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LBA35

Camrelizumab (C) plus rivoceranib (R) vs. sorafenib (S) as first-line therapy for unresectable hepatocellular carcinoma (uHCC): A randomized, phase III trial

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Background

The benefits of immunotherapy plus an anti-angiogenic TKI in uHCC are unclear. This study aimed to assess C (Camrelizumab; anti-PD-1 IgG4 monoclonal antibody) + R (Rivoceranib, Apatinib; VEGFR2-TKI) *vs.* S (Sorafenib) as first-line treatment for uHCC.

Methods

In this international, randomized, open-label, phase III trial, eligible patients (pts) were randomized 1:1 to receive C (200 mg, iv, q2w) + R (250 mg, po, qd) or S (400 mg, po, bid). Pts were stratified by macrovascular invasion and/or extrahepatic metastases, geographical region (Asia *vs.* non-Asia), and baseline serum AFP (<400 *vs.* ≥ 400 ng/mL). The primary endpoints were PFS per RECIST v1.1 criteria by BIRC as well as OS. The primary analysis for PFS was done after 339 PFS events occurred (May 10, 2021) and the planned interim analysis of OS was done after 262 deaths occurred (Feb 8, 2022).

Results

A total of 543 pts (ITT population) were randomized to receive C+R (N=272) or S (N=271) respectively. With a median follow-up time of 7.8 mo, PFS was significantly improved with C+R *vs.* S (median 5.6 mo [95% CI 5.5-6.3] *vs.* 3.7 mo [2.8-3.7]; HR 0.52 [95% CI 0.41-0.65]); 1-sided $p<0.0001$). With a median follow-up of 14.5 mo, OS was significantly prolonged with C+R *vs.* S (median 22.1 mo [95% CI 19.1-27.2] *vs.* 15.2 mo [13.0-18.5]; HR 0.62 [95% CI 0.49-0.80]; 1-sided $p<0.0001$). ORR, DCR and DoR were also better with C+R *vs.* S (Table). A pre-specified subgroup analysis showed that HRs of PFS and OS obviously favored C+R in the majority of the subgroups. Grade ≥3 TRAEs occurred in 80.9% with C+R and 52.4% with S. TRAE led to discontinuation of any treatment in 24.3% (of both agents in 3.7%) with C+R and 4.5% with S. Fatal TRAE occurred in 1 pt in each arm.Table: LBA35

Summary of efficacy outcomes

	C+R (N=272)	S (N=271)	1-sided *p*-value
Median OS (95% CI), mo	22.1 (19.1-27.2)	15.2 (13.0-18.5)	-
HR (95% CI)	0.62 (0.49-0.80)		<0.0001*
Median PFS (95% CI), mo	5.6 (5.5-6.3)	3.7 (2.8-3.7)	-
HR (95% CI)	0.52 (0.41-0.65)		<0.0001*

	C+R (N=272)	S (N=271)	1-sided *p*-value
Confirmed ORR (95% CI), %	25.4 (20.3-31.0)	5.9 (3.4-9.4)	<0.0001†
Median DoR (95% CI), mo	14.8 (8.4-NR)	9.2 (5.3-NR)	-
DCR (95% CI), %	78.3 (72.9-83.1)	53.9 (47.7-59.9)	-
Median TTP (95% CI), mo	7.2 (5.6-8.2)	3.7 (3.6-3.7)	-

All assessed by BIRC per RECIST v1.1 except for OS. Data cutoff was May. 10, 2021 for PFS and Feb. 8, 2022 for other outcomes. * Stratified log-rank test. † Stratified Cochran-Mantel-Haenszel test. NR=not reached.

Conclusions

C+R significantly prolonged PFS and OS and improved ORR *vs.* S, and presents as a new first-line treatment option for uHCC. This is the first positive pivotal trial to show survival benefits with a PD-1/PD-L1 inhibitor plus an anti-angiogenic TKI for uHCC.

Clinical trial identification

NCT03764293.

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Disclosure

X. Liang: Financial Interests, Personal, Full or part-time Employment: Hengrui Pharmaceuticals. C. Chen: Financial Interests, Personal, Full or part-time Employment: Hengrui Pharmaceuticals. Z. Nie: Financial Interests, Personal, Full or part-time Employment: Hengrui Pharmaceuticals. L. Wang: Financial Interests, Personal, Full or part-time Employment: Hengrui Pharmaceuticals. All other authors have declared no conflicts of interest.