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Editorial

Systematic Therapy for Gastrointestinal Tumors

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Systematic therapy for gastrointestinal tumor has revolved around radiation therapy, chemotherapy, targeted therapy, and immunotherapy over the last few decades. Among which, immunotherapy is undoubtedly the most prospective field for tumor treatment. In recent years, immunotherapy, especially immune checkpoint inhibitors (ICIs), has demonstrated promising and exciting results in various clinical trials. The Checkmate-648 and KEYNOTE-590 studies laid the foundation for PD-1 antibodies plus chemotherapy as first-line treatment in advanced esophageal squamous cell carcinoma. The KEYNOTE-181 and ATTRACTION-3 studies secured PD-1 antibodies as second-line treatment for advanced ESCC. In advanced gastric adenocarcinoma, the Checkmate-649 and ATTRACTION-4 studies established PD-1 antibodies plus chemotherapy as first-line treatment, while KEYNOTE-061 and ATTRACTION-2 studies recognized PD-1 antibodies as second- and third-line treatment. The KEYNOTE-177 study showed that pembrolizumab was superior to chemotherapy with respect to PFS (median, 16.5 vs. 8.2 months) in MSI-H/dMMR advanced or metastatic colorectal cancer. The REVONIVO and LEAP-005 studies advocated PD-1 antibodies plus targeted therapy as third-line treatment for metastatic colorectal cancer with MSS.

Immunotherapy as one of the most important part of systemic therapy for gastrointestinal tumor has gained rapidly recognition. A few promising research prospects for gastrointestinal tumors include the following: (1) ICIs combined with low-dose chemotherapy and/or radiation therapy. Low-dose chemotherapy or radiation therapy delivers tumor cytotoxicity, with limited impairment to the systemic immune system, providing a synergistic treatment effect. A low-dose, high-frequency administration continues to kill tumor cells, which releases tumor antigens to activating the antitumor immune response. In addition, the establishment of an optimal duration for ICIs and chemotherapy administration is of clinical significance. (2) ICIs combined with VEGF pathway inhibitors. Through increasing vessel permeability, VEGF pathway inhibitors can improve tumor perfusion, improve hypoxia, encourage immune cell migration, and finally augment the overall treatment efficacy of ICIs. (3) Establishment of a systematic immune evaluation criteria, such as calculating the proportion of inhibitory and activating immune cells. The individual immune system should be evaluated continuously during systematic therapy. If the immune system has been significantly impaired, treatment course should be shortened. (4) Tumor cytotoxicity can cause certain tumor cells to enter the G0 stage of mitosis or complete cell death, which causes the tumor tissue to become fibrotic, but can still be detected by CT or MIR. Continuous treatment will not provide additional antitumor effects, but instead cause systemic damage. Therefore, with the help of new surveillance methods such as PET-CT, a dynamic evaluation of tumor vitality can minimize systemic damage and improve the survival of patients through shortening the course of antitumor treatment. (5) Activation of tumor-specific immune responses may be the key for tumor patients to achieve complete remission. Neoantigen vaccine (including peptide vaccine and RNA vaccine) may be a promising direction in the treatment of gastrointestinal tumors. In conclusion, based on continuous monitoring of tumor vitality and evaluation of the immune system, application of neoantigen immunotherapy combined with PD-1 antibody,

along with chemotherapy and radiotherapy, can altogether provide a new paradigm for the systematic therapy of gastrointestinal tumors.

Conflicts of Interest

The authors declare that they have no conflicts of interest regarding the publication of this special issue.

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