# 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-203)

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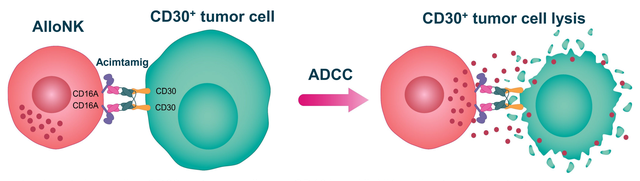
## BACKGROUND AND SIGNIFICANCE

- Limited treatment options are available for patients with relapsed or refractory (R/R) Hodgkin lymphoma (HL) and patients with R/R peripheral T-cell lymphoma (PTCL); novel therapies to improve outcomes and tolerability are required.
- Acimtamig (AFM13) is a tetravalent, bispecific Innate Cell Engager (ICE) that binds CD16A on natural killer (NK) cells and CD30-positive (CD30⁺) on HL and a subset of PTCL, enhancing NK cell-mediated antibody-dependent cellular cytotoxicity (ADCC; **Figure 1**).
- Acimtamig monotherapy trials in patients with R/R HL and R/R PTCL have shown single agent activity and a tolerable safety profile.[1,2]
- Recently, a Phase 1/2 study of acimtamig in combination with cord blood (cb)-derived NK cells showed in patients with R/R CD30⁺ lymphomas treated at the recommended phase 2 dose (n=35), an objective response rate (ORR) of 94% and a complete response (CR) rate of 71%.[3]
- AlloNK (formerly 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.[4]
- AlloNK demonstrated potent killing of tumor cell lines *in vitro* and *in vivo*, and preliminary results of a Phase 1/2 trial of AlloNK alone and in combination with rituximab in patients with R/R B cell non-Hodgkin lymphoma demonstrated that AlloNK is well tolerated.[4]
- Preclinical data suggests the cytotoxic activity of AlloNK is enhanced in combination with acimtamig and adoptive transfer of AlloNK co-administered with acimtamig conferred tumor growth control *in vivo*.[5]

## OBJECTIVE

**To evaluate the safety and efficacy of acimtamig in combination with AlloNK in patients with R/R classical HL and CD30⁺ PTCL**

## Figure 1: Acimtamig + AlloNK mechanism of action




Acimtamig acts by binding CD30 on tumor cells and CD16A on AlloNK, redirecting and potentiating NK cell-mediated lysis of specific tumor cells.
ADCC, antibody-dependent cellular cytotoxicity; NK, natural killer.

## STUDY DESIGN AND METHODS

- This Phase 2, open-label, multi-center, multi-cohort study, with a safety run-in phase followed by an expansion phase, of acimtamig in combination with AlloNK was opened for recruitment in October 2023 (NCT05883449).
- The **primary objective** is to determine the ORR (complete and partial responses) assessed by Independent Radiology Committee (IRC) based on positron emission tomography–computed tomography (PET-CT) per Lugano classification.
- **Secondary objectives** include safety, tolerability, immunogenicity, complete response rate, duration of response and progression free survival.
- Key inclusion and exclusion criteria are shown in **Table 1.**

### Table 1: Key inclusion and exclusion criteria

**Inclusion**

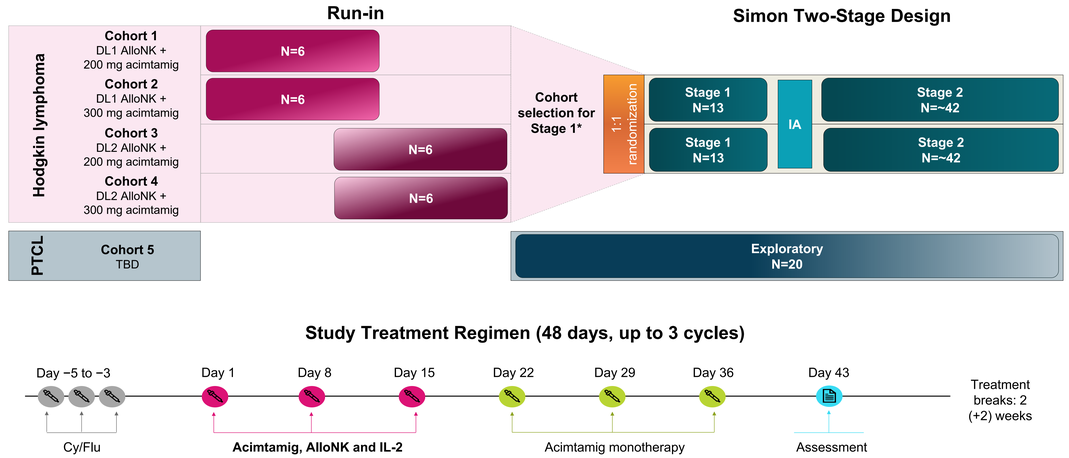
- Adults (≥18 years) that can provide informed consent
- R/R classical HL or CD30⁺ R/R PTCL (confirmed CD30 expression of ≥1% by IHC) subtypes, including:
  - PTCL-NOS
  - AITL
  - ALK⁺ and ALK⁻ ALCL
- Prior treatment consistent with the following:
  - R/R HL: must have received at least two lines of therapy including one line of combination chemotherapy, BV and a PD-1 checkpoint inhibitor)
  - R/R PTCL: must have received at least one line of combination chemotherapy
  - Patients with ALCL must have received or been intolerant to BV
  - Prior ASCT is permitted if completed at least three months prior to the first dose of study treatment

**Exclusion**

- Treatment with any anti-cancer agent ≤21 days prior to enrollment
- Continuing toxicity from a prior therapy
- Active acute or chronic GvHD or GvHD requiring immunosuppressive treatment
- Central nervous system involvement
- Previous treatment with acimtamig or cbNK cells

ALCL, anaplastic large cell lymphoma; AITL, angioimmunoblastic T-cell lymphoma; ALK, anaplastic lymphoma kinase; ASCT, autologous stem cell transplant; BV, brentuximab vedotin; cb, cord blood; GvHD, graft verus host disease; HL, Hodgkin lymphoma; IHC. Immunohistochemistry; NK, natural killer; PD1, programmed death ligand-1; PTCL(-NOS), peripheral T-cell lymphoma (not otherwise specified); R/R, relapsed or refractory

## Figure 2: Phase 2 design for acimtamig in combination with AlloNK (LuminICE-203; NCT05883449)




DL1: 2 ×10⁹ AlloNK on Day 1, Day 8, and Day 15; DL2, 4 ×10⁹ AlloNK at Day 1, 2 ×10⁹ AlloNK at Day 8 and Day 15.
*Following the run-in observation period and after cycle 1 has completed for each subject enrolled in the four HL cohorts, two 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.
Cy/Flu, cyclophosphamide and fludarabine; DL, dose level; HL, Hodgkin lymphoma; IA, interim analysis; IL-2, interleukin-2; IV, intravenously; PTCL, peripheral T-cell lymphoma; TBD, to be determined.

- 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 acimtamig and AlloNK in four cohorts (**Figure 2**).
  - A standard lymphodepletion regimen of fludarabine (30 mg/m²/day) and cyclophosphamide (300 mg/m²/day) will be administered IV from Day −5 to Day −3 at the start of each treatment cycle.
  - Following this, acimtamig (200 mg or 300 mg once weekly) will be given, with AlloNK (dose level 1 or 2, see **Figure 2**) given 1 hour later.
  - Patients will receive 6 ×10⁶ IU of interleukin-2 subcutaneously at least 1 hour after each AlloNK dose.
- Cohorts 1 and 2 will enroll in parallel; cohorts 3 and 4 will start only if cohorts 1 and 2 are cleared per protocol safety criteria.
- Following the safety run-in phase and after cycle 1 has completed for each subject enrolled in all four cohorts, a thorough risk-benefit analysis will be performed in order to determine the two dose levels to be evaluated in the Simon two-stage design part of the study.
- In addition, an exploratory cohort (cohort 5) will begin enrollment of patients with CD30⁺ PTCL.
- Disease assessments will be conducted at baseline and on Day 43 (±3 days) of each cycle.

**The LuminICE-203 study will establish whether the combination of acimtamig and AlloNK leads to improved response rates for patients with CD30⁺ lymphomas where treatment options are currently limited.**

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