



**PEER-REVIEW REPORT**

**Name of journal:** *World Journal of Gastrointestinal Oncology*

**Manuscript NO:** 111171

**Title:** Tumour chemotherapy sensitivity test may predict clinical outcomes in colorectal cancer patients receiving oxaliplatin and fluoropyrimidine-based regimens

**Provenance and peer review:** Unsolicited manuscript; Externally peer reviewed

**Peer-review model:** Single blind

**Reviewer’s code:** 08118307

**Position:** Peer Reviewer

**Academic degree and professional title:** Professor, Research Fellow

**Reviewer’s Country/Territory:** China

**Author’s Country/Territory:** China

**Manuscript submission date:** 2025-06-24

**Reviewer chosen by:** Hong-Xin Jiang

**Reviewer accepted review:** 2025-07-31 06:27

**Reviewer performed review:** 2025-08-11 09:26

**Review time:** 11 Days and 2 Hours

<b>Content to be reviewed</b>	<p>Does the manuscript’s content fall within the scope of the journal? <b>Yes</b></p> <p>Is there any Key Word that is not included in the manuscript title? <b>Yes</b></p> <p>Do authors’ affiliations correspond to the content of the manuscript? <b>Yes</b></p> <p>Does the Abstract contain the contents of each part of the manuscript (IMRaD)? <b>Yes</b></p> <p>Are the Key Words complete? <b>Yes</b></p>
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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? **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? **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 B (Very Good)
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?	Yes
Conclusion	Minor revision
Re-review	No
Peer-reviewer statements	Peer-Review: Onymous
	Conflicts-of-Interest: No
Are your review comments generated by AI tools?	No

### SPECIFIC COMMENTS TO AUTHORS

This study conducted a retrospective analysis of ATP-TCA test results from 1,549 colorectal cancer patients, confirming the independent prognostic value of ATP-TCA in predicting overall survival (OS) and disease-free survival (DFS) among resectable colorectal cancer patients receiving oxaliplatin- and fluorouracil-based adjuvant chemotherapy regimens. The findings demonstrate that ATP-TCA can help optimize postoperative chemotherapy selection, enhance treatment efficacy, and improve patient outcomes. Although certain limitations exist, such as the retrospective design and



inconsistent thresholds, the research provides important evidence for future developments in personalized medicine and recommends further large-scale prospective studies to validate its clinical application value.

The present investigation explores the predictive value of ATP-TCA testing in individualized chemotherapy for colorectal cancer, featuring a sufficient sample size and rigorous statistical analyses (Cox regression, Kaplan-Meier survival analysis, etc.), with clear clinical significance. However, three limitations—sample selection bias, insufficient threshold standardization, and relatively short follow-up periods—require targeted improvements to enhance the reliability of the conclusions.

The revision suggestions are as follows.

1. Sample selection bias: Excluding patients who received neoadjuvant/targeted/immunotherapy (proportion in sample unknown) limits the results to traditional chemotherapy Homo sapiens populations, deviating from modern clinical practice. Discuss the impact of exclusion criteria on the generalizability of conclusions and quantify the proportion of excluded patients in the "Limitations" section.
2. Standardization of ATP-TCA threshold: The self-defined IC50/IC90 threshold lacks validation of consistency with thresholds from other studies (e.g., international consensus). Cite prior literature (e.g., ATP-TCA threshold studies in breast cancer) to justify the current threshold.
3. Insufficient follow-up time: A median follow-up of 2.78 years (33 months) is inadequate for evaluating long-term survival in early-stage colorectal cancer (stages I-II). Extend follow-up to  $\geq 5$  years (especially for early-stage patients) and supplement with 5-year survival rate analysis. If follow-up extension is unfeasible, explicitly state in the discussion that "conclusions are limited to mid-term prognosis."
4. Clinical translation supplement: Discuss the predictive advantages/disadvantages of



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ATP-TCA compared to genetic testing (e.g., RAS mutation) and PD-L1 testing.

5. Rigorous phrasing: For example, replace "fills the research utetheisa kong white" with "supplements evidence on ATP-TCA application in colorectal cancer." Clearly state study limitations (sample selection, follow-up duration) in the abstract/conclusion.

6. Standardize table formats throughout the manuscript (e.g., table titles).



## PEER-REVIEW REPORT

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**Provenance and peer review:** Unsolicited manuscript; Externally peer reviewed

**Peer-review model:** Single blind

**Reviewer's code:** 08523843

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**Academic degree and professional title:** PhD, Professor

**Reviewer's Country/Territory:** China

**Author's Country/Territory:** China

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

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

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Is the Conclusion reasonable? **No**

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? **Yes**

Does the research scope comply with ethics? **Yes**



Scientific quality	Grade D (Fair)
Novelty of this manuscript	Grade C (Good)
Creativity or innovation of this manuscript	Grade C (Good)
Scientific significance of the conclusion in this manuscript	Grade C (Good)
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?	No
Conclusion	Major revision
Re-review	No
Peer-reviewer statements	Peer-Review: Anonymous
	Conflicts-of-Interest: No
Are your review comments generated by AI tools?	No

### SPECIFIC COMMENTS TO AUTHORS

Your research work has conducted an in-depth assessment of the response of colorectal cancer patients to the combined chemotherapy regimen of fluorouracil and oxaliplatin through the ATP-TCA chemical sensitivity test. The research results clearly confirm that there is a significant correlation between the ATP-TCA chemical sensitivity test and the three-year and five-year overall survival and progression-free survival rates of resectable colorectal cancer patients after surgery combined with chemotherapy. This research not only provides a new perspective for the treatment of colorectal cancer, but also your



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findings have important guiding significance for clinical practice.

Although your research has achieved remarkable results, there are still some aspects that may need further improvement and enhancement. For example, you constructed a Cox regression model in your research, which is an extremely important and widely used model in medical statistical analysis. However, the application of the Cox regression model in your research seems to need further refinement. Specifically, your model construction process did not include any internal or external validation steps. An unvalidated model, no matter how excellent its AUC (Area Under the Curve) and C-index (Concordance Index) values are in the training set, has limited practical significance. Moreover, the AUC and C-index values shown by the training set data you used are not particularly outstanding, which raises doubts about the generalization ability of the model and the reliability of the series of conclusions you have drawn based on the current model. An unvalidated Cox regression model may only be able to identify the correlation between parameters and clinical outcomes. Therefore, I strongly recommend that you add model validation steps in your subsequent research, which will greatly enhance the credibility and persuasiveness of your research results.

I firmly believe that if your research can be further optimized and improved in this aspect, it will not only significantly enhance the quality and depth of the research, but also gain wider recognition from the academic and clinical communities, thereby having a more profound impact on the research of colorectal cancer treatment.



**RE-REVIEW REPORT OF REVISED MANUSCRIPT**

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**Peer-review model:** Single blind

**Reviewer’s code:** 08118307

**Position:** Peer Reviewer

**Academic degree and professional title:** Professor, Research Fellow

**Reviewer’s Country/Territory:** China

**Author’s Country/Territory:** China

**Manuscript submission date:** 2025-06-24

**Reviewer chosen by:** Jing-Jie Wang

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**Review time:** 1 Day and 14 Hours

<b>Content to be reviewed</b>	<p>Does the manuscript’s content fall within the scope of the journal? <b>Yes</b></p> <p>Is there any Key Word that is not included in the manuscript title? <b>Yes</b></p> <p>Do authors’ affiliations correspond to the content of the manuscript? <b>Yes</b></p> <p>Does the Abstract contain the contents of each part of the manuscript (IMRaD)? <b>Yes</b></p> <p>Are the Key Words complete? <b>Yes</b></p>
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Are the experimental data of the Results true and reliable? **Yes**

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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 B (Very Good)
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?	Yes
Conclusion	Accept
Peer-reviewer statements	Peer-Review: Onymous
	Conflicts-of-Interest: No
Are your review comments generated by AI tools?	No

### SPECIFIC COMMENTS TO AUTHORS

This paper has made revisions and replies to the suggestions. Conclusion: It is recommended to accept.

The reply is quoted below.

1. Sample selection bias: Excluding patients who received neoadjuvant/targeted/immunotherapy (proportion in sample unknown) limits the results to traditional chemotherapy Homo sapiens populations, deviating from modern clinical practice. Discuss the impact of exclusion criteria on the generalizability of conclusions and quantify the proportion of excluded patients in the "Limitations"

section.

Answer to 1

We thank the reviewers for their valuable suggestions. Please refer to the yellow-highlighted sections in the Methods section, Figure 1 and the Discussion section for details.

2. Standardization of ATP-TCA threshold: The self-defined IC50/IC90 threshold lacks validation of consistency with thresholds from other studies (e.g., international consensus). Cite prior literature (e.g., ATP-TCA threshold studies in breast cancer) to justify the current threshold.

Answer to 2

We appreciate the reviewers' insightful suggestion. The relevant literature has been cited in the Methods section to provide a rationale for the ATP-TCA threshold standardization.

3. Insufficient follow-up time: A median follow-up of 2.78 years (33 months) is inadequate for evaluating long-term survival in early-stage colorectal cancer (stages I-II). Extend follow-up to  $\geq 5$  years (especially for early-stage patients) and supplement with 5-year survival rate analysis. If follow-up extension is unfeasible, explicitly state in the discussion that "conclusions are limited to mid-term prognosis."

Answer to 3

We appreciate the reviewers' insightful suggestion. Given the current limited follow-up duration, we will continue to extend the study period to obtain longer-term data. Furthermore, the Discussion has been revised to explicitly state that the conclusions of this study are limited to midterm prognosis.

4. Clinical translation supplement: Discuss the predictive advantages/disadvantages of ATP-TCA compared to genetic testing (e.g., RAS mutation) and PD-L1 testing.

Answer to 4



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We appreciate the reviewers' insightful suggestion. The Introduction section has been updated with a comparison of ATP-TCA to other individualized methods, such as genetic and PD-L1 testing.

5. Rigorous phrasing: For example, replace "fills the research utetheisa kong white" with "supplements evidence on ATP-TCA application in colorectal cancer." Clearly state study limitations (sample selection, follow-up duration) in the abstract/conclusion.

Answer to 5

We thank the reviewers for their valuable suggestions and have rigorously revised our conclusions and study limitations accordingly. Please refer to the Abstract section, Pg 2, and the Conclusion section for details.

6. Standardize table formats throughout the manuscript (e.g., table titles).

Answer to 6

Thank you for the comments. The formatting settings of all the tables have been standardized.

Article 4 on proposed amendments, "Clinical translation supplement: Discuss the predictive advantages/disadvantages of ATP-TCA compared to genetic testing (e.g., RAS mutation) and PD-L1 testing", the article also responded.