ORIGINAL ARTICLE

Initial Therapy with FOLFOXIRI and Bevacizumab for Metastatic Colorectal Cancer

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ABSTRACT

BACKGROUND

A fluoropyrimidine plus irinotecan or oxaliplatin, combined with bevacizumab (a monoclonal antibody against vascular endothelial growth factor), is standard first-line treatment for metastatic colorectal cancer. Before the introduction of bevacizumab, chemotherapy with fluorouracil, leucovorin, oxaliplatin, and irinotecan (FOLFOXIRI) showed superior efficacy as compared with fluorouracil, leucovorin, and irinotecan (FOLFIRI). In a phase 2 study, FOLFOXIRI plus bevacizumab showed promising activity and an acceptable rate of adverse effects.

METHODS

We randomly assigned 508 patients with untreated metastatic colorectal cancer to receive either FOLFIRI plus bevacizumab (control group) or FOLFOXIRI plus bevacizumab (experimental group). Up to 12 cycles of treatment were administered, followed by fluorouracil plus bevacizumab until disease progression. The primary end point was progression-free survival.

RESULTS

The median progression-free survival was 12.1 months in the experimental group, as compared with 9.7 months in the control group (hazard ratio for progression, 0.75; 95% confidence interval [CI], 0.62 to 0.90; P=0.003). The objective response rate was 65% in the experimental group and 53% in the control group (P=0.006). Overall survival was longer, but not significantly so, in the experimental group (31.0 vs. 25.8 months; hazard ratio for death, 0.79; 95% CI, 0.63 to 1.00; P=0.054). The incidences of grade 3 or 4 neurotoxicity, stomatitis, diarrhea, and neutropenia were significantly higher in the experimental group.

CONCLUSIONS

FOLFOXIRI plus bevacizumab, as compared with FOLFIRI plus bevacizumab, improved the outcome in patients with metastatic colorectal cancer and increased the incidence of some adverse events. (Funded by the Gruppo Oncologico Nord Ovest and others; ClinicalTrials.gov number, NCT00719797.)

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