Clinical outcomes of camrelizumab + rivoceranib vs sorafenib (CARES-310) as first-line treatment for patients with unresectable hepatocellular carcinoma (uHCC) of non-viral and viral etiology.

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Background: CARES-310 (NCT03764293) evaluated the combination of PD-1 inhibitor, camrelizumab (cam), and VEGFR-1-3 inhibitor, rivoceranib (rivo), compared to sorafenib (sor) for the treatment of uHCC. Cam + rivo significantly improved median overall survival (mOS) and median progression-free survival (mPFS) compared to sor (mOS, 23.8 months [mo] [95% CI 20.6, 27.2] vs 15.2 mo [95% CI 13.2, 18.5] hazard ratio [HR] 0.64 [95% CI 0.52, 0.79]; one-sided $p<0.0001$; mPFS, 5.6 mo [95% CI 5.5, 7.4] vs 3.7 mo [95% CI 3.1, 3.7]; HR 0.54 [95% CI 0.44, 0.67]; one-sided $p<0.0001$). The most common (≥10%) grade ≥3 treatment-related adverse events in the cam + rivo arm were hypertension (38.6%) and AST increased (20.2%). **Methods:** A post-hoc analysis of CARES-310 was performed, where mOS and mPFS were estimated using the Kaplan-Meier method and compared between the 3 etiology groups of non-viral, hepatitis C virus (HCV), and hepatitis B virus (HBV) using the log-rank test. **Results:** mOS was longer with camrelizumab plus rivoceranib compared with sorafenib in patients with non-viral (HR 0.68 [95% CI 0.39, 1.19]), HCV (HR 0.37 [95% CI 0.162, 0.84]), and HBV etiologies (HR 0.70 [95% CI 0.55, 0.89]) (Table). Similarly, mPFS was longer with camrelizumab plus rivoceranib compared with sorafenib in patients with non-viral (HR 0.55 [95% CI 0.34, 0.91]), HCV (HR 0.50 [95% CI 0.23, 1.06]), and HBV etiologies (HR 0.57 [95% CI 0.45, 0.72]) (Table). **Conclusions:** Cam + rivo in CARES-310 suggested clinically meaningful mOS benefit in non-viral and viral HCC vs sor and provides assurance of clinical benefit for first line treatment to patients with uHCC independent of etiology. Clinical trial information: NCT03764293. Research Sponsor: Elevar Therapeutics; Jiangsu Hengrui Pharmaceuticals.

Etiology Group	Camrelizumab + Rivoceranib (n=272)	Sorafenib (n=271)
Non-viral, n (%)	42 (15.4%)	45 (16.6)
mOS, mo (95% CI)	26.8 (10.3, NR)	15.2 (9.6, 23.2)
mPFS, mo (95% CI)	6.1 (4.1, 13.8)	3.7 (2.4, 5.5)
HCV, n (%)	22 (8.1)	29 (10.7)
mOS, mo (95% CI)	31.7 (10.8, NR)	13.3 (8.0, 21.5)
mPFS, mo (95% CI)	12.7 (3.7, NR)	3.7 (1.8, 9.1)
HBV, n (%)	208 (76.5)	197 (72.7)
mOS, mo (95% CI)	23.0 (18.9, 26.0)	15.6 (13.3, 19.2)
mPFS, mo (95% CI)	5.6 (5.5, 7.3)	3.7 (2.7, 3.7)

HCC, hepatocellular carcinoma; mOS, median overall survival; mPFS, median progression-free survival; mo, months; HR, hazard ratio; HCV, hepatitis C virus; HBV, hepatitis B virus, NR, not reached.
Results used Cox proportional hazard model.
Confidence Intervals (CI) used the Brookmeyer and Crowley method.