Long-term follow-up of bintrafusp alfa, a bifunctional fusion protein targeting TGF-β and PD-L1, in patients with pretreated bilary tract cancer

**BACKGROUND**

Biliary tract cancer (BTC) is a rare, heterogeneous, and lethal group of cancers with limited treatments. \[\text{[1]}\]

**Germcelline plus capillaries is the standard care of first-line (1L) BTC treatment; however, no global standard of care in second-line (2L) BTC treatment because of the efficacy of 1L chemotherapy in BTC.**

- Recent meta-analysis of 2L chemotherapy in BTC found a median OS of 11.9 months, but the benefit was modest and had heterogeneous treatment regimens.

- The ABC-06 study showed clinical benefit of treatment with mFOLFOX6 (oxaliplatin, leucovorin, and 5-fluorouracil) vs active symptom control for patients with pretreated BTC. However, the median progression-free survival (PFS) was 4.0 months, 12-month OS rate of 25.4%, and ORR of 9.3%.

- Recent studies for the treatment of multiple cancers with immune checkpoint inhibitors (ICIs) have shown promising results, although the efficacy of ICIs has yet to be demonstrated in BTC.

- In a phase 2 study, 12 patients with BTC who received ≥2 prior anticancer regimens with PD-L1–unselected BTC, the ORR was 11% per independent review committee (IRC). Safety was manageable for BTC and recommended 1200 mg every 2 weeks (Q2W).

- Since the initial analysis, the investigator-assessed ORR and DCR remained at 22% per the investigator (11% per independent review committee). Patients supported the selection of 1200 mg every 2 weeks (Q2W) as the recommended dose for BTC treatment.

**RESULTS**

**Table 1. Investigator-assessed efficacy as of October 24, 2019 cutoff**

<table>
<thead>
<tr>
<th>Outcome</th>
<th>12-month OS, % (95% CI)</th>
<th>18-month PFS, % (95% CI)</th>
<th>Median OS, months (95% CI)</th>
<th>Median PFS, months (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>All patients</td>
<td>12.7 (6.7-15.8)</td>
<td>14.8 (9.7-20.7)</td>
<td>18 (12-27)</td>
<td>10 (6-17)</td>
</tr>
<tr>
<td>PD-L1–unselected BTC</td>
<td>18 (11-23)</td>
<td>23.3 (20.0-26.6)</td>
<td>18.9 (14.3-23.3)</td>
<td>10.6 (8.2-13.0)</td>
</tr>
<tr>
<td>PD-L1–selected BTC</td>
<td>13 (9.4-16.8)</td>
<td>26.7 (22.8-30.7)</td>
<td>18 (13-24)</td>
<td>12 (9.4-14.8)</td>
</tr>
<tr>
<td>PD-L1–unselected and IRC</td>
<td>12 (5.7-18.4)</td>
<td>23.3 (20.0-26.6)</td>
<td>18.9 (14.3-23.3)</td>
<td>10.6 (8.2-13.0)</td>
</tr>
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**CONCLUSIONS**

- After 20 months of follow-up, bintrafusp alfa continued to demonstrate safety and durable clinical benefit in patients with pretreated BTC. The median OS was 17.4 months; 24-month OS and PFS rates were 27.7% and 11.6%, respectively.

- The efficacy of bintrafusp alfa in patients with pretreated BTC compares favorably with that of mFOLFOX6 from the ABC-06 study (ORR, 4%; median OS and PFS, 6.9 months).

- Additional safety signals or deaths were observed since the initial analysis. One grade 3/4 TRAE (grade 3/4 keratitis) was observed during the study.

- Bintrafusp alfa showed a 26% response rate with a long duration of response (42.8% with DORs of 18+ months, 23.3% with DORs of 23.5+ months, and 36.7% with DORs of 24+ months).

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**REFERENCES**

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6. Changhoon Yoo, yooc@amc.seoul.kr

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**DISCLOSURES**

The authors declare no potential conflicts of interest. \[\text{[2]}\]

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