.

Conclusions: OCI + TIS showed promising antitumor activity and durable responses, regardless of PD-L1 expression, and was well tolerated in pts with previously treated R/M CC.

Clinical trial identification: NCT04693234.

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745MO Raludotatug deruxtecan (R-DXd; DS-6000) monotherapy in patients with previously treated ovarian cancer (OVC): Subgroup analysis of a first-in-human phase I study

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Background: R-DXd is an antibody–drug conjugate comprised of a humanised IgG1 antibody against cadherin 6 (CDH6), a stable linker selectively cleaved within tumour cells, and a membrane permeable topoisomerase I inhibitor. Overexpression of CDH6, a cell adhesion protein, occurs in the majority of OVC cases and is associated with poor prognosis. In an ongoing phase 1 trial (NCT04707248), R-DXd demonstrated an acceptable safety profile and an early efficacy signal.

Methods: All patients received prior taxane and platinum therapies and were unselected for CDH6 tumour expression. Part A (dose escalation) assessed the tolerability of R-DXd at 1.6 to 9.6 mg/kg, and 8.0 mg/kg was determined to be the maximum tolerated dose. Doses of 4.8 to 8.0 mg/kg were expanded in Part B. A subgroup analysis of patients with OVC who received R-DXd at 4.8 to 8.0 mg/kg is reported here.

Results: As of 03 March 2023, 42 patients with OVC had received R-DXd at 4.8 (n = 7), 6.4 (n = 20), and 8.0 (n = 15) mg/kg: 40 (95%) had platinum-resistant disease, 29 (69%) had received prior bevacizumab, and 26 (62%) had received prior PARP inhibitors. The median prior lines of therapy was 4.0 (range 1 – 13). Twenty-one patients (50%) were still receiving study treatment. The median treatment duration was 18.1 wks (range, 3.0–93.9). Any-grade treatment-emergent adverse events (TEAEs) were experienced by 37 patients (88%), and grade ≥ 3 TEAEs were observed in 21 (50%). The most common all-grade TEAEs were nausea (55%), fatigue (40%), vomiting (38%), and diarrhoea (33%). AEs led to R-DXd discontinuation in 14% of patients. The confirmed overall response rate (RECIST v1.1) in patients with measurable disease was 38% (13 of 34): 67% (95% CI, 22.3 – 95.7; 4/6, including 1 CR) at 4.8 mg/kg, 33% (95% CI, 11.8 – 61.6; 5/15) at 6.4 mg/kg, and 31% (95% CI, 9.1 – 6.4; 4/13) at 8.0 mg/kg. Two patients with unconfirmed partial responses were still on treatment. Eleven of 21 GCIG-evaluable patients (52%) had a CA-125 response.

Conclusions: In heavily pretreated OVC patients without CDH6 preselection, R-DXd demonstrated acceptable safety and encouraging preliminary efficacy, which supports further clinical development in OVC.

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