

# Initial Safety Report of NSABP C-08: A Randomized Phase III Study of Modified FOLFOX6 With or Without Bevacizumab for the Adjuvant Treatment of Patients With Stage II or III Colon Cancer

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**Purpose** The National Surgical Adjuvant Breast and Bowel Project C-08 trial was designed to investigate the safety and effectiveness of adding bevacizumab to modified infusional fluorouracil, leucovorin, and oxaliplatin (FOLFOX) 6 regimen for the adjuvant treatment of patients with stage II or III colon cancer. We present safety information in advance of the planned analysis of efficacy.

**Patients and Methods** Among 2,710 randomly assigned patients, demographic factors were balanced. Patients received modified FOLFOX6 every 2 weeks x 12 or modified FOLFOX6 plus bevacizumab (5 mg/kg every 2 weeks x 26, experimental group).

**Results** Overall rates of grade 4 or 5 toxicities were nearly identical in the FOLFOX6 and FOLFOX6 plus bevacizumab arms (15.2% and 15.0%, respectively). Six-month mortality rates were 0.96% and 0.90% for the control and experimental groups, respectively. Grade 3+ toxicities that occurred more often in the experimental arm versus control arm included hypertension (12% v 1.8%, respectively), wound complications (abdominal incisional hernia or infusion port dehiscence/inflammation; 1.7% v 0.3%, respectively), pain (11.1% v 6.3%, respectively), and proteinuria (2.7% v 0.8%, respectively). Grade 2+ neuropathy was increased in the experimental arm versus the control arm (grade 2, 33% v 29%, respectively; grade 3, 16% v 14%, respectively; and grade 4, < 1% each). In the experimental arm versus control arm, significantly less thrombocytopenia (1.4% v 3.4%, respectively) and fewer allergic reactions (3.1% v 4.7%, respectively) were observed. Advanced age was associated with a significantly greater rate of grade 4 and 5 toxicities regardless of treatment.

**Conclusion** Bevacizumab with modified FOLFOX6 is well tolerated in the surgical adjuvant setting in these patients. No significant increase in GI perforation, hemorrhage, arterial or venous thrombotic events, or death with the addition of bevacizumab to modified FOLFOX6 has been observed. Follow-up for potential delayed adverse effects and efficacy is ongoing.

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