REAL-WORLD EXPERIENCE WITH REVUMENIB: A SINGLE-CENTER ANALYSIS OF EFFICACY AND TOLERABILITY

UMAR IQBAL[1], ONYEE CHAN[1], RORY SHALLIS[1], LORENA LOPEZ-GONZALEZ[2], SYEDA SABA KAREEM[3], ALISON WALKER[1], CRAIG W. FREYER[2], ANDREW KUYKENDALL[1], HUAN HUANG[2], ZOEY XIE[1], ERIC PADRON[1], RAMI KOMROKJI[1], JEFFREY LANCET[1], DAVID A. SALLMAN[1]

1. Department of Malignant Hematology, Moffitt Cancer Center, Tampa, FL
2. Syndax Pharmaceuticals, Inc., New York, NY
3. Department of Pharmacy, Moffitt Cancer Center, Tampa, FL

INTRODUCTION

- Revumenib, a first-in-class, oral, potent, and selective inhibitor of the menin-KMT2A interaction, is used for the treatment of relapsed/refractory (R/R) acute myeloid leukemia (AML) harboring an *NPM1* mutation or R/R acute leukemia with a *KMT2A* translocation in patients ≥1 year[1,2]
- The first real-world evidence for revumenib, based on a single-center experience, demonstrated favorable real-world effectiveness and tolerability in *NPM1*–mutated (*NPM1*m) and *KMT2A*–rearranged (*KMT2A*r) acute leukemia.[3] These findings provided early real-world evidence supporting the use of revumenib in routine clinical practice

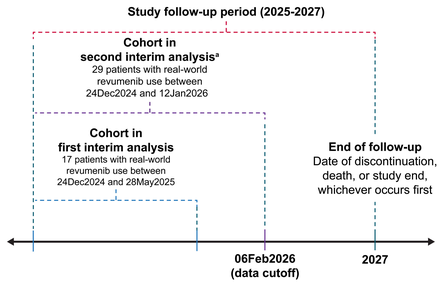
AIM

- To present updated effectiveness and safety/tolerability outcomes from real-world revumenib use at a single academic institution

METHODS

- In this ongoing longitudinal study, institutional prescription data were reviewed to identify patients who received ≥1 dose of revumenib outside of a clinical trial between 24Dec2024 and 12Jan2026
- Patients were followed from revumenib initiation until data cutoff (06Feb2026) or death (**Figure 1**)
- Clinical response was evaluated using ELN 2022 criteria[4] for complete remission (CR), CR with partial hematologic recovery (CRh), and CR with incomplete hematologic recovery (CRi). Overall response rate (ORR) also included morphologic leukemia-free state and partial response. Response in patients treated solely for MRD+ disease was assessed by conversion to MRD− disease
- Safety outcomes included grade ≥3 QTcF prolongation and differentiation syndrome (DS)

Figure 1. Study design



[a]Second interim analysis included patients from first interim analysis with extended follow-up as well as additional patients enrolled since the first data cutoff.

RESULTS

- Twenty-nine patients were included in the total population (12 *KMT2A*r, 11 *NPM1*m, 5 *NUP98*–rearranged, and 1 false-positive *KMT2A*r; **Table 1**)
- Overall, 72% of patients were treated for R/R disease (**Table 2**)
- Median (range) number of prior lines of therapy was 2 (0–5); 72% of patients had prior venetoclax exposure
- Seven patients received revumenib monotherapy and 22 received combination therapy (**Table 3**)
- Seven patients proceeded to HSCT; 3 received revumenib as post-HSCT maintenance

Table 1. Patient characteristics

	Total population (N = 29)[a]
Age, median (range), y	62 (24–82)
Male, n (%)	18 (62)
Follow-up from revumenib initiation, median (range), mo	6.1 (0.4–23.1)
Leukemia subtype, n (%)	
AML	28 (97)
CML-BP	1 (3)
Co-mutations, n (%)	24 (83)
FLT3	5 (17)
DNMT3A	4 (14)
IDH2	3 (10)
IDH1	1 (3)

[a]Included 1 patient with false-positive KMT2Ar (included in safety analysis) and 5 patients with R/R NUP98r disease (4 AML and 1 CML-BP).

Table 2. Treatment history

	Total population (N = 29)[a]
No. of prior lines of therapy, median (range)[b]	2 (0–5)
Prior venetoclax, n (%)	21 (72)
Prior HSCT, n (%)	9 (31)
Treatment setting at revumenib initiation, n (%)	
R/R	21 (72)
MRD+	5 (17)
Frontline	2 (7)
Post-HSCT maintenance only	1 (3)

[a]Included 1 patient with false-positive KMT2Ar (included in safety analysis) and 5 patients with R/R NUP98r disease (4 AML and 1 CML-BP). [b]HSCT was not considered a separate line of therapy.

Table 3. Revumenib treatment characteristics

	Total population (N = 29)[a]
Monotherapy, n (%)	7 (24)
Combination therapy, n (%)[b]	22 (76)
Post-revumenib HSCT, n[c]	7
Post-HSCT revumenib, n/N	3/7

[a]Included 1 patient with false-positive KMT2Ar (included in safety analysis) and 5 patients with R/R NUP98r disease (4 AML and 1 CML-BP). [b]Seventeen patients received revumenib + venetoclax + hypomethylating agent (triplet). [c]Two patients received HSCT as second HSCT.

- Among the R/R response-evaluable cohort (n = 18), ORR was 72% (**Table 4**)
- Five patients (17%) had grade 3 QTcF prolongation (2 increased >60 ms from baseline); no grade 4 events occurred; QTcF prolongation did not lead to treatment discontinuation in any patient (**Table 5**)
- Three patients (10%) had grade 3 DS; no grade 4 events occurred (**Table 5**)
- Six deaths occurred (5 disease-related and 1 HSCT complication); none were related to revumenib

Table 4. Real-world effectiveness of revumenib[a,b]

	R/R cohort (n = 18)
ORR, n (%)	13 (72)
CRc (CR + CRh + CRi), n (%)	9 (50)
CR+CRh, n (%)	6 (33)
Time to first response, median (range), mo	1.0 (0.5–6.5)
Time to best response, median (range), mo	2.6 (0.6–10.1)
Relapse, n (%)	3/13 (23) 1 with CNS-only relapse
	MRD+ cohort (n = 5)
Achieved MRD−, n (%)	4 (80)
Relapse, n (%)	1[c] CNS-only relapse
	Frontline cohort (n = 1)
CR (MRD−), n (%)	1 (100)
Relapse, n (%)	0

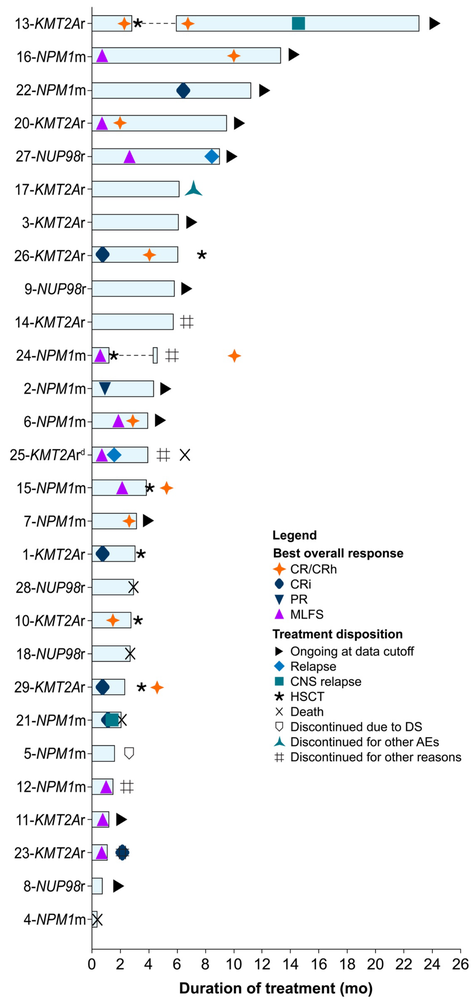
[a]Across all treatment settings (R/R, MRD+, frontline), 18/24 (75%) patients achieved the relevant clinical response. [b]The following patients were excluded from response analyses: 3 patients with marrow not yet evaluated or pending (R/R cohort), 1 patient with false-positive KMT2Ar (frontline cohort), and 1 patient who received revumenib only as post-HSCT maintenance. [c]Relapse occurred in patient who remained MRD+.

Table 5. Real-world safety and tolerability of revumenib

	Total population (N = 29)
Grade 3 QTcF prolongation, n (%)[a]	5 (17)
Revumenib interruption	3 (10)
Revumenib reduction	1 (3)
Revumenib discontinuation	0
Grade 3 DS, n (%)[b]	3 (10)
Revumenib interruption	0
Revumenib reduction	0
Revumenib discontinuation	1 (3)
Death (not related to revumenib)[c]	6 (21)

[a]Regular QTcF monitoring was available for 24 patients. Four patients had grade 1 QTcF prolongation; 2 patients had grade 2 QTcF prolongation. Among the 5 patients who had grade 3 QTcF prolongation, 2 increased >60 ms from baseline and 3 had QTcF ≥501 ms. No grade 4 QTcF prolongation events occurred. [b]One patient had grade 2 DS; 3 patients had grade 3 DS (1 patient on concomitant enasidenib, 1 patient on venetoclax + decitabine, and 1 patient on revumenib monotherapy). No grade 4 DS events occurred. [c]Five deaths were related to disease progression and 1 was related to HSCT; none were related to revumenib.

Figure 2. Swimmer plot[a–c]



[a]Revumenib combination therapy predominated; patients 3, 5, 9, 12, 17, 21, and 27 received monotherapy. [b]Most patients were treated for R/R disease except patient 26 (frontline disease), patient 17 (post-HSCT maintenance only), and patients 7, 10, 12, 21, and 24 (MRD+ disease). [c]Patient with false-positive KMT2Ar was excluded. [d]Discontinued revumenib as post-HSCT maintenance after 1 week due to thrombocytopenia.

CONCLUSIONS

- Findings demonstrate revumenib is an effective and well-tolerated therapeutic option in patients with heavily pretreated AML, with broad activity in combination and in the MRD+ setting
- High ORR and CRc rates were observed among the R/R cohort
- Responses appear durable even for heavily pretreated patients, with only 4 relapses; of these, 2 were limited to the CNS

ACKNOWLEDGMENTS

This study was sponsored by Syndax Pharmaceuticals, Inc.

CONTACT INFORMATION

David.Sallman@moffitt.org

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. Iqbal U, et al. Presented at: 67th American Society of Hematology (ASH) Annual Meeting and Exposition; December 6–9, 2025; Orlando, FL, USA. Abstract 3448.
4. Döhner H, et al. *Blood*. 2022;140(12):1345–1377.