

PEER-REVIEW REPORT

Name of journal: World Journal of Clinical Oncology

Manuscript NO: 62909

Title: iRECIST in the assessment of atypical responses after immunotherapy

Reviewer's code: 03397272

Position: Editorial Board

Academic degree: PhD

Professional title: Associate Professor

Reviewer's Country/Territory: Slovenia

Author's Country/Territory: Italy

Manuscript submission date: 2021-01-24

Reviewer chosen by: Jia-Ping Yan

Reviewer accepted review: 2021-01-25 18:40

Reviewer performed review: 2021-01-27 11:21

Review time: 1 Day and 16 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 Grade E: Do not publish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 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

Please see comments in the attached file.

PEER-REVIEW REPORT

Name of journal: World Journal of Clinical Oncology

Manuscript NO: 62909

Title: iRECIST in the assessment of atypical responses after immunotherapy

Reviewer's code: 01808895

Position: Peer Reviewer

Academic degree: MD

Professional title: Professor

Reviewer's Country/Territory: Austria

Author's Country/Territory: Italy

Manuscript submission date: 2021-01-24

Reviewer chosen by: AI Technique

Reviewer accepted review: 2021-01-25 19:52

Reviewer performed review: 2021-02-12 17:15

Review time: 17 Days and 21 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 Grade E: Do not publish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 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 checked="" type="checkbox"/> Minor revision <input 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



**Baishideng
Publishing
Group**

7041 Koll Center Parkway, Suite
160, Pleasanton, CA 94566, USA
Telephone: +1-925-399-1568
E-mail: bpgoffice@wjgnet.com
<https://www.wjgnet.com>

SPECIFIC COMMENTS TO AUTHORS

This is a review of the iRECIST response evaluation of cancer patients undergoing immunotherapy with a particular focus on atypical response pattern (pseudo-, hyperprogression, dissociated response). The review summarizes the most important findings in different tumor types plus gives a reasonable overview about the potential pathomechanisms of these atypical response types as well -a table summarizing the different findings (percentages) for different tumor-types would be helpful, since this information is very difficult to memorize from the text. -the images in figures 3 and 4 seem to have mixed up: please correctly assign the images to the text

PEER-REVIEW REPORT

Name of journal: World Journal of Clinical Oncology

Manuscript NO: 62909

Title: iRECIST in the assessment of atypical responses after immunotherapy

Reviewer's code: 05493185

Position: Peer Reviewer

Academic degree: MD, PhD

Professional title: Doctor

Reviewer's Country/Territory: China

Author's Country/Territory: Italy

Manuscript submission date: 2021-01-24

Reviewer chosen by: Jia-Ping Yan

Reviewer accepted review: 2021-01-25 03:43

Reviewer performed review: 2021-02-15 16:46

Review time: 21 Days and 13 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 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 type="checkbox"/> Accept (General priority) <input checked="" type="checkbox"/> Minor revision <input 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

Advantages: 1. Immuno-RECIST (IRECIST) standards were introduced in 2017 to better analyze tumor responses to immunotherapy. Even iRECIST standards have been accepted by the world, due to the different mechanism of immunotherapy, clinical experience has shown that the percentage of patients cannot be ignored, is difficult to determine the type of right relief (stability, progress, or complete remission), this review introduces three kinds of "atypical response": pseudoprogression, hyperprogression, dissociated response, summarizes each pattern, wants to make quantitative standard to help clinicians and radiologists to evaluate the effect by immunotherapy in order to help patients get the best treatment plan. 2. Most of the references cited are recent two years and the data are relatively novel. 3. The article format is clear, first of all, it introduces the different views on iRECIST in the assessment of immunotherapy, then, it respectively makes a detailed introduction for the three categories, finally, summarizing atypical response characteristics again.

Insufficiency: Pseudoprogression, hyperprogression and dissociated response sometimes are not easy to distinguish, which affects the judgment of clinical benefit of immunotherapy, and thus affects the choice of subsequent treatment plan. At the same time, it is difficult to capture the tumor growth dynamics before and after treatment in the early stage of disease in practical operation. In clinical practice, in the case of lack of pre-baseline, pseudoprogression will weaken the true positive rate, because it is impossible to get different parameters, it's also impossible to distinguish between pseudoprogression and hyperprogression.

Suggestions: 1. Pseudoprogression gives a few of reference cases, so it is suggested to refer to more cases. The incidence of Pseudoprogression only describes a few tumors, so the data is not enough. 2. It is suggested to adjust the order of paragraphs in writing, because the logic is not smooth enough. 3. The frequency of pseudoprogression is lower than that of routine progression, and the decision to move beyond progression makes



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<https://www.wjgnet.com>

only in patients with obvious clinical benefit from immunotherapy. It is suggested to further explore the criteria for clinical benefit from immunotherapy in order to determine when the progression can be moved beyond progression. 4. Since there is no definition of HPD, how to clarify its incidence and explore relevant predictors? This part of the content is not mature, it is suggested to write down the latest major consensus, more persuasive. 5.① In pseudoprogression, the probability data of this phenomenon in various tumors were not available;② In pseudoprogression, there were less references to the two sections of iRECIST Guidelines. 6.① There are few examples of Dissociated Response;② Since the standard of Dissociated Response in iRECIST Guidelines is not clear, we can find some guiding literatures for its subsequent research and introduce the possibility of its subsequent development. 7. The classification of atypical responses in recent introduce and core tips are different. 8. Reducing the frequency of using Cosequently (the text appears 6 times), and consider replacing it by using other words;

RE-REVIEW REPORT OF REVISED MANUSCRIPT

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Manuscript NO: 62909

Title: iRECIST in the assessment of atypical responses after immunotherapy

Reviewer's code: 05493185

Position: Peer Reviewer

Academic degree: MD, PhD

Professional title: Doctor

Reviewer's Country/Territory: China

Author's Country/Territory: Italy

Manuscript submission date: 2021-01-24

Reviewer chosen by: Jia-Ru Fan

Reviewer accepted review: 2021-03-24 08:52

Reviewer performed review: 2021-03-24 12:58

Review time: 4 Hours

Scientific quality	[<input checked="" type="radio"/>] Grade A: Excellent [<input type="radio"/>] Grade B: Very good [<input type="radio"/>] Grade C: Good [<input type="radio"/>] Grade D: Fair [<input type="radio"/>] Grade E: Do not publish
Language quality	[<input checked="" type="radio"/>] Grade A: Priority publishing [<input type="radio"/>] Grade B: Minor language polishing [<input type="radio"/>] Grade C: A great deal of language polishing [<input type="radio"/>] Grade D: Rejection
Conclusion	[<input checked="" type="radio"/>] Accept (High priority) [<input type="radio"/>] Accept (General priority) [<input type="radio"/>] Minor revision [<input type="radio"/>] Major revision [<input type="radio"/>] Rejection
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

I have no concern to publish this paper in WJCO.