Safety and Efficacy of FLT3 Inhibitors in Acute Myeloid Leukemia: An Updated Meta-Analysis of 2975 Patients

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Introduction

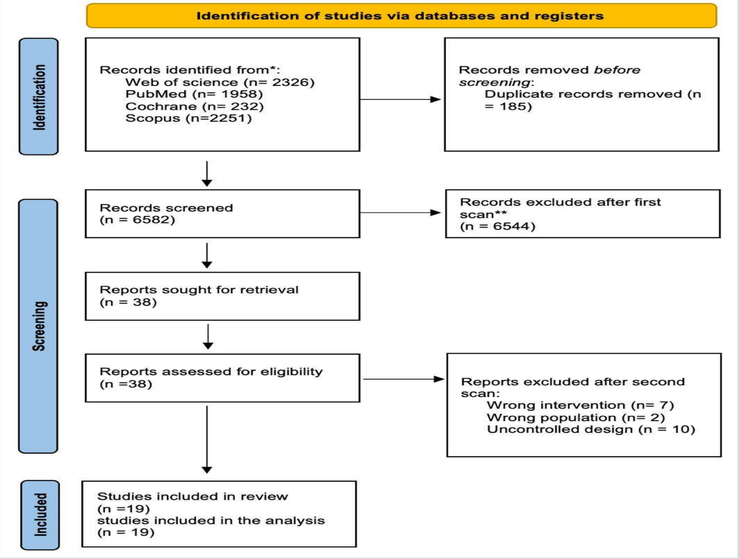
Acute myeloid leukemia (AML) is an aggressive hematological malignancy that arises from myeloid precursor cells within the bone marrow. Mutations in the FMS-like tyrosine kinase 3 (FLT3) gene occur in around one-third of AML patients. These mutations are associated with a worse prognosis. FLT3 gene plays a crucial role in the growth and survival of cancer cells. FLT3 inhibitors have emerged as a promising treatment option to inhibit the aberrant signaling pathways driven by FLT3 mutations.

Results

Pooling data from **19 RCTs** (2975 patients) showed that sorafenib was superior to placebo in terms of overall survival rate (RR= 2.26, 95% CI [1.33, 3.84], P= 0.003). However, the overall effect did not favor either of the two groups in terms of hematological and gastrointestinal side effects (RR= 1.29, 95% CI [0.77, 2.18], P= 0.3) and (RR= 1.40, 95% CI [0.92, 2.14], P= 0.1), respectively. Additionally, an insignificant difference was detected among gilteritinib versus placebo and midostaurin versus placebo in terms of hematological and gastrointestinal side effects (RR= 1.54, 95% CI [0.97, 2.43], P= 0.07, RR= 2.97, 95% CI [0.40, 22.15], P=0.2, RR= 1.27, 95% CI [0.96, 1.68], P=0.09, and RR= 1.16, 95% CI [0.56, 2.43], P= 0.6), respectively.

Objectives

We performed this meta-analysis to update the current evidence about the safety and efficacy of FLT3 inhibitors on the overall survival rate and adverse events in AML patients.



Methodology

Scopus, Web of Science, Cochrane Library, and PubMed were searched for relevant randomized controlled trials (RCTs) from inception until April 2024. We included RCTs comparing **sorafenib, gilteritinib, and midostaurin versus placebo**. Records were screened for eligible studies, and all relevant outcomes were pooled as risk ratio (RR) in a random-effect model meta-analysis, using RevMan software.

Conclusion

Our meta-analysis revealed a statistically significant improvement in overall survival with sorafenib compared to placebo. However, while our findings suggest that sorafenib may offer a survival benefit, a more comprehensive understanding of its safety profile, alongside those of gilteritinib and midostaurin, is necessary. Further research is crucial to optimize treatment strategies and establish definitive guidelines for using FLT3 inhibitors in AML patients.

References:
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