**Protocol Number: ADCT-301-103**

**Official Title: A Phase 1b, Open-label, Dose-escalation and Dose-expansion Study to Evaluate the Safety, Tolerability, Pharmacokinetics, and Antitumor Activity of Camidanlumab Tesirine (ADCT-301) as Monotherapy or in Combination in Patients With Selected Advanced Solid Tumors**

**NCT Number: NCT03621982**

**Document Date: 02 December 2021**

# Statistical Analysis Plan

## A Phase 1b, Open-label, Dose-escalation and Dose-expansion Study to Evaluate the Safety, Tolerability, Pharmacokinetics, and Antitumor Activity of Camidanlumab Tesirine (ADCT-301) as Monotherapy or in Combination in Patients With Selected Advanced Solid Tumors

## PROTOCOL NO.: ADCT-301-103

## SAP Final No./ Date: 30 November 2021

## Statistician: [redacted]

## Confidentiality Statement

# SAP Approval – Sponsor Signatory

| | |
|---|---|
| **Study Title** | A Phase 1b, Open-label, Dose-escalation and Dose-expansion Study to Evaluate the Safety, Tolerability, Pharmacokinetics, and Antitumor Activity of Camidanlumab Tesirine (ADCT-301) as Monotherapy or in Combination in Patients With Selected Advanced Solid Tumors |
| **Protocol Number** | ADCT-301-103 |
| **Original SAP Version Date:** | 30 November 2021 |

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Signature Date

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ADC Therapeutics

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## Glossary of Abbreviations

| Glossary of Abbreviations: | |
|---|---|
| **AE** | Adverse event |
| **AESI** | Adverse event of special interest |
| **BMI** | Body mass index |
| **BOR** | Best overall response |
| **C1D1** | Cycle 1 Day 1 |
| **CI** | Confidence interval |
| **CR** | Complete response |
| **CRF** | Case report form |
| **CSR** | Clinical study report |
| **CTCAE** | Common Terminology Criteria for Adverse Events |
| **DCR** | Disease control rate |
| **DLT** | Dose limiting toxicity |
| **DoR** | Duration of response |
| **DoSD** | Duration of stable disease |
| **ECG** | Electrocardiogram |
| **ECOG** | Eastern Cooperative Oncology Group |
| **IP** | Investigational product |
| [redacted] | [redacted] |
| **IV** | Intravenous |
| **MedDRA** | Medical Dictionary for Regulatory Activities |
| **NCI** | National Cancer Institute |
| **NE** | Not evaluable |
| **ORR** | Overall response rate |
| **OS** | Overall survival |
| **PD** | Progressive disease |
| **PFS** | Progression-free survival |
| **PK** | Pharmacokinetic |
| **PR** | Partial response |
| **PT** | Preferred term |
| **QTc** | Corrected QT interval |
| **RDE** | Recommended Dose for Expansion |
| **SAE** | Serious adverse event |

| | |
|---|---|
| **SAP** | Statistical analysis plan |
| **SD** | Stable disease |
| **SOC** | System organ class |
| **std** | Standard deviation |
| **TEAE** | Treatment-emergent adverse event |
| [redacted] | [redacted] |
| **WHODRUG DD** | World Health Organization Drug Dictionary |

# 1 Introduction

This statistical analysis plan (SAP) describes the statistical methods to be used during the reporting and analysis of data collected under ADC Therapeutics Protocol ADCT-301-103.

This SAP should be read in conjunction with the study protocol and case report form (CRF). This version of the plan has been developed using the Protocol Amendment 7 dated 2 September 2021.

# 2 Study Objectives

## 2.1 Primary Objectives

- Characterize the safety and tolerability of camidanlumab tesirine as monotherapy and camidanlumab tesirine in combination with pembrolizumab, and to identify the recommended dose(s) and schedule(s) for future studies in patients with selected advanced solid tumors

## 2.2 Secondary Objectives

- Evaluate the preliminary anti-tumor activity of camidanlumab tesirine as monotherapy and camidanlumab tesirine in combination with pembrolizumab
- Evaluate the pharmacokinetic (PK) profile of camidanlumab tesirine as monotherapy and camidanlumab tesirine in combination with pembrolizumab
- Evaluate the immunogenicity of camidanlumab tesirine as monotherapy and camidanlumab tesirine in combination with pembrolizumab

# 3 Study Design

This is a Phase 1b, multi-center, open-label study with a dose-escalation part and a dose-expansion part.

In the dose-escalation part (Part 1), patients will receive escalating doses of camidanlumab tesirine as monotherapy, or escalating dose of camidanlumab tesirine in combination with pembrolizumab, guided by a 3+3 design.

Additionally, in the dose-escalation part for camidanlumab tesirine as monotherapy, separate paired-biopsy cohorts have been included:

- The paired-biopsy cohorts will enroll patients, treated only with camidanlumab tesirine as monotherapy, who will be undergoing two mandatory biopsies, one pre- and one on-treatment biopsy, to better understand effects of camidanlumab tesirine on tumor tissue biomarkers. These cohorts will be introduced at dose levels that have been deemed safe during escalation. In order to allow patients to benefit from trial participation, one intra-patient dose escalation (after the mandatory on-treatment biopsy has been obtained) to the highest dose level determined to be safe at that point will be performed, unless deemed by the Investigator not to be in the best interest of the patient.

Two groups are planned in the dose-expansion part (Part 2):

- Group 1: an indication for which camidanlumab tesirine in combination with pembrolizumab at the doses shown in Part 1 to have preliminary activity.

- Group 2: a basket group of patients with advanced solid tumors and MSI-H/dMMR status, who have received a prior regimen containing a PD-1/PD-L1 inhibitors, for which the best response was CR, PR, or SD ≥4 months, and then progressed while under treatment with the PD-1/PD-L1 inhibitor based regimen; no more than 4 patients with the same indication (tunour type) are allowed in this basket group.

## 3.1 Sample Size Consideration

Approximately 95 patients; Part 1 may enroll approximately 65 patients and Part 2 will enroll approximately 30 patients, approximately 16 patients in Group 1 and 14 in Group 2.

## 3.2 Randomization

Not applicable.

## 3.3 Modifications to the statistical section of the protocol

Not applicable.

# 4 Statistical methods

No hypothesis testing will be performed in this study.

All analyses will use SAS® version 9.4 or higher.

Unless otherwise stated, tables, listings, and figures will be broken down by monotherapy and combination therapy and then by dose level in dose-escalation part, and by group in dose-expansion part. Additional tables broken down by indication and by indication at recommded dose for expansion (RDE) will be specificied in later sections. All data will be provided in listings. Tables and figures are based on the defined analysis population.

Categorical data will be presented using counts and percentages, with the number of patients in the analysis population as the denominator for percentages. Percentages will be rounded to 1 decimal place and not be displayed for zero counts.

Continuous data will be summarized using the number of observations (n), mean, standard deviation (std), median, minimum, and maximum. Minima and maxima will be rounded to the precision of the original value, and means, medians, and 95% confidence intervals (CIs) if presented will be rounded to 1 decimal place greater than the precision of the original value. The std will be rounded to 2 decimal places greater than the precision of the original value, up to a maximum of 3 decimal places.

CI will be two-sided and use $\alpha$=0.05 (i.e., 95% CIs), unless otherwise specified. For exact estimates, the CI will be calculated using the Clopper–Pearson exact method. For Kaplan-Meier estimates, the CI will be calculated using the Greenwood's formula with (complementary) log-log transformation.

Kaplan-Meier plots will be provided along with Kaplan-Meier estimates.

The Baseline value is defined as the last non-missing value or measurement taken prior to the first dose of study drug.

## 4.1 Analysis Populations

### 4.1.1 Safety Analysis Set

All patients who receive study drugs.

### 4.1.2 DLT-evaluable Analysis Set

Patients in Part 1who receive study drug. However, this set excludes:

- Patients in Part 1 who discontinue from the study during the dose limiting toxicity (DLT) period (see Protocol Section 6.5) without experiencing a DLT

- Patients in Part 1 enrolled in the paired-biopsy cohort
- Additional patients in Part 1, of same indication, enrolled at a dose level equal or higher to the dose level for which at least 1 patient with documented PR or CR has been observed

### 4.1.3 Efficacy Analysis Set

All patients who receive at least 1 dose of study drug (refer to Protocol Section 6), have valid baseline disease assessment(s), and at least one valid post baseline disease assessment. Patients who do not have a post baseline assessment due to early clinical progression or death (after receiving study drug) will also be included.

### 4.1.4 Pharmacokinetics (PK) Analysis Set

All patients who receive study drugs and have at least 1 pre-(C1D1) and 1 post-dose valid PK assessment.

[redacted]

## 4.2 Patient Disposition

Enrolled subjects include all patients who signed informed consent forms. All subjects enrolled, including screen fails, will be summarized. Subjects who discontinued treatment and discontinued from the study will be summarized, along with the primary reasons for discontinuation. The disposition summary will be based on the Safety Analysis Set.

Patient disposition data will be listed.

## 4.3 Protocol Deviations

All protocol deviations will be determined prior to database lock and will be agreed upon by a review of individual subject data. Major protocol deviation criteria will be established and subjects with major protocol deviations will be identified and documented before the database lock for the primary analysis.

The number and percentage of patients with any important clinical study report (CSR)-reportable protocol deviation will be summarized overall and by type of deviation. The pre-defined important CSR-reportable protocol deviations are listed below; in addition, any other protocol deviations deemed by ADCT medical to be important CSR-reportable deviations will be included in the summary.

- Patient entered the study even though they did not satisfy the entry criteria

- Patient received a prohibited concomitant treatment during the study
- Patient who met criteria for mandatory study drug discontinuation during the study but did not have study drug withdrawn
- Patient who received the wrong treatment or incorrect dose, including dose not specified in the protocol and actual dose of study drug was greater than 15% more or less than protocol planned dose.

Important protocol deviations will be summarized and listed.

## 4.4 Demographic and Baseline Characteristics

Demographic and baseline characteristics will be tabulated for the Safety Analysis Set.

Demographic and baseline characteristics data will also be listed.

## 4.5 Cancer History and Medical History

Cancer history, prior radiotherapy, prior cancer surgery, and prior system treatments will be tabulated for the Safety Analysis Set.

Cancer history, including each tumor type, medical history, prior radiotherapy, prior cancer surgery, and prior system treatments will be listed.

## 4.6 Prior and Concomitant Medications (other than anticancer therapies)

All medications will be recorded in the CRF starting from the ICF signature date or from 14 days prior to C1D1, whichever is earlier, and continuing until 30 days after last dose of study drug.

All medications will be coded using the World Health Organization-Drug Dictionary (WHO-DD) version 2018 March 01.

Prior and concomitant medications will be listed.

## 4.7 Exposure to Treatment

### 4.7.1 Extent of Study Drug Exposure

Study drug exposures will be based on the Safety Analysis Set.

A treatment cycle is defined as 3 weeks (i.e., 21 days).

For patients receiving camidanlumab tesirine as monotherapy, camidanlumab tesirine will be administered as an intravenous (IV) infusion on Day 1 of each cycle starting from Cycle 1 onwards.

For patients receiving camidanlumab tesirine in combination with pembrolizumab, camidanlumab tesirine will be administered for 2 cycles (on C1D1 and C2D1), and pembrolizumab at a dose of 200 mg Q3W will be administered on Day 1 of each cycle starting from Cycle 1 onwards (dosing schedule 1). If unacceptable toxicity (Protocol section 6.5) occurs during Cycle 1 at dose level -1 and dose level -2, dosing schedule 2, where pembrolizumab administration may start at Cycle 2, may be investigated in newly enrolled patients.

Patients who tolerate the study treatment (i.e., no liver enzyme increase ≥ Grade 2, no pleural effusion ≥ Grade 2, no edema ≥ Grade 2) and are in disease control (defined as disease control ≥ SD) may receive additional doses of camidanlumab tesirine in combination with pembrolizumab, upon informing the Sponsor.

Additional administrations of camidanlumab tesirine in combination with pembrolizumab will be given as follows: 2 consecutive Cycles every 2 Cycles (2 cycles on, 2 cycles off schedule), starting from Cycle 5 up to a year (i.e., Cycle 5 and 6, Cycle 9 and 10, Cycle 13 and 14, Cycle 17 and 18) if there is no delay in the planed treatment schedule: Between these cycles, patients should receive pembrolizumab as a single agent

Study treatment is given for up to a year. Continued administration of camidanlumab tesirine as monotherapy or camidanlumab in combination with pembrolizumab, or pembrolizumab alone after a year will be discussed with the Sponsor in the context of the likely risk benefit assessment for each individual patient. The dose amounts of camidanlumab tesirine monotherapy are given according to Protocol section 6.3 and for the combination with pembrolizumab according to Protocol section 6.4.

Duration of treatment (days) is calculated as date of last treatment – date of first treatment + 1.

- Camidanlumab tesirine

Dose administered at each infusion (µg) of camidanlumab tesirine is calculated by concentrated investigational product (IP) volume (in mL) * 5 mg/mL * 1000. For cases of incomplete infusion, adjust the calculated prepared dose by multiplying a factor of (1- volume of dosing solution not administered [in mL]/ 50 mL). If volume of dosing solution not administered is missing, then adjust the calculated prepared dose by multiply the factor of (end time – start time [in minutes])/30 minutes.

Relative dose intensity (%) for camidanlumab tesirine is calculated as 100 * [total weighted adjusted dose received (µg/kg) / total planned dose (µg/kg)], where total planned dose is number of cycles should be for camidanlumab tesirine dosing during treatment * protocol planned dose (µg/kg) per cycle.

Table 1 Target study day for camidanlumab tesirine

| Study Visit | Target Study Day when Camidanlumab Tesirine as Monotherapy | Target Study Day when Camidanlumab Tesirine in Combination with Pembrolizumab |
|---|---|---|
| C1D1 | 1 | 1 |
| C2D1 | 22 | 22 |
| C3D1 | 43 | NA |
| C4D1 | 64 | NA |
| C5D1 | 85 | 85 |
| C6D1 | 106 | 106 |
| C7D1 | 127 | NA |
| C8D1 | 148 | NA |
| C9D1 | 169 | 169 |
| C10D1 | 190 | 190 |
| C11D1 | 211 | NA |
| C12D1 | 232 | NA |
| C13D1 | 253 | 253 |
| C14D1 | 274 | 274 |
| C15D1 | 295 | NA |
| C16D1 | 316 | NA |
| C17D1 | 337 | 337 |
| C18D1 | 358 | 358 |

Note: If patients receive doses beyond C18, target study day at each cycle will be calculated by adding 21 days from target study day in the previous cycle.

Duration of treatment, number of cycles dosed, total dose received (µg), total weight adjusted dose received (µg/kg), average dose per cycle (µg/kg), dose modification, delay, reduction, and interruption, and relative dose intensity for camidanlumab tesirine will be summarized.

- Pembrolizumab

Dose administered at each infusion (mg) of pembrolizumab is fixed at 200 mg as a 30 minutes IV infusion (starting 1 hour after the end of the camidanlumab tesirine infusion), and dose modifications are not expected. For incomplete infusion, adjust the calculated prepared dose by multiplying a factor of (1- volume of dosing solution not administered [in mL]/ 50 mL). If volume of dosing solution not administered is missing, then adjust the calculated prepared dose by multiply the factor of (end time – start time [in minutes])/30 minutes.

Relative dose intensity (%) for pembrolizumab is calculated as 100 * [total dose received (mg) / total planned dose (mg)], where total planned dose is number of cycles should be for pembrolizumab dosing during treatment * 200 (mg) per cycle.

Duration of treatment, number of cycles dosed, total dose received (mg), average dose per cycle (mg), dose delay, reduction, and interruption, and relative dose intensity for pembrolizumab will be summarized.

Exposure data and infusion details in both camidanlumab tesirine and pembrolizumab will be listed.

### 4.7.2 Subsequent Anticancer Therapy or Procedure

Patients' subsequent anticancer therapies or procedures including systemic therapy, radiation, transplant, or other, along with the start date of new anticancer therapy or procedure will be listed.

## 4.8 Efficacy Analyses

Efficacy analyses will be based on the Efficacy Analysis Set.

Derived efficacy endpoints and tumor assessment data will be listed.

### 4.8.1 Overall Response Rate

An objective responder is defined as any patient who had a best overall response (BOR) of CR or PR per RECIST 1.1. Overall response rate (ORR) is defined as the proportion of objective responders.

For the analysis of ORR,

- The category of BOR includes complete response (CR), partial response (PR), stable disease (SD), progressive disease (PD), and inevaluable (NE).
- Overall responses derived for BOR must be assessed on or before the start of subsequent anti-cancer therapy or procedure.
- A BOR of SD requires the patient on-study for a minimum of 35 days after the first dose of study drug. A patient with SD only before this time will be considered as NE.
- For patients who do not have post-baseline assessment due to early clinical progression or death (after receiving study drug), they will be categorized separately from patients with assessments.

Disease control rate (DCR) is defined as the proportion of objective responders and patients with SD at least 35 days after the first dose of study drug.

The ORR and DCR and their 95% two-sided exact CIs will be presented. Time to first response and time to BOR will aso be summarized.

BOR will also be presented by indication and by indication at RP2D. In addition, extent of study drug exposure will be summarized according to BOR category.

### 4.8.2 Duration of Response

Duration of response (DoR) is defined among objective responders (CR or PR per RECIST 1.1) as the time from the earliest date of first response until the first date of either disease progression (based on radiographic or clinical progression at end of treatment [EOT]/end of study [EOS]) or death due to any cause.

The censoring rules for DoR are as follow:

- For patients who are still alive at the time of analysis and without objective evidence of progression, patients will be censored at the last tumor assessment.
- For patients who receive subsequent anti-cancer therapy or procedure prior to disease progression or death, patients will be censored at the last tumor assessment on or prior to subsequent therapy or procedure.
- A sensitivity analysis might be considered:if a clinical disease progression or toxicity is observed without radiographic tumor progression assessment being confirmed, then the patient will be censored at the last tumor assessment.

The DoR will be estimated by Kaplan-Meier method. The median DoR and its 95% two-sided CI will be presented.

DoR will also be presented by indication and by indication at RP2D.

### 4.8.3 Duration of Stable Disease

Duration of stable disese (DoSD) is defined among patients of SD per RECIST 1.1 as the time from first dose of study drug until disease progression (based on radiographic or clinical progression at end of treatment [EOT]/end of study [EOS]) or death due to any cause.

The censoring rules for DoR in Section 4.8.2 apply to DoSD.

The DoSD will be estimated by Kaplan-Meier method. The median DoSD and its 95% two-sided CI will be presented.

DoSD will be presented by dose, by indication, and by indication at RP2D.

### 4.8.4 Progression-Free Survival

Progression-Free Survival (PFS) is defined as the time from first dose of study drug until disease progression (based on radiographic or clinical progression at end of treatment [EOT]/end of study [EOS]) or death due to any cause, whichever occurs first.

The censoring rules for PFS are as follow:

- For patients who are still alive at the time of analysis and without objective evidence of progression, patients will be censored at the last tumor assessment.

- For patients who receive subsequent anti-cancer therapy or procedure prior to disease progression or death, patients will be censored at the last tumor assessment on or prior to subsequent therapy or procedure.
- For patients who have no post baseline tumor assessment, and have no disease progression or death, or receive subsequent anti-cancer therapy or procedure(s), patients will be censored at the first dose date of study drug.
- A sensitivity analysis might be considered: if a clinical progression or toxicity is observed without radiographic progression assessment being confirmed, then the patient will be censored at the last tumor assessment.

The PFS will be estimated by Kaplan-Meier method. The median PFS and its 95% two-sided CI will be presented.

### 4.8.5 Overall Survival

Overall survival (OS) is defined as the time from first dose of study drug until death due to any cause.

For patients who are still alive or unknown at the time of analysis, patients will be censored at the date the patient was known to be alive.

The OS will be estimated by Kaplan-Meier method. The median OS and its 95% two-sided CI will be presented.

[redacted]

[redacted]

## 4.9 Safety Analyses

All safety analyses will be based on the Safety Analysis Set.

### 4.9.1 Adverse Events

#### 4.9.1.1 Analyses of Adverse Events

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

The definition of SAEs is referred to the Protocol section 8.1.

A treatment-emergent AE (TEAE) is defined as an AE that occurs or worsens in the period extending from the first dose of study drug to 30 days after the last dose of study drug in this study or start of a new anticancer therapy, whichever is earlier.

AEs will be coded according to MedDRA Version 22.0, and the severity of the toxicities will be graded according to the National Cancer Institute (NCI) Common Terminology Criteria for Adverse Events (CTCAE) Version 4.0, where applicable.

The summary of overall TEAEs includes:

- TEAEs
- Drug-related TEAEs
- Grade ≥3 TEAEs
- Drug-related Grade ≥3 TEAEs
- Serious Adverse Events (SAEs)
- Drug-related SAEs
- TEAEs leading to dose delayed, reduced or interrupted (camidanlumab tesirine or pembrolizumab)
- TEAEs leading to discontinuation of camidanlumab tesirine or pembrolizumab
- TEAEs leading to death
- Infusion related reactions

The incidence of TEAEs will be summarized by system organ class (SOC) and preferred term (PT). A subject will be counted only once within a SOC and PT, even if the subject experienced more than one AE within a specific SOC and PT. Below TEAEs will be summarized in the same fashion:

- Drug-related TEAEs by SOC and PT
- Grade ≥3 TEAEs by SOC and PT
- Drug-related Grade ≥3 TEAEs by SOC and PT
- The most common TEAEs (≥ 10% incidence) by PT
- TEAEs by SOC, PT and maximum CTCAE grade
- TEAEs by relationship to study drug, maximum CTCAE grade, SOC and PT

Listing of all AEs, including non-TEAEs, will be provided. Besides, TEAEs leading to dose reduced, delayed or interrupted (camidanlumab tesirine or pembrolizumab), TEAEs leading to discontinuation of camidanlumab tesirine or pembrolizumab, and TEAEs leading to death will also be provided.

Details on classification of AEs with missing or partial onset dates are provided in Section 6.

### 4.9.1.2 Dose-Limiting Toxities

Definition of DLT is referred to the Protocol section 6.5. DLTs will be summarized in each dose level in the dose-escalation part for the DLT-evaluable Analysis Set.

Listings of DLTs will be provided.

### 4.9.1.3 Serious Adverse Events

A post-dose AE is defined as an AE during treatment that occurs or worsens from the first dose of study drug.

Below SAEs will be summarized in both TEAE and post-dose AE:

- SAEs by PT
- SAEs by SOC and PT
- SAEs by SOC, PT and maximum CTCAE grade

Listings of SAEs will be provided.

### 4.9.1.4 Deaths

Listing of all deaths will be provided.

### 4.9.1.5 Adverse Events of Special Interest

Definition of AESI is referred to the Protocol section 8.1.1.

Below AESIs will be summarized in both TEAE and post-dose AE:

- AESIs by PT
- AESIs by SOC and PT
- AESIs by SOC, PT and maximum CTCAE grade

Listings of AESIs will be provided.

## 4.9.2 Laboratory Data

Laboratory data for hematology, chemistry, and coagulation will be summarized for the actual values and the change from baseline value at each scheduled assessment. In addition, all data will be graded according to the NCI CTCAE Version 4.0, and summarized by baseline and maximum post-baseline CTCAE grade, including unscheduled visits. Shift tables will summarize the shift from baseline grade to maximum post-baseline CTCAE grade.

Listings of laboratory data for hematology, chemistry, and coagulation will be provided. In addition, listings of urinalysis, thyroid function testing, influenza testing, SARS-CoV-2 testing, and any microbiological tests performed will also be provided.

### 4.9.3 Electrocardiogram

Electrocardiogram (ECG) data will be summarized for the actual values and the change from baseline value at each scheduled assessment. Shift tables will summarize the shift from baseline to End of Treatment and worst post-baseline visit in ECG interpretation (categorized as normal; abnormal, not clinically significant; and abnormal, clinically significant).

Corrected QT interval by Fredericia (QTcF) will be summarized by categories as follows:

- QTcF interval > 450 ms
- QTcF interval > 480 ms
- QTcF interval > 500 ms
- QTcF interval increases from baseline > 30 ms
- QTcF interval increases from baseline > 60 ms

Listings of ECG data will be provided from both local and central reads of the data.

### 4.9.4 Vital Signs

Vital signs data, including weight, will be summarized for the actual values and the change from baseline value at each scheduled assessment.

Listings of vital signs data, including height and weight, will be provided.

### 4.9.5 ECOG Performance Status

ECOG performance status will be summarized at each scheduled assessment. Shift tables will summarize the shift from baseline to End of Treatment and to the worst post-baseline visit in ECOG performance status.

Listing of ECOG performance status will be provided.

### 4.9.6 Physical Examinations

Listing of physical examinations will be provided.

### 4.9.7 Pregnancy Test

Listing of pregnancy test results, if applicalble, will be provided.

# 5 Final Analysis

All efficacy and safety endpoints will be analyzed and reported in the clinical study report (CSR). Results of PK analysis, immunogenicity analysis, [redacted] will be reported separately.

# 6 Data handling conventions

## 6.1 General conventions

### 6.1.1 Missing data

In general, missing data including dates will be treated as missing and no data imputation will be applied, unless otherwise specified. Data that are potentially spurious or erroneous will be queried and examined during the review of the study data.

If there are partial or missing dates for an AE, then it will be considered as a TEAE. If the assessment of the relationship of an AE to study drug is missing, then the relationship will be as possibly related.

If the severity/grade is missing for one of the treatment emergent occurrences of an AE, the maximal severity of the remaining occurrences will be considered. If the severity is missing for all the occurrences a “missing” category will be added in summary table.

### 6.1.2 Unscheduled visits

Unscheduled visit measurements of laboratory data, vital signs, and ECG will be used for computation of baseline and worst values and/or grades. Re-windowing for unscheduled visits will not be performed.

### 6.1.3 Duplicated visits

Depending on the statistical analysis method, single values may be required for each analysis window. For example, change from baseline by visit usually requires a single value per visit. Unless otherwise noted throughout the rest of this document, when a single value is needed, the following rule(s) will be used:

- If more than 1 assessment occurs during the same nominal visit, select the record closest to the nominal day for that visit.
- If there are 2 assessments that are equidistant from the nominal day, the data of the assessment after the scheduled study day will be used.
- The last measurement will be used if multiple measurements are taken on the same day.

# 7 Reference List