

The point to point responses are as following.

Reviewer #1 (Comments to the Author):

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 specificly be used due to reduced costs but this implies more studies from more centers. 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!

Response: We are extremely grateful for your insightful comments on our manuscript. We truly respect your expertise and are committed to ensuring that our manuscript is of the highest quality.

Reviewer #2 (Comments to the Author):

Weakness 1: Limited Sample Size and Lack of External Validation Issue.

Response: Thank you for your constructive feedback and valuable suggestions on our manuscript. We have carefully considered each of your points and have made the necessary revisions to address the concerns raised. This manuscript is a editorial discussing the *WJGO*

article written by Zhao JL, et al. We acknowledge the limitations of the retrospective study design with a small sample size and the lack of external validation for the line chart prediction model. We agreed that their study should expand sample size and designed a prospective study in their future research and we mentioned this on page 3, lines 99-107.

Weakness 2: Superficial Exploration of Novel Biomarkers Issue.

Response: We agree that a more in-depth analysis of the novel biomarkers SLITRK3 and PENK is necessary to support their clinical adoption. The study conducted by Zhao JL, et al should perform a comparative analysis of the performance and utility of SLITRK3 and PENK with traditional inflammatory indices and propose a clear roadmap for incorporating SLITRK3 and PENK into clinical workflows. We mentioned this on page 3, lines 99-107.

Weakness 3: Insufficient Consideration of Confounding Factors Issue.

Response: We recognize the importance of addressing confounding factors that may affect the interpretation of the results. The authors have incorporated additional control measures in their analysis to adjust for confounding variables. They should perform subgroup analyses based on the presence or absence of infections and chronic diseases. Besides, they should consider combining inflammatory markers with more stable parameters, such as genetic or molecular data, to enhance the overall predictive accuracy. We mentioned this on page 3, lines 99-107.

Weakness 4: Inadequate Discussion on Clinical Implications of Targeted Therapy Issue.

Response: We appreciate the suggestion to expand the discussion on the clinical implications of targeted therapy. We agree that a step-by-step guide should be proposed for clinicians on how to adjust treatment plans based on marker dynamics. A meta-analysis of relevant studies would be helpful to discuss the clinical implications of these combined findings, providing a more comprehensive view of the role of inflammatory markers in targeted therapy for GIST. We mentioned this on page 3, lines 99-107.

Weakness 5: Limited Practical Application of Findings Issue.

Response: We understand the need for the findings to have practical applications in routine clinical practice. We agree to create a user-friendly online platform where clinicians can input patient data and obtain prognostic predictions based on the model proposed by Zhao JL, et al. Moreover, it is important to establish and validate standardized thresholds for the inflammatory markers used in the model. We mentioned this on page 3, lines 99-107.

In conclusion, we agree the suggestion the concerns raised by you. We believe that the study of Zhao JL, et al provide valuable insights and practical tools for the clinical management of GIST patients.

Reviewer #3 (Comments to the Author):

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 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.

Response: We would like to express our sincere gratitude for the constructive comments and suggestions, which have significantly enhanced the quality of this manuscript. We truly appreciate the time and effort you put into providing such comprehensive feedback.