

PEER-REVIEW REPORT

Name of journal: World Journal of Cardiology

Manuscript NO: 33910

Title: Is Entresto Good for the Brain?

Reviewer's code: 01955969

Reviewer's country: United States

Science editor: Xiu-Xia Song

Date sent for review: 2017-03-14

Date reviewed: 2017-03-25

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"/> 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 type="checkbox"/> Plagiarism	<input type="checkbox"/> Minor revision
<input type="checkbox"/> Grade E: Poor		<input checked="" type="checkbox"/> No	<input type="checkbox"/> Major revision
		BPG Search:	
		<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, submitted by Nirav Patel et al., discusses safety paradigms associated with chronic use of the heart drug, valsartan/sacubitril (formerly known as LCZ696 and currently marketed by Novartis as Entresto) in patients at risk of Alzheimer's disease (AD). Valsartan/sacubitril has been approved by the US Food and Drug Administration for the treatment of heart failure, and functions by inhibiting an enzyme known as neprilysin. Neprilysin plays a critical role in breaking down various peptides in cells, including natriuretic peptides (NPs), vasoactive peptides (e.g. endothelin-1, bradykinins), neuropeptides (e.g. substance P, enkephalins), and the beta-amyloid (A β) peptide. Although some cardiovascular benefits are achieved using a neprilysin inhibitor (NPi), recent laboratory studies involving the central nervous system implicate NPi in the development of AD in animal models. Therefore, a prudent approach involves following high-risk patients closely with cognitive assessments. Tests for detecting cerebrospinal fluid (CSF) β A peptide levels and amyloid plaques in clinical trials are also necessary. Comments: 1) It should be noted that patients with heart failure AND preserved ejection

fraction (HFpEF) currently represent almost half of all HF cases, and is projected to become the predominant form of HF in the future. The authors should summarize the most recent and ongoing HFpEF clinical trials in this manuscript. 2) The mechanism proposed for underlying neprilysin inhibitor in the metabolism of cardiovascular peptides and the A β peptide is not well elucidated. A schematic description is necessary. 3) The authors split the review paper into different sections with subtitles. However, some sections are overlapping. 4) Some of the most recent publications related to this topic are not included, such as Feldman AM et al JAMA 2016 and Hubers SA et al circulation 2016. 5) Occasional grammatical and spelling errors are found throughout the manuscript.

PEER-REVIEW REPORT

Name of journal: World Journal of Cardiology

Manuscript NO: 33910

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Date sent for review: 2017-03-14

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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 type="checkbox"/> High priority for publication
<input 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
<input type="checkbox"/> Grade E: Poor		<input checked="" type="checkbox"/> No	<input checked="" type="checkbox"/> Minor revision
	<input type="checkbox"/> Grade D: Rejected	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 is a nice review of the novel agent Entresto with some focus on potential neurological side effects. Overall the article is well written, please correct some grammatical and typo issues In the first para of "Goals of Therapy" section please add Sympathetic nervous system to RAAS since beta blockers are also listed Please use Entresto consistently since LCZ696 is no mor applicable as a name Please also mention ongoing cognitive function studies with Entresto