Journal of Clinical Question

Decision Letter (JCQ-2026-0026)

From: [redacted]
To:
CC:
BCC:

Subject: Journal of Clinical Question - Decision on Manuscript ID JCQ-2026-0026

Body: 15-Aug-2026

Dear Dr Wang:

Manuscript ID JCQ-2026-0026 entitled "Targeting RAS in Pancreatic Ductal Adenocarcinoma: From Molecular Breakthroughs to Phase III Clinical Validation and Beyond" 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.

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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).

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
The manuscript is timely and well structured, with a valuable overview of the rapidly evolving RAS-targeted treatment landscape in PDAC. The integration of phase III evidence with emerging KRAS G12D-directed approaches is particularly relevant.

A few minor revisions are recommended:

Clearly distinguish peer-reviewed clinical evidence, conference-reported data, and ongoing trials throughout the manuscript and tables.

Ensure that preliminary response data are presented with appropriate caution and are not directly compared across heterogeneous trials.

Please carefully audit the reference list for duplicate or inconsistent citations, including the apparent duplication of references 21 and 22.

Clarify the distinction between currently actionable molecular testing and investigational ctDNA-based monitoring.

Addressing these points would further improve the accuracy and clinical clarity of the review.

Reviewer: 2

Comments to the Author
If needed you are welcome to site more papers in PDAC, for example Clin Cancer Res (2025) 31 (17): 3644–3651.
https://doi.org/10.1158/1078-0432.CCR-24-1821

Date Sent: 15-Aug-2026

Journal of Clinical Question

Author's Response to Decision Letter for (JCQ-2026-0026)

Targeting RAS in Pancreatic Ductal Adenocarcinoma: From Molecular Breakthroughs to Phase III Clinical Validation and Beyond

Dear Reviewers,
We sincerely thank the reviewers for their careful evaluation of our manuscript and for their constructive and helpful comments. We have revised the manuscript accordingly and believe that these revisions have improved its accuracy, clarity, and clinical relevance. Our point-by-point responses are provided below, and all changes made in response to the reviewers' comments are indicated in the revised manuscript.

Reviewer 1
Comment 1: Clearly distinguish peer-reviewed clinical evidence, conference-reported data, and ongoing trials throughout the manuscript and tables.
Response: Thank you for this important suggestion. To make the maturity of the evidence explicit without unnecessarily expanding the main text, we revised Table 1 so that conference abstract/presentation data are identified with a dagger symbol (†), while unmarked clinical studies are identified as full peer-reviewed publications. Ongoing phase II/III trials remain summarized separately in Table 2. This presentation now clearly separates peer-reviewed clinical evidence, preliminary conference-reported data, and ongoing trials.(Table 1, lines 568–569)

Comment 2: Ensure that preliminary response data are presented with appropriate caution and are not directly compared across heterogeneous trials.
Response: We agree. The main text already emphasizes that cross-trial numerical comparisons are potentially misleading because the available studies differ in treatment setting, molecular eligibility, study design, follow-up, and response assessment. To reinforce this caution at the point where efficacy results are summarized, we added an explicit statement to the Notes of Table 1 indicating that efficacy estimates should not be directly compared across studies. This is intended to ensure that preliminary response data are interpreted as signals of clinical activity rather than as evidence of comparative efficacy. (lines 153–159, lines 570–571.)

Comment 3: Please carefully audit the reference list for duplicate or inconsistent citations, including the apparent duplication of references 21 and 22.
Response: Thank you for identifying this issue. We rechecked references 21 and 22 and corrected the reference-list issue noted by the reviewer. The corresponding in-text citations were also verified in the revised manuscript.

Comment 4: Clarify the distinction between currently actionable molecular testing and investigational ctDNA-based monitoring.
Response: We appreciate this important comment. We revised the Future Directions section to explicitly distinguish baseline molecular profiling used to identify actionable alterations for treatment selection from serial ctDNA monitoring for treatment response or emerging resistance. We now state directly that serial ctDNA monitoring remains investigational and is not currently established as a standard-of-care decision tool in PDAC. (lines 361–364)

We thank the reviewer again for these constructive comments, which have improved the accuracy and clinical clarity of the manuscript.

Reviewer 2
Comment: If needed you are welcome to cite more papers in PDAC, for example Clin Cancer Res (2025) 31 (17): 3644–3651. https://doi.org/10.1158/1078-0432.CCR-24-1821
Response: Thank you for this helpful recommendation. We reviewed the suggested study and incorporated it into the revised manuscript as Reference 54. Because this study concerns modulation of the immunosuppressive tumor microenvironment rather than direct RAS inhibition, we cited it in the Combination Strategies section to provide relevant clinical context for immunotherapy-based approaches in PDAC. We also added a brief description of the reported reduction in intratumoral monocytes/macrophages and enhancement of T-cell activation, while retaining appropriate caution regarding the need for larger studies to establish clinical benefit. (lines 347–350)

We sincerely thank the reviewers again for their thoughtful and constructive comments. We believe that the revisions made in response to these suggestions have strengthened the manuscript and improved the clarity and clinical relevance of the review. We appreciate the reviewers' time and consideration and hope that the revised manuscript is now suitable for publication.

Best Regards

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