PHASE 1 FIRST-IN-HUMAN TRIAL OF AMV564, A BIVALENT BISPECIFIC (2×2) CD33/CD3 T-CELL ENGAGER, IN PATIENTS WITH RELAPSED/REFRACTORY ACUTE MYELOID LEUKEMIA (AML)

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European Hematology Association

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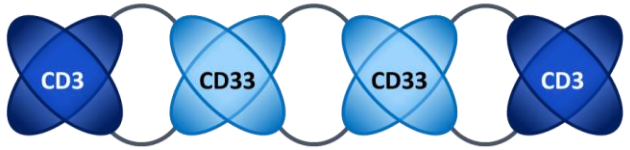
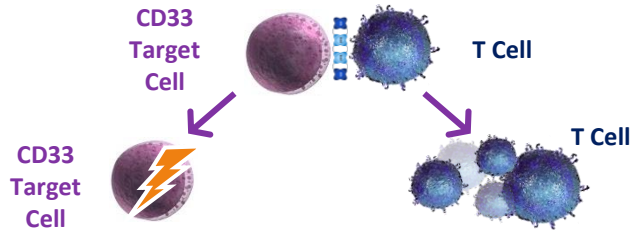
AMV564 Is a Bivalent, Bispecific CD33/CD3 T-cell Engager

AMV564



Unique homodimer that forms 4 scFvs

T-Cell Engager Mechanism of Action



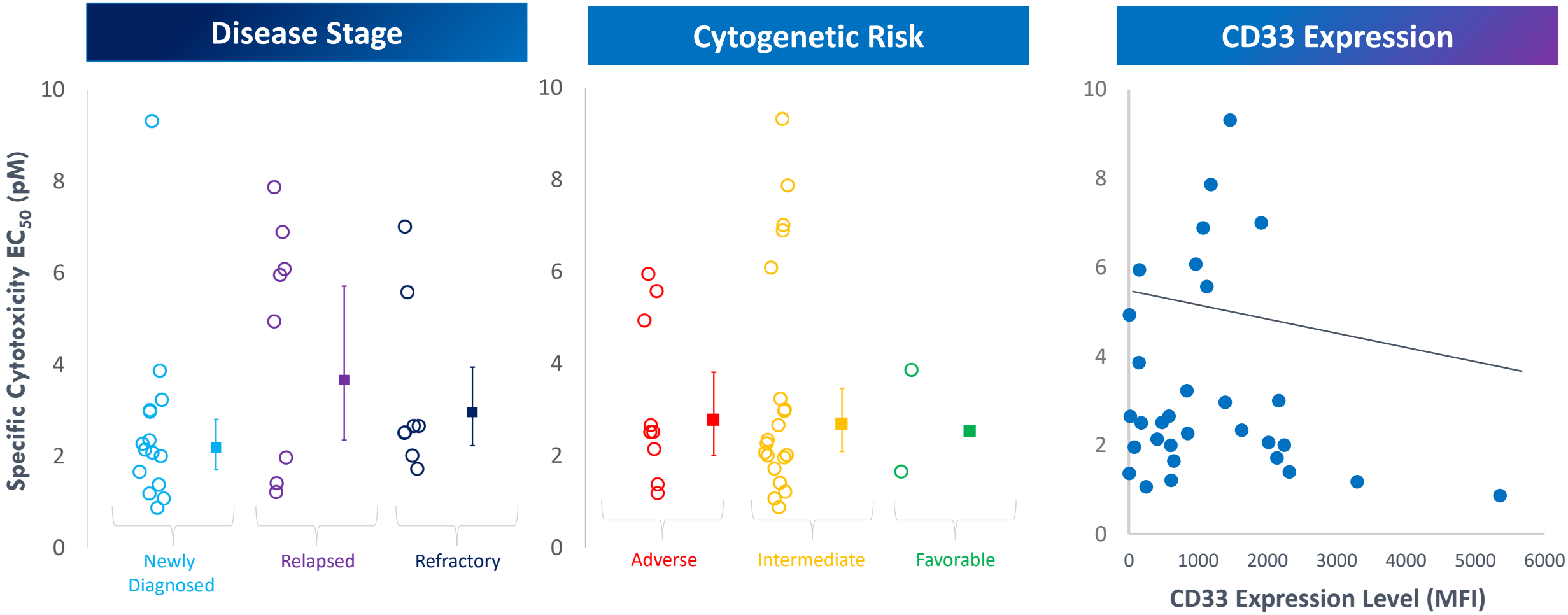
Highly specific CD33 target cell killing

- Activation
- Cytokine release
- Proliferation
- Differentiation

Potential Advantages

- Intermediate half-life
  - Not renally cleared due to size (103 kDa)
  - Gradual drug accumulation for controlled T cell activation
  - Enables rapid hematologic recovery
  - Intermittent dosing possible
- High CD3 and CD33 affinity
  - Greater activity/avidity
- Minimal risk of off-target T-cell activation
  - No risk of FcRn and Fc-gamma mediated cytokine release
- CD33 targeted
  - Well characterized target and clinically validated for AML

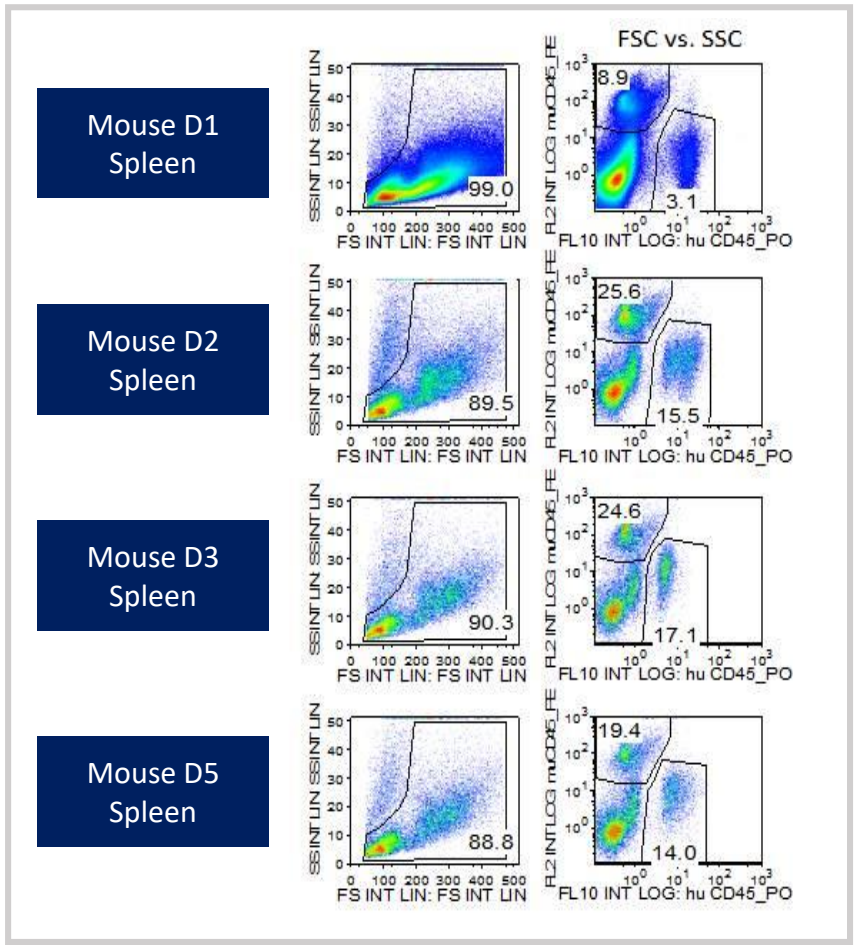
Potent and Broadly Active in AML Patient Samples



Equipotent across the disease spectrum with single digit pM activity

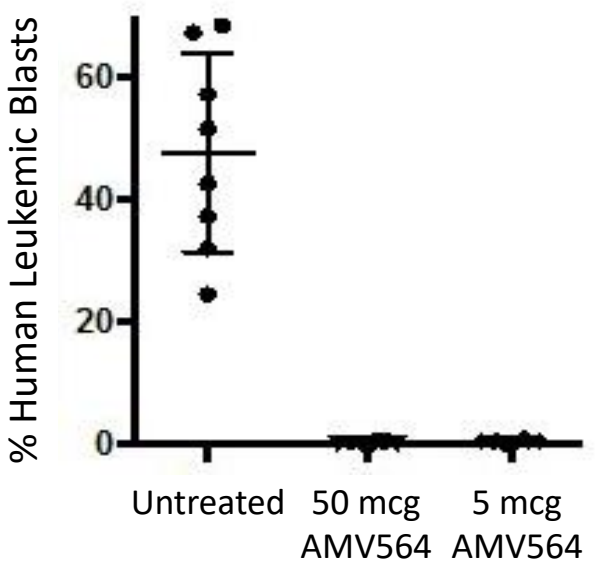
Data: R. Walter Group, FHCRC (Note: Positive T cell selection)

Eliminates AML Patient-Derived Xenograft (PDX) Tumor in Stringent Mouse Model with Autologous T Cells

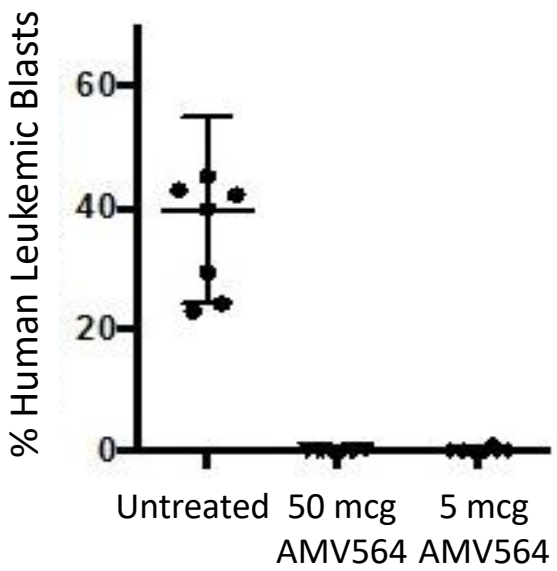


In NSG mice injected with leukemic cells alone >40% of spleen cells and >45% of BM cells were confirmed by FACS to be leukemic blasts by Day 38.

Bone Marrow



Spleen

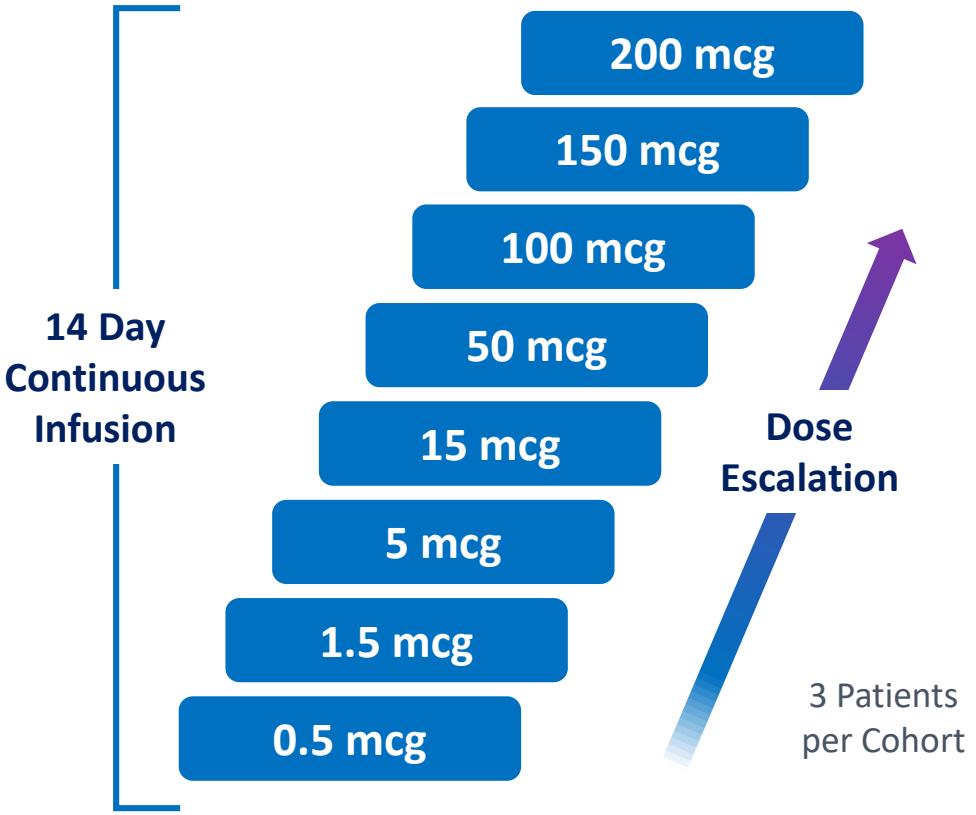


- Eliminated blasts from both bone marrow and spleen at low doses

Data: J. DiPersio, ASCO 2015

Phase 1 Clinical Study Design: AMV564 in R/R AML
(NCT03144245)

3+3 DESIGN



PATIENTS

- 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/BMx

Phase 1 Study in AML: High Risk Patient Population

	0.5 – 50 mcg x 14 d (N = 17)
Median age (range), y	72 (24, 84)
Sex, male, n (%)	9 (53)
ECOG score, n (%)	
0	11 (65)
1	5 (29)
2	1 (6)
Secondary AML, n (%)	9 (53)
≥ Second salvage, n (%)	13 (76)
Prior intensive chemotherapy, n (%)	9 (53)
MRC cytogenetic risk group, n (%)	
Favorable	0 (0)
Intermediate	7 (41)
Adverse	10 (59)
Enrollment BM, median (range)	30% (5%, 95%)
Baseline WBC, median (range), × 10^9/L	1.7 (0.4, 31.8)

MRC, Medical Research Council; WBC, white blood cell

Data: 07JUN2018

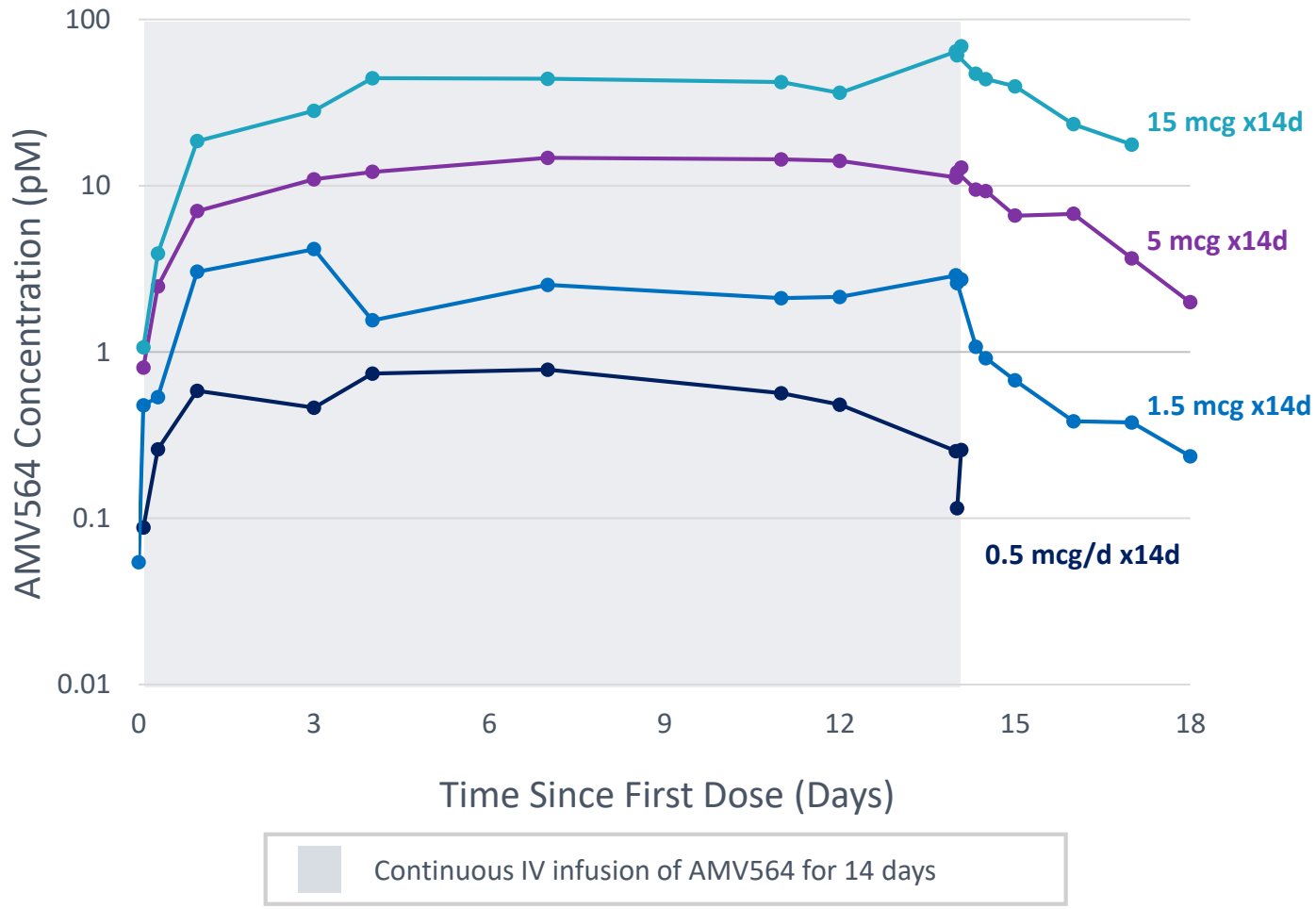
AMV564 Clinical Pharmacokinetics

PK Attributes:

- Gradual accumulation to steady-state
- Terminal $t_{1/2}$ ~ 2 d
- Lower clearance than monovalent BiTE®/DART

Preclinical Comparisons:

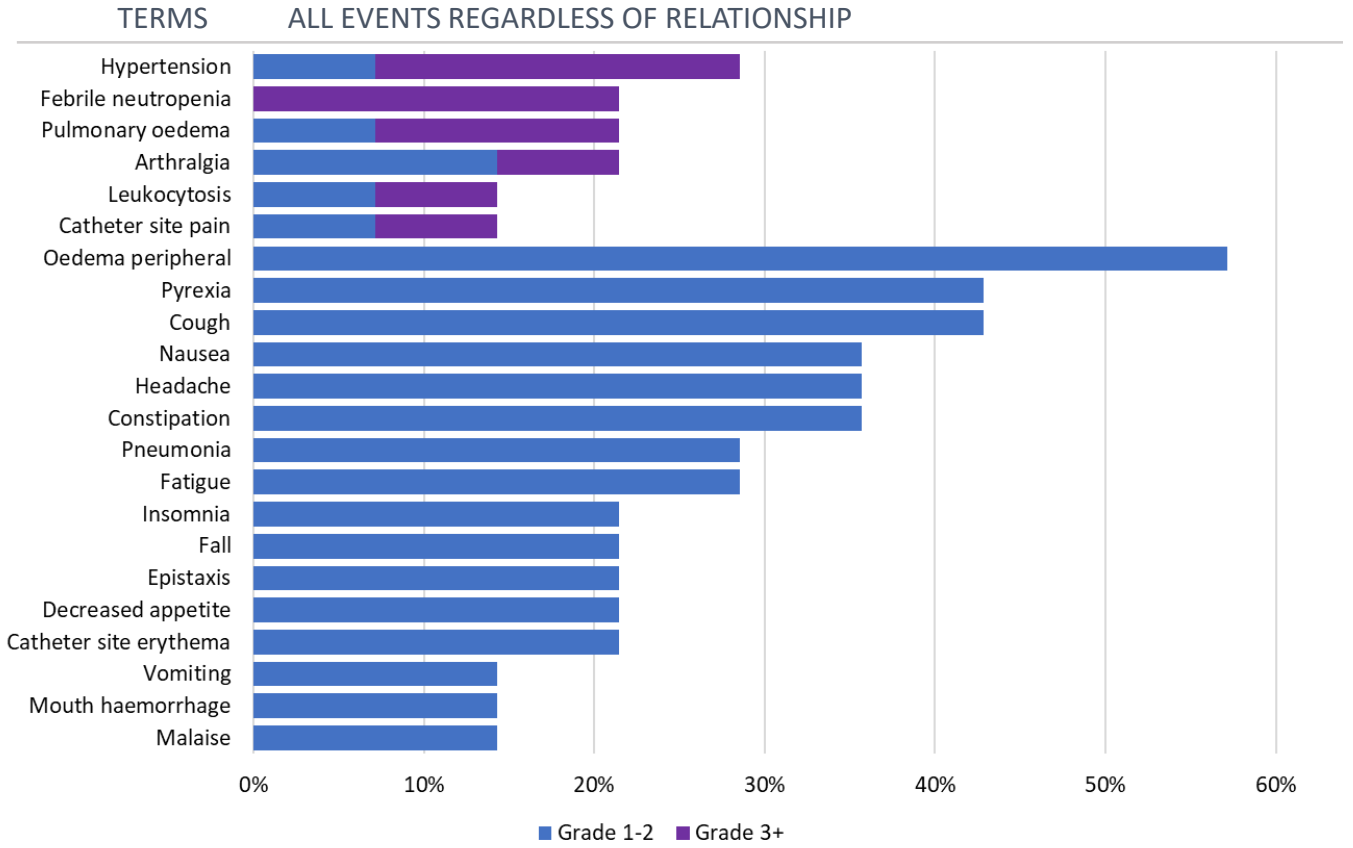
- Leukemic Blast Elimination
  - EC_{95} ~ 13 – 58 pM
- NHP HNSTD Exposure
  - C_{ss} ~ 100 pM



Safety Summary: Only Mild Treatment-Emergent Adverse Events (AEs)

No Dose Limiting Toxicities through 50 mcg

- No related Grade 3+ adverse events
- No cytokine release syndrome (CRS) ≤ 15 mcg; manageable Grade 2 CRS at 50 mcg (1 pt)
- 0% 30-day mortality
- Repeat cycles well tolerated



Data: 07JUN2018

Activity Observed at Doses ≤ 50 mcg

T-cell activation

- Increased cytokine levels following administration of AMV564
- Increased antigen markers of T cell activation

Modest bone marrow blast reductions

- 13 – 38% reductions in bone marrow blasts 10 of 16 evaluable patients

Extramedullary improvements

- Reduction in spleen size

Patient 03-016 Treated at 50 mcg

Background

- Severe myelofibrosis
- Received 2 cycles of AMV564 at 50 mcg

AGE/SEX	DIAGNOSIS	SALVAGE #	CG RISK	BLAST %	PRIOR IC
70/F	2nd AML[a]	2nd	Intermediate	45%	No

T cell activation accompanied by manageable CRS

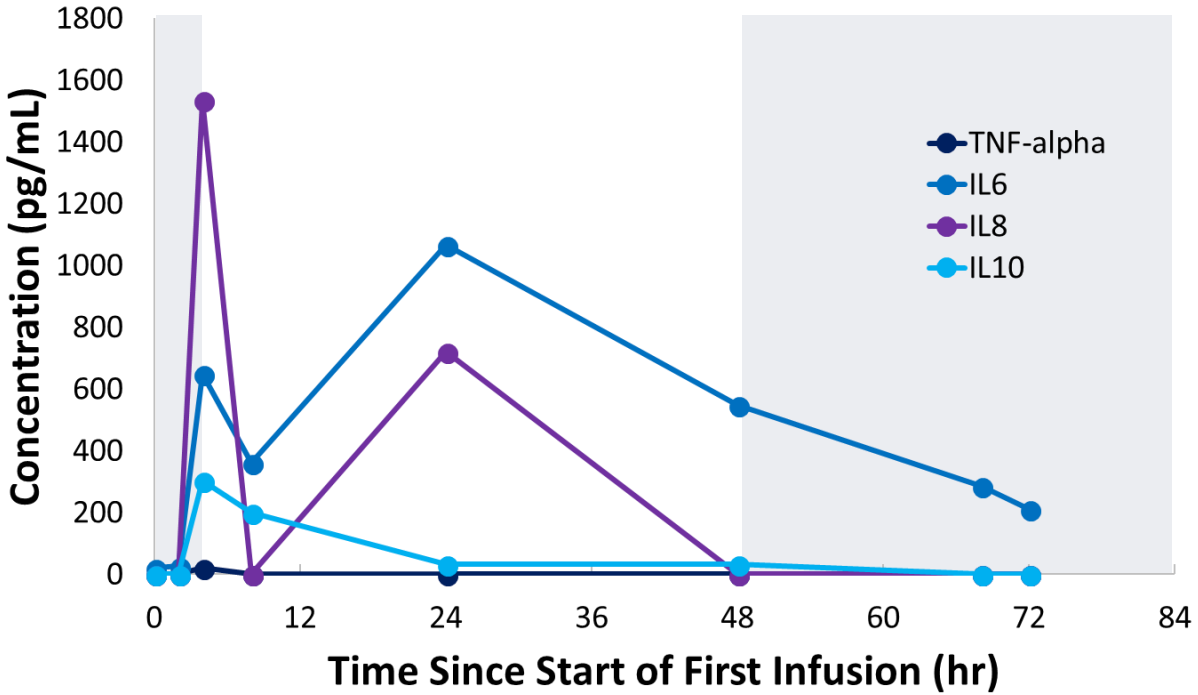
- Fever, mild hypotension onset ~6 hours of infusion
- Managed with tocilizumab, IVF's, temporary cessation of infusion
- Subsequent resumption of infusion well-tolerated

Efficacy: Activity observed

- Spleen size reduction from 18 cm to 11 cm
- Decrease in BM cellularity from 30% to 10%
- Reduction in BM blasts from 45% to 23%

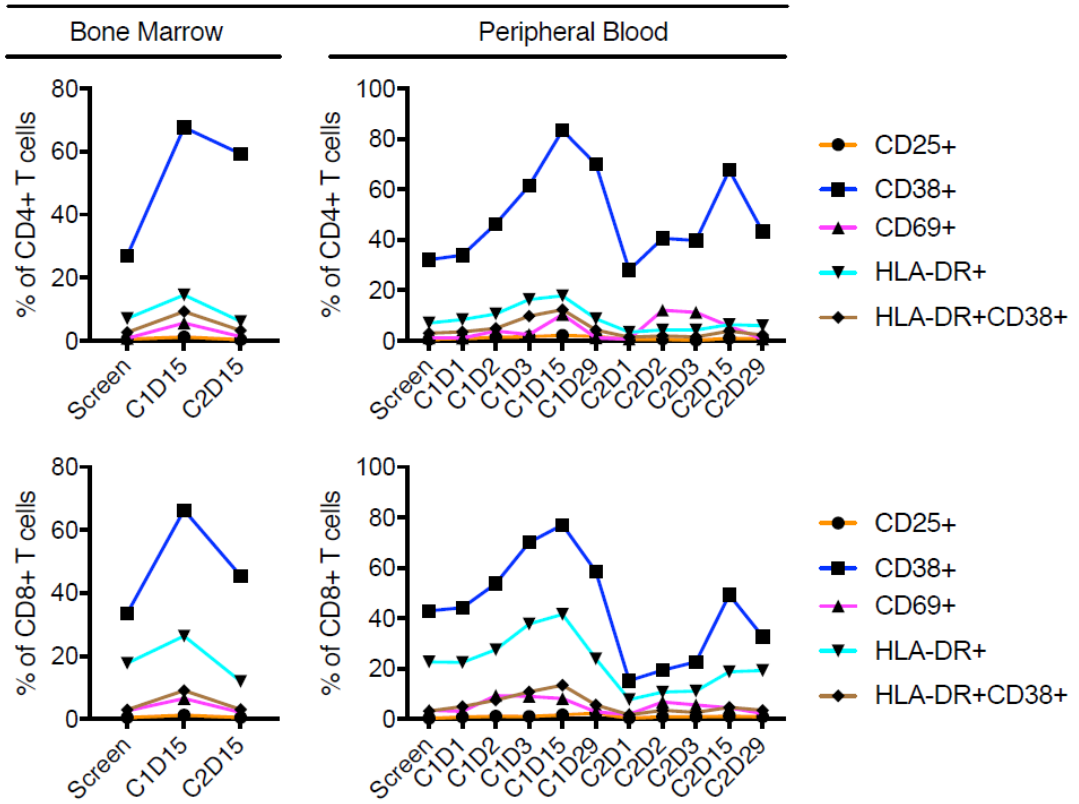
T Cell Activation at 50 mcg: Patient 03-016 (Preliminary)

Cytokines Increased



IL2, IL4, and IFN-gamma were below the LLOQ

T-Cells Activated



AMV564 Phase 1 Study in AML: Summary

Unprecedented and Differentiated PK Profile

- ~2 day terminal half-life
- Gradual drug accumulation to steady-state concentrations

Well Tolerated

- No DLTs, manageable CRS observed
- 0% 30-day mortality rate in high-risk AML population

Activity Observed at Low Doses

- Reductions in bone marrow blasts at doses below EC95
- Evidence of significant T-cell activation at doses $\geq$ 15 mcg
- Evidence of response in extramedullary sites (Decrease in spleen size)