# Electronic Signature Page

Document title: Statistical Analysis Plan (version 2.0)

Sign-off status: FINAL

Digitally signed by:

Certified by PSI CRO AG

| NAME, POSITION | ROLE | DATE TIME STAMP |
|---|---|---|
| [redacted] | [redacted] | [redacted] |
| [redacted] | [redacted] | [redacted] |
| [redacted] | [redacted] | [redacted] |
| [redacted] | [redacted] | [redacted] |
| [redacted] | [redacted] | [redacted] |
| [redacted] | [redacted] | [redacted] |

This signoff page has been automatically generated to capture the digital signatures of authorized signatories. Each record has been time-stamped and verified as authentic by certified software, providing evidence that the signed document has not been altered or tampered with post-signature.

# STATISTICAL ANALYSIS PLAN

## PROTOCOL AFM13-203

**A Phase 2, Open-Label, Multi-Center Study of Innate Cell Engager AFM13 in Combination with Allogeneic Natural Killer Cells (AB-101) in Subjects with Recurrent or Refractory Hodgkin Lymphoma and CD30-Positive Peripheral T-Cell Lymphoma (LuminICE-203)**

| | |
|---|---|
| **Protocol code:** | AFM13-203 |
| **SAP Version:** | Final 2.0 |
| **SAP Date:** | 20-SEP-2024 |
| **Author:** | [redacted] |

# DOCUMENT HISTORY

## VERSION HISTORY

| Version # | Version Date |
|---|---|
| 1 | 11-SEP-2023 |
| 2 | 20-SEP-2024 |

## REVISION HISTORY

| [redacted] | [redacted] | [redacted] | [redacted] |
|---|---|---|---|
| [redacted] | [redacted] | [redacted] | [redacted] |
| [redacted] | [redacted] | [redacted] | [redacted] |
| [redacted] | [redacted] | [redacted] | [redacted] |
| [redacted] | [redacted] | [redacted] | [redacted] |
| [redacted] | [redacted] | [redacted] | [redacted] |
| [redacted] | [redacted] | [redacted] | [redacted] |
| [redacted] | [redacted] | [redacted] | [redacted] |
| [redacted] | [redacted] | [redacted] | [redacted] |
| [redacted] | [redacted] | [redacted] | [redacted] |
| [redacted] | [redacted] | [redacted] | [redacted] |
| [redacted] | [redacted] | [redacted] | [redacted] |
| [redacted] | [redacted] | [redacted] | [redacted] |
| [redacted] | [redacted] | [redacted] | [redacted] |
| [redacted] | [redacted] | [redacted] | [redacted] |
| 2 | [redacted] | [redacted] | [redacted] |

# APPROVAL SIGNATURES

**STUDY TITLE:** A Phase 2, Open-Label, Multi-Center Study of Innate Cell Engager AFM13 in Combination with Allogeneic Natural Killer Cells (AB-101) in Subjects with Recurrent or Refractory Hodgkin Lymphoma and CD30-Positive Peripheral T-Cell Lymphoma (LuminICE-203)

**PROTOCOL NUMBER:** AFM13-203

**SAP** Final 2.0, 20-SEP-2024

PSI

[redacted]

Signature: ..... Date: .....

[redacted]

Signature: ..... ..... Date: .....

[redacted]

Signature: ..... Date: .....

[redacted]

Signature: ..... ..... Date: .....

Affimed GmbH

[redacted]

Signature: ..... Date: .....

[redacted]

Signature: ..... Date: .....

# TABLE OF CONTENTS

# LIST OF ABBREVIATIONS

| | |
|---|---|
| ADA | Anti-drug antibody |
| AE | Adverse event |
| AESI | Adverse events of special interest |
| ASTCT | American Society for Transplantation and Cellular Therapy |
| ATC | Anatomical Therapeutic Chemical (classification system) |
| CI | Confidence interval |
| CR | Complete response/remission |
| CRR | Complete response rate |
| CRS | Cytokine release syndrome |
| CTCAE | Common Terminology Criteria for Adverse Events |
| CV | Coefficient of variation |
| DCR | Disease control rate |
| DOR | Duration of response |
| ECOG | Eastern Cooperative Oncology Group |
| eCRF | Electronic Case Report Form |
| EORTC | European Organisation for Research and Treatment of Cancer |
| FAS | Full analysis set |
| HL | Hodgkin lymphoma |
| IA | Interim analysis |
| ICANS | Immune effector cell-associated neurotoxicity syndrome |
| IL-2 | Interleukin-2 |
| IRC | Independent Radiology Committee |
| ITT | Intention-to-treat |
| LTEAE | Lymphodepletion-TEAEs |
| MAGIC | Mount Sinai Acute GvHD International Consortium |
| Max | Maximum |
| MedDRA | Medical Dictionary of Regulatory Activities |
| mFAS | Modified full analysis set |
| Min | Minimum |
| MRD | Measurable residual disease |
| NCI | National Cancer Institute |
| NK | Natural killer |
| oFAS | Overall full analysis set |
| ORR | Objective response rate |
| OS | Overall survival |
| PET-CT | Positron emission tomography-computed tomography |
| PFS | Progression-free survival |
| PK | Pharmacokinetic(s) |
| PPS | Per-protocol set |
| PR | Partial response |
| PRR | Partial responses rate |
| PRO | Patient-reported outcome |
| PT | Preferred term |
| PTCL | Peripheral T-cell lymphoma |
| QoL | Quality of Life |
| R/R | Refractory/relapsed |

| | |
|---|---|
| SAE | Serious adverse event |
| SAS | Safety analysis set |
| SAP | Statistical Analysis Plan |
| SD | Standard deviation |
| SOC | System organ class |
| SRC | Safety Review Committee |
| SRI | Safety run-in set |
| TEAE | Treatment emergent adverse event |
| TFL | Tables, figures, listings |
| TLS | Tumor lysis syndrome |
| WHO | World Health Organization |

# 1. INTRODUCTION

This Statistical Analysis Plan (SAP) covers the statistical analysis and reporting for the AFM13-203 Clinical Study. The SAP is based on the Study Protocol version 3.0, dated 03-JUL-2024, and electronic Case Report Form (eCRF) dated 12-SEP-2024.

The study design, assessments, and variables to be analyzed are described in detail in the study protocol. Protocol Section 9 provides the instruction for the statistical analyses. Statistical methods will be implemented accordingly.

The SAP will be finalized before the first participant is enrolled to the study, if possible. It will be finalized before any analysis of the study data.

# 2. STUDY OBJECTIVES

## 2.1 PRIMARY OBJECTIVES

The primary objective of this study is to assess the antitumor activity of acimtamig in combination with AlloNK® in participants with refractory/relapsed (R/R) classical Hodgkin lymphoma (HL) and CD30-positive peripheral T-cell lymphomas (PTCLs) by objective response rate (ORR).

## 2.2 SECONDARY OBJECTIVES

The secondary objectives are the following:

- To assess efficacy of acimtamig in combination with AlloNK®
- To assess the incidence of post-treatment transplant
- To assess the safety and tolerability of acimtamig in combination with AlloNK®
- To assess the immunogenicity of acimtamig in combination with AlloNK®

## 2.3 EXPLORATORY OBJECTIVES

[redacted]

# 3. STUDY DESCRIPTION

The study design and study treatments can be found in the study protocol.

# 4. SAMPLE SIZE AND POWER CALCULATION

Details about the sample size and power calculations can be found in the study protocol (Section 9.2).

# 5. ANALYSIS ENDPOINTS

## 5.1 PRIMARY ENDPOINT AND ESTIMAND

[redacted]

## 5.2 SECONDARY ENDPOINTS

Secondary endpoints are:

- Duration of response (DOR) reported by the Investigator and IRC
- Complete response rate (CRR) reported by the Investigator and IRC
- ORR reported by the Investigator based on PET-CT as assessed by the Lugano classification
- Incidence of participants receiving subsequent transplant
- Frequency of participants with study-drug related treatment-emergent adverse events (TEAEs) and serious adverse events (SAEs) (evaluated using the National Cancer Institute [NCI] Common Terminology Criteria for Adverse Events [CTCAE] v5.0 and American Society for Transplantation and Cellular Therapy [ASTCT] grading for TEAEs related to cytokine release syndrome [CRS] and immune effector cell-associated neurotoxicity syndrome [ICANS])
- Frequency of participants developing anti-drug antibodies (ADAs) against acimtamig or AlloNK®
- Progression-free survival (PFS) by IRC

- Overall survival (OS)

## 5.3 EXPLORATORY ENDPOINTS

[redacted]

# 6. ANALYSIS POPULATIONS

The populations for the statistical analyses are defined as follow:

- Safety analysis set (SAS): The SAS will consist of all participants (enrolled in run-in phase, Stage 1, Stage 2, and exploratory cohorts) who received any amount of any component of the regimen [acimtamig, AlloNK®, or any study treatment such as lymphodepletion or interleukin-2 (IL-2)]. The SAS will be the primary population for all safety-related endpoints.
- Full analysis set (FAS): Following the intention-to-treat (ITT) principle, the FAS will consist of all participants enrolled into one of the two selected cHL Cohorts in Stage 1 and Stage 2 or exploratory PTCL cohort (Cohort 5) who received at least 1 dose of both acimtamig and AlloNK®. The FAS will be the primary population for all efficacy-related endpoints.
- NK full analysis set (NK-FAS): Following the ITT principle for analysis of Cohort 6, the NK-FAS will consist of all participants who received at least 1 dose of AlloNK® in Cohort 6. The NK-FAS will be the primary population for all efficacy related endpoints concerning Cohort 6.
- Per protocol set (PPS): The PPS will consist of all participants in FAS who did not have any major protocol deviations. The primary analysis will be repeated on the PPS to support the results of the primary analysis on the FAS.
- Modified full analysis set (mFAS): The mFAS will consist of all participants in the FAS who have at least one post-baseline response assessment by IRC according to the Lugano classification. The mFAS will be used for sensitivity analyses of the primary endpoint.
- [redacted]
- Overall full analysis set (oFAS): The oFAS will consist of all participants enrolled to the HL

cohorts of the study except for Cohort 6 (in run-in phase, Stage 1, and Stage 2) who received at least 1 dose of both acimtamig and AlloNK®. The oFAS will be used for sensitivity analyses of the primary endpoint. The exploratory cohorts are not included in oFAS because the results would be identical with those from the FAS analyses.

- Safety run-in set (SRI): The SRI consists of all participants of the 4 safety run-in cohorts who received at least 66% of the acimtamig and AlloNK® combination during Cycle 1. The SRI will be used for the analysis of run-in phase data.
- Acimtamig PK set: The acimtamig PK set consists of all participants (except those from Cohort 6) who have received at least 1 dose of acimtamig and have at least 1 post dose acimtamig PK measurement.
- AlloNK PK set: The AlloNK PK set consists of all participants who have received at least 1 dose of AlloNK® drug and have at least 1 post dose AlloNK® PK measurement.

Participants who were screened and signed the informed consent but did not receive any treatment will be listed, including the reason for screen failure and any SAE that is related to a study procedure. These participants will not be part of any summary table except for summarizing disposition.

# 7. ANALYTICAL PLAN AND STATISTICAL METHODS

## 7.1 GENERAL CONVENTIONS AND STATISTICAL CONSIDERATIONS

Continuous variables will be summarized with the following statistics: number of non-missing observations, number of missing observations, mean, standard deviation (SD), median, 1st quartile, 3rd quartile, minimum (min), and maximum (max). Moreover, geometric mean, coefficient of variation (CV), and geometric CV will be calculated for certain PK parameters.

Categorical variables will be summarized using frequency table with counts for all categories including missing, and percentages for all non-missing category, calculated with the total number of non-missing values as denominator.

Percentages for categorical data summaries will be displayed with 1 decimal point (e.g. 51.4%), except for 100% which will be presented with no decimals (i.e. 100%). Unless otherwise specified, percentages for baseline summaries will be based on the total number of participants in the analysis set, percentages for post-baseline summaries will be based on the total number of participants with non-missing values.

Use of decimal places in descriptive statistics:

- Min, Max: same as the actual data
- Mean, Median, Q1, Q3: actual data + 1 decimal
- SD: actual data + 2 decimals

A maximum of 3 significant digits will be displayed.

Analysis will be presented by cohort. Moreover, all HL cohorts (except Cohort 6) pooled will be analyzed (2 pooled cohorts for FAS, 4 pooled cohorts for oFAS and SAS).

Those subjects who initially consented under protocol v3.0 and later versions, and thus will not receive IL-2 after the AlloNK treatment, will be analyzed separately, but only a limited set of analyses (Disposition, PK, AE Overview, Exposure) will be created for this.

The PET-CT response assessed by IRC used for efficacy endpoints by IRC following the Lugano classification is identified in the data as from the Oncologist.

For all efficacy analyses using local investigator PET-CT response assessments, the Overall response assessment (integrating all radiographic and non-radiographic data) as captured in the eCRF) following the Lugano classification will be used.

## 7.2 Definition of Baseline, Study Visits, and Visit Windows

The baseline value is the last value observed/measured before the first administration of any study treatment, i.e., acimtamig, AlloNK® or any study treatment such as lymphodepletion.

Study Day 1 is the day of first administration of any acimtamig or AlloNK®; study days before Study Day 1 are calculated as [date - date of 1st acimtamig administration], study days after Study Day 1 are calculated as [date - date of 1st acimtamig administration + 1].

All by-visit summaries will be created using the visits as recorded in the eCRF. No reassignment of visits will be done.

## 7.3 Handling of Missing Data

[redacted]

## 7.4 Protocol Deviations

Protocol deviations will be classified as major or minor; the classification will be done manually during the medical review as described in Protocol Deviation Management Plan. In general, major protocol deviations are those with likely impact on the efficacy or safety of the study treatment.

Major and minor protocol deviations will be summarized by number of protocol deviations and number and percentage of participants with at least 1 protocol deviation; protocol deviations by type (e.g., violation of eligibility criterion) will also be summarized.

The protocol deviations will be presented in FAS.

A listing of all protocol deviations, along with their grade as major or minor, will be provided for all participants.

## 7.5 PARTICIPANT DISPOSITION

The disposition summaries of participants will include:

- Number of participants screened, number and percentage of screening failures with reasons for screening failure; percentages will be calculated from all screened participants.

For all enrolled participants, the following will be presented for each cohort, and moreover separately in each cohort for participants who received and who did not receive IL-2 (percentages will be calculated from all enrolled participants in each cohort / from all participants who received and who did not receive IL-2 in each cohort):

- Number and percentage of participants enrolled, overall and by site
- Number and percentage of participants in the analysis sets
- Number and percentage of participants discontinued treatment (with reason for treatment discontinuation)

For all participants in FAS, the following will be presented (percentages will be calculated from all participants in FAS):

- Number and percentage of participants continued and not continued into follow-up period
- Reason for end of study for participants, with number and percentage of participants
- Number and percentage of participants in each treatment cycle

Inclusion and exclusion criteria violations and enrollment will be presented for all screened participants in data listings. The disposition listing will be created for all enrolled participants.

## 7.6 PARTICIPANT CHARACTERISTICS

### 7.6.1 BASELINE AND DEMOGRAPHIC CHARACTERISTICS

The following characteristics will be summarized by treatment arms in FAS:

- Demography: age at screening, sex, ethnicity, race
- Vital signs: height, weight, temperature, respiratory rate, heart rate, systolic and diastolic blood pressure, overall vital signs assessment,
- Physical examination result
- Childbearing potential

Listings of demography and baseline characteristics data will be created.

### 7.6.2 MEDICAL HISTORY AND CURRENT MEDICAL CONDITIONS

The following will be summarized in FAS, and also listed:

- The lymphoma history:
    - Subtype, time since initial cytological/histological diagnosis until screening
    - Stage and B-symptoms presence at initial diagnosis and at screening

  - For HL cohorts: Classical HL-specific prognostic factors (erythrocyte sedimentation rate, lymph node involvement, Extranodal disease sites) at initial diagnosis and at screening, International Prognostic Score for HL at initial diagnosis, soluble CD30 result at screening
  - For PTCL cohort: Non-Hodgkin Lymphoma-specific prognostic factors (extranodal disease sites) at initial diagnosis and at screening, International Prognostic Index at initial diagnosis, local CD30 result (%) and soluble CD30 result

- Medical history other than lymphoma
- Prior anti-cancer therapies and surgeries (number of prior therapies, therapeutic agents, prior stem cell transplant, PD1 Inhibitor therapy, Brentuximab Vedotin (BV) therapy, Car-T therapy and radiotherapy, best response to the last line prior to the study start)

Prior anti-cancer therapies will be coded by World Health Organization (WHO) Anatomical, Therapeutic, and Chemical (ATC) terms, summarized and listed.

Medical history will be coded utilizing corresponding Medical Dictionary for Regulatory Activities (MedDRA; version 26 or later), summarized by System Organ Classes (SOCs) and Preferred Terms (PTs) and listed.

#### 7.6.3 PRIOR AND CONCOMITANT MEDICATION

Medication will be coded by World Health Organization (WHO) Anatomical, Therapeutic, and Chemical (ATC) terms (version March 2023 or later). All prior (ended before the first day of any study treatment, including lymphodepletion) and concomitant (started on or after the first day of study treatment or ongoing on that day) medications will be summarized by ATC level 2 term and PT for FAS. Where start and end dates are partially available, imputation will be done as outlined in Section 7.3. If start and end dates are completely missing or classifications cannot be conclusively made based on the available information, such treatments will be classified as concomitant medications.

Prior and concomitant medications will be also presented in data listings.

## 7.7 EFFICACY ENDPOINTS AND ANALYSIS

The endpoints by IRC assessments will be derived using only responses provided by IRC regardless of Investigator responses. Similarly, endpoints by Investigator assessments will be derived using only responses provided by Investigator regardless of IRC responses. All cohorts will be analyzed independently.

All the efficacy endpoints values and original variables used for their evaluation will be listed; the subgroups (as defined in Section 7.9.1) will be included in the primary endpoint listing.

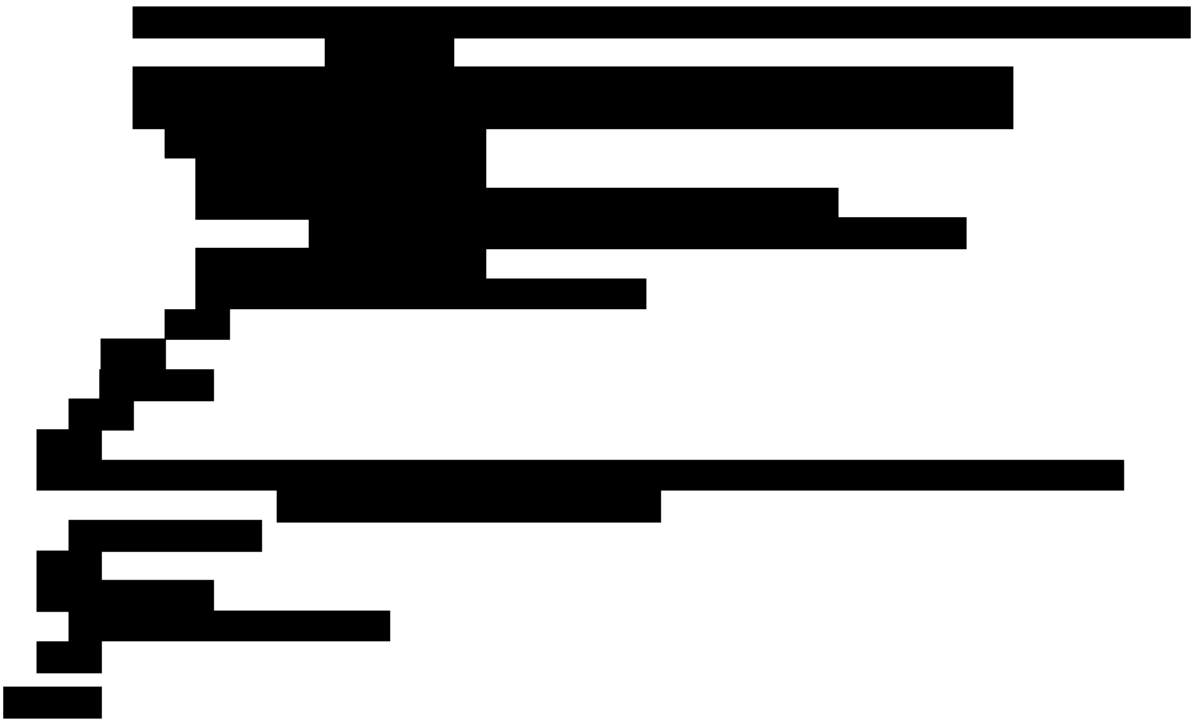
### 7.7.1 ANALYSIS OF PRIMARY EFFICACY ENDPOINT

#### 7.7.1.1 ENDPOINT DESCRIPTION

The primary endpoint is based on the ORR, calculated as the proportion of participants with having a best response of CR or PR as assessed by IRC according to the Lugano classification. A participant will be assumed as a responder if he/she achieves complete or partial response at any postbaseline visit; otherwise, he/she will be a non-responder. Participants with missing post-baseline response will be classified as non-responders.

#### 7.7.1.2 PRIMARY ANALYSIS

[redacted]



In addition, the CRR and Partial Responses Rate (PRR) will be provided, calculated as the proportion of participants with the best result being CR or with the best result being PR, respectively; for the calculation of CI for PRR, the participants with CR are assumed to be non-responders.

The number and percentage of participants with objective response, CR and PR at each treatment cycle will be presented. The swimmer plot, showing the response by Lugano classification for each participant by time in trial, will be plotted.

The primary endpoint analysis will be based on the FAS.

#### 7.7.1.3 Primary Analysis for Cohort 6

The ORR for Cohort 6 will be analyzed in a similar way as described in Section 7.7.1.2 but on the NK-FAS, with exact binomial CI used and no p-value calculated. Furthermore, participants who do not develop a response (at least PR) after cycle 1 (i.e., after the first assessment) will be counted as treatment failures.

The CRR and PRR will be provided, calculated as described in Section 7.7.1.2. In addition, shift table from response assessed at the end of cycle 1 to later cycles will be presented, including counts and percentages.

### 7.7.2 Analysis of Secondary Efficacy Endpoints

Secondary endpoints will be analyzed in FAS. For Cohort 6 the NK-FAS will be used instead, but for this cohort only ORR by Investigator will be presented in a summary table and the remaining secondary endpoints will only be listed.

#### 7.7.2.1 Duration of Response

DOR by Investigator and DOR by IRC will be analyzed for the participants who achieved PR or

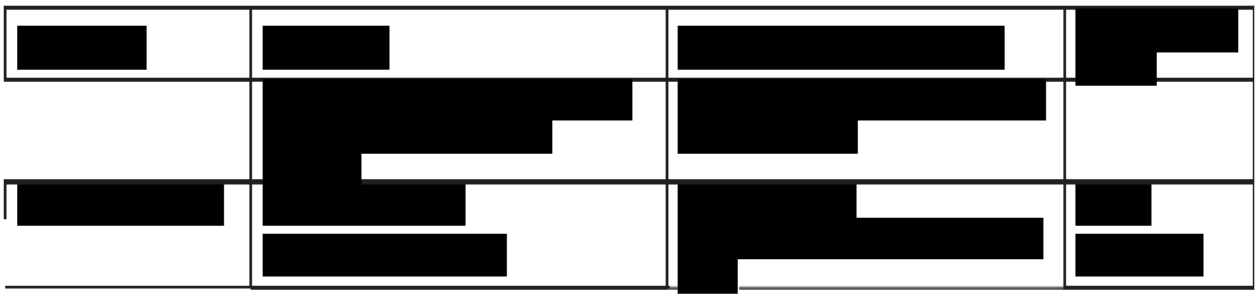
CR only. The DOR is defined as time from first assessment of PR or CR to the first assessment of progressive disease or death.

Participants who started a new anti-lymphoma therapy prior to a documented progressive disease will be censored at the last disease assessment prior to initiation of new anti-lymphoma therapy. Participants who discontinued the study before the first assessment of progressive disease or death will be censored at their last disease assessment. The censoring rules are summarized in Table 1.

[redacted]

DOR will be summarized by descriptive statistics including median DOR, first and third quartile and Kaplan - Meier estimates at 3, 6, 9, 12, etc. months with respective 95% CIs. The Kaplan – Meier curve will be plotted.

[redacted]



#### 7.7.2.2 ORR BY INVESTIGATOR

The ORR by investigator will be analyzed in the same way as the primary endpoint. The only exception is that exact binomial CI will be used, and no p-value will be calculated.

The swimmer plot showing the response reported for each participant by time in trial will be plotted.

#### 7.7.2.3 CRR BY INVESTIGATOR AND BY IRC

Both the CRR (proportion of participants with the best post-baseline assessment being CR; participants without assessment are assumed to be non-responders) by Investigator and by IRC will be analyzed in a similar way as the primary endpoint, i.e., the CRR will be presented as percentage in the whole population, including the 95% CI; exact binomial CI will be used instead of the Koyama and Chen interval because no futility conclusion will be done for this endpoint during the interim analysis (IA).

#### 7.7.2.4 ORR, CRR AND PRR BY INVESTIGATOR FOR COHORT 6

The ORR, CRR and PRR by investigator will be analyzed in the same way as described in Section 7.7.1.3, including the shift table.

#### 7.7.2.5 PFS BY IRC

PFS is the time from the first treatment of acimtamig or AlloNK® received until the first progression disease assessed by IRC or death.

Participants who started a new anti-lymphoma therapy prior to a documented progressive disease will be censored at the last disease assessment prior to initiation of new anti-lymphoma therapy. Participants who discontinued the study before the first assessment of progressive disease or death will be censored at their last disease assessment. The censoring rules are summarized in Table 1.

PFS will be summarized by Kaplan-Meier estimates in the analogous way as DOR. The Kaplan – Meier curve will be plotted.

#### 7.7.2.6 OVERALL SURVIVAL

OS is the time from the first treatment of acimtamig or AlloNK® received until the death. Participants with no death recorded will be censored at the last available contact date. The censoring rules are summarized in Table 1.

[redacted]

OS will be summarized by Kaplan-Meier estimates in the analogous way as DOR. The Kaplan – Meier curve will be plotted.

#### 7.7.2.7 INCIDENCE OF PARTICIPANTS RECEIVING SUBSEQUENT TRANSPLANT

The incidence of participants receiving subsequent transplant will be assessed and summarized by percentage rate and 95% CI. The number of participants who miss the information about the subsequent transplant will be reported but these participants will not be included in the percentage calculation.

#### 7.7.2.8 IMMUNOGENICITY PARAMETERS

Immunogenicity parameters, including frequency of participants developing ADAs against acimtamig or AlloNK®, will be analyzed by cohort and visits. It will be summarized by descriptive statistics and listed for both acimtamig and AlloNK®.

### 7.7.3 ANALYSIS OF EXPLORATORY ENDPOINTS

[redacted]

### 7.7.4 SENSITIVITY ANALYSIS

The primary endpoint will be analyzed in PPS, mFAS, and oFAS as sensitivity analyses; for oFAS,

the analysis will be repeated for participants who received and who did not receive IL-2.

[redacted]

## 7.8 SAFETY ENDPOINTS AND ANALYSIS

The following secondary safety endpoint will be analyzed:

- Frequency of participants with study-drug related TEAEs and SAEs (evaluated using NCI CTCAE v5.0 and ASTCT grading for TEAEs related to CRS and ICANS)

Moreover, exposure to study treatment, other AE summaries and laboratory parameters will be analyzed for safety.

All safety analyses will be done in SAS.

### 7.8.1 EXPOSURE TO STUDY TREATMENT

The duration of the study treatment will be summarized in weeks.

[redacted]

Moreover, the following characteristics of the treatment exposure will be summarized by descriptive statistics and listed for all study treatments separately; it will be summarized for each treatment cycle and over the entire study period:

- Number of participants who received at least 1 dose of the treatment
- Number of doses administered for a participant
- Cumulative dose amount received by a participant
- Dose intensity (mg/weeks)
- Treatment compliance of a participant measured as the percentage of the actual received cumulative dose amounts throughout the period compared to the planned doses

The characteristics above will be summarized for each cohort separately, and for acimtamig and AlloNK® also separately for participants who received and who did not receive IL-2 in each cohort. Also, for all the study treatments, the number of and percentage of the administration, its delays, dose adjustments, reasons for adjustments and actual dose will be presented by cycle and treatment day. Analysis of exposure as described above will be repeated using the FAS.

The summaries for exposure to study treatment will be presented for acimtamig, AlloNK® and lymphodepletion. Exposure for IL-2 will be listed only.

### 7.8.2 ADVERSE EVENTS

TEAEs are those events with onset at/or after the first administration of any study drug of the regimen (acimtamig, AlloNK® or any study treatment such as lymphodepletion or IL-2) until 30 days after last administration of any study drug.

Lymphodepletion-TEAEs (LTEAEs) are the TEAEs with onset at/or after the date of the first lymphodepletion and before the first administration of acimtamig or AlloNK®.

The acimtamig/AlloNK®-TEAEs (ATEAEs) are the TEAEs with onset at/or after the first administration of acimtamig or AlloNK®.

TEAEs and SAEs will be coded using MedDRA, version 26 or later, and graded using NCI CTCAE v5.0 (including neurotoxicities that are not considered ICANS) except for CRS and ICANS, which will be graded according to the ASTCT grading, tumor lysis syndrome (TLS) will be graded according to the Cairo-Bishop TLS grading system and acute GVHD will be grading according to the Mount Sinai Acute GvHD International Consortium (MAGIC) criteria.

Changes in the severity of one and the same AE will be collected as separate records in the eCRF, but they will be linked. As it is only a change of grading in one and the same AE, such an AE will be counted only once in AE tables, using the highest grade reported. If such an AE is recorded as both serious and non-serious, it will be counted as serious AE in the tables. If such an AE is recorded as both related (possibly, probably, definitely related) and not-related, it will be counted as related AE in the tables.

The number and percentage of participants with an AE and the number of AEs will be summarized for the following TEAEs:

- TEAE, serious TEAE, LTEAE, serious LTEAE, ATEAE, serious ATEAE
- AE of special interest (AESI)
- TEAE of severity grade 3, 4 or 5 for CTCAE 5.0, ASTCT, ASTCT ICANS, MAGIC, Cairo-Bishop grading
- TEAE and serious TEAE related to acimtamig, to AlloNK® and to acimtamig or AlloNK®; an AE is considered a study drug related if it is possibly, probably or definitely related according to eCRF
- TEAE of CTCAE Grade 3, 4 or 5 related to acimtamig, to AlloNK® and to acimtamig or AlloNK®
- TEAE leading to acimtamig interruption, to AlloNK® interruption, to permanent discontinuation of acimtamig, to permanent discontinuation of AlloNK®
- Fatal TEAE, fatal TEAE related to acimtamig, fatal TEAE related to AlloNK®
- TEAE of preferred term “Infusion-Related Reactions”

The summary described above will be repeated for participants who received and who did not receive IL-2 in each cohort.

The incidence of following TEAEs will be tabulated by system organ class (SOC) and preferred term (PT):

- TEAE, LTEAE, ATEAE
- TEAE by SOC, PT and severity grade (CTCAE 5.0, ASTCT, ASTCT ICANS, MAGIC, Cairo-Bishop grading)
- TEAE leading to acimtamig discontinuation, TEAE leading to AlloNK® discontinuation
- TEAE related to acimtamig, TEAE related to AlloNK®, TEAE related to acimtamig or AlloNK®
- Serious TEAE, serious TEAE related to acimtamig, serious TEAE related to AlloNK®, serious TEAE related to acimtamig or AlloNK®
- Fatal TEAE, fatal TEAE related to acimtamig, fatal TEAE related to AlloNK®, fatal TEAE related to acimtamig or AlloNK®
- TEAE with CTCAE Grade ⩾3, TEAE with CTCAE Grade ≥3 related to acimtamig, TEAE with CTCAE Grade ≥3 related to AlloNK®, TEAE with CTCAE Grade ≥3 related to acimtamig or AlloNK®
- Non-serious TEAE

Deaths during the treatment phase until 30 days after the last dose and the corresponding reasons will be summarized.

The not treatment-emergent AEs will be only listed.

### 7.8.3 Laboratory Data

Safety laboratory results for hematology, chemistry and coagulation will be graded by NCI CTCAE v5.0. If no grading exists, values will be classified into low/normal/high based on laboratory normal ranges.

If a lab value is reported using a nonnumeric qualifier e.g., less than (<) a certain value, or greater than (>) a certain value, the given numeric value will be used in the analyses, ignoring the nonnumeric qualifier.

Descriptive statistics summarizing laboratory results for hematology, chemistry and coagulation will be presented for all study visits. The change from baseline to each post-baseline and the CTCAE grades will also be summarized.

All laboratory values will be listed. A separate listing for abnormal lab values (Grade 3 and higher, and low/high values) will be presented for hematology, chemistry, and coagulation. Urinalysis results will be listed only.

### 7.8.4 ECG, Vital Signs, Physical Examination and ECOG Status

ECG, vital signs, physical examination and Eastern Cooperative Oncology Group (ECOG) status will be summarized by descriptive statistics at each visit, including change from baseline for continuous variables; ECOG status will be analyzed as categorical variable.

All values will also be listed.

[redacted]

[redacted]

## 7.9 Other Endpoints and Analysis

### 7.9.1 Subgroup Analysis

Subgroup analyses will be performed to better characterize specific sub-populations. It will be performed in the two selected cohorts with R/R classical HL. The FAS will be used for efficacy and SAS for safety endpoints.

The following subgroup analyses are planned:

[redacted]

For those pre-specified subgroups, the ORR (primary endpoint), CRR, duration of response, PFS (all assessed by IRC), overall survival and AE (summary table) analyses will be repeated.

Each subgroup must contain at least 10 participants per category per cohort to perform a subgroup analysis. If a subgroup analysis is not conducted due to this restriction, data listings of the primary endpoint showing the data for this subgroup will be provided.

# 8. INTERIM ANALYSIS

## 8.1 Risk-Benefit Analysis of Safety Run In Period

[redacted]

[redacted]

## 8.2 INTERIM ANALYSIS AFTER 1ST STAGE OF SIMON'S DESIGN PART

[redacted]

[redacted]

## 8.3 PRIMARY ANALYSIS

[redacted]

# 9. Final Analysis

[redacted]

# 10. Independent Safety Review Committee (SRC)

An independent SRC will be established prior to the enrollment of the first participant. The independent SRC will be responsible for reviewing at regular intervals the safety data of all participants throughout the conduct of the study. Detailed recruitment status and interim safety reports will be provided to the SRC on a regular basis. Further details regarding the constitution of the SRC and its specific roles and responsibilities and timing of reviews will be provided in the SRC charter.

# 11. DEVIATIONS FROM ANALYSIS AS DESCRIBED IN THE PROTOCOL

The analysis populations mFAS and oFAS were added for sensitivity analysis of the primary endpoint.

# 12. PROGRAMMING SPECIFICATIONS

All outputs will be produced using SAS version 9.4 or a later version.

The margins should be at least 1.50 inches for the binding edge and 1.0 inches for all others.

In the top left portion of each table/listing, the *protocol number* will be presented. On the next line, a *table/listing number* followed by the *title* of the table/listing and p*opulation* information will be displayed. Horizontal lines will appear after the column heading of the table/listing. *Footnotes* will be put under the main body of text at the bottom of the page. The source listing number will be displayed for all tables. The *SAS program name* will appear on the bottom left corner of each table/listing in a string, followed by the database lock date, and the *page number* will appear on the bottom right corner of each table/listing. The *date and time of creation* of the table/listing will appear on the bottom left corner under to the SAS program name line.

Courier New 8-point bold font will be used for all tables and listings. Usually, a landscape layout is suggested for both tables and listings, but it is not mandatory. Any date information in the listing will use the date9. format, for example, 07MAY2002.

The list of tables, listings, and figures, and shells for unique tables are provided in a separate Mock-Up tables, figures, and listings (TFLs) document.

# 13. REFERENCES

Koyama T, Chen H. Proper inference from Simon's two-stage designs. Stat Med. 2008;27(16):3145-3154. Doi:10.1002/sim.3123.