

Peer Review File

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Response to the comments of Reviewer A

Comment 1: It is important to score the causality of the potential effect to the the drug. Please use some standard causality listings like the Naranjo scale

Reply 1: We thank the reviewer for pointing out this issue. We indeed should have applied some standard causality listings to score the causality of the potential effect to the the drug. Now, we have evaluated the possible causal relationship between adverse events and drugs with reference to the Naranjo probability scale, which is evaluated as probable, and the specific details are shown in supplementary Table 1.

Changes in the text: see Page 4, line 80-83 and Supplementary Table 1.

Comment 2: Please also complete the manuscript wit other risk factors for aortic dissection like smoking history or Marfan syndrome

Reply 2: Thank you for your comment. We have added this part according to your suggestion.

Changes in the text: see page 3, Line 53-55.

Comment 3: It is important to explain to the readers why there might be a difference in the occurrence of this important side effect and the use of VEGF antibodies versus TKIs

Reply 3: VEGF and VEGFR, PDGFR, c-Kit and FGFR1-4 expressed on the surface of vascular endothelial cells play an important role in maintaining the development and stability of vascular endothelial cells. VEGF antibodies mainly antagonizes VEGF, for example, bevacizumab is a specific inhibitor of VEGF-A; VEGFR-TKIs is usually a multi-target inhibitor that can target VEGFR1/2/3, PDGFR, c-Kit, FGFR1-4, such as fruquintinib can selectively target VEGFR1/2/3. Different targets and degrees of antagonism may lead to differences in this side reaction.

Changes in the text: see Page 5, line 89-94.

Comment 4: Whij was chosen to proceed with bevacizumab (VEGF-i) after surgery?

Reply 4: The reason why we continue to use bevacizumab after surgery is that, first of all, the overall treatment of this patient has never stopped antiangiogenic therapy, although we stopped using fruquintinib, but in order to control the progression of the tumor, patients still need to choose antiangiogenic drugs as systemic treatment. In addition, during the reexamination 3 months after operation, the patient's aortic dissection had recovered and the patient had recovered to grade 0 from the point of view of adverse reaction grading, so we chose low-dose bevacizumab according to the patient's previous treatment history. during the treatment of bevacizumab, we also continue to monitor the occurrence of cardiovascular adverse events in patients.

Comment 5: line 77: "and so on": please remove since the important side effects have been summarized

Reply 5: We have modified our text as advised (see Page 1, line 7-8)

Changes in the text: Page 1, line 7-8

Response to the comments of Reviewer B

Comment 1: The suggestion for researchers is to smooth the implication of the drug in the event by describing it as the possible causative agent.

Reply 1: Thank you very much for your comments and advice, we have evaluated the possible causal relationship with reference to the Naranjo probability scale, which is evaluated as probable. And we have revised this relationship.

Changes in the text: see Page 1, line 14-15 and Supplementary Table 1.