Addition of aflibercept to fluorouracil, leucovorin, and irinotecan improves survival in a phase III randomized trial in patients with metastatic colorectal cancer previously treated with an oxaliplatin-based regimen.

Abstract
PURPOSE: Treatment for metastatic colorectal cancer (mCRC) commonly involves a fluoropyrimidine-based chemotherapy regimen such as infusional fluorouracil, leucovorin, and irinotecan (FOLFIRI) or fluorouracil, leucovorin, and oxaliplatin, often combined with bevacizumab or an epidermal growth factor receptor monoclonal antibody. We studied the effect of adding the novel antiangiogenic agent aflibercept (also known as ziv-aflibercept in the United States) to FOLFIRI in patients with mCRC previously treated with oxaliplatin, including patients who received prior bevacizumab. PATIENTS AND METHODS: Patients were randomly assigned to receive aflibercept (4 mg/kg intravenously; 612 patients) or placebo (614 patients) every 2 weeks in combination with FOLFIRI. Treatment was administered until disease progression or unacceptable toxicity. The primary end point was overall survival. RESULTS: Adding aflibercept to FOLFIRI significantly
improved overall survival relative to placebo plus FOLFIRI (hazard ratio [HR], 0.817; 95.34% CI, 0.713 to 0.937; P = .0032) with median survival times of 13.50 versus 12.06 months, respectively. Aflibercept also significantly improved progression-free survival (PFS; HR, 0.758; 95% CI, 0.661 to 0.869; P < .0001), with median PFS times of 6.90 versus 4.67 months, respectively. The effects on overall survival and PFS exhibited a consistent trend across prespecified subgroup analyses, including bevacizumab pretreated patients. Response rate was 19.8% (95% CI, 16.4% to 23.2%) with aflibercept plus FOLFIRI compared with 11.1% (95% CI, 8.5% to 13.8%) with placebo plus FOLFIRI (P = .0001). Adverse effects reported with aflibercept combined with FOLFIRI included the characteristic anti-vascular endothelial growth factor effects and also reflected an increased incidence of some chemotherapy-related toxicities. CONCLUSION: Aflibercept in combination with FOLFIRI conferred a statistically significant survival benefit over FOLFIRI combined with placebo in patients with mCRC previously treated with oxaliplatin.

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