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AdvanTIG-206: Phase 2 Randomized Open-Label Study of Ociperlimab (OCI) + Tislelizumab (TIS) + BAT1706 (Bevacizumab Biosimilar) Versus TIS + BAT1706 in Patients (pts) With Advanced Hepatocellular Carcinoma (HCC)

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DECLARATION OF INTERESTS

Zhenggang Ren: *Nothing to disclose*
Yao Huang: *Nothing to disclose*
Yabing Guo: *Nothing to disclose*
Ming-Mo Hou: *Nothing to disclose*
Wei Wang: *Nothing to disclose*
Ming Kuang: *Nothing to disclose*
Chunyi Hao: *Nothing to disclose*
Wentao Wang: *Nothing to disclose*
Yanqiao Zhang: *Nothing to disclose*
Tianqiang Song: *Nothing to disclose*
Chaoliu Dai: *Grants from Education Department of Liaoning Province*
Hsing-Tao Kuo: *Nothing to disclose*
Vincent Li: *Employed by BeiGene; stock or other ownership at BeiGene*
Ramil Abdrashitov: *Employed by BeiGene; stock or other ownership at BeiGene*
Lei Wang: *Employed by BeiGene; stock or other ownership at BeiGene*
Jia Fan: *Nothing to disclose*

Background

- Despite current treatment options, a high unmet medical need remains for patients with HCC, the most common type of primary liver cancer worldwide[1]
- Co-inhibition of PD-L1 and VEGF provided survival benefit compared with sorafenib in 1L advanced unresectable HCC[2,3]
- Co-inhibition of TIGIT and PD-1/PD-L1 has demonstrated antitumor activity in studies of HCC[4,5]
- **Ociperlimab (OCI)** is an IgG1 mAb engineered to bind TIGIT with high specificity and affinity[6,7]
- Tislelizumab (TIS) is an IgG4 anti–PD-1 mAb designed to minimize binding to FcγR on macrophages[8]
- BAT1706 has been approved in China as a bevacizumab (anti-VEGF mAb) biosimilar[9]
- The **phase 2, randomized, open-label, multicenter AdvanTIG-206 (NCT04948697)** study is investigating the addition of **OCI** to the TIS + BAT1706 backbone as 1L treatment of advanced HCC

Here, we report the primary analysis of efficacy and safety outcomes from **AdvanTIG-206**

Abbreviations: 1L, first-line; FcγR, Fc-gamma receptor; HCC, hepatocellular carcinoma; IgG, immunoglobulin gamma; mAb, monoclonal antibody; PD-1, programmed cell death protein-1; PD-L1, programmed death-ligand 1; TIGIT, T-cell immunoreceptor with immunoglobulin and tyrosine-based inhibitory motif domains; VEGF, vascular endothelial growth factor.

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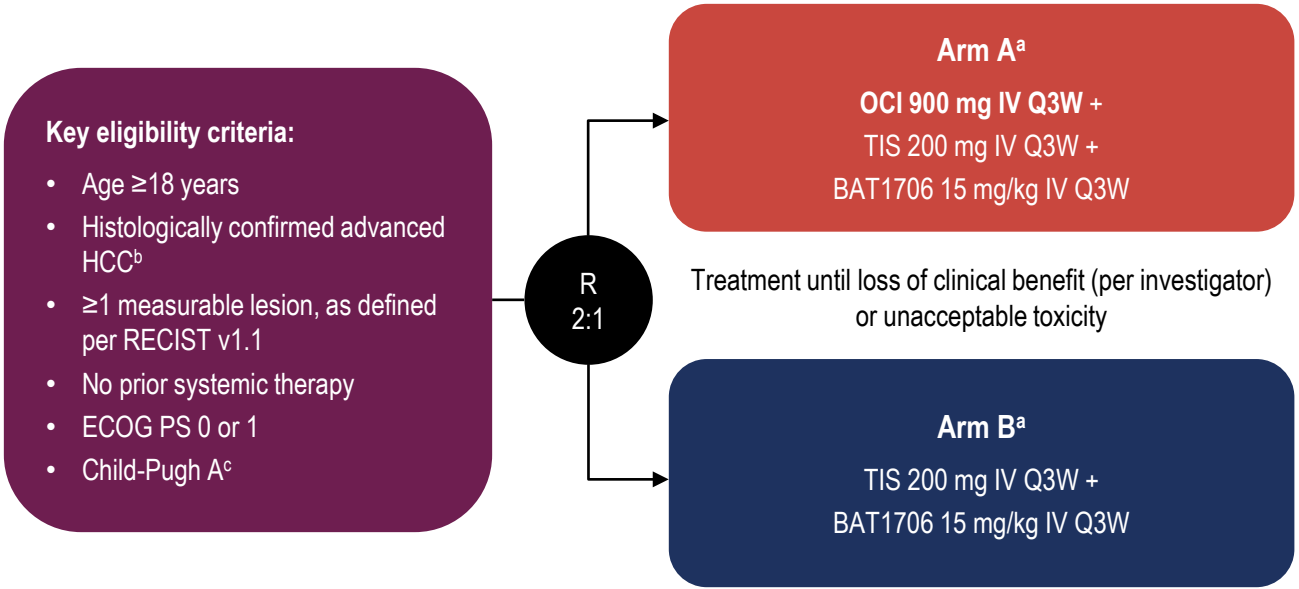
Study Design

Phase 2, randomized, open-label study conducted at 26 centers in Chinese mainland and Taiwan



Primary endpoint:
- Investigator-assessed ORR (per RECIST v1.1)

Key secondary endpoints:
- Investigator-assessed DoR (per RECIST v1.1), PFS, OS
- Safety

Exploratory endpoint:
- Correlation of biomarkers with clinical responses/resistance

Stratification factors:
- PD-L1 vCPS[d,e] (<1% vs ≥1%)
- MVI/EHS (present vs absent)

[a]All study drugs dosed in 21-day cycles. [b]Either BCLC Stage C disease or BCLC Stage B disease that is not amenable to or has progressed after loco-regional therapy and is not amenable to a curative treatment approach. [c]Assessed within 7 days of randomization. [d]PD-L1 expression was centrally assessed using the analytically validated VENTANA PD-L1 (SP263) assay. [e]Defined as the total percentage of the tumor area covered by tumor cells with PD-L1 membrane staining at any intensity and tumor-associated immune cells with PD-L1 staining at any intensity.

Abbreviations: BCLC, Barcelona Clinic Liver Cancer; DoR, duration of response; ECOG, Eastern Cooperative Oncology Group; EHS, extrahepatic spread; HCC, hepatocellular carcinoma; IV, intravenously; MVI, macrovascular invasion; OCI, ociperlimab; ORR, objective response rate; OS, overall survival; PD-L1, programmed death-ligand 1; PFS, progression-free survival; PS, performance status; Q3W, every 3 weeks; RECIST v1.1, Response Evaluation Criteria in Solid Tumors version 1.1; TIS, tislelizumab; vCPS, visually estimated combined positive score.

Baseline Characteristics

	Arm A (n=62)	Arm B (n=32)
Median (range) age, years	57.0 (28, 85)	60.0 (30, 78)
Male	57 (91.9)	30 (93.8)
ECOG PS 1	23 (37.1)	14 (43.8)
PD-L1 expression per IRT		
<1%	33 (53.2)	18 (56.3)
≥1%	29 (46.8)	14 (43.8)
TIGIT expression[a]		
<1%	28 (46.7)	16 (50.0)
≥1%	32 (53.3)	16 (50.0)
MVI/EHS per IRT		
Present	41 (66.1)	21 (65.6)
Absent	21 (33.9)	11 (34.4)

	Arm A (n=62)	Arm B (n=32)
Viral status		
HBV infected only	52 (83.9)	24 (75.0)
HCV infected only	2 (3.2)	3 (9.4)
HBV and HCV coinfected	1 (1.6)	0 (0.0)
Uninfected[b]	7 (11.3)	5 (15.6)
Other relevant medical history	46 (74.2)	27 (84.4)
Alcoholic hepatitis	3 (4.8)	0 (0.0)
NASH/fatty liver	1 (1.6)	1 (3.1)
Underlying cirrhosis	39 (62.9)	20 (62.5)
Partial or complete portal vein thrombosis	13 (21.0)	7 (21.9)
Esophageal varices	10 (16.1)	12 (37.5)
Ascites	10 (16.1)	4 (12.5)
Jaundice	1 (1.6)	0 (0.0)

Baseline characteristics, including PD-L1 and TIGIT expression, were generally well balanced between arms

ITT analysis set. Data cutoff February 27, 2023. Data are n (%) unless otherwise stated. [a]TIGIT expression is available in 60 patients in Arm A and 32 patients in Arm B. Two patients in Arm A have no result of TIGIT expression due to technical issues. [b]"Uninfected" includes patients without a medical history of HBV and/or HCV infections.

Abbreviations: ECOG, Eastern Cooperative Oncology Group; EHS, extrahepatic spread; HBV, hepatitis B virus; HCV, hepatitis C virus; IRT, Interactive Response Technology; ITT, intention-to-treat; MVI, macrovascular invasion; NASH, nonalcoholic steatohepatitis; PD-L1 programmed death-ligand 1; PS, performance status; TIGIT, T-cell immunoreceptor with immunoglobulin and tyrosine-based inhibitory motif domains.

Disease Response

Median study follow-up time of 9.2 months

	Arm A (n=62)	Arm B (n=32)
***Primary endpoint*—ORR, % (95% CI)**	35.5 (23.7, 48.7)	37.5 (21.1, 56.3)
	2-sided P=0.8350[a]	
Best overall response, n (%)		
CR	0	0
PR	22 (35.5)	12 (37.5)
SD	26 (41.9)	11 (34.4)
PD	10 (16.1)	7 (21.9)
NE	4 (6.5)	2 (6.3)
Median DoR, months (95% CI)	12.6 (7.0, NE)	10.6 (4.2, NE)
Response ongoing without event at data cutoff, n (%)	16 (72.7)	9 (75.0)

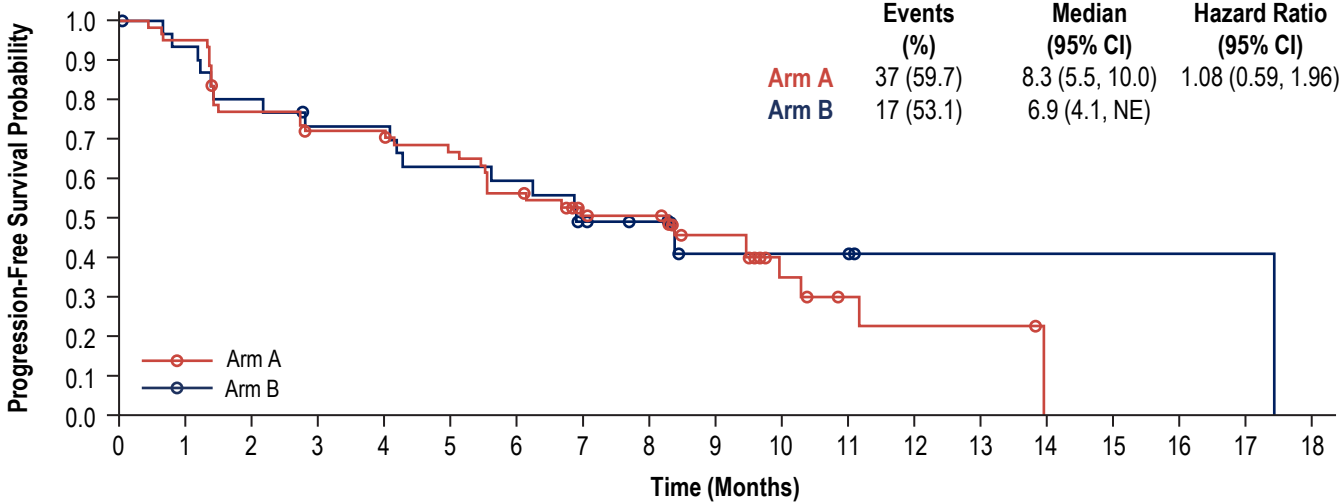
- In patients with baseline PD-L1 expression of ≥1% (29 in Arm A, 14 in Arm B), the ORR was numerically higher in those receiving OCI + TIS + BAT1706 (44.8%) compared with those receiving TIS + BAT1706 (35.7%)

TIS + BAT1706 demonstrated a promising ORR in patients with advanced HCC

Adding **OCI** to TIS + BAT1706 was not associated with improved antitumor activity in the overall population

ITT analysis set. Data cutoff February 27, 2023. ORR, best overall response, and DoR per investigator assessment using RECIST v1.1. After first documentation of response (CR or PR), confirmation of tumor response occurred ≥4 weeks later. [a]*P*-value for descriptive purposes only.
Abbreviations: CI, confidence interval; CR, complete response; DoR, duration of response; HCC, hepatocellular carcinoma; ITT, intention-to-treat; NE, not estimable; OCI, ociperlimab; ORR, objective response rate; PD, progressive disease; PD-L1 programmed death-ligand 1; PR, partial response; SD, stable disease; RECIST v1.1, Response Evaluation Criteria in Solid Tumors version 1.1; TIS, tislelizumab.

Progression-Free Survival



	Events (%)	Median (95% CI)	Hazard Ratio (95% CI)	*P*-value
Arm A	37 (59.7)	8.3 (5.5, 10.0)	1.08 (0.59, 1.96)	0.4056
Arm B	17 (53.1)	6.9 (4.1, NE)		

Number at Risk:

Arm A	62	58	46	42	42	38	32	24	23	16	7	4	3	3	0	0	0	0	0
Arm B	32	28	24	21	21	18	17	12	10	4	4	4	1	1	1	1	1	1	0

PFS was similar between treatment arms; OS data require further follow-up

ITT analysis set. Data cutoff February 27, 2023. Median study follow-up time of 9.2 months. Median was estimated by the Kaplan-Meier method with 95% CIs estimated using the Brookmeyer and Crowley method with log-log transformation. HR and 95% CIs were estimated using a Cox regression model stratified by PD-L1 expression and MVI/EHS. Efron method will be used to handle ties if there are any. The 1-sided P-value was calculated using a log-rank test stratified by PD-L1 expression and MVI/EHS. *P*-value is for descriptive purposes only.
Abbreviations: CI, confidence interval; EHS, extrahepatic spread; HR, hazard ratio; ITT, intention-to treat; MVI, macrovascular invasion; NE, not estimable; OS, overall survival; PD-L1, programmed death-ligand 1; PFS, progression-free survival.

Safety

	Arm A (n=62)	Arm B (n=31)
Patients with any TEAE	62 (100.0)	31 (100.0)
≥Grade 3	40 (64.5)	15 (48.4)
Serious	30 (48.4)	10 (32.3)
Leading to death[a]	3 (4.8)	0 (0.0)
Leading to treatment discontinuation	14 (22.6)	4 (12.9)
Patients with any TRAE	56 (90.3)	24 (77.4)
≥Grade 3	31 (50.0)	8 (25.8)
Serious	16 (25.8)	2 (6.5)
Leading to death[a]	3 (4.8)	0 (0.0)
Leading to treatment discontinuation	10 (16.1)	2 (6.5)
Patients with any imAE	27 (43.5)	12 (38.7)
Patients with any IRR	1 (1.6)[b]	0 (0.0)

- Grade ≥3 TRAEs occurring in ≥5% of patients in both arms were hypertension (14.5% Arm A, 6.5% Arm B) and proteinuria (6.5% in both arms); all were of Grade 3

OCI + TIS + BAT1706 was generally well tolerated with an acceptable safety profile

Safety analysis set. Data cutoff February 27, 2023. Data are n (%). AEs were graded using NCI-CTCAE v5.0. Treatment-related TEAEs include those events considered by the investigator to be related or with missing assessment of the causal relationship. [a]Excluding death due to disease under study. Included cerebral ischemia, hepatitis, and upper gastrointestinal perforation and deemed treatment-related by investigator. [b]IRR was of Grade < 3.

Abbreviations: AE, adverse event; imAE, immune-mediated adverse event; IRR, infusion-related reaction; NCI-CTCAE, National Cancer Institute Common Terminology Criteria for Adverse Events; OCI, ociperlimab; TEAE, treatment-emergent adverse event; TIS, tislelizumab; TRAE, treatment-related adverse event.

Conclusions

- In **AdvanTIG-206**, adding **OCI** to the doublet of TIS + BAT1706 was not associated with improved antitumor activity in the overall population
  - TIS + BAT1706 demonstrated a promising ORR in patients with advanced HCC
  - In patients with baseline PD-L1 expression of ≥1%, the response rate was numerically higher in those receiving **OCI** + TIS + BAT1706 compared with those receiving TIS + BAT1706
  - PFS was similar between treatment arms; OS data require further follow-up
- No new safety signals were identified in either study arm

Abbreviations: HCC, hepatocellular carcinoma; OCI, ociperlimab; ORR, objective response rate; OS, overall survival; PD-L1, programmed death-ligand 1; PFS, progression-free survival; TIS, tislelizumab.

Thank you!

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