

PEER-REVIEW REPORT

Name of journal: *World Journal of Gastrointestinal Oncology*

Manuscript NO: 74597

Title: Claudin 18.2 is a potential therapeutic target for zolbetuximab in pancreatic ductal adenocarcinoma

Provenance and peer review: Unsolicited Manuscript; Externally peer reviewed

Peer-review model: Single blind

Reviewer's code: 05429162

Position: Peer Reviewer

Academic degree: MD, PhD

Professional title: Academic Fellow, Chief Doctor, Research Fellow, Research Scientist

Reviewer's Country/Territory: Japan

Author's Country/Territory: China

Manuscript submission date: 2021-12-31

Reviewer chosen by: AI Technique

Reviewer accepted review: 2022-01-02 06:00

Reviewer performed review: 2022-01-11 14:42

Review time: 9 Days and 8 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 Grade E: Do not publish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: [☒] Anonymous [☐] Onymous

Conflicts-of-Interest: [☐] Yes [☒] No

SPECIFIC COMMENTS TO AUTHORS

Summary Xi et al. analyzed the expression of Claudin 18.2 in pancreatic ductal adenocarcinoma (PDAC). Although the authors showed increased expression level of Claudin 18.2 in PDAC, I cannot recommend this article for publication because it has extensive problems. Major points 1) Introduction; There is no evidence showed that chemotherapy with/without targeted therapy is the first-line treatment in PDAC. In NCCN guidelines, there is no evidence that the chemotherapy with targeted therapy showed favorable prognosis (<https://www.nccn.org/guidelines/guidelines-detail?category=1&id=1455>). 2) The authors showed that the p53MVA and PD-1 inhibitor combination therapy is “pretty safe” regimen. However, as authors cited the article, there is many patients who suffered Grade1-2 adverse events albeit small sample size (Chung et al. Clin Transl Oncol. 2019 Mar;21(3):363-372. doi: 10.1007/s12094-018-1932-2) 3) Materials and methods [Scoring of CLDN 18.2 staining] The authors have not stated how many slides were used for IHC-score evaluation. Please clarify the number of slides used. 4) Results: Considering the heterogeneity of patients’ characteristics shown in table 2, the authors should perform multivariate analysis to evaluate if the significant factors correlated to CLDN18.2 expression is independent factor. 5) Discussion; In the result section, the authors showed that there is no significant survival difference between CLDN18.2 high/low expression patients. I think it is a hard to say that the zolbetuximab is a potential treatment target on PDAC. If the authors would like to show the zolbetuximab is a candidate agent, the authors should show more basic evidence related to zolbetuximab.

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Provenance and peer review: Unsolicited Manuscript; Externally peer reviewed

Peer-review model: Single blind

Reviewer's code: 05260764

Position: Peer Reviewer

Academic degree: Doctor, MD

Professional title: Surgeon

Reviewer's Country/Territory: Denmark

Author's Country/Territory: China

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Reviewer accepted review: 2022-01-16 18:45

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Review time: 3 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
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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
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SPECIFIC COMMENTS TO AUTHORS

This is an interesting study which propose a new and exciting target for the treatment of PDAC, as well as potentially more types of cancer, if validated in other studies. Therefore the value of the findings and topic of this paper is of great interest. However, several things have to be revised in order to make this paper acceptable for publication - I have tried to illuminate these things in the attached review of your paper, but overall concerns are; - Language level is not of high enough quality - A clearer aim is needed - Method section is very confusing and you have to find a lot of facts about how the study was conducted in the discussion section. - The statistics behind the number of samples you chose to evaluate is lacking - More than one part of the results section is a discussion - You lack a "strength and weaknesses" section were you illuminate the pros and cons of your study and critically evaluate your own work.