Abstract 201P: A phase 2 study of serplulimab (a programmed death-1 inhibitor) with or without HLX04 (a bevacizumab biosimilar) for the treatment of advanced hepatocellular carcinoma

Zhenggang Ren[1], Guoliang Shao[2], Jie Shen[3], Li Zhang[4], Xu Zhu[5], Weijia Fang[6], Guoping Sun[7], Yuxian Bai[8], Jianbing Wu[9], Lianxin Liu[10], Yuan Yuan[11], Jingdong Zhang[12], Zhen Li[13], Ling Zhang[14], Tao Yin[15], Jincai Wu[16], Xiaoli Hou[17], Qingyu Wang[17], Jun Zhu[17], Jia Fan[1,*]

1. Liver Cancer Institute, Zhongshan Hospital, Fudan University, Shanghai, China; 2. Department of Interventional Radiology, Cancer Hospital of the University of Chinese Academy of Sciences (Zhejiang Cancer Hospital), Hangzhou, China; 3. Department of Oncology, Nanjing Drum Tower Hospital, the Affiliated Hospital of Nanjing University Medical School, Nanjing, China; 4. Department of Oncology, Chongqing University Three Gorges Hospital, Chongqing, China; 5. Key Laboratory of Carcinogenesis and Translational Research (Ministry of Education/Beijing), Department of Interventional Therapy, Peking University Cancer Hospital & Institute, Beijing, China; 6. Department of Medical Oncology, The First Affiliated Hospital, Zhejiang University School of Medicine, Hangzhou, China; 7. Department of Oncology, The First Affiliated Hospital of Anhui Medical University, Hefei, China; 8. Department of Gastrointestinal Oncology, Harbin Medical University Cancer Hospital, Harbin, China; 9. Department of Oncology, The Second Affiliated Hospital of Nanchang University, Nanchang, China; 10. Department of Hepatobiliary Surgery, Anhui Provincial Hospital, the First Affiliated Hospital of University of Science and Technology of China, Hefei, China; 11. Department of Oncology, Xuzhou Central Hospital, Xuzhou, China; 12. Medical Oncology Department of Gastrointestinal Cancer, Liaoning Cancer Hospital & Institute, Cancer Hospital of China Medical University, Shenyang, China; 13. Department of Medical Oncology, Linyi Cancer Hospital, Linyi, China; 14. Department of Hepatobiliary and Pancreatic Surgery, Henan Cancer Hospital, the Affiliated Cancer Hospital of Zhengzhou University, Zhengzhou, China; 15. Department of Hepatobiliary and Pancreatic Surgery, Hubei Cancer Hospital, Wuhan, China; 16. Department of Hepatobiliary and Pancreatic Surgery, Hainan General Hospital, Haikou, China; 17. Shanghai Henlius Biotech, Inc., Shanghai, China

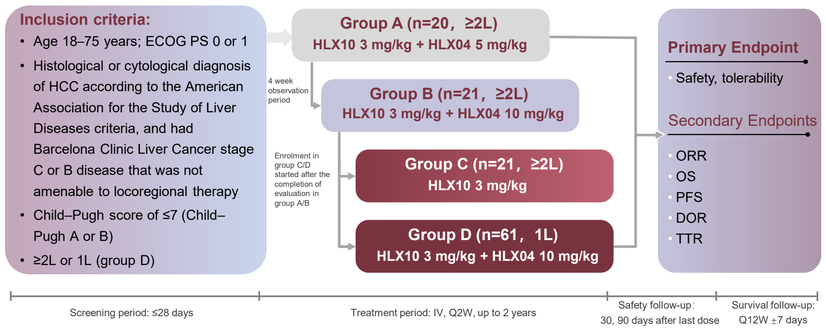
Background

- Primary liver cancer ranked as the sixth most common cancer and the third leading cause of cancer death worldwide in 2020[1]. Hepatocellular carcinoma (HCC) is the predominant type of liver cancer, comprising about 90% of cases[2].
- First-line treatments recommended for advanced HCC include tyrosine kinase inhibitors (TKI) and the anti-programmed death-ligand 1 (PD-L1) plus anti-angiogenesis combination therapy[3-4].
- Serplulimab is a fully humanized monoclonal anti-programmed death 1 (PD-1) antibody. HLX04 (Han-Bei-Tai®) is a bevacizumab biosimilar approved by the China National Medical Products Administration (NMPA) which has shown equivalences to reference bevacizumab[5-6].
- The effect of serplulimab plus HLX04 in previously treated HCC patients (group A and B) have been published[7].
- Here we report the results of serplulimab as monotherapy in previously treatment HCC patients (group C) or as combination therapy with HLX04 for previously untreated HCC patients (group D).

Methods

- This is a multicenter, open-label, single-arm, phase 2 clinical trial in China to assess the safety and tolerability of serplulimab alone or in combination with HLX04 for treating advanced HCC in a first-line or subsequent-line setting (NCT03973112).
- Tumor imaging by computed tomography or magnetic resonance imaging was scheduled at baseline, every 6 weeks for 24 weeks from the first dose, every 8 weeks from week 25 to week 48, and every 12 weeks thereafter. Tumor response was assessed by the IRRC and by investigators per RECIST v1.1.

Figure 1. Study design



1L, first line; 2L, second line; DOR, duration of response; ECOG PS, Eastern Cooperative Oncology Group performance status; HCC, hepatocellular carcinoma; IV, intravenous; ORR, objective response rate; OS, overall survival; PFS, progression-free survival; Q2W: every 2 weeks; Q12W: every 12 weeks; RECIST, Response Evaluation Criteria in Solid Tumors; TTR, time to response.

Results

- As of the data cut-off date (7 February 2023), 238 subjects were screened, and 123 (51.7%) were enrolled in group A (N = 20), group B (N = 21), group C (N = 21), and group D (N = 61).
- The median follow-up durations in group C and D were 26.0 months and 25.5 months, respectively.
- Baseline demographics and characteristics of group C and group D are shown in Table 1.

References

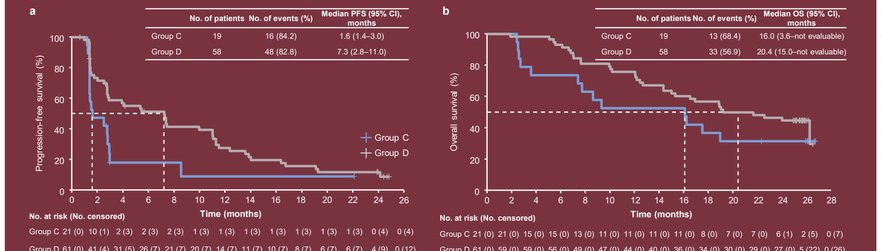
1. CA Cancer J Clin. 2021 May;71(3):209-49.
2. Nat Rev Dis Primers. 2021 Jan 21;7(1):6.
3. Guidelines of Chinese Society of Clinical Oncology. Hepatocellular carcinoma. 2020.
4. NCCN Guideline Version 2.2023.
5. Cancer Chemother Pharmacol. 2021 Sep;88(3):465-74.
6. BioDrugs. 2021 Jul;35(4):445-58.
7. Liver Cancer. 2023 Jun;12(2):116-128.

Presenter: Professor Zhenggang Ren; E-mail: ren.zhenggang@zs-hospital.sh.cn

In the first-line and subsequent-line settings, serplulimab plus HLX04 and serplulimab monotherapy, respectively, showed a manageable safety profile together with encouraging efficacy in patients with advanced HCC.

Efficacy

Figure 2. Kaplan–Meier curves of progression-free survival assessed by the IRRC (a) and overall survival (b)*



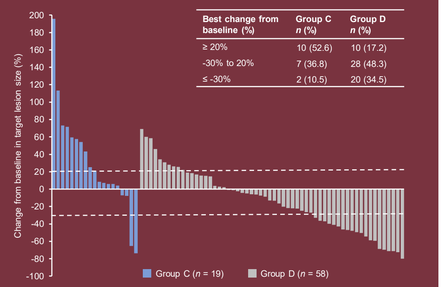
**Results in efficacy evaluable patients, of which five patients without post-baseline tumor assessment were excluded.*
CI, confidence interval; HCC, Hepatocellular carcinoma; IRRC, Independent Radiology Review Committee; No., number; OS, overall survival; PFS, progression-free survival.

- With serplulimab monotherapy, the median PFS (95% CI) and OS (95% CI) were 1.6 (1.4-3.0) months and 16.0 (3.6-not evaluable) months, respectively, in group C among the efficacy evaluable patients (n=19) （Figure 2）. For all the 21 patients treated in group C, the median PFS (95% CI) and OS (95% CI) were 1.8 (1.4-2.8) months and 16.0 (3.6-not evaluable) months, respectively.
- The first-line treatment of serplulimab plus HLX04 resulted in a median PFS (95% CI) of 7.3 (2.8–11.0) months, and a median OS (95% CI) of 20.4 (15.0–not evaluable) months in group D among the efficacy evaluable patients (n=58) (Figure 2). For all the 61 patients treated in group D, the median PFS (95% CI) and OS (95% CI) were 7.3 (2.8-11.0) months and 19.1 (14.3-not evaluable) months, respectively.

Table 2. Tumor response assessed by IRRC per RECIST 1.1

	Group C (n = 21)	Group D (n = 61)
ORR, % (95% CI)	4.8 (0.1, 23.8)	27.9 (17.1, 40.8)
DCR, % (95% CI)	33.3 (14.6, 57.0)	63.9 (50.6, 75.8)
CR, n (%)	0	0
PR, n (%)	1 (4.8)	17 (27.9)
SD, n (%)	6 (28.6)	22 (36.1)
PD, n (%)	12 (57.1)	18 (29.5)
NE, n (%)	0	1 (1.6)
Missing, n (%)	2 (9.5)	3 (4.9)
DOR, % (95% CI)	NE (NE, NE)	12.7 (4.5, NE)

Figure 3. Best percentage change from baseline in target lesion size assessed by IRRC



CI, confidence interval; CR, complete response; DCR, disease control rate; DOR, duration of response; IRRC, Independent Radiology Review Committee; NE, not evaluable; ORR, objective response rate; PD, progressive disease; PFS, progression-free survival; PR, partial response; RECIST, Response Evaluation Criteria in Solid Tumors; SD, stable disease.

- The ORR and DCR in group C (n=21) were 4.8% (95% CI: 0.1–23.8) and 33.3% (95% CI: 14.6–57.0), respectively.
- The ORR and DCR in group D (n=61) were 27.9% (95% CI: 17.1–40.8) and 63.9% (95% CI: 50.6–75.8), respectively.
- The median DOR in group C was not reached (95% CI: NE, NE). 1 (100%) patient had a DOR ≥ 6 months.
- The median DOR in group D was 12.65 months (95% CI: 4.47, NE). 12 (70.6%) patients had a DOR ≥ 6 months.

Table 1. Patient demographics and baseline characteristics

	Group C (n = 21)	Group D (n = 61)
Median age (range), years	57.0 (35-71)	55.0 (31-73)
Sex, n (%)		
Male	19 (90.5)	54 (88.5)
Female	2 (9.5)	7 (11.5)
Ethnicity, n (%)		
Han	20 (95.2)	61 (100)
Others	1 (4.8)	0
Median BMI (range), kg/m²	22.7 (16.4-28.1)	23.1 (15.2-29.3)
ECOG PS, n (%)		
0	8 (38.1)	36 (59.0)
1	13 (61.9)	25 (41.0)
Distant metastasis stage, n (%)		
M0	3 (14.3)	32 (52.5)
M1	18 (85.7)	29 (47.5)
BCLC stage, n (%)		
B	1 (4.8)	11 (18.0)
C	20 (95.2)	50 (82.0)
Chid-Pugh class		
A	20 (95.2)	61 (100)
B	1 (4.8)	0
Macrovascular invasion, n (%)	5 (23.8)	21 (34.4)
Alpha-fetoprotein >400 ng/mL, n (%)	11 (52.4)	27 (44.3)
HBV infection, n (%)	21 (100)	60 (98.4)
HCV antibody positive, n (%)	0	3 (4.9)

BCLC, Barcelona clinic liver cancer; BMI, body mass index; ECOG PS, Eastern Cooperative Oncology Group performance status; HBV, hepatitis B virus; HCV, hepatitis C virus.

Safety

- Grade 3 or higher TEAEs were observed in 10 (47.6%) and 29 (47.5%) patients in group C and D, respectively. (Table 3). The most common Grade 3 or higher TEAEs in group C and group D are listed in Table 4.
- Grade 3 or higher TRAEs were observed in 6 (28.6%) and 25 (41.0%) patients in group C and D, respectively.
- TRAEs leading to death were reported in two patients, one each in group C (hepatic failure) and group D (hepatic failure and disease progression).
- irAEs were reported in 3 (14.3%) and 20 (32.8%) patients in group C and group D, respectively.

Table 3. Summary of TEAEs

n (%)	Group C (n = 21)	Group D (n = 61)
Any TEAEs	21 (100)	60 (98.4)
Grade ≥ 3 TEAEs	10 (47.6)	29 (47.5)
TESAEs	7 (33.3)	17 (27.9)
TEAEs leading to drug discontinuation[a]	1 (4.8)	9 (14.8)
TEAEs leading to death	3 (14.3)	3 (4.9)
TRAEs[b]	17 (81.0)	57 (93.4)
Grade ≥ 3 TRAEs	6 (28.6)	25 (41.0)
TRSAEs	2 (9.5)	9 (14.8)
TRAEs leading to drug discontinuation[a]	1 (4.8)	7 (11.5)
TRAEs leading to death	1 (4.8)	1 (1.6)
AESIs	5 (23.8)	25 (41.0)
IRRs	0	0
irAEs	3 (14.3)	20 (32.8)
Others	2 (9.5)	10 (16.4)

Table 4. Most common Grade ≥ 3 TEAEs (≥5%)

SOC PT	Group C (n = 21)	Group D (n = 61)
All Grade ≥ 3 TEAEs	10 (47.6)	29 (47.5)
Investigations	5 (23.8)	15 (24.6)
Platelet count decreased	0	6 (9.8)
Blood bilirubin increased	3 (14.3)	3 (4.9)
Aspartate aminotransferase increased	1 (4.8)	5 (8.2)
Lymphocyte count decreased	0	6 (9.8)
Metabolism and nutrition disorders	4 (19.0)	4 (6.6)
Hyponatraemia	2 (9.5)	1 (1.6)
Vascular disorders	2 (9.5)	5 (8.2)
Hypertension	2 (9.5)	4 (6.6)
Renal and urinary disorders	0	7 (11.5)
Proteinuria	0	6 (9.8)
General disorders and administration site conditions	2 (9.5)	2 (3.3)
Disease progression	2 (9.5)	2 (3.3)

[a] Discontinuation of HLX10 or HLX04; [b] Related to HLX10 or HLX04.
AESI, adverse event of special interest; irAE, immune-related adverse event; IRR, infusion-related reactions; PT, preferred term; SOC, System Organ Class; TEAE, treatment-emergent adverse event; TESAE, serious TEAE; TRSAE, serious TRAE; TRAE, treatment-related adverse event.

Acknowledgments and Disclosures

- The authors would like to acknowledge the participants in this study and their families, the investigators and staff at all clinical sites and the members of the Independent Data Monitoring Committee.
- This study was funded by Shanghai Henlius Biotech, Inc. Editorial support was provided by Shiqi Zhong, and Chen Hu from Shanghai Henlius Biotech, Inc.
- Xiaoli Hou, Qingyu Wang, and Jun Zhu are employees of Shanghai Henlius Biotech, Inc.

2023 European Society for Medical Oncology (ESMO) Asia Congress, December 1 – 3, 2023