Rectal

PD-1 Blockade in Mismatch Repair-Deficient, Locally Advanced Rectal Cancer

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BACKGROUND

Neoadjuvant chemotherapy and radiation followed by surgical resection of the rectum is a standard treatment for locally advanced rectal cancer. A subset of rectal cancer is caused by a deficiency in mismatch repair. Because mismatch repair-deficient colorectal cancer is responsive to programmed death 1 (PD-1) blockade in the context of metastatic disease, it was hypothesised that checkpoint blockade could be effective in patients with mismatch repair-deficient, locally advanced rectal cancer.

METHODS

We initiated a prospective phase II study in which single-agent dostarlimab, an anti-PD-1 monoclonal antibody, was administered every three weeks for six months in patients with mismatch repair-deficient stage II or III rectal adenocarcinoma. This treatment was to be followed by standard chemoradiotherapy and surgery. Patients who had a clinical complete response after completion of dostarlimab therapy would proceed without chemoradiotherapy and surgery. The primary end points are sustained clinical complete response 12 months after completion of dostarlimab therapy or pathological complete response after completion of dostarlimab therapy with or without chemoradiotherapy and overall response to neoadjuvant dostarlimab therapy with or without chemoradiotherapy.

RESULTS

A total of 12 patients have completed treatment with dostarlimab and have undergone at least six months of follow-up. All 12 patients (100%; 95% confidence interval, 74 to 100) had a clinical complete response, with no evidence of tumour on magnetic resonance imaging, 18F-fluorodeoxyglucose-positron-emission tomography, endoscopic evaluation, digital rectal examination, or biopsy. At the time of this report, no patients had received chemoradiotherapy or undergone surgery, and no cases of progression or recurrence had been reported during follow-up (range, six to 25 months). No adverse events of grade 3 or higher have been reported.

CONCLUSIONS

Mismatch repair-deficient, locally advanced rectal cancer was highly sensitive to single-agent PD-1 blockade. Longer follow-up is needed to assess the duration of response.