

Decision Letter (JCQ-2025-0021)

From:

To:

CC:

BCC:

Subject: Journal of Clinical Question - Decision on Manuscript ID JCQ-2025-0021

Body: 04-Jul-2025

Dear Dr Kitamura:

Manuscript ID JCQ-2025-0021 entitled "Oral Antifibrotic Agents for the Treatment of Idiopathic Pulmonary Fibrosis: A Systematic Review and Network Meta-Analysis of Randomized Controlled Trials" 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 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.

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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).

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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 Isaacs
Editor in Chief, Journal of Clinical Question
jcqeic@gleampub.com

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

[Reviewer(s)' Comments]

Reviewer: 1

Comments to the Author

The authors performed a literature review of anti-fibrosis drug. These two drugs have been clinically applied for many years, if the authors focus on the drug effects and pharmacokinetics, or ADE, the scientific meaning of this article is more prominent.

Reviewer: 2

Comments to the Author

Overall the presentation of manuscript is great.

The minor comments are

(1) the representations of Network graphs (Figure 1, Figure S4, and S6) are not clear. The explanation of node, edges, vertex, sparsity, and dense can be improved. The graph does not seem to be the direct output from R code. It is important to use the output of figures from the software since the size of node, edge, and other factors are calculated from the Bayesian Network analyses

(2) explain the ranking Figure S2. the number of bar is not nine ranks.

(3) provide the prior information that was used in this analyses.

Date Sent: 04-Jul-2025

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Author's Response to Decision Letter for (JCQ-2025-0021)

Oral Antifibrotic Agents for the Treatment of Idiopathic Pulmonary Fibrosis: A Systematic Review and Network Meta-Analysis of Randomized Controlled Trials

Dear Editor and Reviewers,

We sincerely thank the Editor and both reviewers for their thoughtful and constructive comments on our manuscript. We greatly appreciate the time and effort you dedicated to evaluating our work, as well as the insightful suggestions that have helped us improve the clarity, rigor, and overall quality of the paper. Below, we provide a detailed point-by-point response to each comment, along with the corresponding revisions made in the manuscript.

Reviewer 1

Comment: The authors performed a literature review of anti-fibrosis drug. These two drugs have been clinically applied for many years, if the authors focus on the drug effects and pharmacokinetics, or ADE, the scientific meaning of this article is more prominent.

Response: We sincerely appreciate the reviewer's insightful comment. As noted, the two currently approved agents for IPF have been in clinical use for many years, and a deeper exploration of their pharmacological profiles and adverse events is highly relevant. In response, we have expanded our data analysis to include the novel agent nerandomilast, evaluating its role both as monotherapy and in combination with the existing agents. Furthermore, we have compared their respective therapeutic effects and highlighted differences in serious adverse events (SAEs). We have also added a more detailed discussion of the previous two agents, as follows: "Nintedanib, a tyrosine kinase inhibitor, targets multiple growth factor receptors implicated in fibrotic signaling pathways. Pirfenidone exerts both antifibrotic and anti-inflammatory effects, primarily through modulation of transforming growth factor-beta and other cytokines. These agents differ in their pharmacokinetic profiles and safety characteristics, but both have been shown to significantly reduce the rate of forced vital capacity (FVC) decline and are recommended for patients with mild to moderate disease." We believe these additions significantly enhance the scientific rigor and clinical relevance of the manuscript.

Reviewer 2

Comment (1): The representations of Network graphs (Figure 1, Figure S4, and S6) are not clear. The explanation of node, edges, vertex, sparsity, and dense can be improved. The graph does not seem to be the direct output from R code. It is important to use the output of figures from the software since the size of node, edge, and other factors are calculated from the Bayesian Network analyses.

Response: Thank you for pointing this out. We have revised Figures 1, S4, and S6 to improve clarity. The appearance of the network graphs was enhanced using the *igraph* and *viridis* packages in R, while preserving the calculated sizes of nodes, edges, and other relevant parameters. Additionally, we improved the figure legends and the corresponding manuscript text to provide clearer explanations of the node as suggested. We have added the the following contents to the methods section as follows "The appearance of the network graphs was enhanced using the "igraph" and "viridis" packages."

Comment (2): Explain the ranking Figure S2. The number of bar is not nine ranks.

Response: Thank you for pointing this out. The number of bars for each treatment in Figure S2 reflects the number of possible ranks based on the treatments included in the analysis. The tallest bar for each treatment indicates the most probable rank. We have revised the figure caption and added a brief explanation in the text to clarify this for readers.

Comment (3): Provide the prior information that was used in this analyses.

Response: Thank you for this important comment. We have revised the Methods section to include a detailed description as follows "A rankogram is a bar plot that displays the probability of each treatment occupying each possible rank, with the tallest bar indicating the most likely rank for that treatment."

We sincerely thank the reviewers for their constructive comments, which have improved the quality and scientific rigor of our manuscript.

Best regards,

Hideya Kitamura

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