Title: Statistical Analysis Plan (SAP) for "A Phase 1/2a, Open-label, Dose-escalation, Dose-expansion, Parallel Assignment Study to Evaluate the Safety and Clinical Activity of PBCAR20A in Study Subjects with Relapsed/Refractory (r/r) Non-Hodgkin Lymphoma (NHL) or r/r Chronic Lymphocytic Leukemia (CLL) or Small Lymphocytic Lymphoma (SLL)"

Protocol number: PBCAR20A-01 v5.0 10FEB2021
Product: PBCAR20A
Sponsor: Precision BioSciences, Inc.

Effective date: March 29, 2022

Description:

The purpose of this SAP is to describe the planned analyses and outputs to be included in the Clinical Study Report for Protocol PBCAR20A-01 (version 5.0), dated 10 February 2021.

This SAP is intended to describe the efficacy, safety analyses required for the study.

This SAP will be provided to the study team members to convey the content of statistical package.

SAP Authors and Signatures

Author's Name and Functional Area:

Function	Name/title
Lead Author	[redacted] Precision BioSciences, Inc.
Contributing Author	[redacted] Precision BioSciences, Inc.
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I give my approval for the attached SAP entitled "A Phase 1/2a, Open-label, Dose-escalation, Dose-expansion, Parallel Assignment Study to Evaluate the Safety and Clinical Activity of PBCAR20A in Study Subjects with Relapsed/Refractory (r/r) Non-Hodgkin Lymphoma (NHL) or r/r Chronic Lymphocytic Leukemia (CLL) or Small Lymphocytic Lymphoma (SLL)" dated March 29, 2022.

SAP Approval Signatures

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List of Abbreviations

Abbreviation	**Definition**
AE	adverse event
AESI	adverse events of special interest
ALL	acute lymphoblastic leukemia
ASTCT	American Society for Transplantation and Cellular Therapy
B-ALL	B-cell acute lymphoblastic leukemia
BMA	bone marrow aspiration
BMI	body mass index
BOR	best overall response
CAR	chimeric antigen receptor
CBC	complete blood count
CI	confidence interval
CLL	Chronic lymphocytic leukemia
CNS	Central nervous system
CS	clinically significant
CR	complete response
CRi	complete response with incomplete recovery of counts
CRP	C-reactive protein
CRS	cytokine release syndrome
CT	computed tomography
CTCAE	Common Terminology Criteria for Adverse Events
DLT	dose-limiting toxicity
DoR	duration of response
ECG	electrocardiogram
ECHO	echocardiogram
ECOG	Eastern Cooperative Oncology Group
eCRF	electronic case report form
FDA	Food and Drug Administration
GvHD	graft-versus-host disease
HIV	human immunodeficiency virus
HLA	human leukocyte antigen
ICANS	immune effector cell-mediated neurotoxicity syndrome

ICF	Informed consent form
ICH	International Council for harmonization
ITT	Intent-to-Treat
IV	intravenous
kg	kilogram
KM	Kaplan-Meier
LTFU	long-term follow-up
LVEF	Left ventricular ejection fraction
MedDRA	Medical Dictionary for Regulatory Activities
mg	milligram
MRD	minimal residual disease
MRI	Magnetic Resonance Imaging
MTD	maximum tolerated dose
MUGA	Multiple gated acquisition scan
NCCN	National Comprehensive Cancer Network
NCI	National Cancer Institute
NCS	Not clinically significant
NHL	non-Hodgkin lymphoma
ORR	objective response rate
OS	overall survival
PD	progressive disease
PET	positron emission tomography
PFS	progression-free survival
PK	pharmacokinetic(s)
PR	partial response
PT	Preferred Term
QC	quality control
qPCR	quantitative polymerase chain reaction
RE	Response Evaluable
RNA	ribonucleic acid
r/r	relapsed/refractory
SAE	serious adverse event
SAP	Statistical Analysis Plan

SD	stable disease
SLL	Small lymphocytic leukemia
SoA	Schedule of Activities
SOC	System Organ Class
TEAE	treatment-emergent adverse event
TESAE	treatment-emergent serious adverse event
WHO	World Health Organization

1 SUMMARY OF KEY PROTOCOL INFORMATION

1.1 Change to the Protocol Defined Statistical Analysis Plan

Any changes from the originally planned statistical analysis specified in the protocol are outlined in Table 1.

Table 1: Change to protocol defined analysis plan

Protocol	Statistical Analysis Plan	Rationale for Changes
PBCAR20A-01 v4.0 09SEP2020	Cohort A(NHL) and Cohort B (CLL/SLL) will be combined for all analyses.	Protocol V4 has combined the two cohorts into one cohort, and dose level 3 has been changed to a flat dose of 480x10^6 cells.
PBCAR20A-01 v5.0 10FEB2021	Subject enrollment will be discontinued after the completion of Phase 1. The study will not progress to Phase 2a. All subsequent sections in the SAP apply to only Phase 1. Actual dose level given in the study will be used for summary tables	This study includes only Phase 1 due to the project not moving forward. Dose level 2: 240x10^6 cells were not given as dose level 2 dosing has been completed based on protocol V4.

1.2 Study Objectives and Endpoints

The primary, secondary, and exploratory objectives and corresponding endpoints for Phase 1 are listed in Table 2. Due to early study termination, only a synopsis will be generated, and exploratory endpoints will not be included.

Table 2: Study objectives and endpoints

Objective	Endpoints
Primary Objective	Primary Endpoints
Evaluate the safety and tolerability of PBCAR20A in subjects with r/r $CD20^+$ NHL including r/r$CD20^+$ CLL/SLL and find an appropriate dose to optimize safety and efficacy	The identification of the maximum tolerated dose (MTD) based on the incidence of dose-limiting toxicities (DLTs)
Secondary Objectives	Secondary Endpoints
Evaluate the clinical activity and safety profile of PBCAR20A in study subjects with r/r $CD20^+$ NHL including r/r $CD20^+$ CLL/SLL	Objective response rate (ORR) • NHL: Lugano 2016 criteria • CLL/SLL: International Workshop on Chronic Lymphocytic Leukemia (iwCLL) 2018 guidelines
	Progression-free survival (PFS) • Defined as the duration (days) from Day 0 to disease progression or death
	Incidence of AESI, SAEs, and DLTs related

	to the investigational product

1.3 General Study Design

This study is a nonrandomized, open-label, dose escalation Phase 1 study. Essential components of the study design and key features are summarized in Table 3.

Table 3: Overview of study design and key features

Design Features	Three escalating dose groups will be enrolled and treated sequentially, with the possibility of a single de-escalation. • Within each dose group, at least 3 and at most 6 study subjects will be treated with a single dose of PBCAR20A using a standard 3 + 3 design. • The starting dose of PBCAR20A will be 1×10^6 CAR T cells/kg body weight. • In the absence of DLTs, subsequent dose groups will be treated with escalating doses to a maximum flat dose of 480×10^6 CAR T cells. • If a DLT is observed in 1 of 3 study subjects at a given dose level, 3 additional study subjects (for a total of up to 6 study subjects) will be enrolled and treated at that dose level. • When 3 additional study subjects are added to the dose group, the dose will be increased to the next dose level if ≤1 of 6 study subjects experiences a DLT. • If ≥2 of the 3 to 6 study subjects in a dose group experience DLTs then the MTD has been exceeded. The dose level will then be lowered to the previous dose and up to 3 additional study subjects (for a total of 6) will be treated at the previous (lower) dose level. • See the flow chart of the dose escalation algorithm in Figure 1.
Dosing Schedule	• Lymphodepletion (LD) chemotherapy will be administered during the Screening Period from Days -5 to -3. • All subjects will receive an intravenous (IV) PBCAR20A on Day 0 of the study. • The first treated subject in each dose level (including the dose de-escalation group, i.e., Dose -1) will be observed for 14 days for safety before any subsequent subject receives any study treatment to provide an adequate safety monitoring window. • Once the first study subject in each dose level has completed Day 14 after dosing with no DLTs, then subsequent subjects can be enrolled without delays into that dose level. • See Figure 2 for the study design schematic.

Treatment assignment	No randomization scheme or treatment arm assignment applies. Three PBCARCD20A doses are planned: Dose 1: 1x10^6 cells/kg, Protocol V3 Dose 2: 3x10^6 cells/kg, Protocol V3 Dose 3: 480x10^6 cells, Protocol V4 All subjects will receive fludarabine 30 mg/m^2/day and cyclophosphamide 500 mg/m^2/day from Day -5 to Day -3.
Blinding	Blinding of study subjects or study staff does not apply.
Interim /Analysis	• No formal interim analyses are planned. • A Safety Monitoring Committee will review safety data at regular intervals and to determine whether dose escalation is appropriate

Figure 1: Dose escalation algorithm

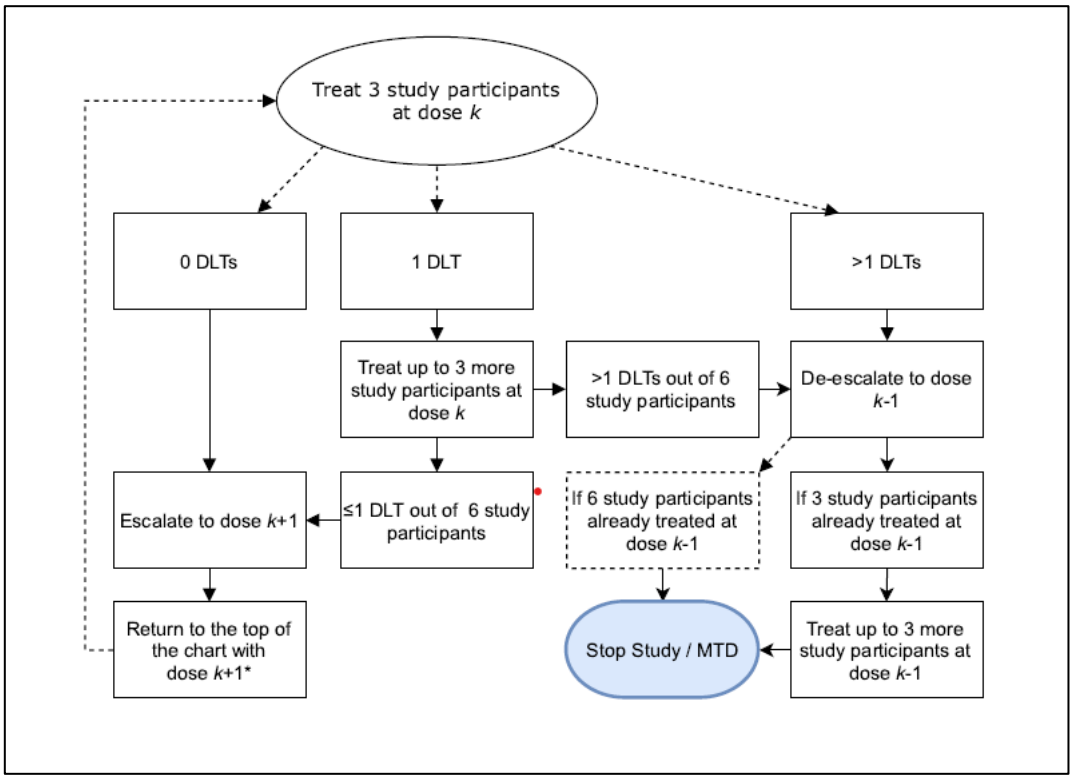
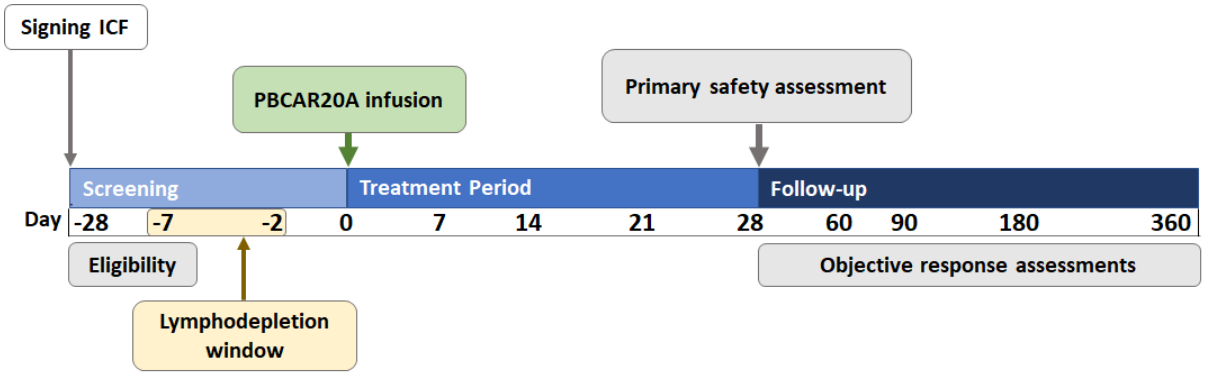


Figure 2: Study schema



Abbreviations: ICF=informed consent form.

1.4 Statistical Hypotheses

Statistical analysis for all safety and efficacy parameters will be descriptive in nature. Categorical variables will be summarized by frequency distributions (number and percentages of study subjects). Continuous variables will be summarized by mean, standard deviation, median, minimum, and maximum, and time-to-event variables will be summarized using Kaplan-Meier methods and figures for the estimated median time.

No formal statistical hypothesis testing is planned; however, if exploratory analyses are conducted and confidence intervals (CIs) are provided for estimates, the 95% CIs are consistent with a 2-sided 5% significance level. All analyses, summaries, and listings will be performed using SAS® (Cary, North Carolina) software (version 9.4 or higher).

2 SAMPLE SIZE

Subjects will be enrolled in dose groups with 3 to 6 subjects for each dose. Dose escalation of PBCAR20A will follow a standard 3 + 3 design with sequential groups of 3 subjects treated with incrementally higher doses of PBCAR20A until a DLT is observed and the MTD is established. Per the standard oncology 3 + 3 Phase 1 dose-escalation design, the total number of subjects to be enrolled cannot be precisely determined because the sample size is dependent upon the observed safety profile, which will determine the number of subjects per dose group and the number of dose escalations required to achieve the MTD. For this Phase 1 study, 4 dose levels (including possible de-escalation) may be tested. It is anticipated that approximately 9-30 study subjects will be required to reach the MTD.

3 PLANNED ANALYSES

3.1 Interim Analyses and Data Monitoring

No formal interim analyses are planned.

Dose escalation investigator calls consisting of the investigators, the medical monitor, and sponsor representative(s) will meet regularly to review safety and efficacy data and to provide safety oversight during the study. The group will review safety data at regular intervals to discuss any unexpected significant toxicities and to determine whether dose

escalation is appropriate.

3.2 Final analysis

The final planned primary analyses will be performed after the completion of the following sequential steps:

1. All subjects have completed a 28 Day Safety observation period of the study as defined in the protocol.
2. All required database cleaning activities have been completed, and the final database release and database freeze have been declared by Data Management.

4 ANALYSIS POPULATIONS

The analysis populations along with their inclusion criteria are defined in Table 4.

Following protocol amendment V4, enrolment for CLL/SLL and NHL cohorts have been combined, therefore, these two cohorts will be combined in the tables/figures and will be identified in the data listings if needed.

Table 4: Analysis populations

Population	Definition / Criteria	Analyses Evaluated
All Screened	• All subjects who sign the informed consent form (ICF) and participate the screening assessments. • Note: screening failures, screened but never enrolled are included in this population.	• Study population display • Screening failures display
Intent-To-Treat (ITT) / Enrolled	• Includes all subjects who are eligible for treatment based on inclusion and exclusion criteria and enrolled into the study. • Subjects will only appear once in the ITT population, even if they are retreated with PBCAR20A.	• Study population • Safety displays (vital sign, ECG, labs, etc.)
Safety	• Includes all subjects who receive study treatment, starting with Lymphodepletion. • This population will be used to summarize the demographic and baseline characteristics and safety data. • Subjects will only appear once in the Safety population, even if they are retreated with PBCAR20A.	• TEAE-related safety displays • Demographic and baseline characteristics
Response Evaluable (RE)	• Includes all subjects who received study treatment PBCAR20A and have at least 1 post-Baseline efficacy assessment.	• Efficacy displays

Population	Definition / Criteria	Analyses Evaluated
	• Subjects who discontinue due to disease progression, have a transplant, die, or have a treatment-related toxicity prior to having a disease assessment will be included in the Response Evaluable population. • Subjects who are retreated will be included in the Response Evaluable population for each treatment of PBCAR20A	

Enrolled (ITT) and Safety population consists of the same subjects for this study. 'Safety' population will be used tables and listings.

4.1 Protocol Deviations

Protocol deviations (including deviations related to study inclusion/exclusion criteria, conduct of the trial, patient management or patient assessment) will be summarized or listed.

A separate summary and listing of all inclusion/exclusion criteria deviations will also be provided, if any. This summary will be based on data as recorded on the inclusion/exclusion page of the eCRF.

Major protocol deviations will be summarized for the Safety Population. A listing of all protocol deviations will be provided.

Protocol deviations will be tracked by the study team throughout the conduct of the study in accordance with the Protocol Deviation Management Plan. Data will be reviewed prior to freezing the database to ensure all important deviations are captured and categorized on the protocol deviations dataset. This dataset will be the basis for the summaries or listings of protocol deviations. If there are many protocol deviations, a summary will be produced. If there are only a few protocol deviations, a listing will be produced.

5 CONSIDERATIONS FOR DATA ANALYSES AND DATA HANDLING CONVENTIONS

Statistical analyses will be primarily descriptive in nature. Unless otherwise specified, continuous variables will be summarized by presenting the number of non-missing observations, mean, standard deviation, median, minimum, and maximum. Categorical variables will be summarized by presenting the number of subjects and percentage for each category.

Time-to-event variables will be summarized using Kaplan-Meier (KM) methods and figures for the estimated median time. No formal statistical hypothesis testing is planned; however, if exploratory analyses are conducted and confidence intervals (CIs) are provided for estimates, the 95% CIs are consistent with a 2-sided 5% significance level.

Results of statistical analyses, descriptive statistics, and supporting listings will be presented by PBCAR20A dose levels.

All tabulations will be based on pooled data across centers.

Analyses will be performed using SAS for Windows statistical software, version 9.4 or higher (SAS, Cary, NC), except where other software may be deemed more appropriate.

Pharstat will perform all efficacy and safety statistical analyses described in this SAP.

5.1 Data Quality Assurance

Once all the source verification is complete, all queries are resolved, and the database has been updated accordingly, the database will be locked and made available to Pharstat for final analysis.

PBI's biostatisticians will review the data when:

1. Final analysis: All subjects complete Day 360 visit or discontinue from the study.
2. Ad-hoc analyses: Based on planned publications and presentations, ad-hoc analyses will be requested. Source verification and query resolution will be an ongoing process. Targeted data quality checks will be performed by Data Management when ad-hoc analyses are requested.

5.2 Study Assessments Windows

Data will be summarized by nominal study visit recorded in the database.

See Table 9 in Section 12.1 (Appendix A) for the timing of all relevant assessments.

5.3 Study Treatment Display Descriptors

The treatment descriptions to be used for the displays are listed in Table 5.

Table 5: Treatment descriptions for displays

Footnote Description	Table Header	Order
1×10^6 cells/kg	DL1	1
3×10^6 cells/kg	DL2	2
480×10^6 cells	DL3	3

5.4 Handling of Missing Data

Except for the time-to-event endpoints (described below), partial first diagnosis date and partial end dates of concomitant medications will be listed as they are recorded, all other "Unknown" or "not done" data will be treated as missing; unless otherwise specified, no method for imputation is planned.

Missing data on the PFS endpoint will have events coded as right censored per Table 6 based on the FDA's Guidance for Industry document Clinical Trial Endpoints for the Approval of Non-small Cell Lung Cancer Drugs and Biologics (April 2015) [1]; Table C1.

Table 6: Censoring methods for PFS

Situation	Date of Progression or Censoring	Outcome
Progression documented between scheduled visits	Earliest date of radiological assessment documenting progression	PFS event
No progression	Date of last radiological assessment of measured lesions	Censored
Treatment discontinuation for undocumented progression	Date of discontinuation	PFS event
Treatment discontinuation for toxicity or other reason	Date of discontinuation	PFS event
New anticancer treatment started	Date of start of new anticancer treatment	PFS event
Death before first progressive disease (PD) assessment	Date of death	PFS event
Death between adequate assessment visits	Date of death	PFS event
Death or progression after more than 1 missed visit	Date of first missed visit	PFS event

5.5 Multiple Comparisons

There are no multiple comparisons.

5.6 Covariates and Subgroups Analysis

Given this is a dose escalation study, no covariates or subgroups analysis will be done.

5.7 Data Derivations and Transformations

The following derivations will be used in this study:

Study day:

- =Date of assessment – Day 0 date (first PBCAR20A administration) + 1 for assessments done **after** date of first PBCAR20A administration.
- =Date of assessment – Day 0 date (first PBCAR20A administration) for assessments done **before** date of first PBCAR20A administration.

Weight: Baseline weight extracted from screening visit.

Duration:

- Duration on study (days) (or Time to Next Treatment) = end of study date – screening date + 1
- Time to AEs onset = AE onset date – Day0 date + 1

- Duration of AE = AE end date -AE start date + 1
- Follow-up time = Last contact/assessment date – Day 0 date +1

5.8 Reporting Process and Standards

Table 7

Software	SAS version 9.4 will be used
Datasets	SDTM: Not applicable ADAM: Not applicable RAW: Medidata will be used to create analysis datasets
Location	Programs will be located at Box\ClinFinalData\PBCAR20A\PBCAR20A-01\Program Datasets will be located at Box\ClinFinalData\PBCAR20A\PBCAR20A-01\Data\RAW Outputs will be located at Box\ClinFinalData\PBCAR20A\PBCAR20A-01\Output
QC	QC programs and output will be located at \Box\ClinFinalData\PBCAR20A\PBCAR20A-01\QC
Precision	Calculated values will be presented at no more than 3 significant digits
Unscheduled visits	Unscheduled visits will not be included in summary tables. Unscheduled visits will be included in figures. All unscheduled visits will be only included in figures and listings.
Descriptive Summary	Categorical Data: N, n, frequency, % Continuous Data: N, n, mean, median, standard deviation (SD), min, max.

6 STUDY POPULATION

6.1 Subject Disposition

A summary table (frequency counts and percentages) of all subjects in the All Screened population be provided including study completion status and reasons for early termination.

Subject disposition will be tabulated by dose level and overall. First screening (first subject first visit) and last contact/assessment date as well as first and last PBCAR20A injection dates for each dose will be presented in the table.

Screen failures with reasons (inclusion/exclusion criteria numbers recorded in the eCRF) as well as early discontinuations with reasons will be listed for all subjects.

A by-subject listing for screened population will be created. It will include Screen failure subjects with reasons (inclusion/exclusion criteria numbers recorded in the eCRF) and subjects who started LD but did not dose with their reasons for discontinuation and time on study.

6.2 Demographic and Baseline Variables

Descriptive statistics will be used to summarize the demographic characteristics (including age (≥65 years vs. <65 years), gender, race, ethnicity, height, weight, and body mass index (BMI) at Screening) for the Safety population.

Descriptive statistics will be used to summarize the baseline characteristics for subjects in the Safety population with the data collected at Screening or Day 0 pre-dose only. Baseline data will include disease type, disease stage, prior autologous stem cell transplant, prior line therapy, refractory subgroup, and baseline Eastern Cooperative Oncology Group (ECOG) performance status.

7 EFFICACY ANALYSES

All efficacy analyses described below will be carried out on the RE population. Unless otherwise specified, data will be summarized by dose level and overall.

7.1 Efficacy Analysis

Efficacy analyses on ORR and PFS will be performed.

7.1.1 Objective Response Rate (ORR)

The ORR is defined as the proportion of study subjects as responder, including partial response (PR) and complete response (CR) rates (i.e., the ORR is the rate of CR + PR). The response to treatment with PBCAR20A through Day 360 will be evaluated using the Lugano criteria for NHL and iwCLL for CLL/SLL (see Protocol Section 8.1).

Since the primary objective of this study is to determine the safety and tolerability of PBCAR20A, to identify an appropriate dose to optimize safety and efficacy, and to optimize the treatment regimen, an estimation approach will be applied to efficacy data analyses. The ORR will be summarized by number and percentage of subjects for all dose levels and along with the corresponding exact 95% CIs (Exact binomial CI: Clopper-Pearson method).

7.1.2 Progression-Free Survival (PFS)

PFS is defined as the interval between the date of first PBCAR20A administration and the date of disease relapse, progression, or death, whichever occurs (i.e., the number of days from Day 0 to disease relapse, progression, or death). Details on censoring method can be found in Section 5.4, Table 6.

$$PFS\ (days) = Date\ of\ disease\ relapse\ or\ progression\ or\ death\ or\ last\ assessment\ (or\ retreatment\ date) - Date\ of\ first\ PBCAR20A\ administration + 1$$

A PFS summary by dose will also be provided.

Individual PFS will be plotted with swimmer plot and grouped by dose level and indicated as responder, non-responder, starting new SCT treatment or death.

For subjects who meet the retreatment criteria and have had a study visit within 30 days, their PFS will be calculated from each PBCAR20A infusion.

8 SAFETY ANALYSES

All subjects in the Safety population will be included in the summaries and listings of safety data. No formal hypothesis testing will be performed to compare differences between dose groups. The safety data will be summarized for the overall AEs and specially AESI. Any clinically significant events related to laboratory tests, electrocardiograms (ECGs), and vital signs will be captured as AEs. All summaries will be descriptive.

8.1 Extent of Exposure

Study treatment administrations (including both LD and PBCAR20A) will be listed for each subject with drug name, dose, total cells infused (in 10^6 cells), and total lymphodepletion administered. Subject compliance with treatment will also be noted in this listing.

8.2 Adverse Events

An adverse event (AE) is defined as any untoward medical occurrence in a subject or clinical investigation subject administered a pharmaceutical product and which does not necessarily have to have a causal relationship with this treatment.

All AEs will be collected until death, disease progression, stem cell transplant, withdrawal due to intolerable toxicity, withdrawal of consent, or Day 360, whichever occurs first, and recorded on the eCRF, regardless of whether they are related to the study treatment. All AEs collected through Day 28 will be used for assessment of DLTs; any AEs occurring after Day 28 will be considered in dose-escalation decisions and monitoring procedures as appropriate.

AEs, including SAEs, that occur after signing of informed consent and before administration of any protocol-specified medication will be recorded as Medical History on the appropriate eCRF.

The AEs will be classified using the Medical Dictionary for Regulatory Activities (MedDRA) classification system version 22.1. The severity of the toxicities will be graded according to the NCI CTCAE version 5.0.

8.2.1 Adverse Event Summaries

A treatment-emergent adverse event (TEAE) is an AE with initial onset or that worsens in severity after the first dose of PBCAR20A.

Non-TEAE is defined as an AE that occurred prior to the PBCAR20A injection, but after the initiation of lymphodepletion, and they will be summarized separately from TEAEs by system organ class (SOC) and prefer term (PT) based on ITT (Enrolled) population.

The following summaries will be tabulated:

i. The number and percentage of subjects experiencing a TEAE,
ii. The number and percentage of subjects experiencing a SAE,
iii. The number and percentage of subjects experiencing an AESI,
iv. The number and percentage of subjects experiencing a fatal AE.

Additionally, the following information will be provided:

v. The number and percentage of subjects experiencing a serious adverse event related to each of the study medications (PBCAR20A, Lymphodepletion (Cyclophosphamide & Fludarabine)) by max toxicity grade,
vi. Listing of all TESAEs,
vii. Listing of all subjects who died on study.

All TEAEs will be listed. The listing will contain the following information: dose level, PT, PT grade, whether the event was an SAE, DLT, or AESI, symptom grade, relationship to study medications (PBCAR20A, Cyclophosphamide, Fludarabine), whether the adverse event attributed to the disease, study day at onset, duration of the adverse event in days, treatment given to treat the adverse event, and the outcome. Listings will be sorted by subject and AE

onsite date.

8.2.2 Adverse Events of Special Interest (AESI)

The following AESI are AEs are of particular concern in CAR T cell therapy:

- CRS
- ICANS
- GvHD

Subjects will be assessed for AESI from the administration of PBCAR20A through Day 360.

The following will be presented by dose and overall:

i. Summary of onset and duration of All AESIs,
ii. The number and percentage of subjects with symptoms from each type of AESI (CRS, ICANS, GvHD) by dose and by max grade (ASTCT grade or GvHD grade),
iii. Summary of AESIs and symptoms by max toxicity grade and dose,
iv. The number and percentage of AESIs and Infections by max toxicity grade and dose,
v. Summary of medications given for AESIs,

Listing of all Cytokine Release Syndrome, ICANS, and GvHD will also be provided. All occurrences of these AESIs will be listed for each subject. The listing will contain the following information: dose level, AE PT, PT grade, associated symptoms of the AESI, associated symptoms grade, AE onset days on study, duration of the AESI in days, treatment given to treat the adverse event, and the outcome. Listings will be sorted by subject and AE onset date.

The median time (range) to onset of an AESI from the first dose of PBCAR20A and the median duration (range) of an AESI:

$$\textit{Duration of AESI (days)} = \textit{Date of Resolution} - \textit{Date of Onset} + 1.$$

$$\textit{Time to AESI onset(days)} = \textit{Date of AE onset} - \textit{Day 0 Date} + 1.$$

For an AESI that is ongoing at the time of the analysis, the date of data cutoff will be used to calculate the duration.

9 REPORTING CONVENTIONS

The mean, standard deviation, and any other statistics other than quantiles, will be reported to one decimal place greater than the original data. Quantiles, such as median, minimum, and maximum, will use the same number of decimal places as the original data.

10 QUALITY ASSURANCE OF STATISTICAL PROGRAMMING

Analyses will be performed using SAS for Windows statistical software, version 9.4 or higher (SAS, Cary, NC), except where other software may be deemed more appropriate.

To provide high quality code that is understandable and allows reproduction of the analysis, the following points will be followed:

- The population to be used in a table or figure will be explicitly set at the start of a block of code that computes the output, ideally by looking up the population from the table of tables.
- Any outputs will have the
    - date and time included,
    - the name of the code file that produced the analysis,
    - programmer initials or user IDs.
- At the start of any code file there will be a set of comments that give
    - the author,
    - the date and time of writing,
    - references to inputs and outputs,
    - reference to any parent code file that runs the child code file.

All coding and output should adhere to one of three levels of quality control (QC), as outlined below:

- Level 1: the QC programmer/statistician will conduct a manual review of the data and compare the output to the raw listing.
- Level 2: the QC programmer/statistician will review the program, output, and log to ensure that these files are error-free.
- Level 3: a second review programmer/statistician will independently reproduce the analyses and output.

Most listings are classified as QC level 1, most summaries are classified as QC level 2, and all summaries and analyses involving primary endpoints and AESI are classified as QC level 3 (see Section 11 for QC level classifications for specific listings and tables).

11 LISTING OF TABLES, LISTINGS AND FIGURES

This section is to give precise details for each table, listing or figure to be produced.

Mock tables, listings and figures should be provided. Including the title, number, analysis population, etc.

Tables: # of decimal digits, formatting (e.g., confidence in brackets, in parentheses, in separate columns).

Figures: labels for all axes, legends, plotting symbols.

These detailed specifications can have minor revisions during the production phase without needing to revise the SAP, this may include changing the table numbers if a reordering or deletion is appropriate, providing that the specifications in the main body of the SAP sections 4 to 8 are met.

Suggestions for ordering or organizing TLFs:

e.g., Tables E for efficacy and S for safety and nothing for patient disposition.

Disposition is Table of Figure 1.xxx

Efficacy is Table or Figure 2.xxx

Safety is Table or Figure 3.xxx

The following numbering will be applied for SAP generated displays:

Table 8: Numbering for SAP generated displays

Section	**Tables**	**Figures**
Study Population	1.1 to 1.xxx	1.1 to 1.xxx
Efficacy	2.1 to 2.xxx	2.1 to 2.xxx
Safety	3.1 to 3.xxx	3.1 to 3.xxx
Section	**Listings**	
ICH Listings	1 to xx	
Other Listings	xx+1 to yy	

Table 10: Study population tables and listings

No.	Population	Example Shell	Title	Programming Notes	Quality Control	Deliverable [Priority]
Subject Disposition						
1.1	All Screened	SD1	Summary of Subject Disposition	Retreated subject will be included under actual dose level received	3	FP [1]
1	All Screened	L-SD1	Listing of Screen Failures		1	FP [1]
Protocol Deviation						
1.2	Safety	PD1	Summary/Listing of Major Protocol Deviations	If no major deviations, then put a blank table as 'As no data to present. If few, only listing needed	1	FP [1]
Demographic and Baseline Characteristics						
1.3	Safety	DMBC1	Summary of Demographics and Baseline Characteristics	Retreated subject will not be included in the summary	3	FP [1]

Table 11: Efficacy tables, figures and listings

No.	Population	Example Shell	Title	Programming Notes	Quality Control	Deliverable [Priority]
Response						
2.1	RE	ORR1	Summary of Objective Response Rate by Initial Treatment	Responder=CR+PR, no retreatment data	3	FP [1]
2	RE	L-ORR1	Listing of Objective Response Data	Include retreatment data	3	FP [1]
2.1	RE	F-SW	Swimmer plot for Progression Free Survival	For retreatment subject, combine the initial data with retreatment	1	FP [1]

				data		

Table 12: Safety tables and listings

No.	Population	Example Shell	Title	Programming Notes	Quality Control	Deliverable [Priority]
Extent of Exposure						
3.1	Safety	L-TA1	Listing of Planned and Actual Treatment Administered	Including dose level, lot number, date and time, drug name, compliance, and total quantity administered	1	FP [1]
All AEs						
3.2	Safety	AEAll1	Summary of Overall Adverse Events by Treatment	Combine the initial and retreatment periods safety data, this will be the summary for each individual	2	FP [1]
3	Safety	L-AE1	Listing of All Treatment Emergent Adverse Events		2	FP [1]
AEs of Special Interest						
3.3	Safety	AEAll2	Summary of Onset and Duration for all AESIs	Onset and duration are related to max grade of each type of AE	3	FP [1]
3.4	Safety	AESI2	Summary of AESIs and Symptoms by Dose and Max Toxicity Grade	AE and CRS data should be combined to identify the CRS events and symptoms	3	FP [1]
3.5	Safety	AESI1	Summary of AEs of Special Interest and Infections by Max Toxicity Grade and Dose	Infection will combine all infection Aes, and max grade	3	FP [1]
3.6	Safety	CM1	Summary of Concomitant Medications Given for AESI	Select the Toxi, Dex and other medications for fever,	1	FP [1]
4	Safety	L-AEAll1	Listing of All Cytokine Release Syndrome, ICANS, GvHD		1	FP [1]

SAEs						
3.7	Safety	SAE1	Summary of All PBCARCD20A-related Serious Adverse Event By Max Toxicity Grade		1	FP [1]
3.8	Safety	SAE1	Summary of All Lymphodepletion-related Serious Adverse Event By Max Toxicity Grade		1	FP [1]
5	Safety	L-SAE1	Listing of All TESAEs		1	FP [1]
6	Safety	L-SAE1	Listing of All Deaths		1	FP [1]

12 APPENDICES

12.1 Appendix A: Schedule of Activities

Table 9: Study schedule

	Treatment Period									**Follow-up**							
Month	**-**	**1**								**2**		**3**	**4**	**5**	**6**	**9**	**12**
Day	**-28**[a]	**0**	**1**	**3**	**7**	**10**	**14**	**21**	**28**	**42**	**60**	**90**	**120**	**150**	**180**	**270**	**360/ ET**
Visit window (days)			**+1**	**+1**	**±1**	**±1**	**±2**	**±2**	**±2**	**±5**	**±5**	**±5**	**±5**	**±5**	**±5**	**±7**	**±7**
Informed consent	X																
Inclusion and exclusion criteria	X																
Demography	X																
Weight	X	X							X			X			X	X	X
Full physical examination	X	X							X			X			X	X	X
Medical history	X	X								X[b]	X[b]	X[b]	X[b]	X[b]	X[b]	X[b]	X[b]
Viral serology[c]	X																
HLA haplotype	X																
Anti-HLA antibodies	X								X			X					
Brain MRI	X[d]																
Lumbar puncture (History of CNS involvement)	X[e]																

	Treatment Period									**Follow-up**							
Month	**-**	**1**								**2**		**3**	**4**	**5**	**6**	**9**	**12**
Day	**-28**[a]	**0**	**1**	**3**	**7**	**10**	**14**	**21**	**28**	**42**	**60**	**90**	**120**	**150**	**180**	**270**	**360/ ET**
Visit window (days)			**+1**	**+1**	**±1**	**±1**	**±2**	**±2**	**±2**	**±5**	**±5**	**±5**	**±5**	**±5**	**±5**	**±7**	**±7**
LVEF (ECHO or MUGA)	X																
Serum pregnancy test (WOCBP only)	X																
Clinical laboratory assessments[f]	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
Coagulation panel[g]	X	X															
Vital signs[h]	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
12-lead ECG (triplicate)[i]	X																
ECOG Performance Status	X	X							X			X			X	X	X
Fludarabine + cyclophosphamide[j]																	
Study treatment administration[k]		X															
Study participant diary[l]		----------X----------															
PET-CT scan (NHL only)	X[m]						X[n]		X		X	X			X	X	X
Tumor/liquid biopsy	X[o]						X[p]										
Serum and whole blood samples for analyses[q]	X	X[r]	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X

	Treatment Period									Follow-up							
Month	**-**	**1**								**2**		**3**	**4**	**5**	**6**	**9**	**12**
Day	**-28**[a]	**0**	**1**	**3**	**7**	**10**	**14**	**21**	**28**	**42**	**60**	**90**	**120**	**150**	**180**	**270**	**360/ ET**
Visit window (days)			**+1**	**+1**	**±1**	**±1**	**±2**	**±2**	**±2**	**±5**	**±5**	**±5**	**±5**	**±5**	**±5**	**±7**	**±7**
BMA/bone marrow biopsy (Diagnosed w BM involvement)[s]	X								X		X	X			X	X	X
CT scan (if preferred to PET/CT for CLL/SLL only)	X								X		X	X			X	X	X
Objective response assessment									X		X	X			X	X	X
MRD assessment[t]	X								X		X	X			X	X	X
Concomitant medications	X																
AE review	X																
AESI[u]		X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X

Abbreviations: AE=adverse event; AESI=adverse event of special interest; BMA=bone marrow aspiration; CAR=chimeric antigen receptor; CLL=chronic lymphocytic leukemia; CNS=central nervous system; CT=computed tomography; DLBCL=diffuse large B-cell lymphoma; ECG=electrocardiogram; ECOG=Eastern Cooperative Oncology Group; ECHO=echocardiogram; ET=early termination; eCRF=electronic case report form; HLA=human leukocyte antigen; HIV=human immunodeficiency virus; IV=intravenous; LD=lymphodepletion; LVEF=left ventricular ejection fraction; MRI=magnetic resonance imaging; MUGA=multigated acquisition scan; NHL=non-Hodgkin lymphoma; PBMC=peripheral blood mononuclear cell; PET=positron emission tomography; SLL=small lymphocytic lymphoma; WOCBP=women of childbearing potential.

[a] Lymphodepletion regimens will be administered as described in the Pharmacy Manual.

[b] Study subjects are asked about the current status of their disease and treatment, including stem cell transplant.

[c] Viral screening to include HIV antibody, hepatitis B surface antigen, hepatitis B core antibody, hepatitis C antibody, HLA haplotype, and anti-HLA antibodies.

[d] Brain MRI is recommended for all study subjects at Baseline to assess the presence of brain disease or abnormalities. A negative MRI is required at Screening for NHL study subjects with a history of CNS disease. An MRI conducted as a part of the routine care within 6 weeks of initiating lymphodepletion chemotherapy may be used for Screening.

[e] A negative lumbar puncture is required at Screening only if the study participant has a history of CNS disease. A lumbar puncture conducted as a part of the routine care within 6 weeks of initiating lymphodepletion chemotherapy may be used for Screening.

[f] Clinical laboratory tests for safety assessments are outlined in Protocol Section 7.1.4. Clinical laboratory tests can be performed up to 24 hours before dosing on Day 0.

[g] Coagulation panel may be performed after Baseline if the investigator considers it necessary.

[h] Vital signs should be measured on the day of dosing at 5 minutes (±2 minutes) before dosing, then at the end of infusion (±5 minutes), 60 minutes after the end of infusion (±10 minutes), and 4 hours (±15 minutes) after the end of infusion. Vital signs should also be collected as clinically indicated.

[i] Additional ECGs will be collected as clinically indicated.

[j] The initial lymphodepletion chemotherapy regimen will be composed of fludarabine (30 mg/m^2/day IV) and cyclophosphamide (500 mg/m^2/day IV) during the Screening Period from Days -5 to -3. However, modified lymphodepletion regimens may be used after safety is established in dose level. The lymphodepletion regimen will be specified at the time of registration. Please refer to the Pharmacy Manual for the lymphodepletion dosing regimen; lymphodepletion status may be discussed between the Sponsor Medical Monitor, Principal Investigators, and contract research organization Medical Monitor prior to registration.

[k] Study subjects are evaluated for the following restrictions 2 hours (±60 minutes) prior to receiving the PBCAR20A infusion: new uncontrolled infection after receipt of lymphodepletion, fever, taking any corticosteroid beyond the replacement details, rapid acceleration of malignant disease, and any organ dysfunction since Screening. Additional details are provided in Protocol Section 5.1.1. At the investigator's discretion, study subjects may receive premedication 1 hour (±15 minutes) prior to receiving the PBCAR20A infusion with oral acetaminophen and oral or IV diphenhydramine according to the institutional standards.

[l] Study participant diaries will be provided to study subjects on Day 0 to monitor temperature, at least daily, during the first 28 days.

[m] . The PET-CT scan conducted as part of the routine care within 4 weeks of PBCAR20A administration may be used for Screening purposes. If the scan is performed as a part of routine care, the result will be obtained from the study participant's physician or medical record.

[n] A PET-CT scan on Day 14 is optional and will be determined by the investigator. Additional details are provided in Protocol Section 8.4.

[o] Screening tumor biopsy may be omitted if a study participant has had a biopsy showing CD20$^+$ disease within 6 months before Screening and has not received any anti-CD20$^+$ therapy since then. Note: If the tumor is CD20-negative by flow cytometry, it should be evaluated by immunohistochemistry as flow assays may result in false negatives due to competition with CD20 targeting treatment antibodies (e.g. rituximab).

[p] Tumor biopsy may be performed to confirm imaging changes as clinically indicated. Additional biopsies may be performed pending Sponsor approval.

[q] Exploratory analyses will be performed by the central laboratory. Additional analyses performed at the site that are not required by the protocol should be captured in the eCRF.

[r] Blood samples will be collected before PBCAR20A administration on Day 0.

[s] If available, the central laboratory will also test fresh BMA or bone marrow core samples for CAR T cells.

[t] MRD assessment will be performed at Screening for all study subjects. Please consult the Laboratory Manual for specific sample requirements at Screening. At subsequent visits, MRD assessment will only be performed for study subjects who meet other standard response criteria (see Protocol Section 8.1). Please consult the Laboratory Manual for specific sample requirements at all subsequent visits. Note that these samples are disease-specific and may be different between Screening and all subsequent visits.

[u] AESIs are listed in Protocol Section 7.2.1.3.