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GIST Management: A Multidisciplinary Approach

Chen Wei*

Department of Digestive Medicine, Eastern Asia Medical University, Shanghai, China

Introduction

Gastrointestinal stromal tumors (GISTs) represent the predominant mesenchymal neoplasms encountered within the gastrointestinal tract. The therapeutic landscape for GISTs has undergone substantial evolution, largely propelled by the advent of targeted therapies, most notably tyrosine kinase inhibitors (TKIs) such as imatinib. This review meticulously examines the contemporary panorama of GIST clinical management, encompassing the diagnostic process, risk stratification methodologies, surgical interventions, and systemic therapeutic strategies. A central theme is the paramount importance of molecular profiling in guiding personalized treatment decisions. Adjuvant and neoadjuvant TKI therapies are recognized as critical components in enhancing patient outcomes, while ongoing research actively investigates the mechanisms underlying emergent resistance to these agents [1].

The surgical dimension in GIST management, particularly for localized disease presentations, retains its fundamental significance. This article elucidates current surgical techniques, including conventional open procedures, laparoscopic approaches, and robotic-assisted surgery, alongside the underlying principles aimed at achieving complete tumor resection. Furthermore, it addresses the management paradigms for unresectable or metastatic GISTs, where systemic therapy assumes a primary role. The impact of surgical margin status on recurrence rates and the strategic utility of neoadjuvant therapy in facilitating surgical resection are also explored in detail [2].

Tyrosine kinase inhibitors (TKIs) are firmly established as the cornerstone of systemic treatment for advanced GIST. This paper undertakes a comprehensive review of the efficacy and safety profiles of the approved TKIs, namely imatinib, sunitinib, and regorafenib, across first-line, second-line, and third-line treatment settings. Strategies designed to address and manage TKI resistance, encompassing dose adjustments and sequential therapeutic regimens, are thoroughly discussed. Emerging TKIs and novel combination therapies are also brought to the forefront [3].

Molecular profiling has emerged as an indispensable tool in the effective management of GIST. This article underscores the critical role of accurately identifying specific gene mutations, particularly within the KIT and PDGFRA genes, for predicting therapeutic responses and making informed TKI selections. The significance of secondary mutations in the pathogenesis of resistance, as well as the increasing importance of next-generation sequencing technologies in routine clinical practice, are also examined [4].

Risk stratification tools, including the well-established National Institutes of Health (NIH) and Miettinen-Lasota criteria, are pivotal in guiding therapeutic decisions for patients with GIST. This review elaborates on the integration of tumor size, mitotic index, and anatomical location into these scoring systems to accurately predict the risk of recurrence and metastasis. The article also addresses the continually evolving understanding of GIST risk categories and their direct influence on the recommended duration of adjuvant therapy [5].

Adjuvant imatinib therapy is considered a standard of care for patients with completely resected GISTs that carry a high risk of recurrence. This article offers an evidence-based overview of the optimal duration of adjuvant therapy, which is typically recommended for three years, and discusses the various factors that inform this critical decision. It further addresses the inherent challenges and discernible benefits associated with extending the duration of adjuvant therapy, alongside the management strategies for patients who experience recurrence following adjuvant treatment [6].

Resistance to TKIs presents a formidable challenge in the clinical management of GIST. This paper provides an in-depth exploration of the molecular mechanisms that underpin acquired resistance, including the emergence of secondary mutations in KIT or PDGFRA genes and the activation of alternative signaling pathways. The article also discusses various strategies aimed at overcoming resistance, such as switching to different TKIs, employing combination therapies, and utilizing investigational agents [7].

Neoadjuvant TKI therapy is gaining increasing traction as a therapeutic modality for downstaging locally advanced GISTs, thereby facilitating complete surgical resection and potentially improving overall survival. This article reviews the existing body of evidence supporting the use of neoadjuvant therapy, highlighting its impact on tumor shrinkage, surgical feasibility, and the achievement of pathological response. It also addresses crucial aspects such as the optimal timing and duration of neoadjuvant treatment regimens [8].

The management of rare GIST variants, including pediatric GISTs or those harboring specific uncommon mutations, necessitates highly tailored therapeutic approaches. This review critically examines the distinct biological characteristics and clinical behaviors associated with these less common subtypes, discussing the inherent challenges in applying standard treatment protocols. Emerging therapeutic targets specifically relevant to these distinct GIST populations are also brought to light [9].

A multidisciplinary care approach is recognized as essential for achieving optimal management outcomes in GIST patients. This article underscores the critical importance of seamless collaboration among oncologists, surgeons, radiologists, pathologists, and gastroenterologists throughout the entire patient journey, from diagnosis and staging to treatment planning and long-term follow-up. It discusses how such a coordinated and integrated approach can significantly contribute to improved patient outcomes and an enhanced quality of life [10].

Description

Gastrointestinal stromal tumors (GISTs) are the most common mesenchymal tumors of the GI tract. Management strategies have evolved significantly with the advent of tyrosine kinase inhibitors (TKIs) like imatinib. This review covers the current landscape of GIST clinical management, from diagnosis and risk stratification to surgical approaches and systemic therapy, emphasizing the importance of molecular profiling for guiding treatment decisions. Adjuvant and neoadjuvant TKI therapy plays a crucial role in improving outcomes, and emerging resistance mechanisms are being actively investigated [1].

The role of surgery in GIST management, particularly for localized disease, remains central. This article details current surgical techniques, including open, laparoscopic, and robotic approaches, and discusses the principles of achieving complete resection. It also addresses the management of unresectable or metastatic GISTs, where systemic therapy is the mainstay. The impact of surgical margins on recurrence rates and the utility of neoadjuvant therapy in facilitating surgical resection are explored [2].

Tyrosine kinase inhibitors (TKIs) are the cornerstone of systemic therapy for advanced GIST. This paper reviews the efficacy and safety profiles of approved TKIs, including imatinib, sunitinib, and regorafenib, in the first-line, second-line, and third-line settings. Strategies for managing TKI resistance, including dose modifications and sequential therapy, are discussed. Emerging TKIs and combinations are also highlighted [3].

Molecular profiling is indispensable for GIST management. This article emphasizes the critical role of identifying specific mutations, particularly in KIT and PDGFRA, for predicting treatment response and guiding TKI selection. It also discusses the significance of secondary mutations in the development of resistance and the importance of next-generation sequencing in clinical practice [4].

Risk stratification tools, such as the National Institutes of Health (NIH) and Miettinen-Lasota criteria, are vital for guiding treatment decisions in GIST. This review elaborates on how tumor size, mitotic index, and tumor location are integrated into these scoring systems to predict the risk of recurrence and metastasis. The article also discusses the evolving understanding of risk categories and their impact on the duration of adjuvant therapy [5].

Adjuvant imatinib therapy is a standard of care for completely resected GISTs at high risk of recurrence. This article provides an evidence-based overview of the optimal duration of adjuvant therapy, typically 3 years, and discusses the factors influencing this decision. It also addresses the challenges and benefits of extending adjuvant therapy and the management of patients who develop recurrence after adjuvant treatment [6].

Resistance to TKIs is a significant challenge in GIST management. This paper delves into the molecular mechanisms of acquired resistance, including secondary mutations in KIT or PDGFRA, and the development of alternative signaling pathways. It also explores strategies to overcome resistance, such as switching to different TKIs, combination therapies, and investigational agents [7].

Neoadjuvant TKI therapy is increasingly used to downstage locally advanced GISTs, facilitate complete surgical resection, and potentially improve survival. This article reviews the evidence supporting neoadjuvant therapy, including its impact on tumor shrinkage, surgical feasibility, and pathological response. It also discusses optimal timing and duration of neoadjuvant treatment [8].

The management of rare GIST variants, such as pediatric GISTs or those with specific uncommon mutations, requires tailored approaches. This review examines the distinct biological features and clinical behaviors of these rare subtypes and discusses the challenges in applying standard treatment protocols. Emerging therapeutic targets for these specific GIST populations are also highlighted [9].

Multidisciplinary care is essential for optimal GIST management. This article emphasizes the importance of collaboration among oncologists, surgeons, radiologists, pathologists, and gastroenterologists in the diagnosis, staging, treatment planning, and follow-up of GIST patients. It discusses how a coordinated approach can lead to improved patient outcomes and quality of life [10].

Conclusion

Gastrointestinal stromal tumors (GISTs) are the most common mesenchymal tumors of the GI tract. Their management has been revolutionized by tyrosine kinase inhibitors (TKIs) like imatinib. The current approach integrates diagnosis, risk stratification, surgical techniques, and systemic therapy, with molecular profiling being crucial for treatment decisions. Adjuvant and neoadjuvant TKI therapies are important for improving outcomes, while resistance mechanisms are actively studied. Surgery remains key for localized disease, with various techniques available. For advanced GISTs, TKIs are the primary treatment, with strategies for managing resistance and exploring new agents. Molecular analysis of mutations in KIT and PDGFRA guides TKI selection and predicts resistance. Risk stratification tools help determine treatment duration and intensity. Neoadjuvant TKI therapy is used to facilitate surgery in advanced cases. Management of rare GIST variants requires specialized approaches. A multidisciplinary team approach is essential for comprehensive patient care.

Acknowledgement

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Conflict of Interest

None.

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Address for Correspondence: Chen, Wei, Department of Digestive Medicine, Eastern Asia Medical University, Shanghai, China , E-mail: chen.wei@eamu.cn

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