STATISTICAL ANALYSIS PLAN

CER-FT011-SSc01

A PHASE II, RANDOMISED, DOUBLE BLIND, PLACEBO-CONTROLLED STUDY OF THE PHARMACOKINETICS, PHARMACODYNAMIC EFFECTS, AND SAFETY, OF ORAL FT011 IN PARTICIPANTS WITH DIFFUSE SYSTEMIC SCLEROSIS

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VERSION NUMBER AND DATE: FINAL v1.1, 16Nov2022

Statistical Analysis Plan Signature Page - authors

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STATISTICAL ANALYSIS PLAN SIGNATURE PAGE - APPROVAL

Upon review of this document, the undersigned approves this version of the Statistical Analysis Plan, authorizing that the content is acceptable for the reporting of this study.

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MODIFICATION HISTORY

Listed below are modifications made to the SAP after the signed approval(s).

Unique Identifier for this Version	Date of the Document Version	Author	Significant Changes from Previous Authorized Version
Draft 1.0	01Oct2021	[redacted]	Not Applicable – First Version
Draft 2.0	02Jun2022	[redacted]	Addressing Sponsor and Medical Writing review comments
Final 1.0	24Aug2022	[redacted]	Final Version
Final 1.1	16Nov2022	[redacted]	Minor update to algorithm for SHAQ-DI for programming purposes.

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1. INTRODUCTION

This document describes the rules and conventions to be used in the presentation and analysis of pharmacokinetic (PK), pharmacodynamic (PD), and safety data for Protocol CER-FT011-SSc01 version 2.1, dated 01 November 2021. It describes the data to be summarized and analysed, including specifics of the statistical analyses to be performed.

A subset of the analyses described in this SAP will form the basis of reports provided to the Data Safety Monitoring Board (DSMB) while the study is ongoing. The tables and listings prepared for the DSMB are additionally identified in the Table, Listing and Figures Template document that accompanies this SAP. It is recognised that this analysis plan may be modified by the study team as new information becomes available outside of the study, or to reflect recommendations made by DSMB. In addition, some analyses, tables or listings may be omitted at DSMB if there are insufficient data to warrant analysis or at the request of the DSMB. Where the SAP is updated after initial approval, the changes will result in a new version and a brief description in the Modification History of this SAP.

This statistical analysis plan (SAP) is based on protocol Version 2.1 dated 01 November 2021, DSMB charter version 1.0 dated 15 July 2021 and eCRF Version 7.3 dated 10 November 2021.

2. STUDY OBJECTIVES AND ENDPOINTS

2.1. PRIMARY OBJECTIVE AND ENDPOINTS

The primary objective is:

- To assess the PK of oral FT011 in participants with diffuse systemic sclerosis (SSc)

The primary endpoints are:

- FT011 (Maximum plasma concentration (C_{max}), Time to maximum concentration (t_{max}), and Areas under the Curve (AUC) in plasma after a single dose and after 12-weeks of treatment.
- Measurement of steady state FT011 levels in plasma.

  Note: additional calculations may be performed, and metabolites may also be measured.

2.2. SECONDARY OBJECTIVES AND ENDPOINTS

The secondary objectives are:

- To assess the safety and tolerability of oral FT011 compared to placebo in participants with diffuse SSc.
- To evaluate the short-term efficacy of oral FT011 compared to placebo in improving disease activity in participants with diffuse SSc.

The secondary endpoints are:

- Safety will be assessed by:
  - Treatment-emergent adverse events from first dose of study drug to End of Study.
  - Physical examination.
  - Vital signs (blood pressure, heart rate, respiratory rate, and temperature).
  - 12-lead electrocardiograms (ECG).
  - Safety laboratory results (haematology, biochemistry, coagulation, and urinalysis).
  - Use of concomitant medications.
- Efficacy will be assessed by:
  - Change in modified Rodnan skin score (mRSS) from Baseline at each visit.
  - Change in percent predicted forced vital capacity (FVC) from Baseline to Week 4, Week 8, and Week 12.
  - Change in Scleroderma Health Assessment Questionnaire - Disability Index (SHAQ-DI) Score from Baseline to Week 4, Week 8, and Week 12.
  - Change in Patient Global Assessment Score from Baseline to Week 4, Week 8, and Week 12.
  - Change in Physician Global Assessment Score from Baseline to Week 4, Week 8, and Week 12.
  - The proportion of patients showing an improvement (defined as ACR Composite Response Index in Diffuse Cutaneous Systemic Sclerosis (CRISS) score predicted probability of ≥0.60) at Week 12.
  - Change in the Scleroderma Clinical Trials Consortium Damage Index (SCTC-DI) score from Baseline to Week 12.
  - Change in the 5-D Itch Scale from Baseline to Week 12.

2.3. EXPLORATORY OBJECTIVES AND ENDPOINTS

[redacted]

3. STUDY DESIGN

3.1. GENERAL DESCRIPTION

This is a multi-centre, randomised, double blind, placebo-controlled study to assess the PK and PD effects and safety of FT011 in participants with diffuse SSc.

A total of approximately 30 participants, 10 per treatment group, will be randomised and treated. The sample size for this study is sized based on practical considerations and a formal sample size calculation was not performed.

The targeted study population is participants with diffuse SSc with a disease duration of ≤10 years from onset of first non-Raynauds symptom, and a modified Rodnan Skin Score (mRSS) of 15 to 40 at the screening visit. Participants meeting all eligibility criteria will have a baseline skin biopsy (2 x 3 mm punch biopsies) taken before being randomised 1:1:1 to FT011 200 mg, FT011 400 mg, or placebo.

Participants will take their study drug once a day for 3 months (12 weeks), in addition to their standard-of-care scleroderma medications. They will return to the site for study visits at Weeks 4, 8, and 12. Week 12 is the end of the study Treatment Period. A final study follow-up visit will be conducted one month after they complete treatment (Week 16).

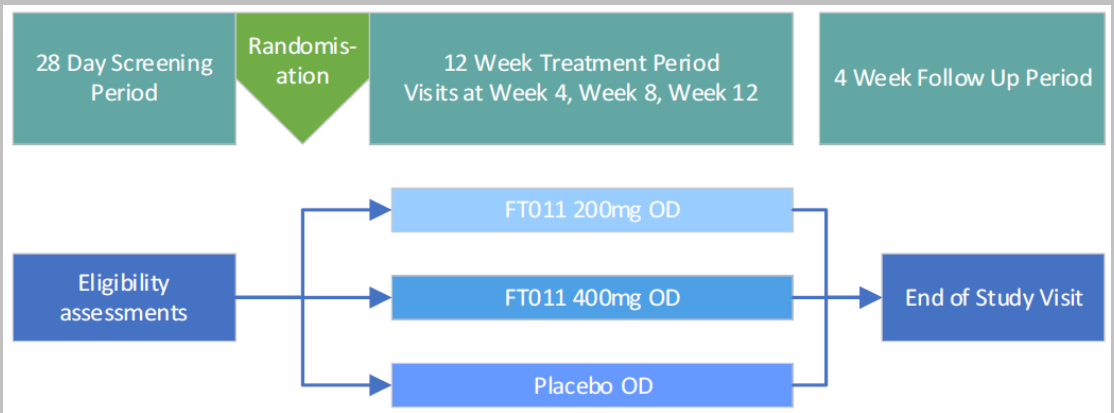
Visit procedures will include skin thickness assessments using the mRSS at every visit, and forced vital capacity (FVC), the Scleroderma Health Assessment Questionnaire-Disability Index (SHAQ-DI), and Physician and Patient Global Assessments at all visits during the Treatment Period. A follow up skin biopsy will be taken at Week 12. On Day 1 and at Week 12 participants will have serial PK samples collected out to 8 hours post-dose, and trough samples will be collected at each interim visit. Other on-study visit assessments will include additional participant questionnaires, physical examinations, vital signs measurements, safety laboratory blood and urine tests, and electrocardiograms. Adverse events and concomitant medications will be assessed and recorded at each study visit.

Additional blood samples will be collected at Day 1 and Week 12 for exploratory assessments.

With the exception of methotrexate, which is excluded, participants should be maintained on their current SSc medications during the course of the Treatment Period unless they meet the following progression criteria; those who have a mRSS increase from Baseline of 5 or more may start immunosuppressive medications, or, if already taking these, have their immunosuppressive medications or doses changed.

A Data Safety Monitoring Board (DSMB) will review safety and PK data at agreed recruitment and progression milestones to provide independent oversight of participant safety.

Figure A: Study Flow Diagram



Abbreviations: OD – Once Daily.

3.2. SCHEDULE OF EVENTS

Schedule of events can be found in section 2, Table 1 of the protocol.

3.3. CHANGES TO ANALYSIS FROM PROTOCOL

There are two planned changes to this SAP that aren't included in protocol:

1) The SAP includes the addition of an All Participants Screened Set, which is used for disposition reporting.
2) The patient global assessment scores will be inverted for the CRISS calculations. This is described in section 14 of the SAP.

4. PLANNED ANALYSES

4.1. DATA SAFETY MONITORING BOARD

An independent DSMB will be established prior to recruitment start, with appropriate charter that defines its roles and responsibilities. The DSMB will monitor accruing trial safety results and PK data at intervals throughout the study. The main purpose of the DSMB will be to protect the interests of the participants included in the trial.

The DSMB will convey to Certa Therapeutics their recommendations as to whether the trial may continue as planned or if the trial should be modified or stopped. The final decision on whether the

study should be modified or stopped will be the responsibility of Certa Therapeutics. Any decision to modify or stop will be communicated to investigators and regulatory authorities (RA) by Certa Therapeutics (or their representatives). The DSMB may also review PK data in a blinded fashion.

The DSMB will also review any serious adverse events (SAE) that occur during the study.

The DSMB meetings will be held when data is available at the following time points:

- First meeting will be scheduled after 10 participants have been randomised, or at 6 months after start of recruitment, whichever is earlier.
- Second meeting will be scheduled after 10 participants have completed treatment.
- Third meeting will be scheduled after 20 participants have completed treatment.

Meetings will be scheduled for approximately three weeks after the data cut off to allow time for preparation of summaries, tables and listings.

As outlined in the DSMB charter, two separate reports will be prepared and distributed as follows for each DSMB meeting. The summary below provides details of the relevant sections of this analysis plan that are relevant to each report, a broader description of the planned analyses that will be provided at each DSMB review can be found in the relevant sections of the charter.

The proposed tables and listings proposed for the DSMB appears in Appendix 4 of the charter and are reproduced in Appendix 3 of the SAP. The full structure is presented in the Tables, Listings and Figure Templates.

Open Session: Distributed to the DSMB members, Certa Therapeutics and others as requested by the DSMB. Data presented in the open sessions will not identify the dosing regimens of the participants. The report will include analyses from the following section of this analysis plan pooled over the treatment groups unless specified otherwise.

- Information on participant recruitment (provided by Project Manager)
- Protocol Changes (provided by Project Manager)
- Eligibility/Protocol Deviations (provided by Project Manager)
- Study disposition
- Baseline demographics
- Baseline scleroderma signs and symptoms
- Study treatment status (including completion of 12 week treatment period).

Closed Session: Distributed to the DSMB members only. The report will include analyses from the following sections of this analysis plan with summaries of treatment groups masked as Group A, Group B, and Group C unless specified otherwise. The DSMB may request the unmasking of treatment codes from the independent unblinded biostatistician when such information is needed.

- Study disposition
- Baseline demographics

- Baseline scleroderma signs and symptoms
- Disease history
- Study treatment status
- Treatment-emergent adverse event
- PK (depends on data availability)
- Data completeness

4.2. INTERIM ANALYSIS

There will be no interim analysis for this study.

4.3. FINAL ANALYSIS

All final, planned analysis identified in this SAP will be performed by IQVIA Biostatistics following Certa Therapeutics Pty Ltd authorization of this Statistical Analysis Plan, database lock and determination of analysis sets and unblinding of the study.

5. ANALYSIS SET

Agreement of participants included/excluded from each analysis set will be conducted after database lock.

5.1. ALL PARTICIPANTS SCREENED SET

The All Participants Enrolled Set will include all participants who provided informed consent for this study. This analysis set will be used to describe disposition and listings.

5.2. INTENTION-TO-TREAT ANALYSIS SET

The Intention-to-Treat (ITT) Analysis Set will include all participants who were randomised. Participants in this set will be analysed based on the treatment that they were randomised to. The ITT set will be used to present demographic and summary of study treatment summaries.

5.3. MODIFIED INTENTION-TO-TREAT ANALYSIS SET

The modified Intention-to-Treat (mITT) Analysis Set will include all randomised participants who received at least one dose of study drug and had a post-baseline efficacy data for at least one of the efficacy outcome measures. Participants in this set will be analysed based on the treatment that they were randomised to. All efficacy analyses will be based on the mITT Analysis Set.

5.4. SAFETY ANALYSIS SET

The Safety Analysis Set will include all randomised participants who received at least one dose of study drug. Participants in this set will be analysed based on the actual treatment that they received. All safety summaries will be based on the Safety Analysis Set.

5.5. PHARMACOKINETIC ANALYSIS SET

The pharmacokinetic (PK) Analysis Set will include all participants included in the safety set who have sufficient concentrations to allow for the calculation of at least one PK parameter. Participants who experience any adverse events or have protocol deviations that could affect the PK profiles may be excluded from the PK analysis set at the pharmacokineticist's discretion. Participants in this set will be analysed based on the actual treatment that they received. All PK analyses will be based on the PK Analysis Set.

6. GENERAL CONSIDERATIONS

Listings will be presented using All Participants Enrolled Set for those participants with data available.

6.1. SUMMARY STATISTICS

For categorical variables, the population size (N for population group totals and n for available data for each treatment group) and the percentage (of available data) for each class of the variable will be presented. Continuous variables will be summarized using descriptive statistics, including number of participants (n), mean, standard deviation (SD), median, minimum, and maximum values. The coefficient of variation (CV%), geometric mean and geometric CV% will be presented for the PK tables.

95% Confidence Intervals will be reported where appropriate. If not mentioned otherwise, all statistical tests will be performed with a type I two-sided error rate of 5%.

6.2. TREATMENT SUMMARIZATION

Results will be presented for each treatment group, for the pooled FT011 group and overall.

6.3. PRECISION

All continuous demographic and safety variables (i.e., clinical laboratory values, vital signs, body weight and ECG intervals), including derivations thereof, will be reported to the same precision as the source data.

For the reporting of descriptive statistics, the mean and median will be presented to one digit more than the source data. The standard deviation will be presented to two digits more than the source data. The minimum and maximum will be presented to the same precision as the source data.

PK data (concentration-time and PK parameters) will be presented to three significant digits.

Percentages will be reported to one decimal point.

6.4. REFERENCE START DATE AND STUDY DAY

Study Day will be calculated from the date of first study drug administration and will be used to show start/stop day of assessments and events.

- If the date of the event is on or after the date of first study drug administration then:

Study Day = (date of event – date of first study drug administration) + 1

- If the date of the event is prior to the date of first study drug administration then:

Study Day = (date of event – date of first study drug administration)

There will be no Study Day 0.

In the situation where the event date is partial or missing, study day and any corresponding durations will appear partial or missing in the listings.

6.5. BASELINE

In general, baseline is defined as the last available, valid, non-missing measurement taken prior to first study drug administration (including unscheduled assessments). In the case where the last non-missing measurement and the reference start date coincide, that measurement will be considered pre-baseline, but adverse events (AEs) and medications commencing on the reference start date will be considered post-baseline.

6.6. ON-TREATMENT

A participant will be identified as on-treatment if the last available, valid, non-missing measurement taken prior to cut-off date indicates the participant is receiving a study drug.

6.7. RETESTS, UNSCHEDULED VISITS AND EARLY TERMINATION DATA

Unscheduled measurements will not be included in summaries at each protocol specified time point. However, unscheduled assessments will be taken into consideration in the calculation of baseline values.

Early termination results will be recorded as such and included with the end-of-study summaries.

In the case of a retest of a scheduled assessment, the retested measurement for that scheduled time (i.e., the original assessment) will be used for summaries unless flagged as invalid.

In the case of duplicate tests with the same sample date/time (in particular, where a lab sample is analysed at two separate labs), for quantitative results, the mean of the values will be used in the

summary tables and for qualitative results, the most abnormal of the values will be used in the summary tables. The listings will present the duplicate values.

Data from unscheduled visits/time points will be included in the figures (where appropriate) and data listings.

6.8. WINDOWING CONVENTIONS

No visit windowing will be performed for this study.

6.9. STATISTICAL TESTS

Where indicated, two-sided confidence intervals will be assessed at the 5% significance and two-sided p-value will be reported.

6.10. COMMON CALCULATIONS

For continuous measurements:

Actual change from baseline will be calculated as:

- Test Value at Visit X (after baseline) – Baseline Value

6.11. SOFTWARE VERSION

All derivations, statistical analyses, summaries and listings will be generated using SAS version 9.4 or higher (SAS Institute, Inc., Cary, North Carolina). PK Parameters will be calculated using WinNonlin version 8.3 or higher (Certara, LP Princeton, New Jersey, USA).

7. STATISTICAL CONSIDERATIONS

7.1. ADJUSTMENTS FOR COVARIATES AND FACTORS TO BE INCLUDED IN ANALYSES

The baseline values will be included as a covariate, treatment group will be included as a fixed effect, and the interaction effect between study visit and treatment group, and participant will be included as random effects in the mixed models for efficacy analysis.

No additional adjustments for covariates will be made.

7.2. MULTICENTER STUDIES

All centers are to be pooled by treatment group for analysis purposes and no by-center analyses are to be performed.

7.3. MISSING DATA

Missing data will not be imputed. Missing or incomplete dates will not be imputed if not indicated otherwise.

Unless otherwise specified, all analysis will be based on the number of observations in the relative analysis set, i.e. participants with missing information will be included in the denominator when calculating percentages.

7.3.1 MISSING OR PARTIAL ADVERSE EVENT DATES

Missing dates will not be imputed.

7.4. EXAMINATION OF SUBGROUPS

No subgroup analyses will be performed for this study.

8. OUTPUT PRESENTATIONS

APPENDIX 1 shows conventions for presentation of data in outputs.

The templates provided with this SAP describe the presentations for this study and therefore the format and content of the summary tables and listings to be provided by IQVIA Biostatistics.

9. DISPOSITION AND PROTOCOL DEVIATIONS

All participants who provide informed consent will be accounted for in this study.

9.1. DISPOSITION

Participant disposition will be tabulated for each treatment group and for all participants in the following categories:

- Total number of participants Screened (Overall summary only)
- Number of screen failures (Overall summary only)

- Screen failures reason

- Number of participants enrolled but not randomised (Overall summary only)
- Number of participants replaced (Overall summary only)
- Number of participants randomised
  - Number and percentage of participants started study drug
  - Number and percentage of participants did not start study drug
- Number and percentage of participants on-treatment (DSMB only)
- Number and percentage of participants off-treatment (DSMB only)
- Number and percentage of participants completing treatment
- Number and percentage of participants with study drug discontinuation
  - Primary reason for treatment discontinuation
- Number and percentage of participants completed study
- Number and percentage of participants with study discontinuation
  - Primary reason for study discontinuation

Percentages for the reasons for failed screening are based on the number of participants who failed screening; percentages for the reasons for study discontinuation are based on the number of participants who prematurely discontinued from the study; all other percentage are based on the number of randomised participants.

The number and percentage of participants included in each analysis set (definitions provided in Section 5) will also be summarized by treatment group and for all participants using frequency tabulations, based on the number of randomized participants.

Listings of study disposition, analysis set assignments, study eligibility, and study drug administration will be provided.

9.2. PROTOCOL DEVIATIONS

A protocol deviation is any noncompliance with the clinical trial protocol, Good Clinical Practice (GCP), or Manual of Procedure requirements. The noncompliance may be either on the part of the participant, the site principal investigator (PI), or the study site staff. Any participant enrolled who does not meet eligibility criteria will be considered an enrolment deviation.

Protocol deviations will be summarized by severity classification (critical, major or minor) and deviation type by treatment group and for all participants.

Protocol deviations will be listed including a severity classification of critical, minor or major, as determined by clinical staff. All participants whose study participation was impacted by COVID-19 will be flagged.

10. DEMOGRAPHIC AND OTHER BASELINE CHARACTERISTICS

Demographic data and other baseline characteristics will be presented for the ITT Analysis Set. Individual participant demographics and baseline characteristics will be presented in listings.

Demographic and baseline characteristics (age, sex, of childbearing potential, race, ethnicity, mRSS at Screening and scleroderma signs and symptoms, FVC, CRISS score, SHAQ-DI, SCTC-DI, 5-D Itch Scale, Patient Global Assessment, Physician Global Assessment) will be summarised and tabulated by treatment group and for all participants.

11. MEDICAL HISTORY/CURRENT MEDICAL CONDITION

Medical history or current medical condition will be presented for the Safety Analysis Set.

Medical history and current medical condition will be coded using Medical Dictionary for Regulatory Activities (MedDRA) central coding dictionary, Version 23.0 or higher. Medical history conditions are defined as those conditions which stop prior to first study drug administration. The number and percentage of participants for each system organ class (SOC) and preferred term (PT) will be summarized by treatment group and for all participants.

Summaries will be presented by SOC and PT, sorted by decreasing overall frequency. In cases of SOC classes or PTs with equal frequencies, it will be sorted alphabetically. Participants will be counted only once for each SOC or PT in the event that they have multiple records of the same SOC or PT term in the database. Medical history will be listed per treatment group.

12. PRIOR AND CONCOMITANT MEDICATIONS

Prior and concomitant medications will be coded using the World Health Organization (WHO)Drug Global Version 01MAR2021 (or later). Prior medications will be recorded up to 1 month prior to baseline observations.

Medications will be grouped by Anatomical Therapeutic Chemical (ATC) system (Level 2) and drug preferred term and summarized by treatment group for the Safety Analysis Set.

- Prior medications are those medications which stopped prior to the first study drug administration.
- Concomitant medications are medications which were taken at least once after the first study drug administration:
  - started prior to, on or after the first study drug administration AND ended on or after the date of first study drug administration or were ongoing at the end of the study.
  - Started on or after the date of first study drug administration.

In the listings, each medication will be identified as a prior medication (P), a concomitant medication that started prior to first study drug administration and continued after the first dose of study drug (PC) or a concomitant medication that started after the first dose of study drug ©.

In the summary tables, prior and concomitant medications will be presented by decreasing frequency of total medications overall within each ATC class and then similarly by decreasing frequency of total medications overall within each preferred term. In cases of ATC classes or preferred terms with equal frequencies, medications will be sorted alphabetically.

Systemic Sclerosis Related Concomitant Medications will be summarised separately. Systemic sclerosis (immunosuppressive medications) related concomitant medications will also be summarized separately for participants who have an mRSS increase of 5 or more.

13. STUDY DRUG EXPOSURE AND COMPLIANCE

Participants will be instructed to take two (2) capsules once per day during the treatment period.

Exposure to study drug will be presented for the Safety Analysis Set. A data listing containing the study drug administration details will be provided.

The date of first and last study drug administration will be taken from the drug administration eCRF form. Interruptions and compliance are not taken into account for duration of exposure.

Duration of exposure will be summarized by treatment group and for all participants.

13.1. DERIVATION

Duration of exposure (weeks) = (date of last study drug administration – date of first study drug administration + 1) / 7

13.2. STUDY DRUG COMPLIANCE

Compliance to the study drug will be presented for the ITT Analysis Set.

Overall treatment compliance will be summarized by treatment group and for all participants.

Kit dispensed, kit return details and study drug compliance will be listed per treatment group.

13.3. DERIVATION

$$Compliance\ (\%) = \frac{\text{number of capsules taken}}{(\text{date of kit returned} - \text{date of kit dispensed} + 1)\ \text{x}\ 2} \times 100$$

Overall study drug compliance will be calculated as:

$$Overall\ Treatment\ Compliance = [1 - (\frac{total\ number\ number\ of\ days\ of\ study\ drug\ interruption}{Duration\ of\ study\ drug\ exposure\ in\ days})] \times$$

100,

Where duration of study drug exposure is derived as date/time of last treatment – date/time of first treatment + 1.

14. PHARMACOKINETIC, EFFICACY AND PHARMACODYNAMIC ANALYSIS

14.1. PHARMACOKINETIC ANALYSIS

Pharmacokinetic data collected and analysed will be presented as described in this section. All PK analysis will be presented using the PK Analysis set.

14.1.1 PHARMACOKINETIC SAMPLE COLLECTION

Blood samples for plasma PK analyses will be collected at the following time points:

- Day 1: within 30 minutes prior to IMP administration, and at 1, 2, 3, 4, 5, 6, 7 and 8 hours post dose.
- Week 4: within 30 minutes prior to IMP administration.
- Week 8: within 30 minutes prior to IMP administration.
- Week 12: within 30 minutes prior to IMP administration, and at 1, 2, 3, 4, 5, 6, 7 and 8 hours post dose.

A window of ± 10 minutes is allowed for all time points. Collections outside of these windows will be recorded as protocol deviations. Actual collection time must be recorded. At each visit, the time of administration of the previous dose of IMP, and the time the dose is taken at the study site, must be recorded.

14.1.2 PHARMACOKINETIC CONCENTRATIONS

Plasma FT011 (and any metabolite) concentrations data will be summarised by visit and nominal collection time points using descriptive statistics including the number of concentrations below the limit of quantification (BLQ), CV%, geometric mean, and geometric CV%.

Results reported as BLQ will be treated as zero for the calculation of the summary statistics, and as missing for the calculation of the geometric statistics.

Spaghetti plots of the individual plasma FT011 concentrations vs. actual time profiles (relative to the dose at the visit) will be presented on linear and log-linear scales. Plots will be presented by treatment group and visit. BLQ concentrations will be set to 0 in the linear plots and will be treated as half of lower limit of quantification (0.5*LLOQ) in the log-linear plots.

Mean concentration profiles (± SD bars) vs. nominal time curves will be presented by visit on linear and log-linear scales.

All plasma FT011 concentration data will be listed, and the listing will include the calculated elapsed time since the study drug administration at the specific visit and the time deviations between the actual and planned sample collection times.

14.1.3 PHARMACOKINETIC PARAMETERS

Two sets of plasma FT011 PK parameters will be calculated based on the concentrations collected after the single dose on Day 1 and based on the concentrations collected after the last dose at Week 12. Plasma PK parameters will be calculated using a non-compartmental approach (Phoenix WinNonlin version 8.3 or higher) based on the observed concentration-time profiles. Actual sampling times relative to the dose at the visit will be used in all PK calculations. The PK set will be used for the pharmacokinetic parameter calculations. The following PK parameters will be determined for FT011 and additional parameters may be added at the discretion of the pharmacokineticist.

PK Parameter	Method
C_{max}	Maximum observed concentration
t_{max}	Time to reach maximum concentration
AUC_{0-8}	Area under the plasma concentration-time curve from the time of the dose administration to the time of the 8-hour post-dose concentration calculated by the linear up log down trapezoidal method
AUC_{last}	Area under the concentration-time curve from the time of the dose administration to the time of the last measurable concentration calculated by the linear up log down trapezoidal method

All predose BLQ values will be substituted by zeros. Thereafter BLQ values will be set as “missing”.

The plasma PK parameter results will be summarised by treatment group and visit using summary statistics and the geometric statistics described for the PK concentrations. All plasma PK parameter results will be listed.

Results will also be presented graphically using box-and-whisker plots.

14.2. EFFICACY ANALYSIS

All efficacy analysis will be presented using the mITT Analysis set. The statistical comparisons described in this SAP for the efficacy variables are exploratory only, and no formal hypotheses testing will be undertaken.

14.2.1 EFFICACY VARIABLES AND DERIVATION

14.2.1.1 MODIFIED RODNAN SKIN SCORE (MRSS)

The mRSS is a validated physical evaluation of participant's skin thickness rated by clinical palpation

using a 0-3 scale (0 = normal skin; 1 = mild thickness; 2 = moderate thickness with difficulty in making skin folds and no wrinkles; 3 = severe thickness with inability to pinch the skin into a fold) for each of 17 surface anatomic areas of the body: face, anterior chest, abdomen, and with right and left sides of the body separately evaluated, the fingers, forearms, upper arms, thighs, lower legs, dorsum of hands and feet. Individual values are summed and defined as the total skin score. Total score is 0 to 51 with higher scores indicating worse symptomology. Minimally clinically significant difference in mRSS is 3-5 points.[1]

14.2.1.2 Percent Predicted Forced Vital Capacity (FVC)

Percent predicted FVC is calculated using equations incorporating age, sex, and race. It is calculated as (FVC Observed / FVC Predicted) x 100, where FVC predicted is calculated relative to a reference population. Forced expiratory manoeuvres will be performed at least in triplicate with the minimal requirement that three manoeuvres are "acceptable" and that two of these manoeuvres meet end-of-test and repeatability criteria for FVC and forced expiratory volume in 1 second (FEV1).

14.2.1.3 Scleroderma Health Assessment Questionnaire-Disability Index (SHAQ-DI)

The SHAQ-DI consists of 20 questions referring to eight domains of activity: dressing/grooming, arising, eating, walking, hygiene, reach, grip, and activities. Each item is scored on a 4-point scale from 0 to 3: 0 = without any difficulty; 1 = with some difficulty; 2 = with much difficulty; 3 = unable to do.

The highest (0 is lowest, 3 is highest) score reported by a patient for any individual item in each of the domains is the score for that domain. Additionally, for each category if the patient indicates that they have used an aid or device, then the minimum score for that domain is 2. If the domain is previously scored as 3, then the domain score is 3. For example, if the highest score for dressing/grooming is ‘1’ and the patient says that they use a device for dressing, then the domain score for dressing/grooming would be set to ‘2’.

The overall composite SHAQ-DI (Standard Disability Index) for a patient is derived as the average of the computed domain scores (where the domain scores are set as described above), with the denominator based on the number of domains in which the patient has provided a response.

The composite score indicates the participant's self-assessed level of disability - higher scores indicate worse symptomology. The outcome is the change in mean score from baseline. A negative change from baseline indicates improvement.

The Scleroderma HAQ (SHAQ) includes an additional five scleroderma-specific visual analogue scales (VAS), addressing overall disease activity, Raynaud's phenomenon, finger ulcers, breathing, and intestinal problems. A composite VAS score is not created nor are the individual VAS scores incorporated into the HAQ DI score.

14.2.1.4 Patient Global Assessment Score

The Patient's Global Assessment represents the patient's overall health status on a 100-mm horizontal

VAS, ranging from 0 on the extreme left end of the scale indicating "extremely poor health status", and 100 on the extreme right end indicating "excellent health status".

14.2.1.5 Physician Global Assessment Score

The Physician's Global Assessment is to be completed based on examination and overall assessment of the participant. The physician's assessment of the participant's SSc status will be scored on a 100-mm horizontal VAS, ranging from 0 on the extreme left end of the scale indicating "no disease activity" (symptom free), and 100 on the extreme right end indicating "worst imaginable disease activity".

14.2.1.6 Composite Response Index in Diffuse Cutaneous Systemic Sclerosis (CRISS)

The ACR CRISS was developed using expert consensus and data driven approaches for use in clinical trials.[2,3] The exponential algorithm determines the predicted probability of improvement from baseline, incorporating change in the mRSS, FVC percent predicted, physician and patient global assessments, and HAQ-DI. The outcome is a continuous variable between 0.0 and 1.0 (0 - 100%). A higher score indicates greater improvement.

The application of CRISS algorithm in a randomised clinical trial is a 2-step process.

In the first step, participants will be clinically evaluated to determine whether the participant has improved or not. A participant is considered not improved and is assigned a probability score of improving equal to 0.0, irrespective of improvement on other core items, if he/she develops:

1. New scleroderma renal crisis.
2. Decline in FVC % predicted ≥15% (relative), confirmed by another FVC % within a month, high resolution computed tomography (HRCT) to confirm interstitial lung disease (if previous HRCT did not show interstitial lung disease) and FVC % predicted below 80% predicted (attributable to SSc).
3. New onset of left ventricular failure (defined as ejection fraction ≤45%) or new onset of pulmonary arterial hypertension requiring treatment (attributable to SSc).

If the participant is determined to exhibit improvement in the first step (i.e., not assigned a 0.0), the second step involves computing the predicted probability of improving (a score between 0.0 and 1.0, inclusive) using the equation:

$$\frac{exp\left[-5.54-0.81*\Delta_{MRSS}+0.21*\Delta_{FVC\%}-0.40*\Delta_{Pt-glob}-0.44*\Delta_{MD-glob}-3.41*\Delta_{HAQ-DI}\right]}{1+exp\left[-5.54-0.81*\Delta_{MRSS}+0.21*\Delta_{FVC\%}-0.40*\Delta_{Pt-glob}-0.44*\Delta_{MD-glob}-3.41*\Delta_{HAQ-DI}\right]}$$

where ΔMRSS indicates the change in mRSS from baseline to the visit, ΔFVC denotes the change in FVC % predicted from baseline to the visit, ΔPt-glob indicates the change in patient global assessment, ΔMD-glob denotes the change in physician global assessment, and ΔHAQ-DI is the change in HAQ-DI. Note that all changes are absolute changes. Additionally, Pt-glob will be calculated as 100-reported score. ΔPt-glob and ΔMD-glob will be divided by 10.

Participants for which the predicted probability is greater or equal to 0.60 are considered improved, while participants for which the predicted probability is below 0.60 are considered not improved.

14.2.1.7 Scleroderma Clinical Trials Consortium Damage Index (SCTC-DI)

The SCTC-DI is a 23-item composite damage index to quantify organ damage in systemic sclerosis (0-55 scale: >5 moderate damage, >12 severe damage). The total SCTC-DI score is reported on the eCRF.

14.2.1.8 5-D Itch Scale

The 5-D itch scale is a validated brief multidimensional questionnaire designed to be useful as an outcome measure in clinical trials. The five dimensions are degree, duration, direction, disability, and distribution.

14.2.1.9 Missing Data Methods for Efficacy Variable

Missing data will not be imputed, unless otherwise stated.

14.2.1.10 Analysis of Efficacy Variables

The observed values and change from baseline values for mRSS, percent predicted FVC, HAQ-DI, patient global assessment score, and physician global assessment score, and SCTC-DI score will be listed for each participant at each protocol specified visit and will be summarised using descriptive statistics over time by treatment group and for all participants.

Actual and change from baseline values will be presented graphically by treatment group using a jitter plot and overlaid box-whisker plot (median, 25th and 75th percentiles) over time.

For mRSS, HAQ-DI, SCTC-DI and 5-D Itch Scale the individual item responses will also be summarised and listed for each participant.

The 5-D itch scale at baseline and at Week 12 will be listed for each participant and will be summarised using descriptive statistics. The change from baseline to Week 12 will also be summarised.

Even though no formal hypothesis testing is planned for this study, exploratory analyses may be performed to assess the treatment effect of FT011 on the efficacy outcomes if data indicates trend and model assumptions hold.

For mRSS, percent predicted FVC, HAQ-DI, patient global assessment score, and physician global assessment score, the change from baseline values will be compared between the FT011 and placebo groups using a mixed model for repeated measures with the baseline value as a covariate, treatment group as fixed effect, the interaction effect between study visit and treatment group, and participant as random effect using an unstructured covariance structure. Parameter estimates will be calculated using restricted maximum likelihood methods (REML), and the Kenward-Rogers method for determining the degrees of freedom. This method will assume that any missing data is Missing at Random (MAR). Example SAS code for the mixed model (using SAS Proc Mixed) is:

```
PROC MIXED data=libname.ADXX REML;
CLASS TRT01P VISIT SUBJID;
MODEL AVAL = TRT01P|VISIT BASELINE / DDFM = KENWARDROGER;
RANDOM VISIT / SUBJECT = SUBJID TYPE = UN;
LSMEANS TRT01P|VISIT / PDIFF = CONTROL('PLACEBO') CL ;
RUN;
```

Details of model including covariance structure will be decided based on the model fit. The least squares means, estimated treatment differences (compared to placebo) with two-sided 95% confidence intervals and p-values will be presented.

The CRISS score and SCTC-DI score will be compared between FT011 and placebo group using a Wilcoxon rank-sum test at each post-baseline visit. Example SAS code for this is:

```
PROC NPAR1WAY DATA=LIBNAME.ADXX (where=(trt01p in (placebo treatment_groupX)) WILCOXON;
CLASS TRT01P;
VAR AVAL;
EXACT WILCOXON;
RUN;
```

The proportions (binary outcomes) of participants showing an:

- improvement in CRISS at Week 12

will be listed, summarised and compared using the Cochran-Mantel-Haenszel test. Example SAS code for the Cochran-Mantel-Haenszel test in SAS Proc Freq is:

```
PROC FREQ DATA=LIBNAME.ADXX;
        TABLES TRT01P*AVAL / CMH;
RUN;
```

14.3. PHARMACODYNAMIC ANALYSIS

14.3.1 PHARMACODYNAMIC VARIABLES AND DERIVATION

At each visit during the Treatment Period, samples will be collected for measurement of the following cytokines and chemokines: IL-6, CCL2, CXCL8 (IL-8), CXCL4 (MCP-1), TGFβ, CTGF, ICAM-1, VEGF, IL-4, IL-10, and IL-1β.

14.3.2 MISSING DATA METHODS FOR PHARMACODYNAMIC VARIABLE

Missing data will not be imputed, unless otherwise stated.

14.2.3 ANALYSIS OF PHARMACODYNAMIC VARIABLE

The observed values and change from baseline values will be listed for each participant at each protocol specified visit and will be summarised using descriptive statistics over time by treatment

group and for all participants.

15. SAFETY OUTCOMES

All safety summaries will be based on the Safety Analysis Set.

There will be no statistical comparisons between the treatment groups for safety outcomes.

15.1. ADVERSE EVENTS

AEs will be coded to system organ class (SOC) and preferred term (PT) using MedDRA central coding dictionary, Version 23.0 (or higher).

Treatment-emergent adverse events (TEAEs) are defined as AEs which commence or worsen on or after the date and time of first study drug administration. AEs without an onset date and time will be defined as treatment-emergent except if an incomplete date (e.g., month and year) clearly indicates that the event started prior to start of first study drug administration or if the AE stop date indicates that the event started and/or stopped prior to start of first study drug administration.

All Adverse Events (AEs) summaries will be restricted to the TEAEs only. The number and percentage of TEAEs, Serious TEAEs, TEAEs leading to discontinuation of study treatment and study, and TEAEs related to study treatment will be summarized by SOC, PT and treatment group. The number and percentage of TEAEs by maximum severity will also be summarized.

An overall summary of the number and percentage of participants who had events in each of the categories described below will be produced by treatment group and for all participants.

The following AE summaries will be provided:

- Overview of TEAEs, including:
    - At least one TEAE
    - At least one study treatment related TEAE
    - At least one serious TEAE
    - At least one study treatment related serious TEAE
    - Any TEAE leading to death
    - TEAE leading to study discontinuation
    - TEAE leading to study drug withdrawal
    - TEAE leading to study drug interruption
    - At least one TEAE by maximum severity
    - At least one study treatment related TEAE by maximum severity
- Incidence of TEAEs by SOC and PT
- Incidence of study treatment related TEAEs by SOC and PT

- Incidence of TEAEs by maximum severity
- Incidence of study treatment related TEAEs by maximum severity
- Incidence of serious TEAEs by SOC and PT
- Incidence of study treatment related serious TEAEs by SOC and PT.

In the summary tables, AEs will be presented by decreasing frequency of total participants overall within each SOC and then similarly by decreasing frequency of total participants overall within each PT. SOC or PTs with equal frequencies will be sorted alphabetically.

An overall summary of number of participants within each of the categories described in the sub-section below, will be provided as specified in the templates.

The overall Listing of adverse events will include TEAEs and Non-TEAEs. All other listings will include TEAEs only.

15.1.1 All TEAEs

Incidence of TEAEs will be presented by SOC and PT and broken down further by maximum severity and relationship to study treatment. In these tables, SOC and PT will be presented by decreasing frequency.

15.1.1.1 Severity

Adverse event severity is classified as mild, moderate, or severe. TEAEs starting after the first dose of study treatment with a missing severity will be classified as severe. If a participant, reports a TEAE more than once within that SOC/ PT, the AE with the worst-case severity will be used in the corresponding severity summaries.

15.1.1.2 Relationship to Study Treatment

Relationship to study treatment, as assessed by the Investigator, is classified as definitely related, probably related, possibly related, unlikely related or not related. TEAEs reported as having a definitely related, probably related, or possibly related relationship to study treatment are classified as related. TEAEs with a missing or unknown relationship to study treatment will be considered related to study treatment. If a participant, reports the same AE more than once within that SOC/ PT, the AE with the worst relationship to study treatment will be used in the corresponding relationship summaries.

15.1.1.3 TEAEs Leading to Study Drug interruption

TEAEs leading to drug interruption will be identified by using the variable pertaining to action taken with study treatment on the AE page of the eCRF indicated as 'Drug interrupted' and all TEAEs meeting this criteria will be listed separately.

15.1.1.4 TEAEs Leading to Study Drug Withdrawal

TEAEs leading to permanent discontinuation of study drug will be identified by using the variable pertaining to action taken with IP on the AE page of the eCRF indicated as 'Drug withdrawn' and all TEAEs meeting this criteria will be listed separately.

15.1.1.5 TEAEs Leading to Study Discontinuation

TEAEs leading to study discontinuation will be identified by using the variable pertaining to 'specify action taken' on the AE page of the eCRF indicated as 'Withdrawn from study' and all TEAEs meeting this criteria will be listed separately.

15.1.1.6 Adverse Events Leading to Death

TEAEs leading to death will be identified by using the variable pertaining to seriousness criteria on the AE page of the eCRF indicated as 'Death' and all TEAEs leading to death will be listed separately.

15.1.1.7 Serious Adverse Events

Serious adverse events (SAEs) are those events recorded as "Serious" on the AE page of the eCRF and all Serious Treatment-Emergent AEs will be summarized and listed separately.

15.2. Laboratory Evaluations

Central safety laboratory results will be included in the reporting of this study for haematology, biochemistry, coagulation, urinalysis, and serum pregnancy testing. No lab data imputation will be performed. Incomplete data may be excluded from some analyses. In cases where an analysis depends on identifying an abnormal value, only values which are non-missing and which can be clearly identified programmatically as abnormal will be counted.

Presentations will use SI Units, as provided by the laboratory.

Quantitative laboratory measurements reported as "<X", i.e. below the lower limit of quantification, or "> X", i.e. above the upper limit of quantification, will be converted to X for the purpose of quantitative summaries, but will be presented as recorded, i.e. as "<X" or "> X" in the listings.

Laboratory data will be summarized using descriptive statistics. Clinical laboratory data collected during study conduct, which were not required per protocol, such as for special testing to evaluate an AE, will be listed and not summarized.

All laboratory data is summarised and listed for all visits where data is collected. The following summaries are provided for laboratory data:

Actual values and change from baseline will be summarized using descriptive statistics at each protocol specified time point, by treatment group.

- Shift from baseline will be summarized at each post-baseline protocol scheduled time by treatment group , using frequency tabulations.

- Separate listings will be produced for all participants with at least one out-of-range or abnormal clinical laboratory result. In these listings, the full time point profile will be presented for the parameter with the out-of-range or abnormal value.

A list of laboratory assessments to be included in the outputs is included below:

- Haematology: Haemoglobin, haematocrit, red blood cell count, red cell distribution width, mean corpuscular volume, mean corpuscular haemoglobin, mean corpuscular haemoglobin concentration, white blood cell count, neutrophils, lymphocytes, monocytes, eosinophils, basophils, and platelet count
- Biochemistry: Sodium, potassium, magnesium, bicarbonate, phosphate, calcium, urea, urate, serum albumin, total protein, gamma-glutamyl transferase, alanine transaminase, aspartate transaminase, direct bilirubin, alkaline phosphatase, glucose, cholesterol, triglycerides, high-density lipoprotein, low-density lipoprotein, creatine phosphokinase, lactate dehydrogenase, creatinine, eGFR.
- Coagulation: Activated partial thromboplastin time (aPTT), Prothrombin time, International normalized ratio (INR), Fibrinogen
- Urinalysis: urine culture, sensitivities, antibiotic susceptibility, urine albumin, urine creatinine, urinary albumin creatinine ratio (UACR)

LABORATORY SPECIFIC DERIVATIONS

Unit conversions for laboratory data will be provided in the programming specifications documents.

LABORATORY REFERENCE RANGE

Continuous laboratory measurements will be compared with the relevant laboratory reference ranges by the laboratory vendors and categorized as:

- Low: Below the lower limit of the laboratory reference range.
- Normal: Within the laboratory reference range (upper and lower limit included).
- High: Above the upper limit of the laboratory reference range.
- Laboratory values that do not have a reference range will not be categorized.

15.3. 12-LEAD ELECTROCARDIOGRAM EVALUATIONS

12-Lead Electrocardiogram (ECG) parameters (heart rate [beats/min], PR interval[msec], QRS duration[msec], QT interval [msec], QTcF interval [msec], QTcB interval [msec] and RR interval [msec]) will be reported for this study.

The following summaries will be provided for ECG data:

- All ECG data will be presented in data listings.

- Actual values and change from baseline for ECG parameter values will be summarized using descriptive statistic at each protocol specified time point by treatment group .
- Shift from baseline according to the investigator's interpretation of ECG results (Normal, Abnormal NCS, Abnormal CS) will be summarized at each post-baseline protocol scheduled time by treatment group , using frequency tabulations.

15.4. VITAL SIGNS

The following vital signs measurements will be reported for this study: height [cm], body weight [kg], BMI [kg/m^2], body temperature[˚C], heart rate [beats/min], respiratory rate [breaths/min], systolic blood pressure [mmHg], diastolic blood pressure [mmHg].

The following summaries will be provided for vital sign data:

- Actual values and change from baseline for vital signs parameter values will be summarized using descriptive statistics at each protocol specified time point by treatment group.
- All vital signs data will be presented in data listings.

DERIVATIONS

- BMI (kg/ m^2) = Body weight (kg)/ Height $(m)^2$

15.5. PHYSICAL EXAMINATION

Physical examination will include examination of general appearance, skin, head, neck (including thyroid), ears, eyes, nose, throat, heart, lungs, abdomen, lymph nodes, extremities and nervous system will be evaluated by the Investigator as Normal, Abnormal NCS or Abnormal CS. New abnormalities occurring after IP administration will be recorded as AEs. Full physical exam will be given at screening and symptom directed physical examination will be given thereafter.

The Investigator's assessment of the physical examination for the various body systems will be listed.

16. DATA NOT SUMMARISED OR PRESENTED

The other variables and/or domains not summarized or presented are:

- Comments
- Skin Biopsy.

These domains and/or variables will not be summarized or presented, but will be available in the clinical study database, SDTM and/or ADaM datasets and listed.

17. REFERENCES

Protocol Version 32.1, dated 01 November 2021.

eCRF Version 7.3, dated 10 November 2021.

1 Amjadi et al., American College of Rheumatology; Aug 2009; 2493-2494

2 Khanna D, Lovell DJ, Giannini E, Clements PJ, Merkel PA, Seibold JR, et al. Development of a provisional core set of response measures for clinical trials of systemic sclerosis. Ann Rheum Dis. 2008;67(5):703-709

3 Khanna D, Berrocal VJ, Giannini EH, Seibold JR, Merkel PA, Mayes MD, et al. The American College of Rheumatology Provisional Composite Response Index for Clinical Trials in Early Diffuse Cutaneous Systemic Sclerosis. Arthritis Rheumatol. 2016; 68(2):299-311.

APPENDIX 1. PROGRAMMING CONVENTIONS FOR OUTPUTS

OUTPUT CONVENTIONS

Outputs will be presented according to the following IQVIA Global Biostatistics Standard Output Conventions.

DATES & TIMES

Depending on data available, dates and times will take the format DDMMMYYYY; times will take the format HH:MM; combined dates and times will take the format DDMMMYYYY/HH:MM. Time will be based on a 24 hour clock.

SPELLING FORMAT

British (UK), except for MedDRA where British English is used.

PRESENTATION OF TREATMENT GROUPS

Only the treatment groups that were actually dosed will be presented in the tables, listings and figures. Study groups that are planned in the protocol but were not conducted will not be included in the outputs.

For outputs, treatment groups will be represented as follows and in that order:

Treatment Group	For Tables and Graphs	For Listings
Placebo	Placebo	Placebo
FT011 200 mg QD	FT011 200 mg	FT011 200 mg
FT011 400 mg QD	FT011 400 mg	FT011 400 mg
Pooled FT011	Pooled FT011	NA
All Participants	All Participants	NA

LISTINGS

The listings will contain data from all scheduled and unscheduled visits, as per the schedule of events Section 2 of the protocol.

All listings will be ordered by the following (unless otherwise indicated in the template):

- Treatment group
- Participant ID
- Date and time (where applicable).

APPENDIX 2. PARTIAL DATE CONVENTIONS

Imputed dates will NOT be presented in the listings.

ALGORITHM FOR DEFINITION OF TREATMENT-EMERGENT ADVERSE EVENTS:

START DATE	STOP DATE	ACTION
Known	Known/Partial/ Missing	If start date < study med start date, then not TEAE If start date >= study med start date, then TEAE
Partial, but known components show that it cannot be on or after study med start date	Known/Partial/ Missing	Not TEAE
Partial, could be on or after study med start date OR Missing	Known	If stop date < study med start date, then not TEAE If stop date >= study med start date, then TEAE
	Partial	Impute stop date as latest possible date (i.e. last day of month if day unknown or 31st December if day and month are unknown), then: If stop date < study med start date, then not TEAE If stop date >= study med start date, then TEAE
	Missing	Assumed TEAE

ALGORITHM FOR DEFINITION OF PRIOR / CONCOMITANT MEDICATIONS:

START DATE	STOP DATE	ACTION
Known	Known	If stop date < study med start date, assign as prior If stop date >= study med start date and start date <= end of treatment, assign as concomitant
	Partial	Impute stop date as latest possible date (i.e. last day of month if day unknown or 31st December if day and month are unknown), then: If stop date < study med start date, assign as prior If stop date >= study med start date and start date <= end of treatment, assign as concomitant
	Missing	If stop date is missing could never be assumed a prior medication If start date <= end of treatment, assign as concomitant
Partial	Known	Impute start date as earliest possible date (i.e. first day of month if day unknown or 1st January if day and month are unknown), then: If stop date < study med start date, assign as prior If stop date >= study med start date and start date <= end of treatment, assign as concomitant
	Partial	Impute start date as earliest possible date (i.e. first day of month if day unknown or 1st January if day and month are unknown) and impute stop date as latest possible date (i.e. last day of month if day unknown or 31st December if day and month are unknown), then: If stop date < study med start date, assign as prior If stop date >= study med start date and start date <= end of treatment, assign as concomitant
	Missing	Impute start date as earliest possible date (i.e. first day of month if day unknown or 1st January if day and month are unknown), then: If stop date is missing could never be assumed a prior medication If start date <= end of treatment, assign as concomitant
Missing	Known	If stop date < study med start date, assign as prior If stop date >= study med start date, assign as concomitant
	Partial	Impute stop date as latest possible date (i.e. last day of month if day unknown or 31st December if day and month are unknown), then: If stop date < study med start date, assign as prior If stop date >= study med start date, assign as concomitant
	Missing	Assign as concomitant

APPENDIX 3. TABLES AND LISTINGS FOR DSMB MEETINGS

TABLES

- STUDY DISPOSITION, ALL PARTICIPANTS ENROLLED SET
- DEMOGRAPHICS, INTENTION-TO-TREAT SET
- DISEASE HISTORY, SAFETY ANALYSIS SET
- TREATMENT-EMERGENT ADVERSE EVENTS, SAFETY ANALYSIS SET
- TREATMENT-EMERGENT SEVERE ADVERSE EVENTS, SAFETY SET
- TREATMENT-EMERGENT SERIOUS ADVERSE EVENTS, SAFETY SET
- TREATMENT RELATED TREATMENT-EMERGENT ADVERSE EVENTS, SAFETY SET
- CLINICALLY SIGNIFICANT LABORATORY VALUES , SAFETY SET
- ELECTROCARDIOGRAM FINDINGS, SAFETY SET
- SCLERODERMA RELATED CONCOMITANT MEDICATIONS , SAFETY SET

LISTINGS

- STUDY DISPOSITION, INTENTION-TO-TREAT SET
- DEMOGRAPHICS, INTENTION-TO-TREAT SET
- DISEASE HISTORY, INTENTION-TO-TREAT SET
- CONCOMITANT MEDICATION, SAFETY ANALYSIS SET
- PARTICIPANT QUESTIONNAIRES, PHYSICAL EXAMINATIONS, VITAL SIGNS MEASUREMENTS
- ADVERSE EVENTS, SAFETY SET
- SERIOUS ADVERSE EVENTS, SAFETY SET
- ADVERSE EVENTS LEADING TO DISCONTINUATION OF STUDY DRUG, SAFETY SET
- LABORATORY MEASURES, SAFETY SET
- ELECTROCARDIOGRAM, SAFETY SET