

97

Niraparib

52

Snapshot of AON Practice

Ovarian Cancer — Antibody-Drug Conjugates

Mirvetuximab soravtansine

25

Trastuzumab deruxtecan

6

Updates in Ovarian Cancer 2025

Gottfried E. Konecny M.D.
University of California Los Angeles



David Geffen School of Medicine

- **Update on PARP Inhibitors**
- Novel Antibody Drug Conjugates
- Immunotherapy in Recurrent Disease
- Inhibiting the Glucocorticoid Receptor

PARP Inhibitors in Ovarian Cancer 2025



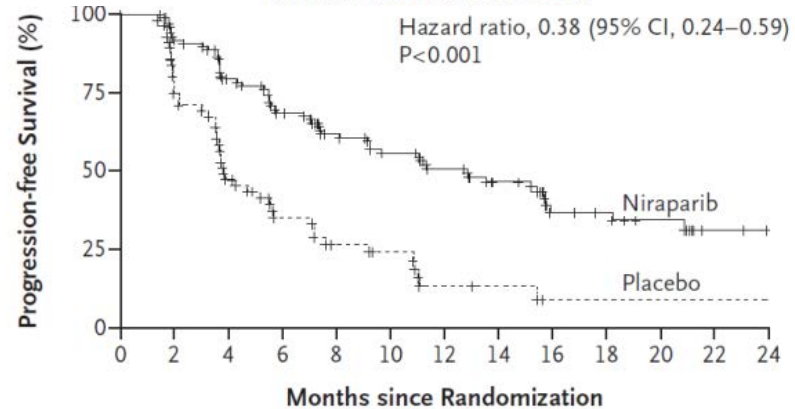
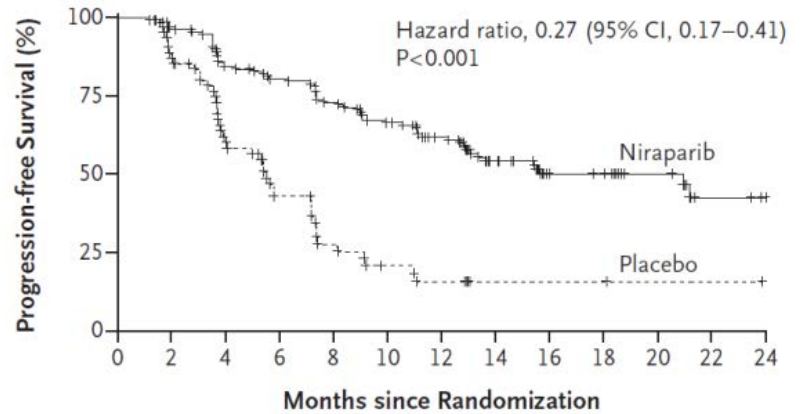
Population

BRCA mutated	Phase III	SOLO-1 (olaparib)	SOLO-2 (olaparib)	SOLO-3 (olaparib vs chemo)	ARIEL 4 (rucaparib v chemo)
	II			ARIEL 2 (rucaparib)	
(*BRCAm or HRD)	III	PAOLA-1 (olaparib/bev*)		QUADRA (niraparib)	QUADRA (niraparib)
	III	PRIMA (niraparib)	Study 19 (olaparib)	AVANOVA2 (niraparib+/- bev)	
All Comers		ATHENA MONO (rucaparib)	NOVA (niraparib)		
			ARIEL3 (rucaparib)		
	II	OVARIO (niraparib/bev)			

NOVA – Niraparib as Maintenance

2016 - PFS NEJM

Germline BRCA Mutation



2022 - OS

Dear Health Care Letter

- **gBRCAmut**
OS was **43.6** months for niraparib vs. **41.6** months for placebo
(HR = 0.93 [95% CI 0.63, 1.36])
- **Non-gBRCAmut, HRDpos**
OS was **37.3** months for niraparib vs **41.4** months for placebo
(HR = 1.32 [95% CI 0.84, 2.06])
- **Non-gBRCAmut**
OS was **31.1** months for niraparib vs. **36.5** months for placebo
(HR = 1.10 [95% CI 0.83, 1.46])

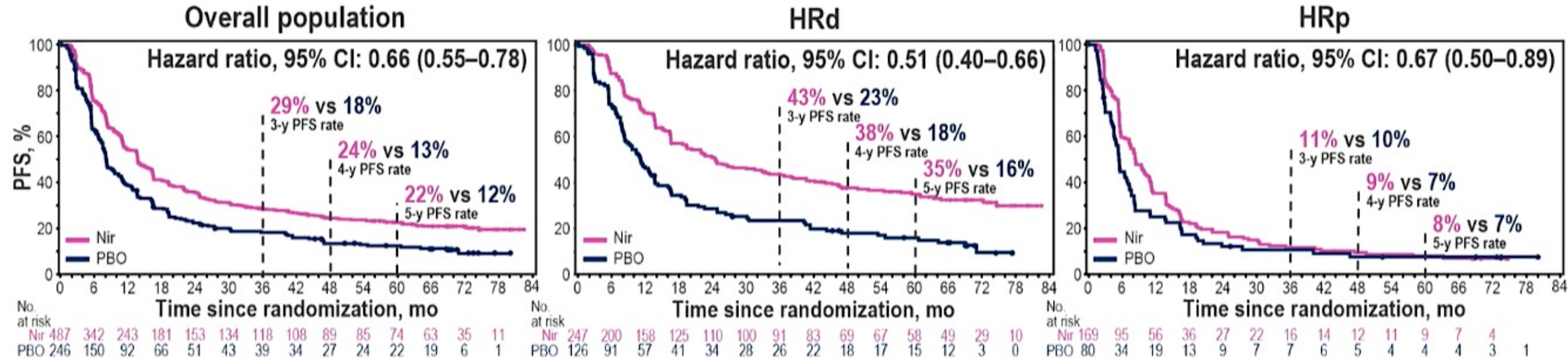
MDS/AML in Randomized Ovarian Cancer PARP Inhibitor Maintenance Trials

			PARPi	MDS/AML Events by arm	
Trial	Setting	Agent	Duration	PARPi, n (%)	Comparator, n (%)
SOLO1 ⁴	1L maint	Olaparib	2 years	3/260 (1.5)	1/130 (0.8)
PRIMA ⁶	1L maint	Niraparib	3 years	1/484 (<1)	0/244
PAOLA1 ⁵	1L maint	Olaparib	2 years	6/535 (1)	1/267 (0.4)
ATHENA MONO ⁹	1L maint	Rucaparib	2 years	2/425 (0.5)	0/110
Study19 ⁸	PS maint	Olaparib	UDP, 18% >3yrs	2/136 (1.5)	1/129 (<1)
SOLO2 ²	PS maint	Olaparib	UDP, mean 29.1 mos	16/195 (8)	4/99 (4)
NOVA ³	PS maint	Niraparib	UDP	13/367 (3.5)	3/179 (1.7)
gBRCAm				9/136 (6.6)	2/65 (3.1)
non-gBRCAm				4/231 (1.7)	1/114 (0.9)
ARIEL3 ⁷	PS maint	Rucaparib	UDP, median 8.3 mos	14/375 (3.8)	6/189 (3.2)
PARPi ≥24m ¹⁰				9/79 (11.4)	
non-gBRCAm				5/245 (2.0)	1/123 (0.8)
gBRCAm				9/130 (6.9)	3/63 (4.8)
PARPi ≥24 mos				7/46 (15.2)	

²Poveda A, et al. Lancet Oncol 2021, ³Matulonis U. et al. SGO 2021, ⁴DiSilvestro P, et al. J Clin Oncol 2022, ⁵Ray-Coquard I et al. NEJM Dec 2019, ⁶Gonzalez-Martin A et al. NEJM 2019, ⁷Coleman RL et al. IGCS 2022, ⁸Lederman J et al. Lancet 2016 17: 1579-89, ⁹Monk B et al. J Clin Oncol 2022, ¹⁰O'Malley et al. Gyn Onc 10/2022

Updated long-term PFS (ad hoc, investigator-assessed)^{a,b}

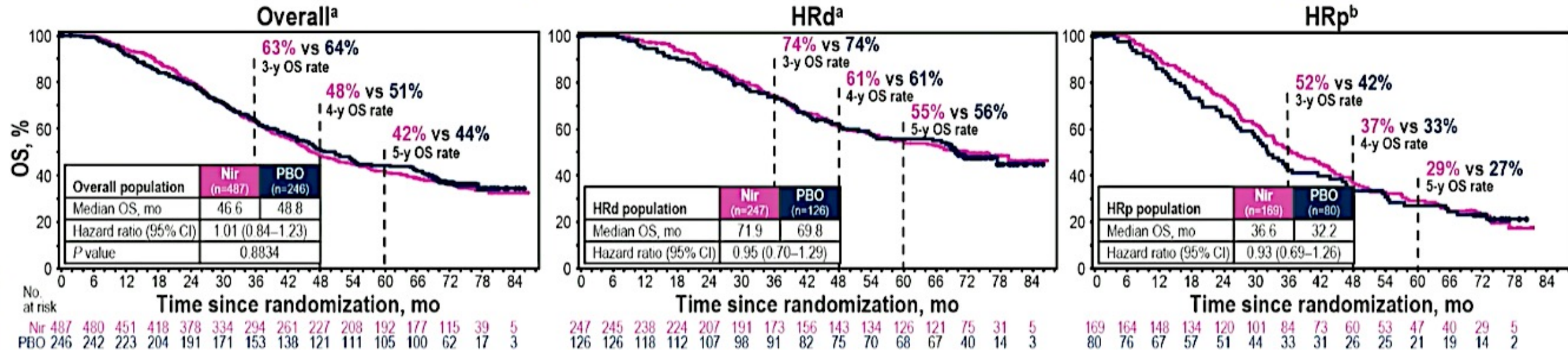
Niraparib PFS benefit sustained with additional follow-up in the overall and HRd populations



- Data cutoff date, 8 April 2024; median follow-up, 6.2 years
- Among patients alive at 5 years in the HRd population, patients who received niraparib were twice as likely to be progression free (35%) than patients who received placebo (16%)
- Delaying progression is critical to maintain health-related quality of life¹

Final OS (62.5% maturity in overall population)

No difference in OS between niraparib and placebo arms in the overall, HRd, and HRp populations

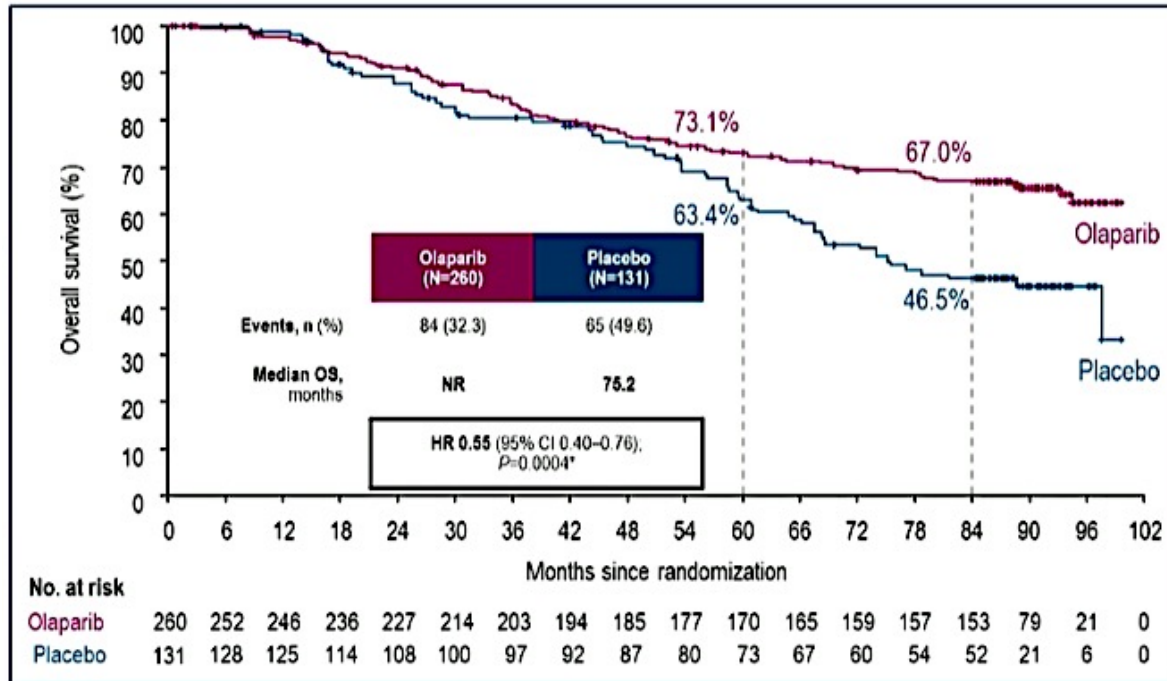


- OS results for all prespecified biomarker-defined subgroups consistent with overall population^c

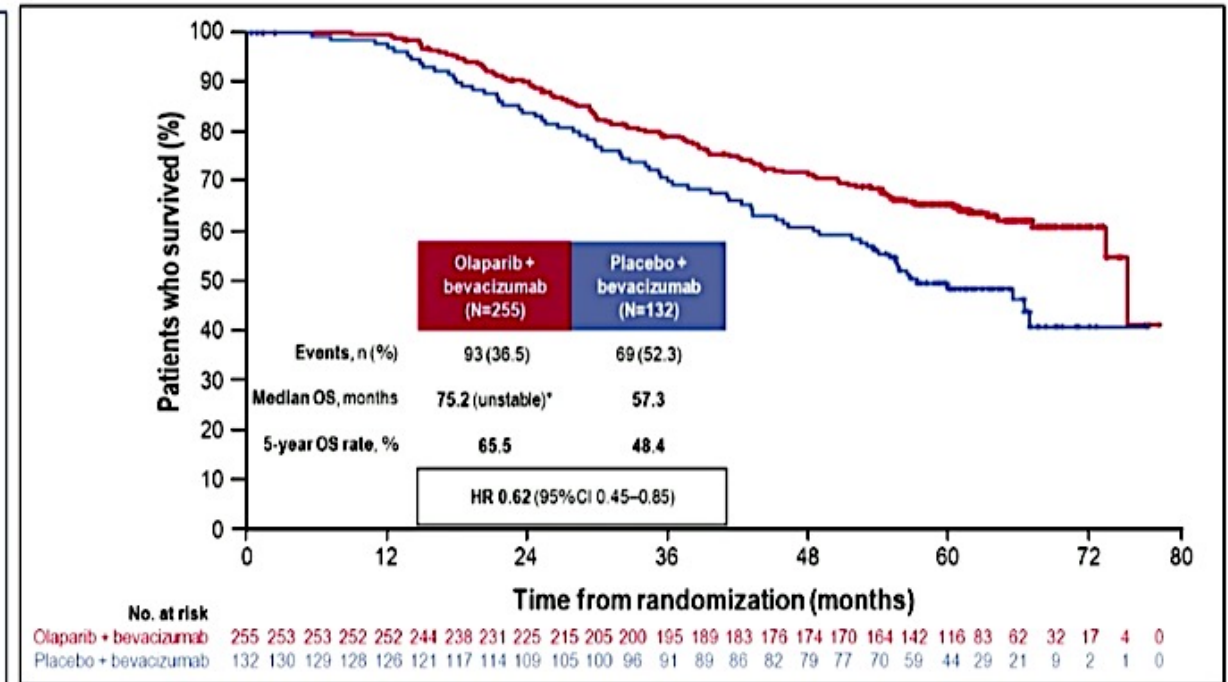
And now we waited 5 years for OS data...

What have we seen in the meantime?

BRCA+: SOLO-1 Overall Survival



BRCA+/HRD+: PAOLA Overall Survival

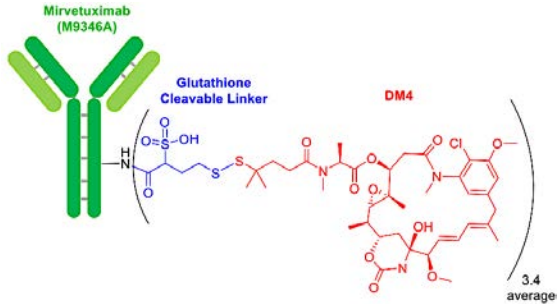
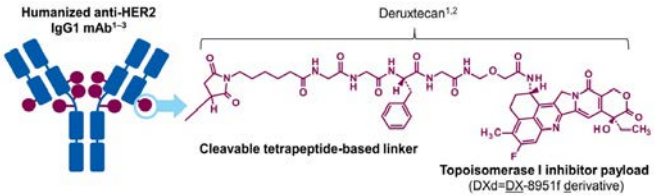
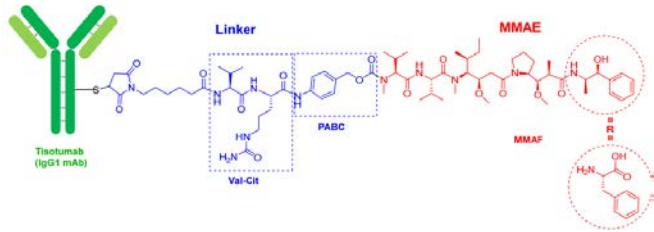


Di Silvestro P, et al. J Clin Oncol 2023

Ray-Coquard I, et al. Ann Oncol 2023

- Update on PARP Inhibitors
- **Novel Antibody Drug Conjugates**
- Immunotherapy in Recurrent Disease
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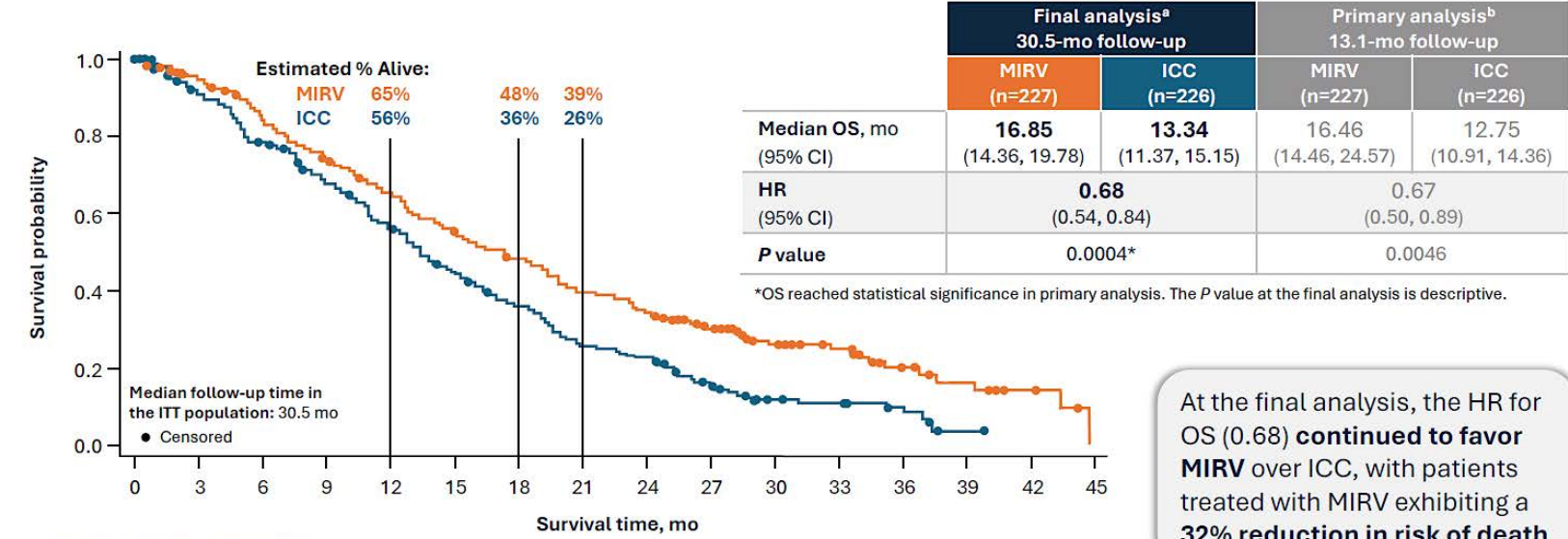
ADCs FDA Approved for Gynecologic Cancer

	Mirvetuximab soravtansine (MIRV) ^{1,2}	Trastuzumab deruxtecan (T-DXd) ^{3,4}	Tisotumab vedotin ^{5,6}
Target	FR α	HER2	Tissue factor
Payload	DM4	Topoisomerase I inhibitor	MMAE (microtubule disruptor)
Regulatory Status	Ovarian: Full FDA approval	HER2 IHC 3+ tumor agnostic: accelerated FDA	Cervical Cancer: Full FDA approval
Pivotal Trial	MIRASOL	DESTINY-PanTumor02	InnovaTV-301
Structure			

1. Mirvetuximab soravtansine. Prescribing information. https://www.accessdata.fda.gov/drugsatfda_docs/label/2024/761310Orig1s005lbl.pdf; 2. de la Torre BG, & Albericio F. *Molecules*. 2023;28(3):1038.; 3. Trastuzumab deruxtecan. Prescribing information. https://www.accessdata.fda.gov/drugsatfda_docs/label/2024/761139s028lbl.pdf; 4. Meric-Bernstam F, et al. ASCO 2023. Abstract LBA3000; 5. Tisotumab vedotin-tftv. Prescribing information https://www.accessdata.fda.gov/drugsatfda_docs/label/2024/761208s007lbl.pdf; 6. de la Torre BG & Albericio F. *Molecules*. 2022;27(3):1075.

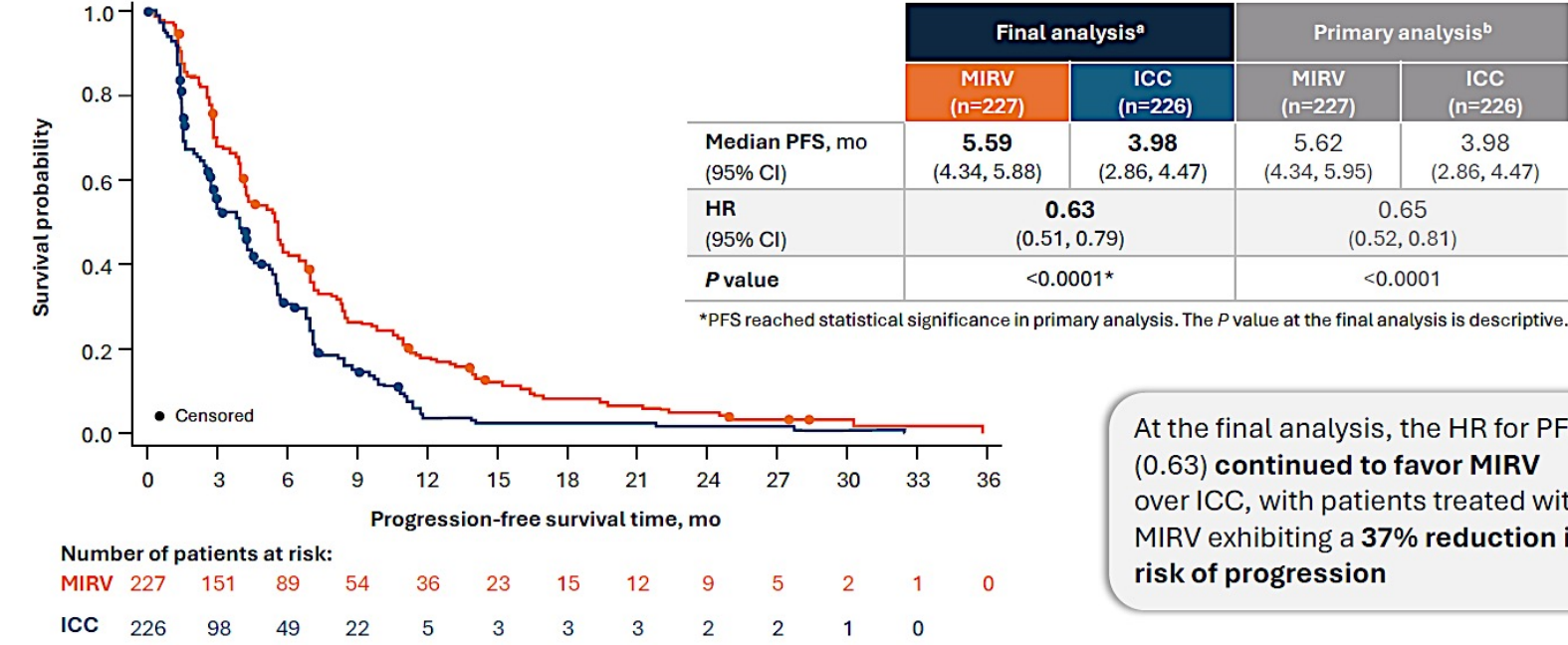
MIRASOL: Final OS and PFS

Overall Survival



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**

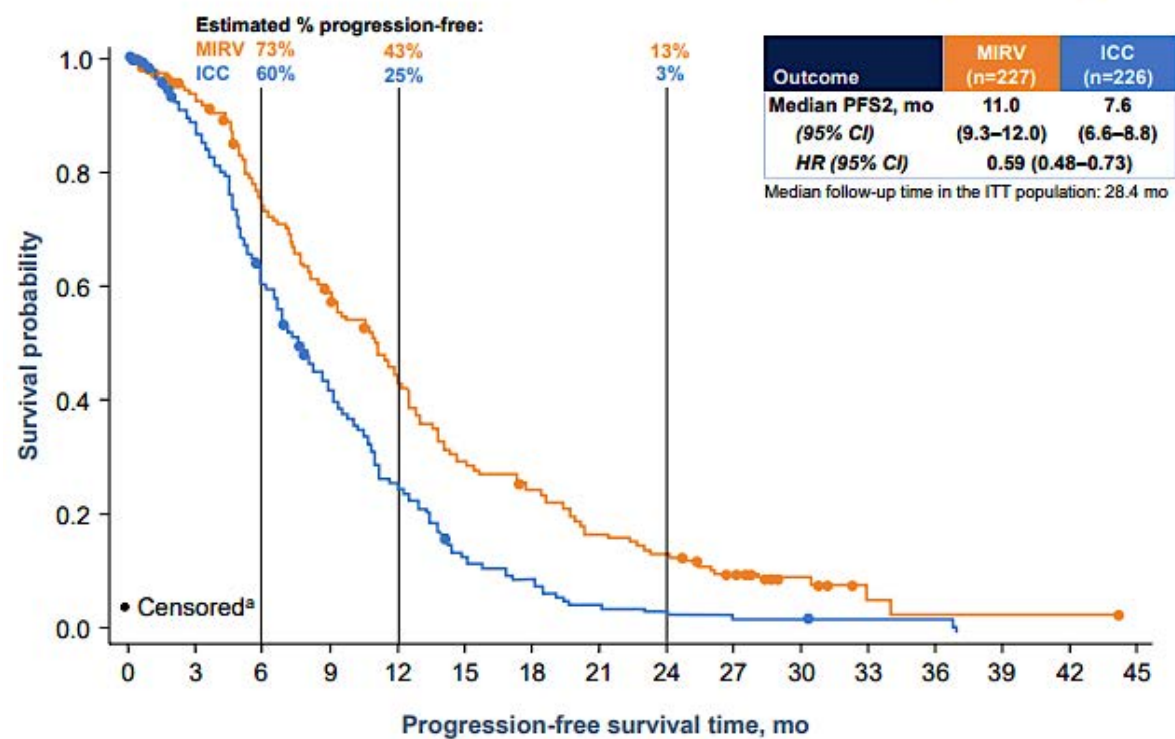
Progression-Free Survival



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**

MIRASOL: PFS2

PFS2 ITT Population (Median follow-up 28.4 mo)



Number of patients at risk:

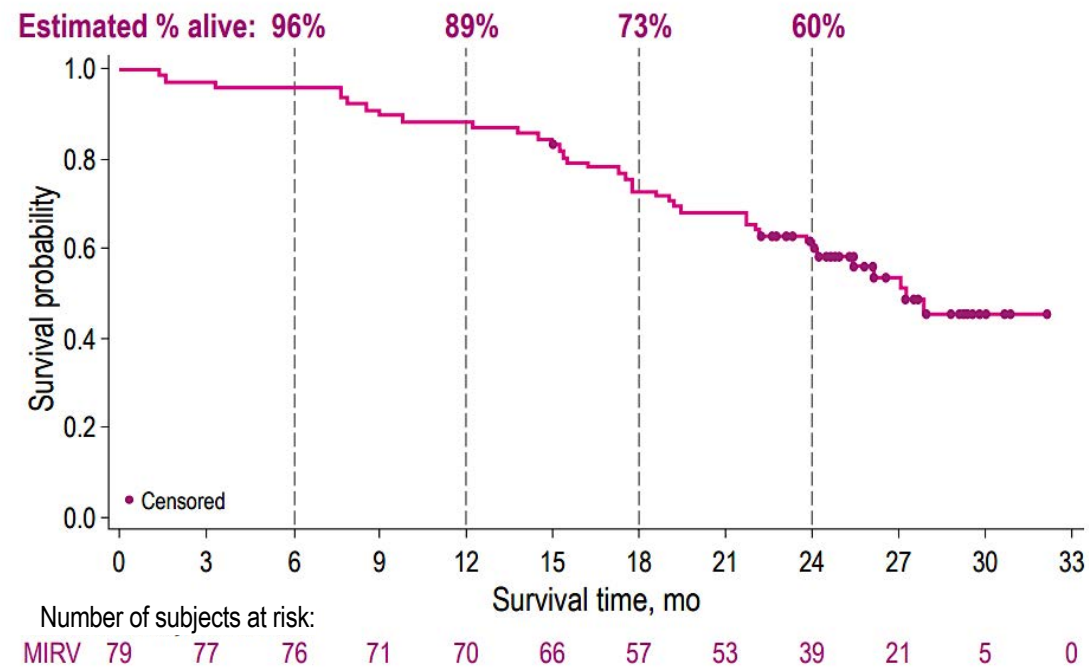
MIRV	227	201	155	123	90	61	50	34	27	15	7	2	1	1	1	0
ICC	226	177	122	83	49	24	17	8	6	4	4	3	2	0	0	0

*Reasons for censor included no next-line treatment with no PD or death during long-term follow-up, next-line treatment ongoing with no PD or death during long-term follow-up, lost to follow-up, and no follow-up contact.

PFS2 by Baseline Clinicodemographic Subgroup

		No. of patients	No. of events	Hazard ratio (95% CI) ^a	Hazard ratio (95% CI)	P value ^b
All		453	390	0.59 (0.48, 0.73)		<0.0001
Stage at diagnosis	III	284	244	0.58 (0.45, 0.76)		<0.0001
	IV	141	122	0.60 (0.41, 0.86)		0.0048
BRCA status	Positive	65	58	0.31 (0.17, 0.56)		<0.0001
	Negative	388	332	0.65 (0.53, 0.81)		0.0001
Age (years)	18-64	254	216	0.62 (0.47, 0.81)		0.0005
	≥65	199	174	0.57 (0.42, 0.78)		0.0003
ECOG PS at baseline	0	250	215	0.61 (0.46, 0.80)		0.0003
	1	198	171	0.58 (0.43, 0.79)		0.0005
Prior exposure to bevacizumab	Yes	281	247	0.61 (0.47, 0.78)		0.0001
	No	172	143	0.57 (0.41, 0.79)		0.0008
Prior exposure to PARPi maintenance	Yes ^c	252	219	0.49 (0.37, 0.65)		<0.0001
	No	190	160	0.74 (0.54, 1.02)		0.0656
	Uncertain	11	11	0.45 (0.12, 1.71)		0.2308
Number of prior lines of therapy	1 or 2	245	212	0.55 (0.42, 0.73)		<0.0001
	3	208	178	0.65 (0.48, 0.87)		0.0040
Type of ICC	PLD	163	141	0.56 (0.40, 0.79)		0.0007
	Paclitaxel	185	156	0.62 (0.45, 0.86)		0.0036
	Topotecan	105	93	0.62 (0.41, 0.93)		0.0204
Primary PFI ^d	≤6 months	147	126	0.69 (0.48, 0.99)		0.0404
	>6 months	305	264	0.56 (0.44, 0.72)		<0.0001
Most recent PFI ^e	≤3 months	187	161	0.62 (0.45, 0.85)		0.0027
	>3 months	266	229	0.56 (0.43, 0.74)		<0.0001

PICCOLO: Final OS and Efficacy Summary with Mirvetuximab Soravtansine



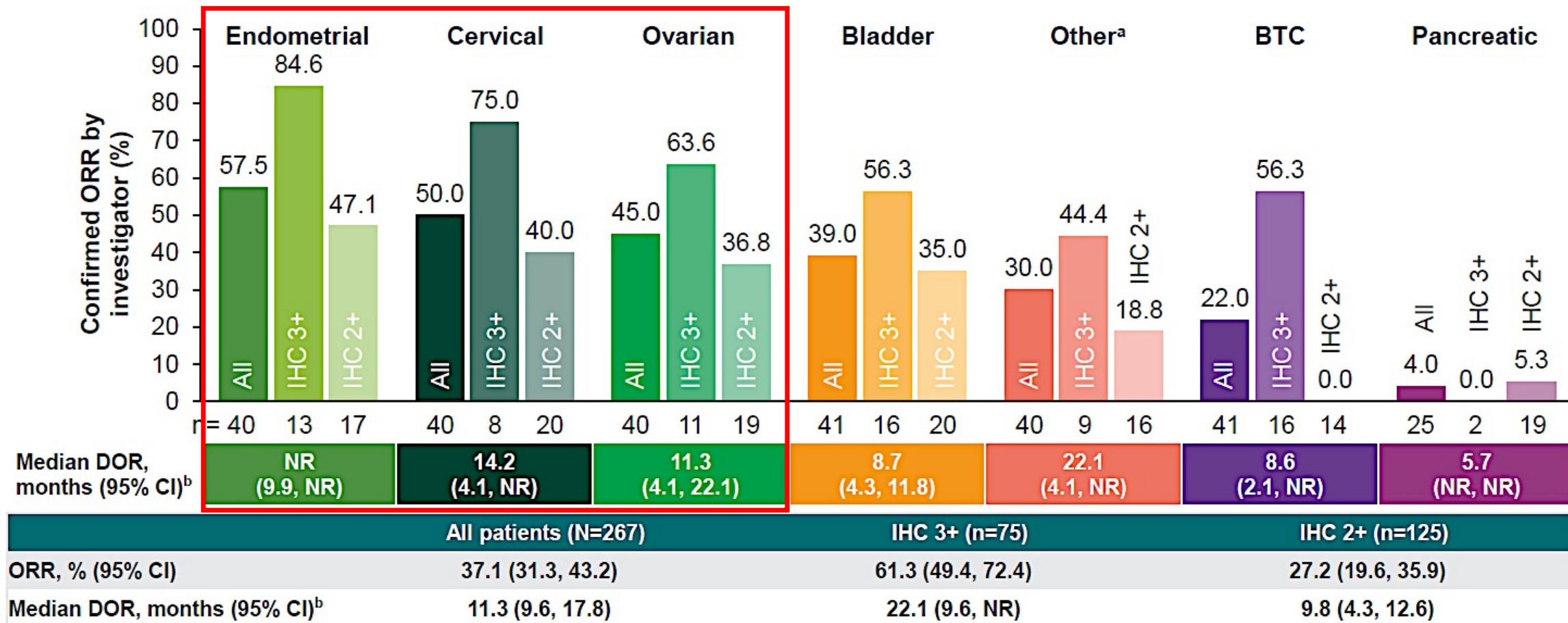
Median OS
27.17 months (95% CI, 23.79–NR)

61 patients (77%) received a new anticancer therapy^a, most commonly:

- Platinum-based regimen (47%)
- Gemcitabine (32%)
- Anthracyclines (30%)
- Other chemotherapy (28%)
- Bevacizumab (25%)
- Taxanes (23%)

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

DESTINY-PanTumor02: Objective Response Rate



Analysis of ORR by investigator was performed in patients who received ≥ 1 dose of T-DXd; all patients (n=267; including 67 patients with IHC 1+ [n=25], IHC 0 [n=30], or unknown IHC status [n=12] by central testing) and patients with centrally confirmed HER2 IHC 3+ (n=75) or IHC 2+ (n=125) status. Analysis of DOR was performed in patients with objective response who received ≥ 1 dose of T-DXd; all patients (n=99; including 19 patients with IHC 1+ [n=6], IHC 0 [n=9], or unknown IHC status [n=4] by central testing) and patients with centrally confirmed HER2 IHC 3+ (n=46) or IHC 2+ (n=34) status. ^aResponses in extramammary Paget's disease, head and neck cancer, oropharyngeal neoplasm, and salivary gland cancer; ^bincludes patients with a confirmed objective response only

BTC, biliary tract cancer; CI, confidence interval; DOR, duration of response; HER2, human epidermal growth factor receptor 2; IHC, immunohistochemistry; NR, not reached; ORR, objective response rate; T-DXd, trastuzumab deruxtecan

DESTINY-PanTumor02

Secondary Endpoints –

Final PFS and OS

(Investigator Assessed)

mPFS

Median PFS, months (95% CI) [n]*	All patients	HER2 IHC status by central testing		HER2 IHC status at enrollment†	
		IHC 3+	IHC 2+	IHC 3+	IHC 2+
All	6.9 (5.6, 8.0) [267]	11.9 (8.2, 13.0) [75]	5.4 (4.2, 6.0) [125]	9.7 (7.0, 12.5) [111]	5.1 (4.1, 6.0) [151]
Endometrial	11.1 (7.1, 25.8) [40]	28.1 (7.3, NE) [13]	8.5 (4.6, 15.1) [17]	24.8 (4.5, 35.7) [16]	11.0 (6.0, 19.5) [24]
Cervical	7.0 (4.2, 11.1) [40]	NE (3.9, NE) [8]	4.8 (2.7, 5.7) [20]	NE (3.9, NE) [10]	4.6 (1.4, 8.1) [25]
Ovarian	5.9 (4.0, 8.3) [40]	12.5 (3.1, NE) [11]	4.1 (2.3, 12.6) [19]	12.6 (4.1, NE) [15]	4.4 (2.3, 7.1) [25]
Bladder	7.0 (4.2, 9.7) [41]	7.4 (3.0, 11.9) [16]	7.8 (2.6, 11.6) [20]	7.0 (3.9, 11.5) [27]	7.0 (2.6, 13.0) [14]
Other†	8.8 (5.5, 12.5) [40]	22.3 (5.6, NE) [9]	5.5 (2.8, 8.7) [16]	13.0 (6.3, 23.4) [16]	6.6 (2.9, 8.8) [24]
Biliary tract	4.6 (3.1, 6.0) [41]	7.4 (2.8, 12.5) [16]	4.2 (2.8, 6.0) [14]	6.9 (3.0, 8.0) [22]	3.7 (2.8, 5.1) [19]
Pancreatic	3.2 (1.8, 7.2) [25]	5.4 (2.8, NE) [2]	2.8 (1.4, 9.1) [19]	8.0 (1.2, NE) [5]	3.2 (1.4, 4.9) [20]

mOS

Median OS, months (95% CI) [n]	All patients	HER2 IHC status by central testing		HER2 IHC status at enrollment†	
		IHC 3+	IHC 2+	IHC 3+	IHC 2+
All	13.4 (11.9, 15.3) [267]	21.1 (16.0, 26.0) [75]	12.2 (10.7, 13.6) [125]	17.7 (12.8, 23.4) [111]	12.0 (9.6, 13.5) [151]
Endometrial	24.2 (12.8, 33.7) [40]	33.7 (18.9, NE) [13]	16.4 (8.0, 34.7) [17]	29.0 (4.5, NE) [16]	20.3 (8.1, 33.1) [24]
Cervical	13.6 (11.1, 19.7) [40]	35.8 (3.9, NE) [8]	11.6 (5.1, 18.0) [20]	35.8 (3.9, NE) [10]	11.7 (8.0, 13.6) [25]
Ovarian	13.2 (8.0, 17.7) [40]	20.0 (3.8, NE) [11]	13.0 (4.7, 21.9) [19]	20.0 (7.2, NE) [15]	10.7 (5.9, 14.8) [25]
Bladder	12.8 (11.2, 15.1) [41]	13.4 (6.7, 19.8) [16]	13.1 (11.0, 19.9) [20]	12.6 (6.7, 17.2) [27]	13.5 (8.0, 19.9) [14]
Other*	21.0 (12.9, 25.1) [40]	25.1 (11.1, NE) [9]	14.6 (6.8, 22.4) [16]	25.2 (11.1, 40.0) [16]	15.5 (9.6, 22.4) [24]
Biliary tract	7.0 (4.6, 10.2) [41]	12.4 (2.8, 26.3) [16]	6.0 (3.7, 11.7) [14]	7.6 (4.6, 23.7) [22]	5.3 (3.1, 10.2) [19]
Pancreatic	5.0 (3.8, 14.2) [25]	12.4 (8.8, NE) [2]	4.9 (2.4, 15.7) [19]	8.8 (2.4, NE) [5]	4.7 (3.2, 14.2) [20]

Novel Deruxtecan ADCs in Development

ADC	Datopotamab deruxtecan (Dato-DXd)	Raludotatug deruxtecan (R-DXd)	Ifinatamab Deruxtecan (I-DXd)
Gynecological Malignancy	Ovarian & Endometrial	Ovarian, Endometrial & Cervical	Ovarian, Endometrial & Cervical
Target	TROP2	CDH6	B7-H3
Target Expression	Highly expressed in a majority of ovarian and endometrial cancers ¹	Minimal expression in normal tissue but aberrantly expressed and linked to poorer prognosis in many solid tumors ²	Minimal or no expression in normal tissues but highly expressed in many solid tumors ³
Payload	Exatecan (Topoisomerase I inhibitor)		
Key Trials for Gynecologic Cancer	TROPION-PanTumor03	REJOICE-PanTumor01 REJOICE-Ovarian01	Ideate-PanTumor02
Development Stage	Phase 3	Phase 2/3	Phase 1/2
Development Status	Ongoing	Ongoing	Ongoing

1. Oaknin A et al. ESMO 2024. Abstract 714MO; 2. Albiges L et al. ASCO 2025. Abstract TPS3158; 3. Kogawa T et al. ASCO 2025. Abstract TPS3157.

Raludotatug deruxtecan (R-DXd) in patients with platinum-resistant ovarian cancer: Primary analysis of the Phase 2, dose-optimization part of the REJOICE-Ovarian01 study

Isabelle Ray-Coquard,¹ Kosei Hasegawa,² Nicoletta Colombo,³ Jung-Yun Lee,⁴ David Cibula,⁵ Yunong Gao,⁶ Sabrina Chiara Cecere,⁷ Peng-Hui Wang,⁸ Lubomir Bodnar,⁹ Sally Baron-Hay,¹⁰ Diana Bello Roufai,¹¹ Mayu Yunokawa,¹² David Garcia-Illescas,¹³ Sook-hee Hong,¹⁴ Maria Cristina Petrella,¹⁵ Sandra Re,¹⁶ Madan Gopal Kundu,¹⁶ Karin Yamada,¹⁷ Veronique D'Hondt,¹⁹ Lydia Gaba¹⁹

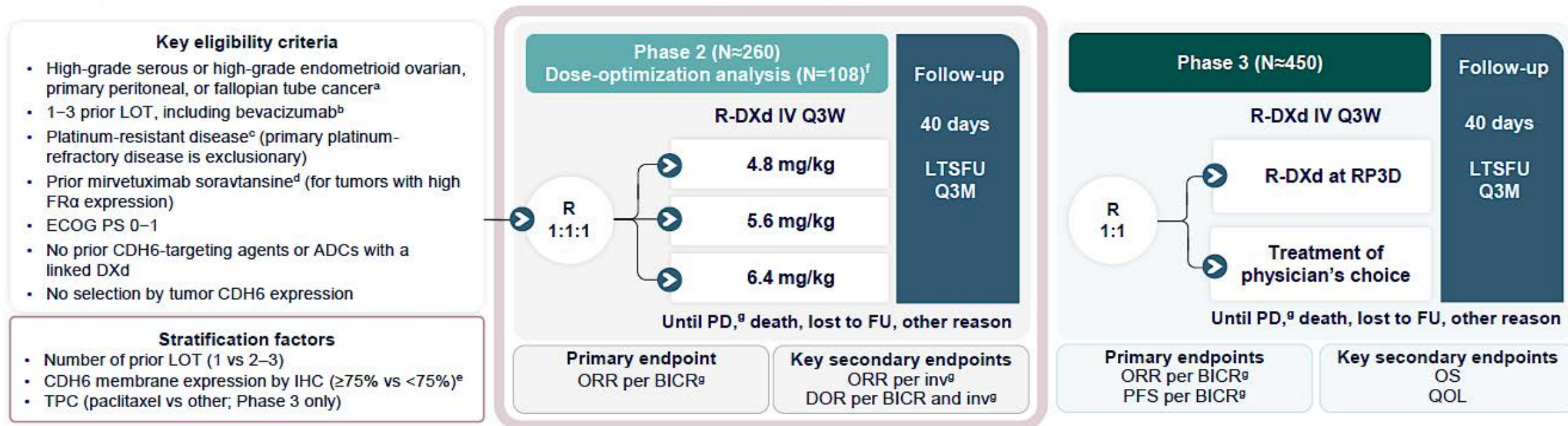
¹Centre Léon Bérard, University Claude Bernard, and GINECO, Lyon, France; ²Saitama Medical University International Medical Center, Hidaka, Saitama, Japan; ³European Institute of Oncology, IRCCS, Milan, Italy; ⁴Yonsei Cancer Center and Severance Hospital, Yonsei University College of Medicine, Seoul, Republic of Korea; ⁵Charles University and General University Hospital, Prague, Czech Republic; ⁶Beijing Cancer Hospital, Beijing Institute for Cancer Research, Beijing, China; ⁷IRCCS Fondazione G. Pascale, Naples, Italy; ⁸Taipei Veterans General Hospital, Taipei, Taiwan; ⁹University of Siedlce, Siedlce, Poland; ¹⁰GenesisCare North Shore, St Leonards, NSW, Australia; ¹¹Institut Curie, Saint-Cloud, France; ¹²The Cancer Institute Hospital of Japanese Foundation for Cancer, Tokyo, Japan; ¹³Vall d'Hebron Institute of Oncology (VHIO), Hospital Universitari Vall d'Hebron, Vall d'Hebron Barcelona Hospital Campus, Barcelona, Spain; ¹⁴Seoul St. Mary's Hospital, The Catholic University of Korea, Seoul, Republic of Korea; ¹⁵Azienda Ospedaliera Universitaria Careggi, Florence, Italy; ¹⁶Daiichi Sankyo, Inc., Basking Ridge, NJ, USA; ¹⁷Merck & Co., Inc., Rahway, NJ, USA; ¹⁸Institut du Cancer de Montpellier Val d'Aurelle, Parc Euromedecine, GINECO, Montpellier, France; ¹⁹Hospital Clinic Barcelona and GEICO, Barcelona, Spain.

19 October 2025

Presentation number: LBA42

REJOICE-Ovarian01 study design

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



We present the primary analysis from the dose-optimization part of the Phase 2/3 REJOICE-Ovarian01 study, in 107 patients with platinum-resistant OC who had a follow-up of ≥18 weeks or discontinued treatment

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

1. ClinicalTrials.gov. <https://clinicaltrials.gov/study/NCT06161025>. Accessed October 7, 2025. 2. Ray-Coquard I, et al. Poster presentation at American Society of Clinical Oncology 2024; May 31–June 4; Chicago, IL, USA. Poster TPS5625. 3. Moore KN, et al. Oral presentation at the Society of Gynecologic Oncology 2024 Annual Meeting on Women's Cancer, March 16–18, 2024; San Diego, CA, USA.

R-DXd monotherapy demonstrated promising antitumor activity at all doses in patients with platinum-resistant OC

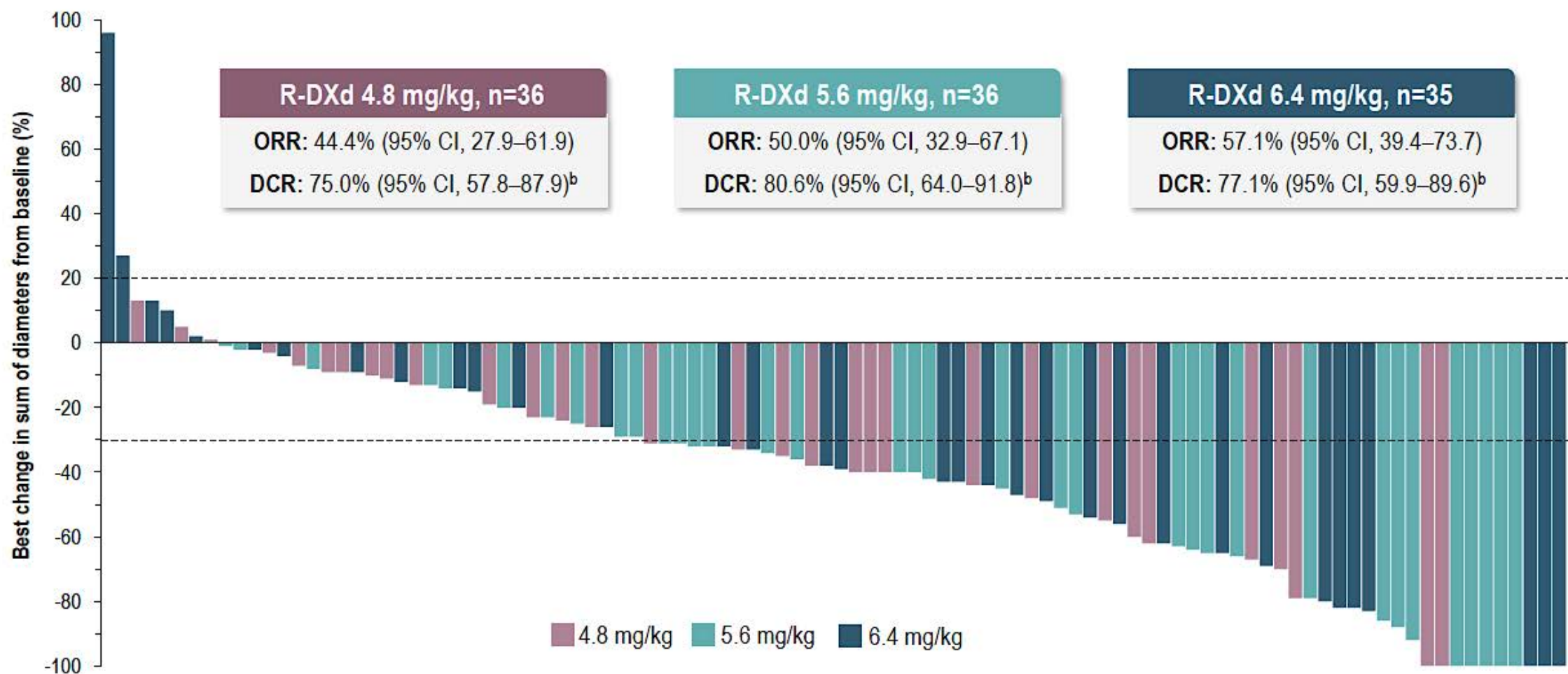
Confirmed response by BICR ^a	R-DXd 4.8 mg/kg n=36	R-DXd 5.6 mg/kg n=36	R-DXd 6.4 mg/kg n=35	R-DXd 4.8–6.4 mg/kg N=107
ORR, % (95% CI)	44.4 (27.9–61.9)	50.0 (32.9–67.1)	57.1 (39.4–73.7)	50.5 (40.6–60.3)
BOR,^b n (%)				
CR	1 (2.8)	2 (5.6)	0	3 (2.8)
PR	15 (41.7)	16 (44.4)	20 (57.1)	51 (47.7)
SD	17 (47.2)	15 (41.7)	10 (28.6)	42 (39.3)
PD	2 (5.6)	2 (5.6)	4 (11.4)	8 (7.5)
Not evaluable	1 (2.8) ^c	1 (2.8) ^d	1 (2.9) ^c	3 (2.8)
DCR,^e % (95% CI)	75.0 (57.8–87.9)	80.6 (64.0–91.8)	77.1 (59.9–89.6)	77.6 (68.5–85.1)
TTR, median (range), weeks	7.1 (5.4–18.7)	6.6 (5.1–18.3)	7.2 (5.3–19.1)	7.1 (5.1–19.1)

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

^aPer RECIST 1.1. ^bBOR was defined as the best response across all timepoints; CR, ≥2 assessments of CR ≥4 weeks apart, prior to progression; PR, ≥2 assessments of PR (or CR) ≥4 weeks apart, prior to progression (not meeting criteria for CR); SD, ≥1 assessment of SD (or better) ≥5 weeks following treatment initiation, and before progression (not meeting criteria for CR or PR); PD, progression ≥12 weeks following treatment initiation (not meeting criteria for CR, PR, or SD); ^cPatient had no baseline tumor assessment by BICR. ^dPatient had no adequate post-baseline tumor assessment by BICR. ^eDCR was defined as percentage of patients with BOR of CR, PR, or SD (per RECIST 1.1).

BICR, blinded independent central review; BOR, best overall response; CI, confidence interval; CR, complete response; DCR, disease control rate; OC, ovarian cancer; ORR, objective response rate; PD, progressive disease; PR, partial response; RECIST 1.1, Response Evaluation Criteria in Solid Tumours, version 1.1; SD, stable disease; TTR, time to response.

Clinically meaningful tumor responses were seen irrespective of dose^a



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

^aAntitumor 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. ^bDCR 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.

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

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

The safety profile of the 4.8 and 5.6 mg/kg cohorts were similar.

Treatment-related TEAEs occurred more frequently in the 6.4 mg/kg cohort (vs 4.8 and 5.6 mg/kg cohorts)

Data cutoff: February 26, 2025.

Reported safety events are defined using MedDRA Preferred Terms and CTCAE criteria.

^aGrade 5 events were hepatic failure, ovarian cancer, and malignant neoplasm progression. ^bGrade 5 events were ovarian cancer and aspiration. ^cGrade 5 event was influenza infection. ^dDose modifications associated with treatment-related TEAEs defined as: dose discontinuation, no subsequent administration of R-DXd; dose reduction, R-DXd dose was reduced at next administration; dose delay, study drug was not administered at the next scheduled cycle but was administered at a later date. ^eILD/pneumonitis events were adjudicated by an independent ILD adjudication committee. ^fILD/pneumonitis Grade ≥3 event (adjudicated as treatment related) was grade 3.

CTCAE, Common Terminology Criteria for Adverse Events; ILD, interstitial lung disease; MedDRA, Medical Dictionary for Regulatory Activities; SAE, serious adverse event; TEAE, treatment-emergent adverse event.

- Update on PARP Inhibitors
- Novel Antibody Drug Conjugates
- **Immunotherapy in Recurrent Disease**
- Inhibiting the Glucocorticoid Receptor

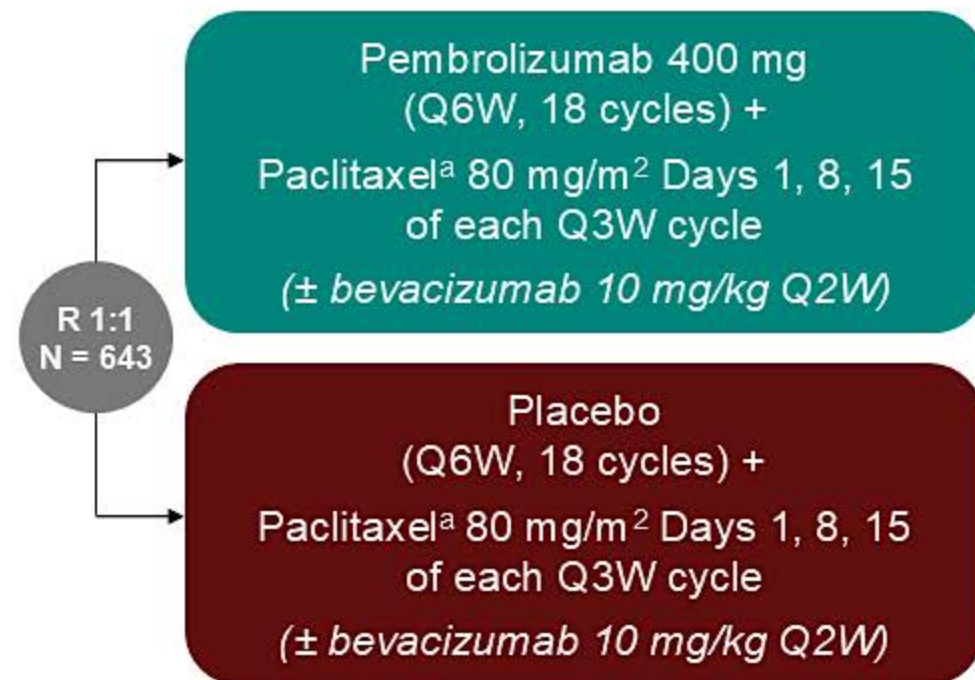
ENGOT-ov65/KEYNOTE-B96 Study Design (NCT05116189)

Key Eligibility Criteria

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

Stratification Factors

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



Primary Endpoint: PFS per RECIST v1.1 by investigator
Key Secondary: OS

^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.

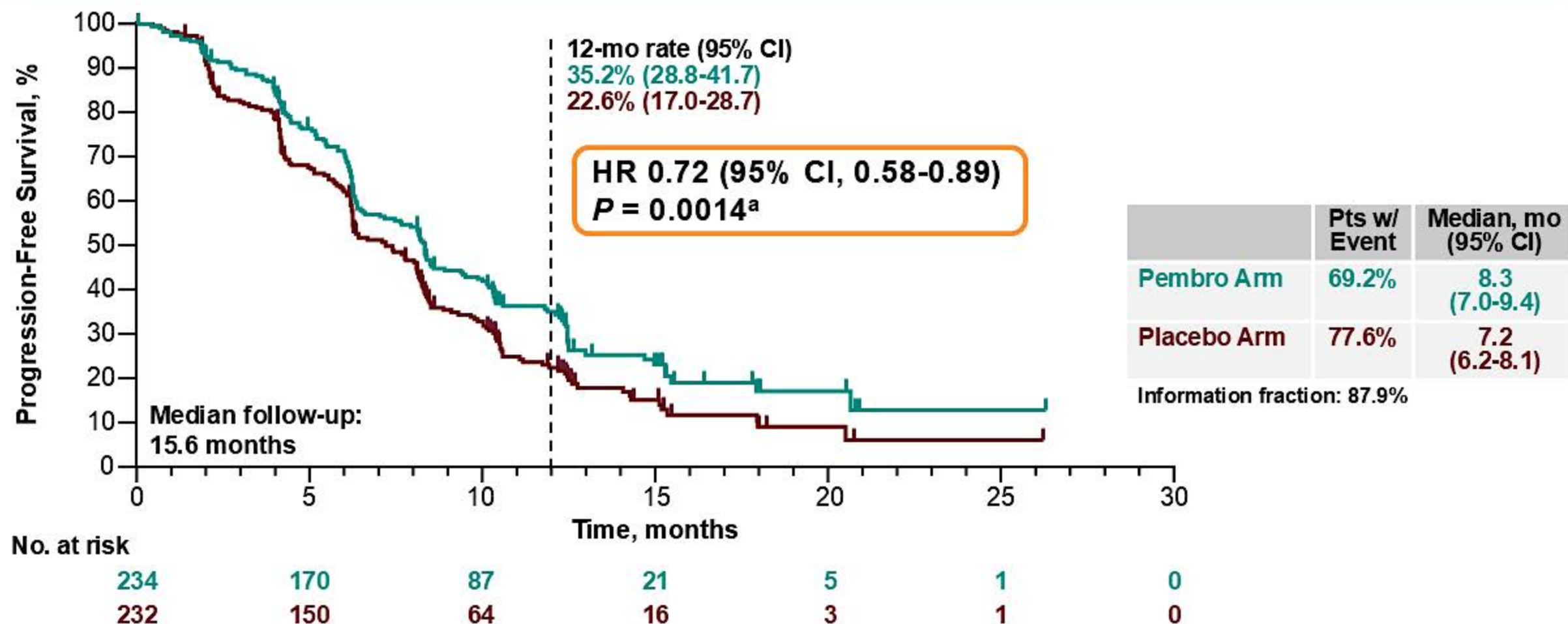
Baseline Characteristics

	Pembro Arm (N = 322)	Placebo Arm (N = 321)
Age, median (range)	62 y (37-85)	61 y (37-82)
Race ^a		
White	207 (64.3%)	217 (67.6%)
Asian	72 (22.4%)	58 (18.1%)
Multiple	12 (3.7%)	17 (5.3%)
Black or African American	8 (2.5%)	6 (1.9%)
Hawaiian/Pacific Islander	1 (0.3%)	1 (0.3%)
PD-L1 CPS		
<1	88 (27.3%)	89 (27.7%)
1 to <10	133 (41.3%)	132 (41.1%)
≥10	101 (31.4%)	100 (31.2%)
Stage at diagnosis (FIGO 2014 criteria)		
IA-IIB	25 (7.8%)	26 (8.1%)
III-IIIC	183 (56.8%)	189 (58.9%)
IVA-IVB	114 (35.4%)	106 (33.0%)

	Pembro Arm (N = 322)	Placebo Arm (N = 321)
ECOG PS 1	142 (44.1%)	144 (44.9%)
High-grade serous histology ^b	278 (86.3%)	275 (85.7%)
Bevacizumab use	235 (73.0%)	236 (73.5%)
Prior lines of therapy ^c		
1 line	121 (37.6%)	113 (35.2%)
2 lines	200 (62.1%)	207 (64.5%)
Prior anticancer therapy		
Anti-PD-1 or PD-L1	7 (2.2%)	7 (2.2%)
Bevacizumab	149 (46.3%)	146 (45.5%)
PARP inhibitor	112 (34.8%)	123 (38.3%)
Platinum-free interval ^d		
<3 mo	137 (42.5%)	162 (50.5%)
≥3 to ≤6 mo	183 (56.8%)	154 (48.0%)
>6 mo	2 (0.6%)	4 (1.2%)

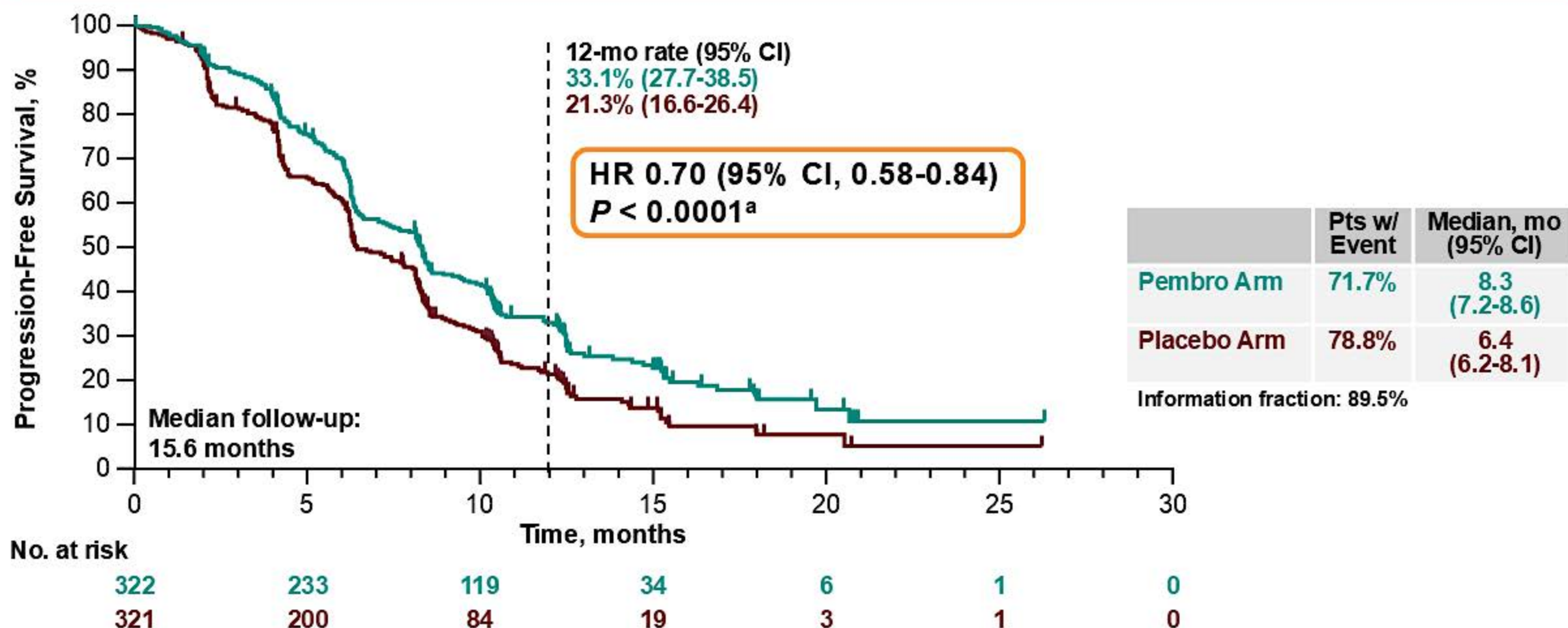
^a44 participants had missing information for race, 22 (6.8%) in the pembro arm and 22 (6.9%) in the placebo arm. ^bOther histology subtypes in the pembro and placebo arms, respectively, were clear cell in 24 (7.5%) and 26 (8.1%), endometrioid in 9 (2.8%) and 4 (1.2%), low-grade serous in 6 (1.9%) and 10 (3.1%), carcinosarcoma in 3 (0.9%) and 5 (1.6%), and other carcinoma in 2 (0.6%) and 1 (0.3%). ^c2 participants had 3 prior lines of therapy, 1 (0.3%) in each treatment arm. ^d1 participant in the placebo arm had missing information for platinum-free interval. Data cutoff date: March 5, 2025.

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



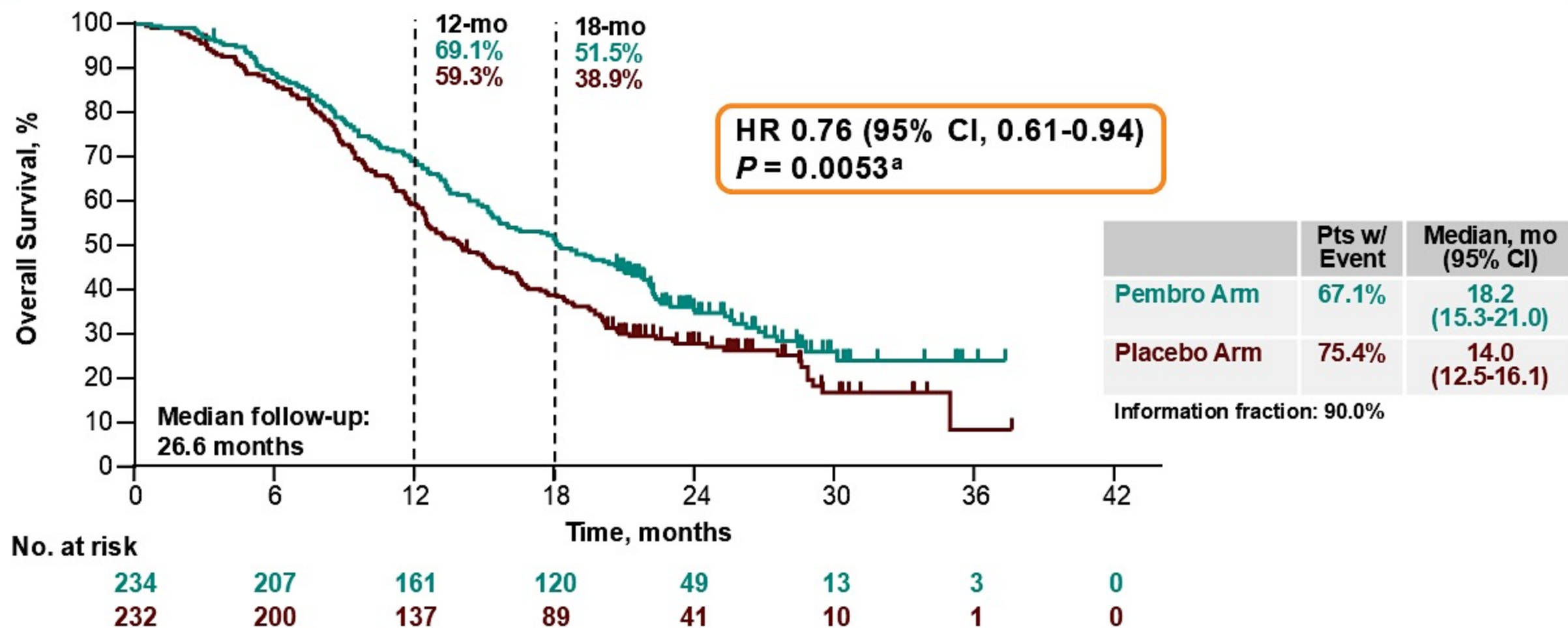
Response assessed per RECIST v1.1 by investigator review. ^aHazard ratio (CI) analyzed based on a Cox regression model with treatment as a covariate stratified by the randomization stratification factors. The observed p-value crossed the prespecified nominal boundary of 0.0116 at this planned first interim analysis; because the success criterion of the PFS hypothesis was met, no formal testing of PFS will be performed at later analyses. Data cutoff date: April 3, 2024.

Progression-Free Survival in the ITT Population at IA1



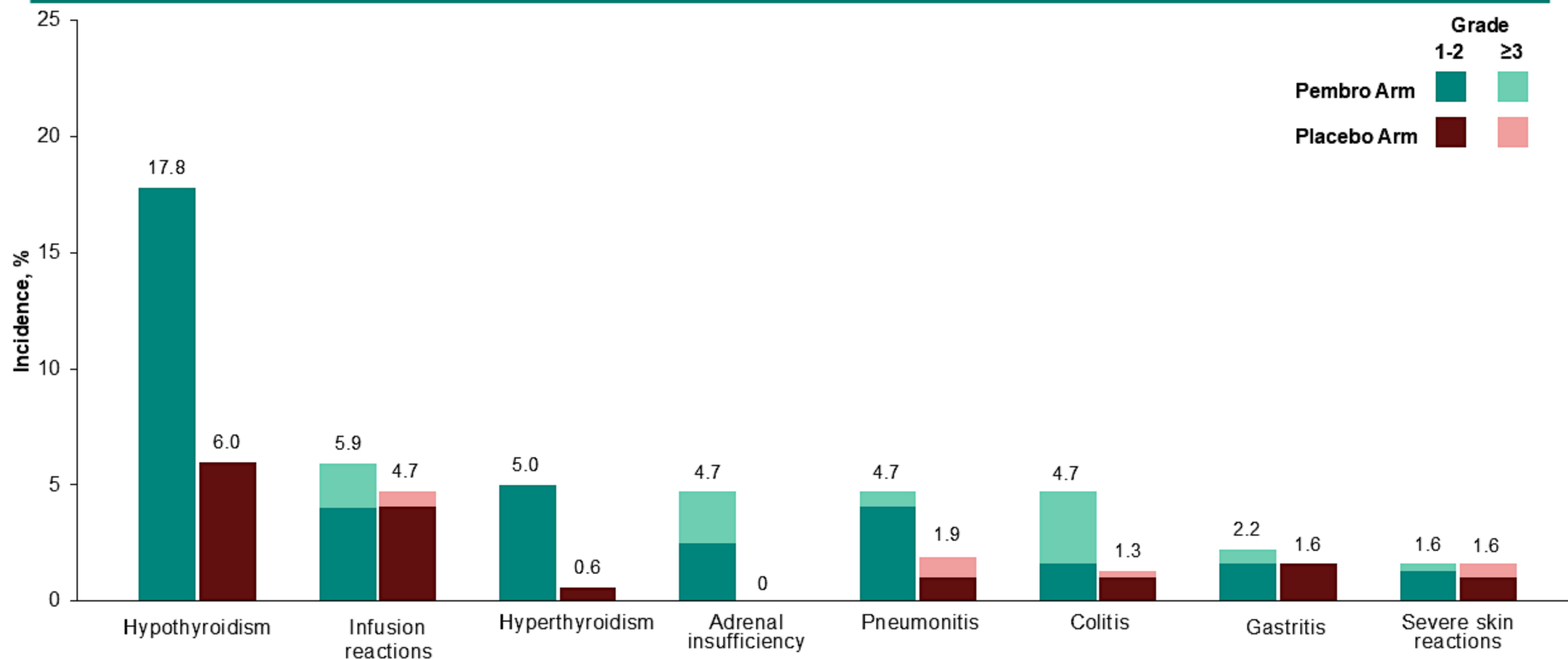
Response assessed per RECIST v1.1 by investigator review. ^aHazard ratio (CI) analyzed based on a Cox regression model with treatment as a covariate stratified by the randomization stratification factors. The observed p-value crossed the prespecified nominal boundary of 0.0023 at this planned first interim analysis; because the success criterion of the PFS hypothesis was met, no formal testing of PFS will be performed at later analyses. Data cutoff date: April 3, 2024.

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



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

Immune-Mediated Adverse Events and Infusion Reactions at IA2, Incidence ≥ 5 Participants in Either Arm



Events were based on a list of preferred terms intended to capture the known risks of pembrolizumab and considered regardless of attribution to treatment by the investigator.
Data cutoff date: March 5, 2025.

Phase 3 KEYNOTE-B96 Trial Met Secondary Endpoint of Overall Survival in All Comers Population of Patients With Platinum-Resistant Recurrent Ovarian Cancer

Press Release: October 16, 2025

The Phase 3 KEYNOTE-B96 trial, also known as ENGOT-ov65, met its secondary endpoint of overall survival (OS) for the treatment of patients with platinum-resistant recurrent ovarian cancer in all comers. The trial studied pembrolizumab in combination with chemotherapy (paclitaxel) with or without bevacizumab for these patients.

“As previously announced, KEYNOTE-B96 met its primary endpoint of progression-free survival PFS in patients with platinum-resistant recurrent ovarian cancer whose tumors express PD-L1 and in all comers, as well as its secondary endpoint of OS for patients whose tumors express PD-L1, at previous interim analyses.

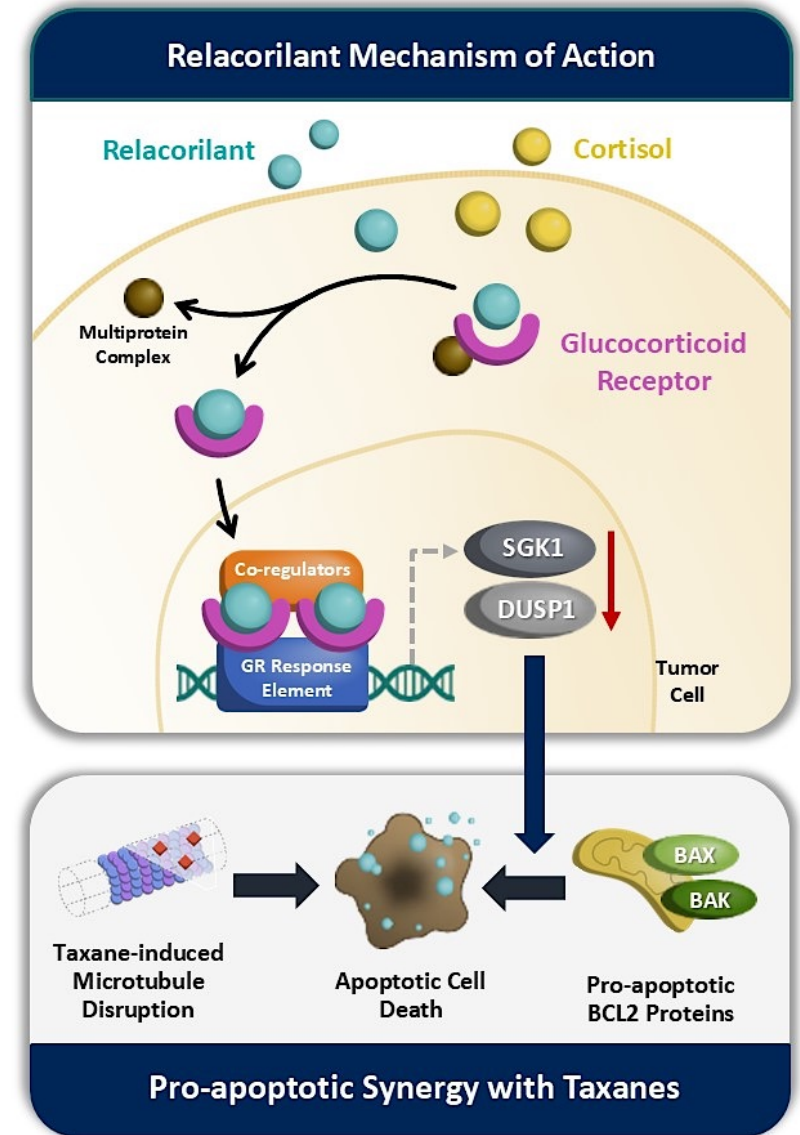
Findings from these prior analyses will be presented in a Presidential Symposium at the upcoming European Society for Medical Oncology (ESMO) Congress 2025.”

- Update on PARP Inhibitors
- Novel Antibody Drug Conjugates
- Immunotherapy in Recurrent Disease
- **Inhibiting the Glucocorticoid Receptor**

Background

- Patients with platinum-resistant ovarian cancer have an overall survival of ~1 year and need new treatments¹
- Ovarian cancers express the glucocorticoid receptor (GR), a marker of poor prognosis²
- GR signaling reduces sensitivity to chemotherapy^{3,4}
- Relacorilant is a novel, selective GR antagonist (SGRA) that restores the sensitivity of cancers to cytotoxic chemotherapy^{3,5,6}

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

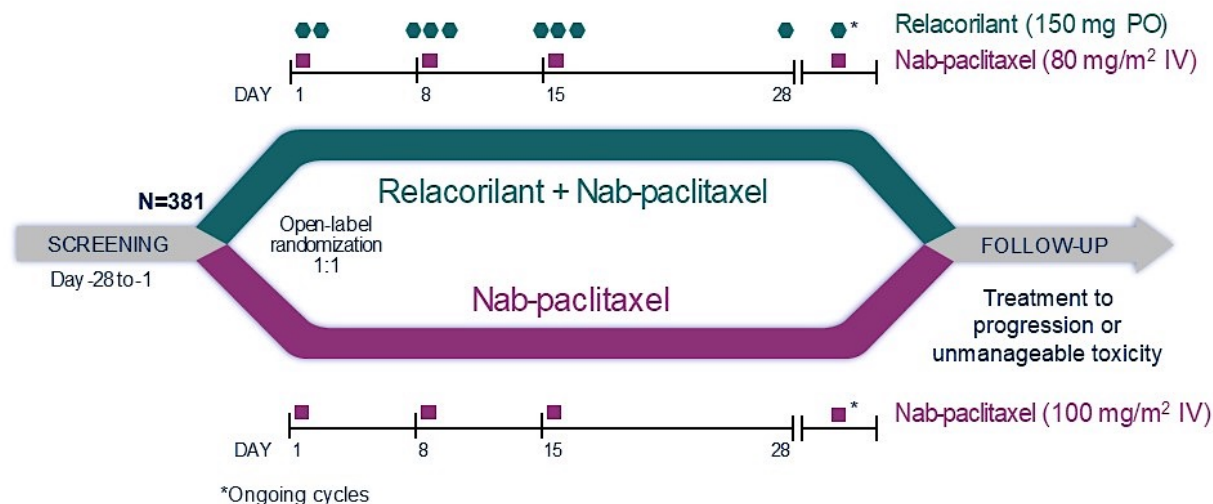


ROSELLA | Study Schema

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

Secondary Endpoints

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

First patient enrolled: 5th January 2023

Last patient enrolled: 8th April 2024

Data cutoff: 24th February 2025

Conducted at 117 sites in 14 countries.

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; PFS, progression-free survival; PO, by mouth; RECIST, Response Evaluation Criteria in Solid Tumors.

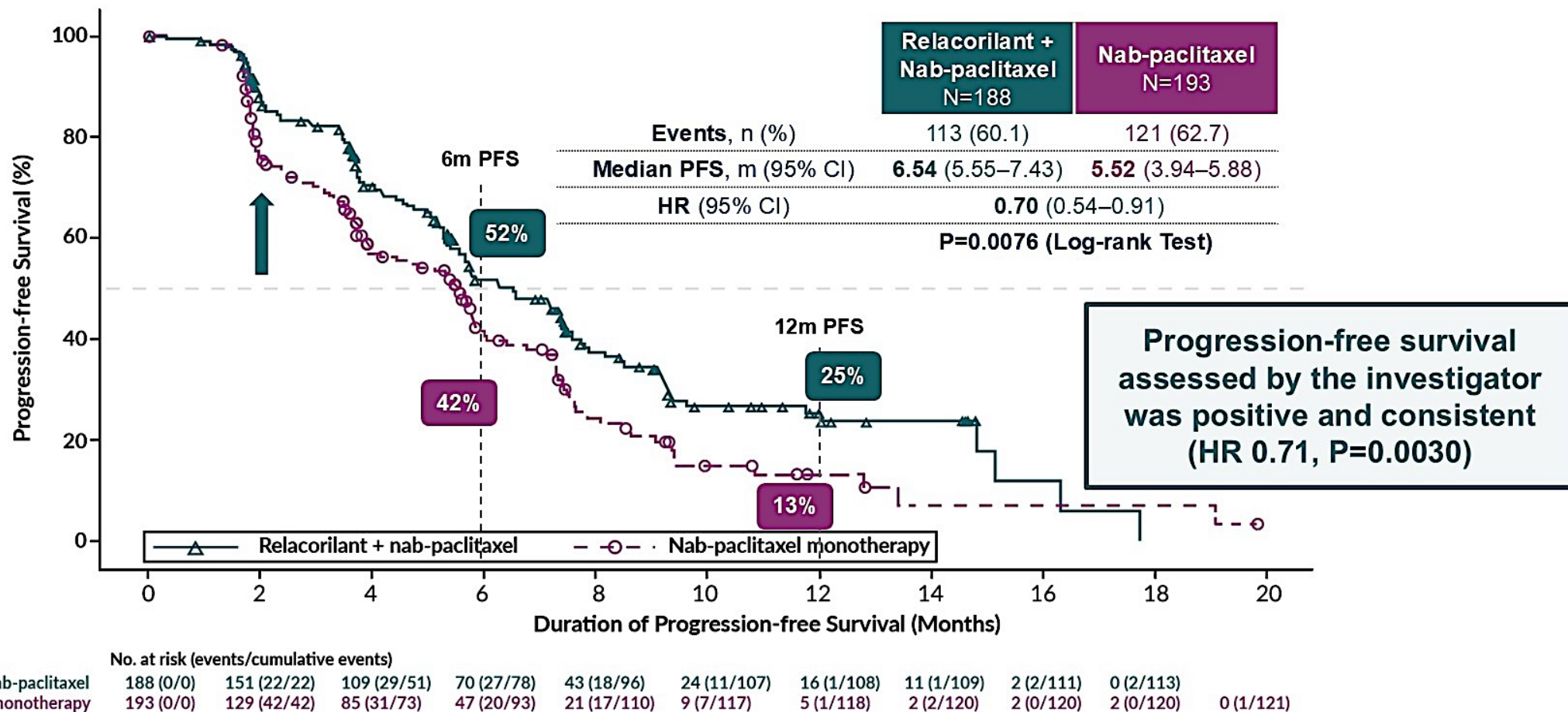
ROSELLA | Baseline Characteristics Were Well Balanced ⁸

		Relacorilant + Nab-paclitaxel (N=188)	Nab-paclitaxel (N=193)
Age, median (range), years		61 (26–85)	62 (33–86)
Race, n (%)	White	136 (72.3)	135 (69.9)
	Black or African-American	3 (1.6)	2 (1.0)
	Asian (92% Korean)	22 (11.7)	26 (13.5)
	Other / Not Reported	27 (14.4)	30 (15.5)
Ethnicity, n (%)	Hispanic	16 (8.5)	17 (8.8)
Region	North America	45 (23.9)	45 (23.3)
	Europe	107 (56.9)	109 (56.5)
	Korea, Australia, and Latin America	36 (19.1)	39 (20.2)
ECOG Performance Status, n (%) [*]	1 or 2	53 (28.2)	63 (32.6)
BRCA1/2 Mutation, n (%)	Yes	23 (12.2)	24 (12.4)
Prior Lines of Therapy, n (%)	1	15 (8.0)	18 (9.3)
	2	92 (48.9)	89 (46.1)
	3	81 (43.1)	86 (44.6)
Primary Platinum Refractory, n (%) [†]	Yes	13 (6.9)	13 (6.7)
Prior Lines of Therapy in the Platinum-resistant Setting, n (%)	≥1	67 (35.6)	82 (42.5)
Prior Taxane in the Platinum-resistant Setting, n (%)	Yes	8 (4.3)	7 (3.6)
Prior Therapies, n (%)	Bevacizumab	188 (100)	193 (100)
	Taxanes	187 (99.5)	192 (99.5)
	Pegylated Liposomal Doxorubicin	121 (64.4)	125 (64.8)
	PARP Inhibitor	114 (60.6)	120 (62.2)

^{*}In the nab-paclitaxel monotherapy arm, 1 patient had an ECOG performance status of 2. [†]Progressed within 3 months of the last dose of platinum from their first line platinum regimen. 97% of patients had high-grade serous carcinoma; 8 patients had high-grade endometrioid carcinoma and 2 patients had carcinosarcoma. BRCA, Breast Cancer Gene; ECOG, Eastern Cooperative Oncology Group.

Data cutoff: Feb 24, 2025

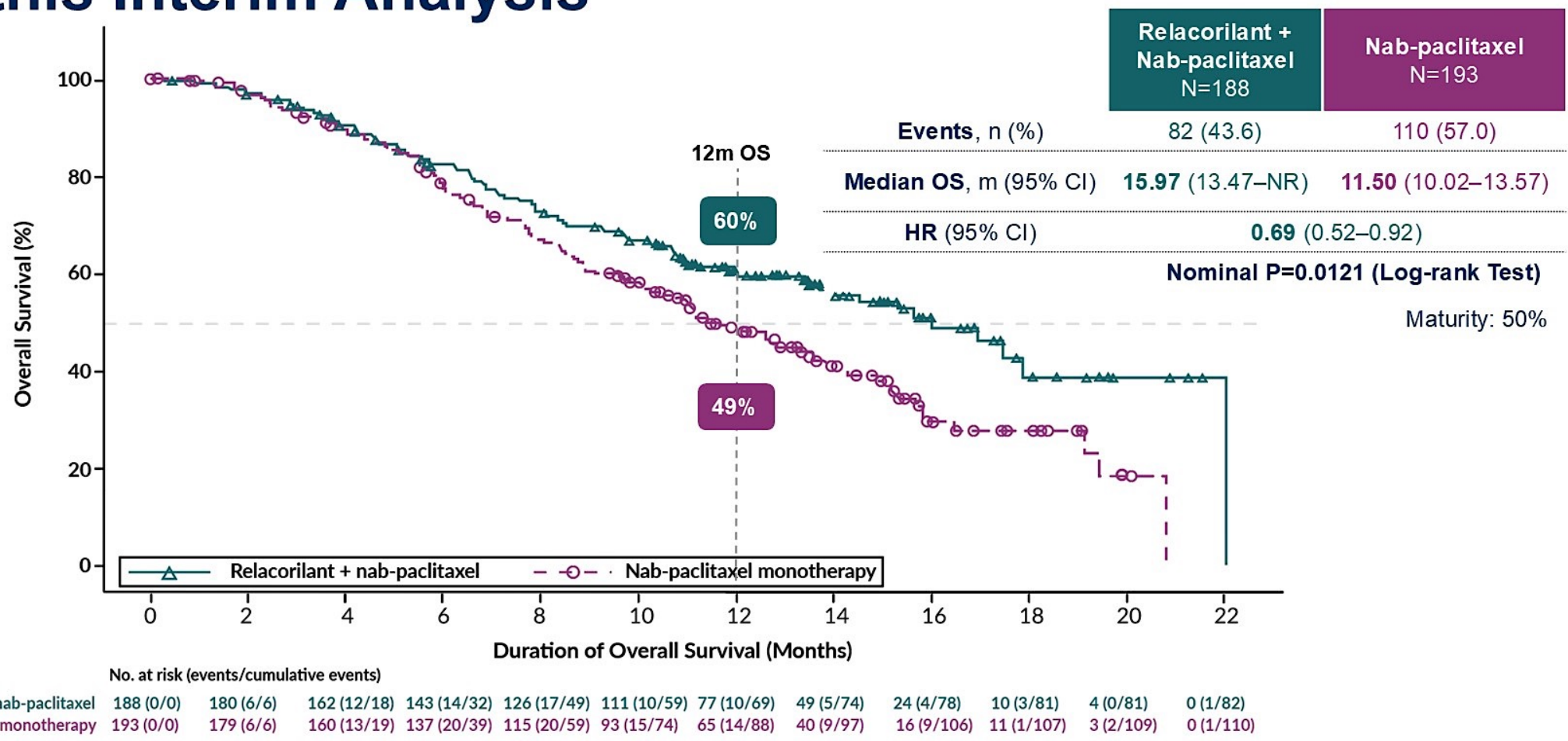
ROSELLA | Relacorilant Significantly Improved Progression-Free Survival Assessed by Blinded Review



Median follow-up time: 9.0 months; statistical significance threshold: $P \leq 0.04$. 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. BICR, blinded-independent central review; CI, confidence interval; HR, hazard ratio; m, months; PFS, progression-free survival.

Data cutoff: Feb 24, 2025

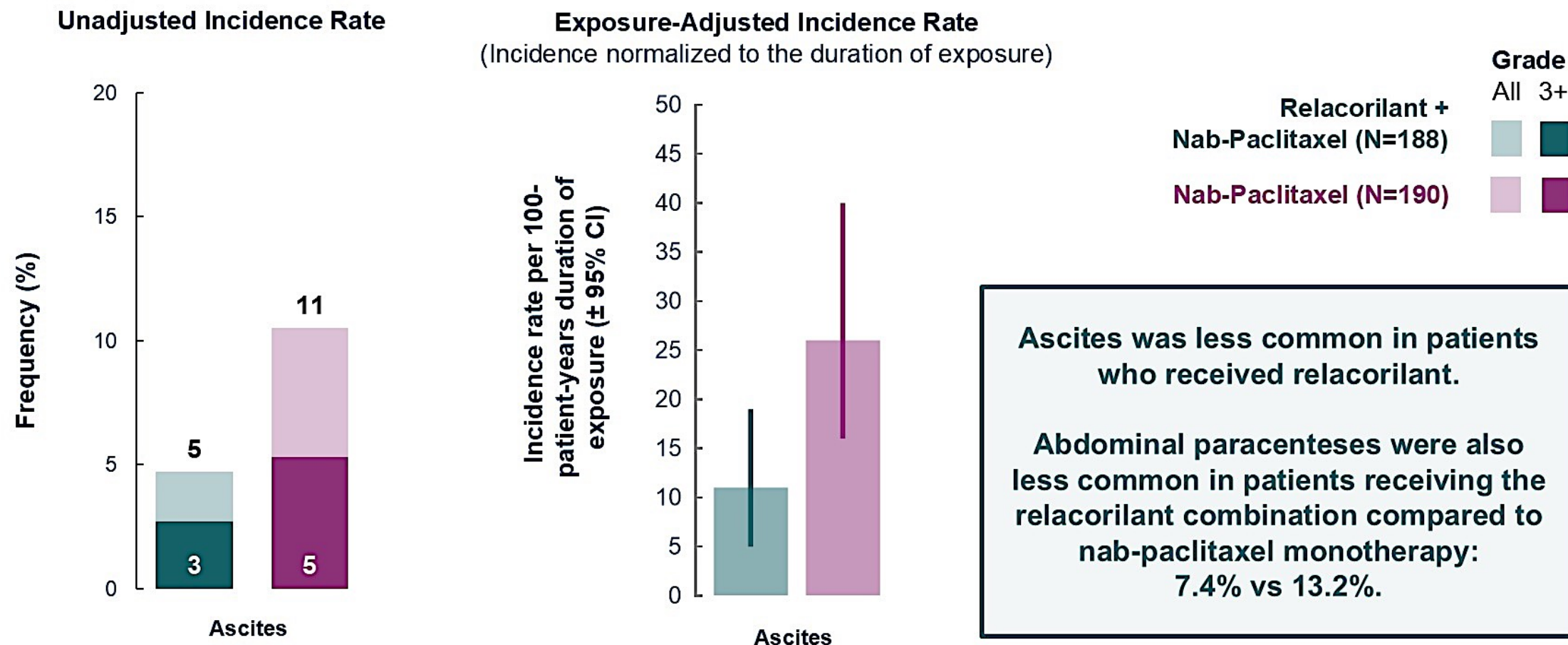
ROSELLA | Relacorilant Improved Overall Survival at this Interim Analysis



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

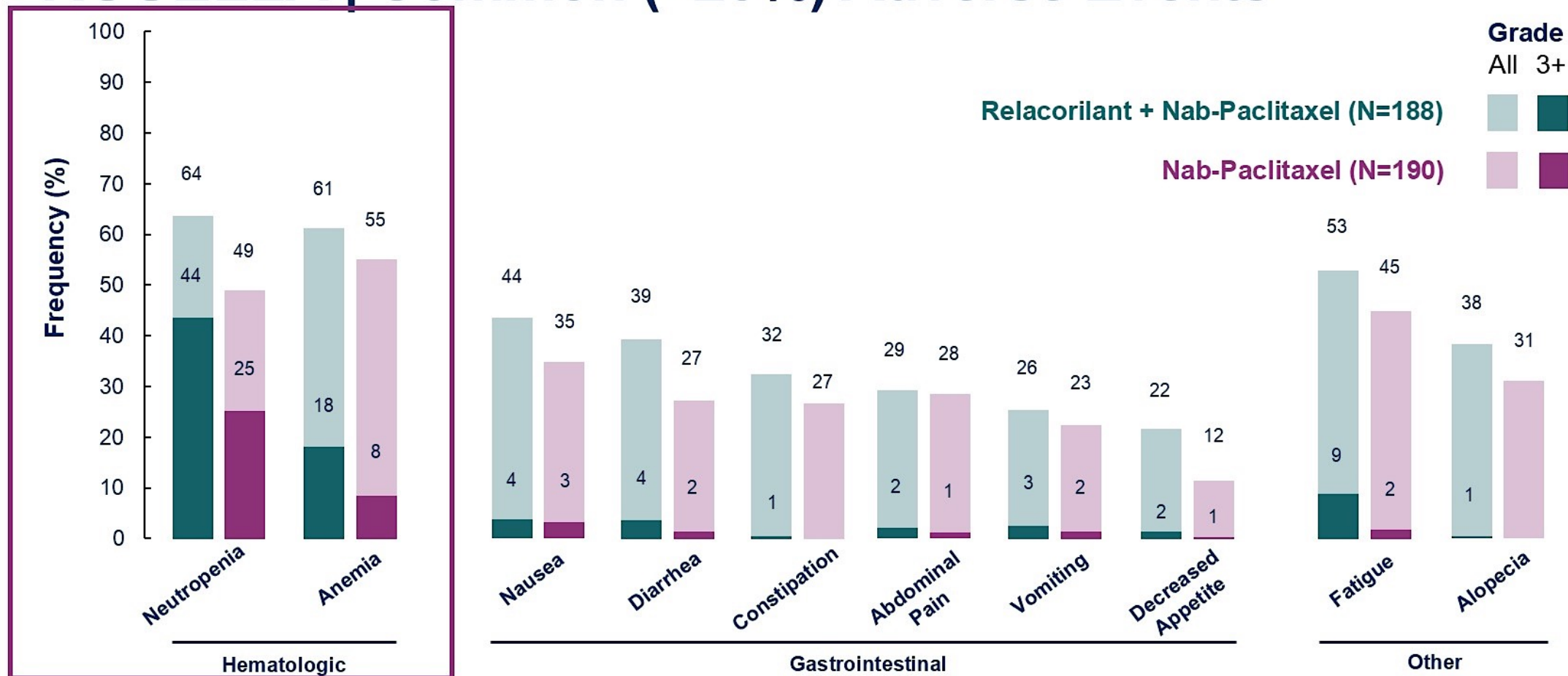
Data cutoff: Feb 24, 2025

ROSELLA | Lower Incidence of Ascites with Relacorilant + Nab-paclitaxel



Data cutoff: Feb 24, 2025

ROSELLA | Common (>20%) Adverse Events



Peripheral neuropathy occurred with similar frequency in both arms (19.1% and 17.4%).

5 SAEs of febrile neutropenia were reported, 4 (2.1%) with relacorilant + nab-paclitaxel and 1 (0.5%) with nab-paclitaxel monotherapy.

5 SAEs of sepsis were reported, 3 (1.6%) with relacorilant + nab-paclitaxel and 2 (1.1%) with nab-paclitaxel monotherapy.

TEAEs that occurred in >20% of patients. Assessed in the safety population of patients who received at least one dose of study drug, N=378. Combined terms are presented for neutropenia (neutropenia, reduced neutrophil count, and febrile neutropenia), anemia (anemia, reduced hemoglobin, and reduced red blood cell count) and fatigue (fatigue and asthenia). SAEs, serious adverse events; TEAEs, treatment-emergent adverse events.

Data cutoff: Feb 24, 2025

Case Presentation: 56-year-old woman with ovarian cancer; PALB2 germline mutation



Dr Brian Mulherin (Indianapolis, Indiana)

QUESTIONS FOR THE FACULTY

How do you decide whether to start with neoadjuvant chemotherapy or proceed straight to primary debulking surgery for patients with newly diagnosed advanced ovarian cancer?

QUESTIONS FOR THE FACULTY

A 65-year-old woman with OC undergoes R0 resection and receives adjuvant carboplatin/paclitaxel with good response. What would you most likely recommend as maintenance therapy if genetic testing revealed a germline PALB2 mutation?

Under what circumstances, if any, are you recommending PARP inhibitor maintenance to a patient with homologous recombination-proficient OC?

QUESTIONS FOR THE FACULTY

In addition to evaluating germline and somatic HRD mutations, what other actionable biomarkers, if any, do you test for in the adjuvant setting (eg, FR-alpha)?

Case Presentation: 61-year-old woman with Stage IVB fallopian tube carcinoma; BRCA2 germline mutation



Dr Jennifer Yannucci (Savannah, Georgia)

QUESTIONS FOR THE FACULTY

In general, when administering olaparib maintenance, do you stop after 2 years? What about maintenance niraparib? Is using ctDNA, in addition to imaging, to determine how long to administer PARP inhibitor maintenance a reasonable approach?

QUESTIONS FOR THE FACULTY

What do you quote patients in terms of the risk of AML/MDS associated with PARP inhibitor therapy? Does this risk increase with longer exposure?

QUESTIONS FOR THE FACULTY

For patients who receive PARP inhibitor maintenance and progress, are there situations in which you will rechallenge with a PARP inhibitor?

Case Presentation: 64-year-old woman with ovarian cancer and BRCA2 somatic mutation who develops cytopenias on maintenance olaparib



Dr Zanetta Lamar (Naples, Florida)

QUESTIONS FOR THE FACULTY

Is there any way to anticipate which patients receiving a PARP inhibitor will experience cytopenias? In general, how do you manage PARP inhibitor-associated cytopenias? How far can you dose-reduce without impacting efficacy?

QUESTIONS FOR THE FACULTY

Given the recent ESMO presentation of findings from the KEYNOTE-B96 trial, are you attempting to access pembrolizumab/chemotherapy for your patients with platinum-resistant recurrent PD-L1-positive OC? Do you think this strategy will soon be relevant for all patients with platinum-resistant disease?

QUESTIONS FOR THE FACULTY

What is the mechanism of action of relacorilant? What is the rationale for combining this agent with *nab* paclitaxel? What are the primary toxicities associated with this agent?

If both pembrolizumab/chemotherapy and relacorilant/*nab* paclitaxel become available, how do you think you will likely sequence them for platinum-resistant OC?

Case Presentation: 72-year-old woman with HER2 IHC 2+, ER-expressing, FOLR1-positive ovarian cancer



Dr Sean Warsch (Asheville, North Carolina)

QUESTIONS FOR THE FACULTY

In general, for a patient with FR α -positive, HER2-positive (IHC 3+) recurrent ovarian cancer, would you recommend mirvetuximab soravtansine or trastuzumab deruxtecan (T-DXd) first?

Are you typically sticking with the FDA indication or will you employ T-DXd for a patient with HER2 IHC2+ ovarian cancer? In general, in which line of therapy do you administer T-DXd?

QUESTIONS FOR THE FACULTY

What other novel antibody-drug conjugates (ADCs) are you excited about for patients with advanced ovarian cancer?

Given what we currently know about raludotatug deruxtecan, would you like to have access to it at the current time? If so, for which types of patients would you like to employ it? What are the primary toxicities associated with this ADC?

Integrating New Advances into the Care of Patients with Cancer

**A Multitumor Symposium in Partnership
with the American Oncology Network**

CME/MOC, NCPD and ACPE Accredited

**Saturday, November 8, 2025
10:00 AM – 3:00 PM CT**

Up Next ...

**Dr Manish A Shah discusses
the management of gastroesophageal cancers**