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PEER-REVIEW REPORT

Name of journal: World Journal of Clinical Oncology

Manuscript NO: 53938

Title: Targeting Metabolism to Overcome Bcl-2 Inhibitor Resistance in AML

Reviewer's code: 02739495
Position: Peer Reviewer
Academic degree: PhD
Professional title: Professor
Reviewer's Country/Territory: China
Author's Country/Territory: United States

Manuscript submission date: 2020-01-03
Reviewer chosen by: Le Zhang
Reviewer accepted review: 2020-02-24 02:05
Reviewer performed review: 2020-02-24 03:21
Review time: 1 Hour

Scientific quality	[ ] Grade A: Excellent [Y] Grade B: Very good [ ] Grade C: Good [ ] Grade D: Fair [ ] Grade E: Do not publish
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) [Y] Accept (General priority) [ ] Minor revision [ ] Major revision [ ] Rejection
Re-review	[ ] Yes [ ] No
Peer-reviewer statements	Peer-Review: [Y] Anonymous [ ] Onymous Conflicts-of-Interest: [ ] Yes [Y] No

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SPECIFIC COMMENTS TO AUTHORS

The manuscript is well designed. I recomment it to be published in the World Journal of Clinical Oncology.

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PEER-REVIEW REPORT

Name of journal: World Journal of Clinical Oncology

Manuscript NO: 53938

Title: Targeting Metabolism to Overcome Bcl-2 Inhibitor Resistance in AML

Reviewer's code: 00503195
Position: Editorial Board
Academic degree: MD, PhD
Professional title: Assistant Professor, Professor
Reviewer's Country/Territory: Greece
Author's Country/Territory: United States

Manuscript submission date: 2020-01-03
Reviewer chosen by: Ying Dou
Reviewer accepted review: 2020-03-25 09:16
Reviewer performed review: 2020-03-25 10:32
Review time: 1 Hour

Scientific quality	[ ] Grade A: Excellent [ ] Grade B: Very good [ ] Grade C: Good [Y] Grade D: Fair [ ] Grade E: Do not publish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

The review is interesting but requires improvements Major points 1. Generally, although in the title and abstract, the authors focused on cell metabolism, in the main text, cell metabolism was almost not discussed. This point should be corrected, or otherwise, the title and the abstract should be changed. 2. Many sentences simply describe the results of various studies in a very brief way, and they require further explanation or discussion by the authors. Otherwise, the review is like a collection of loosely connected sentences. 3. Please explain abbreviations when they appear for the first time in the text. 4. "A number of oncogenes and pathways work to activate glutamine addiction in AML, the rate-limiting step for mTORC1 pathway." mTORC1 pathway is activated or better deactivated by certain amino acids. There are studies showing that the sensitivity of this system is against certain amino acids and, more precisely, to leucine, isoleucine, valine, and possibly arginine (Gallinetti J, Biochem J 449: 1-10, 2013), but not against glutamine. Please comment. Also, the notion of mTORC1 at the above point requires a previous introduction about its role in AML. A comment about the role of glutamine in cell metabolism, mainly its conversion by glutaminases to a-ketoglutarate and entry into the Krebs cycle as a source of energy, is required. 5. A figure that describes in some detail the discussed apoptotic pathways and the effect of venetoclax on them is necessary. Minor points Genearrly, the text should be re-checked. Here are some examples. 1. In the above sentence, there are two contradictory means. "As such, redox-based treatment of hematologic malignancies by either inducing apoptosis with ROS generation or reducing ROS production, thereby depleting proliferative advantage, has been proposed." 2. "BH3 mimetics are a novel class of inhibitors specifically designed to disrupt the binding between the BH3 domain of proapoptotic proteins like BIM and BID and Bcl-2." Bcl-2? 3. "Interestingly, however, on subset analysis 38% of patients were noted to be positive for IDH 1/2 mutations, of

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whom 33% achieved a CR. The suggestion of a greater response in this molecular subpopulation was a clue to the potential metabolic effects of venetoclax treatment." At this point, the role of IDH in metabolism requires explanation. 4. "Interestingly, a glycine-to-valine mutation at amino acid position 101 (Gly101Val) was not identified in VRCs." Of which gene?