



**PEER-REVIEW REPORT**

**Name of journal:** World Journal of Meta-Analysis

**Manuscript NO:** 49567

**Title:** Tofacitinib for the treatment of ulcerative colitis: A review of the literature

**Reviewer's code:** 03645427

**Reviewer's country:** South Korea

**Science editor:** Ying Dou

**Reviewer accepted review:** 2019-06-21 13:17

**Reviewer performed review:** 2019-06-22 06:26

**Review time:** 17 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 checked="" 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 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 article is very timely and pertinent. Although you did not suggested the data analyses or aauthor's opinion concerning efficacy and safety of tofacitinib in comparison with other existing biologic agents, I think this reviewing is informative and summarized well.



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#### INITIAL REVIEW OF THE MANUSCRIPT

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**PEER-REVIEW REPORT**

**Name of journal:** World Journal of Meta-Analysis

**Manuscript NO:** 49567

**Title:** Tofacitinib for the treatment of ulcerative colitis: A review of the literature

**Reviewer’s code:** 02446483

**Reviewer’s country:** Canada

**Science editor:** Ying Dou

**Reviewer accepted review:** 2019-06-23 14:18

**Reviewer performed review:** 2019-06-23 14:30

**Review time:** 1 Hour

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**

It remains challenging the management of patients with ulcerative colitis who are dependent on corticosteroid for control of symptoms, or refractory to corticosteroids or standard immunosuppressive therapy. The development of newer medical therapies has increased the options for managing patients with ulcerative colitis in this situation.



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Access and funding may remain limited for some countries and the potential access for children is not clear. The editorial is well written. I would add and emphasize the potentiality and causalities for failure using Tofacitinib and when a pediatric access may be considered.

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**PEER-REVIEW REPORT**

**Name of journal:** World Journal of Meta-Analysis

**Manuscript NO:** 49567

**Title:** Tofacitinib for the treatment of ulcerative colitis: A review of the literature

**Reviewer's code:** 04091933

**Reviewer's country:** Russia

**Science editor:** Ying Dou

**Reviewer accepted review:** 2019-06-21 10:35

**Reviewer performed review:** 2019-06-25 10:20

**Review time:** 3 Days and 23 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**

The review is of undoubted interest, since such phenomena as steroid dependence, steroid resistance and lack of response to biological preparations are widespread. Small molecules like tofacitinib are a real therapeutic alternative for patients with IBD. The review is well written (with the latest literary references) and can be published, however



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a minor revision is required. 1. The authors made the right safety emphasis on HZ infection and probable thromboembolic events. However, given the lack of safety information, it is desirable to describe the main infectious (not only HZ, but *C. difficile* colitis, abscesses, etc.), oncological (NMSCs) and other side effects (gastrointestinal perforations, MACE, etc.) of tofacitinib. 2. Since the review reflects the real experience, it is desirable to give an example of a successful combining a biologic with tofacitinib as rescue therapy [Griller & Cohen, 2019]. 3. It may be worth mentioning the potential efficacy of tofacitinib in pyoderma gangrenosum that affects IBD patients (CD cases on tofacitinib for severe inflammatory arthritis have been described to date [Kochar et al., 2019]). 4. It is advisable to discuss the cost of treatment with tofacitinib, since it is likely that tofacitinib could also be economically viable in comparison with other biologics due to its lower production cost [Milev et al., 2019]. 5. Another brand name for tofacitinib (Jaquinus) is also worth mentioning.

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**PEER-REVIEW REPORT**

**Name of journal:** World Journal of Meta-Analysis

**Manuscript NO:** 49567

**Title:** Tofacitinib for the treatment of ulcerative colitis: A review of the literature

**Reviewer's code:** 00036517

**Reviewer's country:** Japan

**Science editor:** Ying Dou

**Reviewer accepted review:** 2019-06-24 07:35

**Reviewer performed review:** 2019-07-01 06:50

**Review time:** 6 Days and 23 Hours

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 polishing	(High priority)	<input checked="" type="checkbox"/> Anonymous
<input type="checkbox"/> Grade C: Good		<input type="checkbox"/> Accept	<input type="checkbox"/> Onymous
<input checked="" type="checkbox"/> Grade D: Fair	<input type="checkbox"/> Grade C: A great deal of language polishing	(General priority)	Peer-reviewer's expertise on the topic of the manuscript:
<input type="checkbox"/> Grade E: Do not publish	<input type="checkbox"/> Grade D: Rejection	<input type="checkbox"/> Minor revision	<input type="checkbox"/> Advanced
		<input checked="" type="checkbox"/> Major revision	<input type="checkbox"/> General
		<input type="checkbox"/> Rejection	<input checked="" type="checkbox"/> No expertise
			Conflicts-of-Interest:
			<input type="checkbox"/> Yes
			<input checked="" type="checkbox"/> No

**SPECIFIC COMMENTS TO AUTHORS**

I think authors need to compare the efficacy of tofacitinib for UC patients clearly, and also the difference of efficacy of tofacitinib than TNF alpha antibodies. In discussion, there are many data from papers of references, but I suggest that suthors need to add their speculations for use tofacitinib to UC patients.



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**PEER-REVIEW REPORT**

**Name of journal:** World Journal of Meta-Analysis

**Manuscript NO:** 49567

**Title:** Tofacitinib for the treatment of ulcerative colitis: A review of the literature

**Reviewer's code:** 03442128

**Reviewer's country:** United States

**Science editor:** Ying Dou

**Reviewer accepted review:** 2019-06-21 11:17

**Reviewer performed review:** 2019-07-04 15:26

**Review time:** 13 Days and 4 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 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 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:
publish	<input type="checkbox"/> Grade D: Rejection	<input checked="" 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**

The authors present a timely and concise overview of the newest therapy for Ulcerative Colitis, the JAK inhibitor tofacitinib. The authors do a good job of summarizing the limited available data, but a number of structural elements the manuscript need to be addressed, along with some additions to content. Suggested revisions: Title: Would



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remove the reference to “Real-World Experience” from the manuscript title. In fact, very few of the studies reviewed in the manuscript reflect real-world experience. Abstract: The abstract is too generalized, and needs to more specifically touch on the major points/subjects to be discussed in the manuscript that follows. E.g. review of efficacy, safety, Minor point: Would also avoid use of superlatives such as “incredible” and “exciting”. This should also be the case in the manuscript itself. Core tip: Again, would not address “real world efficacy”. The vast majority of the review reflects clinical trial experience. Manuscript: Introduction: Minor point: use the trademark symbol following us of the word Xeljanz, ® Paragraph 2: Would place the discussion of long term safety AFTER review of shorter term efficacy Major point: WOULD NOT discuss the authors own center’s experience until it is either published in a peer review journal or presented at GI conference. Review of the Literature: Would start with a review of the Octave clinical trial results before addressing the real world literature When discussing the Berinstein JA paper about rescue tofacitinib, should address that these were INPATIENTS and prior biologic failures: this is what makes the paper’s results important Minor: overall a good discussion of varicella issues. Would just address the packaging recommendation regarding live vaccinations in those on tofacitinib, and the differences between the older and newer type of VZV vaccines and. Pregnancy is addressed, but would include what (if anything) the prescribing information for tofacitinib has to say about pregnancy. Would add a line or two about lactation issues, recommendations as well. Would add a brief paragraph regarding malignancy risk, if any. While little to no data available for UC, may find some more information/reporting in the RA literature Perspective: Would again downplay the “Real world post marketing data...” given the limited real world data presented

**INITIAL REVIEW OF THE MANUSCRIPT**



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