TPS3158 **Poster Session**

REJOICE-PanTumor01: A phase 2 signal-seeking study of raludotatug deruxtecan (R-DXd) in patients with advanced or metastatic gynecologic or genitourinary tumors.

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Background: Cadherin-6 (CDH6), a transmembrane protein involved in cell–cell adhesion and epithelial–mesenchymal transition, is overexpressed in many cancer types. R-DXd is an anti-CDH6 antibody–drug conjugate composed of a humanized CDH6 antibody covalently linked to a potent topoisomerase I inhibitor payload (DXd) via a plasma-stable linker. In an ongoing Phase 1 study (NCT04707248), a subgroup of patients with heavily pretreated ovarian cancer (OC) who received R-DXd 4.8–6.4 mg/kg, had an objective response rate (ORR) of 48.6% (95% confidence interval [CI], 31.9–65.6); median duration of response (DOR) was 11.2 months (95% CI, 3.1–not estimable), and progression-free survival (PFS) was 8.1 months (95% CI, 5.3–not estimable), irrespective of CDH6 expression level (data cut-off: July 14, 2023). The safety profile of R-DXd was manageable. In total, 11.1% of patients discontinued R-DXd due to treatment-emergent adverse events. These promising data warranted further investigation of R-DXd in REJOICE-Ovarian01 (NCT06161025), a Phase 2/3 study in patients with platinum-resistant high-grade serous OC (HGSOC), and in the REJOICE-PanTumor01 Phase 2 study, which is described here. **Methods:** REJOICE-PanTumor01 (NCT06660654) is a global, open-label Phase 2 study in patients with locally advanced or metastatic gynecologic (endometrial cancer [EC], cervical cancer, or non-HGSOC) or genitourinary (urothelial cancer [UC] or clear cell renal cell carcinoma [ccRCC]) tumors. Cohorts are tumor type–specific; patients in all cohorts must have relapsed or progressive disease after receiving ≥1 prior line (and ≤3 prior lines in the EC, UC, and ccRCC cohorts only) of standard treatment. Adult patients with ECOG performance status 0–1 are eligible; there is no selection for tumor CDH6 expression. Approximately 40 patients will be enrolled into each cohort to receive R-DXd 5.6 mg/kg IV every 3 weeks until disease progression per RECIST 1.1, unacceptable toxicity, death, or other reason per protocol. In each cohort, a nonbinding futility interim analysis will be conducted after 20 patients complete a minimum of 12 weeks of follow-up, the results of which may determine whether the remaining (~20) patients will be treated. Primary endpoints are ORR for the gynecological and UC cohorts, disease control rate (DCR) for the ccRCC cohort (both investigator-assessed), and safety and tolerability for all cohorts. Secondary endpoints are ORR (ccRCC cohort only), DCR (except ccRCC cohort), PFS, DOR, time to response (all investigator-assessed per RECIST 1.1), pharmacokinetics, and immunogenicity. No formal hypothesis testing will be performed; ORR and DCR will be analyzed using a Clopper–Pearson method to determine 95% CI. PFS and DOR will be analyzed using the Kaplan–Meier method (2-sided 95% CI). Study enrollment began in January 2025. Clinical trial information: NCT06660654. Research Sponsor: Daiichi Sankyo, Inc., Merck Inc.