

How Can the Integration of Targeted Agents With Chemoradiation Help Rectal Cancer Patients?

Christopher H. Crane, MD

University of Texas M. D. Anderson Cancer Center

Houston, Texas

The landmark Gastrointestinal Tumor Study Group (GITSG)¹ and North Central Cancer Treatment Group (NCTTG)² trials defined the role of postoperative chemoradiation in the treatment of stage II-III localized rectal cancer. More recently, the German CAO/ARO/AIO trial demonstrated that preoperative chemoradiation yields higher rates of local control and sphincter preservation with lower rates of toxicity compared with postoperative chemoradiation.³ However, it is clear that significant limitations remain even with the use of neoadjuvant chemoradiation in the highest risk patients (T3/N+ and T4 patients).⁴ Enhancement of pelvic control through the use of more effective radiosensitization is a goal for future trials. The concept of organ preservation after pathologic complete response to chemoradiation in cT3/N0 rectal cancer is also gaining interest.⁵ It may be possible to substitute either full thickness local excision⁶ or possibly even surveillance alone⁷ for radical surgery in highly selected patients who respond well to chemoradiation. In order for such a strategy to be feasible on a large scale, dramatically more effective chemoradiation regimens are needed. Many single-arm studies that incorporated novel cytotoxic radiosensitizers such as capecitabine, irinotecan, and oxaliplatin with 5-fluorouracil (5-FU)-based chemoradiation in the neoadjuvant setting have shown a suggestion of modest increases in pathologic response, at the price of increased acute toxicity. The National Surgical Breast and Bowel Project (NSABP) R-04 is a phase III trial that is evaluating two of these promising new agents, oxaliplatin and capecitabine. Preliminary studies have evaluated the addition of targeted agents such as bevacizumab and cetuximab to standard chemoradiation for rectal cancer.

Selected References

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