A Phase 1 Dose Escalation with Expansion Study to Evaluate the Safety, Tolerability, Pharmacokinetics, and Efficacy of AMV564 in Subjects with Advanced Solid Tumors

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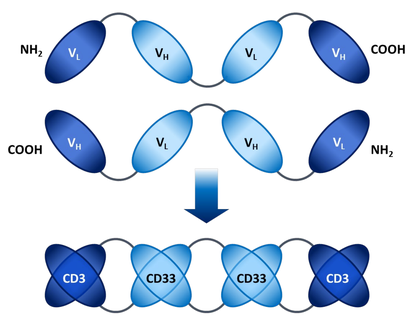
BACKGROUND

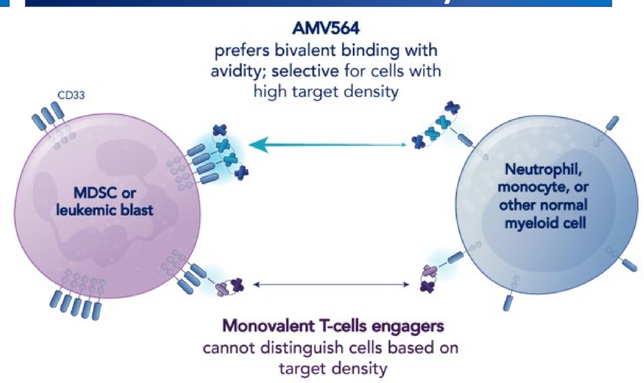
- Critical effectors of the suppressive tumor microenvironment are myeloid-derived suppressor cells (MDSCs), which elicit a range of suppressive functions that inhibit normal T cell responses and cause unresponsiveness to immune checkpoint blockade.
- MDSC expansion and production of immune-suppressive cytokines is driven by binding of CD33 by its ligand S100A9[1]
- AMV564 is a novel bivalent, bispecific (2:2) CD33/CD3 T-cell engager that binds CD33 on target cells and CD3 on T-cells leading to selective elimination of MDSCs, sparing normal neutrophils and monocytes, in acute myeloid leukemia (AML) patients.[2-3]
- The selectivity of AMV564 is driven by avid binding to cells where CD33 is highly expressed and actively signaling, such as MDSC
- Preliminary results from the first-in-human phase 1 study patients have demonstrated safety and single-agent activity in patients with AML.[3]

AMV564



- AMV564 is a homodimeric protein with 4 single-chain variable fragment (scFv) binding sites, 2 that bind CD33 and 2 that bind CD3
- > 100 kD in size

AMV564 Selectivity



- Selectivity of AMV564 is driven by avid binding to cells where CD33 is highly expressed and clustered in an activated configuration, such as MDSC

STUDY DESIGN AND OBJECTIVES

AMV564-301 is a Phase 1, open label, multicenter dose-escalation with expansion study in patients with advanced solid tumors for which no recognized standard therapy exists. This study is registered at ClinicalTrials.gov (NCT04128423).

Dose Escalation Stage

- 3+3 dose escalation
- Dose levels of 15 mcg/day up to a maximum of 2400 mcg/day
- Planned enrollment of ~42 patients

Primary Objectives

- To characterize AMV564 safety and tolerability
- To determine the maximum-tolerated dose (MTD) of AMV564 in patients with advanced solid tumors

Dose Expansion Stage

- Enrollment of up to 50 patients to receive AMV564 at the recommended dose identified in the Dose-Escalation Stage.

Primary Objectives

- To further characterize AMV564 safety and tolerability
- To evaluate preliminary efficacy of AMV564 in patients with advanced solid tumors

KEY ELIGIBILITY CRITERIA

Inclusion Criteria

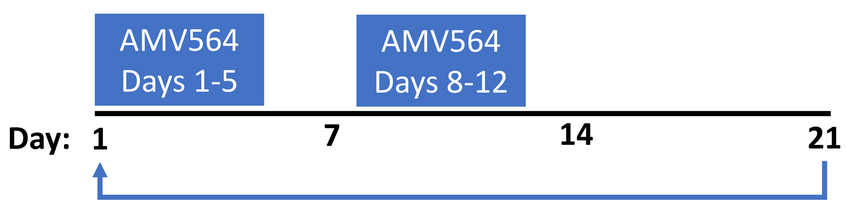
- ≥ 18 years of age
- Histologically or cytologically documented, incurable or metastatic solid tumor that is advanced (non-resectable) or recurrent and progressing since the last anti-tumor therapy and for which no recognized standard therapy exists
- ECOG performance status of ≤2.
- Measurable disease per RECIST v1.1 or per other criteria best suited for the specific tumor type being evaluated
- Adequate organ function

Exclusion Criteria

- Prior treatment with chimeric antigen receptor (CAR) T-cell therapy or T-cell engager therapy
- Chronic use of corticosteroids in excess of 10 mg daily of prednisone or equivalent within 4 weeks prior to first dose of AMV564 (replacement doses of corticosteroids, e.g. prednisone 5-7.5 mg daily are acceptable)

STUDY TREATMENT

AMV564 is administered daily as a subcutaneous (SC) injection on Days 1-5 and 8-12 of a 21-day cycle.



ENROLLMENT

- The first patient initiated treatment in Study AMV564-301 on 14 October 2019.
- To date, no dose-limiting toxicities (DLTs) have been reported and dose escalation continues.

Dose Level	Target Dose (mcg/d)	Enrolled Patients, n	DLT-Evaluable Patients, n	DLT Observed
1	15	2	1[a]	None
2-7	50-2400	Not yet enrolling		

[a] One patient enrolled at the 15 mcg/day dose level has not completed the DLT-evaluation period as of 9 November 2019.

REFERENCES

1. Chen *et. al*. J. Clin. Inv. (2013) 123: 4595-4611 Reusch U, Harrington KH, Gudgeon CJ, et al. Characterization of CD33/CD3 Tetravalent Bispecific Tandem Diabodies (TandAbs) for the Treatment of Acute Myeloid Leukemia. *Clin Cancer Res.* 2016; 22: 5829-38.
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3. Cheng P, Eksioglu E, Chen X, et al. Immunodepletion of MDSC By AMV564, a Novel Tetravalent Bispecific CD33/CD3 T Cell Engager Restores Immune Homeostasis in MDS in Vitro. *Blood*. 2017; 130:51 (abstract).

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