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Review article

Current progress and challenges of immunotherapy in gastric cancer: A focus on CAR-T cells therapeutic approach

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Abstract

Gastric cancer (GC) is a severe malignancy, accounting for the third most common cancer death worldwide. Despite the development of chemo-radiation therapy, there has not been sufficient survival advantage in patients with GC who were treated by these methods. GC immunogenicity is hampered by a highly immunosuppressive microenvironment; therefore, further understanding of the molecular biology of GC is the potential to achieve new therapeutic strategies in GC therapy, including specific immunotherapy. Current immunotherapies are mainly based on cytokines, immune checkpoints, monoclonal antibodies (mAb), bispecific antibodies (BisAbs), antibody-drug conjugates (ADCs), and chimeric antigen receptor (CAR). Immunotherapy has made significant progress in the treatment of GC, so that studies show that nivolumab as a programmed death 1 (PD1) inhibitor has proper safety and effectiveness as a third-line treatment for GC patients. Multiple monoclonal antibodies like ramucirumab and claudiximab were effective in treating GC patients, especially in combination with other treatments. Despite the challenges of CAR therapy in solid tumors, CAR therapy targets various GC cells targets; among them, intercellular adhesion molecule (ICAM)-1 CAR-T cell and CLDN18.2 CAR-T cell have shown promising results. Although responses to all these treatments are encouraging and in some cases, durable, these successes are not seen in all treated patients. The present review represents the development of various immunotherapies especially CAR-T cell therapy, its current use, clinical data in GC, and their limitations.