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

Title	:	A multicentre, randomised, double-blind (sponsor-unblinded), placebo-controlled, repeat dose study to investigate the safety and tolerability, pharmacokinetics, pharmacodynamics, and efficacy of GSK2982772 in subjects with active plaque-type psoriasis.
Compound Number	:	GSK2982772
Effective Date	:	24-May-2017

Description :

- The purpose of this RAP is to describe the planned analyses and output to be included in the Clinical Study Report for Protocol 203167.
- This RAP is intended to describe the safety, tolerability, PK, PD, and efficacy analyses required for the study.
- This RAP will be provided to the study team members to convey the content of the Statistical Analysis Complete (SAC) deliverable.

Author's Name and Functional Area:

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Approved by:

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1. REPORTING & ANALYSIS PLAN SYNOPSIS

Overview	Key Elements of the RAP
Purpose	This is the first study with GSK2982772 in subjects with active, plaque-type psoriasis. The purpose of this study is to evaluate the safety, tolerability, pharmacokinetic (PK), pharmacodynamics (PD) and preliminary efficacy of GSK2982772. The intention of this study is to enable a fuller understanding of the mechanism of action and potential for clinical efficacy of GSK2982772 in PsO.
Protocol	This RAP is based on protocol amendment #2 [(Dated: 12/04/2017) of study GSK2982772 (GSK Document No. : 2015N251765_02)] and eCRF Version 3.0
Primary Objective	To investigate the safety and tolerability of 60 mg twice daily doses and 60 mg three times daily doses of GSK2982772 in subjects with active plaque-type psoriasis.
Primary Endpoint	Safety and tolerability of GSK2982772 as assessed by clinical monitoring and reporting of adverse events, change in laboratory values, ECG, vital signs.
Study Design	A multicentre, randomised, double-blind (sponsor-unblinded), placebo-controlled, repeat dose study proof of mechanism study. Approximately 30 subjects with active PsO will be randomised in a 2:1 ratio to GSK2982772 60mg BID and placebo respectively. Approximately 24 subjects with active PsO will be randomised in a 3:1 ratio to GSK2982772 60mg TID and placebo respectively
Planned Analyses	Safety and tolerability (primary). Pharmacokinetic (PK), Pharmacodynamic (PD) and clinical efficacy (secondary/exploratory).
Analysis Populations	All subjects: all subjects screened for eligibility Safety population: comprised all subjects who receive one dose of study treatment (placebo or GSK2982772). PK population: comprised subjects in the 'Safety' population for whom a pharmacokinetic sample was obtained and analysed.
Hypothesis	The primary objective of the study is to investigate the safety and tolerability of GSK2982772 60mg BID and 60mg TID following 12 weeks of treatment. No formal statistical hypotheses will be conducted to assess this objective. If appropriate, comparisons between the GSK2982772 60mg BID / 60mg TID arms and the placebo arm will be made to investigate the secondary inflammatory, mechanistic and efficacy objectives. Trends over time will be investigated for both treatment arms along with associations between each of the parameters.
Primary	<u>Safety:</u>

Overview	Key Elements of the RAP
Analyses	• All data will be descriptively summarised, graphically presented and listed appropriately according to GSK's Integrated Data Standard Library (IDSL) standards.
Secondary Analyses	<u>General:</u> • All data will be descriptively summarised, graphically presented and listed appropriately according to GSK's Integrated Data Standard Library (IDSL) standards. • Modelling relationships between each of the mechanistic endpoints and also with the clinical endpoints using appropriate statistical modelling techniques to identify any trends. • Trends over time will be investigated for all treatment arms along with associations between each of the key secondary and exploratory parameters. • If appropriate, formal comparisons between each GSK2982772 arm and placebo will be made to investigate the secondary PD, mechanistic endpoints and efficacy. <u>Pharmacokinetic</u>: • No formal statistical analyses will be conducted. <u>Pharmacodynamic/biomarker</u>: • Descriptive statistics and/or graphical summaries for all PD and biomarker endpoints by treatment and time point. <u>Efficacy:</u> • Descriptive statistics and/or graphical summaries of index lesion PLSS score by treatment and time point. • (Percentage) change from baseline for the index lesion PLSS score will be analysed using repeated measures mixed effects model (MMRM), where appropriate.

2. SUMMARY OF KEY PROTOCOL INFORMATION

2.1. Changes to the Protocol Defined Statistical Analysis Plan

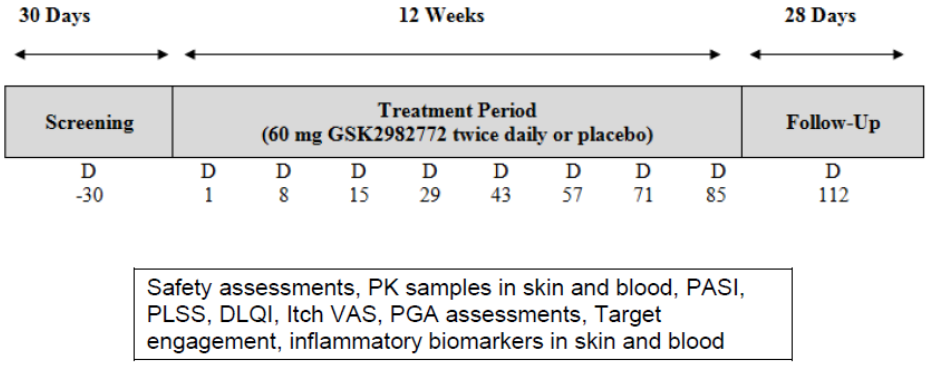
There were no changes or deviations to the originally planned statistical analysis specified in the protocol amendment 2 [(Dated: 12-Apr-2017)].

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

Objectives	Endpoints
Primary Objectives	**Primary Endpoints**
• To investigate the safety and tolerability of 60 mg twice daily and 60 mg three times daily doses doses of GSK2982772 in subjects with active plaque-type psoriasis.	• Adverse events • Clinical laboratory values (clinical chemistry, haematology and urinalysis) • Vital sign measurements (blood pressure, heart rate, respiratory rate and body • temperature) • 12-Lead ECG monitoring
Secondary Objectives	**Primary Objectives**
• To investigate the pharmacokinetics of GSK2982772 in blood following 60 mg twice daily doses and 60 mg three times daily doses of GSK2982772 in subjects with active plaque-type psoriasis.	• Pre-dose plasma concentrations of GSK2982772 at Days 43 (Week 6) and 85 (Week 12). • Post-dose plasma concentrations of GSK2982772 on Days 1 and 43 (Week 6) at 1, 2, 4 and 6 hours post dose.
• To investigate the effect of 60 mg twice daily doses and 60 mg three times daily doses of GSK2982772 on inflammatory biomarkers in skin biopsies from psoriatic skin lesions in subjects with active plaque-type psoriasis.	• Change from baseline in histopathological scoring of psoriatic lesional biopsies which may include, but are not limited to the following as data permit: K16, CD3/CD11c, CD161, elastase positive dermal cells and epidermal thickness. • mRNA expression of inflammatory gene transcripts which may include, but are not limited to the following as data permit: IL-4, IL-10, IL-17, IL-21, IL-22, IL-23, TNF and IFNγ on Days 1 (Week 0) and 43 (Week 6).
• To investigate the effect of 60 mg twice daily doses and 60 mg three times daily doses of GSK2982772 on disease activity in subjects with active plaque-type psoriasis.	• Percentage change from baseline and actual Psoriatic Lesion Severity Sum (PLSS) scores in the index lesion.
Exploratory Objectives	**Exploratory Endpoints**
• To investigate the effect of 60 mg twice daily doses and 60 mg three times daily doses of GSK2982772 on disease activity in subjects with	• Change from baseline in Psoriasis Area Severity Index (PASI) scores. • The proportion of subjects who achieve PASI ≥ 50%, 75%, and 90% improvement from baseline score.

Objectives	Endpoints
active plaque type psoriasis	• Change from baseline and actual Physician Global Assessment (PGA). • The proportion of subjects who achieve "clear" (0) or "almost clear" (1) on PGA. • Change from baseline in body surface area (BSA).
• To investigate the effect of 60 mg twice daily doses and 60 mg three times daily doses of GSK2982772 on inflammatory biomarkers in the blood of subjects with active plaque-type psoriasis.	• Change from baseline in blood inflammatory markers which may include, but are not limited to the following as data permit: CRP, VEGF, S100A8, S100A9, IL-17, IL-22, and TNF.
• To investigate the effect of 60 mg twice daily doses and 60 mg three times daily doses of GSK2982772 on transcriptome profiling of both blood and skin of subjects with active plaque-type psoriasis.	• Transcriptomic analysis of mRNA isolated from blood and skin at Day 1 (Week 0) and Day 43 (Week 6).
• To investigate pathway and target engagement following 60 mg twice daily doses and 60 mg three times daily doses of GSK2982772 in blood and skin biopsy tissue in subjects with active plaque-type psoriasis.	• Pharmacology biomarker endpoints may include, but are not limited to the following Days 1 (Week 0), 43 (Week 6) and 85 (Week 12), as data permit: o Target Engagement Assay RIP1 (TEAR1) in blood and skin. o Total or phosprylated RIP1, MLKL, and RIP3, cleaved and total caspase 3 and caspase 8 signatures in skin.
• To investigate the concentration of GSK2982772 in the skin of subjects with active plaque-type psoriasis after 60 mg twice daily doses of and 60 mg three times daily doses GSK2982772.	• Pre-dose GSK2982772 concentrations in skin biopsies at Days 1 (Week 0) and 43 (Week 6), as data permit.
• To investigate the effect of 60 mg twice daily doses and 60 mg three times daily doses of GSK2982772 on the patient reported outcomes (PROs) of subjects with active plaque-type psoriasis.	• Change from baseline in Dermatology Life Quality Index (DLQI) score. • Change from baseline and actual Visual Analogue Scale (VAS) itch score.

2.3. Study Design

Overview of Study Design and Key Features	
	
Design Features	• A multicentre, randomised, double-blind (sponsor-unblinded), placebo-controlled, repeat dose study proof of mechanism study. • Investigate the safety and tolerability, pharmacokinetic (PK), pharmacodynamic (PD) and clinical efficacy of repeat doses of GSK2982772.
Dosing	• Subjects will be screened up to 30 days before the treatment phase. • Approximately 30 subjects randomised in 2:1 ratio to receive GSK2982772 60mg or placebo orally twice daily (approximately 12 hours apart) for 84 days. • Approximately 24 subjects randomised in 3:1 ratio to receive GSK2982772 60mg or placebo orally three times daily (approximately 12 hours apart) for 84 days.
Treatment Assignment	• At screening a unique Subject Number (CRF number) is assigned. • Subjects who meet screening eligibility criteria and complete the Pre-Treatment assessments will be randomised through an Interactive Response Technology (IRT). • IRT will confirm the subject's CRF number and provide the randomisation number. • Randomisation number is generated by Clinical Statistics and will assign the subject to a treatment. • Approximately 30 subjects randomised in 2:1 ratio to receive GSK2982772 60mg BID or placebo BID. • Approximately 24 subjects randomised in 3:1 ratio to receive GSK2982772 60mg TID or placebo TID.
Interim	• Blinded safety, clinical and adverse event data will be reviewed at

Overview of Study Design and Key Features	
Analysis	appropriate intervals by the GSK Safety Review Team (SRT). See SRT charter for further details. • The PLSS data will be reviewed in an unblinded manner when an appropriate number of subjects have completed Day 43. See the interim analysis chapter for further details. • A formal interim analysis will be conducted after the completion of Cohort 1 and will only include those subjects randomised to a BID dosing regimen.

2.4. Statistical Hypotheses

The primary objective of the study is to investigate the safety and tolerability of GSK2982772 60mg BID and 60mg TID following 12 weeks of treatment. No formal statistical hypotheses will be conducted to assess this objective.

If appropriate, comparisons between each GSK2982772 arm and the placebo arm will be made to investigate the secondary inflammatory, mechanistic and efficacy objectives. Trends over time will be investigated for both treatment arms along with associations between each of the parameters.

3. PLANNED ANALYSES

3.1. Interim Analyses

In line with routine pharmacovigilance, an internal GSK Safety Review Team (SRT) which will include members of the 203167 study team, will review blinded safety data, including clinical laboratory parameters and adverse events, at appropriate intervals during the period of study conduct. Further details are outlined in the SRT charter.

In both cohorts, once an appropriate number of subjects randomised to GSK2982772 have completed Day 43 (Week 6), the PLSS data will be reviewed in an unblinded manner by a Data Review Committee (DRC) consisting of the GSK Project Physician Lead (PPL), the study statistician, the study pharmacokineticist, the Pattern Recognition Receptor (PRR) Discovery Performance Unit (DPU) Head, the Early Development Lead (EDL), the Safety Review Team (SRT) leader, or their designees on an ongoing basis. A physician external to the GSK2982772 project team may also be involved in the data review. Additional inflammatory biomarkers, clinical and mechanistic endpoints (e.g. target engagement) may be reviewed if available. No other member of the GSK core study team will be unblinded to this data. The primary purpose of these reviews will be to monitor PLSS changes for internal decision making purposes. A data review charter will identify the specific GSK individuals involved, outline in detail the activities of this review and how the integrity of the study will be maintained.

A formal interim analysis will be conducted after the completion of Cohort 1 and will only include those subjects randomised to a BID dosing regimen. The purpose of the

interim analysis is primarily to provide the project team and key GSK stakeholders with an early indication of the safety and efficacy from the trial, and to facilitate decision making regarding the subsequent clinical development of GSK2982772.

3.2. Final Analyses

The final planned primary 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. A completed subject is one who has completed all phases of the study including the follow-up visit.
3. All required database cleaning activities have been completed and final database release and database freeze has been declared by Data Management.
4. All criteria for unblinding the randomisation codes have been met.
5. Randomisation codes have been distributed according to RandAll NG procedures.

4. ANALYSIS POPULATIONS

Population	Definition / Criteria	Analyses Evaluated
All subjects	• All subjects who were screened for eligibility.	• Selected study population
Safety	• All subjects who receive at least one dose of study treatment. • This population will be based on the treatment the subject actually received[1]	• Study population • Safety • Efficacy • PD
Pharmacokinetic	• Subjects in the 'Safety' population for whom a pharmacokinetic sample was obtained and analysed.	• PK

NOTES :

1. Any subjects who actually received both placebo and GSK2982772 due to dispensing errors will be assigned to GSK2982772, regardless of treatment duration

Please refer to Appendix 13: List of Data Displays which details the population to be used for each displays 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 unblinding and 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: Assessment Windows
11.3	Appendix 3: Treatment States and Phases
11.4	Appendix 4: Data Display Standards & Handling Conventions
11.5	Appendix 5: Derived and Transformed Data
11.6	Appendix 6: Premature Withdrawals & Handling of Missing Data
11.7	Appendix 7: Values of Potential Clinical Importance
11.8	Appendix 8: Multicentre Studies
11.9	Appendix 9: Examination of Covariates, Subgroups & Other Strata
11.10	Appendix 10: Multiple Comparisons & Multiplicity
11.11	Appendix 11: Model Checking and Diagnostics for Statistical Analyses.
11.13	Appendix 12: Abbreviations & Trade Marks
11.14	Appendix 13: Data Displays
11.15	Appendix 14: Example Mock Shells for Data Displays

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 13: List of Data Displays.

Table 2 Overview of Planned Study Population Analyses

Endpoint / Parameter / Display Type	Data Displays Generated		
	Table	Figure	Listing
Randomisation			
Randomisation			Y
Subject Disposition			
Subject Disposition	Y		
Reasons for Screen Failure	Y		Y
Subjects by 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
PsO baseline characteristics – BSA,disease duration , prior treatments, naive phototherapy, PASI score, PLSS index lesions, PGA, Lesion severity area and score, history of tobacco use	Y		Y
Race and Racial Combinations	Y		Y [2]
Prior and Concomitant Medications			
Current/Past Medical Conditions	Y		
Concomitant Medications	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 SafetyAnalyses

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

Table 3 provides an overview of the planned safety analyses, with full details of data displays being presented in Appendix 13: List of Data Displays.

Table 3 Overview of Planned Adverse Event Analyses

Endpoint / Parameter/ Display Type	Absolute		
	Summary		Individual
	T	F	L
Adverse Events (AEs)			
All AEs by SOC	Y		Y
Common (>=10%) AEs by Overall Frequency	Y	Y [1]	
All AEs by Maximum Intensity/Grade by SOC (and PT)	Y		
All Drug-Related AEs by SOC	Y		
Subjects & No. of Occurrences of Common Non-Serious AEs by SOC and PT	Y		
Subject Numbers for Individual AEs			Y
Relationship Between AE SOCs, PT & Verbatim Text			Y
Serious and Other Significant AEs			
Fatal Serious AEs			Y
Non-Fatal Serious AEs			Y
Serious AEs by SOC	Y		
Reasons for Considering as a Serious AE			Y
Drug-Related Serious AEs by SOC	Y		
AEs Leading to Withdrawal from Study / Permanent Discontinuation of Study Treatment by Overall Frequency	Y		Y
Subjects and Number of Occurrences of Serious, Drug-Related Serious, Fatal Serious, and Drug-Related Fatal Serious AEs	Y		
Other Significant Adverse Events			Y

NOTES:

- T = Table, F = Figures, L = Listings, Y = Yes display generated, SOC = System Organ Class, PT = Preferred Term.
- Summary = Represents TF 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] Plot of common AEs and relative risk will be generated.

7.1.2. Overview of Clinical Laboratory Analyses

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

Table provides an overview of the planned analyses, with further details of data displays being presented in Appendix 1: List of Data Displays.

Table 5 Overview of Planned Clinical Laboratory Analyses

Endpoint / Parameter/ Display Type	Absolute			Change from BL		
	Summary		Individual	Summary		Individual
	T	F	L	T	F	L
Chemistry						
Chemistry Results	Y			Y		
Emergent Chemistry Results by PCI Criteria	Y					
Hematology						
Hematology Results	Y			Y		
Emergent Hematology Results by PCI Criteria	Y					
Urinalysis						
Urine Concentration				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			
Scatter Plot of Maximum vs. Baseline for ALT		Y				
Scatter Plot of Maximum ALT vs Maximum Total Bilirubin		Y				
All Laboratory						
Laboratory Data for Subjects with Abnormalities of Potential Clinical Concern			Y			
Laboratory Data Abnormalities of Potential Clinical Importance			Y			

NOTES:

- T = Table, F = Figures, L = Listings, Y = Yes display generated, PCI = Potential Clinical Importance
- 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 provides an overview of the planned analyses, with further details of data displays being presented in Appendix 13: List of Data Displays.

Table 6 Overview of Planned Other Safety Analyses

Endpoint / Parameter/ Display Type	Absolute			Change from BL		
	Summary		Individual	Summary		Individual
	T	F	L	T	F	L
ECG						
ECG Findings	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			
ECG Values of PCI			Y			
Abnormal ECG Findings			Y			
Vital Signs						
Vital Signs by Visit	Y			Y		
Emergent Vital Signs Results by PCI Criteria	Y					
All Vital Signs for Subjects with Values of PCI			Y			

NOTES:

- T = Table, F = Figures, L = Listings, Y = Yes display generated, PCI = Potential Clinical Importance
- 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.

8. SECONDARY STATISTICAL ANALYSES

8.1. Plasma Pharmacokinetic Analyses

8.1.1. Overview of Planned Pharmacokinetic Analyses

The pharmacokinetic (PK) analyses will be based on the "Pharmacokinetic" population, unless otherwise specified. There are no planned statistical analyses.

GUI_51487 (4.0), effective October 2014, contains the pharmacokinetic methods to be used in non-compartmental analysis (NCA) and reporting of pharmacokinetic studies. This document should be used as a reference.

8.1.2. Overview of Planned pharmacokinetic Analyses

Table provides an overview of the planned pharmacokinetic analyses, with further details of data displays being presented in Appendix 13: List of Data Displays.

Table 8 Overview of Planned Pharmacokinetic Analyses

Endpoints	Untransformed				Log-transformed			
	Summary		Individual		Summary		Individual	
	T	F	F	L	T	F	F	L
Pharmacokinetic								
Plasma Drug concentration	Y	Y[1][2]	Y[1]	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 plots will be generated.

8.1.3. Drug Concentration Measures

Refer to Appendix 4: Data Display Standards & Handling Conventions, Section 11.4.3 Reporting process & standards for details on how the concentration data will be derived.

8.1.3.1. Statistical Analysis of Pharmacokinetic Parameters

No formal pharmacokinetic statistical analyses will be performed.

8.2. Pharmacodynamic/Biomarker Analyses

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

8.2.1. Overview of Planned Analyses

Table 10 provides an overview of the planned analyses, with further details of data displays being presented in Appendix 13: List of Data Displays.

Table 10 Overview of Planned Pharmacodynamic/biomarker Analyses

Endpoint	Absolute							Change from Baseline						
	Stats Analysis			Summary		Individual		Stats Analysis			Summary		Individual	
	T	F	L	T	F	F	L	T	F	L	T	F	F	L
Pharmacodynamic and Biomarkers														
Inflammatory biomarkers in skin biopsy[1]				Y		Y	Y	Y	Y	Y	Y			
mRNA from skin biopsy[2]				Y		Y	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 (i.e. descriptive statistics) of the observed raw data.
- Individual = Represents FL related to any displays of individual subject observed raw data
- 1: Histopathloogical Scoring of Skin biopsy may include epidermal thickness, elastase positive dermal cells, K16, CD3/CD11c and CD161.
- 2: mRNA expression of inflammatory gene transcripts including but not limited to:IL-4, IL-10, IL-17, IL-21, IL-22, IL-23, TNF, IFNγ

8.2.2. Statistical Analysis of Inflammatory Biomarkers in the Skin Biopsy (Histopathological Scoring of Psoriatic Lesional Biopsies)

Primary Statistical Analyses
Endpoint(s)
• Change from baseline on log transformed inflammatory biomarkers from skin biopsy on Day 43 pre-dose: Log_e Change = Log_e (Visit) – log_e (Baseline)
Model Specification
• Endpoints will be statistically analyzed using an Analysis of Covariance (ANCOVA) model. • Terms fitted in the ANCOVA model will include: o Fixed Category : Treatment o Fixed Continuous Covariates : Log_e Baseline score
Model Checking & Diagnostics
Refer to Appendix 1: Model Checking and Diagnostics for Statistical Analyses.
Presentation of results

Primary Statistical Analyses
➢ Adjusted geometric means, the mean difference between each dose (test) and the placebo (reference) at each timepoint and associated 95% confidence interval will be constructed using the residual variance ➢ The treatment ratios and 95% CI will be calculated by back-transforming the difference between the least square means and associated 95% CI ➢ Percentage change from baseline at each timepoint will be calculated from the adjusted geometric means using the formula 100% x (exp(adj mean)- 1)

8.2.3. Statistical Analysis of mRNA from Skin Biopsies: Transcriptomic Data

8.2.3.1. Fold Change Analysis

The log_2 normalised copy numbers (also referred to as log2(intensity)) received from the normalised process will be listed and summarised appropriately.

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

- If ratio ≥ 0 then fold change = ratio
- If ratio <0 then fold change = -1/ratio

Primary Statistical Analyses
Endpoint(s)
• Log2(intensity) mRNA expression of inflammatory gene transcripts which may include, but are not limited to the following as data permit: IL-4, IL-10, IL-17, IL-21, IL-22, IL-23, TNF and IFNγ
Model Specification
• Endpoints will be statistically analyzed using a linear repeated measures mixed effects model. • Terms fitted in the linear repeated measures mixed effects model will include: o Fixed Category : Treatment, Visit, Treatment * Visit o Random Effect : Subject
Model Checking & Diagnostics
Refer to Appendix 1: Model Checking and Diagnostics for Statistical Analyses.
Presentation of Results
• For each probeset analysed adjusted means with corresponding 95% CI and fold changes with corresponding 95% CI's can be outputted. The fold change is derived from the ratio of the back-transformed estimate of the difference between adjusted means. • Plots of LS means and 95% confidence intervals from the model will be generated for each treatment by time. Additionally, plots of differences and 95% confidence intervals for the comparison between the treatment groups will be generated.

For each comparison subsets of probesets will be identified based on an appropriate fold-change, for example, fold changes >1.5 or <-1.5. The proportion of probesets with fold changes >1.5 or <-1.5 will be summarised in a frequency table.

Exploratory graphical reporting on the back-transformed scale can include:

- Log_2 (intensity) plotted against time point separately for individual subjects, grouped by treatment group
- Adjusted mean intensity and 95 CI% plotted by treatment group and time point

8.3. Efficacy Analyses

8.3.1. Overview of Planned Efficacy Analyses

The secondary efficacy analyses will be based on the "Safety" population, unless otherwise specified.

Table 11 provides an overview of the planned efficacy analyses, with further details of data displays being presented in Appendix 13: List of Data Displays.

Table 11 Overview of Planned Efficacy Analyses

ENDPOINT	Absolute							% Change from Baseline						
	Stats Analysis			Summary		Individual		Stats Analysis			Summary		Individual	
	T	F	L	T	F	F	L	T	F	L	T	F	F	L
Psoriatic Lesion Severity Sum (PLSS)														
PLSS				Y	Y	Y	Y	Y	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 (i.e. descriptive statistics) of the observed raw data.
- Individual = Represents FL related to any displays of individual subject observed raw data.

8.3.2. Statistical Analysis of Efficacy Data

Statistical Analyses
Secondary Endpoint(s)
• Percentage change from baseline (pre-dose Day 1) in PLSS score at Days 15, 29, 43 (pre-dose), 57, 71 and 85.
Model Specification
• Endpoints will be statistically analyzed using a mixed models repeated measures (MMRM) approach. • Terms fitted in the MMRM model will include: o Fixed Category : Treatment, Day, Treatment*Day

Statistical Analyses
○ Fixed Continuous Covariates : Baseline Score ○ Repeated Effect : Day Note: Other covariates maybe explored, if deemed appropriate for sensitivity analyses.
Model Checking & Diagnostics
• Refer to Appendix 11: Model Checking and Diagnostics for Statistical Analyses.
Presentation of results
• LS means and corresponding standard error of means (SEs) and 95% confidence intervals will be presented for each treatment by time interaction, together with estimated treatment differences (GSK2982772 – Placebo) and the corresponding 95% confidence intervals will be produced. • Plots of LS means and 95% confidence intervals from the model will be generated over time by treatment. Additionally, plots of differences and 95% confidence intervals for the comparison of interest will be generated over time.

9. OTHER STATISTICAL ANALYSES

9.1. Skin Pharmacokinetic Analyses

9.1.1. Overview of Planned Pharmacokinetic Analyses

The pharmacokinetic (PK) analyses will be based on the "Pharmacokinetic" population, unless otherwise specified. There are no planned statistical analyses.

GUI_51487 (4.0), effective October 2014, contains the pharmacokinetic methods to be used in non-compartmental analysis (NCA) and reporting of pharmacokinetic studies. This document should be used as a reference.

9.1.2. Overview of Planned pharmacokinetic Analyses

Table provides an overview of the planned pharmacokinetic analyses, with further details of data displays being presented in Appendix 13: List of Data Displays.

Table 8 Overview of Planned Pharmacokinetic Analyses

Endpoints	Untransformed				Log-transformed			
	Summary		Individual		Summary		Individual	
	T	F	F	L	T	F	F	L
Pharmacokinetic								
Skin Drug concentration	Y	Y[1][2]	Y[1]	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 plots will be generated.

9.1.3. Drug Concentration Measures

Refer to Appendix 4: Data Display Standards & Handling Conventions, Section 11.4.3 Reporting process & standards for details on how the concentration data will be derived.

9.1.3.1. Statistical Analysis of Pharmacokinetic Parameters

No formal pharmacokinetic statistical analyses will be performed.

9.2. Exploratory Pharmacodynamic and Biomarker Analyses

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

Table 13 provides an overview of the planned Pharmacodynamic/Biomarker analyses, with full details of data displays being presented in Appendix 13: List of Data Displays.

Table 13 Overview of Planned Exploratory Biomarker Analyses

Endpoint	Absolute							Change from Baseline						
	Stats Analysis			Summary		Individual		Stats Analysis			Summary		Individual	
	T	F	L	T	F	F	L	T	F	L	T	F	F	L
Pharmacodynamic and Biomarkers														
Inflammatory biomarkers in blood[1]				Y		Y	Y	Y	Y	Y	Y			Y
Target Engagament Assay RIP1 (TEAR1)[2]	Y	Y	Y	Y		Y	Y							
Pharmacology biomarker in skin[3]														
Blood Transcptomics sample[4]														

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: Including, but not limited to CRP, VEGF, S100A8, IL-17, IL-22 and TNF
- 2: In blood and skin
- 3: Total or phosprylated RIP1, MLKL, and RIP3, cleaved and total caspase 8 signatures are not intended to be delivered as part of DBF by first intent. Any future summaries and/or analyses will be deemed post-hoc
- 4. Transcriptomic analysis of mRNA are not intended to be delivered as part of DBF by first intent. Any future summaries and/or analyses will be deemed post-hoc.

Scatter plots of Skin Target Engagement and skin biomarkers for Day 43 and Day 85 will also be produced.

If deemed appropriate, the relationship between Skin Target Engagement and the skin biomarkers will be explored further using multivariate statistical analyses. The consistency in the changes over time between the endpoints will also be assessed. Any such analyses will be defined after unblinding of the data and thus deemed post-hoc.

9.2.1. Planned Exploratory Biomarker Statistical Analyses

Planned Statistical Analyses
Endpoint(s)
• Percentage change from baseline in blood inflammatory markers, including, but not limited to the following as data permits: CRP, VEGF, S100A8, IL-17, IL-22 and TNF across Days 43 (pre-dose) and 84 (pre-dose).
Model Specification
• Change from baseline scores will be analysed using a mixed models repeated measures (MMRM) across Day 43(pre-dose) and 85.

Planned Statistical Analyses
• Terms fitted in the MMRM model will include: o Fixed Category : Treatment, Day, Treatment*Day o Fixed Continuous effect : Baseline scores o Repeated Effect : Day
Model Checking
• Refer to Appendix 1: Model Checking and Diagnostics for Statistical Analyses.
Model Results Presentation
• Adjusted means and corresponding standard error of means (SEs) and 95% confidence intervals will be presented for each treatment by time interaction, together with estimated treatment differences (GSK2982772 – Placebo) and the corresponding 95% confidence intervals will be produced for respective endpoints. • Plots of LS means and 95% confidence intervals from the model will be generated for each treatment by time. Additionally, plots of differences and 95% confidence intervals for the comparison of interest will be generated.

Target Engagement
Endpoints
• Log Ratio = Log (free TEAR1) – log (total TEAR1)
Model Specification
➢ A mixed effect model will be fitted with treatment, period, time (i.e. planned relative time) and treatment * time as a fixed effect and subject as a random effect. Baseline log ratio will be fitted as a continuous covariate ➢ The Kenward & Roger (KR) degrees of freedom approach will be used.
Model Checking
➢ Refer to Section 11.11.
Presentation of Results
➢ Adjusted geometric means, the mean difference between each dose (test) and the placebo (reference) at each timepoint and associated 95% confidence interval will be constructed using the residual variance ➢ The treatment ratios and 95% CI will be calculated by back-transforming the difference between the least square means and associated 95% CI ➢ Percentage target engagement at each timepoint will be calculated from the adjusted geometric means using the formula 100% x (exp ln (v2 / v1) - 1) percentage target engagement = (100 – engagement ratio) * 100

9.3. Exploratory Efficacy Analyses

The exploratory efficacy analyses will be based on the "Safety" population, unless otherwise specified.

Table 14 provides an overview of the planned exploratory efficacy analyses, with further details of data displays being presented in Appendix 13: List of Data Displays.

Table 14 Overview of Planned Exploratory Efficacy Analyses

Endpoint(s)	Absolute							Change from Baseline						
	Stats Analysis			Summary		Individual		Stats Analysis			Summary		Individual	
	T	F	L	T	F	F	L	T	F	L	T	F	F	L
Psoriasis Area Severity Index (PASI)														
PASI score				Y	Y	Y	Y	Y	Y	Y	Y			Y
PASI50, PASI75, PASI90[1]	Y		Y	Y			Y							
Physician Global Assessment (PGA)														
PGA				Y	Y		Y	Y		Y	Y			Y
PGA (clear vs almost clear)	Y		Y	Y			Y							
Psoriatic Body Surface Area														
BSA				Y	Y	Y	Y	Y	Y	Y	Y			Y
Patient Reported Outcomes (PROs)														
Dermatology Life Quality Index (DLQI)				Y	Y	Y	Y	Y	Y	Y	Y			Y
Visual Analogue Scale (VAS) itch score				Y	Y	Y	Y	Y	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 (i.e. descriptive statistics) of the observed raw data.
- Individual = Represents FL related to any displays of individual subject observed raw data.

- PASI 50/75/90 will only be analysed if >50% of subjects have a BSA >5% at baseline

9.3.1. Planned Exploratory Efficacy Statistical Analyses

GEE modelling will only be performed if at least 30% response rate and Day 43 or Day 85 for any one treatment group. Further the proportion of subjects achieving PASI50/75/90 will only be performed if >50% of subjects have a BSA >5% at baseline.

Exploratory Endpoint(s)
• Proportion of subjects who achieve ≥ xx% improvement from baseline in PASI score at Days 15, 29, 43 (pre-dose), 57, 71 and 85 (if sufficient number of subjects are enrolled with a >5% BSA). • Proportion of subjects who have a PGA score of 'clear' (0) or 'almost clear' (1) at Days 15,29,

43(pre-dose), 57, 71 and 85.
Model Specification
• Will be analysed using a GEE (Generalized Estimating Equations) model across Day 15, 29, 43 (pre-dose), 57, 71 and 85. • Terms fitted in the GEE model will include: o Fixed Category : Treatment, Day, Treatment*Day o Repeated Effect : Day
Presentation of results
• Adjusted Odds Ratios and corresponding 95% confidence intervals will be generated from contrasts for treatment by day interactions. • Plots of the adjusted Odds Ratios and 95% confidence intervals from the model will be generated for each treatment by time. Additionally plots of differences and 95% confidence intervals for the comparisons of interest will be generated.

Exploratory Endpoint(s)
• Psoriasis Area Severity Index (PASI) score (if sufficient number of subjects are enrolled with a >5% BSA). • Physician Global Assessment (PGA) • Visual Analogue Scale (VAS) itch score.
Model Specification
• Change from baseline scores will be analysed using a mixed models repeated measures (MMRM) across Day 15, 29, 43 (pre-dose), 57, 71 and 85. • Terms fitted in the MMRM model will include: o Fixed Category : Treatment, Day, Treatment*Day o Fixed Continuous effect : Baseline scores o Repeated Effect : Day Note: Other covariates maybe explored, if deemed appropriate for sensitivity analyses.
Presentation of results
• Adjusted means and corresponding standard error of means (SEs) and 95% confidence intervals will be presented for each treatment by time interaction, together with estimated treatment differences (GSK2982772 – Placebo) and the corresponding 95% confidence intervals will be produced for respective endpoints. • Plots of LS means and 95% confidence intervals from the model will be generated for each treatment by time. Additionally, plots of differences and 95% confidence intervals for the comparison of interest will be generated.

Exploratory Endpoint(s)
• Body Surface Area (BSA)
Model Specification
• Change from baseline scores will be analysed using an Analysis of Covariance (ANCOVA) model at Day 85. • Terms fitted in the ANCOVA model will include: o Fixed Category : Treatment o Fixed Continuous effect : Baseline scores

Presentation of results
• Adjusted means and corresponding standard error of means (SEs) and 95% confidence intervals will be presented for each treatment, together with estimated treatment differences (GSK2982772 – Placebo) and the corresponding 95% confidence intervals will be produced. • Plots of LS means and 95% confidence intervals from the model will be generated for each treatment. Additionally, plots of differences and 95% confidence intervals for the comparison of interest will be generated.

Exploratory Endpoint(s)
• Dermatology Life Quality Index (DLQI) score.
Model Specification
• Change from baseline scores will be analysed using a mixed models repeated measures (MMRM) across Day 43 (pre-dose) and 85. • Terms fitted in the MMRM model will include: o Fixed Category : Treatment, Day, Treatment*Day o Fixed Continuous effect : Baseline scores o Repeated Effect : Day
Presentation of results
• Adjusted means and corresponding standard error of means (SEs) and 95% confidence intervals will be presented for each treatment by time interaction, together with estimated treatment differences (GSK2982772 – Placebo) and the corresponding 95% confidence intervals will be produced for respective endpoints. • Plots of LS means and 95% confidence intervals from the model will be generated for each treatment by time. Additionally, plots of differences and 95% confidence intervals for the comparison of interest will be generated.
Model Checking
• Refer to Appendix 1: Model Checking and Diagnostics for Statistical Analyses.

9.4. Exploratory Pharmacodynamic / Efficacy Analyses

If deemed appropriate, the relationship between the skin biomarkers and efficacy endpoints will be explored further using multivariate statistical methods and/or Bayesian methodology as recommended by the GSK PCPS Experimental Medicine working group. The consistency in the changes over time between the endpoints will also be assessed. Any such analyses will be defined after unblinding of the interim data and thus deemed post-hoc.

10. REFERENCES

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: Assessment Windows
Section 11.3	Appendix 3: Treatment States & Phases
Section 11.4	Appendix 4: Data Display Standards & Handling Conventions
Section 11.5	Appendix 5: Derived and Transformed Data
Section 11.6	Appendix 6: Premature Withdrawals & Handling of Missing Data
Section 11.7	Appendix 7: Values of Potential Clinical Importance
Section 11.8	Appendix 8: Multicentre Studies
Section 11.9	Appendix 9: Examination of Covariates and Subgroups
Section 11.10	Appendix 10: Multiple Comparisons and Multiplicity
Section 11.11	Appendix 11: Model Checking and Diagnostics for Statistical Analyses
Other RAP Appendices	
Section 11.12	Appendix 12: Abbreviations & Trade Marks
Section 11.13	Appendix 13: List of Data Displays
Section 11.14	Appendix 14: Example Mock Shells for Data Displays

11.1. Appendix 1: Time & Events

11.1.1. Protocol Defined Time & Events

Procedures	Screening	Treatment Period													Early Withdrawal[14]	Follow Up	Notes
		Day 1	Day 8	Day 15	Day 22	Day 29	Day 36	Day 43 (week 6)	Day 50	Day 57	Day 64	Day 71	Day 78	Day 85 (week 12)			**Visit windows** Screening: up to 30d before Day 1. Treatment Period (except Day 1 & 85): ± 3d. Day 1 NA; Day 85 ± 2d. Early Withdrawal: NA Follow Up: 28d after last dose ± 3d
Screening Procedures	Screening procedures in addition to those listed below are (outpatient visit): informed consent; inclusion/ exclusion criteria; demography; medical history (includes past and current conditions, medication history, and family history of premature CV disease); HIV, Hep B and Hep C screen; serum pregnancy test (WCBP only).																
Site Visit	X	X	X	X		X		X		X		X		X	X	X	1. Full physical exam: height/weight at Screening, height not required at later timepoints. 2. Vitals: BP, HR, RR, temperature. ECG triplicate at Screening only. 3. Urinalysis not required on Days 29, 57 and 71. 4. If urine test is positive, confirmatory serum test must be performed. 5. Pre-dose 6. In Cohort 1, subjects must take study medication twice a day approx. 12h apart. In Cohort 2, subjects must take study medication three times a day approx. 8h apart. Exact time of dosing to be recorded in diary cards. On Days 43 and 85, subjects must not take medication at home in the morning. Subjects will complete pre-dose assessments and then will be administered their morning dose of medication at site on Day 43 only. On Day 85, subjects no longer dosed.
Phone call					X		X		X		X		X				
Safety Assessments																	
Full physical exam[1]	X													X	X	X	
Brief physical exam		X[5]		X		X		X[5]		X		X					
12-lead ECG, vital signs[2]	X	X[5]	X	X		X		X[5]		X		X		X	X	X	
Columbia Suicide Severity Rating Scale (C-SSRS)	X	X[5]						X[5]						X	X		
Hematology, chemistry, urinalysis	X	X[5]	X	X		X[3]		X[5]		X[3]		X[3]		X	X	X	
FSH & estradiol (if applicable)	X																
Serum pregnancy (WCBP)	X																
Urine pregnancy test (WCBP only)[4]		X[5]	X	X		X		X[5]		X		X		X	X	X	
Study Treatment																	
Randomisation		X															
Study medication[6]		X	X----------														
Dispensing of study medication		X				X				X							
Dispensing of diary cards[7]		X	X	X		X		X		X		X					

Procedures	Screening	Treatment Period													Early Withdrawal [14]	Follow Up	Notes
		Day 1	Day 8	Day 15	Day 22	Day 29	Day 36	Day 43 (week 6)	Day 50	Day 57	Day 64	Day 71	Day 78	Day 85 (week 12)			**Visit windows** Screening: up to 30d before Day 1. Treatment Period (except Day 1 & 85): ± 3d. Day 1 NA; Day 85 ± 2d. Early Withdrawal: NA Follow Up: 28d after last dose ± 3d
PROs/ Disease Assessments																	7. Diary card checked by site staff and new diary card dispensed at every study visit. 8. Blood samples for inflammatory biomarkers and mRNA taken pre-dose on Day 1, Day 43 and Day 85. 9. PK blood samples taken pre-dose on Day 43. Post-dose serial PK samples taken on Day 1 and Day 43 at 1, 2, 4, and 6 hours post-dose. 10. Pre-dose Day 1 one biopsy taken from non-lesional skin and two biopsies taken from biopsy target lesion. 11. On Day 43, two biopsies taken from the same target lesion that was selected at Day 1. Punch biopsies on Day 43 are to be taken pre-dose. 12. Biopsy only required at Early Withdrawal visit if completed at least 14 days of treatment and prior to Day 43. 13. PGx sample collected at Day 1, after randomization and separate informed consent. If sample not collected at Day 1, can be collected at any time post-randomization. 14. If subject withdraws early, every effort will be made for the subject to complete an Early Withdrawal visit prior to Follow Up.
Psoriatic Body Surface Area	X	X [5]												X	X		
PASI, PGA, PLSS, Itch	X	X [5]		X		X		X [5]		X		X		X	X		
DLQI	X	X [5]						X [5]						X	X		
Photograph of lesions		X [5]						X [5]						X	X		
Other Assessments and Procedures																	
Blood sample for inflammatory biomarkers[8]		X [5]						X [5]						X	X		
Blood sample for mRNA analysis[8]		X [5]						X [5]						X	X		
Blood sample for Target Engagement		X [5]						X [5]						X	X		
PK blood samples[9]		X						X [5]						X	X		
Skin punch biopsies for PK, inflammatory biomarkers, mRNA, target engagement & pathway engagement		X [5,10]						X [11]							X[12]		
Pharmacogenetic sample (PGx)		X [13]															
Con med review & AE/SAE reporting		X----------X															

11.2. Appendix 2: Assessment Windows

11.2.1. Definitions of Assessment Windows for Analyses

No Assessment Windows will be defined for Analysis, and summaries and analyses will be based on nominal visits.

11.3. Appendix 3: Treatment States and Phases

11.3.1. Treatment Phases

Assessments and events will be classified according to the time of occurrence relative to study treatment unless otherwise specified. Treatment phases are to be included on A&R datasets.

Treatment Phase	Definition
Pre-Treatment	Date ≤ Study Treatment Start Date
On-Treatment	Study Treatment Start Date < Date ≤ Study Treatment Stop Date
Post-Treatment	Date > Study Treatment Stop Date

11.3.2. Treatment States

Assessments and events will be classified according to time of occurrence relative to the start and/or stop date of the study treatment.

11.3.2.1. Treatment States for Safety Data

Treatment State	Definition
Pre-Treatment	Date ≤ Study Treatment Start Date
On-Treatment	Study Treatment Start Date < Date ≤ Study Treatment Stop Date +1
Post-Treatment	Date > Study Treatment Stop Date +1

NOTES:

- If the study treatment stop date is missing then the assessment will be considered to be On-Treatment

Treatment States for AE Data

Treatment State	Definition
AE = Pre-Treatment	AE Start Date < Study Treatment Start Date
AE = On-Treatment	If AE onset date is on or after treatment start date & on or before treatment stop date. Study Treatment Start Date ≤ AE Start Date ≤ Study Treatment Stop Date +1
AE = Post-Treatment	If AE onset date is after the treatment stop date. AE Start Date > Study Treatment Stop Date
AE Onset Time Since 1st Dose (Days)	If Treatment Start Date > AE Onset Date: **= AE Onset Date - Treatment Start Date** If Treatment Start Date ≤ AE Onset Date: **= AE Onset Date - Treatment Start Date +1** Missing otherwise.
AE Duration (Days)	**AE Resolution Date – AE Onset Date + 1**
AE = Drug-related	If relationship is marked 'YES' on [Inform/CRF OR value is missing].

NOTES:

- If the study treatment stop date is missing then the AE will be considered to be On-Treatment.

11.4. Appendix 4: Data Display Standards & Handling Conventions

11.4.1. Study Treatment & Sub-group Display Descriptors

Treatment Group Descriptions			
RandAll NG		Data Displays for Reporting	
Code	Description	Description	Order [1]
A	GSK2982772 60mg BID	GSK2982772 60mg BID	2
C	GSK2982772 60mg TID	GSK2982772 60mg TID	3
P	Placebo	Placebo [2]	1
Q	Placebo TID		

NOTES:

1. Order represents treatments being presented in TFL, as appropriate.
2. Placebo BID and Placebo TID will be combined for reporting purposes

Should a subject receive the wrong medication at any point during the study in error, that subject will be treated as having received GSK2982772 60mg BID or GSK2982772 60mg TID, dependent on whether Cohort 1 or Cohort 2, for the duration of the study. Such subjects will have a footnote on Table 1.12 and Listing 1.

11.4.2. Baseline Definition & Derivations

11.4.2.1. Baseline Definitions

For all endpoints (expect as noted in baseline definitions) the baseline value will be the latest pre-dose assessment.

Parameter	Study Assessments Considered As Baseline		Baseline Used in Data Display
	Screening	Day 1 (Pre-Dose)	
Safety Assessments			
Vital signs[1]	X	X	Day 1 (Pre-Dose)
12-lead ECG[2]	X	X	Day 1 (Pre-Dose)
Laboratory (Haematology, clinical chemistry and urinalysis)	X	X	Day 1 (Pre-Dose)
Columbia Suicide Severity Rating Scale (C-SSRS)	X	X	Day 1 (Pre-Dose)
PROs/Disease Assessments			
Psoriatic Body	X	X	Day 1 (Pre-Dose)

Parameter	Study Assessments Considered As Baseline		Baseline Used in Data Display
	Screening	Day 1 (Pre-Dose)	
Surface Area			
PASI, PGA, PLSS, itch	X	X	Day 1 (Pre-Dose)
DLQI	X	X	Day 1 (Pre-Dose)
Other Assessments and Procedures			
Blood sample for inflammatory biomarkers		X	Day 1 (Pre-Dose)
Blood sample for mRNA analysis		X	Day 1 (Pre-Dose)
Blood sample for Target Engagement		X	Day 1 (Pre-Dose)
PK blood samples		X	Day 1 (Pre-Dose)
Skin punch biopsies for PK, inflammatory biomarkers, mRNA, target engagement & pathway engagement		X	Day 1 (Pre-Dose)

NOTES :

- Unless otherwise stated, the mean of replicate assessments at any given time point will be used as the value for that time point.
- 1 = Vitals: BP, HR, RR, temperature
- 2 = ECG triplicate at screening only

11.4.2.2. 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]
Maximum Change from Baseline	= Calculate the change from baseline at each given timepoint and determine the maximum change

NOTES :

- Unless otherwise specified, the baseline definitions specified in Section 11.4.2.1 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.

11.4.3. Reporting Process & Standards

Reporting Process
Software

Reporting Process	
• The currently supported versions of SAS software will be used.	
Reporting Area	
HARP Server	UK1SALX00175
HARP Area	arenv \ arprod \ gsk2982772 \ mid203167 \ internal_03 arenv \ arprod \ gsk2982772 \ mid203167 \ final
QC Spreadsheet	arenv \ arprod \ gsk2982772 \ mid203167 \ internal_03 arenv \ arwork \ gsk2982772 \ mid203167 \ final \ documents
Analysis Datasets	
• Analysis datasets will be created according to Integrated Data Standards Library (IDSL) GSK A&R dataset standards.	
Generation of RTF Files	
• RTF files will be generated for key outputs at the time of the IA, SAC.	

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 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

Reporting Standards	
• Unscheduled visits will not be included in summary tables or figures, unless otherwise stated.. • All unscheduled visits will be listed.	
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 and or within] 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).
Parameters Not Being Log Transformed	tmax, first point, last point and number of points used in the determination of Lambda_z.
Summary Tables	The following PK parameters will not be summarised: tmax, first point, last point and number of points used in the determination of Lambda_z.
Listings	Additionally, include the first point, last point and number of points used in the determination of lambda_z for listings.
Graphical Displays	
• Refer to IDSL Statistical Principals 7.01 to 7.13.	

11.5. Appendix 5: Derived and Transformed Data

11.5.1. 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. • If there are two values within a time window the value closest to the target day for that window will be used. If values are the same distance from the target then the mean will be taken. • 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

11.5.2. Study Population

Demographics
Date of Birth
• Only the year of birth will be captured, and therefore the date of birth is then derived as follows: Year of birth = YYYY → Date of birth = 30th June YYYY
Age
• Calculated as the integer part of (date of baseline – date of birth) Age = integer part (date of baseline – 30th June YYYY) • Birth date will be presented in listings as 'YYYY'.
Body Mass Index (BMI)
• Calculated as **Weight (kg) / [Height (m)^2**
Race category
• White: 'White: Arabic/North African Heritage' and 'White: White/Caucasian/European Heritage', or both of these, but no other category checked • African descent: 'African American/African Heritage', and no other category checked • Asian: 'Asian – Central/South Asian Heritage', 'Asian – East Asian Heritage', 'Asian – Japanese Heritage', and 'Asian – South East Asian Heritage', or any combination of these, but no other category checked • Other: Any combination that has not been categorized above ('mixed race')

Extent of Exposure
• Number of days of exposure to study drug will be calculated based on the formula:

Extent of Exposure

Duration of Exposure in Days = Treatment Stop Date – (Treatment Start Date) + 1

- Subjects who were randomized but did not report a treatment start date will be categorised as having zero days of exposure.
- The cumulative dose will be based on the formula:

  Cumulative Dose = Sum of (Number of Days x Total Daily Dose)
- If there are any treatment breaks during the study, exposure data will be adjusted accordingly.

11.5.3. 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

11.5.4. Pharmacokinetic

Skin Pharmacokinetic Concentrations

Skin PK Conc
• The density of human skin tissue is 1.184 g/mL per Gastroplus V9.0. • The volume of solvent added to each tissue sample was 0.5 mL. • For actual tissue weights, please refer to the Excel spreadsheet
Skin PK Concentration (ng/mL) 1. PK Conc in Weight of Tissue Sample = SMS PK Conc in Soln (ng/mL) X [0.5 mL + (Tissue Weight (g) / 1.184 g/mL)] 2. PK Conc in tissue as concentration (ng/g) = PK Conc in Weight of Tissue Sample / Tissue Weight 3. PK Conc in tissue as concentration (ng/mL) = PK Conc in tissue as concentration (ng/g) 1.184 g/mL
Example (fictitious) data: SMS tissue homogenate concentration = 2 ng/mL Tissue weight = 0.014 g SMS plasma concentration= 400 ng/mL Example Calculations: 1. Convert GSK2982772 concentration in the homogenate to GSK2982772 concentration in the tissue sample as follows: 2 ng/mL X [0.5 mL + (0.014 g/1.184 g/mL)] = 2ng/mL X 0.512 mL = 1.024 ng GSK2982772 in a 0.014 g tissue sample 2. Convert absolute amount of GSK2982772 in this skin tissue sample to a tissue concentration as follows: 1.024 ng / 0.014 g tissue = 73.1 ng GSK2982772/g tissue = 73.1 ng/g 3. Convert ng/g tissue to ng/mL tissue as follows : 73.1 ng/g X 1.184 g/mL = 86.5 ng GSK2982772/mL tissue = 86.5 ng/mL 4. Determine the ratio of GSK2982772 tissue concentration to GSK2982772 plasma concentration for a given patient as follows: 86.5 ng/mL / 400 ng/mL = 0.216

11.5.5. Efficacy

Clinical Efficacy
Plaque Lesional Severity Score (PLSS) and index plaque selection
Two plaques will be selected at Day -1, one for clinical assessment (index plaque) and one for biopsy. Ideally the index plaque should be the most severe plaque. At a minimum each plaque will have an induration score of ≥2 (moderate or above) and a score of ≥1 in erythema and scaling, as detailed in the scoring list below. Each lesion must have a PLSS score of ≥5. The PLSS is the sum of the erythema, scaling and induration. The PLSS assessment will be performed by the same qualified dermatologist throughout, wherever possible and will be scored using the same scale (0-4 point rating scale) as the PASI.

Clinical Efficacy

Psoriasis Area Severity Index (PASI), PASI50, PASI75, PASI90

Psoriatic lesions will be assessed using the PASI. The PASI assessment will be performed by the investigator or a suitably trained delegate, and whenever possible, the PASI assessments for an individual subject will be completed by the same assessor at all time-points. Each area of the body (head, upper extremities, trunk, lower extremities) will be assessed for the following symptoms: erythema, induration, scaling. A 0–4 point rating scale will be used, as follows:

0 = No symptom
1 = Slight
2 = Moderate
3 = Marked
4 = Very Marked

After calculating the BSA as detailed above, use the multiplier for that body region to calculate the area score for each region as detailed below:

• Head

Number of palms x 10% = % of head

• Upper extremities

Number of palms x 5% = % of upper extremities

• Trunk

Number of palms x 3.3% = % of area trunk

• Lower extremities

Number of palms x 2.5% = % of lower extremities

The area of psoriatic involvement for each area of the body (head, upper extremities, trunk, lower extremities) will be assessed using a 0–6 point rating scale, as follows:

0 = 0%
1 = 0–9%
2 = 10–29%
3 = 30–49%
4 = 50–69%
5 = 70–89%
6 = 90–100%

Total PASI score will be calculated using the following method:

- Add up the 3 intensity scores for each area of the body to give 4 subtotals (A1–A4):
  - **A1** (head intensity score) = head **redness** score + head **thickness** score + head **scaling** score

Clinical Efficacy

- **A2** (upper extremities intensity score) = upper extremities **redness** score + upper extremities **thickness** score + upper extremities **scaling** score
- **A3** (trunk intensity score) = trunk **redness** score + trunk **thickness** score + trunk **scaling** score
- **A4** (lower extremities intensity score) = lower extremities **redness** score + lower extremities **thickness** score + lower extremities **scaling** score

- Multiply each subtotal (A1–A4) by the body surface area represented by that region to give 4 new subtotals (B1–B4):
  - **B1** (head) = A1 x 0.1
  - **B2** (upper extremities) = A2 x 0.2
  - **B3** (trunk) = A3 x 0.3
  - **B4** (lower extremities) = A4 x 0.4
- Multiply each subtotal (B1–B4) by the area affected for that region to give 4 new subtotals (C1–C4):
  - **C1** (head) = B1 x 1–6
  - **C2** (upper extremities) = B2 x 1–6
  - **C3** (trunk) = B3 x 1–6
  - **C4** (lower extremities) = B4 x 1–6
- Calculate the total PASI score = C1 + C2 + C3 + C4

From the total scores, the following will be derived: change from baseline, percentage change from baseline, PASI50, PASI75 and PASI90 at each time point. Calculation of change from baseline and percentage change from baseline is described in Section 11.4.2.2.

Where PASI50, PASI75 and PASI90 are given by:

PASI50	Yes: No:	≥ 50% reduction in PASI total score from baseline at time point < 50% reduction in PASI total score from baseline at time point
PASI75	Yes: No:	≥ 75% reduction in PASI total score from baseline at time point < 75% reduction in PASI total score from baseline at time point
PASI90	Yes: No:	≥ 90% reduction in PASI total score from baseline at time point < 90% reduction in PASI total score from baseline at time point

Physician Global Assessment (PGA)

Psoriatic lesions will be assessed using the PGA. The PGA assessment will be performed by the investigator or a suitably trained delegate, and whenever possible, the PGA assessments for an individual subject will be completed by the same assessor at all time-points. A 6-point scoring system will be used to measure the severity of psoriatic lesions over the whole body, at the time of the evaluation:

CCI - This section contained Clinical Outcome Assessment data collection questionnaires or indices, which are protected by third party copyright laws and therefore have been excluded.

Clinical Efficacy

CCI

[redacted]

PGA (clear and almost clear)

PGA is given by:

PGA	Clear (0): Almost Clear (1):	No signs of psoriasis (post-inflammatory hypopigmentation or hyperpigmentaition could be present) slight elevation, scale and/or erythema

Body Surface Area (BSA)

As part of the inclusion criteria the patients Psoarisis plaques need to cover 2-10% of body surface area. This will be calculated based on the areas outlined as part of the PASI score (see section 9.6.4.2). Where body surface area is calculated based on the palm method, where a patient's palm to PIP and thumb = 1%, and so:

Head and Neck	10% (10 palms)
Upper extremities	20% (20 palms)
Trunk (axillae and groin)	30% (30 palms)
Lower extremities (buttocks)	40% (40 palms)

Therefore the total BSA = 100% (100 palms)

So these proportions are applied to the absolute areas identified at Baseline to determine the overall body surface area, assuming that the areas are available. If only the categories are available (eg. 0-9%, 10-29%) then this calculation cannot be calculated.

Dermatology Life Quality Index (DLQI)

The Dermatology Life Quality Index (DLQI) is a ten-question questionnaire used to measure the impact of skin disease on the quality of life of an affected person. It is designed for people aged 16 years and above.

Clinical Efficacy

CCI - This section contained Clinical Outcome Assessment data collection questionnaires or indices, which are protected by third party copyright laws and therefore have been excluded.

Clinical Efficacy
CCI [redacted]

Visual Analogue Scale (VAS) itch score
The subject will be asked to rate the intensity of itch over the past week by marking a line on a 10 cm VAS with anchors “0” (no noticeable itching) to “10” (maximum itching sensation).

11.5.6. Pharmacodynamic and Biomarker

TEAR
Target Engagement
• Ratio = free / total • Target Engagement = 100 – (ratio $_{post}$/ratio $_{baseline}$) * 100)) • BIOMARK dataset: BICATCD = TRALBP1 (total) or RALB1F (free) BITESTCD = CONC (Sample = Target Engagement) and CONCTSZ (Sample = Tru Culture)

11.6. Appendix 6: Premature Withdrawals & Handling of Missing Data

11.6.1. Premature Withdrawals

Element	Reporting Detail
General	• Subject study completion (i.e. as specified in the protocol) was defined as one who has completed all phases of the study including the follow-up visit. • Withdrawn subjects may be replaced in the study at the discretion of the investigator. • 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.

11.6.2. 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 : o 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. o 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.

11.6.2.1. Handling of Missing Dates

Element	Reporting Detail
General	Partial dates will be displayed as captured in subject listing displays. Imputed dates should be stored in variables IMPSTDT (Imputed Start Date) and IMPENDT (Imputed End Date)
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 as per Appendix : Treatment States and Phases. 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

Element	Reporting Detail
	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.

11.6.2.2. 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.

11.6.2.3. Handling of Missing Data for Statistical Analysis

Element	Reporting Detail
PLSS	• Actual score: The mixed models repeated measures model will be applied to the data in the analysis and account for missing data in the repeated measures analysis over time. • Percentage change from baseline: o If baseline missing: Exclude from analysis o If baseline not missing: The mixed models repeated measures model will be applied to the data in the analysis and account for missing data in the repeated measures analysis over time
PASI	• Change from baseline: o If baseline missing: Exclude from analysis o If baseline not missing: The mixed models repeated measures model will be applied to the data in the analysis and account for missing data in the repeated measures analysis over time.
PASI50	• If the data is missing then failure is assumed, and therefore a 'non-response'

Element	Reporting Detail
PASI75 PASI90	assigned to the missing data point.
PGA	• Actual score: The mixed models repeated measures model will be applied to the data in the analysis and account for missing data in the repeated measures analysis over time. • Change from baseline: o If baseline missing: Exclude from analysis o If baseline not missing: The mixed models repeated measures model will be applied to the data in the analysis and account for missing data in the repeated measures analysis over time.
PGA (clear and almost)	• If the data is missing then failure is assumed, and therefore a 'non-response' assigned to the missing data point.
BSA	• Change from baseline: o If data is missing, exclude from analysis as it is not possible to calculate change from baseline since BSA is measured at only two time points; baseline (Day 1 pre-dose) and at Day 85.
DLQI	• Actual score: The mixed models repeated measures model will be applied to the data in the analysis and account for missing data in the repeated measures analysis over time. • Change from baseline: o If baseline missing: Exclude from analysis If baseline not missing: The mixed models repeated measures model will be applied to the data in the analysis and account for missing data in the repeated measures analysis over time.
VAS	• Actual score: The mixed models repeated measures model will be applied to the data in the analysis and account for missing data in the repeated measures analysis over time. • Change from baseline: o If baseline missing: Exclude from analysis • If baseline not missing: The mixed models repeated measures model will be applied to the data in the analysis and account for missing data in the repeated measures analysis over time.

11.7. Appendix 7: Values of Potential Clinical Importance

11.7.1. 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	
Lymphocytes	$x10^9$/ L		0.8	
Neutrophil Count	$x10^9$/ L		1.5	
Platelet Count	$x10^9$/ L		100	550
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	mmol/L		30	
Calcium	mmol/L		2	2.75
Creatinine	mmol/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 U/L	High	1.5xULN T. Bilirubin + ≥ 2x ULN ALT

11.7.2. ECG

ECG Parameter	Units	Clinical Concern Range	
		Lower	Upper
Absolute			
Absolute QTc Interval	msec	> 450 [1]	
		> 450 [2]	≤ 479 [2]
		≥ 480 [2]	≤ 499 [2]
		≥ 500 [2]	
Absolute PR Interval	msec	< 110 [1]	> 220 [1]
Absolute QRS Interval	msec	< 75 [1]	> 110 [1]
Change from Baseline			
Increase from Baseline QTc	msec	> 60 [1]	
	msec	> 30 [2]	≤ 59 [2]
	msec	≥ 60 [2]	

NOTES: [Remove footnotes for RAP development]

1. Represent standard ECG values of PCI for HV studies
2. Represent further subdivisions of ECG values for analysis whereby the RAP team needs to decide whether these need to be generated in addition to standard ECG values being flagged. IF not required, then delete.

11.7.3. 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	≥ 20	≥ 40	≥ 20	≥ 40
Diastolic Blood Pressure	mmHg	≥ 10	≥ 20	≥ 10	≥ 20
Heart Rate	bpm	≥ 15	≥ 30	≥ 15	≥ 30

NOTES: : [Remove footnotes for RAP development]

Represent further subdivisions of BP & HR for analysis whereby the RAP team needs to decide whether these need to be generated in addition to standard absolute BP & HR values being flagged. IF not required, then delete.

Vital Sign Parameter (Change from Baseline)	Units	Clinical Concern Range			
		Decrease		Increase	
		Lower	Upper	Lower	Upper

11.8. Appendix 8: Multicenter Studies

No specific outputs will be produced by centre or highlighting the recruitment by site.

11.9. Appendix 9: Examination of Covariates, Subgroups & Other Strata

No sub group analyses are to be conducted in this study.

11.10. Appendix 10: Multiple Comparisons & Multiplicity

No adjustments will be made for multiplicity.

11.11. Appendix 11: Model Checking and Diagnostics for Statistical Analyses

11.11.1. Statistical Analysis Assumptions

Analysis	• MMRM

- For the MMRM, model assumptions will be applied, but appropriate adjustments maybe applied 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.
- An unstructured covariance structure for the R matrix will be used by specifying 'type=UN' on the REPEATED line.
    - In the event that this model fails to converge, alternative correlation structures may be considered such as CSH or CS.
    - Akaike's Information Criteria (AIC) will be used to assist with the selection of covariance structure.
- 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.

11.12. Appendix 12 – Abbreviations & Trade Marks

11.12.1. Abbreviations

Abbreviation	Description
ADaM	Analysis Data Model
AE	Adverse Event
AIC	Akaike's Information Criteria
A&R	Analysis and Reporting
CDISC	Clinical Data Interchange Standards Consortium
CI	Confidence Interval
CPMS	Clinical Pharmacology Modelling & Simulation
CS	Clinical Statistics
CSR	Clinical Study Report
CTR	Clinical Trial Register
CV_b / CV_w	Coefficient of Variation (Between) / Coefficient of Variation (Within)
DOB	Date of Birth
DP	Decimal Places
eCRF	Electronic Case Record Form
IA	Interim Analysis
ICH	International Conference on Harmonisation
IDMC	Independent Data Monitoring Committee
IDSL	Integrated Data Standards Library
IMMS	International Modules Management System
IP	Investigational Product
ITT	Intent-To-Treat
GUI	Guidance
LOC	Last Observation Carries Forward
MMRM	Mixed Model Repeated Measures
PCI	Potential Clinical Importance
PD	Pharmacodynamic
PDMP	Protocol Deviation Management Plan
PK	Pharmacokinetic
PP	Per Protocol
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
IA, SAC	Statistical Analysis Complete
SDTM	Study Data Tabulation Model
SOP	Standard Operation Procedure
TA	Therapeutic Area
TFL	Tables, Figures & Listings
GSK	GlaxoSmithKline

11.12.2. Trademarks

Trademarks of the GlaxoSmithKline Group of Companies
ADVAIR

Trademarks not owned by the GlaxoSmithKline Group of Companies
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SAS

11.13. Appendix 13: List of Data Displays

11.13.1. Data Display Numbering

The following numbering will be applied for RAP generated displays:

Section	Tables	Figures
Study Population	1.1 to 1.n	1.1 to 1.n
Efficacy	2.1 to 2.n	2.1 to 2.n
Safety	3.1 to 3.n	3.1 to 3.n
Pharmacokinetic	4.1 to 4.n	4.1 to 4.n
Pharmacodynamic and / or Biomarker	5.1 to 5.n	5.1 to 5.n
Pharmacokinetic / Pharmacodynamic	6.1 to 6.n	6.1 to 6.n
Section	**Listings**	
ICH Listings	1 to x	
Other Listings	y to z	

11.13.2. Mock Example Shell Referencing

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

Section	Figure	Table	Listing
Study Population	POP_Fn	POP_Tn	POP_Ln
Efficacy	EFF_Fn	EFF_Tn	EFF_Ln
Safety	SAFE_Fn	SAFE_Tn	SAFE_Ln
Pharmacokinetic	PK_Fn	PK_Tn	PK_Ln
Pharmacodynamic and / or Biomarker	PD_Fn	PD_Tn	PD_Ln
Pharmacokinetic / Pharmacodynamic	PKPD_Fn	PKPD_Tn	PK/PD_Ln

NOTES:

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

11.13.3. Deliverable [Priority]

Delivery	Description
IA	Interim Analysis Statistical Analysis Complete
IA, SAC	Final Statistical Analysis Complete

11.13.4. Study Population Tables

Study Population Tables					
No.	**Population**	**IDSL / TST ID / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
Subject Disposition					
1.1.	Safety	ES1	Summary of Subject Disposition	ICH E3, GSK CTR, FDAAA, EudraCT	IA, SAC
1.2.	All screened	ES6	Summary of Reasons for Screen Failure	Journal Requirements	IA, SAC
1.3.	Safety	NS1	Summary of Number of Subjects by Centre	EudraCT	IA, SAC
Protocol Deviation					
1.4.	Safety	DV1	Summary of Important Protocol Deviations	ICH E3	IA, SAC
Population Analysed					
1.5.	Safety	SP1	Summary of Study Populations and Exclusions	IDSL	IA, SAC
Demographic and Baseline Characteristics					
1.6.	Safety	DM1	Summary of Demographic Characteristics	ICH E3, GSK CTR, FDAAA, EudraCT	IA, SAC
1.7.	Safety	DM5	Summary of Race and Racial Combinations	ICH E3, FDA, GSK CTR, FDAAA, EudraCT	IA, SAC
1.8.	Safety	DM6	Summary of Race and Racial Combination Details	ICH E3, FDA	IA, SAC
1.9.	Safety		Summary of Psoarsis Baseline Characteristics	Based on DM1 to include: Baseline BSA, Duration, Prior Treatment, Naive to Phototherapy, Baseline PASI Score, Baseline PLSS score, Baseline PGA, Lesion Seveirty (area and score), history of tobacco use	IA, SAC
Prior and Concomitant Medications					

Study Population Tables					
No.	**Population**	**IDSL / TST ID / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
1.10.	Safety	MH4	Summary of Current/Past Medical Conditions	ICH E3 Separate summaries for Current & Past conditions, if collected.	IA, SAC
1.11.	Safety	CM1	Summary of Concomitant Medications	ICH E3	IA, SAC
Exposure and Treatment Compliance					
1.12.	Safety	EX1, EX2, OEX1, OEX5	Summary of Exposure to Study Treatment	ICH E3 Dose and/or time on treatment, as applicable.	IA, SAC

11.13.5. Safety Tables

Safety : Tables					
No.	**Population**	**IDSL / TST ID / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
Adverse Events (AEs)					
2.1.	Safety	AE5a	Summary of All Adverse Events by System Organ Class and Maximum Intensity	ICH E3	IA, SAC
2.2.	Safety	AE3	Summary of Common (>10%) Adverse Events by Overall Frequency	GSK CTR	IA, SAC
2.3.	Safety	AE5a	Summary of All Drug-Related Adverse Events by System Organ Class and Maximum Intensity	GSK CTR	IA, SAC
Serious and Other Significant Adverse Events					
2.4.	Safety	AE1	Summary of Serious Adverse Events by System Organ Class	IDSL / GSK CTR	IA, SAC
2.5.	Safety	CP_AE8a	Listing of Fatal Adverse Events		IA, SAC

Safety : Tables					
No.	**Population**	**IDSL / TST ID / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
2.6.	Safety	AE1	Summary of Drug-Related Serious Adverse Events by System Organ Class	GSK CTR	IA, SAC
2.7.	Safety	AE3	Summary of Adverse Events Leading to Withdrawal from Study / Permanent Discontinuation of Study Treatment by Overall Frequency	IDSL	IA, SAC
2.8.	Safety	AE16	Summary of Subjects and Number of Occurrences of Serious, Drug-Related Serious, Fatal Serious, and Drug-Related Fatal Serious Adverse Events	FDAAA, EudraCT	IA, SAC
Laboratory: Chemistry					
2.9.	Safety	LB1	Summary of Clinical Chemistry Changes from Baseline	ICH E3 Includes Baseline values. Includes pre-specified parameters repeated in conventional units.	IA, SAC
2.10.	Safety	LB1	Summary of Clinical Chemistry Values		IA, SAC
2.11.	Safety	LB3	Summary of Emergent Clinical Chemistry Results by Potential Clinical Importance Criteria		IA, SAC
Laboratory: Hematology					
2.12.	Safety	LB1	Summary of Hematology Changes From Baseline	ICH E3 Includes baseline values.	IA, SAC
2.13.	Safety	LB1	Summary of Hematology Values	ICH E3 Includes baseline values.	IA, SAC
2.14.	Safety	LB3	Summary of Emergent Hematology Results by Potential Clinical Importance Criteria		IA, SAC
Laboratory: Urinalysis					

Safety : Tables					
No.	**Population**	**IDSL / TST ID / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
2.15.	Safety	LB1	Summary of Urine Concentration Changes from Baseline	ICH E3 Includes Baseline values.	IA, SAC
Laboratory: Hepatobiliary (Liver)					
2.16.	Safety	LIVER1	Summary of Liver Monitoring/Stopping Event Reporting	IDSL	IA, SAC
2.17.	Safety	LIVER10	Summary of Hepatobiliary Laboratory Abnormalities		IA, SAC
ECG					
2.18.	Safety	EG1	Summary of ECG Findings	IDSL As above for Chemistry, using ECG findings categories (and change from baseline categories, if applicable).	IA, SAC
2.19.	Safety	EG2	Summary of Change from Baseline in ECG Values by Visit	IDSL	IA, SAC
2.20.	Safety	CP_EG12	Summary of Maximum Change from Baseline in QTc Values by Category	IDSL	IA, SAC
Vital Signs					
2.21.	Safety	VS1	Summary of Change From Baseline in Vital Signs by Visit	ICH E3 Includes Baseline values.	IA, SAC
2.22.	Safety	VS1	Summary of Vital Signs by Visit		IA, SAC

11.13.6. Safety Figures

Safety : Figures					
No.	**Population**	**IDSL / TST ID / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
Adverse Events					
2.1.	Safety	AE10	Plot of Common Adverse Events and Relative Risk	IDSL Common defined as >10%	IA, SAC
Hepatobilary (Liver)					
2.2.	Safety	LIVER14	Scatter Plot of Maximum vs Baseline for ALT		IA, SAC
2.3.	Safety	LIVER9	Scatter Ploy for Maximum ALT va Maximum Total Bilirubin		IA, SAC

11.13.7. Efficacy Tables

Efficacy: Tables					
No.	**Population**	**IDSL / TST ID / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
PLSS					
3.1.	Safety	EFF_T3	Summary Statistics for PLSS scores by Treatment and Visit		IA, SAC
3.2.	Safety	EFF_T3	Summary Statistics for % change from baseline PLSS scores by Treatment and Visit		IA, SAC
3.3.	Safety	EFF_T4	Summary of Statistical Analysis Results for Percentage Change from Baseline PLSS score by Visit		IA, SAC
PASI					
3.4.	Safety	EFF_T3	Summary Statistics for PASI scores by Treatment and Visit		IA, SAC
3.5.	Safety	EFF_T3	Summary Statistics for Change from baseline PASI scores by Treatment and Visit		IA, SAC
3.6.	Safety	EFF_T4	Summary of Statistical Analysis Results for Percentage Change from Baseline PASI score by Visit		IA, SAC
3.7.	Safety	EFF_T2	Frequency: Proportion of subjects improving from baseline in PASI Score (PASI 50. PASI 75 and PASI 90) by Treatment and Visit		IA, SAC
3.8.	Safety	EFF_T1	GEE adjusted odds ratio and 95% CI for PASI50 by Visit		IA, SAC
3.9.	Safety	EFF_T1	GEE adjusted odds ratio and 95% CI for PASI75 by Visit		IA, SAC
3.10.	Safety	EFF_T1	GEE adjusted odds ratio and 95% CI for PASI90 by Visit		IA, SAC
PGA					
3.11.	Safety	EFF_T3	Summary Statistics for PGA Scores by Treatment and Visit		IA, SAC
3.12.	Safety	EFF_T3	Summary Statistics for change from baseline PGA Scores by Treatment and Visit		IA, SAC

Efficacy: Tables					
No.	**Population**	**IDSL / TST ID / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
3.13.	Safety	EFF_T4	Summary of Statistical Analysis Results for Change from Baseline PGA Score by Visit	Include related estimated LSMeans and treatment differences. Footnote:	IA, SAC
PGA "Clear"/"Almost Clear"					
3.14.	Safety	EFF_T2	Frequency: PGA score of Clear/Almost Clear by Treatment and Visit	Clear/Almost is a score of 0 or 1	IA, SAC
3.15.	Safety	EFF_T1	GEE Point Estimate and 95% CI for PGA Score of Clear / Almost Clear by Visit	Footnote:	IA, SAC
BSA					
3.16.	Safety	EFF_T3	Summary Statistics for BSA scores by Treatment and Visit		IA, SAC
3.17.	Safety	EFF_T3	Summary Statistics for change from baseline BSA scores by Treatment and Visit		IA, SAC
3.18.	Safety	EFF_T4	Summary of Statistical Analysis Results for Change from Baseline BSA score by Visit		IA, SAC
DLQI					
3.19.	Safety	EFF_T3	Summary Statistics for DLQI scores by Treatment and Visit		IA, SAC
3.20.	Safety	EFF_T3	Summary Statistics for change from baseline DLQI scores by Treatment and Visit		IA, SAC
3.21.	Safety	EFF_T4	Summary of Statistical Analysis Results for Change from Baseline DLQI score by Visit		IA, SAC
VAS Itch Score					
3.22.	Safety	EFF_T3	Summary Statistics for VAS scores by Treatment and Visit		IA, SAC
3.23.	Safety	EFF_T3	Summary Statistics for change from baseline VAS scores by Treatment and Visit		IA, SAC

Efficacy: Tables					
No.	**Population**	**IDSL / TST ID / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
3.24.	Safety	EFF_T4	Summary of Statistical Analysis Results for Change from Baseline VAS score by Visit		IA, SAC

11.13.8. Efficacy Figures

Efficacy: Figures					
No.	**Population**	**IDSL / TST ID / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
PLSS					
3.1.	Safety	FE1	Individual PLSS scores over Time by Treatment	Panel plot by subject, line colour to reflect treatment group, subjid as cell header	IA, SAC
3.2.	Safety	FE2	Mean (+/-SD) PLSS Scores over Time by Treatment		IA, SAC
3.3.	Safety	FE2	Point Estimates and 95% CI for Change from Baseline in PLSS Score over Time by Treatment	Grey dashed ref line at y=0	IA, SAC
PASI					
3.4.	Safety	FE1	Individual PASI Scores over Time by Treatment	Panel plot by subject, line colour to reflect treatment group, subjid as cell header	IA, SAC
3.5.	Safety	FE2	Mean (+/-SD) PASI Scores over Time by Treatment		IA, SAC
3.6.	Safety	FE2	Point Estimates and 95% CI for Change from Baseline in PASI Score over Time by Treatment	Grey dashed ref line ay y=0	IA, SAC
3.7.	Safety	FE2	Proportion of Subjects Who Achieved PASI50 over Time by Treatment	Line graph Treatment on the same plot	IA, SAC
3.8.	Safety	FE3	Odds Ratio and 95% CI for Achieving PASI50 over Time by Treatment		IA, SAC
3.9.	Safety	FE2	Proportion of Subjects Who Achieved PASI75 over Time by Treatment	Line graph Treatment on the same plot	IA, SAC
3.10.	Safety	FE3	Odds Ratio and 95% CI for Achieving PASI75 over Time by Treatment		IA, SAC
3.11.	Safety	FE2	Proportion of Subjects Who Achieved PASI90 over Time by Treatment	Line graph Treatment on the same plot	IA, SAC

Efficacy: Figures					
No.	**Population**	**IDSL / TST ID / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
3.12.	Safety	FE3	Odds Ratio and 95% CI for Achieving PASI90 over Time by Treatment		IA, SAC
PGA					
3.13.	Safety	FE1	Individual PGA Scores over Time by Treatment	Panel plot by subject, line colour to reflect treatment group, subjid as cell header	IA, SAC
3.14.	Safety	FE2	Mean (+/-SD) PGA Scores over Time by Treatment		IA, SAC
3.15.	Safety	FE3	Point Estimates and 95% CI for Change from Baseline in PGA Score over Time by Treatment	Grey dashed ref line ay y=0	IA, SAC
PGA "Clear"/"Almost Clear"					
3.16.	Safety	FE2	Proportion of Subjects Who Achieve PGA Score of Clear / Almost Clear over Time by Treatment		IA, SAC
3.17.	Safety	FE3	Odds Ratio and 95% CI for Achieving PGA Score of Clear over Time by Treatment		IA, SAC
BSA					
3.18.	Safety	FE1	Individual BSA Scores over Time by Treatment	Panel plot by subject, line colour to reflect treatment group, subjid as cell header	IA, SAC
3.19.	Safety	FE2	Mean (+/-SD) BSA Scores over Time by Treatment		IA, SAC
3.20.	Safety	FE3	Point Estimates and 95% CI for Change from Baseline in BSA Score over Time by Treatment	Grey dashed ref line ay y=0	IA, SAC
DLQI					
3.21.	Safety	FE1	Individual DLQI Scores over Time by Treatment	Panel plot by subject, line colour to reflect treatment group, subjid as cell header	IA, SAC

Efficacy: Figures					
No.	**Population**	**IDSL / TST ID / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
3.22.	Safety	FE2	Mean (+/-SD) DLQI Scores over Time by Treatment		IA, SAC
3.23.	Safety	FE3	Point Estimates and 95% CI for Change from Baseline in DLQI Score over Time by Treatment	Grey dashed ref line ay y=0	IA, SAC
VAS itch score					
3.24.	Safety	FE1	Individual VAS itch Scores over Time by Treatment	Panel plot by subject, line colour to reflect treatment group	IA, SAC
3.25.	Safety	FE2	Mean (+/-SD) VAS itch Scores over Time by Treatment		IA, SAC
3.26.	Safety	FE3	Point Estimates and 95% CI for Change from Baseline in VAS itch Score over Time by Treatment	Grey dashed ref line ay y=0	IA, SAC

11.13.9. Pharmacokinetic Tables

Pharmacokinetic : Tables					
No.	**Population**	**IDSL / TST ID / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
PK concentration data					
4.1.	PK	PKPT1	Summary of Plasma GSK2982772 Pharmacokinetic Concentration-Time Data (ng/mL)		IA, SAC
4.2.	PK	PKPT1	Summary of Skin GSK2982772 Pharmacokinetic Concentration-Time Data (ng/mL)		IA, SAC

11.13.10. Pharmacokinetic Figures

Pharmacokinetic : Figures					
No.	**Population**	**IDSL / TST ID / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
Individual concentration plots					
4.1.	PK	PKCF1P	Individual Plasma GSK2982772 Concentration-Time Plot by Subject (Linear and Semi-Log)	Page by: subject Panel: linear and semi-log x-axis: actual relative time y-axis: PK concentration Legend: Visit	IA, SAC
Mean/median concentration plots					
4.2.	PK	PKCF2	Mean (+ SD) plot: Plasma GSK2982772 concentrations (linear and semi-log)	Panel: linear and semi-log x-axis: planned relative time y-axis: PK concentration Legend: active treatment	IA, SAC
4.3.	PK	PKCF3	Median (range) plot: GSK2982772 Plasma concentrations (linear and semi-log)	Panel: linear and semi-log x-axis: planned relative time y-axis: PK concentration Legend: active treatment	IA, SAC
Individual concentration plots					
4.4.	PK	PKCF1P	Individual Skin GSK2982772 Concentration-Time Plot by Subject (Linear and Semi-Log)	Page by: subject Panel: linear and semi-log x-axis: actual relative time y-axis: PK concentration Legend: Visit	IA, SAC
Mean/median concentration plots					
4.5.	PK	PKCF2	Mean (+ SD) plot: Skin GSK2982772 concentrations (linear and semi-log)	Panel: linear and semi-log x-axis: planned relative time y-axis: PK concentration Legend: active treatment	IA, SAC

Pharmacokinetic : Figures					
No.	**Population**	**IDSL / TST ID / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
4.6.	PK	PKCF3	Median (range) plot: Skin GSK2982772 concentrations (linear and semi-log)	Panel: linear and semi-log x-axis: planned relative time y-axis: PK concentration Legend: active treatment	IA, SAC

11.13.11. Pharmacodynamic and / or Biomarker Tables

Pharmacodynamic (and or Biomarker) : Tables					
No.	**Population**	**IDSL / TST ID / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
Inflammatory Biomarkers in Skin					
5.1.	Safety	PD1	Summary of Histopathological Scoring in Psoriatic Lesional Biopsies	By parameter / (epidermis/dermis) K16: 0 or 1	IA, SAC
5.2.	Safety	PD3	Summary of Percentage Change in Histopathological Scoring in Psoriatic Lesional Biopsies		IA, SAC
5.3.	Safety	EFF_T4	Adjusted Mean (95% CI) Percentage Change in Histopathological Scoring of Psoriatic Lesional Biopsy	Present %CVb instead of SE	IA, SAC
mRNA in Skin					
5.4.	Safety	PD2	Summary of mRNA Expression of Inflammatory Gene Transcripts in Psoriatic Lesional Biopsies		IA, SAC
5.5.	Safety	PD_T2	Frequency Table Summarising the Number of Probe Sets with Various Fold Change in Psoriatic Lesional Biopsies	Use cut-offs 1.5 and -1.5 initially. Change to -1.25 and 1.5 if no one achieves the initial cut-offs	IA, SAC
5.6.	Safety	PD_T3	Summary of Adjusted Mean Fold Changes in mRNA Expression of Inflammatory Gene Transcripts in Psoriatic Lesional Biopsies	If Adj Mean FC lies between -1 and 1 then do not include on table	IA, SAC
Inflammatory Biomarkers in Blood					
5.7.	Safety	PD1	Summary Statistics of Blood Inflammatory Biomarkers	One page for each cell type/measure by visit/time and treatment	IA, SAC
5.8.	Safety	PD2	Summary of Percentage Change in Blood Inflammatory Biomarkers	One page for each cell type/measure by visit/time and treatment	IA, SAC
5.9.	Safety	EFF_T4	Adjusted Mean (95% CI) Percentage Change in Blood Inflammatory Biomarkers	Present %CVb instead of SE	IA, SAC
Pathway and Target Engagement					

Pharmacodynamic (and or Biomarker) : Tables					
No.	**Population**	**IDSL / TST ID / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
5.10.	Safety		Summary of TEAR1 % Target Engagement in Blood	% Target Engagement by visit/time, Refer to 200975/Partb_final for display	IA, SAC
5.11.	Safety		Adjusted Mean (95% CI) TEAR1 % Target Engagement in Blood	Refer to 200975/Partb_final for display	IA, SAC
5.12.	Safety		Summary of TEAR1 % Target Engagement in Skin	% Target Engagement by visit/time, Refer to 200975/Partb_final for display	IA, SAC
5.13.	Safety		Adjusted Mean (95% CI) TEAR1 % Target Engagement in Skin	Refer to 200975/Partb_final for display	IA, SAC

11.13.12. Pharmacodynamic (and / or Biomarker) Figures

Pharmacodynamic (and or Biomarker) : Figures					
No.	**Population**	**IDSL / TST ID / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
Inflammatory Biomarkers in Skin					
5.14.	Safety	FE1	Individual Subject Profiles for Histopathological Scoring in Psoriatic Lesional Biopsies	Page by biomarker and location (dermis/epidermis) Panel plot, line colours by treatment group, subjid as cell header	IA, SAC
5.15.	Safety	FE2	Adjusted Mean (95% CI) Percentage Change in Histopathological Scoring of Psoriatic Lesional Biopsy	Reference line at y=0, grey dashed style	IA, SAC
mRNA in Skin					
5.16.	Safety	FE1	Individual Subject Profiles for mRNA Expression of Inflammatory Gene Transcripts in Psoriatic Lesional Biopsies	Panel plot, line colours by treatment group, subjid as cell header	IA, SAC
5.17.	Safety	FE4	Adjusted Mean Intensities for for mRNA Expression of Inflammatory Gene Transcripts in Psoriatic Lesional Biopsies	Y xais – log2 scale	IA, SAC
5.18.	Safety	FE5	Adjusted Mean (95% CI) Fold Change in mRNA Expression of Inflammatory Gene Transcripts in Psoriatic Lesional Biopsies	If Adj Mean FC lies between -1 and 1 then do not include on table Include band from FC -1 to 1, transparency 0.5	IA, SAC
Inflammatory Biomarkers in Blood					
5.19.	Safety	FE1	Summary Statistics of Blood Inflammatory Biomarkers	Page by biomarker Panel plot, line colours by treatment group, subjid as cell header	IA, SAC
5.20.	Safety	FE2	Adjusted Mean (95% CI) Percentage Change in Blood Inflammatory Biomarkers	Reference line at y=0, grey dashed style	IA, SAC

<table>
<tr><th colspan="6">Pharmacodynamic (and or Biomarker) : Figures</th></tr>
<tr><th>No.</th><th>Population</th><th>IDSL / TST ID / Example Shell</th><th>Title</th><th>Programming Notes</th><th>Deliverable [Priority]</th></tr>
<tr><td colspan="6">Pathway and Target Engagement</td></tr>
<tr><td>5.21.</td><td>Safety</td><td>FE1</td><td>Individual Subject Profiles for TEAR1 % Target Engagement in Blood</td><td>Panel plot, line colours by treatment group, subjid as cell header</td><td>IA, SAC</td></tr>
<tr><td>5.22.</td><td>Safety</td><td>FE2</td><td>Adjusted Mean (95% CI) TEAR1 % Target Engagement in Blood</td><td></td><td>IA, SAC</td></tr>
<tr><td>5.23.</td><td>Safety</td><td>FE1</td><td>Individual Subject Profiles for TEAR1 % Target Engagement in Skin</td><td>Panel plot, line colours by treatment group, subjid as cell header</td><td>IA, SAC</td></tr>
<tr><td>5.24.</td><td>Safety</td><td>FE2</td><td>Adjusted Mean (95% CI) TEAR1 % Target Engagement in Skin</td><td></td><td>IA, SAC</td></tr>
<tr><td>5.25.</td><td>Safety</td><td>FE6</td><td>Scatter Plot of TEAR 1 % Target Engagement in Blood vs. TEAR1 % Target Engagement in Skin by Treatment Group</td><td>X axis- TE Blood, y axis TE Skin
Include bands for lower 10th and 90th percentile from PKPD, and grey dashed ref line at median
60mg BID PKPD model:
<table><tr><th></th><th>10th percentile</th><th>Median</th><th>90th Percentile</th></tr><tr><td>Blood</td><td>85.3%</td><td>95%</td><td>98.4%</td></tr><tr><td>Skin</td><td>70.3%</td><td>88.5%</td><td>96.1 %</td></tr></table></td><td>IA, SAC</td></tr>
<tr><td colspan="6">Exploratory</td></tr>
</table>

Pharmacodynamic (and or Biomarker) : Figures					
No.	**Population**	**IDSL / TST ID / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
5.26.	Safety	FE7	Scatter Plot of TEAR1 % Target Engagement in Skin vs. Percentage Change in Histopathological Scoring in Psoriatic Lesional Biopsies	Page by biomarker and location (dermis/epidermis) X axis – TE Skin, y axis - % Chg Biomarker Markers by treatment group	IA, SAC
5.27.	Safety	FE7	Scatter Plot of TEAR1 % Target Engagement in Skin vs. Fold Change in mRNA Expression of Inflammatory Gene Transcripts in Psoriatic Lesional Biopsies	Page by biomarker and location (dermis/epidermis) X axis – TE Skin, y axis - % Chg Biomarker Markers by treatment group Band for FC between -1 to 1	IA, SAC

11.13.13. Biomarker / Efficacy Figures

Pharmacodynamic (and or Biomarker) : Figures					
No.	**Population**	**IDSL / TST ID / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
5.28.	Safety	FE7	Scatter Plot of TEAR1 % Target Engagement in Skin vs. Percentage Change in PLSS	Page by biomarker and location (dermis/epidermis) X axis – TE Skin, y axis - % Chg Biomarker Markers by treatment group Band for FC between -1 to 1	IA, SAC
5.29.	Safety	FE7	Scatter Plot of TEAR1 % Target Engagement in Skin vs. Percentage Change in PASI	Page by biomarker and location (dermis/epidermis) X axis – TE Skin, y axis - % Chg Biomarker Markers by treatment group Band for FC between -1 to 1	IA, SAC

11.13.14. ICH Listings

ICH : Listings					
No.	**Population**	**IDSL / TST ID / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
Randomisation					
1.	Safety	CP_TA1	Listings of Randomised and Actual Treatments		IA, SAC
Subject Disposition					
2.	All subjects	ES7	Listing of Reasons for Screen Failure	Journal Guidelines	IA, SAC
3.	Safety	ES2	Listing of Reasons for Study Withdrawal	ICH E3	IA, SAC
4.	Safety	BL1	Listing of Subjects for Whom the Treatment Blind was Broken	ICH E3	IA, SAC
5.	Safety	TA1	Listing of Planned and Actual Treatments	IDSL	IA, SAC
Protocol Deviations					
6.	Safety	DV2	Listing of Important Protocol Deviations	ICH E3 Listing also includes analysis population exclusions.	IA, SAC
7.	Safety	IE3	Listing of Subjects with Inclusion/Exclusion Criteria Deviations	ICH E3	IA, SAC
Population Analysed					
8.	All Subjects	SA3a	Listing of Subjects Excluded from Any Population	ICH E3 e.g., subjects screened but not randomized, subjects randomized but not treated, subjects with deviations leading to exclusion from per protocol population (can be separate listing per population).	IA, SAC

Demographic and Baseline Characteristics					
9.	Safety	DM2	Listing of Demographic Characteristics	ICH E3	IA, SAC
10.	Safety	DM9	Listing of Race	ICH E3	IA, SAC
Prior and Concomitant Medications					
11.	Safety	CP_CM3	Listing of Concomitant Medications	IDSL	IA, SAC
Exposure and Treatment Compliance					
12.	Safety	EX3	Listing of Exposure Data	ICH E3	IA, SAC
Adverse Events					
13.	Safety	AE8	Listing of All Adverse Events	ICH E3	IA, SAC
14.	Safety	AE7	Listing of Subject Numbers for Individual Adverse Events	ICH E3	IA, SAC
15.	Safety	AE2	Listing of Relationship Between Adverse Event System Organ Classes, Preferred Terms, and Verbatim Text	IDSL	IA, SAC
Serious and Other Significant Adverse Events					
16.	Safety	CP_AE8a	Listing of Serious Adverse events	ICH E3	IA, SAC
17.	Safety	SAE Reasons	Listing of Reasons for Considering as a Serious Adverse Event	FDA Note: IDSL shell in development.	IA, SAC
18.	Safety	CP_AE8	Listing of Adverse Events Leading to Withdrawal from Study / Permanent Discontinuation of Study Treatment	ICH E3	IA, SAC
Hepatobiliary (Liver)					
19.	Safety	MH2	Listing of Medical Conditions for Subjects with Liver Stopping Events	IDSL	IA, SAC
20.	Safety	SU2	Listing of Substance Use for Subjects with Liver Stopping Events	IDSL	IA, SAC

All Laboratory					
21.	Safety	LB5	Listing of Laboratory Data for Subjects with Abnormalities of Potential Clinical Concern	ICH E3 Include fasted or non-fasted. Include subjects that have both absolute and change from baseline PCI	IA, SAC
22.	Safety	LB5 / LB6	Listing of Laboratory Data Abnormalities of Potential Clinical Importance	Include fasted or non-fasted.	IA, SAC
ECG					
23.	Safety	CP_EG3	Listing of All ECG Values for Subjects with a Value of Potential Clinical Importance	IDSL Include absolute PCI subjects. Footnote: H=High absolute, L= Low absolute."	IA, SAC
24.	Safety	CP_EG3	Listing of All ECG Changes for Subjects with a Value of Potential Clinical Importance	IDSL Include change from baseline PCI subjects. Footnote: H=High change from baseline value, L= Low change from baseline value	IA, SAC
25.	Safety	CP_EG3	Listing of ECG Values of Potential Clinical Importance	"Include absolute PCIs. Footnote: H=High absolute, L= Low absolute."	IA, SAC
26.	Safety	CP_EG3	Listing of ECG Changes of Potential Clinical Importance	"Include change from baseline PCIs. Footnote: H=High change, L= Low changee."	IA, SAC
27.	Safety	CP_EG5	Listing of Abnormal ECG Findings	IDSL	IA, SAC
Vital Signs					

28.	Safety	CP_VS4	Listing of All Vital Signs for Subjects with Values of Potential Clinical Importance	"Include both absolute and change from baseline PCI subjects. Footnote: H=High, L=Low H1=Lower Increase, H2=Upper Increase, L1=Lower Decrease, L2=Upper Decrease"	IA, SAC

11.13.15. Non-ICH Listings

Non-ICH : Listings					
No.	**Population**	**IDSL / TST ID / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
Columbia Suicide Severity Rating Scale (C-SSRS)					
29.	Safety	ECSSRS4	Listing of C-SSRS suicidal Ideation and Behaviour Data		IA, SAC
30.	Safety	ECSSRS5	Listing of C-SSRS Suicidal Behaviour Details		IA, SAC
Pharmacokinetic					
31.	PK	PKCL1X	Listing of Blood GSK2982772 Pharmacokinetic Concentration-Time (ng/mL) Data		IA, SAC
32.	PK	PKCL1X	Listing of Skin GSK2982772 Pharmacokinetic Concentration-Time (ng/mL) Data		IA, SAC
Pharmacodynamic					
33.	Safety	LS2	Listing of Histopathological Scoring in Psoriatic Lesional Biopsies	Including, but not limited to K16, CD3/Cd11c, CD161, elastase positive dermal cells and epidermal thickness.	IA, SAC
34.	Safety	LS1	Listing of mRNA Expression of Inflammatory Gene Transcripts in Psoriatic Lesional Biopsies	Including, but not limited to CRP, VEGF, S100A8, S100A9, IL-17, IL-22 and TNF.	IA, SAC
35.	Safety	LS2	Listing of Blood Inflammatory Biomarkers		IA, SAC
36.	Safety		Listings of TEAR1 % Target Engagement	See 200975/partb_final	IA, SAC
37.	Safety	n/a	Raw SAS Output of Statistical Analysis of Histopathological Scoring in Psoriatic Lesional Biopsies		IA, SAC
38.	Safety	n/a	Raw SAS Output of Statistical Analysis of Inflammatory Gene Transcripts in Psoriatic Lesional Biopsies		IA, SAC
39.	Safety	n/a	Raw SAS Output of Statistical Analysis of Blood Inflammatory Biomarkers		IA, SAC

Non-ICH : Listings					
No.	**Population**	**IDSL / TST ID / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
40.	Safety	n/a	Raw SAS Output of Statistical Analysis of TEAR1 % Target Engagement		IA, SAC
Efficacy					
41.	Safety	LS2	Listings of PLSS absolute and change from baseline score		IA, SAC
42.	Safety	LS2	Listings of PASI absolute, change from baseline, percentage change from baseline, PASI50, PASI75 and PASI90 status		IA, SAC
43.	Safety	LS2	Listing of PGA categories by treatment over time		IA, SAC
44.	Safety	LS2	Listing of BSA absolute and change from baseline score		IA, SAC
45.	Safety	LS2	Listing of DLQI Absolute and Change From Baseline Score		IA, SAC
46.	Safety	LS2	Listings of VAS Absolute and Change From Baseline Score		IA, SAC
47.	Safety	n/a	RAW SAS Output of Statistical Analysis Results for Percentage Change From Baseline PLSS Score		IA, SAC
48.	Safety	n/a	RAW SAS Output of Statistical Analysis Results for Change From Baseline PASI Score		IA, SAC
49.	Safety	n/a	RAW SAS Output of Statistical Analysis Results for PASI50 Score		IA, SAC
50.	Safety	n/a	RAW SAS Output of Statistical Analysis Results for PASI75 Score		IA, SAC
51.	Safety	n/a	RAW SAS Output of Statistical Analysis Results for PASI90 Score		IA, SAC
52.	Safety	n/a	RAW SAS Output of Statistical Analysis Results for Change from Baseline PGA Score		IA, SAC

Non-ICH : Listings					
No.	**Population**	**IDSL / TST ID / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
53.	Safety	n/a	RAW SAS Output of Statistical Analysis Results for PGA Score of Clear / Almost Clear		IA, SAC
54.	Safety	n/a	RAW SAS Output of Statistical Analysis Results for Change From Baseline BSA score		IA, SAC
55.	Safety	n/a	RAW SAS Output of Statistical Analysis Results for Change From Baseline BSA score		IA, SAC
56.	Safety	n/a	RAW SAS Output of Statistical Analysis Results for Change From Baseline DLQI score		IA, SAC
57.	Safety	n/a	RAW SAS Output of Statistical Analysis Results for Change From Baseline VAS score		IA, SAC

11.14. Appendix 14: Example Mock Shells for Data Displays

Example : LS1
Protocol : 203167
Population : Safety

Listing XX:
Listing of Absolute, Percentage Inhibition and Maximum Percentage Inhibition in qPCR Expression

Gene	Treatment	Subject	Visit	CT1/CT2/ CTAVG/ Copy Number	Value	Percentage Inhibition [1]	Maximum Percentage Inhibition [2]
XXXXGENE	GSKXXXXXX XXmg	XXXX	Screening	CT1	XX.XXX		
				CT2	XX.XXX		
				CTAVG	XX.XXX		
				NORMALISED	XX.XXX		
			Baseline	CT1	XX.XXX		
				CT2	XX.XXX		
				CTAVG	XX.XXX		
				NORMALISED	XX.XXX	x.xxx	
			Week X	CT1	XX.XXX		
				CT2	XX.XXX		
				CTAVG	XX.XXX		
				NORMALISED	XX.XXX	x.xxx	

Example : LS2
Protocol : 203167
Population : Safety

Listing XX:
Listing of Raw, Change from baseline and Percent Change in [variable}

Treatment	Subject	Visit	Visit date	Study day	Histopatholgical Scoring	Raw	Change	Percent Change
Placebo	XXX	XXX	XX/XX/XX	Day 1	K16	XXX.X		
					CD3/CD11c	XXX.X		
					CD161	XXX.X		
					Elactase +ve cels	XXX.X		
					epidermal thickness	XXX.X		
		XXX	XX/XX/XX	Day 43	K16	XXX.X	XXX.X	XXX.X
					CD3/CD11c	XXX.X	XXX.X	XXX.X
					CD161	XXX.X	XXX.X	XXX.X
					Elactase +ve cels	XXX.X	XXX.X	XXX.X
					epidermal thickness	XXX.X	XXX.X	XXX.X

Example EFF_T1 Page 1 of 1
Protocol: 203167
Population: Safety

Table XX: GEE Point Estimate and 95% CI for PASI*XX* by Week

Comparison	Parameter	Odds Ratio	95% CI of Odds Ratio	
GSK2982772 vs Placebo	PASI*XX* at Day 1	x.xx	(x.xx, x.xx)	
GSK2982772 vs Placebo	PASI*XX* at Day 15	x.xx	(x.xx, x.xx)	
GSK2982772 vs Placebo	PASI*XX* at Day 29	x.xx	(x.xx, x.xx)	....
.... ..	.... ..			

Example EFF_T2
Protocol: 203167
Population: Safety

Table XX: Frequency Table for PASI50, PASI75 by week

Parameter	Visit	Placebo N=x	100mg N=x	200mg N=x	400mg N =x
PASI50	Day 1	nn/nn (xx.xx)	nn / nn (xx.xx)	nn / nn (xx.xx)	nn / nn (xx.xx)
	Day 15	nn / nn (xx.xx)	nn / nn (xx.xx)	nn / nn (xx.xx)	nn / nn (xx.xx)
	Day 29	nn / nn (xx.xx)	nn / nn (xx.xx)	nn / nn (xx.xx)	nn / nn (xx.xx)
	...				
PASI75	Day 1	nn / nn (xx.xx)	nn / nn (xx.xx)	nn / nn (xx.xx)	nn / nn (xx.xx)
	Day 15	nn / nn (xx.xx)	nn / nn (xx.xx)	nn / nn (xx.xx)	nn / nn (xx.xx)
	Day 29	nn / nn (xx.xx)	nn / nn (xx.xx)	nn / nn (xx.xx)	nn / nn (xx.xx)
	...				
PASI90	Day 1	nn / nn (xx.xx)	nn / nn (xx.xx)	nn / nn (xx.xx)	nn / nn (xx.xx)
	Day 15	nn / nn (xx.xx)	nn / nn (xx.xx)	nn / nn (xx.xx)	nn / nn (xx.xx)
	Day 29	nn / nn (xx.xx)	nn / nn (xx.xx)	nn / nn (xx.xx)	nn / nn (xx.xx)
	...				

Example EFF_T3 Page 1 of 1
Protocol: 203167
Population: Safety

Table XX: Summary Statistics (Mean +/- SD) for Actual and Change from Baseline [*Continuous Parameter*] by Treatment and Week

Parameter	Treatment	N	Visit	n	Mean	{95% CI (Lower,Upper)}	SD	Median	Min.	Max.
Continuous Parameter	GSK2982772	18	Day 1	18	xxxx.xx	(xxxx.xx,xxxx.xx)	xx.xxx	xxxx.xx	xxxx.x	xxxx.x
			Day 15	18	xxxx.xx	(xxxx.xx,xxxx.xx)	xx.xxx	xxxx.xx	xxxx.x	xxxx.x
			Day 29	18	xxxx.xx	(xxxx.xx,xxxx.xx)	xx.xxx	xxxx.xx	xxxx.x	xxxx.x
			...							
	Placebo	6	Day 1	6	xxxx.xx	(xxxx.xx,xxxx.xx)	xx.xxx	xxxx.xx	xxxx.x	xxxx.x
			Day 15	6	xxxx.xx	(xxxx.xx,xxxx.xx)	xx.xxx	xxxx.xx	xxxx.x	xxxx.x
			Day 29	6	xxxx.xx	(xxxx.xx,xxxx.xx)	xx.xxx	xxxx.xx	xxxx.x	xxxx.x
			...							

Example: EFF_T4
Protocol: 203167
Population: Safety

Table x.x:
Repeated Measures Analysis of the Change from Baseline in [*Continuous Parameter*] at Each Visit

Visit	Treatment Group	n	LSMean	Standard Error	95% CI for LS Mean	Difference from Placebo	95% CI for Difference (Lower,Upper)
Week 1	Placebo	x	x.xx	x.xxx	(x.xx, x.xx)		
	GSK2982772	x	x.xx	x.xxx		x.xx	(x.xx, x.xx)
Week 2	Placebo	x	x.xx	x.xxx	(x.xx, x.xx)		
	GSK2982772	x	x.xx	x.xxx	(x.xx, x.xx)	x.xx	(x.xx, x.xx)

...

Repeated Measures Analysis adjusted for Baseline Score, Treatment Group, Visit and Treatment Group by Visit Interaction

Example: PD_T1
Protocol: 203167
Population: Safety

Listing XX:
Listing of Absolute, Percentage Inhibition and Maximum Percentage Inhibition in mRNA Expression

Gene	Treatment	Subject	Visit	CT1/CT2/ CTAVG/ Copy Number	Value	Percentage Inhibition [1]	Maximum Percentage Inhibition [2]
XXXXGENE	GSKXXXXXX XXmg	XXXX	Screening	CT1	XX.XXX		
				CT2	XX.XXX		
				CTAVG	XX.XXX		
				NORMALISED	XX.XXX		
			Baseline	CT1	XX.XXX		
				CT2	XX.XXX		
				CTAVG	XX.XXX		
				NORMALISED	XX.XXX	x.xxx	
			Week X	CT1	XX.XXX		
				CT2	XX.XXX		
				CTAVG	XX.XXX		
				NORMALISED	XX.XXX	x.xxx	

Example: PD_T2
Protocol: 203167
Population: Safety

Table XX.XX :
Frequency table summarising the number of probe sets in various fold change

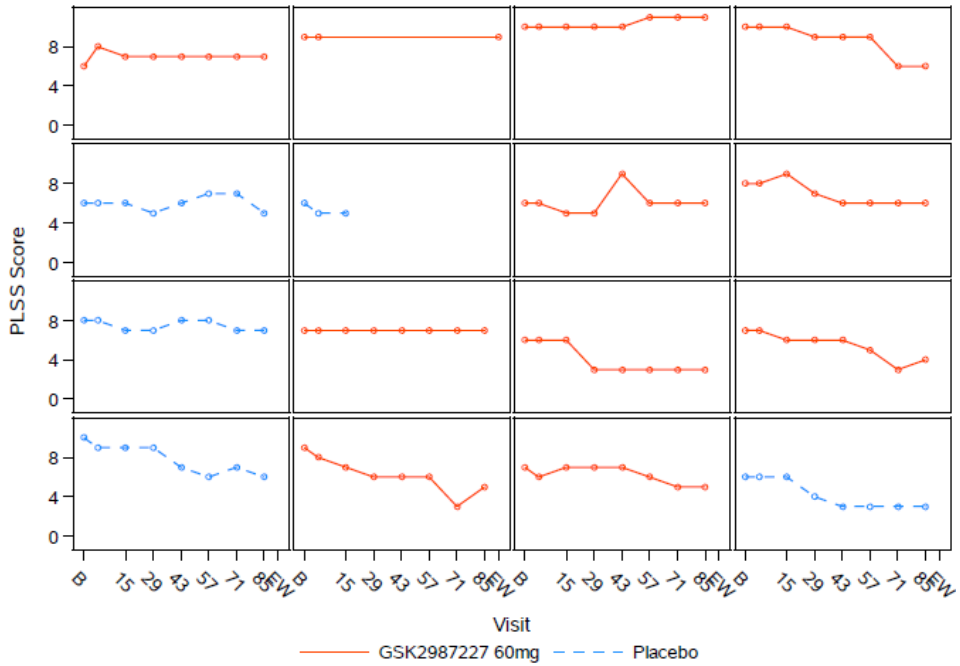
Probeset	Gene	Visit	N	n	Treatment	Fold Change < 1.5	Fold Change >1.5
XXXXXX	XXXXXX	Baseline	XX	XX	Placebo	xx (xx.xx)	xx (xx.xx)
					GSKXXXXXX XXmg	xx (xx.xx)	xx (xx.xx)
		WEEK xx	XX	XX	Placebo	xx (xx.xx)	xx (xx.xx)
					GSKXXXXXX XXmg	xx (xx.xx)	xx (xx.xx)
		WEEK xx	XX	XX	Placebo	xx (xx.xx)	xx (xx.xx)
					GSKXXXXXX XXmg	xx (xx.xx)	xx (xx.xx)

Example: PD_T3
Protocol: 203167
Population: Safety

Treatment Group	n Adjusted Mean 95% CI	n Adjusted Mean 95% CI	Fold Chg. From Baseline 95% CI	Comparison to Placebo Fold Change 95% CI
Placebo SD/RD (4W) (N=6)	4 10033.48 (5015.87, 20070.45)	4 13337.45 (4806.65, 37008.63)	1.33 (-1.24, 2.19)	
GSK 60mg BID (N=4)	8118.18 (3264.70, 20187.10)	6830.11 (2150.27, 21695.19)	-1.19 (-1.96, 1.39)	-1.58 (-3.21, 1.28)
GSK 60mg TID 15mg/kg (N=15)	9 6459.95 (3943.96, 10580.99)	9 6471.40 (3139.22, 13340.56)	1.00 (-1.42, 1.43)	-1.33 (-2.45, 1.39)

Example: FE1
Protocol: 203167
Population: Safety

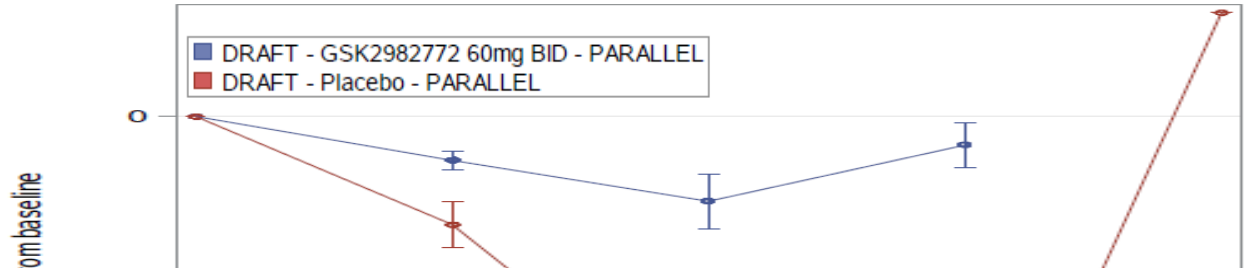
Table X
Individual [*Continuous Parameter*] Scores over Time by Treatment



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

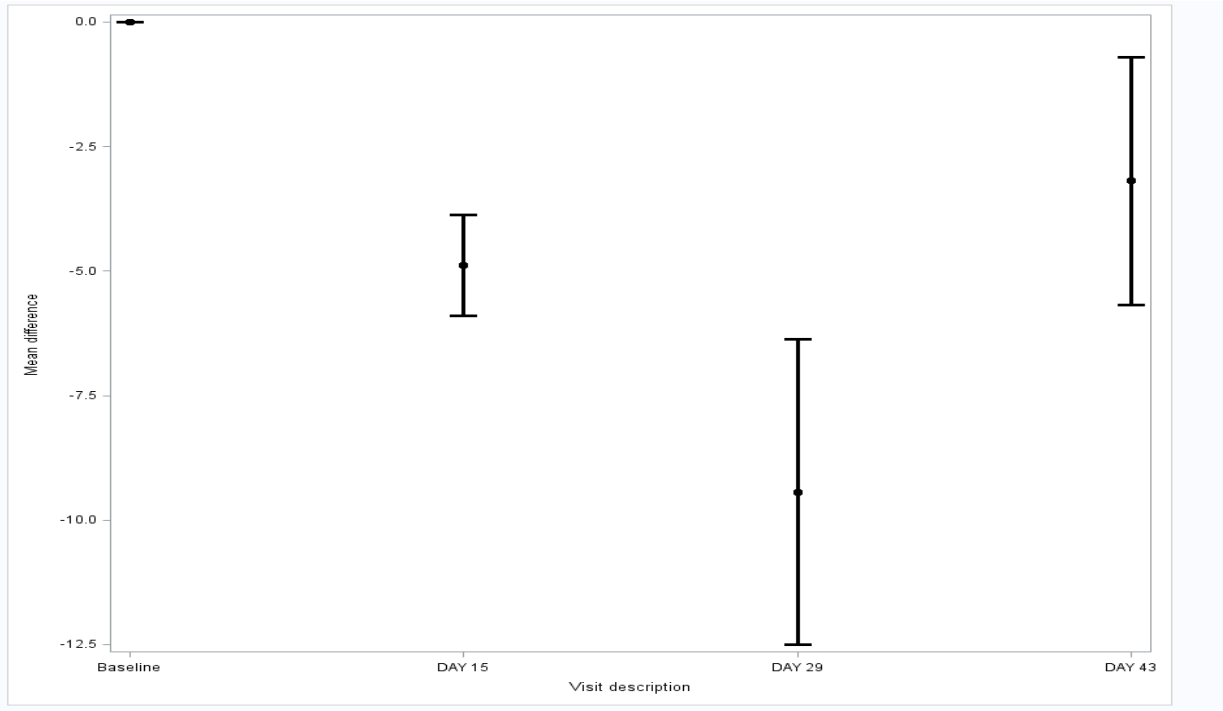
Example: FE2
Protocol: 203167
Population: Safety

Table X
Mean (+/-SD) [*Continuous Parameter*] over Time by Treatment



Example: FE3
Protocol: 203167
Population: Safety

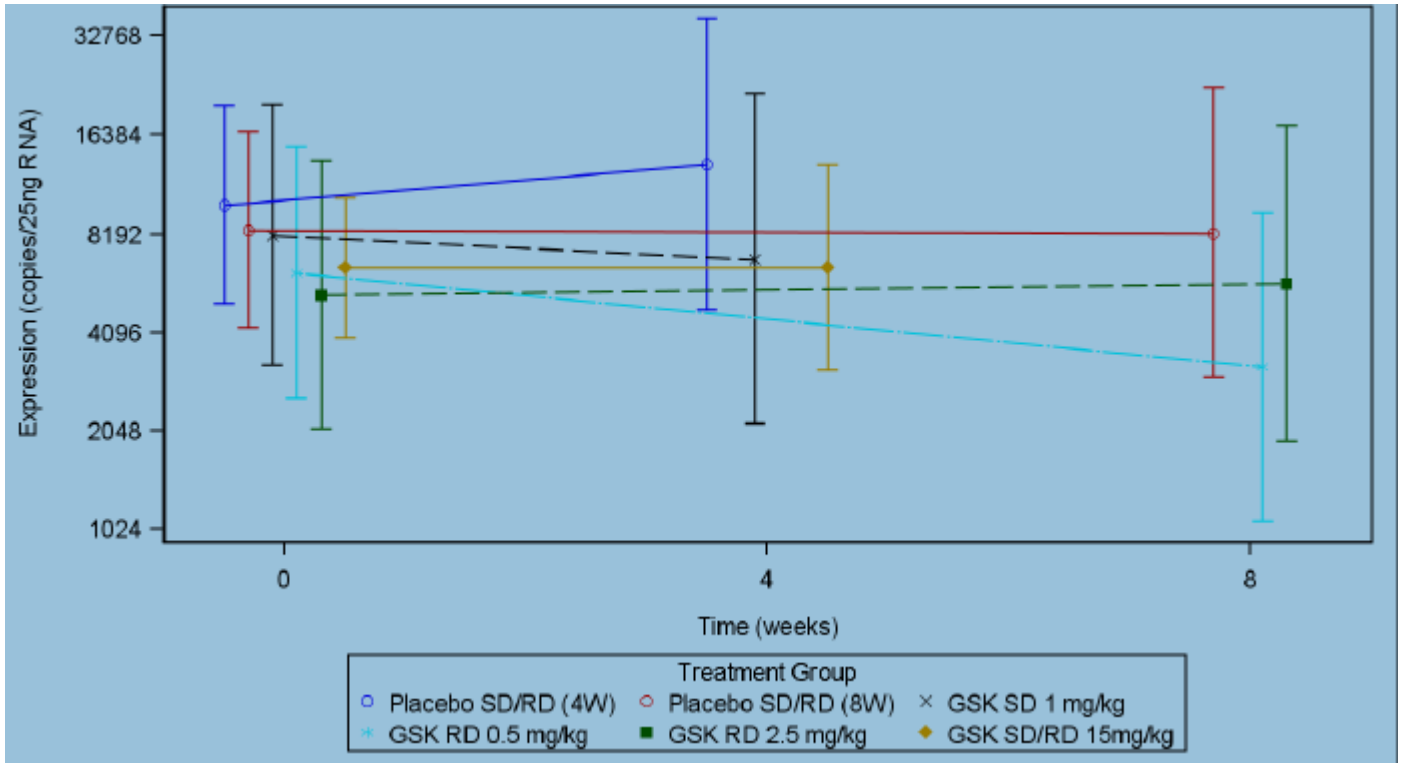
Table X
Treatment Difference and 95% CI of [*Continuous Parameter*]



Example: FE4
Protocol: 203167
Population: Safety

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

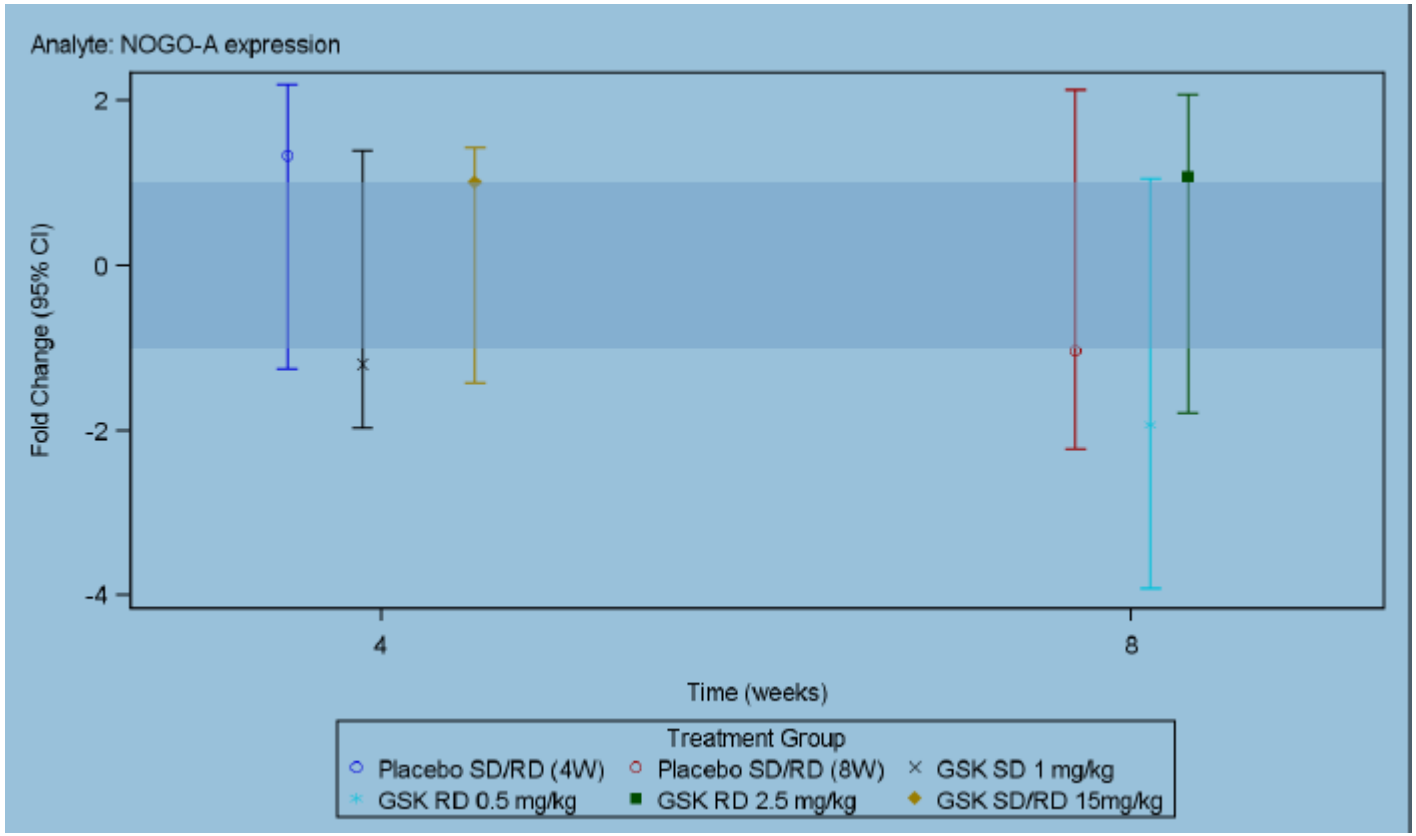
Gene ID: XXXX



Example: FE5
Protocol: 203167
Population: Safety

Figure XX.XX:
Adjusted Fold Change in mRNA Expression

Gene ID: XXXX



Example: FE6
Protocol: 203167
Population: Safety

Figure XX.XX:

Plasma TE vs Skin TE

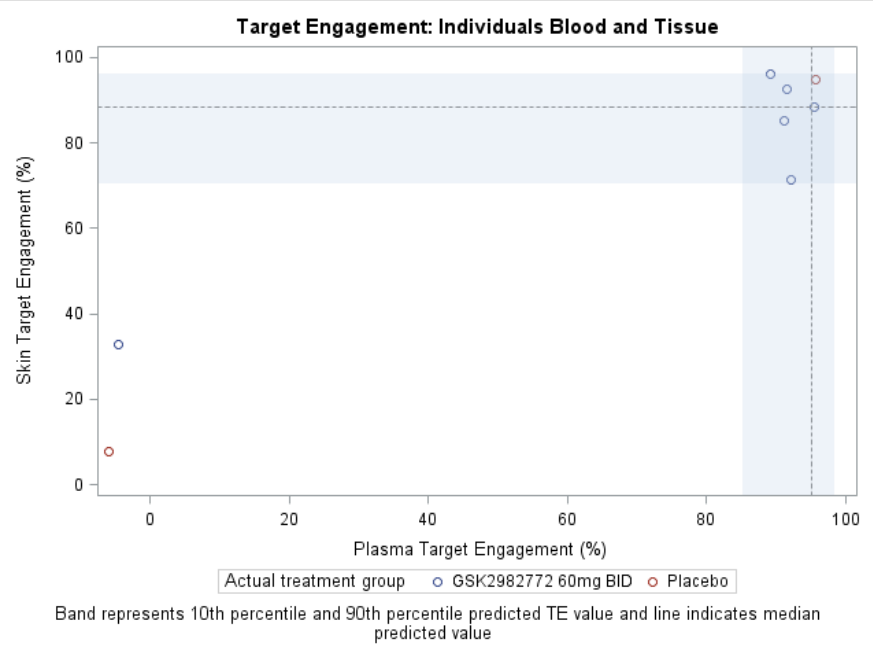
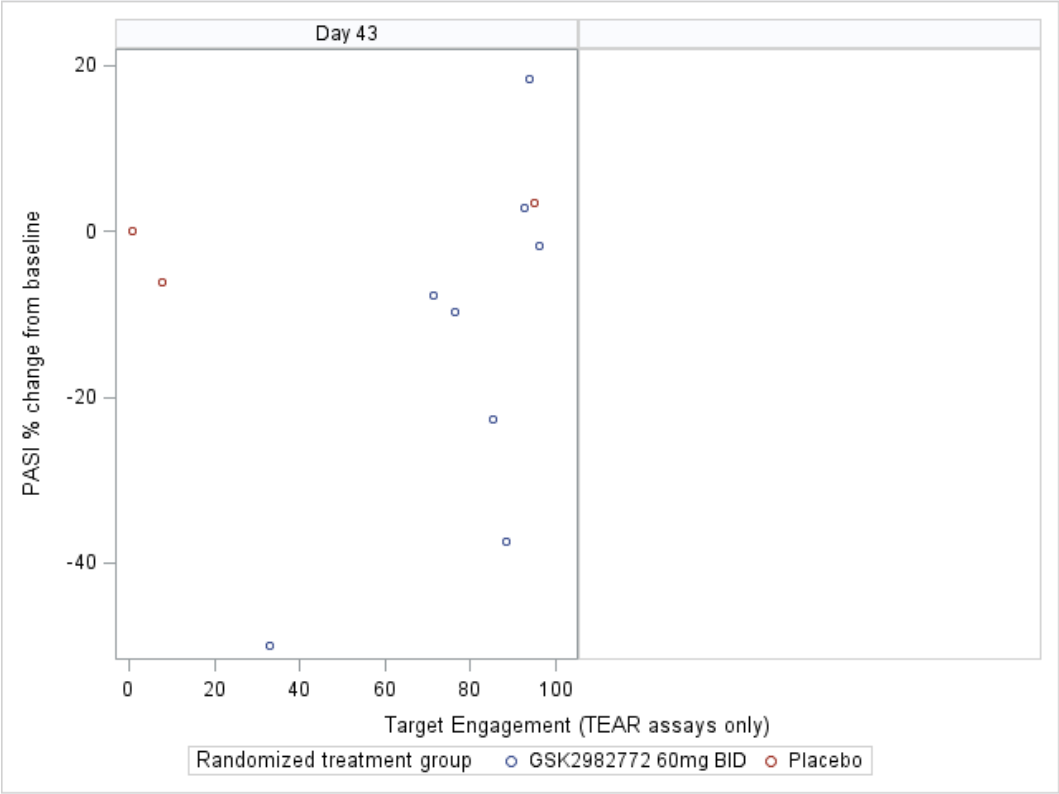


Figure XX.XX:
Skin TE vs Effiacy/Biomarkers


Day 43
20
0
-20
-40
PASI % change from baseline
0
20
40
60
80
100
Target Engagement (TEAR assays only)
Randomized treatment group
GSK2982772 60mg BID
Placebo