Efficacy of Gilteritinib Versus Salvage Chemotherapy in Relapsed or Refractory FLT3-Mutated AML: A Meta-Analysis

Vedant Shah[1], Abhi Shah[2], Pragya Jain[3], Viraj Panchal[4], Bolivia Crocete Aloysia Fernandes[1], Swapna Gangasani[1], Diviya Joshi[5], Michael Maroules[6]

1 The New York Medical College Graduate Medicine Program at St. Mary's General Hospital and Saint Clare's Health, Denville, NJ, USA

2 Smt. NHL Municipal Medical College, Ahmedabad, Gujarat, India

3 Baptist Hospital of Southeast Texas, Beaumont, TX, USA

4 Louisiana State University, Shreveport, LA, USA

5 GMC, Thane, Maharashtra, India

6 St. Michael Medical Center, Newark, NJ, USA

Introduction

- Patients with relapsed or refractory acute myeloid leukemia (AML) have an infrequent response to salvage chemotherapy when associated with mutations in the FMS-like tyrosine kinase 3 gene (FLT3)
- Gilteritinib, a selective oral FLT3 inhibitor targeting both ITD and TKD mutations, demonstrated superior overall survival (OS) in the phase III ADMIRAL trial and has since become a standard of care in the relapsed refractory R/R setting.

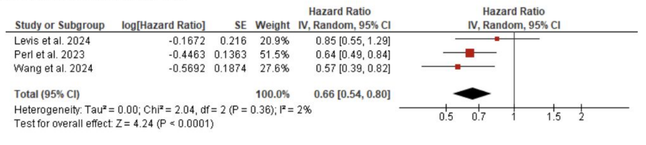
Objective

- This meta-analysis synthesizes available evidence from comparative and single-arm studies to provide a comprehensive evaluation of Gilteritinib efficacy relative to salvage chemotherapy in R/R FLT3-mutated AML

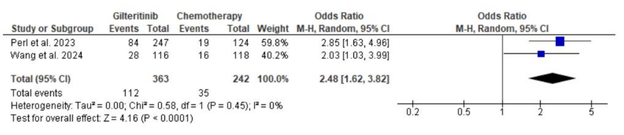
Methods

- **Search sources**: PubMed, clinicaltrials.gov.
- **Endpoints**:
  - Overall Survival (OS)
  - Complete Remission (CR), CR with partial hematologic recovery (CRh)
  - Partial Response (PR)
  - Overall Response Rate (ORR)
- **Meta Analysis**: Done wih Mantel–Haenszel method, random-effects model, pooled hazard ratios (HR) and odds ratios (OR) with 95% CI (RevMan 5.4).

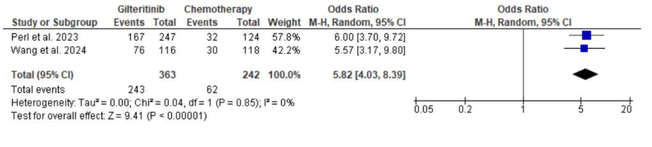
Median Overall survival HR



Complete remission or complete remission with partial hematologic recovery



Overall response



Results

Study Characteristics

- **7 studies (n = 1,464 patients)** with FLT3-mutated R/R AML were included.
- **4 comparative trials (n = 1,138)** evaluated gilteritinib versus salvage chemotherapy.
- **3 single-arm studies (n = 326)** assessed gilteritinib outcomes alone.

Comparative Meta-Analysis (Gilteritinib vs Salvage Chemotherapy)

- **Overall Survival (OS):** Gilteritinib significantly improved survival (HR = 0.66, 95% CI: 0.54–0.80; p < 0.0001), representing a **34% reduction in risk of death**.
- **Complete Remission (CR/CRh):** Higher odds of remission with gilteritinib (OR = 2.48, 95% CI: 1.62–3.82; p < 0.0001).
- **Overall Response Rate (ORR):** Increased with gilteritinib (OR = 5.82, 95% CI: 4.03–8.39; p < 0.00001).

Single-Arm Gilteritinib Studies

- **CR:** 16.2% (95% CI: 10.7–21.6).
- **CR/CRh:** 22.6% (95% CI: 10.4–34.8).
- **Partial Response (PR):** 17.2% (95% CI: 11.1–23.3).
- **Composite CR:** 48% (95% CI: 39.7–56.2).
- **Overall Response Rate (ORR):** 67.2% (95% CI: 62.4–72.0).
- **No Response:** 26.2% (95% CI: 22.4–30.0).

Discussion

- Gilteritinib demonstrates **superiority** over salvage chemotherapy in R/R FLT3-mutated AML.
- Benefits observed across **OS, remission, and response rates**, with minimal heterogeneity.
- Single-arm data reinforces **consistent efficacy**, with ORR >67%.
- These findings support the use of Gilteritinib as an effective treatment option in R/R AML patients and reinforce its role in improving clinical outcomes.

References

1. Targeting FLT3 Mutation in Acute Myeloid Leukemia: Current Strategies and Future Directions. *Cancers (Basel)*.
2. Follow-up of patients with R/R FLT3-mutation-positive AML treated with gilteritinib in the phase 3 ADMIRAL trial. *Blood*. 2022;139(23):3366-3375.

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