A Phase II Open-label Multicenter Study to Assess the Efficacy and Safety of AFM13 in Patients With Relapsed or Refractory CD30-positive Peripheral T-cell Lymphoma (REDIRECT)

Introduction

Adult T-cell lymphoproliferative disease

- In hematologic malignancies, CD30 expression is strongly increased in Hodgkin lymphoma [6] and angiocentric large-cell lymphomas [62], but has also been found in other lymphoid malignancies, such as peripheral T-cell lymphoma (PTCL).
- While the identified subtypes of the PTCL can lead to different survival rates, chemotherapy treatment results in a median time from diagnosis to relapse or progression, and median overall survival of patients with PTCL, measured in months.
- In an international prospective cohort study, the majority of PTCL patients (several subtypes) were included, not otherwise specified (NOS) received chemotherapy +/- radiotherapy as first- or second-line treatment including consolidative high-dose therapy and hematopoietic stem cell transplantation (HCT) [7].
- It is observed that chemotherapy is administered +/- 5.8 months, 3 years with some (3%) for HSCT, for relapsed-patients, respectively.
- There is no clear standard of care treatment for PTCL/PN with the exception of brentuximab vedotin (BV) for the ALCL subtype and there is a paucity of data regarding long-term outcomes.

Targeting CD30-Positive Lymphoma with AFM13

**Objective:**

The objective of the REDIRECT clinical trial is to investigate the efficacy and safety of AFM13 in patients with relapsed or refractory CD30-positive peripheral T-cell lymphoma or transformed mycosis fungoides.

- An open-label, phase 2A/A, investigator-sponsored study is ongoing for patients in R/R (30 mg) or P/NS (60 mg) CD30-positive lymphoma with cutaneous involvement at the Columbia University Medical Center.
- Data presented from the Columbia University clinical study is summarized below (Table 1).  

**Methodology:**

- AFM13 demonstrated a high overall response rate of 50% (95% CI 24-79) and 14.3% complete response rate.
- AFM13 was active in 85% of patients with relapsed/refractory ANLL, of whom 50% were PR or complete responders.
- Currently only trials target patients who specifically have lymphoma as biomarker phase 2 and centrally (exception: patients with ≤Grade 2 peripheral neuropathy will be allowed).

**Table 1:** Monotherapy Response Rates in Patients With CD30-Positive Lymphoma

<table>
<thead>
<tr>
<th>Lymphoma Subtype</th>
<th>Complete Response</th>
<th>Partial Response</th>
<th>Stable Disease</th>
<th>Progression</th>
</tr>
</thead>
<tbody>
<tr>
<td>DLBCL</td>
<td>2/15 (13%)</td>
<td>6/15 (40%)</td>
<td>6/15 (40%)</td>
<td>1/15 (7%)</td>
</tr>
<tr>
<td>HL</td>
<td>1/10 (10%)</td>
<td>2/10 (20%)</td>
<td>6/10 (60%)</td>
<td>1/10 (10%)</td>
</tr>
<tr>
<td>ALCL</td>
<td>1/13 (8%)</td>
<td>4/13 (31%)</td>
<td>5/13 (38%)</td>
<td>3/13 (23%)</td>
</tr>
<tr>
<td>PTCL</td>
<td>1/11 (9%)</td>
<td>3/11 (27%)</td>
<td>6/11 (55%)</td>
<td>1/11 (9%)</td>
</tr>
</tbody>
</table>

**Figure 1:** AFM13 Structure

- AFM13 is a bispecific, tetravalent, innate cell engager that binds and activates natural killer (NK) cells and macrophages via CD16A as well as to CD30+ on lymphoma cells.
- Such transformation is often associated with poor prognosis and a mean 5-year survival rate of 20-40%.
- AFM13 therefore acts as a bridge to innate immunity by recruiting and activating innate immune cells and tumor-infiltrating lymphocytes (TILs) and is currently in clinical investigation.

**DISCLOSURE OF NOTES:**

- Patients with the following subtypes of lymphoma:
  1. T-cell and NK-cell lymphomas
  2. Angiocentric small-vessel lymphoma
  3. Primary cutaneous CD30+ T-cell lymphoma
  4. Primary cutaneous ALCL (lymphoma of cutaneous T-cell origin)
  5. Primary cutaneous ALCL (cutaneous T-cell lymphoma, not otherwise specified)
- Chemotherapy and brentuximab vedotin (BV) failure or be intolerant to brentuximab vedotin (Cohorts A and B)
- Patient must not have received brentuximab vedotin within 12 weeks (2 cycles of maintenance) of the first dose of study drug
- Results in a median time from original diagnosis to relapse or progression, and median overall survival of patients with PTCL, measured in months.
- In an international prospective cohort study, the majority of PTCL patients (several subtypes) were included, not otherwise specified (NOS) received chemotherapy +/- radiotherapy as first- or second-line treatment including consolidative high-dose therapy and hematopoietic stem cell transplantation (HCT) [7].
- It is observed that chemotherapy is administered +/- 5.8 months, 3 years with some (3%) for HSCT, for relapsed-patients, respectively.
- There is no clear standard of care treatment for PTCL/PN with the exception of brentuximab vedotin (BV) for the ALCL subtype and there is a paucity of data regarding long-term outcomes.

**Figure 2:** AFM13 Function

For refractory/relapsed (R/R) patients receiving HSCT or not receiving HSCT as salvage therapy, median survival after relapse (SAR) was 5.8 months, 3 years with some (3%) for HSCT, for relapsed-patients, respectively.

**Methods**

- **AFM13 (REDIRECT) is phase 2 open-label, multicenter, global study to investigate the efficacy and safety of AFM13 in patients R/R CD30+ PTCL and NHL (Figure 2)**
- **REDIRECT is a registration-directed study and is currently recruiting.**

**Figure 3. REDIRECT Phase 2 Study to Assess AFM13 in Patients With R/R CD30-positive T-cell Lymphoma or Transformed Mycosis Fungoides (NCT04015133)**

**DISCLOSURE OF NOTES:**

- Patients with the following subtypes of lymphoma:
  1. T-cell and NK-cell lymphomas
  2. Angiocentric small-vessel lymphoma
  3. Primary cutaneous CD30+ T-cell lymphoma
  4. Primary cutaneous ALCL (lymphoma of cutaneous T-cell origin)
  5. Primary cutaneous ALCL (cutaneous T-cell lymphoma, not otherwise specified)

**PRINCIPAL INVESTIGATORS:**

- **AFM13 (REDIRECT) is phase 2 open-label, multicenter, global study to investigate the efficacy and safety of AFM13 in patients R/R CD30+ PTCL and NHL**
- **REDIRECT is a registration-directed study and is currently recruiting.**

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**REFERENCES:**

- References:  
  1. Kim, KJ, Lee, S, Yoon, JH, et al. Boosted Affimed studying more patients with ≤Grade 2 peripheral neuropathy will be allowed.  
  3. J, LG, HR, DR, SS are employees of Affimed GmbH.  
  5. The results of this study are consistent with the REDIRECT trial and ongoing Affimed monoclonal antibody for the treatment of patients with R/R PTCL and NHL.
  6. The study is currently enrolling as of May 11th, 2020.
  7. Patients may have relapsed or refractory disease AND the following:
  8. Complete response established by validated immunohistochemistry, cytotoxicity, flow cytometry, radioimmunoassay, and/or another investigational agent at least 2 full courses of the drug administration schedule per the first dose of study drug.
  9. Ensuring sustainability of the clinical development of AFM13 in patients who do not meet the conditions for the enrolment of the study.  
  10. A Phase II Open-label Multicenter Study to Assess the Efficacy and Safety of AFM13 in Patients With Relapsed or Refractory CD30-positive Peripheral T-cell Lymphoma (REDIRECT)

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**ABBREVIATIONS:**

- **CD30**: CD30 antigen; **MCL**: mantle cell lymphoma; **B-ALL**: B-cell acute lymphoblastic leukemia; **AIDS**: acquired immune deficiency syndrome; **NSCLC**: non-small cell lung cancer; **PSC**: primary sclerosing cholangitis; **PFS**: progression-free survival; **OS**: overall survival; **ORR**: objective response rate; **CR**: complete response; **PR**: partial response; **SD**: stable disease; **PD**: progressive disease; **AE**: adverse event; **HCT**: hematopoietic stem cell transplantation; **EBMT**: European Group for Blood and Marrow Transplantation; **MDS**: myelodysplastic syndrome; **CML**: chronic myeloid leukemia; **KPS**: Karnofsky performance status; **mHCT**: autologous hematopoietic cell transplantation; **AML**: acute myeloid leukemia; **PR**: partial response; **CR**: complete response; **CBP**: center for bortezomib/pomalidomide; **HRS**: histiocytic sarcoma; **POD**: postoperative day