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PEER-REVIEW REPORT

Name of journal: *World Journal of Clinical Oncology*

Manuscript NO: 87101

Title: Classification of patients with metastatic colorectal cancer into consensus molecular subtypes into real-world: A pilot study

Provenance and peer review: Invited Manuscript; Externally peer reviewed

Peer-review model: Single blind

Reviewer's code: 05097817
Position: Editorial Board
Academic degree: MD, PhD

Professional title: Professor

Reviewer's Country/Territory: China

Author's Country/Territory: Chile

Manuscript submission date: 2023-07-26

Reviewer chosen by: AI Technique

Reviewer accepted review: 2023-08-07 03:02

Reviewer performed review: 2023-08-11 11:31

Review time: 4 Days and 8 Hours

Scientific quality	[ ] Grade A: Excellent [ ] Grade B: Very good [Y] Grade C: Good [ ] Grade D: Fair [ ] Grade E: Do not publish
Novelty of this manuscript	[ ] Grade A: Excellent [ ] Grade B: Good [Y] 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	[Y] Grade A: Priority publishing [ ] Grade B: Minor language polishing [ ] Grade C: A great deal of language polishing [ ] Grade D: Rejection
Conclusion	[ ] Accept (High priority) [ ] Accept (General priority) [ ] Minor revision [Y] 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 authors aimed to generate an alternative protocol as a validated tool from prospective studies for accurately classifying patients of metastatic colorectal cancer into the four Consensus Molecular Subtype (CMS) categories, by using RT-PCR and next-generation genomic sequencing (NGS) techniques, potentially leading to precise selection and guiding targeted therapy of mCRC patients. They conclude that they successfully classified mCRC patients into CMS categories using an RT-PCR- and NGS-based workflow. However, there are some points that need more clarification and statements in the manuscript, as shown in below: 1- The methods for RT-PCR experiments, CMS categories identification and data analysis, described in this manuscript doesn't present in adequate detail. What is the information for those RT-PCR primers which should be provided in a supplementary table? The original dataset of all those gene mutations or expression for each patient better be shown in a supplementary table according to the detailed criteria to classify their CMS categories. 2- Figure 1 need be more clarified and better replaced with a spot diagram. 3- To provide a comprehensive overview of the mutations in those 25 genes with their 25-gene

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TumorSec panel, a clarified and classified table is much more informative including each genetic status within each group of patients rather than a simple figure with the proportion of patients harboring mutation in Figure 2. 4- The results in Figure 3 is confused and too inadequate to describe those four identified CMS system together with 6 unclassifiable patients. Based on their results, the authors addressed that among those 24 identifiable patients, the remaining 8 patients (33%) were classified as non-categorical but probable for a CMS, but how they further determined those are CMS4 patients? Need more clear statement and discussion. The same correction need be done in the Abstract where they declared that "Thirty patients ….. in this study. Among them, 20% (n=6), 10% (n=3), 23% (n=7), and 27% (n=8) were classified as CMS1, CMS2, CMS3, and CMS4, respectively……Notably, 67% of cases were determined to belong to categorical CMSs, while the remaining 33% belonged to non-categorical CMSs". 5- They since have obtained the gene expression- /or mutation-based subtype signatures for those genes, I am very interested in that they might also be able to find important associations between the CMS groups and clinical variables/ and differences in prognosis. There would be more scientific significance in their findings if the results could confirm that the clinical relevance of the intrinsic biological processes implicated in each CMS. 6- What are the new findings or novelty of this study? Or brought any new concepts in this study proposes? The author might describe more in the Discussion section.

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Reviewer's code: 03656584
Position: Editorial Board
Academic degree: MD, MSc
Professional title: Associate Professor, Associate Specialist, Director, Doctor
Reviewer's Country/Territory: China
Author's Country/Territory: Chile

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Reviewer chosen by: Geng-Long Liu

Reviewer accepted review: 2023-09-07 15:51

Reviewer performed review: 2023-09-14 06:06

Review time: 6 Days and 14 Hours

Scientific quality	[ ] Grade A: Excellent [ ] Grade B: Very good [Y] Grade C: Good [ ] Grade D: Fair [ ] Grade E: Do not publish
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) [ ] Accept (General priority) [ ] Minor revision [Y] Major revision [ ] Rejection
Re-review	[Y] Yes [ ] No

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Peer-reviewer statements	Peer-Review: [Y] Anonymous [ ] Onymous
	Conflicts-of-Interest: [ ] Yes [Y] No

SPECIFIC COMMENTS TO AUTHORS

The authors conducted a study on the molecular typing of non resectable metastatic colorectal cancer, and the experimental design of the relevant research had certain flaws. It is best to select patients who were initially diagnosed with non resectable metastatic colorectal cancer at the researcher's unit for treatment, and who have started hospitalization for the first time. If colorectal cancer patients who have already been treated in other hospitals but later experience recurrence, metastasis, and irremovable colorectal cancer, the relevant observation indicators and prognosis may be affected by the initial treatment. Additionally, the sample size is too small and divided into many layers, resulting in patients in each layer being single digits. This leads to a significant impact on statistical differences. This directly leads to a decrease in the credibility of its research conclusions. The innovation of related research is average, and the sample size is too small, which has limited practical guidance significance for clinical practice. Suggest the author to increase the sample size.