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EFFICACY OF FLT3 INHIBITORS IN ACUTE MYELOID LEUKEMIA (AML): A NETWORK META-ANALYSIS OF RANDOMIZED CONTROLLED TRIALS

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INTRODUCTION

- FMS-like tyrosine kinase 3 (FLT3) is crucial for hematopoietic cell proliferation and differentiation.
- FLT3 mutations occur in about one-third of acute myeloid leukemia (AML) cases.
- Recently, several FLT3 inhibitors have entered various clinical trial stages and approvals.

AIM

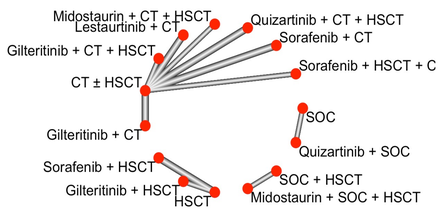
To investigate the clinical benefits of FLT3 inhibitors in patients with FLT3-mutated AML.

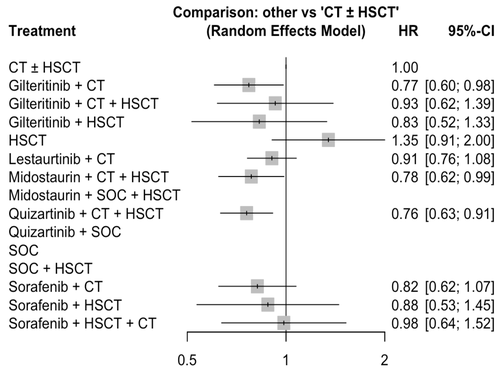
METHODS

- Systematic search- PubMed/MEDLINE, Cochrane, EMBASE, Scopus, and ClinicalTrials.gov until April 2024
- Primary outcome - Hazard ratio (HR) of overall survival, CIs. (If not reported, median survival times were converted to HRs)
- Data analysis - frequentist approach in R, with back-transformation of log(HRs) for treatment comparisons.
- An additive model estimated incremental treatment effects, with significance tested via z scores and *P* values.

RESULTS

Component network meta-analysis with 16 studies including 3806 patients, 8 active components, and 4 subnetworks.





- Significant risk reductions were found for quizartinib + CT + HSCT (HR, 0.7584 [0.6312; 0.9112), gilteritinib + CT (HR, 0.7703 [0.6045; 0.9815]) and Midostaurin+CT+HSCT (HR, 0. 7837 [0.6230; 0.9857]).
- Examining incremental effects, quizartinib + CT + HSCT (incremental HR (iHR), 0.6780 [0.5276-0.8713]), gilteritinib + CT (iHR, 0.6886 [0.5484-0.8647]), and sorafenib + CT (iHR, 0.7312 [0.5669-0.9432]) showed significant risk reductions.
- Component analysis revealed significant risk reductions for quizartinib (iHR, 0.5035 [0.3210-0.7899]), midostaurin (iHR, 0.5202 [0.3241-0.8350]), gilteritinib (iHR, 0.6156 [0.4423-0.8567]), and sorafenib (iHR, 0.6537 [0.4624-0.9242]). Heterogeneity was low ($\tau^2 = 0.0027$, $\tau = 0.0516$, $I^2 = 4.4\%$ [0.0%-64.0%]).

CONCLUSIONS

- Quizartinib + CT + HSCT and gilteritinib + CT significantly reduce mortality risk compared with chemotherapy ± HSCT.
- Incremental effects analysis highlights significant benefits for quizartinib, midostaurin, gilteritinib, and sorafenib, indicating their efficacy in managing FLT3-mutated AML.

REFERENCES (a few)

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