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Reimagining Cancer Treatment

Syndax Investor Meeting
American Society of Hematology Annual Meeting
December 9, 2024

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Welcome and Introduction to Syndax

Steve Closter
Chief Commercial Officer, Syndax

Syndax: A commercial-stage oncology company with two first-in-class medicines with practice-changing and billion-dollar potential

Revuforj® (revumenib)

- First and only FDA-approved menin inhibitor
- Only targeted therapy for KMT2A translocations
- Launched in the U.S. in November 2024
- In development for mNPM1 AML and solid tumors

Three oral sessions and one poster at ASH 2024
highlighted the potential of Revuforj as both a monotherapy and in combination with SOC agents

Niktimvo™ (axatilimab-csfr)

- FDA approved in 3L chronic GVHD (cGVHD)
- U.S. launch, in partnership with Incyte, expected no later than early first quarter 2025
- In development for patients with newly diagnosed cGVHD, and IPF

One oral session and two posters at ASH 2024
highlighted Niktimvo's clinical profile and unique mechanism of action in cGVHD

mNPM1, mutant nucleophosmin 1; GVHD, graft-versus-host disease; IPF, idiopathic pulmonary fibrosis; SOC, standard of care

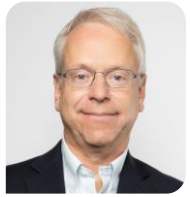
High interest in the first and only FDA-approved menin inhibitor at ASH 2024

Driving Revuforj awareness at ASH 2024:

- ✓ Branded booth
- ✓ Product theater
- ✓ Three oral sessions
- ✓ Robust HCP engagement

Today's guest speakers

Niktimvo™ (axatilimab-csfr)



Chronic GVHD AGAVE-201 Results & Ongoing MAXPIRe IPF Trial

Peter Ordentlich, Ph.D.
Chief Scientific Officer and Founder, Syndax

Revuforj® (revumenib)

Acute Leukemia Overview & R/R mNPM1 AUGMENT-101 Results

Eytan Stein, M.D
Chief, Leukemia Service, Memorial Sloan Kettering Cancer Center

R/R KMT2Ar AUGMENT-101 Results & SAVE Trial Results

Ghayas Issa, M.D.
Associate Professor of Leukemia, The University of Texas MD Anderson Cancer Center

BEAT AML Frontline Combination Trial Results

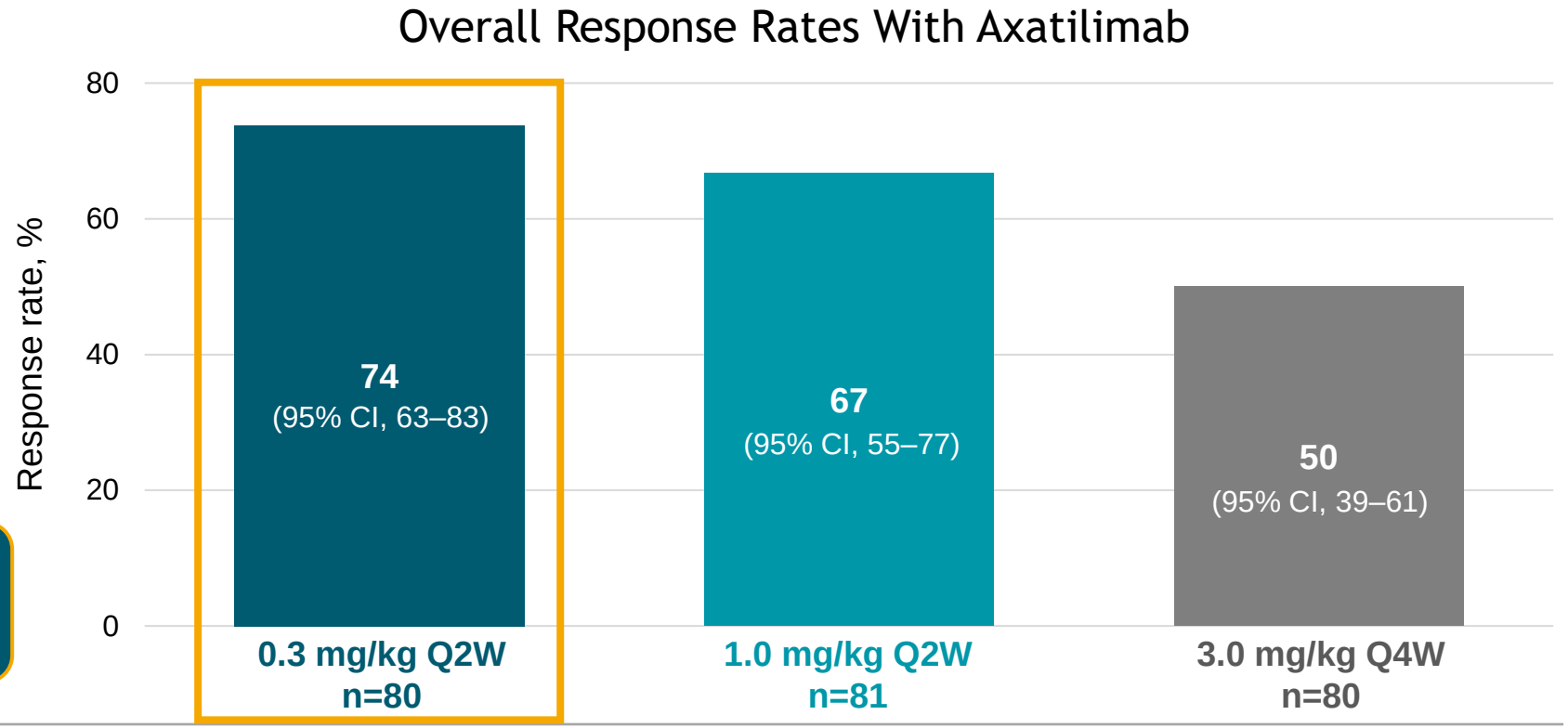
Joshua Zeidner, M.D.
Chief, Leukemia Research, University of North Carolina, Lineberger Comprehensive Cancer Center

Recent AGAVE-201 Trial Results & Ongoing MAXPIRe IPF Trial

Peter Ordentlich, Ph.D.
Chief Scientific Officer and Founder, Syndax

AGAVE-201 met the primary efficacy endpoint across all cohorts of cGVHD patients receiving axatilimab

0.3 mg/kg Q2W is now the FDA-approved dose of Niktimvo (axatilimab-csfr)



	0.3 mg/kg Q2W n=80	1.0 mg/kg Q2W n=81	3.0 mg/kg Q4W n=80
Time to response, median months (range)	1.7 (0.9–8.1)	1.9 (0.9–8.6)	1.4 (0.9–5.6)
Response maintained for ≥12 months, % (95% CI)	60 (43–74)	60 (43–74)	53 (30–71)

Q2W, every 2 weeks; Q4W, every 4 weeks.
Primary endpoint was overall response rate in the first 6 cycles as defined by NIH 2014 Consensus Criteria.

AGAVE-201 positive results observed in a heavily pretreated, late stage cGVHD population

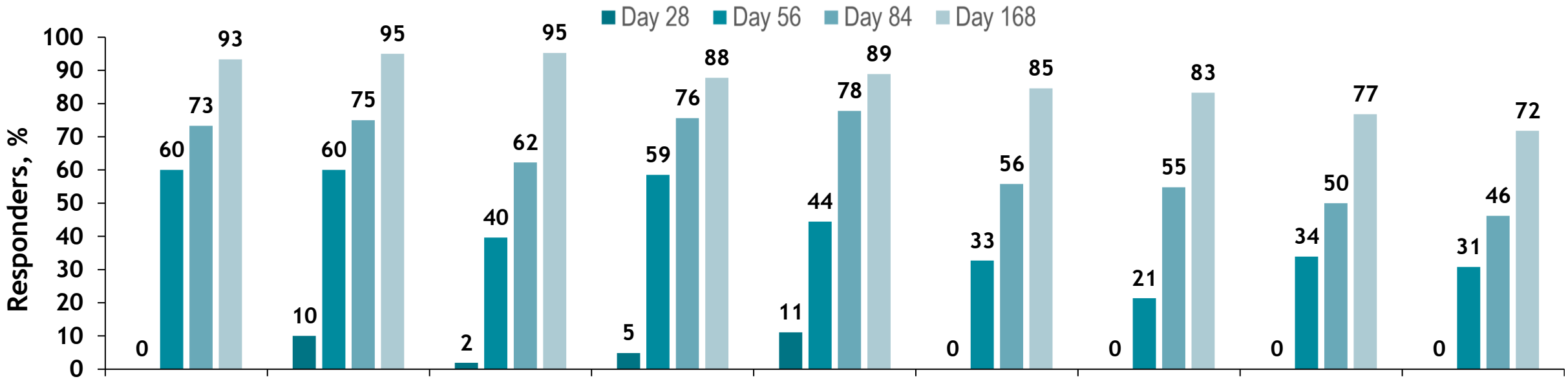
Population (ITT)	AGAVE-201 N=241
Age median (min, max), years	53 (7, 81)
Median time since cGVHD diagnosis	48 months
≥ 4 organs involved	54%
% Patients with lung manifestations	45%
% Patients with NIH severe cGVHD	80%
Median prior therapies	4
≥ 4 prior lines of treatment	65%
Prior ruxolitinib	74%
Prior ibrutinib	31%
Prior belumosudil	23%

AGAVE-201 study population differentiation vs belumosudil study population
Significantly longer time since diagnosis
More severe cGVHD
More exposure to prior therapies

Secondary analyses from AGAVE-201 highlight the potential for rapid onset of clinical activity with axatilimab in cGVHD patients

Data presented at ASH 2024 (abstract #98)

Median times to organ-specific responses ranged from 1.0-3.2 months across organs



	Lower GI (n=15)	Upper GI (n=20)	Joints/fascia (n=106)	Esophagus (n=41)	Liver (n=9)	Mouth (n=52)	Lungs (n=42)	Eyes (n=56)	Skin (n=39)
TTR, months									
Median	1.2	1.0	1.9	1.1	1.9	2.1	2.6	2.7	3.2
Range	1.0–10.5	0.9–6.0	0.9–9.5	0.9–10.5	0.9–6.1	1.0–9.6	1.0–14.8	1.0–9.1	1.0–14.4

Additional data presented at ASH show patient-reported symptom improvements were more rapid than the respective organ-specific NIH response in the lungs, eyes, mouth and skin

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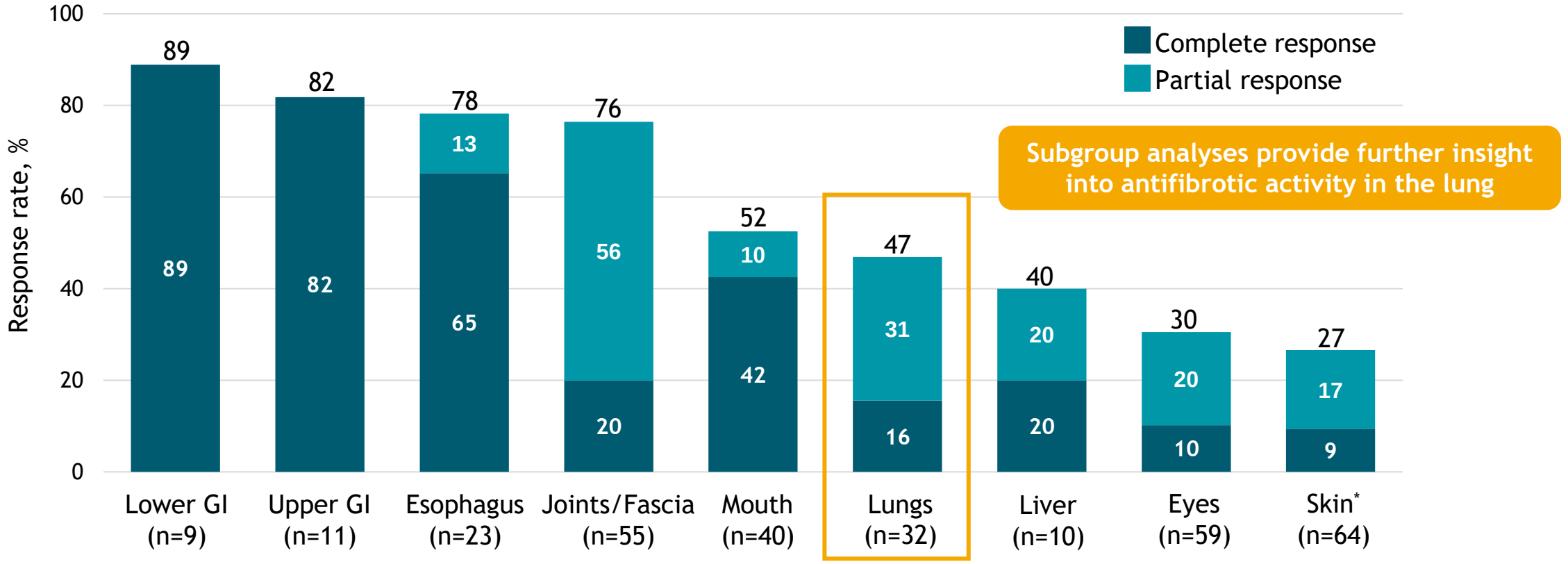
Data from all doses tested in the AGAVE-201 trial (0.3 mg/kg Q2W; 1 mg/kg Q2W; 3 mg/kg Q4W).
TTR, time to response

Niktimvo showed robust responses across all organs studied in the heavily pre-treated population enrolled in AGAVE-201

AGAVE-201

Niktimvo 0.3 mg/kg every two weeks



Subgroup analyses provide further insight into antifibrotic activity in the lung

Responses were notable in fibrosis-dominated organs, including esophagus (78%), joints and fascia (76%), lung (47%), and skin (27%)

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*Due to rounding, complete response and partial response numbers may not add up to total response rate. GI, gastrointestinal.

Antifibrotic activity of axatilimab highlighted in AGAVE-201 subgroup analysis of patients with cGVHD related bronchiolitis obliterans syndrome (BOS)

Data presented at ERS 2024

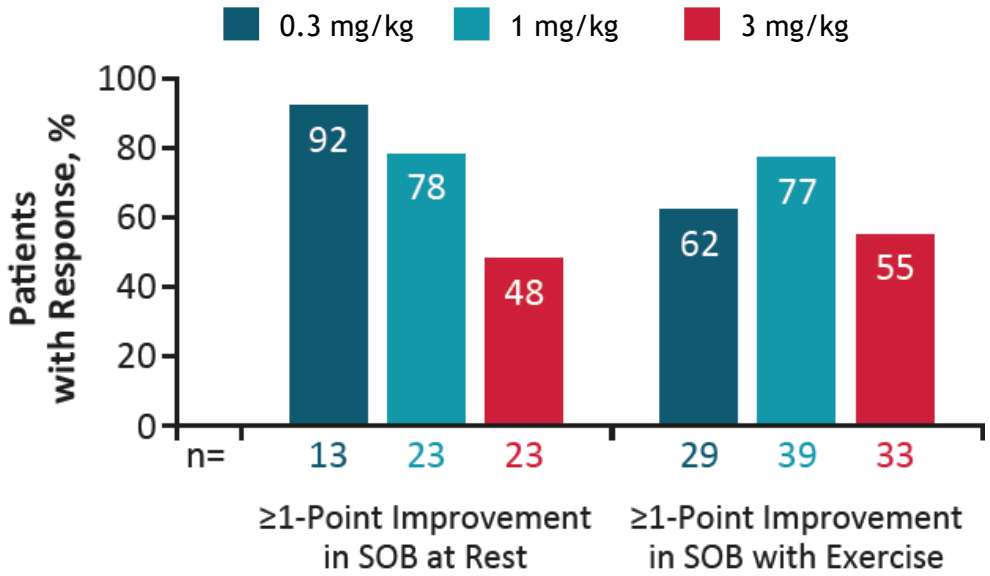
Rapid and robust BOS response rates despite inclusion of patients with severe BOS

Patients with BOS in AGAVE-201	0.3 mg/kg (n=32)	1mg/kg (n=41)	3 mg/kg (n=35)
Characteristics			
Number of prior systemic cGVHD therapies, median (range)	4 (2–10)	4 (2–10)	4 (2–12)
Lung involvement at baseline, n (%)	32 (100)	41 (100)	35 (100)
FEV_1 ≤39%	14 (47)	15 (42)	7 (26)
NIH cGVHD lung symptom score of 3	8 (25)	10 (26)	8 (23)
Efficacy			
BOS response, n (%)	**15 (47)**	**14 (34)**	**13 (37)**

Median time to first BOS response was <3 months

Clinically meaningful improvements in symptoms of shortness of breath (SOB) at rest or with exertion

Patient reported improvements in SOB based on mLSS



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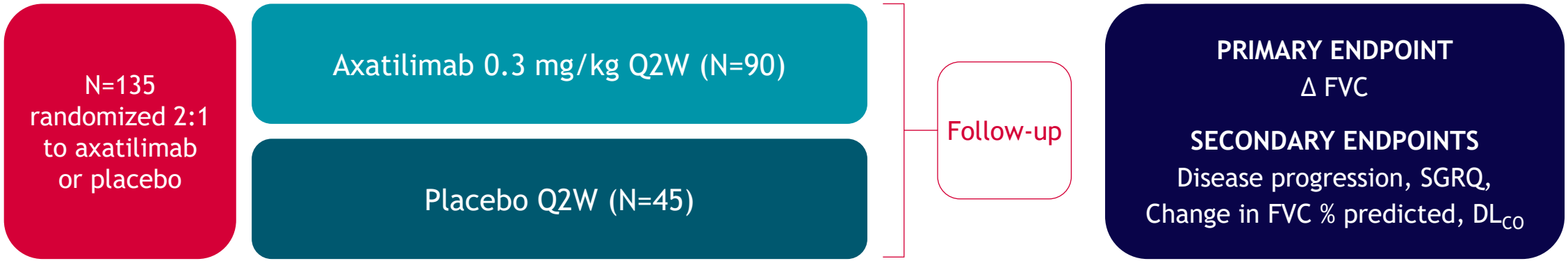
FEV_1, forced expiratory volume in 1 second; mLSS, modified Lee Symptom Score

MAXPIRe Phase 2 trial of axatilimab in IPF is now enrolling patients with topline data anticipated in 2026

A 26-Week, Randomized, Double-Blind, Placebo-Controlled, Multi-Center Study to Evaluate the Efficacy, Safety, and Tolerability of Axatilimab in Subjects with Idiopathic Pulmonary Fibrosis (IPF)



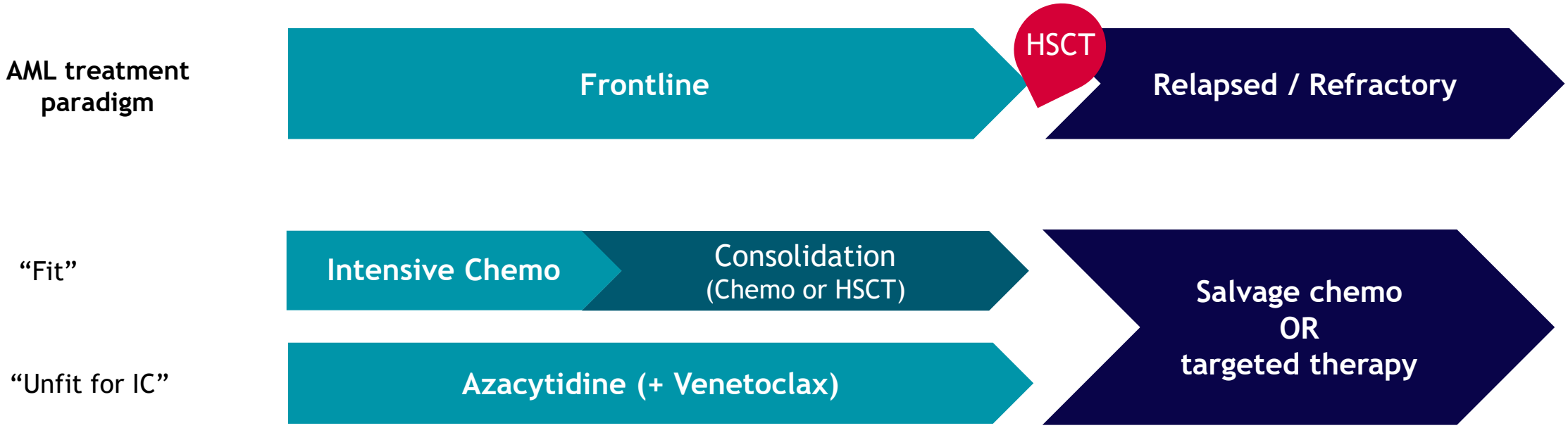
Axatilimab's advancement into IPF supported by:

- Published preclinical and clinical rationale for CSF-1 pathway inhibition in IPF
- Clinical results from chronic GVHD trials showing the positive impact on lung fibrosis

Acute Leukemia Overview

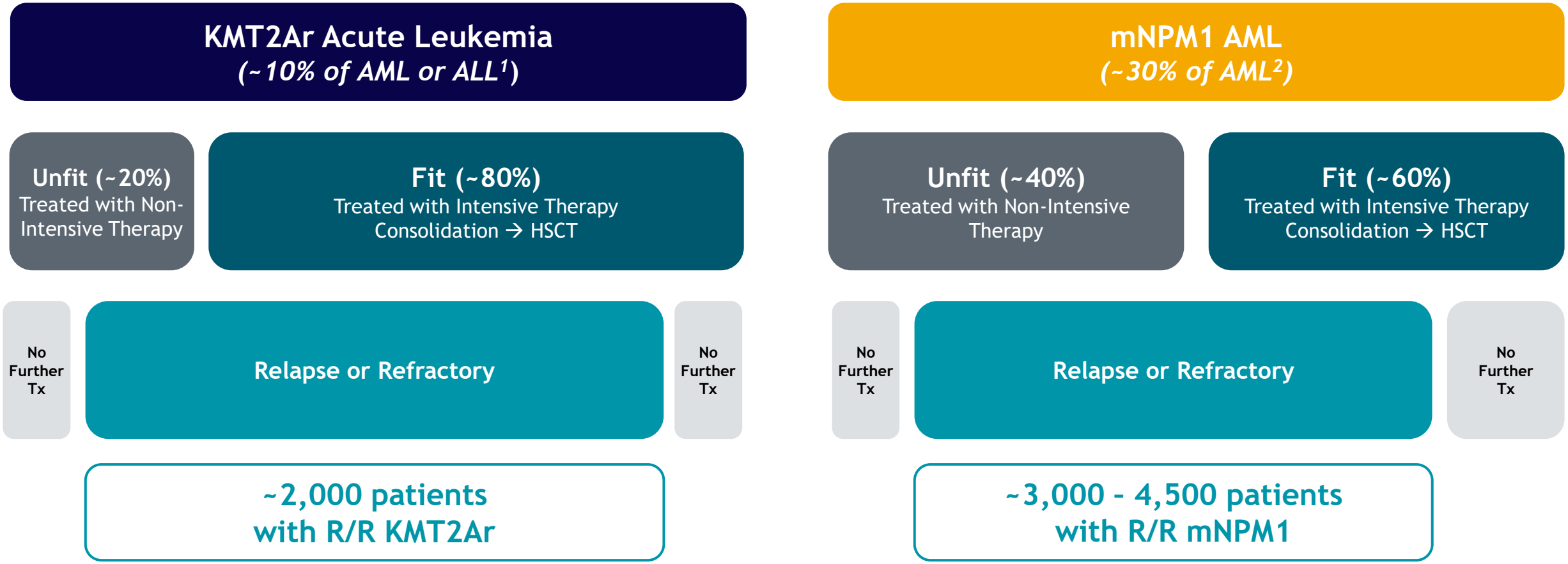
Eytan Stein, M.D.
Chief, Leukemia Service
Memorial Sloan Kettering Cancer Center

Acute myeloid leukemia (AML) treatment paradigm



Despite recent advances, most patients will be refractory to their initial therapy or relapse

Menin inhibition has a near-term potential to impact a significant number of patients with R/R KMT2Ar acute leukemia or mNPM1 AML



1. Issa, GC, et al. Therapeutic implications of menin inhibition in acute leukemias. Leukemia 35, 2482–2495 (2021); 2. Issa G., et al. Clinical outcomes associated with NPM1 mutations in patients with relapsed or refractory AML. Blood Adv. 2023; 7(6):933-942. 3. Data on file for other estimates; Tx, treatment.

Treatment response criteria in AML: Tumor clearance equivalent across MLFS and CRc

Response	Tumor	Platelets recovered	Neutrophils recovered	ORR	CRc	CR/CRh
CR	< 5%	Yes	Yes	✓	✓	✓
CRh	< 5%	Half normal levels	Half normal levels	✓	✓	✓
CRp	< 5%	No	Yes	✓	✓	
CRi	< 5%	Either has recovered		✓	✓	
MLFS	< 5%	Neither has recovered		✓		
PR	5-25% and a ≥50% reduction	Yes	Yes	✓		
No response	> 5%	No	No			
Non-evaluable	Lack an adequate BM response evaluation					

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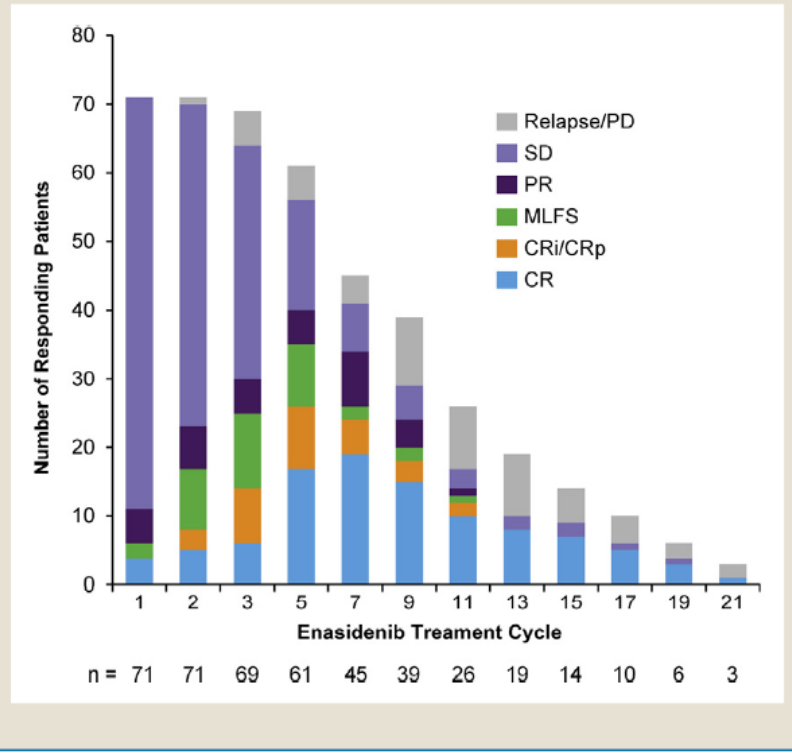
2022 ELN recommendations for the management of AML in adults (aml-hub.com); ORR, Overall response rate; CRc, Composite complete remission; ANC, absolute neutrophil count; BM, bone marrow; CR, complete remission; CRh, CR with partial hematologic recovery; CRi, CR with incomplete hematologic recovery; MLFS, morphologic leukemia-free state; PR, partial remission.

Mutation testing, treatment decisions and response cadence can vary with targeted therapies

Hematologic response curve example – Enasidenib in patients with R/R AML



Time on treatment (TTR + DOR)

Diagnosis & testing

Time to response (TTR)

Varies by mutation

Duration of response (DOR)

Impacted by:

Depth of response
- Morphologic CR (<5% blasts)
- MRD negative CR

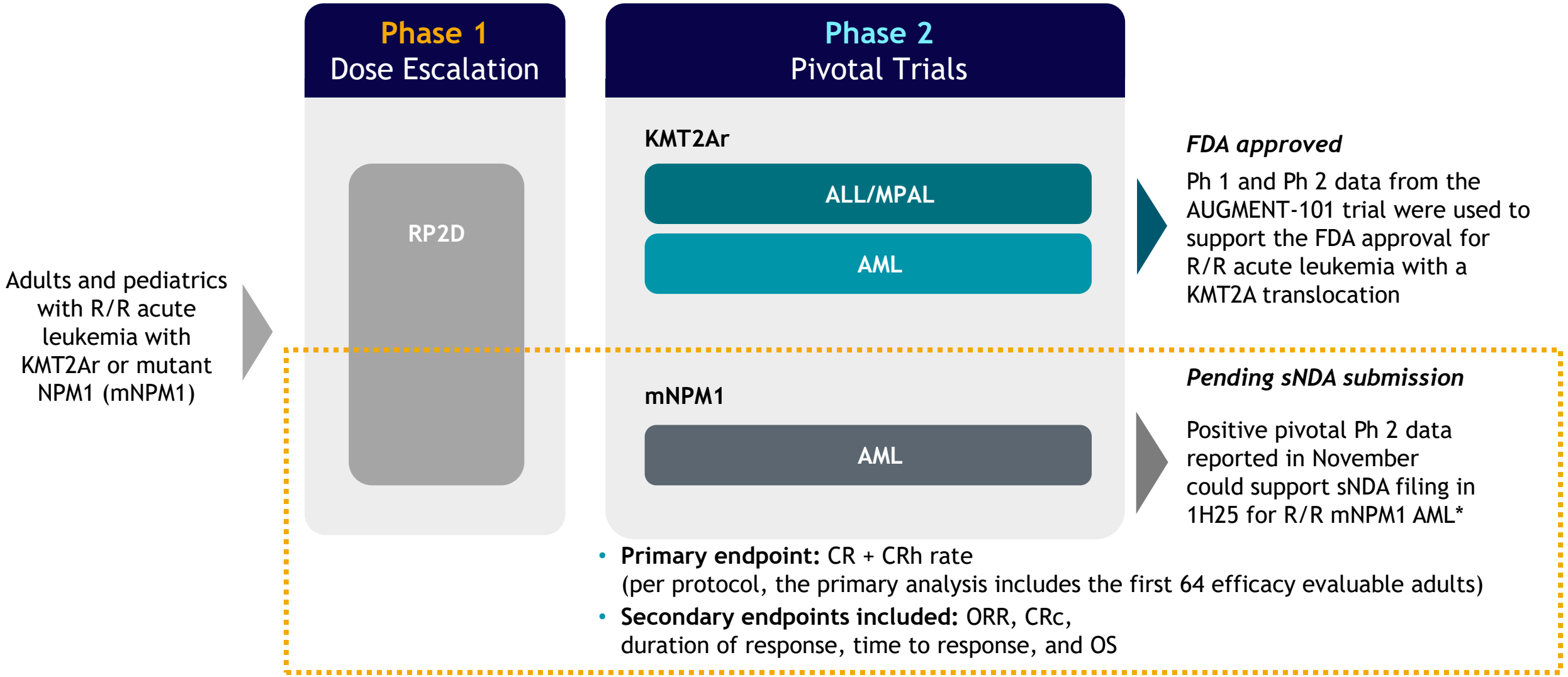
Ability to receive transplant
- Is maintenance a good option?

Figure 1. Stein, E. et al. Response kinetics and clinical benefits of nonintensive AML therapies in the absence of morphologic response. Clinical Lymphoma, Myeloma and Leukemia vol. 20, e66-75 (2019).

AUGMENT-101 R/R mNPM1 AML Trial Results

Eytan Stein, M.D.
Chief, Leukemia Service
Memorial Sloan Kettering Cancer Center

AUGMENT-101: A Phase 1/2 trial of revumenib monotherapy in R/R mNPM1 and KMT2Ar acute leukemia



*The use of revumenib in R/R mNPM1 AML is still under investigation and has not been approved by the FDA.
ORR, overall response rate; CR, Complete remission; CRh, Complete remission with partial hematological recovery; CRc, Composite complete remission; OS, overall survival; R/R, relapsed or refractory

AUGMENT-101 baseline characteristics in Phase 2 cohort of patients with R/R mNPM1 AML

Baseline Characteristics	Protocol-Defined Adult Efficacy Population N = 64	Safety Population N = 84
Age, years, median (range)	65 (19, 84)	63 (11, 84)
≥ 18 to <65, n (%)	31 (48)	42 (50)
≥ 65, n (%)	33 (52)	41 (49)
Female, n (%)	38 (59)	50 (60)
Baseline co-mutations of interest, n (%)		
FLT3-ITD	22 (34)	26 (31)
FLT3-TKD	4 (6)	6 (7)
IDH1	8 (13)	11 (13)
IDH2	8 (13)	10 (12)
Disease Status at Baseline, n (%)		
Primary refractory (persistent leukemia following induction chemotherapy)	5 (8)	7 (8)
Refractory relapse (unresponsive to most recent salvage treatment)	35 (55)	41 (49)
Prior lines of therapy, median (range)	2 (1, 7)	2 (1, 7)
≥3 lines, n (%)	23 (36)	29 (35)
Prior venetoclax, n (%)	48 (75)	62 (74)
Prior HSCT, n (%)	14 (22)	20 (24)

Safety population includes 20 additional patients who were enrolled after the first 64 efficacy evaluable adults

Patients were **significantly older** than R/R KMT2Ar cohort

75% had prior venetoclax exposure in efficacy population

36% received revumenib in the 4L or later in efficacy population

Revumenib demonstrated compelling efficacy in R/R mNPM1 AML patients in Ph 2 portion of AUGMENT-101

Best Response, n (%)	Protocol-Defined Adult Efficacy Population N = 64
CR/CRh *(95% CI); one-sided p-value*	15 (23%) *(14%, 36%); 0.0014*
CR	12 (19%)
CRh	3 (5%)
MRD^{neg} CR/CRh*	**9/14 (64%)**
Median duration of CR/CRh	4.7 months
Overall Response Rate (ORR)	**30 (47%)**
Composite complete remission (CRc)	19 (30%)
MRD^{neg} CRc*	**10/17 (59%)**
Proceeded to HSCT after response	5/30 (17%)
Resumed revumenib post-HSCT	3/5 (60%)

ORR = CR+CRh+CRp+CRi+MLFS+PR; CRc = CR+CRh+CRp+CRi; * Not all patients had MRD status reported.
Note: Totals may not sum due to rounding.

Results in protocol-defined Ph 2 efficacy population:

~50% of patients achieved an overall response in heavily pre-treated population

Deep, meaningfully durable CR/CRh responses

Consistent with R/R KMT2Ar acute leukemia cohort

Post-hoc analysis of larger Ph 2 R/R mNPM1 AML population highlights consistency of revumenib's profile

Best Response, n (%)	Post-Hoc Efficacy Evaluable Adult + Pediatric Population[1] N=77
CR/CRh *(95% CI)*	20 (26%) *(17%, 37%)*
CR	16 (21%)
CRh	4 (5%)
MRD^{neg} CR/CRh*	**12/19 (63%)**
Median duration of CR/CRh	4.7 months
Overall Response Rate (ORR)	**37 (48%)**
Composite complete remission (CRc)	25 (32%)
MRD^{neg} CRc*	**13/23 (57%)**

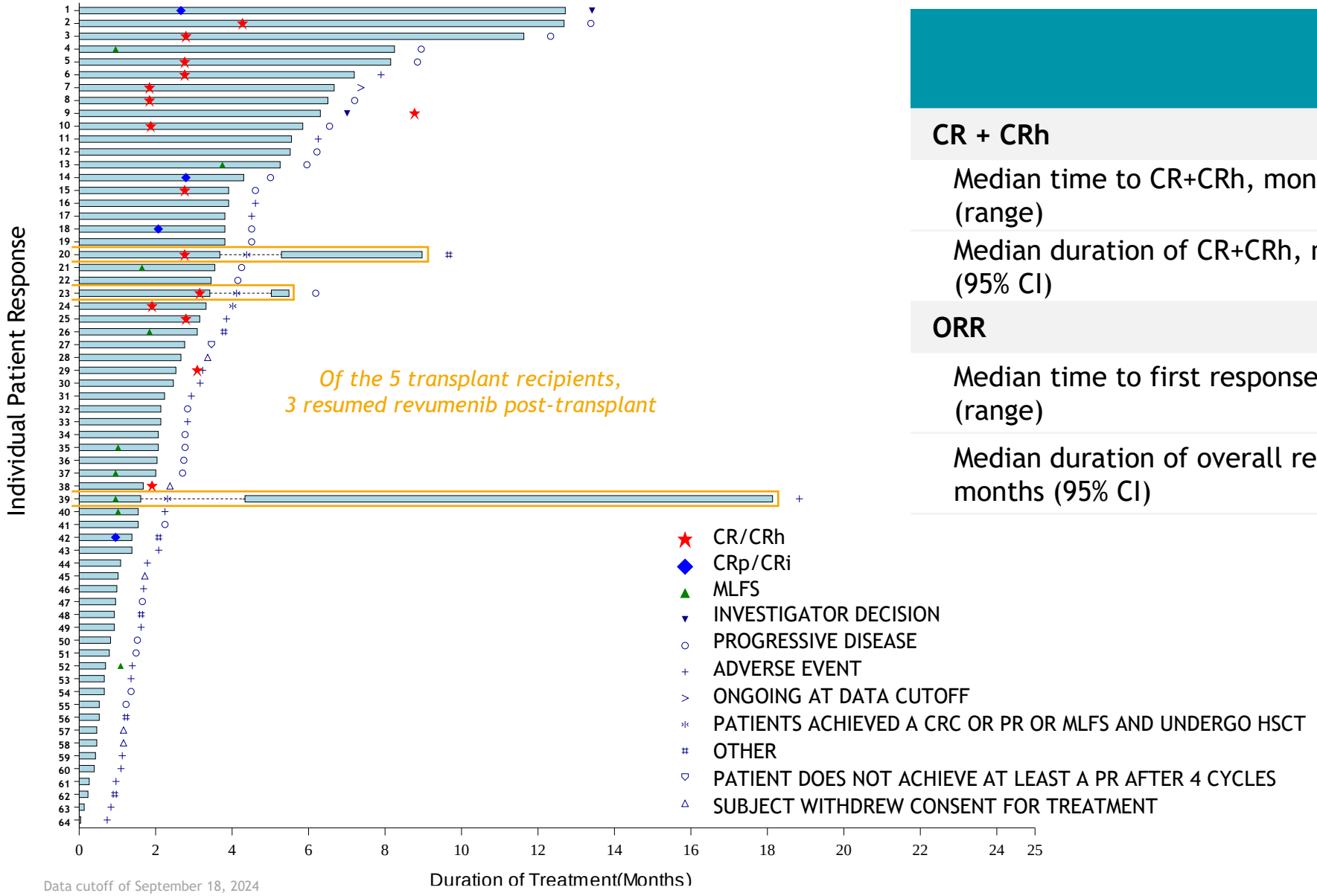
ORR = CR+CRh+CRp+CRi+MLFS+PR; CRc = CR+CRh+CRp+CRi; * Not all patients had MRD status reported.

77 of 84 enrolled patients met the efficacy evaluable criteria (i.e., blast counts >5% measured within 28 days prior to treatment and centrally confirmed mNPM1)

Results from larger population are **consistent with the protocol-defined Ph 2 efficacy analysis**

Data cutoff of September 18, 2024; 1. Post-hoc efficacy evaluable population consists of all Phase 2 R/R mNPM1 AML patients with central confirmation of NPM1 mutation and blast counts >5% measured within 28 days prior to treatment. Of the 84 patients in the Phase 2 R/R mNPM1 safety population, 7 patients did not meet the efficacy evaluable criteria and were therefore excluded from the post-hoc efficacy analysis.

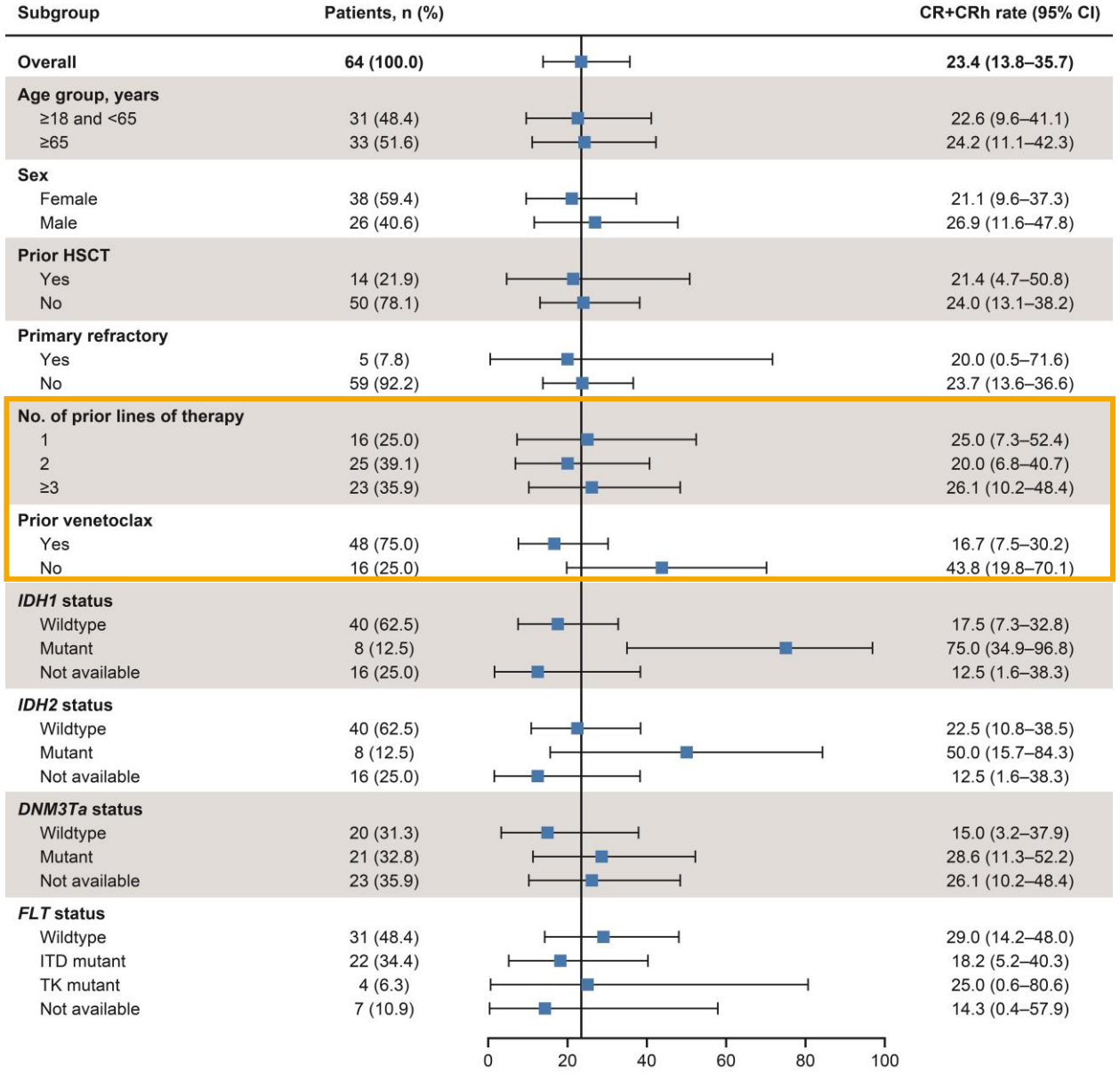
Responses were rapid and meaningfully durable in R/R mNPM1 AML patients in Ph 2 portion of AUGMENT-101



	Protocol-Defined Adult Efficacy Population N = 64
CR + CRh	**15 (23%)**
Median time to CR+CRh, months (range)	2.76 (1.8-8.8)
Median duration of CR+CRh, months (95% CI)	4.7 (1.2-8.2)
ORR	**30 (47%)**
Median time to first response, months (range)	1.84 (0.9-4.6)
Median duration of overall response, months (95% CI)	4.4 (1.2-5.6)

Data cutoff of September 18, 2024

Responses were observed across all major subgroups of R/R mNPM1 AML patients in Ph 2 portion of AUGMENT-101



Subgroup	Patients, n (%)	CR+CRh rate (95% CI)
Overall	**64 (100.0)**	**23.4 (13.8–35.7)**
Age group, years		
≥18 and <65	31 (48.4)	22.6 (9.6–41.1)
≥65	33 (51.6)	24.2 (11.1–42.3)
Sex		
Female	38 (59.4)	21.1 (9.6–37.3)
Male	26 (40.6)	26.9 (11.6–47.8)
Prior HSCT		
Yes	14 (21.9)	21.4 (4.7–50.8)
No	50 (78.1)	24.0 (13.1–38.2)
Primary refractory		
Yes	5 (7.8)	20.0 (0.5–71.6)
No	59 (92.2)	23.7 (13.6–36.6)
No. of prior lines of therapy		
1	16 (25.0)	25.0 (7.3–52.4)
2	25 (39.1)	20.0 (6.8–40.7)
≥3	23 (35.9)	26.1 (10.2–48.4)
Prior venetoclax		
Yes	48 (75.0)	16.7 (7.5–30.2)
No	16 (25.0)	43.8 (19.8–70.1)
***IDH1* status**		
Wildtype	40 (62.5)	17.5 (7.3–32.8)
Mutant	8 (12.5)	75.0 (34.9–96.8)
Not available	16 (25.0)	12.5 (1.6–38.3)
***IDH2* status**		
Wildtype	40 (62.5)	22.5 (10.8–38.5)
Mutant	8 (12.5)	50.0 (15.7–84.3)
Not available	16 (25.0)	12.5 (1.6–38.3)
***DNM3Ta* status**		
Wildtype	20 (31.3)	15.0 (3.2–37.9)
Mutant	21 (32.8)	28.6 (11.3–52.2)
Not available	23 (35.9)	26.1 (10.2–48.4)
***FLT* status**		
Wildtype	31 (48.4)	29.0 (14.2–48.0)
ITD mutant	22 (34.4)	18.2 (5.2–40.3)
TK mutant	4 (6.3)	25.0 (0.6–80.6)
Not available	7 (10.9)	14.3 (0.4–57.9)

Importantly, responses were seen in:

- Heavily pretreated patients
- Patients with prior venetoclax exposure

Safety results from Phase 2 R/R mNPM1 AML cohort in the AUGMENT-101 trial support favorable revumenib safety and tolerability profile

Grade ≥3 Treatment-Related Adverse Events [TRAEs] (≥5% of patients)	Safety Population N = 84
Patients with Grade ≥3 TRAE	50 (60%)
Electrocardiogram QT prolonged	18 (21%) *(Gr 3: 19% | Gr 4: 2%)*
Anemia	12 (14%)
Febrile neutropenia	11 (13%)
Differentiation syndrome	11 (13%) *(Gr 3: 11% | Gr 4: 2%)*
Platelet count decreased	9 (11%)
Thrombocytopenia	8 (10%)
White blood cell count decreased	7 (8%)
Neutrophil count decreased	6 (7%)

- Safety results in this older, heavily pre-treated population were consistent with previously reported data
- Low rate of treatment-related discontinuations (5%)
- Most common adverse events observed are largely characteristic of symptoms experienced by patients undergoing treatment for AML

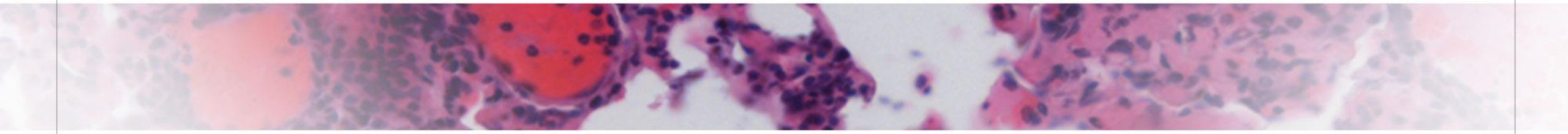
* Data cutoff of September 18, 2024

Latest AUGMENT-101 R/R KMT2Ar and SAVE Trial Results

Ghayas Issa, M.D.
Associate Professor of Leukemia
The University of Texas MD Anderson Cancer Center

American Society *of* Hematology

Helping hematologists conquer blood diseases worldwide



Updated Results and Longer Follow-Up From the AUGMENT-101 Phase 2 Study of Revumenib in All Patients With Relapsed or Refractory (R/R) *KMT2Ar* Acute Leukemia

Ibrahim Aldoss, Ghayas C. Issa, James S. Blachly, Michael J. Thirman, Gabriel N. Mannis, Martha L. Arellano, John F. DiPersio, Elie Traer, C. Michel Zwaan, Neerav Shukla, Branko Cuglievan, Carolyn S. Grove, Matthew Greenwood, Christine M. McMahon, Alexander E. Perl, Richard M. Stone, Cristina Papayannidis, David S. Dickens, Maël Heiblig, Andrius Žučenka, Pau Montesinos, Ioannis Mantzaris, Tibor Kovacsovics, Paul J. Shami, Li Yu, Rebecca G. Bagley, Nicole McNeer, Eytan M. Stein

Presented at the 66th ASH Annual Meeting & Exposition; December 7–10, 2024; San Diego, CA. Oral abstract 211.

Treatments Are Needed for *KMT2Ar* Acute Leukemia

- Many patients experience relapse after chemotherapy and/or HSCT[1]
- In adults, remission rates after relapse (CR, 5%) and median OS (2.4 months) after ≥2 salvage therapies remain low[1]
- Outcomes in pediatric patients after relapse are also poor[2]

OS in Adult Patients With R/R *KMT2Ar* AML After ≥3L Therapy

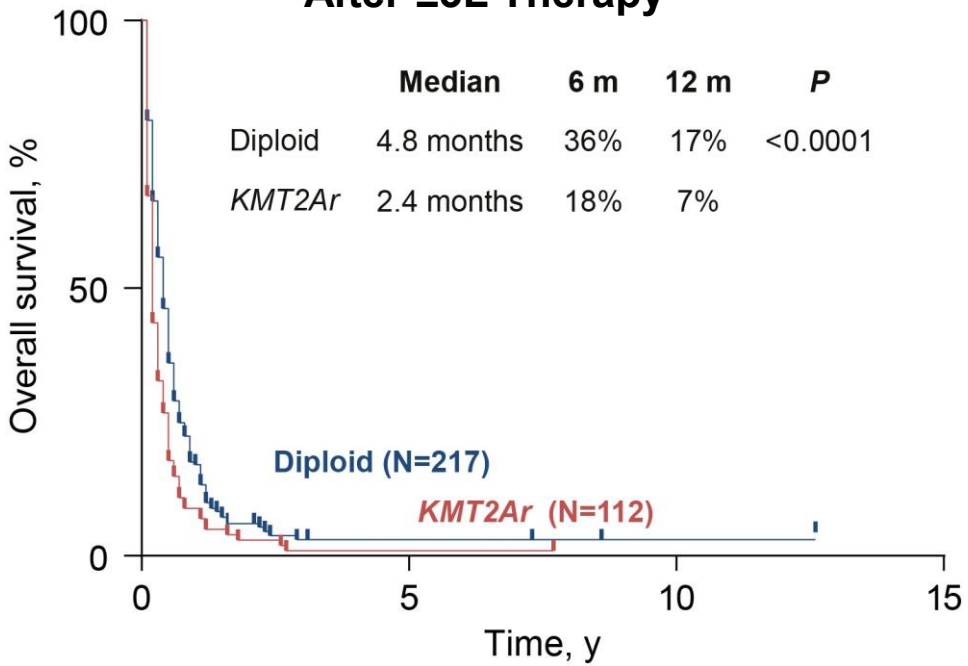


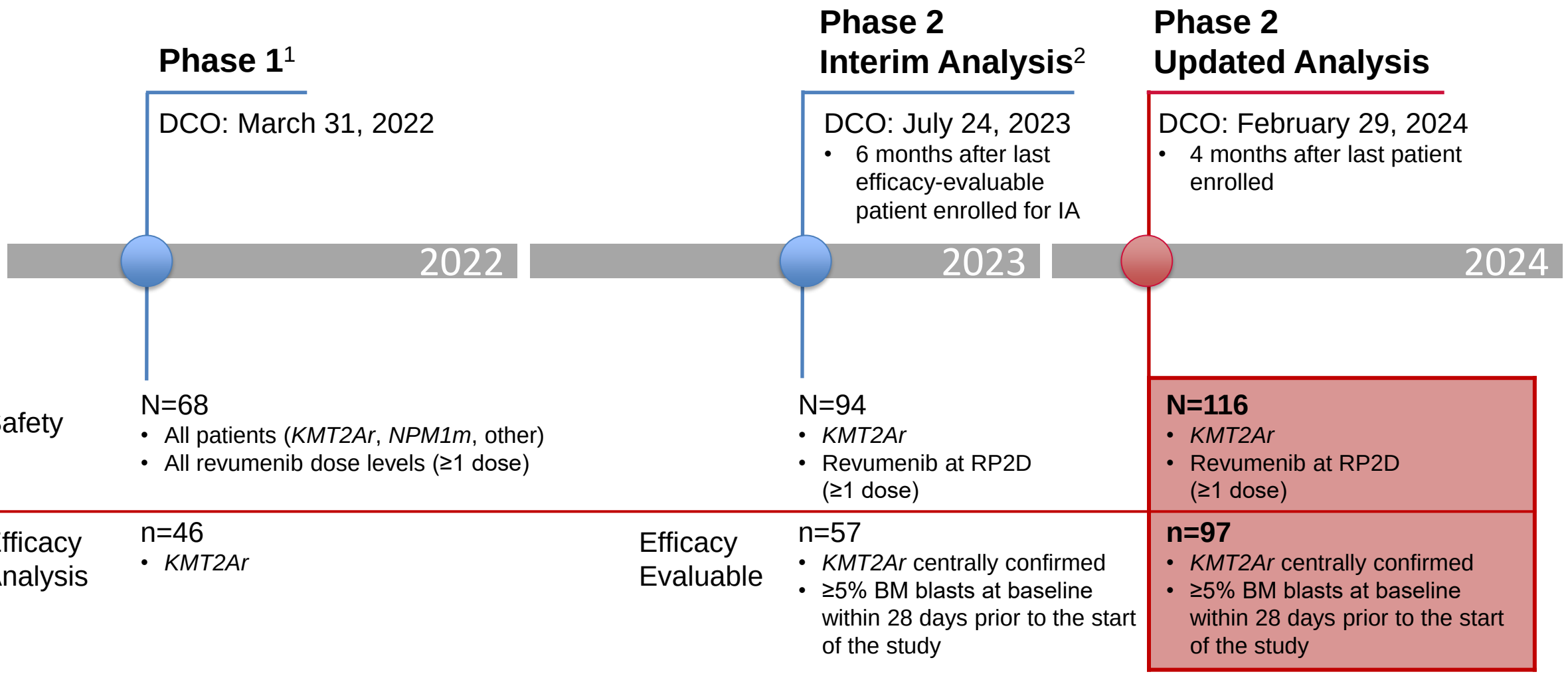
Figure reproduced from Issa GC, et al. *Blood Cancer J*. 2021;11:162 Creative Commons Attribution (CC BY) license. http://creativecommons.org/licenses/by/4.0/

Approved treatments for *KMT2Ar* disease are needed

3L, third-line; AML, acute myeloid leukemia; CR, complete remission; HSCT, hematopoietic stem cell transplant; *KMT2Ar*, lysine N-methyltransferase 2A rearranged; OS, overall survival; R/R, relapsed/refractory.

1. Issa GC, et al. *Blood Cancer J*. 2021;11:162. 2. Attarbaschi A, et al. *J Clin Oncol.* 2022;41(7):1404–1422.

AUGMENT-101 *KMT2Ar* Analyses



BM, bone marrow; DCO, data cutoff date; *KMT2Ar*, lysine N-methyltransferase 2A rearranged; IA, interim analysis; RP2D, recommended phase 2 dose.

1. Issa GC, et al. *Nature*. 2023;615(7954):920–924. 2. Issa GC, et al. *J Clin Oncol*. Published online August 9, 2024.

Phase 2 *KMT2Ar*: Patient Demographics

Parameter	Efficacy population (n=97)[a]	Safety population (N=116)[b]
Age, y, median (range)	37.0 (0.6–75.0)	35.5 (0.6–75.0)
Age <18 y, n (%)	20 (20.6)	28 (24.1)
Age ≥18 to <65 y, n (%)	65 (67.0)	74 (63.8)
Age ≥65 y, n (%)	12 (12.4)	14 (12.1)
Female, n (%)	55 (56.7)	67 (57.8)
Race, n (%)		
White	69 (71.1)	80 (69.0)
Non-White	16 (16.5)	18 (15.5)
Unknown	12 (12.4)	18 (15.5)

Data cutoff: February 29, 2024.

[a]All patients who have received ≥1 dose of revumenib, have been centrally confirmed for *KMT2Ar* acute leukemia, and have ≥5% blasts in bone marrow at baseline.

[b]All patients with *KMT2Ar* acute leukemia who received ≥1 dose of revumenib.

Phase 2 *KMT2Ar*: Baseline Characteristics

Parameter	Efficacy population (n=97)[a]	Safety population (N=116)[b]
Leukemia type, n (%)		
AML	78 (80.4)	95 (81.9)
ALL	13 (13.4)	15 (12.9)
MPAL/other	6 (6.2)	6 (5.2)
Co-mutations, n (%)[c]		
FLT3-ITD	5 (5.2)	7 (6.0)
FLT3-TKD	2 (2.1)	3 (2.6)
RAS	12 (12.4)	12 (10.3)
TP53	5 (5.2)	5 (4.3)
Primary refractory, n (%)	19 (19.6)	20 (17.2)
No. of prior lines of therapy, median (range)	2 (1–11)	2 (1–11)
≥3, n (%)	41 (42.3)	51 (44.0)
Prior venetoclax, n (%)	62 (63.9)	73 (62.9)
Prior HSCT, n (%)	46 (47.4)	59 (50.9)

Data cutoff: February 29, 2024.

[a]All patients who have received ≥1 dose of revumenib, have been centrally confirmed for *KMT2Ar* acute leukemia, and have ≥5% blasts in bone marrow at baseline. [b]All patients with *KMT2Ar* acute leukemia who received ≥1 dose of revumenib. [c]In patients who had co-mutation status reported.

ALL, acute lymphoblastic leukemia; AML, acute myeloid leukemia; FLT3, fms-related tyrosine kinase 3; HSCT, hematopoietic stem cell transplant; ITD, internal tandem duplication; *KMT2Ar*, lysine N-methyltransferase 2A rearranged; MPAL, mixed phenotype acute leukemia; *RAS*, rat sarcoma virus; TKD, tyrosine kinase domain; TP53, tumor protein 53.

Phase 2 *KMT2Ar*: Revumenib Efficacy

Parameter	Efficacy population (n=97)[a]
ORR, n (%)	**62 (63.9)**
CR+CRh rate, n (%)	22 (22.7)
95% CI	14.8–32.3
CRc, n (%)	41 (42.3)
95% CI	32.3–52.7
Negative MRD status, n (%)[b]	
CR+CRh	11/18 (61.1)
CRc	21/36 (58.3)

Parameter	Efficacy population (n=97)[a]
Best response, n (%)	
CR	15 (15.5)
CRh	7 (7.2)
CRi	2 (2.1)
CRp	17 (17.5)
MLFS	20 (20.6)
PR	1 (1.0)
PD	7 (7.2)
No response	21 (21.6)
Other[c]	7 (7.2)

Data cutoff: February 29, 2024.

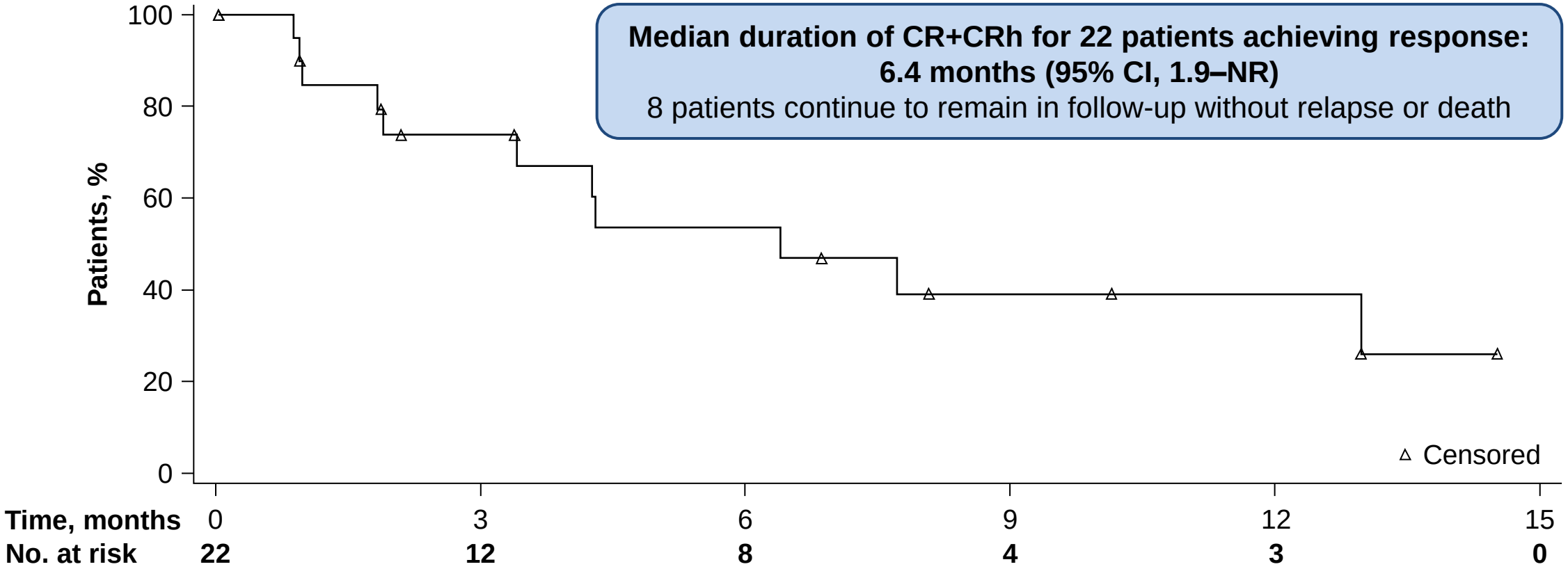
[a]All patients who have received ≥1 dose of revumenib, have been centrally confirmed for *KMT2Ar* acute leukemia, and have ≥5% blasts in bone marrow at baseline.

[b]MRD done locally; not all patients had MRD status reported.

[c]Includes patients without postbaseline disease assessment.

CR, complete remission; CRc, composite CR (CR+CRh+CRp+CRi); CRh, CR with partial hematologic recovery; CRi, CR with incomplete hematologic recovery; CRp, CR with incomplete platelet recovery; *KMT2Ar*, lysine N-methyltransferase 2A rearranged; MLFS, morphological leukemia-free state; MRD, measurable residual disease; ORR, overall response rate (CRc+MLFS+PR); PD, progressive disease; PR, partial remission.

Phase 2 *KMT2Ar*: Duration of CR+CRh



Median duration of CR+CRh for 22 patients achieving response: 6.4 months (95% CI, 1.9–NR)
8 patients continue to remain in follow-up without relapse or death

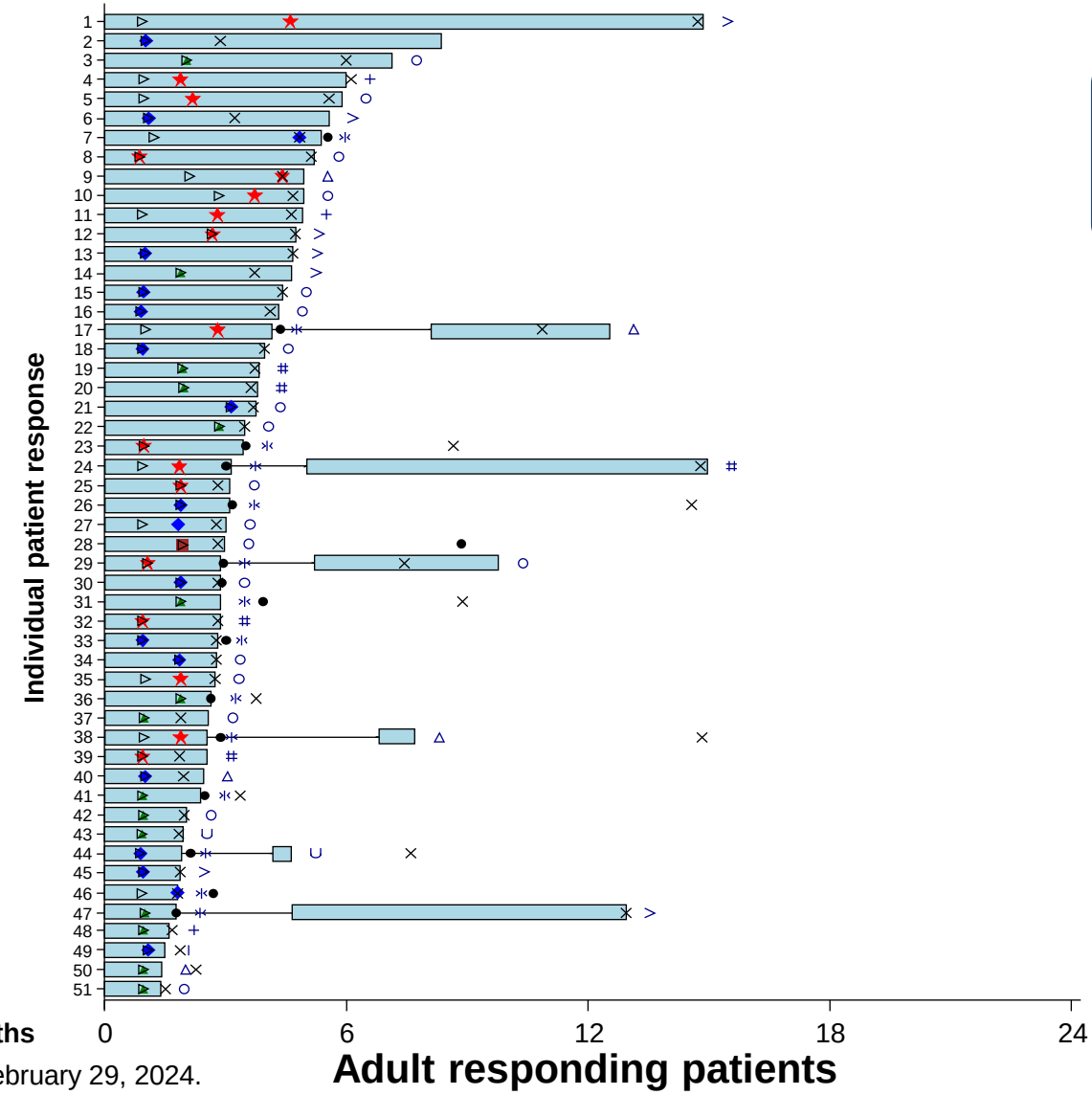
The updated median duration of CR+CRh for the 13 patients who achieved response in the interim analysis[1] was 13.0 months (95% CI, 3.4–NR)

Data cutoff: February 29, 2024.

CR, complete remission; CRh, CR with partial hematologic recovery; *KMT2Ar*, lysine N-methyltransferase 2A rearranged; NR, not reached.

1. Issa GC, et al. *J Clin Oncol*. Published online August 9, 2024.

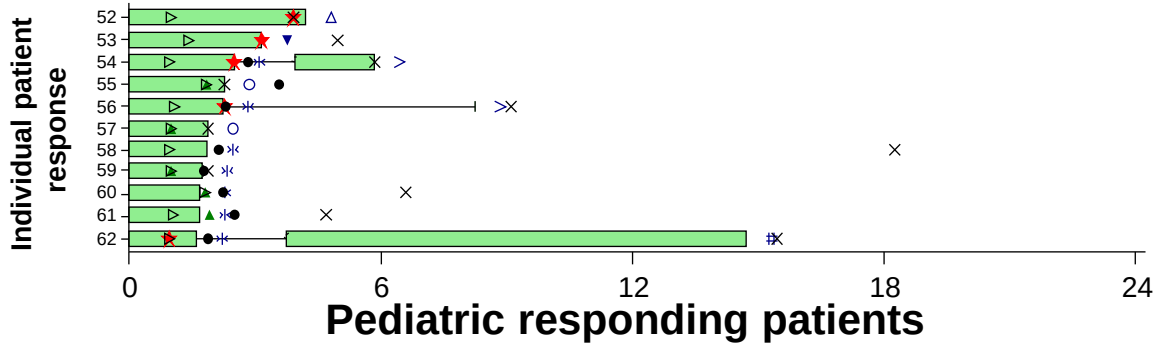
Phase 2 *KMT2Ar*: Duration of Treatment



Time to first response, median (range):

- **ORR (n=62): 1.0 month (0.9–3.1)**
- **CR+CRh (n=22): 2.0 months (0.9–4.6)**

Adult
Pediatrics
CR/CRh
CRp/CRi
MLFS
PR
ORR start
DOR end
HSCT
Ongoing treatment at data cutoff
PD
AE
Patient achieved a CRc, PR, or MLFS and underwent HSCT
Patient withdrew consent for treatment
Other
Investigator decision
Prohibited concomitant medication



Data cutoff: February 29, 2024.

AE, adverse event; CR, complete remission; CRc, CR composite (CR+CRh+CRp+CRi); CRh, CR with partial hematologic recovery; CRi, CR with incomplete hematologic recovery; CRp, CR with incomplete platelet recovery; DOR, duration of response; HSCT, hematopoietic stem cell transplant; *KMT2Ar*, lysine N-methyltransferase 2A rearranged; MLFS, morphological leukemia-free state; ORR, overall response rate; PD, progressive disease; PR, partial remission.

Phase 2 *KMT2Ar*: Patients Who Proceeded to HSCT

Parameter	n (%)
Proceeded to HSCT in ORR, n (%)	**21/62 (33.9)**
Proceeded to HSCT in CR or CRh	8/21 (38.1)
Proceeded to HSCT in CRp or CRi	6/21 (28.6)
Proceeded to HSCT in MLFS	7/21 (33.3)
Restarted revumenib post HSCT, n (%)	**9/21 (42.9)**
Time from HSCT to resuming revumenib post HSCT, days, median (range)	70 (35–182)

Data cutoff: February 29, 2024.

[a]MRD assessment was not required as part of the study; reported MRD is of available samples conducted locally by flow cytometry or PCR (n=1) at the discretion of the investigator.

Of patients who proceeded to HSCT:

- 11/14 patients with CRc had MRD status available[a]:
  - 9 (81.8%) MRD negative
- 6/8 patients with CR or CRh had MRD status available[a]:
  - 4 (66.7%) MRD negative

CR, complete remission; CRc, composite CR (CR+CRh+CRp+CRi); CRh, CR with partial hematologic recovery; CRi, CR with incomplete hematologic recovery; CRp, CR with incomplete platelet recovery; HSCT, hematopoietic stem cell transplant; *KMT2Ar,* lysine N-methyltransferase 2A rearranged; MLFS, morphological leukemia-free state; MRD, measurable residual disease; PCR, polymerase chain reaction.

Phase 2 *KMT2Ar*: Revumenib Safety Profile

	Safety population (N=116)[a]	
All terms, n (%)	**TEAEs**	**TRAEs**
Any grade	116 (100.0)	96 (82.8)
Grade ≥3	106 (91.4)	63 (54.3)
Serious AE	90 (77.6)	42 (36.2)
AEs leading to:		
Dose reduction	11 (9.5)	10 (8.6)
Discontinuation	16 (13.8)	6 (5.2)
Death	19 (16.4)	4 (3.4)

Data cutoff: February 29, 2024.
[a]All patients with *KMT2Ar* acute leukemia who received ≥1 dose of revumenib.

AE, adverse event; *KMT2Ar*, lysine N-methyltransferase 2A rearranged; TEAE, treatment-emergent adverse event; TRAE, treatment-related adverse event.

Phase 2 *KMT2Ar*: Revumenib Safety Profile (cont)

Any-grade TEAEs that occurred in ≥25% patients

All terms, n (%)	Safety population (N=116)[a]
Nausea	52 (44.8)
Febrile neutropenia	46 (39.7)
Vomiting	40 (34.5)
Diarrhea	35 (30.2)
QTc prolongation	34 (29.3)
Anemia	31 (26.7)
Differentiation syndrome	31 (26.7)
Epistaxis	30 (25.9)

Grade ≥3 TEAEs that occurred in ≥10% patients

All terms, n (%)	Safety population (N=116)[a]
Febrile neutropenia	45 (38.8)
Anemia	23 (19.8)
Decreased platelet count	19 (16.4)
Differentiation syndrome	17 (14.7)
Decreased neutrophil count	17 (14.7)
Decreased white blood cell count	17 (14.7)
Sepsis	16 (13.8)
QTc prolongation	15 (12.9)

Data cutoff: February 29, 2024.

[a]All patients with *KMT2Ar* acute leukemia who received ≥1 dose of revumenib.

No new safety signals were reported in this larger patient population
No patients discontinued revumenib due to cytopenias, differentiation syndrome, or QTc prolongation

KMT2Ar, lysine N-methyltransferase 2A rearranged; TEAE, treatment-emergent adverse event.

Phase 2 *KMT2Ar*: DS and QTc Prolongation

	Safety population (N=116)[a]	
All terms	**DS**	**QTc prolongation**
Any grade TEAE, n (%)	31 (26.7)	34 (29.3)
Grade 3[b]	16 (51.6)	15 (44.1)
Grade 4[b]	1 (3.2)	0
Grade 5	0	0
Dose interruptions[b]	9 (29.0)	14 (41.2)
Dose reductions[b]	0	4 (11.8)
Discontinuations	0	0
Time to initial onset, days, median (range)	10 (3–41)	8 (1–72)
Duration of initial event, days, median (range)	12 (3–31)	1 (1–8)

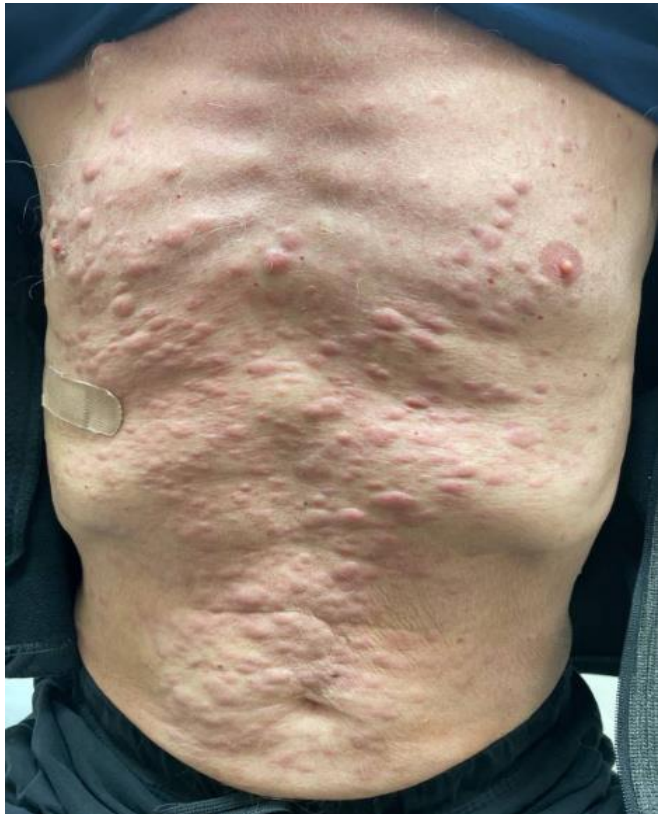
- Steroids were used to treat DS in 100% of cases, and hydroxyurea was used in 32.3% of those cases
- QTc prolongation was manageable and most patients with grade 3 were able to continue treatment in ≤1 day

Data cutoff: February 29, 2024.
[a]All patients with *KMT2Ar* acute leukemia who received ≥1 dose of revumenib.
[b]Of the total as reported by any grade TEAE.

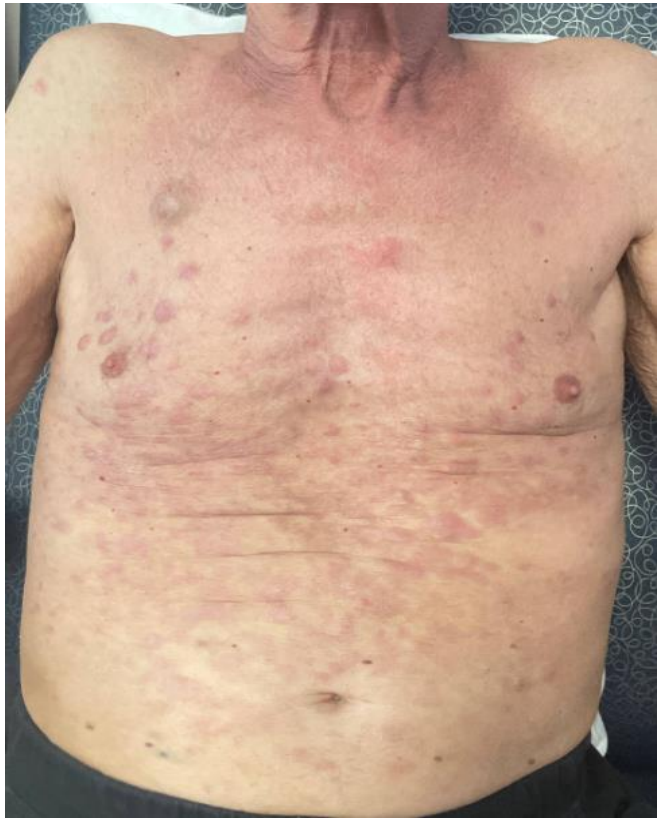
DS, differentiation syndrome; *KMT2Ar*, lysine N-methyltransferase 2A rearranged; TEAE, treatment-emergent adverse event.

NPM1mt with Extramedullary AML on SAVE

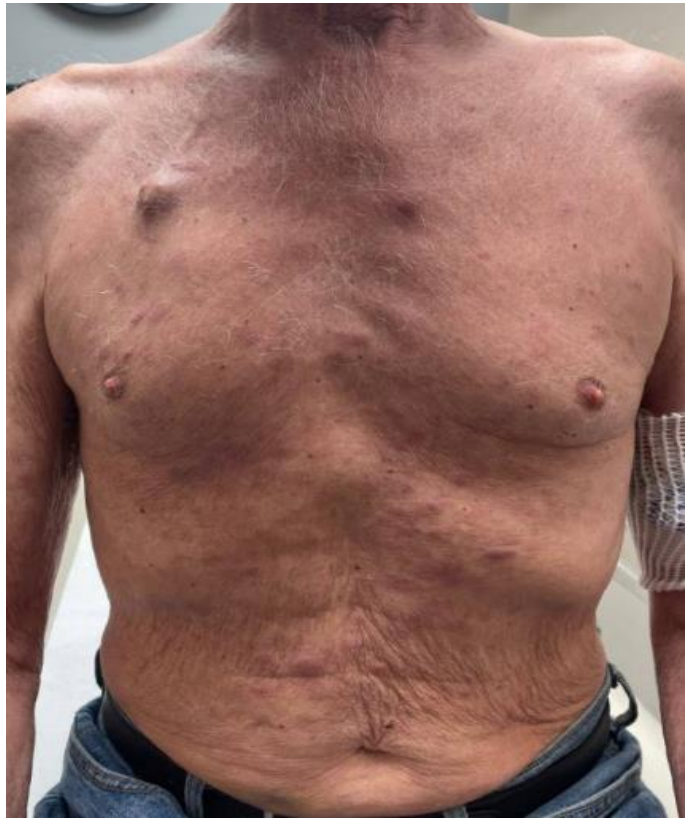
74 yo M, R/R AML, *NPM1*, *KRAS*, *PTPN11*, *FLT3*-TKD mutations, previously treated with 7+3+Mido → HIDAC+GO+Mido → Aza+Ven: NR → SAVE: NR (reduction in disease burden but residual PET+)



Pre-treatment
BM blasts 1%, MRD MFC neg



C1 D28
BM blasts 6%, MRD MFC neg



C2 D28

Conclusions

- In this updated phase 2 analysis, revumenib continues to consistently provide clinically meaningful responses in heavily pretreated patients with R/R *KMT2Ar* acute leukemias, including high rates of MRD negativity and ability to proceed to HSCT
- The safety profile of revumenib is manageable; no patients discontinued due to differentiation syndrome or QTc prolongation
- This trial represents the largest evaluation of a targeted therapy for patients with R/R *KMT2Ar* acute leukemias to date, including the largest pediatric menin inhibitor cohort
- The independent *NPM1m* AML cohort results will be presented in future publications

Revumenib is the first approved menin inhibitor

and first approved treatment for *KMT2Ar* acute leukemia

AML, acute myeloid leukemia; HSCT, hematopoietic stem cell transplant; *KMT2Ar*, lysine N-methyltransferase 2A rearranged; MRD, measurable residual disease; NPM1m, mutated nucleophosmin 1; R/R, relapsed/refractory;

American Society of Hematology
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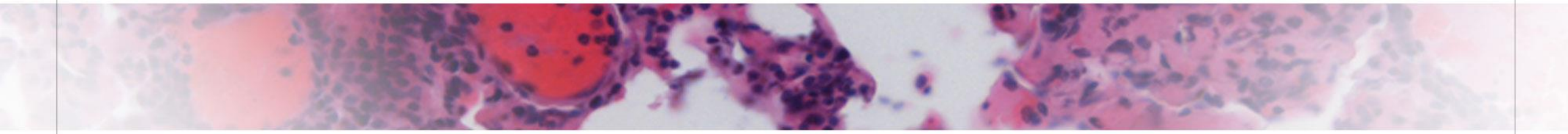

Phase I/II Study of the All-Oral Combination of Revumenib (SNDX-5613) with Decitabine/Cedazuridine (ASTX727) and Venetoclax in R/R AML (SAVE)

Ghayas C. Issa[1], Branko Cuglievan[2], Naval Daver[1], Courtney D. DiNardo[1], Aziz Farhat[1], Nicholas J. Short[1], David McCall[2], Allison Pike[1], Sheila Tan[1], Brianna Kammerer[2], Aimee Marshal[1], Musa Yilmaz[1], Tapan M. Kadia[1], Naveen Pemmaraju[1], Maro Ohanian[1], Hussein A. Abbas[1], Abhishek Maiti[1], Alexandre Bazinet[1], Elias Jabbour[1], Koji Sasaki[1], Gautam Borthakur[1], Guillermo Montalban-Bravo[1], Nitin Jain[1], Yesid Alvarado[1], Farhad Ravandi[1], Guillermo Garcia-Manero[1], Michael Andreeff[1], and Hagop M. Kantarjian[1]

[1]Department of Leukemia, [2]Division of Pediatrics, The University of Texas MD Anderson Cancer Center, Houston, TX

Rationale for SAVE Combination

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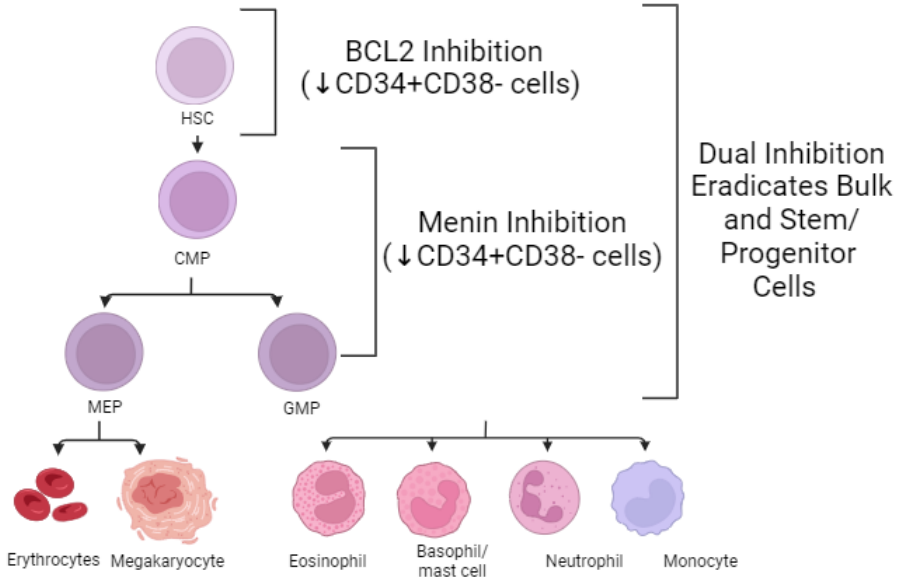
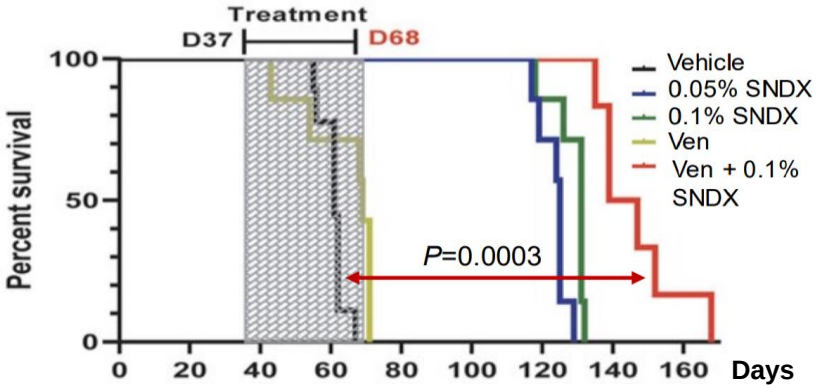
- HMA + **venetoclax** is standard for older/unfit AML
- **Oral decitabine/cedazuridine (ASTX727)** approved (MDS,CMML), equivalent efficacy as IV decitabine[1]
- *KMT2Ar* or *NPM1mt* leukemias susceptible to apoptosis through BCL2 inhibition[2-5]
- **Bcl-2 + menin inhibition** → eradication of bulk and stem/progenitor cells and improved survival in preclinical models[6,7]
- All-oral combination of **S**NDX-5613 + **A**STX727 + **VE**netoclax (**SAVE**)



PDX: *NPM1*, *FLT3* ITD/TKD[6]



1. Garcia-Manero G et al. Lancet Haematol. 2024 Jan;11(1):e15-e26. 2. Benito JM et al. Cell reports 2015;13:2715-27. 3. Tiong IS et al. Br J Haematol. 2021 Mar;192(6):1026-1030. 4. Lachowiez CA et al. Blood Adv. 2020 Apr 14;4(7):1311-1320. 5. Issa GC et al. Blood Adv. 2023 Mar 28;7(6):933-942. 6. Carter BZ et al. Blood. 2021 Oct 28;138(17):1637-1641. 7. Fiskus W et al . Blood cancer journal 2022;12:5

SAVE Phase I/II Study Design

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- Age ≥12 years
- R/R AML or Myeloid MPAL
- *KMT2Ar* or *NPM1mt* or *NUP98r*
- ECOG ≤2
- Adequate organ function

Revumenib (SNDX-5613)
DL 0: 113 mg
DL 1: 163 mg (**RP2D of monotherapy**)
PO Q12h D1-D28 + a strong CYP3A4i (posaconazole or voriconazole)

ASTX727
1 tablet (35 mg decitabine and 100 mg cedazuridine) PO daily for D1-D5

Venetoclax
400 mg target dose* with ramp up
PO D1-D14
*adjusted with azoles

D14 bone marrow for early response

Amendment: hold revumenib after D21 if D14 BM blasts <5%

Primary objectives:
- **Phase I (3+3 design)**
  Safety, MTD and RP2D
- **Phase II**
  Efficacy

Secondary objectives:
- Phase 2
  OS, RFS, CRD, MRD

Maintenance revumenib post-HSCT for 1 year

Baseline Characteristics - SAVE in R/R AML

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Characteristic	N = 33
Median age, years [range]	35 [12-81]
12-17 years, n (%)	5 (15%)
Female, n (%)	19 (58%)
BM blasts, % [range]	36 [1-94]
AML, n (%)	32 (97%)
MPAL, n (%)	1 (3%)
Medullary and EMD	5 (15%)
Therapy-related AML	4 (12%)
Genotype, n (%)	
KMT2Ar	16 (49%)
NPM1mt	12 (36%)
NUP98r	5 (15%)

Co-mutations, n (%)	
FLT3	10 (30%)
ITD/TKD	5 (15%) / 5 (15%)
WT1	10 (30%)
RAS	7 (21%)
Median no. of prior lines Tx [range]	3 [1-5]
Prior venetoclax, n (%)	19 (58%)
Prior HMA, n (%)	15 (45%)
Prior menin inhibitor, n (%)	2 (6%)
Prior FLT3 inhibitor, n(%)	10 (30%)
Prior HSCT, n (%)	12 (36%)

Data Cutoff 11/18/2024

Dose Escalation – Ph1 SAVE (3+3 Design)

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Revumenib (SNDX-5613)

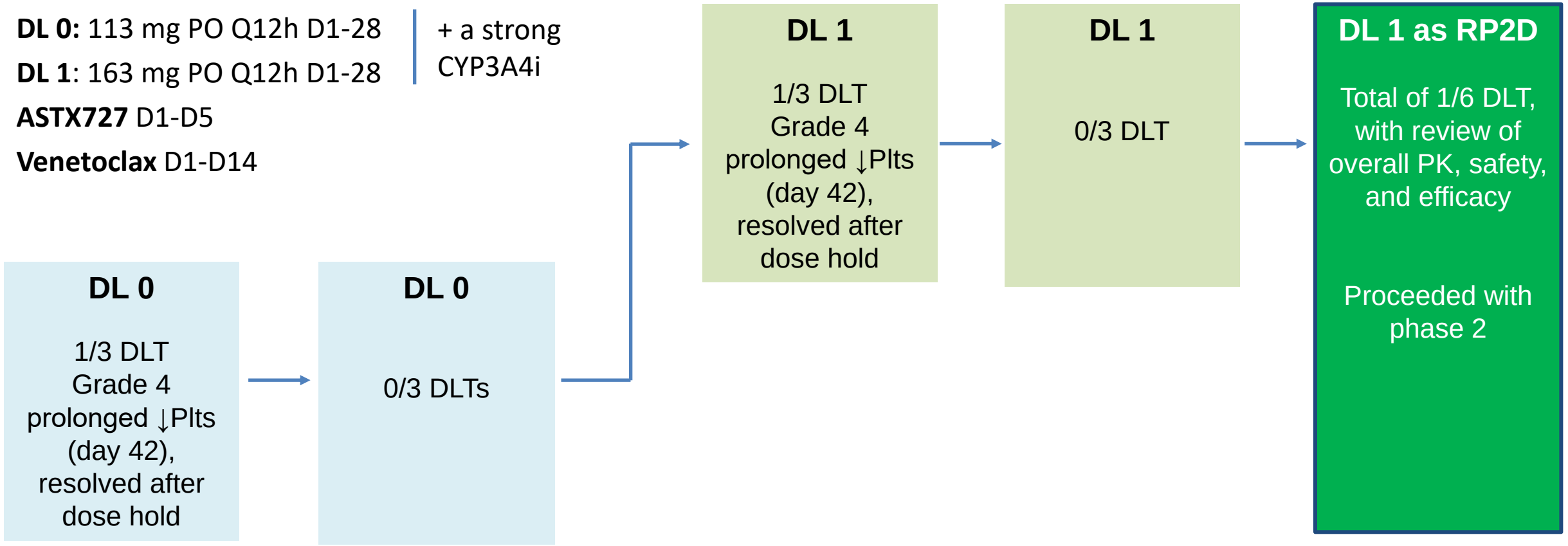
DL 0: 113 mg PO Q12h D1-28

DL 1: 163 mg PO Q12h D1-28

+ a strong CYP3A4i

ASTX727 D1-D5

Venetoclax D1-D14



Patient Disposition – SAVE in R/R AML

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Patient Disposition, n (%)	N = 33
Remaining on study	**13 (39%)**
Ongoing response without HSCT	10 (30%)
Maintenance post-HSCT	3 (9%)
Completed study including maintenance post-HSCT	**2 (6%)**
Proceeded to HSCT	13 (39%)
Proceeded to maintenance	7 (54%)
Off study (reason below)	**18 (55%)**
Progression or no response	10 (30%)
Death (unrelated) [1 (3%) early mortality in 60 days]	4 (12%)
AE (1 related, 1 unrelated)	2 (6%)
Other (1 for HSCT no maintenance; 1 no insurance coverage)	2 (6%)

Data Cutoff 11/18/2024

Adverse Events – SAVE in R/R AML

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TEAEs (any grade, >30%)	N = 33
QT prolongation	21 (64%)
Elevated AST/ALT	19 (58%)
Nausea	18 (55%)
↓K+	17 (52%)
Vomiting	17 (52%)
↑Phos	15 (45%)
↑K+	13 (39%)
Febrile neutropenia	12 (36%)
Hyponatremia	12 (36%)
Constipation	11 (33%)
Diarrhea	11 (33%)
Lung infection	11 (33%)
Sinus tachycardia	10 (30%)
[…]	
Differentiation syndrome	3 (9%)

TEAEs (Grade ≥3, and any G4-5)	G3	G4	G5	G ≥3
Febrile neutropenia	11 (33%)	0	0	11 (33%)
Lung infection	11 (33%)	0	0	11 (33%)
Elevated AST/ALT	5 (15%)	1 (3%)	0	6 (18%)
Sepsis	4 (12%)	2 (6%)	0	6 (18%)
Respiratory failure	0	5 (15%)	1 (3%)	6 (18%)
↓Platelets	3 (9%)	3 (9%)	0	6 (18%)
Sinusitis	5 (15%)	0	0	5 (15%)
Bacteremia	3 (9%)	0	1 (3%)	4 (12%)
AKI	2 (6%)	1 (3%)	0	3 (9%)
Hypokalemia	3 (9%)	0	0	3 (9%)
Nausea	3 (9%)	0	0	3 (9%)
Intracranial hemorrhage	2 (6%)	1 (3%)	0	3 (9%)
QT prolongation	2 (6%)	1 (3%)	0	3 (9%)
Colitis	2 (6%)	0	0	2 (6%)
Differentiation syndrome	1 (3%)	0	0	1 (3%)

TEAEs, treatment emergent adverse events regardless of attribution to study drugs. All cases of differentiation syndrome and QT prolongation were considered at least possibly related to revumenib. Data Cutoff 11/18/2024.

High response rate with SAVE in R/R AML

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Best Response n (%)	All patients (N=33)	*KMT2Ar* (N=16)	*NPM1mt* (N=12)	*NUP98r* (N=5)
ORR	27 (82%)	14 (88%)	8 (67%)	5 (100%)
CR/CRh	**16 (48%)**	7 (44%)	6 (50%)	3 (60%)
CR	**13 (39%)**	6 (38%)	6 (50%)	1 (20%)
CRh	3 (9%)	1 (6%)	0	2 (40%)
CRp	4 (12%)	3 (19%)	1 (8%)	0
PR	1 (3%)	0	0	1 (20%)
MLFS	6 (18%)	4 (25%)	1 (8%)	1 (20%)
No response/NE*	6 (18%)*	2 (13%)	4 (33%)*	0
MRD neg by MFC (10^{-4}) in responders	17/26 (65%)[#]	9/13 (69%)[#]	7/7 (100%)	1/5 (20%)
Within CR/CRh	14/16 (88%)	7/7 (100%)	6/6 (100%)	1/3 (33%)
Proceeded to HSCT	13 (39%)	9 (56%)	2 (17%)	2 (40%)

ORR= CR+CRh+CRp+PR+MLFS. *One pt with *NPM1mt* with early death prior to response assessment. [#]One responding pt had inadequate MRD by MFC. Data Cutoff 11/18/2024

SAVE leads to rapid responses in refractory cases

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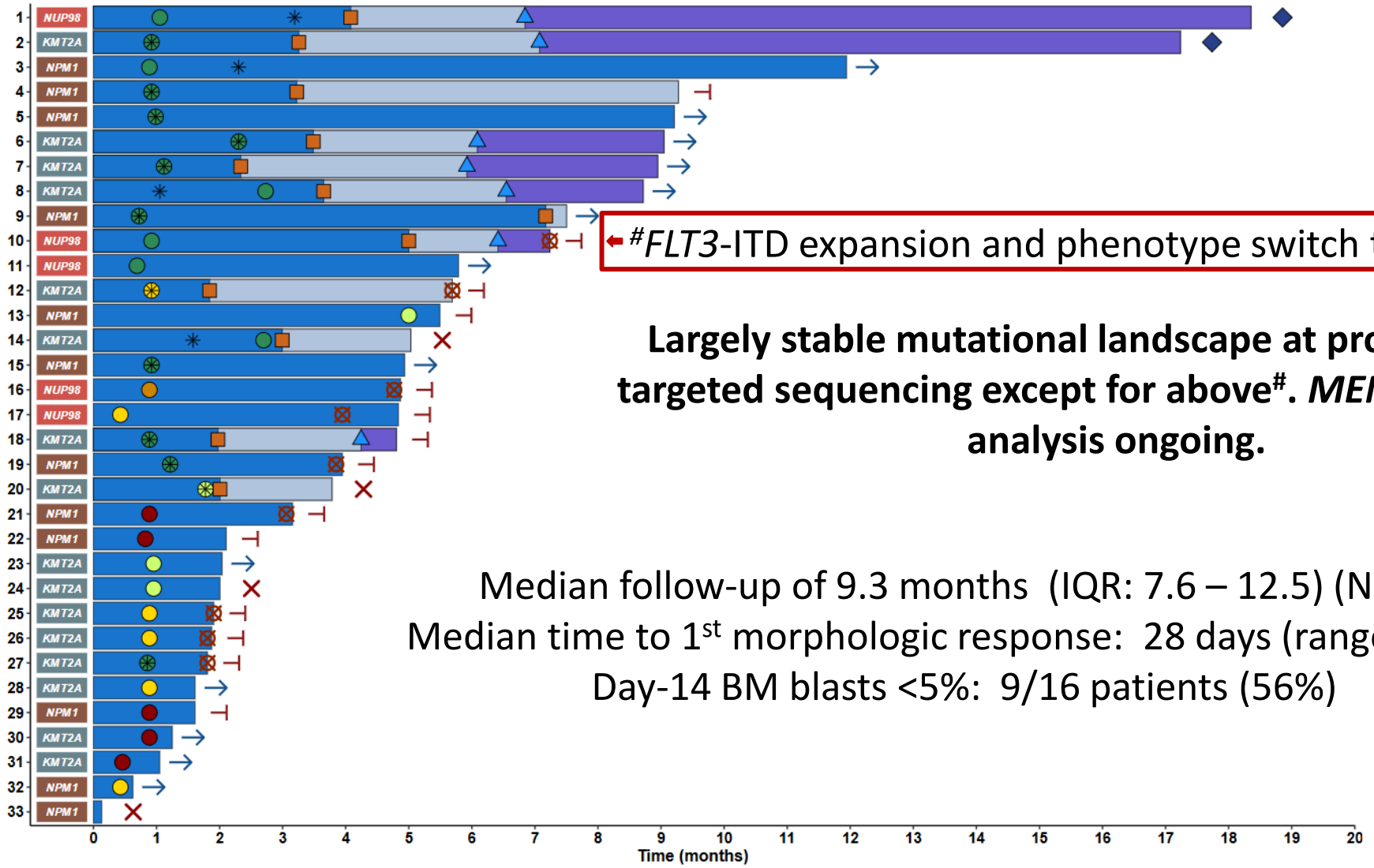


#*FLT3*-ITD expansion and phenotype switch to B-ALL + AML

Largely stable mutational landscape at progression on targeted sequencing except for above#. *MEN1* mutational analysis ongoing.

Median follow-up of 9.3 months (IQR: 7.6 – 12.5) (N=33)
Median time to 1st morphologic response: 28 days (range, 14-70)
Day-14 BM blasts <5%: 9/16 patients (56%)

Response
- CR/CRh
- CRi/CRp
- MLFS
- PR
- NR
- MRD neg

Time
- On study drug
- Post HSCT
- Maintenance

Events
- Completed
- Ongoing
- Off-treatment
- Dead
- Maintenance
- HSCT
- Relapse

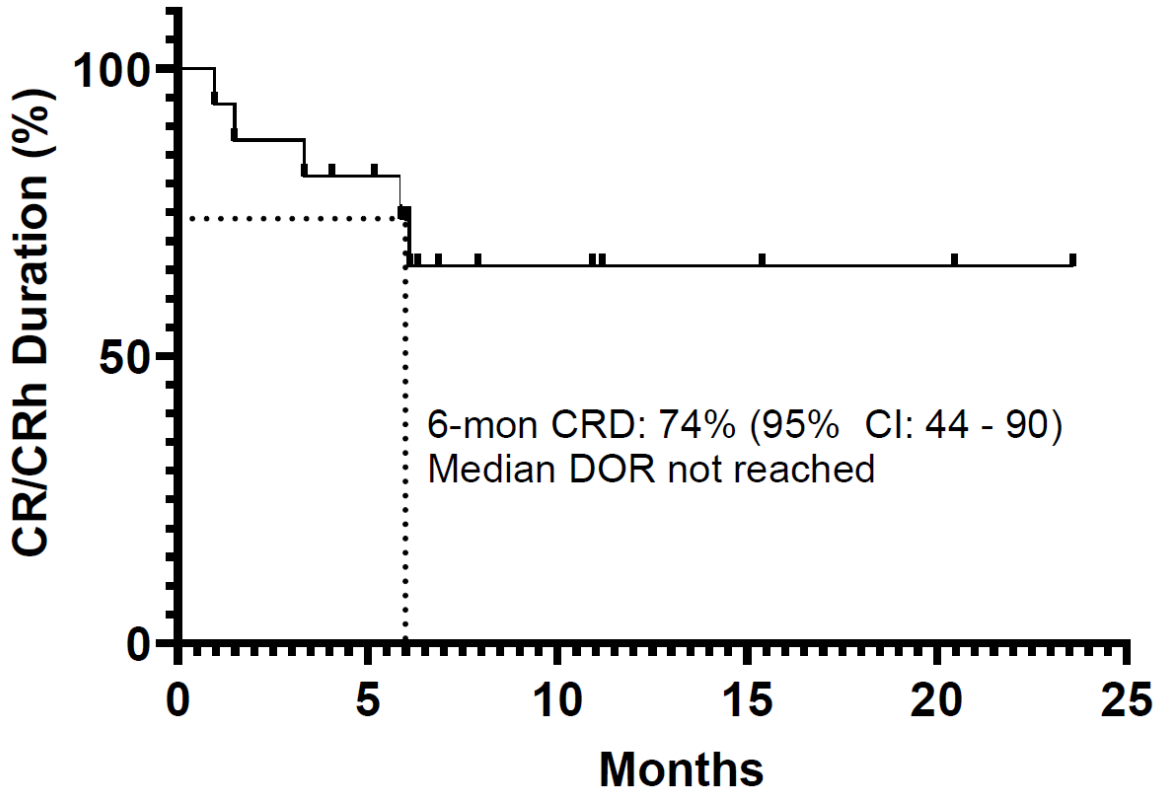
Data Cutoff 11/18/2024

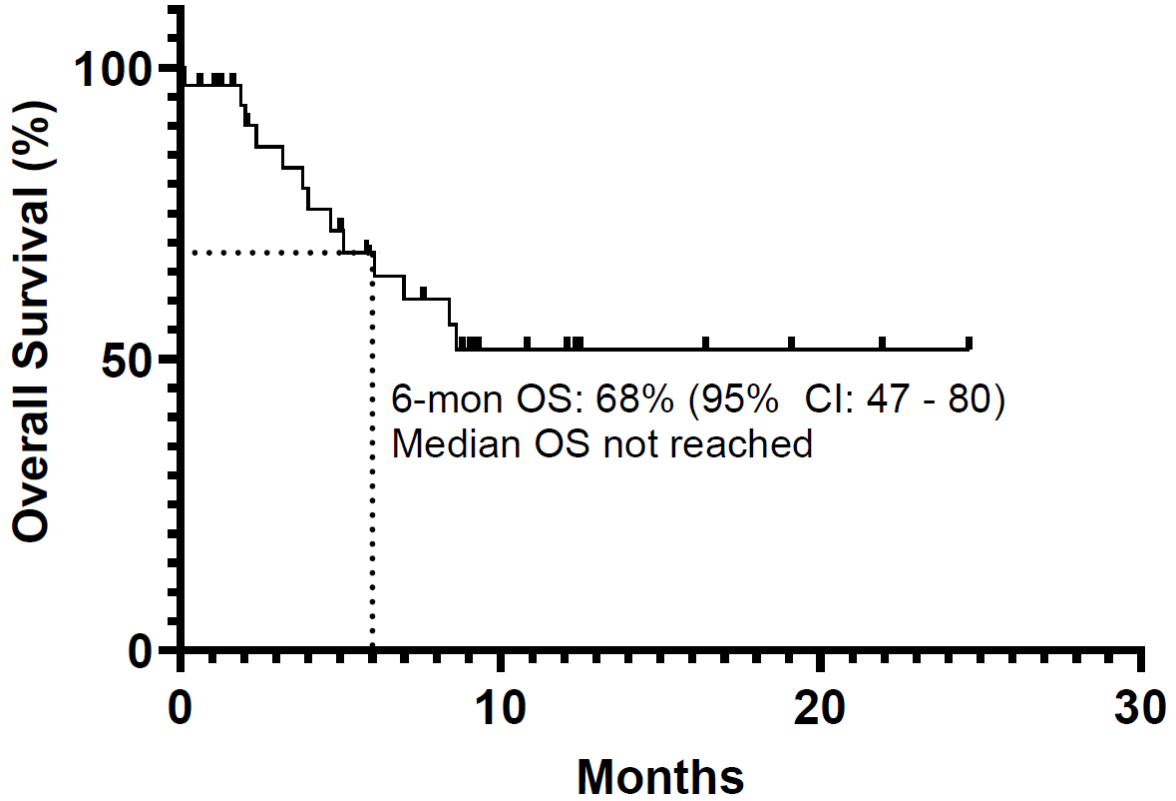
Duration of Response on SAVE for R/R AML

THE UNIVERSITY OF TEXAS MD Anderson Cancer Center Making Cancer History®

Abstract #216 SAVE

Median follow-up of 9.3 months (IQR: 7.6 – 12.5) (N=33)





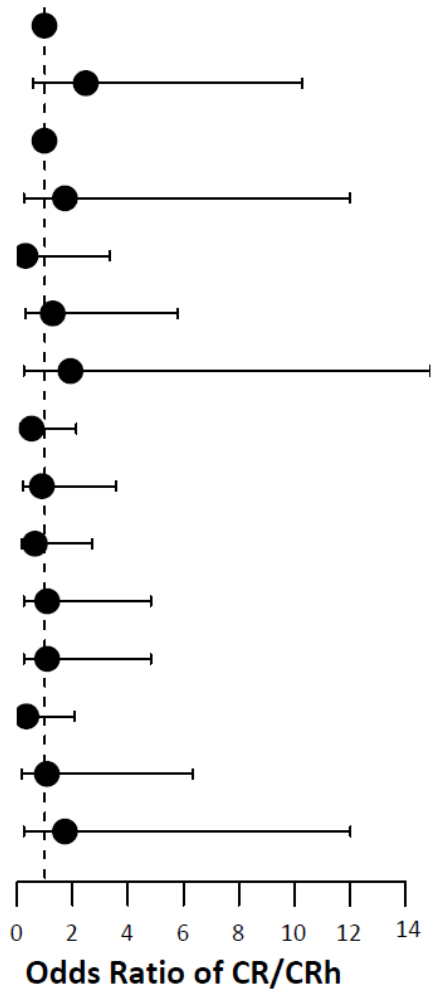
Data Cutoff 11/18/2024

Efficacy by Subgroups on SAVE in R/R AML

THE UNIVERSITY OF TEXAS MD Anderson Cancer Center
Making Cancer History®

Abstract #216 SAVE

		n (%)	*P*	Odds Ratio
Baseline Ch.	Age		0.5	0.9 (0.9–1.0)
	Female	19 (58)	0.2	2.5 (0.6–10.3)
	BM blast %		0.4	0.9 (0.9–1.0)
	EMD	5 (15)	0.6	1.7 (0.3–12.0)
	t–AML	4 (12)	0.3	0.3 (0.03–3.4)
Genotype	*NPM1mt* vs *KMT2Ar*	12 (36)	0.7	1.3 (0.3–5.8)
	NUP98r vs *KMT2Ar*	5 (15)	0.5	1.9 (0.3–14.9)
Prior Tx	≥ 3 lines of therapy	15 (45)	0.9	0.5 (0.1–2.1)
	Previous venetoclax	19 (58)	0.9	0.9 (0.2–3.6)
	Previous HSCT	12 (36)	0.6	0.7 (0.2–2.7)
Co-mutation	*FLT3*	10 (30)	0.9	1.1 (0.3–4.8)
	WT1	10 (30)	0.9	1.1 (0.3–4.8)
	RAS	7 (21)	0.2	0.3 (0.06–2.1)
	RUNX1	6 (18)	0.9	1.1 (0.2–6.3)
	IDH2	5 (15)	0.6	1.7 (0.3–12.0)



Data Cutoff 11/18/2024

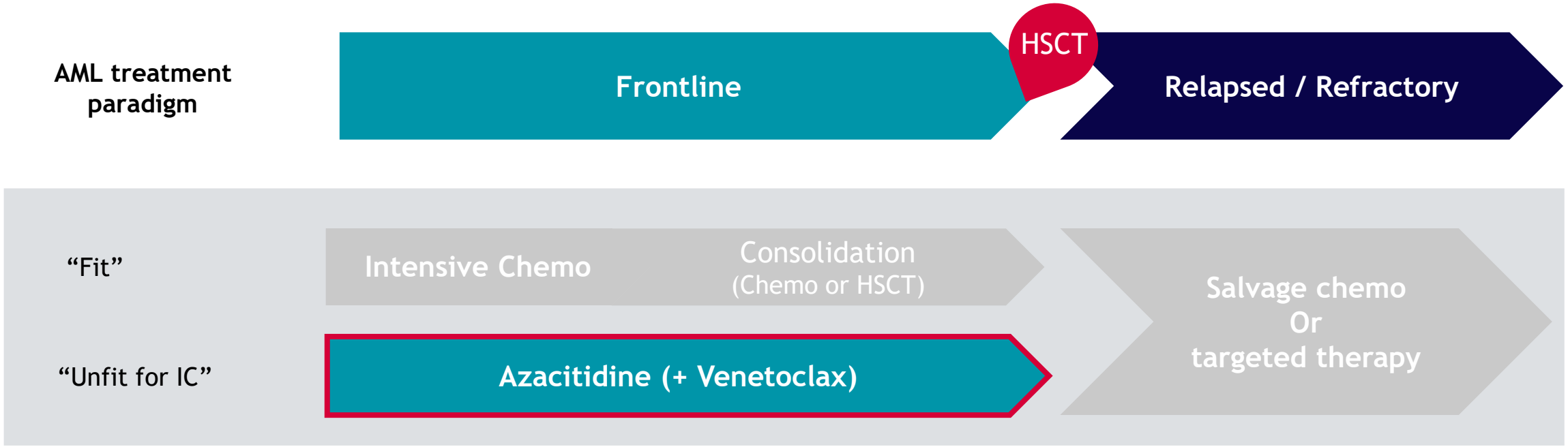
Conclusions

- The **all-oral SAVE** [**revumenib (SNDX-5613)**, **oral decitabine/cedazuridine (ASTX727)** and **VEnetoclax**] → acceptable safety and high efficacy in **children and adults** with R/R AML susceptible to menin inhibition
- High rates of response in heavily pretreated population
  - **ORR 82%, CR/CRh 48% → MRD-neg 88% in responders. Median DOR not reached**
  - 39% (13/33 pts) proceeded to HSCT, 7 pts resumed revumenib maintenance
  - Lower rate of DS compared to monotherapy with similar incidence of QT prolongation
- Myelosuppression, confounded by expected risk with HMA + Ven in R/R AML
- This study is now enrolling newly diagnosed patients with AML and *KMT2Ar*, *NPM1mt*, *NUP98r,* ineligible for intensive chemotherapy.

BEAT AML Frontline Combination Trial Results

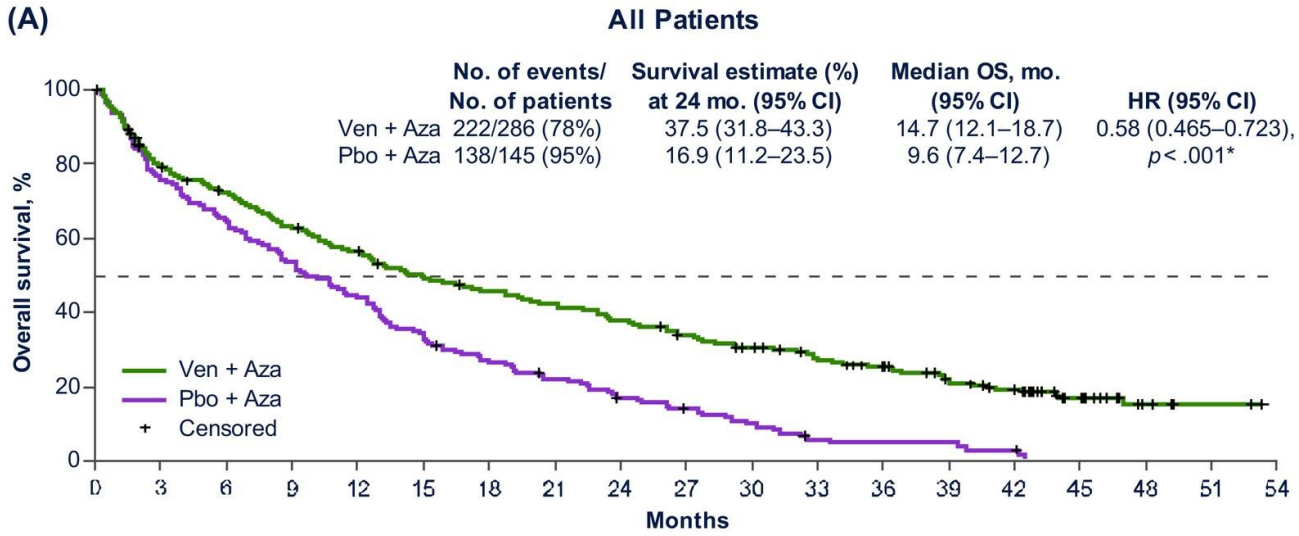
Joshua Zeidner, M.D.
Associate Professor of Medicine, Chief, Leukemia Research, University of North Carolina, Lineberger Comprehensive Cancer Center

BEAT-AML and Syndax partnered on frontline SOC combos based on strong efficacy and tolerability observed in relapsed / refractory patients



Azacitidine/venetoclax (aza/ven) outcomes in frontline therapy

- Aza/Ven is an important Tx advance for newly diagnosed older/unfit AML

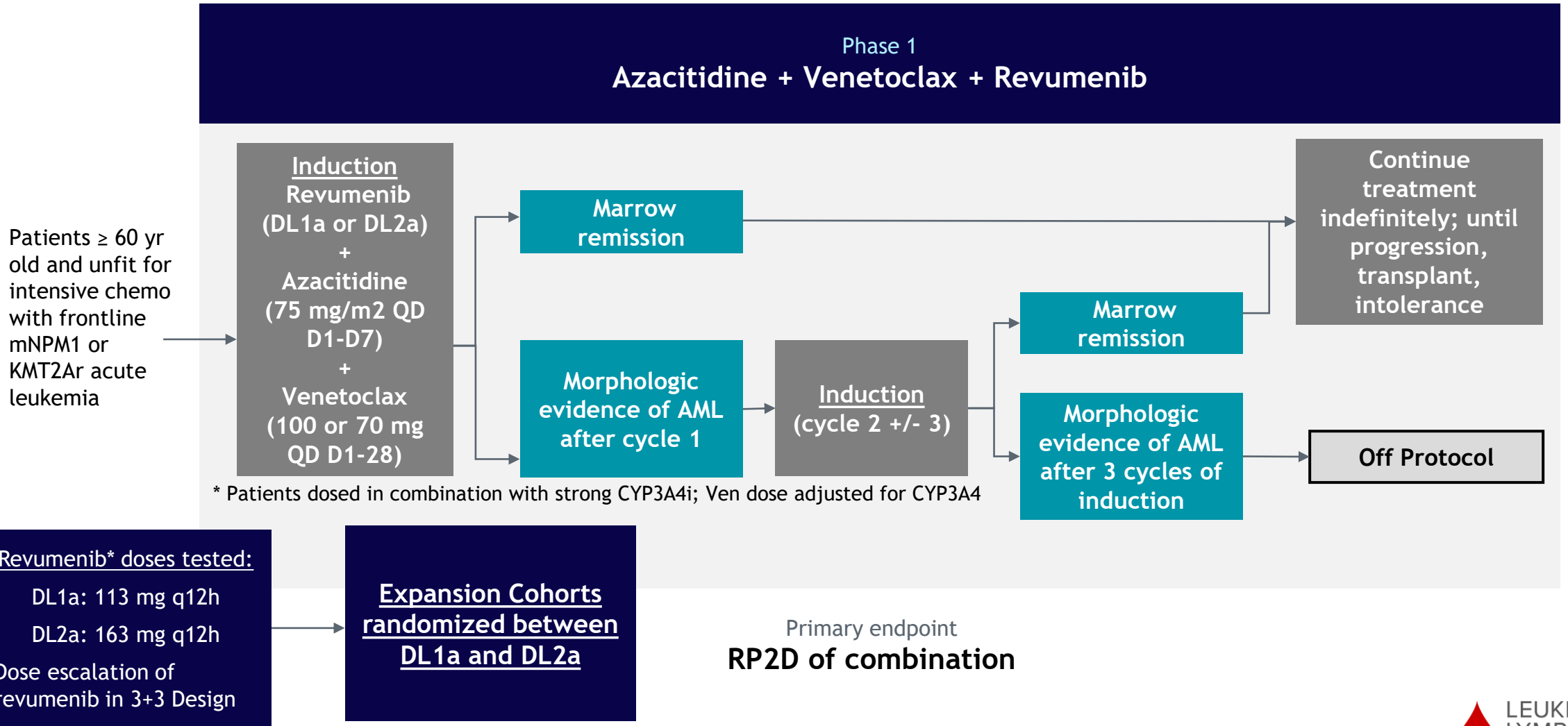


- CR rates = 37%
- Composite CR rates = 66%
- CR+CRh = 65%
  - 40% achieved CR+CRh after cycle 1

- However, long-term outcomes are poor (2-year OS = 38%) and majority of pts will relapse
- No significant OS advantage of Aza/Ven in *NPM1* mutations (*mNPM1*) or poor-risk cytogenetics
  - ~50% of *NPM1* mut have concomitant FLT3-ITD or NRAS/KRAS mut-> intermediate benefit by mPRS
  - Median OS 39 months vs. 9.9 months w/o and w/ signaling mutations, respectively

Pratz, *Am J Hematol* 2024; Dohner, *Blood* 2024

BEAT AML: Aza/Ven + Rev in frontline *mNPM1* or *KMT2Ar* AML



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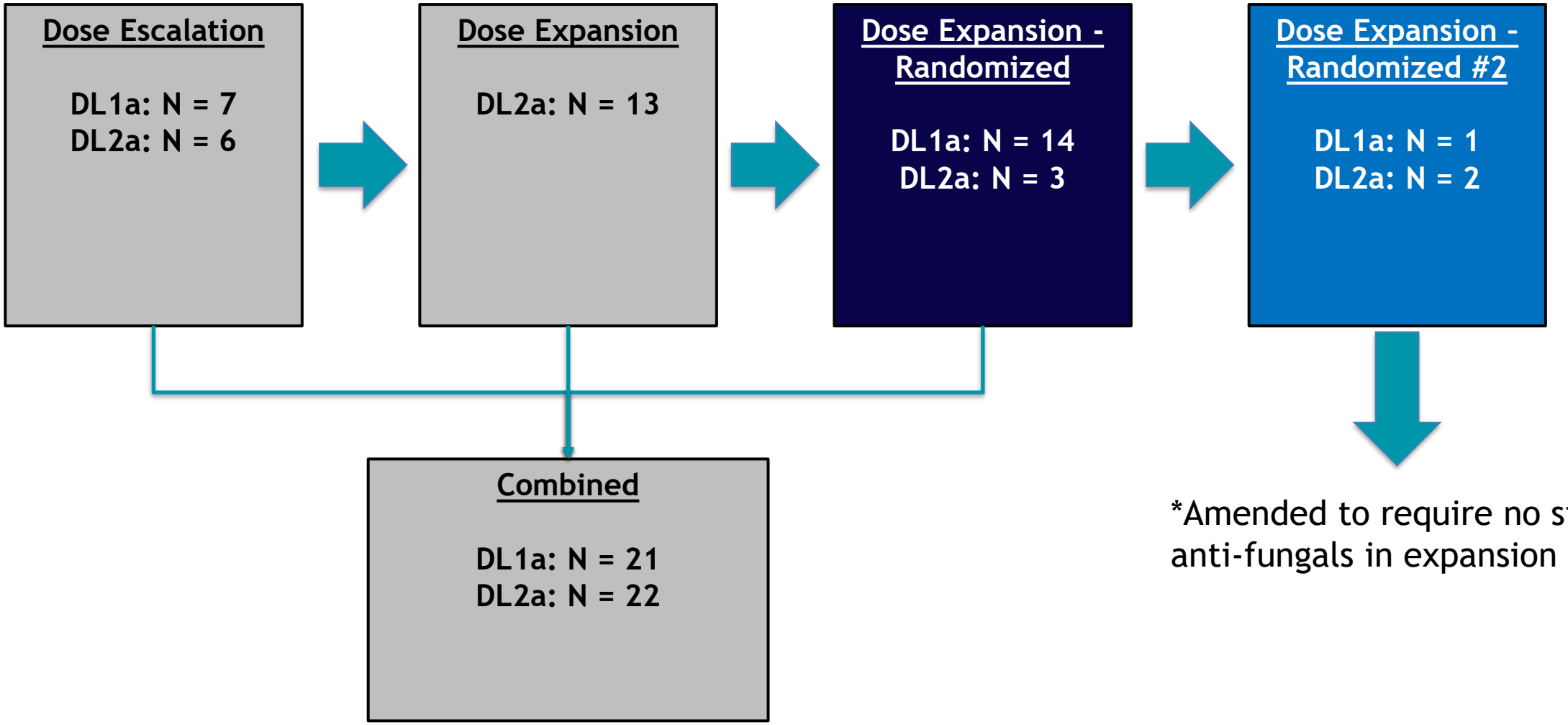
Current status of enrollment



*Amended to require no strong anti-fungals in expansion 2

BEAT AML patient demographics

Patient Demographics	DL1	DL2	All patients enrolled		
Genetics	All	All	*NPM1*	*KMT2A*	All
Number of Patients (%)	N=22	N=24	N=37 (80%)	N=9 (20%)	N=46
Age (Years), Median (Range)	73 (61-92)	69.5 (60-84)	72 (61-92)	67 (60-81)	71 (60-92)
Age ≥ 75 Years, no. (%)	10 (45)	7 (29)	16 (43)	1 (11)	17 (37)
Sex, %M/F	32/68	58/42	43/57	56/44	46/54
BM Blasts (%), Median (Range)	63 (15-94)	55 (16-81.8)	54 (15-94)	78 (55-84)	58 (15-94)

Data as of November 26, 2024, Enrolled Population

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Clinical outcomes of Aza/Ven/Rev

Treatment Outcomes	DL1 (n=18)	DL2 (n=19)	All (n=37)		
Genetics	All	All	NPM1	KMT2a	All
Response Rates for Efficacy Evaluable Patients[1]					
Number of Patients (%)	18	19	28 (76%)	9 (24%)	37
Composite CR (CRc)[2], no. (%)	17/18 (94)	18/19 (95)	27/28 (96)	8/9 (89)	**35/37 (95)**
Overall Response Rate (ORR)[3], no. (%)	18/18 (100)	19/19 (100)	28/28 (100)	9/9 (100)	**37/37 (100)**
Marrow Remission Achieved in 1 Cycle	15 (83)	16 (84)	23 (82)	8 (89)	31 (84)
End of Induction (Cycles 1-2) Responses					
CR	13 (72%)	15 (79%)	22 (79%)	6 (67%)	28 (76%)
CRh	1 (6%)	2 (11%)	2 (7%)	1 (11%)	3 (8%)
CRi	3 (17%)	1 (5%)	2 (7%)	1 (11%)	4 (11%)
MLFS	1 (6%)	1 (5%)	1 (4%)	1 (11%)	2 (5%)
Flow MRD Negative, no. (%)	18 (100)	17 (89)	26 (93)	9 (100)	35 (95)
Allo-Stem Cell Transplant, no. (%)	3 (17)	7 (37)	7 (25)	3 (33)	10 (27)
Relapse, no. (%)	2 (11)	1 (5)	1 (3)	2 (22)	3 (8)

1: Response Evaluable patients included patients alive and who received disease assessment after at least 1 cycle
2: CRc = CR+CRh+CRp+CRi; 3: ORR = CRc+MLFS+PR

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Safety of Aza/Ven/Rev

- No non-hematologic DLT's seen at any dose level
  - 1 Hematologic DLT observed in DL1a escalation: platelets exceeded 42 days to recover, no other DLTs across both dose levels
- Grade ≥3 non-hematologic AE's rarely observed and no difference between dose levels
- Most common treatment-related AE's: QTcF Prolongation (33%), nausea (30%), vomiting (26%), dysgeusia (26%)

Adverse Event, no. (% of Patients) Number of Patients Number of Patients with Reported Events	**DL1a** 22 12 (55)	**DL2a** 24 12 (50)	**All** 46 24 (52)
Differentiation Syndrome (DS) Grade 3+	6 (27) 2 (9)	1 (4) 0 (0)	7 (15) 2 (4)
QTcF Prolongation Grade 3+	8 (36) 2 (9)	12 (50) 3 (13)	20 (43) 5 (11)
Peripheral Neuropathy Grade 3+	0 (0) 0 (0)	0 (0) 0 (0)	0 (0) 0 (0)

- QTcF Prolongation and DS self-limiting with no discontinuations
- Only 1 pt required dose reduction due to QTcF prolongation: G3 QTcF prolongation on DL1a

- Overall, 13/46 (28%) died on study to date: DL1: 5/22 (23%); DL2: 8/24 (33%); *NPM1m*: 10/37 (27%); *KMT2Ar*: 3/9 (33%)

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Treatment cycle duration analysis supports cytopenias related to ventoclax

Induction Cycle Duration

Treatment Cycle Lengths	DL1a	DL2a	All
No. of Patients	7	19	26
Median Cycles, (range)	3 (1-11)	3 (1-6)	(1-11)
Induction Cycle Length[1]			
No. of Patients	5	15	20
Median Days per Cycle, (range)	38 (29-49)	35 (28-42)	**36 (28-49)**

ANC $\geq 0.5 \times 10^9$/L and platelets $\geq 50 \times 10^9$/L needed prior to each cycle of continuation

Time to Initiation of Continuation Cycles

Delay (weeks)	# of Continuation Cycles	Proportion of All Continuation Cycles
No Delay	6	17%
<1 week	11	31%
1-2 weeks	7	19%
2+ weeks	12	33%

Median duration of continuation phase cycles was **38 days** (range = 28-188 days)

- 16 (80%) patients had a delay prior to continuation phase due to cytopenias
- **No difference in time to initiation of continuation phase b/w DL1a and DL2a suggesting that cytopenias related to venetoclax not revumenib**
  - **Venetoclax now dose reduced to 14 days each continuation cycle**
- Dose reductions were made to revumenib (28 to 21 days), then venetoclax (28 to 21 days), then Azacitidine (7 to 5 days)
  - 13 total dose reductions were made in 5 patients: 6 revumenib, 5 venetoclax, and 2 azacitidine

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[1]Includes only patients and induction cycles where a remission is achieved, and continuation cycle is started; Data cut off: May, 2024

Revumenib randomized Phase 3 study design

Newly diagnosed AML w/ *NPM1mut*
- ≥75 years or unfit for intensive chemo

1:1

Azacitidine
Venetoclax
Revumenib*

Azacitidine
Venetoclax
Placebo

- *KMT2Ar to be included but not as part of primary analysis*
- *HSCT allowed*

Primary endpoint: OS

* Final results from BEAT-AML to support revumenib dose and schedule, and placebo schedule.

STUDY AML GROUP · ALFA · FRENCH INNOVATIVE LEUKEMIA ORGANIZATION · UK AML Clinical Trials Group · CETLAM · fondazione GIMEMA onlus · ALLG Australasian Leukaemia & Lymphoma Group · Leukemia & Lymphoma Society BEAT AML · Nordic AML Group · SAKK · HOVON

Conclusions and next steps

- **Revumenib can be safely added to Aza/Ven**
  - No new safety signals or toxicity seen
  - Enrollment ongoing in an expansion cohort randomized between DL1 and DL2
- **Aza/Ven/Rev is highly active in newly diagnosed unfit AML patients with *NPM1* mut or *KMT2Ar***
  - Overall Response rate = 100% in 37 evaluable patients
  - Remissions occur rapidly (84% w/in 1 cycle) and are deep (Flow MRD negative = 95%)

Next Steps

- Present final analysis of first expansion cohort (43 patients) in 2025 with subsequent publication
- **Initiate HOVON-sponsored International Randomized Phase 3 Study**
  - Aza/Ven ± Rev in newly diagnosed unfit AML patients with *mNPM1;* Primary Endpoint = OS
    - Venetoclax dose modifications for continuation cycles mirroring clinical practice

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Close and Q&A

Steve Closter
Chief Commercial Officer, Syndax

Expected upcoming milestones

Revuforj (revumenib)

Menin-KMT2A inhibition

- Initiation of pivotal combination trial with ven/aza in newly diagnosed mNPM1 or KMT2Ar acute leukemias by YE24
- Publish and present pivotal R/R mNPM1 AML data at a medical conference in 1H25
- sNDA filing in R/R mNPM1 AML in 1H25

Niktimvo (axatilimab-csfr)

CSF-1R inhibition

- Launch in refractory chronic GVHD no later than early first quarter 2025
- Chronic GVHD frontline combination trial with steroids in preparation
- Topline readout from Phase 2 IPF trial in 2026

Building blocks to Syndax's transformational era

Before 2023

Established scientific leadership

- Built innovative oncology company with industry-leading scientific, clinical development, and regulatory expertise
- Strategically expanded pipeline with differentiated therapies

2023-2024

Advanced clinical, regulatory, and operational excellence

- Prepared organization for transition to commercial stage, including the establishment of commercial capabilities
- **Received FDA approvals for two first-in-class products** with practice-changing potential, Revuforj and Niktimvo

2025 and beyond

Transformational era of sustainable and profitable growth

- Well positioned to change the treatment landscape and drive sustained, profitable growth supported by:
  - Commercialization of first-in-class therapies
  - Strong financial foundation to fund Syndax through profitability
  - Targeted strategy to expand pipeline and drive long-term success and value creation


Determined to realize a future in
which people with cancer live longer
and better than ever before.