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Review

Novel immunotherapyapproachesformetastatic urothelial and renal cell carcinoma

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Running title: Immune checkpoint inhibitor approaches for metastatic GU cancers

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Abstract

The treatment of metastatic renal cell carcinoma (RCC) and urothelial carcinoma (UC)remains a major challenge.Past research has implicated the immune system in tumor surveillance of both malignancies, leading to the application ofimmunotherapy agents for both cancers. Among them, the most promising agents are the checkpoint blockade drugs, such asantibodies targeting the cytotoxic T-lymphocyte-associated antigen 4 (CTLA-4), programmed death receptor 1 (PD-1), and PD-1 ligand (PD-L1). In normal physiology, these immune checkpoints act as inhibitory signalsto fine-tune the duration and strength of immune reactions, which is pivotal for maintaining self-tolerance. However,tumor cells also utilize immune checkpoint pathways to evade anti-tumor immune response, leading to disease progression and metastasis.Thus, there has been intense preclinical and clinical effort focused on the application of checkpoint inhibitors in metastatic RCC and UC. To date, nivolumab (anti-PD-1) and atezolizumab (anti-PD-L1) have been approved for the treatment of metastatic RCCandUC, respectively. Despite these successes, challenges remain in how to further improve response rates to immunotherapy and how to select patients that will benefit from this approach. In this report, we review existing data and research on immunotherapy in metastatic RCC and UC.

Keywords: Immune checkpoint inhibitors, nivolumab, atezolizumab, pembrolizumab, renal cell carcinoma, urothelial carcinoma