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).

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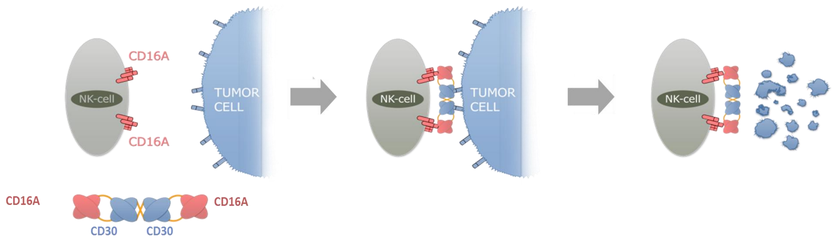
BACKGROUND

- AFM13 is a CD30/CD16A targeting high affinity bispecific tetravalent antibody that engages and activates NK cells and macrophages.



METHODS

- Population: subjects with relapsed or refractory CD30 expressing lymphoma with cutaneous involvement

Cohort	Dose regimen			Total exposure
	Dose	Schedule	Duration	
Cohort 1	1.5 mg/kg	weekly	weeks 1-8	12 mg/kg
Cohort 2	7.0 mg/kg	weekly	weeks 1-8	56 mg/kg
Cohort 3	7.0 mg/kg CIVI *	weekly	weeks 1-8	56 mg/kg
Cohort 4	200mg flat dose	weekly	weeks 1-8	1600 mg

*1 mg/kg loading 6mg/kg as continuous infusion for 5 days per week

- Response assessment performed by mSWAT, photography, PET imaging and peripheral blood flow cytometry.
- A second cycle was administered if there was no progression of disease.
- 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.

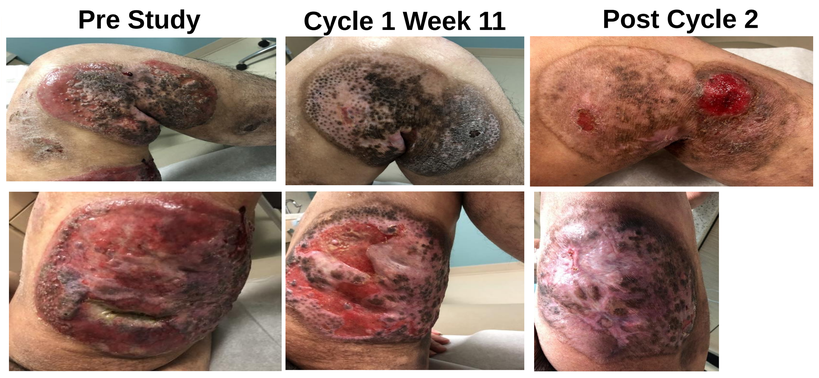
RESULTS

Patient Demographics Table	N= 10
Median age, (range)	65 (37-79)
Male (%)	7 (70%)
Race (% white/ non-white)	30%/70%
Median number of prior therapy, (range)	4 (1-11)
Patients progressed on brentuximab vedotin	2
Total Skin Electron Beam Radiotherapy	5
Disease Histologies	
Transformed Mycosis Fungoides (T-MF)	5
Mycosis Fungoides, non-transformed (MF)	2
Systemic Anaplastic Large Cell Lymphoma-ALK negative (S- ALCL, ALK -)	2
Cutaneous Anaplastic Large Cell Lymphoma (C-ALCL)	1

RESULTS

Cohort	Disease	Toxicity	Response
1	S-ALCL, Alk (-)	No AE	PR
	T-MF	No AE	POD
	C- ALCL	Rash (G4) Skin infection (G3)	CR
2	MF	IRR (G1)	SD
	T-MF	IRR (G1)	SD
	T-MF	Skin infection (G3) IRR (G1)	Not assessed
3	T-MF	No AE	PR
	S-ALCL, Alk (-)	No AE	PR
	MF	No AE	POD
4	T-MF	No AE	PR

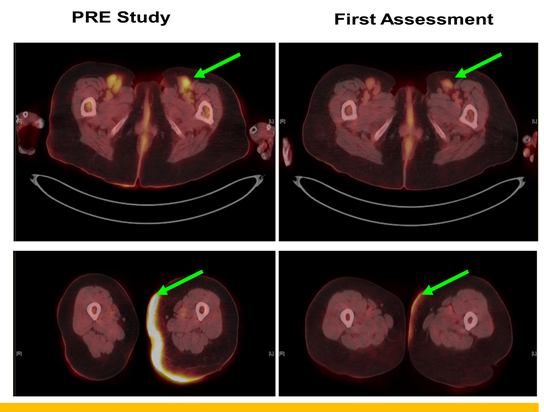
Skin Response in T-MF Patient



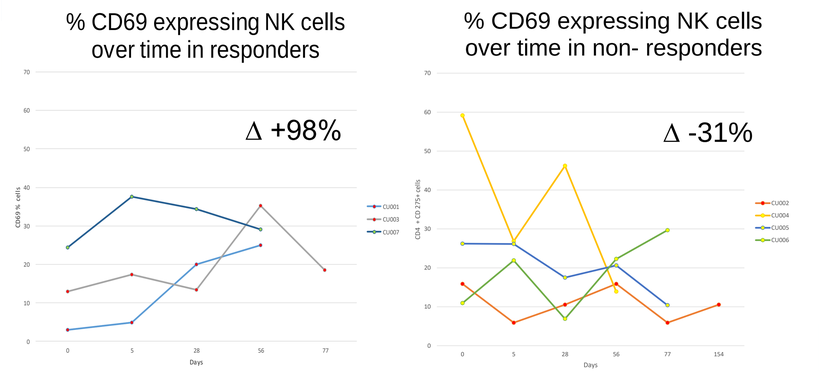
Rapid and Durable Response in T-MF

Response in a T-MF subject then consolidated with an Allogenic stem cell transplant. Responses were seen in:

- Nodes
- Skin
- Peripheral blood

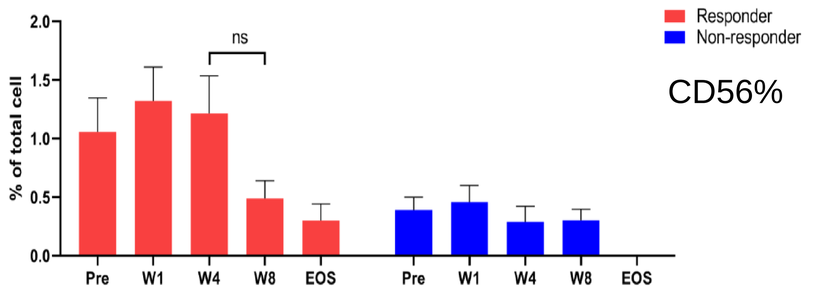


Peripheral Blood Biomarker Correlatives

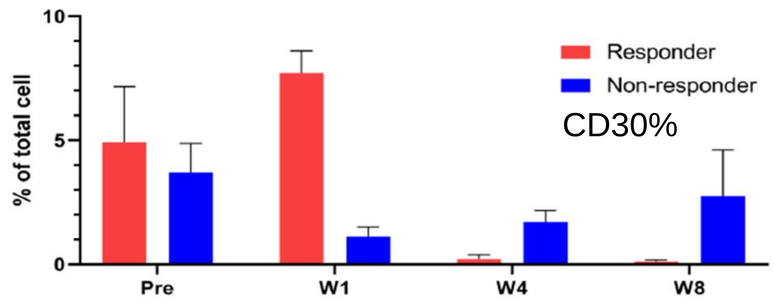


- Increased CD69 expression (activation marker) on circulating NK cells from responders vs. non-responders.
- Decreased in circulating NK cells during therapy with post therapy recovery, by following cells CD56+ CD3- , CD56+ CD16+ and NKp46+.
- Circulating CD4+ CD25+ T cells (Tregs) decrease in responders vs. non-responders.

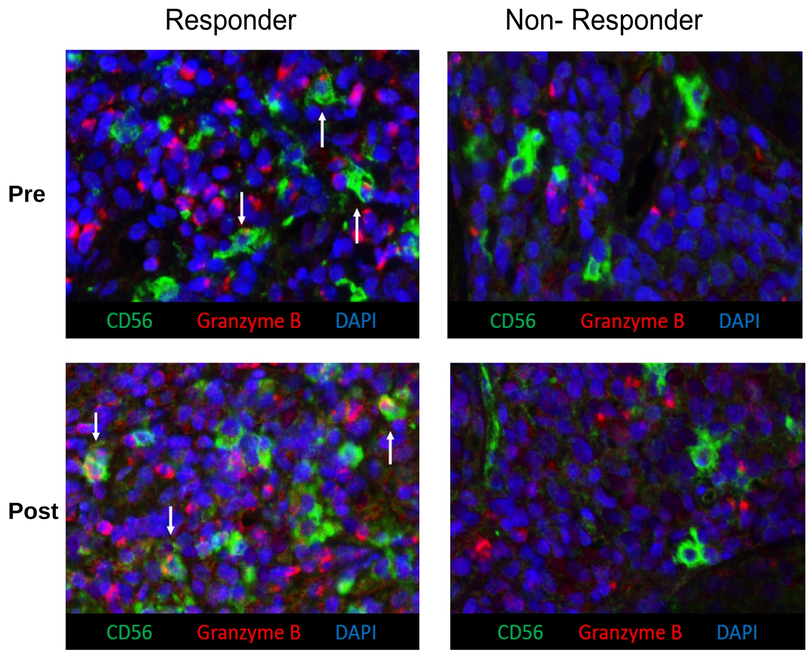
Tumor Biopsies Biomarker Correlatives



- Tumor biopsies showed increased infiltration of CD56+ NK cells pre therapy and during therapy in responders (red) vs. non-responders (blue).



- Tumor CD30 expressing cells decrease significantly in response to therapy in responders (red) vs. non-responders (blue).



- 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 was well tolerated.
- AFM13 demonstrated a high ORR of 50% and showed activity post-brentuximab vedotin failure.
- Tumor biopsies in patients who were responding to AFM13 showed increased NK cells both before and during treatment.
- A phase II multicenter international study of AFM13 in PTCL and T-MF is planned.

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