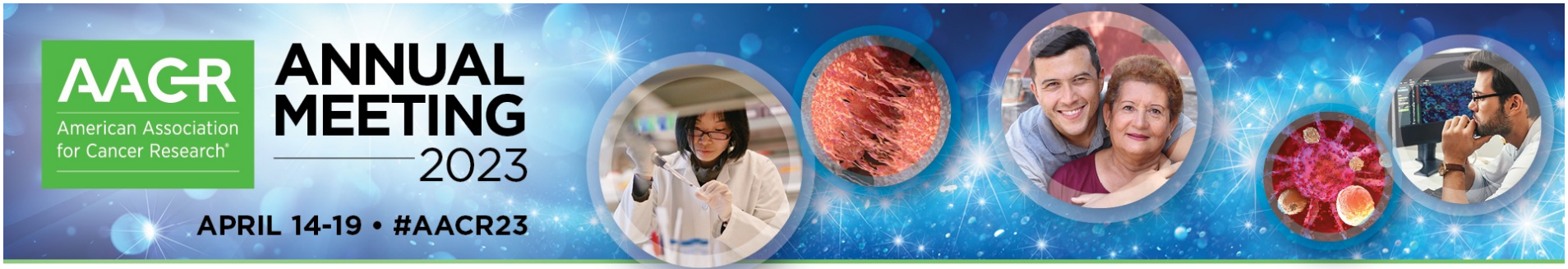

REDIRECT: A Phase 2 study of AFM13 in patients with CD30-positive relapsed or refractory (R/R) peripheral T-cell lymphoma (PTCL)

Won Seog Kim, MD
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SUNG KYUN KWAN UNIVERSITY

Disclosure Information

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Won Seog Kim

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There is high unmet need in R/R PTCL

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PTCLs are a heterogeneous group of aggressive lymphomas with generally poor prognoses[1]

PTCL accounts for **10–15% of all new cases** of NHL worldwide[2,3]

Median OS of most PTCL subtypes is **1–3 years**; the 5-year OS rate is ~26%[3]

Many patients do not respond to frontline therapy; **no standard-of-care therapy is established for patients with R/R PTCL[4]**

Many patients with PTCL have tumor cells that express CD30 (37–100% depending on PTCL subtype), providing a therapeutic target for developing novel treatment approaches[5]

1. Khan et al. *Cancers (Basel)* 2021; 13:5627 | 2. Vose et al. *J Clin Oncol* 2008;26(25):4124–30 | 3. Casulo et al. *J Natl Cancer Inst* 2017;109 | 4. Park et al. *BMC Cancer* 2020; 20:1157 | 5. Bossard et al. Blood 2014; 124:2983–86.
NHL, non-Hodgkin's lymphoma; OS, overall survival; PTCL, peripheral T-cell lymphoma; R/R, relapsed/refractory.

AFM13: Enhancing the innate immune response to target CD30⁺ tumor cells

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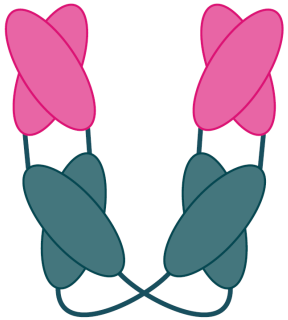
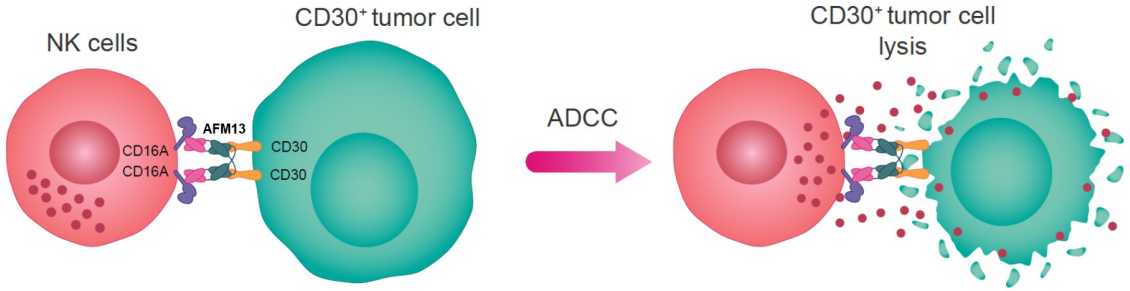
AFM13



AFM13 is a tetravalent, bispecific CD30/CD16A, designed to redirect and enhance NK cell-mediated ADCC towards CD30⁺ PTCL tumor cells[1,2]

AFM13 mechanism of action[3]



Augmenting innate immunity with AFM13 may provide an effective treatment approach for patients with R/R CD30⁺ PTCLs

1. Reiners et al. *Mol Ther* 2013; 21:895–903 | 2. Wu et al. *J Hematol Oncol* 2015; 8:96 | 3. Reusch et al. *MAbs* 2014; 6:728–39.
ADCC, antibody-dependent cellular cytotoxicity; NK, natural killer; PTCL, peripheral T-cell lymphoma; R/R relapsed/refractory.

Previous studies with AFM13 demonstrate proof-of-concept for targeting CD30+ lymphomas

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AFM13 monotherapy in patients with CD30+ R/R HL[1] and R/R lymphomas with cutaneous presentation[2]

- **AFM13 exhibited targeted lysis of CD30+ tumor cells**, with **ORRs of 11.5%–42.0%**
- **A well-managed safety profile was observed**; the most common TEAEs were IRRs, and **no cases of CRS**
- Early correlative science data showed **enhanced activation of NK cells** immediately after AFM13 infusion[1] and **greater NK cell activation and tumor infiltration of NK cells in the presence of AFM13**[2]

Based on these trials, the RP2D of 200 mg AFM13 was established

1. Rothe et al. *Blood*. 2015; 125:4024-31 | 2. Sawas et al. Oral presentation at the 2020 American Society of Hematology Annual Meeting and Exposition; December 5–8, 2020, Atlanta, Georgia, USA.
CRS, cytokine release syndrome; HL, Hodgkin lymphoma; NK, natural killer; ORR, overall response rate; IRR, infusion related reaction; RP2D, recommended phase 2 dose; R/R relapsed/refractory; TEAE, treatment emergent adverse event.

The REDIRECT study (NCT04101331)

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A Phase 2 open-label, global, multicenter, registration-directed study in patients with CD30$^+$ R/R PTCL

Inclusion criteria

- Histologically confirmed CD30$^+$ R/R PTCL by Ber-H2 targeted IHC in ≥1% tumor cells
- PTCL subtypes: PTCL-NOS, AITL, sALCL (ALK$^+$ and ALK$^-$; including patients who are refractory or progressed on BV), EATL, MEITL, HSTCL, SPTCL, FTCL, PTCL-TFH, and BIA-ALCL
- Received ≥1 prior line of systemic therapy

Exclusion criteria

- Non-PTCL subtypes of lymphoma: T-PLL, T-LGL, CLPD-NK, ANKL, ENKTCL, iTLPD-GI, ATL
- Requirement for systemic immunosuppressive therapy
- CNS involvement
- Allogeneic hematopoietic cell/solid organ transplant within the last 3 years

AITL, angioimmunoblastic T-cell lymphoma; ALK, anaplastic lymphoma kinase; ANKL, aggressive NK-cell lymphoma; ATL, adult T-cell leukemia/lymphoma; BIA-ALCL, breast implant-associated anaplastic large-cell lymphoma; BV, brentuximab vedotin; CLPD-NK, chronic lymphoproliferative disorder of NK cells; CNS, central nervous system; EATL, enteropathy-associated T-cell lymphoma; ENKTCL, extranodal NK/T-cell lymphoma; FTCL, follicular T-cell lymphoma; HSTCL, hepatosplenic T-cell lymphoma; iTLPD-GI, indolent T-cell lymphoproliferative disorder of the gastrointestinal tract; MEITL, monomorphic epitheliotropic intestinal T-cell lymphoma; PTCL, peripheral T-cell lymphoma; PTCL-NOS, peripheral T-cell lymphoma not-otherwise-specified; PTCL-TFH, nodal peripheral T-cell lymphoma with T follicular helper phenotype; SPTCL, subcutaneous panniculitis-like T-cell lymphoma; R/R, relapsed/refractory; sALCL, systemic anaplastic large-cell lymphoma; T-LGL, T-cell large granular lymphocytic leukemia; T-PLL, T-cell prolymphocytic leukemia.

The REDIRECT study (NCT04101331)

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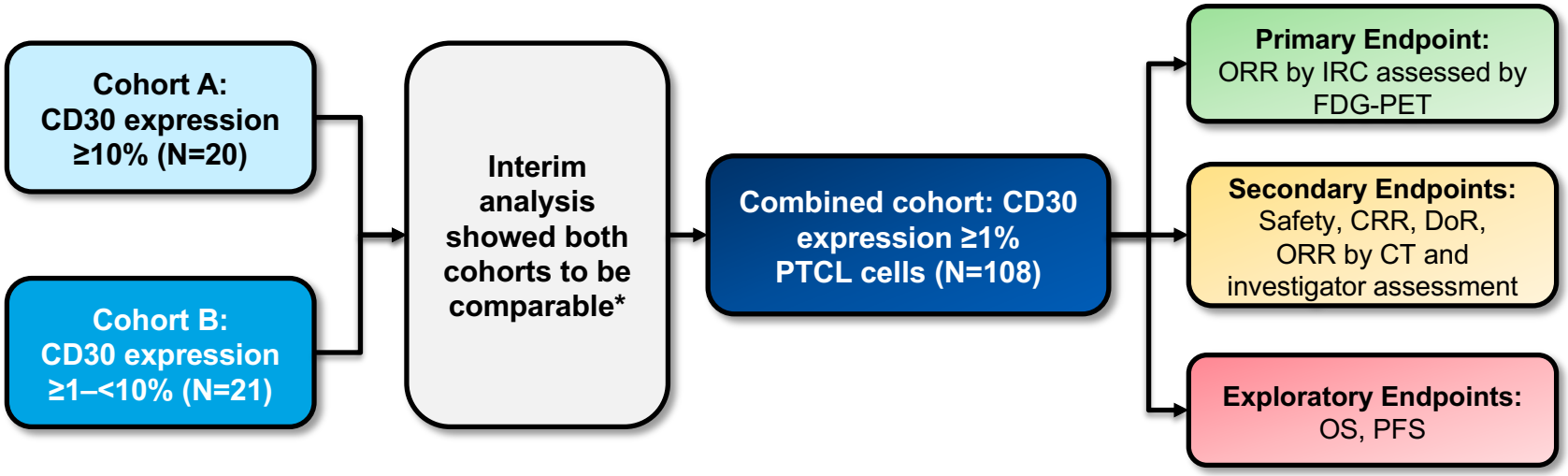
200 mg AFM13 was administered IV Q1W until disease progression, unacceptable toxicity, termination at the investigator's discretion, or withdrawal of consent



*An optimum Simon's two-stage design was used to calculate the sample size with H0=25 and H1=40. The pre-planned interim futility analysis at N=20 demonstrated that the response rate in Cohort A met the pre-defined threshold for continuation of the study. The response rate in Cohort B was sufficiently comparable to Cohort A, allowing merging of both cohorts into a single cohort for all patients with CD30 ≥1%, per the study protocol.
CRR, complete response rate; CT, computerized tomography; DoR, duration of response; FDG-PET, fluorodeoxyglucose-positron emission tomography; IRC, independent review committee; IV, intravenously
OS, overall survival; PFS, progression-free survival; PTCL, peripheral T-cell lymphoma; Q1W, once weekly; R/R, relapsed/refractory.

Patient and tumor characteristics (N=108)

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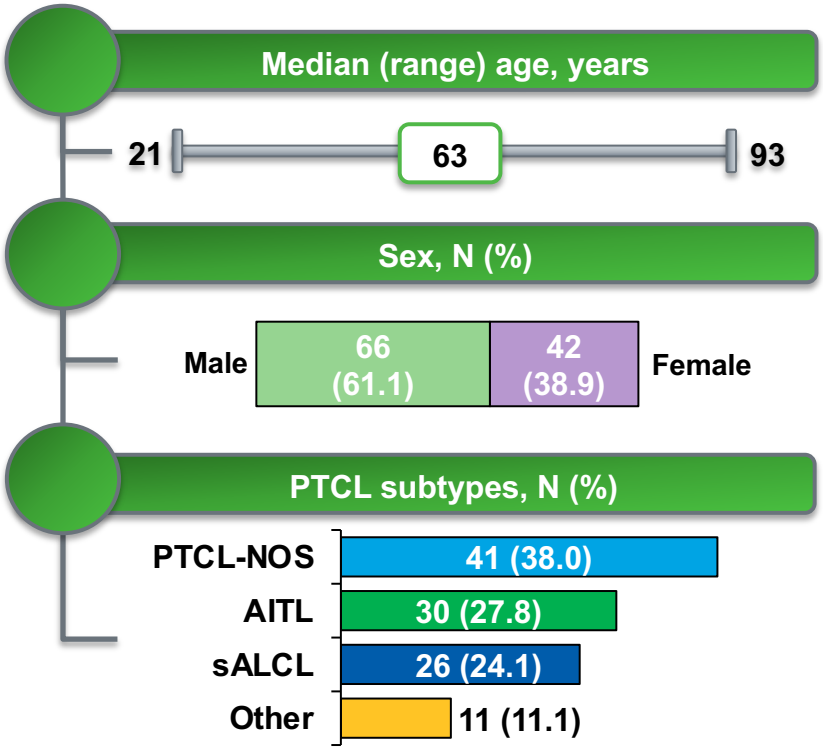

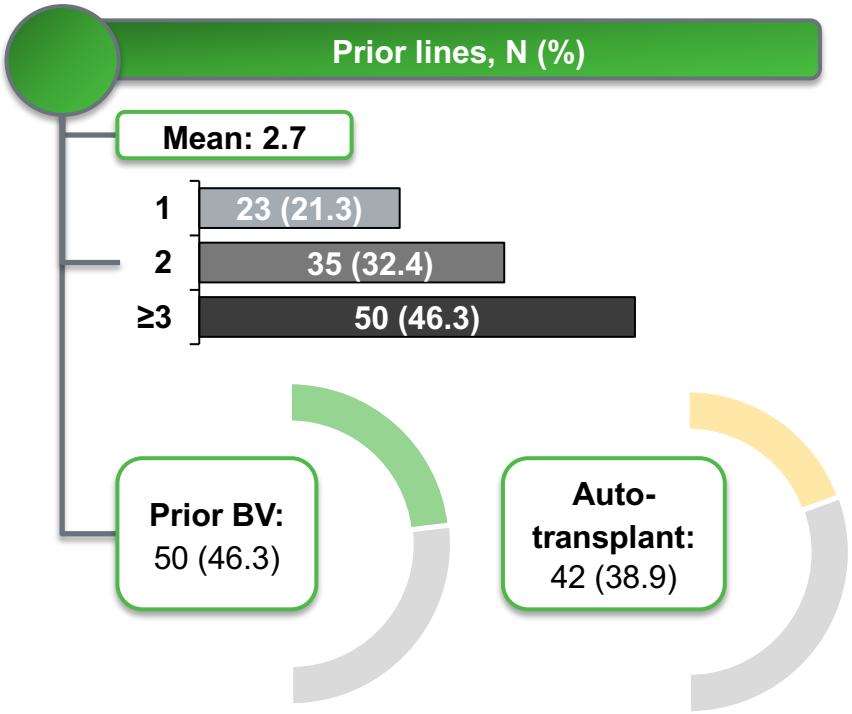

AITL, angioimmunoblastic T-cell lymphoma; BV, brentuximab vedotin; N, number; PTCL, peripheral T-cell lymphoma; PTCL-NOS, peripheral T-cell lymphoma not-otherwise-specified; sALCL, systemic anaplastic large-cell lymphoma.

Exposure to study treatment (N=108)

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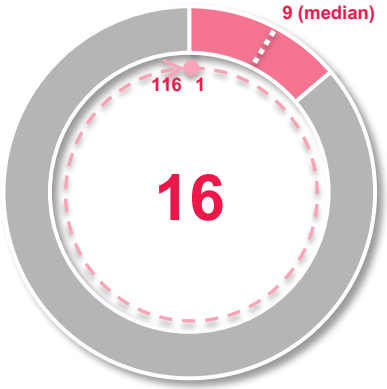
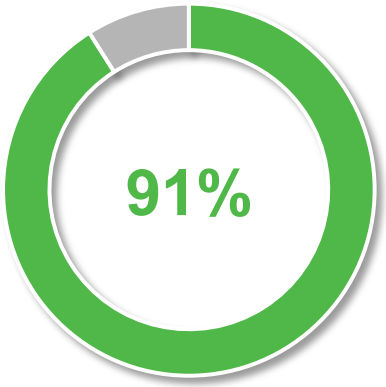
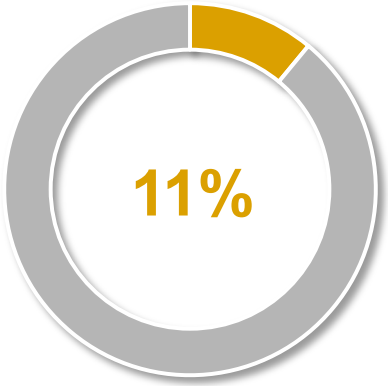
Number of infusions (mean)



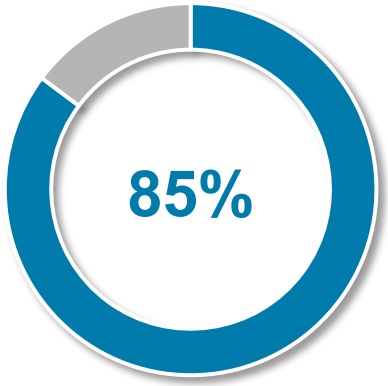
Relative dose intensity (mean)



Patients with at least one dose reduction*



Patients who received 200 mg at all infusions



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

AFM13 exhibited a tolerable safety profile (N=108)

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No new or unexpected safety findings were observed

Summary of adverse events, N patients (%)		
	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 infusion related reactions, pneumonia, chills, pyrexia, hepatic enzyme increase, and pulmonary embolism
**All AFM13-related TEAEs leading to discontinuation were IRRs

Summary of AFM13-related TEAEs by Grade (≥5% patients), N patients (%)			
	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)

No AFM13-related Grade 5 TEAEs were observed

IRR, infusion-related reaction; N, number; TEAE, treatment-emergent adverse event.

AFM13 exhibited clinical efficacy in a heavily pre-treated cohort of patients (N=108)

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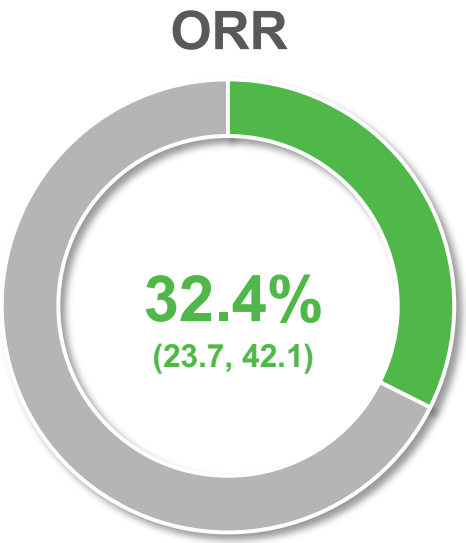

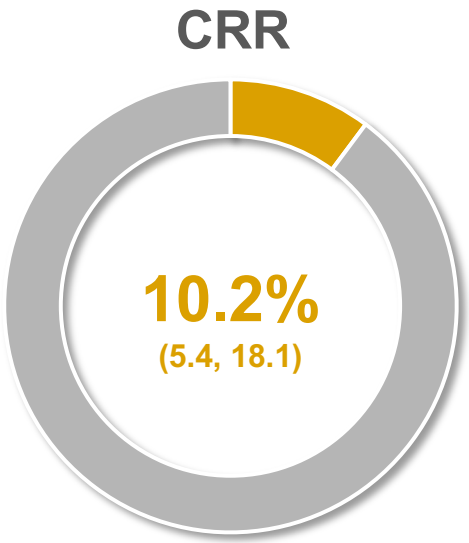

Metabolic responses were determined by FDG-PET per IRC assessment

ORR, CRR, and DCR (95% CI) values are presented.
CI, confidence interval; CRR, complete response rate; FDG-PET, fluorodeoxyglucose-positron emission tomography; IRC, independent review committee; N, number; ORR, overall response rate.

Tumor shrinkage was observed in over half of evaluable patients (N=82)

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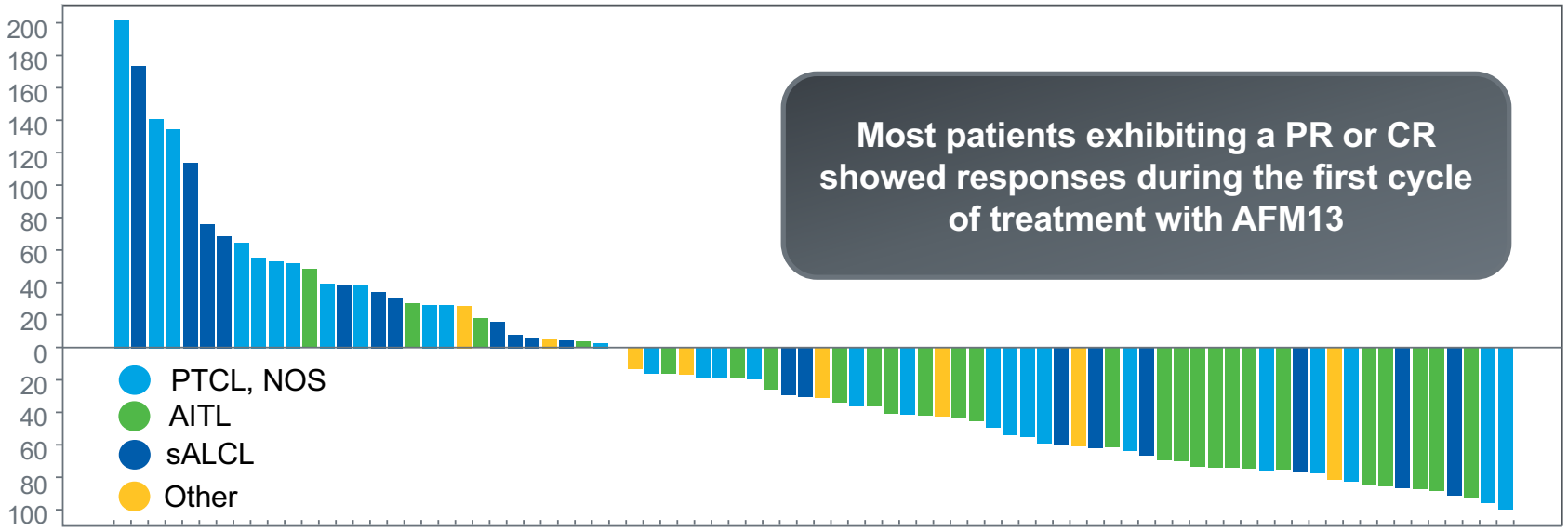
Greatest percentage tumor change from baseline in SPD based on CT per IRC assessment in individual patients*



*One bar represents one patient; only patients with measurable post-baseline assessment are included.
AITL, angioimmunoblastic T-cell lymphoma; CR, complete response; CT, computerized tomography; IRC, independent review committee; N, number; PR, partial response; PTCL-NOS, peripheral T-cell lymphoma not-otherwise-specified; sALCL, systemic anaplastic large-cell lymphoma; SD, stable disease; SPD, sum of the products of diameters.

Patients with AITL exhibited the highest ORR and CRR

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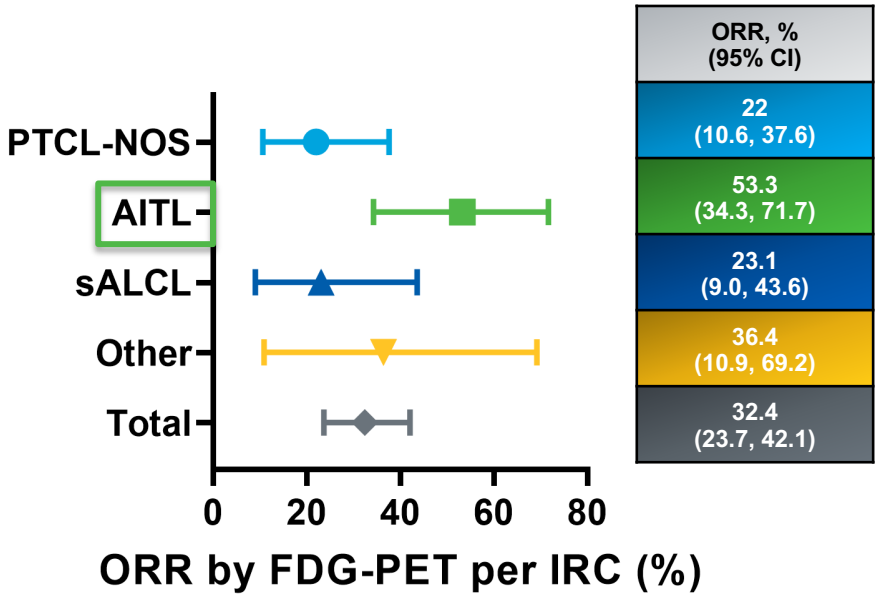

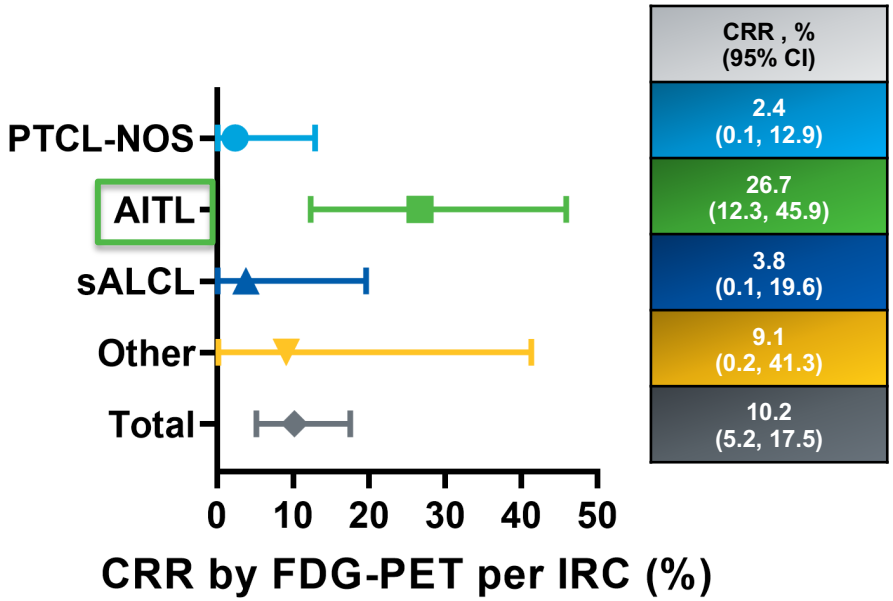

AITL, angioimmunoblastic T-cell lymphoma; CI, confidence interval; CRR, complete response rate; FDG-PET, fluorodeoxyglucose-positron emission tomography; IRC, independent review committee; N, number; ORR, overall response rate; PTCL-NOS, peripheral T-cell lymphoma not-otherwise-specified; sALCL, systemic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

No meaningful differences in response amongst patients stratified by CD30 expression level

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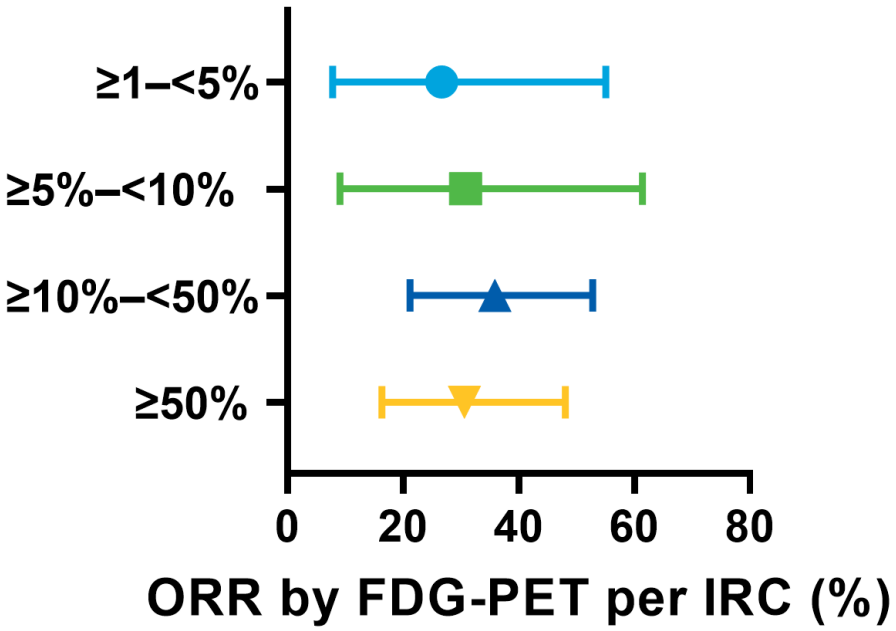

CD30 expression level	ORR, % (95% CI)
≥1–<5%	26.7 (7.8, 55.1)
≥5%–<10%	30.8 (9.1, 61.4)
≥10%–<50%	35.9 (21.2, 52.8)
≥50%	30.6 (16.4, 48.1)

CI, confidence interval; FDG-PET, fluorodeoxyglucose-positron emission tomography; IRC, independent review committee; ORR, overall response rate.

Duration of responses

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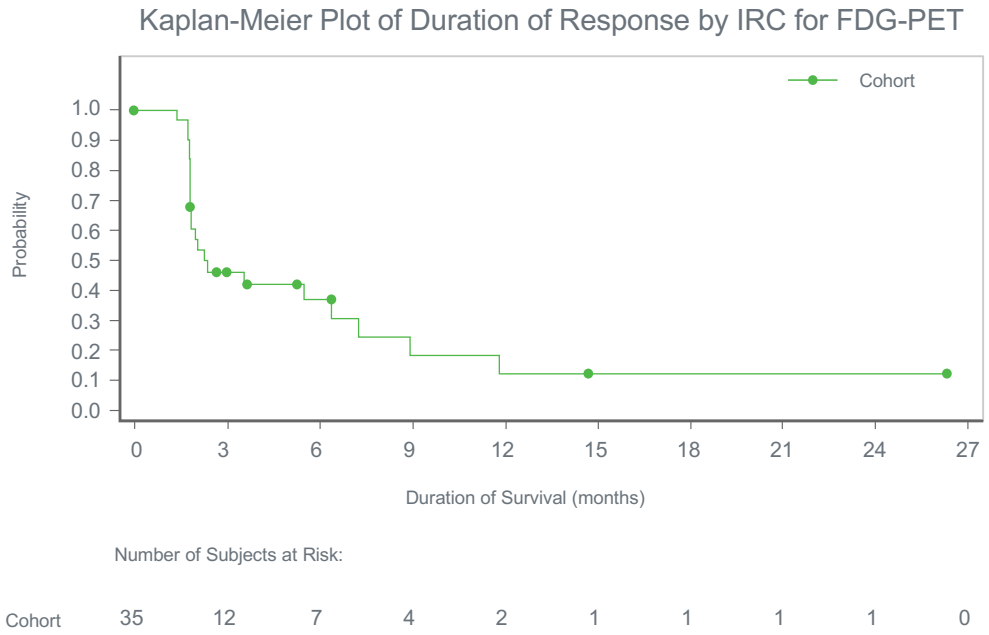

	DoR, N=35 DoCR, N=11
Patients censored, N	13
Median DoR, months (95% CI)	2.3 (1.9, 6.5)
Median DoCR, months (95% CI)	3.6 (1.9, NE)

CI, confidence interval; DoCR, duration of complete response; DoR, duration of response; FDG-PET, fluorodeoxyglucose-positron emission tomography; IRC, independent review committee; N, number; NE, not estimable.

Progression-free survival

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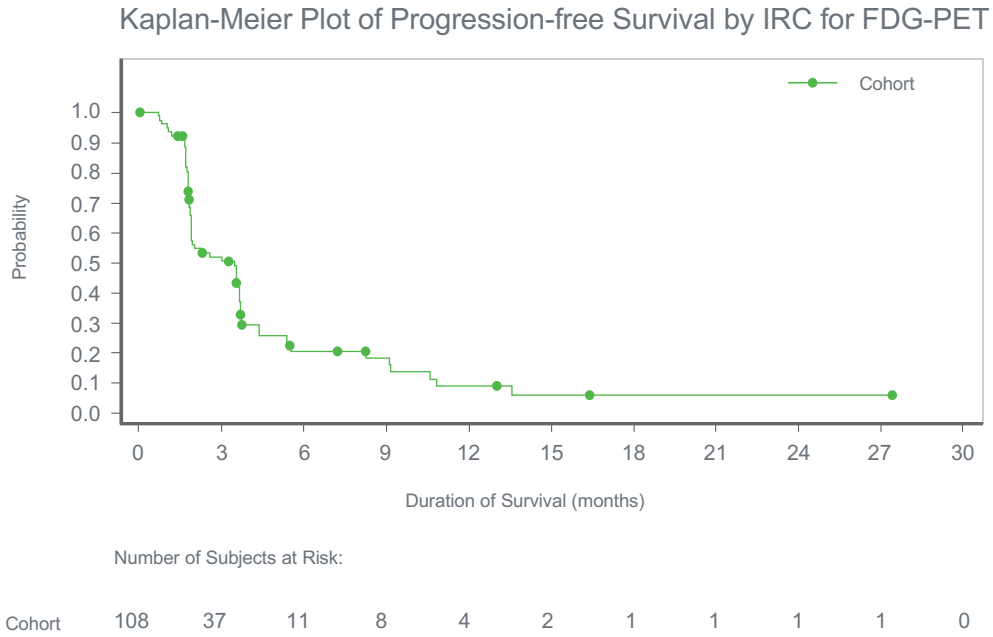

	N=108
Patients censored, N	46
Median PFS, months (95% CI)	3.5 (1.9, 3.6)

Percentage (%) based on number of subjects in the full analysis set. Subjects who had no recorded event (progressive disease or death) were censored at the date of their last disease assessment; those who began a new anti-cancer therapy or had a transplant prior to documented progression were censored at the last disease assessment prior to initiation of new anti-cancer therapy or prior to the transplant. Censor numbers included subjects who did not have any baseline assessments, or no post-baseline disease assessment performed even if baseline disease assessment was done.
CI, confidence interval; FDG-PET, fluorodeoxyglucose-positron emission tomography; IRC, independent review committee; N, number; PFS, progression-free survival.

Overall survival

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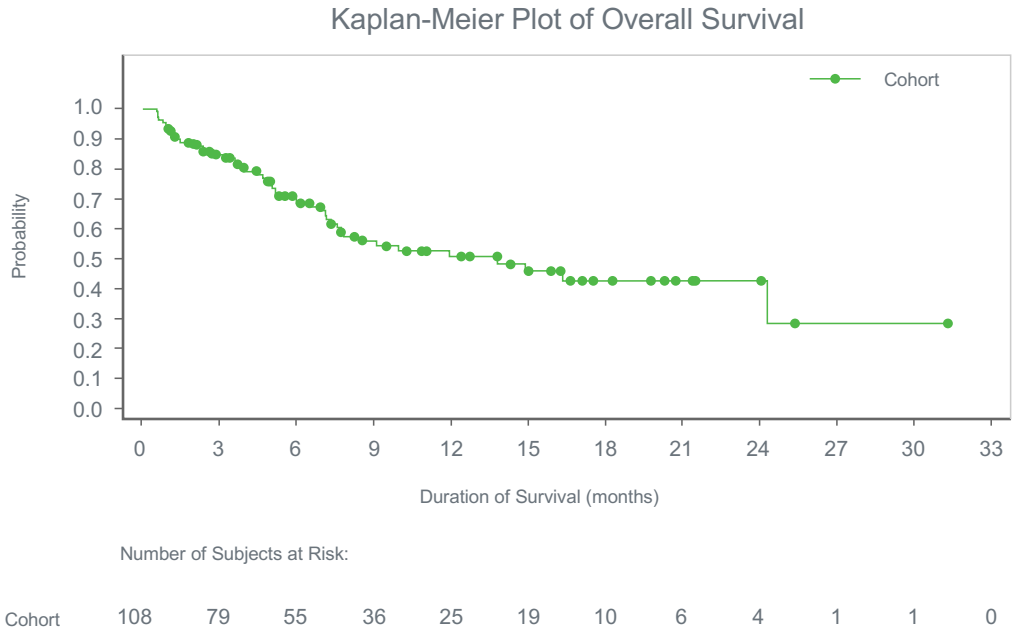

	N=108
Patients censored, N	62
Median OS, months (95% CI)	13.8 (5.0, NE)

Percentage (%) based on number of subjects in the full analysis set. Subjects who had no recorded event were censored at the date of their last disease assessment; those who began a new anti-cancer therapy or had a transplant prior to documented progression were censored at the last disease assessment prior to initiation of new anti-cancer therapy or prior to the transplant. Censor numbers included subjects who did not have any baseline assessments, or no post-baseline disease assessment performed even if baseline disease assessment was done.
CI, confidence interval; N, number; NE, not estimable; OS, overall survival.

Conclusion

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AFM13 exhibited clinical efficacy in a heavily pre-treated cohort with CD30+ R/R PTCL; the greatest ORR was observed in patients with AITL

AFM13 showed a tolerable safety profile; no new or unexpected safety findings were observed compared with previous AFM13 clinical studies

Enhancing the innate immune response with AFM13 may provide the basis for an alternative treatment approach for patients with R/R CD30+ PTCL

Beyond monotherapy: AFM13 in combination with allogeneic NK cells

- A trial of **AFM13 in combination with AB-101 allogeneic NK cells is planned** based on the results of a Phase 1/2a trial of AFM13 in combination with cbNK cells predominantly in patients with R/R HL[1,2]
  - **An ORR of 94.2%** was observed in patients treated at the RP2D
  - **The combination was well tolerated;** no DLTs were encountered during the dose escalation phase
- Data from REDIRECT provide **proof-of-concept for development of AFM13 in combination with NK cells in R/R CD30+ PTCL**

1. Nieto et al. Blood 2022;140:415–16 | 2. Nieto et al. Oral presentation at the 2022 American Society of Hematology Annual Meeting and Exposition; December 10–13, 2022; New Orleans, Louisiana, USA.
AITL, angioimmunoblastic T-cell lymphoma; cbNK, cord blood natural killer; DLT, dose-limiting toxicity; HL, Hodgkin lymphoma; NK, natural killer; ORR, overall response rate; PTCL, peripheral T-cell lymphoma; RP2D, recommended phase 2 dose; R/R, relapsed/refractory.

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- Saratov State Medical University
- GUZ Leningrad Regional Clinical Hospital
- Russian Research Institute of Hematology and Transfusiology of the Federal Biomedical Agency
- Regional Clinical Hospital

Spain
- Duran I Reynals Hospital Catalan Institute Of Oncology
- Hospital de la Santa Creu i Sant Pau
- Hospital del Mar Barcelona
- Hospital Universitari Vall d'Hebron
- Institut Catala d'Oncologia Badalona, Hospital Germans Trias I Pujol
- Institut Catala d' Oncologia Girona
- Hospital Universitario 12 de Octubre-Centro de Actividades Ambulatorias
- Hospital Universitario Fundacion Jimenez Diaz
- Hospital Universitario Virgen del Rocio
- Institut Catala d'Oncologia Tarragona

Turkey
- Ankara University Faculty of Medicine, Department of Internal Diseases, Hematology Division
- Dr. Abdurrahman Yurtaslan Ankara Onkoloji Egitim Arastirma Hastanesi Hematoloji Klinigi Ankara
- Gazi University Faculty of Medicine, Department of Internal Diseases
- Sağlık Bilimleri Üniversitesi Gülhane Eğitim ve Araştırm Hastanesi
- Istanbul Universitesi Istanbul Tip Fakultesi Ic Hastaliklari Anabilim Dali Hematoloji Bilim Dali Fatih
- Ege University Medical Faculty
- Kocaeli University Faculty of Medicine, Department of Internal Diseases, Hematology Division
- Ondokuz Mayis Universitesi Tip Fakultesi Saglik Uyg. ve Egitim Merkezi
- Tekirdag Namik Kemal Universitesi Saglik Uygulama ve Arastirma Hastanesi
- KaradenizTeknik Universitesi Tip Fakultesi Farabi Hastanesi

USA
- University of Alabama at Birmingham (O'Neal Comprehensive Cancer Center)
- City of Hope Comprehensive Cancer Center
- University of California Los Angeles (UCLA) Health
- Emory University Clinic, Winship Cancer Institute
- Ochsner Clinic Foundation, Precision Cancer Therapies Program
- University of Michigan Health, Rogel Cancer Center
- Mayo Clinic
- Center for Lymphoid Malignancies, New York
- Memorial Sloan Kettering Cancer Center
- Abramson Cancer Center of the University of Pennsylvania
- University of Pittsburgh Medical Center
- MD Anderson Cancer Center
- University of Washington Seattle Cancer Care Alliance

Thank you for listening