



PEER-REVIEW REPORT

Name of journal: World Journal of Gastroenterology

Manuscript NO: 42571

Title: The role of cenicriviroc in the management of nonalcoholic fatty liver disease

Reviewer's code: 03647461

Reviewer's country: United States

Science editor: Xue-Jiao Wang

Date sent for review: 2018-09-28

Date reviewed: 2018-09-29

Review time: 1 Day

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

The emphasis of this short communication seems to be on the anti-fibrotic effect of cenicriviroc (CVC) in curtailing the progression of NAFLD to cirrhosis. It was also related in this manuscript that CVC, an oral CCR2/CCR5 antagonist, averts macrophage trafficking and hepatic infiltration by CCR2+ MoMFs, thus blocking the fibrotic process



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enhanced by CCR2 and CCR5 activation. The increase in CCL-2 and -4 in CVC - treated patients is also another testament to its effect. However, it is not evident that CVC can reverse cirrhosis, which is an advanced stage of fibrosis (stage 4). This in contrast to the statement made in the manuscript, which states that “Preclinical studies and a phase 2b study in humans suggest that this agent might hold promise in the management of NAFLD, particularly in patients with advanced fibrosis.” Some of the studies conducted in human patients do not have statistically significant results. Although the manuscript details NAFLD treatment regimen with CVC, in large part, the impact on NASH could also be important according to the CENTAUR study. Therefore, the efficacy of CVC is high as this is also a multinational study. However, it remains that patients in the initial stages of fibrosis can still reverse it without the need for CVC with lifestyle changes in diet and exercise. Nevertheless, this report adds value to pharmacotherapeutic options such as CVC suggested by ongoing clinical phase studies. This is especially significant if taking 150 mg once daily does not interfere with the safety and tolerability of CVC as reported by Friedman S. [Placebo-Controlled Trial of Cenicrivitoc for Treatment of Nonalcoholic Steatohepatitis With Fibrosis. *Hepatology* 2018; 67: 1754-1767]. The authors do acknowledge, however, that larger studies are required to accurately determine the safety and efficacy of the drug.

INITIAL REVIEW OF THE MANUSCRIPT

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PEER-REVIEW REPORT

Name of journal: World Journal of Gastroenterology

Manuscript NO: 42571

Title: The role of cenicriviroc in the management of nonalcoholic fatty liver disease

Reviewer's code: 00034151

Reviewer's country: South Korea

Science editor: Xue-Jiao Wang

Date sent for review: 2018-09-28

Date reviewed: 2018-10-10

Review time: 12 Days

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 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

The manuscript entitled "The role of cenicriviroc in the management of nonalcoholic fatty liver disease" was an informative review regarding cenicriviroc and its phase 2b study in patients with NAFLD. However, the scope of the manuscript was somewhat narrow as a review. The manuscript was an optimal one as an editorial.



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PEER-REVIEW REPORT

Name of journal: World Journal of Gastroenterology

Manuscript NO: 42571

Title: The role of cenicriviroc in the management of nonalcoholic fatty liver disease

Reviewer's code: 03388095

Reviewer's country: United States

Science editor: Xue-Jiao Wang

Date sent for review: 2018-09-28

Date reviewed: 2018-10-14

Review time: 15 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 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 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

This is a well-written, quite focused review on the role of Cenicriviroc in fatty liver disease, particularly in patients with advanced fibrosis. The review detailed the molecular pathway, animal studies, and on-going clinical trials. It will be nice if the authors can provide some diagram to illustrate the molecular pathway so readers can



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better understand it.

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