Statistical Analysis Plan

Official Title of Study: A randomized, double blind (sponsor open), comparative, multi-center study to evaluate the safety and efficacy of subcutaneous belimumab (GSK1550188) and intravenous rituximab co-administration in subjects with primary Sjögren's syndrome.

NCT ID: NCT02631538

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Information Type	:	Reporting and Analysis Plan (RAP)

Title	:	Reporting and Analysis Plan for a randomized, double blind (sponsor open), comparative, multi-center study to evaluate the safety and efficacy of subcutaneous belimumab (GSK1550188) and intravenous rituximab co-administration in subjects with primary Sjögren's syndrome.
Compound Number	:	GSK1550188
Effective Date	:	18-AUG-2020

Description:

The purpose of this RAP is to describe the planned analyses and outputs to be included in the Clinical Study Report for Protocol 201842.

This RAP is intended to describe the planned safety & tolerability, efficacy, biomarker/pharmacodynamic, pharmacokinetic and health outcomes analyses required for the study.

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

RAP Section 3.3 (Final Analyses) outlined the intended purpose of the RAP was for the planned analyses for Primary and End of Study (EoS) SAC deliverables. However, in the event that the Primary Analysis reporting does not identify treatment benefit, an abridged set of analysis may be conducted for EoS analysis, which will be detailed in a RAP amendment or addendum. Therefore, this RAP amendment includes updates to the approved version for the Primary Analysis. As the milestone (Last Subject Last Visit) for RAP approval as per SOP_54838 has been achieved, agreement and approval steps allow confirmation of any planned changes outside the steps outlined in the RAP SOP.

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1. REPORTING & ANALYSIS PLAN SYNOPSIS

Overview	Key Elements of the RAP
Purpose	This RAP details all planned analyses and outputs required for: 1. Primary Analyses (post completion of all week 52 assessments) 2. End of Study (EoS) Analyses (Week 104)
Protocol	• This RAP is based on the protocol amendment 06 (Dated 25/Jun/2019) of study 201842 (GSK Document Number 2014N220285_06 and eCRF Version 1.02).
Primary Objective	• Investigate the safety and tolerability of anti-BLyS / anti-CD20 co-administration therapy and anti-BLyS and anti-CD20 monotherapies for subjects with active primary Sjögren's syndrome (pSS).
Primary Endpoint	• Safety and tolerability; including incidence of SAEs and AESIs.
Study Design	• A randomized, double blind (sponsor open), comparative, multi-national, multi-center, placebo-controlled trial in subjects with active pSS. • Approximately 70 subjects will be recruited into the study initially. At Day 0, subjects will be randomized 1:2:2:2 into one of 4 treatment arms. Withdrawals may be replaced. • Study 201842 consisted of 3 phases: ○ **A 52-week treatment phase** during which subjects were randomized to one of four arms ○ **A 16-week general follow (GFU**) up period focused on safety assessments ○ **An individualized follow (IFU)** up period for subjects with persistently low B cell counts • **NOTE:** All subjects will enter a 16-week general follow-up period after the Week 52 visit or after discontinuation if a subject discontinues IP and withdraws from the treatment phase visits prior to Week 52. Assessments to be performed are included in protocol Time and Events Table. During the general follow up period subjects will remain off of investigational product, endeavor not to change concomitant medication regimen, receive monthly safety follow up phone calls, and will return to the clinic for asite visit at the end of the general follow up period • Subjects entering IFU are assessed every 12 wks (± 7 days), with calls every 4 wks (±7 days) between visits. Subjects exit IFU when: CD19+ B-lymphocyte counts are within normal range or 10% of baseline levels (if baseline < LLN), OR at investigator's discretion starts receiving disease modifying therapy that may affect B-cell numbers OR for up to a maximum of 2 years (i.e., up to Week 104) – whichever comes first. Subjects exiting IFU period will attend a

Overview	Key Elements of the RAP
	final visit (within 28 days of decision) for final assessments (IFU Final Visit). • Subjects who withdrew (WD) prematurely from investigational product (IP) during treatment phase & refused to attend further visits through wk 52, were encouraged to participate in the GFU & IFU for safety purposes.
Planned Analyses	• Quarterly blinded safety data summaries for SRT. • Quarterly un-blinded safety data summaries and secondary efficacy endpoint, ESSDAI for iSRC. • Interim analyses occurring once approximately 35 subjects have completed their Week 24 assessments. • Primary Analysis ○ The primary analyses will be conducted following completion of all Week 52 visits, with inclusion of the FU visit data which is available at this time. The analyses will be performed once the data from all visits up to and including this Week 52 cutoff have been collected, verified and validated. Week 68 data will also be included, if available. • <u>End of Study</u> • The follow-up (end of study) analyses will include all follow-up data (i.e. general follow-up data between Week 52 and Week 68 and individualized follow-up data from Week 68 through Week 104/IFU final visit). These analyses will be performed once data from Week 52 through Week 104/IFU final visit has been collected, verified and validated.
Analysis Populations	• 'Screened Population' will be used to evaluate selected study population. • 'Enrolled Population' will be used to evaluate selected study population. • 'Safety Population' will be used to evaluate study population, efficacy, safety, PD, exploratory and health outcomes data. • 'PK' populations will be used to evaluate belimumab and rituximab pharmacokinetics. • 'Per-protocol Population' may be used to evaluate a subset of Efficacy, PD, and biomarker data.
Hypothesis	• The study is designed to investigate the safety and tolerability of the co-administration of belimumab with rituximab and belimumab monotherapy in subjects with pSS. • No formal hypotheses will be tested. • For secondary endpoints, an estimation approach will be adopted with derivation of estimates and 95% confidence interval (CI) for the comparisons of interest (see Section 2.5)
Primary Endpoint Analysis	• Safety data will be presented in a tabular and graphical format. • Clinical interpretation will be based upon review of AEs, laboratory values and vital signs. • No formal statistical testing will be performed on the safety data.
Secondary	• Secondary endpoints will be analysed to provide point estimates and

Overview	Key Elements of the RAP
Endpoints Analysis	corresponding 95% CIs for the comparisons of interest. • In addition, probabilities of success of the co-administration therapy and belimumab monotherapy will be conducted.

2. SUMMARY OF KEY PROTOCOL INFORMATION

2.1. Changes to the Protocol Defined Statistical Analysis Plan

There were no changes or deviations to the planned statistical analysis specified in the protocol amendment 06 [(Dated: 25/Jun/2019)].

Changes from the originally planned statistical analysis specified in the protocol are outlined:

Protocol	Reporting & Analysis Plan	
Statistical Analysis Plan	**Statistical Analysis Plan**	**Rationale for Changes**
• Section 9.3.1: Analysis Population	• Section 4: Analysis Populations	• "Screened" and "Enrolled" populations were included to support data disclosure displays • Per Protocol analysis population was also defined for sensitivity analysis
• Section 9.4.2 Primary Analyses	• Section 8.1.1.1 ESSDAI	• A corrected ESSDAI score will also be calculated. ESSDAI scores disease activity in 12 domains. In 5 (renal, PNS, CNS, cutaneous and pulmonary) of the domains, ESSDAI requires that if activity has been present for greater than or equal to 12 months then it must be treated as irreversible damage and the activity should be scored as zero (Seror, 2015a). This is a problem for clinical trials of long duration such as study 201842 because it can result in misleading evidence of reduced activity.

All data displays (Tables, Figures & Listings) will use the term "Subject" which reflects CDISC and GSK Data Display Standards terminology.

2.2. Changes to the Final RAP for End of Study Reporting

This section outlines key (not limited too) updates from the RAP version approved prior to the RAP SOP milestone (Last Subject Last Visit).

Additional updates post EoS Database Release (DBR) have also been included to clarify timepoints included for the general follow up period and individualised follow up period. Subjects who withdrew (WD) prematurely from investigational product (IP) during the treatment phase and refused to attend further visits through week 52, were encouraged to participate in the GFU period and the IFU period (if required) for safety purposes. For several subjects withdrawing early from IP, this resulted in a temporal misalignment of data such that data which were collected during their follow up calls and visits were allocated to visits which occurred much later in the study (i.e. in the post W52 general and individualized follow up periods). Additional analyses have been included to assess the response in the GFU and IFU.

RAP Section	Summary of Change
4.0 Study Population	**EoS Analysis:** A completer population was included to support additional Week 68/FU / IFU analyses.
7.1 Safety Analyses 11.5.3 Safety Appendix 13: List of Data Displays	**Primary Analysis:** Implemented MedDRA V22.0. **EoS Analysis:** Implement MedDRA V23.0 which constitutes a major release and relevant sections are updated.
	Primary Analysis: Summarized safety data for all completed visits up to W68 (where reported by visit) and up to W104 (where not reported by visit), with cut-off date of 09/09/19 (W52 LSLV). **EoS Analysis:** Will summarize (Tables, Figures and Listings) AE/AESI safety endpoints for all completed visits **up to Week 68 only.** Other safety endpoints will be reported using scheduled visits, unless specified.
7.1.4. Adverse Events of Special Interest	**EoS Analysis:** Specified additional AESI details for post-administration systemic reactions by Rituximab/Placebo Infusion.
8. Secondary Statistical Analyses 9. Other Statistical Analyses Appendix 13: List of Data Displays	**Primary Analysis:** Specified any formal model based statistical analyses included visits upto Week 52. **EoS Analysis:** Additional ESSDAI statistical analyses included using the completer population.
8. Secondary Statistical Analyses Appendix 13: List of Data Displays	**Primary Analysis:** % change from baseline in No. of B Cells (CD20)/mm2 in salivary gland biopsy at Week 24 was reported. **EoS Analysis:** Change from baseline will be reported instead of % change from baseline.
11.5.3 Appendices: Safety	**EoS Analysis:** Added Section 11.5.3.2. Coronavirus Disease 2019 (COVID-19) Environment Onset Date.
11.5.6 Biomarker Appendix 13: List of Data Displays 11.8.1 Laboratory Parameters	**EoS Analysis:** Table 11 (Flow Cytometry Parameters) & Table 13 (Minor Salivary Gland Parameters) updated to reflect final EoS delivery. Additional details included for imputation of Flow Cytometry Parameters.
11.5.6.1. Immunogenicity	**EoS Analysis:** Additional details have been included to clarify the reporting of Antibodies to Rituximab
Appendix 13: List of Data Displays	**EoS Analysis:** Any selected Primary Analysis displays that has been identified for generation for EoS has been allocated unique numbering. **EoS Analysis:** All figures will be displayed up to Week 68/FU only and a line break after Week 52 will be included, so as to indicate Week 68/FU timepoint is not sequential for all subjects.
	EoS Analysis: The following display will not be generated: • T2.13: ESSDAI and ClinESSDAI Bland-Altman Plot at Week 24 (Corrected) • T2.14: Scatter Plot of Wk 24 Changes for Total ESSDAI Score vs Salivary Gland B Cells • T2.15: Median Free Blys Vs Median CD19+ B cell by Treatment • T7.3: Summary Statistics: Lacrimal Gland Function (Schirmer's Test) • T7.4: Summary Statistics of Change from Baseline: Lacrimal Gland Function (Schirmer's Test) • T7.5: Summary Statistics of PGA • T7.6: Summary Statistics of Change from Baseline: PGA • T2.1009: Summary of Statistical Analysis Results of Change from Baseline: ESSDAI Total Score (Uncorrected)

RAP Section	Summary of Change
	• T2.1010: Summary of Statistical Analysis Results of Change from Baseline: ESSDAI Total Score (Uncorrected) – Per Protocol Population • T2.1011: Summary of Statistical Analysis Results of Change from Baseline: ESSDAI Total Score (Corrected) • T2.1012: Summary of Statistical Analysis Results of Change from Baseline: ESSDAI Total Score (Corrected) - Per Protocol Population • T2.1021: Summary of Statistical Analysis of Responder on Total ESSDAI Score (Corrected) • F2.1005: Adjusted Mean (95% CI) Change from Baseline: ESSDAI Total Score (Uncorrected) • F2.1006: Adjusted Mean (95% CI) Change from Baseline: ESSDAI Total Score (Corrected) • T2.1029: Summary of Statistical Analysis Results of Change from Baseline: Stimulated Salivary Flow • T2.1030: Summary of Statistical Analysis Results of Change from Baseline: Stimulated Salivary Flow - Per Protocol Population • T2.1033: Summary of Statistical Analysis Results of Change from Baseline: Oral Dryness Numeric Response Scale • T2.1034: Summary of Statistical Analysis Results of Change from Baseline: Oral Dryness Numeric Response Scale - Per Protocol Population • T6.1006: Summary of Statistical Analysis of Responders on ESSPRI
	EoS Analysis: The following additional displays will be generated: • Table 1.1006 Summary of Study Populations • T1.1023: Summary of Overall Subject Status • T.1.1025: Serious Acute Post-Injection Systemic Reactions per GSK Adjudication by PT, in First Six Doses of Belimumab/Placebo • T.3.63: Post-IV Systemic Reactions per Anaphylactic Reactions CMQ Broad search by PT, in First Two 2 Infusions of Rituximab/Placebo • T2.1040: Summary Statistics of ESSDAI Total Score (Corrected) - Completers • T2.1041: Summary of Statistical Analysis Results of Change from Baseline: ESSDAI Total Score (Corrected) - Completers • T2.1042: Summary Statistics of Stimulated and Unstimulated Salivary Flow - Completers • T2.1043: Summary Statistics of Oral Dryness Numeric Response Scale - Completers • T6.1015: Summary Statistics of ESSPRI Total Score and Domains - Completers • T7.023: Summary Statistics of Flow Cytometry Flow Parameters- Completers • L1059: Listing of Overall Subject Status • L1061: Listing of Protocol Deviations Related to Covid-19

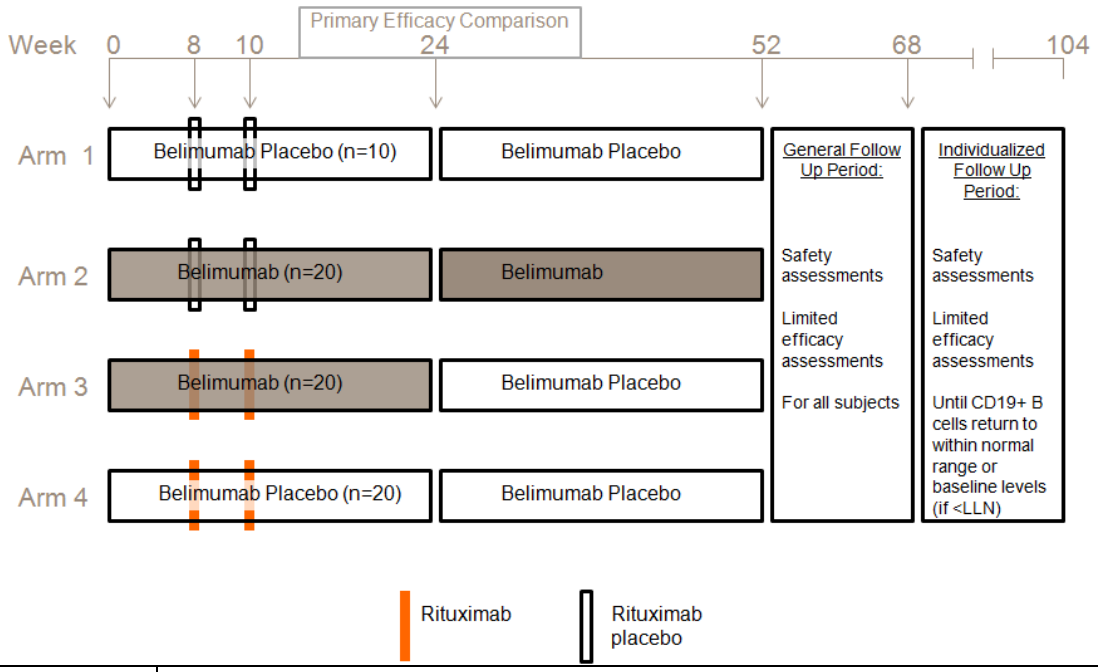
2.3. Study Objective(s) and Endpoint(s)

Objectives	Endpoints
Primary	
• Safety and tolerability of anti-BLyS / anti-CD20 co-administration therapy and anti-BLyS and anti-CD20 monotherapies	• Safety and tolerability; including incidence of SAEs and AESIs.
Secondary	
Clinical efficacy of anti-BLyS / anti-CD20 co-administration therapy and anti-BLyS and anti-CD20 monotherapies	• ESSDAI score over time • Stimulated salivary flow over time • Oral dryness numeric response scale over time
• Assessment of anti-BLyS / anti-CD20 co-administration therapy and anti-BLyS and anti-CD20 monotherapies on tissue B-cells.	• B cell quantification within salivary gland biopsy at Week 24
Exploratory	
Assessment of mechanism and durability of effect of anti-BLyS/anti-CD20 co-administration therapy and anti-BLyS and anti-CD20 monotherapies.	<u>Clinical efficacy</u> • Ocular dryness numeric response scale over time • Lacrimal gland function as measured by Schirmer's test • Physician's Global Assessment (PGA) of disease activity over time <u>Biomarkers</u> • Serologic markers over time • Change in peripheral blood leukocytes including B cell subsets over time • BLyS levels in blood • Immunogenicity of rituximab and belimumab • Pharmacokinetics of rituximab and belimumab • Change from baseline in the cellular composition of the salivary gland • Sustained efficacy of anti-BLyS/anti-CD20 co-administration at Week 52. Additional exploratory biomarkers may be evaluated [1] o Transcriptomic analysis of blood and salivary gland o B and T cell receptor clonal analysis in peripheral blood and salivary gland o Proteomic assessment of the saliva
Health Outcomes	
Gather preliminary information on patient reported outcomes of anti-BLyS/anti-CD20 co-administration	• ESSPRI score (and individual scale sub-scores) over time • Fatigue and Discomfort- SICCA Symptom Inventory

Objectives	Endpoints
therapy and anti-BLyS and anti-CD20 monotherapies.	(PROFAD SSI SF) over time • Patient Global Assessment (PtGA) of disease activity over time. • Subject exit interviews.
NOTE: [1] Analysis will be implemented post week 52 primary analysis	

2.4. Study Design

Overview of Study Design and Key Features



Design Features	• Multi-national, multi-center, double-blind (sponsor open), randomized, placebo-controlled trial in subjects with active pSS. • Disease activity assessment at Week 52 will allow determination of whether any clinical effects of co-administration therapy achieved at Week 24 are sustained after discontinuation of therapy and/or whether chronic treatment with belimumab monotherapy is effective.
Dosing	• Belimumab/ Placebo weekly subcutaneous injections • Rituximab/Placebo infusions at Weeks 8 and 10.
Treatment Assignment	• At Day 0, subjects will be randomized 1:2:2:2 to one of 4 treatment arms. • Subjects will be stratified based on their baseline disease activity severity [ESSDAI total 5-12 (moderate) vs. >12 (severe)]. • GSK RandAll NG used to generate randomization schedules. • Centralized randomization using GSK RAMOS NG for treatment allocation.
Safety Review	• Periodic blinded review by SRT, and un-blinded reviews by iSRC, focusing on key safety parameters.

Overview of Study Design and Key Features	
Interim Analysis	• Formal planned interim analysis was performed once approximately 35 subjects had completed their Week 24 assessments.

2.5. Statistical Hypotheses

The primary objective of the study is to investigate the safety and tolerability of the co-administration of belimumab with rituximab and belimumab monotherapy in subjects with pSS. No formal statistical comparisons will be conducted to assess this objective.

Secondary efficacy and mechanistic endpoints will be investigated. The following exploratory comparisons will be conducted:

1. Co-administration belimumab/rituximab treatment arm vs. Placebo arm
2. Co-administration belimumab/rituximab treatment arm vs. Rituximab monotherapy arm
3. Co-administration belimumab/rituximab treatment arm vs. Belimumab monotherapy arm
4. Belimumab monotherapy arm vs. Placebo arm
5. Belimumab monotherapy arm vs. Rituximab monotherapy arm

3. PLANNED ANALYSES

3.1. Regular Data Reviews

Safety data will be reviewed on a quarterly basis in a blinded fashion by an internal safety review team (SRT). Summaries will be produced in order to describe the baseline demography and the following safety parameters:

1. Adverse events and serious adverse events including fatalities
2. Adverse events of special interest as defined in the belimumab PSAP
3. Withdrawals and reasons for withdrawal
4. Blood chemistry
5. Hematology
6. CD4 and CD8 as measured by flow cytometry
7. Immunoglobulin levels (IgG)

The displays for the SRT meetings will not include any laboratory data that could potentially un-blind the treatments. IgA, IgM and CD19 assessment are excluded.

Additionally, summaries of the above parameters plus IgA, IgM, vital signs and ESSDAI will be reviewed in an unblinded manner by the internal Safety Review Committee (iSRC) as outlined in protocol and in the iSRC charter. In order to protect the blinding status, these displays will be produced by a third party (Quanticate).

3.2. Interim Analyses

A formal interim analysis was planned to take place once half of the planned subjects (i.e.: approximately 35 subjects) have completed their Week 24 assessments. The interim analysis displays included the available data for all visits up to Week 68 as indicated in the table below. The interim analysis reviewed safety outputs produced for iSRC and additional summaries for efficacy, biomarkers and health outcomes parameters. The interim analysis summaries were produced by treatment group and reviewed by the TA-DAC and the iSRC. At the interim analysis, to aid internal decision making, predictive probabilities for ESSDAI effects were computed for comparison of combination (belimumab/rituximab) vs placebo at Week 24 and for comparison of belimumab monotherapy vs placebo at Week 24. The predictive probabilities for ESSDAI treatment differences greater than 3 and greater than 5, under varying assumptions for target sample size were assessed to support potential sample size re-estimation for the study. Access to interim outputs were restricted to individuals specified in the iSRC charter. There were no changes made to the sample size/study as a result of the interim analysis.

Section	Interim Analysis
Study Population	Baseline demography Disease History Disposition
Safety **(Primary study objective)**	Adverse events and serious adverse events Adverse events of special interest as defined in Belimumab PSAP Withdrawals and reasons for withdrawal Immunoglobulin (IgG, IgA, IgM) Haematology Blood chemistry Vital Signs CD4 and CD8
Clinical Efficacy	ESSDAI Total Score and Domains
Biomarkers	B cells (CD20) count/mm^2 in salivary gland biopsy (by histology) B cell (CD20) / T cell (CD3) ratio in salivary gland biopsy (by histology) Lymphocyte Focus Score (expressed per $4mm^2$) in salivary gland biopsy (by histology) Plasma cells (CD138+; both CD20pos and CD20neg) count/mm^2 in salivary gland tissue (by histology). Frequency of B cells[1], naïve[2], memory[3], and plasmablast[4] in peripheral blood (by flow cytometry) Serum SS-A concentration

Section	Interim Analysis
Health Outcomes	ESSPRI (total score and the pain, fatigue and dryness domains)

1. CD19+ B cells (CD3-CD19+)
2. Naïve B cells (CD19+CD20+CD27-)
3. Memory B cells (CD19+CD20+CD27+)
4. Plasmablast All (CD19+CD27+CD38+)

3.3. Final Analyses

There will be two database freezes for this study, corresponding to the Primary Analyses and the End of Study Analyses (Week 104).

Primary Analysis

The cut-off date in the Primary Analysis datasets will be 09-Sep-2019 (i.e. the date the last subject completed their Week 52 visit). Data after 09-Sep-2019 will be removed from the extracted data after DBR based on the algorithms detailed in refer to Appendix 5: Derived and Transformed Data for details. The data cut off will be applied on DMDATA before generating any analysis datasets and outputs.

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

1. All subjects have completed their Week 52 (or early withdrawal assessment for subjects withdrawing consent prior to Week 52).
2. All required database cleaning activities have been completed and final database release (DBR) and database freeze (DBF) has been declared by Data Management.
3. All criteria for un-blinding the randomization codes have been met:
   - AESI adjudication through Week 68/FU assessments.
   - Protocol deviation review as described in Protocol Deviation Management Plan (PDMP) is completed.
   - Exclusions from the per protocol population have been agreed and documented.
4. Randomisation codes have been distributed according to RandAll NG procedures.
5. Database freeze (DBF) has been declared by Data Management.

All outputs as described in Section 6 to Section 9 of the RAP and detailed in Appendix 13 will be reported for the primary analyses:

- Summary tables reported by visit will include only data collected till Week 68/FU
- Summary tables not reported by visit will include all date collected based on the date-cut date, unless otherwise specified/ required.
- All collected data from the Individualized Follow Up (IFU) period will be listed.

End of Study Analysis

The end of study (after week 104) analyses will be performed after the completion of the following sequential steps:

1. All subjects have completed the 16-week generalized follow-up visit (Week 68) and individualized follow up visit (up to Week 104 or IFU final visit for subjects leaving the IFU prior to W104) or Early Withdrawal visit for those subjects who withdraw from the study prior to the Week 104 visit.

2. All required database cleaning activities have been completed and final database release and database freeze has been declared by Data Management as described in Steps 2, 3 and 5 above.

For the End of Study Analysis reporting, selected Primary Analysis displays (Appendix 13: List of Data Displays) have been identified and will be generated, using the final data.

The displays will be updated (as required) to capture the additional visits and to reflect the final data. If further details are required, a RAP amendment or addendum will be generated to specify the changes.

This RAP details the planned analysis for both database freezes, with the expectation of an observed treatment benefit being observed following the Primary Analysis. In the event that the Primary Analysis reporting does not identify treatment benefit, an abridged set of analysis may be conducted for the end of study analysis, which will be detailed in a RAP amendment or addendum.

4. ANALYSIS POPULATIONS

Population	Definition / Criteria	Analyses Evaluated
Screened	• All participants who were screened for eligibility	• Selected Study Population
Enrolled	• All participants who passed screening and entered the study. Includes Randomized Participants. • 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.	• Selected Study Population
Safety	• Comprises all subjects who receive at least one dose of study treatment. • This population will be based on the treatment the subject actually received.	• Study Population • Efficacy • Safety/tolerability • PD/Biomarker • Exploratory • Health Outcomes
Belimumab Pharmacokinetic (PK-B)	• Subjects in the “Safety” population for whom a post treatment belimumab pharmacokinetic sample was obtained and analysed.	• Belimumab PK

Population	Definition / Criteria	Analyses Evaluated
Rituximab Pharmacokinetic (PK-R)	• Subjects in the "Safety" population for whom a post treatment rituximab pharmacokinetic sample was obtained and analysed	• Rituximab PK
Per-Protocol (PP)	• All participants in the safety population who comply with the protocol. • Protocol deviations that would exclude participants from the PP population are defined in Section 4.1 (Protocol Deviations) and Appendix 1: Protocol Deviation Management and Definitions for Per Protocol Population. • The Per-Protocol set will not be analysed if this population comprises more than 85% of the safety population.	• Subset of Efficacy/PD/ Biomarker
Completer	• Subjects who completed the 52 Week treatment visits AND general follow up phase of the study including the visit at Week 68 **NOTE:** • Definition as per protocol Section 5.5 Subject and Study Completion • Does not include any subjects with a study treatment discontinuation flag.	• Efficacy • Health Outcomes • PD/Biomarkers • Exploratory

NOTES:

- Please refer to Appendix 13, List of Data Displays which details the population to be used for each display being generated.

4.1. Protocol Deviations

Important protocol deviations (including deviations related to study inclusion/exclusion criteria, conduct of the trial, patient management or patient assessment) will be summarized and listed.

Separately, important deviations which result in exclusion from the per-protocol analysis population will also be summarized and listed.

Protocol deviations will be tracked by the study team throughout the conduct of the study in accordance with the current Protocol Deviation Management Plan. [Version 007 (18-Sep-2019 or higher)].

- Data related to the Primary Analysis will be reviewed prior to unblinding and freezing the database to ensure all important deviations and deviations which lead to the exclusion from the analyses are captured and categorized on the protocol deviations dataset.
- This dataset will be the basis for the summaries and listings of the protocol deviations.

All deviations will be discussed and adjudicated as important or not important.

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.

4.2. Per-Protocol Population

Periodic review of the per-protocol population will be conducted during the course of the study, with the final assessment made prior to unblinding the data for Primary Analysis reporting.

The per-protocol population will be primarily based on an assessment of the important protocol deviations. However, non-important deviations or other study conduct issues may be identified during the study and warrant a subject's exclusion from the per-protocol population. This will be documented in the protocol deviation adjudication meeting minutes prior to database freeze. Only protocol deviations or study conduct issues that have the potential to impact a subset of Efficacy/PD/Biomarker evaluations will lead to a subject's exclusion from the per-protocol population.

5. CONSIDERATIONS FOR DATA ANALYSES AND DATA HANDLING CONVENTIONS

5.1. Study Treatment & Sub-group Display Descriptors

Treatment Group Descriptions			
RandAll NG		Data Displays for Reporting	
Code	Description	Description	Order [1]
A	Co-administration therapy	Co-administration	2
B	Belimumab 200 mg SC injection	Belimumab	3
C	Rituximab 1,000 mg IV infusion	Rituximab	4
P	Placebo	Placebo	1

NOTES:

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

Treatment Descriptors, Colors, Line Style and Symbols for Reporting

Treatment Descriptor	Color	SAS Color	Line Style	Symbol
Co-administration	Green	CX228B22	LongDash	Circle (filled)
Belimumab	Blue	CX0000FF	Dash	Triangle (filled)
Rituximab	Purple	CX800080	ShortDash	Diamond (filled)
Placebo	Brown	CXA05000	Solid	Square (filled)

5.2. Baseline Definitions

For all endpoints (except as noted in baseline definitions) the baseline value will be the latest pre-dose assessment with a non-missing value, including those from unscheduled visits. If time is not collected, Day 0 assessments are assumed to be taken prior to first dose and used as baseline.

Parameter	Study Assessments Considered as Baseline			Baseline Used in Data Display
	Screening	Day 0 (Pre-Dose)	Week 8	
Safety				
Laboratory [1]	X	X		Day 0 (Pre Dose) [3]
Vital Signs	X	X		Day 0 (Pre Dose) [3]
CSSRS		X		Day 0 (Pre Dose)
Neurological Assessment		X		Day 0 (Pre Dose)
Immunogenicity (Rituximab)			X	Week 8

Parameter	Study Assessments Considered as Baseline			Baseline Used in Data Display
	Screening	Day 0 (Pre-Dose)	Week 8	
Efficacy				
ESSDAI/ClinESSDAI	X			Screening
Salivary Flow	X			Screening
Oral Dryness	X			Screening
Salivary Gland B Cell Quantification	X			Screening
Exploratory				
Ocular Dryness	X			Screening
Lacrimal Gland Function	X			Screening
PGA	X			Screening
Unstimulated Salivary Flow	X			Screening
BLyS		X		Day 0 (Pre Dose)
Serologic Markers	X	X		Day 0 (Pre Dose) [3]
Flow Cytometry	X	X		Day 0 (Pre Dose) [3]
Minor Salivary Gland Histology Assessments [2]	X			Screening
Health Outcomes				
ESSPRI	X			Screening
PRO FAD SSI SF	X			Screening
PtGA	X			Screening

Notes:

1. Includes Clinical Chemistry, Hematology, Urinalysis and Other Screening Tests
2. Salivary gland biopsy may be conducted at any time during screening up to day 0
3. If day 0 pre dose assessment is missing, the screening assessment will be used as baseline.

- Unless otherwise stated, the mean of replicate assessments at any given time point will be used as the value for that time point.
- Unless otherwise stated, if baseline data are missing no derivation will be performed and baseline will be set to missing.

Changes from baseline will be derived as follows.

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

NOTES:

- Unless otherwise specified, the baseline definitions specified in Section 5.2 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.

5.3. Multi-center Studies

In this multicenter global study, enrolment will be presented by country and site.

5.4. Examination of Covariates, Other Strata and Subgroups

5.4.1. Covariates and Other Strata

Independent variables to be included in efficacy and exploratory analyses are described in Section 8 and Section 9, respectively.

5.4.2. Examination of Subgroups

Subgroup analysis based on following Randomization Stratum ESSDAI categories may be analysed as a post SAC analysis.

ESSDAI groups:

- Low (<5)
- Moderate (>=5 & <=12)
- Severe (>12)
- High Activity (>=14)

5.5. Multiple Comparisons and Multiplicity

No adjustments for multiple comparisons are planned.

5.6. Other Considerations for Data Analysis and Data Handling Conventions

Other considerations for Data Analysis are described in the appendices;

Section	Component
11.3	Appendix 3: Treatment States and Phases
11.4	Appendix 4: Data Display Standards and Handling Conventions
11.5	Appendix 5: Derived and Transformed Data
11.6	Appendix 6: Reporting Standards for Missing Data
11.7	Appendix 7: Values of Potential Clinical Importance

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 1 provides an overview of the planned study population analyses for the primary analyses, and the specific data displays are captured in Appendix 13: List of Data Displays.

Table 1 Overview of Planned Study Population Analyses

Display Type	Data Displays Generated		
	Table	Figure	Listing
Randomization			
Randomization and Actual Treatments			Y
Subject Disposition			
Subject Disposition	Y [1]		
Reasons for Screening Failures	Y		Y
Reasons for Withdrawals	Y		Y
Treatment Discontinuations			Y
Important Protocol Deviations	Y		Y [2]
Enrolment	Y		
Exclusions from Study Populations	Y		Y
Demographic and Baseline Characteristics			
Demographic Characteristics	Y		Y
Race & Racial Combinations	Y		Y
Smoking Use	Y		
Family History of Cardiovascular Risk Factors	Y		
Physical Examination			Y
Medical Condition & Concomitant Medications			
Medical Conditions (Sjögren specific)	Y		Y
Medical Conditions (non-Sjögren specific)	Y		Y
Concomitant Medication	Y		Y

NOTES:
Y = Yes display generated.
[1] For End of Study, a further subject disposition table will be generated to summarize subject's completion status upto Week 52 & W68, subjects withdrawn and who continued or discontinued study visits.
[2] For End of Study, a further listing will be generated to capture important PDs related to COVID-19.

Selected Primary Analysis study population displays will also be generated for the End of Study Analysis and are identified in Appendix 13: List of Data Displays. Where required, programming notes (Appendix 13 or Mock Shell Examples) have been included for any specific changes based on the Primary Analysis displays.

7. PRIMARY STATISTICAL ANALYSES

7.1. Safety Analyses

7.1.1. Overview of Planned Analyses

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

Table 2 provides an overview of the planned safety Primary Analyses, with further details of data displays being presented in Appendix 13: List of Data Displays.

Table 2 Overview of Planned Safety Analyses

Endpoint	Absolute				Change from Baseline			
	Summary		Individual		Summary		Individual	
	T	F	F	L	T	F	F	L
Exposure								
Extent of Exposure	Y			Y				
Adverse Events								
All AEs [1]	Y			Y				
All Drug-Related AEs	Y							
AEs of Special Interest	Y			Y				
Serious AEs	Y							
Withdrawal AEs	Y			Y				
Fatal Adverse Events	Y			Y				
Common AEs [2]	Y							
Reasons for Considering as SAE				Y				
Laboratory Values								
Immunoglobulins	Y	Y		Y	Y	Y [3]		
Clinical Chemistry	Y [4]			Y	Y [4]			
Hematology	Y [4]	Y		Y	Y [4] [5]			
Liver	Y							Y
Urinalysis (Dipstick)	Y			Y				
Other Screening Tests [6] [7]				Y				
C-Reactive Protein	Y				Y			
CD4 and CD8	Y	Y		Y				
ECGs								
ECG	Y							
Abnormal ECG				Y				
Vital Signs								
Vital Signs	Y [8]			Y	Y [8]			

Endpoint	Absolute				Change from Baseline			
	Summary		Individual		Summary		Individual	
	T	F	F	L	T	F	F	L
Neurological Symptoms								
Neurological Symptoms	Y			Y				
Columbia-Suicide Severity Rating Scale								
C-SSRS	Y			Y				
Immunogenicity								
Belimumab Immunogenicity	Y			Y				
Rituximab Immunogenicity[9]	Y			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. Listing will include subject's numbers for individual AE's & AE system organ classes, preferred terms and verbatim text. A separate listing will be generated for Primary & EoS to capture with subjects with post Week 68/FU events.
2. Common AEs are adverse events occurring with a frequency > 5%.
3. IgG, IgA & IgM will be reported
4. Including summaries of Toxicity grading
5. Including evaluation of shifts from baseline.
6. Positive/abnormal findings
7. Other screening tests include HIV, Hepatitis B (HBsAg), HbcAb, Hepatitis C (Hep C antibody), FSH, estradiol and serum or urine hCG pregnancy test.
8. Including evaluation of PCI criteria
9. Reported only for End of Study (Baseline is defined as Week 8)

Selected Primary Analysis safety displays will also be generated for the End of Study Analysis and are identified in Appendix 13: List of Data Displays. Where required, programming notes (Appendix 13 or Mock Shell Examples) have been included for any specific changes based on the Primary Analysis displays.

Primary Analysis: Summarized safety data for all completed visits up to Week 68 (where reported by visit) and up to Week 104 (where not reported by visit), with a cut-off date of 9 September 2019 (Week 52 LSLV).

On completion of the Primary Analysis, it was noted that the safety data included 39 AEs (out of a total of 49) reported during the IFU phase that were not within the defined scope of the protocol for AE collection. The over-reported AEs included 2 SAEs reported by 2 subjects; both were assessed as unrelated to study treatment. An additional blinded listing of the 49 AEs reported during the IFU period was generated. Full details are included in the Primary Analysis CSR.

End of Study Analysis: Summarize AE/AESI safety data for all completed visits up to Week 68 only to include AEs collected in the defined protocol AE collection period. An unblinded listing of the AEs reported during the IFU period will be generated, which will also include information as to whether the AE occurred pre or during the COVID-19 pandemic.

Additional safety analyses may (if required) also be conducted to further assess the impact of the over-reported AEs in the FU or COVID-19 pandemic.

7.1.2. Immunogenicity

Exploratory Analyses: Immunogenicity
Endpoints
• Immunogenic Response to Belimumab • Immunogenic response to Rituximab (will not be reported until all subjects have completed the follow-up phases of the study)
Summary Results Presentation
The method for calculation of belimumab & rituximab immunogenic response is given in Section 11.5.6.1. The belimumab and rituximab immunogenicity response will be summarized for the binding antibody assay by treatment group and visit. The table will include the number and proportion of subjects in each result category for each visit. Binding confirmatory assay results will be categorized as Negative, Positive, or Unknown. Positive samples in the binding assay are further categorized as Transient Positive (i.e. single positive response that does not occur at the final assessment) or Persistent Positive (i.e. positive response that occurs at least 2 consecutive assessments or a single result at the final assessment) Belimumab only: Presence of neutralizing antibodies and titre for samples confirming positive in the blinding assay will be listed. Rituximab: Baseline is Week 8. Titre for samples confirming positive in the blinding assay will be listed.

7.1.3. Immunoglobulin

Exploratory Analyses: Immunoglobulin
Endpoints
The number and percentage of subjects with immunoglobulin values (IgG, IgA, and IgM) below the LLN at each visit will be presented The number and percentage of subjects with immunoglobulin values (IgG, IgA, and IgM) above the ULN at each visit will be presented **Worst IgG toxicity grade** The number and percentage of subjects at each toxicity grade will be assessed at baseline and also for anytime post baseline. **IgG toxicity ≥ 2 grade shift post-baseline** The number and percentage of subjects with at least one ≥ 2 grade shift as well as the specific shift categories: Grade 0 to 2, Grade 0 to 3, Grade 0 to 4, Grade 1 to 3, Grade 1 to 4 and Grade 2 to 4 will be computed by treatment group.

7.1.4. Adverse Events of Special Interest

The AESI definitions from Section 15 and Section 16 of the current belimumab PSAP (Note: Version 5 was used for the interim analysis and version 6 for the final analysis) will be followed to identify the program level AESI. Search terms based on the current version of MedDRA (Primary Analysis = 22.0 and End of Study = 23.0) at the time of database release will be utilized. The additional study specific AESI are:

Severe skin reaction: All events identified by Severe Cutaneous Adverse Reactions SMQ broad search will be adjudicated (Preferred terms corresponding to broad search from SMQ are given in the Section 11.5.3.1)

Cardiac Disorders: All events identified by applying Cardiac Arrhythmias SMQ, Cardiac Failure SMQ, Cardiomyopathy SMQ, and Ischaemic heart disease SMQ will be adjudicated (Preferred terms corresponding to broad search from SMQ are given in Section 11.5.3.1)

Posterior Reversible Encephalopathy Syndrome (PRES): Defined as all events identified in the preferred term "Posterior Reversible Encephalopathy Syndrome".

Progressive Multifocal Leukoencephalopathy (PML): Defined as all events identified in the preferred term "Progressive multifocal leukoencephalopathy"

Adverse events related to the biopsy: Preferred terms corresponding to adverse events related to biopsy will be reviewed and adjudicated.

Malignancies, serious post-administration systemic reactions, potential opportunistic infections, suicide/self-injury, fatalities, severe infections and skin reactions will be adjudicated at the subject level by the GSK blinded Safety Review Team (SRT). Additionally, the study specific AESI's will be adjudicated at the subject level by the study team. Adjudication will be conducted periodically with a final adjudication completed prior to the DBF for the primary analysis. Further adjudications (periodically and prior to End of Study DBF) will also be performed for the End of Study analysis. Only adjudicated study specific AESI's will be reported.

An overall summary of AESI will be presented and each specific category of AESI will be presented separately by PT. Infection AESIs will also be presented by PT for all infections leading to discontinuation. The number and percentage of subjects with at least one occurrence and the number of events for each AESI will be provided. The AESI categories are:

Malignant Neoplasms

- Malignancies Excluding non-melanoma skin cancer (NMSC)
- Malignancies Including NMSC
- Solid Tumor
- Hematologic
- Skin (All)
    - NMSC

- Excluding NMSC
- Tumors of unspecified malignancy adjudicated as malignant per GSK adjudication

Post-Administration Systemic Reactions

- Post-Administration Systemic Reactions per Anaphylactic Reaction Customized MedDRA Query (CMQ) narrow search
- Post-Administration Systemic Reactions per Anaphylactic Reaction CMQ broad search
- Post-Administration Systemic Reactions per Anaphylactic Reaction CMQ algorithmic search
- Serious Anaphylaxis per Sampson Criteria
- Serious Acute Post-Administration Systemic Reactions/Hypersensitivity per GSK adjudication
  - Serious Acute Post-Administration Systemic Reactions Excluding Hypersensitivity per GSK adjudication
  - Serious Acute Hypersensitivity Reactions per GSK adjudication
- Serious Delayed Acute Hypersensitivity Reactions per GSK adjudication
- Serious Delayed Non-Acute Hypersensitivity Reactions per GSK adjudication

All Infections of Special Interest

- All opportunistic infections per GSK adjudication
- Opportunistic infections per GSK adjudication excluding Tuberculosis and Herpes Zoster
  - Serious opportunistic infections per GSK adjudication excluding Tuberculosis and Herpes Zoster
- Active Tuberculosis
  - Non-Opportunistic
  - Opportunistic
- Herpes Zoster
  - Non-Opportunistic
  - Opportunistic
    - Recurrent
    - Disseminated
- Sepsis

Depression/suicide/self-injury

- Depression (Inc. mood disorders and anxiety)
- Suicide/self-injury
- Serious Suicide/Self-injury per GSK Adjudication
  - Suicidal Behaviour per GSK Adjudication
    - Completed Suicide per GSK Adjudication
  - Suicidal Ideation per GSK Adjudication
  - Self-injurious Behaviour Without Suicidal Intent per GSK Adjudication

Deaths

Study Specific AESI

- Severe skin reaction per GSK Adjudication
- Cardiac Disorders
- Posterior Reversible Encephalopathy Syndrome (PRES)
- Progressive multifocal leukoencephalopathy (PML)
- Adverse events related to the biopsy

7.1.4.1. Post-Administration systemic reactions by Belimumab/Placebo Injection

Summaries of post-injection systemic reactions will be presented by the first six injections (belimumab/placebo) in addition to overall injections for the following categories:

- Post-Injection Systemic Reactions per Anaphylactic Reaction CMQ broad search (on the day of the injection or within 3 days after the injection)
- Serious Post-Injection Systemic Reactions per Anaphylactic Reaction CMQ broad search (on the day of the injection or within 3 days after the injection)
- Serious Acute Post-Injection Systemic Reactions/Hypersensitivity per GSK adjudication
- Serious Delayed Acute Post-Injection Systemic Reactions per GSK adjudication
- Serious Delayed Non-Acute Post-Injection Systemic Reactions per GSK adjudication

7.1.4.2. Post-Administration Systemic Reactions by Rituximab/Placebo Infusion

Summaries of post-infusion systemic reactions will be presented by the first two infusions (rituximab/placebo):

- Post-Injection Systemic Reactions per Anaphylactic Reaction CMQ broad search (on the day of the infusion or within 3 days after the infusion)

8. SECONDARY STATISTICAL ANALYSES

8.1. Efficacy and Biomarker Analyses

8.1.1. Overview of Planned Efficacy and Biomarker Analyses

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

Table 3 provides an overview of the planned efficacy Primary Analyses, with further details of data displays being presented in Appendix 13: List of Data Displays.

Table 3 Overview of Planned Efficacy and Biomarker Analyses

Endpoint	Absolute							Change from Baseline						
	Stats Analysis			Summary		Individual		Stats Analysis			Summary		Individual	
	T	F	L	T	F	F	L	T	F	L	T	F	F	L
Clinical Efficacy														
ESSDAI Score (Uncorrected & Corrected)				Y	Y		Y	Y	Y [2]		Y	Y		
ESSDAI Domains (Uncorrected & Corrected)				Y	Y		Y				Y			
ESSDAI Responder (Corrected)	Y [2]			Y	Y									
ClinESSDAI (Corrected)				Y			Y	Y [2]			Y			
ClinESSDAI Responder (Corrected)				Y										
ESSDAI Corrected /ClinESSDAI Corrected Correlations												Y[2]		
Stimulated Salivary Flow				Y			Y	Y [2]			Y	Y		
Oral Dryness NRS				Y			Y	Y [2]			Y	Y		
Biomarker														
Number of B cells (CD20) /mm^2 in Salivary Gland Biopsy				Y			Y	Y [1]			Y[1]	Y[1]		Y

NOTES:

- T = Table, F = Figure, L = Listing, Y = Yes display generated.
- Stats Analysis = Represents TFL related to any formal statistical analyses (i.e. modeling) 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.
- NRS, Numeric Response Scale

[1] Based on change from baseline
[2] Will not be generated for EoS

Selected Primary Analysis efficacy displays will also be generated for the End of Study Analysis and are identified in Appendix 13: List of Data Displays. Where required, programming notes (Appendix 13 or Mock Shell Examples) have been included for any specific changes based on the Primary Analysis displays.

8.1.1.1. ESSDAI

ESSDAI scores disease activity in 12 domains. In 5 (renal, PNS, CNS, cutaneous and pulmonary) of the domains, ESSDAI requires that if activity has been present for greater than or equal to 12 months then it must be treated as irreversible damage and the activity should be scored as zero (Seror, 2015a). This is a problem for clinical trials of long duration such as study 201842 because it can result in misleading evidence of reduced activity. For that reason, a corrected ESSDAI score will be calculated.

The ESSDAI Corrected score will be calculated as:

- For each damage eligible domain
  - where damage is scored as present for 1st time after screening **THEN** corrected activity score = damage score for that domain for that visit and the activity score for all subsequent visits should be changed to equal the corresponding damage domain score
  - Except in rare cases where the activity score for the visit concerned is already equal to or greater than the damage score, in which case no change should be made.
- If damage is scored as present at screening **AND** if the damage score increases in level of involvement (low to moderate or moderate to high) after the screening visit then the activity score for that domain for that visit and all subsequent visits should be changed to equal the corresponding damage domain score
  - Except in rare cases where the activity score for the visit concerned is already equal to or greater than the damage score, in which case no change should be made.
- If damage is scored at screening and remains constant across visits, then no programmed correction can or should be made to the activity scores.

Further details are included in Section 11.5.4 Efficacy.

The primary inference will be based on the corrected ESSDAI score, with the uncorrected score being used as a supporting sensitivity analysis to assess any impact.

For the Primary Analysis, the correction could not be applied for 1 subject (ID PPD) for one domain of ESSDAI. The complexity of disease scoring in the PNS domain for this subject prevented the correction algorithm from appropriately recording low activity for this domain from Week 24 onwards. Consequently, the total corrected ESSDAI score for this subject is underestimated by 5 points for each visit from Week 24 onwards. Only a single domain of ESSDAI was affected and there is thought to be no impact on the interpretation of the overall corrected ESSDAI data. This subject will subsequently not be corrected for the End of Study Analysis.

8.1.2. Planned Efficacy and Biomarker Statistical Analyses

Secondary Statistical Analyses – Efficacy (MMRM)
Endpoint(s)
• Change from Baseline in ESSDAI Total Score (Uncorrected & Corrected) • ESSDAI Domain Scores (Corrected) • ESSDAI Improvements (At Least 1 Category on Domain Score) (Corrected) • ESSDAI Worsening (At Least 1 Category on Domain Score) (Corrected) • Change from Baseline in Stimulated Salivary Flow • Change from Baseline in Oral Dryness Numeric Response Scale
Model Specification
• Endpoints will be statistically analyzed using a mixed model repeated measures (MMRM) • Terms fitted in MMRM models will include: Fixed Categorical : Treatment, Visit, Treatment * Visit Interaction Fixed Continuous Covariates : Baseline (see Section 5.2 for baseline definition) Repeated : Visit • For the analysis of salivary flow and oral dryness numeric response, ESSDAI stratification (moderate or severe) will also be included as a fixed categorical term.
Model Checking & Diagnostics
• Refer to Appendix 9: Model Checking and Diagnostics for Statistical analyses.
Model Results Presentation
• Adjusted means and corresponding standard error of means (SEs) and 95% confidence intervals will be presented for changes from baseline on each treatment by Visit. together with estimates and the corresponding 95% confidence intervals for the comparisons of interest. • If the model checking deems the above parametric analysis to be unsuitable, nonparametric rank Hodges-Lehmann's confidence intervals will be provided in order to assess the robustness of the parametric analysis. This will be carried out in addition to the parametric analyses • For ESSDAI Total Score (Uncorrected and Corrected), plots of LS means and SE for changes from baseline for each treatment at all visits up to Week 52 as derived from the MMRM model will be presented.
Summary Results Presentation
• Summary statistics (n, mean, median, minimum and maximum), will be presented on the absolute values at each visit and the change from baseline at each visit. • Plots of the mean and corresponding SE on changes from baseline over time for each treatment will also be presented.
Supportive Analyses
• For ESSDAI, additional statistical analysis using MMRM will be conducted for changes from baseline for each treatment at all visits up to Week 68/FU, using the completer population. • The relationship between Scoring of ESSDAI (corrected) and Clinical ESSDAI (corrected) will be assessed graphically. • ESSDAI domain scores (Corrected) will be summarized. The number and proportion of subjects reporting no, Low, moderate (and high response where applicable), will be computed for each of the 12 domains by treatment and visit. • Improvements in ESSDAI Domain Scores (corrected) will be evaluated. For each domain, the number and proportion of improvers (i.e. higher to lower category) out of the subjects who had an activity score on the specific domain at baseline will be computed. The number and proportion of subjects with worsening will be assessed for each ESSDAI Domain (Corrected). The domain level denominator is the subset of subjects who do not have highest level of symptom at baseline.

Secondary Statistical Analyses – Efficacy (Bayesian)

Endpoint(s)

- Change from baseline in Total ESSDAI Score (Corrected)

Model Specification

- A Bayesian repeated Measures model will be used to fit the change from baseline in Total ESSDAI Score (Corrected).
- A multivariate (MVN) normal distribution is assumed for the vector of changes from baseline for each subject (i.e. the change from baseline at weeks 12, 24, 36 & 52).
- Markov-Chain-Monte-Carlo (MCMC) method in SAS will be used to derive the posterior distributions of the endpoint.
- A linear model for Change from Baseline (CFB) in Total ESSDAI Score at each Week (visit) will be constructed to model the within-subject covariance structures:

  CFB = Intercept + Treatment + Baseline + Week + Treatment*Week

  Terms fitted in the model will include:
  Fixed Categorical: Week (Week 12 to Week 52), Treatment, Treatment*Week Interaction
  Fixed Continuous: Baseline
  Random: Subject

- The prior for the variance covariance matrix will follow an Inverse Wishart Distribution.
- Set seed=123456 with simulation size of 100,000 (i.e. every 10th iteration will be kept which will form the final MCMC (thinned) sample of 10,000) & 10,000 burn-in iterations. The simulation size and number of burn-in iterations may be updated during the convergence check.
- Vague priors (normal (0, var=1e6)) will be used for regression parameters.

Model Checking & Diagnostics

- Refer to Appendix 9: Model Checking and Diagnostics for Statistical analyses.

Summary Results Presentation

- The sample size n, mean, median, standard deviation and highest posterior density (HPD: smallest interval width among all credible intervals) interval will be presented from the posterior density function.
- The posterior distribution will be used to produce several probability statements (where θ is the ESSDAI change from baseline), such as (but not limited to and maybe refined):
  - Pr ($\theta_{\text{Co-administration}}$, 24w – θ_{Placebo}, 24w < 0 | 201842 data)
  - Pr ($\theta_{\text{Co-administration}}$, 52w – θ_{Placebo}, 52w < 0 | 201842 data)
  - Pr ($\theta_{\text{Co-administration}}$, 24w – θ_{Placebo}, 24w < 3 | 201842 data)
  - Pr ($\theta_{\text{Co-administration}}$, 52w – θ_{Placebo}, 52w < 3 | 201842 data)

  - Pr ($\theta_{\text{Co-administration}}$, 24w – $\theta_{\text{Belimumab}}$, 24w < 0 | 201842 data)
  - Pr ($\theta_{\text{Co-administration}}$, 52w – $\theta_{\text{Belimumab}}$, 52w < 0 | 201842 data)

  - Pr ($\theta_{\text{Co-administration}}$, 24w – $\theta_{\text{Rituximab,}}$ 24w < 0 | 201842 data)
  - Pr ($\theta_{\text{Co-administration}}$, 52w – $\theta_{\text{Rituximab,}}$ 52w < 0 | 201842 data)

  - Pr ($\theta_{\text{Belimumab}}$, 24w – θ_{Placebo}, 24w < 0 | 201842 data)
  - Pr ($\theta_{\text{Belimumab}}$, 52w – θ_{Placebo}, 52w < 0 | 201842 data)
  - Pr ($\theta_{\text{Belimumab}}$, 24w – θ_{Placebo}, 24w < 3 | 201842 data)
  - Pr ($\theta_{\text{Belimumab}}$, 52w – θ_{Placebo}, 52w < 3 | 201842 data)

Secondary Statistical Analyses – Efficacy
Endpoints
• ESSDAI Responders (Corrected)
Summary Results Presentation

• The proportion of ESSDAI responders based on corrected total ESSDAI score will be summarized descriptively using counts and percentages by treatment and visit. Responders are defined as below
  • **Responders 1** - Subjects with a reduction in total ESSDAI of at least 5 points over baseline
  • **Responders 2** - Subjects with a reduction in total ESSDAI of at least 3 points over baseline
  • **Responders 3** - Subjects with a reduction in total ESSDAI of at least 3 points over baseline, and ESSDAI Total Score <5
  • **Responders 4** - ESSDAI Total Score < 5
• The proportion of ESSDAI responders will be presented as a bar chart grouped by treatment for each visit.

Model Specification
• Responder endpoints will be statistically analysed using a Generalised Estimating Equations (GEE) model • The model will be fitted using an unstructured covariance structure of the correlated responses. • Terms fitted in GEE models will include: Fixed Categorical : Treatment, Visit, Treatment*Visit Interaction Fixed Continuous Covariate: Baseline Total ESSDAI Score Repeated : Visit
Model Checking & Diagnostics
• Refer to Appendix 9: Model Checking and Diagnostics for Statistical analyses.
Model Results Presentation
• The Binary endpoints will be summarized using counts and proportions of subjects achieving a response by treatment group. • Differences in the proportions of subjects achieving response between treatment groups will be summarized by Visit (up to Week 52). 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.

Secondary Statistical Analyses – Efficacy
Endpoint(s)
• ClinESSDAI Responders (Corrected)
Summary Results Presentation
• The proportion of ESSDAI responders based on corrected total ESSDAI score will be summarized descriptively using counts and percentages by treatment and visit. Responders are defined as subjects with a reduction in total ClinESSDAI of at least 3 points over baseline

Secondary Statistical Analyses – Biomarker
Endpoint(s)
• Absolute change from baseline in Number of B Cells (CD20)/mm^2 in salivary gland biopsy at Week 24
Model Specification
• The absolute change at Week 24 will be analysed using the Hodges-Lehmann method to provide a

Secondary Statistical Analyses – Biomarker
95% confidence interval for the contrasts of interest specified in Section 2.5 at Week 24
Model Result Presentation
• Along with the number of subjects (n) and median of absolute change from baseline of each treatment group, median difference with 95% Confidence intervals estimated from the H-L method will be presented at week 24 for the contrasts of interest.
Summary Results Presentation
• Summary statistics (n, mean, median, minimum and maximum) will be presented on the absolute values and the absolute change from baseline at Week 24.

8.2. Pharmacokinetic Analyses

8.2.1. Overview of Planned Pharmacokinetic Analyses

The pharmacokinetic (PK) analyses will be based on the Pharmacokinetic (PK-B and PK-R) populations, unless otherwise specified.

Table 4 provides an overview of the planned primary analyses, with full details being presented in Appendix 13: List of Data Displays.

Table 4 Overview of Planned Pharmacokinetic Analyses

Endpoint	Untransformed							Log-Transformed						
	Stats Analysis			Summary		Individual		Stats Analysis			Summary		Individual	
	T	F	L	T	F	F	L	T	F	L	T	F	F	L
Serum Drug Concentrations				Y	Y	Y[1]								

NOTES:

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

1. Linear and Semi-Log plots will be created on the same display.

8.2.2. Drug Concentration Measures

Refer to Appendix 4: Data Display Standards & Handling Conventions (Section 11.4.1 Reporting Process & Standards).

Serum belimumab concentrations will be listed and summarized by visit and nominal time. Standard summary statistics will be calculated (i.e. mean, standard deviation, and 95% confidence interval of mean, geometric mean, 95% confidence interval for geometric mean, % coefficient of variation (CV), median, minimum and maximum). Individual subject and median PK concentrations profiles will be graphically presented.

8.2.2.1. Statistical Analysis of Pharmacokinetic Parameters

No formal statistical analyses will be performed.

8.3. Pharmacokinetic / Pharmacodynamic Analyses

The Pharmacokinetic / Pharmacodynamic analyses will be based on the "Safety" and "PK-B" populations, unless otherwise specified.

The primary goal of this analysis is to characterize the pharmacokinetic/pharmacodynamic relationship of belimumab administered through injection in subjects with Primary Sjogren's syndrome.

1. No formal population pharmacokinetic/pharmacodynamics analyses are planned. The relationships will be explored using descriptive methods only.

Table 5 provides an overview of the pharmacokinetic/pharmacodynamics analyses, with details being presented in Appendix 13: List of Data Displays.

Table 5 Overview of Pharmacokinetic / Pharmacodynamic 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
Flow cytometry B cells (CD19+) /serum Belimumab concentration Comparison						Y [1]								

NOTES:

- T = Table, F = Figure, L = Listing, Y = Yes display generated.
- Stats Analysis = Represents TFL related to any formal statistical analyses (i.e. modeling) 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] For Belimumab and Combination Treatment Groups

9. OTHER STATISTICAL ANALYSES

9.1. Exploratory

9.1.1. Overview of Exploratory Analysis

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

Table 6 provides an overview of the planned exploratory Primary Analyses, with full details of data displays being presented in Appendix 13: List of Data Displays.

Table 6 Overview of Exploratory 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
Clinical Efficacy														
Ocular Dryness NRS				Y			Y				Y	Y		
Lacrimal Gland Function				Y			Y				Y	Y		
PGA				Y			Y				Y	Y		
Unstimulated Salivary Flow				Y			Y				Y	Y		
ESSDAI Supplementary Damage Assessments				Y			Y							
Biomarkers														
BLyS levels in blood Free BLyS Total BLyS[4]				Y			Y				Y[1]	Y[1]		
Flow CytometryParameters[2]				Y	Y[3]		Y	Y[1, 3, 5]			Y[1]	Y[1,3]		
Serologic Markers[2]				Y			Y				Y[1]	Y[1]		
Complement Factors[2]				Y			Y				Y[1]	Y[1]		
Exploratory Minor Salivary Gland Histology Assessments[2]				Y	Y[3]		Y	Y[1,3, 5]			Y[1]	Y[1,3]		
Serum Chemokines - CXCL13				Y							Y[1]	Y[1]		
ESSDAI/Salivary Gland CD20+ B cell Evaluation					Y[5]									
Flow cytometry B Cells (CD19+) /serum BLyS Evaluation					Y									

NOTES:

- T = Table, F = Figure, L = Listing, Y = Yes display generated.
- Stats Analysis = Represents TFL related to any formal statistical analyses (i.e. modeling) 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.
- NRS; Numeric Response Scale

1. Only Percentage Change from Baseline will be presented
2. See Section 11.5.6 for parameters.
3. Subset of the parameters as defined in Section 9.1.2
4. Total BLyS concentration only for End of Study analyses
5. Will not be reported for End of Study

Selected Primary Analysis exploratory displays will also be generated for the End of Study Analysis and are identified in Appendix 13: List of Data Displays. Where required, programming notes (Appendix 13 or Mock Shell Examples) have been included for any specific changes based on the Primary Analysis displays.

9.1.2. Planned Exploratory Analyses

Exploratory Analyses: Clinical Efficacy and Biomarkers
Endpoints
Salivary Gland Assessments • Absolute values • Change from Baseline • Percentage Change from Baseline Refer to Table 13 for parameters to be included in the summary table
Summary Results Presentation
• Descriptive statistics (N, n, arithmetic mean, standard deviation, median, minimum and maximum) will be calculated and summarized by treatment group and visit for the above endpoints. Absolute values and changes from baseline will be assessed.
Model Results Presentation
• The absolute change from baseline for selected parameters: Lymphocyte Focus Score (in 4mm^2), B (CD20) / T (CD3) cell ratio and Plasma cell (CD138+; both - CD20pos and CD20neg) count/mm^2) at Week 24 will be analysed using Hodges-Lehmann method to provide a non-parametric 95% confidence interval for the contrasts of interest at Week 24 specified in Section 2.5.
Endpoints
• Ocular Dryness NRS • Lacrimal gland function (Schirmers test see Section 11.5.4) • PGA • Unstimulated Salivary flow • Free BLyS • Total BLyS (NOTE: Total BLyS concentration only for End of Study analysis) • Serologic Markers: SS-A, SS-B, Rheumatoid factor, Lambda and kappa free light chains Beta 2 microglobulins • Complement Factors (C3, C4, CH50) • Exploratory Minor Salivary Gland histology assessments (see Section 11.5.6) • Serum chemokine CXCL13 Refer to Table 12 for further parameter details

Exploratory Analyses: Clinical Efficacy and Biomarkers
Summary Results Presentation
• Descriptive statistics (N, n, arithmetic mean, standard deviation, median, minimum maximum) will be calculated and summarized by treatment group and visit for the above endpoints. • Absolute values and changes from baseline will be assessed.
Exploratory Analyses: Damage Scoring
• Damage Scores for Cutaneous, pulmonary, renal, PNS and CNS domains of ESSDAI
Summary Results Presentation
• The number and percentage of subjects who report damage will be summarized for each of these 5 domains by treatment and visit. • For the subset of subjects who report damage, a listing will be produced to display damage scoring alongside ESSDAI domain scores. The listing will include only the subject/domain combinations where there is damage reported, and in each case assessments from all visits to be presented.
Exploratory Analyses: Flow Cytometry
• Refer to Table 11 for further details on parameters
Model Results Presentation
• The absolute change from baseline in cell count for each parameter at Week 24 will be analysed using Hodges-Lehmann method to provide a non-parametric 95% confidence interval for the contrasts of interest at Week 24 specified in Section 2.5. Similarly, this analysis will be repeated for the absolute changes in cell counts for each parameter at Week 52
Summary Results Presentation
• The cell counts and percentage change from baseline in cell counts will be summarized (n, mean, median, sd, min, max). Median (± IQR) will be presented by treatment and visit. • B cells (CD19+) will be summarized by treatment and visit • In addition, Naïve B Cells, Memory, Plasmablasts (all), Plasmablast (CD20+), Plasmablast (CD20-), Transitional and Activated B Cells, will all be additionally expressed as % of CD19+ cells and summarized by treatment and visit.
Sensitivity and Supportive Statistical Analyses
The relationship between the change in salivary gland B cell quantification from baseline and ESSDAI scores will be explored: • Scatter plots of changes from baseline to Week 24 for Total ESSDAI score vs Change from baseline to Week 24 in salivary gland B cells will be produced.

9.2. Health Outcomes

9.2.1. Overview of Health Outcome Analysis

Table 7 provides an overview of the planned health outcomes, with full details of data displays being presented in Appendix 13 : List of Data Displays

Table 7 Overview of Health Outcome 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
Patient reported health outcomes														
ESSPRI Score				Y			Y				Y	Y		
ESSPRI Domains - Dryness, Fatigue, Pain				Y			Y				Y	Y		
ESSPRI Responders	Y [1]			Y	Y									
PtGA				Y			Y				Y			
PROFAD-SSI-SF Subscores – PROF, PROFAD and SSI				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. modeling) 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] Will not be generated for EoS

Selected Primary Analysis health outcomes displays will also be generated for the End of Study Analysis and are identified in Appendix 13: List of Data Displays. Where required, programming notes (Appendix 13 or Mock Shell Examples) have been included for any specific changes based on the Primary Analysis displays.

Exploratory analyses of the EXIT Interview Data will be conducted in a separate report under the direction of the VEO/PRO Department after the study is reported and once EXIT Interview data has been delivered by ICON.

9.2.2. Planned Health Outcomes Statistical Analyses

Secondary Statistical Analyses
Endpoint(s)
• Change from Baseline in Total ESSPRI Score • Change from Baseline in ESSPRI Dryness Domain • Change from Baseline in ESSPRI Fatigue Domain • Change from Baseline in ESSPRI Pain Domain • Change from baseline in PROF Subscore

Secondary Statistical Analyses
• Change from baseline in PROFAD Subscore • Change from baseline in SSI Subscore (assessed for female subjects only)
Summary Results Presentation
• Summary statistics for observed values and change from baseline (i.e. screening) will be presented by treatment group and visit, for the dryness domain, fatigue domain, pain domain, and total ESSPRI score • Summary statistics for observed values and change from baseline will be presented by treatment group for the total PROF, PROFAD and SSI Subscore at each time point.
Endpoint(s)
• ESSPRI Responders
Summary Results Presentation

• The proportion of ESSPRI responders will be summarized descriptively using counts and percentages by treatment and visit. The ESSPRI responders are defined as below
  • **Responders 1** - Decrease of Total ESSPRI score of at least 1 point or at least 15% relative to baseline
  • **Responders 2** - Subjects with baseline score of ≥ 5 and Total ESSPRI score of < 5
• The proportion of subjects with an ESSPRI response will be presented as bar chart grouped by treatment for each visit.

Model Specification
• Responder endpoints will be statistically analysed using a Generalised Estimating Equations (GEE) model using visits up to Week 52 • The model will be fitted using an unstructured covariance structure of the correlated responses. • Terms fitted in GEE models will include: Fixed Categorical : Treatment, Visit, Treatment*Visit Interaction Fixed Continuous Covariate : Baseline ESSPRI Score Repeated : Visit
Model Checking & Diagnostics
• Refer to Appendix 9: Model Checking and Diagnostics for Statistical analyses.
Model Results Presentation
• The Binary endpoints will be summarized using counts and proportions of subjects achieving a response by treatment group. • Differences in the proportions of subjects achieving response between treatment groups will be summarized by 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.
Endpoints
• PtGA
Summary Results Presentation
• Summary statistics for actual PtGA scores as well as changes from baseline will be presented for each time-point by treatment group.

Secondary Statistical Analyses (Bayesian)

Endpoint(s)

- Change from Baseline in Total ESSPRI Score

Model Specification

- A Bayesian repeated Measures model will be used to fit the change from baseline in Total ESSPRI Score.
- A multivariate (MVN) normal distribution is assumed for the vector of changes from baseline for each subject (i.e. the change from baseline at weeks 12, 24, 36 & 52).
- Markov-Chain-Monte-Carlo (MCMC) method in SAS will be used to derive the posterior distributions of the endpoint.
- A linear model for Change from Baseline (CFB) at each Week (visit) will be constructed to model the within-subject covariance structures:

  CFB = Intercept + Treatment + Baseline + Week + Treatment*Week

  Terms fitted in the model will include:
  Fixed Categorical: Week (Week 12 to Week 52), Treatment, Treatment*Week Interaction
  Fixed Continuous: Baseline
  Random: Subject

- The prior for the variance covariance matrix will follow an Inverse Wishart Distribution.
- Set seed=123456 with simulation size of 100,000 (i.e. every 10th iteration will be kept which will form the final MCMC (thinned) sample of 10,000) & 10,000 burn-in iterations. The simulation size and number of burn-in iterations may be updated during the convergence check.
- Vague priors (normal (0, var=1e6)) will be used for regression parameters.

Model Checking & Diagnostics

- Refer to Appendix 9: Model Checking and Diagnostics for Statistical analyses.

Summary Results Presentation

- The sample size N, mean, standard deviation and highest posterior density (HPD: smallest interval width among all credible intervals) interval will be presented from the posterior density function.
- The posterior distribution will be used to produce several probability statements (where θ is the Total ESSPRI change from baseline), such as (but not limited to and maybe refined):
  - Pr ($\theta_{\text{Co-administration}}$, 24w – θ_{Placebo}, 24w < 0 | 201842 data)
  - Pr ($\theta_{\text{Co-administration}}$, 52w – θ_{Placebo}, 52w < 0 | 201842 data)
  - Pr ($\theta_{\text{Co-administration}}$, 24w – θ_{Placebo}, 24w < 0.67 | 201842 data)
  - Pr ($\theta_{\text{Co-administration}}$, 52w – θ_{Placebo}, 52w < 0.67 | 201842 data)

  - Pr ($\theta_{\text{Co-administration}}$, 24w – $\theta_{\text{Belimumab}}$, 24w < 0 | 201842 data)
  - Pr ($\theta_{\text{Co-administration}}$, 52w – $\theta_{\text{Belimumab}}$, 52w < 0 | 201842 data)

  - Pr ($\theta_{\text{Co-administration}}$, 24w – $\theta_{\text{Rituximab,}}$ 24w < 0 | 201842data)
    Pr ($\theta_{\text{Co-administration}}$, 52w – $\theta_{\text{Rituximab,}}$ 52w < 0 | 201842data)

  - Pr ($\theta_{\text{Belimumab}}$, 24w – θ_{Placebo}, 24w < 0 | 201842 data)
  - Pr ($\theta_{\text{Belimumab}}$, 52w – θ_{Placebo}, 52w < 0 | 201842 data)
  - Pr ($\theta_{\text{Belimumab}}$, 24w – θ_{Placebo}, 24w < 0.67 | 201842 data)
  - Pr ($\theta_{\text{Belimumab}}$, 52w – θ_{Placebo}, 52w < 0.67 | 201842 data)

9.2.3. Planned Health Outcomes Psychometric Analyses

As the original validation of ESSPRI demonstrated a fairly low sensitivity to change, validation analyses will be repeated to support interpretation of the data (including the ESSPRI responder analysis). The analyses will be conducted by a PRO external vendor, following unblinding for the Primary Analyses have been completed. The analysis will be done under the direction of the VEO-PCO Department.

10. REFERENCES

GlaxoSmithKline Document Number 2014N220285_06 Protocol Amendment 06: A randomized, double blind (sponsor open), comparative, multi-center study to evaluate the safety and efficacy of subcutaneous belimumab (GSK1550188) and intravenous rituximab co-administration in subjects with primary Sjögren's syndrome. Effective date 25-JUN-2019.

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Seror R, Meiners P, Baron G, Bootsma H, Bowman SJ, Vitali C, et al. Development of the ClinESSDAI: a clinical score without biological domain. A tool for biological studies. Ann Rheum Dis. 2016 Nov;75(11):1945–50.

Seror R, Theander E, Brun JG, Ramos-Casals M, Valim V, Dörner T, et al. Validation of EULAR primary Sjögren's syndrome disease activity (ESSDAI) and patient indexes (ESSPRI). Ann Rheum Dis. 2015b May;74(5):859–66.

11. APPENDICES

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

11.1.1. Exclusions from Per-Protocol Population

Subjects will be excluded from the per-protocol population if any of the following criteria apply. The outputs for the per-protocol population will not be produced if the per-protocol population comprises >85% of the safety population subjects.

- Received wrong treatment most of the time (>50% of the time).
- Did not receive treatment most of the time (>50% of the time).
- Did not have a clinical diagnosis of Primary Sjögren's Syndrome according to Inclusion Criterion #2.
- Did not have baseline unstimulated salivary flow >0.0 mL/min or stimulated baseline salivary flow >0.05 mL/min) as defined by inclusion criterion #3.
- Did not have symptomatic oral dryness (≥5/10 on subject completed Numeric Response Scale) as defined by inclusion criterion #4.
- Did not have systemically active disease defined as an ESSDAI score ≥5 at screening (Inclusion Criterion 5).
- Received an excluded systemically administered immunosuppressive or immunomodulatory medication prior to screening (see Exclusion Criteria 17-22).
- Received a prohibited systemically administered immunosuppressive or immunomodulatory medication prior to Week 52.
- Deviation from study blind/unblind procedures: Investigator/site staff did not remain blinded to one or both treatment assignments through Week 52/Early Withdrawal Visit.
- Other, a deviation that does not satisfy the above criteria, however, in the judgment of the clinical team, including the medical monitor, constitutes an exclusion from the Per-Protocol population.

A participant meeting any of the following criteria will be excluded from the Per-Protocol population:

Exclusion Criteria	Protocol Deviation Category	Protocol Deviation Subcategory
Received wrong treatment most of the time (>50% of the time).	Wrong study treatment/ administration/ dose	Wrong study treatment or assignment administered
Did not receive treatment most of the time (>50% of the time).	N/A	N/A
Did not have a clinical diagnosis of Primary Sjögren's according to Inclusion Criterion #2.	Eligibility criteria not met	Documented Primary Sjögren's Syndrome by American European Consensus Group criteria including: either SS-A or SS-B positive.
Did not have baseline unstimulated salivary flow >0.0 mL/min or stimulated baseline salivary flow >0.05 mL/min) as defined by inclusion criterion #3.	Eligibility criteria not met	Baseline unstimulated salivary flow >0.0 mL/min or evidence of glandular reserve function (stimulated baseline salivary flow >0.05 mL/min).
Did not have symptomatic oral dryness (≥5/10 on subject completed Numeric Response Scale) as defined by inclusion criterion #4.	Eligibility criteria not met	Symptomatic oral dryness (≥5/10 on subject completed Numeric Response Scale)
Did not have systemically active disease defined as an ESSDAI score ≥5 at screening (Inclusion Criterion 5).	Eligibility criteria not met	Systemically active disease, ESSDAI ≥5 points OR (for sites in ITALY ONLY) Systemically active disease, ESSDAI≥5 points and with at least: a) 1 extraglandular domain moderate, OR b) 2 extraglandular domains low.
Received an excluded medication prior to screening (per Exclusion Criteria 17-22).	Eligibility criteria not met	Check the Protocol Section 5.2
Received a prohibited medication prior to Week 52.	Excluded medication, vaccine or device	Medication, excluded by the protocol, was administered
Study blind/unblind procedures: Investigator/site staff did not remain blinded to one or both treatment assignments through Week 68/Exit visit efficacy evaluation.	Study Procedures	Study blinding/unblinding procedures
Other, a deviation that does not satisfy the above criteria, however, in the judgment of the clinical team, including the medical monitor, constitutes an exclusion from the Per Protocol population.	N/A	N/A

11.2. Appendix 2: Schedule of Activities

11.2.1. Protocol Defined Schedule of Events

Study Day	**Screening** (up to 35 days prior to Day 0)	**Double Blind Treatment Period**																**General follow up period[1]**	**Individualized follow up period (IFU)[6]**	**IFU Final Visit**
		Day 0	7 ± 1 days	28 ± 7days	56 ± 7days	70 ± 7 days	84 ± 7 days	112 ± 7days	140 ± 7days	168 ± 7days	196± 7days	224 ± 7days	252 ± 7days	280 ± 7days	308 ± 7days	336 ± 7days	364 ± 7days			
Study Week	**W -5**		**W1**	**W4**	**W8**	**W10**	**W12**	**W16**	**W20**	**W24**	**W28**	**W32**	**W36**	**W40**	**W44**	**W48**	**W52**	**W68**		
Informed consent	X																			
Inclusion and exclusion criteria	X																			
Demography	X																			
Full physical exam	X	X[3]															X	X		X
Abbreviated physical exam symptom directed			X	X	X	X	X	X	X	X	X	X	X	X	X	X			X	
Past & current medical conditions [including AECG criteria & CV medical history]	X																			
Urine pregnancy test (WCBP) in clinic[9]	X	X[3]		X	X		X	X	X	X	X	X	X	X	X	X	X	X	X	X
Concomitant medication review	X[10]	X[3]	X	X	X	X	X[10]	X	X	X[10]	X	X	X[10]	X	X	X	X[10]	X[10]	X	X[10]
Study Treatments																				
Randomization		X																		
Belimumab/placebo.(weekly, home, except 1st & 2nd dose), last dose wk 51		X[11]	X[11]	X	X	X	X	X	X	X	X	X	X	X	X	X				
Monitor in clinic after dosing for 3hrs (1st & 2nd dose of belimumab/pbo)		X	X																	
Rituximab/placebo (at site)					X[8]	X[8]														

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Study Day	**Screening** (up to 35 days prior to Day 0)	**Double Blind Treatment Period**																**General follow up period[1]**	**Individualized follow up period (IFU)[6]**	**IFU Final Visit**
		Day 0	7 ± 1 days	28 ± 7days	56 ± 7days	70 ± 7 days	84 ± 7 days	112 ± 7days	140 ± 7days	168 ± 7days	196± 7days	224 ± 7days	252 ± 7days	280 ± 7days	308 ± 7days	336 ± 7days	364 ± 7days			
Study Week	**W -5**		**W1**	**W4**	**W8**	**W10**	**W12**	**W16**	**W20**	**W24**	**W28**	**W32**	**W36**	**W40**	**W44**	**W48**	**W52**	**W68**		
Monitor in clinic after dosing for 1h post rituximab/placebo					X	X														
Efficacy, pharmacokinetics and pharmacodynamics																				
ESSDAI[16]	X						X			X			X				X	X		X
ESSPRI	X						X			X			X				X	X		X
Oral Dryness numerical resp. scale	X						X			X			X				X	X		X
Ocular Dryness numerical resp. scale	X						X			X			X				X	X		X
Salivary gland biopsy	X[5]									X[12]							X[13]			
Lacrimal function (Schirmer's) test	X						X			X			X				X			
Fatigue- (PROFAD SSI SF)	X									X			X				X			
Patient Global Assessment (PtGA)	X									X			X				X			
Physicians Global Assessment (PGA)	X									X			X				X			
Exit interview																	X			
Stimulated Salivary Flow	X						X			X			X				X	X		X
Unstimulated Salivary Flow	X						X			X			X				X	X		X
Blood: Leukocyte population[2]	X	X[3]	X	X	X		X			X	X		X		X		X	X	X	X
Serological biomarkers	X	X[3]			X		X	X		X	X		X		X		X	X	X	X
Saliva sample for proteomics	X						X			X			X				X			
Blood: BLyS levels[2]		X[3]		X	X		X	X		X	X		X		X		X	X		X
Blood: Transcriptomics		X[3]			X					X			X				X			
Salivary gland: Transcriptomics	X									X							X[13]			
Blood: PBMC exploratory endpoints		X[3]			X					X										

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Study Day	**Screening** (up to 35 days prior to Day 0)	**Double Blind Treatment Period**																**General follow up period[1]**	**Individualized follow up period (IFU)[6]**	**IFU Final Visit**
		Day 0	7 ± 1 days	28 ± 7days	56 ± 7days	70 ± 7 days	84 ± 7 days	112 ± 7days	140 ± 7days	168 ± 7days	196± 7days	224 ± 7days	252 ± 7days	280 ± 7days	308 ± 7days	336 ± 7days	364 ± 7days			
Study Week	**W -5**		**W1**	**W4**	**W8**	**W10**	**W12**	**W16**	**W20**	**W24**	**W28**	**W32**	**W36**	**W40**	**W44**	**W48**	**W52**	**W68**		
Blood: Belimumab PK[2]										X			X		X		X			
Blood: Rituximab PK[2]					X[7]	X[7]	X			X			X							
Safety & Laboratory Assessments																				
AE/SAE review	X[17]	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X[18]	X
Vital signs	X	X[3,4]	X[4]	X	X[4]	X[4]	X	X	X	X	X	X	X	X	X	X	X	X	X	X
12-lead ECG	X																			
CSSRS (suicidality assessment)		X[3]	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X		
Neurological assessment		X[3]	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
Urinalysis	X	X[3]					X			X			X				X	X		X
Blood: Immunoglobulin levels (IgG, IgA[2], IgM[2])	X	X[3]		X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
Blood: Cryoglobulins	X						X			X			X				X	X		X
Blood chemistry	X	X[3]		X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
Hematology	X	X[3]		X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
HIV, Hep B and Hep C screen	X[14]																	X		
Pharmacogenetics blood sample[15]		X																		
Blood: Belimumab Immunogenicity[2]		X[3]			X					X							X	X		
Blood: Rituximab Immunogenicity[2]					X[3]					X							X			

1. All subjects, including subjects who are withdrawn from the study and decline to complete the treatment phase visits through Week 52, are required to enter the general follow up period. During this 16-week general follow up period, subjects will receive calls every 4 weeks (±7 days) to evaluate AEs, to check concomitant medications and to complete the neurological assessment.
2. In order to maintain the blind, sites will be blinded to these data following screening - including B-cell flow cytometry panels and IgA, IgM levels.

3. To be measured or collected pre-dose.

4. Subjects will be monitored post study treatment as detailed in protocol.

5. Biopsy can occur on Day 0 or at any time during the screening period provided the subject has met all other entry criteria prior to the biopsy.

6. Subjects will enter the IFU if, following the general follow up period, their CD19+ B-cell levels remain below the lower limit of normal (or less than 90% of baseline, if baseline value was below LLN). During the IFU, subjects will be seen in the clinic every 12 weeks (± 7 days), with calls every 4 weeks (±7 days) between visits to evaluate subjects for AEs & concomitant medications. Subjects will exit the IFU when: CD19+ B-lymphocyte counts are within normal range or 10% of baseline levels (if baseline < LLN), OR at the investigator's discretion the subject starts receiving disease modifying therapy that may affect B-cell numbers OR or for up to a maximum of 2 years (i.e., up to Week 104) – whichever comes first. Subjects exiting IFU period will attend a final visit (within 28 days of that decision) for final assessments (IFU Final Visit) as detailed in the Table.

7. Obtain samples post-dose only, within 10 minutes after end of infusion.

8. Both doses of rituximab/placebo will be administered in the clinic. Approximately 60 minutes prior to rituximab/placebo, subjects will receive orally an antipyretic and an antihistamine. At least 30 minutes prior to administration of rituximab/placebo, subjects will receive IV 100mg methylprednisilone .The 2nd rituximab/placebo administration at the Week10 visit must be given 14 days (13-18 days, see SRM) after the first administration (given at the Week 8 visit). A patient alert card should be sent home with the subject following each dose of rituximab/placebo.

9. If urine test is positive, confirm with serum test. Pregnancy testing & contraception are required until 16 weeks post last administration of study treatment for those subjects who complete Weeks 46- 52 or withdraw from treatment prior to Week 8 dosing. Pregnancy testing and contraception are required for approximately 12 months after the administration of the final rituximab/placebo dose for the subset of subjects who discontinue treatment from Week 8 up to Week 46.

10. Subjects will receive a reminder phone call 48 hours prior to efficacy assessment visits to remind them that they should not be using certain symptomatic therapies prior to visit (see Section 4.1 of Study Reference Manual for details); in addition subjects should document their last use of symptomatic therapies in their self injection log book.

11. First & second dose of belimumab will be administered in clinic by subject or caregiver. A patient alert card will be sent home with the subject each time belimumab is dispensed for home administration.

12. Week 24 biopsy may be taken on a separate day from the other required assessments within the Week 24 study visit window.

13. Week 52 biopsy is optional. Trancriptomics will only be performed if biopsy is taken.

14. If test otherwise performed within 3 months prior to first dose of study treatment, testing at screening is not required.

15. Informed consent for optional substudies e.g.,genetics must be obtained before collecting a sample.

16. If additional tests (e.g., pulmonary function tests, EMG, MRI) are required to complete ESSDAI assessment, these should be scheduled as close as possible to the stipulated study visit window.

17. From signing of consent until initiation of study treatment, only SAEs related to study participation will be collected.

18. From the end of general follow-up phase through the last contact (including the individualized safety follow-up phase), only designated AESIs (i.e., infections, malignancies, and depression/suicidality/self-injury), fatal SAEs, and SAEs assessed as related to the investigational product or to study participation will be collected.

11.3. Appendix 3: Treatment States and Phases

11.3.1. Treatment Phases

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

Treatment Phase	Definition
Pre-Treatment	Date ≤ Study Treatment Start Date
On-Treatment	Study Treatment Start Date < Date ≤ Last Dose + 28
Post-Treatment	Date > Last Dose + 28

11.3.2. Treatment States

Assessments and events will be classified according to time of occurrence relative to the date of first and/or last dose of study treatment.

11.3.2.1. Treatment States for AE Data

Treatment State	Definition
Pre-Treatment	AE Start Date < Study Treatment Start Date
On-Treatment	If AE onset date is on or after treatment start date & up to 28 days after date of last dose. Study Treatment Start Date ≤ AE Start Date ≤ [Last Dose Study Treatment + 28]
Post-Treatment	If AE onset date is > 28 days after the last dose of study drug. AE Start Date >[Last Dose Study Treatment + 28]
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:

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

11.4. Appendix 4: Data Display Standards & Handling Conventions

11.4.1. Reporting Process & Standards

Reporting Process	
Software	
• The currently supported versions of SAS software will be used.	
Reporting Area (Interim)	
HARP Server	: US1SALX00259
HARP Area	: \ARPROD\GSK1550188\MID201842\Interim_01
Reporting Area (Primary Analysis)	
HARP Server	: US1SALX00259
HARP Area	: \ARPROD\GSK1550188\MID201842\Primary_02
NOTE: • Primary_01 has been taken for previous CDISC reporting and hence not available	
Reporting Area (End of Study Analysis)	
HARP Server	: US1SALX00259
HARP Area	: \ARPROD\GSK1550188\MID201842\Final_02
Analysis Datasets	
• Analysis datasets will be created according to IDSL standards	
Generation of RTF Files	
• RTF files will be generated at primary and end of study analysis • XML files in the format expected by DORS (Disclosure Obligation Reporting System) for relevant displays	

Reporting Standards
General

• The current GSK Integrated Data Standards Library (IDSL) will be applied for reporting, unless otherwise stated:
  • 4.03 to 4.23: General Principles
  • 5.01 to 5.08: Principles Related to Data Listings
  • 6.01 to 6.11: Principles Related to Summary Tables
  • 7.01 to 7.13: Principles Related to Graphics

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 with a maximum of 4 DP presented. • 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.

Reporting Standards	
Planned and Actual Time	
• Reporting for tables, figures and formal statistical analyses: o Planned time relative to dosing will be used in figures, summaries, statistical analyses and calculation of any derived parameters, unless otherwise stated. o 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: o Planned and actual time relative to study drug dosing will be shown in listings (Refer to IDSL Statistical Principle 5.05.1). o Unscheduled or unplanned readings will be presented within the subject's listings. o Data will be incorporated in figures, summaries and statistical analyses using the visit recorded in eCRF. No visit slotting is planned.	
Unscheduled Visits	
• Unscheduled visits will not be presented in summary tables or figures, with the exception of any time post baseline/worst toxicities where all data including unscheduled visits are used in derivations. • 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)
Graphical Displays	
• Refer to IDSL Statistical Principals 7.01 to 7.13. • Include ref line (i.e. y=0) for figures having negative values	

11.5. Appendix 5: Derived and Transformed Data

11.5.1. General

Multiple Measurements at One Time Point
• Mean of the measurements will be calculated and used in any derivation of summary statistics but if listed, all data will be presented. • If there are two values within a time window the value closest to the target day for that window will be used. If values are the same distance from the target, then the mean will be taken. • Subjects having both High and Low values for Normal Ranges at any post-baseline visits for safety parameters will be counted in both the High and Low categories of "Any visit post-baseline" row of related summary tables. This will also be applicable to relevant Potential Clinical Importance summary tables.
Study Day
• Calculated as the number of days from randomization date: o Ref Date = Missing → Study Day = Missing o Ref Date < Randomization Date → Study Day = Ref Date – Randomization Date o Ref Data ≥ Randomization Date → Study Day = Ref Date – (Randomization Date) + 1
Data Cutt-off
• The study data cut-off date of the primary analysis is September 9th, 2019. Data after September 9th will be removed from the extracted data after October 30th based on the algorithms detailed below. • The data cut off will be applied on DMDATA before the generating of any analysis datasets and outputs.

Datasets	Label	Algorithm
AE	ADVERSE EVENT	AESTDT <= CUTOFF DATE
BIOLINK	BIOMARKER SAMPLE	BIDT <= CUTOFF DATE
BIOMARK	BIOMARKER	BIDT <= CUTOFF DATE
BLIND	BLIND	BLDT <= CUTOFF DATE
CC	EULAR SJOGRENS SYNDROME DISEASE ACTIVITY INDEX	CCDT <= CUTOFF DATE
CE	CV CLINICAL EVENTS	CESTDT <= CUTOFF DATE
CHDPOT	PREGNANCY INFORMATION	IMPUTED CHDMNFD_, THEN THE IMPUTED DATE <= CUTOFF DATE
CONMEDS	CONCOMITANT MEDICATIONS	IMPUTED CMSTD_, THEN THE IMPUTED DATE <= CUTOFF DATE
CONV	LAB CONVERSION FACTOR	NOT CUT
CSSRSV4	COLUMBIA SUICIDE SEVERITY RATING SCALE	ACTDT <= CUTOFF DATE
CVDXTEST	CEREBROVASCULAR EVENTS	DXDT <= CUTOFF DATE
DEMO	DEMOGRAPH	NOT CUT
DS	STUDY CONCLUSION	DSSTDT <= CUTOFF DATE
DTH	DEATH	DDDT <= CUTOFF DATE
DV1	PROTOCOL DEVIATION	DVSTDT <= CUTOFF DATE
ECG	12-LEAD ECG	EGDT <= CUTOFF DATE
EGCRIT	ECG REFERENCE DATA	NOT CUT

Datasets	Label	Algorithm
ELIG	ELIGIBILIT	NOT CUT
ENROL	INFORM ENROLLMENT	NOT CUT
ESSPRI	EULAR SJOGRENS SYNDROME PATIENT REPORTED INDEX	ACTDT <= CUTOFF DATE
EVIDENCE	DEEP VEIN THROMBOSIS (DVT) /PULMONARY EMBOLISM (PE)	NOT CUT
EXPOSURE	STUDY TREATMENT	FIRST GET THE LARGEST VISITNUM FROM VISIT DATA WHERE VISITDT <= CUTOFF DATE; LEFT JOIN EXPOSURE WITH THE VISIT DATA BY SUBJID; VISITNUM FROM STATUS < = THE LARGEST VISITNUM FROM VISIT DATA WHERE EXSTDT IS MISSING OR EXSTDT < = CUTOFF DATE WHERE SSDT IS NOT MISSING.
FACE	NEUROLOGICAL SYMPTOMS QUESTIONNAIRE	FCEDT <= CUTOFF DATE
FACV	FINDING ABOUT CLINICAL EVENTS	NOT CUT
FADE	INVESTIGATIONAL PRODUCT DEVICE MALFUNCTION (DEV MALFUNCTION)	FDEDT <= CUTOFF DATE
FADTH	FINDINGS ABOUT DEATH	DDORRSDT <= CUTOFF DATE
FAMH	FINDING ABOUT METICAL HISTORY	NOT CUT
FAMHIST	FAMILY HISTORY	NOT CUT
FAPR	UNSTIMULATED AND STIMULATED SALIVARY FLOW	FPRDT <= CUTOFF DATE
GENPRO	PHARMACOGENETIC (PGx) RESEARCH CONSENT	GPSMPDT <= CUTOFF DATE
HRU	HOSPITALISATION	HUHOSTDT <= CUTOFF DATE
IMGEN	IMMUNOGENICITY	IGDT <= CUTOFF DATE
IMGLINK	IMMUNOGENICITY SAMPLING	IGDT <= CUTOFF DATE
INVESTIG	INVESTIGATOR SIGNATUR	NOT CUT
IPDISC	STUDY TREATMENT DISCONTINUATION	SDENDT <= CUTOFF DATE
LAB	LABORATORY TEST	LBDT < = CUTOFF DATE
LABCRIT	LAB REFERENCE DATA	NOT CUT
LBIOPSY	LIVER BIOPSY (BIOPSY)	LPDT < = CUTOFF DATE
LBTESTCD	LAB TEST CODES	NOT CUT
LEREPORT	LIVER MONITORING/STOPPING EVENT REPORTING (LEREPORT)	LERSTDT < = CUTOFF DATE
LIMAGING	LIVER IMAGING (IMAGING)	LIDT < = CUTOFF DATE
MEDHIST	SJOGRENS SYNDROME SPECIFIC MEDICAL HISTORY	NOT CUT
MI	MICROSCOPIC FINDINGS	GET THE LARGEST VISITNUM FROM VISIT DATA WHERE VISITDT <= CUTOFF DATE; LEFT JOIN MI WITH THE VISIT DATA BY SUBJID; VISITNUM FROM MI < = THE LARGEST VISITNUM FROM VISIT DATA
MO	MORPHOLOGY	MODT < = CUTOFF DATE
NYHASCR	NYHA SCORE	NOT CUT
OCULAR	LACRIMAL FUNCTION (SCHIRMERS) TEST	XGDT < = CUTOFF DATE
OROCNRS	ORAL AND OCULAR DRYNESS NUMERIC RATING SCAL	ACTDT < = CUTOFF DATE

Datasets	Label	Algorithm
PFDSSISF	PROFILE OF FATIGUE AND DISCOMFORT - SICCA SYMPTOMS INVENTORY	ACTDT < = CUTOFF DATE
PHGA	PHYSICIAN GLOBAL ASSESSMENT OF DISEASE ACTIVITY	ACTDT < = CUTOFF DATE
PK	PK BLOOD SAMPLE COLLECTION; PHARMACOKINETICS	PKSTDT < = CUTOFF DATE
PR	SCHIRMERS TEST SATURATION PROCEDURE	PRSTDT < = CUTOFF DATE
PSRAE	POSSIBLE SUICIDE RELATED ADVERSE EVENT QUESTION	AESTDT < = CUTOFF DATE
PSRAECOM	POSSIBLE SUICIDE RELATED ADVERSE EVENT QUESTION COMMENT	NOT CUT
PTGA	PATIENT GLOBAL ASSESSMENT OF DISEASE ACTIVITY	ACTDT < = CUTOFF DATE
RACE	COLLECTED RACE	NOT CUT
RAND	RANDOMISATION	NOT CUT
RANDALL	RANDOMISED TREATMENT	NOT CUT
RISK	MEDICAL DEVICE	NOT CUT
RUCAM	LIVER EVENTS (LIVER EVENTS)	RUDT < = CUTOFF DATE
SS	SYMPTOMATIC THERAPY US	FIRST GET THE LARGEST VISITNUM FROM VISIT DATA WHERE VISITDT <= CUTOFF DATE; LEFT JOIN SS WITH THE VISIT DATA BY SUBJID; VISITNUM FROM STATUS < = THE LARGEST VIISTNUM FROM VISIT DATA WHERE SSDT IS MISSING OR SSDT < = CUTOFF DATE WHERE SSDT IS NOT MISSING.
STATUS	VISIT STATUS	GET THE LARGEST VISITNUM FROM VISIT DATA WHERE VISITDT <= CUTOFF DATE; LEFT JOIN STATUS WITH THE VISIT DATA BY SUBJID; VISITNUM FROM STATUS < = THE LARGEST VISiTNUM FROM VISIT DATA
SUBUSE	HISTORY OF TOBACCO USE	NOT CUT
SURGERY	CEREBROVASCULAR SURGERY	SPDT < = CUTOFF DATE
TMSLICE	VISIT AND PERIOD	NOT CUT
VISIT	VISIT	VISITDT < = CUTOFF DATE
VITALS	VITAL SIGNS	VSDT < = CUTOFF DATE
VSCRIT	VITAL SIGNS REFERENCE DATA	NOT CUT
VIRAL	VIRAL LABORATORY RESULTS	LABDT < = CUTOFF DATE

11.5.2. Study Population

Subject Disposition Status – Primary Analysis
Study Completion Status at Week 68

A subject is considered **Completed** at Week 68 if **BOTH** of the following conditions are met:
• The study treatment is not stopped permanently before the scheduled end of the treatment period
• Subject completed Week 68 visit
 	
• A subject is considered **Ongoing** at Week 68 if **ALL** of the following conditions are met:
  • The study treatment is not stopped permanently before the scheduled end of the treatment period subject has not completed Week 68 visit
  • Date of subject completion or withdrawal is missing
 	
• A subject is considered **Withdrawn** at Week 68 if **EITHER** of the following conditions is met:
  • The study treatment is stopped permanently before the scheduled end of the treatment period
  • The study treatment is not stopped permanently before the scheduled end of the treatment period, but subject was withdrawn prior to Week 68

Demographics
Age

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

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

Extent of Exposure to Belimumab
• Number of days of exposure to belimumab will be calculated as: **Duration of Exposure in Days = Date of Last Belimumab Injection – Date of First Belimumab Injection + 7** • Subjects who were randomized but did not report a treatment start date will be categorized as having zero days of exposure.
Baseline Characteristics
Autoantibodies
• SS-A positive subjects are defined as those who have screening SS-A ≥ 7 KU/L. • SS-B positive subjects are defined as those who have screening SS-B ≥ 7 KU/L

Extent of Exposure to Belimumab
Time Since Diagnosis
Time since diagnosis of Primary Sjogren Syndrome is defined as: • If treatment start date >= diagnosis date and then treatment start date - diagnosis date $\frac{\textit{Treatment Start date - diagnosis date + 1}}{\textit{365.25}}$ • If the day and month of diagnosis is missing, this will be imputed as '30th June' • If the year of diagnosis is missing, time since diagnosis will be set to missing
Average Daily Prednisone Dose
• At baseline, the average daily dose of prednisone is the sum of doses over 7 consecutive days up to, but not including Day 0 divided by 7: Days on which a subject does not have prednisone use recorded will be considered as 0 mg for the day in the calculation of average daily prednisone dose.

11.5.3. Safety

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, unless otherwise specified 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. 1. Example 1: 2 Significant Digits = '< x' becomes x – 0.01 2. Example 2: 1 Significant Digit = '> x' becomes x + 0.1 3. Example 3: 0 Significant Digits = '< x' becomes x – 1 Details of rules to apply for biomarker endpoints are covered in Section 11.5.6.

Neurological Symptoms
• Neurological systems are assessed based upon a questionnaire consisting of 7 questions with response of either yes or no. • See Appendix 11 for further information.

Suicidal Risk Monitoring
Columbia Suicidality Severity Rating Scale (C-SSRS)
• The C-SSRS is a measure of suicidal ideation and behavior. • The following outcomes are C-SSRS categories and have binary responses (yes/no). The categories have been re-ordered from the actual scale in an increasing order of severity from 1 to 10 to facilitate the definitions of the comparative endpoints. o Category 1 – CCI - This section contained Clinical Outcome Assessment data collection questionnaires or indices, which are protected by third party copyright laws and therefore have been excluded. o Category 2 – o Category 3 – o Category 4 – o Category 5 – o Category 6 – o Category 7 – o Category 8 – o Category 9 – o Category 10 • The following outcomes are numerical scores derived from the C-SSRS categories. The scores are created at each assessment for each patient. o Suicidal Ideation Score: The maximum suicidal ideation category (1-5 on the C-SSRS) present at the assessment. Assign a score of 0 if no ideation is present. o Suicidal Behavior Score: The maximum suicidal behavior category (6-10 on the C-SSRS) present at the assessment. Assign a score of 0 if no behavior is present. o Suicidal Ideation or Behavior Score: The maximum suicidal ideation or behavior category (1-10 on the C-SSRS) present at the assessment. Assign a score of 0 if no ideation or behavior is present. o See Appendix 11 for further details.

11.5.3.1. Adverse Events of Special Interest

Handling Study specific AESI:

- GSK study statistician will generate cumulative spreadsheets in .csv format which is created by merging DMDATA.AE with MedDRA dictionary by preferred terms corresponding to study specific AESI SMQ's extracted from latest version of MedDRA, as specified in the below table.
- GSK study statistician will distribute spreadsheets via e-mail to the study team for clinical review.
- GSK study statistician will receive returned spreadsheets. A manual review will be performed so that any noted quality issues can be followed up.

  GSK study statistician will create csv versions in the "Adjudicated" folder on arwork (\\us1salx00259.corpnet2.com\arenv\arwork\gsk1550188\refdata\aesi\Adjudication Results\MID201842\Adjudicated).

Study Specific Primary Analysis AESI specification to be capture in the process. For the End of Study Analyses, PTs related the MedDRA version at the time of database release will be used. If a new version of MedDRA is used, then a RAP amendment or addendum will be created to capture updated PTs.

End of Study Reporting

MedDRA 23.0 PTs will be used. This is a major version release that includes changes to any level of the hierarchy and additionally includes COVID-19 related terminology. On this basis the RAP will not be updated, instead MedDRA V23.0 will be implemented. Same search Strategy will be applied to MedDRA V23.0.

Category: Severe skin reaction per GSK Adjudication (Ten and Steven's Johnson Syndrome)	
Search Strategy	**MedDRA 22.0 PTs Included in SMQ**
Broad Search: Severe Cutaneous Adverse Reactions SMQ.	Acquired epidermolysis bullosa
	Blister
	Blister rupture
	Bullous impetigo
	Conjunctivitis
	Corneal exfoliation
	Drug eruption
	Epidermolysis
	Epidermolysis bullosa
	Fixed eruption
	Genital ulceration
	HLA-B*1502 assay positive
	HLA-B*5801 assay positive
	Hypopharyngeal synechiae
	Lip exfoliation
	Mouth ulceration
	Mucocutaneous ulceration
	Mucosa vesicle
	Mucosal erosion
	Mucosal exfoliation
	Mucosal necrosis
	Mucosal ulceration
	Nasal mucosal blistering
	Nikolsky's sign
	Noninfective conjunctivitis
	Oral mucosal blistering
	Oral mucosal exfoliation
	Oral papule
	Oropharyngeal blistering
	Pemphigoid

Category: Severe skin reaction per GSK Adjudication (Ten and Steven's Johnson Syndrome)	
Search Strategy	**MedDRA 22.0 PTs Included in SMQ**
	Pemphigus
	Penile exfoliation
	Skin erosion
	Skin exfoliation
	Staphylococcal scalded skin syndrome
	Stomatitis
	Symmetrical drug-related intertriginous and flexural exanthema
	Tongue exfoliation
	Vaginal exfoliation
	Vaginal ulceration
	Vulval ulceration
	Vulvovaginal rash
	Vulvovaginal ulceration

Category: Cardiac Disorders	
Search Strategy	**MedDRA 22.0 PTs Included in SMQ**
Broad Search: Cardiac Arrhythmias SMQ	**Sub-Category:** Arrhythmia related investigations, signs and symptoms (SMQ)
	Bezold-Jarisch reflex
	Bradycardia
	Cardiac arrest
	Cardiac death
	Cardiac telemetry abnormal
	Cardio-respiratory arrest
	Central bradycardia
	Electrocardiogram abnormal
	Electrocardiogram ambulatory abnormal
	Electrocardiogram change
	Heart rate abnormal
	Heart rate decreased
	Heart rate increased
	Loss of consciousness
	Palpitations
	Rebound tachycardia
	Respiratory sinus arrhythmia magnitude abnormal
	Respiratory sinus arrhythmia magnitude decreased
	Respiratory sinus arrhythmia magnitude increased
	Sudden death
	Syncope
	Tachycardia

Category: Cardiac Disorders	
Search Strategy	**MedDRA 22.0 PTs Included in SMQ**
	Tachycardia paroxysmal
	Sub-Category: Cardiac arrhythmia terms (incl bradyarrhythmias and tachyarrhythmias) (SMQ)
	-NIL-
	Sub-Category: Tachyarrhythmias (incl supraventricular and ventricular tachyarrhythmias) (SMQ)
	-NIL-
	Sub-Category: Supraventricular tachyarrhythmias (SMQ)
	ECG P wave inverted
	Electrocardiogram P wave abnormal
	Retrograde p-waves
Broad Search: Congenital and neonatal arrhythmias (SMQ)	Baseline foetal heart rate variability disorder
	Bradycardia foetal
	Bradycardia neonatal
	Cardiac arrest neonatal
	Cardio-respiratory arrest neonatal
	Foetal heart rate acceleration abnormality
	Foetal heart rate deceleration abnormality
	Neonatal sinus bradycardia
	Neonatal sinus tachycardia
	Neonatal tachycardia
	Nonreassuring foetal heart rate pattern
	Tachycardia foetal
	Nonreassuring foetal heart rate pattern
	Tachycardia foetal
Broad Search: Cardiac Failure SMQ	Artificial heart implant
	Atrial natriuretic peptide abnormal
	Atrial natriuretic peptide increased
	Bendopnoea
	Brain natriuretic peptide abnormal
	Brain natriuretic peptide increased
	Cardiac cirrhosis
	Cardiac contractility modulation therapy
	Cardiac device reprogramming
	Cardiac dysfunction
	Cardiac index decreased
	Cardiac output decreased
	Cardiac resynchronisation therapy
	Cardiac ventriculogram abnormal
	Cardiac ventriculogram left abnormal
	Cardiac ventriculogram right abnormal

Category: Cardiac Disorders	
Search Strategy	**MedDRA 22.0 PTs Included in SMQ**
	Cardiomegaly
	Cardio-respiratory distress
	Cardiothoracic ratio increased
	Central venous pressure increased
	Diastolic dysfunction
	Dilatation ventricular
	Dyspnoea paroxysmal nocturnal
	Heart transplant
	Hepatic vein dilatation
	Implantable cardiac monitor replacement
	Intracardiac pressure increased
	Jugular vein distension
	Left ventricular diastolic collapse
	Left ventricular dilatation
	Left ventricular dysfunction
	Left ventricular enlargement
	Lower respiratory tract congestion
	Myocardial depression
	Nocturnal dyspnoea
	N-terminal prohormone brain natriuretic peptide abnormal
	N-terminal prohormone brain natriuretic peptide increased
	Oedema
	Oedema blister
	Oedema due to cardiac disease
	Oedema neonatal
	Oedema peripheral
	Orthopnoea
	Peripheral oedema neonatal
	Peripheral swelling
	Post cardiac arrest syndrome
	Prohormone brain natriuretic peptide abnormal
	Prohormone brain natriuretic peptide increased
	Pulmonary congestion
	Right ventricular diastolic collapse
	Right ventricular dilatation
	Right ventricular dysfunction
	Right ventricular enlargement
	Scan myocardial perfusion abnormal
	Stroke volume decreased
	Surgical ventricular restoration

Category: Cardiac Disorders	
Search Strategy	**MedDRA 22.0 PTs Included in SMQ**
	Systolic dysfunction
	Venous pressure increased
	Venous pressure jugular abnormal
	Venous pressure jugular increased
	Ventricular assist device insertion
	Ventricular compliance decreased
	Ventricular dysfunction
	Ventricular dyssynchrony
	Wall motion score index abnormal
Broad Search: Cardiomyopathy SMQ	Abnormal precordial movement
	Acquired cardiac septal defect
	Acute left ventricular failure
	Alcohol septal ablation
	Arrhythmia
	Arrhythmia supraventricular
	Artificial heart implant
	Ascites
	Atrial enlargement
	Atrial hypertrophy
	Atrial pressure increased
	Autoimmune myocarditis
	Bendopnoea
	Blood pressure diastolic abnormal
	Blood pressure diastolic decreased
	Blood pressure diastolic increased
	Blood pressure fluctuation
	Blood pressure inadequately controlled
	Blood pressure systolic abnormal
	Blood pressure systolic decreased
	Blood pressure systolic increased
	Cardiac aneurysm
	Cardiac arrest
	Cardiac contractility modulation therapy
	Cardiac device reprogramming
	Cardiac dysfunction
	Cardiac electrophysiologic study abnormal
	Cardiac failure
	Cardiac failure acute
	Cardiac failure chronic
	Cardiac failure congestive

Category: Cardiac Disorders	
Search Strategy	**MedDRA 22.0 PTs Included in SMQ**
	Cardiac function test abnormal
	Cardiac imaging procedure abnormal
	Cardiac index abnormal
	Cardiac index decreased
	Cardiac index increased
	Cardiac monitoring abnormal
	Cardiac operation
	Cardiac output decreased
	Cardiac pseudoaneurysm
	Cardiac resynchronisation therapy
	Cardiac ventricular scarring
	Cardiac ventriculogram abnormal
	Cardiac ventriculogram left abnormal
	Cardiac ventriculogram right abnormal
	Cardiomegaly
	Cardiothoracic ratio increased
	Cardiovascular disorder
	Cardiovascular function test abnormal
	Chest pain
	Chest X-ray abnormal
	Computerised tomogram thorax abnormal
	Coxsackie carditis
	Coxsackie myocarditis
	Cytomegalovirus myocarditis
	Decreased ventricular preload
	Diastolic dysfunction
	Dilatation atrial
	Dilatation ventricular
	Directional Doppler flow tests abnormal
	Dyspnoea
	ECG signs of ventricular hypertrophy
	Echocardiogram abnormal
	Electrocardiogram abnormal
	Electrocardiogram change
	Electrocardiogram PR segment depression
	Electrocardiogram U wave inversion
	Endocardial fibroelastosis
	External counterpulsation
	Gonococcal heart disease
	Heart and lung transplant

Category: Cardiac Disorders	
Search Strategy	**MedDRA 22.0 PTs Included in SMQ**
	Heart transplant
	Hepatomegaly
	Hyperdynamic left ventricle
	Hypersensitivity myocarditis
	Implantable cardiac monitor replacement
	Increased ventricular preload
	Intracardiac pressure increased
	Irregular breathing
	Labile blood pressure
	Left atrial dilatation
	Left atrial enlargement
	Left atrial volume abnormal
	Left atrial volume decreased
	Left atrial volume increased
	Left ventricular dilatation
	Left ventricular dysfunction
	Left ventricular end-diastolic pressure decreased
	Left ventricular enlargement
	Left ventricular failure
	Left ventricular heave
	Lupus myocarditis
	Lyme carditis
	Malarial myocarditis
	Mental status changes
	Multiple gated acquisition scan abnormal
	Myocardiac abscess
	Myocardial necrosis marker increased
	Myocarditis
	Myocarditis bacterial
	Myocarditis helminthic
	Myocarditis infectious
	Myocarditis meningococcal
	Myocarditis mycotic
	Myocarditis post infection
	Myocarditis septic
	Myocarditis syphilitic
	Myocarditis toxoplasmal
	Myoglobinaemia
	Myoglobinuria
	Nocturia

Category: Cardiac Disorders	
Search Strategy	**MedDRA 22.0 PTs Included in SMQ**
	Nuclear magnetic resonance imaging thoracic abnormal
	Oedema
	Orthostatic hypotension
	Palpitations
	Papillary muscle disorder
	Papillary muscle haemorrhage
	Radiation myocarditis
	Right atrial dilatation
	Right atrial enlargement
	Right atrial pressure increased
	Right ventricle outflow tract obstruction
	Right ventricular dilatation
	Right ventricular enlargement
	Right ventricular heave
	Right ventricular systolic pressure decreased
	Scan myocardial perfusion abnormal
	Sudden cardiac death
	Sudden death
	Surgical ventricular restoration
	Syncope
	Systolic anterior motion of mitral valve
	Systolic dysfunction
	Ultrasound Doppler abnormal
	Vascular resistance pulmonary increased
	Ventricular arrhythmia
	Ventricular assist device insertion
	Ventricular dysfunction
	Ventricular dyskinesia
	Ventricular dyssynchrony
	Ventricular enlargement
	Ventricular hyperkinesia
	Ventricular hypertrophy
	Ventricular hypokinesia
	Ventricular remodelling
	Viral myocarditis
	Wall motion score index abnormal
	Wall motion score index abnormal
Broad Search: Ischaemic heart disease SMQ	**Sub-Category:** Myocardial infarction (SMQ)
	Blood creatine phosphokinase abnormal
	Blood creatine phosphokinase increased

Category: Cardiac Disorders	
Search Strategy	**MedDRA 22.0 PTs Included in SMQ**
	Cardiac ventricular scarring
	ECG electrically inactive area
	ECG signs of myocardial infarction
	Electrocardiogram Q wave abnormal
	Electrocardiogram ST segment abnormal
	Electrocardiogram ST segment elevation
	Electrocardiogram ST-T segment elevation
	Electrocardiogram U wave inversion
	Infarction
	Myocardial necrosis marker increased
	Scan myocardial perfusion abnormal
	Vascular graft occlusion
	Vascular stent occlusion
	Vascular stent thrombosis
	Sub-Category: Other ischaemic heart disease (SMQ)
	Arteriogram coronary abnormal
	Cardiac stress test abnormal
	Cardiopulmonary exercise test abnormal
	Cardiovascular event prophylaxis
	Computerised tomogram coronary artery abnormal
	Elastic vessel recoil complication
	Electrocardiogram PR segment depression
	Electrocardiogram ST segment depression
	Electrocardiogram ST-T segment abnormal
	Electrocardiogram ST-T segment depression
	Electrocardiogram T wave abnormal
	Electrocardiogram T wave inversion
	Electrocardiogram U wave inversion
	Exercise electrocardiogram abnormal
	Exercise test abnormal
	Post angioplasty restenosis
	Restenosis
	Stress echocardiogram abnormal
	Vascular stent stenosis
	Wall motion score index abnormal

Category: Posterior Reversible Encephalopathy Syndrome (PRES)	
Search Strategy	**MedDRA 22.0 PTs Included in SMQ**
Search using Preferred Term	Posterior Reversible Encephalopathy Syndrome

Category: PML	
Search Strategy	**MedDRA 22.0 PTs Included in SMQ**
Search using Preferred Term	Progressive Multifocal Leukoencephalopathy

Category: Biopsy Procedure	
Search Strategy	**MedDRA 22.0 PTs Included in SMQ**
Review all AE Preferred Term for biopsy related AESI	All AE terms will be included

11.5.3.2. Coronavirus Disease 2019 (COVID-19) Environment Onset Date

A COVID-19 environment onset date has been defined by GlaxoSmithKline for each Country as:

Country	COVID-19) Environment Onset Date
Argentina	10 FEB 2020
Canada	10 MAR 2020
France	25 FEB 2020
Germany	10 FEB 2020
Italy	10 FEB 2020
Netherlands	10 FEB 2020
Norway	10 FEB 2020
Spain	10 FEB 2020
Sweden	10 FEB 2020
United Kingdom	24 FEB 2020

This represents the best estimate of the outbreak of COVID-19 within each country at this time.

11.5.4. Efficacy

+++Efficacy+++
Calculation of ESSDAI/ClinESSDAI score
• The ESSDAI includes 12 domains (ie, organ systems: cutaneous, respiratory, renal, articular, muscular, peripheral nervous system, central nervous system, hematological, glandular, constitutional, lymphadenopathy and biological). Each domain has 3 or 4 possible activity levels (Table 8).

+++Efficacy+++

Corrected ESSDAI score:

- For each damage eligible domain
  - where damage is scored as present for 1st time after screening **THEN** corrected activity score = damage score for that domain for that visit and the activity score for all subsequent visits should be changed to equal the corresponding damage domain score
  - Except in rare cases where the activity score for the visit concerned is already equal to or greater than the damage score, in which case no change should be made.
- If damage is scored as present at screening **AND** if the damage score increases in level of involvement (low to moderate or moderate to high) after the screening visit then the activity score for that domain for that visit and all subsequent visits should be changed to equal the corresponding damage domain score
  - Except in rare cases where the activity score for the visit concerned is already equal to or greater than the damage score, in which case no change should be made.
- If damage is scored at screening and remains constant across visits, then no programmed correction can or should be made to the activity scores.
- The ClinESSDAI includes 11 of the 12 ESSDAI domains (biological domain is excluded).

Table 8 ESSDAI Domains

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

*Refer to Appendix 11 for details of the domains which incorporate High Response

The Total ESSDAI and Total ClinESSDAI Scores are obtained by multiplying the level of activity(Table 8) by the domain weights (Table 9). There are differing weightings for the ESSDAI and ClinESSDAI, and the biological domain is excluded from the calculation of the ClinESSDAI. The ESSDAI total score can range between 0 and 123. The ClinESSDAI total score can range between 0 and 135.

- Missing domains:
  - If there are missing responses for ≥ 3 domains, the Total ESSDAI and Total ClinESSDAI scores will be set to missing.
  - If <3 domains are missing, imputation of missing domain responses will be applied to enable derivation of total scores. The individual domain scores from the nearest prior assessment which is up to 28 days earlier (and post baseline) will be carried forward and used for computation of total score. If there is no prior assessment meeting this criteria, the total scores will be set to missing.

+++Efficacy+++

Table 9 Weighting for Computation of ESSDAI and ClinESSDAI

Domain	Weight	
	ESSDAI	ClinESSDAI
Constitutional	CCI - This section contained Clinical Outcome Assessment data collection questionnaires or indices, which are protected by third party copyright laws and therefore have been excluded.	
Lymphadenopathy and lymphoma		
Glandular		
Articular		
Cutaneous		
Pulmonary		
Renal		
Muscular		
Peripheral nervous system		
Central nervous system		
Haematological		
Biological		

Calculation of ESSDAI Response (Corrected)

- Three ESSDAI response variables will be computed. Definitions for responders is specified below:
  - **Responders 1** - Subjects with a reduction in total ESSDAI of at least 5 points over baseline
  - **Responders 2** - Subjects with a reduction in total ESSDAI of at least 3 points over baseline
  - **Responders 3** - Subjects with a reduction in total ESSDAI of at least 3 points over baseline, and ESSDAI Total Score <5
  - **Responders 4** - ESSDAI Total Score < 5

Lacrimal Gland Function

- Stirp length wet (mm/min) is calculated as length (mm) paper wet divided by time taken to wet (min) for the left and right eyes. The length of Schirmer's strip is 35mm so wet/min can be calculated accordingly if the entire paper was wet and the time was recorded.
  - If duration is given as 0 or Not Applicable it will be considered as 5 mins.

11.5.5. Health Outcomes

+++Patient Reported Outcomes+++

Calculation of ESSPRI Total Score

- The ESSPRI has 3 domains (dryness, fatigue and pain)
- The ESSPRI total score is the mean of the 3 domain scores, with each domain score being the response between CCI and CCI which is provided in response to the below questions.
  - CCI - This section contained Clinical Outcome Assessment data collection questionnaires or indices, which are protected by third party copyright laws and therefore have been excluded.
  -
  -
- If there are missing responses for >1 domain, the ESSPRI total is set to missing. If 1 domain is missing, the nearest prior assessment up to 28 days earlier (and post baseline) for this domain will be carried forward and used for computation of total ESSPRI score. If there is no prior assessment meeting this criteria, the total score will be set to missing.

Calculation of ESSPRI Response

- Two ESSPRI Response will be calculated.
- **Definition 1** - An ESSPRI response is defined as a decrease in the ESSPRI total score of at least one point or at least 15% compared to baseline.
- **Definition 2** - An ESSPRI response is defined as a patient with baseline of ≥ 5 and ESSPRI score < 5.

Calculation of PROFAD-SSI-SF

- Each of the 19 questions of the short form PROFAD-SSI-SF has a severity scores ranging from 0 to 7 indicating increasing severity.
- Eight domain scores are derived from the 19-item PROFAD-SSI-SF questionnaire by taking averages of available responses to the relevant questions. Where responses are available for less than 50% of the required questions at the specific visit, the domain score for that visit will be set to missing.

Domain	Questions	Domain Score Set to Missing
Somatic fatigue	CCI - This section contained Clinical Outcome Assessment data collection questionnaires or indices, which are protected by third party copyright laws and therefore have been excluded.	
Mental fatigue		
Arthralgia		
Vascular		
Cutaneous dryness		
Vaginal dryness		
Ocular dryness		
Oral dryness		

PROF, PROFAD and SSI subscores are derived by summing the domain scores listed in Table 10. The SSI subscores will be derived for females only.

Table 10 PROFADSSI Domains

PROF	PROFAD	SSI
Somatic fatigue	Somatic fatigue	Cutaneous dryness
Mental fatigue	Mental fatigue	Vaginal dryness
	Arthralgia	Ocular dryness
	Vascular	Oral dryness

11.5.6. Biomarkers

A list of Flow Cytometry Parameters and associated variable names in the Biomarker dataset (BIOMARK) which will be summarized are provided in Table 11.

If BIMETHCD=FLWTBNK AND IF BICATCD = CD19 AND BITESTCD=CONC AND BIORRES = '<5 'then BIORRESN (i.e. Table 11 Column = Low B cell Imputation = Yes) will be imputed by S&P to **result of subset parameter in % * 2.5.**

Example calculation for subset parameter:

Panel [BIMETHCD]	Parameter [BICATCD]	Unit [BITESTCD]	Unit [BIORRESU]	Result (Numerical) [BIORRESN]	Result [BIORRES]
FLWTBNK	CD19	CONC	CELLS/CUMM		< 5
FLWPLSM	CDX136	CONC	CELLS/CUMM	Imputation = 96/100 * 2.5 = 2.4	
FLWPLSM	CDX136	PERCENT	%	96	

IF BIORRES="UNABLE TO CALCULATE" THEN the standard values (BISTRESC and BISTRESN) will be the same as in original values (BIORRES, BIORRESU), do not apply any imputation (i.e. DO NOT set 0).

Any other parameter reported as < x will be imputed to ½*x

Table 11 Flow Cytometry Parameters

Biomarker Testing Method Code (BIMETHCD)	BICATCD	Parameter	BITESTCD	Source Data Units of Measurement (BIORRESU)	Conversion of source data to Cells/mL for reporting	Low B cell Imputation	Label [1]
FLWTBNK	CDX03	CD3+ CD4+	CONC	CELLS/CUMM	N	N	CD4+ T cells
FLWTBNK	CDX02	CD3+ CD8+	CONC	CELLS/CUMM	N	N	CD8+ T cells
FLWTBNK	CD19	CD19+ B Cell	CONC	CELLS/CUMM	N	Imputed	CD19+ Total B cells
FLWPLSM	CDX136	Naïve CD20+ CD27- (% of CD19+ cells)	PERCENT	%	N	N	Naïve B cell CD20+ CD27- (% of CD19 cells)
FLWPLSM	CDX136	Naïve CD20+ CD27-	CONC	CELLS/CUMM	N	Y	Naïve B cell CD20+ CD27-
FLWPLSM	CDX137	Memory CD20+ CD27+	CONC	CELLS/CUMM	N	Y	Memory B cell CD20+ CD27+
FLWPLSM	CDX137	Memory CD20+ CD27+ (% of CD19+ cells)	PERCENT	%	N	N	Memory B cell CD20+ CD27+ (% of CD19+ cells)
FLWPLSM	CDX143	CD20- CD138+	CONC	CELLS/CUMM	Y	Y	Plasmacell CD20- CD138+
FLWPLSM	CDX141	Activated B Cell CD20+ CD69+ (% of CD19+ cells)	PERCENT	%		N	Activated Total B Cells CD20+ CD69+ (% of CD19+ cells)
FLWPLSM	CDX141	Activated B Cell	CONC	CELLS/CU	Y	Y	Activated Total B

Biomarker Testing Method Code (BIMETHCD)	BICATCD	Parameter	BITESTCD	Source Data Units of Measurement (BIORRESU)	Conversion of source data to Cells/mL for reporting	Low B cell Imputation	Label [1]
	[a]	CD20+ CD69+		MM			Cells CD20+ CD69+
FLWPLSM	CDX156	Plasmablast All CD27+CD38+CD19+ (% of CD19+ cells)	PERCENT	%	N	N	Plasmablast All CD27+CD38+CD19+ (% of CD19+ cells)
FLWPLSM	CDX156	Plasmablast All CD27+CD38+CD19+	CONC	CELLS/CUMM	Y	Y	Plasmablast All CD27+CD38+CD19+
FLWPLSM	CDX493	Plasmablast CD20+	CONC	CELLS/ML	NA	Y	Plasmablast CD20+
FLWPLSM	CDX494	Plasmablast CD20-	CONC	CELLS/ML	NA	Y	Plasmablast CD20-
FLWPLSM	CDX145	CD20+ CD138+	CONC	CELLS/CUMM	Y	Y	Plasmacells CD20+CD138+
FLWPLSM	CD20	B cells CD20+	CONC	CELLS/CUMM	N	Y	B cells CD20+
FLWTBNK	CDX04	Natural Killer CD16+ CD56+	CONC	CELLS/CUMM	N	N	Natural Killer CD16+ CD56+
FLWTRANS	CDX198	Transitional T2 CD19+ CD24Int+ CD38Int+ CD27-	CONC	CELLS/CUMM	Y	Y	Transitional T2 CD24Int+ CD38Int+ CD27-
FLWTRANS	CDX199	Transitional CD19+ CD24b+ CD38b+ CD27- (% of CD19+ cells)	%CD19+	%	N	N	Transitional CD24b+ CD38b+ CD27- (% of CD19+ cells)
FLWTRANS	CDX199	Transitional CD19+ CD24b+ CD38b+ CD27-	CONC	CELLS/CUMM	Y	Y	Transitional CD24b+ CD38b+ CD27-
FLWTRANS	CDX202	Memory Breg Phenotype CD19+ CD24b+ CD27+	CONC	CELLS/CUMM	Y	Y	Memory B cells CD24b CD27+
FLWTRANS	CDX203	Naïve IgD+ CD19+ CD27- IgD+	CONC	CELLS/CUMM	N	Y	Naïve B cell IgD+
FLWTRANS	CDX84	Non-Switched Memory CD19+ CD27+ IgD+	CONC	CELLS/CUMM	N	Y	Non-Switched Memory CD27+ IgD+
FLWTRANS	CDX86	Switched Memory CD19+ CD27+ IgD-	CONC	CELLS/CUMM	N	Y	Switched Memory CD27+ IgD-
FLWTRANS	CDX87	Plasmablast CD38br CD27br CD19+	CONC	CELLS/CUMM	Y	Y	Plasmablast CD38br CD27br CD19+
FLWPLSM	CDX154	Short-lived Plasma CD20-	CONC	CELLS/CUMM	Y	Y	Short-lived Plasma CD20-

Biomarker Testing Method Code (BIMETHCD)	BICATCD	Parameter	BITESTCD	Source Data Units of Measurement (BIORRESU)	Conversion of source data to Cells/mL for reporting	Low B cell Imputation	Label [1]
		CD27br					CD27br
FLWTRANS	CDX197	Transitional CD24+ CD27- CD19+	CONC	CELLS/CUMM	N	Y	Transitional CD24+ CD27- CD19+
FLWTRANS	CDX205	Naïve B cells CD24- CD38br CD19+	CONC	CELLS/CUMM	N	Y	Naïve B cell CD24- CD38br CD19+

[1] Label included for reference only

The cells/mL records will be derived from source data as required. Cells/mL =1000 * Cells/CUMM.

The reporting units and database information for serologic biomarkers, complement and serum chemokines are detailed in Table 12.

Table 12 Additional Biomarkers

Biomarker Category	Biomarker	Dataset	Dataset Codes	Reporting Unit	Notes
Serologic Markers	SS-A	LAB	LBTESTCD = ASSARO_PLQ	KU/L	Categories for summary: <7 7 – 10 >10 – 120 >120 – 240 >240
	SS-B	LAB	LBTESTCD = ASSBLA_PLQ	KU/L	Categories for summary: <10 10 – 80 >80 – 160 >160 – 320 >320
	Rheumatoid Factor	LAB	LBTESTCD = RF_PLC	KU/L	Impute values <10 to 5
	Lambda light chain protein	LAB	LBTESTCD = LLCPRO_PLC	mg/L	
	Kappa light chain protein	LAB	LBTESTCD = KLCPRO_PLC	mg/L	
	kappa/lambda ratio*	LAB	LABTESTCD = LKLC_PLQ	mg/L	Derived
	Beta 2 microglobulin	LAB	LBTESTCD = B2M_PLC	NMOL/L=SI or original=mg/L	
Complement	CH50	LAB	LBTESTCD = CH50_PLC	U/ml =original unit	Categories for summary: <10 10-30 >30-60 >60
	C3	BIOMARK	BICATCD=C3	G/L	
	C4	BIOMARK	BICATD=C4	G/L	
Serum cytokine	CXCL13	BIOMARK	BICATCD=BLC = BICCAT= B-lymphocyte chemokine	NG/L	

* The parameter is derived as a ratio of Kappa light chain protein to Lambda light chain protein

A list of Minor Salivary Gland Parameters and associated variable names in the MI dataset which will be summarized are provided in Table 13.

Only baseline and Week 24 data will be reported for Primary Analysis reporting. Any parameter reported as 'No B-cells (CD20)' will be excluded from summary.

Table 13 Minor Salivary Gland Parameters

Parameter	Units	MITESTCD	Replicate Results Databased defined by MIREFID2 (biopsy slices) [3]
[1] Lymphoma Risk	Negative/Positive	AG001	N
[2] Lymphocyte Focus Score	per 4 mm^2	AG006	Y
[2] B cell (CD20)	count/mm^2	AG007	N
[2] B (CD20) / T (CD3) cell ratio		AG008	N
[2] Plasma cell (CD138+; both - CD20pos and CD20neg)	count/mm^2	AG012	N
T cell (CD3)	count/mm^2	AE005	N
Total aggregate area/total glandular area	ratio	AG004	Y
Average Focus size	mm^2	AG005	Y
Percent Foci displaying Germinal centres*	%	AG010	Y
Percent Foci displaying follicular dendritic cells (CD21)	%	AG011	Y
Percent Foci displaying CD3/CD20 segregation	%	AG009	Y
Plasma cell (CD138; both CD20+ and CD20-)/ B cell (CD20)	ratio	AG018	N
Plasma cell (CD138+, CD20+)	count /mm^2	AG020	N
Plasma cell (CD138+, CD20-)	count /mm^2	AG021	N
Memory B Cell (CD20+CD27+)	count /mm^2	AG022	N
Follicular B cell (IgD+, CD20+)	count /mm^2	AG017	N
Non-switched Memory B cell (IgD+, CD20+, CD27+)	count /mm^2	AG023	N
Switched Memory B cell (IgD-, CD20+, CD27+)	count /mm^2	AG024	N

[1] Lymphoma risk assessed at screening only and presented in baseline characteristics summary.
[2] Parameters reported at interim analysis
[3] For some assessments, sections from two different cutting levels are planned, and an additional section may be taken for analysis if discrepant results across cutting levels (difference >2 in focus score).

For the histology parameters where replicate results (i.e. from two different cutting levels) are provided (as indicated by 'Y'), average across all the replicates will be derived for analysis. If no replicate, then available value will be used for summary.

11.5.6.1. Immunogenicity

Anti-drug antibody (ADA) assays (Belimumab and Rituximab):

1. Binding assay: Tiered assay (Screening, confirmation, and titer) to assess the presence of ADA
    - Screening assessment is performed producing a result that is positive or negative. Negative samples in the screening assay are negative for the binding assay.
    - For samples with a positive screening assessment, a confirmation assay is carried out which produces a positive or negative result. A subject is confirmed as positive for the assessment at this step. Samples testing positive in the screening assay, but negative in the confirmation assay are

negative; samples testing positive in both the binding assay and the confirmation assay are positive for the binding assay

- For samples with a positive binding assay (positive in the screening and confirmation) result, a titer value is obtained to quantify the degree of binding in a titration assay step. The titer result is the inverse of the dilution at which the sample no longer tests positive in the screening assay.

2. Neutralizing assay (NAb) (only for Belimumab): Assay to determine if ADA present in a sample is neutralizing to the activity of the drug. Subjects who test positive for the binding assay may be further characterized by testing confirmed positive samples from the binding assay in the neutralizing assay, which produces a positive or negative result.

If a subject has a positive screening assessment from the binding assay, but the confirmatory assessment is missing, the immunogenicity response will be reported as "Unknown".

- **NOTE:** For subjects WD IP and immediately entering Week 68/FU, assess any impact if visits are not in chronological order, when categorizing Persistent Positive. Adjust if required.

Reporting of Rituximab

The following definitions will be applied when summarizing the data.

Persistent Positive (PP)

Baseline (Week 8):

1. Baseline (Week 8) is the first-time immunogenicity is being tested and therefore cannot be PP
2. One exception is IF confirming = positive @ Baseline (Week 8) & subject WD from study prior to Week 24 THEN PP

Post Baseline (Week 8):

Positive response that occurs at least 2 consecutive assessments or a single result at the final assessment (i.e. point 2 above)

Transient Positive (TP)

- Single positive response that does not occur at the final assessment

NOTE: Both the screening and confirming test for the time point in question must be positive

Additional Programming Notes:

- IF your Positive @ Week 8 = TP AND IF the same subject @ Week 24 = Positive then will be classified as PP at Week 24 ONLY BUT cannot be retrospectively applied (i.e. being PP) to the same subject at Week 8

- IF the same subject @ Week 52 was negative then classified as negative at this timepoint (i.e. PP classification cannot be carried forward from previous timepoint)

11.6. Appendix 6: Reporting Standards for Missing Data

11.6.1. Premature Withdrawals

Element	Reporting Detail
General	○ Subject study completion (i.e. as specified in the protocol) was defined as a subject who has completed the treatment and general follow up phase of the study including the Week 68 visit. ○ Subjects may discontinue treatment and continue to complete remaining scheduled visits whilst off treatment or withdraw from study prior to Week 68. ○ All available data from subjects who discontinue treatment or are withdrawn from the study will be included in analysis, summary tables and figures, unless otherwise specified.

11.6.2. Handling of Missing Data

Element	Reporting Detail
General	○ Missing data occurs when any requested data is not provided, leading to blank fields on the collection instrument: • 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.

11.6.2.1. Handling of Missing 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: • 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 3 : Treatment States and Phases. • 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.

11.6.2.2. Handling of Partial Dates

Element	Reporting Detail
Concomitant Medications	○ Partial dates for any concomitant medications recorded in the CRF will be imputed using the following convention: • If the partial date is a start date, a '01' will be used for the day and 'Jan' will be used for the month • 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: • If the partial date is a start date, a '01' will be used for the day and 'Jan' will be used for the month. • 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. • The AE will then be considered to start on-treatment (worst case). • If the partial date is a stop date, a '28/29/30/31' will be used for the day (dependent on the month and year) and 'Dec' will be used for the month. ○ The recorded partial date will be displayed in listings.

11.6.2.3. Handling of Missing Data for Statistical Analysis

Element	Reporting Detail
General	○ Appendix 5 details imputations that will applied to obtain total scores for ESSDAI, ClinESSDAI and ESSPRI where sufficient partial data are collected. An MMRM approach is planned for the key efficacy readouts.

11.7. Appendix 7: Values of Potential Clinical Importance

11.7.1. Laboratory Values

Hematology				
Laboratory Parameter	**Units**	**Category**	**Clinical Concern Range**	
			Low Flag (< x)	**High Flag (>x)**
Lymphocytes	GI/L		0.8	
Neutrophil Count	GI/L		1.5	
Platelet Count	GI/L		100	550
While Blood Cell Count (WBC)	GI/L		3	20
Monocytes	GI/L		1.8	8
Eosinophils	GI/L		0.05	0.55
Basophils	GI/L		0	0.2
Red Blood Cell Count (RBC)	TI/L		3.6	5.1
Hemoglobin	G/L		71	199
Hematocrit	l		0.201	0.599

Clinical Chemistry				
Laboratory Parameter	**Units**	**Category**	**Clinical Concern Range**	
			Low Flag (< x)	**High Flag (>x)**
Albumin	G/L		32	50
Creatinine	umol/L		53	104.3
Glucose	mmol/L		3.9	6.9
Potassium	mmol/L		3.5	5.3
Sodium	mmol/L		135	146
Chloride	mmol/L		95	108
Urea/BUN	mmol/L		2.5	9
Creatinine Kinase	IU/L		0	190
Uric Acid	umol/L		150	450

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

Laboratory Parameter	Units	Normal Ranges	
		Low Flag (< x)	High Flag (>x)
IgG	G/L	6.94	16.18
IgM	G/L	0.48	2.71
IgA	G/L	0.81	4.63

11.7.2. 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
Systolic Blood Pressure	mmHg	≥ 30	≥ 30
Diastolic Blood Pressure	mmHg	≥ 20	≥ 20
Heart Rate	bpm	≥ 30	≥ 30

11.8. Appendix 8: Laboratory Parameters & Toxicity Grading Tables

11.8.1. Laboratory Parameters

Hematology	Urinalysis	Other Screening Tests
CBC: • WBC Count • Hemoglobin • Hematocrit • Platelet Count RBC Indices: • RBC Count • MCV • MCH WBC Differential: • Neutrophils • Lymphocytes • Monocytes • Eosinophils • Basophils	Specific gravity pH, glucose, protein, blood and ketones by dipstick	HIV, Hepatitis B (HBsAg) and HbcAb Hepatitis C (Hep C antibody) FSH and estradiol Serum or urine hCG Pregnancy
Biological Markers	**Immunogenicity**	**PK**
<u>TBNK panel:</u> • CD16+CD56+ (Natural Killer Cell) Count (counts/ml) • % CD16+CD56+ (Natural Killer Cell) (as a proportion of tot lymphocytes) • CD3+CD4+ (Helper T Cell) Count • CD3+CD8+ (Cytotoxic T Cell) Count <u>Serologic Markers</u> • Concentration SS-A and SS-B • Concentration Rheumatoid factor • Concentration Lambda and kappa free light chains • Concentration Beta 2 microglobulins <u>Complement Factors:</u> • Concentration C3 • Concentration C4 • Concentration CH50 <u>Immunoglobulins</u> • IgG, IgA, IgM <u>Core 6-colour B cell assay ('plasma B cell panel'):</u> • B cell (CD19+) • Naïve B cell (CD19+CD20+CD27-) (absolute count)	Rituximab immunogenicity Belimumab immunogenicity	Rituximab PK Belimumab PK

• Naïve B cell (CD19+CD20+CD27-) (percentage of CD19+) • Memory B cell (CD19+CD20+CD27+) (absolute count) • Memory B cell (CD19+CD20+CD27+) (percentage of CD19+) • Plasmablast All (CD19+CD27+CD38+) (absolute count) • Plasmablast All (CD19+CD27+CD38+) (percentage of CD19+) • Plasmablast CD20+ (CD19+CD20+CD27br+CD38br+) (absolute count) • Plasmablast CD20- (CD19+CD20-CD27br+CD38br+) (absolute count) <u>Exploratory 6-colour B cell assay ('plasma B cell panel'):</u> • Activated B cells (CD19+CD20+CD69+) (absolute count) • Activated B cells (CD19+CD20+CD69+) (percentage of CD19+) • Plasmacell (CD20- CD138+) (absolute count) <u>Listings only 6-colour B cell assay ('plasma B cell panel'):</u> • Plasmacells CD20+ (CD20+CD138+) (absolute count) • B cells CD20+ (CD19+CD20+)(absolute count) <u>Core CD24w/Plasma B cell assay ('Transitional B cell Panel'):</u> • Transitional T2 (CD19+ CD24Int+CD38Int+CD27-) (absolute count) • Transitional (CD19+CD24br+CD38br+CD27-) (percentage of CD19+) • Transitional (CD19+CD24br+CD38br+CD27-) (absolute count) • Non-switched memory (CD19+CD27+IgD+) (absolute counts) • Switched memory (CD19+CD27+IgD-) (absolute counts) <u>Exploratory CD24w/Plasma B cell assay ('Translational B cell Panel'):</u> • Memory 'Breg phenotype' (CD19+CD24br+CD27+) (absolute count) • Naïve IgD+ (CD19+CD27-IgD+) (absolute count) <u>Listings only CD24w/Plasma B cell assay ('Transitional B cell Panel')</u> • Plasmablasts (CD38br CD27br CD20+) (absolute count) • Short-lived Plasma (CD20- CD27br) (absolute count) • Transitional (CD24+ CD27-) (absolute count) • Naïve B cells (CD24-CD38br+) (absolute count) Concentration C-Reactive Protein Concentration free BLyS * <u>Core Minor Salivary Gland histology assessments:</u> • Lymphocyte Focus Score (in $4mm^2$) • B cell (CD20) count/mm^2 • B (CD20) / T (CD3) cell ratio		

• Plasma cell (CD138+; both - CD20pos and CD20neg) count/mm^2 • Memory B Cell (CD20+CD27+) count/mm^{2†} Exploratory Minor Salivary Gland Histology Assessments • T (CD3) cell /mm^2 • Total aggregate area/total glandular area (ratio) • Average Focus size (mm^2) • % Foci displaying Germinal centres • % Foci displaying follicular dendritic cells (CD21) • % Foci displaying CD3/CD20 segregation • Plasma cell (CD138; both CD20+ and CD20-)/ B cell (CD20) ratio • Plasma cell (CD138+, CD20+) count /mm^2 • Plasma cell (CD138+, CD20-) count /mm^2 • Lymphoma risk - Assessed as Yes or No End of Study: Additional parameters maybe reported, if available: • Follicular B cell (IgD+, CD20+) • Non-switched Memory B cells (IgD+, CD20+, CD27+) • Switched Memory B cells (IgD-, CD20+, CD27+) Serum cytokines and chemokines: • Concentration CXCL13		

† Will be reported for End of Study
*Total BLyS concentrations only for End of Study analysis

11.8.2. Toxicity Grading Tables

Modified version of DMID is used for the toxicity grading with the exception of IgG (values taken from scientific literature) and lymphocytes (values taken from CTCAE V4).

HEMATOLOGY		GRADE 1	GRADE 2	GRADE 3	GRADE 4
Hemoglobin		9.6-11 G/DL 96-110 G/L	8.1-9.5 G/DL 81-95 G/L	6.5-8 G/DL 65-80 G/L	0-6.4 G/DL 0-64 G/L
Leukocytes		3-3.9 THOU/MCL 3-3.9 GI/L	2-2.9 THOU/MCL 2-2.9 GI/L	1-1.9 THOU/MCL 1-1.9 GI/L	0-0.9 THOU/MCL 0-0.9 GI/L
Absolute Neutrophils		1.5-1.99 THOU/MCL 1.5-1.99 GI/L	1-1.49 THOU/MCL 1-1.49 GI/L	0.5-0.99 THOU/MCL 0.5-0.99 GI/L	0-0.49 THOU/MCL 0-0.49 GI/L
Platelets		75,000-99,999 PER CUMM 75-99 GI/L	50,000-74,999 PER CUMM 50-74 GI/L	25,000-49,999 PER CUMM 25-49 GI/L	0-24,999 PER CUMM 0-24 GI/L

CHEMISTRIES		GRADE 0 (QUEST DB REQUIREMENT)	GRADE 1	GRADE 2	GRADE 3	GRADE 4
Sodium (step-wise grading for Hyponatremia and Hypernatremia combined)		136-145 MEQ/L	130-150 MEQ/L	123-157 MEQ/L	116-165 MEQ/L	0-99,999 MEQ/L
		136-145 MMOL/L	130-150 MMOL/L	123-157 MMOL/L	116-165 MMOL/L	0-99,999 MMOL/L
Hyponatremia			*130-135 MEQ/L*	*123-129 MEQ/L*	*116-122 MEQ/L*	*<116 MEQ/L*
Hypernatremia			*146-150 MEQ/L*	*151-157 MEQ/L*	*158-165 MEQ/L*	*>165 MEQ/L*
Potassium (step-wise grading for Hypokalemia and Hyperkalemia combined)		3.5-5.5 MEQ/L	3-6 MEQ/L	2.5-6.5 MEQ/L	2-7 MEQ/L	0-9,999.9 MEQ/L
		3.5-5.5 MMOL/L	3-6 MMOL/L	2.5-6.5 MMOL/L	2-7 MMOL/L	0-9,999.9 MMOL/L
Hypokalemia			*3.0-3.4 MEQ/L*	*2.5-2.9 MEQ/L*	*2.0-2.4 MEQ/L*	*<2.0 MEQ/L*
Hperkalemia			*5.6-6.0 MEQ/L*	*6.1-6.5*	*6.6-7.0 MEQ/L*	*>7.0 MEQ/L*
Phosphate (analyte not within chem. panel for this protocol so will flag)			2-2.4 MG/DL	1.5-1.9 MG/DL	1-1.4 MG/DL	0-0.9 MG/DL
			0.65-0.75 MMOL/L	0.5-0.64 MMOL/L	0.3-0.49 MMOL/L	0-0.29 MMOL/L
Calcium (corrected for Albumin) (step-wise grading for Hypocalcemia and Hypercalcemia combined)		8.5-10.5 MG/DL	7.8-11.5 MG/DL	7-12.5 MG/DL	6.1-13.5 MG/DL	0-9,999.9 MG/DL
		2.12-2.62 MMOL/L	1.94-2.86 MMOL/L	1.74-3.12 MMOL/L	1.52-3.36 MMOL/L	1.52-9,999.99 MMOL/L
Hypocalcemia			*7.8-8.4 mg/dL*	*7.0-7.7 mg/dL*	*6.4-6.9 mg/dL*	*<6.1 mg/dL*
Hypercalcemia			*10.6-11.5 mg/dL*	*11.6-12.5 mg/dL*	*12.6-13.5 mg/dL*	*>13.5 mg/dL*
Magnesium (analyte not within chem. panel for this protocol so will flag)			1.2-1.4 MEQ/L	0.9-1.1 MEQ/L	0.6-0.8 MEQ/L	0-0.5 MEQ/L
			0.6-0.7 MMOL/L	0.46-0.59 MMOL/L	0.3-0.45 MMOL/L	0-0.29 MMOL/L
Albumin			3-3.4 G/DL	2.5-2.9 G/DL	2-2.4 G/DL	0-1.9 G/DL
			30-34 G/L	25-29 G/L	20-24 G/L	0-19 G/L
Bilirubin (Total)			1.4-1.9 MG/DL	2.0-3.2 MG/DL	3.3-6.5 MG/DL	6.6-9,999.9 MG/DL
			23-33 UMOL/L	34-55 UMOL/L	56-110 UMOL/L	111-9,999.9 UMOL/L
			> 1.0-1.5 x ULN	> 1.2-2.5 x ULN	> 2.5-5 x ULN	>5 x ULN
Glucose (step-wise grading for Hypoglycemia and Hyperglycemia combined)		65-115 MG/DL	55-160 MG/DL	40-250 MG/DL	30-500 MG/DL	0-99,999 MG/DL
		3.6-6.4 MMOL/L	3.1-8.9 MMOL/L	2.2-13.9 MMOL/L	1.7-27.8 MMOL/L	0-9,999.9 MMOL/L
Hypoglycemia			*55-94 mg/dL*	*40-54 mg/dL*	*30-39 mg/dL*	*<30 mg/dL*
Hyperglycemia			*116-160 mg/dL*	*161-250 mg/dL*	*251-500 mg/dL*	*>500 251-500 mg/dL*
Creatinine		*Ref Range MG/DL*			*MG/DL*	
	M 18-19y	0.67-1.26	1.27 - 1.89	1.90 - 3.78	3.79 - 7.56	>7.56
	F 18-19y	0.48-1.01	1.02 - 1.51	1.52 - 3.03	3.04 - 6.06	>6.06
	M 20-29y	0.80-1.30	1.31 - 1.95	1.96 - 3.90	3.91 - 7.80	>7.80
	F 20-29y	0.57-1.03	0.58 - 1.54	1.54 - 3.09	3.10 - 6.18	>6.18
	M 30-39y	0.79-1.33	1.34 - 1.99	2.00 - 3.99	4.00 - 7.98	>7.98
	F 30-39y	0.58-1.06	1.07 - 1.59	1.60 - 3.18	3.19 - 6.36	>6.36
	M 40-49y	0.78-1.34	1.35 - 2.01	2.02 - 4.02	4.03 - 8.04	>8.04
	F 40-49y	0.59-1.07	1.08 - 1.60	1.60 - 3.21	3.22 - 6.42	>6.42
	M 50-59y	0.76-1.46	1.47 - 2.19	2.20 - 4.38	4.39 - 8.76	>8.76
	F 50-59y	0.60-1.10	1.11 - 1.65	1.66 - 3.30	3.31 - 6.60	>6.60
	M 60-69y	0.76-1.46	1.47 - 2.19	2.20 - 4.38	4.39 - 8.76	>8.76
	F 60-69y	0.60-1.18	1.19 - 1.77	1.78 - 3.54	3.55 - 7.08	>7.08
	M >69y	0.67-1.54	1.55 - 2.31	2.32 - 4.62	4.63 - 9.24	>9.24
	F >69y	0.63-1.22	1.23 - 1.83	1.84 - 3.66	3.67 - 7.32	>7.32
		Ref Range UMOL/L			*UMOL/L*	

	M 18-19y	59.2-111.4	111.5 - 167.1	167.2 - 334.2	334.3 - 668.4	>668.4
	F 18-19y	42.4-89.3	89.4 - 133.9	134.0 - 267.9	268.0 - 535.8	>535.8
	M 20-29y	70.7-114.9	115.0 - 172.3	172.4 - 344.7	344.8 - 689.4	>689.4
	F 20-29y	50.4-91.1	91.2 - 136.6	136.7 - 273.3	273.4 - 546.6	>546.6
	M 30-39y	69.8-117.6	117.7 - 176.4	176.5 - 352.8	352.9 - 705.6	>705.6
	F 30-39y	51.3-93.7	93.8 - 140.5	140.6 - 281.1	281.2 - 562.2	>562.2
	M 40-49y	69.0-118.5	118.6 - 177.7	177.8 - 355.5	355.6 - 711.0	>711.0
	F 40-49y	52.2-94.6	94.7 - 141.9	142 - 283.8	283.9 - 567.6	>567.6
	M 50-59y	67.2-129.1	129.2 - 193.6	193.7 - 387.3	387.4 - 774.6	>774.6
	F 50-59y	53.0-97.2	97.3 - 145.8	145.9 - 291.6	291.7 - 583.2	>583.2
	M 60-69y	67.2-129.1	129.2 - 193.6	193.7 - 387.3	387.4 - 774.6	>774.6
	F 60-69y	53.0-104.3	104.4 - 156.4	156.5 - 312.9	313.0 - 625.8	>625.8
	M >69y	59.2-136.1	136.2 - 204.1	204.2 - 408.3	408.4 - 816.6	>816.6
	F >69y	55.7-107.8	107.9 - 161.7	161.8 - 323.4	323.5 - 646.8	>646.8
			>1.0-1.5 x ULN	*>1.5-3 x ULN*	*>3.0-6.0 x ULN*	*>6.0 x ULN*
Uric Acid			7.5-10 MG/DL 450-590 UMOL/L	10.1-12 MG/DL 591-710 UMOL/L	12.1-15 MG/DL 711-890 UMOL/L	15.1-9,999.9 MG/DL 891-99,999 UMOL/L
AST	0-64y		53-105 U/L	106-210 U/L	211-420 U/L	421-99,999 U/L
	65-199y		69-137U/L	138-275 U/L	276-550 U/L	551-99,999 U/L
			1.25-2.5 x ULN	*>2.5-5.0 x ULN*	*>5.0-10.0 x ULN*	*>10.0 x ULN*
ALT			60-120 U/L 1.25-2.5 x ULN	121-240 U/L >2.5-5.0 x ULN	241-480 U/L >5.0-10.0 x ULN	481-99,999 U/L >10.0 x ULN
GGT (analyte not within chem. panel for this protocol so will flag)						
	M 0-64y		82-162 U/L	163-325 U/L	326-650 U/L	651-99,999 U/L
	F 0-64y		57-112 U/L	113-225 U/L	226-450 U/L	451-9,999 U/L
	65-199y		94-187 U/L	188-375 U/L	376-750 U/L	751-99,999 U/L
			1.25-2.5 x ULN	*>2.5-5.0 x ULN*	*>5.0-10.0 x ULN*	*>10.0 x ULN*
Alkaline Phosphatase	M 16-19y		282-562 U/L	563-1,125 U/L	1,126-2,250 U/L	2,251-99,999 U/L
	F 16-19y		207-412 U/L	413-825 U/L	826-1,650 U/L	1,651-99,999 U/L
	20-199y		157-312 U/L	313-625 U/L	626-1,250 U/L	1,251-99,999 U/L
			1.25-2.5 x ULN	*>2.5-5.0 x ULN*	*>5.0-10.0 x ULN*	*>10.0 x ULN*

IMMUNOGLOBULINS			GRADE 1	GRADE 2	GRADE 3	GRADE 4
IgG (Immunoglobulins)			550-700 MG/DL 5.5-7 G/L	400-549 MG/DL 4-5.49 G/L	250-399 MG/DL 2.5-3.99 G/L	0-249 MG/DL 0-2.49 G/L

URINALYSIS		GRADE 0	GRADE 1	GRADE 2	GRADE 3	GRADE 4
Protein			1++	2++, 3++	4++	n/a
RBC		0-1, 1-3	3-5	5-10, 6-10, 10+, 10-15, 10-20, 15-25, 20-40, 20+, 25-50, 50-100, INNUMERABLE	CLUMPING, CLUMPED, RBC CASTS	n/a

PROTEIN/CREATININE RATIO			GRADE 1	GRADE 2	GRADE 3	GRADE 4
Protein/Creatinine Ratio			0.2-1 MG/MG	1.001-2 MG/MG	2.001-3.5 MG/MG	3.501-999.999 MG/MG

Lymphopenia	GRADE 1	GRADE 2	GRADE 3	GRADE 4
Lymphocyte count	<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

11.9. Appendix 9: Model Checking and Diagnostics for Statistical Analyses

11.9.1. Statistical Analysis Assumptions

11.9.1.1. Continuous Endpoints

Endpoint(s)	• Change from Baseline in ESSDAI Score • Change from Baseline in ClinESSDAI Score • Change from Baseline in Stimulated salivary Flow • Change from Baseline in Oral Dryness Numeric Response Scale
Analysis	• 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.
- Akaike's Information Criteria (AIC) will be used to assist with the selection of covariance structure.
- In the event that this model fails to converge, alternative correlation structures may be considered such as CSH or CS.
- 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 serious departures from the distributional assumptions, nonparametric rank Hodges-Lehmann's confidence intervals will be provided in order to assess the robustness of the parametric analysis. This will be carried out in addition to the parametric analyses.

Endpoint(s)	• Change from Baseline in ESSDAI Score • Change from Baseline in ESSPRI Score
Analysis	• Bayesian

General Considerations for Bayesian Analysis:

- Convergence for all the parameters in the model will be verified

Initial Values:

- Unless otherwise specified, initial parameter values of 0.5 will be used for the fixed effect parameters.
- If convergence of the Markov chain Monte Carlo (MCMC) algorithm is problematic, then alternative estimates may be used (for example, these could be based on maximum likelihood estimates).

Convergence Diagnostics:

- To be able to perform Bayesian inference using MCMC simulations the samples for all the parameters in the model need to be obtained from the corresponding target posterior distribution. To ensure that this is the case the following is a list of convergence diagnostics that can be applied for each parameter:

Comparing MCSE vs posterior standard deviation:

- The Monte Carlo Standard Errors (MCSE) should be compared with the standard deviation of the posterior distribution (SD) to ensure that only a fraction of the posterior variability is due to the simulation, i.e., the ratio MCSE/SD should be as small as possible, typically close to 0.01.
- Adequate values for the number of MCMC samples / thinning / number of burn-in samples should be chosen to ensure that the ratio MCSE/SD for all the parameters in the model is approximately 0.01.
- In addition, if possible, the number of tuning units and maximum number of tuning iterations may be increased to find a better proposal distribution for the model parameters, which in turn may reduce the MCSE/SD ratio.
- Where possible the code should be written to allow the SAS compiler to identify and make use of conjugacy, since this can greatly reduce the corresponding MCSE/SD ratio

Diagnostic plots and visual inspection:

- Trace plots of samples versus the simulation index can used to assess some aspects of convergence. The centre of the chain should appear stable with very small fluctuations, i.e., the distribution of points should not change as the chain progresses and the posterior mean and variance are relatively constant.
- Autocorrelation plots can be used to assess degree of autocorrelation (should decline rapidly and show no oscillation patterns).
- The posterior density should look reasonable for each parameter (e.g. for posterior parameters expected to follow a normal distribution, the density plot should not appear bi-modal, but for parameters acting as binary flags, then bi-modal is acceptable).
- Examination of correlation structures between relevant posterior parameters should be used to provide information about what potential issues may be and also what corrective action(s) may be worthwhile attempting.

11.9.1.2. Binary Endpoints

Endpoint(s)	• Binary Endpoints as described in Section 8.1.2
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.

11.10. Appendix 10 – Abbreviations & Trade Marks

Abbreviations

Abbreviation	Description
ADaM	Analysis Data Model
AE	Adverse Event
AIC	Akaike's Information Criteria
A&R	Analysis and Reporting
CDISC	Clinical Data Interchange Standards Consortium
CI	Confidence Interval
CPMS	Clinical Pharmacology Modeling & Simulation
CS	Clinical Statistics
CSR	Clinical Study Report
CTCAE	Common Terminology Criteria for Adverse Events
CTR	Clinical Trial Register
CV_b / CV_w	Coefficient of Variation (Between) / Coefficient of Variation (Within)
DMID	Division of Microbiology and Infectious Diseases
DOB	Date of Birth
DP	Decimal Places
eCRF	Electronic Case Record Form
EoS	End of Study
ESSDAI	Eular Sjögren's Syndrome Disease Activity Index
ClinESSDAI	Clinical Eular Sjögren's Syndrome Disease Activity Index
ESSPRI	Eular Sjögren's Syndrome Patient Reported Index
GSK	GlaxoSmithKline
IA	Interim Analysis
ICH	International Conference on Harmonization
IDMC	Independent Data Monitoring Committee
IDSL	Integrated Data Standards Library
IFU	Individualized Follow Up
IMMS	International Modules Management System
IP	Investigational Product
iSRC	Safety Review Committee
ITT	Intent-To-Treat
LOC	Last Observation Carries Forward
MMRM	Mixed Model Repeated Measures
PCI	Potential Clinical Importance
PD	Pharmacodynamic
PDMP	Protocol Deviation Management Plan
PGA	Physicians Global Assessment
PK	Pharmacokinetic
PP	Per Protocol
PSAP	Program Safety Analysis Plan
pSS	Primary Sjogren's Syndrome
PtGA	Patient Global Assessment

Abbreviation	Description
QC	Quality Control
QTcF	Frederica's QT Interval Corrected for Heart Rate
QTcB	Bazett's QT Interval Corrected for Heart Rate
RAP	Reporting & Analysis Plan
RAMOS	Randomization & Medication Ordering System
SAC	Statistical Analysis Complete
SAE	Serious Adverse Event
SE	Standard Error
SD	Standard Deviation
SOP	Standard Operation Procedure
SRDP	Study Results Dissemination Plan
SRT	Safety Review Team
TA	Therapeutic Area
TFL	Tables, Figures & Listings
VEO-PCO	Value, Evidence and Outcomes, Patient Centred Outcomes.

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11.11. Appendix 11: Questionnaires

11.11.1. Columbia Suicide severity rate scale (CSSRS) post baseline

COLUMBIA SUICIDE-SEVERITY RATING SCALE (C-SSRS)

SUICIDAL IDEATION	
Ask questions 1 and 2. If both are negative, proceed to "Suicidal Behavior" section. If the answer to question 2 is "yes," ask questions 3, 4 and 5. If the answer to question 1 and/or 2 is "yes", complete "Intensity of Ideation" section.	**Since Last Visit**

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

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COLUMBIA SUICIDE-SEVERITY RATING SCALE (C-SSRS) (Continued)

SUICIDAL IDEATION	
	Since Last Visit
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INTENSITY OF IDEATION			
Ideation Type	Type # (1-5)	Description of Ideation	Since Last Visit
Most Severe Ideation			
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COLUMBIA SUICIDE-SEVERITY RATING SCALE (C-SSRS) (Continued)

INTENSITY OF IDEATION (Continued)	
	Since Last Visit
	Most Severe
CCI - This section contained Clinical Outcome Assessment data collection questionnaires or indices, which are protected by third party copyright laws and therefore have been excluded.	

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INTENSITY OF IDEATION (Continued)	
	Since Last Visit
	Most Severe
CCI - This section contained Clinical Outcome Assessment data collection questionnaires or indices, which are protected by third party copyright laws and therefore have been excluded.	

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COLUMBIA SUICIDE-SEVERITY RATING SCALE (C-SSRS) (Continued)

SUICIDAL BEHAVIOR Check (✔) all that apply, so long as these are separate events; must ask about all types.	**Since Last Visit**
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COLUMBIA SUICIDE-SEVERITY RATING SCALE (C-SSRS) (Continued)

SUICIDAL BEHAVIOR (Continued)	Since Last Visit
CCI - This section contained Clinical Outcome Assessment data collection questionnaires or indices, which are protected by third party copyright laws and therefore have been excluded.	

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COLUMBIA SUICIDE-SEVERITY RATING SCALE (C-SSRS) (Continued)

Answer for Actual Attempts Only	Most Lethal Attempt
Date: →	-- --- -- Day Month Year

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US:ENG (United States/English) IDSL Version 01.01 - 15 AUG 11 [CSSRSV4.1 Since Last Visit]

11.11.2. Columbia Suicide severity rate scale (CSSRS) at baseline

COLUMBIA SUICIDE-SEVERITY RATING SCALE (C-SSRS)

SUICIDAL IDEATION

Ask questions 1 and 2. If both are negative, proceed to "Suicidal Behavior" section. If the answer to question 2 is "yes," ask questions 3, 4 and 5. If the answer to question 1 and/or 2 is "yes", complete "Intensity of Ideation" section.

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

US:ENG (United States/English) IDSL Version 01.00 - 20 MAY 11 [CSSRSV4.1 Baseline]

COLUMBIA SUICIDE-SEVERITY RATING SCALE (C-SSRS) (Continued)

SUICIDAL IDEATION		
	Lifetime: Time He/She Felt Most Suicidal	**Current: Within Last 6 Months**
CCI - This section contained Clinical Outcome Assessment data collection questionnaires or indices, which are protected by third party copyright laws and therefore have been excluded.		

US:ENG (United States/English) IDSL Version 01.00 - 20 MAY 11 [CSSRSV4.1 Baseline]

COLUMBIA SUICIDE-SEVERITY RATING SCALE (C-SSRS) (Continued)

SUICIDAL IDEATION		
	Lifetime: Time He/She Felt Most Suicidal	**Current: Within Last 6 Months**
CCI - This section contained Clinical Outcome Assessment data collection questionnaires or indices, which are protected by third party copyright laws and therefore have been excluded.		

US:ENG (United States/English) IDSL Version 01.00 - 20 MAY 11 [CSSRSV4.1 Baseline]

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

US:ENG (United States/English) IDSL Version 01.00 - 20 MAY 11 [CSSRSV4.1 Baseline]

COLUMBIA SUICIDE-SEVERITY RATING SCALE (C-SSRS) (Continued)

INTENSITY OF IDEATION (Continued)		
	Most Severe: Lifetime	**Most Severe: Current**
CCI - This section contained Clinical Outcome Assessment data collection questionnaires or indices, which are protected by third party copyright laws and therefore have been excluded.		

US:ENG (United States/English) IDSL Version 01.00 - 20 MAY 11 [CSSRSV4.1 Baseline]

INTENSITY OF IDEATION (Continued)		
	Most Severe: Lifetime	**Most Severe: Current**
CCI - This section contained Clinical Outcome Assessment data collection questionnaires or indices, which are protected by third party copyright laws and therefore have been excluded.		

US:ENG (United States/English) IDSL Version 01.00 - 20 MAY 11 [CSSRSV4.1 Baseline]

COLUMBIA SUICIDE-SEVERITY RATING SCALE (C-SSRS) (Continued)

SUICIDAL BEHAVIOR Check (✔) all that apply, so long as these are separate events; must ask about all types.	Lifetime
CCI - This section contained Clinical Outcome Assessment data collection questionnaires or indices, which are protected by third party copyright laws and therefore have been excluded.	

US:ENG (United States/English) IDSL Version 01.00 - 20 MAY 11 [CSSRSV4.1 Baseline]

COLUMBIA SUICIDE-SEVERITY RATING SCALE (C-SSRS) (Continued)

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

US:ENG (United States/English) IDSL Version 01.00 - 20 MAY 11 [CSSRSV4.1 Baseline]

COLUMBIA SUICIDE-SEVERITY RATING SCALE (C-SSRS) (Continued)

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

US:ENG (United States/English) IDSL Version 01.00 - 20 MAY 11 [CSSRSV4.1 Baseline]

Answer for Actual Attempts Only	Most Recent Attempt	Most Lethal Attempt	Initial/First Attempt
Date: →	__ ___ __ Day Month Year	__ ___ __ Day Month Year	__ ___ __ Day Month Year
CCI - This section contained Clinical Outcome Assessment data collection questionnaires or indices, which are protected by third party copyright laws and therefore have been excluded.			

US:ENG (United States/English) IDSL Version 01.00 - 20 MAY 11 [CSSRSV4.1 Baseline]

11.11.3. Eular Sjögren's syndrome disease activity index (ESSDAI)

EULAR SJÖGREN'S SYNDROME DISEASE ACTIVITY INDEX (ESSDAI)_Modified

Domain	Activity Level	Description	Abnormality currently present and stable for >12 months and due to damage rather than activity? If yes, indicate level of involvement
1. **Constitutional** *Exclusion of fever of infectious origin and voluntary weight loss*	CCI - This section contained Clinical Outcome Assessment data collection questionnaires or indices, which are protected by third party copyright laws and therefore have been excluded.		
2. **Lymphadenopathy and lymphoma** *Exclusion of infection*			
3. **Glandular** *Exclusion of stone or infection*			
4. **Articular** *Exclusion of osteoarthritis*			

US:ENG (United States/English) IDSL Version 01.00 - 05 JAN 16 [ESSDAI_Modified]

EULAR SJÖGREN'S SYNDROME DISEASE ACTIVITY INDEX (ESSDAI)_Modified (Continued)

Domain	Activity Level	Description	Abnormality currently present and stable for >12 months and due to damage rather than activity? If yes, indicate level of involvement
5. Cutaneous *Rate as 'No activity' stable long-lasting features related to damage*	CCI - This section contained Clinical Outcome Assessment data collection questionnaires or indices, which are protected by third party copyright laws and therefore have been excluded.		
6. Pulmonary *Rate as 'No activity' stable long-lasting features related to damage, or respiratory involvement not related to the disease (tobacco use, etc.)*			

US:ENG (United States/English)

IDSL Version 01.00 - 05 JAN 16 [ESSDAI_Modified]

EULAR SJOGREN'S SYNDROME DISEASE ACTIVITY INDEX (ESSDAI)_Modified (Continued)

Domain	Activity Level	Description	Abnormality currently present and stable for >12 months and due to damage rather than activity? If yes, indicate level of involvement
7. **Renal** *Rate as 'No activity' stable long-lasting features related to damage and renal involvement not related to the disease. If biopsy has been performed, please rate activity based on histological features first*	CCI - This section contained Clinical Outcome Assessment data collection questionnaires or indices, which are protected by third party copyright laws and therefore have been excluded.		
8. **Muscular** *Exclusion of weakness due to corticosteroids*			

US:ENG (United States/English) IDSL Version 01.00 - 05 JAN 16 [ESSDAI_Modified]

EULAR SJOGREN'S SYNDROME DISEASE ACTIVITY INDEX (ESSDAI)_Modified (Continued)

Domain	Activity Level	Description	Abnormality currently present and stable for >12 months and due to damage rather than activity? If yes, indicate level of involvement
9. PNS *Rate as 'No activity' stable long-lasting features related to damage or PNS involvement not related to the disease*	CCI - This section contained Clinical Outcome Assessment data collection questionnaires or indices, which are protected by third party copyright laws and therefore have been excluded.		
10. CNS *Rate as 'No activity' stable long-lasting features related to damage or CNS involvement not related to the disease*			

US:ENG (United States/English) IDSL Version 01.00 - 05 JAN 16 [ESSDAI_Modified]

EULAR SJOGREN'S SYNDROME DISEASE ACTIVITY INDEX (ESSDAI)_Modified (Continued)

Domain	Activity Level	Description	Abnormality currently present and stable for >12 months and due to damage rather than activity? If yes, indicate level of involvement
11. Haematological *For anaemia, neutropenia, and thrombopenia, only autoimmune cytopenia must be considered* *Exclusion of vitamin or iron deficiency, drug-induced cytopenia*	CCI - This section contained Clinical Outcome Assessment data collection questionnaires or indices, which are protected by third party copyright laws and therefore have been excluded.		
12. Biological			

US:ENG (United States/English) IDSL Version 01.00 - 05 JAN 16 [ESSDAI_Modified]

11.11.4. Neurological Symptoms

	YES	NO
CCI - This section contained Clinical Outcome Assessment data collection questionnaires or indices, which are protected by third party copyright laws and therefore have been excluded.		

If any of the above are answered “Yes” at any visit, the investigator will contact the medical monitor.

Any neurological symptom that cannot be attributed to a concurrent medical condition or concomitant medication must be referred to a neurologist.

11.11.5. Oral and Ocular dryness

ORAL AND OCULAR DRYNESS SCALES

People with Primary Sjögren's Syndrome may experience a variety of symptoms. Please indicate how severe the following Sjögren's symptoms are **now** by selecting **one** number:

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

UK:ENG (United Kingdom/English) Non-Standard [Oral And Ocular Dryness Scales]

11.11.6. Physician global assessment of disease activity (PGA)

PHYSICIAN GLOBAL ASSESSMENT OF DISEASE ACTIVITY

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

UK:ENG (United Kingdom/English) Non-Standard [Physician Global Assessment of Disease Activity]

11.11.7. Eular Sjögren's syndrome patient reported index (ESSPRI)

EULAR SJÖGREN'S SYNDROME PATIENT REPORTED INDEX (ESSPRI)

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

US:ENG (United States/English) IDSL Version 01.00 - 22 APR 15 [ESSPRI]

11.11.8. Profile of fatigue and discomfort - SICCA symptoms inventory short form (PROFAD-SSI-SF)

PROFILE OF FATIGUE AND DISCOMFORT - SICCA SYMPTOMS INVENTORY - SHORT FORM - 19 ITEM (PROFAD-SSI-SF)

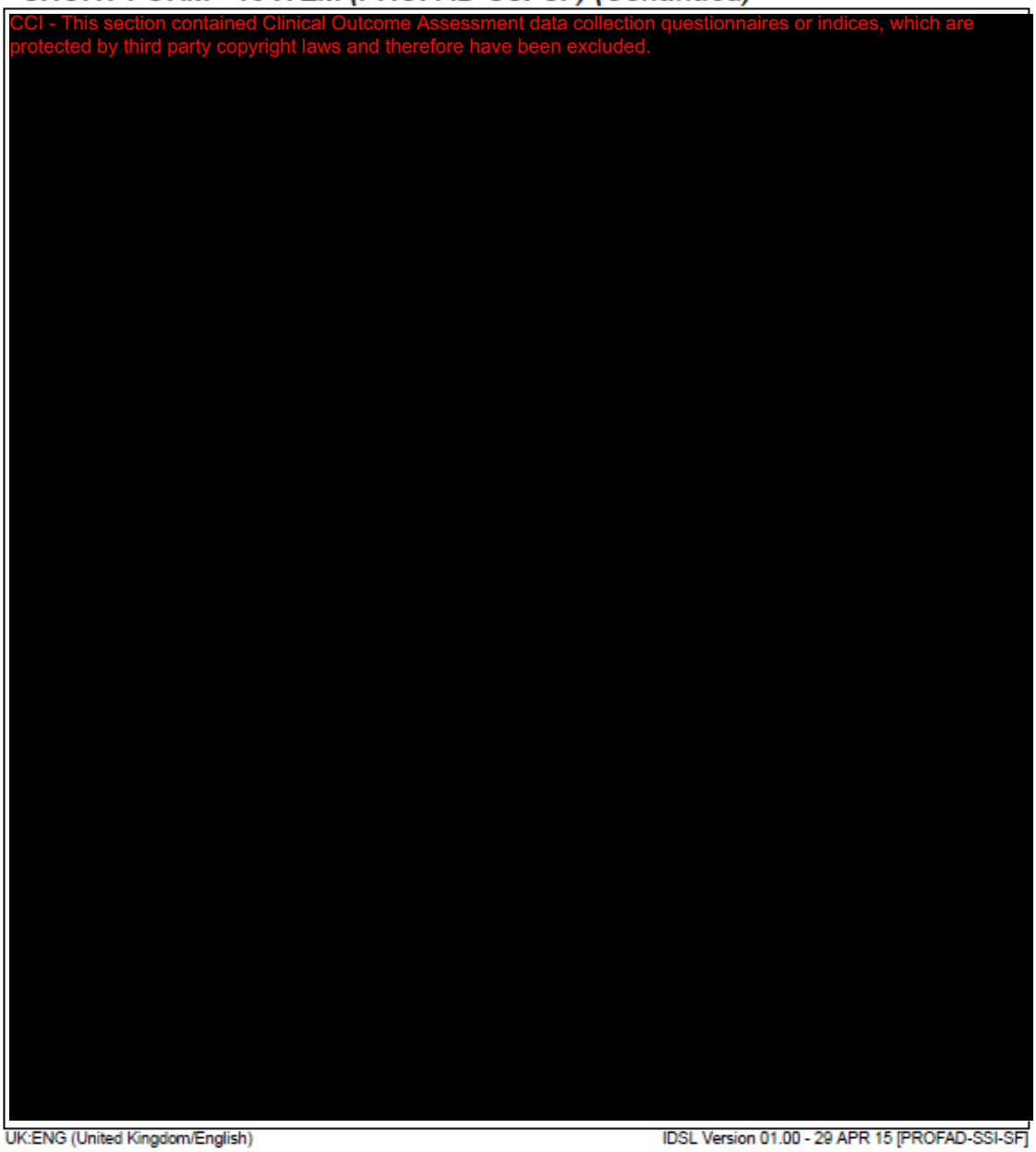
Please assess how bad at worst each symptom has been in the last two weeks by ringing one of the numbers 0 to 7.

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

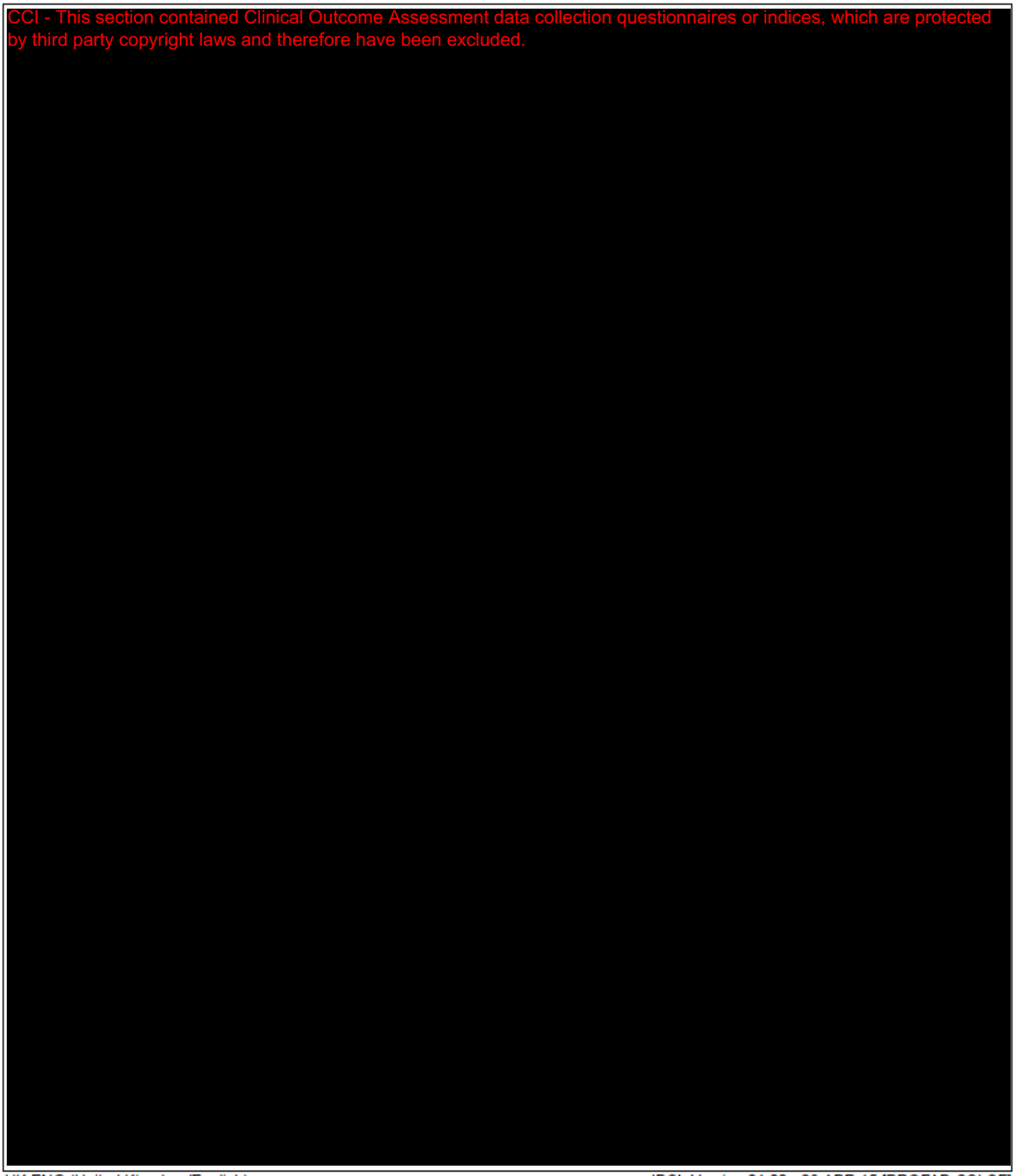
UK:ENG (United Kingdom/English) IDSL Version 01.00 - 29 APR 15 [PROFAD-SSI-SF]

PROFILE OF FATIGUE AND DISCOMFORT - SICCA SYMPTOMS INVENTORY - SHORT FORM - 19 ITEM (PROFAD-SSI-SF) (Continued)

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



UK:ENG (United Kingdom/English) IDSL Version 01.00 - 29 APR 15 [PROFAD-SSI-SF]


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

11.11.9. Patient global assessment of disease activity (PtGA)

PATIENT GLOBAL ASSESSMENT OF DISEASE ACTIVITY (PtGA)

Considering all of the ways your symptoms related to your Sjögren's syndrome (your dryness, your fatigue, your pain and your mental fatigue) are affecting you, how do you rate the severity of your Sjogren's syndrome now? (Select one number)

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

UK:ENG (United Kingdom/English) Non-Standard [Patient Global Assessment of Disease Activity (PtGA)]

11.11.10. Sjogren's Allowable Medication Categories

Medication Category	Rule
Anti-malarials	Set to "ANTIMALARIALS" if the preferred term begins with "QUINACRINE", "QUININE", "HYDROXYCHLOROQUINE", "MEPACRINE", or "CHLOROQUINE", "NOVOCHLOROQUINE" AND the route of administration is "ORAL"
Steroids	Set to 'STEROIDS' if at least one associated ATC code (ATCCD1 – ATCCD6) begins with 'H02' AND Route of administration is "ORAL"
Muscarinic agonists	Refer to Table 14

Table 14 Muscarinic agonists terms

Term Name	Term Code
CARBACHOL + HYPROMELLOSE	01175401
PHENYLEPHRINE + PILOCARPINE	00906001
ACETYLCHOLINE	00611301
METIPRANOLOL HYDROCHLORIDE + PILOCARPINE HYDROCHLORIDE	01482401
PHENYLEPHRINE + PILOCARPINE NITRATE	01309901
PHENYLEPHRINE HYDROCHLORIDE + PILOCARPINE HYDROCHLORIDE	00597501
BORIC ACID + PILOCARPINE HYDROCHLORIDE + THIAMINE HYDROCHLORIDE	00937701
XANOMELINE	01302901
CARTEOLOL HYDROCHLORIDE + PILOCARPINE HYDROCHLORIDE	40521001
XANOMELINE TARTRATE	01302902
PILOCARPINE BORATE	00043504
METHACHOLINE	00978001
METHACHOLINE CHLORIDE	00978002
PILOCARPINE HYDROCHLORIDE + TIMOLOL MALEATE	00971201
CARBACHOL	00060901
EUPHRASIA EXTRACT + PILOCARPINE HYDROCHLORIDE + POTASSIUM IODIDE	01200001
ACECLIDINE HYDROCHLORIDE	00189502
ACETYLCHOLINE CHLORIDE	00611302
NAPHAZOLINE HYDROCHLORIDE + PILOCARPINE BORATE	00981301
NAPHAZOLINE HYDROCHLORIDE + NEOSTIGMINE BROMIDE + PILOCARPINE HYDROCHLORIDE	00280001
BETHANECHOL HYDROCHLORIDE	00115903
PILOCARPINE	00043501
PILOCARPINE HYDROCHLORIDE	00043503
EPINEPHRINE BITARTRATE + PILOCARPINE HYDROCHLORIDE	00458001
ACECLIDINE	00189501
NAPHAZOLINE HYDROCHLORIDE + PILOCARPINE BORATE + PILOCARPINE HYDROCHLORIDE	00981401
PHYSOSTIGMINE SALICYLATE + PILOCARPINE HYDROCHLORIDE	00578301
PILOCARPINE NITRATE	00043502
BETHANECHOL CHLORIDE	00115902
BETHANECHOL HYDROCHLORIDE	54486501
BENZALKONIUM CHLORIDE + HYPROMELLOSE + PHENYLMERCURIC NITRATE + PILOCARPINE HYDROCHLORIDE	00221601
PHYSOSTIGMINE + PILOCARPINE	01017301
BETHANECHOL	00115901
DIPIVEFRINE HYDROCHLORIDE + PILOCARPINE HYDROCHLORIDE	53176901
CEVIMELINE	01435201
BENZALKONIUM CHLORIDE + DIPIVEFRINE HYDROCHLORIDE +	01318101

Term Name	Term Code
PILOCARPINE HYDROCHLORIDE	
CEVIMELINE HYDROCHLORIDE	52131601

11.11.11. Prednisone Conversion Factors

A concomitant medication is identified as a steroid if at least one associated ATC code (ATCCD1 – ATCCD6) begins with 'H02.'

The following routes are considered to provide systemic exposure: oral, subcutaneous, intramuscular, intradermal, and intravenous. Topical routes of administration are excluded (e.g., topical, conjunctival, intranasal).

At data base release all preferred terms identified with an ATC code beginning with 'H02' will be reviewed to ensure a conversion factor and dosing frequency exist for all terms with a systemic route of administration.

Similarly, all routes of administration for preferred terms with an ATC code beginning with 'H02'will be reviewed to ensure all systemic routes have been identified in the list above.

In order to be converted, the frequency and dose of the steroid must be present with the unit dose in milligrams (mg).

Reported dose for systemic steroid is converted to prednisone equivalent dose using conversion factor for each particular medication (refer to online calculator http://www.globalrph.com/corticocalc.htm).

Daily Prednisone Equivalent Dose (mg) = Collected Dose (mg) x Conversion Factor x Frequency Factor

Preferred term	Conversion factor for converting to a prednisone-equivalent dose
BETAMETHASONE	8.333
BETAMETHASONE DIPROPIONATE	8.333
BETAMETHASONE SODIUM PHOSPHATE	8.333
BETAMETHASONE VAL	8.333
BETROSPAM	8.333
BUDESONIDE	0.333
CELESTONA BIFAS	8.333
CORTISONE	0.2
CORTISONE ACETATE	0.2
CRONOLEVEL	8.333
DEFLAZACORT	0.8333
DEPO-MEDROL MED LIDOKAIN	1.25
DEXAMETHASONE	6.667
DEXAMETHASONE ACETATE	6.667
DEXAMETHASONE SODIUM PHOSPHATE	6.667

FLUOCORTOLONE	3
HYDROCORTISONE	0.25
Preferred term	**Conversion factor for converting to a prednisone-equivalent dose**
HYDROCORTISONE ACETATE	0.25
HYDROCORTISONE SODIUM SUCCINATE	0.25
MEPREDNISONE	1.25
METHYLPREDNISOLONE	1.25
METHYLPREDNISOLONE ACEP	1.25
METHYLPREDNISOLONE ACETATE	1.25
METHYLPREDNISOLONE SODIUM SUCCINATE	1.25
PARAMETHASONE	2.5
PREDNISOLONE	1
PREDNISOLONE SODIUM PHOSPHATE	1
PREDNISOLONE SODIUM SUCCINATE	1
PREDNISONE	1
PREDNISONE ACETATE	1
TRIAMCINOLONE	1.25
TRIAMCINOLONE ACETATE	1.25
TRIAMCINOLONE ACETONIDE	1.25

Frequency Factors	
Frequency	**Factor**
BID	2
BIW	2/7
OAM	1/30
Once	1
One	1
OD	1
PRN	null
Q2H	12
Q2W	1/14
Q3H	8
Q3MO	1/84
Q3w	1/21
Q4H	6
Q4W	1/28
Q6H	4
Q8H	3
Q12H	2
QAM	1
QD	1
QH	24
QHS	1

Frequency Factors	
QID	4
QM	1
QOD	½
QPM	1
QW	1/7
QWK	1/7
TID	3
TIW	3/7
UNK	Null
2 TIMES PER WEEK	2/7
3 TIMES PER WEEK	3/7
4 TIMES PER WEEK	4/7
5 TIMES PER WEEK	5/7
5XWK	5/7
5 TIMES PER DAY	5
EVERY 2 WEEKS	1/14
EVERY 3 WEEKS	1/21
EVERY 4 WEEKS	1/28
EVERY WEEK	1/7

11.11.12. Exit Interview

Instructions for Interviewer:

- At the beginning of the interview, please confirm the patient's study number.
- Text written in **bold** is to be read verbatim to each subject.
- Text written in *[italics]* is an instruction to the interviewer.
- Probes are to be used as needed to encourage the subject to provide full responses to each of the questions. They should be used if the subject gives an incomplete or unclear response or explanation with the initial question.
- Actively listen during the interview and take notes as necessary.

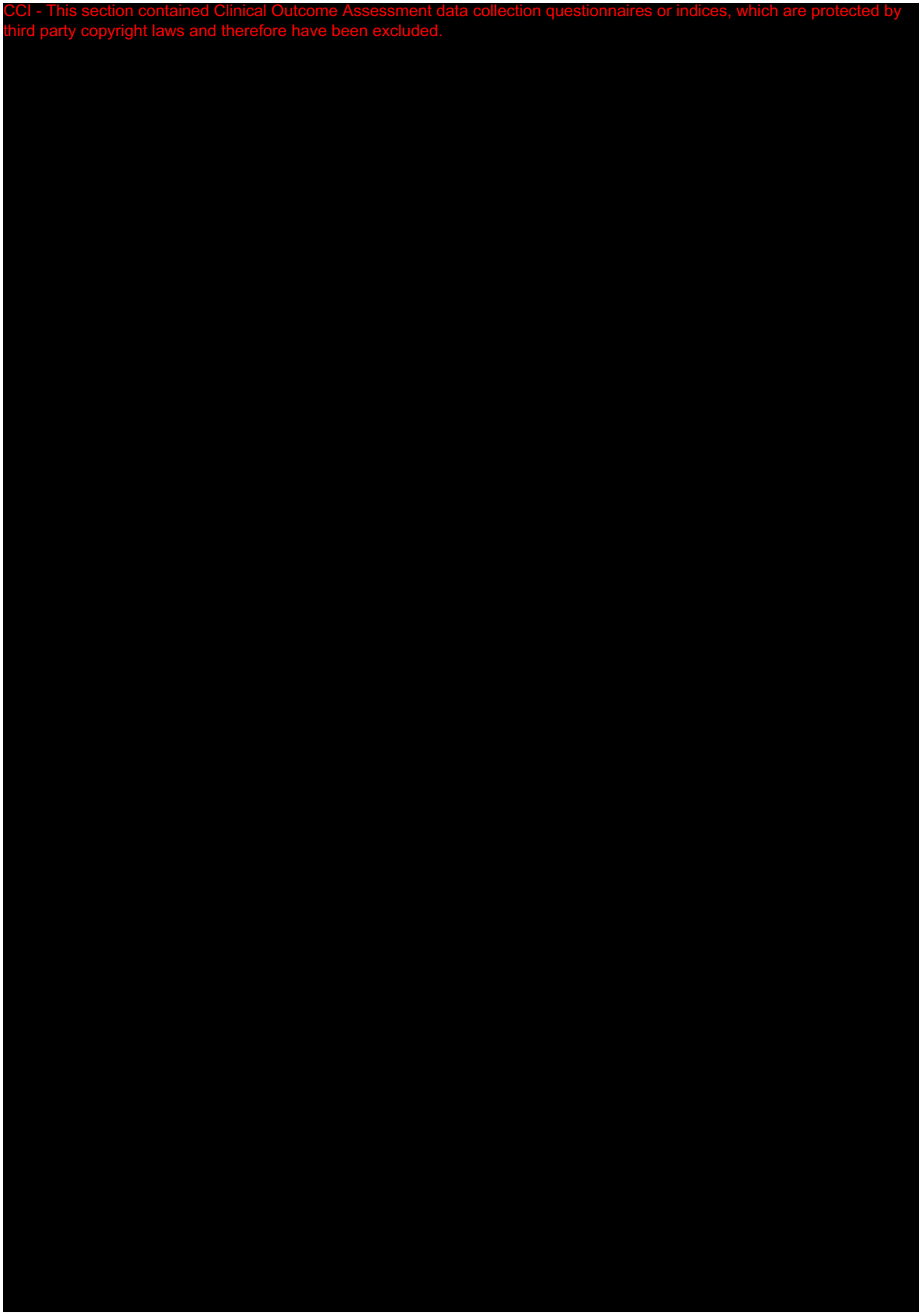
INTRODUCTION:

Hello, my name is [state first name] and I will be asking you some questions about your experience with medications in this study. The interview will be recorded and a transcript will be developed. In order to protect your confidentiality, only your study number will be included in the transcript. You are free to stop the interview at any time if you decide you no longer wish to participate.

The following questions have been developed to provide information on patient experiences with medications. It is important that you give your best answers, so please listen carefully to each question before you respond.

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

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



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

11.12. Appendix 12: Headline Results

11.12.1. Headline Results Output

The following tables will be included as headline results:

Table 15 Headline Results Output

Table	Title
1.1	Summary of Subject Status and Reason for Study Withdrawal
1.8	Summary of Demographic Characteristics
1.20	Summary of Baseline Disease Activity
2.11	Summary of Statistical Analysis Results of Change from Baseline: ESSDAI Total Score (Corrected)
2.19	Summary of Responders on Total ESSDAI
2.29	Summary of Statistical Analysis Results of Change from Baseline: Stimulated Salivary Flow
2.33	Summary of Statistical Analysis Results of Change from Baseline: Oral Dryness Numeric Response Scale
2.37	Summary of Statistical Analysis Results of Percentage Change from Baseline in Core Salivary Gland Histology at Week 24 [1]
2.38	Summary of Bayesian Posterior Probabilities: ESSDAI Total Score (Corrected) [2]
3.2	Summary of All Adverse Events by System Organ Class and Preferred Term
3.9	Adverse Events of Special Interest by Category
3.29	Summary of Serious Adverse Events by System Organ Class and Preferred Term (Number of Subjects and Occurrences)
6.2	Summary Statistics of Change from Baseline: ESSPRI Total Score and Domains
6.4	Summary of ESSPRI Responders
6.11	Summary of Bayesian Posterior Probabilities: ESSPRI Total Score [2]
7.10	Summary Statistics of Percentage Change from Baseline: Flow Cytometry Parameters [1]

NOTE:
[1] Only summarize B cell (CD20)/mm2 in Salivary Gland
[2] If time permits (generated by GSK)

11.13. Appendix 13: List of Data Displays

11.13.1. Data Display Numbering

The following numbering will be applied for RAP generated displays:

Section	Tables	Figures
Study Population	1.1 to 1.22(EOS: 1.1001 to 1.1023)	N/A
Efficacy	2.1 to 2.39 2.2 (EOS: 2.1001 to 2.1043)	to 2.12 (EOS: 2.1001 to 2.1011)
Safety	3.1 to 3.62 (EOS: 3.1002 to 3.1062)	3.1 to 3.4 (EOS: 3.1001 to 3.1004)
Pharmacokinetic	4.1 to 4.4	4.1 to 4.5 (EOS: 4.1001 to 4.1002)
Pharmacokinetic/ Pharmacodynamic	N/A	5.1
Health Outcomes	6.1 to 6.14 (EOS: 6.1001 to 6.1015)	6.1 to 6.3 (EOS: 6.1001 to 6.1002)
Exploratory/Biomarker	7.1 to 7.22 (EOS: 7.1001 to 7.1023)	7.1 to 7.9 (EOS: 7.1001 to 7.1009)
Section	**Listings**	
ICH Listings	1 to 31 (EOS: 1002 to 1030)	
Other Listings	32 to 58 (EOS: 1032 to 1061)	

NOTE: For the End of Study Analysis reporting, selected Primary Analysis displays have been identified and will be generated. All displays generated for the End of Study Analysis will have unique numbering, and their display numbers have been indicated in parentheses in the list of displays.

11.13.2. Mock Example Shell Referencing

Non IDSL specifications will be referenced as indicated and mock up displays are presented separately.

Section	Figure	Table	Listing
Study Population	N/A	POP_Tn	POP_Ln
Efficacy	EFF_Fn	EFF_Tn	EFF_Ln
Safety	N/A	SAFE_Tn	SAFE_Ln
Pharmacokinetic/Pharmacodynamic	PKPD_Fn	N/A	N/A
Exploratory/Biomarker	PD_Fn		

11.13.3. Deliverables

Delivery [Priority]	Description
HL [1]	Primary Analyses (Week 52) Headline Results
SAC_WK52 [2]	Primary Analysis (Week 52) SAC
SAC_EOS [3]	End of Study (Week 104) SAC

NOTES:

- Unless otherwise specified in the Programming Notes, displays will be generated by Quanticate.

For the End of Study Analysis reporting, selected Primary Analysis displays have been identified and will be generated, using the final data. The displays will be updated (as required) to capture the additional visits and to reflect the final data. If further details are required, a RAP amendment or addendum will be generated to specify the changes. If" Per Protocol Population" not run, then no data will be reported".

This RAP details the planned analysis for both database freezes (Primary Analysis and End of Study Analysis), with the expectation of an observed treatment benefit being observed following the Primary Analysis.

In the event that the Primary Analysis reporting does not identify treatment benefit an abridged set of analysis may be conducted for the end of study analysis, which will be detailed in a RAP amendment or addendum.

11.13.4. Study Population Tables

Study Population Tables					
No.	**Population**	**IDSL / TST ID / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
Subject Disposition					
1.1. (1.1001)	Safety	POP_T1	Summary of Subject Status and Reason for Study Withdrawal	ICH E3, FDAAA, EudraCT EoS : Refer to mock shell POP_T1.1	HL [1] SAC_WK52 [2] SAC_EOS [3]
1.2. (1.1002)	Safety	SD1	Summary of Treatment Status and Reasons for Discontinuation of Study Treatment	ICH E3 Add Total column (if feasible) NOTE: Align with eCRF Footnote: Note: Treatment status with respective to Week 52 [1] Subjects may have only one primary reason.	SAC_WK52 [2] SAC_EOS [3]
1.3.	Screened	ES6	Summary of Screening Status and Reasons for Screen Failure	Journal Requirements NOTE: Align with eCRF	SAC_WK52 [2]
1.4.	Enrolled	NS1	Summary of Number of Subjects Enrolled by Country and Site ID	EudraCT/Clinical Operations	SAC_WK52 [2]
Protocol Deviation					
1.5. (1.1005)	Safety	DV1	Summary of Important Protocol Deviations	ICH E3	SAC_WK52 [2] SAC_EOS [3]

Study Population Tables					
No.	**Population**	**IDSL / TST ID / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
Population Analysed					
1.6. (1.006)	Safety	SP1	Summary of Study Populations	IDSL	SAC_WK52 [2] SAC_EoS [3]
1.7.	Safety	SP2	Summary of Exclusions from Per Protocol Population		SAC_WK52 [2]
Demographics					
1.8.	Safety	DM1	Summary of Demographic Characteristics	ICH E3, FDAAA, EudraCT	HL [1] SAC_WK52 [2]
1.9.	Enrolled	DM11	Summary of Age Ranges	EudraCT	SAC_WK52 [2]
1.10.	Safety	DM5	Summary of Race and Racial Combinations		SAC_WK52 [2]
1.11.	Safety	FH1	Summary of Family History of Cardiovascular Risk Factors	Footnote: Women <65 years or men < 55 years. Half siblings are considered first degree relatives	SAC_WK52 [2]
1.12.	Safety	SU1	Summary of Substance Use		SAC_WK52 [2]
Medical Condition & Con Meds					
1.13.	Safety	MH4	Summary of Medical Conditions (Sjögren Specific)	ISRC version with all medical conditions Ref eCRF and align	SAC_WK52 [2]
1.14.	Safety	MH4	Summary of Medical Conditions (non-Sjögren Specific)		SAC_WK52 [2]
1.15.(1.1015)	Safety	CM1	Summary of Concomitant Medications	ICH E3 Add Total column (if feasible)	SAC_WK52 [2] SAC_EOS [3]

Study Population Tables					
No.	**Population**	**IDSL / TST ID / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
1.16.(1.1016)	Safety	CM1	Summary of Most Frequently used Concomitant Medications by Generic Term	Footnote: Includes concomitant medications taken by >= 5% subjects Add Total column (if feasible)	SAC_WK52 [2] SAC_EOS [3]
1.17.	Safety	POP_T2	Summary of Permitted pSS Medication Usage at Baseline	Add Total column (if feasible)	SAC_WK52 [2]
1.18.	Safety	POP_T3	Summary of Steroids, Anti-malarial and Muscarinic Agonists Use at Baseline	Add Total column (if feasible)	SAC_WK52 [2]
Disease History					
1.19.	Safety	POP_T4	Summary of AECG Classification Criteria Reported for Subjects at Baseline	Add Total column (if feasible)	SAC_WK52 [2]
1.20.	Safety	POP_T5	Summary of Baseline Disease Activity	Add Total column (if feasible)	HL [1] SAC_WK52 [2]
1.21.	Safety	POP_T6	Summary of Autoantibody, Immunoglobulin, Complement, and Other Biomarker Measurements at Baseline	Add Total column (if feasible)	SAC_WK52 [2]
Other					
1.22.(1.1022)	Safety	POP_T7	Cumulative Study Withdrawal by Study Week		SAC_WK52 [2] SAC_EOS [3]
1.1023.	Safety	POP_T8	Summary of Overall Subject Status		SAC_EOS [3]

11.13.5. Efficacy Tables

Efficacy: Tables					
No.	**Population**	**IDSL / TST ID / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
ESSDAI Score					
2.1. (2.1001)	Safety	EFF_T1	Summary Statistics of ESSDAI Total Score (Uncorrected)	Include all visits up to Week 68 EoS: Include all scheduled visits	SAC_WK52 [2] SAC_EOS [3]
2.2. (2.1002)	Per Protocol	EFF_T1	Summary Statistics of ESSDAI Total Score (Uncorrected)	Include all visits up to Week 68 EoS: Include all scheduled visits	SAC_WK52 [2] SAC_EOS [3]
2.3. (2.1003)	Safety	EFF_T1	Summary Statistics of ESSDAI Total Score (Corrected)	Include all visits up to Week 68 EoS: Include all scheduled visits	SAC_WK52 [2] SAC_EOS [3]
2.4. (2.1004)	Per Protocol	EFF_T1	Summary Statistics of ESSDAI Total Score (Corrected)	Include all visits up to Week 68 EoS: Include all scheduled visits	SAC_WK52 [2] SAC_EOS [3]
2.5. (2.1005)	Safety	EFF_T1	Summary Statistics of Change from Baseline: ESSDAI Total Score (Uncorrected)	Include all visits up to Week 68 EoS: Include all scheduled visits	SAC_WK52 [2] SAC_EOS [3]
2.6. (2.1006)	Per Protocol	EFF_T1	Summary Statistics of Change from Baseline: ESSDAI Total Score (Uncorrected)	Include all visits up to Week 68 EoS: Include all scheduled visits	SAC_WK52 [2] SAC_EOS [3]
2.7. (2.1007)	Safety	EFF_T1	Summary Statistics of Change from Baseline: ESSDAI Total Score (Corrected)	Include all visits up to Week 68 EoS: Include all scheduled visits	SAC_WK52 [2] SAC_EOS [3]
2.8. (2.1008)	Per Protocol	EFF_T1	Summary Statistics of Change from Baseline: ESSDAI Total Score (Corrected)	Include all visits up to Week 68 EoS: Include all scheduled visits	SAC_WK52 [2] SAC_EOS [3]
2.9.	Safety	EFF_T2	Summary of Statistical Analysis Results of Change from Baseline: ESSDAI Total Score (Uncorrected)	All visits to wk 52 entered to MMRM model. Note: Add the final model parameters	SAC_WK52 [2]

Efficacy: Tables					
No.	**Population**	**IDSL / TST ID / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
2.10.	Per Protocol	EFF_T2	Summary of Statistical Analysis Results of Change from Baseline: ESSDAI Total Score (Uncorrected)	All visits to wk 52 entered to MMRM model. Note: Add the final model parameters	SAC_WK52 [2]
2.11.	Safety	EFF_T2	Summary of Statistical Analysis Results of Change from Baseline: ESSDAI Total Score (Corrected)	All visits to wk 52 entered to MMRM model. Note: Add the final model parameters	HL [1] SAC_WK52 [2]
2.12.	Per Protocol	EFF_T2	Summary of Statistical Analysis Results of Change from Baseline: ESSDAI Total Score (Corrected)	All visits to wk 52 entered to MMRM model. Note: Add the final model parameters	SAC_WK52 [2]
2.13.(2.1013)	Safety	EFF_T3	Summary of ESSDAI Domain Activity (Uncorrected)	Include all visits up to Week 68 EoS: Include all scheduled visits	SAC_WK52 [2] SAC_EOS [3]
2.14.(2.1014)	Per Protocol	EFF_T3	Summary of ESSDAI Domain Activity (Uncorrected)	Include all visits up to Week 68 EoS: Include all scheduled visits	SAC_WK52 [2]
2.15.(2.1015)	Safety	EFF_T3	Summary of ESSDAI Domain Activity (Corrected)	Include all visits up to Week 68 EoS: Include all scheduled visits	SAC_WK52 [2] SAC_EOS [3]
2.16.(2.1016)	Per Protocol	EFF_T3	Summary of ESSDAI Domain Activity (Corrected)	Include all visits up to Week 68 EoS: Include all scheduled visits	SAC_WK52 [2] SAC_EOS [3]
2.17.(2.1017)	Safety	EFF_T4	ESSDAI Improvement (At Least 1 Category on Domain Score) by Domain Among Subjects with Domain Involvement at Baseline (Corrected)	Include all visits up to Week 68 EoS: Include all scheduled visits	SAC_WK52 [2] SAC_EOS [3]
2.18.(2.1018)	Safety	EFF_T5	ESSDAI Worsening (At Least 1 Category on Domain Score) by Domain (Corrected)	Include all visits up to Week 68 EoS: Include all scheduled visits	SAC_WK52 [2] SAC_EOS [3]
2.19.(2.1019)	Safety	EFF_T6	Summary of Responders on Total ESSDAI Score (Corrected)	Corrected ESSDAI score will be used. Include all visits up to Week 68	HL [1] SAC_WK52 [2]

Efficacy: Tables					
No.	**Population**	**IDSL / TST ID / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
				EoS: Include all scheduled visits Footnote: Responders are defined as below: Responder 1: ≥5 point reduction in ESSDAI Total vs baseline Responder 2: ≥3 point reduction in ESSDAI Total vs baseline Responder 3: ≥3 point reduction in ESSDAI Total vs baseline and Total Score < 5 Responder 4: Total score <5	SAC_EOS [3]
2.20.(2.1020)	Per Protocol	EFF_T6	Summary of Responders on Total ESSDAI Score (Corrected)	Corrected ESSDAI score will be used. Include all visits up to Week 68 EoS: Include all scheduled visits Footnote: Responders are defined as below: Responder 1: ≥5 point reduction in ESSDAI Total vs baseline Responder 2: ≥3 point reduction in ESSDAI Total vs baseline Responder 3: ≥3 point reduction in ESSDAI Total vs baseline and Total Score < 5 Responder 4: Total Score <5 Footnote to include model parameter as per mock table	SAC_WK52 [2] SAC_EOS [3]
2.21.	Safety	EFF_T7	Summary of Statistical Analysis of Responder on Total ESSDAI Score (Corrected)	Footnote: Responder definition and include footnotes as per EFF_T7 Note: Add the final model parameters	SAC_WK52 [2]

Efficacy: Tables					
No.	**Population**	**IDSL / TST ID / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
2.22.(2.1022)	Safety	EFF_T8	Proportion of Subjects with Damage by Domain	Additional Supplementary to ESSDAI for 5 domains EoS: Include all scheduled visits	SAC_WK52 [2] SAC_EOS [3]
ClinESSDAI Score					
2.23.(2.1023)	Safety	EFF_T1	Summary Statistics: ClinESSDAI Total Score (Corrected)	Corrected ESSDAI score will be used. Include all visits up to Week 68 EoS: Include all scheduled visits	SAC_WK52 [2] SAC_EOS [3]
2.24.(2.1024)	Safety	EFF_T1	Summary Statistics of Change from Baseline: ClinESSDAI Total Score (Corrected)	Corrected ESSDAI score will be used. Include all visits up to Week 68 EoS: Include all scheduled visits	SAC_WK52 [2] SAC_EOS [3]
2.25.(2.1025)	Safety	EFF_T2	Summary of Statistical Analysis Results of Change from Baseline: ClinESSDAI Total Score (Corrected)	Corrected ESSDAI score will be used. All visits to wk 52 entered to MMRM model. Note: Add the final model parameters	SAC_WK52 [2]
2.26.(2.1026)	Safety	EFF_T6	Summary of ClinESSDAI Responders (Corrected)	Corrected ESSDAI score will be used. Including just one section with Responder Criteria: Reduction from baseline ≥3 EoS: Include all scheduled visits	SAC_WK52 [2] SAC_EOS [3]
Stimulated and Unstimulated Salivary Flow					
2.27.(2.1027)	Safety	EFF_T1	Summary Statistics of Stimulated and Unstimulated Salivary Flow	Include all visits up to Week 68 EoS: Include all scheduled visits Page by parameter – stimulated and unstimulated flow	SAC_WK52 [2] SAC_EOS [3]
2.28.(2.1028)	Safety	EFF_T1	Summary Statistics of Change from Baseline: Stimulated and Unstimulated Salivary Flow	Include all visits up to Week 68 EoS: Include all scheduled visits by parameter	SAC_WK52 [2] SAC_EOS [3]

Efficacy: Tables					
No.	**Population**	**IDSL / TST ID / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
				Page by parameter – stimulated and unstimulated flow	
2.29.	Safety	EFF_T2	Summary of Statistical Analysis Results of Change from Baseline: Stimulated Salivary Flow	All visits to wk 52 entered to MMRM model. Note: Add the final model parameters	HL [1] SAC_WK52 [2]
2.30.	Per Protocol	EFF_T2	Summary of Statistical Analysis Results of Change from Baseline: Stimulated Salivary Flow	All visits to wk 52 entered to MMRM model. Note: Add the final model parameters	SAC_WK52 [2]
Oral Dryness					
2.31.(2.1031)	Safety	EFF_T1	Summary Statistics of Oral Dryness Numeric Response Scale	Include all visits up to Week 68 EoS: Include all scheduled visits	SAC_WK52 [2] SAC_EOS [3]
2.32.(2.1032)	Safety	EFF_T1	Summary Statistics of Change from Baseline: Oral Dryness Numeric Response Scale	Include all visits up to Week 68 EoS: Include all scheduled visits	SAC_WK52 [2] SAC_EOS [3]
2.33.	Safety	EFF_T2	Summary of Statistical Analysis Results of Change from Baseline: Oral Dryness Numeric Response Scale	All visits to wk 52 entered to MMRM model Note: Add the final model parameters	HL [1] SAC_WK52 [2]
2.34.	Per Protocol	EFF_T2	Summary of Statistical Analysis Results of Change from Baseline: Oral Dryness Numeric Response Scale	All visits to wk 52 entered to MMRM model. Note: Add the final model parameters	SAC_WK52 [2]

Efficacy: Tables					
No.	**Population**	**IDSL / TST ID / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
Salivary Gland Histology					
2.35.(2.1035)	Safety	EFF_T9	Summary Statistics for Salivary Gland Histology Assessments	Includes baseline and Week 24 only Include all parameters as specified in RAP Table 13 Note: Include Week 52 for EoS reporting	SAC_WK52 [2] SAC_EOS [3]
2.36.(2.1036)	Safety	EFF_T9	Summary Statistics of Percentage Change from Baseline: Salivary Gland Histology Assessments EOS: Summary Statistics of Change from Baseline: Salivary Gland Histology Assessments	Includes only Week 24 data Include all parameters as specified in RAP Table 13 Note: Include Week 52 for EoS reporting	SAC_WK52 [2] SAC_EOS [3]
2.37.(2.1037)	Safety	EFF_T10	Summary of Statistical Analysis Results of Percentage Change from Baseline in Core Salivary Gland Histology at Week 24 EOS: Summary of Statistical Analysis Results of Change from Baseline in Core Salivary Gland Histology at Week 24	Parameters to be included in the analysis are • B cell (CD20) count/mm^2 • Lymphocyte Focus Score (per 4mm^2) • B (CD20) / T (CD3) cell ratio • Plasma cell (CD138+; both - CD20pos and CD20neg) count/mm^2 Note: Exclude Week 52 for EoS reporting (i.e. only n=6 samples).	HL [1] SAC_WK52 [2] SAC_EOS [3]
Further Efficacy Evaluation					
2.38.	Safety	EFF_T11	Summary of Bayesian Posterior Probabilities: ESSDAI Total Score (Corrected)	Add appropriate footnotes based on final out **To be generated by GSK**	HL [1] SAC_WK52 [2]

Efficacy: Tables					
No.	**Population**	**IDSL / TST ID / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
Further Evaluation					
2.39.(2.1039)	Safety	N/A	Summary of Responders on Total ESSDAI Score	EoS: Include all scheduled visits % responders calculated using n for each visit EoS: Include all scheduled visits	SAC_WK52 [2] SAC_EOS [3]
(2.1040)	Completer	EFF_T1	Summary Statistics of ESSDAI Total Score (Corrected) – Completer	Include all scheduled visits Add footnote: Note: Completer is defined as "Subjects who completed the 52 Week treatment visits AND general follow up phase of the study including the visit at Week 68"	SAC_EOS [3]
(2.1041)	Completer	EFF_T2	Summary of Statistical Analysis Results of Change from Baseline: ESSDAI Total Score (Corrected) - Completer	Include visits upto and including Week 68/FU Add footnote: As T2.1040	SAC_EOS [3]
(2.1042)	Completer	EFF_T1	Summary Statistics of Stimulated and Unstimulated Salivary Flow - Completer	Include all scheduled visits Page by parameter – stimulated and unstimulated flow Add footnote: As T2.1040	SAC_EOS [3]
(2.1043)	Completer	EFF_T1	Summary Statistics of Oral Dryness Numeric Response Scale - Completer	Include all scheduled visits Add footnote: As T2.1040	SAC_EOS [3]

11.13.6. Efficacy Figures

Efficacy: Figures					
No.	**Population**	**IDSL / TST ID / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
ESSDAI					
2.1. (2.1001)	Safety	EFF_F1	Mean (± SE) of ESSDAI Total Score (Uncorrected)	All scheduled visits Legend: Treatment EoS: Include all visits up to Week 68/FU. X-axis: Add line break between Week 52 and Week 68/FU with no joining lines.	SAC_WK52 [2] SAC_EOS [3]
2.2. (2.1002)	Safety	EFF_F1	Mean (± SE) of ESSDAI Total Score (Corrected)	All scheduled visits Legend: Treatment EoS: As F2.1001	SAC_WK52 [2] SAC_EOS [3]
2.3. (2.1003)	Safety	EFF_F1	Mean (± SE) of Change from Baseline in ESSDAI Total Score (Uncorrected)	All scheduled visits Legend: Treatment EoS: As F2.1001	SAC_WK52 [2] SAC_EOS [3]
2.4. (2.1004)	Safety	EFF_F1	Mean (± SE) of Change from Baseline in ESSDAI Total Score (Corrected)	All scheduled visits Legend: Treatment EoS: As F2.1001	SAC_WK52 [2] SAC_EOS [3]
2.5.	Safety	EFF_F1	Adjusted Mean (95% CI) Change from Baseline: ESSDAI Total Score (Uncorrected)	Panel: Rows = 1 by Cols = 1 for parameter X-Axis: Visit: Continuous Scale Y-Axis: ESSDAI total Score and scaled accordingly Legend: Treatment Include all visits to Week 52 Note: Add the final model parameters	SAC_WK52 [2]
2.6.	Safety	EFF_F1	Adjusted Mean (95% CI) Change from Baseline: ESSDAI Total Score (Corrected)	Panel: Rows = 1 by Cols = 1 for parameter X-Axis: Visit: Continuous Scale Y-Axis: ESSDAI total Score and scaled	SAC_WK52 [2] SAC_EOS [3]

Efficacy: Figures					
No.	**Population**	**IDSL / TST ID / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
				accordingly Legend: Treatment Include all visits to Week 52 Note: Add the final model parameters	
2.7. (2.1007)	Safety	EFF_F2	ESSDAI Activity by Domain	Page By: Domain Panel: Visit (Include only Baseline, Week 24 and Week 52) EoS: Panel: Visit (Include only Baseline, Week 24 & Week 52) X-Axis = Treatment Y-Axis = Percentage of Subjects Stacked bar chart SAS colors for the categories are No Activity - CXDCDCDC Low Activity - CX9370DB Moderate Activity - CX7FFF00 High Activity - CXFF8C00	SAC_WK52 [2] SAC_EOS [3]
2.8. (2.1008)	Safety	EFF_F3	ESSDAI Responders Bar Chart by Treatment and Visit (Corrected)	EoS: Include all scheduled visits except IFU, EW & W68/FU Footnote: Responders are defined as below: Responder 1: ≥5 point reduction in ESSDAI Total vs baseline Responder 2: ≥3 point reduction in ESSDAI Total vs baseline Responder 3: ≥3 point reduction in ESSDAI Total vs baseline and Total Score < 5 Responder 4: Total Score <5	SAC_WK52 [2] SAC_EOS [3]

Efficacy: Figures					
No.	**Population**	**IDSL / TST ID / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
Stimulated & Unstimulated Salivary Flow					
2.9. (2.1009)	Safety	EFF_F1	Mean (+/- SE) of Change from Baseline in Stimulated Salivary Flow	EoS: As F2.1001 Panel: Rows = 1 by Cols = 1 for parameter X-Axis: Visit: Continuous Scale Legend: Treatment	SAC_WK52 [2] SAC_EOS [3]
2.10. (2.1010)	Safety	EFF_F1	Mean (+/- SE) of Change from Baseline in Unstimulated Salivary Flow	As F2.1001 Legend: Treatment	SAC_WK52 [2] SAC_EOS [3]
Oral Dryness					
2.11. (2.1011)	Safety	EFF_F1	Mean (+/- SE) of Change from Baseline in Oral Dryness Numeric Response	EoS: As F2.1001 Panel: Rows = 1 by Cols = 1 for parameter X-Axis: Visit: Continuous Scale Y-Axis: Oral dryness numeric response and scaled accordingly Legend: Treatment	SAC_WK52 [2] SAC_EOS [3]
Salivary Gland Histology					
2.12. (2.1012)	Safety	EFF_F4	Median (+/- IQR) of Percentage Change from Baseline in Salivary Gland Core Parameters EoS: Median (+/- IQR) of Change from Baseline in Salivary Gland Core Parameters	Percentage change (Primary) and change (EoS) to wk 24 for • B cell (CD20) count/mm2 • Lymphocyte Focus Score (in $4mm^2$) • B (CD20) / T (CD3) cell ratio • Plasma cell (CD138+; both - CD20pos and CD20neg) count/mm^2 X-Axis: Week 24 visit only Legend: Treatment NOTE: Limited sample at WK52 (i.e. n=6), hence Week 52 not required for EoS.	SAC_WK52 [2] SAC_EOS [3]

Efficacy: Figures					
No.	**Population**	**IDSL / TST ID / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
Exploratory Correlation Evaluation					
2.13.	Safety	PD_F1	ESSDAI and ClinESSDAI Bland-Altman Plot at Week 24 (Corrected)	Panel: Rows = 1 by Cols = 1 for parameter X-Axis: Average of Change from baseline to Wk24 Total ClinESSDAI and Change from baseline to wk 24 Total ESSDAI Y-Axis: Difference of Change from baseline to Wk24 Total ESSDAI and Change from baseline to wk 24 Clin ESSDAI Legend: Treatment Note: Add footnotes as required Note: For SAC_EOS [3]: Include other timepoints and add identifies	SAC_WK52 [2]
2.14.	Safety	PD_F2	Scatter Plot of Wk 24 Changes for Total ESSDAI Score vs Salivary Gland B Cells	Panel: Rows = 1 by Cols = 1 for parameter X-Axis: Percentage Change from baseline to Wk24 Salivary Gland B Cells Y-Axis: Change from baseline to Wk24 Total ESSDAI Legend: Treatment	SAC_WK52 [2]
2.15.	Safety	PD_F3	Median Free Blys Vs Median CD19+ B cell by Treatment	Panel per Treatment. Legend: Visit X-axis: CD19+ B cells Y-axis: Free Blys B Cell measured by flow cytometry	SAC_WK52 [2]

11.13.7. Safety Tables

Safety: Tables					
No.	**Population**	**IDSL / TST ID / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
Exposure					
3.1.	Safety	SAFE_T15	Summary of Extent of Exposure		SAC_WK52 [2]
Adverse Events (AEs)					
3.2. (3.1002)	Safety	AE1	Summary of All Adverse Events by System Organ Class and Preferred Term	ICH E3 Footnote: Note: Subjects are counted only once per SOC/PT EoS: Include visits upto W68/FU EoS Footnote: Note: Includes Treatment & General Follow Up periods only.	HL [1] SAC_WK52 [2] SAC_EOS [3]
3.3. (3.1003)	Safety	AE1	Summary of All Adverse Events by System Organ Class	Excludes Preferred Term breakdown Footnote: Note: Subjects are counted only once per SOC EoS: Include visits upto W68/FU EoS Footnote: Add as T3.1002	SAC_WK52 [2] SAC_EOS [3]
3.4. (3.1004)	Safety	AE3	Summary of Common (>=5%) Adverse Events by Overall Frequency	ICH E3 EoS: Include visits upto W68/FU EoS Footnote: Add as T3.1002	SAC_WK52 [2] SAC_EOS [3]
3.5. (3.1005)	Safety	AE3	Summary of Common (>=5%) Grade 2-4 Adverse Events	ICH E3	SAC_WK52 [2]

Safety: Tables					
No.	**Population**	**IDSL / TST ID / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
			by Overall Frequency	EoS: Include visits upto W68/FU EoS Footnote: Add as T3.1002	SAC_EOS [3]

Safety: Tables					
No.	**Population**	**IDSL / TST ID / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
3.6. (3.1006)	Safety	AE1	Summary of All Drug-Related Adverse Events by System Organ Class and Preferred Term	ICH E3 EoS: Include visits upto W68/FU EoS Footnote: Add as T3.1002	SAC_WK52 [2] SAC_EOS [3]
3.7. (3.1007)	Safety	AE15	Summary of Common (>=5%) Non Serious Adverse Events by System Organ Class and Preferred Term (Number of Participant and Occurrences)	FDAAA EoS: Include visits upto W68/FU EoS Footnote: Add as T3.1002	SAC_WK52 [2] SAC_EOS [3]
3.8. (3.1008)	Safety	AE3	Summary of Common (>=5%) Drug-Related Grade 2-4 Adverse Events by Overall Frequency	ICH E3 EoS: Include visits upto W68/FU EoS Footnote: Add as T3.1002	SAC_WK52 [2] SAC_EOS [3]
3.9. (3.1009)	Safety	SAFE_T7	Adverse Events of Special Interest by Category	Includes events defined in Belimumab PSAP and study specific special interest events EoS: Include visits upto W68/FU EoS Footnote: Add as T3.1002	HL [1] SAC_WK52 [2] SAC_EOS [3]
3.10. (3.1010)	Safety	SAFE_T8	Malignant Neoplasm Adverse Events of Special Interest by Category and PT	EoS: Include visits upto W68/FU EoS Footnote: Add as T3.1002	SAC_WK52 [2] SAC_EOS [3]
3.11. (3.1011)	Safety	SAFE_T9	Post-Administration Systemic Reaction Adverse Events of Special Interest by Category and PT	EoS: Include visits upto W68/FU EoS Footnote: Add as T3.1002	SAC_WK52 [2] SAC_EOS [3]
3.12. (3.1012)	Safety	SAFE_T9	Serious Post-Administration Systemic Reaction Adverse Events of Special Interest by Category and PT	Change title and content so only Serious PASR's are summarized EoS: Include visits upto W68/FU EoS Footnote: Add as T3.1002	SAC_WK52 [2] SAC_EOS [3]

Safety: Tables					
No.	**Population**	**IDSL / TST ID / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
3.13.	Safety	SAFE_T10	Post-Injection Systemic Reactions per Anaphylactic Reactions CMQ Broad search by PT, in First Six Doses of Belimumab/Placebo	All infusion column would include the overall study treatment	SAC_WK52 [2]
3.14.	Safety	SAFE_T10	Serious Post-Injection Systemic Reactions per Anaphylactic Reactions CMQ Broad search by PT, in First Six Doses of Belimumab/Placebo	All infusion column would include the overall study treatment	SAC_WK52 [2]
3.15.	Safety	SAFE_T10	Serious Acute Post-Injection Systemic Reactions per GSK Adjudication by PT, in First Six Doses of Belimumab/Placebo	All infusion column would include the overall study treatment	SAC_WK52 [2]
3.16.	Safety	SAFE_T10	Serious Delayed Acute Post-Injection Systemic Reactions per GSK Adjudication by PT, in First Six Doses of Belimumab/Placebo	All infusion column would include the overall study treatment	SAC_WK52 [2]
3.17.	Safety	SAFE_T10	Serious Delayed Non-Acute Post-Injection Systemic Reactions per GSK Adjudication by PT, in First Six Doses of Belimumab/Placebo	All infusion column would include the overall study treatment	SAC_WK52 [2]
3.18. (3.1018)	Safety	SAFE_T11	Infection Adverse Events of Special Interest by Category and PT	EoS: Include visits upto W68/FU EoS Footnote: Add as T3.1002	SAC_WK52 [2] SAC_EOS [3]
3.19. (3.1019)	Safety	SAFE_T11	Infection Adverse Events of Special Interest Leading to Study Agent Discontinuation by Category and PT by Category and PT	EoS: Include visits upto W68/FU EoS Footnote: Add as T3.1002	SAC_WK52 [2] SAC_EOS [3]
3.20. (3.1020)	Safety	SAFE_T12	Depression/Suicide/Self-injury Adverse Events of Special Interest by Category and PT	EoS: Include visits upto W68/FU EoS Footnote: Add as T3.1002	SAC_WK52 [2] SAC_EOS [3]

Safety: Tables					
No.	**Population**	**IDSL / TST ID / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
3.21. (3.1021)	Safety	SAFE_T13	Severe Skin Reactions Adverse Events of Special Interest by Preferred Term	Study specific AESI EoS: Include visits upto W68/FU EoS Footnote: Add as T3.1002	SAC_WK52 [2] SAC_EOS [3]
3.22. (3.1022)	Safety	SAFE_T13	Cardiac Disorders Adverse Events of Special Interest by Preferred Term	Study specific AESI EoS: Include visits upto W68/FU EoS Footnote: Add as T3.1002	SAC_WK52 [2] SAC_EOS [3]
3.23. (3.1023)	Safety	SAFE_T13	Posterior Reversible Encephalopathy Syndrome (PRES) Adverse Events of Special Interest by Preferred Term	Study specific AESI EoS: Include visits upto W68/FU EoS Footnote: Add as T3.1002	SAC_WK52 [2] SAC_EOS [3]
3.24. (3.1024)	Safety	SAFE_T13	Progressive Multifocal Leukocephalopathy (PML) Adverse Events of Special Interest by Preferred Term	Study specific AESI EoS: Include visits upto W68/FU EoS Footnote: Add as T3.1002	SAC_WK52 [2] SAC_EOS [3]
3.25. (3.1025)	Safety	SAFE_T13	Biopsy Adverse Events of Special Interest by Preferred Term	Study specific AESI EoS: Include visits upto W68/FU EoS Footnote: Add as T3.1002	SAC_WK52 [2] SAC_EOS [3]
3.26. (3.1026)	Safety	AE1	Summary of Serious Adverse Events by System Organ Class and Preferred Term	EoS: Include visits upto W68/FU EoS Footnote: Add as T3.1002	SAC_WK52 [2] SAC_EOS [3]
3.27. (3.1027)	Safety	AE1	Summary of Serious Adverse Events by System Organ Class	No preferred term breakdown EoS: Include visits upto W68/FU EoS Footnote: Add as T3.1002	SAC_WK52 [2] SAC_EOS [3]

Safety: Tables					
No.	**Population**	**IDSL / TST ID / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
3.28. (3.1028)	Safety	AE1	Summary of Adverse Events Leading to Discontinuation of Study Treatment or Withdrawal from Study by System Organ Class and Preferred Term	EACTRCD and AEWD EoS: Include visits upto W68/FU EoS Footnote: Add as T3.1002	SAC_WK52 [2] SAC_EOS [3]
3.29. (3.1029)	Safety	AE16	Summary of Serious Adverse Events by System Organ Class and Preferred Term (Number of Subjects and Occurrences)	FDAAA, EudraCT EoS: Include visits upto W68/FU EoS Footnote: Add as T3.1002	HL [1] SAC_WK52 [2] SAC_EOS [3]
3.30. (3.1030)	Safety	AE5A	Summary of All Adverse Events by Maximum Intensity by System Organ Class and Preferred Term	EoS: Include visits upto W68/FU EoS Footnote: Add as T3.1002	SAC_WK52 [2] SAC_EOS [3]
3.31. (3.1031)	Safety	AE1	Summary of Fatal Adverse Events by System Organ Class and Preferred Term	EoS: Include visits upto W68/FU EoS Footnote: Add as T3.1002	SAC_WK52 [2] SAC_EOS [3]
Labs					
3.32. (3.1032)	Safety	LB1	Summary of Hematology Laboratory Values	EoS: Include all scheduled visits Add footnote: Basophils% = % of leukocytes; Eosinophils% = % of leukocytes	SAC_WK52 [2] SAC_EOS [3]
3.33. (3.1033)	Safety	LB1	Summary of Hematology Changes from Baseline	EoS: Include all scheduled visits ICH E3 Includes baseline values. Add footnote: Basophils% = % of leukocytes; Eosinophils% = % of leukocytes	SAC_WK52 [2] SAC_EOS [3]

Safety: Tables					
No.	**Population**	**IDSL / TST ID / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
3.34. (3.1034)	Safety	SAFE_T5	Laboratory Reference Range Shifts from Baseline: Hematology	EoS: Include all scheduled visits	SAC_WK52 [2] SAC_EOS [3]
3.35. (3.1035)	Safety	SAFE_T1	Worst Laboratory Toxicity Grade: Hematology	EoS: Include all scheduled visits	SAC_WK52 [2] SAC_EOS [3]
3.36. (3.1036)	Safety	SAFE_T2	Laboratory Toxicity Grade Worsening of at Least 2 Grades from Baseline: Hematology	EoS: Include all scheduled visits	SAC_WK52 [2] SAC_EOS [3]
3.37. (3.1037)	Safety	LB1	Summary of Clinical Chemistry Laboratory Values	EoS: Include all scheduled visits	SAC_WK52 [2] SAC_EOS [3]
3.38. (3.1038)	Safety	LB1	Summary of Changes from Baseline: Clinical Chemistry Laboratory Values	EoS: Include all scheduled visits	SAC_WK52 [2] SAC_EOS [3]
3.39. (3.1039)	Safety	SAFE_T1	Worst Laboratory Toxicity Grade: Clinical Chemistry	EoS: Include all scheduled visits	SAC_WK52 [2] SAC_EOS [3]
3.40. (3.1040)	Safety	SAFE_T2	Laboratory Toxicity Grade Worsening of at Least 2 Grades from Baseline: Clinical Chemistry	EoS: Include all scheduled visits	SAC_WK52 [2] SAC_EOS [3]
3.41. (3.1041)	Safety	SAFE_T6	Summary of Liver Assessments	EoS: Include all scheduled visits	SAC_WK52 [2] SAC_EOS [3]
3.42. (3.1042)	Safety	UR3	Summary of Urinalysis Dipstick Results	EoS: Include all scheduled visits	SAC_WK52 [2] SAC_EOS [3]

Safety: Tables					
No.	**Population**	**IDSL / TST ID / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
3.43. (3.1043)	Safety	LB1	Summary of Protein/Creatinine Ratio	EoS: Include all scheduled visits	SAC_WK52 [2] SAC_EOS [3]
3.44. (3.1044)	Safety	LB1	Summary of Immunoglobulins by Visit	EoS: Include all scheduled visits Page by parameter: IgG, IgA, IgM,	SAC_WK52 [2] SAC_EOS [3]
3.45. (3.1045)	Safety	LB1	Summary of Change from Baseline in Immunoglobulins by Visit	EoS: Include all scheduled visits Page by parameter: IgG, IgA, IgM,	SAC_WK52 [2] SAC_EOS [3]
3.46. (3.1046)	Safety	SAFE_T1	Worst Laboratory Toxicity Grade: Immunoglobulin	EoS: Include all scheduled visits Includes IgG only Include footnote for baseline	SAC_WK52 [2] SAC_EOS [3]
3.47. (3.1047)	Safety	SAFE_T2	Laboratory Toxicity Grade Worsening of at Least 2 Grades from Baseline: Immunoglobulin	EoS: Include all scheduled visits Includes IgG only Include footnote for baseline	SAC_WK52 [2] SAC_EOS [3]
3.48. (3.1048)	Safety	SAFE_T4	Immunoglobulins below LLN	EoS: Include all scheduled visits Page by parameter: IgG, IgA, IgM,	SAC_WK52 [2] SAC_EOS [3]
3.49. (3.1049)	Safety	SAFE_T4	Immunoglobulins above ULN	EoS: Include all scheduled visits Page by parameter: IgG, IgA, IgM,	SAC_WK52 [2] SAC_EOS [3]
3.50. (3.1050)	Safety	LB1	Summary of C-Reactive Protein	EoS: Include all scheduled visits	SAC_WK52 [2] SAC_EOS [3]
3.51. (3.1051)	Safety	LB1	Summary of Changes from Baseline in C-Reactive Protein	EoS: Include all scheduled visits	SAC_WK52 [2] SAC_EOS [3]

Safety: Tables					
No.	**Population**	**IDSL / TST ID / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
Vital Signs					
3.52. (3.1052)	Safety	VS1	Summary of Vital Signs	EoS: Include all scheduled visits	SAC_WK52 [2] SAC_EOS [3]
3.53. (3.1053)	Safety	VS1	Summary of Change from Baseline for Vital Signs	EoS: Include all scheduled visits	SAC_WK52 [2] SAC_EOS [3]
ECG					
3.54.	Safety	EG1	Summary of ECG Findings	Screening Visit Only	SAC_WK52 [2]
3.55.	Safety	EG2	Summary of Screening ECG	Include all intervals	SAC_WK52 [2]
TBNK					
3.56. (3.1056)	Safety	LB1	Summary of CD4 and CD8	EoS: Include all scheduled visits	SAC_WK52 [2] SAC_EOS [3]
3.57. (3.1057)	Safety	LB1	Summary of Changes from Baseline in CD4 and CD8	EoS: Include all scheduled visits	SAC_WK52 [2] SAC_EOS [3]

Safety: Tables					
No.	**Population**	**IDSL / TST ID / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
Neurological Symptoms					
3.58. (3.1058)	Safety	SAFE_T3	Summary of Neurological Symptoms	EoS: Include all scheduled visits	SAC_WK52 [2] SAC_EOS [3]
Columbia-Suicide Severity Rating Scale					
3.59. (3.1059)	Safety	ECSSRS1	Summary of C-SSRS Suicidal Ideation or Behaviour During Treatment	EoS: Include all scheduled visits Include summaries for both lifetime and current state.	SAC_WK52 [2] SAC_EOS [3]
3.60. (3.1060)	Safety	ECSSRS2	Summary of Treatment-Emergent C-SSRS Suicidal Ideation or Behaviour Relative to Pre-treatment	EoS: Include all scheduled visits	SAC_WK52 [2] SAC_EOS [3]
3.61. (3.1061)	Safety	ECSSRS3	Shift Table of Changes in C-SSRS Categories from Pre-Treatment to On-Treatment	EoS: Include all scheduled visits	SAC_WK52 [2] SAC_EOS [3]
Immunogenicity					
3.62. (3.1062)	Safety	SAFE_T14	Summary of Immunogenic Response by Visit	EoS: Include all scheduled visits Belimumab antibodies Rituximab antibodies EoS Footnote: For anti-Rituximab, baseline is Week 8	SAC_WK52 [2] SAC_EOS [3]
Further Analyses					
3.1063	Safety	SAFE_10	Post-IV Systemic Reactions per Anaphylactic Reactions CMQ Broad search by PT, in First Two 2 Infusions of Rituximab/Placebo	All infusion column would include the overall study treatment	SAC_EOS [3]

11.13.8. Safety Figures

Safety: Figures					
No.	**Population**	**IDSL / TST ID / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
Lab					
3.1 (3.1001)	Safety	EFF_F1	Mean (+/- SE) of Hematology	EoS: As F2.1001 Parameters for SAC: WBC count, Neutrophil counts, Haemoglobin, Platelets, Lymphocytes, Hematocrit, Monocytes, Eosinophils, Basophils All visits contained with the summary source table, with Day 0 being included as part of the plot	SAC_WK52 [2] SAC_EOS [3]
3.2 (3.1002)	Safety	EFF_F4	Median (+/- IQR) of Immunoglobulins	EoS: As F2.1001 x-axis is visit, line per treatment group.	SAC_WK52 [2] SAC_EOS [3]
3.3 (3.1003)	Safety	EFF_F4	Median (+/- IQR) of Change from baseline of Immunoglobulins	EoS: As F2.1001 x-axis is visit, panel per treatment group. Include IgG, IgA and IgM.	SAC_WK52 [2] SAC_EOS [3]
3.4 (3.1004)	Safety	EFF_F1	Median (+/- IQR) of Absolute Values of CD4 and CD8	EoS: As F2.1001 x-axis is visit, line per treatment group.	SAC_WK52 [2] SAC_EOS [3]

11.13.9. Pharmacokinetic Tables

Pharmacokinetic: Tables					
No.	**Population**	**IDSL / TST ID / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
PK Concentration Data					
4.1.	PK-B	PK01	Summary of Plasma Belimumab Pharmacokinetic Concentration-Time Data (ng/mL)	Include 3 columns: Combination, Belimumab, Total	SAC_WK52 [2]
4.2.	PK-B	PK01	Summary of Plasma Belimumab Pharmacokinetic Concentration-Time Data (μg/mL) by Baseline Body Weight Quartiles	Include 3 columns: Combination, Belimumab, Total	SAC_WK52 [2]
4.3.	PK-R	PK01	Summary of Plasma Rituximab Pharmacokinetic Concentration-Time Data (ng/mL)	Include 3 columns: Combination, Rituximab, Total	SAC_WK52 [2]
4.4.	PK-B	PK01	Summary of Plasma Belimumab Pharmacokinetic Concentration-Time Data (μg/mL) by Belimumab Immunogenicity Status	Include 3 columns: Combination, Belimumab, Total Produce if ≥6 subjects in total have positive belimumab immunogenicity.	SAC_WK52 [2]

11.13.10. Pharmacokinetic Figures

Pharmacokinetic: Figures					
No.	**Population**	**IDSL / TST ID / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
Individual Plots					
4.1. (4.1001)	PK-B	PKCF1P	Individual Belimumab Plasma Concentration-Time Plot by Treatment (Linear and Semi-Log)	Paginate by Treatment Combo and Bel Arms NOTE: Ensure treatment legends can be differentiated	SAC_EOS [3]
4.2. (4.1002)	PK-R	PKCF1P	Individual Rituximab Plasma Concentration-Time Plot by Treatment (Linear and Semi-Log)	Paginate by Treatment Combo and Ritux Arms NOTE: Ensure treatment legends can be differentiated	SAC_EOS [3]
Median Plots					
4.3.	PK-B	PKCF3	Median Plasma Belimumab Concentration-Time Plots by Treatment (Linear and Semi-log)	Combo and Bel Arms	SAC_WK52 [2]
4.4.	PK-B	PKCF3	Median Plasma Belimumab Concentration-Time Plots by Body Weight Quartile (Linear and Semi-log)	Combo and Bel Arms	SAC_WK52 [2]
4.5.	PK-R	PKCF3	Median Plasma Rituximab Concentration-Time Plots by Treatment (Linear and Semi-log)	Combo and Ritux Arms	SAC_WK52 [2]

11.13.11. Pharmacokinetic / Pharmacodynamic Figures

Pharmacokinetic / Pharmacodynamic: Figures					
No.	**Population**	**IDSL / TST ID / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
5.1.	Safety	PKPD_F1	Scatterplot of CD19+ B cells Versus Belimumab Concentration	2 panels: combo and bel Individual subject data y-axis=CD19+ B cells (from TBNK panel CONC record) x-axis=Belimumab concentration	SAC_WK52 [2]

11.13.12. Health Outcomes Tables

Health Outcomes: Tables					
No.	**Population**	**IDSL / TST ID / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
ESSPRI Score					
6.1. (6.1001)	Safety	EFF_T1	Summary Statistics of ESSPRI Total Score and Domains	EoS: Include all scheduled visits Summarize for both the overall score and 3 domains (dryness, fatigue and pain)	SAC_WK52 [2] SAC_EOS [3]
6.2. (6.1002)	Safety	EFF_T1	Summary Statistics of Change from Baseline: ESSPRI Total Score and Domains	EoS: Include all scheduled visits Summarized for both the overall score and 3 domains (dryness, fatigue and pain)	HL [1] SAC_WK52 [2] SAC_EOS [3]
6.3. (6.1003)	Per Protocol	EFF_T1	Summary Statistics of Change from Baseline: ESSPRI Total Score and Domains	EoS: Include all scheduled visits Summarized for both the overall score and 3 domains (dryness, fatigue and pain)	SAC_WK52 [2] SAC_EOS [3]
6.4. (6.1004)	Safety	EFF_T4	Summary of ESSPRI Responders	EoS: Include all scheduled visits Footnote: Responder 1: Decrease in the ESSPRI total score of at least one point or at least 15% compared to baseline	HL [1] SAC_WK52 [2] SAC_EOS [3]
6.5. (6.1005)	Per Protocol	EFF_T4	Summary of ESSPRI Responders	EoS: Include all scheduled visits Footnote: Responder 1: Decrease in the ESSPRI total score of at least one point or at least 15% compared to baseline	SAC_WK52 [2] SAC_EOS [3]

Health Outcomes: Tables					
No.	**Population**	**IDSL / TST ID / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
6.6.	Safety	EFF_T7	Summary of Statistical Analysis of Responders on ESSPRI	Footnote: Responder 1: Decrease in the ESSPRI total score of at least one point or at least 15% compared to baseline Responder 2: Subjects with baseline score of >= 5 and Total ESSPRI score of < 5. The denominator for percentages at each visit are the subjects who had a score >= 5 at baseline. Note: Add the final model parameters	SAC_WK52 [2]
PROFAD SSI SF					
6.7.	Safety	EFF_T1	Summary Statistics of PROFAD SSI SF Subscores	Summarize for the 3 subscores (PROF, PROFAD, SSI) Footnote (if feasible): 1. PROF is calculated as the sum of domains Somatic fatigue and Mental fatigue 2. PROFAD is calculated as the sum of domains Somatic fatigue, Mental fatigue, Arthralgia and Vascular 3. SSI is calculated as the sum of domains Cutaneous dryness, Vaginal dryness, Ocular dryness and Oral dryness. The SSI subscore is derived for females only.	SAC_WK52 [2]

Health Outcomes: Tables					
No.	**Population**	**IDSL / TST ID / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
6.8.	Safety	EFF_T1	Summary Statistics of Change from Baseline in PROFAD SSI SF Subscores	Summarize for the 3 subscores (PROF, PROFAD, SSI) Footnote (if feasible): 1. PROF is calculated as the sum of domains Somatic fatigue and Mental fatigue 2. PROFAD is calculated as the sum of domains Somatic fatigue, Mental fatigue, Arthralgia and Vascular 3. SSI is calculated as the sum of domains Cutaneous dryness, Vaginal dryness, Ocular dryness and Oral dryness. The SSI subscore is derived for females only.	SAC_WK52 [2]
PtGA					
6.9.	Safety	EFF_T1	Summary Statistics of PtGA		SAC_WK52 [2]
6.10.	Safety	EFF_T1	Summary Statistics of Change from Baseline: PtGA		SAC_WK52 [2]
Further Health Outcomes Analyses					
6.11.	Safety	EFF_T11	Summary of Bayesian Posterior Probabilities: ESSPRI Total Score	**To be generated by GSK** Add appropriate footnotes based on final output	SAC_WK52 [2]

Health Outcomes: Tables					
No.	**Population**	**IDSL / TST ID / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
6.14. (6.1014)	Safety	EFF_T4	Summary of ESSPRI Responders	EoS: Include all scheduled visits Footnote: Responder 1: Decrease in the ESSPRI total score of at least one point or at least 15% compared to baseline Responder 2: Subjects with baseline score of >= 5 and Total ESSPRI score of < 5. The denominator for percentages at each visit are the subjects who had a score >= 5 at baseline.	SAC_WK52 [2] SAC_EOS [3]
(6.1015)	Completer	EFF_T1	Summary Statistics of ESSPRI Total Score and Domains – Completer	Include all scheduled visits Summarize for both the overall score and 3 domains (dryness, fatigue and pain) Add footnote: Note: Completer is defined as “Subjects who completed the 52 Week treatment visits AND general follow up phase of the study including the visit at Week 68”	SAC_EOS [3]

11.13.13. Health Outcomes Figures

Health Outcomes: Figures					
No.	**Population**	**IDSL / TST ID / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
ESSPRI Score					
6.1. (6.1001)	Safety	EFF_F1	Mean (+/-± SE) of Change from Baseline of ESSPRI Total Score and Domains	EoS: As F2.1 Intervals with compose of arithmetic mean ± SE. All visits. Legend: Treatment	SAC_WK52 [2] SAC_EOS [3]
6.2. (6.1002)	Safety	EFF_F3	Proportion of Subjects with an ESSPRI Response	EoS: Include all scheduled visits Footnote: Responder 1: Decrease in the ESSPRI total score of at least one point or at least 15% compared to baseline Responder 2: Subjects with baseline score of ≥ 5 and Total ESSPRI score of < 5 at each visit. The denominator for percentages are the subjects who had a score >=5 at baseline at each visit.	SAC_WK52 [2] SAC_EOS [3]
PROFAD SSI SF					
6.3.	Safety	EFF_F1	Mean (+/-± SE) of Change from Baseline PROFAD SSI SF Subscores	Parameter by: Subscores Intervals with compose of arithmetic mean ± SE. All visits. Legend: Treatment	SAC_WK52 [2]

11.13.14. Exploratory Tables

Exploratory: Tables					
No.	**Population**	**IDSL / TST ID / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
Ocular Dryness					
7.1. (7.1001)	Safety	EFF_T1	Summary Statistics of Ocular Dryness Score	EoS: Include all scheduled visits	SAC_WK52 [2] SAC_EOS [3]
7.2. (7.1002)	Safety	EFF_T1	Summary Statistics of Change from Baseline: Ocular Dryness Score	EoS: Include all scheduled visits	SAC_WK52 [2] SAC_EOS [3]
Lacrimal Gland Function					
7.3.	Safety	EFF_T1	Summary Statistics: Lacrimal Gland Function (Schirmer's test)	Page by: Laterality Parameter: Strip length wet (mm/min) Footnote: Note: Unit = mm/min	SAC_WK52 [2]
7.4.	Safety	EFF_T1	Summary Statistics of Change from Baseline: Lacrimal Gland Function (Schirmer's test)	Page by: Laterality Parameter: Strip length wet (mm/min) Footnote: Note: Unit = mm/min	SAC_WK52 [2]
PGA					
7.5.	Safety	EFF_T1	Summary Statistics of PGA		SAC_WK52 [2]
7.6.	Safety	EFF_T1	Summary Statistics of Change from Baseline: PGA		SAC_WK52 [2]

Exploratory: Tables					
No.	**Population**	**IDSL / TST ID / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
Serologic Markers					
7.7. (7.1007)	Safety	EFF_T1	Summary Statistics of Serologic Markers	Page by marker Include all visits up to Week 68 EoS: Include all scheduled visits Lambda and Kappa Light Chains Ratio of Kappa / Lambda Beta 2 Microglobulin Rheumatoid Factor	SAC_WK52 [2] SAC_EOS [3]
7.8. (7.1008)	Safety	EFF_T9	Summary Statistics Percentage Change from Baseline: Serologic Markers	Page by marker Include all visits up to Week 68 EoS: Include all scheduled visits Ratio of Kappa /Lambda Light Chains Beta 2 Microglobulin Rheumatoid Factor	SAC_WK52 [2] SAC_EOS [3]
Flow Cytometry Parameters					
7.9. (7.1009)	Safety	EFF_T9	Summary Statistics of Flow Cytometry Flow Parameters	Include all parameters specified in RAP Table 11 except for: • Plasmablasts (CD38br CD27br CD20+) • Plasmacells CD20+ (CD20+ CD138+) • Short-lived Plasma (CD20- CD27br) • Transitional (CD24+ CD27-) • Naïve B cells (CD24-CD38br+) • B cells CD20+ (CD19+CD20+)	SAC_WK52 [2] SAC_EOS [3]
7.10. (7.1010)	Safety	EFF_T9	Summary Statistics of Percentage Change from Baseline: Flow Cytometry Parameters	Include all parameters specified in RAP Table 11 for the Final Analysis except for: • Plasmablasts (CD38br CD27br CD20+)	HL [1] SAC_WK52 [2] SAC_EOS [3]

Exploratory: Tables					
No.	**Population**	**IDSL / TST ID / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
				• Plasmacells CD20+ (CD20+ CD138+) • Short-lived Plasma (CD20- CD27br) • Transitional (CD24+ CD27-) • Naïve B cells (CD24-CD38br+) • B cells CD20+ (CD19+CD20+)	
7.11. (7.1011)	Safety	EFF_T10	Summary of Statistical Analysis Results of Percentage Change from Baseline in: Flow Cytometry Parameters at Week 24 EOS: Summary of Statistical Analysis Results of Change from Baseline in: Flow Cytometry Parameters at Week 24	Include only the below parameters for analysis • CD19+ B cell (CD3-CD19+) • Naïve B cell (CD19+CD20+CD27-) • Memory B cell (CD19+CD20+CD27+) • Activated B Cell (CD20+ CD69+) • Plasmablast All (CD19+CD27+CD38+) • Plasmablast (CD20+) • Plasmablast (CD20-) • Transitional B cells (CD19+CD24bCD38+CD27-) Footnote: Analysis performed using Hodges-Lehmann estimator based on Wilcoxon rank test for 2 sample populations.	SAC_WK52 [2] SAC_EOS [3]
7.12.	Per Protocol	EFF_T10	Summary of Statistical Analysis Results of Percentage Change from Baseline in: Flow Cytometry Parameters at Week 24	Include only the below parameters for analysis • CD19+ B cell (CD3-CD19+) • Naïve B cell (CD19+CD20+CD27-) • Memory B cell (CD19+CD20+CD27+) • Activated B Cell (CD20+CD69+) • Plasmablast All	SAC_WK52 [2]

Exploratory: Tables					
No.	**Population**	**IDSL / TST ID / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
				(CD19+CD27+CD38+) • Plasmablast (CD20+) • Plasmablast (CD20-) • Transitional B cells (CD19+CD24bCD38+CD27-) Footnote: Analysis performed using Hodges-Lehmann estimator based on Wilcoxon rank test for 2 sample populations.	
7.13. (7.1013)	Safety	EFF_T10	Summary of Statistical Analysis Results of Percentage Change from Baseline in: Flow Cytometry Parameters at Week 52 EoS Summary of Statistical Analysis Results of Change from Baseline in: Flow Cytometry Parameters at Week 52	Include only the below parameters for analysis CD19+ B cell (CD3-CD19+) Naïve B cell (CD19+CD20+CD27-) Memory B cell (CD19+CD20+CD27+) Activated B Cell (CD20+CD69+) Plasmablast All (CD19+CD27+CD38+) Transitional B cells (CD19+CD24bCD38+CD27-) Plasmablast (CD20+) Plasmablast (CD20-) Footnote: Analysis performed using Hodges-Lehmann estimator based on Wilcoxon rank test for 2 sample populations.	SAC_WK52 [2] SAC_EOS [3]

Exploratory: Tables					
No.	**Population**	**IDSL / TST ID / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
BLyS					
7.14. (7.1014)	Safety	EFF_T9	Summary Statistics of Free BLyS Levels in Blood EoS: Summary Statistics of Free and Total BLyS Levels in Blood	EoS: Include all scheduled visits Subset BICATCD = "TNF13BPF"	SAC_WK52 [2] SAC_EOS [3]
7.15. (7.1015)	Safety	EFF_T9	Summary Statistics of Percentage Change from Baseline: Free BLyS Levels in Blood EoS: Summary Statistics of Free and Total BLyS Levels in Blood	EoS: Include all scheduled visits Subset BICATCD = "TNF13BPF"	SAC_WK52 [2] SAC_EOS [3]
7.16. (7.1016)	Per Protocol	EFF_T9	Summary Statistics of Percentage Change from Baseline: Free BLyS Levels in Blood EoS Summary Statistics of Free and Total BLyS Levels in Blood	EoS: Include all scheduled visits Subset BICATCD = "TNF13BPF"	SAC_WK52 [2] SAC_EOS [3]
Complement Factors					
7.17. (7.1017)	Safety	EFF_T9	Summary Statistics of Complement Factors	EoS: Include all scheduled visits To be run on C3, C4	SAC_WK52 [2] SAC_EOS [3]
7.18. (7.1018)	Safety	EFF_T9	Summary Statistics of Percentage Change from Baseline: Complement Factors	EoS: Include all scheduled visits To be run on C3, C4 Note: For SAC_EOS [3] - Include protocol defined Serological biomarkers	SAC_WK52 [2] SAC_EOS [3]
7.19. (7.1019)	Safety	PD_T1	Summary of CH50 by Visit	Frequency count	SAC_WK52 [2]

Exploratory: Tables					
No.	**Population**	**IDSL / TST ID / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
					SAC_EOS [3]
Serum Cytokines and Chemokines					
7.20. (7.1020)	Safety	EFF_T9	Summary Statistics of Serum Cytokines and Chemokines	EoS: Include all scheduled visits CXCL13 NOTE: BICATCD=BLC = BICAT = B-lymphocyte chemokine Add footnote: Note: B-lymphocyte Chemokine = CXCL13	SAC_WK52 [2] SAC_EOS [3]
7.21. (7.1021)	Safety	EFF_T9	Summary Statistics of Percentage Change from Baseline: Serum Cytokines and Chemokines	EoS: Include all scheduled visits CXCL13 NOTE: BICATCD=BLC = BICAT = B-lymphocyte chemokine Add footnote: Note: B-lymphocyte Chemokine = CXCL13	SAC_WK52 [2] SAC_EOS [3]

Exploratory: Tables					
No.	**Population**	**IDSL / TST ID / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
SS-A and SS-B					
7.22. (7.1022)	Safety	PD_T2	Summary of Autoantibodies by Visit	EoS: Include all scheduled visits Frequency count of SS-A and SS-B at final	SAC_WK52 [2] SAC_EOS [3]
Further Evaluation					
(7.1023)	Completer	EFF_T9	Summary Statistics of Flow Cytometry Flow Parameters – Completer	Include all parameters specified in RAP Table 11 except for: • Plasmablasts (CD38br CD27br CD20+) • Plasmacells CD20+ (CD20+ CD138+) • Short-lived Plasma (CD20- CD27br) • Transitional (CD24+ CD27-) • Naïve B cells (CD24-CD38br+) B cells CD20+ (CD19+CD20+) Add footnote: Note: Completer is defined as "Subjects who completed the 52 Week treatment visits AND general follow up phase of the study including the visit at Week 68"	SAC_EOS [3]

11.13.15. Exploratory Figures

Exploratory: Figures					
No.	**Population**	**IDSL / TST ID / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
Ocular Dryness NRS					
7.1. (7.1001)	Safety	EFF_F1	Mean (+/- SE) of Change from Baseline in Ocular Dryness NRS	All scheduled visits Legend: Treatment EoS: As F2.1001	SAC_WK52 [2] SAC_EOS [3]
Lacrimal Gland Function					
7.2.	Safety	EFF_F1	Mean (+/- SE) of Change from Baseline in Lacrimal Gland Function (Schirmers Test)	All scheduled visits Legend: Treatment EoS: As F2.1001	SAC_WK52 [2]
PGA					
7.3.	Safety	EFF_F1	Mean (+/- SE) of Change from Baseline in PGA	All scheduled visits Legend: Treatment	SAC_WK52 [2]
Flow Cytometry					
7.4. (7.1004)	Safety	EFF_F4	Median (+/- IQR) of Absolute Values of Flow Cytometry	EoS: As F2.1001 Include only the following parameters (Page by) • CD19+ B cell (CD3-CD19+) • Naïve B cell (CD19+CD20+CD27-) • Memory B cell (CD19+CD20+CD27+) • Activated B Cell (CD20+CD69+) • Plasmablast All (CD19+CD27+CD38+) • Transitional B cells (CD19+CD24bCD38+CD27-) • Plasmablast CD20+ • Plasmablast CD20- x-axis is visit, y-axis in absolute values of the parameters. Panel per treatment group.	SAC_WK52 [2] SAC_EOS [3]

Exploratory: Figures					
No.	**Population**	**IDSL / TST ID / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
7.5. (7.1005)	Safety	EFF_F4	Median (+/- IQR) for Percentage Change from Baseline in Flow Cytometry	EoS: As F2.1001 • CD19+ B cell (CD3-CD19+) • Naïve B cell (CD19+CD20+CD27-) • Memory B cell (CD19+CD20+CD27+) • Activated B Cell (CD20+CD69+) • Plasmablast All (CD19+CD27+CD38+) • Transitional B cells (CD19+CD24bCD38+CD27-) • Plasmablast CD20+ • Plasmablast CD20- x-axis is visit, y-axis in percentage change from baseline of the parameters. Panel per treatment group.	SAC_WK52 [2] SAC_EOS [3]
Blys					
7.6. (7.1006)	Safety	EFF_F4	Median (+/- IQR) for Percentage Change from Baseline in Free Blys EoS Median (+/- IQR) for Percentage Change from Baseline in Free and Total Blys	EoS: EoS: As F2.1001 x-axis is visit, panel by parameter (Free & Total BLyS).	SAC_WK52 [2] SAC_EOS [3]
Serologic Biomarkers					
7.7. (7.1007)	Safety	EFF_F4	Median (+/- IQR) for Percentage Change from Baseline in Serological Biomarkers	EoS: EoS: As F2.1001 Include Rheumatoid Factor, Lambda light chain protein, Kappa light chain protein, Kappa/Lambda ratio, Beta 2 microglobulin	SAC_WK52 [2] SAC_EOS [3]
Complement Factors					
7.8. (7.1008)	Safety	EFF_F4	Median (+/- IQR) for Percentage Change from Baseline in Complement Factors	EoS: EoS: As F2.1001 Include C3 and C4	SAC_WK52 [2] SAC_EOS [3]

Exploratory: Figures					
No.	**Population**	**IDSL / TST ID / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
Serum Chemokines					
7.9. (7.1009)	Safety	EFF_F4	Median (+/- IQR) for Percentage Change from Baseline in CXCL13	EoS: EoS: As F2.1001 NOTE: BICATCD=BLC = BICAT = B-lymphocyte chemokine	SAC_WK52 [2] SAC_EOS [3]

11.13.16. ICH Listings

ICH: Listings					
No.	**Population**	**IDSL / TST ID / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
Study Population					
1.	Safety	TA1	Listing of Randomized and Actual Treatments		SAC_WK52 [2]
2. (1002)	Safety	ES2	Listing of Reasons for Study Withdrawal		SAC_WK52 [2] SAC_EOS [3]
3.	Safety	POP_L1	Listing of Reasons for Permanent Study Treatment Discontinuation		SAC_WK52 [2]
4.	Screened	ES7	Listing of Reasons for Screening Failure		SAC_WK52 [2]
5. (1005)	Safety	SP3	Listing of Subjects Excluded from Any Populations		SAC_WK52 [2] SAC_EOS [3]
6. (1006)	Safety	DV2	Listing of Important Protocol Deviations		SAC_WK52 [2] SAC_EOS [3]
7.	Safety	IE3	Listing of Subjects with Inclusion/Exclusion Criteria Deviations		SAC_WK52 [2]
Demographics					
8.	Safety	DM2	Listing of Demographic Characteristics		SAC_WK52 [2]
9.	Safety	DM9	Listing of Race		SAC_WK52 [2]
10. (1010)	Safety	POP_L2	Listing of Physical Exam		SAC_WK52 [2] SAC_EOS [3]

ICH: Listings					
No.	**Population**	**IDSL / TST ID / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
Medical Condition & Concomitant Medications					
11.	Safety	MH2	Listing of Medical Conditions (Sjögren specific)	iSRC version has all medical conditions	SAC_WK52 [2]
12.	Safety	MH2	Listing of Medical Conditions (non-Sjögren specific)		SAC_WK52 [2]
13. (1013)	Safety	CP_CM3	Listing of Concomitant Medications		SAC_WK52 [2] SAC_EOS [3]
Disease History					
14.	Safety	POP_L3	Listing of Disease Characteristics (AECG Criteria)		SAC_WK52 [2]
Exposure					
15.	Safety	OEX3a	Listing of Exposure		SAC_WK52 [2]
Adverse Events					
16. (1016)	Safety	AE7	Listings of Subject Numbers for Individual Adverse Events	EoS: Include visits upto W68/FU EoS Footnote: Note: Includes Treatment & General Follow Up periods only.	SAC_WK52 [2] SAC_EOS [3]
17. (1017)	Safety	AE8	Listing of All Adverse Events	EoS: Include visits upto W68/FU EoS Footnote: As Listing 1016	SAC_WK52 [2] SAC_EOS [3]
18. (1018)	Safety	AE8	Listing of Post Treatment Adverse Events	EoS: Include visits upto W68/FU EoS Footnote: As Listing 1016	SAC_WK52 [2] SAC_EOS [3]

ICH: Listings					
No.	**Population**	**IDSL / TST ID / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
19. (1019)	Safety	SAFE_L3	Listing of Adverse Events of Special Interest	EoS: Include visits upto W68/FU EoS Footnote: As Listing 1016 Include all AESI, including study specific	SAC_WK52 [2] SAC_EOS [3]
20. (1020)	Safety	AE8	Listing of Fatal Serious Adverse Events	EoS: Include visits upto W68/FU EoS Footnote: As Listing 1016	SAC_WK52 [2] SAC_EOS [3]
21. (1021)	Safety	AE8	Listing of Non-Fatal Serious Adverse Events	EoS: Include visits upto W68/FU EoS Footnote: As Listing 1016	SAC_WK52 [2] SAC_EOS [3]
22. (1022)	Safety	AE14	Listing of Reasons for Considering as a Serious Adverse Event	EoS: Include visits upto W68/FU EoS Footnote: As Listing 1016	SAC_WK52 [2] SAC_EOS [3]
23. (1023)	Safety	AE8	Listing of Adverse Events Leading to Discontinuation of Treatment or Withdrawal from Study	EoS: Include visits upto W68/FU EoS Footnote: As Listing 1016	SAC_WK52 [2] SAC_EOS [3]
24. (1024)	Safety	AE2	Listing of Relationship between System Organ Class and Verbatim Text	EoS: Include visits upto W68/FU EoS Footnote: As Listing 1016	SAC_WK52 [2] SAC_EOS [3]

ICH: Listings					
No.	**Population**	**IDSL / TST ID / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
Laboratory					
25. (1025)	Safety	LB5	Listing of Hematology Laboratory Data	EoS: Include all scheduled visits EoS Footnote: As Listing 1016	SAC_WK52 [2] SAC_EOS [3]
26. (1026)	Safety	LB5	Listing of Clinical Chemistry Laboratory Data	EoS: Include all scheduled visits EoS Footnote: As Listing 1016	SAC_WK52 [2] SAC_EOS [3]
27. (1027)	Safety	LB5	Listing of Liver Function Laboratory Data	EoS: Include all scheduled visits EoS Footnote: As Listing 1016	SAC_WK52 [2] SAC_EOS [3]
28. (1028)	Safety	UR2a	Listing of Urinalysis Data	EoS: Include all scheduled visits EoS Footnote: As Listing 1016	SAC_WK52 [2] SAC_EOS [3]
29. (1029)	Safety	LIVER5	Listing of Liver Monitoring/Stopping Event Reporting	EoS: Include all scheduled visits EoS Footnote: As Listing 1016	SAC_WK52 [2] SAC_EOS [3]
Vital Signs					
30. (1030)	Safety	VS4	Listing of Vital Signs	EoS: Include all scheduled visits	SAC_WK52 [2] SAC_EOS [3]
ECGs					
31.	Safety	EG5	Listing of Abnormal ECG Findings		SAC_WK52 [2]

ICH: Listings					
No.	**Population**	**IDSL / TST ID / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
Other					
(1061)	Safety	DV2	Listing of Protocol Deviations Related to Covid-19	Include only subjects with related Covid-19 PD's. Subset standard text 'COVID-19'.	SAC_EOS [3]

11.13.17. Non-ICH Listings

Non-ICH: Listings					
No.	**Population**	**IDSL / TST ID / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
Safety					
32. (1032)	Safety	SAFE_L1	Listing of Neurological Symptoms	EoS: Include all scheduled visits	SAC_WK52 [2] SAC_EOS [3]
33. (1033)	Safety	ECSSRS4	Listing of C-SSRS Suicidal Ideation and Behavior Data	EoS: Include all scheduled visits	SAC_WK52 [2] SAC_EOS [3]
34. (1034)	Safety	ECSSRS5	Listing of C-SSRS Suicidal Behavior Details	EoS: Include all scheduled visits	SAC_WK52 [2] SAC_EOS [3]
35. (1035)	Safety	SAFE_L2	Grade 3 or Grade 4 Laboratory Toxicity Results: Hematology	EoS: Include all scheduled visits	SAC_WK52 [2] SAC_EOS [3]
36. (1036)	Safety	SAFE_L2	Grade 3 or Grade 4 Laboratory Toxicity Results: Clinical Chemistry	EoS: Include all scheduled visits	SAC_WK52 [2] SAC_EOS [3]
37. (1037)	Safety	SAFE_L2	Grade 3 or Grade 4 Laboratory Toxicity Results: Immunoglobulin	EoS: Include all scheduled visits IgG only	SAC_WK52 [2] SAC_EOS [3]
38.	Safety	SAFE_L4	Listing of Positive Results for Other Screening Tests	Include HIV, Hepatitis B (HBsAg), HbcAb, Hepatitis C (Hep C antibody), FSH, estradiol and serum or urine hCG pregnancy test.	SAC_WK52 [2]

Non-ICH: Listings					
No.	**Population**	**IDSL / TST ID / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
39. (1039)	Safety	IMM2	Listing of Positive Immunogenicity Results	**Primary** Belimumab **EoS** Belimumab & Rituximab Results All antibody and assay data Footnote: For anti-Rituximab, baseline is Week 8	SAC_WK52 [2] SAC_EOS [3]
40. (1040)	Safety	LB5	Listing of Immunoglobulins	Define flags "I" "N" "U" etc… in the footnotes	SAC_WK52 [2] SAC_EOS [3]
41. (1041)	Safety	LB5	Listing of CD4 and CD8	EoS: Include all scheduled visits	SAC_WK52 [2] SAC_EOS [3]
Efficacy					
42. (1042)	Safety	EFF_L1	Listing of ESSDAI Responses	EoS: Include all scheduled visits At SAC Include Total ESSDAI, ClinESSDAI and individual domains	SAC_WK52 [2] SAC_EOS [3]
43. (1043)	Safety	EFF_L2	Listing of Damage Scoring for Subjects with Damage	EoS: Include all scheduled visits For each subject with damage. All timepoints, but only in domain which has any damage reported.	SAC_WK52 [2] SAC_EOS [3]
44. (1044)	Safety	EFF_L3	Listing of Change from Baseline of Clinical Efficacy Endpoints and Number of B cells (CD20/mm2) in salivary gland.	EoS: Include all scheduled visits **To be generated by GSK**	SAC_WK52 [2] SAC_EOS [3]

Non-ICH: Listings					
No.	**Population**	**IDSL / TST ID / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
45. (1045)	Safety	EFF_L4	Listing of Stimulated and Unstimulated Salivary Flow	EoS: Include all scheduled visits **To be generated by GSK**	SAC_WK52 [2] SAC_EOS [3]
46. (1046)	Safety	EFF_L5	Listing of Oral and Ocular Dryness NRS	EoS: Include all scheduled visits **To be generated by GSK**	SAC_WK52 [2] SAC_EOS [3]
47.	Safety	EFF_L6	Listing of Lacrimal Function (Schirmer's) Test	**To be generated by GSK**	SAC_WK52 [2]
48.	Safety	EFF_L7	Listing of PROFAD-SSI-SF Subscores	**To be generated by GSK**	SAC_WK52 [2]
49.	Safety	EFF_L8	Listing of Patient Global Assessment (PtGA)	**To be generated by GSK**	SAC_WK52 [2]
50.	Safety	EFF_L9	Listing of Physicians Global Assessment (PGA)	**To be generated by GSK**	SAC_WK52 [2]
51. (1051)	Safety	EFF_L10	Listing of Free and Total BLyS Levels	EoS: Include all scheduled visits **To be generated by GSK**	SAC_WK52 [2] SAC_EOS [3]
52. (1052)	Safety	EFF_L11	Listing of Flow Cytometry Parameters	EoS: Include all scheduled visits Include all parameters Page by: Parameters **To be generated by GSK**	SAC_WK52 [2] SAC_EOS [3]
53. (1053)	Safety	EFF_L11	Listing of Serologic Markers	EoS: Include all scheduled visits Include all parameters Page by: Parameters **To be generated by GSK**	SAC_WK52 [2] SAC_EOS [3]

Non-ICH: Listings					
No.	**Population**	**IDSL / TST ID / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
54.	Safety	EFF_L11	Listing of Salivary Gland Assessment	Include all parameters Page by: Parameters **To be generated by GSK**	SAC_WK52 [2]
55. (1056)	Safety	EFF_L12	Listing of ESSPRI Score	EoS: Include all scheduled visits **To be generated by GSK**	SAC_WK52 [2] SAC_EOS [3]
541 (1057)	Safety	EFF_L11	Listing of Complement Factors (CH50)	EoS: Include all scheduled visits **To be generated by GSK**	SAC_WK52 [2] SAC_EOS [3]
542 (1058)	Safety	EFF_L11	Listing of Complement Factors (Biomarkers)	EoS: Include all scheduled visits **To be generated by GSK**	SAC_WK52 [2] SAC_EOS [3]
1059.	Safety	POP_L4	Listing of Overall Subject Status	EoS: Include all scheduled visits **To be generated by GSK**	SAC_EOS [3]
411 (1411)	Safety	SAFE_L4	Listing of All Adverse Events Post Week 68 during the Individualized Follow Up Period	Primary: Blinded listing EoS: Unblinded listing **To be generated by GSK**	SAC_WK52 [2] SAC_EOS [3]

11.14. Appendix 14: Example Mock Ups

Data Display Specification are presented in a separate document.