720MO IBI354 (anti-HER2 antibody-drug conjugate [ADC]) in patients (pts) with advanced gynecological cancers (Gynecol C): Results from a phase I study

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Background: IBI354 is an ADC consisting of trastuzumab (anti-HER2 antibody) conjugated to a topoisomerase I inhibitor. We report safety and efficacy of IBI354 in pts with advanced Gynecol C in a phase 1 study.

Methods: Eligible pts with HER2 IHC 1+, 2+ or 3+ advanced cervical cancer (CC), endometrial cancer (EC), or platinum-resistant ovarian cancer (OC) who failed or were intolerant to standard treatment were enrolled from China and Australia. Pts received IBI354 at 6, 9, or 12 mg/kg Q3W. Primary endpoint was safety. Secondary endpoints were ORR, DCR, DoR, and PFS per RECIST v1.1.

Results: As of Mar 22, 2024, 129 pts were enrolled (median age: 57.0 yrs, ECOG PS 1: 69.8%, prior treatment regimens $\geq$2: 82.2%) including 89 pts with OC, 26 CC, and 14 EC. HER2 alterations in most pts were IHC 1+ (65.6%) and 2+ (27.3%); 7.0% were IHC 3+. Median treatment duration was 12.3 weeks (range: 3.1-33.3). Treatment-related adverse events (TRAEs) occurred in 105 (81.4%) pts and grade $\geq$3 TRAEs in 21 (16.3%) pts. Most common TRAEs ($\geq$ 20%) were anemia (34.1%), leukopenia (30.2%), nausea (29.5%), and neutropenia (21.7%). Interstitial lung disease was not observed. Serious TRAEs occurred in 7.0% pts. No TRAEs led to treatment discontinuation or death. TRAE led to dose reduction in 1 (0.8%) pt. The safety profile of IBI354 in Gynecol C was comparable with the whole study cohort. As of Apr 25, 2024, for pts with at least one tumor assessment (n = 124), ORR was 39.5% (95%CI: 30.9-48.7) and DCR was 83.1% (95% CI:75.3-89.2). In pts with OC (n = 86), ORR was 41.9% (95% CI: 31.3-53.0) and DCR was 81.4% (95% CI: 71.6-89.0). For the 40 OC pts at 12 mg/kg cohort, ORR and DCR were 45.0% (95% CI: 29.3-61.5) and 90.0% (95% CI: 76.3-97.2), respectively. For the 14 pts with $HER2^{2/3+}$ CC and EC, ORR and DCR was 57.1% (95% CI: 28.9-82.3) and 92.9% (95% CI: 66.1-99.8) including 1 pt (EC) achieved complete response and 7 pts (4 CC and 3 EC) achieved partial response. DoR and PFS were immature.

Conclusions: IBI354 was well tolerated and showed promising efficacy in pts with advanced Gynecol C. Clinical development of IBI354 in these tumors is ongoing. More data will be updated at the meeting.

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721MO Phase I, two-part, multicenter first-in-human (FIH) study of TORL-1-23: A novel claudin 6 (CLDN6) targeting antibody drug conjugate (ADC) in patient with advanced solid tumors

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Background: TORL-1-23 is an ADC targeting the oncofetal protein CLDN6. A member of the claudin family of tight junction proteins, CLDN6 expression is limited to early stages of development, with aberrant expression in many cancers, including ovarian, endometrial, and testicular cancers.

Methods: Part 1 (escalation) and part 2 (expansion) enrolled patients (pts) with advanced solid tumors. TORL-1-23 is administered as a 30-min IV infusion Q3W. Study objectives include evaluation of safety, tolerability, DLTs, RP2D, antitumor activity, and correlation of CLDN6 levels with response. Part 1: Pts received TORL-1-23 across 10 dose levels (0.2 to 4.0 mg/kg). Part 2: Pts with CLDN6-expressing cancers will be evaluated to confirm the RP2D in ovarian cancer, NSCLC, and other cancers using a CLDN6 IHC companion diagnostic.

Results: As of 29-Apr-2024, 68 pts have been enrolled. Part 1 enrolled 48 pts with ovarian (n=35), testicular (n=5), endometrial (n=7), and NSCLC (n=1) cancers. Part 2 enrolled 20 pts with ovarian (n=11), endometrial (n=4), NSCLC (n=4), and testicular (n=1) cancers at 2.4 mg/kg (n=12) and 3.0 mg/kg (n=8) with pegfilgrastim. Part 1: Median prior lines of therapy were 4 (1-9). Treatment-related adverse events (TRAE) occurred in 85% of pts. G1/2 TRAEs (>20%) included fatigue (42%), peripheral neuropathy (40%), alopecia (38%), nausea (31%), anemia (31%), WBC count decrease (23%), and arthralgia (23%). The most common ($\geq$10%) G3+ TRAE was neutropenia (23%). Part 2: CLDN6+ ovarian cancer cohort was limited to platinum resistant disease, 1-3 prior lines. The safety profile for 2.4mg/kg and 3.0mg/kg was consistent with previous reports. Febrile neutropenia, ILD, and ocular toxicities were not observed. Pts with CLDN6+ ovarian cancer, ORR was 21% (3/14) at 0.2-2.0mg/kg; 67% (4/6) at 2.4mg/kg, and 50% (6/12) at 3.0 mg/kg. 26 pts remain on treatment with one ongoing >100 weeks.

Conclusions: TORL-1-23 is well tolerated with promising preliminary antitumor activity in heavily-pretreated pts with CLDN6-expressing ovarian, endometrial, and testicular cancers. Dose expansion is ongoing at doses of 2.4mg/kg and 3.0mg/kg in CLDN6+ NSCLC and ovarian cancer, and CLDN6-low expressing tumors.

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