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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Abstract #1455

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 lysos of CD33-expressing cells and T-cell activation and proliferation. AMV564 is broadly active with picomolar potency and activity is independent of cytogenic 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

• Homodimer that forms 4 sFv/sFv
• Two binding sites for CD33 and CD3
• >200 kD, larger than the renal clearance threshold and not rapidly cleared

MECHANISM OF ACTION

AMV564

[Diagram showing the mechanism of action of AMV564]

PHARMACOKINETICS

Terminal half-life of 2 days

PATIENT CHARACTERISTICS

Poor prognosis population

| Median age (range), y | 71 (24, 84) |
| Sex, male, n (%) | 13 (50) |
| WBC, x10⁹/L, n (%) | 4 (15) |
| Secondary AML, n (%) | 73 (24, 84) |
| Prior alloHSCT, n (%) | 1 (4) |
| Prior allogeneic transplant, n (%) | 1 (4) |
| MRC cytogenetic risk group, n (%) | 0% 30% 50% 73% |
| Enrollment BM, median (range) | 1.70 (0.4, 3.10) |

SAFETY

No Dose Limiting Toxocities 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

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REFERENCES


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