



PEER-REVIEW REPORT

Name of journal: *World Journal of Gastrointestinal Oncology*

Manuscript NO: 103855

Title: Combining Immune Checkpoint Inhibitors with Standard Treatment Regimens in Advanced HER-2 Positive Gastric Cancer Patients

Provenance and peer review: Unsolicited Manuscript; Externally peer reviewed

Peer-review model: Single blind

Reviewer's code: 08396805

Position: Peer Reviewer

Academic degree: PhD

Professional title: Doctor

Reviewer's Country/Territory: Brazil

Author's Country/Territory: China

Manuscript submission date: 2024-12-20

Reviewer chosen by: AI Editor

Reviewer accepted review: 2024-12-22 13:53

Reviewer performed review: 2025-01-01 13:28

Review time: 9 Days and 23 Hours

Scientific quality	<input type="checkbox"/> Grade A: Excellent <input checked="" type="checkbox"/> Grade B: Very good <input type="checkbox"/> Grade C: Good <input type="checkbox"/> Grade D: Fair <input type="checkbox"/> Grade E: Do not publish
Novelty of this manuscript	<input type="checkbox"/> Grade A: Excellent <input type="checkbox"/> Grade B: Good <input checked="" type="checkbox"/> Grade C: Fair <input type="checkbox"/> Grade D: No novelty
Creativity or innovation of this manuscript	<input type="checkbox"/> Grade A: Excellent <input checked="" type="checkbox"/> Grade B: Good <input type="checkbox"/> Grade C: Fair <input type="checkbox"/> Grade D: No creativity or innovation



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

SPECIFIC COMMENTS TO AUTHORS

The manuscript presents a study evaluating the efficacy and safety of combining immune checkpoint inhibitors (ICIs) with standard treatment regimens in patients with advanced HER-2-positive gastric cancer. The authors performed a retrospective analysis on 104 patients, comparing outcomes between those receiving trastuzumab with chemotherapy and those additionally receiving ICIs. The study aims to determine prognostic factors influencing progression-free survival and assess the safety profile of the treatment regimen. The addition of immune checkpoint inhibitors to standard treatment regimens shows favorable efficacy in prolonging progression-free survival in advanced HER-2-positive gastric cancer, with manageable safety profiles. The research highlights the significance of HER-2 expression levels and PD-L1 positivity as prognostic factors influencing treatment outcomes. By demonstrating that patients with high HER-2 expression and positive PD-L1 status benefit more significantly from the combined treatment, the study contributes valuable insights into biomarker-driven personalized treatment strategies. The study is well-structured, providing a comprehensive examination of both clinical efficacy and safety outcomes. However, there are several



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areas where clarity and additional detail would strengthen the manuscript: 1. The introduction effectively sets the stage for the research, providing a solid rationale for combining ICIs with standard regimens. However, the current prevalence of HER-2-positive gastric cancer within different demographics could be more detailed to emphasize the study's importance further. 2. While the treatment regimens are described clearly, a table summarizing these could aid comprehension, especially regarding the chemotherapy regimens and ICI options. 3. Expanding on how the study's findings align or differ from previous research will provide a more robust contribution to the existing literature. 4. Abbreviations should be employed consistently, and all should be defined upon first use. 5. The language needs the further improvement. While this manuscript provides a valuable contribution to the field of gastric cancer treatment, addressing the aforementioned areas will enhance its clarity and depth. I recommend revision to incorporate these suggestions, thereby improving the manuscript's overall quality and impact within the field.



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Peer-review model: Single blind

Reviewer's code: 08396808

Position: Peer Reviewer

Academic degree: Associate Chief Physician

Professional title: Doctor

Reviewer's Country/Territory: Malaysia

Author's Country/Territory: China

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Reviewer performed review: 2025-01-04 12:43

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Scientific quality	<input type="checkbox"/> Grade A: Excellent <input type="checkbox"/> Grade B: Very good <input checked="" type="checkbox"/> Grade C: Good <input type="checkbox"/> Grade D: Fair <input type="checkbox"/> Grade E: Do not publish
Novelty of this manuscript	<input type="checkbox"/> Grade A: Excellent <input checked="" type="checkbox"/> Grade B: Good <input type="checkbox"/> Grade C: Fair <input type="checkbox"/> Grade D: No novelty
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Language quality	<input type="checkbox"/> Grade A: Priority publishing <input checked="" type="checkbox"/> Grade B: Minor language polishing <input type="checkbox"/> Grade C: A great deal of language polishing <input type="checkbox"/> Grade D: Rejection
Conclusion	<input type="checkbox"/> Accept (High priority) <input type="checkbox"/> Accept (General priority) <input checked="" type="checkbox"/> Minor revision <input type="checkbox"/> Major revision <input type="checkbox"/> Rejection
Re-review	<input checked="" type="checkbox"/> Yes <input type="checkbox"/> No
Peer-reviewer statements	Peer-Review: <input checked="" type="checkbox"/> Anonymous <input type="checkbox"/> Onymous
	Conflicts-of-Interest: <input type="checkbox"/> Yes <input checked="" type="checkbox"/> No

SPECIFIC COMMENTS TO AUTHORS

This submission by Zhang et al. try to investigate the efficacy and safety of combining immune checkpoint inhibitors with standard treatment regimens in patients with advanced HER-2-positive gastric cancer. The manuscript describes a retrospective analysis conducted on 104 patients with advanced HER-2-positive gastric cancer treated at a single institution from March 2021 to May 2023. Clear criteria are defined, including pathological confirmation of adenocarcinoma, HER-2 positivity, and ECOG performance status. Exclusions are noted, like previous immunotherapy or significant organ dysfunction. Patients were divided into a control group receiving standard treatment with trastuzumab and chemotherapy and an observation group receiving the same standard treatment plus ICIs. The manuscript provided the baseline data for both groups, confirming no significant differences in demographics or disease characteristics. Although no significant differences were observed in overall response rates or disease control rates between groups, the observation group demonstrated significantly improved mPFS compared to the control group, particularly in patients with IHC3+ HER-2 expression. Univariate and multivariate analyses identified independent factors



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affecting PFS, such as ECOG performance status, peritoneal metastasis, and PD-L1 expression. Also, the adverse events were documented and primarily included hypothyroidism and neutropenia, with significant differences between the groups for these side effect. They concluded that high HER-2 expression and positive PD-L1 status are associated with better outcomes, reinforcing their potential roles as biomarkers for treatment optimization. This study underscores the importance of tailoring treatment regimens based on individual patient characteristics, particularly HER-2 and PD-L1 expression levels. This emphasis on personalized medicine aligns with contemporary trends in oncology, where patient-specific factors are increasingly driving therapeutic decisions. Some comments for minor revision: 1) Further detail on monitoring protocols for adverse events and how disease progression was assessed would reinforce methodological transparency. 2) Compare and contrast the findings more thoroughly with existing literature to contextualize the study within the broader field of gastric cancer research. 3) The content of Figures should be focused and merged, such as Figure 1 and Figure 2, Figure 3 and Figure 4, Figure 5 and Figure 6.