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PEER-REVIEW REPORT

Name of journal: *World Journal of Gastrointestinal Oncology*

Manuscript NO: 102831

Title: Potential biomarkers for the prognosis of gastrointestinal stromal tumors

Provenance and peer review: Invited Manuscript; Externally peer reviewed

Peer-review model: Single blind

Reviewer's code: 03629470
Position: Peer Reviewer
Academic degree: MD, PhD, Professor
Professional title: Doctor
Reviewer's Country/Territory: India
Author's Country/Territory: China

Manuscript submission date: 2024-11-05

Reviewer chosen by: Shang Wu

Reviewer accepted review: 2024-12-12 14:08

Reviewer performed review: 2024-12-14 08:31

Review time: 1 Day and 18 Hours

Scientific quality	[ ] Grade A: Excellent [Y] Grade B: Very good [ ] Grade C: Good [ ] Grade D: Fair [ ] Grade E: Do not publish
Novelty of this manuscript	[ ] Grade A: Excellent [Y] Grade B: Good [ ] Grade C: Fair [ ] Grade D: No novelty
Creativity or innovation of this manuscript	[ ] Grade A: Excellent [ ] Grade B: Good [Y] Grade C: Fair [ ] Grade D: No creativity or innovation

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Scientific significance of the conclusion in this manuscript	[ ] Grade A: Excellent [Y] Grade B: Good [ ] Grade C: Fair [ ] Grade D: No scientific significance
Language quality	[ ] Grade A: Priority publishing [Y] Grade B: Minor language polishing [ ] Grade C: A great deal of language polishing [ ] Grade D: Rejection
Conclusion	[ ] Accept (High priority) [Y] Accept (General priority) [ ] Minor revision [ ] Major revision [ ] Rejection
Re-review	[Y] Yes [ ] No
Peer-reviewer statements	Peer-Review: [Y] Anonymous [ ] Onymous
	Conflicts-of-Interest: [ ] Yes [Y] No

SPECIFIC COMMENTS TO AUTHORS

The title effectively conveys the editorial's focus on prognostic parameters and inflammatory markers in GISTs. However, for an editorial, it could be more engaging and opinion-driven, emphasizing its stance or the significance of the topic, such as "Emerging Prognostic Tools in GIST: A Call for Standardization and Innovation." Authors are from a reputed center; Their expertise adds weight to the arguments presented. Abstract: For an editorial, a succinct summary or opening paragraph that emphasizes the key message and its relevance to ongoing debates or advancements in the field could be added for clarity. Key Words: Current keywords like "GIST," "inflammatory markers," and "prognostic parameters" are adequate. However, including terms like "editorial perspective" and "clinical implications" would help frame it as an opinion-driven piece. Introduction: The editorial introduction establishes the clinical importance of prognostic tools in GIST and identifies gaps in current knowledge, particularly around inflammatory markers. It successfully positions the editorial as a bridge between traditional and emerging prognostic approaches. Materials and Methods: Since this is an editorial, a detailed methodology is not applicable. However, the

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editorial could enhance its impact by referencing pivotal studies and the methodologies they employed to support its arguments. Results: The editorial effectively summarizes key findings from relevant literature, focusing on the role of inflammatory markers and their limitations. The integration of these findings into the editorial's broader perspective is logical and contributes to its authoritative tone. Discussion: The editorial's core lies in its discussion, which eloquently explores the potential and challenges of using inflammatory markers as prognostic tools. It highlights limitations in current research, such as small sample sizes and the lack of standardized thresholds. While these points are well-argued, the discussion could be strengthened by offering a clearer direction for future research and clinical applications. Conclusion: The conclusion emphasizes the integration of classical and novel markers for personalized treatment in GIST. For an editorial, it could more strongly advocate for specific actions, such as establishing international consensus on thresholds or prioritizing large-scale validation studies. Overall: This editorial is an insightful and concise commentary on the evolving landscape of GIST prognostic tools. To enhance its impact, it could adopt a more assertive tone, strongly advocating for the standardization and clinical integration of inflammatory markers. Additionally, it should emphasize actionable next steps for the research community.

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Reviewer's code: 08250044
Position: Peer Reviewer
Academic degree: Assistant Professor, PhD
Professional title: Doctor
Reviewer's Country/Territory: China
Author's Country/Territory: China

Manuscript submission date: 2024-11-05
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Review time: 1 Hour

Scientific quality	[ ] Grade A: Excellent [Y] Grade B: Very good [ ] Grade C: Good [ ] Grade D: Fair [ ] Grade E: Do not publish
Novelty of this manuscript	[ ] Grade A: Excellent [Y] Grade B: Good [ ] Grade C: Fair [ ] Grade D: No novelty
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SPECIFIC COMMENTS TO AUTHORS

Weakness 1: Limited Sample Size and Lack of External Validation Issue: The study is based on a retrospective design with a small sample size, which reduces the statistical power and limits the generalizability of its findings. Additionally, the proposed line chart prediction model lacks external or multicenter validation, further affecting its clinical applicability. Recommendations: Expand Sample Size: Collaborate with multiple institutions to conduct a multicenter study, ensuring a more diverse and representative patient population. Validate Externally: Apply the line chart prediction model to independent external datasets to evaluate its robustness and reliability across different clinical settings. Prospective Studies: Shift towards a prospective study design to minimize bias and better assess causality. Weakness 2: Superficial Exploration of Novel Biomarkers Issue: While the manuscript mentions emerging biomarkers like SLITRK3 and PENK, the discussion lacks depth regarding their biological mechanisms, clinical advantages, and potential integration with existing prognostic tools. This underrepresentation weakens the argument for their clinical adoption. Recommendations: Detailed Mechanistic Insights: Include more in-depth analysis of the

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pathways and mechanisms through which these novel markers influence GIST prognosis. Comparative Analysis: Contrast the performance and utility of these biomarkers with traditional inflammatory indices to highlight their unique contributions. Integration Framework: Propose a clear roadmap for incorporating these biomarkers into clinical workflows, supported by potential thresholds or criteria based on existing literature. Weakness 3: Insufficient Consideration of Confounding Factors Issue: The inflammatory markers discussed are susceptible to variability caused by non-cancer-related factors, such as infection, nutritional status, and chronic diseases. These confounding factors are not adequately addressed, potentially leading to false-positive prognostic assessments. Recommendations: Standardization Efforts: Advocate for the development of standardized thresholds for inflammatory markers, accounting for known confounders. Control Measures: Incorporate strategies to control or adjust for confounding variables, such as subgroup analyses or multivariate modeling. Additional Biomarkers: Consider combining inflammatory markers with more stable parameters, such as genetic or molecular data, to enhance the overall predictive accuracy. Weakness 4: Inadequate Discussion on Clinical Implications of Targeted Therapy Issue: The manuscript briefly touches on the interaction between inflammatory markers and targeted therapies, such as imatinib, but lacks a detailed exploration of how these biomarkers could guide treatment strategies or predict therapy outcomes. Recommendations: Expand Discussion: Elaborate on the role of inflammatory markers in predicting response or resistance to targeted therapies and their potential for monitoring disease progression. Propose Clinical Guidelines: Suggest practical approaches for integrating these markers into therapeutic decision-making, such as adjusting treatment plans based on marker dynamics. Combine Data: Incorporate findings from previous studies or real-world evidence to support hypotheses about the relationship between biomarkers and treatment efficacy. Weakness 5: Limited Practical

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Application of Findings Issue: While the line chart prediction model is a promising tool, the manuscript does not provide sufficient guidance on how it could be adopted in routine clinical practice. Additionally, the lack of standardized thresholds for markers reduces its utility. Recommendations: Simplify Implementation: Develop a step-by-step guide for clinicians on how to use the prediction model, including workflows, necessary software, and patient data requirements. Threshold Validation: Establish and validate standardized thresholds for the inflammatory markers to facilitate consistent and reproducible application in different healthcare settings. Pilot Studies: Propose pilot programs in select hospitals to evaluate the feasibility and impact of the model in real-world clinical environments.

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Position: Peer Reviewer
Academic degree: Associate Professor, MD
Professional title: Doctor
Reviewer's Country/Territory: Romania
Author's Country/Territory: China

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Reviewer performed review: 2024-12-26 02:26

Review time: 13 Days and 8 Hours

Scientific quality	[Y] Grade A: Excellent [ ] Grade B: Very good [ ] Grade C: Good [ ] Grade D: Fair [ ] Grade E: Do not publish
Novelty of this manuscript	[Y] Grade A: Excellent [ ] Grade B: Good [ ] Grade C: Fair [ ] Grade D: No novelty
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	Conflicts-of-Interest: [ ] Yes [Y] No

SPECIFIC COMMENTS TO AUTHORS

Dear authors, Thank you for the opportunity to review your manuscript "Potential biomarkers for the prognosis of gastrointestinal stromal tumors". I was really impressed by the indepth and novelty of the informations presented structured and clearly. Gastrointestinal stromal tumors (GISTs) are a mesenchymal tumor with variable behavior, with low-risk, intermediate-risk, and high-risk groups for recurrence In your manuscript it is emphasized the importance of GISTs staging and of the therapy and also the importance of some clear parameters for recurrence assessment. This study provides a new tool for assessing the risk of postoperative recurrence in GIST patients by establishing a line chart prediction model, which is validated by previous research showing that a high platelet-to-lymphocyte ratio (PLR) and neutrophil-to-lymphocyte ratio (NLR) are correlated with increased tumor sizes, more advanced tumor stages and a high mitotic index，Novel prognostic parameters for GIST patients is thriving and new markers, such as cytokines and chemokines, are being explored for their potential role in GIST prognosis. On the other hand proinflammatory markers can be more specificalyy be used due to reduced costs but this implies more studies from more centers.

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Compared with classical prognostic parameters, inflammatory markers are readily accessible and cost effective, providing additional prognostic information that allows clinicians to conduct more comprehensive assessments Overall, this study can offer an additional model for GIST prognosis and recurrence risk assessment, independent of the traditional prognostic factors of GIST. I have nothing to comment or to add on your excelent and solid manuuscript. Congrats for your work!