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PEER-REVIEW REPORT

Name of journal: *World Journal of Gastroenterology*

Manuscript NO: 108298

Title: Real-world comparison of effectiveness and safety of chemotherapy plus bevacizumab with or without anti-PD-1 immunotherapy as first-line therapy in microsatellite stable

Provenance and peer review: Unsolicited Manuscript; Externally peer reviewed

Peer-review model: Single blind

Reviewer's code: 06482162

Position: Peer Reviewer

Academic degree and professional title: MD

Reviewer's Country/Territory: United States

Author's Country/Territory: China

Manuscript submission date: 2025-04-09

Reviewer chosen by: Shang Wu

Reviewer accepted review: 2025-04-16 04:19

Reviewer performed review: 2025-04-28 15:39

Review time: 12 Days and 11 Hours

Content to be reviewed	Does the manuscript's content fall within the scope of the journal? Yes Is there any Key Word that is not included in the manuscript title? Yes Do authors' affiliations correspond to the content of the manuscript? Yes Does the Abstract contain the contents of each part of the manuscript (IMRaD)? Yes
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Are the Key Words complete? **Yes**

Is the content of the Introduction adequate? **Yes**

Is the content of the Materials and Methods complete?
Yes

Is the description of the experiments clear and
complete? **Yes**

Are the experimental data presented in the
manuscript's biostatistics content reliable? **Yes**

Are the experimental data of the Results true and
reliable? **Yes**

Are the quality and resolution of the images up to
standard? **Yes**

Do the selection and design of the figures and tables
follow the principles of necessity and clarity? **Yes**

Is there any duplication between various parts of the
manuscript and between the main text and the content
presented in the figures and tables? **Yes**

Are the figures and tables numbered consecutively in
the order in which they appear in the manuscript? **Yes**

Is the content of the Discussion reasonable? **Yes**

Is the Conclusion reasonable? **Yes**

Are all references necessary and reasonable? **Yes**

Do authors omit important references? **Yes**

Are all references related to the topic of the
manuscript? **Yes**

Do authors only cite their own earlier publications? **No**

Is the manuscript's text correct, concise, and clear? **Yes**

Will the manuscript's content be of interest to readers?
Yes

Are additional experiments needed for the study? **Yes**



	Does the research scope comply with ethics? Yes
Scientific quality	Grade A (Excellent)
Novelty of this manuscript	Grade A (Excellent)
Creativity or innovation of this manuscript	Grade A (Excellent)
Scientific significance of the conclusion in this manuscript	Grade A (Excellent)
Language quality	Grade B (Very good)
Does this manuscript describe a study of the existing knowledge system?	Yes
Does this manuscript report a revolutionary innovation?	No
Does this manuscript report an unconventional innovation?	No
Conclusion	Accept
Re-review	No
Peer-reviewer statements	Peer-Review: Anonymous
	Conflicts-of-Interest: No

SPECIFIC COMMENTS TO AUTHORS

The authors presented a multicenter, retrospective study aimed at evaluating the survival outcomes of combining chemotherapy, bevacizumab, and anti-PD-1 immunotherapy versus using chemotherapy and bevacizumab alone in patients with microsatellite stable (MSS) metastatic colorectal cancer. Overall, the study found that adding anti-PD-1 therapy did not lead to a statistically significant improvement in progression-free survival (PFS), overall survival (OS), or objective response rate (ORR) compared to chemotherapy with bevacizumab alone. An exploratory biomarker analysis



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identified baseline lactate dehydrogenase (LDH) levels as an independent predictor of survival outcomes, suggesting a potential tool for selecting patients who may benefit more from combination therapy. Safety profiles between the two groups were comparable, with no new or unexpected adverse events observed. The study has several notable strengths. It was carefully designed, especially for a real-world analysis, and the authors used robust statistical methods, including propensity score matching (PSM) and inverse probability of treatment weighting (IPTW), to minimize confounding factors and strengthen the validity of their findings. The inclusion of exploratory biomarker and subgroup analyses added further depth, offering valuable insights into possible prognostic factors that could influence treatment decisions in the future. However, there are also important limitations to consider. First, the sample size was relatively small, with only 25 patients remaining in the experimental group after matching. Such a small number reduces the statistical power of the study, making it harder to detect real differences between groups. In fact, when examining the Kaplan-Meier survival curves, there appeared to be a trend favoring improved PFS in the combination therapy group. Yet, this trend did not reach statistical significance, likely due to the limited sample size. Another concern is the use of different anti-PD-1 agents—including penpulimab, pembrolizumab, and sintilimab—across patients, which could introduce variability in treatment effects and complicate interpretation of the results. Overall, while the study offers encouraging early signals, larger, prospective, and more standardized studies are needed to validate these findings and better define the role of anti-PD-1 therapy in this patient population.



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Provenance and peer review: Unsolicited Manuscript; Externally peer reviewed

Peer-review model: Single blind

Reviewer's code: 08359254

Position: Peer Reviewer

Academic degree and professional title: MD

Reviewer's Country/Territory: China

Author's Country/Territory: China

Manuscript submission date: 2025-04-09

Reviewer chosen by: Shang Wu

Reviewer accepted review: 2025-04-22 02:01

Reviewer performed review: 2025-05-06 08:01

Review time: 14 Days and 6 Hours

Content to be reviewed	Does the manuscript's content fall within the scope of the journal? Yes Is there any Key Word that is not included in the manuscript title? No Do authors' affiliations correspond to the content of the manuscript? Yes Does the Abstract contain the contents of each part of the manuscript (IMRaD)? Yes
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Are the Key Words complete? **Yes**

Is the content of the Introduction adequate? **Yes**

Is the content of the Materials and Methods complete?
Yes

Is the description of the experiments clear and
complete? **Not Applicable**

Are the experimental data presented in the
manuscript's biostatistics content reliable? **Not
Applicable**

Are the experimental data of the Results true and
reliable? **Not Applicable**

Are the quality and resolution of the images up to
standard? **Yes**

Do the selection and design of the figures and tables
follow the principles of necessity and clarity? **Yes**

Is there any duplication between various parts of the
manuscript and between the main text and the content
presented in the figures and tables? **No**

Are the figures and tables numbered consecutively in
the order in which they appear in the manuscript? **Yes**

Is the content of the Discussion reasonable? **Yes**

Is the Conclusion reasonable? **Yes**

Are all references necessary and reasonable? **Yes**

Do authors omit important references? **No**

Are all references related to the topic of the
manuscript? **Yes**

Do authors only cite their own earlier publications? **No**

Is the manuscript's text correct, concise, and clear? **Yes**

Will the manuscript's content be of interest to readers?
Yes



	Are additional experiments needed for the study? No Does the research scope comply with ethics? Yes
Scientific quality	Grade A (Excellent)
Novelty of this manuscript	Grade B (Very Good)
Creativity or innovation of this manuscript	Grade B (Very Good)
Scientific significance of the conclusion in this manuscript	Grade A (Excellent)
Language quality	Grade A (Excellent)
Does this manuscript describe a study of the existing knowledge system?	Yes
Does this manuscript report a revolutionary innovation?	No
Does this manuscript report an unconventional innovation?	Yes
Conclusion	Minor revision
Re-review	Yes
Peer-reviewer statements	Peer-Review: Anonymous
	Conflicts-of-Interest: No

SPECIFIC COMMENTS TO AUTHORS

This study, through a multicenter retrospective cohort analysis, explores the efficacy and safety of chemotherapy combined with bevacizumab with or without anti-PD-1 immunotherapy in MSS mCRC patients, which is clinically significant. The study design is relatively rigorous, employing propensity score matching (PSM) and inverse probability treatment weighting (IPTW) to reduce confounding factors, with reasonable data analysis methods. Before acceptance, I believe the following issues should be addressed: 1. Abstract: The results should include specific statistical values (e.g.,



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"HR=0.7076") and clearly highlight the key findings from the subgroup analysis (e.g., benefits for male and right-sided colon cancer patients). 2. Introduction: Recent key clinical trials should be added to compare the treatment challenges faced by MSS patients. 3. The first paragraph of the discussion mentions methods for overcoming the generally poor efficacy of immunotherapy, but the explanation is insufficient. Numerous studies have shown that tertiary lymphoid structures (TLS) are important biomarkers in colorectal cancer (PMID: 39575712). One study indicated that mature TLS can predict the efficacy of immune checkpoint inhibitors in solid tumors, independent of PD-L1 expression (PMID: 35118423). Therefore, TLS has great potential in addressing this challenge. 4. There are numerous Chinese punctuation marks ("。") following citation numbers throughout the manuscript; please correct this. After addressing the above modifications, I believe this article is suitable for publication in the World Journal of Gastroenterology.



RE-REVIEW REPORT OF REVISED MANUSCRIPT

Name of journal: *World Journal of Gastroenterology*

Manuscript NO: 108298

Title: Real-world comparison of effectiveness and safety of chemotherapy plus bevacizumab with or without anti-PD-1 immunotherapy as first-line therapy in microsatellite stable

Provenance and peer review: Unsolicited Manuscript; Externally peer reviewed

Peer-review model: Single blind

Reviewer's code: 08359254

Position: Peer Reviewer

Academic degree and professional title: MD

Reviewer's Country/Territory: China

Author's Country/Territory: China

Manuscript submission date: 2025-04-09

Reviewer chosen by: Yu Bai

Reviewer accepted review: 2025-05-13 14:06

Reviewer performed review: 2025-05-13 14:09

Review time: 1 Hour

Content to be reviewed	Does the manuscript's content fall within the scope of the journal? Yes Is there any Key Word that is not included in the manuscript title? No Do authors' affiliations correspond to the content of the manuscript? Yes Does the Abstract contain the contents of each part of the manuscript (IMRaD)? Yes
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Are the Key Words complete? **Yes**

Is the content of the Introduction adequate? **Yes**

Is the content of the Materials and Methods complete?
Yes

Is the description of the experiments clear and
complete? **Yes**

Are the experimental data presented in the
manuscript's biostatistics content reliable? **Yes**

Are the experimental data of the Results true and
reliable? **Yes**

Are the quality and resolution of the images up to
standard? **Yes**

Do the selection and design of the figures and tables
follow the principles of necessity and clarity? **Yes**

Is there any duplication between various parts of the
manuscript and between the main text and the content
presented in the figures and tables? **No**

Are the figures and tables numbered consecutively in
the order in which they appear in the manuscript? **Yes**

Is the content of the Discussion reasonable? **Yes**

Is the Conclusion reasonable? **Yes**

Are all references necessary and reasonable? **Yes**

Do authors omit important references? **No**

Are all references related to the topic of the
manuscript? **Yes**

Do authors only cite their own earlier publications? **No**

Is the manuscript's text correct, concise, and clear? **Yes**

Will the manuscript's content be of interest to readers?
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Are additional experiments needed for the study? **No**



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	Does the research scope comply with ethics? Yes
Scientific quality	Grade A (Excellent)
Novelty of this manuscript	Grade A (Excellent)
Creativity or innovation of this manuscript	Grade A (Excellent)
Scientific significance of the conclusion in this manuscript	Grade A (Excellent)
Language quality	Grade A (Excellent)
Does this manuscript describe a study of the existing knowledge system?	Yes
Does this manuscript report a revolutionary innovation?	Yes
Does this manuscript report an unconventional innovation?	Yes
Conclusion	Accept
Peer-reviewer statements	Peer-Review: Anonymous
	Conflicts-of-Interest: No

SPECIFIC COMMENTS TO AUTHORS

Accept