

Dear editors,

We would like to express our sincere gratitude for the insightful feedback on our manuscript titled "Immunohistochemical expression of TIM3 as a prognostic indicator in upper gastrointestinal tract tumors: A meta-analysis" bearing reference 87382. We are deeply grateful to you and the reviewers for the time and effort invested in reviewing our manuscript. After discussions with all co-authors, we have made thorough and meticulous revisions to the manuscript in accordance with the reviewers' suggestions. In the manuscript, we have highlighted the revisions in yellow.

Here is a point-by-point response to the reviewers' comments and concerns.

Response to Reviewer Comments:

Response to Reviewer #1:

1. The meta-analysis about the prognostic survival of TIM3 in upper gastrointestinal tract tumors showed that the high expression of TIM3 in upper gastrointestinal tract cancer is associated with poorer prognosis. However, **in Table 1 of the results, the cancer type needs to be classified according to tumor sites and histologic type first, then ordered according to date in the same category of tumors.**

Response: Thank you very much for your suggestion. We have made the suggested changes in the revised manuscript.

2. In Materials and Methods, data extraction and quality assessment, **data extraction should be described in detail to focus on the important parts such as TNM stages, so as to make the focal contents stand out.**

Response: Thank you for your suggestion. We have provided a detailed description regarding data extraction in subsection 2.3 (Data extraction and quality assessment) of the Materials and Methods section.

3. In the introduction and discussion section, TIM3 was not only expressed in cancer tissue, but also could be detected in serum, **so consider adding recent references about TIM3 in serum if available.**

Response: Thank you for the insightful suggestion. We have added references regarding TIM3 expression in serum in the first paragraph of the Discussion section.

Response to Reviewer #2:

This study addresses a current topic. The manuscript is quite well written and organized. **English could be improved.** Figures and tables are comprehensive and clear. The introduction explains in a clear and coherent manner the background of this study.\* Introduction section: although the authors correctly included important papers in this setting, **we believe the systemic treatment scenario for gastric cancer should be further discussed in the Introduction section and some recently published papers added ( PMID: 36633661; PMID: 33508962; PMID: 35031442 ; PMID: 33916206 ), only for a matter of consistency.** We think it might be useful to introduce the topic of this interesting study.

Response: Thanks for your support and suggestions. We have further improved the language in the revised manuscript. In the Introduction section, we have cited additional studies to enrich the background information.

\* Discussion section: Very interesting and timely discussion. Of note, **the authors should expand the Discussion section, including a more personal perspective to reflect on. For example, they could answer the following questions - in order to facilitate the understanding of this complex topic to readers: what potential does this study hold? What are the knowledge gaps and how do researchers tackle them? How do you see this area unfolding in the next 5 years?** We think it would be extremely interesting for the readers. However, we think the authors should be acknowledged for their work. In fact, they correctly addressed an important topic, the methods sound good and their discussion is well balanced. **One additional little flaw: the authors could better explain the limitations of their work, in the last part of the Discussion.**

Response: Your suggestion is sincerely appreciated. We have added the corresponding paragraphs 4, 5, 6, and 7 to the Discussion section.

**We suggest a linguistic revision and the addition of some references for a matter of consistency. Moreover, the authors should better clarify some points.**

Response: Thank you very much for your suggestions. We have revised the language

and have cited additional studies in the Discussion section to ensure consistency.

We sincerely look forward to your valuable feedback on our submissions and are happy to respond to any further queries or suggestions you may have. We hope that our revised manuscript will be published in your journal. It would be a great honor for us.

Thank you very much! Best wishes!

Yours sincerely,

Zhi-Wei Zhang