# Statistical Analysis Plan Addendum

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|---|---|
| **Clinical Trial Protocol Identification No.** | EMR 200017-014 |
| **Title:** | A Phase II, randomized, double-blind, placebo-controlled, parallel-group, multicenter trial to evaluate the efficacy and safety of abituzumab in subjects with systemic sclerosis-associated interstitial lung disease (SSc-ILD) |
| **Trial Phase** | Phase II |
| **Investigational Medicinal Product(s)** | Abituzumab |
| **Clinical Trial Protocol Version** | Version 5.0 (Global), 26 July 2017<br>Version 5.1 (USA, Argentina, Australia and Israel), 09 August 2017 |
| **Statistical Analysis Plan Author** | PPD |
| **Statistical Analysis Plan Addendum Date and Version** | V1 / 05 April 2018 |
| **Statistical Analysis Plan Reviewers** | PPD<br>PPD<br>PPD, EMD Serono.<br>PPD<br>, EMD Serono.<br>PPD, Medical Responsible, EMD Serono.<br>PPD, PPD, EMD Serono.<br>PPD, PPD, EMD Serono. |

# 1 Signature Page

**Statistical Analysis Plan Addendum:** EMR 200017-014

A Phase II, randomized, double-blind, placebo-controlled, parallel-group, multicenter trial to evaluate the efficacy and safety of abituzumab in subjects with systemic sclerosis-associated interstitial lung disease (SSc-ILD)

PPD PPD Date: PPD

Trial Biostatistician

PPD

PPD PPD Date: PPD

PPD

EMD Serono

45A Middlesex Turnpike, Billerica, MA 01821, USA

PPD Date: PPD

PPD

PPD

EMD Serono

45A Middlesex Turnpike, Billerica, MA 01821, USA

PPD PPD Date: PPD

Medical Responsible

EMD Serono

45A Middlesex Turnpike, Billerica, MA 01821, USA

# 2 Table of Contents

# 3 List of Abbreviations and Definition of Terms

Refer to the Study SAP.

# 4 Modification History

| Unique Identifier for SAP Version | Date of SAP Version | Author | Changes from the Previous Version |
|---|---|---|---|
| 1.0 | 05 April 2018 | PPD | N/A – First version |

# 5 Purpose of the Statistical Analysis Plan Addendum

The purpose of this statistical analysis plan (SAP) addendum is to document technical and detailed specifications for the Final Analysis for protocol EMR200017-014.

Due to the early termination of the study and consequently the limited number of subjects and data available, the full pre-planned analyses in the Study SAP (dated 15 November 2017) will not be carried out, since they may lead to unreliable conclusions. Hence this addendum references the applicable parts of the Study SAP and the Independent Data Monitoring Committee (IDMC) SAP (dated 29 June 2016) to produce the tables, listings, and figures (TLFs) to be included in the abbreviated clinical study report (CSR).

# 6 Summary of Clinical Study Features

Refer to the Study SAP.

# 7 Sample Size/Randomization

Refer to the Study SAP.

# 8 Overview of Planned Analyses

## 8.1 Final Analysis

**Cut-off date:**

The data cut-off date for the final analysis will be when all randomized subjects have completed the Week 12 Safety Follow-up visit or been lost to follow-up. No more data are expected to be entered into the database by the sites after this point.

A blinded data review meeting will be held prior to database lock in order to identify and confirm protocol deviations (PDs).

**Dissemination of results:**

The blinded Biostatistics study team will become unblinded after database lock. Results will be generated on the aggregate group level and delivered to the Sponsor as one package (no key TLFs will be produced) following the normal process.

**TLF Shells:**

Refer to Appendix 1 for the TLF shells.

# 9 Changes to the Planned Analyses in the Clinical Study Protocol

See subsequent sections regarding the analyses that will be performed for the abbreviated CSR.

# 10 Protocol Deviations and Analysis Sets

Refer to the Study SAP.

Subject disposition will use the Screening Analysis Set, all baseline and safety summaries will use the Safety Analysis Set and all efficacy summaries will use the mITT Analysis Set. The other analysis sets will not be required for the following reasons:

- Intent-to-treat – All randomized subjects were treated so this is equivalent to the mITT analysis set.
- Per-Protocol – The purpose of this was for sensitivity analysis on the primary and key secondary endpoints, which will no longer be performed.
- PK – No PK analyses will be performed for the abbreviated CSR.
- Pharmacogenetics – No CCI analyses will be performed for the abbreviated CSR.

Since no supportive analyses on the primary endpoint will be performed, no subgroups will be identified.

# 11 General Specifications for Statistical Analyses

Refer to the Study SAP. Only summary statistics will be computed.

**Early Termination Visit:**

Since subjects will be performing their early termination (ET) visits at different stages within the protocol schedule of assessments, for the efficacy by-visit summaries, the ET visits will reference the protocol visits in between which they fell chronologically.

For example, if a subject performed their Week 12 visit, then performed their ET visit at a later date (but before their scheduled Week 24 visit), their ET visit will be shown as “ET (W12 – W24)” to display the weeks that it fell between.

**Missing data:**

No imputation of missing efficacy data or duration of prior mycophenolate use at baseline will be performed.

# 12 Study Subjects

Subject disposition status will be summarized as per the Study SAP. Important PDs will be listed only and clinically important PDs will not be identified.

# 13 Demographics and Other Baseline Characteristics

Demographics, medical history, and disease history will be summarized as per the IDMC SAP.

# 14 Previous or Concomitant Medications/Procedures

Previous and concomitant medications will be summarized as per the IDMC SAP.

# 15 Treatment Compliance and Exposure

The following will be summarized using descriptive statistics:

- Treatment duration (weeks)
- Number of infusions of trial treatment received
- Treatment adherence (%)
- Infusion duration (hours) and volume (mL)
- Number of subjects with at least one dose adjustment (overall and by reason)
- Number of subjects with at least one infusion not completed as planned (overall and by reason)

Refer to the Study SAP for definitions.

# 16 Endpoint Evaluation

Summary statistics of absolute values and change from baseline will be provided for the following efficacy measurements. No statistical tests will be performed or confidence intervals presented.

Pulmonary function tests:

- FVC
- FVC % Predicted
- DLCO – eCRF result
- DLCO % Predicted – eCRF result
- KCO – eCRF result

HRCT results:

- QLF
- Total ILD

QoL questionnaires:

- Mahler TDI
- SGRQ
- Physician's Global Assessment
- Patient's Global Assessment
- SHAQ – VAS scores only
- EQ-5D – VAS score only

- Leicester Cough Index

Skin fibrosis:

- mRSS
- Digital Ulcer Count

Clinically meaningful disease progression and overall survival:

- Disease Progression
- Listing of Deaths

Refer to the Study SAP for details of these measurements and any derivations required.

# 17 Safety Evaluation

Refer to the IDMC SAP for the safety summaries that will be provided.

# 18 Appendix 1 – TLF shells

## 18.1 Tables and Figures

**Programming note:**

**The shells use Treatment A, B & C.**

**The order of the treatment groups in the tables will be as follows:**

| | Placebo | Abituzumab 500 mg | Abituzumab 1500 mg | Total |
|---|---|---|---|---|

**The same order will be used for listings.**

This table of contents details which TLFs have been produced for the IDMCs and which are new for the final analysis:

EMR200017-014_Synoptic_CSR_TOC_for

Red text in the shells is where the IDMC TLF has been adjusted for the final analysis.

The headers will be:

```
Protocol: EMR 200017-014 (Abituzumab) - Cutoff date: DDMMMYYYY (<Purpose>)
-------------------------------------------------------------------------------------------
```

The footers will be:

```
-------------------------------------------------------------------------------------------------------------------------
Source: ADxx DDMMMYYYY hh:mm <creation date of ADAM dataset>; Listing 16.2.xx; SDTM package: DDMMMYYYY
Program_path\pgm_name.sas, DDMMMYYYY hh:mm                                                          Page 1 of x
```

15.1: Demographic and Baseline Data
15.1.1: Subject Disposition
Table 15.1.1.1: Subject Disposition Status

| | Treatment A | Treatment B | Treatment C | Total |
|---|---|---|---|---|
| Number of screened subjects*(a)*, n | | | | xx |
| Number of screen failures, n | | | | xx |
| Subject did not meet all eligibility criteria | | | | xx |
| Withdrew informed consent | | | | xx |
| Progressive disease | | | | xx |
| Adverse event | | | | xx |
| Lost to follow-up | | | | xx |
| Death | | | | xx |
| Other | | | | xx |
| Missing | | | | xx |
| Randomized subjects, n (%) | xx (100.0) | xx (100.0) | xx (100.0) | xx (100.0) |
| Baseline FVC <70% predicted | xx (xx.x) | xx (xx.x) | xx (xx.x) | xx (xx.x) |
| Baseline FVC ≥70% predicted | xx (xx.x) | xx (xx.x) | xx (xx.x) | xx (xx.x) |
| Received no treatment, n (%)* | xx (xx.x) | xx (xx.x) | xx (xx.x) | xx (xx.x) |
| Treatment Ongoing, n (%) | xx (xx.x) | xx (xx.x) | xx (xx.x) | xx (xx.x) |
| Treatment Completed, n (%) | xx (xx.x) | xx (xx.x) | xx (xx.x) | xx (xx.x) |

**Shell continues on the next page**

15.1: Demographic and Baseline Data
15.1.1: Subject Disposition
Table 15.1.1.1: Subject Disposition Status

| | Treatment A | Treatment B | Treatment C | Total |
|---|---|---|---|---|
| Subjects who discontinued trial treatment, n (%) | xx (xx.x) | xx (xx.x) | xx (xx.x) | xx (xx.x) |
| Adverse Event | xx (xx.x) | xx (xx.x) | xx (xx.x) | xx (xx.x) |
| Lost to Follow-up | xx (xx.x) | xx (xx.x) | xx (xx.x) | xx (xx.x) |
| Protocol non-compliance | xx (xx.x) | xx (xx.x) | xx (xx.x) | xx (xx.x) |
| Death | xx (xx.x) | xx (xx.x) | xx (xx.x) | xx (xx.x) |
| Progressive disease | xx (xx.x) | xx (xx.x) | xx (xx.x) | xx (xx.x) |
| Withdrew Consent | xx (xx.x) | xx (xx.x) | xx (xx.x) | xx (xx.x) |
| Other | xx (xx.x) | xx (xx.x) | xx (xx.x) | xx (xx.x) |
| Subjects who discontinued trial treatment and withdrew from the treatment period, n (%) | xx (xx.x) | xx (xx.x) | xx (xx.x) | xx (xx.x) |
| Subjects who withdrew from the trial, n (%) | xx (xx.x) | xx (xx.x) | xx (xx.x) | xx (xx.x) |
| Adverse Event | xx (xx.x) | xx (xx.x) | xx (xx.x) | xx (xx.x) |
| Lost to Follow-up | xx (xx.x) | xx (xx.x) | xx (xx.x) | xx (xx.x) |
| Protocol non-compliance | xx (xx.x) | xx (xx.x) | xx (xx.x) | xx (xx.x) |
| Death | xx (xx.x) | xx (xx.x) | xx (xx.x) | xx (xx.x) |
| Progressive disease | xx (xx.x) | xx (xx.x) | xx (xx.x) | xx (xx.x) |
| Withdrew Consent | xx (xx.x) | xx (xx.x) | xx (xx.x) | xx (xx.x) |
| Other | xx (xx.x) | xx (xx.x) | xx (xx.x) | xx (xx.x) |

Note: Percentages for 'Subjects who discontinued trial treatment' are based on the number of subjects who received at least one infusion of trial treatment. All other percentages are based on the number of subjects randomized.
No subjects were randomized under the new stratification level of < 6 months prior mycophenolate duration, so this stratification factor has not been presented.
* Number of subjects who received no treatment based on current exposure data.

15.1: Demographic and Baseline Data
15.1.4: Demographic Characteristics
Table 15.1.4.1: Demographic Characteristics - SAF Analysis Set

| | Treatment A N=xxx (100%) | Treatment B N=xxx (100%) | Treatment C N=xxx (100%) | Total N=xxx (100%) |
|---|---|---|---|---|
| Sex, n (%) | | | | |
| Male | xx (xx.x) | xx (xx.x) | xx (xx.x) | xx (xx.x) |
| Female | xx (xx.x) | xx (xx.x) | xx (xx.x) | xx (xx.x) |
| Missing | xx (xx.x) | xx (xx.x) | xx (xx.x) | xx (xx.x) |
| Race, n (%) | | | | |
| White | xx (xx.x) | xx (xx.x) | xx (xx.x) | xx (xx.x) |
| Black or African American | xx (xx.x) | xx (xx.x) | xx (xx.x) | xx (xx.x) |
| Asian | xx (xx.x) | xx (xx.x) | xx (xx.x) | xx (xx.x) |
| American Indian or Alaska Native | xx (xx.x) | xx (xx.x) | xx (xx.x) | xx (xx.x) |
| Native Hawaiian or Other Pacific Islander | xx (xx.x) | xx (xx.x) | xx (xx.x) | xx (xx.x) |
| Other | xx (xx.x) | xx (xx.x) | xx (xx.x) | xx (xx.x) |
| Missing (including not collected at site) | xx (xx.x) | xx (xx.x) | xx (xx.x) | xx (xx.x) |
| Ethnicity, n (%) | | | | |
| Hispanic or Latino | xx (xx.x) | xx (xx.x) | xx (xx.x) | xx (xx.x) |
| Not Hispanic or Latino | xx (xx.x) | xx (xx.x) | xx (xx.x) | xx (xx.x) |
| Age (Years) | | | | |
| n (%) | xx (xx.x) | xx (xx.x) | xx (xx.x) | xx (xx.x) |
| Missing (%) | xx (xx.x) | xx (xx.x) | xx (xx.x) | xx (xx.x) |
| Mean ±SD | xx ±xx.xx | xx ±xx.xx | xx ±xx.xx | xx ±xx.xx |
| Median | xx | xx | xx | xx |
| Q1; Q3 | xx; xx | xx; xx | xx; xx | xx; xx |
| Min; Max | xx; xx | xx; xx | xx; xx | xx; xx |

**Shell continues on the next page**

15.1: Demographic and Baseline Data
15.1.4: Demographic Characteristics
Table 15.1.4.1: Demographic Characteristics - SAF Analysis Set

| | Treatment A N=xxx (100%) | Treatment B N=xxx (100%) | Treatment C N=xxx (100%) | Total N=xxx (100%) |
|---|---|---|---|---|
| Age categories, n (%) | | | | |
| < 35 years | xx (xx.x) | xx (xx.x) | xx (xx.x) | xx (xx.x) |
| >= 35 - < 50 years | xx (xx.x) | xx (xx.x) | xx (xx.x) | xx (xx.x) |
| >= 50 - < 76 years | xx (xx.x) | xx (xx.x) | xx (xx.x) | xx (xx.x) |
| Missing | xx (xx.x) | xx (xx.x) | xx (xx.x) | xx (xx.x) |

Note: Age is relative to the date of informed consent.

15.1: Demographic and Baseline Data
15.1.5: Medical History
Table 15.1.5.1: Medical History - SAF Analysis Set

| Primary System Organ Class<br>Preferred Term | Treatment A<br>N=xxx (100%)<br>n (%) | Treatment B<br>N=xxx (100%)<br>n (%) | Treatment C<br>N=xxx (100%)<br>n (%) | Total<br>N=xxx (100%)<br>n (%) |
|---|---|---|---|---|
| Subjects with at least one Medical History | xx (xx.x) | xx (xx.x) | xx (xx.x) | xx (xx.x) |
| SOC1 | xx (xx.x) | xx (xx.x) | xx (xx.x) | xx (xx.x) |
| PT1 | xx (xx.x) | xx (xx.x) | xx (xx.x) | xx (xx.x) |
| PT2 | xx (xx.x) | xx (xx.x) | xx (xx.x) | xx (xx.x) |
| SOC2 | xx (xx.x) | xx (xx.x) | xx (xx.x) | xx (xx.x) |
| PT1 | xx (xx.x) | xx (xx.x) | xx (xx.x) | xx (xx.x) |
| PT2 | xx (xx.x) | xx (xx.x) | xx (xx.x) | xx (xx.x) |

MedDRA version xx.x.

***Programming Note:***
***- Sort order by primary SOC and PT in alphabetical order. If SOC or PT is missing/not coded yet, then 'UNCODED' (or 'UNCODED + verbatim Investigator') will be indicated at the ADaM level. Uncoded SOC/PT should come first.***
***MedDRA version 19.1 or highest at time of data transfer.***

15.1: Demographic and Baseline Data
15.1.6: Other Baseline Characteristics
Table 15.1.6.1: Disease History – SAF Analysis Set

| | Treatment A N=xxx (100%) | Treatment B N=xxx (100%) | Treatment C N=xxx (100%) | Total N=xxx (100%) |
|---|---|---|---|---|
| Time since date of diagnosis (years) | | | | |
| n (%) | xx (xx.x) | xx (xx.x) | xx (xx.x) | xx (xx.x) |
| Missing (%) | xx (xx.x) | xx (xx.x) | xx (xx.x) | xx (xx.x) |
| Mean ±SD | xx ±xx.xx | xx ±xx.xx | xx ±xx.xx | xx ±xx.xx |
| Median | xx | xx | xx | xx |
| Q1; Q3 | xx; xx | xx; xx | xx; xx | xx; xx |
| Min; Max | xx; xx | xx; xx | xx; xx | xx; xx |
| Subject status/ disease history, n (%) | | | | |
| Diffuse cutaneous SSc | xx (xx.x) | xx (xx.x) | xx (xx.x) | xx (xx.x) |
| Limited cutaneous SSc | xx (xx.x) | xx (xx.x) | xx (xx.x) | xx (xx.x) |
| SSc sine scleroderma | xx (xx.x) | xx (xx.x) | xx (xx.x) | xx (xx.x) |
| Systemic sclerosis symptom history (a), n (%) | | | | |
| Skin thickening | xx (xx.x) | xx (xx.x) | xx (xx.x) | xx (xx.x) |
| Digital ulcers | xx (xx.x) | xx (xx.x) | xx (xx.x) | xx (xx.x) |
| Synovitis and/or joint contracture | xx (xx.x) | xx (xx.x) | xx (xx.x) | xx (xx.x) |
| Tendon friction rubs | xx (xx.x) | xx (xx.x) | xx (xx.x) | xx (xx.x) |
| C .K. elevation and/or weakness | xx (xx.x) | xx (xx.x) | xx (xx.x) | xx (xx.x) |
| Atrophy: Upper extremity | xx (xx.x) | xx (xx.x) | xx (xx.x) | xx (xx.x) |
| Atrophy: Lower extremity | xx (xx.x) | xx (xx.x) | xx (xx.x) | xx (xx.x) |
| Atrophy: Right extremity | xx (xx.x) | xx (xx.x) | xx (xx.x) | xx (xx.x) |
| Atrophy: Left extremity | xx (xx.x) | xx (xx.x) | xx (xx.x) | xx (xx.x) |
| Esophagus: Dysphagia | xx (xx.x) | xx (xx.x) | xx (xx.x) | xx (xx.x) |
| Esophagus: Reflux | xx (xx.x) | xx (xx.x) | xx (xx.x) | xx (xx.x) |
| Stomach: Early satiety | xx (xx.x) | xx (xx.x) | xx (xx.x) | xx (xx.x) |
| Stomach: Vomiting | xx (xx.x) | xx (xx.x) | xx (xx.x) | xx (xx.x) |
| Intestinal: Diarrhea | xx (xx.x) | xx (xx.x) | xx (xx.x) | xx (xx.x) |
| Intestinal: Bloating | xx (xx.x) | xx (xx.x) | xx (xx.x) | xx (xx.x) |

**Shell continues on the next page**

15.1: Demographic and Baseline Data
15.1.6: Other Baseline Characteristics
Table 15.1.6.1: Disease History – SAF Analysis Set

| | Treatment A N=xxx (100%) | Treatment B N=xxx (100%) | Treatment C N=xxx (100%) | Total N=xxx (100%) |
|---|---|---|---|---|
| Intestinal: Constipation | xx (xx.x) | xx (xx.x) | xx (xx.x) | xx (xx.x) |
| Incontinence | xx (xx.x) | xx (xx.x) | xx (xx.x) | xx (xx.x) |
| Hypertension | xx (xx.x) | xx (xx.x) | xx (xx.x) | xx (xx.x) |
| Renal crisis | xx (xx.x) | xx (xx.x) | xx (xx.x) | xx (xx.x) |
| Dyspnea (significant) | xx (xx.x) | xx (xx.x) | xx (xx.x) | xx (xx.x) |
| Palpitations (significant) | xx (xx.x) | xx (xx.x) | xx (xx.x) | xx (xx.x) |
| ACR/EULAR Classification Criteria for Systemic Sclerosis (b), n (%) | | | | |
| Skin thickening of the fingers of both hands extending proximal to the metacarpophalangeal joints | xx (xx.x) | xx (xx.x) | xx (xx.x) | xx (xx.x) |
| Skin thickening of the fingers: Puffy fingers | xx (xx.x) | xx (xx.x) | xx (xx.x) | xx (xx.x) |
| Skin thickening of the fingers: Sclerodactyly of the fingers | xx (xx.x) | xx (xx.x) | xx (xx.x) | xx (xx.x) |
| Fingertip lesions: Digital tip ulcers | xx (xx.x) | xx (xx.x) | xx (xx.x) | xx (xx.x) |
| Fingertip lesions: Fingertip pitting scars | xx (xx.x) | xx (xx.x) | xx (xx.x) | xx (xx.x) |
| Telangiectasia | xx (xx.x) | xx (xx.x) | xx (xx.x) | xx (xx.x) |
| Abnormal nailfold capillaries | xx (xx.x) | xx (xx.x) | xx (xx.x) | xx (xx.x) |
| Lung involvement: Pulmonary arterial hypertension | xx (xx.x) | xx (xx.x) | xx (xx.x) | xx (xx.x) |
| Lung involvement: Interstitial lung disease | xx (xx.x) | xx (xx.x) | xx (xx.x) | xx (xx.x) |
| Raynaud's Phenomenon | xx (xx.x) | xx (xx.x) | xx (xx.x) | xx (xx.x) |
| [redacted] | xx (xx.x) | xx (xx.x) | xx (xx.x) | xx (xx.x) |
| [redacted] | xx (xx.x) | xx (xx.x) | xx (xx.x) | xx (xx.x) |
| [redacted] | xx (xx.x) | xx (xx.x) | xx (xx.x) | xx (xx.x) |
| III | | | | |

Note: Partial date of diagnosis is imputed as follows: In case the day of diagnosis is missing, then the day will be imputed as the 1st. In case the month of diagnosis is missing, then the month will be imputed as January.
(a) Counts are the number of subjects who reported 'Yes' to the questions.
(b) Counts are the number of subjects who reported 'Present' to the questions.

15.1: Demographic and Baseline Data
15.1.7: Previous and Concomitant Medications, Procedures, Follow-up Treatments
Table 15.1.7.1: Previous Medication – SAF Analysis Set

| ATC-2nd Level<br>Preferred Term | Treatment A<br>N=xxx (100%)<br>n (%) | Treatment B<br>N=xxx (100%)<br>n (%) | Treatment C<br>N=xxx (100%)<br>n (%) | Total<br>N=xxx (100%)<br>n (%) |
|---|---|---|---|---|
| Subjects with at least one Previous Medication | xx (xx.x) | xx (xx.x) | xx (xx.x) | xx (xx.x) |
| ATC1 | xx (xx.x) | xx (xx.x) | xx (xx.x) | xx (xx.x) |
| MED1 | xx (xx.x) | xx (xx.x) | xx (xx.x) | xx (xx.x) |
| MED2 | xx (xx.x) | xx (xx.x) | xx (xx.x) | xx (xx.x) |
| ATC2 | xx (xx.x) | xx (xx.x) | xx (xx.x) | xx (xx.x) |
| MED1 | xx (xx.x) | xx (xx.x) | xx (xx.x) | xx (xx.x) |
| MED2 | xx (xx.x) | xx (xx.x) | xx (xx.x) | xx (xx.x) |

WHO Drug Dictionary version Enhanced September 2016.
Note: If a subject has more than one medication within a ATC class/preferred term, the subject was counted once in that ATC class/preferred term.
In case multiple ATC-I-s are assigned to a medication, all ATC-I-s will be reported.

***Programming Note:***
***- Sort order by ATC-2nd Level and Preferred Term in alphabetical order.***
***WHO Drug Dictionary version Enhanced September 2016 or highest at time of data transfer.***

***Repeat for table:***
Table 15.1.7.2: Concomitant Medication – SAF Analysis Set
***Change "Previous Medication" to "Concomitant Medication"***

15.2: Efficacy Data
15.2.1: Annual Rate of Absolute FVC Change in Volume (mL)
Table 15.2.1.1: FVC Volume (mL) Observed and Change from Baseline by Visit - mITT Analysis Set

| Visit / Statistic | Treatment A N=xxx | | Treatment B N=xxx | | Treatment C N=xxx | |
|---|---|---|---|---|---|---|
| | Observed | Change from Baseline | Observed | Change from Baseline | Observed | Change from Baseline |
| Baseline | | | | | | |
| n (%) | xxx (xx.x) | | xxx (xx.x) | | xxx (xx.x) | |
| Missing (%) | xxx (xx.x) | | xxx (xx.x) | | xxx (xx.x) | |
| Mean ±SD | xx.x ±xx.xx | | xx.x ±xx.xx | | xx.x ±xx.xx | |
| Median | xx.x | | xx.x | | xx.x | |
| Q1; Q3 | xx.x; xx.x | | xx.x; xx.x | | xx.x; xx.x | |
| Min; Max | xx; xx | | xx; xx | | xx; xx | |
| Week 12 | | | | | | |
| n (%) | xxx (xx.x) | xxx (xx.x) | xxx (xx.x) | xxx (xx.x) | xxx (xx.x) | xxx (xx.x) |
| Missing (%) | xxx (xx.x) | xxx (xx.x) | xxx (xx.x) | xxx (xx.x) | xxx (xx.x) | xxx (xx.x) |
| Mean ±SD | xx.x ±xx.xx | xx.x ±xx.xx | xx.x ±xx.xx | xx.x ±xx.xx | xx.x ±xx.xx | xx.x ±xx.xx |
| Median | xx.x | xx.x | xx.x | xx.x | xx.x | xx.x |
| Q1; Q3 | xx.x; xx.x | xx.x; xx.x | xx.x; xx.x | xx.x; xx.x | xx.x; xx.x | xx.x; xx.x |
| Min; Max | xx; xx | xx; xx | xx; xx | xx; xx | xx; xx | xx; xx |
| Week 24 | | | | | | |
| n (%) | xxx (xx.x) | xxx (xx.x) | xxx (xx.x) | xxx (xx.x) | xxx (xx.x) | xxx (xx.x) |
| Missing (%) | xxx (xx.x) | xxx (xx.x) | xxx (xx.x) | xxx (xx.x) | xxx (xx.x) | xxx (xx.x) |
| Mean ±SD | xx.x ±xx.xx | xx.x ±xx.xx | xx.x ±xx.xx | xx.x ±xx.xx | xx.x ±xx.xx | xx.x ±xx.xx |
| Median | xx.x | xx.x | xx.x | xx.x | xx.x | xx.x |
| Q1; Q3 | xx.x; xx.x | xx.x; xx.x | xx.x; xx.x | xx.x; xx.x | xx.x; xx.x | xx.x; xx.x |
| Min; Max | xx; xx | xx; xx | xx; xx | xx; xx | xx; xx | xx; xx |

Note: Baseline is defined as the last non-missing assessment value prior to randomization. If such a value is missing then the last value prior to the first trial treatment administration will be used.
Percentages are based on the number of subjects present in the trial at that visit.

**Programming note:** Only display visits where FVC assessment is scheduled to be done and where there is data available.

**Repeat table 15.2.1.1 for:**
Table 15.2.1.2: FVC % Predicted Observed and Change from Baseline by Visit - mITT Analysis Set

15.2: Efficacy Data
15.2.2: Key Secondary Endpoints
Table 15.2.2.1: Change in Dyspnea from Baseline as Measured by the Mahler TDI - mITT Analysis Set

| Visit / Statistic | Treatment A N=xxx | Treatment B N=xxx | Treatment C N=xxx |
|---|---|---|---|
| Baseline | | | |
| n (%) | xxx (xx.x) | xxx (xx.x) | xxx (xx.x) |
| Missing (%) | xxx (xx.x) | xxx (xx.x) | xxx (xx.x) |
| Mean ±SD | xx.x ±xx.xx | xx.x ±xx.xx | xx.x ±xx.xx |
| Median | xx.x | xx.x | xx.x |
| Q1; Q3 | xx.x; xx.x | xx.x; xx.x | xx.x; xx.x |
| Min; Max | xx; xx | xx; xx | xx; xx |
| Week 12 | | | |
| Change from Baseline | | | |
| n (%) | xxx (xx.x) | xxx (xx.x) | xxx (xx.x) |
| Missing (%) | xxx (xx.x) | xxx (xx.x) | xxx (xx.x) |
| Mean ±SD | xx.x ±xx.xx | xx.x ±xx.xx | xx.x ±xx.xx |
| Median | xx.x | xx.x | xx.x |
| Q1; Q3 | xx.x; xx.x | xx.x; xx.x | xx.x; xx.x |
| Min; Max | xx; xx | xx; xx | xx; xx |
| …… | | | |

**Repeat table 15.2.1.1 for:**
Table 15.2.2.2: mRSS Total Score Observed and Change from Baseline by Visit - mITT (dcSSc) Analysis Set

**Programming note:** Only display visits where mRSS assessment is scheduled to be done and where there is data available.

**Add the following footnote:**

Note: dcSSc = diffuse cutaneous systemic sclerosis. Only subjects with dcSSc at baseline are included in the mRSS summary.

15.2: Efficacy Data
15.2.2: Key Secondary Endpoints
Table 15.2.2.3: Absolute Change from Baseline in SGRQ Total Score - mITT Analysis Set

| | Treatment A N=xxx | | Treatment B N=xxx | | Treatment C N=xxx | |
|---|---|---|---|---|---|---|
| Visit/ Statistic | Observed | Change from Baseline | Observed | Change from Baseline | Observed | Change from Baseline |
| Baseline | | | | | | |
| n (%) | xxx (xx.x) | | xxx (xx.x) | | xxx (xx.x) | |
| Missing (%) | xxx (xx.x) | | xxx (xx.x) | | xxx (xx.x) | |
| Mean ±SD | xx.x ±xx.xx | | xx.x ±xx.xx | | xx.x ±xx.xx | |
| Median | xx.x | | xx.x | | xx.x | |
| Q1; Q3 | xx.x; xx.x | | xx.x; xx.x | | xx.x; xx.x | |
| Min; Max | xx; xx | | xx; xx | | xx; xx | |
| Week 12 | | | | | | |
| n (%) | xxx (xx.x) | xxx (xx.x) | xxx (xx.x) | xxx (xx.x) | xxx (xx.x) | xxx (xx.x) |
| Missing (%) | xxx (xx.x) | xxx (xx.x) | xxx (xx.x) | xxx (xx.x) | xxx (xx.x) | xxx (xx.x) |
| Mean ±SD | xx.x ±xx.xx | xx.x ±xx.xx | xx.x ±xx.xx | xx.x ±xx.xx | xx.x ±xx.xx | xx.x ±xx.xx |
| Median | xx.x | xx.x | xx.x | xx.x | xx.x | xx.x |
| Q1; Q3 | xx.x; xx.x | xx.x; xx.x | xx.x; xx.x | xx.x; xx.x | xx.x; xx.x | xx.x; xx.x |
| Min; Max | xx; xx | xx; xx | xx; xx | xx; xx | xx; xx | xx; xx |

…

15.2: Efficacy Data
15.2.2: Secondary Endpoints
Table 15.2.2.4: Clinically Meaningful Disease Progression - mITT Analysis Set

| | Treatment A N=xxx (100%) n (%) | Treatment B N=xxx (100%) n (%) | Treatment C N=xxx (100%) n (%) |
|---|---|---|---|
| Number of Subjects with Clinically Meaningful Disease Progression | xxx (xx.x) | xxx (xx.x) | xxx (xx.x) |
| Trial Treatment Discontinued | xxx (xx.x) | xxx (xx.x) | xxx (xx.x) |
| SSc-ILD Progression | xxx (xx.x) | xxx (xx.x) | xxx (xx.x) |
| Relative decrease from baseline in FVC % predicted >10% * | xxx (xx.x) | xxx (xx.x) | xxx (xx.x) |
| Relative decrease from baseline in FVC % predicted of >5% to <10% and relative decrease in DLCO % predicted >15% * | xxx (xx.x) | xxx (xx.x) | xxx (xx.x) |
| Mycophenolate dose increased | xxx (xx.x) | xxx (xx.x) | xxx (xx.x) |
| New immunosuppressant or biologic drug initiated | xxx (xx.x) | xxx (xx.x) | xxx (xx.x) |
| Trial Treatment Discontinued | xxx (xx.x) | xxx (xx.x) | xxx (xx.x) |
| SSc Progression other than ILD | xxx (xx.x) | xxx (xx.x) | xxx (xx.x) |
| Scleroderma renal crisis | xxx (xx.x) | xxx (xx.x) | xxx (xx.x) |
| Left ventricular failure (defined as ejection fraction <45%) | xxx (xx.x) | xxx (xx.x) | xxx (xx.x) |
| Pulmonary arterial hypertension requiring treatment | xxx (xx.x) | xxx (xx.x) | xxx (xx.x) |
| Other | xxx (xx.x) | xxx (xx.x) | xxx (xx.x) |
| Trial Treatment Discontinued | xxx (xx.x) | xxx (xx.x) | xxx (xx.x) |

* Confirmed on 2 occasions within 4 weeks.
Note: A subject may have both SSc-ILD progression and SSc progression other than ILD at the same time, and may progress more than once.

**Repeat table 15.2.1.1 for:**
Table 15.2.2.5: DLCO (mmol of CO/min/kPa) Observed and Change from Baseline by Visit - mITT Analysis Set

**Programming note:** Only display visits where DLCO assessment is scheduled to be done and where there is data available.

**Repeat table 15.2.1.1 for:**

Table 15.2.2.6: Absolute Change from Baseline in QLF - mITT Analysis Set
Table 15.2.2.7: DLCO % Predicted Observed and Change from Baseline by Visit - mITT Analysis Set

**Programming note:** Only display visits where DLCO assessment is scheduled to be done and where there is data available.

Table 15.2.3.1: KCO Observed and Change from Baseline by Visit - mITT Analysis Set
Table 15.2.3.2: Extent of total ILD Observed and Change from Baseline by Visit - mITT Analysis Set

15.2: Efficacy Data
15.2.4: QoL Endpoints
Table 15.2.4.1: Leicester Cough Index Total Score – Observed and Change from Baseline - mITT Analysis Set

| Visit/ Statistic | Treatment A N=xxx | | Treatment B N=xxx | | Treatment C N=xxx | |
|---|---|---|---|---|---|---|
| | Observed | Change from Baseline | Observed | Change from Baseline | Observed | Change from Baseline |
| Baseline | | | | | | |
| n (%) | xxx (xx.x) | | xxx (xx.x) | | xxx (xx.x) | |
| Missing (%) | xxx (xx.x) | | xxx (xx.x) | | xxx (xx.x) | |
| Mean ±SD | xx.x ±xx.xx | | xx.x ±xx.xx | | xx.x ±xx.xx | |
| Median | xx.x | | xx.x | | xx.x | |
| Q1; Q3 | xx.x; xx.x | | xx.x; xx.x | | xx.x; xx.x | |
| Min; Max | xx; xx | | xx; xx | | xx; xx | |
| Week 24 | | | | | | |
| n (%) | xxx (xx.x) | xxx (xx.x) | xxx (xx.x) | xxx (xx.x) | xxx (xx.x) | xxx (xx.x) |
| Missing (%) | xxx (xx.x) | xxx (xx.x) | xxx (xx.x) | xxx (xx.x) | xxx (xx.x) | xxx (xx.x) |
| Mean ±SD | xx.x ±xx.xx | xx.x ±xx.xx | xx.x ±xx.xx | xx.x ±xx.xx | xx.x ±xx.xx | xx.x ±xx.xx |
| Median | xx.x | xx.x | xx.x | xx.x | xx.x | xx.x |
| Q1; Q3 | xx.x; xx.x | xx.x; xx.x | xx.x; xx.x | xx.x; xx.x | xx.x; xx.x | xx.x; xx.x |
| Min; Max | xx; xx | xx; xx | xx; xx | xx; xx | xx; xx | xx; xx |

…

Note: Baseline is defined as the last non-missing measurement prior to randomization. If such a value is missing then the last value prior to the first trial treatment administration will be used.
Percentages are based on the number of subjects present in the trial at that visit.
Note: The domain score is the sum of all scores in that domain divided by the number of questions in that domain (ranging from 1 to 7). The total score is the sum of all domain scores (ranging from 3 to 21).

**Repeat table 15.2.4.1 for:**
Table 15.2.4.2: Physician's Global Assessment – Observed and Change from Baseline - mITT Analysis Set

**Update footnotes:**
Note: Baseline is defined as the last non-missing measurement prior to randomization. If such a value is missing then the last value prior to the first trial treatment administration will be used.
Percentages are based on the number of subjects present in the trial at that visit.
Note: The Physician's Global Assessment consists of one question that is answered on a VAS from of 0 to 100,

where 0 is the most positive response and 100 is the most negative.

**Repeat table 15.2.4.1 for:**
Table 15.2.4.3: Patient's Global Assessment – Observed and Change from Baseline - mITT Analysis Set
**Update footnote to say** 'Patient's Global Assessment' instead of 'Physician's Global Assessment'

15.2: Efficacy Data
15.2.4: QoL Endpoints
Table 15.2.4.4: SHAQ – VAS Scores – Observed and Change from Baseline - mITT Analysis Set

| VAS category/ Visit/ Statistic | Treatment A N=xxx | | Treatment B N=xxx | | Treatment C N=xxx | |
|---|---|---|---|---|---|---|
| | Observed | Change from Baseline | Observed | Change from Baseline | Observed | Change from Baseline |
| Pain: | | | | | | |
| Baseline | | | | | | |
| n (%) | xxx (xx.x) | | xxx (xx.x) | | xxx (xx.x) | |
| Missing (%) | xxx (xx.x) | | xxx (xx.x) | | xxx (xx.x) | |
| Mean ±SD | xx.x ±xx.xx | | xx.x ±xx.xx | | xx.x ±xx.xx | |
| Median | xx.x | | xx.x | | xx.x | |
| Q1; Q3 | xx.x; xx.x | | xx.x; xx.x | | xx.x; xx.x | |
| Min; Max | xx; xx | | xx; xx | | xx; xx | |
| Week 24 | | | | | | |
| n (%) | xxx (xx.x) | xxx (xx.x) | xxx (xx.x) | xxx (xx.x) | xxx (xx.x) | xxx (xx.x) |
| Missing (%) | xxx (xx.x) | xxx (xx.x) | xxx (xx.x) | xxx (xx.x) | xxx (xx.x) | xxx (xx.x) |
| Mean ±SD | xx.x ±xx.xx | xx.x ±xx.xx | xx.x ±xx.xx | xx.x ±xx.xx | xx.x ±xx.xx | xx.x ±xx.xx |
| Median | xx.x | xx.x | xx.x | xx.x | xx.x | xx.x |
| Q1; Q3 | xx.x; xx.x | xx.x; xx.x | xx.x; xx.x | xx.x; xx.x | xx.x; xx.x | xx.x; xx.x |
| Min; Max | xx; xx | xx; xx | xx; xx | xx; xx | xx; xx | xx; xx |
| … | | | | | | |

Note: Baseline is defined as the last non-missing measurement prior to randomization. If such a value is missing then the last value prior to the first trial treatment administration will be used.
Percentages are based on the number of subjects present in the trial at that visit.
Note: The VAS are scored from 0 to 100, where 0 is the most positive response and 100 is the most negative.

15.2: Efficacy Data
15.2.4: QoL Endpoints
Table 15.2.4.5: EQ-5D VAS Score – Observed and Change from Baseline - mITT Analysis Set

| Visit/ Statistic | Treatment A N=xxx | | Treatment B N=xxx | | Treatment C N=xxx | |
|---|---|---|---|---|---|---|
| | Observed | Change from Baseline | Observed | Change from Baseline | Observed | Change from Baseline |
| Baseline | | | | | | |
| n (%) | xxx (xx.x) | | xxx (xx.x) | | xxx (xx.x) | |
| Missing (%) | xxx (xx.x) | | xxx (xx.x) | | xxx (xx.x) | |
| Mean ±SD | xx.x ±xx.xx | | xx.x ±xx.xx | | xx.x ±xx.xx | |
| Median | xx.x | | xx.x | | xx.x | |
| Q1; Q3 | xx.x; xx.x | | xx.x; xx.x | | xx.x; xx.x | |
| Min; Max | xx; xx | | xx; xx | | xx; xx | |
| Week 24 | | | | | | |
| n (%) | xxx (xx.x) | xxx (xx.x) | xxx (xx.x) | xxx (xx.x) | xxx (xx.x) | xxx (xx.x) |
| Missing (%) | xxx (xx.x) | xxx (xx.x) | xxx (xx.x) | xxx (xx.x) | xxx (xx.x) | xxx (xx.x) |
| Mean ±SD | xx.x ±xx.xx | xx.x ±xx.xx | xx.x ±xx.xx | xx.x ±xx.xx | xx.x ±xx.xx | xx.x ±xx.xx |
| Median | xx.x | xx.x | xx.x | xx.x | xx.x | xx.x |
| Q1; Q3 | xx.x; xx.x | xx.x; xx.x | xx.x; xx.x | xx.x; xx.x | xx.x; xx.x | xx.x; xx.x |
| Min; Max | xx; xx | xx; xx | xx; xx | xx; xx | xx; xx | xx; xx |
| … | | | | | | |

Note: Baseline is defined as the last non-missing measurement prior to randomization. If such a value is missing then the last value prior to the first trial treatment administration will be used.
Percentages are based on the number of subjects present in the trial at that visit.
Note: The EQ-5D VAS is numbered from 0 to 100 where the endpoints are labelled ‘Best health you can imagine’ (100) and ‘Worst health you can imagine’ (0).

15.2: Efficacy Data
15.2.5: Skin Fibrosis Endpoints
Table 15.2.5.1: Digital Ulcer Count – Observed and Change from Baseline - mITT Analysis Set

| Ulcer Type/ Visit/ Statistic | Treatment A N=xxx | | Treatment B N=xxx | | Treatment C N=xxx | |
|---|---|---|---|---|---|---|
| | Observed | Change from Baseline | Observed | Change from Baseline | Observed | Change from Baseline |
| Active: | | | | | | |
| Baseline | | | | | | |
| n (%) | xxx (xx.x) | | xxx (xx.x) | | xxx (xx.x) | |
| Missing (%) | xxx (xx.x) | | xxx (xx.x) | | xxx (xx.x) | |
| Mean ±SD | xx.x ±xx.xx | | xx.x ±xx.xx | | xx.x ±xx.xx | |
| Median | xx.x | | xx.x | | xx.x | |
| Q1; Q3 | xx.x; xx.x | | xx.x; xx.x | | xx.x; xx.x | |
| Min; Max | xx; xx | | xx; xx | | xx; xx | |
| Week 12 | | | | | | |
| n (%) | xxx (xx.x) | xxx (xx.x) | xxx (xx.x) | xxx (xx.x) | xxx (xx.x) | xxx (xx.x) |
| Missing (%) | xxx (xx.x) | xxx (xx.x) | xxx (xx.x) | xxx (xx.x) | xxx (xx.x) | xxx (xx.x) |
| Mean ±SD | xx.x ±xx.xx | xx.x ±xx.xx | xx.x ±xx.xx | xx.x ±xx.xx | xx.x ±xx.xx | xx.x ±xx.xx |
| Median | xx.x | xx.x | xx.x | xx.x | xx.x | xx.x |
| Q1; Q3 | xx.x; xx.x | xx.x; xx.x | xx.x; xx.x | xx.x; xx.x | xx.x; xx.x | xx.x; xx.x |
| Min; Max | xx; xx | xx; xx | xx; xx | xx; xx | xx; xx | xx; xx |
| … | | | | | | |

Note: Baseline is defined as the last non-missing measurement prior to randomization. If such a value is missing then the last value prior to the first trial treatment administration will be used.
Percentages are based on the number of subjects present in the trial at that visit.
Note: Only subjects with digital ulcers at baseline continue with the digital ulcer assessment throughout the trial.
The total count is the sum of all active, undetermined and healed ulcers.

15.3: Safety Data
15.3.0: Treatment Compliance and Exposure
Table 15.3.0.1: Duration of Treatment (weeks) – SAF Analysis Set

| | Treatment A N=xxx (100%) | Treatment B N=xxx (100%) | Treatment C N=xxx (100%) |
|---|---|---|---|
| Duration of treatment (weeks), n (%) | | | |
| >=4 and <=28 weeks | xxx (xx.x) | xxx (xx.x) | xxx (xx.x) |
| >28 and <=52 weeks | xxx (xx.x) | xxx (xx.x) | xxx (xx.x) |
| >52 and <=76 weeks | xxx (xx.x) | xxx (xx.x) | xxx (xx.x) |
| >76 and <=100 weeks | xxx (xx.x) | xxx (xx.x) | xxx (xx.x) |
| >100 weeks | xxx (xx.x) | xxx (xx.x) | xxx (xx.x) |
| n (%) | xxx (xx.x) | xxx (xx.x) | xxx (xx.x) |
| Mean ±SD | xx.x ±xx.xx | xx.x ±xx.xx | xx.x ±xx.xx |
| Median | xx.x | xx.x | xx.x |
| Q1; Q3 | xx.x; xx.x | xx.x; xx.x | xx.x; xx.x |
| Min; Max | xx; xx | xx; xx | xx; xx |

Note: Duration of treatment (weeks) is calculated as:
(Last infusion date prior to data cut-off – first infusion date + 28) / 7 days.

***Programming note:***

- ***Summary statistics are based on subjects who received at least one infusion of trial treatment ➔ Min>0 (this should be equivalent to the SAF analysis set)***

15.3: Safety Data
15.3.0: Treatment Compliance and Exposure
Table 15.3.0.2: Number of Infusions – SAF Analysis Set

| | Treatment A N=xxx (100%) | Treatment B N=xxx (100%) | Treatment C N=xxx (100%) |
|---|---|---|---|
| Total number of infusions received, n (%) | | | |
| 1 | xxx (xx.x) | xxx (xx.x) | xxx (xx.x) |
| >1 and <=8 | xxx (xx.x) | xxx (xx.x) | xxx (xx.x) |
| >8 and <=14 | xxx (xx.x) | xxx (xx.x) | xxx (xx.x) |
| >14 and <=20 | xxx (xx.x) | xxx (xx.x) | xxx (xx.x) |
| >20 and <=26 | xxx (xx.x) | xxx (xx.x) | xxx (xx.x) |
| >26 | xxx (xx.x) | xxx (xx.x) | xxx (xx.x) |
| n (%) | xxx (xx.x) | xxx (xx.x) | xxx (xx.x) |
| Mean ±SD | xx.x ±xx.xx | xx.x ±xx.xx | xx.x ±xx.xx |
| Median | xx.x | xx.x | xx.x |
| Q1; Q3 | xx.x; xx.x | xx.x; xx.x | xx.x; xx.x |
| Min; Max | xx; xx | xx; xx | xx; xx |
| Total number of infusions across all subjects, n | xxx | xxx | xxx |

***Programming note:***

- ***Summary statistics are based on subjects who received at least one infusion of trial treatment ➔ Min>0 (this should be equivalent to the SAF analysis set)***

15.3: Safety Data
15.3.0: Treatment Compliance and Exposure
Table 15.3.0.2b: Treatment Adherence – SAF Analysis Set

| | Treatment A N=xxx (100%) | Treatment B N=xxx (100%) | Treatment C N=xxx (100%) |
|---|---|---|---|
| Adherence with Treatment, n (%) | | | |
| n (%) | xxx (xx.x) | xxx (xx.x) | xxx (xx.x) |
| <80% | xxx (xx.x) | xxx (xx.x) | xxx (xx.x) |
| 80% - 100% | xxx (xx.x) | xxx (xx.x) | xxx (xx.x) |
| >100% - 120% | xxx (xx.x) | xxx (xx.x) | xxx (xx.x) |
| >120% | xxx (xx.x) | xxx (xx.x) | xxx (xx.x) |
| Mean ±SD | xx.x ±xx.xx | xx.x ±xx.xx | xx.x ±xx.xx |
| Median | xx.x | xx.x | xx.x |
| Q1; Q3 | xx.x; xx.x | xx.x; xx.x | xx.x; xx.x |
| Min; Max | xx; xx | xx; xx | xx; xx |

Note: Adherence by subject is calculated as: (sum of actual volume received/ sum of planned volume, up to and including their last dose recorded on their treatment termination visit)*100.
For the continuous summary, values >100% are set to 100%.

***Programming note:***

- ***Summary statistics are based on subjects who received at least one infusion of trial treatment (this should be equivalent to the SAF analysis set)***
- ***The Treatment Compliance definition for the IDMC is equivalent to the Treatment Adherence definition in the Study SAP, for the Primary & Final analyses.***

15.3: Safety Data
15.3.0: Treatment Compliance and Exposure
Table 15.3.0.3: Infusion Duration and Volume – SAF Analysis Set

| | Treatment A N=xxx (100%) | Treatment B N=xxx (100%) | Treatment C N=xxx (100%) |
|---|---|---|---|
| Mean infusion duration (hours) | | | |
| n (%) | xxx (xx.x) | xxx (xx.x) | xxx (xx.x) |
| Mean ±SD | xx.x ±xx.xx | xx.x ±xx.xx | xx.x ±xx.xx |
| Median | xx.x | xx.x | xx.x |
| Q1; Q3 | xx.x; xx.x | xx.x; xx.x | xx.x; xx.x |
| Min; Max | xx; xx | xx; xx | xx; xx |
| Mean actual volume infused (mL) | | | |
| n (%) | xxx (xx.x) | xxx (xx.x) | xxx (xx.x) |
| Mean ±SD | xx.x ±xx.xx | xx.x ±xx.xx | xx.x ±xx.xx |
| Median | xx.x | xx.x | xx.x |
| Q1; Q3 | xx.x; xx.x | xx.x; xx.x | xx.x; xx.x |
| Min; Max | xx; xx | xx; xx | xx; xx |

Note: Summary statistics are based on the mean infusion duration and mean volume received per subject.

***Programming note:***

- ***Summary statistics are based on subjects who received at least one infusion of trial treatment ➔ Min>0 (this should be equivalent to the SAF analysis set)***

15.3: Safety Data
15.3.0: Treatment Compliance and Exposure
Table 15.3.0.4: Dose Adjustments – SAF Analysis Set

| | Treatment A N=xxx (100%) n (%) | Treatment B N=xxx (100%) n (%) | Treatment C N=xxx (100%) n (%) |
|---|---|---|---|
| Number of subjects without any dose adjustment (a) | xxx (xx.x) | xxx (xx.x) | xxx (xx.x) |
| Number of subjects with at least one dose adjustment | xxx (xx.x) | xxx (xx.x) | xxx (xx.x) |
| Dose adjusted: | | | |
| Adverse Event | xxx (xx.x) | xxx (xx.x) | xxx (xx.x) |
| Other | xxx (xx.x) | xxx (xx.x) | xxx (xx.x) |
| No dose: | | | |
| Adverse Event | xxx (xx.x) | xxx (xx.x) | xxx (xx.x) |
| Missed Dose | xxx (xx.x) | xxx (xx.x) | xxx (xx.x) |
| Other | xxx (xx.x) | xxx (xx.x) | xxx (xx.x) |
| Number of subjects with at least one missed visit (b) | xxx (xx.x) | xxx (xx.x) | xxx (xx.x) |

Note: A subject may have more than one reason if they have more than one dose adjustment, so will be counted under each reason.
(a) Subjects without any dose adjustment do not include subjects with missed visits.
(b) Subjects with missed visits may not be counted under 'Dose adjusted' or 'No dose' due to not completing the 'STUDY TREATMENT ADMINISTRATION DETAILS' eCRF page at the missed visit.

***Programming note: Summary statistics are based on subjects who received at least one infusion of trial treatment (this should be equivalent to the SAF analysis set)***

15.3: Safety Data
15.3.0: Treatment Compliance and Exposure
Table 15.3.0.5: Infusion Outcome – SAF Analysis Set

| | Treatment A N=xxx (100%) n (%) | Treatment B N=xxx (100%) n (%) | Treatment C N=xxx (100%) n (%) |
|---|---|---|---|
| Number of subjects with all infusions completed as planned | xxx (xx.x) | xxx (xx.x) | xxx (xx.x) |
| Number of subjects with at least one infusion not completed as planned | xxx (xx.x) | xxx (xx.x) | xxx (xx.x) |
| Adverse Event (other than infusion-related reaction or overdose) | xxx (xx.x) | xxx (xx.x) | xxx (xx.x) |
| Infusion-related reaction | xxx (xx.x) | xxx (xx.x) | xxx (xx.x) |
| Overdose | xxx (xx.x) | xxx (xx.x) | xxx (xx.x) |
| Other | xxx (xx.x) | xxx (xx.x) | xxx (xx.x) |

Note: A subject may have more than one reason if they have more than one infusion not completed as planned, so will be counted under each reason.

***Programming note:***

- ***Summary statistics are based on subjects who received at least one infusion of trial treatment (this should be equivalent to the SAF analysis set)***

15.3: Safety Data
15.3.1: Display of Adverse Events
Table 15.3.1.1: Overview of Treatment Emergent Adverse Events (TEAEs) – SAF Analysis Set

| Number of Subjects with: | Treatment A N=xxx (100%) n (%) | Treatment B N=xxx (100%) n (%) | Treatment C N=xxx (100%) n (%) |
|---|---|---|---|
| Any TEAE | xxx (xx.x) | xxx (xx.x) | xxx (xx.x) |
| Any trial treatment related TEAE | xxx (xx.x) | xxx (xx.x) | xxx (xx.x) |
| Any serious TEAE | xxx (xx.x) | xxx (xx.x) | xxx (xx.x) |
| Any trial treatment related serious TEAE | xxx (xx.x) | xxx (xx.x) | xxx (xx.x) |
| Any grade >=3 TEAE | xxx (xx.x) | xxx (xx.x) | xxx (xx.x) |
| Any grade >=4 TEAE | xxx (xx.x) | xxx (xx.x) | xxx (xx.x) |
| Any trial treatment related grade >=3 TEAE | xxx (xx.x) | xxx (xx.x) | xxx (xx.x) |
| Any trial treatment related grade >=4 TEAE | xxx (xx.x) | xxx (xx.x) | xxx (xx.x) |
| Any TEAE leading to death | xxx (xx.x) | xxx (xx.x) | xxx (xx.x) |
| Any trial treatment related TEAE leading to death | xxx (xx.x) | xxx (xx.x) | xxx (xx.x) |
| Any treatment emergent AESI | xxx (xx.x) | xxx (xx.x) | xxx (xx.x) |
| Any trial treatment related treatment emergent AESI | xxx (xx.x) | xxx (xx.x) | xxx (xx.x) |
| Any serious treatment emergent AESI | xxx (xx.x) | xxx (xx.x) | xxx (xx.x) |

**Shell continues on the next page**

15.3: Safety Data
15.3.1: Display of Adverse Events
Table 15.3.1.1: Overview of Treatment Emergent Adverse Events (TEAEs) – SAF Analysis Set

| Number of Subjects with: | Treatment A N=xxx (100%) n (%) | Treatment B N=xxx (100%) n (%) | Treatment C N=xxx (100%) n (%) |
|---|---|---|---|
| Any trial treatment related serious treatment emergent AESI | xxx (xx.x) | xxx (xx.x) | xxx (xx.x) |
| Any grade >=3 treatment emergent AESI | xxx (xx.x) | xxx (xx.x) | xxx (xx.x) |
| Any grade >=4 treatment emergent AESI | xxx (xx.x) | xxx (xx.x) | xxx (xx.x) |
| Any trial treatment related grade >=3 treatment emergent AESI | xxx (xx.x) | xxx (xx.x) | xxx (xx.x) |
| Any trial treatment related grade >=4 treatment emergent AESI | xxx (xx.x) | xxx (xx.x) | xxx (xx.x) |
| Any treatment emergent AESI leading to death | xxx (xx.x) | xxx (xx.x) | xxx (xx.x) |
| Any trial treatment related treatment emergent AESI leading to death | xxx (xx.x) | xxx (xx.x) | xxx (xx.x) |

NCI-CTCAE version 4.03.
Note: TEAEs are defined as events that start within the day of first dose of trial treatment until 28 days after last dose of treatment.
Related TEAEs are events with relationship missing, unknown or related.
AESI = Adverse Event of Special Interest.

15.3: Safety Data
15.3.1: Display of Adverse Events
Table 15.3.1.2: Overview of TEAEs Leading to Discontinuation / Dose Reduction of Treatment – SAF Analysis Set

| Number of Subjects with: | Treatment A N=xxx (100%) n (%) | Treatment B N=xxx (100%) n (%) | Treatment C N=xxx (100%) n (%) |
|---|---|---|---|
| Any TEAE leading to temporary discontinuation of trial treatment | xxx (xx.x) | xxx (xx.x) | xxx (xx.x) |
| Any trial treatment related TEAE leading to temporary discontinuation of trial treatment | xxx (xx.x) | xxx (xx.x) | xxx (xx.x) |
| Any TEAE leading to permanent discontinuation of trial treatment | xxx (xx.x) | xxx (xx.x) | xxx (xx.x) |
| Any trial treatment related TEAE leading to permanent discontinuation of trial treatment | xxx (xx.x) | xxx (xx.x) | xxx (xx.x) |
| Any TEAE leading to dose reduction of trial treatment | xxx (xx.x) | xxx (xx.x) | xxx (xx.x) |
| Any trial treatment related TEAE leading to dose reduction of trial treatment | xxx (xx.x) | xxx (xx.x) | xxx (xx.x) |

Note: TEAEs are defined as events that start within the day of first dose of trial treatment until 28 days after last dose of treatment.
Related TEAEs are events with relationship missing, unknown or related.

15.3: Safety Data
15.3.1: Display of Adverse Events
Table 15.3.1.3: TEAE by Primary System Organ Class (SOC) and Preferred Term (PT) – SAF Analysis Set

| Primary System Organ Class<br>Preferred Term | Treatment A<br>N=xxx (100%)<br>n (%) | Treatment B<br>N=xxx (100%)<br>n (%) | Treatment C<br>N=xxx (100%)<br>n (%) |
|---|---|---|---|
| Subjects with at least one event | xxx (xx.x) | xxx (xx.x) | xxx (xx.x) |
| SOC1 | xxx (xx.x) | xxx (xx.x) | xxx (xx.x) |
| PT11 | xxx (xx.x) | xxx (xx.x) | xxx (xx.x) |
| PT12 | xxx (xx.x) | xxx (xx.x) | xxx (xx.x) |
| PT13 | xxx (xx.x) | xxx (xx.x) | xxx (xx.x) |
| SOC2 | xxx (xx.x) | xxx (xx.x) | xxx (xx.x) |
| PT21 | xxx (xx.x) | xxx (xx.x) | xxx (xx.x) |
| PT22 | xxx (xx.x) | xxx (xx.x) | xxx (xx.x) |

MedDRA version 19.1.
Note: TEAEs are defined as events that start within the day of first dose of trial treatment until 28 days after last dose of treatment.

**Programming Note: sorted by primary SOC and PT in alphabetical order.**
***MedDRA version 19.1 or highest at time of data transfer.***

**Repeat table 15.3.1.3 for:**
Table 15.3.1.4: Trial Treatment Related TEAEs by SOC and PT – SAF Analysis Set

**Add footnote:** Related TEAEs are events with relationship missing, unknown or related.

Table 15.3.1.5: Serious TEAEs by SOC and PT – SAF Analysis Set
Table 15.3.1.6: Trial Treatment Related Serious TEAEs by SOC and PT – SAF Analysis Set

**Add footnote:** Related TEAEs are events with relationship missing, unknown or related.

Table 15.3.1.7: Non-serious TEAEs by SOC and PT at a Frequency Threshold of 5% – SAF Analysis Set

**Add footnote:** Frequency threshold of 5% in any treatment group.

15.3: Safety Data
15.3.1: Display of Adverse Events
Table 15.3.1.8: TEAEs by Worst Grade, SOC and PT – SAF Analysis Set

| | Treatment A N=xxx (100%) | | | | Treatment B N=xxx (100%) | | | | Treatment C N=xxx (100%) | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Primary System Organ Class<br>Preferred Term | Any Grade n (%) | Grade >=3 n (%) | Grade >=4 n (%) | Grade 5 n (%) | Any Grade n (%) | Grade >=3 n (%) | Grade >=4 n (%) | Grade 5 n (%) | Any Grade n (%) | Grade >=3 n (%) | Grade >=4 n (%) | Grade 5 n (%) |
| Subjects with at least one event | xxx (xx.x) | xxx (xx.x) | xxx (xx.x) | xxx (xx.x) | xxx (xx.x) | xxx (xx.x) | xxx (xx.x) | xxx (xx.x) | xxx (xx.x) | xxx (xx.x) | xxx (xx.x) | xxx (xx.x) |
| SOC1 | xxx (xx.x) | xxx (xx.x) | xxx (xx.x) | xxx (xx.x) | xxx (xx.x) | xxx (xx.x) | xxx (xx.x) | xxx (xx.x) | xxx (xx.x) | xxx (xx.x) | xxx (xx.x) | xxx (xx.x) |
| PT11 | xxx (xx.x) | xxx (xx.x) | xxx (xx.x) | xxx (xx.x) | xxx (xx.x) | xxx (xx.x) | xxx (xx.x) | xxx (xx.x) | xxx (xx.x) | xxx (xx.x) | xxx (xx.x) | xxx (xx.x) |
| PT12 | xxx (xx.x) | xxx (xx.x) | xxx (xx.x) | xxx (xx.x) | xxx (xx.x) | xxx (xx.x) | xxx (xx.x) | xxx (xx.x) | xxx (xx.x) | xxx (xx.x) | xxx (xx.x) | xxx (xx.x) |
| SOC2 | xxx (xx.x) | xxx (xx.x) | xxx (xx.x) | xxx (xx.x) | xxx (xx.x) | xxx (xx.x) | xxx (xx.x) | xxx (xx.x) | xxx (xx.x) | xxx (xx.x) | xxx (xx.x) | xxx (xx.x) |
| PT21 | xxx (xx.x) | xxx (xx.x) | xxx (xx.x) | xxx (xx.x) | xxx (xx.x) | xxx (xx.x) | xxx (xx.x) | xxx (xx.x) | xxx (xx.x) | xxx (xx.x) | xxx (xx.x) | xxx (xx.x) |
| … | | | | | | | | | | | | |

MedDRA version 19.1, NCI-CTCAE version 4.03.
Note: Any grade includes 'Missing' grade. Worst grade per subject/SOC/PT is reported.
TEAEs are defined as events that start within the day of first dose of trial treatment until 28 days after last dose of treatment.

**Programming Note:** ***MedDRA version 19.1 or highest at time of data transfer.***

**Repeat table 15.3.1.8 for:**
Table 15.3.1.9: Trial Treatment Related TEAEs by Worst Grade, SOC and PT – SAF Analysis Set

**Add footnote:** Related TEAEs are events with relationship missing, unknown or related.

**Repeat table 15.3.1.3 for:**
Table 15.3.1.10: TEAEs Leading to Death by SOC and PT – SAF Analysis Set
Table 15.3.1.11: TEAEs Leading to Trial Treatment Discontinuation by SOC and PT – SAF Analysis Set
Table 15.3.1.12: TEAEs Leading to Dose Reduction of Trial Treatment by SOC and PT – SAF Analysis Set
Table 15.3.1.13: TEAEs Leading to Withdrawal from Trial by SOC and PT – SAF Analysis Set
Table 15.3.1.14: Treatment Emergent AESIs by SOC and PT – SAF Analysis Set

**Add footnote:** AESI = Adverse Event of Special Interest.

15.3: Safety Data
15.3.2: Listings of Deaths, Other Serious and Significant Adverse Events
Table 15.3.2.1: Deaths by Primary Reason – SAF Analysis Set

| | Treatment A N=xxx (100%) n (%) | Treatment B N=xxx (100%) n (%) | Treatment C N=xxx (100%) n (%) |
|---|---|---|---|
| Subjects who died | xxx (xx.x) | xxx (xx.x) | xxx (xx.x) |
| Primary reason for death | | | |
| Progressive disease and/or disease related condition | xxx (xx.x) | xxx (xx.x) | xxx (xx.x) |
| Event unrelated to trial treatment | xxx (xx.x) | xxx (xx.x) | xxx (xx.x) |
| Event related to trial treatment | xxx (xx.x) | xxx (xx.x) | xxx (xx.x) |
| Unknown | xxx (xx.x) | xxx (xx.x) | xxx (xx.x) |

Note: Reason as reported on death CRF page.

15.3: Safety Data
15.3.2: Listings of Deaths, Other Serious and Significant Adverse Events
Table 15.3.2.3: Listing of Serious TEAEs – SAF Analysis Set

| AE No | Preferred Term/ Investigator Term | Start/ End Date of AE | Dur. of AE (days) | Onset Rel.to Trial Treat. | Rel. to Trial Treat. | Grade | Action on Trial Treat.(a) | Outcome(b) | Rel. Day from First Admin. |
|---|---|---|---|---|---|---|---|---|---|
| Treatment Arm: Treatment A, Subject ID: XXXXXXXXXX, Age: xx, Sex: X, Race: XXXXXXX<br>Treatment Administration: First Date: DDMONYYYY, Last Date: DDMONYYYY, Number of infusions: xx | | | | | | | | | |
| X | XXXXXXXXXXXXXXX/<br>XXXXXXXXXXXXXXX | DDMONYYYY/<br>DDMONYYYY | xx | Before | Unrelated | 1 | No change | Res. | xx |
| Treatment Arm: Treatment A, Subject ID: XXXXXXXXXX, Age: xx, Sex: X, Race: XXXXXXX<br>Treatment Administration: First Date: DDMONYYYY, Last Date: DDMONYYYY, Number of infusions: xx | | | | | | | | | |
| X | XXXXXXXXXXXXXXXX/<br>XXXXXXXXXXXXXXXX | DDMONYYYY/<br>DDMONYYYY | xx | During | Related | 2 | Reduced | Ong. | xx |
| Treatment Arm: Treatment B, Subject ID: XXXXXXXXXX, Age: xx, Sex: X, Race: XXXXXXX<br>Treatment Administration: First Date: DDMONYYYY, Last Date: DDMONYYYY, Number of infusions: xx | | | | | | | | | |
| X | XXXXXXXXXXXXXXXX/<br>XXXXXXXXXXXXXXXX | DDMONYYYY/<br>DDMONYYYY | xx | After | Unrelated | 3 | Interrupted | Res. w. sequ. | xx |

MedDRA version 19.1, NCI-CTCAE version 4.03.
Note: (a) Action: No change = Dose not changed, Reduced = Dose reduced, Interrupted = Drug interrupted, Withdrawn = Drug withdrawn, N/A = Not applicable.
(b) Outcome: Change = Change in severity, Res. = Resolved, Res. w. sequ. = Resolved with sequelae, Ong. = Ongoing, Fatal = Fatal, Unknown = Unknown.

***Programming note: MedDRA version 19.1 or highest at time of data transfer.***

15.3: Safety Data
15.3.5: Clinical Laboratory Evaluations
Table 15.3.5.1: Hematology – Shift from Baseline to Worst On-treatment Value – SAF Analysis Set

| | | | Worst On-treatment Value | | | | |
|---|---|---|---|---|---|---|---|
| Laboratory Test | Treatment | Baseline Classification | Low n (%) | Normal n (%) | High n (%) | Missing n (%) | Total n (%) |
| PARAM1 (Unit1) | Treatment A N=XXX | Low | xxx (xx.x) | xxx (xx.x) | xxx (xx.x) | xxx (xx.x) | xxx (100.0) |
| | | Normal | xxx (xx.x) | xxx (xx.x) | xxx (xx.x) | xxx (xx.x) | xxx (100.0) |
| | | High | xxx (xx.x) | xxx (xx.x) | xxx (xx.x) | xxx (xx.x) | xxx (100.0) |
| | | Missing | xxx (xx.x) | xxx (xx.x) | xxx (xx.x) | xxx (xx.x) | xxx (100.0) |
| | | Total | xxx (xx.x) | xxx (xx.x) | xxx (xx.x) | xxx (xx.x) | xxx (100.0) |
| | Treatment B N=XXX | Low | xxx (xx.x) | xxx (xx.x) | xxx (xx.x) | xxx (xx.x) | xxx (100.0) |
| | | Normal | xxx (xx.x) | xxx (xx.x) | xxx (xx.x) | xxx (xx.x) | xxx (100.0) |
| | | High | xxx (xx.x) | xxx (xx.x) | xxx (xx.x) | xxx (xx.x) | xxx (100.0) |
| | | Missing | xxx (xx.x) | xxx (xx.x) | xxx (xx.x) | xxx (xx.x) | xxx (100.0) |
| | | Total | xxx (xx.x) | xxx (xx.x) | xxx (xx.x) | xxx (xx.x) | xxx (100.0) |
| | ..... | | | | | | |

Note: Baseline is the last measurement prior to the first dose of any trial treatment.
Normal category includes low values for high parameters and high values for low parameters.

**Repeat table 15.3.5.1 for:**
Table 15.3.5.2: Clinical Chemistry – Shift from Baseline to Worst On-treatment Value – SAF Analysis Set

**Programming Note: All parameters and treatments are reported.**

***- For Hematology:*** *Hematocrit, Hemoglobin, Mean cellular hemoglobin, Mean cellular hemoglobin concentration, Mean cellular volume, Platelet count, Red blood cell count, Red cell distribution width, White blood cell count and differential.*
***- For Clinical Chemistry:*** *Gamma glutamyl transferase, ALT, Albumin, AP, AST, Bilirubin – direct (only if total bilirubin is outside the normal range), Bilirubin – total, Calcium, Chloride, Bicarbonate, Serum creatinine, Glucose, Potassium, Protein – total, Sodium, Urea, Uric acid, C-reactive protein.*

***Worst value for non-CTCAE parameters need to be defined with the team for each parameter (e.g. Blood urea nitrogen high). In case worse value could be either low or high for some tests, then report both PARAM low and PARAM high (e.g. Hematocrit low and Hematocrit high).***

***In case, there is not enough space to display the table on one page, merge the columns for parameter and treatment arm.***

15.3: Safety Data
15.3.5: Clinical Laboratory Evaluations
Table 15.3.5.3: Hematology – Shift in Toxicity Grading from Baseline to Highest Grade – SAF Analysis Set

| Laboratory Test | Treatment | Baseline NCI-CTCAE Grade | Worst NCI-CTCAE Grade | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| | | | Grade 0 n (%) | Grade 1 n (%) | Grade 2 n (%) | Grade 3 n (%) | Grade 4 n (%) | Missing n (%) | Total n (%) |
| PARAM1 (Unit1) | Treatment A N=xxx | Grade 0 | xxx (xx.x) | xxx (xx.x) | xxx (xx.x) | xxx (xx.x) | xxx (xx.x) | xxx (xx.x) | xxx (100.0) |
| | | Grade 1 | xxx (xx.x) | xxx (xx.x) | xxx (xx.x) | xxx (xx.x) | xxx (xx.x) | xxx (xx.x) | xxx (100.0) |
| | | Grade 2 | xxx (xx.x) | xxx (xx.x) | xxx (xx.x) | xxx (xx.x) | xxx (xx.x) | xxx (xx.x) | xxx (100.0) |
| | | Grade 3 | xxx (xx.x) | xxx (xx.x) | xxx (xx.x) | xxx (xx.x) | xxx (xx.x) | xxx (xx.x) | xxx (100.0) |
| | | Grade 4 | xxx (xx.x) | xxx (xx.x) | xxx (xx.x) | xxx (xx.x) | xxx (xx.x) | xxx (xx.x) | xxx (100.0) |
| | | Missing | xxx (xx.x) | xxx (xx.x) | xxx (xx.x) | xxx (xx.x) | xxx (xx.x) | xxx (xx.x) | xxx (100.0) |
| | | Total | xxx (xx.x) | xxx (xx.x) | xxx (xx.x) | xxx (xx.x) | xxx (xx.x) | xxx (xx.x) | xxx (100.0) |

**Shell continues on the next page**

15.3: Safety Data
15.3.5: Clinical Laboratory Evaluations
Table 15.3.5.3: Hematology – Shift in Toxicity Grading from Baseline to Highest Grade – SAF Analysis Set

| | | | Worst NCI-CTCAE Grade | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| Laboratory Test | Treatment | Baseline NCI-CTCAE Grade | Grade 0 n (%) | Grade 1 n (%) | Grade 2 n (%) | Grade 3 n (%) | Grade 4 n (%) | Missing n (%) | Total n (%) |
| | Treatment B N=xxx | Grade 0 | xxx (xx.x) | xxx (xx.x) | xxx (xx.x) | xxx (xx.x) | xxx (xx.x) | xxx (xx.x) | xxx (100.0) |
| | | Grade 1 | xxx (xx.x) | xxx (xx.x) | xxx (xx.x) | xxx (xx.x) | xxx (xx.x) | xxx (xx.x) | xxx (100.0) |
| | | Grade 2 | xxx (xx.x) | xxx (xx.x) | xxx (xx.x) | xxx (xx.x) | xxx (xx.x) | xxx (xx.x) | xxx (100.0) |
| | | Grade 3 | xxx (xx.x) | xxx (xx.x) | xxx (xx.x) | xxx (xx.x) | xxx (xx.x) | xxx (xx.x) | xxx (100.0) |
| | | Grade 4 | xxx (xx.x) | xxx (xx.x) | xxx (xx.x) | xxx (xx.x) | xxx (xx.x) | xxx (xx.x) | xxx (100.0) |
| | | Missing | xxx (xx.x) | xxx (xx.x) | xxx (xx.x) | xxx (xx.x) | xxx (xx.x) | xxx (xx.x) | xxx (100.0) |
| | | Total | xxx (xx.x) | xxx (xx.x) | xxx (xx.x) | xxx (xx.x) | xxx (xx.x) | xxx (xx.x) | xxx (100.0) |

**Shell continues on the next page**

15.3: Safety Data
15.3.5: Clinical Laboratory Evaluations
Table 15.3.5.3: Hematology – Shift in Toxicity Grading from Baseline to Highest Grade – SAF Analysis Set

| Laboratory Test | Treatment | Baseline NCI-CTCAE Grade | Worst NCI-CTCAE Grade | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| | | | Grade 0 n (%) | Grade 1 n (%) | Grade 2 n (%) | Grade 3 n (%) | Grade 4 n (%) | Missing n (%) | Total n (%) |
| | Treatment C N=xxx | Grade 0 | xxx (xx.x) | xxx (xx.x) | xxx (xx.x) | xxx (xx.x) | xxx (xx.x) | xxx (xx.x) | xxx (100.0) |
| | | Grade 1 | xxx (xx.x) | xxx (xx.x) | xxx (xx.x) | xxx (xx.x) | xxx (xx.x) | xxx (xx.x) | xxx (100.0) |
| | | Grade 2 | xxx (xx.x) | xxx (xx.x) | xxx (xx.x) | xxx (xx.x) | xxx (xx.x) | xxx (xx.x) | xxx (100.0) |
| | | Grade 3 | xxx (xx.x) | xxx (xx.x) | xxx (xx.x) | xxx (xx.x) | xxx (xx.x) | xxx (xx.x) | xxx (100.0) |
| | | Grade 4 | xxx (xx.x) | xxx (xx.x) | xxx (xx.x) | xxx (xx.x) | xxx (xx.x) | xxx (xx.x) | xxx (100.0) |
| | | Missing | xxx (xx.x) | xxx (xx.x) | xxx (xx.x) | xxx (xx.x) | xxx (xx.x) | xxx (xx.x) | xxx (100.0) |
| | | Total | xxx (xx.x) | xxx (xx.x) | xxx (xx.x) | xxx (xx.x) | xxx (xx.x) | xxx (xx.x) | xxx (100.0) |

NCI-CTCAE version 4.03.
Note: Baseline is the last measurement prior to the first dose of any trial treatment.

**Repeat table 15.3.5.3 for:**
Table 15.3.5.4: Clinical Chemistry – Shift in Toxicity Grading from Baseline to Highest Grade – SAF Analysis Set

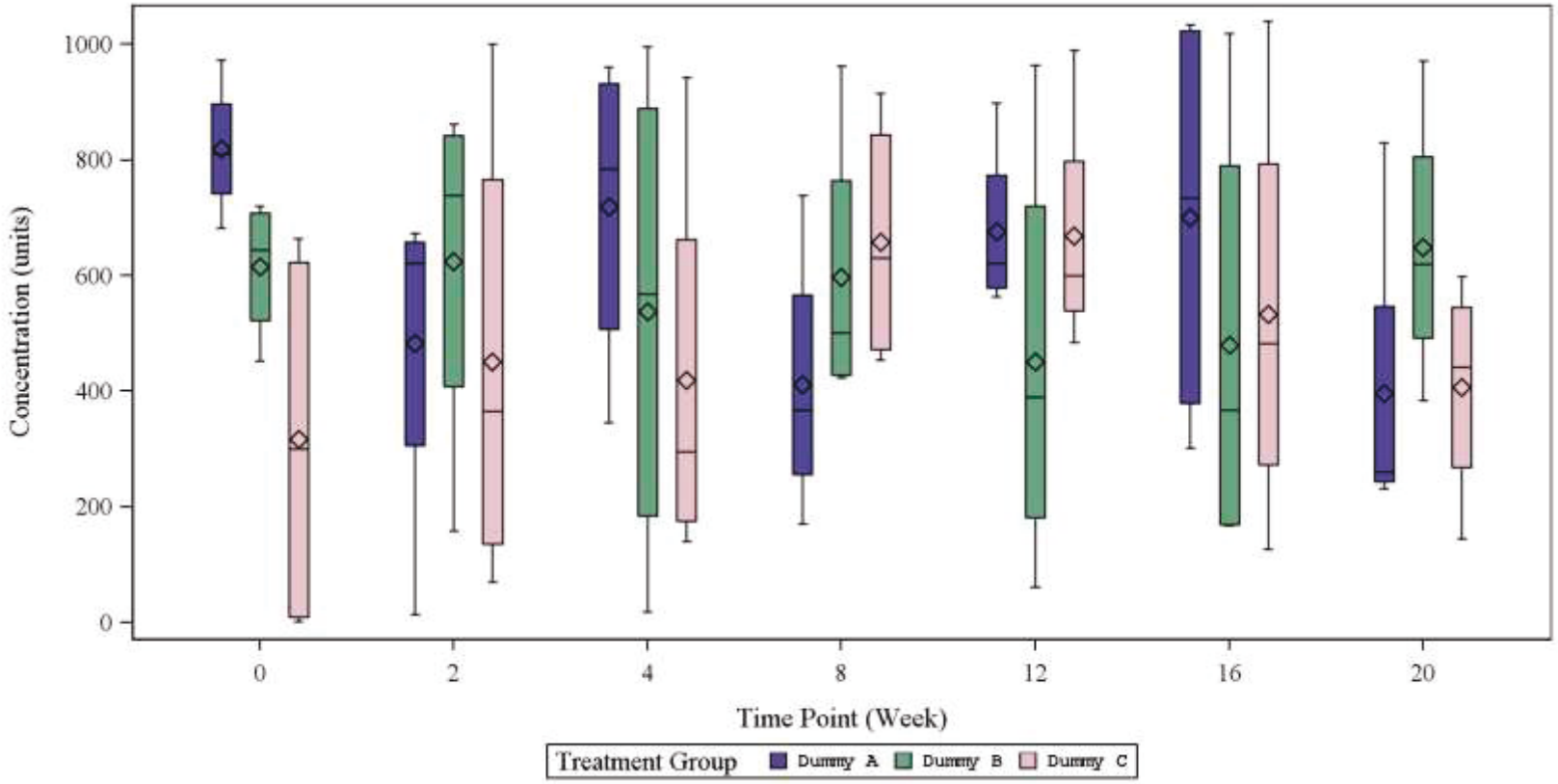
**Programming Note: Only gradable parameters are reported, examples are provided below – present all gradable parameters that are available.**

***- For Hematology: Leukocytes high (10E9/L), Leukocytes low (10E9/L), Hemoglobin high (g/L), Hemoglobin low (G/L), Platelets (10E9/L), Lymphocytes high (10E9/L), Lymphocytes low (10E9/L), Neutrophils (10E9/L)…***

***- For Biochemistry: Bilirubin (µmol/L), AST (U/L), ALT (U/L), Alkaline Phosphatase (U/L), Creatinine (µmol/L), Albumin (G/L), Calcium low (mmol/L), Calcium high (mmol/L), Sodium low (mmol/L), Sodium high (mmol/L), Potassium low (mmol/L), Potassium high (mmol/L), Glucose high (mmol/L), Glucose low (mmol/L), Uric acid high (mmol/L)…***

***In case there is not enough space to display the table on one page, merge the columns for parameter and treatment.***

15.3: Safety Data
15.3.5: Clinical Laboratory Evaluations
Figure 15.3.5.5: Boxplot of Change from Baseline for ALT Values by Visit – SAF Analysis Set




**Programming Note: Split figure across multiple pages as the number of weeks increases.**

**Programming note:** The y-axis label should be "<PARAM> Change from Baseline (*<units>*). The x-axis label should be "Visit". For the partially unblinded outputs, the Treatment Group legend will show "Treatment A" etc.

Use only the following colors (applies to all figures): Cyan, Magenta, Yellow & Black. Also use different symbols for each treatment group.

**Repeat figure 15.3.5.5 for:**

Figure 15.3.5.6: Boxplot of Change from Baseline for AST Values by Visit – SAF Analysis Set

Figure 15.3.5.7: Boxplot of Change from Baseline for Total Bilirubin Values by Visit – SAF Analysis Set

Figure 15.3.5.8: Boxplot of Change from Baseline for Total White Blood Count Values by Visit – SAF Analysis Set

Figure 15.3.5.9: Boxplot of Change from Baseline for Neutrophils Values by Visit – SAF Analysis Set

# 18.2 Listings

16.2.1: Subject Disposition
Listing 16.2.1.1: Subject Disposition and Withdrawals – Screening Analysis Set

| Treatment Group | Subject Identifier | Screening Date | Randomized?/ Date Randomized/ Stratification Factor (a) | Withdrew Prior to Being Treated? | In SAF Analysis Set? | Withdrew from trial treatment/ Reason for Withdrawal | Date of Last Dose | Discont-inued Trial?/ Primary Reason | Date Discont-inued |
|---|---|---|---|---|---|---|---|---|---|
| Treatment A | XXXXXXX | DDMMMYYYY | Yes/DDMMMYYYY/ FVC <70% | XXX | XXX | Yes/XXXXXXXX XXXX | DDMMMYYYY | Yes/ xxxxxxxx | DDMMMYYYY |
| | XXXXXXX | DDMMMYYYY | Yes/DDMMMYYYY/ FVC ≥70% | XXX | XXX | No | | No | |
| | XXXXXXX | DDMMMYYYY | Yes/DDMMMYYYY/ XXXXXX | XXX | XXX | No | | No | |
| | …… | | | | | | | | |
| Treatment B | XXXXXXX | DDMMMYYYY | Yes/DDMMMYYYY/ XXXXXX | XXX | XXX | No | | No | |
| | … | | | | | | | | |
| *Etc.* | | | | | | | | | |

(a) Stratification Factor from eCRF: FVC <70% = Baseline FVC <70% predicted, FVC ≥70% = Baseline FVC ≥70% predicted.
Note: Baseline is defined as the last non-missing assessment value prior to randomization.

**Programming Note: If a subject is screened but not yet randomized, treatment group will be Not Randomized. If they are screen failed then treatment group is Screen Failures.**
**If there are subjects in the Not Randomized group then add the following footnote (note indentation to line up with baseline footnote):**
**'Not Randomized' treatment group contains subjects who are still in screening at time of data cutoff.**
**Ensure any "Other" reasons for treatment and trial termination are specified, "Other: xxxxxx".**

16.2.1: Subject Disposition
Listing 16.2.2.1: Important Protocol Deviations – ITT Analysis Set

| Treatment Group | Subject Identifier | Type | Deviation details |
|---|---|---|---|
| Treatment A | XXXXXXX | Eligibility and Entry Criteria | XXXXXXXXXXXXX/ XXXXXXXXXXXXXXXXX |
| | | Efficacy Criteria | XXXXXXXXXXXXXXXXXXX |
| | XXXXXXX | XXXXXXXXXXX | XXXXXXXXXXXXXX |
| | | XXXXXXXXXXXX | XXXXXXXXXXXXXXXXX |
| | XXXXXXX | XXXXXXXXXXX | XXXXXXXXXXXXXX |
| | | XXXXXXXXXXXX | XXXXXXXXXXXXXXXXX |
| | …… | | |
| Treatment B | XXXXXXX | XXXXXXXXXXX | XXXXXXXXXXXXXX |
| | | XXXXXXXXXXXX | XXXXXXXXXXXXXXXXX |
| | … | | |
| *Etc.* | | | |

**Programming note:** Present each deviation on a new line.

16.2.4: Demographic Data
Listing 16.2.4.1: Subject Demographics – SAF Analysis Set

| Treatment Group | Subject Identifier | Sex | Birth Date | Age (years) | Race | Ethnicity |
|---|---|---|---|---|---|---|
| Treatment A | XXXXXXX | Male | DDMMMYYYY | XX | XXXXXXX | XXXXX |
| | XXXXXXX | Female | YYYY | XX | XXXXXXX | XXXXX |
| | XXXXXXX | XXXX | DDMMMYYYY | XX | XXXXXXX | XXXXX |
| | …… | | | | | |
| Treatment B | XXXXXXX | XXXX | DDMMMYYYY | XX | XXXXXXX | XXXXX |
| | … | | | | | |
| *Etc.* | | | | | | |

Note: Age is relative to the date of informed consent.

16.2.4: Demographic Data
Listing 16.2.4.2: Subject Medical History – SAF Analysis Set

| Treatment Group | Subject Identifier | System Organ Class | Preferred Term | Verbatim Text | Start Date | End Date | Related to Study Condition? |
|---|---|---|---|---|---|---|---|
| Treatment A | XXXXXXX | XXXXXXX | XXXXXXX | XXXXXXX | DDMMMYYYY | Ongoing | Yes |
| | | XXXXXXX | XXXXXXX | XXXXXXX | DDMMMYYYY | DDMMMYYY | No |
| | | XXXXXXX | XXXXXXX | XXXXXXX | DDMMMYYYY | XXXXXXXX | Unknown |
| | …… | | | | | | |
| Treatment B | XXXXXXX | XXXXXXX | XXXXXXX | XXXXXXX | DDMMMYYYY | XXXXXXXX | |
| | … | | | | | | |
| *Etc.* | | | | | | | |

MedDRA version xx.x.

**Programming note:** MedDRA version 19.1 or highest at time of data transfer.

16.2.4: Demographic Data
Listing 16.2.4.3: Subject Disease History – SAF Analysis Set

| Treatment Group | Subject Identifier | Date of Diagnosis | Time Since Date of Diagnosis (years) | Status | Systemic Sclerosis Symptom History (a) | ACR/EULAR Classification Criteria for Systemic Sclerosis (b) |
|---|---|---|---|---|---|---|
| Treatment A | XXXXXXX | DDMMMYYYY | XX.XX | Diffuse cutaneous SSc | Skin Thickening/ Tendon friction rubs/ XXXXXXX | Fingertip lesions: Fingertip pitting scars/ Abnormal nailfold capillaries/ XXXXXX |
| | XXXXXXX | DDMMMYYYY | XX.XX | Limited cutaneous SSc | XXXXXXX/ XXXXXXX / XXXXXXXXX/ XXXXXX | XXXXXXX/ XXXXXXX / XXXXXXXXX/ XXXXXX |
| | XXXXXXX | DDMMMYYYY | XX.XX | XXXXXXX | XXXXXXX/ XXXXXXX / XXXXXXXXX/ XXXXXX | XXXXXXX/ XXXXXXX / XXXXXXXXX/ XXXXXX |
| | …… | | | | | |
| Treatment B | XXXXXXX | DDMMMYYYY | XX.XX | XXXXXXXX | XXXXXXX/ XXXXXXX / XXXXXXXXX/ XXXXXX | |
| | … | | | | | |
| *Etc.* | | | | | | |

(a) Where 'Yes' was selected on the eCRF.
(b) Where 'Present' was selected on the eCRF.
Note: Time since date of diagnosis is relative to date of informed consent.

**Programming note: Concatenate all Systemic Sclerosis Symptom History sub-categories where 'Yes' is ticked on the eCRF, concatenate all ACR/EULAR Classification Criteria for Systemic Sclerosis sub-categories where 'Present' is ticked on the eCRF.**

16.2.4: Demographic Data
Listing 16.2.4.4: Previous Medications – SAF Analysis Set

| Treatment Group | Subject Identifier | ATC Level 2/ Preferred Term/ Reported Name | Start Date/ End Date (Trial Day) | Dose (Unit) | Frequency | Route | Reason (Indication) | Reason(s) |
|---|---|---|---|---|---|---|---|---|
| Treatment A | XXXXXXX | XXXXXXXXXXXX/ XXXXXXXX/ XXXXXXXX | DDMMMYYYY (xx) / DDMMMYYYY (xx) | XXX xx | XX | XX | XXXXXXXX | Adverse event/ Disease related condition |
| | | XXXXXXXXXXXX/ XXXXXXXX/ XXXXXXXX | DDMMMYYYY (xx) / DDMMMYYYY (xx) | XXX xx | Other: XXX | XX | XXXXXXXX | XXXXXXX |
| | …… | | | | | | | |
| Treatment B | XXXXXXX | XXXXXXXXXXXX/ XXXXXXXX/ XXXXXXXX | DDMMMYYYY (xx) / DDMMMYYYY (xx) | XXX | XX | Other: XX | XXXXXXXXXXXX | XXXXXX |
| | … | | | | | | | |
| *Etc.* | | | | | | | | |

WHO Drug Dictionary version Enhanced September 2016.
Note: In case multiple ATCs are assigned to a medication, all ATCs will be reported.

***Programming note: WHO Drug Dictionary version Enhanced September 2016 or highest at time of data transfer.***
**Repeat listing 16.2.4.4 for:**
Listing 16.2.4.5: Concomitant Medications – SAF Analysis Set
***Change "Previous Medication" to "Concomitant Medication"***
Listing 16.2.4.6: Background Therapy – SAF Analysis Set
***Change "Previous Medication" to "Background Therapy".***

16.2.5: Treatment Compliance and Exposure
Listing 16.2.5.1: Trial Treatment Administration Details – SAF Analysis Set

| Treatment Group | Subject Identifier | Visit | Preparation Date (Time)/ Kit Number | Admin. Start Date (Time)/ End Date (Time) | Duration of infusion (hours) | Change in Dose? | Planned Volume (mL) | Actual Volume (mL) | Infusion Completed as Planned? |
|---|---|---|---|---|---|---|---|---|---|
| Treatment A | XXXXXXX | XXXXXXX | DDMMYYY (HH:MM)/ XXXX | DDMMYYY (HH:MM)/ DDMMYYY (HH:MM) | XX.XX | No | XXX | XXX | No: Adverse event |
| | | XXXXXXX | DDMMYYY (HH:MM)/ XXXX | DDMMYYY (HH:MM)/ DDMMYYY (HH:MM) | XX.XX | Dose adjusted: Adverse event | XXX | XXX | Yes |
| | | XXXXXXX | DDMMYYY (HH:MM)/ XXXX | DDMMYYY (HH:MM)/ DDMMYYY (HH:MM) | XX.XX | XXXXXXX | XXX | XXX | XXX |
| | | XXXXXXX* | | | | No dose: Missed visit | XXX | | No: Other, No dose: missed visit |
| *Etc.* | | | | | | | | | |

* = Visit derived due to the subject not completing the "STUDY TREATMENT ADMINISTRATION DETAILS" eCRF page at the missed visit.
Note: Admin. = Administration.
Duration of infusion is calculated as: End time of administration – start time of administration.

16.2.5: Treatment Compliance and Exposure
Listing 16.2.5.2: Overall Exposure to Trial Treatment – SAF Analysis Set

| Treatment Group | Subject Identifier | Treatment Duration (weeks) | Number of Infusions | Number of Dose Adjustments | Number of Infusions Not Completed as Planned | Overall Treatment Adherence (%) |
|---|---|---|---|---|---|---|
| Treatment A | XXXXXXX | XXX | XX | X | X | XX |
| *Etc.* | | | | | | |

Note: Treatment duration is calculated as: (Last infusion date prior to data cut-off – first infusion date + 28) / 7 days.
Subject overall treatment adherence is calculated as: (sum of actual volume received/ sum of planned Volume, up to and including their last dose recorded on their treatment termination visit)*100.

16.2.6: Efficacy Data
Listing 16.2.6.1: FVC Volume (mL) and FVC % Predicted – mITT Analysis Set

| Treatment Group | Subject Identifier | Visit | Date of Assessment (Trial Day) | FVC (mL) | | FVC % Predicted | |
|---|---|---|---|---|---|---|---|
| | | | | Observed | Change from Baseline | Observed | Change from Baseline |
| Treatment A | XXXXXXX | XXXXXXX | DDMMMYYYY (xx) | XX* | | XX* | |
| | | XXXXXXX | DDMMMYYYY (xx) | XX | XX | XX | XX |
| | | XXXXXXX | DDMMMYYYY (xx) | XX | XX | XX | XX |
| *Etc.* | | | | | | | |

* Baseline value.
Note: Baseline is defined as the last non-missing assessment value prior to randomization. If such a value is missing then the last value prior to the first trial treatment administration will be used.
Trial day is defined relative to the date of randomization.

16.2.6: Efficacy Data
Listing 16.2.6.2: mRSS Total Score – mITT Analysis Set

| Treatment Group | Subject Identifier | Visit | Date of Assessment (Trial Day) | mRSS Total Score | |
|---|---|---|---|---|---|
| | | | | Observed | Change from Baseline |
| Treatment A | XXXXXXX | XXXXXXX | DDMMMYYYY (xx) | XX* | |
| | | XXXXXXX | DDMMMYYYY (xx) | XX | XX |
| | | XXXXXXX | DDMMMYYYY (xx) | XX | XX |
| *Etc.* | | | | | |

* Baseline value.
^ = diffuse cutaneous systemic sclerosis at baseline.
Note: Baseline is defined as the last non-missing assessment value prior to randomization. If such a value is missing then the last value prior to the first trial treatment administration will be used.
Trial day is defined relative to the date of randomization.

16.2.6: Efficacy Data
Listing 16.2.6.3: Clinically Meaningful Disease Progression – mITT Analysis Set

| Treatment Group | Subject Identifier | Date of Progression (Trial Day) | Progression Criteria Fulfilled | SSc-ILD progression | | |
|---|---|---|---|---|---|---|
| | | | | Was Mycophenolate Dose Increased? | Was a New Immunosuppressant or Biologic Drug Initiated? | Was the Trial Treatment Discontinued? |
| Treatment A | XXXXXXX | DDMMMYYYY (xx) | SSc-ILD: Relative decrease from baseline in FVC % predicted >10% | No | No | No |
| | | DDMMMYYYY (xx) | SSc other than ILD: Scleroderma renal crisis | | | XX |
| *Etc.* | | | | | | |

Note: Trial day is defined relative to the date of randomization.

**Programming note:** Only display subjects with clinically meaningful disease progression. Concatenate all details selected for SSc other than ILD (including the free text details for 'Other'). If both SSc-ILD and SSc other than ILD were selected on the same date, then display on a new line.

16.2.6: Efficacy Data
Listing 16.2.6.4: DLCO – mITT Analysis Set

| Treatment Group | Subject Identifier | Visit | Date of Assessment (Trial Day) | DLCO as recorded on eCRF | DLCO Result in SI Unit (mmol of CO/min/kPa) | | DLCO % Predicted | |
|---|---|---|---|---|---|---|---|---|
| | | | | Observed (unit) | Observed | Change from Baseline | Observed | Change from Baseline |
| Treatment A | XXXXXXX | XXXXXX | DDMMMYYYY (xx) | XX (xxx) | XX* | | XX* | |
| | | XXXXXX | DDMMMYYYY (xx) | XX (xxx) | XX | XX | XX | XX |
| | | XXXXXX | DDMMMYYYY (xx) | XX (xxx) | XX | XX | XX | XX |
| *Etc.* | | | | | | | | |

* Baseline value.
Note: Baseline is defined as the last non-missing assessment value prior to randomization. If such a value is missing then the last value prior to the first trial treatment administration will be used.
Trial day is defined relative to the date of randomization.

16.2.6: Efficacy Data
Listing 16.2.6.5: KCO – mITT Analysis Set

| Treatment Group | Subject Identifier | Visit | Date of Assessment (Trial Day) | Test overread grading | VA | DLCO/ VA | KCO | |
|---|---|---|---|---|---|---|---|---|
| | | | | | | | Observed | Change from baseline |
| Treatment A | XXXXXXX | XXXXXXX | DDMMMYYYY (xx) | Acceptable | xx | xx+ | xx* | |
| | | XXXXXXX | DDMMMYYYY (xx) | Unacceptable | xx | xx | xx | xx |
| | | XXXXXXX | DDMMMYYYY (xx) | xxxxx | | | | |
| *Etc.* | | | | | | | | |

* Baseline value.
Note: Baseline is defined as the last non-missing assessment value prior to randomization.
Trial day is defined relative to the date of randomization.

16.2.6: Efficacy Data
Listing 16.2.6.6: Digital Ulcers – mITT Analysis Set

| Treatment Group | Subject Identifier | Visit | Completed Status | Date of Assessment (Trial Day) | Number of Active Ulcers | | Undetermined Ulcers | | Healed Ulcers | | Total Digital Ulcer count |
|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | Absolute Value | CFB | Absolute Value | CFB | Absolute Value | CFB | |
| Treatment A | XXXXXXX | XXXXXX | Done | DDMMMYYYY (xx) | XXX* | | XXX* | | XXX* | | XXX |
| | | XXXXXX | Not Done | | | | | | | | |
| | | XXXXXX | XXXXXXX | DDMMMYYYY (xx) | XXX | XXX | XXX | XXX | XXX | XXX | XXX |
| *Etc.* | | | | | | | | | | | |

* Baseline value.
Note: Baseline is defined as the last non-missing assessment value prior to randomization.
CFB = Change from Baseline.
Trial day is defined relative to the date of randomization.

16.2.6: Efficacy Data
Listing 16.2.6.7: Mahler BDI/TDI – mITT Analysis Set

| Treatment Group | Subject Identifier | Visit | Date of Assessment (Trial Day) | Done/ Not done - Reason | Question | Score |
|---|---|---|---|---|---|---|
| Treatment A | XXXXXXX | XXXXXXX | DDMMMYYYY (xx) | Done | Functional Imapairment | x |
| | | | | | Magnitude of Task | x |
| | | | | | Magnitude of Effort | x |
| | | | | | Total | x |
| | | XXXXXXX | DDMMMYYYY (xx) | Done | Changes in Functional Impairment | x |
| | | | | | Changes in Magnitude of Task | x |
| | | | | | Changes in Magnitude of Effort | x |
| | | | | | Total | x |
| | | XXXXXXX | DDMMMYYYY (xx) | Not done – Subject felt too ill | | |

*Etc.*

Note: Baseline is defined as the last non-missing assessment value prior to randomization. The BDI is completed at baseline and the TDI is completed at subsequent visits.
Trial day is defined relative to the date of randomization.

16.2.6: Efficacy Data
Listing 16.2.6.8: SGRQ – Question Scores – mITT Analysis Set

| Treatment Group | Subject Identifier | Visit | Date of Assessment (Trial Day) | Done/ Not done - Reason | Question (component) | Answer(s) | Weight |
|---|---|---|---|---|---|---|---|
| Treatment A | XXXXXXX | XXXXXXX | DDMMMYYYY (xx) | Done | xxxxxx (S) | xxxx | x |
| | | | | | xxxxxx (I) | xxxx | x |
| | | | | | | xxxxx | x |
| | | | | | … | xxxxx | x |
| | | XXXXXXX | DDMMMYYYY (xx) | Done | | xxxx | x |
| | | | | | | xxxxxx | x |
| | | | | | | xxxx | x |
| | | | | | | xxxxxx | x |
| | | XXXXXXX | DDMMMYYYY (xx) | Not done – Subject felt too ill | | | |
| *Etc.* | | | | | | | |

Note: Component abbreviations: S = Symptoms, I = Impacts, A = Activity.
Trial day is defined relative to the date of randomization.

16.2.6: Efficacy Data
Listing 16.2.6.9: SGRQ – Component and Total Scores – mITT Analysis Set

| Treatment Group | Subject Identifier | Visit | Date of Assessment (Trial Day) | Done/ Not done - Reason | Component | Score | Change from baseline |
|---|---|---|---|---|---|---|---|
| Treatment A | XXXXXXX | XXXXXXX | DDMMMYYYY (xx) | Done | Symptoms | x | |
| | | | | | Activity | x | |
| | | | | | Impacts | x | |
| | | | | | Total | x* | |
| | | XXXXXXX | DDMMMYYYY (xx) | Done | Symptoms | x | |
| | | | | | Activity | x | |
| | | | | | Impacts | x | |
| | | | | | Total | x | x |
| | | XXXXXXX | DDMMMYYYY (xx) | Not done – Subject felt too ill | | | |

*Etc.*

* Baseline value (total scores only).
Note: Baseline is defined as the last non-missing measurement prior to randomization.
Trial day is defined relative to the date of randomization.
The component score is 100 x summed weights from all positive items in that component divided by the sum of weights for all items in that component. The total score is 100 x summed weights from all positive items in the questionnaire divided by the sum of weights for all items in the questionnaire.

16.2.6: Efficacy Data
Listing 16.2.6.10: Leicester Cough Index – Question Scores – mITT Analysis Set

| Treatment Group | Subject Identifier | Visit | Date of Assessment (Trial Day) | Done/ Not done - Reason | Question (domain) | Score |
|---|---|---|---|---|---|---|
| Treatment A | XXXXXXX | XXXXXXX | DDMMMYYYY (xx) | Done | xxxxxx (P) | x |
| | | | | | xxxxx (Psy) | x |
| | | | | | xxxxx (S) | x |
| | | XXXXXXX | DDMMMYYYY (xx) | Done | xxxxx | x |
| | | | | | xxxxxx | x |
| | | | | | | x |
| | | | | | | x |
| | | XXXXXXX | DDMMMYYYY (xx) | Not done – Subject felt too ill | | |
| *Etc.* | | | | | | |

Note: Trial day is defined relative to the date of randomization.
Domain abbreviations: P = Physical, Psy = Psychological, S = Social.
1 is the most negative score, 7 is the most positive score.

16.2.6: Efficacy Data
Listing 16.2.6.11: Leicester Cough Index – Domain and Total Scores – mITT Analysis Set

| Treatment Group | Subject Identifier | Visit | Date of Assessment (Trial Day) | Done/ Not done - Reason | Domain | Score | Change from baseline |
|---|---|---|---|---|---|---|---|
| Treatment A | XXXXXXX | XXXXXXX | DDMMMYYYY (xx) | Done | Physical | x | |
| | | | | | Psychological | x | |
| | | | | | Social | x | |
| | | | | | Total | x* | |
| | | XXXXXXX | DDMMMYYYY (xx) | Done | Physical | x | |
| | | | | | Psychological | x | |
| | | | | | Social | x | |
| | | | | | Total | x | x |
| | | XXXXXXX | DDMMMYYYY (xx) | Not done – Subject felt too ill | | | |
| *Etc.* | | | | | | | |

* Baseline value (total score only).
Note: Baseline is defined as the last non-missing assessment value prior to randomization.
Trial day is defined relative to the date of randomization.
Domain scores are the sum of all scores in the domain divided by the number of questions within that domain.

16.2.6: Efficacy Data
Listing 16.2.6.12: Physician's Global Assessment – mITT Analysis Set

| Treatment Group | Subject Identifier | Visit | Date of Assessment (Trial Day) | Done/ Not done - Reason | Score | Change from baseline |
|---|---|---|---|---|---|---|
| Treatment A | XXXXXXX | XXXXXXX | DDMMMYYYY (xx) | Done | x* | |
| | | XXXXXXX | DDMMMYYYY (xx) | Done | x | x |
| | | XXXXXXX | DDMMMYYYY (xx) | Not done – Subject felt too ill | | |
| *Etc.* | | | | | | |

* Baseline value.
Note: Baseline is defined as the last non-missing assessment value prior to randomization.
Trial day is defined relative to the date of randomization.
The score is based on the question: "On a scale of 0–100, where would you rate the overall effect systemic sclerosis has on your patient at this time", where 0 = has no effect at all and 100 = worst possible effect.

**Repeat listing 16.2.6.12 for:**
Listing 16.2.6.13: Patient's Global Assessment – mITT Analysis Set

**Update footnote:** The score is based on the question: "On a scale of 0–100, where would you rate the overall effect systemic sclerosis has on you at this time", where 0 = has no effect at all and 100 = worst possible effect.

16.2.6: Efficacy Data
Listing 16.2.6.14: SHAQ – VAS Scores – mITT Analysis Set

| | | | Overall disease activity | | Raynaud's phenomenon | | Finger ulcers | | Breathing problems | | Intestinal problems | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Treatment Group | Subject Identifier | Visit | Observed | CFB | Observed | CFB | Observed | CFB | Observed | CFB | Observed | CFB |
| Treatment A | XXXXXXX | XXXXX | xx* | | xx* | | xx* | | xx* | | xx* | |
| | | XXXXX | xx | xx | xx | xx | xx | xx | xx | xx | xx | xx |
| | | XXXXX | xx | xx | xx | xx | xx | xx | xx | xx | xx | xx |
| | | XXXXX | xx | xx | xx | xx | xx | xx | xx | xx | xx | xx |
| | | … | | | | | | | | | | |
| | XXXXXXX | XXXXX | xx^ | | xx^ | | xx^ | | xx^ | | xx^ | |
| | | XXXXX | xx | xx | xx | xx | xx | xx | xx | xx | xx | xx |
| | | XXXXX | xx | xx | xx | xx | xx | xx | xx | xx | xx | xx |
| | | … | | | | | | | | | | |
| | XXXXXXX | XXXXX | xx | | xx | | xx | | xx | | xx | |
| *Etc.* | | | | | | | | | | | | |

* Baseline value.
Note: Baseline is defined as the last non-missing assessment value prior to randomization.
The VAS scores range from 0 (most positive response) to 100 (most negative response).
CFB = Change from baseline.

16.2.6: Efficacy Data
Listing 16.2.6.15: EQ-5D VAS Score – mITT Analysis Set

| Treatment Group | Subject Identifier | Visit | Date of Assessment (Trial Day) | VAS Score | |
|---|---|---|---|---|---|
| | | | | Observed | CFB |
| Treatment A | XXXXXXX | XXXXXXX | DDMMMYYYY (xx) | X* | |
| | | | | X | X |
| | | | | X | X |
| | ... | | | | |
| …. | XXXXXXX | | DDMMMYYYY (xx) | X* | |
| | | | | X | X |
| | | | | X | X |
| | ... | | | | |

* Baseline value.
Note: Baseline is defined as the last non-missing assessment value prior to randomization.
Trial day is defined relative to the date of randomization.
CFB = Change from Baseline.

16.2.6: Efficacy Data
Listing 16.2.6.16: HRCT Results – mITT Analysis Set

| Treatment Group | Subject Identifier | Visit | Date of Assessment (Trial Day) | QLF (%) (a) | | Extent of ILD (%) | |
|---|---|---|---|---|---|---|---|
| | | | | Observed | Change from Baseline | Observed | Change from Baseline |
| Treatment A | XXXXXXX | XXXXXXX | DDMMMYYYY (xx) | X* | | X* | |
| | | | DDMMMYYYY (xx) | X | X | X | X |
| | | | DDMMMYYYY (xx) | X | X | X | X |
| | ... | | | | | | |
| …. | XXXXXXX | | DDMMMYYYY (xx) | X* | | X* | |
| | | | DDMMMYYYY (xx) | X | X | X | X |
| | | | DDMMMYYYY (xx) | X | X | X | X |
| | ... | | | | | | |

* Baseline value.
(a) QLF in region of highest severity.
Note: Baseline is defined as the last non-missing assessment value prior to randomization.
Trial day is defined relative to the date of randomization.

16.2.7: Display of Adverse Events
Listing 16.2.7.1: All Adverse Events – SAF Analysis Set

| Treatment Group | Subject Identifier | System Organ Class/ Preferred Term/ Verbatim Text | Start Date/ End Date (Trial Day) | Relationship /Timing to Trial Trt | Toxic-ity Grade | Causal-ity Factors | Action Taken With Trial Trt/Other Action | Outcome |
|---|---|---|---|---|---|---|---|---|
| Treatment A | XXXXXXX | XXXXXXXXXXXXXXX/<br>XXXXXXXXXXXXXXX/<br>XXXXXXXXXXXXX+* | DDMMMYYYY (xx)/<br>DDMMMYYYY (xx) | XXXXXXXXXX/<br>XXXXXXX | X | XX | XXXXXXXXXX/<br>XXXXXXXXXXX | XXXXXXXXX |
| *Etc.* | | | | | | | | |

+ Serious Adverse Event.
# Adverse Event of Special Interest.
* Treatment Emergent Adverse Event.
Note: Trial day is defined relative to the date of randomization.

16.2.7: Display of Adverse Events
Listing 16.2.7.2: Serious Adverse Events – SAF Analysis Set

| Treatment Group | Subject Identifier | System Organ Class/ Preferred Term/ Verbatim Text | Start Date/ End Date (Trial Day) | Seriousness Criteria | Relationship/Action Taken with Trial Trt |
|---|---|---|---|---|---|
| Treatment A | XXXXXXX | XXXXXXXXXXXXXXX/ XXXXXXXXXXXXXXX/ XXXXXXXXXXXXXXX # | DDMMMYYYY (xx)/ DDMMMYYYY (xx) | Requires/prolongs hospitalization | XXXXXXXXXXXXXXXXX/ XXXXXXXXXXX |
| | . . . | | | | |
| *Etc.* | | | | | |

# Adverse Event of Special Interest.
$ Non-Treatment Emergent Adverse Event.
Note: Trial day is defined relative to the date of randomization.

16.2.7: Display of Adverse Events
Listing 16.2.7.3: Listing of Deaths – SAF Analysis Set

| Treatment Group | Subject Identifier | Informed Consent Date | Randomization Date | First/Last Trial Trt. Date | Death Date (days since last dose) | Primary Reason for Death |
|---|---|---|---|---|---|---|
| Treatment A | XXXXXXX | DDMMMYYYY | DDMMMYYYY | DDMMMYYYY/ DDMMMYYYY | DDMMMYYYY (XXX) | XXXXXXXXXXXXXXXXXXXXXXXX |
| | . . . | | | | | |
| *Etc.* | | | | | | |

16.2.8: Clinical Laboratory Evaluations
Listing 16.2.8.1: Hematology Parameters – SAF Analysis Set

| Treatment Group | Subject Identifier | Visit | Date of Sample (Trial Day) | Comment | Parameter (Unit) | Normal Range | Result | NCI-CTC grade (a) |
|---|---|---|---|---|---|---|---|---|
| Treatment A | XXXXXXX | XXXXXXXX | DDMMMYYYY (xx) | XXXXXXXXXX | XXXXXXXXXX | XX - XX | XXX* | x/x |
| | | | | | XXXXXXXXXX | XX - XX | XXX L | x |
| | | | | | XXXXXXXXXX | XX - XX | XXX H | |
| | . . . | | | | | | | |
| *Etc.* | | | | | | | | |

(a) NCI-CTCAE version 4.03 for gradeable parameters. For parameters with both low and high grades, the grades are presented as Low/High.
L = value below normal range, H = value above normal range.
* Baseline value.
Note: Baseline is defined as the last non-missing assessment value prior to first dose of trial treatment.
Trial day is defined relative to the date of randomization.

**Programming Note: Repeat listing 16.2.8.1 for:**
Listing 16.2.8.2: Clinical Chemistry Parameters – SAF Analysis Set

16.2.9: Other Safety Evaluations
Listing 16.2.9.1: Vital Signs – SAF Analysis Set

| Treatment Group | Subject Identifier | Visit | Assessment Date ~~(Trial Day)~~ | Blood Pressure (mmHg) | | Pulse Rate (beats/min) | Temperature (°C) (Location) | Height (cm) | Weight (kg) |
|---|---|---|---|---|---|---|---|---|---|
| | | | | Systolic | Diastolic | | | | |
| Treatment A | XXXXXXX | XXXXXXXX | DDMMMYYYY ~~(xx)~~ | XXX | XXX | XXX | XX (XXXXXX) | XX | XX |
| | | XXXXXXXX | DDMMMYYYY ~~(xx)~~ | XXX | XXX | XXX | XX (XXXXXX) | | |
| | . . . | | | | | | | | |
| *Etc.* | | | | | | | | | |

~~Note: Trial day is defined relative to the date of randomization.~~

16.2.9: Other Safety Evaluations
Listing 16.2.9.2: Electrocardiogram Data – SAF Analysis Set

| Treatment Group | Subject Identifier | Visit | Assessment Date ~~(Trial Day)~~ | Result | Clinically Significant? (a) |
|---|---|---|---|---|---|
| Treatment A | XXXXXXX | XXXXXXXX | DDMMMYYYY ~~(xx)~~ | Normal | |
| | | XXXXXXXX | DDMMMYYYY ~~(xx)~~ | Abnormal | No |
| | | XXXXXXXX | DDMMMYYYY ~~(xx)~~ | XXXXXXXXXX | xxxxxx |
| | . . . | | | | |
| *Etc.* | | | | | |

(a) If result is 'Abnormal'.
~~* Baseline value.~~
~~Note: Baseline is defined as the last non-missing assessment value prior to first dose of trial treatment.~~
~~Trial day is defined relative to the date of randomization.~~