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
Sungkyunkwan University School of Medicine, Seoul, Republic of Korea
Disclosure Information

Won Seog Kim

I have the following relevant financial relationships to disclose:

Grant/Research support from: Sanofi, Beigene, Boryong, Roche, Kyowa-Kirin, Donga
There is high unmet need in R/R PTCL

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\(^5\)

---


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

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

AFM13 mechanism of action³

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


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

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)

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)

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

Cohort A:
CD30 expression ≥10% (N=20)

Interim analysis showed both cohorts to be comparable*

Combined cohort: CD30 expression ≥1% PTCL cells (N=108)

Primary Endpoint:
ORR by IRC assessed by FDG-PET

Secondary Endpoints:
Safety, CRR, DoR, ORR by CT and investigator assessment

Explanation:
- *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.
- ORR, 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)

Median (range) age, years
- 21 - 63 - 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)

Prior lines, N (%)
- Mean: 2.7
- 1: 23 (21.3)
- 2: 35 (32.4)
- ≥3: 50 (46.3)

Prior BV: 50 (46.3)
Auto-transplant: 42 (38.9)

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)

*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)

No new or unexpected safety findings were observed

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

*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

<table>
<thead>
<tr>
<th>Summary of AFM13-related TEAEs by Grade (≥5% patients), N patients (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Grade 1/2</td>
</tr>
<tr>
<td>Any TEAE</td>
</tr>
<tr>
<td>IRRs</td>
</tr>
<tr>
<td>Neutropenia</td>
</tr>
<tr>
<td>Pyrexia</td>
</tr>
<tr>
<td>Nausea</td>
</tr>
<tr>
<td>Anemia</td>
</tr>
<tr>
<td>Chills</td>
</tr>
<tr>
<td>Thrombocytopenia</td>
</tr>
<tr>
<td>Rash</td>
</tr>
</tbody>
</table>

*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

No AFM13-related Grade 5 TEAEs were observed
AFM13 exhibited clinical efficacy in a heavily pre-treated cohort of patients (N=108)

- **ORR**: 32.4% (23.7, 42.1)
- **CRR**: 10.2% (5.4, 18.1)

Metabolic responses were determined by FDG-PET per IRC assessment.

OFR, 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)

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

Most patients exhibiting a PR or CR showed responses during the first cycle of treatment with AFM13

*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

PTCL-NOS

<table>
<thead>
<tr>
<th>Condition</th>
<th>ORR, % (95% CI)</th>
<th>CRR, % (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>AITL</td>
<td>22 (10.6, 37.6)</td>
<td>2.4 (0.1, 12.9)</td>
</tr>
<tr>
<td>sALCL</td>
<td>53.3 (34.3, 71.7)</td>
<td>26.7 (12.3, 45.9)</td>
</tr>
<tr>
<td>Other</td>
<td>23.1 (9.0, 43.6)</td>
<td>3.8 (0.1, 19.6)</td>
</tr>
<tr>
<td>Total</td>
<td>36.4 (10.9, 69.2)</td>
<td>9.1 (0.2, 41.3)</td>
</tr>
<tr>
<td>Total</td>
<td>32.4 (23.7, 42.1)</td>
<td>10.2 (5.2, 17.5)</td>
</tr>
</tbody>
</table>

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

<table>
<thead>
<tr>
<th>CD30 expression level</th>
<th>ORR, % (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>≥1–&lt;5%</td>
<td>26.7 (7.8, 55.1)</td>
</tr>
<tr>
<td>≥5%–&lt;10%</td>
<td>30.8 (9.1, 61.4)</td>
</tr>
<tr>
<td>≥10%–&lt;50%</td>
<td>35.9 (21.2, 52.8)</td>
</tr>
<tr>
<td>≥50%</td>
<td>30.6 (16.4, 48.1)</td>
</tr>
</tbody>
</table>

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

Kaplan-Meier Plot of Duration of Response by IRC for FDG-PET

Cohort

Patients censored, N
DoR, N=35
DoCR, N=11

<table>
<thead>
<tr>
<th>Patients censored, N</th>
<th>13</th>
</tr>
</thead>
<tbody>
<tr>
<td>Median DoR, months (95% CI)</td>
<td>2.3 (1.9, 6.5)</td>
</tr>
<tr>
<td>Median DoCR, months (95% CI)</td>
<td>3.6 (1.9, NE)</td>
</tr>
</tbody>
</table>

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

Kaplan-Meier Plot of Progression-free Survival by IRC for FDG-PET

- **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

Kaplan-Meier Plot of Overall Survival

Number of Subjects at Risk:

<table>
<thead>
<tr>
<th>Cohort</th>
<th>108</th>
<th>79</th>
<th>55</th>
<th>36</th>
<th>25</th>
<th>19</th>
<th>10</th>
<th>6</th>
<th>4</th>
<th>1</th>
<th>1</th>
<th>0</th>
</tr>
</thead>
</table>

Patients censored, N

<table>
<thead>
<tr>
<th></th>
<th>N=108</th>
</tr>
</thead>
<tbody>
<tr>
<td>N=108</td>
<td>62</td>
</tr>
</tbody>
</table>

Median OS, months (95% CI)

<table>
<thead>
<tr>
<th></th>
<th>13.8</th>
</tr>
</thead>
<tbody>
<tr>
<td>(5.0, NE)</td>
<td></td>
</tr>
</tbody>
</table>

CI, confidence interval; N, number; NE, not estimable; OS, overall survival.
Conclusion

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


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.
Acknowledgements

We would like to thank all of the patients, caregivers, investigators and trial site staff who participated in the REDIRECT study.

I would also like to take this opportunity to thank my fellow co-authors and investigators for their valued contribution to this trial:

- Jake Shortt
- Pier Luigi Zinzani
- Natalya Mikhaylova
- Ana Marin-Niebla
- Dejan Radeski
- Vincent Ribrag
- Eva Domingo Domenech
- Ahmed Sawas
- Karenza Alexis
- Michael Emig
- Linta Garcia
- Andre Overesch
- Kerstin Pietzko
- Steven Horwitz
- Tasman Armitage
- Pratyush Giri
- Nicole Wong Doo
- Georg Hess
- Marcus Hentrich
- Peter Reimer
- Blanca Sanchez Gonzalez
- Jose Maria Roncero Vidal
- Raul Cordoba
- Juan Manuel Sancho
- Antonia Rodríguez
- Fatima De La Cruz Vicente
- Adrian Tempesta
- Krimo Bouabdallah
- Stéphane Vigourovix
- Roch Houot
- Emanuele Ravano
- Alessandra Tucci
- Gerardo Musuraca
- Monica Tani
- Jae-Cheol Jo
- Prof. Jong-seok Lee
- Ki-seong Eom
- Wanda Knapinska-Poslusnny
- Wojciech Jurczak
- Alexander Myasnikov
- Serge Voloshin
- Oleg Akilov
- Stefan Bartá
- Andrei Shustov
- Jasmine Zain
- Swaminathan Iyer
- Nora Bennani
- Pamela Allen
- Ryan Wilcox
- Burhan Turgut
- Mehmet Turgut
- Meliha Nalcaci
- Fahri Sahin
- Ozgur Mehtap
- Laura Finn
- Oleg Akilov
- Stefan Bartá
- Andrei Shustov
- Jasmine Zain
- Swaminathan Iyer
- Nora Bennani
- Pamela Allen
- Ryan Wilcox
Acknowledgements for the patients, caregivers and trial staff at the following sites:

**Australia**
- Royal Adelaide Hospital
- Flinders Medical Centre
- Monash Health-Monash Medical Centre
- Concord Repatriation General Hospital
- Gosford Hospital
- Linear Clinical Research

**France**
- Centre Hospitalier Universitaire (CHU) de Bordeaux
- Centre Hospitalier Universitaire de Brest
- CHU Vendée
- CHU Pontchaillou
- Institut Gustave Roussy

**Germany**
- Klinikum Essen Sud - Evangelisches Krankenhaus Essen-Werden gGmbH
- University Hospital Leipzig
- Universitätsmedizin Mainz
- Rotkreuzklinikum Muenchen

**Italy**
- Ist.Ematologia E Oncologia Medica L.E A.Seragnoli
- Azienda Ospedaliera Speciali Civili di Brescia-Università degli Studi Di Brescia
- Istituto Scientifico Romagnolo per lo Studio e la Cura dei Tumori (IRST) IRCCS
- Azienda Unità Sanitaria Locale di Ravenna - Ospedale S. Maria delle Croci di Ravenna
- Republican Korea
- Chonbuk National University Hospital
- Seoul National University Bundang Hospital
- Catholic University of Korea, Seoul St. Mary’s Hospital
- Samsung Medical Center
- Ulsan University Hospital

**Poland**
- Szpitalne Pomorskie Sp. z o.o. Szpital Morski im. PCK, Oddział Hematologii i Transplantology Szpiku
- Pratia MCM Krakow
- Centrum Onkologii - Instytut im. Marii Sklodowskiej-Curie, Klinika Nowotworów Układu Chlonnego
- Instytut Hematologii i Transfuzjologi, Klinika Hematologii
- Uniwersytecki Szpital Kliniczny im. Jana Mikulicza-Radeckiego we Wrocławiu, Klinika Hematologii, Nowotworów Krwi i Transplantacji Szpiku
- Russian Federation
- Republic Hospital n.a. V.A. Baranov
- First State Saint-Petersburg Pavlov Medical University
- 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 Català d’Oncologia Badalona, Hospital Germans Trias I Pujol
- Institut Català d’Oncologia Girona
- Hospital Universitario 12 de Octubre-Centro de Actividades Ambulatorias
- Hospital Universitario Fundacion Jimenez Diaz
- Hospital Universitario Virgen del Rocío
- Institut Català d’Oncologia Tarragona

**Turkey**
- Ankara University Faculty of Medicine, Department of Internal Diseases, Hematology Division
- Dr. Abdurrahman Yurtaslan Ankara Onkoloji Eğitim Arastirma Hastanesi Hematoloji Kliniği Ankara
- Gazi University Faculty of Medicine, Department of Internal Diseases
- Sağlık Bilimleri Üniversitesi Gülhane Eğitim ve Araştırma Hastanesi
- İstanbul Üniversitesi İstanbul Tip Fakültesi İc Hastalıkları Anabilim Dali Hematoloji Bilim Dali Fafth
- Ege University Medical Faculty
- Kocaeli University Faculty of Medicine, Department of Internal Diseases, Hematology Division
- Ondokuz Mayis Üniversitesi Tip Fakültesi Sağlık Uyg. ve Eğitim Merkezi
- Tekirdağ Namık Kemal Üniversitesi Sağlık Uygulama ve Arastirma Hastanesi
- Karadeniz Teknik Üniversitesi Tip Fakültesi 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