Efficacy and Safety of Ibrutinib Combined with Venetoclax in the Treatment of Relapsed or Refractory Mantle Cell Lymphoma: A Systematic Review and Single-Arm Meta-Analysis

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Introduction

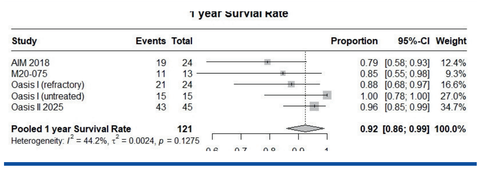
Mantle cell lymphoma (MCL) is an aggressive B-cell malignancy with a poor prognosis despite current therapies. Ibrutinib, a Bruton's tyrosine kinase (BTK) inhibitor, and venetoclax, a BCL-2 inhibitor, have shown individual efficacy in MCL, but their combined therapeutic potential remains underexplored.

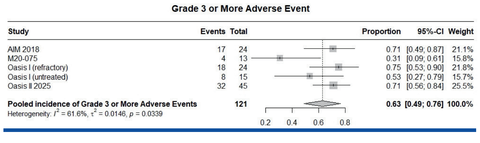
Objectives

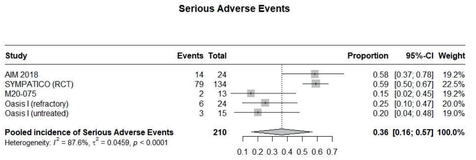
This meta-analysis aims to assess the efficacy and safety of ibrutinib plus venetoclax in the treatment of MCL.

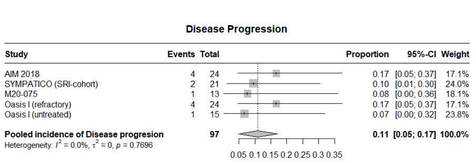
Methods

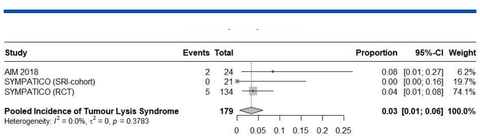
- The PubMed, Embase, Scopus, and Cochrane databases were systematically searched using relevant keywords from inception until April 2025.
- A total of 5 studies fulfilling predefined selection criteria were included in this meta-analysis.
- The pooled prevalence was estimated using the double arcsine transformation with the corresponding 95% confidence interval (CI) using the random effects model.
- The I2 and X2 statistics assessed interstudy heterogeneity. A significant heterogeneity was defined as I2 > 50%.
- Statistical analyses were performed in R Studio 4.4 using the “meta” package.









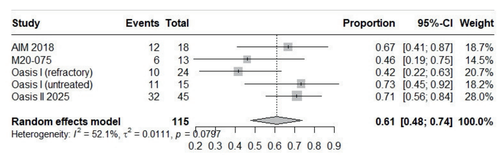


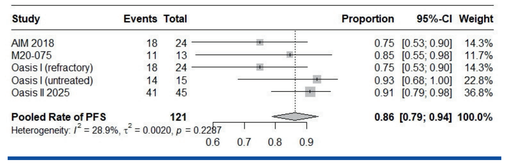
Discussion

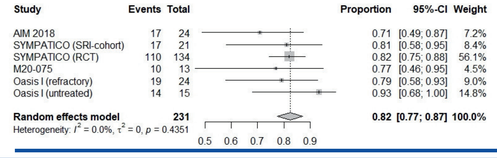
The combination of ibrutinib and venetoclax demonstrates high response and survival rates in relapsed or refractory mantle cell lymphoma, with uMRD findings suggesting the potential for deep and durable remissions. While adverse events are frequent, they are generally manageable with appropriate monitoring, and the low incidence of tumor lysis syndrome indicates effective prophylactic measures. Overall, this regimen shows promise as a treatment option, though further randomized studies are needed to confirm its long-term benefits and safety profile.

Results

- A total of 276 patients across five studies were included, with a median age of 68±7.9years, and a male predominance of 62% to 88%.
- The pooled overall response rate was 82% (95% CI: 77%–87%), with a clinical remission rate of 64% (95% CI: 55%–73%) and uMRD rate of 61% (95% CI: 48%–74%).
- Progression-free survival and 1-year overall survival were 86% (95% CI: 79%–94%) and 92% (95% CI: 86%–99%), respectively.
- Disease progression occurred in 11% (95% CI: 5%–17%).
- Grade ≥3 adverse events and serious adverse events occurred in 63% (95% CI: 49%–76%) and 36% (95% CI: 16%–57%), respectively.
- Treatment discontinuation and tumor lysis syndrome were reported in 26% (95% CI: 20%–32%) and 3% (95% CI: 1%–6%), respectively.







Conclusion

The combination of ibrutinib and venetoclax demonstrates high overall response and survival rates in mantle cell lymphoma, with manageable toxicity. These findings support its potential as an effective therapeutic option, though further studies are warranted to validate long-term outcomes and safety.