Combination Therapy of Envafolimab and Suvemcitug with chemotherapy in Patients with Non-Small Cell Lung Cancer: Results from a Phase II Clinical Trial

#1467P

C. Wu[1], L. Wu[2], X. Meng[3], Y. Wang[4], Q. Fan[5], X. Wang[6], K. Gu[7], R. Ma[8], C. Hu[9], L. Lu[10], F. Su[11], C. Yang[12], Z. Liu[12], J. Tian[12], X. Sun[13], S. Sun[14], Y. Cheng[1];

[1]Internal Medicine, Jilin Cancer Hospital, Changchun, China, [2]Chest medicine 2, Hunan Cancer Hospital, Changsha, China, [3]Radiation Oncology, Shandong Cancer Hospital, Jinan, China, [4]Respiratory Medicine, Harbin Medical University Cancer Hospital, Harbin, China, [5]Oncology Department, The First Affiliated Hospital of Zhengzhou University, Zhengzhou, China, [6]Medical oncology, The First Affiliated Hospital of Gannan Medical University, Ganzhou, China, [7]Medical Oncology, The First Affiliated Hospital of Anhui Medical University, Hefei, China, [8]Chest medicine 2, Liaoning Cancer Hospital & Institute, Shenyang, China, [9]Medical Oncology Department, Anhui Provincial Cancer Hospital, Hefei, China, [10]Medical oncology, Zhejiang Provincial People's Hospital, Hangzhou, China, [11]Medical oncology, The First Affiliated Hospital of Bengbu Medical College, Bengbu, China, [12]Clinical Science,Shandong Simcere Biopharmaceutical Co., Ltd., Shandong, China, [13]Clinical Pharmacology, Shandong Simcere Biopharmaceutical Co., Ltd., Shandong, China, [14]Clinical Statistics, Shandong Simcere Biopharmaceutical Co., Ltd., Shandong, China

BACKGROUND

- The combination of anti–PD-1/PD-L1 antibody and chemotherapy with or without anti-angiogenic agent has shown antitumor activity in non-small cell lung cancer (NSCLC).
- This study aims to assess the efficacy and safety of envafolimab (anti- PD-L1 antibody) in combination with suvemcitug (anti-VEGF antibody) and chemotherapy as second-line or later therapy in patients (pts) with advanced NSCLC.

METHODS

- This was an open-label, multi-cohort, multicenter, phase II trial conducted in China.
- In Cohort C, NSCLC pts with at least one prior line of treatment were enrolled, stratified by the history of prior immunotherapy. Envafolimab (300 mg SC Q3W) plus suvemcitug (2 mg/kg IV Q3W) and docetaxel (75mg/m^2 IV Q3W) were administrated until disease progression or unacceptable toxicity. The primary endpoint was objective response rate (ORR) assessed by investigator review using RECIST v1.1. Secondary endpoints included progression-free survival (PFS), duration of response (DoR), disease control rate (DCR) and safety.

RESULTS

- As of June 30, 2023, 40 pts were enrolled in NSCLC cohort, including 20 immunotherapy (IO) treated NSCLC (Cohort C1) and 20 IO naïve NSCLC (Cohort C2). 72.5% (29/40) pts were treated with one prior therapy and 25.0% (10/40) pts with EGFR alteration.

Table1. Demographic and baseline characteristics

Demographic and baseline characteristics	C1 No.(%)	C2 No.(%)
Age		
Mean (SD)	59.10 (5.79)	59.45 (9.03)
Median (range)	59.00 (50, 72)	60.50 (43, 73)
Sex		
Male	18 (90.00%)	16 (80.00%)
Female	2 (10.00%)	4 (20.00%)
Prior lines of therapy*		
1 prior line	15 (75.00%)	14 (70.00%)
≥ 2 prior lines	5 (25.00%)	6 (30.00%)
Pathological classification		
Adenocarcinoma	12 (60.00%)	19 (95.00%)
Squamous cell carcinoma	8 (40.00%)	1 (5.00%)
PD-L1 expression&		
IC < 1%	8 (40.00%)	12 (60.00%)
IC ≥ 1%	6 (30.00%)	2 (10.00%)
Unknown	6 (30.00%)	6 (30.00%)

Demographic and baseline characteristics	C1 No.(%)	C2 No.(%)
EGFR mutation		
Yes	0	10 (50.00%)
No	16 (80.00%)	9 (45.00%)
Unknown	4 (20.00%)	1 (5.00%)
Baseline ECOG PS		
0	1 (5.00%)	2 (10.00%)
1	19 (95.00%)	18 (90.00%)
Baseline SLD of target lesions(mm)		
Mean (SD)	51.75 (23.54)	61.52 (45.76)
Median (range)	50.44 (13.32, 88.90)	48.50 (14.00, 209.50)
Prior lines of therapy with 3rd generation EGFR-TKI		
Yes	0 (0.00%)	9 (45.00%)#
No	20 (100.00%)	11 (55.00%)

*: In cohort C1 means IO combined with chemotherapy, in cohort C2 means chemotherapy or TKI therapy;
&: Detected by SP263;
#: One patient with EGFR mutation did not receive a 3rd generation EGFR-TKI therapy due to there was no T790M mutation.

- For IO treated NSCLC (C1), 19 pts had at least one post treatment tumor assessment. The ORR and DCR were 26.3% (5/19) and 84.2% (16/19) respectively. The PFS was 6.6 (2.89-NE) months. 6 pts are still on treatment as of cut-off date.
- For IO naïve NSCLC (C2), 17 pts had at least one assessment, 3 pts achieved partial response and the DCR was 82.4% (14/17). The PFS was 8.2 (2,99-NE) months. 3 pts are still on treatment as of cut-off date.

Table2. Summary of the Overall Objective Response

	Cohort C1 N=19	Cohort C2 N=17
ORR , n (%)	5 (26.3%)	3 (17.6%)
95%CI	(9.15,51.20)	(3.80,43.43)
BoR , n (%)		
CR	1 (5.3%)	0
PR	4 (21.1%)	3 (17.6%)
SD	11 (57.9%)	11 (64.7%)
PD	3 (15.8%)	2 (11.8%)
NE	0	1 (5.9%)
DCR , n (%)	16 (84.2%)	14 (82.4%)
95%CI	(60.42,96.62)	(56.57,96.20)

ORR: Objective response rate; BoR: Best overall response;
DCR: Disease control rate; CR: Complete response; PR: Partial response;
SD: Stable disease; PD: Progressive disease; NE: Not evaluable.

Figure1. Kaplan-Meier curves of PFS in patients with NSCLC treated with suvemcitug plus envafolimab and docetaxel

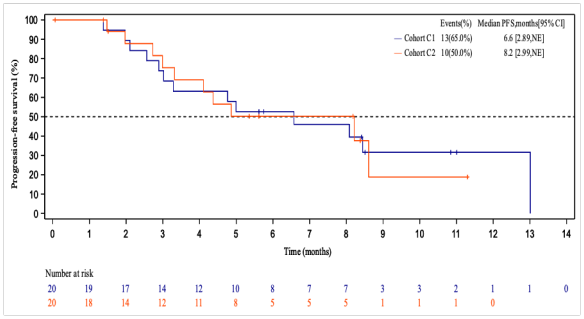


Figure2. Best Change of the Sum of Target Lesions from Baseline

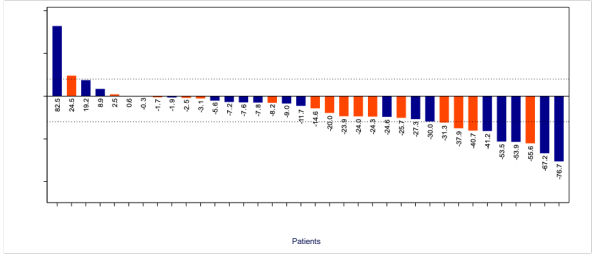
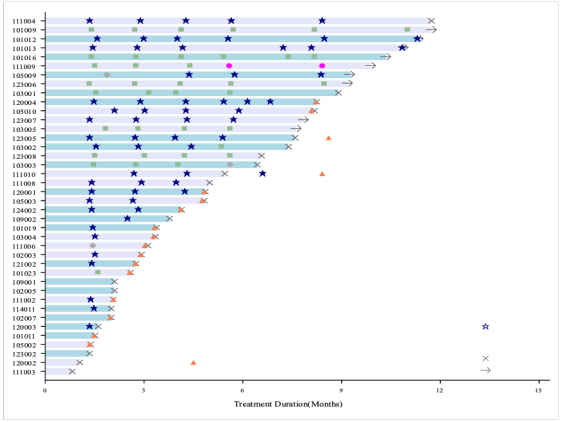


Figure3. Duration of the Treatment



- In NSCLC pts,The most common treatment-related adverse events (TRAEs) were white blood cell count decreased (57.5%, 23/40), neutrophil count decreased (55.0%, 22/40), anaemia (37.5%,15/40), platelet count decreased (35.0%,14/40), asthenia (30.0%,12/40), alanine aminotransferase increased (22.5%,9/40), decreased appetite (22.5%, 9/40), alopecia (20.0%, 8/40), aspartate aminotransferase increased (15.0%,6/40), proteinuria (15.0%,6/40), gamma-glutamyltransferase increased (15.0%,6/40).
- The most common grade ≥ 3 TRAEs were neutrophil count decreased (52.5%, 21/40) and white blood cell count decreased (45.0%, 18/40).
- In total, 3 pts experienced TEAEs leading to death, one due to COVID-19, one due to acute myocardial infarction , and one due to Lung infection. All the three TEAEs were not related study treatment.

Table3. Overview of TEAEs

	N = 40 n (%)
TEAEs	39 (97.5%)
Related to study treatment	39 (97.5%)
Related to suvemcitug	36 (90.0%)
Related to envafolimab	34 (85.0%)
Related to docetaxel	39 (97.5%)
TESAEs	24 (60.0%)
Related to study treatment	19 (47.5%)
Related to suvemcitug	16 (40.0%)
Related to envafolimab	14 (35.0%)
Related to docetaxel	14 (35.0%)
≥ Grade 3 TEAEs	30 (75.0%)
Related to study treatment	27 (67.5%)
Related to suvemcitug	14 (35.0%)
Related to envafolimab	16 (40.0%)
Related to docetaxel	25 (62.5%)

	N = 40 n (%)
AE leading to Death	3 (7.5%)
Related to study treatment	0
Related to suvemcitug	0
Related to envafolimab	0
Related to docetaxel	0
Dose discontinuation	10 (25.0%)
Suvemcitug	8 (20.0%)
Envafolimab	4 (10.0%)
Docetaxel	6 (15.0%)
Dose interruption	21 (52.5%)
Suvemcitug	15 (37.5%)
Envafolimab	16 (40.0%)
Docetaxel	21 (52.5%)
Dose reduction	8 (20.0%)
Suvemcitug	1 (2.5%)
Envafolimab	0
Docetaxel	7 (17.5%)

Table4. Summary of TRAEs (≥15%)

TRAEs	Cohort C N=40	
	All grade	≥3 grade
White blood cell count decreased	23 (57.5%)	18 (45.0%)
Neutrophil count decreased	22 (55.0%)	21 (52.5%)
Anaemia	15 (37.5%)	1 (2.5%)
Platelet count decreased	14 (35.0%)	3 (7.5%)
Asthenia	12 (30.0%)	2 (5.0%)
Alanine aminotransferase increased	9 (22.5%)	2 (5.0%)
Decreased appetite	9 (22.5%)	0
Alopecia	8 (20.0%)	0
Aspartate aminotransferase increased	6 (15.0%)	1 (2.5%)
Proteinuria	6 (15.0%)	1 (2.5%)
Gamma-glutamyltransferase increased	6 (15.0%)	0

- The pharmacokinetic exposure of envafolimab and suvemcitug in Cohort C was comparable with monotherapy.

Figure4. Pharmacokinetcis (PK): Cycle 1 serum concentrations (mean±SD) of Suvemcitug (A) and Envafolimab (B) in Cohort C1 and C2 safety cohort.

Figure 4A. Suvemcitug

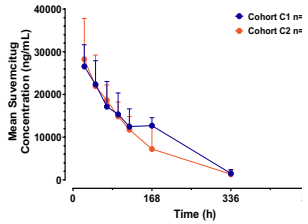
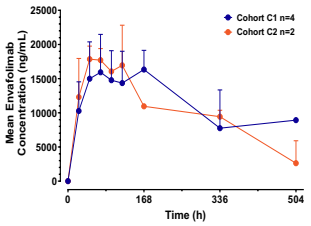


Figure 4B. Envafolimab



CONCLUSIONS

- This phase II clinical trial demonstrated antitumor activity and manageable safety profile of immunotherapy plus anti-angiogenic agent and chemotherapy in pts with NSCLC, who had failed at least one line of therapy.
- The addition of suvemcitug and envafolimab to docetaxel did not lead to significant worsening of TEAE.
- We are exploring if any subgroup might be benefit from this regimen.
- Clinical trial information:NCT05148195.

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Contact information
Ying Cheng, MD, 0431-80596003, jl.cheng@163.com

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