Combination Therapy of Envafolimab and Suvemcitug in Patients with Hepatocellular Carcinoma: Results from a Phase II Clinical Trial

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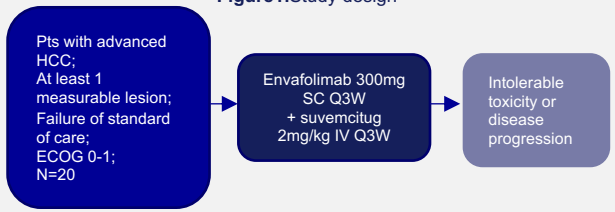
BACKGROUND

- The efficacy of immune checkpoint inhibitors combined with antiangiogenesis agents has been demonstrated in a variety of solid tumors including hepatocellular carcinoma (HCC).
- Suvemcitug, selectively binds to and blocks VEGFA from binding to VEGFR1 and 2, thereby inhibiting its activities and preventing tumour angiogenesis and ultimately suppressing tumour growth and metastasis.
- Envafolimab is a humanized single-domain anti-PD-L1 antibody which is administered subcutaneously (SC).
- This study aims to assess the efficacy and safety of the combination of suvemcitug and envafolimab as second-line or later therapy in patients (pts) with advanced HCC.

METHODS

- This was an open-label, multi-cohort, multicenter, phase II trial conducted in China. In Cohort B, eligible pts had received at least one prior line of treatment for HCC and were treated with suvemcitug (2 mg/kg IV Q3W) plus envafolimab (300 mg SC Q3W) until disease progression or unacceptable toxicity was observed. The primary endpoint was objective response rate (ORR) assessed by investigators based on RECIST v1.1 criteria. Secondary endpoints included disease control rate (DCR), duration of response (DoR), progression-free survival (PFS) and safety.

Figure1. Study desigh



RESULTS

- As of June 30,2023, a total of 20 pts were treated with envafolimab and suvemcitug. 80.0% pts (16/20) received one prior therapy and 40.0% pts (8/20) had been treated with PD-1/L1 antibody.

Table1. Demographic and baseline characteristics

Demographic and baseline characteristics	No.(%)
Age	
Mean (SD)	55.65 (8.18)
Median (range)	54.50 (42, 70)
Sex	
Male	19 (95.00%)
Female	1 (5.00%)
Any previous PD-1/L1 therapy	
Yes	8 (40.00%)
No	12 (60.00%)
Prior lines of therapy	
1 prior line	16 (80.00%)
≥ 2 prior lines	4 (20.00%)
PD-L1 expression*	
IC < 1%	5 (25.00%)
IC ≥ 1%	3 (15.00%)
Unknown	12 (60%)

Demographic and baseline characteristics	No.(%)
Cause of hepatocellular carcinoma	
Hepatitis B	18 (90.00%)
Unknown	2 (10.00%)
Baseline ECOG PS	
ECOG: 0	8 (40.00%)
ECOG: 1	12 (60.00%)
BCLC Stage	
Stage B	6 (30.00%)
Stage C	14 (70.00%)
Previous vascular invasion	
Yes	2 (10.00%)
No	18 (90.00%)
Baseline SLD of target lesions(mm)	
Mean (SD)	96.97 (52.52)
Median (range)	102.30 (13.20, 221.40)

* Detected by SP263

- After a median follow up of 12.71 (95% CI, 9.89, 12.94) months, 3 pts are still on treatment. Among 18 efficacy-evaluable pts, 2 pts achieved partial response, 1 of whom had previously received sorafenib only and the other lenvatinib only. The DCR was 72.2% (13/18).The median PFS was 4.3 (95% CI, 1.4-8.1) months.

Table2. Summary of Objective Response

	N=18
ORR，n（%）	2 (11.1%)
95%CI	(1.38,34.71)
BoR，n（%）	
PR	2 (11.1%)
SD	11 (61.1%)
PD	5 (27.8%)
DCR，n（%）	13 (72.2%)
95%CI	(46.52,90.31)

ORR: Objective response rate; BoR: Best of response;
DCR: Disease control rate; PR: Partial response;
SD: Stable disease; PD: Progressive disease

Figure2. Kaplan-Meier curves of PFS in patients with HCC treated with suvemcitug plus envafolimab

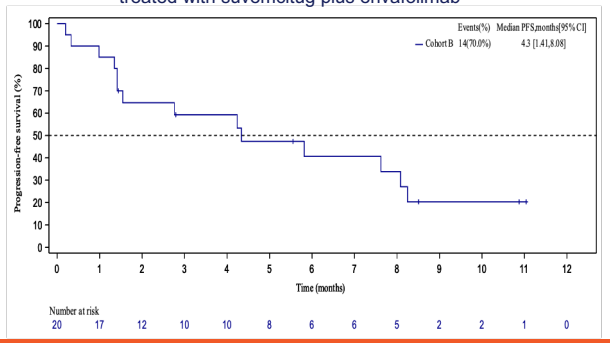


Figure3. Duration of the Treatment

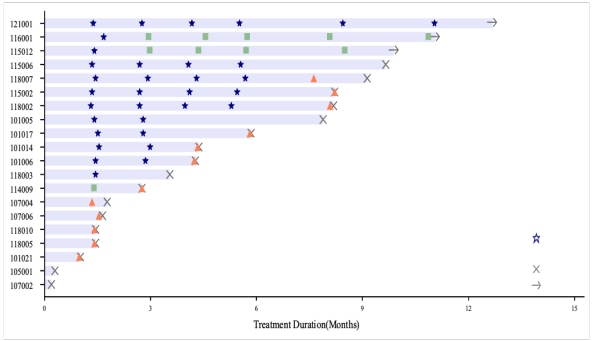
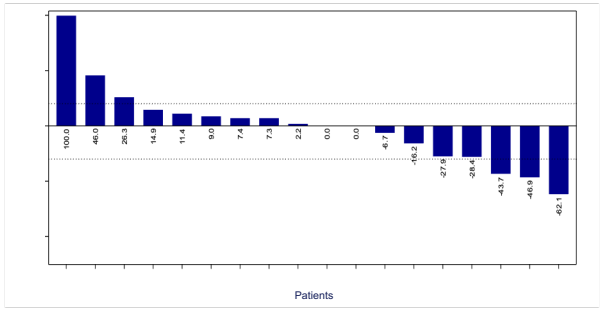


Figure4. Best Change of the Sum of Target Lesions from Baseline



- Any grade treatment-emergent adverse evens(TEAEs) occurred in 100%(n=20) of pts. The most common treatment-related adverse events (TRAEs) were proteinuria (50.0%,10/20), aspartate aminotransferase increased (35.0%,7/20), gamma-glutamyltransferase increased (25.0%,5/20), hypertension (25.0%,5/20), platelet count decreased (25.0%,5/20) and white blood cell count decreased (20.0%,4/20).
- The most common grade ≥ 3 TRAEs were proteinuria (20.0%,4/20), gamma-glutamyltransferase increased (5%,1/20), hypertension (5%,1/20), platelet count decreased (5%, 1/20), anaemia (5%, 1/20), and blood bilirubin increased (5%, 1/20).
- In total, 1 patient experienced acute myocardial infarction leading to death and was not related to study treatment.

Table3. Overview of TEAEs

	N = 20 n (%)
TEAEs	20 (100%)
Related to study treatment	17 (85.0%)
Related to suvemcitug	16 (80.0%)
Related to envafolimab	15 (75.0%)
TESAEs	6 (30.0%)
Related to study treatment	3 (15.0%)
Related to suvemcitug	3 (15.0%)
Related to envafolimab	3 (15.0%)
≥ Grade 3 TEAEs	10 (50.0%)
Related to study treatment	8 (40.0%)
Related to suvemcitug	8 (40.0%)
Related to envafolimab	6 (30.0%)

	N = 20 n (%)
AE leading to Death	1 (5.0%)
Related to study treatment	0
Related to suvemcitug	0
Related to envafolimab	0
Dose discontinuation	1 (5.0%)
Suvemcitug	1 (5.0%)
Envafolimab	0
Dose interruption	9 (45.0%)
Suvemcitug	6 (30.0%)
Envafolimab	9 (45.0%)
Dose reduction	4 (20.0%)
Suvemcitug	4 (20.0%)
Envafolimab	0

Table4. Summary of TRAEs(≥15%)

TRAEs	N=20，n(%)	
	All grade	≥ Grade 3
Proteinuria	10 (50.0%)	4 (20.0%)
Aspartate aminotransferase increased	7 (35.0%)	0
Gamma-glutamyltransferase increased	5 (25.0%)	1 (5.0%)
Hypertension	5 (25.0%)	1 (5.0%)
Platelet count decreased	5 (25.0%)	1 (5.0%)
White blood cell count decreased	4 (20.0%)	0
Anaemia	3 (15.0%)	1 (5.0%)
Blood bilirubin increased	3 (15.0%)	1 (5.0%)
Alanine aminotransferase increased	3 (15.0%)	0
Weight decreased	3 (15.0%)	0

CONCLUSIONS

- The combination of envafolimab and suvemcitug was tolerable and the adverse events were manageable with no new safety concerns.
- Suvemcitug and envafolimab demonstrated modest antitumor activity in previously treated HCC pts which were generally comparable to similar studies.
- Clinical trial information:NCT05148195.

Acknowledgment
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Disclosure
Dr. Cheng confirm that she does not have conflicts of interest to declare.