

ESPS PEER-REVIEW REPORT

Name of journal: World Journal of Cardiology

ESPS manuscript NO: 29448

Title: PCSK9 inhibitors: A new era of lipid lowering therapy

Reviewer's code: 00227622

Reviewer's country: United States

Science editor: Fang-Fang Ji

Date sent for review: 2016-08-16 08:54

Date reviewed: 2016-08-16 21:25

CLASSIFICATION	LANGUAGE EVALUATION	SCIENTIFIC MISCONDUCT	CONCLUSION
<input type="checkbox"/> Grade A: Excellent	<input checked="" type="checkbox"/> Grade A: Priority publishing	Google Search:	<input checked="" type="checkbox"/> Accept
<input checked="" type="checkbox"/> Grade B: Very good	<input 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"/> 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 checked="" type="checkbox"/> Plagiarism	<input type="checkbox"/> Minor revision
<input type="checkbox"/> Grade E: Poor		[Y] No	<input type="checkbox"/> Major revision
		BPG Search:	
		<input type="checkbox"/> The same title	
		<input type="checkbox"/> Duplicate publication	
		<input type="checkbox"/> Plagiarism	
		[Y] No	

COMMENTS TO AUTHORS

This is a satisfactory review of the topic.

ESPS PEER-REVIEW REPORT

Name of journal: World Journal of Cardiology

ESPS manuscript NO: 29448

Title: PCSK9 inhibitors: A new era of lipid lowering therapy

Reviewer's code: 01206034

Reviewer's country: Japan

Science editor: Fang-Fang Ji

Date sent for review: 2016-08-16 08:54

Date reviewed: 2016-08-22 17:23

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

Chaudhary et al described a review article about PCSK9 inhibitors. Basically, the article was well written in terms of extensive search for PCSK9 inhibitors-related articles. This topic is of great interests, however there are a few issues to be concerned as described below. 1. First of all, this work is based on extensive literature search for PCSK9 inhibitors. Prior studies have reported that lipid-lowering effects of statins were different between Caucasians and Asians. If data were available, authors should add a description regarding an effect of race and/or genetic factors on effectiveness and adverse effects of PCSK9 inhibitors. 2. Regarding an effect of PCSK9 inhibitors on reducing cardiovascular effects, several studies examining cardiovascular events have already been published although the outcome data were not the primary endpoints of the studies. Authors are encouraged to add the outcome data of ODYSSEY LONG TERM and OSLER trials. 3. In page 6, the paragraph describing PCSK9 and melanoma metastasis is quite vague. If the circulating cholesterol level per se is associated with metastasis as written, this paragraph could be deleted, because the relationship between PCSK9 and metastasis is not established. 4. There are several grammatical errors and misspelling so that proofreading should be done.

ESPS PEER-REVIEW REPORT

Name of journal: World Journal of Cardiology

ESPS manuscript NO: 29448

Title: PCSK9 inhibitors: A new era of lipid lowering therapy

Reviewer's code: 00504325

Reviewer's country: Austria

Science editor: Fang-Fang Ji

Date sent for review: 2016-08-16 08:54

Date reviewed: 2016-08-23 15:33

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 manuscript is well written, focused and straight forward. There are only minor comments for improvements: #1 Some dates need to be updated, wich may stem from delays in the submission process: p8.:April 2016, should be available?; p.17.: July 2016, results available? #2 p.10, last sentence, first paragraph: It is not possible to induce PCSK9 by statins in patients not taking statins. #3 In the last chapter (p20 ff.) some "left overs" are found and should be corrected. i) "goal" should be removed (line 5 from bottom). ii)The following sentence is hard to follow. iii) p21 top: PCSK9 inhibitors....This sentence does not make sense. #4 The costs for PCSK9 antibodies is estimated from NNT5 is 28. However, until now we have only surrogate parameters which are improved, but no hard end data like OS or CVE. Thus, a not should be added that costs may be reevaluated in the the near future, considering the new endpoints. #5 There is some concern that cognitive impairments may be induced by PCSK9 Inhibitors. A not on this aspect should be added.

ESPS PEER-REVIEW REPORT

Name of journal: World Journal of Cardiology

ESPS manuscript NO: 29448

Title: PCSK9 inhibitors: A new era of lipid lowering therapy

Reviewer's code: 01567591

Reviewer's country: Canada

Science editor: Fang-Fang Ji

Date sent for review: 2016-08-16 08:54

Date reviewed: 2016-08-19 01:44

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 checked="" type="checkbox"/> Plagiarism	<input checked="" type="checkbox"/> Minor revision
<input type="checkbox"/> Grade E: Poor		[Y] No	<input type="checkbox"/> Major revision
		BPG Search:	
		<input type="checkbox"/> The same title	
		<input type="checkbox"/> Duplicate publication	
		<input type="checkbox"/> Plagiarism	
		[Y] No	

COMMENTS TO AUTHORS

This manuscript described the development status of PCSK9 inhibitors. The authors are mainly focusing on the anti-PCSK9 antibodies that are approved or in development. They shed a positive light on the FDA approved antibodies and made a pretty good review of the data available from clinical trials. Although there are several typo errors throughout the manuscript, the overall manuscript worth publication in WJG. Before publishing, if possible, the authors should update their data from clinical trials such as (NCT01968980, NCT01813422 etc..).

ESPS PEER-REVIEW REPORT

Name of journal: World Journal of Cardiology

ESPS manuscript NO: 29448

Title: PCSK9 inhibitors: A new era of lipid lowering therapy

Reviewer's code: 00591996

Reviewer's country: Taiwan

Science editor: Fang-Fang Ji

Date sent for review: 2016-08-16 08:54

Date reviewed: 2016-09-03 02:14

CLASSIFICATION	LANGUAGE EVALUATION	SCIENTIFIC MISCONDUCT	CONCLUSION
<input type="checkbox"/> Grade A: Excellent	<input type="checkbox"/> Grade A: Priority publishing	Google Search:	<input type="checkbox"/> [Y] Accept
<input type="checkbox"/> [Y] Grade B: Very good	<input type="checkbox"/> [Y] 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"/> [] 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"/> [Y] No	<input type="checkbox"/> [] Minor revision
<input type="checkbox"/> [] Grade E: Poor		BPG Search:	<input type="checkbox"/> [] Major revision
		<input type="checkbox"/> [] The same title	
		<input type="checkbox"/> [] Duplicate publication	
		<input type="checkbox"/> [] Plagiarism	
		<input type="checkbox"/> [Y] No	

COMMENTS TO AUTHORS

Reviewer Comments Title: PCSK9 INHIBITORS: A NEW ERA OF LIPID LOWERING THERAPY

Summary The manuscript focused on monoclonal antibodies and other inhibitors that inactivate proprotein convertase subtilisin-kexin type 9 (PCSK9) as a novel class of medications against hyperlipidemia. As a whole, the article is carefully written with the inclusion of sufficient details necessary for the readers' understanding of the topic. It is a good read for both basic medical researchers and clinicians. **Major Comments** The manuscript contains fairly detailed descriptions on LDL cholesterol metabolism and the background of targeting PCSK9 as a therapeutic strategy against hyperlipidemia as well as current concerns regarding the use of PCSK9 inhibitors. Besides, the current clinical status of related medications and descriptions on their uses were included. This reviewer has only the concern that certain information may need to be updated if available. For instance, the results of phase III trials for Bococizumab, the OLE trial, and those of other studies related to PCSK9 inhibition. **Minor Comments** 1. If possible, on describing the role of PCSK9 in lipid metabolism, it would be excellent if a schematic illustration is available to facilitate the understanding of the detailed and yet complicated process. 2. Typos and minor grammatical



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mistakes may be minimized by careful proof-reading.