Statistical Analysis Plan

IPP-201101/005

A 52-Week, Randomized, Double-Blind, Parallel-Group, Placebo-Controlled Study to Evaluate the Efficacy and Safety of a 200-mcg Dose of IPP-201101 Plus Standard of Care in Patients With Systemic Lupus Erythematosus

Prepared for:

ImmuPharma

Prepared by:

ORION Clinical

7 Bath Road, Slough

Berkshire SL1 3UA UK

Tel: +44 (0) 1753 578080

Fax: +44 (0) 1753 578081

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Version	**Author**
Final Version 3	Fahmeeda Sheikh, John Sullivan

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Author: Fahmeeda Sheikh, John Sullivan

Version: Final Version 3

The undersigned have reviewed and revised this SAP and find it to be consistent with the study requirements:

Robert Zimmer, CEO, ImmuPharma — Date: 28 MARCH 2018

Fahmeeda Sheikh, Statistician, Orion Clinical Services Ltd. — Date: 28 MARCH 2018

John Sullivan, Head of Statistics, Simbec-Orion Group Ltd. — Date: 28MAR2018

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GLOSSARY OF ABBREVIATIONS

%CV	Coefficient of Variation
ACR	American College of Rheumatology
AE	Adverse Event
ALT	Alanine Transaminase
AM	Arithmetic Mean
ANA	Antinuclear antibody
ANC	Absolute Neutrophil Count
ANCOVA	Analysis of Covariance
ANOVA	Analysis of Variance
Anti-dsDNA Ab	Anti-double-stranded Deoxyribonucleic Acid Antibody
Anti-Sm Ab	Anti-Smith antibody
Anti-U1-70K snRNP Ab	Anti-uridine rich 70 kilodalton small nuclear ribonucleoprotein particle Ab
AST	Aspartate Transaminase
ATC	Anatomical Therapeutic Chemical
BILAG A	British Isles Lupus Assessment Group A
BILAG B	British Isles Lupus Assessment Group B
BLQ	Below the Limit of Quantification
BMI	Body Mass Index
BUN	Blood Urea Nitrogen
CDISC	Clinical Data Interchange Standards Consortium
CI	Confidence Interval
CRA	Clinical Research Associate
CRF	Case Report Form
CRP	C-reactive protein
CRO	Clinical Research Organisation
CS	Clinically Significant
CSR	Clinical Study Report
C-SSRS	Columbia-Suicide Severity Rating Scale
CTC	Common Toxicity Criteria
DBL	Database Lock
DMP	Data Management Plan

DOB	Date of Birth
DRM	Data Review Meeting
DSMB	Data Safety Monitoring Board
ECG	Electrocardiogram
eCRF	Electronic Case Report Form
FACIT	Functional Assessment of Chronic Illness Therapy
FAS	Full Analysis Set
GM	Geometric Mean
GGT	Gamma-Glutamyl-Transpeptidase
ICH	International Conference on Harmonisation
IDMC	Independent Data Monitoring Committee
IgA	Immunoglobulin A
IgE	Immunoglobulin E
IgG	Immunoglobulin G
IgM	Immunoglobulin M
IMP	Investigational Medicinal Product
IRT	Interactive Response Technology
IV	Intravenous
LDH	Lactate Dehydrogenase
LLQ	Lower limit of quantification
LOCF	Last Observation Carried Forward
LS Mean	Least Squares Mean
MedDRA	Medical Dictionary for Regulatory Activities
mg	Milligram
ml	Millilitre
N	Number of Patients
n	Number of Events
NCS	Not Clinically Significant
PhGA	Physician's Global Assessment
PK	Pharmacokinetics
PT	Preferred Term
QC	Quality Control
QoL	Quality of Life

RBC	Red Blood Cell
SAP	Statistical Analysis Plan
SAS	Statistical Analysis System
SC	Subcutaneous
SD	Standard Deviation
SDI	SLICC/ACR Damage Index
SDTM	Study Data Tabulation Model
SE	Standard Error
SELENA	Safety of Estrogens in Lupus Erythematosus: National Assessment
SF-36	Medical Outcome Survey Short Form 36
SFI	SELENA Flare Index
SLE	Systemic Lupus Erythematosus
SLEDAI-2K	Systemic Lupus Erythematosus Disease Activity Index 2000
SLICC	Systemic Lupus International Collaborative Clinics
SOC	System Organ Class
SRI	SLE Responder Index
TEAE	Treatment Emergent Adverse Event
WBC	White Blood Cell
WHO	World Health Organisation
WHODD	World Health Organisation Drug Dictionary
µg	Microgram

1 INTRODUCTION

1.1 GENERAL

This statistical analysis plan (SAP) describes the statistical methods to be used during the reporting and analyses of data collected under ImmuPharma Protocol IPP-201101/005 and should be read in conjunction with the study protocol and electronic case report form (eCRF).

This version of the plan has been developed using the protocol Version 2.5 dated 27JUL2016 for Germany and 01JUN2016 for all other countries and blank CRF Version 3.1 dated 06FEB2017. Any further changes to the protocol or eCRF will be reviewed for potential impact on the SAP which will be amended if it is deemed necessary.

At the time of writing this version of the SAP, the study is ongoing.

1.2 CHANGES FROM PROTOCOL

A tipping point sensitivity analysis has been added.

A hierarchical testing procedure for the most important secondary endpoints will be used.

Adverse events of special interest have been identified and will be investigated.

2 STUDY OBJECTIVES

The primary objective of this study is to evaluate the efficacy of a 200 mcg dose of IPP-201101 every 4 weeks for 48 weeks compared with placebo in patients with active Systemic Lupus Erythematosus (SLE) as assessed by the SLE Responder Index (SRI) at Week 52. An SRI response is defined as:

- a reduction from baseline in the Systemic Lupus Erythematosus Disease Activity Index 2000 (SLEDAI-2K) score of at least 4 points;
- no worsening in Physician's Global Assessment (PhGA) (with worsening defined as an increase in PhGA of more than 0.30 point from baseline);
- no new British Isles Lupus Assessment Group A (BILAG A) body system score and;
- no more than 1 new BILAG B body system score from baseline

3 STUDY DESIGN

3.1 OVERVIEW

This is a Phase III, randomised, double-blind, parallel-group, placebo-controlled study which was conducted in 28 centres globally, over a period of 52 weeks. The study will enrol approximately 200 men and women aged between 18 and 70, who have serologically active SLE with moderate disease

activity on the basis of a standard assessment of disease activity, validated for use as a measure in clinical studies.

The purpose of the study is to evaluate the efficacy and safety of a 200 mcg dose of IPP-201101 plus standard of care compared with placebo plus standard of care. The study will evaluate the clinical response to treatment with IPP-201101 and will also include assessment of biomarkers and change in steroid use from baseline. Safety assessments will include monitoring of adverse events, clinical laboratory test results, vital signs measurements, 12-lead electrocardiogram (ECG) findings, suicidality assessments, anaphylaxis evaluations and concomitant medication use.

Treatment assignment will be stratified by region (Europe or United States [US]), SLEDAI-2K screening total score (6 to 9, ≥ 10) and racial-ethnic classification (black/Hispanic or others). Within each stratum, eligible patients will be randomly assigned with a 1:1 ratio to receive either 200 mcg of IPP-201101 or placebo.

3.2 Inclusion and Exclusion Criteria

To be eligible for inclusion into this study, each patient must fulfil all inclusion criteria and not violate any exclusion criteria (for the protocol under which they are entered) during screening prior to randomisation. Details of the inclusion and exclusion criteria are presented in the protocol and amendments.

3.3 Study Treatment

Patients randomly assigned to IPP-201101 will be administered a dosage of 200 mcg subcutaneously (SC) every 4 weeks for 48 weeks, and those patients randomly assigned to placebo will be administered placebo SC every 4 weeks for 48 weeks. All patients will be administered a total of 13 doses.

3.4 Study Timepoints

The study consists of a screening period of up to 4 weeks, and a 48 week treatment period. Patients will return to the study centre 4 weeks after administration of the last dose of study drug and a final assessment will take place. Patients are expected to participate in the study for up to 54 weeks.

Visits will be as follows:

Visit		Week
1	Screening	Days -28 to -1
2	Baseline, Randomisation and Date of First Dose	0
3	Blood sample for immunogenicity testing	2
4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15	Treatment period	4, 8, 12, 16, 20, 24, 28, 32, 36, 40, 44, 48
16	Final assessment (or early termination)[a]	52

[a]If a patient is withdrawn from the study before completion of 48 weeks of treatment (13 doses of study drug), final procedures and assessments will be performed at early termination visit.

If more than one visit occurs within a window, the nearest to the scheduled time will be presented within the summaries.

See Section 16.1 for the Study Schedule of procedures and assessments.

3.5 Sample Size Considerations

The study is designed to estimate and assess the significance of the difference between a 200 mcg dose of IPP-201101 and placebo in the proportion of SRI responders at Week 52. It is anticipated that approximately 270 patients will be screened for participation in the study, and 200 of these patients will be enrolled in the study in order to provide 100 evaluable patients per treatment group.

The study will have a 90% or greater power to detect a 25% or greater difference in the proportion of SRI responders between the IPP-201101 group and the placebo group, or to detect a 20% difference with an 80% power. This projection uses the 2-sided Pearson Chi-square test with alpha=0.05, and is based on an anticipated placebo effect at Week 52 of 40% to 45%.

3.6 Randomisation

Randomisation will be stratified for the following 3 baseline characteristics:

- Region (Europe, US)
- SLEDAI-2K screening total score (6 to 9, ≥ 10)
- Racial-ethnic group classification (black/Hispanic, others)

Within each of the stratum, eligible patients will be randomly assigned with a 1:1 ratio to receive either 200 mcg of IPP-201101 or placebo SC every 4 weeks for 48 weeks.

The randomisation will be programmed by the unblinded statistician at Orion, who will send through randomisation and kit lists to Oracle to be loaded into the Interactive Response Technology (IRT).

Upon receiving information for a new patient, the IRT will assign the new patient to the next available randomisation code with the randomisation stratum for the appropriate region, SLEDAI-2K screening score and racial-ethnic group classification.

A more detailed description of the randomisation process can be found in the Randomisation Plan.

4 STUDY VARIABLES AND COVARIATES

4.1 Primary Efficacy Variable

The primary variable for statistical comparison between treatment groups will be the proportion of patients achieving a combined clinical response using the SRI at Week 52. An SRI is defined as:

- a reduction from baseline in the SLEDAI-2K score of at least 4 points;
- no worsening in PGA (with worsening defined as an increase in PhGA of more than 0.30 point from baseline);
- no new BILAG A body system score and;

- no more than 1 new BILAG B body system score from baseline.

The combined clinical response is intended to demonstrate an improvement in overall disease activity without worsening of disease in any organ system as determined by the investigator's quantitative and qualitative assessments.

4.2 SECONDARY EFFICACY VARIABLES

The following secondary efficacy variables and endpoints will be analysed:

Most important secondary efficacy variables:

- Proportion of patients achieving a clinical SLEDAI-2K total score of 0 at Week 52 (remission)
- Proportion of patients who had an assessment of "no" for arthritis symptoms using SLEDAI-2K at Week 52 and had an assessment of "yes" at randomisation
- Proportion of patients who achieved a BILAG C score at week 52 who had a BILAG A or BILAG B score in the BILAG body system score at randomisation
- Absolute change in fatigue using the Functional Assessment of Chronic Illness Therapy-Fatigue (FACIT-Fatigue) at Week 52
- Proportion of patients who achieved a combined clinical response using SRI (see Section 4.1 Primary Efficacy Variable for definition) at Week 52 in the subgroup with screening SLEDAI-2K ≥ 10

Other secondary efficacy variables:

- SLEDAI-2K total score at each visit
- The SRI response at each visit during the study
- The reduction in the SLEDAI-2K total score by at least 4 points at each visit during the treatment period
- The effect of IPP-201101 on disease activity, as assessed by the BILAG-2004 disease activity index, at each visit during the treatment period
- The effect of IPP-201101 on the status of disease (PhGA scale) at each visit during the treatment period
- The reduction of the SLEDAI-2K total score by at least 5 points at each visit during the treatment period
- The reduction of the SLEDAI-2K total score by at least 6 points at each visit during the treatment period
- The SRI-5 response at each visit during the treatment period
- The SRI-6 response at each visit during the treatment period
- The SRI-7 response at each visit during the treatment period
- The SRI-8 response at each visit during the treatment period
- The SRI-9 response at each visit during the treatment period

- The effect of IPP-201101 on arthritis, as assessed by the 28-joint count examination for pain and tenderness at each visit during the treatment period
- The effect of IPP-201101 on health-related quality of life, as assessed by completion of the Medical Outcome Survey Short Form 36 (SF-36) at visits at Weeks 12, 24, 36 and 52 (or final assessment) and change from baseline analysed at Week 52
- The reduction in the SLEDAI-2K total score by at least 4 points from baseline to Week 52
- The effect of IPP-201101 on disease activity, as assessed by the BILAG-2004 disease activity index, from baseline to Week 52
- The effect of IPP-201101 on the status of disease (PhGA scale) from baseline to Week 52
- The effect of IPP-201101 on the incidence of disease flares (i.e. Safety of Estrogens in Lupus Erythematosus: National Assessment [SELENA] Flare Index [SFI] and SLEDAI-2K score of greater than 15) at each visit during the treatment period
- The effect of IPP-201101 on the occurrence of SLE-induced organ damage (e.g. Systemic Lupus International Collaborative Clinics/American College of Rheumatology [SLICC/ACR] Damage Index [SDI] and adverse event inquiry) at visits at Weeks 24 and 52 (or final assessment)
- The effect of IPP-201101 on steroid dose over time throughout the study

4.3 Exploratory Efficacy Variables

The following exploratory efficacy variables and endpoints will be analysed:

- The effect of IPP-201101 on the biologic markers of disease activity, anti-double-stranded deoxyribonucleic acid antibody (anti-dsDNA Ab) complement components (C3 and C4), at each visit during the treatment period
- The effect of IPP-201101 on the following biologic markers of disease activity at Weeks 4, 12, 24, 36 and 52 (or final assessment):
    - Antinuclear antibody (ANA)
    - Anti-uridine rich 70 kilodalton small nuclear ribonucleoprotein particle Ab (Anti-U1-70K snRNP Ab)
    - Anti-Smith antibody (Anti-Sm Ab)
    - C-reactive protein (CRP)
    - Immunoglobulin G (IgG), Immunoglobulin M (IgM), Immunoglobulin E (IgE) and Immunoglobulin A (IgA)
- In vitro intracellular and cytokine response

4.4 Pharmacokinetic and Immunogenicity Variables

A blood sample for measurement of the concentration of IPP-201101 will be obtained from all patients who have a serious adverse event and/or have an adverse event leading to withdrawal from the study.

The immunogenicity of IPP-201101 will be assessed by any presence of anti-IPP-201101 antibodies (anti-IPP-201101 Ab) at visits at Weeks 2, 4, 12, 20, 28, 36, 44 and 52 (or final assessment).

4.5 SAFETY VARIABLES

The safety and tolerability of IPP-201101 will be evaluated by the following:

- Occurrence of adverse events throughout the study.
- Specified adverse events of special interest will be studied in more detail. These are:
    1. immune-mediated adverse reaction,
    2. hepatitis,
    3. pneumonitis,
    4. facial/face oedema or allergic oedema,
    5. nephritis or pyelonephritis,
    6. autoimmune haemolytic anaemia.
- Clinical laboratory parameters (serum chemistry, haematology and urinalysis) at each visit during the treatment period
- Vital signs (systolic and diastolic blood pressures, pulse, temperature and body weight) measurements at each visit during the treatment period
- 12-lead ECG findings at Week 52 (or final assessment)
- Physical examination findings, including physical examination symptom directed findings, at specified time points at each visit during the treatment period
- Evaluation for suicidality at each visit during the treatment period using the Columbia-Suicide Severity Rating Scale (C-SSRS)
- Anaphylaxis assessment using the Clinical Criteria for Diagnosing Anaphylaxis
- Concomitant medication usage throughout the study

5 DEFINITIONS

Study Drug. Study drug is taken to mean either IPP-201101 or placebo.

Baseline. Baseline is defined by patient and by variable as the last non-missing value before the first dose of study drug. This will be the pre-dose assessment at Visit 2/Week 0.

Study Day. Study day is the number of days since start of treatment where the date of first dose is counted as Day 1.

Protocol Deviation: a deviation related to study inclusion or exclusion criteria, conduct of the trial, patient management or patient assessment. This refers to any change, divergence, or departure from the study design or procedures defined in the protocol. Deviations recorded by the Project Manager, CRA, Data Management or by Statistical programming checks will be identified and discussed at the Data Review Meeting (DRM) before database lock (DBL) to agree which should be included in the protocol deviation listing.

6 ANALYSIS SETS

Membership of the analysis sets will be reviewed and agreed at a DRM before DBL.

6.1 RANDOMISED SET

The Randomised Set is defined as all patients who were randomised to a treatment at enrolment, regardless of whether or not they took any study drug.

The Randomised Set will be used for all study population summaries.

6.2 SAFETY SET

The Safety Set is defined as all patients who receive at least one dose of investigational drug.

The Safety Set will be used for all safety analyses. Patients who receive the wrong treatment in error will be analysed as treated for safety analyses.

6.3 FULL ANALYSIS SET

The Full Analysis Set (FAS) will include all patients in the safety set.

The FAS will be used for all efficacy analyses. Patients who receive the wrong treatment in error will be analysed as randomised for efficacy analyses.

7 SAFETY MONITORING

No formal safety monitoring reports will be provided by Orion statistics department.

8 INTERIM ANALYSES

No interim analysis is planned.

9 DATA

9.1 ECRF DATA

eCRF data will be provided by Orion data management to the statistics department as SAS data sets in Orion standard format which will be used for programming the outputs. Populated data sets will be available when programming starts. These may contain dummy data if real data is not yet available.

No laboratory results will be entered on the eCRF.

9.2 External Data

9.2.1 Laboratory Data

Transfers of central laboratory data will be received in an agreed format and uploaded to a SAS dataset by Orion data management. Populated test transfers (using dummy data if necessary) will be received before programming can start.

Laboratory samples and additional assays will be analysed centrally by the following laboratories:

- Seirian Laboratories (Simbec), UK
- Eurofins Central Laboratory, US

Reference ranges will be recorded alongside each parameter as part of the transfer file.

9.2.2 Other non-CRF data

Any PK concentration data will be received from Seirian Laboratories in an Excel spreadsheet in an agreed format. If any PK data is collected then the concentration spreadsheet will be uploaded to a SAS dataset for programming

BILAG, SLEDAI-2K, flare index and PhGA data will be received from ADS-Limathon, UK in an agreed format, and will be uploaded to a SAS dataset for programming.

9.3 Randomisation List

The randomisation list will be uploaded to a SAS dataset following DBL.

9.4 Programming and Data Review

Programming of analysis datasets, tables, figures and listings will be ongoing during the data management of the study. Blind outputs may be reviewed by ImmuPharma before DBL.

When the final data is considered clean, key listings (to be agreed) will be run and distributed to the study team for review. A blind DRM will be held to discuss the outcome of this review and the protocol deviations. Once all data issues have been resolved and the analysis populations approved, the database will be locked. The randomisation codes will be opened and the final run of outputs and final quality control (QC) will then take place.

10 STATISTICAL METHODS

10.1 General Principles

All statistical methods will be based on the International Conference on Harmonisation (ICH) E9 document "Statistical Principles for Clinical Trials".

Data will be summarised by treatment group. A total column showing all patients will be included for baseline and safety summaries. Where appropriate, data will also be summarised by visit with summaries for each visit attended as scheduled and an additional summary for final (last scheduled visit or early withdrawal). The format of the summaries is defined in the shells at the end of this document.

In summary and analysis tables of continuous variables, standard descriptive statistics (N, mean, standard deviation [SD], median, minimum and maximum) will be presented. Least Squares mean (LS mean), standard error (SE) and 95% confidence Interval (CI) will be presented in the statistical analysis outputs as appropriate. The minimum and maximum statistics will be presented in summary tables to the same number of significant figures as the original data. The mean/AM, median, LS mean, CI, SD and SE will be presented to one more decimal place than the original data.

For numeric data which includes non-numeric values (e.g. PK data reported as BLQ or lab results reported as < 10 or >100) the following principles will be applied when summarising the data:

- BLQ will be replaced with a value that is ½ of the lower limit of quantification (LLQ)
- Results reported as < x will be treated in the same way as BLQ with LLQ=x
- Otherwise AM, SD, CI and %CV will not be calculated
- Whenever meaningful, minimum, median and maximum will be presented based on the reported data (e.g. minimum = <10, median = 20, maximum = >100)

In summary tables of categorical variables, the number of non-missing observations by category will be presented with percentages. Categories for missing data will be presented if necessary. Unless otherwise specified, the denominator for each percentage will be the number of non-missing observations within the column. All percentages will be presented to one decimal place.

If changes in severity for the same TEAE have been reported separately but with the same AE number, they will be collapsed to a single AE with maximum severity for the summary tables, but listed as reported. In AE summary tables, a patient will be counted only once in each preferred term or system organ class category, but all results will be listed.

Classifications of medical history, concomitant medication and adverse events will be sorted alphabetically within the summary tables.

If any laboratory assessments are repeated at the same visit, the result from the repeat assessment will be used in summaries. Both values will be listed.

Data collected on the eCRF will be presented within data listings. The data listings will be sorted by treatment group, patient number and visit/week/day. Treatment group will be as allocated (randomised). If any patients receive the wrong treatment this will be flagged in all listings. Visits outside the visit windows will be identified within the listings.

The date format for all output presentations will be 'ddMMMyyyy'.

All statistical analysis will be performed using SAS 9.3 or higher.

All hypothesis testing will be carried out at the 5% (2-sided) significance level unless stated otherwise.

P-values will be rounded to four decimal places. P-values less than 0.0001 will be reported as <0.0001 in tables.

If any of the assumptions underlying the formal statistical methods proposed are violated during the analysis of the final data, alternative statistical methods will be used and any changes documented in the statistical methods section of the clinical study report (CSR), including the rationale for use.

10.2 Stratification Adjustment

Randomisation was stratified by region, SLEDAI-2K screening total score and racial-ethnic classification. The primary endpoint analysis will be adjusted for these stratification factors.

10.3 Missing Data

10.3.1 Individual Questionnaire items

For the purpose of efficacy analysis, missing or invalid values will be imputed using data from the previous visit for individual items and scores in the questionnaires and scales. For a derived score involving multiple items, the missing or invalid individual items will be imputed first before calculating the derived scores based on the complete individual item values.

These rules only apply for visits in which the patient is currently in the study and some data or an individual item is missing. If an assessment is not done at a visit, the missing data will not be imputed.

10.3.2 Sensitivity Analyses

Sensitivity analyses will be performed to investigate the possible impact of violations of assumptions about missing data on the reliability of the efficacy results. A tipping point analysis, where dropouts on IPP-201101 are assigned worse outcomes than those on placebo, will be performed. Additionally the last observation carried forward (LOCF) method will be used. For the continuous secondary endpoint FACIT-Fatigue multiple imputation will be used. See Section 11.3 Efficacy Analyses for more details.

10.4 Pooling of Sites

Sites will be pooled for all analyses. There will be no adjustment for centre effect or treatment by centre interaction.

10.5 Statistical Issues

There are no statistical issues.

11 STATISTICAL OUTPUT

General principles for layout of the statistical output are described in Section 10.1, including specification of the table columns, and these are illustrated for each unique table in the table shells in Section 15. For clarity and brevity in this document the phrase "by treatment group" is understood for all summaries and is not included within the text of this section.

11.1 Patient Disposition

The patient disposition table will summarise the following data for all patients (*Table 14.1.1*):

- number of screened patients
- number of patients randomised
- number of patients who failed screening
- number of patients randomised but not treated
- The number (%) of patients in the FAS
- The number (%) of patients in the Safety Set

The number (%) of patients who complete the study and patients who withdraw from the study by the main reason for withdrawal will be summarised for the set of randomised patients *(Table 14.1.2)*.

A listing of all patients with protocol deviations will be presented. A data listing presenting the eligibility for the analysis sets for each patient will also be presented.

11.2 PATIENT CHARACTERISTICS AT BASELINE

The main analysis set for the baseline summaries will be the set of randomised patients.

11.2.1 Demographic and Baseline Characteristics

Age will be calculated using Date of Birth (DOB) and Date of Informed Consent and presented as age at last birthday as an integer. Height is recorded as part of the physical examination at screening visit only.

Age, gender, ethnicity, race, height, weight and BMI will be summarised by stratification factor and overall (*Table 14.1.3)*.

11.2.2 Medical History and Current Medical Conditions

All conditions will be coded using the version of the Medical Dictionary for Regulatory Activities (MedDRA) defined in the Data Handling Manual. Past medical/surgical history and current medical conditions will be summarised by system organ class (SOC) and preferred term (PT). The number (%) of patients reporting each condition will be presented by stratification factor and overall *(Table 14.1.4.1 and 14.1.4.2)*.

11.2.3 Prior Medications

All medications taken by patients on entry to the study or during the study will be recorded in the CRF. Medications will be classified using the version of the World Health Organisation Drug Dictionary (WHODD) coding dictionary defined in the Data Management Plan (DMP). The Anatomical Therapeutic Chemical (ATC) Classification and WHODD PT will be used to list and summarise the data.

Prior medications are defined as medication that started and stopped before Visit 2 (week 0). Only medications where the stop date is prior to Visit 2 will be considered prior. If the stop date is unknown or incomplete and the medications cannot definitely be considered as stopped prior to Visit 2 then the medications will be considered as concomitant medications.

The number (%) of patients reporting the use of any prior medications by ATC classification and PT will be summarised by stratification factor and overall *(Table 14.1.5)*.

11.2.4 SLE Disease History

Date of diagnosis of SLE is recorded on the eCRF along with information about the patient's last SLE flare and SLE-related hospitalisation. This information will be presented as time since diagnosis of SLE (years), time since last SLE flare (years) and time since SLE-related hospitalisation (years), and will be summarised using descriptive statistics by stratification factor and overall *(Table 14.1.6)*. Time since diagnosis of SLE/ last SLE flare/ SLE-related hospitalisation is calculated as the difference between date of informed consent and date of diagnosis of SLE/ date of last SLE flare/ date of SLE-related hospitalisation.

11.2.5 Other Baseline Characteristics

Physical examination and 12-lead ECG will be performed at screening (Visit 1) and results will be summarised using descriptive statistics by stratification factor and overall *(Table 14.1.7)*.

11.3 Efficacy Analyses

Treatment comparisons will be IPP-201101 vs placebo. The main analysis set for the efficacy analyses will be the FAS.

11.3.1 Primary Efficacy Variable

11.3.1.1 Primary Analysis of the Primary Variable

The primary efficacy variable is the proportion of patients who achieve a combined clinical response using SRI assessed at Week 52. An SRI response is defined as:

- A reduction from baseline in the SLEDAI-2K score of at least 4 points;
- no worsening in PhGA (with worsening defined as an increase in PhGA of more than 0.30 point from baseline);
- no new BILAG A body system score;
- and no more than 1 new BILAG B body system score from baseline.

The SRI will be analysed using a logistic regression model with treatment and stratification factors as main factors and SRI is linked to the model factors through the logit function. Patients who withdraw from the study are classified as non-responders as measured by SRI at Week 52. Patients with no post-baseline efficacy assessment are considered non-responders. The likelihood-ratio-based Chi-square statistics will be used to test treatment difference, at the 5% significance level. Odds ratio and associated 95% CI will be determined from the logistic regression model and presented for IPP-201101 vs placebo *(Table 14.2.1.1)*.

11.3.1.2 Sensitivity Analyses of the Primary Variable

The primary analysis will be repeated using 4 different imputation methods to estimate missing SRI at Week 52 according to the reason for withdrawal.

In the first method, patients who withdrew because of lack of efficacy will be classified as treatment failures assessed by SRI at Week 52. For patients who withdraw because of other reasons, their missing SRI at Week 52 will be estimated using the last observation carried forward (LOCF) multiple imputation (*Table 14.2.1.2.1*).

In the second method, all missing SRI values at Week 52 will be imputed using the last observation carried forward (LOCF) method (*Table 14.2.1.2.2*).

In the third method, patients who withdraw and those completers who used prohibited medication within 8 weeks from Week 52 will be classified as non-responders (*Table 14.2.1.2.3*).

In the fourth method, a tipping point analysis, where dropouts on IPP-201101 are assigned worse outcomes than those on placebo, will be performed. IPP-201101 dropouts will be imputed as non-responders and placebo dropouts will be imputed as responders. This tipping point analysis will be identical to the primary analysis described in Section 11.3.1.1, apart from placebo patients with missing assessments at Week 52 will be imputed as responders and IPP-201101 patients with missing assessments at Week 52 will be imputed as non-responders (*Table 14.2.1.2.4*).

11.3.2 Secondary Efficacy Variables

11.3.2.1 Most Important Secondary Endpoints

The most important secondary endpoints (in order of importance) are:

- Proportion of patients achieving a clinical SLEDAI-2K total score of 0 at Week 52 (remission). This will be summarised using descriptive statistics and analysed using logistic regression in the same way as the primary analysis of the primary variable *(Table 14.2.2.1.1)*. Patients who withdraw early from the study are classified as non-responders at Week 52.
- Proportion of patients who had an assessment of "no" for arthritis symptoms using SLEDAI-2K at Week 52 and had an assessment of "yes" at randomisation. This will be summarised using descriptive statistics and analysed using logistic regression in the same way as the primary analysis of the primary variable *(Table 14.2.2.1.2)*. Patients who withdraw early from the study are classified as non-responders at Week 52.
- Proportion of patients who achieved a BILAG C score at Week 52 who had a BILAG A or BILAG B score in the BILAG body system score at randomisation. This will be summarised using descriptive statistics and analysed using logistic regression in the same way as the primary analysis of the primary variable *(Table 14.2.2.1.3)*. Patients who withdraw early from the study are classified as non-responders at Week 52.
- Absolute change in fatigue using the FACIT-Fatigue at Week 52. The change from baseline at Week 52 will be descriptively summarised and analysed using an Analysis of Covariance (ANCOVA) model including fixed effects for treatment and the randomisation stratification factors region (Europe, US), SLEDAI-2K screening total score (6 to 9, ≥ 10) and racial-ethnic classification (black/Hispanic or others), and also the baseline fatigue score using the FACIT-Fatigue as a covariate. The LOCF method will be used to impute missing values. LS mean estimates of the difference between the two treatment groups, together with 95% CIs, SE and the p-value, will be provided. *(Table 14.2.2.1.4.1)*.
- Proportion of patients who achieved a combined clinical response using SRI (see Section 11.3.1.1 Primary Analysis of the Primary Variable for definition) at Week 52 in the subgroup with screening SLEDAI-2K ≥ 10. This will be summarised using descriptive statistics and analysed using logistic regression in the same way as the primary analysis of the primary variable *(Table 14.2.2.1.5)*. Patients who withdraw early from the study are classified as non-responders at Week 52.

To control for multiplicity a hierarchical testing approach will be used for the 5 most important secondary endpoints. The first will be tested at the 5% significance level. If this test is significant the second most important will be tested, then the third, and so on. This will continue until a test result is not statistically significant, at which point the process will stop.

Sensitivity Analyses of the Secondary Endpoint Variable FACIT-Fatigue

A multiple imputation method will be used to account for missing data at Week 52. The imputation values will be drawn from the categories formed by treatment group and randomisation stratum to which the patient belongs. This will be done as follows:

1. The missing values are filled in *m* times to generate *m* complete data sets (using SAS PROC MI). A value of 5 will be used for *m*.

This is done by fitting *m* linear regression models using patients with observed values for the endpoint and further covariates. Based on the fitted regression model, a new regression model is simulated from the Bayesian posterior predictive distribution of the regression parameters and is used to impute the missing values;

2. The *m* complete datasets are analysed by using the relevant statistical procedure (ANCOVA) for this endpoint;
3. The results from the *m* analyses are combined for statistical inference (using SAS PROC MIANALYZE).

Multiple imputation aims to allow for the uncertainty about the missing data by creating several different plausible imputed data sets and appropriately combining results obtained from each of them. The method assumes that missing values are 'missing at random' (MAR), such that any systematic difference between the missing values and the observed values can be explained by differences in observed data (*Table 14.2.2.1.4.2*).

11.3.2.2 Other Secondary Endpoints

The following other secondary endpoints will be descriptively summarised only, unless otherwise specified:

- SLEDAI-2K total score at each visit *(Table 14.2.2.2.1)*.
- Proportion of patients achieving an SRI response at each visit compared to baseline *(Table 14.2.2.2.2)*.
- Proportion of patients achieving a clinical SLEDAI-2K response at each visit compared to baseline, where a clinical response is defined as a reduction of at least 4 points in the SLEDAI-2K clinical score *(Table 14.2.2.2.3)*
- Proportion of patients achieving a BILAG-2004 clinical response at each visit compared to baseline (an improvement in at least 1 category from a B score to a C or D score, with no worsening in any other category) *(Table 14.2.2.2.4)*
- Proportion of patients showing no worsening on a PhGA scale at each visit compared to baseline (*Table 14.2.2.2.5*).
- Proportion of patients achieving a reduction of 5 points in the SLEDAI-2K total score at each visit compared to baseline *(Table 14.2.2.2.6)*
- Proportion of patients achieving a reduction of 6 points in the SLEDAI-2K total score at each visit compared to baseline *(Table 14.2.2.2.7)*
- Proportion of patients achieving an SRI-5 response at each visit compared to baseline *(Table 14.2.2.2.8)*
- Proportion of patients achieving an SRI-6 response at each visit compared to baseline *(Table 14.2.2.2.9)*
- Proportion of patients achieving an SRI-7 response at each visit compared to baseline *(Table 14.2.2.2.10)*
- Proportion of patients achieving an SRI-8 response at each visit compared to baseline *(Table 14.2.2.2.11)*

- Proportion of patients achieving an SRI-9 response at each visit compared to baseline *(Table 14.2.2.2.12)*
- Proportion of patients showing an improvement from baseline in tender and swollen joint counts using the 28-joint count examination for pain and tenderness *(Table 14.2.2.2.13)*. Tender and swollen joints are a significant cause of morbidity in patients with SLE and lupus arthritis will be evaluated using this assessment.
- Descriptive summary statistics for absolute and relative changes from baseline in the SF-36 total score at Weeks 12, 24, 36 and 52 (or final assessment) will be presented *(Table 14.2.2.2.14)*. Assessments of the SF-36 with missing values will be omitted from the summaries.
- Proportion of patients achieving a reduction of at least 4 points in the SLEDAI-2K total score at Week 52 *(Table 14.2.2.2.15)*.
- Proportion of patients achieving a BILAG-2004 response (no new BILAG A body system score and no more than 1 new BILAG B body system score from baseline) at Week 52 *(Table 14.2.2.2.16)*.
- Proportion of patients showing no worsening on a PhGA scale at Week 52 *(Table 14.2.2.2.17)*.
- SFI time to first mild to moderate flare from time of randomisation to each visit (days), incidence of mild to moderate flare, incidence of severe flare and time to severe flare from time of randomisation to each visit (days) *(Table 14.2.2.2.18)*
- Proportion of patients with SLEDAI-2K score of greater than 15 at each visit *(Table 14.2.2.2.19)*
- Changes in the SDI total score from screening to Week 24 and from screening to Week 52 (or final assessment) *(Table 14.2.2.2.20)*. The SDI assesses specific comorbidities associated with SLE and consists of 39 items covering 12 organ systems.
- Steroid dose will be evaluated to determine the proportion of patients taking a dose less than 7.5 mg of prednisone equivalent/day, a dose of 7.5 mg prednisone equivalent/day or more, and none per day at baseline, Week 24 and Week 52 *(Table 14.2.2.2.21.1)*. Proportion of patients with changes in steroid dose from baseline to Weeks 24 and 52 will be presented in a shift table *(Table 14.2.2.2.21.2)*.
- A reduction from baseline in the SLEDAI-2K score of at least 4 points. This will be summarised using descriptive statistics and analysed using logistic regression in the same way as the primary analysis of the primary variable (*Table 14.2.2.2.22*). Patients who withdraw early from the study are classified as non-responders at Week 52.
- No worsening in PhGA (with worsening defined as an increase in PhGA of more than 0.30 point from baseline). This will be summarised using descriptive statistics and analysed using logistic regression in the same way as the primary analysis of the primary variable (*Table 14.2.2.2.23*). Patients who withdraw early from the study are classified as non-responders at Week 52.
- No new BILAG A body system score. This will be summarised using descriptive statistics and analysed using logistic regression in the same way as the primary analysis of the primary variable (*Table 14.2.2.2.24*). Patients who withdraw early from the study are classified as non-responders at Week 52.

- No more than 1 new BILAG B body system score from baseline. This will be summarised using descriptive statistics and analysed using logistic regression in the same way as the primary analysis of the primary variable (*Table 14.2.2.2.25*). Patients who withdraw early from the study are classified as non-responders at Week 52.

11.3.3 Exploratory Efficacy Variables

The following exploratory efficacy variables will be descriptively summarised:

- Changes from baseline in the anti-dsDNA Ab, C3 and C4 biomarkers at each visit during the treatment period *(Table 14.2.3.1)*. Biomarkers in SLE are often used for diagnosis but do not always correlate with changes in disease activity, so these will be evaluated to determine if a change in level correlates with a change in disease activity.
- Changes in the biomarkers ANA, anti-U1-70K snRNP Ab, anti-Sm Ab, CRP, IgG, IgM, IgA and IgE from baseline to Weeks 4, 12, 24, 36 and 52 (or final assessment) *(Table 14.2.3.2)*. As above, these will be evaluated to determine if a change in level correlates with a change in disease activity.
- Blood samples (5 mL) for in vitro intracellular and cytokine response will be collected from patients at selected study centres via venipuncture or indwelling catheter prior to study drug administration at weeks 0, 4, 24, and 48. In vitro intracellular and cytokine response data will be summarised by time point *(Table 14.2.3.3)*.
- The cumulative distribution of the decrease in the first item of the SRI responder definition (a reduction from baseline in the SLEDAI-2K score of at least 1, 2, 3 etc. points) showing the probability of attaining each decrease, or worse will be summarised (*Table 14.2.3.4*) and plotted by treatment on the FAS (*Figure 1*) at Week 52.

11.4 Pharmacokinetic and Immunogenicity Analyses

A blood sample for measurement of the concentration of IPP-201101 will be obtained from all patients who have a serious adverse event and/or have an adverse event leading to withdrawal from the study.

Any PK samples collected when a patient is withdrawn due to a SAE related to study treatment will be listed.

Anti-IPP-201101 Ab testing will be performed at Weeks 0, 2, 4, 12, 20, 28, 36, 44 and 52 (or final assessment) prior to study drug administration. The immunogenicity of IPP-201101 will be evaluated by determining the presence of any anti-IPP-201101 at Weeks 2, 4, 12, 20, 28, 36, 44 and 52 (or final assessment). Results will be summarised by treatment and visit using the FAS *(Table 14.2.4)* and all results will be listed.

11.5 Safety Analyses

The main analysis set for the safety analyses will be the safety set.

11.5.1 Adverse Events

All adverse events (AE) will be classified using the version of the MedDRA coding dictionary specified in the DMP.

Events will be classified as treatment-emergent if they started or increased in severity on or after the first date and time of medication dosing at Visit 2 and up to study closure or withdrawal date. If an

event start date is partial, then the start day, month, year or stop date will be used to determine if the event is treatment-emergent. If the classification of the AE cannot be determined from the data available, then the event will be considered treatment-emergent.

Treatment-emergent adverse events (TEAEs) will be further classified as follows:

Severe TEAEs: Severity classified as 'severe' (Common Toxicity Criteria [CTC] grade 3 or 4) or missing.

Serious TEAEs: Serious classified as 'yes' or missing.

Drug-related TEAEs: Relationship to study drug classified as 'related' or missing.

Serious drug-related TEAEs: Both serious and drug-related, as specified above.

TEAEs leading to withdrawal from study: Action taken classified as 'discontinued'.

TEAEs overall and in each of the above classifications will be summarised by treatment group and overall. *(Table 14.3.1.1)*. All TEAEs and drug-related TEAEs will also be summarised by severity within the same table.

Summaries by SOC and PT will also be presented for treatment-emergent events *(Table 14.3.1.2)*. Similar tables will be presented for each of the classifications of treatment-emergent events above *(Tables 14.3.1.3 to 14.3.1.7)*.

All AE summary tables will show the number (%) of patients having at least one event and the number of events in each treatment group and overall. Note: If a patient has multiple AEs with the same PT, these will be summarised once within the count for N (%) of patients, but each event will be counted within the number of reports n of each AE. Changes in severity of the same AE (if collected) will be counted only once within the number of reports n of each AE.

The following will be presented in listing format within the data summaries:

- Deaths *(Table 14.3.1.8.1)*
- Serious Adverse Events *(Table 14.3.1.8.2)*
- Adverse Events which Led to Withdrawal *(Table 14.3.1.8.3)*

All adverse events (including non-treatment-emergent events) recorded on the CRF will be listed within the data listings.

11.5.2 Adverse Events of Special interest

The adverse events of special interest are:

- immune-mediated adverse reaction,
- hepatitis,
- pneumonitis,
- facial/face oedema or allergic oedema,
- nephritis or pyelonephritis,
- autoimmune haemolytic anaemia.

A summary by SOC and PT will be presented for these adverse events of special interest (*Table 14.3.1.9*).

11.5.3 Laboratory Data

Clinical laboratory tests (serum chemistry, haematology and urinalysis) will be carried out at screening (Visit 1), baseline/start of study drug treatment (Visit 2), throughout the treatment period, and at the final assessment.

The laboratory tests will be performed using the central laboratory identified at the front of the protocol (and in the Laboratory Procedures Manual provided in the study file documents). Specific laboratory tests to be performed are listed below:

- **Serum chemistry:** calcium, phosphate, sodium, potassium, chloride, bicarbonate or carbon dioxide, glucose, blood urea nitrogen (BUN), creatinine, cholesterol, uric acid, alanine transaminase (ALT), aspartate transaminase (AST), lactate dehydrogenase (LDH), gamma-glutamyl transpeptidase (GGT), alkaline phosphatase, creatinine phosphokinase, total protein, albumin, total bilirubin and direct bilirubin
- **Haematology:** haemaglobin, haematocrit, platelet count, absolute neutrophil count (ANC), white blood cell (WBC) count and differential count (polymorphonuclear leukocytes [neutrophils], lymphocytes, eosinophils, monocytes, basophils, metamyelocytes)
- **Urinalysis:** protein, glucose, ketones, blood (haemoglobin), pH, specific gravity, spot protein-creatinine ratio, creatinine clearance, eGFR and microscopic (bacteria, red blood cells [RBCs], WBCs, casts, crystals)

The absolute values of each parameter and changes from baseline will be descriptively summarised at each visit by treatment and overall *(Tables 14.3.2.1 to 14.3.2.3)*.

If laboratory results are repeated at the same visit, the repeated result will be used in summaries (instead of the original one) provided the sample was taken within the visit window, otherwise the original result will be used. All values will be compared to pre-specified boundaries in order to identify clinically significant changes or values and will be highlighted in listings.

Laboratory results at unscheduled visits will be included in the listings but will not be summarised.

Serum pregnancy data will be listed only.

A Coombs' test will be obtained at screening. At subsequent visits, if hemolysis is suspected or confirmed, Coombs' test, haptoglobin, and a peripheral smear will be obtained. Results of these tests will be listed only.

11.5.4 Vital Signs

Systolic blood pressure, diastolic blood pressure, pulse and body temperature are collected at all visits.

Weight is measured at all visits as part of the physical examination (complete and symptom directed) and will be descriptively summarised as part of vital signs.

The absolute values of the vital signs and changes from baseline will be descriptively summarised at each visit *(Tables 14.3.3)*.

11.5.5 Electrocardiogram

A 12-lead ECG will be completed at Screening and at Week 52.

The number and percentage of patients with Normal / Abnormal NCS / Abnormal CS ECG results at these visits will be summarised in a shift table *(Table 14.3.4)*.

11.5.6 Physical Examination

A complete physical examination will be conducted at screening (Visit 1) and at the final assessment (or early termination). Symptom directed physical examination evaluations and the 28-joint count examination for pain and tenderness will be performed throughout the treatment period (Week 0 through 52).

All physical examination data will be listed and newly occurring physical examination abnormalities will be identified within the listings.

11.5.7 Suicidality Assessment C-SSRS

Suicidality will be assessed using the C-SSRS at baseline and at each visit during the treatment period. The C-SSRS assesses suicidality from ideation to behaviours and monitors the potential emergence of suicidality in clinical studies.

The C-SSRS Baseline version will be performed at baseline (Week 0) and the C-SSRS since Last Visit version will be performed at Weeks 4 to 52 (or final assessment). Cumulative positive C-SSRS outcomes during the study will be descriptively summarised *(Table 14.3.5)*.

11.5.8 Anaphylaxis Evaluation

Anaphylaxis is defined as a serious allergic reaction that is rapid in onset and may cause death. Any patient who experiences an adverse event that presents with signs and/or symptoms that are suggestive of an anaphylactic, anaphylactoid, or drug hypersensitivity reaction will be evaluated using the Clinical Criteria for Diagnosing Anaphylaxis at the DRM before database lock to agree which should be flagged within the adverse event data listing.

11.5.9 Concomitant Medication

Concomitant medications are defined as medications that started before Visit 2 (week 0) and either stopped on the day of Visit 2 or continued into the study. They will also include all medications taken while the patient is treated with study drug. Concomitant medications can be further classified as:

- Present at screening (started before Week 0 and stopped on date of Week 0)
- Ongoing at baseline (started before Week 0 and ongoing at Week 0)
- Started after first dose (started any time after Week 0 through to Week 52)

Partial start dates where the medication cannot definitely be considered as starting prior to Week 0 will lead to a categorisation of the medications as having started on or after Week 0.

The number (%) of patients reporting the use of any concomitant medications in each of the above categories and the number (%) of patients taking each drug by ATC classification and PT will be summarised, by category *(Table 14.3.6)*.

11.6 Study Termination

Time to study termination (days) is calculated as (date of study termination - date of informed consent).

A Kaplan-Meier plot of time to study termination will be presented (*Figure 2*) and summarised using descriptive statistics (*Table 14.3.7*).

If there are sufficient numbers this will also be done by individual primary reason for withdrawal from study.

11.7 Study Drug Exposure

Study drug exposure will be descriptively summarised by treatment and baseline stratification factors *(Table 14.3.8)*. Exposure will be characterised by the duration of treatment and the number of injections received. Treatment duration is calculated as the total number of days from day of first dose to day of last dose.

11.8 Procedures/Non-Drug Therapies

All prior procedures/therapies (started before date of first study drug intake) and current procedures/therapies (started during the treatment period) will be collected on the eCRF but will not be coded. All procedures/non-drug therapy data will be listed.

12 VALIDATION

All tables, figures and listings will be subject to independent quality control and visual review. Unique tables will be independently programmed. Findings will be documented in a quality control form and actions taken will also be documented.

The completed form will be reviewed and signed by both programmers and by the head of biostatistics.

13 LITERATURE CITATIONS/REFERENCES

None

14 LIST OF TABLES, FIGURES AND LISTINGS

14.1 LIST OF TABLES

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Efficacy Data

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Table 14.2.2.2.16	Summary of BILAG-2004 Disease Activity Index	Full Analysis Set
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Listing 16.4.15	Laboratory Sample Collection

15 SHELLS FOR TABLES, FIGURES AND LISTINGS

The intended layouts for tables, figures and listings are presented. However, it may be appropriate for the Orion programmer to change the layouts, upon review of the data available, for completeness and clarity.

QCd output will be produced as Rich Text Format (.rtf) files for convenient inclusion in the CSR.

Subject to this, the following will apply:

- Layout will be landscape, fixed width, font size 8.
- Each output will have the heading:

  IPP-201101/005 (left); date ddMMMyyyy (right)
- Table headings will define the analysis set used for the summary/analysis.
- All outputs will have a footer specifying the SAS program path and filename (left); page x/y (right)
- Tables will have a footer specifying the source listing
- Figures will have a footer specifying the source table or listing
- Additional footnotes will be included where appropriate for clarification.
- Treatment group and patient number and will be included in all listings.

Immupharma IPP-201101/005 ddMMMyyyy

Table 14.1.1 Patient Disposition (All Enrolled Patients)

	IPP-201101 (N=xxx)	Placebo (N=xxx)	Total (N=xxx)
Total number of Enrolled			xx
Failed screening			xx (xx.x%)
Randomised	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Randomised but not treated	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Analysis Sets			
Full Analysis Set	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Safety Set	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)

Enrolled = entered on eCRF
The denominator for each percentage is the number of enrolled subjects

Source: Listing 16.x.x
Path\Filename Page x/y

Immupharma IPP-201101/005 ddMMMyyyy

Table 14.1.2 Study Termination and Primary Reason for Withdrawal (All Randomised Patients)

	IPP-201101 (N=xxx)	Placebo (N=xxx)	Total (N=xxx)
Completed	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Early withdrawal	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Main reason for early withdrawal			
Adverse event	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Etc	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)

The denominator for each percentage is the number of randomised subjects within the column

Source: Listing 16.x.x
Path\Filename Page x/y

Immupharma IPP-201101/005 ddMMMyyyy

Table 14.1.3 Demographic Characteristics (All Randomised Patients)

Region UK, SLEDAI-2K Score 6-9, Race Black/ Hispanic		IPP-201101 (N=xxx)	Placebo (N=xxx)	Total (N=xxx)
Age (years)	N	xx	xx	xx
	Mean	xx.xx	xx.xx	xx.xx
	SD	xx.xx	xx.xx	xx.xx
	Median	xx.xx	xx.xx	xx.xx
	Minimum	xx.x	xx.x	xx.x
	Maximum	xx.x	xx.x	xx.x
Sex	N	xx	xx	xx
	Male	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
	Female	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Ethnicity	N	xx	xx	xx
	Hispanic or Latino	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
	Not Hispanic or Latino	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Race	N	xx	xx	xx
	White	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)

	Black or African American	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
	American Indian or Alaska Native	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
	Native Hawaiian or Other Pacific Islander	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
	Asian	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
	Other	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Height (m)	N	xx	xx	xx
	Mean	xx.xx	xx.xx	xx.xx
	SD	xx.xx	xx.xx	xx.xx
	Median	xx.xx	xx.xx	xx.xx
	Minimum	xx.x	xx.x	xx.x
	Maximum	xx.x	xx.x	xx.x
Weight (kg)	N	xx	xx	xx
	Mean	xx.xx	xx.xx	xx.xx
	SD	xx.xx	xx.xx	xx.xx
	Median	xx.xx	xx.xx	xx.xx
	Minimum	xx.x	xx.x	xx.x
	Maximum	xx.x	xx.x	xx.x
BMI (kg/m^2)	N	xx	xx	xx
	Mean	xx.xx	xx.xx	xx.xx

SD	xx.xx	xx.xx	xx.xx
Median	xx.xx	xx.xx	xx.xx
Minimum	xx.x	xx.x	xx.x
Maximum	xx.x	xx.x	xx.x

The denominator for each percentage is the number of non-missing observations within the column
Age was calculated using DOB and date of informed consent and presented as age at last birthday.

Source: Listing 16.x.x
Path\Filename Page x/y

Programming note: Start each strata on a new page. Order of strata:
Region UK, SLEDAI-2K Score 6-9, Race Black/ Hispanic
Region UK, SLEDAI-2K Score 6-9, Race Other
Region UK, SLEDAI-2K Score ≥ 10, Race Black/ Hispanic
Region UK, SLEDAI-2K Score ≥ 10, Race Other
Region USA, SLEDAI-2K Score 6-9, Race Black/ Hispanic
Region USA, SLEDAI-2K Score 6-9, Race Other
Region USA, SLEDAI-2K Score ≥ 10, Race Black/ Hispanic
Region USA, SLEDAI-2K Score ≥ 10, Race Other
Overall

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Table 14.1.4.1 Medical History (All Randomised Patients)

Region UK, SLEDAI-2K Score 6-9, Race Black/ Hispanic	IPP-201101 (N=xxx)	Placebo (N=xxx)	Total (N=xxx)
Any medical history	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
SOC	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
PT	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
PT	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Etc	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
SOC	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
PT	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
PT	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Etc	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Etc			

The denominator for each percentage is the number of randomised patients within the column
MedDRA version <XX.X>

Source: Listing 16.x.x
Path\Filename Page x/y

Programming note: Start each strata on a new page. Order of strata:
Region UK, SLEDAI-2K Score 6-9, Race Black/ Hispanic
Region UK, SLEDAI-2K Score 6-9, Race Other

Region UK, SLEDAI-2K Score ≥ 10, Race Black/ Hispanic
Region UK, SLEDAI-2K Score ≥ 10, Race Other
Region USA, SLEDAI-2K Score 6-9, Race Black/ Hispanic
Region USA, SLEDAI-2K Score 6-9, Race Other
Region USA, SLEDAI-2K Score ≥ 10, Race Black/ Hispanic
Region USA, SLEDAI-2K Score ≥ 10, Race Other
Overall

This layout also applies to:
Table 14.1.4.2 Current Medical Conditions (All Randomised Patients)

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Table 14.1.5 Prior Medications (All Randomised Patients)

Region UK, SLEDAI-2K Score 6-9, Race Black/ Hispanic	IPP-201101 (N=xxx)	Placebo (N=xxx)	Total (N=xxx)
Any Prior Medications[1]	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
X, xxxxxxxxxxxxx	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
XON, xxxxxxxxxxxxx	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
XONXX, xxxxxxxxxxx	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
xxxxxxxxxxxxx	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
xxxxxxxxxxxx	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Etc			
XONXX, xxxxxxxxxxx	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
xxxxxxxxxxxx	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Etc			
Etc			

[1] Medication that started and stopped prior to first study drug intake
WHO-DDE version <XX.X>
The denominator for each percentage is the number of randomised patients within the column

Source: Listing 16.x.x
Path\Filename Page x/y

Programming note: Start each strata on a new page. Order of strata:
Region UK, SLEDAI-2K Score 6-9, Race Black/ Hispanic

Region UK, SLEDAI-2K Score 6-9, Race Other
Region UK, SLEDAI-2K Score ≥ 10, Race Black/ Hispanic
Region UK, SLEDAI-2K Score ≥ 10, Race Other
Region USA, SLEDAI-2K Score 6-9, Race Black/ Hispanic
Region USA, SLEDAI-2K Score 6-9, Race Other
Region USA, SLEDAI-2K Score ≥ 10, Race Black/ Hispanic
Region USA, SLEDAI-2K Score ≥ 10, Race Other
Overall

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Table 14.1.6 SLE Disease History (All Randomised Patients)

Region UK, SLEDAI-2K Score 6-9, Race Black/ Hispanic		IPP-201101 (N=xxx)	Placebo (N=xxx)	Total (N=xxx)
Time since diagnosis of SLE (years)	N	xx	xx	xx
	Mean	xx.xx	xx.xx	xx.xx
	SD	xx.xx	xx.xx	xx.xx
	Median	xx.xx	xx.xx	xx.xx
	Minimum	xx.x	xx.x	xx.x
	Maximum	xx.x	xx.x	xx.x
Time since last SLE flare (years)	N	xx	xx	xx
	Mean	xx.xx	xx.xx	xx.xx
	SD	xx.xx	xx.xx	xx.xx
	Median	xx.xx	xx.xx	xx.xx
	Minimum	xx.x	xx.x	xx.x
	Maximum	xx.x	xx.x	xx.x
Time since SLE-related hospitalisation (years)	N	xx	xx	xx
	Mean	xx.xx	xx.xx	xx.xx
	SD	xx.xx	xx.xx	xx.xx

Median	xx.xx	xx.xx	xx.xx
Minimum	xx.x	xx.x	xx.x
Maximum	xx.x	xx.x	xx.x

Time since diagnosis of SLE/ last SLE flare/ SLE-related hospitalisation is calculated as the difference between date of informed consent and date of diagnosis of SLE/ date of last SLE flare/ date of SLE-related hospitalisation

Source: Listing 16.x.x
Path\Filename Page x/y

Programming note: Start each strata on a new page. Order of strata:
Region UK, SLEDAI-2K Score 6-9, Race Black/ Hispanic
Region UK, SLEDAI-2K Score 6-9, Race Other
Region UK, SLEDAI-2K Score ≥ 10, Race Black/ Hispanic
Region UK, SLEDAI-2K Score ≥ 10, Race Other
Region USA, SLEDAI-2K Score 6-9, Race Black/ Hispanic
Region USA, SLEDAI-2K Score 6-9, Race Other
Region USA, SLEDAI-2K Score ≥ 10, Race Black/ Hispanic
Region USA, SLEDAI-2K Score ≥ 10, Race Other
Overall

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Table 14.1.7 Other Baseline Characteristics (All Randomised Patients)

Region UK, SLEDAI-2K Score 6-9, Race Black/ Hispanic		IPP-201101 (N=xxx)	Placebo (N=xxx)	Total (N=xxx)
Physical examination				
General appearance	N	xx	xx	xx
	Normal	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
	Abnormal NCS	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
	Abnormal CS	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Skin	N	xx	xx	xx
	Etc			
Etc				
12-Lead ECG	N	xx	xx	xx
	Normal	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
	Abnormal NCS	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
	Abnormal CS	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)

The denominator for each percentage is the number of non-missing observations within the column

Source: Listing 16.x.x
Path\Filename Page x/y

Programming note: Start each strata on a new page. Order of strata:
Region UK, SLEDAI-2K Score 6-9, Race Black/ Hispanic
Region UK, SLEDAI-2K Score 6-9, Race Other
Region UK, SLEDAI-2K Score ≥ 10, Race Black/ Hispanic
Region UK, SLEDAI-2K Score ≥ 10, Race Other
Region USA, SLEDAI-2K Score 6-9, Race Black/ Hispanic
Region USA, SLEDAI-2K Score 6-9, Race Other
Region USA, SLEDAI-2K Score ≥ 10, Race Black/ Hispanic
Region USA, SLEDAI-2K Score ≥ 10, Race Other
Overall

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Table 14.2.1.1 Primary Analysis of SRI Response at Week 52 (Full Analysis Set)

		IPP-201101 (N=xxx)	Placebo (N=xxx)	Odds ratio (95% CI)	p-value
SRI Response at Week 52	N	xx	xx		
	Clinical SRI Response	xx (xx.x%)	xx (xx.x%)		
	No Clinical SRI Response	xx (xx.x%)	xx (xx.x%)		
Logistic regression	Responders	xx	xx		
	Non-responders	xx	xx		
	Treatment: IPP-201101 vs Placebo			x.xx (x.xx, x.xx)	x.xxxx
	Region				x.xxxx
	SLEDAI-2K score at screening				x.xxxx
	Racial-ethnic group classification				x.xxxx

The denominator for each percentage is the number of non-missing observations within the column

Logistic regression model is fitted with treatment and stratification factors as main factors.
Patients who withdrew early from the study are classified as non-responders at Week 52.

Source: Listing 16.x.x
Path\Filename Page x/y

This layout also applies to:

1. Sensitivity Analysis of Primary Variable:
Table 14.2.1.2.1 Sensitivity Analysis 1 of SRI Response at Week 52 (Full Analysis Set) Programming note: Footnote 2 to read 'Patients who withdrew early because of treatment failure are classified as non-responders. Patients who withdrew early because of other reasons have their missing SRI response at Week 52 imputed using the LOCF method.'
Table 14.2.1.2.2 Sensitivity Analysis 2 of SRI Response at Week 52 (Full Analysis Set) Programming note: Footnote 2 to read 'All patients who withdrew early have their missing SRI response at Week 52 imputed using the LOCF method.'
Table 14.2.1.2.3 Sensitivity Analysis 3 of SRI Response at Week 52 (Full Analysis Set) Programming note: Footnote 2 to read 'Patients who withdrew early and completers who used prohibited medication within 8 weeks from Week 52 are classified as non-responders.'
Table 14.2.1.2.4 Sensitivity Analysis 4 of SRI Response at Week 52 (Full Analysis Set) Programming note: Footnote 2 to read 'Patients on IPP-201101 who withdrew early are classified as non-responders at Week 52 and patients on Placebo who withdrew early are classified as responders at Week 52, as part of a tipping point analysis where dropouts on IPP-201101 are assigned worse outcomes than those on Placebo.'

2. Most important secondary endpoints:
Table 14.2.2.1.1 Analysis of Patients Achieving a Clinical SLEDAI-2K Total Score of 0 at Week 52 (remission) (Full Analysis Set)
Table 14.2.2.1.2 Analysis of Patients who had an Assessment of "No" for Arthritis Symptoms using SLEDAI-2K at Week 52 and had an Assessment of "Yes" at Randomisation (Full Analysis Set)
Table 14.2.2.1.3 Analysis of Patients Achieving a BILAG C Score at Week 52 who had a BILAG A or BILAG B Score at Randomisation (Full Analysis Set)
Table 14.2.2.1.5 Analysis of SRI Response at Week 52 in the Subgroup with Screening SLEDAI-2K ≥ 10

3. Other secondary endpoints:
Table 14.2.2.2.22 Reduction from Baseline in SLEDAI-2K Score of at Least 4 Points (Full Analysis Set)
Table 14.2.2.2.23 No Worsening in PhGA (Full Analysis Set)
Table 14.2.2.2.24 No New BILAG A Body System Score
Table 14.2.2.2.25 No More than 1 New BILAG B Body System Score from Baseline (Full Analysis Set)

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Table 14.2.2.1.4.1 Analysis of Absolute Change in Fatigue using the FACIT-Fatigue at Week 52 (Full Analysis Set)

		IPP-201101 (N=xxx)	Placebo (N=xxx)	p-value
Baseline	N	xx	xx	xx
	Mean	xx.xx	xx.xx	xx.xx
	SD	xx.xx	xx.xx	xx.xx
	Median	xx.xx	xx.xx	xx.xx
	Minimum	xx.x	xx.x	xx.x
	Maximum	xx.x	xx.x	xx.x
Week 52	N	xx	xx	xx
	Mean	xx.xx	xx.xx	xx.xx
	Etc			
Changes from baseline to Week 52	N	xx	xx	xx
	Etc			
ANCOVA Model[1]				
Treatment difference: IPP-201101 vs Placebo	LS Mean			xx.xx
	95% CI			xx.x, xx.x

	SE	xx.xx
	p-value	x.xxxx
Fixed effects and covariates	Treatment	x.xxxx
	Region	x.xxxx
	SLEDAI-2K screening total score	x.xxxx
	Racial/ethnic classification	x.xxxx
	Baseline fatigue using the FACIT-Fatigue total score	x.xxxx

Baseline is defined as the last non-missing value before the first dose of study drug.
[1]The ANCOVA model analyses change from baseline in fatigue using the FACIT-Fatigue total score at Week 52 and includes fixed effects for treatment and randomisation factors (region, SLEDAI-2K screening score, racial/ethnic classification) and baseline fatigue using the FACIT-Fatigue total score as covariates

Source: Listing 16.x.x
Path\Filename Page x/y

This layout also applies to:
Table 14.2.2.1.4.2 Sensitivity Analysis of Absolute Change in Fatigue using the FACIT-Fatigue at Week 52 (Full Analysis Set) Programming note: Add footnote 'The multiple imputation method has been used to account for missing data at Week 52.'

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Table 14.2.2.2.1 Summary of SLEDAI-2K Total Score (Full Analysis Set)

		IPP-201101 (N=xxx)	Placebo (N=xxx)	Total (N=xxx)
Baseline	N	xx	xx	xx
	Mean	xx.xx	xx.xx	xx.xx
	SD	xx.xx	xx.xx	xx.xx
	Median	xx.xx	xx.xx	xx.xx
	Minimum	xx.x	xx.x	xx.x
	Maximum	xx.x	xx.x	xx.x
Week 4	N	xx	xx	xx
	Mean	xx.xx	xx.xx	xx.xx
	Etc			
Etc				

Baseline is defined as the last non-missing value before the first dose of study drug.

Source: Listing 16.x.x
Path\Filename

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Table 14.2.2.2.2 Patients Achieving a SRI Response (Full Analysis Set)

		IPP-201101 (N=xxx)	Placebo (N=xxx)	Total (N=xxx)
Baseline to Week 4	N	xx	xx	xx
	Clinical SRI Response	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
	No Clinical SRI Response	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Baseline to Week 8	N	xx	xx	xx
	Clinical SRI Response	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
	No Clinical SRI Response	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Etc				
Baseline to Week 48	Etc	xx	xx	xx
Baseline to Week 52	Etc	xx	xx	xx

The denominator for each percentage is the number of non-missing observations within the column
Baseline is defined as the last non-missing value before the first dose of study drug.

Source: Listing 16.x.x
Path\Filename

Programming Note: display all visits where SRI response is obtained

This layout also applies to:

Table 14.2.2.2.3 Patients Achieving a SLEDAI-2K Clinical Response (Full Analysis Set)
Table 14.2.2.2.4 Patients Achieving a BILAG-2004 Clinical Response (Full Analysis Set)
Table 14.2.2.2.5 Patients Showing No Worsening on PhGA Scale (Full Analysis Set)
Table 14.2.2.2.6 Patients Achieving a Reduction of 5 Points in SLEDAI-2K Total Score (Full Analysis Set)
Table 14.2.2.2.7 Patients Achieving a Reduction of 6 Points in SLEDAI-2K Total Score (Full Analysis Set)
Table 14.2.2.2.8 Patients Achieving a SRI-5 Response (Full Analysis Set)
Table 14.2.2.2.9 Patients Achieving a SRI-6 Response (Full Analysis Set)
Table 14.2.2.2.10 Patients Achieving a SRI-7 Response (Full Analysis Set)
Table 14.2.2.2.11 Patients Achieving a SRI-8 Response (Full Analysis Set)
Table 14.2.2.2.12 Patients Achieving a SRI-9 Response (Full Analysis Set)
Table 14.2.2.2.13 Patients Showing an Improvement in Tender and Swollen Joints Count (Full Analysis Set)
Table 14.2.2.2.17 Summary of Status of Disease (PhGA Scale) (Full Analysis Set)

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Table 14.2.2.2.14 Summary of Medical Outcome Survey SF-36 (Full Analysis Set)

		IPP-201101 (N=xxx)	Placebo (N=xxx)	Total (N=xxx)
Baseline	N	xx	xx	xx
	Mean	xx.xx	xx.xx	xx.xx
	SD	xx.xx	xx.xx	xx.xx
	Median	xx.xx	xx.xx	xx.xx
	Minimum	xx.x	xx.x	xx.x
	Maximum	xx.x	xx.x	xx.x
Week 12	N	xx	xx	xx
	Mean	xx.xx	xx.xx	xx.xx
	Etc			
Change from baseline to Week 12	N	xx	xx	xx
	Mean	xx.xx	xx.xx	xx.xx
	Etc			
Etc				

Baseline is defined as the last non-missing value before the first dose of study drug.

Source: Listing 16.x.x
Path\Filename

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Programming note: display absolute and relative to baseline data for Weeks 12, 24, 36 and 52

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Table 14.2.2.2.16 Summary of BILAG-2004 Disease Activity Index (Full Analysis Set)

		IPP-201101 (N=xxx)	Placebo (N=xxx)	Total (N=xxx)
Baseline to Week 52	N	xx	xx	xx
	BILAG-2004 Response	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
	No BILAG-2004 Response	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)

The denominator for each percentage is the number of non-missing observations within the column
Baseline is defined as the last non-missing value before the first dose of study drug.

Source: Listing 16.x.x
Path\Filename

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This layout also applies to:
Table 14.2.2.2.15 Patients with a Reduction in the SLEDAI-2K Total Score by at Least 4 Points from Baseline to Week 52 (Full Analysis Set)

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Table 14.2.2.2.18 Summary of SFI Variables (Full Analysis Set)

		IPP-201101 (N=xxx)	Placebo (N=xxx)	Total (N=xxx)
Incidence of mild to moderate flare	N	xx	xx	xx
	Yes	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
	No	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Time to first mild to moderate flare (days)	N	xx	xx	xx
	Mean	xx.xx	xx.xx	xx.xx
	SD	xx.xx	xx.xx	xx.xx
	Median	xx.xx	xx.xx	xx.xx
	Minimum	xx.x	xx.x	xx.x
	Maximum	xx.x	xx.x	xx.x
Incidence of severe flare	N	xx	xx	xx
	Yes	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
	No	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Time to severe flare (days)	N	xx	xx	xx
	Mean	xx.xx	xx.xx	xx.xx

SD	xx.xx	xx.xx	xx.xx
Median	xx.xx	xx.xx	xx.xx
Minimum	xx.x	xx.x	xx.x
Maximum	xx.x	xx.x	xx.x

Time to first mild to moderate flare/ time to severe flare is calculated as the difference between date of baseline visit and date of mild to moderate/severe flare
The denominator for each percentage is the number of non-missing observations within the column

Source: Listing 16.x.x
Path\Filename Page x/y

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Table 14.2.2.2.19 Proportion of Patients with SLEDAI-2K Score Greater than 15 at each Visit (Full Analysis Set)

		IPP-201101 (N=xxx)	Placebo (N=xxx)	Total (N=xxx)
Baseline	N	xx	xx	xx
	Score >15	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
	Score ≤15	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Week 4	N	xx	xx	xx
	Score >15	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
	Score ≤15	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Etc				
Week 48	Etc	xx	xx	xx
Week 52	Etc	xx	xx	xx

The denominator for each percentage is the number of non-missing observations within the column
Baseline is defined as the last non-missing value before the first dose of study drug.

Source: Listing 16.x.x
Path\Filename

Programming Note: display all visits where SLEDAI-2K score is obtained

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Table 14.2.2.2.20 Summary of Changes in the SDI Total Score (Full Analysis Set)

		IPP-201101 (N=xxx)	Placebo (N=xxx)	Total (N=xxx)
Screening	N	xx	xx	xx
	Mean	xx.xx	xx.xx	xx.xx
	SD	xx.xx	xx.xx	xx.xx
	Median	xx.xx	xx.xx	xx.xx
	Minimum	xx.x	xx.x	xx.x
	Maximum	xx.x	xx.x	xx.x
Week 24	N	xx	xx	xx
	Mean	xx.xx	xx.xx	xx.xx
	Etc			
Change from Screening to Week 24	N	xx	xx	xx
	Mean	xx.xx	xx.xx	xx.xx
	Etc			
Week 52	N	xx	xx	xx
	Mean	xx.xx	xx.xx	xx.xx

	Etc			
Change from Screening to Week 52	N	xx	xx	xx
	Mean	xx.xx	xx.xx	xx.xx
	Etc			

Source: Listing 16.x.x
Path\Filename

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Table 14.2.2.2.21.1 Summary of Steroid Dose (Full Analysis Set)

		IPP-201101 (N=xxx)	Placebo (N=xxx)	Total (N=xxx)
Baseline	N	xx	xx	xx
	None	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
	<7.5mg	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
	≥7.5mg	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Week 24	N	xx	xx	xx
	None	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
	<7.5mg	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
	≥7.5mg	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Week 52	N	xx	xx	xx
	None	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
	<7.5mg	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
	≥7.5mg	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)

Baseline is defined as the last non-missing value before the first dose of study drug.
The denominator for each percentage is the number of non-missing observations within the column

Source: Listing 16.x.x
Path\Filename

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Table 14.2.2.2.21.2 Shift Table of Changes in Steroid Dose (Full Analysis Set)

	IPP-201101 (N=xxx)			Placebo (N=xxx)			Total (N=xxx)		
	Baseline			Baseline			Baseline		
	None	<7.5mg	≥7.5mg	None	<7.5mg	≥7.5mg	None	<7.5mg	≥7.5mg
Week 24									
None	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
<7.5mg	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
≥7.5mg	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Week 52									
None	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
<7.5mg	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
≥7.5mg	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)

Baseline is defined as the last non-missing value before the first dose of study drug.
The denominator for each percentage is the number of non-missing observations within the column

Source: Listing 16.x.x
Path\Filename Page x/y

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Table 14.2.3.1 Summary of Changes in Biomarkers: Anti-dsDNA Ab, C3 and C4 (Full Analysis Set)

		IPP-201101 (N=xxx)	Placebo (N=xxx)	Total (N=xxx)
Anti-dsDNA Ab				
Baseline	N	xx	xx	xx
	Mean	xx.xx	xx.xx	xx.xx
	SD	xx.xx	xx.xx	xx.xx
	Median	xx.xx	xx.xx	xx.xx
	Minimum	xx.x	xx.x	xx.x
	Maximum	xx.x	xx.x	xx.x
Week 1	N	xx	xx	xx
	Etc			
Changes from Baseline to Week 1	N	xx	xx	xx
	Etc			
Etc				

Baseline is defined as the last non-missing value before the first dose of study drug.

Source: Listing 16.x.x

Path\Filename Page x/y

Include all weeks in treatment period and start each parameter on a new page

This layout also applies to:
Table 14.2.3.2 Summary of Changes in Other Biomarkers (Full Analysis Set) Programming note: display Weeks 4, 12, 24, 36 and 52
Table 14.2.3.3 Summary of In Vitro Intracellular and Cytokine Response (Full Analysis Set) Programming note: display Weeks 4, 24, and 48

Immupharma IPP-201101/005 ddMMMyyyy

Table 14.2.3.4 Cumulative Distribution of the Reduction from Baseline to Week 52 in SLEDAI-2K Score (Full Analysis Set)

	IPP-201101 (N=xxx)		Placebo (N=xxx)		Total (N=xxx)	
	N	Probability	N	Probability	N	Probability
Reduction from Baseline to Week 52						
Total	xx		xx		xx	
Less than or equal to 0	xx	x.xx	xx	x.xx	xx	x.xx
Less than or equal to 1	xx	x.xx	xx	x.xx	xx	x.xx
Less than or equal to 2	xx	x.xx	xx	x.xx	xx	x.xx
Less than or equal to 3	xx	x.xx	xx	x.xx	xx	x.xx
Less than or equal to 4	xx	x.xx	xx	x.xx	xx	x.xx
Etc						

The denominator for each probability is the number of non-missing observations within the column
Baseline is defined as the last non-missing value before the first dose of study drug.
A reduction of less than 0 signifies an increase in the score.

Source: Listing 16.x.x
Path\Filename

Page x/y

Programming note: continue table in one unit increases until all reductions are captured.

Immupharma IPP-201101/005 ddMMMyyyy

Table 14.2.4 Immunogenicity Findings (Full Analysis Set)

		IPP-201101 (N=xxx)	Placebo (N=xxx)	Total (N=xxx)
Presence of anti-IPP-201101				
Baseline	N	xx	xx	xx
	Yes	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
	No	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Week 2	N	xx	xx	xx
	Yes	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
	No	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Week 4	N	xx	xx	xx
	Yes	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
	No	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Etc				

Baseline is defined as the last non-missing value before the first dose of study drug.

Source: Listing 16.x.x
Path\Filename Page x/y

Programming note: Baseline, Weeks 2, 4, 12, 20, 28, 36, 44 and 52 (or final assessment) should be presented in the table

Immupharma IPP-201101/005 ddMMMyyyy

Table 14.3.1.1 Summary of Treatment-Emergent Adverse Events (Safety Set)

	IPP-201101 (N=xxx)	Placebo (N=xxx)	Total (N=xxx)
Any Treatment-Emergent Adverse Events	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Severe Treatment-Emergent Adverse Events	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Serious Treatment-Emergent Adverse Events	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Drug-Related Treatment-Emergent Adverse Events	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Serious Drug-Related Treatment-Emergent Adverse Events	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Treatment-Emergent Adverse Events leading to withdrawal from the study	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Treatment-Emergent Adverse Events leading to death	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)

The denominator for each percentage is the number of subjects within the column

Source: Listing 16.x.x
Path\Filename Page x/y

Immupharma IPP-201101/005 ddMMMyyyy

Table 14.3.1.2 Treatment-Emergent Adverse Events, by SOC and PT (Safety Set)

	IPP-201101 (N=xxx)	Placebo (N=xxx)	Total (N=xxx)
Any Treatment-Emergent Adverse Events	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
SOC	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
PT	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
PT	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Etc	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
SOC	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
PT	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
PT	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Etc	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)

MedDRA version <XX.X>
The denominator for each percentage is the number of subjects within the column

Source: Listing 16.x.x
Path\Filename Page x/y

This layout also applies to:

Table 14.3.1.3 Severe Treatment-Emergent Adverse Events, by SOC and PT (Safety Set)
Table 14.3.1.4 Serious Treatment-Emergent Adverse Events, by SOC and PT (Safety Set)
Table 14.3.1.5 Drug-Related Treatment-Emergent Adverse Events, by SOC and PT (Safety Set)
Table 14.3.1.6 Serious Drug-Related Treatment-Emergent Adverse Events, by SOC and PT (Safety Set)
Table 14.3.1.7 Treatment-Emergent Adverse Events Leading to Withdrawal from the Study, by SOC and PT (Safety Set)
Table 14.3.1.9 Adverse Events of Special Interest, by SOC and PT (Safety Set)

Immupharma IPP-201101/005 ddMMMyyyy

Table 14.3.1.8.1 Listing of Deaths

Treatment	Centre/ Patient number	Date of start of treatment	Date of death
xxxxxxx	xxx-xxxx	ddMMMyyyy	ddMMMyyyy
xxxxxxx	xxx-xxxx	ddMMMyyyy	ddMMMyyyy
Etc	Etc		

Path\Filename Page x/y

Immupharma IPP-201101/005 ddMMMyyyy

Table 14.3.1.8.2 Listing of Serious Adverse Events

IPP-201101

Centre/ Patient number	Adverse Event Preferred Term SOC Term	Start date	Study day	Stop date /ongoing	Duration of adverse event (days)	Severity	Action taken regarding study drug	Concomitant therapy started due to AE	Outcome	Relationship to study drug	Serious
xxx xxxx	xxxxxxxxx xxxxxxxx xxxxxxx	ddMMMyyyy	xx	ddMMMyyyy	xx	Mild /Moderate /etc	None /Discontinued /Etc	Yes /No	Resolved /Etc	Unrelated /Unlikely /Etc	Yes /No
	xxxxxxxxx xxxxxxxx xxxxxxx	ddMMMyyyy	xx	ddMMMyyyy	xx	Mild /Moderate /etc	None /Discontinued /Etc	Yes /No	Resolved /Etc	Unrelated /Unlikely /Etc	Yes /No
xxx xxxx	xxxxxxxxx xxxxxxxx xxxxxxx	ddMMMyyyy	xx	ddMMMyyyy	xx	Mild /Moderate /etc	None /Discontinued /Etc	Yes /No	Resolved /Etc	Unrelated /Unlikely /Etc	Yes /No
Etc											

Repeat for placebo

Path\Filename Page x/y

This layout also applies to:

Table 14.3.1.8.3 Listing of Adverse Events which Led to Withdrawal

Immupharma IPP-201101/005 ddMMMyyyy

Table 14.3.2.1 Summary of Serum Chemistry Parameters (Safety Set)

		IPP-201101 (N=xxx)	Placebo (N=xxx)	Total (N=xxx)
Calcium				
Baseline	N	xx	xx	xx
	Mean	xx.xx	xx.xx	xx.xx
	SD	xx.xx	xx.xx	xx.xx
	Median	xx.xx	xx.xx	xx.xx
	Minimum	xx.x	xx.x	xx.x
	Maximum	xx.x	xx.x	xx.x
Week 4	N	xx	xx	xx
	Mean	xx.xx	xx.xx	xx.xx
	SD	xx.xx	xx.xx	xx.xx
	Median	xx.xx	xx.xx	xx.xx
	Minimum	xx.x	xx.x	xx.x
	Maximum	xx.x	xx.x	xx.x
Change from baseline to Week 4				
Etc				

Baseline is defined as the last non-missing value before the first dose of study drug.

Source: Listing 16.x.x
Path\Filename Page x/y

Programming note: start each parameter on a new page and summarise any non-continuous data with number (%) instead of descriptive stats.

This layout also applies to:
Table 14.3.2.2 Summary of Haematology Parameters (Safety Set)
Table 14.3.2.3 Summary of Urinalysis Parameters (Safety Set)

Immupharma IPP-201101/005 ddMMMyyyy

Table 14.3.3 Vital Signs (Safety Set)

		IPP-201101 (N=xxx)	Placebo (N=xxx)	Total (N=xxx)
Diastolic Blood Pressure				
Baseline	N	xx	xx	xx
	Mean	xx.xx	xx.xx	xx.xx
	SD	xx.xx	xx.xx	xx.xx
	Median	xx.xx	xx.xx	xx.xx
	Minimum	xx.x	xx.x	xx.x
	Maximum	xx.x	xx.x	xx.x
Week 4	N	xx	xx	xx
	Mean	xx.xx	xx.xx	xx.xx
	SD	xx.xx	xx.xx	xx.xx
	Median	xx.xx	xx.xx	xx.xx
	Minimum	xx.x	xx.x	xx.x
	Maximum	xx.x	xx.x	xx.x
Change from baseline to Week 4				
Etc				

```
Baseline is defined as the last non-missing value before the first dose of study drug.

Source: Listing 16.x.x
Path\Filename                                                                    Page x/y
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Immupharma IPP-201101/005 ddMMMyyyy

Table 14.3.4 Shift Table of 12-Lead ECG (Safety Set)

	IPP-201101 (N=xxx)			Placebo (N=xxx)		
	Baseline			Baseline		
	Normal	Abnormal NCS	Abnormal CS	Normal	Abnormal NCS	Abnormal CS
Week 52						
Normal	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Abnormal NCS	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Abnormal CS	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)

NCS=Not Clinically Significant; CS=Clinically Significant

The denominator for each percentage is the number of non-missing observations within the column
Baseline is defined as the last non-missing value before the first dose of study drug.

Source: Listing 16.x.x
Path\Filename Page x/y

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Table 14.3.5 Suicidality Assessment (Safety Set)

		IPP-201101 (N=xxx)	Placebo (N=xxx)	Total (N=xxx)
Columbia-Suicide Severity Rating Scale (C-SSRS)				
Baseline	N	xx	xx	xx
	Mean	xx.xx	xx.xx	xx.xx
	SD	xx.xx	xx.xx	xx.xx
	Median	xx.xx	xx.xx	xx.xx
	Minimum	xx.x	xx.x	xx.x
	Maximum	xx.x	xx.x	xx.x
Week 4	N	xx	xx	xx
	Mean	xx.xx	xx.xx	xx.xx
	SD	xx.xx	xx.xx	xx.xx
	Median	xx.xx	xx.xx	xx.xx
	Minimum	xx.x	xx.x	xx.x
	Maximum	xx.x	xx.x	xx.x
Etc				

Baseline is defined as the last non-missing value before the first dose of study drug.

Source: Listing 16.x.x
Path\Filename Page x/y

Programming note: Baseline, Weeks 4, 8, 12, 16, 20, 24, 28, 32, 36, 40, 44, 48 and 52 (or final assessment) should be presented in the table

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Table 14.3.6 Concomitant Medications (Safety Set)

	IPP-201101 (N=xxx)	Placebo (N=xxx)	Total (N=xxx)
Any Concomitant Medications	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Present at screening[1]	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Ongoing at baseline[2]	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Started after first dose[3]	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Present at screening			
X, xxxxxxxxxxxxx	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
XON, xxxxxxxxxxxxx	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
XONXX, xxxxxxxxxxx	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
xxxxxxxxxxxxx	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Etc			
XONXX, xxxxxxxxxxx	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
xxxxxxxxxxxx	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Etc			

[1]Medication that started prior to first study drug intake and stopped on the day of Week 0/baseline
[2]Medication that started prior to first study drug intake and continued into the study
[3]Medication that started any time after first study drug intake

WHO-DDE version <XX.X>
The denominator for each percentage is the number of patients within the column

Source: Listing 16.x.x

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Table 14.3.7 Time to Study Termination (Safety Set)

		IPP-201101 (N=xxx)	Placebo (N=xxx)	Total (N=xxx)
Time to study termination (days)	N	xx	xx	xx
	Mean	xx.xx	xx.xx	xx.xx
	SD	xx.xx	xx.xx	xx.xx
	Median	xx.xx	xx.xx	xx.xx
	Minimum	xx.x	xx.x	xx.x
	Maximum	xx.x	xx.x	xx.x
Kaplan-Meier estimate (days)	Median (95% CI)	xx.xx (xx.xx, xx.xx)	xx.xx (xx.xx, xx.xx)	xx.xx (xx.xx, xx.xx)

Time to study termination (days) is calculated as (date of study termination - date of informed consent).

Source: Listing 16.x.x
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Table 14.3.8 Study Drug Exposure (Safety Set)

		IPP-201101 (N=xxx)	Placebo (N=xxx)	Total (N=xxx)
Duration of treatment (days)	N	xx	xx	xx
	Mean	xx.xx	xx.xx	xx.xx
	SD	xx.xx	xx.xx	xx.xx
	Median	xx.xx	xx.xx	xx.xx
	Minimum	xx.x	xx.x	xx.x
	Maximum	xx.x	xx.x	xx.x
Number of injections	N	xx	xx	xx
	Mean	xx.xx	xx.xx	xx.xx
	SD	xx.xx	xx.xx	xx.xx
	Median	xx.xx	xx.xx	xx.xx
	Minimum	xx.x	xx.x	xx.x
	Maximum	xx.x	xx.x	xx.x

Duration of treatment is calculated as (day of last dose - day of first dose).

Source: Listing 16.x.x
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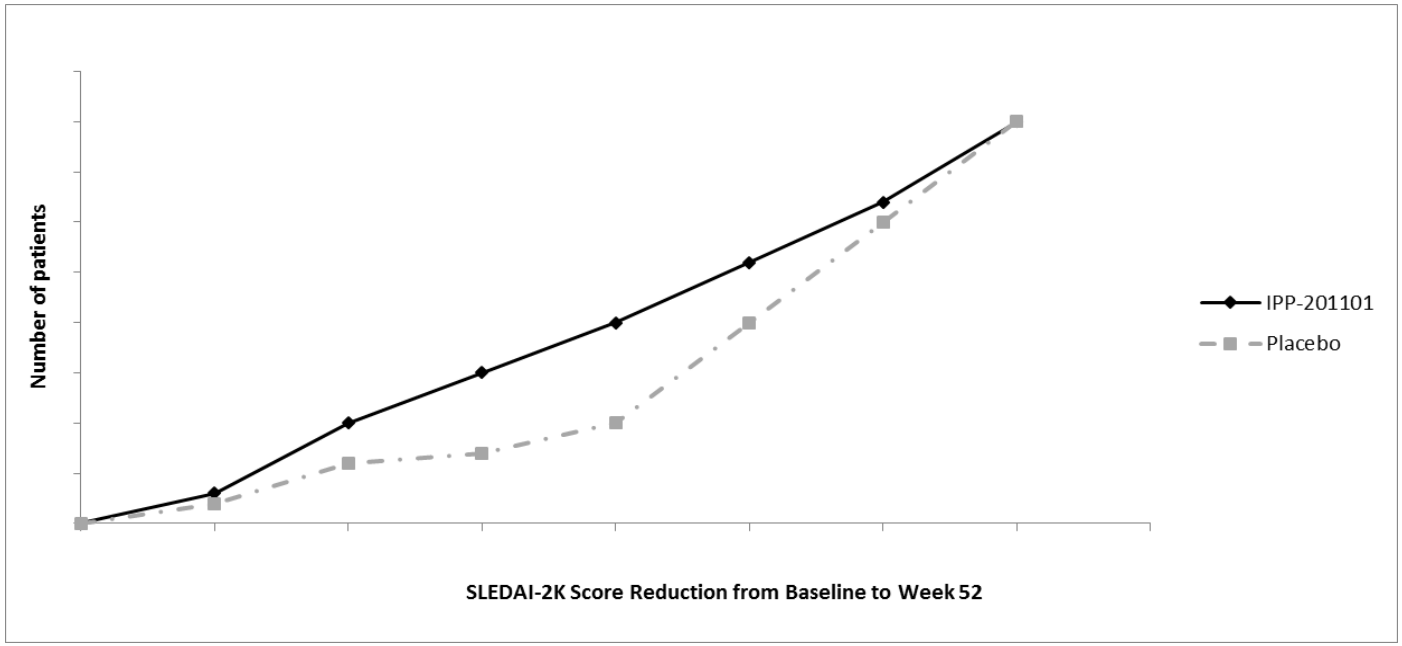
Figure 1 Cumulative Distribution of the Reduction from Baseline to Week 52 in SLEDAI-2K Score (Full Analysis Set)



Source: Listing 16.x.x
Path\Filename Page x/y

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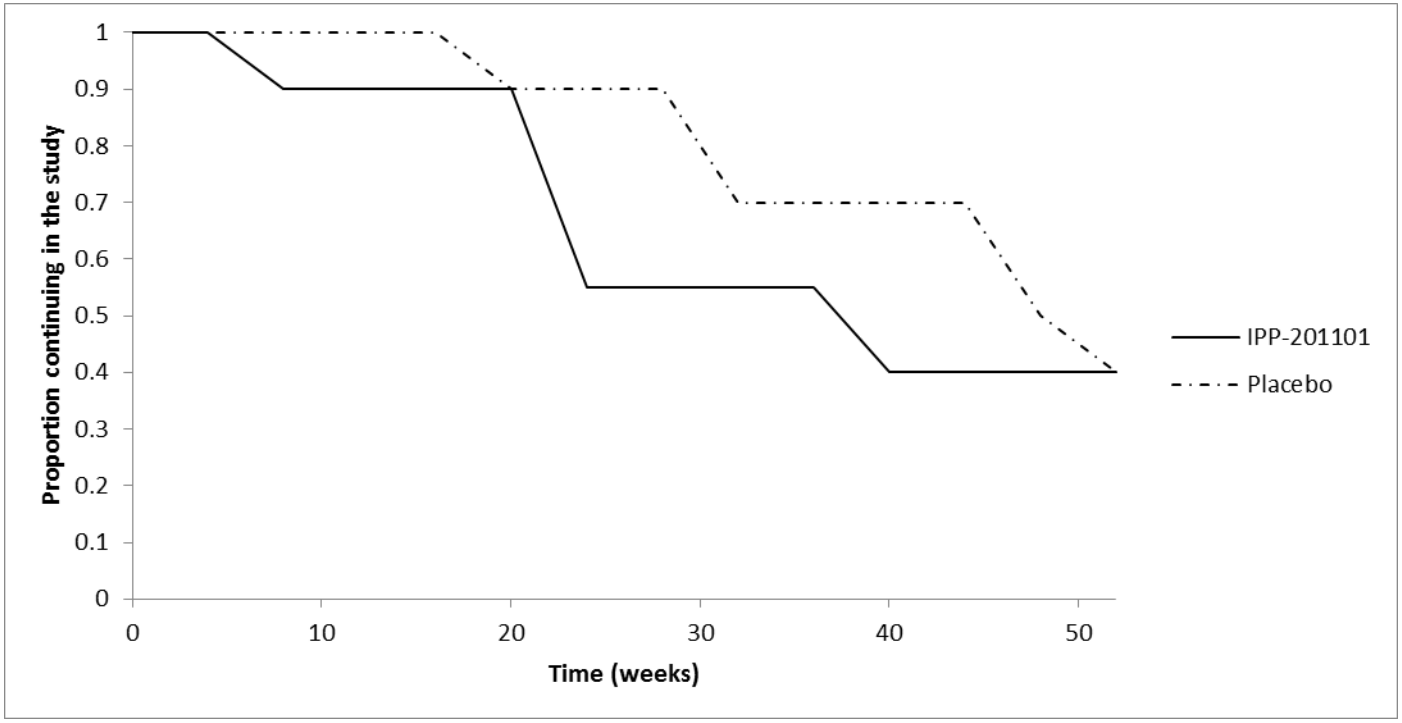
Figure 2 Kaplan-Meier Plot of Time to Study Termination (Safety Set)



Source: Listing 16.x.x
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Listing 16.2.1 Discontinued Patients

Treatment	Centre/ Patient number	First dose date	Last dose date	Date of withdrawal	Main reason for withdrawal
xxxxxxx	xxx-xxxx	ddMMMyyyy	ddMMMyyyy	ddMMMyyyy	xxxxxxxxxxxxxxxxxxxxxxxxx
	xxx-xxxx	ddMMMyyyy	ddMMMyyyy	ddMMMyyyy	xxxxxxxxxxxxxxxxxxxxxxxxx
	xxx-xxxx	ddMMMyyyy	ddMMMyyyy	ddMMMyyyy	xxxxxxxxxxxxxxxxxxxxxxxxx
	xxx-xxxx	ddMMMyyyy	ddMMMyyyy	ddMMMyyyy	xxxxxxxxxxxxxxxxxxxxxxxxx

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Listing 16.2.2 Protocol Deviations

Treatment	Centre/ Subject number	Major deviation	Description of deviation
xxxxxxx	xx/xx-xx	Yes/No	xxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxx
		Yes/No	xxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxx
	Etc		

Path\Filename

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Listing 16.2.3 Analysis Datasets

Treatment	Centre/ Patient number	Full Analysis Set	Safety Set
xxxxxx	xxx-xxxx	Yes/No	Yes/No
	xxx-xxxx	Yes/No	Yes/No
	xxx-xxxx	Yes/No	Yes/No
	xxx-xxxx	Yes/No	Yes/No

Etc

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Listing 16.2.4 Demographic Data

Treatment	Centre/ Patient number	Date of screening	Date of birth	Age* (years)	Gender	Ethnic origin	Race	Weight (kg)	Height (cm)	BMI (kg/m^2)
xxxxxx	xxx-xxxx	ddMMMyyyy	ddMMMyyyy	xx	xxxx	xxxx	xxxx	xx.x	xxx.x	xx.x
	xxx-xxxx	ddMMMyyyy	ddMMMyyyy	xx	xxxx	xxxx	xxxx	xx.x	xxx.x	xx.x
	xxx-xxxx	ddMMMyyyy	ddMMMyyyy	xx	xxxx	xxxx	xxxx	xx.x	xxx.x	xx.x
	xxx-xxxx	ddMMMyyyy	ddMMMyyyy	xx	xxxx	xxxx	xxxx	xx.x	xxx.x	xx.x
	xxx-xxxx	ddMMMyyyy	ddMMMyyyy	xx	xxxx	xxxx	xxxx	xx.x	xxx.x	xx.x

Etc

*Age calculated at Date of Screening

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Listing 16.2.5 Study Drug Exposure and Compliance

Treatment	Centre/ Patient number	Visit	200mcg dose administered	Actual dose administered	Reason for change in dose	Treatment duration (weeks)	Compliance
xxxxxx	xxx-xxxx	x	Yes				
		x	Yes				
		x	No	xxx mcg	xxxxxx		
		x	Yes				
		x*					
						xx	xxx.x%
xxxxxx	xxx-xxxx	x	Yes				
		x	No	xxx mcg	xxxxxx		
		x	Yes				
		x	Yes				
						xx	xxx.x%
Etc							

*Outside the visit window

Immupharma IPP-201101/005 ddMMMyyyy

Listing 16.2.6 Efficacy Response Data

Treatment	Centre/ Patient number	Final Visit	Reduction from baseline in the SLEDAI-2K score of atleast 4 points	No worsening in PGA*	New BILAG A body system score	More than 1 new BILAG B body system score from baseline	Included in primary analysis?	Responser at Week 52?
xxxxxx	xxx-xxxx	Week X	Yes/No	Yes/No	Yes/No	Yes/No	Yes/No	Yes/No
	xxx-xxxx	Week X	Yes/No	Yes/No	Yes/No	Yes/No	Yes/No	Yes/No
	xxx-xxxx	Week X	Yes/No	Yes/No	Yes/No	Yes/No	Yes/No	Yes/No
	Etc							
Etc								

*Worsening defined as an increase in PGA of more than 0.30 point from baseline

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Listing 16.2.7 Adverse Event Listing

IPP-201101

Centre/ Patient number	Adverse Event Preferred Term SOC Term	Date of onset	Study day	Resolution date /ongoing	Duration of adverse event (days)	Outcome	Serious	Severity	Relationship to study drug	Action taken	Action taken with study drug
xxx xxxx	xxxxxxxxx xxxxxxxx xxxxxxx	ddMMMyyyy	xx	ddMMMyyyy	xx	Resolved /Etc	Yes /No	Mild /Moderate /etc	Not related /Related	None /Concomitant medication /Other	None /Discontinued /Etc
	xxxxxxxxx xxxxxxxx xxxxxxx*	ddMMMyyyy	xx	ddMMMyyyy	xx	Resolved /Etc	Yes /No	Mild /Moderate /etc	Not related /Related	None /Concomitant medication /Other	None /Discontinued /Etc
	Etc										
Etc											

*Adverse event classifed as an anaphylactic, anaphylactoid, or drug hypersensitivity reaction

Repeat for Placebo

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Listing 16.2.8.1 Laboratory Measurements: Serum Chemistry

Treatment	Parameter	Centre/ Patient number	Visit	Sample date	Sample time	Standard Result	Standard Unit	Reference range	Is result outside reference range or is test not done?	Clinically significant?
xxxxxx	Calcium	xxx-xxxx	xxxx	ddMMMyyyy	hh:mm	xxx.xx	xxxx	xxx.xx, xxx.xx	Within range/ Outside range/ Test not done	Yes/No
			xxxx	ddMMMyyyy	hh:mm	xxx.xx	xxxx	xxx.xx, xxx.xx	Within range/ Outside range/ Test not done	Yes/No
		xxx-xxxx	xxxx	ddMMMyyyy	hh:mm	xxx.xx	xxxx	xxx.xx, xxx.xx	Within range/ Outside range/ Test not done	Yes/No
		Etc								
	Phosphate	xxx-xxxx	xxxx	ddMMMyyyy	hh:mm	xxx.xx	xxxx	xxx.xx, xxx.xx	Within range/ Outside range/ Test not done	Yes/No
			xxxx	ddMMMyyyy	hh:mm	xxx.xx	xxxx	xxx.xx, xxx.xx	Within range/ Outside range/ Test not done	Yes/No
Etc										

*Outside the visit window

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This layout also applies to:

Listing 16.2.8.2 Laboratory Measurements: Haematology

Listing 16.2.8.3 Laboratory Measurements: Urinalysis

Immupharma IPP-201101/005 ddMMMyyyy

Listing 16.4.1 Final Status

Treatment	Centre/ Patient number	First dose date	Last dose date	Completed treatment	Primary reason for discontinuation
xxxxxx	xxx-xxxx	ddMMMyyyy	ddMMMyyyy	Yes/No	xxxxxxxxxxxxxxxxxxx
	xxx-xxxx	ddMMMyyyy	ddMMMyyyy	Yes/No	xxxxxxxxxxxxxxxxxxx
	xxx-xxxx	ddMMMyyyy	ddMMMyyyy	Yes/No	xxxxxxxxxxxxxxxxxxx
	xxx-xxxx	ddMMMyyyy	ddMMMyyyy	Yes/No	xxxxxxxxxxxxxxxxxxx

Etc

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Immupharma IPP-201101/005 ddMMMyyyy

Listing 16.4.2 Visit Dates

Treatment	Centre/ Patient number	Visit	Date
xxxxxx	xxx-xxxx	xx	ddMMMyyyy
		xx	ddMMMyyyy
		xx*	ddMMMyyyy
		xx	ddMMMyyyy

Etc

*Outside the visit window

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Listing 16.4.3.1 Inclusion Criteria

Criterion No.	Definition of Criterion
1	The patient is a man or woman between 18 and 70 years of age with an established diagnosis of SLE as defined by ACR Classification Revised Criteria. The diagnosis is fulfilled provided that at least 4 criteria are met.
2	The patient has a positive test result for ANA at screening (titer must be at least 1:80 [by human epithelial cell tumor line (HEp-2) ANA assay]) and/or a positive test result for antidsDNA Ab at screening (value must be 30 IU/mL or more by enzyme-linked immunosorbent assay [ELISA]).
3	Written informed consent is obtained.
4	Female and males receiving IPP-201101 and their female partners must use a highly effective contraceptive during treatment and for 30 days after discontinuation of study drug treatment. Women must be surgically sterile, 2 years postmenopausal, or, if of childbearing potential, use a highly effective method of contraception. Men and their partner must have highly effective accepted method of contraception, Single barrier/Double barrier and spermicides are not acceptable methods of contraception. Highly effective methods of contraception include, true abstinence, intrauterine device (IUD), or hormonal contraception associated with inhibition of ovulation (oral, transdermal, implanted, and injected), intrauterine hormone-releasing system (IUS), bilateral tubal occlusion, vasectomised partner. True abstinence is defined when this is in line with the preferred and usual lifestyle of the subject. [Periodic abstinence (e.g., calendar, ovulation, symptothermal, post-ovulation methods), declaration of abstinence for the duration of a trial, and withdrawal are not acceptable methods of contraception]
Etc	

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Programming Note: The list of criteria will be presented on the first page of the listing. Subject data will start on page 2.

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Listing 16.4.3.1 Inclusion Criteria

Treatment	Centre/Patient number	Visit	Criteria								
			1	2	3	4	5	6	7	8	9
xxxxxx	xxx-xxxx	xxxx	Yes/No	Yes/No	Yes/No	Yes/No	Yes/No	Yes/No	Yes/No	Yes/No	Yes/No
	xxx-xxxx	xxxx*	Yes/No	Yes/No	Yes/No	Yes/No	Yes/No	Yes/No	Yes/No	Yes/No	Yes/No
	xxx-xxxx	xxxx	Yes/No	Yes/No	Yes/No	Yes/No	Yes/No	Yes/No	Yes/No	Yes/No	Yes/No
	xxx-xxxx	xxxx	Yes/No	Yes/No	Yes/No	Yes/No	Yes/No	Yes/No	Yes/No	Yes/No	Yes/No

Etc

*Outside the visit window

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This layout also applies to:

Listing 16.4.3.2 Exclusion Criteria

Programming Note: Adjust number of columns according to number in CRF. If too many criteria to fit, split into listings Part 1 and Part 2

Immupharma IPP-201101/005 ddMMMyyyy

Listing 16.4.4.1 Medical History

Treatment	Centre/ Patient number	Condition SOC PT	Start date	End date / Ongoing	Currently treated?	Severity	Intermittent
xxxxxx	xxx-xxxx	xxxxxxxxxxxxx xxxxxxxxxxx xxxxxxxxxx	ddMMMyyyy	ddMMMyyyy / Ongoing	Yes/No	Mild/ Moderate/ Severe/ Life-threatening	Yes/No
		xxxxxxxxxxxxx xxxxxxxxxxx xxxxxxxxxx	ddMMMyyyy	ddMMMyyyy / Ongoing	Yes/No	Mild/ Moderate/ Severe/ Life-threatening	Yes/No
Etc							

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Immupharma IPP-201101/005 ddMMMyyyy

Listing 16.4.4.2 SLE Disease History

Treatment	Centre/ Patient number	Date of SLE Diagnosis	Date of last SLE flare known?	Date of last SLE flare?	Has patient been hospitalised for SLE related illnesss?	Date of hospitalisation
xxxxxx	xxx-xxxx	ddMMMyyyy	Yes/ No/ Not Applicable	ddMMMyyyy	Yes/No	ddMMMyyyy
	xxx-xxxx	ddMMMyyyy	Yes/ No/ Not Applicable	ddMMMyyyy	Yes/No	ddMMMyyyy
	xxx-xxxx	ddMMMyyyy	Yes/ No/ Not Applicable	ddMMMyyyy	Yes/No	ddMMMyyyy

Etc

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Immupharma IPP-201101/005 ddMMMyyyy

Listing 16.4.4.3 BILAG Historical Disease Assessment

Treatment	Centre/ Patient number	Date of assessment	Cardiorespiratory score	Constitutional score	Gastrointestinal score	Haematological score	Mucocutaneous score	Musculoskeletal score	Neuropsychiatric score	Ophthalmic score	Renal score	BILAG total numeric score
xxxxxx	xxx-xxxx	ddMMMyyyy	xx	xx	xx	xx	xx	xx	xx	xx	xx	xx
	xxx-xxxx	ddMMMyyyy	xx	xx	xx	xx	xx	xx	xx	xx	xx	xx
	xxx-xxxx	ddMMMyyyy	xx	xx	xx	xx	xx	xx	xx	xx	xx	xx
Etc												

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This layout also applies to:
Listing 16.4.5.6 Raw Efficacy Data: BILAG (Programming note: add column for 'Visit')

Programming note: if column labels are not fitting on one page, abbreviate 'Cardiorespiratory' to CR, 'Gastrointestinal' to GI etc as necessary. All abbreviations should be included in a footnote e.g. CR = Cardiorespiratory; GI = Gastrointestinal; etc

Immupharma IPP-201101/005 ddMMMyyyy

Listing 16.4.5.1 Raw Efficacy Data: SRI

Treatment	Centre/ Patient number	Visit	SLEDAI-2K Score	PGA Score	New Bilag A Score from baseline	More than 1 BILAG B score from baseline	SRI response	SRI-5 response	SRI-6 response
xxxxxx	xxx-xxxx	xx	xx	xx	Yes/No	Yes/No	Yes/No	Yes/No	Yes/No
		xx*	xx	xx	Yes/No	Yes/No	Yes/No	Yes/No	Yes/No
		xx	xx	xx	Yes/No	Yes/No	Yes/No	Yes/No	Yes/No
		xx	xx	xx	Yes/No	Yes/No	Yes/No	Yes/No	Yes/No
Etc									

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Listing 16.4.5.2 Raw Efficacy Data: 28 Joint Count Examination for Pain and Tenderness

Treatment	Centre/ Patient number	Visit	Was 28 joint count exam performed?	Joint	Right			Left		
					Tenderness	Swelling	Not done	Tenderness	Swelling	Not done
xxxxxx	xxx-xxxx	xx	Yes/No	Shoulder	Not Tender/ Tender	None/ Detectable		Not Tender/ Tender	None/ Detectable	
				Elbow	Not Tender/ Tender	None/ Detectable		Not Tender/ Tender	None/ Detectable	
				Wrist	Not Tender/ Tender	None/ Detectable		Not Tender/ Tender	None/ Detectable	
				Etc						
		xx*	Yes/No	Shoulder	Not Tender/ Tender	None/ Detectable		Not Tender/ Tender	None/ Detectable	
		Etc								
Etc										

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Immupharma IPP-201101/005 ddMMMyyyy

Listing 16.4.5.3 Raw Efficacy Data: SDI

Treatment	Centre/ Patient number	Visit	Was SDI performed?	Date of assessment	Any items present?	Organ System	Item	Score	Total Score
xxxxxx	xxx-xxxx	xx	Yes/No	ddMMMyyyy	Yes	xxxxxxxx	xxxxxxxx	xx	
						xxxxxxxx	xxxxxxxx	xx	
									xxx
		xx	Yes/No	ddMMMyyyy	No				xxx
		xx	Yes/No	ddMMMyyyy	Yes	xxxxxxxx	xxxxxxxx	xx	x
Etc									

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Programming note: Only include organ systems/items where patient has answered yes

Immupharma IPP-201101/005 ddMMMyyyy

Listing 16.4.5.4 Raw Efficacy Data: SF-36

Treatment	Centre/ Patient number	Question	Baseline Week 1	Week 12	Week 24	Week 36	Week 52
xxxxxx	xxx-xxxx	Was SF-36 performed?	Yes/No	Yes/No	Yes/No	Yes/No	Yes/No
		Date	ddMMMyyyy	ddMMMyyyy*	ddMMMyyyy	ddMMMyyyy^	ddMMMyyyy
		1	Excellent/ Very good/ Good/ Fair /Poor	Excellent/ Very good/ Good/ Fair /Poor	Excellent/ Very good/ Good/ Fair /Poor	Excellent/ Very good/ Good/ Fair /Poor	Excellent/ Very good/ Good/ Fair /Poor
		2	Much better/ Somewhat better/ About the same/ Somewhat worse/ Much worse	Much better/ Somewhat better/ About the same/ Somewhat worse/ Much worse	Much better/ Somewhat better/ About the same/ Somewhat worse/ Much worse	Much better/ Somewhat better/ About the same/ Somewhat worse/ Much worse	Much better/ Somewhat better/ About the same/ Somewhat worse/ Much worse
		3a	Yes, a lot / Yes, a little/ No	Yes, a lot / Yes, a little/ No	Yes, a lot / Yes, a little/ No	Yes, a lot / Yes, a little/ No	Yes, a lot / Yes, a little/ No
		3b	Yes, a lot / Yes, a little/ No	Yes, a lot / Yes, a little/ No	Yes, a lot / Yes, a little/ No	Yes, a lot / Yes, a little/ No	Yes, a lot / Yes, a little/ No
Etc		Etc					

*Outside the visit window

^Early termination visit has been mapped to the scheduled visit that occurs immediately after termination

Immupharma IPP-201101/005 ddMMMyyyy

Listing 16.4.5.5 Raw Efficacy Data: FACIT Fatigue Scale

Treatment	Centre/ Patient number	Question	Baseline Week 1	Week 12	Week 24	Week 36	Week 52
xxxxxx	xxx-xxxx	Was FACIT Fatigue Scale performed?	Yes/No	Yes/No	Yes/No	Yes/No	Yes/No
		Date	ddMMMyyyy	ddMMMyyyy*	ddMMMyyyy^	ddMMMyyyy	ddMMMyyyy
		HI7	Not at all/ A little bit / Somewhat / Quite a bit / Very much	Not at all/ A little bit / Somewhat / Quite a bit / Very much	Not at all/ A little bit / Somewhat / Quite a bit / Very much	Not at all/ A little bit / Somewhat / Quite a bit / Very much	Not at all/ A little bit / Somewhat / Quite a bit / Very much
		HI12	Not at all/ A little bit / Somewhat / Quite a bit / Very much	Not at all/ A little bit / Somewhat / Quite a bit / Very much	Not at all/ A little bit / Somewhat / Quite a bit / Very much	Not at all/ A little bit / Somewhat / Quite a bit / Very much	Not at all/ A little bit / Somewhat / Quite a bit / Very much
		An1					
		Etc					
Etc							

*Outside the visit window

^Early termination visit has been mapped to the scheduled visit that occurs immediately after termination

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Listing 16.4.5.7 Raw Efficacy Data: SFI

Treatment	Centre/ Patient number	Date of randomisation	Date of assessment	Visit	Flare Classification
xxxxxx	xxx-xxxx	ddMMMyyyy	ddMMMyyyy	xxxx	No flare/ Mild or moderate/ Severe/Not Done
			ddMMMyyyy	xxxx	No flare/ Mild or moderate/ Severe/Not Done
			ddMMMyyyy	xxxx	No flare/ Mild or moderate/ Severe/Not Done
			Etc		
	xxx-xxxx	ddMMMyyyy	ddMMMyyyy	xxxx	No flare/ Mild or moderate/ Severe/Not Done
		ddMMMyyyy	ddMMMyyyy	xxxx	No flare/ Mild or moderate/ Severe/Not Done
Etc					

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Listing 16.4.5.8 Raw Exploratory Efficacy Data: Biomarkers

Treatment	Parameter	Centre/ Patient number	Visit	Sample date	Sample time	Result	Unit
xxxxxx	ANA	xxx-xxxx	xxxx	ddMMMyyyy	hh:mm	xxx.xx	xxxx
			xxxx	ddMMMyyyy	hh:mm	xxx.xx	xxxx
		xxx-xxxx	xxxx	ddMMMyyyy	hh:mm	xxx.xx	xxxx
		Etc					
	Anti-U1-70K snRNP Ab	xxx-xxxx	xxxx*	ddMMMyyyy	hh:mm	xxx.xx	xxxx
			xxxx	ddMMMyyyy	hh:mm	xxx.xx	xxxx
Etc							

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This layout also applies to:

Listing 16.4.5.9 Raw Exploratory Efficacy Data: Cytokine Response

Immupharma IPP-201101/005 ddMMMyyyy

Listing 16.4.6.1 PK Data: IPP-201101 Plasma Concentration

Treatment	Centre/ Patient number	Visit	Timepoint	Sample taken	Sample collection date	Sample collection time	Concentration
xxxxxx	xxx-xxxx	xx	Pre-dose/5 mins post-dose/1 hour post-dose/2 hours post-dose/ 24 hours post-dose	Yes/No	ddMMMyyyy	hh:mm	xx.x
		xx	Pre-dose/5 mins post-dose/1 hour post-dose/2 hours post-dose/ 24 hours post-dose	Yes/No	ddMMMyyyy	hh:mm	xx.x
		xx	Pre-dose/5 mins post-dose/1 hour post-dose/2 hours post-dose/ 24 hours post-dose	Yes/No	ddMMMyyyy	hh:mm	xx.x
		xx*	Pre-dose/5 mins post-dose/1 hour post-dose/2 hours post-dose/ 24 hours post-dose	Yes/No	ddMMMyyyy	hh:mm	xx.x
Etc							

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Immupharma IPP-201101/005 ddMMMyyyy

Listing 16.4.6.2 Immunogenicity Findings

Treatment	Centre/ Patient number	Visit	Sample date	Sample time	Presence of any anti-IPP-201101
xxxxxx	xxx-xxxx	xxxx	ddMMMyyyy	hh:mm	Yes/No
		xxxx	ddMMMyyyy	hh:mm	Yes/No
	xxx-xxxx	xxxx	ddMMMyyyy	hh:mm	Yes/No
	Etc				
	xxx-xxxx	xxxx*	ddMMMyyyy	hh:mm	Yes/No
		xxxx	ddMMMyyyy	hh:mm	Yes/No
Etc					

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Immupharma IPP-201101/005 ddMMMyyyy

Listing 16.4.7 Vital Signs

Treatment	Centre/ Patient number	Visit	Vital signs measured?	Date of assessment	Blood pressure				Pulse		Body temperature	
					Was blood pressure taken?	Arm	Systolic BP (mmHg)	Diastolic BP (mmHg)	Was pulse taken?	Pulse (beats /min)	Was temperature taken?	Temperature (˚C)
xxxxxx	xxx-xxxx	xx	Yes/No	ddMMMyyyy	Yes/No	Left/Right	xxx	xxx	Yes/No	xxx	Yes/No	xx.x
		xx	Yes/No	ddMMMyyyy	Yes/No	Left/Right	xxx	xxx	Yes/No	xxx	Yes/No	xx.x
		xx*	Yes/No	ddMMMyyyy	Yes/No	Left/Right	xxx	xxx	Yes/No	xxx	Yes/No	xx.x
		xx	Yes/No	ddMMMyyyy	Yes/No	Left/Right	xxx	xxx	Yes/No	xxx	Yes/No	xx.x
Etc												

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Immupharma IPP-201101/005 ddMMMyyyy

Listing 16.4.8.1 Complete Physical Examination

Treatment	Centre/ Patient number	Visit	Was physical examination performed?	Weight		Height		Date of assessment	Body system	Status	Abnormality
				Was weight taken?	Weight (kg)	Was height measured?	Height (cm)				
xxxxxx	xxx-xxxx	xx	Yes/No (reason)	Yes/No	xxx.x	Yes/No	xxx.x	ddMMMyyyy	General appearance	Normal/Abnormal NCS/ Abnormal CS/ Not done	xxxxxxxxxxxxxx
									Skin	Normal/Abnormal NCS/ Abnormal CS/ Not done	xxxxxxxxxxxxxx
									Etc		
		xx*	Yes/No (reason)	Yes/No	xxx.x	Yes/No	xxx.x	ddMMMyyyy	General appearance	Normal/Abnormal NCS/ Abnormal CS/ Not done	xxxxxxxxxxxxxx
Etc									Etc		

*Outside the visit window

NCS=Not Clinically Significant; CS=Clinically Significant

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Immupharma IPP-201101/005 ddMMMyyyy

Listing 16.4.8.2 Symptom Directed Physical Examination

Treatment	Centre/ Patient number	Visit	Was physical examination performed?	Weight		Date of assessment	Body system	Status	Abnormality
				Was weight taken?	Weight (kg)				
xxxxxx	xxx-xxxx	xx	Yes/No (reason)	Yes/No	xxx.x	ddMMMyyyy	General appearance	Normal/Abnormal NCS/ Abnormal CS/ Not done	xxxxxxxxxxxxxx
							Skin	Normal/Abnormal NCS/ Abnormal CS/ Not done	xxxxxxxxxxxxxx
							Etc		
		xx*	Yes/No (reason)	Yes/No	xxx.x	ddMMMyyyy	General appearance	Normal/Abnormal	xxxxxxxxxxxxxx
Etc							Etc		

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Immupharma IPP-201101/005 ddMMMyyyy

Listing 16.4.9 12-Lead ECG

Treatment	Centre/ Patient number	Visit	Was ECG performed?	Date of assessment	Result	Abnormality	Clinically significant?
xxxxxx	xxx-xxxx	xx	Yes/No	ddMMMyyyy	Normal/ Abnormal	xxxxxxxxxx	Yes/No
		xx	Yes/No	ddMMMyyyy	Normal/ Abnormal	xxxxxxxxxx	Yes/No
		xx*	Yes/No	ddMMMyyyy	Normal/ Abnormal	xxxxxxxxxx	Yes/No
	Etc						
Etc							

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Immupharma IPP-201101/005 ddMMMyyyy

Listing 16.4.10.1 Prior Medications

Treatment	Centre/ Patient number	Therapy ATC Code PT	Type of treatment	Dose	Unit	Frequency	Route	Start date (Stop date/ongoing)	Indication	Is treatment prophylactic?	Related event(s)
xxxxxx	xxx-xxxx	xxxxxxxxxxxxxxx xxxxxxxxxxxxx xxxxxxxxxxx	SLE Treatment: Corticosteroids/ SLE Treatment: Other/ Other	xx.x	xxx	xxx	xxx	ddMMMyyyy (ddMMMyyyy/ongoing)	xxxxxxxxx	Yes/No	MH/AE
		xxxxxxxxxxxxxxx xxxxxxxxxxxxx xxxxxxxxxxx	SLE Treatment: Corticosteroids/ SLE Treatment: Other/ Other	xx.x	xxx	xxx	xxx	ddMMMyyyy (ddMMMyyyy/ongoing)	xxxxxxxxx	Yes/No	MH/AE
		xxxxxxxxxxxxxxx xxxxxxxxxxxxx xxxxxxxxxxx	SLE Treatment: Corticosteroids/ SLE Treatment: Other/ Other	xx.x	xxx	xxx	xxx	ddMMMyyyy (ddMMMyyyy/ongoing)	xxxxxxxxx	Yes/No	MH/AE

Etc

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This layout also applies to:

Listing 16.4.10.2 Concomitant Medications

Immupharma IPP-201101/005 ddMMMyyyy

Listing 16.4.11 Procedures/ Non-Drug Therapies

Treatment	Centre/ Patient number	Were there any procedures/non-drug therapies either prior to or during the study?	Therapy	Start date (Stop date/ongoing)	Indication	Is treatment prophylactic?	Given for Adverse Event?	Pre-existing condition?
xxxxxx	xxx-xxxx	Yes/No	xxxxxxxxxxxxxx	ddMMMyyyy (ddMMMyyyy/ ongoing)	xxxxxxxxx	Yes/No	Yes/No	Yes/No
			xxxxxxxxxxxxxx	ddMMMyyyy (ddMMMyyyy/ ongoing)	xxxxxxxxx	Yes/No	Yes/No	Yes/No
	xxx-xxxx	Yes/No	xxxxxxxxxxxxxx	ddMMMyyyy (ddMMMyyyy/ ongoing)	xxxxxxxxx	Yes/No	Yes/No	Yes/No
			xxxxxxxxxxxxxx	ddMMMyyyy (ddMMMyyyy/ ongoing)	xxxxxxxxx	Yes/No	Yes/No	Yes/No
Etc								

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Immupharma IPP-201101/005 ddMMMyyyy

Listing 16.4.12.1 Raw Suicidality Assessment C-SSRS Baseline

Treatment	Centre/ Patient number	Was C-SSRS performed? (Date)	Category	Question	Response
xxxxxx	xxx-xxxx	Yes/No (ddMMMyyyy)	Suicidal ideation	Wish to be dead	Yes (Reason)/ No
				Non-specific active suicidal thoughts	Yes (Reason)/ No
				Active suicidal ideation with any methods (not plan) without intent to act	Yes (Reason)/ No
				Active suicidal ideation with some intent to act, without specific plan	Yes (Reason)/ No
				Active suicidal ideation with specific plan and intent	Yes (Reason)/ No
			Intensity of ideation	Most severe ideation type (description)	1/2/3/4/5 (xxxxxxxxxx)
				Frequency of thoughts	Less than once a week/ Once a week / 2-5 times in week / Daily or almost daily/ Many times each day
Etc					

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This layout also applies to: Listing 16.4.12.2 Raw Suicidality Assessment C-SSRS Since Last Visit (Programming note: Include a Visit column after Centre/ Patient number column)

Immupharma IPP-201101/005 ddMMMyyyy

Listing 16.4.13 Urine Pregnancy Test

Treatment	Centre/ Patient number	Visit	Date of test	Test done	Reason	Result
xxxxxx	xxx-xxxx	xx	ddMMMyyyy	Yes/No/Not applicable	xxxxxxxxxxxx	Positive/ Negative
		xx	ddMMMyyyy	Yes/No/Not applicable	xxxxxxxxxxxx	Positive/ Negative
		xx*	ddMMMyyyy	Yes/No/Not applicable	xxxxxxxxxxxx	Positive/ Negative
		xx	ddMMMyyyy	Yes/No/Not applicable	xxxxxxxxxxxx	Positive/ Negative

Etc

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Immupharma IPP-201101/005 ddMMMyyyy

Listing 16.4.14 Hemolysis Testing

Treatment	Centre/ Patient number	Visit	Was sample taken?	Sampling date	Sampling time	Is hemolysis suspected/ confirmed?	Coomb's Test	Haptoglobin (units)	Peripheral Smear
xxxxxx	xxx-xxxx	xx	Yes/No	ddMMMyyyy	hh:mm	Yes/No	Positive/Negative		
		xx	Yes/No	ddMMMyyyy	hh:mm	Yes/No	Positive/Negative	xxxx	xxxx
		xx*	Yes/No	ddMMMyyyy	hh:mm	Yes/No	Positive/Negative	xxxx	xxxx
		xx	Yes/No	ddMMMyyyy	hh:mm	Yes/No	Positive/Negative	xxxx	xxxx
	xxx-xxxx	xx	Yes/No	ddMMMyyyy	hh:mm	Yes/No	Positive/Negative		
	xxx-xxxx	xx	Yes/No	ddMMMyyyy	hh:mm	Yes/No	Positive/Negative		
		xx	Yes/No	ddMMMyyyy	hh:mm	Yes/No	Positive/Negative	xxxx	xxxx

Etc

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Programming note: Coombs' test should be populated for all screening visits, but for subsequent visits Coombs' test, haptoglobin and peripheral smear will only be measured if hemolysis was suspected. Therefore, some patients will only have screening results.

Immupharma IPP-201101/005 ddMMMyyyy

Listing 16.4.15 Laboratory Sample Collection

Treatment	Centre/ Patient number	Visit	Analyte	Sample taken	Sampling date	Sampling time
xxxxxx	xxx-xxxx	xx	Serum Chemistry	Yes/No	ddMMMyyyy	hh:mm
			Haematology	Yes/No	ddMMMyyyy	hh:mm
			Urinalysis	Yes/No	ddMMMyyyy	hh:mm
			HBsAg, HCV Ab	Yes/No	ddMMMyyyy	hh:mm
			Serology	Yes/No	ddMMMyyyy	hh:mm
			Immunogenicity	Yes/No	ddMMMyyyy	hh:mm
			Cytokine response	Yes/No	ddMMMyyyy	hh:mm
		xx	Serum Chemistry	Yes/No	ddMMMyyyy	hh:mm
			Haematology	Yes/No	ddMMMyyyy	hh:mm
		xx*				
Etc		xx				

*Outside the visit window

Programming note: Analytes include Serum Chemistry; Haematology; Urinalysis; HBsAg and HCV Ab; Serology tests; Immunogenicity; Cytokine response. Note that not all are collected at all visits.

16 APPENDICES

16.1 STUDY SCHEDULE

	Pretreatment	Treatment										FV/ET
	V1	V2	V3	V4	V5	V6	V7/V8	V9	V10/V11	V12	V13/V14/V15	V16
Procedures and assessments	Screening D −14 to −1	BL/Start study treatment W0	W2	W4	W8	W12	W16/W20	W24	W28/W32	W36	W40/W44/W48[a]	W52[a]
Informed consent	X											
I/E criteria review[b]	X	X										
Medical/psychiatric history	X											
PE	X[c]											X[d]
PE symptom directed[d]		X		X	X	X	X	X	X	X	X	
Clinical laboratory tests (serum chemistry,[e] hematology,[f] urinalysis[g])	X	X		X	X	X	X	X	X	X	X	X
HBsAg, HCV Ab	X											
ANA	X	X		X		X		X		X		X
Anti-dsDNA Ab, C3, C4	X	X		X	X	X	X	X	X	X	X	X
Anti–U1-70K snRNP Ab, anti-Sm Ab, CRP, IgG, IgM, IgE, IgA		X		X		X		X		X		X
Hemolysis tests[h]	X											
Pharmacokinetic samples[i]		X					X[i]		X[i]			
In vitro intracellular and cytokine		X		X				X			X	
Vital signs[k]	X	X	X	X	X	X	X	X	X	X	X	X
Pregnancy test[l]	X	X		X	X	X	X	X	X	X	X	X
12-lead ECG	X											X
Concomitant medication review	X[m]	X	X	X	X	X	X	X	X	X	X[m]	X[m]
Adverse event inquiry[n]	X	X	X	X	X	X	X	X	X	X	X	X
SLEDAI-2K[o]	X	X		X	X	X	X	X	X	X	X	X
BILAG-2004[o]	X	X		X	X	X	X	X	X	X	X	X
28-joint count exam for pain and tenderness		X		X	X	X	X	X	X	X	X	X
SFI	X	X		X	X	X	X	X	X	X	X	X
SDI[o]	X							X				X
SF-36		X				X		X		X		X
PhGA		X		X	X	X	X	X	X	X	X	X
FACIT-Fatigue		X				X		X		X		X
C-SSRS[p]		X		X	X	X	X	X	X	X	X	X
Access IRT	X[q]	X[r]		X	X	X	X	X	X	X	X	X[s]
Study drug administration[t,u]		X		X	X	X	X	X	X	X	X	

Footnotes and abbreviations appear on the next page.

[a] If a patient is withdrawn from the study before completion of 48 weeks of treatment, final procedures and assessments will be performed at the last visit.
[b] The clinical SLEDAI-2K score during screening must be at least 6 for the patient to be enrolled.
[c] Physical examination will include measurement of height at screening only and measurement of body weight at week 52 (or final assessment).
[d] Physical examination symptom directed will include measurement of body weight.
[e] Serum chemistry laboratory parameters will include a comprehensive metabolic panel and creatine phosphokinase.
[f] Hematology laboratory parameters will include complete blood count with differential.
[g] Urinalysis parameters will include urine dipstick, microscopic urinalysis, and spot protein-creatinine ratio.
[h] Coombs' test will be obtained at screening. At subsequent visits, Coombs' test, haptoglobin, and peripheral smear will be obtained if hemolysis is suspected or confirmed.
[i] A blood sample (5 mL) for measurement of IPP-201101 concentrations will be obtained prior to and 5 minutes and 1, 2, and 24 hours after study drug administration at weeks 0, 16, and 32 from patients at selected North American and Western European study centers. A blood sample for measurement of the concentration of IPP-201101 will be obtained from all patients who have a serious adverse event and/or have an adverse event leading to withdrawal from the study.
[j] Anti–IPP-201101 Ab testing will be performed at visit 2 (week 0; baseline/start of study drug treatment), visit 3 (week 2), visit 4 (week 4), visit 6 (week 12), visit 8 (week 20), visit 10 (week 28), visit 12 (week 36), visit 14 (week 44), and the final assessment (or early termination) (visit 16 [week 52]). All samples will be collected prior to administration of study drug at that particular visit. Any patient with a positive test result for anti–IPP-201101 Ab at the final study visit will be followed with additional immunogenicity testing at 8-week intervals until the level returns to baseline value or the levels are judged by the investigator to be chronic, or the patient is lost to follow-up.
[k] Vital signs measurements will include systolic and diastolic blood pressures, pulse, and temperature. The same position and arm should be used each time vital signs are measured for a given patient.
[l] At screening, baseline, weeks 4 through 48, and week 52 (or final assessment), urine pregnancy tests will be performed on all women prior to study drug administration regardless of childbearing potential.
[m] Concomitant medication usage will be obtained from the start of screening. Background therapies for SLE may not change from week 44 to week 52.
[n] Adverse events that are suggestive of anaphylaxis or a drug hypersensitivity reaction will be evaluated as per the Clinical Criteria For Diagnosing Anaphylaxis.
[o] Eligibility will be validated by a central reader for concordance.
[p] C-SSRS will be administered directly to the patient using IRT and assessed using C-SSRS Baseline version at baseline (visit 2) and C-SSRS Since Last Visit version at visits 4 through 16.
[q] At screening, using IRT each patient will be assigned with a 6-digit personal identification screening number.
[r] The IRT will be accessed at baseline/start of study drug treatment for drug kit assignment. The IRT will also assign a 4-digit treatment number. In addition, the IRT will be accessed during the study for drug resupply.
[s] The IRT will be accessed at final visit for study disposition.
[t] Patients will be randomly assigned to receive a 200-mcg dose of IPP-201101 or placebo. IPP-201101 or placebo will be administered subcutaneously every 4 weeks from weeks 0 to 48. Patients who continue to meet the inclusion/exclusion criteria will be assigned a permanent 4-digit unique randomization number using the IRT. The IRT will assign a 4-digit treatment number. The 1st dose of study drug will be administered at baseline (visit 2) after all assessments have been completed. Patients should be monitored for at least 1 hour after study drug administration at visits 2 and 4 and then at the discretion of the investigator.
[u] Study drug may not be administered by the same individual performing the SLEDAI-2K, BILAG-2004, PhGA, SFI, and SDI. These disease activity indices must be completed before study drug is administered (at visits at which study drug is administered).

V=visit; D=day; W=week; BL=baseline; FV=final visit; ET=early termination; I/E=inclusion/exclusion; PE=physical examination; HBsAg=hepatitis B surface antigen; HCV Ab=hepatitis C virus antibody; ANA=antinuclear antibody; anti-dsDNA Ab=anti–double-stranded deoxyribonucleic acid antibody; C3=complement component 3; C4=complement component 4; anti–U1-70K snRNP Ab=anti-uridine rich 70 kilodalton small nuclear ribonucleoprotein particle antibody; anti-Sm Ab=anti–Smith antibody; CRP=C-reactive protein; IgG=immunoglobulin G; IgM=immunoglobulin M; IgE=immunoglobulin E, IgA=immunoglobulin A; Ab=antibody; ECG=electrocardiogram; IRT=Interactive Response Technology; SLEDAI-2K=Systemic Lupus Erythematosus Disease Activity Index 2000; BILAG-2004=British Isles Lupus Assessment Group 2004; exam=examination; SELENA=Safety of Estrogens in Lupus Erythematosus: National Assessment; SLICC/ACR=Systemic Lupus International Collaborative Clinics/American College of Rheumatology; SF-36=Medical Outcome Survey Short Form 36; SFI=Safety of Estrogens in Lupus Erythematosus: National Assessment Flare Index; SDI=SLICC/ACR Damage Index; PhGA=Physician's Global Assessment; FACIT-Fatigue=Functional Assessment of Chronic Illness Therapy–Fatigue Scale; C-SSRS=Columbia-Suicide Severity Rating Scale.