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Revumenib as Maintenance for AML Following Allogeneic Stem Cell Transplantation

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INTRODUCTION

- Relapse following allogeneic hematopoietic stem cell transplantation (allo-HSCT) remains a major cause of treatment failure in acute myeloid leukemia (AML)
- AML with *NPM1* mutations (*NPM1mt*), *KMT2A*-rearrangements (*KMT2Ar*), or *NUP98*-rearrangements (*NUP98r*) is susceptible to menin inhibition[1-3]
- Revumenib is approved for adults and pediatrics with relapsed/refractory *NPM1mt* or *KMT2Ar* acute leukemia[4,5]
- Menin inhibition could potentiate the graft versus leukemia effect[6,7]

AIMS

- The safety and efficacy of revumenib as post-HSCT maintenance therapy remain undefined
- We thereby sought to:
  - **Assess the tolerability** of revumenib as maintenance post-HSCT for AML
  - **Evaluate the preliminary efficacy** of revumenib as maintenance post-HSCT in the context of a historical cohort

METHODS

- Conducted a 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 or Expanded Access Program, NCT05918913) or combination (revumenib, oral decitabine/cedazuridine, and venetoclax: SAVE, NCT05360160)
  - Resumed post-HSCT revumenib maintenance
  - Analysed historical cohort with same genotypes prior to advent of menin inhibitors

RESULTS

For all tables, n (%) or median [range]

Table 1. 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 monotherapy*	10 (42)	4 (31)	6 (55)
SAVE†	14 (58)	9 (69)	5 (45)

* All relapsed/refractory
† Frontline n = 6, relapsed/refractory n = 8

Table 2. 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			1 (9)
Reduced Intensity	9 (38)	8 (62)	0 (0)
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]
Pre-Maintenance Labs			
WBC (x10⁹/L)	5 [2 – 14]	6 [2 – 10]	5 [3 – 14]
Hgb (g/dL)	11 [8 – 14]	11 [8 – 14]	12 [9 – 14]
Plt (x10⁹/L)	171 [73 – 411]	146 [73 – 302]	186 [114 – 411]

Table 3. Treatment Emergent Adverse Events (TEAE)

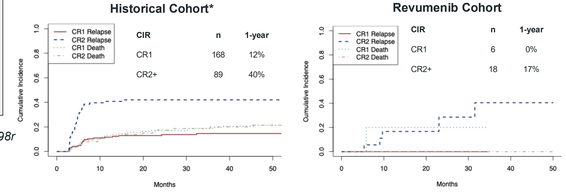
TEAEs	All Grades	≥Grade 3	AE with Dose Interruption/Reduction	AE with Discontinuation
Thrombocytopenia	20 (83)	11 (46)	11 (46)	3 (13)
Neutropenia	5 (21)	1 (4)	1 (4)	1 (4)
Infection	4 (17)	2 (8)	2 (8)	1 (4)
GVHD	3 (13)	1 (4)	0 (0)	0 (0)
Nausea/vomiting	2 (8)	0 (0)	1 (4)	0 (0)
Elevated LFTs	1 (4)	0 (0)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

Table 4. Measurable Residual Disease 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‡	4/5 (80)	4/5 (80)	--
Positive	1 (20)	1 (20)	

* MFC, Multiparameter flow cytometry, sensitivity of 1x10⁻⁴
† NGS, next-generation sequencing, sensitivity of 5x10⁻⁵
‡ One patient NGS MRD positive on Day 25 post-revumenib after tx held for TCP, repeat is pending

Figure 4*. Relapse Vs. Non-Relapse Mortality with Historical Control



***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)
Excluded pts who relapsed/died before landmark of 82 days (median time to initiate post-HSCT menin)

Figure 1. Survival of Entire Cohort

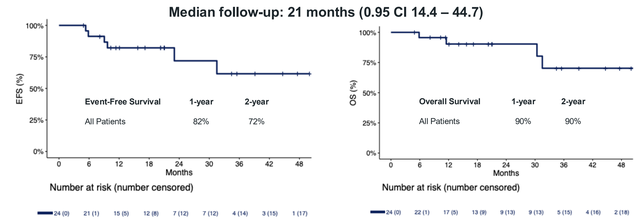


Figure 2. Survival in Adult Vs. Pediatric

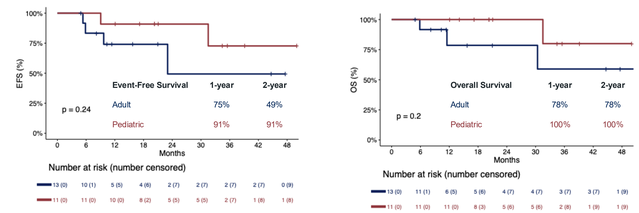


Figure 3. Relapse Vs. Non-Relapse Mortality

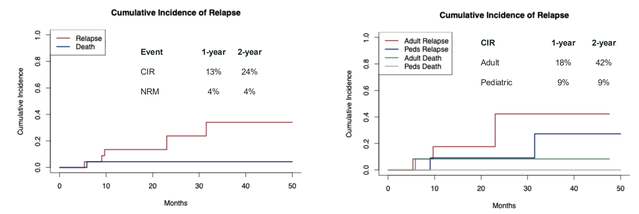
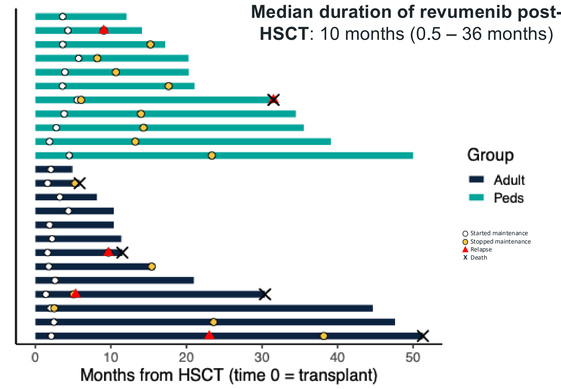


Figure 5. Patient Disposition



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 this was manageable with dose modifications**
- 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 small, singlesingle-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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