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Overall survival in the FOXFIRE-SIRFLOX-FOXFIRE Global prospective randomized studies of first-line SIRT in patients with mCRC

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Background The FOXFIRE randomized studies [FOXFIRE, SIRFLOX and FOXFIRE-Global (FF-SF-FFG)] were designed to evaluate the efficacy and safety of selective internal radiation therapy (SIRT) using yttrium-90 resin microspheres plus first-line chemotherapy for unresectable metastatic colorectal cancer (mCRC). The design and eligibility criteria of the three studies were similar, which facilitated this prospective combined analysis of overall survival (OS).

Methods Chemotherapy-naïve mCRC patients with liver metastases unsuitable for curative resection/ablation were randomized (1:1) to the Control arm with standard oxaliplatin-based chemotherapy (mFOLFOX6 or OxMdG) ± bevacizumab, or the Test arm to receive the same chemotherapy, plus a single SIRT treatment. Limited extra-hepatic metastases and primary tumor in situ were included. The primary endpoint OS was analysed on an intention-to-treat basis using individual participant data. Secondary endpoints included progression-free survival (PFS), liver PFS, response rate and adverse events (AEs).

Results A total of 1103 patients (Control arm n=549; Test arm n=554) with a median age of 63 years were enrolled. Median follow-up was 43.3 months. There was no difference in median OS between the two treatment arms (pooled hazard ratio [HR] 1.04; 95% confidence interval [CI], 0.90–1.19; p=0.609) or in median PFS (pooled HR 0.90; 95% CI, 0.79–1.02; p=0.108). The objective response rate was higher in the SIRT arm than in the Control arm (72.2% and 63.0%, respectively, p=0.001). The risk of progression in the liver as a first event was lower in patients in the SIRT arm (pooled HR 0.51; CI 0.43–0.62; p<0.001). There was a higher likelihood of grade 3–5 AEs in the Test arm than in the Control arm (74.0% vs 66.5%, respectively, p=0.009). The addition of SIRT appeared to have a significant OS benefit in patients with right-sided tumors.

Conclusions This combined analysis showed no improvement when SIRT is added to first-line oxaliplatin-fluorouracil chemotherapy. However, the addition of SIRT achieved higher tumor response rates and improved liver-specific PFS. The addition of SIRT appeared to have a significant OS benefit in patients with right-sided tumors.