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Safety and efficacy of ixotatug vedotin (TORL-1-23), a claudin 6-targeted ADC, as monotherapy in germ cell tumors (GCT)

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Background

Claudin-6 (CLDN6) is a cell surface protein and member of the claudin family of tight junction molecules expressed at high levels in multiple human cancers with little or no expression in normal adult tissues. Overexpression of CLDN6 has been found to be highly prevalent in GCT. Ixotatug vedotin (Ixo-V) is a first-in-class IgG1-vc-MMAE antibody drug conjugate that specifically targets CLDN6 positive (CLDN6+) disease. Ixo-V monotherapy has previously demonstrated promising antitumor activity with a manageable safety profile in heavily pretreated CLDN6+ ovarian cancer. Here, we report safety and efficacy from an ongoing phase 1 study of Ixo-V in patients with heavily pretreated GCT including progression after high-dose chemotherapy with autologous stem cell transplantation (SCT).

Methods

Patients (pts) with previously treated advanced or metastatic GCT, not amenable to surgery, were enrolled across dose escalation and dose expansion cohorts. Pts received Ixo-V (doses ranging from 0.4-3.4 mg/kg) on Day 1 of a 21-day cycle. This analysis includes pts with GCT of testicle (9), ovary (2), and extragonadal disease (1). Responses were assessed by investigator per RECIST 1.1; adverse events (AEs) were graded by CTCAE v5.0.

Results

Of 12 GCT pts treated to date, 11 were CLDN6+, median age 39 years (range 23-76). Pts received a median of 4 prior lines (range 1-11), 3 median platinum lines; 50% had prior SCT. Of 10 efficacy evaluable pts, ORR was 50% (95% CI 18.7-81.3); 3 of 6 SCT pts had confirmed responses. Disease control rate was 80%. Median duration of response was 4.5 months (95% CI; 1.9, NE); 1 pt maintained response for 47.4 months. Most common AEs (all grades) included 6 pts with constipation, and 4 each with arthralgia, back pain, nausea, vomiting. Most common Grade 3/4 AEs included 3 pts with neutropenia and 2 pts with peripheral sensory neuropathy. Two pts discontinued due to treatment-related AEs.

Conclusions

These data suggest meaningful clinical activity of Ixo-V in heavily pretreated pts with recurrent GCT, including pts with disease refractory to SCT. Safety profile is consistent with prior experience. These data support further clinical investigation of Ixo-V across CLDN6-expressing tumor types including recurrent GCT.

Clinical trial identification

NCT05103683.

Legal entity responsible for the study

TORL BioTherapeutics.

Funding

TORL BioTherapeutics.

Disclosure

C. Oliai: Financial Interests, Personal, Research Funding: Pfizer, Jazz Pharmaceuticals, Orca Bio, Seagen, AstraZeneca, Kite, Electra Therapeutics. D. Feldman: Financial Interests, Personal, Invited Speaker, Spouse (not myself): Novo Nordisk; Financial Interests, Personal,

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