

PEER-REVIEW REPORT

Name of journal: World Journal of Gastrointestinal Oncology

Manuscript NO: 46481

Title: Evaluation of the Safety and Effectiveness of Direct Oral Anticoagulants and Low Molecular Weight Heparin in Gastrointestinal Cancer-Associated Venous Thromboembolism

Reviewer's code: 00504156

Reviewer's country: Greece

Science editor: Ying Dou

Reviewer accepted review: 2019-05-24 18:39

Reviewer performed review: 2019-05-29 13:43

Review time: 4 Days and 19 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 checked="" 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 type="checkbox"/> Advanced
		<input type="checkbox"/> Rejection	<input type="checkbox"/> General
			<input checked="" type="checkbox"/> No expertise
			Conflicts-of-Interest:
			<input type="checkbox"/> Yes
			<input checked="" type="checkbox"/> No

SPECIFIC COMMENTS TO AUTHORS

The literature needs to be updated



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INITIAL REVIEW OF THE MANUSCRIPT

Google Search:

- ☐ The same title
- ☐ Duplicate publication
- ☐ Plagiarism
- ☐ No

BPG Search:

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- ☐ No

Response: We thank the reviewer for helpful suggestion on a continuously changing evidence-based medicine topic. Authors searched the database and were able to update Reference 35 meta-analysis with PLoS One. 2019 Mar 21;14(3):e0213940 publication which reflects a more accurate assessment of our manuscript and additionally supports the risk of bleeding among high-risk CAVTE patients on DOACs. Additionally, an ASCO Clinical Practice Guideline Update 2019 was cited on the Discussion section and Limitations subsection by new reference #44, stating the preference of LMWH over DOACs on high-risk GI-CAVTE scenario. Furthermore, we have added commentary on Mcbane et al. 2018 American Society of Hematology preliminary data presentation with regards to oral apixaban therapy [ADAM-VTE trial pending publication]. Authors decided not to include 2019 CASSINI study (Khorana et al. N Engl J Med. 2019 Feb 21;380(8):720-728) because even though authors selected high-risk cancer patients

(Khorana score >2, >30% pancreatic cancer) for primary thromboprophylaxis without a thrombosis event, the clinical setting differs from our retrospective secondary anticoagulation after a cancer thrombosis event, and this may confuse your readers.

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Manuscript NO: 46481

Title: Evaluation of the Safety and Effectiveness of Direct Oral Anticoagulants and Low Molecular Weight Heparin in Gastrointestinal Cancer-Associated Venous Thromboembolism

Reviewer's code: 03270441

Reviewer's country: China

Science editor: Ying Dou

Reviewer accepted review: 2019-05-29 02:59

Reviewer performed review: 2019-05-29 14:36

Review time: 11 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	(High priority)	<input checked="" type="checkbox"/> Anonymous
<input checked="" 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 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

Good paper. It provided useful suggestions for clinical practice. However, due to the small sample size and very few endpoint events, the part of "Conclusion" by the authors



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was too definitive. If I were the author, I prefer to express “Conclusion” as a kind of possibility.

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BPG Search:

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- ☐ No

Response: We thank the reviewer for this important comment. We have added language to address this request. For example on the Discussion section, Limitations subsections, we stated “GI-CAVTE is a high-risk subpopulation deserves additional prospective clinical analysis of the efficacy and safety of DOACs”, “evaluation of clinical predictors that may influence the risk of VTE recurrence and major bleeding could include GICA as a high-risk group”, and furthermore we acknowledge a list of known study limitations.

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Name of journal: World Journal of Gastrointestinal Oncology

Manuscript NO: 46481

Title: Evaluation of the Safety and Effectiveness of Direct Oral Anticoagulants and Low Molecular Weight Heparin in Gastrointestinal Cancer-Associated Venous Thromboembolism

Reviewer's code: 03766000

Reviewer's country: China

Science editor: Ying Dou

Reviewer accepted review: 2019-05-28 06:56

Reviewer performed review: 2019-06-11 03:38

Review time: 13 Days and 20 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:
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			<input checked="" type="checkbox"/> No

SPECIFIC COMMENTS TO AUTHORS

Alejandro Recio-Boiles et al measured the safety and effectiveness of direct oral anticoagulants and low molecular weight heparin in gastrointestinal cancer-associated

venous thromboembolism, and found that Rivaroxaban compared to apixaban and enoxaparin had a significantly higher risk of major bleeding on GICA-VTE patients with equivocal efficacy. 1 Table 1 and 2 consist of data from papers by other researchers, and is described in the Introduction part. Therefore, it seemed to delete the two tables instead of describing these data with details. 2 In the manuscript, the experiment was performed during November 2013-February 2017 (The method part), and “Sixty-four percent of patients completed anticoagulation therapy (range 1 to 43 months).” appeared the second paragraph of the Results part. However, the experiment time including November 2013 and February 2017 was only 40 months (3 months missing???). Please carefully re-check the data. 3 The tables in the manuscript should be three-lined. 4 Patients seemed not to give informed consent to this study.

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Response: We thank the reviewer for the thoughtful recommendations.

1-After attentive consideration, authors believe Table 1 and 2 provides important historical background on the topic developed through the manuscript. On our case, both tables provide a succinct and organized summary of each one evidence-based landmark trial results, which would otherwise require an extensive and tiresome wording to describe. Therefore, we kindly request to keep Table 1 and 2, otherwise would significantly change the extension and content of the manuscript.

2-We acknowledge the time difference by a typographical and editing error, after reviewing the data, we agree with the reviewer that the evaluation only included 40 months. Please find on the Results section, second paragraph ““Sixty-four percent of patients completed anticoagulation therapy (range 1 to 40 months).” This change was also corrected on Table 3.

3-We have changed each tables on the manuscript to be three-lined.

4-We obtained prior to initiating research an Institutional Review Board approval Protocol Number: 1508054987 and further obtained a waiver of personal health information authorization (45 CFR 164.512(i)(2)(ii)): as the use or disclosure of protected health information involves no more than minimal risk to the individuals and the research could not practicably be conducted without the waiver. Prior mentioned statement has been added to the manuscript Material and Methods section, second paragraph.