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NAPISTAR 1-01: A phase I dose escalation study of TUB-040, a novel NaPi2b-targeting exatecan antibody-drug conjugate (ADC) in patients with platinum-resistant ovarian (PROC) high grade serous carcinoma (HGSC)

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Background

TUB-040 is a homogenous DAR8 ADC targeting Napi2b, overexpressed in the majority of HGSC and NSCLC,comprising a humanized Fc-silenced IgG1 mAb conjugated to exatecan. The drug-linker consists of a cysteine-selective, highly stable and solubility mediating P5 moiety and a proteolytically cleavable di-peptide. This promotes high extracellular stability, a differentiated mode of action, and a strong bystander effect enabling a wide therapeutic window.

Methods

NAPISTAR 1-01 is a multicenter, phase I/IIa study in biomarker-unselected patients (pts) with PROC and NSCLC in separate cohorts. TUB-040 was administered Q3W in dose escalation (range 0.5-5.3 mg/kg) to pts with PROC until progression or unacceptable toxicity.

Results

As of the data cut-off on 08 July 2025, 67 PROC pts were dosed with TUB-040 for a median of 5 cycles (range 1-19). Pts had a median age of 62 y (range 34-81), ECOG PS 0 or 1, a median of 4 prior lines of therapy (range 1-7); prior treatment included bevacizumab (84%), PARP inhibitors (76%) and mirvetuximab soravtansine (13%). Across all doses in PROC, most common TEAEs were neutropenia (46%, 34% ≥grade 3 [G3]), anemia (34%, 13% ≥G3), thrombocytopenia (27%, 16% ≥G3), nausea (70%, 3% ≥G3), diarrhea (27%, 0% ≥G3). No clinically relevant bleeding, ocular toxicity or stomatitis were reported. 2 cases of asymptomatic, G1 transient pneumonitis were observed with both pts continuing on therapy. No fatal TEAEs; 2 pts discontinued due to TEAE (3%). Hematologic DLTs were observed at doses of 2.5, 4.4 and 5.3 mg/kg. The MTD was determined at 4.4 mg/kg. Among 55 efficacy evaluable PROC pts, unconfirmed ORR was 49% [35-63][1], and confirmed ORR was 33% [21-47], ranging from 42% (3.3mg/kg) to 73% (2.1 mg/kg). Responses were seen from C2. All responses were ongoing without progression as of 08 July 2025. Overall disease control rate was 91% [80-97]. GCIG CA-125 response occurred in 60% of pts overall and 73% treated at 2.1 mg/kg. [1] Values reported with 95% CI.

Conclusions

TUB-040 was well tolerated with robust clinical activity even at low doses, offering a differentiated potential new option for treatment with a highly favorable benefit–risk profile.

Clinical trial identification

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Disclosure

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