

Zanubrutinib Demonstrates Superior Outcomes Over Ibrutinib and Acalabrutinib in High-Risk Relapsed/Refractory CLL: A PRISMA-Based Systematic Review and Meta-Analysis

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INTRODUCTION

- High-risk R/R CLL (del(17p), TP53 mutation, unmutated IGHV, bulky disease) remains challenging to treat.
- Zanubrutinib is a next-generation BTKi with demonstrated efficacy in CLL.
- Comparative outcomes versus ibrutinib and acalabrutinib in high-risk R/R CLL remain incompletely defined.

AIM

To compare the efficacy and safety of zanubrutinib versus ibrutinib and acalabrutinib in high-risk R/R CLL.

METHOD

- PRISMA-based systematic review & meta-analysis
- 7 studies: 3 RCTs + 3 indirect comparisons + 1 pairwise meta-analysis
- Outcomes: PFS, ORR, CR, OS, adverse events
- Random-effects inverse-variance model
- Evidence certainty assessed using GRADE

CONCLUSIONS

Zanubrutinib demonstrated superior PFS, response rates, and safety compared with ibrutinib in high-risk R/R CLL. Indirect evidence favored zanubrutinib over acalabrutinib for PFS and CR; however, direct head-to-head trials are needed.

RESULTS

Zanubrutinib vs Ibrutinib

- PFS:** HR **0.60** (95% CI 0.47–0.77)
- del(17p)/TP53:** HR **0.51** (95% CI 0.33–0.78)
- ORR:** OR **1.65** (95% CI 1.15–2.37)
- CR:** OR **1.66** (95% CI 1.11–2.49)
- Atrial fibrillation:** RR **0.30** (95% CI 0.19–0.48)
- AE-related discontinuation:** RR **0.45** (95% CI 0.27–0.75)

Zanubrutinib vs Acalabrutinib

- PFS:** HR **0.60** (95% CI 0.45–0.80)
- CR:** OR **2.89** (95% CI 1.13–7.43)

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