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Preoperative Therapy for Rectal Cancer

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For patients with cT3 and or N+ rectal cancer, the German trial confirmed that preoperative combined modality therapy achieves significantly improved local control, less acute short- and long-term toxicity, and increased sphincter preservation compared with postoperative combined modality therapy. The subsequent shift from postoperative to preoperative therapy has resulted in a series of questions. For example, does combining newer chemotherapeutic agents with radiation improve the pathologic complete response (pCR) rate? Is the response rate a surrogate marker for outcome? Are molecular markers available that can help predict the response rate and preoperative nodal stage? Do patients with uT3N0 disease require preoperative adjuvant radiation? Should all patients who receive preoperative combined modality therapy receive postoperative adjuvant chemotherapy?

Most of the trials that combined novel chemotherapeutic agents with preoperative radiation reported higher pCR rates than achieved with continuous infusion 5-fluorouracil (5-FU). Likewise, results of most phase I/II trials suggest that pCR is associated with improvement in local control. However, phase III trials are needed. The European Organisation for Research and Treatment of Cancer (EORTC) 22921 and the French Fédération Francophone de Cancérologie Digestive (FFCD) 9203 trials did not confirm a significant survival benefit for postoperative adjuvant 5-FU-based chemotherapy in patients with node-positive colon and rectal cancers. Despite these controversial data, 4 months of postoperative adjuvant chemotherapy is still appropriate. However, in patients whose tumors do not respond to preoperative treatment, it is reasonable not to use the same chemotherapeutic regimen in the postoperative setting.

Molecular markers will likely help us understand the underlying mechanisms and provide a rationale for selection of the appropriate therapies.