Poster 1620

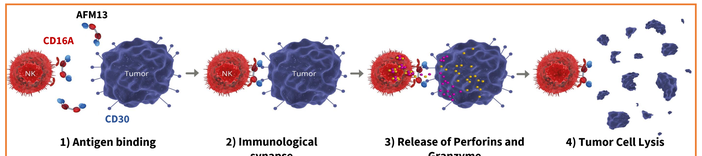
A Phase 1 Study Investigating the Combination of AFM13 and the Monoclonal Anti-PD-1 Antibody Pembrolizumab in Patients with Relapsed/Refractory Hodgkin Lymphoma after Brentuximab Vedotin Failure: Updated Safety and Efficacy Data

Nancy L Bartlett[1], Robert W Chen[2], Eva Domingo-Domenech[3], Andres Forero-Torres[4**], Ramon Garcia-Sanz[5], Philippe Armand[6], Sumana Devata[7], Antonia Rodriguez Izquierdo[8], Izidore S Lossos[9], Craig B Reeder[10], Taimur Sher[11], Cassandra Choe-Juliak[12#], Kim Prier[13], Sylvia E Schwarz[13], Andras Strassz[13], Leila Alland[12], Stephen M Ansell[14]

[1]Siteman Cancer Center, Washington University School of Medicine, Saint Louis, MO, [2]Department of Hematology/Hematopoietic Cell Transplantation, City of Hope, Duarte, CA, [3]Institut Català D'oncología L'Hospitalet de Llobregat, Barcelona, Spain, [4]Comprehensive Cancer Center University of Alabama at Birmingham, Birmingham, AL, [5]University Hospital of Salamanca, Salamanca, Spain, [6]Dana-Farber Cancer Institute, Boston, MA, [7]Internal Medicine/Hematology/Oncology, University of Michigan, Ann Arbor, MI, [8]Hospital Doce de Octubre, Madrid, Spain, [9]Sylvester Comprehensive Cancer Center, University of Miami, Miami, FL, [10]Mayo Clinic, Phoenix, AZ, [11]Mayo Clinic, Jacksonville, FL, [12]Affimed, Inc., New York, NY, [13]Affimed GmbH, Heidelberg, Germany, [14]Mayo Clinic, Rochester, MN

Introduction

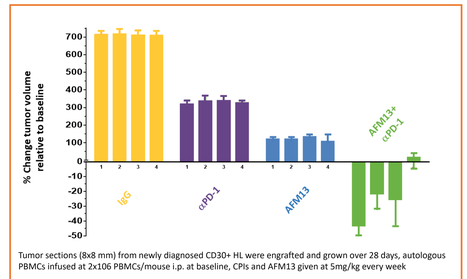
AFM13 is a first-in-class tetravalent, bispecific NK cell engager that binds to CD30 on tumor cells and CD16A on NK cells. By engaging CD16-positive NK cells, AFM13 leads to NK cell-mediated killing of tumor cells.[1] Pembrolizumab (Keytruda®) is approved in patients with R/R classical Hodgkin lymphoma as monotherapy. AFM13 showed single agent clinical activity with solid safety profile in a Phase 1 study[2]. Pre-clinical in vivo data of the combination of AFM13 with PD1-blockade showed synergism and the potential for induction of cross-talk between innate and adaptive immunity.[3] Based on these findings, we conducted a Phase 1b study evaluating the safety and tolerability of AFM13 in combination with pembrolizumab in patients with R/R Hodgkin lymphoma.



Mechanism of action of AFM13

Scientific Rationale

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



Tumor sections (8x8 mm) from newly diagnosed CD30+ HL were engrafted and grown over 28 days, autologous PBMCs infused at 2x106 PBMCs/mouse i.p. at baseline, CPIs and AFM13 given at 5mg/kg every week

Synergy of AFM13 with anti-PD-1

Methods

- **Study design:** 3+3 dose escalation design with 3 dose escalation cohorts (C) and an extension cohort (EC) of up to 24 patients (pts)
- **Primary objectives:**
  - Maximum tolerated dose (MTD) determination
- **Secondary objectives:**
  - Safety/tolerability
  - Anti-tumor activity
  - PK profile evaluation
- **Study assessments:**
  - PET/CT imaging every 12 weeks (Lugano Classification Revised Staging System for Malignant lymphoma)[4]

	Week 2 & 3	Weeks 4, 5, 6, 7,8, 9	Weeks 10, 13, 16, 19, 22 & 25
Cohort 1	0.1 mg/kg x 3	0.5 mg/kg	0.5 mg/kg
Cohort 2	0.5 mg/kg x 3	1.5 mg/kg	1.5 mg/kg
Cohort 3	3 mg/kg x 3	7.0 mg/kg	7.0 mg/kg

Dose escalation of AFM13

Population Characteristics

Characteristic	Total Patient Population (N=30) Number (%)
Age, years, median (range)	34 (18 to 73)
Gender	Female 10 (33%); Male 20 (67%)
Prior therapies, no.	
3	15 (50%)
4	6 (20%)
5	3 (10%)
6	4 (13%)
7	2 (7%)
Prior auto. stem cell transplant.	12 (40%)
Prior brentuximab vedotin (BV)	30 (100%)
BV as last therapy	13 (43%)
Refractory vs. relapsed	57% vs. 43%

Demographic and baseline characteristics, safety population (N=30)

Safety

- **All 30 pts have completed DLT period**
  - 2 DLTs observed
    - Missed ≥25% of AFM13 during DLT period (C3)
    - G4 IRR (EC)
- **MTD not reached; expansion at the highest treated dose and schedule**
- **Treatment-related Adverse Events (TRAE)**
  - Most were Common Terminology Criteria for Adverse Events (CTCAE) G1 or G2 and manageable with standard of care measures

TRAEs, All Grades	Safety population (N=30)
IRR	24 (80%)
Rash	9 (30%)
Nausea	7 (23%)
Pyrexia	7 (23%)
Diarrhea	6 (20%)
Fatigue	5 (17%)
Headache	5 (17%)
Elevated ALT	4 (13%)
Elevated AST	4 (13%)

TRAEs ≥ G3	Safety population (N=30)
IRR	4 (13%)
Elevated AST	1 (3%)
Gastritis	1 (3%)
Hypotension	1 (3%)
Nausea	1 (3%)
Neutropenia	1 (3%)
Vomiting	1 (3%)

Most common TRAEs in at least ≥10% patients for all CTCAE Grades and all TRAEs ≥ G3

Efficacy

- **Patients:** Efficacy analysis included best response amongst all 30 pts (intent to treat, ITT)
- **Overall response:** 88% ORR by both investigator and independent assessments at the highest dose treated/dose chosen for expansion
- **Complete response rate:** 42% by investigator and 46% by independent assessments at the highest dose treated/dose chosen for expansion
- **ITT:** 83% ORR for the ITT population that included dose escalation cohorts (C1 & C2) by both investigator and independent assessments

	Complete Metabolic Response No. (%)	Partial Metabolic Response No. (%)	No Metabolic Response No. (%)	Progressive Disease No. (%)	Overall Response Rate No. (%)
C1 and C2 (N=6)	1 (17%)	3 (50%)	0 (0%)	2 (33%)	4 (67%)
C3 + EC (N=24)	10 (42%)	11 (46%)	2 (8%)	1 (4%)	21 (88%)
ITT (N=30)	11 (37%)	14 (47%)	2 (7%)	3 (10%)	25 (83%)

Best metabolic response by investigator assessment, efficacy (ITT) population (N=30)

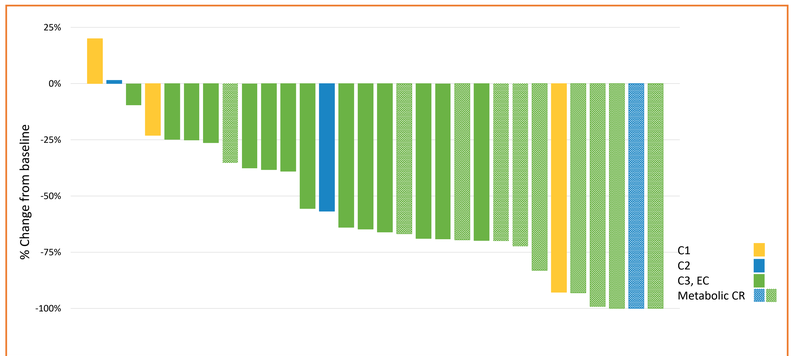
	Complete Metabolic Response No. (%)	Partial Metabolic Response No. (%)	No Metabolic Response No. (%)	Progressive Disease No. (%)	Overall Response Rate No. (%)
C1 and C2 (N=6)	1 (17%)	3 (50%)	2 (33%)	0 (0%)	4 (67%)
C3 + EC (N=24)	11 (46%)	10 (42%)	1 (4%)	2 (8%)	21 (88%)
ITT (N=30)	12 (40%)	13 (43%)	3 (10%)	2 (7%)	25 (83%)

Best metabolic response by independent assessment, efficacy (ITT) population (N=30)

Conclusions

- **The combination of AFM13 and pembrolizumab is well tolerated, with most common AE being IRRs that are mostly mild to moderate in nature and manageable with standard of care measures**
- **Deepening of responses over time was observed in multiple patients, and patients who were previously transplant ineligible transitioned to transplant after achieving an objective response**
- **At the highest treated dose, the ORR of 88% and CR rates of 42% and 46% by local and independent assessments, respectively, compare favorably to the historical data of pembrolizumab in a similar patient population, with the CR rate approximately double that of pembrolizumab[5, 6]**
- **The combination of AFM13 with pembrolizumab is a promising regimen for patients with relapsed/refractory Hodgkin lymphoma**

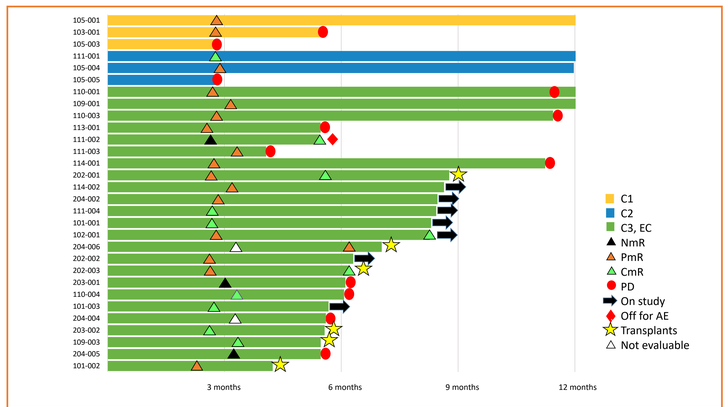
Best Response, Tumor Volume



Change in tumor volume measured by CT-scan, efficacy (ITT) population (N=30)

Duration and Deepening of Responses

- **Deepening of response:** Observed in 4 patients
  - NmR to CmR
  - 2 cases of PmR to CmR
  - Not evaluable to PmR
- **Durable responses:** Estimated 6-month PFS rate at the highest dose treated 77%
- **Transplant:** 6 patients transitioned successfully to stem cell transplant



Swimmers Plot, safety population (N=30)

#Corresponding author; Presenting author;

Disclosures: S.A. and P.A. receive research funding from Affimed; A.S., C.C-J., K.P.S.S., L.A. are employees of Affimed; **A.F-T is a former principal investigator at University of Alabama.

References: 1) Reusch U., et al., *mAbs* 2014; 6(3): 728-39. 2) Rothe A., et al., *Blood* 2015; 125(26): 4024-31. 3) Zhao X., et al., *J Clin Oncol* 2015; 33 (suppl; abstr 3050). 4) Cheson B.D., et al., *J Clin Oncol* 2014; 32(27): 3059-3067. 5) Chen et al., *J Clin Oncol* 2017; 35:2125-2132. 6) Armand, et al., *J Clin Oncol* 2018; 36:1428-1439.