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

Title	:	Reporting and Analysis Plan for a multi-centre Phase IIa double-blind, placebo-controlled study to investigate the efficacy and safety of GSK3196165 in subjects with inflammatory hand osteoarthritis.
Compound Number	:	GSK3196165
Effective Date	:	09-FEB-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 204851.
- This RAP is intended to describe the planned efficacy, safety, pharmacokinetic (PK), PK/PD and Biomarker analyses required for the study.
- This RAP will be provided to the study team members to convey the content of the Interim Analyses and Statistical Analysis Complete (SAC) deliverables.

Author's Name and Functional Area:

Approver	Date	Approval Method
PPD Statistician (Immuno-Inflammation, Clinical Statistics)	NA	NA
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Approver	Date	Approval Method
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RAP Team Approvals:

Approver	Date	Approval Method
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TABLE OF CONTENTS

PAGE

1. REPORTING & ANALYSIS PLAN SYNPOSIS

Overview	Key Elements of the RAP
Purpose	• This RAP details all planned analyses and outputs required for the final Clinical Study Report (CSR) of study 204851.
Protocol	• This RAP is based on the protocol amendment 2(Dated:03Jan2017) of study 204851 (GSK Document No. : 2015N242468_02)
Primary Objective	• To assess the efficacy potential of GSK3196165 on pain in inflammatory Hand Osteoarthritis (HOA).
Primary Endpoint	• Change from baseline in 24h average hand pain intensity at Week 6, as measured by daily pain Numerical Rating Scale (NRS) averaged over the 7 days prior to assessment visit.
Study Design	• Randomised Phase IIa, multicentre, double-blind (sponsor unblind), placebo-controlled parallel group study in patients with active inflammatory HOA. • At least 40 subjects will be randomised to either placebo or GSK3196165 in a 1:1 ratio (n=20 per arm). • 4 week screening period will be followed by a 12 week treatment period (dosing with GSK3196165 or placebo), then a follow up period completing on week 22. • Treatment with GSK3196165 or placebo will be given as a single subcutaneous injection (shielded to subjects) to the abdomen or thigh, by an unblinded administrator weekly for 5 injections, from Week 0 to Week 4 (Days 1, 8, 15, 22, 29), then every other week for 3 further injections, from Week 6 until Week 10 (Days 43, 57 and 71).
Planned Analyses	• Efficacy (Primary Analysis) • Safety, PK, PK/PD, Biomarkers, Imaging (Secondary/Exploratory analyses)
Analysis Populations	• Screened population: all subjects who were screened including those who are classified as screen failures. • Enrolled population: all subjects who passed screening and entered the study. • Intent to Treat (ITT) population: all subjects who were randomised to treatment and who received at least one dose of study treatment. This population will be based on randomised treatment group. • Safety population: all subjects who received at least one dose of study treatment (GSK3196165 or placebo).This population will be based on the treatment actually received. • Pharmacokinetic (PK) population: all subjects in the 'Safety' population who have at least one valid PK assessment.

Overview	Key Elements of the RAP
Hypothesis	• H_0: there is no difference between GSK3196165 and placebo in the change from baseline in the average Pain NRS Scale at Week 6. • H_A: there is a difference between GSK3196165 and placebo in the change from baseline in the average Pain NRS Scale at Week 6.
Primary Analyses	• The primary endpoint will be analysed using a repeated measures model (MMRM).
Secondary Analyses	• Continuous endpoints will be analysed using the same methods as the primary endpoint. For some endpoints this may be after transformation, if applicable. • Binary endpoints will be summarised using counts and proportions and analysed using a Generalised Estimating Equations (GEE) model.

2. SUMMARY OF KEY PROTOCOL INFORMATION

2.1. Changes to the Protocol Defined Statistical Analysis Plan

Any changes from the originally planned statistical analysis specified in the protocol (GSK Document No. 2015N242468_02, Dated:03JAN2017) 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**
• Endpoint is defined as 'Change from Baseline in patient global assessment (PtGA) and physician global assessment (PhGA) of disease activity at Week 6, 12 and 22'.	• Endpoint is defined as 'Change from Baseline in patient global assessment (PtGA) and physician global assessment (PhGA) of disease activity at Weeks 2, 4, 8 12 and 22'.	• PtGA and PhGA timepoints were incorrectly specified in the endpoints list on pages 11 and 16 of protocol, but correct in the time and events table and elsewhere
• Endpoint is defined as 'Change from baseline in structural and inflammatory HOA features in the affected hand (including synovitis, bone erosions, joint space width, and bone marrow edema) as assesses by the RAMRIQ scoring system.	• Endpoint is defined as 'Change from baseline in structural and inflammatory HOA features in the affected hand (including synovitis, bone erosions, joint space width, and bone marrow edema) as assesses by the HOAMRIQ scoring system.	• Incorrect scoring system is specified in the protocol.
• Administrative Interim Review not specified	• Addition of Administrative Interim Review	• Administrative Interim Review was requested by II TA Head. This was requested after the protocol amendment was created and therefore is being documented in the RAP. The administrative interim review was approved by the MDL on 18May2017. The timing of this interim was after unblinding of the study at the protocol defined PK interim.

Protocol	Reporting & Analysis Plan	
Statistical Analysis Plan	**Statistical Analysis Plan**	**Rationale for Changes**
• Protocol specifies 'The primary endpoint will be analysed using a repeated measures model (MMRM) adjusted for baseline pain score, treatment group, visit and the visit by treatment group interaction as fixed effects, patient as a random effect and day within patient as a repeated effect, using an unstructured covariance matrix.'	• The MMRM model will also be investigated with the addition of the baseline*visit interaction term and the most appropriate model selected.	• Error from protocol specified analyses

2.2. Study Objectives and Endpoints

Objectives	Endpoints
Primary Objectives	**Primary Endpoints**
• To assess the efficacy potential of GSK3196165 on pain in inflammatory HOA.	• Change from baseline in 24h average hand pain intensity at week 6, as measured by daily pain Numerical Rating Scale (NRS) averaged over the 7 days prior to assessment visit.
Secondary Objectives	**Secondary Endpoints**
• To evaluate impact of GSK3196165 on average and worst HOA pain, over time.	• Change from baseline in 24h average hand pain intensity at each visit, measured by daily pain NRS and averaged over the 7 days prior to each assessment visit. • Change from baseline of worst hand pain intensity over 24h at each visit, measured by daily NRS and averaged over the 7 days prior to each assessment visit. • Proportion of subjects in each treatment group achieving a 30% reduction in 24h average hand pain intensity at each visit, measured by daily NRS averaged over the 7 days prior to assessment visit. • Proportion of subjects in each treatment group achieving a 50% reduction in 24h average hand pain intensity at each visit, measured by daily NRS averaged over the 7 days prior to assessment visit. • Proportion of subjects in each treatment group achieving a 30% reduction in 24h worst hand pain intensity at each visit, measured by daily NRS averaged over the 7 days prior to assessment visit.

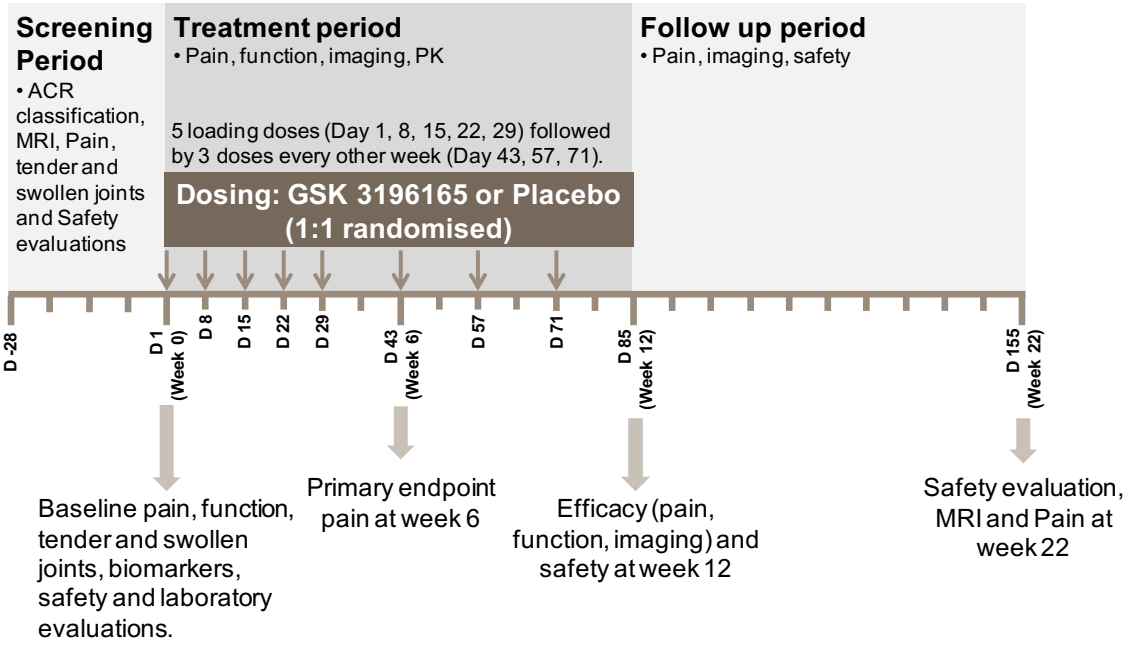
Objectives	Endpoints
	• Proportion of subjects in each treatment group achieving a 50% reduction in 24h worst hand pain intensity at each visit, measured by daily NRS averaged over the 7 days prior to assessment visit.
• To assess the impact of GSK3196165 on hand pain (on use), stiffness and function, over time.	• Change from baseline in Australian Canadian Hand Osteoarthritis Index (AUSCAN) 3.1 NRS, total and domains (pain, morning stiffness, function) scores at each visit.
• To assess the impact of GSK3196165 on HOA inflammation.	• Change in number of swollen and tender hand joints at each visit.
• To assess potential impact of GSK3196165 on disease activity in HOA.	• Change from baseline in patient global assessment (PtGA) and physician global assessment (PhGA) of disease activity at Weeks 2, 4, 8 12 and 22.
• To assess safety of GSK3196165 in HOA patients, over the study duration.	• Incidence of adverse events and serious adverse events. • Incidence of infections. • Incidence of pulmonary events (cough/dyspnea, PAP and D_{LCO}). • Immunogenicty.
• To assess population pharmacokinetics of GSK3196165 in HOA.	• Population pharmacokinetics endpoints such as CL/F, Vss/F, Ka.
Exploratory Objectives	**Exploratory Endpoints**
• To explore the potential impact of GSK3196165 on disease progression/modification in HOA, using MRI imaging.	• Change from baseline in synovitis in the affected hand*, as measured by DCE-MRI including the exchange rate (K^{trans}), interstitial volume (v_e), plasma volume (v_p), volume of synovitis, initial rate of enhancement (IRE), and maximum signal intensity enhancement (ME). • Change from baseline in structural and inflammatory HOA features in the affected hand* (including synovitis, erosive damage, cysts, osteophytes, cartilage space loss, malalignment, and bone marrow lesions) as assessed by the OMERACT HOAMRIS scoring system • Change from baseline in structural and inflammatory HOA features in the affected hand* (including synovitis, bone erosions, joint space width, and bone marrow edema) as assesses by the HOAMRIQ scoring system. • Change from baseline in bone shape as assessed by structural MRI of the affected hand*.

Objectives	Endpoints
• The exploration of the relationship between GSK3196165 PK and PD effects and/or efficacy.	• Relationship between concentration or PK parameters and PD endpoint(s).
• To evaluate the potential of GSK3196165 to affect biomarkers of HOA.	• Change in blood biomarkers from baseline at each visit.

* If only one hand is affected by HOA and meets the inclusion criteria, the affected hand will be documented at screening and used for all assessments. In cases where both hands are affected by HOA and both meet the inclusion criteria, then the dominant hand will be documented at screening and this hand will be used for the MRI assessments throughout the study.

2.3. Study Design

Overview of Study Design and Key Features



Design Features	• Randomised phase IIa, multicentre, double-blind (sponsor unblind), placebo-controlled, parallel group study in patients with active inflammatory HOA.
Dosing	• A screening period of up to 4 weeks. • Treatment with GSK3196165 or placebo will be given as a single subcutaneous injection (shielded to subjects) to the abdomen or thigh, by an unblinded administrator weekly for 5 injections, from Week 0 to Week 4 (Days 1, 8, 15, 22, 29), then every other week for 3 further injections, from Week 6 until Week 10 (Days 43, 57 and 71). • In total, each subject will receive up to 8 doses of study treatment.
Treatment Assignment	• At least 40 subjects will be randomized across the two treatment arms, to receive either placebo or GSK3196165 in a 1:1 ratio (n=20 per arm).
Interim Analysis	• An interim analysis will be performed on available PK and target engagement biomarker data to coincide with other internal decision making across the GSK3196165 project. • Another formal interim analysis may be conducted on the key safety, primary efficacy and key secondary endpoints once a minimum of 30 subjects have completed day 43 (week 6). • In addition to the formal planned interim analyses, further data reviews may be carried out by senior managers not involved in the study conduct to aid in portfolio and budget decisions. These administrative reviews will have no impact on the ongoing study.

2.4. Statistical Hypotheses

The primary endpoint of the study is to evaluate the change from baseline in the average Pain NRS following 6 weeks of treatment with GSK3196165 or placebo in adult subjects with HOA.

The study will test the null hypothesis that there is no difference between GSK3196165 and placebo in the change from baseline in the 24h average Pain NRS Scale at Week 6. The alternative hypothesis is that there is a difference between GSK3196165 and placebo in the change from baseline in the 24h Pain NRS Scale at Week 6 using a two-sided test (α=0.05).

3. PLANNED ANALYSES

3.1. Interim Analyses

An interim analysis will be performed during the study to review the available PK data and target engagement biomarkers. The timing of this analysis will coincide with other internal decision making across the GSK3196165 project.

Another formal interim analysis may be conducted on the key safety, primary efficacy and key secondary endpoints in this study. The purpose of this interim will be to help with decision-making regarding the subsequent clinical development of GSK3196165 for OA. The timing of this analysis will be once a minimum of 30 subjects have completed day 43 (Week 6). It is likely that by the time 30 subjects have completed week 6 the study would have fully recruited and the interim would not lead to early stopping of this study for efficacy.

In addition to the formal planned interim analyses, further data reviews may be carried out by senior managers not involved in the study conduct to aid in portfolio and budget decisions. These administrative reviews will have no impact on the ongoing study.

Full details can be found in Section 10.

3.2. Final Analyses

The final planned end of study analyses on all endpoints will be performed after the completion of the following sequential steps:

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

4. ANALYSIS POPULATIONS

Population	Definition / Criteria	Analyses Evaluated
Screened	• Comprise of all subjects who were screened including those subjects who were classified as Screen Failures	• Study Population
Enrolled	• All participants who passed screening and entered the study. Included are: Run-in Failures; Randomized Participants; in non-randomized study and participants who were assigned a treatment in a non-randomised study. • Note screening failures (who never passed screening even if rescreened) and participants screened but never enrolled into the study (Reserve, Not Used) are excluded from the Enrolled population as they did not enter the study.	• Study Population
Intent-To-Treat (ITT)	• Comprise of all randomised subjects who receive at least one dose of study treatment (GSK3196165 or placebo). • This population will be based on the treatment to which the subject was randomised. • Any subject who receives a treatment randomisation number will be considered to have been randomised.	• Study Population • Efficacy
Safety	• Comprise of all subjects who receive at least one dose of study treatment (GSK3196165 or placebo). • This population will be based on the treatment the subject actually received. • If a subject consistently received the same wrong treatment arm, then this will be considered as the actual treatment arm. The handling of subjects receiving a wrong treatment only for some applications will be decided on a case by case basis.	• Safety • PD/Biomarker
Pharmacokinetic (PK)	• Subjects in the 'Safety' population for whom a pharmacokinetic sample was obtained and analysed.	• PK • PK/PD

NOTES :

- Please refer to Appendix 15: List of Data Displays which details the population to be used for each displays being generated.

4.1. Protocol Deviations

Please refer to the Protocol Deviation Management Plan (PDMP): Dated: 30Nov2017 (Version 3) for full details.

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

5. CONSIDERATIONS FOR DATA ANALYSES AND DATA HANDLING CONVENTIONS

Table 2 provides an overview of appendices within the RAP for outlining general considerations for data analyses and data handling conventions.

Table 2 Overview of Appendices

Section	Component
12.1	Appendix 1: Protocol Deviation Management and Definitions for Per Protocol Population
12.2	Appendix 2: Time & Events
12.3	Appendix 3: Assessment Windows
12.4	Appendix 4: Treatment States and Phases
12.5	Appendix 5: Data Display Standards & Handling Conventions
12.6	Appendix 6: Derived and Transformed Data
12.7	Appendix 7: Premature Withdrawals & Handling of Missing Data
12.8	Appendix 8: Values of Potential Clinical Importance
12.9	Appendix 9: Multicentre Studies
12.10	Appendix 10: Multiple Comparisons & Multiplicity
12.11	Appendix 11: Model Checking and Diagnostics for Statistical Analyses.
12.12	Appendix 12: Definition of some Parameters of Interest
12.13	Appendix 13: Opportunistic Infections: MedDRA Preferred Terms
12.14	Appendix 14: Abbreviations & Trade Marks
12.1512.15	Appendix 15: List of Data Displays
12.16	Appendix 16: Example Mock Shells for Data Displays

5.1. General Considerations

- This is a multi-centre study and there are no planned adjustments for multiple centres or regions.
- There are no planned adjustments for multiple comparisons or multiplicity.

Unless otherwise stated, the following rules will apply:

- Summaries and displays will present data by treatment group.
- Listings will be sorted by treatment group.
- The following statistics will be used to summarise the data, unless otherwise specified:

  - Continuous Variables: number of observations (n), mean, standard deviation (SD), median, minimum and maximum.
  - Categorical Variables: number of observations (n), frequency counts and percentages.

- Summaries by Visit: Only scheduled visits will be presented, unless otherwise stated. Scheduled visits will be slotted as shown in section 12.3.1.
- Unscheduled visits will be listed but will not contribute towards any summary statistics/analyses, unless otherwise stated.
- For continuous endpoints, no imputation for missing values across visits will be done, individual missing item scores contributing to PRO domain scores may be imputed as per the rules given within each PRO (see section 12.7.2.3 for full details)..
- For binary endpoints, subjects with missing values will be considered as non-responders.

6. STUDY POPULATION ANALYSES

6.1. Overview of Planned Analyses

The Study Population analyses will be based on the Screened, Enrolled or Intent-to-Treat (ITT) population, as appropriate unless otherwise specified.

Table 3 provides an overview of the planned study population analyses, with full details of data displays being presented in Appendix 17: List of Data Displays.

Table 3 Overview of Planned Study Population Analyses

Display Type	Data Displays Generated	
	Table	Listing
Randomisation		
Randomised and Actual Treatments		Y
Subject Disposition		
Subject Disposition	Y	
Screening Status and Reasons for Screening Failures	Y	Y
Subjects by Country and Site ID	Y	
Reasons for Subject Withdrawals		Y
Subjects for Whom the Treatment Blind was Broken		Y
Protocol Deviations		
Important protocol deviations	Y	Y
Subjects with Inclusion/Exclusion Criteria Deviations		Y[1]
Populations Analysed		
Study Populations	Y	
Subjects Excluded from Any Population		Y
Demographic and Baseline Characteristics		
Demographics Characteristics	Y	Y
Baseline Efficacy Parameters	Y	
Race and Racial Combinations	Y	Y[2]
OA Disease History	Y	Y
Medical Condition & Concomitant Medications		
Current Medical Conditions	Y	Y
Concomitant medication	Y	Y
Concomitant OA medication	Y	
Prior Medication	Y	Y
Prior OA medication	Y	
Exposure &Treatment Compliance		
Exposure to Study Treatment	Y	Y

NOTES :

- Y = Yes display generated.
- [1] Listing also includes analysis population exclusions.
- [2] Listing of race.

6.1.1. Prior/Concomitant OA Medication

OA medications will be identified by the Medical Monitor through review of unique terms and indications prior to unblinding.

7. PRIMARY STATISTICAL ANALYSES

7.1. Efficacy Analyses

7.1.1. Overview of Planned Primary Efficacy Analyses

The Primary Endpoint is defined as the change from baseline in 24h average hand pain intensity at week 6, as measured by the daily pain Numerical Rating Scale (NRS) averaged over the 7 days prior to assessment visit.

The primary efficacy analyses will be based on the "Intent-To-Treat" population, unless otherwise specified.

Table 4 provides an overview of the planned efficacy analyses, with full details of data displays being presented in Section 12.15: List of Data Displays.

Table 4 Overview of Planned Primary Efficacy Analyses

Endpoint	Absolute							Change from Baseline						
	Stats Analysis			Summary		Individual		Stats Analysis			Summary		Individual	
	T	F	L	T	F	F	L	T	F	L	T	F	F	L
Pain														
24h **average** hand pain NRS score averaged over 7 days prior to assessment	Y[2]		Y [1,2]	Y[2]	Y[2]	Y	Y	Y	Y	Y [1]	Y	Y		Y

NOTES :

- T = Table, F = Figure, L = Listing, Y = Yes display generated.
- Stats Analysis = Represents TFL related to any formal statistical analyses (i.e. modelling) conducted.
- Summary = Represents TFL related to any summaries (i.e. descriptive statistics) of the observed raw data.
- Individual = Represents FL related to any displays of individual subject observed raw data.
- [1] Raw SAS log output from analysis
- [2] Absolute values will be displayed in the same outputs as the change from baseline.

7.1.2. Planned Primary Efficacy Statistical Analyses

Primary Statistical Analyses

Endpoint(s)

- Change from baseline in 24h average hand pain intensity at week 6, as measured by daily pain Numerical Rating Scale (NRS) averaged over the 7 days prior to assessment visit.

Model Specification

- Endpoints will be statistically analysed using a mixed model repeated measures (MMRM) model.
- The model will be fitted using an unstructured covariance matrix.
- Terms fitted in the MMRM model will include:

Fixed Categorical	: Treatment group, Visit, Treatment group * Visit Interaction
Fixed Continuous Covariates	: Baseline pain score #
Random Covariates	: Subject
Repeated	: Visit

A model will also be explored fitting Baseline*Visit & the most appropriate model selected.

Model Checking & Diagnostics

- Refer to Appendix 11: Model Checking and Diagnostics for Statistical Analyses.

Model Results Presentation

- Point estimates and corresponding 95% confidence intervals will be constructed for the treatment differences (GSK3196165-Placebo) at each visit, using the least squared (LS) means obtained from the repeated measures mixed-effects model.
- Plots of LS means and 95% confidence intervals from the model will be generated for each treatment group by time.

Sensitivity and Supportive Statistical Analyses

- Following review of the data, additional analyses maybe conducted to further support the primary statistical analyses, if deemed appropriate.
- Non-parametric analyses may be conducted if the normality assumption does not hold.
- Analyses using different covariance structures may be explored if the unstructured covariance matrix does not converge. The first covariance structures to be tested will be compound symmetry (CS) and then first order autoregressive (AR(1)).
- Sensitivity analyses maybe conducted to assess the impact of missing data.
- Further sensitivity analyses may be conducted to assess the impact of rescue medication use:
- E.g. The impact of imputing all 24h average pain scores to be the 24h worst pain score on days in which paracetamol was used (any dose) may be assessed.
- Further sensitivity analyses may be conducted excluding any subjects taking prohibited medications throughout the study.
-

8. SECONDARY STATISTICAL ANALYSES

8.1. Efficacy Analyses

8.1.1. Overview of Planned Secondary Efficacy Analyses

The secondary efficacy analyses will be based on the "Intent-To-Treat" population, unless otherwise specified.
Table 5 provides an overview of the planned efficacy analyses, with further details of data displays being presented in Appendix 17: List of Data Displays.

Table 5 Overview of Planned Efficacy Analyses

Endpoint	Absolute							Change from Baseline						
	Stats Analysis			Summary		Individual		Stats Analysis			Summary		Individual	
	T	F	L	T	F	F	L	T	F	L	T	F	F	L
24h average hand pain NRS score														
Proportion of subjects achieving a 30% reduction in 24h average hand pain NRS score averaged over 7 days prior to assessment	Y [2]		Y [1]	Y [2]	Y		Y							
Proportion of subjects achieving a 50% reduction in 24h average hand pain NRS score averaged over 7 days prior to assessment	Y [2]		Y [1]	Y [2]	Y		Y							
Daily 24h average hand pain NRS							Y							
24h worst hand pain NRS score														
24h worst pain NRS score averaged over 7 days prior to assessment	Y[3]		Y [1,3]	Y [3]	Y [3]	Y	Y	Y	Y	Y[1]	Y	Y		Y
Daily 24h worst hand pain NRS							Y							
Proportion of subjects achieving a 30% reduction in 24h worst pain NRS score averaged over 7 days prior to assessment	Y [2]		Y [1]	Y [2]	Y		Y							
Proportion of subjects achieving a 50% reduction in 24h worst pain NRS	Y [2]		Y [1]	Y [2]	Y		Y							

Endpoint	Absolute							Change from Baseline						
	Stats Analysis			Summary		Individual		Stats Analysis			Summary		Individual	
	T	F	L	T	F	F	L	T	F	L	T	F	F	L
score averaged over 7 days prior to assessment														
AUSCAN														
AUSCAN 3.1 NRS Components	Y [3]		Y [1,3]	Y [3]	Y [3]	Y	Y	Y	Y	Y [1]	Y	Y		Y
Joint Assessments														
Swollen hand joints	Y [3]		Y[1,3]	Y [3]	Y [3]		Y	Y	Y	Y[1]	Y	Y		Y
Tender hand joints	Y[3]		Y[1,3]	Y [3]	Y [3]		Y	Y	Y	Y[1]	Y	Y		Y
Pain/Tenderness Hand Joint Assessment							Y							
Disease Global Assessment														
PhGA	Y [3]		Y[1,3]	Y [3]	Y [3]		Y	Y	Y	Y[1]	Y	Y		Y
PtGA	Y[3]		Y[1,3]	Y [3]	Y [3]		Y	Y	Y	Y[1]	Y	Y		Y

NOTES :
T = Table, F = Figure, L = Listing, Y = Yes display generated.
Stats Analysis = Represents TFL related to any formal statistical analyses (i.e. modelling) conducted.
Summary = Represents TFL related to any summaries (i.e. descriptive statistics) of the observed raw data.
Individual = Represents FL related to any displays of individual subject observed raw data.
[1] Raw SAS log output from analysis.
[2] Summaries and analysis will be presented together in one output.
[3] Absolute values will be displayed in the same outputs as the change from baseline.

8.1.2. Planned Secondary Efficacy Statistical Analyses

8.1.2.1. Continuous Endpoints

Secondary Statistical Analyses
Endpoint(s)
• Change from baseline in 24h **average** hand pain intensity at each visit, measured by daily pain NRS and averaged over the 7 days prior to each assessment visit. • Change from baseline of **worst** hand pain intensity over 24h at each visit, measured by daily NRS and averaged over the 7 days prior to each assessment visit. • Change from baseline in Australian Canadian Hand Osteoarthritis Index (AUSCAN) 3.1 NRS, total and domains (pain, morning stiffness, function) scores at each visit. • Change from baseline in number of swollen and tender hand joints at each visit. • Change from baseline in patient global assessment (PtGA) and physician global assessment (PhGA) of disease activity at Weeks 2, 4, 8, 12 and 22.
Model Specification

Secondary Statistical Analyses
• Continuous endpoints will be statistically analysed using the same methods as the primary endpoint (MMRM). See Section 7.1.2 for full details.
Model Checking & Diagnostics
• Refer to Appendix 11: Model Checking and Diagnostics for Statistical Analyses.
Model Results Presentation
• Continuous endpoints will be presented using the same methods as the primary endpoint.

Sensitivity and Supportive Statistical Analyses
• Non-parametric analyses may be conducted if the normality assumption does not hold. • Analyses using different covariance structures may be explored if the unstructured covariance matrix does not converge. The first covariance structures to be tested will be compound symmetry and then first order autoregressive (AR(1)). • Further sensitivity analyses may be conducted to assess the impact of missing data. • Further sensitivity analyses may be conducted to assess the impact of rescue medication use: ○ E.g. The impact of imputing all 24h average pain scores to be the 24h worst pain score on days in which paracetamol was used (any dose) may be assessed. • Further sensitivity analyses may be conducted excluding any subjects taking prohibited medications throughout the study.

8.1.2.2. Binary Endpoints

Secondary Statistical Analyses
Endpoint(s)
• Proportion of subjects in each treatment group achieving a 30% reduction in 24h average hand pain intensity at each visit, measured by daily NRS averaged over the 7 days prior to assessment visit. • Proportion of subjects in each treatment group achieving a 50% reduction in 24h average hand pain intensity at each visit, measured by daily NRS averaged over the 7 days prior to assessment visit. • Proportion of subjects in each treatment group achieving a 30% reduction in 24h worst hand pain intensity at each visit, measured by daily NRS averaged over the 7 days prior to assessment visit. • Proportion of subjects in each treatment group achieving a 50% reduction in 24h worst hand pain intensity at each visit, measured by daily NRS averaged over the 7 days prior to assessment visit.
Model Specification
• Binary efficacy endpoints will be statistically analysed using a Generalised Estimating Equations (GEE) model, which will be used to test the treatment comparison of GSK3196165 versus placebo, accounting for the within-subject correlation of outcomes across the multiple visits.

Secondary Statistical Analyses

- The model will be fitted using an unstructured covariance structure of the correlated responses.
- Terms fitted in the GEE model will include:

Fixed Categorical	: Treatment group, Visit, Treatment group * Visit Interaction, Respective Baseline NRS score
Repeated	: Visit

Model Checking & Diagnostics

- Refer to Appendix 11: Model Checking and Diagnostics for Statistical Analyses.

Model Results Presentation

- The Binary endpoints will be summarised using counts and proportions of subjects achieving a response by treatment group.
- Differences in the proportions of subjects achieving response between active and placebo will be summarised at each visit. 95% CI for the differences will be constructed using their asymptotic standard errors (asymptotic Wald confidence limits) without continuity correction.
- Point estimates and corresponding 95% confidence intervals will be constructed using contrasts for the treatment by day interactions.
- Plots of the point estimates and 95% confidence intervals from the model will be generated for each treatment group by time.

Sensitivity and Supportive Statistical Analyses

- Analyses using different covariance structures may be explored if considered appropriate.
- Further sensitivity analyses may be conducted excluding any subjects taking prohibited medications throughout the study.

8.2. Safety Analyses

8.2.1. Overview of Planned Adverse Event Analyses

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

Table 6 provides an overview of the planned analyses, with further details of data displays being presented in Appendix 16: List of Data Displays.

Table 6 Overview of Planned Safety Analyses

Endpoint	Absolute			
	Summary		Individual	
	T	F	F	L
Adverse Events (AEs)				
AE's (Overview)	Y			
All AE's	Y			Y
Common (>=5%) AE's	Y	Y[1]		
All Drug-Related AE's	Y			
Subjects & No. Of Occurrences of Common (>=5%) Non-Serious AE's	Y			
Subject Numbers for Individual AE's				Y
Relationship between AE SOC, PT and Verbatim Text				Y
Serious and Other Significant AE's				
Serious AE's	Y			
Fatal Serious AE's				Y
Non-Fatal Serious AE's				Y
Reasons for Considering as a Serious AE				Y
AE's leading to permanent discontinuation of study treatment/ withdrawal	Y			Y
AESI's	Y			Y
AESI's – Injection site reactions	Y			
AESI's – Systemic Hypersensitivity Reactions	Y			

NOTES:

- T=Table, F=Figure, L=Listing, Y=Yes display generated.
- Summary= Represents TFL related to any summaries (i.e. descriptive statistics) of the observed raw data.
- Individual= Represents FL related to any displays of individual subject observed raw data.

[1] Plot of common AEs and Relative Risk will be generated.

8.2.1.1. Adverse Events

- Adverse events (AEs) will be coded using the Medical Dictionary for Regulatory Activities (MedDRA) in the latest available version.
- Adverse events of special interest (AESI) will be derived using Common Terminology Criteria for Adverse Events, 2009 v4.0 (CTCAE) and will include:

AESI	Programmatical Derivation
Serious infections, including serious respiratory infections.	SAEs, Filter on infections SOC. Also include HLT Respiratory Infections which will be derived from the Respiratory SOC.
Opportunistic infections including TB reactivation	Opportunistic infections will be adjudicated by the SRT, using the preferred terms list given in Section 12.13. Final adjudication conducted by SRT.
Neutropenia	Based on Grade 3 or 4 absolute neutrophil count
PAP (Pulmonary alveolar proteinosis)	Derived using PAP PT.
Hypersensitivity reactions, including anaphylaxis	Hypersensitivity reactions will be adjudicated by the SRT, using AE data and data from hypersensitivity reactions eCRF page. Final adjudication conducted by SRT.
Injection site reactions	Derived from PT.

- AEs with missing intensity will be considered severe.
- Common AEs will be defined as those reported by ≥ 5% of the subjects in either treatment group, with the threshold applied before any rounding.
- AEs with partial or missing start and/or stop dates will be assumed to be treatment-emergent unless there is evidence through comparison of partial dates to suggest otherwise.
- AEs will be summarised and sorted by system organ class (SOC) and preferred term (PT), unless otherwise specified. Tables will be sorted by overall decreasing frequency of the SOC and then decreasing frequency of PT within the AE.
- Summaries will provide the number and percentage of subjects reporting at least one AE and the total number of events reported.

8.2.2. Overview of Planned Clinical Laboratory Analyses

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

Table 7 provides an overview of the planned analyses, with further details of data displays being presented in Appendix 16: List of Data Displays.

Table 7 Overview of Planned Clinical Laboratory Analyses

Endpoint / Parameter/ Display Type	Absolute			Change from BL		
	Summary		Individual	Summary		Individual
	T	F	L	T	F	L
Labs						
Clinical Chemistry				Y		
Haematology				Y		
Urinalysis				Y		
Proportion of Subjects with Urinalysis findings				Y		
Lab Parameters of Interest by CTCAE Grade				Y	Y	
Shift of Lab Parameters of Interest from Baseline to Worst CTCAE Grade	Y					
All Lab Data for Subjects with any value of PCI			Y			
Lab Values of PCI			Y			
Lab Data with Character Results			Y			
Urinalysis Data for Subjects with any value if PCI			Y			

NOTES:

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

8.2.2.1. Laboratory Values

- Refer to Appendix 6 for handling of laboratory values that are above or below the lower limit of quantification.

8.2.3. Overview of Planned Other Safety Analyses

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

Table 8 provides an overview of the planned analyses, with further details of data displays being presented in Appendix 17: List of Data Displays.

Table 8 Overview of Planned Other Safety Analyses

Endpoint / Parameter/ Display Type	Absolute				Change from BL		
	Summary		Individual		Summary		Individual
	T	F	L	F	T	F	L
ECG							
ECG Findings	Y						
ECG Values					Y	Y	
Maximum QTc Values Post-Baseline	Y						
All ECG Values for Subjects with a Value of PCI			Y				
ECG Values of PCI			Y				
Abnormal ECG Findings			Y				
Subjects meeting QTc discontinuation criteria			Y				
Vital Signs							
Vital Signs			Y		Y		
Vital Signs of PCI			Y				
All Vital Signs for Subjects with Values of PCI			Y				
Immunogenicity							
Immunogenicity Results	Y		Y				
Pulmonary Assessments							
Subjects with Pulmonary Findings	Y						
Persistent Cough, Dyspnea and D_{LCO} Decrease	Y						
Pulse Oximetry	Y		Y		Y		
D_{LCO}			Y	Y	Y		
Proportion of Subjects with 15% Relative Decrease in D_{LCO}	Y						
Spirometry (FEV1 and FVC)			Y		Y		
Cough	Y		Y				
Borg CR10	Y		Y		Y		
Lung Auscultation			Y				

NOTES:

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

8.2.3.1. ECGs

- Triplicate 12-lead ECGs will be collected at the various time points throughout the study shown in Appendix 2. All ECG parameters will be calculated by taking the mean of the non-missing values obtained in the up to three 12-lead ECG evaluations at each visit.

8.2.3.2. Vital Signs

- The following vital signs will be assessed at the various time points in the study shown in Appendix 2:
  - Temperature (in °C)
  - Systolic and diastolic blood pressure (mmHg)
  - Heart rate (beats/min)
  - Height (cm)
  - Weight(kg)
  - Calculated BMI (kg/m²)
  - Blood oxygen (%).

8.2.3.3. Immunogenicity

- Serum samples for anti-drug antibody (ADA) measurements will be obtained from all randomized subjects after administration of study drug at the scheduled visits.
- Samples taken after dosing with GSK3196165 that have a value at or above the cut-point will be considered potentially treatment-emergent ADA-positive. A Shift table from baseline to every assessment will be produced for the Immunogenicity population to assess the number of subjects going from:
  1) negative → negative,
  2) negative → positive,
  3) positive → negative, and
  4) positive → positive.
- Serum analysis will be performed under the management of Immunogenicity and Clinical Immunology (ICI), GlaxoSmithKline. Serum will be tested for the presence of anti- GSK3196165 antibodies using the currently approved analytical methodology incorporating screening, confirmation and titration steps.
  Anti-GSK3196165 Binding AB Detection (positive/negative) will be listed together with titre value (mL)

8.2.3.4. Pulmonary Assessments

- The following pulmonary assessments will be performed at the various time points in the study shown in Appendix 2:
  - Cough (as defined by CTCAE)
  - Borg CR10
  - Lung Auscultation
  - Pulse Oximetry
  - Pulmonary Function Tests (PFTs – spirometry, gas transfer [D_{LCO}])

Pulmonary findings are defined as follows:

- At least one 15% relative decrease from baseline in D_{LCO}.

- At least one 15% relative decrease from baseline in D_{LCO} to <70%.
- Cough of any grade.
- Any abnormal lung auscultation.

Respiratory Events are defined as follows:

Event	Definition
Persistent cough	Cough CTCAE grade 2 or greater recorded for 3 consecutive weeks (15 or more days). Identified through Cough 'Yes' entered in the eCRF with Grade determined from AE reporting with the following definition: AESEV=Mild = Grade 1 AESEV=Moderate= Grade 2 AESEV=Severe= Grade 3
Persistent dyspnea	Borg Scale grade 3 or greater recorded for 3 consecutive weeks (15 or more days) on the eCRF page.
Persistent decrease of D_{LCO} by >15%	Relative decrease of D_{LCO} of >15% compared to Baseline for 3 consecutive weeks (15 or more days)

These definitions are provided for guidance to identify potential cases. Final adjudication will be conducted by the SRT.

8.2.3.5. Cardiovascular Events

In the occurrence of a Cardiovascular Event, patient profiles will be produced using IDSL standard templates.

8.3. Pharmacokinetic Analyses

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

GSK3196165 serum concentration data will be analysed using population approach as described in section 8.3.3.

8.3.1. Overview of Planned Pharmacokinetic Analyses

8.3.2. Drug Concentration Measures

Refer to Appendix 5: Data Display Standards & Handling Conventions (Section 12.5.3 Reporting Process & Standards) for details on how the concentration data will be derived.

8.3.3. Population Pharmacokinetic (PopPK) Analyses

The primary goal of this analysis is to characterise the PK of GSK3196165 administered subcutaneously in subjects with HOA and compare it with other populations.

- The influence of subject demographics, baseline characteristics, and immunogenicity on the pharmacokinetics of GSK3196165 in this population will be investigated.
- The individual subject PK parameters will be estimated and documented for the purposes of any subsequent model based exposure-response (PK/PD) analyses.

PK analysis will be performed based on population PK approach. GSK3196165 serum concentration-time data will be subjected to nonlinear mixed effects modelling using the program NONMEM. To support this analysis a NONMEM file will be generated, which will be combined with already existing NONMEM file from pooled population PK analysis (Population Pharmacokinetic Analysis of GSK3196165 Following Intravenous and Subcutaneous Administration to Healthy Volunteers, Subjects with Rheumatoid Arthritis and Multiple Sclerosis (Date: 08-Jan-2016)). PK model from previous pooled analysis will be starting point this analysis. If the current PK model described the PK data from HOA subjects well (as per criteria set in TP-EP.BS-WW-001-01) no further base model development will be done. Effect of following covariates will be tested:

- Population type (HOA, healthy volunteers, rheumatoid arthritis and multiple sclerosis)
- Subject demographics (age, sex, and race)
- Baseline characteristics (body weight, free GM-CSF levels)
- Immunogenicity

Results of population PK analysis and PK/PD described in section 9.2 will be reported in detail in a standalone report which will go as an appendix/attachment to the CSR.

9. OTHER EXPLORATORY STATISTICAL ANALYSES

9.1. Imaging analyses

9.1.1. Overview of planned Imaging analyses

The Imaging analyses will be based on the "Intent-To-Treat" population, unless otherwise specified.

Table 10 provides an overview of the planned Imaging analyses, with further details of data displays being presented in Section 12.15: List of Data Displays.

Table 9 Overview of Planned Imaging Analyses

Endpoint	Absolute							Change from Baseline						
	Stats Analysis			Summary		Individual		Stats Analysis			Summary		Individual	
	T	F	L	T	F	F	L	T	F	L	T	F	F	L
Inflammatory Structural Joint Damage														
HOAMRIS Individual Components	Y[2]		Y [1,2]	Y [2]	Y [2]		Y	Y	Y	Y [1]	Y	Y	Y	Y
HOAMRIQ Individual Components	Y[2]		Y [1,2]	Y [2]	Y [2]		Y	Y	Y	Y [1]	Y	Y	Y	Y
Joint Inflammation														
DCE-MRI quantitative parameters	Y[2]		Y [1,2]	Y [2]	Y [2]		Y	Y	Y	Y [1]	Y	Y	Y	Y
Bone Shape Parameters														
Bone Shape Parameters				Y [2]	Y [2]		Y				Y	Y		Y

NOTES :

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- Summary = Represents TFL related to any summaries (i.e. descriptive statistics) of the observed raw data.
- Individual = Represents FL related to any displays of individual subject observed raw data.
- [1] Raw SAS log output from analysis.
- [2] Absolute values will be displayed in the same outputs as the change from baseline.

9.1.2. Planned Imaging Statistical Analyses

Planned Statistical Analyses
Endpoint(s)
• Change from baseline in structural and inflammatory HOA features in the affected hand* (including synovitis, erosive damage, cysts, osteophytes, cartilage space loss, malalignment, and bone marrow lesions) as assessed by the OMERACT HOAMRIS scoring system • Change from baseline in structural and inflammatory HOA features in the affected hand* (including synovitis, bone erosions, joint space width, and bone marrow edema) as assessed by the HOAMRIQ scoring system.

Planned Statistical Analyses
• Change from baseline in synovitis in the affected hand*, as measured by DCE-MRI including the exchange rate (K^{trans}), interstitial volume (v_e), plasma volume (v_p), volume of synovitis, initial rate of enhancement (IRE), and maximum signal intensity enhancement (ME). • Change from baseline in bone shape as assessed by structural MRI of the affected hand.
Planned Analyses and Model Specification
• Descriptive Statistics will be calculated for the change from baseline in each individual component of the HOAMRIS (i.e. synovitis, erosive damage, cysts, osteophytes, cartilage space loss, malalignment and bone marrow lesions), as a total for the affected/dominant (whichever is scanned) hand. • Individual Components of Interest in the HOAMRIS will be statistically analysed using the same methods as the primary endpoint (MMRM). • Descriptive statistics will be calculated for each individual component of the HOAMRIQ (i.e. synovitis, erosive damage, cysts, osteophytes, cartilage space loss, malalignment and bone marrow lesions), a total for the affected/dominant (whichever is scanned) hand. • Individual Components of Interest in the HOAMRIQ will be statistically analysed using the same methods as the primary endpoint (MMRM). • Individual components of the HOAMRIQ may be presented as measured, standardized or both (see section 12.6.5 for full details). • Descriptive Statistics will be calculated for the change from baseline in DCE-MRI quantitative derived parameters (i.e. K^{trans}, v_e, v_p, IRE, ME and volume of synovitis), as a total for the affected/dominant (whichever is scanned) hand. • DCE-MRI Parameters of interest will be statistically analysed using the same methods as the primary endpoint (MMRM). • Individual components of the DCE-MRI may be presented as measured and standardized (see section 12.6.5 for full details). • Descriptive Statistics will be calculated for the change from baseline in bone shape parameters (i.e. Surface area of bone) as a total for the affected/dominant (whichever is scanned) hand. • All parameters will be listed by subject and joint/bone.
Model Checking & Diagnostics
• Refer to Appendix 11: Model Checking and Diagnostics for Statistical Analyses.
Model Results Presentation
• Results will be presented using the same methods as the primary endpoint.

Sensitivity and Supportive Statistical Analyses
• Non-parametric analyses may be conducted if the normality assumption does not hold. • Analyses using different covariance structures may be explored if the unstructured covariance matrix does not converge.

9.2. Pharmacokinetic / Pharmacodynamic Analyses

The pharmacokinetic / pharmacodynamic (PK/PD) analyses will be based on the "Pharmacokinetic" population, unless otherwise specified.

The primary goal of this analysis is to characterize the PK/PD relationship of GSK3196165 administered subcutaneously in subjects with HOA.

The analysis will be a graphical analysis and if data permits model based analysis might be conducted on adhoc basis. Overall plots will be generated for response/biomarker data against GSK3196165 exposure parameter.

Examples of the PK/PD plots include:

- Scatter plot of change from baseline in 24h average hand pain intensity at week 4 versus pre-dose concentration values (C_{trough}) at week 4.
- Scatter plot of change from baseline in 24h average hand pain intensity at week 6 versus C_{trough} at week 6.

9.3. Biomarker Analyses

9.3.1. Pharmacodynamic Biomarker Analyses

9.3.1.1. Overview of Planned Pharmacodynamic Biomarker Analyses

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

See section 12.6.6.1 for a full list of Pharmacodynamic Biomarkers.

Table 10 provides an overview of the planned pharmacodynamic biomarker analyses, with full details of data displays being presented in Appendix 16: List of Data Displays.

All Biomarkers may require transformations; see Section 12.5.3 regarding the process of presenting log transformed data.

Prior to any data being analysed, the distributions and proportion of data falling within the quantification limits will be assessed to determine if analysis is appropriate.

Additional analysis assessing the relationship between biomarkers and clinical efficacy endpoints may be conducted if considered appropriate.

Table 10 Overview of Planned Pharmacodynamic Biomarker Analyses

Endpoint	Transformed/Untransformed													
	Absolute							Change from Baseline						
	Stats Analysis			Summary		Individual		Stats Analysis			Summary		Individual	
	T	F	L	T	F	F	L	T	F	L	T	F	F	L
Target Engagement Biomarkers														
Distribution					Y									
By Treatment & Time				Y[1]	Y		Y				Y	Y		Y

Endpoint	Transformed/Untransformed													
	Absolute							Change from Baseline						
	Stats Analysis			Summary		Individual		Stats Analysis			Summary		Individual	
	T	F	L	T	F	F	L	T	F	L	T	F	F	L
Predictive Biomarkers														
Distribution					Y									
By Treatment & Time	Y	Y	Y [1,2]	Y[1]	Y		Y	Y	Y	Y[2]	Y	Y		Y
Cartilage Biomarkers														
Distribution					Y									
By Treatment & Time				Y[1]	Y		Y				Y	Y		Y
Mechanistic Biomarkers														
Distribution					Y									
By Treatment & Time				Y[1]	Y		Y				Y	Y		Y

NOTES :

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- Summary = Represents TFL related to any summaries (descriptive statistics) of the observed raw data.
- Individual = Represents FL related to any displays of individual subject observed raw data.
- [1] Absolute values will be displayed in the same outputs as the change from baseline.
- [2] [1] Raw SAS log output from analysis.

9.3.2. Safety Biomarker Analyses

9.3.2.1. Overview of Planned Safety Biomarker Analyses

The safety biomarker analyses will be based on the "Safety" population, unless otherwise specified. See section 12.6.6.2 for a full list of Safety Biomarkers.

Table 11 provides an overview of the planned safety biomarker analyses, with full details of data displays being presented in Appendix 16: List of Data Displays.

Table 11 Overview of Planned Safety Biomarker Analyses

Endpoint	Transformed/Untransformed													
	Absolute							Change from Baseline						
	Stats Analysis			Summary		Individual		Stats Analysis			Summary		Individual	
	T	F	L	T	F	F	L	T	F	L	T	F	F	L
Safety Biomarkers														
Distribution					Y									
By Treatment & Time				Y[1]	Y		Y				Y	Y		Y

NOTES :

- T = Table, F = Figure, L = Listing, Y = Yes display generated.
- Stats Analysis = Represents TFL related to any formal statistical analyses (i.e. modelling) conducted.
- Summary = Represents TFL related to any summaries (descriptive statistics) of the observed raw data.
- Individual = Represents FL related to any displays of individual subject observed raw data.
  - [1] Absolute values will be displayed in the same outputs as the change from baseline.

9.4. Analyses on Paracetamol Data

9.4.1. Overview of Planned Analyses on Paracetamol Data

The analyses on the paracetamol data will be based on the "Intent-to-Treat" population, unless otherwise specified.

Table 12 provides an overview of the planned efficacy analyses, with full details of data displays being presented in Section 12.15: List of Data Displays.

Table 12 Overview of Planned Analyses on Paracetamol Data

Endpoint	Absolute							Change from Baseline						
	Stats Analysis			Summary		Individual		Stats Analysis			Summary		Individual	
	T	F	L	T	F	F	L	T	F	L	T	F	F	L
Paracetamol														
24h Dose of Paracetamol Averaged over 7 Days Prior to Assessment				Y[1]	Y[1]		Y				Y[1]	Y[1]		
Proportion of Subjects Using Paracetamol				Y										

NOTES :

- T = Table, F = Figure, L = Listing, Y = Yes display generated.
- Stats Analysis = Represents TFL related to any formal statistical analyses (i.e. modelling) conducted.
- Summary = Represents TFL related to any summaries (i.e. descriptive statistics) of the observed raw data.
- Individual = Represents FL related to any displays of individual subject observed raw data.
- [1] Absolute values will be displayed in the same outputs as the change from baseline.

10. INTERIM ANALYSES

Two formal interim analyses are planned during the course of this study. In addition to the formal planned interim analyses, further data reviews may be carried out by senior managers not involved in the study conduct to aid in portfolio and budget decisions. These administrative reviews will have no impact on the ongoing study.

The timing and content of each Interim deliverable is summarised in Table 13.

Table 13 Interim Deliveries

Analysis	Timing	Unblinded Team	Main Objective
PK Interim	To coincide with other internal decision making across the GSK3196165 project	Study Pharmacokineticist, Statistics and Programming, Project Statistician, GSK3196165 MDT	To compare PK of GSK3196165 in subjects with HOA with other populations
Week 6 Interim	Once a minimum of 30 subjects have completed day 43 (week 6)	Study Statistician and Programmer, Project Statistician and Programmer, TA Head, Clinical Statistics TA Head, MDL	To assist with decision making regarding the subsequent clinical development of GSK3196165 for OA
Administrative Interim Data Review	At the discretion of Senior Managers not involved in the study conduct	Study Statistician and Programmer, Project Statistician and Programmer, TA Head, Clinical Statistics TA Head, MDL	To aid with dynamic portfolio and budget decisions

10.1. Overview of planned Week 6 Interim Analysis

10.1.1. Overview of Study Population Analysis at Week 6 Interim

The Study Population analyses will be based on the Intent-to-Treat (ITT) population, unless otherwise specified.

Table 14 provides an overview of the planned study population analyses, with full details of data displays being presented in Appendix 16: List of Data Displays.

Table 14 Overview of Planned Study Population Analyses at Week 6 Interim

Display Type	Data Displays Generated	
	Table	Listing
Demographic and Baseline Characteristics		
Demographics Characteristics	Y	

NOTES :
- Y = Yes display generated.

10.1.2. Overview of Safety Analysis at Week 6 Interim

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

Table 15 provides an overview of the planned analyses, with further details of data displays being presented in Appendix 16: List of Data Displays.

Table 15 Overview of Planned Safety Analyses at Week 6 Interim

Endpoint / Parameter/ Display Type	Absolute				Change from BL		
	Summary		Individual		Summary		Individual
	T	F	F	L	T	F	L
Adverse Events (AE's)							
All AE's	Y						
Serious and Other Significant AE's							
Serious AE's	Y						
Withdrawal AE's	Y						
Drug Related AE's	Y						
AE's leading to death							Y

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

10.1.3. Overview of Planned Efficacy Analysis at Week 6 Interim

Table 17 provides an overview of the planned interim analyses, with full details of data displays being presented in Appendix 16: List of Data Displays

Table 16 Overview of Planned Efficacy Analysis at Week 6 Interim

Endpoint	Absolute							Change from Baseline						
	Stats Analysis			Summary		Individual		Stats Analysis			Summary		Individual	
	T	F	L	T	F	F	L	T	F	L	T	F	F	L
Pain														
24h **average** hand pain NRS score averaged over 7				Y [2]	Y[2]			Y	Y	Y[1]	Y[2]	Y[2]		

Endpoint	Absolute							Change from Baseline						
	Stats Analysis			Summary		Individual		Stats Analysis			Summary		Individual	
	T	F	L	T	F	F	L	T	F	L	T	F	F	L
days prior to assessment														
24h **worst** hand pain NRS score averaged over 7 days prior to assessment				Y [2]	Y[2]			Y	Y	Y[1]	Y[2]	Y[2]		
AUSCAN														
AUSCAN 3.1 NRS Components						Y		Y	Y	Y[1]	Y	Y		
C-Reactive Protein														
C-Reactive Protein				Y [2]	Y[2]			Y	Y	Y[1]	Y[2]	Y[2]		

NOTES :

- T = Table, F = Figure, L = Listing, Y = Yes display generated.
- Stats Analysis = Represents TFL related to any formal statistical analyses (i.e. modelling) conducted.
- Summary = Represents TFL related to any summaries (i.e. descriptive statistics) of the observed raw data.
- Individual = Represents FL related to any displays of individual subject observed raw data.

[1] Raw SAS log output from Analysis.
[2] Absolute value and change from baseline will be displayed on the same output

Week 6 Interim Analysis
Model Specification
• Continuous endpoints will be statistically analysed using the same methods as described in Sections 7.1.2 and 8.1.2.1
Model Checking & Diagnostics
• Refer to Appendix 11: Model Checking and Diagnostics for Statistical Analyses.
Model Results Presentation
• Continuous endpoints will be presented using the same methods as described in Sections 7.1.2 and 8.1.2.1

Sensitivity and Supportive Statistical Analyses
• Following review of the data, additional analyses maybe conducted to further support the primary statistical analyses, if deemed appropriate. • Analyses using different covariance structures may be explored if considered appropriate.

10.2. Overview of planned Pharmacokinetic Interim Analysis

The pharmacokinetic (PK) analysis will be based on the "Pharmacokinetic" population, unless otherwise specified.

The primary objective of the interim PK analysis is to compare PK of GSK3196165 in subjects with HOA with other populations. Plot of GSK3196165 concentration with median value by visit will be produced and compared with similar plot from BAROQUE study including data only till week 12 and 180 mg dose group.

To derive PK parameters, GSK3196165 serum concentration-time data from HOA will be pooled with dataset generated for population PK meta analysis (Population Pharmacokinetic Analysis of GSK3196165 Following Intravenous and Subcutaneous Administration to Healthy Volunteers, Subjects with Rheumatoid Arthritis and Multiple Sclerosis (Date: 08-Jan-2016)) and subjected to nonlinear mixed effects modelling using the program NONMEM. Effect of following covariates will be tested:

- Population type (HOA, healthy volunteers, rheumatoid arthritis and multiple sclerosis)
- Subject demographics (age, sex, and race)
- Baseline characteristics (body weight, free GM-CSF levels)
- Immunogenicity

Individual PK parameters will be summarized by population type and distribution of the derived PK parameters will be plotted by population type.

10.3. Overview of Administrative Interim Data Review

The purpose of the Administrative Interim Data Review is to aid with dynamic portfolio and budget decisions. The outcome of the Administrative Interim Data Review will have no direct impact on the ongoing study.

Table 17 provides an overview of the planned analyses, with full details of data displays being presented in Section 12.15: List of Data Displays.

Table 17 Overview of Analyses for Administrative Interim Data Review

Endpoint	Absolute							Change from Baseline						
	Stats Analysis			Summary		Individual		Stats Analysis			Summary		Individual	
	T	F	L	T	F	F	L	T	F	L	T	F	F	L
Pain														
24h **average** hand pain NRS score averaged over 7 days prior to assessment								Y	Y		Y	Y		
24h **worst** hand pain NRS score averaged over 7 days prior to assessment								Y	Y		Y	Y		
Paracetamol														
24h Dose of Paracetamol Averaged over 7												Y		

Endpoint	Absolute							Change from Baseline						
	Stats Analysis			Summary		Individual		Stats Analysis			Summary		Individual	
	T	F	L	T	F	F	L	T	F	L	T	F	F	L
Days Prior to Assessment														
Proportion of Subjects Using Paracetamol				Y										

NOTES :

- T = Table, F = Figure, L = Listing, Y = Yes display generated.
- Stats Analysis = Represents TFL related to any formal statistical analyses (i.e. modelling) conducted.
- Summary = Represents TFL related to any summaries (i.e. descriptive statistics) of the observed raw data.
- Individual = Represents FL related to any displays of individual subject observed raw data.

11. REFERENCES

[1] Population Pharmacokinetic Analysis of GSK3196165 Following Intravenous and Subcutaneous Administration to Healthy Volunteers, Subjects with Rheumatoid Arthritis and Multiple Sclerosis (Date: 08-Jan-2016)

12. APPENDICES

Section	Appendix
RAP Section 4 : Analysis Populations	
Section 12.1	Appendix 1: Protocol Deviation Management and Definitions for Per Protocol Population
RAP Section 5 : General Considerations for Data Analyses & Data Handling Conventions	
Section 12.2	Appendix 2: Time and Events
Section 12.3	Appendix 3: Assessment Windows
Section 12.4	Appendix 4: Treatment States & Phases
Section 12.5	Appendix 5: Data Display Standards & Handling Conventions • Study Treatment & Sub-group Display Descriptors • Baseline Definitions & Derivations • Reporting Process & Standards
Section 12.6	Appendix 6: Derived and Transformed Data • General, Study Population & Safety • Efficacy • Pharmacokinetic • Pharmacodynamic and or Biomarkers
Section 12.7	Appendix 7: Premature Withdrawals & Handling of Missing Data • Premature Withdrawals • Handling of Missing Data
Section 12.8	Appendix 8: Values of Potential Clinical Importance
Section 12.9	Appendix 9: Multicentre Studies
Section 12.10	Appendix 10: Multiple Comparisons and Multiplicity
Section 12.11	Appendix 11: Model Checking and Diagnostics for Statistical Analyses
Section 12.12	Appendix 12: Definition of some Parameters of Interest
Section 12.13	Appendix 13: Opportunistic Infections: MedDRA Preferred Terms
Other RAP Appendices	
Section 12.14	Appendix 14: Abbreviations & Trade Marks
Section 12.15	Appendix 15: List of Data Displays
Section 12.16	Appendix 16: Example Mock Shells for Data Displays

12.1. Appendix 1: Protocol Deviation Management and Definitions for Per Protocol Population

There is no planned Per Protocol population in this phase IIa study.

12.2. Appendix 2: Time & Events

12.2.1. Protocol Defined Time & Events

12.2.1.1. Screening period Time and Events table

Subject Screening (must be carried out ≤ 28 days prior to Day 1)		
Screening Day 1	Screening Days 1-7, at home	Screening Day ≥8
↓		↓
Informed Consent	Daily Pain NRS questionnaire[2]	Pain NRS eligibility assessment[3]
Inclusion/exclusion criteria		MRI[4]
Demographics		
Medical/medication/alcohol history		
Con. Med. Review		
Vital signs		
12-lead ECG		
Full Physical Exam		
Swollen and tender joints[1]		
Haem/Chem/Urinalysis		
HIV, TB, Hepatitis B & Hepatitis C screen		
RF, ACPA (anti-CCP)		
Pregnancy test (serum)		
Urine drug / alcohol screen		
Spirometry (FEV1, FVC) & D_{LCO}		
Pain NRS training		
SAE assessment		

NOTES:

- [1] Where possible, the same individual should perform all disease assessments for an individual subject (with separate joint assessor).
- [2] Pain NRS questions should be completed at approximately the same time each day (recommended between 6pm and 10pm).
- [3] Eligibility assessment will be based on a 7 day average of the '24h average hand pain NRS' question.
- [4] Subjects must have passed all screening assessments, including laboratory tests and 7-day pain NRS assessment, prior to undertaking MRI scanning.

12.2.1.2. Treatment period Time and Events table

Study events	Screening (≤28 days prior to Day 1)	Treatment period										Week 20 phone call (Day 141 ± 5d)	Follow up (Week 22 (Day 155 ± 7d)
		Week 0		Wk 1	Wk 2	Wk 3	Wk 4	Wk 6	Wk 8	Wk 10	Wk 12		
		Baseline & Day 1 treatment visit	Day 3 (± 1d)PK biomarker visit	Day 8 (± 1d) treatment visit	Day 15 (± 1d) treatment visit	Day 22 (± 1d) treatment visit	Day 29 (± 1d) treatment visit	Day 43 (± 3d) treatment visit	Day 57 (± 3d) treatment visit	Day 71 (± 3d) treatment visit	Day 85 (± 3d) treatment visit		
Borg CR10 Scale[1]	See separate T&E table for screening procedures	X		X	X	X	X	X	X	X	X	Site to contact subject by phone and remind them to begin completing the daily Pain NRS questionnaire starting 7 days before their Follow-up visit at Week 22	See separate table for follow-up visit procedures
Patient[1] and physician global assessment[2]		X			X		X		X		X		
AUSCAN 3.1 NRS[1]		X		X	X		X	X	X	X	X		
Brief Physical Exam		X			X		X		X		X		
Vital signs		X			X		X		X		X		
12-lead ECG		X[4]									X		
Swollen and tender joints[2]		X		X	X		X	X	X	X	X		
MRI[3]											X[3]		
Haem/Chem/Urinalysis		X		X	X		X	X	X	X	X		
PK sampling[4]		X	X	X			X	X			X		
Blood Biomarkers[4]		X	X	X	X		X		X		X		
Urine drug/alcohol		X									X		
Study treatment dosing		X		X	X	X	X	X	X	X			
Cough, Auscultation, Pulse Oximetry		X		X	X	X	X	X	X	X	X		
Spirometry (FEV1, FVC) & D_{LCO}		X									X		
Immunogenicity blood sampling		X[5]			X		X				X		
Pharmacogenetics[6]		X											
Pregnancy test (urine)		X					X		X		X		
Post-treatment Interview											X		
Daily Pain NRS questions[7]		<---------- X ---------->											
SAE/AE assessment		<---------- X ---------->											
Con. medication review		<---------- X ---------->											

Treatment period T&E table notes

[1] PROs are performed before any other assessments, or procedures, to avoid influencing subject.

[2] Where possible, the same individual should perform all disease assessments for an individual subject (with separate joint assessor).

[3] MRI scanning at week 12 may take place on a separate day from other assessments and may occur on Day 85 (± 5d).

[4] Before dosing.

[5] Day 1 immunogenicity sample includes anti-GM-CSF auto-antibody analysis

[6] Consenting subjects only.

[7] Pain NRS questions should be completed at approximately the same time each day (recommended between 6pm and 10pm).

12.2.1.3. Follow up visit and early withdrawal* procedures list

Subject Follow-up Visit Task List **Week 22** (Day 155 ± 7d) ↓
Borg CR10 Scale[1]
Patient[1] and physician global assessment[3]
Pain NRS assessment[2]
Vital signs
Full Physical Exam
Swollen and tender joints[3]
SAE/AE assessment
Con. Med. Review
Pregnancy test (urine)
Haem/Chem/Urinalysis
Immunogenicity
MRI[4]
Blood Biomarkers
PK Sampling
Cough, Auscultation, Pulse Oximetry
Spirometry (FEV1, FVC) & D_{LCO}

NOTES:

- [1] PROs are performed before any other assessments, or procedures, to avoid influencing subject.
- [2] Assessment is based on a 7 day average of the Pain NRS questions.
- [3] Where possible, the same individual should perform all disease assessments for an individual subject (with separate joint assessor).
- [4] If scheduling MRI on the same day as the follow up visit is not possible, the MRI visit may take place on a separate day *before the Follow-up visit* but it must occur within the same Day 155 ±7day window.

*for early withdrawal, Day 85 procedures are followed and a follow up visit scheduled.

12.3. Appendix 3: Assessment Windows

12.3.1. Definitions of Assessment Windows for Analyses

Analysis Set / Domain	Parameter (if applicable)	Target	Analysis Window		Analysis Timepoint
			Beginning Timepoint	Ending Timepoint	
All	All	Day -1	Day -28	Day -1	Screening
MRI	MRI	Day -1	Day -28	Day 1	Baseline
All	All	Day 1	Day 1	Day 1	Baseline
PK/Biomarker	PK/Biomarker	Day 3	Day 2	Day 4	Day 3
All	All	Day 8	Day 6	Day 10	Week 1
All	All	Day 15	Day 13	Day 17	Week 2
All	All	Day 22	Day 20	Day 24	Week 3
All	All	Day 29	Day 27	Day 31	Week 4
All	All	Day 43	Day 38	Day 48	Week 6
All	All	Day 57	Day 52	Day 62	Week 8
All	All	Day 71	Day 66	Day 76	Week 10
All	All	Day 85	Day 80	Day 90	Week 12
MRI	MRI	Day 85	Day 76	Day 94	Week 12
All	All	Day 155	Day 148	Day 162	12 Week Follow Up
All (subjects withdrawn early from treatment)	All (subjects withdrawn early from treatment)	84 days after last treatment	77 days after last treatment	91 days after last treatment	12 Week Follow Up

Note: All data will be listed, but 'out of window' data would not contribute towards any summary statistics or analyses.

Note: MRI rescan visits will be slotted to the nearest analysis time window and will contribute towards summary statistics and analyses.

12.4. Appendix 4: Treatment States and Phases

12.4.1. Study Phases

Assessments and events will be classified according to the time of occurrence relative to study treatment start date, unless otherwise specified.

Study Phase	Definition
Pre-Treatment	Date < Study Treatment Start Date
On-Treatment	Study Treatment Start Date ≤ Date ≤ Study Treatment Stop Date + 14 Days
Safety Follow-Up	Date > Study Treatment Stop Date + 14 Days

12.4.1.1. Study Phases for Concomitant Medication

Study Phase	Definition
Prior	If medication end date is not missing and is before first dose of study treatment.
Concomitant	Any medication that is not a prior

NOTES:
Please refer to Appendix 7 for handling of missing and partial dates for concomitant medication. Use the rules in this table if concomitant medication date is completely missing.

12.4.2. Treatment States

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

12.4.2.1. Treatment States for AE Data

Treatment State	Definition
Pre-Treatment	AE Start Date < Study Treatment Start Date
On-Treatment	Study Treatment Start Date ≤ AE Start Date ≤ Study Treatment Stop Date + 14 Days
Safety Follow-Up	AE Start Date > Study Treatment Stop Date + 14 Days
Onset Time Since 1st Dose (Days)	If Treatment Start Date > AE Onset Date = AE Onset Date - Treatment Start Date If Treatment Start Date ≤ AE Onset Date = AE Onset Date - Treatment Start Date +1 Missing otherwise.
Duration (Days)	AE Resolution Date – AE Onset Date + 1
Drug-related	If relationship is marked 'YES' on Inform/CRF OR value is missing.

NOTES:

- AE's with partial start and/stop dates will be assumed to have occurred on treatment unless there is evidence through comparison of partial dates to suggest otherwise.

12.5. Appendix 5: Data Display Standards & Handling Conventions

12.5.1. Study Treatment & Sub-group Display Descriptors

Treatment Group Descriptions			
RandAll NG		Data Displays for Reporting	
Code	Description	Description	Order [1]
A	GSK3196165 180mg	GSK3196165 180mg	2
P	Placebo	Placebo	1

NOTES:

1. Order represents treatments being presented in TFL, as appropriate.

12.5.2. Baseline Definition & Derivations

12.5.2.1. Baseline Definitions

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

Parameter	Study Assessments Considered As Baseline		Baseline Used in Data Display
	Screening	Day 1 (Pre-Dose)	
Primary			
24h average hand pain NRS score averaged over 7 days prior to assessment[1]	X	X	Day 1 (Pre-Dose)
Secondary			
24h worst pain NRS score averaged over 7 days prior to assessment[1]	X	X	Day 1 (Pre-Dose)
AUSCAN 3.1 NRS		X	Day 1 (Pre-Dose)
Swollen/Tender hand joints		X	Day 1 (Pre-Dose)
PtGA/PhGA		X	Day 1 (Pre-Dose)
PK parameters		X	Day 1 (Pre-Dose)
Safety			
Vital signs (HR, BP & temp)[2]	X	X	Day 1 (Pre-Dose)
ECG (12-lead)[2]	X	X	Day 1 (Pre-Dose)
Laboratory (Haematology, clinical chemistry and urinalysis)[2]	X	X	Day 1 (Pre-Dose)

Parameter	Study Assessments Considered As Baseline		Baseline Used in Data Display
	Screening	Day 1 (Pre-Dose)	
Pulmonary Assessments[2]	X	X	Day 1 (Pre-Dose)
Exploratory			
MRI	X		Screening
PK/PD		X	Day 1 (Pre-Dose)

NOTES :

- Unless otherwise stated, the mean of replicate assessments at any given time point will be used as the value for that time point.
- Where both screening and pre-dose are available, the value closest to first dose will be used.
- [1] For all Pain NRS scores averaged over 7 days prior to assessment, the baseline values will be calculated as the average of the 7 days preceding the first dose of study treatment
- [2] For all vital signs, ECG, labs and pulmonary assessments except $D_{LCO,}$ the baseline values will be the latest pre-dose assessment. For $D_{LCO,}$ a subject's baseline will be taken as the lowest value obtained from the Screening or Day 1(Pre-dose) assessment, or any unscheduled visit in between.

12.5.2.2. Derivations and Handling of Missing Baseline Data

Definition	Reporting Details
Change from Baseline	= Post-Dose Visit Value – Baseline
% Change from Baseline	= 100 x [(Post-Dose Visit Value – Baseline) / Baseline]
Maximum Change from Baseline	= Calculate the change from baseline at each given time point and determine the maximum change. Note that for the ECG outputs this is the maximum increase from baseline
Ratio to Baseline	= Post-Dose Visit Value / Baseline

NOTES :

- Unless otherwise specified, the baseline definitions specified in Section 12.5.2.1 Baseline Definitions will be used for derivations for endpoints / parameters and indicated on summaries and listings.
- Unless otherwise stated, if baseline data is missing no derivation will be performed and will be set to missing.
- The baseline definition will be footnoted on all change from baseline displays.

12.5.3. Reporting Process & Standards

Reporting Process	
Software	
• The currently supported versions of SAS software will be used to perform all data analyses, generate tables, figures and listings.	
Reporting Area	
HARP Server	uk1salx00175
HARP Area	arenv \ arprod \ gsk3196165 \ mid204851 \ final arenv \ arprod \ gsk3196165 \ mid204851 \ primary arenv \ arprod \ gsk3196165 \ mid204851 \ internal_01

Reporting Process	
	arenv \ arprod \ gsk3196165 \ mid204851 \ internal_02 arenv \ arprod \ gsk3196165 \ mid204851 \ internal_03 arenv \ arprod \ gsk3196165 \ mid204851 \ internal_04 arenv \ arprod \ gsk3196165 \ mid204851 \ internal_05 arenv \ arprod \ gsk3196165 \ mid204851 \ spotfire
QC Spreadsheet	arenv \ arwork \ gsk3196165 \ mid204851 \ final \ documents arenv \ arwork \ gsk3196165 \ mid204851 \ primary \ documents arenv \ arwork \ gsk3196165 \ mid204851 \ internal_01 \ documents arenv \ arwork \ gsk3196165 \ mid204851 \ internal_02 \ documents arenv \ arwork \ gsk3196165 \ mid204851 \ internal_03 \ documents arenv \ arwork \ gsk3196165 \ mid204851 \ internal_04 \ documents arenv \ arwork \ gsk3196165 \ mid204851 \ internal_05 \ documents arenv \ arwork \ gsk3196165 \ mid204851 \ spotfire \ documents
Analysis Datasets	
• For the final reporting effort, analysis datasets will be created according to CDISC standards (SDTM IG Version 3.1.3 & AdaM IG Version 1.0 • For creation of ADaM datasets (ADCM/ADAE), the same version of dictionary datasets will be implemented for conversion from SI to SDTM. • For the purpose of the Administrative Interim Review and Interim analyses, analysis datasets will be generated from SI Datasets.	
Generation of RTF Files	
• RTF files will be generated for final reporting effort.	

Reporting Standards
General
• The current GSK Integrated Data Standards Library (IDSL)* will be applied for reporting, unless otherwise stated: o 4.03 to 4.23: General Principles o 5.01 to 5.08: Principles Related to Data Listings o 6.01 to 6.11: Principles Related to Summary Tables o 7.01 to 7.13: Principles Related to Graphics * website IDSL → supporting documentation → component → stats displays → principles
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. • 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.

Reporting Standards	

• 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).
  • Visits outside the protocol defined time-windows (i.e. recorded as protocol deviations) will be included in listings but omitted from figures, summaries and statistical analyses.	

Unscheduled Visits	
• Unscheduled visits will not be included in summary tables or contribute to any analyses, unless otherwise stated. • Unscheduled visits will not be included in figures, unless otherwise stated. • All unscheduled visits will be included in listings.	
Descriptive Summary Statistics	
Continuous Data	Refer to IDSL Statistical Principle 6.06.1
Categorical Data	N, n, frequency, %
Reporting of Pharmacokinetic Concentration Data	
Descriptive Summary Statistics	Refer to IDSL Statistical Principle 6.06.1 Assign zero to NQ values (Refer to GUI_51487 for further details)
Reporting of Log-Transformed Parameters	
Descriptive Summary Statistics	N, n, geometric mean, 95% CI of geometric mean, standard deviation (SD) of logged data and geometric coefficient of variation (CV_b (%)) will be reported. [1] $CV_b (\%) = \sqrt{(\exp(SD^2) - 1)} * 100$ (SD = SD of log transformed data)
Figures	Axes will be presented with actual values with an appropriate log-scale (either base 2 or base 10) depending on range of values
Graphical Displays	
• Refer to IDSL Statistical Principals 7.01 to 7.13.	

12.6. Appendix 6: Derived and Transformed Data

12.6.1. General

Multiple Measurements at One Time Point
• Mean of the measurements will be calculated and used in any derivation of summary statistics but if listed, all data will be presented. • If there are two values within a time window the value closest to the target day for that window will be used except for ECGs, Blood Pressure and Pulse Rate Measures. If values are the same distance from the target, then the latest assessment value will be taken. • Triplicate ECG measures will be averaged for each subject and visit prior to generating summary tables. • Duplicate Blood Pressure and Pulse Rate measures will be averaged for each subject and visit prior to generating summary tables. • Subjects having both High and Low values for Normal Ranges at any post-baseline visits for safety parameters will be counted in both the High and Low categories of "Any visit post-baseline" row of related summary tables. This will also be applicable to relevant Potential Clinical Importance summary tables.
Study Day

• Calculated as the number of days from date of first dose of study treatment:
  • Ref Date = Missing → Study Day = Missing
  • Ref Date < Date of First Dose of Study Treatment → Study Day = Ref Date –Date of First Dose of Study Treatment
  • Ref Data ≥ Randomisation Date → Study Day = Ref Date – (First Dose of Study Treatment) + 1

12.6.2. Study Population

Demographics
Age

• GSK standard IDSL algorithms will be used for calculating age where birth date will be imputed as follows:
  ○ Any subject with a missing day will have this imputed as day '15'.
  ○ Any subject with a missing date and month will have this imputed as '30th June'.
• Calculated as the integer part of (latest of (randomisation date, screening date)– date of birth).
• Birth date will be presented in listings as 'YYYY'.
• Age will be categorised into subgroups <18 years, 18-<65 years and >=65 years

Body Mass Index (BMI)
• Calculated as **Weight (kg) / [Height (m)^2]**
Race Category
• White: 'White: Arabic/North African Heritage' and 'White: White/Caucasian/European Heritage', or both of these, but no other category checked • African descent: 'African American/African Heritage', and no other category checked

Demographics
• Asian: 'Asian – Central/South Asian Heritage', 'Asian – East Asian Heritage', 'Asian – Japanese Heritage', and 'Asian – South East Asian Heritage', or any combination of these, but no other category checked Other: Any combination that has not been categorized above ('mixed race')

Extent of Exposure
• Number of days of exposure to study drug will be calculated based on the formula: **Duration of Exposure in Days = Treatment Stop Date – (Treatment Start Date) + 14** • Subjects who were randomized but did not report a treatment start date will be categorised as having zero days of exposure. • The cumulative dose will be based on the formula: **Cumulative Dose = Sum of (Number of Visits x Total Dose at Each Visit)** • If there are any treatment breaks during the study, exposure data will be adjusted accordingly.
Medical History
Disease Duration
• OA duration since diagnosis in months will be calculated based on the formula: **OA Duration Since Diagnosis in Months = (Date of First Dose of Study Treatment - Start date of formal OA diagnosis + 1)/30.25** • OA duration since first symptoms in months will be calculated based on the formula: **OA Duration Since First Symptoms in Months = (Date of First Dose of Study Treatment - Start date of first symptoms + 1)/30.25**

12.6.3. Safety

ECG Parameters
RR Interval
• IF RR interval (msec) is not provided directly, then RR can be derived as : [1] If QTcB is machine read & QTcF is not provided, then : $$RR = \left[\left(\frac{QT}{QTcB}\right)^2\right] * 1000$$ [2] If QTcF is machine read and QTcB is not provided, then: $$RR = \left[\left(\frac{QT}{QTcF}\right)^3\right] * 1000$$ • If ECGs are manually read, the RR value preceding the measurement QT interval should be a collected value, THEN do not derive.
Corrected QT Intervals
• When not entered directly in the eCRF, corrected QT intervals by Bazett's (QTcB) and Fredericia's (QTcF) formulas will be calculated, in msec, depending on the availability of other measurements. • IF RR interval (msec) is provided then missing QTcB and/or QTcF will be derived as :

ECG Parameters

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

Laboratory Parameters

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

Pulmonary Assessments

Borg CR10

- The Borg CR10 Scale is being used to assess patient-reported shortness of breath (difficulty in breathing)
- The Borg CR10 Scale® is graded from:
  - 0, "Nothing at all", = none, to 10, "Extremely Strong", "Maximal", = the most intense perception or feeling the subject has ever experienced.
  - There is allowance for gradings > 10, which are designated as "Absolute Maximum" or "Highest Possible" and is marked with a "●" in the scale
  - A 3 is designated as being "Moderate" on the scale.
- No imputations will be done for missing data.

Pulse Oximetry

- Pulse Oximetry will be categorised into subgroups <80%, 80% to 90% and ≥90%.
- Lower values represent a worse result.

12.6.4. Efficacy

Efficacy

24h average hand pain NRS score

- Measured by a daily pain Numerical Rating Scale (NRS) based on 24h average hand pain intensity with anchors "0" (no pain) and "10" (worst imaginable pain), which is averaged over the 7 days prior to assessment visit with GSK3196165 or placebo.
- The 7 day average score is calculated by

$$\frac{\sum(Daily\ 24h\ average\ hand\ pain\ NRS\ scores\ in\ the\ 7\ days\ prior\ to\ assess}{Total\ numer\ of\ days\ \ 24h\ average\ hand\ pain\ NRS\ is\ recorded\ in\ 7\ days\ prior\ to}$$

- * If a subject records their daily pain NRS scores for less than 4 days out of the 7 days prior to assessment visit, then the average NRS score for the week prior to the assessment visit will be recorded as missing.

Efficacy

- The 7 day average score will be calculated using the 7 days prior to assessment visit, excluding any values that have been used to calculate previous averages, e.g. if a patient attends a visit on Day 9 (hence 7 day average will be calculated using Days 2 to 8) and attends their next visit on Day 14 (hence 7 day average should be calculated using Days 7 to 13), any overlapping days will be excluded from the calculation of the Day 14 average (i.e. Days 7 and 8).

24h worst hand pain NRS score

- Measured by patients using a daily pain Numerical Rating Scale (NRS) based on 24h worst hand pain intensity with anchors "0" (no pain) and "10" (worst imaginable pain, which is averaged over the 7 days prior to assessment visit with GSK3196165 or placebo.
- The score is calculated by

$$\frac{\sum(Daily\ 24h\ worst\ hand\ pain\ NRS\ scores\ in\ the\ 7\ days\ prior\ to\ assessment\ visit)}{Total\ numer\ of\ days\ \ 24h\ worst\ hand\ pain\ NRS\ is\ recorded\ in\ 7\ days\ prior\ to\ assessment\ visit^{*}}$$

- * If a subject records their daily pain NRS scores for less than 4 days out of the 7 days prior to assessment visit, then the average NRS score for the week prior to the assessment visit will be recorded as missing.
- The 7 day average score will be calculated using the 7 days prior to assessment visit, excluding any values that have been used to calculate previous averages, e.g. if a patient attends a visit on Day 9 (hence 7 day average will be calculated using Days 2 to 8) and attends their next visit on Day 14 (hence 7 day average should be calculated using Days 7 to 13), any overlapping days will be excluded from the calculation of the Day 14 average (i.e. Days 7 and 8).

AUSCAN™

- The AUSCAN™ Index is a self-administered questionnaire consisting of a 15-item scale which measures pain (5 items), stiffness (1 item) and degree of disability/physical function (9 items) during the preceding 48h. All items are rated on an NRS scale with anchors "0" (none) to "10" (extreme).
- The scores for each individual domain (Pain/Stiffness/Physical Function) are calculated using a simple summation of the component item scores relating to that domain, therefore the Pain component ranges from 0-50, Stiffness component 0-10 and Physical Function component (0-90).
- The total AUSCAN™ score is calculated using simple summation of the 15 component item scores and therefore ranges from 0-150.
- If ≥2 pain, the stiffness, >2 physical function items are missing, the patient's response on the affected subscale will be regarded as invalid and the deficient subscale(s) will not be used in any analysis.
- Where 1 pain or 1-2 physical function items are missing, the average value for the subscale will be substituted in lieu of the missing item value(s).

Swollen Hand Joint Count

- Measured by the total number of swollen joints out of a possible 30 (8 DIP, 8 PIP, 2 IP, 10 MCP, 2 CMC) across both hands.
- If there are missing observations for swollen joints then the remaining observations will be assessed and weighted by dividing the number presented by the number of non-missing, and by multiplying by 30 for the joint count.

Efficacy

- No imputations for individual joints will be done.
- If a joint is not evaluable at Baseline, then that joint is set to missing throughout the study.
- If data for more than 50% of the joints are missing at the time of a given assessment, then the total count will be set to missing for that visit.

Painful/Tender Hand Joint Count

- Measured by the total number of tender joints out of a possible 30 (8 DIP, 8 PIP, 2 IP, 10 MCP, 2 CMC) across both hands.
- Joints can be rated 0=no pain/tenderness, 1=mild pain, 2=moderate pain and 3=severe pain.
- A joint is considered tender if it is scored >0 on the tender joint severity scale.
- If there are missing observations for tender joints then the remaining observations will be assessed and weighted by dividing the number presented by the number of non-missing, and by multiplying by 30 for the joint count.
- No imputations for individual joints will be done.
- If a joint is not evaluable at Baseline, then that joint is set to missing throughout the study.
- If data for more than 50% of the joints are missing at the time of a given assessment, then the total count will be set to missing for that visit.

Patient Global Assessment (PtGA)

- Measured by patients who will complete a global assessment of disease activity using the patient global assessment (PtGA) item, an NRS with anchors “0” (very well) to “10” (very poor).
- No imputations for missing data will be done.

Physician Global Assessment (PhGA)

- Measured by Physicians who will complete a global assessment of disease activity using the physician global assessment item (PhGA), an NRS with anchors “0” (none) to “10” (extremely active).
- No imputations for missing data will be done.

24h Paracetamol Dose

- Measured by total dose of paracetamol taken in 24 hours, which is averaged over the 7 days prior to assessment visit with GSK3196165 or placebo.
- If paracetamol dose is missing on a particular day but a pain NRS score has been recorded on that day, then paracetamol dose is set to 0mg for that day.
- If paracetamol dose is missing on a particular day and a pain NRS score is also missing on that day, then paracetamol dose is set to missing for that day.
- The 7 day average dose is calculated by

$$\frac{\sum(Daily\ 24h\ paracetamol\ doseage\ in\ the\ 7\ days\ prior\ to\ assessment\ visit)}{Total\ numer\ of\ days\ \ 24h\ paracetamol\ dose\ is\ recorded\ in\ 7\ days\ prior\ to\ assessment\ visit^{*}}$$

- * If a subject is missing more than 3 daily paracetamol doses out of the 7 days prior to assessment visit, then the average paracetamol dose for the week prior to the assessment visit will be recorded as missing.
- The 7 day average dose will be calculated using the 7 days prior to assessment visit, excluding any values that have been used to calculate previous averages, e.g. if a patient attends a visit on Day 9 (hence 7 day average will be calculated using Days 2 to 8) and

Efficacy
attends their next visit on Day 14 (hence 7 day average should be calculated using Days 7 to 13), any overlapping days will be excluded from the calculation of the Day 14 average (i.e. Days 7 and 8).

12.6.5. Imaging

Imaging

HOAMRIS

- HOAMRIS measures consist of 7 different parameters (Synovitis, Erosive Damage, Cyst, Osteophytes, Cartilage Space Loss, Mal-alignment and Bone Marrow Lesions) that are semi-quantitatively assessed by an independent reviewer on a scale of 0-3/3.5, or can be scored as "Not Visible" or "Surgically Modified".
- Each parameter is evaluated on a total of 8 hand joints (DIP Joints 2-5 and PIP Joints 2-5). For erosive damage, cysts, and bone marrow lesions, the distal and proximal ends of the joint are assessed as sub-regions (i.e. D1, D2, P1, and P2).
- There is one score for each parameter per location, per time point.
- Each parameter is scored as follows:
    - Synovitis Scoring:

Score	Description
0	Normal, no synovitis
0.5	Minimal: >0 but decreased from a timepoint scored 1.
1	Mild: 1-33% volume enhancement
1.5	Mild-Moderate: >0 and <2, but increased from a timepoint scored 1 or decreased from a timepoint scored 2.
2	Moderate: 34-67% volume enhancement
2.5	Moderate-Severe: >1 and <3, but increased from a timepoint scored 2 or decreased from a timepoint scored 3.
3	Severe: 68-100% volume enhanced
3.5	Very Severe: Increased from a timepoint scored 3.
N	Not Visible
S	Surgically Modified

    - Erosive Damage Scoring:

Score	Description
0	Normal, no erosive damage
0.5	Minimal: >0 but decreased from a timepoint scored 1.
1	Mild: ≤10% of bone volume or ≤25% joint surface affected
1.5	Mild-Moderate: >0 and <2, but increased from a timepoint scored 1 or decreased from a timepoint scored 2.
2	Moderate: 11-20% of bone volume and/or 26-50% of joint surface affected
2.5	Moderate-Severe: >1 and <3, but increased from a timepoint scored 2 or decreased from a timepoint scored 3.
3	Severe: >20% of bone volume and/or >50% of joint surface affected
3.5	Very Severe: Increased from a timepoint scored 3.

Imaging

N	Not Visible
S	Surgically Modified

- Cyst Scoring:

Score	Description
0	Normal, no cyst development
1	Mild: cysts are ≤10% of bone volume
2	Moderate: cysts are 11-20% of bone volume
3	Severe: cysts are >20% of bone volume
N	Not Visible
S	Surgically Modified

- Osteophyte Scoring:

Score	Description
0	Normal, no osteophytes
1	Mild: 1-3 small osteophytes
2	Moderate: ≥4 small osteophytes and/or ≥1 moderate osteophyte(s)
3	Severe: at least 1 large osteophyte
N	Not Visible
S	Surgically Modified

- Cartilage Space Loss Scoring:

Score	Description
0	Normal, no loss of cartilage Space
1	Mild: loss of cartilage space without bone-to-bone contact
2	Moderate: focal complete loss of cartilage space
3	Severe: complete cartilage space loss affecting >50% of articulating joint area
N	Not Visible
S	Surgically Modified

- Mal-alignment Scoring:

Score	Description
0	Normal, no apparent mal-alignment
1	Mild: ≤10 degree angulation and/or not congruent joint surfaces
2	Moderate: 11-20 degrees angulation and/or moderate subluxation without crossing the midline
3	Severe: >20 degrees angulation and/or subluxation without crossing the midline
N	Not Visible
S	Surgically Modified

- Bone Marrow Lesions:

Score	Description
0	Normal, no bone marrow lesions
0.5	Minimal: >0 but decreased from a timepoint scored 1.
1	Mild: Lesions are 1-33% of bone volume

Imaging

1.5	Mild-Moderate: >0 and <2, but increased from a timepoint scored 1 or decreased from a timepoint scored 2.
2	Moderate: lesions are 34-66% of bone volume
2.5	Moderate-Severe: >1 and <3, but increased from a timepoint scored 2 or decreased from a timepoint scored 3.
3	Severe: lesions are 67-100% of bone volume
3.5	Very Severe: Increased from a timepoint scored 3.
N	Not Visible
S	Surgically Modified

- If an individual location is scored either "Not Visible" or "Surgically Modified" then the score for that location will be set to missing.
- Each individual Parameter will be presented as a total score for the affected/dominant hand which will be calculated by summing scores of all joints at each time point.

HOAMRIQ

- HOAMRIQ measures consist of the quantitative measurements from the bones and synovial capsules of the following joints:
  - DIP Joints 2-5
  - PIP Joints 2-5
  - MCP Joints 1-5
  - CMC-1
- 7 different parameters are quantitatively assessed as follows:
  - **Synovitis (Volume of Enhancing Pannus)**:
    - The total volume (in mm^3) of contrast-enhanced voxels within the synovial capsule.
    - The following joints will be considered:
      - CMC-1
      - DIP 2-5
      - PIP 2-5
      - MCP 1-5
    - Synovitis will be presented as a total measure which is calculated by summing the individual measure for each joint at each time point.
  - **Synovitis (Normalised)**
    - Normalised Synovitis will be calculated using the Volume of Enhancing Pannus (VEP):

$$\frac{\sum_{all\ joints} VEP}{\sum_{all\ joints} Joint\ Volume}$$

    - The following joints will be considered:
      - CMC-1
      - DIP 2-5

Imaging

- PIP 2-5
- MCP 1-5

- **Erosive Damage (Volume of Bone Erosions)**:
  - The volume (in mm^3) difference between the segmented bones and modelled healthy bones within the 3D MR Image. The measure is taken at the extremities of the bones (15mm length from the joint) or the whole bone.
  - The following bones will be considered:
    - D2-5
    - I2-5
    - M2-5
    - P2-5
    - Trapezium
  - Erosive Damage will be presented as a total measure which is calculated by summing the individual measure for each bone at each time point.
- **Erosive Damage (Normalised)**
  - Normalised Erosive Damage will be calculated using the Volume of Bone:

$$\frac{\sum_{all\ bones} Volume\ of\ Bone\ Erosion}{\sum_{all\ bones} Volume\ of\ Bone}$$

- **Cyst:**
  - Measured as part of the erosions measurement and is therefore quantified but not differentiated from the quantification of erosions, hence no measure is presented separately for this parameter.
- **Osteophyte:**
  - Captured by Bone Shape Parameters, hence no measure is presented separately for this parameter.
- **Cartilage Space Loss (Joint Space Width):**
  - The mean difference (in mm) between corresponded patches on the ends of the phalanges of each joint.
  - The following joints will be considered:
    - CMC-1
    - DIP 2-5
    - PIP 2-5
    - MCP 1-5
  - Cartilage Space Loss will be presented as a total measure which is calculated by summing the individual measure for each joint at each time point.
- **Mal-alignment (Alignment of Bone)**:
  - The 2D angle (in degrees) between phalanges at the DIP, PIP, MCP and CMC joints in the plane of the wrist bones.
  - The following joints will be considered:

Imaging

- CMC-1
- DIP 2-5
- PIP 2-5
- MCP 1-5

- Mal-alignment will be presented as a total measure which is calculated by summing the absolute value of the individual measure for each joint at each time point.

- **Bone Marrow Lesions (Volume of Bone Edema) (Normalised)**:
  - The total volume (in mm^3) of enhanced voxels within the segmented bone volumes at each joint. The measure is taken at the extremities of the bones (15mm length from the joint), or the whole bone.
  - The following bones will be considered:
    - D2-5
    - I2-5
    - M2-5
    - P2-5
    - Trapezium
  - Normalised Bone Marrow Lesions will be calculated using the volume of bone:

$$\frac{\sum_{all\ bones} Volume\ of\ Bone\ Edema}{\sum_{all\ bones} Volume\ of\ Bone}$$

- All parameters will be presented as a total measure for the affected/dominant hand at each time point.

DCE-MRI

- Dynamic Contrast-Enhanced Magnetic Resonance Imaging (DCE-MRI) parameters are measured at each individual joint (DIP Joints 2-5, PIP Joints 2-5, MCP Joints 1-5 and CMC-1) and consist of:
  - Exchange Rate (K^{trans})
  - Interstitial Volume (v_e)
  - Plasma Volume (v_p)
  - Initial Rate of Enhancement (IRE)
  - Maximum signal intensity enhancement (ME).
- All DCE-MRI parameters will be presented as a total measure over all joints at each time point.
- DCE-MRI Parameters will be calculated as:

$$\frac{\sum_{all\ joints} Parameter}{Number\ of\ Joints}$$

- All DCE-MRI Parameters will also be presented normalised by the Volume of Enhancing Pannus (VEP).
- Normalised DCE-MRI parameters will be calculated as:

Imaging

$$\frac{\sum_{all\ joints}(VEP * Parameter)}{\sum_{all\ joints} VEP}$$

- All parameters will be presented as a total measure for the affected/dominant hand at each time point.

Bone Shape Parameters

- **Surface Area of the Bone:**
  - Measured as the whole bone area (in mm^2). At the metacarpals, the joint of interest is the MCP and therefore the distal part (15mm length from the joint) shall be measured.
  - The following bones will be considered:
    - D2-5
    - I2-5
    - M2-5
    - P2-5
    - Trapezium
- All bone shape parameters will be presented as a total measure for the affected/dominant hand which is calculated by summing the individual measure for each bone at each time point.

12.6.6. Biomarker

12.6.6.1. Pharmacodynamic Biomarkers

Test Analyte	LBCAT	LBTESTCD	Units	Derived	Details
Target Engagement					
Free Soluble GM-CSF	BIOMARKER	GMCSFFS	ng/L		
GM-CSF: drug complex	BIOMARKER	GMCSFC	ng/L		
Predictive Biomarkers					
HSCRP	CHEMISTRY	CRP	mg/L		
MRP8/14 COMPLEX	BIOMARKER	S100A8A9	mg/L		
CCL17 (TARC)	BIOMARKER	CCL17	ng/L		
14-3-3η	BIOMARKER	ETA1433	mg/L		
MMP-3	BIOMARKER	MMP3	µg/L		
CXCL13 (BLC)	BIOMARKER	CXCL13	ng/L		
SAA	BIOMARKER	AMYLOIDA	ng/L		
YKL-40	BIOMARKER	CHI3L1	µg/L		
IL6	BIOMARKER	INTLK6	ng/L		
CCL22	BIOMARKER	MDC	ng/L		
Cartilage Biomarkers					
ARGS Neoepitope	BIOMARKER	ARGSNEOE			
C1M	BIOMARKER	C1M			
C2M	BIOMARKER	C2M			
C3M	BIOMARKER	C3M			
CRPM	BIOMARKER	CRPM			
VICM	BIOMARKER	VICM			
Mechanistic Biomarkers					
VEGF	BIOMARKER	VEGF	ng/L		
TNFa	BIOMARKER	TNF	ng/L		
IL-1β	BIOMARKER	INTLK1B	ng/L		
IL-8	BIOMARKER	INTLK8	ng/L		
IL-10	BIOMARKER	INTLK10	ng/L		
IL-13	BIOMARKER	INTLK13	ng/L		
IL-4	BIOMARKER	INTLK4	ng/L		

IFN-γ	BIOMARKER	IFNG	ng/L		

12.6.6.2. Safety Biomarkers

Test Analyte	LBCAT	LBTESTCD	Units	Derived	Details
Lung Damage					
Anti-GM-CSF auto AB	BIOMARKER	GMCSFAA			

12.6.6.3. Biomarker Derivations

All Parameters
Below Limit of Quantification
• If a biomarker 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 indicated as less than x in the comment field) is present, the corresponding numeric value will be imputed using one half the lower limit of quantification. • This value will be used in Summary Tables and Figures, but the original recorded result will be listed.

12.7. Appendix 7: Premature Withdrawals & Handling of Missing Data

12.7.1. Premature Withdrawals

Element	Reporting Detail
General	• Subject study completion (i.e. as specified in the protocol) was defined as completion of all phases of the study including the follow-up visit. • Withdrawn subjects will not be replaced in the study. • All available data from subjects who were withdrawn from the study will be listed and all available planned data will be included in summary tables and figures, unless otherwise specified. • Early withdrawal (EW) visits will be assigned to the respective visit according to the Time and Events table in Section 12.2, using the day of the EW visit relative to Day 1. • For the first 4 weeks an EW visit more than ±3 days in comparison to the target visit will be assigned to the closest target visit. Starting at Week 4, an EW visit more than 7 days after target visit day will be assigned to the next visit. • If a scheduled visit and an EW visit occur within the same visit window and are both available, the later visit will be used for any summaries/analyses. The earlier visit will appear in listing only. • For efficacy analyses, if an EW visit is assigned to a non-standard efficacy visit, i.e., a visit at which efficacy assessments are not scheduled per the Time and Events Table, then these EW data will be ignored in the statistical analysis but all data will be listed.

12.7.2. Handling of Missing Data

Element	Reporting Detail

General	• Missing data occurs when any requested data is not provided, leading to blank fields on the collection instrument :
	  ○ These data will be indicated by the use of a “blank” in subject listing displays. Unless all data for a specific visit are missing in which case the data is excluded from the table.
	  ○ Answers such as “Not applicable” and “Not evaluable” are not considered to be missing data and should be displayed as such.

Outliers	• Any subjects excluded from the summaries and/or statistical analyses will be documented along with the reason for exclusion in the clinical study report.

12.7.2.1. 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 On-treatment as per Appendix 4: Treatment States and Phases. o Missing Stop Day: Last day of the month will be used, unless this is after the stop date of study treatment; in this case the study treatment stop date will be used. • Completely missing start or end dates will remain missing, with no imputation 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.

12.7.2.2. Handling of Missing Data for Statistical Analysis

Element	Reporting Detail
NRI	• Subjects with missing pain NRS scores will be considered as non-responders for the purpose of analyses on the binary endpoints.
Change from Baseline	• For any analysis on change from baseline values, if the baseline value is missing then all following assessment values are excluded from the analysis.

12.7.2.3. Handling of Endpoint Specific Missing Data

Element	Reporting Detail
NRS score	• If a subject records their daily pain NRS scores for less than 4 days out of the 7 days prior to assessment visit, then the average NRS score for the week prior to the assessment visit will be recorded as missing. • For the purpose of the analyses on the continuous endpoints, no imputations for the missing data will be done. • For the purpose of the analyses on the binary endpoints, subjects with missing NRS scores will be considered as non-responders.
AUSCAN™	• If ≥2 pain, the stiffness item or >2 physical function items are missing, the subject's response on the affected subscale will be regarded as invalid and the deficient subscale(s) will not be used in any analysis. • Where 1 pain or 1-2 physical function items are missing, the average value for the subscale will be substituted in lieu of the missing item value(s). • Where any individual component score is missing, total score will be set to missing. • No imputation for missing total individual component scores will be done.
Swollen Hand Joint Count	• If there are missing observations for swollen joints then the remaining observations will be assessed and weighted by dividing the number presented by the number of non-missing, and by multiplying by 30 for the joint count. • No imputations for individual joints will be done. • If a joint is not evaluable at Baseline, then that joint is set to missing throughout the study. • If data for more than 50% of the joints are missing at the time of a given assessment, then the total count will be set to missing for that visit.
Tender Hand Joint Count	• If there are missing observations for tender joints then the remaining observations will be assessed and weighted by dividing the number presented by the number of non-missing, and by multiplying by 30 for the joint count. • No imputations for individual joints will be done. • If a joint is not evaluable at Baseline, then that joint is set to missing throughout the study. • If data for more than 50% of the joints are missing at the time of a given assessment, then the total count will be set to missing for that visit.
PtGA	• No imputations for missing data will be done.
PhGA	• No imputations for missing data will be done.

Element	Reporting Detail
HOAMRIS	• If an individual joint has a missing score, then the score will be imputed using the average score across all available evaluable joints for each individual component. • If data for more than 50% of locations are missing at the time of a given assessment, then the total individual component score will be set to missing for that visit. This threshold may be altered after review of the actual raw data. • No imputation for missing total individual component scores will be done.
HOAMRIQ	• If an individual joint has a missing value, then the value will be imputed using the average score across all available evaluable joints for each individual component. • If data for more than 50% of locations are missing at the time of a given assessment, then the total individual component score will be set to missing for that visit. This threshold may be altered after review of the actual raw data. • No imputation for missing total individual component values will be done.
DCE-MRI	• If an individual joint has a missing value, then the value will be imputed using the average score across all available evaluable joints for each individual component. • If data for more than 50% of locations are missing at the time of a given assessment, then the total individual component score will be set to missing for that visit. This threshold may be altered after review of the actual raw data. • No imputation for missing total individual component values will be done.

12.8. Appendix 8: Values of Potential Clinical Importance

12.8.1. 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

12.8.2. 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			

ECG Parameter	Units	Clinical Concern Range	
		Lower	Upper
Increase from Baseline QTc	msec		>60

12.8.3. Vital Signs

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

Vital Sign Parameter (Change from Baseline)	Units	Clinical Concern Range			
		Decrease		Increase	
		Lower	Upper	Lower	Upper
Systolic Blood Pressure	mmHg	≥ 20	≥ 40	≥ 20	≥ 40
Diastolic Blood Pressure	mmHg	≥ 10	≥ 20	≥ 10	≥ 20
Heart Rate	bpm	≥ 15	≥ 30	≥ 15	≥ 30

12.9. Appendix 9: Multicenter Studies

There are no planned adjustments for multiple centres or regions. For all analyses, all sites, countries and regions will be pooled.

12.10. Appendix 10: Multiple Comparisons & Multiplicity

12.10.1. Handling of Multiple Comparisons & Multiplicity

In this phase IIa study, no adjustments will be made for multiple comparisons or multiplicity.

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

12.11.1. Statistical Analysis Assumptions

12.11.1.1. Continuous Endpoints

Endpoint(s)	• Continuous Endpoints as described in Section 8.1.2.1 .
Analysis	• MMRM

- For the MMRM, model assumptions will be applied, but appropriate adjustments may be made based on the data.
- The Kenward and Roger method for approximating the denominator degrees of freedom and correcting for bias in the estimated variance-covariance of the fixed effects will be used.
- An unstructured covariance structure for the R matrix will be used by specifying 'type=UN' on the REPEATED line.
  - In the event that this model fails to converge, alternative correlation structures may be considered such as spatial power, CS or AR(1).
  - Akaike's Information Criteria (AIC) will be used to assist with the selection of covariance structure.
- Distributional assumptions underlying the model used for analysis will be examined by obtaining a normal probability plot of the residuals and a plot of the residuals versus the fitted values (i.e. checking the normality assumption and constant variance assumption of the model respectively) to gain confidence that the model assumptions are reasonable.
- If there are any departures from the distributional assumptions, alternative models will be explored using appropriate transformed data.

12.11.1.2. Binary Endpoints

Endpoint(s)	• Binary Endpoints as described in Section 8.1.2.2
Analysis	• Generalised Estimating Equations (GEE)

- For the GEE analyses, model assumptions will be applied, but appropriate adjustments may be made based on the data.
- An unstructured working correlation structure will be assumed and standard errors will be calculated based on the empirical sandwich covariance estimate (default setting for PROC GENMOD in SAS)
- An unstructured correlation structure will be used by specifying 'type=UN' on the REPEATED line.
  - In the event that this model fails to converge, alternative correlation structures may be considered such as Independent, CS or AR(1).
  - Quasilikelihood under the Independence Model Criteria (QIC) will be used to assist with the selection of covariance structure.

12.12. Appendix 12: Definitions of some Parameters of Interest

12.12.1. Laboratory Parameters of Interest

Lab parameters of interest	Grade			
	1	2	3	4
HEMOGLOBIN decrease	Hemoglobin (Hgb) <LLN - 10.0 g/dL; <LLN - 6.2 mmol/L; <LLN - 100 g/L	Hgb <10.0 - 8.0 g/dL; <6.2 - 4.9 mmol/L; <100 - 80g/L	Hgb <8.0 g/dL; <4.9 mmol/L; <80 g/L; transfusion indicated	Life-threatening consequences; urgent intervention indicated
WHITE CELL COUNT decrease	<LLN - 3000/mm3; <LLN - 3.0 x 10e9 /L	<3000 - 2000/mm3; <3.0 - 2.0 x 10e9 /L	<2000 - 1000/mm3; <2.0 - 1.0 x 10e9 /L	<1000/mm3; <1.0 x 10e9 /L
TOTAL NEUTROPHILS ABSOLUTE COUNT	<LLN - 1500/mm3; <LLN - 1.5 x 10e9 /L	<1500 - 1000/mm3; <1.5 - 1.0 x 10e9 /L	<1000 - 500/mm3; <1.0 - 0.5 x 10e9 /L	<500/mm3; <0.5 x 10e9 /L
LYMPHOCYTES ABSOLUTE COUNT decreased	<LLN - 800/mm3; <LLN - 0.8 x 10e9 /L	<800 - 500/mm3; <0.8 - 0.5 x 10e9 /L	<500 - 200/mm3; <0.5 - 0.2 x 10e9 /L	<200/mm3; <0.2 x 10e9 /L
LYMPHOCYTES ABSOLUTE increased		>4000/mm3 - 20,000/mm3 ; >4-20 x 10e9 /L	>20,000/mm3; >20 x 10e9 /L	
PLATELET COUNT	<LLN - 75,000/mm3; <LLN - 75.0 x 10e9 /L	<75,000 - 50,000/mm3; <75.0 - 50.0 x 10e9 /L	<50,000 - 25,000/mm3; <50.0 - 25.0 x 10e9 /L	<25,000/mm3; <25.0 x 10e9 /L
CREATININE	>1 - 1.5 x baseline; >ULN - 1.5 x ULN	>1.5 - 3.0 x baseline; >1.5 - 3.0 x ULN	>3.0 baseline; >3.0 - 6.0 x ULN	>6.0 x ULN

SODIUM decrease	<LLN - 130 mmol/L		<130 - 120 mmol/L	<120 mmol/L;
SODIUM increase	>ULN - 150 mmol/L	>150 - 155 mmol/L	>155 - 160 mmol/L	>160 mmol/L
POTASSIUM decrease	<LLN - 3.0 mmol/L	<LLN - 3.0 mmol/L	<3.0 - 2.5 mmol/L	<2.5 mmol/L
POTASSIUM increase	>ULN - 5.5 mmol/L	>5.5 - 6.0 mmol/L	>6.0 - 7.0 mmol/L	>7.0 mmol/L
CALCIUM increase	>ULN - 11.5 mg/dL; >ULN - 2.9 mmol/L	>11.5 - 12.5 mg/dL; >2.9 - 3.1 mmol/L	>12.5 - 13.5 mg/dL; >3.1 - 3.4 mmol/L;	>13.5 mg/dL; >3.4 mmol/L
CALCIUM decrease	<LLN - 1.0 mmol/L	<1.0 - 0.9 mmol/L	<0.9 - 0.8 mmol/L	<0.8 mmol/L
ASAT (SGOT)	>ULN - 3.0 x ULN	>3.0 - 5.0 x ULN	>5.0 - 20.0 x ULN	>20.0 x ULN
ALAT (SGPT)	>ULN - 3.0 x ULN	>3.0 - 5.0 x ULN	>5.0 - 20.0 x ULN	>20.0 x ULN
ALKALINE PHOSPHATASE	>ULN - 2.5 x ULN	>2.5 - 5.0 x ULN	>5.0 - 20.0 x ULN	>20.0 x ULN
BILIRUBIN, TOTAL	>ULN - 1.5 x ULN	>1.5 - 3.0 x ULN	>3.0 - 10.0 x ULN	>10.0 x ULN
ALBUMIN	<LLN - 3 g/dL; <LLN - 30 g/L	<3 - 2 g/dL; <30 - 20 g/L	<2 g/dL; <20 g/L	
GLUCOSE	>ULN -160 mg/dL; >ULN - 8.9 mmol/L	>160 -250 mg/dL; >8.9 - 13.9 mmol/L	>250 - 500 mg/dL; >13.9 - 27.8	>500 mg/dL; >27.8 mmol/L
EST.CREATININE CLEARANCE	<LLN - 60 ml/s/1.73 m2	59 - 30 ml/s/1.73 m2	29 - 15 ml/s/1.73 m2	<15 ml/s/1.73 m2

12.13. Appendix 13: Opportunistic Infections: MedDRA Preferred Terms

12.13.1. Opportunistic Infections: MedDRA Preferred Terms

Opportunistic Infections: MedDRA Preferred Terms	
AIDS retinopathy	Herpes pharyngitis
Acid fast bacilli infection	Herpes sepsis
Acinetobacter bacteraemia	Herpes simplex
Acinetobacter infection	Herpes simplex cervicitis
Acquired immunodeficiency syndrome	Herpes simplex hepatitis
Actinomycosis	Herpes simplex meningoencephalitis
Actinomycotic abdominal infection	Herpes simplex otitis externa
Actinomycotic pulmonary infection	Herpes simplex test positive
Acute HIV infection	Herpes simplex virus conjunctivitis neonatal
Acute hepatitis B	Herpes simplex visceral
Acute hepatitis C	Herpes virus infection
Adrenal gland tuberculosis	Herpes zoster
Arthritis fungal	Herpes zoster cutaneous disseminated
Arthritis salmonella	Herpes zoster disseminated
Aspergilloma	Herpes zoster infection neurological
Aspergillosis oral	Herpes zoster meningitis
Aspergillus infection	Herpes zoster meningoencephalitis
Asymptomatic HIV infection	Herpes zoster meningomyelitis

Opportunistic Infections: MedDRA Preferred Terms	
Asymptomatic viral hepatitis	Herpes zoster necrotising retinopathy
Atypical mycobacterial infection	Herpes zoster oticus
Atypical mycobacterial lower respiratory tract infection	Herpes zoster pharyngitis
Atypical mycobacterial lymphadenitis	Histoplasmosis
Atypical mycobacterial pneumonia	Histoplasmosis cutaneous
Atypical mycobacterium pericarditis	Histoplasmosis disseminated
Bacterial parotitis	Human T-cell lymphocytic virus type II infection
BK virus infection	Human T-cell lymphotropic virus infection
Biliary tract infection cryptosporidial	Human T-cell lymphotropic virus type I infection
Biliary tract infection fungal	Human polyomavirus infection
Blastomycosis	Immune reconstitution inflammatory syndrome associated tuberculosis
Bone tuberculosis	Intestinal tuberculosis
Brachyspira infection	JC virus granule cell neuronopathy
Brain empyema	JC virus infection
Bronchitis fungal	Joint tuberculosis
Bronchopulmonary aspergillosis	Kaposi's sarcoma
Bronchopulmonary aspergillosis allergic	Kaposi's sarcoma AIDS related
Brucella sepsis	Kaposi's varicelliform eruption
Brucellosis	Leptotrichia infection
Candida endophthalmitis	Listeria encephalitis
Candida infection	Listeria sepsis

Opportunistic Infections: MedDRA Preferred Terms	
Candida osteomyelitis	Listeriosis
Candida pneumonia	Lower respiratory tract herpes infection
Candida retinitis	Lower respiratory tract infection fungal
Candida sepsis	Lymph node tuberculosis
Cerebral aspergillosis	Lymphadenitis fungal
Cerebral fungal infection	Lymphoma AIDS related
Cerebral toxoplasmosis	Male genital tract tuberculosis
Choroid tubercles	Meningitis aspergillus
Chronic hepatitis	Meningitis candida
Chronic hepatitis C	Meningitis coccidioides
Coccidioides encephalitis	Meningitis cryptococcal
Coccidioidomycosis	Meningitis fungal
Colitis herpes	Meningitis herpes
Congenital HIV infection	Meningitis histoplasma
Congenital cytomegalovirus infection	Meningitis listeria
Congenital hepatitis B infection	Meningitis salmonella
Congenital herpes simplex infection	Meningitis toxoplasmal
Congenital toxoplasmosis	Meningitis tuberculous
Congenital tuberculosis	Meningoencephalitis herpes simplex neonatal
Congenital varicella infection	Meningoencephalitis herpetic
Conjunctivitis tuberculous	Minor cognitive motor disorder
Corynebacterium infection	Mucocutaneous candidiasis
Corynebacterium sepsis	Mycobacterial infection

Opportunistic Infections: MedDRA Preferred Terms	
Cryptococcal cutaneous infection	Mycobacterium abscessus infection
Cryptococcal fungaemia	Mycobacterium avium complex immune restoration disease
Cryptococcosis	Mycobacterium avium complex infection
Cryptosporidiosis infection	Mycobacterium chelonae infection
Cutaneous coccidioidomycosis	Mycobacterium fortuitum infection
Cutaneous tuberculosis	Mycobacterium kansasii infection
Cytomegalovirus chorioretinitis	Mycobacterium marinum infection
Cytomegalovirus colitis	Mycobacterium ulcerans infection
Cytomegalovirus duodenitis	Mycotic endophthalmitis
Cytomegalovirus enteritis	Mycotoxicosis
Cytomegalovirus enterocolitis	Myocarditis mycotic
Cytomegalovirus gastritis	Myocarditis toxoplasmal
Cytomegalovirus gastroenteritis	Nasal herpes
Cytomegalovirus gastrointestinal infection	Necrotising fasciitis fungal
Cytomegalovirus gastrointestinal ulcer	Necrotising herpetic retinopathy
Cytomegalovirus infection	Neonatal candida infection
Cytomegalovirus mononucleosis	Neonatal mucocutaneous herpes simplex
Cytomegalovirus mucocutaneous ulcer	Neurocryptococcosis
Cytomegalovirus myelomeningoradiculitis	Neutropenic sepsis
Cytomegalovirus myocarditis	Nocardia sepsis
Cytomegalovirus oesophagitis	Nocardiosis
Cytomegalovirus pancreatitis	Oesophageal candidiasis
Cytomegalovirus pericarditis	Oesophageal tuberculosis

Opportunistic Infections: MedDRA Preferred Terms	
Cytomegalovirus syndrome	Ophthalmic herpes simplex
Cytomegalovirus urinary tract infection	Ophthalmic herpes zoster
Cytomegalovirus viraemia	Oro-pharyngeal aspergillosis
Disseminated cryptococcosis	Oropharyngeal candidiasis
Disseminated cytomegaloviral infection	Osteomyelitis blastomyces
Disseminated tuberculosis	Osteomyelitis fungal
Ear tuberculosis	Osteomyelitis salmonella
Eczema herpeticum	Overgrowth fungal
Encephalitis cytomegalovirus	Pancreatitis fungal
Encephalitis fungal	Paratyphoid fever
Encephalitis post immunisation	Pericarditis fungal
Encephalitis post varicella	Pericarditis histoplasma
End stage AIDS	Pericarditis tuberculous
Endocarditis candida	Perinatal HIV infection
Endocarditis histoplasma	Peritoneal candidiasis
Enterocolitis AIDS	Peritoneal tuberculosis
Enterocolitis fungal	Persistent generalised lymphadenopathy
Epididymitis blastomyces	Pneumocystis jirovecii infection
Epididymitis tuberculous	Pneumocystis jirovecii pneumonia
Epstein-Barr virus associated lymphoma	Pneumonia blastomyces
Erythema induratum	Pneumonia cytomegaloviral
Erythrasma	Pneumonia fungal
Exanthema subitum	Pneumonia herpes viral
Extrapulmonary tuberculosis	Pneumonia salmonella

Opportunistic Infections: MedDRA Preferred Terms	
Eye infection toxoplasmal	Pneumonia toxoplasmal
Female genital tract tuberculosis	Polyomavirus-associated nephropathy
Fungaemia	Presumed ocular histoplasmosis syndrome
Fungal abscess central nervous system	Proctitis herpes
Fungal endocarditis	Proctitis monilial
Fungal infection	Progressive multifocal leukoencephalopathy
Fungal oesophagitis	Prostatitis tuberculous
Fungal peritonitis	Pulmonary mycosis
Fungal sepsis	Pulmonary trichosporonosis
Fungal tracheitis	Pulmonary tuberculoma
Funguria	Pulmonary tuberculosis
Gastritis fungal	Pyelonephritis fungal
Gastritis herpes	Renal tuberculosis
Gastroenteritis cryptococcal	Respiratory moniliasis
Gastroenteritis cryptosporidial	Respiratory tract infection fungal
Gastrointestinal candidiasis	Retinitis histoplasma
Gastrointestinal fungal infection	Retroviral infection
Genital blister	Retroviral rebound syndrome
Genital herpes	Salmonella bacteraemia
Genital herpes zoster	Salmonella sepsis
Haemorrhagic pneumonia	Salmonellosis
Hepatosplenic abscess	Salpingitis tuberculous
HIV associated nephropathy	Silicotuberculosis

Opportunistic Infections: MedDRA Preferred Terms	
HIV cardiomyopathy	Sinusitis aspergillus
HIV enteropathy	Skin candida
HIV infection	Spleen tuberculosis
HIV infection CDC Group I	Splenic candidiasis
HIV infection CDC Group II	Splenic infection fungal
HIV infection CDC Group III	Stoma site candida
HIV infection CDC Group IV subgroup A	Stoma site infection
HIV infection CDC Group IV subgroup B	Superinfection fungal
HIV infection CDC Group IV subgroup C1	Superinfection mycobacterial
HIV infection CDC Group IV subgroup C2	Systemic candida
HIV infection CDC Group IV subgroup D	Systemic mycosis
HIV infection CDC Group IV subgroup E	T-cell lymphoma
HIV infection CDC category A	T-cell type acute leukaemia
HIV infection CDC category B	Thyroid tuberculosis
HIV infection CDC category C	Tongue fungal infection
HIV infection CDC group IV	Toxoplasmosis
HIV infection WHO clinical stage I	Tropical spastic paresis
HIV infection WHO clinical stage II	Tuberculoma of central nervous system
HIV infection WHO clinical stage III	Tuberculosis
HIV infection WHO clinical stage IV	Tuberculosis bladder
HIV peripheral neuropathy	Tuberculosis gastrointestinal
HIV wasting syndrome	Tuberculosis liver
Hepatic candidiasis	Tuberculosis of central nervous system
Hepatic infection fungal	Tuberculosis of eye

Opportunistic Infections: MedDRA Preferred Terms	
Hepatitis B	Tuberculosis of genitourinary system
Hepatitis C	Tuberculosis of intrathoracic lymph nodes
Hepatitis chronic persistent	Tuberculosis of peripheral lymph nodes
Hepatitis fulminant	Tuberculosis ureter
Hepatitis toxoplasmal	Tuberculous abscess central nervous system
Hepatitis viral	Tuberculous endometritis
Hepatitis virus-associated nephropathy	Tuberculous laryngitis
Hepatosplenic candidiasis	Tuberculous pleurisy
Herpes dermatitis	Tuberculous tenosynovitis
Herpes oesophagitis	Typhoid fever
Herpes ophthalmic	Varicella keratitis

12.14. Appendix 14 – Abbreviations & Trade Marks

12.14.1. Abbreviations

Abbreviation	Description
ADaM	Analysis Data Model
AE	Adverse Event
AESI	Adverse Event of Special Interest
AIC	Akaike's Information Criteria
A&R	Analysis and Reporting
AUC	Area under the curve
AUSCAN	Australian Canadian Hand Osteoarthritis Index
C_{ave}	Average steady state concentration during dosing interval
CDISC	Clinical Data Interchange Standards Consortium
CI	Confidence Interval
CL	Clearance
CL/F	Total body clearance from plasma after SC administration
CPMS	Clinical Pharmacology Modelling & Simulation
CRF	Case Report Form
CS	Clinical Statistics
CSR	Clinical Study Report
CTR	Clinical Trial Register
CV_b / CV_w	Coefficient of Variation (Between) / Coefficient of Variation (Within)
D_{LCO}	Diffusing capacity of the lung for carbon monoxide
DCE-MRI	Dynamic Contrast Enhanced Magnetic Resonance Imaging
DOB	Date of Birth
DP	Decimal Places
eCRF	Electronic Case Report Form
ECG	Electrocardiogram
FEV1	Forced Expiratory Volume in one Second
FVC	Forced Vital Capacity
GM-CSF	Granulocyte-macrophage colony stimulating factor
GUI	Guidance
GSK	GlaxoSmithKline
H	Hour
HIV	Human Immunodeficiency Virus
HOA	Hand Osteoarthritis
HOAMRIS	Hand Osteoarthritis Magnetic Resonance Imaging Scoring System
HOAMRIQ	Hand Osteoarthritis Magnetic Resonance Imaging Quantitative score
IA	Interim Analysis
ICH	International Conference on Harmonisation
IDMC	Independent Data Monitoring Committee
IDSL	Integrated Data Standards Library
Ig	Immunoglobulin
IMMS	International Modules Management System

Abbreviation	Description
IP	Investigational Product
ITT	Intent-To-Treat
Ka	Absorption rate constant
Kg	Kilogram
K^{trans}	Exchange rate
L	Litre
MDL	Medicines Development Lead
MDT	Medicines Development Team
MedDRA	Medical Dictionary for Regulatory Activities
Mg	Milligram
mL	Milliliter
MMRM	Mixed Model Repeated Measures
MRI	Magnetic Resonance Imaging
NRI	Non-responder Imputation
NRS	Numerical Rating Scale
OA	Osteoarthritis
OMERACT	Outcome measures in Rheumatology
PAP	Pulmonary alveolar proteinosis
PCI	Potential Clinical Importance
PD	Pharmacodynamic
PDMP	Protocol Deviation Management Plan
PhGA	Physician's Global Assessment
PtGA	Patient's Global Assessment
PK	Pharmacokinetic
PP	Per Protocol
PRO	Patient reported outcome
QC	Quality Control
QTc	Corrected QT interval
QTcF	Frederica's QT Interval Corrected for Heart Rate
QTcB	Bazett's QT Interval Corrected for Heart Rate
RAMOS	Randomization & Medication Ordering System
RAMRIS	Rheumatoid Arthritis Magnetic Resonance Imaging Scoring System
RAP	Reporting & Analysis Plan
SAC	Statistical Analysis Complete
SAE	Serious adverse event
SC	Subcutaneous
SDTM	Study Data Tabulation Model
SOP	Standard Operation Procedure
t ½	Elimination half life
TA	Therapeutic Area
TFL	Tables, Figures & Listings
v_e	Interstitial volume
v_p	Plasma volume
V_{ss}/F	Total volume of distribution after SC administration

12.14.2. Trademarks

Trademarks of the GlaxoSmithKline Group of Companies
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12.15. Appendix 15: List of Data Displays

12.15.1. Data Display Numbering

The following numbering will be applied for RAP generated displays:

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

12.15.2. Mock Example Shell Referencing

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

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

NOTES:

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

12.15.3. Deliverable [Priority]

Delivery [Priority] [1]	Description
PK IA [X]	PK Interim Statistical Analysis Complete
Wk6 IA [X]	Week 6 Interim Statistical Analysis Complete
AIR [X]	Administrative Interim Review Complete
SAC [X]	Final Statistical Analysis Complete

NOTES:

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

12.15.4. Study Population Tables

Study Population Tables					
No.	**Population**	**IDSL / TST ID / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
Subject Disposition					
1.1.	ITT	ES1	Summary of Subject Disposition for the Subject Conclusion Record	ICH E3, FDAAA, EudraCT	SAC
1.3.	Screened	ES6	Summary of Screening Status and Reasons for Screen Failures	Journal Requirements Add footnote: For rescreened subjects, the earlier screening is not included. Subjects who got rescreened successfully are not seen as subjects with screening failures.	SAC
1.4.	Enrolled	NS1	Summary of Number of Subjects by Country and Site ID	EudraCT/Clinical Operations	SAC
Protocol Deviation					
1.5.	ITT	DV1	Summary of Important Protocol Deviations	ICH E3	SAC
Population Analysed					
1.6.	Screened	SP1	Summary of Study Populations	IDSL	SAC
Demographic and Baseline Characteristics					
1.7.	ITT	DM1	Summary of Demographic Characteristics	ICH E3, GSK CTR, FDAAA, EudraCT Programming note: Include smoking history	Wk6 IA, SAC
1.8.	ITT	Non Standard POP_T1	Summary of Baseline Efficacy Parameters	Include all Efficacy Parameters	SAC
1.9.	ITT	DM5	Summary of Race and Racial Combinations	ICH E3, FDA, , GSK CTR, FDAAA, EudraCT	SAC

Study Population Tables					
No.	**Population**	**IDSL / TST ID / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
1.10.	ITT	Non Standard POP_T2	Summary of Hand OA Disease History		SAC
Medical condition & Concomitant Medications					
1.11.	ITT	Non Standard POP_T3	Summary of Current Medical Conditions	ICH E3	SAC
1.12.	ITT	CM1	Summary of Concomitant Medication	ICH E3	SAC
1.13.	ITT	CM1	Summary of Concomitant OA Medication		SAC
1.14.	ITT	CM1	Summary of Prior Medication		SAC
1.15.	ITT	CM1	Summary of Prior OA Medication		SAC
Exposure and Treatment Compliance					
1.16.	Safety	EX1	Summary of Exposure to Study Treatment	ICH E3 Rows include: - Duration of Drug Exposure (Days) - Number of Injections - Volume of Doses Received (ml) Footnote 'Note: Exposure includes 13 days after the last injection.'	SAC

12.15.5. Efficacy Tables

Efficacy: Tables					
No.	**Population**	**IDSL / TST ID / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
24h average hand pain NRS score					
2.1.	ITT	Non Standard EFF_T1	Summary of Observed Result and Change from Baseline in 24h average hand pain NRS Averaged over 7 days Prior to Each Visit		AIR, Wk6 IA, SAC
2.2.	ITT	Non Standard EFF_T2	Mixed Model Repeated Measures Analysis (MMRM) of Change from Baseline in 24h average hand pain NRS Averaged over 7 days Prior to Each Visit		AIR, Wk6 IA, SAC
24h worst hand pain NRS score					
2.3.	ITT	Non Standard EFF_T1	Summary of Observed Result and Change from Baseline in 24h worst hand pain NRS Averaged over 7 days Prior to Each Visit		AIR, Wk6 IA, SAC
2.4.	ITT	Non Standard EFF_T2	Mixed Model Repeated Measures Analysis (MMRM) of Change from Baseline in 24h worst hand pain NRS Averaged over 7 days Prior to Each Visit		AIR, Wk6 IA, SAC
Proportion of subjects with percentage reduction in 24h average hand pain NRS					
2.5.	ITT	Non Standard EFF_T3	Summary and Analysis of the Proportion of Subjects Achieving a 30% or More Reduction in 24h average hand pain NRS Averaged over 7 days Prior to Each Visit		SAC
2.6.	ITT	Non Standard EFF_T3	Summary and Analysis of the Proportion of Subjects Achieving a 50% or More Reduction in 24h average hand pain NRS Averaged over 7 days Prior to Each Visit, at Each Visit		SAC
Proportion of subjects with percentage reduction in 24h worst hand pain NRS					
2.7.	ITT	Non Standard EFF_T3	Summary and Analysis of the Proportion of Subjects Achieving a 30% or More Reduction in 24h worst hand pain NRS Averaged over 7 days Prior to Each Visit, at Each Visit		SAC

Efficacy: Tables					
No.	**Population**	**IDSL / TST ID / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
2.8.	ITT	Non Standard EFF_T3	Summary and Analysis of the Proportion of Subjects Achieving a 50% or More Reduction in 24h worst hand pain NRS Averaged over 7 days Prior to Each Visit, at Each Visit		SAC
AUSCAN 3.1 NRS					
2.9.	ITT	Non Standard EFF_T1	Summary of Observed Result and Change from Baseline in AUSCAN 3.1 NRS Individual Components Scores, at Each Visit	Include: AUSCAN Pain, AUSCAN Physical Function, AUSCAN Stiffness, AUSCAN Total Note: Page by Component.	Wk6 IA, SAC
2.10.	ITT	Non Standard EFF_T2	Mixed Model Repeated Measures Analysis (MMRM) of Change from Baseline in AUSCAN 3.1 NRS Individual Components Scores	Include: AUSCAN Pain, AUSCAN Physical Function, AUSCAN Stiffness, AUSCAN Total Note: Page by Component.	Wk6 IA, SAC
Joint Assessments					
2.11.	ITT	Non Standard EFF_T1	Summary of Observed Result and Change from Baseline in the Number of Soft Tissue Swollen Hand Joints, at Each Visit		SAC
2.12.	ITT	Non Standard EFF_T2	Mixed Model Repeated Measures Analysis (MMRM) of Change from Baseline in the Number of Soft Tissue Swollen Hand Joints		SAC
2.13.	ITT	Non Standard EFF_T1	Summary of Observed Result and Change from Baseline in the Number of Tender Hand Joints, at Each Visit		SAC
2.14.	ITT	Non Standard EFF_T2	Mixed Model Repeated Measures Analysis (MMRM) of Change from Baseline in the Number of Tender Hand Joints		SAC
Disease Global Assessment					
2.16.	ITT	Non Standard EFF_T1	Summary of Observed Result and Change from Baseline in the Physician's Global Assessment (NRS 0-10), at Each Visit		SAC

Efficacy: Tables					
No.	**Population**	**IDSL / TST ID / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
2.17.	ITT	Non Standard EFF_T2	Mixed Model Repeated Measures Analysis (MMRM) of Change from Baseline in the Physician's Global Assessment (NRS 0-10)		SAC
2.18.	ITT	Non Standard EFF_T1	Summary of Observed Result and Change from Baseline in the Patients' Global Assessment (NRS 0-10), at Each Visit		SAC
2.19.	ITT	Non Standard EFF_T2	Mixed Model Repeated Measures Analysis (MMRM) of Change from Baseline in the Patients' Global Assessment (NRS 0-10)		SAC
Imaging					
2.20.	ITT	Non Standard EFF_T4	Summary of Observed Result and Change from Baseline in Inflammatory Structural Joint Damage: HOAMRIS	• Individual Components Include: Synovitis, Erosive damage, Cyst, Osteophyte Cartilage Space Loss, Mal-alignment and Bone Marrow Lesions	SAC
2.21.	ITT	Non Standard EFF_T5	Mixed Model Repeated Measures Analysis (MMRM) of Change from Baseline in Inflammatory Structural Joint Damage: HOAMRIS	• Individual Components Include: Synovitis, Erosive damage, Cyst, Osteophyte Cartilage Space Loss, Mal-alignment and Bone Marrow Lesions	SAC

Efficacy: Tables					
No.	**Population**	**IDSL / TST ID / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
2.22.	ITT	Non Standard EFF_T4	Summary of Observed Result and Change from Baseline in Inflammatory Structural Joint Damage: HOAMRIQ	• Individual Components Include synovitis, normalised synovitis, normalised erosive damage, cartilage space loss, mal-alignment and normalised bone marrow lesions. • Add footnote 'Note: Synovitis is normalised by the total joint volume, erosive damage and bone marrow lesions are normalised by volume of bone.'	SAC
2.23.	ITT	Non Standard EFF_T5	Mixed Model Repeated Measures Analysis (MMRM) of Change from Baseline in Inflammatory Structural Joint Damage: HOAMRIQ	• Individual Components Include synovitis, normalised synovitis, normalised erosive damage, cartilage space loss, mal-alignment and normalised bone marrow lesions. • Add footnote 'Note: Synovitis is normalised by the total joint volume, erosive damage and bone marrow lesions are normalised by volume of bone.'	SAC

Efficacy: Tables					
No.	**Population**	**IDSL / TST ID / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
2.24.	ITT	Non Standard EFF_T4	Summary of Observed Result and Change from Baseline in Joint Inflammation: DCE-MRI	• Includes ktrans, normalised Ktrans, VE, normalised VE, VP, normalised VP, IRE, normalised IRE, ME, normalised ME. • Add Footnote: 'Note: All normalised parameters have been normalised using the Volume of Enhancing Pannus (VEP).' • Add units to parameter line.	SAC
2.25.	ITT	Non Standard EFF_T5	Mixed Model Repeated Measures Analysis (MMRM) of Change from Baseline in Joint Inflammation: DCE-MRI	• Includes ktrans, normalised Ktrans, VE, normalised VE, VP, normalised VP, IRE, normalised IRE, ME, normalised ME. • Add Footnote: 'Note: All normalised parameters have been normalised using the Volume of Enhancing Pannus (VEP).' • Add units to parameter line.	SAC
2.26.	ITT	Non Standard EFF_T4	Summary of Observed Result and Change from Baseline in Bone Shape Parameters	• Includes Surface Area of Bone	SAC
Paracetamol					
2.27.	ITT	Non Standard EFF_T1	Summary of Observed Result and Change from Baseline in 24h Total Dosage of Paracetamol Averaged over 7 days Prior to Each Visit		SAC
2.28.	ITT	Non Standard EFF_T6	Summary of the Proportion of Subjects Reporting Paracetamol Use in the 7 days Prior to Each Visit		AIR, SAC

12.15.6. Efficacy Figures

Efficacy: Figures					
No.	**Population**	**IDSL / TST ID / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
24h average hand pain NRS score					
2.1.	ITT	Non Standard EFF_F1	Individual Subject Profile Plots of 24h Average Hand Pain NRS Averaged Over 7 Days Prior to Each Visit, by Treatment Group	X-Axis : Visit : Continuous Scale Y-Axis : Parameter (Unit) scaled accordingly Legend: no legend to be displayed	SAC
2.3	ITT	Non Standard EFF_F2	Plot of Mean and 95% CI of Change from Baseline in 24h Average Hand Pain NRS Averaged over 7 days Prior to Each Visit	X-Axis : Visit Y-Axis : Change from Baseline in Parameter (Unit) scaled accordingly	AIR, Wk6 IA, SAC
2.4.	ITT	Non Standard EFF_F2	Plot of Least Squares Means and 95% CI of Change from Baseline in 24h Average Hand Pain NRS Averaged over 7 days Prior to Each Visit (from Repeated Measures Analysis)	X-Axis : Visit Y-Axis : Change from Baseline in Parameter (Unit) scaled accordingly Add footnote: 'Note: Repeated Measures Analysis adjusted for Baseline Value, Treatment Group, Visit, Treatment Group by Visit Interaction [and Baseline Value by Visit Interaction]'	AIR, Wk6 IA, SAC
24h worst hand pain NRS score					
2.5.	ITT	Non Standard EFF_F1	Individual Subject Profile Plots of 24h Worst Hand Pain NRS Averaged over 7 days Prior to Each Visit, by Treatment Group	X-Axis : Visit : Continuous Scale Y-Axis : Parameter (Unit) scaled accordingly Legend: no legend to be displayed	SAC
2.6.	ITT	Non Standard EFF_F1	Individual Subject Profile Plots of Daily 24h Worst Hand Pain NRS, by Treatment Group	X-Axis : Day : Continuous Scale Y-Axis : Parameter (Unit) scaled accordingly Legend: no legend to be displayed	SAC

Efficacy: Figures					
No.	**Population**	**IDSL / TST ID / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
2.7.	ITT	Non Standard EFF_F2	Plot of Mean and 95% CI of Change from Baseline in 24h Worst Hand Pain NRS Averaged over 7 days Prior to Each Visit, at Each Visit	X-Axis : Visit Y-Axis : Change from Baseline in Parameter (Unit) scaled accordingly	AIR, Wk6 IA, SAC
2.8.	ITT	Non Standard EFF_F2	Plot of Least Squares Means and 95% CI of Change from Baseline in 24h worst hand pain NRS Averaged over 7 days Prior to Each Visit (from Repeated Measures Analysis), at Each Visit	X-Axis : Visit Y-Axis : Change from Baseline in Parameter (Unit) scaled accordingly Add footnote: 'Note: Repeated Measures Analysis adjusted for Baseline Value, Treatment Group, Visit, Treatment Group by Visit Interaction [and Baseline Value by Visit Interaction]'	AIR, Wk6 IA, SAC
Proportion of subjects with percentage reduction in 24h average hand pain NRS					
2.9.	ITT	Non Standard EFF_F2	Proportion of Subjects in Each Treatment Group Achieving a 30% Reduction in 24h Average Hand Pain NRS Averaged over 7 days Prior to Each Visit	X-Axis: Visit Y-Axis: Proportion of Subjects (%) Note: Do not incude CI's	SAC
2.10.	ITT	Non Standard EFF_F3	Proportion of Subjects in Each Treatment Group Achieving a 50% Reduction in 24h Average Hand Pain NRS Averaged over 7 days Prior to Each Visit, at Each Visit	X-Axis: Visit Y-Axis: Proportion of Subjects (%) Note: Do not incude CI's	SAC
Proportion of subjects with percentage reduction in 24h worst hand pain NRS					
2.11.	ITT	Non Standard EFF_F3	Proportion of Subjects in Each Treatment Group Achieving a 30% Reduction in 24h Worst Hand Pain NRS Averaged over 7 days Prior to Each Visit, at Each Visit	X-Axis: Visit Y-Axis: Proportion of Subjects (%) Note: Do not incude CI's	SAC

Efficacy: Figures					
No.	**Population**	**IDSL / TST ID / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
2.12.	ITT	Non Standard EFF_F3	Proportion of Subjects in Each Treatment Group Achieving a 50% Reduction in 24h Worst Hand Pain NRS Averaged over 7 days Prior to Each Visit, at Each Visit	X-Axis: Visit Y-Axis: Proportion of Subjects (%) Note: Do not incude CI's	SAC
AUSCAN 3.1 NRS					
2.13.	ITT	Non Standard EFF_F1	Individual Subject Profile Plots of AUSCAN 3.1 NRS Individual Component Scores, by Treatment Group	X-Axis : Visit Y-Axis : Parameter (Unit) scaled accordingly Individual Components include: AUSCAN Pain, AUSCAN Physical Function, AUSCAN Stiffness, AUSCAN Total	SAC
2.14.	ITT	Non Standard EFF_F2	Plot of Mean and 95% CI of Change from Baseline in AUSCAN 3.1 NRS Individual Component Scores, at Each Visit	X-Axis : Visit Y-Axis : Change from Baseline in Parameter (Unit) scaled accordingly Individual Components include: AUSCAN Pain, AUSCAN Physical Function, AUSCAN Stiffness, AUSCAN Total	Wk6 IA, SAC

Efficacy: Figures					
No.	**Population**	**IDSL / TST ID / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
2.15.	ITT	Non Standard EFF_F2	Plot of Least Squares Means and 95% CI of Change from Baseline in AUSCAN 3.1 NRS Individual Component Scores (from Repeated Measures Analysis)	X-Axis : Visit Y-Axis : Change from Baseline in Parameter (Unit) scaled accordingly Add footnote: 'Note: Repeated Measures Analysis adjusted for Baseline Value, Treatment Group, Visit, Treatment Group by Visit Interaction [and Baseline Value by Visit Interaction]' Individual Components include: AUSCAN Pain, AUSCAN Physical Function, AUSCAN Stiffness, AUSCAN Total	Wk6 IA, SAC
Joint Assessments					
2.16.	ITT	Non Standard EFF_F2	Plot of Mean and 95% CI of Change from Baseline in Number of Soft Tissue Swollen Hand Joints, at Each Visit	X-Axis : Visit Y-Axis : Change from Baseline in Parameter (Unit) scaled accordingly	SAC
2.17.	ITT	Non Standard EFF_F2	Plot of Least Squares Means and 95% CI of Change from Baseline in the Number of Soft Tissue Swollen Hand Joints (from Repeated Measures Analysis)	X-Axis : Visit Y-Axis : Change from Baseline in Parameter (Unit) scaled accordingly Add footnote: 'Note: Repeated Measures Analysis adjusted for Baseline Value, Treatment Group, Visit, Treatment Group by Visit Interaction [and Baseline Value by Visit Interaction]'	SAC

Efficacy: Figures					
No.	**Population**	**IDSL / TST ID / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
2.18.	ITT	Non Standard EFF_F2	Plot of Mean and 95% CI of Change from Baseline in Number of Tender Hand Joints, at Each Visit	X-Axis : Visit Y-Axis : Change from Baseline in Parameter (Unit) scaled accordingly	SAC
2.19.	ITT	Non Standard EFF_F2	Plot of Least Squares Means and 95% CI of Change from Baseline in the Number of Tender Hand Joints (from Repeated Measures Analysis)	X-Axis : Visit Y-Axis : Change from Baseline in Parameter (Unit) scaled accordingly Add footnote: 'Note: Repeated Measures Analysis adjusted for Baseline Value, Treatment Group, Visit, Treatment Group by Visit Interaction [and Baseline Value by Visit Interaction]'	SAC
Disease Global Assessment					
2.20.	ITT	Non Standard EFF_F2	Plot of Mean and 95% CI of Change from Baseline in Physician's Global Assessment (NRS 0-10), at Each Visit	X-Axis : Visit Y-Axis : Change from Baseline in Parameter (Unit) scaled accordingly	SAC
2.21.	ITT	Non Standard EFF_F2	Plot of Least Squares Means and 95% CI of Change from Baseline in Physician's Global Assessment (NRS 0-10) (from Repeated Measures Analysis)	X-Axis : Visit Y-Axis : Change from Baseline in Parameter (Unit) scaled accordingly Add footnote: 'Note: Repeated Measures Analysis adjusted for Baseline Value, Treatment Group, Visit, Treatment Group by Visit Interaction [and Baseline Value by Visit Interaction]'	SAC
2.22.	ITT	Non Standard EFF_F2	Plot of Mean and 95% CI of Change from Baseline in Patients' Global Assessment, at Each Visit	X-Axis : Visit Y-Axis : Change from Baseline in Parameter (Unit) scaled accordingly	SAC

Efficacy: Figures					
No.	**Population**	**IDSL / TST ID / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
2.23.	ITT	Non Standard EFF_F2	Plot of Least Squares Means and 95% CI of Change from Baseline in Patients' Global Assessment (from Repeated Measures Analysis)	X-Axis : Visit Y-Axis : Change from Baseline in Parameter (Unit) scaled accordingly Add footnote: 'Note: Repeated Measures Analysis adjusted for Baseline Value, Treatment Group, Visit, Treatment Group by Visit Interaction [and Baseline Value by Visit Interaction]'	SAC
Imaging					
2.24.	ITT	Non Standard EFF_F2	Plot of Mean and 95% CI of Change from Baseline in Inflammatory Structural Joint Damage: HOAMRIS	X-Axis : Visit Y-Axis : Change from Baseline in Parameter (Unit) scaled accordingly Individual Components Include: Synovitis, Erosive damage, Cyst, Osteophyte Cartilage Space Loss, Mal-alignment and Bone Marrow Lesions	SAC

Efficacy: Figures					
No.	**Population**	**IDSL / TST ID / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
2.25.	ITT	Non Standard EFF_F2	Plot of Least Squares Means and 95% CI of Change from Baseline in Inflammatory Structural Joint Damage: HOAMRIS (from Repeated Measures Analysis)	X-Axis : Visit Y-Axis : Change from Baseline in Parameter (Unit) scaled accordingly Individual Components Include: Synovitis, Erosive damage, Cyst, Osteophyte Cartilage Space Loss, Mal-alignment and Bone Marrow Lesions Add footnote: 'Note: Repeated Measures Analysis adjusted for Baseline Value, Treatment Group, Visit, Treatment Group by Visit Interaction [and Baseline Value by Visit Interaction]'	
2.26.	ITT	Non Standard EFF_F2	Plot of Mean and 95% CI of Change from Baseline in Inflammatory Structural Joint Damage: HOAMRIQ	X-Axis : Visit Y-Axis : Change from Baseline in Parameter (Unit) scaled accordingly Individual Components Include: synovitis, normalised synovitis, normalised erosive damage, cartilage space loss, mal-alignment and normalised bone marrow lesions. Add footnote 'Note: Synovitis is normalised by the total joint volume, erosive damage and bone marrow lesions are normalised by volume of bone.'	SAC

Efficacy: Figures					
No.	**Population**	**IDSL / TST ID / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
2.27.	ITT	Non Standard EFF_F2	Plot of Least Squares Means and 95% CI of Change from Baseline in Inflammatory Structural Joint Damage: HOAMRIQ (from Repeated Measures Analysis)	X-Axis : Visit Y-Axis : Change from Baseline in Parameter (Unit) scaled accordingly Individual Components Include: synovitis, normalised synovitis, normalised erosive damage, cartilage space loss, mal-alignment and normalised bone marrow lesions. Add footnote 'Note: Synovitis is normalised by the total joint volume, erosive damage and bone marrow lesions are normalised by volume of bone.' Add footnote: 'Note: Repeated Measures Analysis adjusted for Baseline Value, Treatment Group, Visit, Treatment Group by Visit Interaction [and Baseline Value by Visit Interaction]'	SAC

Efficacy: Figures					
No.	**Population**	**IDSL / TST ID / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
2.28.	ITT	Non Standard EFF_F2	Plot of Mean and 95% CI of Change from Baseline in Joint Inflammation: DCE-MRI	X-Axis : Visit Y-Axis : Change from Baseline in Parameter (Unit) scaled accordingly Includes ktrans, normalised Ktrans, VE, normalised VE, VP, normalised VP, IRE, normalised IRE, ME, normalised ME. Add Footnote: 'Note: All normalised parameters have been normalised using the Volume of Enhancing Pannus (VEP).' Add units to parameter line.	SAC

Efficacy: Figures					
No.	**Population**	**IDSL / TST ID / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
2.29.	ITT	Non Standard EFF_F2	Plot of Least Squares Means and 95% CI of Change from Baseline in Joint Inflammation: DCE-MRI (from Repeated Measures Analysis)	X-Axis : Visit Y-Axis : Change from Baseline in Parameter (Unit) scaled accordingly Includes ktrans, normalised Ktrans, VE, normalised VE, VP, normalised VP, IRE, normalised IRE, ME, normalised ME. Add Footnote: 'Note: All normalised parameters have been normalised using the Volume of Enhancing Pannus (VEP).' Add units to parameter line. Add footnote: 'Note: Repeated Measures Analysis adjusted for Baseline Value, Treatment Group, Visit, Treatment Group by Visit Interaction [and Baseline Value by Visit Interaction]'	SAC
2.30.	ITT	Non Standard EFF_F2	Plot of Mean and 95% CI of Change from Baseline in Bone Shape Parameters	X-Axis : Visit Y-Axis : Change from Baseline in Parameter (Unit) scaled accordingly Includes Surface Area of Bone Add units to parameter line.	SAC
Paracetamol					

Efficacy: Figures					
No.	**Population**	**IDSL / TST ID / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
2.31.	ITT	Non Standard EFF_F2	Plot of Mean and 95% CI of Change from Baseline in 24h Total Dosage of Paracetamol Averaged over 7 days Prior to Each Visit		AIR, SAC
Additional MRI					
2.32.	ITT	Non Standard	Ordered Scatter Plot of Change from Baseline in Inflammatory Structural Joint Damage: HOAMRIS	X-Axis : Percentile Y-Axis : Change from Baseline in Parameter (Unit) scaled accordingly	SAC
2.33.	ITT	Non Standard	Ordered Scatter Plot of Change from Baseline in Inflammatory Structural Joint Damage: HOAMRIQ	X-Axis : Percentile Y-Axis : Change from Baseline in Parameter (Unit) scaled accordingly	SAC
2.34.	ITT	Non Standard	Ordered Scatter Plot of Change from Baseline in Joint Inflammation: DEC-MRI	X-Axis : Percentile Y-Axis : Change from Baseline in Parameter (Unit) scaled accordingly	SAC
2.35.	ITT	Non Standard	Ordered Scatter Plot of Change from Baseline in Bone Shape Parameters	X-Axis : Percentile Y-Axis : Change from Baseline in Parameter (Unit) scaled accordingly	SAC

12.15.7. Safety Tables

Safety : Tables					
No.	**Population**	**IDSL / TST ID / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
Adverse Events					
3.1.	Safety	Non Standard SAFE_T1	Overall Summary of Adverse Events		SAC
3.2.	Safety	AE1	Summary of All Adverse Events by System Organ Class and Preferred Term	ICH E3	Wk6 IA, SAC
3.3.	Safety	AE3	Summary of Common (>=5%) Adverse Events by Overall Frequency	ICH E3	SAC
3.4.	Safety	AE1	Summary All Drug-Related Adverse Events by System Organ Class and Preferred Term	GSK CTR	Wk6 IA, SAC
3.5.	Safety	AE15	Summary of Common (>=5%) Non-serious Adverse Events by System Organ Class and Preferred Term (Number of Participant and Occurrences)	FDAAA, EudraCT	SAC
Serious and Other Significant Adverse Events					
3.6.	Safety	AE16	Summary of Serious Adverse Events by System Organ Class and Preferred Term (Number of Participants and Occurrences)	FDAAA, EudraCT	Wk 6 IA, SAC
3.7.	Safety	AE1	Summary of Adverse Events Leading to Permanent Discontinuation of Study Treatment or Withdrawal from Study by System Organ Class and Preferred Term	IDSL	Wk6 IA, SAC
3.8.	Safety	Non Standard SAFE_T2	Summary of Adverse Events of Special Interest	Include any AESI, Serious Infections with subgroup of serious respiratory infections, Opportunistic Infections, PAP, Neutropenia, Hypersensitivity Reactions	SAC
3.9.	Safety	Non Standard SAFE_T3	Summary of Adverse Events of Special Interest – Injection Site Reactions		SAC

Safety : Tables					
No.	**Population**	**IDSL / TST ID / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
3.10.	Safety	Non Standard SAFE_T4	Summary of Adverse Events of Special Interest – Systemic Hypersensitivity Reactions related to GSK3196165		SAC
Laboratory					
3.11.	Safety	LB1	Summary of Clinical Chemistry Changes from Baseline	ICH E3	SAC
3.12.	Safety	LB1	Summary of Hematology Changes from Baseline	ICH E3	SAC
3.13.	Safety	LB1	Summary of Urinalysis Changes from Baseline	ICH E3	SAC
3.14.	Safety	Non Standard SAFE_T6	Summary of the Proportion of Subjects with Urinalysis Findings		SAC
3.15.	Safety	Non Standard SAFE_T7	Summary of Laboratory Parameters of Interest by CTCAE Grade	Note: Definitions of Grades can be found in and Laboratory Parameters of Interest can be found in Section 12.12.1. If multiple values are mapped to one visit: the value with the worst CTCAE grade will be considered. If there are more than one value of this grade, the later value will be considered.	SAC

Safety : Tables					
No.	**Population**	**IDSL / TST ID / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
3.16.	Safety	LB18	Shift Table of Laboratory Parameters of Interest from Baseline to Worst CTCAE Grade	Note: Definitions of Grades can be found in and Laboratory Parameters of Interest can be found in Section 12.12.1. Add footnotes: Note: Just parameters which can be classified in CTCAE grades are displayed. Note: Laboratory parameters of interest that have no results with a CTCAE grade were not included.	SAC
ECG					
3.17.	Safety	EG1	Summary of ECG Findings	IDSL	SAC
3.18.	Safety	EG2	Summary of Change from Baseline in ECG Values by Visit	IDSL	SAC
3.19.	Safety	EG10	Summary of Maximum QTc Values Post-Baseline Relative to Baseline by Category	IDSL	SAC
Vital Signs					
3.20.	Safety	VS1	Summary of Change from Baseline in Vital Signs		SAC
Immunogenicity					
3.21.	Safety	Non Standard SAFE_T8	Summary of Immunogenicity Results		SAC
Pulmonary Assessments					
3.22.	Safety	Non Standard SAFE_T9	Summary of Subjects with Pulmonary Findings		SAC

Safety : Tables					
No.	**Population**	**IDSL / TST ID / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
3.23.	Safety	Non Standard SAFE_T5	Summary of Persistent Cough, Dyspnea and D_{LCO} Decrease		SAC
3.24.	Safety	Non Standard SAFE_T10	Summary of Pulse Oximetry		SAC
3.25.	Safety	Non Standard SAFE_T11	Summary of Change from Baseline in Pulse Oximetry (%)		SAC
3.26.	Safety	Non Standard SAFE_T11	Summary of Change from Baseline in D_{LCO}	Note: Baseline is defined as the lowest value during the screening period prior to the first study drug administration.	SAC
3.27.	Safety	Non Standard SAFE_T12	Proportion of Subjects with a 15% Relative Decrease from Baseline in D_{LCO}		SAC
3.28.	Safety	Non Standard SAFE_T11	Summary of Change from Baseline in Spirometry Data	Please add a parameter information above the table for the two separate parameters FEV1 and FVC	SAC
3.29.	Safety	Non Standard SAFE_T13	Summary of Cough Data		SAC
3.30.	Safety	Non Standard SAFE_T11	Summary of Change from Baseline in Borg Dyspnea Score		SAC
3.31.	Safety	Non Standard SAFE_T14	Summary of Borg Dyspnea Questionnaire Data		SAC

12.15.8. Safety Figures

Safety : Figures					
No.	**Population**	**IDSL / TST ID / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
Adverse Events					
3.1.	Safety	AE10	Plot of Common (>=5%) Adverse Events and Relative Risks	Sorted by decreasing relative risk	SAC
Laboratory Values					
3.2.	Safety	LB9	Distribution of Laboratory Parameters of Interest by Visit and Treatment with Maximum over Time	Generate plots for the following parameters Hemoglobin, Total WBCs, Neutrophil Counts, Platelet Counts, ALT, AST and Total Bilirubin.	SAC
ECGs					
3.3.	Safety	EG8	Distribution of QTc Change by Time and Treatment		SAC
Pulmonary Assessments					
3.4.	Safety	Non Standard SAFE_F1	D_{LCO} Patient Profiles Over Time by Treatment		SAC

12.15.9. Pharmacokinetic Tables

Pharmacokinetic : Tables					
No.	**Population**	**IDSL / TST ID / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
PK Concentration					
4.1.	PK	Non Standard EFF_T1	Summary of GSK3196165 serum concentrations by visit		PK IA, Wk6 IA, SAC
4.2.	PK	Non Standard	Summary of derived steady state exposure parameters		PK IA, Wk6 IA
PK parameters					
4.3.	PK	Non Standard	Summary of derived PK parameters		PK IA, Wk6 IA

12.15.10. Pharmacokinetic Figures

Pharmacokinetic : Figures					
No.	**Population**	**IDSL / TST ID / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
PK concentration					
4.1.	PK	Non Standard	Plot of GSK3196165 concentration by visit		PK IA, Wk6 IA
4.2.	PK	Non Standard	Comparison of GSK3196165 concentration by visit in HOA and RA population		PK IA, Wk6 IA
4.3.	PK	Non Standard	Comparison of derived GSK3196165 steady state exposure in HOA, RA, healthy volunteers and multiple sclerosis population		PK IA, Wk6 IA
PK parameters					
4.4.	PK	Non Standard	Plot of distribution of the derived PK parameters in HOA, RA, healthy volunteers and multiple sclerosis population		PK IA, Wk6 IA

12.15.11. Pharmacodynamic and / or Biomarker Tables

Pharmacodynamic and/or Biomarker : Tables					
No.	**Population**	**IDSL / TST ID / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
Target Engagement Biomarkers					
5.1.	Safety	Non Standard PD_T1a or PD_T1b	Summary of Observed Result and Change from Baseline in Target Engagement Biomarkers	Use appropriate table shell depending on whether or not log transformation has been performed. If there are both log transformed and not log transformed biomarkers, then display in two separate outputs.	SAC
Predictive Biomarkers					
5.2.	Safety	Non Standard PD_T1a or PD_T1b	Summary of Observed Result and Change from Baseline in Predictive Biomarkers	Use appropriate table shell depending on whether or not log transformation has been performed. If there are both log transformed and not log transformed biomarkers, then display in two separate outputs.	SAC
5.3.	Safety	Non Standard PD_T2a or PD_T2b	Mixed Model Repeated Measures Analysis (MMRM) of Change from Baseline in Predictive Biomarkers	Use appropriate table shell depending on whether or not log transformation has been performed. If there are both log transformed and not log transformed biomarkers, then display in two separate outputs.	SAC
Cartilage Biomarkers					
5.4.	Safety	Non Standard PD_T1a or PD_T1b	Summary of Observed Result and Change from Baseline in Cartilage Biomarkers	Use appropriate table shell depending on whether or not log transformation has been performed. If there are both log transformed and not log transformed biomarkers, then display in two separate outputs.	SAC
Mechanistic Biomarkers					

Pharmacodynamic and/or Biomarker : Tables					
No.	**Population**	**IDSL / TST ID / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
5.5.	Safety	Non Standard PD_T1a or PD_T1b	Summary of Observed Result and Change from Baseline in Mechanistic Biomarkers	Use appropriate table shell depending on whether or not log transformation has been performed. If there are both log transformed and not log transformed biomarkers, then display in two separate outputs.	SAC
Safety Biomarkers					
5.6.	Safety	Non Standard PD_T1a or PD_T1b	Summary of Observed Result and Change from Baseline in Safety Biomarkers	Use appropriate table shell depending on whether or not log transformation has been performed. If there are both log transformed and not log transformed biomarkers, then display in two separate outputs.	SAC

12.15.12. Pharmacodynamic and / or Biomarker Figures

Pharmacodynamic and or Biomarker : Figures					
No.	**Population**	**IDSL / TST ID / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
Target Engagement Biomarkers					
5.1.	Safety	Non Standard PD_F2	Plot of Distribution of Target Engagement Biomarkers		SAC
5.2.	Safety	Non Standard PD_F1	Plot of Mean/Geometric Mean and 95% CI of Change from Baseline in Target Engagement Biomarkers, at Each Visit	X-Axis: Visit Y-axis: "Change from Baseline in <Biomarker>" or "Ratio to Baseline in <Biomarker>" if log-transformation is required	SAC
Predictive Biomarkers					
5.3.	Safety	Non Standard PD_F2	Plot of Distribution of Predictive Biomarkers		SAC
5.4.	Safety	Non Standard PD_F1	Plot of Mean/Geometric Mean and 95% CI of Change from Baseline in Predictive Biomarkers, at Each Visit	X-Axis: Visit Y-axis: "Change from Baseline in <Biomarker>" or "Ratio to Baseline in <Biomarker>" if log-transformation is required	SAC
5.5.	Safety	Non Standard PD_F1	Plot of Least Squares Means and 95% CI of Change from Baseline in Predictive Biomarkers (from Repeated Measures Analysis)	X-Axis: Visit Y-axis: "Change from Baseline in <Biomarker>" or "Ratio to Baseline in <Biomarker>" if log-transformation is required	SAC
Cartilage Biomarkers					
5.6.	Safety	Non Standard PD_F2	Plot of Distribution of Cartilage Biomarkers		SAC

Pharmacodynamic and or Biomarker : Figures					
No.	**Population**	**IDSL / TST ID / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
5.7.	Safety	Non Standard PD_F1	Plot of Mean/Geometric Mean and 95% CI of Change from Baseline in Cartilage Biomarkers, at Each Visit	X-Axis: Visit Y-axis: “Change from Baseline in <Biomarker>” or “Ratio to Baseline in <Biomarker>” if log-transformation is required	SAC
Mechanistic Biomarkers					
5.8.	Safety	Non Standard PD_F2	Plot of Distribution of Mechanistic Biomarkers		SAC
5.9.	Safety	Non Standard PD_F1	Plot of Mean/Geometric Mean and 95% CI of Change from Baseline in Mechanistic Biomarkers, at Each Visit	X-Axis: Visit Y-axis: “Change from Baseline in <Biomarker>” or “Ratio to Baseline in <Biomarker>” if log-transformation is required	SAC
Safety Biomarkers					
5.10.	Safety	Non Standard PD_F2	Plot of Distribution of Safety Biomarkers		SAC
5.11.	Safety	Non Standard PD_F1	Plot of Mean/Geometric Mean and 95% CI of Change from Baseline in Safety Biomarkers, at Each Visit	X-Axis: Visit Y-axis: “Change from Baseline in <Biomarker>” or “Ratio to Baseline in <Biomarker>” if log-transformation is required	SAC

12.15.13. Pharmacokinetic / Pharmacodynamic Figures

Pharmacokinetic / Pharmacodynamic : Figures					
No.	**Population**	**IDSL / TST ID / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
6.1.	PK	Non Standard	Plot of change from baseline in 24h average hand pain intensity at week 4 versus pre-dose concentration at week 4		SAC
6.2.	PK	Non Standard	Plot of change from baseline in 24h average hand pain intensity at week 6versus pre-dose concentration at week 6		SAC

12.15.14. ICH Listings

ICH : Listings					
No.	**Population**	**IDSL / TST ID / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
Subject Disposition					
1.	Screened	ES7	Listing of Reasons for Screening Failure	Journal guidelines	SAC
2.	Enrolled	ES2	Listing of Reasons for Study Withdrawal	ICH E3	SAC
4.	Enrolled	BL1	Listing of Subjects for Whom the Treatment Blind was Broken	ICH E3	SAC
5.	Enrolled	TA1	Listing of Planned and Actual Treatments	IDSL	SAC
Protocol Deviations					
6.	Enrolled	DV2	Listing of Important Protocol Deviations	ICH E3	SAC
7.	Enrolled	IE3	Listing of Subjects with Inclusion/Exclusion Criteria Deviations	ICH E3	SAC
Populations Analysed					
8.	Enrolled	SA3	Listing of Subjects Excluded from Any Population	ICH E3	SAC
Demography					
9.	ITT	DM2	Listing of Demographic Characteristics	ICH E3	SAC
10.	ITT	DM9	Listing of Race	ICH E3	SAC
Medical condition & concomitant medications					
11.	ITT	MH2	Listing of Current/Past Medical Conditions		SAC
12.	ITT	CM3	Listing of Prior and Concomitant Medications (Non-OA)	IDSL	SAC
13.	ITT	CM3	Listing of Prior and Concomitant OA Medications		SAC
16.	ITT	Non Standard POP_L1	Listing of OA Disease History		SAC

ICH : Listings					
No.	**Population**	**IDSL / TST ID / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
Exposure					
17.	Safety	EX1	Listing of Exposure to Study Treatment Data	ICH E3	SAC
Adverse Events					
18.	Safety	AE8	Listing of All Adverse Events	ICH E3	SAC
19.	Safety	AE7	Listing of Subject Numbers for Individual Adverse Events	ICH E3	SAC
20.	Safety	AE2	Listing of Relationship Between Adverse Event System Organ Classes, Preferred Terms, and Verbatim Text	IDSL	SAC
Serious and Other Significant Adverse Events					
21.	Safety	AE8	Listing of Fatal Serious Adverse Events	ICH E3	Wk6 IA, SAC
22.	Safety	AE8	Listing of Non-Fatal Serious Adverse Events	ICH E3	SAC
23.	Safety	AE14	Listing of Reasons for Considering as a Serious Adverse Event	ICH E3	SAC
24.	Safety	AE8	Listing of Adverse Events Leading to Withdrawal from Study / Permanent Discontinuation of Study Treatment	ICH E3	SAC
25.	Safety	AE7	Listing of Subject Numbers for Adverse Events of Special Interest (AESIs)	ICH E3	SAC
Labs					
26.	Safety	LB5	Listing of All Laboratory Data for Subjects with Any Value of Potential Clinical Importance	ICH E3	SAC
27.	Safety	LB5	Listing of Laboratory Values of Potential Clinical Importance		SAC
28.	Safety	LB14	Listing of Laboratory Data with Character Results	ICH E3	SAC
29.	Safety	UR2a	Listing of Urinalysis Data for Subjects with Abnormalities of Potential Clinical Importance	ICH E3	SAC
Vital signs					

ICH : Listings					
No.	**Population**	**IDSL / TST ID / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
30.	Safety	VS4	Listing of Vital Signs Data		SAC
ECG					
31.	Safety	EG3	Listing of ECG Values for Subjects with Any Value of Potential Clinical Importance	IDSL	SAC
32.	Safety	EG3	Listing of ECG Values of Potential Clinical Importance	IDSL	SAC
33.	Safety	EG5	Listing of All ECG Findings for Subjects with an Abnormal ECG Finding	IDSL	SAC
34.	Safety	EG5	Listing of Abnormal ECG Findings	IDSL	SAC
Vital signs					
35.	Safety	VS4	Listing of Vital Signs of Potential Clinical Importance	IDSL Include Systolic BP, Diastolic BP, Pulse and Oxygen Saturation.	SAC
36.	Safety	VS4	Listing of All Vital Signs Data for Subjects with Any Value of Potential Clinical Importance	IDSL	SAC
Immunogenicity					
37.	Safety	IMM2	Listing of Immunogenicity Results		SAC
Pulmonary Assessments					
38.	Safety	Non Standard POP_L2	Listing of Subjects with Persistent Cough, Dyspnea or D_{LCO} Decrease		SAC
39.	Safety	Non Standard POP_L3	Listing of Pulmonary Assessments		SAC
40.	Safety	Non Standard POP_L4	Listing of Pulmonary Function Tests		SAC

12.15.15. Non-ICH Listings

Non-ICH : Listings					
No.	**Population**	**IDSL / TST ID / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
Efficacy					
41.	ITT	Non Standard EFF_L1	Listing of Individual Subject Hand Pain NRS Averaged over 7 Days Prior to Each Visit		SAC
42.	ITT	Non-Standard EFF_L2	Statistical Listing of Repeated Measures Analysis of Change from Baseline in Average Hand Pain NRS Averaged over 7 Days Prior to Each Visit		SAC
43.	ITT	Non-Standard EFF_L2	Statistical Listing of GEE Analysis on Proportion of Subjects Achieving 30% Reduction in Average Hand Pain NRS Averaged over 7 Days Prior to Each Visit		SAC
44.	ITT	Non-Standard EFF_L2	Statistical Listing of GEE Analysis on Proportion of Subjects Achieving 50% Reduction in Average Hand Pain NRS Averaged over 7 Days Prior to Each Visit		SAC
45.	ITT	Non-Standard EFF_L2	Statistical Listing of Repeated Measures Analysis of Change from Baseline in Worst Hand Pain NRS Averaged over 7 Days Prior to Each Visit, by Visit		SAC
46.	ITT	Non-Standard EFF_L2	Statistical Listing of GEE Analysis on Proportion of Subjects Achieving 30% Reduction in Worst Hand Pain NRS Averaged over 7 Days Prior to Each Visit		SAC
47.	ITT	Non-Standard EFF_L2	Statistical Listing of GEE Analysis on Proportion of Subjects Achieving 50% Reduction in Worst Hand Pain NRS Averaged over 7 Days Prior to Each Visit		SAC
48.	ITT	Non-Standard EFF_L3	Listing of Individual Subject AUSCAN 3.1 NRS Individual Component Scores		SAC
49.	ITT	Non-Standard EFF_L2	Statistical Listing of Repeated Measures Analysis of Change from Baseline in AUSCAN 3.1 NRS Individual Component Scores, by Visit		SAC

Non-ICH : Listings					
No.	**Population**	**IDSL / TST ID / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
50.	ITT	Non-Standard EFF_L4	Listing of Individual Subject Number of Soft Tissue Swollen or Tender Hand Joints, by Visit		SAC
51.	ITT	Non-Standard EFF_L2	Statistical Listing of Repeated Measures Analysis of Change from Baseline in Number of Soft Tissue Swollen Hand Joints, by Visit		SAC
52.	ITT	Non-Standard EFF_L2	Statistical Listing of Repeated Measures Analysis of Change from Baseline in Number of Tender Hand Joints, by Visit		SAC
53.	ITT	Non Standard EFF_L5	Listing of Individual Subject Pain/Tenderness Hand Joint Assessment, by Visit		SAC
54.	ITT	GA4	Listing of Individual Subject Patient's and Physician's Global Assessments, by Visit	List both the Patients and Physicians Global Assessments in the same output with separate columns for each	SAC
55.	ITT	Non-Standard EFF_L2	Statistical Listing of Repeated Measures Analysis of Change from Baseline in Physician's Global Assessment, by Visit		SAC
56.	ITT	Non-Standard EFF_L2	Statistical Listing of Repeated Measures Analysis of Change from Baseline in Patient's Global Assessment, by Visit		SAC
Imaging					
57.	ITT	Non Standard EFF_L6	Listing of Individual Subject Inflammatory Structural Joint Damage: HOAMRIS	Individual Components Include: Synovitis, Erosive damage, Cyst, Osteophyte Cartilage Space Loss, Mal-alignment and Bone Marrow Lesions	SAC
58.	ITT	Non Standard EFF_L6	Listing of Individual Subject Inflammatory Structural Joint Damage: HOAMRIQ	Individual Components Include: synovitis, normalised synovitis, normalised erosive damage, cartilage space loss, mal-alignment and normalised bone marrow lesions	SAC

Non-ICH : Listings					
No.	**Population**	**IDSL / TST ID / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
59.	ITT	Non Standard EFF_L6	Listing of Individual Subject Joint Inflammation: DCE-MRI	Includes ktrans, normalised Ktrans, VE, normalised VE, VP, normalised VP, IRE, normalised IRE, ME, normalised ME.	SAC
60.	ITT	Non Standard EFF_L6	Listing of Individual Subject Bone Shape Parameter	Includes Surface Area of Bone	SAC
PK					
61.	PK	Non Standard PK_L1	Listing of Individual Subject Pharmacokinetic Data		SAC
Biomarker					
62.	Safety	Non Standard PD_L1	Listing of Individual Subject Target Engagement		SAC
63.	Safety	Non Standard PD_L1	Listing of Individual Subject Predictive Biomarkers		SAC
64.	Safety	Non Standard PD_L1	Listing of Individual Subject Cartilage Biomarkers		SAC
65.	Safety	Non Standard PD_L1	Listing of Individual Subject Mechanistic Biomarkers		SAC
66.	Safety	Non Standard PD_L1	Listing of Individual Subject Safety Biomarkers		SAC
67.	Safety	Non Standard EFF_ L2	Statistical Listing of Repeated Measures Analysis of Change from Baseline in Predictive Biomarkers		SAC
Additional					

Non-ICH : Listings					
No.	**Population**	**IDSL / TST ID / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
68.	ITT	GA4	Listing of Individual Subject Daily Hand Pain NRS Scores	List both the 24h Average and 24h Worst Hand Pain Score in the same output with separate columns for each. Only display absolute values	SAC
69.	ITT	Non Standard EFF_L6	Listing of Individual Subject Change from Baseline in Inflammatory Structural Joint Damage: HOAMRIS	Individual Components Include: Synovitis, Erosive damage, Cyst, Osteophyte Cartilage Space Loss, Mal-alignment and Bone Marrow Lesions	SAC
70.	ITT	Non Standard EFF_L6	Listing of Individual Subject Change from Baseline in Inflammatory Structural Joint Damage: HOAMRIQ	Individual Components Include: synovitis, normalised synovitis, normalised erosive damage, cartilage space loss, mal-alignment and normalised bone marrow lesions	SAC
71.	ITT	Non Standard EFF_L6	Listing of Individual Subject Change from Baseline in Joint Inflammation: DCE-MRI	Includes ktrans, normalised Ktrans, VE, normalised VE, VP, normalised VP, IRE, normalised IRE, ME, normalised ME.	SAC
72.	ITT	Non Standard EFF_L6	Listing of Individual Subject Change from Baseline in Bone Shape Parameter	Includes Surface Area of Bone	SAC

12.16. Appendix 17: Example Mock Shells for Data Displays

Example: POP_T1
Protocol: 204851 Confidential
Population: Intent-to-Treat

Table 1.x
Summary of Baseline Efficacy Parameters

	Statistic	Placebo N=xx	GSK3196165 180mg N=xx	Total N=xx
24h average hand pain NRS score averaged over 7 days prior to BL	n	xx	xx	xx
	Mean	xx.xx	xx.xx	xx.xx
	SD	xx.xxx	xx.xxx	xx.xxx
	Median	xx.xx	xx.xx	xx.xx
	Min	xx.x	xx.x	xx.x
	Max	xx.x	xx.x	xx.x
	n	xx	xx	xx
	…	…	…	…
24h worst hand pain NRS score averaged over 7 days prior to BL	n	xx	xx	xx
AUSCAN 3.1 NRS Total Score	n	xx	xx	xx
AUSCAN 3.1 NRS Pain Score	n	xx	xx	xx
	…	…	…	…
AUSCAN 3.1 NRS Physical Function Score	n	xx	xx	xx
	…	…	…	…

	Statistic	Placebo N=xx	GSK3196165 180mg N=xx	Total N=xx
AUSCAN 3.1 NRS Stiffness Score	n	xx	xx	xx
	…	…	…	…
Number of Soft Tissue Swollen Hand Joints	n	xx	xx	xx
	…	…	…	…
Number of Tender Hand Joints	n	xx	xx	xx
	…	…	…	…
PhGA	n	xx	xx	xx
	…	…	…	…
PtGA	n	xx	xx	xx
	…	…	…	…
CRP (mg/L)	n	xx	xx	xx
	…	…	…	…

Note: PtGA= Patient's Global Assessment of Disease Activity, PhGA= Physician's Global Assessment of Disease Activity, CRP= C-Reactive Protein

Programming Note: Make sure to use the correct number of decimal places for each of the variables.
Programming Note: show for all variables all descriptive statistics

Example: POP_T2
Protocol: 204851 Confidential
Population: Intent-to-Treat

Table 1.x
Summary of OA Disease History

	Statistic	Placebo N=xx	GSK3196165 180mg N=xx	Total N=xx
Time since OA diagnosis (months)	n	xx	xx	xx
	Mean	xxx.x	xxx.x	xxx.x
	SD	xx.xx	xx.xx	xx.xx
	Min	xxx	xxx	xxx
	Median	xxx	xxx	xxx
	Max	xxx	xxx	xxx
Time since start of OA symptoms (months)	n	xx	xx	xx
	Mean	xxx.x	xxx.x	xxx.x
	SD	xx.xx	xx.xx	xx.xx
	Min	xxx	xxx	xxx
	Median	xxx	xxx	xxx
	Max	xxx	xxx	xxx

Note: Time since OA diagnosis and start of 0A symptoms is calculated up to date of first study drug administration.

Example: POP_T3
Protocol: 204851 Confidential
Population: Intent-to-Treat

Table 1.x
Summary of Current Medical Conditions

MedDRA vX.X System Organ Class Preferred Term	Placebo N=xx n (%)	GSK3196165 180mg N=xx n (%)	Total
Number of subjects with at least one medical history condition	xx (xx)	xx (xx)	xx (xx)
Cardiovascular Risk Factors	xx (xx)	xx (xx)	xx (xx)
Coronary Artery Disease	xx (xx)	xx (xx)	xx (xx)
Myocardial Infarction	xx (xx)	xx (xx)	xx (xx)
...	xx (xx)	xx (xx)	xx (xx)
System Organ Class 1	xx (xx)	xx (xx)	xx (xx)
Preferred Term 1	xx (xx)	xx (xx)	xx (xx)
Preferred Term 2	xx (xx)	xx (xx)	xx (xx)
...	xx (xx)	xx (xx)	xx (xx)
…			

Notes to Programming Team:

- Cardiac Disorders to be taken from CRF.

Example: EFF_T1
Protocol: 204851 Confidential
Population: Intent-to-Treat

Table 2.x
Summary of Observed Result and Change from Baseline in [Parameter]

[Component: AUSCAN Pain/AUSCAN Physical Function/AUSCAN Stiffness/AUSCAN Total]

		Observed Results				Change from Baseline Results				
Treatment Group	Visit	n	Mean (95% CI)	SD	Median (Min,Max)	n	BL Mean	Mean (95% CI)	SD	Median (Min,Max)
Placebo (N=XX)	Baseline	x x	x.xx (x.xx, x.xx)	x.xxx	x.xx (x.x, x.x)					
	Week 1	x x	x.xx (x.xx, x.xx)	x.xxx	x.xx (x.xx, x.xx)	xx	x.xx	x.x (x.x,x.x)	x.xx	x.x (x.x, x.x)
	Week 2	x x	x.xx (x.xx, x.xx)	x.xxx	x.xx (x.xx, x.xx)	xx	x.xx	x.x (x.x,x.x)	x.xx	x.x (x.x, x.x)
	…	…	…	…	…	…	…	…	…	…
GSK319616 5 180mg (N=XX)	Baseline	x x	x.xxx (x.xx, x.xx)	x.xxx	x.xx (x.xx, x.xx)					
	Week 1	x x	x.xxx (x.xx, x.xx)	x.xxx	x.xx (x.xx, x.xx)	xx	x.xx	x.x (x.x,x.x)	x.xx	x.x (x.x, x.x)
	…	…	…	…	…	…	…	…	…	…

Note: BL Mean for Week X is the mean of the Baseline values of all subjects with a non-missing value at Week X.

Example: EFF_T2
Protocol: 204851 Confidential
Population: Intent-to-Treat

Table 2.x
Mixed Model Repeated Measures Analysis (MMRM)of the Change from Baseline in [Parameter]

[Component: AUSCAN Pain/AUSCAN Physical Function/AUSCAN Stiffness/AUSCAN Total]

Visit	Statistic	Placebo N=xx	GSK3196165 180mg N=xx
Week 1	n	xx	xx
	LS Mean	x.xx	x.xx
	LS Mean Change	x.xx	x.xx
	Standard Error	x.xxx	x.xxx
	Difference from Placebo		x.xx
	95% Confidence Interval		(x.xx, x.xx)
	p-value		0.xxx
Week 2	n		
	LS Mean	x.xx	x.xx
	LS Mean Change	x.xx	x.xx
	Standard Error	x.xxx	x.xxx
	Difference from Placebo		x.xx
	95% CI for Difference		(x.xx, x.xx)
…			

Note: Repeated Measures Analysis adjusted for Baseline Value, Treatment Group, Visit and Treatment Group by Visit Interaction [and Baseline Value by Visit Interaction]
Note: n is the number of subjects with non-missing data at that visit.

Example: EFF_T3
Protocol: 204851 Confidential
Population: Intent-to-Treat

Table 2.x
Summary and Analysis of the Proportion of Subjects Achieving a [30/50]% or More Reduction in [Parameter] at Each Visit

Visit	Statistic	Placebo N=xx	GSK3196165 180mg N=xx
Week 1	n (%)	xx (xx)	xx (xx)
	Difference to Placebo (%)		xx
	95% CI (%)		(xx.x, xx.x)
	Odds Ratio		xx.x
	95% CI (%)		(xx.xx, xx.xx)
Week 2	n (%)	xx (xx)	xx (xx)
	Difference to Placebo (%)		xx
	95% CI (%)		(xx.x, xx.x)
	Odds Ratio		xx.x
	95% CI (%)		(xx.xx, xx.xx)
…			

Note: Missing subjects have been assumed to be non-responders.
Note: Positive differences and Odds Ratios >1 indicate an improvement of treatment over placebo.
Note: 95% confidence intervals for the difference to placebo are constructed using asymptotic Wald confidence limits without correction.
Note: 95% confidence intervals for odds ratios are constructed using exact confidence limits.
Note: Generalised Estimating Equations Analysis adjusted for Baseline Score, Treatment Group, Visit and Treatment Group by Visit Interaction

Example: EFF_T4
Protocol: 204851 Confidential
Population: Intent-to-Treat

Table 2.x
Summary of Observed Result and Change from Baseline in [Inflammatory Structural Joint Damage/Joint Inflammation/Bone Shape Parameters]: [HOAMRIS/HOAMRIQ/DCE-MRI]

Parameter (Unit): <Synovitis/ Erosive Damage/ Cysts/ Osteophyte/ Cartilage Space Loss/ Mal-alignment/ Bone Marrow Lesions>
< Synovitis/ Synovitis (Normalised)/ Erosive Damage/ Erosive Damage (Normalised)/ Cartilage Space Loss/ Mal-alignment/ Bone Marrow Lesions (Normalised)>
< Exchange rate, Interstitial volume, Plasma volume, Initial rate of enhancement, Maximal signal intensity enhancement>
<Surface Area of Bone>

		Observed Results				Change from Baseline Results				
Treatment Group	Visit	n	Mean (95% CI)	SD	Median (Min,Max)	n	BL Mean	Mean (95% CI)	SD	Median (Min,Max)
Placebo (N=XX)	Baseline	xx	x.xx (x.xx,x.xx)	x.xxx	x.xx (x.x, x.x)					
	Week 1	xx	x.xx (x.xx,x.xx)	x.xxx	x.xx (x.xx, x.xx)	xx	x.xx	x.x (x.x,x.x)	x.xx	x.x (x.x, x.x)
	Week 2	xx	x.xx (x.xx,x.xx)	x.xxx	x.xx (x.xx, x.xx)	xx	x.xx	x.x (x.x,x.x)	x.xx	x.x (x.x, x.x)
	Week 4	xx	x.xx (x.xx,x.xx)	x.xxx	x.xx (x.xx, x.xx)	xx	x.xx	x.x (x.x,x.x)	x.xx	x.x (x.x, x.x)
	…	…	…	…	…	…	…	…	…	…
GSK3196165 180mg (N=XX)	Baseline	xx	x.xxx (x.xx,x.xx)	x.xxx	x.xx (x.xx, x.xx)					
	Week 1	xx	x.xxx (x.xx,x.xx)	x.xxx	x.xx (x.xx, x.xx)	xx	x.xx	x.x (x.x,x.x)	x.xx	x.x (x.x, x.x)
	…	…	…	…	…	…	…	…	…	…

<Note: Synovitis is normalized by the total joint volume, erosive damage and bone marrow lesions are normalized by volume of bone.>
< Note: All parameters have been normalized by the Volume of Enhancing Pannus (VEP).>

Example: EFF_T5
Protocol: 204851 Confidential
Population: Intent-to-Treat

Table 2.x
Repeated Measures Analysis of Observed Result and Change from Baseline in [Inflammatory Structural Joint Damage/Joint Inflammation]: [HOAMRIS/HOAMRIQ/DCE-MRI]

Parameter (Unit): <Synovitis/ Erosive Damage/ Cyst/ Osteophyte Cartilage Space Loss/ Mal-alignment/ Bone Marrow Lesions>
< Synovitis/ Synovitis (Normalised)/ Erosive Damage (Normalised)/ Cartilage Space Loss/ Mal-alignment/ Bone Marrow Lesions (Normalised)>
< Exchange Rate, Interstitial Volume, Plasma Volume, Initial Rate of Enhancement, Maximal Signal Intensity Enhancement>

Visit	Statistic	Placebo N=xx	GSK3196165 180mg N=xx
Week 1	n	xx	xx
	LS Mean	x.xx	x.xx
	LS Mean Change	x.xx	x.xx
	Standard Error	x.xxx	x.xxx
	Difference from Placebo		x.xx
	95% Confidence Interval		x.xx - x.xx
	p-value		0.xxx
Week 2	n		
	LS Mean	x.xx	x.xx
	LS Mean Change	x.xx	x.xx
	Standard Error	x.xxx	x.xxx
	Difference from Placebo		x.xx
	95% CI for Difference		x.xx - x.xx
	p-value		0.xxx
…			

Note: Repeated measures analysis adjusted for <Parameter> baseline value, treatment group, visit, treatment group by visit interaction and baseline value by visit interaction.
Note: n is the number of subjects with non-missing data at that visit.
<Note: Synovitis is normalized by the total joint volume, erosive damage and bone marrow lesions are normalized by volume of bone.>
< Note: All parameters have been normalized by the Volume of Enhancing Pannus (VEP).>

Example: EFF_T6
Protocol: 204851 Confidential
Population: Intent-to-Treat

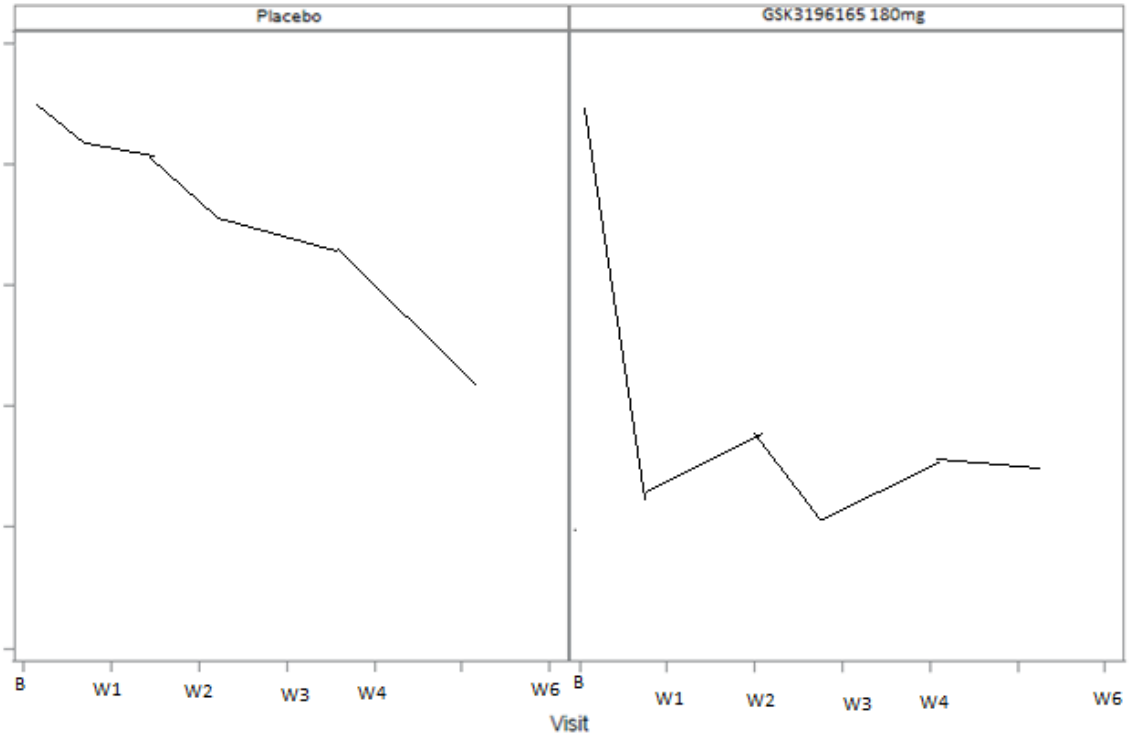
2.x
Summary of the Proportion of Subjects Reporting Paracetamol Use in the 7 Days Prior to Each Visit

Visit	Statistic	Placebo N=xx	GSK3196165 180mg N=xx
Baseline	n	xx	xx
	No Paracetamol (%)	xx (xx)	xx (xx)
	Paracetamol for >=1 day (%)	xx (xx)	xx (xx)
Week 1	n	xx	xx
	No Paracetamol (%)	xx (xx)	xx (xx)
	Paracetamol for >=1 day (%)	xx (xx)	xx (xx)
…			

Example: EFF_F1
Protocol: 204851 Confidential
Population: Intent-to-Treat

Figure 2.x
Individual Subject Profile Plots of [Parameter], by Treatment Group

Component: <AUSCAN Pain/AUSCAN Physical Function/AUSCAN Stiffness/ AUSCAN Total>

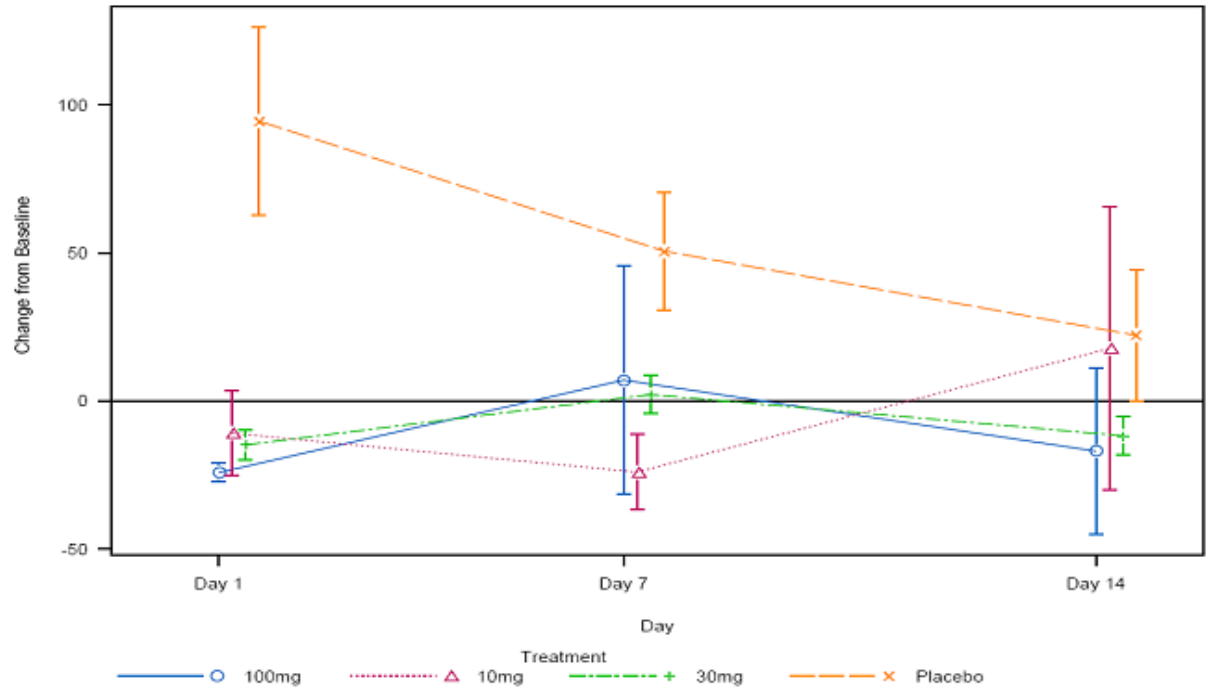


Note: Each of the lines represents one subject.
Note: B=Baseline

Example: EFF_F2
Protocol: 204851 Confidential
Population: Intent-to-Treat

Figure 2.x
Plot of Mean and 95% CI of Change from Baseline in [Parameter], at Each Visit

[Component/Parameter(Unit)]: <AUSCAN Pain/AUSCAN Physical Function/AUSCAN Stiffness/ AUSCAN Total>
<Synovitis/ Erosive Damage/ Cyst/ Osteophyte Cartilage Space Loss/ Mal-alignment/ Bone Marrow Lesions>
< Synovitis/ Synovitis (Normalised)/ Erosive Damage (Normalised)/ Cartilage Space Loss/ Mal-alignment/ Bone Marrow Lesions (Normalised)>
< Exchange Rate, Interstitial Volume, Plasma Volume, Initial Rate of Enhancement, Maximal Signal Intensity Enhancement>



Programming Note: Legend to be centered.

Example: SAFE_T1
Protocol: 204851 Confidential
Population: Safety

Table 3.x
Overall Summary of Adverse Events

Category	Placebo N=xx n (%) [#]	GSK3196165 180mg N=xx n (%) [#]
Any AEs	xx (xx) [x]	xx (xx) [x]
Serious AEs	xx (xx) [x]	xx (xx) [x]
AEs leading to permanent discontinuation of study treatment	xx (xx) [x]	xx (xx) [x]
Drug-related AEs	xx (xx) [x]	xx (xx) [x]
AEs leading to Death	xx (xx) [x]	xx (xx) [x]

Note: n=number of subjects with at least one event. #=number of individual occurrences

Programming note: Include Withdrawals due to AE to “permanent discontinuation of study drug”.

Example: SAFE_T2
Protocol: 204851 Confidential
Population: Safety

Table 3.x
Summary of Adverse Events of Special Interest

Category	Placebo (N=xx) n (%) [#]	GSK3196165 180mg (N=xx) n (%) [#]
Any AESI	xx (xx%) [xx]	xx (xx%) [xx]
Serious Infections	xx (xx%) [xx]	xx (xx%) [xx]
Serious Respiratory Infections	xx (xx%) [xx]	xx (xx%) [xx]
Opportunistic Infections	xx (xx%) [xx]	xx (xx%) [xx]
Neutropenia	xx (xx%) [xx]	xx (xx%) [xx]
Pulmonary Alveolar Proteinosis	xx (xx%) [xx]	xx (xx%) [xx]
Hypersensitivity Reactions	xx (xx%) [xx]	xx (xx%) [xx]
Injection Site Reactions	xx (xx%) [xx]	xx (xx%) [xx]

AESI = Adverse Event of Special Interest.
Note: n=number of subjects reporting at least one event. [#] is the number of individual occurrences.

Example: SAFE_T3
Protocol: 204851 Confidential
Population: Safety

Table 3.x
Summary of Adverse Events of Special Interest - Injection Site Reactions

Number of Subjects with an	Placebo N=xx n (%) [#]	GSK3196165 180mg N=xx n (%) [#]
Injection Site Reaction	xx (xx) [xx]	xx (xx) [xx]
<= 1 Day Post Injection	xx (xx) [xx]	xx (xx) [xx]
> 1 Day Post Injection ($)	xx (xx) [xx]	xx (xx) [xx]
Reported as AE	xx (xx) [xx]	xx (xx) [xx]
Reported as SAE	xx (xx) [xx]	xx (xx) [xx]
Itching/pruritis occurrence	xx (xx) [xx]	xx (xx) [xx]
Redness/erythema occurrence	xx (xx) [xx]	xx (xx) [xx]
Pain occurrence	xx (xx) [xx]	xx (xx) [xx]
Bruising occurrence	xx (xx) [xx]	xx (xx) [xx]
Swelling/edema	xx (xx) [xx]	xx (xx) [xx]
Warm to touch	xx (xx) [xx]	xx (xx) [xx]

Note: n=number of subjects with at least one event. #=number of individual occurrences
Note: ($) until 1 day before next injection.

Example: SAFE_T4
Protocol: 204851 Confidential
Population: Safety

Table 3.x
Summary of Adverse Events of Special Interest - Systemic Hypersensitivity Reactions Related to GSK3196165

Type of Systemic Reaction	Placebo N=xx n (%) [#]	GSK3196165 180mg N=xx n (%) [#]
Systemic Hypersensitivity Reaction	xx (xx) [xx]	xx (xx) [xx]
<= 1 Day Post Injection	xx (xx) [xx]	xx (xx) [xx]
> 1 Day Post Injection ($)	xx (xx) [xx]	xx (xx) [xx]
Reported as an AE	xx (xx) [xx]	xx (xx) [xx]
Reported as an SAE	xx (xx) [xx]	xx (xx) [xx]
Headache	xx (xx) [xx]	xx (xx) [xx]
Pruritis	xx (xx) [xx]	xx (xx) [xx]
Urticaria	xx (xx) [xx]	xx (xx) [xx]
Rash	xx (xx) [xx]	xx (xx) [xx]
Angioedema	xx (xx) [xx]	xx (xx) [xx]
…		
Met an Anaphylaxis Criterion	xx (xx) [xx]	xx (xx) [xx]
Anaphylactic Criterion 1	xx (xx) [xx]	xx (xx) [xx]
Anaphylactic Criterion 2	xx (xx) [xx]	xx (xx) [xx]
Anaphylactic Criterion 3		

Note: n=number of subjects with at least one event. #=number of individual occurrences
Note: ($) until 1 day before next injection.

Example: SAFE_T5
Protocol: 204851 Confidential
Population: Safety

Table 3.x
Summary of Persistent Cough, Dyspnea and D_{LCO} Decrease

	Placebo N=xx n (%)	GSK3196165 180mg N=xx n (%)
Persistent Cough	xx (xx)	xx (xx)
Persistent Dyspnea	xx (xx)	xx (xx)
Persistent D_{LCO} decrease >15% from baseline	xx (xx)	xx (xx)

Note: n=number of subjects reporting at least one event in that category.
Note: Persistent is defined as any event with duration >=15 days. Cough must be grade 2 or 3. Dyspnea is determined from Borg scores >=3. Events were confirmed by the Safety Review Team.

Example: SAFE_T6
Protocol: 204851 Confidential
Population: Safety

Table 3.x
Laboratory Evaluation: Summary of Proportion of Subjects with Urinalysis Findings
(Intent-to-Treat Population)

Laboratory Parameter: Protein

	Placebo N=xx n (%)	GSK3196165 180mg N=xx n (%)
Baseline		
n	xx	xx
1+	xx (xx)	xx (xx)
2+	xx (xx)	xx (xx)
3+	xx (xx)	xx (xx)
Negative	xx (xx)	xx (xx)
Trace	xx (xx)	xx (xx)
Week xx		
n	xx	xx
1+	xx (xx)	xx (xx)
2+	xx (xx)	xx (xx)
3+	xx (xx)	xx (xx)
Negative	xx (xx)	xx (xx)
Trace	xx (xx)	xx (xx)
Week xx		
…	xx	xx
…		

Note: Percentages calculated based on the number of subjects with a valid assessment at the respective visit (n/M*100%).

Programming Note: If multiple values are mapped to one visit: the value with the worst CTCAE grade will be considered. If there are more than one value of this grade, the later value will be considered.
Programming Note: Use this shell for all categorical parameters of Urinalysis, in case there are more than only Protein.

Example: SAFE_T7
Protocol: 204851 Confidential
Population: Safety

Table 3.x
Summary of Laboratory Parameters of Interest by CTCAE Grade

Parameter	Visit	CTCAE Version 4.0	Placebo N=xx n(%)	GSK3196165 180mg N=xx n(%)
Parameter 1	Baseline	n	xx	xx
		Grade 1	xx(xx)	xx(xx)
		Grade 2	xx(xx)	xx(xx)
		Grade 3	xx(xx)	xx(xx)
		Grade 4	xx(xx)	xx(xx)
	Week x	n	xx	xx
		Grade 1	xx(xx)	xx(xx)
		Grade 2	xx(xx)	xx(xx)
		Grade 3	xx(xx)	xx(xx)
		Grade 4	xx(xx)	xx(xx)
	…			
Parameter 2	…			

Note: Just parameters which can be classified in CTCAE grades are displayed.
Note: Laboratory parameters of interest that have no results with a CTCAE grade were not included.
Note: Percentages calculated based on the number of subjects with a valid assessment at the respective visit.

Programming Note: Laboratory Parameters of Interest and according CTCAE Grades can be found in the RAP Appendix 12.
Programming Note: If multiple values are mapped to one visit: the value with the worst CTCAE grade will be considered. If there are more than one value of this grade, the later value will be considered.

Example: SAFE_T8
Protocol: 204851 Confidential
Population: Safety

Table 3.x
Summary of Immunogenicity Results

Assay: [Anti-GSK3196165 Binding AB Detection]

Visit		Placebo N=xx n (%)	GSK3196165 180mg N=xx n (%)
Baseline	n	xx	xx
	Positive	xx (xx%)	xx (xx%)
	Negative	xx (xx%)	xx (xx%)
Anytime Post-Baseline	n	xx	xx
	Positive	xx (xx%)	xx (xx%)
	- to +	xx (xx%)	xx (xx%)
	+ to +	xx (xx%)	xx (xx%)
	Negative	xx (xx%)	xx (xx%)
	+ to -	xx (xx%)	xx (xx%)
	- to -	xx (xx%)	xx (xx%)
Week 1	n	xx	xx
	Positive	xx (xx%)	xx (xx%)
	Negative	xx (xx%)	xx (xx%)
Week X	n	xx	xx
	…	…	…

Note: Change refers to change from Baseline. Percentages for change are based on the number at risk at baseline, e.g. "- to +" and "- to -" are based on "Negative" at baseline.
Note: Percentages for Positive/Negative are based on the number of subjects at each visit.
Programming Note: Positive here refers to confirmed positive results, this should be evident from the dataset.
Programming Note: "Anti-GSK3196165 Binding AB Detection" might have a slightly different naming convention in the dataset. Use the term from the dataset.
Programming Note: Include all relevant assessments.

Example: SAFE_T9
Protocol: 204851 Confidential
Population: Safety

Table 3.x
Summary of Subjects with Pulmonary Findings

Subjects with at least one event of	Placebo N=xx n (%)	GSK3196165 180mg N=xx n (%)
15% relative decrease from Baseline in D_{LCO}	xx (xx)	xx (xx)
15% relative decrease from Baseline in D_{LCO} to <70%	xx (xx)	xx (xx)
Cough	xx (xx)	xx (xx)
Abnormal Lung Auscultation	xx (xx)	xx (xx)

Note: Subjects with at least one event of 15% relative decrease from baseline in DLCO includes any subject with at least one decrease >15%. Cough includes subjects who reported cough of any grade. Abnormal lung auscultation includes subjects with any abnormality reported.

Example: SAFE_T10
Protocol: 204851 Confidential
Population: Safety

Table 3.x
Summary of Pulse Oximetry

Visit Blood Oxygen	Placebo N=xx n (%)	GSK3196165 180mg N=xx n (%)
Baseline		
n	xx	xx
< 80%	xx (xx)	xx (xx)
80% to 90%	xx (xx)	xx (xx)
>=90%	xx (xx)	xx (xx)
Worst Post-Baseline Result		
n	xx	xx
< 80%	xx (xx)	xx (xx)
80% to 90%	xx (xx)	xx (xx)
>=90%	xx (xx)	xx (xx)

Note: Post-baseline percentages calculated based on the number of subjects in the relevant subgroup (n/M*100%).

Example: SAFE_T11
Protocol: 204851 Confidential
Population: Safety

Table 3.x
Summary of Change from Baseline in D_{LCO}

		Observed Results						Change from Baseline Results						
Treatment Group	Visit	n	Mean	SD	Median	Min	Max	n	BL Mean	Mean	SD	Median	Min	Max
Placebo (N=XX)	Baseline	xx	x.xx	x.xxx	x.xx	x.x	x.x							
	Week 1	xx	x.xx	x.xxx	x.xx	x.x	x.x	xx	x.xx	x.xx	x.xxx	x.xx	x.x	x.x
	Week 2	xx	x.xx	x.xxx	x.xx	x.x	x.x	xx	x.xx	x.xx	x.xxx	x.xx	x.x	x.x
	Week 3	xx	x.xx	x.xxx	x.xx	x.x	x.x	xx	x.xx	x.xx	x.xxx	x.xx	x.x	x.x
	Week 4	xx	x.xx	x.xxx	x.xx	x.x	x.x	xx	x.xx	x.xx	x.xxx	x.xx	x.x	x.x
	...													
GSK3196165 180mg (N=XX)	Baseline	xx	x.xx	x.xxx	x.xx	x.x	x.x							
	...	xx	x.xx	x.xxx	x.xx	x.x	x.x	xx		x.xx	x.xxx	x.xx	x.x	x.x

Note: Baseline is defined as the lowest value during the screening period prior to the first study drug administration.
Note: BL Mean for Week X is the mean of the Baseline values of all subjects with a non-missing value at Week X.

Programming note: First footnote only applies to DLCO outputs.

Example: SAFE_T12
Protocol: 204851 Confidential
Population: Safety

Table 3.x
Summary of Proportion of Subjects with a 15% Relative Decrease from Baseline in D_{LCO}

Visit Decrease	Placebo N=xx n (%)	GSK3196165 180mg N=xx n (%)
Week 12		
n	xx	xx
≥15%	xx (xx)	xx (xx)
<15%	xx (xx)	xx (xx)
Missing	xx (xx)	xx (xx)

Note: Percentages calculated based on the number of subjects attending the respective visit.
Notes to Programming Team:
- Compare Baseline value with value from Visit X. Count all subjects with a decrease of at least 15%.

Example: SAFE_T13
Protocol: 204851 Confidential
Population: Safety

Table 3.x
Summary of Cough Data

Visit	Category	Placebo N=xx n(%)	GSK3196165 180mg N=xx n(%)
Baseline	n	xx	xx
	Had a Cough	xx (xx)	xx (xx)
	New	xx (xx)	xx (xx)
	Stable	xx (xx)	xx (xx)
	Worsening	xx (xx)	xx (xx)
	No Cough	xx (xx)	xx (xx)
	Missing	xx (xx)	xx (xx)
Week <1, …, X>	n	xx	xx
	Had a Cough Since last Visit	xx (xx)	xx (xx)
	New	xx (xx)	xx (xx)
	Stable	xx (xx)	xx (xx)
	Worsening	xx (xx)	xx (xx)
	No Cough	xx (xx)	xx (xx)
	Missing	xx (xx)	xx (xx)

Note: Percentages calculated based on the number of subjects attending the respective visit.

Example: SAFE_T14
Protocol: 204851 Confidential
Population: Safety

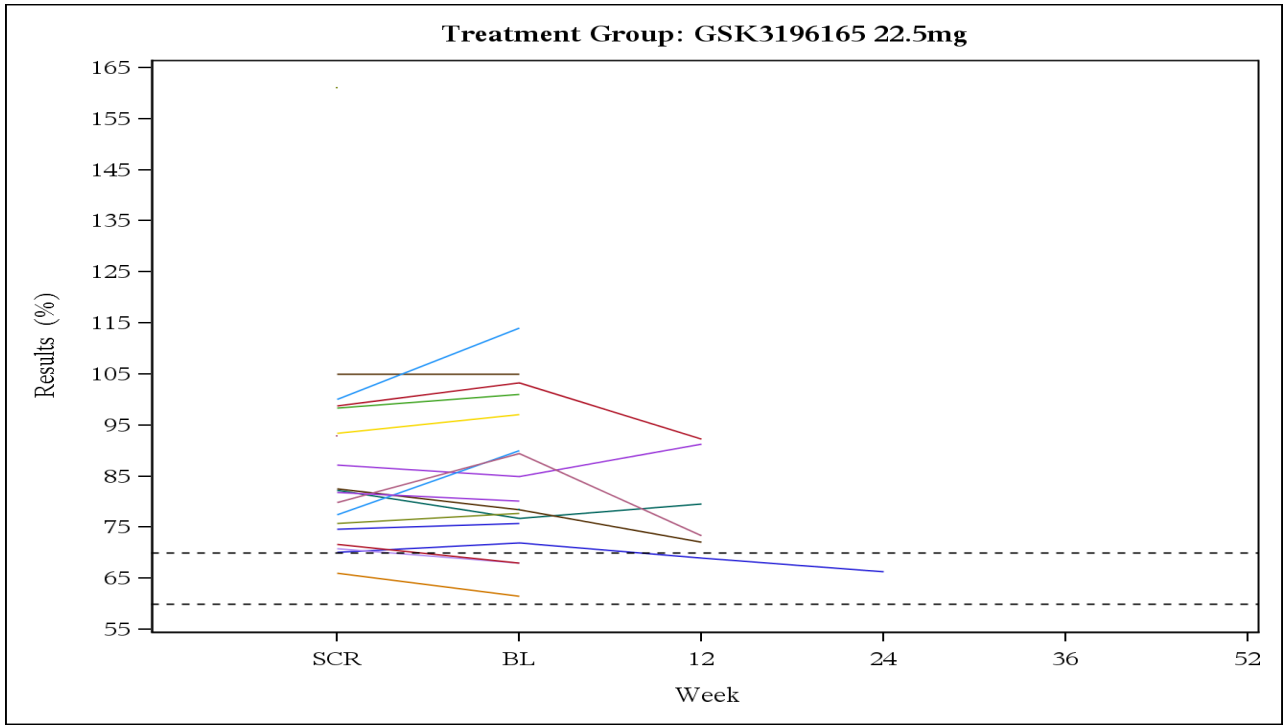
Table 3.x
Summary of Borg Dyspnea Questionnaire Data

Visit	Result	Placebo N=xx n (%)	GSK3196165 180mg N=xx n (%)
Baseline	n	xx	xx
	0 Nothing at all	xx (xx)	xx (xx)
	0.3	xx (xx)	xx (xx)
	0.5 Extremely weak (Just noticeable)	xx (xx)	xx (xx)
	0.7	xx (xx)	xx (xx)
	1 Very weak	xx (xx)	xx (xx)
	1.5	xx (xx)	xx (xx)
	2 Weak (Light)	xx (xx)	xx (xx)
	2.5	xx (xx)	xx (xx)
	3 Moderate	xx (xx)	xx (xx)
	4	xx (xx)	xx (xx)
	5 Strong (Heavy)	xx (xx)	xx (xx)
	…	xx (xx)	xx (xx)
	Missing	xx (xx)	xx (xx)
Week <1, …, X>	n	xx	xx
	0 Nothing at all	xx (xx)	xx (xx)
	0.3	xx (xx)	xx (xx)
	0.5 Extremely weak (Just noticeable)	xx (xx)	xx (xx)
	…		

Note: Percentages calculated based on the number of subjects with a valid assessment at the respective visit.

Example: SAFE_F1
Protocol: 204851 Confidential
Population: Safety

Figure 3.x
D_{LCO} Patient Profiles over Time by Treatment



Example: PD_T1a
Protocol: 204851 Confidential
Population: Safety

Table 5.x
Summary of Observed Result and Change from Baseline in Target Engagement Biomarkers
##For Not Log Transformed Biomarkers##

Biomarker (Unit): <Name of Biomarker>

		Observed Results				Change from Baseline Results				
Treatment Group	Visit	n	Mean (95% CI)	SD	Median (Min,Max)	n	BL Mean	Mean (95% CI)	SD	Median (Min,Max)
Placebo (N=XX)	Baseline	xx	x.xx (x.xx,x.xx)	x.xxx	x.xx (x.x, x.x)					
	Week 1	xx	x.xx (x.xx,x.xx)	x.xxx	x.xx (x.xx, x.xx)	xx	x.xx	x.x (x.x,x.x)	x.xx	x.x (x.x, x.x)
	Week 2	xx	x.xx (x.xx,x.xx)	x.xxx	x.xx (x.xx, x.xx)	xx	x.xx	x.x (x.x,x.x)	x.xx	x.x (x.x, x.x)
	Week 4	xx	x.xx (x.xx,x.xx)	x.xxx	x.xx (x.xx, x.xx)	xx	x.xx	x.x (x.x,x.x)	x.xx	x.x (x.x, x.x)
	…	…	…	…	…	…	…	…	…	…
GSK3196165 180mg (N=XX)	Baseline	xx	x.xxx (x.xx,x.xx)	x.xxx	x.xx (x.xx, x.xx)					
	Week 1	xx	x.xxx (x.xx,x.xx)	x.xxx	x.xx (x.xx, x.xx)	xx	x.xx	x.x (x.x,x.x)	x.xx	x.x (x.x, x.x)
	…	…	…	…	…	…	…	…	…	…

Note: The baseline value is the latest pre-dose assessment.
Note: BL Mean for Week X is the mean of the Baseline values of all subjects with a non-missing value at Week X.
Note: Values below LLQ are imputed to 0.5*LLQ

Programming Note: The number of displayed decimal digits in the table can be different for each Biomarker.

Example: PD_T1b
Protocol: 204851 Confidential
Population: Safety

Table 5.x
Summary of Observed Result and Change from Baseline in Target Engagement Biomarkers
for log transformed biomarkers

Biomarker (Unit): <Name of Biomarker>

		Observed Results				Ratio to Baseline Results				
Treatment Group	Visit	n	Geometric Mean (95% CI)	CV_b (%)	Median (Min,Max)	n	BL Geometric Mean	Geometric Mean Ratio (95% CI)	CV_b (%)	Median (Min,Max)
Placebo (N=XX)	Baseline	xx	x.xx (x.xx,x.xx)	x.xxx	x.xx (x.x, x.x)					
	Week 1	xx	x.xx (x.xx,x.xx)	x.xxx	x.xx (x.xx, x.xx)	xx	x.xx	x.x (x.x,x.x)	x.xx	x.x (x.x, x.x)
	Week 2	xx	x.xx (x.xx,x.xx)	x.xxx	x.xx (x.xx, x.xx)	xx	x.xx	x.x (x.x,x.x)	x.xx	x.x (x.x, x.x)
	Week 4	xx	x.xx (x.xx,x.xx)	x.xxx	x.xx (x.xx, x.xx)	xx	x.xx	x.x (x.x,x.x)	x.xx	x.x (x.x, x.x)
	…	…	…	…	…	…	…	…	…	…
GSK3196165 180mg (N=XX)	Baseline	xx	x.xxx (x.xx,x.xx)	x.xxx	x.xx (x.xx, x.xx)					
	Week 1	xx	x.xxx (x.xx,x.xx)	x.xxx	x.xx (x.xx, x.xx)	xx	x.xx	x.x (x.x,x.x)	x.xx	x.x (x.x, x.x)
	…	…	…	…	…	…	…	…	…	…

Note: CV_b = geometric coefficient of variation.
Note: The baseline value is the latest pre-dose assessment. BL Geometric Mean for Week X is the geometric mean of the Baseline values of all subjects with a non-missing value at Week X.
Note: Values below LLQ are imputed to 0.5*LLQ

Programming Note: The number of displayed decimal digits in the table can be different for each Biomarker.

Example: PD_T2a
Protocol: 204851 Confidential
Population: Safety

Table 5.x
Mixed Model Repeated Measures Analysis (MMRM) of Change from Baseline in Target Engagement Biomarkers
for not-log transformed biomarkers

Biomarker (Unit): <Biomarker>

Visit	Statistic	Placebo N=xx	GSK3196165 180mg N=xx
Week 1	n	xx	xx
	LS Mean	x.xx	x.xx
	LS Mean Change	x.xx	x.xx
	Standard Error	x.xxx	x.xxx
	Difference from Placebo		x.xx
	95% Confidence Interval		x.xx - x.xx
	p-value		0.xxx
Week 2	n		
	LS Mean	x.xx	x.xx
	LS Mean Change	x.xx	x.xx
	Standard Error	x.xxx	x.xxx
	Difference from Placebo		x.xx
	95% CI for Difference		x.xx - x.xx

…

Note: Repeated measures analysis adjusted for <Biomarker> baseline value, treatment group, visit, treatment group by visit and baseline by visit interactions.
Note: n is the number of subjects with non-missing data at that visit.

Example: PD_T2b
Protocol: 204851 Confidential

Table 5.x
Mixed Model Repeated Measures Analysis (MMRM) of Change from Baseline in Target Engagement Biomarkers
for log transformed biomarkers

Biomarker (Unit): <Biomarker>

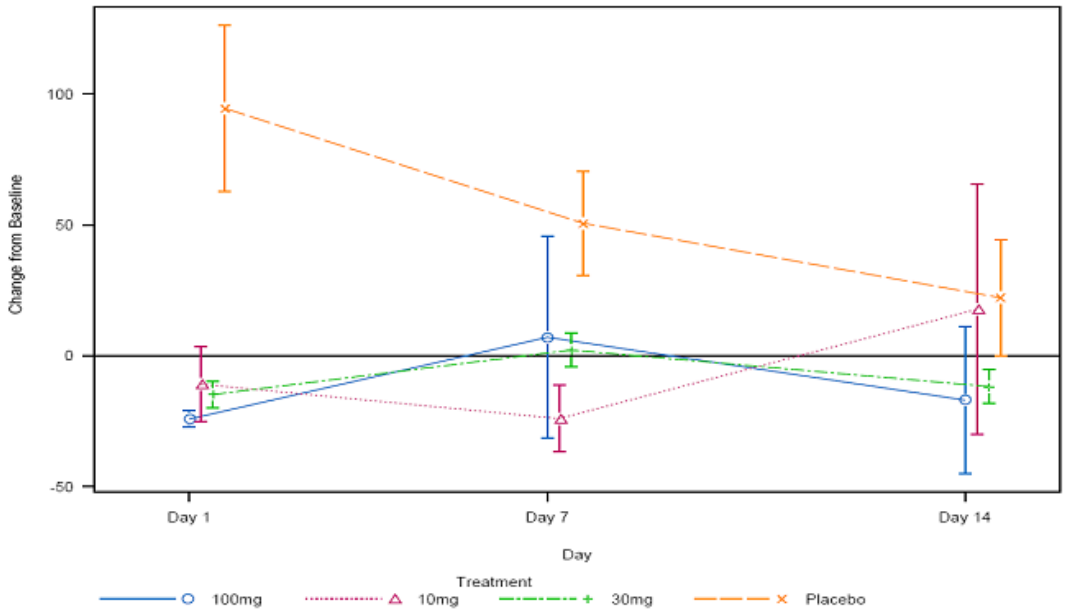
Visit	Statistic	Placebo N=xx	GSK3196165 180mg N=xx
Week 1	n	xx	xx
	LS Geometric Mean	x.xx	x.xx
	LS Geometric Mean Ratio to Baseline	x.xx	x.xx
	Standard Error	x.xxx	x.xxx
	Ratio to Placebo		x.xx
	95% Confidence Interval		x.xx - x.xx
	p-value		0.xxx
Week 2	n		
	LS Geometric Mean	x.xx	x.xx
	LS Geometric Mean Ratio	x.xx	x.xx
	Standard Error	x.xxx	x.xxx
	Ratio to Placebo		x.xx
	95% Confidence Interval		x.xx - x.xx
	p-value		0.xxx
…			

Note: Repeated measures analysis adjusted for <Biomarker> baseline value, treatment group, visit, treatment group by visit and baseline by visit interactions.
Note: n is the number of subjects with non-missing data at that visit.

Example: PD_F1
Protocol: 204851 Confidential
Population: Intent-to-Treat

Figure 5.x
Plot of Mean/Geometric Mean and 95% CI of Change from Baseline in Target Engagement Biomarkers, at Each Visit

Biomarker(Unit): <Biomarker>

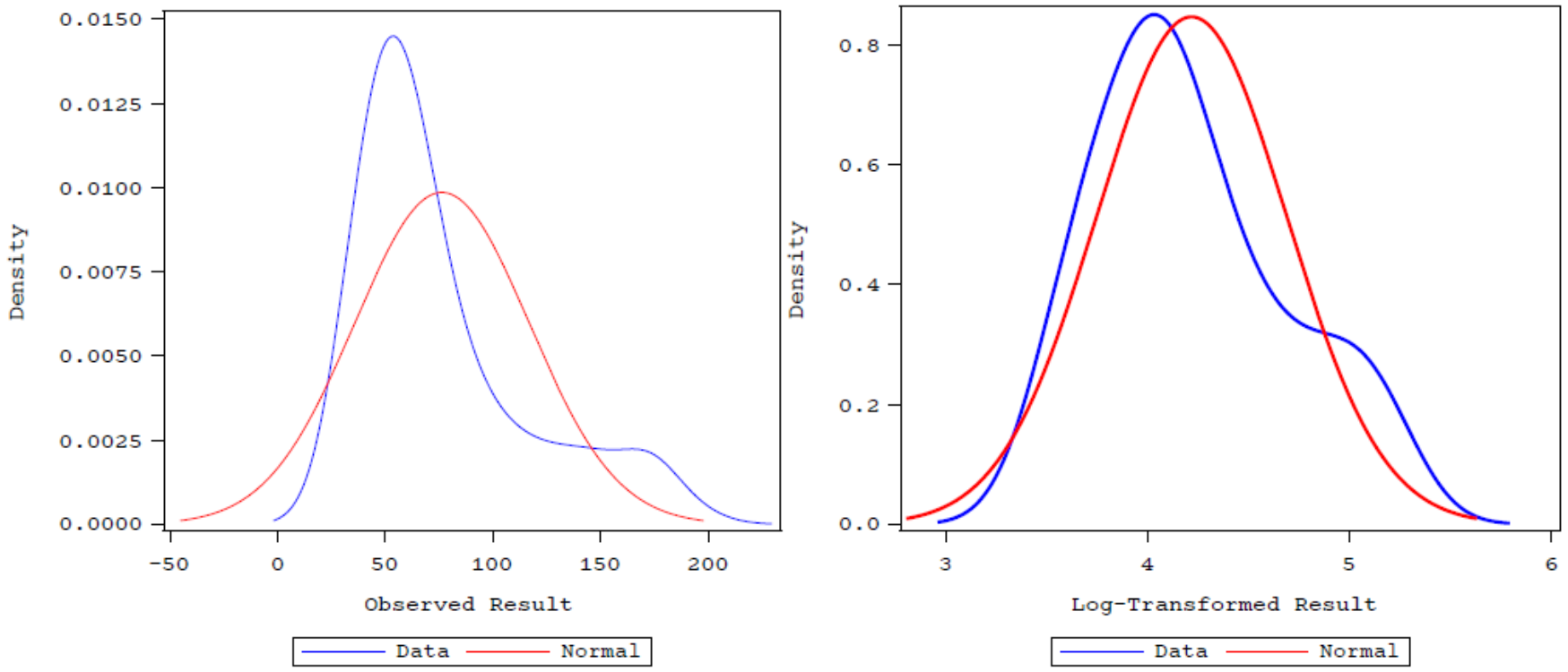


Note: Values below LLQ are imputed to 0.5*LLQ.
Note: The baseline value is the latest pre-dose assessment.
<Note: Repeated measures analysis adjusted for <Biomarker> baseline value, treatment group, visit and treatment group by visit and baseline by visit interactions.>
Programming Note: Legend to be centered.
Programming Note: Y-axis label is "Change from Baseline in <Biomarker>" or "Ratio to Baseline in <Biomarker>" if log-transformation is required

Example: PD_F2
Protocol: 204851 Confidential
Population: Intent-to-Treat

Figure 5.x
Plot of Distribution of <Biomarkers>

Biomarker(Unit): <Biomarker>
Treatment: <Overall/Placebo/GSK3196165 180mg>



Note: Values below LLQ are imputed to 0.5*LLQ.
Note: The baseline value is the latest pre-dose assessment.

Example: POP_L1
Protocol: 204851 Confidential
Population: Intent-to-Treat

Listing x
Listing of OA Disease History

Treatment Group: <Placebo, GSK3196165 180mg>

Site ID/ Subject ID	Date of OA Diagnosis	Time since OA Diagnosis (months) [a]	Start Date of OA Symptoms	Time since Start of OA Symptoms (months) [a]
XX/XXXXX	DD-MMM-YYYY	XX.X	DD-MMM-YYYY	XX.X
XX/XXXXX				
XX/XXXXX				

[a] Up to date of first study medication administration.

Example: POP_L2
Protocol: 204851 Confidential
Population: Intent-to-Treat

Listing x
Subjects with Persistent Cough, Dyspnea or D_{LCO} Decrease

Site ID/ Subject ID	Gender/Age(years)/Race/Weight(kg):	Treatment at Event Onset	Type of Event	Start of Event (Relative Day)
XXXX/XXXXXX	F/XX/XXXX/XX	Placebo	DLCO Cough	DD-MMM-YYYY (XX)

Programming Note: Just show subjects who experienced at least one of the events during the study.

Example: POP_L3
Protocol: 204851 Confidential
Population: Intent-to-Treat

Listing x
Listing of Pulmonary Assessments

Treatment Group: <Placebo, GSK3196165 180mg>
Site ID/ Subject ID: XXXX/XXXXXX Gender/Age(years)/Race/Weight(kg): F/XX/XXXX/XX

Visit	Date of Assessment DD-MMM-YYYY (Relative Day)	Chest X-Ray	Blood Oxygen (%)	Cough/ Grade	Borg Dyspnea Result	Chest Auscultation abnormal/ Classification of Chest Auscultation abnormal
Screening	DD-MMM-YYYY (XX)	<normal, Abnormal - Not Clinically Significant, Abnormal - Clinically Significant >	xx	Yes/ x	XXXX	Yes/ Stable
Baseline	DD-MMM-YYYY (XX)		xx	No	XXXX	No
Week 1						
Etc.						

Example: POP_L4
Protocol: 204851 Confidential
Population: Intent-to-Treat

Listing x
Listing of Pulmonary Function Tests

Treatment Group: <Placebo, GSK3196165 180 mg>
Site ID/ Subject ID: XXXX/XXXXXX Gender/Age(years)/Race/Weight(kg): F/XX/XXXX/XX

Visit	Date of Assessment DD-MMM-YYYY (Relative Day)	Spirometry FEV1 (L)	Spirometry FVC (L)	Reason of Missed Spirometry	Gas Transfer (D_{LCO}) (%)	Reason of Missed D_{LCO}	D_{LCO} Lower than 85% of Baseline Value
Screening	DD-MMM-YYYY (XX)	xx.x	xx.x	XXXXXXXX	xx.x	XXXXXXXX	Yes
Baseline	DD-MMM-YYYY (XX)	xx.x	xx.x	XXXXXXXX	xx.x	XXXXXXXX	No
Week 1							
Etc.							

Note: Baseline is the visit recording the lowest DLCO value obtained from the Screening or Day 1 assessment, or any unscheduled visit in between.

Example: EFF_L1
Protocol: 204851 Confidential
Population: Intent-to-Treat

Listing x
Listing of Individual Subject Hand Pain NRS Averaged over 7 Days Prior to Each Visit

Treatment Group: <Placebo, GSK3196165 180mg>

		24h Average Hand Pain NRS Averaged over 7 Days Prior to Visit			24h Worst Hand Pain NRS Averaged over 7 Days Prior to Visit		
Site ID/ Subject ID	Visit	Observed/CfB	30% Reduction from Baseline	50% Reduction from Baseline	Observed/ CfB	30% Reduction from Baseline	50% Reduction from Baseline
XXXX/ XXXXX	Baseline	x.xx			x.xx		
	Week X	x.xx/ -x.xx	Yes	No	x.xx/ x.xx	No	No
	Etc.	Etc.			Etc.		
XXXX/ XXXXX	Baseline	x.xx			x.xx		
	Week X	x.xx/ x.xx	No	No	x.xx/ -x.xx	Yes	Yes
	Etc.	Etc.			Etc.		

Note: CfB= Change from Baseline.
Notes to Programming Team:
- This listing will be sorted by Site ID, Subject ID, Visit Date

Example: EFF_L2
Protocol: 204851 Confidential
Population: Intent-to-Treat

Listing x
Statistical Listing of […]

Display all SAS Output from Analysis

Example: EFF_L3
Protocol: 204851 Confidential
Population: Intent-to-Treat

Listing x
Listing of Individual Subject AUSCAN 3.1 NRS Individual Component Scores

Treatment Group: <Placebo, GSK3196165 180mg>

Site ID/ Subject ID	Visit	Pain Subscale Score	Physical Function Subscale Score	Stiffness Subscale Score	Total Score
XXXX/ XXXX	Baseline	Xx	Xx	Xx	Xxx
	Week X	Xx	Xx	Xx	Xxx
	Etc.	…	…	…	…
XXXX/ XXXX	Baseline	Xx	Xx	Xx	Xxx
	Week X	Xx	Xx	Xx	Xxx
	Etc.	…	…	…	…

Notes to Programming Team:
- This listing will be sorted by Site ID, Subject ID, Visit Date

Example: EFF_L4
Protocol: 204851 Confidential
Population: Intent-to-Treat

Listing x
Listing of Individual Subject Number of Tender or Swollen Hand Joints, by Visit

Treatment Group: <Placebo, GSK3196165 180mg>
Site ID/Subject ID: XXXXX/ XXXXXXX

Visit		Right Hand Joints	Left Hand Joints	Total Number of Joints
Baseline	Tender	PIP 2, PIP3, PIP4, MCP1	PIP2, PIP3	6
	Swollen	PIP2, PIP4		2
Week 1	Tender	PIP 2, PIP3, PIP4, MCP1	PIP2, PIP3	6
	Swollen	PIP2, PIP4		2

Notes to Programming Team:

- This listing will be sorted by Site ID, Subject ID, Visit Date

Example: EFF_L5
Protocol: 204851 Confidential
Population: Intent-to-Treat

Listing x
Listing of Individual Subject Pain/Tenderness Hand Joint Assessment, by Visit

Treatment Group: <Placebo, GSK3196165 180mg>
Site ID/Subject ID: XXXXX/ XXXXXXX

Visit	Pain/Tenderness Severity	Right Hand Joints	Left Hand Joints	Total Number of Joints
Baseline	Mild	PIP 2, PIP3, PIP4, MCP1	PIP2, PIP3	6
	Moderate	PIP2, PIP4		2
	Severe	PIP5		1
Week 1	Mild	PIP 2, PIP3, PIP4, MCP1	PIP2, PIP3	6
	Moderate	PIP2, PIP4		2
	Severe	PIP5		1

Notes to Programming Team:

- This listing will be sorted by Site ID, Subject ID, Visit

Example: EFF_L6
Protocol: 204851 Confidential
Population: Intent-to-Treat

Listing x
Listing of Individual Subject Inflammatory Structural Joint Damage: HOAMRIS

Treatment Group: <Placebo, GSK3196165 180mg>

Site ID/ Subject ID	Visit	Number of Available Joints	Synovitis	Erosive Damage	Cyst	Osteophyte	Cartilage Space Loss	Mal-alignment	Bone Marrow Lesions
XXXX/ XXXXX	Baseline	Xx	Xxx	Xxx	Xxx	Xxx	Xxx	Xxx	Xxx
	Week X	Xx	Xxx	Xxx	Xxx	Xxx	Xxx	Xxx	Xxx
	…	…	…	…	…	…	…	…	…
XXXX/ XXXXX	Baseline	Xx	Xxx	Xxx	Xxx	Xxx	Xxx	Xxx	Xxx
	Week X	Xx	Xxx	Xxx	Xxx	Xxx	Xxx	Xxx	Xxx
	…	…	…	…	…	…	…	…	…

Notes to Programming Team:
- This listing will be sorted by Site ID, Subject ID, Visit

Example: PK_L1
Protocol: 204851 Confidential
Population: Intent-to-Treat

Listing x
Listing of Individual Subject Pharmacokinetic Data

Treatment Group: <Placebo, GSK3196165 180mg>
Site ID/ Subject ID: XXXX/XXXXXX Gender/Age(years)/Race/Weight(kg): F/XX/XXXX/XX

Visit	Date and Time Sample Taken (Relative Day)	Dose Volume administered (mL)	PLASMA GSK3196165 ng/mL	Reason Test not Done
Screening	DDMMMYYY/ HH:MM (XX)	x.x	xxx	
Baseline	DDMMMYYY/ HH:MM (XX)	x.x		XXXXX
Week X		x.x	xxx	

Example: PD_L1
Protocol: 204851 Confidential
Population: Intent-to-Treat

Listing x
Listing of Individual Subject <Target Engagement/Predictive/…> Biomarkers

Treatment Group: <Placebo, GSK3196165 180mg >
Site ID/ Subject ID: XXXX/XXXXXX Gender/Age(years)/Race/Weight(kg): F/XX/XXXX/XX

Biomarker (Unit)	Visit	Date and Time Sample Taken (Relative Day)	Result	Change from Baseline	Ratio from Baseline (%)
XXXXX (XX)	Screening	DD-MMM-YYYY / HH:MM (xx)	xx.x	xx.x	xx.x
	Baseline	DD-MMM-YYYY / HH:MM (xx)	xx.x	xx.x	xx.x
	Week X				
	Etc.				
XXXXX (XX)	Baseline	DD-MMM-YYYY / HH:MM (xx)	xx.x	xx.x	xx.x
	Week X				
	Etc.				

Note: Values below LLQ are imputed to 0.5*LLQ.