gastrointestinal disorders

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Editorial

New Tools for Precision and Personalized Treatment in Gastrointestinal Cancers

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1. Background

Precision medicine aims at treating patients with the most tailored treatments based on individual biological and molecular features. This strategy is made possible by the high accessibility of tumor genome sequencing technologies, such as next-generation sequencing (NGS), with the subsequent detection of targetable molecular alterations [1].

Gastrointestinal (GI) cancer has a high tumor incidence worldwide, with a poor prognosis associated with the advanced stage of the disease. Although molecular alterations in GI cancer exist and are commonly checked to guide the treatment selection (*RAS*, *BRAF*, and *HER-2* status), the development of new biomarkers has fallen behind compared to those developed for other malignancies, such as melanoma and non-small-cell lung cancer [2]. Moreover, the use of immunotherapy is reduced to a small portion of GI cancer patients, with limited efficacy. The use of new tools, such as liquid biopsies, multiple gene panels, and the discovery of new biomarkers is necessary to improve the treatment of GI cancer [2].

This special issue focuses on the key innovative aspects in the diagnosis and surgical and oncological treatment of gastrointestinal cancers.

2. Risk Factors for Colorectal Cancer (CRC) Development

Colorectal cancer (CRC) typically develops from precancerous lesions due to the exposure of the colonic mucosa to carcinogens with the subsequent formation of polyps [3].

Ali A. Alkhaldy explored various risk factors favoring CRC development in thirty Saudi Arabian patients harboring colorectal polyps and subjected to endoscopic polypectomy. Most patients were non-active, with a median body mass index within the overweight cut-off range. The serum levels of vitamin D were mostly inadequate, with the median fat consumption above the recommended dietary allowance (RDA) and the median fiber intake below the RDA [4]. Similarly, V.K. Chattu evaluated the major risk factors for the development of CRC in the Trinidadian population. A population of 88 CRC-diagnosed patients was retrospectively considered. The majority of the patients (68%) were found to have either diabetes or hypertension as comorbid conditions, 50% reported alcohol consumption, while 30% were cigarette smokers. Remarkably, 91% of the patients had never been screened for CRC prior to their diagnosis. This study proves the absence of screening programs in developing countries and the lack of knowledge about correct lifestyle methods and food habits [5].

3. Prognostic Factors in GI Tumors

De Lorenzis et al. retrospectively analyzed a series of 51 patients with malignant ureteral obstruction (MUO) treated with a ureteral stent or nephrostomy tube positioning. The presence of MUO was associated with poorer survival rates, especially if it was present at the time of the tumor diagnosis and in those receiving no cancer treatment after decompression. Moreover, upper GI tumors causing MUO were associated with reduced survival rates, compared to lower GI tumors [6].

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4. Nutritional Assessment in GI Tumors

Nutritional risk screening and the assessment of nutritional status are of primary importance in the management of GI tumors. Despite cachexia and sarcopenia being two common conditions related to GI tumors, an important under-recognition of cancer-related nutritional impairments has been reported among cancer specialists, with subsequent cancer treatment failure and prognostic significance on clinical outcomes. Sarcopenia is described as a progressive and generalized loss of skeletal muscle mass and function. Malnutrition may be a cause of secondary sarcopenia in cancer [7]. Conversely, cachexia is a multifactorial syndrome characterized by involuntary weight loss and an ongoing loss of skeletal muscle mass, with or without the loss of fat mass [7]. Mascaretti et al. focused on recent updates in this field attained from the ASCO and ESMO World GI meetings [8]. Pereira et al. reviewed the impact of sarcopenia on short- and long-term outcomes in patients undergoing a surgical resection of GI tumors. During the preoperative evaluation, the measurement of muscle mass is an easy and inexpensive diagnostic method of sarcopenia. Preoperative sarcopenia is a negative prognostic factor for the rate for survival and a predictor of increased postoperative morbidity. Therefore, sarcopenic patients should undergo preoperative strategies of prehabilitation in order to prevent adverse events following surgery [9].

5. Molecular Determinants of GI Tumors

Lengyel et al. evaluated the role of *HER-2* as a predictive biomarker for GI tumors that did not include gastric cancer. The landscape of anti-*HER2* therapeutics for non-gastric GI tumors is rapidly evolving, with the amplification of *HER-2* being recognized as a driver mechanism of tumorigenesis in multiple tumor types. In addition, the demonstration of a membrane stain for *HER-2* with immunohistochemistry is emerging as a possible diagnostic marker for cancer treatment, using treatment delivery modalities that target the cancer cells via membrane antigen recognition. Among the new available tools for the evaluation of molecular determinants of GI tumors, liquid biopsies are minimally invasive and can overcome the limitations of tissue biopsies in capturing the complexity of tumor heterogeneity within the primary cancer and among different metastatic sites. Liquid biopsies can also detect early tumor formations or monitor cancer responses to therapy with greater sensitivity compared with the currently available blood biomarkers [10]. Lampis et al. reviewed the role of circulating tumor DNA and non-coding RNA in the management of colorectal cancer patients. The evaluation of the mismatch repair system is of paramount importance in the molecular profiling of GI tumors, too [11]. A frequent outcome of mismatch repair system deficiency (dMMR) is represented by microsatellite instability (MSI), a condition characterized by multiple alterations in the length of microsatellite regions [12]. Although dMMR/MSI high (MSI-H) is not a common condition in gastroesophageal cancers (GEC) (7–22%), it has been associated with a better prognosis and higher response rate to immune checkpoint inhibitors [13]. Lopez et al. discussed the value of dMMR/MSI testing for GEC management in real-life clinical practices, the use of which remains a matter of debate [14].

A further frontier in the treatment of GI tumors is gene therapy that consists of different techniques, such as chimeric antigen receptor (CAR)-T Cells, viral vectors, and nanoparticles. In particular, CAR-T cells are created from the extraction of T cells from the patient that are infected with a virus. The delivered transgene causes the cells to express a CAR that can target specific genes known to be expressed by cancer cells. After CAR-T cells have been generated, they are then delivered back to the patients to target and destroy cancer cells that express the CAR-specific antigen [15]. Mckiver et al. highlighted genetic targets, techniques, and current clinical trials in hepatocarcinoma utilizing gene therapy [16].

6. Conclusions

The treatment of GI tumors remains challenging and the prognosis of advanced tumors is often poor. Moreover, the availability of molecular biomarkers in GI cancers is still scarce, and the role of immunotherapy is limited. An awareness of risk factors is fundamental for the prevention of GI cancers, while the proper management of nutritional aspects affects prognosis and treatment outcomes. Future developments in the treatment of GI cancers include the systematic use of new tools, such as NGS both on tissue samples and liquid biopsies. Although gene therapy does not yet find application in clinical practice, it represents an incredibly promising cellular immunotherapy approach, especially with the use of CAR-T cells.

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