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Radioembolization with chemotherapy for colorectal liver metastases: A randomized, open-label, international, multicenter, phase III trial (EPOCH study)

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Background

Safety and efficacy of trans-arterial Yttrium-90 radioembolization (TARE) in combination with systemic chemotherapy in the second-line setting for colorectal liver metastases is unknown.

Methods

In this phase 3 trial, patients with colorectal liver metastases who progressed on first-line therapy were randomized 1:1 to receive second-line chemotherapy with or without glass microsphere TARE. The two primary endpoints were progression-free survival (PFS) and hepatic PFS (hPFS), assessed by blinded-independent central review. Randomization was stratified by unilobar/bilobar disease, oxaliplatin/irinotecan-based first-line chemotherapy, and KRAS mutation status.

Results

428 patients from 94 centers were randomized to chemotherapy +/- TARE. The hazard ratio (HR) for PFS was 0.69 (95% confidence interval [CI], 0.54-0.88; 1-sided p=0.0013), with a median PFS of 8.0 (CI, 7.2-9.2) and 7.2 (CI, 5.7-7.6) months, respectively. The HR for hPFS was 0.59 (CI, 0.46-0.77; 1-sided p<0.0001), with a median hPFS of 9.1 (CI, 7.8-9.7) and 7.2 (CI, 5.7-7.6) months, respectively. Objective response rates were 34.0% (CI, 28.0-40.5%) and 21.1% (CI, 16.2-27.1%; 1-sided p=0.0019) for TARE and chemotherapy groups, respectively. Median overall survival was 14.0 (CI, 11.8-15.5) and 14.4 months (CI, 12.8-16.4; 1-sided p=0.7229) with a HR of 1.07 (CI, 0.86-1.32) for TARE and chemotherapy groups, respectively. Grade 3 adverse events were reported more frequently in the TARE group (68.4 vs 49.3%). The PFS benefit of TARE was observed for tumors with KRAS mutation (HR 0.57, CI: 0.40-0.80), left-side primary tumor (HR 0.65, CI: 0.48-0.88), hepatic tumor burden 10-25% (HR 0.43, CI: 0.26-0.72), ≤3 lesions (HR 0.33, CI: 0.14-0.76), addition of a biologic agent (HR 0.58, CI: 0.40-0.84), and resected primary (HR 0.63, CI: 0.46-0.85).

Conclusions

EPOCH study met both primary endpoints, demonstrating the addition of TARE to systemic therapy for second-line colorectal liver metastases leads to significantly longer PFS and hPFS. Further subset analyses will better define the ideal patient population benefitting from TARE.

Clinical trial identification

NCT01483027.

Legal entity responsible for the study

Boston Scientific Corporation.

Funding

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Disclosure

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