Decision Letter (JCQ-2026-0023)

From: [redacted]
To:
CC:
BCC:

Subject: Journal of Clinical Question - Decision on Manuscript ID JCQ-2026-0023

Body: 25-Jul-2026

Dear Dr Melford:

Manuscript ID JCQ-2026-0023 entitled "Thrombopoietin Receptor Agonists for Chemotherapy-Induced Thrombocytopenia: A Systematic Review and Network Meta-analysis" which you submitted to the Journal of Clinical Question, has been reviewed. The comments of the reviewer(s) are included at the bottom of this letter.

The reviewer(s) have recommended publication, but also suggest some minor revisions to your manuscript. Therefore, I invite you to respond to the reviewer(s)' comments and revise your manuscript.

To submit your revised manuscript, follow the below steps.
1. Access to https://mc.manuscriptcentral.com/jcq and log into the site.
2. Click "Author" at the top left of the screen at "Home" page.
3. Click "Manuscripts with Decisions" on Author Dashboard page.
4. Click "create a revision" on the manuscript you are going to revise.
5. The system creates your revision manuscript form. Provide your comments about the revised points at the response field, fill in on each field step by step as same as you did for the original submission, and submit your revised manuscript.
IMPORTANT: Your original files are available to you when you upload your revised manuscript. Please delete any redundant files before completing the submission.
Your manuscript number has been appended to denote a revision.

You will be unable to make your revisions on the originally submitted version of the manuscript. Instead, revise your manuscript using a word processing program and save it on your computer. Please also highlight the changes to your manuscript within the document by using the track changes mode in MS Word or by using bold or colored text.

Once the revised manuscript is prepared, you can upload it and submit it through your Author Center.

When submitting your revised manuscript, you will be able to respond to the comments made by the reviewer(s) in the space provided. You can use this space to document any changes you make to the original manuscript. In order to expedite the processing of the revised manuscript, please be as specific as possible in your response to the reviewer(s).

IMPORTANT: Your original files are available to you when you upload your revised manuscript. Please delete any redundant files before completing the submission.

Because we are trying to facilitate timely publication of manuscripts submitted to the Journal of Clinical Question, your revised manuscript should be uploaded as soon as possible. If it is not possible for you to submit your revision in a reasonable amount of time, we may have to consider your paper as a new submission.

Once again, thank you for submitting your manuscript to the Journal of Clinical Question and I look forward to receiving your revision.

Sincerely,
Richard S. Isaacs
Editor in Chief
Journal of Clinical Question

[Editor's Comments]
Associate Editor
Comments to the Author:
(There are no comments.)

[Reviewer(s)' Comments]

Reviewer: 1

Comments to the Author
Thank you for submitting your manuscript that discusses an important and interesting topic which is still considered a gap in the field of oncology.
Kindly find below a few comments to be addressed in order to strengthen the manuscript and its conclusions:
- The English of the whole manuscript needs to be reviewed and some spelling mistakes to be corrected including the abstract.
- The introduction provides a strong background. However, it is advised to discuss briefly the current data/practice of TPO-RAs in the field of hematologic malignancies to highlight that experience especially post bone-marrow transplantation and the gap in the field of solid tumors
- It is advised in the discussion, to discuss the possible drug-drug interactions of TPO-RAs with chemotherapies and list the most common side effects that might occur. Also, it will be beneficial to discuss the current data even if limited about the dose reductions to decrease those interactions and if this strategy has been already tried.
- The financial toxicity of the addition of these medications to the chemotherapy should be addressed briefly knowing that those medications are highly expensive and will not be available to all countries.
- It is recommended to expand the discussion about the the chemo-immuno/TKIs regimens highlighting the possible different side effects and drug-drug interactions especially with TKIs the oral medications that might have more interactions

Reviewer: 2

Comments to the Author
Well, the authors investigated an ongoing and timely topic. They evaluated a systematic review and a network meta-analysis comparing the efficacy and safety of TPO-RAs in CIT. The paper fills a gap in the current database of TPO-RAs in CIT.

I have no concerns about the manuscript, but ı would like to suggest removing the TKI-associated CIT and ICI-associated thrombocytopenia in the discussion part, which is unnecessary.

Date Sent: 25-Jul-2026

Response Letter

Dear Reviewers,

We sincerely thank the reviewers for their careful evaluation of our manuscript and for their constructive comments. We have revised the manuscript accordingly. The reviewers' comments are reproduced below, followed by our responses.

Reviewer 1

Comment 1: The English of the whole manuscript needs to be reviewed and some spelling mistakes to be corrected, including the abstract.

Response: Thank you for this comment. The entire manuscript, including the abstract, has been carefully reviewed and edited to improve grammar, spelling, clarity, and academic style. Several typographical and linguistic errors have also been corrected throughout the manuscript.

Comment 2: The introduction provides a strong background. However, it is advised to discuss briefly the current data/practice of TPO-RAs in the field of hematologic malignancies to highlight that experience, especially post bone-marrow transplantation, and the gap in the field of solid tumors.

Response: Thank you for this valuable suggestion. We have added a brief overview of the clinical experience with thrombopoietin receptor agonists in patients with hematologic malignancies, including their use for persistent thrombocytopenia following hematopoietic stem cell transplantation. The following text has been added to the Introduction:

"Experience with TPO-RAs has also accumulated in haematologic malignancies, particularly for persistent thrombocytopenia after haematopoietic stem cell transplantation. Eltrombopag and other TPO-RAs have shown platelet responses in clinical studies, although the evidence remains limited and is largely based on small or non-randomised cohorts. Because post-transplant thrombocytopenia has mechanisms distinct from chemotherapy-induced thrombocytopenia, these findings cannot be directly extrapolated to patients with solid tumours, in whom comparative randomised evidence remains scarce." （Line 98-104）

Comment 3: It is advised in the discussion to discuss the possible drug-drug interactions of TPO-RAs with chemotherapies and list the most common side effects that might occur. Also, it will be beneficial to discuss the current data, even if limited, about dose reductions to decrease those interactions and whether this strategy has already been tried.

Response: Thank you for this important suggestion. We have expanded the Discussion to address potential drug–drug interactions between TPO-RAs and concomitant anticancer treatments, as well as their common and clinically important adverse effects. We have also clarified that dose or treatment-duration adjustments have been evaluated for certain metabolic or transporter-mediated interactions; however, these studies were not conducted in patients receiving chemotherapy, and no chemotherapy-specific strategy of empirical TPO-RA dose reduction has been established. The following paragraph has been added to the Discussion:

"Potential drug–drug interactions should be considered when TPO-RAs are combined with anticancer therapy. Avatrombopag is metabolised by CYP2C9 and CYP3A, while eltrombopag inhibits OATP1B1 and BCRP; therefore, concomitant medications affecting these pathways may alter drug exposure. Common adverse effects include headache, fatigue, nausea, diarrhoea, hepatic enzyme elevations, thrombocytosis, and thromboembolic events. However, no chemotherapy-specific strategy of empirical TPO-RA dose reduction has been established, and dose modification should be individualised according

to concomitant medications, platelet response, hepatic function, and toxicity."(Line 292-301)

Comment 4: The financial toxicity of the addition of these medications to chemotherapy should be addressed briefly, knowing that these medications are highly expensive and will not be available to all countries.

Response: Thank you for this important comment. We have added a brief discussion of the financial burden and unequal accessibility of TPO-RAs. We also note that cost-effectiveness evidence specific to CIT remains lacking and that treatment decisions should consider local availability and reimbursement.

"Cost and access are additional considerations. TPO-RAs may impose substantial treatment costs, potentially increasing financial toxicity and limiting access in countries with restricted healthcare resources or reimbursement. Although these agents may reduce platelet transfusions and chemotherapy disruption, evidence regarding the cost-effectiveness of thrombopoietic agents specifically for CIT remains limited. Treatment decisions should therefore consider the expected clinical benefit, treatment duration, local availability, and reimbursement."(Line301-307)

Comment 5: It is recommended to expand the discussion about chemo-immunotherapy/TKI regimens, highlighting the possible different side effects and drug-drug interactions, especially with TKIs, as oral medications might have more interactions.

Response: Thank you for this valuable suggestion. We have added a concise statement regarding potential drug–drug interactions between oral TPO-RAs and concomitant anticancer therapies, particularly TKIs. To maintain the focus of this review on chemotherapy-induced thrombocytopenia, we did not expand the discussion of TKI- or ICI-associated thrombocytopenia. The revised text reads:

"Potential interactions with concomitant anticancer therapies should also be considered because oral TPO-RAs differ in their pharmacokinetic properties and interaction profiles. In patients receiving TKI-containing regimens, careful medication review and monitoring are warranted, although direct evidence regarding TPO-RA/TKI combinations remains limited." (Line 292-297)

Reviewer 2

Comment 1: The authors investigated an ongoing and timely topic. They evaluated a systematic review and a network meta-analysis comparing the efficacy and safety of TPO-RAs in CIT. The paper fills a gap in the current database of TPO-RAs in CIT. I have no concerns about the manuscript.

Response: We sincerely thank the reviewer for the positive assessment of our work and for recognizing the clinical relevance of this systematic review and network meta-analysis.

Comment 2: I would like to suggest removing TKI-associated CIT and ICI-associated thrombocytopenia in the Discussion, which is unnecessary.

Response: Thank you for this helpful suggestion. We agree that thrombocytopenia associated with TKI or ICI therapy is mechanistically distinct from conventional chemotherapy-induced thrombocytopenia and lies beyond the primary scope of this review. We have therefore removed the detailed discussion of TKI-associated and ICI-associated thrombocytopenia. A brief statement regarding potential drug–drug interactions with concomitant anticancer therapies has been retained because it is clinically relevant to the use of oral TPO-RAs.

We again thank the reviewers for their thoughtful and constructive comments. We believe that the revisions have improved the clarity, clinical relevance, and methodological focus of the manuscript.

Best Regards

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