Division	:	Worldwide Development
Information Type	:	Reporting and Analysis Plan (RAP)
Title	:	Reporting and Analysis Plan for 200630: A randomised, double blind (sponsor unblinded), placebo controlled, single ascending dose study to investigate the safety, tolerability, pharmacokinetics, and pharmacodynamics of a IV dose of GSK2831781 in healthy volunteers and patients with plaque psoriasis
Compound Number	:	GSK2831781
Effective Date	:	24-JAN-2018

Description:

The purpose of this RAP is to describe the planned analyses and output to be included in the Clinical Study Report for Protocol 2014N192690_11.

This RAP is intended to describe the safety, tolerability, pharmacodynamic and efficacy analyses required for the study.

This RAP will be provided to the study team members to convey the content of the reporting efforts, specifically Statistical Analysis Complete (SAC).

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1. INTRODUCTION

The purpose of this reporting and analysis plan (RAP) is to describe the analyses to be included in the Clinical Study Report for Protocol

1.1. RAP Amendments

Revision chronology:

RAP Section	Amendment Details
Reporting and Analysis Plan_Study200630_Final_V1 [7-Nov-2017]	
Reporting and Analysis Plan_Study200630_Amendment_Final_V1 [23-Jan-2018]	
Soluble LAG3 concentrations	• Change from free and complex sLAG-3 to total sLAG-3
Transcriptomics	• Analyses included
PK / PD Dataset Specification	• Details removed as per current TMF guidelines, the specifications for these datasets will need to be in a separate document, which will reside in eTMF.
Minor updates	• Clarification of some outputs • Added details for the Bayesian analyses • Separate sections/outputs for IHC parameters and epidermis thickness • Categories for ECG to match the protocol

2. SUMMARY OF KEY PROTOCOL INFORMATION

2.1. Changes to the Protocol Defined Statistical Analysis Plan

Changes from the originally planned statistical analysis specified in the protocol are outlined in Table 1.

Table 1 Changes to Protocol Defined Analysis Plan

Protocol	Reporting & Analysis Plan	
Statistical Analysis Plan	**Statistical Analysis Plan**	**Rationale for Changes**
• PK parameters to be derived include AUC(0-week4), Vss and MRT	• PK parameters AUC(0-week4), Vss and MRT will not be derived	• These parameters are not relevant for the study/program and/or a monoclonal antibody
• Dose proportionality will be assessed using the power model	• No statistical analysis (e.g. using a power model) will be performed	• Interim analyses to support DEC meetings showed that the PK data is clearly non-linear (less than proportional increase in exposure with increasing dose), and hence a statistical analysis to test dose proportionality is redundant
• Effect on free and GSK2831781 bound sLAG-3 concentrations	• Total sLAG-3 concentrations will be used instead of free and complex sLAG-3	• The assays for free and complex sLAG-3 are not quantitative, and therefore a new assay to measure total sLAG-3 was developed. PK/PD modelling will be used to investigate the time course of

Protocol	Reporting & Analysis Plan	
Statistical Analysis Plan	**Statistical Analysis Plan**	**Rationale for Changes**
		free and complex sLAG-3.

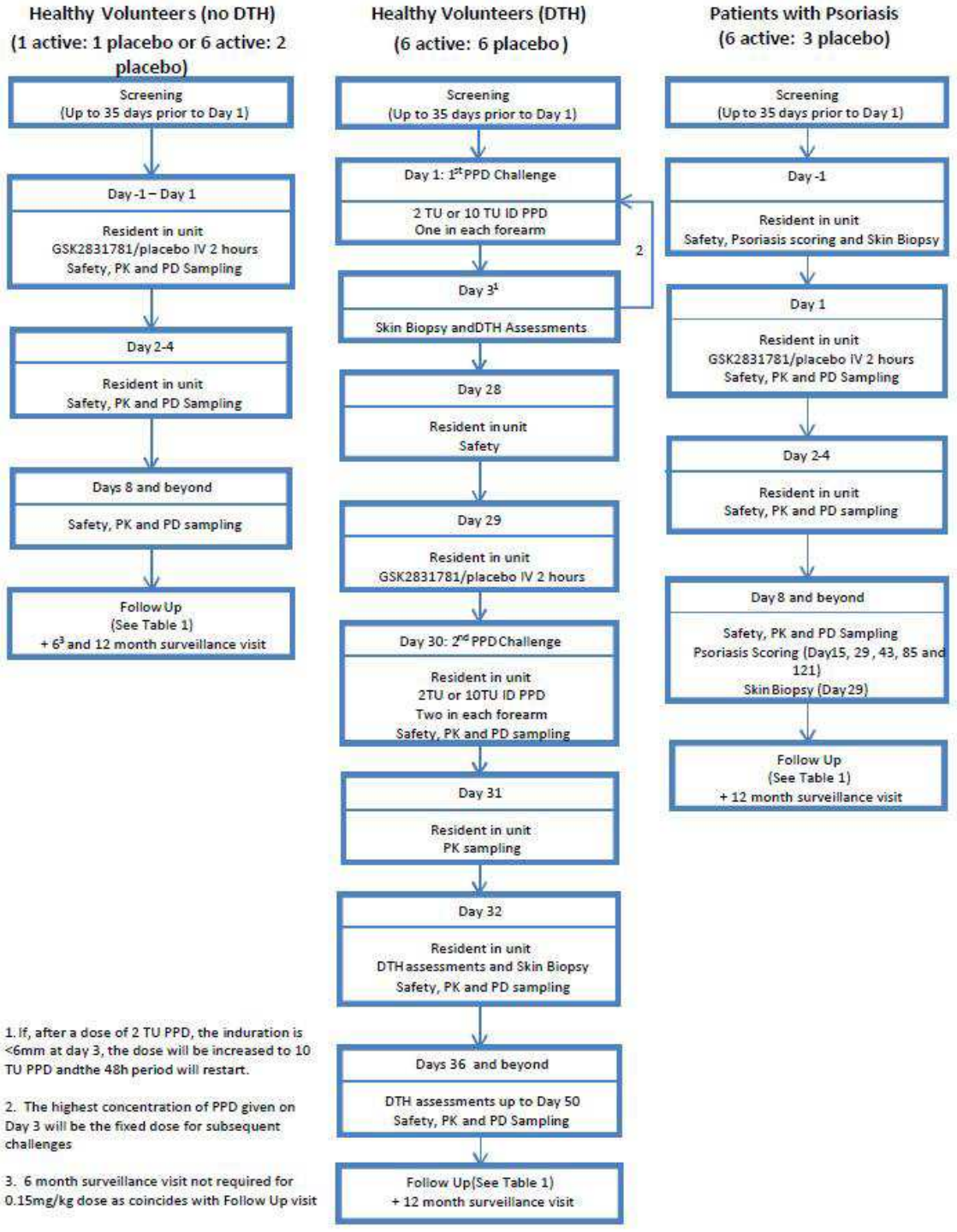
2.2. Study Objectives and Endpoints

Objectives	Endpoints
Primary	**Primary**
To assess the safety and tolerability of single IV doses of GSK2831781 in healthy volunteers and psoriasis patients.	• Laboratory safety data (haematology, clinical chemistry, urinalysis) • Vital signs (blood pressure, heart rate, body temperature) • 12-lead ECGs • Adverse events • Inflammatory cytokine levels
Secondary Objectives	**Secondary Endpoints**
To evaluate the pharmacology and clinical effect of a single IV dose of GSK2831781 in a DTH model in healthy volunteers.	• Change from baseline (PPD 1st challenge) of induration diameter from re-challenge at 3 days post-dose • Duration of induration in the re-challenge • Change from baseline (PPD 1st challenge) of LAG-3+ cells in biopsies of re-challenged skin at 3 days post-dose, measured by IHC
To evaluate the pharmacology of a single IV dose of GSK2831781 in psoriasis patients.	• Change from baseline in LAG-3+ cells in lesional biopsies at Day 29 measured by IHC
To evaluate the pharmacokinetics of single IV doses of GSK2831781 in healthy volunteers and psoriasis patients.	• GSK2831781 PK parameters following single intravenous dose: AUC(0-∞), AUC(0-t), AUC(0-Week4), %AUCex, Cmax, tmax, tlast, CL, Vss, MRT, λz and t ½ when assessable
To evaluate the immunogenicity of GSK2831781 administered as a single IV dose in healthy volunteers and psoriasis patients.	• Antibodies to GSK2831781 in serum
To evaluate the effect of a single IV dose of GSK2831781 on disease activity in psoriasis patients.	• Change from baseline and actual PASI scores at Day 15, 29, 43, 85, 121 and follow-up • Proportion of subjects who achieve ≥50% and ≥75% improvement from baseline in PASI score at Day 15, 29, 43, 85, 121 and follow-up (PASI 50 and PASI 75) • Change from baseline and actual PLSS scores at Day 15, 29, 43, 85, 121 and follow-up • Change from baseline and actual PGA scores at Day 15, 29, 43, 85 and 121 • Proportion of subjects in each PGA score category at Day 15, 29, 43, 85 and 121 • Proportion of subjects achieving PGA 0/1 and at least a 2-point improvement at Day 15, 29, 43, 85 and 121

Objectives	Endpoints
Exploratory Objectives	**Exploratory Endpoints**
To evaluate the effect of a single IV dose of GSK2831781 in psoriasis patients on biomarkers.	• Histopathological scoring of psoriatic lesional biopsies in subjects with psoriasis - Ki67, CD3 and epidermal thickness • Transcriptomic analysis of psoriatic lesional biopsies in subjects with psoriasis
To evaluate the effect of a single IV dose of GSK2831781 in healthy volunteers and psoriasis patients on pharmacodynamic biomarkers.	Proof of pharmacology biomarker endpoints may include, but not limited to, the following as data permit: • LAG-3 expression on different blood immune cell populations including T-cells • Transcriptomic profiling to assess mRNA levels in peripheral blood • Quantification of LAG-3 mRNA in whole blood • Inflammatory cytokine levels • sLAG-3 concentrations • NK cell CD16 receptor occupancy in whole blood • NK cell activation marker expression in whole blood
To explore the impact of pre-existing ADAs on the PK of GSK2831781	• GSK2831781 PK parameters following single intravenous dose: AUC(0-∞), AUC(0-t), AUC(0-Week4), %AUCex, Cmax, tmax, tlast, CL, Vss, MRT, λz and t ½ when assessable

2.3. Study Design

Overview of Study Design and Key Features



Design Features	This is a FTIH, phase I, randomised, double-blind (sponsor unblind), placebo-controlled, single ascending dose study in healthy volunteers (part A) and subjects with plaque psoriasis (part B). Part A will include a cohort of those previously vaccinated with Bacillus Calmette Guérin (BCG) (Part A delayed type hypersensitivity [DTH] cohort).

Overview of Study Design and Key Features

Dosing

This is a dose escalation study, the planned dosing as per protocol is as below:

Planned Doses	Number of subjects randomised (active:placebo)	Safety Follow-up period to progress to next subjects/cohorts	PPD DTH Challenge if Healthy volunteer/ Biopsy if subject	Follow-up and end of exclusion of systemic immunosuppressives
Healthy Volunteers				
0.0003mg/kg	1:1	1:1 wait 28 days post-dose	No DTH	Day 29 ± 1 day (28 days post-dosing)
0.0015mg/kg				Day 43 ± 1 day (42 days post-dosing)
0.0075mg/kg	6:2	1:1 wait 48 hours post-dose 5:1 wait 28 days post-dose	No DTH	Day 85 ± 2 days (84 days post-dosing)
0.04mg/kg				Day 147 ± 3 days (146 days post-dosing)
0.15mg/kg	6:6	1:1 wait 48 hours post-dose 5:5 wait 28 days post-dose	DTH	Day 219 ± 7 days (190 days post-dosing)
0.15mg/kg*	6:2	1:1 wait 48 hours post-dose 5:1 wait 28 days post-dose	No DTH	Day 189 ± 7 days (190 days post-dosing)
Notes: 1. Cohort with a DTH starts dosing on Day 29 2. DTH cohort at dose level 0.15mg/kg is in subjects with pre-existing ADA. All previous cohorts are in subjects without pre-existing ADA 3. Maximum dose for healthy volunteers may change based on emerging exposure				

Psoriasis patients (Pre-existing ADA- and ADA +)				
0.5mg/kg	6:3	1:1 wait 48 hours post-dose 5:2 wait 28 days post-dose	Biopsy	230 days post-dosing ± 7 days [no change with amend #10]
1.5mg/kg				183 days post-dosing ± 7† days (prior to Amendment 10 was 270 days)
5mg/kg				183 days post-dosing ± 7† days (prior to Amendment 10 was 300 days)
Note: All follow-up days may be increased or decreased during the study based on emerging data † All subjects in Cohort 7 (0.5mg/kg) completed the day 230 ± 7 follow up visit. Any subjects in Cohort 7 who have not had a 12-month surveillance visit when the amendment is approved should instead have a surveillance telephone call as soon as practically possible after the amendment is approved, rather than waiting to month 12 after dosing. Subjects in Cohort 8 (1.5mg/kg) who have already completed their follow up visit should also have a surveillance telephone call as soon as protocol amendment 10 is approved.				

Overview of Study Design and Key Features	
	Subjects in Cohort 8 (1.5mg/kg) and Cohort 9 (5mg/kg) who have not yet had a follow up visit when protocol amendment 10 is approved should have final assement, a combined follow up/surveillance visit at day 183 ± 7, or as soon as practically possible if they have already been monitored for longer than 183 ± 7 days after dosing. Subjects in Cohort 8 (1.5mg/kg) who have already completed their follow up visit should have their final assessment, a surveillance telephone call as soon as the protocol amendment is approved.

2.4. Statistical Analyses

The primary objective is to determine the safety and tolerability of single IV doses of GSK2831781 in healthy volunteers and with mild to moderate psoriasis patients. There are no formal hypotheses being tested in the study; instead an estimation and inference approach will be adopted to evaluate the objectives.

3. PLANNED ANALYSES

3.1. Interim Analyses

Interim Analysis	Details (Protocol Defined)
Dose escalation	For Parts A and B of the study, review of safety, tolerability, available pharmacokinetic, DTH induration, available biomarker and PD for healthy volunteers or PASI and PLSS for psoriasis patients at the end of each cohort will be performed by DEC to aid decisions to proceed to higher dose strengths or to subjects with pre-existing ADA. This analysis can include review of individual subject data, summaries, graphical presentations and/or statistical analysis. Safety/tolerability data monitoring and the decision to proceed to the next dose level of GSK2831781 or to subjects with pre-existing ADA will be made by the DEC. The GSK Clinical Pharmacology Modeling and Simulation (CPMS) representative will extract PK data (including treatment information) from SMS2000 using unscrambled subject IDs. PK data will provide supporting evidence for each dose modification decision. Importantly, if the emerging PK data is significantly different from the predicted values, adjustment may have to be made to the planned doses. Dose modification decisions will take into account the emerging PK data, new PK prediction for the next dose and thus the expected safety cover for the next dose.
Interim 1	• Formal unblinded interim analysis when the last subject in DTH cohort (cohort 5) has completed W4 visit. Data for healthy volunteers in cohorts 1-5 will be included. • The purpose of this interim analysis is to provide the project team and GSK stakeholders with key data to inform internal decision making, in order to plan future studies within the clinical development for the asset. • There are no planned implications for the conduct of the study. • Appropriate data summaries will be at the subject and treatment group level for key endpoints of interest and the circulation of results will be restricted to selected members of the project team and key GSK stakeholders. Results or discussions will

Interim Analysis	Details (Protocol Defined)
	not be circulated to blinded staff involved in the conduct of the study at the sites.
Interim 2	• Formal unblinded interim analysis will be conducted during part B. The PASI and PLSS will be evaluated when the last psoriasis patient in cohort 9 has completed D43 visit, and the full interim 2 evaluation will be conducted after all patients have completed their day 85 visit. Data for healthy volunteers and psoriasis patients will be included . • The purpose of this interim analysis is to provide the project team and GSK stakeholders with key data to inform internal decision making, in order to plan future studies within the clinical development for the asset. • There are no planned implications for the conduct of the study. • Appropriate data summaries will be at the subject and treatment group level for key endpoints of interest and the circulation of results will be restricted to selected members of the project team and key GSK stakeholders. Results or discussions will not be circulated to blinded staff involved in the conduct of the study at the sites.

3.2. Final Analyses

Final analyses will be reported when all subjects in all cohorts have completed their final scheduled visits (combined follow-up/surveillance visit or surveillance telephone call), and the following sequential steps have occurred:

- All subjects have completed the study as defined in the protocol.
- All required database cleaning activities have been completed and final database release and database freeze has been declared by Data Management.
- All criteria for unblinding the randomisation codes have been met.
- Randomisation codes have been distributed according to RandAll NG procedures.

4. ANALYSIS POPULATIONS

Population	Definition / Criteria	Analyses Evaluated
Screened	• All participants who were screened for eligibility	• Study Population
Safety	• All randomized participants who received at least one dose of study treatment. • This population will be based on the treatment the subject actually received. • Note: Participants who were not randomized but received at least one dose of study treatment should be listed.	• Study Population • Safety • Efficacy • PD • Ig
Pharmacokinetic (PK)	• All participants in the Safety population who had at least 1 non-missing PK assessment (Non-quantifiable [NQ] values will be considered as non-missing values). • This population will be based on the treatment the subject actually received.	• PK

Refer to Appendix 9 which details the population used for each display.

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, separately for healthy volunteers and psoriasis patients.

Protocol deviations will be tracked by the study team throughout the conduct of the study in accordance with the Protocol Deviation Management Plan (30 September 2015 - version 2).

- Data will be reviewed and deviation will be finalised before freezing the database to ensure all important deviations are captured and categorised on the protocol deviations dataset.
- This dataset will be the basis for the summaries and listings of protocol deviations.

A listing of all inclusion/exclusion criteria deviations will also be provided, separately for healthy volunteers and psoriasis patients. This listing will be based on data as recorded on the inclusion/exclusion page of the eCRF.

5. CONSIDERATIONS FOR DATA ANALYSES AND DATA HANDLING CONVENTIONS

- There are no planned examination of covariates and subgroups.
- There are no planned adjustments made for multiple centres in this study.
- There are no planned adjustments for multiple comparisons or multiplicity.

5.1. Study Treatment & Sub-group Display Descriptors

Treatment Group Descriptions			
RandAll NG		**Output**	
Code	**Description**	**Treatment Label**	**Order**
A	0.0003mg/kg GSK2831781 IV single dose	0.0003mg/kg (ADA-ve)	2
B	0.0015mg/kg GSK2831781 IV single dose	0.0015mg/kg (ADA-ve)	3
C	0.0075mg/kg GSK2831781 IV single dose	0.0075mg/kg (ADA-ve)	4
D	0.04mg/kg GSK2831781 IV single dose	0.04mg/kg (ADA-ve)	5
E	0.15mg/kg GSK2831781 IV single dose	0.15mg/kg (ADA-ve)	6
		0.15mg/kg (ADA+ve)	7
		0.15mg/kg Combined	8
F	0.5mg/kg GSK2831781 IV single dose	0.5mg/kg	10
G	1.5mg/kg GSK2831781 IV single dose	1.5mg/kg	11
H	5mg/kg GSK2831781 IV single dose	5mg/kg	12
P	Placebo IV single dose	Placebo for HV Combined	1
		Placebo for PSO	9

Notes:
1. ADA status as defined at screening
2. Combined treatment groups include subjects with ADA-ve and ADA+ve (only for healthy volunteers (HV))

5.2. Baseline Definitions

For all endpoints (except as noted in baseline definitions) the baseline value will be the latest pre-dose assessment with a non-missing value, including those from unscheduled visits. If time is not collected, Day 1 assessments are assumed to be taken prior to first dose and used as baseline.

Unless otherwise stated, if baseline data is missing no derivation will be performed and baseline will be set to missing.

Table 2 Baseline Definitions - SAFETY ENDPOINTS

Parameter[1]	Study assessments considered as baseline			Baseline used in data display
	Screening	Day -1	Day 1 (pre-dose)	
Healthy Volunteers (No DTH)				
12 Lead ECG & Vital Signs	X	X	X	Day 1 (pre-dose)
Lab results	X	X		Day -1
Cytokine			X	Day 1 (pre-dose)
Psoriasis patients				
Vitals Signs	X	X	X	Day 1 (pre-dose)
12-Lead ECG	X		X	Day 1 (pre-dose)
Lab results	X	X		Day -1
Cytokines			X	Day 1 (pre-dose)

Parameter[1]	Study assessments considered as baseline				Baseline used in data display
	Challenge DTH Day -26	Challenge DTH Day -24	Day -1	Day 1 (pre-dose)	
Healthy Volunteers (DTH)					
Vitals Signs	X	X		X	Day 1 (pre-dose)
12-Lead ECG	X			X	Day 1 (pre-dose)
Lab results	X		X		Day -1
Cytokines				X	Day 1 (pre-dose)

Table 3 Baseline Definitions – EFFICACY / PHARMACODYNAMIC AND BIOMARKER ENDPOINTS

Parameter	Visit considered as baseline		Baseline used for data displays
	Day -1	Day 1 (pre-dose)	
Healthy Volunteers (No DTH)			
Flow cytometry		X	Day 1 (pre-dose)
G-CSF		X	Day 1 (pre-dose)
sLAG-3		X	Day 1 (pre-dose)
Blood transcriptomics		X	Day 1 (pre-dose)
Psoriasis patients			
PBSA	X		Day -1
PASI	X		Day -1
PLSS	X		Day -1
PGA	X		Day -1
Flow cytomery		X	Day 1 (pre-dose)
G-CSF		X	Day 1 (pre-dose)
sLAG-3		X	Day 1 (pre-dose)
Blood transcriptomics		X	Day 1 (pre-dose)
Skin Biopsy (transcriptomics)	X		Day -1

Parameter	Visit considered as baseline				Baseline used for data displays
	Challenge DTH Day -26	Challenge DTH Day -24	Challenge DTH Day -1	Challenge DTH Day 1 (pre-dose)	
Healthy Volunteers (DTH)					
Induration [*]	X	X			DTH Day -24 if 2 assessments DTH Day -26 if only 1 assessment (see footnote)
Flow cytometry				X	DTH Day 1 (pre-dose)
G-CSF				X	DTH Day 1 (pre-dose)
sLAG-3				X	DTH Day 1 (pre-dose)
Blood Transcriptomics				X	DTH Day 1 (pre-dose)
Skin Biopsy - Lag3 and CD3	X				DTH Day -26
[*] HV may be re-challenged on Day -24 if the challenge on Day -26 is not sufficient.					

6. STUDY POPULATION ANALYSES

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

Study population analyses including analyses of subject's disposition, protocol deviations, demographic characteristics, prior and concomitant medications will be based on GSK core data standards.

Screen failures for part A and B will be identified using the cutoff date of 2nd June 2016.

Details of the planned displays are presented in Appendix 9.

7. SAFETY ANALYSES

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

7.1. Adverse Events Analyses

Adverse events analyses including the analysis of adverse events (AEs), Serious (SAEs) and other significant AEs will be based on GSK Core Data Standards.

The details of the planned displays are provided in Appendix 9.

7.2. Clinical Laboratory Analyses

Laboratory evaluations including the analyses of chemistry laboratory tests (at some visits, only liver chemistry and CRP – see e.g. footnote d in T&E for HV (no DTH)), hematology laboratory tests, urinalysis, cytokines and liver function tests will be based on GSK Core Data Standards. In addition, CMV and EBV serology sample will be listed.

Blood samples for viral load monitoring (CMV, EBV, HSV, VZV) taken at baseline and archived will be listed if subsequently analysed (i.e. when a subject demonstrates any clinical symptoms consistent with viral reactivation).

The cytokines are:

- IL-6
- TNF-α
- IL-8
- IFN-γ
- G-CSF

The details of the planned displays are provided in Appendix 9. In tables/figures, if BLQ, LLQ/2 imputed

7.3. Other Safety Analyses

The analyses of non-laboratory safety test results will be based on GSK Core Data Standards, unless otherwise specified. The non-laboratory safety test results include:

- ECGs
- Vital signs

The details of the planned displays are provided in Appendix 9.

8. EFFICACY ANALYSES

8.1. DTH Induration (only for HV)

8.1.1. Endpoint / Variables

1. The induration diameter (mm) by challenge site is defined as the average of the 2 skin response test values (vertical and horizontal) at each challenge site.
   A challenge site is defined by skin response (SR) directionality (upper/lower) and SR laterality (left/right). There are 4 categories:
   - Left upper
   - Right upper
   - Left lower
   - Right lower
2. The overall induration diameter (mm) is defined as the average of the non-missing induration diameters over the challenge sites.
3. The duration of induration is the time (in days) to achieve an overall induration less than 6mm from baseline (see Section 5.2 for baseline definition). It will be calculated as: Date of 1st overall induration < 6mm – Date of baseline induration assessment + 1. For these subjects who do not achieve an overall induration less than 6mm from the time of the PPD re-challenge post dose, the duration of induration is calculated as time from the PPD re-challenge post dose up to the last available induration measurement +1.

8.1.2. Summary Measure

Induration diameter: absolute and change from baseline for HV (DTH subjects only).

Duration of induration: absolute

Data related to ID PPD challenge will be listed.

8.1.3. Population of Interest

The efficacy analyses will be based on the Safety population.

8.1.4. Statistical Analyses / Methods

Details of the planned displays are provided in Appendix 9 and will be based on GSK data standards and statistical principles.

Unless otherwise specified, endpoints / variables defined in Section 8.1.1 will be summarised using descriptive statistics, graphically presented (where appropriate) and listed.

8.1.4.1. Statistical Methodology Specification

Endpoint
Change from baseline in induration diameter (mm) (Overall induration diameter only)
Model Specification

• Mixed models repeated measures (MMRM) model.
• Terms fitted in the MMRM model will include:
  ○ Fixed categorical covariates: Treatment, day (visit), treatment * day (visit) interaction
  ○ Fixed continuous covariates: Baseline (see Section 5.2 for baseline definition)
  ○ Repeated: Day (visit)
• An unstructured covariance will be used to account for the within-subject correlation. by specifying 'type=UN' on the REPEATED line.
• 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.
• LSmeans of the CFB will be calculated using the observed margins (OM argument added in the LSmeans function)

Model Checking & Diagnostics
• In the event that this model fails to converge, alternative correlation structures may be considered.
Model Results Presentation
• Table/Figure of the LS means and 95% CI (by treatment and visit)

Endpoint / Variables
Duration of induration of at least 6mm (days)
Model Specification
• Hasard ratios will be estimated using the Pike estimator.
Model Results Presentation
• Summary table of the hazard ratios • No plot

8.2. Body Surface Area (only for PsO)

8.2.1. Endpoint / Variables

Total body surface area (BSA), in %, measures the area covered with psoriatic plaques.

In the FACE dataset, 4 regional BSA scores (%) are available ((head, upper extremities, trunk, and lower extremities). The total BSA score for each subject at each timepoint is calculated as the sum of the 4 regional BSA scores. If at least one of the 4 regional BSA scores is missing, the total will be set to missing as well.

8.2.2. Summary Measure

Absolute BSA scores (4 regional and total), change from baseline and percent change from baseline in BSA scores over time.

8.2.3. Population of Interest

The efficacy analyses will be based on the Safety population.

8.2.4. Statistical Analyses / Methods

Details of the planned displays are provided in Appendix 9 and will be based on GSK data standards and statistical principles.

Unless otherwise specified, endpoints / variables defined in the section above will be summarised using descriptive statistics, and listed.

8.3. PASI-related endpoints (only for PsO)

8.3.1. Endpoint / Variables

Psoriatic lesions will be assessed using the PASI (Psoriasis Assessment Severity Index), single score ranging from 0 (no disease) to 72 (maximal disease). A negative (%) change from baseline in PASI score indicates an improvement.

The PASI score for each subject at each timepoint is derived as follows.

Data available (PASI SI dataset):

- Areas of the body: head (1), upper extremities (2), trunk (3), lower extremities (4)
- For each of the 4 areas of the body, the intensity of 3 symptoms is assessed on a 0-4-point rating scale
    - Symptoms: erythema (redness of the skin), induration (thickness) and scaling of the psoriasis

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.

- For each of the 4 areas of the body, the percentage area affected by psoriasis is evaluated and expressed as nil (0), 1-9% (1), 10-29% (2), 30-49% (3), 50-69% (4), 70-89% (5) or 90-100% (6)

Derivation

1. Calculation for intensity: the three intensity scores are added up for each of the 4 areas of the body to give 4 subtotals A1, A2, A3, A4.

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.

2. Multiply each subtotal (A1, A2, A3, A4) by the body surface area (BSA) represented by that region to give 4 new subtotals (B1, B2, B3, B4).

   Note: The BSA will not be calculated using the palm's method as categories above are collected. Fixed weights are used.

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.

3. Multiply each subtotal (B1, B2, B3, B4) by the area affected (PASIAREA) for that region to give 4 new subtotals (C1, C2, C3, C4):

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.

4. Calculate the total PASI score = C1 + C2 + C3 + C4
5. If any variable is missing, set PASI score to missing

8.3.2. Summary Measure

- Absolute PASI scores, change from baseline and percent change from baseline in PASI scores over time

- Proportion of subjects who achieve ≥50% improvement from baseline in PASI score (PASI 50), at each post-baseline visit Proportion of subjects who achieve ≥75% improvement from baseline in PASI score (PASI 75) at each post-baseline visit.
  If the PASI score is missing, set PASI 50 or 70 to missing.

Note: Day 85 was not assessed for 0.5mg/Kg dosing cohort (cohort 7).

8.3.3. Population of Interest

The efficacy analyses will be based on the Safety population.

8.3.4. Statistical Analyses / Methods

Details of the planned displays are provided in Appendix 9 and will be based on GSK data standards and statistical principles.

Unless otherwise specified, endpoints / variables defined in Section 8.3.1 will be summarised using descriptive statistics, graphically presented and listed. For the responder endpoints, the exact Binomial 95% CI will be calculated.

8.3.4.1. Statistical Methodology Specification

Endpoint / Variables
Change from baseline in PASI scores
Model Specification
Same MMRM model as for CFB in induration (Section 8.1.4.1)
Model Checking & Diagnostics
Same approach as in Section 8.1.4.1
Model Results Presentation
• Table/Figure of the LS means of CFB and 95% CI (by treatment and visit), as well as treatment differences and 95%CI

8.4. PLSS-related endpoints (only for PsO)

8.4.1. Endpoint / Variables

The PLSS (Psoriatic Lesion Severity Sum) score for each subject at each timepoint is derived as follows.

Data available (CC SI dataset):

For each of the 2 plaques (biopsy or index), the following data will be available:

- The location of the plaque - head, face, arm, leg or trunk
- For each plaque , the intensity of 3 symptoms is assessed on a 0-4-point rating scale

- Symptoms: induration, erythema, and scaling.
  PLSS total score calculated by the investigator will be in the dataset, but the PLSS score for analysis should be derived from the raw data.
- 0-4-point rating scale: no symptoms (0), slight (1), moderate (2), marked (3) or very marked (4).

Derivation

The PLSS total score for each of the plaques (biopsy and index)is the sum of the scores for the 3 symptoms (induration, erythema, and scaling).

8.4.2. Summary Measure

- Absolute PLSS scores, change from baseline and percent change from baseline in PLSS scores over time, for index and biopsy plaques, separately.

8.4.3. Population of Interest

The efficacy analyses will be based on the Safety population.

8.4.4. Statistical Analyses / Methods

Details of the planned displays are provided in Appendix 9 and will be based on GSK data standards and statistical principles.

Unless otherwise specified, endpoints / variables defined in Section 8.4.1 will be summarised using descriptive statistics, graphically presented and listed.

8.4.4.1. Statistical Methodology Specification

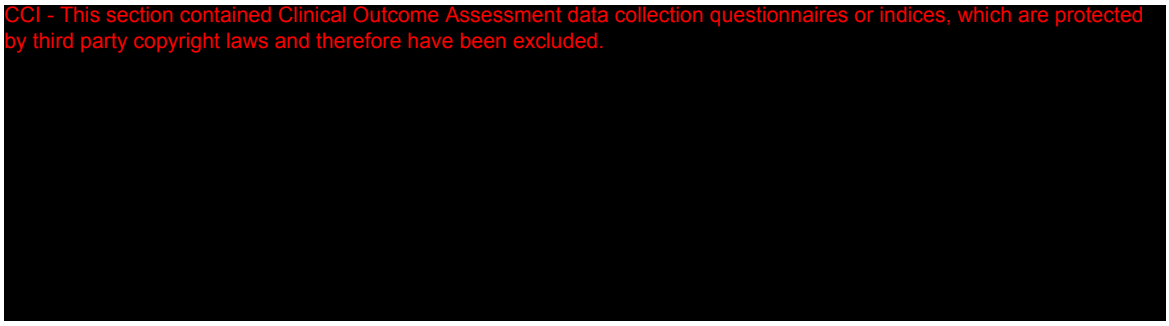
Endpoint / Variables
Change from baseline in PLSS scores for the index plaque only
Model Specification
Same MMRM model as for CFB in induration (Section 8.1.4.1)
Model Checking & Diagnostics
Same approach as in Section 8.1.4.1
Model Results Presentation
• Table/Figure of the LS means of CFB and 95% CI (by treatment and visit), as well as treatment differences and 95%CI

8.5. PGA-related endpoints (only for PsO)

8.5.1. Endpoint / Variables

The Physician Global Assessment (PGA) score for each subject at each timepoint is already in the PGA SI dataset.

A 7-point scoring system will be used to measure the severity of psoriatic lesions over the whole body:



8.5.2. Summary Measure

- PGA scores, change from baseline in PGA scores (categories treated as continuous)
- PGA responses (categorical)
- PGA responders defined as subjects achieving PGA 0/1 (clear or almost clear) and at least a 2-point improvement from baseline. This will be performed on subjects with a baseline PGA score of at least 2. Set to missing if baseline PGA is 0 or 1.

8.5.3. Population of Interest

The efficacy analyses will be based on the Safety population.

8.5.4. Statistical Analyses / Methods

Details of the planned displays are provided in Appendix 9 and will be based on GSK data standards and statistical principles.

Unless otherwise specified, endpoints / variables defined in Section 8.5.1 will be summarised using descriptive statistics, graphically presented and listed.

For the responder endpoint, the exact Binomial 95% CI will also be calculated.

9. PHARMACOKINETIC 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. Drug Concentration Measures

Refer to Section 14.4.3.

9.2. Derived Pharmacokinetic Parameters

Pharmacokinetic parameters will be calculated by standard non-compartmental analysis according to current working practices and using the currently supported version of WinNonlin All calculations of non-compartmental parameters will be based on actual

sampling times. Pharmacokinetic parameters listed will be determined from the plasma concentration-time data, as data permits.

Parameter	Parameter Description
AUC(0-t)	Area under the concentration-time curve from time zero to the time of the last quantifiable concentration (C(t))
AUC(0-inf)	Area under the concentration-time curve from time zero and extrapolated to "infinity"
Cmax	Maximum observed concentration,
tmax	Time to reach Cmax,
CL	Clearance
t½	Apparent terminal half-life
tlast	Time of last quantifiable concentration

NOTES:

- Additional parameters may be included as required.

9.2.1. Population of Interest

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

9.2.2. Statistical Methods

Details of the planned displays are provided in Appendix 9 and will be based on GSK data standards and statistical principles.

Unless otherwise specified, endpoints / variables defined in the section above will be summarised using descriptive statistics, graphically presented (where appropriate) and listed.

10. PHARMACODYNAMIC AND BIOMARKER ANALYSES

10.1. IHC parameters

Cells in lesional biopsies are measured by IHC. There are 3 (epidermis thickness is not IHC parameters – separate section) endpoints of interest: LAG3+, CD3+, Ki67 (SI dataset: BIOMARK).

In the dataset, perivascular infiltrates (PVI) cells are also collected:

- HV (DTH): The PVI are used to locate region of interest high power fields (HPFs) for CD3+ and Lag3+ analysis. It is not a biomarker reportable (only listing)
- PVI is not required for PsO cohorts as regions of interest for HPFs are defined by an alternative approach.

In HV (DTH) LAG3+ and CD3+ were assessed across 3 layers (slices) of the biopsy. A layer represents a section from the lesional skin biopsy tissue. Layers 1-3 represent sections obtained by cutting into the biopsy tissue block at different depths. 10 sections were discarded between each level.

In PsO, LAG3+, CD3+, Ki67 were assessed across 1 layer. The regions of interest (HPFs) for LAG3+ and CD3+ are located in either the epidermis or the superficial dermis. For Ki67, the regions of interest (HPFs) are located in the epidermis only. Epidermal thickness is also only measured in the epidermis.

LAG3+, CD3+ and Ki67 are measured in up to 5 HPFs per layer for HV or epidermis / dermis for PsO. A minimum of 3 HPFs should be present in order for samples to be evaluated.

10.1.1. Endpoint / Variables

Parameter	Endpoint	Derivation	HV (DTH)	PsO
LAG3+	Total number of LAG3+ cells HPFs (A)	For each layer (HV) or epidemis/dermis (PsO) 1. if **5 HPFs** for **all** subjects total # of cells (per layer for HV or epidermis/dermis for PsO) = sum of cells in all HPFs (1-5) 2. If **3 or 4 HPFs** for at least one subject Total # of cells of 3/4 HPFs for **all** subjects = sum of HPFs 1-3, or sum of HPFs 1-4 3. If less than **3 HPFs** for some subjects (i.e 0, 1 or 2 HPFs), set to missing for these subjects Note: There is only 1 layer for PsO	Y (3 layers)	Y (epidermis and dermis)
	Total number of LAG3+ cells averaged across skin layers	Sum of (A) as defined above for layers 1, 2 and-3 / 3 layers Note: there will be always 3 layers per subject and timepoint	Y	N
		Programming notes: 1. Exclude from summary tables/figures if missing (but will be included in listing and individual plots) 2. No LLQ/ULQ for these assays 3. If only some values HPF are missing, it's always in sequential order: e.g. it's not possible to have only HPF2 missing, this should be HPF5		
CD3+	Total number of CD3+ cells HPFs (B)	Same derivation as for LAG3+	Y (3 layers)	Y (epidermis and dermis)
	Total number of CD3+ cells averaged across skin layers	Same derivation as for LAG3+	Y	N
	CD3+ (cells/mm^2)	(B) as defined above / number of HPFs	N	Y

Parameter	Endpoint	Derivation	HV (DTH)	PsO
		assessed (from 3 to 5 depending on the min number of HPFs available)		(epidermis and dermis)
Perivascular infiltrates (PV) cells		No derivation	Y	N
Ki67	Total number of Ki67+ cells HPFs (C)	Same as for as for LAG3+ but only for epidermis	N	Y (epidermis)
	Ki67 (cells/mm^2)	Same as for CD3+ (cells/mm^2) (C) as defined above / number of HPFs assessed (from 3 to 5 depending on the min number of HPFs available)	N	Y (epidermis)

10.1.2. Summary Measure

Absolute, change from baseline and percent change from baseline are of interest for HV and PsO.

Data will be available at baseline and Day 4 (for HV) or Day 29 (for PsO).

10.1.3. Population of Interest

The primary pharmacodynamics and biomarker analyses will be based on the Safety population, unless otherwise specified.

10.1.4. Statistical Methods

Details of the planned displays are provided in Appendix 9 and will be based on GSK data standards and statistical principles.

Unless otherwise specified, endpoints / variables defined in Section 10.1.1 will be summarised using descriptive statistics, graphically presented (where appropriate) and listed.

10.1.4.1. Statistical Methodology Specification

Endpoint / Variables

o Change from baseline in
  o LAG3+ (total cells averaged across 3 skin layers for HV and total cells in dermis and epidermis separately for PsO)
  o CD3+:
  ▪ total cells averaged across 3 skin layers for HV
  ▪ cells per mm^2 in dermis and epidermis separately for PsO
o For epidermis only (PsO), change from baseline in
  o Ki67 (cells/mm)

Model Specification
• Endpoints will be statistically analysed using an ANCOVA model. • Terms fitted in the model will include: Treatment and baseline
Model Results Presentation
• Summary table of the LS means and 95% CI for CFB (by treatment) • [No plot as only 1 post-dose assessment]

10.2. Epidermis thickness (only for PsO)

10.2.1. Endpoint / Variables

Epidermal thickness is measured by making 35 transect measurements across the entire diameter of the epidermis. The values are in the following SI dataset: MI.

Parameter	Endpoint	Derivation	HV (DTH)	PsO
Epidermis thickness	Epidermis thickness (µm)	Mean of the 35 measurements	N	Y (epidermis)

10.2.2. Summary Measure

Absolute, change from baseline and percent change from baseline are of interest for PsO.

Data will be available at baseline and Day 29 (for PsO).

10.2.3. Population of Interest

The primary pharmacodynamics and biomarker analyses will be based on the Safety population, unless otherwise specified.

10.2.4. Statistical Methods

Details of the planned displays are provided in Appendix 9 and will be based on GSK data standards and statistical principles.

Unless otherwise specified, endpoints / variables defined in Section 10.2.1 will be summarised using descriptive statistics, graphically presented (where appropriate) and listed.

10.2.4.1. Statistical Methodology Specification

Endpoint / Variables
○ For epidermis only (PsO), change from baseline in ○ Epidermis thickness (µm)
Model Specification
• Endpoints will be statistically analysed using an ANCOVA model. • Terms fitted in the model will include: Treatment and baseline
Model Results Presentation
• Summary table of the LS means and 95% CI for CFB (by treatment) • [No plot as only 1 post-dose assessment]

10.3. Other PD parameters

10.3.1. Endpoint / Variables

The following endpoints are of interest (SI dataset: BIOMARK):

- s-LAG3 parameters - no derivation is needed
- Flow cytometry – 6 key parameters only described below:

Marker code	Marker	Type (BITESTCD)	Unit (BISTRESU)
CDX226	CD45+ CD3- CD19+	Concentration	CELLS/UL
CDX258	CD45+ CD3+ CD69+	Concentration	CELLS/UL
CDX444	CD4+CD45RA+1B4+	Number of events	COUNT
CDX445	CD4+CD45RA+J11L1+	Number of events	COUNT
CDX446	CD4+CD45RA-1B4+	Number of events	COUNT
CDX447	CD4+CD45RA-J11L1+	Number of events	COUNT

For 4 of these endpoints (CDX444, CDX445, CDX446, CDX447), the derivation below should be applied (same derivation as for PK analyses):

The count at each time point is the difference: BISTRESN value in the row with BIEXPS = “Stained Sample - T cell markers including J11 and 1B4” - BISTRESN value in the row with BIEXPS = ‘LAG3 FMO Control - T cell markers excluding J11 and 1B4’

10.3.2. Summary Measure

- S-LAG3: absolute, change from baseline for total soluble LAG3 concentrations
- Flow cytometry: absolute, change from baseline and **percent of baseline**, where the percent of baseline is: $100 * \frac{\text{post-dose visit value}}{\text{Baseline}}$

10.3.3. Population of Interest

The primary pharmacodynamics and biomarker analyses will be based on the Safety population, unless otherwise specified.

10.3.4. Statistical Methods

Details of the planned displays are provided in Appendix 9 and will be based on GSK data standards and statistical principles.

Unless otherwise specified, endpoints / variables defined in Section 10.3.1 will be summarised using descriptive statistics, graphically presented and listed.

10.4. Transcriptomics (biopsy and blood)

10.4.1. Endpoint / Variables

The following endpoints are of interest:

- Blood transcriptomics (HV, PSO):
    1. 2 genes: LAG-3 long, LAG-3 short
    2. 2 housekeeping genes: POL2RG, POL2RJ
- Biopsy (skin) transcriptomics (PSO only)
    1. 18 genes (including the 2 common genes for blood transcriptomics)

LAG-3 Long	LAG-3 Long Gene mRNA Expression
LAG-3 short	LAG-3 short Gene mRNA Expression
IL-17A	IL-17A Gene mRNA Expression
IL-17F	IL-17F Gene mRNA Expression
IL-22	IL-22 Gene mRNA Expression
IL-23	IL-23a Gene mRNA Expression
IFNg	IFNg Gene mRNA Expression
IL-12A	IL-12A Gene mRNA Expression
IL-10	IL-10 Gene mRNA Expression
FOXP3	FOXP3 Gene mRNA Expression
S100A12	S100A12 Gene mRNA Expression
Ki67	Ki67 Gene mRNA Expression

K16	K16 Gene mRNA Expression
CD3g	CD3g Gene mRNA Expression
TSPAN8	TSPAN8 Gene mRNA Expression
CLDN8	CLDN8 Gene mRNA Expression
CCL27	CCL27 Gene mRNA Expression
CDHR1	CDHR1 Gene mRNA Expression

2. 2 housekeeping genes (same as for blood transcriptomics): POL2RG, POL2RJ

Data available (SI dataset: PF – pharmacogenomics findings):

- Analyte (Collected Specimen Type code): skin or blood

- Gene (Genetic Region of Interest code)

- Type of values (Pharmacogenomics Test code)

  - Cycle times (Ct) – 3 per subject
  - Mean of the Cts
  - Delta Ct
  - Delta Delta Ct
  - Fold change

No derivation is needed by S&P as provided by the vendor.

10.4.2. Summary Measure

For all endpoints above:
- Delta delta Ct baseline versus post-baseline visit
- Fold change from baseline to post-baseline visit: always strictly positive (=2^ - delta delta Ct)

Post-baseline visits:
- HV (DTH and non DTH): Day 2 (Blood only)
- PsO: Day 2 (blood), Day 15 (skin, only cohort 7, removed for cohorts 8 and 9 in amendment 8), Day 29 (skin)

10.4.3. Population of Interest

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

10.4.4. Statistical Methods

Details of the planned displays are provided in Appendix 9 and will be based on GSK data standards and statistical principles.

Unless otherwise specified, endpoints / variables will be summarised using descriptive statistics, graphically presented and listed.

11. PHARMACOKINETIC / PHARMACODYNAMIC ANALYSES

The PK/PD analyses will be based on the PK population, unless otherwise specified.

The primary goal of this analysis is to characterise the PK/PD relationship of GSK2831781 administered IV in healthy subjects and psoriasis patients. The influence of subject demographics and baseline characteristics will be investigated.

A summary of the planned population PK/PD analyses are outlined below:

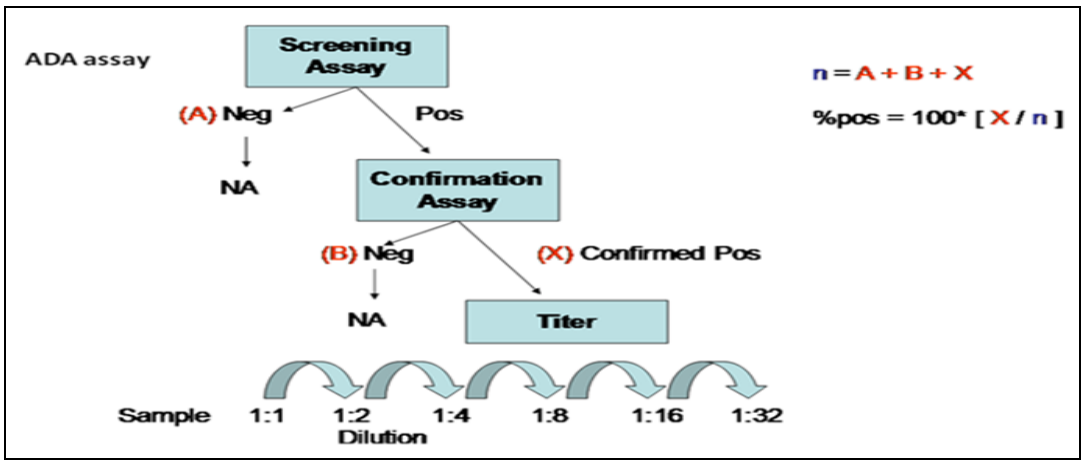
- Drug GSK2831781 plasma concentration and corresponding receptor occupancy data will be subjected to nonlinear mixed effects modelling using the program NONMEM to develop a population PK/PD model.
- To support this analysis a PK/PD dataset will be generated. The details for the dataset specifications are provided in Appendix 7.
- Detailed PK/PD methodology is presented in Appendix 7.

A PK/PD report will be produced by CPMS, and will be included as an appendix to the CSR.

12. IMMUNOGENICITY ANALYSES

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

Information from the screening assay contributes to the number at risk for the calculation of % positive. The calculation of 'n' is displayed in the diagram below as a guide.



There are no planned statistical analyses.

Details of the planned displays are provided in Appendix 9 and will be based on GSK data standards and statistical principles.

13. BAYESIAN ANALYSES (PART B)

To aid decision making, the following posterior probabilities, will be evaluated:

For **PASI/PLSS**:
- Difference of interest = Difference (active – placebo) in % CFB,
- Probabilities of interest
  P(difference < 0)
  P(difference ≤ 10%)
  P(difference ≤ 20%)
  P(difference ≤ 30%)
  P(difference ≤ 40%)

For **total LAG3 cells** for the epidermis and dermis:
- Difference of interest = Difference (active – placebo) in % CFB
- Probabilities of interest
  P(difference < 0)
  P(difference ≤ 30%)

For **Ki67 and epidermis thickness**:
- Difference of interest = Difference (active – placebo) in CFB
- Probabilities of interest
  P(difference < 0)

The active and placebo treatment groups mentioned above are defined as follows:
- Subjects in the active group are defined as psoriasis patients that received the doses 1.5mg/kg and 5mg/kg (pooled cohorts 8 and 9). In total, 12 subjects are on active.
- Subjects in the placebo group are defined as psoriasis patients that received placebo in cohorts 7-9. In total, 9 subjects are on placebo.

The propobabilities described above may also be calculated for each dose (i.e. 1.5mg/kg versus placebo and 5mg/kg versus placebo).

For PASI and PLSS, the change from baseline to lowest non-missing post-baseline response will be derived for each subject, considering all their available asssessments out to day 85. The Bayesian analyses will be conducted for these derived endpoints to provide an overall summary, as oppose to a distinct assessment at each timepoint. For the other endpoints changes from baseline to day 29 will be assessed.

Changes from baseline in each parameter will be analysed using a linear regression, including treatment (active and control as defined above) and baseline score:

$Y_i \sim \text{Normal}(\mu_i, \text{precision} = \tau)$

$\mu_i = \beta_0 + \beta_1 Base_i + \beta_2 Treatment_i$

Where Y_i is the observed change from baseline response for each subject as defined above.

Non-informative conjugate prior distributions are assigned to the unknown parameters:

- Intercept and slope coefficients: β_0 , $\beta_1, \beta_2 \sim$ Normal(0, precision = $10^{-3)}$
  Sensitivity analysis with precion=0.1
- Between-subject precision (1/variance): $\tau \sim$ Gamma (shape = 0.001, rate = 0.001) , i.e. E(τ) = 1

One MCMC chain will be run. At least 10 000 iterations will be used for the burn-in period as well as for the inference. The number of iterations may be increased to ensure that the ratio MCSE/SD for all the parameters in the model is ≤ 0.01.

Visual inspection of MCMC output (including, but not limited to, trace and autocorrelation plots) will be used to assess the convergence.

The posteriror distribution of the difference in % CFB will be generated as β_2 / *mean_Base*. The later is modelled as a normal distribution and assumed that there is no treatment difference for baseline values before treatment: $Base_i \sim Normal(mean\_Base,$ precision = $\tau\_Base)$. Non-informative conjugate prior distributions are assigned to the unknown parameters:

- *mean_Base* ~ Normal(0, precision = $10^{-3)}$
- Between-subject precision (1/variance): $\tau\_Base \sim$ Gamma (shape = 0.001, rate = 0.001) , i.e. E(τ) = 1

The posterior probabilities that the difference in %CFB or CFB is above a pre-defined threshold will be calculated based on the above posterior distributions.

Results will be displayed in a table, with the number of subjects in each group, active and control.

14. APPENDICES

14.1. Appendix 1: Protocol Defined Schedule of Events

14.1.1. Healthy volunteers (no DTH)

Protocol Activity	Base-line	In Clinic Period									Out Patient Visits										
		Day 1						Day 2	Day 3	Day 4	Day 8										
	Day -1	Pre-dose	0 hour	2 hour post-infusion start	4 hour post-infusion start	6 hour post-infusion start	12 hour post-infusion start	24 hour post-infusion start	48 hour post-infusion start	72 hour post-infusion start	168 hour post-infusion start	Day 11	Day 15	Day 18	Day 22	Day 25[a]	Day 29[k]	Day 43	Day 57[l]	Day 85	Day 121
Window											±1d	±1d	±1d	±1d	±1d	±1d	±1d	±2d	±2d	±2d	±3d
Admission to the unit	X																				
Discharge from the unit										X											
Brief physical	X																				
Urine Drug and Alcohol Screen	X																				
Administer IV Dose (2 hour infusion)			◄----► [i]																		
Safety Assessments																					
Vital Signs	X	X		X	X	X	X	X	X	X	X		X		X		X	X	X	X	X
12 - Lead ECG	X[j]	X	◄----► [b]			X				X											
Concomitant Medications	◄----------																				----►
Adverse Events Assessment / SAE's[c]	◄----------																				----►
Laboratory Assessments																					
Haematology	X					X	X			X	X	X	X	X	X	X	X	X	X	X	X
Chemistry	X					X[d]	X[d]			X	X		X		X		X	X	X	X	X
Urinalysis	X					X	X			X	X		X		X		X	X	X	X	X

Protocol Activity	Base-line	In Clinic Period									Out Patient Visits										
		Day 1						Day 2	Day 3	Day 4	Day 8										
	Day -1	Pre-dose	0 hour	2 hour post-infusion start	4 hour post-infusion start	6 hour post-infusion start	12 hour post-infusion start	24 hour post-infusion start	48 hour post-infusion start	72 hour post-infusion start	168 hour post-infusion start	Day 11	Day 15	Day 18	Day 22	Day 25[a]	Day 29[k]	Day 43	Day 57[l]	Day 85	Day 121
Window											±1d	±1d	±1d	±1d	±1d	±1d	±1d	±2d	±2d	±2d	±3d
CMV and EBV serology sample	X																				
Viral load sample (CMV, EBV, HSV, VZV)[e]	X																				
PK Sample[f]		◄													►						
Immunogenicity Sample		X									X						X			X	
Immune Cell Phenotyping[g]		X				X		X		X	X		X				X		X	X	X
CD16 and LAG-3 Receptor occupancy		X				X		X		X	X		X				X		X	X	X
Cytokine Sample		X				X	X	X	X												
G-CSF Sample		X				X		X		X	X		X				X	X	X	X	X
sLAG-3 Sample		X				X		X		X	X		X				X	X	X	X	X
Blood Transcriptomics Sample		X						X													
Ex Vivo Antigen/Cytokine Stimulation Test		X						X													

Protocol Activity	Base-line	In Clinic Period									Out Patient Visits										
		Day 1						Day 2	Day 3	Day 4	Day 8										
	Day -1	Pre-dose	0 hour	2 hour post-infusion start	4 hour post-infusion start	6 hour post-infusion start	12 hour post-infusion start	24 hour post-infusion start	48 hour post-infusion start	72 hour post-infusion start	168 hour post-infusion start	Day 11	Day 15	Day 18	Day 22	Day 25[a]	Day 29[k]	Day 43	Day 57[l]	Day 85	Day 121
Window											±1d	±1d	±1d	±1d	±1d	±1d	±1d	±2d	±2d	±2d	±3d
In vitro LAG-3+ activity		X		X							X										
PGx Sample	X[h]																				

a. Cohort 0.0003mg/kg last out patient visit will be on Day 25.
b. Continuous 2-lead ECG during infusion. Only significant abnormalities during this time will be databased.
c. A targeted physical examination may take place if guided by AE reporting relating to Section 6.3.4, Section 6.3.5 and Section 6.3.6..
d. Liver Chemistry and CRP only
e. Viral load sample for storage as baseline. If symptoms suggestive of viral infection develop then a sample will be taken and analysed with the baseline sample (See Section 6.3).
f. See Pharmacokinetic time and events table for dose specific timepoints.
g. Additional blood samples may be taken during the study if subject develops infection in order to measure LAG-3+ cells or other parameters as may be clinically or immunologically indicated.
h. Pharmacogenetics sample can be taken any time after consent is signed.
i. To calculate the correct dose, weight must be measured on Day -1 or Day 1 pre-dose.
j. Triplicate. Only required if screening ECG not within 35 days of Day 1.
k. Cohort 0.0015mg/kg last out patient visit will be on Day 29.
l. Cohort 0.0075mg/kg last out patient visit will be on Day 57.

14.1.2. Healthy volunteers (DTH subjects)

Protocol Activity	1st Challenge		In Clinic Period										Out Patient Visits										
			Day 28	Day 29 (Day 1)							Day 30 (Day 2 post-dose)	Day 31 (Day 3 post-dose)	Day 32 (Day 4 post-dose)										
	Day 1	Day 3	Day 28	Pre-dose	0 hour	2 hour post-infusion start	4 hour post-infusion start	6 hour post-infusion start	12 hour post-infusion start	24 hour post-infusion start	48 hours post-infusion start	72 hour post-infusion start	Day 36 (Day 8 post-dose)	Day 39 (Day 11 post-dose)	Day 43 (Day 15 post-dose)	Day 46 (Day 18 post-dose)	Day 50 (Day 22 post-dose)	Day 53 (Day 25 post-dose)	Day 57 (Day 29 post-dose)	Day 71 (Day 43 post-dose)	Day 85 (Day 57 post-dose)	Day 113 (Day 85 post-dose)	Day 149 (Day 121 post-dose)
Window			±3d										±1d	±1d	±1d	±1d	±1d	±1d	±1d	±2d	±2d	±2d	±3d
Admission to the unit			X																				
Discharge from the unit												X											
Brief Physical	X		X																				
Urine Drug and Alcohol Screen	X																						
Administer IV Dose (2 hour infusion)					◄----► n																		
Safety Assessments																							
Vital Signs	X	X		X		X	X	X	X	X	X	X	X		X		X		X	X	X	X	X
12 - Lead ECG	Xa			X	◄----► b		X					X											
Concomitant Medications	◄----------																						----------►
Adverse Events Assessment / SAE's[c]	◄----------																						----------►

Protocol Activity	1st Challenge		In Clinic Period										Out Patient Visits										
			Day 28	Day 29 (Day 1)							Day 30 (Day 2 post-dose)	Day 31 (Day 3 post-dose)	Day 32 (Day 4 post-dose)										
	Day 1	Day 3	Day 28	Pre-dose	0 hour	2 hour post-infusion start	4 hour post-infusion start	6 hour post-infusion start	12 hour post-infusion start	24 hour post-infusion start	48 hours post-infusion start	72 hour post-infusion start	Day 36 (Day 8 post-dose)	Day 39 (Day 11 post-dose)	Day 43 (Day 15 post-dose)	Day 46 (Day 18 post-dose)	Day 50 (Day 22 post-dose)	Day 53 (Day 25 post-dose)	Day 57 (Day 29 post-dose)	Day 71 (Day 43 post-dose)	Day 85 (Day 57 post-dose)	Day 113 (Day 85 post-dose)	Day 149 (Day 121 post-dose)
Window			±3d										±1d	±1d	±1d	±1d	±1d	±1d	±1d	±2d	±2d	±2d	±3d
Efficacy Assessments																							
Visual Arm Inspection	Xe									Xe													
ID PPD Challenge	Xf									Xf													
Bleb/ILH Assessment	Xe									Xe													
Ball Point Pen Technique		X										X	X		X		X						
Skin Biopsy		Xg										Xg											

Protocol Activity	1st Challenge		In Clinic Period										Out Patient Visits										
			Day 28	Day 29 (Day 1)						Day 30 (Day 2 post-dose)	Day 31 (Day 3 post-dose)	Day 32 (Day 4 post-dose)											
	Day 1	Day 3	Day 28	Pre-dose	0 hour	2 hour post-infusion start	4 hour post-infusion start	6 hour post-infusion start	12 hour post-infusion start	24 hour post-infusion start	48 hours post-infusion start	72 hour post-infusion start	Day 36 (Day 8 post-dose)	Day 39 (Day 11 post-dose)	Day 43 (Day 15 post-dose)	Day 46 (Day 18 post-dose)	Day 50 (Day 22 post-dose)	Day 53 (Day 25 post-dose)	Day 57 (Day 29 post-dose)	Day 71 (Day 43 post-dose)	Day 85 (Day 57 post-dose)	Day 113 (Day 85 post-dose)	Day 149 (Day 121 post-dose)
Window			±3d										±1d	±1d	±1d	±1d	±1d	±1d	±1d	±2d	±2d	±2d	±3d
Laboratory Assessments																							
Haematology	X[h]		X					X	X			X	X	X	X	X	X	X	X	X	X	X	X
Chemistry	X[h]		X					X[i]	X[i]			X	X		X		X		X	X	X	X	X
Urinalysis	X[h]		X					X	X			X	X		X		X		X	X	X	X	X
CMV and EBV serology sample			X																				
Viral load sample (CMV, EBV, HSV, VZV)[j]			X																				
Immunogenicity Sample				X									X						X			X	
PK Sample[k]				◄																		►	
Immune Cell Phenotyping[l]				X				X		X		X	X		X				X		X	X	X
CD16 and LAG-3 Receptor occupancy				X				X		X		X	X		X				X		X	X	X
Cytokine Sample				X				X	X	X	X												
G-CSF Sample				X				X		X		X	X		X				X	X	X	X	X

Protocol Activity	1st Challenge		In Clinic Period										Out Patient Visits										
			Day 28	Day 29 (Day 1)						Day 30 (Day 2 post-dose)	Day 31 (Day 3 post-dose)	Day 32 (Day 4 post-dose)											
	Day 1	Day 3	Day 28	Pre-dose	0 hour	2 hour post-infusion start	4 hour post-infusion start	6 hour post-infusion start	12 hour post-infusion start	24 hour post-infusion start	48 hours post-infusion start	72 hour post-infusion start	Day 36 (Day 8 post-dose)	Day 39 (Day 11 post-dose)	Day 43 (Day 15 post-dose)	Day 46 (Day 18 post-dose)	Day 50 (Day 22 post-dose)	Day 53 (Day 25 post-dose)	Day 57 (Day 29 post-dose)	Day 71 (Day 43 post-dose)	Day 85 (Day 57 post-dose)	Day 113 (Day 85 post-dose)	Day 149 (Day 121 post-dose)
Window			±3d										±1d	±1d	±1d	±1d	±1d	±1d	±1d	±2d	±2d	±2d	±3d
sLAG-3 Sample				X				X		X		X	X		X				X	X	X	X	X
Blood Transcriptomics Sample				X						X													
Ex vivo antigen/cytokine stimulation				X						X													
In vitro LAG-3+ activity				X		X							X										
PGx Sample	X[m]																						

a. Triplicate. Only required if screening ECG not within 35 days of Day 1.
b. Continuous 2-lead ECG during infusion. Only significant abnormalities during this time will be databased.
c. A targeted physical examination may take place if guided by AE reporting relating to Section 6.3.4, Section 6.3.5 and Section 6.3.6..
d. Must be performed before ID PPD Challenge
e. Bleb is assessed 5 minutes after ID injection and the immediate local hypersensitivity assessment 15-30 minutes after ID injection.
f. See Section 5.10.1 for details.
g. Only biopsy from one of the PPD sites preferably from the subjects non-dominant arm.
h. If safety labs have been taken ≤7 days prior to challenge then these safety labs are not required. These samples can be taken on Day 1 or Day -1.
i. Liver Chemistry and CRP only
j. Viral load sample for storage as baseline. If symptoms suggestive of viral infection develop then a sample will be taken and analysed with the baseline sample (See Section 6.3).
k. See Pharmacokinetic time and events table for dose specific timepoints.
l. Additional blood samples may be taken during the study if subject develops infection in order to measure LAG-3+ cells or other parameters as may be clinically or immunologically indicated.
m. Pharmacogenetics sample can be taken any time after consent is signed.
n. To calculate the correct dose, weight must be measured on Day 28 or Day 29 pre-dose.

14.1.3. Psoriasis patients

Protocol Activity	Base-line	In Clinic Period										Out Patient Visits [l]												
		Day 1							Day 2	Day 3	Day 4	Day 8												
	Day -1	Pre-dose	0 hour	2 hour post-infusion start	4 hour post-infusion start	6 hour post-infusion start	12 hour post-infusion start	24 hour post-infusion start	48 hour post-infusion start	72 hour post-infusion start	168 post-infusion start	Day 11	Day 15	Day 18	Day 22	Day 25	Day 29	Day 36 [n]	Day 43	Day 57	Day 71 [n]	Day 85	Day 121
Window											±1d	±1d	±1d	±1d	±1d	±1d	±1d	±1d	±2d	±2d	±2d	±2d	±3d
Admission to the unit	X																						
Discharge from the unit										X													
Reassess 2 target lesions for suitability	X																						
Brief physical	X																						
Urine Drug and Alcohol Screen	X																						
Administer IV Dose (2 hour infusion)			◄----► [j]																				
Safety Assessments																							
Vital Signs	X	X		X	X	X	X	X	X	X	X		X		X		X		X	X		X	X
12 - Lead ECG	X [k]	X	◄----► [a]			X				X													
Concomitant Medications			◄----------																			►	
Adverse Events / SAEs [b]			◄----------																			►	

Protocol Activity	Base-line	In Clinic Period										Out Patient Visits [l]												
		Day 1							Day 2	Day 3	Day 4	Day 8												
	Day -1	Pre-dose	0 hour	2 hour post-infusion start	4 hour post-infusion start	6 hour post-infusion start	12 hour post-infusion start	24 hour post-infusion start	48 hour post-infusion start	72 hour post-infusion start	168 post-infusion start	Day 11	Day 15	Day 18	Day 22	Day 25	Day 29	Day 36 [n]	Day 43	Day 57	Day 71 [n]	Day 85	Day 121
Window											±1d	±1d	±1d	±1d	±1d	±1d	±1d	±1d	±2d	±2d	±2d	±2d	±3d
Efficacy Assessments																							
Psoriatic Body Surface Area	X												X				X		X			X	X
Psoriasis Area Severity Index	X												X				X		X			X	X
Psoriatic Lesion Severity Score	X [c]												X [c]				X [c]		X [d]			X [d]	X [d]
Phys. Global Assessment Scale	X												X				X		X			X	X
Skin Biopsy	X																X						
Photograph of index lesion	X												X				X		X			X	X
Photograph of biopsy lesion [e]	X																X						

Protocol Activity	Base-line	In Clinic Period									Out Patient Visits [l]												
		Day 1						Day 2	Day 3	Day 4	Day 8												
	Day -1	Pre-dose	0 hour	2 hour post-infusion start	4 hour post-infusion start	6 hour post-infusion start	12 hour post-infusion start	24 hour post-infusion start	48 hour post-infusion start	72 hour post-infusion start	168 post-infusion start	Day 11	Day 15	Day 18	Day 22	Day 25	Day 29	Day 36 [n]	Day 43	Day 57	Day 71 [n]	Day 85	Day 121
Window											±1d	±1d	±1d	±1d	±1d	±1d	±1d	±1d	±2d	±2d	±2d	±2d	±3d
Laboratory Assessments																							
Haematology	X[o]					X	X[o]			X[o]	X[o]	X	X	X	X	X	X		X	X		X	X
Chemistry	X					X [f]	X [f]			X	X		X		X		X		X	X		X	X
Urinalysis	X					X	X			X	X		X		X		X		X	X		X	X
Urine Pregnancy Test (FRP)	X																X			X		X	X
CMV and EBV serology sample	X																						
Viral load sample (CMV, EBV, HSV, VZV) [g]	X																						
Immunogenicity Sample		X									X						X					X	
PK Sample [h]				◄																			►
Immune Cell Phenotyping [i] (Flow)		X				X		X		X	X		X				X		X	X		X	X
Immune Cell Phenotyping [m] (Chip)		X		◄							[m]												►
CD16 and LAG-3 Receptor occupancy		X				X		X		X	X		X				X		X	X		X	X

Protocol Activity	Base-line	In Clinic Period									Out Patient Visits [l]												
		Day 1						Day 2	Day 3	Day 4	Day 8												
	Day -1	Pre-dose	0 hour	2 hour post-infusion start	4 hour post-infusion start	6 hour post-infusion start	12 hour post-infusion start	24 hour post-infusion start	48 hour post-infusion start	72 hour post-infusion start	168 post-infusion start	Day 11	Day 15	Day 18	Day 22	Day 25	Day 29	Day 36 [n]	Day 43	Day 57	Day 71 [n]	Day 85	Day 121
Window											±1d	±1d	±1d	±1d	±1d	±1d	±1d	±1d	±2d	±2d	±2d	±2d	±3d
Cytokine Sample		X				X	X	X	X														
G-CSF Sample		X				X		X		X	X		X				X		X	X		X	X
sLAG-3 Sample		X				X		X		X	X		X				X		X	X		X	X
Blood Transcriptomics Sample		X						X															
PGx Sample	X																						

a. Continuous 2-lead ECG during infusion. Only significant abnormalities during this time will be databased.
b. A targeted physical examination may take place if guided by AE reporting relating to Section 6.3.4, Section 6.3.5 and Section 6.3.6..
c. PLSS will be recorded for the index lesion and the biopsy lesion (prior to the biopsy being performed).
d. Index lesion only.
e. Photographs of the biopsy lesion will be taken before the skin biopsy.
f. Liver Chemistry and CRP only
g. Viral load sample for storage as baseline. If symptoms suggestive of viral infection develop then a sample will be taken and analysed with the baseline sample (See Section 6.3).
h. See Pharmacokinetic time and events table for dose specific timepoints.
i. Additional blood samples may be taken during the study if e.g. subject develops infection (measure LAG-3+ cells), hypersensitivity reactions (serum tryptase), signs/symptoms suggestive of viral reaction, or other parameters as may be clinically or immunologically indicated (See Section 6.3).
j. To calculate the correct dose, weight must be measured on Day -1 or Day 1 pre-dose.
k. Triplicate. Only required if screening ECG not within 35 days of Day 1.
l. Investigator/designee should remind subjects to comply with contraception requirements on an ~ monthly basis until Follow-Up (either at study visits or by telephone call).
m. Immune Phenotyping (Chip) Cohort 7: at Baseline, 6 hours post-start of infusion, Day 8 and 15. Cohorts 8 and 9: at Baseline, 6 hours post start of infusion, Day 43 and 85.
n. Additional visit introduced at Day 36 (Cohort 8 only) and Day 71 (Cohort 9 only).
o. Samples taken for haematology at Day -1, 12 hours, 72 hours and 168 hours are to include analysis for CD3, CD4 and CD8 lymphocyte subsets.

14.2. Appendix 2: Study Phases and Treatment Emergent Adverse Events

14.2.1. Study Phases for Concomitant Medication

Study Phase	Definition
Prior	If medication end date is not missing and is before 28 days prior to screening visit
Concomitant	Any medication that is not a prior, and up to the last scheduled visit attended (follow-up or combined FU/surveillance)
Off-treatment	Medication started between the last scheduled visit and the surveillance visit will be included in the listing, and flagged.
Refer to Appendix 5 for handling of missing and partial dates for concomitant medication. Use the rules in this table if concomitant medication date is completely missing.	

14.2.2. Treatment Emergent Flag for Adverse Events

Flag	Definition
Prior	Any starting date before 1st dose
Treatment Emergent	Any starting date between 1st dose and last scheduled visit (follow-up or combined FU/surveillance)
Off treatment	AE occurring between the last scheduled visit and the surveillance visit will be included in the listing, and flagged.
Refer to Appendix 5 for handling of missing and partial dates for AE. Use the rules in this table if date is completely missing.	

14.3. Appendix 3: A&R Data sets

14.3.1. Subject-Level Variables

14.3.1.1. ADA Status

ADASTACD/ADASTAT should be included in POP, AE plus any other data sets with outputs split by ADA status.

- If a subject has one “positive” record for the confirmatory assayin IMGEN (IGSCATCD=2 and IGORRSCD=1) at screening then set to positive (ADASTATCD=1 / ADASTAT=”ADA Positive”)
- Otherwise set to negative (ADASTATCD=2 / ADASTAT=”ADA Negative”)

14.3.1.2. Treatment

TRTCD/TRTGRP should be completed as specified in RAP Section 5.1.

Complete as follows:

1. Merge DM data sets RAND and RANDALL by RANDNUM to get the PTRTGRP and SCHEDNUM/SCHEDTX for each SUBJID.
2. TRTCD/TRTGRP are then completed from PTRTGRP and SCHEDNUM as described below.
3. Check the ADA status (IMGEN screening data) of all subjects compared with the treatment group assignment.
4. Unrandomised subjects (i.e. subjects with no RANDNUM) will have TRTCD/TRTGRP missing.
5. The actual treatment variables ATRTCD/ATRTGRP should just be copied from TRTCD/TRTGRP unless any subject is known to have taken the wrong treatment. In addition, ATRTCD/ATRTGRP can be set to 888/”No Treatment” for untreated subjects as in the SPOTFIRE version of POP.

14.4. Appendix 4: Data Display Standards & Handling Conventions

14.4.1. Reporting Process

Software	
• The currently supported versions of SAS software will be used.	
Reporting Area	
HARP Server	us1salx00259
HARP Compound	\ARPROD\GSK2831781\MID200630
Analysis Datasets	
• Analysis datasets will be created according to Legacy GSK A&R dataset standards.	
Generation of RTF Files	
• RTF files will be generated for Interim 2 and SAC.	

14.4.2. Reporting Standards

General

• The current GSK Integrated Data Standards Library (IDSL) will be applied for reporting, unless otherwise stated (IDSL Standards Location: https://spope.gsk.com/sites/IDSLLibrary/SitePages/Home.aspx):
• Under Supporting Documentation > Component > Statistical Displays
  • 4.03 to 4.23: General Principles
  • 5.01 to 5.08: Principles Related to Data Listings
  • 6.01 to 6.11: Principles Related to Summary Tables
  • 7.01 to 7.13: Principles Related to Graphics
• Do not include subject level listings in the main body of the GSK Clinical Study Report. All subject level listings should be located in the modular appendices as ICH or non-ICH listings

Formats
• 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, unless otherwise stated. • 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.

Unscheduled Visits	
• Unscheduled visits will not be included in by-visit summary tables and figures. • Unscheduled visits will be considered when deriving maximum/worse post-baseline values. • All unscheduled visits will be included in listings.	
Descriptive Summary Statistics	
Continuous Data	Refer to IDSL Statistical Principle 6.06.1
Categorical Data	N, n, frequency, %
Graphical Displays	
• Refer to IDSL Statistical Principals 7.01 to 7.13.	
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. o Example 1: 2 Decimal Places= '< x ' becomes x – 0.01 o Example 2: 1 Decimal Place= '> x' becomes x + 0.1 o Example 3: 0 Decimal Places= '< x' becomes x – 1	

14.4.3. Reporting Standards for 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)
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, tlast

14.5. Appendix 5: Reporting Standards for Missing Data

14.5.1. 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 participants excluded from the summaries and/or statistical analyses will be documented along with the reason for exclusion in the clinical study report.

14.5.1.1. Handling of Missing and Partial Dates

Element	Reporting Detail
General	• Partial dates will be displayed as captured in subject listing displays.
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 as treatment-emergent. o Last day of the month will be used, unless this is after the stop date of study treatment; in this case the study treatment stop date will be used. • Completely missing start or end dates will remain missing, with no imputation applied. Consequently, time to onset and duration of such events will be missing. • Start or end dates which are completely missing (i.e. no year specified) will remain missing, with no imputation applied.
Concomitant Medications/Medical History	• 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.

14.6. Appendix 6: Values of Potential Clinical Importance

14.6.1. 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

14.6.2. ECG

ECG Parameter	Units	Clinical Concern Range	
		Lower	Upper
Absolute			
Absolute QTc Interval	msec		> 450
Absolute PR Interval	msec	< 110	> 220
Absolute QRS Interval	msec	< 75	> 110
Change from Baseline			
Increase in Baseline in QTc	msec		>60

The following categories will be used for summarising by:
- the maximum QTc values post-baseline relative to baseline
- the maximum increase in QTc values post-baseline relative to baseline

ECG Parameter	Units	Clinical Concern Range	
Absolute QTcB and QTcF Interval	msec	< 450	
		≥ 450	≤ 479
		≥ 480	≤ 500
		> 500	
Change from baseline in QTcB and QTcF	msec	< 30	
		≥ 30	≤ 60
		> 60	

14.6.3. 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

14.7. Appendix 7: Pharmacokinetic/Pharmacodynamic Analyses

All non-linear mixed effects modelling will be performed using NONMEM (ICON Solutions), PsN (Perl Speaks NONMEM) and Pirana (Pirana Software & Consulting BV 2016).

R (The R Foundation for Statistical Computing) will be used for exploratory graphical analysis, graphical model diagnostics and, if needed, modifications of the dataset.

The analysis will be performed by, or under the direct auspices of, Clinical Pharmacology Modelling and Simulation (CPMS), GlaxoSmithKline in the GSK modelling environment MAP (Model-based Analyses Platform) using the currently supported versions of all software packages.

14.7.1. Pharmacokinetic / Pharmacodynamic Dataset Specification

The merging of aLAG3, regiment, biomarker and demographic data together with the creation of the NONMEM-specific dataset will be performed by, or under the direct auspices of, Clinical Statistics (Programmer), GlaxoSmithKline.

This dataset programming will be conducted in a HARP environment using the currently supported version of SAS.

14.7.2. Pharmacokinetic / Pharmacodynamic Methodology

An exploratory graphical analysis of the data will be performed by generating the plots as presented in Appendix 9.

Model development will be data driven.

The initial PK model of choice will be a compartmental model with linear and nonlinear drug elimination. Further model testing will include, but it is not limited to, a compartmental model with target mediated drug disposition (TMDD) and a minimal PBPK model with TMDD incorporated. We anticipate TMDD to be driven by soluble LAG3 (sLAG3). However, if data allow, we plan to test also more complex models with TMDD driven by both, sLAG3 and T-cell bound LAG3.

The final PK model, possibly incorporating TMDD, will be used to develop a PK-RO model. Data relative to CD4+CD45RA- cell count will be used to model RO (quantified by J11L1 marker) and T-cell depletion (quantified by 1B4 marker). The initial RO model will likely be an Emax model. More complex models might be investigated if the data support it.

If plots (and summary) of NCA derived PK parameters identified ADA status, and/or HV vs Pso as possible significant covariates, we will investigate the influence of these covariates in the PK and RO models. Other covariates may be explored as appropriate.

Model acceptability will be judged by convergence, covariance estimation and standard goodness-of-fit plots that may include, but are not limited to:

- Population and individual predictions versus observations
- Conditional weighted residuals versus population predictions and time

For the final PK and the final RO models visual predictive checks (VPCs) will be conducted to assess graphically whether simulations from the developed models are able to reproduce both the central trend and variability in the observed data from the current study as a function of time.

The VPC will be based on 1000 simulations with the model and the design structure of the observed data (i.e. dose level and time, time of PK sampling and individual values of model covariates, if any). The median and the 10th and 90th will be compared to the observed data. Stratification by dose level of GSK2831781 will be used. Other stratification, such as healthy/ psoriasis will be applied in case these covariates were tested in the model.

14.8. Appendix 8: Abbreviations & Trade Marks

14.8.1. Abbreviations

Abbreviation	Description
%AUCex	Percentage of AUC(0-¥) obtained by extrapolation
µg	Microgram
A&R	Analysis and Reporting
ABC	airway, breathing, and circulation from Basic Life Support
aCCR4	Anti C-C chemokine receptor type 4
ADA	Anti-drug antibody
ADA	Anti-drug antibodies
ADCC	Antibody Dependent Cell Cytotoxicity
AE	Adverse Event
AIC	Akaike's Information Criteria
ALT	Alanine aminotransferase (SGPT)
AST	Aspartate aminotransferase (SGOT)
AUC	Area under the concentration-time curve
AUC(0-∞)	Area under the concentration-time curve from time zero (pre-dose) extrapolated to infinite time
AUC(0-t)	Area under the concentration-time curve from time zero (pre-dose) to last time of quantifiable concentration within a subject across all treatments
AUC(0-x)	Area under the concentration-time curve from zero (pre-dose) to some fixed nominal time x
BCG	Bacillus Calmette Guérin vaccine
BMI	Body mass index
BSA	Body surface area
CFB	Change from baseline
CI	Confidence Interval
CL	Systemic clearance of parent drug
Cmax	Maximum observed concentration
CMV	Cytomegalovirus
CPK	Creatine phosphokinase
CPMS	Clinical Pharmacology Modelling and Simulation
CPR	Cardio-Pulmonary Resuscitation
CPSSO	Clinical Pharmacology Sciences and Study Operations
CRF	Case Report Form
CRP	C-Reactive Protein
CS	Clinical Statistics
CSR	Clinical Study Report
CTLA	Cytotoxic T-Lymphocyte Antigen
CTR	Clinical Trial Register
CVb / CVw	Coefficient of Variation (Between) / Coefficient of Variation (Within)
CXCR	CXC Chemokine Receptor
DC	Dendritic Cells

Abbreviation	Description
DEC	Dose Escalation Committee
DMPK	Drug Metabolism and Pharmacokinetics
DOB	Date of Birth
DP	Decimal Places
DPT	Diphtheria, pertussis, tetanus
DTH	Delayed type hypersensitivity
EBV	Epstein-Barr Virus
ECG	Electrocardiogram
ECL	Immunoelectrochemiluminescent
eCRF	Electronic Case Record Form
EDTA	Ethylenediaminetetraacetic acid
EMA	European Medicines Agency
FCS	Foetal Calf Serum
FDA	Food and Drug Administration
FDAAA	Food and Drug Administration Clinical Results Disclosure Requirements
FTIH	First Time In Human
GCP	Good Clinical Practice
G-CSF	Granulocyte-Colony Stimulating Factor
GGT	Gamma glutamyltransferase
GI	Gastrointestinal
GLP	Good Laboratory Practice
GSK	GlaxoSmithKline
h	Hour
HBcAb	Hepatitis B core antibody
HBsAg	Hepatitis B surface antigen
Hep B	Hepatitis B
Hep C	Hepatitis C
HIV	Human Immunodeficiency Virus
HRT	Hormone Replacement Therapy
HSV	Herpes Simplex Virus
IA	Interim Analysis
IB	Investigator's Brochure
ICH	International Conference on Harmonization
ICU	Intensive Care Unit
ID	Intradermal
IDMC	Independent Data Monitoring Committee
IDSL	Integrated Data Standards Library
IEC	Independent Ethics Committee
IFN-γ	Interferon-gamma
Ig	Immunoglobulin
IgM	Immunoglobulin M
IHC	Immunohistochemistry
ii TAU	Immuno-Inflammation Therapeutic Area Unity
IL2R	Interleukin 2 Receptor
ILH	Immediate local hypersensitivity

Abbreviation	Description
IMMS	International Modules Management System
INR	International Normalised Ratio
IP	Investigational Product
kg	Kilogram
L	Litres
LAG-3	Lymphocyte Activation Gene 3
LLQ	Lower Limit of Quantification
mg	Milligram
ml	Millilitre
MlU/mL	milli-international units per millilitre
mm	Millimetre
MMR	Measles, mumps, rubella
MMRM	Mixed Model Repeated Measures
mRNA	Messenger Ribonucleic Acid
MRT	Mean Residence Time
NK	Natural Killer
nM	Nanomolar
NOAEL	No Observed Adverse Effect Level
PASI	Psoriasis Area Severity Index
PBMC	Peripheral Blood Mononuclear Cell
PCI	Potential Clinical Importance
PD	Pharmacodynamic
PDMP	Protocol Deviation Management Plan
PGA	Physicians Global Assessment
PK	Pharmacokinetic
PLSS	Plaque Lesional Severity Score
PPD	Tuberculin Purified Protein Derivative
QTc	Electrocardiogram QT interval corrected for heart rate
QTcB	Bazett's QT Interval Corrected for Heart Rate
QTcF	Frederica's QT Interval Corrected for Heart Rate
RAP	Reporting and Analysis Plan
RBC	Red blood cells
RNA	Ribonucleic acid
RO	Receptor Occupancy
RT-PCR	Reverse transcription polymerase chain reaction
SAC	Statistical Analysis Complete
SAE	Serious adverse event(s)
SGOT	Serum glutamic-oxaloacetic transaminase
SGPT	Serum glutamic pyruvic transaminase
sLAG-3	Soluble Lymphocyte Activation Gene 3
SOP	Standard Operation Procedure
SPC	Summary of Product Characteristics
SPM	Study Procedures Manual
t½	Terminal phase half-life
TA	Therapeutic Area

Abbreviation	Description
TB	Tuberculosis
TFL	Tables, Figures & Listings
tlast	Time of last quantifiable concentration
tmax	Time of occurrence of Cmax
UK	United Kingdom
USA	United States of America
Vss	Volume of distribution at steady state
VZV	Varicella Zoster Virus
WBC	White blood cells
λz	Terminal elimination rate

14.8.2. Trademarks

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14.9. Appendix 9: List of Data Displays

14.9.1. Data Display Numbering

The following numbering will be applied for RAP generated displays:

Section	Tables	Figures
Study Population	1.1 to 1.14	Not applicable
Efficacy	2.1 to 2.23	2.1 to 2.n
Safety	3.1 to 3.35	3.1 to 3.6
Pharmacokinetic	4.1 to 4.6	4.1 to 4.6
Population Pharmacokinetic (PopPK)	Not applicable	Not applicable
Pharmacodynamic and / or Biomarker	6.1 to 6.14	6.1 to 6.18
Pharmacokinetic / Pharmacodynamic	Not applicable	Not applicable
Section	**Listings**	
ICH Listings	1 to 31	
Other Listings	32 to 63	

14.9.2. Mock Example Shell Referencing

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

Non-Standard displays are indicated in the 'IDSL / TST ID / Example Shell' column as 'Reference.'

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
Population Pharmacokinetic (PopPK)	POPPK_Fn	POPPK_Tn	POPPK_Ln
Pharmacodynamic and / or Biomarker	PD_Fn	PD_Tn	PD_Ln
Pharmacokinetic / Pharmacodynamic	PKPD_Fn	PKPD_Tn	PK/PD_Ln

14.9.3. Deliverables

Following review of the IA2 and IA W2 outputs and finalisation of the database, the final list of outputs to be re-run at SAC will be reviewed.

Delivery	Description
IA1	Interim Analysis 1 Statistical Analysis Complete
IA2 EFF	Interim Analysis 2 Statistical Analysis Complete for Efficacy endpoints
IA2	Interim Analysis 2 Statistical Analysis Complete
IA2 W2	Interim Analysis 2 Wave 2 Statistical Analysis Complete
SAC	Final Statistical Analysis Complete

14.9.4. Study Population Tables

Study Population Tables					
No.	**Population**	**IDSL / Example Shell**	**Title**	**Programming Notes**	**Deliverable**
Subject Disposition					
1.1.	safety	ES1	Summary of subject disposition for healthy volunteers	by treatment group - 8 groups	IA1 IA2 W2
1.2.	safety	ES1	Summary of subject disposition for psoriasis patients	Same as for HV - 4 groups	IA2W2
1.3.	All screened	ES6	Summary of reasons for screen failures for healthy volunteers	Not by treatment group	SAC
1.4.	All screened	ES6	Summary of reasons for screen failures for psoriasis patients	Same as for HV	SAC
Protocol Deviation					
1.5.	Safety	DV1A	Summary of important protocol deviations for healthy volunteers	by treatment group - 8 groups	SAC
1.6.	Safety	DV1A	Summary of important protocol deviations for psoriasis patients	Same as for HV - 4 groups	SAC
Population Analysed					
1.7.	All screened	SA1	Summary of study populations for healthy volunteers	by treatment group - 8 groups See text for screen failures	IA2 W2
1.8.	All screened	SA1	Summary of study populations for psoriasis patients	Same as for HV - 4 groups See text for screen failures	IA2 W2

Study Population Tables					
No.	**Population**	**IDSL / Example Shell**	**Title**	**Programming Notes**	**Deliverable**
Demographic and Baseline Characteristics					
1.9.	safety	DM1	Summary of demographic characteristics for healthy volunteers	1. by treatment group - 8 groups 2. Include: Gender, height, weight and BMI 3. Include age category: <18 years, 18 to 65 years, 66 to 75 years and >75 years	IA2 W2
1.10.	safety	DM1	Summary of demographic characteristics for psoriasis patients	Same as for HV - 4 groups	IA2 W2
1.11.	safety	DM5	Summary of race and racial combinations for healthy volunteers	1. by treatment group - 8 groups 2. Report only categories where n>0 count	SAC
1.12.	safety	DM5	Summary of race and racial combinations for psoriasis patients	Same as for HV - 4 groups	SAC
1.13.	safety	DM11	Summary of age ranges for healthy volunteers	by treatment group - 8 groups	SAC
1.14.	safety	DM11	Summary of age ranges for psoriasis patients	by treatment group - 4 groups	SAC

14.9.5. Efficacy Tables

Efficacy: Tables					
No.	**Population**	**IDSL / Example Shell**	**Title**	**Programming Notes**	**Deliverable**
DTH induration					
2.1.	Safety		Summary of induration diameter for healthy volunteers (DTH subjects)	1. Absolute and CFB 2. by challenge site (4) and overall => 5 parameters 3. 2 treatment groups (cohort 5): placebo (DTH) and 0.15mg (DTH=ADA-ve)	IA1
2.2.	Safety		Summary results of statistical analysis of change from baseline in induration diameter for healthy volunteers (DTH subjects)	1. for overall only (1 parameter) 3. 2 treatment groups (cohort 5): placebo (DTH) and 0.15mg (DTH=ADA-ve)	IA1
2.3.	safety		Summary of duration of induration for healthy volunteers (DTH subjects)	1. Absolute 2. 2 treatment groups: placebo (DTH) and 0.15mg (DTH=ADA-ve) 3. If needed for SAC, include only the summary of observed duration (no HR estimate)	IA1
BSA					
2.4.	Safety		Summary of body surface area by visit for psoriasis patients	1. Absolute, CFB, %CFB 2. 4 regional BSA 3. Total BSA (sum of the 4 regional BS)	SAC

Efficacy: Tables					
No.	**Population**	**IDSL / Example Shell**	**Title**	**Programming Notes**	**Deliverable**
PASI					
2.5.	Safety	TE1	Summary of PASI scores by visit for psoriasis patients	1. By treatment group - 4 groups 2. Absolute, CFB, %CBF (byline)	IA2 EFF
2.6.	Safety	TE2	Summary of PASI50 and PASI75 responders by visit for psoriasis patients	1. By treatment group - 4 groups 2. PASI50/75 3. Footnote: PASI50 or PASI75 responders are patients with a ≥ 50% or 75% reduction in PASI score from baseline	IA2 EFF
2.7.	Safety	TE3	Summary of statistical analysis results for change from baseline in PASI scores over time for psoriasis patients		IA2 EFF
PLSS					
2.8.	Safety	TE1	Summary of PLSS scores by visit for psoriasis patients	1. Same table as for PASI 2. Index and biospy lesions (byline) 3. Absolute, CFB, %CBF (byline)	IA2 EFF
2.9.	Safety	TE3	Summary of statistical analysis results for change from baseline in PLSS scores over time for psoriasis patients	1. Same as for PASI 2. Index lesion only 3. CFB	IA2 EFF

Efficacy: Tables					
No.	**Population**	**IDSL / Example Shell**	**Title**	**Programming Notes**	**Deliverable**
PGA					
2.10.	Safety	TE1	Summary of PGA scores by visit for psoriasis patients	1. Absolute, CFB 2. Considers categories as continuous	IA2 EFF
2.11.	Safety	TE2	Summary of PGA responders by visit for psoriasis patients	1. Same table as for PASI50/75 (include exact CI) 2. Footnote: definition of PGA responders	IA2 EFF
2.12.	Safety	TE4	Summary of PGA responses by visit for psoriasis patients	Frequency count (categorical variable)	IA2 EFF
Endpoints for go/no go decisions					
2.13.	Safety		Bayesian analyses of key endpoints	See Section 13 IA2 EFF: PASI and PLSS IA2: total LAG3 cells, Ki67, epidermis thickness Need to add SAS log + CV plots	IA2 EFF IA2

14.9.6. Efficacy Figures

Efficacy: Figures					
No.	**Population**	**IDSL / Example Shell**	**Title**	**Programming Notes**	**Deliverable**
DTH induration					
2.1.	safety	F_PD1	Individual plot of induration diameter over time for healthy volunteers (DTH subjects)	1. Absolute 2. by challenge site (4) and overall => 5 parameters 3. 2 treatment groups (cohort 5): placebo (DTH) and 0.15mg (DTH=ADA-ve) 4. ADA+ve subjects identified in legend	lA1
2.2.	safety	F_PD3	Mean (±SD) induration diameter over time for healthy volunteers (DTH subjects)	1. Absolute 2. by challenge site (4) and overall => 5 parameters - 3. 2 treatment groups (cohort 5): placebo (DTH) and 0.15mg (DTH=ADA-ve)	lA1
2.3.	safety	F_PD3	Adjusted mean (95% CI) of change from baseline in induration diameter over time for healthy volunteers (DTH subjects)	1. CFB (LS means) 2. overall only 3. 2 treatment groups (cohort 5): placebo (DTH) and 0.15mg (DTH=ADA-ve)	lA1

Efficacy: Figures					
No.	**Population**	**IDSL / Example Shell**	**Title**	**Programming Notes**	**Deliverable**
PASI					
2.4.	Safety	F_PD1	Individual plot of PASI scores over time for psoriasis patients	1. Absolute and %CFB 2. ADA+ve subjects identified in legend	IA2 EFF
2.5.	Safety	F_PD3	Mean (±SD) PASI scores over time for psoriasis patients	Absolute, %CFB	IA2 EFF
2.6.	Safety	F_PD3	Adjusted mean (95% CI) of change from baseline in PASI scores over time for psoriasis patients	CFB	IA2 EFF
PLSS					
2.7.	Safety	F_PD1	Individual plot of PLSS scores over time for psoriasis patients	1. Absolute and %CFB 2. Index and biospy lesions 3. ADA+ve subjects identified in legend	IA2 EFF
2.8.	Safety	F_PD3	Mean (±SD) PLSS scores over time for psoriasis patients	Absolute, %CFB Index lesion only	IA2 EFF
2.9.	Safety	F_PD3	Adjusted mean (95% CI) of change from baseline in PLSS scores over time for psoriasis patients	CFB Index lesion only	IA2 EFF
PGA					
2.10.	Safety	F_PD1	Individual plot of PGA responses over time for psoriasis patients	1. Absolute only 2. Considers categories as continuous 3. ADA+ve subjects identified in legend	IA2 EFF

14.9.7. Safety Tables

Safety: Tables					
No.	**Population**	**IDSL / Example Shell**	**Title**	**Programming Notes**	**Deliverable**
Adverse Events (AEs)					
3.1.	safety	CP_AE1P	Summary of all adverse events for healthy volunteers	1. by treatment group - 9 groups (including total active) 2. Only TEAE 3. by SOC then PT 4. Notes: 1. Total Active: Total over the 5 doses (except Placebo for HV Combined). 2. ADA status as defined at screening. 3. Combined treatment groups include subjects with ADA-ve and ADA+ve. 4. Only treatment-emergent AEs are summarised: starting date between 1st dose and last scheduled visit (follow-up or combined FU/surveillance)	IA1 IA2 W2
3.2.	safety	CP_AE1P	Summary of all adverse events for psoriasis patients	Same as for HV - 5 groups (including total active)	IA2 W2
3.3.	safety	CP_AE1P	Summary of drug-related adverse events for healthy volunteers	same output as for all AEs	IA1 IA2 W2
3.4.	safety	CP_AE1P	Summary of drug-related adverse events for psoriasis patients	Same as for HV - 5 groups (including total active)	IA2 W2

Safety: Tables					
No.	**Population**	**IDSL / Example Shell**	**Title**	**Programming Notes**	**Deliverable**
3.5.	safety	CP_AE1P	Summary of all adverse events for ADA+ve subjects	1. ADA+ve defined as subject who were ADA+ve at screening visit 2. Parts A and B (cohorts 5, 7-9) => groups: Pbo HV, 0.15mg/kg, Pbo PsO, 0.5mg/kg, 1.5mg/kg, 5mg/kg 3. Only TEAE 4. by SOC then PT	SAC
3.6.	safety	AE3	Summary of common adverse events for healthy volunteers	1. Common defined as at least 2 patients with the event in any of the treatment groups, separately for parts A and B 2. by treatment group - 9 groups (including total active) 3. Only TEAE 4. by PT	IA2 W2
3.7.	safety	AE3	Summary of common adverse events for psoriasis patients	Same as for HV - 5 groups (including total active)	IA2 W2
3.8.	safety	CP_AE1P	Summary of all adverse events (healthy volunteers and psoriasis patients)	Same as for HV or PsO Include 4 columns - Placebo for HV - Total Active (HV) - Placebo for PsO - Total active (PsO)	IA2 W2

Safety: Tables					
No.	**Population**	**IDSL / Example Shell**	**Title**	**Programming Notes**	**Deliverable**
3.9.	safety	AE2	Relationship between system organ class and verbatim text	HV and PsO in the same summary table	SAC
Serious Adverse Events					
3.10.	safety	AE1	Summary of serious adverse events for healthy volunteers	1. by treatment group - 9 groups (including total active) 2. Only TEAE 3. by PT	IA1 IA2 W2
3.11.	safety	AE1	Summary of serious adverse events for psoriasis patients	Same as for HV - 5 groups (including total active)	IA2 W2

Safety: Tables					
No.	**Population**	**IDSL / Example Shell**	**Title**	**Programming Notes**	**Deliverable**
Laboratory: Chemistry					
3.12.	safety	LB1	Summary of chemistry by visit for healthy volunteers	1. by treatment group - 8 groups 2. By visit, from baseline to last scheduled visit (excluding surveillance visit)	IA1 IA2 W2
3.13.	safety	LB1	Summary of chemistry by visit for psoriasis patients	Same as for HV - 4 groups	IA2 W2
3.14.	safety	LB3	Summary of change from baseline in chemistry by visit for healthy volunteers	1. by treatment group - 8 groups 2. All post-baseline visits, excluding surveillance visits	IA1 SAC
3.15.	safety	LB3	Summary of change from baseline in chemistry by visit for psoriasis patients	Same as for HV - 4 groups	SAC
Laboratory: Hematology					
3.16.	safety	LB1	Summary of haematology by visit for healthy volunteers	same output as for chemistry parameters	IA1 IA2 W2
3.17.	safety	LB1	Summary of haematology by visit for psoriasis patients	same output as for chemistry parameters	IA2 W2
3.18.	safety	LB3	Summary of change from baseline in haematology by visit for healthy volunteers	same output as for chemistry parameters	IA1 SAC
3.19.	safety	LB3	Summary of change from baseline in haematology by visit for psoriasis patients	same output as for chemistry parameters	SAC

Safety: Tables					
No.	**Population**	**IDSL / Example Shell**	**Title**	**Programming Notes**	**Deliverable**
Laboratory: Urinalysis					
3.20.	safety	UR3	Summary of urinalysis dipstick results by visit for healthy volunteers	1. by treatment group - 8 groups 2. By visit, from screening to last scheduled visit (excluding surveillance visit)	IA1 SAC
3.21.	safety	UR3	Summary of urinalysis dipstick results by visit for psoriasis patients	Same as for HV - 4 groups	SAC
ECG					
3.22.	safety	EG1	Summary of ECG findings by visit for healthy volunteers	1. by treatment group - 8 groups 2. By visit, from screening to last scheduled visit (excluding surveillance visit) 3. For screening, use the worst finding out of the 3 values – add the following footonote for screening visit only: At screening, the finding for a subject is the worst finding observed across the 3 findings.	IA1 IA W2
3.23.	safety	EG1	Summary of ECG findings by visit for psoriasis patients	Same as for HV - 4 groups	IA W2

Safety: Tables					
No.	**Population**	**IDSL / Example Shell**	**Title**	**Programming Notes**	**Deliverable**
3.24.	safety	EG2	Summary of ECG values by visit for healthy volunteers	1. by treatment group - 8 groups 2. By visit, from baseline to last scheduled visit (excluding surveillance visit)	SAC
3.25.	safety	EG2	Summary of ECG values by visit for psoriasis patients	Same as for HV - 4 groups	SAC
3.26.	safety	EG2	Summary of change from baseline in ECG values by visit for healthy volunteers	by treatment group - 8 groups	SAC
3.27.	safety	EG2	Summary of change from baseline in ECG values by visit for psoriasis patients	Same as for HV - 4 groups	SAC
3.28.	safety	EG10/EG11 combined	Summary of maximum emergent QTc values by category (absolute and change from baseline) for healthy volunteers	Includes baseline values, and footnote: note: the maximum change for a subject is the maximum increase from baseline observed across all time points for the subject	SAC
3.29.	safety	EG10/EG11 combined	Summary of maximum emergent QTc values by category (absolute and change from baseline) for psoriasis patients	Same as for HV - 4 groups	SAC
Vital Signs					
3.30.	safety	VS1	Summary of vital signs by visit for healthy volunteers	1. by treatment group - 8 groups 2. Include the temperature	IA1 IA2 W2
3.31.	safety	VS1	Summary of vital signs by visit for psoriasis patients	Same as for HV - 4 groups	IA2 W2

Safety: Tables					
No.	**Population**	**IDSL / Example Shell**	**Title**	**Programming Notes**	**Deliverable**
3.32.	safety	VS1	Summary of change from baseline in vital signs by visit for healthy volunteers	Same as for absolute values	SAC
3.33.	safety	VS1	Summary of change from baseline in vital signs by visit for psoriasis patients	Same as for HV - 4 groups	SAC
Cytokines					
3.34.	Safety		Summary of cytokines for healthy volunteers	1. Absolute, CFB 2. See parameters in RAP text	IA1 SAC
3.35.	Safety		Summary of cytokines for psoriasis patients	Same as HV	IA2
Adverse events (additional)					
3.36.	Safety	CP_AE1P	Summary of drug-related adverse events for healthy volunteers and psoriasis patients	Same as for HV or PsO only For HV, remove combined 0.15mg/kg (only keep separate ADA status	SAC
3.37.	Safety	CP_AE1P	Summary of all adverse events for healthy volunteers and psoriasis patients	Same as for HV or PsO only For HV, remove combined 0.15mg/kg (only keep separate ADA status	SAC

Safety: Tables					
No.	**Population**	**IDSL / Example Shell**	**Title**	**Programming Notes**	**Deliverable**
Immunophenotyping					
3.38.	Safety		Summary of immunophenotyping for healthy volunteers	Same output as for flow cytometry for the following parameters. For the 4 of them concentration should be used. No derivation is needed. marker code / marker / endpoint: CDX219 / CD45+ CD3+ / Pan T cells CDX220 / CD45+ CD3+ CD8+ / CD8 T cells CDX221 / CD45+ CD3+ CD8- / CD4 T cells CDX225 / CD45+ CD3- CD16+ CD56+ / NK cells	SAC

Safety: Tables					
No.	**Population**	**IDSL / Example Shell**	**Title**	**Programming Notes**	**Deliverable**
3.39.	Safety		Summary of immunophenotyping for psoriasis patients	Same output as for flow cytometry for the following parameters. For the 4 of them concentration should be used. No derivation is needed. marker code / marker / endpoint: CDX219 / CD45+ CD3+ / Pan T cells CDX220 / CD45+ CD3+ CD8+ / CD8 T cells CDX221 / CD45+ CD3+ CD8- / CD4 T cells CDX225 / CD45+ CD3- CD16+ CD56+ / NK cells	SAC

14.9.8. Safety Figures

Safety: Figures					
No.	**Population**	**IDSL / Example Shell**	**Title**	**Programming Notes**	**Deliverable**
Laboratory					
3.1.	safety	LB11	Individual plot of lymphocytes and neutrophils over time for healthy volunteers	1. panel per treatment group - 8 groups 2. ADA+ve subjects identified in legend	SAC
3.2.	safety	LB11	Individual plot of lymphocytes and neutrophils over time for psoriasis patients	Same as for HV - 4 groups	SAC
ECG					
3.3.	safety	EG7	Empirical distribution function for maximum increase from baseline in QTcF interval for healthy volunteers	1. 8 treatment groups on one plot 2. Calculate the maximum change from baseline	SAC
3.4.	safety	EG7	Empirical distribution function for maximum increase from baseline in QTcF interval for psoriasis patients	Same as for HV - 4 groups	SAC
3.5.	safety	EG7	Empirical distribution function for maximum increase from baseline in QTcB interval for healthy volunteers	Same as QTcF	SAC
3.6.	safety	EG7	Empirical distribution function for maximum increase from baseline in QTcB interval for psoriasis patients	Same as for HV - 4 groups	SAC
Immunophenotyping					
3.7.	Safety		Individual plot of immunophenotyping over time for healthy volunteers	Same plot as for key flow parameters (see Figure 6.8)	SAC
3.8.	Safety		Individual plot of immunophenotyping over time for psoarisis patients	Same plot as for key flow parameters (see Figure 6.9)	SAC

14.9.9. Pharmacokinetic Tables

Pharmacokinetic: Tables					
No.	**Population**	**IDSL / Example Shell**	**Title**	**Programming Notes**	**Deliverable**
PK concentration					
4.1.	PK	PK01	Summary of plasma GSK2831781 pharmacokinetic concentration-time data for healthy volunteers	1. by treatment group - 7 groups (placebo not included) 2. Remove 95%CI as not normally distributed	IA2 W2
4.2.	PK	PK01	Summary of plasma GSK2831781 pharmacokinetic concentration-time data for psoriasis patients	same as HV – 3 groups (placeo not included)	IA2 W2
PK derived parameters					
4.3.	PK	PK03	Summary of derived plasma GSK2831781 pharmacokinetic parameters for healthy volunteers	by treatment group - 7 groups (placebo not included)	IA2 W2
4.4.	PK	PK03	Summary of derived plasma GSK2831781 pharmacokinetic parameters for psoriasis patients	same as HV – 3 groups (placeo not included)	IA2 W2
4.5.	PK	PK05	Summary of log-transformed derived plasma GSK2831781 pharmacokinetic parameters for healthy volunteers	1. by treatment group - 7 groups (placebo not included)¶ 2. Exclude tmax and tlast	IA2 W2
4.6.	PK	PK05	Summary of log-transformed derived plasma GSK2831781 pharmacokinetic parameters for psoriasis patients	same as HV – 3 groups (placeo not included)	IA2 W2

14.9.10. Pharmacokinetic Figures

Pharmacokinetic: Figures					
No.	**Population**	**IDSL / Example Shell**	**Title**	**Programming Notes**	**Deliverable**
PK concentration					
4.1.	PK	PK24	Individual GSK2831781 plasma concentration-time plot (linear and semi-log) for healthy volunteers	1. by treatment group - 8 groups 2. Treatment group as page variable 3. x-axis displays actual relative time. 4. Include line for LLQ along with footnote defining LLQ value 5. ADA +ve patients identified in legend	IA2 W2
4.2.	PK	PK24	Individual GSK2831781 plasma concentration-time plot (linear and semi-log) for psoriasis patients	Same as for HV - 4 groups	IA2 W2
4.3.	PK	PK17	Mean plasma GSK2831781 concentration-time plots (linear and semi-log) for healthy volunteers	1. by treatment group - 7 groups (placebo not included)3. x-axis displays actual relative time. 4. Same y-axis for HV and PsO 5. Include line for LLQ along with footnote defining LLQ value	IA2 W2
4.4.	PK	PK17	Mean plasma GSK2831781 concentration-time plots (linear and semi-log) for psoriasis patients	same as for HV	IA2 W2

Pharmacokinetic: Figures					
No.	**Population**	**IDSL / Example Shell**	**Title**	**Programming Notes**	**Deliverable**
PK derived parameters					
4.5.	PK	PK28	Individual GSK2831781 pharmacokinetic parameters versus dose for healthy volunteers	1. For Cmax, AUC[0-last] - Parameters as page variable 2. x-axis: 5 doses (0.15 combined) 4. ADA +ve patients identified in legend	IA2 W2
4.6.	PK	PK28	Individual GSK2831781 pharmacokinetic parameters versus dose for psoriasis patients	Same as for HV - 3 doses	IA2 W2

14.9.11. Pharmacodynamic / Biomarker Tables

Pharmacodynamic and Biomarker: Tables					
No.	**Population**	**IDSL / Example Shell**	**Title**	**Programming Notes**	**Deliverable**
IHC parameters					
6.1.	Safety		Summary of LAG3+ and CD3+ in skin by visit for healthy volunteers (DTH subjects)	1. Absolute, CFB, %CFB 2. 2 visits: baseline and day 4 3. Endpoints: CD3+, LAG3+ (check RAP text) 4. 2 treatment groups: placebo (DTH) and 0.15mg (DTH=ADA-ve)	IA1 IA2
6.2.	Safety		Summary of cells in lesional biopsies measured by IHC by visit for psoriasis patients	1. Results for dermis and epidermis for CD3+, lag3+; epidermis only for Ki67 2. Absolute, CFB, %CFB 3. 2 visits: baseline and day 29 4. 4 treatment groups	IA2
6.3.	Safety		Summary of epidermis thickness by visit for psoriasis patients	Same as for IHC parameters	IA2
6.4.	Safety		Summary of statistical analysis results for change from baseline in LAG3+ and CD3+ values for healthy volunteers (DTH subjects)	1. CFB 2. Endpoints: CD3+, LAG3+ (check RAP text) 3. 2 treatment groups: placebo (DTH) and 0.15mg (DTH=ADA-ve)	IA1 IA2

Pharmacodynamic and Biomarker: Tables					
No.	**Population**	**IDSL / Example Shell**	**Title**	**Programming Notes**	**Deliverable**
6.5.	Safey		Summary of statistical analysis results for change from baseline in cells in lesional biopsies measured by IHC for psoriasis patients	1. Results for dermis and epidermis for CD3+, lag3+; epidermis only for Ki67 and epidermis thickness 2. CFB 3. 4 treatment groups	IA2
Flow cytometry					
6.6.	Safety		Summary of flow cytometry by visit for healthy volunteers	1. Only the 6 key flow parameters - see RAP text 2. Absolute, CFB, **% of baseline**	IA1 IA2
6.7.	Safety		Summary of flow cytometry by visit for psoriasis patients	Same as for HV	IA2
s-LAG3					
6.8.	Safety		Summary of sLAG-3 by visit for healthy volunteers	1. Absolute, CFB	IA1 IA2
6.9.	Safety		Summary of sLAG-3 by visit for psoriasis patients	Same as for HV	IA2
Immunogenicity					
6.10.	Safety	IMM1	Summary of positive immunogenicity results for healthy volunteers		IA1 IA2 W2
6.11.	Safety	IMM1	Summary of positive immunogenicity results for psoriasis patients	Same as for HV	IA2 W2

Pharmacodynamic and Biomarker: Tables					
No.	**Population**	**IDSL / Example Shell**	**Title**	**Programming Notes**	**Deliverable**
Transcriptomics					
6.12.	Safety		Summary of blood transcriptomics for healthy volunteers	(same mockshell as for any efficacy endpoint, e.g. pasi) By gene (2 as not housekeeping genes) and summary (delta delta Ct and fold change)	SAC
6.13.	Safety		Summary of blood transcriptomics for psoriasis patients	Same as for HV	SAC
6.14.	Safety		Summary of biopsy transcriptomics for psoriasis patients	Same as for blood transcriptomics No data for HV Displays visit 15 (only cohort 7 – 3 on placebo, 6 on 0.5mg/kg) and Day 29 (all PSO)	IA2 W2 (as issue with mapping program from raw data to SI data – 3 gene codes missing)

14.9.12. Pharmacodynamic / Biomarker Figures

Pharmacodynamic and Biomarker: Figures					
No.	**Population**	**IDSL / Example Shell**	**Title**	**Programming Notes**	**Deliverable**
IHC parameters					
6.1.	Safety	F_PD1	Individual plot of LAG3+ and CD3+ in skin over time for healthy volunteers (DTH subjects)	1. Absolute and CFB 2. Total cells (HPF 1-5) - average across 3 skin layers (check RAP text) 3. 2 visits: baseline and day 4 4. Endpoints: CD3+, lag3+	IA1 IA2
6.2.	Safety	F_PD1	Individual plot of cells in lesional biopsies measured by IHC over time for psoriasis patients	1. Results for dermis and epidermis for CD3+ and lag3+; epidermis only for Ki67 2. Absolute and CFB 3. 2 visits: baseline and day 29 4. Endpoints: CD3+, lag3+, Ki67, (seprate table as different dataset) 5. See RAP text for endpoints	IA2
6.3.	Safety	F_PD1	Individual plot of epidermis thickness over time for psoriasis patients	Same as for IHC endpoints	IA2

Pharmacodynamic and Biomarker: Figures					
No.	**Population**	**IDSL / Example Shell**	**Title**	**Programming Notes**	**Deliverable**
6.4.	Safety	F_PD2	Subject profiles of LAG3+ and CD3+ in skin for healthy volunteers (DTH subjects)	1. LAG3+, CD3+ (check RAP text) 2. 2 treatment groups: placebo (DTH) and 0.15mg (DTH=ADA-ve) 3. Total number of cells per layer (3) + average => 4 lines per subjects 4. Absolute 5. Panel with subjects 6. Footnote to be added	IA1 IA2
6.5.	Safety	F_PD3	Mean (±SD) LAG3+ and CD3+ in skin over time for healthy volunteers(DTH subjects)	1. LAG3+, CD3+ (check RAP text) Only average 2. 2 treatment groups: placebo (DTH) and 0.15mg (DTH=ADA-ve) 3. Absolute	IA1 IA2 W2
6.6.	Safety	F_PD3	Mean (±SD) cells in lesional biopsies measured by IHC over time for psoriasis patients	1. Results for dermis and epidermis for CD3+, lag3+; epidermis only for Ki67 2. Absolute 3. 2 visits: baseline and day 29 4. Endpoints: CD3+, lag3+, Ki67 5. 4 treatment groups	IA2 W2
6.7.	Safety	F_PD3	Mean (±SD) epidermis thickness over time for psoriasis patients	Same as for IHC endpoints	IA2 W2

Pharmacodynamic and Biomarker: Figures					
No.	**Population**	**IDSL / Example Shell**	**Title**	**Programming Notes**	**Deliverable**
Flow cytometry					
6.8.	Safety	F_PD1	Individual plot of flow cytometry key parameters over time for healthy volunteers	1. Only the 6 key flow parameters - see RAP text 2. Absolute, **% of baseline** 3. ADA+ve subjects identified in legend	IA1 IA2
6.9.	Safety	F_PD1	Individual plot of flow cytometry key parameters over time for psoriasis patients	Same as for HV	IA2
6.10.	Safety	F_PD3	Mean (±SD) flow cytometry key parameters over time for healthy volunteers	1. Only the 6 key flow parameters - see RAP 2. **% of baseline**	IA2
6.11.	Safety	F_PD3	Mean (±SD) flow cytometry key parameters over time for psoriasis patients	Same as for HV	IA2
s-LAG3					
6.12.	Safety	F_PD1	Individual plot of s-LAG3 over time for healthy volunteers	1. Absolute, CFB 2. ADA+ve subjects identified in legend	IA1 IA2
6.13.	Safety	F_PD1	Individual plot of s-LAG3 over time for psoriasis patients	Same as for HV	IA2
6.14.	Safety	F_PD3	Mean (±SD) s-LAG3 over time for healthy volunteers	CFB	IA2 W2
6.15.	Safety	F_PD3	Mean (±SD) s-LAG3 over time for psoriasis patients	Same as for HV	IA2 W2

Pharmacodynamic and Biomarker: Figures					
No.	**Population**	**IDSL / Example Shell**	**Title**	**Programming Notes**	**Deliverable**
Transcriptomics					
6.16.	Safety	F_PD4	Boxplot of the blood transcriptomics for healthy volunteers	1. By gene (not including housekeeping genes) and summary (delta delta Ct and fold change) - only 1 visit Day 2 2. x-axis: treatment group 3. Individual values (jittered) displayed on top of the boxplot 4. Add footnote about the values in the boxplot	SAC
6.17.	Safety	F_PD4	Boxplot of the blood transcriptomics for psoriasis patients	Same as for HV	SAC
6.18.	Safety	F_PD4	Boxplot of the biopsy transcriptomics for psoriasis patients	Same as for HV Display only versus Day 29 (not day 15)	IA2 W2
Flow cytometry					
6.19.	Safety	F_PD3	Mean (±SE) flow cytometry key parameters up to Day 29 Visit for healthy volunteers	1. Only the 6 key flow parameters - see RAP 2. % of baseline	SAC
6.20.	Safety	F_PD3	Mean (±SE) flow cytometry key parameters up to Day 29 Visit for psoriasis patients	1. Only the 6 key flow parameters - see RAP 2. % of baseline	SAC
s-LAG3					
6.21.	Safety	F_PD3	Mean (±SD) s-LAG3 up to Day 29 Visit for healthy volunteers	CFB	SAC

Pharmacodynamic and Biomarker: Figures					
No.	**Population**	**IDSL / Example Shell**	**Title**	**Programming Notes**	**Deliverable**
6.22.	Safety	F_PD3	Mean (±SD) s-LAG3 up to Day 29 Visit for psoriasis patients	CFB	SAC

14.9.13. ICH Listings

ICH: Listings					
No.	**Population**	**IDSL / Example Shell**	**Title**	**Programming Notes**	**Deliverable**
1.	Safety	DM2	Listing of demographic characteristics for healthy volunteers		IA1
2.	Safety	DM2	Listing of demographic characteristics for psoriasis patients		IA2 W2
3.	Safety	AE7	Listings of subject numbers for individual adverse events for healthy volunteers		SAC
4.	Safety	AE7	Listings of subject numbers for individual adverse events for psoriasis patients	same as for HV	IA2 W2
5.	Safety	CP_AE8	Listing of all adverse events for healthy volunteers		IA2 W2
6.	Safety	CP_AE8	Listing of all adverse events for psoriasis patients	same as for HV	IA2 W2
7.	Safety	CP_AE8a	Listing of serious adverse events for healthy volunteers	Same as for all Aes	IA2 W2
8.	Safety	CP_AE8a	Listing of serious adverse events for psoriasis patients	same as for HV	IA2 W2
9.	Safety	CP_AE8	Listing of adverse events leading to withdrawal from study for healthy volunteers		SAC
10.	Safety	CP_AE8	Listing of adverse events leading to withdrawal from study for psoriasis patients		SAC
11.	Safety	CP_LB5	Listing of clinical chemistry abnormalities of potential clinical importance for healthy volunteers		IA2 W2
12.	Safety	CP_LB5	Listing of clinical chemistry abnormalities of potential clinical importance for psoriasis patients		IA2 W2
13.	Safety	CP_LB6	Listing of all clinical chemistry laboratory data for subjects with PCI abnormalities for healthy volunteers		IA1 SAC

ICH: Listings					
No.	**Population**	**IDSL / Example Shell**	**Title**	**Programming Notes**	**Deliverable**
14.	Safety	CP_LB6	Listing of all clinical chemistry laboratory data for subjects with PCI abnormalities for psoriasis patients		IA2 W2
15.	Safety	CP_LB5	Listing of haematology abnormalities of potential clinical importance for healthy volunteers		IA2 W2
16.	Safety	CP_LB5	Listing of haematology abnormalities of potential clinical importance for psoriasis patients		IA2 W2
17.	Safety	CP_LB6	Listing of all haematology laboratory data for subjects with PCI abnormalities for healthy volunteers		SAC
18.	Safety	CP_LB6	Listing of all haematology laboratory data for subjects with PCI abnormalities for psoriasis patients		IA2 W2
19.	Safety	UR2a	Listing of urinalysis data for healthy volunteers		IA1 SAC
20.	Safety	UR2a	Listing of urinalysis data for psoriasis patients		SAC
21.	Safety		Listing of CMV and EBV serology for healthy volunteers		SAC
22.	Safety		Listing of CMV and EBV serology for psoriasis patients		SAC
23.	Safety	CP_EG3	Listing of ECG values of potential clinical importance for healthy volunteers		IA2 W2
24.	Safety	CP_EG3	Listing of ECG values of potential clinical importance for psoriasis patients		IA2 W2
25.	Safety	CP_EG3	Listing of all ECG values for subjects with any value of potential clinical importance for healthy volunteers		IA2 W2
26.	Safety	CP_EG3	Listing of all ECG values for subjects with any value of potential clinical importance for psoriasis patients		IA2 W2
27.	Safety	CP_EG5	Listing of abnormal ECG findings for psoriasis patients		IA2 W2

ICH: Listings					
No.	**Population**	**IDSL / Example Shell**	**Title**	**Programming Notes**	**Deliverable**
28.	Safety	CP_VS4	Listing of vital signs of potential clinical importance for healthy volunteers		IA2 W2
29.	Safety	CP_VS4	Listing of vital signs of potential clinical importance for psoriasis patients		IA2 W2
30.	Safety	CP_VS4	Listing of all vital signs for subjects with any value of potential clinical importance for healthy volunteers		IA1 SAC
31.	Safety	CP_VS4	Listing of all vital signs for subjects with any value of potential clinical importance for psoriasis patients		SAC
64	Safety	CP_TA1	Listing of randomised and actual treatments for healthy volunteers		SAC
65	Safety	CP_TA1	Listing of randomised and actual treatments for psoriasis patients		SAC
66	Safety	ES2	Listing of reasons for study withdrawal for healthy volunteers		SAC
67	Safety	ES2	Listing of reasons for study withdrawal for psoriasis patients		SAC
68	All screened	ES7	Listing of reasons for screening failure for healthy volunteers		SAC
69	All screened	ES7	Listing of reasons for screening failure for psoriasis patients		SAC
70	Safety	DV2	Listing of important protocol deviations for healthy volunteers		SAC
71	Safety	DV2	Listing of important protocol deviations for psoriasis patients		SAC

ICH: Listings					
No.	**Population**	**IDSL / Example Shell**	**Title**	**Programming Notes**	**Deliverable**
72	Safety		Listing of Subjects with Inclusion/Exclusion Criteria Deviations for Healthy Volunteers		SAC
73	Safety		Listing of Subjects with Inclusion/Exclusion Criteria Deviations for Psoarisis Patients		SAC
74	Safety		Listing of Race for Healthy Volunteers		SAC
75	Safety		Listing of Race for Psoarisis Patients		SAC
76	Safety	SA3a	Listing of subjects excluded from any population for healthy volunteers		SAC
77	Safety	SA3a	Listing of subjects excluded from any population for psoriasis patients		SAC
78	Safety	CP_CM3	Listing of concomitant medications by generic term for healthy volunteers		SAC
79	Safety	CP_CM3	Listing of concomitant medications by generic term for psoarisis patients		SAC
80	Safety	CP_EG5	Listing of abnormal ECG findings for healthy volunteers		SAC

14.9.14. Non-ICH Listings

Non-ICH: Listings					
No.	**Population**	**IDSL / Example Shell**	**Title**	**Programming Notes**	**Deliverable**
32.	PK	PK07	Listing of plasma GSK2831781 pharmacokinetic concentration-time data for healthy volunteers		IA2 W2
33.	PK	PK07	Listing of plasma GSK2831781 pharmacokinetic concentration-time data for psoriasis patients		IA2 W2
34.	PK	PK13	Listing of derived plasma GSK2831781 pharmacokinetic parameters for healthy volunteers		IA2 W2
35.	PK	PK13	Listing of derived plasma GSK2831781 pharmacokinetic parameters for psoriasis patients		IA2 W2
36.	Safety	IMM2	Listing of immunogenicity results for healthy volunteers	NAB assay results included for SAC	IA2 W2
37.	Safety	IMM2	Listing of immunogenicity results for psoriasis patients	same as for HV	IA2 W2
38.	Safety		Listing of induration diameter for healthy volunteers (DTH subjects)		IA1
39.	Safety		Listing of duration of induration for healthy volunteers (DTH subjects)		IA1
40.	safety		Raw sas output statistical analysis results of change from baseline in induration diameter for healthy volunteers (DTH subjects)		IA1
41.	safety		Raw sas output statistical analysis results of duration of induration for healthy volunteers (DTH subjects)		IA1
42.	Safety	LS1	Listing of PASI-related endpoints for psoriasis patientss		SAC
43.	Safety		Listing of PASI components for psoriasis patients		SAC

Non-ICH: Listings					
No.	**Population**	**IDSL / Example Shell**	**Title**	**Programming Notes**	**Deliverable**
44.	Safety		Listing of BSA scores for psoriasis patients		SAC
45.	Safety		Raw sas output of statistical analysis results for change from baseline in PASI scores for psoriasis patients		IA2 EFF IA2
46.	Safety		Raw sas output of statistical analysis results for change from baseline in PLSS score for psoriasis patients		IA2 EFF IA2
47.	Safety		Listing of PLSS-related endpoints for psoriasis patients		SAC
48.	Safety		Listing of PGA-related endpoints for psoriasis patients		SAC
49.	Safety		Listing of cytokines for healthy volunteers		IA1
50.	Safety		Listing of cytokines for psoriasis patients		SAC
51.	Safety		Listing of flow cytometry for healthy volunteers	All the parameters, not only the 6 key ones	IA1
52.	Safety		Listing of flow cytometry for psoriasis patients	All the parameters, not only the 6 key ones	SAC
53.	Safety		Listing of LAG3+ and CD3+ in skin for healthy volunteers (DTH subjects)		IA1
54.	Safety		Listing of cells in lesional biopsies measured by IHC for psoriasis patients		SAC
55.	Safety		Listing of epidermis thickness for psoriasis patients		SAC
56.	Safety		Raw sas output of statistical analysis results for change from baseline LAG3+ and CD3+ for healthy volunteers (DTH subjects)		SAC

Non-ICH: Listings					
No.	**Population**	**IDSL / Example Shell**	**Title**	**Programming Notes**	**Deliverable**
57.	Safety		Raw sas output of statistical analysis results for change from baseline in cells in lesional biopsies measured by IHC for psoriasis patients		SAC
58.	Safety		Raw sas output of statistical analysis results for change from baseline in epidermis thickness for psoriasis patients		SAC
59.	Safety		Listing of sLAG-3 for healthy volunteers		SAC
60.	Safety		Listing of sLAG-3 for psoriasis patients		SAC
61.	Safety		Listing of blood transcriptomics for healthy volunteers	Includes raw Ct as well as average (mean delta Ct, delta delta Ct and fold change)	SAC
62.	Safety		Listing of blood transcriptomics for psoriasis patients		SAC
63.	Safety		Listing of biopsy transcriptomics for psoriasis patients		IA2 W2
81	Safety	other	Listing of PPD challenge for healthy volunteers (DTH subjects)		SAC

14.10. Appendix 10: Example Mock Shells for Data Displays

Data Display Specification will be made available on Request.