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ORIGINAL REPORT

Randomized Trial of Short-Course Radiotherapy Versus Long-Course Chemoradiation Comparing Rates of Local Recurrence in Patients With T3 Rectal Cancer: Trans-Tasman Radiation Oncology Group Trial 01.04

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ABSTRACT

Purpose
To compare the local recurrence (LR) rate between short-course (SC) and long-course (LC) neoadjuvant radiotherapy for rectal cancer.

Patients and Methods
Eligible patients had ultrasound- or magnetic resonance imaging–staged T3N0-2M0 rectal adenocarcinoma within 12 cm from anal verge. SC consisted of pelvic radiotherapy 5 × 5 Gy in 1 week, early surgery, and six courses of adjuvant chemotherapy. LC was 50.4 Gy, 1.8 Gy/fraction, in 5.5 weeks, with continuous infusional fluorouracil 225 mg/m^2 per day, surgery in 4 to 6 weeks, and four courses of chemotherapy.

Results
Three hundred twenty-six patients were randomly assigned; 163 patients to SC and 163 to LC. Median potential follow-up time was 5.9 years (range, 3.0 to 7.8 years). Three-year LR rates (cumulative incidence) were 7.5% for SC and 4.4% for LC (difference, 3.1%; 95% CI, −2.1 to 8.3; $P = .24$). For distal tumors (< 5 cm), six of 48 SC patients and one of 31 LC patients experienced local recurrence ($P = .21$). Five-year distant recurrence rates were 27% for SC and 30% for LC (log-rank $P = 0.92$; hazard ratio [HR] for LC:SC, 1.04; 95% CI, 0.69 to 1.56). Overall survival rates at 5 years were 74% for SC and 70% for LC (log-rank $P = 0.62$; HR, 1.12; 95% CI, 0.76 to 1.67). Late toxicity rates were not substantially different (Radiation Therapy Oncology Group/European Organisation for Research and Treatment of Cancer G3-4: SC, 5.8%; LC, 8.2%; $P = .53$).

Conclusion
Three-year LR rates between SC and LC were not statistically significantly different; the CI for the difference is consistent with either no clinically important difference or differences in favor of LC. LC may be more effective in reducing LR for distal tumors. No differences in rates of distant recurrence, relapse-free survival, overall survival, or late toxicity were detected.

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INTRODUCTION

Adding radiotherapy to surgery has been shown conclusively to improve local control for rectal cancer.[1,2] Short-course preoperative radiotherapy of 25 Gy in 5 consecutive days has been shown to be effective in tumor control. The Swedish Rectal Cancer Trial[3] demonstrated that short-course preoperative radiotherapy reduced the risk of local recurrence (LR) by half. In this study, improved overall survival was also evident. The Dutch Rectal Cancer Trial[4] demonstrated that short-course preoperative radiotherapy maintains its benefit when combined with the best surgical practice—total mesorectal excision. It was through meticulous study design and quality assurance that the value of short-course preoperative radiotherapy in addition to surgery was put beyond doubt. The MRC (Medical Research Council) CR07 rectal trial,[5] which compared short-course preoperative radiotherapy with selective postoperative chemoradiotherapy, provided further support for the short course approach.

Long-course preoperative chemoradiotherapy of 50.4 Gy in 5 weeks and 3 days with concurrent