Cancer immunotherapy: recent advances and challenges

Since the 1890s, attempts have been made to harness the immune system to treat cancer (1). However, only over the last decade have we witnessed the true potential of immunotherapy. Activating the immune system by removing negative regulators has shown benefit in many cancers and continues to shape our understanding of the immune response to cancer. This tremendous success has led to the establishment of immunotherapy as one of the main pillars of cancer treatment. Immune checkpoint inhibitors (ICI) are the poster child of this success with more than 50 Food and Drug Administration approvals for the treatment of various cancers (2).

The immune-oncology landscape is rapidly evolving and currently spans T-cell targeted agents, cell therapies, cancer vaccines, oncolytic viruses, CD3-targeted bispecific antibodies, and various other immunomodulators. A recent report, in 2020, showed that approximately 4,720 immuno-oncology drugs were in the developmental pipeline, and around 6,281 clinical trials were actively investigating these agents (3). There are still several challenges with these agents. At present we lack robust predictive biomarkers and have sparse knowledge of the mechanisms of primary and secondary resistance and the causality of immune-related adverse events. A deeper understanding of these roadblocks will help us with the development of a more personalized treatment approach which will be not only more effective but also much better tolerated.

In this focused series, we celebrate the success of these agents and provide a comprehensive overview of challenges with cancer immunotherapy. Discussed topics include immune-related adverse events and financial toxicities, safety concerns in patients with pre-existing immune dysfunction, current and emerging biomarkers of response along with a detailed discussion on the role of the gut microbiome in modulating response to ICI. Other reviewed topics include chimeric antigen receptor T-cell (CAR T-cell) therapy and ICI in lymphoid malignancies, clinical studies exploring ways to turn immunologically inert "cold" sarcomas "hot" and intralesional agents in the treatment of malignant melanoma.

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Umang Swami

Mohammed Milhem

Umang Swami, MD, MS^
Assistant Professor; *Division of Medical Oncology*, *Department of Internal Medicine*, *Huntsman Cancer Institute*, *University of Utah*, *Salt Lake City*, *UT*, *USA*.
(Email: umang.swami@hci.utah.edu)
Mohammed Milhem, MBBS
Clinical Professor; *Department of Internal Medicine*, *Division of Hematology*, *Oncology*, *and Blood and Marrow Transplantation*, *University of Iowa*, *Iowa City*, *IA*, *USA*.
(Email: mohammed-milhem@uiowa.edu)
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^ ORCID: 0000-0003-3518-0411.

