

Review Comments

- 1) First, the title needs to indicate the clinical research design of this study, i.e., a retrospective cohort study.

Reply 1): We have modified our text as advised (see Page 1, line 5).

Changes in the text: Tumor immune microenvironment remodeling and prognosis of patients with esophageal squamous cell carcinoma after neoadjuvant chemotherapy with and without immunotherapy: a retrospective cohort study.

- 2) Second, the abstract needs some revisions. The background did not describe the potential clinical needs for this research focus. The methods did not describe the inclusion criteria, the assessment of clinical characteristics, laboratory test methods of the biomarkers, measurements of clinical outcomes, and follow up procedures. The results need to briefly describe the clinical characteristics of the study sample. The conclusion needs some comments for the clinical implications of the findings.

Reply 2): We have modified our text as advised.(see Page 2, line 34-40, line 41-53, line 55-58, and Page 3, line 72-76)

Changes are in the background, methods, results and conclusion parts of the abstract.

- 3) Third, the introduction needs to review what has been known and unknown on the current research focus, analyze the limitations of existing studies, and explain the potential clinical significance of this research focus.

Reply 3): We have modified the introduction as advised.(see Page 4, line 111-131)

Changes are in the introduction parts of the main text.

- 4) Fourth, the methodology of the main text needs to correctly describe the clinical research design, sample size estimation procedures, and how the prognosis outcomes were collected. The statistical analysis needs to report details of Cox regression analysis.

Reply 4): We have modified the methodology of the main text as advised(see Page 5, line 137-143. Page 7, line 229-232.)

- 5) Finally, please consider to cite several related papers: 1. Lian L, Teng SB, Xia YY, Shen XM, Zheng Y, Han SG, Wang WJ, Xu XF, Zhou C. Development and verification of a hypoxia- and immune-associated prognosis signature for esophageal squamous cell carcinoma. J Gastrointest Oncol 2022;13(2):462-477. doi: 10.21037/jgo-22-69. 2. Chen Z, Chen Q, Li S, Tu S, Chen Q, Wang A. IL-12RB1: a novel immune prognostic

biomarker for oral squamous cell carcinoma and linked to PD-1/PD-L1 expression in the tumor immune microenvironment. *Ann Transl Med* 2022;10(3):144. doi: 10.21037/atm-21-6915. 3. Huang B, Shi H, Gong X, Yu J, Xiao C, Zhou B, Liang Z, Li X. Comparison of efficacy and safety between pembrolizumab combined with chemotherapy and simple chemotherapy in neoadjuvant therapy for esophageal squamous cell carcinoma. *J Gastrointest Oncol* 2021;12(5):2013-2021. doi: 10.21037/jgo-21-610. 4. Wu Z, Zheng Q, Chen H, Xiang J, Hu H, Li H, Pan Y, Peng Y, Yao X, Liu P, Sun Y, Li B, Zhang Y. Efficacy and safety of neoadjuvant chemotherapy and immunotherapy in locally resectable advanced esophageal squamous cell carcinoma. *J Thorac Dis* 2021;13(6):3518-3528. doi: 10.21037/jtd-21-340.

[Reply 5\): We have cited several related papers in our text as advised.\(References 14 and 21 and 25\)](#)
