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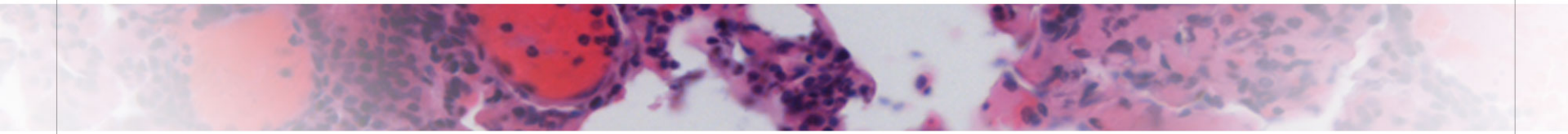


Revumenib Monotherapy in Patients with Relapsed/Refractory *KMT2Ar* Acute Leukemia: Topline Efficacy and Safety Results from the Pivotal AUGMENT-101 Phase 2 Study

Ibrahim Aldoss, Ghayas C. Issa, Michael Thirman, John DiPersio, Martha Arellano, James S. Blachly, Gabriel N. Mannis, Alexander Perl, David S. Dickens, Christine M. McMahon, Elie Traer, C. Michel Zwaan, Carolyn Grove, Richard Stone, Paul J. Shami, Ioannis Mantzaris, Matthew Greenwood, Neerav Shukla, Branko Cuglievan, Yu Gu, Rebecca G. Bagley, Kate Madigan, Soujanya Sunkaraneni, Huy Van Nguyen, Nicole McNeer, Eytan M. Stein

KMT2Ar Acute Leukemia

- Many patients relapse after chemotherapy and/or HSCT[1]
- In adults, remission rates after relapse (CR, 5%) and median OS (2.4 months) after ≥2 salvage therapies remain low[1]
- Outcomes in infants/children after relapse remain poor

No approved targeted therapies for *KMT2Ar* disease

OS in Adult Patients With R/R *KMT2Ar* AML After ≥3rd-Line Therapy

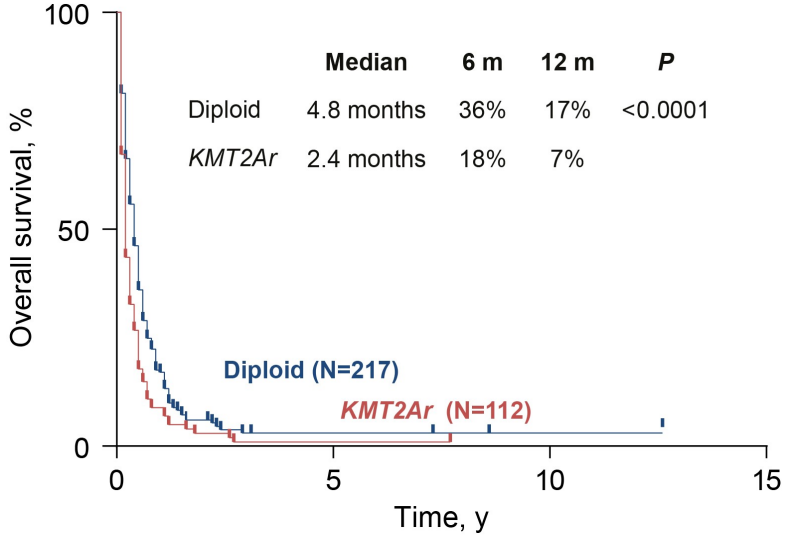


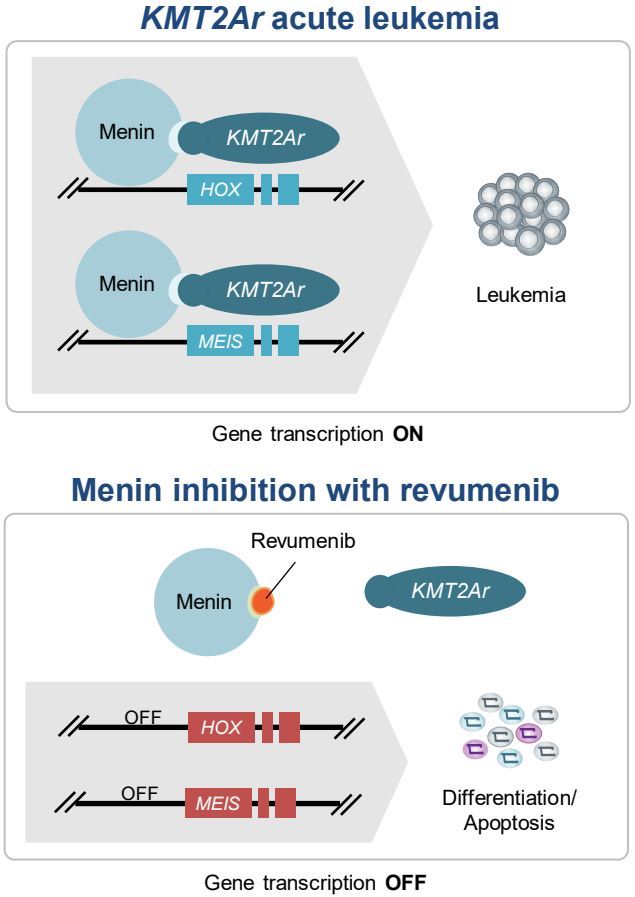
Figure reproduced from Issa GC, Zarka J, Sasaki K, et al. *Blood Cancer J*. 2021;11:162

AML, acute myeloid leukemia; CR, complete remission; HSCT, hematopoietic stem cell transplant; *KMT2Ar*, histone-lysine N-methyltransferase 2A rearrangements; OS, overall survival; R/R, relapsed/refractory.

1. Issa GC, Zarka J, Sasaki K, et al. *Blood Cancer J*. 2021;11:162.

Revumenib

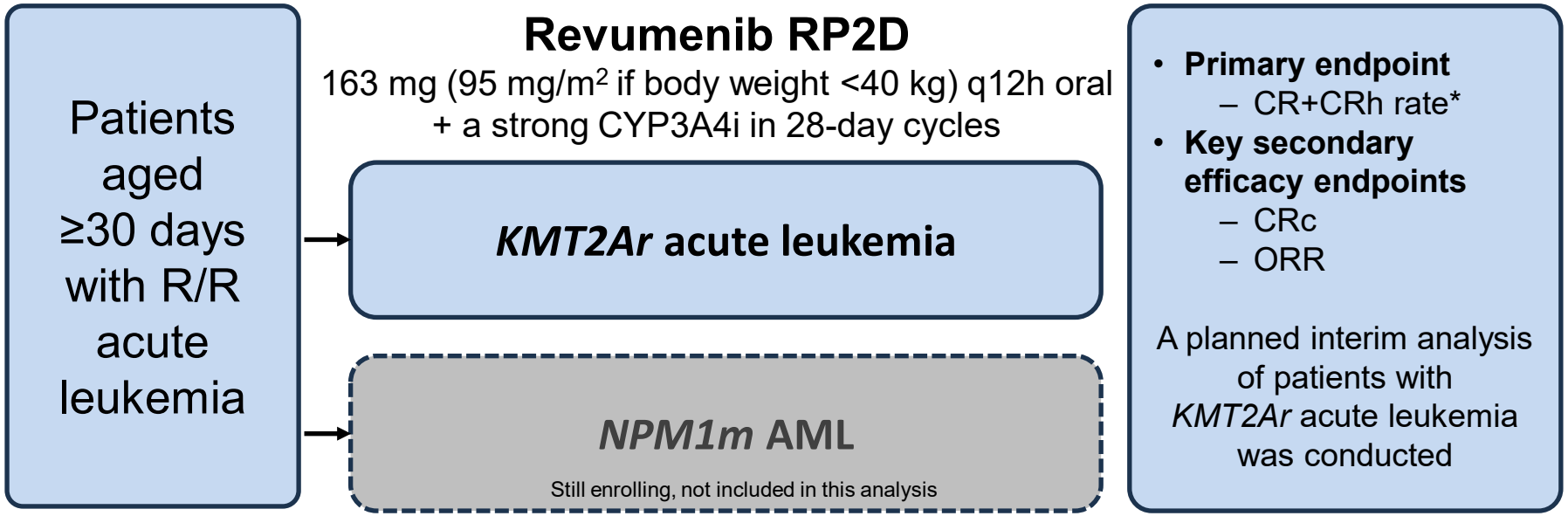
- The menin-KMT2A interaction is a key driver of leukemogenesis[1]
- In a phase 1 study of R/R *KMT2Ar* and *NPM1m* acute leukemias, revumenib demonstrated
  - Clinically meaningful responses that were consistent across subgroups[2]
  - High percentage (67%) of responders proceeding to transplant[2]
  - Manageable safety profile[2]



HOX, homeobox; KMT2A, histone-lysine N-methyltransferase 2A; *KMT2Ar*, KMT2A rearrangements; *MEIS*, Meis homeobox; *NPM1m*, nucleophosmin 1–mutated; R/R, relapsed/refractory.

1. Issa GC, Zarka J, Sasaki K, et al. *Blood Cancer J*. 2021;11:162. **2.** Issa GC, Aldoss I, DiPersio J, et al. *Nature*. 2023;615:920-924.

AUGMENT-101 Phase 2 Study Design



*CR+CRh rate >10% in adult evaluable population considered lower efficacy bound

AML, acute myeloid leukemia; CR, complete remission; CRc, CR composite (CR+CRh+CRp+CRi); CRh, CR with partial hematologic recovery; CRi, CR with incomplete hematologic recovery; CRp, CR with incomplete platelet recovery; CYP3A4i, cytochrome P450 3A4 inhibitor; *KMT2Ar*, histone-lysine N-methyltransferase 2A rearrangements; *NPM1m*, nucleophosmin 1–mutated; ORR, overall response rate; q12h, every 12 hours; RP2D, recommended phase 2 dose; R/R, relapsed/refractory.

Patient Demographics

Parameter	Efficacy population (n=57)	Safety population (n=94)[a]
Median age, y (range)	34.0 (1.3–75)	37.0 (1.3–75)
Age <18 y, n (%)	13 (23)	23 (25)
Age ≥18 y, n (%)	44 (77)	71 (76)
Sex, n (%)		
Female	33 (58)	56 (60)
Race, n (%)		
White	43 (75)	68 (72)
Non-White	10 (18)	14 (15)
Unknown	4 (7)	12 (13)

Data cutoff: July 24, 2023. [a]Defined as patients with *KMT2Ar* acute leukemia having received at least 1 dose of revumenib.

KMT2Ar, histone-lysine N-methyltransferase 2A rearrangements rearrangements.

Baseline Characteristics

Parameter	Efficacy population (n=57)	Safety population (n=94)[a]
Leukemia type, n (%)		
AML	49 (86)	78 (83)
ALL	7 (12)	14 (15)
MPAL/Other	1 (2)	2 (2)
Co-mutations[b], n (%)		
FLT3	5 (9)	7 (7)
RAS	9 (16)	12 (13)
p53	4 (7)	5 (5)
Primary refractory, n (%)	14 (25)	18 (19)
Number of prior lines of therapy, median (range)	2 (1–11)	2 (1–11)
1, n (%)	17 (30)	25 (27)
2, n (%)	14 (25)	28 (30)
≥3, n (%)	26 (46)	41 (44)
Prior venetoclax, n (%)	41 (72)	61 (65)
Prior HSCT, n (%)	26 (46)	47 (50)

Data cutoff: July 24, 2023. [a]Defined as patients with *KMT2Ar* acute leukemia having received at least 1 dose of revumenib. [b]In patients that had co-mutation status reported.

ALL, acute lymphoblastic leukemia; AML, acute myeloid leukemia; *FLT3*, fms-related tyrosine kinase 3; HSCT, hematopoietic stem cell transplant; *KMT2Ar*, histone-lysine N-methyltransferase 2A rearrangements; MPAL, mixed phenotype acute leukemia; *RAS*, rat sarcoma virus.

Response

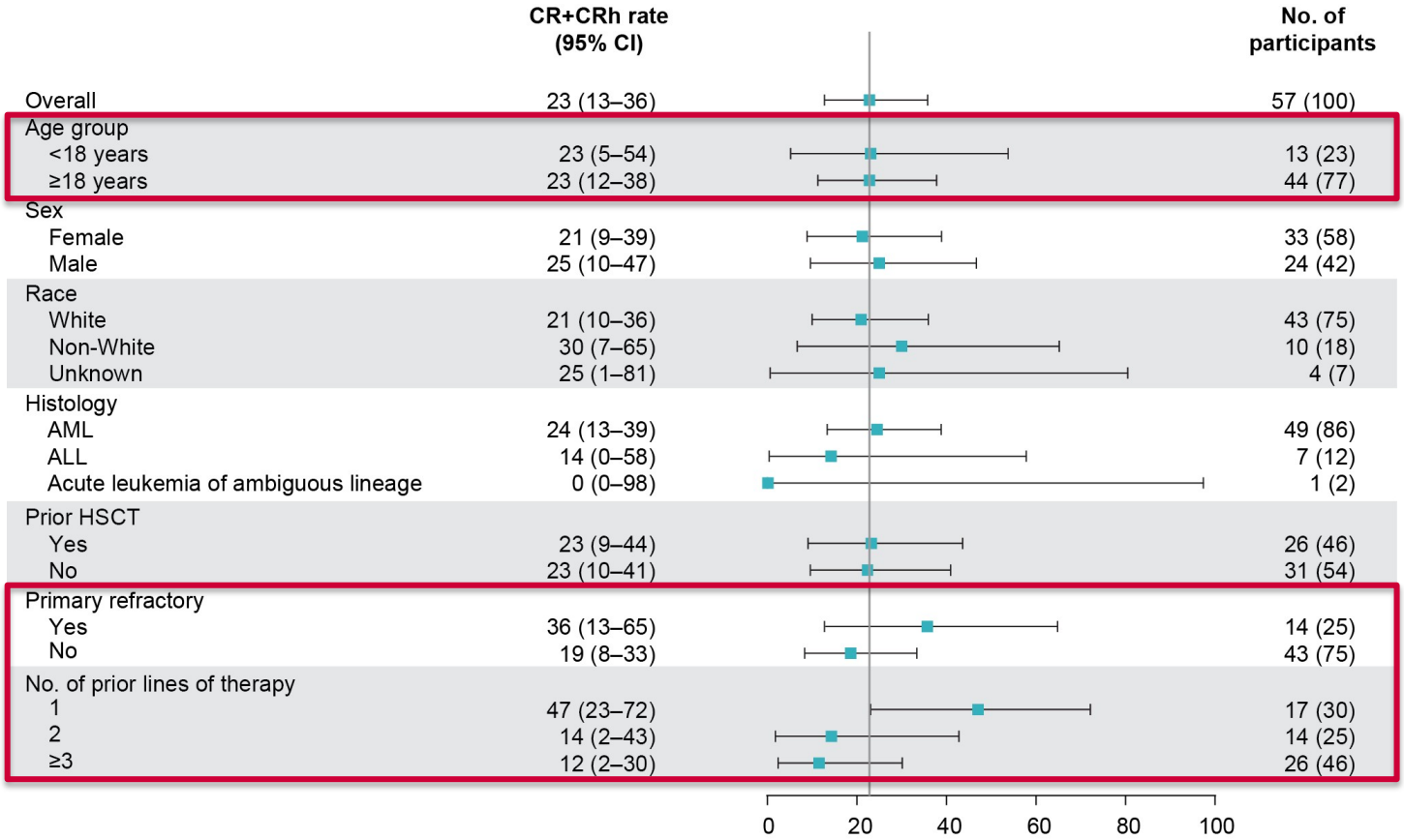
Parameter	Efficacy population (n=57)
ORR, n (%)	**36 (63)**
CR+CRh rate, n (%)	13 (23)
95% CI	12.7–35.8
P value, 1-sided	0.0036
CRc	25 (44)
95% CI	30.7–57.6
Negative MRD status[a]	
CR+CRh	7/10 (70)
CRc	15/22 (68)

Parameter	Efficacy population (n=57)
Best response, n (%)	
CR	10 (18)
CRh	3 (5)
CRi	1 (1.8)
CRp	11 (19)
MLFS	10 (18)
PR	1 (1.8)
PD	4 (7)
No response	14 (25)
Other[b]	3 (5)

Data cutoff: July 24, 2023. [a]MRD done locally; not all patients had MRD status reported. [b]Includes patients without postbaseline disease assessment.

CR, complete remission; CRc, composite CR (CR+CRh+CRp+CRi); CRh, CR with partial hematologic recovery; CRi, CR with incomplete hematologic recovery; CRp, CR with incomplete platelet recovery; MLFS, morphological leukemia-free state; MRD, minimal residual disease; ORR, overall response rate (CRc+MLFS+PR); PD, progressive disease; PR, partial remission.

Subgroup Analyses



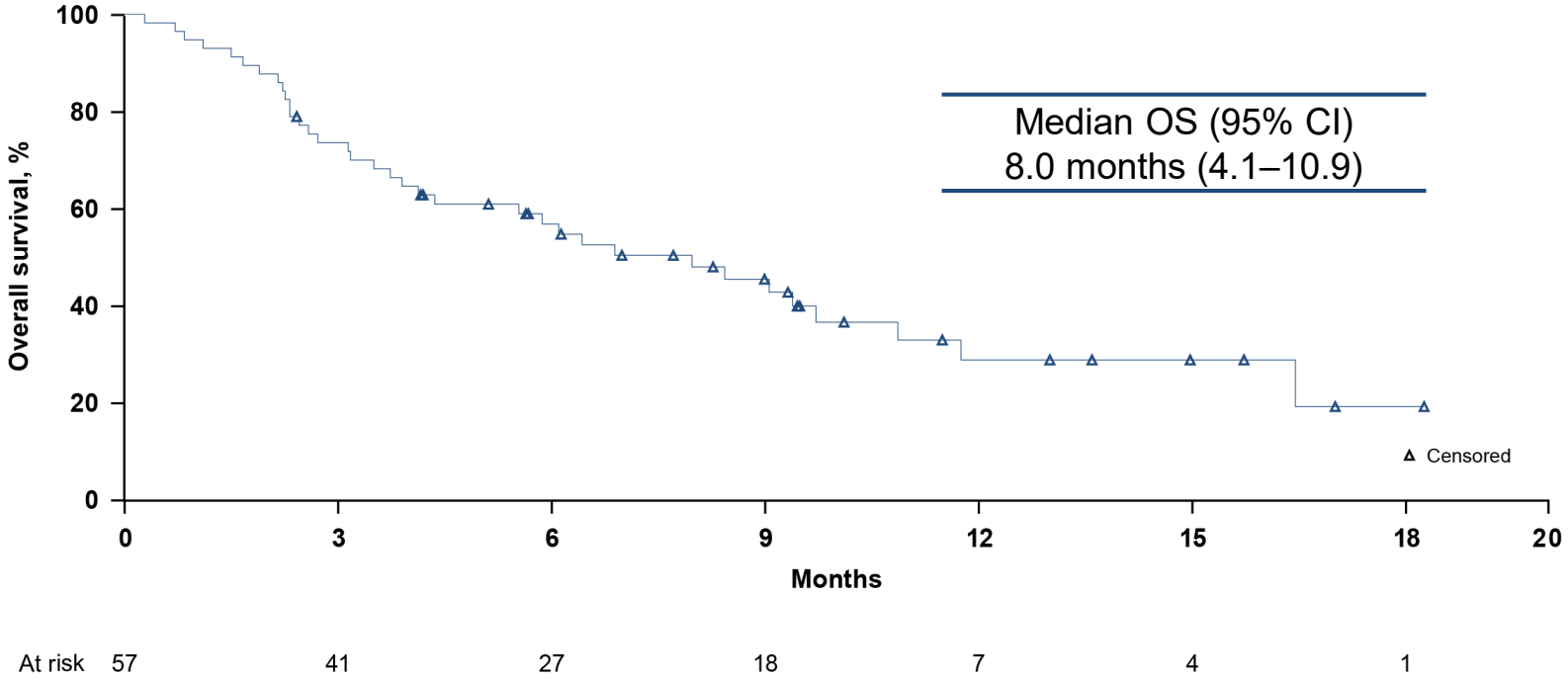
ALL, acute lymphoblastic leukemia; AML, acute myeloid leukemia; CR, complete remission; CRh, CR with partial hematologic recovery; HSCT, hematopoietic stem cell transplant.

Responses Observed Across *KMT2A* Rearrangements

KMT2A rearrangement/ translocation	Summary of ORR		Summary of CR+CRh rate	
	n/N	ORR (95% CI)	n/N	CR+CRh rate (95% CI)
9;11	10/11	91 (58.7–99.8)	2/11	18 (2.3–51.8)
11;19	7/13	54 (25.1–80.8)	2/13	15 (1.9–45.4)
10;11	5/7	71 (29.0–96.3)	2/7	29 (3.7–71.0)
6;11	5/7	71 (29.0–96.3)	2/7	29 (3.7–71.0)
4;11	2/2	100 (15.8–100.0)	0/2	0 (0.0–84.2)
1;11	0/2	0 (0.0–84.2)	0/2	0 (0.0–84.2)
11;16	1/1	100	0/1	0
11;22	1/1	100	1/1	100
Unknown *KMT2A* fusion partner	5/13	39 (13.9–68.4)	4/13	31 (9.1–61.4)

CR, complete remission; CRh, CR with partial hematologic recovery; CRi, CR with incomplete hematologic recovery; CRp, CR with incomplete platelet recovery; *KMT2A*, histone-lysine N-methyltransferase 2A; ORR, overall response rate (CR+CRh+CRp+CRi+MLFS+PR); PR, partial remission.

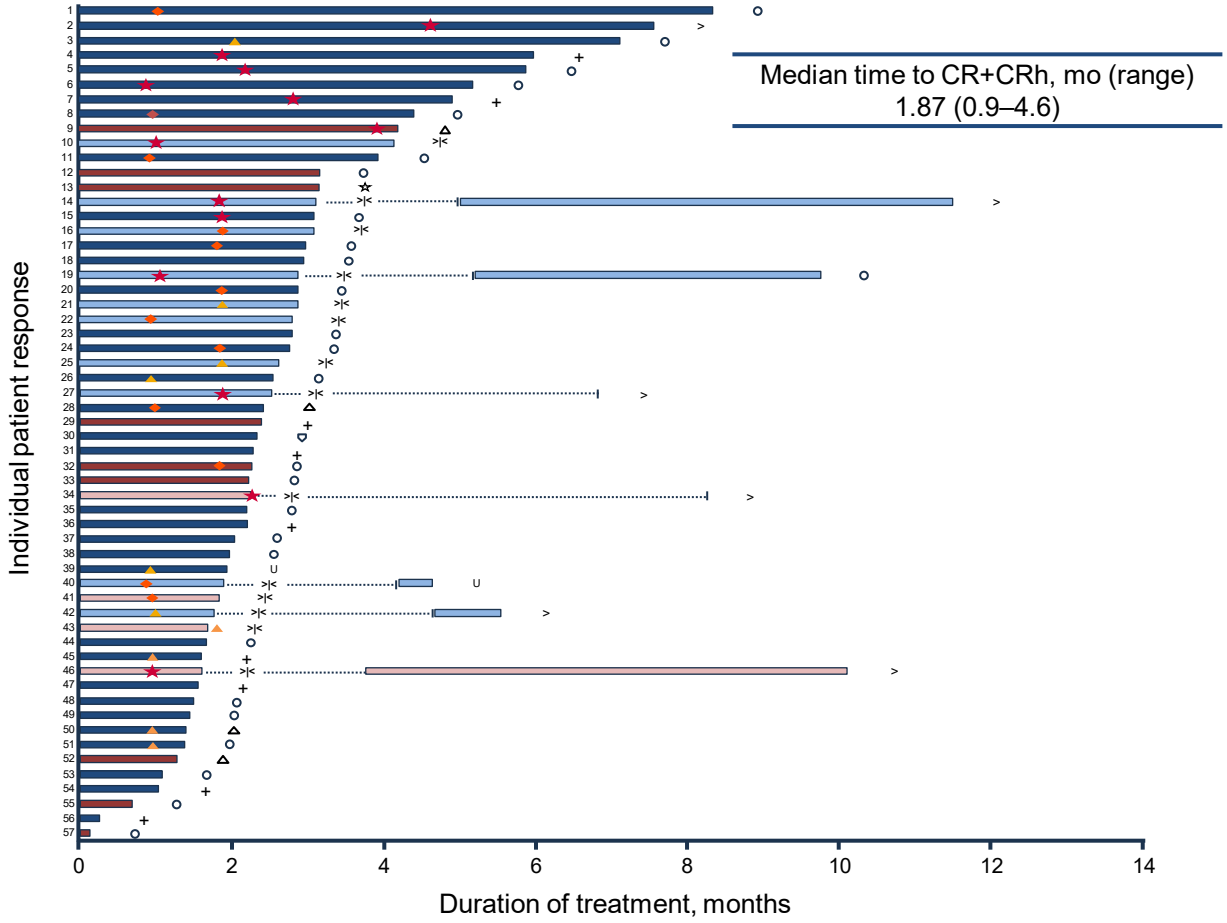
Overall Survival



OS, overall survival.

Duration of Treatment

- Adult
- Adult, underwent HSCT
- Pediatric
- Pediatric, underwent HSCT
- ★ CR/CRh
- ◆ CRp/CRi
- ▲ MLFS
- ○ Progressive disease
- > Ongoing at data cutoff
- \+ Adverse event
- △ Subject withdrew consent for treatment
- >|< HSCT
- ☆ Noncompliance
- Patient did not achieve at least a PR after 4 cycles
- U Prohibited concomitant medication



CR, complete remission; CRh, CR with partial hematologic recovery; CRi, CR with incomplete hematologic recovery; CRp, CR with incomplete platelet recovery; HSCT, hematopoietic stem cell transplant; MLFS, morphological leukemia-free state; PR, partial remission.

Duration of Response

Parameter	Patients achieving CR+CRh (n=13)
Median duration of CR+CRh, months (95% CI)	6.4 (3.4–NR)
Proceeded to HSCT, n (%)	14/36 (39)
Proceeded to HSCT in CR or CRh	6/14 (43)
Proceeded to HSCT in MLFS or CRp	8/14 (57)
Restarted revumenib post HSCT, n (%)	7/14 (50)*

Data cutoff: July 24, 2023

*3 additional patients remained eligible to initiate revumenib after HSCT at the time of data cutoff.

CR, complete remission; CRh, CR with partial hematologic recovery; CRp, CR with incomplete platelet recovery; HSCT, hematopoietic stem cell transplant; MLFS, morphological leukemia-free state; NR, not reached.

Revumenib Safety Profile

All terms	Safety population (n=94)[a] TEAEs
Any grade, n (%)	93 (99)
≥Grade 3, n (%)	86 (92)
Serious AE, n (%)	72 (77)
AEs leading to:	
Dose reduction	9 (10)
Discontinuation	12 (13)
Death	14 (15)

Data cutoff: July 24, 2023. [a]Defined as patients with *KMT2Ar* acute leukemia having received at least 1 dose of revumenib.

R/R, relapsed/refractory; TEAE, treatment-emergent adverse event; TRAE, treatment-related adverse event.

Revumenib Safety Profile (cont)

Any grade TEAEs that occurred in ≥25% patients

All terms, n (%)	Safety population (n=94)[a]
Nausea	42 (45)
Febrile neutropenia	36 (38)
Diarrhea	33 (35)
Vomiting	29 (31)
Differentiation syndrome	26 (28)
Hypokalemia	26 (28)
Epistaxis	25 (27)
QTc prolongation	24 (26)

Grade ≥3 TEAEs that occurred in ≥10% patients

All terms, n (%)	Safety population (n=94)[a]
Febrile neutropenia	35 (37)
Decreased neutrophil count	15 (16)
Decreased white blood cell count	15 (16)
Decreased platelet count	14 (15)
Anemia	17 (18)
Differentiation syndrome	15 (16)
QTc prolongation	13 (14)
Sepsis	11 (12)
Hypokalemia	10 (11)

Data cutoff: July 24, 2023. [a]Defined as patients with *KMT2Ar* acute leukemia having received at least 1 dose of revumenib.

No patients discontinued due to differentiation syndrome, QTc prolongation, or cytopenias

KMT2Ar, histone-lysine N-methyltransferase 2A rearrangements; TEAE, treatment-emergent adverse event.

Conclusions

- Revumenib is effective and safe in pediatric and adult patients with R/R *KMT2Ar* acute leukemia
- Durable MRD-negative remissions were observed in responders
- High rates of transplants among responders
- Discontinuations and dose reductions due to adverse events were low
- Study was stopped early after meeting the primary efficacy endpoint at the predefined interim analysis
  - A New Drug Application for *KMT2Ar* leukemia has been initiated under the FDA Real-Time Oncology Review program based on these data

The independent NPM1m cohort continues to enroll at all sites

KMT2Ar, histone-lysine N-methyltransferase 2A rearrangements; MRD, minimal residual disease; *NPM1m*, mutated nucleophosmin 1; R/R, relapsed/refractory; TEAE, treatment-emergent adverse event; TRAE, treatment-related adverse event.

Acknowledgements

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