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POSTER ABSTRACTS

704.CELLULAR IMMUNOTHERAPIES: EARLY PHASE AND INVESTIGATIONAL THERAPIES

AFM13 in Combination with Allogeneic Natural Killer Cells (AB-101) in Relapsed or Refractory Hodgkin Lymphoma and CD30 $^{+}$ Peripheral T-Cell Lymphoma: A Phase 2 Study (LuminICE)

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Background and Significance

Limited treatment options are available for patients with relapsed or refractory (R/R) Hodgkin lymphoma (HL) and no standard-of-care therapy is established for R/R peripheral T-cell lymphoma (PTCL); novel therapies to improve outcomes in these patients are required.

AFM13 is a tetravalent, bispecific innate cell engager that binds CD16A on natural killer (NK) cells and CD30 expressed (CD30 $^{+}$) on HL and PTCL cells, enhancing NK cell-mediated antibody-dependent cellular cytotoxicity (ADCC). AFM13 monotherapy trials in patients with R/R HL and PTCL have shown promising clinical activity and a tolerable safety profile (Sasse *et al. Blood* 2020; Kim *et al. Cancer Res* 2023). Recently, a Phase 1/2 study of AFM13 in combination with cord blood (cb)-derived NK cells in patients with R/R CD30 $^{+}$ lymphomas treated at the recommended phase 2 dose (n=35) achieved an objective response rate (ORR) of 94% and a complete response (CR) rate of 71% (Nieto *et al. Blood* 2022, oral presentation).

AB-101 is a non-genetically modified, allogeneic, cryopreserved, off-the-shelf, cb-derived NK cell product optimized for enhanced ADCC through selection for the KIR-B haplotype and the CD16 F158V polymorphism. AB-101 has demonstrated potent killing of tumor cell lines *in vitro* and *in vivo* and preliminary results of a Phase 1/2 trial of AB-101 alone and in combination with rituximab in patients with R/R B cell non-Hodgkin lymphoma demonstrated AB-101 is well tolerated (Khanal *et al. J Clin Oncol* 2023).

Combining AFM13 with AB-101 has the potential to synergistically enhance and redirect antitumor immune responses to target HL and CD30 $^{+}$ PTCL cells.

Study Design and Methods

This Phase 2, open-label, multi-center, multi-cohort study (NCT05883449) aims to evaluate the efficacy and safety of AFM13 in combination with AB-101 in patients with R/R HL and certain R/R CD30 $^{+}$ PTCL subtypes. PTCL subtypes permitted are PTCL not-otherwise specified, angioimmunoblastic T-cell lymphoma, and ALK-positive and -negative anaplastic large cell lymphoma (ALCL). Patients aged $\geq$18 years are planned for enrolment and patients with R/R HL must have received at least two prior lines of therapy including prior combination chemotherapy, brentuximab vedotin (BV) and a checkpoint inhibitor. Patients with R/R PTCL must have confirmed CD30 expression of $\geq$1% by immunohistochemistry and have received at least one prior line of combination chemotherapy; patients with ALCL must have received or been intolerant to BV. Prior autologous or allogeneic hematopoietic stem cell transplant is permitted. Exclusion criteria include treatment with any anti-cancer agent $\leq$21 days prior to enrolment, continuing toxicity from a prior therapy, central nervous system involvement, or previous treatment with AFM13 or NK cells.

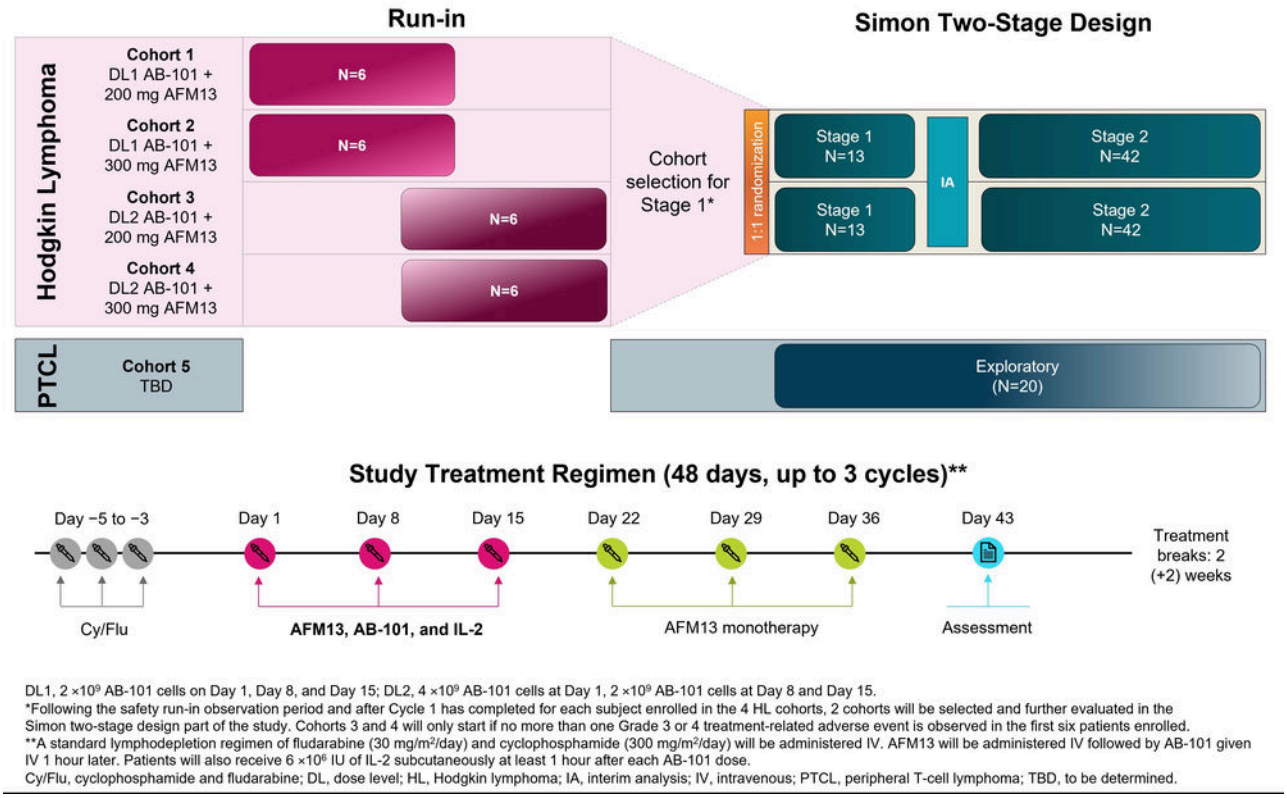
The primary objective is to determine the ORR (complete and partial responses) by Independent Radiology Committee (IRC) based on PET-CT per Lugano classification. Secondary objectives include safety and immunogenicity, complete response rate, duration of response and progression free survival.

Treatment will be given intravenously (IV) over 48-day cycles for up to 3 cycles. A run-in phase will assess two dose levels of AFM13 and AB-101 in 4 cohorts (Figure). A standard lymphodepletion regimen of fludarabine (30 mg/m ^{2}/day) and cyclophosphamide (300 mg/m ^{2}/day) will be administered IV from Day −5 to Day −3 at the start of each treatment cycle. Following this, AFM13 (200 mg or 300 mg once weekly) will be given, with AB-101 (dose level 1 or 2, see Figure) given 1 hour later per cycle. Patients will also receive 6 $\times 10^{6}$ IU of IL-2 subcutaneously at least 1 hour after each AB-101 dose. Cohorts 1 and 2 will enrol in

parallel; cohorts 3 and 4 will start only if cohorts 1 and 2 are cleared per protocol safety criteria. After cycle 1 has completed for each subject enrolled in all 4 cohorts, an analysis of the safety and clinical responses will be performed to determine the two dose levels to be evaluated in the main study. In addition, an exploratory cohort (cohort 5) will begin enrolment of patients with CD30 $^{+}$ PTCL. Disease and efficacy assessments will be conducted at screening and on Day 43 (± 3 days) of each cycle.

Disclosures Moskowitz: *Incyte:* Research Funding; *Bristol-Myers Squibb:* Research Funding; *Beigene:* Research Funding; *Seattle Genetics:* Honoraria, Research Funding; *Merck:* Honoraria, Research Funding; *ADC Therapeutics:* Research Funding. **Harstrick:** *Affimed:* Current Employment, Current holder of *stock options* in a privately-held company. **Emig:** *Affimed:* Current Employment, Current holder of *stock options* in a privately-held company. **Overesch:** *Affimed:* Current Employment, Current holder of *stock options* in a privately-held company. **Pinto:** *Affimed:* Current Employment, Current holder of *stock options* in a privately-held company. **Ravenstijn:** *Affimed:* Current Employment, Current holder of *stock options* in a privately-held company. **Schlüter:** *Affimed:* Current Employment, Current holder of *stock options* in a privately-held company. **Rubel:** *Affimed:* Current Employment, Current holder of *stock options* in a privately-held company. **Rebscher:** *Affimed:* Current Employment, Current holder of *stock options* in a privately-held company. **Graefe:** *J&J, ABBVIE, BMS:* Current equity holder in publicly-traded company; *Artiva Biotherapeutics:* Current Employment, Current holder of *stock options* in a privately-held company. **Lim:** *Artiva Biotherapeutics:* Current Employment, Current holder of *stock options* in a privately-held company, Patents & Royalties: Co-inventor on 10 Artiva patents; no royalties. **Raymon:** *Artiva Biotherapeutics:* Current Employment, Current holder of *stock options* in a privately-held company. **Alexis:** *Affimed:* Current Employment, Current holder of *stock options* in a privately-held company.

Figure: Phase 2 Study Design of AFM13 in Combination with AB-101 (NCT05883449; LuminICE)



DL1, 2 ×10^{9} AB-101 cells on Day 1, Day 8, and Day 15; DL2, 4 ×10^{9} AB-101 cells at Day 1, 2 ×10^{9} AB-101 cells at Day 8 and Day 15.
*Following the safety run-in observation period and after Cycle 1 has completed for each subject enrolled in the 4 HL cohorts, 2 cohorts will be selected and further evaluated in the Simon two-stage design part of the study. Cohorts 3 and 4 will only start if no more than one Grade 3 or 4 treatment-related adverse event is observed in the first six patients enrolled.
**A standard lymphodepletion regimen of fludarabine (30 mg/m^{2}/day) and cyclophosphamide (300 mg/m^{2}/day) will be administered IV. AFM13 will be administered IV followed by AB-101 given IV 1 hour later. Patients will also receive 6 ×10^{6} IU of IL-2 subcutaneously at least 1 hour after each AB-101 dose.
Cy/Flu, cyclophosphamide and fludarabine; DL, dose level; HL, Hodgkin lymphoma; IA, interim analysis; IV, intravenous; PTCL, peripheral T-cell lymphoma; TBD, to be determined.

Figure 1

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