REJOICE-Ovarian01: Phase 2 dose-optimization subgroup analysis – R-DXd in Asian patients with platinum-resistant ovarian cancer

P118-12

Jung-Yun Lee,[1] Xiaohua Wu,[2,3] Peng-Hui Wang,[4] Kyung Hae Jung,[5] Isabelle Ray-Coquard,[6] Mayu Yunokawa,[7] Kenichi Harano,[8] Kazuki Sudo,[9] Yunong Gao,[10] Jianqing Zhu,[11] Akira Kikuchi,[12] Hidemichi Watari,[13] Connor Mailley,[14] Sandra Re,[14] Madan Gopal Kundu,[14] Tsvetomir Mitov,[15] Karin Yamada,[16] Kosei Hasegawa[17]

[1]Yonsei Cancer Center and Severance Hospital, Yonsei University College of Medicine, Seoul, Republic of Korea; [2]Fudan University Shanghai Cancer Center, Shanghai, China; [3]Shanghai Medical College, Fudan University, Shanghai, China; [4]Taipei Veterans General Hospital, Taipei, Taiwan; [5]Asan Medical Center, University of Ulsan College of Medicine, Seoul, Republic of Korea; [6]Centre Léon Bérard, University Claude Bernard, and GINECO, Lyon, France; [7]The Cancer Institute Hospital of the Japanese Foundation of Cancer Research, Tokyo, Japan; [8]National Cancer Center Hospital East, Kashiwa, Japan; [9]National Cancer Center Hospital, Tokyo, Japan; [10]Beijing Cancer Hospital, Beijing Institute for Cancer Research, Beijing, China; [11]Zhejiang Cancer Hospital, Hangzhou, China; [12]Niigata Cancer Center Hospital, Niigata, Japan; [13]Hokkaido University Hospital, Sapporo, Japan; [14]Daiichi Sankyo, Inc., Basking Ridge, NJ, USA; [15]Daiichi Sankyo, Ltd. Uxbridge, UK; [16]Merck & Co., Inc., Rahway, NJ, USA; [17]Saitama Medical University International Medical Center, Hidaka, Japan.

OBJECTIVE

- To report a subgroup analysis of Asian patients with platinum-resistant OC included in the Phase 2 dose-optimization part of the Phase 2/3 REJOICE-Ovarian01 study

CONCLUSIONS

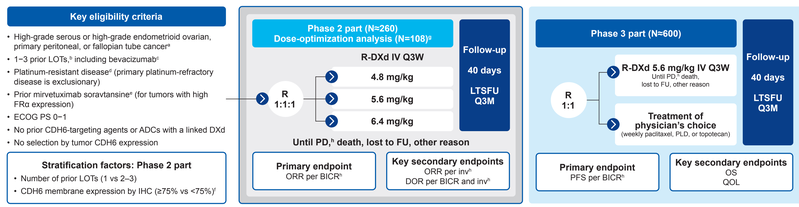
- In this dose-optimization analysis, 45 Asian patients with platinum-resistant OC received R-DXd at doses of 4.8–6.4 mg/kg
  - In the Asian subgroup, 95.2% of tumors demonstrated positive CDH6 membrane expression by IHC
- Baseline characteristics were consistent between Asian patients and the overall population
- 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[1]
  - 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 pharmacokinetics and exposure–response data,[2] R-DXd 5.6 mg/kg provided a positive benefit–risk profile and was considered the optimal dose
- The ongoing 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

INTRODUCTION

- Platinum-resistant OC is associated with poor outcomes.[3,4] Standard of care is single-agent non-platinum chemotherapy, which provides only a modest benefit; median OS is 10–12 months[3]
- Expression of CDH6 is observed in up to 94% of epithelial OC tumors[5–7]
- R-DXd is a CDH6-directed ADC comprising a humanized anti-CDH6 IgG1 mAb, covalently linked to a topoisomerase I inhibitor payload via a tetrapeptide-based cleavable linker[8]
- In the primary analysis of the dose-optimization part of REJOICE-Ovarian01, patients with platinum-resistant OC (defined as treatment-free interval from last platinum dose <6 months) 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[5]
- Here, we present a subgroup analysis of Asian patients included in the Phase 2 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 had discontinued treatment

METHODS

REJOICE-Ovarian01 study design (NCT06161025)[9]



[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 are eligible. [c]Unless ineligible. [d]Defined as 1 line of prior platinum therapy (24 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.[10] [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.

RESULTS

Patient baseline characteristics and treatment exposure

- At the February 26, 2025 data cutoff, 45 Asian patients had received R-DXd 4.8–6.4 mg/kg and were included in the Asian subgroup analysis (Japan, n=18; Republic of Korea, n=17; China, n=8; Taiwan, n=2) (**Table 1**)

Table 1: Baseline characteristics and prior systemic therapies

Patient 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
Age, median (range), years	58 (34–80)	60 (34–81)
Age >70 years, n (%)	5 (11.1)	17 (15.9)
ECOG PS, n (%)		
0	30 (66.7)	61 (57.0)
1	15 (33.3)	46 (43.0)
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[b]	n=42[c]	n=101[c]
Any positivity, n (%)	40 (95.2)	95 (94.1)

[a]Only patients treated with ≥1 dose were included in this analysis and made up the safety analysis cohort. [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). [c]Three tumor samples in the Asian subgroup and 6 tumor samples in the overall population were of insufficient quality to determine CDH6 membrane positivity.

- The median number of prior lines of therapy for Asian patients was 2 (range, 1–3)
- Overall, 37 (82.2%) Asian patients had received prior bevacizumab, 33 (73.3%) prior PARP inhibitor, and 2 (4.4%) prior mirvetuximab soravtansine
- Among 42 Asian patients with available baseline tumor CDH6 expression data, 40 (95.2%) had CDH6 membrane positivity at any intensity
- At the data cutoff, 23 (51.1%) Asian patients remained on study treatment and 22 (48.9%) patients had discontinued R-DXd, including 13 (28.9%) due to PD, 2 (4.4%) due to clinical progression, 4 (8.9%) due to adverse events, and 3 (6.7%) due to death
- The median duration on study treatment for Asian patients was 5.1 months (range, 0.7–9.7) and the median follow-up for the 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

Tumor response

- R-DXd monotherapy demonstrated promising antitumor activity at all doses in Asian patients with platinum-resistant OC (**Table 2**)
- Clinically meaningful tumor responses were seen irrespective of dose (**Figure 1**)
  - ORR was 47.4% (95% CI, 24.4–71.1) in the 4.8-mg/kg cohort, 46.2% (95% CI, 19.2–74.9) in the 5.6-mg/kg cohort, and 53.8% (95% CI, 25.1–80.8) in the 6.4-mg/kg cohort
- Clinically meaningful tumor responses were observed across a range of CDH6 expression levels[1] (n=35; data not shown)
- R-DXd treatment was associated with rapid responses at all doses in Asian patients (**Figure 2**)

Safety

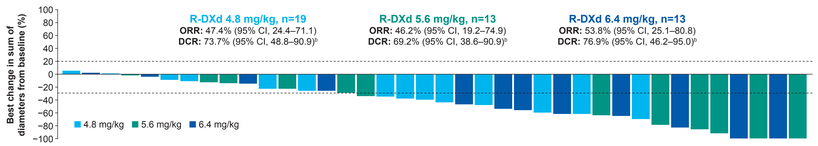
- Across all doses, any-grade TRAEs were reported in 41 (91.1%) Asian patients and Grade ≥3 TRAEs were reported in 18 (40.0%); there were no Grade 5 TRAEs (**Table 3**)
  - No Grade 5 hematologic TEAEs were reported at any dose; Grade 3 febrile neutropenia was reported in 2 Asian patients, one each in the R-DXd 5.6-mg/kg and 6.4-mg/kg cohorts
- In Asian patients, TRAEs led to R-DXd delay, reduction, or discontinuation in 12 (26.7%), 10 (22.2%), and 3 (6.7%) patients, respectively
  - Dose reductions were more frequent with the 6.4-mg/kg dose in both the Asian subgroup and the overall population
- Any-grade adjudicated treatment-related ILD/pneumonitis was reported in 2 (4.4%) Asian patients (4.8 mg/kg, Grade 3; 6.4 mg/kg, Grade 2)
- The most common TEAEs reported in Asian patients by R-DXd dose are shown in **Figure 3**

Table 2: Summary of efficacy in the Asian subgroup and the overall population

Confirmed response by BICR[a]	Asian subgroup by dose			Asian subgroup R-DXd 4.8–6.4 mg/kg n=45	Overall population R-DXd 4.8–6.4 mg/kg N=107
	R-DXd 4.8 mg/kg n=19	R-DXd 5.6 mg/kg n=13	R-DXd 6.4 mg/kg n=13		
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)

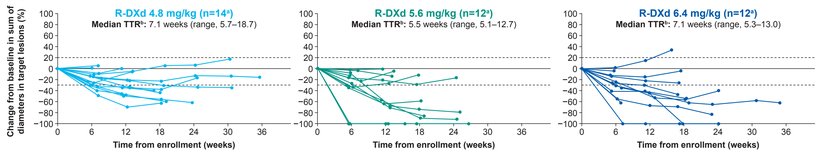
[a]Per RECIST 1.1. [b]BOR was defined as the best response across all timepoints; CR, ≥2 assessments of CR ≥4 weeks apart, prior to progression; PR, ≥2 assessments of PR (or CR) ≥4 weeks apart, prior to progression (not meeting criteria for CR); SD, ≥1 assessment of SD (or better) ≥5 weeks following 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).

Figure 1: Tumor responses in Asian patients with platinum-resistant OC[a]



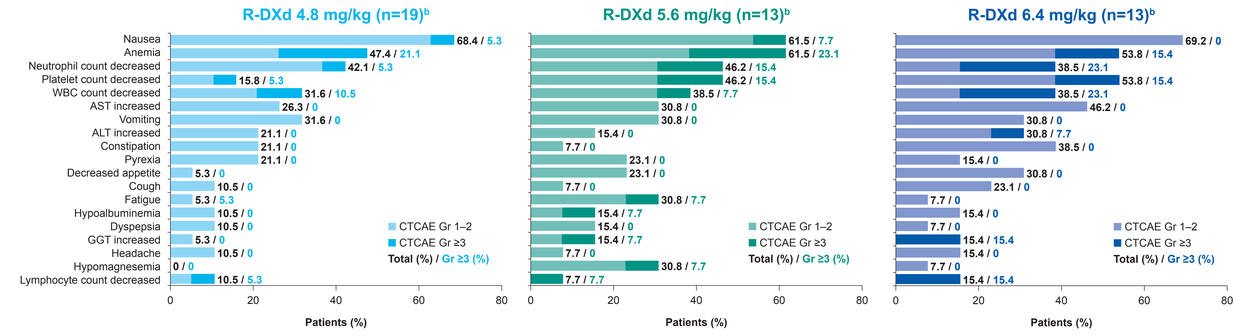
[a]Tumor response assessed by BICR per RECIST 1.1. Only patients with measurable disease at baseline and ≥1 post-baseline tumor scan, both by BICR, were included in the waterfall plot (n=38). Six patients (R-DXd 4.8 mg/kg [n=5]; 6.4 mg/kg [n=1]) did not have measurable disease at baseline, and 1 patient (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 ≥77 days (per RECIST 1.1).

Figure 2: Depth and durability of response in target lesions



[a]Tumor 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).

Figure 3: Most common TEAEs in Asian patients (≥10% across all doses)[a]



[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).

Table 3: Safety summary

	Asian subgroup		Overall population
	R-DXd 5.6 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 (%)	13 (100)	44 (97.8)	106 (99.1)
Grade ≥3	9 (69.2)	27 (60.0)	56 (52.3)
Any TRAE, n (%)	12 (92.3)	41 (91.1)	100 (93.5)
Grade ≥3	6 (46.2)	18 (40.0)	38 (35.5)
Grade 5	0	0	0
Dose modifications associated with TRAEs,[a] n (%)			
Drug discontinuation	0	3 (6.7)	6 (5.6)
Dose reduction	2 (15.4)	10 (22.2)	20 (18.7)
Dose delay	4 (30.8)	12 (26.7)	25 (23.4)
ILD/pneumonitis adjudicated as treatment related,[b] n (%)			
Any grade	0	2 (4.4)	4 (3.7)
Grade ≥3	0	1 (2.2)[c]	1 (0.9)[c]
Grade 5	0	0	0

[a]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. [b]ILD/pneumonitis events were adjudicated by an independent ILD adjudication committee. [c]ILD/pneumonitis Grade ≥3 event (adjudicated as treatment related) was Grade 3.

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 ratudotatug deruxtecan (R-DXd).
Medical writing support was provided by Rachael Bailey, 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).
The content in this poster was previously presented at the European Society of Medical Oncology (ESMO) Asia Congress; December 5–7, 2025; Singapore, Republic of Singapore.

ABBREVIATIONS

ADC, antibody–drug conjugate; **ALT**, alanine aminotransferase; **AST**, aspartate aminotransferase; **BICR**, blinded independent central review; **BOR**, best overall response; **CDH6**, cadherin 6; **CI**, confidence interval; **CR**, complete response; **CTCAE**, Common Terminology Criteria for Adverse Events; **DCR**, disease control rate; **DOR**, duration of response; **ECOG PS**, Eastern Cooperative Oncology Group performance status; **FRα**, folate receptor alpha; **FU**, follow-up; **GGT**, gamma-glutamyl transferase; **Gr**, grade; **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; **MedDRA**, Medical Dictionary for Regulatory Activities; **N**, ovarian cancer; **ORR**, objective response rate; **OS**, overall survival; **PARP**, poly (ADP-ribose) polymerase; **PD**, progressive disease; **PFS**, progression-free survival; **PLD**, pegylated liposomal doxorubicin; **PR**, partial response; **Q3W**, every 3 months; **QOL**, quality of life; **R**, randomization; **R-DXd**, ratudotatug deruxtecan; **RECIST 1.1**, Response Evaluation Criteria in Solid Tumors, version 1.1; **SD**, stable disease; **TEAE**, treatment-emergent adverse event; **TRAE**, treatment-related adverse event; **TTR**, time to response; **WBC**, white blood cell.

REFERENCES

1. Lee J-Y, et al. Oral presentation at the European Society for Medical Oncology Asia congress. December 5–7, 2025; Singapore, Republic of Singapore. Presentation 1658.
2. Daiichi Sankyo, Inc. Data on file.
3. González-Martín A, et al. Ann Oncol. 2023;34:833–848.
4. Richardson DL, et al. JAMA Oncol. 2023;9:851–859.
5. Harano K, et al. Poster presentation at the European Society for Medical Oncology Congress. October 17–21, 2025; Berlin, Germany. Presentation LBA42.
6. Sheldon D, et al. Poster presentation at the European Society for Medical Oncology Congress. October 20–24, 2023; Madrid, Spain. Presentation 777P.
7. Suzuki H, et al. Poster presentation at the European Society for Medical Oncology Congress. September 17–21, 2021; Virtual. Presentation 919.
8. Suzuki H, et al. Med Cancer Ther. 2024;2:257–271.
9. ClinicalTrials.gov. https://clinicaltrials.gov/study/NCT06161025. Accessed February 4, 2026.
10. 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.

kharano@east.ncc.go.jp