SAFETY AND CLINICAL ACTIVITY OF AMV564, A CD33/CD3 T-CELL ENGAGER, IN PATIENTS WITH RELAPSED/REFRACTORY ACUTE MYELOID LEUKEMIA (AML): UPDATED RESULTS FROM THE PHASE 1 FIRST-IN-HUMAN TRIAL

Peter Westervelt[1], **Gail J. Roboz[2]**, Jorge E. Cortes[3], Jessica K. Altman[4], Vivian G. Oehler[5], Meixiao Long[6], Hagop M. Kantarjian[3], Sangmin Lee[2], Tae H. Han[7], Jeanmarie Guenot[7], Eric J. Feldman[7], John F. DiPersio[1]

[1]Washington University School of Medicine, Saint Louis, MO, [2]Weill Cornell Medicine and The Weill Medical College of Cornell University, New York, NY, [3]The University of Texas MD Anderson Cancer Center, Houston, TX, [4]Northwestern University, Chicago, IL, [5]Fred Hutchinson Cancer Research Center, Seattle, WA, [6]Ohio State University, Columbus, OH, [7]Amphivena Therapeutics Inc, South San Francisco, CA, United States

European Hematology Association

June 2019

Most AML Patients Die Within 1 Year After Relapsed/Refractory Disease

Therapy	Data Source	n	Overall Response (CR + CRi)	Median OS, Months
IDAC	Phase 3 study[1]	355	19	6.1
Intensive salvage[a]	Phase 2 study[2]	44	41	6.3
Investigator's choice[b]	Phase 3 study[3]	190	21	3.3
Hypomethylating agents	Multicenter retrospective (2006-2016)[4]	514	18	6.9

1. Ravandi F, et al. *Lancet Oncol*. 2015;16:1025-1036.
2. Cortes JE, et al. *Cancer*. 2015;121:234-242.
3. Roboz GJ, et al. *J Clin Oncol*. 2014;32:1919-1926.
4. Stahl M, et al. *Blood*. 2016;128:1063.

a. Intensive salvage regimens included: MEC (n=23); idarubicin/cytarabine (n=8); cytarabine-based induction + fludarabine ± Mylotarg (n=5); cytarabine-based induction + amsacrine (n=2); cytarabine-based induction + mitoxantrone ± Mylotarg (n=2); cytarabine-based induction + Mylotarg (n=1); cytarabine-based induction + cladribine (n=1); cytarabine alone (n=1); mitoxantrone + etoposide (n=1)

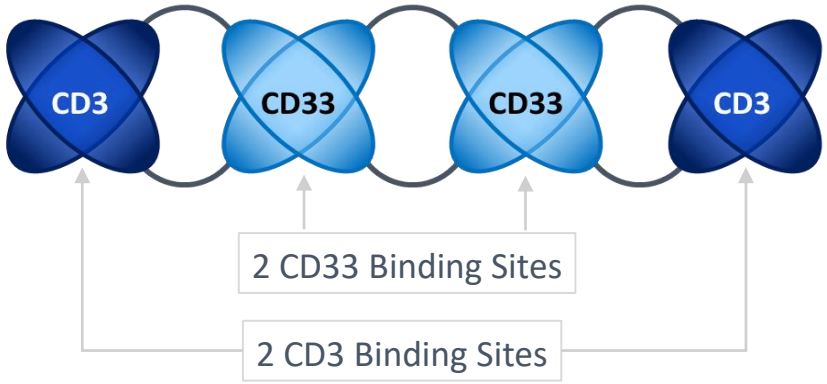
b. Investigator's choice included: high-dose cytarabine (n=22); mitoxantrone, etoposide, cytarabine (MEC; n=44); fludarabine, cytarabine, granulocyte colony-stimulating factor with or without idarubicin (n=65); low-dose cytarabine (n=12); hypomethlyating agents (n=34); hydroxyurea (n=6); or supportive care (n=7)

IDAC=Intermediate-Dose Cytarabine; MEC=Mitoxantrone, Etoposide and intermediate dose Cytarabine

AMV564: A Bivalent, Bispecific CD33/CD3 T-cell Engager

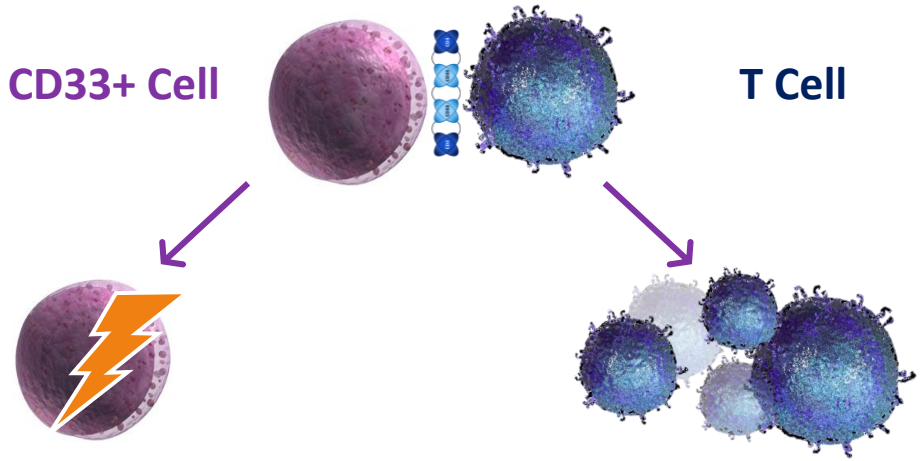
AMV564

- Selected from > 100 lead candidates based on activity in AML patient samples



- CD33
  - Expressed on >95% of AML blasts
  - Highly expressed on myeloid derived suppressor cells (MDSCs)

T-Cell Engager Mechanism of Action

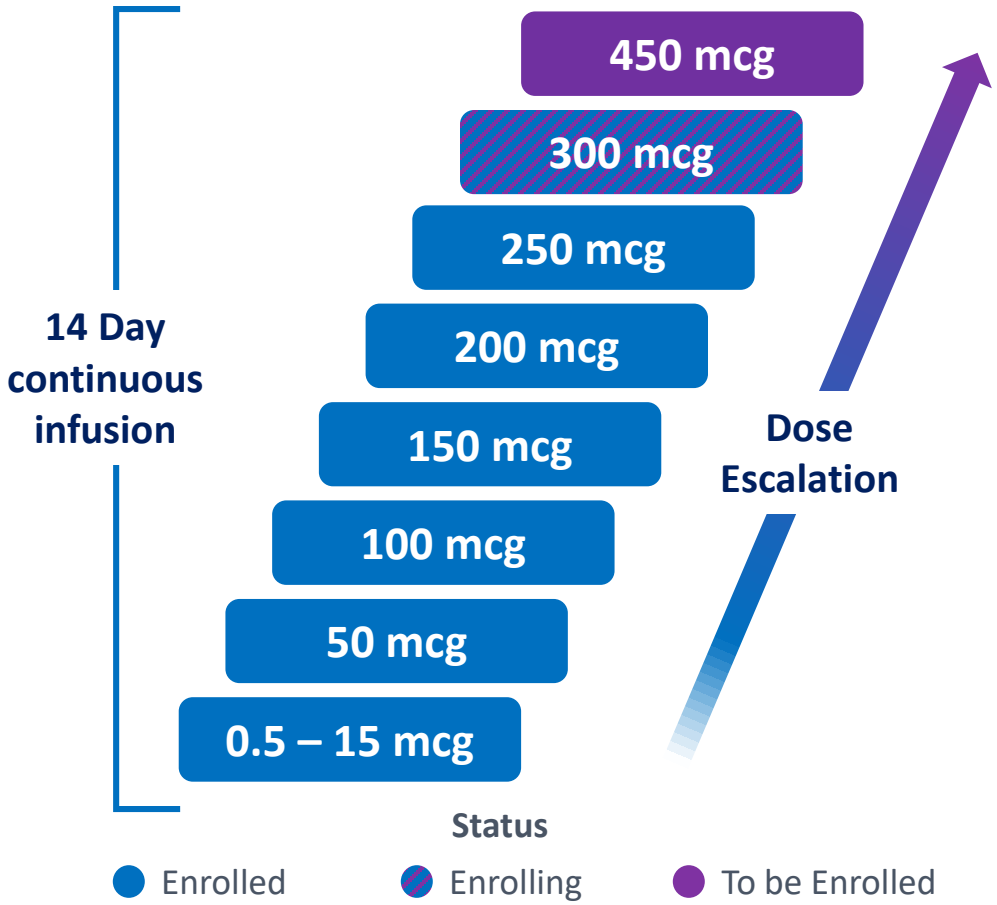


Highly specific target cell killing

- Activation
- Cytokine release
- Proliferation
- Differentiation

AMV564-101 Phase 1 Clinical Study Design: Relapsed/Refractory AML

3+3 DESIGN



PATIENTS

33 Patients dosed to date

- Age ≥ 18 years
- High-risk disease
  - 1-4 prior induction regimens
  - Post AlloHSCT relapse allowed
  - 2nd AML allowed
- Normal renal/hepatic function

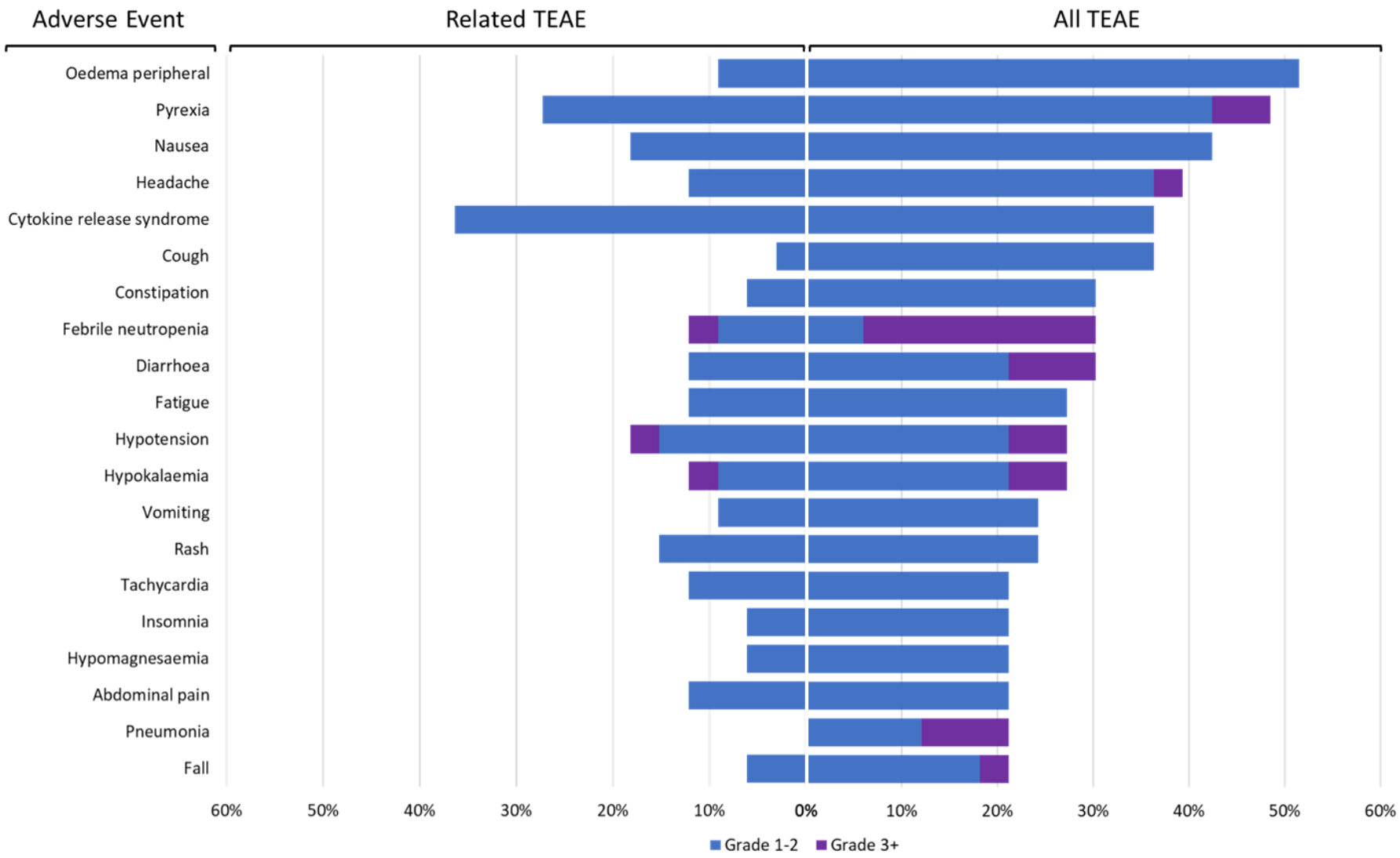
KEY OBJECTIVES

- Define MTD/RP2D
- Evaluate preliminary efficacy
- Assess PK
- Assess Biomarkers

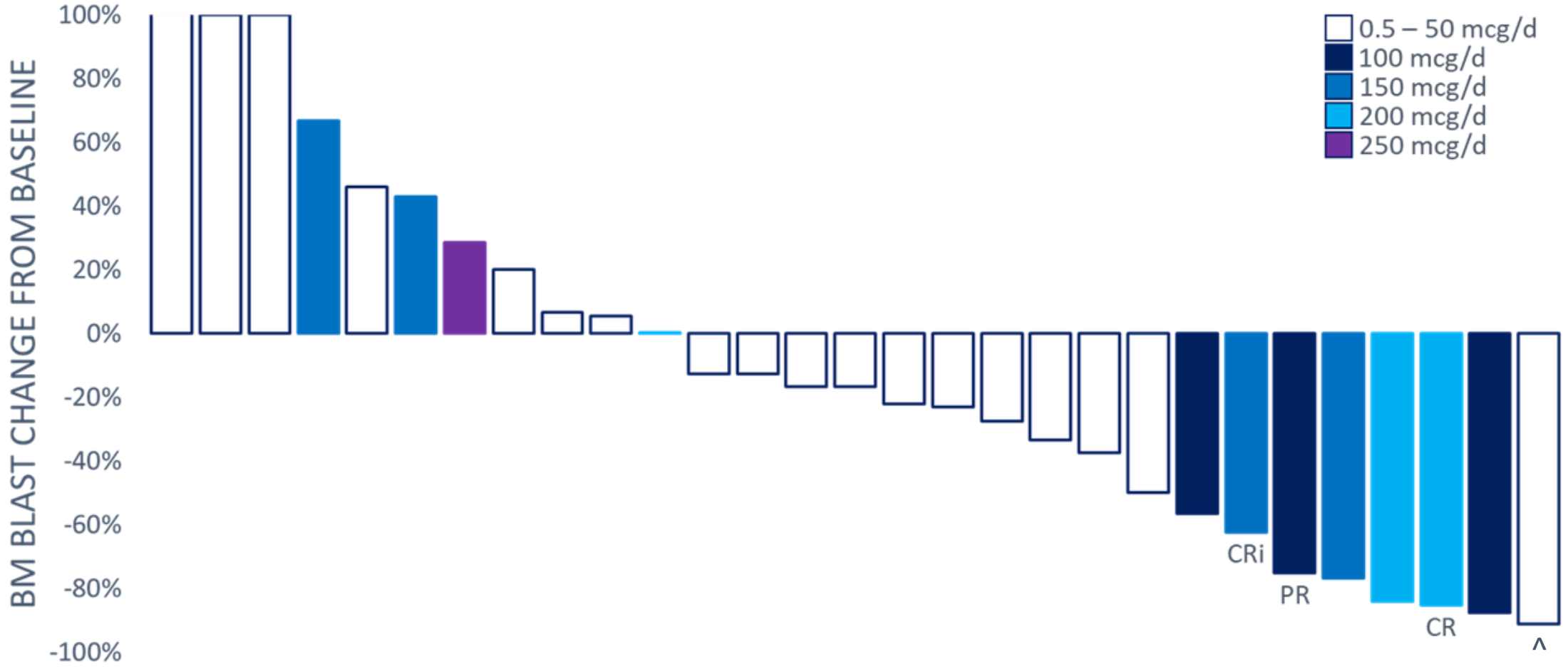
AMV564-101: High Risk Patient Population

	0.5 - 250 mcg (x 14 days)
Total N	33
Median age (range), y	71.5 (24, 85)
Sex, male, n (%)	19 (58)
ECOG score, n (%)	
0	7 (21)
1	22 (67)
2	4 (12)
Secondary AML, n (%)	24 (73)
Prior intensive chemotherapy, n (%)	21 (64)
Prior allogeneic transplant, n (%)	3 (9)
MRC cytogenetic risk group, n (%)	
Favorable	1 (3)
Intermediate	13 (39)
Unfavorable	19 (58)
Enrollment BM, median (range)	30% (3%, 96%)
Baseline WBC, median (range), X 10^9/L	2.1 (0.2, 13.8)

AMV564 Is Well Tolerated – No Dose Limiting Toxicity Through 250 mcg



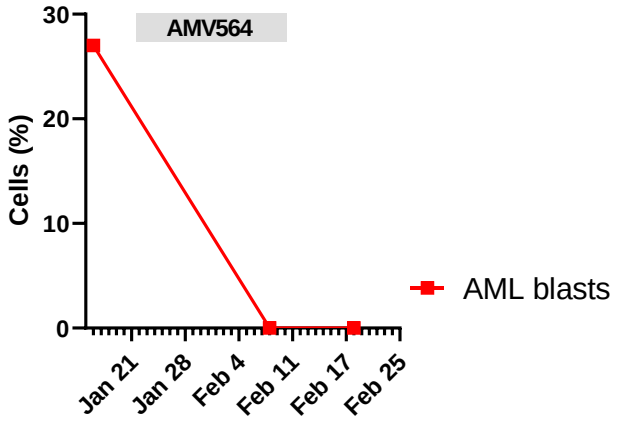
Best Response in Bone Marrow with a 14 Day Dosing Regimen



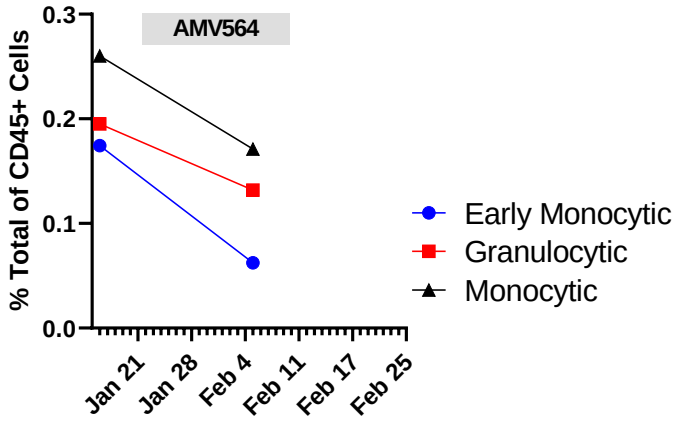
^ reduction in spleen size

Patient 02-041 (CR): Selective Depletion of Leukemic Blasts and MDSCs

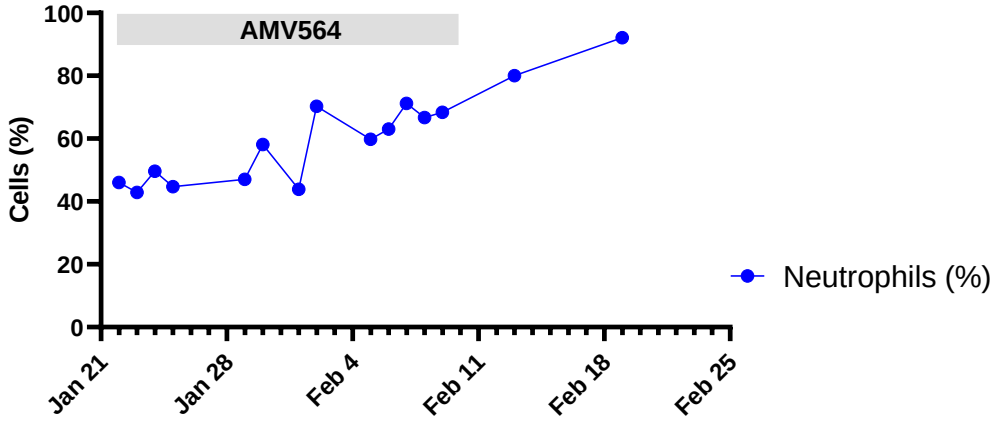
Blasts: Bone Marrow



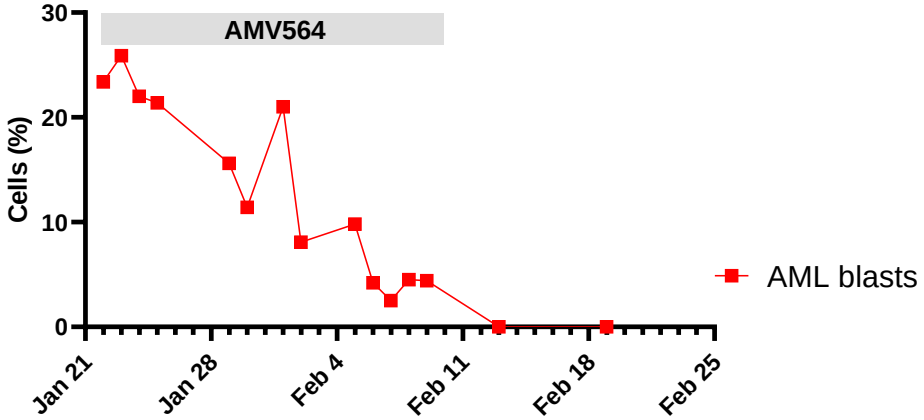
MDSCs: Bone Marrow



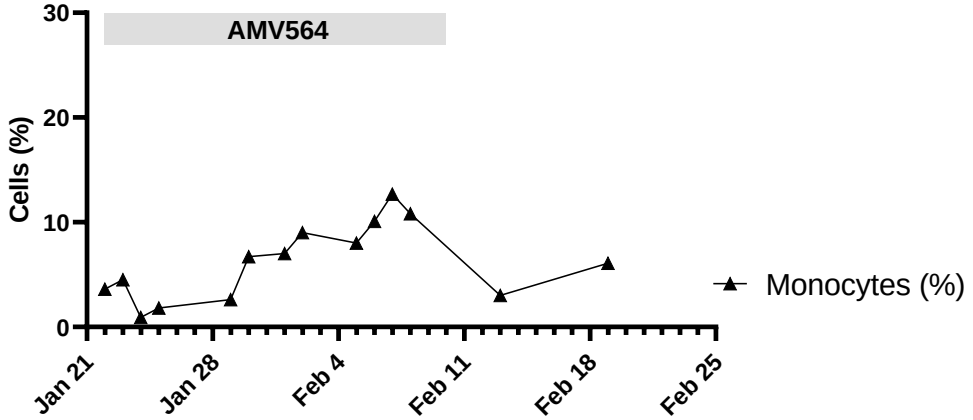
Neutrophils: Peripheral Blood



Blasts: Peripheral Blood



Monocytes: Peripheral Blood



New Lead-in Dose Regimen without Steroids for Continued Dose Escalation

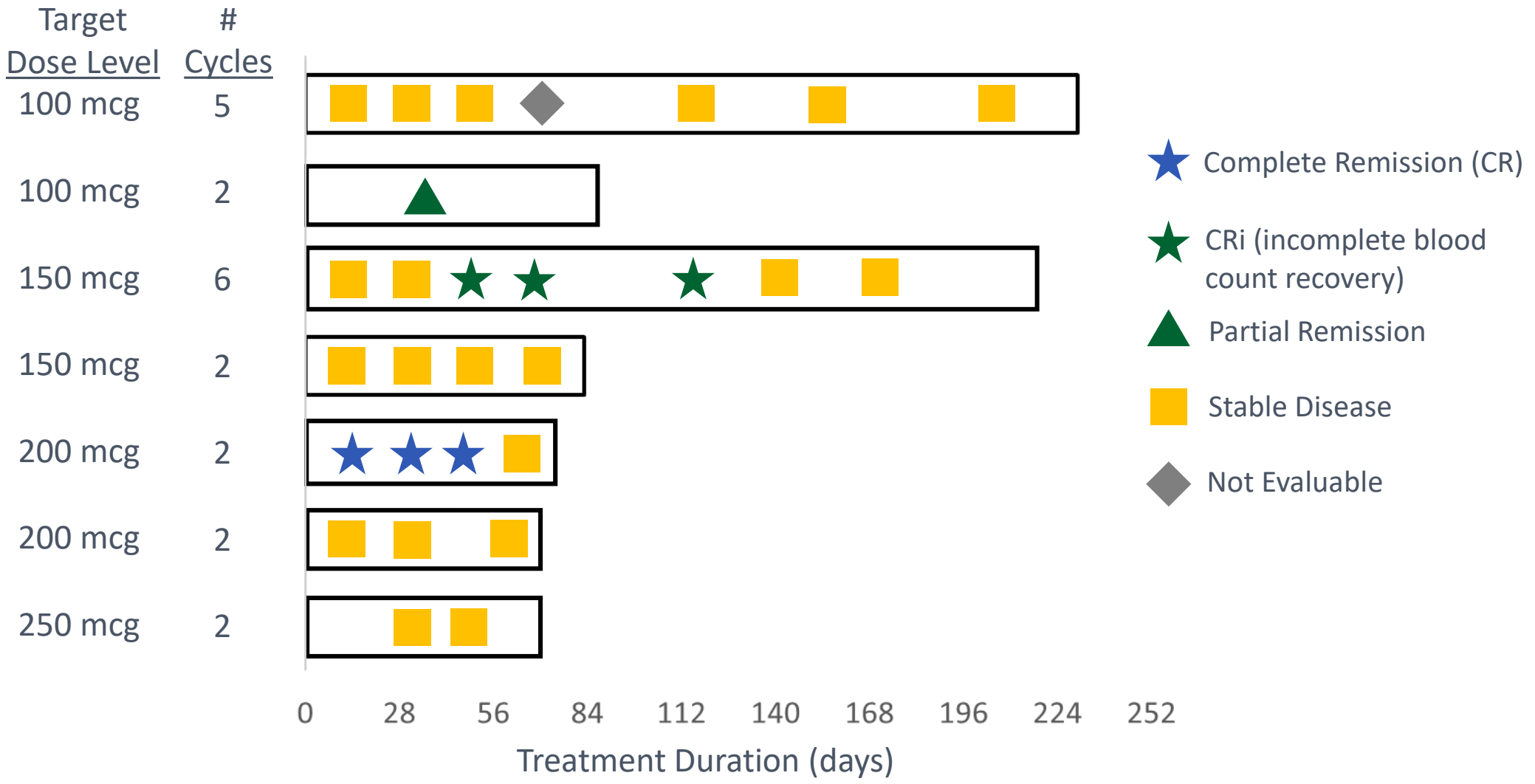
No Grade 3 or Grade 4 CRS

Lead-in Dose	Target Dose	# of Cycles	Grade 1	Grade 2	≥ Grade 3
N/A	15 mcg	30	3	1	0
15 mcg	100 mcg	21	4	0	0
15 → 100 mcg	150 mcg	4	2	0	0
15 → 100 mcg	200 mcg	3	0	2	0
15 → 100 mcg	250 mcg	1	0	1	0
15→30→100→150→200 mcg	250 mcg	3	0	1*	0

*Grade 2 CRS (hypotension) occurred at 15 mcg (Day 1) without dose interruption

15 → 100 mcg: 3 days at 15 mcg and 3 days at 100 mcg
15→30→100→150→200 mcg: 1 day at each of 15 mcg, 30 mcg, 100 mcg, 150 mcg and 200 mcg with no prophylactic steroids

Duration of Response for Patients Receiving ≥2 Cycles of AMV564



AMV564-101 Summary

- Well tolerated, with no DLTs and limited Grade 1 and Grade 2 CRS
- Incremental dosing regimen with reduced lead in and without steroids tolerated at higher doses
- Monotherapy activity with CR, CRi and PR responses observed with a 14-day dosing regimen
- Seven-month duration of response observed (1 CRi, 1 SD)
- Rapid and selective elimination of leukemic blasts and MDSCs observed

Acknowledgments

- Patients and their families
- Investigators, study teams, and site personnel