INFECTIOUS COMPLICATIONS IN CLL/SLL PATIENTS RECEIVING BRUTON TYROSINE KINASE INHIBITORS – SYSTEMATIC REVIEW AND META-ANALYSIS OF RANDOMIZED CONTROLLED TRIALS

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Introduction

The development of Bruton Tyrosine Kinase inhibitors (BTKis) has revolutionized the management of chronic lymphocytic leukemia/small lymphocytic lymphoma (CLL/SLL). However, increased infection rates have been reported in patients receiving BTKis.

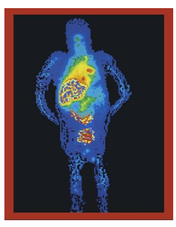
Aim

This study aimed to evaluate the risk of infections associated with BTKis compared to other therapeutic regimens in CLL/SLL patients.

Objectives

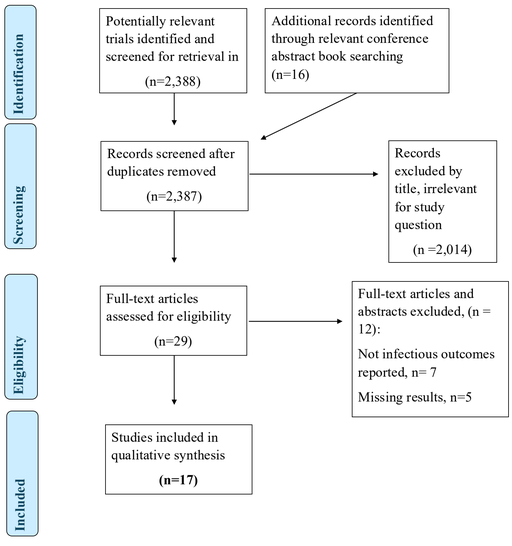
- Quantify pooled risk ratios (95% CIs) for any infection and grade 3–4 infections.
- Estimate risks for prespecified infection subtypes.

Methods



- We searched PubMed (1966–July 2024), CENTRAL (July 2024), and ASH/EHA proceedings (2020–2024) for published and unpublished BTKi RCTs in CLL/SLL.
- Pooled risk ratios (RR) with 95% confidence intervals (CIs) were estimated using fixed or random-effects models based on heterogeneity.

Figure 1. Trial flow according to Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA



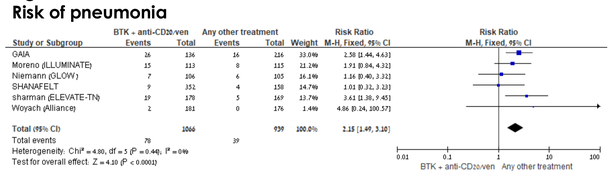
Results

- Seventeen trials encompassing 7,457 patients were included.
- BTKi-containing regimens, either as monotherapy or combined with anti-CD20 or venetoclax, were not associated with a significantly increased risk of any infection compared to other regimens [BTKi + anti-CD20 or venetoclax: RR 0.93 (95% CI: 0.79–1.09, I^2 = 46%), 3 trials; BTKi monotherapy: RR 1.12 (95% CI: 0.94–1.34, I^2 = 73%), 3 trials].
- BTKi-containing regimens were associated with a significantly increased risk of pneumonia compared to other regimens [RR 2.15 (95% CI: 1.49–3.1, I^2 = 0%), 6 trials].
- The risk of febrile neutropenia was reduced in trials comparing BTKi-containing regimens to other therapies.

Figure 2. BTKi vs other treatment: Risk of any infection



Figure 3. BTKi with anti-CD20/venetoclax vs other treatment: Risk of pneumonia



Discussion

- BTKi-containing regimens were not associated with an increased risk of overall infections or grade 3–4 infections compared to other regimens.
- However, an elevated risk of pneumonia was observed with BTKi combinations, highlighting the need for careful consideration when selecting treatment regimens for CLL/SLL patients.

References

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