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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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.

**STUDY DESIGN**

- **3+3 Design**
  - 14 Day Continuous Infusion
  - 300 mcg
  - 150 mcg
  - 60 mg
  - 50 mcg
  - 40 mg
  - 30 mg
  - 500 mcg

**KEY OBJECTIVES**

- Define MTD/PD/P2D
- Evaluate preliminary efficacy
- Assess PK
- Assess biomarkers
- CD33 expression not required

**MECHANISM OF ACTION**

- Homodimer that forms 4 scFvs
- Two binding sites for CD33 and CD3
- >200 KD, larger than the renal clearance threshold and not rapidly cleared

**AMV564**


**REFERENCES**


**PATIENT CHARACTERISTICS**

<table>
<thead>
<tr>
<th><strong>Poor prognosis population</strong></th>
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<tbody>
<tr>
<td>Median age (range), y</td>
</tr>
<tr>
<td>Sex, male, n (%)</td>
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<tr>
<td>ECOG score, n (%)</td>
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<tr>
<td>ECOG score, n (%)</td>
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<tr>
<td>Secondary AML, n (%)</td>
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<tr>
<td><strong>Spleen</strong></td>
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<td>Baseline WBC, median (range)</td>
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**MECHANISM OF ACTION**

- CD33 Target Cell
- CD33 Target Cell
- T Cell
- Highly specific CD33 target cell lysis
- Activation
- Cytokine release
- Proliferation
- Differentiation

**SAFETY**

No Dose Limiting Toxocities through 150 mcg

- No related Grade 3/4 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

**PHARMACOKINETICS**

Terminal half-life of 2 days

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

**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 CR at 100 mcg
  - Response in extramedullary disease in the spleen
  - T-cell activation and proliferation in bone marrow and blood