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「Randomized phase III study of bevacizumab plus FOLFIRI and bevacizumab plus mFOLFOX6 as first-line treatment for patients with metastatic colorectal cancer (WJOG4407G)」

BACKGROUND: FOLFIRI and FOLFOX have shown equivalent efficacy for metastatic colorectal cancer (mCRC), but their comparative effectiveness is unknown when combined with bevacizumab.

PATIENTS AND METHODS: WJOG4407G was a randomized, open-label, phase III trial conducted in Japan. Patients with previously untreated mCRC were randomized 1:1 to receive either FOLFIRI plus bevacizumab (FOLFIRI + Bev) or mFOLFOX6 plus bevacizumab (mFOLFOX6 + Bev), stratified by institution, adjuvant chemotherapy, and liver-limited disease. The primary end point was non-inferiority of FOLFIRI + Bev to mFOLFOX6 + Bev in progression-free survival (PFS), with an expected hazard ratio (HR) of 0.9 and non-inferiority margin of 1.25 (power 0.85, one-sided alpha-error 0.025). The secondary end points were response rate (RR), overall survival (OS), safety, and quality of life (QoL) during 18 months. This trial is registered to the University Hospital Medical Information Network, number UMIN000001396.

RESULTS: Among 402 patients enrolled from September 2008 to January 2012, 395 patients were eligible for efficacy analysis. The median PFS for FOLFIRI + Bev (n = 197) and mFOLFOX6 + Bev (n = 198) were 12.1 and 10.7 months, respectively [HR, 0.905; 95% confidence interval (CI) 0.723-1.133; P = 0.003 for non-inferiority]. The median OS for FOLFIRI + Bev and mFOLFOX6 + Bev were 31.4 and 30.1 months, respectively (HR, 0.990; 95% CI 0.785-1.249). The best overall RRs were 64% for FOLFIRI + Bev and 62% for mFOLFOX6 + Bev. The common grade 3 or higher adverse events were leukopenia (11% in FOLFIRI + Bev/5% in mFOLFOX6 + Bev), neutropenia (46%/35%), diarrhea (9%/5%), febrile neutropenia (5%/2%), peripheral neuropathy (0%/22%), and venous thromboembolism (6%/2%). The QoL assessed by FACT-C (TOI-PFC) and FACT/GOG-Ntx was favorable for FOLFIRI + Bev during 18 months.

CONCLUSION: FOLFIRI plus bevacizumab was non-inferior for PFS, compared with mFOLFOX6 plus bevacizumab, as the first-line systemic treatment for mCRC.