Combination Therapy of Envafolimab, Suvemcitug, and FOLFIRI in Patients with Metastatic Microsatellite Stable or Mismatch-repair Proficient Colorectal Cancer: Results from a Phase II Clinical Trial

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BACKGROUND

- Envafolimab is a humanized single-domain anti-PD-L1 antibody which is administered subcutaneously (SC).
- Suvemcitug is a humanized monoclonal antibody against vascular endothelial growth factor (VEGF).
- This study aims to assess the efficacy and safety of the combination of envafolimab and suvemcitug with chemotherapy as second-line or later therapy in patients (pts) with with metastatic microsatellite stable or mismatch-repair proficient colorectal cancer (MSS/ pMMR CRC).

METHODS

- This was an open-label, multi-cohort, multicenter, phase II trial conducted in China. Eligible pts had received at least one prior line of treatment for MSS/pMMR mCRC (Cohort D) and were treated with envafolimab plus suvemcitug and FOLFIRI (Irinotecan, Leucovorin, and 5-Fluorouracil). The primary endpoint was objective response rate (ORR). Secondary endpoints included duration of response (DoR), disease control rate (DCR), and progression-free survival (PFS) and safety.

RESULTS

- As of June 30, 2023, 20 pts with MSS/pMMR mCRC were enrolled. 25.0% pts (5/20) received two prior or later therapies and 50.0% pts (10/20) were prior treated with antiangiogenic agents.

Table1. Demographic and baseline characteristics

Demographic and baseline characteristics	No.(%)	Demographic and baseline characteristics	No.(%)
Age		With or without lung metastasis	
Mean (SD)	56.45 (10.60)	Yes	11 (55.00%)
Median (range)	56.00 (36, 74)	No	9 (45.00%)
Sex		Prior lines of therapy	
Male	12 (60.00%)	1 prior line	15 (75.00%)
Female	8 (40.00%)	≥ 2 prior lines	5 (25.00%)
Tumor site		Any previous antiangiogenic therapy	
Left-sided or Rectum	15 (75.00%)	Yes	10 (50.00%)
Right-sided	5 (25.00%)	No	10 (50.00%)
Baseline ECOG PS		Any previous anti-EGFR antibody therapy	
0	2 (10.00%)	Yes	2 (10.00%)
1	18 (90.00%)	No	18 (90.00%)
KRAS status		Baseline SLD of target lesions(mm)	
KRAS mut	7 (35.00%)	Mean (SD)	52.62 (29.81)
KRAS wt	7 (35.00%)	Median (range)	46.75 (16.92, 108.50)
Unknown	6 (30.00%)	PD-L1 expression*	
With or without liver metastasis		IC ≥ 1%	11 (55.00%)
Yes	11 (55.00%)	IC < 1%	5 (25.00%)
No	9 (45.00%)	Unknown	4 (20.00%)

* Detected by SP263

- All pts had at least one post treatment tumor assessment, the confirmed ORR was 25.0% (95% CI, 8.7-49.1) and DCR was 90.0% (95% CI, 68.3-98.8). With a median follow-up time of 10.81 months, the median PFS was 5.6 months (95% CI, 4.01-8.25), 1 patient still on treatment as of cut-off date.

Table2. Summary of Objective Response

	N=20
ORR , n (%)	5 (25.0%)
95%CI	(8.66,49.10)
BoR , n (%)	
PR	5 (25.0%)
SD	13 (65.0%)
PD	2 (10.0%)
DCR , n (%)	18 (90.0%)
95%CI	(68.30,98.77)

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

Figure1. Kaplan-Meier curves of PFS in patients with CRC

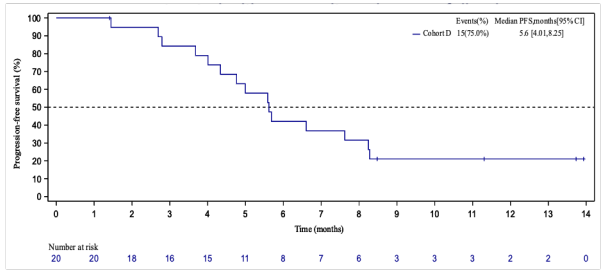


Figure2. Duration of the Treatment

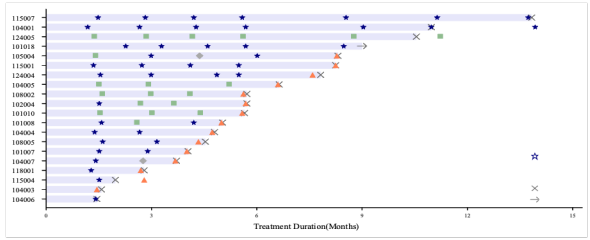
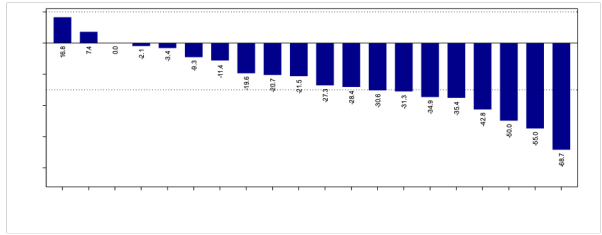


Figure3. Best Change of the Sum of Target Lesions from Baseline



- The most common treatment-related adverse events (TRAEs) were white blood cell count decreased (85.0%, 17/20), neutrophil count decreased (75.0%, 15/20), proteinuria (65.0%, 13/20), nausea (60.0%, 12/20), diarrhea (55.0%, 11/20), hypertension (45.0%, 9/20), platelet count decreased (45.0%, 9/20) and anaemia (45.0%, 9/20).
- The most common grade ≥ 3 TRAEs were neutrophil count decreased (60.0%, 12/20), white blood cell count decreased (25.0%, 5/20) and hypertension (25.0%, 5/20).
- No death reported.

Table3. Overview of TEAEs

	N = 20 n (%)		N = 20 n (%)
TEAEs	20 (100.0%)	AE leading to Death	0
Related to study treatment	20 (100.0%)	Related to study treatment	0
Related to suvemcitug	19 (95.0%)	Related to suvemcitug	0
Related to envafolimab	17 (85.0%)	Related to envafolimab	0
Related to chemotherapy	20 (100.0%)	Related to chemotherapy	0
TESAEs	8 (40.0%)	Dose discontinuation	0
Related to study treatment	7 (35.0%)	Suvemcitug	0
Related to suvemcitug	4 (20.0%)	Envafolimab	0
Related to envafolimab	4 (20.0%)	Chemotherapy	0
Related to chemotherapy	7 (35.0%)	Dose interruption	15 (75.0%)
≥ Grade 3 TEAEs	18 (90.0%)	Suvemcitug	14 (70.0%)
Related to study treatment	18 (90.0%)	Envafolimab	9 (45.0%)
Related to suvemcitug	13 (65.0%)	Chemotherapy	11 (55.0%)
Related to envafolimab	8 (40.0%)	Dose reduction	13 (65.0%)
Related to chemotherapy	15 (75.0%)	Suvemcitug	2 (10.0%)
		Envafolimab	0
		Chemotherapy	13 (65.0%)

Table4. Summary of TRAEs(≥15%)

TRAE	All grade	≥Grade 3
White blood cell count decreased	17 (85.0%)	5 (25.0%)
Neutrophil count decreased	15 (75.0%)	12 (60.0%)
Proteinuria	13 (65.0%)	2 (10.0%)
Nausea	12 (60.0%)	0
Diarrhoea	11(55.0%)	1 (5.0%)
Hypertension	9 (45.0%)	5 (25.0%)
Platelet count decreased	9 (45.0%)	2 (10.0%)
Anaemia	9 (45.0%)	1 (5.0%)
Lymphocyte count decreased	7 (35.0%)	3 (15.0%)
Hypothyroidism	7 (35.0%)	0
Vomiting	5 (25.0%)	1 (5.0%)
Blood thyroid stimulating hormone increased	5 (25.0%)	0
Stomatitis	4 (20.0%)	3 (15.0%)
Alanine aminotransferase increased	4 (20.0%)	0
Decreased appetite	4(20.0%)	0
Asthenia	3 (15.0%)	0
Constipation	3 (15.0%)	0
Hypoaesthesia	3 (15.0%)	0
Mouth ulceration	3 (15.0%)	0
Pyrexia	3 (15.0%)	0
Weight decreased	3 (15.0%)	0

- The pharmacokinetic profile of envafolimab and suvemcitug in Cohort D was similar with other cohorts and prior mono therapy studies.

Figure4.
Pharmacokinetcis (PK): Cycle 1 serum concentrations (mean ±SD) of Sevemcitug (A) and Envafolimab (B) in Cohort D safety coh ort.

Figure 4A

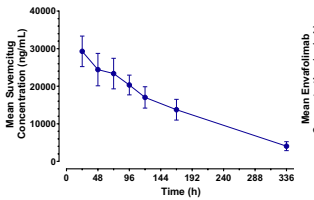
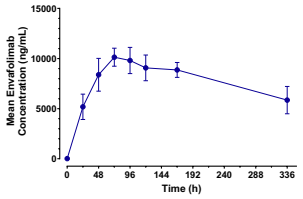


Figure 4B



CONCLUSIONS

- This study demonstrated modest antitumor activity and a manageable safety profile of immunotherapy plus anti-angiogenic agent and chemotherapy in pts with MSS/ pMMR mCRC who had failed at least one line of therapy.
- The results support further evaluation of this combination therapy in a larger population.
- We are exploring if any subgroup might be benefit from this regimen.
- Clinical trial information:NCT05148195.

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