Protocol C4671028

A PHASE 1, OPEN-LABEL, NON-RANDOMIZED STUDY TO INVESTIGATE THE SAFETY AND PK FOLLOWING MULTIPLE ORAL DOSES OF PF-07321332 (NIRMATRELVIR)/RITONAVIR IN ADULT PARTICIPANTS WITH COVID-19 AND SEVERE RENAL IMPAIRMENT EITHER ON HEMODIALYSIS OR NOT ON HEMODIALYSIS

Statistical Analysis Plan
(SAP)

Version: **1.0**

Date: **19 August 2022**

[redacted]

[redacted]

[redacted]

TABLE OF CONTENTS

[redacted]

[redacted]

[redacted]

LIST OF TABLES

LIST OF FIGURES

APPENDICES

1. VERSION HISTORY

Table 1. Summary of Changes

Version/ Date	Associated Protocol Amendment	Rationale	Specific Changes
1.0	1.0		SAP original version

For the entire document, text in *Italic* format will represent language copied directly from protocol.

2. INTRODUCTION

The purpose of this study is to evaluate the safety and PK of PF-07321332 (nirmatrelvir)/ritonavir in adults with severe renal impairment and COVID-19. Eligible participants include those with severe renal impairment (defined as eGFR <30 mL/min/1.73 m^2) and not yet receiving HD (Cohort 1) and individuals receiving HD (Cohort 2).

2.1. Modifications to the Analysis Plan Described in the Protocol

Not applicable.

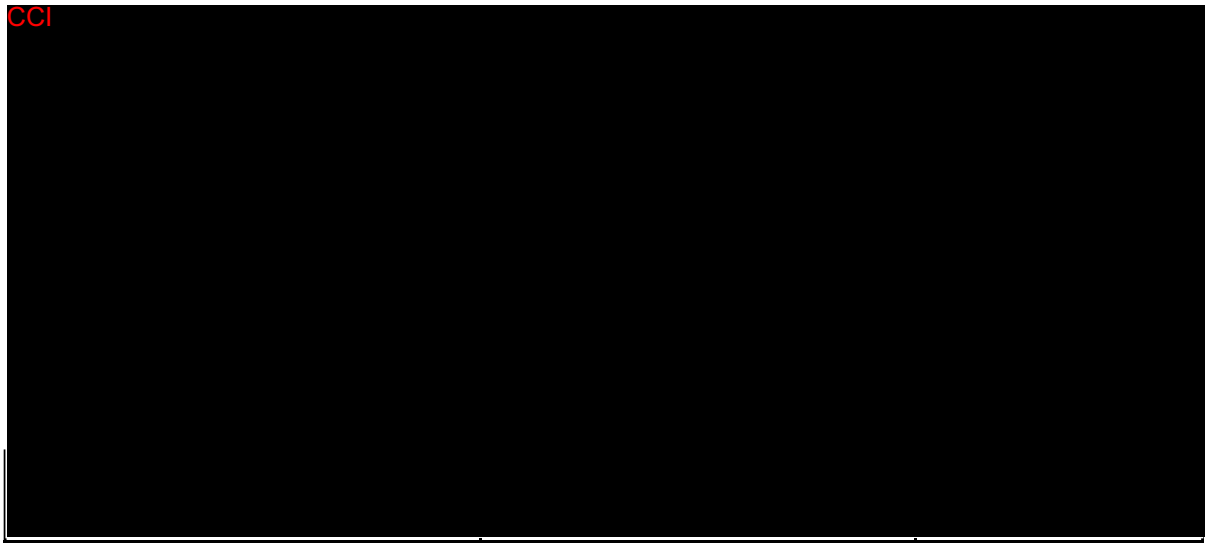
2.2. Study Objectives, Endpoints, and Estimands

Table 2. Objectives and Endpoints

Objectives	***Endpoints***	***Estimands***
Primary:	***Primary:***	***Primary:***
• *To describe the safety and tolerability of nirmatrelvir/ritonavir in adult participants with COVID-19 and severe renal impairment.*	• *Incidence of TEAEs.* • *Incidence of SAEs and AEs leading to discontinuations.*	• *Not Applicable.*
Secondary:	***Secondary:***	***Secondary:***
• *To evaluate the effect of severe renal impairment on the PK of nirmatrelvir in participants not on HD.* • *To evaluate the effect of severe renal impairment on the PK of nirmatrelvir in participants on HD.*	• *Plasma nirmatrelvir PK parameters including C_{max}, CL/F, Vz/F, $AUC_{0\text{-}tau}$, $t_{½}$, and C_{trough} estimated from the population PK model.*	• *Not Applicable.*
• *To evaluate the effect of HD on the PK of nirmatrelvir.*	• *HD clearance (CLd) of nirmatrelvir.* • *Fraction of nirmatrelvir dose removed from the body by dialysis (Fd)*	• *Not Applicable.*
CCI [redacted]		

[redacted]

[redacted]



2.2.1. Primary Estimand(s)

Not applicable.

2.2.2. Secondary Estimand(s)

Not applicable.

2.2.3. Additional Estimand(s)

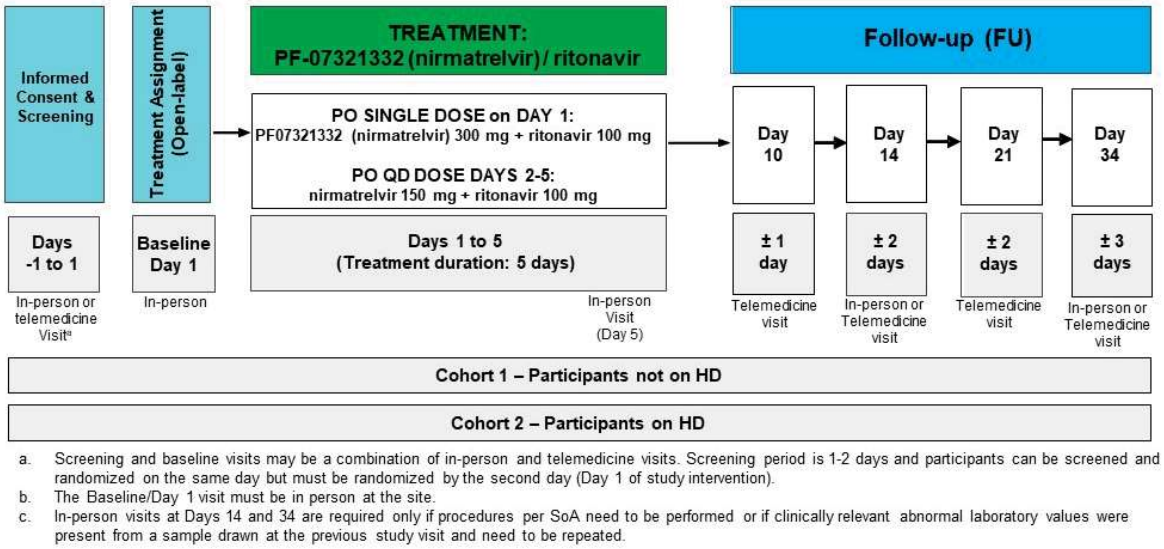
Not applicable.

2.3. Study Design

This is a Phase 1, open-label study to evaluate the effect of severe renal impairment on the PK of nirmatrelvir/ritonavir and the safety and tolerability of nirmatrelvir/ritonavir in adult participants with COVID-19 and severe renal impairment and not yet receiving intermittent hemodialysis (Cohort 1) and severe renal impairment receiving intermittent hemodialysis (Cohort 2). The study will be conducted in 2 parallel cohorts. Cohort 1 will enroll eligible participants with severe renal impairment (defined as eGFR <30 mL/min/1.73 m2) not on hemodialysis. Cohort 2 will enroll eligible participants with severe renal impairment on hemodialysis. All eligible participants will be assigned to receive a single dose of PF-07321332 (nirmatrelvir)/ritonavir 300 mg/100 mg orally on Day 1 followed by PF-07321332 (nirmatrelvir)/ritonavir 150 mg/100 mg QD from Day 2 to Day 5.

Approximately 24 participants (12 participants in Cohort 1 and 12 participants in Cohort 2) will be assigned to study intervention.

Figure 1. Study Design



a. Screening and baseline visits may be a combination of in-person and telemedicine visits. Screening period is 1-2 days and participants can be screened and randomized on the same day but must be randomized by the second day (Day 1 of study intervention).
b. The Baseline/Day 1 visit must be in person at the site.
c. In-person visits at Days 14 and 34 are required only if procedures per SoA need to be performed or if clinically relevant abnormal laboratory values were present from a sample drawn at the previous study visit and need to be repeated.

2.4. Sample Size Determination

The 12 evaluable participants per cohort is considered sufficient to provide a suitable estimate of precision of PK parameters of nirmatrelvir in severe renal impairment participants on HD and not on HD, in which provides approximately 40% precision (the width of 90% confidence interval) for AUC_{inf} and C_{max}. To ensure sufficient PK data for analysis, any participant with insufficient PK samples for analysis may be replaced.

To identify an adequate sample size for PK, we assessed the precision of estimating the PK parameter using different sample sizes, as defined by the width of the resultant confidence intervals represented as a percentage of the mean value of the PK parameter. Currently, no PK data is available in severe renal impairment following multiple doses of nirmatrelvir; therefore, a single dose PK data of nirmatrelvir in severe renal impairment adults not on dialysis (Table 3) was used to determine the CV estimates for nirmatrelvir PK parameters. The CV estimates in Table 3, for nirmatrelvir AUC_{inf} and C_{max} range from 33% to 38% (ie, 0.33 to 0.38).

Table 3. PF-07321332 (nirmatrelvir) PK Parameters Following Single Dose of PF-07321332 (nirmatrelvir) /Ritonavir 100 mg/100 mg in Severe Renal Impairment Patients

PK Parameter (units)	Nirmatrelvir (N=8)
C_{max} (ng/mL)	2369 (38)
AUC_{inf} (ng*hr/mL)	44040 (33)
T_{max} (hr)	3.00 (1.00-6.05)
$t_{1/2}$ (hr)	13.37 ± 3.3225

Values are presented as geometric mean (geometric % CV) except median (range) for T_{max} and arithmetic mean ± SD for $t_{½}$.

The study participants may experience more variability in PK parameters than the available data given the wider range of multiple doses, thus a precision is described with an anticipated CV of 0.2, 0.3, or 0.4.

Table 4 below shows the upper and lower confidence limits and 90% CI width for the mean PK parameter (eg, AUC, $t_{½}$, or C_{max}), presented as a percentage of the mean, for different N and CV. With a sample size of 12 evaluable participants and a CV equal to 0.4, the 90% CI will range from 79.3% – 120.7 % of the mean, and the corresponding CI width will be 41.4% of the mean. The PK parameter will be estimated with a tight 95% CI in the a severe renal impaired population.

Table 4. Percentile Range and Width of 90% Confidence Intervals for the Mean PK Parameter

N	CV=0.2		CV=0.3		CV=0.4	
	Range	Width	Range	Width	Range	Width
8	86.6-113.4%	26.8%	79.9-120.1%	40.2%	73.2-126.8%	53.6%
10	88.5-111.5%	23.1%	82.7-117.3%	34.6%	76.9-123.1%	46.2%
12	89.6-110.4%	20.7%	84.5-115.5%	31.1%	**79.3-120.7%**	**41.4%**
14	90.5-109.5%	19.0%	85.8-114.2%	28.4%	81.1 -119.0%	37.9%

3. ENDPOINTS AND BASELINE VARIABLES: DEFINITIONS AND CONVENTIONS

3.1. Primary Endpoint

- Incidence of TEAEs
- Incidence of SAEs and AEs leading to discontinuations.

3.2. Secondary Endpoint(s)

- Plasma PF-07321332 (nirmatrelvir) PK parameters including C_{max}, CL/F, Vz/F,

$AUC_{0\text{-}tau}$, $t_{½}$, and C_{trough} estimated from the population PK model.

- HD clearance (CL_d) of PF-07321332 (nirmatrelvir).
- Fraction of PF-07321332 (nirmatrelvir) dose removed from the body by dialysis (F_d).

CCI

[redacted]

3.4. Baseline Variables

Baseline visit is set up according to study days of Day -1 to Day 1. Only non-missing results that are prior to the first dose intervention will be considered as Baseline data. The variables for baseline include vital signs, labs (hematology, chemistry, and additional tests), COVID-19 vaccination status, SARS-CoV-2 serology, SARS-CoV-2 RNA, and prior medications. For SARS-CoV-2 RNA concentration data, the Baseline data is on Day 1.

3.5. Safety Endpoints

The safety endpoints of this study are:

- Incidence of TEAEs.
- Incidence of SAEs and AEs leading to discontinuations.

Clinical Data Interchange Standards Consortium (CDISC) and Pfizer Standards (CaPS) will be used for the analysis of standard safety data.

3.5.1. Adverse Events

An adverse event (AE) is any untoward medical occurrence in a study participant administered a product or medical device; the event need not necessarily have a causal relationship with the treatment or usage. An adverse event is considered a Treatment-

[redacted]

Emergent Adverse Event (TEAE) if the event started on or after the study medication start date and time.

3.5.2. Medical History

Medical history in addition to COVID-19 disease history and demographics will be collected at screening. Smoking status will be collected. Medication history of prescription or nonprescription drugs (including vaccinations), and dietary and herbal supplements taken within 30 days prior to the planned first dose will be collected. All doses of COVID-19 vaccinations administered at any time before study participation will be collected and summarized.

3.5.3. Height and Weight

Height and weight will be measured and recorded at screening.

3.5.4. Laboratory Data

The Appendix 3 lists clinical safety laboratory tests to be performed and the protocol SoA for the timing and frequency.

3.5.5. Vital Signs

Vital signs measure include temperature, pulse rate, respiratory rate, oxygen saturation level, and blood pressure.

4. ANALYSIS SETS (POPULATIONS FOR ANALYSIS)

Data for all participants will be assessed to determine if participants meet the criteria for inclusion in each analysis population.

Participant Analysis Set	***Description***
Enrolled	*"Enrolled" means a participant's, or their legally authorized representative's, agreement to participate in a clinical study following completion of the informed consent process and assignment to study intervention. A participant will be considered enrolled if the informed consent is not withdrawn prior to participating in any study activity after screening. Potential participants who are screened for the purpose of determining eligibility for the study, but do not participate in the study, are not considered enrolled, unless otherwise specified by the protocol.*
SAS	*All participants assigned to study intervention and who take at least 1 dose of study intervention. Participants will be analyzed according to the product they actually received.*

Defined Analysis Set	***Description***
PK Concentration	*The PK concentration population is defined as all participants assigned to investigational product and treated who have at least 1 concentration measured.*
PK Parameter	*The PK parameter analysis population is defined as all participants assigned to investigational product and treated who have at least 1 of the PK parameters of interest measured.*

5. GENERAL METHODOLOGY AND CONVENTIONS

5.1. Hypotheses and Decision Rules

This is single arm study and has no statistical hypotheses tested and no formal decision rules for interpreting the study results. All analyses will be descriptive.

5.2. General Methods

Descriptive statistics for all endpoints will be provided by cohort and time point. For most summary tables, unless stated otherwise, cohorts will be presented both separately and combined.

5.2.1. Analyses for Binary Endpoints

For binary endpoints, number and proportion of participants with the event of interest (with corresponding sample size) will be summarized for each cohort and overall.

5.2.2. Analyses for Continuous Endpoints

For continuous endpoints, values and/or changes from baseline over time, as applicable, will be summarized for each cohort and overall. Standard descriptive statistics (n, mean, standard deviation, median, interquartile range, minimum, and maximum) will be utilized.

5.2.3. Analyses for Categorical Endpoints

For categorical endpoints, number and proportion of participants for each category (with corresponding sample size) will be summarized for each cohort and overall.

5.3. Methods to Manage Missing Data and Non-Quantifiable Data

In summary tables of concentration data by cohort, visit day and time, statistics will be calculated having set concentrations to missing if one of the following applies:

- A concentration has been collected as ND (not done) or NS (no sample), or
- A deviation in sampling time is of sufficient concern or a concentration has been flagged anomalous by the pharmacokineticist. In such cases, data for all participants will be assessed to determine if samples meet the criteria for exclusion from analysis prior to releasing the database, and classifications will be documented per standard operating procedures.

SARS-CoV-2 RNA < LLOQ is imputed as $1.7 = \log_{10}(50)$ for non-missing results.

As all analyses are descriptive, missing endpoint data will result in a summary where the N for that endpoint (and time point) is smaller than the total N of the corresponding analysis set. No imputation of the missing data will be performed.

Missing PK concentration values will generally be handled as described above. Non-missing concentrations that are below the limit of quantitation will be reported as such in listings and imputed as zero for summary tables and figures.

Additional details for handling missing data in the population PK modeling will be described in a population modeling analysis plan.

Missing safety data such as dates or severities of adverse events will be handled using standard algorithms in accordance with CDISC and CaPS standards.

6. ANALYSES AND SUMMARIES

6.1. Primary Endpoint

6.1.1. Primary Endpoint/Estimand Analysis

6.1.1.1. Main Analysis

Incidence of TEAEs through Day 34, SAEs, and AEs leading to discontinuation will be summarized with number and percent of participants in the SAS for each cohort, and overall, in accordance with CDISC and CaPS standards.

6.1.1.2. Sensitivity/Supplementary Analysis

Not applicable.

6.2. Secondary Endpoint(s)

6.2.1. Plasma nirmatrelvir PK parameters: CL/F, V_z/F, $AUC_{0\text{-}tau}$, C_{max}, $t_{1/2}$ and C_{trough}

- Nonlinear mixed effect modeling will be performed using the PK concentration analysis set (see Section 4) to evaluate pharmacokinetic parameters of nirmatrelvir (CL/F, V_z/F, $AUC_{0\text{-}tau}$, C_{max}, $t_{1/2}$ and C_{trough}). The detailed procedures for the population PK analysis, including the model implementation and evaluation will be described in a population modeling analysis plan. Also, the results of the analysis will be summarized in a population modeling and analysis report, separate from the clinical study report.

- Plasma concentrations of nirmatrelvir from venous or Tasso samples will be summarized using the PK concentration analysis set. A listing of plasma concentrations at the nominal sampling time by participant, method of blood collection, and cohort will be provided. A listing of deviations from the nominal sampling time will also be provided. For each cohort, and overall, the plasma concentrations will be summarized by nominal sampling time using appropriate descriptive statistics (eg, number of participants/samples, number of concentrations at or above the lower limit of quantification (NALQ), mean, SD, minimum, median, maximum, and coefficient of variation).

- Individual nirmatrelvir plasma concentration profiles (ie, concentration vs. time data) will be presented graphically by cohort (ie, spaghetti plots) using actual sample collection time on both linear and semilogarithmic scales. Median concentration time profiles will be presented by cohort on both linear and semilogarithmic scales using nominal sampling time. Additional graphical presentations of PK data may be included at the discretion of the PK scientist.

6.2.2. HD clearance (CL_d) of PF-07321332 (nirmatrelvir)

Hemodialysis clearance (CL_d) of nirmatrelvir will be calculated using the following relationship:

$$CL_d = [(C_{in} - C_{out}) / C_{in}] \times [Qb \times (1 - HCT)]$$

where C_{in} and C_{out} are plasma concentrations measured in blood samples entering and exiting the dialyzer, respectively; Q_b and HCT are blood flow rate entering the dialyzer and hematocrit measured at each collection time, respectively. Individual time point CL_d values obtained using this method will be used to calculate an average subject CL_d.

6.2.3. Fraction of PF-07321332 (nirmatrelvir) dose removed from the body by dialysis (F_d)

Fraction of nirmatrelvir dose removed from the body by dialysis (F_d) will be calculated as follow:

$$F_d = 100\% \times A_d / Dose$$

[redacted]

[redacted]

where A_d is the amount of drug removed by the dialysis and is calculated as follows:

$$A_d = CL_d \times AUC_{t0\text{-}t1}$$

where for $AUC_{t0\text{-}t1}$, t_0 marks the start time and t_1 the termination of the hemodialysis session.

CCI

[redacted]

CCI

[redacted]

[redacted]

[redacted]

CCI

[redacted]

6.4. Subset Analyses

Not applicable.

6.5. Baseline and Other Summaries and Analyses

6.5.1. Baseline Summaries

Baseline demographic and other characteristics described in 3.4 will be tabulated for the SAS and summarized by cohort, and overall. Quantitative variables will be described by standard descriptive statistics (N, mean, standard deviation, median, minimum, and maximum), and qualitative variables will be summarized by number and proportion in each category.

Demographic data collected at screening will be reported.

6.5.2. Study Conduct and Participant Disposition

The number of participants screened, assigned to study treatment, completing study treatment, and completing the study will be summarized. The reasons for discontinuation will be summarized by cohort.

6.5.3. Study Treatment Exposure

The number of doses of the study treatment received and the percentage compliance will be summarized.

6.5.4. Concomitant Medications and Nondrug Treatments

Concomitant medications and non-drug treatments will be summarized by cohort in accordance with CDISC and CaPS standards.

The types of vaccines received will be summarized for number and percent of participants for each vaccine type overall and each cohort.

6.5.5. Vaccination

Vaccination data will be collected in con-med data set (ADCM), the variable MCAT represents the type of vaccine (i.e., Pfizer, J&J and others). For participant who have more than one dose of vaccine, there are more than one record in the ADCM data set. So the number of doses can be derived from the record.

The number of doses received will be summarized for number and percent of subject for each vaccine dose overall and each cohort.

6.6. Safety Summaries and Analyses

All safety analyses will be performed on the safety population, ie, Safety Analysis Set (SAS). Safety summaries and analyses will utilize CDISC and CaPS standards.

6.6.1. Adverse Events

As this study has only one treatment, the 3-tier approach to adverse event reporting will not be utilized. For each AE, the number and percent incidence will be summarized by cohort, but the incidence will not be formally compared among cohorts. No p-values or confidence intervals will be generated and therefore, no multiplicity adjustment will be used. AEs will be arranged alphabetically within system organ class in the summary tables.

It should be recognized that most studies are not designed to reliably demonstrate a causal relationship between the use of a pharmaceutical product and an adverse event or a group of adverse events. Except for select events in unique situations, studies do not employ formal adjudication procedures for the purpose of event classification. As such, safety analysis is generally considered as an exploratory analysis and its purpose is to generate hypotheses for further investigation.

6.6.2. Laboratory Data

Lab data and the corresponding changes from baseline will be summarized over time (Day 1, 5) by cohort, and overall using standard descriptive statistics. Any abnormalities of potential clinical concern according to the criteria specified by the Pfizer reporting standards will be described. Data will be presented in tabular and/or graphical format, as appropriate.

Data collected at screening that are used for inclusion/exclusion criteria will be considered source data, and will not be required to be reported, unless otherwise noted.

6.6.3. Vital Signs

SBP, DBP, pulse rate, respiratory rate, oral temperature, and SpO_2 will be summarized over time (Day 1, 5, 14, 34) by cohort, and overall using standard descriptive statistics. Any abnormalities of potential clinical concern (see Table 5) will be described. Data will be presented in tabular and/or graphical format, as appropriate.

Table 5. Post-Baseline Vital Signs Categories

Parameter (units)	Criteria
Systolic Blood Pressure (mmHg)	Value < 90
	Increase ≥ 30
	Decrease ≥ 30
Diastolic Blood Pressure (mmHg)	Value < 50
	Increase ≥ 20
	Decrease ≥ 20
Pulse Rate (bpm)	Value < 40
	Value > 120

6.6.4. Electrocardiograms

Not applicable.

6.6.5. Physical Examination

Medical history and physical examination collected during the course of the study will be considered source data and will not be required to be reported, unless otherwise noted. However, any untoward findings identified on physical and/or neurological examinations conducted during the active collection period will be captured as AEs, if those findings meet the definition of an AE.

7. INTERIM ANALYSES

No interim analysis will be conducted for this study.

As this is an open-label, unblinded study, the sponsor may conduct reviews of the data during the study for the purpose of safety assessment, facilitating PK/PD modeling, and/or supporting clinical development.

8. REFERENCES

None.

9. APPENDICES

Appendix 1. Summary of PK Concentration Analyses

Endpoint	Analysis Type	Population	Data Inclusion and Rules for Handling Intercurrent Events and Missing Data	Analysis Model
PK concentration	Summary (nominal sampling time)	PK concentration analysis set	Missing data will not be imputed. Concentrations BLQ imputed as zero.	Descriptive stats for overall, Cohort 1 and Cohort 2
	Figure – Individual concentration vs. time profiles (actual sampling time)	PK concentration analysis set	Missing data will not be imputed. Concentrations BLQ imputed as zero.	Spaghetti plots for Cohort 1, Cohort 2
	Figure – Median concentration vs. time profile (nominal sampling time)	PK concentration analysis set	Missing data will not be imputed. Concentrations BLQ imputed as zero.	Summary plots for Cohort 1 and Cohort 2
	Listing (nominal sampling time)	PK concentration analysis set	Concentrations BLQ reported as such.	Listing by cohort, participant, nominal sampling time; includes method of blood collection, actual sampling time, and deviation from nominal sampling time

Appendix 2. Data Derivation Details

Appendix 2.1. Definition and Use of Visit Windows in Reporting

Reporting will be based on nominal visits. When categorizing dated assessments under nominal times for the purpose of reporting, the protocol-defined visit windows will be utilized (see the protocol schedule of activities). Unplanned visits will be listed, but generally not summarized, except in the case of lab abnormalities and vital sign categories summary tables.

Appendix 2.2. Endpoint Derivations

See the Analysis and Reporting Plan for any relevant endpoint derivations.

Appendix 2.3. Definition of Protocol Deviations That Relate to Statistical Analyses/Populations

Protocol deviations that may result in exclusion of specific data points (eg, PK concentrations) from analysis include deviations related to:

- Compliance, missed doses, dosing/administration errors.
- Prohibited concomitant medications.
- Participant conditions affecting drug metabolism such as hepatic impairment.
- PK samples not done or not properly collected, stored, or handled.

Appendix 3. Clinical Laboratory Tests

The following safety laboratory tests will be performed at times defined in the SoA section of this protocol. Unscheduled clinical laboratory measurements may be obtained at any time during the study to assess any perceived safety issues.

Table 6. Protocol-Required Safety Laboratory Assessments

Hematology	Chemistry	Other	Additional Tests
Hemoglobin Hematocrit RBC count Platelet count WBC count Total neutrophils (Abs) Eosinophils (Abs) Monocytes (Abs) Basophils (Abs) Lymphocytes (Abs)	Urea and creatinine eGFR Glucose Calcium Sodium Potassium Chloride Total CO2 (bicarbonate) AST, ALT Total bilirubin Alkaline phosphatase Albumin Total protein	Pregnancy test (β-hCG)a SARS-CoV-2 serology (IgG and IgM)	**For suspected DICI/DIKI:** Creatinine (Scr) **Needed for Hy's Law** AST, ALT (repeat) Total bilirubin (repeat) Albumin Alkaline phosphatase (repeat) Direct bilirubin Indirect bilirubin Creatine kinase GGT PT/INR Total bile acids Acetaminophen drug and/or protein adduct levels Hepatitis serology

a. Local urine testing using the central lab-provided test (locally purchased test is acceptable after Day 1 if the participant and/or home health staff does not have one provided by the central lab) will be standard for the protocol unless serum testing is required by local regulation or IRB/EC or the participant is anuric. A negative urine or serum (β-hCG) pregnancy test must be confirmed at screening and prior to dispensing treatment for ALL WOCBP.

Appendix 4. List of Abbreviations

Abbreviation	Term
Abs	Absolute
AE	adverse event
AUC	area under the curve
$AUC_{0\text{-}tau}$	AUC over a dosing interval
AUC_{inf}	AUC from time 0 extrapolated to infinite time
BLQ	below the limit of quantitation
BP	blood pressure
CaPS	CDISC aligned Pfizer Standards
CDISC	Clinical Data Interchange Standards Consortium
CI	confidence interval
CL_d	hemodialysis clearance
CL/F	apparent oral clearance
C_{max}	maximum observed concentration
C_{min}	minimum plasma concentration
COVID-19	coronavirus disease 2019
CRF	case report form
CSR	clinical study report
C_{trough}	Pre-dose trough concentration
CV	Coefficient of variation
DMC	data monitoring committee
EC	Ethics committee
ECG	electrocardiogram
E-DMC	external data monitoring committee
eDiary	Electronic diary
ET	early termination
F_d	fraction of drug removed from the body
FDA	Food and Drug Administration
GCP	Good Clinical Practice
HD	hemodialysis
ICD	informed consent document
IRB	Institutional Review Board
LLOQ	lower limit of quantitation
LOD	limit of detection
MedDRA	Medical Dictionary for Regulatory Activities
N/A	not applicable
NALQ	Number of concentrations at or above the lower limit of quantification
NP	nasopharyngeal
PK	pharmacokinetic(s)
PR	pulse rate

Abbreviation	Term
PT	preferred term
RR	relative risk
RT-PCR	real time polymerase chain reaction
SAE	serious adverse event
SAP	statistical analysis plan
SAS	Safety analysis set
SARS-CoV-2	severe acute respiratory syndrome coronavirus 2
SD	standard deviation
SGS	Statistical Guidance Standards
SOP	standard operating procedure
SoA	schedule of activities
SpO_2	oxygen saturation
TEAE	treatment emergent adverse event
ULN	upper limit of normal
WHO	World Health Organization
WHODD	World Health Organization Drug Dictionary

CLINICAL AND MEDICAL CONTROLLED DOCUMENT (CMCD) REQUIRED FORM			
Identifier	**Version**	**Title**	**Effective Date**
DMB02-GSOP-RF01	8.0	STATISTICAL ANALYSIS PLAN APPROVAL SIGNATURE FORM	27-Jan-2020

NOTE: This form is used to document the approval of a Statistical Analysis Plan (SAP) and any subsequent amendment of the SAP.

SAP Title: Include protocol number and format per following example: A### Statistical Analysis Plan	C4671028 Final Statistical Analysis Plan v1.0 19AUG22
☒ **Approval of SAP**	**SAP Version:** v1.0
☐ **Approval of Amendment to SAP**	
Name and Title of Person Submitting form: (SAP Author)	PPD
Date Submitted: (dd-Mmm-yyyy)	25-AUG-2022

Approval indicates that the SAP provides analysis specifications consistent with the analysis outlined in the protocol and meets the standards and requirements used for programming of tables, listings and figures.

SAP Approver's Name:	PPD
SAP Approver's Title:	PPD
Signature:	PPD
Date: (dd-Mmm-yyyy)	25 Aug 2022 12:38:038-0400

[redacted]