Peer Review File

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Reviewer A

Comment 1:The use of Dasatinib was validates for FDA in adult patients from 2005 but not for pediatric patients until 2017. This must be specified in the article.
Reply 1:I'm sorry we didn't choose our words carefully here.In order to determine the time when dasatinib was approved for CML by the US FDA, relevant literature and the US FDA website were searched, and the approval time for CML in children was determined to be November 9, 2017. Adult CML was first approved in the United States and EU in 2006 as mentioned in Reference 3.
Changes in the text: We have modified our text as advised (see Page 4, line 56). Dasatinib was approved in 2006 for the treatment of adult patients with CML. It was not approved for use in children with CML until 2017.

Comment 2:The characteristic toxicities of dasatinib are: Pleural effusion, Pulmonary arterial hypertension and Hematological toxicity (platelet dysfunction) [1, 2]. I do not understand your conclusions. “Compared with adult data, imatinib exhibits stronger correlation signals with pericardial effusion and pulmonary hypertension compared to dasatinib in children” but in your case, and adolescents” but in this case, the patient suffers pulmonary arterial hypertension and pleural effusion when she started treatment with dasatinib.
Reply 2:Thank you for reminding us that we are not clear enough here. What we want to express is that according to the FAERS data collected on OpenVigil, in people under the age of 18 years, the signal related to pericardial effusion of imatinib is stronger than that of dasatinib (this is exactly the opposite of the results in the adult group) . But this does not mean that the safety of dasatinib is better in the minor group. Our case is about adverse reactions such as pericardial effusion caused by dasatinib. Therefore, during the use of TKIs in pediatric patients, we still need to strengthen monitoring, especially pulmonary and cardiovascular toxicity, and promptly intervene in possible serious adverse reactions. At the same time, these adverse reactions should be reported as much as possible to provide more useful pediatric data for minor patients using TKIs.
Changes in the text: We have modified our text as advised (see Page 2, line 29). We express that in pediatric CML patients, dasatinib may not be better than imatinib in terms of safety in causing pericardial effusion, and more pediatric data and more drug monitoring are needed to help select TKIs. and use.

Comment 3:The authors could briefly recall the hypotheses about the pathophysiology by which Dasatinib can produce pleural effusion, such as the inhibition of Src kinase, which is involved in the regulation of vascular permeability and the stability of the pleural epithelium.
Reply 3:Thanks for giving us a good suggestion. Although the exact mechanism of pleural effusion caused by dasatinib is not clear, there are several hypotheses that we will supplement succinctly.
Changes in the text: We have modified our text as advised (see Page 9, line 183). Here we succinctly supplement the three mainstream hypotheses: (1) dasatinib inhibits PDGFR-P, (2) increased pleural and / or pulmonary vascular permeability due to inhibition of SRC family kinases, and (3) allergic or immune-mediated reaction rather than liquid reaction.

Comment 4: Line 351. In the conclusions the following statement could be drafted briefly: “This decision was primarily based on the consideration that while imatinib may not be as effective as dasatinib for this particular patient, no significant adverse events were observed during the initial two years of treatment.”
Reply 4:Thank you for your advice and we will add the reasons for re-selecting imatinib in the conclusion section to make our report more complete.
Changes in the text:We have modified our text as advised (see Page 13, line 261). We explained that the withdrawal of dasatinib and the re-use of imatinib was due to the fact that although the effect of imatinib in this patient was not as good as that of dasatinib, no serious adverse reactions were observed in the first two years.

Reviewer B

Comment 5: In 100-102 lines there are too many world repetitions; please, change the section:” To summarize the experience of diagnosis and treatment of severe adverse drug reactions of dasatinib, in order to improve medical staff's understanding of adverse drug reactions, especially the different characteristics of adverse drug reactions in children and adults.”
Reply 5: Thank you for your suggestion, which has drawn our attention to the deficiencies in the case description section. We will make revisions to focus on pertinent diagnoses and treatments.
Changes in the text: We have modified our text as advised (see Page 5, line 80). Based on the recommendations, we are streamlining the case description to retain essential information, with an emphasis on the diagnosis and treatment of adverse drug reactions.

Comment 6:Please, provide details about CML details including blood count, bcr-abl transcript type, etc.
Reply 6:Thank you for the reminder, we will work on improving the content of this section.
Changes in the text: we added some data about CML details including blood count, bcr-abl transcript type (see Page 6, line 108;Page 7, line 117;Page 8, line 150).

Comment 7:What is the rationale for using imatinib in the first line?
Reply 7:Thank you for your question. The child was diagnosed with CML in February 2017, and at that time, only imatinib was approved for the treatment of this disease. In November 2017, the U.S. FDA approved dasatinib for the treatment of pediatric CML. However, in China, up until now, the CFDA has not officially approved dasatinib for use in pediatric patients. That is why imatinib was chosen for the initial treatment of this child.
Changes in the text: We have modified our text as advised (see Page 9, line 169). We have explained here why imatinib was the initially preferred treatment for the child.

Comment 8: lines 140-141 Why was imatinib started immediately, at the risk of worsening the clinical condition?
Reply 8:Thank you for your inquiry. Based on our analysis of the child's condition, she has experienced severe adverse reactions caused by dasatinib; however, her overall status remains manageable, and her CML treatment is not yet complete. Although the efficacy of imatinib may not be as high as dasatinib, she did not experience any serious adverse reactions during the two years of prior imatinib use. After carefully weighing the pros and cons, and with the intention to intensify monitoring after administering imatinib, we boldly chose to switch to imatinib instead of discontinuing all TKIs.
Changes in the text: We have modified our text as advised (see Page 13, line 261). In this explanation, the reason for reverting to the use of imatinib is due to the absence of severe adverse reactions during previous use, while also considering the continuity of the child's CML treatment.

Comment 9:Line 183, Bosentan to be written in lower case
Reply 9:Thank you for your suggestion, we will make the modification here.
Changes in the text: We have modified our text as advised (see Page 7, line 124).

Comment 10:The main text consists of too many short and concise sentences
Reply 10:Thank you for bringing this to our attention, we will revise this section.
Changes in the text: We have modified our text as advised (see Page 5, line 80).

Comment 11:Please summaries the case description section
Reply 11:Thank you for your suggestion. We will describe this section more concisely and highlight the key points.
Changes in the text: We have modified our text as advised (see Page 5, line 80).

Comment 12:What are your plans on bosentan? will it ever be discontinued?
Reply 12:Thank you for your question. Upon discharge, our doctors discontinued bosentan because the child's pulmonary hypertension was primarily due to pleural effusion related to dasatinib. Once the pleural effusion was resolved, the pulmonary hypertension was also expected to alleviate and return to normal. However, during subsequent follow-ups, an echocardiogram in June 2023, conducted in Sichuan locally, showed a slight increase in pulmonary artery pressure, and the local doctors prescribed bosentan to the child again. But during our follow-up in September 2023, the family reported that they had discontinued bosentan and that the pulmonary hypertension had disappeared.
Changes in the text: We have modified our text as advised (see Page 8, line 148). We have added the discontinuation date of bosentan here.

Comment 13:Please, delete "also known as chronic myelogenous leukemia" in the discussion section
Reply 13:Thank you for your suggestion, we will delete this sentence.
Changes in the text: We have modified our text as advised (see Page 9, line 158).

Comment 14:correct the use of abbreviations, please
Reply 14:Thank you for noticing our irregularity, we will make the necessary amendments.
Changes in the text: We have modified our text as advised (see Page 2, line 26).

Comment 15:In lines 318 319 "Currently, many experts agree on discontinuing dasatinib in patients experiencing adverse reactions such as PAH" needs a reference
Reply 15:Thank you for bringing this to our attention. We have reviewed the relevant literature and made appropriate modifications to our statement. Pulmonary hypertension induced by dasatinib may require treatment with vasodilators, but numerous reports indicate that there is improvement when dasatinib is discontinued on its own.
Changes in the text: We have modified our text as advised (see Page 12, line 224).We have provided the relevant references.

Reference: Orlikow E, Weatherald J, Hirani N. Dasatinib-Induced Pulmonary Arterial Hypertension. Can J Cardiol. 2019 Nov;35(11):1604.
Tamura Y, Tamura Y. Dasatinib-induced Pulmonary Hypertension. Intern Med. 2022 Aug 1;61(15):2245-2246.

Comment 16:Please reformulate the discussion section as it is confusing and difficult to read and understand
Reply 16:Thank you for your suggestions. Our discussion section does seem a bit confusing and we will be reorganizing and consolidating the content.
Changes in the text: We have modified our text as advised (see Page 9, line 167).

Comment 17:Obtaining a deep and sustained molecular response with the aim of discontinuing therapy should be added to the reasons for choosing a TKI
Reply 17:Thank you for your suggestion, and we will include this sentence in our conclusion.
Changes in the text: We have modified our text as advised (see Page 13, line 259).