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Advancing Knowledge, Discovery, and Collaboration

PIVOTAL PHASE 2 RESULTS OF AUGMENT-101 FOR REVUMENIB IN *KMT2Ar* ACUTE LEUKEMIA: PEDIATRIC EXPERIENCE

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Plenary Oral Presentation

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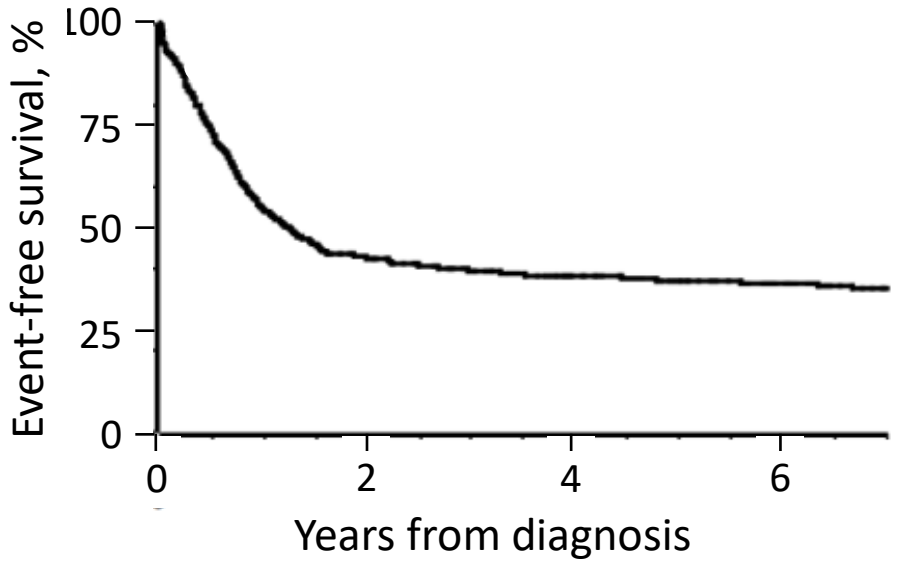
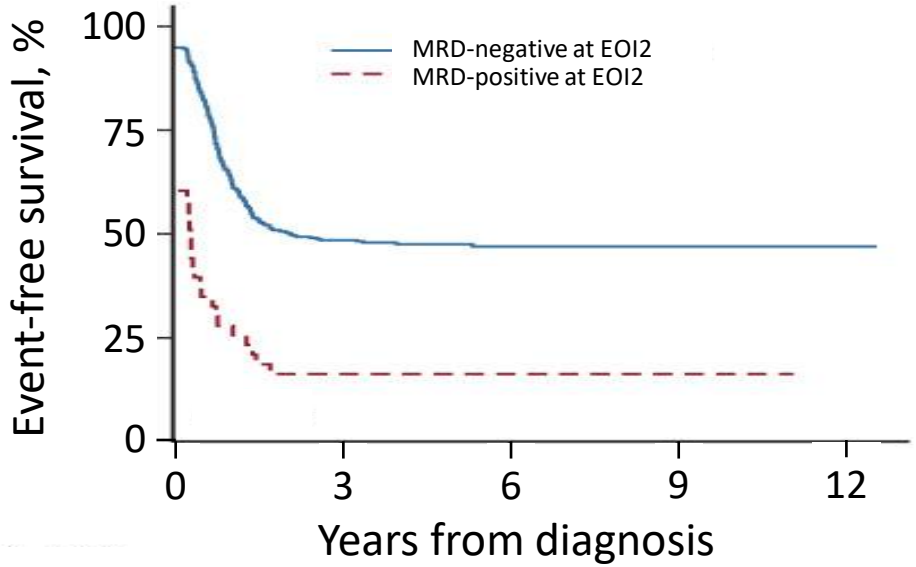
Outcomes in Pediatric *KMT2Ar* Acute Leukemia Remain Poor[1-3]

Event-free survival in infants with *KMT2Ar* ALL (n=476)[1]



Event-free survival in pediatric patients with *KMT2Ar* AML (n=456)[3]



No approved targeted therapies for *KMT2Ar* disease

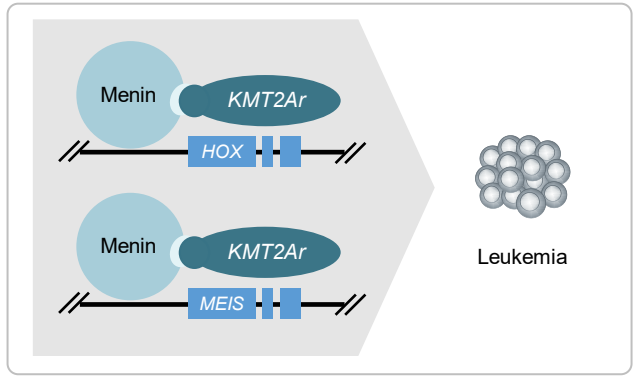
ALL, acute lymphoblastic leukemia; AML, acute myeloid leukemia; EOI2, end of induction 2; *KMT2Ar*, histone-lysine N-methyltransferase 2A rearrangements; MRD, measurable residual disease.

1. Pieters et al. *J Clin Oncol.* 2019;37:2246-2256. **2**. Hilden et al. *Blood*. 2006;108:441-451. **3.** van Weelderen RE et al. *J Clin Oncol*. 2023 Jun 1;41:2963-2974.

Revumenib

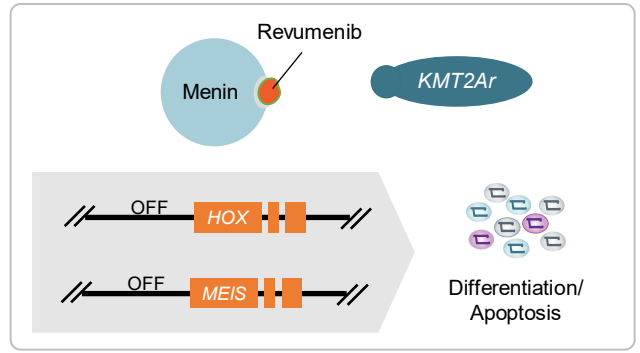
- The menin-KMT2A interaction is a key driver of leukemogenesis[1]
- In a phase 1 study of R/R *KMT2Ar* and *NPM1m* acute leukemias, revumenib demonstrated[2]
  - Clinically meaningful responses that were consistent across subgroups
  - High percentage (67%) of responders proceeding to transplant
  - Acceptable safety profile
  - Preliminary antileukemic activity in children
- Revumenib was administered with or without a CYP3A4 inhibitor[2]

KMT2Ar acute leukemia



Gene transcription **ON**

Menin inhibition with revumenib

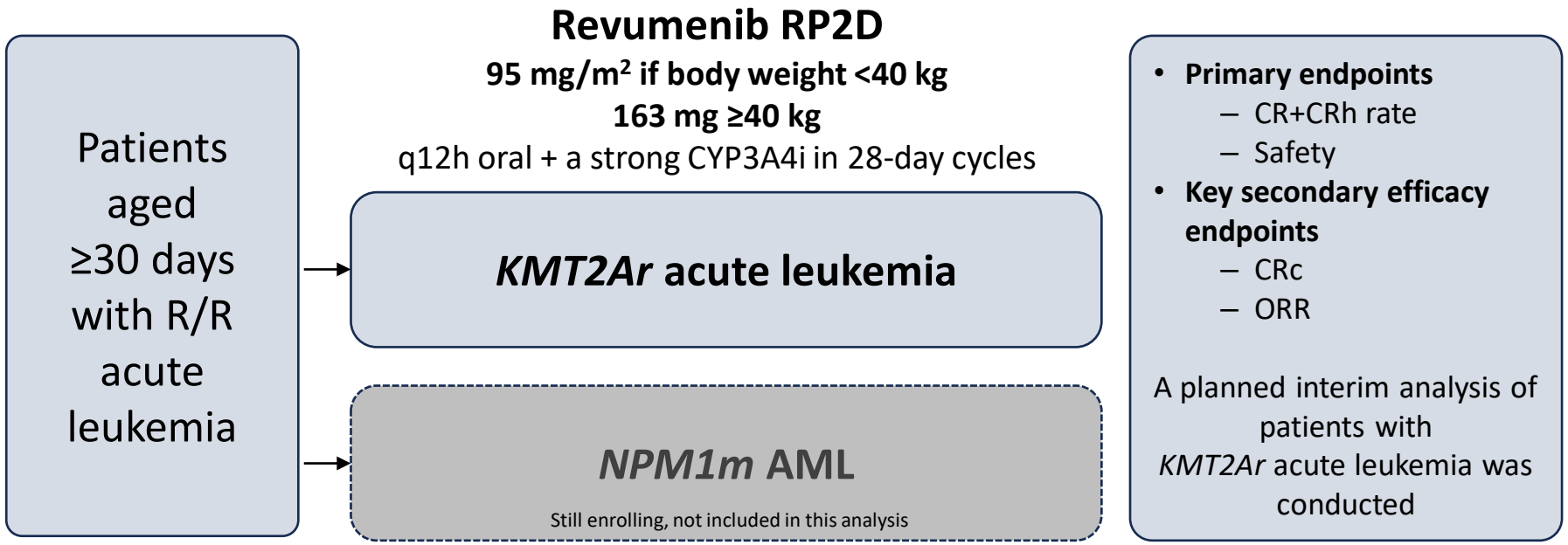


Gene transcription **OFF**

CYP3A4, cytochrome P450 3A4; *HOX*, homeobox; KMT2A, histone-lysine N-methyltransferase 2A; *KMT2Ar*, KMT2A rearrangements; *MEIS*, Meis homeobox; *NPM1m*, nucleophosmin 1–mutated; R/R, relapsed/refractory.

1. Issa. *Blood Cancer J*. 2021;11:162. **2.** Issa GC. *Nature*. 2023;615:920-924.

AUGMENT-101 Phase 2 Study Design



Administration: capsules or oral solution taken orally or through NG/G or duodenal tube

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; NG/G, nasogastric/gastric; *NPM1m*, nucleophosmin 1–mutated; ORR, overall response rate; q12h, every 12 hours; RP2D, recommended phase 2 dose; R/R, relapsed/refractory.

Patient Demographics

Parameter	Safety population (n=23)[a]	Efficacy population (n=13)[b]
Median age, y (range)	4.0 (1.3–17.0)	5.0 (1.3–17.0)
<2 y, n (%)	4 (17)	3 (23)
≥2 to <12 y, n (%)	16 (70)	7 (54)
≥12 to <18 y, n (%)	3 (13)	3 (23)
Sex, n (%)		
Female	13 (57)	6 (46)
Race, n (%)		
White	14 (61)	9 (69)
Non-White	4 (17)	2 (15)
Unknown	5 (22)	2 (15)

[a]Pediactric patients with *KMT2Ar* acute leukemia having received at least 1 dose of revumenib. [b]Pediatric patients in the IA efficacy population at data cutoff.

IA, interim analysis; *KMT2Ar*, histone-lysine N-methyltransferase 2A rearrangements.

Baseline Characteristics

Parameter	Safety population (n=23)[a]	Efficacy population (n=13)[b]
Leukemia type, n (%)		
AML	17 (74)	11 (85)
ALL	5 (22)	2 (15)
ALAL	1 (4)	0 (0)
Disease status at baseline, n (%)		
Primary refractory	5 (22)	5 (38)
Refractory relapse	14 (61)	5 (38)
Early untreated relapse	4 (17)	3 (23)
Number of prior lines of therapy, median (range)	3 (1–11)	4 (1–11)
1, n (%)	5 (22)	4 (31)
2, n (%)	4 (17)	2 (15)
≥3, n (%)	14 (61)	7 (54)
Prior venetoclax, n (%)	13 (57)	8 (62)
Prior CAR-T, n (%)	4 (17)	2 (15)
Prior HSCT, n (%)	12 (52)	6 (46)
>1 prior HSCT	4 (17)	2 (15)

[a]Pediactric patients with *KMT2Ar* acute leukemia having received at least 1 dose of revumenib. [b]Pediatric patients in the IA efficacy population at data cutoff.

ALAL, acute leukemia of ambiguous lineage; ALL, acute lymphoblastic leukemia; AML, acute myeloid leukemia; CAR-T, chimeric antigen receptor-T cell; HSCT, hematopoietic stem cell transplant; IA, interim analysis; *KMT2Ar*, histone-lysine N-methyltransferase 2A rearrangements.

Response

Primary Endpoint

CR+CRh= 22.8% (13/57; 95% CI, 12.7–35.8; 1-sided *P* value 0.0036)

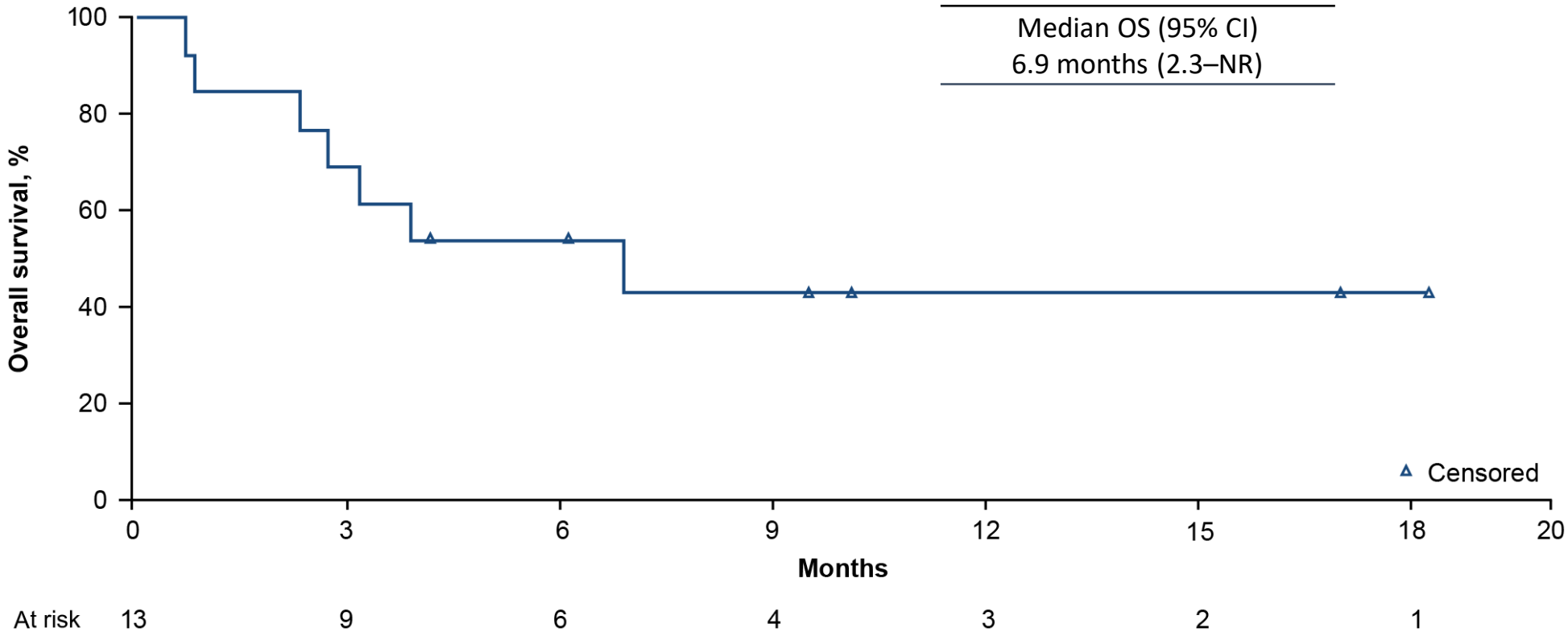
Parameter	Efficacy population (n=13)[a]
ORR, n (%)	**6 (46)**
CR+CRh rate, n (%)	3 (23)
95% CI	5.0–53.8
CRc	5 (38.5)
95% CI	13.9–68.4
Negative MRD status by flow[b]	
CR+CRh	2/3 (67)
CRc	3/5 (60)

Parameter	Efficacy population (n=13)[a]
Best response, n (%)	
CR[c]	1 (8)
CRh[d]	2 (15)
CRi[e]	1 (8)
CRp[f]	1 (8)
MLFS	1 (8)
PR	0 (0)
PD	3 (23)
No response	3 (23)
Other[g]	1 (8)

[a]Pediactric patients in the IA efficacy population at data cutoff. [b]MRD done locally; not all patients had MRD status reported. [c]Bone marrow blasts <5%; absence of circulating blasts and blasts with Auer rods; absence of extramedullary disease; ANC ≥1.0 × 10^9/L (1000/µL) and platelet count ≥100 × 10^9/L (100,000/µL). [d]Bone marrow blasts <5%; absence of circulating blasts and blasts with Auer rods; absence of extramedullary disease; residual neutropenia (>0.5 × 10^9/L [500/µL]) and thrombocytopenia (>50 × 10^9/L [50,000/µL]). [e]Bone marrow blasts <5%; absence of circulating blasts and blasts with Auer rods; absence of extramedullary disease; residual neutropenia (<1.0 × 10^9/L [1000/µL]) or thrombocytopenia (<100 × 10^9/L [100,000/µL]). [f]Bone marrow blasts <5%; absence of circulating blasts and blasts with Auer rods; absence of extramedullary disease; ANC ≥1.0 × 10^9/L (1000/µL) and platelet count <100 × 10^9/L (100,000/µL). [g]Includes patients without postbaseline disease assessment.

ANC, absolute neutrophil count; 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, measurable residual disease; ORR, overall response rate (CRc+MLFS+PR); PD, progressive disease; PR, partial remission.

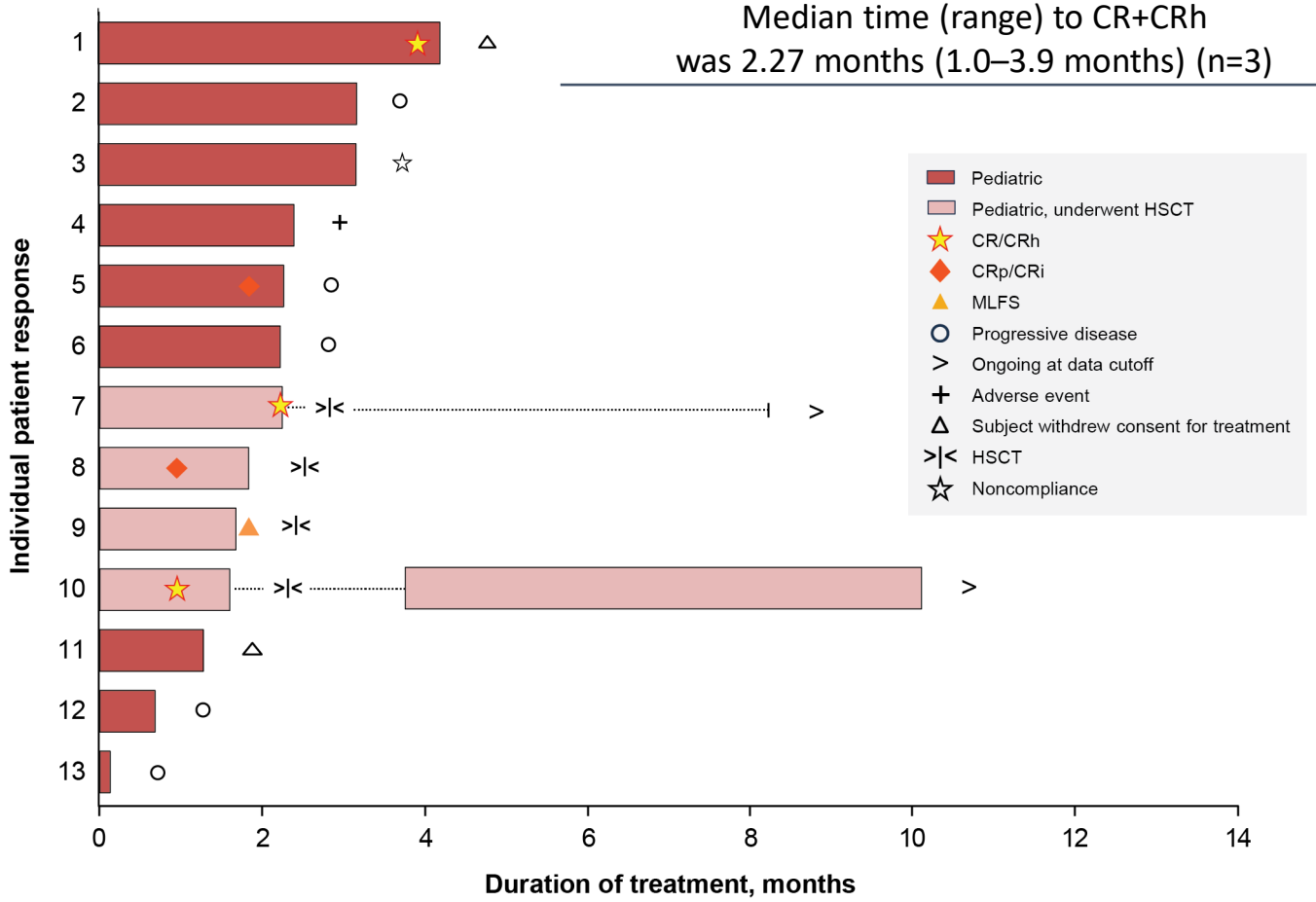
Overall Survival



NR, not reached; OS, overall survival.

Duration of Treatment and Patients Who Proceeded to Transplant

Median time (range) to CR+CRh was 2.27 months (1.0–3.9 months) (n=3)



Parameter	Patients achieving response (n=6)
Proceeded to HSCT, n (%)	4/6 (67)
Proceeded to HSCT in CR or CRh	2/4 (50)
Proceeded to HSCT in MLFS or CRp	2/4 (50)
Restarted revumenib post HSCT, n (%)	2/4 (50)

Data cutoff: July 24, 2023.

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.

Revumenib Safety Profile

AEs of special interest

All terms, n (%)	Safety population (n=23)[a]
Differentiation syndrome grade ≥2	8 (35)
QTc prolongation grade ≥2	1 (4)
AEs leading to:	
Dose reduction	0 (0)
Discontinuation[b]	1 (4)[c]

[a]Pediatric patients with *KMT2Ar* acute leukemia having received at least 1 dose of revumenib.
[b]No treatment-related discontinuations occurred. [c]Febrile neutropenia.

Grade ≥3 TRAEs that occurred in ≥10% patients

All terms, n (%)	Safety population (n=23)[a]
Any treatment-related AE grade ≥3	7 (30)
Febrile neutropenia	3 (13)
Neutrophil count decreased	3 (13)

[a]Pediatric patients with *KMT2Ar* acute leukemia having received at least 1 dose of revumenib.

No discontinuations due to differentiation syndrome or QTc prolongation

AE, adverse event; *KMT2Ar*, histone-lysine N-methyltransferase 2A rearrangements; TRAE, treatment-related adverse event.

Conclusions

- AUGMENT-101 met its primary efficacy endpoint in an aggregate population of adults and children with R/R *KMT2Ar* acute leukemia, validating phase 1 results
- The majority of responding children (67%) were able to proceed to transplant, with 2 resuming revumenib maintenance post transplant
- Safety profile in children was manageable and consistent with safety profile in adults

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; *NPM1m*, nucleophosmin 1–mutated; R/R, relapsed/refractory.

Acknowledgements

- All study patients, their families, and caregivers for participating in this study
- Study teams at the individual sites
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