SCT-I10A combined with a bevacizumab biosimilar (SCT510) versus sorafenib in the first-line treatment of advanced hepatocellular carcinoma: A randomized phase 3 trial.

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Background: Hepatocellular carcinoma (HCC) is a significant health concern in China, and it has been a leading cause of cancer-related deaths. Immunotherapy combined with anti-vascular growth therapy is the first recommended therapy. In this study, we evaluated the safety and efficacy of SCT-I10A (an anti-programmed death 1 [PD-1] monoclonal antibody) combined with SCT510 (a bevacizumab biosimilar) compared to sorafenib as the first-line treatment for advanced HCC. **Methods:** In this open-label, multicenter, phase 3 trial (NCT04560894) conducted in China, patients with advanced HCC who had not received prior system therapy were enrolled and randomly assigned (2:1) to receive SCT-I10A (200 mg every three weeks [Q3W]) plus SCT510 (a bevacizumab biosimilar, 15 mg/kg Q3W) or sorafenib (400 mg orally twice daily) until no clinical benefit or unacceptable toxicity. Randomization was stratified by ECOG performance status (0 vs. 1), baseline alpha-fetoprotein level (<400ng/ml vs. ≥400ng/ml), macrovascular invasion or extrahepatic metastasis (yes vs. no). The co-primary endpoints were overall survival (OS) and progression-free survival (PFS) as assessed by the blinded independent central review (BICR) according to Response Evaluation Criteria in Solid Tumors (RECIST) version 1.1 in the full analysis set. **Results:** At the data cutoff for the interim analysis (November 2, 2023), a total of 346 patients were enrolled and received at least one dose (SCT-I10A plus SCT510 group, n=230; sorafenib group, n=116), and the median follow-up was 19.7 months. The SCT-I10A plus SCT510 group exhibited a significantly longer median OS than that in the sorafenib group (22.1 vs. 14.2 months, hazard ratio [HR] 0.60; 95% confidence interval [CI]: 0.44, 0.81; p=0.0008). Median PFS was prolonged significantly in the SCT-I10A plus SCT510 group compared to the sorafenib group (7.1 vs. 2.9 months; HR 0.50; 95%CI: 0.38, 0.65; p<0.0001). The objective response rate (ORR) was higher in the SCT-I10A plus SCT510 group (32.8% [75/229]) than in the sorafenib group (4.3% [5/116]). Grade ≥3 treatment-related adverse events (TRAEs) were observed in 42.6% (98/230) of patients in the SCT-I10A plus SCT510 group and 33.6% (39/116) of patients in the sorafenib group. The most common grade ≥3 TRAE was hypertension (SCT-I10A plus SCT510 group vs. sorafenib group: 7.8% [18/230] vs. 4.3% [5/116]). Three drug-related deaths (unknown cause, hemorrhage intracranial, or upper gastrointestinal hemorrhage in 1 patient each) occurred and were related to SCT510. **Conclusions:** The combination of SCT-I10A and SCT510 showed substantial clinical advantages and an acceptable safety profile in patients with advanced HCC, thereby supporting its suitability as a first-line treatment option for HCC. Clinical trial information: NCT04560894. Research Sponsor: Sinocelltech Ltd.