

Answering reviewers' comments

Dear Editors and Reviewers:

Thank you very much for your letter and for the reviewers' comments concerning our manuscript entitled "Immunotherapy of Gastric cancer: Present status and future perspectives." Those comments are very helpful for revising and improving our paper.

We have studied comments carefully and have made corrections which we hope meet with approval. The process of change was highlighted with yellow color in the revised manuscript, and I also recorded the paragraph that was changed for this question in each response. The main corrections in the paper and the responses to the reviewer's comments are as follows:

Responds to the Reviewer #1's comments:

- 1. Given the title "Immunotherapy of Gastric cancer: Present status and future perspectives.", readers would expect the content to mainly cover the current status and potential future developments of gastric cancer immunotherapy. However, the provided paragraphs touch on various aspects beyond immunotherapy, including epidemiology, pathophysiology, and other treatment strategies of gastric cancer. While these contents are important for readers to comprehensively understand gastric cancer, they can be confusing and divert attention from the main focus on immunotherapy. In addition, there does not seem to be sufficient coverage on the details of the present situation and future of immunotherapy, which may disappoint readers. Hence, I agree the structure of the paper needs refinement to make it more coherent and targeted. It would be helpful to first briefly introduce the epidemiology and pathophysiology of gastric cancer, then thoroughly discuss the status quo of gastric cancer immunotherapy, including current treatment methods, efficacy, and existing issues, before exploring likely developmental trends and research directions moving forward. Other treatment strategies can be mentioned as references where appropriate but should not dominate.**

Answer

*The invitation of the editorial board of the Journal was to write an editorial based on the published article **Advances and key focus areas in gastric cancer immunotherapy: A comprehensive scientometric and clinical trial review (1999-2023)**. Since the main topic of the published article was related to immunotherapy of gastric cancer we thought that this should be the main topic of the editorial along with a reference to the very interesting current data on the changing epidemiology and etiopathogenesis of the disease. We felt that the topic of treatment should also be discussed but with more emphasis on immunotherapy. Based on the above considerations and within the short time allowed by the editorial board for the revision of the article we made a revision of the title of the editorial proposing the title "Gastric Cancer: epidemiology, pathogenesis and treatment strategies with emphasis on immunotherapy". Subsequently we revised several sections of the article referring to the reviewer's proposed changes such as current treatment methods, efficacy, and existing issues that are mentioned subsequently.*

- 2. While the paper provides an in-depth introduction of the different types and methods of immunotherapy for gastric cancer, including immune checkpoint inhibitors and cell-based therapies, the analysis of the specific efficacy, advantages and limitations of these therapies is insufficient. More in-depth discussion is needed on the mechanisms of immunotherapy and practical applications of biomarkers, especially regarding immune checkpoint inhibitors and interactions with the unique tumor microenvironment in gastric cancer.**

Answer

Based on the reviewer's suggestions we proceeded to a more extensive discussion of the mechanisms of immunotherapy as well as the practical applications of biomarkers, such as immune checkpoint inhibitors and interactions with the tumor microenvironment.

- 3. The paper does not thoroughly review some of the most recent immunotherapy strategies such as non-specific immune modulators and tumor vaccines. Enriching the discussion with these emerging areas will broaden and deepen the scope of the paper, thus providing a more**

comprehensive overview of the current state of cancer immunotherapy. I would suggest the author expand the literature review to include recent advancements in various aspects of immunotherapy: for example, novel tumor vaccine methods such as oncolytic virus vaccines and cutting-edge areas like neoantigen-based personalized vaccines.

Answer

In the revised paper we included the theoretical part of the non-specific immune modulators, oncolytic virus vaccines, and neoantigen-based personalized vaccines.

4. **Regarding the use of technical terminology, I recommend the author provide brief explanations or definitions when specialized terms first appear, to aid comprehension for non-expert readers. For example, “cytokine-induced killer (CIK) cells”, “chimeric antigen receptor T cell (CAR-T cell) therapy”, and other concepts should be explained on their maiden appearance - clarifying what they are and their roles and significance in gastric cancer immunotherapy.**

Όσον αφορά τη χρήση τεχνικής ορολογίας, συνιστώ στον συγγραφέα να παρέχει σύντομες εξηγήσεις ή ορισμούς όταν εμφανίζονται για πρώτη φορά εξειδικευμένοι όροι, για να βοηθήσουν στην κατανόηση των μη ειδικών αναγνωστών. Για παράδειγμα, «κύτταρα δολοφονίας που προκαλούνται από κυτοκίνη (CIK), «θεραπεία χιμαιρικού αντιγονικού υποδοχέα T-λεμφοκυττάρων (CAR-T cell)» και άλλες έννοιες θα πρέπει να εξηγηθούν στην παρθενική τους εμφάνιση - διευκρινίζοντας τι είναι και τους ρόλους και τη σημασία τους σε ανοσοθεραπεία καρκίνου του στομάχου.

Answer

In the various parts of the article, the specialized terms were briefly explained and their role in GC immunotherapy was clarified. In addition, we have included an aggregated list of abbreviations used in this article.

5. **For consistency, the format of the cited references should be uniform throughout. Additionally, please verify that all referenced sources are**

accurate and contain no errors. I noticed some references are missing the digital object identifier (DOI) or PubMed ID (PMID).

Answer

A detailed review of the literature was carried out with regard to the accuracy and correctness of the bibliographic references.

Reviewer #2:

This is a very well written Editorial concerning the recently published paper of Li YN et al. entitled "Advances and key focus areas in gastric cancer immunotherapy: A comprehensive scientometric and clinical trial review (1999-2023)" in the World Journal of Gastroenterology. In present Editorial, the author discusses the conservative treatment (chemotherapy) of the various forms of gastric cancer. Special attention is given to modern therapeutic approaches with emphasis on immunotherapy which seems to be the future of GC treatment, especially in combination with chemotherapy. In this Editorial, the authors give their suggestions for immunotherapy of Gastric cancer.

Answer:

Thank you very much for your comments.

Reviewer #3:

Thank you for inviting me to evaluate the editorial titled "Immunotherapy of Gastric cancer: Present status and future perspectives". In this editorial, they briefly described the recent data concerning the epidemiological parameters of gastric cancer (GC) in different countries, attempting to give an interpretation based on the etiological factors involved in the etiopathogenesis of the neoplasm. Then they briefly discussed the conservative treatment (chemotherapy) of the various forms of this malignant neoplasm. Special attention was given to modern therapeutic approaches with emphasis on immunotherapy which seems to be the future

of GC treatment, especially in combination with chemotherapy. Then they commented on the article by Li YN et al. entitled "Advances and key focus areas in gastric cancer immunotherapy: A comprehensive scientometric and clinical trial review (1999-2023)" published in the recent issue of the World Journal of Gastroenterology. Finally, they believed the trends in clinical trials were the discovery of new biomarkers and the investigation of more specific treatment options, and the combination of several therapeutic agents will constitute future therapeutic strategies. The paper is well arranged and the logic is clear. The cited literature is comprehensive and modern. The quality of language of the manuscript is acceptable for me. So, I recommend that this manuscript may be accepted after minor revision. There are some advices for the authors:

- In "1.1. Incidence-prevalence"

The Incidence of gastric cancer in China may affect the conclusion of this part is not discussed, although this part was mentioned in the introduction.

Answer:

We thank the reviewer for his constructive comments. Concerning the incidence of GC in China we added the relevant data (marked in yellow in the revised paper).

- In "4.TREATMENT MODALITIES"

Targeted therapy of gastric cancer is not sufficiently discussed. For example, targeted therapy of claudin18.2 needs to be supplemented.

Answer:

The relevant part of the paper was expanded to include also claudin18.2 targeted therapy (marked in yellow in the revised paper).