Randomized Phase II trial of the carboxylerase (CES)-converted novel drug EDO-S7.1 in patients (pts) with advanced biliary tract cancers (BTC)

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Introduction and Objectives
- Study design: A randomized Phase II, open-label, single-center, two-arm, parallel-group, single-blind, placebo-controlled, multicenter trial (Table 1).
- Patients were randomized 1:1 to receive either etoposide toniribate or best supportive care (BSC).
- The primary endpoint was to assess the anti-tumor activity of etoposide toniribate in patients with BTC who have progressed despite one or more previous lines of treatment.

Methods
- This was a Phase II, multicenter, open-label study to assess the anti-tumor activity of etoposide toniribate in adult patients with advanced BTC. Patients were randomized 1:1 to receive either etoposide toniribate or best supportive care (BSC) as per institutional standard (Figure 1).
- The full 28-day treatment cycle was repeated until disease progression, unmanageable toxicity, or withdraw of consent (achieved scored trial). Patients were considered adequate.
- Patients receiving BSC who experienced disease progression could cross-over to receive therapy compared with those treated with BSC.
- This was a Phase II, multicenter, open-label study to assess the anti-tumor activity of etoposide toniribate.

Results
- A total of 22 patients with BTC were randomized, 11 to receive etoposide toniribate and 11 to BSC (Table 1).
- The safety analysis set included 22 patients (11 etoposide toniribate, 11 BSC) who received at least one dose of study medication.
- The per protocol analysis set (PP) included 10 patients (5 etoposide toniribate, 5 BSC) who had been correctly randomized and had sufficient treatment and efficacy assessment information.

Primary endpoints
- Median PFS, Time to Treatment Failure (TTF), Overall Survival (OS), and Safety
- Median PFS, TTF, and OS were greater in those treated with etoposide toniribate compared with BSC (Table 2).
- All patients who received etoposide toniribate achieved a partial response (PR) or stable disease (SD) compared with those treated with BSC.

Secondary endpoints
- Median PFS, TTF, and OS were greater in those treated with etoposide toniribate compared with BSC (Table 2).
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Conclusions
- The targeted conversion and slow release of inactive etoposide toniribate allows for an increase in the dose of the active ingredient that may overcome drug resistance without excessive toxicities.
- These findings will be explored in a Phase III study in a larger patient cohort.

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Figure 1. Study design

Table 1. Patient demographics and baseline characteristics

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<tr>
<th>Etoposide toniribate</th>
<th>BSC</th>
<th>Number of patients</th>
<th>14</th>
<th>13</th>
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<tr>
<td>Age (y)</td>
<td>60.3 ± 10.8</td>
<td>65.8 ± 8.7</td>
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<td>Race white (n)</td>
<td>8 (57)</td>
<td>6 (46)</td>
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<td>TNM stage at diagnosis, n (%)</td>
<td>3 (21)</td>
<td>2 (15)</td>
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<td>Primary tumor site, n (%)</td>
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<td>IVC metastases, n (%)</td>
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<tr>
<td>IV metastases, n (%)</td>
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Figure 2. Progression-free survival (PFS)

Figure 3. Time to treatment failure (TTF)

Figure 4. Overall survival (OS)