ANSWERS TO REVIEWERS

1. We have started with a short introduction about molecular characteristics of pancreatic cancer in order to highlight on the one hand how progresses in PDAC biology knowledge have been made, but no results are actually useful in clinical practice, and on the other hand how one of the major problems in developing target therapies for this tumor is the large genetic complexity and heterogeneity. Anyway we have removed less relevant contents.
2. Unfortunately almost all target therapy trials in PDAC have failed. We have reported only the main phase II and phase III trials for each target agent type, not mentioning many other negative trials, especially phase I studies. We have summarized trials in respect of the target pathways to make the text clearer.
3. As suggested, we have included some new molecular agents recently presented at the 2015 ASCO meeting, such as Demcizumab.
4. Our conclusions about unsatisfying results of target agents in PDAC are derived from the large number of trials analyzed and from a correlation with PDAC genomic landscape. Of course they are also in line with other reviews in literature.
5. We have reduced the title.
6. As suggested, we have separated conclusion and future challenges in two different sections.
7. We have included a mention of antibody drug conjugates in the future challenges section to give a more complete overview of biological agents' applications in pancreatic cancer.