Revumenib as Maintenance for AML Following Allogeneic Stem Cell Transplantation

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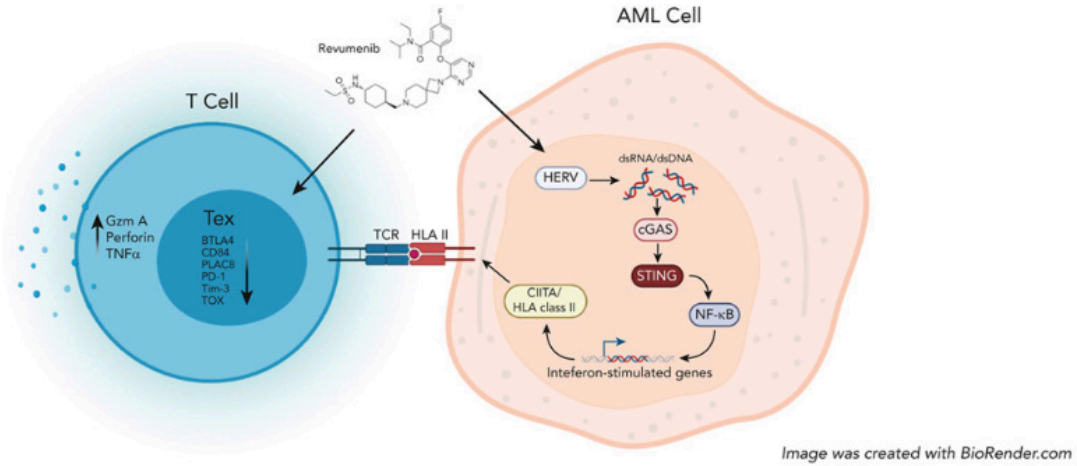
Key Takeaway Points/Conclusions

Revumenib as maintenance for AML post-HSCT is feasible, and thrombocytopenia is common but manageable

Promising efficacy vs historical benchmarks support evaluation of menin inhibition as post-HSCT maintenance

Background

- Relapse following allo-HSCT remains a major cause of treatment failure in AML
- AML with *NPM1mt*, *KMT2Ar,* or *NUP98r* is susceptible to menin inhibition[1-3]
- Revumenib is approved for R/R *NPM1mt* or *KMT2Ar* acute leukemia[4,5]
- Menin inhibition could potentiate GVL[6,7]
- The safety and efficacy of revumenib as post-HSCT maintenance therapy remain unknown



Adapted from Visual abstract, Fetsch V et al, Blood 2026

[1]Grembecka J et al. Nat Chem Biol 2012; [2]Uckelmann HJ et al. Science 2020; [3]Heikamp EB et al. Blood 2022; [4]Issa et al. J Clin Oncol 2025; [5]Arellano et al. Blood 2025; [6]Fetsch V et al. Blood 2026; [7]Hogeling SM et al. Haematologica 2025.

Aims

- **To assess the tolerability** of revumenib as maintenance post-HSCT for AML
- **To evaluate the preliminary efficacy** of revumenib as maintenance post-HSCT in the context of a historical cohort

Methods

- Single-center, pooled analysis of patients with *NPM1mt*, *KMT2Ar*, or *NUP98r* AML treated with revumenib prior to HSCT
  - In **any line of remission**
  - **Revumenib monotherapy** (AUGMENT-101, NCT04065399; EAP, NCT05918913) or **combination** (revumenib, decitabine/cedazuridine and venetoclax: SAVE, NCT05360160)
  - **Resumed post-HSCT revumenib maintenance**
- Analyzed a historical control cohort with same genotypes prior to advent of menin inhibitors

Baseline Characteristics

Characteristic*	All Patients (N = 24)	Adult (N = 13)	Pediatric (N = 11)
Median age, years	22 [1 – 74]	58 [21 – 74]	13 [1 – 17]
Female	14 (58)	10 (77)	4 (36)
Genotype			
NPM1mt	6 (25)	6 (46)	0 (0)
KMT2Ar	17 (71)	7 (54)	10 (91)
NUP98r	1 (4)	0 (0)	1 (9)
Prior HSCT	13 (54)	5 (38)	8 (73)
Lines of Therapy	3 [1 – 11]	3 [1 – 11]	3 [1 – 6]
CR Status at HSCT			
CR1	6 (25)	5 (38)	1 (9)
CR2+	18 (75)	8 (62)	10 (91)
Regimen Pre-HSCT			
Revumenib†	10 (42)	4 (31)	6 (55)
SAVE‡	14 (58)	9 (69)	5 (45)

* N (%), or median [range]
† All relapsed/refractory
‡ Frontline n = 6, relapsed/refractory n = 8

Transplant Characteristics

Characteristic*	All Patients (N = 24)	Adult (N = 13)	Pediatric (N = 11)
Type of HSCT			
MUD	9 (38)	8 (62)	1 (9)
Haplo	5 (21)	2 (15)	3 (27)
MSD	4 (17)	2 (15)	2 (18)
Cord	4 (17)	0 (0)	4 (36)
MMUD	2 (8)	1 (8)	1 (9)
Conditioning			
Reduced Intensity	9 (38)	8 (62)	1 (9)
Myeloablative	15 (63)	5 (39)	10 (91)
GVHD Prophylaxis			
Tacrolimus	21 (88)	10 (77)	11 (100)
PTCy	13 (54)	9 (69)	5 (46)
Time to Revumenib Maintenance (days)	82 [42 – 174]	62 [42 – 133]	116 [57 – 174]
Baseline Parameters before Maintenance			
WBC (x10^9/L)	5 [2 – 14]	6 [2 – 10]	5 [3 – 14]
Hgb (g/dL)	11 [8 – 14]	11 [8 – 14]	12 [9 – 14]
Plt (x10^9/L)	171 [73 – 411]	146 [73 – 302]	186 [114 – 411]

* N (%), or median [range]

MRD Status at the time of HSCT

Characteristic*	All Patients (N = 24)	Adult (N = 13)	Pediatric (N = 11)
MFC† MRD Pre-HSCT			
Negative	19 (79)	12 (92)	7 (64)
Positive	2 (8)	1 (8)	1 (9)
Unknown	3 (13)	0 (0)	3 (27)
MFC MRD Post-HSCT			
Negative	21 (88)	11 (85)	10 (91)
Positive	0 (0)	0 (0)	0 (0)
Unknown	3 (13)	2 (15)	1 (9)
***NPM1* NGS‡ MRD Pre-Maintenance**			--
Negative	2/5 (40)	2/5 (40)	
Below Level of Detection	3/5 (60)	3/5 (60)	
***NPM1* NGS MRD Post-Maintenance**			--
Negative§	4/5 (80)	4/5 (80)	
Positive	1/5 (20)	1/5 (20)	

* N (%), or median [range]
† MFC, Multiparameter flow cytometry; sensitivity of 1 x 10^{-4}
‡ NGS, Next-generation sequencing; sensitivity of 5 x 10^{-5}
§ One patient NGS MRD positive on Day 25 post revumenib after treatment held for thrombocytopenia, repeat is pending

Safety

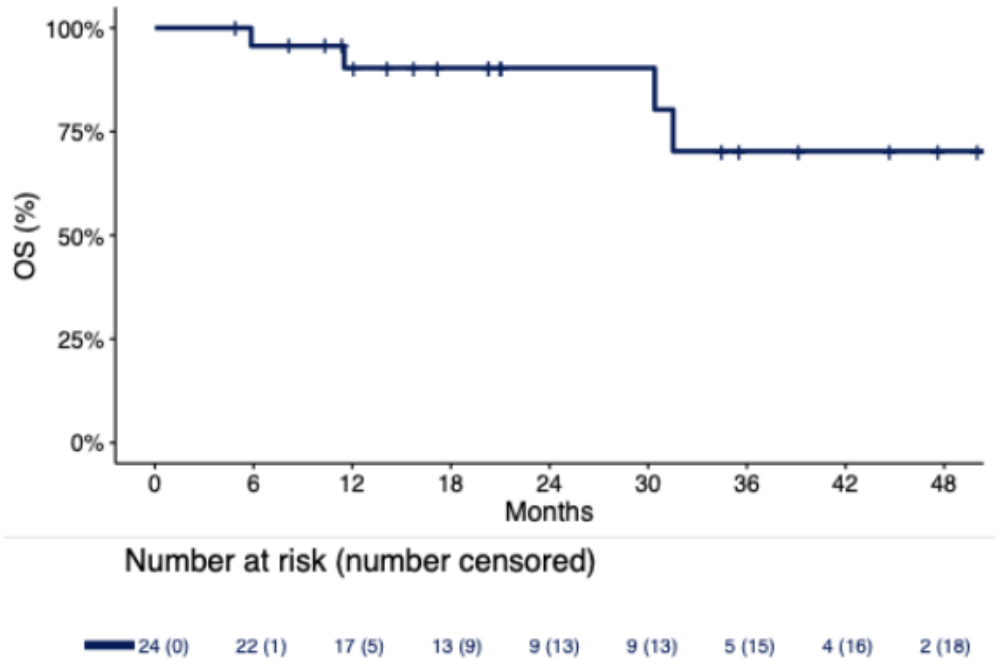
TEAEs	All Grades	≥Grade 3	AE with Dose Interruption/Reduction	AE with Discontinuation
Thrombocytopenia	20 (83)	11 (46)	11 (46)	3 (13)
Neutropenia	5 (21)	1 (4)	1 (4)	1 (4)
Infection*	4 (17)	2 (8)	2 (8)	1 (4)
GVHD†	3 (13)	1 (4)	0 (0)	0 (0)
Nausea/vomiting	2 (8)	0 (0)	1 (4)	0 (0)
Elevated LFTs	1 (4)	0 (0)	0 (0)	0 (0)
Diarrhea	1 (4)	1 (4)	0 (0)	0 (0)
Prolonged QTc	0 (0)	0 (0)	0 (0)	0 (0)
Differentiation syndrome	0 (0)	0 (0)	0 (0)	0 (0)

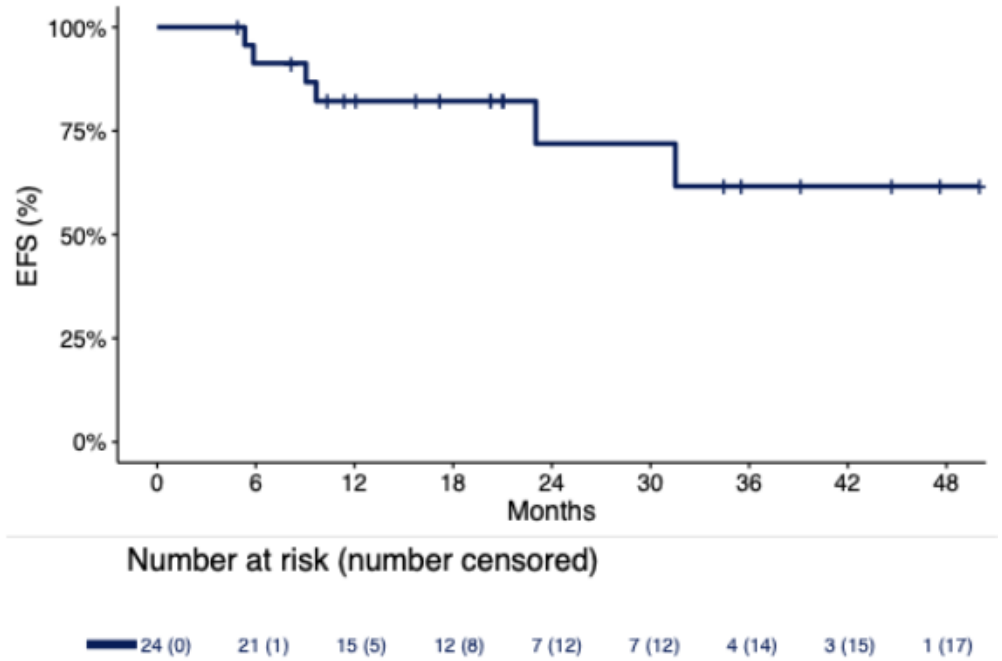
*Infection: n = 1 BK cystitis, n = 1 UTI, n = 1 septic shock, n = 1 CMV gastritis
†GVHD: n = 1 G1 chronic skin GHVD, n = 1 G4 acute GI GVHD, n = 1 unknown grade

TEAEs: treatment-emergent adverse events. Adverse events leading to revumenib post-HSCT dose interruption, reduction or discontinuation are shown. Reported as N (%).

Survival with revumenib post-HSCT maintenance

Median follow-up time: 21 months (0.95 CI 14.4 – 44.7)





Overall Survival	1-year	2-year
All Patients	90%	90%

Event-Free Survival	1-year	2-year
All Patients	82%	72%

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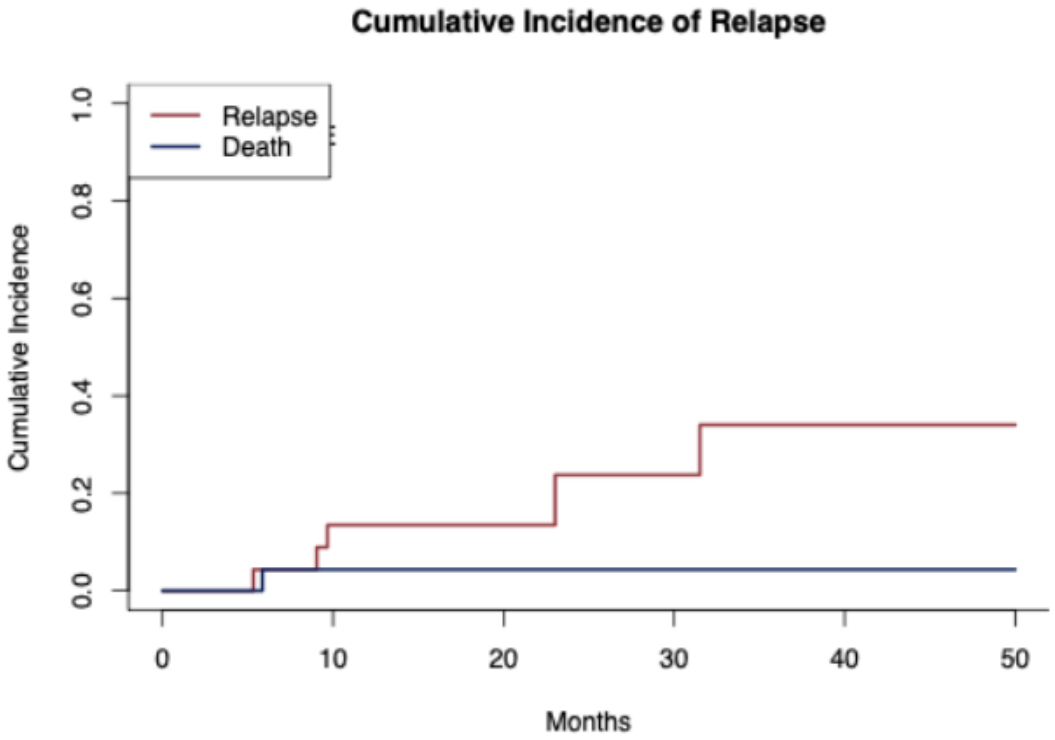
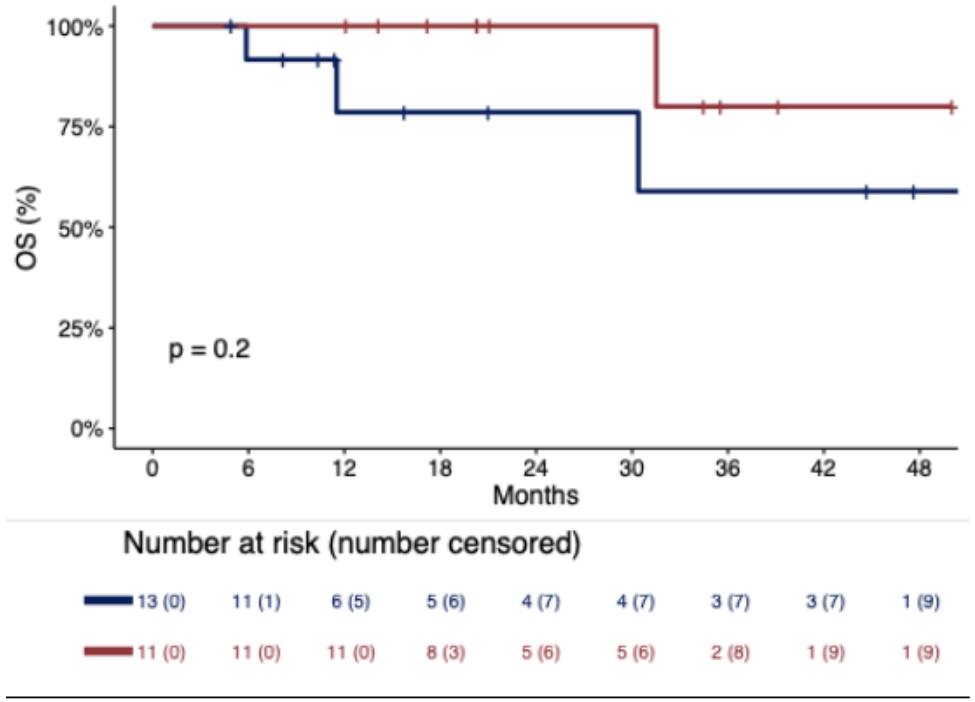
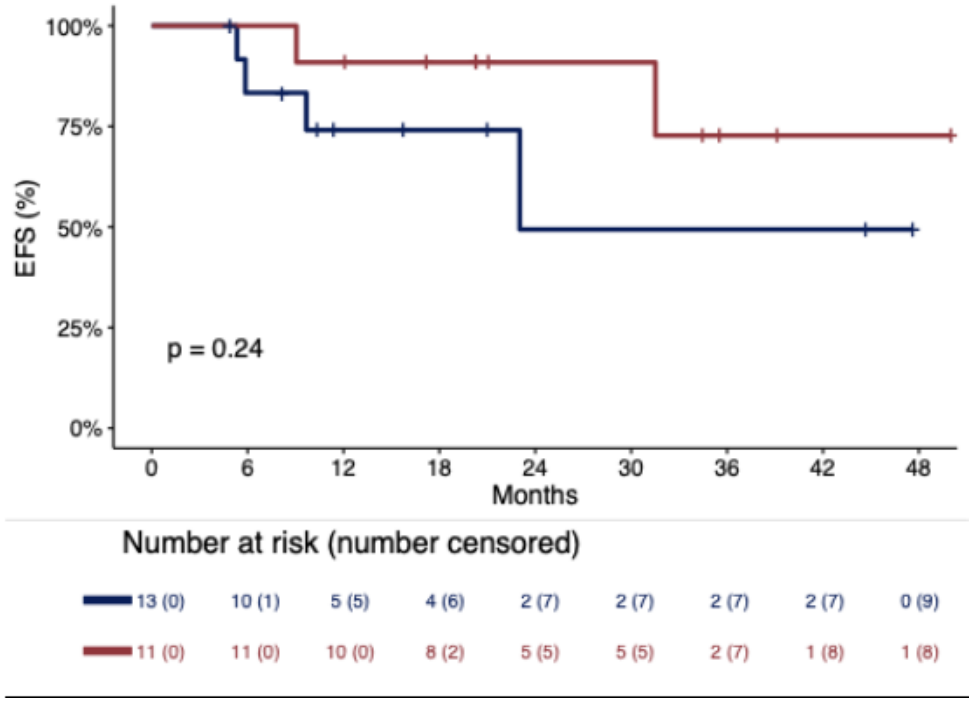
Relapse or Death with revumenib post-HSCT maintenance



Event	1-year	2-year
Cumulative Relapse Rate	13%	24%
Non-relapse Mortality	4%	4%

Survival with revumenib post-HSCT maintenance

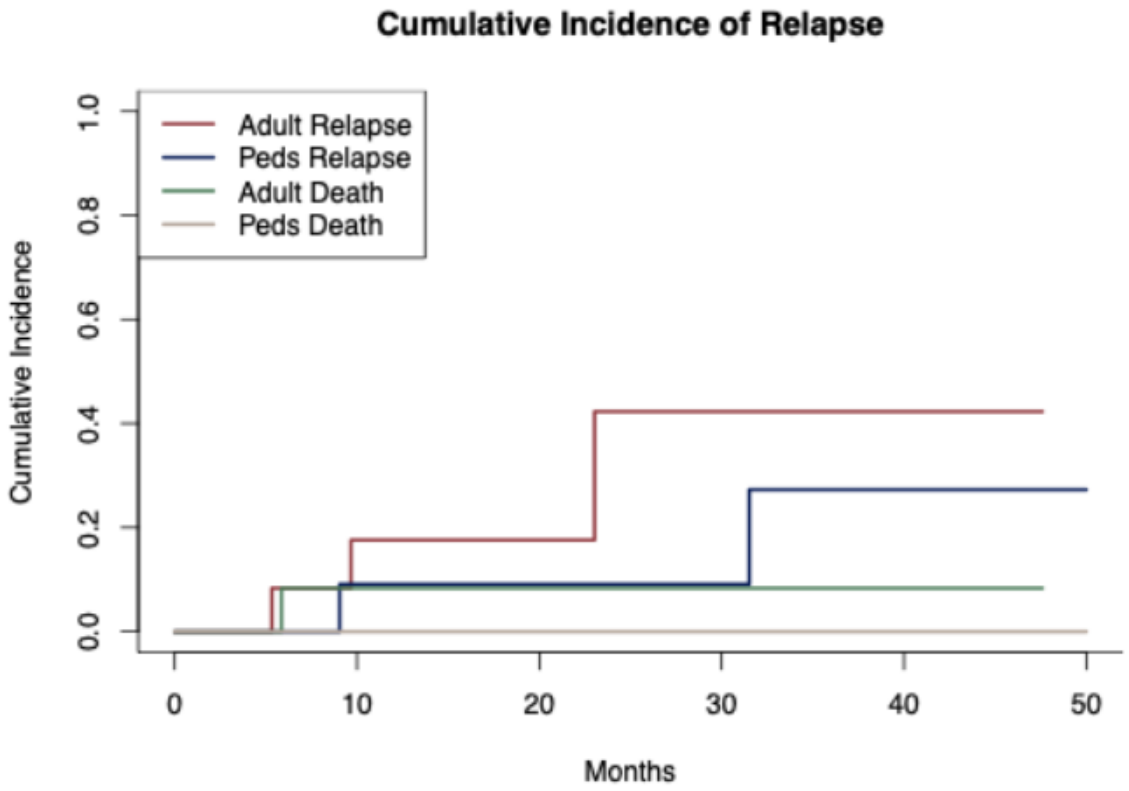




Overall Survival	1-year	2-year
Adult	78%	78%
Pediatric	100%	100%

Event-Free Survival	1-year	2-year
Adult	75%	49%
Pediatric	91%	91%

Relapse or Death with revumenib post-HSCT maintenance



Cumulative Relapse Rate	1-year	2-year
Adult	18%	42%
Pediatric	9%	9%

Non-Relapse Mortality	1-year	2-year
Adult	8%	8%
Pediatric	0%	0%

Relapse *p*-value 0.43
Non-Relapse Mortality *p*-value 0.33

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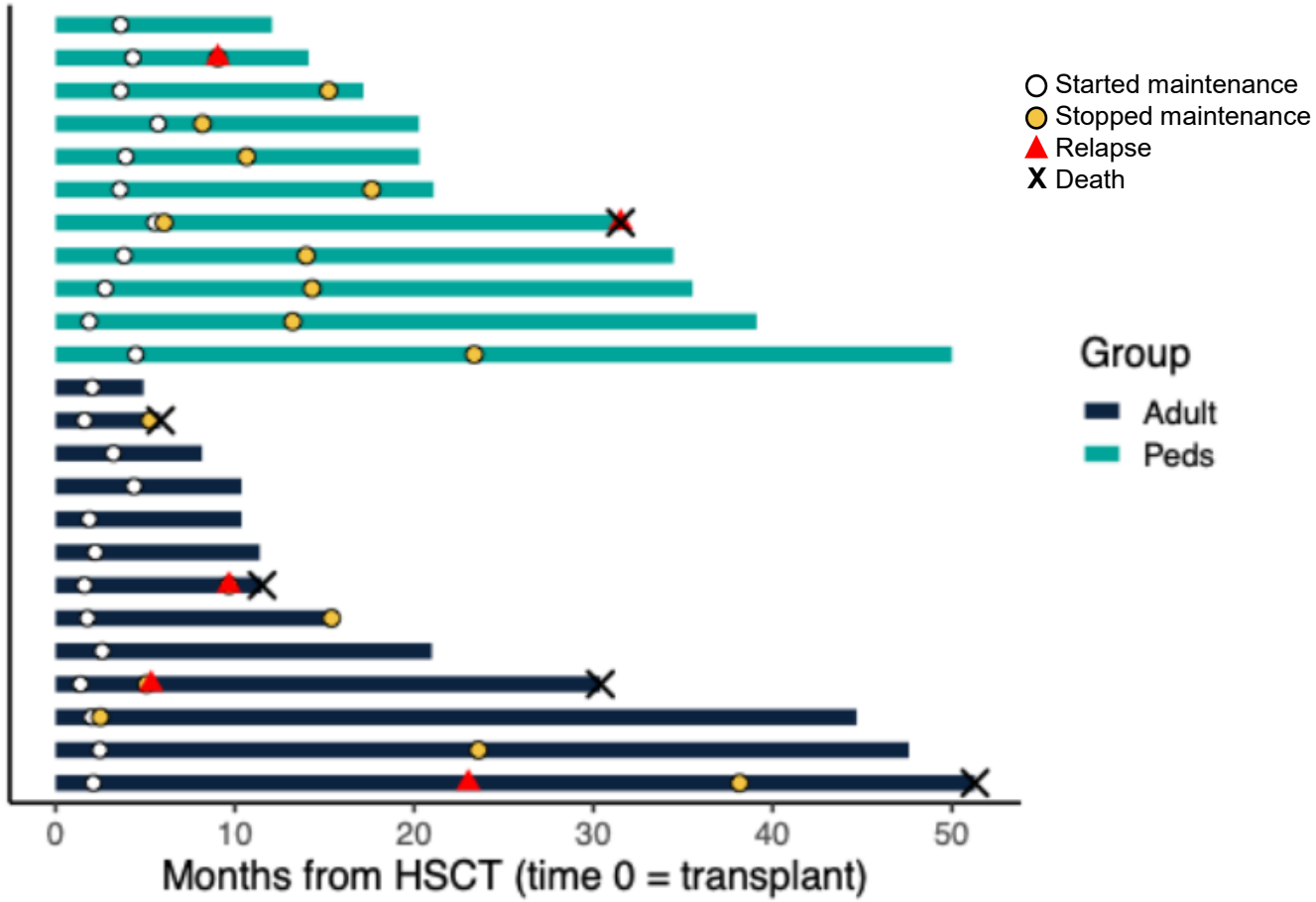
Patient Disposition

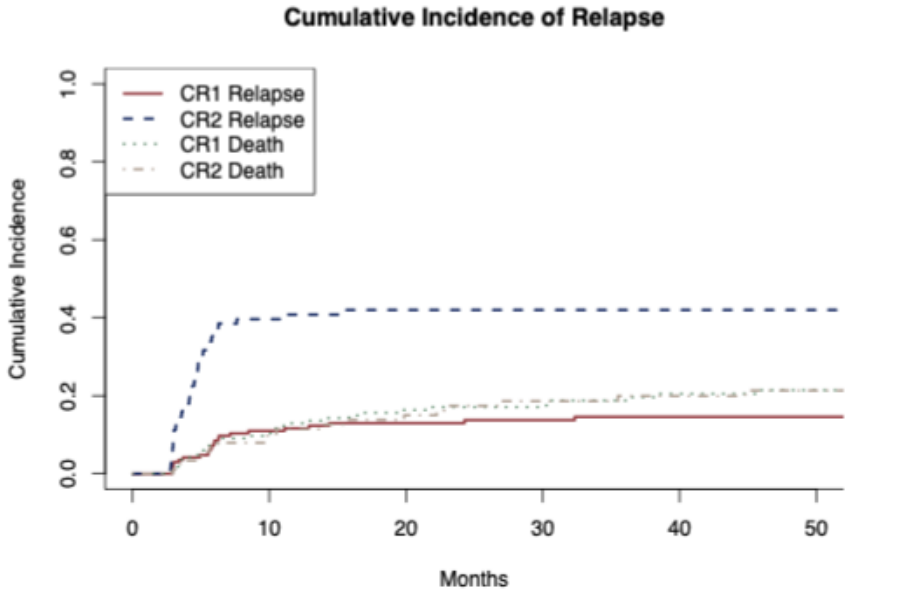


- Median duration of revumenib post-HSCT: **10 months (0.5 – 36 months)**
  - 7 remain on revumenib
- 2 pediatric *KMT2Ar* relapses
  - 1 while on revumenib
  - 1 death
- 3 adult relapses
  - 3 while on revumenib
  - 2 *NPM1mt*, 1 *KMT2Ar*
  - 3 deaths
- 1 adult death in CR
- All relapses CR2+

Relapse or Death with Historical Context

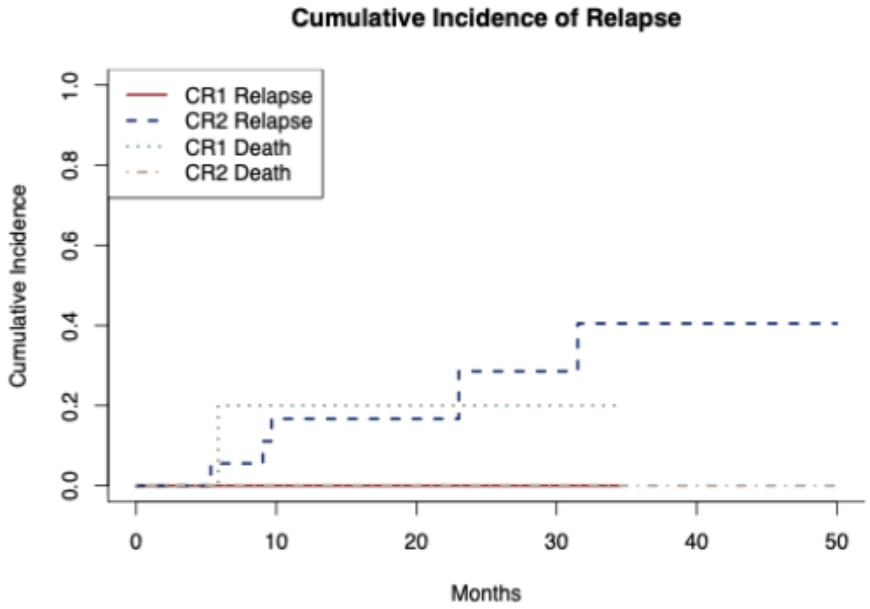
Historical Cohort

Historical Cohort (2005-2025) of *NPM1mt*, *KMT2Ar*, *NUP98r* AML
S/p allo-HSCT in CR1 and salvage ≥1
Median follow-up time: 83 months (0.95 CI 61.9 – 96.9)



Cumulative Relapse Rate	n	1-year
CR1	168	12%
CR2+	89	40%

Revumenib Cohort



Cumulative Relapse Rate	n	1-year
CR1	6	0%
CR2+	18	17%

Conclusions

- Revumenib as maintenance post-HSCT was feasible with no unexpected safety signals
- **Thrombocytopenia was common**, occurring in 83% of patients (grade ≥3 46%), however was manageable with dose modifications
- QTc prolongation events in the post-HSCT setting were not observed
- In our heavily pre-treated cohort (**CR2+ 74%, prior HSCT >50%**), survival outcomes appear encouraging relative to historical expectations with **2-year overall survival and event-free survival rates of 90% and 72%**, respectively
- Limitations include the single-center, single-arm design with heterogeneity in disease biology
- These findings support **further prospective evaluation of menin inhibition as maintenance therapy post-HSCT**

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Lay Summary

- Relapse after stem cell transplant remains a major challenge for patients with acute myeloid leukemia (AML)
- Certain subtypes of AML, including those with mutations in *NPM1* or rearrangements in *KMT2A* or *NUP98* are sensitive to treatment with a targeted therapy called revumenib, which is a type of menin-inhibitor
- Treatment with revumenib after stem cell transplant for these types of AML may help prevent relapse
- We studied how safe and effective using revumenib was in patients after transplant
- Overall, the treatment appears safe, and the rates of relapse appeared lower than expected compared to historical outcomes
- Our findings support further study of this approach