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

Title	:	Reporting and Analysis Plan for a randomised, multi-center, double blind (sponsor open), placebo-controlled study to assess the efficacy, safety, tolerability, pharmacokinetics and pharmacodynamics of GSK3117391 in subjects with severe, active rheumatoid arthritis
Compound Number	:	GSK3117391
Effective Date	:	12-JAN-2018

Description :

- The purpose of this RAP is to describe the planned analyses and output to be included in the Clinical Study Report for Protocol 204957.
- A final approved version of the full RAP for each interim reporting and final effort including the list of data displays will be made available prior to the respective Database Release (DBR).
- This study has been terminated early due to business prioritisation.

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1. REPORTING & ANALYSIS PLAN SYNOPSIS

Overview	Key Elements of the RAP
Purpose	• The purpose of this RAP is to describe the planned analyses and output to be included in the Clinical Study Report for Protocol 204957. • This study has been terminated early due to business prioritisation.
Protocol	• This RAP is based on the version 3 of the protocol (Dated: 01/Jun/2017) of study 204957 (GSK Document No. : 2016N270377_03)
Primary Objective	• To assess the efficacy of GSK3117391 in subjects with severe RA following every other day dosing
Primary Endpoint	• Change from baseline in DAS 28-CRP at Day 28
Secondary Objectives	• To assess the safety and tolerability of GSK3117391 following every other day dosing. • To assess the efficacy of GSK3117391 on other clinical endpoints following every other day dosing. • To assess the pharmacokinetics following every other day dosing of GSK3117391. • To investigate the monocyte numbers after every other day dosing with GSK3117391. • To assess the effects of GSK3117391 on biomarkers of inflammation in the blood.
Secondary Endpoints	• Adverse events, Vital signs (HR, BP & Temperature), ECGs, Clinical laboratory tests (haematology, biochemistry and urinalysis). • ACR responders (ACR20, ACR50, ACR70) • Number of swollen joints assessed using 28-joint counts • Number of tender/painful joints assessed using 28-joint counts • Change from baseline in DAS28-CRP over time • Plasma concentrations and derived pharmacokinetics (PK) parameters of GSK3117391 and GSK3339189. • Changes in monocyte numbers over time • Changes from baseline in blood biomarkers, including but not limited to: C-reactive protein (CRP), soluble cytokine and inflammatory mediators and Myeloid-related protein 8/14 (MRP8/14).
Exploratory Objectives	• To assess the intracellular pharmacokinetics following every other day dosing of GSK3117391. • To evaluate the PD of GSK3117391 following every other day dosing. • To explore the effects of GSK3117391 on the leukocyte population. • To investigate the effect of GSK3117391 on inflammatory gene expression in blood.
Exploratory Endpoints	• Where possible, intracellular concentrations and derived PK parameters of GSK3339189 following every other day repeat doses. • Acetylation levels in monocytes, lymphocytes and granulocytes in peripheral blood.

Overview	Key Elements of the RAP
	• Cell marker quantification using flow cytometry. • Change from baseline in inflammatory gene expression in blood.
Study Design	• This is a randomised, double-blind (sponsor open), multicentre, placebo-controlled, parallel group study to evaluate the efficacy, safety and tolerability, PK and PD of GSK3117391 in subjects with RA resistant to DMARD therapy. • Approximately 40 subjects with severe RA despite treatment with DMARDs will be randomised into the study. • The total maximum study duration is approximately 10 weeks (not including any rescreen). Following a screening period of up to 28 days, subjects will be randomised (1:1) to placebo or 40 mg GSK3117391 orally-administered every other day for a period of 28 days. Subjects will be followed up for 7-14 days post final dose. • Study schematic is included below. • Due to early termination of the study, the study had 3 randomised patients, with 2 completing the study.
Termination	• This study has been terminated early due to business prioritisation. • There were 3 randomised subjects. • A synoptic CSR will be generated with disclosure of safety and key primary/secondary endpoints. The final outputs will include listings of all safety/tolerability endpoints, the primary endpoint and the key secondary endpoint.
Analysis Populations	• All Screened: The "All Screened" population is defined as all subjects who screened. • Enrolled Population: The "Enrolled Population" is defined as subjects (who ultimately passed screening, even if rescreened). Randomised Subjects and Subjects where no treatment was assigned (e.g. never randomised) even though they passed screening. • Safety Population: The 'Safety Population' is defined as subjects who receive at least one dose of study medication
Hypothesis	• No hypothesis is to be tested because of early termination of the study.
Primary Analyses	• Due to early termination of the study and with 2 completers, listings of the raw and change from baseline DAS28 score over time will be produced for each subject.
Secondary Analyses	• The safety and tolerability data will be listed. • Componenetsof the DAS28 score – Tender Joint count using 28-joint counts and swollen joint counts using 28-joint counts, CRP and patient's global assessment of disease activitywill be listed. • Absolute and change from baseline monocyte numbers and MRP8/14 levels will be listed and ploted over time.

Overview	Key Elements of the RAP
	• PK ouptuts will not be generated as the sample were not assayed. • ACR20, 50 and 70 response will not be calulcated due to the small sample size.
Exploratory Analyses	• No exploratory analysis will be conducted.

2. SUMMARY OF KEY PROTOCOL INFORMATION

2.1. Changes to the Protocol Defined Statistical Analysis Plan

Due to the termination of the study, only listings will be produced for the safety events and the DAS28 score. This differs to the planned analyses outlined in the protocol.

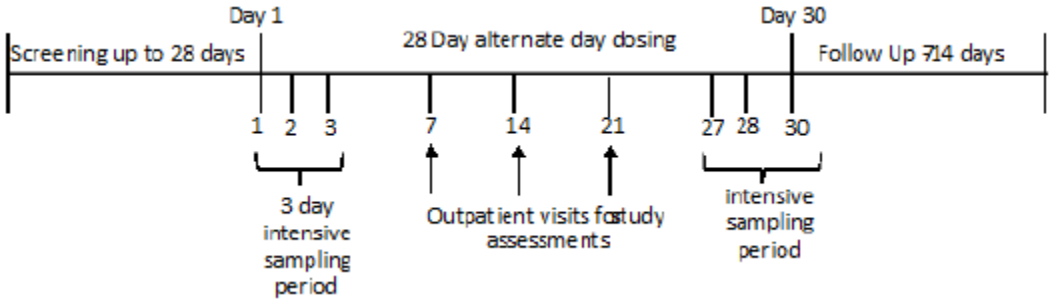
2.2. Study Objective(s) and Endpoint(s)

Objectives	Endpoints
Primary Objectives	**Primary Endpoints**
• To assess the efficacy of GSK3117391 in subjects with severe RA following every other day dosing	• Change from baseline in DAS 28-CRP at Day 28.
Secondary Objectives	**Secondary Endpoints**
• To assess the safety and tolerability of GSK3117391 following every other day dosing	• Adverse events • Vital signs (HR, BP & Temperature) • ECGs • Clinical laboratory tests (haematology, biochemistry and urinalysis)
• To assess the efficacy of GSK3117391 on other clinical endpoints following every other day dosing	• ACR responders (ACR20, ACR50, ACR70) • Number of swollen joints assessed using 28-joint counts • Number of tender/painful joints assessed using 28-joint counts • Change from baseline in DAS28-CRP over time • Components of composite endpoints (ACR response, DAS28-CRP) at all assessment timepoints will also be reported separately
• To assess the pharmacokinetics following every other day dosing of GSK3117391	• Plasma concentrations and derived pharmacokinetics (PK) parameters of GSK3117391 and GSK3339189
• To investigate the monocyte numbers after every other day dosing with GSK3117391	• Changes in monocyte numbers over time

• To assess the effects of GSK3117391 on biomarkers of inflammation in the blood	• Changes from baseline in blood biomarkers, including but not limited to:
	  • C-reactive protein (CRP),
	  • Soluble cytokine and inflammatory mediators

Objectives	Endpoints
	• Myeloid-related protein 8/14 (MRP8/14)
Exploratory Objectives	**Exploratory Endpoints**
• To assess the intracellular pharmacokinetics following every other day dosing of GSK3117391	• Where possible, intracellular concentrations and derived PK parameters of GSK3339189 following every other day repeat doses
• To evaluate the PD of GSK3117391 following every other day dosing	• Acetylation levels in monocytes, lymphocytes and granulocytes in peripheral blood
• To explore the effects of GSK3117391 on the leukocyte population	• Cell marker quantification using flow cytometry
• To investigate the effect of GSK3117391 on inflammatory gene expression in blood	• Change from baseline in inflammatory gene expression in blood

2.3. Study Design

Overview of Study Design and Key Features	
	
Design Features	This is a randomised, double-blind (sponsor open), multicentre, placebo-controlled, parallel group study to evaluate the efficacy, safety and tolerability, PK and PD of GSK3117391 in subjects with severe RA resistant to DMARD therapy. 40 subjects will be randomised to either GSK3117391 or placebo to be taken every other day for 28 days of treatment. The maximum total duration of the study is approximately 10 weeks from screening to the last study visit
Dosing	Subjects in this study will be treated with 40 mg of GSK3117391 every other day for a 28-day period.
Interim Analysis	No formal interim analysis will be conducted due to the termination of the study. An administrative interim analysis was conducted for internal decision making, based on unblinded DAS28 (absolute and change from baseline) and its components in November 2017.

2.4. Statistical Hypotheses

As a result of the termination, no statistical hypothesis will be tested.

3. PLANNED ANALYSES

3.1. Instream Analyses

In line with routine pharmacovigilance, an internal GSK Safety Review Team (SRT) which will include members of the 204957 study team, will review blinded safety data, including clinical laboratory parameters and adverse events, at appropriate intervals during the period of study conduct. Further details are outlined in the SRT charter.

3.2. Interim Analyses

No formal interim analysis will be conducted as the study has been terminated after 3 randomised patients.

An administrative interim was conducted based on listing of the unblinded DAS28 score and its components.

3.3. Final Analyses

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

1. All required database cleaning activities have been completed
2. Final database release and database freeze has been declared by Data Management.
3. Unblinding of the randomisation codes and distribution according to RandAll NG procedures prior to performing the final planned analysis.

4. ANALYSIS POPULATIONS

Population	Definition / Criteria	Analyses Evaluated
All Screened	This population is defined as all subjects who were screened.	• Screen Failure
Enrolled	The following subjects (who ultimately passed screening, even if rescreened) are included in the Enrolled population: Randomised Subjects and Subjects where no treatment was assigned (e.g. never randomised) even though they passed screening	• Study Population (sub-set, see TOC in Appendix 15)
Safety Population	Subjects who receive at least one dose of study medication.	• Safety • Study Population (main outputs) • Efficacy • Disease and PD Biomarkers

NOTES :

- Please refer to Section 11.15: List of Data Displays which details the population to be used for each displays being generated.

4.1. Protocol Deviations

- Important protocol deviations (including deviations related to study inclusion/exclusion criteria, conduct of the trial, patient management or patient assessment) will be summarised and listed.
- Important deviations which result in exclusion from the analysis population will also be summarised and listed. (Please refer to Section 11.1: Protocol Deviation Management and Definitions for Per Protocol Population).

- 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 DBR 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 listing of all inclusion/exclusion criteria deviations will also be provided. This summary will be based on data as recorded on the inclusion/exclusion page of the eCRF.

5. CONSIDERATIONS FOR DATA ANALYSES AND DATA HANDLING CONVENTIONS

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

Table 1 Overview of Appendices

Section	Component
11.1	Appendix 1: Protocol Deviation Management and Definitions for Per Protocol Population
11.2	Appendix 2: Time & Events
11.3	Appendix 3: Assessment Windows
11.4	Appendix 4: Treatment States and Phases
11.5	Appendix 5: Data Display Standards & Handling Conventions
11.6	Appendix 6: Derived and Transformed Data
11.7	Appendix 7: Premature Withdrawals & Handling of Missing Data
11.8	Appendix 8: Values of Potential Clinical Importance
11.9	Appendix 9: Multicenter Studies
11.10	Appendix 10: Examination of Covariates, Subgroups & Other Strata
11.11	Appendix 11: Multiple Comparisons & Multiplicity
11.12	Appendix 12: Model Checking and Diagnostics for Statistical Analyses.
11.13	Appendix 13: Pharmacokinetic/Pharmacodynamic (Or Biomarker) Analysis

6. STUDY POPULATION ANALYSES

6.1. Overview of Planned Analyses

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

Table 2 provides an overview of the planned study population analyses, with full details of data displays being presented in Appendix 15: List of Data Displays

Table 2 Overview of Planned Study Population Analyses

Endpoint / Parameter / Display Type	Data Displays Generated
	Listing
Randomisation	
Randomisation	Y
Subject Disposition	
Reasons for Subject Withdrawal	Y
Reasons for Screen Failure	Y
Subjects for Whom the Treatment Blind was Broken	Y
Planned and Actual Treatments	Y
Protocol Deviations	
Important Protocol Deviations	Y
Subjects with Inclusion/Exclusion Criteria Deviations	Y
Populations Analysed	
Subjects Excluded from Any Population	Y
Demographic and Baseline Characteristics	
Demographic Characteristics	Y
Race and Racial Combinations	Y [1]
Prior and Concomitant Medications	
Concomitant Medications	Y
Exposure and Treatment Compliance	
Exposure to Study Treatment	Y

NOTES :

- Y = Yes display generated.

1. [1] Listing of race.

7. PRIMARY STATISTICAL ANALYSES

7.1. Primary Efficacy Analyses

7.1.1. Overview of Planned Primary Efficacy Analyses

The efficacy analyses will be based on the Safety population.

Table 3 provides an overview of the planned analyses, with further details of data displays being presented in Appendix 15: List of Data Displays

Due to the early termination of study, listings and individual subjects profile plots of DAS28-CRP absolute, and change from baseline score will be produced. No summary tables or statistical analysis will be generated or conducted.

Table 3 Overview of Planned Primary Efficacy Analyses

Endpoint	Individual	
	Figure	Listing
DAS-28 CRP		
Absolute and Change from Baseline	Y	Y

NOTES :

- Y = Yes display generated.
- Individual = Represents FL related to any displays of individual subject observed raw data.

8. SECONDARY STATISTICAL ANALYSES

8.1. Secondary Efficacy Analyses

8.1.1. Overview of Planned Secondary Efficacy Analyses

The efficacy analyses will be based on the Safety population.

Table 4 provides an overview of the planned analyses, with further details of data displays being presented in Appendix 15: List of Data Displays

Table 4 Overview of Planned Efficacy Analyses

Endpoint / Parameter/ Display Type	Absolute	
	Individual	
	Figure	Listing
Efficacy		
TJC68, SJC66, PtGA, CRP		Y

NOTES :
- Y = Yes display generated.
- Individual = Represents FL related to any displays of individual subject observed raw data.

8.2. Pharmacodynamic/Biomarker Analyses

8.2.1. Overview of Planned Pharmacodynamic/Biomarker Analyses

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

Table 5 provides an overview of the planned analyses, with further details of data displays being presented in Appendix 15: List of Data Displays

Table 5 Overview of Planned Pharmacodynamic/Biomarker Analyses

Endpoint / Parameter/ Display Type	Absolute and change from baseline	
	Individual	
	Listing	Figure
Blood Biomarkers		
MRP8/14	Y	
Monocyte count	Y	Y

NOTES :
- Y = Yes display generated.
- Individual = Represents FL related to any displays of individual subject observed raw data.

8.3. Safety Analyses

8.3.1. Overview of Planned Adverse Event Analyses

The safety 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 15: List of Data Displays.

Table 6 Overview of Planned Adverse Event Analyses

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

NOTES :

- Y = Yes display generated.
- Individual = Represents FL related to any displays of individual subject observed raw data.

8.3.2. Overview of Planned Clinical Laboratory Analyses

The safety analyses will be based on the Safety population.

Table 7 provides an overview of the planned analyses, with further details of data displays being presented Appendix 15: List of Data Displays.

Table 7 Overview of Planned Clinical Laboratory Analyses

Endpoint / Parameter/ Display Type	Absolute
	Individual
	Listing
All Laboratory	Y
All Laboratory Data for Subjects with any Value of Potential Clinical Concern/PCI	
Laboratory Values of PCI	Y

NOTES :

- Y = Yes display generated.
- Individual = Represents FL related to any displays of individual subject observed raw data.

8.3.3. Overview of Planned Other Safety Analyses

The safety analyses will be based on the Safety population.

Table 8 provides an overview of the planned analyses, with further details of data displays being presented in Appendix 15: List of Data Displays.

Table 8 Overview of Planned Other Safety Analyses

Endpoint / Parameter/ Display Type	Absolute
	Individual
	Listing
ECG	
All ECG Values for Subjects with any Value of PCI	Y
ECG Values of PCI	Y
Abnormal ECG Findings	Y
Vital Signs	
All Vital Signs for Subjects with any Value of PCI	Y

NOTES:

- Y = Yes display generated, PCI = Potential Clinical Importance
- Individual = Represents FL related to any displays of individual subject observed raw data.

8.4. Pharmacokinetic Analyses

Due to the sample analysis issues, PK samples will not be analysed and hence the data will not be available.

9. OTHER STATISTICAL ANALYSES

9.1. Exploratory Analyses

No exploratory outputs will be generated.

10. REFERENCES

GlaxoSmithKline Document Number 2016N270377_03 Study ID 204957. A randomised, multi-center, double blind (sponsor open), placebo-controlled study to assess the efficacy, safety, tolerability, pharmacokinetics and pharmacodynamics of GSK3117391 in subjects with severe, active rheumatoid arthritis. Effective Date: 01-Jul-2017

11. APPENDICES

Section	Appendix
RAP Section 4 : Analysis Populations	
Section 11.1	Appendix 1: Protocol Deviation Management and Definitions for Per Protocol Population
RAP Section 5 : General Considerations for Data Analyses & Data Handling Conventions	
Section 11.2	Appendix 2: Time and Events
Section 11.3	Appendix 3: Assessment Windows
Section 11.4	Appendix 4: Treatment States & Phases
Section 11.5	Appendix 5: Data Display Standards & Handling Conventions • Study Treatment & Sub-group Display Descriptors • Baseline Definitions & Derivations • Reporting Process & Standards
Section 11.6	Appendix 6: Derived and Transformed Data • General, Study Population & Safety • Efficacy • Pharmacokinetic • Pharmacodynamic and or Biomarkers
Section 11.7	Appendix 7: Premature Withdrawals & Handling of Missing Data • Premature Withdrawals • Handling of Missing Data
Section 11.8	Appendix 8: Values of Potential Clinical Importance
Section 11.9	Appendix 9: Multicentre Studies • Laboratory Values • ECG • Vital Signs
Section 11.10	Appendix 10: Examination of Covariates and Subgroups
Section 11.11	Appendix 11: Multiple Comparisons and Multiplicity
Section 11.12	Appendix 12: Model Checking and Diagnostics for Statistical Analyses
Section 11.13	Appendix 13: Pharmacokinetic / Pharmacodynamic (or Biomarker) Analyses
Other RAP Appendices	
Section 11.14	Appendix 14: Abbreviations & Trade Marks
Section 11.15	Appendix 15: List of Data Displays
Section 11.16	Appendix 16 Example Mock Shells for Data Displays

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

11.1.1. Exclusions from the Per Protocol Population

Not applicable

11.1.1.1. Exclusions from Per Protocol Efficacy Dataset

Not applicable.

11.2. Appendix 2: Time & Events

11.2.1. Protocol Defined Time & Events

Table 9 Screening and Follow-up Assessments

Procedure	**Screening** (up to 28 days prior to Day 1[1])	**Follow-up Visit** (7-14 days post last dose or EW[2])	***Notes***
			1. Screening period can be extended to 56 days to allow ONLY the washout of background DMARD therapy where necessary. All other assessments must be completed within 28 days prior to Day 1. Some assessment can occur on separate visit 2. For EW (Early Withdrawal) visit, assessments are to be conducted as deemed necessary based on PI's judgment and to be recorded as an unscheduled visit in the subject's CRF
Outpatient Visit	X	X	Additional screening visit needed for FRP pregnancy test 4 to 7 days before day 1
Informed Consent	X		Informed consent must be obtained prior to any study procedures being conducted including DMARD therapy washout period.
Medical/medication/drug/alcohol history	X		
Demographics	X		
Height and weight	X		
Full Physical Examination	X		Additional examinations may be performed, or brief examinations made full examinations, by the Investigator, as deemed necessary (e.g. where safety or laboratory findings indicate).
Brief Physical Examination		X	
Eligibility criteria	X		
12-lead ECG and vital signs	X	X	Vital signs include HR, BP and temp.
Pregnancy test	X	X	First test in screening is serum pregnancy test, all subsequent testing urine. An additional pregnancy test during screening visit (urine) is required 4-7 days prior to Day 1. This test may be performed at home. FRP only.
Contraception use compliance	X	X	
HIV, Hep B and Hep C screen, TB, G6PD	X		
RF, ACPA (i.e. aCCP)	X		
Haem/Chem/Urinalysis tests	X	X	Including INR/APTT (coagulation) and MetHb (MetHb, performed locally)
PK blood sample and Met ID		X	Sample to be collected only if the 24h-post last dose sample (at D28) has not been collected

Procedure	**Screening** (up to 28 days prior to Day 1[1])	**Follow-up Visit** (7-14 days post last dose or EW[2])	***Notes***
			1. Screening period can be extended to 56 days to allow ONLY the washout of background DMARD therapy where necessary. All other assessments must be completed within 28 days prior to Day 1. Some assessment can occur on separate visit 2. For EW (Early Withdrawal) visit, assessments are to be conducted as deemed necessary based on PI's judgment and to be recorded as an unscheduled visit in the subject's CRF
PD biomarker sample		X	This includes biomarkers for RA disease and exploratory PD, acetylation
HAQ-DI, PtGA, PtAAP	X	X	Complete before any other assessment at a clinic visit
Joint counts: TJC(68), SJC(66)	X	X	Independent joint assessor
Physician Global Assessment of Arthritis (PhGA)	X	X	Where possible, the same physician should perform all disease assessments for an individual subject.
hsCRP	X	X	
Chest x-ray	X		Only required at screening if no CXR performed within 12 weeks of Day 1 visit
Adverse Event Review		X	
Concomitant Medication Review		X	
Gene expression blood		X	

Table 10 Day 1 to Day 30 On-Study Assessments

	D1								D2	D3						D7[3]	D14[4]	D21[3]	D27							D28	D30
Study treatment every other day including clinic visit days as shown	X									X						X		X	X								
Time in relation to dose[1]	pre	0.25h	0.5h	1h	2h	4h	6h	10h	24h[5]	pre	0.25h	0.5h	1h	4h	8h	pre		pre	pre	0.25h	0.5h	1h	2h	4h	6h	10h	24h[5]	72h[5]
12 lead ECG and vital signs	X					X		X	X					X		X	X	X	X									
Brief physical examination	X														X	X	X	X	X								X	X
Pregnancy test (FRP)	X															X	X	X	X									
Contraception use compliance	X								X	X						X	X	X	X								X	X
Haematology test	X			X		X	X	X	X	X			X	X	X	X	X	X	X			X		X	X	X	X	X	X
Chem/Urinalysis test	X							X	X	X						X	X	X	X									
Coagulation (INR/APTT)	X							X	X	X						X	X	X	X								X	X
Joint counts: TJC(68), SJC(66)	X															X	X	X									X	
Patient reported outcomes PtGA, PtAAP, HAQ-DI	X															X	X	X									X	
PhGA	X															X	X	X									X	
hsCRP	X															X	X	X									X	
RF, ACPA	X																											
Met Hb[7]																	X										X	
RA disease biomarker blood	X			X[8]		X[8]		X[8]	X[8]	X[8]					X[8]	X	X	X	X[8]								X	
Exploratory PD and acetylation blood	X			X		X		X	X	X			X	X	X	X	X	X	X			X		X		X	X	X	X
PK blood	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	
MET ID blood	X	X	X	X	X	X	X	X	X										X	X	X	X	X	X	X	X	X	

	D1								D2	D3						D7[3]	D14[4]	D21[3]	D27								D28	D30
Study treatment every other day including clinic visit days as shown	X									X						X		X	X									
Time in relation to dose[1]	pre	0.25h	0.5h	1h	2h	4h	6h	10h	24h[5]	pre	0.25h	0.5h	1h	4h	8h	pre		pre	pre	0.25h	0.5h	1h	2h	4h	6h	10h	24h[5]	72h[5]
Isolated monocyte PK[9]	X			X		X		X	X	X			X	X	X				X			X		X		X	X	X
Gene expression blood	X																											
PK unrine sample	X	Collect urine for 24h after dose																										
PGx	X																											
Drug compliance assessment[10]																X	X	X	X									
AE and concurrent med review	Collect AE's from D1 to end of follow up visit																											

FRP, Females of reproductive potential; HAQ-DI, Health Assessment Questionnaire Disability Index; hsCRP, high sensitivity C-reactive protein; ESR: erythrocyte sedimentation rate; INR/APTT, International normalised ratio/partial thromboplastin time; PhGA, Physician Global Assessment of Arthritis; PtGA, Patient Global Assessment of Arthritis; TJC, Tender Joint Count; SJC, Swollen Joint Count; PtAAP, Patient Assessment of Arthritis Pain; ACPA, Anti-citrullinated protein antibodies; RF, rheumatoid factor; PK, pharmacokinetics ; MET ID: metabolite identification; PGx, pharmacogenomics.

1. Sample collection and assessments to be conducted in accordance with the time and events table.
2. Visits may be conducted on previous or next DOSING day.
3. The D14 visit has a ± 2 day window and may be on a DOSING or NON DOSING day. If on a dosing day, assessments should be per formed pre-dose.
4. Blood samples to be collected within a ±1h window of the scheduled time.
5. Patient Reported Outcomes questionnaires should be completed by subjects before any other assessment at a clinic visit.
6. Sample will be collected and stored for future analysis.
7. Applicable to selected sites only.
8. Record number of capsules in bottle and check patient diary. On non-visit days, phone subject to remind them to take dose.
9. Applicable to selected sites only.
10. Record number of capsules in bottle and check patient diary. On non-visit days, phone subject to remind them to take dose.

11.3. Appendix 3: Assessment Windows

11.3.1. Definitions of Assessment Windows for Analyses

No Assessment Windows will be defined, and listings will be based on nominal visits.

11.4. Appendix 4: Treatment States and Phases

11.4.1. Treatment Phases

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

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

11.4.2. 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.

11.4.2.1. Treatment States for Safety Data

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

NOTES:

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

11.4.2.2. Treatment States for AE Data

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

NOTES:

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

11.5. Appendix 5: Data Display Standards & Handling Conventions

11.5.1. Study Treatment & Sub-group Display Descriptors

Treatment Group Descriptions			
RandAll NG		Data Displays for Reporting	
Code	Description	Description	Order [1]
A	GSK3117391 40 mg	GSK3117391 40 mg	2
P	Placebo	Placebo	1

NOTES:

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

11.5.2. Baseline Definition & Derivations

11.5.2.1. Baseline Definitions

For efficacy, PD biomarker and RA disease biomarker endpoints, the value from the Day 1 (pre-dose) time point will be used as baseline.

For all other endpoints the baseline value will be the latest non-missing pre-dose assessment before the first dose (including unscheduled visits).

11.5.2.2. 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

NOTES :

- Unless otherwise specified, the baseline definitions specified in Section 11.5.2.1 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.

11.5.3. Reporting Process & Standards

Reporting Process	
Software	
• The currently supported versions of SAS software will be used.	
Reporting Area	
HARP Server	: UK1SALX00175
HARP Area	: arenv \ arprod \ gsk3117391 \ mid204957 \ final
QC Spreadsheet	: arenv \ arprod \ gsk3117391 \ mid204957 \ final \ documents

Reporting Process
Analysis Datasets
• Analysis datasets will be created according to Integrated Data Standards Library (IDSL) GSK A&R dataset standards.
Generation of RTF Files
• No RTF files are being generated.

Reporting Standards	
General	
• The current GSK Integrated Data Standards Library (IDSL) will be applied for reporting, unless otherwise stated: o 4.03 to 4.23: General Principles o 5.01 to 5.08: Principles Related to Data Listings o 6.01 to 6.11: Principles Related to Summary Tables o 7.01 to 7.13: Principles Related to Graphics	
Formats	
• All data will be reported according to the actual treatment the subject received unless otherwise stated. • GSK IDSL Statistical Principles (5.03 & 6.06.3) for decimal places (DP's) will be adopted for reporting of data based on the raw data collected. • Numeric data will be reported at the precision collected on the eCRF. • The reported precision from non eCRF sources will follow the IDSL statistical principles but may be adjusted to a clinically interpretable number of DP's.	
Planned and Actual Time	
• Reporting for tables, figures and formal statistical analyses : • Planned time relative to first dosing will be used in figures, listings and calculation of any derived parameters, unless otherwise stated.. • Reporting for Data Listings: • Planned and actual time relative to study drug dosing will be shown in listings (Refer to IDSL Statistical Principle 5.05.1). • Unscheduled or unplanned readings will be presented within the subject's listings. • Visits outside the protocol-defined time windows (i.e. recorded as protocol deviations) will be included in listings but omitted from figures.	
Unscheduled Visits	
• 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, %
Graphical Displays	
• Refer to IDSL Statistical Principals 7.01 to 7.13.	

11.6. Appendix 6: Derived and Transformed Data

11.6.1. General

Multiple Measurements at One Time Point
• All data will be listed.
Study Day

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

11.6.2. Study Population

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

Extent of Exposure
• Number of days of exposure to study drug will be calculated based on the formula: **Duration of Exposure in Days = Treatment Stop Date – (Treatment Start Date) + 1** • Subjects who were randomised but did not report a treatment start date will be categorised as having zero days of exposure. • The cumulative dose will be based on the formula: **Cumulative Dose = Sum of (Number of Days x Total Daily Dose)** • If there are any treatment breaks during the study, exposure data will be adjusted accordingly.

11.6.3. 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 :

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

Laboratory Parameters

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

11.6.4. Efficacy derivations

DAS28-CRP

The DAS assessment is a derived measurement with differential weighting given to each component.

The DAS28(CRP) will be calculated at each assessment time point. The components of the DAS28 arthritis assessment include:

- Tender Joint Count 28 (TJC28)
- Swollen Joint Count 28 (SJC28)

- C-reactive protein (CRP) (in mg/L)
- Patient's Global Assessment of Arthritis Disease Activity (PtGA) (visual analogue scale with values from 0=best to 100=worst)

DAS28(CRP)

The DAS28(CRP) score will be calculated using the following formula:

$$DAS28(CRP) = 0.56\sqrt{TJC28} + 0.28\sqrt{SJC28} + 0.36\ln(CRP + 1) + 0.014PtGA + 0.96$$

If one of the components is missing at an individual assessment point, the DAS28(CRP) value for that assessment will be set to missing. See Section 11.7.2.3 for further details of missing data approaches.

Swollen and Tender Joint Counts

Four different scores will be calculated to evaluate swelling and tenderness of joints. TJC28 and SJC28 will take 28 joints into account.

The assessment for swelling is the total number of joints with a present swelling and ranges from 0 to 28 for SJC28.

The assessment for tenderness is the total number of joints with a present tenderness and ranges from 0 to 28 for TJC28.

The following 28 joints will be taken into account for TJC28 and SJC28: Shoulder (2 joints), Knee (2), Elbow (2), Wrist (2), Fingers (PIP, MCP: 20).

Artificial, ankylosed and missing joints are excluded from swelling and tenderness assessment.

If there are missing observations for tender or swollen joints then the remaining observations will be assessed and weighted by dividing the number presented by number of non-missing and by multiplying by 28 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.

For example, for a patient with 2 missing tender or swollen joint counts at a given post-baseline time, the final score will be based on the 26 that are non-missing. Suppose if 12 of the 26 are tender/swollen then final score will be (12/26)x28=12.92.

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.

Observed joint states will be listed without any modification for every subject and visit.

Patient's Global Assessment of Arthritis Disease Activity (PtGA)

Subjects will assess the severity of their current arthritis pain using a continuous visual analog scale (VAS) with anchors "0" (no pain) and "100" (most severe pain).

No imputations for missing data will be done.

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

11.7.1. Premature Withdrawals

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

11.7.2. Handling of Missing Data

Element	Reporting Detail
General	• Missing data occur when any requested data are not provided, leading to blank fields on the collection instrument : o These data will be indicated by the use of a "blank" in subject listing displays (unless all data for a specific visit are missing in which case the data are excluded from the table). o Answers such as "Not applicable" and "Not evaluable" are not considered to be missing data and should be displayed as recorded.
Outliers	• Any subjects excluded from the summaries and/or statistical analyses will be documented along with the reason for exclusion in the clinical study report.

11.7.2.1. Handling of Missing Dates

Element	Reporting Detail
General	Partial dates will be displayed as captured in subject listing displays. Imputed dates should be stored in variables IMPSTDT (Imputed Start Date) and IMPENDT (Imputed End Date)
Adverse Events	• The eCRF allows for the possibility of partial dates (i.e., only month and year) to be recorded for AE start and end dates; that is, the day of the month may be missing. In such a case, the following conventions will be applied for calculating the time to onset and the duration of the event: o Missing Start Day: First of the month will be used unless this is before the start date of study treatment; in this case the study treatment start date will be used and hence the event is considered On-treatment as per Appendix 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

Element	Reporting Detail
	missing. • Start or end dates which are completely missing (i.e. no year specified) will remain missing, with no imputation applied.

11.7.2.2. Handling of Partial Dates

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

11.7.2.3. Handling of Missing Data for Statistical Analysis

Element	Reporting Detail
Efficacy: DAS28-CRP	• If one of the components is missing at an individual assessment point, the DAS28(CRP) value for that assessment will be set to missing.
Tender and swollen joint counts	• If there are missing observations for tender or swollen joints then the relevant joint count will be set to missing. • If a joint is “not applicable” or “‘non-evaluable, other’” at Baseline, then that joint is set to that value throughout the study for the subject.
Patient’s Global Assessment of Arthritis Disease Activity (PtGA)	• No imputations for missing data will be conducted

11.8. Appendix 8: Values of Potential Clinical Importance

11.8.1. Laboratory Values

Haematology				
Laboratory Parameter	**Units**	**Category**	**Clinical Concern Range**	
			Low Flag (< x)	**High Flag (>x)**
Haematocrit	Ratio of 1	Male	0.3	0.54
		Female	0.3	0.54
		Δ from BL	↓0.075	
Haemoglobin	g/L	Male	90	180
		Female	90	180
		Δ from BL	↓20	
Lymphocytes	$x10^9$/ L		0.5	
Neutrophil Count	$x10^9$/ L		1.0	
Platelet Count	$x10^9$/ L		50	550
While Blood Cell Count (WBC)	$x10^9$/ L		3	14
Monocyte	$x10^9$/ L		0.2	1.5

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

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

11.8.2. ECG

ECG Parameter	Units	Clinical Concern Range	
		Lower	Upper
Absolute			
Absolute QTc Interval	msec	> 450	
		> 450	≤ 479
		≥ 480	≤ 499
		≥ 500	
Absolute PR Interval	msec	< 110	> 220
Absolute QRS Interval	msec	< 75	> 110

11.8.3. 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

11.9. Appendix 9: Multicentre Studies

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

11.10. Appendix 10: Examination of Covariates, Subgroups & Other Strata

11.10.1. Handling of Covariates, Subgroups & Other Strata

No subgroup analyses are to be conducted in this study.

11.11. Appendix 11: Multiple Comparisons & Multiplicity

No formal statistical analyses are planned for the study.

11.12. Appendix 12: Model Checking and Diagnostics for Statistical Analyses

11.12.1. Statistical Analysis Assumptions

No formal statistical analyses are planned for the study.

11.13. Appendix 13: Population Pharmacokinetic and Pharmacokinetic / Pharmacodynamic (Or Biomarker) Analyses

No population PK and PK/PD analyses are planned for the study.

11.14. Appendix 14 – Abbreviations & Trade Marks

11.14.1. Abbreviations

Abbreviation	Description
ACR	American College of Rheumatology
ADaM	Analysis Data Model
AE	Adverse Event
AIC	Akaike's Information Criteria
A&R	Analysis and Reporting
CDISC	Clinical Data Interchange Standards Consortium
CI	Confidence Interval
CL/F	Apparent Clearance
CPMS	Clinical Pharmacology Modelling & Simulation
CRP	C-reactive protein
CS	Clinical Statistics
CSR	Clinical Study Report
CTR	Clinical Trial Register
CV_b / CV_w	Coefficient of Variation (Between) / Coefficient of Variation (Within)
DAS28	Disease Activity Score for 28 different joints
DRC	Data Review Committee
DOB	Date of Birth
DP	Decimal Places
ECG	Electrocardiogram
eCRF	Electronic Case Record Form
ESR	Erythrocyte sedimentation rate
EULAR	European League against Rheumatism
GEE	Generalized Estimating Equation
IA	Interim Analysis
ICH	International Conference on Harmonisation
IDMC	Independent Data Monitoring Committee
IDSL	Integrated Data Standards Library
IMMS	International Modules Management System
IP	Investigational Product
ITT	Intent-To-Treat
GUI	Guidance
HARP	Harmonised Analysis and Reporting Platform
LLN	Lower Limit of Normal
LOC	Last Observation Carries Forward
MMRM	Mixed Model Repeated Measures
NRS	Numeric rating scale
PCI	Potential Clinical Importance
PD	Pharmacodynamic
PDMP	Protocol Deviation Management Plan
PhGA	Physician's Global Assessment of Arthritis

Abbreviation	Description
PK	Pharmacokinetic
PK/PD	Pharmacokinetics/Pharmacodynamics
PP	Per Protocol
PT	Preferred Term
PtGA	Patient's Global Assessment of Arthritis Disease Activity
QC	Quality Control
QTcF	Frederica's QT Interval Corrected for Heart Rate
QTcB	Bazett's QT Interval Corrected for Heart Rate
RA	Rheumatoid arthritis
RAP	Reporting & Analysis Plan
RAMOS	Randomization & Medication Ordering System
SAC	Statistical Analysis Complete
SAE	Serious Adverse Events
SDTM	Study Data Tabulation Model
SJC	Swollen joint count
SJC28	Swollen joint count for 28 different joints
SOC	System Organ Class
SOP	Standard Operation Procedure
TA	Therapeutic Area
TFL	Tables, Figures & Listings
TJC	Tender joint count
TJC28	Tender joint count for 28 different joints
ULN	Upper Limit of Normal
VAS	Visual Analogue Scale
V/F	Apparent Volume of Distribution
GSK	GlaxoSmithKline

11.14.2. Trademarks

Trademarks of the GlaxoSmithKline Group of Companies
NONE

Trademarks not owned by the GlaxoSmithKline Group of Companies
SAS

11.15. Appendix 15: List of Data Displays

11.15.1. Data Display Numbering

The following numbering will be applied for RAP generated displays:

Section	Tables	Figures
Study Population	N/A	N/A
Efficacy	N/A	2.1 to 2.2
Safety	N/A	3.1 to 3.2
Pharmacodynamic and / or Biomarker	N/A	N/A
Section	**Listings**	
ICH Listings	1 to 28	
Other Listings	29 to 31	

11.15.2. Mock Example Shell Referencing

Non IDSL specifications will be referenced as indicated and if required an example mock-up displays provided in Appendix 16: 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
Pharmacodynamic and / or Biomarker	PD_Fn	PD_Tn	PD_Ln

NOTES:

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

11.15.3. Deliverable [Priority]

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

NOTES:

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

11.15.4. Efficacy Figures

Efficacy: Figures					
No.	**Population**	**IDSL / TST ID / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
DAS28					
2.1.	Safety	EFF_F1	Individual patient profiles of DAS28-CRP score over time		SAC
2.2.	Safety	EFF_F1	Individual patient profiles of change from baseline in DAS28-CRP score over time		SAC

11.15.5. Pharmacodynamic Figures

Efficacy: Figures					
No.	**Population**	**IDSL / TST ID / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
Biomarkers					
2.3.	Safety	EFF_F1	Individual patient profiles of monocyte count over time		SAC

11.15.6. ICH Listings

ICH : Listings					
No.	**Population**	**IDSL / TST ID / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
Randomisation					
1.	Safety	CP_TA1	Listings of Randomised and Actual Treatments		SAC

ICH : Listings					
No.	**Population**	**IDSL / TST ID / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
Subject Disposition					
2.	All subjects	ES7	Listing of Reasons for Screen Failure	Journal Guidelines	SAC
3.	Safety	ES2	Listing of Reasons for Study Withdrawal	ICH E3	SAC
4.	Safety	BL1	Listing of Subjects for Whom the Treatment Blind was Broken	ICH E3	SAC
5.	Safety	TA1	Listing of Planned and Actual Treatments	IDSL	SAC
Protocol Deviations					
6.	Safety	DV2	Listing of Important Protocol Deviations	ICH E3	SAC
7.	Safety	IE3	Listing of Subjects with Inclusion/Exclusion Criteria Deviations	ICH E3	SAC
Demographic and Baseline Characteristics					
8.	Safety	DM2	Listing of Demographic Characteristics	ICH E3	SAC
9.	Safety	DM9	Listing of Race	ICH E3	SAC
Prior and Concomitant Medications					
10.	Safety	CP_CM3	Listing of Concomitant Medications	IDSL	SAC
Exposure and Treatment Compliance					
11.	Safety	EX3	Listing of Exposure Data	ICH E3	SAC
Adverse Events					
12.	Safety	CP_AE8	Listing of All Adverse Events	ICH E3	SAC
13.	Safety	AE7	Listing of Subject Numbers for Individual Adverse Events	ICH E3	SAC
14.	Safety	AE2	Listing of Relationship Between Adverse Event System Organ Classes, Preferred Terms, and Verbatim Text	IDSL	SAC

ICH : Listings					
No.	**Population**	**IDSL / TST ID / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
Serious and Other Significant Adverse Events					
15.	Safety	CP_AE8a	Listing of Fatal Serious Adverse events	ICH E3	SAC
16.	Safety	CP_AE8a	Listing of Non-Fatal Serious Adverse Events	ICH E3	SAC
17.	Safety	AE14	Listing of Reasons for Considering as a Serious Adverse Event	ICHE3	SAC
18.	Safety	CP_AE8	Listing of Adverse Events Leading to Withdrawal from Study / Permanent Discontinuation of Study Treatment	ICH E3	SAC
All Laboratory					
19.	Safety	LB5	Listing of Laboratory Data for Subjects with Abnormalities of Potential Clinical Concern	ICH E3	SAC
20.	Safety	LB5 / LB6	Listing of Laboratory Data Abnormalities of Potential Clinical Importance		SAC
ECG					
21.	Safety	CP_EG3	Listing of All ECG Values for Subjects with a Value of Potential Clinical Importance	IDSL Include absolute PCI subjects. Footnote: H=High absolute, L= Low absolute."	SAC
22.	Safety	CP_EG3	Listing of All ECG Changes for Subjects with a Value of Potential Clinical Importance	IDSL Include change from baseline PCI subjects. Footnote: H=High change from baseline value, L= Low change from baseline value	SAC

ICH : Listings					
No.	**Population**	**IDSL / TST ID / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
23.	Safety	CP_EG3	Listing of ECG Values of Potential Clinical Importance	"Include absolute PCIs. Footnote: H=High absolute, L= Low absolute."	SAC
24.	Safety	CP_EG3	Listing of ECG Changes of Potential Clinical Importance	"Include change from baseline PCIs. Footnote: H=High change, L= Low change."	SAC
25.	Safety	CP_EG5	Listing of Abnormal ECG Findings	IDSL	SAC
Vital Signs					
26.	Safety	CP_VS4	Listing of All Vital Signs for Subjects with Values of Potential Clinical Importance	"Include both absolute and change from baseline PCI subjects. Footnote: H=High, L=Low H1=Lower Increase, H2=Upper Increase, L1=Lower Decrease, L2=Upper Decrease"	SAC

11.15.7. Non-ICH Listings

Non-ICH : Listings					
No.	**Population**	**IDSL / TST ID / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
Efficacy					
27.	Safety	LS2	Listing of DAS28-CRP Score and Components	Footnote: Swollen Joint Count based on 28 and 66 joints. Tender Joint Count based on 28 and 68 joints. Patient's Global Assessment of Arthritis Disease Activity measured on VAS scale. CRP – C-Reatove protein	SAC
Pharmacodynamics/Biomarkers					
28.	Safety	LS1	Listing of Absolute and Change from Baseline MRP8/14 level		SAC
29.	Safety	LS1	Listing of Absolute and Change from Baseline in Monocyte Count		SAC

11.16. Appendix 16: Example Mock Shells for Data Displays

Example : LS1
Protocol : 204957
Population : Safety

Listing xx: Listing of Absolute and Change from Baseline in [variable]

Treatment: Placebo

Subject	Visit	Visit Date	Study Day	Absolute	CFB
XX	SCREENING	13SEP2016	XX	XX	
	DAY 1	26SEP2016	XX	XX	
	EARLY WITHDRAWAL	12OCT2016	XX	XX	XX
XX	SCREENING	28SEP2016	XX		
	DAY 1	19OCT2016	XX	XX	
	DAY 7	02NOV2016	XX	XX	XX
	DAY 14	16NOV2016	XX	XX	XX
	DAY 21	30NOV2016	XX	XX	XX
	DAY 28	14DEC2016	XX	XX	XX
XX	SCREENING	16NOV2016	XX	XX	
	DAY 1	05DEC2016	XX	XX	
	DAY 7	19DEC2016	XX	XX	XX
	DAY 14	04JAN2017	XX	XX	XX
	DAY 21	16JAN2017	XX	XX	XX
	DAY 28	01FEB2017	XX	XX	XX

Example : LS2
Protocol : 204957
Population : Safety

Listing X
Listing of DAS28-CRP Score and Components
Treatment: <Placebo, GSKXXXXXXX XXmg>

Site ID/ Subject ID	Visit	DAS28(CRP)/ DAS28(CRP) CfB/	PGA	TJC28/ TJC68	SJC28/ SJC66	CRP
XXXX/ XXXXX	Baseline	x.xx/ x.xx	XX	xx.x/ xx.xx	xx.x/ xx.xx	xx.x/ xx.xx
	Week X	x.xx/ -x.xx	XX	xx.x/ xx.xx	xx.x/ xx.xx	xx.x/ xx.xx
	Etc.	Etc.	Etc.	Etc.	Etc.	Etc.
XXXX/ XXXXX	Baseline	x.xx/ -x.xx	XX	xx.x/ xx.xx	xx.x/ xx.xx	xx.x/ xx.xx
	Week X	x.xx/ x.xx	XX	xx.x/ xx.xx	xx.x/ xx.xx	xx.x/ xx.xx
	Etc.	Etc.	Etc.	Etc.	Etc.	Etc.

Example :EFF_F1
Protocol : 204957
Population : Safety

Figure xx: Individual patient profiles of [variable] over time