Statistical Analysis Plan

Study ID: 116543

Official Title of Study: Reporting and Analysis Plan for BEL116543, a 5-Year Prospective Observational Registry to Assess Adverse Events of Interest and Effectiveness in Adults with Active, Autoantibody-Positive Systemic Lupus Erythematosus Treated with or without BENLYSTA™ (Belimumab)

NCT number: NCT01729455

Date of Document: 20 Mar 2025

Note: A typographical error appears in Section 2.3 of the Study Design (third bullet under 'Design Features'). The phrase currently reads 'assessment of **secondary** endpoints', but it is intended to state 'assessment of **other** endpoints", in line with other sections of the SAP and the protocol.

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Division	:	Worldwide Development
Information Type	:	Reporting and Analysis Plan (RAP)
Title	:	Reporting and Analysis Plan for BEL116543, a 5-Year Prospective Observational Registry to Assess Adverse Events of Interest and Effectiveness in Adults with Active, Autoantibody-Positive Systemic Lupus Erythematosus Treated with or without BENLYSTA™ (Belimumab)
Compound Number	:	GSK1550188
Clinical Study Identifier		BEL116543
Effective Date	:	14 March 2025

Description:

This document describes the safety and effectiveness analysis and outputs required for Clinical Study Report BEL116543 [HGS10006-C1124].

RAP Author(s):

Lead Author	Signatures	Dates
PPD Statistical Team Lead	PPD	3/14/2025
PPD Manager, Biostatistics		3/17/2025
Co-Author		
PPD Biostatistician		3/19/2025

RAP Team Reviews:
(Method: Electronic Approval)

Reviewers	Signatures	Dates
PPD Senior Statistical Programmer	PPD	3/17/2025
PPD Senior Statistician		3/17/2025
PPD Principal Programmer, Development Biostatistics (Programming Development)		3/17/2025
PPD PPD, Immunology (Medical Monitor)		3/20/2025
PPD PPD		3/20/2025
PPD PPD Epidemiology Immunology		3/20/2025
PPD Senior Biostatistician		3/19/2025

Clinical Statistics and Clinical Programming Line Approvals:
(Method: Electronic Approval)

Approver	Signatures	Dates
PPD PPD, Development Biostatistics	PPD	3/17/2025
PPD, PPD (Immunology Clinical Programming)		3/17/2025

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1. INTRODUCTION

The purpose of this reporting and analysis plan (RAP) is to describe the analyses required for the final Clinical Study Report (CSR) for study BEL116543 [HGS10006-C1124] based on the study protocol amendment 5.

Protocol Revision Chronology:		
Global	14-Aug-2012	Original
Global	01-Nov-2012	Amendment No 01
Local 2013N183013_00	10-Dec-2013	Local Addendum No 01 for Sweden
Global 2017N316452_00	19-Jun-2017	Amendment No 02
Global 2017N316452_01	12-Mar-2018	Amendment No 03
Global 2017N316452_02	25-Nov-2020	Amendment No 04
GlobalTMF-14148167	25 May 2022	Amendment No 05

This RAP is based upon the following study documents:

- Study Protocol Amendment 05 (25 May 2022)
- Case Report Form (CRF) Version 7.0 (27 Jul 2020)

The protocol amendment 03 excludes collection of the following data: quality of life (as assessed by SF-12v2 Health Survey), fatigue (as assessed by the functional assessment of chronic illness therapy [FACIT]-Fatigue Scale) and limits collection of systemic lupus erythematosus (SLE) disease activity (as assessed by the SLEDAI 2000) to the baseline visit only. The protocol amendment 04 updated the General Medical Status (current status of medical condition and/or medical procedure/surgery since last reported) to be collected at 24 and 48 months. The data collection modifications for protocol amendments 3 and 4 are shown in Appendix 1.

2. SUMMARY OF KEY PROTOCOL INFORMATION

2.1. Changes to the Protocol Defined Reporting Analysis Plan and Previous RAP

2.1.1. Changes to the Protocol Defined Reporting Analysis Plan

This RAP provides a more detailed elaboration of the high-level summary of statistical analysis provided in the protocol. There are no changes to the approach originally planned for statistical analysis. However, the following slight modifications have been made:

- Computation of rates (incidence and event) will be done separately for Opportunistic Infections and Other Infections of Interest (these were combined as one in the protocol).

2.1.2. Changes to the Previous RAP

This version of the RAP for final analysis includes amendments to the approved interim analysis 11 (IA11) RAP. Changes are listed below:

- Section 3.1: details on Interim analysis have been deleted as not applicable for final analysis
  Along the document, non relevant statements related to interim analysis have been deleted.
- Section 4.2: last version of Protocol Deviation Management Plan (PDMP) added
- Section 5.1: Table presented analysis strategy per endpoints: Correction added for hospitalization for “As-Exposed time varying”, that is applicable to the 14 weeks risk window (Y1) and 6-months risk window (Y2) was made applicable for Serious Psychiatric Events
- Sections 5.2 and 9.5.1: updated laboratory measurement reporting
- Section 5.4: “Ongoing” status deleted as RAP applies for final analysis
- Section 5.5: clarification added regarding reporting of subjects transferred to a new site in table of enrollement
- Section 7.2: Effectiveness analysis will not be conducted separately for the two study cohorts (Current users and treatment initiators). All link in the RAP deleted.
- Section 7.3: New section added to include propensity scores analysis
- Section 8: AESI work instruction reference added, , references regarding propensity scores analysis also added
- Section 9: first appendix presented in previous version was removed, impacting the numbering of the subsequent sections.
- Section 9.4: GSK standards updated
- Section 9.9: new appendix added.
- Section 9.10: new appendix added.
- Section 9.11: updated for final analysis (was previously section 9.10)
- Section 9.12: section renumbered (was previous section 9.11)

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

Objectives	Endpoints
Primary	**Primary**
To evaluate the incidence of selected adverse events of special interest (AESI) over 5 years in adults with active autoantibody-positive systemic lupus erythematosus (SLE) who are treated with or without BENLYSTA	Comparison of incidence rates, over a 5-year period, of listed Adverse Events of Special Interest (AESI) among adult SLE subjects who are exposed or unexposed to BENLYSTA: 1. Malignancies (excluding non-melanoma skin cancers) 2. Mortality 3. Opportunistic infections (serious and non-serious)* 4. Other infections of interest (serious and non-serious)* 5. Non-melanoma skin cancers (NMSC) 6. Serious psychiatric events 7. Serious infections
Other	**Other**
To evaluate selected effectiveness measures in adults with active autoantibody-positive SLE who are treated with or without BENLYSTA	1. Comparison of mean change from baseline in SLICC/ACR Damage Index (SDI) score over a 5-year period in adult SLE subjects who are exposed or unexposed to BENLYSTA 2a. Comparison of proportions of subjects with concomitant SLE medication use, including steroids (as defined below), over a 5-year period in adult SLE subjects who are exposed or unexposed to BENLYSTA Over the past six months the daily dose was either: i. Always < 7.5 mg/day ii. >= 7.5 mg/day for <= 2 weeks iii. >= 7.5 mg/day for > 2 weeks 2b. Comparison of mean change from baseline in six-month average daily corticosteroid dose (prednisone equivalent, mg/day) assessed over 5-year period in adult SLE subjects who are exposed or unexposed to BENLYSTA 3. Comparison of incidence rates, over a 5-year period, of hospitalizations (as shown below) among adults SLE subjects who are exposed or unexposed to BENLYSTA: i. All hospitalizations ii. SLE-related hospitalization
Tertiary/Exploratory	**Tertiary/Exploratory**
NA	NA

* Computation of rates will be done separately for opportunistic infections and other infections of interest (these were combined as one in the protocol)

2.3. Study Design

Overview of Study Design and Key Features	
Design Features	• Multi-centre, prospective, observational cohort study (registry). • Subjects receiving or initiating BENLYSTA and/or other immunosuppressant SLE medications (e.g. azathioprine, methotrexate, cyclophosphamide, mycophenolate, and biologics) (all medication decisions are at the discretion of the subject and their healthcare provider, and are not mandated by study design or protocol). • Subjects are followed-up approximately every 6 months for 5 years for occurrence of AESI (primary endpoint) and assessment of secondary endpoints including SDI organ damage. • Assessments are intended to be performed every 6 months based on information gathered during routine care and hospital attendance as there are no protocol mandated study visits*
Time & Events	Appendix 1: Schedule of Activities provides details of study activity timelines and data collection.
Exposure Assignment	• No formal or protocol defined treatment assignment. • Subjects are enrolled into 1 of 2 exposure groups; those who, at baseline, are receiving or initiating BENLYSTA (BENLYSTA or Exposed group) or are not receiving BENLYSTA (Non-BENLYSTA or Unexposed group).
Interim Analyses	• Annual interim analyses were planned throughout the study life cycle until the end of study in 2025.The interims were done for monitoring the safety of BENLYSTA and for reporting study progress to the external Scientific Advisory Committee, Benlysta Safety Review Team and Regulators.
Final Analysis	• Final analysis is planned for 2025 such that the enrollment and 5-year follow-up of every subject will have been completed.

* Study setup to collect data during routine visits at approximately 6-month intervals ± 2months; this data collection interval is intended to align with routine standard of care visits for SLE subjects.

2.4. Statistical Hypotheses / Statistical Analyses

The purpose of the study is to evaluate the incidence of AESI over 5 years in adults with SLE being treated with and without BENLYSTA in a real-world setting. No formal statistical hypotheses testing will be conducted since there is no pre-specified hypothesis for any of the study endpoints.

Unless otherwise specified, the following measures will be used:

- Categorical variables will be summarized as the number of subjects and percentages (%) of subjects in each category. Percentages will not include the missing category and will be calculated over the number of subjects with available (non-missing) data.
- Continuous variables will be summarized using the mean, standard deviation (SD), median, first and third quartiles (Q1, Q3), minimum (min), maximum (max).
- Computed percentages will be presented with one decimal place. Percentages equal to 100 will be presented as 100% and no percentage will be presented for zero frequencies. In case of presenting CIs for categorical/qualitative data, exact methods for deriving these intervals will be used in case of descriptive statistics.
- The 95% CI will be computed for rates to contextualize the extent of random error but will not be used for formal statistical hypothesis testing.

3. PLANNED ANALYSES

3.1. Interim Analyses

Annual interim analyses were conducted throughout the study life cycle at a prospectively pre-determined data cut-off date until end of study reporting in 2025 for the monitoring and reporting of study progress to either the external Scientific Advisory Committee, Benlysta Safety Review Team and/or regulators.

3.2. Final Analyses

The final planned analyses will be performed after the completion of the following procedure:

1. All subjects have completed their 5-year follow-up (or early withdrawal assessment for subjects withdrawing prior to completion of the 5-year follow-up), i.e. the last subject last visit milestone.
2. All required database cleaning activities have been completed and final database lock (DBL) has been declared by Data Management.

Further details of the sequential steps above, along with the relevant timelines can be found in the Clinical Study Activity Plan (CSAP).

This RAP describes the planned statistical analyses to be conducted for the final reporting. The AE review/categorization process is detailed in Appendix 3 (Section 9.3). The descriptive summary of baseline characteristics will be produced by exposure group (i.e. Benlysta or Exposed vs Non-Benlysta or Unexposed) using the 'Eligible' analysis population (see Section 4). A separate descriptive summary may be produced for the two study cohorts ('Current Users' and 'Treatment Initiators', see Section 5.6.2).

Safety and effectiveness endpoints will be analysed using the 'Evaluable' population. Results will be summarized by subjects' exposure group (i.e. Benlysta or Exposed vs Non-Benlysta or Unexposed) defined using the 'Initial Exposure', 'Ever-Exposed', and/or 'As-Exposed (Time Varying)' strategies (Section 9.2). In addition, separate summary display tables may be produced for the two study cohorts). The list of the planned data displays for each analysis population is provided in Appendix 11 (Section 9.11).

Description of the statistical methods to be used to minimize selection bias and confounding bias of safety analysis is also presented.

4. ANALYSIS POPULATIONS

4.1. Study analysis population

Population	Definition / Criteria	Analyses Evaluated
Enrolled	• All subjects who were enrolled irrespective of whether they meet the inclusion/exclusion criteria	• Study Progress
Eligible	• Subjects in the 'Enrolled' population who met the inclusion/exclusion criteria [1]	• Study Population • Other Covariates
Evaluable [3]	• Subset of the 'Eligible' population with a collection of enrollment data and at least 1 post-baseline assessment	• Safety • Effectiveness
Sensitivity Analysis		
Sensitivity	• Subjects in the 'Enrolled' population who are on combination of medications that include both anti-malarials and corticosteroids, or who are in the 'Eligible' population [2]	• Study Population
Evaluable Sensitivity [3]	• Subset of the 'Sensitivity' population with a collection of enrollment data and at least 1 post-baseline assessment	• Safety

Refer to Appendix 11: List of Tables, Listings and Figures (TLF) Data Displays for details of the population used for each analysis endpoint.

[*1] Based on medications reported in the SLE medications page and/or baseline corticosteroids page of the eCRF. In the SDTM data, eligible subjects who are taking Benlysta at enrollment (refer to section 9.5.2 for more details) will be assigned study exposure group = BENLYSTA. Subjects on immunosuppressants other than Benlysta at enrollment will be assigned exposure group = NON-BENLYSTA. Subjects who are only on anti-malarials or steroids at enrollment will not be included in any analyses. Moreover subjects who are on combination of medications at enrollment that include both anti-malarials and corticosteroids, but not immunosuppressants, will not be included in the 'Eligible' population.*

***Note for programming**: some medications recorded as "Other" in CRF are immunosuppresants and should be considered when confirming eligibility. The manual review and selection of immunosuppressants reported as free text in "Other" field is under the responsibility of the GSK clinical team. At each data cut, review of new medications will manually be done and reported in an external Excel file.*

[*2] Compared to the 'Eligible' population, the 'Sensitivity' population will also include subjects on combination of medications that include both anti-malarials and corticosteroids, without immunosuppressant at enrollment. These subjects will be assigned exposure group = NON-BENLYSTA and used only for a sensitivity analysis.*

*[3]. **Note for programming:** subjects are considered 'Evaluable' if i) study day > 91 and visit is not end of study or ii) if previous point is not satisfied, last date of Adverse Events, Hospitalization and Concomitant Medications datasets is "day > 1" and Exposure dataset "day > 4". If previous point is not satisfied, the last contact date (as defined in Section 9.5.3) > 91 will be considered.*

4.2. Protocol Deviations

Protocol deviations will be tracked by the study team throughout the conduct of the study in accordance with the Protocol Deviation Management Plan (PDMP) [22 April 2024 Version 5.0]. If the PDMP is updated, the most current version of the PDMP will be used.

Data will be reviewed on an ongoing basis and prior to locking the database to ensure all important deviations are captured and categorized in the protocol deviations dataset. This dataset will be the basis for the table and listing of protocol deviations.

A summary of subjects who did not meet inclusion/exclusion criteria will also be provided.

5. CONSIDERATIONS FOR DATA ANALYSES AND DATA HANDLING CONVENTIONS

5.1. Study Exposure & Sub-group Display Descriptors

Exposure Group Descriptions			
Study Exposure Group		Data Displays for Reporting	
Code	Description	Description	Order in TLF
A	BENLYSTA	BENLYSTA	2
B	NON-BENLYSTA	NON-BENLYSTA	1

Exposure group comparisons will be displayed using the following specified descriptors:

- BENLYSTA vs NON-BENLYSTA

BENLYSTA group is used for subjects who are exposed to Benlysta while NON-BENLYSTA group is used for subjects who are not exposed to Benlysta. For summary description of baseline characteristics, the exposure group represents subjects' exposure at enrollment (i.e 'Initial Exposure'). For summary of safety and effectiveness endpoints, the exposure group will be defined using the 'Initial Exposure', 'As-Exposed', and/or 'Ever- Exposed' strategies (see Appendix 2, Section 9.2). 'As-Exposed' is defined based on whether or not a subject is using Benlysta at specific period during the study follow-up time; thus a subject's exposure group can change over time depending on switching[1] to or off Benlysta. 'Ever-Exposed' is defined based on whether a subject was exposed to Benlysta at any point in time after enrollment, in this instance a subject's exposure can change only once over time if they were initially 'Unexposed' and then started using Benlysta; once a subject is exposed to Benlysta, they will always be considered as 'Exposed'.

The specific strategy for defining exposure group and the analysis approach for accrued data will be indicated on the TLFs titles and list of the planned data displays provided in Appendix 11 (Section 9.11).

[1] *Subjects are considered to have switched from BENLYSTA exposure group if they permanently discontinued Benlysta treatment or missed doses of Benlysta for more than 98 days and do not restart doses of Benlysta on or before day 99 after the last Benlysta medication end date. Subjects are considered to have switched from NON-BENLYSTA exposure group if they initiate or start receiving Benlysta dose anytime during the study follow-up period. Change of different study-qualifying Non-Benlysta Standard of Care (SOC) medications does not count as exposure switching.*

Primary analysis will be done on 'Initial Exposure' strategy for all endpoints while 'As--Exposed' and 'Ever-Exposed' will apply for some endpoints as exploratory analysis:

	Primary analysis		Exploratory analysis	
Endpoints	**Initial Exposure Intent-To-Treat (ITT)**	**While on Initial Exposure**	**As-Exposed Time varying***	**Ever-Exposed**
Primary endpoints (AESI)				
Serious Psychiatric events	Y	Y	Y1, Y2	
Serious infections, opportunistic infections and other infections of interest	Y	Y	Y1, Y2	
NMSC and malignancies excluding NMSC	Y	Y	Y1	Y
Mortality	Y	Y	Y1, Y2	Y
Effectiveness endpoints				
SLICC/ACR Damage index (SDI)	Y			
Concomitant SLE medications including steroids	Y			
Hospitalization	Y	Y	Y1	

** For As-Exposed strategy, 14 weeks risk window or 6-months risk window are defined depending on the endpoint (see Appendix 2, Section 9.2). Y=Yes. Y1 = applicable to the 14 weeks risk window, Y2 = applicable to the 6-months risk window.*

For some display Tables and Figures, the 'Total' for the two exposure groups combined may be presented, as shown on the TLFs mock-shell (Appendix 12). The format of Graphs/Figures will follow the graphical display standard and handling convention specified in Appendix 4Appendix 5.

The "Initial Exposure" strategy will be used to derive weights from the Propensity Scores model for the weighted analyses (see section 7.3). This exposure includes two different analysis approaches:

- 'Intent-To-Treat (ITT)' and
- 'While On Initial Exposure'.

Other subgroups will be described in more detail in Section 5.6.2.

5.2. Baseline Definition

The protocol specifies Day 0 as baseline, but the Clinical Data Interchange Standards Consortium (CDISC) standard refers to the baseline as Day 1; therefore, baseline date will be referenced as Day 1 in this document. Further information on the definition of study and SLE medication phases is presented in Section 9.5.2.

In general, the baseline value of a variable will be defined as the value of the variable measured at the enrollment visit per eCRF . The exceptions are:

i. For SLICC, and SLEDAI 2000, measurements done within ±30 days of enrollment day will be considered as baseline. If there are multiple records that meet this criteria for the same measurement, the worst-case value will be selected as the baseline value. If the values are equal, the measurement which takes place first will be selected as the baseline value.

ii. For laboratory, measurements done within ±30 days of enrollment day will be considered as baseline. If there are multiple records that meet this criteria for the same measurement, the measurement which takes place first will be selected as the baseline value.

iii. For SLE medications, a 3-day post enrollment rule is applied such that SLE medications started or initiated between study days 1-4 of enrollment (i.e. Study Day 1, 2, 3 or 4) are counted as baseline medication.

iv. All hospitalizations (SLE-related and non-SLE-related) which occurred (based on admission date) within 6 months prior to or on the enrollment visit date.

5.3. Visit/Assessment Time Window and Descriptor

Follow-up assessments are expected to be performed every six months ±2-month time window. Analysis visit will be created for mapping data assessments into correct visit time point. This variable will be used in all analyses that require a visit number, regardless of the collected visit in the eCRF. If there are multiple visits done within a expected visit time window, the visit with the worst-case value will be used. Further details are provided in Section 9.5.1.

Study Period	Analysis Visit Number (AVISITN)	Target Visit Time	Expected Visit Interval	Expected Assessment Interval (Days)[1]	Target Study Day (for events slotting)[2]	Table/Graph Descriptor (Months)
Enrollment	1	Day 1		<=91 days		
Baseline	1.5					
Follow-up	2	6 Months	4 to 8 Months	92 – 274[3]	183	6
	3	12 Months	10 to 14 Months	275 – 456	366	12
	4	18 Months	16 to 20 Months	457 – 639	548	18
	5	24 Months	22 to 26 Months	640 – 822	731	24
	6	30 Months	28 to 32 Months	823 – 1004	914	30
	7	36 Months	34 to 38 Months	1005 – 1187	1096	36
	8	42 Months	40 to 44 Months	1188 – 1369	1279	42
	9	48 Months	46 to 50 Months	1370 – 1552	1461	48
	10	54 Months	52 to 56 Months	1553 – 1735	1644	54

	11	60 Months	58 to 63 Months[4]	1736 – 1918	1827	60

[1]Expected study day interval for mapping data assessments date to visit. Lower limit = Target Study Day–91 (i.e. approximately 3 months). Upper limit = Lower limit of next interval–1, 60 months upper limit is calculated as Target Study Day+91.
[2]Target study day for slotting events (e.g. AESI and Hospitalization) to time point. Target day is calculated as 365.25/12*<xx months> rounding up to the nearest integer.
[3]Expected assessment days for 6 months visit for all clinical data except for AEs and Hospitalizations (which collection should start from Day 1 for AEs and Day 2 for hospitalizations and then slotted using the target study day), and SLE medications (which starts from Day 5).
[4]Visits and events collected after 63 months will not be summarised or analysed.

All new cases of AESIs, medications, and/or hospitalizations occurring since the last visit assessment will be collected. The analysis time point will be assigned using the target study day and will be used for all corresponding statistical analysis and data summary. The study day will be assigned based on the date of event, measurement, or assessment, if present. Else, study day will be assigned based on the date of the visit.

5.4. Subjects' Study Status

A "study completer" is defined as a subject who did not withdraw from the study, was not lost to follow-up or not deceased prior to the 5-year follow-up. Study subject's completion status will be presented and described as 'Completed' or 'Withdrawn'. 'Ongoing' status will remain for the final analysis dry-run. At that time, subjects with 'Ongoing' status will be further grouped by time since last contact date as at the data cut date. This will be categorized as: 0.5 year, 0.5 - < 1 year, 1 - < 2 years, 2 - < 3 years, < 4 years, 4+ years (see Section 9.5.3). For subjects who withdraw, the following reason for withdrawal will be reported as captured on the eCRF: adverse event including death, lost to follow-up, withdrew consent, investigator discretion and site closed/terminated. Subjects who were still ongoing as of last interim analysis will be considered lost to follow-up (LTFU) only at the final 60-month visit following completion of 5-years + 3 months since enrollment into the study. The last contact date (as defined in Section 9.5.3) will be taken as the date of LTFU.

5.5. Multicentre Studies

In this multicentre global study, enrollment will be presented by country and site. For subjects who switched study sites, the last site where study was completed will be reported. Study sites will be grouped into three regions (US/Canada vs Europe vs Other).

5.6. Examination of Covariates, Other Strata and Subgroups

5.6.1. Covariates and Other Strata

The list of potential confounding factors included in statistical analysis to minimize selection and confounding bias will be listed in Appendix 9.9.

Descriptive summary will be performed for the subject demographic characteristics and some other covariates:

i. Baseline SDI (0 vs ≥ 1)

ii. Hospitalization within 6 months prior to study enrollment (Yes vs No)

iii. SLEDAI 2000 score at baseline (<10 vs ≥ 10)

iv. Baseline Immunosuppressant use (Yes vs No; mycophenolate vs immunosuppressant other than mycophenolate)

v. Duration of prior/baseline medication (i.e. Immunosuppressants, anti-malarials or other) (<1, 1-2 or >2years)

vi. SLE diagnosis duration (<1, 1- <5, 5-<10, 10-<15, 15-<20 ≥20years)

vii. Oral corticosteroids dose (mg/day) use at baseline (Always <7.5mg/day, ≥7.5mg/day for ≤ 2 weeks or ≥7.5mg/day for > 2 weeks)

viii. Region (US/Canada vs Europe vs Other)

ix. Race (Black, White, Asian, Other)

x. Positive anti-dsDNA at baseline

xi. Low complement at baseline

For the elderly population, sub-group summary will be performed as part of the end of study reporting (to fulfil the Elderly analysis post-approval commitment). Any analysis for elderly sub-group will be restricted to subjects aged 65 yrs and older, grouped as ≥65 years and age ≥75 years if feasible.

5.6.2. Examination of Subgroups

Descriptive summaries and statistical analyses will be performed separately for the two study cohorts (Current Users and Treatment Initiators).

Study Cohort	Definition / Criteria
Current Users	• Subjects who have received or started qualifying medication(s) for ≥ 2 months (≥ 62 days) prior to enrollment (Day 1)
Treatment Initiators	• Subjects who have initiated or started qualifying medication(s) in the last 2 months (< 62 days) prior to enrollment into the study (i.e Baseline SLE medication initiation < 62 days from study Day 1)

Study cohort can be determined for 'Eligible' subjects only (see section 4)

For the purpose of study cohort assignment to either a current user or a treatment initiator, the following rules will be used to determine when a subject first received Benlysta and/or Non-Benlysta SLE medications:

- For BENLYSTA subjects: this will be the start date of earliest baseline Benlysta medication.

- For NON-BENLYSTA subjects: this will be the start date of study-qualifying non-benlysta SLE medications or the most recently added immunosuppressant if they are on multiple medications at baseline.

5.7. Multiple Comparisons and Multiplicity

No adjustments for multiple comparisons are planned. There will be no formal statistical testing, analyses including comparison of estimates will be descriptive only..

5.8. Other Considerations for Data Analyses and Data Handling Conventions

Other considerations for data summaries, analyses and data handling conventions are outlined in the following appendices:

Section	Component
9.2	**Appendix 2:** Exposure Strategy, Analysis Approach and Individual's Subject-Years Calculation
9.3	**Appendix 4Appendix 3:** Review and Categorization of Adverse Events of Special Interest
9.4	**Appendix 4:** Data Display Standards & Handling Conventions
9.5	**Appendix 5:** Derived and Transformed Data
9.6	**Appendix 6:** Reporting Standards for Missing Data
9.7	**Appendix 7:** Laboratory Tests

6. STUDY POPULATION ANALYSES

6.1. Overview of Planned Study Population Analyses

Study population analyses will be based on the 'Eligible' population. These analyses will include descriptive summaries of subject's disposition, demographic and baseline characteristics, SLE concomitant medications, historical and baseline medical/disease condition, baseline SLEDAI 2000 (S2K composite score) and SLE diagnosis. All baseline characteristics summaries will be presented by exposure group (BENLYSTA or NON-BENLYSATA) for the two study cohorts ('Current Users' and 'Treatment Initiators').

Table 1 provides an overview of the planned baseline study population analyses. Details of data displays to be generated are presented in Appendix 11 (Section 9.11.1). Frequency (numbers and percentages) and summary statistics including number of observations, mean, SD, median, range (min; max) and interquartile range (Q1; Q3) will be reported as necessary.

Of note, baseline SLEDAI 2000 descriptive summaries will include:

- Summary statistics of continuous SLEDAI score
- Frequency of each SLEDAI 2000 component (see Section 9.5.5)
- Frequence of SLEDAI 2000 score category and SLEDAI 2000 score grouped (<10 vs. ≥ 10)

Table 1 Overview of Planned Study Population Analyses

Display Type	Data Displays to be Generated		
	Table	Figure	Listing
Subjects Disposition			
Subject Population Disposition	Y		
Subject Study Status & Withdrawal Reason	Y		
Inclusion/Exclusion Criteria	Y		
Enrollment	Y		
Subjects Demographic and Baseline Characteristics			
Demographic Characteristics	Y		Y
History of Tobacco Use and Alcohol Use	Y		
Pregnancy**	Y		
SLEDAI 2000	Y		
Disease Condition			
Medical History	Y		
SLE Diagnosis Duration	Y		
Laboratory Tests			
Laboratory Test Parameters*	Y		
Treatment Switching relative to Initial Cohort			
Exposure switching (BENLYSTA start/stop)	Y		Y
Reasons for switching (starting or stopping Benlysta)	Y		Y
Withdrawal and Reason for Withdrawal			
Withdrawal from study	Y		
Reason for withdrawal	Y		Y

NOTES: Y = Yes; implies display type (Table, Figure, Listing) generated. Empty cells implies 'No' display type generated. * See list of tests in Appendix 7 (Section 9.7); ** female participants only

The following statistical analyses to describe the rate and risk/probability of study withdrawal will be performed:

- Study Withdrawal rate (see details of methodology in Section 7.1.5)
- The rate of Study Withdrawal using Kaplan–Meier (KM) estimator (see details of methodology in Section 7.1.5)
- Survival Probability (the probability of not withdrawing from the study)

7. STATISTICAL ANALYSES

The data displays of the final analysis are shown in Appendix 11. Unless otherwise specified, analyses will be performed using 'Evaluable' analysis population, and presented separately for 'Current Users' and 'Treatment Initiators' study cohorts.

7.1. Safety Analyses

For all primary endpoint analyses (AESIs) comparison is by exposure group (BENLYSTA and NON-BENLYSTA) defined based on exposure assignment strategies described in Appendix 2 (Section 9.2): 'Initial Exposure', 'As-Exposed' (Time Varying), and/or 'Ever-Exposed'. The exposure strategy used for each endpoint will be indicated on the data displays list (Appendix 11) and on the actual Tables, Listings and Figures (TLFs).

An overview of planned safety analyses is presented in Table 2. Details of the data displays for the planned analyses are presented in Appendix 11: List of TLF Data Displays (Section 9.11.2).

Table 2 Overview of Planned Safety Analyses

Endpoint	Absolute						Change from Baseline			
	Stats Analysis		Summary		Individual		Summary		Individual	
	T	F	T	F	F	L	T	F	F	L
Adverse Events of Special Interest (AESI)										
Overall and specific AESIs experienced during follow-up (section 2.2)	Y		Y			Y[1]				

[1]Listing will include individual's subject study ID, adverse event's (AE's) & AE system organ classes, preferred terms and verbatim text.

NOTES:

- T = Table, L = Listing, F = Figure, Y = Yes display type generated. Empty cells implies 'No' display type generated.
- Stats Analysis = display type for statistical analysis (i.e. modelling and computation of rates) of event count data.
- Summary = display type for any summaries (i.e. descriptive statistics) of the observed raw data.
- Individual = display of individual subject observed raw data.

7.1.1. Endpoint / Variables

The primary safety endpoint is each category of AESI (listed in Section 2.2) experienced by subjects during study follow-up period.

7.1.2. Summary Measure

The summary measures for the safety endpoints specified in Table 2 are:

AESI endpoints

- Cumulative count of all AESI combined and count of subjects (number and percentage) experiencing at least one AESI.
- Cumulative count of each specific AESI category and count of subjects (number and percentage) experiencing at least one occurrence of each specific AESI category.
- Incidence proportion (expressed as a %) for each specific AESI category.
- Incidence rate (Section 7.1.5.1) for each specific AESI category.
- Event rate (Section 7.1.5.1) for each specific AESI category (except mortality).

7.1.3. Population of Interest

The primary safety analyses will be based on the “Evaluable” analysis population, unless otherwise specified.

7.1.4. Strategy for Intercurrent (Post-Randomization) Events

Not applicable.

7.1.5. Statistical Analyses / Methods

Unless otherwise specified, endpoints/variables displayed in Section 7.1.1 will be summarised as specified in Section 7.1.2. Details of the planned displays for each endpoint are provided in Appendix 11: List of TLF Data Displays.

The statistical analysis method for estimation of rate and 95% CI are described below.

7.1.5.1. Statistical Methodology Specification Related to AESI Endpoints

Endpoint / Variables
Incidence and event rates will be calculated for the following endpoints/variables (unless otherwise specified): • Each category of AESI experienced by subjects as listed in Section 2.2
Endpoint Specification
1. Incidence rate will be calculated for each exposure group as follows: $$Incidence\ \ Rate = \frac{\sum at\ risk\ subjects\ with\ at\ least\ one\ event}{\sum subject\ years\ at\ risk}\ X\ 100$$ - Incidence rate is defined as the number of 'at-risk' subjects experiencing first event (i.e. number of new cases) during the specified follow-up period divided by total subject-years at-risk of that event for all subjects at risk. - Although the categorization of study follow-up time to Benlysta (Exposed) or Non-Benlysta (Unexposed) depends on the exposure assignment strategy (see Appendix 2, Section.9.2.1 for further discussion), the follow-up time included in the subject-years at-risk calculation, for each month xx time period, starts from enrollment date and ends at the earliest of the following: o First event date o Last contact date (as defined in Section 9.5.3) o Month xx target date (Section 5.3) o Censored date (for While on Initial Exposure strategy; see Section 9.2.1.1) o Data cut-off date Additionally, for some exposure strategies (e.g. 'As-Exposed' strategy; see Appendix 2, Section 9.2.1.2), time to treatment switch and risk windows are also considered when categorizing follow-up time into 'Exposed' and 'Unexposed' period. - Calculation of an individual's subject-years at-risk for each exposure strategy is shown in Section 9.2. - Subject-years at-risk will be calculated for each event type separately. - Only the first experience of the event (i.e. new cases) or first primary diagnosis (in the case of a malignant event) which occurred during the 'at-risk' period are counted (see Section 9.2.1 for time period considered for each exposure strategy). - For summary of each specific AESI category, subjects experiencing events in multiple AESI categories will be counted in more than 1 AESI category. 2. Event rate will be computed for each exposure group as follows: $$Event\ rate = \frac{\sum all\ AESI\ events}{\sum subject\ years\ of\ follow\text{–}up} X\ 100$$ - Event rate is estimated for potentially recurrent events and represents the average number of events per unit time of follow-up. It is defined as the total number of events experienced by all subjects during the specified study period divided by subject-years of follow-up. The categorization of study follow-up time depends on the exposure strategy (see Appendix 2, Section 9.2.1). The subject-years of follow-up for each month xx time period takes the same definition above for the subject-years at-risk, however, follow-up does not stop at the time of first event. - Additionally, for some exposure strategies (e.g. 'As-Exposed' strategy), time to treatment switch and risk windows are also considered when categorizing follow-up time into exposed and unexposed period (Section 9.2.1.2) - All events experienced during the follow-up period including recurrent events are counted (see Section 9.2.1 for time period considered for each exposure strategy).

- Calculation of an individual's subject-years of follow-up for each exposure strategy is shown in Appendix 2 (Section 9.2). Incidence and event rates will be calculated and reported per 100 subject-years. The 95% CI for the rate will be calculated assuming an exact Poisson distribution method [Stokes, 2012].
Model Checking & Diagnostics
• No model-based statistical analysis will be performed; hence there is no model checking and diagnostics to be conducted.
Results Presentation
Total number of events, number and % of subjects with events, total subject-years at-risk, and total subject-years of follow-up will be reported. In addition, incidence proportion (where applicable), incidence rate, event rate and their 95% CI will be presented. The mock-shell tables showing details of data displays are presented in Appendix 12.
Subgroup Analyses
This analysis may be conducted for each study cohort separately (Current Users and Treatment Initiators; Section 5.6.2) . The list of TLF Data Displays is presented in Appendix 11.
Sensitivity Analyses
This analysis will also be conducted using the 'Evaluable Sensitivity' population. Details of the planned displays are provided in Appendix 11: List of TLF Data Displays.

7.1.5.2. Statistical Methodology Specification related to study withdrawal event

Endpoint / Variables
• Study Withdrawal event
Endpoint Specification
1. The percentage of subjects withdrawing from the study at the time of the final analysis data cut will be calculated for each exposure group, using the Kaplan-Meier product-limit estimator for the survival probability (the probability of not withdrawing from the study), as follows: $$\hat{S}(t) = \prod_{t_i \le t}(1 - \frac{d_i}{n_i})$$ - t_i is the specific time of interest when at least one event occurred - d_i is the number of dropout events at time t_i. - n_i is the number of subjects at-risk up to time t_i. 2. Withdrawal rates at time *t* will be computed at time *t*, denoted as $\hat{F}(t)$: $$\hat{F}(t) = 1 - \hat{S}(t)$$ The probabilites of survival and study withdrawal will be expressed in percentage (%), along with 95% CI, for the following time points: 12, 24, 36, 48, 60 months. Additionally the cumulative number of withdrawals will be presented, along with percentage (calculated as cumulative number of withdrawals/N). For the following time periods: 0-12, 12-24, 24-36, 36-48, 48-60 months, the number at-risk at the start of each time period, along with number of withdrawals during each time period will be presented. Percentage is calculated as <number of withdrawals during time point> / <the number at risk at the start of time period>
Model Checking & Diagnostics
• No model-based statistical analysis will be performed; hence there is no model checking and diagnostics to be conducted.
Results Presentation
The mock-shell tables showing details of data displays are presented in Appendix 12.
Subgroup Analyses
This analysis may be conducted overall and for each study cohort separately (Current Users and Treatment Initiators; Section 5.6.2) and by relevant clinical covariate listed in Section 5.6.1. The list of TLF Data Displays is presented in Appendix 11.
Sensitivity Analyses
N/A

7.2. Effectiveness Analyses

Overview of planned selected effectiveness measures is shown in Table 3. The analyses will be conducted using 'Evaluable' analysis population and by study exposure defined using the 'Initial Exposure' strategy (see section 9.2.1.1) and/or by strata of clinical covariates listed in Section 5.6.1. Appendix 11: List of TLF Data Displays provides details of the analyses to be conducted.

Table 3 Overview of Planned Effectiveness Analyses

Mock shell 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														
SLICC/ACR Damage Index (SDI)				Y							Y			
Hospitalizations experienced	Y			Y										
Average Corticosteroid dose (mg/day)				Y							Y			
Concomitant SLE medications and corticosteroid use				Y			Y							

NOTES:

- T = Table, F = Figure, L = Listing, Y = Yes display type generated. Empty cell implies 'No' display type generated.
- Stats Analysis = display type for statistical analysis (i.e. modelling and computation of rates) of event count data.
- Summary = display type for summaries (i.e. descriptive statistics) of the observed raw data.
- Individual = display of individual subject observed raw data.

7.2.1. Endpoints

The effectiveness (other) endpoints assessed include:

- Organ damage as assessed by SLICC/ACR Damage Index (SDI)
    - Absolute and change from baseline for SDI composite score
    - Count of subjects with each SDI domain component
    - Count of subjects with no change in SDI, and SDI worsening (i.e. change from baseline ≥0) as SDI score change 0, 1, 2 and >=3
    - Count of subjects in each permutation of baseline score and subsequent follow-up scores , to quantify how the scores change from baseline (0 to 0, 0 to 1, 0 to 2, etc) over the follow-up period
- Concomitant SLE medication and corticosteroid use

- Use of concomitant SLE medication (Yes or No)
- Use of concomitant immunosuppressants (Yes or No)
- Use of concomitant corticosteroids (Yes or No)
- If concomitant corticosteroid use is 'Yes':
  - Concomitant corticosteroid dose (mg/day) (Always <7.5mg/day, ≥7.5mg/day for ≤ 2 weeks or ≥7.5mg/day for > 2 weeks)
  - Absolute and change from baseline of average corticosteroids dose (mg/day)

- Hospitalization events
  - Count of events and subjects hospitalized for All-cause
  - Count of events and subjects hospitalized for SLE-related reasons

7.2.2. Summary Measure

The following measures will be used to summarize endpoints listed on Table 3 and in Section 7.2.1 above.

- Continuous endpoints such as absolute and change from baseline SDI score, absolute and change from baseline average corticosteroids dose (mg/day)
  - Summary statistics including number of observations, mean, SD, median, range (min; max) and interquartile range (Q1; Q3)
- Categorical binary, nominal and/or ordinal endpoints such as SLE medication use (immunosuppressants vs. others), use of corticosteroids (Yes or No), oral corticosteroids dose (mg/day) use (Always <7.5mg/day, ≥7.5mg/day for ≤ 2 weeks or ≥7.5mg/day for > 2 weeks), presence or absence of each SDI domain item, and SDI worsening (change from baseline ≥1)
  - Proportion or frequency (number and percentage) of subjects
- Count of events such as hospitalizations
  - Incidence and events rates with 95% CI (see Section 7.2.4 below for detailed methodology)

7.2.3. Population of Interest

The effectiveness analyses will be based on the "Evaluable" analysis population.

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7.2.4. Statistical Analyses / Methods

Endpoints listed in Section 7.2.1 will be summarised and presented as specified in Section 7.2.2. Details of the planned displays are provided in Appendix 11: List of TLF Data Displays.

Incidence and event rates of hospitalizations will be computed with 95% CI following the same approach described in Section 7.1.5.

7.3. Propensity Score Analysis

This section describes statistical methods to be used to control for confounding bias of the BEL116543 study final analysis.

Of note, statistical methods presented in this section will apply to primary objectives only.

7.3.1. Statistical Considerations

Analysis will be conducted on the evaluable population defined in section 4 as: Subset of the 'Eligible' population with a collection of enrollment data and at least 1 post baseline assessment.

First step of analysis: Inverse probability of treatment weighting (IPTW)

Propensity scores will be computed as the probability of being exposed to Benlysta at enrollment given an individual's baseline characteristics. Logistic regression will be used to derive the PS. Non-stabilized weights (i.e. IPTW) for each individual will be calculated as the inverse of the probability of receiving the actual exposure: 1/PS for the Benlysta arm and 1/(1-PS) for the Non-Benlysta arm.

Inverse probability of treatment weighting (IPTW) (Rosenbaum, 1983) will be used to adjust for differences in covariates balance between exposure groups, Benlysta versus Non-Benlysta. To reduce likelihood of extreme weights being assigned in the analysis, stabilized weights will be computed by multiplying the non-stabilized weight of each individual by the proportion of subjects who were exposed to Benlysta at enrollment : p/PS for the Benlysta arm and (1-p)/(1-PS) for the Non-Benlysta arm., (Chesnaye, 2021). For the remainder of the document, references to "weight" refer to stabilized weights.

These weights will create a *pseudopopulation* whereby confounding factors are balanced among Benlysta and non-Benlysta arms. The weights' distributions will be checked to identify extreme weights which might impact results (see section 7.3.1.3). If the balance assessment reveals that adequate balance cannot be achieved between the Benlysta and non-Benlysta arms (section 7.3.1.2.2), no further analysis using propensity scores will be conducted.

Second step of analysis: Outcome analysis
The primary outcome model will be a weighted Poisson regression based on stabilized weights. Weighted incidence rates and event rates will be calculated and presented. Further details presented in section 7.3.1.5.

7.3.1.1. General Assumptions for Causal Inference

Observational research relies on causal inference methods when deriving unbiased estimates. Hernán & Robins (2019) list 3 conditions to be met, for the valid use of methods like IPTW: conditional exchangeability, positivity and consistency. Additionally, the no interference assumption between subjects should be met. These conditions make

underlying assumptions about the data to be analyzed and violations of the underlying assumptions can bias the estimates, leading to inaccurate conclusions.

7.3.1.1.1. Conditional Exchangeability

The conditional exchangeability assumption allows an observational study to be conceptualized as a conditionally randomized trial, where the probability to receive the treatment depends on the covariates, but not on unmeasured variables. Essentially, this assumption leads to the postulation of no unmeasured confounding, and potential outcomes can be treated as Missing at Random (MAR). In practice, verifying the validity of the conditional exchangeability assumption is not possible. While we assume conditional exchangeability within specific groups (such as treatment arms or covariate levels), it's important to recognize that unmeasured factors may still exist. Therefore, we proceed with caution, acknowledging that perfect validation of this assumption is unattainable.

7.3.1.1.2. Positivity

The positivity assumption specifies that every subject has a probability > 0 to receive either treatment, otherwise no causal inference would be possible. The assumption of positivity will be checked by examining the overlap of the propensity score distribution for both treatment groups graphically. The SAS option WCLOUD will be used within the CAUSALTRT procedure to display weights, and if weights > 10 are observed, the potential for non-positivity will be investigated (see section 7.3.1.4).

7.3.1.1.3. Consistency

The assumption of treatment consistency specifies that there is no ambiguity defining a treatment (Hernán and Robins, 2020). This assumption is also known by the term "treatment variation irrelevance".

7.3.1.1.4. Interference

The assumption of no interference specifies that a potential outcome for any subject does not vary with the treatment assigned to other subjects, i.e., a subject's outcome is not affected by other subjects' exposure to the treatment. In the current study interference is not expected due to the characteristics of the studied disease.

7.3.1.2. IPTW Estimation

7.3.1.2.1. Propensity Score Variables Selection

A PS model will be defined for IPTW estimation.

The pre-specified variables collected at baseline, considered by medical experts to be potentially important covariates, with respect to both treatment assignment and likelihood of experiencing outcome, are presented in Section 9.9 (Table 4).

Firstly, multicollinearity assumption will be assessed by verifying that there are no two or more variables which are highly collinear. Variance Inflation Factor (VIF) will be

computed by specifying the 'vif' option in a PROC REG in SAS (see section 9.10). A VIF higher than 10 indicates co-linearity regarding the concerned covariates. The decision of which covariate(s) to drop, if applicable, will be made based on clinical importance.

Secondly, selected variables will be used as covariates in the SAS CAUSALTRT procedure to fit a logistic regression model and compute propensity scores. The response variable will be the probability of receiving Benlysta at enrollment.

In case the model does not converge, multi-level covariates with sparse counts will be collapsed. If any issues remain thereafter, covariates which generate non-convergence will be removed from the model. In either such case, a corresponding footnote will be added to the corresponding statistical tables.

The propensity score model will be finalized prior to proceeding to estimation of weighted incidence and event rates. An evaluation of all variables used in the PS will be made to allow adjustment prior to the final analysis, considering:

- overlap of the predicted probability of exposure initiation through inspection of graphical and distributional summaries (see section 7.3.1.1.2);
- balancing exposure cohorts through IPTW (Robins et al 2000; see section 7.3.1.2.2);

In addition, the odds ratios of the covariates in the PS model will be reported along with 95% CI and p-value using PROC LOGISTIC to identify PS covariates more associated with the treatment assignment and potentially influencing the weight.

7.3.1.2.2. Balance Assessment of the Propensity Score Model

As described in Rosenbaum and Rubin (1983), the propensity score is also a balancing score. To assess the balance that is produced by a propensity score model, standardized mean differences (SMDs), variance ratios and weighted density plots for the continuous covariates will be displayed using the 'CovDiffPS' and 'PSCovDen' options in the SAS PROC CAUSALTRT statement in SAS.

The resultant table and plots will be provided as supplementary outputs, presenting SMDs and variance ratios before and after weighting (per SAS ODS table name 'PSCovDiff') in order to assess covariate balance after weighting.

An improvement in the covariate balance after weighting would be indicated by the following two observations when the unweighted and weighted columns in the table are compared:

- Smaller SMDs in the weighted column than in the unweighted column
- Variance ratios between 0.5 to 2 in the weighted column

Although there is no universally agreed criterion as to what threshold of the standardized difference can be used to indicate important imbalance, it is commonly agreed that a standardized mean difference of less than 0.1 indicates a negligible difference in the mean

or prevalence of a covariate between treatment groups (Austin, 2011). Of note, variance ratio will be assessed but the main criterion of balance will be based on SMDs.

7.3.1.3. Handling of Extreme Weights

Following satisfaction of positivity assumptions as per section 7.3.1.1.2, if there is evidence of extreme weights (> 10) that cannot be resolved by adjusting the PS model then subjects in the tails of the propensity score distributions will have their propensity score truncated at the 99th percentile value (i.e.: large weight will be replaced with the 99th percentile).

7.3.1.4. Missing Data on Covariates

Considering the background of the study, missingness is known for the baseline confounders. Among variables listed in Table 4, Body Mass index (BMI), Race, Ethnicity, SDI and SLEDAI 2000 score are reported with missing values. The rules below will apply:

- The missing data for individual variables will be coded into a "missing" category for categorical variables to allow all subjects to be used in the analysis; for continuous measures, missing data will be set to a fixed value (i.e. median) and an indicator variable will be added in the model.

- However, in the case of very few missing cases (<10):
    - The modal category will be assumed for categorical variables.
    - The indicator variable will be omitted from the model for continuous variables

- Specific case of baseline SLEDAI 2000 (S2K composite score):
  The Assessments of SLEDAI 2000 score consist of 24 individual items (see section 9.5.5) in which signs and symptoms, laboratory tests, and physician's assessment for each of 9 organ systems are given a weighted score and summed if present (marked 'Yes').
    - A "Clinical SLEDAI 2000 score" (CS2K) will be computed considering all items except "Low Complement" and "Increased DNA Binding". The CS2K is computed based on the remaining 22 items, with either "absent" or "not done" being regarded as 0.

    - A corresponding variable "total not-done points" calculating the sum of not done weights is also included in the model. "Total not done points" = 0 for subjects who were assessed for all items. "Total not done points" = 18 for subjects with maximum (6) not done items. The variable's inclusion is to allow the model to differentiate between subjects who have scored x points/101 available compared to subjects who have score x points/83 available, or anywhere in between.

- If the SLEDAI 2000 form is completely missing, then median CS2K (based on subjects who answered >0 questions) and median "total not done points" will be assumed, and an indicator variable will be added in the model.

7.3.1.5. Incidence and event rate analysis

Weighted incidence rate per 100 person-years and weighted event rate per 100 person years will be presented for 'ITT' and 'While-On-Initial Exposure' treatment strategies. The 95% CI for the rates will be calculated assuming an exact Poisson distribution method.

Incidence rates will be calculated as total weighted incidence divided by total weighted subject years at risk with corresponding weighted exact Poisson CI:

$$Lower = \frac{(quantile('CHISQ', 0.025, 2 * \sum weight * \ subject\ with\ at\ least\ \ one\ event)/2)}{\sum weight * \ subject\ years\ at\ risk}$$

$$Upper = \frac{(quantile('CHISQ', 0.975, 2 * (\sum weight * \ subject\ with\ at\ least\ \ one\ event + 1))/2)}{\sum weight * \ subject\ years\ at\ risk}$$

Event rates will be calculated as total weighted number of events divided by total weighted follow up time. with corresponding weighted exact Poisson CI:

$$Lower = \frac{(quantile('CHISQ', 0.025, 2 * \sum weight * \ events)\ /2)}{\sum weight * \ subject\ years\ of\ follow{-}up}$$

$$Upper = \frac{(quantile('CHISQ', 0.975, 2 * (\sum events\ + 1))/2)}{\sum weight * \ subject\ years\ of\ follow{-}up}$$

7.3.2. Baseline Characteristics

Baseline characteristics (i.e. variables included in the PS-model) will be presented for the evaluable population and appropriate statistical tests will be used for group comparison. P-values, for descriptive purpose only, will be presented.

- For categorical variables:
  - Fisher's exact test will be used for 2*2 frequency tables (FISHER option in TABLES statement of PROC FREQ)
  - Otherwise, Chi-Square test will be used (CHISQ option in TABLES statement of PROC FREQ)
- For continuous variables, t-test will be used (PROC TTEST), normality assumed considering sample.
- Standardized mean differences (SMDs), variance ratios and weighted density plots for the continuous covariates will be displayed before and after weighting as described in section 7.3.1.2.2.

7.3.3. Safety Endpoints with confounding adjustment

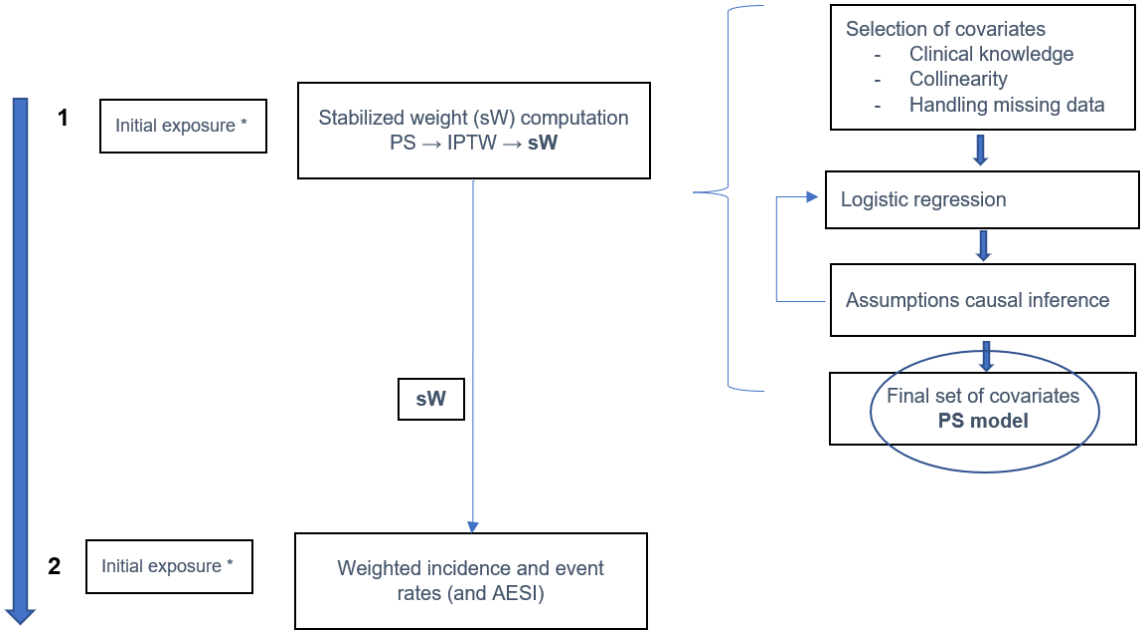
The primary endpoint analysis with confounding adjustment, (weighted incidence rates) will be conducted using ITT and While On Initial Exposure strategies only for the below safety endpoints:

- Malignancies (excluding non-melanoma skin cancers)
- Mortality
- Opportunistic infections (serious and non-serious)
- Other infections of interest (serious and non-serious)
- Non-melanoma skin cancers (NMSC)
- Serious psychiatric events
- Serious infections

For all endpoints, details about outcome-specific baseline covariates, distributions are displayed in the below table:

Analysis	Endpoints	Dependent variable	Distribution	Baseline covariates
Primary	- Weighted Incidence rate	Number of first event	Poisson	Not adjusted
Primary	- Weighted Event rate	Number of all events	Poisson	Not adjusted

7.3.4. Summary



** Initial exposure: ITT strategy and while on initial treatment.*

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9. APPENDICES

9.1. Appendix 1: Schedule of Activities

9.1.1. Protocol Defined Schedule of Events

	Time Points										
Data Collection[7]	Enrollment[1] (Day 1)	6 months (±2months)	12 months (± 2 months)	18 months (± 2 months)	24 months (±2 months)	30 months (±2 months)	36 months (±2 months)	42 months (±2 months)	48 months (± 2 months)	54 months (± 2 months)	60 months (-2/+3 months)[6]
Informed Consent	X										
Demographics	X										
Medical History (including SLE History)/General Medical Status	X				X[3]				X[3]		
Potential Confounders for Malignancies and/or Infections List	X										
Historical SLE Medications	X										
SLEDAI 2000[2]	X										
Verify Eligibility Criteria	X										
SLICC/ACR Damage Index	X	X	X	X	X	X	X	X	X	X	X
Record of Current SLE Medications (including corticosteroids)[4]	X	X	X	X	X	X	X	X	X	X	X
Record of Hospitalizations	X	X	X	X	X	X	X	X	X	X	X
Record of AEs of Special Interest[5]		X	X	X	X	X	X	X	X	X	X

1. Data collection for enrollment may occur over more than one day.
2. Laboratory values should not be attributed on the SLEDAI 2000 unless laboratory values were obtained within 30 days of the assessment.
3. Only General Medical Status (current status of medical condition and/or medical procedure/surgery since last reported) is collected at 24 and 48 months.
4. SLE Medications include immunosuppressants, biologics, antimalarials, corticosteroids, and investigational agents for SLE. If a subject currently using BENLYSTA changes formulation, the original BENLYSTA record must be updated with a stop date and a new BENLYSTA record needs to be created with a start date for the new formulation. The new BENLYSTA record should also include formulation (IV or SC).
5. AEs of special interest for this study include mortality, serious infections, opportunistic infections and other infections of interest, selected serious psychiatric events, and malignancies (including NMSC). In order to collect additional important information on potential suicidality-related events, should any of the events marked with an asterisk in Appendix 2 of the protocol occur, the investigator will be requested to complete the PSRHQ eCRF (only the first time a serious suicidality-related event is reported) and a PSRQ eCRF (each time a serious suicidality-related event is reported). The PSRHQ and PSRQ are provided in Appendix 3 and Appendix 4 of the protocol, respectively.
6. For the last time point (60 months), data collection is extended by an additional 1 month and therefore can occur up to 63 months after enrollment (Day 1). This is to provide sites with additional time to contact subjects before declaring them as lost-to-follow-up.

7. The data collection time intervals of 6 months ±2 months are intended to align with routine standard of care visits for SLE subjects. With the exception of the last time point at 60 months (for which data collection can only be extended up to 63 months), data collection occurring outside the time window (±2 months) should be assigned to the closest time point.

9.2. Appendix 2: Exposure Strategy, Analysis Approach and Individual's Subject-Years Calculation

9.2.1. Exposure Strategy

For the purpose of statistical analysis, subjects' exposure arm (BENLYSTA vs NON-BENLYSTA) will be assigned using the following exposure strategies: 'Initial Exposure', 'As-Exposed (Time Varying)' with Benlysta risk windows of 14 weeks (98 days) and 6 months, and 'Ever-Exposed'. Hypothetical scenarios for each strategy are represented in Section 9.2.2.

Programming Hints for assignment of fatalities applicable to all exposure strategy (see also Section 9.3.2**):**

- For mortality events: the fatal SAE onset date should be used as the 'Event Date' when slotting the death to the relevant analysis time period, and as a result corresponding exposure group. In the case of multiple fatal SAEs, the latest onset date should be used.
- For individual's subject-years at-risk computation, the date of death should be used as the 'Event Date'.

9.2.1.1. Initial Exposure

This is defined as subjects' exposure arm assignment (Benlysta or Non-Benlysta) at the time of enrollment (Baseline). Due to potential for one or more treatment switching during the follow-up, two different analysis approaches will be used for 'Initial Exposure' strategy; namely, 'ITT' and 'While On Initial Exposure'.

1. ITT approach will use all accrued data during the whole follow-up period irrespective of treatment switching. Subjects entering the study on Benlysta medication will be considered 'Exposed' and those on Non-Benlysta SLE medications are considered 'Unexposed' throughout the study period.

A limitation of the ITT is potential bias from mismatch of events to exposure arm since events occurring after exposure switching are attributed to that Initial Exposure. This will attribute events to Benlysta exposure when subjects are no longer exposed and vice-versa (i.e. Non-Benlysta initial cohort switched to Benlysta). See Section 9.2.1.2 for details of 'As-Exposed' (Time Varying) approach to address this limitation

Programming Hints for derivation of essential variables needed for computation of incidence and event rates (presented in Section 7.1.5.1**) under the ITT approach:**

- Compute individual's subject-years at-risk as:

  [(minimum (Event Date, Last Contact Date*) – Study Enrollment Date) +1]/365.25

- Compute individual's subject-years of follow-up as:

  [(Last Contact Date* – Study Enrollment Date) +1]/365.25

- Consider events experienced during the whole study period:

  Study Enrollment Date ≤ Event Date ≤ Last Contact Date*

  - For incidence rate calculation only count new cases (i.e. first onset) of the event experienced during the period
  - For events rate calculation count all the events experienced during the period

  NOTE:

  i. Individual's subject-years at-risk will be calculated for each event type separately and if required for each time period (i.e. for analysis by time period)

  ii. Individual subject-years of follow-up may be required for each time period (i.e. for analysis by time period)

  * Last Contact Date as defined in section 9.5.3

2. While On Initial Exposure analysis approach will be used to analyze all data accrued up to the first treatment switch. Any events and follow-up time accrued after the first exposure switching (switching from Initial Exposure) will be censored (i.e. excluded from analysis) at first exposure switch date (see Section 5.14 for the definition of exposure/medication switching).

A limitation of this analysis approach is potential bias introduced by underreporting of events experienced during the study since data from only a subset of the study period and events collected before the first treatment switch are included in the analysis. The results only present risk of exposure prior to first treatment switch. See Section 9.2.1.2 for details of 'As-Exposed' (Time Varying) approach to address this.

Programming Hints for derivation of essential variables needed for computation of incidence and events rates (presented in Section 7.1.5.1**) under the While On Initial Exposure approach:**

- Compute First Switch Date as:

  Baseline Benlysta Medication End Date + 98 days (for switching from Benlysta to Non-Benlysta) or

  First Post-Baseline Benlysta Start Date – 1) (for switching from Non-Benlysta to Benlysta)

- Compute individual's subject-years at-risk as:

  [(minimum (Event Date, First Switch Date, Last Contact Date*) – Study Enrollment Date) +1]/365.25

- Compute individual's subject-years of follow-up as:

  [(minimum (First Switch Date, Last Contact Date*) – Study Enrollment Date) +1]/365.25

- Consider events experienced up to First Switch Date (if switching from Initial Exposure) or whole study period (if no switch):

  Study Enrollment Date ≤ Event Date ≤ minimum(First Switch date-1, Last Contact Date*)

  - For incidence rate calculation only count new cases (i.e. first onset) of the event experienced during the period
  - For events rate calculation count all the events experienced during the period

  NOTE:

  i. Individual's subject-years at-risk will be calculated for each event type separately and if required for each time period (i.e. for analysis by time period)

  ii. Individual subject-years of follow-up may be required for each time period (i.e. for analysis by time period)

  * Last Contact Date as defined in section 9.5.3

An illustration of follow-up to be counted in each exposure group defined by the two 'Initial Exposure' analysis approaches is shown in Section 9.2.2.

9.2.1.2. As-Exposed (Time Varying)

This exposure strategy specifically accounts for treatment switching to or from BENLYSTA throughout the study. It dynamically assigns subjects' exposure group based on Benlysta/non-Benlysta use at time of event, during study follow-up. Therefore, a subject's exposure group can change over time (time varying) depending on the SLE medication in use at specific time during study follow-up. For Benlysta, exposure does not end on the date when Benlysta stops. Instead, two different risk windows will be used to determine when Benlysta exposure ends:

- 14 weeks: Benlysta exposure ends 14 weeks (98 days) after Benlysta treatment stops.
- 6 months: Benlysta exposure ends 6 months (183 days) after Benlysta treatment stops.

- Subjects may contribute events and follow-up time (i.e. subject-years) to either one or both exposure periods depending on the medication switch pattern (see Section 9.2.2). Data summary and analysis will be done by exposure group assigned using the 'As--Exposed' strategy.

In contrast to the 'Initial Exposure' or 'While on Initial Exposure' strategies, which may only utilize subject level exposure group at Enrollment, the 'As-Exposed' strategy (time--varying) will assign and use exposure group at the time of the event.

Programming Hints for derivation of essential variables needed for computation of incidence and events rates (presented in Section 7.1.5.1**) under the 'As-Exposed' approach:**

- Each subject's follow-up time will be split into different exposure periods categorized as 'Exposed' (when the subject is on Benlysta medication) or 'Unexposed' (when the subject is off Benlysta). Each exposure period will have a distinct *'Period Start Date'* and a distinct *'Period end date'.*
    - Note that for each subject, number of exposure periods = number of switches + 1 (see Section 5.1 4 for definition of switching)
- Identify the start of each period as follows:
    - The first exposure period (i.e. period=1) starts from enrollment date (i.e. ***Period Start Date*** = Enrollment Date). First period exposure status is same as baseline exposure group assignment
    - For subsequent exposure periods, ***Period$_{n+1}$ Start Date*** is ***Period$_n$ End Date*** + 1
- Identify the end of each period as follows:
    - For all exposure periods except the last, ***Period End Date*** = ***Switch Date***

      Switch Date is

      Benlysta End Date + 98 days or 183 days when switching from Benlysta to Non-Benlysta (i.e. Exposed to Unexposed) period. *Period with this end date will be assigned 'Benlysta' or 'Exposed' group.*

      Next Benlysta Start Date – 1 when switching from Non-Benlysta to Benlysta (i.e. Unexposed to Exposed) period. *Period with this end date will be assigned 'Non-Benlysta' or 'Unexposed' cohort*
    - For last or final exposure period, ***Period End Date*** is the ***Last Contact Date****.
- Identify or map events experienced during the study to the specific exposure period satisfying:

  Follow-up Period Start Date ≤ Event Onset Date ≤ Follow-up Period End Date

  NOTE: for incidence rate calculation, first event is retained for each exposure group (i.e. Benlysta and Non-Benlysta).
- Calculate individual's subject-years of follow-up for time spent in each exposure group *j* (where *j* =1(Exposed), 2(Unexposed)) as follows:

- For overall or 60-Month+ time period, calculate '*period follow-up time*' ($pFUt$) in days for each period *i* (*i* =1, 2, …., n) as:

  (Period End Date – Period Start Date) +1

- For other xx-Month time periods (xx = 12, 24, 36, 48), calculate '*period follow-up time*' ($pFUt$) in days as follows:

  - Calculate cumulative follow-up duration for each exposure period i (CM_FUD[i])
  - Identifying qualifying exposure period for each xx-Month time specific computation as period where previous CM_FUD value is less than xx-Month target visit day (i.e. CM_FUD[i-1] < xx-Month target visit day for i= 1, 2,…n; where CM_FUD[0] = 0)
  - For each qualifying exposure period for xx-Month time, calculate xx-M_pFUt =

    CM_FUD[i] – CM_FUD[i-1] if CM_FUD[i] ≤ xx-Month target visit day

    xx-Month target visit day – CM_FUD[i-1] if CM_FUD[i] > xx-Month target visit day

    where CM_FUD[0] = 0

- Calculate each individual subject-year of follow-up $(syFU_j)$ as follows:

  - For each exposure group *j* (*j* =1(Exposed), 2(Unexposed)), sum $pFUt$ over all periods *i* with the same exposure group and divided by 365.25

    $syFU_j = \left(\sum_{i=1}^{n} pFUt_{i(j)}\right)/365.25$ (for overall or 60+Month time period)

    $xxM\_syFU_j = \left(\sum_{i=1}^{n} xxM\_pFUt_{i(j)}\right)/365.25$ (for time period specific computation)

(NOTE: For time period analysis, the above computation will be done for the following time periods: 12-month, 24-month, 36-Month, and 48-Month).

- Individual's subject-years 'at-risk' ($syAR_j$) will be calculated for each exposure group *j* (*j* = 1(Exposed), 2(Unexposed)) as follows:

  - Calculate *period 'at-risk' time* ($pARt_i$) for each exposure period *i* (*i*=1, 2,….,n) or qualifying exposure period for xx-Month time as:

    - if no event occurred in the exposure period (for overall or 60-Month+ time period calculation) or event day > xx-Month target visit day (for xx-Month time period specific calculation)

      $pARt_i$ = *period follow-up time*' ($pFUt$) or

xxM_$pARt_i$ = xxM_pFUt (for time specific calculation)

- for period where first event occurred (per exposure group) or event day <= xx-Month target visit day

  $pARt_i$ = *event day – CM_FUD[i-1]*

  xxM_$pARt_i$ = *event day – CM_FUD[i-1]* (in case of time specific calculation)

  where CM_FUD[0] = 0

- For each exposure group *j* (*j* =1(Exposed), 2(Unexposed)) separatedly compute individual subject-year at-risk $syAR_j$ thus:

  - For subjects with no events in exposure group j, sum $pARt_i$ for all periods *i(j) (i.e. periods occurring while on exposure group j)*

    $syAR_j = \left(\sum_{i=1}^{n} pARt_{i(j)}\right)/365.25$

    $xxM\_syAR_j = \left(\sum_{i=1}^{n} xxM\_pARt_{i(j)}\right)/365.25$ (for time period specific computation)

  - For subjects with at least one event in exposure group j, sum $pARt_i$ for all periods *i(j)* up to period where the first event in exposure group j occurred

    $syAR_j = \left(\sum_{i=1}^{n*} pARt_{i(j)}\right)/365.25$

    $xxM\_syFU_j = \left(\sum_{i=1}^{n*} xxM\_pFUt_{i(j)}\right)/365.25$ (for time period specific computation)

    where *n** is the period where the first event was experienced (NOTE: Time spent in subsequent exposure periods for the same exposure group after an event had occurred will not be counted)

  NOTE: Individual's subject-years at-risk will be calculated for each event category separately

* Last Contact Date as defined in Section 9.5.3

9.2.1.3. Ever-Exposed

This exposure strategy accounts for whether a subject was ever-exposed to Benlysta at any point during the follow-up period, once exposed to Benlysta they will always be considered at risk. Any events accrued and all follow-up time after first Benlysta treatment has started will be allocated to Benlysta exposure. Follow-up time before first Benlysta exposure will be allocated to the comparison cohort. Therefore, a subject's exposure group will only change once if a subject moves from a comparison treatment ('Not exposed' onto Benlysta).

A limitation of this strategy is bias from mismatch of events to exposure arm since events occurring after switching off Benlysta are attributed to Benlysta exposure when subjects are no longer exposed.

Programming Hints for derivation of essential variables needed for computation of incidence and events rates (presented in Section 7.1.5.1**) under the 'Ever-Exposed' approach:**

- Subjects on Benlysta at enrollment will only have one exposure period (period=1) and Period Start Date = Enrollment Date (as ITT strategy).
- Subjects not on Benlysta at enrollment who do not switch on to Benlysta will only have one exposure period (period=1) and Period Start Date = Enrollment Date (as ITT strategy).
- Subjects not on Benlysta at enrollment who do switch on to Benlysta will have two exposure periods:
    - For period = 1, Period Start Date = Enrollment date, Exposure = Non-Benlysta and Period End Date = Benlysta start date -1
    - For period = 2, Period Start Date = Benlysta start date, Exposure = Benlysta and Period End Date = Last contact date*.
- Identify or map events experienced during the study to a specific exposure period by checking the event onset within the period start and end interval.

  Follow-up Period Start Date ≤ Event Date ≤ Follow-up Period End Date

  NOTE: for incidence rate calculation, first event is retained for each exposure group (i.e. Benlysta and Non-Benlysta). This is only applicable for subjects with two exposure periods, i.e. subjects not on Benlysta at enrollment who do switch on to Benlysta.

- Calculate individual's subject-years of follow-up for time spent in each exposure group as follows:

a) Subjects on Benlysta at enrollment:

   Exposed subject-years = (Last contact date* - Enrollment Date+1)/365.25.

b) Subjects not on Benlysta at enrollment who do not switch on to Benlysta:

   Unexposed subject-years = (Last contact date* - Enrollment Date+1)/365.25.

c) Subjects not on Benlysta at enrollment who do switch on to Benlysta:

   Unexposed subject-years = (Benlysta start date – Enrollment date)/365.25

   Exposed subject-years = (Last contact date* - Benlysta start date +1)/365.25

- For other xx-Month time periods (xx = 12, 24, 36, 48), calculate period follow-up years as follows:

a) Subjects on Benlysta at enrollment:

Exposed period follow-up years = (xx-Month period end date - Enrollment Date+1)/365.25.

where xx-Month period end date = earliest of xx-Month target visit date and Last contact date*

b) Subjects not on Benlysta at enrollment who do not switch on to Benlysta before xx-Month target visit date:

Unexposed period follow-up years = (xx-Month period end data - Enrollment Date+1)/365.25.

where xx-Month period end data = earliest of xx-Month target visit date and Last contact date*

c) Subjects not on Benlysta at enrollment who do switch on to Benlysta before xx-Month target visit date:

Unexposed period follow-up years = (Benlysta start date – Enrollment date) /365.25

Exposed period follow-up years = (xx-Month period end date - Benlysta start date +1)/365.25

where xx-Month period end data = earliest of xx-Month target visit date and Last contact date*

- An individual's subject-years 'at-risk' will be calculated for each exposure group as follows:

a) Subjects on Benlysta at enrollment:

Exposed subject-years at-risk = [(minimum (Event Date, Last Contact Date*) – Study Enrollment Date) +1]/365.25

b) Subjects not on Benlysta at enrollment who do not switch on to Benlysta before xx-Month target visit date:

Unexposed subject-years at-risk = [(minimum (Event Date, Last Contact Date*) – Study Enrollment Date) +1]/365.25

c) Subjects not on Benlysta at enrollment who do switch on to Benlysta before xx-Month target visit date:

i) If no event happens in period:

Unexposed subject-years at-risk = (Benlysta start date - Enrollment Date) /365.25.

Exposed subject-years at-risk = (Last contact date* - Benlysta start date+1) /365.25

ii) If event happens in period:

Unexposed subject-years at-risk = (minimum (Event date, Benlysta start date) - Enrollment Date)/365.25

Exposed subject-years at-risk =

If Event date ≥ Benlysta start date: (Event date – Benlysta start date+1) /365.25

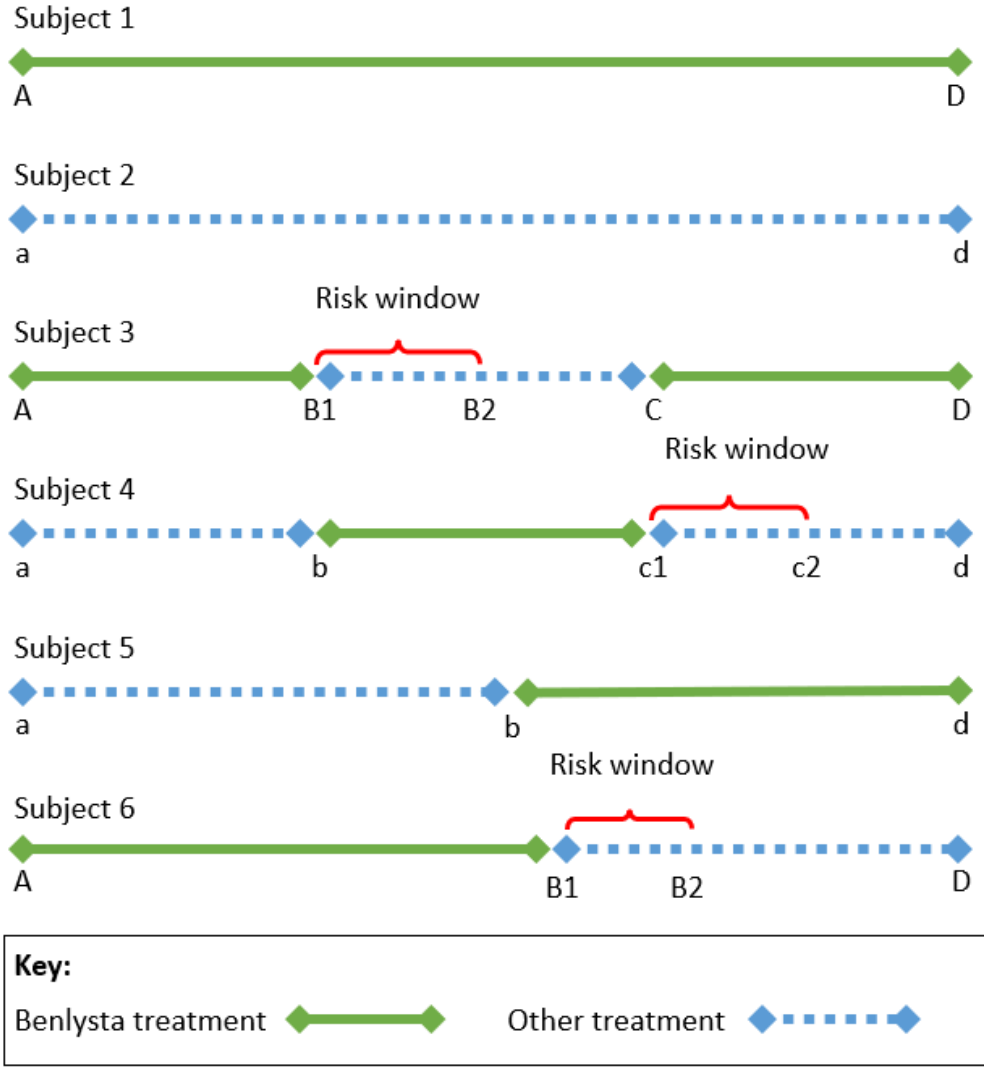
If Event date < Benlysta start date: 0

NOTE: An individual's subject-years at-risk will be calculated for each event category separately

* Last Contact Date as defined in Section 9.5.3

9.2.2. Exposure Strategy Hypothetical Illustration

The exposure status strategies described in Section 9.2.1 are illustrated in the chart below showing treatment profile of six hypothetical subjects.



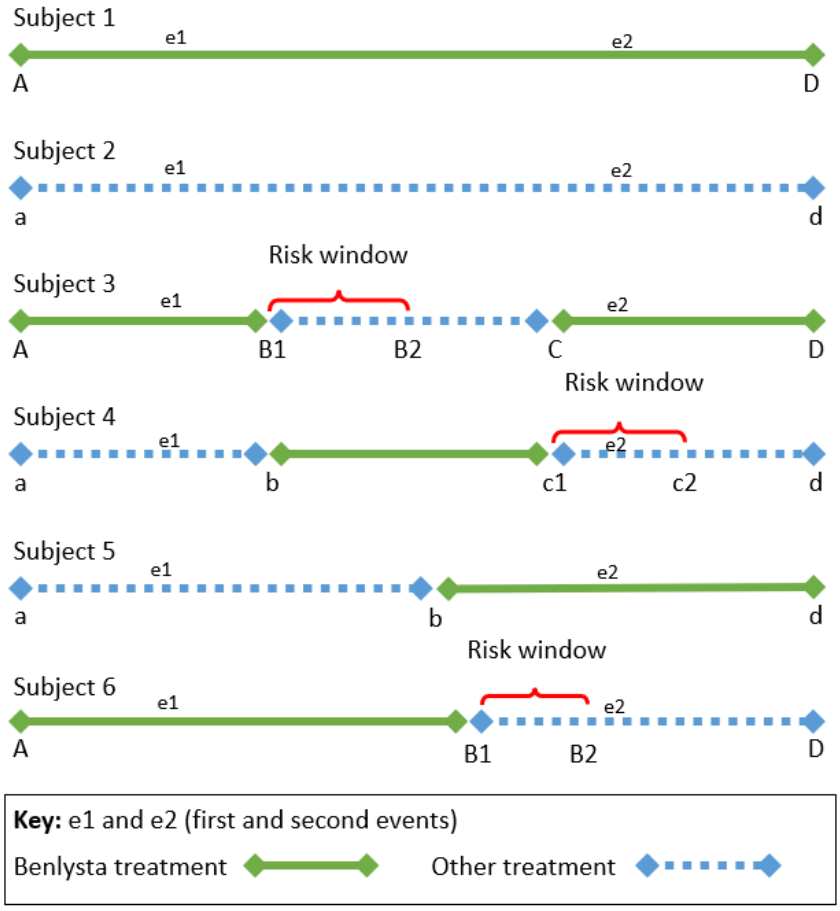
NOTE: The risk windows are only applicable when switching from Benlysta medication to Non-Benlysta Standard of Care (SOC) medication(s). There are two possible risk windows: (1) 14 weeks (98 days) which assumes that Benlysta exposure ends 14 weeks (98 days) after cessation (End Date) of Benlysta medication; and (2) 6 months.

The events and exposure time contributed by each subject to the two exposure status cohorts (Benlysta or Non-Benlysta) depend on the analysis strategy as shown in the Table below.

Exposure Strategy	Highlights	Exposure Time/Events Attribution per risk windows*	
		BENLYSTA	NON-BENLYSTA
Initial Exposure: - Intent-To-Treat (ITT)	ITT • Assign exposure status based on baseline (enrollment) SLE medication • Include all events and exposure time during FU irrespective of switching	D – A (subjects 1, 3, 6)	d – a (subjects 2, 4, 5)
- While On-Initial Exposure	While On-Initial Exposure • Assign exposure status based on baseline (enrollment) SLE medication • Censor (exclude) events and exposure time post switching	D – A (subject 1) B2 – A (subjects 3 & 6)	d – a (subject 2) b - a (subjects 4 & 5)
As-Exposed (Time varying)	• Allows subjects to switch treatment exposure status based on treatment use • Assign time varying treatment exposure group • Subjects treatment exposure group change over follow-up time depending on switch on and off Benlysta medication • Treatment exposure status is assigned at event and visit data level • Used all data since no censoring of events or follow-up exposure time after switching • Subjects can contribute person-year exposure time to any of treatment exposure groups	D – A (subject 1) B2 – A & D – C (subject 3) c2 – b (subject 4) d - b (subject 5) B2 – A (subject 6)	d – a (subject 2) C – B2 (subject 3) b – a & d – c2 (subject 4) b – a (subject 5) D – B2 (subject 6)
Ever-Exposed	• Assigns exposure status based on ever being exposed to Benlysta • Considers whether subject was exposed to Benlysta at any point during the follow up period • When subject has not been exposed to Benlysta at any point in time, the subject is considered as 'Unexposed'. Once a subject is exposed to Benlysta even once, they will be considered as always exposed • Treatment exposure status is assigned at event and visit data level • Uses all data • Subjects who start as 'Unexposed' can contribute person-year exposure time to both of the treatment exposure groups if they start taking Benlysta	D – A (subject 1) D – A (subject 3) d – b (subject 4) d – b (subject 5) D – A (subject 6)	d – a (subject 2) b – a (subject 4) b – a (subject 5)

*** Assume at-risk window is only applicable after switching from Benlysta**

The same chart could be used to illustrate how events are considered to compute incidence rate. Let's note e1 and e2, two events of same AESI occurring for a subject.



- For initial exposure (i.e. ITT and while on initial exposure), events only contribute to the subject's initial exposure assignement, and only the first event will be considered for the incidence rate computation:
  - Subjects 1, 3 and 6: one event for Benlysta group (e1-A)
  - Subjects 2, 4 and 5: one event for Non-Benlysta group (e1-a)

- For the 'As-Exposed' and 'Ever-Exposed' strategies, subjects can contribute subject-years and events to either one or both exposure groups. The following events will be considered for the incidence rate computation:
  - For subjects 1 and 2, there is no medication (exposure) switching, therefore computation remains as per initial exposure.
  - For subject 3, only the first event is considered for Benlysta group and therefore computation remains as per initial exposure.
  - Subject 4:

- For the as-exposed strategy, one event for Non-Benlysta group (e1-a) and one event for Benlysta group (e2-b) as the event occurred during risk-window of Benlysta period.
- The same applies for the ever-exposed strategy, as subject was not on Benlysta at enrollment and switch on to Benlysta.

- Subject 5:
  - For the as-exposed strategy, one event for Non-Benlysta group (e1-a) and one event for Benlysta group (e2-b).
  - The same applies for the ever-exposed strategy, as subject was not on Benlysta at enrollment and switch on to Benlysta.
- Subject 6:
  - For the as-exposed strategy, one event for Benlysta group (e1-a) and one event for Non-Benlysta group (e2-B2).
  - For the ever-exposed strategy, one event for Benlysta group (e1-A) and none for non-Benlysta group. The subject was on Benlysta at enrollment and is always considered as exposed, therefore computation remains as per initial exposure.

9.3. Appendix 3: Review and Categorization of Adverse Events of Special Interest

9.3.1. Semi-Automated Adverse Events of Special Interest Coding Process

A programming process will be performed for the creation of AE flags and adjudication variables for assigning each AE to at least a specific AESI category using the current version of Benlysta Program Safety Analysis Plan (PSAP) term of interest (TOI) and the GSK Medical Dictionary for Regulatory Activities (MedDRA) dictionary in effect at the time of reporting. The automated categorization of the reported AE into AESIs will be based on the following Benlysta pre-specified custom MedDRA queries (CMQ) variables:

- Neoplasms, hematological (CQ02NAM)
- Neoplasms, skin (CQ03NAM)
- Non-melanoma skin cancer-NMSC (CQ03NMFL)
- Neoplasms, solid (CQ01NAM)
- Neoplasms, unspecified (CQ04NAM)
- Opportunistic Infections (CQ06NAM)
- Herpes Zoster (CQ07NAM)
- Pneumonia (CQ10NAM)
- Sepsis (CQ08NAM)
- Tuberculosis (CQ11NAM)
- Suicide/self-injury (SMQ01NAM)
- Depression (CQ09NAM)

Any AEs that cannot be automatically categorized into AESI by the automatic process will be flagged for manual review by the GSK Study Medical Monitor and GSK Safety Evaluation and Risk Management (SERM) physician to adjudicate. The manual review process is as described in Section 9.3.2. The working instruction provided by GSK showing details of the automated steps is available on request from the GSK SABLE Study Lead Programmer or Statistician.

9.3.2. Review and Categorization of Adverse Events of Special Interest

All reported AE terms will be reviewed at the subject level by GSK Medical Monitor. The review and categorization of AEs are used to flag AESIs. The reviewers will categorize each AE into one of the following AESI category.

- Malignancies (excluding non-melanoma skin cancer - NMSC)
- Opportunistic infections (see protocol Appendix 1)
- Other infections of interest (see protocol Appendix 1)
- NMSC
- Serious psychiatric events (see protocol Appendix 2)
- Serious infections

Cases of mortality (death) are reported as all the events captured as fatal SAEs in the eCRF. All other AESI types are assigned based on the review outcome described above. For summary and reporting purpose, the eCRF field for reporting SAE will be used to separate serious and non-serious Opportunistic Infections and Other Infections of Interest AESI.

In addition to review by the GSK Medical Monitor, an independent review and categorization will be performed by safety physician for concurrence with the initial review using the same data and following the same convention of the main review. Identified discrepancies will be discussed and reconciled between the GSK clinical representatives (Medical Monitor and study Clinical Science Lead or designee) and the SERM physician. The reconciled record of categorization will be utilized in study reporting.

The identification, classification and categorization of AESI is planned to occur at least annually prior to the clinical database cut-off date for the scheduled annual post-approval European Medicines Agency (EMA) submission. It is anticipated that since this is an ongoing study and in-stream query process, categorization may change from one report to another, as additional information becomes available on safety events.

9.4. Appendix 4: Data Display Standards & Handling Conventions

9.4.1. Reporting Process

Software	
• All analyses will be conducted using SAS® version 9.4 or higher (SAS Institute, Cary, NC, USA).	
Reporting Area: • Datasets and TLF outputs received from FSO will be uploaded to	
Domino Project	16267_116543_EOS
Compound/Study	GSK1550188\BEL116543
Analysis Datasets	
• Analysis datasets will be created according to CDISC standards (SDTM IG Version 3.2 & Analysis Data Model (ADaM) IG Version 1.1).	
Generation of RTF Files	
• RTF files will be generated for each Table, Listing and Figure.	

9.4.2. Reporting Standards

General
The current GSK Statistical Display Principles will be applied for reporting, unless otherwise stated. I GSK Statistical Display Principles location: https://myteams.gsk.com/sites/IDSLLibrary/PublishingImages/Combined%20Statistical%20Displays%20Principles%20v2.docx). Below sections from "Combined Statistical Displays Principles v2.docx" will be applied: • 4.3 to 4.24: Principles for All Displays • 5.1 to 5.9: Principles for Data Listings • 6.1 to 6.11: Principles for Summary Table • 7.1 to 7.13: Principles for Graphics
Formats
• GSK Statistical Displays Principles (4.24, 6.8.3, & 6.9) for decimal places (DP's) will be adopted for reporting of data based on the raw data collected, unless otherwise stated. • Numeric data will be reported at the precision collected on the eCRF. • The reported precision from non eCRF sources will follow the GSK statistical displays principles but may be adjusted to a clinically interpretable number of DP's.
Planned and Actual Time

• Reporting for Tables, Figures and formal statistical analyses:
  • Target visit dates will be used for slotting events. The analysis visit dates will be used for any displays with time point analysis and derivations.
• Reporting for Data Listings:
  • Unless otherwise stated, planned/scheduled time relative to study assessment will be shown for TLF (Refer to Statistical Displays Principle 5.5).

Unscheduled Visits
• No unscheduled visit in the study

9.5. Appendix 5: Derived and Transformed Data

9.5.1. General

Multiple Measurements at One Analysis Time Point
• All AESIs, SLE medications or hospitalizations reported since the last visit will be reported and analysed. • If there are multiple values available within a visit window, then the worst case will be used for analysis. If the worst-case values are equal, the visit with the earliest date will be selected. For laboratory, the measurement which takes place first will be selected as the value. • For SLICC and SLEDAI 2000, the worst-case value will be that which increases the total score.

9.5.2. Study and Concomitant Medication Phases

Study Phase	Definition
Historical	Date < Enrollment Date
Baseline	Enrollment Date
Follow-up	Date > Enrollment Date

Medication Phase	Definition	
Historical	Medications stopped prior to enrollment date (Day 1). For BENLYSTA only: With regards to interruptions (i.e. stopping & restarting the medication), medications that stop within the 98 days window before enrollment, and don't restart within 98 days of the medication end date, will be classified as historical.	Medication End Date < Study Enrollment Date, excluding interruptions in medications for BENLYSTA only (as defined in the baseline medication phase)
Baseline	Medications started on or prior to enrollment date (Day 1) and still ongoing at or after enrollment, or for BENLYSTA only: Benlysta that stops within 98 days before enrollment and restarts, such that restart date – stop date ≤98 days and subsequent Benlysta end date is ongoing or after enrollment date. Such cases are considered interruptions, the medication is classified as baseline.	Medication Start Date ≤ Enrollment Date* ≤ Medication End Date, or accounting for interruptions for BENLYSTA only: Enrollment Date -98 ≤ Medication(A) End Date < Enrollment Date* and Subsequent Medication(B) Start Date ≤ Medication(A) End Date + 98 and ((Subsequent Medication(B) End date ≥ Enrollment Date) or (Subsequent Medication(B) End Date is missing))
Post-Baseline	Medication is still ongoing after enrollment day or medications end date is after enrollment.	Medication End Date is missing or Medication End Date> Enrollment Date

* Consider SLE medication(s) started within 3 days following the enrollment date (i.e Medication started or initiated at Day 1, 2, 3, or 4) as Baseline Medication (i.e Enrollment Date ≤ Medication Start Date ≤ Enrollment Date +3)

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

For all parameters, changes from baseline will be derived as follows:

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

9.5.3. Study Population

Demographics
Age
• GSK standard integrated data standards library (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 Year will be presented in listings as 'YYYY'.
Body Mass Index (BMI)
• Calculated as Weight (kg) / [Height (m)]^2
Baseline Characteristics
Time since SLE Diagnosis
• Calculated as: $\frac{(Enrollment\ date - Diagnosis\ date + 1)}{365.25}$ ○ Partial dates will be imputed as described in Section 9.6.2.1: Handling of Missing and Partial Dates
Exposure Duration
• Duration or extent of exposure (days) = (Medication End Date – Medication Start Date) +1 ○ Last contact Date (as defined in Section 9.5.3) will be used as Medication End Date if medication is ongoing at the time of data cut ○ May be calculated for historical, at baseline and post (follow-up) enrollment ○ For multiple medication records within each medication predefined category (i.e anti-malarial, Mycophenolate Mofetil etc): • the start date of earliest and end date of latest medications will be used when there is overlap in days of use • total of all durations of exposures will be used when there is no overlap in days of use
Disposition Duration
• Duration since last known visit or last contact date ○ Subject who has an 'Ongoing' status on the database (applicable to final analysis dry-run) will be categorized by duration since last contact calculated as: (DataCut Off Date (DCO) – Last Contact Date +1)/365.25 ○ The following categories will be used: - Last contact date to DCO is < 0.5 year

- Last contact date to DCO is 0.5 - < 1 year - Last contact date to DCO is 1 - < 2 years - Last contact date to DCO is 2 - < 3 years - Last contact date to DCO is 3 - < 4 years - Last contact date to DCO is 4+ years
• Last contact date definition: o maximum (death date [supersedes all other dates], last data assessment date, last visit date, last AE or hospitalization date) o in the case that the above date is greater than the reference end date (date of completion or withdrawal from end of study disposition CRF page), then the last contact date will be replaced with the reference end date. This is equivalent to the risk end period for each subject, and will be used for the subject-years calculations.

9.5.4. Safety

Adverse Events of Special Interest
• Duration of AESI (days) = Date of AESI resolution – AESI start date + 1 (If the AE is ongoing the duration will be left blank and no imputation will be done)

9.5.5. Effectiveness

Effectiveness endpoints
SLICC/ACR Damage Index (SDI) score
• SDI is designed to capture items of irreversible organ damage (present for at least 6 months) occurring in subjects with SLE. It consists of 12 organ system (listed below) scales each having subscales comprised of up to six components. • Scoring will be performed for the following items as per Systemic Lupus International Collaborating Clinics/American College of Rheumatology Damage Index. • Total scores used for analysis will not be obtained directly from the eCRF electronic data capture (EDC), but instead calculated by summing the scores of each domain. • If any item is missing, the total score should be set to missing (see Section 9.6.2.3 for exceptions).

Item	Score
Ocular (either eye, by clinical assessment)	
Any cataract ever	0,1
Retinal change or optic atrophy	0,1
Neuropsychiatric	
Cognitive impairment (e.g. memory deficit, difficulty with calculation, poor concentration, difficulty in spoken or written language, impaired performance levels) or major psychosis	0,1
Seizures requiring therapy for 6 months	0,1
Cerebrovascular accident ever (score 2 if >1)	0,1,2
Cranial or peripheral neuropathy (excluding optic)	0,1
Transverse myelitis	0,1
Renal	
Estimated or measured glomerular filtration rate <50%	0,1
Proteinuria >3.5 g/24hours	0,1
Or	

Effectiveness endpoints	
End-stage renal disease (regardless of dialysis or transplantation)	0,3
Pulmonary	
Pulmonary hypertension (right ventricular prominence, or loud P2)	0,1
Pulmonary fibrosis (physical and radiograph)	0,1
Shrinking lung (radiograph)	0,1
Pleural fibrosis (radiograph)	0,1
Pulmonary infarction (radiograph)	0,1
Cardiovascular	
Angina or coronary artery bypass	0,1
Myocardial infarction ever (score 2 if >1)	0,1,2
Cardiomyopathy (ventricular dysfunction)	0,1
Valvular disease (diastolic, murmur, or systolic murmur >3/6)	0,1
Pericarditis for 6 months, or pericardiectomy	0,1
Peripheral vascular	
Claudication for 6 months	0,1
Minor tissue loss (pulp space)	0,1
Significant tissue loss ever (e.g. loss of digit or limb) (score 2 if >1 site)	0,1,2
Venous thrombosis with swelling, ulceration, or venous stasis	0,1
Gastrointestinal	
Infarction or resection of bowel below duodenum, spleen, liver, or gall bladder ever, for any cause (score 2 if >1 site)	0,1,2
Mesenteric insufficiency	0,1
Chronic peritonitis	0,1
Stricture or upper gastrointestinal tract surgery ever	0,1
Musculoskeletal	
Muscle atrophy or weakness	0,1
Deforming or erosive arthritis (including reducible deformities, excluding avascular necrosis)	0,1
Osteoporosis with fracture or vertebral collapse (excluding avascular necrosis)	0,1
Avascular necrosis (score 2 if >1)	0,1,2
Osteomyelitis	0,1
Skin	
Scarring chronic alopecia	0,1
Extensive scarring or panniculum other than scalp and pulp space	0,1
Skin ulceration (excluding thrombosis) for >6 months	0,1
Premature gonadal failure	0,1
Diabetes (regardless of treatment)	0,1
Malignancy (exclude dysplasia) (score 2 if >1 site)	0,1,2
From the Systemic Lupus International Collaborating Clinics (SLICC) and the American College of Rheumatology Diagnostic and Therapeutic Criteria Committee, 1996 (Gladman, 1996)	

Effectiveness endpoints

SLEDAI**, 2000 (S2K) score**

- Assessments consist of 24 individual items (listed below) in which signs and symptoms, laboratory tests, and physician's assessment for each of 9 organ systems are given a weighted score and summed if present (marked 'Yes') at the time of the visit or ±30 days of enrollment visit.
- The maximum theoretical score is 105 (all 24 descriptors present simultaneously) with 0 indicating inactive disease (marked 'No'), but in practice few subjects have scores >45.
- Total Scores used for analysis are derived based on the sum of the weighted value for each organ system component (see Gladman, 2002).

Descriptor	Weight	Definition
Seizure	8	Recent onset, exclude metabolic, infectious or drug cause.
Psychosis	8	Altered ability to function in normal activity due to severe disturbance in the perception of reality. Include hallucinations, incoherence, marked loose associations, impoverished thought content, marked illogical thinking, bizarre, disorganized, or catatonic behavior. Exclude uremia and drug causes.
Organic Brain Syndrome	8	Altered mental function with impaired orientation, memory or other intellectual function with rapid onset and fluctuating clinical features. Include clouding of consciousness with reduced capacity to focus and inability to sustain attention to environment, plus at least 2 of the following: perceptual disturbance, incoherent speech, insomnia or daytime drowsiness, or increased or decreased psychomotor activity. Exclude metabolic, infectious, or drug causes.
Visual Disturbance	8	Retinal changes of SLE. Include cytoid bodies, retinal hemorrhages, serious exudate or hemorrhages in the choroids, or optic neuritis. Exclude hypertension, infection, or drug causes.
Cranial Nerve Disorder	8	New onset of sensory or motor neuropathy involving cranial nerves. Include vertigo due to lupus.
Lupus Headache	8	Severe persistent headache: may be migrainous but must be non-responsive to narcotic analgesia.
CVA	8	New onset of cerebrovascular accident(s). Exclude arteriosclerosis.
Vasculitis	8	Ulceration, gangrene, tender finger nodules, periungual infarction, splinter hemorrhages, or biopsy or angiogram proof of vasculitis.
Arthritis	4	≥2 joints with pain and signs of inflammation (i.e., tenderness, swelling or effusion).
Myositis	4	Proximal muscle aching/weakness associated with elevated creatine phosphokinase/aldolase or electromyogram changes or a biopsy showing myositis.
Urinary Casts	4	Heme-granular or red blood cell casts.
Hematuria	4	>5 red blood cells/high power field. Exclude stone, infection, or other causes.
Proteinuria	4	>0.5 gm/24 hours.
Pyuria	4	>5 white blood cells/high power field. Exclude infection.
Rash	2	Inflammatory type rash.
Alopecia	2	Abnormal, patchy or diffuse loss of hair.
Mucosal Ulcers	2	Oral or nasal ulcerations.
Pleurisy	2	Pleuritic chest pain with pleural rub or effusion, or pleural thickening.
Pericarditis	2	Pericardial pain with at least one of the following: rub, effusion or electrocardiogram or echocardiogram confirmation.
Low Complement	2	Decrease in CH50, C3, or C4 below the lower limit of normal for testing laboratory.
Increased DNA Binding	2	Increased DNA binding by FARR assay above normal range for testing laboratory.

Effectiveness endpoints		
Fever (move to hematologic)	1	>38 degrees C (38ºC). Exclude infectious cause.
Thrombocytopenia	1	<100,000 platelets/mm^3, exclude drug causes.
Leukopenia	1	<3,000 white blood cells/mm^3, exclude drug causes.

Adapted from: Gladman D Dafna, Ibañez Dominique and Urowitz B Murray. Systemic lupus erythematosus disease activity index 2000. J Rheumatol 2002;29;288-29 [Gladman, 2002]

9.6. Appendix 6: Reporting Standards for Missing Data

9.6.1. Study Withdrawals

Element	Reporting Detail
General	• Subject study completion (i.e. as specified in the protocol) was defined as completion of the 5-year follow-up following enrollment into study. • Withdrawn subjects will not be replaced in the study. Subjects who develop AESI will still remain in the study except for fatality event, withdrawal of consent or withdrawal at physician discretion. • All available data from subjects who were withdrawn from the study will be listed and all available data will be included in summary Tables and Figures.

9.6.2. Handling of Missing Data

Element	Reporting Detail
General	• Missing data occurs when any requested data are not provided, leading to blank fields on the collection instrument: o These data will be indicated using a "blank" in subject listing displays, unless all data for a specific timepoint are missing in which case the data are excluded from the Table. o Answers of "Not applicable" (i.e. within the section 'Serious Adverse Event of Special Interest [SAE-SI]') are not considered to be missing data and should be displayed as such.
Data Collection Stopped	• For effectiveness endpoints where collection of the underlying data have been stopped as per protocol amendment 3. Data collected for these endpoints prior to their removal from the protocol are available in the previous interim analysis reports.

9.6.2.1. Handling of Missing and Partial Dates

Element	Reporting Detail
General	• Partial dates will be displayed as captured in subject listing displays
Adverse Events Concomitant Medications Medical History Hospitalization	• 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 imputation will follow the conventions shown in Section 9.6.2.2. In the event the end date is after to the last contact date, the last contact date (section 9.5.3) 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 (where applicable). • The recorded partial date will be displayed in listings; so, should not be overwritten.

9.6.2.2. Imputation Convention for Missing and Partial Dates

Start date	Stop Date	Imputation
Complete date available	Complete date available	Not applicable
Complete date available	Only day is missing	Impute day of stop date with last day of the same month
Complete date available	Month and day are missing	1. Impute stop date with 'Jun30' 2. If (year of start date=year of stop date) then stop date =max (start date + 1, stop date)
Day is missing	Complete date available	Impute the day part of start date with "01" of the same month
Day is missing	Only day is missing	Impute day of start date with '01' and day of stop date with last day of the same month
Day is missing	Month and day are missing	1. Impute day of start date with '01' and 'Jun 30' for day and month of stop date 2. If (year of start date=year of stop date) then stop date =max (start date + 1, stop date)
Day and Month missing	Complete date available	1. Impute start date with 'Jun01' 2. If (year of start date=year of stop date) then start date =min (start date, stop date-1)
Day and Month missing	Only day is missing	1. Impute day of stop date with '30' and 'Jun 01' for day and month of start date 2. If (year of start date=year of stop date) then start date =min (start date, stop date-1)
Day and Month missing	Month and day are missing	Impute start date with 'Jun01' and stop date with 'JUN30'

9.6.2.3. Handling of Missing Data for Statistical Analysis

Element	Reporting Detail
General	• For endpoints not relying on multiple questionnaire items, missing values will not be imputed • Data will be analysed only for the time point at which they were collected.
SDI Domains	• If any item is missing, the total score should be missing. However, if the missing item has previously been score in previous visits, the worst observation can be carried forward for that item. • If the SDI is scored inconsistently (a decrease score at subsequent follow-up relative to previous visit has occurred) and the data are unable to be queried and/or corrected, the previous score (before the decrease) will be carried forward at the item level for the SLICC/Damage Index questions, this corresponds to worst observation carried forward (WOCF). These carried forward values at items level will then be used to calculate the total score which will be the value summarized and displayed for reporting.
S2K Score	For the calculation of S2K score, all items will be taken from the completed SLEDAI 2000 CRF page; no imputation will be performed. Scores for any S2K items will be used as observed. Subjects with at least one missing i.e. 'not done' value at baseline assessment will be excluded from the analysis of S2K total score.

9.7. Appendix 7: Laboratory Tests

Laboratory Parameter	Units
ANA status	
Anti-dsDNA	
C3	
C4	
CH50	
Lymphocyte differential % / count	
IgA	
IgM	
IgG	
White blood cell (WBC) count	mm^3
Neutrophil differential Count	mm^3
Thrombocytopenia (<100,000 platelets/10^9/L)	
Urinary Casts (Heme-granular or red blood cell casts)	
Hematuria (>5 red blood cells/high power field)	[Units]
Proteinuria (>0.5mg/24 hours)	
Pyuria (>5 white blood cells/high power field)	

9.8. Appendix 8: Abbreviations & Trade Marks

9.8.1. Abbreviations

Abbreviation	Description
ACR	American College of Rheumatology
ADaM	Analysis Data Model
AE	Adverse Event
AESI	Adverse Event of Special Interest
BMI	Body Mass Index
CDISC	Clinical Data Interchange Standards Consortium
CI	Confidence Interval
CSAP	Clinical Study Activity Plan
CSR	Clinical Study Report
DBL	Database Lock
DCO	Data Cut Off date
eCRF	Electronic Case Record Form
EDC	Electronic Data Capture
EMA	European Medicines Agency
FACIT	Functional Assessment of Chronic Illness Therapy
IA	Interim Analysis
IDSL	Integrated Data Standards Library
IPTW	Inverse Probability of Treatment Weighting
ITT	Intent-To-Treat
MAR	Missing at Random
Max	Maximum
Min	Minimum
NMSC	Non-melanoma skin cancers
PDMP	Protocol Deviation Management Plan
PS	Propensity score
Q1	First Quartile
Q3	Third Quartile
RAP	Reporting & Analysis Plan
PSRHQ	Possible Suicidality-Related History Questionnaire
PSRQ	Possible Suicidality-Related Questionnaire
S2K	SLEDAI 2000
SABLE	Safety And effectiveness of Belimumab in Systemic Lupus Erythematosus Registry
SAC	Statistical Analysis Complete
SAE	Serious Adverse Event
SD	Standard Deviation
SDI	SLICC/ACR Damage Index
SDTM	Study Data Tabulation Model
SERM	Safety Evaluation and Risk Management
SLE	Systemic Lupus Erythematosus

Abbreviation	Description
SLEDAI	Systemic Lupus Erythematosus Disease Activity Index
SLICC	Systemic Lupus International Collaborating Clinics
SMDs	standardized mean differences
TLF	Tables, Listings & Figures
VIF	Variance Inflation Factor

9.8.2. Trademarks

Trademarks of the GSK Group of Companies
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MedDRA
SAS® version 9.4 or higher (SAS Institute, Cary, NC, USA)
Domino 5.9.1

9.9. Appendix 9: Treatment Propensity Score Models Covariates

Table 4: Treatment Propensity Score Models Covariates

Variables	Categories/Units	Key covariates*
Year of entry in the study	2013/2014 2015/2016 2017/2018 2019/2020	
Age at baseline	Years	Yes
Sex	Female Male	Yes
BMI	Underweight (<18.5) Normal (18.5 - <25) Overweight (25 - <30) Obese (30 - <40) Extremely obese (>=40)	
Race	Black White Asian Other	Yes
Ethnicity	Hispanic/Latino Not Hispanic/Latino	
Region	US/Canada Europe Other	Yes
Baseline Clinical SLEDAI 2000 score	Score	Yes
Baseline SDI	Score	
SLE duration since diagnosis	Years	
Used corticosteroids for SLE in the past six months	Yes No	Yes
Cardiovascular risk factors	Yes No	
Allergic reactions	Yes No	
Interstitial lung disease	Yes No	
Chronic Obstructive Pulmonary Disease (COPD)	Yes No	
Opportunistic Infection	Yes No	

Variables	Categories/Units	Key covariates*
Any other infection	Yes No	
Autoimmune disorders	Yes No	
Hypogammaglobulinaemia	Yes No	
Cancer	Yes No	
Non-Melanoma Skin Cancer (NMSC)	Yes No	
Family history of cancer	Yes No	
End stage renal failure	Yes No	
Depression and/or anxiety disorder	Yes No	
Suicidal ideation and/or suicidal depression and/or suicidal behavior	Yes No	
Attempted suicide	Yes No	
Dialysis	Yes No	
Transplant	Yes No	
Splenectomy	Yes No	

Treatment propensity score models covariates are collected at baseline.
* Key covariates will be included in PS models. They are selected based on clinical judgment. If during building the PS model, there is a need to simplify the model specification, retention of key variables will be given priority. Any model simplification involving removal of these key covariates, will require further discussions and alignment with study team prior to implementation.

9.10. Appendix 10: SAS example code

Assessing co-linearity:

The option VIF gives the variance inflation factor in SAS REG procedure:

```
PROC REG data=out ;
  MODEL Y= X Z / VIF ;
RUN;
```

Categorical covariates with at least 3 categories will be transformed into dummy variables to be used in the SAS REG procedure.

Example:

The covariate Z could take the 3 categories values: 1, 2 and 3. Three dummy variables will be created:

Z1=1 if Z =1 else Z1=0;
Z2=1 if Z =2 else Z2=0;
Z3=1 if Z =3 else Z3=0;

If we choose the Z=1 as the reference category, the regression will be:

```
PROC REG data=out ;
  MODEL Y= X Z2 Z3 / VIF ;
RUN;
```

Propensity score model(s) definition:

```
proc causaltrt data= ADPS method=IPW noeffect;
   class  X1 X2 Xn ;
   psmodel TRT01Pn(descending) = X1….. Xn;
   model outcome;
   output out=PS ps=PS1 ipw=IPTW1;
run;
```

Note: the CAUSALTRT code contains both PSMODEL (to specify the propensity model) and MODEL (to specify the outcome model) statements. Anyway, the NOEFFECT option will allow finalization of the propensity model prior to conducting any outcome analysis.

9.11. Appendix 11: List of TLF Data Displays

9.11.1. Subjects and Study Characteristics Tables

Subjects and Study Characteristics Tables			
Table No	**Analysis Population**	**Title**	**Programming Note**
Subject Disposition			
1.000	Enrolled	Summary of Subjects Population by Study Cohort, Visit Attendance and Benlysta Medication (Exposure) Switch	
2.000	Eligible	Subject Completion Status	
3.000	Enrolled	Inclusion/Exclusion Criteria Deviations	
4.000	Eligible	Enrollment by Country	
5.000	Eligible	Enrollment by current Site	
Demographic			
6.000	Eligible	Demographic and Baseline Characteristics	
6.001	Sensitivity	Demographic and Baseline Characteristics – Sensitivity Analysis	
6.010	Eligible	Demographic and Baseline Characteristics – Current Users	
6.020	Eligible	Demographic and Baseline Characteristics – Treatment Initiators	
7.000	Eligible	Tobacco Use and Alcohol Abuse History at Baseline	
7.010	Eligible	Tobacco Use and Alcohol Abuse History at Baseline – Current Users	
7.020	Eligible	Tobacco Use and Alcohol Abuse History at Baseline – Treatment Initiators	

Subjects and Study Characteristics Tables			
Table No	**Analysis Population**	**Title**	**Programming Note**
Pregnancy Status			
8.000	Eligible	Baseline Pregnancy Status	
8.010	Eligible	Baseline Pregnancy Status – Current Users	
8.020	Eligible	Baseline Pregnancy Status – Treatment Initiators	
Historical and Current Medical History			
9.011	Eligible	Summary of Past Medical History at Baseline	
9.012	Eligible	Summary of Past Medical History at Baseline – Current Users	
9.013	Eligible	Summary of Past Medical History at Baseline – Treatment Initiators	
9.021	Eligible	Summary of Current Medical History at Baseline	
9.022	Eligible	Summary of Current Medical History at Baseline – Current Users	
9.023	Eligible	Summary of Current Medical History at Baseline – Treatment Initiators	
9.111	Eligible	Summary of Past General Medical Status at Month 24 and 48 Visits [Initial Exposure - ITT Strategy]	
9.112	Eligible	Summary of Past General Medical Status at Month 24 and 48 Visits [Initial Exposure - ITT Strategy] – Current Users	
9.113	Eligible	Summary of Past General Medical Status at Month 24 and 48 Visits [Initial Exposure - ITT Strategy] – Treatment Initiators	
9.121	Eligible	Summary of Current General Medical Status at Month 24 and 48 Visits [Initial Exposure - ITT Strategy]	
9.122	Eligible	Summary of Current General Medical Status at Month 24 and 48 Visits [Initial Exposure - ITT Strategy] – Current Users	

Subjects and Study Characteristics Tables			
Table No	**Analysis Population**	**Title**	**Programming Note**
9.123	Eligible	Summary of Current General Medical Status at Month 24 and 48 Visits [Initial Exposure - ITT Strategy] – Treatment Initiators	
SLEDAI 2000			
10.011	Eligible	Summary of SLEDAI 2000 at Baseline	
10.012	Eligible	Summary of SLEDAI 2000 at Baseline – Current Users	
10.013	Eligible	Summary of SLEDAI 2000 at Baseline – Treatment Initiators	
SLE Disease Duration			
12.000	Eligible	Summary of SLE Disease Duration at Baseline by Study Cohort	

Subjects and Study Characteristics Tables			
Table No	**Analysis Population**	**Title**	**Programming Note**
Laboratory Values			
19.000	Eligible	Summary of Baseline Laboratory Values	
19.010	Eligible	Summary of Baseline Laboratory Values – Current Users	
19.020	Eligible	Summary of Baseline Laboratory Values – Treatment Initiators	
Vaccinations			
20.000	Eligible	Summary of Baseline Vaccination Status by Study Cohort	
Exposure Switching			
17.000	Eligible	Summary of Medication Switching During Study Follow-up Period	
17.010	Eligible	Summary of Medication Switching During Study Follow-up Period – Current Users	
17.020	Eligible	Summary of Medication Switching During Study Follow-up Period – Treatment Initiators	
Withdrawal from Study			
50.000	Eligible	Time to Study Withdrawal [Initial Exposure - ITT Strategy]	
50.001	Eligible	Time to Study Withdrawal [Initial Exposure - ITT Strategy] – Current Users	
50.002	Eligible	Time to Study Withdrawal [Initial Exposure - ITT Strategy] – Treatment Initiators	
Protocol Deviations			
52.000	Eligible	Protocol Deviations	

9.11.2. Safety Endpoints Tables

Safety Endpoints Tables			
Table No	**Analysis Population**	**Title**	**Programming Note**
AESI			
23.000	Evaluable	Summary of Adverse Events of Special Interest by Time Period [Initial Exposure - ITT Strategy]	
23.001	Evaluable Sensitivity	Summary of Adverse Events of Special Interest by Time Period [Initial Exposure - ITT Strategy] – Sensitivity Analysis	
23.010	Evaluable	Summary of Adverse Events of Special Interest by Time Period [Initial Exposure - ITT Strategy] – Current Users	
23.020	Evaluable	Summary of Adverse Events of Special Interest by Time Period [Initial Exposure - ITT Strategy] – Treatment Initiators	
23.100	Evaluable	Summary of Adverse Events of Special Interest by Time Period [While On Initial Exposure Strategy]	
23.101	Evaluable Sensitivity	Summary of Adverse Events of Special Interest by Time Period [While On Initial Exposure Strategy] – Sensitivity Analysis	
23.110	Evaluable	Summary of Adverse Events of Special Interes by Time Period [While On Initial Exposure Strategy] – Current Users	
23.120	Evaluable	Summary of Adverse Events of Special Interest by Time Period [While On Initial Exposure Strategy] – Treatment Initiators	
23.200	Evaluable	Summary of Fatal AESI by SOC, PT and Study Cohort	
23.201	Evaluable Sensitivity	Summary of Fatal AESI by SOC, PT and Study Cohort – Sensitivity Analysis	
24.110	Evaluable	Overall Proportion and Rates of Adverse Events of Special Interest [Initial Exposure - ITT Strategy]	
24.1101	Evaluable Sensitivity	Overall Proportion and Rates of Adverse Events of Special Interest [Initial Exposure - ITT Strategy] – Sensitivity Analysis	

Safety Endpoints Tables			
Table No	**Analysis Population**	**Title**	**Programming Note**
24.111	Evaluable	Overall Proportion and Rates of Adverse Events of Special Interest [Initial Exposure - ITT Strategy] – Current Users	
24.112	Evaluable	Overall Proportion and Rates of Adverse Events of Special Interest [Initial Exposure - ITT Strategy] – Treatment Initiators	
24.120	Evaluable	Overall Proportion and Rates of Adverse Events of Special Interest [While On Initial Exposure Strategy]	
24.1201	Evaluable Sensitivity	Overall Proportion and Rates of Adverse Events of Special Interest [While On Initial Exposure Strategy] – Sensitivity Analysis	
24.121	Evaluable	Overall Proportion and Rates of Adverse Events of Special Interest [While On Initial Exposure Strategy] – Current Users	
24.122	Evaluable	Overall Proportion and Rates of Adverse Events of Special Interest [While On Initial Exposure Strategy] – Treatment Initiators	
24.210	Evaluable	Rates of Adverse Events of Special Interest by Time Period [As-Exposed – Time Varying Strategy with 14 Weeks Risk Window]	
24.211	Evaluable	Rates of Adverse Events of Special Interest by Time Period [As-Exposed – Time Varying Strategy with 14 Weeks Risk Window] – Current Users	
24.212	Evaluable	Rates of Adverse Events of Special Interest by Time Period [As-Exposed – Time Varying Strategy with 14 Weeks Risk Window] – Treatment Initiators	
24.310	Evaluable	Rates of Mortality, Serious Infections, Opportunistic Infections, Other Infections of Interest and Serious Psychiatric Events by Time Period [As-Exposed - Time Varying Strategy with 6 Months Risk Window]	
24.311	Evaluable	Rates of Mortality, Serious Infections, Opportunistic Infections, Other Infections of Interest and Serious Psychiatric Events by Time Period [As-Exposed – Time Varying Strategy with 6 Months Risk Window] – Current Users	

Safety Endpoints Tables			
Table No	**Analysis Population**	**Title**	**Programming Note**
24.312	Evaluable	Rates of Mortality, Serious Infections, Opportunistic Infections, Other Infections of Interest and Serious Psychiatric Events by Time Period [As-Exposed – Time Varying Strategy with 6 Months Risk Window] – Treatment Initiators	
24.410	Evaluable	Rates of Mortality, NMSC and Malignancies by Time Period [Ever-Exposed Strategy]	
24.411	Evaluable	Rates of Mortality, NMSC and Malignancies by Time Period [Ever-Exposed Strategy] – Current Users	
24.412	Evaluable	Rates of mortality, NMSC and Malignancies by Time Period [Ever-Exposed Strategy] – Treatment Initiators	

9.11.3. Effectiveness Endpoints Tables

Effectiveness Endpoints Tables			
Table No	**Analysis Population**	**Title**	**Programming Note**
SLICC/ACR Damage Index (SDI)			
11.000	Eligible	Summary of Baseline SLICC/ACR Damage Index (SDI)	
11.100	Evaluable	Change from Baseline in SLICC/ACR Damage Index (SDI) by Visit [Initial Exposure – ITT Strategy]	
Hospitalizations			
13.000	Eligible	Summary of Hospitalizations at Baseline by Study Cohort	
13.110	Evaluable	Summary of Hospitalizations Rate by Time Period [Initial Exposure – ITT Strategy]	
13.210	Evaluable	Summary of Hospitalizations Rate by Time Period [While On Initial Exposure Strategy]	
13.310	Evaluable	Summary of Hospitalizations Rate by Time Period [As-Exposed – Time Varying Strategy with 14 Weeks Risk Window]	
SLE Medications			
14.000	Eligible	Duration of Prior SLE Medications Not in Use at Baseline (Historical) by Study Cohort	
14.100	Eligible	Duration of Prior SLE Medications in Use at Baseline by Study Cohort	
14.200	Eligible	Frequency of Prior SLE Medications in Use at Baseline by Study Cohort	
14.300	Eligible	Frequency of Concomitant SLE Medications by Study Cohort	

Corticosteroids Use			
15.000	Eligible	Summary of Corticosteroids Usage at Baseline	
15.101	Evaluable	Change from Baseline in Average Corticosteroids Dose by Visit [Initial Exposure – ITT Strategy]	
15.201	Evaluable	Summary of Corticosteroids Usage by Visit [Initial Exposure – ITT Strategy]	

9.11.4. Propensity Scores Tables

Propensity Scores Tables			
Table No	**Analysis Population**	**Title**	**Programming Note**
53.011	Evaluable	Baseline Characteristics Included in the Propensity Score Model as Covariates	
53.012	Evaluable	Propensity Score Model Building: Associations between Baseline Characteristics and Treatment Initiation	
53.020	Evaluable	Standardized Mean Differences before and after IPTW Adjustment [Initial Exposure]	
53.031	Evaluable	IPTW Distribution [Initial Exposure]	
53.032	Evaluable	Stabilized IPTW Distribution [Initial Exposure]	
54.010	Evaluable	Weighted Rates of Adverse Events of Special Interest [Initial Exposure - ITT Strategy]	
54.020	Evaluable	Weighted Rates of Adverse Events of Special Interest [While On Initial Exposure Strategy]	

9.11.5. Listings

Listings			
No.	**Population**	**Title**	**Programming Notes**
1.000	Eligible	Subjects Demographic Characteristics	Separate page by Initial Exposure Group [ITT Strategy]/Study Cohort: NON-BENLYSTA/Current Users BENLYSTA/Current Users NON-BENLYSTA/Treatment Initiators BENLYSTA/Treatment Initiators
2.000	Eligible	SLE Medication	Separate page by Initial Exposure Group [ITT Strategy]/Study Cohort: NON-BENLYSTA/Current Users BENLYSTA/Current Users NON-BENLYSTA/Treatment Initiators BENLYSTA/Treatment Initiators
3.010	Eligible	All Adverse Events	Separate page by Initial Exposure Group [ITT Strategy]/Study Cohort: NON-BENLYSTA/Current Users BENLYSTA/Current Users NON-BENLYSTA/Treatment Initiators BENLYSTA/Treatment Initiators
4.000	Eligible	Exposure Switching (BENLYSTA Start/Stop) Information	Separate page by Initial Exposure Group [ITT Strategy]/Study Cohort: NON-BENLYSTA/Current Users BENLYSTA/Current Users NON-BENLYSTA/Treatment Initiators BENLYSTA/Treatment Initiators

Listings			
No.	**Population**	**Title**	**Programming Notes**
5.000	Eligible	Baseline General Medical History - Other Specify Medical Conditions	Separate page by Initial Exposure Group [ITT Strategy]/Study Cohort: NON-BENLYSTA/Current Users BENLYSTA/Current Users NON-BENLYSTA/Treatment Initiators BENLYSTA/Treatment Initiators
6.000	Eligible	Medical Conditions Relevant to AESI	Separate page by Initial Exposure Group [ITT Strategy]/Study Cohort: NON-BENLYSTA/Current Users BENLYSTA/Current Users NON-BENLYSTA/Treatment Initiators BENLYSTA/Treatment Initiators
7.000	Eligible	Fatality by Initial Exposure Group and Study Cohort	Separate page by Initial Exposure Group [ITT Strategy]/Study Cohort: NON-BENLYSTA/Current Users BENLYSTA/Current Users NON-BENLYSTA/Treatment Initiators BENLYSTA/Treatment Initiators
8.000	Eligible	Serious Psychiatric AESI	Separate page by Initial Exposure Group [ITT Strategy]/Study Cohort: NON-BENLYSTA/Current Users BENLYSTA/Current Users NON-BENLYSTA/Treatment Initiators BENLYSTA/Treatment Initiators

Listings			
No.	**Population**	**Title**	**Programming Notes**
8.100	Eligible	Possible Suicidality-Related Questionnaire	Separate page by Initial Exposure Group [ITT Strategy]/Study Cohort: NON-BENLYSTA/Current Users BENLYSTA/Current Users NON-BENLYSTA/Treatment Initiators BENLYSTA/Treatment Initiators
9.000	Eligible	Study Withdrawal	Separate page by Initial Exposure Group [ITT Strategy]/Study Cohort: NON-BENLYSTA/Current Users BENLYSTA/Current Users NON-BENLYSTA/Treatment Initiators BENLYSTA/Treatment Initiators
10.000	Eligible	Protocol Deviations	Separate page by Initial Exposure Group [ITT Strategy]/Study Cohort: NON-BENLYSTA/Current Users BENLYSTA/Current Users NON-BENLYSTA/Treatment Initiators BENLYSTA/Treatment Initiators

9.11.6. Figures

Figures			
Table No	**Population**	**Title**	**Programming Notes**
1.000	Eligible	Baseline Medication Groupings	
2.000	Eligible	Plot of Projected vs. Observed Withdrawal Probabilities	
53.020	Evaluable	Supplementary Results (Original SAS Output) - [Initial Exposure]	Figure referred to the table 53.020 (Proposensity Score Table)

9.11.7. Elderly Study (Subjects ≥ 65 years old) Data Display Tables

Study Population Tables			
Table No	**Population**	**Title**	**Programming Notes**
Subject Disposition			
2.0001	Eligible	Subject Completion Status (Subjects ≥65 Years Old)	Repeat for ≥75 years and change population label to Elderly (Subjects ≥75 Years Old)
Demographic			
6.0001	Eligible	Demographic and Baseline Characteristics (Subjects ≥65 Years Old)	Repeat for ≥75 years and change population label to Elderly (Subjects ≥75 Years Old)

Effectiveness Endpoints Tables			
Table No.	**Population**	**Title**	**Programming Notes**
SLICC/ACR Damage Index (SDI)			
11.0001	Eligible	Summary of Baseline SLICC/ACR Damage Index (SDI) (Subjects ≥65 Years Old)	Repeat for ≥75 years and change population label to Elderly (Subjects ≥75 Years Old)
SLE Disease Duration			
12.0001	Eligible	Summary of SLE Disease Duration at Baseline by Study Cohort (Subjects ≥65 Years Old)	Repeat for ≥75 years and change population label to Elderly (Subjects ≥75 Years Old)
Historical and Baseline Concomitant SLE Medications			
15.0001	Eligible	Summary of Corticosteroids Usage at Baseline (Subjects ≥65 Years Old)	Repeat for ≥75 years and change population label to Elderly (Subjects ≥75 Years Old)
Safety Endpoints Tables			
23.0001	Eligible	Summary of Adverse Events of Special Interest by Time Period (Subjects ≥65 Years Old)	Repeat for ≥75 years and change population label to Elderly (Subjects ≥75 Years Old)

9.11.8. Elderly Study (Subjects ≥ 65 years old) Data Display Listings

Listings			
No.	**Population**	**Title**	**Programming Notes**
Subject Disposition			
1.0001	Eligible	Subjects Demographic Characteristics (subjects ≥65 Years Old)	Repeat for ≥75 years and change population label to Elderly (Subjects ≥75 Years Old)
2.0001	Eligible	SLE Medication (Subjects ≥65 Years Old)	Repeat for ≥75 years and change population label to Elderly (Subjects ≥75 Years Old) Separate page by Initial Exposure Group [ITT Strategy]/Study Cohort: NON-BENLYSTA/Current Users BENLYSTA/Current Users NON-BENLYSTA/Treatment Initiators BENLYSTA/Treatment Initiators
Adverse Events of Special Interest (AESI)			
3.0101	Eligible	All Adverse Events (Subjects ≥65 Years Old)	Repeat for ≥75 years and change population label to Elderly (Subjects ≥75 Years Old) Separate page by Initial Exposure Group [ITT Strategy]/Study Cohort: NON-BENLYSTA/Current Users BENLYSTA/Current Users NON-BENLYSTA/Treatment Initiators BENLYSTA/Treatment Initiator

9.12. Appendix 12: Example Mock Shells for Data Displays

TLF displays mock shells is on a separate file and available on request.

Certificate Of Completion

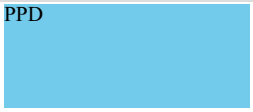
Envelope Id: PPD
Status: Completed
Subject: Complete with Docusign: SABLE FA Merged RAP_20250314_Final_Clean.pdf
Source Envelope:
Document Pages: 85
Signatures: 12
Certificate Pages: 6
Initials: 0
AutoNav: Enabled
EnvelopeId Stamping: Enabled
Time Zone: (UTC+01:00) Brussels, Copenhagen, Madrid, Paris

Envelope Originator:
PPD
PPD
PPD
IP Address: PPD

Record Tracking

Status: Original
14-Mar-2025 | 19:35
Holder: PPD
PPD
Location: DocuSign

Signer Events	Signature	Timestamp
PPD PPD Security Level: Email, Account Authentication (None)	PPD Signature Adoption: Pre-selected Style Using IP Address: PPD	Sent: 14-Mar-2025 | 19:44 Viewed: 17-Mar-2025 | 05:11 Signed: 17-Mar-2025 | 05:11
Electronic Record and Signature Disclosure: Accepted: 17-Mar-2025 | 05:11 ID: PPD		
PPD PPD Security Level: Email, Account Authentication (None)	PPD Signature Adoption: Pre-selected Style Using IP Address: PPD	Sent: 14-Mar-2025 | 19:44 Viewed: 17-Mar-2025 | 17:35 Signed: 17-Mar-2025 | 17:36
Electronic Record and Signature Disclosure: Accepted: 17-Mar-2025 | 17:35 ID: PPD		
PPD PPD Security Level: Email, Account Authentication (None)	PPD Signature Adoption: Pre-selected Style Using IP Address: PPD	Sent: 14-Mar-2025 | 19:44 Viewed: 17-Mar-2025 | 13:58 Signed: 17-Mar-2025 | 13:58
Electronic Record and Signature Disclosure: Accepted: 17-Mar-2025 | 13:58 ID: PPD		
PPD PPD Security Level: Email, Account Authentication (None)	PPD Signature Adoption: Pre-selected Style Using IP Address: PPD	Sent: 14-Mar-2025 | 19:44 Resent: 19-Mar-2025 | 13:16 Viewed: 19-Mar-2025 | 13:17 Signed: 19-Mar-2025 | 13:17
Electronic Record and Signature Disclosure: Accepted: 13-Oct-2023 | 16:20 ID: PPD		

Signer Events	Signature	Timestamp
PPD PPD Security Level: Email, Account Authentication (None)	 Signature Adoption: Pre-selected Style Using IP Address: PPD	Sent: 14-Mar-2025 | 19:44 Resent: 19-Mar-2025 | 13:16 Viewed: 19-Mar-2025 | 13:36 Signed: 19-Mar-2025 | 13:36
Electronic Record and Signature Disclosure: Accepted: 19-Mar-2025 | 13:36 ID: PPD		
PPD PPD Security Level: Email, Account Authentication (None)	 Signature Adoption: Pre-selected Style Using IP Address: PPD	Sent: 14-Mar-2025 | 19:44 Viewed: 14-Mar-2025 | 19:44 Signed: 14-Mar-2025 | 19:45
Electronic Record and Signature Disclosure: Not Offered via Docusign		
PPD PPD Security Level: Email, Account Authentication (None)	 Signature Adoption: Pre-selected Style Using IP Address: PPD	Sent: 14-Mar-2025 | 19:44 Resent: 19-Mar-2025 | 13:16 Viewed: 20-Mar-2025 | 12:29 Signed: 20-Mar-2025 | 12:29
Electronic Record and Signature Disclosure: Accepted: 20-Mar-2025 | 12:29 ID: PPD		
PPD PPD Security Level: Email, Account Authentication (None)	 Signature Adoption: Pre-selected Style Using IP Address: PPD	Sent: 14-Mar-2025 | 19:44 Resent: 19-Mar-2025 | 13:16 Viewed: 20-Mar-2025 | 19:23 Signed: 20-Mar-2025 | 19:23
Electronic Record and Signature Disclosure: Accepted: 20-Mar-2025 | 19:23 ID: PPD		
PPD PPD Security Level: Email, Account Authentication (None)	 Signature Adoption: Pre-selected Style Using IP Address: PPD	Sent: 14-Mar-2025 | 19:44 Viewed: 17-Mar-2025 | 05:24 Signed: 17-Mar-2025 | 05:24
Electronic Record and Signature Disclosure: Accepted: 17-Mar-2025 | 05:24 ID: PPD		
PPD PPD Security Level: Email, Account Authentication (None)	 Signature Adoption: Pre-selected Style Using IP Address: PPD	Sent: 14-Mar-2025 | 19:44 Resent: 19-Mar-2025 | 13:16 Viewed: 20-Mar-2025 | 18:07 Signed: 20-Mar-2025 | 18:08
Electronic Record and Signature Disclosure:		

Signer Events	Signature	Timestamp
Accepted: 20-Mar-2025 | 18:07 ID: PPD		
PPD PPD Security Level: Email, Account Authentication (None)	PPD Signature Adoption: Drawn on Device Using IP Address: PPD	Sent: 14-Mar-2025 | 19:44 Viewed: 17-Mar-2025 | 10:55 Signed: 17-Mar-2025 | 10:56
Electronic Record and Signature Disclosure: Accepted: 17-Mar-2025 | 10:55 ID: PPD		
PPD PPD Security Level: Email, Account Authentication (None)	PPD Signature Adoption: Pre-selected Style Using IP Address: PPD	Sent: 14-Mar-2025 | 19:44 Viewed: 17-Mar-2025 | 13:20 Signed: 17-Mar-2025 | 13:20
Electronic Record and Signature Disclosure: Accepted: 06-Apr-2022 | 16:01 ID: PPD		

In Person Signer Events	Signature	Timestamp

Editor Delivery Events	Status	Timestamp

Agent Delivery Events	Status	Timestamp

Intermediary Delivery Events	Status	Timestamp

Certified Delivery Events	Status	Timestamp

Carbon Copy Events	Status	Timestamp

Witness Events	Signature	Timestamp

Notary Events	Signature	Timestamp

Envelope Summary Events	Status	Timestamps
Envelope Sent	Hashed/Encrypted	14-Mar-2025 | 19:44
Certified Delivered	Security Checked	17-Mar-2025 | 13:20
Signing Complete	Security Checked	17-Mar-2025 | 13:20
Completed	Security Checked	20-Mar-2025 | 19:23

Payment Events	Status	Timestamps

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