

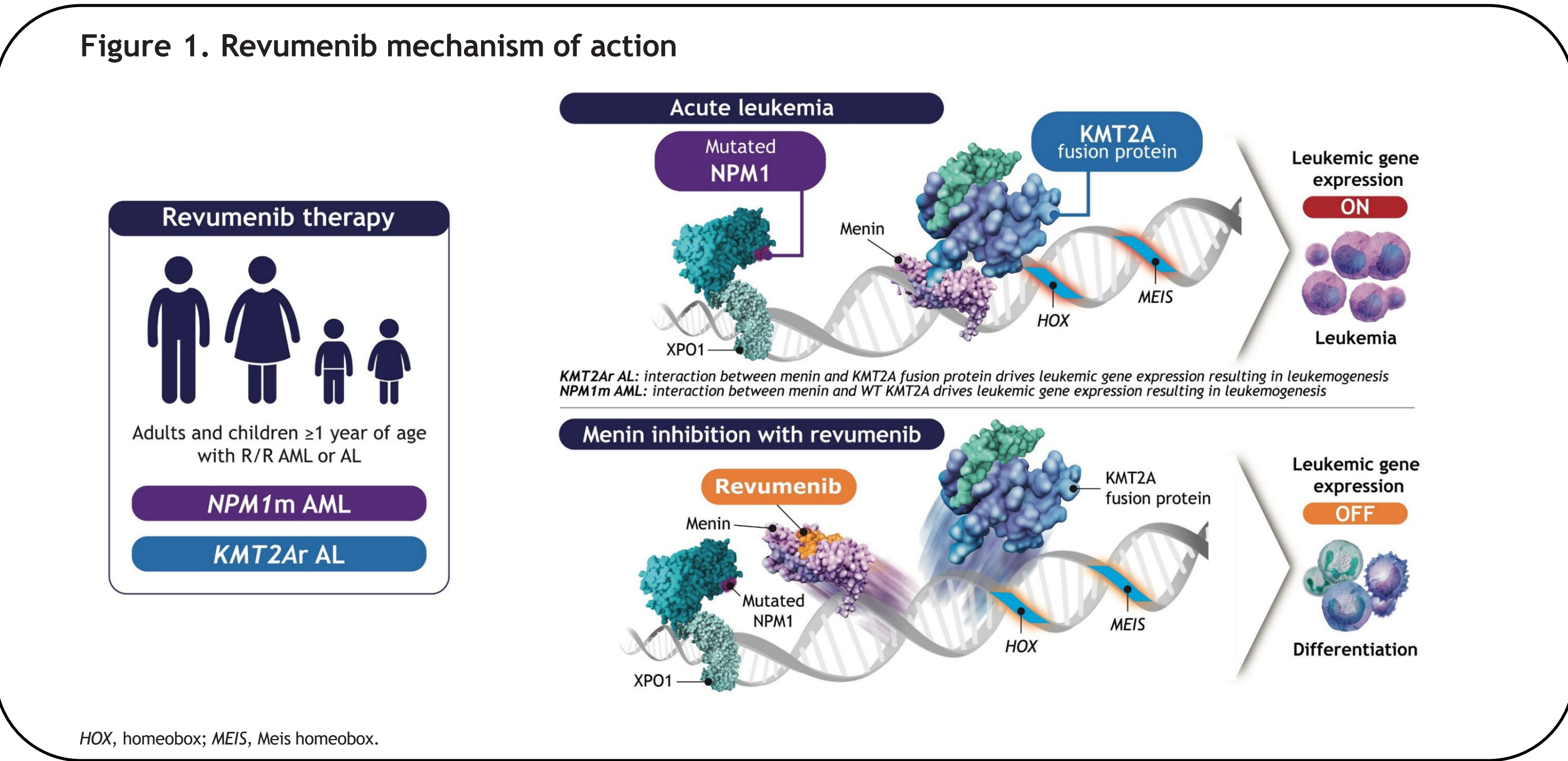
AML - 632

# Revumenib Therapy Post Hematopoietic Stem Cell Transplant for Patients With Relapsed/Refractory *KMT2A*r, *NPM1*m, and *NUP98*r Acute Myeloid Leukemia: Post Hoc Analysis of Outcomes From AUGMENT-101

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## INTRODUCTION

- Hematopoietic stem cell transplant (HSCT) is widely used as a standard-of-care approach for acute myeloid leukemia (AML), yet disease recurrence after HSCT remains a major limitation<sup>1</sup>
  - Approximately 30% to 40% of patients (regardless of age) relapse, often within 6 to 7 months after HSCT<sup>2,3</sup>
  - Among young adult and adult patients with *KMT2A*-rearranged (*KMT2A*r) AML, relapse often occurs early (median time to relapse, 4.7 months)<sup>4</sup>
- Revumenib, a first-in-class, oral, potent, and selective inhibitor of the menin-*KMT2A* interaction (Figure 1), is used for the treatment of relapsed/refractory (R/R) AML harboring an *NPM1* mutation (*NPM1*m) or R/R acute leukemia with a *KMT2A* translocation in adult and pediatric patients 1 year and older<sup>5,6</sup>
- In addition to the well-characterized antileukemic action of menin inhibitors, preclinical data indicate that menin inhibition may also enhance donor T-cell antitumor activity, which supports revumenib as a potential post-HSCT maintenance treatment and thus as a strategy to reduce the risk of relapse<sup>7</sup>



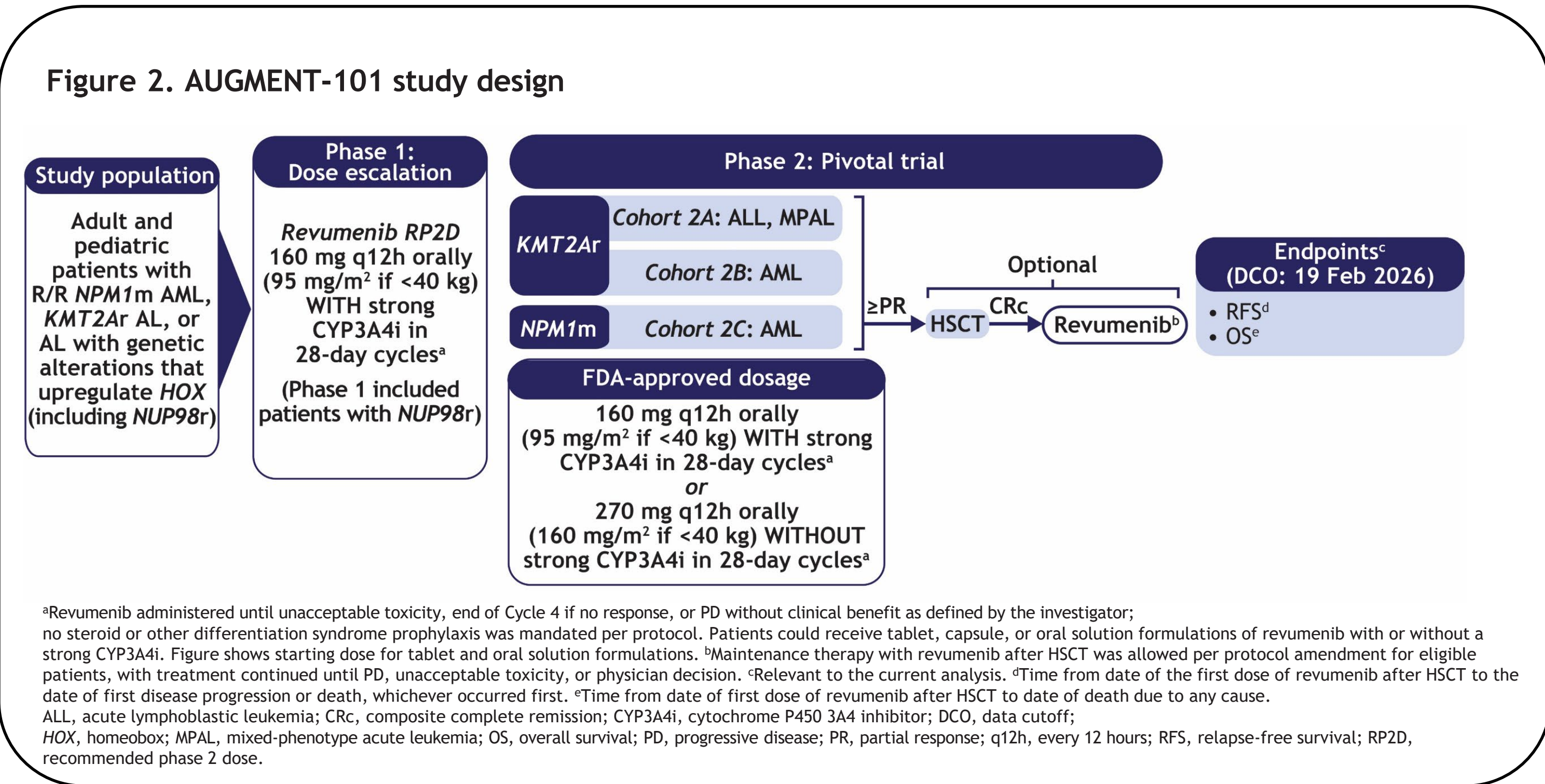
## OBJECTIVE

- To evaluate the efficacy and safety of revumenib monotherapy as post-HSCT maintenance treatment in patients with R/R *NPM1*m, *KMT2A*r, or *NUP98* rearranged (*NUP98*r) AML using data from AUGMENT-101 (NCT04065399)

## METHODS

### Study design

- AUGMENT-101 is an ongoing phase 1/2, open-label, dose-escalation and -expansion study of revumenib in pediatric and adult patients with R/R *NPM1*m, *KMT2A*r, or *NUP98*r acute leukemia (Figure 2)
- Post-HSCT maintenance therapy with revumenib was allowed for eligible patients, with treatment continuing until disease progression, unacceptable toxicity, or physician decision
  - Eligible patients were between 30 to 180 days after HSCT, had achieved composite complete remission, had successful engraftment, and had no acute or chronic graft-versus-host disease (GVHD) that required immunosuppression
  - Revumenib maintenance was administered at the same dose the patient was receiving immediately prior to HSCT, with adjustments for patients starting or stopping a strong cytochrome P450 3A4 inhibitor peri-HSCT



## RESULTS

### Patients

- As of 19 February 2026, 19/59 (32%) patients with R/R AML who received HSCT after achieving a response with revumenib monotherapy had resumed revumenib treatment after HSCT
- Four (21%) patients had *NPM1*m AML, 14 (74%) had *KMT2A*r, and 1 (5%) had *NUP98*r (Table 1)
  - Two of 4 patients with *NPM1*m had co-mutations (*IDH1*, *DNM3TA*, and *FLT3*-ITD)
- Patients had received a median (range) of 2 (1-7) prior lines of treatment; 10 (53%) patients had received prior HSCT
- Median (range) time from HSCT to initiation of revumenib maintenance was 65 (34-181) days

| Table 1. Demographic and baseline characteristics                |                          |                            |                           |                   |
|------------------------------------------------------------------|--------------------------|----------------------------|---------------------------|-------------------|
|                                                                  | <i>NPM1</i> m<br>(n = 4) | <i>KMT2A</i> r<br>(n = 14) | <i>NUP98</i> r<br>(n = 1) | Total<br>(N = 19) |
| Age, median (range), y                                           | 42.5 (19.0-56.0)         | 40.0 (1.3-75.0)            | 17.0 (17.0-17.0)          | 39.0 (1.3-75.0)   |
| Age group, n (%)                                                 |                          |                            |                           |                   |
| <18 y                                                            | 0                        | 3 (21)                     | 1 (100)                   | 4 (21)            |
| 18-≤65 y                                                         | 4 (100)                  | 10 (71)                    | 0                         | 14 (74)           |
| ≥65 y                                                            | 0                        | 1 (7)                      | 0                         | 1 (5)             |
| Female, n (%)                                                    | 3 (75)                   | 6 (43)                     | 0                         | 9 (47)            |
| Race, n (%)                                                      |                          |                            |                           |                   |
| White                                                            | 4 (100)                  | 8 (57)                     | 1 (100)                   | 13 (68)           |
| Non-White <sup>a</sup>                                           | 0                        | 3 (21)                     | 0                         | 3 (16)            |
| Unknown                                                          | 0                        | 3 (21)                     | 0                         | 3 (16)            |
| No. of prior lines of therapy, median (range)                    | 2 (1-7)                  | 2 (1-6)                    | 5 (5-5)                   | 2 (1-7)           |
| Disease status at baseline, n (%)                                |                          |                            |                           |                   |
| Primary refractory                                               | 0                        | 4 (29)                     | 0                         | 4 (21)            |
| Refractory relapse                                               | 2 (50)                   | 6 (43)                     | 1 (100)                   | 9 (47)            |
| Early untreated relapse                                          | 1 (25)                   | 2 (14)                     | 0                         | 3 (16)            |
| Late untreated relapse                                           | 1 (25)                   | 2 (14)                     | 0                         | 3 (16)            |
| Prior treatment, n (%)                                           |                          |                            |                           |                   |
| Venetoclax                                                       | 2 (50)                   | 6 (43)                     | 1 (100)                   | 9 (47)            |
| HSCT                                                             | 2 (50)                   | 7 (50)                     | 1 (100)                   | 10 (53)           |
| Days from HSCT to initiating revumenib treatment, median (range) | 43 (40-59)               | 78 (34-181)                | 145 (145-145)             | 65 (34-181)       |

<sup>a</sup>Includes Black or African American and Asian.

### Post-HSCT maintenance exposure

- Median relative dose intensity was high, regardless of genotype, which supports tolerability of revumenib as a post-HSCT maintenance therapy (Table 2)
- Median (range) duration of post-HSCT maintenance therapy was 20.0 (2.0-137.0) weeks

| Table 2. Exposure                          |                          |                            |                           |                   |
|--------------------------------------------|--------------------------|----------------------------|---------------------------|-------------------|
|                                            | <i>NPM1</i> m<br>(n = 4) | <i>KMT2A</i> r<br>(n = 14) | <i>NUP98</i> r<br>(n = 1) | Total<br>(N = 19) |
| No. of cycles started, median (range)      | 2.5 (1.0-24.0)           | 5.0 (1.0-33.0)             | 11.0 (11.0-11.0)          | 5.0 (1.0-33.0)    |
| Relative dose intensity, median (range), % | 78.7 (55.8-100.0)        | 95.5 (15.7-159.5)          | 95.7 (95.7-95.7)          | 95.7 (15.7-159.5) |
| Duration of therapy, median (range), wk    | 38.1 (2.0-99.0)          | 19.7 (2.0-137.0)           | 41.7 (42.0-42.0)          | 20.0 (2.0-137.0)  |

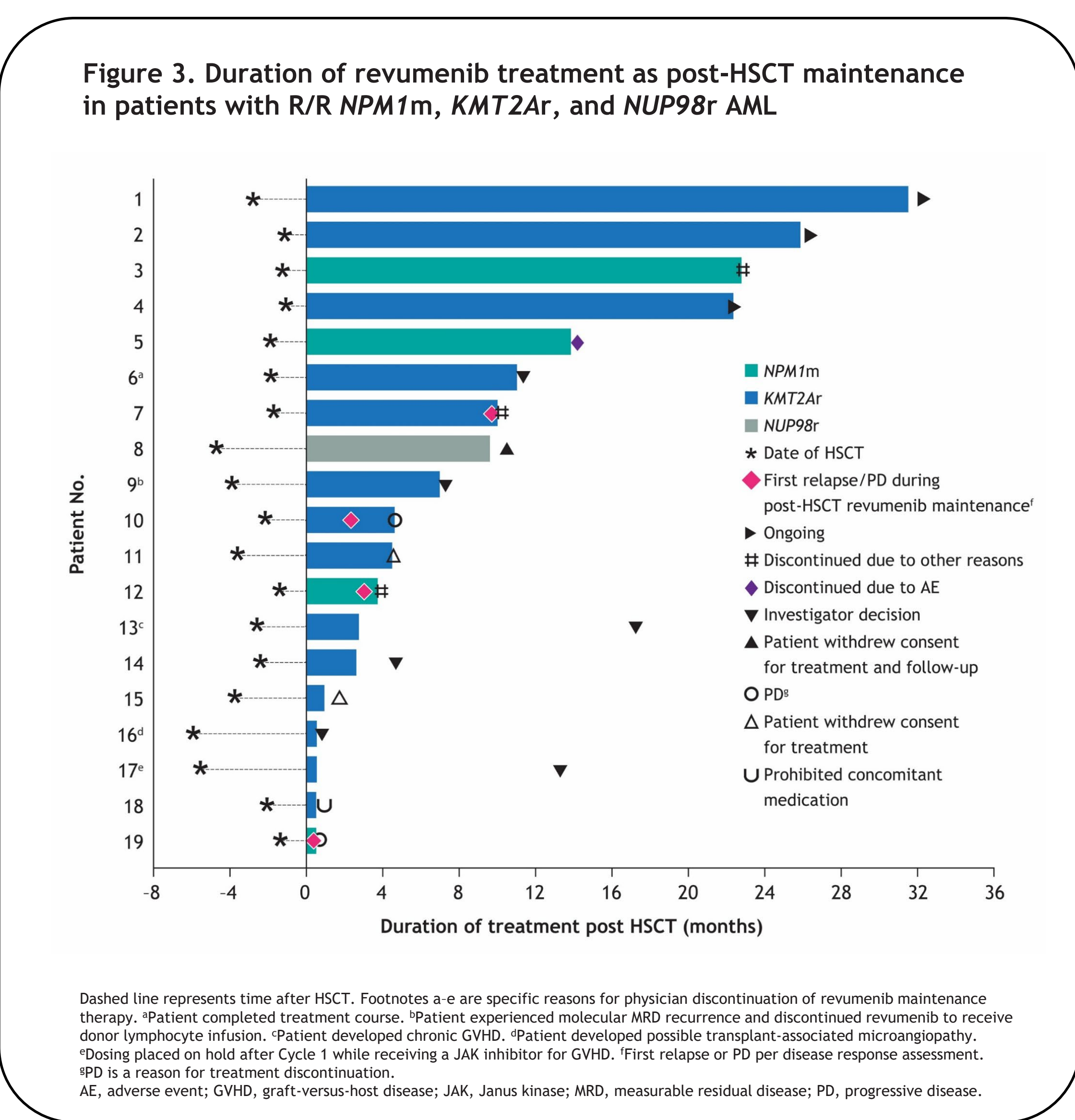
### Efficacy

- Median relapse-free survival was not reached in patients receiving post-HSCT revumenib, regardless of genotype, and 78.6% of patients remained alive and relapse free at 12 months (Table 3)
  - 85.1% of patients in the *KMT2A*r group were alive and relapse free at 12 months
- Median overall survival was not reached in patients receiving post-HSCT revumenib, regardless of genotype (Table 3)

| Table 3. Efficacy                |                          |                            |                           |                   |
|----------------------------------|--------------------------|----------------------------|---------------------------|-------------------|
|                                  | <i>NPM1</i> m<br>(n = 4) | <i>KMT2A</i> r<br>(n = 14) | <i>NUP98</i> r<br>(n = 1) | Total<br>(N = 19) |
| RFS                              |                          |                            |                           |                   |
| Events, <sup>a</sup> n (%)       | 2 (50.0)                 | 3 (21.4)                   | 0                         | 5 (26.3)          |
| Median (95% CI), mo              | NR (0.3-NR)              | NR (26.0-NR)               | N/A                       | NR (26.0-NR)      |
| Estimated 12-mo rate (95% CI), % | 50.0 (5.8-84.5)          | 85.1 (52.3-96.1)           | N/A                       | 78.6 (52.5-91.4)  |
| OS                               |                          |                            |                           |                   |
| Events, <sup>b</sup> n (%)       | 2 (50.0)                 | 2 (14.3)                   | 0                         | 4 (21.1)          |
| Median (95% CI), mo              | NR (0.9-NR)              | NR (26.0-NR)               | N/A                       | NR (26.0-NR)      |
| Estimated 12-mo rate (95% CI), % | 75.0 (12.8-96.1)         | 100.0 (100.0-100.0)        | N/A                       | 94.7 (68.1-99.2)  |

<sup>a</sup>Four patients due to PD, 1 patient due to death. <sup>b</sup>Due to death.  
N/A, not applicable; NR, not reached; OS, overall survival; PD, progressive disease; RFS, relapse-free survival.

- As of 19 February 2026, 3 patients remained on post-HSCT maintenance treatment (Figure 3)



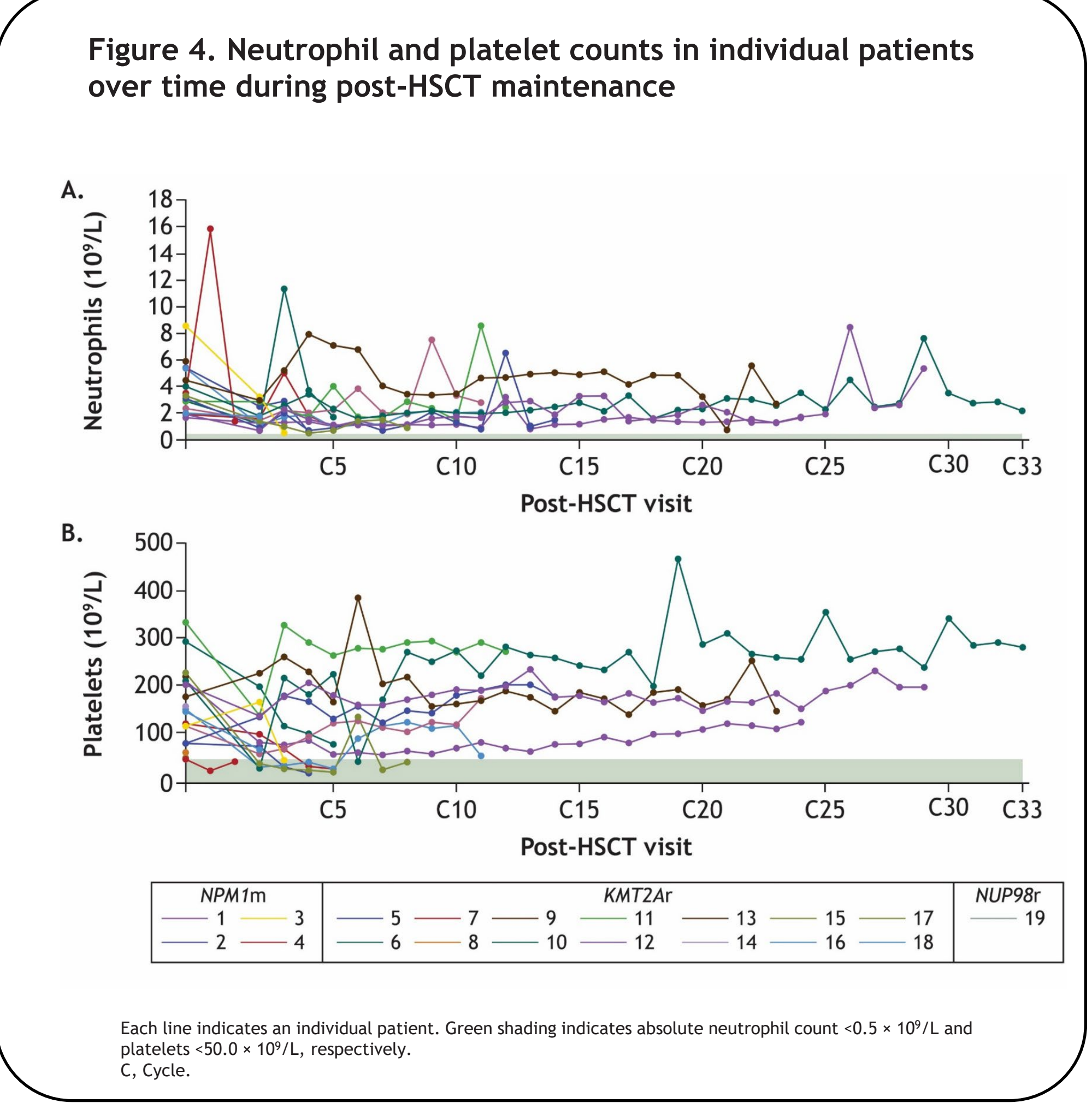
### Safety

- Any-grade treatment-emergent adverse events (TEAEs) occurred in 84% of patients (Table 4); most common were thrombocytopenia/platelet count decreased (53%) and rhinorrhea (37%)
- Most common grade ≥3 TEAEs were thrombocytopenia/platelet count decreased (42%) and neutrophil count decreased (16%)

| Table 4. Summary of AEs                   |                |
|-------------------------------------------|----------------|
| Parameter, n (%)                          | Total (N = 19) |
| Any-grade TEAE                            | 16 (84)        |
| Grade ≥3                                  | 14 (74)        |
| Any-grade TRAE                            | 9 (47)         |
| Grade ≥3                                  | 8 (42)         |
| SAE                                       | 8 (42)         |
| TEAE leading to dose modification         | 11 (58)        |
| Reduction                                 | 2 (11)         |
| Interruption                              | 11 (58)        |
| TEAE leading to revumenib discontinuation | 1 (5)          |
| TEAE leading to death                     | 0              |
| TRAE leading to dose modification         | 7 (37)         |
| Reduction <sup>a</sup>                    | 2 (11)         |
| Interruption <sup>b</sup>                 | 7 (37)         |
| TRAE leading to revumenib discontinuation | 1 (5)          |
| TRAE leading to death                     | 0              |

<sup>a</sup>Due to AEs (platelet count decreased, n = 2; neutrophil count decreased, n = 1; 1 patient experienced both events).  
<sup>b</sup>Dose interruptions included dose delayed or dose skipped.  
AE, adverse event; SAE, serious adverse event; TEAE, treatment-emergent adverse event; TRAE, treatment-related adverse event.

- Relative to post-HSCT starting dose levels, 2 (11%) patients had a revumenib dose reduction due to cytopenia; no patients discontinued revumenib treatment due to cytopenia
- Most patients maintained neutrophils >0.5 × 10<sup>9</sup>/L and platelets >50.0 × 10<sup>9</sup>/L during revumenib maintenance therapy (Figure 4)



- 11/19 (58%) patients had dose interruptions during treatment
  - Reasons for skipped doses included platelet count decreased/thrombocytopenia (6/19; 32%), nausea/vomiting (3/19; 16%), neutropenia (1/19; 5%), and GVHD (3/19; 16%)
- One grade ≥2 QTcF prolongation event occurred in 1 (5%) patient, lasting 1 day, and was unrelated to revumenib
- No differentiation syndrome events were reported with revumenib post-HSCT maintenance therapy
- GVHD occurred in 4 (21%) patients, and onset ranged from 17 to 83 days after initiation of revumenib maintenance
  - Three events were grade 3, and none were considered related to revumenib

## CONCLUSIONS

- Revumenib demonstrated promising efficacy and a tolerable safety profile as post-HSCT maintenance treatment in adult and pediatric patients with R/R *NPM1*m, *KMT2A*r, and *NUP98*r AML
- Sustained relapse-free survival across genotypes supports the potential ability of revumenib to reduce post-HSCT relapse in this high-risk population
- The safety profile of revumenib was consistent with that of the broader AUGMENT-101 trial,<sup>5</sup> and no differentiation syndrome was reported
  - No patients discontinued treatment due to cytopenias
- Collectively, these data support continued evaluation of revumenib as a post-HSCT maintenance treatment, with ongoing assessment in the post-transplant setting (NCT06575296)

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AUGMENT-101 is sponsored by Syndax Pharmaceuticals, Inc. Medical writing and editorial assistance were provided by Kirsty Lee, MPH, of Luminary Communications Inc., and were funded by Syndax Pharmaceuticals, Inc. Poster previously presented at 31<sup>st</sup> Congress of the European Hematology Association (EHA); 11-14 June 2026; Stockholm, Sweden.

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