Safety and Treatment-Free Outcomes of Ibrutinib-Based Regimens in Relapsed/Refractory Chronic Lymphocytic Leukemia: A systematic review and meta-analysis,

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Background

The emergence of Bruton tyrosine Kinase inhibitors(BTKi) such as Ibrutinib has significantly advanced the treatment of relapsed/refractory chronic lymphocytic leukemia (CLL). However, adverse events like atrial fibrillation (AF), bleeding, and hypertension remain concerns. This study aimed to compare the safety and treatment free survival (TFS) of Ibrutinib mono therapy versus Ibrutinib-based combination (IBCs).

Methods

A systematic review and meta-analysis were conducted, incorporating 10 randomized controlled trials (RCT) reporting on Ibrutinib monotherapy (IB) and IBCs in R/R CLL. Outcomes analyses included the odds ratio (OR) for Atrial Fibrillation, bleeding , hypertension, and hazard ratio (HR) for treatment-free survival. Subgroup analysis compared IB vs IBC regimens. Heterogeneity I^2 statistic.

Results

For Atrial fibrillation the pooled odds ratio was 1.054 (95% CI: 0.74 - 1.36; $I^2 = 0\%$), indicating no significant difference across treatment types. In the Bleeding analysis (9 studies), IB regimens showed a trend toward increased risk (OR: 0.911 ; 95% CI: 0.36 - 1.45) compared to IBCs (OR: 0.76; 95% CI: 0.495 - 1.034), though not statistically significant (P = 0.637). In contrast, hypertension was significantly more common in the IB group (OR: 0.57; 95% CI: 0.06 - 1.07) compared to IBCs (OR: 0.94; 95% CI: 0.56 - 1.31), with overall heterogeneity $I^2 = 62.7\%$. For treatment free survival, Ibrutinib regimens were associated with a pooled HR of 0.415 (95% CI: 0.28 - 0.54), indicating a favorable treatment free survival benefit. Subgroup hazards ratio were 0.480 for IB and 0.354 for IBC, suggesting comparable efficacy.

Conclusion

Ibrutnib and its combinations remain effective in prolonging treatment-free survival in refractory CLL. While overall safety is acceptable, hypertension and bleeding events are more frequent with ibrutinib mono therapy. These findings highlight the importance of balancing efficacy with safety when selecting BTKi regimens and suggest that combination therapies may offer a modest safety advantage without compromising outcomes.text.

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