Peer Review File

Article Information: http://dx.doi.org/10.21037/atm-21-539

Reviewer A:

1. Although NK cell immunotherapy is a promising therapy, today more promising immunotherapy is immune checkpoint inhibitor. The reviewer thinks that it would be ideal to combine with IRE and so far, there have already been published many studies on this topic. Thus, I prefer you should address not only NK cell-based immunotherapy but also immune checkpoint inhibitor.
   Thank you for your comment. We completely agree with the reviewer that there are recent studies that showed promising results in combination with IRE for effective cancer immunotherapy. However, our recent study focused on the mechanism of NK cells and the advancement of the therapeutic outcome as combined with the IRE ablation method. This combination therapy has been investigated for several research groups and there are still ongoing clinical trials. Despite that other immunotherapies have improved the clinical outcome when combined with IRE ablation, we are not able to maintain the main framework of the recent study while including other approaches and their mechanisms within the limited timeframe provided for returning the revision of the study. Therefore, we presented this limitation in our study by citing the most recent studies obtained with our literature search. The conclusion section of the manuscript is amended as follows,
   Page 13, Conclusion
   "***Besides, several studies that combine other immunotherapeutic methods with the IRE ablation method have presented promising outcomes for the treatment of pancreatic tumors in which comprehensive reports will be beneficial for the researchers with the focus of cancer research (108-112).”***

Reviewer B:

1. P9,Ln11-12: the MRI reversible zone is not well defined given limitations of the pixels. However this is a good place to describe the MRI findings of the zones as well.
   Thank you for your comment. We have amended the manuscript as follows,
   Page 9, IRE Ablation
   *"***In MRI, the IRE zone was observed as hyperintense on T1w and T2w images due to the coagulative necrosis while the RE zone is described as hypointense on T1w and hyperintense T2w MRI images (69).***"*

2. Pg 10, Ln 14. Citations 86,87, please in body report that this is only done in animals to be completely transparent
   Thank you for your comment. We have amended the manuscript by emphasizing the utilization of the animal HCC model for the study as follows,
   Page 10, IRE Ablation
   *"***More recently, an advanced MRI technique was performed on the VX2 rabbit HCC model to differentiate irreversibly ablated regions from reversibly electroporated zones which will be beneficial for intraprocedural assessment (86,87).***"*

3. Pg 10, Ln 22-23, please state the adverse effects mentioned.
   Thank you for your comment. We have presented the adverse effects encountered with the study.
   *"***Of 44 patients undergoing IRE treatment, five patients had 9 adverse effects which were classified as unrelated (leukocytosis, urinary tract infection), indirectly related (dehydration, biliary stent occlusion, cholangitis, and acute renal failure), procedure-related (neurogenic bladder, abdominal pain, and flank pain) and all these effects were resolved in 30 days.***"*

4. Pg 12, LN 8-9, improved median OS, please state the numbers and results.
   Thank you for your comment. We have amended the manuscript as directed.
   Page, 12, IRE plus NK cell-based treatment
   "***The study showed that the patient cohort that received combination treatment had significantly improved median overall survival (10.1 months) compared to patients treated with a single therapy (8.9 months, p = 0.0078). Moreover, the observation data acquired 3 months following the treatments demonstrated a significant difference in tumor size among the groups (IRE: 2.68±1.01 vs NK-IRE: 2.31±0.68 p<0.05), and the combination group obtained a higher disease control rate than the IRE group.***"

5. Table 1 & 2, the tables of clinical trials registered alone is not useful. Please state the findings in those completed, and the intended size of each study.
   Thank you for your comment. We have updated tables 1 and 2 by including the study findings and the intended size of each study.