4007 **Oral Abstract Session**

Hepatic arterial infusion chemotherapy of oxaliplatin plus fluorouracil versus sorafenib in advanced hepatocellular carcinoma: A biomolecular exploratory, randomized, phase 3 trial (The FOHAIC-1 study).

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Background: Advanced hepatocellular carcinoma (HCC) with mega liver masses and macrovascular invasion were commonly observed at the first diagnosis, while with less extrahepatic metastases (77.5% vs. 37.9%). However, in clinical trials IMbrave150, SHARP, and Asia-Pacific SHARP, the percentage of extrahepatic metastases reached 63%, 53%, and 68.7%, respectively, while macrovascular invasion only accounted for 38%, 36%, and 36%. Unlike the previous and ongoing phase 3 clinical trials exploring the optimal systemic medication in the first-line treatment of advanced HCC, this study mainly focused on a population with a heavy intrahepatic tumor burden. **Methods:** In this open-label, phase 3 trial, patients were randomly assigned in a 1:1 ratio to undergo hepatic arterial infusion chemotherapy (HAIC) of FOLFOX regimens (HAIC-FO) or sorafenib treatment. Patients in the HAIC-FO group were recommended to receive tumor and normal tissue biopsy to search for the potential genomic biomarkers in predicting the response to treatment. **Results:** Between May 2017 and May 2020, 551 patients were recruited. Two hundred sixty eligible patients were randomly assigned to receive HAIC-FO (n = 130) or sorafenib (n = 132) and were included in the intention-to-treatment population. Macrovascular invasion with or without extrahepatic metastasis was present in 82.8% of patients (84.6% and 81.1%; P = 0.446). The median tumor diameter was 11.7 cm (IQR 8.3-14.0) of the HAIC-FO group and 10.8 cm (8.7-13.6) of the sorafenib group (P = 0.439). The percentage of patients with $>$ 50% tumor volume involvement of the liver was 41.5% and 39.4%, respectively (P = 0.724). At the time of data cutoff (Oct 31, 2020, at 190 deaths [79 of HAIC-FO and 111 of sorafenib]), patients receiving HAIC-FO had a median overall survival of 13.9 months (95%CI 10.6-17.2), compared with 8.2 months (7.5-9.0) for those receiving sorafenib (HR 0.408 [95%CI 0.301-0.552], P $<$ 0.001). Tumor downstaging occurred in 16 (12.3% of 130) patients of the HAIC-FO group, including 15 (93.8%) receiving curative surgery or ablation and finally achieving a median overall survival (progression-free survival) of 20.8 (16.4) months (95%CI 9.1-32.5 [7.5-25.3]) with a 1-year rate of 93.8% (68.8%). Analyses of predictive biomarkers based on the whole genome sequencing were ongoing in the HAIC-FO group. **Conclusions:** This randomized phase 3 study proved that HAIC-FO had superior efficacy and survival outcome than sorafenib in the first-line treatment of primary diagnostic, advanced HCC, indicating that patients with heavy intrahepatic tumor burden, HAIC-FO monotherapy might be a better strategy than sorafenib. Clinical trial information: NCT03164382. Research Sponsor: The clinical trial was supported by the Sun Yat--sen University Clinical Research 5010 Program of China (No. 2018013).