A paradigm shift in rectal cancer treatment: The PROSPECT trial

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The “Miles” procedure, or abdominal-perineal resection (APR), recently celebrated a 100-year anniversary, which should remind us that while some things change, others remain the same. Whereas the APR is still practiced, numerous additional options have evolved, including sphincter-preserving procedures to improve quality of life, and neoadjuvant and adjuvant radiation and chemotherapy to reduce rates of local, regional, and systemic relapse. Indeed, our current paradigm calls for neoadjuvant radiation and sensitizing chemotherapy followed by surgery and postoperative chemotherapy as the standard of care for Stage II and Stage III rectal cancer. This standard is now challenged by rising concerns about the long-term toxicities of current regimens and new standards are encouraged by improvements in surgery and radiographic imaging and chemotherapy options.

To safely challenge the existing paradigm, the Alliance for Clinical Trials in Oncology Cooperative Group is launching a new trial titled the “PROSPECT” trial. PROSPECT is the acronym for Preoperative Radiation Or Selective Preoperative Radiation and Evaluation before Chemotherapy and Total Mesorectal Excision (TME).

The PROSPECT trial, by offering preoperative radiation or selective preoperative radiation and evaluation before chemotherapy and TME, provides the opportunity of reducing the use of pelvic radiation in patients who might not benefit from this treatment. In this phase II/III multicenter trial, neoadjuvant FOLFOX (Oxaliplatin, Leucovorin, and 5-Fluorouracil) with selective use of chemoradiation (5-Fluorouracil and pelvic radiation), is being tested against the current standard of preoperative chemoradiation (5-Fluorouracil and pelvic radiation) for rectal cancer patients undergoing low anterior resection with TME (NCCTG-N1048; N1048; NCT01515787; see figure, this page).

The rationales for conducting the trial are as follows: (1) pelvic radiation is associated with significant morbidities; (2) neoadjuvant chemoradiation may overtreat some patients whose risk of local failure is low after TME alone; and (3) moving systemic chemotherapy more proximately in the treatment regimen may benefit some patients. The trial’s primary endpoints are R0 resection rate, time to local recurrence, and disease-free survival.

Adult patients (ages ≥18 years) with biopsy-proven rectal adenocarcinoma of the following characteristics are eligible:

- Clinical stage T2N1, T3N0, or T3N1 (stage II, IIIA, or IIIB) as...