AFM13 in Patients with R/R Peripheral T cell Lymphoma (PTCL): A *Post-hoc* Subgroup Analysis From the REDIRECT Study

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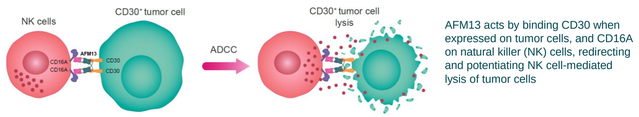
BACKGROUND

- PTCLs are a group of aggressive hematologic malignancies with generally poor prognoses. No standard-of-care therapy is established for patients with relapsed or refractory (R/R) PTCL and novel treatments are required[1]
- Proof-of-concept Phase 1 studies of AFM13, a tetravalent, bispecific Innate Cell Engager (ICE®), have shown a well-managed safety profile and promising clinical activity in patients with R/R Hodgkin lymphoma (HL) and cutaneous CD30-positive (CD30+) lymphomas[2,3]

AFM13 mechanism of action[4]



AFM13 acts by binding CD30 when expressed on tumor cells, and CD16A on natural killer (NK) cells, redirecting and potentiating NK cell-mediated lysis of tumor cells

ADCC, antibody-dependent cellular cytotoxicity; NK, natural killer.

- Analysis of a small group of patients with T-cell lymphoma with cutaneous presentation showed a correlation between increased NK cell infiltration into tumors and response to the treatment. AFM13 may provide an effective treatment approach for patients with CD30+ PTCL[5]
- This study (NCT04101331; REDIRECT trial) was a Phase 2 open-label, global, multicenter, study of AFM13 in patients with CD30+ R/R PTCL[6]

OBJECTIVES

To perform an analysis of AFM13 efficacy (overall response rate [ORR]) in patient subgroups from the REDIRECT study based on key patient characteristics

STUDY DESIGN

200 mg AFM13 was administered intravenously once weekly until disease progression, unacceptable toxicity, termination at the investigator's discretion, or withdrawal of consent

CRR, complete response rate; CT, computerized tomography; DoR, duration of response; FDG-PET, fluorodeoxyglucose-positron emission tomography; IRC, independent review committee; OS, overall survival; PFS, progression-free survival; PTCL, peripheral T-cell lymphoma.

Baseline characteristics

Patient characteristics	Total cohort (N=108)
Age, median (range)	63 (21–93)
Sex, N (%)	
Male	66 (61.1)
Female	42 (38.9)
PTCL subtypes, N (%)	
PTCL-NOS	41 (38.0)
AITL	30 (27.8)
sALCL	26 (24.1)
Other	11 (11.1)
Number of prior lines, N (%)	
Mean	2.7
1	23 (21.3)
2	35 (32.4)
≥3	50 (46.3)
Number of patients receiving prior BV, N (%)	50 (46.3)
Number of patients receiving prior auto transplant, N (%)	19 (17.6)

AITL, angioimmunoblastic T-cell lymphoma; BV, brentuximab vedotin; N, number of patients; PTCL, peripheral T-cell lymphoma; PTCL-NOS, peripheral T-cell lymphoma not-otherwise-specified; sALCL, systemic anaplastic large-cell lymphoma.

RESULTS

Exposure to study treatments (N=108)

*The dose was reduced to 100 mg AFM13 as per the protocol, in the case of repeated Grade 2 infusion-related reactions, or on a case-by-case basis following discussion with the Medical Monitor for patients exhibiting an AFM13-related, ≥Grade 3 non-infusion-related reactions. No amended had more than one dose reduction.
N, number of patients.

Safety

- AFM13 showed a well-managed safety profile; the most common treatment-emergent adverse events (TEAEs) were infusion-related reactions (IRRs)
- Steroid premedication reduced the incidence of IRRs

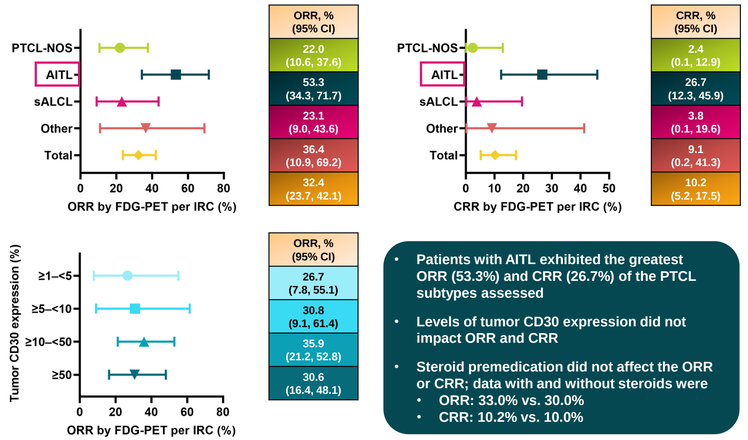
Summary of adverse events, N patients (N=108, %)	All	AFM13-related
TEAE	105 (97.2)	79 (73.1)
TEAE Grade ≥3	58 (53.7)	33 (30.6)
Serious TEAE*	43 (39.8)	9 (8.3)
Fatal TEAE	6 (5.6)	0
TEAEs leading to study drug discontinuation**	13 (12.0)	2 (1.9)

*Related, serious TEAEs were IRRs, pneumonia, chills, pyrexia, hepatic enzyme increase, and pulmonary embolism.

**All AFM13-related TEAEs leading to discontinuation were IRRs.
IRR, infusion-related reaction; N, number of patients;
TEAE, treatment-emergent adverse event.

Summary of AFM13-related TEAEs by Grade (≥5% patients), N patients (N=108, %)	Grade 1/2	Grade 3/4	Overall
Any TEAE	46 (42.6)	33 (30.6)	79 (73.1)
IRRs	21 (19.4)	6 (5.6)	27 (25.0)
Neutropenia	3 (2.8)	8 (7.4)	11 (10.2)
Pyrexia	8 (7.4)	1 (0.9)	9 (8.3)
Nausea	7 (6.5)	1 (0.9)	8 (7.4)
Anemia	3 (2.8)	4 (3.7)	7 (6.5)
Chills	6 (5.6)	1 (0.9)	7 (6.5)
Thrombocytopenia	5 (4.6)	2 (1.9)	7 (6.5)
Rash	5 (4.6)	1 (0.9)	6 (5.6)

Patients with AITL exhibited the highest ORR and CRR; no meaningful difference in efficacy was observed among patients stratified by CD30 expression levels



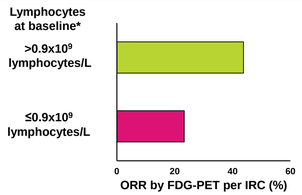
- Patients with AITL exhibited the greatest ORR (53.3%) and CRR (26.7%) of the PTCL subtypes assessed
- Levels of tumor CD30 expression did not impact ORR and CRR
- Steroid premedication did not affect the ORR or CRR; data with and without steroids were
  - ORR: 33.0% vs. 30.0%
  - CRR: 10.2% vs. 10.0%

AITL, angioimmunoblastic T-cell lymphoma; CI, confidence interval; CRR, complete response rate; FDG-PET, fluorodeoxyglucose-positron emission tomography; IRC, independent review committee; ORR, overall response rate; PTCL-NOS, peripheral T-cell lymphoma not-otherwise-specified; sALCL, systemic anaplastic large-cell lymphoma.

POST-HOC SUBGROUP ANALYSIS

- A *post-hoc* analysis was performed on subgroups defined by premedication (with or without steroids and number of prior lines of treatment), baseline lymphocytes counts, C-reactive protein (CRP) levels at baseline, and sex
- The displayed parameters were selected by a multivariate analyses to show a difference in ORR
- No meaningful differences were observed in subgroups defined by the number of prior lines of treatment and steroid premedication

Patients with high lymphocyte counts exhibited greater ORR, with minimal differences in AFM13-related TEAEs, compared with patients with low lymphocyte counts

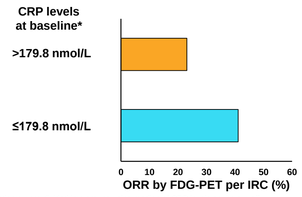


* Patients were divided into subgroups using median baseline lymphocyte levels as the cut-off

Summary of adverse events by subgroup, N patients (%)	AFM13-related	Serious AFM13-related	Grade ≥3 AFM13-related	IRRs
Lymphocytes levels				
high >0.9x10⁹ lymphocytes/L (N=48)	34 (70.8)	2 (4.2)	14 (29.2)	16 (33.3)
low ≤0.9x10⁹ lymphocytes/L (N=60)	45 (75.0)	7 (11.7)	19 (31.7)	18 (30.0)

- The ORR of patients with high baseline lymphocyte counts (above median) was greater than that of patients with low lymphocyte counts (43.8% [95% CI: 0.13, 0.36] vs. 23.3% [0.30, 0.59])
- The safety profiles were similar irrespective of lymphocyte counts

Patients with low CRP exhibited greater ORR, fewer Grade ≥3 AFM13-related reactions and IRRs compared with patients with high CRP

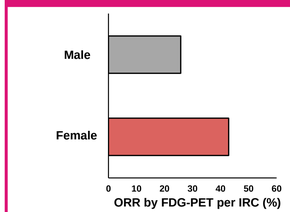


* Patients were divided into groups using median of CRP levels as the cut-off

Summary of adverse events by subgroup, N patients (%)	AFM13-related	Serious AFM13-related	Grade ≥3 AFM13-related	IRRs
CRP levels				
high >179.8 nmol/L (N=52)	41 (78.8)|	5 (9.6)	22 (42.3)	22 (42.3)
low ≤179.8 nmol/L (N=56)	38 (67.9)	4 (7.1)	11 (19.6)	12 (21.4)

- Patients with low CRP (below or equal to median) at baseline had a greater ORR than patients with high CRP at baseline (41.1% [95% CI: 0.28, 0.67] vs. 23.1% [0.13, 0.37])
- Patients with low CRP reported fewer Grade ≥3 AFM13-related reactions and IRRs compared with patients from the high CRP subgroup (19.6% vs. 42.3% and 21.4% vs. 42.3%, respectively)

Female patients demonstrated a higher ORR than male patients



Summary of adverse events by subgroup, N patients (%)	AFM13-related	Serious AFM13-related	Grade ≥3 AFM13-related	IRRs
Sex				
Male (N=66)	49 (74.2)	4 (6.1)	22 (33.3)	17 (25.8)
Female (N=42)	30 (71.4)	5 (11.9)	11 (26.2)	17 (40.5)

- The ORR of female patients was higher than that of male patients (42.9% [95% CI: 0.28, 0.59] vs. 25.8% [0.16, 0.38])
- Overall, female patients experienced fewer Grade ≥3 AFM13-related events than male patients (26.2% vs. 33.3%) but a higher incidence of IRRs (40.5% vs. 25.8%)

CONCLUSIONS

- AFM13 continues to show single-agent activity and a well-managed safety profile in patients with R/R PTCL
- The ORR is comparable to therapies approved for this indication[7–12]; subgroup analyses suggest potential patient characteristics which may predict a more favorable response to AFM13, such as sex, baseline lymphocyte counts, and CRP levels at baseline
- No meaningful difference in ORR was found in subgroups based on CD30 expression levels, number of prior lines or steroid premedication
- These data support further clinical development of AFM13, including in combination with cord blood-derived allogeneic NK cells, to augment the innate immune response to CD30+ tumors

The authors would like to thank all patients, carers, investigators and site staff for their invaluable contributions to the study.
Poster presented at the European Hematology Association meeting, Frankfurt, Germany, June 8–11, 2023. Medical writing support provided by Meridian HealthComms, Plumley, UK. For more information, please contact Karenza Alexis at K.Alexis@affimed.com

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