Division	:	Worldwide Development
Information Type	:	Reporting and Analysis Plan (RAP)

Title	:	Reporting and Analysis Plan for a double-blind (sponsor unblinded) study to investigate safety, tolerability, pharmacokinetics, pharmacodynamics and clinical effect of repeat dosing of GSK2646264 in cutaneous lupus erythematosus patients
Compound Number	:	GSK2646264
Effective Date	:	28-JUN-2018

Description :

- This RAP is intended to describe the safety, tolerability, pharmacokinetics, pharmacodynamics and clinical efficacy analyses required for the study.
- This RAP will be provided to the study team members to convey the content of the final Statistical Analysis Complete (SAC) deliverable.

Author's Name and Functional Area:

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1. REPORTING & ANALYSIS PLAN SYNPOSIS

Overview	Key Elements of the RAP
Purpose	• The purpose of this reporting and analysis plan (RAP) is to describe the planned analyses and outputs for the final reporting of group A and group B.
Protocol	• This RAP is based on the protocol amendment 3 [(Dated: 14/DEC/2017) of study GSK204860 (GSK Document No.: 2015N246677_04] and eCRF Version (Version 1).
Primary Objective	• To evaluate the safety and tolerability of repeat doses of a cream formulation of GSK2646264 in patients with CLE
Primary Endpoint	• Safety and tolerability by laboratory tests, vital signs, 12 lead ECG and AE reporting
Study Design	• This is a double blind (sponsor unblinded) Phase Ib two group study to investigate repeat doses of GSK2646264, a spleen tyrosine kinase (SYK) inhibitor administered via topical delivery, on safety, pharmacodynamic effect and clinical efficacy in active CLE lesions and in acute CLE like lesions induced by an established protocol of Photoprovocation (PV). • The study population will be adult subjects (at least 18 years of age) that have been diagnosed with either subacute or chronic CLE. • Group A: Patients with fewer than two active lesions will be enrolled into group A and exposed to PV for 3 consecutive days. (Patients with LET, presenting with any number of lesions can enrol into Group A). Patients will be assessed for the development of lesions up to 14 days from the first PV. Patients that develop PV lesions at any time during this period, as determined by the local investigative team, will receive 1% strength GSK2646264 on 1 lesion and placebo on 1 lesion daily and either 1% strength GSK2646264 or placebo on an area of uninvolved skin, for skin PK of study drug, for 28 days. • Group B: Patients that have a minimum of 2 active existing CLE lesions as determined by the investigators will be enrolled into group B and have one lesion treated with 1% GSK2646264 and 1 lesion with placebo.
Planned Analyses	• Final analysis of groups A and B will be reported together after all subjects in groups A (up to 5 subjects) and B (approximately 15 subjects) have completed their follow-up visit.
Analysis Populations	• **Safety Population:** The 'Safety Population' is defined as subjects who receive at least one dose of study medication. This population is used for the summary of all data including safety, efficacy and pharmacodynamic (PD) data but excluding PK data. • **Pharmacokinetic Population:** The 'PK Population' is defined as subjects in the 'Safety' population who received an active dose and for whom a pharmacokinetic sample was obtained and analysed. This population is used for the summary of PK data only. • **PV failures:** The 'PV Failures Population' is defined as subjects who enrolled into Group A but were not randomised to a treatment. This population is used to present concomitant medications and Adverse event information for these subjects.

Overview	Key Elements of the RAP
	• **All Screened:** The 'All Screened Population' comprises of all subjects who have entered the study and will be used for the listing and summary of screen failures.
Hypothesis	• The primary objective of the study is to evaluate the safety and tolerability of repeat doses of a cream formulation of GSK2646264 in patients with CLE. • No formal statistical comparisons will be conducted to assess this primary objective. • If deemed appropriate to assess key efficacy and pharmacodynamic endpoints, the following exploratory comparisons may be conducted: GSK2646264 treatment vs. Placebo in PV lesions GSK2646264 treatment vs. Placebo in natural CLE lesions
Primary Analyses	• Safety data will be presented in tabular and/or graphical format and summarized descriptively according to GSK's Integrated Data Standards Library (IDSL) standards.
Secondary Analyses	• All plasma GSK2646264 concentration data will be graphically represented, descriptively summarised and listed appropriately. Plasma GSK2646264 concentration time data will be analysed using a Non-compartmental Analysis (NCA), if data permit. Pharmacokinetic data will be presented in graphical and/or tabular form and will be summarized descriptively. • Descriptive statistics of both raw and change from baseline, where appropriate will be calculated for erythema, oedema, dyspigmentation (and scaling in existing lesions only) and modified RCLASI. Change from baseline in each clinical activity assessment will be analysed using a repeated measures mixed effects model with subject random effect and treatment and baseline activity score as the fixed effect. • IFN mRNA data will be normalised, back transformed and log2 transformed mRNA intensity data in each IFN mRNA signature endpoints will be analysed using a mixed model with subject random effect and treatment and baseline intensity as the fixed effect. Fold changes will be derived form the back-transformed estimate of the difference between adjusted means.
Exploratory Analyses	• Descriptive statistics of both raw and change from baseline will be calculated for exploratory Pharmacodynamic/Biomarker endpoints. Change from baseline in these endpoints may be analysed using a mixed model with subject random effect and treatment and baseline activity score as the fixed effect. If data permits, endpoints may be analysed using a mixed model with subject random effect and skin type as the fixed effect to study the difference due to skin type.

2. SUMMARY OF KEY PROTOCOL INFORMATION

2.1. Changes to the Protocol Defined Statistical Analysis Plan

The following changes were made to the originally planned statistical analysis specified in the protocol amendment 3 [(Dated: 14/DEC/2017)]:

- The secondary endpoint for the plasma concentration of GSK2646264 is clarified in the RAP:

Secondary Objectives	Secondary Endpoints
• To evaluate the plasma concentrations of GSK2646264 in patients with CLE	• PK parameters, including but not limited to AUC, Cmax, tmax, half-life ($t_{1/2}$) if data permits.

Since no subjects were randomised into Group A, no outputs will be generated for this part. Listings will be produced for the enrolled (PV failure) subjects in Group A who were not randomised.

In the protocol Section 9.4.2, it states that 'Change from baseline in each clinical activity assessment will be analysed for each lesions type'. Due to the small number of patients in the study, no formal statistical analysis will be conducted for the RCLASI scores. Descriptive summary for raw and change baseline scores will be calculated and presented.

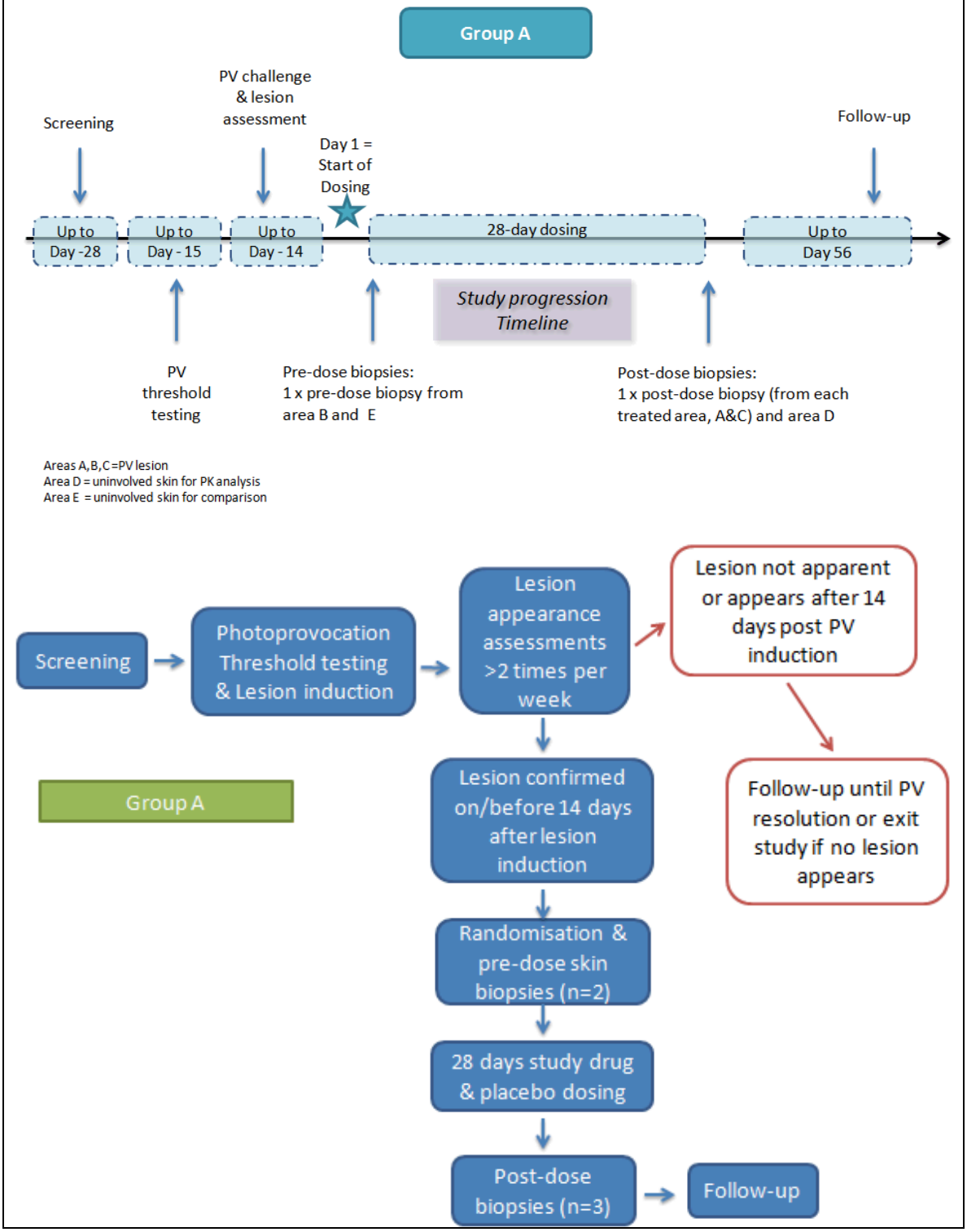
2.2. Study Objective(s) and Endpoint(s)

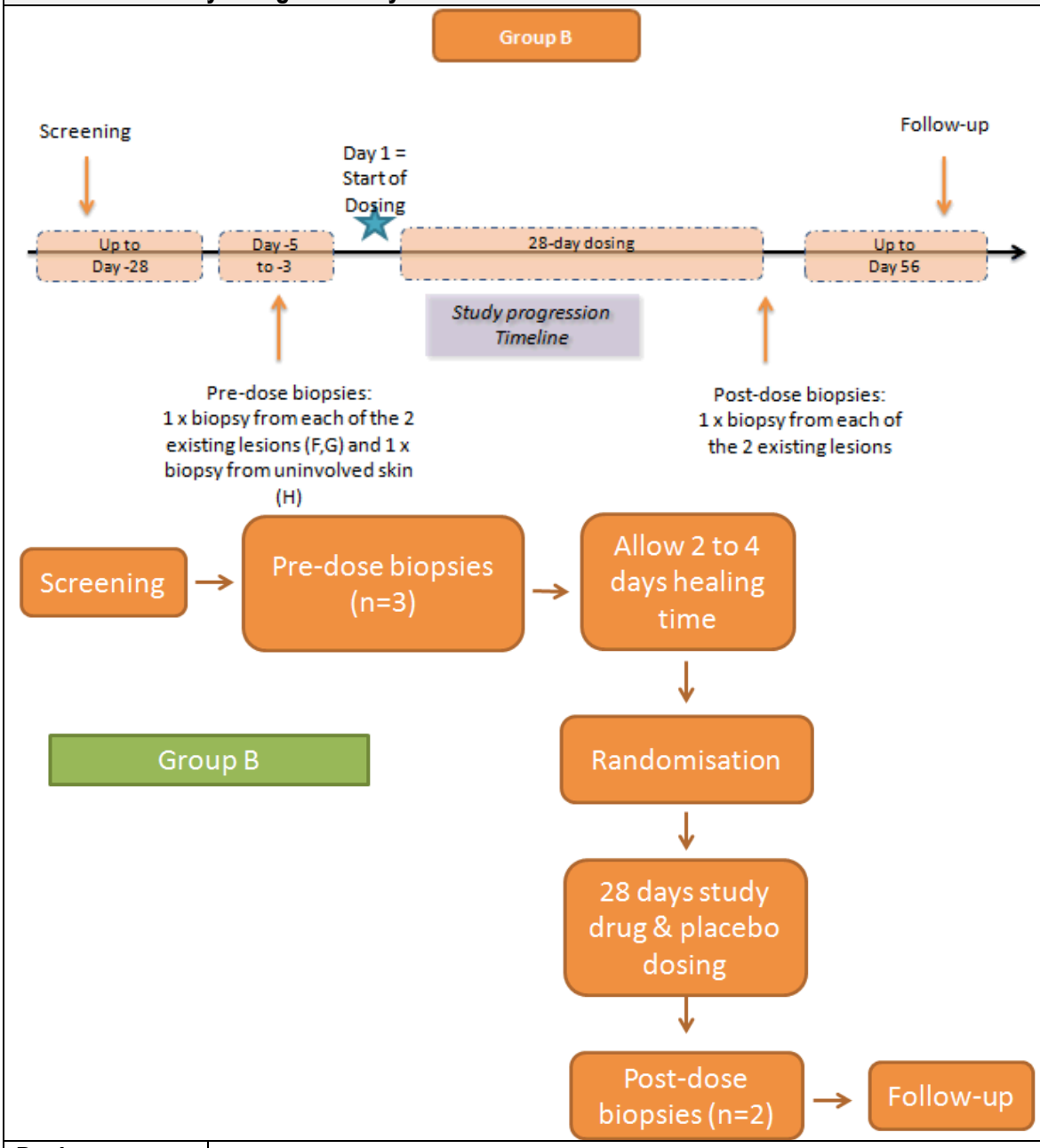
Objectives	Endpoints
Primary Objectives	**Primary Endpoints**
• To evaluate the safety and tolerability of repeat doses of a cream formulation of GSK2646264 in patients with CLE	• Safety and tolerability by laboratory tests, vital signs, 12-lead ECG, and AE reporting.
Secondary Objectives	**Secondary Endpoints**
• To determine the effect of GSK2646264 on the reduction in clinical activity score from baseline in treated PV and existing CLE lesions	• Change from baseline of components of a modified RCLASI- composite clinical activity score at day 14 and day 28 in PV and existing lesions in erythema, oedema, dyspigmentation and (scaling in existing CLE lesions only)
• To evaluate the plasma concentrations of GSK2646264 in patients with CLE	• PK parameters, including but not limited to AUC, Cmax, tmax, half-life ($t_{1/2}$) if data permits.
• To determine the effect of GSK2646264 on expression of IFN mRNA signature in skin biopsies in treated PV and existing CLE	• Change from baseline in IFN mRNA signature in skin biopsies at day 28 in PV and existing CLE lesions

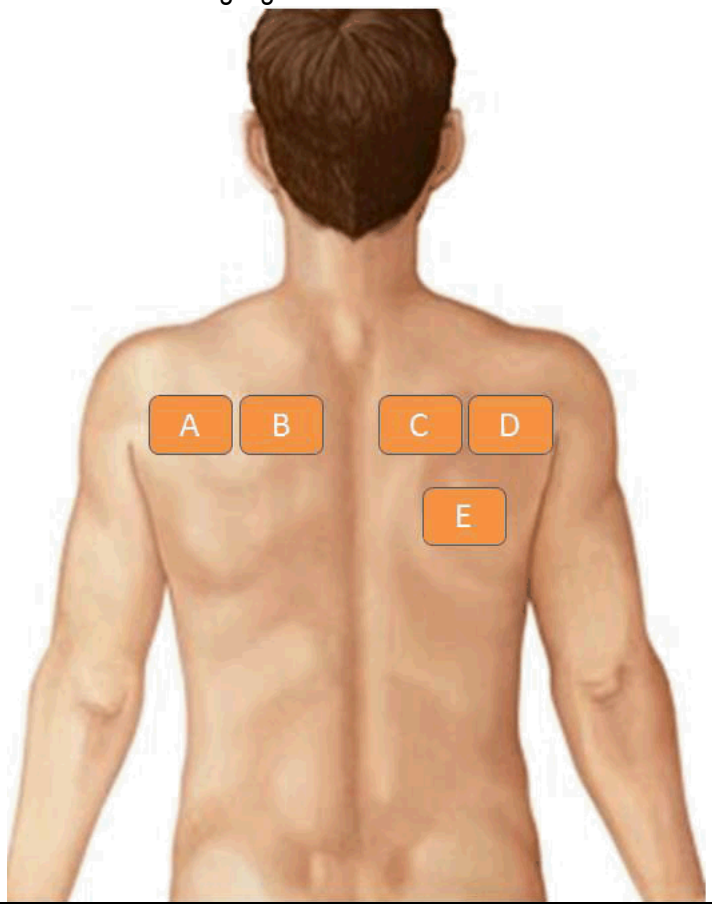
Objectives	Endpoints
lesions	
Exploratory Objectives	**Exploratory Endpoints**
• To determine the effect of GSK2646264 on expression of IFN protein markers in skin biopsies in treated PV and existing CLE lesions	• Change from baseline in IFN proteins (e.g. MxA, CXCL10) in skin biopsies at day 28 in PV and existing CLE lesions
• To determine the effect of GSK2646264 on expression of pSYK and SYK protein in skin biopsies in treated PV and existing CLE lesions	• Change from baseline in pSYK and SYK protein in skin biopsies at day 28 in PV and existing CLE lesions
• To determine the effect of GSK2646264 on immune cell markers in skin biopsies in treated PV and existing CLE lesions	• Change from baseline in immune cell proteins (e.g. CD3, CD20, CD11c, CD123, CD68) in skin biopsies at day 28 in PV and existing CLE lesions
• To determine the effect of GSK2646264 on the histological disease activity in PV and existing CLE lesions	• Change from baseline in histopathology score (including parakeratosis, ballooning/hydropic degeneration, epidermal cell-death, junctional and dermal inflammation) in skin biopsies at day 28 in PV and existing CLE lesions
• To evaluate the skin concentrations of GSK2646264 in patients with CLE	• Skin biopsy concentrations and derived pharmacokinetic parameters of GSK2646264

2.3. Study Design

Overview of Study Design and Key Features



Overview of Study Design and Key Features	
	
Design Features	• This is a double blind (sponsor unblinded) Phase Ib two group study to investigate repeat doses of GSK2646264, a spleen tyrosine kinase (SYK) inhibitor administered via topical delivery, on safety, pharmacodynamic effect and clinical efficacy in active CLE lesions and in acute CLE like lesions induced by an established protocol of PV. The study population will be adult subjects (at least 18 years of age) that have been diagnosed with either subacute or chronic CLE. Patients with Lupus Erythematosus Tumidus (LET) are allowed in group A only. • Group A: Patients with fewer than two active lesions will be enrolled into group A and exposed to PV for 3 consecutive days (Patients with LET presenting with any number of lesions can also be enrolled into Part A). Patients will be assessed for the development of lesions up to 14 days

<table>
<tr><th colspan="2">Overview of Study Design and Key Features</th></tr>
<tr><td></td><td>from the first PV. Patients that develop PV lesions at any time during this period, as determined by the local investigative team, will receive 1% strength GSK2646264 on 1 lesion and placebo on 1 lesion daily and either 1% strength GSK2646264 or placebo on an area of uninvolved skin, for skin PK of study drug, for 28 days.
• Group B: Patients that have a minimum of 2 active existing CLE lesions as determined by the investigators will be enrolled into group B and have one lesion treated with 1% GSK2646264 and 1 lesion with placebo.</td></tr>
<tr><td>Dosing</td><td>• Topical application daily for 28 days</td></tr>
<tr><td>Treatment Assignment</td><td>• Group A Subjects will be assigned the following regimens:
<table>
<tr><th></th><th>Skin Sites A/C/D</th><th>Sequence assignment ratio</th></tr>
<tr><td>Sequence 1</td><td>A/P/A</td><td>4</td></tr>
<tr><td>Sequence 2</td><td>A/P/P</td><td>1</td></tr>
<tr><td>Sequence 3</td><td>P/A/A</td><td>4</td></tr>
<tr><td>Sequence 4</td><td>P/A/P</td><td>1</td></tr>
</table>
P=Placebo, A= GSK2646264 1%
Where sites are highlighted below:

</td></tr>
</table>

<table>
<tr><th colspan="2">Overview of Study Design and Key Features</th></tr>
<tr><td></td><td>PV lesion and area uninvolved skin (area B and E respectively) will be used solely to take biopsy.
• Group B Subjects will be assigned the following regimens:
<table>
<tr><th></th><th>Skin Sites F/ G</th><th>Sequence assignment ratio</th></tr>
<tr><td>Sequence 1</td><td>A/P</td><td>1</td></tr>
<tr><td>Sequence 2</td><td>P/A</td><td>1</td></tr>
</table>
P=Placebo, A= GSK2646264 1%
Where skin sites F and G will be chosen, lesions F> in size than G, and an area of uninvolved skin (area H) will be used solely to take biopsy.</td></tr>
<tr><td>Final analysis</td><td>• Final analysis of groups A and B will be reported together after all subjects in groups A (up to 5 subjects) and B (approximately 15 subjects) have completed their follow-up visit.</td></tr>
</table>

2.4. Statistical Hypotheses

The primary objective of the study is to evaluate the safety and tolerability of repeat doses of a cream formulation of GSK2646264 in patients with CLE. No formal statistical comparisons will be conducted to assess this objective. If deemed appropriate to assess key efficacy and pharmacodynamic endpoints, the following exploratory comparisons may be conducted:

- Group B
    - GSK2646264 treatment vs. Placebo in natural CLE lesions

If deemed appropriate the following exploratory comparisons may be conducted for pharmacodynamic markers from the skin biopsies:

- Group B
    - Baseline GSK2646264 lesion vs uninvolved skin (skin area H)
    - Baseline Placebo lesion vs uninvolved skin (skin area H)
    - GSK2646264 lesion at Day 28 vs uninvolved skin (skin area H)
    - Placebo lesion at Day 28 vs uninvolved skin (skin area H)

3. PLANNED ANALYSES

3.1. Final Analyses

The final planned analyses will be performed after the completion of the following sequential steps:

1. All subjects have completed the study as defined in the protocol.
2. All required database cleaning activities have been completed and final database release and database freeze has been declared by Data Management.
3. All criteria for unblinding the randomisation codes have been met.

4. Randomisation codes have been distributed according to RandAll NG procedures.

4. ANALYSIS POPULATIONS

Population	Definition / Criteria	Analyses Evaluated
Safety	• Comprise of all subjects who receive at least one dose of study treatment. • This population will be based on the treatment the subject actually received.	• Study Population • Safety • Efficacy • Pharmacodynamic
Pharmacokinetic	• Subjects in the 'Safety' population for whom a pharmacokinetic sample was obtained and analysed.	• PK
PV Failures	• Subjects who enrolled into Group A but were not randomised to a treatment.	• AEs relating to PV • Concomitant medications
All Screened	• Comprises of all subjects who have entered the study	• Screen failures

NOTES :

- Please refer to Appendix 8: List of Data Displays which details the population to be used for each display being generated.

4.1. Protocol Deviations

- Important protocol deviations (including deviations related to study inclusion/exclusion criteria, conduct of the trial, patient management or patient assessment) will be summarised and listed.
- Protocol deviations will be tracked by the study team throughout the conduct of the study in accordance with the Protocol Deviation Management Plan.
    - Data will be reviewed prior to freezing the database to ensure all important deviations and deviations which may lead to exclusion from the analysis are captured and categorised on the protocol deviations dataset.
    - This dataset will be the basis for the summaries and listings of protocol deviations.
- A separate summary and listing of all inclusion/exclusion criteria deviations will also be provided. This summary will be based on data as recorded on the inclusion/exclusion page of the eCRF.

5. CONSIDERATIONS FOR DATA ANALYSES AND DATA HANDLING CONVENTIONS

Table 1 provides an overview of appendices within the RAP for outlining general considerations for data analyses and data handling conventions.

Table 1 Overview of Appendices

Section	Component
11.1	Appendix 1: Time & Events
11.2	Appendix 2: Data Display Standards & Handling Conventions
11.3	Appendix 3: Derived and Transformed Data
11.4	Appendix 4: Premature Withdrawals & Handling of Missing Data
11.5	Appendix 5: Values of Potential Clinical Importance
11.6	Appendix 6: Model Checking and Diagnostics for Statistical Analyses.

6. STUDY POPULATION ANALYSES

6.1. Overview of Planned Analyses

The study population analyses will be based on the Safety population, unless otherwise specified.

Table 2 provides an overview of the planned study population analyses, with full details of data displays being presented in Appendix 8: List of Data Displays.

Table 2 Overview of Planned Study Population Analyses

Endpoint / Parameter / Display Type	Data Displays Generated		
	Table	Figure	Listing
Subject Disposition			
Subject Disposition	Y		
Reasons for Screen Failure	Y		Y
Subjects by Country and Centre	Y		
Reasons for Subject Withdrawal			Y
Subjects for Whom the Treatment Blind was Broken			Y
Planned and Actual Treatments			Y
Protocol Deviations			
Important Protocol Deviations	Y		Y
Subjects with Inclusion/Exclusion Criteria Deviations			Y [1]
Populations Analysed			
Study Populations and Exclusions	Y		
Subjects Excluded from Any Population			Y
Demographic and Baseline Characteristics			
Demographic Characteristics	Y		Y
Race and Racial Combinations	Y		Y [2]
Race and Racial Combination Details	Y		
Prior and Concomitant Medications			
Current/Past Medical Conditions	Y		Y
Concomitant Medications	Y		Y
Type of CLE	Y		Y
Exposure and Treatment Compliance			
Exposure to Study Treatment	Y		Y

NOTES :

- Y = Yes display generated.

[1] Listing also includes analysis population exclusions.
[2] Listing of race.

7. PRIMARY STATISTICAL ANALYSES

7.1. Safety Analyses

7.1.1. Overview of Planned Adverse Events Analyses

The safety analyses will be based on the Safety population, unless otherwise specified.

Table 3 provides an overview of the planned analyses, with full details of data displays being presented in Appendix 8: List of Data Displays.

Table 3 Overview of Planned Adverse Events Analyses

Endpoint / Parameter/ Display Type	Absolute		
	Summary		Individual
	T	F	L
Adverse Events (AEs)			
All AEs by SOC	Y		Y
All Drug-Related AEs by SOC	Y		
Subject Numbers for Individual AEs			Y
Relationship Between AE SOCs, PT & Verbatim Text			Y
Serious and Other Significant AEs			
Non-Fatal Serious AEs			Y
Serious AEs by SOC	Y		
Reasons for Considering as a Serious AE			Y
AEs Leading to Withdrawal from Study / Permanent Discontinuation of Study Treatment by Overall Frequency	Y		Y

[1] Plot of common AEs and relative risk will be generated.

7.1.2. Overview of Planned Clinical Laboratory Analyses

The safety analyses will be based on the safety population, unless otherwise specified.

Table 4 provides an overview of the planned analyses, with further details of data displays being presented in Appendix 8: List of Data Displays.

Table 4 Overview of Planned Clinical Laboratory Analyses

Endpoint / Parameter/ Display Type	Absolute		Change from BL	
	Summary	Individual	Summary	Individual
	T	L	T	L
Chemistry				
Chemistry Changes from Baseline			Y	
Emergent Chemistry Results Relative to Normal Range	Y			
Hematology				
Hematology Changes from Baseline			Y	
Emergent Hematology Results Relative to Normal Range	Y			
Urinalysis				
Urine Concentration Changes from Baseline			Y	
Emergent Urinalysis Dipstick Results	Y			
Hepatobiliary (Liver)				
Liver Monitoring/Stopping Event Reporting	Y			
Hepatobiliary Laboratory Abnormalities	Y			
Medical Conditions for Subjects with Liver Stopping Events		Y		
Substance Use for Subjects with Liver Stopping Events		Y		
All Laboratory				
Laboratory Data for Subjects with Abnormalities of Potential Clinical Concern		Y		Y
Laboratory Data Abnormalities of Potential Clinical Importance		Y		Y

NOTES:

- T = Table, L = Listings, Y = Yes display generated, PCI = Potential Clinical Importance, BL = Baseline
- Summary = Represents TFL related to any summaries (i.e. descriptive statistics) of the observed raw data.
- Individual = Represents FL related to any displays of individual subject observed raw data.

7.1.3. Overview of Planned Other Safety Analyses

The safety analyses will be based on the Safety population, unless otherwise specified.

Table 5 provides an overview of the planned analyses, with further details of data displays being presented in Appendix 8: List of Data Displays.

Table 5 Overview of Planned Other Safety Analyses

Endpoint / Parameter/ Display Type	Absolute		Change from BL	
	Summary	Individual	Summary	Individual
	T	L	T	L
ECG				
ECG Findings	Y			
Maximum Emergent QTc Values by Category	Y			
Change from Baseline in ECG Values by Visit			Y	
Maximum Change from Baseline in QTc Values by Category			Y	
All ECG Values for Subjects with a Value of PCI		Y		Y
ECG Values of PCI		Y		Y
Abnormal ECG Findings		Y		
Vital Signs				
Change From Baseline in Vital Signs by Visit			Y	
Emergent Vital Signs Results by Grade Relative to Normal Range by PCI Criteria	Y			
All Vital Signs for Subjects with Values of PCI		Y		Y
Local Tolerability				
Skin Irritation Score[1]	Y[2]	Y[2]	Y[2]	Y[2]
Dermal Response and Other Dermal Effects	Y	Y		

NOTES:

- T = Table, L = Listings, Y = Yes display generated, PCI = Potential Clinical Importance, BL = Baseline
- Summary = Represents TFL related to any summaries (i.e. descriptive statistics) of the observed raw data.
- Individual = Represents FL related to any displays of individual subject observed raw data.
- [1]: See Section 11.3.3 for more details.
- [2]: Absolute and change from baseline will be displayed on the same output.

8. SECONDARY STATISTICAL ANALYSES

8.1. Efficacy Analyses

8.1.1. Overview of Planned Efficacy Analyses

The secondary efficacy analyses will be based on the safety population, unless otherwise specified and will be based on Group B subjects only.

Table 6 provides an overview of the planned efficacy analyses, with further details of data displays being presented in Appendix 8: List of Data Displays.

Table 6 Overview of Planned Efficacy Analyses

Endpoint	Absolute			
	Summary		Individual	
	T	F	F	L
Clinical Score				
RCLASI and Components	Y[1,2]	Y[2]	Y[2]	Y[1]

NOTES :

- T = Table, F = Figure, L = Listing, Y = Yes display generated.
- Stats Analysis = Represents TFL related to any formal statistical analyses (i.e. modelling) conducted.
- Summary = Represents TFL related to any summaries (i.e. descriptive statistics) of the observed raw data.
- Individual = Represents FL related to any displays of individual subject observed raw data.
- [1]: Include both absolute and change from baseline
- [2]: By Disease Characteristics (Chronic CLE, Acute CLE, Sub-acute CLE, LET and All).

8.1.2. Planned Efficacy Statistical Analyses

Due to the small number of patients in the study, no formal statistical analysis will be conducted.

8.2. Pharmacokinetic Analyses

8.2.1. Overview of Planned Pharmacokinetic Analyses

The pharmacokinetic (PK) analyses will be based on the Pharmacokinetic population, unless otherwise specified and will be based on Group B subjects only.

The pharmacokinetic analyses will be performed by, or under the direct auspices of Clinical Pharmacokinetic Modelling Simulation (CPMS), GlaxoSmithKline.
Table 7 provides an overview of the planned analyses, with full details being presented in Appendix 8: List of Data Displays.

Table 7 Overview of Planned Pharmacokinetic Analyses

Endpoint	Untransformed				Log-Transformed
	Summary		Individual		Summary
	T	F	F	L	T
Plasma					
Plasma concentrations	Y	Y[1,2]	Y[1]	Y	
Plasma PK Parameters[3]	Y			Y	Y

NOTES :

- T = Table, F = Figure, L = Listings, Y = Display generated.
- Stats Analysis = Represents TFL related to any formal statistical analyses (i.e. modelling) conducted.
- Summary = Represents TFL related to any summaries (i.e. descriptive statistics) of the observed raw data.
- Individual = Represents FL related to any displays of individual subject observed raw data.
- [1] Linear and Semi-log plots will be created on the same display
- [2] Separate Mean (±SD) and Median (range) plots will be generated
- [3] if data permit

8.2.2. Drug Concentration Measures

Refer to Appendix 5: Data Display Standards & Handling Conventions (Section 11.2.3 Reporting Process & Standards).

8.2.3. Pharmacokinetic Parameters

8.2.3.1. Deriving Pharmacokinetic Parameters

- Refer to Appendix 5: Data Display Standards & Handling Conventions (Section 11.2.3 Reporting Process & Standards).
- The pharmacokinetic parameters will be calculated by standard non-compartmental analysis according to current working practices and using WinNonLin, if data permit.
- All calculations of non-compartmental parameters will be based on actual sampling times.

Table 8 Derived Pharmacokinetic Parameters

Parameter	Parameter Description
AUC(0-t)	Area under the concentration-time curve from time zero to the time of the last quantifiable concentration (C(t)) will be calculated using the linear trapezoidal rule for each incremental trapezoid and the log trapezoidal rule for each decremental trapezoid.
AUC(0-∞)	Area under the concentration-time curve extrapolated to infinity will be calculated as: **AUC = AUC(0-t) + C(t) / lambda_z**
%AUCex	The percentage of AUC (0-∞) obtained by extrapolation (%AUCex) will be calculated as: **[AUC(0-inf) – AUC(0-t)] / AUC(0-inf) x 100**
Cmax	Maximum observed concentration, determined directly from the concentration-time data.
tmax	Time to reach Cmax, determined directly from the concentration-time data.
t½	Apparent terminal half-life will be calculated as: **t½ = ln2 / lambda_z**

NOTES:

- Additional parameters may be included as required.
- Lambda_z is the terminal phase rate constant.

8.2.3. Pharmacokinetics from Skin biopsy

The PK analysis of the skin biopsy was from Group A in the study. Since no subjects were randomised in this group, there were no skin biopsies for the PK analysis and therefore no outputs will be generated.

8.3. Pharmacodynamic and Biomarker Analyses

8.3.1. Overview of Planned Pharmacodynamic and Biomarker Analyses

The pharmacodynamic analyses will be based on the Safety population, unless otherwise specified and will be based on Group B subjects only.

The transcriptomic data handling, qc and normalisation will be performed by, or under the direct auspices of Target Sciences (TSci) Statistics, GlaxoSmithKline.
Table 9 provides an overview of the planned pharmacodynamic and Biomarker analyses, with full details of data displays being presented in Appendix 8: List of Data Displays.

Table 9 Overview of Planned Pharmacodynamic and Biomarker Analyses

Endpoint	Absolute				Fold change		
	Summary		Individual		Stats Analysis		
	T	F	F	L	T	F	L
IFN mRNA signature in skin biopsies[2]	Y[1]		Y[1]	Y	Y	Y	Y

NOTES :

- T = Table, F = Figure, L = Listing, Y = Yes display generated.
- Stats Analysis = Represents TFL related to any formal statistical analyses (i.e. modelling) conducted.
- Summary = Represents TFL related to any summaries (descriptive statistics) of the observed raw data.
- Individual = Represents FL related to any displays of individual subject observed raw data.
- [1]: By Disease Characteristics (Chronic CLE, Acute CLE, Sub-acute CLE, LET and All).
- [2]: List of genes and probesets are given in Section 11.3.5

RNA will be extracted and hybridised using a balanced batch design. An appropriate microarray platform will be determined at the time of hybridisation, to allow for improvements in technology. The quality of the data will be assessed and then normalised using appropriate methodologies and software.

Microarray mRNA data will be normalised using gcRMA or RMA in Array Studio v5.0 or later. After normalisation, the data will be quality assessed and any samples deemed as QC fails will be excluded from any further analysis. This quality assessment will involve looking for outlying signals in both the normalised expression data and the MAS5 QC metrics generated from each sample. If any samples are excluded, the remaining data will be re-normalised. The output from the normalisation will be $\log_2$ transformed mRNA intensity data (measured in arbitrary units).

8.3.2. Planned Pharmacodynamic and Biomarker Statistical Analyses

Planned Statistical Analyses
Endpoint(s)
• IFN mRNA signatures
Model Specification
Microarray mRNA data have been collected from the skin biopsy in both GSK2646264 and placebo

Planned Statistical Analyses

treated lesions on Day -5 to -3 (Baseline) and Day 28.

To compare the expression value for each probe set, the following mixed- effects model will be fitted to each probe set, with mRNA intensity ($log_{2\ scale}$) as the response variable.

Baseline is defined as the measurement taken pre-dose at baseline of each treated lesions (i.e lesion-specific baseline).

The baseline observation will be defined as an additional response measured on the same subject prior to application of the treatment. Then this observation is not affected by any of the effects included in the basic model for the response.

Visit	Trt	XTrt
Baseline	GSK2646264	NA
Baseline	Placebo	NA
Day 28	GSK2646264	GSK2646264
Day 28	Placebo	Placebo

The model will include:

- Fixed terms: Treatment (Xtrt: Placebo, GSK2646264, NA), Visit, Visit and Treatment (Xtrt) interaction
- Random: Subject (in sas Random intercept /subject=subjid)
- Repeated: Visit (in SAS Repeated visit / subject=subjid type=un)

For each probe set analysed adjusted means with corresponding 95% CI and fold changes with corresponding 95% CI's will be outputted. The fold change is derived from the ratio of the back-transformed estimate of the difference (GSK2646264 – Placebo) between adjusted means.

Since the data will be log_2 transformed prior to the analysis the treatment effects will be expressed as ratios after back transformation. These ratios can be converted from treatment ratios to fold change values as follows:

- If ratio ≥ 1 then fold change = ratio
- If ratio < 1 then fold change = -1/ratio

Model Checking

- Refer to Appendix 6 : Model Checking and Diagnostics for Statistical Analyses.

Model Results Presentation

- Back transformed baseline-adjusted means along with 95% CIs will be calculated for each treatment group. Additionally, fold changes between active and placebo in change from

Planned Statistical Analyses
baseline intensity will be calculated, along with 95% CI.
Endpoint(s)
• IFN mRNA signatures
Model Specification
Microarray mRNA data have been collected from the skin biopsy in from different lesions on Day -5 to -3 (Baseline) and Day 28. To compare the expression value for each probe set, the following mixed- effects model will be fitted to each probe set, with mRNA intensity (log2 scale) as the response variable. The model will include: • Fixed terms: Skin Type • Random: Subject (in sas Random intercept /subject=subjid) Notes Group B: Skin type refers to uninvolved skin, baseline GSK2646264 lesion, baseline Placebo lesion, GSK2646264 lesion at day 28 and Placebo lesion at day 28 For each probe set analysed adjusted means with corresponding 95% CI and fold changes with corresponding 95% CI's will be outputted. The fold change is derived from the ratio of the back-transformed estimate of the difference (GSK2646264 – Placebo) between adjusted means. Since the data will be log2 transformed prior to the analysis the lesion effects will be expressed as ratios after back transformation. These ratios can be converted from treatment ratios to fold change values as follows: • If ratio ≥ 1 then fold change = ratio • If ratio < 1 then fold change = -1/ratio
Model Checking
• Refer to Appendix 6: Model Checking and Diagnostics for Statistical Analyses.
Model Results Presentation
Back transformed baseline-adjusted means along with 95% CIs will be calculated for each skin type group. Additionally, following fold changes with 95% CI will also be presented: - GSK2646264 lesion at day 28 – Uninvolved Skin (skin area H) - Placebo lesion at day 28 – Uninvolved Skin (skin area H) - Baseline GSK2646264 lesion – Uninvolved Skin (skin area H) - Baseline Placebo lesion – Uninvolved Skin (skin area H)

9. OTHER STATISTICAL ANALYSES

9.1. Exploratory Pharmacodynamic and Biomarker Analyses

9.1.1. Overview of Planned Exploratory Pharmacodynamic and Biomarker Analyses

The pharmacodynamic analyses will be based on the Safety population, unless otherwise specified.

Table 9 provides an overview of the planned pharmacodynamic and Biomarker analyses, with full details of data displays being presented in Appendix 8: List of Data Displays.

Table 10 Overview of Planned Exploratory Pharmacodynamic and Biomarker Analyses

Endpoint	Untransformed			
	Absolute			
	Summary		Individual	
	T	F	L	F
Skin Biopsy				
IFN proteins (e.g. MxA, CXCL10) in skin biopsies	Y[2,3]	Y[3]	Y[2]	Y[3]
Immune cell proteins (e.g. CD3, CD20, CD11c, CD123, CD68) in skin biopsies	Y[2,3]	Y[3]	Y[2]	Y[3]
Histopathology score in skin biopsies [1]	Y[2,3]	Y[3]	Y[2]	Y[3]
pSYK and SYK protein in skin biopsies	Y[2,3]	Y[3]	Y[2]	Y[3]

NOTES :

- T = Table, F = Figure, L = Listing, Y = Yes display generated.
- Stats Analysis = Represents TFL related to any formal statistical analyses (i.e. modelling) conducted.
- Summary = Represents TFL related to any summaries (descriptive statistics) of the observed raw data.
- Individual = Represents FL related to any displays of individual subject observed raw data.
- [1] component scores; parakeratosis, ballooning/hydropic degeneration, epidermal cell-death, junctional and dermal inflammation will not be statistically analysed.
- [2] Include both absolute and change from baseline
- [3]: By Disease Characteristics (Chronic CLE, Acute CLE, Sub-acute CLE, LET and All).

10. REFERENCES

GlaxoSmithKline Document Number 2015N246677_04: A double-blind (sponsor unblinded) study to investigate safety, tolerability, pharmacokinetics, pharmacodynamics and clinical effect of repeat dosing of GSK2646264 in cutaneous lupus erythematosus patients Effective date: 14-DEC-2017

11. APPENDICES

Section	Appendix
RAP Section 5 : General Considerations for Data Analyses & Data Handling Conventions	
Section 11.1	Appendix 1: Time and Events
Section 11.2	Appendix 2: Data Display Standards & Handling Conventions • Study Treatment & Sub-group Display Descriptors • Baseline Definitions & Derivations • Reporting Process & Standards
Section 11.3	Appendix 3: Derived and Transformed Data • General, Study Population & Safety • Efficacy • Pharmacodynamic and or Biomarkers
Section 11.4	Appendix 4: Premature Withdrawals & Handling of Missing Data • Premature Withdrawals • Handling of Missing Data
Section 11.5	Appendix 5: Values of Potential Clinical Importance
Section 11.6	Appendix 6: Model Checking and Diagnostics for Statistical Analyses
Other RAP Appendices	
Section 11.7	Appendix 7: Abbreviations & Trade Marks
Section 11.8	Appendix 8: List of Data Displays
Section 11.9	Appendix 9: Example Mock Shells for Data Displays

11.1. Appendix 1: Time & Events

11.1.1. Protocol Defined Time & Events

11.1.2. Group A

Procedure	Screening (up to Day -28)	Day -15	Day -14	Day -13 to -1	Day 1	Day 2 to Day 13	Day 14	Day 15 to Day 20	Day 21 to Day 27	Day 28	Day 29 to 42	Follow-up[a]	[a] All procedures listed to also be conducted if a subject decides to prematurely withdraw/discontinue
Informed Consent	X												
Inc/Exc criteria assessment	X												
Demography	X												
Pregnancy Test (women)	X				X		X					X	Pregnancy testing to be performed at Screening, on Day 1 (pre-dose), Day 14 (pre-dose) and once during follow-up, with day recorded
TSH, free T4, free T3	X				X		X					X	
Vital Signs	X	X			X		X			X			
Safety Lab Samples (clin chem, haematol, Urinalysis)	X	X		X	X		X			X		X	On days of dosing samples should be taken predose. Sample timepoints during the Day-13 to Day-1 period are as follows: – once weekly during visits to assess PV lesion development
Full Physical Exam	X											X	

Procedure	Screening (up to Day -28)	Day -15	Day -14	Day -13 to -1	Day 1	Day 2 to Day 13	Day 14	Day 15 to Day 20	Day 21 to Day 27	Day 28	Day 29 to 42	Follow-up[a]	[a] All procedures listed to also be conducted if a subject decides to prematurely withdraw/discontinue
Brief Physical Exam				X									Assessment to be performed pre-dose Sample timepoints during the Day-13 to Day-1 period are as follows: – once weekly during visits to assess PV lesion development
12-lead ECG	X				X		X					X	On days of dosing assessments should be performed predose
SLE clinical assessment	X				X					X		X	On days of dosing assessment as defined by the investigator to be performed pre-dose .
ANA, anti-dsDNA , anti-Ro and anti-La antibodies, HIV, Hep B, Hep C, FSH, Drug screen	X												
Skin Biopsies					X[b]					X[b]			[b]Day 1 biopsies will be taken pre-dose. Day 28 biopsies will be taken 4 hours post-dose
UV threshold testing		X											
Photoprovocation			X[c, d]										Performed 24 hours after UV threshold testing. [c]PV occurs once every 24 hours for 3 days on Day-14, Day-13 & Day-12. [d] If PV induced lesions appear at all 3 sites after Day -14 or Day -13, PV treatment can be stopped early

Procedure	Screening (up to Day -28)	Day -15	Day -14	Day -13 to -1	Day 1	Day 2 to Day 13	Day 14	Day 15 to Day 20	Day 21 to Day 27	Day 28	Day 29 to 42	Follow-up[a]	[a] All procedures listed to also be conducted if a subject decides to prematurely withdraw/discontinue
Lesion induction assessment			<- ----X------>										
Lesion resolution assessment											X	X	
Clinical score					X		X			X			Components of the RCLASI as defined in Section 11.3.4 Assessments to be performed pre-dose
Local Tolerability Assessment					X	X	X	X	X	X	X		Assessments to be performed pre-dose and up to one hour following dosing on days of dosing
Dosing					X	X	X	X	X	X			Once daily
Randomisation					X								Pre-dose

Procedure	Screening (up to Day -28)	Day -15	Day -14	Day -13 to -1	Day 1	Day 2 to Day 13	Day 14	Day 15 to Day 20	Day 21 to Day 27	Day 28	Day 29 to 42	Follow-up[a]	[a] All procedures listed to also be conducted if a subject decides to prematurely withdraw/discontinue
PK blood sample					X	X	X		X	X	X	X	Sampling timepoints: Day 1 = pre-dose; and 5hrs (±1 hr) Between Day 2 and Day13: one pre-dose sample or postdose sample with time recorded since last dose Day 14: predose sample Between Day 21 and Day27: one pre-dose sample or postdose sample with time recorded since last dose Day 28: one postdose sample with time recorded since last dose Between Day 29 and Day 42: one sample with time recorded since last dose Follow-up visit: one sample with sampling day recorded
AE/SAE Review	X	<----------X---------->											
Concomitant Medication Review	X	<----------X---------->											

11.1.3. Group A PV non-responders

Procedure	Once-weekly up to 28 days after first photoprovocation	Final Follow-up visit(s) (occurs until final PV induced lesion has resolved)	Notes
Brief Physical Exam	X	X	IMPORTANT: This table is **ONLY** applicable for subjects in group A that do not develop PV induced lesions within 14 days of the start of photoprovocation Once-weekly assessments will occur from 15 days post first photoprovocation up until 28 days post first photoprovocation. Any PV lesion that develops after 15 days post-photoprovocation will be followed up until resolution.
PV Lesion assessment (if present)	X	X	
AE/SAE Review	X	X	
Concomitant Medication Review	X		

11.1.4. Group B

Procedure	Screening (up to Day -28)	Day -5 to -3	Day 1	Day 2 to Day 13	Day 14	Day 15 to Day 20	Day 21 to Day 27	Day 28	Day 29 to 42	Follow-up (between Day 43 to Day 56)[a]	[a] All procedures listed to also be conducted if a subject decides to prematurely withdraw/discontinue
Informed Consent	X										
Inc/Exc criteria assessment	X										
Demography	X										
Pregnancy Test (women)	X		X		X					X	Pregnancy testing to be performed at Screening, on Day 1 (pre-dose), Day 14 (pre-dose) and once during follow-up, with day recorded
TSH, free T4, freeT3	X		X		X					X	
Vital Signs	X	X			X			X			
Safety Lab Samples (clin chem ,haematol, Urinalysis)	X	X	X		X			x		X	On days of dosing samples should be taken predose
Full Physical Exam	X									X	
Brief Physical Exam			X								Assessment to be performed pre-dose
12-lead ECG	X		X		X					X	On days of dosing assessments should be performed predose
SLE clinical assessment	X		X					X		X	On days of dosing assessment as defined by the investigator to be performed pre-dose .
ANA, anti-dsDNA antibodies, anti-Ro and anti-La antibodies, HIV, Hep B, Hep C, FSH, Drug screen	X										
Lesion selection		X									

Procedure	**Screening (up to Day -28)**	**Day -5 to -3**	**Day 1**	**Day 2 to Day 13**	**Day 14**	**Day 15 to Day 20**	**Day 21 to Day 27**	**Day 28**	**Day 29 to 42**	**Follow-up (between Day 43 to Day 56)[a]**	[a] All procedures listed to also be conducted if a subject decides to prematurely withdraw/discontinue
Skin Biopsies		X[b]						X[b]			[b]2 to 4 days healing time will be allowed prior to randomisation and the first dose. Day 28 biopsies will be taken 4 hours post-dose
Clinical score			X		X			X			
Local tolerability Assessment			X	X	X	X	X	X	X		Assessments to be performed pre-dose and up to one hour following dosing on days of dosing
Dosing			X	X	X	X	X	X			Once daily
Randomisation			X								Pre-dose

Procedure	**Screening (up to Day -28)**	**Day -5 to -3**	**Day 1**	**Day 2 to Day 13**	**Day 14**	**Day 15 to Day 20**	**Day 21 to Day 27**	**Day 28**	**Day 29 to 42**	**Follow-up (between Day 43 to Day 56)[a]**	[a] All procedures listed to also be conducted if a subject decides to prematurely withdraw/discontinue
PK blood sample			X	X	X		X	X	X	X	Sampling timepoints: Day 1 = pre-dose; and 5hrs (±1 hr) Between Day 2 and Day13: one pre-dose sample or postdose sample with time recorded since last dose Day 14: predose sample Between Day 21 and Day27: one pre-dose sample or postdose sample with time recorded since last dose Day 28:one postdose sample with time recorded since last dose Between Day 29 and Day 42: one sample with time recorded since last dose Follow-up visit: one sample with sampling day recorded
AE/SAE Review	X										
Concomitant Medication Review	X										
Lesion resolution assessment									X	X	

11.2. Appendix 2: Data Display Standards & Handling Conventions

11.2.1. Study Treatment & Sub-group Display Descriptors

Study population and Safety displays will be presented by sequence. Treatment will not be used to summarise these endpoints as all subjects will receive both active and placebo concurrently.

Study Group Descriptions			
RandAll NG		Data Displays for Reporting	
Strata Code	Description	Description	Order [1]
A	Group A - Fewer than 2 active lesions (PV)	Group A - (PV lesions)	1
B	Group B - At least 2 active CLE lesions	Group B – (CLE lesions)	2

Group A sequence descriptions:

Sequence Descriptions			
RandAll NG		Data Displays for Reporting	
Code	Description	Description	Order [1]
AA/PC/AD	GSK2646264 skin site A/ Placebo skin site C/ GSK2646264 skin site D	GSK2646264 skin area A/ Placebo skin area C/ GSK2646264 skin area D	1
AA/PC/PD	GSK2646264 skin site A/ Placebo skin site C/ Placebo skin site D	GSK2646264 skin area A/ Placebo skin area C/ Placebo skin area D	2
PA/AC/AD	Placebo skin site A/ GSK2646264 skin site C/ GSK2646264 skin site D	Placebo skin area A/ GSK2646264 skin area C/ GSK2646264 skin area D	3
PA/AC/PD	Placebo skin site A / GSK2646264 skin site C/ Placebo skin site D	Placebo skin area A/ GSK2646264 skin area C/ Placebo skin area D	4

NOTES:

1. Order represents treatments being presented in TFL, as appropriate.
2. Present code as well as description in displays

Group B sequence descriptions:

Sequence Group Descriptions			
RandAll NG		Data Displays for Reporting	
Code	Description	Description	Order [1]
AF/PG	GSK2646264 skin site F/ Placebo skin site G	GSK2646264 skin area F/ Placebo skin area G	1
PF/AG	Placebo skin site F/ GSK2646264 skin site G	Placebo skin area F/ GSK2646264 skin area G	2

NOTES:

1. Order represents treatments being presented in TFL, as appropriate.
2. Present code as well as description in displays.

Based on the randomisation schedule, treatments/descriptions will be programmatically assigned to each skin site area. Local tolerability, Efficacy and Pharmacodynamic endpoints are measured at a skin site level and therefore the following treatments will be used:

Group A

Treatment group descriptions			
Skin area		Data Displays for Reporting	
Code	Type	Description	Order
A	PV lesion	GSK2646264 or Placebo [2]	1 or 2
B	PV lesion	Baseline lesion	3
C	PV lesion	GSK2646264 or Placebo [2]	1 or 2
D	Uninvolved Skin	GSK2646264 or Placebo [2]	1 or 2
E	Uninvolved Skin	Uninvolved skin	4

NOTES:

1. Order represents treatments being presented in TFL, as appropriate.
2. Based on randomisation schedule
3. GSK2646264 will have a code of 1, Placebo will have a code of 2

Group B

Treatment group descriptions			
Skin area		Data Displays for Reporting	
Code	Type	Description	Order
F	Natural Lesion	GSK2646264 or Placebo [2]	1 or 2
G	Natural Lesion	GSK2646264 or Placebo [2]	1 or 2
H	Uninvolved Skin	Uninvolved skin	4

NOTES:

1. Order represents treatments being presented in TFL, as appropriate.
2. Based on randomisation schedule
3. GSK2646264 will have a code of 1, Placebo will have a code of 2

11.2.2. Baseline Definition & Derivations

11.2.2.1. Baseline Definitions

Group A:

	Study Assessments Considered as Baseline				Baseline Used in Data Display
	Screening	Day -15	Day -13 to Day -1	Day 1 (Pre-Dose)	
Safety					
Vital Signs	X	X		X	Day 1 [1]
Safety Lab Samples	X	X	X		Day 1
12-lead ECG	X			X	Day 1
Pharmacodynamic					
Skin Biopsy (IFN, mRNA, IFN proteins, pSYK and SYK proteins, immune cell proteins)				X	Day 1 (Lesion B will be used as baseline)
Efficacy					
RCLASI and components				X	Day 1
Pharmacokinetic					
Plasma PK				X	Day 1

NOTES :

- [1] Unless otherwise stated, the mean of replicate assessments at any given time point will be used as the value for that time point.

Group B:

	Study Assessments Considered as Baseline			Baseline Used in Data Display
	Screening	Day -5 to Day -3	Day 1 (Pre-Dose)	
Safety				
Vital Signs	X	X		Day -5 to Day -3 [1]
Safety Lab Samples	X	X	X	Day 1
12-lead ECG	X		X	Day 1
Pharmacodynamic				
Skin Biopsy (IFN, mRNA, IFN proteins, pSYK and SYK proteins, immune cell proteins)		X		Day -5 to Day -3
Efficacy				
RCLASI and components			X	Day 1
Pharmacokinetics				
Plasma PK			X	Day 1

NOTES :

- Unless otherwise stated, the mean of replicate assessments at any given time point will be used as the value for that time point.

11.2.2.2. Derivations and Handling of Missing Baseline Data

Definition	Reporting Details
Change from Baseline	= Post-Dose Visit Value – Baseline
% Change from Baseline	= 100 x [(Post-Dose Visit Value – Baseline) / Baseline]

NOTES :

- Unless otherwise specified, the baseline definitions specified in Section 11.2.2.1 Baseline Definitions will be used for derivations for endpoints / parameters and indicated on summaries and listings.
- Unless otherwise stated, if baseline data is missing no derivation will be performed and will be set to missing.
- The baseline definition will be footnoted on all change from baseline displays.

11.2.3. Reporting Process & Standards

Reporting Process	
Software	
• The currently supported versions of SAS software will be used to perform all data analyses and generation of displays.	
Reporting Area	
HARP Server	: us1salx00259
HARP Area	:\us1salx00259\arprod\gsk2646264\mid204860\final_01
QC Spreadsheet	:\us1salx00259\arprod\gsk2646264\mid204860\final_01\document
Analysis Datasets	
• Analysis datasets will be created according to Legacy GSK A&R dataset standards	
Generation of RTF Files	
• RTF files will be generated for listings and tables • PDF flies will be generated for figures	

Reporting Standards
General
• The current GSK Integrated Data Standards Library (IDSL) will be applied for reporting, unless otherwise stated: o 4.03 to 4.23: General Principles o 5.01 to 5.08: Principles Related to Data Listings o 6.01 to 6.11: Principles Related to Summary Tables o 7.01 to 7.13: Principles Related to Graphics
Formats
• All data will be reported according to the actual treatment the subject received unless otherwise stated. • GSK IDSL Statistical Principles (5.03 & 6.06.3) for decimal places (DP's) will be adopted for reporting of data based on the raw data collected. • Numeric data will be reported at the precision collected on the eCRF. • The reported precision from non eCRF sources will follow the IDSL statistical principles but

Reporting Standards	
may be adjusted to a clinically interpretable number of DP's.	
Planned and Actual Time	

• Reporting for tables, figures and formal statistical analyses :
  • Planned time relative to dosing will be used in figures, summaries, statistical analyses and calculation of any derived parameters, unless otherwise stated.
  • The impact of any major deviation from the planned assessment times and/or scheduled visit days on the analyses and interpretation of the results will be assessed as appropriate.
• Reporting for Data Listings:
  • Planned and actual time relative to study drug dosing will be shown in listings (Refer to IDSL Statistical Principle 5.05.1).
  • Unscheduled or unplanned readings will be presented within the subject's listings.
  • Visits outside the protocol defined time-windows (i.e. recorded as protocol deviations) will be included in listings but omitted from figures, summaries and statistical analyses.	

Unscheduled Visits	
• Unscheduled visits will not be included in summary tables. • Unscheduled visits will not be included in figures. • All unscheduled visits will be included in listings.	
Descriptive Summary Statistics	
Continuous Data	Refer to IDSL Statistical Principle 6.06.1
Categorical Data	N, n, frequency, %
Reporting of Pharmacokinetic Concentration Data	
Descriptive Summary Statistics	Refer to IDSL Statistical Principle 6.06.1 Assign zero to NQ values (Refer to GUI_51487 for further details)
Reporting of Pharmacokinetic Parameters	
Descriptive Summary Statistics (Log Transformed)	N, n, geometric mean, 95% CI of geometric mean, standard deviation (SD) of logged data and between geometric coefficient of variation (CVb/w (%)) will be reported. [1] CV_b (%) = $\sqrt{}$ (exp(SD^2) - 1) * 100 (SD = SD of log transformed data) [2] CV_w (%) = $\sqrt{}$ (exp(MSE) - 1) * 100 (MSE = mean square error from mixed effect model of loge-transformed data).
Graphical Displays	
• Refer to IDSL Statistical Principals 7.01 to 7.13.	

11.3. Appendix 3: Derived and Transformed Data

11.3.1. General

Multiple Measurements at One Time Point
• Mean of the measurements will be calculated and used in any derivation of summary statistics but if listed, all data will be presented. • Subjects having both High and Low values for Normal Ranges at any post-baseline visits for safety parameters will be counted in both the High and Low categories of "Any visit post-baseline" row of related summary tables. This will also be applicable to relevant Potential Clinical Importance summary tables.
Study Day

• Calculated as the number of days from randomisation date :
  • Ref Date = Missing → Study Day = Missing
  • Ref Date < Randomisation Date → Study Day = Ref Date – Randomisation Date
  • Ref Data ≥ Randomisation Date → Study Day = Ref Date – (Randomisation Date) + 1

11.3.2. Study Population

Demographics
Age

• GSK standard IDSL algorithms will be used for calculating age where birth date will be imputed as follows:
  o Any subject with a missing day will have this imputed as day '15'.
  o Any subject with a missing date and month will have this imputed as '30th June'.
• Birth date will be presented in listings as 'YYYY'.

Body Mass Index (BMI)
• Calculated as **Weight (kg) / Height (m)^2**

Extent of Exposure

• Number of days of exposure to study cream will be calculated based on the formula:
Duration of Exposure in Days = Treatment Stop Date – (Treatment Start Date) + 1
• Subjects who were randomised but did not report a treatment start date will be categorised as having zero days of exposure.
• Exposure data on a day is recorded in the eCRF in the following manner:
  • Weight of container and ancillary kit BEFORE application (A)
  • Weight of container and ancillary kit AFTER application (B)
  • Location of cream application, where all locations that apply are ticked (C)
This means that the weight of cream that was applied on that day (calculated as B-A) is the total dose of cream, with part of the total dose of cream applied to each of all the body locations (C) that are ticked.
• The cumulative dose of cream will be based on the formula:

Extent of Exposure

Cumulative Dose = Sum of (Number of Days x Total Daily Dose of cream)

- If there are any treatment breaks during the study, exposure data will be adjusted accordingly.

11.3.3. Safety

ECG Parameters

RR Interval

- IF RR interval (msec) is not provided directly, then RR can be derived as :

  [1] If QTcB is machine read & QTcF is not provided, then :

$$RR = \left[\left(\frac{QT}{QTcB}\right)^2\right] * 1000$$

  [2] If QTcF is machine read and QTcB is not provided, then:

$$RR = \left[\left(\frac{QT}{QTcF}\right)^3\right] * 1000$$

- If ECGs are manually read, the RR value preceding the measurement QT interval should be a collected value THEN do not derive.

Corrected QT Intervals

- When not entered directly in the eCRF, corrected QT intervals by Bazett's (QTcB) and Fredericia's (QTcF) formulas will be calculated, in msec, depending on the availability of other measurements.
- IF RR interval (msec) is provided then missing QTcB and/or QTcF will be derived as :

$$QTcB = \frac{QT}{\sqrt{\frac{RR}{1000}}} \qquad QTcF = \frac{QT}{\sqrt[3]{\frac{RR}{1000}}}$$

Laboratory Parameters

- If a laboratory value which is expected to have a numeric value for summary purposes, has a non-detectable level reported in the database, where the numeric value is missing, but typically a character value starting with '<x' or '>x' (or indicated as less than x or greater than x in the comment field) is present, the number of significant digits in the observed values will be used to determine how much to add or subtract in order to impute the corresponding numeric value.
  - Example 1: 2 Significant Digits = '< x ' becomes x – 0.01
  - Example 2: 1 Significant Digit = '> x' becomes x + 0.1
  - Example 3: 0 Significant Digits = '< x' becomes x – 1

Tolerability score

Tolerability will be assessed with the skin irritation scoring system for Part A and B of study, where the score consists of a numeric score according to the dermal response scoring i), and a letter according to the other effects scoring ii), as follows:

i) Dermal response scoring:
0 = no evidence of irritation
1 = minimal erythema, barely perceptible (pink)
2 = moderate erythema (definite redness), readily visible; minimal edema or minimal papular response
3 = strong erythema (intense redness), or erythema and papules
4 = definite edema
5 = erythema, edema, and papules
6 = vesicular eruption
7 = strong reaction spreading beyond test site

ii) Other effects:
Z = no other effect
A = slight glazed appearance
B = marked glazing
C = glazing with peeling and cracking
F = glazing with fissures
G = film of dried serous exudate covering all or part of the patch site
H = small petechial erosions and/or scabs

For each skin assessment, letter grade will be converted to numeric values as below:
A=0, Z=0, B=1, C=2, F=3, G=3, H=3.
A combined score for each subject will be calculated by adding all numeric and letter scores
The Skin Irritation Score for will be calculated for each subject at each timepoint and for each body part.

11.3.4. Efficacy

RCLASI

- Modified RCLASI Activity score will be derived by adding together patient's score for Erythema, Scaling/Hyperkeratosis (group B only) and Edema/infiltration. If any one of these components are missing, then the modified RCLASI Activity Score will be set to missing.

  Modified RCLASI Activity score = Erythema + Scaling/Hyperkeratosis (group B only) + Edema/Infiltration

- Overall Modified RCLASI score will be derived by summing the activity and dyspigmentation score. If any one of these components is missing, then the overall modified RCLASI Score will be set to missing.
-

  Overall Modified RCLASI Score = Modified RCLASI Activity score + Dyspigmentation

11.3.5. Biomarker

IFN mRNA signature

- Genes to be reported in the descriptive and analysis summary include, but not limited to:
    - CXCL10
    - IFI16
    - IFI44
    - IFI44L
    - IFIH1
    - MX1
    - MX2
    - OAS1
    - OAS2
    - OAS3
    - IFIT1
    - IFIT3
    - OASL
    - ISG15
    - IL1A
    - IL1B
    - IL6

Since each gene has multiple probesets, the following table highlights the probesets which have, historically, been of good quality and hence will be used for the analysis in this study. Entrez ID is also specified, which is a unique code a gene. These can be used at the programming stage to subset from multiple genes and probesets.

PROBSID	GENESYMB	Entrez_ID
204533_at	CXCL10	3627
206332_s_at	IFI16	3428
208965_s_at	IFI16	3428
208966_x_at	IFI16	3428
214059_at	IFI44	10561
214453_s_at	IFI44	10561
204439_at	IFI44L	10964
1555464_at	IFIH1	64135
216020_at	IFIH1	64135
219209_at	IFIH1	64135
203153_at	IFIT1	3434
204747_at	IFIT3	3437
229450_at	IFIT3	3437
208200_at	IL1A	3552
210118_s_at	IL1A	3552
205067_at	IL1B	3553
39402_at	IL1B	3553
205207_at	IL6	3569

205483_s_at	ISG15	9636
202086_at	MX1	4599
204994_at	MX2	4600
202869_at	OAS1	4938
205552_s_at	OAS1	4938
204972_at	OAS2	4939
206553_at	OAS2	4939
228607_at	OAS2	4939
218400_at	OAS3	4940
232666_at	OAS3	4940
205660_at	OASL	8638
210797_s_at	OASL	8638

Immunohistochemistry (IHC) biomarkers

Cells in lesional biopsies are measured by IHC. Single stains include but are not limited to; pSyk+, tSyk+, MxA+, CD3+, CD20+, CD68+, CD11c+, CD123+, Dual stains include but are not limited to; pSyk/tSyk, pSyk/CD11c, pSyk/CD123, in Epidermal, Dermal and combined areas of skin.

Each single/dual stain is assessed at 20x magnification across the whole 1 layer (3.5um slice) of the biopsy by automated image analysis and normalised by area (mm2). The regions of interest are the epidermis, dermis and glass, however only cells within the epidermis and dermis are analysed, which are classified by the automated image analysis software HALO. A manual QC process will be conducted on the software assigned regions of interest if necessary at the discretion of the operator, including but not limited to removal or addition of incorrectly classified areas within HALO. Other artefacts (tissue folding, stain precipitation) will be excluded from the ROI manually at the discretion of the operator and confirmation by the pathologist.

The number of positive cells for each marker will be calculated from the single or dual stain where appropriate. The reportables will include but are not limited to the total number of cells for each marker normalised by area (mm^2), total area (mm^2), total number of cells per mm^2, percentage of dual positive cells from total cells and percentage of each marker that is positive for both markers in the dual stains where applicable. These values will be provided for both dermis and epidermis separately, and combined, and will be derived by the BIB group within GSK prior to data transfer.

Histopathology score

- The component scores (patient's parakeratosis, ballooning\hydropic degeneration, epidermal cell-death, junctional inflammation and dermal inflammation scores) are scored twice by two independent investigators. Derivation,

  Mean component score = (score 1 + score 2)/2

  will be used to derive the mean component scores for each patient. This will be used for the

descriptive summaries. If one of the scores missing then the other score will be used as the mean component score.

- Overall histopathology score will be derived by summing derived **mean** component scores for patient's parakeratosis, ballooning\hydropic degeneration, epidermal cell-death, junctional inflammation and dermal inflammation scores. This will be used for the descriptive summaries.

- Note for listing only: For each score, the overall histopathology score will be derived by summing component scores for patient's parakeratosis, ballooning\hydropic degeneration, epidermal cell-death, junctional inflammation and dermal inflammation scores. This will be used for the descriptive summaries.

11.4. Appendix 4: Premature Withdrawals & Handling of Missing Data

11.4.1. Premature Withdrawals

Element	Reporting Detail
General	• Subject study completion (i.e. as specified in the protocol) was defined as subject who receives at least 25 days of study drug and completes the end of treatment biopsy and assessment. • Withdrawn subjects may be replaced in the study. • All available data from subjects who were withdrawn from the study will be listed and all available planned data will be included in summary tables and figures, unless otherwise specified.

11.4.2. Handling of Missing Data

Element	Reporting Detail
General	• Missing data occurs when any requested data is not provided, leading to blank fields on the collection instrument: ○ These data will be indicated by the use of a "blank" in subject listing displays. Unless all data for a specific visit are missing in which case the data is excluded from the table. ○ Answers such as "Not applicable" and "Not evaluable" are not considered to be missing data and should be displayed as such.
Outliers	• Any subjects excluded from the summaries and/or statistical analyses will be documented along with the reason for exclusion in the clinical study report.
IFN mRNA signatures	• No imputation methods will be used for missing value.
IHC biomarkers	• Change from baseline will be derived for this marker (see Section 11.2.2.2). If data is missing at any particular time point, then the change from baseline will be set to missing.
Histopathology score	• Change from baseline score will be derived (see Section 11.2.2.2) for individual components. If one or more of the components are missing then final score will be set to missing. If a score is missing at any particular time point, then the change from baseline score will be set to missing.
Histopathology component score	• Change from baseline score will be derived for individual components for each subject. If a score is missing at any particular time point, then the change from baseline score will be set to missing.

11.4.2.1. Handling of Missing Dates

Element	Reporting Detail
General	Partial dates will be displayed as captured in subject listing displays.

Element	Reporting Detail
Adverse Events	• The eCRF allows for the possibility of partial dates (i.e., only month and year) to be recorded for AE start and end dates; that is, the day of the month may be missing. In such a case, the following conventions will be applied for calculating the time to onset and the duration of the event: o Missing Start Day: First of the month will be used unless this is before the start date of study treatment; in this case the study treatment start date will be used and hence the event is considered On-treatment o Missing Stop Day: Last day of the month will be used, unless this is after the stop date of study treatment; in this case the study treatment stop date will be used. • Completely missing start or end dates will remain missing, with no imputation applied. Consequently, time to onset and duration of such events will be missing. • Start or end dates which are completely missing (i.e. no year specified) will remain missing, with no imputation applied.

11.4.2.2. Handling of Partial Dates

Element	Reporting Detail
Concomitant Medications	• Partial dates for any concomitant medications recorded in the CRF will be imputed using the following convention: o If the partial date is a start date, a '01' will be used for the day and 'Jan' will be used for the month o If the partial date is a stop date, a '28/29/30/31' will be used for the day (dependent on the month and year) and 'Dec' will be used for the month. • The recorded partial date will be displayed in listings.
Adverse Events	• Any partial dates for adverse events will be raised to data management. If the full date cannot be ascertained, the following assumptions will be made: o If the partial date is a start date, a '01' will be used for the day and 'Jan' will be used for the month. o However, if these results in a date prior to Week 1 Day 1 and the event could possibly have occurred during treatment from the partial information, then the Week 1 Day 1 date will be assumed to be the start date. o The AE will then be considered to start on-treatment (worst case). o If the partial date is a stop date, a '28/29/30/31' will be used for the day (dependent on the month and year) and 'Dec' will be used for the month. • The recorded partial date will be displayed in listings.

11.5. Appendix 5: Values of Potential Clinical Importance

11.5.1. Laboratory Values

Haematology				
Laboratory Parameter	**Units**	**Category**	**Clinical Concern Range**	
			Low Flag (< x)	**High Flag (>x)**
Hematocrit	Ratio of 1	Male		0.54
		Female		0.54
		Δ from BL	↓0.075	
Hemoglobin	g/L	Male		180
		Female		180
		Δ from BL	↓25	
Red Blood Cell Count (RBC)	$x10^{12}$/ L		4.2	5.9
Lymphocytes	$x10^{9}$/ L		0.8	
Neutrophil Count	$x10^{9}$/ L		1.5	
Platelet Count	$x10^{9}$/ L		100	550
Monocytes	$x10^{9}$/ L		0.14	1.3
Eosinophils	$x10^{9}$/ L			0.55
Basophils	$x10^{9}$/ L			0.22
While Blood Cell Count (WBC)	$x10^{9}$/ L		3	20

Clinical Chemistry				
Laboratory Parameter	**Units**	**Category**	**Clinical Concern Range**	
			Low Flag (< x)	**High Flag (>x)**
Albumin	G/L		30	
Calcium	mmol/L		2	2.75
Creatinine	umol/L	Δ from BL		↑ 44.2
Glucose	mmol/L		3	9
Magnesium	mmol/L		0.5	1.23
Phosphorus	mmol/L		0.8	1.6
Potassium	mmol/L		3	5.5
Sodium	mmol/L		130	150
Total CO2	mmol/L		18	32

Liver Function			
Test Analyte	**Units**	**Category**	**Clinical Concern Range**
ALT/SGPT	U/L	High	≥ 2x ULN
AST/SGOT	U/L	High	≥ 2x ULN
AlkPhos	U/L	High	≥ 2x ULN
T Bilirubin	µmol/L	High	≥ 1.5xULN
T. Bilirubin + ALT	µmol/L	High	1.5xULN T. Bilirubin

Liver Function			
Test Analyte	**Units**	**Category**	**Clinical Concern Range**
	U/L		+ ≥ 2x ULN ALT

11.5.2. ECG

ECG Parameter	Units	Clinical Concern Range	
		Lower	Upper
Absolute			
Absolute QTc Interval	msec		> 450
Absolute PR Interval	msec	< 110	> 220
Absolute QRS Interval	msec	< 75	> 110
Change from Baseline			
Increase from Baseline QTc	msec		>30

11.5.3. Vital Signs

Vital Sign Parameter (Absolute)	Units	Clinical Concern Range	
		Lower	Upper
Systolic Blood Pressure	mmHg	< 85	> 160
Diastolic Blood Pressure	mmHg	< 45	> 100
Heart Rate	bpm	< 40	> 110

Vital Sign Parameter (Change from Baseline)	Units	Clinical Concern Range			
		Decrease		Increase	
		Lower	Upper	Lower	Upper
Systolic Blood Pressure	mmHg		≥ 40		≥ 40
Diastolic Blood Pressure	mmHg		≥ 20		≥ 20
Heart Rate	bpm		≥ 30		≥ 30

11.6. Appendix 6: Model Checking and Diagnostics for Statistical Analyses

11.6.1. Statistical Analysis Assumptions

Endpoint(s)	• IFN mRNA signatures
Analysis	• Mixed model

- Model assumptions will be applied, but appropriate adjustments maybe made based on the data.
- The Kenward and Roger method for approximating the denominator degrees of freedom and correcting for bias in the estimated variance-covariance of the fixed effects will be used.
- Distributional assumptions underlying the model used for analysis will be examined by obtaining a normal probability plot of the residuals and a plot of the residuals versus the fitted values (i.e. checking the normality assumption and constant variance assumption of the model respectively) to gain confidence that the model assumptions are reasonable.
- If there are any departures from the distributional assumptions, alternative models will be explored using appropriate transformed data.

11.7. Appendix 7 – Abbreviations & Trade Marks

11.7.1. Abbreviations

Abbreviation	Description
AE	Adverse Event
A&R	Analysis and Reporting
BMI	Body Mass Index
CI	Confidence Interval
CLE	Cutaneous Lupus Erythematosus
CPMS	Clinical Pharmacology Modelling & Simulation
CS	Clinical Statistics
CSR	Clinical Study Report
CTR	Clinical Trial Register
DOB	Date of Birth
DP	Decimal Places
eCRF	Electronic Case Record Form
FRP	Females of Reproductive Potential
FTIH	First Time in Human
GUI	Guidance
IA	Interim Analysis
ICH	International Conference on Harmonisation
IDSL	Integrated Data Standards Library
IFN	Interferon
IMMS	International Modules Management System
IP	Investigational Product
LET	Lupus Erythematosus Tumidus
MMRM	Mixed Model Repeated Measures
mRNA	Messenger-Ribonucleaic Acid
PCI	Potential Clinical Importance
PD	Pharmacodynamic
PDMP	Protocol Deviation Management Plan
PK	Pharmacokinetic
pSYK	Phosporylated- Spleen Tyrosine Kinase
PV	Photoprovocation
QC	Quality Control
QTcF	Frederica's QT Interval Corrected for Heart Rate
QTcB	Bazett's QT Interval Corrected for Heart Rate
RAP	Reporting & Analysis Plan
RAMOS	Randomization & Medication Ordering System
RCLASI	Revised Cutaneous Lupus Erythematosus Disease Area and Severity Index
SAC	Statistical Analysis Complete
SAE	Serious Adverse Event
SOP	Standard Operation Procedure

Abbreviation	Description
SYK	Spleen Tyrosine Kinase
TA	Therapeutic Area
TFL	Tables, Figures & Listings
GSK	GlaxoSmithKline

11.7.2. Trademarks

Trademarks of the GlaxoSmithKline Group of Companies
NONE

Trademarks not owned by the GlaxoSmithKline Group of Companies
SAS
WinNonlin

11.8. Appendix 8: List of Data Displays

11.8.1. Data Display Numbering

The following numbering will be applied for RAP generated displays:

Section	Tables	Figures
Study Population	1.1 to 1.14	
Safety	2.1 to 2.20	
Efficacy	3.1	3.1 to 3.2
Pharmacokinetic	4.1 to 4.3	4.1 to 4.3
Pharmacodynamic	5.1 to 5.5	5.1 to 5.12
Section	**Listings**	
ICH Listings	1 to 33	
Other Listings	34 to 44	

11.8.2. Mock Example Shell Referencing

Non IDSL specifications will be referenced as indicated and if required an example mock-up displays provided in Appendix 9: Example Mock Shells for Data Displays.

Section	Figure	Table	Listing
Safety	SAFE_Fn	SAFE_Tn	SAFE_Ln
Pharmacodynamic	PD_Fn	PD_Tn	PD_Ln

NOTES:

- Non-Standard displays are indicated in the 'IDSL / TST ID / Example Shell' or 'Programming Notes' column as '[Non-Standard] + Reference.'

11.8.3. Deliverable [Priority]

Delivery [Priority] [1]	Description
SAC	Final Statistical Analysis Complete

NOTES:

1. Indicates priority (i.e. order) in which displays will be generated for the reporting effort.

11.8.4. Study Population Tables

Study Population Tables					
No.	**Population**	**IDSL / TST ID / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
Subject Disposition					
1.1.	Safety	CP_ES1p	Summary of Subject Disposition (Group B-Natural Lesions)		SAC
1.2.	All Screened	ES6	Summary of Reasons for Screen Failure (Group A- PV lesions)		SAC
1.3.	All Screened	ES6	Summary of Reasons for Screen Failure (Group B-Natural Lesions)		SAC
1.4.	Safety	NS1	Summary of Number of Subjects by Country and Centre (Group B-Natural Lesions)		SAC
Protocol Deviation					
1.5.	Safety	DV1	Summary of Important Protocol Deviations (Group B-Natural Lesions)		SAC
Population Analysed					
1.6.	All Screened	SP1	Summary of Study Populations and Exclusions (Group A- PV lesions)		SAC
1.7.	All Screened	SP1	Summary of Study Populations and Exclusions (Group B-Natural Lesions)		SAC

Study Population Tables					
No.	**Population**	**IDSL / TST ID / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
Demographic and Baseline Characteristics					
1.8.	Safety	DM3	Summary of Demographic Characteristics (Group B-Natural Lesions)	Include BMI	SAC
1.9.	Safety	DM5	Summary of Race and Racial Combinations (Group B-Natural Lesions)		SAC
1.10.	Safety	DM6	Summary of Race and Racial Combination Details (Group B-Natural Lesions)		SAC
Prior and Concomitant medications					
1.11.	Safety	MH1, MH4	Summary of [Current/Past] Medical Conditions (Group B-Natural Lesions)		SAC
1.12.	Safety	CM1	Summary of Concomitant Medications (Group B-Natural Lesions)		SAC
1.13.	Safety	SAFE_T3	Summary of Type of CLE (Group B-Natural Lesions)	Obtained from medical conditions page in eCRF. Under Disease Diagnosis – 2. Disease characteristics.	SAC
Exposure and Treatment Compliance					
1.14.	Safety	EX1	Summary of Weight of Study Cream Applied (Group B-Natural Lesions)	See Section 11.3.2 regarding total daily dose of cream; label first row as “Daily Weight of Cream (g)” with following footnote: “Note: Daily Dose refers to the one lesion that either active or placebo treatment is applied to; Label second row as “Cumulative Weight of Cream (g)”.	SAC

11.8.5. Safety Tables

Safety : Tables					
No.	**Population**	**IDSL / TST ID / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
Adverse Events					
2.1.	Safety	CP_AE1p	Summary of All Adverse Events by System Organ Class (Group B-Natural Lesions)	Only Total adverse events will be summarised.	SAC
2.2.	Safety	CP_AE1p	Summary All Drug-Related Adverse Events by System Organ Class (Group B-Natural Lesions)	Only Total adverse events will be summarised.	SAC

Safety : Tables					
No.	**Population**	**IDSL / TST ID / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
Serious and Other Significant Adverse Events					
2.3.	Safety	CP_AE1p	Summary of Serious Adverse Events by System Organ Class (Group B-Natural Lesions)	Only Total adverse events will be summarised.	SAC
2.4.	Safety	CP_AE1p	Summary of Adverse Events Leading to Withdrawal from Study / Permanent Discontinuation of Study Treatment by Overall Frequency (Group B-Natural Lesions)	Only Total adverse events will be summarised.	SAC
Laboratory: Chemistry					
2.5.	Safety	LB1	Summary of Chemistry Changes from Baseline (Group B-Natural Lesions)	Treatment column will not be displayed.	SAC
2.6.	Safety	LB3	Summary of Emergent Chemistry Results Relative to Normal Range (Group B-Natural Lesions)	Treatment columns will be replaced by one 'Part B' column	SAC
Laboratory: Hematology					
2.7.	Safety	LB1	Summary of Hematology Changes from Baseline (Group B-Natural Lesions)	Includes baseline values. Treatment column will not be displayed.	SAC
2.8.	Safety	LB3	Summary of Emergent Hematology Results Relative to Normal Range (Group B-Natural Lesions)	As notes for Chemistry T2.12.	SAC
Laboratory: Urinalysis					
2.9.	Safety	LB1	Summary of Urine Concentration Changes from Baseline (Group B-Natural Lesions)	Includes Baseline values. Treatment column will not be displayed.	SAC
2.10.	Safety	LB2	Summary of Emergent Urinalysis Dipstick Results (Group B-Natural Lesions)	As above for Chemistry, using dipstick categories.	SAC
Laboratory: Hepatobiliary (Liver)					
2.11.	Safety	LIVER1	Summary of Liver Monitoring/Stopping Event Reporting (Group B-Natural Lesions)	Treatment columns will be replaced by one 'Part B' column	SAC

Safety : Tables					
No.	**Population**	**IDSL / TST ID / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
2.12.	Safety	LIVER10	Summary of Subjects Meeting Emergent Hepatobiliary Laboratory Abnormality Criteria (Group B-Natural Lesions)	Treatment columns will be replaced by one 'Part B' column	SAC
ECG					
2.13.	Safety	EG1	Summary of ECG Findings (Group B-Natural Lesions)	Treatment columns will be replaced by one 'Part B' column	SAC
2.14.	Safety	CP_EG11	Summary of Maximum Emergent QTc Values by Category (Group B-Natural Lesions)	Treatment columns will be replaced by one 'Part B' column	SAC
2.15.	Safety	EG2	Summary of Change from Baseline in ECG Values by Visit (Group B-Natural Lesions)	Note: IDSL shell in development. Includes Baseline values. Treatment columns will be replaced by one 'Part B' column	SAC
2.16.	Safety	CP_EG12	Summary of Maximum Change from Baseline in QTc Values by Category (Group B-Natural Lesions)	Treatment columns will be replaced by one 'Part B' column	SAC
Vital Signs					
2.17.	Safety	VS1	Summary of Change from Baseline in Vital Signs by Visit (Group B-Natural Lesions)	Treatment column will not be displayed.	SAC
2.18.	Safety	VS3	Summary of Emergent Vital Signs Results Relative to Normal Range (Group B-Natural Lesions)	Treatment columns will be replaced by one 'Part B' column	SAC
Local Tolerability					
2.19.	Safety	SAFE_T1	Summary (Absolute and Change from Baseline) of Mean irritation score assessment – (Group B-Natural Lesions)		SAC
2.20.	Safety	SAFE_T2	Assessment of Maximum Dermal Reactions and Response (Group B-Natural Lesions)		SAC

11.8.6. Efficacy Tables

Efficacy: Tables					
No.	**Population**	**IDSL / TST ID / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
RCLASI					
3.1.	Safety	PD_T1	Summary of RCLASI and components (Absolute and Change from Baseline) (Group B-Natural Lesions)	Page by score type (e.g. component/final) Include absolute and change from baseline. First variable for Type of CLE – include All. Include footnote for derivation (see Section 11.3.4)	SAC

11.8.7. Efficacy Figures

Efficacy: Figures					
No.	**Population**	**IDSL / TST ID / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
RCLASI					
3.1.	Safety	PD_F1	Individual profile plots of RCLASI and components (Group B-Natural Lesions)	Page by score type (e.g. component/final) Column panel by treatment group Symbol by subject Id. Line pattern by CLE type. Include footnote for derivation (see Section 11.3.4)	SAC
3.2.	Safety	PD_F2	Summary of Mean (±SE) in RCLASI and components (Group B-Natural Lesions)	Panel by CLE type (include All). Include footnote for derivation (see Section 11.3.4)	SAC

11.8.8. Pharmacokinetic Tables

Pharmacokinetic : Tables					
No.	**Population**	**IDSL / TST ID / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
4.1.	PK	PKPT1	Summary of Serum GSK2646264 Pharmacokinetic concentrations versus time by actual dose (Group B-Natural Lesions)		SAC
4.2.	PK	PKPT1	Summary of Derived Serum GSK2646264 Pharmacokinetic Parameters by actual dose (Group B-Natural Lesions)		SAC
4.3.	PK	PKPT1	Summary of Log-Transformed Derived Serum GSK2646264 Pharmacokinetic Parameters by actual dose (Group B-Natural Lesions)		SAC

11.8.9. Pharmacokinetic Figures

Pharmacokinetic : Figures					
No.	**Population**	**IDSL / TST ID / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
4.1.	PK	PKCF1P	Individual GSK2646264 Plasma Concentration-Time Plot by Subject (Linear and Semi-Log) (Group B-Natural Lesions)	Refer Table1 treatment description table 1.X-axis display actual relative time 2.Include line for LLQ along with footnote defining LLQ value 3.Include values below LLQ	SAC
4.2.	PK	PKCF2	Mean (±SD) Plasma GSK2646264 Concentration-Time Plots (Linear and Semi-log) (Group B-Natural Lesions)	1.Refer Table 1 treatment description table 2. Include the full SD bars i.e.(not just the +ve SD) at each time point. 3. X-axis displays planned relative time 4. Include line for LLQ along with footnote defining LLQ value.	SAC
4.3.	PK	PKCF3	Median (Range) Plasma GSK2646264 Concentration-Time Plot (Linear and Semi-log) (Group B-Natural Lesions)	1.Refer Table 1 treatment description table 2. X-axis displays planned relative time 3. Include line for LLQ along with footnote defining LLQ value. 4. Combine data per dose group; i.e. no distinction of ADA status	SAC

11.8.10. Pharmacodynamic Tables

Pharmacodynamic (and or Biomarker) : Tables					
No.	**Population**	**IDSL / TST ID / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
IFN mRNA signature					
5.1.	Safety	PD2	Summary of mRNA Expression of Inflammatory Gene Transcripts in Biopsy (Group B-Natural Lesions)	Summary by treatment group (Placebo, GSK2646264 and uninvolved skin) First variable for Type of CLE – include All. See Section 11.3.5 for list of genes and probe-sets to be summarised	SAC
5.2.	Safety	PD_T2	Summary of Adjusted Mean and Fold Changes in mRNA Expression of Inflammatory Gene Transcripts in Biopsies (Group B-Natural Lesions)	Summary by treatment group (Placebo and GSK2646264) See Section 11.3.5 for list of genes and probe-sets to be analysed Footnote: 'Comparison to placebo fold change' is the fold change on GSK2646264 relative to placebo in $\log_2$ intensity at day 28.'	SAC
5.3.	Safety	PD_T3	Summary of Adjusted Mean and Fold Changes in mRNA Expression of Inflammatory Gene Transcripts in Biopsies by Skin Type (Group B-Natural Lesions)	Summary by skin type See Section 11.3.5 for list of genes and probe-sets to be analysed Footnote: 'Comparison to uninvolved fold change' is the fold change on GSK2646264 relative to placebo in $\log_2$ intensity.'	SAC

Pharmacodynamic (and or Biomarker) : Tables					
No.	**Population**	**IDSL / TST ID / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
Other biomarkers					
5.4.	Safety	PD_T1	Summary of Cell Markers from Immunohistochemistry (Absolute and Change from baseline) (Group B-Natural Lesions)	Summary by lesion type (Placebo, GSK2646264 and uninvolved skin). Replace treatment title with 'Lesion type' First variable for Type of CLE – include All.	SAC
5.5.	Safety	PD_T1	Summary of Histopathology score and components in skin biopsies (Absolute and Change from baseline) (Group B-Natural Lesions)	Page by score type – e.g final score then component score summaries Summary by lesion type (Placebo, GSK2646264 and uninvolved skin). Include change from baseline column where applicable. Replace treatment title with 'Lesion type' First variable for Type of CLE – include All.	SAC

11.8.11. Pharmacodynamic Figures

Pharmacodynamic (and or Biomarker) : Figures					
No.	**Population**	**IDSL / TST ID / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
IFN mRNA signature					
5.1.	Safety	PD_F1	Individual Subject Profiles for mRNA Expression of IFN Signatures in Skin Biopsies (Group B-Natural Lesions)	Symbol by subject id, column panel by treatment group (Placebo and GSK2646264) Symbol by subject Id. Line pattern by CLE type See Section 11.3.5 for list of genes and probe-sets to be summarised	SAC
5.2.	Safety	PD_F3	Adjusted Mean Intensities (95% CI) for mRNA Expression IFN Signatures in Skin Biopsies (Group B-Natural Lesions)	Y xais – log2 scale By treatment group (Placebo and GSK2646264) Jitter by treatment (i.e. do not overlay the mean error bars.)	SAC
5.3.	Safety	PD_F4	Adjusted Mean (95% CI) Fold Change in mRNA Expression of IFN Signatures in Skin Biopsies (Group B-Natural Lesions)	Page by Gene ID. X-axis - probeset ID Include band from FC -1 to 1, transparency 0.5 Footnote: 'Comparison to placebo' is the fold change on GSK2646264 relative to placebo in log_2 intensity at day 28.'	SAC
5.4.	Safety	PD_F5	Individual Plot of mRNA Expression of IFN Signatures in Skin Biopsies by Skin Type (Group B-Natural Lesions)	Symbol by CLE type, column panel by skin type. X-axis – subject id Symbol by CLE type See Section 11.3.5 for list of genes and probe-sets to be summarised	SAC

Pharmacodynamic (and or Biomarker) : Figures					
No.	**Population**	**IDSL / TST ID / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
5.5.	Safety	PD_F6	Adjusted Mean Intensities (95% CI) for mRNA Expression IFN Signatures in Skin Biopsies (Group B-Natural Lesions)	Since only one timepoint, replace x-axis with skin type. Symbol by subject Id. Include individual raw values	SAC
5.6.	Safety	PD_F6	Adjusted Mean (95% CI) Fold Change in mRNA Expression of IFN Signatures in Skin Biopsies by Skin Type (Group B-Natural Lesions)	Page by Gene ID. X-axis - probeset ID By Skin Type – symbol by skin type Include band from FC -1 to 1, transparency 0.5 Footnote: 'Comparison to uninvolved' is the fold change on GSK2646264 relative to placebo in log_2 intensity.'	SAC
Exploratory PD endpoints					
5.7.	Safety	PD_F1	Individual plot of cell markers from Immunohistochemistry (Group B-Natural Lesions)	Symbol by subject id, column panel by treatment group (Placebo and GSK2646264) Symbol by subject Id. Line pattern by CLE type Heading: [marker name and description]	SAC
5.8.	Safety	Similar to PD_F2	Plot of Mean and SE of cell markers from Immunohistochemistry (Group B-Natural Lesions)	By treatment group (Placebo and GSK2646264) Panel by CLE type (include All). Heading: [marker name and description]	SAC

Pharmacodynamic (and or Biomarker) : Figures					
No.	**Population**	**IDSL / TST ID / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
5.9.	Safety	PD_F6	Plot of Mean and SE of cell markers from Immunohistochemistry by Skin Type(Group B-Natural Lesions)	Since only one timepoint, replace x-axis with skin type. Include individual raw values Symbol by subject Id. Panel by CLE type (include All) Heading: [marker name and description]	SAC
5.10.	Safety	PD_F1	Individual plot of Histopathology score and components in skin biopsies (Group B-Natural Lesions)	Symbol by subject id, column panel by treatment group (Placebo and GSK2646264) Symbol by subject Id. Line pattern by CLE type	SAC
5.11.	Safety	Similar to PD_F2	Plot of Mean and SE in Histopathology score and components in skin biopsies (Group B-Natural Lesions)	By treatment group (Placebo and GSK2646264) Panel by CLE type (include All)	SAC
5.12.	Safety	PD_F6	Plot of Mean and SE in Histopathology score and components in skin biopsies by skin type (Group B-Natural Lesions)	Since only one timepoint, replace x-axis with skin type Include individual raw values Symbol by subject Id. Panel by CLE type (include All) Heading: [type of score]	SAC

11.8.12. ICH Listings

ICH : Listings					
No.	**Population**	**IDSL / TST ID / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
Subject Disposition					
1.	PV Failures	ES7	Listing of Reasons for Screen Failure (Group A- PV lesions)		SAC
2.	All Screened	ES7	Listing of Reasons for Screen Failure (Group B-Natural Lesions)		SAC
3.	Safety	ES2	Listing of Reasons for Study Withdrawal (Group B-Natural Lesions)		SAC
4.	Safety	BL1 / BL2	Listing of Subjects for Whom the Treatment Blind was Broken (Group B-Natural Lesions)		SAC
5.	Safety	CP_RD1x	Listing of Planned and Actual Treatments (Group B-Natural Lesions)		SAC
Protocol Deviations					
6.	Safety	DV2	Listing of Important Protocol Deviations (Group B-Natural Lesions)		SAC
7.	Safety	IE3	Listing of Subjects with Inclusion/Exclusion Criteria Deviations (Group B-Natural Lesions)		SAC
Populations Analysed					
8.	All Screened	SA3a	Listing of Subjects Excluded from Any Population (Group B-Natural Lesions)		SAC
Demographic and Baseline Characteristics					
9.	Safety	DM2	Listing of Demographic Characteristics (Group B-Natural Lesions)	Include BMI	SAC
10.	Safety	DM9	Listing of Race (Group B-Natural Lesions)		SAC

ICH : Listings					
No.	**Population**	**IDSL / TST ID / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
Medical History					
11.	Safety	MH2	Listing of Medical History (Group B-Natural Lesions)		SAC
Prior and Concomitant Medications					
12.	Safety	CP_CM3	Listing of Concomitant Medications (Group B-Natural Lesions)		SAC
Exposure and Treatment Compliance					
13.	Safety	EX3	Listing of Weight of Study Cream Applied (Group B-Natural Lesions)	If applicable adapt to study data See Section 11.3.2 regarding total daily dose of cream i.e. each subject to have one row per day, with weight of cream listed (the total weight calculated from the weight before and after application), column labelled as "Weight of Cream (g)" and each body location/side listed together on that single row.	SAC
Adverse Events					
14.	Safety	CP_AE8	Listing of All Adverse Events (Group B-Natural Lesions)	No treatment heading.	SAC
15.	PV failures	CP_AE8	Listing of All Adverse Events for subjects that were PV failures (Group A-PV Lesions)	No treatment heading.	SAC
16.	Safety	AE7	Listing of Subject Numbers for Individual Adverse Events (Group B-Natural Lesions)	Treatment column will not be displayed.	SAC
17.	Safety	AE2	Listing of Relationship Between Adverse Event System Organ Classes, Preferred Terms, and Verbatim Text (Group B-Natural Lesions)		SAC

ICH : Listings					
No.	**Population**	**IDSL / TST ID / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
Serious and Other Significant Adverse Events					
18.	Safety	CP_AE8a	Listing of Serious Adverse Events (Group B-Natural Lesions)	No treatment heading.	SAC
19.	Safety	AE14	Listing of Reasons for Considering as a Serious Adverse Event (Group B-Natural Lesions)		SAC
20.	Safety	CP_AE8	Listing of Adverse Events Leading to Withdrawal from Study / Permanent Discontinuation of Study Treatment (Group B-Natural Lesions)	No treatment heading.	SAC
Hepatobiliary (Liver)					
21.	Safety	MH2	Listing of Medical Conditions for Subjects with Liver Stopping Events (Group B-Natural Lesions)	Treatment column will not be displayed	SAC
22.	Safety	SU2	Listing of Substance Use for Subjects with Liver Stopping Events (Group B-Natural Lesions)	Treatment column will not be displayed	SAC
All Laboratory					
23.	Safety	LB5	Listing of Laboratory Data for Subjects with Abnormalities of Potential Clinical Concern (Group B-Natural Lesions)	No treatment heading.	SAC
24.	Safety	LB5	Listing of Laboratory Data for Subjects with Abnormalities of Potential Clinical Concern-Change from Baseline (Group B-Natural Lesions)	No treatment heading.	SAC
25.	Safety	LB5	Listing of Laboratory Data Abnormalities of Potential Clinical Importance (Group B-Natural Lesions)	No treatment heading.	SAC
26.	Safety	LB5	Listing of Laboratory Data Abnormalities of Potential Clinical Importance- change from baseline (Group B-Natural Lesions)	No treatment heading.	SAC

ICH : Listings					
No.	**Population**	**IDSL / TST ID / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
ECG					
27.	Safety	CP_EG3	Listing of All ECG Values for Subjects with a Value of Potential Clinical Importance (Group B-Natural Lesions)	No treatment heading.	SAC
28.	Safety	CP_EG3	Listing of ECG Values of Potential Clinical Importance (Group B-Natural Lesions)	No treatment heading.	SAC
29.	Safety	CP_EG3	Listing of All ECG Values for Subjects with a Value of Potential Clinical Importance- Change from Baseline (Group B-Natural Lesions)	No treatment heading.	SAC
30.	Safety	CP_EG3	Listing of ECG Values of Potential Clinical Importance-Change from Baseline (Group B-Natural Lesions)	No treatment heading.	SAC
31.	Safety	CP_EG5	Listing of Abnormal ECG Findings (Group B-Natural Lesions)	No treatment heading.	SAC
Vital Signs					
32.	Safety	CP_VS4	Listing of All Vital Signs for Subjects with Values of Potential Clinical Importance (Group B-Natural Lesions)	Treatment column will not be displayed	SAC
33.	Safety	CP_VS4	Listing of All Vital Signs for Subjects with Values of Potential Clinical Importance –Change from baseline (Group B-Natural Lesions)	Treatment column will not be displayed	SAC

11.8.13. Non-ICH Listings

Non-ICH : Listings					
No.	**Population**	**IDSL / TST ID / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
Study Population					
34.	Safety	SAFE_L2	Listing of Type of CLE (Group B-Natural Lesions)	Obtained from medical conditions page in eCRF. Under Disease Diagnosis – 2. Disease characteristics.	
Local tolerability					
35.	Safety	SAFE_L1	Listing of local tolerability (Group B-Natural Lesions)	Include maximal dermal response	SAC
RCLASI					
36.	Safety	PD_L1	Listing of RCLASI and components (Group B-Natural Lesions)	Include change from baseline. Include a footnote to explain the derivation	SAC

Non-ICH : Listings					
No.	**Population**	**IDSL / TST ID / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
Pharmacokinetic					
37.	PK	PKCl1P	Listing of Plasma GSK2646264 Pharmacokinetic Concentration-Time Data (Group B-Natural Lesions)		SAC
38.	PK	PKPL1P	Listing of Derived Plasma GSK2646264 Pharmacokinetic Parameters (Group B-Natural Lesions)		SAC
Pharmacodynamic					
39.	Safety	PD_L2	Listing of transcriptomic mRNA expression in skin biopsies for selected probesets (Group B-Natural Lesions)	See Section 11.3.5 for list of genes and probe-sets to be listed	SAC
40.	Safety		Raw SAS output from the statistical analysis of change from baseline IFN proteins in skin biopsies (Group B-Natural Lesions)		SAC
41.	Safety		Raw SAS output from the statistical analysis of IFN proteins in skin biopsies by skin type (Group B-Natural Lesions)		SAC
42.	Safety	PD10	Listing of Cell Markers from Immunohistochemistry (Group B-Natural Lesions)	Include change from baseline	SAC
43.	Safety	PD_L3	Listing of Histopathology score and components in skin biopsies (Group B-Natural Lesions)	Include change from baseline. Column for Skin Area (e.g. F, G and H). Each subject has two forms. Thus listing will include both values.	SAC
44.	Safety	PD_L4	Listing of QC criteria from Histological scoring form (Group B-Natural Lesions)	This will include listing of QC Criteria section of the form.	SAC

11.9. Appendix 9: Example Mock Shells for Data Displays

Example : SAFE_T1 Page x of y

Protocol : 204860
Population : Safety

Table x.xx

Summary (Absolute and Change from Baseline) of Mean irritation score assessment

Summary: Mean Irritation score (Absolute)

Treatment	Time	N	n	Mean	S.D	Min	Median	Max
Placebo	X	x	X	xxx.x	xx.xx	xxx	xxx	xxx
	X	x	X	xxx.x	xx.xx	xxx	xxx	xxx
	X	x	X	xxx.x	xx.xx	xxx	xxx	xxx
	.	.		.	.	.	.	.
GSK2646264	X	x	X	xxx.x	xx.xx	xxx	xxx	xxx
	X	x	X	xxx.x	xx.xx	xxx	xxx	xxx
	X	x	X	xxx.x	xx.xx	xxx	xxx	xxx
	.	.		.	.	.	.	.

Example : SAFE_T2

Page x of y

Protocol : 204860
Population : Safety

Table x.xx
Summary of Tolerability: Maximum Dermal Response and Maximum Other Dermal Effects

Assessment		Statistic	GSK2646264 (N = XX)	Placebo (N = XX)
Maximum Dermal Response	0	n (%)	XX (XX.XX)	XX (XX.XX)
	1	n (%)	XX (XX.XX)	XX (XX.XX)
	2	n (%)	XX (XX.XX)	XX (XX.XX)
	-	-	-	-
	7	n (%)	XX (XX.XX)	XX (XX.XX)
	Z	n (%)	XX (XX.XX)	XX (XX.XX)
Maximum Other Dermal Effects	A	n (%)	XX (XX.XX)	XX (XX.XX)
	B	n (%)	XX (XX.XX)	XX (XX.XX)
	…	…	…	…
	H	n (%)	XX (XX.XX)	XX (XX.XX)

Note: NA = not applicable
Note: Treatment is GSK2646264 1% and matching Placebo, on the respective body surface area, one side each.
Note: Dermal Response: 0 = no evidence of irritation, 1 = minimal erythema, barely perceptible (pink), 2 = moderate erythema (definite redness), readily visible; minimal edema or minimal papular response, 3 = strong erythema (intense redness), or erythema and papules, 4 = definite edema, 5 = erythema, edema, and papules, 6 = vesicular eruption, 7 = strong reaction spreading beyond test site.
Note: Other Dermal Effects: Z = no other effect, A = slight glazed appearance, B = marked glazing, C = glazing with peeling and cracking, F = glazing with fissures, G = film of dried serous exudate covering all or part of the patch site, H = small petechial erosions and/or scabs.

Example : SAFE_T3

Protocol : 204860
Population : Safety

Table x.xx
Summary of Type of CLE (Group B-Natural Lesions)

CLE type	N=XX
Chronic	n (%)
Acute	n (%)
Sub-acute	n (%)
LTE	n (%)

Example : PD_T1
Protocol : 204860
Population : Safety

Table Summary of [RCLASI/PD endpoints]
[Insert Title]

Type of CLE	Treatment	N	Visit	n	Mean	95% CI of Mean	SD	Median	Min.	Max.
Sub-Acute	GSK2646264	X	Day 1 Predose	24	xxxx.xx	(xxxx.xx, xxxx.xx)	xx.xx	xxxx.x	xxxx	xxxx
			Day 14	24	xxxx.xx	(xxxx.xx, xxxx.xx)	xx.xx	xxxx.x	xxxx	xxxx
			Day 28	23	xxxx.xx	(xxxx.xx, xxxx.xx)	xx.xx	xxxx.x	xxxx	xxxx
	Placebo	X	Day 1 predose	24	xxxx.xx	(xxxx.xx, xxxx.xx)	xx.xx	xxxx.x	xxxx	xxxx
				21	xxxx.xx	(xxxx.xx, xxxx.xx)	xx.xx	xxxx.x	xxxx	xxxx
			Day 14	21	xxxx.xx	(xxxx.xx, xxxx.xx)	xx.xx	xxxx.x	xxxx	xxxx
			Day 28	21	xxxx.xx	(xxxx.xx, xxxx.xx)	xx.xx	xxxx.x	xxxx	xxxx
Chronic	GSK2646264	X	Day 1 Predose	24	xxxx.xx	(xxxx.xx, xxxx.xx)	xx.xx	xxxx.x	xxxx	xxxx
			Day 14	24	xxxx.xx	(xxxx.xx, xxxx.xx)	xx.xx	xxxx.x	xxxx	xxxx
			Day 28	23	xxxx.xx	(xxxx.xx, xxxx.xx)	xx.xx	xxxx.x	xxxx	xxxx
	Placebo	X	Day 1 predose	24	xxxx.xx	(xxxx.xx, xxxx.xx)	xx.xx	xxxx.x	xxxx	xxxx
				21	xxxx.xx	(xxxx.xx, xxxx.xx)	xx.xx	xxxx.x	xxxx	xxxx
			Day 14	21	xxxx.xx	(xxxx.xx, xxxx.xx)	xx.xx	xxxx.x	xxxx	xxxx
			Day 28	21	xxxx.xx	(xxxx.xx, xxxx.xx)	xx.xx	xxxx.x	xxxx	xxxx
All										

Example: PD_T2
Protocol: 204860
Population: Safety

Table XX.XX :

Treatment Group	Visit	n Adjusted Mean 95% CI	n Adjusted Mean 95% CI	Fold Change 95% CI	Comparison to Placebo Fold Change 95% CI
Placebo	Baseline	4 10033.48 (5015.87, 20070.45)	4 13337.45 (4806.65, 37008.63)		
(N=XX)					
	Day 28	4 8118.18 (3264.70, 20187.10)	4 6830.11 (2150.27, 21695.19)	-1.19 (-1.96, 1.39)	
GSKXXXXX	Baseline	4 10033.48 (5015.87, 20070.45)	4 13337.45 (4806.65, 37008.63)		
(N=XX)					
	Day 28	4 8118.18 (3264.70, 20187.10)	4 6830.11 (2150.27, 21695.19)	-1.19 (-1.96, 1.39)	-1.19 (-1.96, 1.39)

Example: PD_T3
Protocol: 204860
Population: Safety

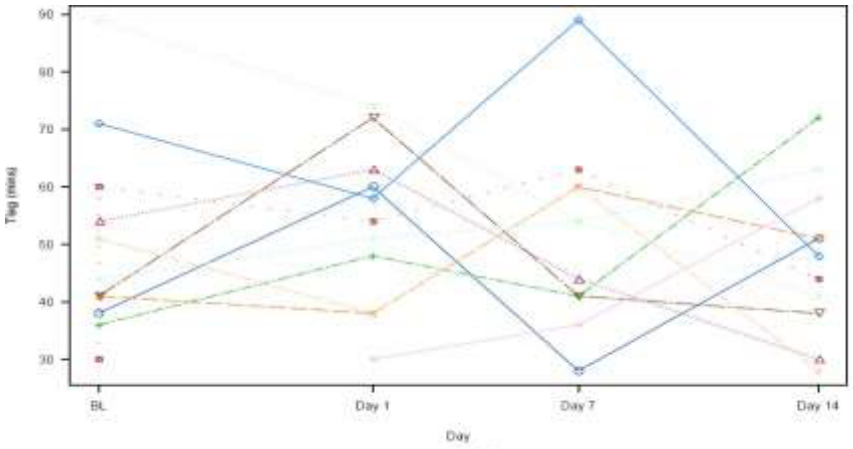
Table XX.XX :
Summary of Analysis for Microarray mRNA Data from xxxx

Skin Type	n Adjusted Mean 95% CI	n Adjusted Mean 95% CI	Comparison to Uninvolved Fold Change 95% CI
Uninvolved	4 10033.48 (5015.87, 20070.45)	4 13337.45 (4806.65, 37008.63)	
Placebo	5 8118.18 (3264.70, 20187.10)	5 6830.11 (2150.27, 21695.19)	-1.19 (-1.96, 1.39)
GSKXXXXXX	8 8118.18 (3264.70, 20187.10)	8 6830.11 (2150.27, 21695.19)	-1.19 (-1.96, 1.39)

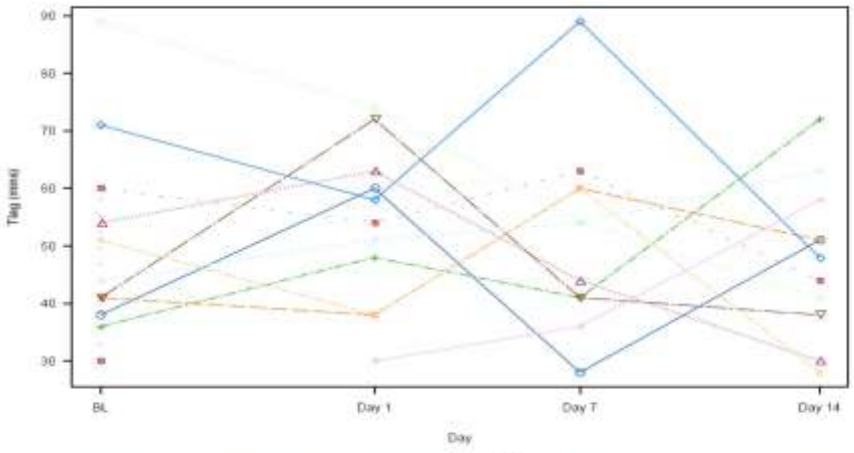
Example : PD_F1
Protocol : 204860
Population : Safety

Figure: Individual profile plot of {RCLASI/PD endpoints]
[Insert Title]

Placebo



GSK2646264



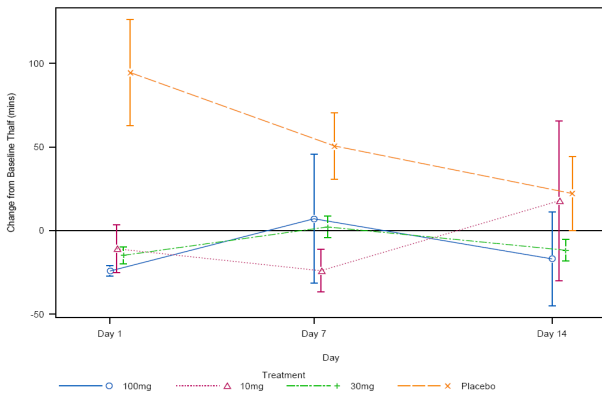
PPD

USER ID:directory/program.sas 01JAN2002 12:01

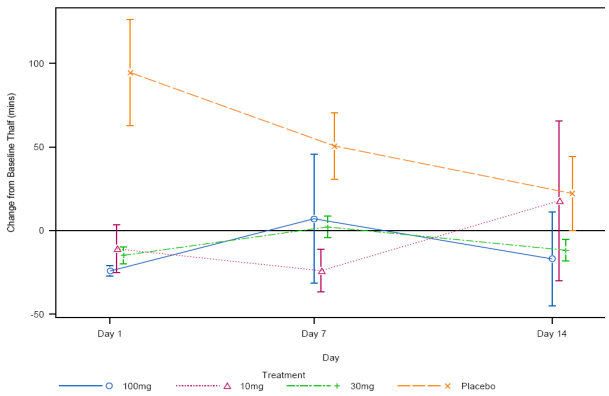
Example : PD_F2
Protocol : 204860
Population : Safety

Figure: Mean (±95% CI) [RCLASI/PD endpoints]
[Insert Title]

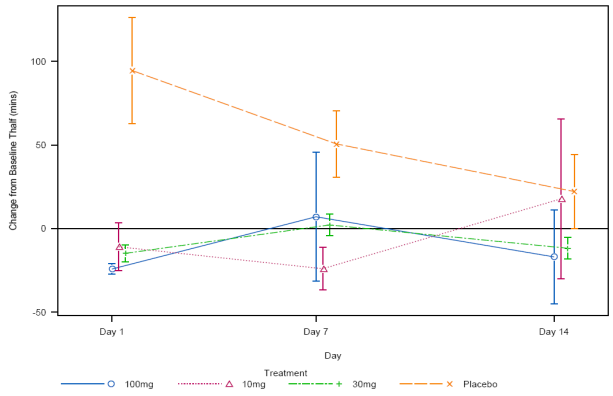
CLE type: Chronic



CLE type: Sub-Acute



CLE type: All

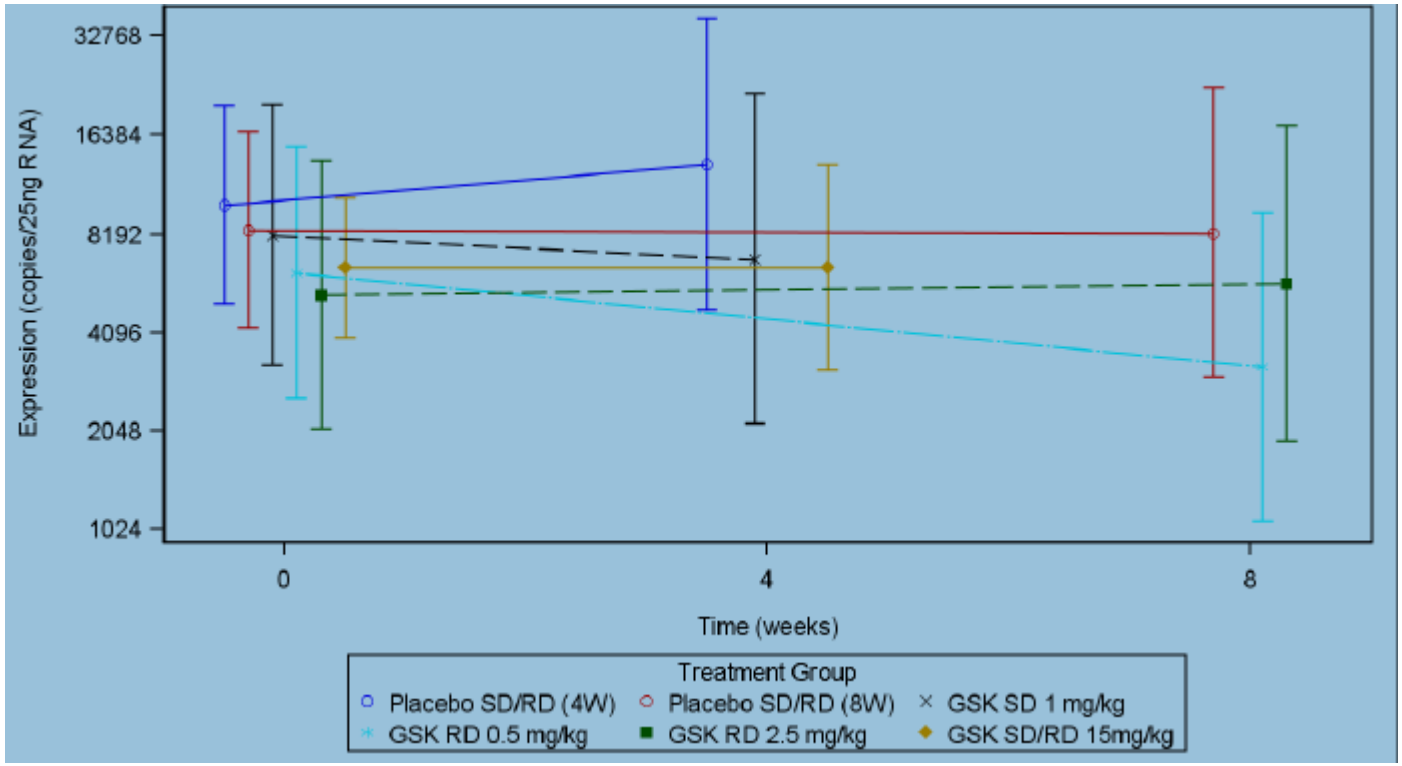


USER ID:directory/program.sas 01JAN2002 12:01

Example: PD_F3

Figure XX.XX:
Adjusted mean probe set intensity values (95% CI) by time from xxxx

Gene ID: XXXX Probeset ID: xxxx

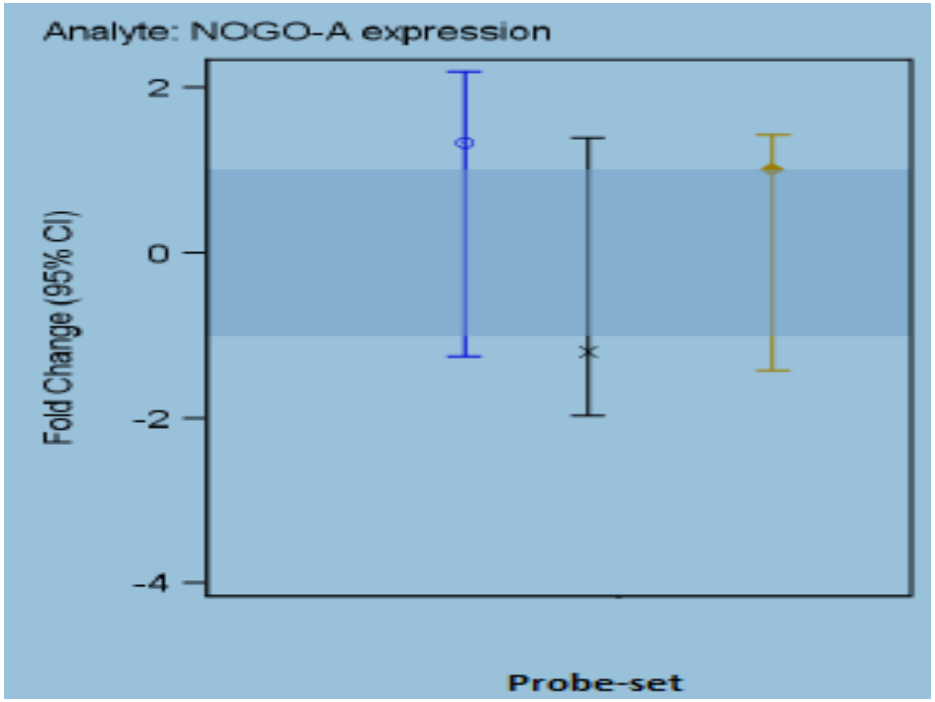


Example: PD_F4

Protocol: 204860 Page 1 of x
Population: Safety

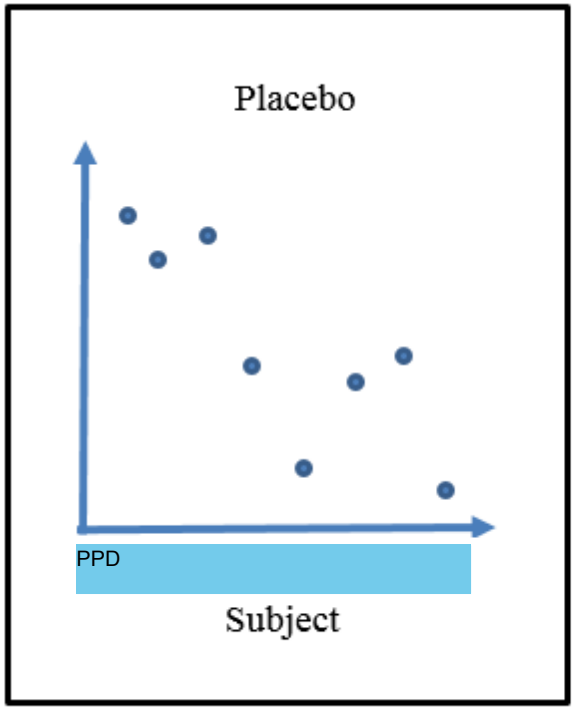
Figure XX.XX:
Adjusted Fold Change in mRNA Expression

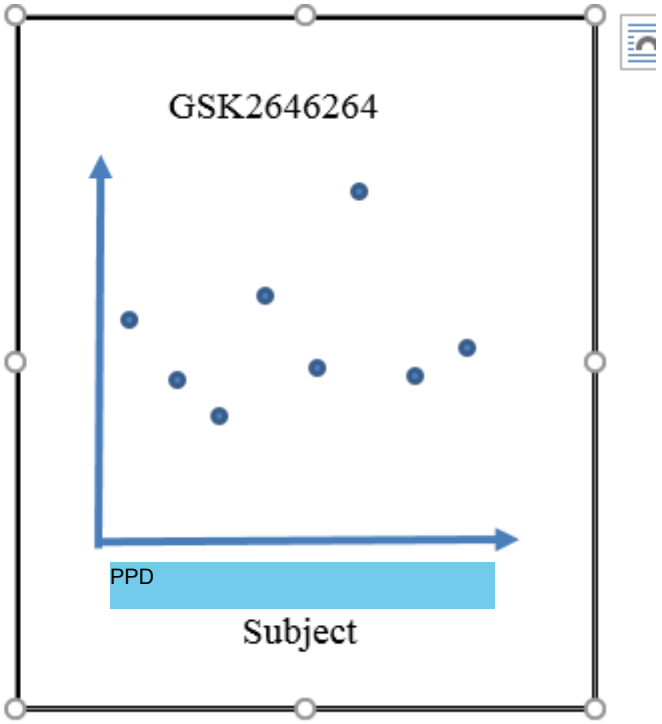
Gene ID: XXXX



Example: PD_F5
Protocol: 204860 Page 1 of x
Population: Safety

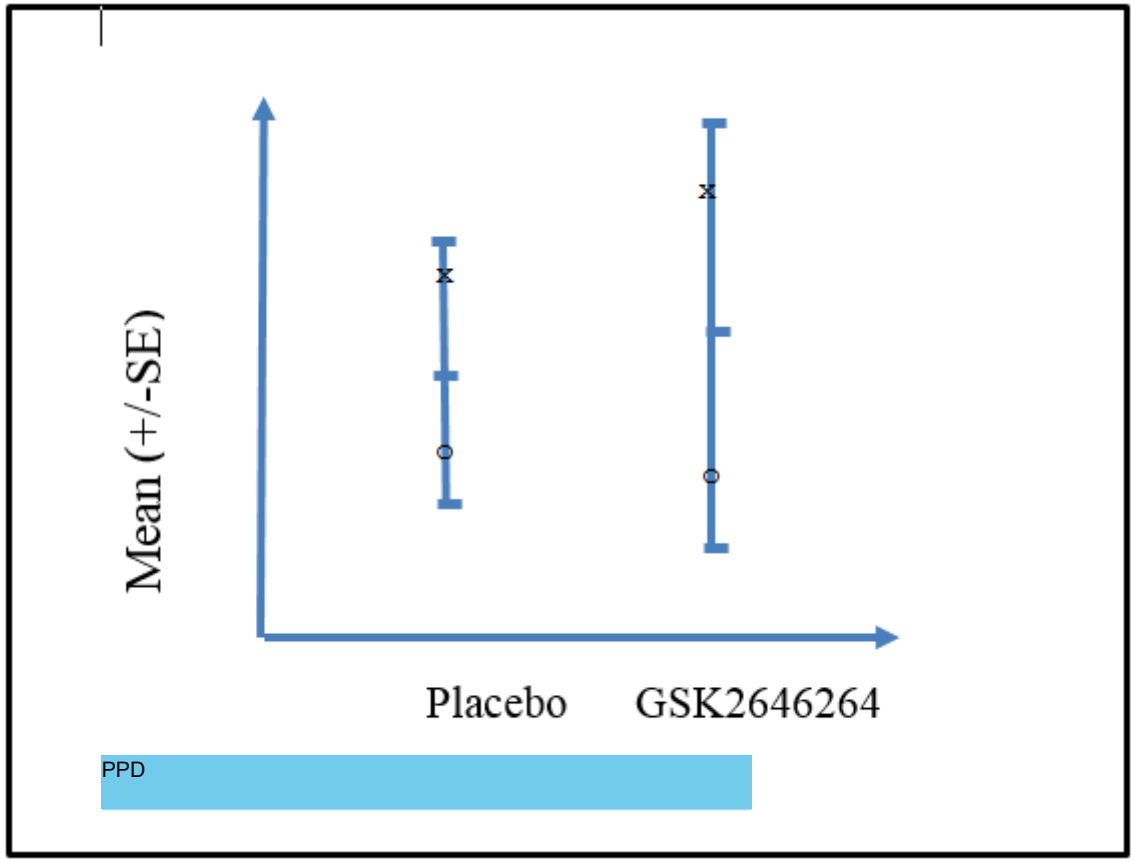
Figure XX.XX:





Example: PD_F6
Protocol: 204860
Population: Safety

Figure XX.XX:



Example : SAFE_L1
Protocol : 204860
Population : Safety

Listing: Listing of local tolerability

Subject	Treatment	Visit	Location	Side	Dermal Response	Other Dermal Effects	Skin Irritation Score	Skin Irritation Score Cfb
XXX	GSK2646264	XX	XX	XX	XX	XX	XX	XX
		XX	XX	XX	XX	XX	XX	XX
	--	--	--	--	--	--	--	--
	XXX	XX	XX	XX	XX	XX	XX	XX

Note: Dermal Response 0-7, Other Dermal Effects Z, A-H.
Note: cfb: Change from baseline

Example : SAFE_L2
Protocol : 204860
Population : Safety

Listing of Type of CLE (Group B-Natural Lesions)

Subject	CLE Type	Disease Diagnosis
XXX	Chronic	DD/MMM/YYYY
XXX	Acute	DD/MMM/YYYY
XXX	Acute	DD/MMM/YYYY

Example : PD_L1
Protocol : 204860
Population : Safety

Listing of RCLASI and components

Subject	Sequence	Skin site	Treatment	Visit	Planned time	Eyrthema	Scaling	.....	RCLASI score	RCLASI activity score
XXX	xxxx	xxxx	XX	XX	XX	XX	XX	XX	XX	XX
			XX	XX	XX	XX	XX	XX	XX	XX
			XX	XX	XX	XX	XX	XX	XX	XX
		--		--	--	--	--	--	--	--
		XXX		XX	XX	XX	XX	XX	XX	XX

Programming notes: include all RCLASI components.

Example : PD_L2
Protocol : 204860
Population : Safety

Listing XX:
Listing of transcriptomic mRNA expression for selected probesets by visit from xxxx

Skin Site	Subj.	Visit./ Visit date./ Study day	Probeset	GeneID	Normalised Expression
Placebo	XXX	XXX/ XX/XX/XX/ Baseline	XXXXXX	XXXXXXXXXXXXXXX	XX.X
		XXX/ XX/XX/XX/ Week XX	XXXXXX	XXXXXXXXXXXXXXX	XX.X
		XXX/ XX/XX/XX/ Week XX	XXXXXX	XXXXXXXXXXXXXXX	XX.X
		XXX/ XX/XX/XX/ Week XX	XXXXXX	XXXXXXXXXXXXXXX	XX.X

Example : PD_L3
Protocol : 204860
Population : Safety

Table x.xx
Listing of Histopathology score and components in skin biopsies (Group B-Natural Lesions)

Subj	Skin Area	Scoring: Histological Features	Score 1	Score 2	Score 1	Score 2	Average Score
XXXX	F	Parakeratosis	None	None	0	0	0
		Ballooning / Hydropic Degeneration	Weak	None	1	0	0.5
		Epidermal Cell Death	Fair	None	2	0	1
		Junctional Inflammation	Fair	None	2	0	1
		Dermal Inflammation	Fair	None	2	0	1
		Histological Score	NA	NA	7	0	3.5

Example : PD_L4
Protocol : 204860
Population : Safety

Table x.xx
Listing of QC criteria from Histological scoring form (Group B-Natural Lesions)

Subj	Skin Area	QC Criteria	Score 1	Score 2
XXXX	F	Quality of the skin specimen is sufficient	Yes	Yes
		This is a lesional skin biopsy form an inflamed skin area	Yes	No
		The correct diagnosis for this skins specimen most probably is CLE	Yes	Yes
		Correct CLE subtype for this skin sample		