Peer Review File

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Reviewer A

Comment 1: In the study selection, there are very small RCTs included, of e.g. 10 patients per group. Some of these are not published in regular peer-reviewed journals. I was unable to read some the articles, also because links in de reference list to online resources (rather than regular journal references) did not work. Taken together, I could not verify the quality of some of the studies that this network analysis was based on.

Reply 1: Thank you for highlighting these concerns. We have systematically reviewed and included all studies that met our inclusion criteria to minimize selection bias. All included studies are published in peer-reviewed journals. Some of the online links provided direct access to the articles through Chinese databases. Although some studies have small sample sizes, we have conducted a quality assessment of all included studies, which is available for readers' reference. If necessary, a subgroup analysis based on study quality can be conducted in future.

Comment 2: There is no reporting on cardiovascular toxicity, which could be considered the most relevant adverse effect of second generation TKI

Reply 2: Thank you for your constructive suggestion. We agree on the importance of evaluating cardiovascular toxicity in assessing the overall safety of TKIs. Unfortunately, our initial systematic review revealed a scarcity of sufficient data for a robust statistical comparison of these specific extra-hematological adverse effects across the TKIs studied. This limitation constrains our ability to perform a network meta-analysis on cardiovascular toxicity.

Reviewer B

Comment 1: Add what you considered 'statistically significant' as you mention it at several points.

Reply 1: Thank you for your suggestion. We have clarified the criteria for statistical significance throughout the manuscript.

Changes in the text: We have added a statement in the methods section: “Results were considered statistically significant if the RR value's 95% confidence interval did not include 1.0.” Please see Page 5, line 197-199 in the methods section.

Comment 2: It would be beneficial if you added the p-value for each RR.

Reply 2: Thank you for your suggestion. While we understand the importance of including p-values, we believe that presenting the risk ratios (RR) values along with their 95% confidence intervals provides sufficient information regarding the statistical significance and effect size. This approach ensures clarity and conciseness in our reporting.

Comment 3: The study included drugs that are currently not available for international use, with existing scientific evidence being limited to Asia. This is the case for flumatinib, for which the volume of literature is very limited, and the cited multicenter article only includes representation from a few Asian countries. Therefore, its efficacy and safety need to be confirmed in future studies that include greater racial representation.

At this time, it would not be possible to generalize some of the present results to populations outside of the Asian continent, where this medication has been studied.

A considerable part of the discussion focuses on the results of flumatinib. However, since it is not a globally available medication and the cited studies have limited racial representation, the applicability of the cited literature should be stated as limited. It would be beneficial to clarify this as a limitation of the study so that readers take this information into consideration.

Reply 3: Thank you for your insightful comments. We acknowledge the limitations regarding
the generalizability of flumatinib's results due to its limited availability and the regional focus of existing studies. We have revised the discussion section to emphasize these points and to clarify the limitations of our study.
Changes in the text: We have added a paragraph in the discussion section highlighting the limited availability of flumatinib and the regional focus of existing studies, stating: “Given that flumatinib is not widely available internationally and the existing literature predominantly includes data from a few Asian countries, the applicability of our findings is limited. ” Please see Page 9, line 401-403 in the discussion section.

Comment 4: In line 374, it mentions the following: 'literature from other sources indicated a superior efficacy of flumatinib over imatinib in treating newly diagnosed CP-CML.' The 'other sources' are not cited. Please include the references for your assertion, or if that is not possible, remove that statement.

Reply 4: Thank you for pointing this out. We have addressed this issue by including the appropriate references to support our assertion regarding the superior efficacy of flumatinib over imatinib in treating newly diagnosed CP-CML.
Changes in the text: We have added a statement: “Moreover, a real-world study also indicated a superior efficacy of flumatinib over imatinib in treating newly diagnosed

CP-CML(55).” Please see Page 9, line 392-394 in the discussion section.