Author’s response to reviews

Title: Application effect of apatinib in patients with failure of standard treatment for advanced malignant tumours

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Author’s response to reviews:

Dear Editor:

Based on the comments we received, the manuscript was carefully revised, and also checked the references. We must thank you and all other reviewers for the critical feedback. We feel lucky that the valuable comments helped us with the improvement of our manuscript. Please do forward our heartfelt thanks to these experts.

Below you will find our point-by-point responses to the comments/questions:

1. Please provide a List of abbreviations after the Conclusions section. If abbreviations are used in the text, they should be defined in the text at first use and included in this list.

Abbreviations:

VEGF: Vascular Endothelial Growth Factor

VEGFR: Vascular Endothelial Growth Factor Receptor

GC: Gastric Cancer

PD: Progressive Disease

ECOG: Eastern Cooperative Oncology Group

RECIST: Response Evaluation Criteria in Solid Tumours
SD: Stable Disease

PR: Partial Response

CR: Complete Remission

ORR: Objective Response Rate

DCR: Disease Control Rate

PFS: Progression-free survival

ABCB1: ATP-binding cassette subfamily B member 1 transporter gene

MRP1: Multidrug Resistance Associated Protein 1

BCRP: Breast Cancer Resistance Protein

We have already added the abbreviations as required. These can be seen after the Conclusions section, on page 13 (Abbreviations section).

2. Thank you for including the supplemental file containing information regarding your ethics approval. However, in the Ethics approval section of your Declarations, please provide the full name of the committee that approved this study and a reference number if appropriate. Please then remove the Ethics supplemental file and also remove the statement regarding treatment of animals, as no animal experiments were conducted during your study.

We have revised the Ethics approval and consent to participate part according to the regulations: “This article was approved by the Ethics Committee of the Cancer Hospital of Harbin Medical University.” These can be seen on page 14 (Ethics approval and consent to participate section).

3. In the same section, please clarify whether consent obtained from participants was written or verbal. If the consent was verbal please include reasoning for this and state if an ethics committee approved this method of obtaining consent.

As a post-third-line treatment, to date, apatinib has shown positive results in multiple tumours, such as gastric cancer, breast cancer, lung cancer, oesophageal cancer and other cancers. This study focused on the short-term efficacy and adverse effects of apatinib in patients with multiple malignancies with failure after standard treatment, and the study mainly needs to collect case information and data from patients with advanced malignant tumors after treatment, and does not increase the patients’ pain. The patient is treated strictly in accordance with the drug instructions during treatment and sign an informed document. Based on the principles of voluntary and informed consent, and will maximize the protection of patients' rights and privacy.
The following are the drug instructions and informed consent.

4. Please note that the Consent for publication statement refers to consent obtained to include any individual person’s data in any form (including individual details, images or videos). Therefore, please state "Not applicable" in this section as no personal information is provided in your manuscript. The statement regarding authors’ approval of the final manuscript should instead be included in the Authors’ contributions section of the Declarations.

We have stated "Not applicable" in this Consent for publication section. And the statement regarding authors’ approval of the final manuscript have been included in the Authors’ contributions section of the Declarations. These can be seen on page 14 (Consent to publication section).

5. In the Authors' contributions section, please refer to all authors by their initials rather than full names.

We have made changes as required, thank you for your guidance. These can be seen on page 14-15 (Authors' contributions section).

6. In your Funding section, please also state the role of the funding body in the design of the study; collection, analysis, and interpretation of data; and in writing the manuscript.

This study was part of the Program on The Haiyan Research Fund Youth Project of Harbin Medical University Cancer Hospital (Grant No. JJQN2019-14). Funds are mainly analytical and statistical data in research design, language editing, and finally completed the manuscript.

7. Please remove your response to the reviewers from the main manuscript.

We have removed the response to the reviewers from the main manuscript as requested.

8. Please remove the supplementary declarations, cover letter, title page, and editorial certificate files from the file inventory, as they are no longer needed at this stage of the editorial process.

We have removed the supplementary declarations, cover letter, title page, and editorial certificate files from the file inventory as requested, thank you for your editing.

9. We kindly ask that you please remove the last sentence from the Acknowledgements, as this section should only include contributors who do not meet the criteria for authorship.

We have removed the last sentence from the Acknowledgements, thank you for your suggestions and tips. These can be seen on page 15 (Acknowledgements section).
10. While assessing your manuscript in-house, we found several instances where the text displayed similarities to text found in other previously published sources. While we understand that you may wish to express some of the same ideas contained in these publications, please be aware that we cannot condone the use of text from previously published work. We would therefore be grateful if you could reformulate the sections listed below to resolve the overlap between your manuscript and other sources. Please ensure that, where relevant, these sources are also referenced as appropriate:

Background:

Pg. 3, lines 16-25


The content that needs to be changed has been modified to “Cancer is the leading cause of death in China. It is also a major public health issue. Due to the large population of China, an aging population and an unhealthy lifestyle. It is expected that the incidence and mortality of cancer will increase significantly.”

The newly modified content can be seen on the page 3. lines 16-23 (Background section).

Pg. 3, lines 35-45 & pg. 4, lines 40-52


The content that needs to be changed has been modified to “In recent years, clinical scholars have proposed targeted therapy. Unlike previous surgery, radiotherapy and chemotherapy, targeted therapy has highly efficient and selective, which can greatly reduce toxic side effects and bring new hope to patients with recurrent tumors. With the rapid development of molecular biology, targeted anticancer drugs has gradually become a research hotspot for clinical scholars.”

“Currently, apatinib has been experimentally studied in different types of cancer. The results confirmed that apatinib is an effective method for the treatment of malignant tumors. Moreover, related experiments show that apatinib is superior to other anti-angiogenic drugs and has good safety. Therefore, apatinib may be an effective treatment for different advanced cancers.”

The newly modified content can be seen on the page 3, lines 35-45 & page. 4, lines 40-48 (Background section)

Discussion:

Pg. 10, lines 42-51 & pg. 11, lines 2-21
The content that needs to be changed has been modified to “With the development of precision medicine and in-depth research on cancer, targeted therapy is expected to become a new breakthrough point in the treatment of malignant tumors. Now there are some targeted drugs applied to clinical treatment, and combined with other treatment methods, which will provide a new therapeutic concept for the standard treatment of many malignancies.” “Apatinib is one of most promising antiangiogenic target drugs. Currently, apatinib has been experimentally studied in different types of cancer. The results confirmed that apatinib is an effective method for the treatment of malignant tumors. Apatinib combined with chemotherapy or targeted therapy may further improve the clinical efficacy. Moreover, related experiments show that apatinib is superior to other anti-angiogenic drugs and has good safety. Therefore, apatinib is reasonable and effective for the treatment of different advanced cancers.”

The newly modified content can be seen on the page 10, lines 42-53 & page. 11, lines 2-17 (Discussion section)

Thank you very much for your suggestion, we have carefully reviewed and revised the duplicates.

11. At this stage, please upload your manuscript as a single, final, clean version that does not contain any tracked changes, comments, highlights, strikethroughs or text in different colors. All relevant tables/figures/additional files should also be clean versions. Figures (and additional files) should remain uploaded as separate files.

We have uploaded the manuscript as required. Thank you very much for your suggestion and make my manuscript more perfect. We really want to publish this article in BMC Pharmacology and Toxicology. This will be our pleasure. Thank you.