Zanidatamab (ZW25; Zani) in Patients (pts) with Previously Treated Advanced Human Epidermal Growth Factor Receptor 2 (HER2)-Amplified Biliary Tract Cancer (BTC): Asia Subgroup Analysis of the Phase 2b HERIZON-BTC-01 Study


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Background

Zani, a HER2-targeted bispecific antibody, has shown antitumor activity and a tolerable and manageable safety profile in pts with HER2-amplified, treatment (Tx)-refractory, advanced BTC (HERIZON-BTC-01; NCT04466891). Here, we report a post-hoc analysis of the Asia subgroup in predetermined cohort 1 (HER2 immunohistochemistry 2+ or 3+) comprising pts from China and South Korea.

Methods

This phase 2b, open-label, single-arm study evaluated zani monotherapy (20 mg/kg IV Q2W) in adults with HER2-amplified, inoperable, locally advanced/metastatic BTC. Pts had received ≥1 prior systemic Tx for advanced disease, including gemcitabine. The primary endpoint was confirmed objective response rate. Secondary endpoints included disease control rate, duration of response, progression-free survival, and adverse events (AEs).

Results

Of 80 pts enrolled in cohort 1, 50 were from Asia (median age 63.5 years; 29 [58%] gallbladder cancer, 11 [22%] intra-, and 10 [20%] extra-hepatic cholangiocarcinoma). At data cutoff (Oct 10, 2022), median study follow-up was 11.3 months (range 6.9-22.3); 7 (14%) pts remained on Tx. Pts had median 1 prior line (range 1-5) of Tx for advanced disease. Efficacy is summarized in Table 1. Tx-related AEs (TRAEs) were experienced by...
70% of pts, the most common being infusion-related reactions (42%), diarrhea (28%), and decreased ejection fraction (EF; 12%). In all, 10% of pts experienced grade 3 TRAEs (decreased EF [4%]; diarrhea, increased blood bilirubin, and enteritis [all 2%]); none had grade 4/5 TRAEs. A total of 4% of pts had serious TRAEs and 2% discontinued Tx due to decreased EF.

<table>
<thead>
<tr>
<th>Asia subgroup (n=50)</th>
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<tbody>
<tr>
<td><strong>Objective response rate</strong>, % (95% CI)</td>
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<tr>
<td><strong>Best overall response</strong>, n (%)</td>
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<tr>
<td>Complete response</td>
</tr>
<tr>
<td>Partial response</td>
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<tr>
<td>Stable disease</td>
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<tr>
<td>Progressive disease</td>
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<td>Not evaluable</td>
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<td><strong>Disease control rate</strong>, % (95% CI)</td>
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<td><strong>Median duration of response, months (95% CI)</strong></td>
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<td><strong>Duration of response ≥16 weeks, n (%) (95% CI)</strong></td>
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<td><strong>Median progression-free survival, months (95% CI)</strong></td>
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</table>

CI, confidence interval

*aConfirmed by independent central review per RECIST v1.1; **Estimated using Clopper-Pearson method; ***Estimated using Brookmeyer & Crowley method with log-log transformation.

**Conclusions**

Zani demonstrated durable tumor responses and a tolerable and manageable safety profile in pts in the Asia subgroup with Tx-refractory HER2- amplified advanced BTC, consistent with the overall study population (Harding J, et al. Lancet Oncol. 2023).