Protocol C5041034

A Phase 1, Open-Label, Randomized, Single Dose, Crossover Study to Estimate the Relative Bioavailability of Etrasimod (PF-07915503) Mini Tablets in Water and 3 Food Vehicles Compared to the Etrasimod (PF-07915503) Clinical IR Tablets Under Fasted Conditions, and to Evaluate Mini Tablet Palatability in Healthy Adult Participants

Statistical Analysis Plan (SAP)

Version: 1

Date: 25 May 2023

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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 / 25 May 2023	Original 03 Apr 2023	N/A	N/A

2. INTRODUCTION

Etrasimod is an orally administered, selective, synthetic $S1P_{1,4,5}$ modulator that is being developed to treat immune-mediated inflammatory disorders, including UC, AA, AD, CD and EoE. The $S1P_1$ is a cell surface expressed protein that has been shown to regulate lymphocyte migration out of lymphoid tissues. Synthetic small molecule $S1P_1$ agonists have been observed to act as functional antagonists by inducing sustained receptor internalization, thus inhibiting lymphocyte migration out of lymphoid tissues and lowering the amount of peripheral blood lymphocytes available to be recruited to sites of inflammation. Modulation of the S1P/S1P receptor axis is thought to be a potential therapeutic approach to the management of immune-mediated inflammatory disorders.

The purpose of the study is to estimate the rBA of etrasimod mini tablets 2 mg in water and 3 food vehicles relative to etrasimod clinical IR tablet 2 mg under fasting conditions in healthy adult participants. The study will also assess the safety, tolerability, and palatability of etrasimod mini tablets (total dose of 2 mg) in healthy adult participants. The etrasimod mini tablets are intended for dosing in pediatric population 2 years old to <12 years old.

This SAP provides the detailed methodology for summary and statistical analyses of the data collected in Study C5041034.

2.1. Modifications to the Analysis Plan Described in the Protocol

None.

2.2. Study Objectives and Endpoints

Objectives	***Endpoints***
Primary:	***Primary:***
• *To estimate the rBA of etrasimod 2 mg mini tablets mixed with water compared with etrasimod 2 mg clinical IR tablets under fasted conditions* • *To estimate the rBA of the etrasimod 2 mg mini tablets mixed with apple sauce compared with the etrasimod 2 mg clinical IR tablets under fasted conditions*	• *Plasma AUC_{last}, AUC_{inf} and C_{max} of etrasimod*

Objectives	***Endpoints***
• *To estimate the rBA of the etrasimod 2 mg mini tablets mixed with chocolate pudding compared with the etrasimod 2 mg clinical IR tablets under fasted conditions* • *To estimate the rBA of the etrasimod 2 mg mini tablets mixed with yogurt compared with the etrasimod 2 mg clinical IR tablets under fasted conditions*	
Secondary:	***Secondary:***
• *To evaluate the safety and tolerability of etrasimod in healthy participants* • *To assess the palatability of etrasimod mini tablets mixed with water/apple sauce/chocolate pudding/yogurt*	• *Assessment of first dose HR reduction, TEAEs, clinical laboratory abnormalities, vital signs, PEs, and 12-lead ECGs* • *Assessment of palatability via questionnaire: mouth feel, bitterness, tongue/mouth burns, throat burn, and overall liking*
Tertiary/Exploratory:	***Tertiary/Exploratory:***
• *To characterize the PK parameters of etrasimod 2 mg mini tablets mixed with water or soft foods (apple sauce, chocolate pudding, or yogurt) compared with etrasimod 2 mg clinical IR tablet* • *To validate the PK measurement of etrasimod in capillary blood sample collected using a micro sampling device against the PK measurement of etrasimod in venous blood samples.*	• *Plasma etrasimod: $t_{½}$, CL/F, V_z/F and T_{max} of etrasimod* • *Plasma concentration of etrasimod obtained via micro sampling compared to venous sampling*

2.3. Study Design

This is a Phase 1, open-label, single-dose, randomized 4-crossover periods and 1-fixed period design in a single cohort of approximately 16 healthy male or female participants .

The study will consist of 5 treatments as shown below:

1. *Treatment A: Single oral dose of etrasimod 2 mg clinical IR tablet under fasted conditions (Reference)*
2. *Treatment B: Single oral dose of etrasimod 2 mg mini tablets mixed with applesauce under fasted conditions (Test 1)*
3. *Treatment C: Single oral dose of etrasimod 2 mg mini tablets mixed with chocolate pudding under fasted conditions (Test 2)*
4. *Treatment D: Single oral dose of etrasimod 2 mg mini tablets mixed with water under fasted conditions (Test 3)*
5. *Treatment E: Single oral dose of etrasimod 2 mg mini tablets mixed with yogurt under fasted conditions (Test 4)*

Sixteen participants will be enrolled in Period 1 for a total of 12 evaluable participants to complete study. Participants will be randomly assigned to 1 of the 4 sequences shown in Table 2 in which participants are randomized in crossover design to receive Treatments A to D in Periods 1 to 4 with Treatment E being fixed in Period 5. Participants will be discharged on Day 9 of Period 5, following completion of all assessments. Each treatment is 9 days that includes dosing, PK sampling and an extra day to minimize any residual etrasimod concentrations prior to start of the next treatment. The total planned duration of participation from the screening visit to the last follow-up phone call, is approximately 14 weeks.

Table 2. Treatment Sequence

Treatment sequence (n=4 per sequence)	*Period 1*	*Period 2*	*Period 3*	*Period 4*	*Period 5 (fixed)*
1	*A*	*B*	*C*	*D*	*E*
2	*B*	*D*	*A*	*C*	*E*
3	*C*	*A*	*D*	*B*	*E*
4	*D*	*C*	*B*	*A*	*E*

Since etrasimod has a half-life approximately 30 hours, there will be a 9-day washout between each dose.

3. ENDPOINTS AND BASELINE VARIABLES: DEFINITIONS AND CONVENTIONS

3.1. Primary Endpoints

The primary endpoints are the plasma AUC_{last}, AUC_{inf} and C_{max} of etrasimod. The test/reference ratios for AUC_{last}, AUC_{inf} and C_{max} will be derived with Treatment B (etrasimod 2 mg mini tablets mixed with applesauce under fasted conditions), Treatment C (etrasimod 2 mg mini tablets mixed with chocolate pudding under fasted conditions), and Treatment D (etrasimod 2 mg mini tablets mixed with water under fasted conditions) as the test treatments and Treatment A (etrasimod 2 mg clinical IR tablets under fasted conditions) as the reference treatment. In addition, the test/reference ratios for AUC_{last}, AUC_{inf} and C_{max} will be derived with Treatment E (etrasimod 2 mg mini tablets mixed with yogurt under fasted conditions) as the test treatment and Treatment A (etrasimod 2 mg clinical IR tablets under fasted conditions) as the reference treatment.

Plasma PK parameters of etrasimod will be derived (as data permit) from the concentration-time data using standard noncompartmental methods as outlined in the Table 3 below. Actual PK sampling times will be used in the derivation of PK parameters. 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_{inf}	*Area under the concentration-time curve from time zero extrapolated to infinity*	$AUC_{last} + (C_{last}*/k_{el})$, *where* $C_{last}*$ *is the predicted plasma concentration at the last quantifiable time point from the log-linear regression analysis*
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.*
C_{max}	*Maximum observed concentration*	*Observed directly from data*
T_{max}	*Time for* C_{max}	*Observed directly from data as time of first occurrence*
$t_{½}$	*Terminal half-life*	$Log_e(2)/k_{el}$, *where* k_{el} *is the terminal phase rate constant calculated by a linear regression of the loglinear concentration-time curve. Only those data points judged to describe the terminal loglinear decline will be used in the regression.*
CL/F	*Apparent clearance*	$Dose/AUC_{inf}$
V_z/F	*Apparent volume of distribution*	$Dose/(AUC_{inf} \bullet k_{el})$

3.2. Secondary Endpoints

3.2.1. Safety data

The secondary endpoints include the safety and tolerability data, discussed in Section 3.5.

3.2.2. Palatability of etrasimod mini tablets

The data collected for palatability assessment using the sponsor-provided palatability questionnaire will be numerically derived by measuring length (using a scale with gradations of at least 0.1 cm) of the "x" marked by the participant relative to the "good trait". For palatability assessment, the data used in the analysis will be transcribed and rescaled to a score from 0 to 100 from the raw measurements on the questionnaire.

3.3. Baseline Variables

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

3.4. Other Endpoints

3.4.1. Other PK parameters of etrasimod

Exploratory endpoints include other plasma PK parameters of etrasimod such as T_{max}, $t_{1/2}$, CL/F and V_z/F.

3.4.2. Etrasimod microsampling concentration

Etrasimod micro sampling concentration using Tasso device will be collected according to the SoA as specified in the protocol.

3.5. Safety Endpoints

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

- first dose HR reduction
- adverse events (AE)
- laboratory data
- vital signs data
- electrocardiogram (ECG) results

3.5.1. First Dose HR reduction

For all periods, HR will be measured every hour up to 6 hours, at 8 and 24 hours post-etrasimod dose at Day 1. The baseline HR value is the average of the HR values from the triplicate ECG measurements collected predose on Day 1 of each period. Changes from baseline will be defined as the change between the postdose measurements and baseline value. In addition, the nadir HR value on Day 1 will be derived.

3.5.2. 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 35 days after the last dose of study intervention will be counted as treatment emergent and attributed to the last treatment taken. The time period for collecting AEs ("active collection period") for each participant begins from the time the participant provides informed consent.

3.5.3. 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 participant's baseline test result is within or outside the laboratory reference range for the particular laboratory parameter.

For all periods, the baseline measurement is the predose measurement on Period 1 Day -1. Changes from baseline will be defined as the change between the postdose and baseline measurements.

3.5.4. Vital Signs

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

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

3.5.5. Electrocardiograms

QT interval, QTcF, PR interval, QRS and heart rate (HR) will be recorded at each 12-lead ECG assessment time indicated in the SoA given in the protocol. QTcF will be derived using Fridericia's heart rate correction formula:

QTcF = QT / (RR)^(1/3) where RR = 60/HR (if not provided)

For all periods, the baseline value is the average of triplicate ECG measurements collected predose on Day 1 of each period. Changes from baseline will be defined as the change between the postdose measurements and baseline value.

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***
Safety Analysis Set	*All participants who take at least 1 dose of study intervention. Participants will be analyzed according to the product they actually received.*
PK Concentration Set	*All participants who take at least 1 dose of study intervention and in whom at least 1 concentration value is reported.*
PK Parameter Set	*All participants who take at least 1 dose of study intervention and in whom at least 1 of the PK parameters of interest are reported.*

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 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.

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 not be presented for a particular treatment group if more than 50% of the data are NC. For statistical analyses, PK parameters coded as NC will also be set to missing, and statistics will be presented for a particular treatment with ≥3 evaluable measurements.

If an individual participant has a known biased estimate of a PK parameter (due for example to a dosing error or 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. For instance, if a participant has a vomiting event post dose that is within a duration of time that is 2-times the derived median T_{max} for the population for the administered treatment, then the pharmacokineticist should consider the exclusion of the PK concentration data collected following the initial vomiting event in that treatment period and the PK parameter data reported for that treatment period from the datasets used to calculate summary statistics or statistical analyses.

5.3.2. Safety Data

Missing values in standard summaries of safety data will be imputed according to CaPS.

6. ANALYSES AND SUMMARIES

6.1. Primary Endpoints

Plasma AUC_{last}, AUC_{inf} and C_{max} of etrasimod will be summarized by treatment group and will include the set of summary statistics as specified in Table 4.

For the evaluation of relative bioavailability of etrasimod 2 mg mini tablets mixed with applesauce, chocolate pudding and water compared to etrasimod 2 mg clinical IR tablets, *natural log transformed AUC_{inf}, AUC_{last} and C_{max} will be analyzed using a mixed effect model with sequence, period and treatment as fixed effects and participant within the 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% CI for the ratios. Treatment A (etrasimod 2 mg clinical IR tablets under fasted conditions) will be the Reference treatment while Treatment B (etrasimod 2 mg mini tablets mixed with applesauce under fasted conditions), Treatment C (etrasimod 2 mg mini tablets mixed with chocolate pudding under fasted conditions), and Treatment D (etrasimod 2 mg mini tablets mixed with water under fasted conditions) will be the Test treatments.*

For the evaluation of relative bioavailability of etrasimod 2 mg mini tablets mixed with yogurt compared to etrasimod 2 mg clinical IR tablets, *natural log transformed AUC_{inf}, AUC_{last} and C_{max} will be analyzed using a mixed effect model with sequence and treatment as fixed effects and participant within the sequence as a random effect. Treatment A (etrasimod*

2 mg clinical IR tablets under fasted conditions) will be the Reference treatment while Treatment E (etrasimod 2 mg mini tablets mixed with yogurt under fasted conditions) will be the Test treatment.

For AUC_{inf}, AUC_{last} and C_{max}, a listing of the individual participant ratios (Test/Reference) will be provided. Box and whisker plots for AUC_{inf}, AUC_{last} and C_{max}, will be plotted by treatment and overlaid with geometric means.

Residuals from the models 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.

6.2. Secondary Endpoints

6.2.1. Safety data

Analyses and summaries of safety data are described in Section 6.6.

6.2.2. Palatability of etrasimod mini tablets

The sensory attributes (mouth feel, bitterness, sweetness, sourness, saltiness, tongue/mouth burn, overall liking) from the Taste Assessment Questionnaire will be listed and descriptively summarized by treatment, and question across participants. Summary statistics (mean and 90% CI) will be calculated for the various questions. Radar plots for each of 4 time points (1, 5, 10 and 20 minutes after dosing), summarizing all attributes for each treatment will be generated.

6.3. Other Endpoints

6.3.1. Other PK parameters of etrasimod

Exploratory endpoints include other PK parameters of etrasimod such as T_{max}, $t_{1/2}$, CL/F and V_z/F. The PK parameters will be listed and summarized descriptively by treatment group in accordance with Pfizer data standards on the PK Parameter Set, as data permit. Missing values will be handled as detailed in Section 5.3.1. Each 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

Supporting data from the estimation of $t_{½}$ and AUC_{inf} will be listed by analyte and group: terminal phase rate constant (k_{el}); goodness of fit statistic from the log-linear regression (r^2); the percent of AUC_{inf} based on extrapolation (AUC_{extrap}%); 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.

PK Concentrations:

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

Presentations of 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 given 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].

6.3.2. Etrasimod micro sampling concentration

The micro sampling will be performed in this study, but the results of analyzing this data will not be included in the CSR. Instead, a separate internal bioanalytical report will be issued to document data and conclusions from this analysis. However, *etrasimod concentration at sampling time points, C_{max} and AUC_{0-24} from paired samples obtained via micro sampling and venous sampling will be compared. Individual participant differences and % differences*

of concentrations by PK sampling time, C_{max} and AUC_{0-24} will be listed and summarized descriptively.

6.4. Subset Analyses

There are no planned subset analyses.

6.5. Baseline and Other Summaries and Analyses

6.5.1. Demographic Summaries

Demographic characteristics will be summarized for Safety Analysis Set in accordance with the CaPS.

6.5.2. 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.

6.5.3. Study Treatment Exposure

Study treatment exposure will be listed.

6.5.4. Concomitant Medications and Nondrug Treatments

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

6.6. 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.

6.6.1. First Dose HR reduction

Changes from predose baseline in HR at every hour up to 6 hours, at 8 and 24 hours on Day 1, as well as the nadir HR value on Day 1, will be summarized by treatment.

6.6.2. Adverse Events

AEs 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.

6.6.3. Laboratory Data

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

6.6.4. Vital Signs

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

6.6.5. Electrocardiograms

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

Changes from baseline for the ECG parameters will be summarized by treatment. The number (%) of participants with maximum postdose QTcF values and maximum increases from baseline in the following categories will be tabulated by treatment.

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

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/PD modeling, and/or supporting clinical development.

Final analysis will follow the official database release. As this will be an open-label study, there is no formal unblinding of the randomization code.

APPENDICES

Appendix 1. SAS Code for Analyses

An example of the PROC MIXED code is provided below:

For the primary objective – relative BA (B,C,D vs A):

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

For the primary objective – relative BA (E vs A):

```
proc mixed data=tab.pk;
        class seq trt participant;
        model l&var=seq trt/ ddfm=KR;
        random participant(seq) /subject=participant(seq);
        lsmeans trt;
        estimate 'E vs A' trt -1 0 0 0 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
Treatment A: Single oral dose of etrasimod 2 mg clinical IR tablet under fasted conditions (Reference)

Treatment B: Single oral dose of etrasimod 2 mg mini tablets mixed with applesauce under fasted conditions (Test 1)

Treatment C: Single oral dose of etrasimod 2 mg mini tablets mixed with chocolate pudding under fasted conditions (Test 2)

Treatment D: Single oral dose of etrasimod 2 mg mini tablets mixed with water under fasted conditions (Test 3)

Treatment E: Single oral dose of etrasimod 2 mg mini tablets mixed with yogurt under fasted conditions (Test 4) */

Appendix 2. List of Abbreviations

Abbreviation	Term
%CV	coefficient of variation
AA	alopecia areata
AD	atopic dermatitis
AE	adverse event
AUC_{extrap}%	the percent of AUC_{inf} based on extrapolation
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
CaPS	Clinical Data Interchange Standards Consortium and Pfizer Standards
CD	Crohn's Disease
CI	confidence interval
C_{last}	last quantifiable concentration
CL/F	apparent clearance after oral dose
C_{max}	maximum plasma concentration
CSR	clinical study report
ECG	electrocardiogram
EoE	eosinophilic esophagitis
HR	heart rate
IR	immediate-release
k_{el}	terminal phase rate constant
LLQ	lower limit of quantitation
mg	milligram
ms	millisecond
N/A	not applicable
NC	not calculated
ND	not done
NS	no sample
PD	pharmacodynamic(s)
PK	pharmacokinetic(s)
PR	pulse rate
PR interval	time from the beginning of the P wave to the beginning of the QRS complex
QRS	Combination of Q-, R- and S- wave on an electrocardiogram representing ventricular depolarization
QTc	corrected QT
QTcF	corrected QT (Fridericia method)
r^2	goodness of fit statistic from the log-linear regression

Abbreviation	Term
rBA	relative bioavailability
RR	the time between the start of one QRS complex and the start of the next QRS complex
SAP	statistical analysis plan
SD	standard deviation
S1P	sphingosine 1-phosphate
$S1P_{1,4,5}$	S1P receptors 1, 4, and 5
SoA	schedule of activities
$t_{½}$	terminal elimination half-life
TEAE	treatment emergent adverse event
T_{max}	time for C_{max}
UC	ulcerative colitis
V_z/F	apparent volume of distribution after oral dose