# NSABP Trial R-04 and ECOG Trial 5204

A national platform for the neoadjuvant and adjuvant treatment of patients with stage II or III rectal adenocarcinoma

**by Nicholas Petrelli, MD**

NSABP protocol R-04 and ECOG protocol 5204 are complementary trials that set the stage for a national agenda for the adjuvant treatment of patients with stage II or stage III rectal adenocarcinoma. NSABP protocol R-04 is a trial comparing preoperative radiation therapy and capecitabine with or without oxaliplatin to preoperative radiation therapy and continuous intravenous infusion of 5-fluorouracil with or without oxaliplatin. Following surgery, patients on NSABP R-04 are candidates for ECOG 5204, which is a randomized Phase III trial of postoperative oxaliplatin, 5-fluorouracil, and leucovorin versus oxaliplatin, 5-fluorouracil, leucovorin, and bevacizumab for stage II or III rectal adenocarcinoma. As part of their eligibility criteria, both trials require:

1. ECOG performance status of 0-1
2. Histologically confirmed adenocarcinoma of the rectum
3. No evidence of metastatic disease
4. Adequate bone marrow, liver, and kidney function.

## Ancillary Studies

NSABP R-04 also includes a quality of life study that will examine differences between the four treatment regimens and the two approaches of sphincter saving and non-sphincter saving surgery. Core biopsy tissue in RNAlater® (an aqueous, non-toxic tissue storage reagent that rapidly permeates tissues to stabilize and protect cellular RNA); serum collection before therapy begins; and tumor blocks and serum collected at the time of surgery are all required for NSABP R-04 as part of a tissue library to correlate gene expression profiling with response and prognosis. ECOG 5204 also has ancillary studies dealing with assessing long-term rectal function, validating the FACT-Diarrhea subscale questionnaire, and assessing long-term symptoms of oxaliplatin-related neurotoxicity and tissue sample collection to assess laboratory correlates. The schemas for ECOG 5204 and NSABP R-04 are illustrated in Figures 1 and 2, respectively.

## Primary and Secondary Endpoints

The primary endpoint for NSABP R-04 is the time from randomization to first local regional failure. Local recurrence is defined as evidence of tumor in the anastomotic or perineal area. Regional recurrence is defined as evidence of tumor in the pelvic or retroperitoneal nodes. Secondary endpoints include:

- Pathologic complete response to preoperative therapy
- Comparison of oral capecitabine and continuous infusion of 5-fluorouracil with or without oxaliplatin on quality of life
- The impact of the type of surgical management of rectal cancer on quality of life at one year after surgical treatment.

The primary end point for ECOG 5204 is overall survival. Secondary endpoints include 1) disease free survival, 2) tolerance of treatment, 3) patterns of failure, 4) evaluation of molecular markers of treatment efficacy, and 5) correlation of tumor molecular prognostic markers with survival.

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**Figure 1. E5204 Trial Schema**

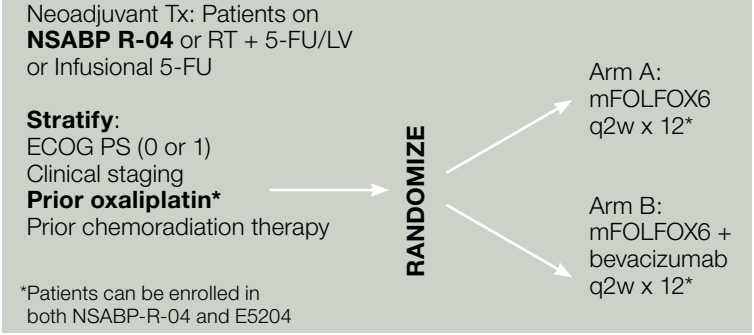
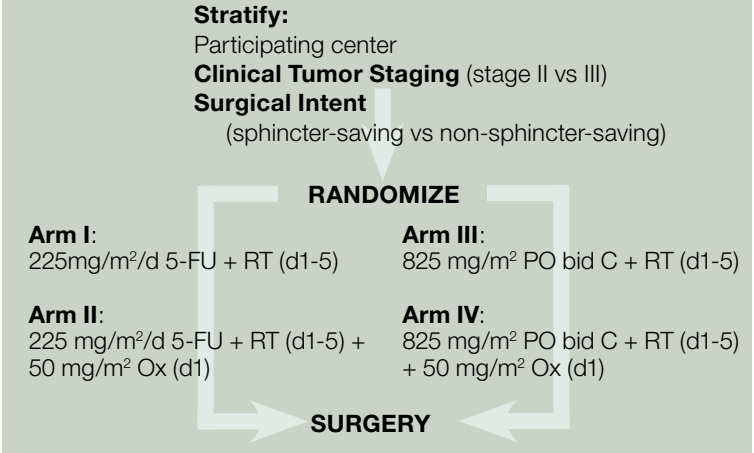



**Figure 2. NSABP R-04 Trial Schema**




RT = radiotherapy; Ox = oxaliplatin; C = capecitabine.