

## Peer Review File

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### Reviewer A

In this study, the safety and short-term outcomes after neoadjuvant immunotherapy combined with chemotherapy or chemoradiotherapy were shown. I think this is a precious study with new knowledge. However, several revisions are required.

1. Line 204-210. Was pneumonitis immune-related adverse event? Please show your opinion. In addition, how did grade 5 pneumonitis occur?

Reply 1: Yes, we believe pneumonitis is immune-related adverse event. The patient had completed neoadjuvant treatment. During the preoperative examination, he complained that he developed a cold after catching a cold. After climbing stairs, the chest tightness and shortness of breath worsened. There was no improvement after steroid treatment. The condition worsened rapidly within one day. He was transferred to ICU for treatment but did not improve and later died.

Changes in the text: None.

2. Line 235-241. Table 3. Please show the grade of postoperative complication in Clavien-Dindo classification.

Reply 2: Most of the major complications in the table are grade 3, and only one patient was grade 5, which resulted in death from multiple organ failure due to anastomotic leakage and pneumonia.

Changes in the text: None.

3. Occurrence of grade 5 pneumonitis among relatively small number patients is unmissable fact. Please discuss this point in Discussion section.

Reply 3: Thank you for your suggestion. There was one case of grade 5 pneumonitis associated with immune checkpoint inhibitor (ICI) in the nICT group. ICI therapy alters the balance of immune cells in the body, which in turn cause damage to certain organ system, such as pneumonitis, colitis and endocrine disorders. And a meta-analysis paper showed compared with chemotherapy, PD-1 inhibitors showed significant increase in grade 1-5 and grade 3-5 pneumonitis (RR, 5.17, 95% CI: 2.82–9.47,  $p < 0.001$ ; RR, 4.14, 95% CI: 1.82–9.42,  $p < 0.001$ ). The morbidity for immune-related pneumonitis after ICI inhibitor therapy has been about 3.02(95%CI: 2.31-3.93) % for PD-1 inhibitors. ICI therapy-related pneumonitis is an uncommon but important complication of ICI therapy, with potential for significant morbidity and mortality. As the clinical manifestation is often nonspecific, CT plays an important role in diagnosis. In this article, we believe that this is an incidental event, and as surgeons are more

concerned about postoperative complications, we do not specifically discuss this case of pneumonia in the discussion section.

Changes in the text: None.

References

Su Q, Zhu EC, Wu JB, Li T, Hou YL, et al. Risk of Pneumonitis and Pneumonia Associated With Immune Checkpoint Inhibitors for Solid Tumors: A Systematic Review and Meta-Analysis. *Front Immunol.* 2019 Feb 4:10:108.

## **Reviewer B**

I want to congratulate the authors for this study which presents evidence supporting the safety of esophagectomy following induction chemotherapy or chemoradiation therapy with immunotherapy. The authors acknowledged the limitations of the study: non-randomized, small sample and single center. It does, however, add up to the growing evidence of the benefits and safety of immunotherapy in the induction setting.

Reply 1: Thank you for your recognition and encouragement of the article.

Changes in the text: None.