

Cardiovascular Events of Bruton's Tyrosine Kinase Inhibitors: A Real-World Study Based on the FDA Adverse Events Reporting System (FAERS) Database

Zeng-xiang Zhao¹, Tian-yi Yang², Yuan-hui Wang¹, Li Zhang³, Li Ji⁴, and Yu-wen Su⁵

¹Department of Clinical Pharmacology, Sir Run Run Hospital, Nanjing Medical University, Nanjing 211166, China

²Hubert Department of Global Health, Rollins School of Public Health, Emory University, Atlanta, Georgia 30329, United States

³Dongfang Hospital, Beijing University of Chinese Medicine, Beijing 100078, China

⁴Department of Clinical Pharmacy, School of Basic Medical Sciences and Clinical Pharmacy, China pharmaceutical university, Nanjing 211198, China.

⁵School of Pharmacy, Nanjing Medical University, Nanjing 211166, China

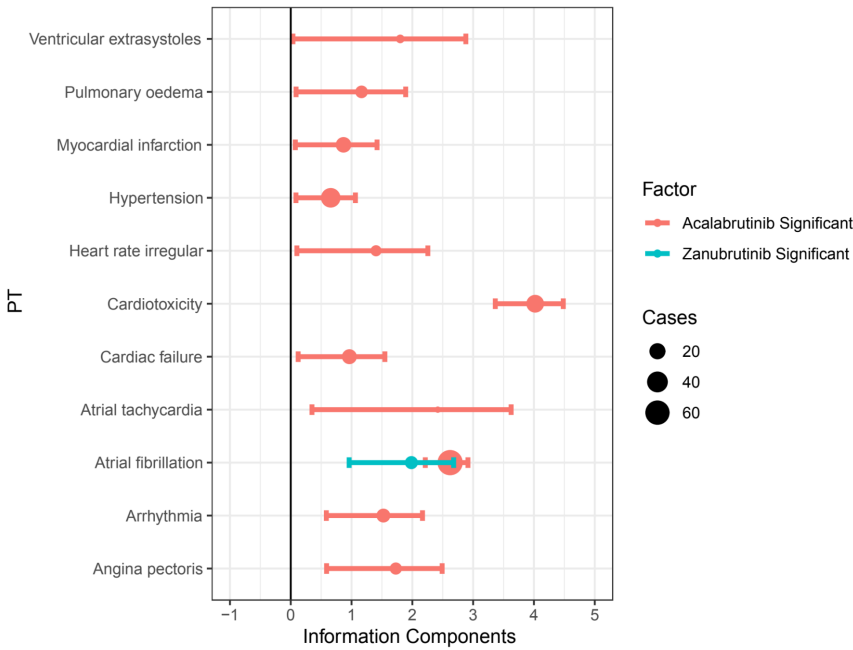
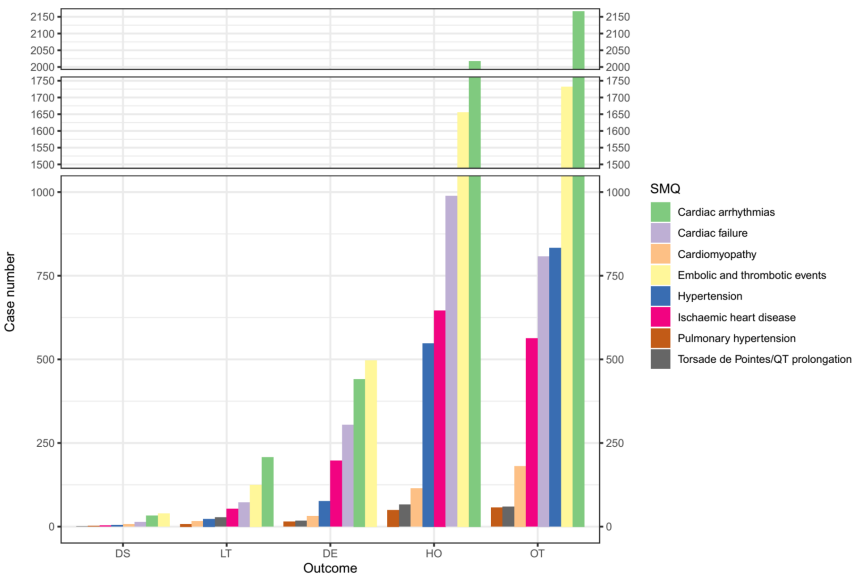
May 7, 2023

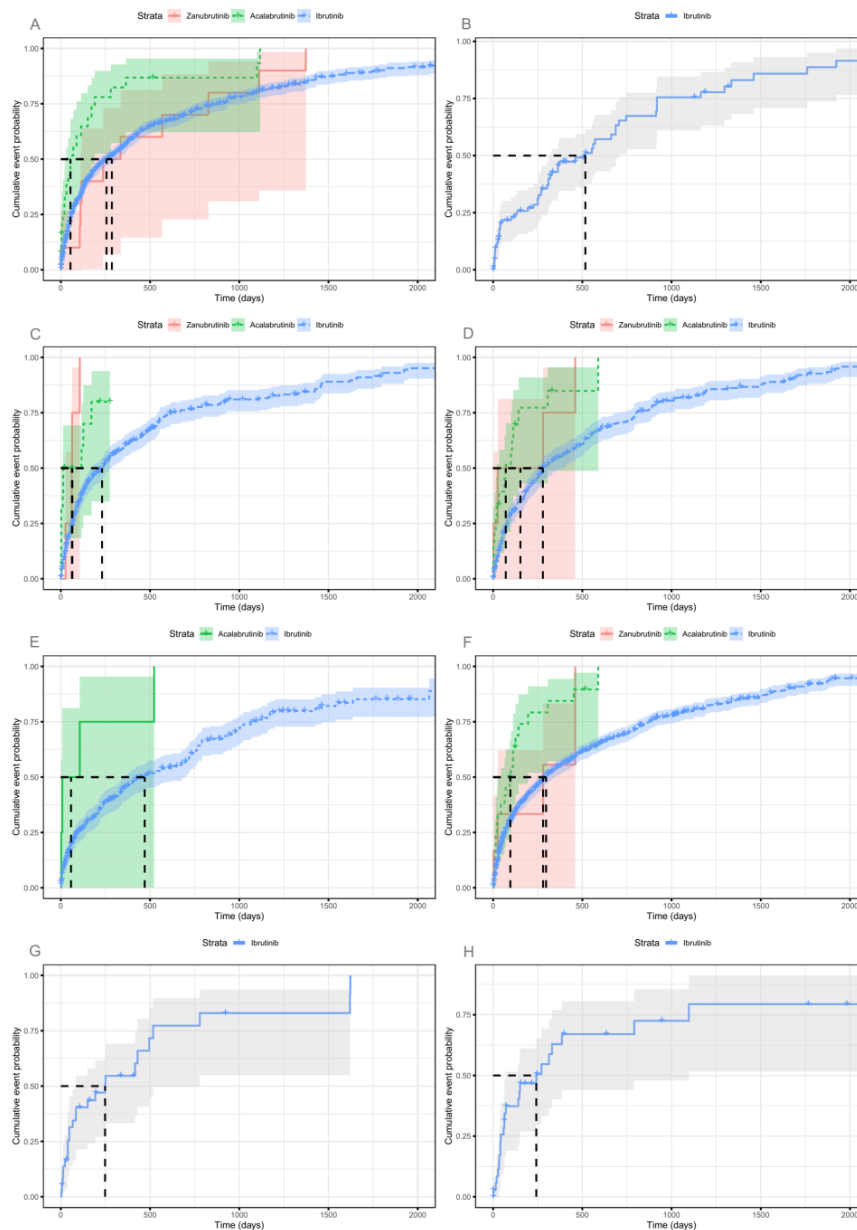
Abstract

Abstract Aims Bruton's tyrosine kinase inhibitors (BTKIs), including first-generation ibrutinib, second-generation acalabrutinib, and zanubrutinib may have certain mechanisms of action (MOAs) related to adverse effects (AEs) on the cardiovascular system. We aimed to evaluate the cardiac AEs of BTKIs reported to the U.S. Food and Drug Administration Adverse Event Reporting System (FAERS) and to compare the differences in cardiovascular toxicity of ibrutinib, acalabrutinib, and zanubrutinib. **Methods** Only primary suspect drugs from the FAERS database were extracted from January 2013 to December 2022 across all indications of FDA-approved BTKIs. Disproportionality was measured by reporting odds ratios (RORs) and information components (ICs). An additional disproportionality analysis was also performed from January 2020 to December 2022. **Results** A total of 10,353 cases involving ibrutinib, acalabrutinib and zanubrutinib were included. Ibrutinib was significantly associated with the incidence of cerebrovascular accidents, myocardial infarction and other thrombotic events. Acalabrutinib was associated with new signals, including cardiac failure, ventricular extrasystoles, pulmonary edema and angina pectoris, and hypertension and myocardial infarction were found in additional analyses. Furthermore, acalabrutinib was characterized by a much earlier onset of cardiovascular events. Only atrial fibrillation was associated with zanubrutinib use. Acalabrutinib and zanubrutinib had lower ROR values for cardiac AEs, and fewer signals for these two drugs compared with ibrutinib. **Conclusion** This study indicated that new AEs were not clearly noted on the label for acalabrutinib. It is suggested that the cardiovascular risks of BTKIs remain a concern and worth attention as next-generation BTKIs are discovered and developed.

Hosted file

Manuscript.docx available at <https://authorea.com/users/615430/articles/641860-cardiovascular-events-of-bruton-s-tyrosine-kinase-inhibitors-a-real-world-study-based-on-the-fda-adverse-events-reporting-system-faers-database>





Hosted file

Table 1.docx available at <https://authorea.com/users/615430/articles/641860-cardiovascular-events-of-bruton-s-tyrosine-kinase-inhibitors-a-real-world-study-based-on-the-fda-adverse-events-reporting-system-faers-database>

Hosted file

Table 2.docx available at <https://authorea.com/users/615430/articles/641860-cardiovascular-events-of-bruton-s-tyrosine-kinase-inhibitors-a-real-world-study-based-on-the-fda-adverse-events-reporting-system-faers-database>

Hosted file

Table 3.docx available at <https://authorea.com/users/615430/articles/641860-cardiovascular-events-of-bruton-s-tyrosine-kinase-inhibitors-a-real-world-study-based-on-the-fda-adverse-events-reporting-system-faers-database>

Hosted file

Table 4.docx available at <https://authorea.com/users/615430/articles/641860-cardiovascular-events-of-bruton-s-tyrosine-kinase-inhibitors-a-real-world-study-based-on-the-fda-adverse-events-reporting-system-faers-database>

Hosted file

Table 5.docx available at <https://authorea.com/users/615430/articles/641860-cardiovascular-events-of-bruton-s-tyrosine-kinase-inhibitors-a-real-world-study-based-on-the-fda-adverse-events-reporting-system-faers-database>

Hosted file

Table 6.docx available at <https://authorea.com/users/615430/articles/641860-cardiovascular-events-of-bruton-s-tyrosine-kinase-inhibitors-a-real-world-study-based-on-the-fda-adverse-events-reporting-system-faers-database>