Abstract #1455

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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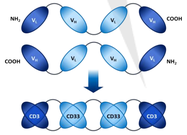
BACKGROUND

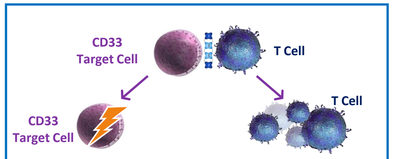
AMV564 is a novel bivalent, bispecific (2:2) CD33/CD3 T cell engager that binds CD33 on leukemic blasts and other CD33-expressing cells and the invariant CD3ε on the T-cell receptor creating an immune synapse that results in T-cell directed lysis of CD33-expressing cells and T cell activation and proliferation. AMV564 is broadly active with picomolar potency and activity is independent of cytogenetic or molecular abnormalities, CD33 expression level and disease stage, based on preclinical studies with AML patient samples (Reusch et al. 2016). AMV564 is well-tolerated in AML patients and demonstrates single agent anti-leukemic activity through T-cell engagement.

AMV564



- Homodimer that forms 4 scFvs
- Two binding sites for CD33 and CD3
- >100 kD, larger than the renal clearance threshold and not rapidly cleared

MECHANISM OF ACTION

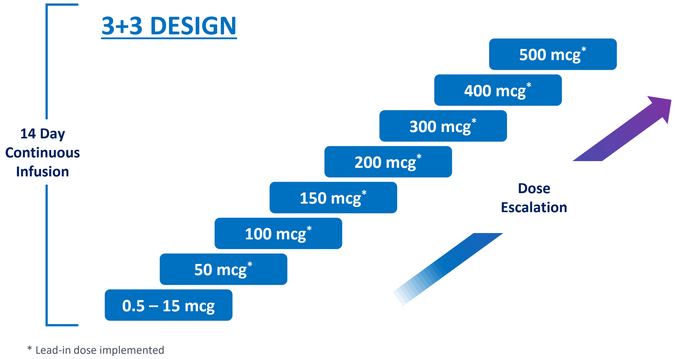


Highly specific CD33 target cell killing

- Activation
- Cytokine release
- Proliferation
- Differentiation

STUDY DESIGN

3+3 DESIGN



* Lead-in dose implemented

KEY ELIGIBILTY

- Age ≥ 18 years
- High-risk R/R AML
  - 1-4 prior induction regimens
  - Post AlloHSCT relapse allowed
  - 2nd AML allowed
- Normal renal/hepatic function
- CD33 expression not required

KEY OBJECTIVES

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

PATIENT CHARACTERISTICS

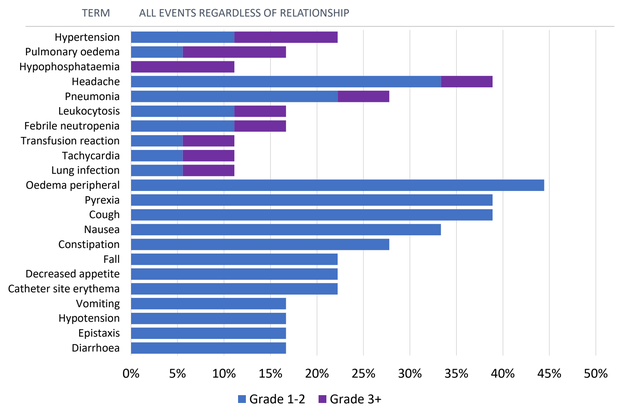
Poor prognosis population

	0.5 – 150 mcg x 14 d (N = 26)
Median age (range), y	73 (24, 84)
Sex, male, n (%)	13 (50)
ECOG score, n (%)	
0	5 (19)
1	17 (65)
2	4 (15)
Secondary AML, n (%)	17 (65)
≥ Second salvage, n (%)	18 (69)
Prior intensive chemotherapy, n (%)	16 (62)
Prior allogeneic transplant, n (%)	1 (4)
MRC cytogenetic risk group*, n (%)	
Favorable	0 (0)
Intermediate	13 (50)
Adverse	13 (50)
Enrollment BM, median (range)	28% (5%, 95%)
Baseline WBC, median (range), × 10^9/L	1.7 (0.4, 31.8)

SAFETY

No Dose Limiting Toxicities through 150 mcg

- No related Grade 3+ adverse events including cytokine release syndrome (CRS)
- 0% 30-day mortality
- Repeat cycles also well tolerated



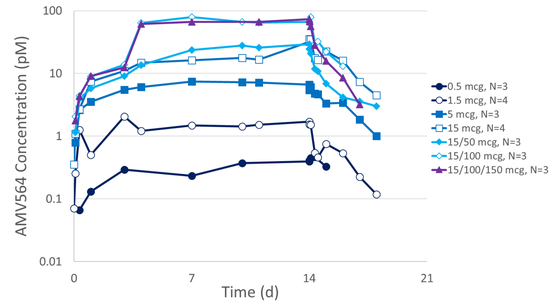
Cytokine Release Syndrome

- **No Grade 3+ CRS**
- **No Grade 2+ CRS with Lead-in Dose Strategy**

Lead-in Dose	Target Dose	# of Cycles	Grade 1	Grade 2	≥ Grade 3
N/A	15 mcg	20	3	0	0
15 mcg	100 mcg	13	4	0	0
15 → 100 mcg	150 mcg	4	2	0	0

PHARMACOKINETCS

Terminal half-life of 2 days

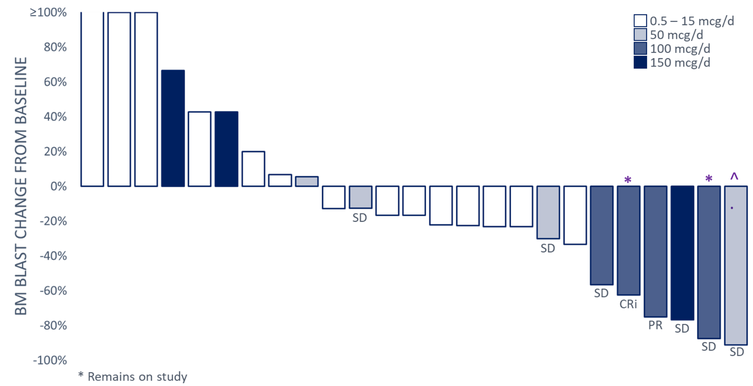


Lead-in dosing of 15 mcg for patients at the 50 and 100 mcg dose levels
Lead-in dosing of 15 mcg and 100 mcg for patients at 150 mcg dose levels

- Gradual concentration increase to steady-state with continuous intravenous infusion
- Concentrations decline with a multi-phasic profile

ANTI-LEUKEMIC ACTIVITY

Complete and partial responses observed



* Remains on study

^. Spleen size reduced from 18 cm to 11 cm (patient with 1° myelofibrosis evolved to AML)
Response as per ELN AML criteria 2017

CONCLUSIONS

Summary through 150 mcg cohort

- **Safe and Well Tolerated**
- **Novel Pharmacokinetic Profile**
- **Single Agent Activity in Relapsed/Refractory AML**
  - Blast reductions in 16/26 poor prognosis AML patients, with PR and CRi at 100 mcg
  - Response in extramedullary disease in the spleen
  - T cell activation and proliferation in bone marrow and blood

REFERENCES

- Döhner H et al. Diagnosis and management of AML in adults: 2017 ELN recommendations from an international expert panel. Blood. 2017 Jan 26;129(4):424-447. doi: 10.1182/blood-2016-08-733196. Epub 2016 Nov 28
- Reusch U et al. Characterization of CD33/CD3 Tetravalent Bispecific Tandem Diabodies (TandAbs) for the Treatment of Acute Myeloid Leukemia. Clin Cancer Res. 2016 Dec 1;22(23):5829-5838. Epub 2016 May 17.

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