

PEER-REVIEW REPORT

Name of journal: *World Journal of Gastroenterology*

Manuscript NO: 80268

Title: Resistance to targeted therapy and new developments in metastatic colorectal cancer,

Provenance and peer review: Invited Manuscript; Externally peer reviewed

Peer-review model: Single blind

Reviewer's code: 05387405

Position: Peer Reviewer

Academic degree: MSc, PhD

Professional title: Research Scientist

Reviewer's Country/Territory: Hungary

Author's Country/Territory: China

Manuscript submission date: 2022-09-20

Reviewer chosen by: AI Technique

Reviewer accepted review: 2022-10-26 08:26

Reviewer performed review: 2022-11-01 20:37

Review time: 6 Days and 12 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 Grade E: Do not publish
Language quality	<input type="checkbox"/> Grade A: Priority publishing <input type="checkbox"/> Grade B: Minor language polishing <input checked="" 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 type="checkbox"/> Minor revision <input checked="" 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

Authors presented a review detailing resistance of targeted therapy in metastatic CRC.

1. Although it was reported that the English of the article was revised by "a professional linguistic reviewer", the readability of the text suffers several times due to grammar issues. Two examples: - "The American Society of Clinical Oncology (ASCO) recommends that population with left-sided tumors versus right-sided tumors seem to benefit more from anti-EGFR therapy, and are associated with better prognosis" - "A phase I trial to explore the pharmacodynamic effects of TVB-2640 (FASN inhibitor) for patients with resectable tumors (NCT02980029)" The text would significantly benefit from the edit of a native English speaking professional. 2. There are several abbreviations throughout the text that were never resolved, eg. MT (mutated). Please check the manuscript for unresolved abbreviations. 3. There were several currently running RCT-s that were not cited. Eg.: "Besides, a phase 3 trial is assessing the effect of adagrasib plus cetuximab as the second-line treatment of KRASG12C mutated-type (MT) mCRC." The journal gives specific citation types for clintrials.gov sites, therefore, please, carefully look and add the citations for all, currently running but previously non-cited studies as well. 4. Authors should further discuss that line of thought that was just mentioned in the conclusion, that no study ever investigated these molecular markers in complete for treatment selection. 5. The paragraph presenting the current therapeutic options is very rough. 6. Although the title of the manuscript suggest a broader topic, the article deals with mCRC only. The change of the title is highly suggested. Eg.: "Resistance to targeted therapy and new developments in metastatic colorectal cancer"

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Peer-review model: Single blind

Reviewer's code: 03478911

Position: Associate Editor

Academic degree: PhD

Professional title: Chief Technician, Executive Vice President, Research Assistant Professor

Reviewer's Country/Territory: South Korea

Author's Country/Territory: China

Manuscript submission date: 2022-09-20

Reviewer chosen by: Dong-Mei Wang

Reviewer accepted review: 2022-11-22 12:09

Reviewer performed review: 2022-11-29 06:35

Review time: 6 Days and 18 Hours

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
Language quality	<input type="checkbox"/> Grade A: Priority publishing <input type="checkbox"/> Grade B: Minor language polishing <input checked="" 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 type="checkbox"/> Minor revision <input checked="" 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

The author summarized the recent regimens for colorectal cancer and the resulting resistance problems, they also summarized the latest therapeutics that can overcome them. However, the following two points should be considered. 1. There is a distinction between the treatments for colon and rectal cancer. For rectal cancer, radiotherapy is included in the standard regimen. Therefore, it needs to be organized into a separate section for the summarization of regimens for rectal cancer treatment. 2. Immunotherapy is less effective in MMR proficient or microsatellite stable (MSS) mCRC. This is because the MMR/MSS CRC is classified as a cold tumor. As various therapies are being investigated clinically to overcome the characteristics of cold tumors, supplementing the contents is necessary.

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Peer-review model: Single blind

Reviewer's code: 03004840

Position: Editorial Board

Academic degree: MSc, PhD

Professional title: Academic Research, Postdoc, Senior Researcher

Reviewer's Country/Territory: Turkey

Author's Country/Territory: China

Manuscript submission date: 2022-09-20

Reviewer chosen by: Dong-Mei Wang

Reviewer accepted review: 2022-11-08 10:27

Reviewer performed review: 2022-11-30 07:53

Review time: 21 Days and 21 Hours

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
Language quality	<input checked="" type="checkbox"/> Grade A: Priority publishing <input 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 type="checkbox"/> Minor revision <input checked="" 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="radio"/>] Anonymous [<input type="radio"/>] Onymous
	Conflicts-of-Interest: [<input type="radio"/>] Yes [<input checked="" type="radio"/>] No

SPECIFIC COMMENTS TO AUTHORS

Name of Journal: World Journal of Gastroenterology Manuscript Type: REVIEW

Resistance to targeted therapy and new developments in colorectal cancer This review article summarizes the resistance mechanisms for targeted therapy alternatives used in colorectal cancer. Resistance mechanism and potential treatments for CRC were also discussed. Overall paper is well written and intellectually sound, however it could be improved by expanding on a few points. Below are suggestions for improving the manuscript. 1. Minor typos should be corrected. 2. Full form of the abbreviations should be provided when used for the first time. 3. Some limitations for chemotherapy like systemic toxicity, low tumor-specific selectivity, response rate issues, and resistance should be included in the review paper. 4. There is no figure or table in the paper. Authors are requested to support their review with some figures and tables. It will help readers in keeping track of the relevant details. For instance, pathways for targeted therapy could be represented as a schematic diagram to the readers. Agents which targets EGFR or EGFR-related pathways under clinical investigation could be given as a table. 5. The side effects of targeted therapy such as asthenia, mucositis, anorexia, diarrhea, vomiting, skin rash, hand-foot syndrome, fatigue and cardiotoxicity should be discussed briefly in the manuscript. 6. Contribution of tumor microenvironment, microbiota and exosomes to resistance mechanism should be given briefly in the manuscript.

RE-REVIEW REPORT OF REVISED MANUSCRIPT

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Peer-review model: Single blind

Reviewer's code: 03478911

Position: Associate Editor

Academic degree: PhD

Professional title: Chief Technician, Executive Vice President, Research Assistant Professor

Reviewer's Country/Territory: South Korea

Author's Country/Territory: China

Manuscript submission date: 2022-09-20

Reviewer chosen by: Yu-Lu Chen

Reviewer accepted review: 2022-12-26 08:41

Reviewer performed review: 2022-12-27 04:34

Review time: 19 Hours

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
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 checked="" type="checkbox"/> Accept (General priority) <input type="checkbox"/> Minor revision <input type="checkbox"/> Major revision <input type="checkbox"/> Rejection
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



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SPECIFIC COMMENTS TO AUTHORS

All concerns have been well addressed. There is no additional issue to raise.