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ESPS PEER-REVIEW REPORT

Name of journal: World Journal of Gastroenterology

ESPS manuscript NO: 15847

Title: New targeted therapies in pancreatic cancer

Reviewer's code: 00052016

Reviewer's country: Japan

Science editor: Ya-Juan Ma

Date sent for review: 2014-12-12 09:58

Date reviewed: 2015-01-07 23:01

| CLASSIFICATION | LANGUAGE EVALUATION | SCIENTIFIC MISCONDUCT | CONCLUSION |
|---|--|--|--|
| <input type="checkbox"/> Grade A: Excellent | <input checked="" type="checkbox"/> Grade A: Priority publishing | Google Search: | <input type="checkbox"/> Accept |
| <input type="checkbox"/> Grade B: Very good | <input type="checkbox"/> Grade B: Minor language polishing | <input type="checkbox"/> The same title | <input type="checkbox"/> High priority for publication |
| <input type="checkbox"/> Grade C: Good | | <input type="checkbox"/> Duplicate publication | |
| <input checked="" type="checkbox"/> Grade D: Fair | <input type="checkbox"/> Grade C: A great deal of language polishing | <input type="checkbox"/> Plagiarism | <input type="checkbox"/> Rejection |
| <input type="checkbox"/> Grade E: Poor | <input type="checkbox"/> Grade D: Rejected | <input checked="" type="checkbox"/> No | <input checked="" type="checkbox"/> Minor revision |
| | | BPG Search: | <input type="checkbox"/> Major revision |
| | | <input type="checkbox"/> The same title | |
| | | <input type="checkbox"/> Duplicate publication | |
| | | <input type="checkbox"/> Plagiarism | |
| | | <input checked="" type="checkbox"/> No | |

COMMENTS TO AUTHORS

This manuscript summarizes the molecular targets in pancreatic cancer. This review is well described and informative to understand current concept. However, there is an issue to be considered before acceptance. 1. Possibility of anti-IGF-1R, ganitumab, was mentioned in the manuscript. However, press release said that phase 3 trial for metastatic pancreatic adenocarcinoma was terminated because ganitumab with gemcitabine is unlikely to demonstrate an improvement in the primary endpoint of overall survival (http://www.amgen.com/media/media_pr_detail.jsp?releaseID=1723925).



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ESPS PEER-REVIEW REPORT

Name of journal: World Journal of Gastroenterology

ESPS manuscript NO: 15847

Title: New targeted therapies in pancreatic cancer

Reviewer's code: 00068348

Reviewer's country: Greece

Science editor: Ya-Juan Ma

Date sent for review: 2014-12-12 09:58

Date reviewed: 2015-01-08 00:14

| CLASSIFICATION | LANGUAGE EVALUATION | SCIENTIFIC MISCONDUCT | CONCLUSION |
|--|--|--|--|
| <input type="checkbox"/> Grade A: Excellent | <input checked="" type="checkbox"/> Grade A: Priority publishing | Google Search: | <input type="checkbox"/> Accept |
| <input checked="" type="checkbox"/> Grade B: Very good | <input type="checkbox"/> Grade B: Minor language polishing | <input type="checkbox"/> The same title | <input type="checkbox"/> High priority for publication |
| <input type="checkbox"/> Grade C: Good | <input type="checkbox"/> Grade C: A great deal of language polishing | <input type="checkbox"/> Duplicate publication | <input type="checkbox"/> Rejection |
| <input type="checkbox"/> Grade D: Fair | <input type="checkbox"/> Grade D: Rejected | <input checked="" type="checkbox"/> Plagiarism | <input checked="" type="checkbox"/> Minor revision |
| <input type="checkbox"/> Grade E: Poor | | [Y] No | <input type="checkbox"/> Major revision |
| | | BPG Search: | |
| | | <input type="checkbox"/> The same title | |
| | | <input type="checkbox"/> Duplicate publication | |
| | | <input type="checkbox"/> Plagiarism | |
| | | [Y] No | |

COMMENTS TO AUTHORS

This article refers to the new leading targeted therapies in pancreatic cancer with emphasis to the immunotherapies. To my opinion is a very well written article and gives all the necessary information about new treatment options. My only remark is to make some more comments in respect to advanced pancreatic cancer.

ESPS PEER-REVIEW REPORT

Name of journal: World Journal of Gastroenterology

ESPS manuscript NO: 15847

Title: New targeted therapies in pancreatic cancer

Reviewer's code: 00069406

Reviewer's country: China

Science editor: Ya-Juan Ma

Date sent for review: 2014-12-12 09:58

Date reviewed: 2014-12-30 21:44

| CLASSIFICATION | LANGUAGE EVALUATION | SCIENTIFIC MISCONDUCT | CONCLUSION |
|--|---|--|---|
| <input type="checkbox"/> Grade A: Excellent | <input type="checkbox"/> Grade A: Priority publishing | Google Search: | <input type="checkbox"/> Accept |
| <input checked="" type="checkbox"/> Grade B: Very good | <input checked="" type="checkbox"/> Grade B: Minor language polishing | <input type="checkbox"/> The same title | <input checked="" type="checkbox"/> High priority for publication |
| <input type="checkbox"/> Grade C: Good | <input type="checkbox"/> Grade C: A great deal of language polishing | <input type="checkbox"/> Duplicate publication | <input type="checkbox"/> Rejection |
| <input type="checkbox"/> Grade D: Fair | <input type="checkbox"/> Grade D: Rejected | <input checked="" type="checkbox"/> Plagiarism | <input type="checkbox"/> Minor revision |
| <input type="checkbox"/> Grade E: Poor | | [Y] No | <input type="checkbox"/> Major revision |
| | | BPG Search: | |
| | | <input type="checkbox"/> The same title | |
| | | <input type="checkbox"/> Duplicate publication | |
| | | <input type="checkbox"/> Plagiarism | |
| | | [Y] No | |

COMMENTS TO AUTHORS

This is a well-organized review on the progress of targeted therapies in pancreatic cancer. The author listed many targets of PDAC as well as some clinical trial results. In general, the article is worth to read and can provide some new information instead of reading multiple papers in this area. There are some recommendations from the reviewer, 1. It's better to show some important tumor survival indexes such as OS, PFS in the text. For example, in Anti-EGFR agents, Erlotinib's result was not show in detail. For some in vitro studies, which is far from clinic usage, the author need to reduce the text. 2. A graph with the link between the pathways or factors related to PDAC is needed to present more clearly for readers. 3. A table with the effect of target agents is suggested to compare their difference on the OS or PFS, or labelled with "failed" as mentioned by the author.

ESPS PEER-REVIEW REPORT

Name of journal: World Journal of Gastroenterology

ESPS manuscript NO: 15847

Title: New targeted therapies in pancreatic cancer

Reviewer's code: 00029319

Reviewer's country: Germany

Science editor: Ya-Juan Ma

Date sent for review: 2014-12-12 09:58

Date reviewed: 2015-01-09 00:48

| CLASSIFICATION | LANGUAGE EVALUATION | SCIENTIFIC MISCONDUCT | CONCLUSION |
|---|---|--|--|
| <input type="checkbox"/> Grade A: Excellent | <input type="checkbox"/> Grade A: Priority publishing | Google Search: | <input type="checkbox"/> Accept |
| <input type="checkbox"/> Grade B: Very good | <input checked="" type="checkbox"/> Grade B: Minor language polishing | <input type="checkbox"/> The same title | <input type="checkbox"/> High priority for publication |
| <input checked="" type="checkbox"/> Grade C: Good | | <input type="checkbox"/> Duplicate publication | |
| <input type="checkbox"/> Grade D: Fair | <input type="checkbox"/> Grade C: A great deal of language polishing | <input type="checkbox"/> Plagiarism | <input type="checkbox"/> Rejection |
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| | | <input type="checkbox"/> The same title | |
| | | <input type="checkbox"/> Duplicate publication | |
| | | <input type="checkbox"/> Plagiarism | |
| | | <input checked="" type="checkbox"/> No | |

COMMENTS TO AUTHORS

This review summarizes the new leading targeted therapies in pancreatic cancers, focussing on passive and specific immunotherapies. The analysis includes experimental studies as well as clinical trials. Passive immunotherapy includes mainly therapies targeting against kinases, including epidermal growth factor receptor, Ras/Raf/mitogen-activated protein kinase cascade, human epidermal growth factor receptor 2, insulin growth factor-1 receptor, phosphoinositide 3-kinase/Akt/mTOR and hepatocyte growth factor receptor. Specific immunotherapies activate antitumor immune responses. The tailored target therapy via multiple pathways will leading to personalized medicine in the near future.

The following aspects are recommended to make revision:

- There is a brief introduction into the topic. Current therapeutic strategies are not explained sufficiently: what are the indications for adjuvant or operative therapy? Whats the difference in the therapy between curative or palliative regime?
- The targeted therapies are explained well, but without discussing its clinical useage. In which stage of disease are they used in pancreatic cancer?



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- The explanation of therapies against intracellular signaling pathways is too detailed and far from clinical practice.
- A graph with the link between the pathways or factors related to pancreatic cancer is needed to present more clearly for readers.

ESPS PEER-REVIEW REPORT

Name of journal: World Journal of Gastroenterology

ESPS manuscript NO: 15847

Title: New targeted therapies in pancreatic cancer

Reviewer's code: 00069015

Reviewer's country: China

Science editor: Ya-Juan Ma

Date sent for review: 2014-12-12 09:58

Date reviewed: 2015-01-02 16:56

| CLASSIFICATION | LANGUAGE EVALUATION | SCIENTIFIC MISCONDUCT | CONCLUSION |
|---|---|--|--|
| <input type="checkbox"/> Grade A: Excellent | <input type="checkbox"/> Grade A: Priority publishing | Google Search: | <input type="checkbox"/> Accept |
| <input type="checkbox"/> Grade B: Very good | <input checked="" type="checkbox"/> Grade B: Minor language polishing | <input type="checkbox"/> The same title | <input type="checkbox"/> High priority for publication |
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| | | <input type="checkbox"/> The same title | |
| | | <input type="checkbox"/> Duplicate publication | |
| | | <input type="checkbox"/> Plagiarism | |
| | | <input checked="" type="checkbox"/> No | |

COMMENTS TO AUTHORS

This review summarizes the new leading targeted therapies in pancreatic cancers, mainly focusing on passive and specific immunotherapies. Passive immunotherapy includes mainly therapies targeting against kinases, including epidermal growth factor receptor, Ras/Raf/mitogen-activated protein kinase cascade, human epidermal growth factor receptor 2, insulin growth factor-1 receptor, phosphoinositide 3-kinase/Akt/mTOR and hepatocyte growth factor receptor. Specific immunotherapies activate antitumor immune responses. The tailored target therapy via multiple pathways will leading to personalized medicine in the near future. The following aspects are recommended to make revision: 1. A brief diagram of the passive immunotherapy pathway network would help illustrate. 2. The author draw a panorama of targeted therapies in PCs including some well-know "new drugs" which already been discussed in a number of publications. More detailed discuss on advancing therapy pathways which ongoing trail would help to learning new leading therapies. 3. Some clinical trials number are not provided, such as inhibitors of the P13K/Akt/mTOR, MAPK cascade inhibitors (pimasertib and refametinib) , vorinostat+GEM+bortezomib, anti-TGF treatment in advanced PC. More result details of this



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ongoing clinical trials would help to understand the perspective of the therapy.