Is Day 14 Bone Marrow Useful to Predict CR and Guide Reinduction after "7+3"? - a systematic review and meta-analysis

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Introduction

In AML, a bone marrow biopsy around day 14 (D14BM) post-intensive induction is "standard of care". Current guidelines recommend reinduction if >5% blasts are detected (Positive D14BM). However, the predictive value of D14BM and the benefit of reinduction based on this strategy remain under-studied. Although tremendous progress has occurred in targeted therapy for AML, FLT3 mutations and IDH-1/-2 mutations account for ~30% and less than 20% of AML cases diagnosed in patients younger than 65 years old.

Aim

To evaluate the predictive power of D14BM for refractory leukemia at hematological recovery and the efficacy of reinduction based on Positive D14BM.

Design

Databases: PubMed, Embase, Web of Science, Cochrane through December 2024.

Search terms: "acute myeloid leukemia" and "day 14 bone marrow".

Eligibility: adult population, reporting interim BM findings (Day 7-21), remission status at hematological recovery, and the numbers of patients who received reinduction.

Meta-analysis of paired sensitivity and specificity was performed with a bivariate model. The positive predictive value was calculated based on the pooled mean sensitivity, specificity, and historical prevalence of refractory leukemia.

In patients with Positive D14BM, risk ratios (RR) for CR rates between reinduction and observation were meta-analyzed with the inverse variance method.

Results

A total of 1,044 research articles were identified. Twelve retrospective studies were included in this study.

None of the studies reported using venetoclax-based regimen or targeted therapy. The median percentage of patients with Positive D14BM after induction was 33.6% (20.4-48.1%), among whom a median of 47.8% (10.5-84.4%) received reinduction. CR was uniformly defined as blast <5%, absolute neutrophil count > 1,000 /μL, and platelet > 100,000/μL.

A total of 1,683 patients from 10 studies who did not receive reinduction regardless of D14BM results were used to evaluate the predictive value of D14BM. The **pooled mean sensitivity and specificity of D14BM were 49.7% (95% CI 40.4-59.0%) and 86.2% (95% CI 80.4-90.6%),** respectively. Assuming the prevalence of refractory leukemia is 15%, the **positive predictive value of D14BM was estimated to be 38.9%.**

A total of 832 patients from 11 studies were included to compare the CR rates following reinduction vs observation following Positive D14BM. The meta-analysis **RR of CR at cell count recovery was 1.00 (61% vs 60%, 95% CI 0.76-1.31, I^2 = 56.6%).**

Conclusion

Positive D14BM is poorly associated with refractory leukemia at hematological recovery. Reinduction based on Positive D14BM resulted in a nearly identical CR rate as observation-only. Omitting reinduction may spare significant toxicity without compromising outcomes.

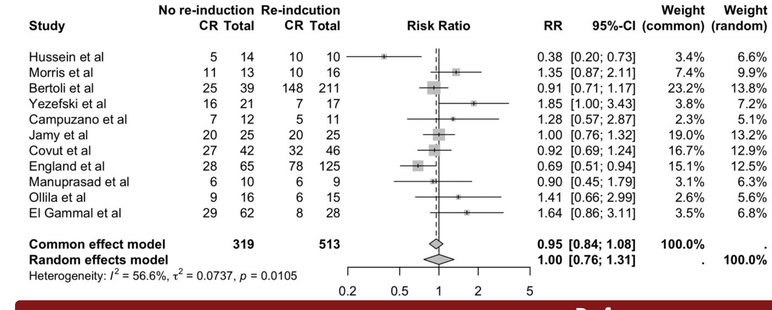


Figure. Random effects forest plot for 11 studies evaluating RR of CR among AML patients with Positive D14BM

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