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Phase III study of SHR-1701 versus placebo in combination with chemo as first-line (1L) therapy for HER2-negative gastric/gastroesophageal junction adenocarcinoma (G/GEJA)

Z. Peng[1], J. Wang[2], Y. Zhang[3], H. Li[4], Q. Zhao[5], X. Zhu[6], S. Wei[7], Y. Cheng[8], W. Yang[9], J. Yao[10], M. Zhang[11], L. Xie[12], X. Zhang[13], P. Zhao[14], C. Hu[15], J. Zhang[16], Z. Wang[17], W. Wang[17], H. Han[17], L. Shen[1]

[1] Department of Gastrointestinal Oncology, Key laboratory of Carcinogenesis and Translational Research (Ministry of Education/Beijing), Peking University Cancer Hospital & Institute, Beijing, China, [2] Department of Digestive Diseases 2, Henan Cancer Hospital, Zhengzhou, China, [3] Gastroenterology Department, Harbin Medical University Cancer Hospital, Harbin, China, [4] Gastrointestinal Medical Oncology, Tianjin Medical University Cancer Institution & Hospital, Tianjin, China, [5] Third Department of Surgery, The Fourth Hospital of Hebei Medical University, Shijiazhuang, China, [6] Medical Oncology, Fudan University Shanghai Cancer Center, Shanghai, China, [7] Gastrointestinal Surgery, Hubei Cancer Hospital, Wuhan, China, [8] Department of Medical Oncology, Jilin Cancer Hospital, Changchun, China, [9] Gastroenterology Department, Shanxi Cancer Hospital, Taiyuan, China, [10] Oncology Department, The First Affiliated Hospital of Henan University of Science and Technology, Luoyang, China, [11] Oncology Department, The Second Hospital of Anhui Medical University, Hefei, China, [12] Gastrooncology Department, Yunnan Cancer Hospital & Third Affiliated Hospital of Kunming Medical University, Kunming, China, [13] Oncology Department, North Jiangsu People's Hospital, Yangzhou, China, [14] Gastrointestinal Surgery, Sichuan Cancer Hospital, Chengdu, China, [15] Department of Chemotherapy Oncology, Anhui Provincial Hospital, Hefei, China, [16] Department of Digestive Diseases 2, Liaoning Cancer Hospital and Institute, Shenyang, China[17] Clinical Research & Development, Jiangsu Hengrui Pharmaceuticals Co., Ltd., Shanghai, China

Background

SHR-1701 is a bifunctional agent composed of an IgG4 mAb targeting PD-L1 fused with extracellular domain of the TGF-βIIR. We aimed to assess the addition of SHR-1701 to standard chemo in patients (pts) with previously untreated, unresectable locally advanced or metastatic HER2-negative G/GEJA.

Methods

This was a 2-part phase 3 study. In part 1, the recommended dose of SHR-1701 was determined to be 30 mg/kg, when combined with CAPOX. In the multicenter, randomized, double-blind, part 2, pts were randomized (1:1) to receive SHR-1701 (30 mg/kg, iv, q3w) or matching placebo, plus CAPOX. Randomization was stratified by PD-L1 CPS (≥5 vs <5), ECOG PS (0 vs 1), and peritoneal metastasis (yes vs no). Primary endpoint was OS, assessed in population with PD-L1 CPS ≥5 and in ITT population.

Results

From Mar 11, 2022 to Jan 13, 2024, 731 pts were randomly assigned to SHR-1701+chemo (N=365) or placebo+chemo (N=366). As of May 20, 2024, median follow-up was 8.5 mo (IQR 5.6–13.2). In pts with PD-L1 CPS ≥5, median OS was significantly prolonged with SHR-1701+chemo versus placebo+chemo (16.8 vs 10.4 mo; HR, 0.53 [95% CI 0.40–0.68]; p<0.0001). In ITT population, median OS was significantly improved with SHR-1701+chemo over placebo+chemo (15.8 vs 11.2 mo; HR, 0.66 [95% CI 0.53–0.81]; p<0.0001). PFS, ORR, and DoR with SHR-1701+chemo were also superior to placebo+chemo (Table). Grade ≥3 TRAEs were comparable between the two arms (62.6% vs 59.0%), with the most common being decreased platelet count (19.0% vs 28.1%), decreased neutrophil count (12.1% vs 16.4%), and anemia (19.8% vs 12.6%).Table: LBA60

Efficacy summary

	PD-L1 CPS ≥5		ITT	
	SHR-1701+Chemo (N=246)	Placebo+Chemo (N=248)	SHR-1701+Chemo (N=365)	Placebo+Chemo (N=366)
Median OS (95% CI), mo	16.8 (14.7–NR)	10.4 (9.0–12.1)	15.8 (14.0–16.9)	11.2 (9.4–12.1)
HR (95% CI); p	0.53 (0.40–0.68); p<0.0001	0.66 (0.53–0.81); p<0.0001		
Median PFS (95% CI), mo*	7.6 (6.5–9.3)	5.5 (4.4–5.6)	7.0 (6.6–8.3)	5.5 (5.1–5.6)
HR (95% CI)	0.52 (0.42–0.66)	0.57 (0.48–0.69)		
Confirmed ORR, % (95% CI)*	56.5% (50.1–62.8)	32.7% (26.9–38.9)	53.4% (48.2–58.6)	32.8% (28.0–37.9)
Difference, % (95% CI)	23.8% (15.1–32.0)	20.6% (13.5–27.5)		
Median DoR (95% CI), mo*	10.2 (7.7–17.6)	5.1 (4.3–5.6)	8.5 (7.0–13.0)	5.3 (4.5–5.8)

*assessed per BICR.

Conclusions

1L SHR-1701 plus CAPOX showed a statistically significant and clinically meaningful benefit in OS compared with placebo plus CAPOX in pts with HER2-negative G/GEJA, both in PD-L1 CPS ≥5 population and in overall population regardless of PD-L1 level, presenting as a new treatment option.

Clinical trial identification

NCT04950322, Release date: July 6, 2021.

Legal entity responsible for the study

Jiangsu Hengrui Pharmaceuticals Co., Ltd.

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Disclosure

Z. Wang, W. Wang, H. Han: Financial Interests, Personal, Full or part-time Employment: Jiangsu Hengrui Pharmaceuticals. All other authors have declared no conflicts of interest.

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