Phase I/II study of a fully oral combination of decitabine/cedazuridine, venetoclax and gilteritinib in *FLT3* mutated AML

KEY TAKEAWAYS

- *FLT3* mutations are common in AML, linked to poor outcomes, especially in older patients
- A fully oral treatment with decitabine/cedazuridine in combination with venetoclax and gilteritinib shows encouraging response rates in patients with newly-diagnosed and R/R AML with *FLT3* mutations

In a Phase I/II study, a fully oral combination of decitabine/cedazuridine (DEC-C), venetoclax (Ven), and gilteritinib was tolerable and showed **encouraging response rates in patients with *FLT3* mutated AML**. The Phase I (dose escalation) part of the trial focused on finding the best dose of gilteritinib and the Phase II (dose expansion) evaluated the efficacy and safety of DEC-C with Ven and gilteritinib.

The trial had two cohorts of patients:

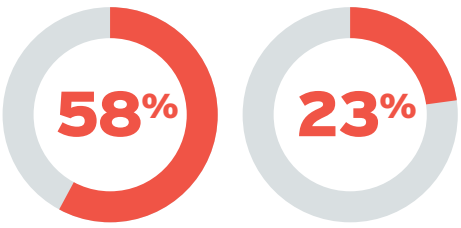
- Patients with newly-diagnosed (ND) AML with mutated *FLT3*
- Patients with relapsed/refractory (R/R) AML or high-risk myelodysplastic syndrome (MDS) with mutated *FLT3*

Patients received DEC-C 100 mg plus Ven 400 mg in combination with gilteritinib 80 mg (dose level 1) or 120 mg (dose level 2). There were no dose-limiting toxicities at either dose of gilteritinib and **the 80 mg dose (dose level 1) was chosen for the Phase II part of the trial.**

The primary objective of the study was to establish the **safety and efficacy** of a fully oral combination of DEC-C with Ven and gilteritinib in patients with ND AML or R/R AML or MDS with *FLT3* mutations.

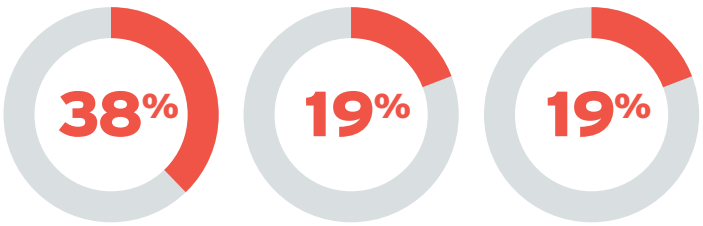
Response rates	ND AML cohort AML (n=7)	R/R AML cohort (n=18)
Overall response rate	86%	44%
Complete remission rate	71%	17%
Complete remission with incomplete hematological recovery	14%	28%

Safety results in both cohorts



Grade 3 adverse events | Grade 4 adverse events

Most frequent Grade 3-4 adverse events



Sepsis | Febrile neutropenia | Lung infection

Two patients (8%) in the R/R AML cohort died due to septic shock in Cycle 1 and Cyle 2.

Low blood count and delayed count recovery were the main limiting factors of treatment

Platelets recovery duration
38 days

Neutrophils recovery duration
48 days

Patients often needed dose adjustments to avoid prolonged low blood counts.

WHAT DOES THIS MEAN FOR PATIENTS?

FLT3 mutations are common in AML, affecting about one-third of patients. These mutations are linked to poor outcomes, especially in older patients. This study tested a fully oral combination of DEC-C, venetoclax, and gilteritinib in patients with ND or R/R AML with *FLT3* mutations. The treatment was feasible and showed promising response rates. However, challenges included low blood cell counts with slow recovery, often leading to dose adjustments. Overall, these results are promising but need to be confirmed in larger studies with longer follow-up periods. If validated, this treatment could offer a more convenient and effective option for patients with *FLT3*-mutated AML.

Reference: *Bataller A, et al. Presentation at 29th European Hematology Association (EHA) Congress, Madrid. June 13-16, 2024. Abstract #S139.*

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