STUDENTS' CORNER
LETTER TO THE EDITOR

Immune check point inhibition in Colorectal Cancer: Current challenges and concerns

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Esteemed Editor, The incidence of colorectal cancer (CRC), which accounts for 10% of all cancer cases worldwide, ranges from 4 to 6.8% in Pakistan to 11% in the UK[1] making it the 3rd most common type of cancer. Blood in the stool, changes in bowel habits, exhaustion, and weight loss are possible signs and symptoms.

Neoadjuvant chemotherapy and radiation accompanied by rectal resection surgery is the mainstay of care for locally advanced colorectal cancer. Immune checkpoint inhibitors have proved to be a novel first-line therapy for various forms of cancer, along with chemo and immunotherapy. A class of checkpoint inhibitor medications known as PD-1 (programmed cell death protein 1) inhibitors and PD-L1 (programmed death-ligand 1) inhibitors function by inhibiting the activation of immunological checkpoint proteins mostly on the cell surface known PD-1, PD-L1. The FDA has approved five antibodies that suppress the PD-1 signalling pathway for cancer treatment, including Dostarlimab. Another recent trial successfully supports the possibility that checkpoint blockage may benefit people with mismatch repair–deficient, locally advanced rectal cancer. Dostarlimab effectively provided a clinically complete response.[2]

The challenges in therapy include the fact that in a recent trial,[2] the clinical use of PD-1/PD-L1 targeting checkpoint inhibitors in rectal cancer has primarily focused on a subset of microsatellite unstable (MSI-high) patients, whose DNA sequence is different from typical healthy cells and accounts only for 5% of metastatic CRC. Immune Checkpoint Inhibitors (ICIs) failed to exhibit anticancer action in the remaining 95% of CRC patients, whose DNA sequence matches that of healthy normal cells (MSS/pMMR).[3] Furthermore, in studies,[4] PD-1 blockade induced antitumour memory in mice models after recovery. If produced in humans could pave a new line of treatment for cancer recurrence. Additionally, Dostarlimab has many side effects and contraindications like Type1 Diabetes Mellitus and pregnancy.[5] More research is needed to obtain drugs having fewer contraindications and more potency.

Along with the combined use of analyzed data already present, using nanocarriers for drug delivery, reporting timing and mode of delivery of the immunotherapy on people from demographic diversities, researchers could optimize therapeutic effects on anti–PD-1 efficacy and bring another breakthrough in cancer treatment, prevention and spread. We are hopeful that further studies along with personalized cancer vaccines, cell therapy, gene editing, microbiome-based therapeutics, and combination drug therapy could pave the way toward more effective cancer treatment.

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