Editorial

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Precision medicine for primary rectal cancer will become a reality

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Although precision medicine is the goal, in reality, rectal cancer treatment follows standard guidelines. Currently, the routine treatment for locally advanced rectal cancer includes neoadjuvant chemoradiotherapy and surgery, and this "one-size-fits-all" approach improves oncologic outcomes. However, bowel dysfunction, even in the case of sphincter preservation, has been an intractable problem and a major cause of worsening quality of life [1]. Therefore, there have been efforts to keep oncologic safety and improve quality of life as well in treatment of rectal cancer. The watch-and-wait approach which can preserve rectum has been used in a very small subset of patients who had complete clinical regression after neoadjuvant chemoradiotherapy. This approach presents a paradigm shift in rectal cancer treatment, making it a subject of great interest [2]. Intensifying multimodal neoadjuvant treatment accelerates the paradigm shift towards the watch-and-wait approach, i.e., surgery deferral [3].

Intensified neoadjuvant treatment relieves approximately 50% of patients from the functional deterioration of radical resection; however, it also causes dysfunction caused by chemoradiotherapy. The side effect of chemoradiotherapy is substantial and results in long-term discomfort. Although many studies have been conducted to address this problem, there is still no sufficient result that can help to reduce side effects. Indeed, patients who have mismatch repair–deficient rectal cancer may respond less to the current neoadjuvant treatment [4]. Therefore, these patients are prone to receive neoadjuvant therapy which might not be effective but toxic.

These patients have been targeted for immunotherapy, a game-changing treatment, because of their unique genetic properties. Therapeutic possibility of immunotherapy was studied and proved in the patients with metastatic colorectal cancer [5].

Cercek et al. [6] examined the therapeutic possibility of immunotherapy in rectal cancer treatment. In June, 12 patients with mismatch repair–deficient stage II or III rectal cancer were administered immunotherapy with dostarlimab, a programmed death 1 inhibitor. All patients who completed 6 months of dostarlimab treatment showed complete clinical regression upon magnetic resonance imaging, ^{18}F-fluorodeoxyglucose–positron-emission tomography, and endoscopy. All were free of tumor regrowth and other treatments during a median follow-up period of 1 year. The report is very promising because the treatment outcome was obtained without serious adverse events and further chemoradiotherapy. However, waiting for the long-term report is important because regrowth and distant metastasis can occur later on. Nevertheless, these patients have an increased potential to be cured without functional deterioration, which is common in the current treatment modality.

Aside from the insufficient follow-up period and small study population, the indication for treatment is also an issue. Although the authors included those with stage II and III rectal cancer, 25% of the patients had T1/T2 disease. These patients will have favorable outcomes even if they have lymph node metastasis with the current treatment strategy [7, 8]. In this regard, the proposed treatment strategy may change the disease status of these patients from curable to merely controllable. This necessitates reasonable and reliable response evaluation method and interval while considering both the clinical implication and medical cost.

Although only a short-term report, the study of Cercek et al. [6] is a step closer to precision medicine considering genetic and tumor status, as well as quality of life in 5% to 10% of patients with rectal cancer. Globally diverse clinical trial groups are needed to examine the possibility of using immunotherapy as a primary treatment for mismatch repair–deficient rectal cancer in the clinical setting.

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CONFLICT OF INTEREST

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