**CT-P59 1.2**

# A Pilot Phase 1, Randomized, Double-Blind, Placebo-controlled, Parallel-Group, Single Ascending Dose Study to Evaluate the Safety, Tolerability and Virology of CT-P59 in patient with Mild Symptoms of Severe Acute Respiratory Syndrome Coronavirus (SARS-CoV-2) Infection

**14th Apr 2021**
Statistical Analysis Plan

**Version 3.0**

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Upon review of this document, including table, listing and figure shells, the undersigned approves the final statistical analysis plan. The analysis methods and data presentation are acceptable, and the table, listing and figure production can begin.

**TABLE OF CONTENTS**

## LIST OF ABBREVIATIONS

| Abbreviation | Definition |
|---|---|
| $\%AUC_{ext}$ | Percentage of the area extrapolated |
| ADA | Anti-Drug Antibody |
| ADE | Antibody Dependent Enhancement |
| AESI(s) | Adverse Event(s) of Special Interest |
| AE | Adverse Event |
| ATC | Anatomical Therapeutic Chemical |
| $AUC_{0\text{-}inf}$ | Area under the Concentration-Time Curve from Time zero to Infinity |
| $AUC_{0\text{-}last}$ | Area under the Serum Concentration-Time Curve from time zero to the Last Quantifiable Concentration |
| BLQ | Below the Lower limit of Quantification |
| BMI | Body Mass Index |
| CI | Confidence Interval |
| CL | Total Body Clearance |
| $C_{max}$ | Maximum Observed Serum Concentration |
| CSR | Clinical Study Report |
| CTCAE | Common Terminology Criteria for Adverse Events |
| CV% | Percent Coefficient of Variation |
| DEC | Dose Escalation Committee |
| DRM | Date Review Meeting |
| DSMB | Data and Safety Monitoring Board |
| ECG | Electrocardiogram |
| eCRF | Electronic Case Report Form |
| EOT | End-of-treatment |
| GCP | Good Clinical Practice |
| HBsAg | Hepatitis B Surface Antigen |
| HBcAb | Hepatitis B Core Antibody |
| HIV | Human Immunodeficiency Virus |
| ICF | Informed Consent Form |
| ICH | International Council for Harmonisation |
| IRR | Infusion Related Reaction |
| ITT | Intent-to-treat |
| LLoQ | Lower Limit of Quantification |
| N/A | Not Applicable |
| NAb | Neutralizing Antibody |
| MedDRA | Medical Dictionary for Regulatory Activities |
| PK | Pharmacokinetic |
| PT | Preferred Term |
| qPCR | Quantitative Polymerase chain reaction |
| RT-PCR | Reverse Transcription Polymerase Chain Reaction |

| Abbreviation | Definition |
|---|---|
| SAE | Serious Adverse Event |
| SAP | Statistical Analysis Plan |
| SARS-CoV-2 | Severe Acute Respiratory Syndrome Coronavirus 2 |
| SD | Standard Deviation |
| SI | International System |
| SoC | Standard of Care |
| SOC | System Organ Class |
| $t_{1/2}$ | Terminal Elimination Half-life |
| TEAE | Treatment-emergent Adverse Event |
| TEAESI | Treatment-emergent Adverse Events of Special Interest |
| TESAE | Treatment-emergent Serious Adverse Event |
| TLF | Table, Listing and Figure |
| $T_{max}$ | Time to $C_{max}$ |
| $V_z$ | Volume of Distribution during the Terminal Phase |
| $\lambda_z$ | Terminal Elimination Rate Constant |
| WHO | World Health Organization |

## 1. ADMINISTRATIVE STRUCTURE

This study is being conducted under the sponsorship of CELLTRION, Inc. (hereinafter referred to as "CELLTRION"). The clinical monitoring, and pharmacokinetic (PK) parameter calculation are being performed under contract with [redacted] the PK and immunogenicity samples are being performed under contract with [redacted] and the virology samples is being performed under contract with [redacted] in collaboration with CELLTRION. The data management and statistical analyses are being performed by CELLTRION.

## 2. INTRODUCTION

This Statistical Analysis Plan (SAP) defines the statistical methods to be used by CELLTRION Clinical Statistics team in the analysis and presentation of data from CELLTRION study number CT-P59 1.2, entitled as "A Pilot Phase 1, Randomized, Double-blind, Placebo-controlled, Parallel Group, Single Ascending Dose Study to Evaluate the Safety, Tolerability and Virology of CT-P59 in Patient with Mild Symptoms of Severe Acute Respiratory Syndrome Coronavirus (SARS-CoV-2) Infection".

There are two clinical study reports (CSRs) planned for the following time points:

- First CSR: The following data will be included, and list of TLFs is presented in Appendix 5.

  - Virology (quantitative polymerase chain reaction [qPCR]) data up to Day 7 of each patient

  - PK and immunogenicity data up to Day 14 of each patient

  - Other safety data up to Day 14 of last enrolled patient

- Final CSR: All data after completion of the study.

If additional CSRs are required for regulatory or academic purposes, CSRs will be generated after the first database lock and unblinding process.

This SAP covers all specified analyses and is based on the following documents:

- Study Protocol Version 1.3 – 27th July 2020
- Study Protocol Version 1.3, including country specific A.2 – 02nd September 2020
- Unique Case Report Form Version 1.2 – 17th July 2020

Table, Listing and Figure (TLF) mock shells will be provided as an addendum to this document.

# 3. Study Objective

Primary and secondary objectives are described as below.

## 3.1. Primary Objective

- To evaluate the preliminary safety and tolerability of CT-P59 up to Day 14 of the last enrolled patient.

## 3.2. Secondary Objectives

The secondary objectives are as follows:

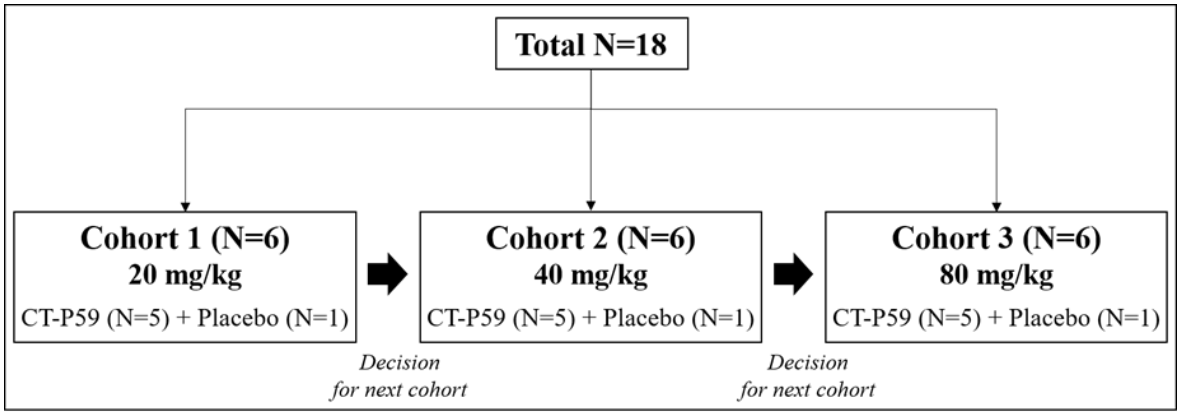
- To evaluate the viral efficacy and characterization of SARS-CoV-2 viral isolates
- To evaluate the efficacy of CT-P59
- To evaluate the PK of CT-P59
- To evaluate additional safety of CT-P59 including immunogenicity

# 4. INVESTIGATIONAL PLAN

## 4.1. Study Design and Plan

This is a randomized, double-blind, placebo-controlled, parallel group, single ascending dose, Phase 1, pilot study to evaluate the safety, tolerability and virology of CT-P59 in combination with standard of care (SoC), except potential antiviral drugs and/or immune-based therapy under evaluation for treatment of SARS-CoV-2 infection, in patients with mild symptoms of SARS-CoV-2 infection. Approximately 18 patients in 3 cohorts are planned for enrollment and each cohort will consist of 6 patients, 5 of whom will receive CT-P59 and 1 of whom will receive a placebo. In each cohort, patients will be randomized in a 5:1 ratio to receive CT-P59 or placebo. This study will be started with the lowest dose that will maximize safety and the dose levels will be escalated to the higher doses.
The overview of the study is presented in Figure 1.

**Figure 1: Study Design Overview**




After each study drug administration, patients will be observed for 48 hours for evaluation of the safety and tolerability of study drug.

When escalating dose from previous cohort to next cohort, Dose Escalation Committee (DEC) will review all available safety data of all patients in each cohort, within an observation period of 48 hours after study drug administration. If no safety or tolerability concern is observed, patients in next cohort will receive study drug. The dose escalation from a previous cohort to the next cohort will be stopped if one or more of the following stopping criteria are met:

- Two or more patients in one cohort experience treatment-emergent adverse event (TEAE)s of grade 3 or higher, which are considered to be related to study drug
- Four or more patients in one cohort experience TEAEs of grade 2 or higher, which are considered to be related to study drug
- One or more patients in one cohort experience a treatment-emergent serious adverse event (TESAE), which are considered to be related to study drug

If an event corresponding to the above criteria occurs within the observation period of 48 hours in each cohort and the dosing is temporarily stopped under the decision of DEC, the appointed independent Data and Safety Monitoring Board (DSMB) members will evaluate the relationship to CT-P59 of the event with unblinded manner and make a decision on continuation and the dose escalation of the study. If an event corresponding to the above criteria occurs after observation period of 48 hours in the previous cohort, further progression to next cohort will be temporarily stopped and the appointed independent DSMB members will review data and make a decision on continuation and the dose escalation of the study.
If it was revealed that an event corresponding to the above criteria occurs and all the TEAEs are related to CT-P59 as reviewed by DSMB members, the study will be temporarily stopped and the information will be submitted to regulatory authority for further evaluation and confirmation on continuation of the dose escalation of the study.

This study will comprise 4 study periods including Screening, Treatment Period, End-of-Treatment Visit and Follow-Up Period.

**Screening** (Day -7 to Day 1): Patients will sign and date the informed consent form (ICF) and undergo procedures to determine eligibility. During the Screening Period, retest for Screening is permitted only once by the Investigator's judgement. If the repeated test result is again not suitable or indeterminate for inclusion, the patient will be screen failed. Only one retest for reverse transcription polymerase chain reaction (RT-PCR) will be allowed, if study drug can be administered no more than 7 days from onset of symptom based on retest results. And, if there is available RT-PCR result confirming SARS-CoV-2 infection prior to obtaining written informed consent (but no more than 7 days from the onset of symptoms), the result can be allowed. If Screening visit date and the administration of study drug date (Day 1) are same, all assessments scheduled for the Screening and Day 1 visit can be performed only once on the date before randomization

**Treatment Period** (Day 1 to prior to End-of-Treatment Visit): Inclusion and exclusion criteria will be re-confirmed on Day 1. If it is concluded that the patients are not eligible in Day 1 assessments, the patient will be considered as Screening failure even if he/she was eligible based on assessments results performed during Screening Period. Patients will be randomized in 5:1 ratio to receive CT-P59 or placebo once all eligibility criteria have been confirmed. Patients will receive a single dose of CT-P59 or placebo on Day 1. All patients will be admitted to the study center on Day 1 and it is recommended to be confined up to Day 7. In-house stay period can be determined by Investigator considering the isolation regulation and/or public health capacity of the country, however all patients should be confined to the study center for at least 72 hours (until completion of all assessments on Day 3). After discharge, the consecutive study visits will be carried out on an out-patient basis. During the isolation period according to the local regulation, patients will visit the study center using the transportation provided by Sponsor.

**End-of-Treatment Visit** (Day 90): End-of-treatment (EOT) visit assessments will be performed on Day 90. If a patient is early terminated from the study, the patient will be asked to return to the study center as soon as possible for the safety assessments predefined for EOT visit.

**Follow-Up Period** (From End-of-Treatment Visit to Day 180): For all patients including a patient who early terminated from the study, each telephone call follow-up will occur bi-weekly from 2 weeks after the EOT visit to Day 180. During the Follow-Up Period, SARS-CoV-2 infection related signs and symptoms will be assessed by telephone call to capture the suspicious antibody dependent enhancement (ADE) occurrence. For patients with suspicious ADE occurrence, additional assessments will be conducted on unscheduled visit.

# 5. GENERAL STATISTICAL CONSIDERATIONS

Continuous data will be summarized using descriptive statistics: number of patients (n), mean, standard deviation (SD), minimum, median and maximum, unless otherwise specified. The descriptive statistics will be calculated using raw data before rounding although rounded values are listed. The following rules will be followed with regards to the number of decimal places:

- Minimum and maximum will be presented to the same number of decimal places in the source listing.
- Mean, median, geometric mean and percent coefficient of variation (CV%) will be rounded to one more decimal place than the maximum decimal place of values in the source listing.
- Standard deviation (SD) will be rounded to one more decimal place than mean.
- Only for PK section, point estimate and confidence intervals (CI) obtained from statistical procedures will be displayed to three decimal places. Also, standard error (SE) obtained from statistical procedures will be displayed to four decimal places.
- Kaplan-Meier estimates and days calculated using data/time will be displayed to two decimal places.

Geometric mean will not be reported if the dataset includes zero values and CV% will not be reported if the mean is zero.

Categorical data will be summarized using frequency tables showing numbers and percentages of patients. Percentages will be rounded to one decimal place and will be suppressed when the count is zero. The denominator for all percentages will be the number of patients within each treatment group for the set of interest, unless otherwise specified. Treatment group is defined in Section 5.4.

Unscheduled visit will not be summarized in visit-based tables, unless otherwise specified. However, all data will be displayed in listings. Unless otherwise specified, listings will be sorted by the treatment group, patient number and visit, if applicable. In cases where more ordering is required, other variables will be included in the sort order as applicable.

When combining data from Electronic Case Report (eCRF) and analytical facilities such as Central Laboratory for PK, virology or immunogenicity, discrepancy will be handled as following:

1) Recorded as sample collected in eCRF but no corresponding results from analytical facility – listing will display only sample collection visit/date from eCRF;

2) No corresponding records in eCRF for results from analytical facility – listing will display only specimen collection visit/date and results from analytical facility;

3) Discrepancy in sample collection date from eCRF and analytical facility – listing will display results from analytical facility and visit/date from eCRF if not missing; if sample collection date is missing in eCRF then use specimen collection visit/date from analytical facility.

All available results from analytical facilities will be included in the summary table.

This SAP could be updated after the Data Review Meeting (DRM) but prior to database hard lock to document any deviations.

### 5.1. Software

All statistical analyses will be conducted using [redacted]

PK parameters will be computed by [redacted]

### 5.2. Sample Size

The total sample size of 18 patients is not based on a formal statistical hypothesis. A sample size justification based on statistical hypothesis is not relevant in this study. The proposed number of 6 patients (5 patients for CT-P59 and 1 patient for placebo) in each cohort is set empirically based on sample sizes in other Phase 1 studies investigating the safety and tolerability of their study drugs and is considered to be sufficient to achieve the objective of the study.

### 5.3. Randomization, Stratification, and Blinding

On Day 1, eligible patients will be randomly assigned in 5:1 ratio to receive CT-P59 or placebo.

Patients who receive study drug and discontinue before the study completion will generally not be replaced. However, if a patient who receives study drug discontinues the study for a reason other than patient's safety, additional patient can be recruited upon decision of DEC. If a patient who randomized but did not receive study drug decides to discontinue the study, this patient can be replaced.

The randomization codes will not be revealed to study patients, investigator, and study center personnel except for delegated unblinded staff who will handle the study drug and predefined unblinded teams in the CELLTRION and [redacted] until all final data have been entered into the database and the database is locked and released for analysis.

Under normal circumstances, the blind should not be broken. The blind should only be broken if specific emergency treatment would be dictated as knowing the study drug assignment is required for medical management. In such cases, the investigator may, in emergency, determine the identity of the study drug by using the [redacted]

The date, time and reason for the unblinding must be documented in the source document and the appropriate field of the eCRF and the medical monitor will be informed as soon as possible.

All unblinding events will be reported to the medical monitor and CELLTRION. Any patients for whom the blind is broken may continue in the study at the investigator's discretion.

The overall randomization code will be broken only for reporting purposes. This will occur after database lock for data up to Day 14 of the last enrolled patient. The unblinded personnel will be predefined and documented before performing the analyses.

## 5.4. Analysis sets

Analysis sets and its definitions are described in this section. The analysis set will be identified and included as a subtitle of each TLF.

The following treatment groups will be used for analysis: CT-P59 20 mg/kg, CT-P59 40 mg/kg, CT-P59 80 mg/kg and placebo. For placebo group, pooling of patients assigned to placebo treatment within each cohort is considered for analysis.

For Intent-to-treat (ITT) set, patients will be assigned to either "CT-P59 20 mg/kg", "CT-P59 40 mg/kg", "CT-P59 80 mg/kg" or placebo treatment group according to the treatment they were randomized to. The PK and Safety sets will be analyzed according to actual treatment group. Patients receiving at least one kit of CT-P59 will be assigned to the actual treatment group of CT-P59 of corresponding cohort, even if the patient is randomized to placebo group.

The number and percentage of patients in all sets will be tabulated by the treatment group on ITT set. A listing will also be produced displaying data on ITT set.

### 5.4.1. Intent-to-Treat Set

The ITT set is defined as all patients enrolled and randomly assigned to receive a dose of either of the study drugs, regardless of whether or not any study drug dosing was completed.

### 5.4.2. Safety Set

The safety set will consist of all patients who receive a full or partial dose of the study drugs.

### 5.4.3. Pharmacokinetic Set

The PK set will consist of all patients who receive a full dose of CT-P59 and have at least 1 evaluable post-treatment PK concentration result.

## 5.5. Definition of Baseline

The baseline value will be considered to be the last non-missing value before the study drug administration. Post-baseline values will be considered to be all measurements collected after the study drug administration.

## 5.6. Protocol Deviations

Protocol deviation will be categorized as “major” or “minor”. A major protocol deviation is one that may affect the interpretation of study results or the patient’s rights, safety or welfare, and will be identified prior to study unblinding. Major protocol deviations include, but are not limited to, the following:

- Mis-randomization (defined as patients who received treatment other than randomly assigned treatment)
- Non-adherence to Inclusion or Exclusion criteria (to be identified through review of data)
- Significant Good Clinical Practice (GCP) non-compliance

A listing of major protocol deviations for each patient will be provided by treatment group for the ITT set.

## 5.7. Outliers

Any outliers that are detected during the review of the data will be investigated and discussed during the DRM. In general, outliers will not be excluded.

# 6. PATIENT DISPOSITION

The number of patients who were screened will be displayed. The number of patients who failed at screening will be also displayed along with the primary reason for screening failure based on the ‘Eligibility Criteria’ page of eCRF.

The number and percentage of patients who were randomized, initiated study treatment, completed the period including EOT, discontinued the period including EOT will be displayed for the ITT set with percentage by treatment group.

Patient disposition will be defined as follows:

- A patient will be considered to have failed the Screening if the screening failure date is recorded on the 'Eligibility Criteria' page of eCRF.

- A patient will be considered to be randomized if a randomization ID was allocated to the patient based on the 'Randomization' page of eCRF.

- A patient will be considered to be initiated study treatment if it is recorded as 'Yes' to study drug administration on the 'Study Drug Administration' page of eCRF.

- A patient will be considered to have completed the treatment period including EOT if it is recorded that the patient was completed from the study ('Yes' box checked) on the 'End of Treatment Period' page of eCRF.

- A patient will be considered to have discontinued the treatment period including EOT if it is recorded that the patient was discontinued from the study ('No' box checked) on the 'End of Treatment Period' page of eCRF.

The number and percentage of patients who discontinued the treatment period including EOT and ended the study participation including follow-up period will be displayed by primary reason for discontinuation and ending participation based on the 'End of Treatment Period' and 'End of Study Participation' page of eCRF, and treatment group respectively.

In addition, time on study prior to discontinuation will be displayed using descriptive statistics, for those patients who initiate the study treatment and discontinue. Time on study to end of study participation will be displayed using descriptive statistics, for those patients who initiate the study treatment and end.

The study duration in days will be calculated as (study discontinuation date [for end of study participation, end of study participation date] – study drug administration date + 1). The study discontinuation date, end of study participation date and study drug administration date will be taken as the date on the 'End of Treatment Period' page, 'End of Study Participation' page and on the 'Study Drug Administration' page of eCRF respectively.

Patient disposition data will be listed for the ITT set by treatment group. A listing will also be provided to display data from 'Eligibility Criteria' page of eCRF.

# 7. DEMOGRAPHICS, BASELINE, AND BACKGROUND CHARACTERISTICS

## 7.1. Demographics and Stratification Details

The following demographic measures and stratification details will be summarized for the ITT set: Age (years); Sex (Male, Female); Fertility Status (Pre-Menarche, Surgically Sterilized, Post-Menopausal, and Potentially Able to Bear Children. For female patient only); Race (White, Black or African American, American Indian or Alaska Native, Asian, Native Hawaiian or

Other Pacific Islander, Not Allowed by Investigator Country Regulations, Other); Ethnicity (Hispanic or Latino, Non-Hispanic or Non-Latino, Unknown); Height (cm), Weight (kg) and Body Mass Index (BMI) ($kg/m^2$) as recorded at Screening.

Age will be automatically calculated in eCRF system based on the date of the informed consent day and the year of birth considering whether birth date has passed the informed consent date or not.

Demographics will be listed for the ITT set by treatment group.

### 7.2. Viral Serology Test

At Screening, the following assessments for serologic markers will be performed:

- Hepatitis B Surface Antigen (HBsAg)
- Hepatitis B Core Antibody (HBcAb)
- Hepatitis C Antibody
- Human Immunodeficiency Virus (HIV) -1 and -2

All viral serology test result will be listed for ITT set by treatment group.

### 7.3. Urine Drug Test

A urine drug test will be performed at Screening. The screen for drug abuse includes methamphetamine, barbiturates, benzodiazepines, cocaine, tetrahydrocannabinol, and opiates. The urine test can be repeated once at the discretion of the Investigator. All urine drug test result will be listed for the ITT set by treatment group.

### 7.4. Medical History

Medical history is captured at Screening and will be coded using Medical Dictionary for Regulatory Activities (MedDRA Version 23.0 or the later version). Medical history will be summarized by treatment group, system organ class (SOC) and preferred term (PT) for the ITT set. Medical history will be listed for the ITT set by treatment group.

### 7.5. Disease Characteristic

Disease characteristic is captured at Screening visit. The number and percentage of patients with symptoms will be summarized by treatment group for the ITT set. Time (days) since the earliest symptom start will be calculated as (date of study drug administration – date of earliest symptom start). Time (days) since the earliest symptom start will be summarized by treatment group using descriptive statistics. All disease characteristic will be listed for the ITT set by treatment group.

# 8. TREATMENTS AND MEDICATIONS

## 8.1. Prior and Concomitant Medications

All medications used during the study, taken within 30 days before the patient signs the ICF until the EOT visit will be collected on the eCRF. All medications will be coded according to the World Health Organization drug dictionary (WHO Drug Dictionary March 2020 or the later version). Medications will be classified as either prior or concomitant.

A prior medication is defined as following, and all other medications will be defined as concomitant medication.

- A medication checked as "Yes" to "If stop date is unknown, was this drug stopped before the study drug administration (Day 1)?" on eCRF or
- A medication having stop date of medication before the date of study drug administration.

The prior medications will be summarized by treatment group, drug class (using Anatomical Therapeutic Chemical [ATC] level 2), and PT along with the total number of prior medications and the number and percentage of patients with at least one prior medication for the Safety set. The separate tables will be also generated for the concomitant medications by treatment group, drug class (using ATC level 2), and PT along with the total number of concomitant medications and the number and percentage of patients with at least one concomitant medication for the Safety set. At each level of summarization, a patient is counted only once if the patient reported one or more medications at that level. When ATC Level 2 for drug class is not available, Level 1 will be used instead.

All prior and concomitant medications will be listed separately by treatment group for the Safety set.

## 8.2. Exposure to Study Drug

The number and percentage of patients who received the study drugs will be summarized by treatment group for the Safety set. The prescribed and actual administered dose (mg) of study drug will also be summarized using descriptive statistics.

A listing will be provided by treatment group for the ITT set showing the details collected on the "Study Drug Administration" page of eCRF.

## 8.3. Study Restriction Assessment

Patients who follow or not any of the study restriction will be listed for the Safety set by

treatment group, visit and category.

## 9. VIROLOGY ANALYSIS

Virology analysis will be conducted on the ITT set unless otherwise stated.

Virology analysis consists of viral efficacy (viral shedding based on qPCR), characterization of SARS-CoV-2 viral isolate (genotyping) and RT-PCR. Viral shedding (qPCR) and genotype samples will be analyzed at the central laboratory and RT-PCR sample will be analyzed at the local laboratory.

If the patient had RT-PCR result confirming SARS-CoV-2 infection prior to obtaining written informed consent (but no more than 7 days from the onset of symptoms), the result can be allowed. During the Screening Period, only one retest for RT-PCR will be allowed, if study drug can be administered no more than 7 days from onset of symptom based on retest results.

Nasopharyngeal swab samples for virology analysis will be collected and corresponding virology analysis will be performed at the time point specified in Appendix 1 and Appendix 2.

Viral titers will be assessed in $\log_{10}$cp/mL for qPCR. The following Table 2 presents how viral titers will be treated in descriptive summary and AUC calculation, and categorized to Positive or Negative.

**Table 2 Handling of Viral Titers (qPCR)**

| | Treated as | Classified as |
|---|---|---|
| Quantitative value | Reported value | Positive |
| BLQ | LLoQ | Positive |
| Negative | 0 | Negative |

Abbreviations: qPCR= quantitative polymerase chain reaction; BLQ=below the low limit of quantification; LLoQ=lower limit of quantification. NA= Not Applicable.

Actual results and change from baseline for viral shedding in nasopharyngeal swab specimens (titers) for qPCR will be summarized by treatment groups at each scheduled time point. The number and percentage of patients with positive / negative for qPCR will also be summarized by treatment group and scheduled time point.

Duration (days) of viral shedding in nasopharyngeal swab specimens for qPCR will be calculated as (date/time of post-baseline last positive sample - date/time of study drug administration). Patients with at least one positive sample after baseline will be included in the summary. Duration of viral shedding for qPCR will be summarized by treatment groups using descriptive statistics.

AUC of viral titers for qPCR is calculated from date/time of study drug administration to date/time of last measurable value of patients who have at least one post-baseline result

(including BLQ and negative values) using linear trapezoidal rule. Viral titer at baseline will be considered as result at study drug administration. AUC of viral titers for qPCR will be summarized by treatment groups using descriptive statistics.

Mean (±SD) viral titer of qPCR for each scheduled time point will be plotted by treatment group.

All virology results including qPCR and RT-PCR will be listed for each patient by treatment group and time point respectively.

Genotype results will be listed by treatment group in patients with predose sample with > 3 $log_{10}$cp/mL in ITT set. Day 1 (SARS-CoV-2 positive sample) and the last SARS-CoV-2 positive sample in time with > 3 $log_{10}$cp/mL will be analyzed. Additional samples were analyzed if SARS-CoV-2 infection symptoms were deteriorated or viral titers were not noticeably reduced.

The first CSR will present viral shedding in nasopharyngeal swab specimens based on qPCR up to Day 7 of each patient displaying descriptive statistics for actual results and change from baseline, and frequency table for categorized results and figure for mean (±SD) of viral titer. All virology analysis will be presented in the Final CSR.

## 10. EFFICACY ANALYSES

All Efficacy analysis will be conducted on the ITT set unless otherwise stated.

### 10.1. SARS-CoV-2 Infection Symptom Checklist

All patients will be issued a patient diary for SARS-CoV-2 Infection Symptom Checklist at screening and will be required to record it in the diary from Day 1 until Clinical recovery or Day 28 whichever comes first. After Day 28, additional recording of the diary will be required if following conditions are met:

- For patients who will achieve clinical recovery at Day 28, patients will record the diary until Day 29 to confirm whether it is maintained at least 24 hours.
- For patients who will show deterioration (at the discretion of the Investigator) after the achievement of clinical recovery, patient will record the diary until secondary achievement of clinical recovery.
- After Day 28 of regular scheduled study visit, for patients with suspicious ADE occurrence, patient will record the diary for 7 days from the day of suspicious ADE occurrence specified in Appendix 2.

All patients will be instructed to complete the diary twice a day in the following time point at approximately 12-hour intervals except for screening: In the morning (between 6 and 10 AM, approximately) and in the evening (between 6 and 10 PM, approximately). The patient will be recorded once at screening. On the date of study drug administration (Day 1), the patient diary

will be recorded twice before and after the study drug administration. If screening visit date and the administration of study drug date are same, the patient diary will be recorded twice before and after the study drug administration (Day 1).

SARS-CoV-2 Infection Symptom Checklist consists of 7 symptoms and the intensity of patient's self-aware for each symptom. The 7 symptoms are feeling feverish, cough, shortness of breath or difficulty breathing, sore throat, body pain or muscle pain, fatigue, and headache. Scores for SARS-CoV-2 infection symptom are "Absent (0)", "Mild (1)", "Moderate (2)", "Severe (3)" and "Not Done".

Clinical recovery is defined by all symptoms on the SARS-CoV-2 infection symptom Checklist are recorded as 'absent' or 'mild' in intensity for at least 24 hours. To satisfy the clinical recovery, symptoms of the moderate or severe in intensity at baseline should be scored as mild or absent, or symptoms of the mild or absent in intensity at baseline should be scored as absent, after study treatment. Patients who meet the clinical recovery criteria for at least three consecutive time points will be considered as satisfying condition of 24 hours, and achieving clinical recovery at the first time point. The three consecutive time points for each symptom can be different because the three consecutive time points will be determined excluding missing data if the results of some symptoms are missing on the SARS-CoV-2 infection symptom Checklist. However, results of all 7 symptoms have to be recorded at the first time point achieving clinical recovery. The example of a patients achieving clinical recovery on Day 14 Morning is presented the following Table 3.

**Table 3 Example of a Patients Achieving Clinical Recovery**

| | Day 14 Morning | Day 14 Evening | Day 15 Morning | Day 15 Evening |
|---|---|---|---|---|
| Feeling feverish | 0 | 0 | Missing | 0 |
| Cough | 0 | Missing | 0 | 0 |
| Shortness of breath or difficulty breathing | 0 | 0 | 0 | 0 |
| Sore throat | 0 | 0 | 0 | 0 |
| Body pain or muscle pain | 0 | 0 | 0 | 0 |
| Fatigue | 0 | 0 | 0 | 0 |
| Headache | 0 | 0 | 0 | 0 |

The time to clinical recovery (days) will be calculated as [date/time achieving clinical recovery (or censoring) – date/time of study drug administration]. Patients who are ongoing in the study without event, with death or early withdrawal for any reason will be considered as censored at the day of their scheduled visit of interest (Day 28). Missing time of completion of diary will be assumed to be 10:00 AM and 10:00 PM for calculation of time to recovery.

The number and percentage of patients with clinical recovery up to Day 7, Day 14, and Day 28 and Censored up to Day 28 along with censoring reason will be displayed by treatment group. The 25th percentile, 50th percentile (median) and 75th percentile will be estimated from Kaplan-Meier curve for the time to clinical recovery up to Day 28 and displayed by treatment group. Kaplan-Meier plots for each treatment group will be presented.

This listing will include all data collected on the "SARS-CoV-2 Infection Symptom Checklist" page of eCRF.

### 10.2. Disease Status Monitoring

Disease status including requirement of supplemental oxygen, intensive care unit transfer, mechanical ventilation use and hospitalization will be monitored during the study period (from signing of ICF to EOT).

The number and percentage of patients with supplemental oxygen, intensive care unit transfer, mechanical ventilation use up to Day 7, 14 and Day 28 and hospitalization up to Day 14 and Day 28 will be summarized by treatment group respectively.
A listing will be provided by treatment group for the ITT set showing the details collected on the "Disease Status Monitoring" page of eCRF.

## 11. PHARMACOKINETIC ANALYSIS

All PK analyses will be conducted on the PK set unless otherwise specified.

### 11.1. Serum Concentrations

Blood samples for PK analyses will be collected from all patients at the time points specified in PK Blood Sampling Time Points and acceptable tolerance windows (Table 4). If the PK blood sample is unable to be analyzed or is missing at certain time point, some blood samples collected for immunogenicity assessment at the same time point can be used for PK assessment.

Descriptive statistics (n, mean, SD, geometric mean, CV%, minimum, median, and maximum) for serum concentrations will be summarized by CT-P59 treatment groups at each scheduled visit and time point. Individual serum concentrations, collection date/time, and deviations from scheduled time will be listed for the Safety set by CT-P59 treatment groups, visit and time points.

Concentration that are below the lower limit of quantification (BLQ) prior to the study drug administration will be treated as zero (0), and all other BLQ values will be treated as missing for calculation of descriptive statistics of serum PK concentrations and for PK parameter estimation. Measurable concentrations after consecutive BLQs during the terminal phase will also be set to missing.

The mean (±SD) serum concentration versus scheduled sample time profiles for the CT-P59 will be presented graphically on both linear and semi-logarithmic scales by CT-P59 treatment groups. In addition, the spaghetti plot of serum concentrations versus scheduled sample time profiles will be presented graphically on both linear and semi-logarithmic scales by CT-P59 treatment groups.

**Table 4 Blood Sampling Time Points for Pharmacokinetic Assessment**

| Day | Time point | Window |
|---|---|---|
| Day 1 | Predose | Predose within the day |
| | End of infusion | + 15 minutes |

| | | |
|---|---|---|
| | 1 hour after end of infusion | |
| Day 2 | 24 hours after start of infusion | ± 1 hour |
| Day 3 | 48 hours after start of infusion | |
| Day 5 | 96 hours after start of infusion | ± 4 hours |
| Day 7 | 144 hours after start of infusion | |
| Day 10 | 216 hours after start of infusion | |
| Day 14 | 312 hours after start of infusion | ± 1 day |
| Day 28 | 648 hours after start of infusion | ± 3 days |
| Day 56 | 1,320 hours after start of infusion | ± 5 days |
| Day 90/EOT visit | 2,136 hours after start of infusion | |

The first CSR will present PK serum concentration results up to Day 14 of each patient.

## 11.2. Pharmacokinetic Parameters

The following PK parameters will be calculated by noncompartmental methods based on the actual sampling time points using [redacted]

| **Parameter** | **Definition** |
|---|---|
| $AUC_{0\text{-}inf}$ | Area under the concentration-time curve from time zero to infinity, calculated using the linear up and log down trapezoidal rule |
| $AUC_{0\text{-}inf}$/Dose | Dose normalized $AUC_{0\text{-}inf}$ (normalized to total body dose and dose/body weight) |
| $AUC_{0\text{-}last}$ | Area under the concentration-time curve from time zero to the last quantifiable concentration, calculated using the linear up and log down trapezoidal rule |
| $AUC_{0\text{-}last}$/Dose | Dose normalized $AUC_{0\text{-}last}$ (normalized to total body dose and dose/body weight) |
| $C_{max}$ | Maximum serum concentration |
| $C_{max}$/Dose | Dose normalized $C_{max}$ (normalized to total body dose and dose/body weight) |
| $T_{max}$ | Time to $C_{max}$ |
| $t_{1/2}$ | Terminal half-life, calculated as:<br>$t_{1/2} = \ln 2/\lambda_z$ |
| $\%AUC_{ext}$ | Percentage of $AUC_{0\text{-}inf}$ obtained by extrapolation. |
| $\lambda_z$ | Terminal elimination rate constant estimated from the linear regression of the natural log-transformed concentration over time at the terminal phase. At least 3 time points (excluding $C_{max}$) and in general, adjusted correlation coefficient ($r^2$) greater than or equal to 0.85 is needed to |

| | |
|---|---|
| | calculate and retain $\lambda_z$ and its associated parameters ($t_{1/2}$, $AUC_{0\text{-inf}}$, $AUC_{0\text{-inf}}$/Dose, CL, and $V_z$). Values of adjusted $r^2$ less than 0.85 will be examined on a case-by-case basis for reliability to calculate and retain $\lambda_z$ and its associated parameters ($t_{1/2}$, $AUC_{0\text{-inf}}$, $AUC_{0\text{-inf}}$/Dose, CL, and $V_z$). Pharmacokinetic parameters that do not meet this criterion will be listed but not summarized |
| CL | Total body clearance, calculated as:<br>$CL = Dose/AUC_{0\text{-inf}}$ where Dose is the total body dose |
| $V_z$ | Volume of distribution during the terminal phase, calculated as:<br>$V_z = (CL)/\lambda_z$ |

Pharmacokinetic parameters will be summarized by CT-P59 treatment groups using descriptive statistics (n, mean, SD, geometric mean, CV%, minimum, median, and maximum values for all parameters).

All data for the PK parameters will be listed by CT-P59 treatment groups using the following rules: $C_{max}$ and $C_{max}$/Dose will be presented to same level of precision as the PK concentration results, $T_{max}$ will be presented to 2 decimal places, $AUC_{0\text{-last}}$, $AUC_{0\text{-last}}$/Dose, $AUC_{0\text{-inf}}$ and $AUC_{0\text{-inf}}$ /Dose will be rounded to integer, and all other PK parameters will be presented to 3 significant digits.

Scatter plots of individual values and geometric mean versus dose (in mg/kg on numeric scale and log-transformed scale) will be presented for $AUC_{0\text{-inf}}$, $AUC_{0\text{-last}}$, $C_{max}$, and the corresponding dose-normalized parameters.

Dose proportionality of the PK parameters, $AUC_{0\text{-inf}}$, $AUC_{0\text{-last}}$, and $C_{max}$, over the administered dose range (in mg/kg) will be quantified using the following power model:

log (parameter) = a + b * log (dose)

where 'a' is the intercept and 'b' is the slope.

The power model parameters (slope and intercept) along with the corresponding 90% CIs and SE will be estimated using least-squares regression or an equivalent method, and will be presented in tabular format and graphically.

The first CSR will present summaries only for $C_{max}$, $C_{max}$/Dose (normalized to dose/body weight) and $T_{max}$, derived from serum concentration up to Day 14, scatter plots only for $C_{max}$, $C_{max}$/Dose (normalized to dose/body weight) and dose proportionality assessment only for $C_{max}$ using [redacted]

## 12. SAFETY ANALYSES

All Safety analyses will be conducted on the Safety set unless otherwise stated.

### 12.1. Adverse Events

An adverse event (AE) is defined as any untoward medical occurrence in any patient during the study which does not necessarily have a causal relationship with the study drug. Any new

condition noted at Screening would be regarded as an AE, but not a TEAE.

A TEAE includes any untoward medical occurrence in a patient after administration of a study drug, which does not necessarily have to have a causal relationship with this the study drug. A TEAE can therefore be any unfavorable and unintended sign (including an abnormal laboratory finding), symptom, or disease temporally associated with the use of the product, whether or not related to the study drug.

All AEs will be reported by the Investigator via eCRF from the date patients signs the ICF until EOT visit, regardless of the relationship to the study drug, and graded for intensity according to the Common Terminology Criteria (CTCAE) Version 5.0 and coded to SOC and PT according to MedDRA Version 23.0 or later.

If the stop date of an AE is incomplete or unknown, the following rules will be applied.

- Missing day (e.g., XXSEP2020): Assume the last day of the month. (e.g. 30SEP2020)
- Missing day and month (e.g., XXXXX2020): Assume December 31st. (e.g., 31DEC2020)
- Missing day, month and year (e.g., XXXXXXXXX): Leave it as Missing.

In case a patient dies during the study, the stop date will be imputed with the date of death if the imputed stop date is after the date of death.

If the start date of an AE is incomplete or unknown, the following rules will be applied. If the stop date of the AE is incomplete, imputed stop date will be used instead of reported stop date:

- If the day an AE is missing (e.g. XXSEP2020), the month and year of the incomplete date will be compared to the date of study drug administration.
    - If the month and year are equal for both dates, the AE start date will be imputed as the earlier of: (i) the date of study drug administration, and (ii) the stop date of the AE.
    - If the month and year are not equal, the AE start date will be imputed as the first day of the month (e.g. 01SEP2020).
- If the day and month are missing (e.g. XXXXX2020), the year of the incomplete date will be compared to the date of study drug administration.
    - If the years of both dates are equal, start date will be imputed as earlier date of: (i) the date of study drug administration, and (ii) the stop date of the AE.
    - If the year is not equal, start date will be imputed as the 1st of January of the incomplete date year (e.g. 01JAN2020).
- If the AE start date is missing (e.g. XXXXXXXXX), start date will be imputed as the earlier date of: (i) the date of study drug administration, and (ii) the stop date of the AE.

The recorded/imputed dates of AEs will be used for decision whether the event is TEAE.

All AEs recorded will be presented in a data listing. Listings for AEs will include the following information: SOC, PT and Verbatim term; start and stop date/time; Time to Occurrence (for TEAE) [calculated as (AE start date – date of study drug administration +1)]; AE Duration [calculated as (AE stop date – AE start date +1)]; TEAE flag; intensity (CTCAE Grade 1 to 5); outcome (recovered/resolved, recovering/resolving, recovered/resolved with sequelae: type of sequelae, not recovered/not resolved, fatal, unknown); type of sequelae (if recovered/resolved with sequelae); relationship with study drug (unrelated, possible, probable, definite); action taken with study drug (dose not changed, drug interrupted, drug withdrawn, not applicable); any treatment received (no, medication, non-medication treatment: specify, both medication and non-medication treatment: specify the non-medication treatment); whether the event was serious (no, yes); whether the AE is classified as an infusion related reactions (IRR) including hypersensitivity and anaphylactic reaction (no, yes).

In summaries, AEs will be considered to be related if the relationship is possible, probable, or definite. If relationship or intensity is missing, it will be summarized separately under a missing category.

### 12.1.1. Incidence of Treatment-Emergent Adverse Events

The TEAEs will be summarized by treatment group, SOC, PT, relationship and intensity, displaying the number and percentage of patients with at least one TEAE using only the worst intensity recorded at each level of summarization. The total number of events and number and percentage of patients with at least one TEAE over all SOCs will also be displayed.

### 12.1.2. Serious Adverse Events

A serious adverse event (SAE) is defined as any event that results in death, is life threatening, requires inpatient hospitalization or prolongation of existing hospitalization, results in persistent or significant disability/incapacity, or is a congenital anomaly/birth defect. Medical and scientific judgment should be exercised in deciding whether expedited reporting is appropriate in other situations, such as important medical events that may not be immediately life-threatening or result in death or hospitalization but may jeopardize the patient or may require medical or surgical intervention to prevent one of the outcomes listed in the definition above. These should also be considered serious.

The TESAE will be summarized by treatment group, SOC, PT, relationship and intensity, displaying the number and percentage of patients with at least one TESAE using only the most severe intensity recorded at each level of summarization. The total number of events and number and percentage of patients with at least one TESAE over all SOCs will also be displayed. All SAEs including serious criteria and SAE description will be presented in an additional information listing.

### 12.1.3. Deaths

All patients who have a SAE with serious criteria of “Death” will be presented in a listing and

the following variables will be included; date of study drug administration, date of last visit, date of death, time (days) to death from study drug administration, TEAE flag, SOC/PT, whether an autopsy was performed (no, yes), whether a death certificate was completed (no, yes), relationship to study drug. Time (days) to death from study drug administration will be calculated as (date of death – date of study drug administration + 1).

### 12.1.4. Treatment-Emergent Adverse Events Leading to Discontinuation

All patients who have a TEAE with an action taken with study drug of "Drug Withdrawn" will be summarized by treatment group, SOC, PT, relationship and intensity, displaying the number and percentage of patients with at least one TEAE leading to study drug discontinuation, using only the most severe TEAE recorded at each level of summarization. The total number of events and number and percentage of patients with at least one TEAE which led to study drug discontinuation over all SOCs will also be displayed.

### 12.1.5. Treatment-Emergent Adverse Events of Special Interest

The AEs checked as "Yes" to "Is Adverse event classified Infusion Related Reactions including Hypersensitivity and Anaphylactic Reactions?" on the "Adverse Event" page of eCRF will be classified as Infusion Related Reaction (IRR) including Hypersensitivity and Anaphylactic Reaction, and considered as adverse events of special interest (AESI) because AE related to infusion related reactions (hypersensitivity/anaphylactic reactions).

TEAEs of special interest (TEAESI; IRR including hypersensitivity/anaphylaxis reaction) will be summarized by treatment group, SOC, PT, relationship and intensity, displaying number and percentage of patients with at least one TEAESI using only the most severe TEAESI recorded at each levels of summarization. The total number of events and number and percentage of patients with at least one TEAESI over all SOCs will also be displayed. Additionally, table for signs and symptoms of TEAESI will be provided separately by SOC, PT and intensity.

Experienced signs and symptoms of TEAESI will be presented in additional information listings for TEAESI.

## 12.2. Clinical Laboratory Evaluations

Blood and urine samples for clinical laboratory assessments including clinical chemistry, hematology, and urinalysis will be collected at the time points specified in Appendix 1 and Appendix 2. Laboratory analyses will be performed by the local laboratories. For the first CSR, results will be listed based on local laboratories units. Results converted to International System of Units (SI units) will be listed and summarized in the Final CSR. The results in local unit that cannot be converted to SI unit are collected, the results will be listed and summarized separately in local unit in the Final CSR.

The following clinical laboratory assessments will be performed:

| | |
|---|---|
| Clinical chemistry: | Total protein, serum bilirubin (total, direct), ALT, AST, alkaline phosphatase, γ-glutamyl transferase, blood urea nitrogen, creatinine, |

| | |
|---|---|
| | creatine kinase, creatine kinase-myocardial band isoenzyme, troponin (I or T, [only one applicable]), albumin, sodium, potassium, calcium, chloride, inorganic phosphorus, glucose, lactate dehydrogenase, total cholesterol, triglyceride, high-density lipoprotein cholesterol, and CRP |
| Hematology: | Red blood cells, erythrocyte sedimentation rate, total white blood cell count, absolute neutrophil count, eosinophil count, lymphocyte count, platelet count, hemoglobin, mean corpuscular volume, mean corpuscular hemoglobin, mean corpuscular hemoglobin concentration, and hematocrit |
| Urinalysis: | Bilirubin, blood, glucose, ketones, leukocytes, nitrite, pH, protein, specific gravity, urobilinogen, and microscopic examination of white blood cell count, red blood cell count, and bacteria |

Abnormal clinical laboratory values will be flagged as either “High” or “Low” based on the reference ranges for each laboratory parameter. The investigator will determine whether any of the abnormal clinical laboratory values are clinically significant or not clinically significant.

Some numeric parameters will be labeled with a CTCAE term, and grading will be applied to post-baseline values for numeric parameters where possible according to CTCAE version 5.0. Grades that require clinical input only will not be assigned to these parameters. Grades which are part numeric and part clinical input will be assigned based on the numeric portion only. If different grades share the same criteria due to exclusion of clinical input, lower grade will be used. The CTCAE terms and grades for applicable parameters are listed in Appendix 4. The CTCAE grades for this analysis will be Grade 1 (Mild), Grade 2 (Moderate), Grade 3 (Severe) and Grade 4 (Life-threatening). The CTCAE Grade 5 (Death) will not be applied in this analysis since death cannot be determined from a numeric laboratory result. If the post-baseline result for a patient does not satisfy any CTCAE grade, it will be classified as “No Grade”.

Actual results and changes from baseline of numeric laboratory parameters including clinical chemistry, hematology, and urinalysis will be summarized using descriptive statistics by treatment group, parameter and scheduled visit in separate tables by laboratory category. For the purpose of summarization, any numeric values recorded from the clinical laboratory tests which are below the lower limit or above the upper limit of quantification will be set to the respective limit for all related summaries. In listings, original results containing inequality signs will be displayed.

The number and percentage of patients for clinical laboratory test results (clinical chemistry, hematology, and urinalysis) will be summarized using {“Normal”, “Abnormal, Not Clinically Significant”, “Abnormal, Clinically Significant”} categories as appropriate, by treatment group, parameter and visit, in the form of a shift table to detect changes from baseline, in separate tables by laboratory category.

The number and percentage of patients with a result for each CTCAE grade will be summarized by treatment group, laboratory category, CTCAE term and scheduled visit. Additional tables

will be generated using the most severe grade after study drug administration. The most severe grade will be selected including all post-baseline scheduled and unscheduled visits.

All clinical laboratory test results of clinical chemistry, hematology, and urinalysis will be presented in separate listings by laboratory category. For values that are outside the normal range, high and low flags and clinical significance as evaluated by the investigator will be presented if applicable, and CTCAE results will also be presented for applicable parameters.

### 12.3. Vital Signs and Weight

Vital signs and weight measurements will be performed at the time points specified in Appendix 1 and Appendix 2. Vital signs (including systolic and diastolic blood pressures, heart rate, respiratory rate, body temperature and $SpO_2$) will be measured after the patient has rested quietly for at least 5 minutes. $SpO_2$ will be measured while breathing normal room air. Body temperature will be measured using tympanic thermometer throughout the study.

All vital signs will be summarized using descriptive statistics of actual result and change from baseline by treatment group, parameter and scheduled visit. All vital signs and weight except for hypersensitivity monitoring results will be listed for each patient by treatment group, parameter and visit.

### 12.4. Hypersensitivity Monitoring

For hypersensitivity monitoring, additional vital signs measurements including systolic and diastolic blood pressure, heart rate, respiratory rate and body temperature will be performed at the following time points in Table 5.

**Table 5 Schedule of Assessments for Hypersensitivity Monitoring**

| Day | Time points | Window |
|---|---|---|
| Day 1 | Predose | Within 30 minutes |
| | 15 minutes from start of infusion | ± 5 minutes |
| | 30 minutes from start of infusion | |
| | 60 minutes from start of infusion | |
| | 90 minutes from start of infusion | |
| | 2 hours from start of infusion | ± 15 minutes |
| | 3 hours from start of infusion | |
| | 6 hours from start of infusion | |
| | 12 hours from start of infusion | |
| Day 2 | 24 hours from start of infusion | ± 30 minutes |

The number and percentage of patients who have clinically notable hypersensitivity result will be summarized in a table by treatment group, scheduled time points and parameter. The criteria for clinically notable results are defined as follows in Table 6.

**Table 6 Hypersensitivity Classification for Vital signs**

| Parameter | Low | High |
|---|---|---|
| Systolic blood pressure (mmHg) | ≤ 90 | ≥ 160 |
| Diastolic blood pressure (mmHg) | ≤ 50 | ≥ 90 |
| Heart rate (beats per minute) | ≤ 50 | ≥ 100 |
| Respiratory rate (breaths per minute) | ≤ 12 | ≥ 20 |
| Body temperature (°C) | ≤ 35.0 | ≥ 38.0 |

All vital signs data for hypersensitivity monitoring will be listed for each patient by treatment group, time point and parameter. High and low flags will also be presented in the listing to show whether a hypersensitivity result is outside of normal range.

### 12.5. Electrocardiogram

A 12-lead Electrocardiogram (ECG) will be performed at the time points specified in Appendix 1 and Appendix 2 and if the patient experienced cardiac symptoms during study drug administration. All scheduled 12-lead ECGs will be performed after the patient has rested quietly for at least 5 minutes. In case of hypersensitivity monitoring, any type of ECG can be performed. The findings of 12-lead ECG will be classified as either "Normal", "Abnormal, Not Clinically Significant", or "Abnormal, Clinically Significant".

The number and percentage of patients will be summarized by treatment group, scheduled visit, in the form of a shift table to detect changes from baseline. All ECG data including hypersensitivity monitoring results will be listed for each patient by treatment group and visit.

### 12.6. Physical Examination

A physical examination will be performed at Screening, on Day 1 and at EOT visit. The examination will include an assessment of general appearance, head and neck, skin, cardiovascular, respiratory, abdominal, neurological, musculoskeletal, lymphatic systems. The findings of physical examination will be classified as either "Normal", "Abnormal, Not Clinically Significant", or "Abnormal, Clinically Significant".

The number and percentage of patients will be summarized by treatment group, scheduled visit, category, in the form of a shift table to detect changes from baseline. All physical examination data will be listed for each patient by treatment group, visit and category.

### 12.7. Pregnancy Test

Pregnancy tests consist of serum and urine pregnancy tests. Serum pregnancy test will be performed for female patients with childbearing potential at Screening and EOT visit. The serum pregnancy test samples will be analyzed at the local laboratory. If serum pregnancy test is unavailable, urine pregnancy test can be performed instead. Pregnancy test results will be classified as "Positive", "Negative".

All pregnancy test results will be listed for each patient tested by treatment group, visit.

### 12.8. Radiography

Radiography (chest x-ray and/or chest CT) will be performed at the time points specified in

Appendix 1. Results for radiography will be classified as either "Normal", "Abnormal, Not Clinically Significant" or "Abnormal, Clinically Significant".

The number and percentage of patients will be summarized by treatment group, scheduled visit, in the form of a shift table to detect changes from baseline. All radiography results will be listed by treatment group, visit.

### 12.9. Immunogenicity

Blood samples for immunogenicity assessments will be collected prior to study drug administration on Day 1 and on Days 7, 14, 28, 56, and EOT visit. The immunogenicity of CT-P59 will be assessed by anti-drug antibody (ADA) and neutralizing antibody (NAb) test in validated immunoassay. If the blood sample is unable to be analyzed or is missing at certain time point, some blood samples collected for PK assessment at the same time point can be used for immunogenicity assessment. Additional immunogenicity will be assessed when immune-related AEs occurs. Analysis will be performed at the central laboratory.

The ADA assay will follow a three-tiered approach consisting of (i) screening assay, (ii) specificity/confirmatory assay, and (iii) titration. The test outcome for the screening assay will be either "Potential Positive" or "Negative". Samples that are "Potential Positive" in the screening assay will be undergone further testing in the specificity/confirmatory assay to determine if patients are a true positive. The test outcome for the specificity/confirmatory assay will be either "Reactive", "Negative", or "Not applicable (N/A)". "Reactive" indicates a true positive test outcome and will be labeled as "Positive" in outputs. "Negative" is considered negative, and "N/A" indicates the assay was negative at the screening phase of the process. Patients with a "Negative" test outcome for either screening or specificity/confirmatory assays will be considered negative for the overall ADA assessment. For further characterization, the antibody level will be assessed by titration in confirmed positive samples.

Samples that are positive in the ADA assay will be analyzed further to conduct a NAb assessment. The test outcome for the screening assay will be either "Positive" or "Negative".

The number and percentage of patients for the results of the final ADA and the screening NAb assay will be summarized by treatment group, scheduled visit and test.

Descriptive statistics of ADA titer will be displayed by treatment group, scheduled visit and test. The results of ADA titer will also be presented in the listing of immunogenicity results.

All immunogenicity data will be listed for each patient by treatment group and visit.

The first CSR will present only results of ADA screening and confirmatory assay up to Day 14 of each patient.

### 12.10. SARS-CoV-2 Infection Related Signs and Symptoms

During the Screening, Treatment Period, and EOT visit, the Investigator or designee will perform a respiratory signs and symptoms assessment (including the examination of ear, nose, throat, sinuses, lungs and other) and assessment for non-respiratory signs and symptoms and/or potential complications of SARS-CoV-2 infection. During the Follow-Up Period, patients will

be asked if they have any SARS-CoV-2 infection related signs and symptoms by telephone call. The assessment will be performed at the scheduled time points specified in Appendix 1 and Appendix 2. The findings of assessment for respiratory signs and symptoms will be classified as either "Normal", "Abnormal, Not Clinically Significant", or "Abnormal, Clinically Significant".

The assessment results for respiratory signs and symptoms at each scheduled visit (excluding follow-up period) with those at baseline will be summarized by treatment group, scheduled visit, category, in the form of a shift table to detect changes from baseline. All assessment data will be listed for each patient by treatment group, visit, assessment type and category.

### 12.11. Antibody-dependent Enhancement

A patient will be considered to have suspicious Antibody-dependent Enhancement (ADE) if it is checked as "Yes" to "Has the subject experienced any suspicious Antibody-dependent Enhancement (ADE) during the study?" on eCRF.

If a patient has suspicious ADE, additional evaluations will be performed as specified in Appendix 2 during the Treatment Period, EOT, and Follow-Up Period. If symptoms have not resolved or have worsened up to Day 7 after the day of suspicious ADE occurrence, same procedure will be repeated until when the symptoms are resolved and/or no SARS-CoV-2 infection is confirmed by RT-PCT (local).

Proportion of patients with suspicious ADE will be summarized by treatment group.

Additional evaluation results will be listed in each evaluation listing. Only ADE Yes/No data will be listed for each patient by treatment group, separately.

## 13. Changes in the Planned Analysis

### 13.1. Changes in the Protocol

1. To use more information in determination of the clinical recovery, 'at Screening' was modified to 'at Baseline' in the sentence "To satisfy the clinical recovery, symptoms of the moderate or severe in intensity at Screening should be scored as mild or absent, or symptoms of the mild or absent in intensity at Screening should be scored as absent, after study treatment.".

2. Although 'Virology analysis vendor ([redacted])' conducted an analysis for 'Cell culture', statistical analysis was not possible because results were not derived from most of the analysis, so related sentences about 'Cell culture' was deleted in the SAP.

## 14. Reference List

International Council for Harmonisation (ICH) Assembly. ICH E9: Statistical principles for clinical trials – Step 5. 01 September 1998.

US Department of Health and Human Services. (2010). National Institutes of Health, National Cancer Institute. Common Terminology Criteria for Adverse Events (CTCAE) version 5.0. Available from: http://evs.nci.nih.gov/ftp1/CTCAE/About.html

# 15. APPENDIX

## Appendix 1: Schedule of Assessments

| | Screening [1] | Treatment Period | | | | | | | | | | | | EOT [2] | Follow-Up Period [3] |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| **Study Day (Visit windows)** | **-7 to 1** | **1** | **2** | **3** | **4** | **5** | **6** | **7** | **10** | **14 (±1)** | **21 (±1)** | **28 (±3)** | **56 (±5)** | **90 (±5)** | **Bi-weekly up to 180 (±5)** |
| **In-house Stay [4]** | | **X** | **X** | **X** | **(X)** | **(X)** | **(X)** | **(X)** | | | | | | | |
| **Telephone Follow-Up Visit** | | | | | | | | | | | | | | | **X** |
| Informed consent | X | | | | | | | | | | | | | | |
| Medical history | X | | | | | | | | | | | | | | |
| Demographics | X | | | | | | | | | | | | | | |
| Inclusion/exclusion criteria [5] | X | X[6] | | | | | | | | | | | | | |
| Weight, BMI and height [7] | X | X[6] | | | | | | | | | | | | X | |
| Physical Examination | X | X[6] | | | | | | | | | | | | X | |
| Urine drug abuse check [8] | X | | | | | | | | | | | | | | |
| Hepatitis B/C and HIV test [9] | X | | | | | | | | | | | | | | |
| Serum pregnancy test [10] | X | | | | | | | | | | | | | X | |
| Clinical laboratory analyses [11] | X | X[6] | X | X | | X | | X | X | X | | X | X | X | |
| Vital Signs (blood pressure, heart rate, respiratory rate, $SpO_2$ and body temperature) [12] | X | X[6] | X | X | X[26] | X | X[26] | X | X | X | X | X | X | X | |
| 12-lead ECG [13] | X | X[6] | X | | | | | X | | X | | X | X | X | |
| Radiography [14] | X | | | X[26] | | | | | | X | | | | | |
| **Randomization** | | X[6] | | | | | | | | | | | | | |
| **Administration of study drug [15]** | | X | | | | | | | | | | | | | |
| Nasopharyngeal swab [16] | | | | | | | | | | | | | | | |
| • RT-PCR (local) [17] | X | | | | | | | | | | | | | | |
| • Viral shedding (central, qPCR and Cell culture) | | X[6] | X | X | X | X | X | X | X | X | X | X | | | |

| Study Day (Visit windows) | Screening [1] | Treatment Period | | | | | | | | | | | | EOT [2] | Follow-Up Period [3] |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | -7 to 1 | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 10 | 14 (±1) | 21 (±1) | 28 (±3) | 56 (±5) | 90 (±5) | Bi-weekly up to 180 (±5) |
| **In-house Stay** [4] | | X | X | X | (X) | (X) | (X) | (X) | | | | | | | |
| **Telephone Follow-Up Visit** | | | | | | | | | | | | | | | X |
| • Genotyping of SARS-CoV-2 viral isolates (central) | | X [6] | (X) [18] | | | | | | | | | | | | |
| Patient diary for SARS-CoV-2 Infection Symptom Checklist [19] | X | X | | | | | | | | | | | (X) | (X) | |
| SARS-CoV-2 infection related signs and symptoms assessment [20] | X | X [6] | X | X | | X | | X | X | X | | X | X | X | X |
| Pharmacokinetic sampling [21] | | X | X | X | | X | | X | X | X | | X | X | X | |
| Immunogenicity sampling | | X [6] | | | | | | X | | X | | X | X | X | |
| Hypersensitivity monitoring [22] | | X | X | | | | | | | | | | | | |
| Disease status monitoring [23] | X | | | | | | | | | | | | | | |
| Restriction assessment | X | | | | | | | | | | | | | | |
| Prior, concomitant medication [24] | X | | | | | | | | | | | | | | |
| Adverse events [25] | X | | | | | | | | | | | | | | |

Abbreviations: ADE=antibody-dependent enhancement; AE=adverse event; ALT=alanine aminotransferase; AST=aspartate aminotransferase; BMI=body mass index; CRP=C-reactive protein; CT=computed tomography; ECG=electrocardiogram; EOT=End-of-Treatment; ESR=erythrocyte sedimentation rate; HBcAb=hepatitis B core antibody, HBsAg=hepatitis B surface antigen; HIV=human immunodeficiency virus; ICF=informed consent form; PK=pharmacokinetic; qPCR= quantitative polymerase chain reaction; RT-PCR=reverse-transcription polymerase chain reaction; SARS-CoV-2=severe acute respiratory syndrome coronavirus 2; $SpO_2$= peripheral capillary oxygen saturation

1. If Screening visit date and the administration of study drug date (Day 1) are same, all assessments scheduled for the Screening and Day 1 visit can be performed only once on the date before randomization.
2. End-of-Treatment visit assessments will be performed on Day 90. If a patient is early terminated from the study, the patient will be asked to return to the study site for the safety assessments predefined on an EOT visit. If deemed necessary by the investigator, then the patient will be asked to return at the scheduled EOT visit.
3. For all patients, (including a patient who early terminated from the study, if possible) each telephone call follow-up will occur bi-weekly from 2 weeks after the EOT visit to Day 180. During the Follow-Up Period, SARS-CoV-2 infection related signs and symptoms will be assessed by telephone call to capture the suspicious ADE occurrence. For patients with suspicious ADE occurrence, all assessments specified in Table 11-2 (in protocol V1.3) will be conducted on unscheduled visit.
4. All patients will be admitted to the study center on Day 1 and it is recommended to be confined up to Day 7. In-house stay period can be determined by investigator considering the isolation regulation and/or public health capacity of the country, however all patients should be confined to the study center for at least 72 hours (until completion of all assessments on Day 3). After discharge, the consecutive study visits will be carried out on an out-patient basis. During the isolation period according to the regulatory of the country, patients will visit the study center using the transportation provided by Sponsor.

5. Inclusion and exclusion criteria will be confirmed at Screening and on Day 1. If it is concluded that the patients are not eligible in Day 1 assessments, the patients will be considered as Screening failure even if he/she was eligible based on assessments results performed during Screening Period.
6. These assessments should be performed prior to the study drug administration.
7. Measurement of height and BMI will be performed once at Screening.
8. A urine drug tests will be performed at Screening. The screen for drug abuse includes methamphetamine, barbiturates, benzodiazepines, cocaine, tetrahydrocannabinol, and opiates. The urine test can be repeated once at the discretion of the Investigator.
9. At Screening, HBsAg, HBcAb, hepatitis C antibody, HIV-1 or -2 test must be assessed in all patients (mandatory). If HBsAg test result is positive, the patient cannot be enrolled in the study. If HBcAb test is positive, the patient also cannot be enrolled. If hepatitis C antibody, HIV-1 or -2 test result is positive ([Only for protocol V1.3, including country specific A.2], HBsAg, HIV-1 or -2 test result is positive), the patient must be excluded from the study.
10. For female patients with childbearing potential, serum pregnancy test will be performed at Screening and EOT visit. If serum pregnancy test is unavailable, urine pregnancy test can be performed instead. Only patients who are confirmed as nonpregnant can be enrolled in the study.
11. Clinical laboratory testing (clinical chemistry, hematology, and urinalysis) will be performed.

| | |
|---|---|
| Clinical chemistry | Total protein, serum bilirubin (total, direct), ALT, AST, alkaline phosphatase, γ-glutamyl transferase, blood urea nitrogen, creatinine, creatine kinase, creatine kinase-myocardial band isoenzyme, troponin (I or T, only one applicable), albumin, sodium, potassium, calcium, chloride, inorganic phosphorus, glucose, lactate dehydrogenase, total cholesterol, triglyceride, high-density lipoprotein cholesterol, and CRP |
| Hematology | Red blood cells, ESR, total white blood cell count, absolute neutrophil count, eosinophil count, lymphocyte count, platelet count, hemoglobin, mean corpuscular volume, mean corpuscular hemoglobin, mean corpuscular hemoglobin concentration, and hematocrit |
| Urinalysis | Bilirubin, blood, glucose, ketones, leukocytes, nitrite, pH, protein, specific gravity, urobilinogen, and microscopic examination of white blood cell count, red blood cell count, and bacteria |

12. Blood pressure, heart rate, respiratory rate, $SpO_2$ and body temperature will be measured after the patient has rested quietly for at least 5 minutes. $SpO_2$ will be measured while breathing normal room air. Temperature will be measured using tympanic thermometer throughout the study.
13. All scheduled 12-lead ECGs must be performed after the patient has rested quietly for at least 5 minutes. Regardless of the 12-lead ECG result, further cardiological evaluation can be performed at the Investigator's discretion.
14. Radiography (chest x-ray and/or chest CT) will be performed at the scheduled time point and when the investigator considers it is clinically necessary (e.g., abnormal findings of $SpO_2$).
15. Study drug will be administered as an IV infusion for 90 minutes (±15 minutes) on Day 1. When calculating total volume of study drug to be administered, the body weight of each patient measured on Day 1 will be used.
16. Nasopharyngeal swabbing will be performed by trained site personnel. A nasopharyngeal swab sampling time points and acceptable tolerance windows are specified in Table 6-2 (in protocol V1.3) and below:
    - Screening: If Screening and administration of study drug occur on the same day, sampling of nasopharyngeal swab will be performed twice both for RT-PCR (local) of Screening and viral shedding and genotype (central) of Day 1, respectively.
    - Day 1: predose (within the day)
    - Day 2: 24 hours (±4 hours) after the start of the study drug infusion.
    - Day 3: 48 hours (±4 hours) after the start of the study drug infusion.
    - Day 4: 72 hours (±4 hours) after the start of the study drug infusion.
    - Day 5: 96 hours (±4 hours) after the start of the study drug infusion.

- Day 6: 120 hours (±4 hours) after the start of the study drug infusion.
- Day 7: 144 hours (±4 hours) after the start of the study drug infusion.
- Day 10: 216 hours (±4 hours) after the start of the study drug infusion.
- Day 21 (±1 day)
- Day 14 (±1 day)
- Day 28 (±3 days)

17. If the patient had RT-PCR result confirming SARS-CoV-2 infection prior to obtaining written informed consent (but no more than 7 days from the onset of symptoms), the result can be allowed. During the Screening Period, only one retest for RT-PCR will be allowed, if study drug can be administered no more than 7 days from onset of symptom based on retest results.
18. The genotyping will be performed on samples at time point when resistance is suspected, but not limited to.
19. study drug administration, patients will be instructed to complete the patient diary for SARS-CoV-2 Infection Symptom Checklist twice a day at approximately 12-hour intervals in the morning (between 6 and 10 AM, approximately) and in the evening (between 6 and 10 PM, approximately) from Day 1 until clinical recovery or Day 28, whichever comes first. The patient diary will be recorded once at Screening. On the date of study drug administration (Day 1), the patient diary will be recorded twice before and after the study drug administration. After Day 28, additional recording of the diary will be required if following conditions are met:
    - For patients who will achieve clinical recovery at Day 28, patients will record the diary until Day 29 to confirm whether it is maintained at least 24 hours.
    - For patients who will show deterioration (at the discretion of the investigator) after the achievement of clinical recovery, patient will record the diary until secondary achievement of clinical recovery.
    - After Day 28 of regular scheduled study visit, for patients with suspicious ADE occurrence, patient will record the diary for 7 days from the day of suspicious ADE occurrence (specified in Table 11-2 (in protocol V1.3)).
    - However, if patient's condition is not available to record the diary at the discretion of investigator (e.g. sedation state for mechanical ventilator therapy), recording can be discontinued.
20. During the Screening, Treatment Period, and EOT visit, the Investigator or designee will perform a respiratory signs and symptoms assessment (which should include, at a minimum, the examination of ear, nose, throat, sinuses, and lungs) and assessment for potential complications of SARS-CoV-2 infection. During the Follow-Up Period, patients will be asked if they have any SARS-Cov-2 infection related signs and symptoms by telephone call.
21. PK analysis will be performed at the central laboratory. Blood sampling time points and acceptable tolerance windows for PK assessments are specified in Table 6-3 (in protocol V1.3) and below:
    - Day 1: predose (within the day), end of infusion (+15 minutes), and 1 hour (+15 minutes) after the end of infusion.
    - Day 2: 24 hours (±1 hour) after start of infusion.
    - Day 3: 48 hours (±1 hour) after start of infusion.
    - Day 5: 96 hours (±4 hours) after start of infusion.
    - Day 7: 144 hours (±4 hours) after start of infusion.
    - Day 10: 216 hours (±4 hours) after start of the infusion.
    - Day 14 (±1 day), Day 28 (±3 days), Day 56 (±5 days), and Day 90 (±5 days)/EOT visit.

22. Hypersensitivity monitoring will be performed at Day 1 predose (within 30 minutes), 15 minutes (±5 minutes), 30 minutes (±5 minutes), 60 minutes (±5 minutes), 90 minutes (±5 minutes), 2 hours (±15 minutes), 3 hours (±15 minutes), 6 hours (±15 minutes), 12 hours (±15 minutes), 24 hours (±30 minutes) from the start of infusion (specified in Table 6-1 (in protocol V1.3)). Vital signs including blood pressure, heart rate, respiratory rate and body temperature will be evaluated for possible hypersensitivity reactions. Any type of ECG will be performed if a patient experiences cardiac symptoms. Emergency equipment, such as adrenaline, antihistamines, corticosteroids, and respiratory support (inhalational therapy, oxygen and artificial ventilator) must be available.
23. Disease status including requirement of supplemental oxygen, intensive care unit transfer, mechanical ventilation use, hospitalization will be monitored during the study period (from signing of ICF to EOT).
24. Prior and/or concomitant medication use will be recorded for the 30 days before the signed date of ICF until the EOT visit.
25. Adverse events will be assessed from the date the ICF is signed until up to EOT visit, regardless of the relationship to the study drug. All incidences of ADE occurring during the follow-up period will be reported as an AE, irrespective of causal relationship.
26. Assessment will be performed according to protocol V1.3, including country specific A.2.

## Appendix 2: Schedule of Assessments for Patients with Suspicious ADE Occurrence (Unscheduled Visits)

| Evaluation | Suspicious ADE Assessment | | | | |
|---|---|---|---|---|---|
| | Day of occurrence [1] | Day 2 | Day 3 | Day 5 | Day 7 [2] |
| Nasopharyngeal swab | | | | | |
| • RT-PCR (local) [3] | (X) | | | | |
| • Viral shedding (central, qPCR and Cell culture) | X | X | X | X | X |
| • Genotyping of SARS-CoV-2 viral isolates (central) [4] | (X) | | | | |
| Patient diary for SARS-CoV-2 Infection Symptom Checklist [5] | X | | | | |
| SARS-CoV-2 infection related signs & symptoms assessment [6] | X | X | X | X | X |
| Vital Signs [7] | X | X | X | X | X |
| 12-lead ECG [8] | X | | X | | X |
| Troponin test (I or T, only one applicable) | X | | X | | X |

Abbreviations: ADE=antibody-dependent enhancement; ECG=electrocardiogram; qPCR= quantitative polymerase chain reaction; RT-PCR= reverse-transcription polymerase chain reaction; SARS-CoV-2=severe acute respiratory syndrome coronavirus 2; $SpO_2$= peripheral capillary oxygen saturation

**Note**: For suspicious ADE assessment, patients can be hospitalized based on the investigator's decision. If required, additional assessments can be performed by investigator's discretion during the hospitalization period. Otherwise, the assessment will be done by out-patient visit. The genotype assessment marked as (X) will be performed in selected visits under the conditions explained in the relevant document of virology analysis.

1. Adverse events will be assessed from the date the ICF is signed until up to EOT visit, regardless of the relationship to the study drug. All incidences of ADE occurring during the follow-up period will be reported as an AE, irrespective of causal relationship.
2. If symptoms have not resolved or have worsened up to Day 7 after the day of suspicious ADE occurrence, same procedure will repeat until when the symptoms are resolved and/or no SARS-CoV-2 infection is confirmed by RT-PCR (local).
3. If required, RT-PCR (local) can be performed at any time by Investigator's discretion.
4. The genotyping will be performed on samples at time point when resistance is suspected, but not limited to.

5. For patients with suspicious ADE occurrence, patient will record the patient diary for SARS-CoV-2 Infection Symptom Checklist for 7 days from the day of suspicious ADE occurrence. Patients will be instructed to complete the diary twice a day at approximately 12-hour intervals in the morning (between 6 and 10 AM, approximately) and in the evening (between 6 and 10 PM, approximately).
6. The Investigator or designee will perform a respiratory signs and symptoms assessment (which should include, at a minimum, the examination of ear, nose, throat, sinuses, and lungs) and assessment for potential complications of SARS-CoV-2 infection.
7. Blood pressure, heart rate, respiratory rate, $SpO_2$ and body temperature will be measured after the patient has rested quietly for at least 5 minutes. $SpO_2$ will be measured while breathing normal room air. Temperature will be measured using tympanic thermometer throughout the study.
8. All scheduled 12-lead ECGs must be performed after the patient has rested quietly for at least 5 minutes. Regardless of the 12-lead ECG result, further cardiological evaluation can be performed at the Investigator's discretion.

## Appendix 3: SARS-CoV-2 Infection SYMPTOM CHECKLIST

**Please read the below question and check one box that describes your symptoms of the following SARS-CoV-2 infection symptoms.**

| | | Absent (0) | Mild (1) | Moderate (2) | Severe (3) |
|---|---|---|---|---|---|
| 1 | **Feeling feverish** | | | | |
| 2 | **Cough** | | | | |
| 3 | **Shortness of breath or difficulty breathing** | | | | |
| 4 | **Sore throat** | | | | |
| 5 | **Body pain or muscle pain** | | | | |
| 6 | **Fatigue** | | | | |
| 7 | **Headache** | | | | |

## Appendix 4: CTCAE v5.0 for Clinical Laboratory Test Results

| CTCAE Term | Laboratory Parameter | Level | Grade 1 | Grade 2 | Grade 3 | Grade 4 |
|---|---|---|---|---|---|---|
| Alanine aminotransferase increased | Alanine Aminotransferase (ALT) | High | >ULN - 3.0 x ULN if baseline was normal; 1.5 - 3.0 x baseline if baseline was abnormal | >3.0 - 5.0 x ULN if baseline was normal; >3.0 - 5.0 x baseline if baseline was abnormal | >5.0 - 20.0 x ULN if baseline was normal; >5.0 - 20.0 x baseline if baseline was abnormal | >20.0 x ULN if baseline was normal; >20.0 x baseline if baseline was abnormal |
| Hypoalbuminemia | Albumin | Low | <LLN - 3 g/dL; <LLN - 30 g/L | <3 - 2 g/dL; <30 - 20 g/L | <2 g/dL; <20 g/L | - |
| Alkaline phosphatase increased | Alkaline phosphatase (ALP) | High | >ULN - 2.5 x ULN if baseline was normal; 2.0 - 2.5 x baseline if baseline was abnormal | >2.5 - 5.0 x ULN if baseline was normal; >2.5 - 5.0 x baseline if baseline was abnormal | >5.0 - 20.0 x ULN if baseline was normal; >5.0 - 20.0 x baseline if baseline was abnormal | >20.0 x ULN if baseline was normal; >20.0 x baseline if baseline was abnormal |
| Aspartate aminotransferase increased | Aspartate Aminotransferase (AST) | High | >ULN - 3.0 x ULN if baseline was normal; 1.5 - 3.0 x baseline if baseline was abnormal | >3.0 - 5.0 x ULN if baseline was normal; >3.0 - 5.0 x baseline if baseline was abnormal | >5.0 - 20.0 x ULN if baseline was normal; >5.0 - 20.0 x baseline if baseline was abnormal | >20.0 x ULN if baseline was normal; >20.0 x baseline if baseline was abnormal |
| Blood bilirubin increased | Total Bilirubin | High | >ULN - 1.5 x ULN if baseline was normal; > 1.0 - 1.5 x baseline if baseline was abnormal | >1.5 - 3.0 x ULN if baseline was normal; >1.5 - 3.0 x baseline if baseline was abnormal | >3.0 - 10.0 x ULN if baseline was normal; >3.0 - 10.0 x baseline if baseline was abnormal | >10.0 x ULN if baseline was normal; >10.0 x baseline if baseline was abnormal |
| Leukocytosis | White Blood Cells | High | - | - | >100,000/$mm^3$ | - |
| White blood cell decreased | White Blood Cells | Low | <LLN - 3000/$mm^3$; <LLN - 3.0 x $10e^9$ /L | <3000 - 2000/$mm^3$; <3.0 - 2.0 x $10e^9$ /L | <2000 - 1000/mm3; <2.0 - 1.0 x $10e^9$ /L | <1000/$mm^3$; <1.0 x $10e^9$ /L |
| Creatinine increased [1)] | Creatinine | High | >ULN - 1.5 x ULN | >1.5 - 3.0 x baseline; >1.5 - 3.0 x ULN | >3.0 x baseline; >3.0 - 6.0 x ULN | >6.0 x ULN |
| Eosinophilia | Eosinophils (Absolute Ct) | High | >ULN and >Baseline | - | - | - |
| GGT increased | Gamma Glutamyl Transferase (GGT) | High | >ULN - 2.5 x ULN if baseline was normal; 2.0 - 2.5 x baseline if | >2.5 - 5.0 x ULN if baseline was normal; >2.5 - 5.0 x baseline | >5.0 - 20.0 x ULN if baseline was normal; >5.0 - 20.0 x baseline | >20.0 x ULN if baseline was normal; >20.0 x baseline if |

| | | | | | | |
|---|---|---|---|---|---|---|
| | | | baseline was abnormal | if baseline was abnormal | if baseline was abnormal | baseline was abnormal |
| Hypercalcemia | Calcium | High | Corrected serum calcium of >ULN - 11.5 mg/dL; >ULN - 2.9 mmol/L; @ | Corrected serum calcium of >11.5 - 12.5 mg/dL; >2.9 - 3.1 mmol/L; @ | Corrected serum calcium of >12.5 - 13.5 mg/dL; >3.1 - 3.4 mmol/L; @ | Corrected serum calcium of >13.5 mg/dL; >3.4 mmol/L; @ |
| Hypocalcemia | Calcium | Low | Corrected serum calcium of <LLN - 8.0 mg/dL; <LLN - 2.0 mmol/L; @ | Corrected serum calcium of <8.0 - 7.0 mg/dL; <2.0 - 1.75 mmol/L; @ | Corrected serum calcium of <7.0 - 6.0 mg/dL; <1.75 - 1.5 mmol/L; @ | Corrected serum calcium of <6.0 mg/dL; <1.5 mmol/L; @ |
| Hypoglycemia | Glucose | Low | <LLN - 55 mg/dL; <LLN - 3.0 mmol/L | <55 – 40 mg/dL; <3.0 – 2.2 mmol/L | <40 – 30 mg/dL; <2.2 – 1.7 mmol/L | <30 mg/dL; <1.7 mmol/L |
| Anemia | Hemoglobin | Low | <LLN - 10.0 g/dL; <LLN – 6.2 mmol/L; <LLN - 100 g/L | <10.0 - 8.0 g/dL; <6.2 - 4.9 mmol/L; <100 – 80 g/L | <8.0 g/dL; <4.9 mmol/L; <80 g/L | - |
| Hemoglobin increased | Hemoglobin | High | Increase in >0 – 2 g/dL from ULN or above baseline if baseline is above ULN | Increase in >2 - 4 g/dL from ULN or above baseline if baseline is above ULN | Increase in >4 g/dL from ULN or above baseline if baseline is above ULN | - |
| Blood lactate dehydrogenase increased | Lactate Dehydrogenase (LDH) | High | >ULN | - | - | - |
| Lymphocyte count decreased | WBC Differential, Lymphocytes | Low | <LLN - 800/$mm^3$; <LLN - 0.8 x $10e^9$/L | <800 - 500/$mm^3$; <0.8 - 0.5 x $10e^9$ /L | <500 - 200/$mm^3$; <0.5 - 0.2 x $10e^9$ /L | <200/$mm^3$; <0.2 x $10e^9$ /L |
| Lymphocyte count increased | WBC Differential, Lymphocytes | High | - | >4000/$mm^3$ - 20,000/$mm^3$ | >20,000/$mm^3$ | - |
| Platelet count decreased | Platelet count | Low | <LLN - 75,000/$mm^3$; <LLN - 75.0 x $10e^9$ /L | <75,000-50,000/$mm^3$; <75.0 - 50.0 x $10e^9$ /L | <50,000-25,000/$mm^3$; <50.0 - 25.0 x $10e^9$ /L | <25,000/mm3; <25.0 x $10e^9$ /L |
| Hyperkalemia | Potassium | High | >ULN - 5.5 mmol/L | >5.5 - 6.0 mmol/L | >6.0 - 7.0 mmol/L | >7.0 mmol/L |
| Hypokalemia | Potassium | Low | <LLN - 3.0 mmol/L | | <3.0 - 2.5 mmol/L | <2.5 mmol/L |
| Hypernatremia | Sodium | High | >ULN - 150 mmol/L | >150 - 155 mmol/L | >155 - 160 mmol/L; | >160 mmol/L |
| Hyponatremia | Sodium | Low | <LLN - 130 mmol/L | 125-129 mmol/L | 120-124 mmol/L regardless of symptoms | <120 mmol/L |

| | | | | | | |
|---|---|---|---|---|---|---|
| Cholesterol high | Total Cholesterol | High | >ULN - 300 mg/dL;<br>>ULN - 7.75 mmol/L | >300 - 400 mg/dL;<br>>7.75 - 10.34 mmol/L | >400 - 500 mg/dL;<br>>10.34 - 12.92 mmol/L | >500 mg/dL;<br>>12.92 mmol/L |
| Neutrophil count decreased | WBC Differential, Neutrophils | Low | <LLN - 1500/$mm^3$;<br><LLN - 1.5 x $10e^9$ /L | <1500 - 1000/$mm^3$;<br><1.5 - 1.0 x $10e^9$ /L | <1000 - 500/$mm^3$;<br><1.0 - 0.5 x $10e^9$ /L | <500/$mm^3$;<br><0.5 x $10e^9$ /L |
| Hypertriglyceridemia | Triglyceride | High | 150 mg/dL - 300 mg/dL;<br>1.71 mmol/L - 3.42 mmol/L | >300 mg/dL - 500 mg/dL;<br>>3.42 mmol/L - 5.7 mmol/L | >500 mg/dL - 1000 mg/dL;<br>>5.7 mmol/L - 11.4 mmol/L | >1000 mg/dL;<br>>11.4 mmol/L |

LLN = lower limit of normal, ULN = upper limit of normal.
1) The most severe grade is counted if the CTCAE grade is discrepant by multiple definitions.
Note: The LLN and ULN values will be the lower and upper limits of the normal ranges as provided by the local laboratory at each relevant transfer. In case numeric value for grading is identical such as Hypokalemia, CTCAE grade which includes numeric value will only be applied, because abnormal laboratory value with clinical input was reported as an adverse event and graded accordingly. @ indicates that corrected calcium (mg/dL) = measured total calcium (mg/dL) + 0.8 (4.0 – serum albumin [g/dL]), where 4.0 represents the average albumin level. For SI units as: Corrected calcium (mmol/l) = total Ca (mmol/l) + 0.02 (40 –serum albumin [g/l]).

## *Appendix 5: Tables, Listings and Figures in the Initial Analysis (For first CSR)*

| Output Number | Title | Analysis set |
|---|---|---|
| **Listings:** | | |
| Listing 16.2.1.1 | Patient Disposition | ITT set |
| Listing 16.2.2.1 | Analysis Sets | ITT set |
| Listing 16.2.2.2 | Major Protocol Deviations | ITT set |
| Listing 16.2.2.3 | Screening Failures | |
| Listing 16.2.4.1 | Demographics | ITT set |
| Listing 16.2.4.4 | Medical History | ITT set |
| Listing 16.2.4.5 | Prior Medication | ITT set |
| Listing 16.2.4.6 | Concomitant Medication | ITT set |
| Listing 16.2.5.1 | Study Drug Administration | ITT set |
| Listing 16.2.6.1 | Reverse Transcription Polymerase Chain Reaction (RT-PCR) | ITT set |
| Listing 16.2.6.2 | Viral Shedding in Nasopharyngeal Swab Specimens based on qPCR | ITT set |
| Listing 16.2.6.7 | Individual Serum Concentration of CT-P59 (Unit) | Safety set |
| Listing 16.2.6.8 | Individual Serum Pharmacokinetic Parameters of CT-P59 | PK set |
| Listing 16.2.7.1 | Adverse Events | Safety set |
| Listing 14.3.2.1 | Deaths | Safety set |
| Listing 14.3.2.2 | Serious Adverse Events: Additional Information | Safety set |
| Listing 14.3.2.3 | Infusion Related Reaction including hypersensitivity/anaphylactic reactions: Additional Information | Safety set |
| Listing 16.2.8.1 | Clinical Chemistry | Safety set |
| Listing 16.2.8.2 | Hematology | Safety set |
| Listing 16.2.8.3 | Urinalysis | Safety set |
| Listing 16.2.9.1 | Vital Signs and Weight | Safety set |
| Listing 16.2.9.2 | Vital Signs for Hypersensitivity Monitoring | Safety set |
| Listing 16.2.9.3 | Electrocardiograms | Safety set |
| Listing 16.2.9.4 | Physical Examinations | Safety set |
| Listing 16.2.9.6 | Radiography | Safety set |

| | | |
|---|---|---|
| Listing 16.2.9.7 | Immunogenicity Results | Safety set |
| Listing 16.2.9.8 | SARS-CoV-2 Infection Related Signs and Symptoms | Safety set |
| Listing 16.2.9.9 | Antibody-dependent Enhancement | Safety set |
| **Tables:** | | |
| Table 14.1.1 | Summary of Patient Disposition | ITT set |
| Table 14.1.2 | Analysis Sets | ITT set |
| Table 14.1.3 | Summary of Demographics | ITT set |
| Table 14.1.7 | Study Drug Administration | Safety set |
| Table 14.2.1.1 | Summary of Viral Shedding in Nasopharyngeal Swab Specimens (qPCR) | ITT set |
| Table 14.2.1.7 | Actual Result and Change from Baseline for Viral Shedding in Nasopharyngeal Swab Specimens (qPCR) | ITT set |
| Table 14.2.3.1 | Summary of Serum Concentration of CT-P59 (Unit) | PK set |
| Table 14.2.3.2 | Summary of Serum Pharmacokinetic Parameters of CT-P59 | PK set |
| Table 14.2.3.3 | Statistical Analysis to Assess Dose Proportionality | PK set |
| Table 14.3.1.1 | Treatment-Emergent Adverse Events by Intensity | Safety set |
| Table 14.3.1.2 | Treatment-Emergent Serious Adverse Events by Intensity | Safety set |
| Table 14.3.1.4 | Treatment-Emergent Adverse Events classified as Infusion related reaction including hypersensitivity/anaphylactic reactions | Safety set |
| Table 14.3.1.5 | Signs and Symptoms of Treatment-Emergent Adverse Events Classified as Infusion Related Reaction including hypersensitivity/anaphylactic reactions | Safety set |
| Table 14.3.6.7 | Summary of Immunogenicity | Safety set |
| Table 14.3.6.10 | Proportion of patients with Suspicious Antibody-dependent Enhancement | ITT set |
| **Figures:** | | |
| Figure 14.2.2.1 | Mean (+/- SD) Serum Concentration of (unit) | PK set |
| Figure 14.2.2.2 | Individual Serum Concentration of (unit) | PK set |
| Figure 14.2.2.3 | Scatter plot of PK Parameter versus Dose | PK set |
| Figure 14.2.3.1 | Mean (+/-SD) Viral Titer (log values) from qPCR | ITT set |