

Advances in Gastrointestinal Cancer Research

Guest Editor



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Message from the Guest Editor

Dear Colleagues,

In the last decade, immunocheckpoint inhibitors have proved to be a turning point in the treatment of several malignancies, including NSCLC, melanoma and renal cell carcinoma. Although their activity

against gastrointestinal tract cancers took longer to be demonstrated, recent studies have shown interesting results in selected patient groups.

In gastro-esophageal cancers, immunocheckpoint inhibitors are effective as adjuvant monotherapy for esophageal carcinoma, and as first line treatment for gastric cancer when used in combination with chemotherapy.

In colorectal cancers, immunotherapy is effective both as monotherapy and also in combination with other immunocheckpoint inhibitors. More recent results show that immunotherapy is also effective in combination with chemotherapy for the treatment of metastatic disease. This efficacy was demonstrated only in patients with tumors showing microsatellite instability (dMMR/MSI-H). However, the most recent combination study with temozolomide in patients with MGMT-silenced and microsatellite stable (MSS) metastatic colorectal cancer showed these tumors were also responsive to immunotherapy.

In all studies, the tumor biomarkers most frequently associated with a better response to immunocheckpoint inhibitors were dMMR/MSI-H and the expression of PD-L1 (CPS > 5%). MSI-H in particular appears to represent a subgroup of malignancies with distinctive clinical and molecular features and that are characterized by a striking response to immunocheckpoint inhibitor treatments. For these reasons, in 2017 the FDA approved the use of pembrolizumab as an agnostic therapy in MSI-H malignancies.

At the same time, molecular targeted therapies have led to some encouraging results. Anti-HER2 drugs are now used in routine clinical practice for the treatment of both colorectal and gastro-oesophageal cancers. Recently, trastuzumab deruxtecan alone and in combination with immunocheckpoint inhibitor showed benefit for disease-free progression and overall survival in the metastatic setting for gastric adenocarcinoma. Phase II studies have also evaluated claudin 18.2 and FGFR2b as potential predictive biomarkers. Treatments with anti-claudin 18.2 and anti-FGFR2b monoclonal antibodies were able to delay tumor progression and showed a trend for longer overall survival.

Taken together, these results indicate a promising but constantly evolving therapeutic scenario. However, they also indicate the need to identify additional and accurate biomarkers to improve the molecular-based selection of patients. Another issue to be clarified concerns the best therapeutic sequence to follow in patients who are able to receive a second or even third line of treatment.

For this special issue, researchers are invited to contribute original manuscripts and reviews that explore the role of immunotherapy, targeted therapy and precision medicine. These can include agnostic indications in gastrointestinal tumours that focus on the state of the art, challenges, mechanisms of resistance and ongoing research.

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