First-Line Treatment Outcomes in *TP53*-Mutated Acute Myeloid Leukemia: A Systematic Review and Meta-Analysis

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Background

- **TP53m AML is an adverse-risk subtype** with treatment resistance, frequent relapse, and poor survival.
- Frontline approaches include **IC, LIT, and HMA ± VEN**.
- **The optimal frontline strategy remains uncertain** due to variable response and survival outcomes.

LIT: *HMA monotherapy/combinations, HMA + VEN, or other lower-intensity therapies.*

Aims

- **Evaluate the efficacy of frontline treatment strategies in TP53-mutated AML** by comparing response to different therapies
- **Assess whether improved treatment responses translate into meaningful** survival **benefit**

Methods

1 STUDY DESIGN
- Systematic review and meta-analysis of studies in adults with newly diagnosed, treatment-naïve *TP53*-mutated AML.

2 LITERATURE SEARCH
- PubMed, Embase, Web of Science, and Scopus searched; manual reference review.

3 OUTCOMES
- CR, CRi, ORR, PR, refractory disease, HCT rate, and median OS.

4 STATISTICAL ANALYSIS
- Pooled using inverse-variance fixed-effect models; heterogeneity assessed by I^2 in RStudio.

Results

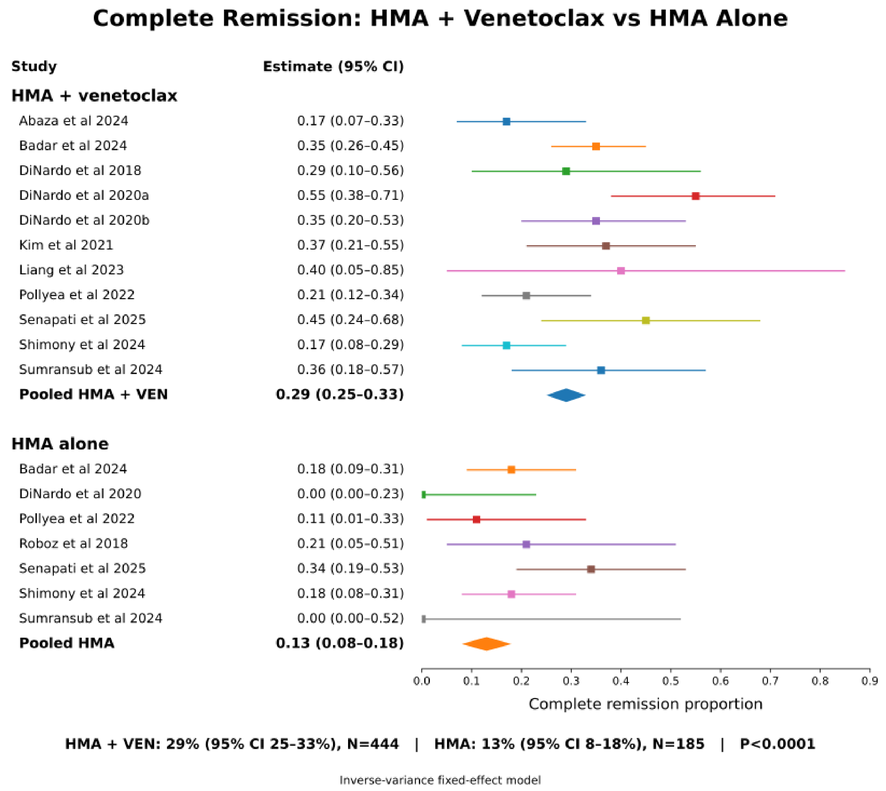

Figure 1: Comparison of CR amongst HMA + Venetoclax vs HMA Alone.

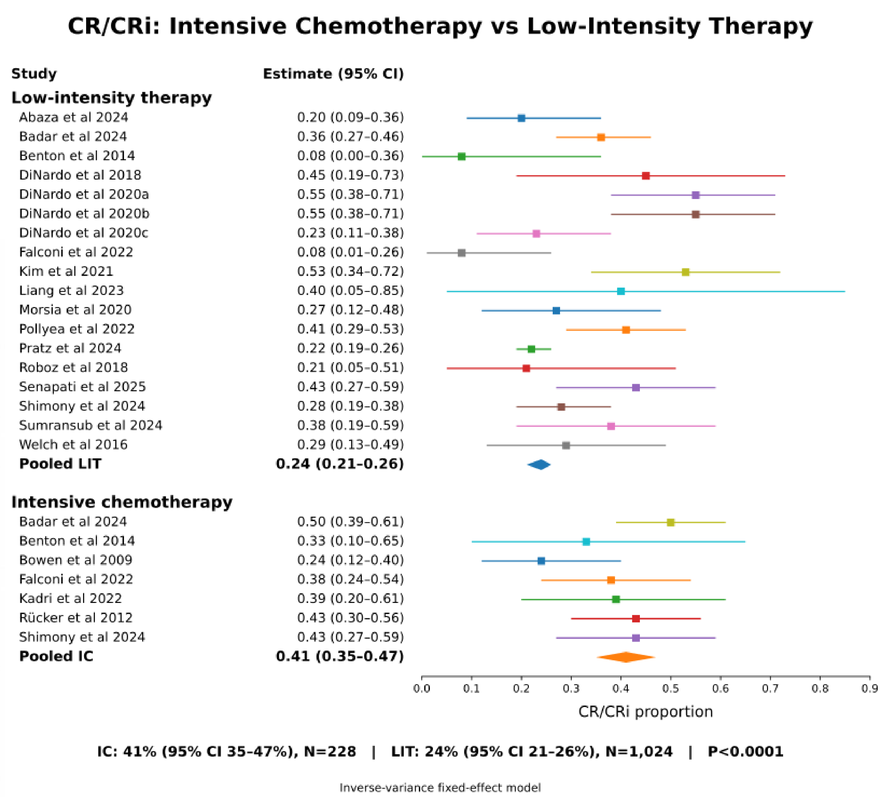

Figure 2: CR/Ri comparison of IC vs LIT

Conclusions

- **IC and HMA+VEN achieved higher CR rates**, with IC also producing higher CR/CRi than LIT.
- **More patients proceeded to HCT with IC than LIT** (**30% vs 9%; P=0.007**).
- **Despite improved responses, median OS remained ~6 months**, highlighting the need for rapid disease control and early HCT in eligible patients.

Discussion

- **Persistent TP53m clones may contribute to treatment resistance and relapse**
- **Allo-HCT** remains the **principal** potentially **curative strategy**
- Substantial study heterogeneity limit direct treatment comparisons, highlighting the **need for therapies capable of achieving deeper TP53 clonal clearance and durable disease control**.

Selected References

- DiNardo CD, et al. Azacitidine and venetoclax in previously untreated acute myeloid leukemia. *N Engl J Med.* 2020;383:617–629.
- Pollyea DA, et al. Outcomes in patients with poor-risk cytogenetics with or without TP53 mutations treated with venetoclax and azacitidine. *Clin Cancer Res.* 2022;28:5272–5279.
- Daver NG, et al. TP53-mutated myelodysplastic syndrome and acute myeloid leukemia: biology, current therapy, and future directions. *Cancer Discov.* 2022;12:2516–2529.

Full reference list will be available in manuscript