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

Raghad Karim, MD1; Alexander Starodub, MD, PhD2; Anthony Tolcher, MD1; Victoria Smith, PhD3; Sterling Eckard, PhD3; Jeanmarie Guenot, PhD3; Patrick Chun, MD3

1NEXT Oncology, San Antonio, TX; 2Riverside Peninsula Cancer Institute, Newport News, VA; 3Amphivena Therapeutics Inc., South San Francisco, CA

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 S100A91
- 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.
- The selectivity of AMV564 is driven by avid binding to cells where CD33 is highly expressed and clustered in an activated configuration, such as MDSC
- Preliminary results from the first-in-human phase 1 study patients have demonstrated safety and single-agent activity in patients with AML3

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).

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

STUDY TREATMENT

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

<table>
<thead>
<tr>
<th>AMV564</th>
<th>AMV564 Selectivity</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>AMV564 prefers bivalent binding with avidity; selective for cells with high target density</td>
</tr>
<tr>
<td></td>
<td>Selectivity of AMV564 is driven by avid binding to cells where CD33 is highly expressed and clustered in an activated configuration, such as MDSC</td>
</tr>
</tbody>
</table>

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.

<table>
<thead>
<tr>
<th>Dose Level</th>
<th>Target Dose (mcg/d)</th>
<th>Enrolled Patients, n</th>
<th>DLT-Evaluable Patients, n</th>
<th>DLT Observed</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>15</td>
<td>2</td>
<td>1</td>
<td>None</td>
</tr>
<tr>
<td>2-7</td>
<td>50-2400</td>
<td>2</td>
<td>1</td>
<td>None</td>
</tr>
<tr>
<td>8-30</td>
<td>450-3600</td>
<td>2</td>
<td>1</td>
<td>None</td>
</tr>
<tr>
<td>31-60</td>
<td>4000-7200</td>
<td>2</td>
<td>1</td>
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</tr>
<tr>
<td>61-120</td>
<td>6000-12000</td>
<td>2</td>
<td>1</td>
<td>None</td>
</tr>
<tr>
<td>121-2400</td>
<td>12,000-24,000</td>
<td>2</td>
<td>1</td>
<td>None</td>
</tr>
</tbody>
</table>

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

REFERENCES


Presented at the Society for Immunotherapy of Cancer Annual Meeting; November 6-10, 2019; National Harbor, MD. www.amphivena.com