

Number of patients needed to treat to prevent one atrial fibrillation event with zanubrutinib versus ibrutinib and acalabrutinib in B-cell malignancies

Authors: Talha Munir¹, Paolo Sportoletti², Leyla Mohseninejad³, Lianne Barnieh³, Tushar Srivastava⁴, Kate Ren⁴, Wassim Aldairy³, Ayad K. Ali³, Keri Yang³, Rhys Williams³, Joe-Elie Salem⁵

Affiliations: ¹ Leeds University, Leeds, UK; ² University Degli Studi di Perugia, Perugia, Italy; ³ BeOne Medicines Ltd, San Carlos, USA; ⁴ ConnectHEOR, London, UK; ⁵ Sorbonne Université, Paris, France

ABSTRACT

Introduction

Bruton tyrosine kinase inhibitors (BTKis) are used for the treatment of B-cell malignancies. Second generation (acalabrutinib) and next generation (zanubrutinib) BTKis have demonstrated improved cardiovascular safety profiles compared to first-generation BTKi, ibrutinib. A recent systematic review and network meta-analysis of randomized controlled trials by Alqassas et al. (*JACC*. 2025) assessed the cardiovascular risk of BTKis and reported significantly higher odds of atrial fibrillation (AFib) with either ibrutinib or acalabrutinib compared to zanubrutinib. AFib remains an event of concern for practicing hematologists, thus, this study estimated the number of patients needed to treat (NNT) with zanubrutinib, compared to ibrutinib and acalabrutinib, to prevent one AFib event in patients with B-cell malignancies.

Methods

To estimate the NNT, a two-step approach was considered. First, the baseline incidence probability of AFib with zanubrutinib was determined. This was derived from a safety analysis by Moslehi et al. (*Blood Adv*. 2024), which pooled the safety data from ten clinical trials and a total of 1550 patients treated with zanubrutinib. The cumulative incidence probability of all-grade AFib was estimated at 4.5% (95% confidence interval [CI]: 3.5% to 5.5%). Odds ratios (ORs) for AFib were then taken from Alqassas et al. (2025) for zanubrutinib versus ibrutinib (OR: 3.5; 95% CI: 2.35 to 5.22) and zanubrutinib versus acalabrutinib (OR: 2.06; 95% CI: 1.13 to 3.77). These ORs were then applied to the incidence probability of AFib with zanubrutinib to calculate the absolute risk difference (ARD) versus ibrutinib and acalabrutinib. NNT was then calculated based on ARDs. To test the robustness of the findings, probabilistic sensitivity analyses (PSA) were conducted, where the 95% CI of the NNT was also estimated based on Monte Carlo simulation methodology.

Results

The analysis estimated an NNT of 11 for zanubrutinib versus ibrutinib, meaning that treating 11 patients with zanubrutinib instead of ibrutinib would prevent one AFib event. For the comparison versus acalabrutinib, treating 24 patients with zanubrutinib instead of acalabrutinib would prevent one AFib event. The PSA yielded consistent findings with the base case versus both ibrutinib (estimated as 11; 95% CI: 9 to 14) and acalabrutinib (estimated as 24; 95% CI: 14 to 47).

Conclusions

This NNT analysis demonstrates the clinical value of zanubrutinib in reducing the risk of AFib compared to both ibrutinib and acalabrutinib in patients with B-cell malignancies. This is an important consideration in clinical decision making where cardiovascular safety is a priority. Study findings should be interpreted within the context of the limitations including possible differential follow-up across studies, which may impact the incidence of AFib over time.