STATISTICAL ANALYSIS PLAN
FOR PROTOCOL NIT-119

Sponsor: NEOIMMUNETECH	NeoImmuneTech, Inc. 2400 Research Blvd, Suite 250 Rockville, MD 20850	Email:NIT119@neoimmunetech.com
Protocol Number:	NIT-119	
Protocol Title:	A multicenter, open-label, single-arm Phase II study to evaluate anti-tumor efficacy and safety of NT-I7 (efineptakin alfa) in combination with atezolizumab in subjects with previously untreated, PD-L1-expressing, locally advanced or metastatic Non-Small Cell Lung Cancer	
Protocol Version / Date:	Version 3.0/15-NOV-2022	

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Plan Version:	SAP-Final Version 2.1		
Plan Date:	30-Oct -2024		

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SAP Version:	SAP-Final Version 2.1
SAP Date:	30-Oct-2024

I have read and approve the Statistical Analysis Plan specified above and agree on its content:

Signature: QIAOQIAO ZHANG *Electronically signed by: QIAOQIAO ZHANG Reason: I approve this document Date: Oct 30, 2024 14:02 EDT*

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Statistician, Amarex Clinical Research — Date

Signature: *Luke Yun Suk Oh* *Electronically signed by: Luke Yun Suk Oh Reason: I approve this document Date: Oct 30, 2024 15:02 EDT*

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NeoImmuneTech, Inc. Representative — Date

TABLE OF CONTENTS

ABBREVIATIONS, ACRONYMS, AND DEFINITIONS

Abbreviation/Acronym	**Definition**
ADA	Anti-Drug Antibody
AEs	Adverse Events
AESI	Adverse Event of Special Interest
ALC	Absolute Lymphocyte Count
ALT	Alanine Amino Transferase
ANC	Absolute Neutrophil Count
ASA	American Statistical Association
AUC	Area Under the Curve
aPTT	Activated Partial Thromboplastin Time
AST	Aspartate Amino Transferase
BMI	Body Mass Index
BOR	Best Overall Response
BUN	Blood Urea Nitrogen
CBC	Complete Blood Count
CD	Cluster of Differentiation
CI	Confidence Interval
C_{max}	Maximum Concentration
CR	Complete Response
CRF	Case Report Form
CSR	Clinical Study Report
CT	Computed Tomography
CxDx	Cycle x Day x
DAIDS	The Division of AIDS
D1	Day 1
DCR	Disease Control Rate
DL	Dose Level
DMC	Data Monitoring Committee
DoR	Duration of Response
ECI	Events of Clinical Interest
ECOG	Eastern Cooperative Oncology Group
eCRF	Electronic Case Report Form
EDC	Electronic Data Capture
eGFR	Epidermal Growth Factor Receptor
ECG	Electrocardiogram
EOT	End of Treatment
ER	Estrogen Receptor
FDA	Food and Drug Administration
FU	Follow Up
GCP	Good Clinical Practice
HER2	Human Epidermal Growth Factor Receptor 2
HIV	Human Immunodeficiency Virus
HR	Hazard Ratio

Abbreviation/Acronym	**Definition**
hyFC	hybrid Fc
IA	Interim Analysis
ICF	Informed Consent Form
ICH	International Council for Harmonization
iCPD	Confirmed Progressive Disease (per iRECIST)
iCR	Complete Response (per iRECIST)
IHC	Immunohistochemistry
IM	Intramuscular
IME	Important Medical Events
INR	International Normalized Ratio
iPR	Partial Response (per iRECIST)
irAE	Immune-related Adverse Event
iSD	Stable Disease (per iRECIST)
ISR	Injection Site Reaction
ITT	Intent-To-Treat
iUPD	Unconfirmed Progressive Disease (per iRECIST)
IV	Intravenous
LDH	Lactate Dehydrogenase
MAS	Macrophage Activation Syndrome
MedDRA	Medical Dictionary for Regulatory Activities
MRI	Magnetic Resonance Imaging
NCI-CTCAE	National Cancer Institute – Common Terminology Criteria for Adverse Events
NIT	NeoImmuneTech
NSCLC	Non-Small Cell Lung Cancer
NT-I7	rh-IL-7-hyFc; also known as efineptakin alfa
ORR	Objective Response Rate
OS	Overall Survival
OTC	Over-the-counter
PASS	Power Analysis & Sample Size Software
PBMC	Peripheral Blood Mononuclear Cells
PD	Progressive Disease
PD-1	Programmed Cell Death Protein 1 Protein - Ligand 1
PD-L1	Programmed Death-Ligand 1
PFS	Progression Free Survival
PI	Principal Investigator
PK	Pharmacokinetic
PR	Partial Response
PT	Preferred Term
Q3W	Every 3 Weeks
Q6W	Every 6 Weeks
QTc	Corrected QT interval
R/R	Relapsed/Refractory
RBC	Red Blood Cells

Abbreviation/Acronym	**Definition**
RECIST 1.1	Response Evaluation Criteria in Solid Tumors 1.1
iRECIST	Immune Response Evaluation Criteria in Solid Tumors
SAEs	Serious Adverse Events
SAP	Statistical Analysis Plan
SC	Subcutaneous
SD	Stable Disease
SGOT	Serum Glutamic-Oxaloacetic Transaminase
SGPT	Serum Glutamic-Pyruvate Transaminase
SOC	System Organ Class
$T_{1/2}$	Terminal Half-life
Tmax	Time to Reach Cmax
T_{reg}	Regulatory T cells
TEAE	Treatment Emergent Adverse Event
TIL	Tumor-Infiltrating Lymphocyte
TMB	Tumor Mutational Burden
TPS	Tumor Proportion Score
TSH	Thyroid Stimulating Hormone
Tx	Treatment
WBC	White Blood Cells
WHO	World Health Organization

1. INTRODUCTION

This Statistical Analysis Plan (SAP) describes the planned analyses and reporting for the clinical trial protocol NIT-119, conducted by NeoImmuneTech, Inc. The reader of this SAP is encouraged to review the complete protocol and amendments as this plan contains only a limited overview of protocol information. The main objectives of this plan are to provide details pertaining to statistical methodology, data conventions, and processes used for the analysis of data from this trial.

The format and content of this SAP are structured to provide sufficient detail to meet the requirements specified by the International Council on Harmonization (ICH) E9: Guidance on Statistical Principles in Clinical Trials. All work planned and presented in this SAP will follow the ethical guidelines published by the American Statistical Association (ASA).

The following documents were reviewed in preparation of this SAP:

- Final protocol 3.0/15-NOV-2022
- ASA Ethical Guidelines for Statistical Practice (2016)
- The Royal Statistical Society: Code of Conduct (2014)
- ICH Guidance on the Structure and Content of Clinical Study Reports (ICH E3, 1996)
- ICH Guidance on the Structure and Content of Clinical Study Reports (ICH E3(R1), 2013)
- ICH Guidance on the Statistical Principles for Clinical Trials (ICH E9, 1998)
- ICH Guidance on the Statistical Principles for Clinical Trials (ICH E9(R1), 2017)

2. PROTOCOL DESIGN

2.1 Design Overview

This is a multicenter, open-label, single-arm Phase II study to evaluate anti-tumor efficacy and safety of NT-I7 in combination with atezolizumab in subjects with program-death ligand 1 (PD-L1)-expressing (tumor proportion score [TPS]≥1%), metastatic (Stage IV) or locally advanced squamous or non-squamous non-small cell lung cancer (NSCLC) who have not received prior systemic therapy in the metastatic or locally advanced setting.

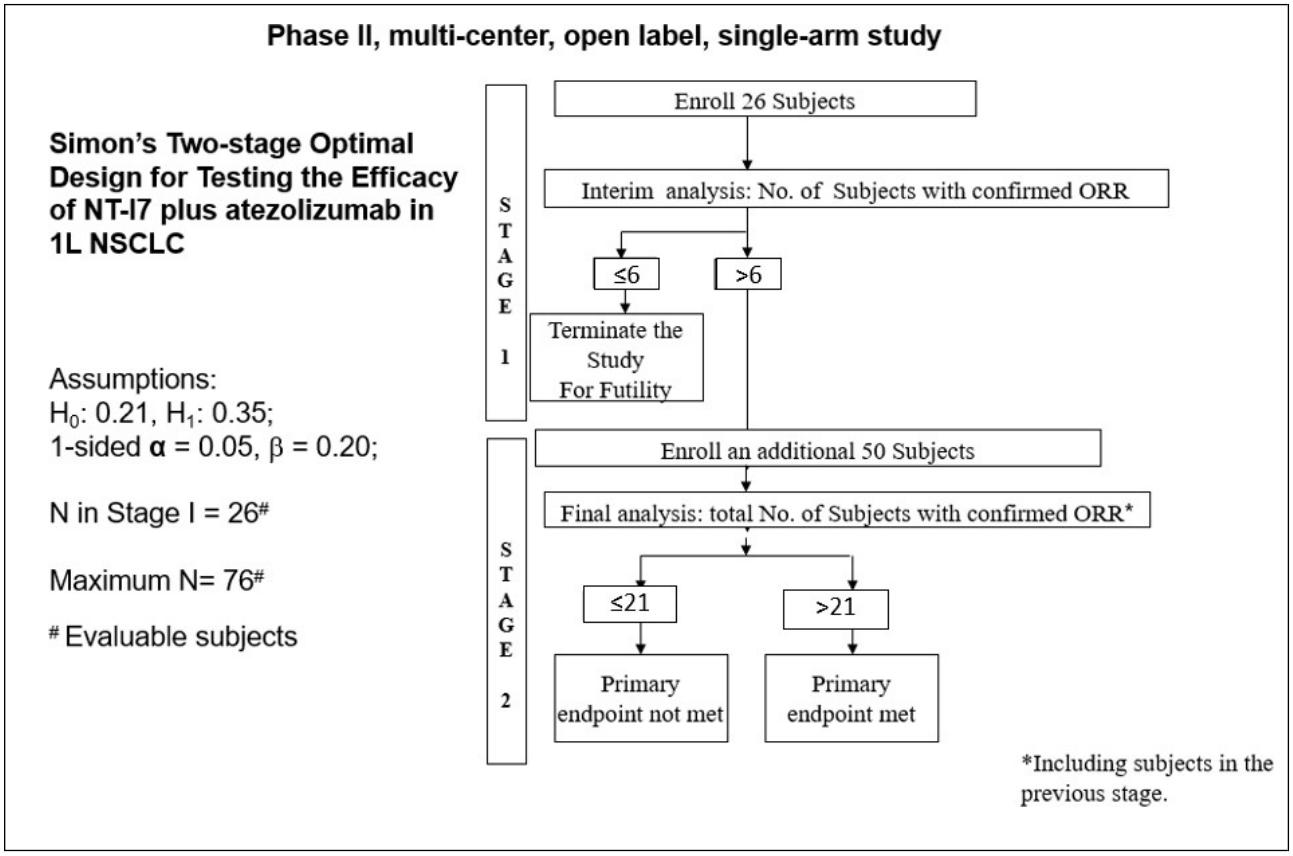
Eligible subjects must have measurable disease according to Investigators using Response Evaluation Criteria in Solid Tumors 1.1 (RECIST 1.1). This Phase II study will enroll a minimum of 26 evaluable subjects and a maximum of 76 evaluable subjects; taking into account a non-evaluable rate of approximately 5%, it is planned to enroll up to 83 subjects.

The study will follow Simon's 2-stage optimal design with null objective response rate (ORR) test rate 21% and alternative ("promising") rate 35%, powered at 80% for 1-sided alpha = 0.05 primary

test with 76 evaluable subjects for the final analysis and interim analysis for futility at 26 evaluable subjects.

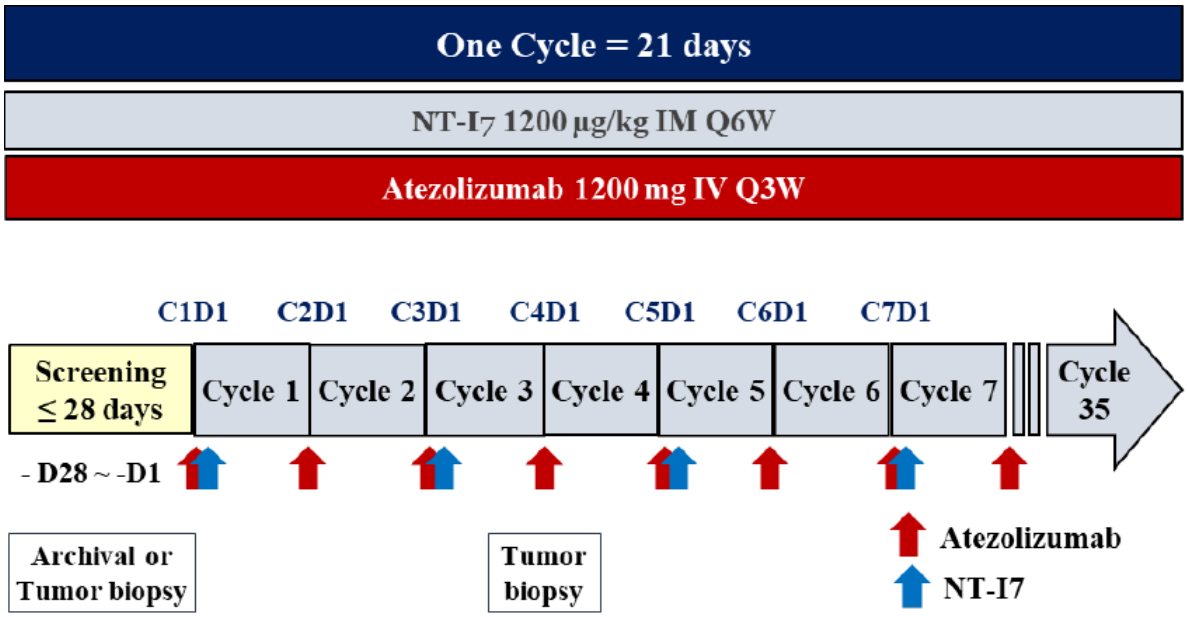
One treatment cycle is defined as 21 days (3 weeks) with 1200 µg/kg NT-I7 administered intramuscularly (IM) once every 6 weeks (Q6W) starting on Cycle 1, and 1200 mg atezolizumab administered intravenously (IV) once every 3 weeks (Q3W) starting on Cycle 1. On days where both drugs are given, atezolizumab will be given prior to NT-I7. The treatment will be continued up to a maximum of 35 cycles (approximately 2 years).

Figure 2-1: Study Flow Diagram



2.2 Treatment Schema

All subjects will receive the combination therapy in this single arm design. The treatment schema is presented as below:



CT/MRI

Radiological tumor assessments will be conducted every 2 cycles (6 weeks ±1 week) during the first 6 months, and every 3 cycles (9 weeks ±1 week) thereafter. Confirmatory scans must be performed at >4 weeks after initial assessment of response to confirm a best response of CR or PR, whenever disease progression is suspected (e.g., symptomatic deterioration), and at End of Treatment visit. If disease progression is identified by RECIST v1.1, a second scan will be scheduled 4-8 weeks later to confirm disease progression by iRECIST. (See Appendix 3 for details.)

Tumor Biopsy

Pre-treatment biopsy/tissue collection (fresh) must be obtained within 28 days prior to Cycle 1, Day 1, unless archival tissue is available. On-treatment tumor biopsy must be obtained before treatment on C4D1.

2.3 Treatment Group

The treatment group is NT-I7 in combination with atezolizumab.

2.4 Randomization and Stratification

Not applicable.

2.5 Blinding

Not applicable.

2.6 Protocol Objectives

2.6.1 Primary Objective

To assess the preliminary anti-tumor activity of NT-I7 in combination with atezolizumab, based on ORR as assessed by Investigators using RECIST 1.1 and immune Response Evaluation Criteria in

Solid Tumors (iRECIST), in subjects with PD-L1 TPS≥1%, metastatic (Stage IV) or locally advanced squamous or non-squamous NSCLC who have not received prior systemic therapy in the metastatic or locally advanced setting.

2.6.2 Secondary Objective

- To make further assessment of the anti-tumor activity and efficacy of NT-I7 in combination with atezolizumab based on Duration of Response (DoR), Disease Control Rate (DCR), Progression-Free Survival (PFS), and Overall Survival (OS) by RECIST 1.1 and iRECIST.
- To evaluate the safety and tolerability of NT- I7 in combination with atezolizumab in subjects with PD-L1 TPS≥1%, metastatic (Stage IV) or locally advanced squamous or non-squamous NSCLC who have not received prior systemic therapy in the metastatic or locally advanced setting.

2.6.3 Exploratory Objective

- To assess pharmacokinetics (PK) parameters for NT-I7.
- To evaluate the immunogenicity of NT-I7.
- To explore biomarkers that may predict and/or act as pharmacodynamic (PD) indicators of pharmacologic activity of NT-I7 in combination with atezolizumab.
- To explore the relationship(s) between tumor and peripheral blood biomarkers with efficacy, adverse events (AEs), and/or safety parameters.

2.7 Efficacy Outcome Measures

2.7.1 Primary Outcome Measure

ORR, defined as the percentage of subjects with a best overall response (BOR) of a complete response (CR/iCR) or partial response (PR/iPR), per RECIST 1.1 and iRECIST as determined by the investigator.

2.7.2 Secondary Outcome Measures

- DoR for the responders, defined as the time from the first occurrence of a documented objective response to the time of the first documented disease progression or death from any cause, whichever occurs first, per RECIST 1.1 and iRECIST as determined by the investigator.
- DCR, defined as proportion of subjects with a BOR of CR/iCR, PR/iPR or stable response (SD/iSD), per RECIST 1.1 and iRECIST as determined by the investigator.
- PFS, defined as the time from the first study treatment (Cycle 1, Day 1) to the first

occurrence of progression or death from any cause, whichever occurs first, per RECIST .1.1 and iRECIST as determined by the investigator.

- OS, defined as the time from first study treatment (Cycle 1, Day 1) to death from any cause.

2.7.3 Exploratory Analysis

- Assess PK parameters for NT-I7: Respective serum concentration of NT-I7 administered at specified timepoints for the following non-compartmental PK parameters: Area under the curve (AUC), maximum observed concentration (Cmax), time to reach Cmax (Tmax), clearance, volume of distribution, and terminal half-life ($T_{1/2}$).
- Evaluate the immunogenicity of NT-I7: Incidence of anti-drug antibody (ADA) to NT- I7 during the study relative to baseline.
- Explore biomarkers that may predict and/or act as pharmacodynamic indicators of pharmacologic activity of NT-I7 in combination with atezolizumab:
  - Effect of NT-I7 assessed in tumor tissue and peripheral blood including but not limited to the following:
    - ✓ Tumor biopsy analyses of tumor mutational burden (TMB), tumor-infiltrating lymphocytes (TILs), and PD-L1
    - ✓ Immunophenotyping of circulating peripheral blood mononuclear cells (PBMCs).
  - Assessment of cytokines and chemokines as markers of immune modulation
- Explore the relationship(s) between tumor and peripheral blood biomarkers with efficacy, AEs, and/or safety parameters:
  - Correlation of tumor and peripheral blood biomarkers including but not limited to PD-L1 and TMB with ORR, PFS, and OS.
  - Correlation of tumor and peripheral blood biomarkers including but not limited to PD-L1 and TMB with incidence of AEs.

2.7.4 Safety Assessments

The following assessments will be conducted for safety analysis:

- Incidence of treatment-emergent AEs (TEAEs)
- Incidence of withdrawals from the study due to TEAEs
- Changes and shifts in laboratory measurements over time
- Changes in vital signs and weight over time
- Changes and shifts in Electrocardiogram (ECG) parameters over time

- Physical examination

3. SAMPLE SIZE DETERMINATION, STATISTICAL POWER, AND SIGNIFICANCE LEVEL

This Phase II study will enroll a minimum of 26 evaluable subjects and a maximum of 76 evaluable subjects; taking into account a non-evaluable rate of approximately 5% it is planned to enroll up to 83 subjects.

The study will follow Simon's 2-stage optimal design (R. Simon, Controlled Clinical Trials 10:1-10 (1989)) with null ORR test rate 21% and alternative ("promising") rate 35%, powered at 80% for 1-sided alpha = 0.05 primary test with 76 evaluable subjects for the final analysis and interim analysis for futility at 26 evaluable subjects.

4. INTERIM ANALYSIS

The futility interim analysis (IA) for the Simon optimal design will be conducted at 26 evaluable subjects.

An IA is planned and will be conducted when the first 26 evaluable subjects have completed at least one post treatment scan.

4.1 Goals

The objectives of this IA are:

- Futility analysis for the Simon optimal design
- Safety of NT-I7

4.2 Analysis Population

The IA population will be the first 26 evaluable subjects who have completed at least one post treatment scan.

4.3 Procedures for Data Preparation

The procedures of the IA include the following:

1. Cutoff dates for collection of electronic case report forms (eCRFs), data querying, database lock and analysis will be established based on an estimated target date when 26 evaluable subjects have completed at least one post treatment scan.
2. All data received by the cutoff date will be entered, validated, queries generated and resolved or pending queries documented.

4.4 Metrics to be Calculated for the Interim Analysis

Using this data, the independent statistician will prepare safety summaries and calculate the Objective

Response Rate (ORR), i.e., the proportion of subjects with a best overall response (BOR) of a complete response (CR/iCR) or partial response (PR/iPR) in the group.

4.5 Stopping Rule

Futility will be assessed based on ORR at the time of the interim analysis. If there are at least 7 responders in stage 1, then the study will continue to stage 2. The responder criteria is calculated using PASS v14.0.

The above information, along with basic descriptive analyses of safety data, is included in this report for the data monitoring committee (DMC) review. Based on these data, the DMC will make recommendations to the sponsor on futility and safety.

4.6 Data Provided to DMC

The DMC will receive a statistical report. The details on the content of the report are described in the DMC charter.

4.7 Information Provided to Sponsor by DMC

The recommendations to the sponsor will be either "continue with the study" or "stop for futility" based on the data reviewed.

5. PRIMARY HYPOTHESIS

This clinical trial is designed to primarily test the below hypotheses:

H_0: $P_{ORR} = 0.21$ (i.e., the Objective Response Rate (ORR) is 0.21)

H_1: $P_{ORR} = 0.35$ (i.e., the Objective Response Rate (ORR) is 0.35)

ORR is defined as the percentage of subjects with a BOR of a CR/iCR or PR/iPR, per RECIST 1.1 and iRECIST as determined by the investigator.

6. ANALYSIS POPULATIONS

6.1 Safety Population

The Safety population is defined as any subject who received at least one dose of the study treatment. This population will be used for the analysis of safety parameters.

6.2 Efficacy Evaluable Population

Subjects are required to complete at least Cycle 1 treatment and at least one post-baseline tumor scan to be considered evaluable. The evaluable population will be used for efficacy analysis.

6.3 All Enrolled Subjects

All Enrolled Subjects are defined as all subjects that are not screen failed. All Enrolled Subjects will be used for demographic and baseline characteristic listings and tables (i.e., listings/tables for the data

collected before treatment administration).

7. DATA CONVENTION AND RELATED DEFINITIONS

7.1 Baseline Definition

For all parameters, baseline will be defined as the last available value on or prior to the date of the first treatment. For assessments where both pre-dose and post-dose measurements are collected on the date of the first treatment, the pre-dose assessment will be used as the baseline value.

7.2 Duplicate Data

For unplanned duplicate data within a protocol-specified visit, the last measured value will be used for the analysis. If it is not possible to identify the "last measured value", the average of the duplicate values will be used. In cases where additional ECGs are performed at the same visit, the Duplicate ECGs[1] measurements will be used for the analysis.

7.3 Handling of Missing Data

7.3.1 Handling of Missing Data for Efficacy Evaluations

Every effort will be made to obtain required data at each scheduled evaluation from all subjects who have been randomized to minimize missing data. Missing data will not be imputed.

7.3.2 Handling of Missing Data for Safety Evaluations

The imputation rules below will be followed for imputation of missing dates:

Partial/Missing Start Date	Missing day - Impute the 1st of the month unless month is same as month and year of first dose of study drug then impute first dose date. Missing month – Impute January unless year is the same as first dose date then impute first dose month. Completely missing – impute first dose date unless the end date suggests it could have started prior to this in which case impute Jan 1st of the same year as the end date. When imputing a start date, ensure that the new imputed date is sensible i.e. is prior to the end date of the AE or medications.
Partial Start Time (applicable to AE only)	If the minute or second part is missing, then impute as 00.

[1] Duplicate ECGs refers to the additional ECG collection section with the leading question "Was a duplicate ECG performed" from the eCRF.

Missing Start Time (applicable to AE only)	If the start date or the imputed start date is the same as the date of first treatment administration, then the start time will be estimated to be equal to the time of first treatment administration; unless the end date & time suggests it could have started prior to this in which case impute as 00. If the start date or the imputed start date is prior to or after the date of first treatment administration, then the start time will be set to 00:00:00 (24-hour clock).

Partial/Missing End Date	If the date of death is non missing, then use it as the last date else if the date of death is missing, then use the end of study date as the last date. Missing day - If year and month is the same as the last date, then impute the last date; else impute the last day of the month. Missing month – If the year is the same as the last date, then impute last date; else impute the last month of the year. Completely missing – Impute last date.
Missing End Time (applicable to AE only)	If the minute or second part is missing, then impute as 59 Completely missing – Impute 23:59:59.

7.4 Multicenter Clinical Trials

This is a multicenter clinical trial that includes approximately 20 centers in the United States.

7.5 Multiple Comparisons and Multiplicity

No multiplicity adjustment is planned for multiple analyses on this Phase II study.

7.6 Covariates and Prognostic Factors

There are no pre-planned covariates analyses of the data from this study.

7.7 Standard Calculations

7.7.1 Age

Age will be calculated as the number of completed years between the date of informed consent and the subject's birth date.

Age (years) = integer of [(date of informed consent – date of birth)/ 365.25]

7.7.2 Body Mass Index (BMI)

BMI will be calculated using height (in cm) and weight (in kg) according to the formula noted below.

BMI (kg/m^2) = weight (kg) / [height (cm)/100]^2

7.7.3 Change from baseline

Change from baseline will be calculated for each post baseline visit as follows:

Change From Baseline = Post baseline result at time - Baseline result

7.7.4 Time to event

Time to event (months) will be calculated according to the formula noted below:

Time to event = (Date of Event – Date of first treatment administration + 1) / 30.4

7.7.5 Duration of response (DoR)

DoR (months) will be calculated according to the formula noted below.

DoR= (Date of the first disease progression/death – Date of the first objective response + 1)/30.4

7.8 Data Standardization

The study data will be tabulated according to the CDISC SDTM standard to facilitate regulatory submission, with all clinical data mapped to the appropriate SDTM domains.

All analysis datasets will be structured in compliance with CDISC ADaM standards to support statistical analysis. The derivation of key variables and endpoints will be traceable from raw data (SDTM datasets) to analysis-ready data (ADaM datasets). The ADaM datasets will include the necessary derived variables for the analysis of endpoints as outlined in this plan, including both Define-XML and the corresponding Reviewer Guides (SDRG and ADRG).

8. STATISTICAL METHODS

All statistical analyses will be performed using SAS® for Windows, version 9.4 or later. All data collected during this study will be presented in subject data listings.

All the efficacy analyses presented here will be conducted using evaluable populations. All safety analyses will be conducted using the safety population.

For continuous variables, descriptive statistics (n, mean, standard deviation, median, minimum, and maximum) will be presented. For categorical variables both frequencies and percentages will be presented.

8.1 Summarizing Disposition and Baseline Data

8.1.1 Subject Disposition and Withdrawals

There will be a detailed accounting of all subjects that signed the informed consent to participate in this trial. The following will be summarized:

- The number of subjects who signed the informed consent
- The number of subjects who are screen failures
- The number of subjects who received at least one study treatment
- The number of subjects who completed the treatment
- The number of subjects who discontinued prior to completion
- Reasons for discontinuation prior to completion will also be summarized descriptively

The number of subjects in each analysis population will be summarized, reason for exclusion from analysis populations will be listed.

In addition, there will also be a listing of all subjects, which will provide the clinical trial center, nation, study completion status, and the specific reason for discontinuation.

8.1.2 Protocol Deviations

Protocol deviations for all subjects will be listed as by-subject listing and/or summarized.

8.1.3 Demographics and Baseline Characteristics

Demographics and baseline characteristics (i.e., Age, Gender, etc.) will be presented as by-subject listing and summarized descriptively for all enrolled subjects.

Medical history will be coded using Medical Dictionary for Regulatory Activities (MedDRA) version 24.0 and will be summarized by system organ class (SOC) and preferred term (PT). Medical history results will be provided as by-subject listings and summarized.

8.1.4 Prior and Concomitant Medications

Prior medication is defined as any medication with an end date prior to the first treatment date.

All prior and concomitant medications recorded in the eCRF will be listed and coded to the drug substance level (i.e., generic term) using WHO Drug dictionary version Y2021MARB3 and summarized by the number and percentage of subjects taking each medication for the Safety population. CM will be summarized by Anatomical Therapeutic Classification (ATC) class (2nd level, chemical subgroup) and PT. Subject will only be counted once within each ATC-2 code and within each preferred name.

8.1.5 Prior Anti-Cancer Treatments

All prior anti-cancer treatments (i.e., Radiotherapy, Chemotherapy/Immunotherapy, and Surgery)

recorded in the eCRF will be presented as by-subject listings.

8.1.6 Extent of Exposure

All treatment administration data will be listed and summarized for the Safety population.

In addition, extent of exposure will be summarized using total number of Cycles, the duration (weeks) of exposure, cumulative actual dose received.

The duration of treatment administration will be determined by the following formula:

Duration = (date of last treatment administration – date of first treatment administration + 1) / 7

8.1.7 Study Treatment Compliance

All accountability and compliance data will be listed and summarized for the Safety population.

8.2 Analysis of Efficacy Data

The primary analysis will be conducted on the Evaluable Population. Any observations excluded from the efficacy analyses will be listed as by-subject listings.

8.2.1 Primary Outcome Measure

ORR is defined as the percentage of subjects with a BOR of a CR/iCR or PR/iPR, per RECIST 1.1 and iRECIST as determined by the investigator. Per RECIST 1.1, an objective response should be confirmed by a repeat imaging assessment. Tumor imaging to confirm PR or CR should be performed at least 4 weeks after the first indication of a response is observed. The ORR point estimate and 95% Confidence Interval will be calculated.

At the final analysis, if the total number of responders is not greater than 21, then the primary endpoint is considered as not met and the treatment is deemed unworthy of further study. The rejection number of responders is calculated using PASS v14.0.

8.2.2 Secondary Outcome Measure

8.2.2.1 Duration of Response (DoR)

The DoR for the responders is defined as the time from the first occurrence of a documented objective response to the time of the first documented disease progression or death from any cause, whichever occurs first, per RECIST 1.1 and iRECIST as determined by the investigator. The censoring rule for DoR is described in Table 8-1. Kaplan-Meier methods will be used to depict the DoR and it will also be presented descriptively for the responders.

8.2.2.2 Disease Control Rate (DCR)

DCR is defined as proportion of subjects with a BOR of CR/iCR, PR/iPR or SD/iSD, per RECIST 1.1 and iRECIST as determined by the investigator. The DCR point estimate and 95% confidence

interval will be calculated.

8.2.2.3 Progression-free Survival (PFS)

PFS will be calculated using the formula in Section 7.7.4**Error! Reference source not found.**. The censoring rule for PFS is described in Table 8-1. These conventions are based on the April 2015 FDA Guidance for Industry, "Clinical Trial Endpoints for the Approval of Non-Small Cell Lung Cancer Drugs and Biologics". Kaplan-Meier analysis will be used to depict the median PFS (months).

Table 8-1 Date of Progression or Censoring for Progression-Free Survival Situation

Situation	Date of Progression or Censoring	Outcome
Progression documented between scheduled visits	Date of last disease assessment	Progressed
No progression	Date of last disease assessment with no documented progression	Censored
Treatment discontinuation for undocumented progression	Date of last disease assessment with no documented progression	Censored
Treatment discontinuation for toxicity or other reason	Date of last disease assessment with no documented progression	Censored
New anticancer treatment started	Date of last disease assessment with documented non progression before start of new treatment	Censored
Death before first PD assessment	Date of death	Progressed
Death between adequate assessment visits	Date of death	Progressed

8.2.2.4 Overall Survival (OS)

OS will be calculated using the formula in Section 7.7.4**Error! Reference source not found.**. The censoring rule for OS is described in Table 8-2. Kaplan-Meier analysis will be used to depict the median OS (months).

Table 8-2 Censoring Rule for Overall Survival Situation

Situation	Date of Event or Censoring	Outcome
Subject died	Date of Death	Dead
Subject known to be alive in the survival follow-up	Date of last day known to be alive	Censored

Situation	Date of Event or Censoring	Outcome
Subject completed the study	Date of study completion	Censored
Subject discontinued from the study	Date of discontinuation	Censored
Subject did not withdrawal nor lost to follow-up and is still in the study	Date of last visit	Censored

8.3 Analysis of Safety Data

All safety analyses will be conducted using the Safety population. All data collected will be summarized according to the variable type. No inferential statistics are planned.

8.3.1 Adverse Events (AEs)

AEs will be classified by SOC and PT according to the MedDRA dictionary v24.0.

TEAEs are defined as adverse events with onset date on or after the first dose and 90 days within the last treatment. The following TEAE summaries will be provided:

a) TEAEs
b) TEAEs by severity
c) Treatment related TEAEs (NT-I7, Atezolizumab, NT-I7 or Atezolizumab)
d) SAEs
e) Treatment related SAEs
f) AE of Special Interest (AESI)
g) Immune-related AEs (irAEs)
h) Injection site reaction (ISR)
i) TEAEs leading to treatment discontinuation/interruption
j) TEAEs leading to death

The severity will be assessed using the National Cancer Institute – Common Terminology Criteria for Adverse Events (NCI-CTCAE) v5.0. Unless otherwise specified, at each level of subject summarization, a subject will be counted only once. If there is more than one occurrence of an event, the event of the worst severity or the worst-case relationship category will be summarized.

All AEs recorded in the eCRF will be presented as by-subject listings.

8.3.2 Clinical Laboratory Evaluations

All results of laboratory evaluations will be presented as by-subject listings.

8.3.2.1 Laboratory Values over Time

Summary statistics of raw data and change from baseline values for each laboratory parameter will be presented by time point. Data will be summarized as appropriate for the variable type.

For change from baseline summaries, subjects with an undefined change from baseline, because of missing data, will be excluded.

8.3.2.2 Individual Subject Changes on Interpretation

Shift tables will be presented based on physician/investigator interpretation (i.e., Normal, Abnormal (not clinically significant) and Abnormal (clinically significant)) with counts and percentages of subjects to compare baseline to the worse post-baseline value.

8.3.2.3 Individual Clinically Significant Abnormalities

Clinically significant laboratory abnormalities will be listed.

8.3.3 Vital Signs

Vital sign assessments are performed to characterize basic body function. All vital signs results will be listed as by-subject listings.

8.3.3.1 Vital Signs Values over Times

Summary statistics of raw data and change from baseline values for each vital sign parameter will be presented by time point. Data will be summarized as appropriate for the variable type.

For change from baseline summaries, subjects with an undefined change from baseline, because of missing data, will be excluded.

8.3.3.2 Individual Patient Changes on Notable Vital Sign Values

Clinically notable elevated values

- Systolic BP: >= 160 mmHg and an increase >= 20 mmHg from baseline
- Diastolic BP: >= 100 mmHg and an increase >= 15 mmHg from baseline.
- Body temperature: >= 39.1°C
- Weight: increase from baseline of >= 10%
- Heart rate: >= 120 bpm with increase from baseline of >=15 bpm
- Respiration rate: >= 24 breaths per minute with increase from baseline of >= 6 breaths per minute from baseline.

Clinically notable below normal values

- Systolic BP: <= 90 mmHg and a decrease >= 20 mmHg from baseline
- Diastolic BP: <= 50 mmHg and a decrease >= 15 mmHg from baseline
- Body temperature: <= 35°C
- Weight: decrease from baseline of >= 20%
- Heart rate: <= 50 bpm with decrease from baseline of >= 15 bpm

- Respiration rate: <= 8 breaths per minute with decrease from baseline of >= 6 breaths per minute from baseline

The number and percentage of patients with at least one post-baseline vital sign abnormality (in both directions, i.e., both elevated and below normal values) will be summarized.

8.3.3.3 Individual Clinically Significant Abnormalities

Clinically significant vital sign abnormalities (i.e., those vital sign abnormalities recorded as AEs) will be listed.

8.3.4 Electrocardiogram (ECGs)

The ECG parameters include ventricular rate (beats per minute), PR interval (msec), QRS interval (msec), QT interval (msec), and QTc interval (msec).

8.3.4.1 ECG Values over Time

Summary statistics of raw data and change from baseline values for each ECG parameter will be presented by time point. Data will be summarized as appropriate for the variable type.

For change from baseline summaries, subjects with an undefined change from baseline, because of missing data, will be excluded.

8.3.4.2 Individual Patient Changes on Notable ECG Values

The number and percentage of patients having notable ECG interval values and newly occurring qualitative ECG abnormalities will be summarized.

The following notable ECG interval values for each parameter will be presented as by-subject listing. Number and percentage of subjects with at least one occurrence of the below notable ECG changes will be summarized.

QT and QTc:

(1) New >450 msec
(2) New >480 msec
(3) New >500 msec
(4) Increase from baseline >30 msec
(5) Increase from baseline >60 msec

Shift tables will also be presented using frequency and percentages for the categories of QT results (<=450, >450-480, >480-500, >500) with counts and percentages of subjects, for shift (change) from baseline.

PR:

(1) An increase of >25% from baseline and PR >200 msec at any post-baseline assessment

QRS:

(1) An increase of >25% from baseline and QRS >110 msec at any post-baseline assessment

Ventricular rate:

(1) Increase >25% from baseline and HR >100 bpm at any post-baseline assessment

(2) Decrease >25% from baseline and HR <50 bpm at any post-baseline assessment

8.3.5 Physical Examination

Physical Examination findings will be presented as by-subject listing.

8.3.6 Serum Pregnancy Test

All the results for serum pregnancy test will be presented as a by-subject listing.

8.3.7 Urine Pregnancy Test

All data from Urine Pregnancy test will be presented as a by-subject listing.

8.4 Exploratory Outcome Measure

8.4.1 Pharmacokinetics Assessment

PK samples for NT-I7 will be analyzed from all subjects following the PK timepoints in Table 8-3 by BioAgilytix and transferred to Amarex. All data from these assessments will be presented and/or summarized.

Respective serum concentration of NT-I7 administered at specified timepoints for the following non-compartmental PK parameters: AUC, Cmax, Tmax, clearance, volume of distribution, and T1/2 will be calculated, as applicable.

Table 8-3 Pharmacokinetic (PK) and Immunogenicity Sample Collections*

Treatment Cycle/Visit	Cycle 1				Cycle 2	Cycle 3		Cycle 4	Cycle 5		Cycle 7	Cycle 9	Subsequent Cycles	End of Tx (EOT)	Safety FU
Scheduling Window	Day 1			Day 8 ±2 days	Day 1 ±2 days	Day 1 ±2 days		Day 1 ±2 days	Day 1 ±2 days		Day 1 ±2 days	Day 1 ±2 days	Day 1 ±2 days		90 days after last dose ±7 days
Hours	0 h	2 h (±15mins)	6 h (±30mins)			0 h			0 h						
NT-I7 PK	X[a]	X[b]	X[b]	X	X[a]	X[a]		X[a]	X[a]					X	
NT-I7 ADA[c]	X[a]				X[a]	X[a]			X[a]		X[a]	X[a]	Every 4 Cycles[a]	X[d]	X[e]

[a] PK and immunogenicity samples shall be collected for NT-I7 in all subjects prior to study agent(s) administration on a dosing day, preferably within 1 hour of dosing.
[b] Blood draws are timed after NT-I7 administration is complete.
[c] Immunogenicity samples shall be collected pre-dose on C1D1, C2D1, C3D1, C5D1, C7D1, and C9D1. Thereafter, samples shall be collected pre-dose on every 4 cycles such as C13D1, C17D1, C21D1, and so on, and at time End-of-Treatment (EOT) visit.
[d] End-of-treatment (EOT) testing can be omitted if the last ADA sample collection is within 2 weeks of EOT visit.
[e] Repeat testing at 90-day Safety follow-up visit, if positive at the EOT visit or the last cycle testing (if within 2-weeks of EOT), whichever is applicable.
* Details on blood collection, handling, and shipping are provided in the *NIT-119 Generic Laboratory Manual*.

8.4.2 Immunogenicity Assessment

Immunogenicity samples for NT-I7 will be analyzed from all subjects following Table 8-3 by BioAgilytix and transferred to Amarex. Incidence of ADA to NT-I7 during the study will be assessed. All data of ADA and neutralizing antibody (NADA) will be presented as by-subject listing. The number and percentage of subjects with ADA and NADA will be summarized by time point.

8.4.3 Correlative Studies and Biomarker Assessments

The correlative studies and biomarker assessments will be performed by NIT. Data will be transferred from vendors to NIT directly. There will be no data transfer to Amarex except for data from Q2 Solutions. Amarex will not perform statistical analysis on exploratory data from any vendors, including Q2 solutions.

8.4.4 Peripheral Blood Biomarker Analyses

The peripheral blood biomarker will be performed by NIT. Data will be transferred from vendors to NIT directly. There will be no data transfer to Amarex except for data from Q2 Solutions. Amarex will not perform statistical analysis on data from any vendors, including Q2 solutions.

8.5 Additional Outcome Measure

8.5.1 ECOG Performance Assessment

ECOG performance status will be presented as a by-subject listing.

A shift table will be presented based on ECOG Grade with counts and percentages of subjects to

compare baseline to the worst post-baseline value.

9. APPENDIX 1

FIGURE 9-1: SCHEDULE OF ASSESSMENTS

Treatment (Tx) Cycle/ Visit*	Screening	Cycle 1		Cycle 2		Cycle 3	Cycle 4	Cycle 5	Subsequent Cycles	End of Tx (EOT)[19]	Post Tx Follow Up			
											Safety FU[20]			Survival FU[21]
Scheduling Window	Within 28 days	Day 1	Day 8 ±2 days	Day 1 ±2 days	Day 8 ±2 days	Day 1 ±2 days	Day 1 ±2 days	Day 1 ±2 days	Day 1 ±2 days		30 days after last dose ±7 days	60 days after last dose ± 7 days	90 days after last dose ±7 days	Every 90 days after FU Visit 3 ±7 days
Atezolizumab[1]		X		X		X	X	X	X					
NT-I7[2]		X				X		X	X (odd cycles only)					
Informed consent[3]	X													
Inclusion/Exclusion Criteria[4]	X													
Demographics	X													
Medical history	X													
Safety Assessments**														
Prior and concomitant medications[5]	X	X	X	X	X	X	X	X	X	X	X	X	X	X
Physical exam[6]	X	X		X		X	X	X	X	X	X	X	X	
ECOG Performance Status	X	X		X		X	X	X	X	X	X	X	X	
Vital signs[7]	X	X	X	X	X	X	X	X	X	X	X			
Height	X													
Weight	X	X		X		X	X	X	X	X	X			
Adverse Events Assessments[8]	X	X	X	X	X	X	X	X	X	X	X	X	X	X
12-lead ECG[9]	X	X (as indicated)												
CBC w/diff, platelets[10]	X	X	X	X		X	X	X	X	X	X			
Serum chemistry[11]	X	X	X	X		X	X	X	X	X	X			
PT/INR and aPTT	X	X								X				
Thyroid Function[12]	X	X				X		X	Odd cycles	X				
Serum or Urine Pregnancy Test[13]	X	X		X		X	X	X	X	X	X			

Treatment (Tx) Cycle/ Visit*	Screening	Cycle 1		Cycle 2		Cycle 3	Cycle 4	Cycle 5	Subsequent Cycles	End of Tx (EOT)[19]	Post Tx Follow Up			
											Safety FU[20]			Survival FU[21]
Scheduling Window	Within 28 days	Day 1	Day 8 ±2 days	Day 1 ±2 days	Day 8 ±2 days	Day 1 ±2 days	Day 1 ±2 days	Day 1 ±2 days	Day 1 ±2 days		30 days after last dose ±7 days	60 days after last dose ± 7 days	90 days after last dose ±7 days	Every 90 days after FU Visit 3 ±7 days
Urine Analysis[14]	X	X		X		X	X	X	X	X				
Survival Status[15]														X
Efficacy Measurements														
Tumor evaluation (CT/MRI)[16]	X	RECIST 1.1 and iRECIST algorithm: Every 6 weeks (± 1 week) for the first 6 months, then every 9 weeks (± 1 week) until disease progression or study discontinuation.								X		X[20]	X[20]	X[16]
Tumor Biopsies/Archival Tissue Collection														
Archived Tumor Tissue or Fresh Tumor Biopsy[17]	X						X							
Correlative Studies**														
Immunophenotyping[18]		X	X	X	X	X	X			X				
Cytokines[18]		X	X	X	X	X	X			X				
Blood samples for biomarker analysis[18]		X					X							
Pharmacokinetics	Refer to Table 3, Section 6.4 for PK sampling													
Immunogenicity	Refer to Table 3, Section 6.4 for ADA sampling													

* One treatment cycle is defined as 21 days (3 weeks) with NT-I7 administered IM on Day 1 of every other cycle (Q6W) starting in Cycle 1, and atezolizumab 1200 mg administered IV on Day 1 of every cycle (Q3W).

** Unless otherwise specified, all clinic procedures and sample collection are to be done prior to NT-I7 and/or atezolizumab dosing.

[1] Atezolizumab: Dose as assigned; once every 3 weeks, starting Cycle 1, Day 1.

[2] NT-I7: Dose as assigned; once every 6 weeks, starting Cycle 1, Day 1. NT-I7 must be dosed 45 (±15) minutes after atezolizumab on days where concurrent administration is planned.

[3] Written consent must be obtained prior to performing any protocol specified procedure. A copy of the signed and dated ICF will be provided to the subject. The original ICF will be retained by the Investigator.

[4] All inclusion/exclusion criteria should be assessed during screening period, prior to first dose.

[5] Prior medications – Record all medications (prescription and over-the-counter [OTC]) taken within 28 days (4 weeks) prior to the first dose of study treatment). Concomitant medications – Enter all medications (prescription and OTC) taken after first dose of study treatment on Cycle 1, Day 1 through the Safety Follow-up visit Day 90 (± 7 days) after the last dose.

[6] Full physical exam is required during Screening, Day 1 of every cycle, End of Treatment, and Safety Follow-up visits. A directed physical exam may be performed on other days as clinically indicated.

[7] Vital signs consist of blood pressure, heart rate, respiratory rate, and temperature. See Sections 7.1.1.2 (NT-I7) and 7.1.2 (Atezolizumab) for vital sign collection requirements on treatment days.

[8] All AEs meeting serious criteria, from the time of consent through 90 days following cessation of study treatment. See Section 9 for additional details on reporting of AEs.

[9] 12-lead duplicate ECGs (+/- 5 minutes apart) will be obtained at Screening. If clinically indicated, additional ECGs may be obtained during the study.

[10] Hematology includes complete blood count (CBC) with differential, including but not limited to red blood cell (RBC) count, hemoglobin, hematocrit, white blood cell (WBC) count with differential (neutrophil count including lymphocyte, monocyte, eosinophil, basophil counts and bands), absolute neutrophil count (ANC), and platelet count.

[11]Chemistry includes (but is not limited to) sodium, potassium, calcium, phosphorus, chloride, magnesium, bicarbonate, blood urea nitrogen (BUN) or urea, serum creatinine, glucose, uric acid, albumin, total protein, alkaline phosphatase, lactate dehydrogenase, bilirubin (indirect and direct), aspartate serum glutamic oxaloacetic transaminase (AST/SGOT), alanine aminotransferase/serum pyruvic transaminase (ALT/SGPT).

[12]At screening, thyroid function testing is to include TSH, free T3 and free T4. At subsequent timepoints, thyroid function testing consists of TSH only. However, if the TSH is abnormal, reflexive testing of free T3 and free T4 are to be performed.

[13]Serum pregnancy test to be performed at the screening visit for all females except those surgically sterile for at least 6 weeks or postmenopausal for at least 1 year. Subsequent tests to be performed on urine samples. If positive, then test to be repeated with serum pregnancy test.

[14]Urinalysis (a urine dipstick may be used) at screening and Day 1 of each cycle.

[15]Survival status and additional subsequent cancer therapy details (if applicable) such as regimen, setting of the regimen, start date and end date of the regimen, best response to the regimen and date of progression after the subsequent therapy will be collected.

[16]Baseline CT/MRI tumor imaging must be performed within 28 days (4 weeks) prior to first dose. Scans performed as part of routine clinical management are acceptable for use as the baseline scan if they are of diagnostic quality and performed within the allotted screening window. The exact same image acquisition and processing parameters should be used throughout the study. On-study radiological tumor assessments will begin at week 6 post first dose date (± 7 days) and be performed every 2 cycles (6 weeks ± 1 week) until 6 months, at which time scans will be performed every 3 cycles (9 weeks ± 1 week). (Note: Subjects do not need to undergo the next scheduled tumor imaging if it is less than 4 weeks after the previous scan). Refer to section 6.3, Appendix 2 (RECIST 1.1) and Appendix 3 (iRECIST) for additional guidance.

[17]Pre-treatment tumor tissue sample should be obtained either from freshly collected biopsy during screening or from previous surgery or biopsy and prior to the start of treatment in this study. On-treatment tumor tissue sample should be freshly collected from all available patients at the Cycle 4 visit. For newly collected biopsies (screening and Cycle 4), fresh tumor biopsies or formalin-fixed paraffin embedded tumor tissue blocks should be preferentially obtained from tumor tissues that are safely accessible as determined by the investigator and collected via non-significant risk procedures. Tumor lesions used for biopsy should not be lesions used as RECIST 1.1 target lesions. For archival tissue a minimum of 25 unstained tumor tissue sections are acceptable. Submission of fewer than 25 unstained slides may be acceptable in some circumstances following discussion with the Study Medical Monitor.

[18]Whole blood will be collected for the multispectral immunophenotyping to obtain absolute cell counts for CD4+ and CD8+ T-cell subsets and activation states, NK cells, B cells, and other cell types as necessary, cytokines, and other biomarker analysis. Additional information on handling and shipping are provided in the *NIT-119 Generic Laboratory Manual*

[19]End of Treatment (EOT) visit will occur approximately anytime within 7 days after disease progression determination or treatment discontinuation, or immediately before initiation of any other cancer therapy whichever occurs first.

[20]Safety Follow-Up visits will be performed in clinic at 30 days (± 7 days), 60 days (± 7 days), and 90 days (± 7 days) after the last dose. Tumor imaging can be performed at Safety Follow-Up day 60 (±_7 days) or Day 90 (± 7 days).

[21]Survival Follow-Up Visits will be done via documented telephone calls every 90 days (± 7 days) from Safety Follow-Up Day 90, to assess the subject's status until death, lost to follow up, withdrawal of consent, or end of study, whichever occurs first to find out the survival status, new anti-cancer treatments and the outcome of any ongoing adverse event.
Survival Follow-Up CT/MRI tumor imaging will be performed every 60-90 days for the first nine months (270 days).

10. APPENDIX 2

10.1 Planned by-subject listings

DISPOSITION/WITHDRAWALS (LISTINGS 16.2.1.X)

PROTOCOL DEVIATIONS (LISTINGS 16.2.2.X)

SUBJECTS EXCLUDED FROM THE EFFICACY ANALYSIS (LISTINGS 16.2.3.X)

DEMOGRAPHIC DATA (LISTINGS 16.2.4.1.X)

MEDICAL HISTORY (LISTINGS 16.2.4.2.X)

PRIOR AND CONCOMITANT MEDICATIONS (LISTINGS 16.2.4.3.X)

PRIOR ANTI-CANCER TREATMENTS

- SURGERY in LISTINGS 16.2.4.2.X
- CHEMOTHERAPY/IMMUNOTHERAPY, RADIOTHERAPY in LISTINGS 16.2.4.3.X

DRUG COMPLIANCE AND DRUG CONCENTRATION DATA (LISTINGS 16.2.5.X)

INDIVIDUAL EFFICACY RESPONSE DATA (LISTINGS 16.2.6.X)

ADVERSE EVENT LISTINGS (LISTINGS 16.2.7.X)

INDIVIDUAL LABORATORY MEASUREMENTS (LISTINGS 16.2.8.X)

- OTHER SAFETY DATA (LISTINGS 16.2.9.X)
- VITAL SIGNS
- ECGs
- PHYSICAL EXAMINATION
- OTHER LISTINGS (LISTINGS 16.2.10.X)ECOG
- PK
- IMMUNOGENICITY

10.2 Planned Summary Tables

POPULATION DISPOSITION AND PROTOCOL DEVIATIONS

POPULATION DEMOGRAPHICS

EXPOSURE AND STUDY TREATMENT COMPLIANCE

MEDICAL HISTORY AND CANCER HISTORY/STATUS

PRIOR AND CONCOMITANT MEDICATIONS

EFFICACY SUMMARIES

SAFETY SUMMARIES

- ADVERSE EVENT
- LABORATORY
- VITAL SIGNS
- ECGs

ECOG

PK

IMMUNOGENICITY

11. REFERENCES

1. ASA Ethical Guidelines for Statistical Practice (2016)
2. The Royal Statistical Society: Code of Conduct (2014)
3. ICH Guidance on the Structure and Content of Clinical Study Reports (ICH E3, 1996)
4. ICH Guidance on the Structure and Content of Clinical Study Reports (ICH E3(R1), 2013)
5. ICH Guidance on the Statistical Principles for Clinical Trials (ICH E9, 1998)
6. ICH Guidance on the Statistical Principles for Clinical Trials (ICH E9(R1), 2017)

12. VERSION HISTORY

Version	Date of Issue	Summar of Changes
Original SAP v1.0	2021-08-24	Not Applicable
SAP v2.0	2023-04-19	1. Addition of iRECIST to primary and secondary objectives 2. Updated the Study Flow Diagram to include defined values of X and Y, as well as to specify that subject numbers are for evaluable subjects 3. Updated the Treatment Schema to include C4D1 tumor biopsy as well as language around iRECIST 4. Final Safety Follow Up visit changed from 100 days to 90 days 5. Revisions to Appendix 1 – Figure 9-1: • iRECIST • C2D1 cytokines • C2D8 immunophenotyping and cytokines • Addition of C4D1 peripheral blood sampling and biopsy for exploratory biomarker evaluation • Addition of serious adverse event assessment from time of consent • Removal of EOT peripheral blood sampling for exploratory biomarker evaluation (TCRseq) • Addition of imaging at Safety Follow-Up Day 60 or Day 90 • Addition of imaging every 60-90 days during the first nine months (270 days) of Survival Follow-Up • Removal of language about TCRseq • Updates to footnotes 4, 5, 7, 8, 11, 13, 16, 17,18, 19, 20, and added footnote 21. 6. Updated the PK table number and updated footnotes to clarify timing 7. Changed DSMC to DMC and details surrounding DMC 8. Some language updated to eliminate redundancy and improve readability 9. Updated section 7.3 Handling of Missing Data to add the safety evaluation part. 10. Section 8.1.3 updated to reflect the coded Medical History. 11. Switched section 6.1 and 6.2 and updated the definition of efficacy evaluable population to be consistent with the protocol section 12.4. 12. Updated the Study Flow Diagram (i) from “<6 v.s. >=6” to “<=6 v.s. >6” for the stage I criteria, and (ii) from “<21 v.s. >=21” to “<=21 v.s. >21” for the stage II criteria. Corresponding change from 6 to 7 in section 4.5 Stopping Rule for Interim Analysis. 13. Added the specification for censoring rule and the Kaplan-Meier method for Duration of Response in section 8.2.2.

		14. Removed AE of special interest specification part. 15. Added "as applicable" for PK estimates in section 8.4.1. 16. Revised the timing for Interim Analysis in Section 4 from "when the first 26 evaluable subjects have completed the first follow-up visit" to "when the first 26 evaluable subjects have completed the post treatment scans". 17. Added Subgroup Analyses in Section 7.7 18. Added definition and scope of All Enrolled Subjects in Section 6. 19. Changed the scope of demographic and baseline characteristics in Section 8.1.3 from "for all evaluable population and safety population" to "for all enrolled subjects". 20. Revised the Baseline definition in section 7.1 21. Added specification of duplicate ECGs in section 7.2 Duplicate Data Handling. 22. Removed the second row from Table 8-2 and updated the Table 8-2 title and column header. 23. Updated Listing Numbers in Appendix 2 section 10.1 24. Replaced "Physical Examination" with "ECGs" in Section 10.2 Planned Summary Table to be consistent with the context in section 8.3
SAP v2.1	2024-10-30	25. Added iRECIST response values where iRECIST is mentioned as the guidance to use. 26. Added ECOG performance review as one of the interim analysis goals 27. Added ECOG performance review in section 8.5 as an additional outcome measure 28. Refined the imputation rules for safety evaluation in section 7.3.2 29. Added the Prior Anti-Cancer Treatment analysis as part of the Baseline Data summary in section 8.1.5 30. Added the specification on confirmation of objective response for Primary Outcome Measure in section 8.2.1 31. Revise the specification on DCR outcome presentation in section 8.2.2.2 32. Added specification on Amarex's responsibilities on external data in section 8.4 33. Decoded terms in section 7.3.2, Handling of Missing Data for Safety Evaluations, to improve clearance 34. Revised the formula in section 7.7.5, Duration of Response (DoR) to report DoR in months instead of Days 35. Added specification on ATC to be used in section 8.1.4 for Prior and Concomitant Medications 36. Changed the reporting unit duration of exposure from days to weeks in section 8.1.6 37. Revised the censoring rules in Section 8.2.2.3 to be more specific to this study 38. Updated the specification of AE analysis outline in Section 8.3.1 39. Added section 7.8 Data Standardization

		40. Fixed typos Fixed typos