Peer Review File

Article Information: https://dx.doi.org/10.21037/tlcr-21-950

Reviewer #1: The idea of the authors is fine, but the text is for the overwhelming majority a recapitulation of the three phase 2 trials. Only the last two small paragraphs elaborate on the interesting topic of the editorial.

I suggest that the authors focus on the points they want to make after a small, focused review of the three trials.
Lastly, in IO, the long-term OS gain is more striking than the PFS increase. That important point is missing in the editorial.

Authors: We thank the first reviewer for his thoughtful comments and feedback. We are aware of relevant limitations and the short format of our manuscript. In briefly describing the studies, we felt it was important to highlight oncological outcome and adverse events in addition to the treatment regimen. We have further elaborated the paragraphs describing the benefits of the escalation of conventionally fractionated chemoradioimmunotherapy, hoping to give them more importance. We added a paragraph of the highly beneficial survival outcome concerning OS rather than PFS in our discussion.

Reviewer #2: This manuscript is a good summary of the three clinical trials, and there are no major problems. Thus, there are only a few minor points. In these 3 trials, the authors should describe the primary endpoint.
They used the "primary" many times. This can be confusing to the readers. "Primary" shoud be used for primary endpoints. Line 107, ECOG 2 should be ECOG PS 2.

Authors: We thank the second reviewer for the positive feedback on our work and the valuable suggestions. To provide the reader with a more uniform understanding of primary endpoints, we used the term only once per study and made it uniform. Furthermore, we made the small correction regarding the ECOG performance status.

Reviewer #2: The frequency of grade 3 or higher pneumonitis in PACIFIC trial should be described. These 3 trials still seem to have a high frequency.

Authors: Dear Reviewer 2, this point is indeed very important and was accordingly included by us to the editorial (see line 116). Due to the word count limit, we decided to address this as briefly and precisely as possible in the discussion and hope that it will be brought to the point in this way, see line 123 and following.

Reviewer #3: In this editorial, the authors reviewed three nonrandomized phase II trials evaluating chemoradiotherapy concurrently with immunotherapy and summarized the efficacy and safety results. However I missed a deeper discussion of the study limitations and they did not delve much into most relevant point: does it worth to assume higher toxicity related with the concurrent administration of chemoradiation and immunotherapy? Based on indirect comparison of those studies with PACIFIC and LUN 14-179 (not covered by the editorial), concurrent vs sequential immunotherapy does not seem to yield to significantly higher efficacy in terms of PFS or OS particularly in the long term.

Authors:

We thank the third reviewer for his thoughtful comments and valuable feedback. We included LUN 14-179 as the third reviewer mentioned in our manuscript and discussed the role of concurrent versus sequential immune checkpoint inhibition in more detail. We hope to adequately address the issues raised by the reviewer.

Reviewer #3:

Other issues that should be addressed are:

-The authors commented the efficacy results of DETERRED study but skipped the safety results. The rate of grade 3 or higher was remarkable (80%) and despite there were not immune-related grade 5 toxicities, there were 3 patients who died due to chemotherapy-induced neutropenic sepsis, gastric hemorrhage attributed to steroid-induced gastric ulceration during consolidation chemotherapy, and acute myocardial infarction (thought to be unrelated to atezolizumab). Additionally, one patient in part A died from a tracheoesophageal fistula. This should be discussed by the authors.

Authors:

We added detailed information about both study parts of the DETERRED trial in our manuscript (l. 59-68) and added a paragraph in the discussion part concerning treatment-related side effects.

Reviewer #3:

-Regarding Keynote-799 discussion, please remind that overall response rate has been considered a dim endpoint in the setting of unresectable stage III NSCLC. In addition, the study design lacking a control arm and the fact that response asssessement was perfomed by investigators may have had an impact on the results. Could the authors elaborate more their discussion taking this into account?

Authors:

Thank you very much for your valuable comments. We included the mentioned study limitations of KEYNOTE-799 in our manuscript (l. 76-78) and our

discussion part.

Reviewer #3:
-The authors did not mention other therapeutic approaches which consisted in intensifying the treatment after completing the chemoratiation by combining anti-PD(L)1 with other immunotherapies like it has been reported in the COAST trial (Martinez-Marti et al. ESMO 2021).

Authors:
We included a statement about further intensification and new combinations in our manuscript (discussion and summary) (l. 130-131, l. 137)

Reviewer #3:
-English should be reviewed by a native English speaker.

Authors:
A proof reader with full professional proficiency in English checked the manuscript again.