Revumenib Therapy Post Hematopoietic Stem Cell Transplant for Patients With Relapsed/Refractory *KMT2A*r, *NPM1*m, and *NUP98*r Acute Myeloid Leukemia: Post Hoc Analysis of Outcomes From AUGMENT-101

PS1631

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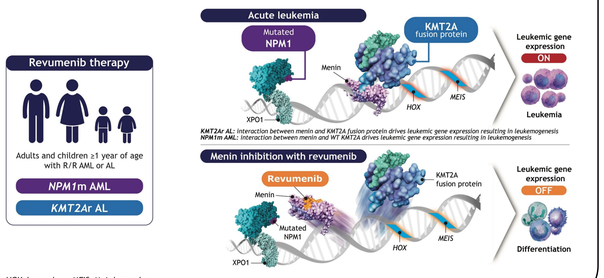
INTRODUCTION

- Hematopoietic stem cell transplant (HSCT) is widely used as a standard-of-care approach for acute myeloid leukemia (AML), yet disease recurrence after HSCT remains a major limitation[1]
  - Approximately 30% to 40% of patients (regardless of age) relapse, often within 6 to 7 months after HSCT[2,3]
  - Among young adult and adult patients with *KMT2A*-rearranged (*KMT2A*r) AML, relapse often occurs early (median time to relapse, 4.7 months)[4]
- Revumenib, a first-in-class, oral, potent, and selective inhibitor of the menin-KMT2A interaction (**Figure 1**), is used for the treatment of relapsed/refractory (R/R) AML harboring an ***NPM1* mutation** (*NPM1*m) or R/R acute leukemia with a ***KMT2A* translocation** in adult and pediatric patients 1 year and older[5,6]
- In addition to the well-characterized antileukemic action of menin inhibitors, preclinical data indicate that menin inhibition may also enhance donor T-cell antitumor activity, which supports revumenib as a potential post-HSCT maintenance treatment and thus as a strategy to reduce the risk of relapse[7]

Figure 1. Revumenib mechanism of action



HOX, homeobox; *MEIS*, Meis homeobox.

OBJECTIVE

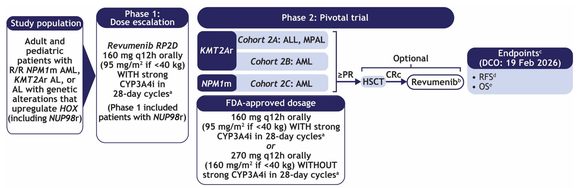
- To evaluate the efficacy and safety of revumenib monotherapy as post-HSCT maintenance treatment in patients with R/R *NPM1*m, *KMT2A*r, or *NUP98* rearranged (*NUP98*r) AML from pooled phase 1/2 data from AUGMENT-101 (NCT04065399)

METHODS

Study design

- AUGMENT-101 is an ongoing phase 1/2, open-label, dose-escalation and -expansion study of revumenib in pediatric and adult patients with R/R *NPM1*m, *KMT2A*r, or *NUP98*r acute leukemia (**Figure 2**)
- Post-HSCT maintenance therapy with revumenib was allowed for eligible patients, with treatment continuing until disease progression, unacceptable toxicity, or physician decision
  - Eligible patients were between 30 to 180 days after HSCT, had achieved composite complete remission, had successful engraftment, and had no acute or chronic graft-versus-host disease (GVHD) that required immunosuppression
  - Revumenib maintenance was administered at the same dose the patient was receiving immediately prior to HSCT, with adjustments for patients starting or stopping a strong cytochrome P450 3A4 inhibitor peri-HSCT

Figure 2. AUGMENT-101 study design



[a]Revumenib administered until unacceptable toxicity, end of Cycle 4 if no response, or PD without clinical benefit as defined by the investigator; no steroid or other differentiation syndrome prophylaxis was mandated per protocol. Patients could receive tablet, capsule, or oral solution formulations of revumenib with or without a strong CYP3A4i. Figure shows starting dose for tablet and oral solution formulations. [b]Maintenance therapy with revumenib after HSCT was allowed per protocol amendment for eligible patients, with treatment continued until PD, unacceptable toxicity, or physician decision. [c]Relevant to the current analysis. [d]Time from date of the first dose of revumenib after HSCT to the date of first disease progression or death, whichever occurred first. [e]Time from date of first dose of revumenib after HSCT to date of death due to any cause.
ALL, acute lymphoblastic leukemia; CRc, composite complete remission; CYP3A4i, cytochrome P450 3A4 inhibitor; DCO, data cutoff; *HOX*, homeobox; MPAL, mixed-phenotype acute leukemia; OS, overall survival; PD, progressive disease; PR, partial response; q12h, every 12 hours; RFS, relapse-free survival; RP2D, recommended phase 2 dose.

RESULTS

Patients

- As of 19 February 2026, 19/59 (32%) patients with R/R AML who received HSCT after achieving a response with revumenib monotherapy had resumed revumenib treatment after HSCT
- Four (21%) patients had *NPM1*m AML, 14 (74%) had *KMT2A*r, and 1 (5%) had *NUP98*r (**Table 1**)
  - Two of 4 patients with *NPM1*m had co-mutations (*IDH1*, *DNM3TA*, and *FLT3*-ITD)
- Patients had received a median (range) of 2 (1-7) prior lines of treatment; 10 (53%) patients had received prior HSCT
- Median (range) time from HSCT to initiation of revumenib maintenance was 65 (34-181) days

Table 1. Demographic and baseline characteristics

	*NPM1*m (n = 4)	*KMT2A*r (n = 14)	*NUP98*r (n = 1)	Total (N = 19)
Age, median (range), y	42.5 (19.0-56.0)	40.0 (1.3-75.0)	17.0 (17.0-17.0)	39.0 (1.3-75.0)
Age group, n (%)				
<18 y	0	3 (21)	1 (100)	4 (21)
18-<65 y	4 (100)	10 (71)	0	14 (74)
≥65 y	0	1 (7)	0	1 (5)
Female, n (%)	3 (75)	6 (43)	0	9 (47)
Race, n (%)				
White	4 (100)	8 (57)	1 (100)	13 (68)
Non-White[a]	0	3 (21)	0	3 (16)
Unknown	0	3 (21)	0	3 (16)
No. of prior lines of therapy, median (range)	2 (1-7)	2 (1-6)	5 (5-5)	2 (1-7)
Disease status at baseline, n (%)				
Primary refractory	0	4 (29)	0	4 (21)
Refractory relapse	2 (50)	6 (43)	1 (100)	9 (47)
Early untreated relapse	1 (25)	2 (14)	0	3 (16)
Late untreated relapse	1 (25)	2 (14)	0	3 (16)
Prior treatment, n (%)				
Venetoclax	2 (50)	6 (43)	1 (100)	9 (47)
HSCT	2 (50)	7 (50)	1 (100)	10 (53)
Days from HSCT to initiating revumenib treatment, median (range)	43 (40-59)	78 (34-181)	145 (145-145)	65 (34-181)

[a]Includes Black or African American and Asian.

Post-HSCT maintenance exposure

- Median relative dose intensity was high, regardless of genotype, which supports tolerability of revumenib as a post-HSCT maintenance therapy (**Table 2**)
- Median (range) duration of post-HSCT maintenance therapy was 20.0 (2.0-137.0) weeks

Table 2. Exposure

	*NPM1*m (n = 4)	*KMT2A*r (n = 14)	*NUP98*r (n = 1)	Total (N = 19)
No. of cycles started, median (range)	2.5 (1.0-24.0)	5.0 (1.0-33.0)	11.0 (11.0-11.0)	5.0 (1.0-33.0)
Relative dose intensity, median (range), %	78.7 (55.8-100.0)	95.5 (15.7-159.5)	95.7 (95.7-95.7)	95.7 (15.7-159.5)
Duration of therapy, median (range), wk	38.1 (2.0-99.0)	19.7 (2.0-137.0)	41.7 (42.0-42.0)	20.0 (2.0-137.0)

Efficacy

- Median relapse-free survival was not reached in patients receiving post-HSCT revumenib, regardless of genotype, and 78.6% of patients remained alive and relapse free at 12 months (**Table 3**)
  - 85.1% of patients in the *KMT2A*r group were alive and relapse free at 12 months
- Median overall survival was not reached in patients receiving post-HSCT revumenib, regardless of genotype (**Table 3**)

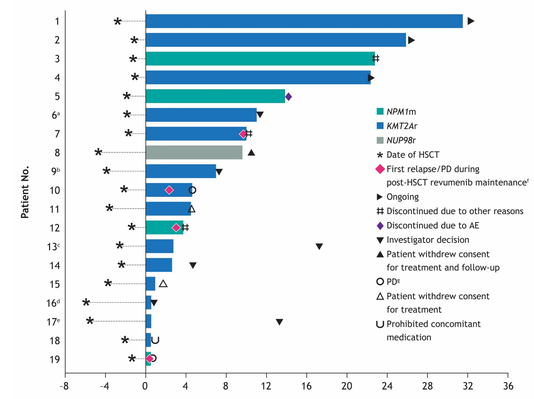
Table 3. Efficacy

	*NPM1*m (n = 4)	*KMT2A*r (n = 14)	*NUP98*r (n = 1)	Total (N = 19)
RFS				
Events,[a] n (%)	2 (50.0)	3 (21.4)	0	5 (26.3)
Median (95% CI), mo	NR (0.3-NR)	NR (26.0-NR)	N/A	NR (26.0-NR)
Estimated 12-mo rate (95% CI), %	50.0 (5.8-84.5)	85.1 (52.3-96.1)	N/A	78.6 (52.5-91.4)
OS				
Events,[b] n (%)	2 (50.0)	2 (14.3)	0	4 (21.1)
Median (95% CI), mo	NR (0.9-NR)	NR (26.0-NR)	N/A	NR (26.0-NR)
Estimated 12-mo rate (95% CI), %	75.0 (12.8-96.1)	100.0 (100.0-100.0)	N/A	94.7 (68.1-99.2)

[a]Four patients due to PD, 1 patient due to death. [b]Due to death.
N/A, not applicable; NR, not reached; OS, overall survival; PD, progressive disease; RFS, relapse-free survival.

- As of 19 February 2026, 3 patients remained on post-HSCT maintenance treatment (**Figure 3**)

Figure 3. Duration of revumenib treatment as post-HSCT maintenance in patients with R/R *NPM1*m, *KMT2A*r, and *NUP98*r AML



Dashed line represents time after HSCT. Footnotes a-e are specific reasons for physician discontinuation of revumenib maintenance therapy. [a]Patient completed treatment course. [b]Patient experienced molecular MRD recurrence and discontinued revumenib to receive donor lymphocyte infusion. [c]Patient developed chronic GVHD. [d]Patient developed possible transplant-associated microangiopathy. [e]Dosing placed on hold after Cycle 1 while receiving a JAK inhibitor for GVHD. [f]First relapse or PD per disease response assessment. [g]PD is a reason for treatment discontinuation.
AE, adverse event; GVHD, graft-versus-host disease; JAK, Janus kinase; MRD, measurable residual disease; PD, progressive disease.

Safety

- Any-grade treatment-emergent adverse events (TEAEs) occurred in 84% of patients (**Table 4**); most common were thrombocytopenia/platelet count decreased (53%) and rhinorrhea (37%)
- Most common grade ≥3 TEAEs were thrombocytopenia/platelet count decreased (42%) and neutrophil count decreased (16%)

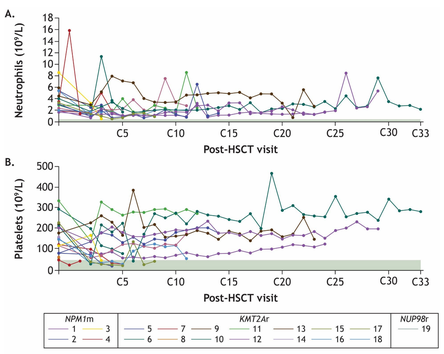
Table 4. Summary of AEs

Parameter, n (%)	Total (N = 19)
Any-grade TEAE	16 (84)
Grade ≥3	14 (74)
Any-grade TRAE	9 (47)
Grade ≥3	8 (42)
SAE	8 (42)
TEAE leading to dose modification	11 (58)
Reduction	2 (11)
Interruption	11 (58)
TEAE leading to revumenib discontinuation	1 (5)
TEAE leading to death	0
TRAE leading to dose modification	7 (37)
Reduction[a]	2 (11)
Interruption[b]	7 (37)
TRAE leading to revumenib discontinuation	1 (5)
TRAE leading to death	0

[a]Due to AEs (platelet count decreased, n = 2; neutrophil count decreased, n = 1; 1 patient experienced both events).
[b]Dose interruptions included dose delayed or dose skipped.
AE, adverse event; SAE, serious adverse event; TEAE, treatment-emergent adverse event; TRAE, treatment-related adverse event.

- Relative to post-HSCT starting dose levels, 2 (11%) patients had a revumenib dose reduction due to cytopenia; no patients discontinued revumenib treatment due to cytopenia
- Most patients maintained neutrophils >0.5 × 10^9/L and platelets >50.0 × 10^9/L during revumenib maintenance therapy (**Figure 4**)

Figure 4. Neutrophil and platelet counts in individual patients over time during post-HSCT maintenance



Each line indicates an individual patient. Green shading indicates absolute neutrophil count <0.5 × 10^9/L and platelets <50.0 × 10^9/L, respectively.
C, Cycle.

- 11/19 (58%) patients had dose interruptions during treatment
  - Reasons for skipped doses included platelet count decreased/thrombocytopenia (6/19; 32%), nausea/vomiting (3/19; 16%), neutropenia (1/19; 5%), and GVHD (3/19; 16%)
- One grade ≥2 QTcF prolongation event occurred in 1 (5%) patient, lasting 1 day, and was unrelated to revumenib
- No differentiation syndrome events were reported with revumenib post-HSCT maintenance therapy
- GVHD occurred in 4 (21%) patients, and onset ranged from 17 to 83 days after initiation of revumenib maintenance
  - Three events were grade 3, and none were considered related to revumenib

CONCLUSIONS

- Revumenib demonstrated promising efficacy and a tolerable safety profile as post-HSCT maintenance treatment in adult and pediatric patients with R/R *NPM1*m, *KMT2A*r, and *NUP98*r AML
- Sustained relapse-free survival across genotypes supports the potential ability of revumenib to reduce post-HSCT relapse in this high-risk population
- The safety profile of revumenib was consistent with that of the broader AUGMENT-101 trial,[5] and no differentiation syndrome was reported
  - No patients discontinued treatment due to cytopenias
- Collectively, these data support continued evaluation of revumenib as a post-HSCT maintenance treatment, with ongoing assessment in the post-transplant setting (NCT06575296)

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