Author’s response to reviews

Title: Does External Beam Radiation Boost to Pelvic Lymph Nodes Improve Outcomes in Patients with Locally Advanced Cervical Cancer?

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Reviewer’s comments:

1. Page 6. Table 1. Why was a IA cervix cancer patient treated with chemoradiation?

Thank you for noting this. The patient with FIGO stage IA2 cervical cancer opted for pelvic radiotherapy as an alternative to modified radical hysterectomy (as per NCCN guideline for stage IA1 with lymphovascular invasion and stage IA2 cervical cancer).

2. FIGO recently revised cervix cancer staging, noting that +PLN/PALNs now classify cervical cancer patients as stage IIIC. Would recommend addressing this very new and pertinent change in the background.

Thank you for the recommendation. We have added the following to the background:
“In the recently revised FIGO staging, patients with positive pelvic LN have been included and classified as stage IIIC1 and those who also had positive para-aortic nodes were classified as stage IIIC2 (ADD REF). Prior to this, FIGO staging did not formally classify lymph node involvement and to date there is no standardized guideline on external beam radiation boost to pelvic lymph nodes.”

3. Page 6 line 46-48. Error in math. 53.6%+46.2% does not add up to 100%.
Thank you for highlighting this and apologies for our error. We have amended this to 53.7% (36 out of 67) and 46.3% (31 out of 67).

4. Page 6 line 53-55. Was there a statistically significant difference in the mean size of positive pelvic lymph nodes that received the boost vs not?
The difference in the mean size of positive pelvic lymph nodes that received pelvic nodal boost was not statistically significant.

5. Page 7 Lines 42-Page 8 Line 27. Would appreciate seeing this data in table format.
Thank you for the suggestion. We have now amended the paragraphs and added tables to this section.

6. Page 9 Line 22. Is this "slightly higher proportion of patients w positive PLNs who had no nodal boost received concurrent chemotherapy" - is this statistically significant?
Thank you for noting this. This was not statistically significant and we have now removed this to avoid confusion and included this small imbalance as part of our limitation.

7. Discussion. What are other factors that may have impacted the negative results of this study?
Other factors that may have contributed to the negative results include the different proportion of patients who received concurrent chemotherapy with 96.8% of patients with positive pelvic lymph nodes who had no nodal boost receiving concurrent chemotherapy compared to 83.3% of patients with positive pelvic lymph nodes who had nodal boost. However, this was not statistically significant. We briefly mentioned radiotherapy resistance in our manuscript and we
believe that further studies to evaluate the role of biomarkers play a crucial part in improving outcome of treatment in cervical cancer.

8. Need a table comparing the baseline characteristics of patients w +PLNs who receive boost vs those who do not. Would recommend including median SUV w range, median size LN w range.

Thank you for the recommendation. We have added age and median size of lymph nodes with range for patients with positive pelvic nodes in table 1. However, only 18.7% of our patients had PET scan hence we did not include this in our table of comparison.

9. Why did the radiation oncologists choose to give boost in some patients, but not in others?

As there is no standardized guideline for pelvic nodal irradiation, this was based on physician’s preference which gave us a good opportunity to study the outcome of such patients.