Effect of Interval (7 or 11 weeks) Between Neoadjuvant Radiochemotherapy and Surgery on Complete Pathologic Response in Rectal Cancer: A Multicenter, Randomized, Controlled Trial (GRECCAR-6)

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Purpose
A pathologic complete response (pCR; ypT0N0) of a rectal tumor after neoadjuvant radio-chemotherapy (RCT) is associated with an excellent prognosis. Several retrospective studies have investigated the effect of increasing the delay after RCT. The aim of this study was to evaluate the effect of increasing the interval between the end of RCT and surgery on the pCR rate.
Methods
GRECCAR6 was a phase III, multicenter, randomized, open-label, parallel-group controlled trial. Patients with cT3/T4 or Tx N+ tumors of the mid or lower rectum who had received RCT (45 to 50 Gy with fluorouracil or capecitabine) were included. Patients were randomly included in the 7-week or the 11- week (11w) group. Primary end point was the pCR rate defined as a ypT0N0 specimen (NCT01648894).
Results
A total of 265 patients from 24 centers were enrolled between October 2012 and February 2015. The majority of the tumors were cT3 (82%). After RCT, surgery was not performed in nine patients (3.4%) because of the occurrence of distant metastasis (n = 5) or other reasons. Two patients underwent local resection of the tumor scar. A total of 47 (18.6%) specimens were classified as ypT0 (four had invaded lymph nodes [8.5%]). The primary end point (ypT0N0) was not different (7 weeks: 20 of 133, 15.0% v 11w: 23 of 132, 17.4%; P = .5983). Morbidity was significantly increased in the 11w group (44.5% v 32%; P = .0404) as a result of increased medical complications (32.8% v 19.2%; P = .0137). The 11w group had a worse quality of mesorectal resection (complete mesorectum [I] 78.7% v 90%; P = .0156).
Conclusion
Waiting 11 weeks after RCT did not increase the rate of pCR after surgical resection. A longer waiting period may be associated with higher morbidity and more difficult surgical resection.