SAFETY AND CLINICAL ACTIVITY OF AMV564, A CD33/CD3 T-CELL ENGAGER, IN PATIENTS WITH RELAPSED/REFRACTORY ACUTE MYELOID LEUKEMIA (AML): UPDATED RESULTS FROM THE PHASE 1 FIRST-IN-HUMAN TRIAL

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European Hematology Association
June 2019
Most AML Patients Die Within 1 Year After Relapsed/Refractory Disease

<table>
<thead>
<tr>
<th>Therapy</th>
<th>Data Source</th>
<th>n</th>
<th>Overall Response (CR + CRi)</th>
<th>Median OS, Months</th>
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<tbody>
<tr>
<td>IDAC</td>
<td>Phase 3 study¹</td>
<td>355</td>
<td>19</td>
<td>6.1</td>
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<tr>
<td>Intensive salvageᵃ</td>
<td>Phase 2 study²</td>
<td>44</td>
<td>41</td>
<td>6.3</td>
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<tr>
<td>Investigator’s choiceᵇ</td>
<td>Phase 3 study³</td>
<td>190</td>
<td>21</td>
<td>3.3</td>
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<tr>
<td>Hypomethylating agents</td>
<td>Multicenter retrospective (2006-2016)⁴</td>
<td>514</td>
<td>18</td>
<td>6.9</td>
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</tbody>
</table>


a. Intensive salvage regimens included: MEC (n=23); idarubicin/cytarabine (n=8); cytarabine-based induction + fludarabine ± Mylotarg (n=5); cytarabine-based induction + amsacrine (n=2); cytarabine-based induction + mitoxantrone ± Mylotarg (n=2); cytarabine-based induction + Mylotarg (n=1); cytarabine-based induction + cladribine (n=1); cytarabine alone (n=1); mitoxantrone + etoposide (n=1)
b. Investigator’s choice included: high-dose cytarabine (n=22); mitoxantrone, etoposide, cytarabine (MEC; n=44); fludarabine, cytarabine, granulocyte colony-stimulating factor with or without idarubicin (n=65); low-dose cytarabine (n=12); hypomethlyating agents (n=34); hydroxyurea (n=6); or supportive care (n=7)

IDAC=Intermediate-Dose Cytarabine; MEC=Mitoxantrone, Etoposide and intermediate dose Cytarabine
AMV564: A Bivalent, Bispecific CD33/CD3 T-cell Engager

**AMV564**

- Selected from > 100 lead candidates based on activity in AML patient samples

- CD33
  - Expressed on >95% of AML blasts
  - Highly expressed on myeloid derived suppressor cells (MDSCs)

**T-Cell Engager Mechanism of Action**

- Activation
- Cytokine release
- Proliferation
- Differentiation

***CD33+ Cell***

**Highly specific target cell killing**

***T Cell***
AMV564-101 Phase 1 Clinical Study Design: Relapsed/Refractory AML

### 3+3 DESIGN

- 0.5 – 15 mcg
- 50 mcg
- 100 mcg
- 150 mcg
- 200 mcg
- 250 mcg
- 300 mcg
- 450 mcg

### PATIENTS

33 Patients dosed to date

- Age ≥ 18 years
- High-risk disease
  - 1-4 prior induction regimens
  - Post AlloHSCT relapse allowed
  - 2nd AML allowed
- Normal renal/hepatic function

### KEY OBJECTIVES

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

### Status

- Enrolled
- Enrolling
- To be Enrolled
## AMV564-101: High Risk Patient Population

<table>
<thead>
<tr>
<th></th>
<th>0.5 - 250 mcg (x 14 days)</th>
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</thead>
<tbody>
<tr>
<td>Total N</td>
<td>33</td>
</tr>
<tr>
<td>Median age (range), y</td>
<td>71.5 (24, 85)</td>
</tr>
<tr>
<td>Sex, male, n (%)</td>
<td>19 (58)</td>
</tr>
<tr>
<td>ECOG score, n (%)</td>
<td></td>
</tr>
<tr>
<td>0</td>
<td>7 (21)</td>
</tr>
<tr>
<td>1</td>
<td>22 (67)</td>
</tr>
<tr>
<td>2</td>
<td>4 (12)</td>
</tr>
<tr>
<td>Secondary AML, n (%)</td>
<td>24 (73)</td>
</tr>
<tr>
<td>Prior intensive chemotherapy, n (%)</td>
<td>21 (64)</td>
</tr>
<tr>
<td>Prior allogeneic transplant, n (%)</td>
<td>3 (9)</td>
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<tr>
<td>MRC cytogenetic risk group, n (%)</td>
<td></td>
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<tr>
<td>Favorable</td>
<td>1 (3)</td>
</tr>
<tr>
<td>Intermediate</td>
<td>13 (39)</td>
</tr>
<tr>
<td>Unfavorable</td>
<td>19 (58)</td>
</tr>
<tr>
<td>Enrollment BM, median (range)</td>
<td>30% (3%, 96%)</td>
</tr>
<tr>
<td>Baseline WBC, median (range), X 10^9/L</td>
<td>2.1 (0.2, 13.8)</td>
</tr>
</tbody>
</table>
AMV564 Is Well Tolerated – No Dose Limiting Toxicity Through 250 mcg

- Oedema peripheral
- Pyrexia
- Nausea
- Headache
- Cytokine release syndrome
- Cough
- Constipation
- Febrile neutropenia
- Diarrhoea
- Fatigue
- Hypotension
- Hypokalaemia
- Vomiting
- Rash
- Tachycardia
- Insomnia
- Hypomagnesaemia
- Abdominal pain
- Pneumonia
- Fall
Best Response in Bone Marrow with a 14 Day Dosing Regimen

^ reduction in spleen size
Patient 02-041 (CR): Selective Depletion of Leukemic Blasts and MDSCs

Blasts: Bone Marrow

MDSCs: Bone Marrow

Neutrophils: Peripheral Blood

Blasts: Peripheral Blood

Monocytes: Peripheral Blood

MDSCs: Bone Marrow

% Total of CD45+ Cells

Early Monocytic
Granulocytic
Monocytic

AMV564

AMV564

AMV564

AMV564
New Lead-in Dose Regimen without Steroids for Continued Dose Escalation

No Grade 3 or Grade 4 CRS

<table>
<thead>
<tr>
<th>Lead-in Dose</th>
<th>Target Dose</th>
<th># of Cycles</th>
<th>Grade 1</th>
<th>Grade 2</th>
<th>≥ Grade 3</th>
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</thead>
<tbody>
<tr>
<td>N/A</td>
<td>15 mcg</td>
<td>30</td>
<td>3</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>15 mcg</td>
<td>100 mcg</td>
<td>21</td>
<td>4</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>15 → 100 mcg</td>
<td>150 mcg</td>
<td>4</td>
<td>2</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>15 → 100 mcg</td>
<td>200 mcg</td>
<td>3</td>
<td>0</td>
<td>2</td>
<td>0</td>
</tr>
<tr>
<td>15 → 100 mcg</td>
<td>250 mcg</td>
<td>1</td>
<td>0</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>15→30→100→150→200 mcg</td>
<td>250 mcg</td>
<td>3</td>
<td>0</td>
<td>1*</td>
<td>0</td>
</tr>
</tbody>
</table>

*Grade 2 CRS (hypotension) occurred at 15 mcg (Day 1) without dose interruption

15 → 100 mcg: 3 days at 15 mcg and 3 days at 100 mcg
15→30→100→150→200 mcg: 1 day at each of 15 mcg, 30 mcg, 100 mcg, 150 mcg and 200 mcg with no prophylactic steroids
AMV564-101 Summary

• Well tolerated, with no DLTs and limited Grade 1 and Grade 2 CRS
• Incremental dosing regimen with reduced lead in and without steroids tolerated at higher doses
• Monotherapy activity with CR, CRi and PR responses observed with a 14-day dosing regimen
• Seven-month duration of response observed (1 CRi, 1 SD)
• Rapid and selective elimination of leukemic blasts and MDSCs observed
Acknowledgments

- Patients and their families
- Investigators, study teams, and site personnel