

Peer Review File

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Review comments

Review manuscript entitled ‘Interventional Oncology Approaches to treating Pancreatic Cancer’

The authors of the manuscript entitled ‘interventional oncology approaches to treating pancreatic cancer’ performed a narrative review on ablation options for pancreatic cancer and focused on IRE and percutaneous ablation.

This subject is relevant since the prognosis of pancreatic cancer remains poor and we are awaiting results of several randomized controlled trials (CROSSFIRE, DIRECT and PELICAN trial) to give more insight with respect to the potential survival benefit of ablative therapies. Especially the immunomodulatory effects of IRE are interesting and give potential for combination treatment with immunotherapy, as discussed by the authors in the future perspectives section of the manuscript.

However, there are some major concerns:

1. Already a lot of reviews exist on this subject. In which way is this narrative review of additional value when for example compared to the review of Narayanan et. al published in 2021 (reference 11) or Ruarus et. al. published in 2018 (reference 4).

Reply: Dr. Narayanan and corresponding authors were invited to write a review on this topic.

Re: It is not WHO wrote the review but WHAT NEW information is reviewed in this NEW REVIEW. The authors should clearly state this in the manuscript.

I have seen the author instruction of DMR and found that the authors could address the issue by adding a rationale section in Introduction which is missing in the revised version.

Reply: A rationale section has been added at the start of the introduction.

2. While the authors state that most data is available on RFA and IRE, the paragraph on RFA is rather short compared to other ablative therapies and moreover it does not represent the existing published data on RFA. Only a review published in 2018 is mentioned while for example a phase II study on RFA has been published (Fegrachi et al.) on which a randomized controlled trial has been based (PELICAN trial). At least this phase II study and the PELICAN trial should be mentioned (trial protocol published in Trials).

Reply: Sources have been added to the RFA paragraph.

3. Some conclusions are very premature. It cannot be concluded from only one reference (a retrospective comparative study with a high risk of bias), that IRE is superior to other ablation modalities (line 420). Moreover, major complications like duodenal hemorrhage have been described for IRE as well. Ongoing randomized controlled trials should give more insight on the

true efficacy and safety of the several ablative therapies. Only after prospective and/or randomized comparative studies have been performed, these conclusions can be made.

Reply: For this comment, we have edited some of the conclusions in the paragraph that seemed premature. We also added a section in the paper describing the risks of IRE with the appropriate references.

4. Most of above mentioned concerns are because of the narrative character of the review. There is no transparency on the methods that are used nor is a search strategy available. The manuscript is at risk to give a subjective view, which is also shown by the lack of data on RFA.

5. The upcoming of FOLFIRINOX in more recent years should be elaborated on within the manuscript. A lot of data that is used is published before the 'FOLFIRINOX era'. Currently the overall survival with only FOLFIRINOX treatment is already more than 17 months for patients with LAPC.

Reply: We have added more paragraphs talking about FOLFIRINOX in the manuscript with the appropriate references.

Minor concerns

1. The references do not seem to be compatible with the sentences that they are referring to (i.e. reference 2 in background section refers to an publication on EUS guided RFA).

Reply: We have looked over the citations in order to make sure they are correct. For reference 2 specifically, the publication is about EUS guided RFA but we used a fact about pancreatic cancer from that article so we wanted to add that citation to show our source.

2. It would be nice if some illustrations of figures would have been used.

Reply: Figure has been added.

Re : the figure should be cited in text. The figure 1b and figure 1c should have separated figure legends.

Reply: This has been fixed. The figure has been cited in the manuscript.