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Opinion Article

Targeted Immunotherapies for Gastrointestinal Cancer in Molecular Mechanisms and Implications

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DESCRIPTION

A significant obstacle to cancer treatment continues to be gastrointestinal cancer, which is a primary cause of cancer-related mortality. Due to the rapid disease development, metastasis, and CRT resistance, the overall 5-year survival rate of gastrointestinal cancer patients in late stage disease is less than 15%, even with the combined administration of contemporary surgical procedures and Chemo Radiotherapy (CRT). The mechanisms driving cancer progression must be better understood, and gastrointestinal cancer treatment plans must be improved immediately. Due to mounting evidence that immune responses play a protective role in the development and spread of cancer, immunotherapy has emerged as a popular area of study in the integrative oncology field. Gastrointestinal cancer treatment. Here is a summary of what is known about the molecular basis of gastric, esophageal, and colorectal cancers. Then, recently created immunotherapy techniques have been discussed, such as immune checkpoint inhibitors, chimeric antigen receptor T cell therapies, tumour vaccines, and treatments that target other immune cells. Finally, each agent's foundational research, clinical trials, and underlying mechanisms are discussed. This review, taken as a whole, highlights recent developments and suggests future prospects for immunotherapy treating people with gastrointestinal cancers. In the top 10 most common and lethal tumours worldwide, Gastrointestinal (GI) cancers account for 26% of global cancer incidence and 35% of all cancer-related deaths. Patients with Colorectal Cancer (CRC), Gastric Cancer (GC), and Esophageal Cancer are currently treated mostly with surgical resection (EC). Many patients still develop distant metastases and therapeutic resistance despite advancements in adjuvant and neoadjuvant Chemoradiotherapy (CRT). There is an urgent need for innovative therapeutic approaches to enhance the prognosis of GI malignancies. Immune-targeted therapy has become a cutting-edge cancer treatment option over the past few decades. However, it is still unclear what regulatory role the immune system plays in GI malignancies. Thankfully, with the advancement of immunotherapy, cancer immunotherapy based mostly on checkpoint inhibitors has demonstrated excellent clinical research potential, demonstrating the significance of immunotherapy in the treatment of cancer. We first give a general summary of GI in this study, including its epidemiology, molecular pathogenesis, and recommended treatment plans. The functional and molecular underpinnings of oncoimmunology are outlined in the sections that follow, with an emphasis on novel immunological checkpoint targets and illustrations of applications in both laboratory studies and clinical trials. For oncologists and immunologists, we anticipate that this review will provide fresh perspective on cancer immunotherapy. The upper GI tract, which is a component of the digestive system, includes the oesophagus and stomach. There are two main kinds of EC: Esophageal Squamous Cell Carcinoma (ESCC) and esophageal adenocarcinoma, both of which are more frequent in the upper or middle region of the oesophagus. Any area of the stomach can develop GC, which can then spread to other organs like the colon, lymph nodes, liver, pancreas, and small intestines. The seventh and fourth most common malignancies worldwide, respectively, are EC and GC. According to estimates from 2018, the 5-year overall survival rate for digestive malignancies in China, including stomach, liver, and esophageal tumours, is just 36.4%. (OS) Surgery is generally very important for the early treatment of both GC and EC. Additionally, systemic therapy for advanced, metastatic stomach and esophageal cancer employs a mix of various cytotoxic chemotherapy drugs. Trastuzumab is frequently added to chemotherapy regimens that include a platinum and fluoropyrimidine doublet, such as FOLFOX, CAPOX, cisplatin/5-fluorouracil (5-FU), or cisplatin/capecitabine, for the treatment of HER2-positive illness. For patients who cannot take fluoropyrimidines, platinum, or ramicurumab, other medications, such as irinotecan or taxanes, may be used alone or in conjunction with these drugs. The body has an immune system, and the complete immune system is responsible for carrying out immune function. Immune organs, immunological cells, and immune chemicals make up the immune system. The tumour microenvironment is made up of these cell types that surround cancer cells, including fibroblasts, endothelial cells, immune cells, and extracellular chemicals such cytokines, hormones, cellular matrix, and growth factors. The Tumour Immune Microenvironment (TIME), which is described in pertinent papers as being able to govern the formation and

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growth of tumours, is anticipated to become a promising target for cancer immunotherapy. Despite significant advancements in molecularly targeted therapy, the outlook for GI malignancies is still dismal. Potential therapeutic options are opened up by advancements in immune checkpoint blockage, especially when combined with methods for getting beyond the TME's immunosuppressive processes. Numerous recent articles show the TIME's crucial functions in GI malignancies, including CRC and GC. The TIME, a crucial regulator of tumour development and prognosis in GI malignancies, interacts with malignant cells directly or indirectly through chemokine and cytokine signalling to influence cancer cell phenotypes and therapeutic responses. Numerous studies have shown that TIME factors as well as genetic changes inside tumour cells affect how tumours develop and metastasize. Briefly, it has been demonstrated that the presence of CD4+ T helper cells, CD8+ CTLs, NK cells, M1 macrophages, and DCs is correlated with a favourable prognosis. On the other hand, a negative outcome has been linked to CD4 + FOXP3+ Th2 cells, M2 macrophages, and Myeloid-Derived Suppressor Cells (MDSCs).