Protocol C4711001

A PHASE 1, RANDOMIZED, DOUBLE-BLIND, SPONSOR-OPEN, VEHICLE-CONTROLLED, FIRST-IN-HUMAN, MULTIPLE-DOSE STUDY, TO INVESTIGATE THE SAFETY, TOLERABILITY, AND PHARMACOKINETICS, OF TOPICALLY ADMINISTERED PF-07295324 AND PF-07259955, IN HEALTHY ADULT PARTICIPANTS

Statistical Analysis Plan (SAP)

Version: 1

Date: 03 Feb 2022

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1. VERSION HISTORY

Table 1. Summary of Changes

Version/ Date	Associated Protocol Amendment	Rationale	Specific Changes
1 03 Feb 2022	Original 06 Dec 2021	N/A	N/A

2. INTRODUCTION

PF-07295324 and PF-07259955 are JAK inhibitors, and are proposed for topical treatment of mild to moderate AD.

The purpose of the study is to evaluate the safety, local and systemic tolerability, and pharmacokinetics following multiple doses of topically applied, maximum feasible formulation of PF-07295324 (0.12% w/w) and PF-07259955 (2% w/w), on approximately 20% BSA in healthy adult participants.

As is typical for first-in-human (FIH) studies, the population envisioned for this study will be healthy, adult, male and female participants. Female participants will be confirmed to be categorized as women of non-childbearing potential (WONCBP) as, at the present time, embryo fetal developmental toxicology studies with PF-07295324 and PF-07259955 have not been conducted. In male participants, appropriate measures to minimize potential transfer of PF-07295324 and PF-07259955 via semen to partners are expected to be followed (refer to Section 10.4).

As this is the first time PF-07295324 and PF-07259955 will be topically administered in humans, safety risks to participants will be minimized by conducting the study in in-patient settings, with adequate monitoring of local and systemic AEs, safety laboratory parameters, 12-lead ECGs, and vital signs. Cumulative safety data will be reviewed after the completion of each cohort.

The safety, local and systemic tolerability, and PK from this study will support the parallel clinical development of PF-07295324 and PF-07259955.

This statistical analysis plan (SAP) provides the detailed methodology for summary and statistical analyses of the data collected in Study C4711001. This document may modify the plans outlined in the protocol; however, any major modifications of the primary endpoint definition or its analysis will also be reflected in a protocol amendment.

2.1. Study Objectives, Endpoints, and Estimands

Objectives	*Endpoints*
Primary:	***Primary:***
• *To evaluate the safety, and local and systemic tolerability, of PF-07295324 and PF-07259955, following multiple doses of topically administered PF-07295324 or PF-07259955, on approximately 20% BSA in healthy adult participants.*	• *Incidence and severity of systemic AEs, safety laboratory tests, vital signs (including blood pressure and pulse rate), and heart rhythms as assessed via 12-lead electrocardiogram (ECG).* • *Incidence and severity of application site AEs as assessed by Draize score.*
Secondary:	***Secondary:***
• *To characterize plasma PK following multiple topical applications of PF-07295324 and PF-07259955.*	• *Plasma PK of multiple topical doses of PF-07295324 and PF-07259955, as data permits:* *Day 1: C_{max}, T_{max}, C_{avg}, C_{trough}, AUC_{tau}* *Day 10: C_{max}, T_{max}, C_{avg}, C_{trough}, AUC_{tau}, R_{ac} (C_{max}), R_{ac}(AUC_{tau}), $t_{½}$, CL/F, and V_z/F*
CCI [redacted]	[redacted]
[redacted]	[redacted]

2.2. Study Design

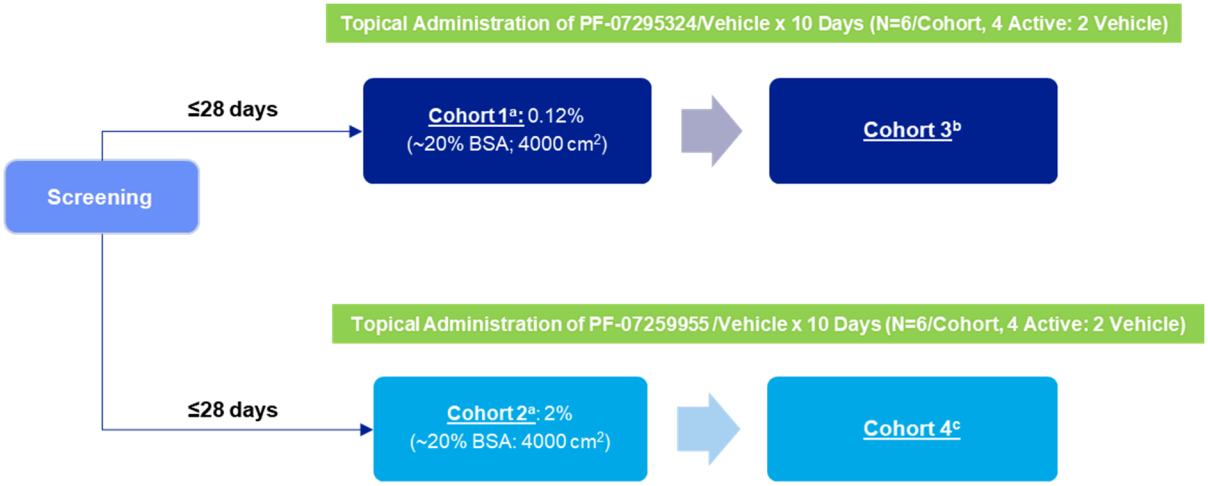
C4711001 is an investigator- and participant-blinded, interventional, randomized, vehicle-controlled, Phase 1 study to evaluate the safety, and local and systemic tolerability and pharmacokinetics of maximum feasible formulation of topical JAK inhibitors, PF-07295324 (0.12%) and PF-07259955 (2%) in healthy adult participants.

This study will enroll healthy adult participants in ≤4 cohorts: 2 planned cohorts and 2 optional cohorts. Approximately 6 participants will be enrolled in each cohort, randomized as 4 active:2 vehicle. Cohort 1 and the optional Cohort 3 will be assigned to PF-07295324/vehicle, administered topically as an ointment. Cohort 2 and the optional Cohort 4 will be assigned to PF-07259955/vehicle administered topically as a cream.

Participants will be enrolled in the optional cohorts in a sequential design to the respective planned cohort, as shown in Figure 1. Planned cohorts assigned to different interventions may progress simultaneously. Similarly, optional cohorts assigned to different interventions may progress simultaneously (Figure 1).

Up to 2 optional cohorts (Cohort 3 and Cohort 4) of up to 6 participants/cohort may be enrolled in this study. Participants enrolled in the optional cohort will be randomized to either active or vehicle (4:2). The optional cohorts may be used to explore lower strength formulations on approximately 20% BSA, or to repeat the maximum feasible formulation on lower body surface area, or to administer maximum feasible formulation at a less frequent dosing regimen on approximately 20% BSA. Participants enrolled in the optional cohorts will be guided by the same stopping criteria as the planned cohorts.

Figure 1. Study Schema



a. PF-07295324 (0.12%)/vehicle in Cohort 1 or PF-07259955 (2%)/vehicle in Cohort 2, will be topically applied on approximately 20% body surface area, Q12H from D1 to D9; only morning (AM) dose will be applied on D10.

b. Based on review of emerging safety from Cohort 1, optional Cohort 3 may be enrolled to explore lower formulation strength of PF-07295324, topically applied on approximately 20% BSA or PF-07295324 (0.12%) on lower body surface area or at a less frequent dosing regimen on approximately 20% BSA.

c. Based on review of emerging safety assessments from Cohort 2, optional Cohort 4 may be enrolled to explore lower formulation strength of PF-07259955 topically applied on approximately 20% BSA or PF-07259955 (2%) on lower body surface area or at a less frequent dosing regimen on approximately 20% BSA.

3. ENDPOINTS AND BASELINE VARIABLES: DEFINITIONS AND CONVENTIONS

3.1. Primary Endpoint(s): Safety Endpoints

- *Incidence and severity of systemic AEs, safety laboratory tests, vital signs (including blood pressure and pulse rate), and heart rhythms as assessed via 12-lead electrocardiogram (ECG).*

- *Incidence and severity of application site AEs as assessed by Draize score.*

The following data are considered in standard safety summaries (see protocol for collection days, baseline assessment, and list of parameters):

- AEs;
- Safety laboratory tests;
- Vital signs (Blood Pressure and Pulse rate);
- ECG.

3.1.1. Adverse Events

An adverse event (AE) is considered a Treatment-Emergent Adverse Event (TEAE) if the event started during the effective duration of treatment. All events that start on or after the first dosing day and time/start time, if collected, but before the last dose plus the lag time, will be flagged as TEAEs. The lag time is defined by the Pfizer Standard of 365 days post last dose. The algorithm will not consider any events that started prior to the first dose date. If an AE starts on the same day as the first dose date, it will be considered treatment emergent unless the CRF data indicates otherwise via explicitly recording time for AE onset which was occurred before the first treatment dosing.

Local toleration of skin irritation assessment will be assessed as specified in the Schedule of Activities (SoA) given in the protocol, by Draize scoring and via clinical observation (see Section 8.2.5 in the protocol).

3.1.2. Laboratory Data

Safety laboratory tests will be performed as described in the protocol. See Protocol Appendix 2 for the list of clinical safety laboratory tests to be performed.

To determine if there are any clinically significant laboratory abnormalities, the hematological, clinical chemistry (serum) and urinalysis safety tests will be assessed against the criteria specified in the sponsor reporting standards. The assessment will not take into account whether each subject's baseline test result is within or outside the laboratory reference range for the particular laboratory parameter.

Baseline of safety laboratory tests is defined as the pre-dose measurement on Day -1. If a value is missing on Day -1, then the last pre-dose measurement will be used as baseline.

3.1.3. Vital Signs

Supine blood pressure and pulse rate measurements will be taken at all time points listed in the SoA given in the protocol.

The baseline measurement is the pre-dose measurement at Hour 0 taken on Day 1. If a value is missing on Day 1, then the last pre-dose measurement will be used as baseline.

3.1.4. ECG

Triplicate 12-lead ECGs will be obtained approximately 2 to 4 minutes apart; the average of the triplicate ECG measurements collected before dose administration on Day 1 will serve as each participant's time-controlled baseline QTcF value. If a value is missing on Day 1, then the last pre-dose measurement will be used as baseline.

The QT, QTc, PR, QRS and heart rate will be recorded at each assessment time.

If not supplied, QTcF will be derived using Fridericia's heart rate correction formula:

$$QTcF = QT/(RR)^{1/3} \qquad \text{where RR} = 60/\text{HR (if not provided)}$$

3.2. Secondary Endpoint(s): PK Parameters

- *Plasma PK of multiple topical doses of PF-07295324 and PF-07259955, as data permits:*

  Day 1: C_{max}, T_{max}, C_{avg}, C_{trough}, AUC_{tau}

  Day 10: C_{max}, T_{max}, C_{avg}, C_{trough}, AUC_{tau}, R_{ac} (C_{max}), R_{ac}(AUC_{tau}), $t_{½}$, CL/F, and V_z/F

Actual PK sampling times will be used in the derivation of PK parameters.

PK parameters for PF-07295324 and PF-07259955, following topical administration, will be derived from the plasma concentration-time profiles using non-compartmental methods, as data permit.

The PK parameters to be assessed in this study, their definition, and method of determination are listed in Table 2. Actual PK sampling times will be used in the derivation of PK parameters.

Table 2. Plasma PK Parameters

Parameter	Day	Definition	Method of Determination
C_{max}	1, 10	Maximum plasma concentration	Observed directly from data
T_{max}	1, 10	Time at which maximum plasma concentration occurs	Observed directly from data
C_{avg}	1, 10	Average plasma concentration	AUC_{tau}/tau; where tau is the dosing interval and AUC_{tau} is area under the plasma concentration-time profile from time zero to time tau (τ), the dosing interval
C_{trough}	1, 5, 7 and 10	Pre-dose Concentration	Observed directly from data
$t_{½}$[a]	10	Terminal half-life	$Log_e(2)/k_{el}$, where k_{el} is the terminal phase rate constant calculated by a linear regression of the log-linear concentration-time curve
AUC_{tau}	1, 10	Area under the plasma concentration-time profile from time zero to time tau (τ), the dosing interval	Linear/Log trapezoidal method up to tau, the dosing interval
CL/F	10	Apparent clearance	$Dose/AUC_{tau}$
V_z/F[a]	10	Apparent volume of distribution	$Dose/(AUC_{tau} \times k_{el})$
R_{ac} (C_{max})	10	Accumulation ratio for C_{max}	$C_{max,\ Day\ 10}/C_{max,\ (first\ dose)}$
R_{ac} (AUC_{tau})	10	Accumulation ratio for AUC_{tau}	$AUC_{tau,\ Day\ 10}/AUC_{tau,\ (first\ dose)}$

a. as data permit.

CCI

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 prior to unblinding and releasing the database and classifications will be documented per standard operating procedures.

Population	Description
Enrolled	All participants who sign the ICD.
Randomly assigned to investigational product	All participants who sign the ICD and determined eligible to participate in the study.
Evaluable	The evaluable population is defined as all participants who are randomly assigned to IP and who are applied at least 1 dose of IP.
Safety	All participants randomly assigned to IP and who are applied at least 1 dose of IP. Participants will be analyzed according to the product they actually received.
PK concentration	All participants randomly assigned to investigational product who received an application of PF-07295324 or PF-07259955 and in whom at least 1 plasma sample concentration value is reported.
PK parameter	All participants randomly assigned to investigational product who received an application of PF-07295324 or PF-07259955 and who have at least 1 of the PK parameters of interest calculated.

4.1. Treatment Misallocations

All analyses will be performed on an "as-treated" basis and will not include data from participants who are randomized but not treated.

If a participant takes a treatment that is not consistent with the treatment they are randomized to, for example takes a treatment out of sequence or takes the same treatment twice, then they will be reported under the treatment that they actually receive for all safety, PK and pharmacodynamic analyses, where applicable.

4.2. Protocol Deviations

Participants who experience events that may affect their PK profile may be excluded from the PK analysis. At the discretion of the pharmacokineticist, a concentration value may also be excluded if the deviation in sampling time is of sufficient concern or if the concentration is anomalous for any other reason.

A full list of protocol deviations will be compiled and reviewed to identify major and minor deviations prior to database closure.

5. GENERAL METHODOLOGY AND CONVENTIONS

5.1. Hypotheses and Decision Rules

No formal hypothesis testing will be performed in this study.

5.2. General Methods

Descriptive analyses will be performed. Some measures will be summarized using graphical representations, where appropriate.

5.2.1. Analyses for Continuous Endpoints

For continuous variables, the data will be summarized using the number of subjects, mean, median, standard deviation, minimum, and maximum in accordance with current Pfizer's data and reporting standards. For appropriate PK parameters, geometric mean and geometric coefficient of variation (geocv%) will also be summarized.

5.2.2. Analyses for Categorical Endpoints

For categorical or ordinal variables, number of subjects, numbers and percentages of subjects meeting the categorical criteria will be supplied in accordance with current Pfizer's data and reporting standards.

5.3. Methods to Manage Missing Data

For the analysis of safety endpoints, the sponsor data standard rules for imputation will be applied.

Methods to handle missing PK data are described below.

Concentrations Below the Limit of Quantification:

In all data presentations (except listings), concentrations below the limit of quantification (BLQ) will be set to zero. (In listings BLQ values will be reported as "<LLQ" where LLQ will be replaced with the value for the lower limit of quantification).

Deviations, Missing Concentrations and Anomalous Values:

In summary tables and plots of median profiles, statistics will be calculated having set concentrations to missing if 1 of the following cases is true:

1. A concentration has been collected as ND (ie, not done) or NS (ie, no sample),

2. A deviation in sampling time is of sufficient concern or a concentration has been flagged anomalous by the pharmacokineticist.

Note that summary statistics will not be presented at a particular time point if more than 50% of the data are missing.

Pharmacokinetic Parameters:

Actual PK sampling times will be used in the derivation of PK parameters. If a PK parameter cannot be derived from a subject's concentration data, the parameter will be coded as NC (ie, not calculated). (Note that NC values will not be generated beyond the day that a subject discontinues). In summary tables, statistics will be calculated by setting NC values to

missing; and statistics will be presented for a particular dose with ≥3 evaluable measurements.

If an individual subject has a known biased estimate of a PK parameter (due for example to an unexpected event such as vomiting before all the compound is adequately absorbed from the gastrointestinal tract), this will be footnoted in summary tables and will not be included in the calculation of summary statistics or statistical analyses.

6. ANALYSES AND SUMMARIES

6.1. Primary Endpoint(s)

6.1.1. Safety Summaries and Analyses

All safety analyses will be performed on the safety population (See Section 4).

AEs, ECGs, BP, pulse rate, skin irritation assessment, and safety laboratory data will be reviewed and summarized on an ongoing basis during the study, to evaluate the safety of participants. Any clinical laboratory, ECG, BP, and pulse rate abnormalities of potential clinical concern will be described. Safety data will be presented in tabular and/or graphical format and summarized descriptively, where appropriate.

Medical history and physical examination and neurological examination information, as applicable, collected during the course of the study will be considered as 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. Data collected at screening that are used for inclusion/exclusion criteria, such as laboratory data, ECGs, and vital signs, will be considered source data, and will not be required to be reported, unless otherwise noted. Demographic data collected at screening will be reported.

PF-07295324 and PF-07259955 will have corresponding vehicle groups throughout, ie, vehicle groups will be summarized by administration type (ointment and cream).

6.1.1.1. Adverse Events

Adverse events will be reported in accordance with the sponsor reporting standards.

Subject discontinuations due to adverse events will be detailed by treatment. Data will be reported in accordance with sponsor reporting standards.

Skin irritation assessment using Draize Score will be listed and summarized by treatment.

6.1.1.2. Laboratory Data

Laboratory data will be listed and summarized by treatment in accordance with the sponsor reporting standards.

6.1.1.3. Vital Signs

Single supine blood pressure and pulse will be collected at times specified in the SoA in the protocol.

The following vital signs endpoints will be determined and summarized for each treatment group:

- Actual values, change from baseline in supine blood pressure and pulse rate over all measurements taken postdose;
- The maximum decrease and increase from baseline over all measurements taken postdose for supine blood pressure.

The increase from baseline will be calculated by subtracting the baseline value from each post-dose measurement to give the change from baseline for each participant. The maximum of these values over the duration of dosing will be reported as maximum increase from baseline, except where a participant does not show an increase. In such an instance, the minimum decrease will be reported.

Similarly, decrease from baseline will be calculated by subtracting each post-dose measurement from individual participant's baseline value. Maximum decrease from baseline will be reported as the minimum value of the changes from baseline. In cases where a participant does not show a decrease, the minimum increase will be reported.

Maximum absolute values and changes from baseline for vital signs will also be tabulated by treatment using categories as defined in Appendix.

6.1.1.4. ECG

Changes from baseline for the ECG parameters QT interval, heart rate, QTc interval, PR interval, and QRS complex will be summarized by treatment and time.

The maximum absolute value (post-dose) and the maximum increase from baseline for QTcF, QT, heart rate, PR and QRS, will be determined over all measurements taken post-dose and reported.

The number (%) of participants with maximum postdose QTc values and maximum increases from baseline in the following categories will be tabulated by treatment:

Safety QTc Assessment

Degree of Prolongation	***Mild (msec)***	***Moderate (msec)***	***Severe (msec)***
Absolute value	*>450-480*	*>480-500*	*>500*
Increase from baseline		*30-60*	*>60*

In addition, the number of participants with uncorrected QT values >500 msec will be summarized.

If more than 1 ECG is collected at a nominal time after dose administration (for example, triplicate ECGs), the mean of the replicate measurements will be used to represent a single observation at that time point. If any of the 3 individual ECG tracings has a QTc value >500 msec, but the mean of the triplicates is not >500 msec, the data from the participant's individual tracing will be described in a safety section of the clinical study report (CSR) in order to place the >500-msec value in appropriate clinical context. However, values from individual tracings within triplicate measurements that are >500 msec will not be included in the categorical analysis unless the average from the triplicate measurements is also >500 msec. Changes from baseline will be defined as the change between the postdose QTc value and the average of the time-matched baseline triplicate values on Day -1, or the average of the predose triplicate values on Day 1.

6.2. Secondary Endpoint(s)

6.2.1. PK Parameters

All PK analysis will be performed on the PK analysis set (See Section 4).

The PK parameters detailed in Table 2 will be listed and summarized for participants in the PK concentration population (see Section 4). Missing values will be handled as detailed in Section 5.3. The PK parameters will be calculated using standard non-compartmental methods. Each PK parameter will be summarized by cohort, dose and will include the set of summary statistics as specified in the table below.

Table 3. PK Parameters to be Summarized Descriptively

Parameter	Summary Statistics
AUC_{tau}, C_{avg}, C_{max}, C_{trough}, R_{ac} (C_{max}), R_{ac}(AUC_{tau}), CL/F, V_z/F	N, arithmetic mean, median, cv%, standard deviation, minimum, maximum, geometric mean and geometric cv%.
T_{max}	N, median, minimum, maximum.
$t_{1/2}$	N, arithmetic mean, median, cv%, standard deviation, minimum, maximum.

No formal inferential statistics will be applied to the PK data.

The plasma concentration of PF-07295324 and PF-07259955 will be listed and descriptively summarized, by nominal PK sampling time and by treatment group. Individual participant, mean and median profiles of the plasma concentration-time data of PF-07295324 and PF-07259955 will be plotted by treatment group using actual (for individual) and nominal (for mean and median) times, respectively. Mean and median profiles of PF-07295324 and PF-07259955 will be presented separately, on both linear and log scales.

The plasma PK parameters of PF-07295324 and PF-07259955 listed in Table 2, will be summarized descriptively by treatment group and by day, in accordance with Pfizer data standards, as data permit.

Supporting data from the estimation of t½ will be listed by analyte where applicable: terminal phase rate constant (k_{el}); goodness of fit statistic from the log-linear regression (r^2); and the first, last, and number of time points used in the estimation of k_{el}. This data may be included in the clinical study report.

Presentations for PF-07295324 and PF-07259955 concentrations will include:

- A listing of all concentrations sorted by subject ID, cohort, dose and nominal time postdose. The concentration listing will also include the actual times. Deviations from the nominal time will be given in a separate listing.

- A summary of concentrations by cohort, dose and nominal time postdose, where the set of statistics will include n, mean, median, standard deviation, coefficient of variation (cv), minimum, maximum and the number of concentrations above the lower limit of quantification.

- Median concentrations time plots (on both linear and semi-log scales) against nominal time postdose by cohort and dose (all treatments on the same plot per scale, based on the summary of concentrations by cohort, dose and time postdose).

- Mean concentrations time plots (on both linear and semi-log scales) against nominal time postdose by cohort and dose (all treatments on the same plot per scale, based on the summary of concentrations by cohort, dose and time postdose).

- Individual concentration time plots by cohort and dose (on both linear and semi-log scales) against actual time postdose (there will be separate spaghetti plots for each dose per scale).

- Individual concentration time plots by subject (on both linear and semi-log scales) against actual time postdose [there will be separate plots for each subject (containing all doses) per scale].

For summary statistics, median and mean plots by sampling time, the nominal PK sampling time will be used, for individual subject plots by time, the actual PK sampling time will be used.

Additional PK analyses may be performed if deemed appropriate.

6.4. Subset Analyses

No subset analyses are planned.

6.5. Baseline and Other Summaries and Analyses

6.5.1. Baseline Summaries

Baseline summary of demographic characteristics (height, weight, BMI, age and race) will be presented for safety population. Each participant's gender will be summarized by sex at birth for each cohort separately and overall in accordance with the sponsor reporting standards.

6.5.2. Study Conduct and Participant Disposition

Subject discontinuations and temporary discontinuations will be detailed and summarized using safety population according to Pfizer standards.

6.5.3. Concomitant Medications and Nondrug Treatments

All concomitant medication(s) as well as non-drug treatment(s) will be reported in the listings.

7. INTERIM ANALYSES

No formal interim analysis will be conducted for this study. As this is an sponsor-open study, the sponsor may conduct unblinded reviews of the data during the course of the study for the purpose of safety assessment, facilitating dosing decisions for optional cohorts, and/or supporting clinical development.

7.1. Introduction

Not applicable.

7.2. Interim Analyses and Summaries

Available safety and PK data may be reviewed.

8. APPENDICES

Appendix 1. Categorical Classes for ECG and Vital Signs of Potential Clinical Concern

Categories for QTcF

Degree of Prolongation	Mild (msec)	Moderate (msec)	Severe (msec)
Absolute value	>450-480	>480-500	>500
Increase from baseline		30-60	>60

Categories for PR and QRS

PR (ms)	max. ≥300	
PR (ms) increase from baseline	Baseline >200 and max. ≥25% increase	Baseline ≤200 and max. ≥50% increase
QRS (ms)	max. ≥140	
QRS (ms) increase from baseline	≥50% increase	

Categories for Vital Signs

Systolic BP (mm Hg)	min. <90	
Systolic BP (mm Hg) change from baseline	max. decrease ≥30	max. increase ≥30
Diastolic BP (mm Hg)	min. <50	
Diastolic BP (mm Hg) change from baseline	max. decrease ≥20	max. increase ≥20
Supine pulse rate (bpm)	min. <40	max. >120

Measurements that fulfill these criteria are to be listed in the clinical study report.

Appendix 2. List of Abbreviations

Abbreviation	Term
Abs	absolute
AD	atopic dermatitis
ADL	activities of daily living
AE	adverse event
ALT	alanine aminotransferase
AST	aspartate aminotransferase
AUC	area under the curve
AUC_{24}	area under the plasma concentration-time curve from 0 to 24 hours
AUC_{tau}	Area under the plasma concentration-time profile from time zero to time tau (τ), the dosing interval
AV	atrioventricular
BBS	Biospecimen Banking System
BID	twice daily
BLQ	below the limit of quantification
BMI	body mass index
BP	blood pressure
bpm	beats per minute
BSA	body surface area
BUN	blood urea nitrogen
BW	body weight
C_{av}/C_{avg}	average concentration
C_{trough}	pre-dose Concentration
CCL26	chemokine (C-C motif) ligand 26
CFR	Code of Federal Regulations
CIOMS	Council for International Organizations of Medical Sciences
CK	creatine kinase
CL_p	clearance of the drug from plasma
CL/F	apparent clearance
C_{max}	maximum observed concentration
CO_2	carbon dioxide (bicarbonate)
Coh	cohort
COVID-19	coronavirus disease 2019
CRF	case report form
CRO	contract research organization
CRU	clinical research unit
CSR	clinical study report
CXCL10	C-X-C motif chemokine 10
CYP	cytochrome P450

Abbreviation	Term
DCT	data collection tool
DDI	drug-drug interaction
DILI	Drug -induced liver injury
DMC	data monitoring committee
DNA	deoxyribonucleic acid
EC	ethics committee
ECC	emergency contact card
ECG	electrocardiogram
eCRF	electronic case report form
EDB	exposure during breastfeeding
EDP	exposure during pregnancy
EMA	European Medicines Agency
EOS	end of study
EPO	erythropoietin
ET	early termination
EU	European Union
EudraCT	European Clinical Trials Database
Fa	fraction of drug absorbed
Fg	fraction of drug extracted at intestine
FIH	first-in-human
f_m	fraction metabolized
FSH	Follicle -stimulating hormone
$F_{u,p}$	Fraction Unbound in plasma
GCP	Good Clinical Practice
GGT	gamma-glutamyl transferase
GLP	Good Laboratory Practice
GM-CSF	granulocyte/macrophage colony stimulating factor
HBcAb	hepatitis B core antibody
HCVAb	hepatitis C antibody
HBsAb	hepatitis B surface antibody
HBsAg	hepatitis B surface antigen
HIV	human immunodeficiency virus
HR	heart rate
CCI [redacted]	
IB	investigator's brochure
IC_{50}	50% inhibitive concentration
ICD	informed consent document
ICH	International Council for Harmonisation
ID	identity

Abbreviation	Term
IFN	interferon
IFNα	interferon alpha
IFNγ/IFNg	interferon gamma
IL	interleukin
IND	investigational new drug
INR	international normalized ratio
IP	investigational product
CCI	[redacted]
IP manual	investigational product manual
IPAL	Investigational Product Accountability Log
IQMP	integrated quality management plan
IRB	institutional review board
IV	intravenous
JAK	janus kinase
k_{el}	terminal phase rate constant
LBBB	left bundle branch block
LFT	liver function test
LLQ	limit of quantification
MCH	mean corpuscular hemoglobin
MCHC	mean corpuscular hemoglobin concentration
MCV	mean corpuscular volume
MFD	maximum feasible dose
NC	not calculated
ND	not done
NS	no sample
mL	milliliter
MMP12	matrix metallopeptidase 12
mRNA	messenger ribonucleic acid
msec	millisecond
N/A	not applicable
nM	nanomolar
NOAEL	No -observed -adverse -effect level
OCT2	organic cation transporter 2
SYS	systemic
PD	pharmacodynamic(s)
CCI	[redacted]
PI	principle investigator
PK	pharmacokinetic(s)
PT	prothrombin time

Abbreviation	Term
PVC	premature ventricular contraction/complex
Q12H	every 12 hours
QD	once daily
QTc	corrected QT
QTcF	corrected QT (Fridericia method)
qual	qualitative
R_{ac} (C_{max})	Accumulation ratio for C_{max}
R_{ac} (AUC_{tau})	Accumulation ratio for AUC_{tau}
RBC	red blood cell
CCI [redacted]	
SAE	serious adverse event
SAP	statistical analysis plan
SCr	serum creatinine
SoA	schedule of activities
SOP	standard operating procedure
SRSD	single reference safety document
STAT	signal transducer and activator of transcription
STOD	study team on demand
SUSAR	suspected unexpected serious adverse reaction
$t_{½}$	apparent terminal half-life
TEAE	Treatment-Emergent Adverse Event
T_{max}	time to first occurrence of C_{max}
TB	tuberculosis
TBili	total bilirubin
TDD	total daily dose
Th	T helper cell
THC	tetrahydrocannabinol
TSLP	thymic stromal lymphopoietin
TYK	tyrosine kinase
uC_{avg}	Unbound average concentration
UGT	uridine diphosphate-glucuronosyltransferase
ULN	upper limit of normal
US	United States
V_d	Volume of distribution
V_{ss}	volume of distribution at steady state
V_z/F	apparent volume of distribution
WBC	white blood cell
WOCBP	woman/women of childbearing potential
WONCBP	woman/women of non-childbearing potential