EHA2026 Congress
June 11-14
Stockholm, Sweden

A Phase 1/2 Study of the Menin inhibitor revumenib with the CELMod mezigdomide in Relapsed/Refractory *KMT2A*-rearranged, *NPM1*-mutant, and *NUP98*-rearranged Acute Leukemias

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INTRODUCTION

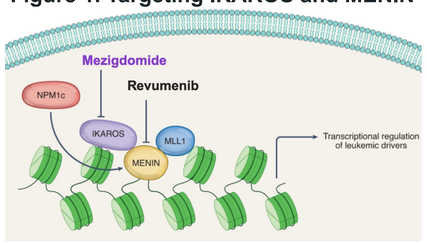
Menin inhibitors (MENINi) are promising for *HOX*-high acute leukemias, but resistance often emerges

- **Revumenib** (REV) is associated with ~50-60% ORR and ~21-23% CR/CRh rate in R/R *KMT2A*r and *NPM1m* acute leuekmias[1,2]
- **Median duration of response of CR/CRh for revumenib is ~5-6 months** in this context
- ***MEN1*** mutations frequently and rapidly emerge to confer resistance[3]
- **Outcomes after MENINi failure** are generally poor[4]

IKAROS is a potential therapeutic target in *HOX*-high acute leukemias

- **IKAROS** is an essential transcription factor in *KMT2A*r AML with cooperativity and chromatin co-occupancy with KMT2A-Menin[5]
- The cereblon E3 ligase modulator **mezigdomide** (MEZ) degrades IKAROS in AML cells and with revumenib **prevents and overcomes resistance** in patient derived xenografts (Figure 1)[6]

Figure 1. Targeting IKAROS and MENIN



Adapted from Jones et al. *Nature Cancer* 2022

HYPOTHESIS

The combination of revumenib and mezigdomide will be safe and efficacious in patients with R/R *KMT2A*r, *NPM1*m, or *NUP98*r acute leukemia.

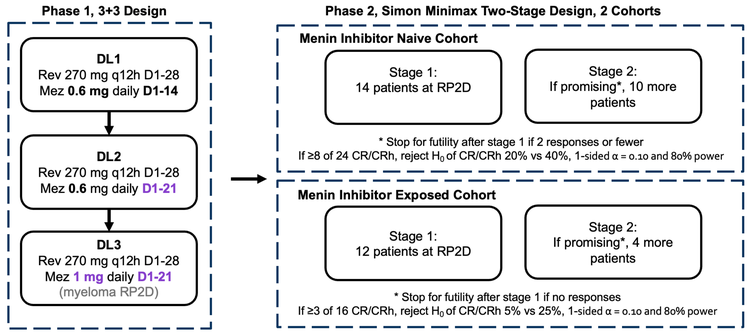
DESIGN

- Multicenter, phase 1/2, investigator-initiated study

Figure 2. Study Summary

Population	• Pts with relapsed/refractory *KMT2A*r, *NPM1*m, or *NUP98*r acute leukemia age 12+; prior menin inhibitor permitted
Intervention	• Revumenib & mezigdomide • **Phase 1/2 Design**
Comparison	• Single-arm, open-label phase 1/2 vs historical controls
Outcomes	• **Primary:** safety, tolerability (phase 1), CR/CRh by 6 cycles (phase 2) • **Secondary:** PK, CRc, ORR, DOR, OS, EFS • **Exploratory:** MRD, Mutation Profiling, PD
Timeframe	• Up to 4 cycles of treatment if no response

Figure 3. Study Schema



- **Phase 1:** 3+3 dose escalation; MEZ doses based on myeloma literature, REV doses based on FDA approved dose
- **Phase 2:** 2 cohorts based on prior MENINi, both Simon Minimax Two-Stage Design
- Treatment until unacceptable toxicity, death, or lack of response (at least MLFS) after 4 cycles

Figure 4. Key Inclusion and Exclusion Criteria

KEY INCLUSION CRITERIA

- Age ≥ 12 AND ≥ 40kg
- Relapsed/Refractory acute leukemia
- *NPM1*m, *KMT2A*r, or *NUP98*r
- ECOG 0-2 if ≥18, KPS of ≥50 (if ≥16 and < 18), Lansky ≥50 (if <16)
- >60 days from alloHCT
- WBC <25,000 (hydroxyurea, leukapheresis permitted)
- Adequate organ function (AST/ALT/Bili ≤ 3x ULN, Cr < 2x ULN or GFR > 60, LVEF >50%)
- Prior menin inhibitor permitted in phase 1, phase 2 cohort 2

KEY EXCLUSION CRITERIA

- APL
- Prior mezigdomide
- Strong or moderate CYP3A4 inhibitors or strong CYP3A4 inducers*
- Proton pump inhibitors
- Uncontrolled infection
- Active cardiac disease (NYHA III/IV heart failure, ACS, stroke)
- GI condition affecting drug absorption
- Prolonged QTcF ≥ 450

*Amendment pending

ENDPOINTS

- **Primary endpoint**: Incidence of DLTs (Phase 1), CR/CRh by 6 cycles (Phase 2)
- **N=18 for phase 1, N=40 for phase 2;** using different promising response rates depending on prior MENINi, α=0.1, power 80%
- **Secondary endpoints**: CRc, ORR, EFS, OS, DOR
- **Exploratory endpoints**: TTR, Transfusion independence, alloHCT rate, MRD negativity, mutational profiling, immunologic effects, *HOX* gene profiling

STUDY STATUS

- Funding and **revumenib** supplied by Syndax Pharmaceuticals
- **Mezigdomide** supplied by Bristol-Myers Squibb
- Study open at MSKCC and actively recruiting
- Additional sites to follow

Recruiting

A Study of Revumenib and Mezigdomide in People With Leukemia

ClinicalTrials.gov ID NCT07356154
Sponsor Memorial Sloan Kettering Cancer Center
Information provided by Memorial Sloan Kettering Cancer Center (Responsible Party)
Last Update Posted 2026-01-21

Clinicaltrials.gov

REFERENCES

1. Issa et al. *JCO* 2024.
2. Arellano et al. *Blood* 2025.
3. Perner et al. *Nature* 2023.
4. Chin et al. *Blood Advances* 2026.
5. Aubrey et al. *Nature Cancer* 2022.
6. Bourgeois et al. *Blood* 2024.

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