Early Real-World Experience with Revumenib Outside of a Clinical Trial Setting: A Single Center Retrospective Review of Efficacy and Tolerability

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INTRODUCTION

- Revumenib was approved by the US Food and Drug Administration on November 15, 2024 as the first menin inhibitor for treatment of relapsed or refractory (R/R) acute leukemias with a *KMT2A* translocation and on October 24, 2025 for treatment of R/R AML with a *NPM1* mutation based on results from the AUGMENT-101 trial[1-4]
- Other molecular subgroups (e.g., *NUP98* rearrangements), disease states (e.g., MRD-positive), or therapeutic strategies (e.g., combination regimens and post-transplant maintenance) may also derive benefit from revumenib[5]
- Here, we present early real-world data on the efficacy and tolerability of revumenib across molecularly defined AML subsets

METHODS

- We reviewed institutional prescription records to identify patients who received ≥1 dose of revumenib between December 12, 2024 and May 28, 2025, outside the context of a clinical trial
- Patients were followed from the date of first revumenib dispensing until October 25, 2025, or death, whichever occurred first
- Efficacy was assessed according to the ELN 2022 criteria and included complete remission (CR), CR with partial hematologic recovery (CRh), and CR with incomplete hematologic recovery (CRi). The composite complete remission (CRc) rate was defined as CR + CRh + CRi, and the overall response rate (ORR) additionally included patients who achieved a morphologic leukemia-free state (MLFS) or partial remission (PR)
- Safety analyses included all treated patients, with grade ≥3 (G3–4) adverse events (AEs) recorded
- Differentiation syndrome and QTc prolongation were captured at any grade

REFERENCES

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RESULTS

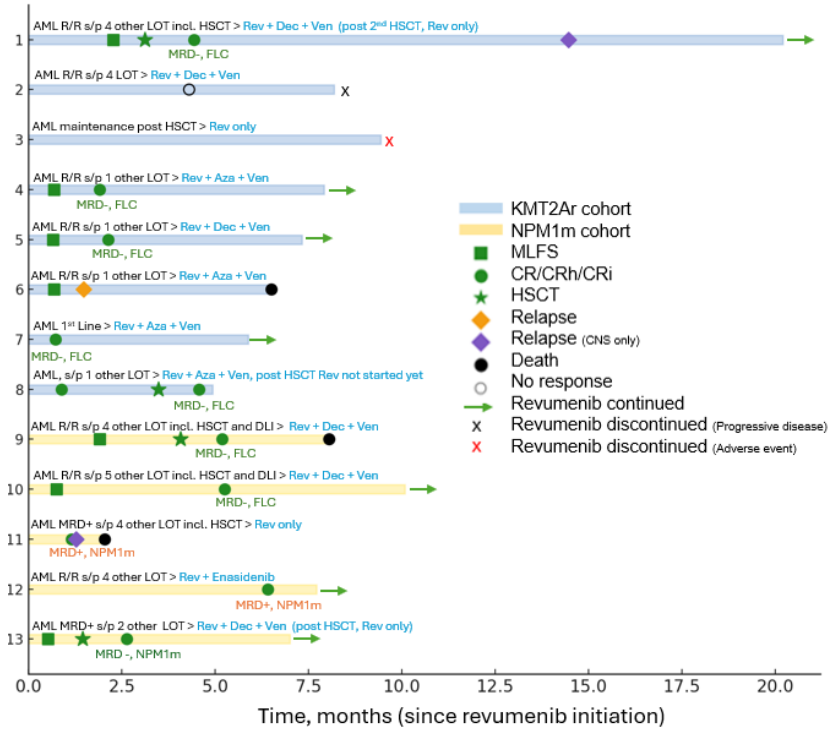

Figure 1. Swimmer plot of duration of treatment

- Patient "1" initiated revumenib while on a clinical trial and continued it post HSCT as maintenance (off trial). CNS relapse was treated definitively and pt maintains MRD negative CR in bone marrow.
- Patient "3" received revumenib only as maintenance post HSCT and it was discontinued due to recurrent pneumonias.
- Patients "11" and "13" were treated for MRD+ disease.
- Patient "7" was treated in the frontline setting and continues to maintain MRD negative CR at 6 months
- Median overall survival not reached at 7.1 months of median follow-up

Results for NUP98 patients

- In addition to *KMT2Ar* and *NPM1m*, 3 patients were treated for *NUP98r* (R/R AML, n=2 and CML-BP, n=1). Of these, 1 R/R AML pt responded and has MLFS (ongoing durable MLFS x 7 months+).
- Two patients with *NUP98r* died due to disease progression

Patient Characteristics	
Total patients, n	17
Age, median (range), years	54 (23-79)
Female, n (%)	7 (41)
Co-mutations, n (%)	13 (76)
Most common co-mutations (*DNMT3A*, *TET2*, and *WT*), n (%)	4 (24) for each
Targetable co-mutations, n	*FLT3*-ITD (2) *IDH1* (1), *IDH2* (1)
Prior lines of therapy, median (range)	4 (0-6)
Prior venetoclax, n (%)	12 (71)
Prior HSCT, n (%)	6 (35)
Follow up, median (range), months	7.1 (2.1-20.5)

Treatment Characteristics	
Single agent revumenib, n/N (%)	3/17 (18)
Revumenib + venetoclax + hypomethylating agent (triplet), n/N (%)	13/17 (76)
Post revumenib HSCT, n/N (%)	4/17 (26) (2 as 2nd HSCT)
Post HSCT revumenib, n/N (%)	3/4 (75) (2 as continuation, 1 as maintenance)

Efficacy Data[a]	
ORR, n/N (%)	10/13 (77)
CRc (CR + CRh + CRi), n/N (%)	8/13 (62)
CR + CRh, n/N (%)	4/13 (31)
MRD negative at best response, n/N (%)	9/12 (75)
Relapse, n/N (%)	3/15 (20) 2 with CNS only relapse
Time to first response, median (range), months	0.8 (0.5-6.5)
Time to best response, median (range), months	2.2 (0.7-6.5)

[a]The following patients were excluded from ORR/CRc/CR+CRh analysis: 1 patient for *KMT2Ar* deemed to be an artifact, 1 patient who received revumenib only as post HSCT maintenance, and 2 patients treated for MRD+ disease. 2 patients treated for MRD+ disease were included in the relapse analysis

Safety Data	
Any grade 3 or 4 AE (non-hematological), n /N (%)	4 /17 (24)
Grade ≥3 QTc prolongation, n/N (%)[a]	3/15 (20)
Grade ≥3 differentiation syndrome, n/N (%)[b]	2/17 (12)
Revumenib interruption, n/N (%)	8/17 (47)
Revumenib reduction, n/N (%)	1/17 (6)
Revumenib discontinuation, n (%)	1 (6)
Deaths	5 (4 disease related, 1 HSCT complication)

[a]Regular QTc monitoring was available for 15 patients; 2 patients had Grade 2 QTc prolongation, 1 patient had Grade 1 QTc prolongation. [b]One event of grade 3 differentiation syndrome occurred in a patient on concomitant enasidenib. 1 patient had Grade 2 differentiation syndrome

CONCLUSIONS

- **Early real-world data for revumenib suggests excellent tolerability and no new safety signals.**
- **QTc prolongation and differentiation syndrome did not lead to treatment discontinuation in any patient.**
- **Responses appear to be durable even for heavily pretreated patients, with only 3 relapses in our cohort of which 2 were limited to CNS.**
- **Triplet therapy with revumenib in combination with HMAs and venetoclax results in earlier responses and with acceptable toxicity profiles.**