Health-Related Quality of Life in Patients With Zanidatamab-Treated HER2-Positive Biliary Tract Cancer in the Phase 2b HERIZON-BTC-01 Study

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Background
- Biliary tract cancer (BTC) is an encompassing term used to describe a group of malignancies, including gallbladder cancer (GBC), extrahepatic cholangiocarcinoma (ECC) and intrahepatic cholangiocarcinoma (ICC). BTC patients present with locally advanced or metastatic disease in over 90% of cases. BTC is a highly chemo-resistant cancer, and treatment options are limited, with a poor prognosis.
- Zanidatamab is a bispecific antibody that simultaneously binds to two separate HER2 domains (extracellular domain 2 and 4) in a 1:1 stoichiometry. This bispecificity results in the formation of homo- and hetero-oligomers with high affinity and_submit to induce internalization of HER2. Zanidatamab has been shown to have anti-tumor activity in a variety of HER2-positive solid tumors.

Methods
- HERIZON-BTC-01 (NCT04466891) is an ongoing, open-label, global phase 2b study of zanidatamab in patients with centrally confirmed HER2-positive BTC. Patients were prospectively assigned into one of two cohorts: Cohort 1 (immunohistochemistry [IHC] 2+ or 3+; defined as HER2-positive) and Cohort 2 (IHC 1+). The study included the following eligibility criteria: adults (≥18 years) with HER2-positive BTC, with a measurable target lesion according to Response Evaluation Criteria in Solid Tumours (RECIST) v1.1. Patients were to be pretreated with ≤4 prior regimens and have a Karnofsky performance status (KPS) ≥50%.

Objectives
- To report the HRQoL outcomes for patients with HER2-positive BTC treated with zanidatamab in the HERIZON-BTC-01 study

Results

- **Patient-reported outcomes**: The EQ-5D visual analogue scale (VAS) was used to assess HRQoL. Patients reported a median VAS score of 75 (range 0-100) at baseline. At the end of the study, the median VAS score was 78 (range 0-100). The EQ-5D descriptive system questionnaire was used to assess health-related quality of life. The mean EQ-5D-5L index score was 0.64 at baseline and 0.67 at the end of the study. The percentage of patients reporting no problem in any domain was 40% at both time points.

- **Safety and tolerability**: The most common treatment-emergent adverse events (TEAEs) were nausea, vomiting, and diarrhea. Grade 3/4 TEAEs occurred in 15% of patients. No grade 4 or 5 TEAEs were reported. No grade 4 or 5 treatment-related adverse events (TRAEs) were reported. The most common grade 3/4 TRAEs were lymphopenia (9%), anemia (8%), and neutropenia (7%).

- **Efficacy**: The primary endpoint of the study was progression-free survival (PFS). At the time of the analysis, 32 patients had progressed, and 22 patients were ongoing at the study cut-off. The median PFS was 7.8 months (95% CI 5.3-17.4). A total of 40 patients were evaluable in Cohort 1 between September 2020 and May 2021. The median PFS was 7.8 months (95% CI 5.3-18.9).

- **Quality of life outcomes**: The EQ-5D VAS scores at baseline and time of best overall tumor response (BONT) were compared. The median change in VAS score from baseline to time of BONT was 10 (range -40 to 20). The EQ-5D index scores at baseline and time of BONT were compared. The median change in EQ-5D index score from baseline to time of BONT was 0.03 (range -0.20 to 0.20).

Conclusions

- The results of HERIZON-BTC-01, including the HRQoL results, support the continued development of zanidatamab as a HER2-positive BTC treatment option.

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**Table 1. Baseline Demographics and Patient Disease Characteristics (Cohort 1)**

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>n=80</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>65% of patients in Cohort 1 were Asian</td>
</tr>
<tr>
<td>Gender</td>
<td>60% of patients in Cohort 1 had an IHC 3+ score</td>
</tr>
<tr>
<td>Race</td>
<td>80% of patients in Cohort 1 were Asian</td>
</tr>
<tr>
<td>KPS</td>
<td>90% of patients in Cohort 1 were Asian</td>
</tr>
<tr>
<td>Prior treatments</td>
<td>100% of patients in Cohort 1 were Asian</td>
</tr>
<tr>
<td>Previous systemic therapy</td>
<td>100% of patients in Cohort 1 were Asian</td>
</tr>
<tr>
<td>Progression status</td>
<td>100% of patients in Cohort 1 were Asian</td>
</tr>
<tr>
<td>Prior chemotherapy</td>
<td>100% of patients in Cohort 1 were Asian</td>
</tr>
</tbody>
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**Figure 2. (A) Proportion of Patients by Type of Response and (B) Disease Response Endpoints Following Zanidatamab Treatment in Cohort 1**

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**Figure 3. Individual Dimensions of the EQ-5D-5L Questionnaire (A-E) by Tumor Response at Baseline and Time of BONT (Cohort 1)**

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**Figure 4. EQ-5D VAS Scores at (A) Baseline and Time of BONT and (B) Change From Baseline at Time of BONT by Tumor Response (Cohort 1)**

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**References**