Editorial

Immunotherapy for gastrointestinal malignancies: the journey does not end here!

Gastrointestinal malignancies represent a common and heterogeneous group of tumors and account for a high percentage of adult cancers. Over the past decades, early detection, advanced endoscopy and surgery, along with the additional benefit in some cases from perioperative treatment, have led to improved outcomes in localized disease. Disease recurrence and metastatic disease, as the primary presentation, are not uncommon and they carry a very poor prognosis with median overall survival (OS) of less than 12 months from metastatic diagnosis with the exception of colon cancer where survival for stage IV disease is approaching 3 years.

Cytotoxic chemotherapy remains the mainstay treatment of advanced GI cancer offering a limited period of disease control. Targeted molecular therapies have been approved for the treatment of several GI cancers leading to improvement in overall outcome. However, the disease does ultimately progress, leaving an apparent and urgent need for effective novel therapies.

Immunotherapy and GI malignancies

The exploitation of the immune system to recognize and treat cancer has represented an attractive therapeutic option for cancer for more than a century. From interleukin 2 (IL-2) in renal cell carcinoma to expanded tumor-infiltrating lymphocytes (TILs) in combination with lymphodepleting chemotherapy in melanoma. These treatments were promising, however, expense and toxicity limited its expansion to other solid tumors.

Within the past decade, a new generation of immunotherapeutic agents has revolutionized oncology. Immune checkpoint inhibitors have demonstrated promising activities across a range of malignancies with acceptable and manageable toxicity. They are now approved for the use in the treatment of advanced melanoma, lung cancer and bladder cancer among others.

In GI malignancies, immune checkpoint inhibitors showed promising early signs of activity, however, research into the immune biology of these diseases has been slower than in other disease groups. Beyond tumors with microsatellite instability, Immune checkpoints inhibitors have generated responses leading to approval in gastric, esophageal, and hepatocellular carcinoma. The responses, however, have been modest compared to other tumor types. Identifying the subset of patients who might benefit from immune check inhibitors in GI cancer has been challenging.

Moving forward, future efforts should be focusing on understanding tumor biology and tumor microenvironment as well as novel approaches to enhance the efficacy of immune check inhibitors. Ongoing trials are evaluating innovative treatments of PD-1 or PD-L1 blockade in combination with chemotherapy, radiation and other immune modulators such as anti-CTLA4, anti-LAG3, TLRs agonists as well as targeted therapy (anti-HER2, anti-VEGFR2).

In this issue of Translational Gastroenterology and Hepatology, authors will summarize the approved immunotherapies in the treatment of GI malignancies including neuroendocrine tumors. They will review the lessons to be learned from the success of immunotherapy in other tumor type and touch on the road to identifying the subset of tumors that might respond to immune check inhibitors.

Acknowledgments

None.

Footnote

Conflicts of Interest: The author has no conflicts of interest to declare.

Ethical Statement: The author is accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

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doi: 10.21037/tgh.2019.11.04
View this article at: http://dx.doi.org/10.21037/tgh.2019.11.04

doi: 10.21037/tgh.2019.11.04
Cite this article as: Almhanna K. Immunotherapy for gastrointestinal malignancies: the journey does not end here! Transl Gastroenterol Hepatol 2020;5:2.

