ISSN: 2475-6296

Review Article

Journal of Clinical & Experimental Immunology

Redefining Gastrointestinal Oncology in the Precision Era: Immunotherapy Integration and Systemic Disparities

Bilal Rahimuddin*

Department of Internal Medicine, Norton Community Hospital, Norton, Virginia

***Corresponding Author**
Bilal Rahimuddin, Department of Internal Medicine, Norton Community Hospital, Norton, Virginia.

Submitted: 2025, Dec 15; **Accepted:** 2026, Jan 09; **Published:** 2026, Jan 16

Citation: Rahimuddin, B. (2026). Redefining Gastrointestinal Oncology in the Precision Era: Immunotherapy Integration and Systemic Disparities. *J Clin Exp Immunol, 11*(1), 01-03.

Abstract

Gastrointestinal (GI) malignancies account for a disproportionate share of global cancer mortality and remain among the most biologically complex and therapeutically challenging tumors in clinical oncology. Historically limited by late-stage diagnosis and modest treatment efficacy, the field has recently undergone a fundamental transformation driven by advances in genomic profiling, immunotherapy, perioperative optimization, and real-world outcomes research. This review synthesizes contemporary developments across gastroesophageal, pancreatic, hepatobiliary, and colorectal cancers, emphasizing the growing role of precision oncology, immune checkpoint inhibition, circulating tumor DNA (ctDNA), and population-level insights into health disparities. Integrating data from randomized trials, translational studies, registry analyses, and recent international conference reports, we explore how these innovations are reshaping risk stratification and therapeutic decision-making while simultaneously exposing persistent inequities in access, outcomes, and survivorship. The convergence of biologic innovation with structural reform will be essential to ensure that scientific progress translates into equitable clinical benefit.

1. Introduction

Cancers of the gastrointestinal tract—including malignancies of the esophagus, stomach, pancreas, liver, biliary system, small intestine, and colorectum—collectively represent one of the leading causes of cancer-related death worldwide. Despite advances in screening and supportive care, overall survival remains poor for many GI cancers, particularly hepatocellular carcinoma (HCC), pancreatic ductal adenocarcinoma (PDAC), and gastric cancer [1,2]. Historically, therapeutic progress was constrained by late presentation, aggressive tumor biology, and limited systemic treatment options.

Over the past decade, however, gastrointestinal oncology has undergone a paradigmatic reorientation. The integration of next-generation sequencing, immune-based therapeutics, perioperative systemic therapy, and population-based analytics has fundamentally reshaped the field [3-6]. Genomic profiling has revealed biologically distinct subsets with actionable vulnerabilities; immune checkpoint inhibitors (ICIs) have improved survival in molecularly selected populations; and liquid biopsy technologies now permit dynamic monitoring of disease Burden [6-9]. Concurrently, epidemiologic and real-world studies have illuminated profound disparities in outcomes shaped by race, socioeconomic status, nutrition, geography, and social support [10-13] .

This review examines recent advances across major GI cancer subtypes, focusing on four intersecting domains: (1) precision oncology and biomarker-driven therapy, (2) immunotherapeutic integration, (3) liquid biopsy and disease monitoring, and (4) structural inequities in cancer care.

2. Gastroesophageal Malignancies

2.1. Precision-guided Therapeutic Evolution

Gastric and esophageal cancers have transitioned from uniform chemotherapy-based regimens toward biomarker-driven, multimodal treatment strategies. Contemporary frameworks emphasize the clinical relevance of HER2 amplification, PD-

L1 expression, microsatellite instability (MSI), and emerging molecular subtypes in guiding therapy selection [3,4]. The incorporation of immune checkpoint inhibitors into first-line and perioperative regimens has significantly improved outcomes in selected populations, particularly in PD-L1–expressing and MSI-high tumors [3,4,14].

The ESOPEC trial further refined perioperative strategies for esophageal adenocarcinoma, underscoring the importance of optimizing neoadjuvant and adjuvant sequencing [6]. These developments reflect a shift from tumor location-based treatment to biology-informed therapy.

2.1. Supportive Care and Outcomes

Host factors exert substantial influence on outcomes. Protein-energy malnutrition is highly prevalent among patients with upper GI cancers and independently predicts increased morbidity, prolonged hospitalization, and mortality [15]. This highlights the necessity of early nutritional screening and intervention as part of comprehensive oncologic care.

3. Pancreatic Cancer

PDAC remains one of the most lethal solid tumors, with 5-year survival rates below 15%. While immunotherapy has limited activity in unselected populations, research increasingly focuses on microenvironmental modulation, stromal targeting, metabolic vulnerabilities, and rational combinations [9].

Real-world analyses demonstrate that malignant portal vein thrombosis significantly worsens outcomes and increases complication rates, emphasizing the need for early detection and multidisciplinary management [16]. Nutritional status, frailty, and thrombotic risk increasingly inform treatment decisions alongside tumor stage.

4. Hepatobiliary and Biliary Tract Cancers

4.1. Molecular and Immune-based Advances

HCC and cholangiocarcinoma are now treated using combinations of immunotherapy and targeted agents. A multidisciplinary consensus emphasizes comprehensive molecular profiling in intrahepatic cholangiocarcinoma to identify FGFR2 fusions, IDH1 mutations, and other actionable alterations [8]. Combination immunotherapy, such as atezolizumab plus bevacizumab, has replaced tyrosine kinase inhibitors as first-line therapy in HCC [17]. Recent conference data suggest expanding benefit from immunotherapy combinations in biliary tract cancers [11].

4.2. Disparities and Population Health

Survival disparities associated with ethnicity, socioeconomic status, and access to care persist across hepatobiliary cancers [2,13]. Rising obesity rates have further contributed to increasing liver cancer incidence and mortality [18].

5. Colorectal and Small Intestinal Tumors

5.1. Precision oncology and biomarkers

Colorectal cancer exemplifies the success of molecular stratification. MSI-high and POLE-mutated tumors exhibit exceptional sensitivity to immunotherapy [6,19]. Circulating tumor DNA enables early relapse detection and minimal residual disease monitoring [6,20].

Bone metastasis predicts poor prognosis in early-onset CRC [1]. Social determinants such as marital status independently influence survival, reflecting the impact of psychosocial support on outcomes [12].

5.2. Neuroendocrine neoplasms

SEER-based analyses reveal significant survival disparities in small intestinal neuroendocrine tumors, reinforcing inequities in early detection and specialty access [14].

6. Immunotherapy in GI Oncology

ICIs now constitute a foundational pillar of therapy in multiple GI cancers [4,5]. However, immune-related adverse events and resistance remain clinically significant challenges [7,21]. Primary resistance arises from low tumor mutational burden, immunosuppressive microenvironments, and impaired antigen presentation. Emerging strategies include combination checkpoint blockade, integration with chemotherapy or radiation to enhance immunogenicity, and targeting myeloid and stromal components of the tumor microenvironment.

7. Liquid Biopsy and Dynamic Monitoring

Liquid biopsy has revolutionized disease monitoring. ctDNA enables noninvasive detection of minimal residual disease, early relapse, and therapeutic response [6,20]. Ongoing trials are validating ctDNA-guided treatment escalation and de-escalation strategies.

8. Supportive Care and Holistic Outcomes

Nutrition, thrombosis, infection, and psychosocial support significantly affect survival independent of oncologic therapy [12,15,16]. These findings emphasize that advances in systemic therapy must be matched by investment in supportive and equitable care delivery.

9. Structural Inequities and Health Disparities

Across GI malignancies, disparities in screening, diagnosis, treatment access, and survivorship persist [1,2,13,14]. These inequities are driven by systemic barriers including insurance status, geographic isolation, institutional resources, and implicit bias.

10. Future Directions

Future priorities include:

- Expanded genomic and ctDNA integration into routine care
- Development of predictive biomarkers for immunotherapy response
- Integration of metabolic and microbiome research
- System-level interventions to reduce disparities

11. Conclusion

Gastrointestinal oncology stands at a transformative juncture. Precision medicine and immunotherapy have reshaped outcomes for selected populations, yet inequities remain pervasive. The future of GI cancer care depends on aligning scientific innovation with ethical and structural commitments to equity.

References

1. Vadehra D, Awidi M, Peshin S, et al. (2025). Bone metastasis in EOCRC. *Ann Oncol*. 36:S38.
2. Sung, H., Ferlay, J., Siegel, R. L., Laversanne, M., Soerjomataram, I., Jemal, A., & Bray, F. (2021). Global cancer statistics 2020: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries. *CA: a cancer journal for clinicians, 71*(3), 209-249.
3. Peshin, S., Takrori, E., Kodali, N. A., Bashir, F., Gibson, M., & Singal, S. (2025). Therapeutic Frontiers in Gastroesophageal Cancer: Contemporary Concepts in Management and Therapy. *International Journal of Molecular Sciences, 26*(23), 11424.
4. Peshin, S., Bashir, F., Kodali, N. A., Dharia, A., Zaiter, S., Singal, S., & Moka, N. (2025). Immunotherapy in GI cancers: lessons from key trials and future clinical applications. *Antibodies, 14*(3), 58.
5. Peshin, S., Modi, S., & Singh, S. (2024). Advancements in cancer immunotherapy: a comprehensive review of immune checkpoint inhibitors with a focus on pembrolizumab and emerging strategies. *Medi Clin Case Rep J, 2*(3), 430-434.
6. Ramachandran, R., Cannon, M., Peshin, S., Kundranda, M., & Scott, A. J. (2025). Unveiling ctDNA Response: Immune Checkpoint Blockade Therapy in a Patient with POLE Mutation-Associated Early-Onset Colon Cancer. *Current Oncology, 32*(7), 370.
7. Kotla, N. K., Bhanushali, C., Vojjala, N., Peshin, S., Goyal, K., Shah, R., ... & Ahmed, N. (2025). Incident reporting and outcomes of gastrointestinal adverse events with immune checkpoint inhibitors. *J Clin Oncol*. 2025;43:e14663.
8. Gujarathi R, Peshin S, Zhang X, et al. (2025). Intrahepatic cholangiocarcinoma. *Hepatol Commun*. 9:e0743.
9. Peshin, S., Takrori, E., Kodali, N. A., Bashir, F., & Singal, S. (2025). Advances in the management of pancreatic cancer: Current strategies and emerging therapies. *International Journal of Molecular Sciences, 26*(15), 7055.
10. Dharia, A., Mahayni, A. A., Borra, R., Peshin, S., Ser-Manukyan, H., Mangu, S., ... & Muddassir, S. (2025). Ethnic and socioeconomic disparities in cancer-free and all-cause survival in cholangiocarcinoma patients under 60: A population-based study.
11. ASCO Abstract e14663. Immunotherapy in hepatobiliary cancers. *J Clin Oncol*. 2025.
12. Liu L, Peshin S, Barboza AZ, et al. (2025). Marital status in CRC survival. *J Clin Oncol*. 43:3628.
13. Sivasubramanian, B. P., Ravikumar, D. B., Dhabuwala, A., Yakout, A., Peshin, S., & Nash III, C. H. (2025). Exploring racial disparities in biliary tract cancer with sepsis. *J Clin Oncol*. e16185.
14. Dharia A, Borra R, Peshin S, et al. (2025). Small intestine carcinoid disparities. *J Clin Oncol*. 43:653.
15. Iqbal, R., Kimball, H., Gaddam, M., Peshin, S., Sinha, S., & Quadri, K. (2025). The impact of protein-energy malnutrition on clinical outcomes in hospitalized gastric cancer patients: A population-based analysis. *J Clin Oncol*. 43:503.
16. Iqbal R, Kimball H, Peshin S, et al. (2025). Portal vein thrombosis in pancreatic cancer. *J Clin Oncol*. 43:784.
17. Finn, R. S., Qin, S., Ikeda, M., Galle, P. R., Ducreux, M., Kim, T. Y., ... & Cheng, A. L. (2020). Atezolizumab plus bevacizumab in unresectable hepatocellular carcinoma. *New England Journal of Medicine, 382*(20), 1894-1905.
18. Rahib L, Smith BD, Aizenberg R, et al. (2014). Cancer statistics. *Cancer Res*. 74:2913-2921.
19. André, T., Shiu, K. K., Kim, T. W., Jensen, B. V., Jensen, L. H., Punt, C., ... & Diaz Jr, L. A. (2020). Pembrolizumab in microsatellite-instability–high advanced colorectal cancer. *New England Journal of Medicine, 383*(23), 2207-2218.
20. Reinert, T., Henriksen, T. V., Christensen, E., Sharma, S., Salari, R., Sethi, H., ... & Andersen, C. L. (2019). Analysis of plasma cell-free DNA by ultradeep sequencing in patients with stages I to III colorectal cancer. *JAMA oncology, 5*(8), 1124-1131.
21. Zaretsky, J. M., Garcia-Diaz, A., Shin, D. S., Escuin-Ordinas, H., Hugo, W., Hu-Lieskovan, S., ... & Ribas, A. (2016). Mutations associated with acquired resistance to PD-1 blockade in melanoma. *New England Journal of Medicine, 375*(9), 819-829.