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PEER-REVIEW REPORT

Name of journal: *World Journal of Clinical Cases*

Manuscript NO: 75684

Title: Proprotein convertase subtilisin/kexin type 9 inhibitor non responses in an adult with a history of coronary revascularization: A case report

Provenance and peer review: Unsolicited Manuscript; Externally peer reviewed

Peer-review model: Single blind

Reviewer's code: 05227810
Position: Editorial Board
Academic degree: FACC, FESC, MBBS, MD
Professional title: Additional Professor
Reviewer's Country/Territory: India
Author's Country/Territory: China

Manuscript submission date: 2022-02-12

Reviewer chosen by: AI Technique

Reviewer accepted review: 2022-02-12 10:44

Reviewer performed review: 2022-02-23 16:41

Review time: 11 Days and 5 Hours

Scientific quality	[ ] Grade A: Excellent [ ] Grade B: Very good [ ] Grade C: Good [Y] Grade D: Fair [ ] Grade E: Do not publish
Language quality	[ ] Grade A: Priority publishing [Y] Grade B: Minor language polishing [ ] Grade C: A great deal of language polishing [ ] Grade D: Rejection
Conclusion	[ ] Accept (High priority) [ ] Accept (General priority) [ ] Minor revision [Y] Major revision [ ] Rejection
Re-review	[Y] Yes [ ] No

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Peer-reviewer statements	Peer-Review: [Y] Anonymous [ ] Onymous Conflicts-of-Interest: [ ] Yes [Y] No

SPECIFIC COMMENTS TO AUTHORS

The authors dwell upon an interesting case of PCSK-9 inhibitor non response in patient with FH with ASCVD - a Very High risk group (designated by ESC 2019) guideline & an Extreme risk group (designated by LAI 2020 lipid guidelines).The article is fairly well written and language quality is good. My comments - 1.The description of the case is inadequate with respect to clinical history, Investigation and therapy administered. Please see comments in the file attached. 2.Moreover, the attribution of genetic defects to drug resistance needs clarity. Please refer to - B.A. Warden, S. Fazio and M.D. Shapiro. Trends in Cardiovascular Medicine 30 (2020) 179–185 for further clarity. 3.Please discuss whether PCSK-9 levels were obtained on therapy or off therapy. 4.The LDL graph looks incomplete - please add drug doses below corresponding LDL levels. 5.The chronology of LDL lowering doesn't fit the picture described. -With simvastatin 20 mg,LDL moved from 402 to 141 (65% Reduction). This is unlikely as Simvastatin 20 mg is moderate dose statin which is expected to have 30%-50% LDL reduction.(ACC/AHA 2018 Cholesterol Guidelines- Grundy et.Circulation. 2018;DOI: 10.1161/CIR.0000000000000625) Do the authors suggest that the patient was a super-responder ? if yes, quote the literature. - The LDL then bounces back to 289-229-220. Was the patient off or on statin? Is it a case of statin tolerance too ? Please explain. - when was PCSK-9 inhibitor initiated - not clear form text or graph? - what was the criteria used to define hypo-responsiveness to drug- < 10% LDL decline or < 15% LDL decline or < 20% LDL decline ? 5. It would be more informative to have therapy and corresponding LDL levels side by side in text for better understanding of the case. 6.The figure 3 doesn't show angiographically severe stenosis. Please omit the

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figures or provide a better one. 7. It would be worthwhile to note the course of other patients with this mutation described in reference 16.

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Peer-review model: Single blind

Reviewer's code: 05430684
Position: Peer Reviewer
Academic degree: MD, MSc, PhD
Professional title: Chief Doctor
Reviewer's Country/Territory: Greece
Author's Country/Territory: China

Manuscript submission date: 2022-02-12

Reviewer chosen by: AI Technique

Reviewer accepted review: 2022-03-10 07:08

Reviewer performed review: 2022-03-10 19:15

Review time: 12 Hours

Scientific quality	[ ] Grade A: Excellent [ ] Grade B: Very good [Y] Grade C: Good [ ] Grade D: Fair [ ] Grade E: Do not publish
Language quality	[ ] Grade A: Priority publishing [ ] Grade B: Minor language polishing [Y] Grade C: A great deal of language polishing [ ] Grade D: Rejection
Conclusion	[ ] Accept (High priority) [ ] Accept (General priority) [ ] Minor revision [Y] Major revision [ ] Rejection
Re-review	[Y] Yes [ ] No

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Peer-reviewer statements	Peer-Review: [ ] Anonymous [Y] Onymous Conflicts-of-Interest: [ ] Yes [Y] No

SPECIFIC COMMENTS TO AUTHORS

I studied carefully the manuscript entitled "Proprotein convertase subtilisin/kexin type 9 (PCSK9) inhibitor nonresponses in an adult with a history of coronary revascularization: A case report" by Yang L et al. The authors report a case of familial hypoercholesterolemia (FH) characterized by moderate response to proprotein convertase subtilisin/kexin type 9 inhibitors (PCSK9i). The authors reported that they had detected a heterozugous mutation of the LDL receptor, namely the 1448G>A (W483X) mutation. Based on their findings, they have hypothesized that the seemingly ineffecticeness of the PCSK9i tretatment could have been attributed to that loss-of-function mutation. This is an interesting case report, which could be considered to be eligible for publication. However, there are some issues that might be discussed with the authors: Major issue: 1) Which APOB mutation was identified in the patient and his mother? Was that mutation crucial for the patient's phentoype? Please discuss. 2) Since an APOB mutation has also been detected, was the patient's case type I FH (OMIM: 143890) or type 2 FH (OMIM: 144010)? Minor issues 1) Please correct the phrase "Nonetheless, our patient refused this treatment. as it was too expensive for him." (page 7) 2) Please correct the phrase "The patient had received aspirin 100 mg QD, clopidogrel 75 mg QD (clopidogrel resistance have been excluded). and simvastatin 20mg QN. before the admission to our hospital." 3) Please amend the ohrase "(Guidelines for the treatment of coronary artery disease)." for a suitable reference.

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RE-REVIEW REPORT OF REVISED MANUSCRIPT

Name of journal: *World Journal of Clinical Cases*

Manuscript NO: 75684

Title: Proprotein convertase subtilisin/kexin type 9 inhibitor non responses in an adult with a history of coronary revascularization: A case report

Provenance and peer review: Unsolicited Manuscript; Externally peer reviewed

Peer-review model: Single blind

Reviewer's code: 05430684
Position: Peer Reviewer
Academic degree: MD, MSc, PhD
Professional title: Chief Doctor
Reviewer's Country/Territory: Greece
Author's Country/Territory: China

Manuscript submission date: 2022-02-12

Reviewer chosen by: Li-Li Wang

Reviewer accepted review: 2022-04-20 15:56

Reviewer performed review: 2022-04-20 16:56

Review time: 1 Hour

Scientific quality	[ ] Grade A: Excellent [ ] Grade B: Very good [ ] Grade C: Good [Y] Grade D: Fair [ ] Grade E: Do not publish
Language quality	[ ] Grade A: Priority publishing [Y] Grade B: Minor language polishing [ ] Grade C: A great deal of language polishing [ ] Grade D: Rejection
Conclusion	[ ] Accept (High priority) [ ] Accept (General priority) [ ] Minor revision [Y] Major revision [ ] Rejection
Peer-reviewer	Peer-Review: [ ] Anonymous [Y] Onymous

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statements	Conflicts-of-Interest: [ ] Yes [Y] No

SPECIFIC COMMENTS TO AUTHORS

I re-reviewed the manuscript entitled "Proprotein convertase subtilisin/kexin type 9 (PCSK9) inhibitor non responses in an adult with a history of coronary revascularization: A case report" by Liu Y. et al. The authors report that "We also note that one APOB mutation were identified in the patient and his mother. However, the LDL level in FH who caused by APOB gene mutations are significantly lower than the others. We think that mutation WAS NOT crucial for the patient's phenotype". Major points 1) The authors are requested to further consolidate their findings regarding the genotype-phenotype correlation (please see: i) Di Taranto MD et al. Genetic spectrum of familial hypercholesterolemia and correlations with clinical expression: Implications for diagnosis improvement. Clin Genet. 2021;100(5):529-541. doi: 10.1111/cge.14036 with special focus to Table 1 and Figure 2 which explicitly refers to the topic; ii) Reeskamp LF et al. Next-generation sequencing to confirm clinical familial hypercholesterolemia, European Journal of Preventive Cardiology, 2021;28(8):875–883, https://doi.org/10.1093/eurjpc/zwaa451. 2) Please add the genetic profile of the APOB mutation. Minor point Please amend capital letters ("WAS NOT") for small ones.