Protocol *C4221024*

A Phase 1, Randomized, Open-Label Study in Healthy Participants to Estimate the Bioavailability of two new Encorafenib Formulations Relative to the Current Formulation and to Evaluate the Effect of a Proton-Pump Inhibitor on Encorafenib Plasma Pharmacokinetics

Statistical Analysis Plan
(SAP)

Version: 1

Date: 04 Jul 2022

[redacted]

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NOTE: *Italicized* text within this document has been taken verbatim from the Protocol.

1. VERSION HISTORY

Table 1. Summary of Changes

Version/ Date	Associated Protocol Amendment	Rationale	Specific Changes
1 04 Jul 2022	Original 05 May 2022	N/A	N/A

2. INTRODUCTION

Encorafenib is a kinase inhibitor indicated, in combination with binimetinib, for the treatment of patients with unresectable or metastatic melanoma with a BRAF V600E or V600K mutation, as detected by an FDA-approved test, or in combination with cetuximab, for the treatment of patients with mCRC with a BRAF V600E mutation, as detected by an FDA approved test, after prior therapy.

Formulated drug product containing encorafenib is currently available as a 75-mg size double zero capsule for commercial uses. At the approved dose for metastatic melanoma (450 mg QD), patients are required to swallow 6 capsules each day within a short period of time. The capsule burden and challenge for many patients to consistently ingest six double-zero capsules has been noted during clinical development and subsequently post-commercialization. Patients have often requested the option to open the capsules because they are too large to swallow.

In order to decrease the size of the current formulated encorafenib capsule and improve the physical stability, 2 new encorafenib tablet formulations have been developed. This study is intended to select the optimal tablet formulation for commercialization based on the pharmacokinetics. In addition, the present dissolution data does not provide enough confidence to exclude the achlorhydric population (PPI effect) from the rBA study. Because of this difference, a preliminary assessment of the effect of a proton-pump inhibitor on the pharmacokinetics of the 2 encorafenib tablet formulations will also be conducted to assist in the formulation selection.

This SAP provides the detailed methodology for summary and statistical analyses of the data collected in Study C4221024.

2.1. Modifications to the Analysis Plan Described in the Protocol

Not applicable.

2.2. Study Objectives, Endpoints, and Estimands

The following are the objectives and endpoints in this study. Estimand framework will not be applied to this Phase 1 study in healthy participants.

Objectives	*Endpoints*
Primary:	***Primary:***
• *To estimate the relative BA of 2 new encorafenib 75-mg tablet formulations (eMCC and eMCCL) to the commercially available encorafenib formulated capsule (CAP) administered under fasted conditions to adult healthy participants.*	• *Plasma AUC_{inf}, AUC_{last} and C_{max} for encorafenib (alone and with rabeprazole).*
Secondary:	***Secondary:***
• *To assess the safety and tolerability of the 3 formulations (eMCC, eMCCL and CAP) encorafenib 75-mg, when given alone and in combination with rabeprazole in adult healthy participants.* • *To estimate the effect of rabeprazole on the PK of eMCC and eMCCL.*	• *Overall safety profile as characterized by laboratory tests, vital signs, ECGs, and adverse events.* • *Other plasma PK parameters for encorafenib (alone and with rabeprazole): T_{max}, $t_{1/2}$, CL/F, and V_z/F, if possible.*

2.3. Study Design

This study will be an open-label, randomized, 4-period, 6-sequence study in adult healthy participants.

Periods 1 through 3 will estimate the relative bioavailability of the 2 new encorafenib tablet formulations (eMCC and eMCCL) compared to the commercially available CAP formulation using a 75-mg encorafenib single dose administered under fasted condition. Period 4 will explore the potential effect of a PPI (rabeprazole) on the PK of encorafenib administered as the eMCC and eMCCL tablet formulations. Participants will receive either the eMCC or eMCCL formulation with rabeprazole in Period 4.

Participants will be randomized into 1 of 6 treatment sequences as outlined in Table 2. *Approximately 18 participants will be enrolled into the study. The total duration of the study will be approximately 90 days including screening.*

Table 2. Trial Design

Treatment Sequence	***Period 1***	***Washout***	***Period 2***	***Washout***	***Period 3***	***Washout***	***Period 4***
1 (N=3)	*A*	*At least 5 day washout[a]*	*B*	*At least 5 day washout[a]*	*C*	*At least 5 day washout[a]*	*D*
2 (N=3)	*A*		*C*		*B*		*E*
3 (N=3)	*B*		*C*		*A*		*D*
4 (N=3)	*B*		*A*		*C*		*E*
5 (N=3)	*C*		*A*		*B*		*D*
6 (N=3)	*C*		*B*		*A*		*E*

a. between successive encorafenib doses.

Treatments:

- *Treatment A (Test 1 for BA evaluation, Reference 1 for PPI effect): A single 75 mg encorafenib dose as the eMCC formulation will be administered on the morning of Day 1 after an overnight fast of at least 10 hours.*

- *Treatment B (Test 2 for BA evaluation, Reference 2 PPI effect): A single 75 mg encorafenib dose as the eMCCL formulation will be administered on the morning of Day 1 after an overnight fast of at least 10 hours.*

- *Treatment C (Reference for BA evaluation): A single 75 mg encorafenib dose as CAP formulation will be administered on the morning of Day 1 after an overnight fast of at least 10 hours.*

- *Treatment D (Test 1 for PPI evaluation): 20 mg rabeprazole will be administered approximately 1 hour prior to dinner on Day -5 through Day -1* and staggered with *a single 75 mg encorafenib dose as eMCC formulation will be administered on the morning of Day 1 after an overnight fast of at least 10 hours.*

- *Treatment E (Test 2 for PPI evaluation): 20 mg rabeprazole will be administered approximately 1 hour prior to dinner on Day -5 through Day -1* and staggered with *a single 75 mg encorafenib dose as eMCCL formulation will be administered on the morning of Day 1 after an overnight fast of at least 10 hours.*

3. ENDPOINTS AND BASELINE VARIABLES: DEFINITIONS AND CONVENTIONS

3.1. Primary Endpoints

The primary endpoints of the study are plasma AUC_{inf} (if data permits), AUC_{last} and C_{max} for encorafenib (alone) under fasted conditions following administration of tablet (eMCC and eMCCL) and capsule (CAP) formulations. Ratios of AUC_{inf}, AUC_{last} and C_{max} of encorafenib administered as eMCC and eMCCL relative to CAP will be derived.

Encorafenib PK parameters following a single dose administration will be derived from the encorafenib plasma concentration versus 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 outlined in Table 3. Actual PK sampling times will be used in the derivation of PK parameters whenever possible. In the case that actual PK sampling times are not available, nominal PK sampling time will be used in the derivation of PK parameters.

Table 3. Definitions of PK Parameters

Parameter	***Definition***	***Method of Determination***
AUC_{last}	*Area under the plasma concentration-time profile from time zero to the time of the last quantifiable concentration (C_{last})*	*Linear-log trapezoidal method.*
AUC_{inf}[a]	*Area under the plasma concentration-time profile from time zero extrapolated to infinite time*	$AUC_{last} + (C_{last}/k_{el})$, *where C_{last} is the predicted plasma concentration at the last quantifiable time point and k_{el} is the elimination rate constant estimated from the log-linear regression analysis.*
C_{max}	*Maximum plasma concentration*	*Observed directly from the data.*
T_{max}	*Time for C_{max}*	*Observed directly from the data as time of first occurrence.*
$t_{½}$[a]	*Terminal plasma elimination half-life*	$Log_e(2)/k_{el}$, *Only those data points judged to describe the terminal log-linear decline will be used in the regression.*
CL/F[a]	*Apparent clearance after oral dose*	*Dose/AUC_{inf} after oral dose.*
V_z/F[a]	*Apparent volume of distribution after oral dosing*	*Dose/(AUC_{inf} • k_{el}) after oral dose.*
T_{last}	*The time for C_{last}*	*Observed directly from the data.*

a. As data permits

3.2. Secondary Endpoints

The secondary endpoint of the study is the overall safety profile of the 3 formulations (eMCC, eMCCL and CAP) of encorafenib when given alone and in combination with rabeprazole, as characterized by laboratory tests, vital signs, ECGs, and adverse events (discussed in Section 3.5).

Other secondary endpoints include additional plasma PK parameters (including T_{max}, $t_{1/2}$, CL/F, and V_z/F, defined in Table 3) for encorafenib (alone and with rabeprazole) and the ratios of AUC_{inf}, AUC_{last} and C_{max} of encorafenib (alone) relative to encorafenib (with rabeprazole) following administration of the eMCC and eMCCL formulations.

3.3. Other Endpoint(s)

None.

3.4. Baseline Variables

Baseline characteristics will be collected according to the schedule of activities (SoA) as specified in the protocol.

3.5. Safety Endpoints

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

- Adverse events (AE)
- Laboratory data
- Vital signs data
- Electrocardiogram (ECG) results

3.5.1. Adverse Events

Any adverse events occurring following start of treatment will be considered as treatment emergent adverse event (TEAE). Events that occur during follow-up within the lag time of up to 28 days after the last encorafenib dose will be counted as treatment emergent and attributed to the last treatment taken. Events that occur during the washout period (up to 28 days from the last treatment) between study periods will be counted as treatment emergent and attributed to the previous treatment taken. The time period for collecting AEs ("active collection period") for each participant begins from the time the participant provides informed consent.

3.5.2. Laboratory Data

Safety laboratory tests will be performed as described in the protocol. To determine if there are any clinically significant laboratory abnormalities, the haematological, 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 participants's baseline test result is within or outside the laboratory reference range for the particular laboratory parameter.

For Periods 1 to 3, the baseline measurement is the predose measurement on Day -1 of each period. For Period 4, the baseline measurement is the predose measurement on Day -1 of Period 3.

3.5.3. Vital Signs

Supine blood pressure (BP) and pulse rate (PR) will be measured at times specified in the SoA given in the protocol.

For each period, the baseline measurement is the predose measurement on Day 1. Changes from baseline will be defined as the change between the postdose and baseline measurements.

3.5.4. Electrocardiograms

QT interval, QTcF, PR, QRS and heart rate (HR) will be recorded at each assessment time indicated in the SoA given in the protocol. If not supplied, QTcF will be derived using Fridericia's heart rate correction formula:

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

For each period, the baseline value is the average of the triplicate ECG measurements collected before dose administration on Day 1. Changes from baseline will be defined as the change between the postdose ECG measurement and the derived baseline ECG.

The maximum absolute value (postdose) and the maximum increase from baseline for QTcF, PR and QRS, over all measurements taken postdose, will be determined.

The maximum increase from baseline will be calculated by first subtracting the baseline value from each postdose measurement to give the change from baseline. The maximum of these values over the respective period will then be selected, except in the case where a participant does not show an increase. In such an instance, the minimum decrease should be taken.

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

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 screening. A participant will be considered enrolled if the informed consent is not withdrawn prior to participating in*

Participant Analysis Set	***Description***
	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.
Safety Analysis Set	*All participants randomly assigned to a treatment sequence and who take at least 1 dose of encorafenib. Participants will be analyzed according to the formulation they actually received.*
PK Concentration Population	*The PK concentration population is defined as all participants randomized and treated who have at least 1 encorafenib concentration in at least 1 period.*
PK Parameter Analysis Population	*The PK parameter analysis population is defined as all participants randomized and treated who have at least 1 of the encorafenib plasma PK parameters of primary interest in at least 1 treatment period.*

5. GENERAL METHODOLOGY AND CONVENTIONS

Final analysis will be performed after study participant data set release following last participant last visit.

5.1. Hypotheses and Decision Rules

No statistical hypothesis will be tested in this study.

5.2. General Methods

5.2.1. Analyses for Binary/Categorical Endpoints

For binary or categorical variables, number of participants, numbers and percentages of participants meeting the categorical criteria will be presented in accordance with the Clinical Data Interchange Standards Consortium and Pfizer Standards (CaPS).

5.2.2. Analyses for Continuous Endpoints

For continuous variables, the data will be summarized using the number of participants, mean, median, standard deviation (SD), minimum, and maximum in accordance with the CaPS. For appropriate PK parameters, geometric mean and geometric coefficient of variation (%CV) will also be summarized.

5.3. Methods to Manage Missing Data

5.3.1. Pharmacokinetic Data

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 one 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 as 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.

An anomalous concentration value is one that, after verification of bioanalytical validity, is grossly inconsistent with other concentration data from the same individual or from other participants. For example, a BLQ concentration that is between quantifiable values from the same dose is considered as anomalous. Anomalous concentration values may be excluded from PK analysis at the discretion of the PK analyst or pharmacokineticist.

PK Parameters:

Actual PK sampling times will be used in the derivation of PK parameters. If a PK parameter cannot be derived from a participant'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 participant 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 participant 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.

5.3.2. Safety Data

Missing values in standard summaries of AEs, laboratory data, vital signs, and ECGs will be imputed according to CaPS.

6. ANALYSES AND SUMMARIES

6.1. Primary Endpoints

For assessment of the primary objectives of the study, *natural log transformed encorafenib AUC_{inf} (if data permit), AUC_{last} and C_{max} will be analyzed using a mixed effect model with sequence, period and treatment as fixed effects and participant within sequence as a random effect. Estimates of the adjusted mean differences (Test-Reference) and corresponding 90% CIs will be obtained from the model. The adjusted mean differences and 90% CIs for the differences will be exponentiated to provide estimates of the ratio of adjusted geometric means (Test/Reference) and 90% CIs for the ratios. Treatment C (encorafenib CAP) is the Reference Treatment while Treatments A and B (eMCC and eMCCL tablet formulations) are the Test Treatments. This analysis will include only data from Treatments A, B and C.*

Residuals from the model will be examined for normality and the presence of outliers via visual inspection of plots of residuals vs predicted values and normal probability plots of residuals but these will not be included in the CSR. If there are major deviations from normality or outliers then the effect of these on the conclusions will be investigated through alternative transformations and/or analyses excluding outliers. Justification for any alternative to the planned analysis will be provided in the clinical study report.

6.2. Secondary Endpoints

Safety data:

Safety data will be analyzed in accordance with the CaPS (see Section 6.5).

PK data for evaluation of the effect of rabeprazole:

For the assessment of the effect of rabeprazole on the PK of eMCC and eMCCL formulations of encorafenib, *natural log transformed encorafenib AUC_{inf} (if data permit), AUC_{last} and C_{max} will be analyzed using ANOVA with treatment and sequence as a fixed effect and subject within sequence as a random effect. Estimates of the adjusted mean differences (Test-Reference) and corresponding 90% CIs will be obtained from the model. The adjusted mean differences and 90% CIs for the differences will be exponentiated to provide estimates of the ratio of adjusted geometric means (Test/Reference) and 90% CIs for the ratios. For the eMCC tablet formulation, Treatment A (eMCC tablet) is the Reference Treatment while Treatment D (eMCC tablet administered with rabeprazole) is the Test Treatment (this analysis will only include data from Treatments A and D). For the eMCCL tablet formulation, Treatment B (eMCCL tablet) is the Reference Treatment while Treatment E (eMCCL tablet administered with rabeprazole) is the Test Treatment (this analysis will only include data from Treatments B and E).*

Residuals from the model will be examined for normality and the presence of outliers via visual inspection of plots of residuals vs predicted values and normal probability plots of residuals but these will not be included in the CSR. If there are major deviations from normality or outliers then the effect of these on the conclusions will be investigated through

alternative transformations and/or analyses excluding outliers. Justification for any alternative to the planned analysis will be given in the report of the study.

PK summaries:

The encorafenib PK parameters will be summarized descriptively by treatment group in accordance with Pfizer data standards for the PK Parameter Analysis Population, as data permit. A listing of the individual participant ratios (Test-Reference) will be provided. Missing values will be handled as detailed in Section 5.3.1. Each encorafenib PK parameter will be summarized by treatment group and will include the set of summary statistics as specified in Table 4.

Table 4. PK Parameters to be Summarized Descriptively by Treatment

Parameter	Summary Statistics
AUC_{inf}, AUC_{last}, C_{max}, CL/F, V_z/F	N, arithmetic mean, median, SD, %CV, minimum, maximum, geometric mean and geometric %CV
T_{max}	N, median, minimum, maximum
$t_{½}$	N, arithmetic mean, median, SD, %CV, minimum, maximum

Box and whisker plots for individual participant parameters (AUC_{inf}, AUC_{last} and C_{max}) will be presented by treatment and overlaid with geometric means.

The plasma concentrations of encorafenib will be listed and descriptively summarized by nominal PK sampling time and treatment for the PK Concentration Population. Individual participant and summary profiles (mean and median plots) of the plasma concentration-time data will be plotted by treatment using actual and nominal times, respectively. Mean and median encorafenib plasma concentration profiles will be presented on both linear and semi-log scales.

Presentations for encorafenib plasma concentrations will include:

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

- A summary of concentrations by treatment and nominal time postdose, where the set of statistics will include n, mean, median, SD, %CV, minimum, maximum and the number of concentrations above the LLQ.

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

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

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

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

6.3. Subset Analyses

There are no planned subset analyses.

6.4. Baseline and Other Summaries and Analyses

6.4.1. Demographic Summaries

Demographic characteristics will be summarized for enrolled population in accordance with the CaPS.

6.4.2. Study Conduct and Participant Disposition

Participants evaluation groups will show end of study participant disposition. Frequency counts will be supplied for participant discontinuation(s) by treatment. Data will be reported in accordance with the CaPS.

6.4.3. Study Treatment Exposure

Study treatment exposure will be listed.

6.4.4. Concomitant Medications and Nondrug Treatments

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

6.5. Safety Summaries and Analyses

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

Safety data will be presented in tabular and/or graphical format and summarized descriptively, where appropriate.

6.5.1. Adverse Events

Adverse events will be reported in accordance with the CaPS.

Participant discontinuations due to adverse events will be detailed by treatment. Data will be reported in accordance with the CaPS.

6.5.2. Laboratory Data

Laboratory data will be listed and summarized by treatment in accordance with the CaPS.

6.5.3. Vital Signs

Vital signs data will be listed and summarized by treatment in accordance with the CaPS.

6.5.4. Electrocardiograms

ECG data will be databased and available upon request.

7. INTERIM ANALYSES

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

7.1. Introduction

Not applicable.

7.2. Interim Analyses and Summaries

Available safety and PK data may be reviewed.

APPENDICES

Appendix 1. Summary of Analyses

Endpoint	Population	Data Inclusion and Rules for Handling Intercurrent Events and Missing Data	Analysis Method
Ratio of encorafenib AUC_{inf}, AUC_{last}, C_{max}	PK Parameter Analysis Population	Observed data	Mixed effect ANOVA model
Encorafenib PK parameters	PK Parameter Analysis Population	Observed data	Descriptive statistics
Encorafenib PK concentrations	PK Concentration Population	Observed and imputed (Section 5.3.1) data	Descriptive statistics
Safety data	Safety analysis set	Observed and imputed (Section 5.3.2) data	Descriptive statistics

Appendix 2. SAS Code for Analyses

An example of the PROC MIXED code is provided below:

For primary objectives:

- **Treatment A (Test) vs Treatment C (Reference)**
- **Treatment B (Test) vs Treatment C (Reference)**

```
proc mixed data=tab.pk;
where trt in ("A", "B", "C");
        class seq period trt participant;
        model l&var=seq period trt/ ddfm=KR;
        random participant(seq) /participant=participant(seq);
        lsmeans trt;
        estimate 'A vs C' trt  1  0  -1   /cl alpha=0.1;
        estimate 'B vs C' trt  0  1  -1  /cl alpha=0.1;

        ods 'Estimates' out=est&var;
        ods 'lsmeans' out=ls&var;
        ods 'covparms' out=cov&var;
        ods 'tests3' out=tst&var;
run;

/* Letter assignments for treatments (trt) within the estimate statement above are as follows
A: 75 mg encorafenib dose as eMCC formulation, fasted condition.
B: 75 mg encorafenib dose as eMCCL formulation, fasted condition.
C: 75 mg encorafenib dose as CAP formulation, fasted condition.
*/
```

For secondary objectives:

- **Treatment A (Reference) vs Treatment D (Test)**

```
proc mixed data=tab.pk;
where trt in ("A", "D");
        class seq trt participant;
        model l&var=seq trt / ddfm=KR;
        random participant(seq) / subject=participant(seq);
        lsmeans trt;
        estimate 'D vs A' trt -1  1 / cl alpha=0.1;
        ods 'Estimates' out=est&var;
        ods 'lsmeans' out=ls&var;
        ods 'covparms' out=cov&var;
        ods 'tests3' out=tst&var;
```

```
run;

/* Letter assignments for treatments (trt) within the estimate statement above are as follows
A: 75 mg encorafenib dose as eMCC formulation, fasted condition.
D: 20 mg rabeprazole with coadministered of 75 mg encorafenib dose as eMCC formulation,
fasted condition.
*/
```

- **Treatment B (Reference) vs Treatment E (Test)**

```
proc mixed data=tab.pk;
where trt in (“B”, “E”);
        class seq trt participant;
        model l&var=seq trt / ddfm=KR;
        random participant(seq) / subject=participant(seq);
        lsmeans trt;
        estimate 'E vs B' trt -1  1 / cl alpha=0.1;
        ods 'Estimates' out=est&var;
        ods 'lsmeans' out=ls&var;
        ods 'covparms' out=cov&var;
        ods 'tests3' out=tst&var;
run;

/* Letter assignments for treatments (trt) within the estimate statement above are as follows
B: 75 mg encorafenib dose as eMCCL formulation, fasted condition.
E: 20 mg rabeprazole with staggered coadministered of 75 mg encorafenib dose as eMCCL
formulation, fasted condition.
*/
```

Appendix 3. List of Abbreviations

Abbreviation	Term
AE	adverse event
ANOVA	analysis of variance
AUC_{inf}	area under the plasma concentration-time profile from time zero extrapolated to infinite time
AUC_{last}	area under the plasma concentration-time profile from time zero to the time of the last quantifiable concentration
BA	Bioavailability
BLQ	below the limit of quantitation
BP	blood pressure
CAP	capsule formulation
CaPS	Clinical Data Interchange Standards Consortium and Pfizer Standards
CI	confidence interval
CL/F	apparent clearance
C_{last}	predicted plasma concentration at the last quantifiable time point from the log-linear regression analysis
C_{max}	maximum plasma concentration
CSR	clinical study report
%CV	coefficient of variation
ECG	Electrocardiogram
eMCC	Immediate-release tablet formulated with MCC as the single extragranular diluent
eMCCL	Immediate-release tablet formulated with both MCC and lactose as extragranular diluents
HR	Heart rate
k_{el}	the terminal phase rate constant calculated by a linear regression of the loglinear concentration-time curve
LLQ	lower limit of quantitation
N/A	not applicable
NC	not calculated
ND	not done
NS	no sample
PK	pharmacokinetic(s)
PPI	proton-pump inhibitor
PR	pulse rate
QRS	Combination of Q-, R- and S- wave on an electrocardiogram representing ventricular depolarization
QTc	corrected QT
QTcF	corrected QT (Fridericia method)
rBA	relative bioavailability
RR	respiratory rate
SAP	statistical analysis plan

Abbreviation	Term
SD	standard deviation
SoA	schedule of activities
$t_{1/2}$	terminal plasma elimination half-life
TEAE	treatment emergent adverse event
T_{last}	the time for C_{last}
T_{max}	time to C_{max}
V_z/F	apparent volume of distribution for extravascular dosing