SINGAPORE 2025 ESMO ASIA

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

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December 05, 2025

Presentation number: #1668

Declaration of interests

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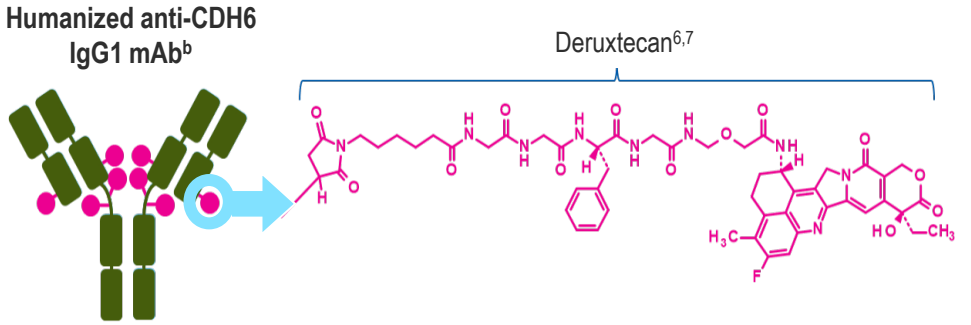
- **Grants:** AbbVie, Advenchen, Ascendis Pharma, Alkermes, AstraZeneca, Beigene, BerGenBio, BMS, CanariaBio, Corcept, Cellid, CKD, Clovis Oncology, Daiichi Sankyo, Eisai, Genmab, Genemedicine, GII, GSK, ImmunoGen, Janssen, Kelun, Merck, Mersana, MSD, Novartis, Onconic Therapeutics, ONO, Regeneron, Roche, Seagen, Sutro, Synthon, TORL BioTherapeutics, Takeda, Zymeworks
- **Consulting fees:** AbbVie, AstraZeneca, CanariaBio, Daiichi Sankyo, Eisai, Genmab , GII, ImmunoGen, Merck, MSD, Seagen, Sutro, Regeneron
- **Honoraria:** AbbVie, AstraZeneca, Daiichi Sankyo, Eisai, MSD, Takeda

Background

- Platinum-resistant OC is associated with poor outcomes[1,2]; standard of care is single-agent non-platinum chemotherapy, which provides only a modest benefit; ORR is 10–15% and median OS is 10–12 months[1]
- Expression of CDH6 is observed in up to 94% of epithelial OC tumors[3–5]
- Raludotatug deruxtecan (R-DXd) is a CDH6-directed ADC comprising a humanized anti-CDH6 IgG1 mAb, covalently linked to a TOPO I inhibitor payload via a tetrapeptide-based cleavable linker[6,7]
- In the primary analysis of the dose-optimization part of REJOICE-Ovarian01, patients with platinum-resistant OC[a] received R-DXd at doses of 4.8, 5.6, or 6.4 mg/kg IV Q3W. Across doses, 50.5% achieved a confirmed objective response[3]

R-DXd was designed with 7 key attributes:



1	Payload mechanism of action: TOPO I inhibitor[7,c]
2	High potency of payload[6,7,c]
3	High drug-to-antibody ratio of ≈8[6,c]
4	Payload with short systemic half-life[7,c,d]
5	Plasma-stable linker-payload[6,7,c]
6	Tumor-selective cleavable linker[6,7,c]
7	Bystander antitumor effect[6,c]

[a]Defined as TFIp <6 months. [b]Image is for illustrative purposes only; actual drug positions may vary. [c]The clinical relevance of these features is under investigation. [d]On the basis of animal data.
ADC, antibody–drug conjugate; CDH6, cadherin 6; DXd, exatecan derivative; IgG1, immunoglobulin G1; IV, intravenous; mAb, monoclonal antibody; OC, ovarian cancer; ORR, objective response rate; OS, overall survival; Q3W, every 3 weeks; TFIp, treatment-free interval from last platinum dose; TOPO I, topoisomerase I.
1. González-Martín A, et al. *Ann Oncol.* 2023;34:833–848. 2. Richardson DL, et al. *JAMA Oncol.* 2023;9:851–859; 3. Ray-Coquard I, et al. Oral presentation at the European Society for Medical Oncology Congress. October 17–21, 2025; Berlin, Germany. Presentation LBA42. 4. Shintani D, et al. Poster presentation at the European Society for Medical Oncology Congress. October 20–24, 2023; Madrid, Spain. Presentation 777P. 5. Suzuki H, et al Poster presentation at the European Society for Medical Oncology Congress. October 17–21, 2021; Virtual. Presentation #919. 6. Suzuki H, et al. *Mol Cancer Ther.* 2024;23:257–271. 7. Nakada T, et al. *Chem Pharm Bull (Tokyo).* 2019;67:173–185.

REJOICE-Ovarian01 study design

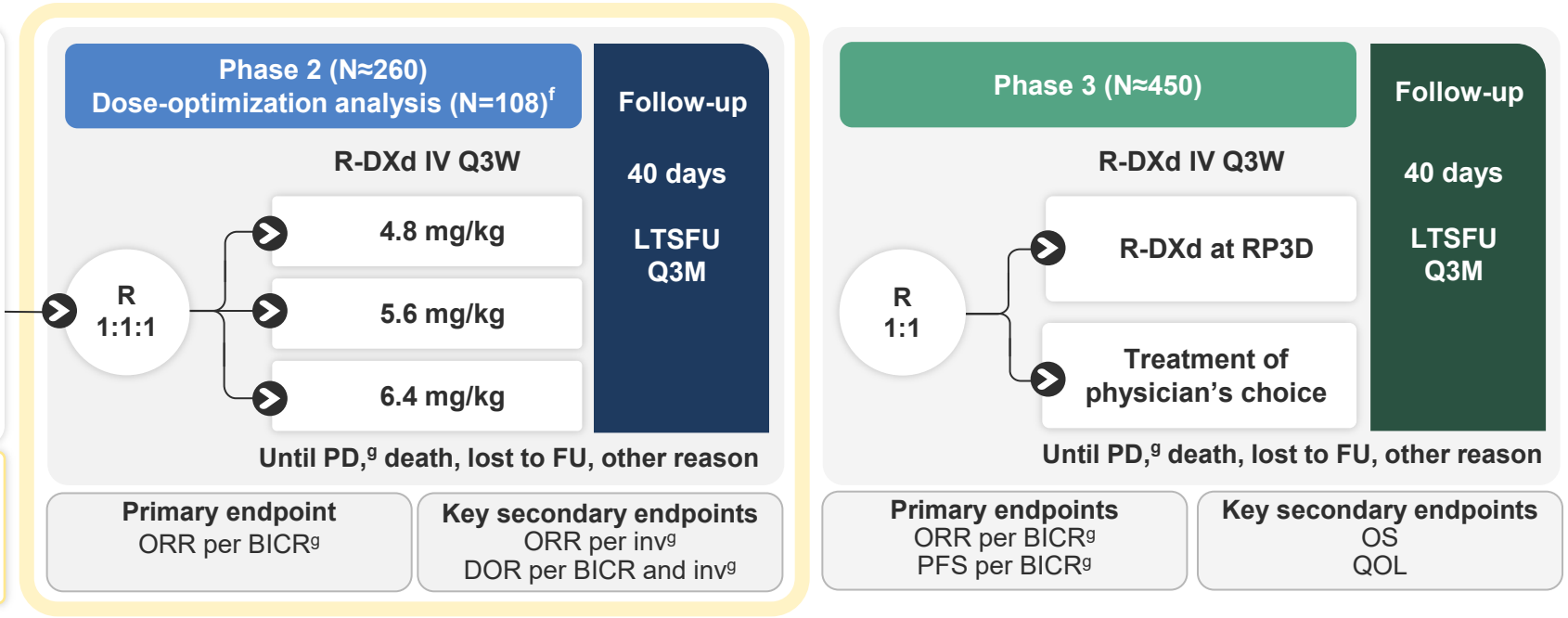
A Phase 2/3 multicenter, randomized study of R-DXd in patients with platinum-resistant, high-grade serous or endometrioid ovarian, primary peritoneal, or fallopian tube cancer[1–3]

Key eligibility criteria

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

Stratification factors

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



We present a subgroup analysis of Asian patients (n=45) included in the dose-optimization part of the Phase 2/3 REJOICE-Ovarian01 study, in patients with platinum-resistant OC who had a follow-up of ≥18 weeks or discontinued treatment

[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]Unless ineligible. [c]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. [d]Unless ineligible, not approved, or not available locally. [e]A stratification cutoff of 75% tumor cell membrane staining at any intensity was selected on the basis of the median observed percentage tumor cell membrane staining (at any intensity) in the Phase 1 study population.[4] [f]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 safety analysis set. [g]Per RECIST 1.1.

ADC, antibody–drug conjugate; BICR, blinded independent central review; CDH6, cadherin 6; DOR, duration of response; DXd, exatecan derivative; ECOG PS, Eastern Cooperative Oncology Group performance status; FRα, folate receptor alpha; FU, follow-up; IHC, immunohistochemistry; inv, investigator; IV, intravenous; LOT, lines of therapy; LTSFU, long-term survival follow-up; OC, ovarian cancer; ORR, objective response rate; OS, overall survival; PD, progressive disease; PFS, progression-free survival; 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; RP3D, recommended Phase 3 dose; 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 Annual Meeting; May 31–June 4, 2024; Chicago, IL, USA. Poster TPS5625. 3. Ray-Coquard I, et al. Oral presentation at the European Society for Medical Oncology Congress. October 17–21, 2025; Berlin, Germany. Presentation LBA42. 4. 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.

Baseline characteristics and prior systemic therapies

Patient and tumor characteristics	Asian subgroup R-DXd 4.8–6.4 mg/kg[a] n=45	Overall population R-DXd 4.8–6.4 mg/kg[a] N=107
Age, median (range), years	58 (34–80)	60 (34–81)
Age >70 years, n (%)	5 (11.1)	17 (15.9)
Region, n (%)		
Asia	45 (100)[b]	45 (42.1)
Europe	—	61 (57.0)
Australia	—	1 (0.9)
ECOG PS, n (%)		
0	30 (66.7)	61 (57.0)
1	15 (33.3)	46 (43.0)
Cancer type, n (%)		
Ovarian	34 (75.6)	91 (85.0)
Peritoneal	2 (4.4)	4 (3.7)
Fallopian tube	9 (20.0)	12 (11.2)
Tumor FIGO stage at initial diagnosis, n (%)		
I–II	5 (11.1)	11 (10.3)
III	21 (46.7)	53 (49.5)
IV	17 (37.8)	39 (36.4)
Unknown	2 (4.4)	4 (3.7)

Tumor characteristics and prior therapies	Asian subgroup R-DXd 4.8–6.4 mg/kg[a] n=45	Overall population R-DXd 4.8–6.4 mg/kg[a] N=107
Number of prior lines of systemic therapy, n (%)		
1	6 (13.3)	10 (9.3)
2	18 (40.0)	42 (39.3)
3	21 (46.7)	55 (51.4)
Received prior therapy, n (%)		
Bevacizumab	37 (82.2)	89 (83.2)
PARP inhibitor	33 (73.3)	75 (70.1)
Mirvetuximab soravtansine	2 (4.4)	3 (2.8)
Last platinum-free interval, n (%)		
<3 months	17 (37.8)	47 (43.9)
3–6 months	28 (62.2)	60 (56.1)
Tumor CDH6 membrane positivity at any intensity at baseline,[c] n (%)	n=42[d]	n=101[d]
Any positivity	**40 (95.2)**	**95 (94.1)**
<75% positive	21 (50.0)	41 (40.6)
≥75% positive[e]	21 (50.0)	60 (59.4)

Data cutoff: February 26, 2025. Study was initiated on February 27, 2024.

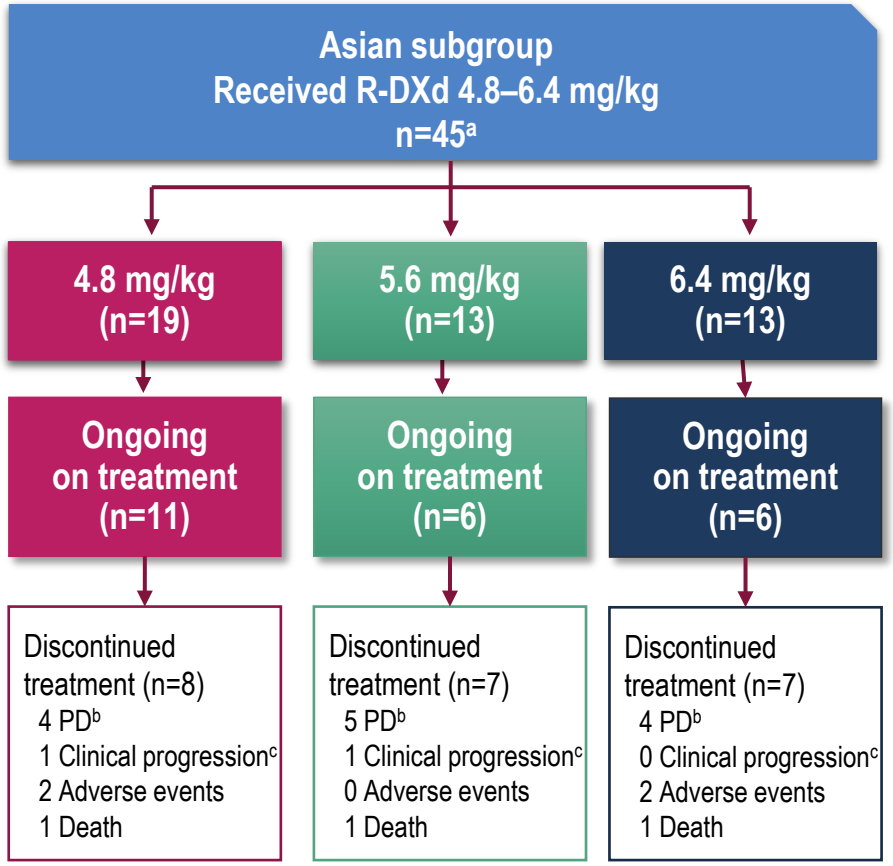
[a]Only patients treated with ≥1 dose were included in this analysis and made up the safety analysis cohort. [b]Asian patients were from China (n=8), Japan (n=18), Republic of Korea (n=17), and Taiwan (n=2). [c]Tumor CDH6 positivity was defined as the percentage of viable tumor cells positive for CDH6 membrane staining at any intensity (1+/2+/3+) determined by CDH6 clinical trial assay (SP450; Roche Diagnostics). [d]Three tumor samples in the Asian subgroup and 6 tumor samples in the overall population were of insufficient quality to determine CDH6 membrane positivity. [e]A stratification cutoff of 75% tumor cell membrane staining at any intensity was selected on the basis of the median observed percentage tumor cell membrane staining (at any intensity) in the Phase 1 study population.[1]

CDH6, cadherin 6; ECOG PS, Eastern Cooperative Oncology Group performance status; FIGO, Fédération Internationale de Gynécologie et d'Obstétrique; PARP, poly (adenosine diphosphate [ADP]-ribose) polymerase; R-DXd, raludotatug deruxtecan.

1. 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.

Patient disposition and treatment exposure

Data cutoff: February 26, 2025



	Asian subgroup R-DXd 4.8–6.4 mg/kg n=45[a]
Ongoing on study treatment, n (%)	23 (51.1)
Discontinued from study treatment, n (%)	22 (48.9)
PD[b]	13 (28.9)
Clinical progression[c]	2 (4.4)
Adverse events	4 (8.9)
Death	3 (6.7)
Duration on study treatment, median (range), months	5.1 (0.7–9.7)
Relative dose intensity,[d] %, median (range)	97.3 (67.2–108.0)

Patients included in the dose-optimization analysis had completed ≥18 weeks of follow-up or discontinued treatment due to an adverse event, PD, or death

The median follow-up for 4.8-mg/kg, 5.6-mg/kg, and 6.4-mg/kg cohorts was 6.3 months (95% CI, 4.5–6.7), 5.9 months (95% CI, 4.5–6.7), and 5.2 months (95% CI, 4.2–7.7), respectively.

[a]Only patients treated with ≥1 dose were included in this analysis and made up the safety analysis cohort. [b]Per RECIST 1.1. [c]Clinical progression was defined as definitive clinical signs of PD, but the most recent radiographic assessment did not meet the criteria for PD according to RECIST 1.1. [d]Relative dose intensity was defined as the administered dose intensity (mg/kg/cycle) expressed as a percentage of the planned dose intensity (mg/kg/cycle).

CI, confidence interval; PD, progressive disease; R-DXd, raludotatug deruxtecan; RECIST 1.1, Response Evaluation Criteria in Solid Tumours, version 1.1.

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

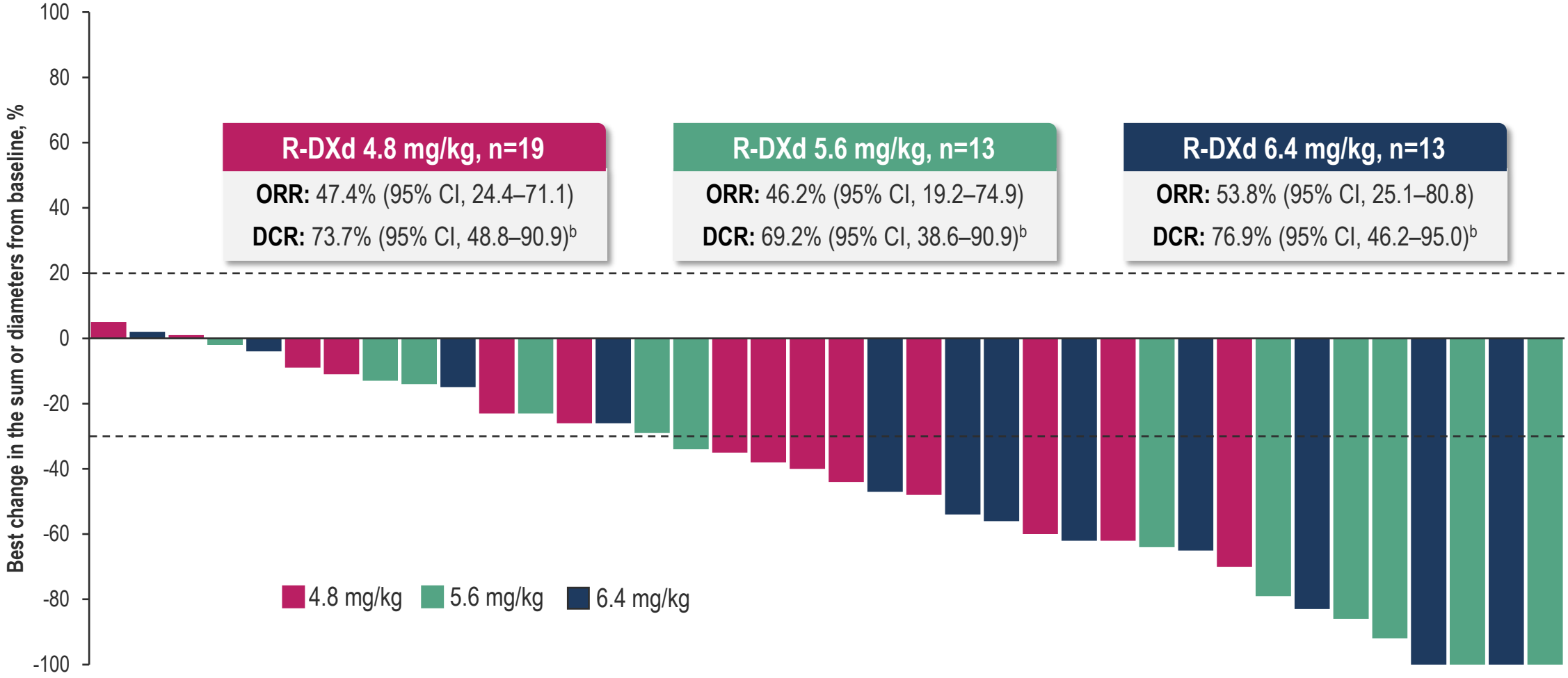
Confirmed response by BICR[a]	Asian subgroup by dose			Asian subgroup	Overall population
	R-DXd 4.8 mg/kg n=19	R-DXd 5.6 mg/kg n=13	R-DXd 6.4 mg/kg n=13	R-DXd 4.8–6.4 mg/kg n=45	R-DXd 4.8–6.4 mg/kg N=107
ORR, % (95% CI)	47.4 (24.4–71.1)	46.2 (19.2–74.9)	53.8 (25.1–80.8)	48.9 (33.7–64.2)	50.5 (40.6–60.3)
BOR,[b] n (%)					
CR	1 (5.3)	2 (15.4)	0	3 (6.7)	3 (2.8)
PR	8 (42.1)	4 (30.8)	7 (53.8)	19 (42.2)	51 (47.7)
SD	8 (42.1)	5 (38.5)	5 (38.5)	18 (40.0)	42 (39.3)
PD	1 (5.3)	1 (7.7)	0	2 (4.4)	8 (7.5)
Not evaluable	1 (5.3)[c]	1 (7.7)[d]	1 (7.7)[c]	3 (6.7)	3 (2.8)
DCR,[e] % (95% CI)	73.7 (48.8–90.9)	69.2 (38.6–90.9)	76.9 (46.2–95.0)	73.3 (58.1–85.4)	77.6 (68.5–85.1)
TTR, median (range), weeks	7.1 (5.7–18.7)	5.5 (5.1–12.7)	7.1 (5.3–13.0)	7.1 (5.1–18.7)	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 6.3 months (95% CI, 4.5–6.7), 5.9 months (95% CI, 4.5–6.7), and 5.2 months (95% CI, 4.2–7.7), respectively.

[a]Per RECIST 1.1. [b]BOR 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). [c]Patient had no baseline tumor assessment by BICR. [d]Patient had no adequate post-baseline tumor assessment by BICR. [e]DCR was defined as percentage of patients with BOR of CR, PR, or SD ≥77 days (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; R-DXd, raludotatug deruxtecan; 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 in Asian patients with platinum-resistant OC[a]

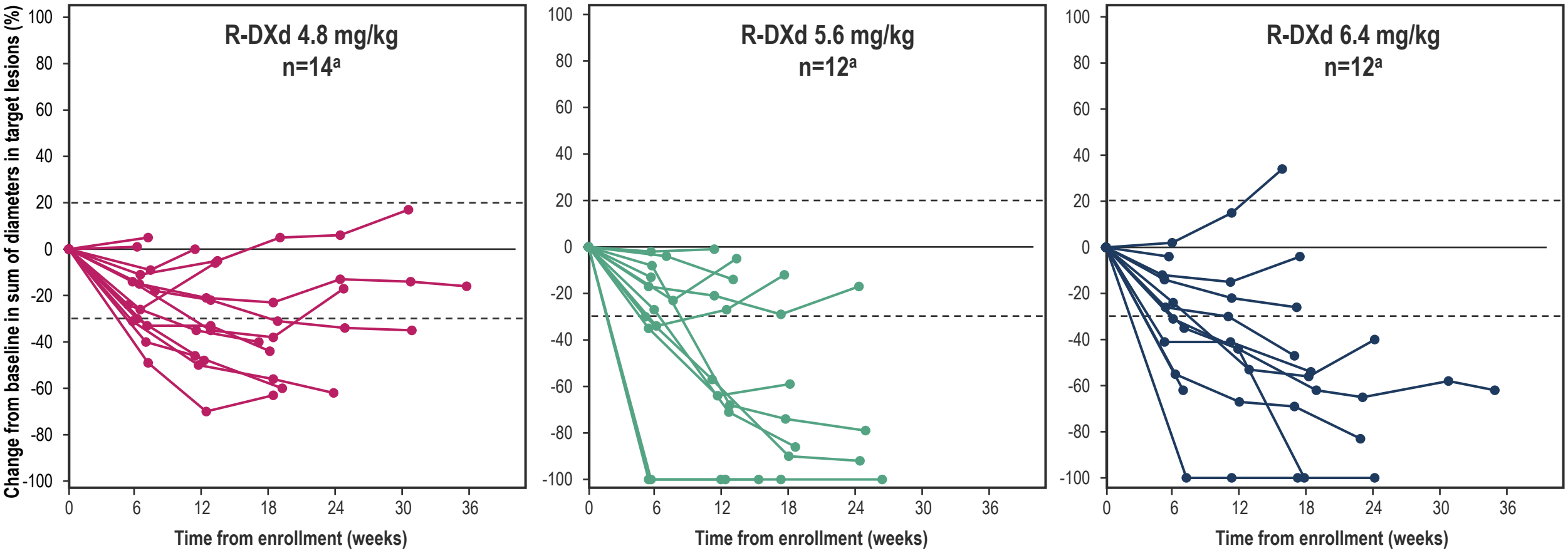


Data cutoff: February 26, 2025. The median follow-up for 4.8-mg/kg, 5.6-mg/kg, and 6.4-mg/kg cohorts was 6.3 months (95% CI, 4.5–6.7), 5.9 months (95% CI, 4.5–6.7), and 5.2 months (95% CI, 4.2–7.7), respectively.

[a]Antitumor response assessed by BICR per RECIST 1.1. Only patients with measurable disease at baseline and ≥1 post-baseline tumor scan, both by BICR, were included in the waterfall plot (n=38). Six patients (R-DXd 4.8 mg/kg [n=5]; 6.4 mg/kg [n=1]) did not have measurable disease at baseline, and 1 patient (R-DXd 5.6 mg/kg) had no adequate post-baseline tumor assessment. [b]DCR was defined as percentage of patients with BOR of CR, PR, or SD (per RECIST 1.1).

BICR, blinded independent central review; BOR, best overall response; CI, confidence interval; CR, complete response; DCR, disease control rate; ORR, objective response rate; PR, partial response; R-DXd, raludotatug deruxtecan; RECIST 1.1, Response Evaluation Criteria in Solid Tumours, version 1.1; SD, stable disease.

R-DXd treatment was associated with rapid responses at all doses in Asian patients



Median TTR[b]: 7.1 weeks (range, 5.7–18.7)

Median TTR[b]: 5.5 weeks (range, 5.1–12.7)

Median TTR[b]: 7.1 weeks (range, 5.3–13.0)

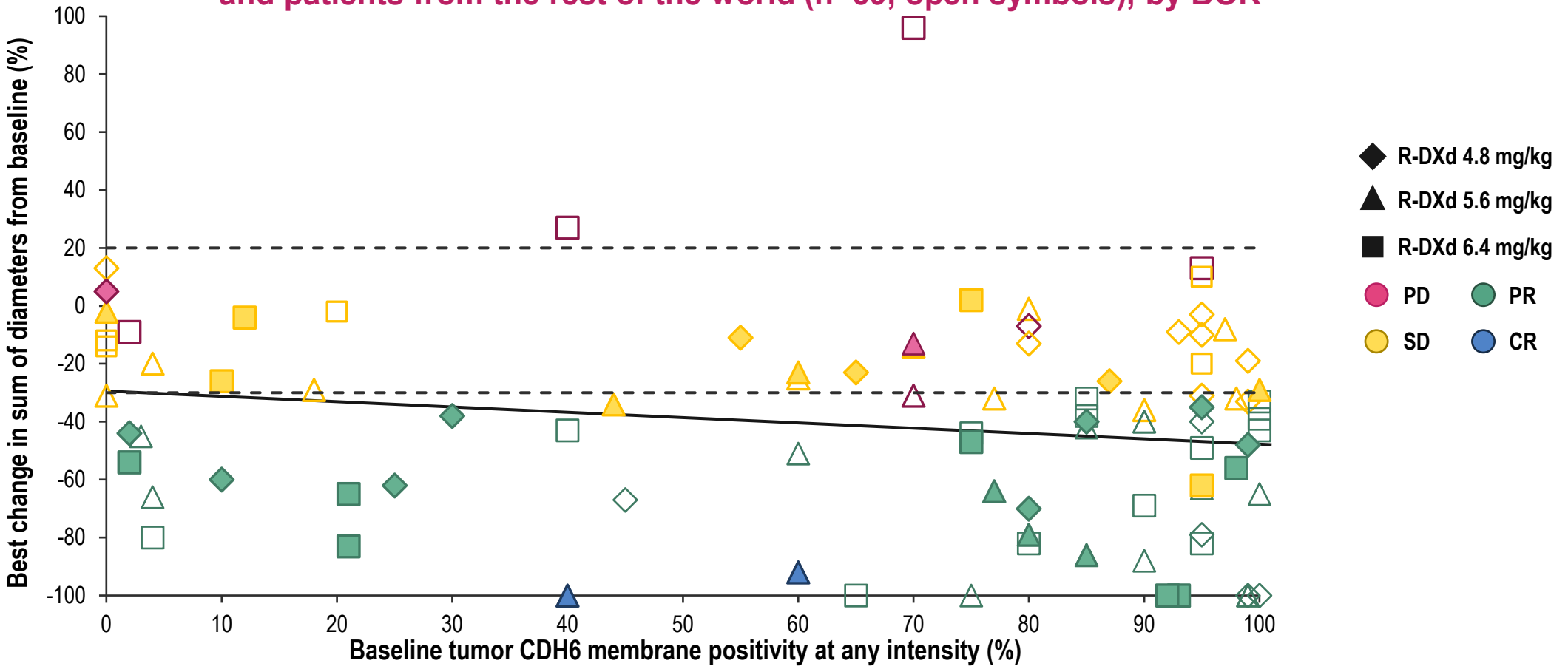
Data cutoff: February 26, 2025. The median follow-up for 4.8-mg/kg, 5.6-mg/kg, and 6.4-mg/kg cohorts was 6.3 months (95% CI, 4.5–6.7), 5.9 months (95% CI, 4.5–6.7), and 5.2 months (95% CI, 4.2–7.7), respectively.

[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=38). Six patients (R-DXd 4.8 mg/kg [n=5]; 6.4 mg/kg [n=1]) did not have measurable disease at baseline, and 1 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, 5.1–18.7).

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

Clinically meaningful tumor responses were observed across a range of CDH6 expression levels

CDH6 membrane positivity from patients in the Asian subgroup (n=35, filled symbols) and patients from the rest of the world (n=59, open symbols), by BOR[a,b]



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]Patients with available baseline tumor CDH6 expression data, who had measurable disease at baseline and ≥1 post-baseline tumor scan (assessed by BICR per RECIST 1.1). [b]Tumor CDH6 positivity was defined as the percentage of viable tumor cells positive for CDH6 membrane staining at any intensity (1+/2+/3+) determined by CDH6 clinical trial assay (SP450; Roche Diagnostics).

BICR, blinded independent central review; BOR, best overall response; CDH6, cadherin 6; CI, confidence interval; CR, complete response; PD, progressive disease; PR, partial response; RECIST 1.1, Response Evaluation Criteria in Solid Tumors, version 1.1; SD, stable disease.

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

	Asian subgroup				Overall population
	R-DXd 4.8 mg/kg n=19	R-DXd 5.6 mg/kg n=13	R-DXd 6.4 mg/kg n=13	R-DXd 4.8–6.4 mg/kg n=45	R-DXd 4.8–6.4 mg/kg N=107
Any TEAE, n (%)	18 (94.7)	13 (100)	13 (100)	44 (97.8)	106 (99.1)
Grade ≥3	9 (47.4)	9 (69.2)	9 (69.2)	27 (60.0)	56 (52.3)
Any TRAE, n (%)	16 (84.2)	12 (92.3)	13 (100)	41 (91.1)	100 (93.5)
Grade ≥3	6 (31.6)	6 (46.2)	6 (46.2)	18 (40.0)	38 (35.5)
Grade 5	0	0	0	0	0
Any SAE, n (%)	8 (42.1)	6 (46.2)	6 (46.2)	20 (44.4)	40 (37.4)
Grade ≥3	8 (42.1)	5 (38.5)	6 (46.2)	19 (42.2)	34 (31.8)
Grade 5	2 (10.5)[a]	1 (7.7)[b]	1 (7.7)[c]	4 (8.9)	6 (5.6)[d]
Any treatment-related SAE, n (%)	2 (10.5)	2 (15.4)	2 (15.4)	6 (13.3)	13 (12.1)
Grade ≥3	2 (10.5)	2 (15.4)	2 (15.4)	6 (13.3)	11 (10.3)
Grade 5	0	0	0	0	0
Dose modifications associated with TRAEs,[e] n (%)					
Drug discontinuation	2 (10.5)	0	1 (7.7)	3 (6.7)	6 (5.6)
Dose reduction	4 (21.1)	2 (15.4)	4 (30.8)	10 (22.2)	20 (18.7)
Dose delay	4 (21.1)	4 (30.8)	4 (30.8)	12 (26.7)	25 (23.4)
ILD/pneumonitis adjudicated as treatment related,[f] n (%)					
Any grade	1 (5.3)	0	1 (7.7)	2 (4.4)	4 (3.7)
Grade ≥3	1 (5.3)[g]	0	0	1 (2.2)[g]	1 (0.9)[g]
Grade 5	0	0	0	0	0

Dose reductions were more frequent with the 6.4-mg/kg dose in both the Asian subgroup and the overall population

Data cutoff: February 26, 2025. Reported safety events are defined using MedDRA Preferred Terms and CTCAE criteria.
[a]Grade 5 events were hepatic failure and ovarian cancer. [b]Grade 5 event was aspiration. [c]Grade 5 event was influenza infection. [d]Grade 5 events were hepatic failure, malignant neoplasm progression, aspiration and influenza infection (each n=1), and ovarian cancer (n=2). [e]Dose 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. [f]ILD/pneumonitis events were adjudicated by an independent ILD adjudication committee. [g]ILD/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; TRAE, treatment-related AE.

Most common TEAEs in Asian patients (≥10% across all doses)[a]

Data cutoff: February 26, 2025.

[a]TEAEs reported in ≥10% of all Asian patients who received R-DXd 4.8–6.4 mg/kg. Reported safety events are defined by MedDRA preferred terminology. [b]Grade 4 hematologic TEAEs reported at 4.8 mg/kg: neutrophil count decreased (n=1), platelet count decreased (n=1); at 5.6 mg/kg: neutrophil count decreased (n=2), platelet count decreased (n=1), leukocyte count decreased (n=2); at 6.4 mg/kg: neutrophil count decreased (n=3), platelet count decreased (n=1), lymphocyte count decreased (n=1). No Grade 5 hematologic TEAEs were reported at any dose. Grade 3 febrile neutropenia was reported in 2 patients, one each in the R-DXd 5.6-mg/kg and 6.4-mg/kg cohorts.

ALT, alanine aminotransferase; AST, aspartate aminotransferase; CTCAE, Common Terminology Criteria for Adverse Events; GGT, gamma-glutamyltransferase; Gr, grade; MedDRA, Medical Dictionary for Regulatory Activities; R-DXd, raludotatug deruxtecan; TEAE, treatment-emergent adverse event; WBC, white blood cell count.

Conclusions

- In this dose-optimization analysis, 45 Asian patients with platinum-resistant OC received R-DXd at doses of 4.8–6.4 mg/kg
  - In this Asian subgroup, 95.2% of tumors demonstrated positive CDH6 membrane expression by IHC
- After a minimum of 18 weeks of follow-up, R-DXd demonstrated promising efficacy across all evaluated doses in Asian patients, with responses similar to that observed in the overall population:
  - The confirmed ORR was 48.9%, including 3 CRs (6.7%)
  - In the Asian population (n=35), clinically meaningful tumor responses were observed across a range of CDH6 expression levels
  - Further follow-up is required to obtain mature data on DOR and PFS
- The safety profile of R-DXd in Asian patients appears to be manageable and is consistent with the safety profile observed in the overall population
  - One adjudicated treatment-related Grade ≥3 ILD event (Grade 3) was reported in this analysis
- On the basis of the efficacy and safety results observed in the Asian subgroup, which were consistent with those in the overall population, together with PK and ER data,[1] R-DXd 5.6 mg/kg provided a positive benefit–risk profile and was considered the optimal dose
- The Phase 3 part of the REJOICE-Ovarian01 study will evaluate R-DXd 5.6 mg/kg versus treatment of physician's choice in patients with platinum-resistant OC

Data cutoff: February 26, 2025.
CDH6, cadherin 6; CR, complete response; DOR, duration of response; ER, exposure–response; IHC, immunohistochemistry; ILD, interstitial lung disease; OC, ovarian cancer; ORR, objective response rate; PFS, progression-free survival; PK, pharmacokinetic; R-DXd, raludotatug deruxtecan.
1. Daiichi Sankyo, Inc. Data on file.

Acknowledgments

- We thank the patients, their families, and their caregivers for study participation, and the study staff for their contributions
- We thank all patients and investigators participating in this study from sites across China, Japan, Republic of Korea, and Taiwan, who contributed to the current analysis
- This study is sponsored by Daiichi Sankyo, Inc. In October 2023, Daiichi Sankyo entered into a global development and commercialization collaboration agreement with Merck Sharp & Dohme LLC, a subsidiary of Merck & Co., Inc., Rahway, NJ, USA (MSD) for raludotatug deruxtecan (R-DXd)
- Medical writing support was provided by Anna Atkinson, PhD, of BOLDSCIENCE Inc., and was funded by Daiichi Sankyo, Inc. Editorial support was provided in accordance with Good Publication Practice guidelines (https://www.ismpp.org/gpp-2022)