# Quizartinib in Combination with Cladribine, Idarubicin and Cytarabine in Acute Myeloid Leukemia

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## INTRODUCTION

- In the phase 3 QuANTUM-First trial, addition of quizartinib 35.4mg to standard induction and consolidation chemotherapy, then as quizartinib 53mg monotherapy improved survival in newly diagnosed FLT3-ITD AML.[2]
- The QUIWI study also supported the activity of quizartinib 53mg in combination with intensive chemotherapy, then as quizartinib 53mg maintenance monotherapy in newly diagnosed FLT3-ITD negative AML.[3]
- CLIA (cladribine, idarubicin, cytarabine) is an intensive chemotherapy backbone with established efficacy in AML.[4]
- Combining quizartinib with CLIA may enhance anti-leukemic activity by targeting FLT3-driven disease while maintaining the cytotoxic benefit of intensive chemotherapy.

## AIM

- In this phase 1/2 study, we evaluated the safety and efficacy of quizartinib (17.7 mg/day and 26.5mg/day) in combination with CLIA in patients with newly diagnosed and relapsed/refractory FLT3-ITD mutated and wild-type AML.

## METHODS

### Key Eligibility Criteria

- **Age**: <75 years
- **Treatment fitness**: Fit for intensive chemotherapy
- **Performance status**: ECOG ≤2
- **Renal function**: Creatinine <1.5 mg/dL
- **Hepatic function**: Total bilirubin <1.5 mg/dL
- **Cardiac function**: LVEF ≥50%

ECOG, Eastern Cooperative Oncology Group, LVEF, left ventricular ejection fraction

### Dosing schedule

**Induction Cycle** — CLIA + quizartinib

| Agent | Dose | Cycle day 1–28 |
|---|---|---|
| Cladribine | 5 mg/m² | Days 1-6 |
| Cytarabine | 1.5 g/m² | Days 1-5 |
| Idarubicin | 10 mg/m² | Days 1-3 |
| Quizartinib | 17.7 or 26.5 mg | Days 6-19 |

**Consolidation** — Up to 5 total cycles

| Agent | Dose | Cycle day 1–28 |
|---|---|---|
| Cladribine | 5 mg/m² | Days 1-3 |
| Cytarabine | 1 g/m² | Days 1-3 |
| Idarubicin | 8 mg/m² | Days 1-2 |
| Quizartinib | 17.7 or 26.5 mg | Days 4-28 |

Quizartinib dose levels evaluated in phase 1: 17.7 mg and 26.5 mg. CLIA, cladribine/cytarabine/idarubicin.

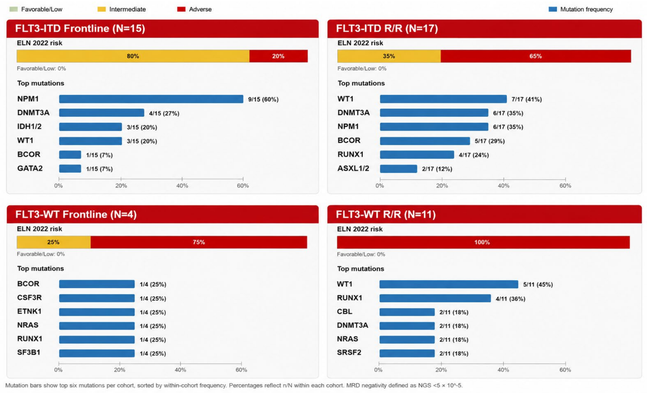
- 47 patients treated overall
- 17 patients enrolled in phase 1; 30 patients enrolled in phase 2
- No dose-limiting toxicities were observed at quizartinib 17.7 mg dose level
- One DLT, myocarditis/pericarditis, was observed at quizartinib 26.5 mg
- Quizartinib 26.5 mg was selected as RP2D

## RESULTS

### Patient Characteristics

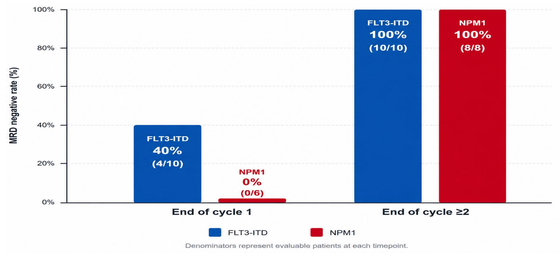
| Clinical Characteristics | FLT3 Positive | | FLT3 Negative | |
|---|---|---|---|---|
| | Frontline (N=15) | R/R (N=17) | Frontline (N=4) | R/R (N=11) |
| **Age** | | | | |
| Median (range), years | 38 (22-60) | 52 (23-72) | 39 (33-60) | 49 (22-71) |
| Age <60 years, n (%) | 14 (93) | 11 (65) | 3 (75) | 8 (73) |
| **Gender** | | | | |
| Female, n (%) | 11 (73) | 8 (47) | 1 (25) | 5 (45) |
| Male, n (%) | 4 (27) | 9 (53) | 3 (75) | 6 (55) |
| **Diagnosis** | | | | |
| De novo AML, n (%) | 15 (100) | 14 (82) | 1 (25) | 9 (82) |
| sAML, n (%) | 0 (0) | 2 (12) | 2 (50) | 1 (9) |
| tAML, n (%) | 0 (0) | 0 (0) | 0 (0) | 1 (9) |
| tsAML, n (%) | 0 (0) | 1 (6) | 1 (25) | 0 (0) |
| **BM blasts**, med. (range), % | 78 (25-93) | 46 (5-82) | 24 (1-30) | 30 (6-99) |
| **Karyotype** | | | | |
| Adverse, n (%) | 0 (0) | 6 (35) | 2 (50) | 7 (64) |
| Diploid, n (%) | 12 (80) | 8 (47) | 2 (50) | 2 (18) |
| Other, n (%) | 3 (20) | 2 (12) | 0 (0) | 0 (0) |
| Insufficient metap., n (%) | 0 (0) | 1 (6) | 0 (0) | 2 (18) |
| **Prior therapies**, median (range) | 0 (0-0) | 3 (1-7) | 0 (0-0) | 3 (1-8) |
| **Prior FLT3 inhibitor therapy**, n (%) | 0 (0) | 12 (71) | 0 (0) | 3 (27) |

### ELN2022 Risk and Molecular Profile by Cohort




Mutation bars show top six mutations per cohort, sorted by within-cohort frequency. Percentages reflect n/N within each cohort. MRD negativity defined as NGS <5 × 10⁻⁵.

### MRD Negativity (<5 x10⁻⁵) by NGS – Frontline FLT3+ Cohort

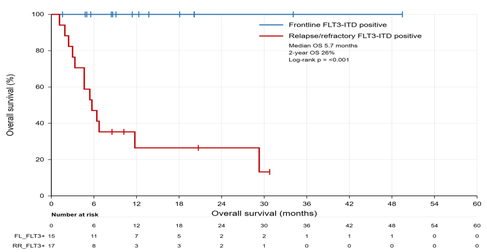



Denominators represent evaluable patients at each timepoint.

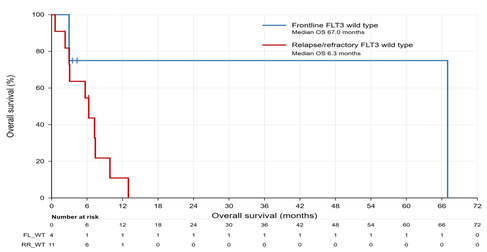
### Response Rates

| Response*, N (%) | FLT3 Positive | | FLT3 Negative | |
|---|---|---|---|---|
| | Frontline (N=15) | R/R (N=17) | Frontline (N=4) | R/R (N=11) |
| **Hematologic Response** | | | | |
| mCRc | 14 (93) | 10 (59) | 2 (50) | 3 (27) |
| CR | 13 (86) | 3 (18) | 2 (50) | 0 (0) |
| CRi | 1 (7) | 4 (23) | 0 (0) | 1 (9) |
| MLFS | 0 (0) | 3 (18) | 0 (0) | 2 (18) |
| No response | 1 (7) | 7 (41) | 2 (50) | 7 (64) |
| Induction death | 0 (0) | 0 (0) | 0 (0) | 1 (9) |
| **MRD at the end of cycle 1, N (%)** | | | | |
| Flow Cytometry Negative | 12/13 (92) | 3/9 (33) | 1/1 (100) | 0/1 (0) |
| FLT3-ITD PCR Negative | 4/4 (100) | 1/5 (20) | - | - |
| FLT3-ITD NGS Negative (< 5 x $10^{-5}$) | 4/10 (40) | 0/3 (0) | - | - |
| NPM1 NGS Negative (< 5 x $10^{-5}$) | 0/6 (0) | 0/2 (0) | - | - |
| **MRD at the end of cycle ≥2 (best), N (%)** | | | | |
| Flow Cytometry Negative | 13/13 (100) | 2/3 (66) | 1/1 (100) | 0/1 (0) |
| FLT3-ITD PCR Negative | 4/4 (100) | 1/1 (100) | - | - |
| FLT3-ITD NGS Negative (< 5 x $10^{-5}$) | 10/10 (100) | 1/2 (5) | - | - |
| NPM1 NGS Negative (< 5 x $10^{-5}$) | 8/8 (100) | 1/1 (100) | - | - |
| **Bridge to bone marrow transplant** | 8 (53) | 7 (41) | 3 (75) | 2 (18) |

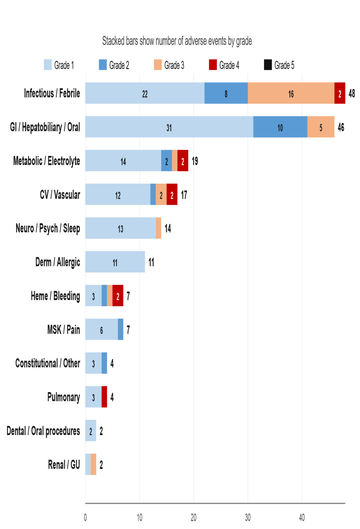
### Overall Survival in *FLT3-ITD* Positive Cohort



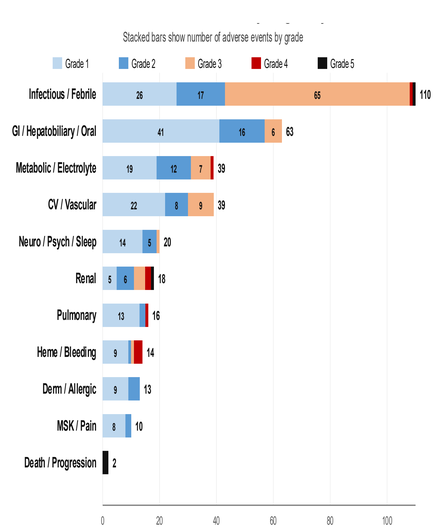

### Overall Survival in *FLT3-ITD* Negative Cohort




### Adverse Events: Newly Diagnosed Patients




### Adverse Events: R/R Patients




## CONCLUSIONS

- High remission rates in newly diagnosed *FLT3-ITD*m
  - CRc 93% (CR 86%), med OS not reached, 2-yr OS 100%%
  - All responding patients achieved deep molecular response by NGS
  - No relapse or death observed at current follow-up
- CLIA+ Quizartinib is active in heavily pretreated pts R/R FLT3-ITDm pts
  - CRc 59%, 41% bridged to allo-transplant
  - Med OS 5.7 m, 2-yr OS 26%
- A lower dose of quizartinib 26.5mg was administered in the *FLT3-ITD* negative cohort compared to QUIWI and the ongoing QuANTUM-Wild 53mg dose, suggesting that a higher dose in this *FLT3-ITD* negative population may be warranted.
- This clinical trial continuous to accrue

## REFERENCES/CONTACT:

1) Cortes JE, et al. J Hematol. Oncol. 2024;17:146. 2) Erba HP, et al. Lancet. 2023;401:1571-1583. 3) Montesinos P, et al. J Clin Oncol. 2025. 4) Goulart H, et al. Cancer. 2025.

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