A PHASE III STUDY OF EAGLE COMPARING TWO DOSES OF BEVACIZUMAB COMBINED WITH FOLFIRI IN THE SECOND-LINE SETTING AFTER FIRST-LINE TREATMENT WITH BEVACIZUMAB PLUS OXALIPLATIN-BASED THERAPY: KRAS SUBGROUP FINDINGS


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Aim: ML18147 showed continued bevacizumab (BEV) with second-line chemotherapy for patients with metastatic colorectal cancer (mCRC) treated with BEV plus standard first-line chemotherapy, represents an option for patients with mCRC independent of KRAS status. EAGLE study evaluated two doses of BEV (10 mg/kg or 5 mg/kg) combined with FOLFIRI in the second-line setting after first-line treatment with BEV plus oxaliplatin-based therapy. Bev 10 mg/kg plus FOLFIRI as second-line treatment did not prolong progression-free survival (PFS) compared with bev 5 mg/kg plus FOLFIRI in patients with mCRC.

Methods: Outcomes according to tumor KRAS status were evaluated as an exploratory analysis. KRAS data were collected from each institution. Survival analyses using Cox regression and Log-rank test were conducted by subgroups of the KRAS status.

Results: Of 387 patients, 326 (84%) had KRAS data; 164 (50%) had KRAS wild-type tumors and 162 (50%) had mutant KRAS tumors. The median PFS was 7.1 months for bev 10 mg/kg and 5.9 months for bev 5 mg/kg (P = 0.568; HR = 1.04; 95% confidence interval (CI): 0.76-1.43) for wild-type KRAS and 5.6 months for bev 10 mg/kg and 6.5 months for bev 5 mg/kg, respectively (P = 0.89; HR = 1.10; 95% CI: 0.80-1.51) for mutant KRAS. The P value of test for treatment-subgroup interaction was 0.956. The median overall survival (OS) was 17.9 months for bev 10 mg/kg and 15.5 months for bev 5 mg/kg, respectively (P = 0.244; HR = 0.80; 95% CI: 0.55-1.17) for wild-type KRAS and 15.9 months for bev 10 mg/kg versus 17.7 months for bev 5 mg/kg, respectively (P = 0.312; HR = 1.21; 95% CI 0.84-1.74) for mutant KRAS.

Conclusions: Although possible differences of treatment effect between bev 5 mg/kg and 10 mg/kg groups were observed for patients with wild-type KRAS, these results revealed bev 10 mg/kg plus FOLFIRI as second-line treatment did not prolong PFS compared with bev 5 mg/kg plus FOLFIRI in patients with mCRC depending on KRAS status.

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