Poster 4095

The Safety and Efficacy of Ivonescimab in Combination With Chemotherapy as First-Line Treatment for Advanced Biliary Tract Cancer

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BACKGROUND

- Although programmed cell death protein 1 (PD-1)/programmed death-ligand 1 (PD-L1) inhibitors combined with chemotherapy are approved as first-line treatment for advanced biliary tract cancer (BTC), the overall survival (OS) benefit is limited, particularly for patients with gall bladder cancer (GBC)[1]
- The combination of PD-1/PD-L1 and vascular endothelial growth factor (VEGF) antibodies have shown clinical benefit in patients with BTC[2,3]
- Ivonescimab is a novel, investigational bispecific antibody against PD-1 and VEGF that has exhibited cooperative binding in vitro[4] and could produce complementary and synergistic antitumor effects through both the PD-1 and VEGF pathways[4-6]
- A phase 1b/2 trial (NCT05214482) of ivonescimab plus chemotherapy with or without AK117 (an investigational antibody against CD47) for patients with advanced malignant tumors is ongoing
- Initial results from a cohort of the phase 2 portion of the study in which ivonescimab plus chemotherapy was assessed in participants with locally advanced or metastatic BTC are described herein

OBJECTIVE

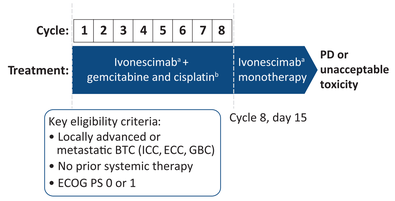
- To assess the safety and preliminary antitumor activity of ivonescimab plus chemotherapy in participants with locally advanced or metastatic BTC

METHODS

Study Design

- This study includes 1 cohort of an open-label, multicenter phase 2 trial being conducted in China to evaluate ivonescimab plus chemotherapy in adults with unresectable locally advanced or metastatic intrahepatic cholangiocarcinoma (ICC), extrahepatic cholangiocarcinoma (ECC), or GBC (**Figure 1**)

Figure 1. Study Design



BTC, biliary tract cancer; ECC, extrahepatic cholangiocarcinoma; ECOG PS, Eastern Cooperative Oncology Group performance status; GBC, gall bladder cancer; ICC, intrahepatic cholangiocarcinoma; PD, progressive disease; Q3W, once every 3 weeks.

[a]Ivonescimab 20 mg/kg or 30 mg/kg administered Q3W on day 1 for up to 8 cycles (21 days per cycle) and administered as monotherapy Q3W until PD or unacceptable toxicity.

[b]Gemcitabine 1000 mg/m^2 and cisplatin 25 mg/m^2 administered Q3W on day 1 and day 8 for up to 8 cycles.

Outcome Measures

- Primary end points were safety and investigator-assessed objective response rate (ORR) based on Response Evaluation Criteria in Solid Tumors, version 1.1
- Secondary end points included disease control rate (DCR), progression-free survival (PFS), and OS

RESULTS

Participants

- As of January 31, 2024, a total of 22 participants with advanced BTC had enrolled in the study: 12 patients (54.5%) with ICC, 1 (4.5%) with ECC, and 9 (40.9%) with GBC (**Table 1**)
  - At the time of data analysis, 13 participants remained in the study and 5 were still receiving the study treatment
- The median age of participants was 65.3 years (range, 47.7-75.6 years) and 81.8% of the patients (18/22) had an Eastern Cooperative Oncology Group performance status score of 1 at baseline (**Table 1**)
- The median duration of follow-up was 13.8 months, and median duration of exposure to ivonescimab was 8.3 months (interquartile range, 6.2-8.6 months)

Table 1. Baseline Characteristics

	Ivonescimab + chemotherapy N = 22
Dosing groups	
Ivonescimab 20 mg/kg + chemotherapy	13 (59.0)
Ivonescimab 30 mg/kg + chemotherapy	9 (41.0)
Age, median (range), years	65.3 (47.7-75.6)
Age <65 years	11 (50.0)
Sex	
Male	7 (31.8)
Female	15 (68.2)
ECOG PS score	
0	4 (18.2)
1	18 (81.8)
Primary tumor type	
ICC	12 (54.5)
ECC	1 (4.5)
GBC	9 (40.9)
Disease classification	
Locally advanced	3 (13.6)
Metastatic	19 (86.4)
PD-L1 combined positive score	
<1	6 (27.3)
≥1	10 (45.5)
Unknown	6 (27.3)

ECC, extrahepatic cholangiocarcinoma; ECOG PS, Eastern Cooperative Oncology Group performance status; GBC, gall bladder cancer; ICC, intrahepatic cholangiocarcinoma; PD-L1, programmed death-ligand 1.
Values are No. (%) unless otherwise noted.
Race/ethnicity demographics data were not collected.

Safety

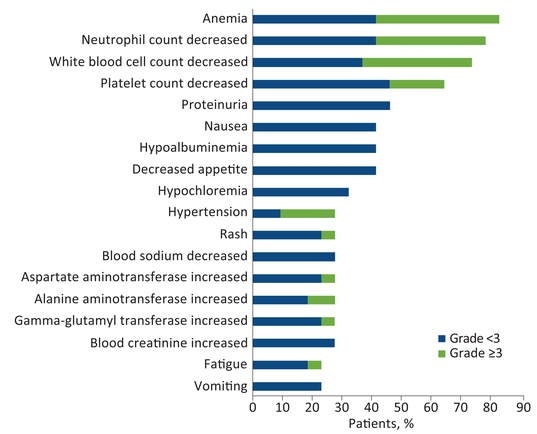
- Grade ≥3 treatment-related adverse events (TRAEs) were reported in 86.4% of participants, but none led to discontinuation of treatment or to death (**Table 2**)
- The most common grade 3 or 4 TRAEs, with a frequency of at least 10%, were anemia (40.9%), white blood cell count decreased (36.4%), neutrophil count decreased (36.4%), platelet count decreased (18.2%), and hypertension (18.2%; **Figure 2**)

Table 2. Summary of Safety Results

	Ivonescimab + chemotherapy N = 22
TEAEs	
Grade ≥3	21 (95.5)
Serious TEAEs	15 (68.2)
Leading to discontinuation	0
Leading to death	0
TRAEs	
Grade ≥3	19 (86.4)
Treatment-related serious AEs	8 (36.4)
Leading to discontinuation	0
Leading to death	0
Immune-related AEs	7 (31.8)
Grade ≥3	4 (18.2)
Gamma-glutamyl transferase increased	1 (4.5)
Lipase increased	1 (4.5)
Platelet count decreased	1 (4.5)
Rash	1 (4.5)

AE, adverse event; TEAE, treatment-emergent adverse event; TRAE, treatment-related adverse event.
Values are No. (%) unless otherwise noted.

Figure 2. Most Common (≥10%) TRAEs



TRAE, treatment-related adverse event.

Efficacy

- ORR by investigator assessment was 63.6% (14/22) overall (**Table 3**) and was 77.8% (7/9) for participants with GBC
  - Results were consistent between the ivonescimab 20 mg/kg and 30 mg/kg Q3W dosing groups
  - Individual patient-level response is shown in **Figures 3** and **4**
- DCR was 100% (22/22, 95% confidence interval [CI], 84.6-100)

Table 3. Overview of Objective Response Rate

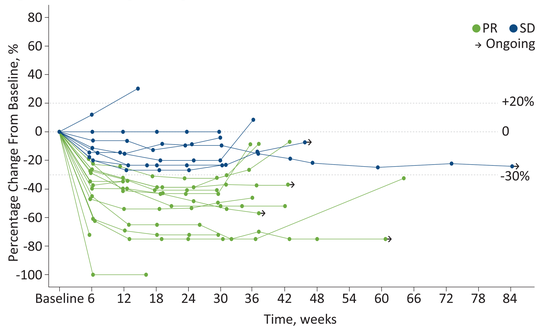
	Ivonescimab + chemotherapy N = 22
Patients who had an objective response, No. ORR (95% CI), %	14 63.6 (40.7-82.8)
Best overall response, No. (%)	
CR	0
PR	14 (63.6)
SD	8 (36.4)
PD	0

CR, complete response; ORR, objective response rate; PD, progressive disease; PR, partial response; SD, stable disease

Figure 3. Best Percentage Change From Baseline in Sum of Tumor Diameters

n, number of participants; PR, partial response; SD, stable disease.

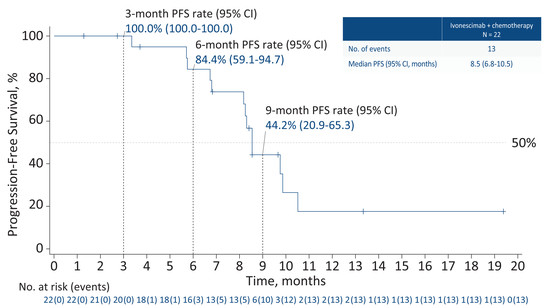
Figure 4. Percentage Change from Baseline in Sum of Diameters Over Time



PR, partial response; SD, stable disease.

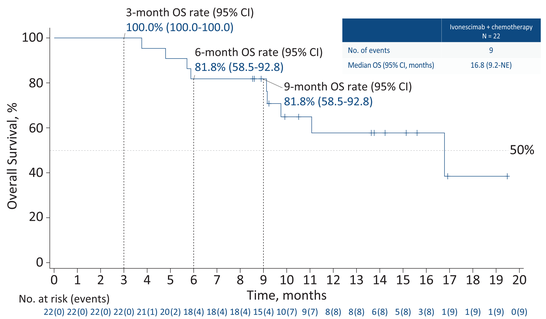
- The median PFS was 8.5 months (95% CI, 6.8-10.5), with a 6-month PFS rate of 84.4% (95% CI, 59.1-94.7; **Figure 5**)
- The median OS was 16.8 months (95% CI, 9.2 to not estimable [NE]), with a 9-month OS rate of 81.8% (95% CI, 58.5-92.8; **Figure 6**)
  - In patients with GBC, the median OS was 16.8 months (95% CI, 3.8-NE)

Figure 5. Kaplan-Meier Curve of Progression-Free Survival



N, total number of participants; PFS, progression-free survival.

Figure 6. Kaplan-Meier Curve of Overall Survival



N, total number of participants; NE, not estimable; OS, overall survival.

CONCLUSIONS

- Ivonescimab (20 or 30 mg/kg Q3W) combined with chemotherapy showed promising antitumor activity and an acceptable safety profile in participants with unresectable locally advanced or metastatic BTC
  - ORRs were comparable across dose groups in this preliminary analysis
- The most frequently reported grade 3 or 4 TRAEs (≥10%) were anemia, white blood cell count decreased, neutrophil count decreased, platelet count decreased, and hypertension
- Results of this analysis support further evaluation of ivonescimab plus chemotherapy for the treatment of BTC
- Ivonescimab is an investigational therapy that is not approved by any regulatory authority

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DISCLOSURES

Wenting Li and Yu Xia are employees of Akeso Biopharma, Inc.

Please contact the author at hzyingjieer@163.com for questions or comments.

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