105P - A phase 2 study of SHR-1316 plus IBI310 in patients with advanced intrahepatic cholangiocarcinoma after failure of first-line therapy

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Background

- Advanced intrahepatic cholangiocarcinoma (iCCA) is highly invasive and holds high mortality due to limited therapeutic strategies after failure of first-line therapy.
- Our previous study demonstrated a heterogeneous inhibitory immune microenvironment characterized by the activation of CTLA-4 or PD1/PD-L1 signaling in the clinical setting of iCCA. This provided a rationale for combining anti-CTLA-4 therapy with anti-PD-L1 therapy.
- This study aimed to evaluate the efficacy and safety of anti-PD-L1 antibody SHR-1316 in combination with anti-CTLA-4 antibody IBI310 for patients (pts) with previously treated advanced iCCA.

Methods

- This was an open-label, single-arm, phase 2 trial (NCT04634058).
- Assuming a target ORR of 20%, the sample size of 40 pts would provide 88% power to reject the null hypothesis of a 5% ORR at a 1-sided α of 2.5%.

Figure 1. Study design

Key Eligibility Criteria
- ≥18 years
- ECOG PS: 0~1
- Unresectable, locally advanced or metastatic, histologically confirmed advanced iCCA
- Failed of first or subsequent-line treatment (prior immunotherapy with anti-CTLA-4 was not permitted)

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SHR-1316 + IBI310 × 4 cycles → SHR-1316 maintenance
IBI310 (IV 3mg/kg D1) Q3W 4 cycles
SHR-1316 (IV 20mg/kg D1) Q3W

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Treatment continued until disease progression, unacceptable toxicity, or a maximum of 2 years after enrollment.

- **Primary endpoint:** objective response rate (ORR) per RECIST v1.1
- **Secondary endpoints:** overall survival (OS), progression-free survival (PFS), disease control rate (DCR), and safety with adverse events summarized using NCI-CTCAE v5.0

Results

Patients

- Up to May 1, 2023, 39 pathologically confirmed advanced iCCA pts who have failed ≥1 prior therapies were enrolled in this study (Table 1).

Table 1. Demographics and Baseline Characteristics

Characteristics	All patients (N = 39)
Median age, y(range)	59 (28-74)
Sex, n (%)	
Male	23 (59.0)
Female	16 (41.0)
TNM stage at baseline, n (%)	
ⅢA	6 (15.4)
ⅢB	5 (12.8)
Ⅳ	28 (71.8)
Prior lines of therapy, n (%)	
1	9 (23.1)
2	12 (30.8)
≥3	18 (46.2)
Prior therapy, n (%)	
Chemotherapy	39 (100.0)
PD-1/PD-L1 inhibitor	21 (53.8)
Tyrosine kinase inhibitors	26 (66.7)

Efficacy

- Of 25 evaluable pts, the confirmed ORR and DCR were 20.0% and 60.0%, respectively (Table 2).
- At date cut-off, the median follow-up was 6.1 months (95%CI, 0.2-18.7), 28 pts were alive, 18 pts remained on treatment. The median PFS and OS were not reached yet.

Table 2. Best overall responses in evaluable pts

Response Parameters n (%)	Total (n=25)	ICIs naïve (n=12)	ICI experienced (n=13)
Complete response	2 (8.0)	1 (8.3)	1 (7.7)
Partial response	3 (12.0)	2 (16.7)	1 (7.7)
Stable disease	10 (40.0)	4 (33.3)	6 (46.1)
Objective response rate	20.0%	25.0%	15.4%
Disease control rate	60.0%	58.3%	61.5%

Safety

- Overall, 38 pts (97.4%) experienced at least one treatment-emergent AE (TEAE) during the study.
- Grade ≥ 3 TEAEs occurred in 16 pts (41.0%).
- No treatment-related death occurred.
- No new or unexpected safety signals were detected.

Table 3. Grade ≥3 TEAEs occurring in ≥5% patients

TEAE	n (%)
Jaundice	6 (15.4)
Rash	4 (10.3)
ALT elevation	3 (7.7)
Hypersensitivity	3 (7.7)
AST elevation	2 (5.1)
Diarrhea	2 (5.1)

AST, Aspartate aminotransferase; ALT, Alanine aminotransferase

Conclusions

- The treatment of SHR-1316 combined with IBI310 was tolerable and showed promising antitumor activity in iCCA refractory to standard therapy.
- Further studies are required to identify predictive/prognostic biomarkers to improve selection of pts most likely to benefit from this treatment strategy.

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Conflict of interest: None