Syndax

Reimagining Cancer Treatment

Syndax Investor Meeting
American Society of Hematology Meeting
December 11, 2023

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Welcome and Introduction to Syndax

Michael Metzger
Chief Executive Officer, Syndax

Syndax: An oncology company with 2 near-commercial heme assets

- Two clinically **potential first-** and **best-in-class** hematology assets
  - **Revumenib**, novel menin inhibitor, targeting KMT2Ar and mNPM1 acute leukemia
  - **Axatilimab**, first CSF-1R mAb **targeting cGVHD**
- Revumenib is on track for **NDA submission by year-end under RTOR**
  - Potential to access ~$2B market opportunity in R/R KMT2Ar and mNPM1 acute leukemia; opportunity to access larger markets with expansion into frontline
- Axatilimab is on track **for BLA submission by year-end** with partner Incyte
  - ~$2B market opportunity for 3L+ cGVHD; opportunity to access larger markets with expansion into earlier lines
- Strong IP supporting both assets with LOE to 2040

ASH 2023
Plenary and Late-Breaker

Safety and Efficacy of Axatilimab at 3 Different Doses in Patients with Chronic Graft-Versus-Host Disease (AGAVE-201)

Session: Plenary Scientific

Revumenib Monotherapy in Patients with Relapsed/Refractory *KMT2Ar* Acute Leukemia: Topline Efficacy and Safety Results from the Pivotal Augment-101 Phase 2 Study

Session: Late-Breaking Abstracts

Axatilimab and revumenib at ASH

Syndax goals at the American Society of Hematology 2023 Annual Meeting

- Showcase axatilimab and revumenib as potential first- and best-in-class agents with potential as monotherapy and in combination
- Educate the physician community ahead of expected 2024 launches
- Generate excitement for ongoing and upcoming trials

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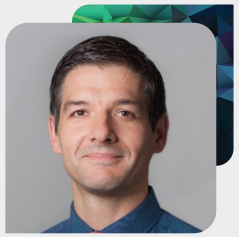
Today’s guest speakers

Axatilimab (cGVHD)



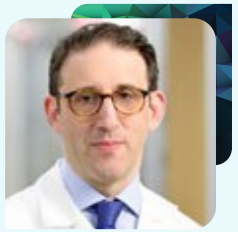
Vedran Radojcic, MD

Senior Medical Director and Clinical Leader for Axatilimab, Syndax Pharmaceuticals

Daniel Wolff, MD

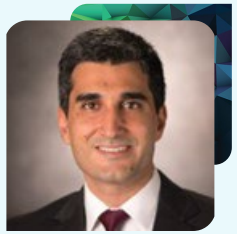
Professor of Hematology, Department of Internal Medicine III of the University of Regensburg

Revumenib (acute leukemia)



Eytan Stein, MD

Chief, Leukemia Service, Director, Program for Drug Development in Leukemia, Memorial Sloan Kettering Cancer Center

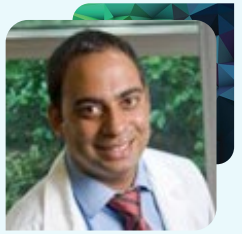


Ghayas Issa, MD

Assistant Professor, Department of Leukemia, Division of Cancer Medicine, The University of Texas MD Anderson Cancer Center

Joshua Zeidner, MD

Associate Professor of Medicine, Chief, Leukemia Research, University of North Carolina, Lineberger Comprehensive Cancer Center



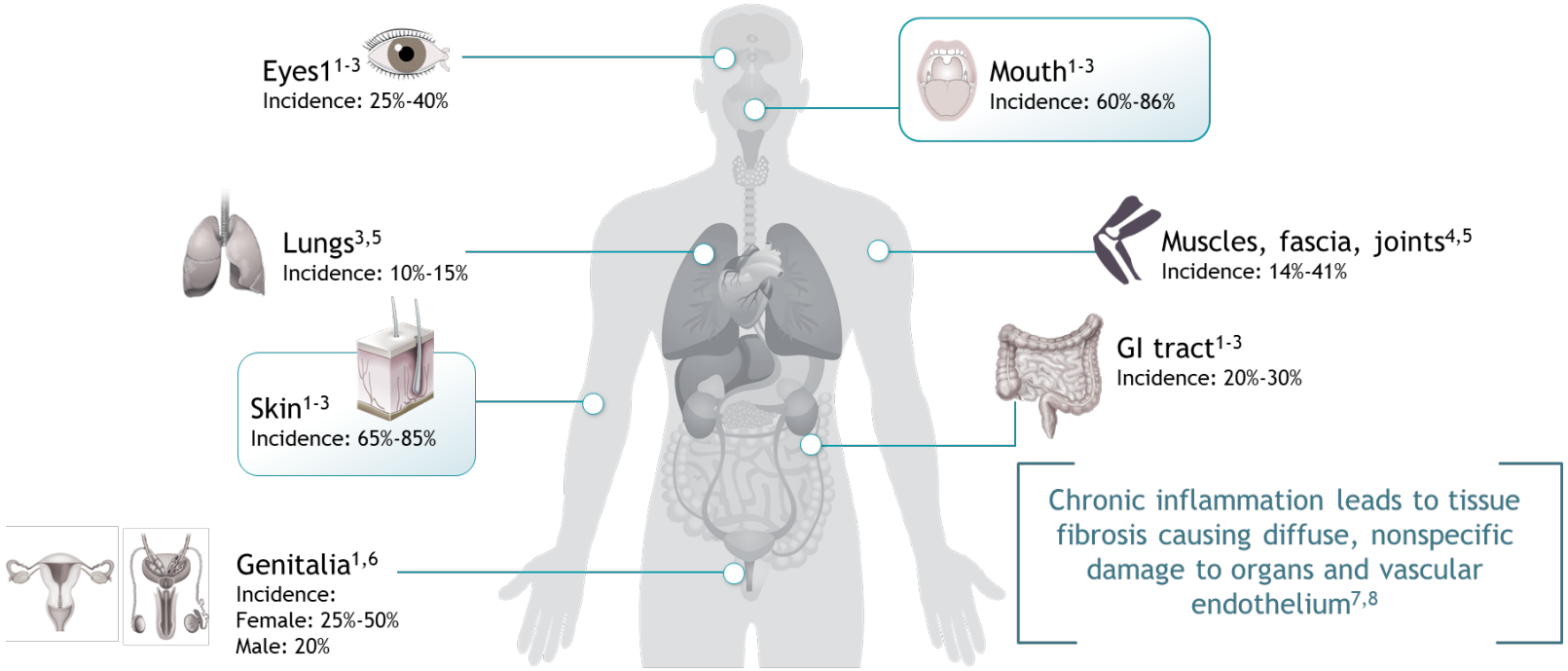
Neerav Shukla, MD

Chief, Pediatric Translational Medicine Service at Memorial Sloan Kettering Cancer Center

Chronic GVHD and Axatilimab Overview

Dr. Vedran Radojcic
Senior Medical Director and Clinical Leader for
Axatilimab, Syndax Pharmaceuticals

Multiorgan involvement in cGVHD drives morbidity and QOL impairment



- Chronic GVHD effects up to 50% of allo-HSCT recipients[8-10]
- Complete responses are rare and many organs respond poorly to available therapy
- Patients need prolonged treatment to control disease burden

1. Jagasia MH, et al. *Biol Blood Marrow Transplant*. 2015;21(3):389-401. 2. Vigorito AC, et al. *Blood*. 2009;114(3):702-708. 3. Lee SJ, et al. *Blood*. 2002;100(2):406-414. 4. Vukic T, et al. *Croat Med J*. 2016;57(3):266-275. 5. Inamoto Y, et al. *Arthritis Rheumatol*. 2014;66(4):1044-1052. 6. Hamilton BK, et al. *Bone Marrow Transplant*. 2017;52(6):803-810. 7. Blazar BR, et al. *Nat Rev Immunol*. 2012;12(6):443-458. 8. Cooke KR, et al. *Biol Blood Marrow Transplant*. 2017;23(2):211-234. 8. Arai et al. *Biol Blood Marrow Transplant*. 2015;21:266-274. 9. Arora et al. *Biol Blood Marrow Transplant*. 2016;22:449-455. 10. Velickovic et al. *Ther Adv Hematol*. 2020;11:1-18.

Significant unmet need remains across all lines of therapy

If approved, axatilimab will provide a differentiated mechanism from currently approved agents

Corticosteroids are the cornerstone of therapy

- ~60% of patients develop corticosteroid resistance or dependence

Currently approved agents are small molecules targeting intracellular signaling to impact the disease

Approved therapies after steroid failure (ibrutinib, belumosudil, ruxolitinib) are not curative[2]

Current Standard of Care[1]

1st Line	Corticosteroids
2nd Line	JAKAFI® IMBRUVICA®
3rd Line	REZUROCK®

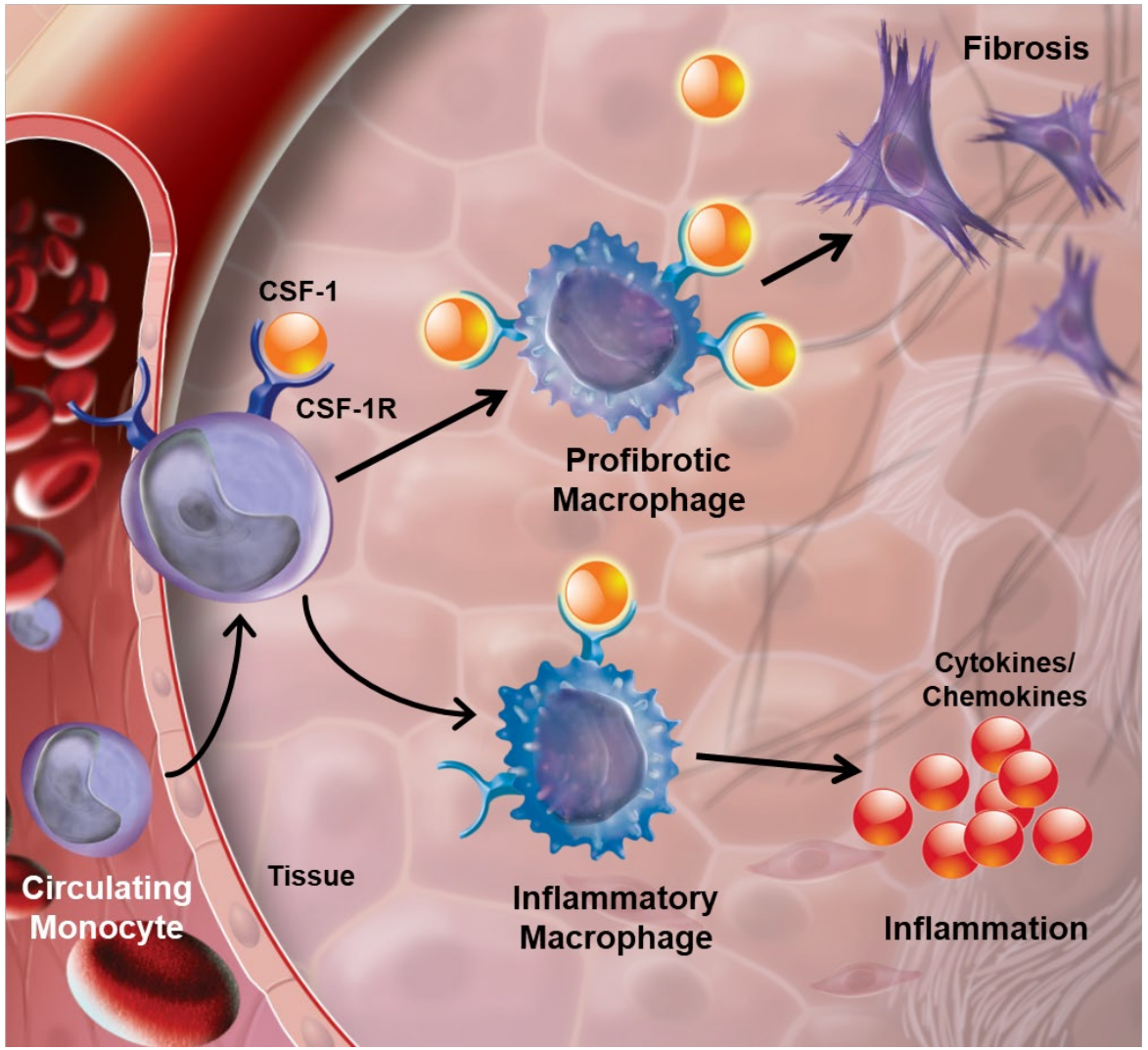
Despite recent approvals, >50% of patients receive ≥3 therapy lines with decreasing efficacy[2] so there remains a significant need for new medications

1. U.S. Regulatory approvals in cGVHD: Imbruvica® - August 2017, Rezurock® - July 2021, Jakafi® - September 2021; 2. Lee et al. *Biol Blood Marrow Transplant*. 2018;24:555-562. 2. Wolff, D.,. *et al.* Steroid-refractory chronic graft-versus-host disease: treatment options and patient management. *Bone Marrow Transplant* **56**, 2079–2087 (2021).

CSF-1R: The key regulator of macrophage and monocyte functions in cGVHD

Targeting monocyte-derived macrophages may control fibrosis and inflammation

- CSF-1/CSF-1R pathway regulates monocyte proliferation and macrophage differentiation and activity[1]
- CSF-1R signaling is critical for development and function of alternatively polarized macrophages which can exert profibrotic and inflammatory functions
- In cGVHD monocytes and macrophages can mediate inflammation and fibrosis[2,3,4]



1. Hume and Macdonald. *Blood* 2012;119:1810-1820. 2. Alexander et al. *J Clin Invest* 2014;124:4266-4280. 3. MacDonald et al. *Blood*. 2017;129:13-21. 4. Jardine et al. *J Clin Invest*. 2020;130:4574-4586.

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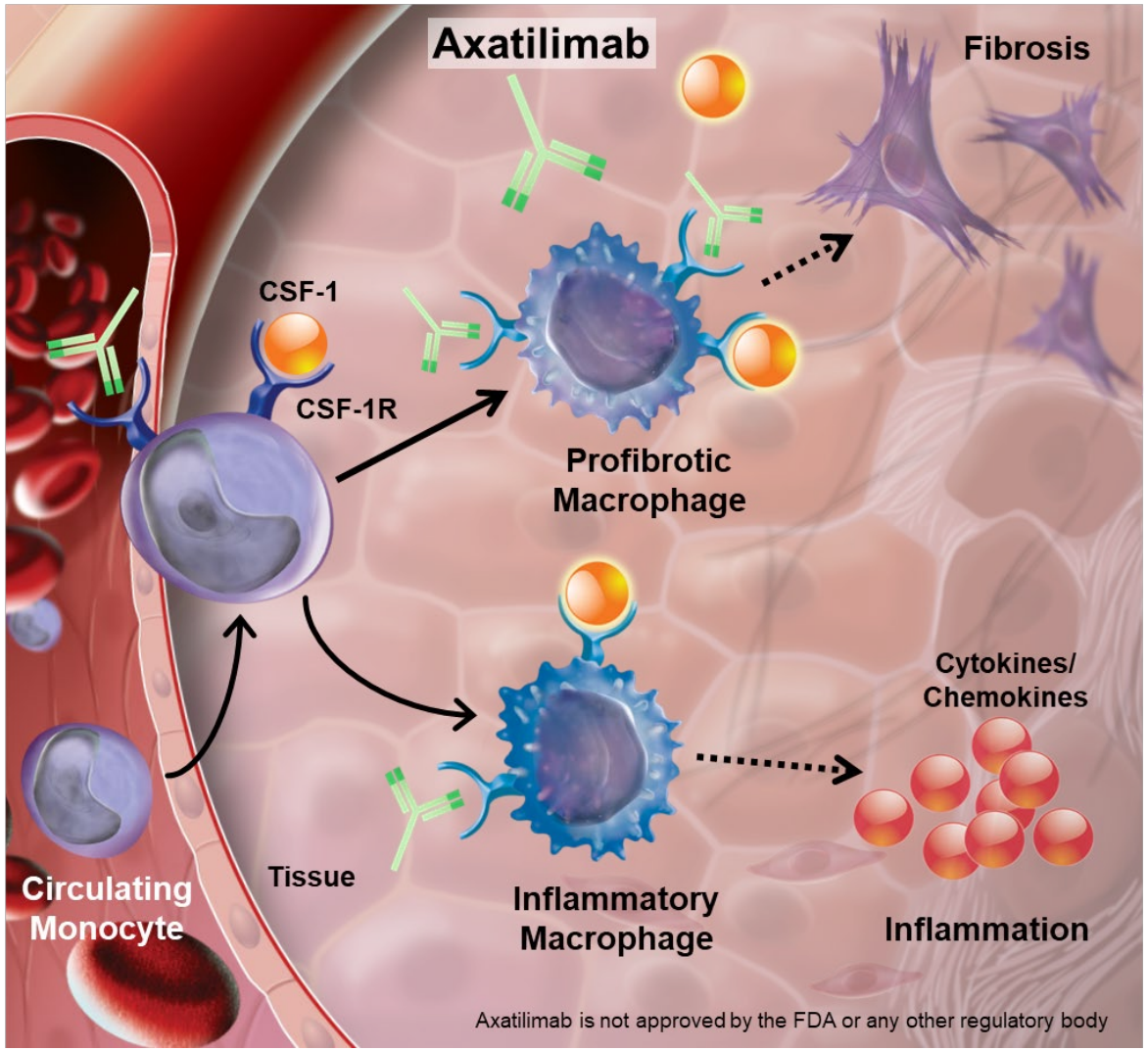
cGVHD, Chronic graft-versus-host disease; CSF-1, Colony-stimulating factor 1; CSF-1R, Colony-stimulating factor 1 receptor

Axatilimab targets key cGVHD pathology mediators

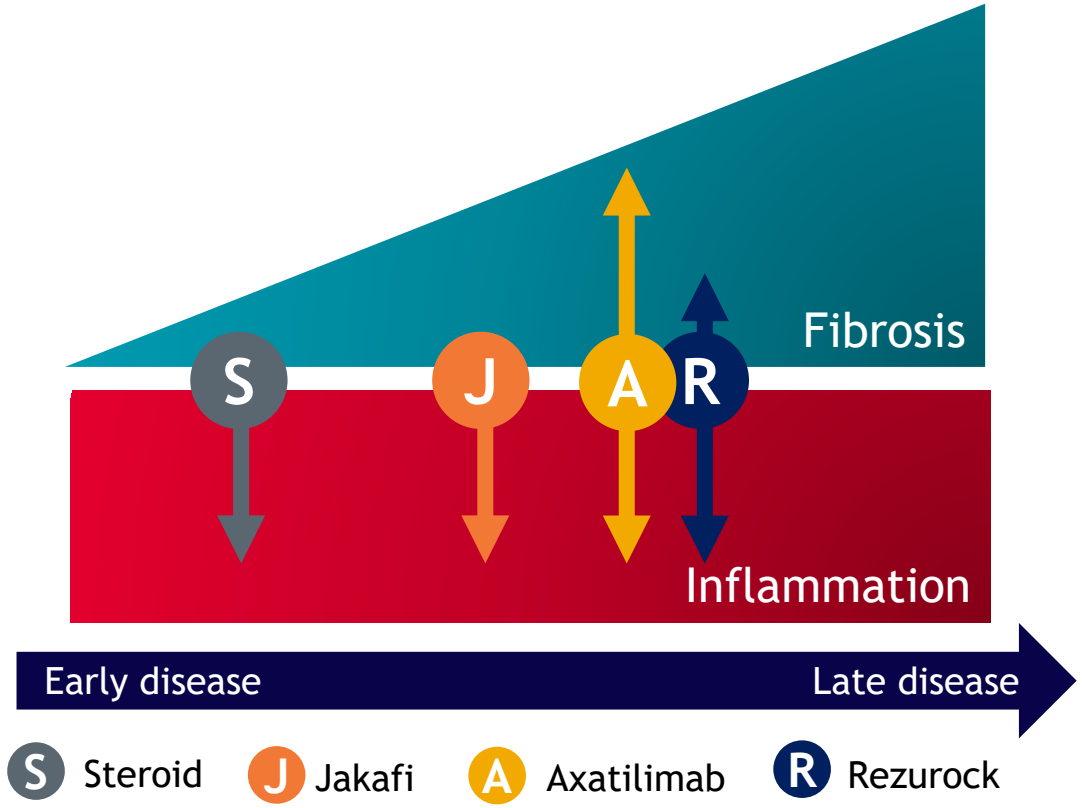
Developing a differentiated, practice-changing intervention in cGVHD

- Axatilimab is a monoclonal antibody that targets CSF-1R on monocytes and macrophages[1]
- Axatilimab inhibits ligand-dependent monocyte and macrophage differentiation and function
- Favorable safety and tolerability profile with promising results in Ph1/2 trial in recurrent/ refractory cGVHD, with an ORR of 67%[1]



1. Kitko et al. *J Clin Oncol*. 2022;41:1864-1875.

Inflammation and fibrosis drive cGVHD

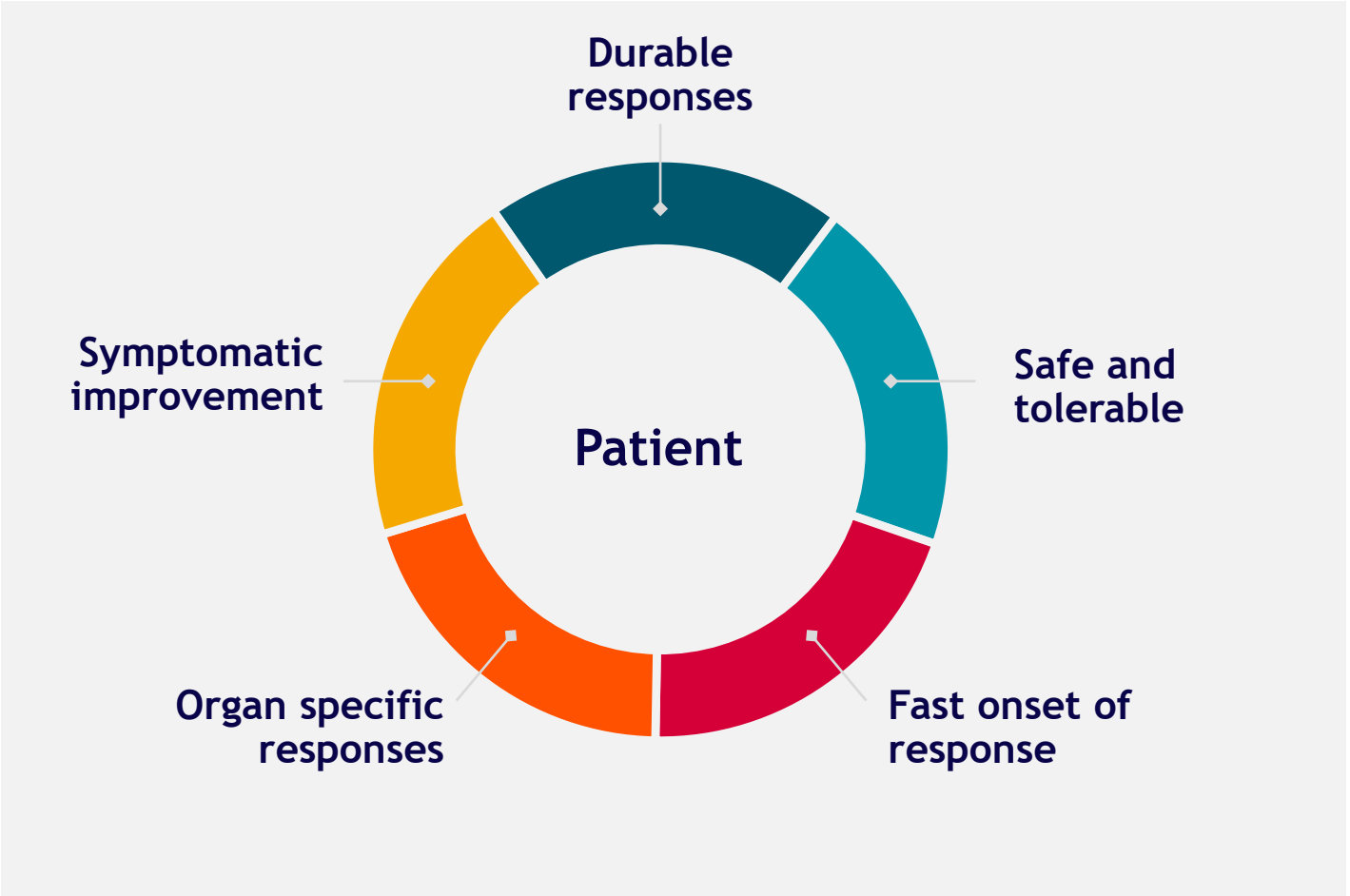


Through CSF-1R inhibition, axatilimab is uniquely positioned to address both hallmarks of cGVHD—inflammation and fibrosis

Currently approved agents inadequately address both inflammation and fibrosis, potentially resulting in suboptimal responses

cGVHD, Chronic graft-versus-host disease; CSF-1R, Colony-stimulating factor 1 receptor

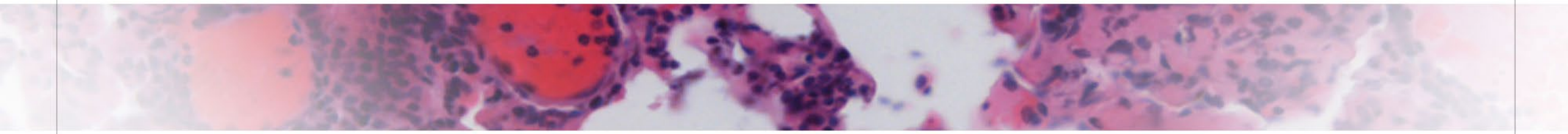
Axatilimab is positioned to address what physicians and patients are seeking in a new cGVHD therapy



Axatilimab Key Attributes

- Demonstrates compelling clinical profile
- Unique MOA in cGVHD
- Benefits in fibrotic and inflammatory components
- Consistent results across all key patient subsets with responses in all organ systems

American Society *of* Hematology
Helping hematologists conquer blood diseases worldwide



Safety and Efficacy of Axatilimab at 3 Different Doses in Patients with Chronic Graft-Versus-Host Disease (AGAVE-201)

Daniel Wolff*, MD, PhD; Corey Cutler,* MD, MPH, FRCPC; Stephanie J. Lee, MD, MPH; Iskra Pusic, MD; Henrique Bittencourt MD, PhD; Jennifer White MD, MSc, FRCPC; Mehdi Hamadani MD; Sally Arai, MD; Amandeep Salhotra, MD; Jose A. Perez-Simon, MD; Amin Alousi, MD; Hannah Choe, MD; Mi Kwon, MD; Arancha Bermúdez, MD; Inho Kim, MD, PhD; Gerard Socie, MD, PhD; Vedran Radojcic, MD; Timothy O'Toole, MS; Chuan Tian, PhD; Peter Ordentlich, PhD; Zachariah DeFilipp,† MD; and Carrie L. Kitko,† MD

*/†Authors contributed equally to this work.

ASH Plenary Session, December 10, 2023

AGAVE-201: Study Design and Methods

Key eligibility criteria

- Age ≥2 years with ≥2 prior lines of systemic therapy
- Active cGVHD defined per 2014 NIH Consensus Criteria[1]
- Concomitant use of corticosteroids (65%), calcineurin inhibitors (28%), or mTOR inhibitors (12%) was allowed but not required
- No additional systemic cGVHD therapy was allowed

Primary endpoint

- ORR in the first 6 cycles as defined by NIH 2014 Consensus Criteria[1]
- Endpoint was met if lower bound of 95% CI >30%

Secondary and exploratory endpoints

- Clinically meaningful improvement in mLSS (≥7 points)
- Organ-specific response rates, DOR, FFS, OS
- Safety

DOR, duration of response; FFS, failure-free survival; mLSS, modified Lee Symptom Scale; mTOR, mammalian target of rapamycin; NIH, National Institutes of Health; OS, overall survival.

1. Jagasia et al. *Biol Blood Marrow Transplant.* 2015;21:389-401.

Baseline Characteristics (ITT Population)

Patient characteristic	Total cohort (N=241)
Age, median (min, max), y	53 (7, 81)
Sex, male, n (%)	151 (63)
Race, White, n (%)	200 (83)
Time from cGVHD diagnosis to randomization, median (max), y	4 (18)
Patients with severe disease, n (%)	192 (80)
Number of organs involved at baseline, median (max)	4 (8)
≥ 4 organs involved, n (%)	130 (54)
Number of prior systemic cGVHD therapies, median (max)	4 (15)
Refractory to last prior cGVHD treatment,[a] n (%)	132 (55)
Prior ruxolitinib, ibrutinib, and/or belumosudil, n (%)	204 (85)
Prior ruxolitinib, n (%)	179 (74)
Prior ibrutinib, n (%)	75 (31)
Prior belumosudil, n (%)	56 (23)

Patient characteristics were well balanced among cohorts

ITT, intention to treat. [a]Defined as patients with a best response to last prior treatment of no change or progressive disease reported at baseline.

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

Population (ITT)	ROCKSTAR N=132	AGAVE-201 N=241
Age median (min, max), years	56 (21, 77)	53 (7, 81)
Median time since cGVHD diagnosis	25.3 months	48 months
≥ 4 organs involved	52%	54%
% Patients with lung manifestations	36%	45%
% patients with NIH severe cGVHD	67%	80%
Median prior therapies	3	4
≥ 4 prior lines of treatment	49%	65%
Prior ruxolitinib	29%	74%
Prior ibrutinib	34%	31%
Prior belumosudil	N/A	23%

AGAVE-201 Differentiation

Significantly longer time since diagnosis

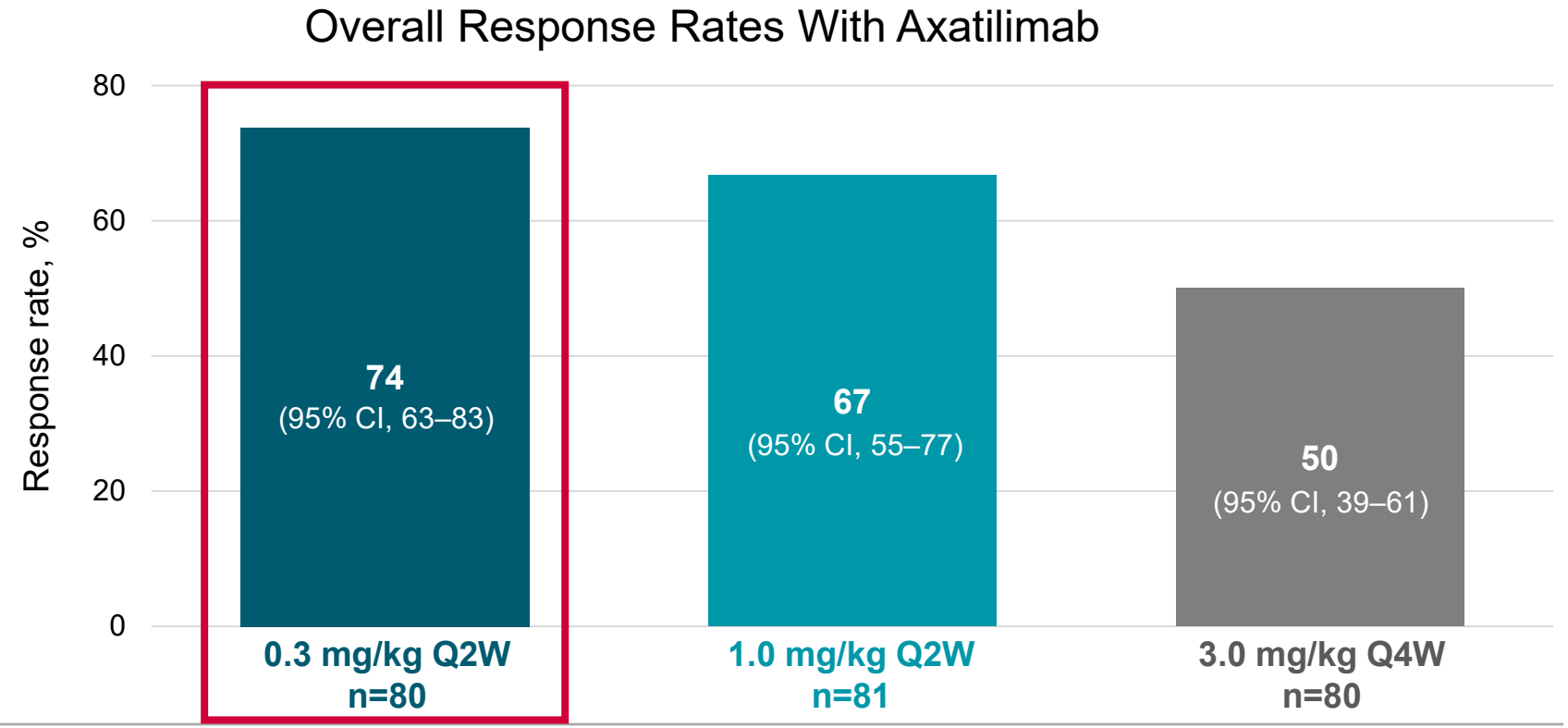
More severe cGVHD

More reflective of real-world treatment

Axatilimab AGAVE-201 Data

Dr. Daniel Wolff
Professor of Hematology, Department of Internal Medicine III of the University of Regensburg

Primary Efficacy Endpoint[a] Met in All Cohorts

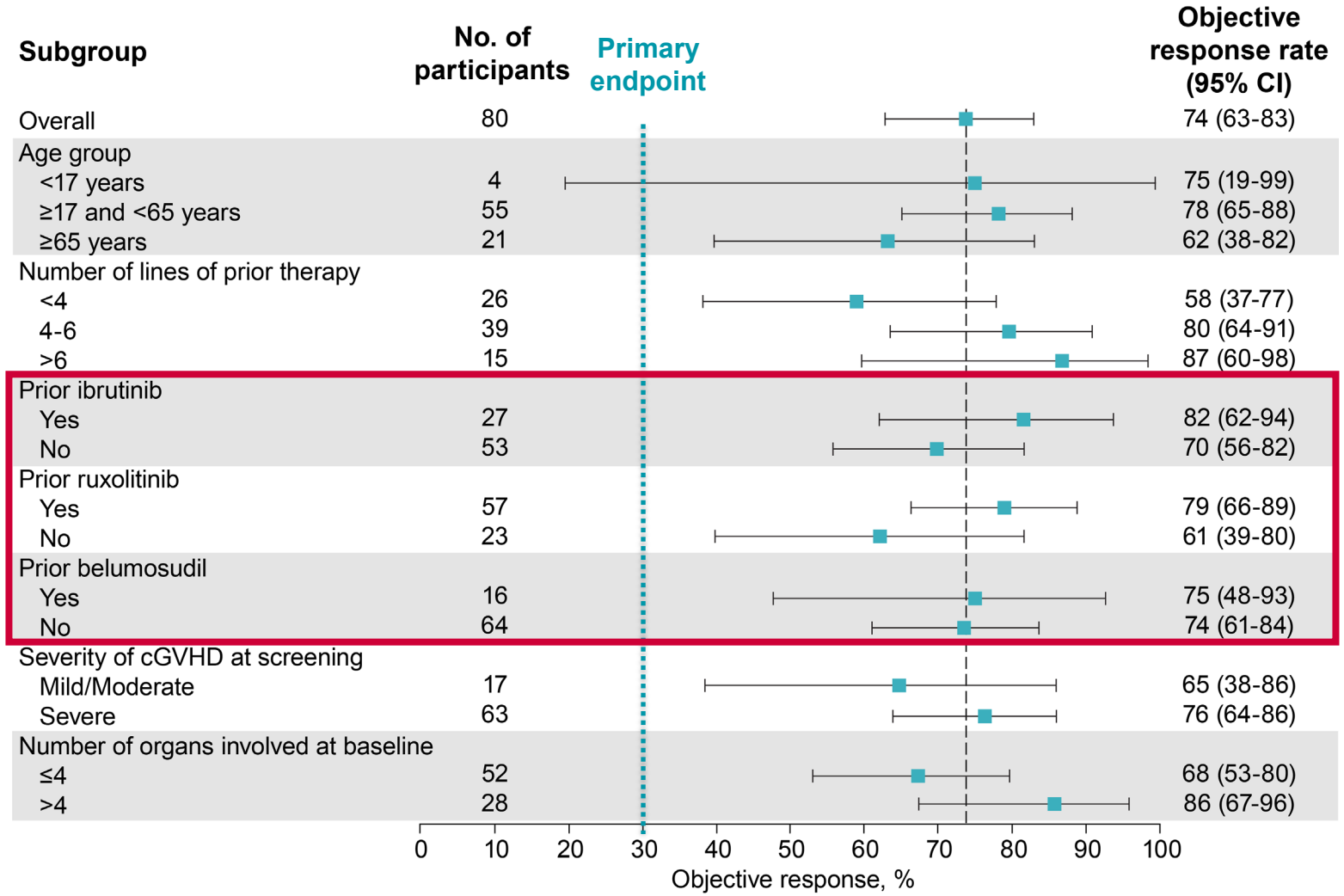


	0.3 mg/kg Q2W n=80	1.0 mg/kg Q2W n=81	3.0 mg/kg Q4W n=80
Time to response, median months (range)	1.7 (0.9–8.1)	1.9 (0.9–8.6)	1.4 (0.9–5.6)
Response maintained for ≥12 months, % (95% CI)	60 (43–74)	60 (43–74)	53 (30–71)

Q2W, every 2 weeks; Q4W, every 4 weeks.
[a]Primary endpoint was overall response rate in the first 6 cycles as defined by NIH 2014 Consensus Criteria.[1]

1. Lee at al. *Biol Blood Marrow Transplant*. 2015;21:984-999.

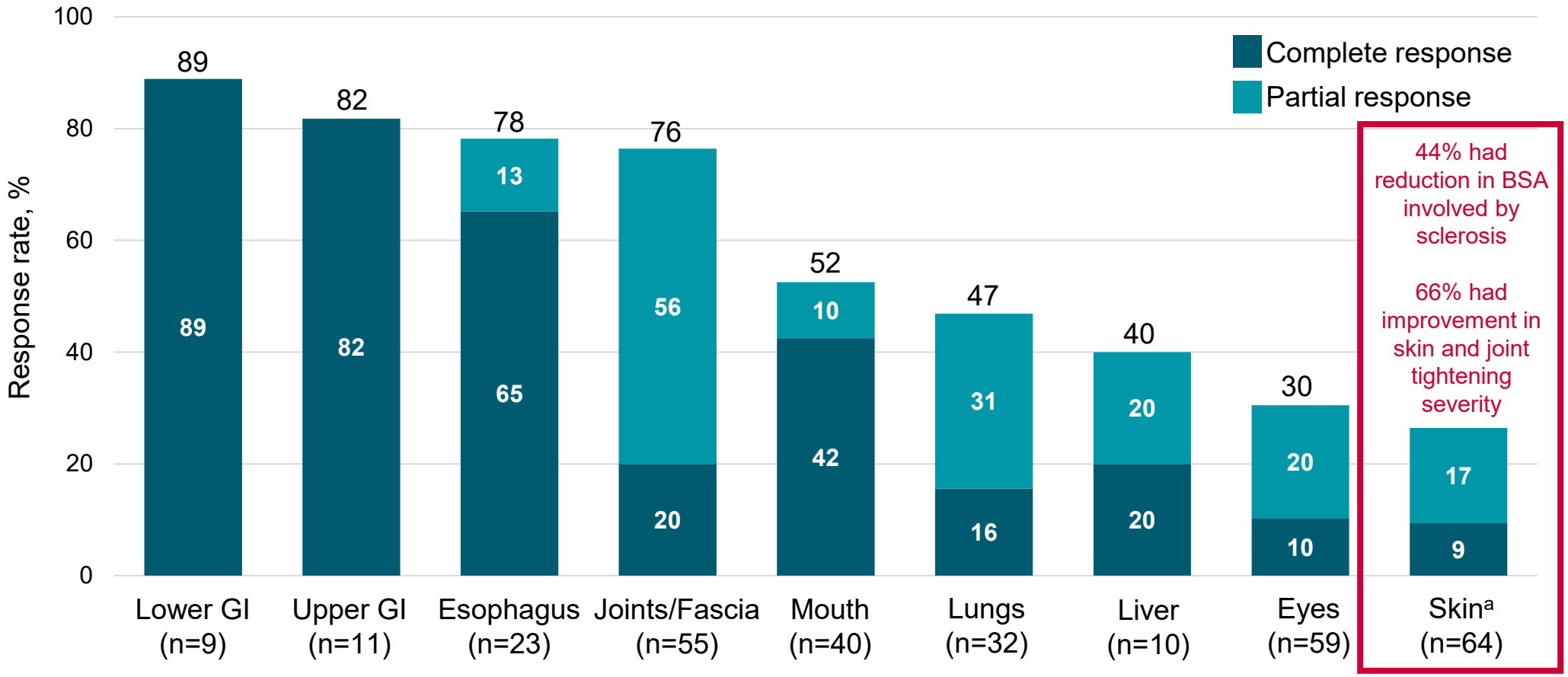
Efficacy Across Subgroups in 0.3 mg/kg Q2W



High response rates (≥75%) were seen in patients who received prior FDA-approved therapies

Q2W, every 2 weeks.

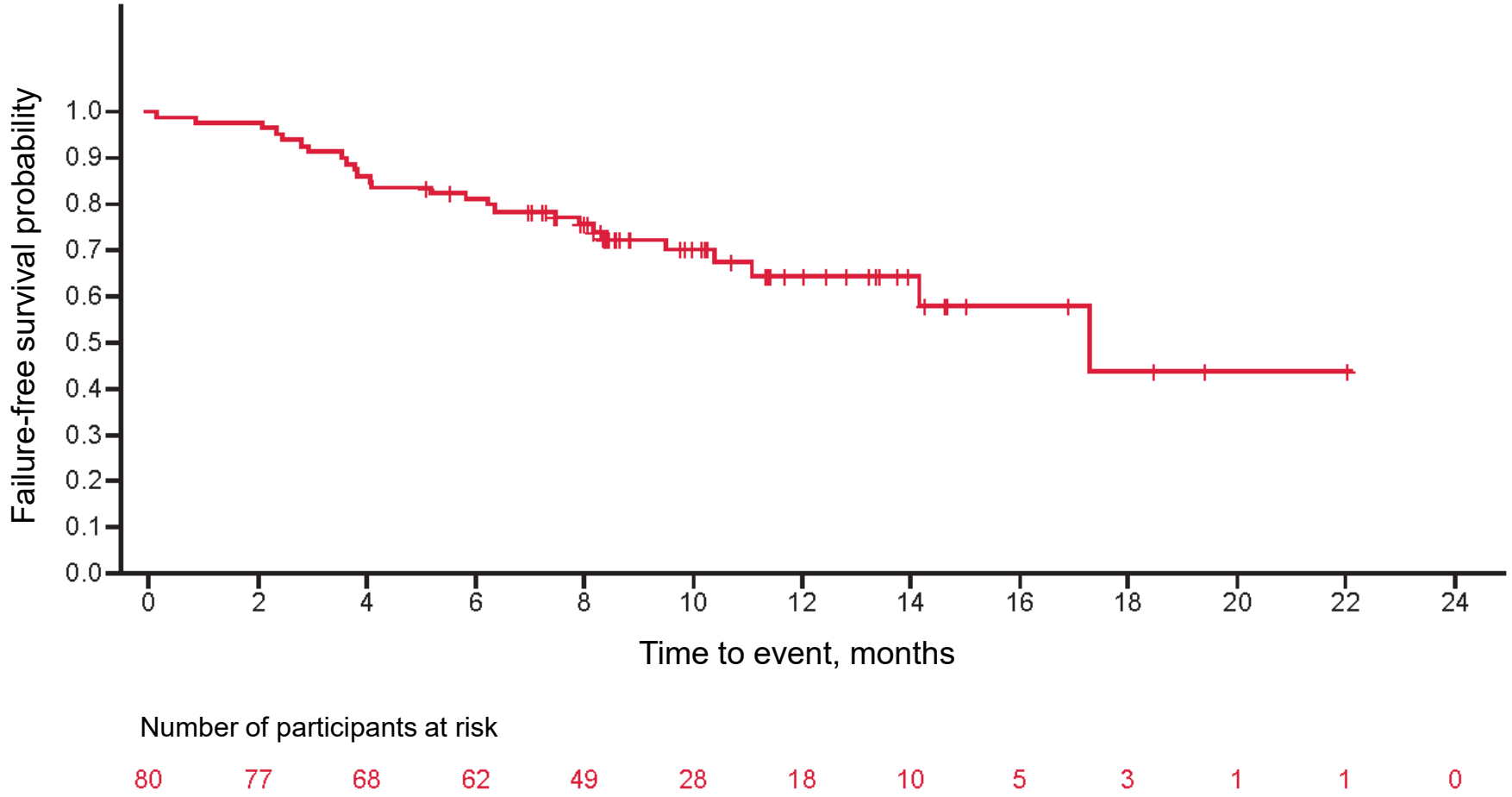
Organ Responses in 0.3 mg/kg Q2W



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

BSA; body surface area; GI, gastrointestinal; Q2W, every 2 weeks. [a]Due to rounding, complete response and partial response numbers may not add up to total response rate.

Failure-free Survival[a] in 0.3 mg/kg Q2W

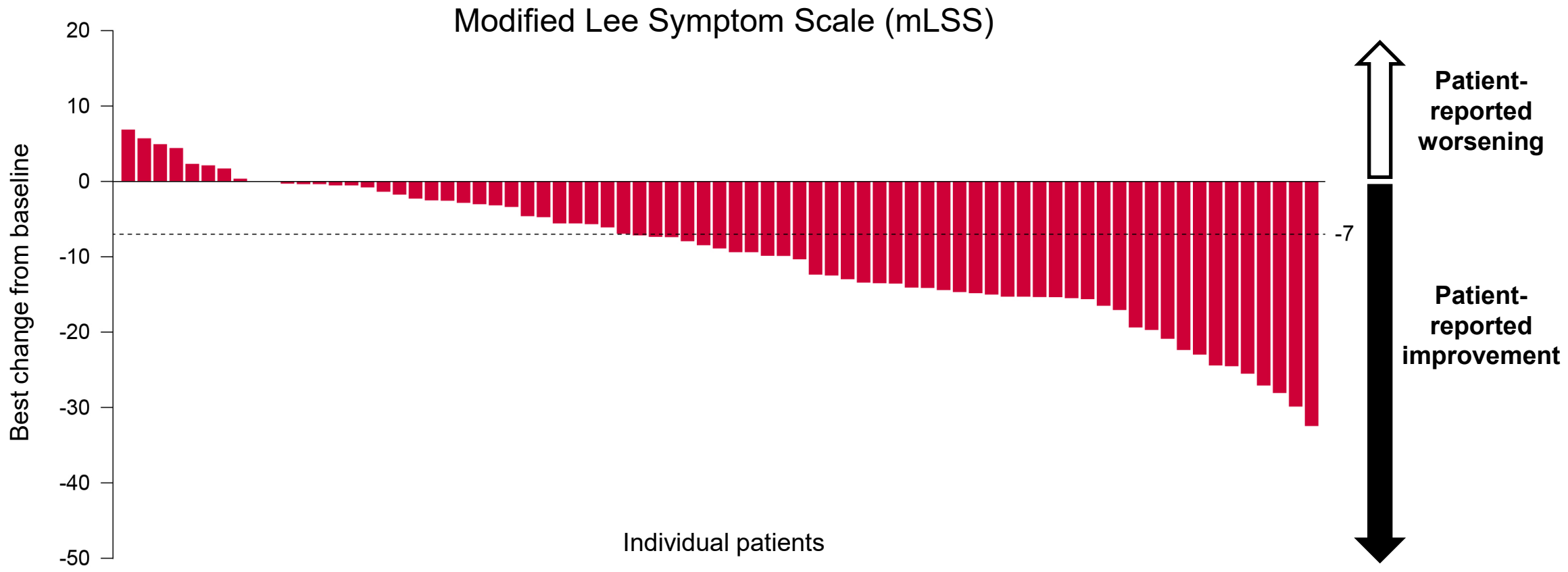


Median FFS was 17.3 (95% CI, 14.2–NE) months

NE, not estimable; Q2W, every 2 weeks.

[a]Defined as time from randomization to death or new systemic cGVHD therapy, where axatilimab dose increase is not considered new therapy.

Patient-Reported Symptom Burden Change in 0.3 mg/kg Q2W



- 55% clinically meaningful change of ≥7-point improvement in mLSS
- Median time to ≥7-point mLSS improvement was 1.5 months
- 73% had improved mLSS skin thickened score from baseline

Q2W, every 2 weeks.

Axatilimab Safety Profile

	Axatilimab 0.3 mg/kg Q2W n=79	Axatilimab 1.0 mg/kg Q2W n=81	Axatilimab 3.0 mg/kg Q4W n=79
Axatilimab dose changes owing to AE, n (%)			
Discontinuation	5 (6.3)	18 (22.2)	14 (17.7)
Dose decrease	5 (6.3)	6 (7.4)	13 (16.5)
Any grade AE in ≥20% of total patients			
Fatigue	18 (22.8)	16 (19.8)	21 (26.6)
Headache	15 (19.0)	14 (17.3)	16 (20.3)
Periorbital edema	2 (2.5)	19 (23.5)	23 (29.1)
COVID-19	13 (16.5)	18 (22.2)	11 (13.9)
Laboratory-based abnormalities			
AST increase	11 (13.9)	31 (38.3)	43 (54.4)
CPK increase	9 (11.4)	26 (32.1)	49 (62.0)
Lipase increased	9 (11.4)	21 (25.9)	39 (49.4)
Lactate dehydrogenase increased	11 (13.9)	22 (27.2)	32 (40.5)
ALT increase	10 (12.7)	18 (22.2)	31(39.2)
Amylase increase	3 (3.8)	10 (12.3)	34 (43.0)
At least 1 related Grade ≥3 AE, n (%)	14 (17.7)	28 (34.6)	37 (46.8)
Fatal AE	1 (1.3)[a]	7 (8.6)[b]	6 (7.6)[c]

AE, adverse event; ALT, alanine aminotransferase; AST, aspartate aminotransferase; CPK, blood creatine kinase; Q2W, every 2 weeks; Q4W, every 4 weeks. [a]Dyspnea. [b]Sudden cardiac death, bronchopulmonary aspergillosis, pneumonia (n=2), sepsis, leukemia recurrent, respiratory failure. [c]Leukemia recurrent, dyspnea, respiratory failure, shock hemorrhagic, neutropenic sepsis, pneumonia.

Conclusion: Axatilimab 0.3 mg/kg Q2W is highly effective in patients with recurrent/refractory cGVHD

- Responses documented in all organs and patient subgroups, including those with fibrotic cGVHD manifestations
  - Complete responses observed in all organ systems including the most difficult to treat organs such as lung

- Rapid and significant symptom burden reduction reported by 85% of patients
  - Clinical responses in symptom reduction occurred rapidly at a median of 1.5 months
  - Patient improvement and clinical response occurred simultaneously

cGVHD, Chronic graft-versus-host disease; Q2W, Every 2 weeks

Conclusion: Axatilimab 0.3 mg/kg Q2W is well tolerated in patients with recurrent/refractory cGVHD

- No unexpected safety concerns
  - AEs consistent with vulnerabilities of cGHVD patients
  - Mostly low grade, reversible, and dose dependent
- Potential to benefit patients alone or in combination with SOC therapies already available
- Robust, well powered clinical trial
  - Real world population with a low steroid dose, no concomitant use for cGVHD
- The recommended axatilimab dose for future trials in cGVHD is 0.3 mg/kg q2wks
  - Phase 2 Jakafi® combo and Phase 3 steroid combo trials to begin in mid-2024

AE, Adverse event; cGVHD, Chronic graft-versus-host disease; Q2W, Every 2 weeks, SOC, Standard of care

Axatilimab Close and Q&A

Michael Metzger
Chief Executive Officer, Syndax

Axatilimab has the potential to be a differentiated treatment option for cGHVD

Unique MOA for cGVHD

- First agent to target disease causing macrophages to impact fibrosis & inflammation
- Potential synergy with SOC

High and durable responses

- 74% ORR at 0.3 mg/kg
- 60% of patients treated at 0.3 mg/kg remained in response at 12 months

Well tolerated supporting broad use

- Low rate of SAEs and discontinuations at 0.3 mg/kg
- Antibody reduces potential for DDIs vs small molecule competitors

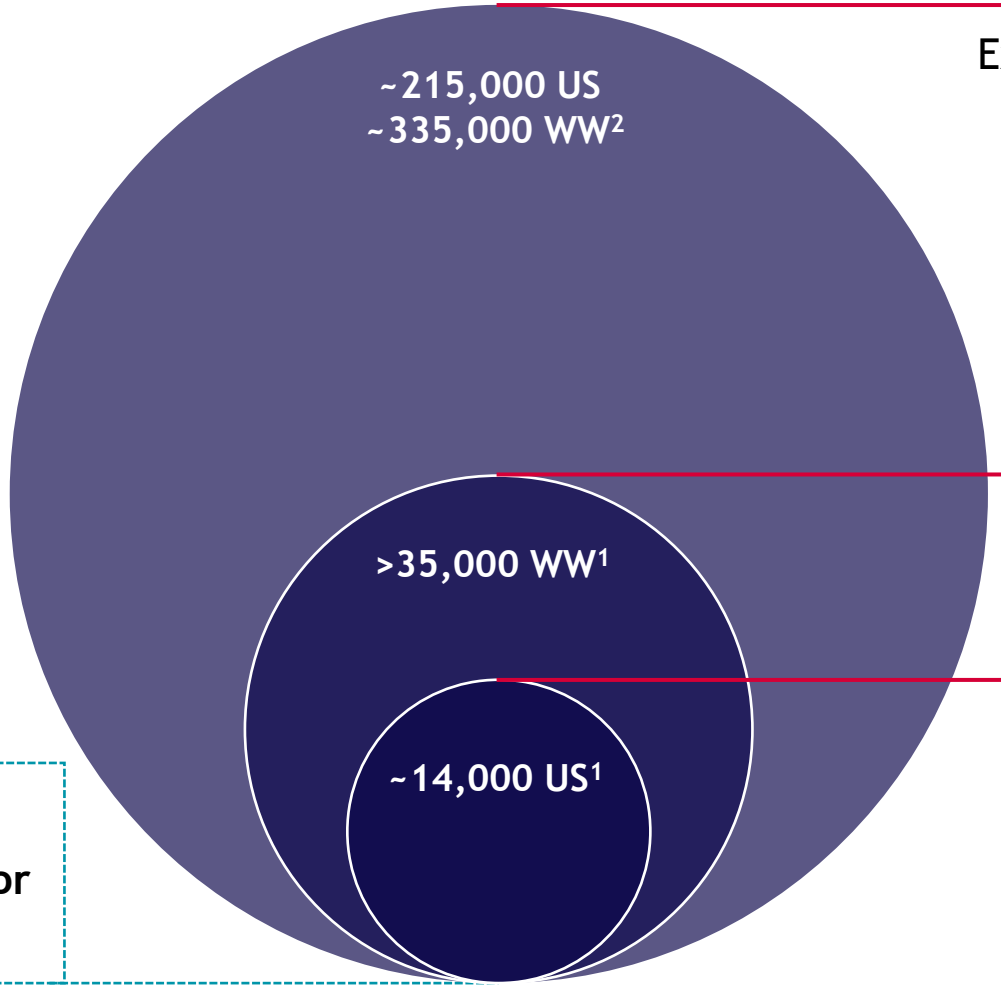
Enrolled population reflects real world

- Efficacy results observed in patients following treatment with current SOC
- Option to switch to Q4W dose at 6 months

DDI, Drug-drug interaction; SOC, Standard of care; ORR, Overall response rate; SAEs, Serious adverse events; Q4W, Every 4 weeks

Axatilimab has the potential to expand into additional high value indications and new geographies

2024 & Beyond



Expansion into fibrotic indications:
IPF POC* init YE23

Expansion into EU, Japan, ROW

R/R chronic GVHD:
BLA submission expected YE23

Expansion into 1st L chronic GVHD:
Jakafi® combo trial init mid-24
Steroid combo trial init mid-24

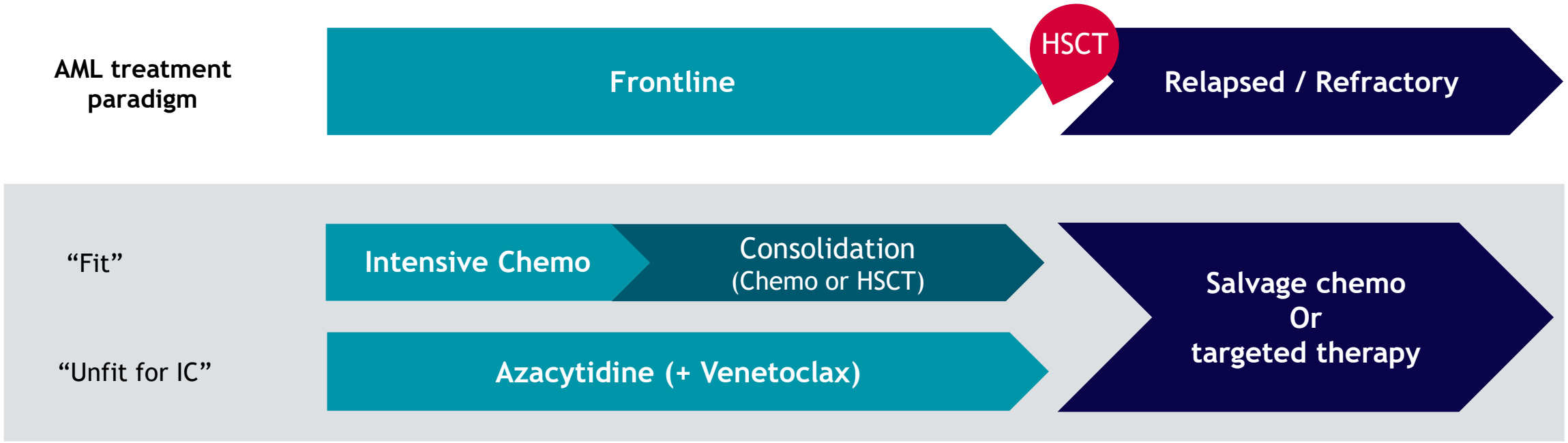
2024
Potential approval for R/R chronic GVHD

1 SmartImmunology Insights cGVHD report March 2020; 2 SmartImmunology Insights IPF report March 2020. * IPF trial will be conducted and funded by Syndax

Acute Leukemia Overview

Dr. Eytan Stein
Chief, Leukemia Service, Director, Program for Drug Development in Leukemia, Memorial Sloan Kettering Cancer Center

AML treatment paradigm



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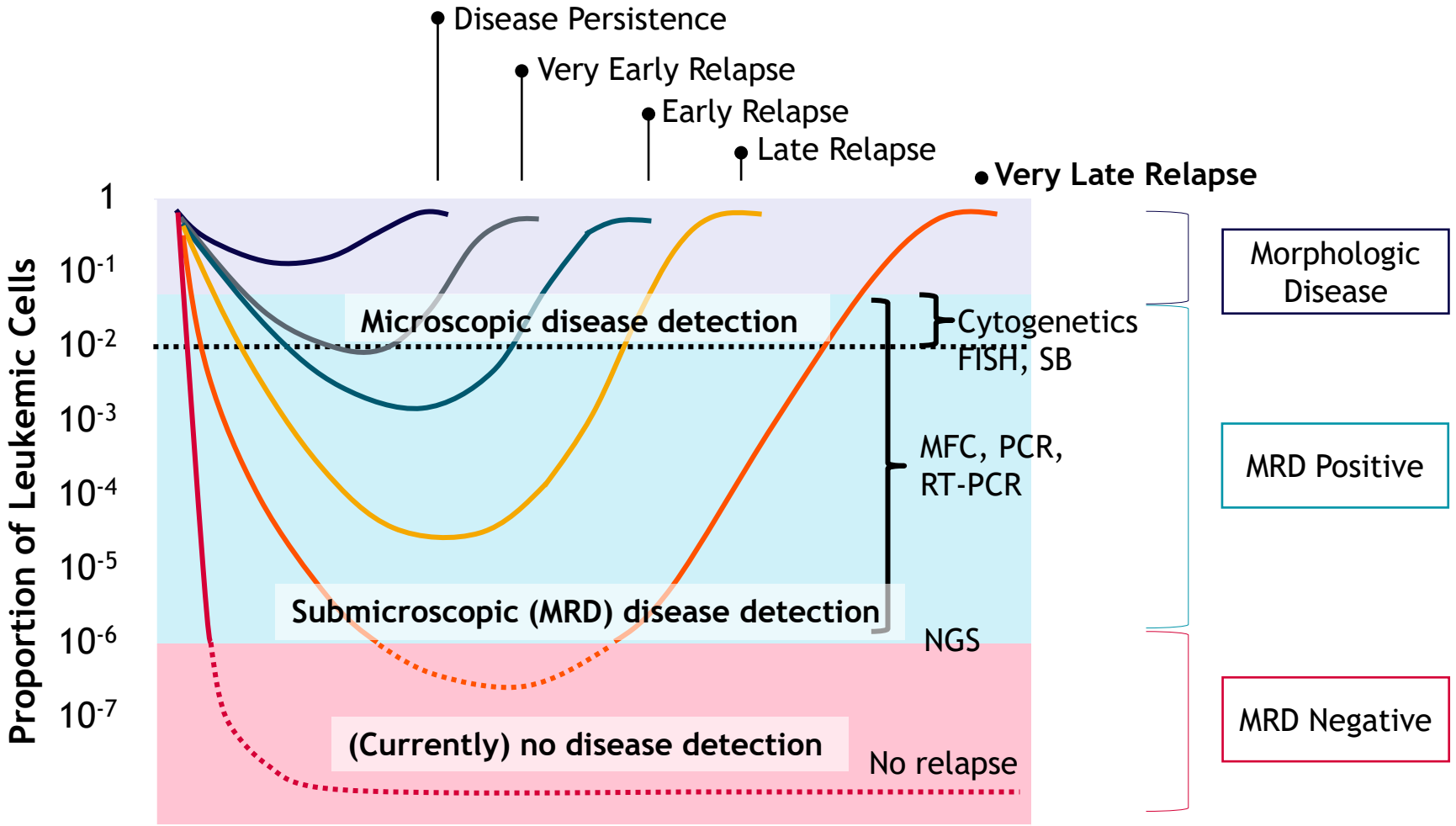
2022 ELN recommendations for the management of AML in adults (aml-hub.com); ORR, Overall response rate; CRc, Composite complete remission; ANC, absolute neutrophil count; BM, bone marrow; CR, complete remission; CRh, CR with partial hematologic recovery; CRi, CR with incomplete hematologic recovery;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

Measurable residual disease has prognostic implications for clinical practice



MRD Definition:
Residual leukemia not detected by morphology (<5% blasts)

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Adapted from: Buckley. Bone Marrow Transplant. 2013;48:630.

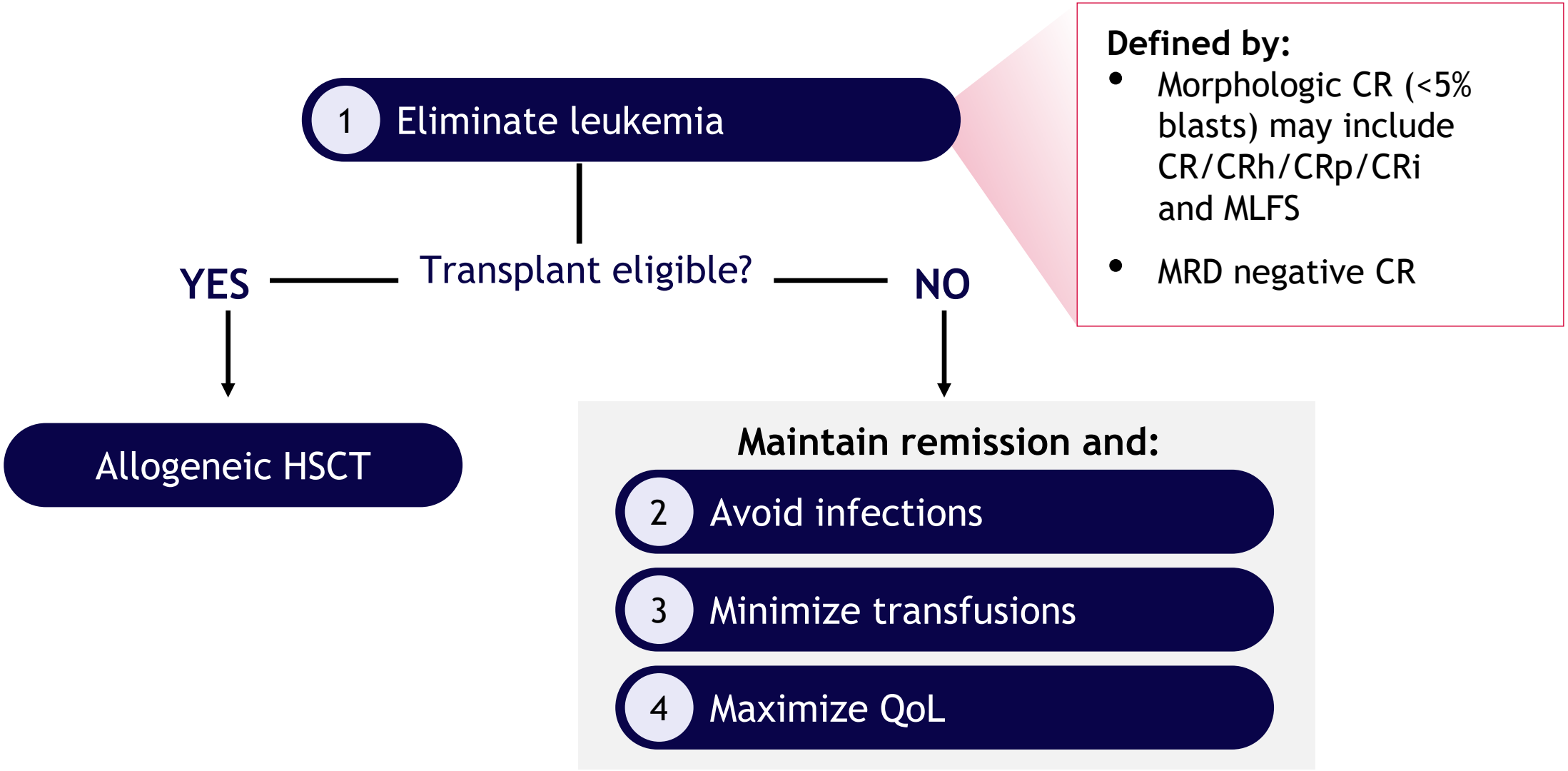
Treatment goals for patients with relapsed/refractory acute leukemia

1 Eliminate leukemia

Defined by:

- Morphologic CR (<5% blasts) may include CR/CRh/CRp/CRi and MLFS
- MRD negative CR

Treatment goals for patients with relapsed/refractory acute leukemia



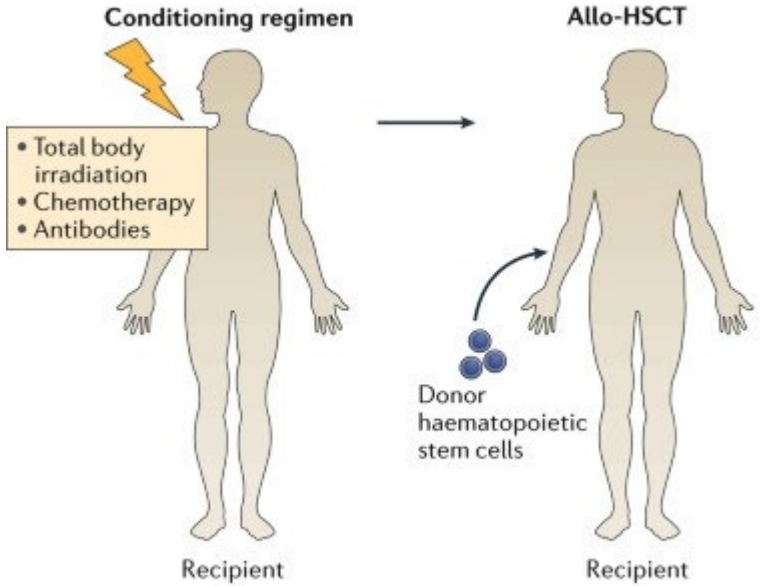
Goals and rationale for transplantation

HSCT

Allogeneic HSCT is the only known method to completely cure AML

Step 1:
Marrow cleared to ≤ 5% tumor blast count (CRc or MLFS); & BM donor identified

Step 2:
Conditioning* performed to ablate bone marrow and enable engraftment



Step 3:
Bone marrow or peripheral blood stem-cell graft infused

Potential complications:

- **Pancytopenia**, gastrointestinal toxicities, infections, and organ dysfunction (conditioning regimens can be more aggressive than intensive chemotherapy)
- Development of GVHD (acute and/or chronic)

Despite recent advances in AML and ALL, treatment options are needed for patients with KMT2Ar and mNPM1 acute leukemias

KMT2Ar Acute Leukemia

10%

of AML or ALL[1]

Most patients relapse after chemotherapy and HSCT

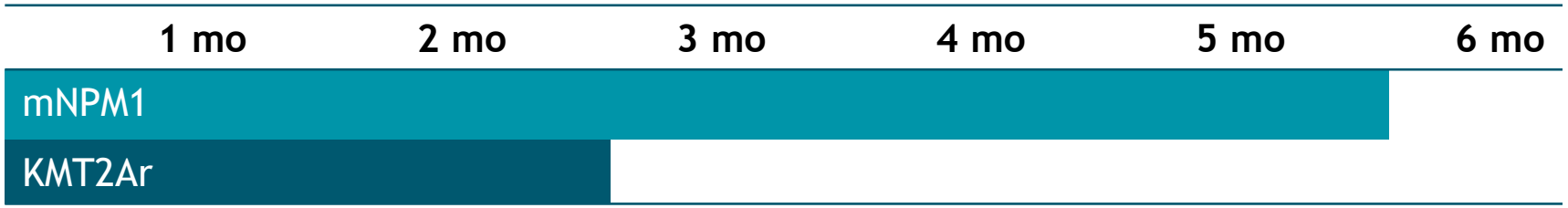
NPM1 Mutant AML

30%

of AML[2]

Most frequent genetic alteration in AML

Median overall survival in 3rd line AML[1,3]

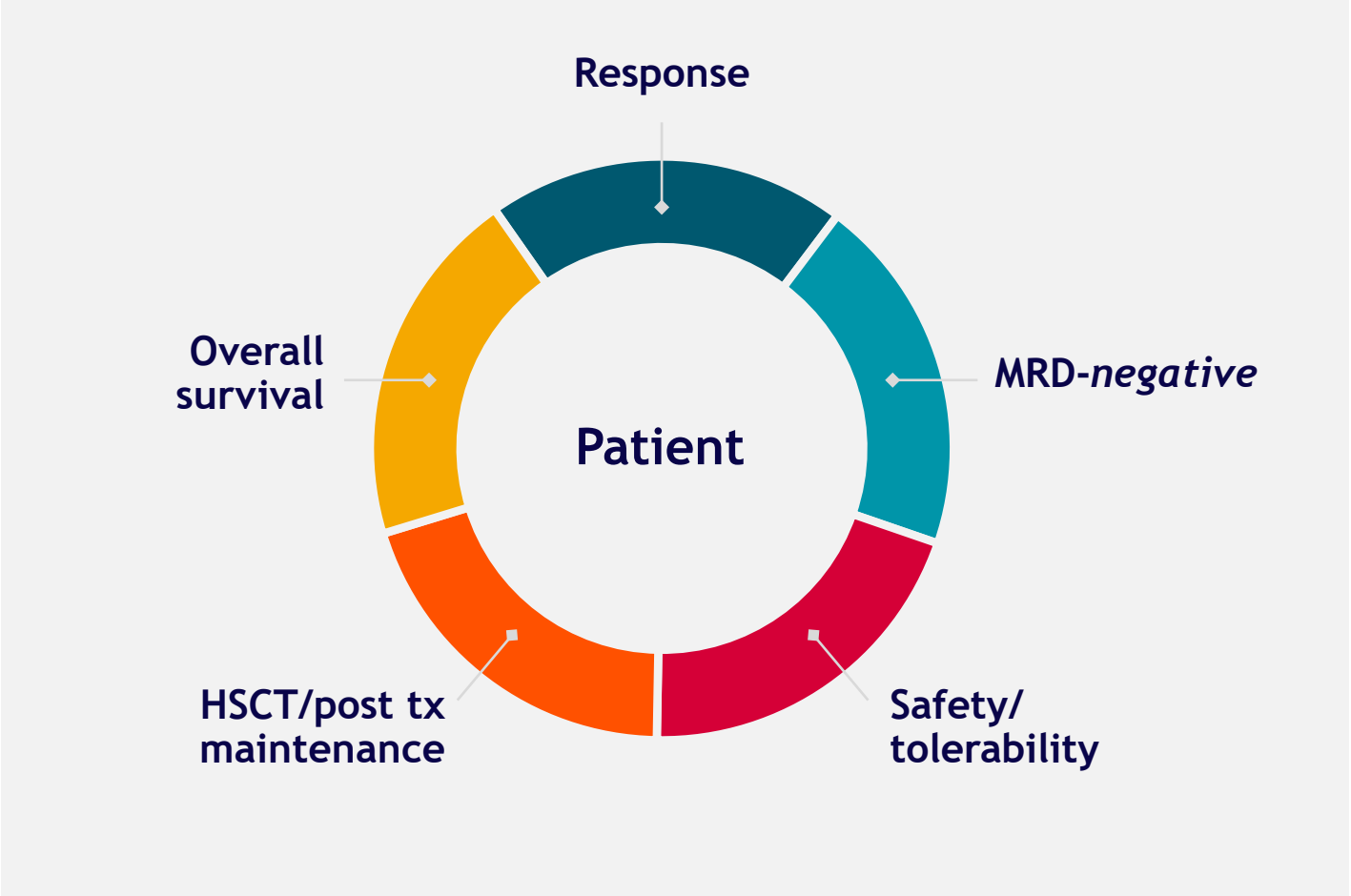


Revumenib has demonstrated positive clinical results in both KMT2Ar and mNPM1 acute leukemia populations

Syndax

1) Issa, G. et al. (2021). Predictors of outcomes in adults with acute myeloid leukemia and KMT2A rearrangements. 2). Falini, B. et al, NPM1-mutated acute myeloid leukemia: from bench to bedside. Blood (2020) 136 (15) 3) Issa G. et al. Clinical outcomes associated with NPM1 mutations in patients with relapsed or refractory AML. Blood Adv. 2023 Mar 28;7(6) ; OS, Overall response

Revumenib is positioned to deliver on key metrics that would address the needs of patients



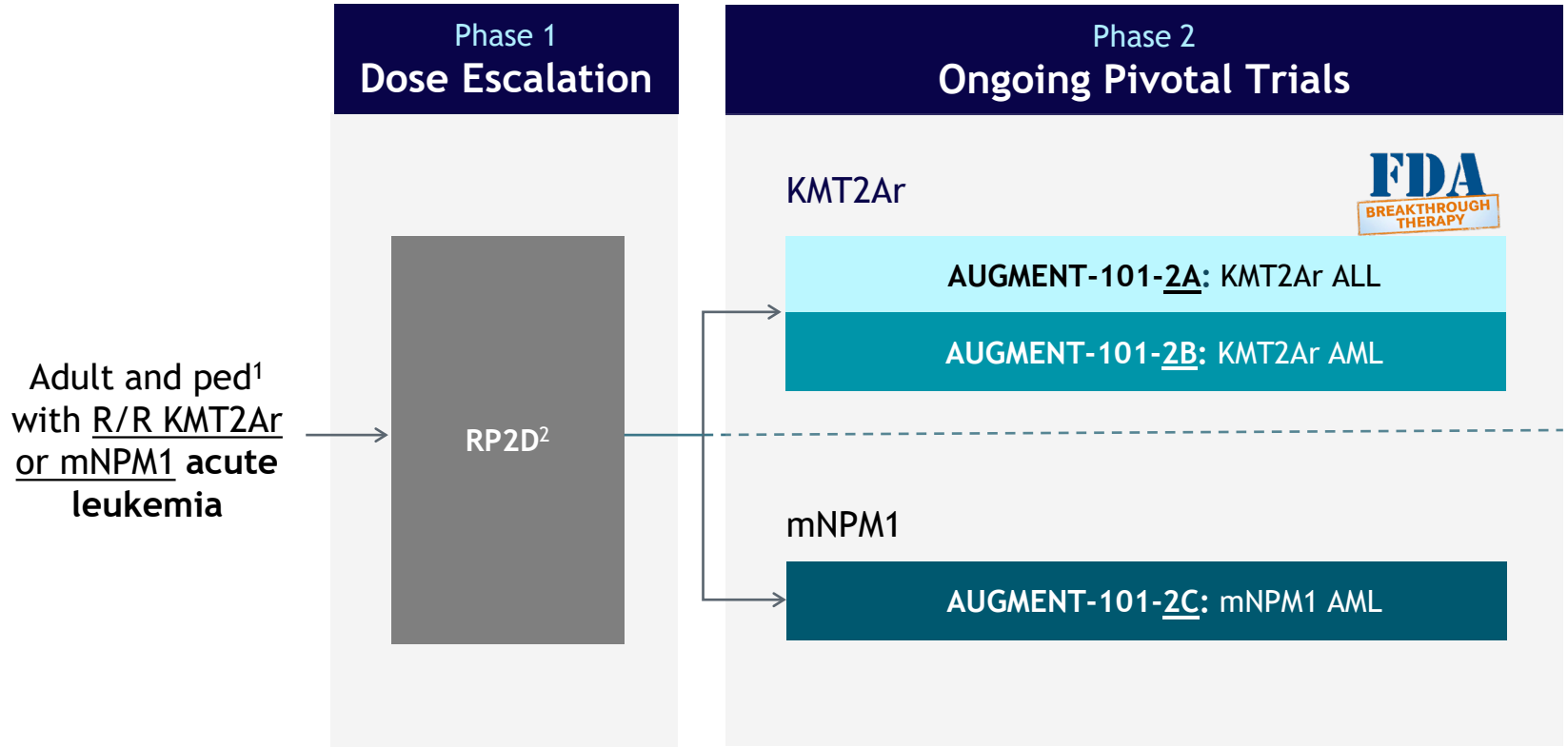
Revumenib Key Attributes

- Demonstrates encouraging clinical profile
- Overall treatment profile that enables R/R to receive HSCT, and post-Tx maintenance
- Convenient route of administration

AUGMENT-101 and SAVE Trial Results

Dr. Ghayas Issa
Assistant Professor, Department of Leukemia, Division of Cancer Medicine, The University of Texas MD Anderson Cancer Center

Pivotal AUGMENT-101 in KMT2Ar and mNPM1 acute leukemias trial design



Patients taken to HSCT can restart treatment with revumenib post-transplant; Abbreviations: KMT2Ar, KMT2A rearrangement, mNPM1, mutated nucleophosmin

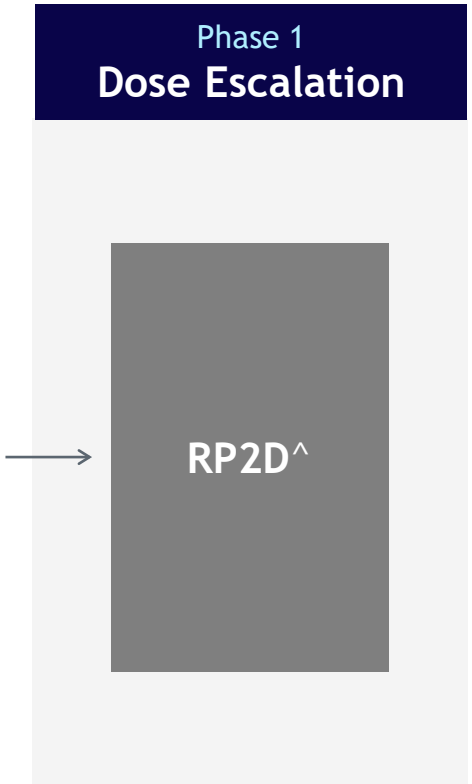
[1] Allows patients ≥30 days of age

[2] 2276mg q12h or 163mg q12h w/ strong CYP3A4 inhibitor

Demographics and design of KMT2Ar patients enrolled into AUGMENT-101 Phase 1 trial

ASH23 #2907

Adult and ped[1] with R/R KMT2Ar **acute leukemia (including AML, ALL, MPAL)**



^ pts assigned to 1 of 6 cohorts to identify RP2D for concomitant use of mod or strong or no CYP3A4i

Demographics	Phase 1 *KMT2Ar* population				
Parameter	Adult AML (n=51)	ALL / Other[b] (n=15)	Peds[c] (n=15)	Efficacy *KMT2Ar* (n=77)	Safety population (n=132)
Median age, y (range)	40.0 (19.0-79.0)	34.0 (1.0-74.0)	9.0 (1.0-16.0)	33.0 (1.0-79.0)	41.0 (0.8-82.0)
Sex, n (%)					
Female	30 (58.8)	10 (66.7)	10 (66.7)	46 (59.7)	70 (53.0)
Ethnicity, n (%)					
Hispanic/Latino	12 (23.5)	1 (6.7)	9 (60.0)	21 (27.3)	31 (23.5)
Not Hispanic/Latino	34 (66.7)	13 (86.7)	6 (40.0)	50 (64.9)	95 (72.0)
Unknown	5 (9.8)	1 (6.7)	0	6 (7.8)	6 (4.5)
Race					
White	28 (54.9)	11 (73.3)	8 (53.3)	46 (59.7)	93 (70.5)
Non-White	14 (27.5)	2 (13.3)	5 (33.3)	19 (24.7)	26 (19.7)
Unknown	9 (17.6)	2 (13.3)	2 (13.3)	12 (15.6)	13 (9.8)
Leukemia type, n (%)					
AML	51 (100.0)	0	11 (73.3)	62 (80.5)	114 (86.4)
ALL	0	13 (86.7)	4 (26.7)	13 (16.9)	14 (10.6)
MPAL/Other	0	2 (13.3)	0	2 (2.6)	4 (3.0)
Median prior Tx (range)	3 (1-8)	3 (1-9)	3 (1-9)	3 (1-9)	3 (1-12)
≥4 prior Tx, n (%)	16 (31.4)	5 (33.3)	7 (46.7)	26 (33.8)	44 (33.3)
Prior venetoclax, n (%)	33 (64.7)	5 (33.3)	9 (60.0)	46 (59.7)	85 (64.4)
Prior HSCT, n (%)	26 (51.0)	5 (33.3)	6 (40.0)	36 (46.8)	58 (43.9)
>1 prior HSCT	12 (23.5)	2 (13.3)	2 (13.3)	15 (19.5)	20 (15.2)

ALL, acute lymphoblastic leukemia; AML, acute myeloid leukemia; HSCT, hematopoietic stem cell transplant; *KMT2Ar*, histone-lysine N-methyltransferase 2A rearrangements; MPAL, mixed phenotype acute leukemia; *mNPM1*, mutated nucleophosmin 1. [a]Data cutoff: July 24, 2023. Some patients may have had <4 months of follow-up. Two pediatric patients switched from *KMT2Ar* to *nNPM1*. Another patient's *KMT2Ar* status changed to "no" at screening. [b]Includes all ages. [c]Includes all leukemia subtypes.

In Phase 1, KMT2Ar patients experienced strong response to revumenib

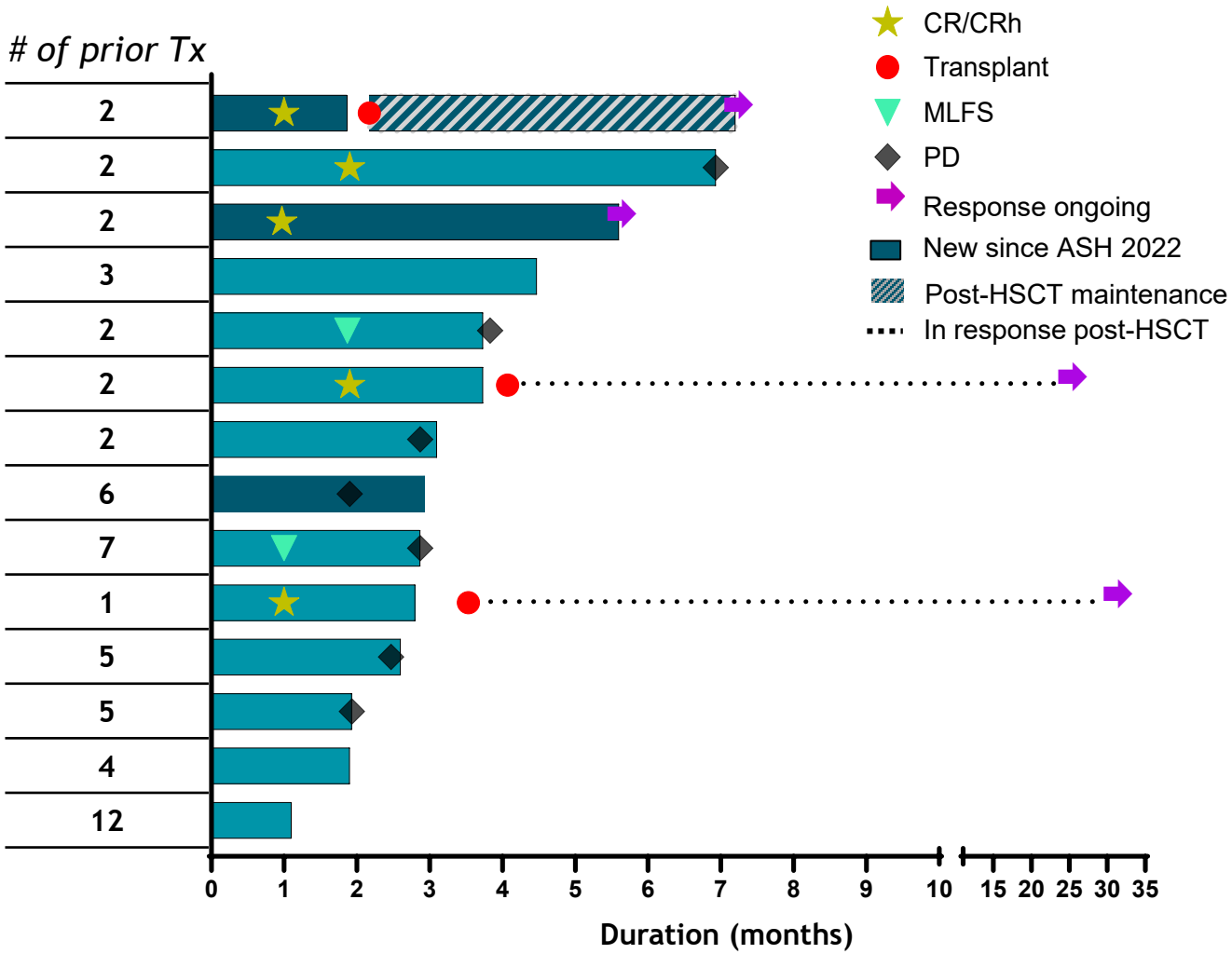
ASH23 #2907

Efficacy (*KMT2Ar* acute leukemia)				
Parameter	Adult AML (n=51)	ALL/Other (n=15)	Peds[c] (n=15)	Overall *KMT2Ar* (n=77)
ORR, n (%)	35 (69)	8 (47)	10 (67)	50 (65)
Best response, n (%)				
CR+CRh rate, n (%)	19 (37)	4 (27)	3 (20)	24 (31)
CRc, n (%)	26 (51)	5 (33)	5 (33)	34 (44)
CR	*15 (29)*	*3 (20)*	*1 (7)*	*18 (23)*
CRh	*4 (8)*	*1 (7)*	*2 (13)*	*6 (8)*
CRi	*2 (4)*	*--*	*--*	*2 (3)*
CRp	*5 (10)*	*1 (7)*	*2 (13)*	*8 (10)*
MLFS	*9 (18)*	*2 (13)*	*5 (33)*	*15 (19.5)*
PR	*--*	*1 (7)*	*0*	*1 (1)*
Other[d]	16 (31)	7 (47)	5 (33)	27 (35)
MRD-neg status in CR+CRh, n (%)	12/17 (71)	3/3 (100)	2/2 (100)	16/21 (76)
MRD-neg status in CRc, n (%)	18/24 (75)	4/4 (100)	4/4 (100)	25/31 (81)
Responders going to HSCT, n (%)	14 /35 (40)	1/8 (13)	4/10 (40)	19/50 (38)

Safety (all patients)	
All terms	Safety pop (n=132)
Any grade TEAE, n (%)	128 (97)
Any grade TEAEs in ≥25% patients	
Nausea	63 (48)
QTc prolongation	48 (36)
Vomiting	46 (35)
Febrile neutropenia	40 (30)
Fatigue	38 (29)
Diarrhea	33 (25)
≥Grade 3 TEAE, n (%)	107 (81)
≥Grade 3 TEAE in ≥10% patients	
Febrile neutropenia	39 (30)
Decreased platelet count	20 (15)
Anemia	18 (14)
Sepsis	17 (13)
Decreased neutrophil count	15 (11)
Decreased white blood cell count	15 (11)

AE, adverse event; ALL, acute lymphoblastic leukemia; AML, acute myeloid leukemia; 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*, histone-lysine N-methyltransferase 2A rearrangements; MLFS, morphological leukemia-free state; MRD, measurable residual disease; *NPM1m*, mutated nucleophosmin 1; ORR, overall response rate (CRc+MLFS+PR); PR, partial remission; TEAE, treatment-emergent adverse event. [a]Data cutoff: July 24, 2023. Some patients may have had <4 months of follow-up. Two pediatric patients switched from *KMT2Ar* to *NPM1m*. Another patient's *KMT2Ar* status changed to "no" at screening. [b]Includes all ages. [c]Includes all leukemia subtypes. [d]Includes no response, disease progression, and patients without postbaseline disease assessment.

AUGMENT-101: Phase 1 R/R mNPM1 patients achieve durable, MRD-negative responses with revumenib



	n (%)
Total mNPM1 @ RP2D	14
CR/CRh	5 (36%)
MRD- CR/CRh	5 (100%)
ORR	7 (50%)

- 3/7 responders proceeded to HSCT
- 1 patient restarted revumenib post HSCT*
- 3/5 of CR/CRh maintained response beyond 6 months, 2 over 22 months
- TRAEs in-line with overall AUGMENT-101 Phase 1/2 experience
  - No treatment related discontinuations
  - No Grade 4 or 5 QTc events
  - ≤ Grade 2 differentiation syndrome

Syndax

2023 amendment allowed patients to restart treatment with revumenib post-transplant following HSCT; mNPM1, mutated nucleophosmin; HSCT, Haematopoietic stem cell transplant; RP2D, Doses that met exposure equivalent of 226 mg q12h or 276mg q12h without strong CYP3A4 inhibitor or 113 mg q12h or 163 mg q12h with strong CYP3A4 inhibitor; * Data cutoff of July 24, 2023

AUGMENT-101 KMT2Ar data shows a high rate of durable, MRD^{neg} responses

ASH23 #LBA5

63%	Overall response rate in pooled analysis
23%	CR/CRh rate in pooled analysis
6.4mos	Median duration of CR/CRh at data cutoff
70%	MRD negative rate among CR/CRh responses

Enables a high rate of deep, durable MRD^{neg} responses in late line R/R patients

Well tolerated, only 6% discontinued due to TRAEs

Profile supports a new treatment paradigm: HSCT followed by revumenib post-transplant maintenance

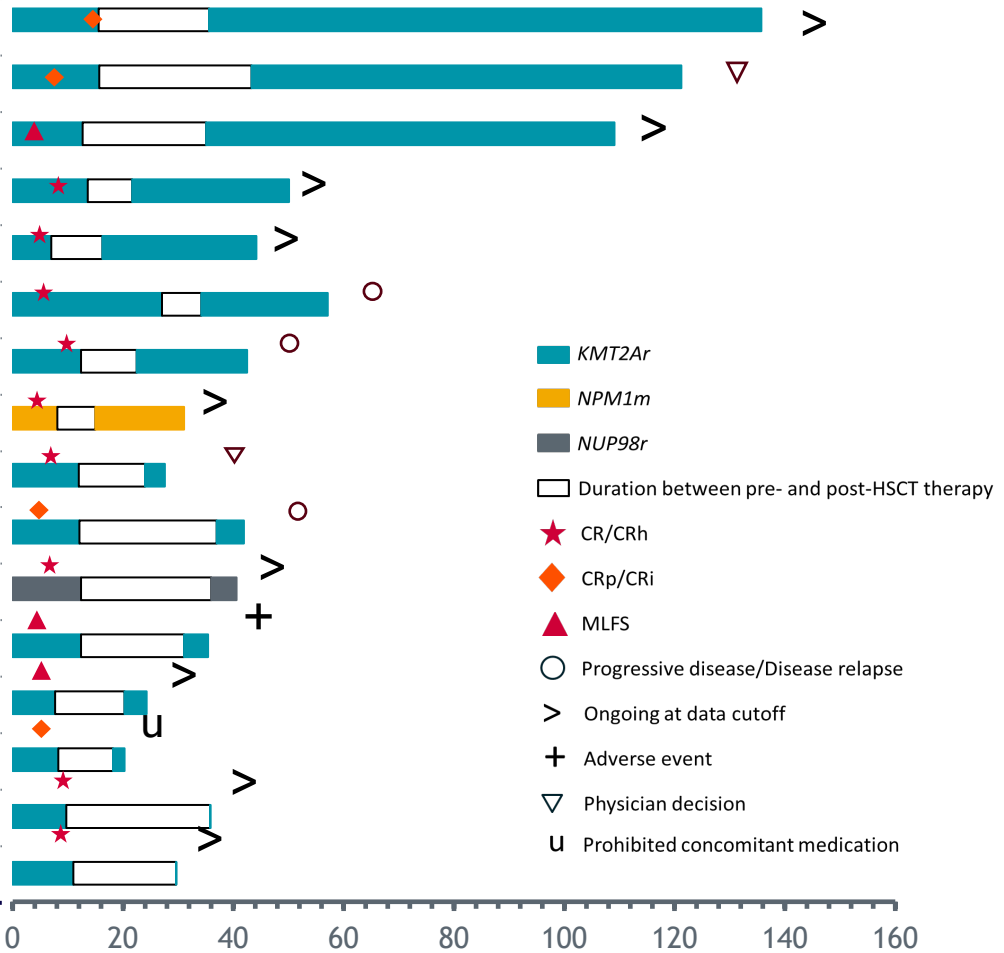
Syndax plans to complete NDA submission by year-end 2023 under RTOR

TRAEs, Treatment related adverse events; HSCT, Hematopoietic stem-cell transplantation; RTOR, Real-Time Oncology Review

Post-transplant maintenance experience supports long-term revumenib use

ASH23 #4950

Age	# prior regimens	Prior HSCT (#)[a]	Last response reported[b]	TRAE leading to dose modification post HSCT
22	4	Yes (2)	MRD− (BM)[c]	Decreased: leg pain
40	1	Yes (1)	CR, MRD−	Decreased: thrombocytopenia
11	3	No	CR, MRD−	Held: thrombocytopenia
41	1	No	CR, MRD−	None
1.3	1	No	CR, MRD not tested	None
71	1	Yes (1)	CRh, MRD+	Decreased: thrombocytopenia
35	2	Yes (1)	Relapse	Skipped: nausea and vomiting
39	2	Yes (1)	CRh, MRD not tested	None
39	6	Yes (1)	CR, MRD−[e]	Skipped: hyperbilirubinemia, thrombocytopenia
41	3	No	PD	None
17	5	Yes (1)	CRh, MRD not tested	None
26	3	No	NA	Discontinued: cytopenia, diarrhea
55	2	Yes (1)	CRp, MRD not tested	Skipped: thrombocytopenia
57	1	Yes (1)	CRi, MRD−	None
5	2	No	CR, MRD not tested	None
56	1	No	CR, MRD not tested	None



3 patients treated beyond 2 years, 1 discontinued after 2 years of post-transplant maintenance and remains in remission

Syndax

[a]All patients went on to HSCT/CD34 infusion after response to on-study revumenib. [b]Last response reported while on revumenib or prior to new antileukemic therapy. [c]Isolated CNS relapse

Thought leaders indicate revumenib may change the treatment paradigm for R/R KMT2Ar acute leukemia

ASH23 #4950

Anticipated KMT2Ar treatment paradigm upon revumenib approval

Relapsed or Refractory
(n = 57)

Revumenib

63% respond
(36/57)

HSCT

39% receive transplant^

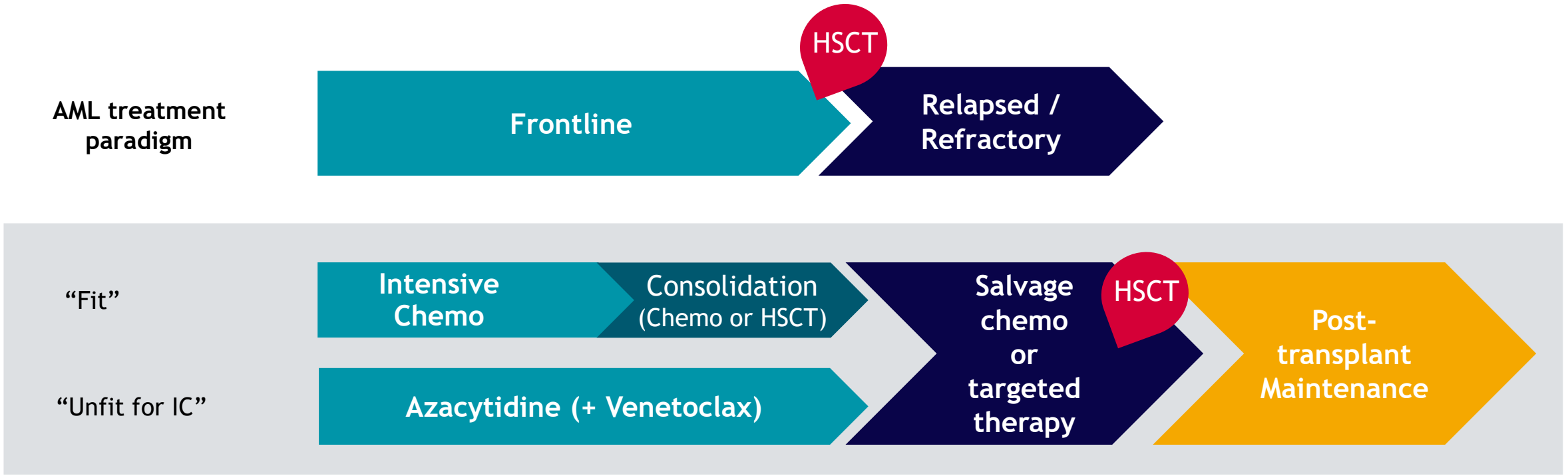
Revumenib maintenance

71% received or eligible for post-transplant maintenance*
(10/14)

^ *8 of 14 patients went to transplant without achieving a CR or CRh*
* *7 patients received post-transplant maintenance, 3 remained eligible to choose post-transplant maintenance as of data cut*

Revumenib induces MRD- complete responses, supports high rates of stem cell transplant and long-term post-transplant maintenance

Revumenib is evolving the AML treatment paradigm



SAVE AML: Revumenib plus Ven/HMA combo in R/R mNPM1, NUP98r or KMT2Ar AML/MPAL

ASH23 #58

Phase 1 in R/R mNPM1, NUP98r or KMT2Ar AML/MPAL

Revumenib + venetoclax + decitabine/cedazuridine (ASTX727)

Primary Endpoints: Safety, MTD, RP2D of combination

DL0:
Revumenib*: 113 mg q12h

DL1:
Revumenib*: 163 mg q12h

Venetoclax*: 400 mg target dose QD D1-D14
ASTX727: 35 mg QD D1-D5

* Patients dosed in combination with strong CYP3A4i; Ven dose adjusted for CYP3A4

KMT2Ar, KMT2A rearrangement; mNPM1, mutated nucleophosmin, NUP98r, Nucleoporin 98

100% ORR for patients treated with Revumenib/Venetoclax/Decitibine

ASH23 #58

Summary of Enrolled Patients & Response Data		
	N (%)	**Subtype**
Total enrolled	**9**	KMT2Ar: 5; mNPM1: 1 NUP98r: 3
Median prior Tx	**3**	55% received prior VEN 67% received prior HSCT
Best response		**Subtype**
ORR	**9 (100%)**	KMT2Ar + NUP98r + mNPM1
CRc 78% — **CR / CRh***	4 (44%)	3 KMT2Ar + 1 NUP98r
CRc 78% — **CRp**	3 (33%)	1 mNPM1 + 2 KMT2Ar
MLFS	1 (11%)	1 NUP98r
PR	1 (11%)	1 NUP98r
MRD^{neg} (MFC)	6 (67%)	* 100% MRD^{neg} CR/CRh

- 100% Response rate in heavily pre-treated pts
  - 67% received prior HMA and/or prior HSCT
  - 56% of patients enrolled in SAVE had relapsed on prior venetoclax therapy
- 67% MRD^{neg} rate, with 100% MRD^{neg} in CR/CRh
- Expected rates venetoclax-naïve R/R AML:
  - CRc ≤ 50%
  - ORR ≤ 60%

Syndax

Data Cutoff Nov 01, 2023

*1. Maximilian Stahl et. al, Clinical and molecular predictors of response and survival following venetoclax therapy in relapsed/refractory AML, Blood Adv, 2021, 2. Jonas, B.A., Pollyea, D.A. How we use venetoclax with hypomethylating agents for the treatment of newly diagnosed patients with acute myeloid leukemia. Leukemia 33, 2795-2804 (2019) 3.*ASH2023 abstract #833 A Phase 2 Study of the Fully Oral Combination of ASTX727 (Decitabine/Cedazuridine) Plus Venetoclax for Older and/or Unfit Patients with Acute Myeloid Leukemia; 4.Curtis A. Lachowiez, et al, A Phase Ib/II Study of Ivosidenib with Venetoclax ± Azacitidine in IDH1-Mutated Myeloid Malignancies *Blood Cancer Discov* (2023) 4 (4): 276-293. 5. Advisory board discussion

SAVE AML supports favorable safety and tolerability profile of all-oral revumenib-venetoclax-decitabine/cedazurine combo in R/R acute leukemia

ASH23 #58

SAVE trial safety summary		
Treatment Related AEs	All Grades in ≥25%	Grade ≥3
Hyperphosphatemia	56%	--
Nausea	56%	--
Febrile neutropenia	--	56%
Vomiting	44%	--
QTc prolongation	33%	--
Differentiation Syndrome	22%	--
Thrombocytopenia	--	22%
Neutropenia	--	22%
Lung infection	--	22%

- No discontinuations for TRAEs, No ≥ Gr 3 QTc
- Myelosuppression comparable to venetoclax-HMA
- No new safety signals observed beyond those reported for venetoclax-HMA

Syndax

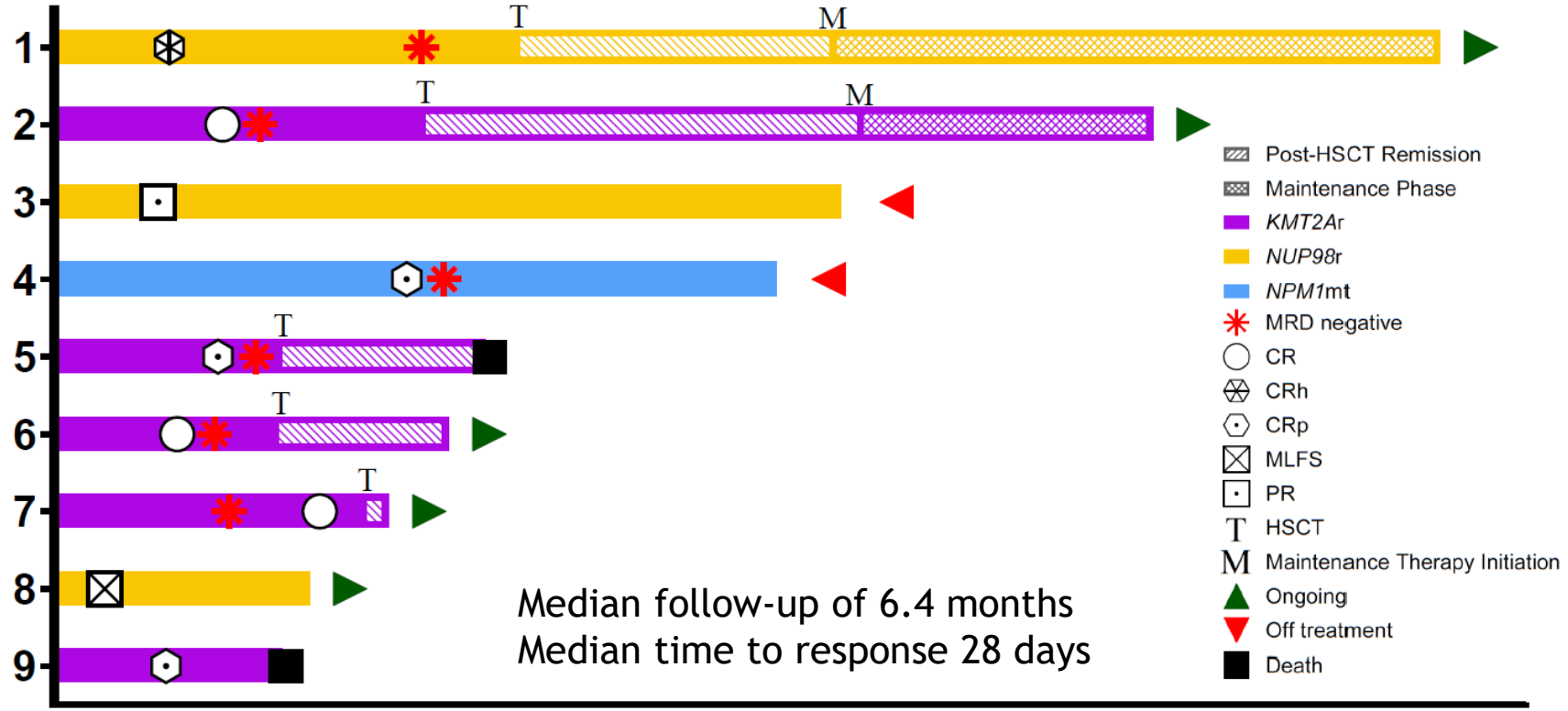
Data Cutoff Nov 01, 2023

1. DiNardo, C. D., Thirman, M., et al., Safety and preliminary efficacy of venetoclax with decitabine or azacitidine in elderly patients with previously untreated acute myeloid leukaemia: a non-randomised, open-label, phase 1b study 2018 Vol 19, Issue 2, p216-228

SAVE AML leads to rapid responses in refractory cases

ASH23 #58

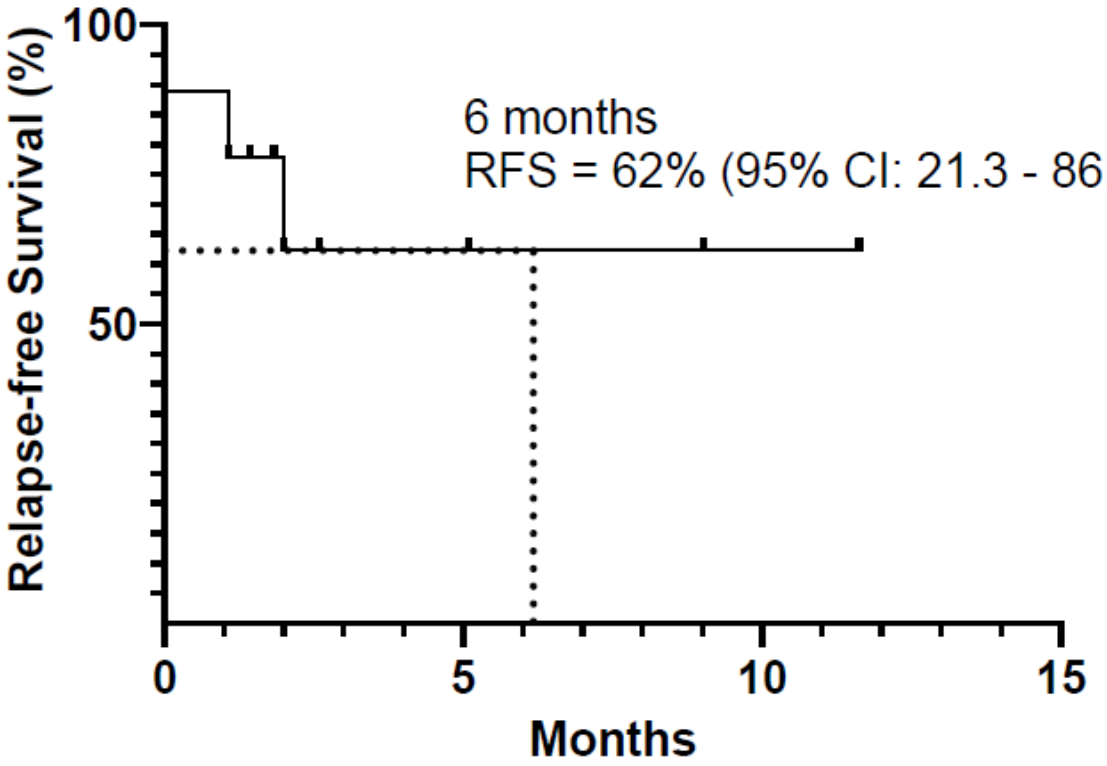
Prior Therapies			
HSCT	HMA	Ven	Menin-i
+	-	-	-
-	-	+	-
+	+	+	-
+	+	+	+
-	+	+	-
+	+	-	-
-	-	-	-
+	+	-	-
+	+	+	-

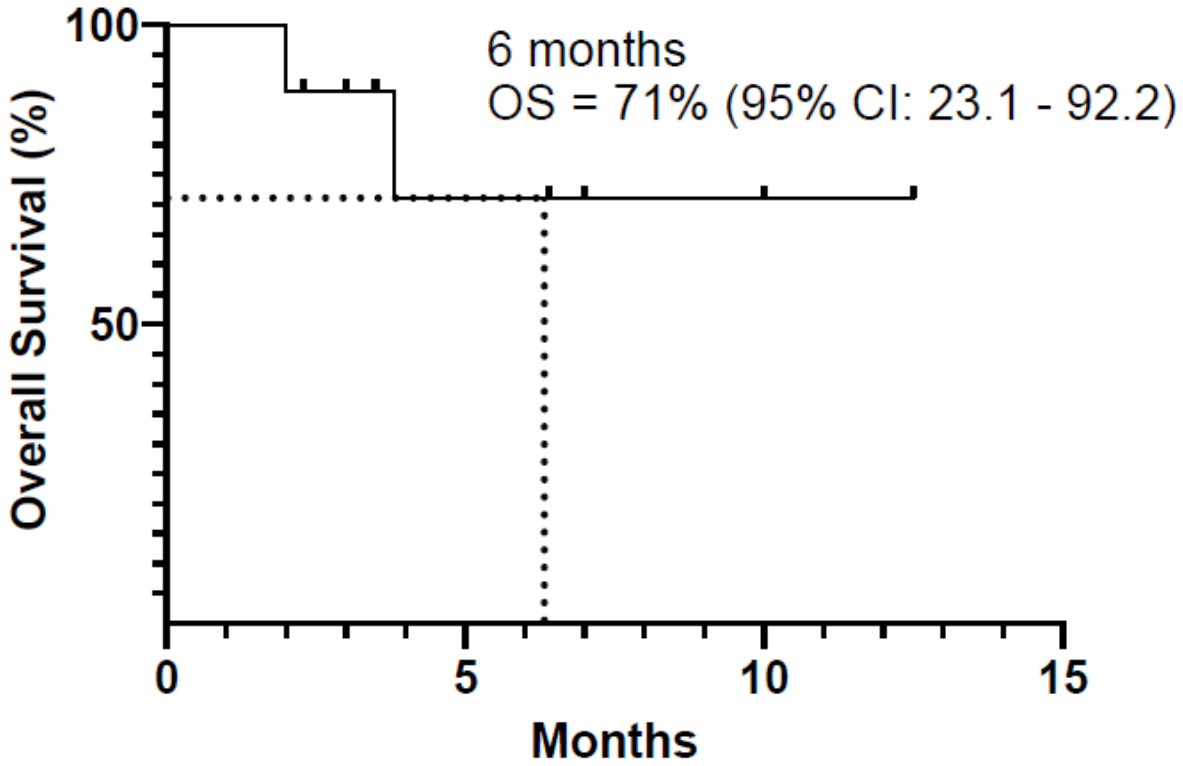


5 patients received HSCT consolidation
2 resumed revumenib maintenance with ongoing remission > 11 months

SAVE AML early results indicate durable remissions

ASH23 #58



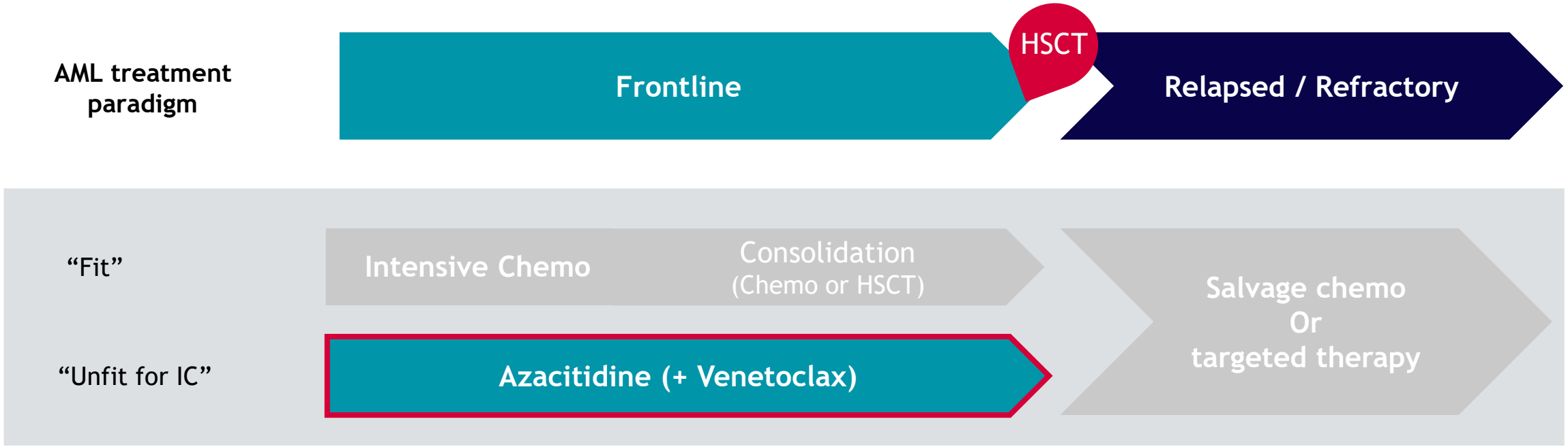


Median RFS and OS not reached with 2 patients having ongoing remission beyond 11 months

BEAT AML Trial Results

Dr. Joshua Zeidner, MD
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



VIALE-A trial establishes the SOC for treatment of newly diagnosed AML patients unable to tolerate intensive chemotherapy

VIALE-A: Ph3, RCT to evaluate the efficacy and safety of azacitidine plus venetoclax vs azacitidine alone

- **Median Overall Survival -- 14.7 mo** (Primary Endpoint)
- **Composite Complete Remission (CRc) -- 66.4%** (Key Secondary Endpoint)

Azacitidine-Venetoclax Group	Safety analysis set (n=283)	
Event	**All Grades†**	**≥ Grade 3‡**
All adverse events	283 (100)	279 (99)
Hematologic adverse events	236 (83)	233 (82)
Thrombocytopenia	130 (46)	126 (45)
Neutropenia	119 (42)	119 (42)
Febrile neutropenia	118 (42)	118 (42)
Anemia	78 (28)	74 (26)
Leukopenia	58 (21)	58 (21)

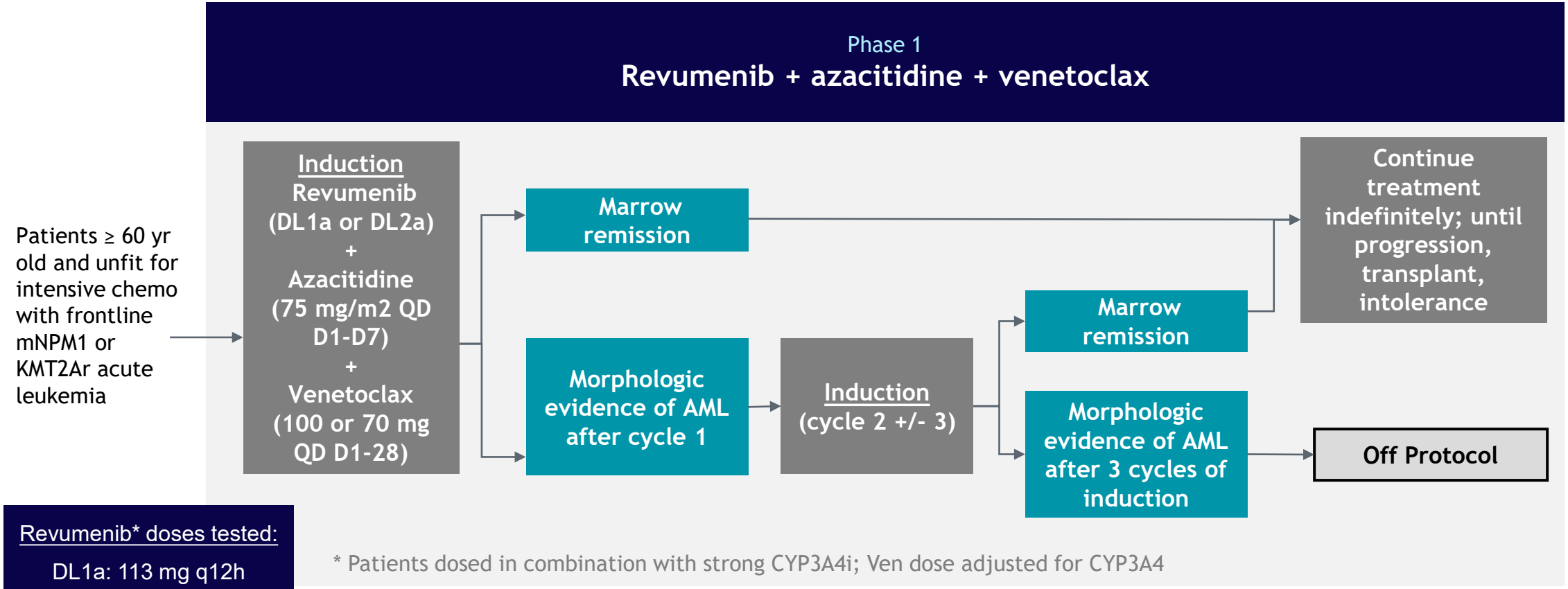
* The safety population included all patients who received at least one dose of azacitidine-venetoclax or azacitidine-placebo.
† Adverse events reported in at least 20% of patients in either treatment group are listed.
‡ Adverse events of grade 3 or higher that were reported in at least 10% of patients in either treatment group are listed.

In VIALE-A, VEN/AZA group:

- Observed a higher incidence of dose interruptions to allow for hematologic recovery
- The majority of patients who received azacitidine-venetoclax (53%) had modifications to the duration of venetoclax
- Used bone marrow assessments to promote appropriate interruptions in venetoclax between treatment cycles to augment hematologic recovery

DiNardo et al. N Engl J Med 2020; 383:617-629

BEAT AML: Revumenib +Ven/Aza combo in frontline mNPM1 or KMT2Ar AML



Revumenib* doses tested:

DL1a: 113 mg q12h

DL2a: 163 mg q12h

Dose escalation of revumenib in 3+3 Design

Primary endpoint

RP2D of combination

BEAT AML patient demographics

	Dose Level 1a n = 7	Dose Level 2a n = 6	Total n = 13
Median Age (yrs), (range)	67 (61-85)	75 (65-84)	73 (61-85)
Age ≥75 years, % (n)	*43% (3)*	*17% (1)*	*4 (31)*
Gender, % M	14%	83%	46%
NPM1 mut, % (n)	57% (4)	66% (4)	62% (8)
KMT2Ar, % (n)	43% (3)	33% (2)	38% (5)
BM Blasts, % (range)	67% (15-84)	58% (21-82)	60% (15-84)

Data as of Dec 01, 2023; Enrolled Population

Newly diagnosed mNPM1 or KMT2Ar AML patients achieved CRc within 1-2 cycles of induction with the triplet combination of rev-ven-aza

	113 mg q12h Dose Level 1a		163 mg q12h Dose Level 2a		All Treated Patients
	KMT2Ar	mNPM1	KMT2Ar	mNPM1	(DL1a + DL2a)
Total # Patients	3	4	2	4	13
Best Response					
CRc	3 (100%)	4(100%)	2 (100%)	4 (100%)*	13 (100%)
CR/CRh	2 (67%)	3 (75%)	2 (100%)	4 (100%)*	11 (85%)
CRi	1 (33%)	1 (25%)	--	--	2 (15%)
MRD flow status					
Negative	3 (100%)	3 (75%)	2 (100%)	4 (100%)	12 (92%)
Unk	--	1 (25%)	--	--	1 (8%)
Transplant	--	1	1	--	2
Relapse	1	--	--	--	1

Data as of Dec 01, 2023; Enrolled Population

BEAT-AML safety and status

- Cytopenias manageable with continuous dosing of venetoclax and full dose revumenib
  - 1 Hematologic DLT observed in DL1a: platelets exceeded 42 days to recover, no other DLTs across both dose levels
- 4/13 (31%) patients experienced differentiation syndrome; 8% Grade 3, 15% Grade 2, 8% Grade 1
- 4/13 (31%) patients experienced QTC prolongation managed without dose reductions; 8% Grade 3, 15% Grade 2, 8% Grade 1

No increased safety issues outside of known reported ven/aza toxicities

- Triplet has cleared DLT window for both revumenib dose levels
- Cohort expansion planned to validate RP2D
- Data to be presented at an upcoming medical meeting

Data as of Dec 01, 2023; Enrolled Population

AUGMENT-102 Trial Results

Dr. Neerav Shukla, MD
Chief, Pediatric Translational Medicine Service at
Memorial Sloan Kettering Cancer Center

AUGMENT-102: Revumenib plus FLA combo in R/R mNPM1, NUP98r or KMT2Ar AML

Phase 1 in R/R mNPM1, NUP98r or KMT2Ar Acute Leukemia

Revumenib + fludarabine + cytarabine

Primary Endpoints: Safety, MTD, RP2D of combination

DL0:
Revumenib*: 113 mg q12h

DL1:
Revumenib*: 163 mg q12h

Fludarabine: 30 mg/m^2 QD D1-D5
Cytarabine: 2,000 mg/m^2 QD D1-D5

* Patients dosed in combination with strong CYP3A4i

Enrolled heavily pretreated pediatric KMT2Ar patients including multiply relapsed KMT2Ar infant leukemia

KMT2Ar, KMT2A rearrangement; mNPM1, Mutated nucleophosmin; NUP98r, Nucleoporin 98

Safety and tolerability data observed with fludarabine-cytarabine (FLA) combinations in patients with R/R AML

First relapse or primary refractory Pediatric AML treated with FLAG[1]

Grade 3 or 4 toxicity	n = 175
Anemia	89 (51%)
Neutropenia	98 (56%)
Thrombocytopenia	98 (56%)
Severe infection	31 (18%)

FLAG = fludarabine, cytarabine, granulocyte colony-stimulating factor

First relapse adult AML with leukemia following 1 course of mitoxantrone-etoposide treated with FLA[2]

Grade 3 or 4 toxicity	n = 18
Neutropenia (Gr 4)	18 (100%)
Febrile neutropenia	18 (100%)
Thrombocytopenia (Gr 4)	18 (100%)

FLA = fludarabine, cytarabine

Chemotherapy is associated with high levels of hematological toxicity

1.Kaspers GJL, et al., Improved Outcome in Pediatric Relapsed Acute Myeloid Leukemia: Results of a Randomized Trial on Liposomal Daunorubicin by the International BFM Study Group. 2. B McLaughlin, MBoyiadzis et al., Fludarabine and cytarabine in patients with relapsed acute myeloid leukemia refractory to initial salvage therapy Int J Hematol (2012) 96:743-747

AUGMENT-102 shows benefit in chemo combo (FLA) in late line R/R KMT2Ar, mNPM1 or NUP98r AML without added AEs

Demographics

Total evaluable	DL1 (N=3)	DL2 (N=12)
Median age (range)	20 yrs (0.75,29)	4 yrs (1,37)
Median prior therapies	3 (3,3)	4 (1,18)
AML/ALL	2/1	12/0
KMT2Ar/mNPM1 /NUP98r	3/0/0	10/1/1

Efficacy Results

Total evaluable	DL1 (N=3)	DL2 (N=12)
CRc	1 (33%)	4 (33%)
CR	--	3 (25%)
CRi	1 (33%)	1 (8%)
Undergo HSCT	--	4*

Safety summary

Gr ≥3 revumenib treatment-related AEs	% N=15
Platelet count decreased	53%
White blood cell count decreased	40%
Anemia	33%
Febrile neutropenia	27%
Neutrophil count decreased	27%
Lymphocyte count decreased	20%

Late line, predominantly pediatric population

- 50% had failed FLA prior to enrollment

Encouraging efficacy results

- Patient receiving post-HSCT maintenance remains in response >10 mos

AE profile consistent with intensive chemo in R/R AML

- No TRAE's leading to dose reduction or discontinuation

Syndax

Data Cutoff September 20, 2023; *Includes 1 mNPM1 patient who went to transplant following 5 days of decitabine

AUGMENT-102 Summary

- AUGMENT-102 Phase 1 trial examined the safety of revumenib in combination with standard AML salvage chemotherapy (FLA – fludarabine-cytarabine)
  - AE profile was consistent with intensive chemo in R/R AML
  - 50% of patients in the trial already failed prior FLA
  - 33% CRc rate exceeded the expected rate in heavily pretreated AML
- Data from expansion cohorts to support the RP2D are expected in 2024
- Based on the AUGMENT-102 results, PedAL consortium is planning a Phase 2 trial in early-first relapse pediatric KMT2Ar leukemia

AE, Adverse event; cGVHD, Chronic graft-versus-host disease; ORR, Overall response rate; Q2W, Every 2 weeks; RP2D, Recommended Phase 2 dose

Close and Q&A

Michael Metzger
Chief Executive Officer, Syndax

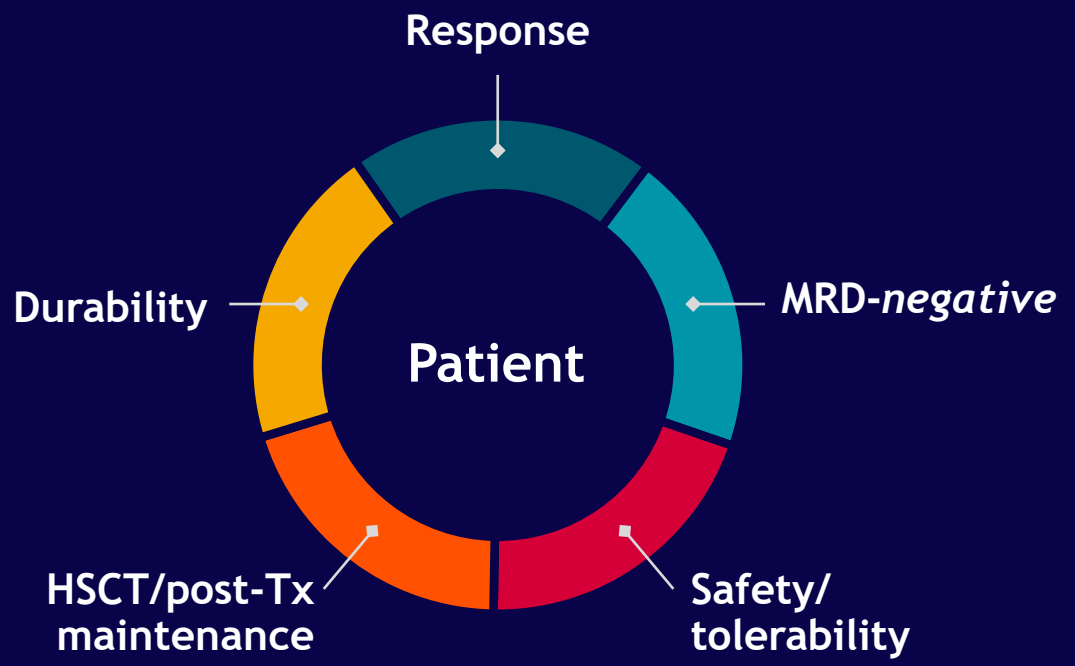
Revumenib is a potential first- and best-in-class therapy for KMT2Ar and mNPM1 acute leukemia

Positive monotherapy results to date:

- Clinically meaningful efficacy data in R/R KMT2Ar acute leukemia; mNPM1 results consistent with KMT2Ar
- Durable responses observed in post-transplant maintenance, even in heavily pretreated patients
- FDA submission for KMT2Ar acute leukemia under RTOR expected to complete by YE23; mNPM1 data expected 4Q24

Combination results to date show revumenib has a favorable safety and efficacy profile:

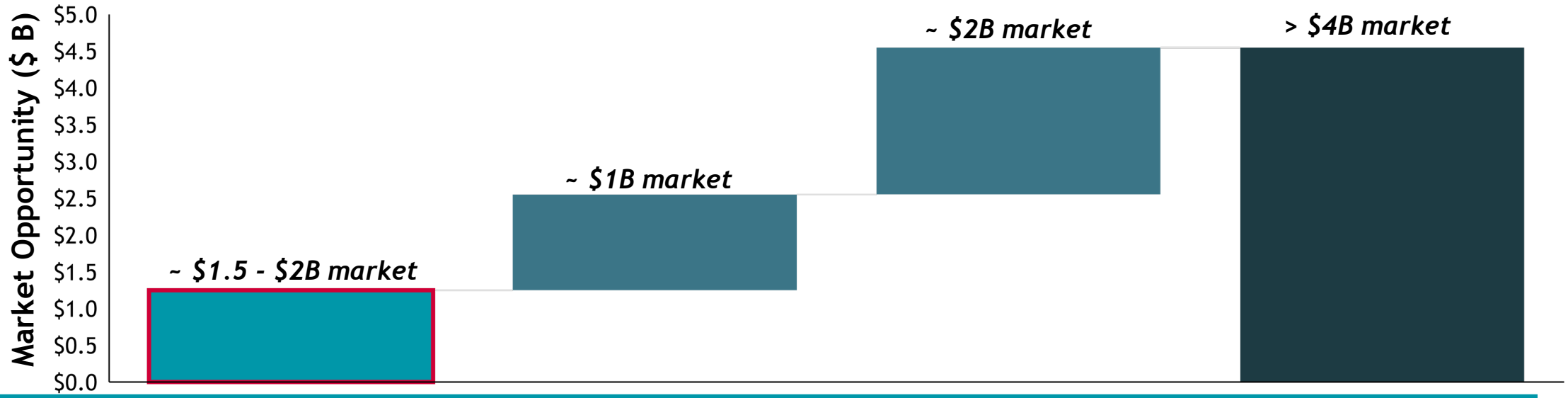
- In combination with ven-HMA in both frontline and R/R AML and includes an increased frequency of MRD^{neg} and CRc
- In combination with FLA chemo combo in R/R pediatric patients, including those who relapsed on FLA



Revumenib delivers on key metrics that address the needs of patients and drive physician utilization

Revumenib's profile supports use as backbone therapy across treatment continuum — providing access to >$4B US market opportunity

Significant growth potential with indications in earlier lines of treatment



	R/R KMT2Ar + NPM1 Acute Leukemia	1L "Unfit" KMT2Ar + NPM1 Acute Leukemia	1L "Fit" KMT2Ar + NPM1 Acute Leukemia	Total
Est. patient population	5,000 - 6,500	~3,500	~5,500	

Source: Data on file; Redbook 2023