Neoadjuvant transarterial infusion chemotherapy with FOLFOX could improve outcomes of resectable BCLC stage A/B hepatocellular carcinoma patients beyond Milan criteria: An interim analysis of a multi-center, phase 3, randomized, controlled clinical trial.

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Background: The efficacy of operation, as the only radical option for resectable BCLC stage A/B hepatocellular carcinoma (HCC) patients beyond Milan criteria, is still unsatisfactory. This study aimed to investigate to efficacy and safety of preoperative neoadjuvant transarterial infusion chemotherapy (TAI) with FOLFOX regimen for these patients. Methods: In this multi-center, prospective, phase 3, randomized, open-labeled, controlled clinical trial, resectable BCLC stage A/B HCC patients beyond Milan criteria were randomly assigned (1:1) before hepatectomy to receive either neoadjuvant TAI (NT group) or operation directly without any neoadjuvant treatment (OP group). The primary endpoint was overall survival (OS), the secondary endpoints are progression-free survival (PFS), recurrence free survival (RFS), and safety. Results: Between March, 2016 and July, 2020, 208 patients enrolled from five Chinese hospitals were randomly assigned to NT group (n=104) or OP group (n=104), with 99 patients in NT group and 100 patients in OP group included in the efficacy and safety analysis. Clinicopathological characteristics were balanced between the two groups. The 1-, 2-, and 3-year OS rates for NT group were 92.9%, 78.6%, and 63.5%, and were 79.5%, 62.0%, and 46.3% for OP group, respectively. The 6-, 12-, and 18-month PFS rates for NT group were 77.6%, 50.4%, and 47.4%, and were 52.7%, 42.8%, and 34.8% for OP group, respectively. The OS and PFS were significantly better in NT group than in OP group (p=0.016 and 0.017, respectively). The 6-, 12-, and 18-month RFS rates for NT group were 63.8%, 47.3%, and 47.3%, and were 52.7%, 42.8%, and 34.8% for OP group, respectively. The RFS between the two group had no difference (p=0.385). No patients in NT group experienced grade 3 or more severe TAI related adverse events. The operation related adverse events were similar between two groups (p=0.300). Conclusions: Neoadjuvant TAI before hepatectomy may bring survival benefits for resectable BCLC stage A/B HCC patients beyond Milan criteria. Trial number: NCT03851913. Clinical trial information: NCT03851913. Research Sponsor: None.