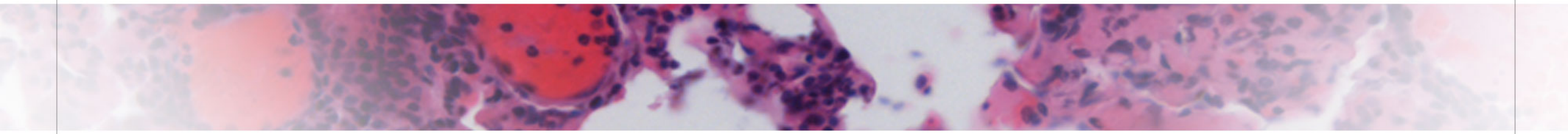
American Society of Hematology
Helping hematologists conquer blood diseases worldwide



Outcomes After Transplant in Relapsed/Refractory *KMT2Ar* (*MLLr*) and *mNPM1* (*NPM1c*) Leukemia Patients Achieving Remissions After Menin Inhibition: Revumenib (SNDX-5613) Ph1 Experience

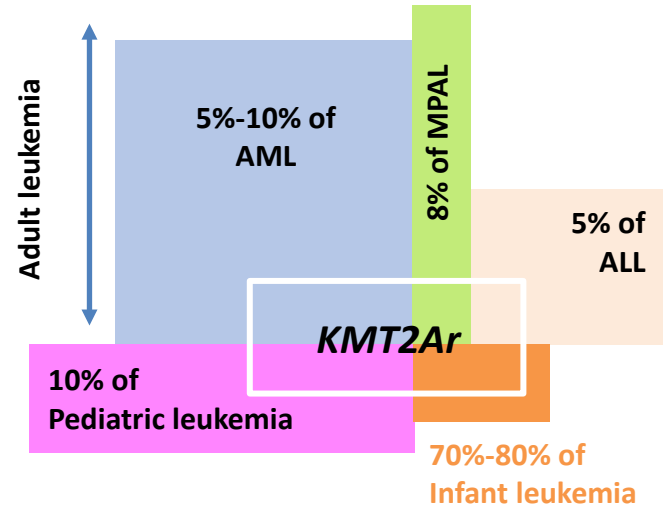
Ghayas C. Issa, MD,[1] Branko Cuglievan, MD,[2] Eytan M. Stein, MD,[3] Martha L. Arellano, MD,[4] Andrius Žucenka,[5] Nandita Khera, MD, MPH,[6] Richard M. Stone, MD,[7] Michael Thirman, MD,[8] John F. DiPersio, MD, PhD,[9] Nicole Karras, MD,[10] Yu Gu, PhD,[11] Rebecca G. Bagley, MA,[11] Galit Rosen, MD,[11] David Tamang, PhD,[11] Kimberly Dishman, NP,[11] Sushama Scalera, MD,[11] Michael L. Meyers, MD, PhD,[11] Kate Madigan, MD,[11] Nicole McNeer, MD, PhD[11] and Ibrahim Aldoss, MD[12]

[1]Department of Leukemia, The University of Texas MD Anderson Cancer Center, Houston, TX; [2]Division of Pediatric Hematology Oncology, The University of Texas MD Anderson Cancer Center, Houston, TX; [3]Leukemia Service, Department of Medicine, Memorial Sloan Kettering Cancer Center, New York, NY; [4]Winship Cancer Institute, Emory University School of Medicine, Atlanta, GA; [5]Hematology, Oncology and Transfusion Medicine Center, Vilnius University Hospital Santaros Klinikos, Vilnius, Lithuania; [6]Division of Hematology/Oncology, Mayo Clinic, Phoenix, AZ; [7]Department of Medical Oncology, Dana-Farber Cancer Institute, Boston, MA; [8]Departmentof Medicine, Section of Hematology/Oncology, University of Chicago, Chicago, IL; [9]Division of Oncology, Department of Medicine, Washington University School of Medicine, Saint Louis, MO; [10]Department of Pediatrics, City of Hope National Medical Center, Duarte, CA; [11]Syndax Pharmaceuticals, Inc., Waltham, MA; [12]City of Hope, Duarte, CA

Leukemias with *KMT2Ar or mNPM1*

KMT2Ar Acute Leukemias

Global incidence ~7,000



- ***KMT2Ar* leukemias are a therapeutic challenge**

NPM1 Mutant AML

Global incidence ~20,000

~30% AML

- **Known *NPM1* co-mutations offer rational combination approaches**

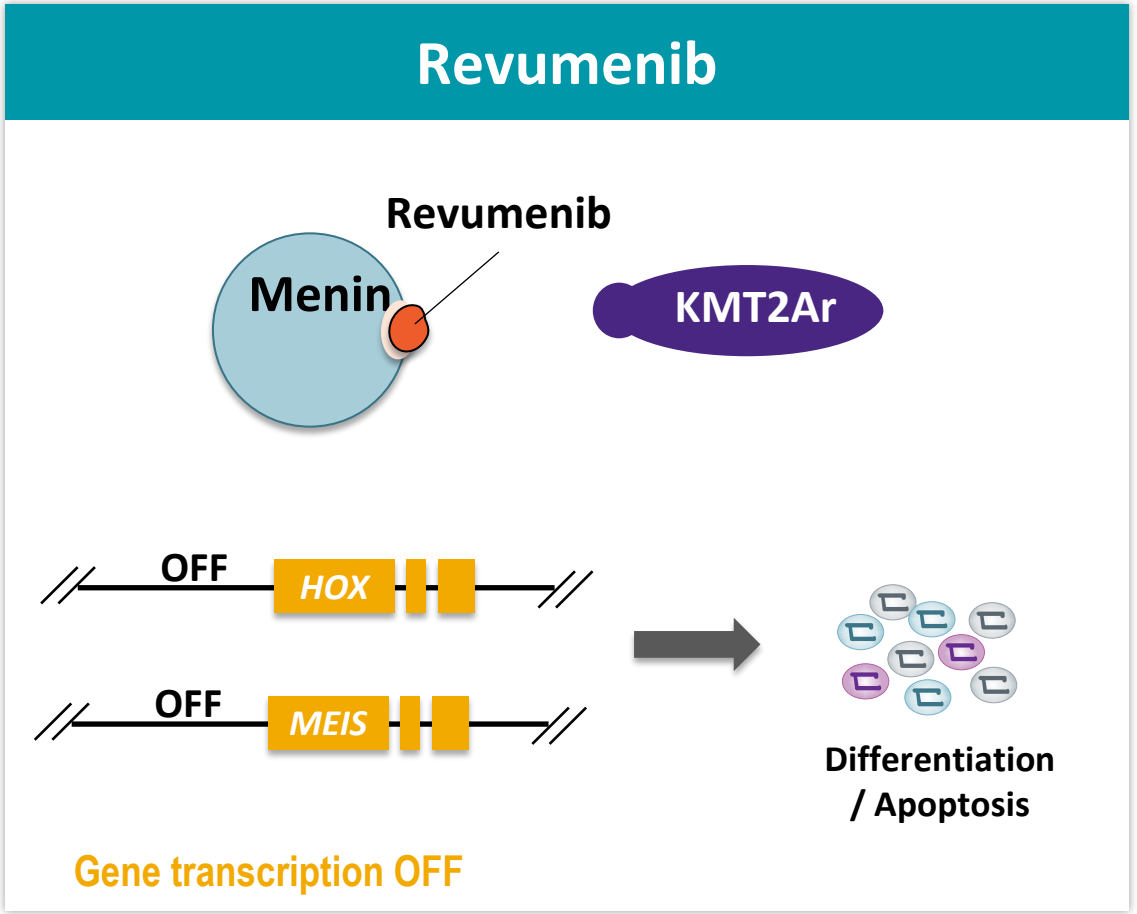
No FDA-approved targeted therapies to treat *KMT2Ar* or *mNPM1* acute leukemias

Sources: NCCN conference and meetings: NCCN guidelines; Issa, GC, et al. *Leukemia*. 2021;35:2482–2495; Papaemmanuil, E. et al. *N Engl J Med*. 2016;374: 2209-2221; Dohner, H. et al. *Blood*, 2017; 129(4):424-447; Falini, B. et al. *Blood,* 2011; 117(4): 1109-1120.

ALL, acute lymphoblastic leukemia; AML, acute myeloid leukemia; FDA, Food and Drug Administration; *KMT2Ar*, lysine methyltransferase 2A rearrangements; *mNPM1*, mutated nucleophosmin 1; MPAL, mixed-phenotype acute leukemia.

Revumenib (SNDX-5613) turns off leukemic transcriptional programs by binding to menin and displacing KMT2A complexes

- *KMT2Ar* and *mNPM1* acute leukemias are driven by aberrant expression of *HOX/MEIS1* that is dependent on menin-KMT2A interaction[1,2]
- Revumenib is a potent, selective inhibitor that disrupts this interaction and blocks this leukemogenic gene transcription program by binding menin within a well-defined pocket, preventing the binding of menin to both wild-type KMT2A and KMT2A fusion proteins[3]

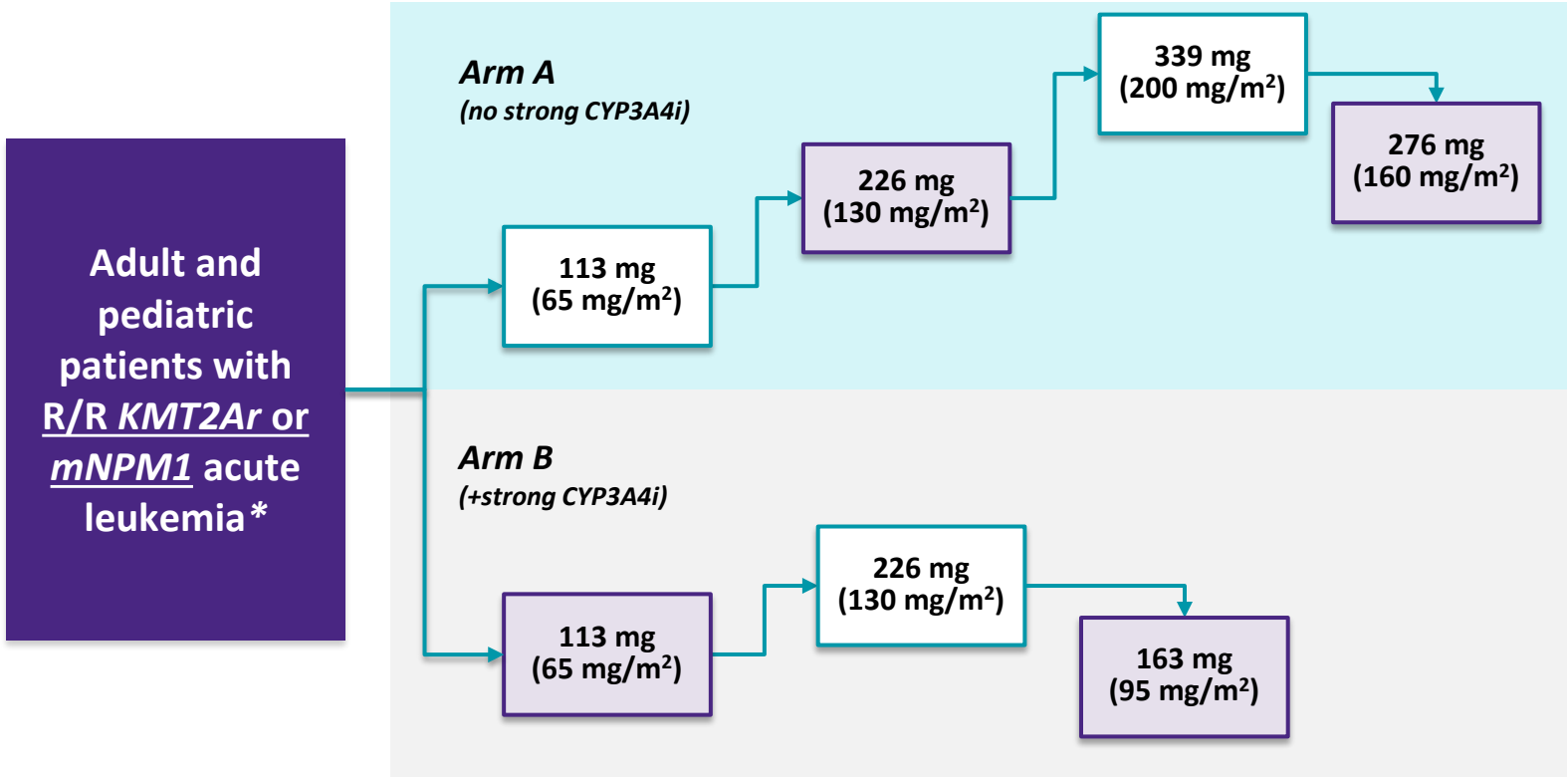


1. Spencer DH, et al. *Leukemia*. 2015;29(6):1279-1289; 2. Issa GC, et al. *Leukemia*. 2021;35:2482–2495; 3. Krivtsov A, et al. *Cancer Cell*. 2019;36(6):660-673.

AUGMENT-101: Phase 1 study design

Treatment

- Revumenib oral, q12h continuous dosing, 28-day cycle
- Accelerated titration into a rolling 6 design



Focus of this abstract:

- **12 patients in remission who proceeded to transplant**
- **3 patients who received revumenib maintenance post-transplant as compassionate use**

*Protocol originally allowed any R/R leukemia regardless of genotype but was amended to *KMT2Ar* or *mNPM1* patients only.
A majority of patients (n=60; 88%) were *KMT2Ar* or *mNPM1* and evaluable as the efficacy population.
q12h, every 12 hours; R/R, relapsed or refractory.

AUGMENT-101 Phase 1 Update
Abstract #63, Issa GC, et al.

12 patients proceeded to HSCT after treatment with revumenib

Patient Disposition	Safety Population N=68
Treatment Ongoing, n (%)	**2 (3)**
Discontinued Treatment, n (%)	**66 (97)**
Progressive disease/No response	39 (57)
Transplant	12 (18)
Adverse event (all unrelated)	7 (10)
Withdrew consent	3 (4)
Other*	3 (4)
Physician decision	2 (3)

AUGMENT-101 Phase 1 Update
Abstract #63, Issa GC, et al.

Efficacy Population:
***KMT2Ar* or m*NPM1* (n=60)**
ORR = 53%
CR/CRh = 18 (30%); MRD-neg 78%

Post-transplant:
- 9 remission
- 2 relapse
- 1 death

3 patients went on to receive revumenib as maintenance therapy
- 1 after HSCT
- 1 after nonmyeloablative stem cell boost
- 1 after subsequent therapy and a 3rd HSCT

*Other: death (not related to treatment), n=2; donor lymphocyte infusion, n=1
CR, complete remission; CRh, complete remission with partial hematologic recovery; HSCT, hematopoietic stem cell transplant.

Data cutoff: 31 March 2022

Baseline characteristics

Baseline Characteristics	Transplant Population N=12
Median age, years (range)	35 (3, 66)
Female, n (%)	12 (100)
Leukemia type, n (%)	
AML	11 (92)
ALL	1 (8)
Median prior therapies (range)	3 (1, 7)
≥1 Stem cell transplant, n (%)	7 (58)
Venetoclax, n (%)	4 (33)

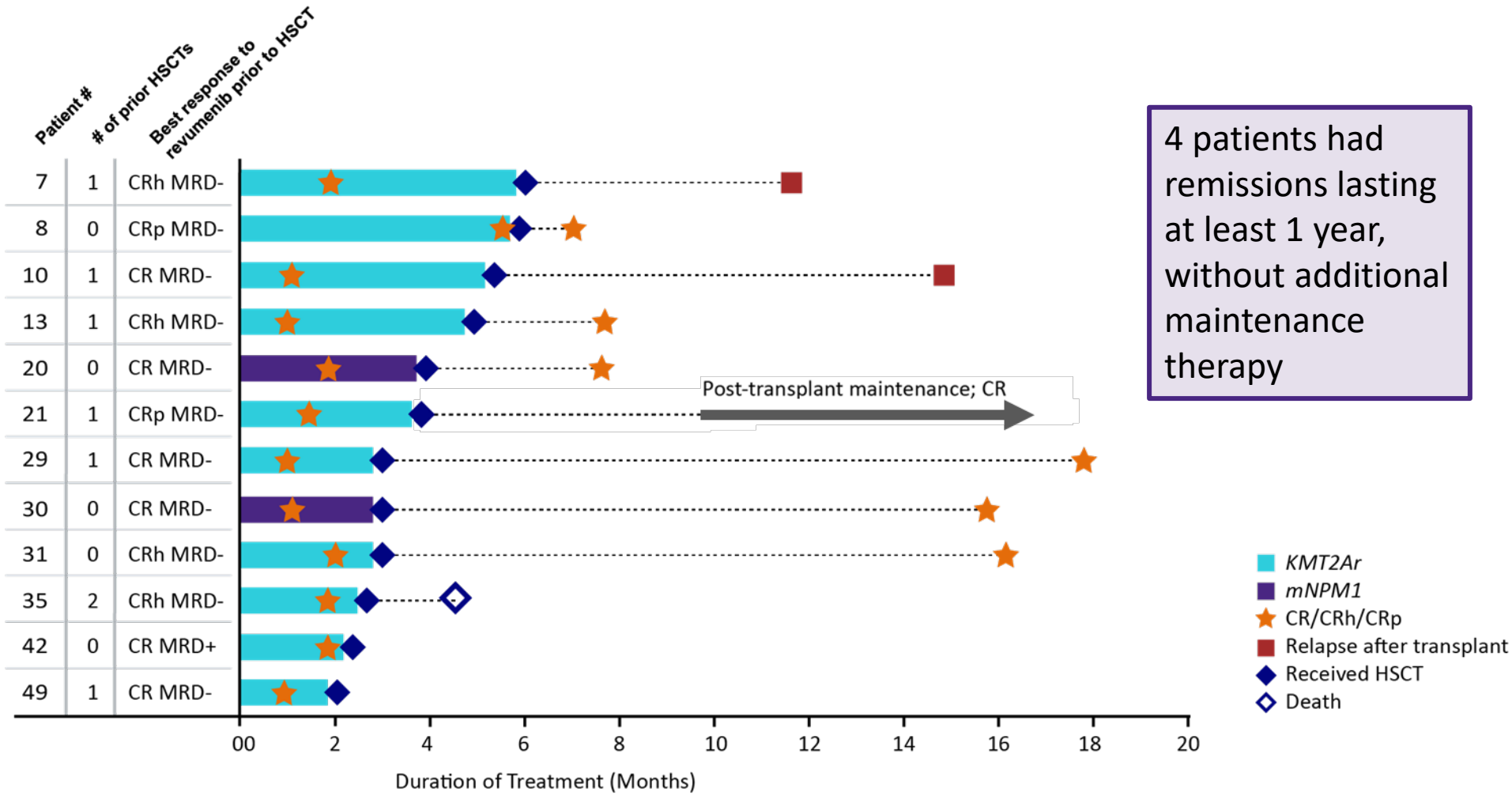
Baseline Characteristics	Transplant Population N=12
***KMT2Ar*, n (%)**	10 (83)
t(9;11)	2 (17)
t(11;19)	5 (42)
t(11;17)	2 (17)
Not specified	1 (8)
***mNPM1*, n (%)**	2 (17)
Co-occurring mutations*, n (%)	
FLT3	1 (9)
RAS	2 (14)
IDH1	1 (13)
DNM3Ta	1 (13)

*In patients for whom co-occurring mutation data were available.

Data cutoff: 31 March 2022

Duration of revumenib treatment and response status

- 38% of responders in AUGMENT-101 proceeded to transplant
- Patients with CR, CRh, and CRp after revumenib monotherapy went on to receive HSCT
- 11 of the 12 patients were MRD-negative prior to transplant



4 patients had remissions lasting at least 1 year, without additional maintenance therapy

CR, complete remission; CRh, complete remission with partial hematologic recovery; CRp, complete remission with incomplete platelet recovery; MRD, measurable residual disease.

Data cutoff: 31 March 2022

Conclusions: Transplant Experience

- Revumenib results in deep responses in heavily pre-treated R/R *KMT2Ar* and *mNPM1* acute leukemia
- Patients who attained CR, CRh, or CRp on revumenib monotherapy had durable remissions after transplant

Maintenance after transplant: Patient 21 update

Diagnosed

- **40 yo F with *KMT2Ar* AML with *FLT3* TKD co-mutation**
- 3 prior lines of therapy including 7+3+midostaurin and HSCT

Revumenib started
— 163 mg q12h with strong CYP3A4i (Arm B)

CRp MRD-negative on AUGMENT-101

Proceeded to a 2nd HSCT; post transplant received 2 cycles azacytidine

+ 6 months*

Revumenib maintenance started on single patient protocol
— 163 mg q12h with strong CYP3A4i

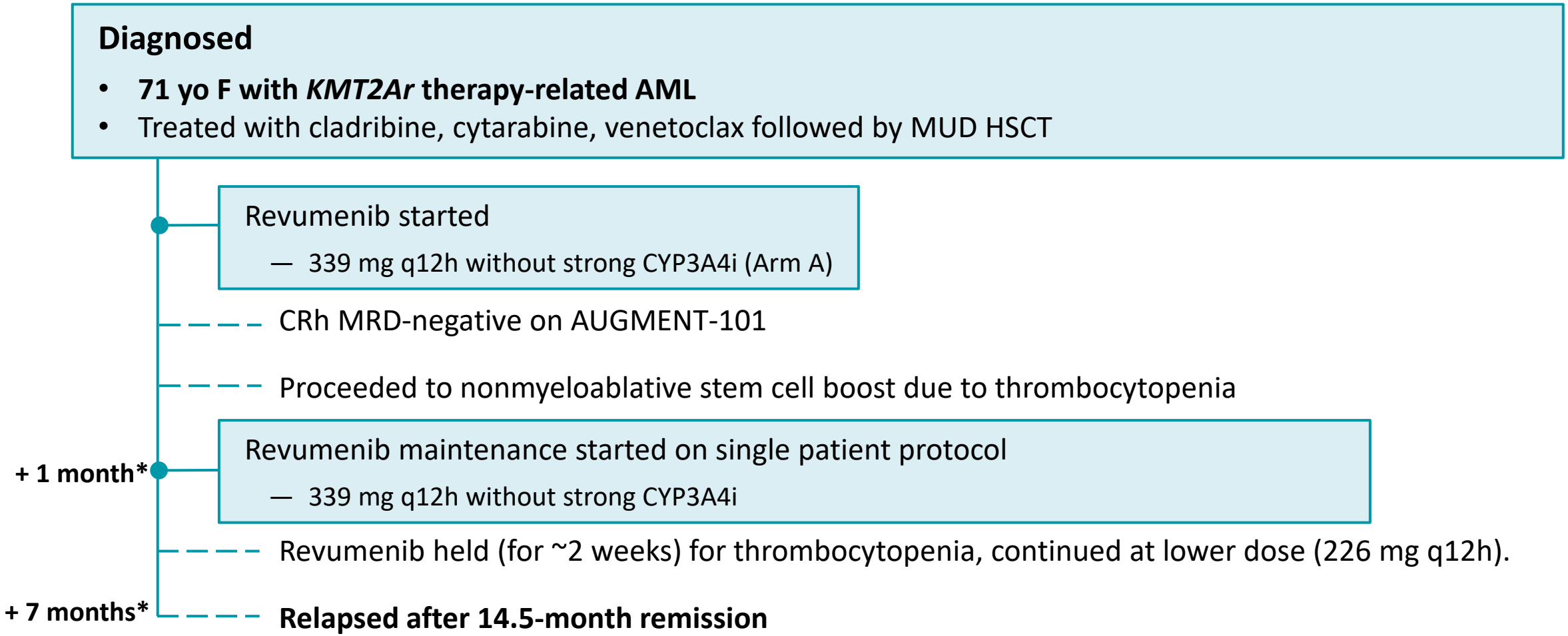
Revumenib held twice (for ~1 month each) for thrombocytopenia, continued at lower dose (113 mg q12h). Platelets recovered to >100K by ~6 months post-transplant

+ 12 months*

MRD-negative by flow 1-year post-transplant

*Follow-up after transplant following response on AUGMENT-101.

Maintenance after stem cell boost



*Follow-up after transplant following response on AUGMENT-101.
MUD, matched unrelated donor.

Conclusions: Post-Transplant Maintenance

- Revumenib maintenance after transplant appears feasible; ongoing studies with revumenib include the option to continue study drug post-transplant
- The safety profile is clinically manageable

AUGMENT-101 Study Update:

- Patients treated in AUGMENT-101 who achieve a response and proceed to HSCT may resume revumenib after HSCT if the following conditions are met:
  - Between 30 to 180 days post HSCT and still in CRc
  - ANC ≥500/mm^3 and platelets ≥50,000/mm^3 without transfusions
  - No acute or chronic GVHD requiring systemic immunosuppression, but may continue prophylaxis with agents including calcineurin inhibitors

GVHD, graft versus host disease.

Active revumenib trials and role of maintenance

Frontline

***mNPM1* or *KMT2Ar* AML**

Beat AML (LLS):
- Revumenib + venetoclax/azacitidine
- Patients not eligible for intensive chemotherapy

R/R

***mNPM1* or *KMT2Ar* AML/ALL**

Chemotherapy combinations (AUGMENT-102):
- AML: Revumenib + FLA x 2
- ALL: Revumenib + 4-drug regimen

All-oral combination (SAVE; MDACC):
- Revumenib (SNDX-5613), ASTX727, venetoclax

AME:
- Radiolabeled revumenib

Maintenance

Post-transplant maintenance incorporated into :
- AUGMENT-101
- AUGMENT-102

Early Intervention: MRD

INTERCEPT (ALLG):
- Revumenib monotherapy
- m*NPM1* or *KMT2Ar* AML patients with MRD^{pos} disease

Breakthrough Cancer (MDACC, DFCI, JH, MSKCC, MIT):
- Revumenib + venetoclax
- m*NPM1, KMT2Ar, or NUP98r* AML patients with MRD^{pos} disease

Acknowledgements

We thank all AUGMENT-101 study patients, their families, and caregivers for participating in this trial.

Principal Investigators, staff, and sites where the trial was conducted:

Memorial Sloan Kettering Cancer Center
Eytan Stein
Kait Tkachuk

Dana-Farber Cancer Institute
Richard Stone
Emilie Baxter

Emory University School of Medicine
Martha Arellano
Temitayo Obajuluwa

University of Chicago
Michael Thirman
Adriana Koziol

Florida Cancer Specialists
Manish Patel
Terri Peterson

The University of Texas MD Anderson Cancer Center
Ghayas Issa
Branko Cuglievan
Allison Pike

Washington University School of Medicine
John DiPersio
Jennifer Reed

City of Hope
Ibrahim Aldoss
Manjyot Nanhwan

Montefiore Medical Center
Ioannis Mantzaris
David Loeb
Joel Victor

University of Iowa
David Dickens
Christopher Stamy

This research was sponsored by Syndax Pharmaceuticals, Inc.