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LBA42

Raludotatug deruxtecan (R-DXd) in patients (pts) with platinum-resistant ovarian cancer (PROC): Primary analysis of the phase II dose-optimization part of REJOICE-Ovarian01

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Background

R-DXd, an antibody–drug conjugate, comprises a humanized cadherin 6 (CDH6) IgG1 monoclonal antibody attached to a topoisomerase I inhibitor payload (DXd) via a tumor-selective cleavable linker. CDH6, a mediator of cell adhesion, is aberrantly expressed in 65–85% of epithelial OC tumors.

Methods

Pts with platinum-resistant high-grade serous or endometrioid OC, primary peritoneal, or fallopian tube cancer who received 1–3 prior lines of systemic therapy (LOT), including bevacizumab (bev) and/or PARP inhibitor (PARPi) if eligible, were enrolled in the phase 2, dose-optimization part of REJOICE-Ovarian01 (NCT06161025), irrespective of tumor CDH6 expression by immunohistochemistry. Pts were randomized to R-DXd 4.8, 5.6 or 6.4 mg/kg IV Q3W until disease progression or unacceptable toxicity and stratified by prior LOT and CDH6 expression. Pts had completed ≥18 weeks of follow-up or discontinued treatment. The primary endpoint was objective response rate (ORR) by blinded independent central review (BICR) per RECIST 1.1.

Results

At data cutoff (Feb 26, 2025), 107 pts with PROC had received R-DXd and were included in the dose-optimization analysis. Median number of prior LOT was 3; 83.2% received prior bev, and 70.1% prior PARPi. Median treatment duration was 23.9 weeks (range, 3.0–42.1). Across doses, ORR by BICR was 50.5%, including 3 complete responses (Table). Clinically meaningful responses were observed across a range of tumor CDH6 expression levels. Most frequent any-grade treatment-emergent adverse events (TEAEs) were nausea (69.2%), anemia (57.0%), and asthenia (46.7%). Treatment-related AEs led to R-DXd delay, reduction, or discontinuation in 23.4%, 18.7%, and 5.6% of pts, respectively.Table: LBA42

	4.8 mg/kg n=36	5.6 mg/kg n=36	6.4 mg/kg n=35	Total N=107
ORR by BICR, %(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)

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Best overall response, n (%) CR PR	1 (2.8) 15 (41.7)	2 (5.6) 16 (44.4)	0 20 (57.1)	3 (2.8) 51 (47.7)
Disease control rate, %(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)
Median time to response,weeks (range)	7.1 (5.4–18.7)	6.6 (5.1–18.3)	7.2 (5.3–19.1)	7.1 (5.1–19.1)
Any-grade TEAEs, n (%)	35 (97.2)	36 (100)	35 (100)	106 (99.1)
Gr ≥3 TEAEs, n (%)	16 (44.4)	20 (55.6)	20 (57.1)	56 (52.3)
Interstitial lung disease adjudicated as treatment-related, n (%)Any-gradeGr ≥3	1 (2.8) 1 (2.8) (*Gr 3*)	1 (2.8) 0	2 (5.7) 0	4 (3.7) 1 (0.9)

Conclusions

R-DXd 5.6 mg/kg is considered the optimal dose to be further evaluated in the ongoing phase 3 study. R-DXd demonstrated promising efficacy and a manageable safety profile in pts with PROC.

Clinical trial identification

NCT06161025.

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Legal entity responsible for the study

Daiichi Sankyo, Inc.

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Disclosure

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