Subgroup analysis of tumor response with raludotatug deruxtecan (R-DXd) by number and type of prior therapy in patients with platinum-resistant ovarian cancer in the Phase 2 part of REJOICE-Ovarian01

P06-21

Isabelle Ray-Coquard,[1] Kosei Hasegawa,[2] Giuseppe Caruso,[3] Jung-Yun Lee,[4] Anna Nohejlovà Medkovà,[5] Xiaohua Wu,[6] Sabrina Chiara Cecere,[7] Peng-Hui Wang,[8] Lubomir Bodnar,[9] Sally Baron-Hay,[10] Cyriac Blonz,[11] Mayu Yunokawa,[12] Luis Manso Sánchez,[13] Sook-hee Hong,[14] Maria Cristina Petrella,[15] Connor Mailley,[16] Madan Gopal Kundu,[16] Karin Yamada,[17] Antoine Angelergues,[18] Lydia Gaba[19]

[1]Centre Léon Bérard, University Claude Bernard, and GINECO, Lyon, France; [2]Saitama Medical University International Medical Center, Hidaka, Saitama, Japan; [3]European Institute of Oncology IRCCS, Milan, Italy; [4]Yonsei Cancer Center and Severance Hospital, Yonsei University College of Medicine, Seoul, Republic of Korea; [5]Second Faculty of Medicine, Charles University and Motol University Hospital, Prague, Czech Republic; [6]Fudan University Shanghai Cancer Center, Shanghai, China; [7]Istituto Nazionale Tumori IRCCS Fondazione G. Pascale, Naples, Italy; [8]Taipei Veterans General Hospital, Taipei, Taiwan; [9]University of Siedlce, Siedlce, Poland and PGOG; [10]Genesis Care North Shore, St Leonards, NSW, Australia; [11]Hôpital Privé du Confluent, and GINECO, Nantes, France; [12]The Cancer Institute Hospital of The Japanese Foundation of Cancer Research, Tokyo, Japan; [13]Hospital Universitario 12 de Octubre, and GEICO, Madrid, Spain; [14]Seoul St. Mary's Hospital, The Catholic University of Korea, Seoul, Republic of Korea; [15]Azienda Universitaria Ospedaliera Careggi, Firenze, Italy; [16]Daiichi Sankyo, Inc., Basking Ridge, NJ, USA; [17]Merck & Co., Inc., Rahway, NJ, USA; [18]Groupe Hospitalier Diaconesses Croix Saint-Simon, and GINECO, Paris, France; [19]Hospital Clinic, and GEICO, Barcelona, Spain.

OBJECTIVES

- This is a subgroup analysis of patients with platinum-resistant OC treated with R-DXd 4.8–6.4 mg/kg in the Phase 2 dose-optimization part of REJOICE-Ovarian01. It evaluates whether tumor response is affected by prior therapy, including number of prior LOTs, prior bevacizumab, prior PARPi, time to progression on/after prior PARPi, and last platinum-free interval

CONCLUSIONS

- In this subgroup analysis of the Phase 2 dose-optimization part of the REJOICE-Ovarian01 study, R-DXd 4.8–6.4 mg/kg demonstrated clinically meaningful activity regardless of prior treatment
- Minor numerical differences in ORR were observed according to the number of prior LOTs, prior treatment (bevacizumab and PARPi), and prior response to therapy (last platinum-free interval and time to progression on/after prior PARPi)
- PFS and OS data are immature; therefore, longer follow-up will be required to evaluate any association between prior therapy and PFS and/or OS
- The safety profile of R-DXd was similar and manageable regardless of the number of prior LOTs, and no new safety signals were identified
  - Four patients (3.7%) had adjudicated treatment-related ILD, including one Grade 3 event (0.9%)
- The ongoing Phase 3 part of the REJOICE-Ovarian01 trial is evaluating R-DXd 5.6 mg/kg versus treatment of physician's choice in patients with platinum-resistant OC

INTRODUCTION

- Patients with platinum-resistant OC often receive multiple prior therapies, leading to cumulative toxicity and acquired resistance which may reduce the tolerability and efficacy of subsequent treatment regimens[1,2]; as such, these patients have poor clinical outcomes and a high unmet need[3,4]
- Standard-of-care non-platinum chemotherapy ± bevacizumab provides only modest benefit (median OS, 10–17 months)[3,5,6]
- The FRα-directed ADC mirvetuximab soravtansine has improved outcomes; however, only approximately one-third of patients are eligible[7–9]
- Raludotatug deruxtecan (R-DXd) is a CDH6-directed ADC comprising a humanized anti-CDH6 IgG1 mAb, linked to a topoisomerase I inhibitor payload via a tetrapeptide-based cleavable linker[10,11]
- In the Phase 2 dose-optimization part of the ongoing Phase 2/3 REJOICE-Ovarian01 trial (data cutoff: February 26, 2025), R-DXd 4.8, 5.6, and 6.4 mg/kg Q3W demonstrated promising efficacy and a manageable safety profile in patients with platinum-resistant OC[12]
  - The confirmed ORR with R-DXd 4.8–6.4 mg/kg was 50.5%, including three confirmed CRs (2.8%)[12]
  - Overall, 94% of patients had positive tumor cell membrane expression of CDH6 at any intensity
- Here, we report a subgroup analysis of efficacy and safety according to prior therapy, in patients in the Phase 2 dose-optimization part of REJOICE-Ovarian01 who had a follow-up of ≥18 weeks or discontinued treatment

METHODS

- REJOICE-Ovarian01 (NCT06161025) is a Phase 2/3 global, multicenter, randomized, open-label study of R-DXd in patients with platinum-resistant, high-grade serous or high-grade endometrioid ovarian, primary peritoneal, or fallopian tube cancer who have received 1–3 prior LOTs (**Figure 1**)
- This analysis evaluated tumor response by prior therapy subgroup in patients included in the Phase 2 dose-optimization part of REJOICE-Ovarian01 who had a follow-up of ≥18 weeks or discontinued treatment
  - Subgroups include number of prior LOTs, prior bevacizumab, prior PARPi, time to progression on/after prior PARPi, and last platinum-free interval
  - Prior bevacizumab and PARPi exposure were defined as any treatment received before randomization at any LOT. Patients may have received bevacizumab or PARPi in multiple prior LOTs; however, prior exposure was counted only once per patient
  - Last platinum-free interval was defined as the time from completion of the last dose of PBC to disease progression

RESULTS

Patient characteristics and treatment exposure

- At the February 26, 2025, data cutoff, 108 patients had been randomized to receive R-DXd doses of 4.8, 5.6, or 6.4 mg/kg, of whom 107 patients had received R-DXd 4.8–6.4 mg/kg and were included in the dose-optimization analysis set (**Table 1**)
- Among patients in the dose-optimization analysis set, the median number of prior LOTs was 3; 10 patients (9.3%) had received 1 prior line, 42 (39.3%) had received 2 prior lines, and 55 (51.4%) had received 3 prior lines
- Overall, 89 (83.2%) patients received prior bevacizumab, and 75 (70.1%) received prior PARPi (of these, 86.7% had progressed within ≤30 days of the last PARPi dose); 47 (43.9%) patients had a last platinum-free interval of <3 months
- At the data cutoff, across the three doses, the median duration on study treatment was 5.5 months (range, 0.7–9.7) and median follow-up was 5.4 months (95% CI, 5.0–5.8)

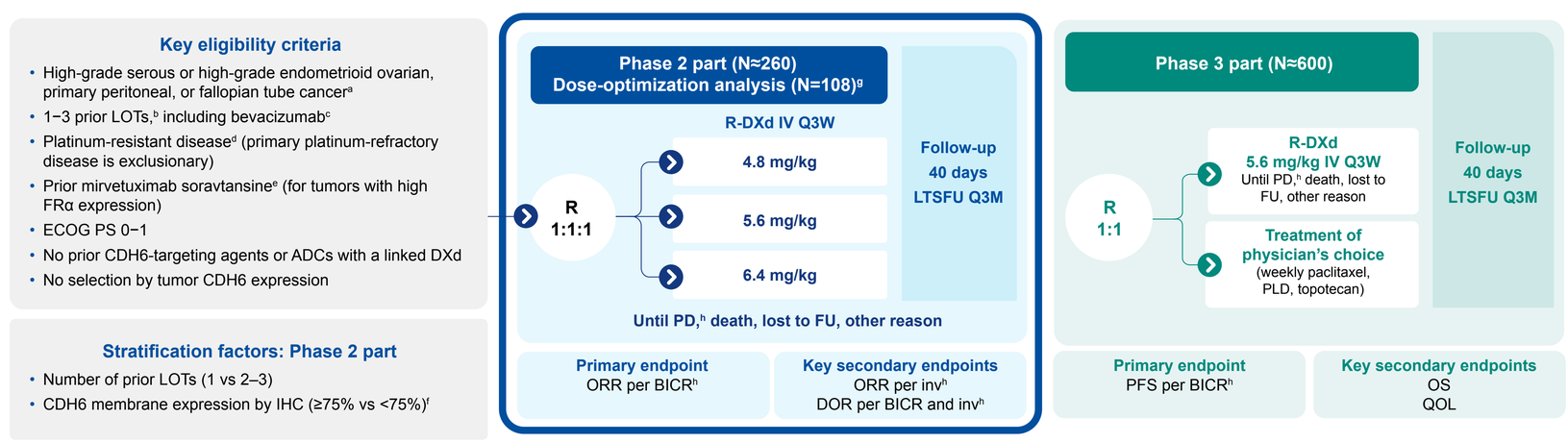
Tumor response by prior therapy

- Clinically meaningful tumor responses were observed across all prior therapy subgroups (**Figure 2**)
- The confirmed ORR by number of prior LOTs was 50.0% (95% CI, 18.7–81.3) in patients with 1 prior line, 59.5% (95% CI, 43.3–74.4) in those with 2 prior lines, and 43.6% (95% CI, 30.3–57.7) in those with 3 prior lines (**Table 2**)
- The observed TTRs were mostly similar across subgroups, including by number of prior LOTs, patients with/without prior bevacizumab, and patients with progression ≤30 or >30 days after prior PARPi

Safety signals by prior therapy

- No major differences were observed in adverse events according to number of prior LOTs (**Figure 3**)
- Grade ≥3 TEAEs, any-grade and Grade ≥3 treatment-related TEAEs, and SAEs were more numerically frequent in patients who had received prior bevacizumab or prior PARPi versus those who had not, and in patients with a last platinum-free interval of <3 months versus 3–6 months. SAEs were also more frequent in patients with progression ≤30 days versus >30 days after prior PARPi
- Four patients (3.7%) overall had adjudicated treatment-related ILD, including one Grade 3 event (0.9%)

Figure 1: REJOICE-Ovarian01 study design (NCT06161025)[13]



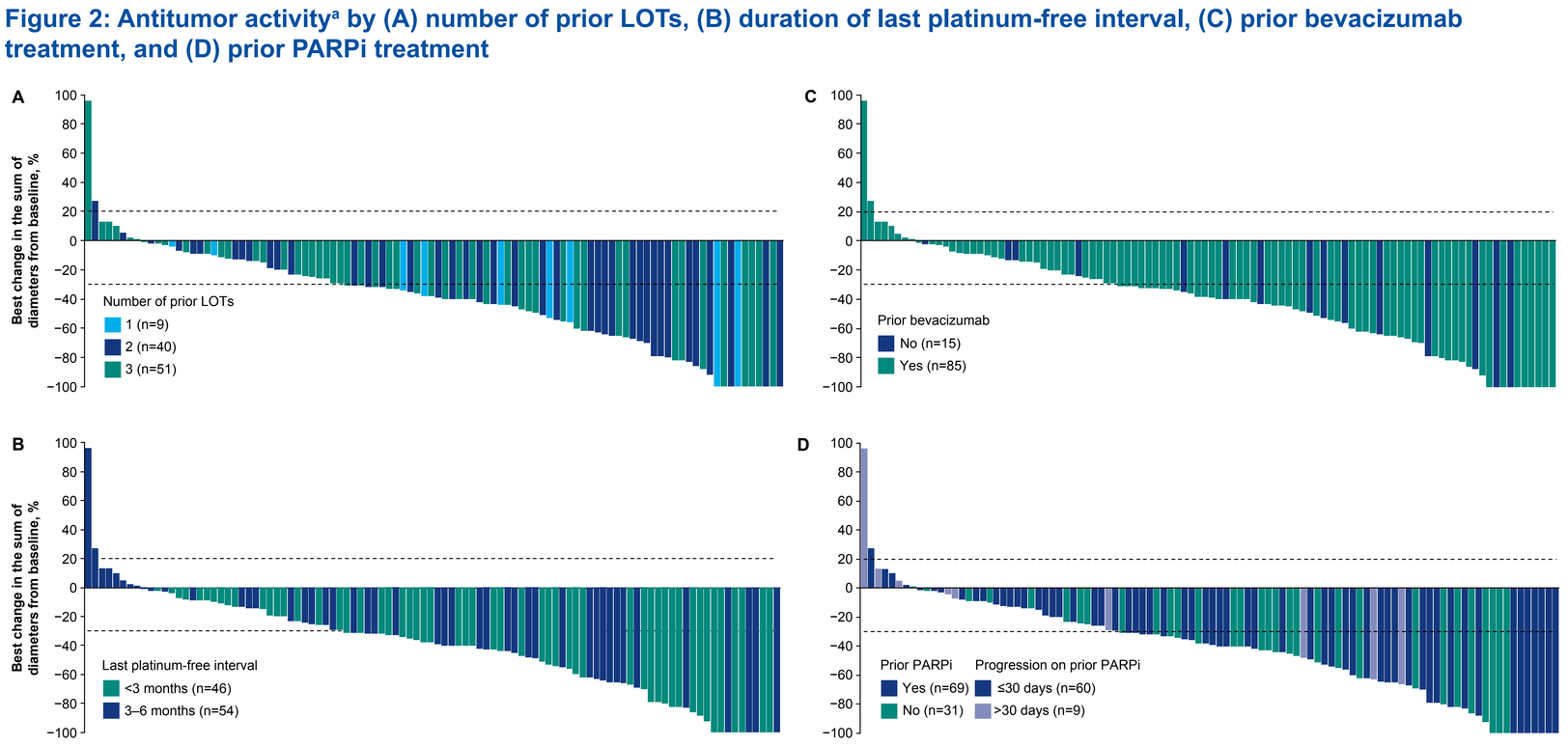
[a]Patients must have ≥1 lesion not previously irradiated and amenable to biopsy; must consent to provide a pretreatment biopsy and, in Phase 2 only, an on-treatment biopsy tissue sample and have ≥1 measurable lesion per RECIST 1.1. [b]In the Phase 3 part, patients with 1–4 prior LOTs will be eligible. [c]Unless ineligible. [d]Defined 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. [e]Unless ineligible, not approved, or not available locally. [f]A 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.[14] [g]Overall, 108 patients were randomized to receive R-DXd. One patient did not receive treatment, so 107 patients were treated and were included in the dose-optimization analysis set. [h]Per RECIST 1.1.

Table 1: Baseline characteristics of patient subgroups included in the dose-optimization analysis set (N=107)

	Number of prior LOTs			Last platinum-free interval		Prior bevacizumab		Prior PARPi		Progression on/after prior PARPi	
	1 (n=10)	2 (n=42)	3 (n=55)	<3 months (n=47)	3–6 months (n=60)	Yes (n=89)	No (n=18)	Yes (n=75)	No (n=32)	≤30 days (n=65)	>30 days (n=10)
ECOG PS, n (%)											
0	5 (50.0)	26 (61.9)	30 (54.5)	25 (53.2)	36 (60.0)	49 (55.1)	12 (66.7)	42 (56.0)	19 (59.4)	38 (58.5)	4 (40.0)
1	5 (50.0)	16 (38.1)	25 (45.5)	22 (46.8)	24 (40.0)	40 (44.9)	6 (33.3)	33 (44.0)	13 (40.6)	27 (41.5)	6 (60.0)
Number of prior LOTs											
1	10 (100)	0	0	0	10 (16.7)	6 (6.7)	4 (22.2)	4 (5.3)	6 (18.8)	3 (4.6)	1 (10.0)
2	0	42 (100)	0	21 (44.7)	21 (35.0)	35 (39.3)	7 (38.9)	29 (38.7)	13 (40.6)	25 (38.5)	4 (40.0)
3	0	0	55 (100)	26 (55.3)	29 (48.3)	48 (53.9)	7 (38.9)	42 (56.0)	13 (40.6)	37 (56.9)	5 (50.0)
Prior therapy											
Bevacizumab	6 (60.0)	35 (83.3)	48 (87.3)	39 (83.0)	50 (83.3)	89 (100)	0	62 (82.7)	27 (84.4)	52 (80.0)	10 (100)
PARPi	4 (40.0)	29 (69.0)	42 (76.4)	34 (72.3)	41 (68.3)	62 (69.7)	13 (72.2)	75 (100)	0	65 (100)	10 (100)
Mirvetuximab soravtansine	0	0	3 (5.5)	1 (2.1)	2 (3.3)	2 (2.2)	1 (5.6)	2 (2.7)	1 (3.1)	2 (3.1)	0
Last platinum-free interval											
<3 months	0	21 (50.0)	26 (47.3)	47 (100)	0	39 (43.8)	8 (44.4)	34 (45.3)	13 (40.6)	27 (41.5)	7 (70.0)
3–6 months	10 (100)	21 (50.0)	29 (52.7)	0	60 (100)	50 (56.2)	10 (55.6)	41 (54.7)	19 (59.4)	38 (58.5)	3 (30.0)
CDH6 membrane positivity at any intensity at baseline,[a] n (%)	9 (90.0)	39 (92.9)	47 (85.5)	40 (85.1)	55 (91.7)	80 (89.9)	15 (83.3)	68 (90.7)	27 (84.4)	60 (92.3)	8 (80.0)

[a]Tumor CDH6 positivity was defined as the percentage of viable tumor cells showing CDH6 membrane staining at any intensity (1+/2+/3+), as determined by the CDH6 clinical trial assay (SP450; Roche Diagnostics). The denominator was the overall population, which included tumor samples of insufficient quality for assessment (n=6).

Figure 2: Antitumor activity[a] by (A) number of prior LOTs, (B) duration of last platinum-free interval, (C) prior bevacizumab treatment, and (D) prior PARPi treatment

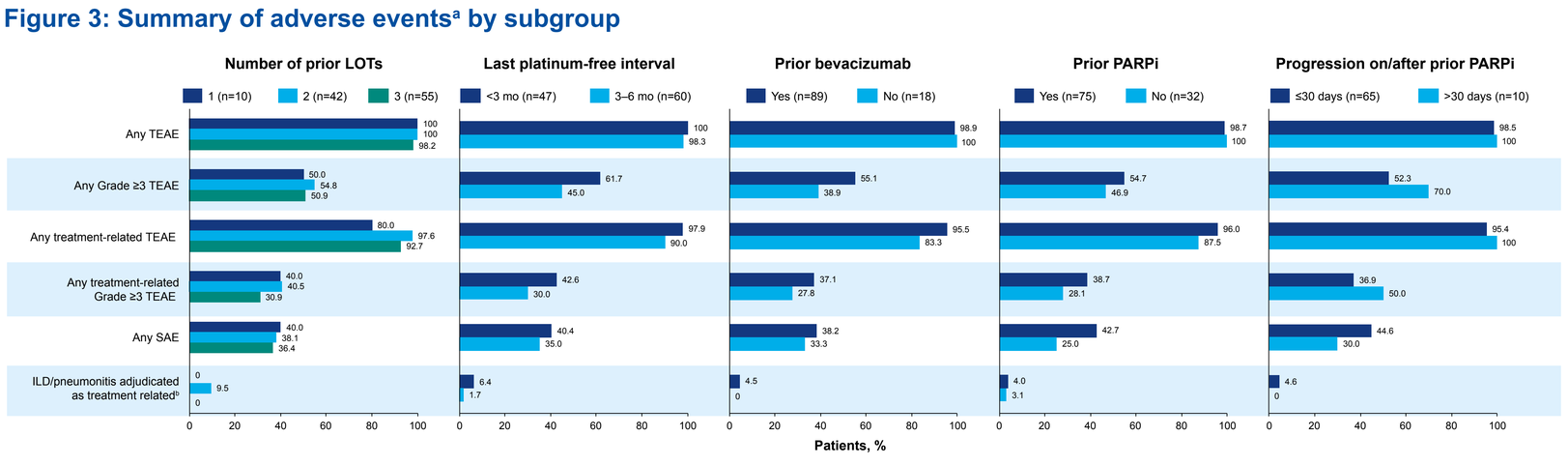


[a]Only patients with measurable disease at baseline and ≥1 post-baseline tumor scan (both by BICR) were included (n=100). Six patients had no measurable baseline disease, and one had no adequate post-baseline assessment.

Table 2: Summary of tumor responses by number, type, and response to prior therapy

	Number of prior LOTs			Last platinum-free interval		Prior bevacizumab		Prior PARPi		Progression on/after prior PARPi	
Confirmed response by BICR per RECIST 1.1	1 (n=10)	2 (n=42)	3 (n=55)	<3 months (n=47)	3–6 months (n=60)	Yes (n=89)	No (n=18)	Yes (n=75)	No (n=32)	≤30 days (n=65)	>30 days (n=10)
BOR, n (%)											
CR	0	1 (2.4)	2 (3.6)	2 (4.3)	1 (1.7)	2 (2.2)	1 (5.6)	2 (2.7)	1 (3.1)	2 (3.1)	0
PR	5 (50.0)	24 (57.1)	22 (40.0)	21 (44.7)	30 (50.0)	41 (46.1)	10 (55.6)	31 (41.3)	20 (62.5)	28 (43.1)	3 (30.0)
SD	4 (40.0)	10 (23.8)	28 (50.9)	18 (38.3)	24 (40.0)	37 (41.6)	5 (27.8)	32 (42.7)	10 (31.3)	29 (44.6)	3 (30.0)
PD	0	5 (11.9)	3 (5.5)	6 (12.8)	2 (3.3)	7 (7.9)	1 (5.6)	8 (10.7)	0	5 (7.7)	3 (30.0)
Not evaluable	1 (10.0)	2 (4.8)	0	0	3 (5.0)	2 (2.2)	1 (5.6)	2 (2.7)	1 (3.1)	1 (1.5)	1 (10.0)
ORR, %, (95% CI)	50.0 (18.7–81.3)	59.5 (43.3–74.4)	43.6 (30.3–57.7)	48.9 (34.1–63.9)	51.7 (38.4–64.8)	48.3 (37.6–59.2)	61.1 (35.7–82.7)	44.0 (32.5–55.9)	65.6 (46.8–81.4)	46.2 (33.7–59.0)	30.0 (6.7–65.2)
Median TTR, weeks, (range)	7.0 (5.4–13.0)	6.3 (5.1–19.1)	9.2 (5.4–18.0)	6.3 (5.4–19.1)	10.9 (5.1–19.1)	7.1 (5.1–19.1)	7.0 (5.4–18.7)	7.0 (5.3–19.1)	11.3 (5.1–19.1)	7.0 (5.3–19.1)	6.1 (6.0–12.1)

Figure 3: Summary of adverse events[a] by subgroup



[a]TEAEs were graded according to Common Terminology Criteria for Adverse Events, version 5.0 criteria. [b]ILD/pneumonitis events were adjudicated by an independent ILD adjudication committee.

REFERENCES

1. Fotopoulou C. *EJC Suppl*. 2014;12:13–16.
2. Havasi A, et al. *Medicina (Kaunas)*. 2023;59:544.
3. González-Martín A, et al. *Ann Oncol*. 2023;34:833–848.
4. Richardson DL, et al. *JAMA Oncol*. 2023;9:851–859.
5. Colombo N, et al. *Ann Oncol*. 2025;36(Suppl S2). Abstract LBA3.
6. Pujade-Lauraine E, et al. *J Clin Oncol*. 2014;32:1302–1308.
7. Matulonis UA, et al. *J Clin Oncol*. 2023;41:2436–2445.
8. Moore KN, et al. *NEJM*. 2023;389:2162–2174. (Suppl)
9. ELAHERE® Prescribing Information. Revised July 2025. Available at: https://www.rxabbvie.com/pdf/elahere_pi.pdf. Accessed January 28, 2026.
10. Suzuki H, et al. *Mol Cancer Ther*. 2024;23:257–271.
11. Nakada T, et al. *Chem Pharm Bull (Tokyo)*. 2019;67:173–185.
12. Ray-Coquard IL, et al. Oral presentation at the European Society for Medical Oncology congress. October 17–21, 2025; Berlin, Germany. Presentation LBA42.
13. ClinicalTrials.gov. https://clinicaltrials.gov/study/NCT06161025. Accessed January 26, 2025.
14. 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.

ABBREVIATIONS

ADC, antibody–drug conjugate; **BICR**, blinded independent central review; **BOR**, best overall response; **CDH6**, cadherin 6; **CI**, confidence interval; **CR**, complete response; **DOR**, duration of response; **ECOG PS**, Eastern Cooperative Oncology Group performance status; **FRα**, folate receptor alpha; **FU**, follow-up; **IgG1**, immunoglobulin G1; **IHC**, immunohistochemistry; **ILD**, interstitial lung disease; **inv**, investigator; **IV**, intravenous; **LOT**, line of therapy; **LTSFU**, long-term survival follow-up; **mAb**, monoclonal antibody; **mo**, months; **OC**, ovarian cancer; **ORR**, objective response rate; **OS**, overall survival; **PARPi**, poly (ADP-ribose) polymerase inhibitor; **PBC**, platinum-based chemotherapy; **PD**, progressive disease; **PFS**, progression free survival; **PLD**, pegylated liposomal doxorubicin; **PR**, partial response; **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; **SAE**, serious adverse event; **SD**, stable disease; **TEAE**, treatment-emergent adverse event; **TTR**, time to response.

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isabelle.ray-coquard@lyon.unicancer.fr