BERLIN 2025 ESMO congress

1470O

Perioperative camrelizumab plus rivoceranib in resectable hepatocellular carcinoma (CARES-009): A randomized, multicenter, phase III trial

J. Zhou[1], J. Fan[1], Z. Wang[1], F. Liang[2], Y. Ji[3], F. Gu[4], T. Li[5], L. Peng[6], T. Peng[7], X. Huang[8], Z. Ding[9], D. Bai[10], B. Xiang[11], G. Tan[12], T. Wen[13], Y. Zeng[14], F. Han[15], Y. Zhang[16], S. Wu[17], Z.G. Hou[18]

[1] Department of Hepatobiliary Surgery and Liver Transplantation, Liver Cancer Institute and Key Laboratory of Carcinogenesis and Cancer Invasion (Ministry of Education), Zhongshan Hospital, Fudan University, Shanghai, China, [2] Department of Biostatistics, Zhongshan Hospital, Fudan University, Shanghai, China, [3] Department of Pathology, Zhongshan Hospital, Fudan University, Shanghai, China, [4] Department of Hepatic Surgery (III), The Third Affiliated Hospital of Naval Medical University (Eastern Hepatobiliary Surgery Hospital), Shanghai, China, [5] Department of General Surgery, Qilu Hospital of Shandong University, Jinan, China, [6] Department of Hepatobiliary Surgery, The Fourth Hospital of Hebei Medical University, Shijiazhuang, China, [7] Department of Hepatobiliary Surgery, The First Affiliated Hospital of Guangxi Medical University, Nanning, China, [8] Department of Liver Transplantation and HBP Surgery, Sichuan Clinical Research Center for Cancer, Sichuan Cancer Hospital & Institute, Sichuan Cancer Center, University of Electronic Science and Technology of China, Chengdu, China, [9] Department of Liver Surgery, Zhongshan Hospital (Xiamen), Fudan University, Xiamen, China, [10] Department of Hepatobiliary Surgery, Northern Jiangsu People's Hospital, Yangzhou, China, [11] Department of Hepatobiliary Surgery, Guangxi Medical University Cancer Hospital & Guangxi Cancer Institute, Nanning, China, [12] Department of General Surgery, The First Affiliated Hospital of Dalian Medical University, Dalian, China, [13] Department of Liver Surgery & Liver Transplantation Center, West China Hospital, Sichuan University, Chengdu, China, [14] Department of Hepatobiliary Surgery, MengChao Hepatobiliary Hospital of Fujian Medical University, Fuzhou, China, [15] Department of Hepatopancreatobiliary Surgery, Henan Cancer Hospital (Affiliated Cancer Hospital of Zhengzhou University), Zhengzhou, China, [16] Department of Hepatobiliary Surgery, Sichuan Academy of Medical Sciences, Sichuan Provincial People's Hospital, Chengdu, China, [17] Department of Hepatopancreatobiliary Surgery, Ningbo Medical Center Lihuili Hospital, Ningbo, China[18] Department of Medical Affairs, Jiangsu Hengrui Pharmaceuticals Co., Ltd., Shanghai, China

Background

The CARES-009 study aims to assess the efficacy and safety of perioperative camrelizumab plus rivoceranib in patients with resectable hepatocellular carcinoma (HCC) at intermediate or high-risk of recurrence.

Methods

Patients with resectable CNLC stage Ib-IIIa HCC (namely BCLC A with tumor size >5 cm, BCLC B and BCLC C without main portal vein tumor thrombus and extrahepatic metastasis) were randomized 1:1 to the perioperative group or the surgery group, stratified by CNLC stage and HBV infection status. In the perioperative group, patients received 2 cycles of neoadjuvant camrelizumab (200 mg q2w) and rivoceranib (250 mg qd), followed by surgical resection and at least 6 cycles of adjuvant camrelizumab (200 mg q3w) and rivoceranib (250 mg qd). In the surgery group, patients underwent upfront surgical resection. The primary endpoint was event-free survival (EFS) assessed by investigators per RECIST v1.1. Key secondary endpoints included major pathological response (MPR, ≤50% viable tumor cells in resected specimens) and overall survival (OS). EFS was also retrospectively assessed by blinded independent review committee (BIRC).

Results

A total of 294 patients were randomized to the perioperative group (n=148) or the surgery group (n=146). At the prespecified interim analysis, the median follow-up was 21.3 months. Median EFS was significantly prolonged in the perioperative group *vs* in the surgery group (42.1 months vs 19.4 months; HR, 0.59; 95% CI, 0.41-0.85; p=0.0040 [significance boundary 0.0148]). MPR was achieved in 35.1% of patients in the perioperative group (3.4% with pathological complete response) compared with 7.5% in the surgery group (p<0.001). EFS assessed by the BIRC were consistent with investigator-assessed findings (the perioperative group *vs* the surgery group, HR, 0.63; 95% CI, 0.44 to 0.90). With only 39 events, OS data remained immature. Grade ≥3 treatment-related adverse events occurred in 37.6% of patients in the perioperative group.

Conclusions

Perioperative camrelizumab plus rivoceranib significantly improved EFS and MPR compared with surgery alone in patients with resectable HCC at intermediate or high-risk of recurrence.

Clinical trial identification

NCT04521153.

Legal entity responsible for the study

The authors.

Funding

Jiangsu Hengrui Pharmaceuticals Co, Ltd.

Disclosure

Z.G. Hou: Financial Interests, Personal, Full or part-time Employment: Jiangsu Hengrui Pharmaceuticals Co, Ltd. All other authors have declared no conflicts of interest.