Background: The TRICOLORE trial previously demonstrated that S-1 and irinotecan (IRI) plus bevacizumab (Bmab) was non-inferior to mFOLFOX6 or CapeOX plus Bmab in terms of progression-free survival (PFS) as first-line treatment for metastatic colorectal cancer (mCRC), irrespective of RAS status (Komatsu Y, et al. ESMO 2017, and Yamada Y, et al. Ann Oncol. 2018). We now report the final overall survival (OS) after a median follow-up of more than 3 years. The results of this trial were subjected to an exploratory analysis to determine if primary tumor location (TL) influenced the response to S-1 and IRI plus Bmab.

Methods: This trial was a randomized, open-label, phase 3 trial. Chemotherapy-naïve patients with mCRC were randomly assigned to receive either mFOLFOX6 or CapeOX plus Bmab (arm A) or S-1 and IRI plus Bmab (arm B, given as a 3-week regimen [7.5 mg/kg Bmab, 150 mg/m² IRI on day 1, and 40–60 mg S-1 twice daily for 2 weeks, followed by a 1-week rest] or a 4-week regimen [5 mg/kg Bmab, 100 mg/m² IRI on days 1 and 15, and 40–60 mg S-1 twice daily for 2 weeks, followed by a 2-week rest]). Patients’ data were finally updated in September 2017.

Results: At this final analysis, the median overall survival (mOS) was 32.6 months with arm A and 34.3 months with arm B (median follow-up, 48.7 months). The hazard ratio (HR) for Os was 0.89 (95% CI 0.72 – 1.10). Median progression-free survival (mPFS) in arm A/B were 10.8/14.0 months (HR 0.86, 95% CI: 0.71–1.04, p < 0.0001 for non-inferiority). In right-sided TL, mOS and mPFS in arm A/B were 25.6/28.1 months (HR 0.82, 95% CI 0.66–1.21) and 9.6/11.4 months (HR 0.85, 95% CI 0.60–1.22), respectively. In left-sided TL, mOS and mPFS in arm A/B were 35.5/36.8 months (HR 0.95, 95% CI 0.68–1.15) and 13.3/15.0 months (HR 0.82, 95% CI 0.66–1.03), respectively.

Conclusions: Our updated analysis reconfirms that S-1 and IRI plus Bmab is non-inferior to mFOLFOX6 or CapeOX plus Bmab in terms of PFS. S-1 and IRI plus Bmab is now recommended as a 1st-line treatment for mCRC irrespective of primary TL and RAS status.

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