Statistical Analysis Plan

Study Name: IFN-K-002 SAP version & date: v4, 18/Jun/2018

Neovacs

IFN-K-002 (VST123)

A Phase IIb, Randomized, Double-Blind, Placebo-Controlled Study to Evaluate the Neutralization of the Interferon Gene Signature and the Clinical Efficacy of IFNα-Kinoid in Adult Subjects with Systemic Lupus Erythematosus

Version: v4

Date: 18/Jun/2018

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Document version history

Version	Date	Author	Modifications since previous version
V4	18/Jun/2018	Alice Tourneroche	1) Precision on population added for analyses performed on status of IFNα neutralizing antibodies (sections 5.2.4.2, 5.2.4.3.1, 5.2.4.4.5.2, 5.2.5.2) 2) Variable "status of IFNα neutralizing antibodies" and corresponding interactions removed from MMRM. (Variable not relevant for Placebo group). Dependent variable has been updated to percent change from baseline and adjustment on baseline removed (section 5.2.4.2) 3) Cox model adjusted on treatment group added (5.2.4.5.2) 4) Correlation graphes replaced by quantitative and qualitative description due to the nature of the variable (section 5.2.4.5.13
V3	28/May/2018	Alice Tourneroche	5) New period added for analysis of Adverse event and rules for analysis of the occurrence of AE according to the status of IFNα neutralizing antibodies (positive/negative) added (section 5.2.5.2) 6) Analysis on change for ANA removed (results of ANA are qualitative) (section 5.2.4.5.7) 7) Rules added for handling of missing items for SLEDAI-2K and SELENA SLEDAI questionnaires (section 5.3.2.2)

V2	17/May/2018	Alice Tourneroche	8) Main efficacy analyses (both for first and second co-primary endpoints) have been modified. Given its definition, BICLA is only relevant at Week 36, making the model for repeated measures as proposed in SAP version 1 not appropriate. The model for repeated measures has been replaced by the model initially planned in the protocol (Logistic regression). To be consistent with the analysis of the second co-primary endpoint, the main analysis of the first co-primary endpoint has also been replaced by the analysis initially planned in the protocol (ANCOVA). The mixed model for repeated measures has been kept as a sensitivity analysis. For consistency purposes, other models for repeated measures have been removed. 9) Definition of Per Protocol Set has been updated (section 3.3.2) 10) Precisions have been added in the SRI definition (section 4.1.2.1) 4) Analysis on change is Lupus therapy (Proportion of patients with an increase or addition in lupus therapy) has been removed. This analysis is considered as redundant with BICLA analysis. (section 5.2.4.5.4)
V1	26/Feb/2018	Alice Tourneroche	NA for initial release

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Abbreviations and definitions

˚C	Degrees Celsius
ACR	American College of Rheumatology
ACS	American Cancer Society
AE	Adverse Event
ALT	Alanine aminotransferase
ANA	Anti-Nuclear Antibodies
ANCOVA	Analysis of Covariance
Anti-RNP	Anti-Ribonucleoprotein
Anti-SSA	Anti-Sjögren's-syndrome A
Anti-SSB	Anti-Sjögren's-syndrome B
AST	Aspartate aminotransferase
ATC	Anatomical Therapeutic Class
AZA	Azathioprine
BICLA	British Isles Lupus Assessment Group-based Composite Lupus Assessment
BILAG	British Isles Lupus Assessment Group
BMI	Body Mass Index
CI	Confidence Interval
CLASI	Cutaneous Lupus Erythematosus Disease Area and Severity Index
CMV	Cytomegalovirus
CPK	Creatine PhosphoKinase
CRO	Contract Research Organization
CRP	C-Reactive Protein
CS	Clinically Significant
CS	Corticosteroid
CVS	Cardio Vascular System
DNA	Deoxyribonucleic acid
dsDNA	Double-stranded DNA
EBV	Epstein Barr Virus
ECG	Electrocardiogram
eCRF	Electronic Case Report Form
FACIT	Functional Assessment of Chronic Illness Therapy

FAS	Full Analysis Set
FDA	Food and Drug Administration
FU	Follow-Up
GMT	Geometric Mean Titer
HIA	Hemagglutination Inhibition Assay
HCQ	Hydroxychloroquinine
HCV	Hepatitis C Virus
HIV	Human Immunodeficiency Virus
HPV	Human Papillomavirus
HSV	Herpes Simplex Virus
huIFN-α	Human interferon α
ICH	International Conference on Harmonization
iDSMB	Independent Data and Safety Monitoring Board
IFN	Interferon
IFN-K	Interferon α-kinoid
IM	Intramuscular
INR	International Normalized Ratio
ITT	Intention-to-treat
IWRS	Interactive Web Response System
KLH	Keyhole Limpet Hemocyanin
LLDAS	Lupus Low Disease Activity State
Mcg	micrograms
MCID	Minimum Clinically Important Difference
MCS	Mental Component Summary
MedDRA	Medical Dictionary for Regulatory Activities
mL	milliliter
mm	millimeter
MMF	Mycophenolate mofetil
MTX	Methotrexate
NCS	Not Clinically Significant
PCS	Physical Component Summary
PGA	Physician Global Assessment
PP	Per Protocol
PT	Preferred Term

PT	Prothrombin time
PTT	Partial Thromboplastin Time
Q1	First Quartile
Q3	Third Quartile
RBC	Red Blood Cell
RT qPCR	Reverse Transcription quantitative Polymerase Chain Reaction
SAF	Safety Population
SAE	Serious Adverse Event
SAP	Statistical Analysis Plan
SAS®	Statistical Analysis System
SELENA	Safety of Estrogen in Lupus Erythematosus National Assessment
SF-36	Short Form-36
SJC	Swollen Joint Count
SLE	Systemic Lupus Erythematosus
SLEDAI	Systemic Lupus Erythematosus Disease Activity Index-2000
SLICC/ACR-DI	Systemic Lupus International Collaborating Clinics/American College of
SOC	System Organ Class
SRI	SLE Responder Index
TEAE	Treatment Emergent Adverse Event
TESAE	Treatment Emergent Serious Adverse Event
VAS	Visual Analog Scale
VZV	Varicella Zoster Virus
WBC	White Blood Cell
WHO	World Health Organization

1 Introduction

This document is the statistical analysis plan (SAP) for the IFN-K-002 study. Please note that this SAP applies only for the main visit up to week 36 (visit 12). The purpose of this SAP is to provide a comprehensive and detailed description of the statistical analyses that will be carried out to assess the efficacy (biological and clinical) and safety of the study treatment, as outlined in the study protocol version 6, dated 11 Apr 2016. The SAP pre-specifies the statistical approaches to be used and is validated prior to the study database lock and the unblinding of the randomization schedule, to ensure the credibility of the study findings.

This SAP covers the analysis of all data until Week 36. The analysis of the extended follow-up data will be detailed in a separate SAP according to protocol.

2 Highlights from study protocol

2.1 Background/Rationale

Full details of the background and rationale for the study are provided in Section 5 of the protocol version 6.0.

2.2 Study Objectives

2.2.1 Primary objective(s)

The primary objective of this study is to evaluate the neutralization of the IFN gene signature following treatment with IFN-K, as measured by the change from baseline of the expression of IFN-induced genes **and** to evaluate the efficacy of treatment with IFN-K using the British Isles Lupus Assessment Group (BILAG)-based Composite Lupus Assessment (BICLA) response criteria. The study will be considered as positive if a statistically significant better effect of IFN-K compared to placebo is observed on the neutralization of the IFN gene signature and if at least a trend favoring IFN-K is observed on the BICLA response.

2.2.2 Secondary objectives

The secondary objectives of this study are:

- To evaluate the efficacy of treatment with IFN-K using:
  - The SLE Responder Index [(SRI)-4 and above]
  - The SLE Disease Activity Index-2000 index (SLEDAI-2K)
  - The BILAG-2004 index
  - The Safety of Estrogen in Lupus Erythematosus National Assessment-SLEDAI (SELENA-SLEDAI) Flare index
  - The Systemic Lupus International Collaborating Clinics/American College of Rheumatology Damage Index for Systemic Lupus Erythematosus (SLICC/ACR-DI)
  - The Cutaneous Lupus Erythematosus Disease Area and Severity Index (CLASI) in patients with cutaneous lesions at baseline
- To evaluate the immune response induced by IFN-K:

- Anti-IFNα antibody response
- Anti-IFNα antibody neutralizing capacities
- Anti-KLH antibody response

- To assess the safety of IFN-K emulsified with ISA 51 VG

2.2.3 Exploratory objectives

The exploratory objectives of this study are:

- To assess disease activity using:
  - The Physician Global Assessment (PGA) score
  - The 28-Tender and Swollen joint counts
  - A Joint Pain Visual Analog Scale (VAS)
  - The flare description
  - The changes in Lupus therapy
- To assess quality-of-life using:
  - The Short Form-36 (SF-36) questionnaire
  - The Functional Assessment of Chronic Illness Therapy (FACIT) fatigue score.
- To assess biological parameters:
  - Levels of lupus-related serum auto-antibodies and biomarkers
  - Neutralizing Anti-IFNα antibodies towards IFNα subtypes
  - Anti-IFNα and anti-KLH antibody isotyping
  - IFNβ cross neutralization
  - Antibody response to influenza vaccination
- To assess correlations between immune responses, IFN gene signature and clinical responses

2.3 Investigational plan

2.3.1 Study design and randomization

This is a Phase IIb, randomized, double-blind, placebo-controlled, multicenter study assessing intramuscular (IM) administration of IFN-K against an adjuvanted placebo. Study patients are enrolled into one of two treatment groups and allocated with a 1:1 randomization ratio to receive the study product: IFN-K or placebo as outlined below:

- Group 1: IFN-K emulsified in ISA 51 VG
- Group 2: placebo emulsified in ISA 51 VG

The study consists in a main study (double-blind) followed by an Extended Follow up Period (open label).

During the main study, each patient receives two injections of study product (corresponding to 240 mcg of IFN-K or placebo) at three visits during the Induction Period (at Week 0 [Visit 2], Week 1 [Visit 3], and Week 4 [Visit 4]). Each patient is administered one injection of study product (corresponding to 120 mcg of IFN-K or placebo) during the Maintenance Period (at Week 12 [Visit 6] and Week 24 [Visit 9]).

The main study comprises a total of 12 visits occurring over a period of 40 weeks. The study is divided into four periods: a 4-week Screening Period that is performed to determine eligibility of the patients for randomization into the study, a 12-week Induction Period, a 12-week Maintenance Period and a 12-week Follow-up Period.

The Extended Follow up Period applies to all patients who have completed the main study. Then, when the results of the main study are available, only patients who have received IFN-K will continue the Extended Follow-up Period for up to 60 months (240 weeks) after Visit 12 (Week 36).

Treatment allocation at each site is performed using central randomization via an Interactive Web Response System (IWRS). The randomization algorithm was developed using a stochastic minimization with a minimization assignment probability parameter of 0.80. Randomization is minimized on:

- Ethnic Origin: Black, Asian, Caucasian/Hispanic, other
- Age: 18-40 or 41-65 years old
- Presence or absence of renal BILAG at screening
- With or without CS treatment at randomization
- With or without HCQ treatment at randomization
- With or without MMF treatment at randomization

At the time of randomization, the IWRS assigns the patient to a treatment arm and provides the number of the treatment kit for the first injection. The actual kit number administered to the patient is recorded in the eCRF.

2.3.2 Determination of sample size

The primary objective of this study is to evaluate the neutralization of the IFN gene signature following treatment with IFN-K, as measured by the change from baseline of the expression of IFN-induced genes **and** to evaluate the efficacy of treatment with IFN-K using the British Isles Lupus Assessment Group (BILAG)-based Composite Lupus Assessment (BICLA) response criteria. The following assumptions were made for the sample size calculation:

- The error probability for a 2-sided t-test should not exceed 5%;
- The power should be 80% or higher;
- The change of the expression of IFN-induced genes in patients treated with IFN-K is assumed to be -22.6% (data from study IFN-K-001, Lauwerys et al., 2013);
- The change of the expression of IFN-induced genes in patients treated with placebo is assumed to be 10% (data from study IFN-K-001, Lauwerys et al., 2013);
- The common standard deviation of the change is 68 (data from study IFN-K-001, Lauwerys et al., 2013).

The assumptions for the change in expression of IFN gene signature and the standard deviation are based on the original data of study IFN-K-001 as presented in Lauwerys *et al.*, 2013.

With 80 evaluable patients per group i.e. a total of 160 evaluable patients, the study will have a power of 85% to detect a difference of 32.6% in the expression of IFN-induced genes in patients treated with IFN-K compared to patients treated with placebo, assuming that the common standard deviation is 68% and using

a two group t-test with a 0.050 two-sided significance level. Assuming a rate of 10% drop-out patients, 178 patients should be enrolled in order to have 160 evaluable patients at Week 36 (80 evaluable patients in each treatment arm=90% of the enrolled patients).

Assuming a BICLA response of 20.6% in the placebo group and 40.6% in IFN-K treated patients (i.e. an absolute difference of 20%) with 80 evaluable patients per group, there will be a 73% power to detect a difference of 20% in the BICLA response criterion.

The sample size needed to ensure a 80% power to the comparison of BICLA response rates between IFN-K and placebo for different response rates in the placebo arm and varying between groups differences are presented in Figure 2 of the protocol. 97 evaluable patients per group would be needed for a power of 80% to detect a difference of 20% with a placebo response rate of 20.6%.

2.3.3 Study assessments and study plan

Visit	1	2	3	4	5	6	7	8	9	10	11	12	FU1*	FU2*
Week	max -4	0	1	4	8	12	16	20	24	28	32	36	60 108 156 204 252	84 132 180 228 276
		Dose 1 240 mcg	Dose 2 240 mcg	Dose 3 240 mcg		Dose 4 120 mcg			Dose 5 120 mcg					
Informed consent	●													
Demographic data	●													
SLE-specific and general medical history including alcohol, drug, and tobacco use. For US patient ONLY, screening for malignancy within the previous 12 months according to ACS	●													
Complete physical examination[1]	●	●	●	●	●	●	●	●	●	●	●	●	●	●
Gynecological examination[2]	●											●		
ECG (12-lead)	●	●				●			●			●		
Chest X-ray		●										●		

Visit	1	2	3	4	5	6	7	8	9	10	11	12	FU1*	FU2*
Week	max -4	0	1	4	8	12	16	20	24	28	32	36	60 108 156 204 252	84 132 180 228 276
		Dose 1 240 mcg	Dose 2 240 mcg	Dose 3 240 mcg		Dose 4 120 mcg			Dose 5 120 mcg					
Vital signs[3]	●	●	●	●	●	●	●	●	●	●	●	●	●	●
Evaluation of eligibility	●	●												
Randomization		●												
Check contraindications		●	●	●		●			●					
Administration of study product[4]		●	●	●		●			●					
Hematology, coagulation and biochemistry (complete)[5]	●	●		●		●			●			●		
Hematology, coagulation and biochemistry (disease-oriented)[5]					●		●	●		●	●		●	●
Lymphocytes count (Total, CD4+, CD8+)		●				●			●			●	●	●
Viral serology[6]	●													
Anti-IFNα binding antibodies		●		●	●	●	●		●	●		●	●	●

Visit	1	2	3	4	5	6	7	8	9	10	11	12	FU1*	FU2*
Week	max -4	0	1	4	8	12	16	20	24	28	32	36	60 108 156 204 252	84 132 180 228 276
		Dose 1 240 mcg	Dose 2 240 mcg	Dose 3 240 mcg		Dose 4 120 mcg			Dose 5 120 mcg					
Anti-IFNα neutralizing antibodies		●				●	●		●	●		●	●	●
Neutralizing Anti-IFNα antibodies towards IFNα subtypes		●				●	●		●	●		●		●[11]
Anti-IFNα and anti-KLH antibody isotyping		●				●			●			●		
IFNβ cross neutralization		●				●			●			●		
Anti-KLH binding antibodies		●				●	●		●	●		●	●	●
Anti-dsDNA antibodies	●	●				●			●			●	●	●
ANA	●	●				●			●			●	●	●
Other auto-antibodies (anti-Sm, anti-RNP, anti-SSA/Ro, anti-SSB/La, anti-cardiolipin and anti-β_2-glycoprotein I antibodies)		●				●			●			●		●[11]
Inflammatory markers (C3, C4, CH50)	●	●		●	●	●	●		●	●		●	●	●

Visit	1	2	3	4	5	6	7	8	9	10	11	12	FU1*	FU2*
Week	max -4	0	1	4	8	12	16	20	24	28	32	36	60 108 156 204 252	84 132 180 228 276
		Dose 1 240 mcg	Dose 2 240 mcg	Dose 3 240 mcg		Dose 4 120 mcg			Dose 5 120 mcg					
IFN gene signature (RT-qPCR)	●													●
IFN gene signature (Affymetrix)		●				●			●			●		●[11]
Serum pregnancy test[7]	●													
Urine pregnancy test[7]		●	●	●	●	●	●	●	●	●	●	●	●	●
Urine analysis including dipstick and microscopic examination	●	●		●	●	●	●	●	●	●	●	●	●	●
SLEDAI-2K	●	●				●			●			●	●	●
PGA	●	●				●			●			●	●	●
BILAG-2004 index	●	●		●	●	●	●	●	●	●	●	●		
SELENA-SLEDAI flare index		●							●			●	●	●
SLICC/ACR DI		●										●		

Visit	1	2	3	4	5	6	7	8	9	10	11	12	FU1*	FU2*
Week	**max -4**	**0**	**1**	**4**	**8**	**12**	**16**	**20**	**24**	**28**	**32**	**36**	**60 108 156 204 252**	**84 132 180 228 276**
		Dose 1 240 mcg	Dose 2 240 mcg	Dose 3 240 mcg		Dose 4 120 mcg			Dose 5 120 mcg					
28-Tender and Swollen joint counts		●				●			●			●		
Joint Pain VAS		●				●			●			●	●	●
CLASI		●				●			●			●		
SF-36 survey score		●				●			●			●	●	●
FACIT fatigue score		●				●			●			●	●	●
Record prior medication and vaccination	●													
Record concomitant medication		●	●	●	●	●	●	●	●	●	●	●	●	●
Influenza vaccination	As needed from Visit 5 at each influenza season except within 7 days before or after study product administration													
Anti-Influenza antibody response	Should be performed 28 days +/-7 days after each flu vaccination													
Record solicited injection site reactions 1 hour post study product administration[8]		●	●	●		●			●					

Visit	1	2	3	4	5	6	7	8	9	10	11	12	FU1*	FU2*
Week	max -4	0	1	4	8	12	16	20	24	28	32	36	60 108 156 204 252	84 132 180 228 276
		Dose 1 240 mcg	Dose 2 240 mcg	Dose 3 240 mcg		Dose 4 120 mcg			Dose 5 120 mcg					
Record solicited systemic AEs 1 hour post study product administration[9]		●	●	●		●			●					
Provision of diary card for daily recording of solicited AEs by patients[10]		●	●	●		●			●					
Return, checking and transcription of diary card			●	●	●		●			●				
Record all AEs		●	●	●	●	●	●	●	●	●	●	●	●	●

ACR = American College of Rheumatology; ACS = American Cancer Society; AE = Adverse event; ANA = Anti-nuclear antibodies; BILAG = British Isles lupus assessment group; CLASI = Cutaneous lupus erythematosus disease area and severity index; CRP = C-reactive protein; CS = corticosteroids; DNA = Deoxyribonucleic acid; ECG = Electrocardiogram; FACIT = Functional assessment of chronic illness therapy; IFN = Interferon; KLH = Keyhole limpet hemocyanin; PGA = Physician's global assessment; RT qPCR = Reverse transcription quantitative polymerase chain reaction; SELENA = Safety of estrogen in lupus erythematosus national assessment; SF-36 = Short form-36 questionnaire; SLE = Systemic lupus erythematosus; SLEDAI = SLE disease activity index; SLICC = System Lupus International Collaborating Clinics; VAS = Visual analog scale.

[1] Including body temperature, weight and height; height being measured only during screening.

[2] Including examination of the cervix, and detection of high risk HPV (by RT qPCR) on PAP smear; unless performed and documented 3 months prior to the first planned study product administration.

[3] Vital signs include brachial pulse and blood pressure. They will be performed after patient has been in a supine position for 3 minutes. At Visits 2, 3, 4, 6 and 9, vital signs will be performed prior to and 1 hour post study product administration.

[4] 240 mcg study product administration at Visit 2, 3 and 4. 120 mcg study product administration at Visit 6 and 9.

[5] Blood samples are to be taken prior to administration of the study product, when applicable.

- Complete means Hemoglobin, complete blood cell count and differential (Red Blood Cells, White Blood Cells, Neutrophil, Lymphocyte, Platelet), INR, PT, PTT, fibrinogen, serum Urea, serum Albumine, serum creatinine level, serum Total protein, Creatinine clearance GFR, Serum Alanine Aminotransferase, Aspartate Aminotransferase, Alkaline Phosphatase, Coombs test, Circulating Anti-Coagulant, Creatine Phospho Kinase. CD19 counts will be performed at Visit 2.
- Disease oriented means Hemoglobin, complete blood cell count and differential (Red Blood Cells, White Blood Cells, Neutrophil, Lymphocyte, Platelet), INR, PT, PTT, fibrinogen, serum Urea, serum Albumine, serum creatinine level, serum Total protein, Creatinine clearance GFR, Coombs test, Circulating Anti-Coagulant, Creatine Phospho Kinase

[6] Screening virology testing at Visit 1: HBV [HBsAg], HCV, HIV, CMV, VZV, EBV, HTLV 1-2, and HSV-1, HSV-2.

[7] Serum and urine pregnancy tests for female patients of childbearing potential only.

[8] Solicited injection site reactions will be recorded by study staff 1 hour post study product administration by asking the patient about his/her perception of pain and itching sensation and via visual assessment of redness, swelling and induration.

[9]Solicited systemic AE will be recorded by study staff 1 hour post study product administration, in particular headache, fatigue, myalgia, nausea, and fever.

[10] Daily recording by patients of the presence or absence and severity of solicited local and systemic reactions on the day of the injection and the six subsequent days (i.e., 7 days in total)

[11] At extended follow-up, to be tested at patient's last visit only.

* The extended follow-up period will last for 5 years (i.e. 60 additional months, 69 months since 1st injection), with one visit every 6 months.

3 Analysis datasets

3.1 Reasons for excluding patients from analysis datasets

All deviations will be reviewed and adjudicated as either major or minor during the blind data review meeting before database lock and code break.

3.1.1 Major protocol deviations

Major protocol deviations leading to patient's exclusion from the Per Protocol population are defined as deviations liable to prevent or change the interpretation of the results of the primary efficacy analysis of the study. The following deviations may be considered as major (the list is not exhaustive and maybe modified at the time of the blind review):

- Non-compliance with the inclusion or non-inclusion criteria
- non-compliance with the randomization procedure
- non-compliance with study treatment
- intake of forbidden medication

3.1.2 Minor protocol deviations

Deviations not identified as 'major' will be considered to be minor.

3.2 Study treatment discontinuations - Study discontinuations

3.2.1 Study treatment discontinuations

If any of these AEs or conditions occur during the study, the patient must not receive additional doses of study product but should be encouraged to continue other study procedures until at least Week 36. The patient must be followed until resolution of the event or condition:

- Bronchospasm or anaphylactic reaction following the administration of study product.
- Any confirmed or suspected immunosuppressive or immunodeficient condition.
- Medications leading to discontinuation of study product (list in Protocol Section 10.7.2).

3.2.2 Study discontinuations

A patient is considered to have completed the main study when he or she completes the final assessment visit (Visit 12 at Week 36), A study termination eCRF page should be completed for every patient who received study product, whether or not the patient completed the study (applicable for both main study and Extended Follow up study). Therefore, study termination page will not be available for patients who achieved visit 12 (week 36) and entered Extended Follow-up period during the double blind period.

If a patient is discontinued prematurely at any time after entering the study, the Investigator makes every effort to see the patient and complete an early termination visit.

The reason for any early discontinuation should be indicated on the termination page. The primary reason for a patient withdrawing prematurely should be selected from the following standard categories of early termination:

- Inclusion not met / Exclusion criteria met
- Adverse event
- Protocol deviation
- Medical decision: Clinical or laboratory events occurred that in the medical judgment of the Investigator for the best interest of the patient are grounds for discontinuation. This includes serious and non-serious AEs regardless of relation to study medication.
- Death: The patient died.
- Pregnancy: The patient became pregnant.
- Withdrawal of Consent: The patient desired to withdraw from further participation in the study in the absence of an Investigator-determined medical need to withdraw. If the patient gave a reason for withdrawal, it should be recorded in the eCRF.
- Lost to Follow-Up: The patient stopped coming for visits, and study personnel were unable to contact the patient.
- Other: The patient was terminated for a reason other than those listed above, such as termination of the study by the Sponsor.

3.3 Analysis dataset definitions

3.3.1 Full Analysis Set (FAS)

The primary efficacy analysis population is the Full Analysis Set (FAS). It will include all randomized patients who received at least one dose of the study product (IFN-K or placebo). This population will be analyzed according to the result of the random treatment assignment.

3.3.2 Per-protocol (PP) dataset

The PP population will be a subset of the FAS including all randomized patients having received at least one dose of study product (IFN-K or placebo), and who complied with the procedures defined in the protocol (*i.e.*, who did not have major protocol deviations that could impact the primary endpoint analysis).

In addition, patients with at least one of the following cases will be excluded from the PP population:

- missing IFN gene signature at baseline
- missing IFN gene signature at week 24 and week 36
- missing BICLA at week 36, i.e:
  - all missing BILAG at baseline
  - or missing BILAG at week 36 corresponding to a BILAG A or B at baseline
  - or all missing BILAG at week 36

- or missing SLEDAI-2K at baseline
- or missing SLEDAI-2K at week 36
- or missing PGA on VAS 100 mm at baseline
- or missing PGA on VAS 100 mm at week 36

- less than 4 doses of study product received (out of 5)

This will also be the population used for the immunogenicity, autoantibodies and biomarkers analyses.

3.3.3 Safety (SAF) dataset

The safety population (SAF) will include all patients who received at least one dose of study product (placebo or IFN-K). The patients in the SAF are analyzed according to the treatment actually received. This will be the population used for the safety analysis.

4 Endpoints for analysis

4.1 Efficacy endpoints

4.1.1 Primary efficacy endpoint(s)

Two co-primary endpoints are evaluated in the trial:

- Change from baseline in the expression of IFN-induced genes at Week 36.
- Response to treatment with IFN-K as measured by the British Isles Lupus Assessment Group (BILAG)-based Composite Lupus Assessment (BICLA) response criteria at Week 36:
  - All BILAG A scores at baseline improve to B/C/D and all BILAG B scores improve to C/D at Week 36

  and

  - No BILAG worsening in other body systems: no new BILAG A or ≥ 2 new BILAG B scores at Week 36

  and

  - No worsening in SLEDAI-2K total score at Week 36 compared with baseline

  and

  - No deterioration in PGA (< 10% worsening) on VAS 100 mm at Week 36 compared with baseline

  and

  - No addition or increased dose level of anti-malarial drugs or immunosuppressive drugs or corticosteroids between Week 24 and Week 36 (this criterion will be identified by medical review)

4.1.2 Secondary efficacy endpoints

4.1.2.1 Clinical Secondary Endpoints

- Response to treatment with IFN-K, as measured by the SLE Responder Index (SRI)-4 response criteria at Week 36:
  - Reduction ≥ 4 points in SELENA-SLEDAI at week 36 compared with baseline

  and
  - No new BILAG A at Week 36

  and
  - No more than 1 new BILAG B at Week 36

  and
  - No deterioration at Week 36 in PGA (< 10% worsening) on VAS 100 mm compared with baseline
- Response to treatment with IFN-K, as measured by the composite SLE Responder Index (SRI)-4 response criteria at Week 36:
  - Same criteria as above

  and
  - Sustained reduction in oral corticosteroids (≤ 5 mg and ≤7.5mg/day) at Week 36 (these criteria will be identified by medical review)
- Response to treatment with IFN-K, as measured by SLEDAI response, defined as a reduction of the SLEDAI-2K score of at least 4 points at Week 36 compared to baseline
- Response to treatment with IFN-K, as measured by BILAG grade changes by body system
- Response to treatment with IFN-K, as measured by Incidence of SLE flare (SELENA SLEDAI flare index. BILAG flares)
- Response to treatment with IFN-K, as measured by SLICC/ACR-DI
- Response to treatment with IFN-K, as measured by Cutaneous LE Disease Area and Severity Index (CLASI)
- Response to treatment with IFN-K, as measured by LLDAS (Franklin *et al*, 2016)

4.1.2.2 Immunogenicity Secondary Endpoints

- Anti-IFNα binding antibody titers
- Anti-IFNα neutralizing antibody titers
- Anti-KLH binding antibody titers

4.1.3 Exploratory efficacy endpoints

- Evaluation of clinical response by assessing disease activity using:
  - PGA scores,
  - number of SLE flares,
  - Time to first SLE flare in patients post randomization,

- 28-Tender and Swollen Joint Counts (SJC),
- Joint Pain VAS
- the incidence of an increase or addition in lupus therapy (intensification and/or add of drugs). (this criterion will be identified by medical review)

- Quality of life using:
  - FACIT fatigue score
  - Changes in the SF-36 score: Physical Component Summary (PCS) and Mental Component Summary (MCS) scores
- Evaluation of biological response by assessing:
  - Changes in the levels of auto-antibodies (ANA, anti-dsDNA, anti-Smith antigen [anti-Sm], anti-RNP, anti-SSA/Ro, anti-SSB/La, anti-cardiolipin, and anti-β2-glycoprotein I antibodies)
  - Changes in levels of biomarkers (C3, C4, CH50)
  - Anti-IFNα and anti-KLH antibody isotyping
  - Neutralizing Anti-IFNα antibodies towards IFNα subtypes
  - IFNβ and IFNω cross neutralization
  - Anti-Hemagglutinin antibody response

4.2 Safety endpoints

The safety and tolerability will be evaluated by the monitoring of the occurrence of AEs and SAEs, clinical laboratory results, physical examinations, vital signs, electrocardiogram and concomitant medications.

4.2.1 Adverse events

Adverse events (AE) will be coded using the MedDRA Version 18 and will be classified by Preferred Term (PT) and System Organ Class (SOC).

A Treatment Emergent Adverse Events (TEAE) will be defined as any adverse event that occurs from the time of first study treatment dose administered to the patient until last study visit.

An SAE is defined as an AE that meets one of the following conditions:

- Death.
- Life threatening event (defined as any AE that places the patient, in the view of the Investigator, at immediate risk of death from the event as it occurred, i.e., it does not include an event that had occurred in a more severe form, might have caused death).
- An event requiring inpatient hospitalization or prolongation of existing hospitalization during the period of protocol defined surveillance.
- Results in a persistent or significant disability/incapacity.
- Congenital anomaly or birth defect in the offspring of a study participant.
- Any other important medical event that may not result in death, be life threatening, or require hospitalization, may be considered a serious adverse experience when, based upon appropriate

medical judgment, the event may jeopardize the patient and may require medical or surgical intervention to prevent one of the outcomes listed above. Examples of such medical events include allergic bronchospasm requiring intensive treatment in an emergency room or at home, blood dyscrasias or convulsions that do not result in inpatient hospitalization, or the development of drug dependency or drug abuse.

Tolerability/safety will be assessed over the 36 weeks study period. The analysis will focus on:

- Occurrence and intensity of any solicited local and systemic reactions during a 7-day follow-up period (i.e. day of study product administration and 6 subsequent days) after each IFN-K or placebo dose
- Occurrence, intensity and relationship of unsolicited AEs occurring throughout the study period
- Occurrence, intensity and relationship of all SAEs occurring throughout the study period
- Rate and severity of viral infections
- Flares (time of occurrence in relation to product administration)

4.2.2 Laboratory endpoints

The following clinical laboratory tests are to be performed on collected blood samples:

- Clinical chemistry: Alanine Aminotransferase (ALT), Aspartate Aminotransferase (AST), Alkaline phosphatase, Creatine phosphokinase (CPK), Creatinine, Urea, Total proteins, Albumin, Circulating Anti-Coagulant
- Hematology: Complete blood cell count and differential (RBC, WBC, Lymphocytes, Neutrophils, Platelets); CD19; Total lymphocytes, CD4+, CD8+, Hemoglobin
- Coagulation: INR, Prothrombin time (PT), Partial Thromboplastin Time (PTT), Fibrinogen, Coomb's test (direct)
- Urine: RBC, WBC, Urinary casts, Albumin, Creatinine, Protein concentration, Albumin/Creatinine ratio, Protein/Creatinine ratio
- Dipstick Urinalysis: pH, glucose, etc

Hematology, clinical chemistry, coagulation and urine analysis data will be graded at each scheduled assessment by Modified WHO Toxicity Scale (See Protocol Appendix 10).

Hematological, clinical chemistry and coagulation safety will be based at each visit on raw value, percent change from baseline and categories (grade or normal, Abnormal CS/N, Abnormal CS/AE, Abnormal NCS).

4.2.3 Other safety endpoints

4.2.3.1 Physical examinations

A complete physical examination is performed at each visit.

The complete physical examination comprises measurements of oral body temperature (in ˚C), weight, height (Visit 1 only), and routine medical examination of body systems (constitutional, mucocutaneous, neuropsychiatric, musculoskeletal, cardiorespiratory, gastrointestinal, ophthalmic, renal or other).

Safety will be based on abnormalities (normal, Abnormal CS/N, Abnormal CS/AE, Abnormal NCS) in the body systems and raw value for height, weight and body temperature.

4.2.3.2 Vital signs

Vital signs are evaluated during each visit. Vital signs include brachial pulse rate and systolic and diastolic blood pressures. These recordings are made after at least 3 minutes of rest, measured in the supine position. Recordings are made prior to and 1-hour post study product administration, when applicable.

Safety will be based at each visit on raw value and change from baseline.

4.2.3.3 Electrocardiograms (ECG

Standard 12-lead ECG recordings are made during the Screening Visit, Visit 2 (Week 0), Visit 6 (Week 12), Visit 9 (Week 24) and Visit 12 (Week 36).

Safety will be based on abnormalities (normal, Abnormal CS/N, Abnormal CS/AE, Abnormal NCS).

4.2.3.4 Concomitant medications

Safety will also be assessed based on the analysis of Concomitant medications coded according to the version WHO-DDE 1Q2015 of the WHO-Drug dictionary.

Medication are considered as concomitant if their start date >= date of first administration or if ongoing at the time of the first administration.

All others will be considered “Prior”.

5 Statistical and Analytical Methods

5.1 General considerations

The statistical analyses are performed in accordance with the ICH E9 guideline and will be based on the pooled data from the individual study sites, unless otherwise stated.

The statistical analyses will be performed by an external Contract Research Organization (CRO), Venn Life Sciences, under the responsibility of the Sponsor.

5.1.1 Presentation of results

The following descriptive statistics will be presented:

- For quantitative variables: number of available values, number of missing values, mean, standard deviation, median, Q1 (or first quartiles), Q3 (third quartiles), minimum, maximum values. When

relevant, confidence intervals will be calculated for the mean (Student CI) or the median (Hahn & Meeker 1991).

- For qualitative variables: number of available values, number of missing values, number and percentage of observations in each category of the variable. Except if otherwise specified, percentages will be calculated using the number of available values as denominator (i.e., not including missing values). When relevant, confidence intervals of proportions will be calculated using the Wald method or Clopper-Pearson if Wald is not applicable.

5.1.2 Significance testing and estimation

Two-sided 95% CIs for two-sample differences in means/proportions between the treated and control groups and one-sample means/proportions will be calculated using:

- The normal-approximation method for GMT and other continuous endpoints,
- The "score" method without the continuity correction (Newcombe, 1998a) for binary endpoints.

Unless specified otherwise in the SAP, statistical tests will be two-sided at a 5% significance level.

5.2 Planned analysis

The lists of statistical Tables, Figures and Listings are provided in Section 10.

5.2.1 Demographics and baseline characteristics

The following demographics variables will be summarized by treatment group on the SAF and then in the FAS, if the two analysis sets are different. (Statistical table 14.1.4):

- Age (continuous and class [18-40], [41-65])
- Gender
- Ethnic origin (see section 9 Derived data)
- Presence or absence of renal BILAG at screening
- With or without CS treatment at randomization
- With or without HCQ treatment at randomization
- With or without MMF treatment at randomization
- With or without MTX treatment at randomization
- With or without AZA treatment at randomization

The following baseline characteristics will be summarized by treatment group on the FAS set:

- Alcohol, drug and tobacco use (Statistical table 14.1.5)
- Vital signs at baseline (Statistical table 14.1.6)
- ECG at baseline (Statistical table 14.1.7)
- Physical examination (including Weight, Height and BMI) at baseline (Statistical table 14.1.8)

- Laboratory test: Haematology (Statistical table 14.1.9), clinical chemistry (Statistical table 14.1.10), Coagulation (Statistical table 14.1.11) and Urinalysis (Statistical table 14.1.12) at baseline
- Laboratory test abnormalities (grade or normal, Abnormal CS/N, Abnormal CS/AE, Abnormal NCS): Haematology abnormalities (Statistical table 14.1.13), Chemistry abnormalities (Statistical table 14.1.14), Coagulation abnormalities (Statistical table 14.1.15) and Urinalysis abnormalities (Statistical table 14.1.16) at baseline
- Viral serology, autoantibodies and inflammatory markers at baseline
- Gynecological examination (Cytological examination and HPV on PAP smear) (Statistical table 14.1.20)
- Efficacy variable at baseline (IFN score, SLEDAI-2K score, BILAG global score, SELENA-SLEDAI flare index, CLASI, SLICC/ACR-DI, PGA score, 28-Tender and Swollen Joint Counts, Joint Pain VAS, SF-36 (Physical Component Summary (PCS) and Mental Component Summary (MCS) scores), FACIT (Statistical table 14.1.21)

All demographics data, Alcohol, drug and tobacco use data and gynecological examination data of each patient will be reported in listing 16.2.4.1, 16.2.4.2 and 16.2.4.3 respectively.

Viral serology and pregnancy test data will be listed in Listing 16.2.4.10 and 16.2.4.11.

The definition of baseline is provided in section 5.4.1.

5.2.2 Patient disposition and study discontinuations

Patient disposition will be described (Statistical table 14.1.1). The following variables will be tabulated:

- Number of patients screened
- Number of randomized patients, total and per treatment group
- Number of randomized patient by visit, total and per treatment group
- Number of randomized patients who completed the study as planned (until V12), total and by treatment group
- Number of randomized patients who prematurely discontinued the study (before V12), total and by treatment group
- Reasons for study discontinuations, total and by treatment group

Patient disposition information will be provided in Listing 16.2.1.1. Screen failure will be included in this listing. The reason of screen failure will be presented.

Inclusion and exclusion criteria will be listed in Listings 16.2.1.2 and 16.2.1.3.

The numbers of patient within each dataset (SAF, FAS, PP), globally and by treatment group, will be provided (Statistical table 14.1.2.1, Listing 16.2.3.1) along with reasons for exclusion from the FAS and PP populations (Statistical table 14.1.2.2 and 14.1.2.3 respectively). Reasons for exclusion from the FAS and PP populations will also be provided in Listing 16.2.3.2, according to ICH E3.

All protocol deviations classified during the blinded data review meeting according to definitions provided in section 3.1.1 (Major deviations) and 3.1.2 (Minor deviations) will be tabulated by treatment group for

the FAS population (Statistical table 14.1.3). All major and minor protocol deviations will also be provided in Listing 16.2.2, according to ICHE3.

5.2.3 Medical history – Previous medications

Time since diagnosis (year) and ACR criteria will be presented for SLE medical history (Statistical table 14.1.22 and Listing 16.2.4.4).

SLE flare history will be presented by body system (Statistical table 14.1.23 and Listing 16.2.4.5)

General Medical & Surgical history will be presented by SOC & PT by treatment group (Statistical table 14.1.24).

Medical and Surgical history for each patient will be reported in Listing 16.2.4.6.

Permitted, Prohibited and Previous medications will be presented by ATC code and Preferred Name by treatment group (Statistical tables 14.1.25 to 14.1.27).

Permitted and Prohibited medications for each patient will be reported in Listings 16.2.4.7 and 16.2.4.8.

5.2.4 Efficacy analyses

5.2.4.1 Primary efficacy analysis

Descriptive statistics for IFN gene signature (first co-primary endpoint) at each visit and % of change from baseline by treatment group will be presented (Statistical tables 14.2.1.1.1 and 14.1.1.2).

The first co-primary efficacy endpoint - Percent of change from baseline after 36 weeks of treatment in the expression of IFN-induced genes – will be analyzed using an ANCOVA model (Statistical table 14.2.1.1.3).

The dependent variable will be the percentage of change from baseline in the expression of IFN-induced genes with the treatment as independent variable. The minimization factors used for randomization – Ethnic origin (see section 9 Derived data), Age group, Presence or absence of renal involvement according to BILAG at screening, corticosteroid treatment, hydroxychloroquine treatment and MMF treatment at screening - will be included as covariates. See section 5.3.2 for handling of missing data.

All IFN gene signature data will be listed in Listing 16.2.6.1.1.

Descriptive statistics for the response to treatment according to BICLA (second co-primary efficacy endpoint) at Week 36 will be presented by treatment group (Statistical table 14.2.1.2.1)

The second co-primary efficacy endpoint - response to treatment according to BICLA - will be analyzed using a logistic regression with the response rate as dependent variable and treatment as independent variable, while adjusting for the minimization factors used for randomization, as listed for the analysis of the first primary end-point (Statistical table 14.2.1.2.2).

Response to treatment according to BICLA will be listed in Listing 16.2.6.1.2

First, the hypothesis with respect to the change from baseline in the expression of IFN-induced genes will be tested at an error probability of 5% for a 2-sided test. If and only if this Null-hypothesis can be rejected, the hypothesis with respect to the response to treatment according to BICLA will be tested also at an error probability of 5% for a 2-sided test.

The study will be considered as positive if a statistically significant better effect of IFN-K compared to placebo is observed on the neutralization of the IFN gene signature (i.e. the first co-primary endpoint) and if at least a trend favoring IFN-K is observed on the BICLA response (i.e. the second co-primary endpoint). An observed 10% difference will be considered a marginal effect and a 15% difference will be considered as an important effect, whatever the statistical significance observed.

The primary efficacy analysis will be performed on the FAS set.

5.2.4.2 Sensitivity and supplementary analyses

The primary efficacy analysis will be repeated on the PP set as a supplementary analysis (Statistical tables 14.2.2.1.1 to 14.2.2.2.2).

It will be also repeated on the FAS population excluding patients with unblinding issue (see section 5.3.6) (Statistical tables 14.2.3.1.1 to 14.2.3.1.3 & 14.2.3.2.1 to 14.2.3.2.2.).

Then, the primary efficacy analysis will be repeated on the FAS for patients IFN-K treated with status of IFNα neutralizing antibodies (positive/negative) at Week 36 as dependent variable.

(Statistical tables 14.2.3.3.1 & 14.2.3.3.2).

Finally, the following analysis will be presented as a sensitivity analysis.

The time variation in IFN gene signature (first co-primary endpoint) will be modelled using a MMRM (mixed model for repeated measures) with random intercept, with percent change at each time point as dependent variable, and minimization factors used for randomization (Ethnic origin (see section 9 Derived data), Age group, Presence or absence of renal involvement according to BILAG at screening, corticosteroid treatment, hydroxychloroquine treatment and MMF treatment at screening, treatment and time as explanatory variables.

The treatment by time interaction will also be included in the model. (Statistical table 14.2.4).

Linearity will be checked graphically. In case of absence of evidence of non-linearity, time will be treated as continuous (variable calculated as the actual number of days since baseline). Otherwise, it will be treated as categorical. (Statistical figure 14.2.1)

5.2.4.3 Secondary efficacy analyses

Secondary efficacy analyses will be performed on the FAS population except if otherwise specified.

5.2.4.3.1 *SRI response*

The SRI-4, 6, 8, 10 responses will be described at Week 36. (Statistical tables 14.2.5.1, 14.2.5.4, 14.2.6.1, 14.2.7.1, 14.2.8.1)

The SRI-4 response (section 4.1.2.1) will be analyzed using the same method as the primary analysis for the second co-primary endpoint (logistic regression). This analysis will be performed both on the FAS and PP sets. (Statistical tables 14.2.5.2 & 14.2.5.5)

The model on FAS for patients IFN-K treated with the status of IFNα neutralizing antibodies (positive/negative) at Week 36 as dependent variable will be also presented (Statistical table 14.2.5.3).

The SRI-6, 8, 10 responses to treatment at week 36 will also be analyzed using a logistic regression using the response rate as dependent variable and treatment as independent variable, while adjusting for the minimization factors used for randomization. (Statistical tables 14.2.6.2, 14.2.7.2, 14.2.8.2)

All analyses performed on SRI-4 will also be conducted on the composite SRI-4 (both with tapering CS ≤5 mg and ≤7.5 mg) on the FAS population only. (Statistical tables 14.2.5.6 to 14.2.5.11)

The SRI-4 response is an important and alternative endpoint assessing the clinical response. In case, there will be no trend on the BICLA response, the SRI-4 response could be chosen as primary endpoint for further development of IFN-K.

5.2.4.3.2 *SLEDAI response*

Number of patients achieving a SLEDAI response, defined as a reduction of the SLEDAI-2K score of at least 4 points at Week 36 compared to baseline will be analyzed using frequency table methods (Statistical table 14.2.9).

SLEDAI-2K score at each visit and change from baseline by treatment group will also be presented (Statistical tables 14.2.10.1 to 14.2.10.2).

All SLEDAI data will be listed in Listing 16.2.6.2.

5.2.4.3.3 *BILAG*

Shift tables between Baseline and LVA (last available value between Week 36 and Week 24) will also be presented for each body system. (Statistical table 14.2.11)

Finally, descriptive statistics for the BILAG global score at each visit and change from baseline to LVA will be presented. The difference between treatment groups for the change from baseline to LVA will be analyzed using the non-parametric Wilcoxon-test. (Statistical table 14.2.12)

The BILAG global score will be defined as the summation of the numerical values for the nine-system scores as given by the following formula:

Numerical global score (xs) = A*12 + B*8 + C*1

Where A, B and C represent the number of Grades A, B and C respectively at each assessment. Grades D and E are considered as 0 (Chee-Seng Yee *et al, 2010*).

All BILAG data will be listed in Listing 16.2.6.3.

5.2.4.3.4 *SELENA SLEDAI flare index*

The numbers of patients with a mild or moderate, or severe SLE flare (SELENA-SLEDAI flare index) and corresponding number of SLE flare will be presented. (Statistical table 14.2.13).

The total score at each visit (planned in the protocol) and change from baseline by treatment group will also be presented. The change at Week 36 will be analyzed using a t-test. (Statistical tables 14.2.14.1 to 14.2.14.2).

All SELENA-SLEDAI flare index data will be listed in Listing 16.2.6.4.

5.2.4.3.5 *SLICC/ACR-DI*

Total score at each visit and change from baseline by treatment group will be presented. The change at Week 36 will be analyzed using a t-test. (Statistical tables 14.2.15.1 to 14.2.15.2).

All SLICC/ACR-DI data will be listed in Listing 16.2.6.5.

5.2.4.3.6 *CLASI*

Total activity score and Total damage score at each visit and change from baseline by treatment group will also be presented. The changes at Week 36 will be analyzed using a t-test. (Statistical tables 14.2.16.1 to 14.2.17.2).

All CLASI data will be listed in Listing 16.2.6.6.

5.2.4.3.7 *LLDAS*

Number of patients achieving a LLDAS at Week 36 will be presented by treatment group (Statistical table 14.2.18). It is defined as:

- SLEDAI-2K ≤4, with no activity in major organ systems (renal, CNS, cardiopulmonary, vasculitis, fever) and no haemolytic anaemia or gastrointestinal activity
- No new features of lupus disease activity compared with the previous assessment (New feature is defined as any BILAG item recorded as “new” (modality 4) at Week 36)
- Physician global assessment (PGA, scale 0–3) ≤1
- Current prednisolone (or equivalent) dose ≤7.5 mg daily (this criterion will be identified by medical review)
- Well tolerated standard maintenance doses of immunosuppressive drugs and approved biological agents, excluding investigational drugs (this criterion will be identified by medical review)

5.2.4.4 Immunogenicity analysis

The following analysis will be performed on the PP population.

5.2.4.4.1 *Anti-IFNα binding antibody titers.*

- The number of patients with a positive antibody response over time (seropositivity) will be analyzed using frequency table methods (Statistical table 14.2.19). The definitions are the followings:
  - Seropositivity: A positive result (seropositivity) is defined when titer was ≥ 400 dil-1 and a negative result when titer is < 400 dil-1.
- Descriptive analysis will be done on Log-transformed dilution titers for anti-IFNα binding antibodies expressed as dilution factors at each time point. (Statistical table 14.2.20)
- Reverse cumulative distribution curves will be generated using anti-IFNα antibody titers (Statistical figure 14.2.2)
- GMT for anti-IFNα binding antibodies will be presented. Results will be expressed with 95% CI (Statistical table 14.2.21).

All corresponding data will be listed in Listing 16.2.6.7.

5.2.4.4.2 *Anti-IFNα antibody neutralizing capacity (NC50).*

- The number of patients with a positive antibody response over time (seropositivity) will be analyzed using frequency table methods (Statistical table 14.2.22). The definitions are the followings:
  - Seropositivity: A positive result (seropositivity) is defined when NC50 was ≥ 200 dil-1 and a negative result when NC50 is <200 dil-1.
- Descriptive analysis will be done on Log-transformed NC50 for anti-IFNα neutralizing antibodies expressed as dilution factors at each time point (Statistical table 14.2.23)
- Reverse cumulative distribution curves will be generated using NC50 (Statistical figure 14.2.3)
- GMT for anti-IFNα neutralizing antibodies will be presented. Results will be expressed with 95% CI (Statistical table 14.2.24).

All corresponding data will be listed in Listing 16.2.6.8.

5.2.4.4.3 *Anti-KLH binding antibody titers.*

- The number of patients with a positive antibody response over time (seropositivity) will be analyzed using frequency table methods (Statistical table 14.2.25). The definitions are the followings:

- Seropositivity: A positive result (seropositivity) is defined when titer was ≥ 400 dil-1 and a negative result when titer is <400 dil-1.

- Descriptive analysis will be done on Log-transformed dilution titers for anti-KLH binding antibodies expressed as dilution factors at each time (Statistical table 14.2.26)
- Reverse cumulative distribution curves will be generated using anti-KLH antibody titers (Statistical figure 14.2.14)
- GMT for anti- KLH binding antibodies will be presented. Results will be expressed with 95% CI (Statistical table 14.2.27).

All corresponding data will be listed in Listing 16.2.6.9.

5.2.4.5 Exploratory analyses

The following analysis will be performed on the FAS population except if otherwise specified.

5.2.4.5.1 *PGA scores*

PGA score at each visit and change from baseline by treatment group will be presented. (Statistical tables 14.2.28.1 to 14.2.28.2)

All PGA data will be listed in Listing 16.2.6.10.

5.2.4.5.2 *SLE flares*

Time to first SLE flare in patients will be analyzed using a cox regression model.

The first model will be adjusted on treatment group.

The second model will be performed only on patients IFN-K treated and will be adjusted on presence/absence of neutralizing antibodies. (Statistical tables 14.2.29.1 to 14.2.29.2)

5.2.4.5.3 *28-Tender and Swollen Joint Counts (SJC)*

28-Tender and Swollen Joint Counts and Joint Pain VAS at each visit and change from baseline will be presented. The changes at Week 36 will be analyzed using a t-test. (Statistical tables 14.2.30.1 to 14.2.32.2).

28-Tender and Swollen joint counts data will be listed in Listing 16.2.6.11, and joint Pain VAS data in Listing 16.2.6.12.

5.2.4.5.4 *Treatment failure*

- Proportion of treatment failure will be analyzed using frequency table methods. Patients will be considered as treatment failure if they receive more than 5 mg prednisone equivalent/day at any time between Week 24 (Visit 9) and Week 36 (Visit 12) or if their CS dose is increased above the Week 24 level is recorded (this criterion will be identified by medical review) (Statistical table 14.2.33)

5.2.4.5.5 *SF-36*

Physical Component Summary (PCS) and Mental Component Summary (MCS) scores at each visit and change from baseline will be presented. The changes at Week 36 will be analyzed using a non-parametric Wilcoxon rank sum test (Statistical tables 14.2.34.1 to 14.2.35.2). If one is statistically significant then the individual domain scores will also be described.

In addition, number of patients with clinically meaningful improvements ≥ Minimum Clinically Important Differences (MCID) of 2.5 points for summary and 5.0 points for domain scores between baseline and Week 36 will be presented. (Statistical tables 14.2.36 to 14.2.37)

All SF-36 data will be presented in Listing 16.2.6.13.

5.2.4.5.6 *FACIT*

Total scores at each visit and change from baseline by treatment group will be presented. The change at Week 36 will be analyzed using a t-test. (Statistical tables 14.2.39.1 to 14.2.39.2)

All FACIT data will be presented in Listing 16.2.6.14.

5.2.4.5.7 *Autoantibodies*

The levels of auto-antibodies (ANA, anti-dsDNA, anti-Smith antigen [anti-Sm], anti-RNP, anti-SSA/Ro, anti-SSB/La, anti-cardiolipin, and anti-β2-glycoprotein I antibodies) will be described at each visit by treatment group. Change from baseline by treatment group will be presented for quantitative parameters. For anti-dsDNA, the change at Week 36 will be analyzed using a t-test. (Statistical tables 14.2.40.1 to 14.2.40.2). These analyses will be performed on the PP population.

All auto-antibodies data will be listed in Listing 16.2.6.15.

5.2.4.5.8 *Biomarkers*

The biomarkers (C3, C4, CH50) at each visit and change from baseline by treatment group will be presented. (Statistical tables 14.2.41.1 to 14.2.41.2). For C3 the change at Week 36 will be analyzed using a t-test. These analyses will be performed on the PP population.

All biomarkers data will be listed in Listing 16.2.6.16.

5.2.4.5.9 *Anti-IFNα and anti-KLH antibody isotyping*

Descriptive analysis will be performed on Anti-IFNα and anti-KLH antibody isotyping data. (Statistical table 14.2.42)

All corresponding data will be listed in Listing 16.2.6.17.

5.2.4.5.10 *Anti-Hemagglutinin antibody response following influenza vaccination*

Seroconversion (four folds increase in antibody titers post-vaccination) and seroprotection (HIA antibody titers ≥1:40 post-vaccination) will be presented by treatment group for each visit. In addition, results by visit will be presented according to status of anti-IFNα neutralizing antibodies (positive/negative) at the corresponding visit (Statistical table 14.2.43). These analyses will be performed on the FAS population, only on patients vaccinated with seasonal Flu and with sample at baseline and post-baseline.

All corresponding data will be listed in Listing 16.2.6.18.

5.2.4.5.11 *Neutralizing Anti-IFNα antibodies towards IFNα subtypes*

Descriptive analysis will be performed on Neutralizing Anti-IFNα antibodies towards IFNα subtypes data. (Statistical table 14.2.44)

All corresponding data will be listed in Listing 16.2.6.19.

5.2.4.5.12 *Other*

IFNβ and IFNω cross neutralization data will be provided in Listing 16.2.6.20

5.2.4.5.13 *Correlation*

Correlation between immunogenicity responses (Anti-IFNα binding positive / neutralizing antibodies positive vs anti-IFNα binding positive / neutralizing antibodies negative) and clinical parameters (BICLA & SRI-4); between clinical and biological parameters (IFN gene signature, C3, dsDNA, ANA), and between immunogenicity responses and biological parameters will be presented on the PP population. The following analyses will be performed:

- Qualitative description for clinical parameters at V12 by status (positive/negative) of anti IFNα neutralizing antibodies at V12 on patients treated with IFN-K and with positive anti IFNα binding antibodies at V12
- Quantitative or qualitative description for biological parameters at V12 by treatment group on patients responder for BICLA at V12
- Quantitative or qualitative description for biological parameters at V12 by treatment group on patients non responder for BICLA at V12
- Quantitative or qualitative description for biological parameters at V12 by treatment group on patients responder for SRI4 at V12
- Quantitative or qualitative description for biological parameters at V12 by treatment group on patients non responder for SRI4 at V12
- Quantitative or qualitative description for biological parameters at V12 by status (positive/negative) of anti IFNα neutralizing antibodies at V12 on patients treated with IFN-K and with positive anti IFNα binding antibodies at V12

(Statistical Tables 14.2.45.1 to 14.2.45.6)

5.2.5 Safety analyses

Safety variables will be tabulated and presented for all patients included in the Safety population (SAF).

5.2.5.1 Extent of exposure and compliance

Compliance (see section 9) with study treatment will be presented by treatment group on the FAS and the PP populations. Treatment compliance will then be analyzed as a numerical variable as well as a categorical variable (Statistical table 14.1.28, Listing 16.2.5.1).

To analyze the extent of exposure the following variables will be summarized by treatment group for the SAF (Statistical table 14.3.1, Listing 16.2.5.2):

- Number of administrations received and cumulative dose
- Duration (number of days) between first IP application and last IP application.
- Presence of anti-IFN α neutralizing antibodies

All administration of study product data will be provided in Listing 16.2.5.3.

5.2.5.2 Adverse events

Adverse event tabulations:

Tabulation of adverse events will present for each cell the following information: number of patients with at least one occurrence of the event, corresponding percentage and number of events (if relevant).

The following tables will be produced for the Safety population as well as by treatment group:

The definition of TEAEs is described in section 4.2.1.

The following period will be defined:

- before first dose
- [1st dose; 2nd dose[
- [2nd dose; 3rd dose[
- [3rd dose; 4th dose[
- [4th dose; 5th dose[
- [5th dose; Week 36]
- [Last dose; Week 36/Early Termination] (for AE which cannot be classified in the previous periods due to dose not received or premature study termination)

Summary table of adverse events (Statistical Table 14.3.2):

- Any AE
- Any TEAE
- Any TEAE by period
- Any TEAE leading to study treatment temporarily discontinuation
- Any TEAE leading to study treatment permanent discontinuation
- Any TEAE of intensity severe or more
- Any TEAE considered related to the study treatment (possibly or probably related)
- Any SAE
- Any SAE by period
- Any Treatment Emergent SAE (TESAE)
- Any TESAE leading to study treatment temporarily discontinuation
- Any TESAE leading to study treatment permanent discontinuation
- Any TESAE considered related to the study treatment (possibly or probably related)
- Any TESAE of intensity severe or more

- Death

Detailed Tables:

All tables listed below will be presented by period (except if otherwise specified):

- Solicited local reactions during a 7-day follow-up period after each study product administration by SOC and PT (Statistical Tables 14.3.3.1 to 14.3.3.6)
- Solicited local reactions during a 7-day follow-up period after each study product administration by SOC, PT and intensity (Statistical Tables 14.3.4.1 to 14.3.4.6)
- Solicited systemic reactions during a 7-day follow-up period after each study product administration by SOC and PT (Statistical Tables 14.3.5.1 to 14.3.5.6)
- Solicited systemic reactions during a 7-day follow-up period after each study product administration by SOC, PT and intensity (Statistical Tables 14.3.6.1 to 14.3.6.6)
- TEAEs by SOC and PT (Statistical Tables 14.3.7.1 to 14.3.7.6)
- TEAEs by SOC, PT and status of IFNα neutralizing antibodies (positive/negative) at time of event (only on patients IFN-K treated) (Statistical Tables 14.3.7.7 to 14.3.7.10)
- TEAEs by SOC, PT and relationship (Statistical Tables 14.3.8.1 to 14.3.8.6)
- TEAEs by SOC, PT and intensity (Statistical Tables 14.3.9.1 to 14.3.9.6)
- TEAEs leading to permanent study treatment discontinuation by SOC and PT (Statistical Table 14.3.10) (only throughout the study)
- SAEs by SOC and PT (Statistical Tables 14.3.11.1 to 14.3.11.7)
- SAEs by SOC, PT and status of IFNα neutralizing antibodies (positive/negative) at time of event (only on patients IFN-K treated) (Statistical Tables 14.3.11.8 to 14.3.11.11)
- SAEs by SOC, PT and relationship (Statistical Tables 14.3.12.1 to 14.3.12.7)
- SAEs by SOC, PT and intensity (Statistical Tables 14.3.13.1 to 14.3.13.7)
- SAEs leading to permanent study treatment discontinuation by SOC and PT (Statistical Table 14.3.14)

The following rules will be applied to analyze the occurrence of AE according to the status of IFNα neutralizing antibodies (positive/negative):

- For adverse event which occurred between dose 1 and dose 3 included, status of neutralizing capacity will not be assessed
- For adverse event which occurred between 3rd dose (excluded) and Visit 6 (included), status of neutralizing capacity at visit 6 will be used
- For adverse event which occurred between Visit 6 (excluded) and Visit 9 (included), status of neutralizing capacity at visit 9 will be used
- For adverse event which occurred between Visit 9 (excluded) and Visit 12 (included), status of neutralizing capacity at visit 12 will be used

Adverse events listings:

All adverse events (including solicited local and systemic reactions) recorded during the study will be presented in Listings. The following information (if available) will be included in the listings (non-exhaustive list):

- Patient identifier
- Age, Ethnic origin (see section 9 Derived data), gender, weight
- The adverse event (System organ class, preferred term, reported term)
- Start date, end date, duration, period
- Severity (e.g., mild, moderate, severe)
- Seriousness (serious/non-serious)
- Action taken
- Outcome
- Relatedness assessment

Listings will be provided for:

- Solicited local reactions during a 7-day follow-up period after each study product administration (Listing 16.2.7.1)
- Solicited systemic reactions during a 7-day follow-up period after each study product administration (Listing 16.2.7.2)
- All other adverse events (Listing 16.2.7.3)
- Death, other Serious Adverse Events and Other Significant Adverse Events (Listing 16.2.7.4). Other significant Adverse Events will include cancer and severe infection (not exhaustive list)

5.2.5.3 Laboratory safety variables

Laboratory evaluations will be summarized by visit and by treatment group on the Safety population.

For each hematology, chemistry and coagulation variables:

- Quantitative descriptive statistics will be tabulated at each visit over the course of the study for raw values and change from baseline (Statistical tables 14.3.15.1, 14.3.15.2, 14.3.16.1, 14.3.16.2, 14.3.17.1, 14.3.17.2,)
- Qualitative descriptive statistics will be tabulated for each laboratory variable at each time over the course of the study:
    - By clinical significance (normal, Abnormal CS/N, Abnormal CS/AE, Abnormal NCS) (Statistical tables 14.3.15.3, 14.3.16.3, 14.3.17.3)
    - by grade (if applicable) (Statistical tables 14.3.15.4, 14.3.16.4, 14.3.17.4)

All urinalysis parameters will also be analyzed as quantitative variables (Statistical table 14.3.18)

In addition, the incidence of severe infections based on the total T-lymphocyte count (lymphocytes < 1000 versus lymphocytes > 1000/mm3) at the visit 2 (D0) will be presented (Statistical table 14.3.19).

All laboratory results will also be presented in Listings 16.2.8.1 to 16.2.8.3.

Urine analysis data will be listed in Listing 16.2.8.4.

5.2.5.4 Physical examinations

Weight and BMI will be presented at each visit with raw value and change from baseline (Statistical tables 14.3.20.1 & 14.3.20.2). Number of normal, Abnormal CS/N, Abnormal CS/AE, Abnormal NCS values will be presented at each visit by body systems for each treatment group (Statistical table 14.3.19).

All individual measurements will be provided in Listing 16.2.9.

5.2.5.1 Vital signs

Quantitative descriptive statistics will be tabulated for each vital sign recorded (heart rate, temperature, systolic and diastolic blood pressure) at each time over the course of the study (e.g., at each timepoint for each visit) for raw values and change from baseline (Statistical tables 14.3.22.1 & 14.3.22.2)

All individual measurements will be provided in Listing 16.2.10.

5.2.5.2 Electrocardiogram (ECG)

For 12-lead ECG assessments variables collected, the frequencies of normal, Abnormal CS/N, Abnormal CS/AE, Abnormal NCS values will be reported by visit and treatment group (Statistical table 14.3.23).

All individual measurements will be provided in Listing 16.2.11.

5.2.5.3 Concomitant medications

Concomitant medications will be presented by ATC code and Preferred Name by treatment group (Statistical table 14.3.24)

Previous and concomitant medications for each patient will be reported in Listings 16.2.4.9.

5.3 Statistical/Analytical issues

5.3.1 Adjustments for Covariates

All models ANCOVA, MMRM, Logistic regression) will be adjusted on the minimization factors used for randomization (Ethnic (see section 9 Derived data) Origin, Age group, Presence or absence of renal involvement according to the BILAG at screening, With or without CS treatment at screening, With or without HCQ treatment at screening, With or without MMF treatment at screening).

In addition, MMRM will be adjusted on the baseline value.

For “Ethnic origin”, the reclassified values (see section 9 Derived data) will be used for primary analysis. The values from the eCRF will be used for sensitivity analysis. In the same way, for “Presence or absence of renal BILAG at screening”, the re-computed renal BILAG score derived in the statistics analysis datasets will

be used for primary analysis. The values from the eCRF will be used as sensitivity analysis. (Statistical tables 14.2.3.1.4 & 14.2.3.2.3)

5.3.2 Handling of Dropouts or Missing Data

Missing data in efficacy analysis:

For the primary endpoint – IFN gene signature – the last available value either at Visit 9 or 12 will be used for the ANCOVA model.

Missing items in questionnaires:

- SLEDAI-2K and SELENA SLEDAI:
  - At visit 6, 9 and 12 (SLEDAI-2K) or at visit 9 and 12 (SLENA-SLEDAI flare index) respectively, for descriptors "Urinary casts, Hematuria, Proteinuria, Pyuria, Low complement, Increased DNA binding, Thrombocytopenia, Leukopenia", if value "Not done" is recorded because of no urinary/lab results available, corresponding descriptor from previous visit will be used
  - Other missing data should be considered as not present (protocol rule: items should be recorded if the descriptor is present at the time of the visit or in the preceding 10 days)

- CLASI: missing data will not be replaced. The score will be considered as missing.

- SF-36: scores for each scale are calculated for respondents completing 50% or more of the items within a scale. Among these respondents, the value for any missing item is imputed as the mean value for non-missing items (John E. Ware)

- FACIT fatigue: if there are missing items, subscale scores can be prorated. This is done by multiplying the sum of the subscale by the number of items in the subscale, then dividing by the number of items actually answered. When there are missing data, prorating by subscale in this way is acceptable as long as more than 50% of the items were answered (e.g., a minimum of 4 of 7 items, 4 of 6 items, etc). (Facit Administration and Scoring Guidelines)

- BILAG: For renal BILAG change in renal function over the last four weeks: if previous renal function is not known it will be assumed to be normal and urinalysis will be given values of 0, serum creatinine will be given a value of 100 µmol/L and creatinine clearance (GFR) will be given a value of 100 mL/min. The results entered at the first assessment will be carried forward unless replaced by new values and they should be overwritten if no longer applicable (DA Isenberg). For other cases, score is calculated with the available data.

Missing or incomplete dates:

For calculation / sorting / assignation based on dates (e.g., treatment emergent AEs, concomitant medications…), the following rules will apply:

- The most conservative approach will be considered (i.e., if the onset date of an AE/concomitant medication is missing / incomplete, it will be assumed to have occurred during the study treatment phase (i.e., a TEAE for AEs) except when the partial onset date or other available data indicates differently (e.g., start date day missing, but month before the month of baseline date, or stop date before baseline date).
- Medical history or disease diagnosis with missing/incomplete date will be assumed to have occurred before any study treatment except when the partial onset date or other available data indicates differently.
- Assignations based on dates will be reviewed and confirmed or infirmed during the data review meeting

No other missing data will be imputed, and all available efficacy and safety data will be included in data listings and tabulations.

5.3.3 Interim Analyses and Data Monitoring

No formal interim data analysis is planned for the study.

An Independent Data Safety Monitoring Board (iDSMB) has reviewed safety data on a regular basis during the course of the study. More details are provided on the iDSMB charter.

5.3.4 Multicentre studies

Randomized patients are included in 65 sites. With regards to the large number of sites compared to the planned number of patients, no adjustment for centre effect will be done. In addition, randomization was centralized and using a minimization.

5.3.5 Multiple Comparison/Multiplicity

This study has 2 co-primary endpoints tested by sequence (ie: First, the first co-primary endpoint will be tested at an error probability of 5% for a 2-sided test). If and only if this Null-hypothesis can be rejected, the second co-primary endpoint will be tested also at an error probability of 5% for a 2-sided test). Consequently, no problem for multiplicity in this study.

5.3.6 Use of an "Efficacy Subset" of Patients

Two efficacy analyses populations were defined, the FAS and the PP. The definition of these populations is given in Section 3.3. The primary efficacy analysis will be conducted on the FAS. The PP population will be used to conduct a sensitivity analysis and assess the robustness of the primary efficacy analysis conclusions. Any substantial difference between the two analyses will be explored and discussed.

Some unblinding (for SAEs/SUSARs reporting and/or upon FDA request) have led to involuntary potential access to unblinded information by the concerned investigator. An analysis excluding these patients will be done for the primary efficacy analysis to assess the robustness of the expected results.

5.3.7 Active-Control Studies Intended to Show Equivalence

Not applicable.

5.3.8 Examination of Subgroups

No subgroups have been defined.

5.4 Data handling conventions

5.4.1 Baseline definitions

For IFN gene signature, only Week 0 (visit 2) will be considered as baseline.

For BILAG scores, a baseline value will be defined for each body system. This baseline will be the value at Week 0 (visit 2).

For other efficacy and safety endpoints the last observation prior to the first dose of study treatment administration will be used as the baseline value. This will usually correspond to the measurement performed at Week 0 before first-dose. However, in case of missing value at Week 0, the last available value recorded during screening will be used as baseline value.

5.4.2 Outliers

All outlier data will be reviewed during the data-review meeting and decisions regarding their use in the statistical analyses will be made.

5.4.3 Windows for time points

All visits will be analyzed as entered in the database except if otherwise specified during the data-review meeting.

5.4.4 Retest and Unscheduled visits

During the data review meeting, any data from unscheduled visit which must be taken into account in the analysis will be identified.

Other data from unscheduled visits will only be tabulated in listings.

6 Interim analysis

No interim analysis is planned.

7 Modifications from the statistical sections in the protocol

7.1 Analysis dataset

Intention to Treat population has been re-labeled Full Analysis Set.

7.2 Efficacy analysis

7.2.1 Primary efficacy analysis

A mixed model for repeated measures with random intercept using all measurements available (IFN gene signature/Score) until Week 36 has been added for the first co-primary endpoint to compute the estimate of the between group difference in change from baseline at week 36 as a sensitivity analysis.

7.2.2 Secondary efficacy & exploratory analyses

The criterion “composite SRI-4 response (tapering CS ≤5mg and ≤7.5mg)”, initially not planned in the protocol, will be analyzed (same method as SRI-4).

The analysis on exploratory endpoint “changes in Lupus Therapy” has been removed because it is redundant with the BICLA and LLDAS analyses.

7.3 Adverse events

Analysis of solicited local & systemic reactions 1-hour post study product administration was planned in the protocol. Time of these AEs was not recorded into the eCRF. This analysis will not be done.

7.4 Laboratory

Analysis on percent change was planned in the protocol. This type of analysis is not always relevant. This analysis will be replaced by an analysis on the change.

7.5 LLDAS

Analysis for LLDAS, initially not planned in the protocol, will be done.

8 Software documentation

All summaries and statistical analyses will be generated using SAS version 9.4 or higher.

9 Derived data

Derived variable	Derivation algorithm
Change from baseline to visit V (continuous)	Change from baseline of variable X=X(Visit V)-X(Baseline) ○ Negative values indicate a decrease in X ○ Positive values indicate an increase in X
Percent change from baseline to visit V (continuous)	Percent change from baseline of variable X=100 *[X(Visit V)-X(Baseline)]/ X(Baseline) ○ Negative values indicate a decrease in X ○ Positive values indicate an increase in X
Treatment Compliance (continuous)	The compliance Ci for patient i will be computed according to: $$C_i = \frac{D_i^t * 100}{D_i^p}$$ where D_i^p mg is the total amount (mg) of IP prescribed to patient i and D_i^t is the total amount (mg) of IP actually taken by the patient during the study i.e., before the end of study for patient i.
Treatment compliance (categorical) (if relevant)	Categorial variable with three modalities: • $C_i < 80\%$ • $80\% \leq C_i < 120\%$ • $C_i \geq 120\%$
Event Duration	(End Date) – (Start Date) + 1
BILAG score	See BILAG-2004 Index scoring
SLEDAI-2K and SELENA SLEDAI	Sum of the weights
SLICC/ACR	Sum of items
CLASI	Sum of items
FACIT	See FACIT-Fatigue Subscale Scoring Guidelines (Version 4)

Derived variable	Derivation algorithm
SF-36	See SF-36 Health Survey, Manual and Interpretation Guide
Time to event SLE flare	SLE flare will be identified in BILAG-2004 scoring. SLE flares are predefined as a BILAG A or B score due to items that were new or worse in any of the eight organ system (Isenberg et Al). For patient with a SLE flare: Time to event = Visit date of corresponding BILAG – Date of Week 0 + 1 For patient without SLE flare: Time to event = Date of Week 36 (or date of end of study for patients prematurely withdrawn before Week 36) – Date of Week 0 +1
Ethnic origin	Ethnic will be derived using race variable existing in the CRF. The other ethnic origin “Black, Asian, Caucasian or Hispanic” will be re-classified in the predetermined modalities (Black, Asian, Caucasian/Hispanic)

10 Tables, Figures and Listings

10.1 List of tables

Number	Title	Screened	SAF	FAS	PP	Other
Demographics and Baseline characteristics						
14.1.1	Patient dispositions	X				
14.1.2.1	Datasets analyzed	X				
14.1.2.2	Reasons for exclusion from the FAS population		X			
14.1.2.3	Reasons for exclusion from the PP population			X		
14.1.3	Protocol deviations		X			
14.1.4	Demographics data		X	X		
14.1.5	Alcohol, drug and tobacco use			X		
14.1.6	Vital signs at baseline			X		
14.1.7	ECG at baseline			X		
14.1.8	Physical examination at baseline			X		
14.1.9	Hematology at baseline			X		
14.1.10	Chemistry at baseline			X		
14.1.11	Coagulation at baseline			X		
14.1.12	Urinalysis at baseline			X		
14.1.13	Hematology abnormalities at baseline			X		
14.1.14	Chemistry abnormalities at baseline			X		
14.1.15	Coagulation abnormalities at baseline			X		
14.1.16	Urinalysis abnormalities at baseline			X		
14.1.17	Viral serology at baseline			X		
14.1.18	Autoantibodies at baseline			X		
14.1.19	Inflammatory markers at baseline			X		
14.1.20	Gynecological examination			X		
14.1.21	Efficacy variables at baseline			X		
14.1.22	SLE medical history			X		
14.1.23	SLE flare history			X		
14.1.24	General Medical & Surgical history			X		
14.1.25	Permitted medications			X		
14.1.26	Prohibited medications			X		
14.1.27	Previous medications			X		
14.1.28	Compliance			X	X	
Efficacy						

Number	Title	Screened	SAF	FAS	PP	Other
14.2.1.1.1	Primary efficacy analysis - First co-primary endpoint - Value at each visit			X		
14.2.1.1.2	Primary efficacy analysis - First co-primary endpoint - Change from baseline			X		
14.2.1.1.3	Primary efficacy analysis - First co-primary endpoint - ANCOVA model			X		
14.2.1.2.1	Primary efficacy analysis - Second co-primary endpoint - Response at Week 36			X		
14.2.1.2.2	Primary efficacy analysis - Second co-primary endpoint - Logistic regression model			X		
14.2.2.1.1	Primary efficacy analysis - First co-primary endpoint - Value at each visit				X	
14.2.2.1.2	Primary efficacy analysis - First co-primary endpoint - Change from baseline				X	
14.2.2.1.3	Primary efficacy analysis - First co-primary endpoint - ANCOVA model				X	
14.2.2.2.1	Primary efficacy analysis - Second co-primary endpoint - Response at Week 36				X	
14.2.2.2.2	Primary efficacy analysis - Second co-primary endpoint - Logistic regression model				X	
14.2.3.1.1	Primary efficacy analysis - First co-primary endpoint - Value at each visit					X
14.2.3.1.2	Primary efficacy analysis - First co-primary endpoint - Change from baseline					X
14.2.3.1.3	Primary efficacy analysis - First co-primary endpoint - ANCOVA model					X
14.2.3.1.4	Primary efficacy analysis - First co-primary endpoint - ANCOVA model - Covariates as randomized			X		
14.2.3.2.1	Primary efficacy analysis - Second co-primary endpoint - Response at Week 36					X
14.2.3.2.2	Primary efficacy analysis - Second co-primary endpoint - Logistic regression model					X
14.2.3.2.3	Primary efficacy analysis - Second co-primary endpoint - Logistic regression model - Covariates as randomized			X		
14.2.3.3.1	Primary efficacy analysis - First co-primary endpoint - ANCOVA model with status of IFNα neutralizing antibodies (positive/negative) at Week 36 as dependent variable			X		

Number	Title	Screened	SAF	FAS	PP	Other
14.2.3.3.2	Primary efficacy analysis - Second co-primary endpoint - Logistic regression model with status of IFNα neutralizing antibodies (positive/negative) at Week 36 as dependent variable			X		
14.2.4	Sensitivity efficacy analysis - First co-primary endpoint - MMRM			X		
14.2.5.1	Secondary efficacy analysis - SRI-4 response at Week 36			X		
14.2.5.2	Secondary efficacy analysis - SRI-4 response - Logistic regression model			X		
14.2.5.3	Secondary efficacy analysis - SRI-4 response - Logistic regression model with status of IFNα neutralizing antibodies (positive/negative) at Week 36 as dependent variable			X		
14.2.5.4	Secondary efficacy analysis - SRI-4 response at Week 36				X	
14.2.5.5	Secondary efficacy analysis - SRI-4 response - Logistic regression model				X	
14.2.5.6	Secondary efficacy analysis - Composite SRI-4 response (CS 5 mg) at Week 36			X		
14.2.5.7	Secondary efficacy analysis - Composite SRI-4 response (CS 5 mg) - Logistic regression model			X		
14.2.5.8	Secondary efficacy analysis - Composite SRI-4 response (CS 5 mg) - Logistic regression model with status of IFNα neutralizing antibodies (positive/negative) at Week 36 as dependent variable			X		
14.2.5.9	Secondary efficacy analysis - Composite SRI-4 response (CS 7.5 mg) at Week 36			X		
14.2.5.10	Secondary efficacy analysis - Composite SRI-4 response (CS 7.5 mg) - Logistic regression model			X		
14.2.5.11	Secondary efficacy analysis - Composite SRI-4 response (CS 7.5 mg) - Logistic regression model with status of IFNα neutralizing antibodies (positive/negative) at Week 36 as dependent variable			X		
14.2.6.1	Secondary efficacy analysis - SRI-6 response at Week 36			X		
14.2.6.2	Secondary efficacy analysis - SRI-6 response at Week 36 - Logistic regression model			X		

Number	Title	Screened	SAF	FAS	PP	Other
14.2.7.1	Secondary efficacy analysis - SRI-8 response at each visit			X		
14.2.7.2	Secondary efficacy analysis - SRI-8 response at Week 36 - Logistic regression model			X		
14.2.8.1	Secondary efficacy analysis - SRI-10 response at each visit			X		
14.2.8.2	Secondary efficacy analysis - SRI-10 response at Week 36 - Logistic regression model			X		
14.2.9	Secondary efficacy analysis - SLEDAI response at week 36			X		
14.2.10.1	Secondary efficacy analysis - SLEDAI-2K scores - Value at each visit			X		
14.2.10.2	Secondary efficacy analysis - SLEDAI-2K scores - Change from baseline			X		
14.2.11	Secondary efficacy analysis - BILAG - Shift table			X		
14.2.12	Secondary efficacy analysis - BILAG global score			X		
14.2.13	Secondary efficacy analysis - SELENA-SLEDAI - Mild, moderate or severe SLE flare			X		
14.2.14.1	Secondary efficacy analysis - SELENA-SLEDAI score - Value at each visit			X		
14.2.14.2	Secondary efficacy analysis - SELENA-SLEDAI score - Change from baseline			X		
14.2.15.1	Secondary efficacy analysis - SLICC/ACR-DI score - Value at each visit			X		
14.2.15.2	Secondary efficacy analysis - SLICC/ACR-DI score - Change from baseline			X		
14.2.16.1	Secondary efficacy analysis - CLASI - Total activity score - Value at each visit			X		
14.2.16.2	Secondary efficacy analysis - CLASI - Total activity score - Change from baseline			X		
14.2.17.1	Secondary efficacy analysis - CLASI - Total damage score - Value at each visit			X		
14.2.17.2	Secondary efficacy analysis - CLASI - Total damage score - Change from baseline			X		
14.2.18	Secondary efficacy analysis - LLDAS			X		
14.2.19	Immunogenicity analysis - Anti-IFNα binding antibody titers - Positive antibody response over time				X	
14.2.20	Immunogenicity analysis - Log-transformed dilution titers for anti-IFNα binding antibodies				X	

Number	Title	Screened	SAF	FAS	PP	Other
14.2.21	Immunogenicity analysis - Anti-IFNα binding antibodies - GMT				X	
14.2.22	Immunogenicity analysis - Anti-IFNα antibody neutralizing capacity (NC50) - Positive antibody response over time				X	
14.2.23	Immunogenicity analysis - Log-transformed NC50 for anti-IFNα neutralizing antibodies				X	
14.2.24	Immunogenicity analysis - Anti-IFNα neutralizing antibodies - GMT				X	
14.2.25	Immunogenicity analysis - Anti-KLH binding antibody titers - Positive antibody response over time				X	
14.2.26	Immunogenicity analysis - Log-transformed dilution titers for anti-KLH binding antibodies				X	
14.2.27	Immunogenicity analysis - Anti-KLH binding antibodies - GMT				X	
14.2.28.1	Exploratory analysis - PGA score - Value at each visit			X		
14.2.28.2	Exploratory analysis - PGA score - Change from baseline			X		
14.2.29.1	Exploratory analysis - SLE Flare - Cox model adjusted on treatment group			X		
14.2.29.2	Exploratory analysis - SLE Flare - Cox model adjusted on presence/absence of neutralizing antibodies			X		
14.2.30.1	Exploratory analysis - 28-Tender joints counts - Value at each visit			X		
14.2.30.2	Exploratory analysis - 28-Tender joints counts - Change from baseline			X		
14.2.31.1	Exploratory analysis - 28-Swollen joints counts - Value at each visit			X		
14.2.31.2	Exploratory analysis - 28-Swollen joints counts - Change from baseline			X		
14.2.32.1	Exploratory analysis - Joint Pain VAS - Value at each visit			X		
14.2.32.2	Exploratory analysis - Joint Pain VAS - Change from baseline			X		
14.2.33	Exploratory analysis - Treatment failure			X		
14.2.34.1	Exploratory analysis - SF-36 - Physical Component Summary (PCS) - Value at each visit			X		
14.2.34.2	Exploratory analysis - SF-36 - Physical Component Summary (PCS) - Change from baseline			X		

Number	Title	Screened	SAF	FAS	PP	Other
14.2.35.1	Exploratory analysis - SF-36 - Mental Component Summary (MCS) - Value at each visit			X		
14.2.35.2	Exploratory analysis - SF-36 - Mental Component Summary (MCS) - Change from baseline			X		
14.2.36	Exploratory analysis - Clinically meaningful improvements - Physical Component Summary (PCS)			X		
14.2.37	Exploratory analysis - Clinically meaningful improvements - Mental Component Summary (MCS)			X		
14.2.38	Exploratory analysis - Clinically meaningful improvements - Domains			X		
14.2.39.1	Exploratory analysis - FACIT total score - Value at each visit			X		
14.2.39.2	Exploratory analysis - FACIT total score - Change from baseline			X		
14.2.40.1	Exploratory analysis - Autoantibodies - Value at each visit				X	
14.2.40.2	Exploratory analysis - Autoantibodies - Change from baseline				X	
14.2.41.1	Exploratory analysis - Biomarkers - Value at each visit				X	
14.2.41.2	Exploratory analysis - Biomarkers - Change from baseline				X	
14.2.42	Exploratory analysis - Anti-IFNα and anti-KLH antibody isotyping				X	
14.2.43	Exploratory analysis - Anti-Hemagglutinin antibody response following influenza vaccination				X	
14.2.44	Exploratory analysis - Neutralizing Anti-IFNα antibodies towards IFNα subtypes				X	
14.2.45.1	Correlation - Qualitative description for clinical parameters at V12 by status of neutra at V12 on patients treated with IFN-K and with positive binding at V12				X	
14.2.45.2	Correlation - Quantitative or qualitative description for biological parameters at V12 by treatment group on patients responder for BICLA at V12				X	
14.2.45.3	Correlation - Quantitative or qualitative description for biological parameters at V12 by treatment group on patients non responder for BICLA at V12				X	

Number	Title	Screened	SAF	FAS	PP	Other
14.2.45.4	Correlation - Quantitative or qualitative description for biological parameters at V12 by treatment group on patients responder for SRI4 at V12				X	
14.2.45.5	Correlation - Quantitative or qualitative description for biological parameters at V12 by treatment group on patients non responder for SRI4 at V12				X	
14.2.45.6	Correlation - Quantitative or qualitative description for biological parameters at V12 by status of neutral at V12 on patients patients treated with IFN-K and with positive binding at V12				X	
Safety						
14.3.1	Extent of exposure		X			
14.3.2	Summary of Adverse events		X			
14.3.3.1	Solicited local reactions during a 7-day follow-up period after each study product administration by SOC and PT - Period [1st dose; 2nd dose[		X			
14.3.3.2	Solicited local reactions during a 7-day follow-up period after each study product administration by SOC and PT - Period [2nd dose; 3rd dose[		X			
14.3.3.3	Solicited local reactions during a 7-day follow-up period after each study product administration by SOC and PT - Period [3rd dose; 4th dose[		X			
14.3.3.4	Solicited local reactions during a 7-day follow-up period after each study product administration by SOC and PT - Period [4th dose; 5th dose[		X			
14.3.3.5	Solicited local reactions during a 7-day follow-up period after each study product administration by SOC and PT - Period [5th dose; Week 36]		X			
14.3.3.6	Solicited local reactions during a 7-day follow-up period after each study product administration by SOC and PT - Period [Last dose;Week 36/Early Termination]		X			
14.3.4.1	Solicited local reactions during a 7-day follow-up period after each study product administration by SOC, PT and intensity - Period [1st dose; 2nd dose[		X			
14.3.4.2	Solicited local reactions during a 7-day follow-up period after each study product administration by SOC, PT and intensity - Period [2nd dose; 3rd dose[		X			

Number	Title	Screened	SAF	FAS	PP	Other
14.3.4.3	Solicited local reactions during a 7-day follow-up period after each study product administration by SOC, PT and intensity - Period [3rd dose; 4th dose[		X			
14.3.4.4	Solicited local reactions during a 7-day follow-up period after each study product administration by SOC, PT and intensity - Period [4th dose; 5th dose[		X			
14.3.4.5	Solicited local reactions during a 7-day follow-up period after each study product administration by SOC, PT and intensity - Period [5th dose; Week 36]		X			
14.3.4.6	Solicited local reactions during a 7-day follow-up period after each study product administration by SOC, PT and intensity - Period [Last dose;Week 36/Early Termination]		X			
14.3.5.1	Solicited systemic reactions during a 7-day follow-up period after each study product administration by SOC and PT - Period [1st dose; 2nd dose[		X			
14.3.5.2	Solicited systemic reactions during a 7-day follow-up period after each study product administration by SOC and PT - Period [2nd dose; 3rd dose[		X			
14.3.5.3	Solicited systemic reactions during a 7-day follow-up period after each study product administration by SOC and PT - Period [3rd dose; 4th dose[		X			
14.3.5.4	Solicited systemic reactions during a 7-day follow-up period after each study product administration by SOC and PT - Period [4th dose; 5th dose[		X			
14.3.5.5	Solicited systemic reactions during a 7-day follow-up period after each study product administration by SOC and PT - Period [5th dose; Week 36]		X			
14.3.5.6	Solicited systemic reactions during a 7-day follow-up period after each study product administration by SOC and PT - Period [Last dose;Week 36/Early Termination]		X			
14.3.6.1	Solicited systemic reactions during a 7-day follow-up period after each study product administration by SOC, PT and intensity - Period [1st dose; 2nd dose[		X			
14.3.6.2	Solicited systemic reactions during a 7-day follow-up period after each study product administration by SOC, PT and intensity - Period [2nd dose; 3rd dose[		X			
14.3.6.3	Solicited systemic reactions during a 7-day follow-up period after each study product administration by SOC, PT and intensity - Period [3rd dose; 4th dose[		X			

Number	Title	Screened	SAF	FAS	PP	Other
14.3.6.4	Solicited systemic reactions during a 7-day follow-up period after each study product administration by SOC, PT and intensity - Period [4th dose; 5th dose[		X			
14.3.6.5	Solicited systemic reactions during a 7-day follow-up period after each study product administration by SOC, PT and intensity - Period [5th dose; Week 36]		X			
14.3.6.6	Solicited systemic reactions during a 7-day follow-up period after each study product administration by SOC, PT and intensity - Period [Last dose;Week 36/Early Termination]		X			
14.3.7.1	TEAEs by SOC and PT - Period [1st dose; 2nd dose[		X			
14.3.7.2	TEAEs by SOC and PT - Period [2nd dose; 3rd dose[		X			
14.3.7.3	TEAEs by SOC and PT - Period [3rd dose; 4th dose[		X			
14.3.7.4	TEAEs by SOC and PT - Period [4th dose; 5th dose[		X			
14.3.7.5	TEAEs by SOC and PT - Period [5th dose; Week 36]		X			
14.3.7.6	TEAEs by SOC and PT - Period [Last dose;Week 36/Early Termination]		X			
14.3.7.7	TEAEs by SOC, PT and status of anti-IFNα neutralizing antibodies and anti-IFNα binding antibodies at time of event - Period [3rd dose; 4th dose[		X			
14.3.7.8	TEAEs by SOC, PT and status of anti-IFNα neutralizing antibodies and anti-IFNα binding antibodies at time of event - Period [4th dose; 5th dose[		X			
14.3.7.9	TEAEs by SOC, PT and status of anti-IFNα neutralizing antibodies and anti-IFNα binding antibodies at time of event - Period [5th dose; Week 36]		X			
14.3.7.10	TEAEs by SOC, PT and status of anti-IFNα neutralizing antibodies and anti-IFNα binding antibodies at time of event - Period [Last dose;Week 36/Early Termination]		X			
14.3.8.1	TEAEs by SOC, PT and relationship - Period [1st dose; 2nd dose[		X			
14.3.8.2	TEAEs by SOC, PT and relationship - Period [2nd dose; 3rd dose[		X			
14.3.8.3	TEAEs by SOC, PT and relationship - Period [3rd dose; 4th dose[		X			

Number	Title	Screened	SAF	FAS	PP	Other
14.3.8.4	TEAEs by SOC, PT and relationship - Period [4th dose; 5th dose[		X			
14.3.8.5	TEAEs by SOC, PT and relationship - Period [5th dose; Week 36]		X			
14.3.8.6	TEAEs by SOC, PT and relationship - Period [Last dose;Week 36/Early Termination]		X			
14.3.9.1	TEAEs by SOC, PT and intensity - Period [1st dose; 2nd dose[		X			
14.3.9.2	TEAEs by SOC, PT and intensity - Period [2nd dose; 3rd dose[		X			
14.3.9.3	TEAEs by SOC, PT and intensity - Period [3rd dose; 4th dose[		X			
14.3.9.4	TEAEs by SOC, PT and intensity - Period [4th dose; 5th dose[		X			
14.3.9.5	TEAEs by SOC, PT and intensity - Period [5th dose; Week 36]		X			
14.3.9.6	TEAEs by SOC, PT and intensity - Period [Last dose;Week 36/Early Termination]		X			
14.3.10	TEAEs leading to permanent study drug discontinuation by SOC and PT		X			
14.3.11.1	SAEs by SOC and PT - Before 1st dose		X			
14.3.11.2	SAEs by SOC and PT - Period [1st dose; 2nd dose[		X			
14.3.11.3	SAEs by SOC and PT - Period [2nd dose; 3rd dose[		X			
14.3.11.4	SAEs by SOC and PT - Period [3rd dose; 4th dose[		X			
14.3.11.5	SAEs by SOC and PT - Period [4th dose; 5th dose[		X			
14.3.11.6	SAEs by SOC and PT - Period [5th dose; Week 36]		X			
14.3.11.7	SAEs by SOC and PT - Period [Last dose;Week 36/Early Termination]		X			
14.3.11.8	SAEs by SOC, PT and status of IFNα neutra (postitive/negative) at time of event - Period [3rd dose; 4th dose[		X			
14.3.11.9	SAEs by SOC, PT and status of IFNα neutra (postitive/negative) at time of event - Period [4th dose; 5th dose[		X			
14.3.11.10	SAEs by SOC, PT and status of IFNα neutra (postitive/negative) at time of event - Period [5th dose; Week 36]		X			
14.3.11.11	SAEs by SOC, PT and status of IFNα neutra (postitive/negative) at time of event - Period [Last dose;Week 36/Early Termination]		X			

Number	Title	Screened	SAF	FAS	PP	Other
14.3.12.1	SAEs by SOC, PT and relationship - Before 1st dose		X			
14.3.12.2	SAEs by SOC, PT and relationship - Period [1st dose; 2nd dose[		X			
14.3.12.3	SAEs by SOC, PT and relationship - Period [2nd dose; 3rd dose[		X			
14.3.12.4	SAEs by SOC, PT and relationship - Period [3rd dose; 4th dose[		X			
14.3.12.5	SAEs by SOC, PT and relationship - Period [4th dose; 5th dose[		X			
14.3.12.6	SAEs by SOC, PT and relationship - Period [5th dose; Week 36]		X			
14.3.12.7	SAEs by SOC, PT and relationship - Period [Last dose;Week 36/Early Termination]		X			
14.3.13.1	SAEs by SOC, PT and intensity - Before 1st dose		X			
14.3.13.2	SAEs by SOC, PT and intensity - Period [1st dose; 2nd dose[		X			
14.3.13.3	SAEs by SOC, PT and intensity - Period [2nd dose; 3rd dose[		X			
14.3.13.4	SAEs by SOC, PT and intensity - Period [3rd dose; 4th dose[		X			
14.3.13.5	SAEs by SOC, PT and intensity - Period [4th dose; 5th dose[		X			
14.3.13.6	SAEs by SOC, PT and intensity - Period [5th dose; Week 36]		X			
14.3.13.7	SAEs by SOC, PT and intensity - Period [Last dose;Week 36/Early Termination]		X			
14.3.14	SAEs leading to permanent study drug discontinuation by SOC and PT		X			
14.3.15.1	Hematology - Value at each visit		X			
14.3.15.2	Hematology - Change from baseline		X			
14.3.15.3	Hematology - Abnormalities at each visit		X			
14.3.15.4	Hematology - Grade at each visit		X			
14.3.16.1	Chemistry - Value at each visit		X			
14.3.16.2	Chemistry - Change from baseline		X			
14.3.16.3	Chemistry - Abnormalities at each visit		X			
14.3.16.4	Chemistry - Grade at each visit		X			
14.3.17.1	Coagulation - Value at each visit		X			
14.3.17.2	Coagulation - Change from baseline		X			
14.3.17.3	Coagulation - Abnormalities at each visit		X			

Number	Title	Screened	SAF	FAS	PP	Other
14.3.17.4	Coagulation - Grade at each visit		X			
14.3.18	Urinalysis - Value at each visit		X			
14.3.19	Incidence of severe infections at D0		X			
14.3.20.1	Weight and BMI - Value at each visit		X			
14.3.20.2	Weight and BMI - Change from baseline		X			
14.3.21	Physical examination, Body system at each visit		X			
14.3.22.1	Vital signs - Value at each visit		X			
14.3.22.2	Vital signs - Change from baseline		X			
14.3.23	ECG - Abnormalities at each visit		X			
14.3.24	Concomitant medications		X			

10.2 List of figures

Number	Title	Screened	SAF	FAS	PP	Other
14.2.1	Sensitivity efficacy analysis - First co-primary endpoint - MMRM - Model diagnostic			X		
14.2.2	Immunogenicity analysis - Anti-IFNα binding antibody titers - Reverse cumulative distribution curves				X	
14.2.3	Immunogenicity analysis - NC50 - Reverse cumulative distribution curves				X	
14.2.4	Immunogenicity analysis - Anti-KLH binding antibody titers - Reverse cumulative distribution curves				X	

10.3 List of listings

Number	Title
16.2.1.1	Patient dispositions
16.2.1.2	Inclusion criteria
16.2.1.3	Exclusion criteria
16.2.2	Protocol deviations
16.2.3.1	Dataset Analyzed
16.2.3.2	Reasons for exclusion from the FAS and PP populations
16.2.4.1	Demographics data
16.2.4.2	Alcohol, drug and tobacco use
16.2.4.3	Gynecological examination
16.2.4.4	SLE medical history

Number	Title
16.2.4.5	SLE flare medical history
16.2.4.6	General Medical & Surgical history
16.2.4.7	Permitted medications
16.2.4.8	Prohibited medications
16.2.4.9	Previous and concomitant medications
16.2.4.10	Viral serology
16.2.4.11	Pregnancy test
16.2.5.1	Compliance
16.2.5.2	Extent of exposure
16.2.5.3	Administration of study product
16.2.6.1.1	IFN gene signature
16.2.6.1.2	Response to treatment according to BICLA
16.2.6.2	SLEDAI-2K
16.2.6.3	BILAG
16.2.6.4	SELENA-SLEDAI flare index
16.2.6.5	SLICC/ACR-DI
16.2.6.6	CLASI
16.2.6.7	Anti-IFNα binding antibodies
16.2.6.8	Anti-IFNα neutralizing antibodies
16.2.6.9	Anti-KLH binding antibodies
16.2.6.10	PGA
16.2.6.11	28-Tender and Swollen joint counts
16.2.6.12	Joint Pain VAS
16.2.6.13	SF-36
16.2.6.14	FACIT
16.2.6.15	Autoantibodies
16.2.6.16	Biomarkers

Number	Title
16.2.6.17	Anti-IFNα and anti-KLH antibody isotyping
16.2.6.18	Anti-Hemagglutinin antibody response
16.2.6.19	Neutralizing Anti-IFNα antibodies towards IFNα subtypes
16.2.6.20	IFNβ and IFNω cross neutralization
16.2.7.1	Solicited local reactions during a 7-day follow-up period after each study product administration
16.2.7.2	Solicited systemic reactions during a 7-day follow-up period after each study product administration
16.2.7.3	All other adverse events
16.2.7.4	Death, other Serious Adverse Events and Other Significant Adverse Events
16.2.8.1	Laboratory - Hematology
16.2.8.2	Laboratory - Chemistry
16.2.8.3	Laboratory - Coagulation
16.2.8.4	Urine analysis
16.2.9	Physical examination
16.2.10	Vital signs
16.2.11	ECG

11 References

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