Article type: Perspective
Home Page URL: https://www.alliedacademies.org/journal-clinical-oncology-cancer-research/

Overcoming Drug Resistance in Metastatic Colorectal Cancer: Novel Therapeutic Strategies.

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Received: *27-May-2025, Manuscript No. AACOCR-25-169758;* ***Editor assigned:*** *01-Jun-2025, PreQC No. AACOCR-25-169758 (PQ);* ***Reviewed:*** *15- Jun-2025, QC No. AACOCR-25-169758;* ***Revised:*** *22- Jun-2025, Manuscript No. AACOCR-25-169758 (R);* ***Published:*** *29- Jun-2025, DOI:10.35841/AACOCR-8.1.180*

Introduction

Metastatic colorectal cancer (mCRC) remains a leading cause of cancer-related mortality worldwide, despite advances in early detection, targeted therapy, and personalized medicine. One of the most formidable challenges in its management is the emergence of drug resistance, which severely limits the efficacy of conventional chemotherapeutics, targeted agents, and even novel immunotherapies. Resistance mechanisms in mCRC are multifactorial, involving genetic mutations, epigenetic alterations, tumor microenvironment modulation, and phenotypic plasticity of cancer cells. These adaptive processes enable tumor cells to evade cytotoxic effects, leading to disease progression and poor patient prognosis. Addressing drug resistance in mCRC requires an integrated approach, combining molecular profiling, biomarker-guided therapy selection, and innovative treatment modalities. Recent research has focused on novel strategies such as combination regimens targeting multiple signaling pathways, immune checkpoint inhibitors, epigenetic modulators, and advanced drug delivery systems. By understanding the complex interplay between tumor biology and therapeutic response, clinicians and researchers aim to develop more durable and effective treatments for patients with mCRC [1, 2, 3, 4, 5].

Conclusion

Overcoming drug resistance in metastatic colorectal cancer demands a paradigm shift in therapeutic development and clinical practice. Emerging strategies, including rational drug combinations, biomarker-based precision medicine, and immunomodulatory approaches, offer promising avenues to circumvent resistance mechanisms. Moreover, leveraging cutting-edge technologies such as liquid biopsy, single-cell sequencing, and nanomedicine can provide real-time insights into tumor evolution, enabling timely treatment adaptation. Ultimately, translating these novel therapeutic strategies into routine clinical care will require robust clinical trials, interdisciplinary collaboration, and patient-centered research. By integrating innovation with precision oncology, the long-standing barrier of drug resistance in mCRC can be progressively dismantled, improving survival outcomes and quality of life for affected individuals.

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Citation: Reid A M. Overcoming Drug Resistance in Metastatic Colorectal Cancer: Novel Therapeutic Strategies. *J Oral Med Surg*. 2025; 8(1):180