

Peer Review File

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Reviewer A

We greatly appreciate your constructive comments, which have helped us significantly improve the quality of our revised manuscript.

This study addresses a current topic.

The manuscript is quite well written and organized. English could be improved.

Figures and tables are comprehensive and clear.

The introduction explains in a clear and coherent manner the background of this study.

We suggest the following modifications:

- Introduction section: although the authors correctly included important papers in this setting, we believe the evolving systemic treatment scenario for biliary tract cancer should be further discussed and some recent papers added within the introduction (PMID: 36695827; PMID: 36533070; PMID: 33756174; PMID: 33571059), only for a matter of consistency. We think it might be useful to introduce the topic of this interesting paper.

Response: Thank you for this constructive comment. Important references on biliary tract cancer specifically you pointed out are cited in the text (PMID: 36695827 (page 8, lines 1-3); PMID: 36533070 (page 7, lines 18- page 8, lines 1); PMID: 33756174 (page 6, lines 15-17); PMID: 33571059 (page 6, lines 15-17)).

- Methods and Statistical Analysis: nothing to add.
- Discussion section: Very interesting and timely discussion. Of note, the authors should expand the Discussion section, including a more personal perspective to reflect on. For example, they could answer the following questions – in order to facilitate the understanding of this complex topic to readers: what potential does this study hold? What are the knowledge gaps and how do researchers tackle them? How do you see this area unfolding in the next 5 years? We think it would be extremely interesting for the readers.

Response: Thank you for highlighting this. We apologize for the lack of clarity. As you have mentioned here and in your other comments, we also believe the points you raised are important. To further clarify the significance of this study, we have detailed the knowledge gaps and future directions in current biliary tract cancer treatment, and we have added the significance of this study (page 18, lines 1-9).

However, we think the authors should be acknowledged for their work. In fact, they correctly addressed an important topic, the methods sound good and their discussion is well balanced.

One additional little flaw: the authors could better explain the limitations of their work, in the last part of the Discussion.

Response: Thank you for your suggestion, I have added more details about limitation (page 17, lines 9-15).

We believe this article is suitable for publication in the journal although major revisions are needed. The main strengths of this paper are that it addresses an interesting and very timely question and provides a clear answer, with some limitations.

We suggest a linguistic revision and addition of references for consistency. However, some points must be clarified.

Response: Thank you for your suggestion. We have revised the manuscript as noted above.

Reviewer B

We greatly appreciate your comments, which could improve our revised manuscript.

Some changes are needed. Some parts should be improved, and a linguistic revision is needed.

Response: Thank you for this comment. As pointed out by Reviewers A and B, some parts were revised. As for the English editing, we have asked Editage (<https://www.editage.com>), a language editing company, to correct any language-related errors in the revised manuscript.

Some references should be updated and the authors should include some recent papers regarding this very important topic in biliary tumors (PMID: 33756174; PMID: 36533070; PMID: 36695827; PMID: 33571059).

Response: Thank you for this comment. Some references have been updated, as you indicated.

Especially, essential references on biliary tract cancer specifically pointed out are cited in the text (PMID: 33756174 (page 6, lines 15-17); PMID: 36533070 (page 7, lines 18- page 8, lines 1); PMID: 36695827 (page 8, lines 1-3); PMID: 33571059 (page 6, lines 15-17)).