Rectal

Multicenter, Randomised, Phase III Trial of Neoadjuvant Chemoradiation With Capecitabine and Irinotecan Guided by UGT1A1 Status in Patients With Locally Advanced Rectal Cancer

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PURPOSE

Differentiating the irinotecan dose on the basis of the uridine diphosphate glucuronosyltransferase 1A1 (UGT1A1) genotype improves the pathologic complete response (pCR) rate. In this study, we further investigated preoperative irinotecan combined with capecitabine-based chemoradiotherapy for locally advanced rectal cancer.

PATIENTS AND METHODS

We conducted this randomised, open-label, multicenter, phase III trial in China. Eligible patients with clinical T3-4 and/or N+ rectal adenocarcinoma, UGT1A1 genotype *1*1 or *1*28 were randomly allocated to the control group: pelvic radiation of 50 Gy/25 fractions with concurrent capecitabine, followed by oxaliplatin and capecitabine; or the experimental group: radiation with capecitabine combined with weekly irinotecan 80 mg/m2 for patients with UGT1A1*1*1 or 65 mg/m2 for patients with UGT1A1*1*28, followed by irinotecan and capecitabine. The primary end point was pCR. This trial was registered with ClinicalTrials.gov (ClinicalTrials.gov identifier: NCT02605265).

RESULTS

Of the 360 patients initially enrolled, 356 were evaluated as the modified intention-to-treat population (n = 178 in both groups). Surgery was performed in 87% and 88% of patients in the control and experimental groups, respectively. The pCR rates were 15% (n = 27 of 178) and 30% (n = 53 of 178) in the control and experimental groups (risk ratio, 1.96; 95% CI, 1.30 to 2.97; P = .001). Four and six patients achieved complete clinical response in the control and experimental groups, respectively. Grade 3-4 toxicities were recorded in 11 (6%) and 68 (38%) patients in the control and experimental groups, respectively (P < .001). The commonest grade 3-4 toxicities were leukopenia, neutropenia, and diarrhea. The overall surgical complication rate was not significantly different between the two groups (11% v 15%; P < .001).

CONCLUSION

Adding irinotecan guided by UGT1A1 genotype to capecitabine-based neoadjuvant chemoradiotherapy significantly increased complete tumour response in Chinese patients.