

A phase III trial comparing mFOLFOX6 to mFOLFOX6 plus bevacizumab in stage II or III carcinoma of the colon: Results of NSABP Protocol C-08

N. Wolmark, G. Yothers, M. J. O'Connell, S. Sharif, J. N. Atkins, T. E. Seay, L. Feherenbacher, S. O'Reilly and C. J. Allegra

NSABP, Pittsburgh, PA; University of Florida, Gainesville, FL; Department of Biostatistics, University of Pittsburgh, Pittsburgh, PA; Allegheny General Hospital, Pittsburgh, PA; Southeast Cancer Control Consortium CCOP, Goldsboro, NC; Atlanta Cancer Care, Atlanta, GA; Kaiser Permanente Northern California, Vallejo, CA; All Ireland Cooperative Oncology Research Group, Dublin, Ireland

J Clin Oncol 27:18s, 2009 (suppl; abstr LBA4)

Background: The primary aim of this two-arm randomized prospective study was to determine whether mFOLFOX6 plus bevacizumab (mFF6+B) would prolong disease-free survival (DFS) compared to mFOLFOX6 (mFF6) alone. **Methods:** Between September 2004 and October 2006, 2,672 patients with follow-up (1,338 and 1,334 in respective arms) with stage II (24.9%) or III carcinoma of the colon were randomized to receive either mFF6 (oxaliplatin 85 mg/m² IV d1, leucovorin 400 mg/m² IV d1, 5-FU 400 mg/m² IV bolus d1, and 5-FU 2400 mg/m² CI over 46 hrs (d1+2) q14d x 12 cycles) or mFF6+B (same mFF6 regimen + bevacizumab 5 mg/kg IV q 2 wks x 1 yr). The primary end point was DFS. Events were defined as first recurrence, second primary cancer, or death. **Results:** The median follow-up for patients still alive was 36 months. The hazard ratio (HR: FF6+B vs. mFF6) was 0.89; 95% CI (0.76=1.04); p=0.15. Data censored at intervals disclosed an initial benefit for bevacizumab that diminished over time: The smoothed estimate of the DFS HR over time indicated that bevacizumab significantly reduced the risk of a DFS event during the interval from 0.5 to 1.0 year. There was no evidence that patients receiving bevacizumab had a worse DFS compared to those receiving mFF6 alone following treatment. **Conclusions:** The addition of bevacizumab to mFF6 did not result in an overall statistically significant prolongation in DFS. There was a transient benefit in DFS during the one-year interval that bevacizumab was utilized. Consideration may be given to clinical trials assessing longer duration of bevacizumab administration. Supported by PHS grants U10CA-12027, -69974, -37377, and -69651 from the NCI and a grant from Genentech, Inc.

	N	Ev	3yDFS	P	Yr	1	1.5	2	2.5	3
mFF6	1338	312	75.5		HR	0.60	0.74	0.81	0.85	0.87
mFF6+B	1334	291	77.4	0.15	P	0.0004	0.004	0.02	0.05	0.08