Breaking BTK, Not Hearts:
Cardiac Safety Review With Covalent and Non-Covalent BTK Inhibitors

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INTRODUCTION

- CLL is the most common leukemia in older adults and increasingly treated with targeted therapies that are generally better tolerated than conventional chemoimmunotherapy.
- **Pirtobrutinib**, a non-covalent Bruton tyrosine kinase inhibitor (BTKi), was recently FDA approved for relapsed/refractory CLL/SLL after prior covalent BTKi therapy and may demonstrate a more favorable cardiovascular safety profile compared with covalent BTK inhibitors.

AIM

To characterize and compare reported cardiac adverse events among BTK inhibitors used in CLL using the FDA Adverse Event Reporting System (FAERS) database.

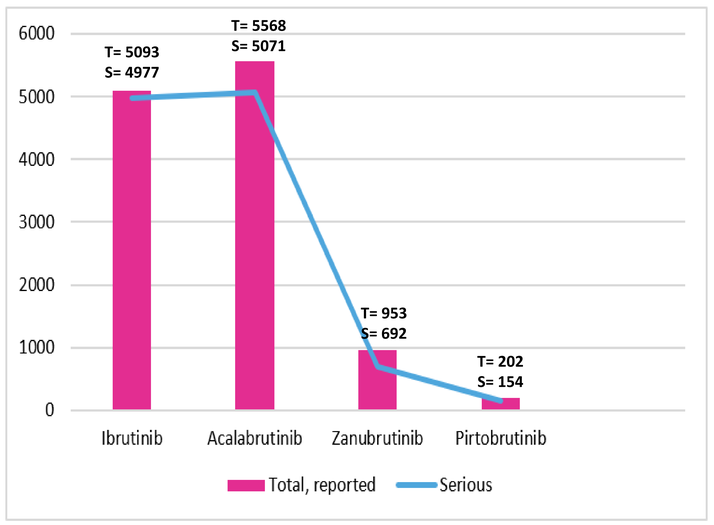
METHOD

- A pharmacovigilance review was conducted using FAERS data from 2013–2026.
- Individual drug reports for ibrutinib, acalabrutinib, zanubrutinib, and pirtobrutinib were filtered to include adult patients (≥18 years) with CLL as the reported indication.
- Cardiac adverse events and serious outcomes were analyzed and compared across agents.

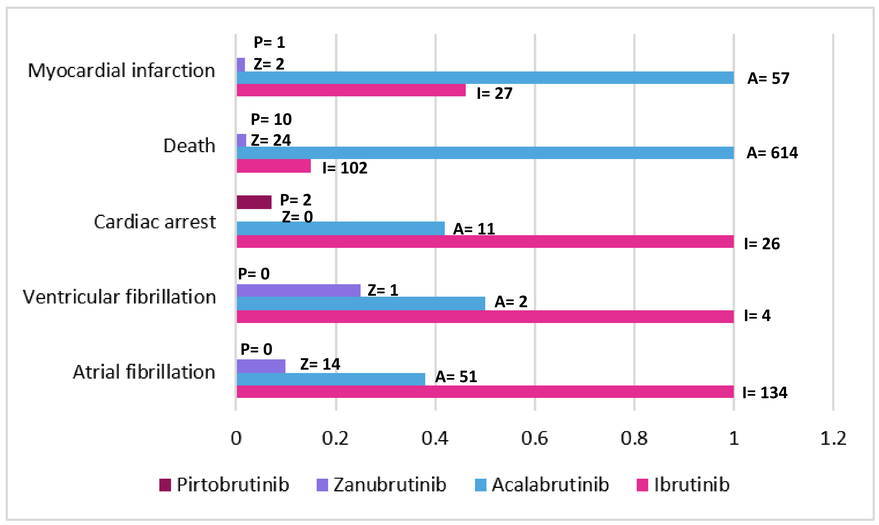
CONCLUSIONS

- Covalent BTK inhibitors demonstrated a substantially greater cardiac adverse event reporting burden compared with pirtobrutinib.
- These findings should be interpreted cautiously given pirtobrutinib's more recent introduction and shorter real-world exposure duration.
- Continued post-marketing surveillance is needed to better define the long-term cardiovascular side effects.

RESULTS



GRAPH 1: Total reported and serious side effects by drug - *The graph shows the number of total reported side effects for the four study drugs, with the line graph indicating the number of serious side effects reported for each drug.*



GRAPH 2: Major cardiac side effects reported for each drug - *The graph shows the number of major cardiac side effects reported for four drugs. The values have been normalized to a scale of 0 to 1 to allow for easier visual representation and comparison.*

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