

A Review on Cancer immunotherapy

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Introduction

Compared with previous standards of care (including chemotherapy, radiotherapy, and surgery), cancer immunotherapy has brought significant improvements for patients in terms of survival and quality of life. Immunotherapy has now firmly established itself as a novel pillar of cancer care, from the metastatic stage to the adjuvant and neoadjuvant settings in numerous cancer types. In this review article, we highlight how the history of cancer immunotherapy paved the way for discoveries that are now part of the standard of care. We also highlight the current pitfalls and limitations of cancer checkpoint immunotherapy and how novel research in the fields of personalized cancer vaccines, autoimmunity, the microbiome, the tumour microenvironment, and metabolomics is aiming to solve those challenges.

Cancer immunotherapies, including checkpoint inhibitors and adoptive cell therapy, manipulate the immune system to recognize and attack cancer cells. These therapies have the potential to induce durable responses in multiple solid and hematologic malignancies and thus have transformed treatment algorithms for numerous tumor types. Cancer immunotherapies lead to unique toxicity profiles distinct from the toxicities of other cancer therapies, depending on their mechanism of action. These toxicities often require specific management, which can

include steroids and immune-modulating therapy and for which consensus guidelines have been published. This review will focus on the toxicities of checkpoint inhibitors and chimeric antigen receptor T cells, including pathophysiology, diagnosis, and management.

The immune system has developed a complex series of mechanisms to detect and eradicate cancer cells. These pathways protect against the development of malignancy but can promote the selection of tumor cells, which are equipped to avoid the host's immune response. The concept of cancer immunoediting, which highlights the dual role of the immune system in protecting against tumor growth while also shaping tumor immunogenicity, describes the process of tumor development using 3 steps: elimination, equilibrium, and escape. During the elimination phase, the host's innate and adaptive immune systems recognize and respond to tumor-specific antigens. Some tumor cells survive elimination and enter the equilibrium phase, during which the adaptive immune system prevents outright tumor growth but exerts a selective pressure on the remaining malignant clones. Tumor cells escape when they develop resistance to the antitumor immune response. Multiple mechanisms have been described to account for the evolution of this escape, including alteration or loss of antigens, manipulation of cytokine expression, and upregulation of immune checkpoint proteins.

Cancer immunotherapies, which were developed based on studies of the mechanisms of tumor escape, manipulate the immune system to reactivate the antitumor immune response and overcome the pathways leading to escape. Early approaches to cancer immunotherapy targeted cytokines to affect immune cell function. For example, high-dose interleukin 2 (IL-2) and interferon (IFN) α -2b lead to multiple downstream effects⁴ and have been used to treat advanced melanoma and renal cell carcinoma (RCC). Therapeutic approaches to manipulate multiple aspects of the immune system have subsequently been investigated, including immune checkpoint inhibitors (ICIs), adoptive cell therapy, oncolytic viruses, and cancer vaccines. Immunotherapies have transformed the treatment landscape for multiple solid and hematologic malignancies but confer unique toxicity profiles, which vary depending on the type of immunotherapy and are related to the specific mechanism of action. Cytokines, such as high-dose IL-2, lead to multiple downstream effects on T cells and natural killer (NK) cells, which, in turn, cause capillary leakage and a sepsis-like syndrome.