REVUMENIB AS MAINTENANCE FOR AML FOLLOWING ALLOGENEIC STEM CELL TRANSPLANTATION

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INTRODUCTION

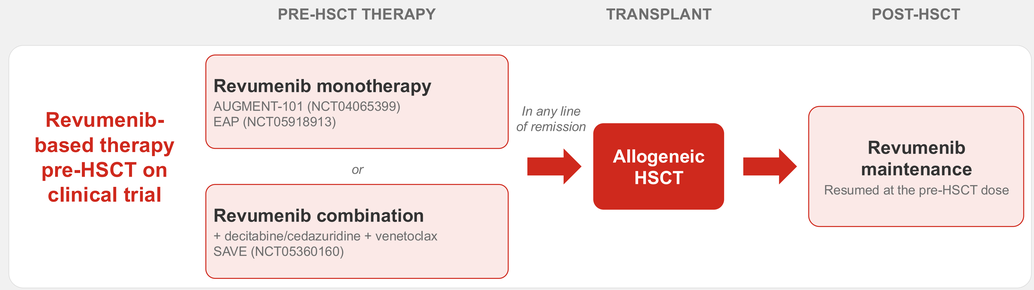
- Relapse after allogeneic hematopoietic stem cell transplantation (allo-HSCT) remains common in acute myeloid leukemia (AML)
- Revumenib is approved for relapsed and/or refractory *NPM1*-mutated or *KMT2A*-rearranged acute leukemia[1-2], however its safety and efficacy as post allo-SCT maintenance therapy is unknown
- Here, we report the outcomes of revumenib as maintenance therapy post allo-SCT in adult and pediatric patients treated at our institution

1. Issa, GC. et al., JCO 2025
2. Arellano, M. et al., Blood 2025

AIM AND METHODS

- Patients with *NPM1*-mutated, *KMT2A*-rearranged, or *NUP98*-rearranged AML were eligible to continue post allo-HSCT maintenance therapy with revumenib following a response to pre allo-SCT revumenib monotherapy orf combination on clinical trial
- Following allo-SCT, revumenib was resumed at the pre allo-SCT dose with adjustment for concomitant azole

Single-center pooled analysis: *NPM1*mt, *KMT2A*r, or *NUP98*r AML undergoing allogeneic HSCT



RESULTS

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]

Response and MRD status

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	5/5 (100)	5/5 (100)	

* MFC, Multiparameter flow cytometry, sensitivity of 1x10^{-4}
† NGS, next-generation sequencing, sensitivity of 5x10^{-5}

Treatment-emergent adverse events

TEAEs	All Grades	≥Grade 3	AE with Dose Interruption/Reduction	AE with Discontinuation
Thrombocytopenia	21 (83)	11 (46)	12 (50)	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)

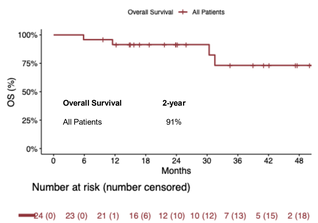
TEAEs: treatment-emergent adverse events. Adverse events leading to revumenib post-HSCT dose interruption, reduction or discontinuation are shown. Reported as N (%).

*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

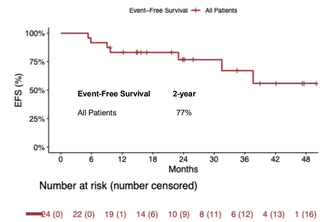
A total of **15 patients (63%)** required either a dose interruption or reduction of revumenib maintenance at any time during their follow-up.
A total of **11 patients (46%)** required dose reduction of revumenib maintenance at any time during their follow-up.

Overall survival
Whole cohort

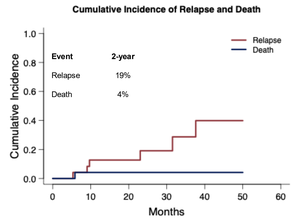
Median follow-up time: 26 months (0.95% CI 21.6 – 47.2)



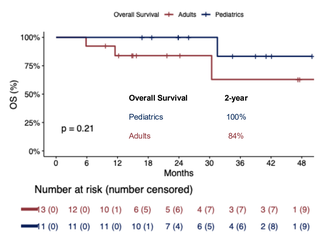
Event-free survival
Whole cohort



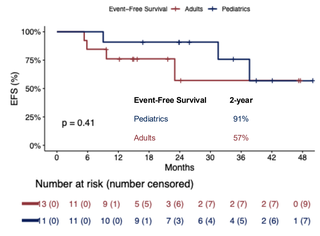
Cumulative incidence of relapse vs death
Whole cohort



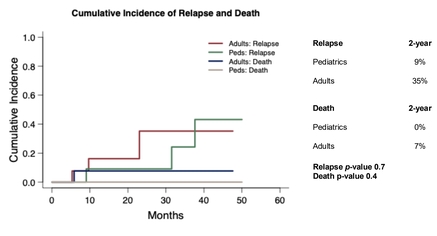
Overall survival
Adults vs. pediatrics



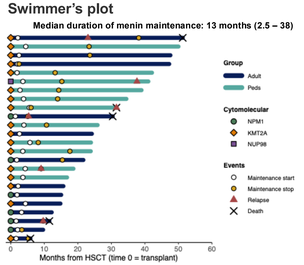
Event-free survival
Adults vs. pediatrics



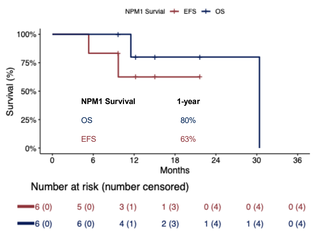
Cumulative incidence of relapse vs death
Adults vs. pediatrics



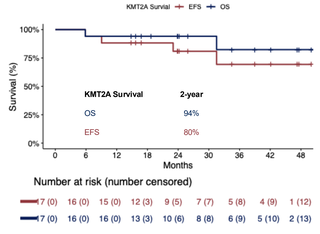
Swimmer's plot



Survival
NPM1 mutated cohort



Survival
KMT2A rearranged cohort



CONCLUSIONS

- Revumenib as maintenance therapy post allo-SCT was feasible with no unexpected safety signals
- Thrombocytopenia was common, occurring in 83% of patients (grade ≥3 46%) and was the most common reason for dose reduction and/or interruption, however this was manageable with dose modification, and most patients could maintain maintenance therapy
- In our heavily pre-treated cohort (CR2+ 74%, prior allo-SCT >50%), survival outcomes appear encouraging with 2-year event-free survival and overall survival rates of 77% and 91%, 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 allo-SCT

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