

## PEER-REVIEW REPORT

**Name of journal:** World Journal of Gastroenterology

**Manuscript NO:** 42512

**Title:** Checkpoint inhibitors: What Gastroenterologists need to know

**Reviewer's code:** 03551817

**Reviewer's country:** China

**Science editor:** Xue-Jiao Wang

**Date sent for review:** 2018-10-12

**Date reviewed:** 2018-10-12

**Review time:** 7 Hours

SCIENTIFIC QUALITY	LANGUAGE QUALITY	CONCLUSION	PEER-REVIEWER STATEMENTS
<input type="checkbox"/> Grade A: Excellent	<input checked="" type="checkbox"/> Grade A: Priority publishing	<input type="checkbox"/> Accept	Peer-Review:
<input checked="" type="checkbox"/> Grade B: Very good	<input type="checkbox"/> Grade B: Minor language	(High priority)	<input checked="" type="checkbox"/> Anonymous
<input type="checkbox"/> Grade C: Good	polishing	<input type="checkbox"/> Accept	<input type="checkbox"/> Onymous
<input type="checkbox"/> Grade D: Fair	<input type="checkbox"/> Grade C: A great deal of	(General priority)	Peer-reviewer's expertise on the
<input type="checkbox"/> Grade E: Do not	language polishing	<input checked="" type="checkbox"/> Minor revision	topic of the manuscript:
publish	<input type="checkbox"/> Grade D: Rejection	<input type="checkbox"/> Major revision	<input checked="" type="checkbox"/> Advanced
		<input type="checkbox"/> Rejection	<input type="checkbox"/> General
			<input type="checkbox"/> No expertise
			Conflicts-of-Interest:
			<input type="checkbox"/> Yes
			<input checked="" type="checkbox"/> No

### SPECIFIC COMMENTS TO AUTHORS

This paper mainly intended to discuss the mechanism and indications of different checkpoint inhibitors currently (PD-1, PD-L1 or CTLA-4) as well as the evaluation and management of gastrointestinal, hepatic and pancreatic side effects. However, there are several suggestions or questions as following: 1. There are a lot of different kinds of



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immune checkpoints, such as TIM3, LAG3, TIGIT, BTLA, why choose PD-1, PD-L1 or CTLA-4. Actually, PD-1 and PD-L1 are the same kind of sort. 2. The mechanism of action of checkpoint inhibitors has not been comprehensively explored in this paper. 3. This paper was talking about the use of checkpoint inhibitors alone, but what if using those inhibitors in combination?

#### **INITIAL REVIEW OF THE MANUSCRIPT**

##### ***Google Search:***

- ☐ The same title
- ☐ Duplicate publication
- ☐ Plagiarism
- ☐ No

##### ***BPG Search:***

- ☐ The same title
- ☐ Duplicate publication
- ☐ Plagiarism
- ☐ No

## PEER-REVIEW REPORT

**Name of journal:** World Journal of Gastroenterology

**Manuscript NO:** 42512

**Title:** Checkpoint inhibitors: What Gastroenterologists need to know

**Reviewer's code:** 00504187

**Reviewer's country:** Italy

**Science editor:** Xue-Jiao Wang

**Date sent for review:** 2018-10-12

**Date reviewed:** 2018-10-13

**Review time:** 1 Day

SCIENTIFIC QUALITY	LANGUAGE QUALITY	CONCLUSION	PEER-REVIEWER STATEMENTS
<input type="checkbox"/> Grade A: Excellent	<input type="checkbox"/> Grade A: Priority publishing	<input type="checkbox"/> Accept	Peer-Review:
<input type="checkbox"/> Grade B: Very good	<input type="checkbox"/> Grade B: Minor language	(High priority)	<input type="checkbox"/> Anonymous
<input type="checkbox"/> Grade C: Good	polishing	<input type="checkbox"/> Accept	<input type="checkbox"/> Onymous
<input type="checkbox"/> Grade D: Fair	<input type="checkbox"/> Grade C: A great deal of	(General priority)	Peer-reviewer's expertise on the
<input type="checkbox"/> Grade E: Do not	language polishing	<input type="checkbox"/> Minor revision	topic of the manuscript:
publish	<input type="checkbox"/> Grade D: Rejection	<input type="checkbox"/> Major revision	<input type="checkbox"/> Advanced
		<input type="checkbox"/> Rejection	<input type="checkbox"/> General
			<input type="checkbox"/> No expertise
			Conflicts-of-Interest:
			<input type="checkbox"/> Yes
			<input type="checkbox"/> No

### SPECIFIC COMMENTS TO AUTHORS

This minireview, aimed to focalize the side effects of Checkpoint inhibitors, is likely addressed to gastroenterologists, who rarely would perform this treatment. The review is useful, but, being addressed to other specialists than oncologists, is probably too long and the paragraphs dedicated to the differential diagnosis of side effects and to the



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different degrees of severity of diarrhea could be shortened. English language and construction need to be strongly improved and the description of the mechanism of these new drugs could be simpler explained for not oncologists, while references are updated and appropriate.

#### **INITIAL REVIEW OF THE MANUSCRIPT**

##### ***Google Search:***

- ☐ The same title
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- ☐ Plagiarism
- ☐ No

##### ***BPG Search:***

- ☐ The same title
- ☐ Duplicate publication
- ☐ Plagiarism
- ☐ No

## PEER-REVIEW REPORT

**Name of journal:** World Journal of Gastroenterology

**Manuscript NO:** 42512

**Title:** Checkpoint inhibitors: What Gastroenterologists need to know

**Reviewer's code:** 01851506

**Reviewer's country:** Japan

**Science editor:** Xue-Jiao Wang

**Date sent for review:** 2018-10-12

**Date reviewed:** 2018-10-16

**Review time:** 4 Days

SCIENTIFIC QUALITY	LANGUAGE QUALITY	CONCLUSION	PEER-REVIEWER STATEMENTS
<input type="checkbox"/> Grade A: Excellent	<input type="checkbox"/> Grade A: Priority publishing	<input type="checkbox"/> Accept	Peer-Review:
<input type="checkbox"/> Grade B: Very good	<input type="checkbox"/> Grade B: Minor language	(High priority)	<input type="checkbox"/> Anonymous
<input type="checkbox"/> Grade C: Good	polishing	<input type="checkbox"/> Accept	<input type="checkbox"/> Onymous
<input type="checkbox"/> Grade D: Fair	<input type="checkbox"/> Grade C: A great deal of	(General priority)	Peer-reviewer's expertise on the
<input type="checkbox"/> Grade E: Do not	language polishing	<input type="checkbox"/> Minor revision	topic of the manuscript:
publish	<input type="checkbox"/> Grade D: Rejection	<input type="checkbox"/> Major revision	<input type="checkbox"/> Advanced
		<input type="checkbox"/> Rejection	<input type="checkbox"/> General
			<input type="checkbox"/> No expertise
			Conflicts-of-Interest:
			<input type="checkbox"/> Yes
			<input type="checkbox"/> No

## SPECIFIC COMMENTS TO AUTHORS

In this review, the author has summarized the status quo of the immune check inhibitors and the relevant side effects with possible remedy. The text is interesting for clinicians, however, difficult for those who are not. This is largely due to the usage of jargons such as "lab", "Rx" and "IV". When abbreviation is used, show the list of abbreviation with full



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text. While the author declares that he/she is good in English writing, there is a doubt, as there are grammatical and typographical errors in the text.

#### **INITIAL REVIEW OF THE MANUSCRIPT**

##### ***Google Search:***

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- ☐ No

##### ***BPG Search:***

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- ☐ Duplicate publication
- ☐ Plagiarism
- ☐ No

## PEER-REVIEW REPORT

**Name of journal:** World Journal of Gastroenterology

**Manuscript NO:** 42512

**Title:** Checkpoint inhibitors: What Gastroenterologists need to know

**Reviewer's code:** 03004570

**Reviewer's country:** Turkey

**Science editor:** Xue-Jiao Wang

**Date sent for review:** 2018-10-12

**Date reviewed:** 2018-10-17

**Review time:** 5 Days

SCIENTIFIC QUALITY	LANGUAGE QUALITY	CONCLUSION	PEER-REVIEWER STATEMENTS
<input type="checkbox"/> Grade A: Excellent	<input type="checkbox"/> Grade A: Priority publishing	<input type="checkbox"/> Accept	Peer-Review:
<input type="checkbox"/> Grade B: Very good	<input checked="" type="checkbox"/> Grade B: Minor language	(High priority)	<input checked="" type="checkbox"/> Anonymous
<input checked="" type="checkbox"/> Grade C: Good	polishing	<input type="checkbox"/> Accept	<input type="checkbox"/> Onymous
<input type="checkbox"/> Grade D: Fair	<input type="checkbox"/> Grade C: A great deal of	(General priority)	Peer-reviewer's expertise on the
<input type="checkbox"/> Grade E: Do not	language polishing	<input checked="" type="checkbox"/> Minor revision	topic of the manuscript:
publish	<input type="checkbox"/> Grade D: Rejection	<input type="checkbox"/> Major revision	<input checked="" type="checkbox"/> Advanced
		<input type="checkbox"/> Rejection	<input type="checkbox"/> General
			<input type="checkbox"/> No expertise
			Conflicts-of-Interest:
			<input type="checkbox"/> Yes
			<input checked="" type="checkbox"/> No

### SPECIFIC COMMENTS TO AUTHORS

This mini-review is about one of the hot topics in oncology. Checkpoint inhibitors are increasingly used for treatment of solid tumors and their adverse effects have special importance. Author summarizes gastrointestinal side effects of these drugs. Article contains 31 references. In general, this mini-review worth publishing, but it needs some

revisions; The indications of current checkpoint inhibitors should be revised. Ipilimumab and nivolumab are indicated for the treatment of patients with melanoma with lymph node involvement, in the adjuvant setting, besides metastatic disease. Nivolumab is indicated also in the treatment of patients with microsatellite instability-high (MSI-H) or mismatch repair deficient (dMMR) metastatic colorectal cancer. Similarly, pembrolizumab is also indicated for the treatment of metastatic, MSI-H or dMMR solid tumors. Indications need current references. Author should refer to the FDA and EMA guidelines. The author mentions that “CTLA-4 down regulates immune system by primarily limiting T-cell activation without linking with a specific protein”; the last part of the sentence must be corrected, because CTLA-4 binds to B7 ligands (B7.1/B7.2) on APCs. By the way, Figure 1 looks pale and is missing some information; I recommend refreshing or redrawing. The interaction between APC and T-cell must be shown. After these minor but important revisions, this manuscript can be published.

## INITIAL REVIEW OF THE MANUSCRIPT

### *Google Search:*

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## PEER-REVIEW REPORT

**Name of journal:** World Journal of Gastroenterology

**Manuscript NO:** 42512

**Title:** Checkpoint inhibitors: What Gastroenterologists need to know

**Reviewer's code:** 00058401

**Reviewer's country:** Brazil

**Science editor:** Xue-Jiao Wang

**Date sent for review:** 2018-10-12

**Date reviewed:** 2018-10-17

**Review time:** 5 Days

SCIENTIFIC QUALITY	LANGUAGE QUALITY	CONCLUSION	PEER-REVIEWER STATEMENTS
<input type="checkbox"/> Grade A: Excellent	<input type="checkbox"/> Grade A: Priority publishing	<input checked="" type="checkbox"/> Accept	Peer-Review:
<input type="checkbox"/> Grade B: Very good	<input checked="" type="checkbox"/> Grade B: Minor language	(High priority)	<input checked="" type="checkbox"/> Anonymous
<input checked="" type="checkbox"/> Grade C: Good	polishing	<input type="checkbox"/> Accept	<input type="checkbox"/> Onymous
<input type="checkbox"/> Grade D: Fair	<input type="checkbox"/> Grade C: A great deal of	(General priority)	Peer-reviewer's expertise on the
<input type="checkbox"/> Grade E: Do not	language polishing	<input type="checkbox"/> Minor revision	topic of the manuscript:
publish	<input type="checkbox"/> Grade D: Rejection	<input type="checkbox"/> Major revision	<input type="checkbox"/> Advanced
		<input type="checkbox"/> Rejection	<input checked="" type="checkbox"/> General
			<input type="checkbox"/> No expertise
			Conflicts-of-Interest:
			<input type="checkbox"/> Yes
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### SPECIFIC COMMENTS TO AUTHORS

Congratulations

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## PEER-REVIEW REPORT

**Name of journal:** World Journal of Gastroenterology

**Manuscript NO:** 42512

**Title:** Checkpoint inhibitors: What Gastroenterologists need to know

**Reviewer's code:** 00070916

**Reviewer's country:** Germany

**Science editor:** Xue-Jiao Wang

**Date sent for review:** 2018-10-12

**Date reviewed:** 2018-10-19

**Review time:** 7 Days

SCIENTIFIC QUALITY	LANGUAGE QUALITY	CONCLUSION	PEER-REVIEWER STATEMENTS
<input type="checkbox"/> Grade A: Excellent	<input type="checkbox"/> Grade A: Priority publishing	<input type="checkbox"/> Accept	Peer-Review:
<input type="checkbox"/> Grade B: Very good	<input type="checkbox"/> Grade B: Minor language	(High priority)	<input type="checkbox"/> Anonymous
<input checked="" type="checkbox"/> Grade C: Good	polishing	<input type="checkbox"/> Accept	<input checked="" type="checkbox"/> Onymous
<input type="checkbox"/> Grade D: Fair	<input checked="" type="checkbox"/> Grade C: A great deal of	(General priority)	Peer-reviewer's expertise on the
<input type="checkbox"/> Grade E: Do not	language polishing	<input checked="" type="checkbox"/> Minor revision	topic of the manuscript:
publish	<input type="checkbox"/> Grade D: Rejection	<input type="checkbox"/> Major revision	<input type="checkbox"/> Advanced
		<input type="checkbox"/> Rejection	<input checked="" type="checkbox"/> General
			<input type="checkbox"/> No expertise
			Conflicts-of-Interest:
			<input type="checkbox"/> Yes
			<input checked="" type="checkbox"/> No

### SPECIFIC COMMENTS TO AUTHORS

In the minireview "Checkpoint Inhibitors: What Gastroenterologists need to know", the author describes first shortly the mode of action of this novel class of therapeutics before he focuses on their side effects and especially their clinical management. The topic is very timely and well selected. However, since I am not a clinician, I recommend having



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at least one reviewer check the manuscript with a clinical background. Still, a few points fall into my area of expertise and I would like to suggest the following to substantially improve this manuscript before it is suited for publication: 1. Overall, the quality of the English language has to be improved! 2. The description of the mechanisms of action of the checkpoint inhibitors is partly wrong and partly very vague. For example: “When the PD-1 receptors ... and attacks are not initiated” is not the mechanism of action. T cells are “pacified” and send into anergy – but some tumor cells are killed by pre-activated T cells when they enter the tumor bed; specificity for tumor cells is of course a prerequisite. Another example is the subsequent sentence “... by primarily limiting T-cell activation without linking with a specific protein” – what should this mean? Consequently, this first part of the manuscript must be substantially improved! 3. A review of this topic aiming at gastroenterologists must also mention and discuss the great success for hypermutated colorectal cancers! 4. The conclusion is again at least partly too vague – the manuscript would benefit from a make-over. 5. Finally, it would make sense to Adept the title to the main Focus - the clinical Management of the side effects.

## **INITIAL REVIEW OF THE MANUSCRIPT**

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## PEER-REVIEW REPORT

**Name of journal:** World Journal of Gastroenterology

**Manuscript NO:** 42512

**Title:** Checkpoint inhibitors: What Gastroenterologists need to know

**Reviewer's code:** 02460781

**Reviewer's country:** China

**Science editor:** Xue-Jiao Wang

**Date sent for review:** 2018-10-12

**Date reviewed:** 2018-10-20

**Review time:** 8 Days

SCIENTIFIC QUALITY	LANGUAGE QUALITY	CONCLUSION	PEER-REVIEWER STATEMENTS
<input type="checkbox"/> Grade A: Excellent	<input type="checkbox"/> Grade A: Priority publishing	<input type="checkbox"/> Accept	Peer-Review:
<input type="checkbox"/> Grade B: Very good	<input checked="" type="checkbox"/> Grade B: Minor language	(High priority)	<input checked="" type="checkbox"/> Anonymous
<input type="checkbox"/> Grade C: Good	polishing	<input type="checkbox"/> Accept	<input type="checkbox"/> Onymous
<input checked="" type="checkbox"/> Grade D: Fair	<input type="checkbox"/> Grade C: A great deal of	(General priority)	Peer-reviewer's expertise on the
<input type="checkbox"/> Grade E: Do not	language polishing	<input type="checkbox"/> Minor revision	topic of the manuscript:
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		<input checked="" type="checkbox"/> Rejection	<input checked="" type="checkbox"/> General
			<input type="checkbox"/> No expertise
			Conflicts-of-Interest:
			<input type="checkbox"/> Yes
			<input checked="" type="checkbox"/> No

### SPECIFIC COMMENTS TO AUTHORS

Many articles summarized managements and side effects of Checkpoint inhibitors. The article has no more new contents.

### INITIAL REVIEW OF THE MANUSCRIPT



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