Clinical and Biological Evaluation of the Novel CD30/CD16A Tetravalent Bispecific Antibody (AFM13) in Relapsed or Refractory CD30-Positive Lymphoma with Cutaneous Presentation: A Biomarker Phase Ib/IIa Study (NCT03192202)

Ahmed Sawas, MD¹
Pei-Hsuan Chen², Mikel Lipschitz², Scott Rodig, MD PhD², George Vlad, PhD¹

¹Columbia University Medical Center, New York, NY; ²Brigham & Women's Hospital, Boston, Massachusetts; Boston, MA.
Main Findings

- AFM13 is active in CD30 expressing lymphomas
- AFM13 is well tolerated in patients
- Biomarker studies demonstrate that AFM13 is able to recruit and activate NK cells

Disclosures:

AS: Roche: Current equity holder in publicly-traded company; Affimed: Research Funding; Daiichi Sankyo: Speakers Bureau; Seattle Genetics: Speakers Bureau; Gilead: Speakers Bureau; Flatiron Health: Current Employment. PC: Affimed: Research Funding. ML: Affimed: Research Funding. SR: Bristol Myers Squibb: Research Funding; Merck: Research Funding; Affimed: Research Funding; KITE/Gilead: Research Funding; Immunitas: Current equity holder in private company, Membership on an entity’s Board of Directors or advisory committees.
Background

- AFM13 is a CD30/CD16A targeting high affinity bispecific tetravalent antibody that engages and activates NK cells and macrophages.
- This study evaluates AFM13’s clinical and immunological activity.
- The study examines the immunologic changes in the tumor and in peripheral blood (PB) as a function of the dose and method of administration of AFM13.
Methods:

- Population: subjects with relapsed or refractory CD30 expressing lymphoma with cutaneous involvement
- A second cycle was administered if there was no progression of disease.
- Response assessment performed by mSWAT, photography, PET imaging and peripheral blood flow cytometry.
- Skin biopsies, whole blood and plasma were collected: pretreatment, day 5 post first dose, week 4 and week 8 of therapy.
- Tumor biopsies were analyzed and evaluated by a pathologist and IHC image analyzer to characterize immune cell subpopulations.
- Peripheral blood samples were analyzed by flow cytometry.

<table>
<thead>
<tr>
<th>Cohort</th>
<th>Dosage</th>
<th>Total Exposure</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cohort 1</td>
<td>1.5 mg/kg</td>
<td>12mg/kg</td>
</tr>
<tr>
<td>Cohort 2</td>
<td>7.0 mg/kg</td>
<td>56mg/kg</td>
</tr>
<tr>
<td>Cohort 3</td>
<td>7.0 mg/kg CIVI*</td>
<td>56mg/kg</td>
</tr>
<tr>
<td>Cohort 4</td>
<td>200 mg</td>
<td>1600mg</td>
</tr>
</tbody>
</table>

AFM13 was administered weekly for 8 weeks

*1 mg/kg loading over 1 hour followed by 6mg/kg as continuous infusion for 5 days per week
## Results: Clinical results displayed by cohort, disease, toxicity and response

<table>
<thead>
<tr>
<th>Cohort</th>
<th>Disease</th>
<th>Toxicity</th>
<th>Response</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.5 mg/kg IV weekly</td>
<td>S-ALCL Alk-</td>
<td>No AE</td>
<td>PR</td>
</tr>
<tr>
<td></td>
<td>T-MF</td>
<td>No AE</td>
<td>POD</td>
</tr>
<tr>
<td></td>
<td>C-ALCL</td>
<td>Rash (G4), Skin infection (G3)</td>
<td>CR</td>
</tr>
<tr>
<td>7 mg/kg IV weekly</td>
<td>MF</td>
<td>IRR (G1)</td>
<td>SD</td>
</tr>
<tr>
<td></td>
<td>T-MF*</td>
<td>IRR (G1)</td>
<td>SD</td>
</tr>
<tr>
<td></td>
<td>T-MF</td>
<td>Skin infection (G3), IRR (G1)</td>
<td>Not assessed</td>
</tr>
<tr>
<td>7 mg/kg CIVI</td>
<td>T-MF</td>
<td>No AE</td>
<td>PR</td>
</tr>
<tr>
<td></td>
<td>S-ALCL Alk-*</td>
<td>No AE</td>
<td>PR</td>
</tr>
<tr>
<td></td>
<td>MF</td>
<td>No AE</td>
<td>POD</td>
</tr>
<tr>
<td>200 mg weekly</td>
<td>T-MF</td>
<td>No AE</td>
<td>PR</td>
</tr>
<tr>
<td></td>
<td>MF</td>
<td>No AE</td>
<td>SD</td>
</tr>
<tr>
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<td>PTCL-NOS</td>
<td>No AE</td>
<td>SD</td>
</tr>
<tr>
<td></td>
<td>T-PLL*</td>
<td>No AE</td>
<td>SD</td>
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<td>AITL</td>
<td>No AE</td>
<td>POD</td>
</tr>
<tr>
<td></td>
<td>T-MF*</td>
<td>No AE</td>
<td>PR</td>
</tr>
</tbody>
</table>

The ORR is 42%

*Patients progressed on Brentuximab vedotin prior to AFM 13 exposure

**Abbreviations:**
- **AE:** Adverse Events
- **AITL:** Angioimmunoblastic T-cell lymphoma
- **C-ALCL:** Cutaneous Anaplastic Large Cell lymphoma
- **CR:** Complete Response
- **PR:** Partial Response
- **POD:** Progression of Disease
- **PTCL-NOS:** Peripheral T-cell lymphoma not otherwise specified
- **MF:** Mycosis Fungoides
- **S-ALCL Alk-:** Systemic Anaplastic Large Cell Lymphoma-ALK negative
- **SD:** Stable Disease
- **T-MF:** Transformed Mycosis Fungoides
- **T-PLL:** T-cell Prolymphocytic Leukemia
**Results:** serial flow cytometry biomarker results

- Decrease in circulating NK cells during therapy with post therapy recovery, by following cells CD56+CD3- , CD56+CD16+ and NKp46+.

- Increase CD69 expression on circulating NK cells from responders vs. non-responders.

- Circulating CD4+ CD25+ T cells (Tregs) decrease in responders vs. non-responders.
Results: serial tumor tissue IHC biomarker

- Tumor biopsies showed increased infiltration of CD56+ NK cells pre therapy in responders vs. non-responders.

- NK cell (green) cytotoxicity through the expression of Granzyme B (red) was seen in responders vs. non-responders by comparing pre therapy tumor biopsy (top panel) to W4 tumor biopsy (bottom panel).

- No change in CD68 expressing cells (not shown).
Conclusion:

- AFM13 demonstrated ORR of 42%.
- AFM13 is well tolerated.
- AFM13 is active post brentuximab vedotin failure.
- Possible correlation between response and tumor NK cell infiltration pre therapy.
- A phase II multicenter international study of AFM13 in PTCL and T-MF is accruing (NCT04101331).

Skin response in a T-MF patient left knee and left inner thigh

Pre Study  Cycle 1 Week 11  Post Cycle 2