GILTERITINIB IN COMBINATION WITH VENETOCLAX, LOW-DOSE CYTARABINE, AND ACTINOMYCIN D AS SALVAGE THERAPY FOR RELAPSED/REFRACTORY *FLT3* MUTATED ACUTE MYELOID LEUKEMIA - A SINGLE-CENTER RETROSPECTIVE STUDY

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Introduction

Combining Gilteritinib with Venetoclax-based regimens shows potentially better efficacy in treating *FLT3*-mutated relapsed/refractory AML cases, compared to Gilteritinib alone.[1,2] We report retrospective results of the quadruplet G-ACTIVE regimen (Gilteritinib, Actinomycin D, Cytarabine, Venetoclax) as salvage therapy in *FLT3*-mutated R/R AML.

Objectives

To evaluate the efficacy and toxicity of the G-ACTIVE regimen in *FLT3*-mutated R/R AML patients.

Methods

We conducted a single-center retrospective study of 28 patients who received G-ACTIVE as salvage therapy for *FLT3*-mutated R/R AML (2020-2024).

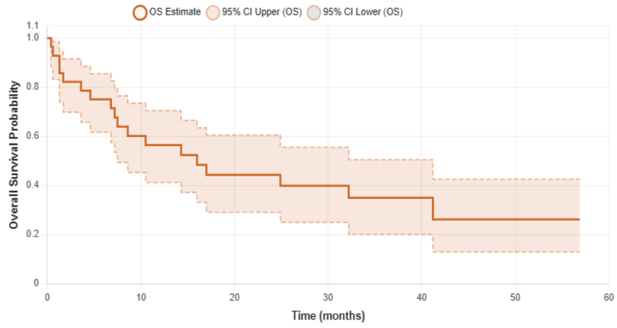
G-ACTIVE regimen included Gilteritinib 80 or 120 mg/day (starting any day from 1 to 28, continued individually), Actinomycin D 12.5 µg/kg (days 1-3, days 1-2 for patients aged ≥65), Cytarabine 20 mg/m2 (days 1-10), and Venetoclax 600 mg/day (starting on day 1, continued individually for up to 28 days).

Results

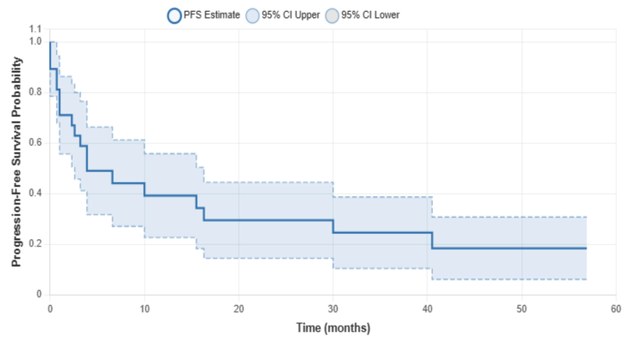
- 28 patients (18 female) were enrolled in the study and received G-ACTIVE.

Patient characteristics	
Median age, years (range)	64.5 (34-87)
FLT3-ITD mutation, n/N (%)	18/28 (64.1)
FLT3-TKD mutation, n/N (%)	6/28 (21.6)
FLT3-ITD* + *FLT3-TKD mutation, n/N (%)	4/28 (14.3)
ELN 2022 risk stratification:	
Favorable risk, n/N (%)	3/28 (10.7)
Intermediate risk, n/N (%)	15/28 (53.6)
Adverse risk, n/N (%)	10/28 (35.7)
Previous intensive chemo, n/N (%)	22/28 (78.5)
Previous *FLT3* inhibitors, n/N (%)	16/28 (57.1)
Previous Venetoclax, n/N (%)	5/28 (17.8)
Previous allo-SCT, n/N (%)	4/28 (14.3)
ORR, n/N (%)	27/28 (96.4)
CR, n/N (%)	12/28 (42.9)
CRi, n/N (%)	6/28 (21.4)
MLFS, n/N (%)	9/28 (32.1)
MRD negativity, n/N (%)	14/28 (50.0)
Bridge to allo-SCT, n/N (%)	15/28 (53.5)

Kaplan-Meier Curve: Overall Survival (OS)



Kaplan-Meier Curve: Progression-Free Survival (PFS)



- **Median OS - 16** (0.4-56.9) months.
- **Median PFS - 10** (0-56.1) months.
- **Day 60 mortality** rate was **18%**.
- Median time to ANC and PLT recovery was 23.5 (14-59) and 22 (6-54) days, respectively.
- The most common severe non-hematological adverse events were **infections** (39.3%).

Summary

G-ACTIVE shows promising efficacy as salvage therapy in *FLT3*-mutated R/R AML, with 96.4% ORR and 64.3% CR + CRi rate in our cohort.

Discussion

Overall, the **G-ACTIVE regimen demonstrates high response rates and effective bridging to allo-SCT**, with encouraging remission durability and OS in patients with R/R *FLT3*-mutated AML.[2,3] The G-ACTIVE regimen exhibits antileukemic activity in patients with prior exposure to FLT3 inhibitors; however, this remains to be proven in clinical trials. Nevertheless, several patients in our cohort demonstrated delayed hematologic recovery, and early mortality was notable, with a cumulative incidence of 18% at day 60.

Our results should be interpreted with caution due to the small sample size and retrospective study design.

References:

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2. Perl AE, Larson RA, Podoltsev NA, et al. Follow-up of patients with R/R FLT3-mutated AML treated with gilteritinib in the phase 3 ADMIRAL trial. Blood. 2022;139(23):3366–75.
3. Zucenka A, Griskevicius L. Gilteritinib in combination with venetoclax, low-dose cytarabine and actinomycin D for R/R FLT3-mutated AML. Br J Haematol. 2024;204(4):1227–31.