Comparative Safety and Efficacy of BTK inhibitors for Patients with Treatment-Naive vs. Relapsed/Refractory Chronic Lymphocytic Leukemia/Small Lymphocytic Lymphoma: A Systematic Review and Network Meta-Analysis of Randomized Controlled Trials

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Introduction

Bruton's tyrosine kinase (BTK) inhibitors have transformed the therapeutic landscape of chronic lymphocytic leukemia (CLL) and small lymphocytic lymphoma (SLL). With the availability of multiple BTK inhibitors and their use in both treatment-naïve and relapsed/refractory (R/R) settings, direct head-to-head evidence remains limited. role of different BTK inhibitors in CLL/SLL management.

Aim

To conduct a systematic review and network meta-analysis (NMA) provides a robust framework to integrate evidence across randomized controlled trials (RCTs), enabling both direct and indirect comparisons. By synthesizing efficacy and safety outcomes, this approach helps clarify the comparative

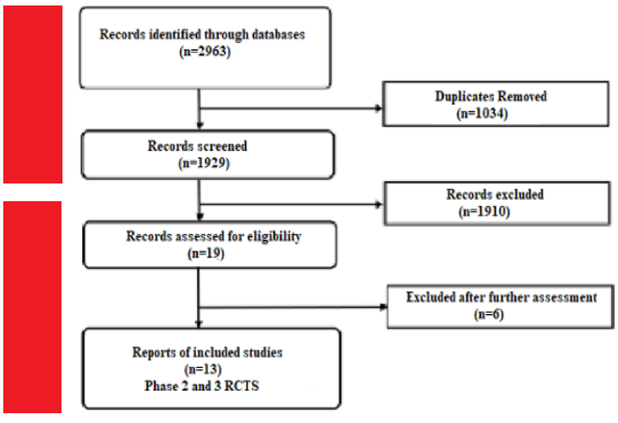
Objectives

To conduct an NMA for the indirect comparisons of progression free survival (PFS), overall survival (OS), Adverse events (AE), and objective response rate (ORR) among BTK inhibitors for CLL/SLL.

Methods

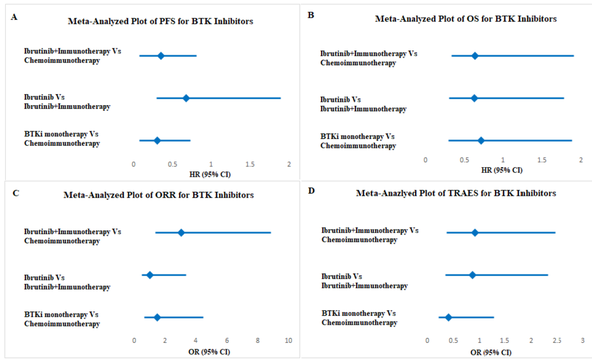
We performed a Bayesian NMA of 13 randomized controlled trials (n=6,763),We used the random effects model for main analysis and node-splitting for consistency checking. We assessed PFS, OS, ORR, and Aes. Surface under the curve ranking (SUCRA) was used for ranking treatments according to each outcome. Subgroup meta-regression (SMR) compared drug performance between TN and R/R patients.

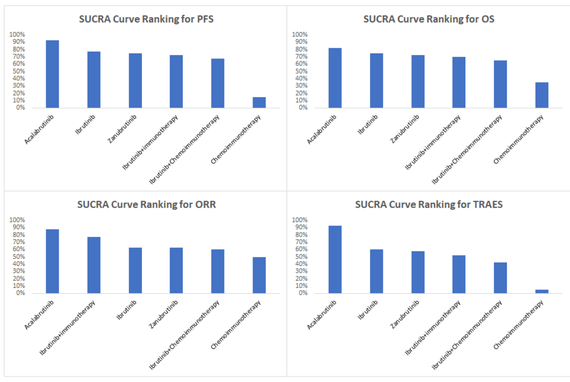
Identification of Studies through Record



Results

Acalabrutinib ranked highest across OS (HR=0.60, 95% CI: 0.42–0.85), PFS (HR=0.31, 95% CI: 0.22–0.42), ORR (OR=2.05, 95% CI: 1.30–3.25), and AE (OR=0.14, 95% CI: 0.09–0.22). Ibrutinib + Chemoimmunotherapy showed the poorest outcomes across all profiles. Subgroup analysis showed that TN patients derived significantly greater clinical benefit and fewer toxicities from BTKi therapies than R/R patients, as shown by the Interaction effect of (+0.44) for PFS, by acalabrutinib. Notably, Ibrutinib and Zanubrutinib demonstrated superior outcomes in TN cohorts, while efficacy was attenuated and toxicity increased in R/R populations.





Discussion

BTKi therapies—particularly acalabrutinib—outperform other BTKi and chemoimmunotherapy in both efficacy and safety, with TN patients experiencing more favourable outcomes. These findings show the importance of individualised treatment selection based on disease status and suggest that early use of selective BTKi may offer optimal benefits.

References

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