Abstract #2592: Updated efficacy and safety results from the phase 2 study of serplulimab, a novel anti-PD-1 antibody, in patients with previously treated unresectable or metastatic microsatellite instability-high or mismatch repair-deficient solid tumors

Jin Li[1], Shukui Qin[2], Haijun Zhong[3], Chuan Jin[4], Lili Chen[5], Xianglin Yuan[6], Qingxia Fan[7], Kehe Chen[8], Peiguo Cao[9], Jianjun Xiao[10], Da Jiang[11], Tao Zhang[12], Hongyu Zhang[13], Xicheng Wang[14], Wei Wang[15], Lin Han[16], Qingyu Wang[16], Jun Zhu[16]

[1]Tongji University Shanghai East Hospital, Shanghai, China; [2]Qinhuai Medical Area, Eastern Theater General Hospital of PLA China, Nanjing, China; [3]Cancer Hospital of the University of Chinese Academy of Sciences (Zhejiang Cancer Hospital), Hangzhou, China; [4]Affiliated Cancer Hospital and Institute of Guangzhou Medical University, Guangzhou, China; [5]Taizhou First People's Hospital, Taizhou, China; [6]Tongji Hospital, Huazhong University of Science and Technology, Wuhan, China; [7]The First Affiliated Hospital of Zhengzhou University, Zhengzhou, China; [8]The People's Hospital of Guangxi Zhuang Autonomous Region, Nanning, China; [9]The Third Xiangya Hospital of Central South University, Changsha, China; [10]Zhongshan City People's Hospital, Zhongshan, China; [11]The Fourth Hospital of Hebei Medical University, Shijiazhuang, China; [12]The First Affiliated Hospital of Chongqing Medical University, Chongqing, China; [13]The Fifth Affiliated Hospital Sun Yat-sen University, Zhuhai, China; [14]The First Affiliated Hospital of Guangdong Pharmaceutical University, Guangzhou, China; [15]The First People's Hospital of Foshan, Foshan, China; [16]Shanghai Henlius Biotech, Inc., Shanghai, China

Background

- Unresectable or metastatic microsatellite instability-high or mismatch repair-deficient (MSI-H/dMMR) solid tumors have a poor prognosis after treatment with conventional chemotherapy, but usually have higher response rates to immune checkpoint inhibitors[1-3].
- The anti-PD-1/L1 mAb treatment was first approved in May 2017 for later line MSI-H/dMMR solid tumor patients and in June 2020 for first line MSI-H/dMMR metastatic colorectal cancer patients[3,4].
- Serplulimab, a novel fully humanized IgG4 anti-PD-1 mAb, has been approved for the treatment of unresectable or metastatic MSI-H solid tumors by China National Medical Products Administration (NMPA), base on the data from pivotal study ASTRUM-010 (NCT03941574)[5,6].
- Here, we report the updated efficacy and safety results of ASTRUM-010.

Methods

- This single-arm, open-label, multicenter, phase 2 study aimed to evaluate the efficacy and safety of serplulimab in unresectable or metastatic MSI-H/dMMR solid tumor patients who had progressed on or been intolerant to standard therapies (Figure 1).
- Patients received 3 mg/kg serplulimab Q2W intravenously for up to 2 years until loss of clinical benefit, death, intolerable toxicity, withdrawal of informed consent or other reasons as specified in the protocol (whichever occurred first).
- CT or MRI scans were conducted at baseline, Q6W for 48 weeks, then Q12W until disease progression or treatment discontinuation. PD was confirmed if the second PD (per iRECIST) was observed by imaging at least 4 weeks after the first PD (per RECIST v1.1).

Figure 1. Study design

Inclusion criteria:

- Age 18–75 years
- ECOG PS 0/1
- With unresectable or metastatic MSI-H/dMMR solid tumors which were histologically or cytologically confirmed by the central laboratory or a local study site
- With disease progression or intolerability after ≥1 prior standard anti-cancer therapy

Serplulimab 3mg/kg IV Q2W

Primary endpoint: ORR assessed by IRRC per RECIST v1.1

Secondary endpoints:

- ORR* **
- DCR***
- DOR
- PK
- Biomarkers
- OS, 6- and 12-month OS rate
- PFS, 6- and 12-month PFS rate***
- Safety
- Immunogenicity
- Quality of life

* Assessed by investigators per RECIST v1.1
** Assessed by IRRC and investigators per iRECIST
*** Assessed by IRRC and investigators per RECIST v1.1 and iRECIST

CT, computed tomography; DCR, disease control rate; dMMR, mismatch repair-deficient; D, day; DOR, duration of response; ECOG PS, Eastern Cooperative Oncology Group performance status; iRECIST, immunotherapy-related RECIST; IRRC, independent radiological review committee; IV, intravenous; MRI, magnetic resonance imaging; MSI-H, microsatellite instability-high; OS, overall survival; PD, progressive disease; PFS, progression-free survival; PK, pharmacokinetics; Q2W: every 2 weeks; Q6W: every 6 weeks; Q12W: every 12 weeks; RECIST, Response Evaluation Criteria in Solid Tumors.

Results

- By the data cut-off date (July 10, 2021), 108 patients had received at least one dose of study treatment and were included in the safety set (SS). 72 (66.7%) patients ended the treatment and 49 (45.4%) patients ended the study. Among the whole population, 68 patients with confirmed MSI-H (by local sites or central lab) were included in the main efficacy analysis population (MEAP); 58 patients with confirmed MSI-H (by central lab) and had no major protocol deviations were included in the sensitivity analysis population (SAP).

References

1. Overman MJ, *et al. Lancet Oncol*. **2017**;18(9):1182–1191.
2. Le DT, *et al. Science*. **2017**;357(6349):409–413.
3. Lemery S, *et al. N Engl J Med*. **2017**;377(15): 1409–1412.
4. https://www.accessdata.fda.gov/drugsatfda_docs/label/2020/125514s084lbl.pdf.
5. Qin SK *et al. JCO*. **2021**;39:15_suppl, 2566-2566
6. https://www.henlius.com/en/NewsDetails-3512-26.html

Presenter: Jin Li, MD, PhD; Email: lijin@csco.org.cn

Serplulimab provides encouraging anti-tumor activity with a manageable safety profile, and has been approved for the treatment of unresectable or metastatic MSI-H solid tumors by China NMPA

Efficacy

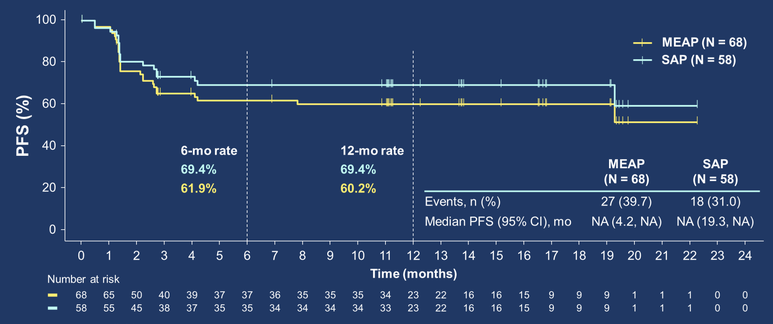
Table 2. Summary of Response by IRRC per RECIST 1.1

	MEAP (N = 68)	SAP (N = 58)
ORR, % (95% CI)	**39.7** (28.0, 52.3)	**43.1** (30.2, 56.8)
DCR, % (95% CI)	67.6 (55.2, 78.5)	72.4 (59.1, 83.3)
CR, n (%)	3 (4.4)	2 (3.4)
PR, n (%)	24 (35.3)	23 (39.7)
SD, n (%)	19 (27.9)	17 (29.3)
PD, n (%)	18 (26.5)	13 (22.4)
NE, n (%)	4 (5.9)	3 (5.2)

- The median follow-up duration were 13.5 months and 14.0 months in MEAP and SAP.
- ORR assessed by IRRC were **39.7%** and **43.1%** in MEAP and SAP, respectively (Table 2). The ORR of 45 colorectal cancer patients in SAP was **46.7%**.
- Median DOR, PFS and OS were not reached. The 6-mo and 12-mo DOR rates in MEAP were both 92.1%, and in SAP were both 95.8%.

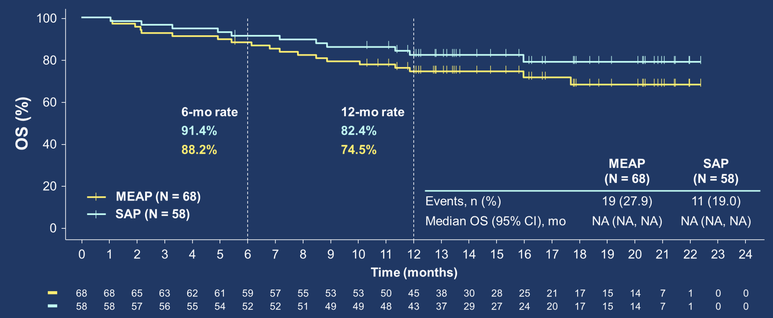
CI, confidence interval; CR, complete response; NE, not evaluable; PD, progressive disease; PR, partial response; SD, stable disease.

Figure 2. Progression-free survival by IRRC per RECIST 1.1



mo, month; NA, not available;

Figure 3. Overall Survival



- Baseline demographics and characteristics of MEAP and SAP are shown in Table 1.

Table 1. Patient demographics and baseline characteristics

	MEAP (N = 68)	SAP (N = 58)
Median age (range), years	53.0 (23.0–72.0)	50.5 (23.0–72.0)
Male, n (%)	36 (52.9)	30 (51.7)
ECOG PS, n (%)		
1	43 (63.2)	36 (62.1)
Tumor types, n (%)		
Colorectal cancer	53 (77.9)	45 (77.6)
Endometrial cancer	5 (7.4)	5 (8.6)
Gastric cancer	4 (5.9)	3 (5.2)
Other	6 (8.8)	5 (8.6)
PD-L1 expression levels[a], n (%)		
Negative	29 (42.6)	20 (34.5)
Positive	30 (44.1)	30 (51.7)
Missing	9 (13.2)	8 (13.8)
TMB[b], n (%)		
High	55 (80.9)	55 (94.8)
Low	8 (11.8)	1 (1.7)
Missing	5 (7.4)	2 (3.4)
Prior lines of chemotherapies, n (%)		
1	26 (38.2)	25 (43.1)
2	16 (23.5)	14 (24.1)
≥3	26 (38.2)	19 (32.8)
Prior therapies, n (%)		
Oxaliplatin	57 (83.8)	48 (82.8)
Capecitabine	48 (70.6)	41 (70.7)
Fluorouracil	37 (54.4)	29 (50.0)
Irinotecan	34 (50.0)	26 (44.8)
Bevacizumab	28 (41.2)	22 (37.9)
Cetuximab	7 (10.3)	6 (10.3)

[a] Positive PD-L1 status was defined as a combined positive score ≥1; [b] Tumour mutational burden (TMB) high was defined as a score ≥10.

Safety

- 105 (97.2%) patients in SS experienced TEAEs (Table 3), most commonly anemia (36.1%), hypoproteinemia (30.6%) and increased aspartate aminotransferase (25.0%), increased alanine aminotransferase (22.2%) and hypothyroidism (20.4%).
- 57 (52.8%) patients in SS had grade 3 or worse TEAEs, of which the most common were anemia (9.3%), disease progression (6.5%), increased γ-glutamyltransferase (5.6%) and intestinal obstruction (5.6%) (Tables 3 and 4).
- No IRRs were observed. 52 (48.1%) patients in SS had irAEs and 13 (12.0%) had grade 3 or worse irAEs (Tables 3). 3 (2.8%) ADRs leading to death (2 disease progression and 1 intestinal obstruction) were reported during the study.

Table 3. Safety summary

	SS (N = 108)	MEAP (N = 68)
Any TEAEs	105 (97.2)	67 (98.5)
Grade ≥3	57 (52.8)	32 (47.1)
Grade 5	16 (14.8)	6 (8.8)
TEAEs leading to treatment discontinuation	6 (5.6)	3 (4.4)
Serious TEAEs	36 (33.3)	19 (27.9)
irAEs	52 (48.1)	39 (57.4)
Grade ≥3	13 (12.0)	10 (14.7)
Any ADRs	85 (78.7)	58 (85.3)
Grade ≥3	30 (27.8)	22 (32.4)
Grade 5	3 (2.8)	2 (2.9)
ADRs leading to treatment discontinuation	3 (2.8)	2 (2.9)

Table 4. CTCAE grade ≥3 TEAEs (≥5%) and irAEs (≥3%)

	SS (N = 108)	MEAP (N = 68)
Grade ≥3 TEAEs (≥5%), n (%)		
Anemia	10 (9.3)	5 (7.4)
Disease progression	7 (6.5)	2 (2.9)
Increased γ-glutamyltransferase	6 (5.6)	3 (4.4)
Intestinal obstruction	6 (5.6)	5 (7.4)
Abnormal liver function	5 (4.6)	4 (5.9)
irAEs (≥3%), n (%)		
Hypothyroidism	19 (17.6)	14 (20.6)
Hyperthyroidism	9 (8.3)	7 (10.3)
Lung inflammation	5 (4.6)	1 (1.5)
Elevated thyroid-stimulating hormone	5 (4.6)	3 (4.4)
Abnormal liver function	4 (3.7)	4 (5.9)
Ventricular extrasystoles	3 (2.8)	3 (4.4)

ADR, adverse drug reaction; CTCAE, Common Terminology Criteria for Adverse Events; irAE, immune-related adverse event; IRR, infusion-related reaction; TEAE, treatment-emergent adverse event.

Acknowledgments and Disclosures

- The authors would like to acknowledge the participants in this study and their families, other 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 Parexel, and funded by Shanghai Henlius Biotech, Inc.
- Lin Han, Qingyu Wang and Jun Zhu are employees of Shanghai Henlius Biotech, Inc.

2022 American Society of Clinical Oncology (ASCO) Annual Meeting, June 3 – June 7, 2022