Methods: A Phase 1 dose escalation/limitation study is ongoing to evaluate the safety and tolerability and preliminary efficacy of the combination of AFM13 with pembrolizumab (Keytruda) as salvage therapy after failure of standard therapies including brentuximab vedotin in pts with NCT02686560). Pts receive escalating doses of AFM13 (Table 1) in combination with pembrolizumab at the approved dose of 200 mg following the classical 3+3 design. Upon completion of dose escalation, recruitment continues into an Extension Cohort. Response assessment is performed every 12 weeks by PET/CT according to the Lugano Classification Revised Staging System for malignant lymphoma. All available safety/efficacy data as of Apr 2016 are presented.

Results: Thirty pts have been enrolled into the study. The median age is 34 years (range, 18-73), with a median of 4 (range 3-7) prior lines of therapy. All pts have relapsed or refractory disease and have listed standard treatments including brentuximab vedotin (BV) and 43% of pts (13/30) died at their last therapy. Thirty seven percent (11/30) have undergone prior autologous stem cell transplantation. Twelve pts were escalated to the dose escalation cohorts (Cohorts 1, 2, 3, 4, and 5) and 18 into the Extension Cohort. All 30 pts completed the 6 week dose limiting toxicity (DLT) observation period. No DLTs occurred in Cohorts 1 and 2, one DLT occurred in Cohort 3 (mixed grade 3/4 DLT for AFM13 during the DLT period due to persistent Grade 1/2 infusion related reactions (IRR) and one DLT occurred in the Extension Cohort (Grade 4 IRR). Treatment-related adverse events (TRAEs) were mainly GI/G1 and included IRRs (8%), nausea (23%), pyrexia (23%) and rash (23%). Treatment related G3 AEs included IRRs (13%), elevated aspartate aminotransferase (2%), gastritis (3%), hypotension (3%), nausea (3%), neutropenia (3%) and vomiting (3%). An interim efficacy analysis was performed for all pts who had a baseline and at least one post-baseline disease assessment as of April 16, 2016 (n=24). The best overall response rate (ORR) and complete response rate (CR) rates treated at the dose and schedule chosen for expansion (n=28; Cohort 3 and Extension Cohort) were 89% and 26%, respectively, by both investigator assessment and independent central review.

Conclusions: Preliminary data suggest that the combination of AFM13 and pembrolizumab is a well tolerable in a patient population with most AEs mild to moderate in nature. The ORR of 89% and CR rate of 26% seen at the dose and schedule chosen for the Extension Cohort compare favorably to monotherapy pembrolizumab in a similar NHL population.

Background
- AFM13 shows synergy with anti-PD-1 in a PDX model

Introduction
- AFM13 is a first-in-class tetravalent, bispecific NK cell engaging agent in clinical development
- High affinity binding to CD30 and CD20, independent of polymorphism, virtually no competition with IgG and potent cytotoxicity
- Synergy with checkpoint modulators in pre-clinical studies
- Established clinical activity with solid safety profile (Phase 1 study)

Safety
- All 30 pts have completed DLT period
- 2 DLTs observed • Mixed 25% of AFM13 during DLT period (Cohort 3)
- 4 IRR (Extension Cohort)
- MTD not reached
- Extended dose/schedule of Cohort 3 (3 mg/kg followed by 7 mg/kg)
- Treatment-related adverse events (TRAE)
- Most common Terminology Criteria for Adverse Events (CTCAE) G1 or G2 and manageable with standard of care measures

Key Conclusions
- The combination of AFM13 and pembrolizumab is well tolerated with most AEs mild to moderate in nature and manageable with standard of care measures.
- Based on local and independent assessments, the ORR and CR rate for the combination at the dose selected for the extension cohort to date compare favorably to the historical data of pembrolizumab in a similar patient population.
- Based on these preliminary data, the combination of AFM13 and pembrolizumab might also be an attractive therapeutic option to be evaluated in patients who are relapsed/refractory to anti-PD1 therapy.

Population Characteristics
- Characteristics
- Total Patient Population (N=30)

Best Response, Tumor Volume
- Change in tumor volume measured by CT-scan, efficacy population (N=24)

A Phase 1 Study Investigating the Combination of AFM13 and the Monoclonal Anti-PD-1 Antibody Pembrolizumab in Patients with Relapsed/Refractory Hodgkin Lymphoma after Brentuximab Vedotin Failure: Updated Safety and Efficacy Data

Nancy L Bartlett1, Robert W Chen2, Eva Domingo3, Andres Forero-Torres4, Ramon Garcia-Sanz5, Philippe Armand6, Sumana Devata7, Antonia Rodriguez6, Izidore S Lossos8, Craig B Reeder9, Taimur Sheri10, Cassandra Choe-Julius11, Andras Strassas12, Anne Kerber12, Leila Alland13, Stephen M Ansell14

1:Slamtan Cancer Center, Washington University School of Medicine, Saint Louis, MO; 2:Department of Hematology, Dana Farber Cancer Institute, Boston, MA; 3:Instituto Catalán de Oncología L'Hospitalet, Barcelona, Spain; 4:University of Alabama at Birmingham, Birmingham, AL; 5:Hospita Universitario de Salamanca, Salamanca, Spain; 6:Clara-Farber Cancer Institute, Boston, MA; 7:University of Michigan, Ann Arbor, MI; 8:Hospital Universitario 12 de Octubre, Madrid, Spain; 9:Sybvestre Comprehensive Cancer Center, University of Miami Miller School of Medicine, Miami, FL; 10:Mayo Clinic, Scottsdale, AZ; 11:Mayo Clinic, Jacksonville, FL; 12:Affimed GmbH, Heidelberg, Germany; 13:Mayo Clinic, Rochester, MN

Abstract

PD429