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PEER-REVIEW REPORT

Name of journal: *World Journal of Gastrointestinal Oncology*

Manuscript NO: 80348

Title: Is the combination of immunotherapy with conventional chemotherapy the key to increase the efficacy of colorectal cancer treatment?

Provenance and peer review: Invited Manuscript; Externally peer reviewed

Peer-review model: Single blind

Reviewer's code: 03261315
Position: Editorial Board
Academic degree: FACE, PhD
Professional title: Academic Research, Chief Doctor, Doctor, Postdoc, Professor, Senior Researcher
Reviewer's Country/Territory: Romania
Author's Country/Territory: Mexico

Manuscript submission date: 2022-09-24

Reviewer chosen by: AI Technique

Reviewer accepted review: 2022-09-28 08:41

Reviewer performed review: 2022-09-28 09:49

Review time: 1 Hour

Scientific quality	[ ] Grade A: Excellent [ ] Grade B: Very good [Y] Grade C: Good [ ] Grade D: Fair [ ] Grade E: Do not publish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

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

SPECIFIC COMMENTS TO AUTHORS

The review is too long. The title is not suitable. The authors present the efficacy of conventional chemotherapy, the immunotherapy and immunosuppression of CRC in separate subchapters . They preset in only 1 page the studies regarding the immunotherapy plus chemotherapy for treatment of CRC. In my opinion they should give up the following subchapters: Conventional treatments of colon cancer and mechanisms of action from a genetic perspective. The 5-Fluorouracil mechanism of action. Use chemotherapeutic strategies for colon cancer treatment; which is the right drug? Chemoresistance to treatment in colon cancer. The authors should focus on the topic. The conclusions are too long. There are bibliographic indices which are missing.

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Reviewer's code: 06392060
Position: Peer Reviewer
Academic degree:

Professional title:

Reviewer's Country/Territory: Reviewer_Country

Author's Country/Territory: Mexico

Manuscript submission date: 2022-09-24

Reviewer chosen by: AI Technique

Reviewer accepted review: 2022-10-02 07:11

Reviewer performed review: 2022-10-11 08:31

Review time: 9 Days and 1 Hour

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 [ ] Grade B: Minor language polishing [Y] Grade C: A great deal of language polishing [ ] Grade D: Rejection
Conclusion	[ ] Accept (High priority) [ ] Accept (General priority) [Y] Minor revision [ ] 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

This is an interesting review article on potential therapies used for treating CRC. Whilst some of the information given in the review is novel other facts regarding treatment are well known. At times English language needed correction particularly in the statement and I quote: 'In another study in Australasian and Canadian populations with asymptomatic patients using the same chemotherapy regimen, NON-DIFFERENCES were reported between early and delayed chemoterapy use until symptoms...[42]. Please use 'no difference'. The NRAS gene is associated with malignant proliferation and metastases of CRC. The authors should refer to a recent meta-analysis which showed that NRAS could predict the poor prognosis for CRC (Yue Hu et al., 2018). Please include this reference and include some more recent references. Please define FOLFIRI in a list of abbreviations. Please include all abbreviations in a list before the references. There were no diagramatic representations of the text. Flow diagrams will help in this regard especially when explaining the pathways of tumorigenesis. The authors mention ICI avelumab monotherapy and darvalumab in microsatellite-instability high/mismatch repair-deficient metastatic CRC patients, and an improvement in progression-free survival. What is the mechanism of action of these monotherapies? A diagram may also be used to explain the mechanism. The advantages of using combined immunotherapy egs: ipilimumab plus nivolumab before surgery is well explained. How were the lack of signs of cancer after surgery assessed?