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PF508

Long-Term Follow-Up of Pediatric/Young Adult Patients With Relapsed/Refractory *KMT2A*r Acute Leukemia Treated With Revumenib in AUGMENT-101

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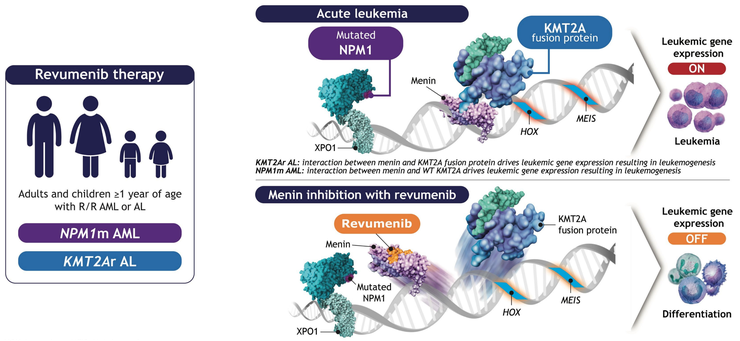
INTRODUCTION

- The menin-KMT2A interaction is critical for leukemogenesis, and up to 10% of adult and pediatric patients with acute leukemia (AL) have a *KMT2A* gene rearrangement (*KMT2A*r)[1,2]
- *KMT2A*r is the most frequent chromosomal rearrangement in pediatric acute myeloid leukemia (AML), occurring in 20%–30% of cases,[3] and is associated with poor prognosis[4]
  - In pediatric patients, 5-year event-free survival (EFS) ranges from 29%–66% and overall survival ranges from 47%–68%[5-10]
- 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** or R/R AL with a ***KMT2A* translocation** in adult and pediatric patients 1 year and older[11,12]

Figure 1. Revumenib mechanism of action



HOX, homeobox; *MEIS*, Meis homeobox.

OBJECTIVE

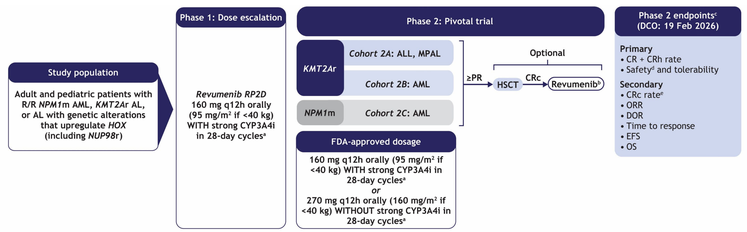
- To report long-term follow-up data for pediatric and young adult patients with R/R *KMT2A*r AL treated with revumenib monotherapy in AUGMENT-101 (NCT04065399)

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 AL with an *NPM1* mutation, *KMT2A*r, or *NUP98* rearrangement (**Figure 2**)
- Pediatric and young adult patients 30 days to <21 years of age pooled from phases 1 and 2 were included in this analysis
- Efficacy outcomes are shown by AL subtype in the efficacy population (patients with *KMT2A*r [local testing], treated at recommended phase 2 dose, with ≥5% baseline morphologic blasts)

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. Patients could receive equivalent 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 or unacceptable toxicity. [c]Relevant to the current analysis. [d]No steroid or other differentiation syndrome prophylaxis was mandated per protocol. [e]CRc rate = CR + CRh + CRp + CRi.
ALL, acute lymphoblastic leukemia; CR, complete remission; CRc, composite CR; CRh, CR with partial hematologic recovery; CRi, CR with incomplete hematologic recovery; CRp, CR with incomplete platelet recovery; CYP3A4i, cytochrome P450 3A4 inhibitor; DCO, data cutoff; DOR, duration of response; EFS, event-free survival; *HOX*, homeobox; MPAL, mixed-phenotype acute leukemia; ORR, overall response rate; OS, overall survival; PD, progressive disease; PR, partial remission; q12h, every 12 hours; RP2D, recommended phase 2 dose.

RESULTS

Patients

- At data cutoff (19 February 2026), 38 pediatric and young adult patients with *KMT2A*r AL who were treated at the recommended phase 2 dose were included in the safety population: 27 with AML, 8 with acute lymphoblastic leukemia (ALL), and 3 with mixed-phenotype acute leukemia (MPAL; **Table 1**)
- Median duration of follow-up was 6.9 months for patients with AML, 2.9 for ALL, and 5.7 for MPAL; 7 patients remained on study at data cutoff
- Majority of patients were 2-<12 years of age and had R/R AML

Table 1. Demographic and baseline characteristics[a]

	AML (n = 27)	ALL (n = 8)	MPAL (n = 3)	Total (N = 38)
Age, median (range), y	6.0 (1.3-20.0)	2.5 (0.6-20.0)	1.5 (1.0-2.0)	5.0 (0.6-20.0)
Age group, n (%)				
0-<2 y	4 (15)	1 (13)	2 (67)	7 (18)
2-<12 y	15 (56)	5 (63)	1 (33)	21 (55)
12-<17 y	4 (15)	1 (13)	0	5 (13)
17-20 y	4 (15)	1 (13)	0	5 (13)
Female, n (%)	16 (59)	5 (63)	2 (67)	23 (61)
Race, n (%)				
White	19 (70)	2 (25)	1 (33)	22 (58)
Non-White[b]	4 (15)	3 (38)	0	7 (18)
Unknown	4 (15)	3 (38)	2 (67)	9 (24)
Disease status at baseline, n (%)				
Primary refractory	5 (19)	2 (25)	0	7 (18)
Refractory relapse	16 (59)	5 (63)	3 (100)	24 (63)
Early untreated relapse	6 (22)	1 (13)	0	7 (18)
No. of prior lines of therapy, median (range)	3.0 (1-11)	4.0 (1-9)	4.0 (2-4)	3.0 (1-11)
Prior therapy, n (%)				
Venetoclax	16 (59)	4 (50)	1 (33)	21 (55)
HSCT	15 (56)	2 (25)	2 (67)	19 (50)
CAR-T	1 (4)	4 (50)	1 (33)	6 (16)

[a]In the safety population (those with *KMT2A*r per local testing who were treated at RP2D). [b]Includes Black or African American, Asian, and multiple.
ALL, acute lymphoblastic leukemia; CAR-T, chimeric antigen receptor T-cell therapy; MPAL, mixed-phenotype acute leukemia; RP2D, recommended phase 2 dose.

Efficacy

- In the efficacy population, durable CR/CRh responses were achieved across AL subtypes in pediatric and young adult patients and observed within ~1 month after initiation of revumenib therapy (**Table 2**)
  - For CR/CRh responders, the median duration of CR/CRh in patients with AML was 32.3 months
- Among patients in the efficacy population with a response, 10/26 (38.5%) patients with AML and 1/3 (33.3%) patients with MPAL proceeded to hematopoietic stem cell transplant (HSCT); 3 patients (all with AML) resumed revumenib monotherapy post HSCT
- Median EFS was similar in patients with AML and MPAL (4.5 and 5.0 months, respectively) and slightly higher than for ALL (1.9 months)

Table 2. Efficacy[a]

	AML (n = 26)	ALL (n = 7)	MPAL (n = 3)	Total (N = 36)
CR + CRh rate, n (%)	8 (30.8)	1 (14.3)	1 (33.3)	10 (27.8)
95% CI	14.3–51.8	0.4–57.9	0.8–90.6	14.2–45.2
Duration of CR/CRh, median (95% CI), mo	32.3 (2.7-NR)	1.9 (NR-NR)	1.8 (NR-NR)	32.3 (1.8-NR)
Time to CR/CRh, median (range), mo	1.9 (1.0-5.6)	1.8 (1.8-1.8)	3.2 (3.2-3.2)	1.9 (1.0-5.6)
CRc rate, n (%)	9 (34.6)	1 (14.3)	1 (33.3)	11 (30.6)
95% CI	17.2–55.7	0.4–57.9	0.8–90.6	16.3–48.1
ORR, n (%)	15 (57.7)	3 (42.9)	2 (66.7)	20 (55.6)
95% CI	36.9–76.6	9.9–81.6	9.4–99.2	38.1–72.1
MRD-negative status,[b] n/N (%)				
CR + CRh	6/7 (85.7)	0	1/1 (100)	7/8 (87.5)
CRc	7/8 (87.5)	0	1/1 (100)	8/9 (88.9)
EFS, median (95% CI), mo	4.5 (2.3-11.7)	1.9 (0.3-NR)	5.0 (0.9-NR)	3.6 (1.9-6.6)
OS, median (95% CI), mo	6.9 (2.9-NR)	3.9 (0.3-NR)	5.7 (0.9-NR)	6.4 (2.9-34.2)

[a]In the efficacy population (those with *KMT2A*r per local testing who were treated at RP2D, with ≥5% baseline morphologic blasts). [b]Among those with MRD status available. MRD assessed by flow cytometry or polymerase chain reaction. One patient with AML and CRp was MRD negative from an unknown method.
ALL, acute lymphoblastic leukemia; CR, complete remission; CRc, composite CR; CRh, CR with partial hematologic recovery; CRp, CR with incomplete platelet recovery; EFS, event-free survival; MPAL, mixed-phenotype acute leukemia; MRD, measurable residual disease; NR, not reached; ORR, overall response rate; OS, overall survival; RP2D, recommended phase 2 dose.

Safety

- Grade ≥3 treatment-emergent adverse events (TEAEs) and treatment-related adverse events occurred in 92% and 37% of all patients, respectively (**Table 3**)
- Overall, 3/38 (8%) patients (all with AML) had a TEAE that led to treatment discontinuation (febrile neutropenia, sepsis, and septic shock)
- Differentiation syndrome (DS) occurred in 13/38 (34%) patients; prophylaxis was not mandated per protocol, and no patients discontinued revumenib due to DS
  - Majority (n = 9; 69%) of patients had a maximum of grade 2 DS; 3 (23%) patients had a maximum of grade 3 DS, and 1 (8%) patient had a maximum of grade 4 DS
  - Median (range) time to initial onset was 7.0 days (3.0-41.0), and median duration of initial event was 14.5 days (4.0-30.0) among all patients
- QTcF prolongation occurred in 8/38 (21%) patients; all patients recovered/resolved, and no patients discontinued revumenib due to QTcF prolongation
  - Four (4/8; 50%) patients had a maximum of grade 2 or 3 QTcF prolongation
  - Median (range) time to initial onset was 4.0 days (1.0-56.0), and median duration was 1.0 day (1.0-18.0)

Table 3. Summary of AEs[a]

Parameter, n (%)	AML (n = 27)	ALL (n = 8)	MPAL (n = 3)	Total (N = 38)
Any grade TEAE	27 (100)	7 (88)	3 (100)	37 (97)
Grade ≥3	25 (93)	7 (88)	3 (100)	35 (92)
Any grade TRAE	21 (78)	4 (50)	3 (100)	28 (74)
Grade ≥3	9 (33)	2 (25)	3 (100)	14 (37)
SAE	22 (81)	5 (63)	3 (100)	30 (79)
TEAE leading to dose modification	7 (26)	3 (38)	2 (67)	12 (32)
Reduction	1 (4)	2 (25)	0	3 (8)
Interruption	7 (26)	3 (38)	2 (67)	12 (32)
TEAE leading to revumenib discontinuation	3 (11)	0	0	3 (8)
TEAE leading to death	4 (15)	0	1 (33)	5 (13)
TRAE leading to dose modification	2 (7)	1 (13)	1 (33)	4 (11)
Reduction	0	1 (13)	0	1 (3)
Interruption	2 (7)	1 (13)	1 (33)	4 (11)
TRAE leading to revumenib discontinuation	0	0	0	0
TRAE leading to death	0	0	0	0

[a]In the safety population (those with *KMT2A*r per local testing who were treated at RP2D).
AE, adverse event; ALL, acute lymphoblastic leukemia; MPAL, mixed-phenotype acute leukemia; RP2D, recommended phase 2 dose; SAE, serious AE; TEAE, treatment-emergent AE; TRAE, treatment-related AE.

CONCLUSIONS

- In pediatric and young adult patients with R/R *KMT2A*r AL, revumenib demonstrated clinically meaningful responses with longer follow-up
- Revumenib showed a notable median duration of CR/CRh (32.3 months) among pediatric and young adult patients with AML
- The safety profile of revumenib was consistent with previously reported data and remained manageable, with no new safety signals identified
- Overall, these long-term follow-up results confirm revumenib as an effective treatment option for pediatric and young adult patients with R/R *KMT2A*r AL across multiple leukemia types

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