

# A Phase II Trial of Hepatic Arterial Infusion Chemotherapy and Bevacizumab in combination with Toripalimab for Advanced Biliary Tract Cancers: Interim Report

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## Background

The prognosis of first-line standard chemotherapy for advanced biliary tract cancers (BTCs) is still unsatisfactory. Based on phase III trial TOPAZ-1, chemotherapy plus PD-L1 inhibitor had shown positive survival improvement. Other evidence showed that VEGF inhibitor could modify tumor immune-microenvironment while hepatic arterial infusion chemotherapy (HAIC) could improve the survival in cholangiocarcinoma. Combining these modalities may improve outcomes. Here we conducted a prospective study to evaluate the efficacy and safety of HAIC combined with bevacizumab (VEGF inhibitor) and toripalimab (PD-1 inhibitor) for advanced BTCs.

## Study design

This open-label, single-arm, single-center prospective phase II trial was initiated by Peking University Cancer Hospital, China, and registered at clinical trials.gov (NCT04217954).

**Patients:** From October 2019 to December 2021, 32 patients with advanced untreated BTCs were enrolled . The baseline characteristics were listed in Table 1.

**Treatments:** The combination regimen was composed of hepatic arterial bevacizumab (300 mg for 2h d1), followed by oxaliplatin (40 mg/m<sup>2</sup> for 2h, days 1-3) and 5-fluorouracil (800 mg/m<sup>2</sup> for 22h, days 1-3), with intravenous toripalimab (240 mg) on day 1 prior to HAIC, every 4 weeks. A maximum of six consecutive HAIC cycles. Then toripalimab (240 mg) and bevacizumab (300 mg) were intravenously infused every four weeks as maintenance treatment(Figure 1).

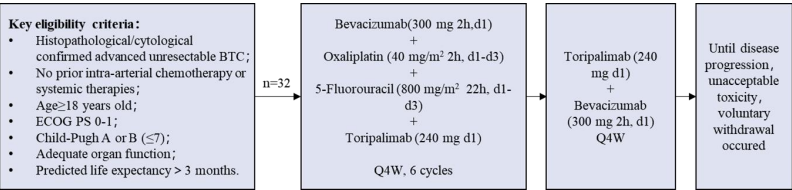


Figure 1: Study schema.

**Endpoints:** The primary endpoint was overall survival (OS). Secondary endpoints included objective response rate (ORR), which was evaluated according to Immune-Modified Response Evaluation Criteria In Solid Tumors (imRECIST), progression-free survival (PFS), and safety.

## Results

### Patient characteristics:

The baseline characteristics were listed in Table 1.

Characteristics	Patients (n=32)
Primary tumor site, n (%)	
Intrahepatic Cholangiocarcinoma	11 (34.4%)
Perihilar Cholangiocarcinoma	17 (53.1%)
Gallbladder Carcinoma	4 (12.5%)
Age (years), mean ± SD	62.06 ± 8.82
Gender, n (%)	
Male	20 (62.5%)
Female	12 (37.5%)
ECOG performance status, n (%)	
0	19 (59.4%)
1	13 (40.6%)
Child-Pugh class	
A	22 (68.8%)
B	10 (31.2%)
Hepatitis, n (%)	
Hepatitis B	4 (12.5%)
Hepatitis C	1 (3.1%)
None	27 (84.4%)
CEA (ng/mL), median (range)	4.35 (1.05-314.31)
CA199 (U/mL), median (range)	513.3 (23.9-69665.0)
Extrahepatic metastasis, n (%)	6 (18.8%)

Table 1: Baseline characteristics of all patients.

### Efficacy:

At the cutoff date (July 26, 2022), the median follow-up was 14.9 months. As shown in Table 2, the overall response rate (ORR) was 84.3% (27/32), with 1 complete responses (CR) and 26 partial responses (PR). Stable disease (SD) was observed in 4 patients (12.5%) and progressive disease (PD) occurred in 1 patient (3.1%). Disease control rate (DCR) was 96.9% (31/32). Six-month PFS rate and OS rate were 80.7% and 90.6%, respectively. One-year PFS rate and OS rate were 53.8% and 80.4%, respectively.

Best response, n (%)	No. of All Patients (n=32)
CR	1 (3.1%)
PR	26 (81.3%)
SD	4 (12.5%)
PD	1 (3.1%)
ORR, (%)	27(84.3%)
DCR, (%)	31(96.9%)
Survival	Value
Six-month PFS rate	80.7%
Six-month OS rate	90.6%
One-year PFS rate	53.8%
One-year OS rate	80.4%

Table 2: Best treatment response of all patients.

### Safety:

The most common grade 3 or 4 treatment-related AEs (TRAEs) were liver dysfunction (6 [18.8%]), hematotoxicity (4 [12.5%]) and Diarrhea (1 [3.1%]). The Immune-Related Adverse Events (irAEs) occurred in 2 [6.3%] patients. One treatment-related death occurred.

## Conclusions

These promising results from HAIC and Bevacizumab in combination with Toripalimab may contribute to a paradigm shift in the first-line treatment for advanced BTC patients. Follow-up for survival is ongoing.

Conflict of interest: None

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