SOHO 2026 ANNUAL MEETING | ABSTRACT AML-848

Efficacy and Differentiation Syndrome With Menin Inhibitors in Relapsed/Refractory KMT2A-Rearranged or NPM1-Mutated Acute Leukemia

An Exploratory Proportional Meta-Analysis of Three Pivotal Trials

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KEY RESULTS 3 prospective trials • 213 efficacy-evaluable • 270 safety-evaluable patients

PRIMARY ENDPOINT
22.5%
Pooled CR/CRh
95% CI 17.4–28.6 • I^2 = 0.0%

SECONDARY ENDPOINT
46.9%
Pooled overall response rate
95% CI 32.8–61.4 • I^2 = 84.5%

SECONDARY ENDPOINT
24.1%
Differentiation syndrome, any grade
95% CI 19.3–29.5 • I^2 = 0.0%

SECONDARY ENDPOINT
14.8%
Differentiation syndrome, grade ≥3
95% CI 11.1–19.6 • I^2 = 0.0%

BACKGROUND

R/R acute leukemias harboring KMT2A rearrangements or NPM1 mutations are driven by HOX/MEIS1-dependent leukemogenesis and carry a poor prognosis with few targeted options. Menin inhibitors restore blast differentiation, but pooled estimates of remission, and of differentiation syndrome (DS), the class-defining toxicity, have not been established.

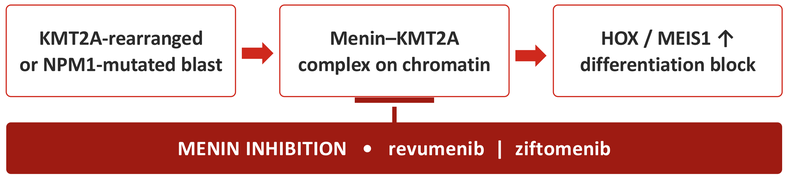

Figure 5. Menin inhibition relieves the HOX/MEIS1-driven differentiation block — the mechanism underlying both remission and differentiation syndrome.

OBJECTIVE

To generate pooled, exploratory estimates of CR/CRh, overall response rate (ORR), and differentiation syndrome (any grade and grade ≥3) across prospective trials of menin inhibitors in R/R KMT2A-rearranged or NPM1-mutated acute leukemia.

METHODS

Exploratory proportional meta-analysis of prospective trials of menin inhibitors in this population. Efficacy events were drawn from efficacy-evaluable populations, safety events from safety-evaluable populations. Single-arm proportions were pooled with a random-effects logistic-normal model (logit transformation); study-level 95% CIs used exact Clopper–Pearson. Heterogeneity was assessed with Cochran Q, τ^2, and I^2. Given few studies and differing populations and response definitions, estimates are exploratory and descriptive rather than comparative.

RESULTS

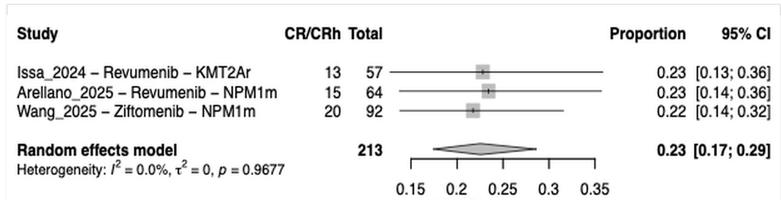

Figure 1. Pooled CR/CRh rate — 22.5% (17.4–28.6), I^2 = 0.0%

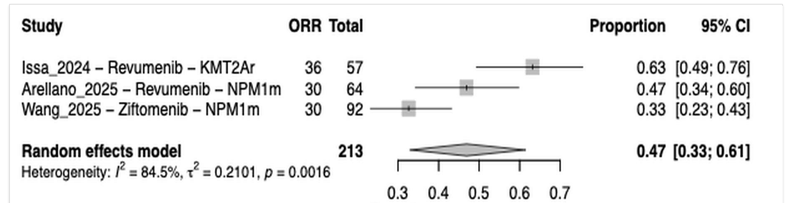

Figure 2. Pooled overall response rate — 46.9% (32.8–61.4), I^2 = 84.5%

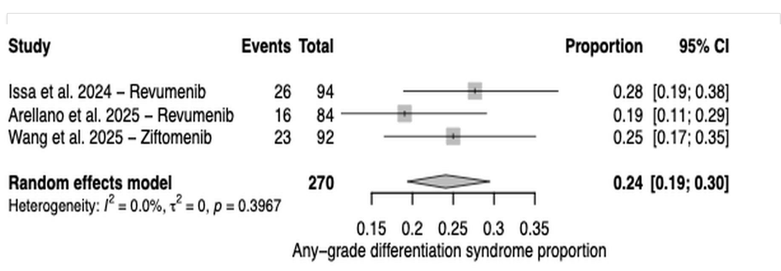

Figure 3. Differentiation syndrome, any grade — 24.1% (19.3–29.5)

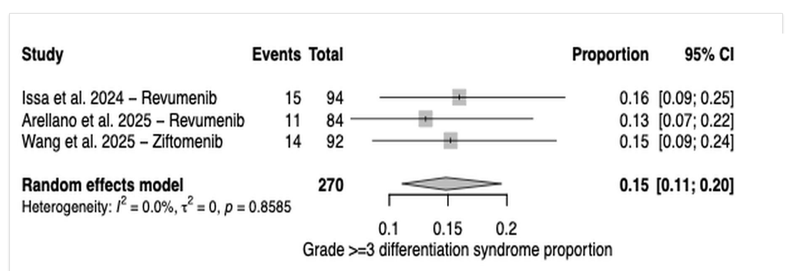

Figure 4. Differentiation syndrome, grade ≥3 — 14.8% (11.1–19.6)

Table 1. Included Studies and Study-Level Response Rates

Study	Trial	Agent	Population	Efficacy N	CR/CRh %	ORR %	Safety N
Issa 2024	AUGMENT-101	Revumenib	KMT2Ar R/R acute leukemia	57	22.8	63.2	94
Arellano 2025	AUGMENT-101	Revumenib	NPM1m R/R AML	64	23.4	46.9	84
Wang 2025	KOMET-001	Ziftomenib	NPM1m R/R AML	92	22.0	33.0	92

CONCLUSIONS

- Menin inhibition yields a reproducible CR/CRh rate of ~23% in heavily pretreated R/R disease, with no between-study heterogeneity (I^2 = 0%).
- Broader response (ORR 46.9%) varied widely across trials (I^2 = 84.5%), reflecting differences in molecular subgroup and response definitions.
- Differentiation syndrome affected ~1 in 4 patients (grade ≥3 in ~15%) and was consistent across agents — a predictable class effect requiring proactive recognition and management.

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REFERENCES 1. Issa GC, et al. J Clin Oncol. 2025;43(1):75-84. 2. Arellano ML, et al. Blood. 2025;146(9):1065-1077. 3. Wang ES, et al. J Clin Oncol. 2025;43(31):3381-3390.

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