Researchers provide a review and update on therapy of gastrointestinal tract tumors

June 18 2024

Credit: Pixabay/CC0 Public Domain

Gastrointestinal (GI) cancers, encompassing esophageal, gastric, small bowel, and colorectal carcinomas, represent a significant global health burden due to their high incidence and mortality rates. A review by M. Jesús Fernández-Aceñero and team provides an in-depth analysis of the molecular characteristics, prognosis, and current therapeutic strategies for these malignancies, highlighting the latest advancements and challenges in the field. The paper is published in the *Journal of Clinical and Translational Pathology*.

Esophageal carcinoma is among the ten most prevalent tumors globally, with squamous cell carcinoma (SCC) being the most common subtype. Despite geographical variations, SCC accounts for approximately 85% of esophageal cancer cases. Adenocarcinoma, particularly arising in Barrett's esophagus, is on the rise in Western countries.

Early-stage esophageal cancer is primarily treated with surgery, while advanced SCC relies on cytotoxic therapies. Neoadjuvant treatments are commonly employed to facilitate surgical resection. Despite these interventions, the prognosis remains poor, with less than 15% of patients achieving disease-free status at a five-year follow-up .

Recent genomic studies have provided valuable insights into the genetic alterations driving esophageal SCC. Technologies like whole-genome and whole-exome sequencing have identified potential therapeutic targets, such as the WNT/Notch1 pathway and the CCL2-CCR2 axis. However, targeted therapies, including EGFR inhibitors, have yet to demonstrate clinical efficacy in phase 3 trials, underscoring the need for predictive biomarkers to personalize treatment strategies .

Gastric cancer (GC) ranks as the fifth most common malignancy and the fourth leading cause of cancer-related deaths worldwide. The incidence

of GC is particularly high in Eastern Asia and Eastern Europe, with significant differences in screening programs, clinical characteristics, and patient management between Asian and Western regions.

Advances in molecular biology have led to the identification of key genetic alterations in GC, contributing to the development of molecular classifications like those by The Cancer Genome Atlas (TCGA) and the Asian Cancer Research Group (ACRG) .

A promising therapeutic target in GC is the tight junction protein claudin-18 isoform 2 (CLDN 18.2), which is overexpressed in up to 30% of gastric and gastroesophageal carcinomas. Zolbetuximab, an anti-CLDN 18.2 antibody, has shown efficacy in clinical trials, offering a new treatment avenue for HER2-negative gastric and gastroesophageal adenocarcinomas. Despite the potential of fibroblast growth factor receptor (FGFR) inhibitors, their success has been limited, likely due to the diverse genetic alterations affecting FGFR .

Small bowel carcinoma is relatively rare compared to other GI cancers. The molecular landscape of these tumors is less understood, but recent studies have started to uncover the genetic changes involved. Treatment strategies for small bowel carcinoma often mirror those for other GI cancers, including surgical resection and chemotherapy. The identification of specific molecular alterations could lead to more targeted therapies in the future .

Colorectal cancer (CRC) is one of the most common malignancies worldwide. Advances in molecular biology have identified several genetic mutations and pathways involved in CRC pathogenesis, including APC, KRAS, and TP53 mutations. These discoveries have paved the way for targeted therapies and personalized treatment approaches. Immunotherapy, particularly immune checkpoint inhibitors, has shown promise in CRC, especially in microsatellite instability-high (MSI-H)

tumors .

The future of gastrointestinal cancer treatment lies in a deeper understanding of the molecular mechanisms underlying these diseases. Research is ongoing to elucidate the molecular pathogenesis of these cancers, which could lead to the development of more effective and personalized therapies. The integration of high-throughput molecular techniques and next-generation sequencing has the potential to identify novel targets and biomarkers, paving the way for personalized medicine in gastrointestinal oncology.

The molecular characterization of GI tumors has significantly advanced our understanding of these malignancies, leading to the development of targeted therapies and personalized treatment strategies. However, challenges remain, including the need for reliable predictive biomarkers and overcoming resistance to targeted treatments. Continued research is essential to improve the prognosis and treatment outcomes for patients with GI cancers.

This comprehensive review underscores the importance of integrating molecular findings into clinical practice to enhance the management of gastrointestinal tumors, ultimately aiming for better patient outcomes and personalized therapeutic approaches .

More information: M. Jesús Fernández-Aceñero et al, A Review and Update on Therapy of Gastrointestinal Tract Tumors: From the Bench to Clinical Practice, *Journal of Clinical and Translational Pathology* (2024). DOI: 10.14218/JCTP.2024.00007

Provided by Xia & He Publishing Inc.