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

Title	:	Reporting and Analysis Plan for A Multi-Center, Multinational, Randomized, Double-Blind Study to Evaluate the Efficacy and Safety of Belimumab (HGS1006) in Combination with Azathioprine for the Maintenance of Remission in Wegener's Granulomatosis and Microscopic Polyangiitis
Compound Number	:	GSK1550188
Effective Date	:	06-MAR-2017

Description :

- The purpose of this RAP is to describe the planned analyses and outputs to be included in the Clinical Study Report of the double-blind and open-label phases for Protocol HGS1006-C1100 (BEL115466).
- This RAP is intended to describe the planned efficacy, safety, pharmacokinetics and biomarker analyses required for the double-blind and open-label phases of the study.
- This RAP will be provided to the study team members to convey the content of the Statistical Analysis Complete (SAC) deliverable for the study.

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1. REPORTING & ANALYSIS PLAN SYNOPSIS

Overview	Key Elements of the RAP
Purpose	• This RAP details all planned analyses and outputs required for the final Clinical Study Report (CSR) of study BEL115466 (HGS1006-C1100).
Protocol	• This RAP is based on protocol amendment 04 (Dated: 26/FEB/2015) and local amendment 01 of protocol amendment 04 (Dated: 06/JUL/2015) of study BEL115466 (HGS1006-C1100; GSK Document No. : 2013N167980_02 and GSK Document No. : 2015N245521_00, respectively), and electronic case report form (eCRF) Version 7.0 (Dated: 05/JUL/2016).
Primary Objective	• To evaluate the efficacy of belimumab the maintenance of remission following a standard induction regimen in subjects with Wegener's Granulomatosis (WG) or Microscopic Polyangiitis (MPA). • To evaluate the safety of belimumab in subjects with WG or MPA.
Primary Endpoint	Time from Day 0 to the first relapse, defined as • at least 1 major BVAS item (Appendix 8) **OR** • a minimum total BVAS score of 6 (Appendix 8) **OR** • receipt of prohibited medications (as defined in Section 5.3)
Major Secondary Endpoint	• Time from Day 0 to the first major relapse (defined as experiencing at least 1 major BVAS item).
Study Design	• Multi-center, multi-national, randomized, double-blind study to evaluate the efficacy and safety of belimumab in combination with azathioprine for the maintenance of remission in subjects with systemic Wegener's Granulomatosis (WG) or Microscopic Polyangiitis (MPA) following a standard induction regimen. • The initial double-blind phase will be followed by a 6 month open-label extension in Belgium as detailed in local amendment 01 of protocol amendment 04. Subjects randomized to 10 mg/kg belimumab + oral 2 mg/kg/day azathioprine (AZA) in the double-blind phase will remain on this treatment and subjects randomized to placebo + 2 mg/kg/day AZA will begin to receive belimumab at 10 mg/kg + AZA 4 weeks after their final dose of placebo. • The sample size has been determined based on the feasibility of enrolling patients into the study within a reasonable time-frame. The sample size is not based on statistical considerations and the analysis of primary and secondary endpoints will be exploratory in nature. The primary efficacy analysis will be performed upon completion of the open label phase of the study. • Parallel-group study in approximately 100 subjects with two treatment groups comprising of one active and one placebo arm. Subjects will be randomized in a 1:1 ratio to receive placebo + AZA or belimumab 10 mg/kg + AZA.
Planned Analyses	• No interim analysis is planned for this study. • All decisions regarding final analysis, as defined in this RAP document, will be made prior to final Database Freeze (unblinding) of the study data. • Five subjects will continue to the open-label phase of the study and therefore data on these subjects for the open-label phase will be listed alongside the double-blind data only.
Analysis Populations	• The Screened population is defined as all subjects who were screened in the study, irrespective of whether or not they received study agent. • The Randomized population is defined as all subjects who were randomized in the

Overview	Key Elements of the RAP
	study, irrespective of whether or not they received study agent. • The Intent-to-Treat (ITT) population is defined as all subjects who are randomized and received at least 1 dose of study agent. • The Per-Protocol population is defined as all randomized subjects who receive at least one dose of study agent and who do not incur any protocol deviations that could affect the primary efficacy endpoint. • The Pharmacokinetic (PK) population is defined as all subjects randomized to belimumab treatment who receive at least one dose of study agent and from whom a pharmacokinetic sample is obtained and analyzed.
Hypothesis	• As the study is exploratory in nature, no formal hypothesis has been specified. However, the study will evaluate the superiority of belimumab versus placebo with respect to the time to first relapse.
Primary Efficacy Analyses	• The primary efficacy analysis will compare the time to first relapse from Day 0 between the placebo/AZA group and the belimumab/AZA combination group using a Cox proportional hazards model, adjusted for anti-neutrophil cytoplasmic antibody (ANCA) type (anti-proteinase 3 [anti-PR3] vs. anti- myeloperoxidase [anti-MPO]), disease stage at induction (initial diagnosis vs. relapsing disease), and induction regimen (rituximab vs. intravenous (IV) cyclophosphamide vs. oral cyclophosphamide). • Adjustment for covariates will be based on the eCRF categorization as oppose to the randomization strata. • The hazard ratio and corresponding 95% confidence interval and Wald chi-squared p-value will be presented for the adjusted difference in risk between the two treatment groups.
Secondary Analyses	**Efficacy - Major Secondary Endpoint**
	• The major secondary endpoint will be listed only due to limited events occurring.
	Efficacy Other - Time to Event
	• Descriptive statistics for time to first event will be presented in tabular format and graphically by treatment group and visit.
	Efficacy Other - Continuous Endpoints
	• Descriptive statistics for continuous endpoints will be presented in tabular format by treatment group and visit.
	Efficacy Other - Binary Endpoints
	• Descriptive statistics for binary endpoints will be presented in tabular format and graphically by treatment group and visit.
	Efficacy - Biomarkers and Autoantibodies
	• Biomarkers and autoantibodies will be summarized using the absolute change from baseline by treatment group and visit with the exception of B lymphocyte Stimulator (BLyS) protein which is only collected at baseline and will be summarized as such. Descriptive statistics will be presented in tabular format and graphically.
	Safety
	• Safety data will be presented in tabular format and summarized descriptively according to GSK's Integrated Data Standards Library (IDSL) standards.
	Pharmacokinetic
	• Serum belimumab concentration data will be summarized descriptively and presented graphically.
Terminology	• The name of Wegener's Granulomatosis (WG) was officially changed in 2011 to

Overview	Key Elements of the RAP
	Granulomatosis with Polyangiitis (GPA). These terms are equivalent and both may be used throughout the RAP. GPA will be presented in displays.

2. SUMMARY OF KEY PROTOCOL INFORMATION

This study was originally intended to support regulatory filings for an ANCA vasculitis treatment indication. That is no longer the intent, and the originally intended enrolment of ~300 subjects has been significantly reduced to ~100 subjects (Protocol HGS1006-C1100 Amend 04 Summary of Modifications; GSK Document No.: 2013N167980_02).

A 6 month open-label extension was originally planned, which would allow participants that completed the double-blind phase the opportunity to subsequently receive open-label belimumab supplied by the sponsor. This was removed from the protocol as part of amendment 04, due to the change in scope of the study. However, ethical objections were raised in Belgium and therefore the open-label extension was reinstated in Belgium only.

2.1. Changes to the Protocol Defined Statistical Analysis Plan

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

Table 1 Changes to Protocol Defined Analysis Plan

Protocol	Reporting & Analysis Plan	
Statistical Analysis Plan	**Statistical Analysis Plan**	**Rationale for Changes**
Synopsis: PK Endpoints and Analysis: Serum samples will be collected from all randomized subjects who receive a dose of study agent during the study and analyzed to determine serum belimumab concentrations. Serum belimumab concentration data will be used in a population PK analysis, which will be reported separately.	Results for this study will be presented using appropriate graphic and tabular summaries.	This study was originally intended to support regulatory filings for an ANCA vasculitis treatment indication. That is no longer the intent, and the originally intended enrolment has been significantly reduced. Therefore, a full population PK analysis is not required for this study.
Section 8.7.2 Analysis of Pharmacokinetics: Serum belimumab concentration will be determined by an electrochemiluminescence (ECL) - based assay. Results for this study will be presented using appropriate graphic and tabular summaries. Serum belimumab concentration data obtained from this study will be used in a population PK analysis, which will be reported separately. Potential effects of demographic characteristics, concurrent medications, renal function or disease stage on belimumab PK will be evaluated.	Results for this study will be presented using appropriate graphic and tabular summaries and no population PK analyses will be conducted.	As above.
Section 8.5.4 Other Efficacy Endpoints	• Absolute change in Vasculitis Damage Index	VDI is not assessed at Week 28 of Year 2; hence the midpoint of

Protocol	Reporting & Analysis Plan	
Statistical Analysis Plan	**Statistical Analysis Plan**	**Rationale for Changes**
Absolute change in Vasculitis Damage Index (VDI) at double-blind Week 48 of Year 1 and double-blind Week 28 of Year 2 and by visit; Proportion of subjects with any increase in VDI at double-blind Week 48 of Year 1 and double-blind Week 28 of Year 2 and by visit;	(VDI) will be analyzed at double-blind Week 48 of Year 1 and double-blind **Week 24 of Year 2** and by visit; • Proportion of subjects with any increase in VDI will be analyzed at double-blind Week 48 of Year 1 and double-blind **Week 24 of Year 2** and by visit;	the study calendar year will be used for analysis.
Study Synopsis: Biological markers will be measured at baseline (Day 0) and at multiple time points thereafter: • Anti-neutrophil cytoplasmic antibody (ANCA: anti-PR3, anti-MPO)	ANCA type will be tabulated for time points at which immunogenicity samples are available.	ANCA type was not evaluated by an immunoassay throughout the study, as specified in the protocol. Instead, only immune-fluorescence assay was performed on the collected samples. However, some remaining immunogenicity samples were available to evaluate ANCA type by immunoassay. Therefore, ANCA (anti-MPO and anti-PR3) will be summarized at the time points where immunogenicity samples are available. These are Day 0, year 1 week 8, year 1 week 24, then every 24 weeks, exit visit and follow-up visit. .
If there are then still less than 5 patients with an event (relapse) in any of the levels of this or any other stratification factor then the stratification term may be removed from the model.	If factors fail to converge they will be removed from the model	More general wording allows removal of factors based on assessment of model fit.
The exploratory analysis of the major secondary efficacy endpoint will be performed using the same method described for the primary efficacy endpoint, but censoring subjects who receive any prohibited medication (as defined in Section 5.5.1) prior to an observation of any major BVAS item. Any censoring will be applied on the date prohibited medications are received.	The major secondary endpoint will be listed only.	Due to a limited number of events occurring during the study, major relapses will be listed only.
Section 8.5.4 Other Efficacy	Proportion of patients in	The protocol was modified to

Protocol	Reporting & Analysis Plan	
Statistical Analysis Plan	**Statistical Analysis Plan**	**Rationale for Changes**
Endpoints: Proportion of patients in remission (defined as BVAS=0 and corticosteroid dose < 10 mg/day) at double-blind Week 48 of Year 1, double-blind Week 28 of Year 2 and by visit.	remission (defined as BVAS=0 and corticosteroid dose ≤ 10 mg/day) at double-blind Week 48 of Year 1, double-blind Week 28 of Year 2 and by visit.	allow doses of prednisone less than or equal to 10mg/day for maintenance at protocol amendment 3 (Protocol HGS1006-C1100 Amend 03 Summary of Modifications; GSK Document No.: 2013N167980_01). Section 8.5.4 should have been updated to be consistent with the protocol but was not. A note to file documenting this was produced.
Section 8.5.4 Other Efficacy Endpoints: CD27-/IgD+/CD10+ transitional	CD19+/CD24b+/CD38b+/CD27-/IgD+/CD10+ transitional.	CD19+/CD24b+/CD38b+/CD27-/IgD+/CD10+ transitional provides a more thorough definition of CD10+ transitional B cells and therefore this been provided by Q^2 solutions rather than the protocol-defined endpoint.

2.2. Study Objectives and Endpoints

2.2.1. Study Objectives

Objectives
• To evaluate the efficacy of belimumab in the maintenance of remission following a standard induction regimen in subjects with Wegener's Granulomatosis (WG) or Microscopic Polyangiitis (MPA).
• To evaluate the safety of belimumab in subjects with WG or MPA.
NOTE: No PK objective was defined in the protocol.

2.2.2. Study Endpoints

2.2.2.1. Efficacy

Primary
Time from Day 0 to the first relapse, defined as • at least 1 major BVAS item (Appendix 8) OR • a minimum total BVAS score of 6 (Appendix 8) **OR** • receipt of prohibited medications (as defined in Section 5.3)

Major Secondary
• Time from Day 0 to the first major relapse (defined as experiencing at least 1 major BVAS item, Appendix 8).

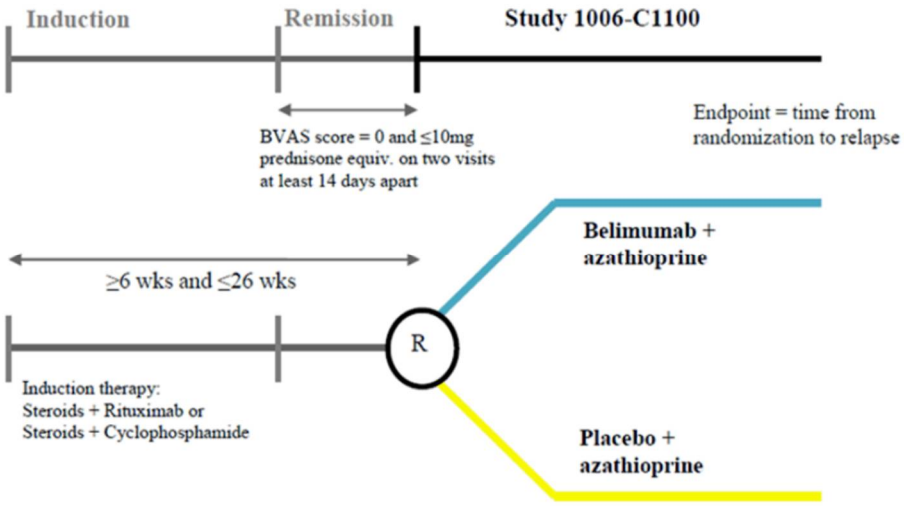
Other
• Time from Day 0 to first minor or major relapse (defined as experiencing at least 1 minor BVAS item and/or using a dose of rescue medication). *Note: (1) Rescue medication (prohibited medications resulting in treatment failure) as defined in Section 5.3. (2) Definition also includes any major relapse, defined as experiencing at least 1 major BVAS item.* • Absolute change in Vasculitis Damage Index (VDI) at DB Week 48 of Year 1 and double-blind Week 24 of Year 2 and by visit; • Proportion of subjects with any increase in VDI at double-blind Week 48 of Year 1 and double-blind Week 24 of Year 2 and by visit; • Absolute change in BVAS at double-blind Week 48 of Year 1 and double-blind Week 28 of Year 2 and by visit; • Proportion of subjects with any increase in BVAS at double-blind Week 48 of Year 1 and double-blind Week 28 of Year 2 and by visit; and • Proportion of subjects with any increase in BVAS organ domains at double-blind Week 48 of Year 1 and double-blind Week 28 of Year 2 and by visit and by domain. • Proportion of patients in remission (defined as BVAS=0 and corticosteroid dose ≤ 10 mg/day) at double-blind Week 48 of Year 1, double-blind Week 28 of Year 2 and by visit. • Proportion of patients with no relapse at double-blind Week 48 of Year 1, double-blind Week 28 of Year 2 and by visit.

Biological Markers and Autoantibodies
• Anti-neutrophil cytoplasmic antibody (ANCA – anti-PR3, anti-MPO) • Serum complement (C3, C4) • Serum immunoglobulin isotypes (IgA, IgM, IgG) • C-reactive Protein (CRP) • Erythrocyte sedimentation rate (ESR) • Urinary protein: urinary creatinine ratio • BLyS protein (Day 0 only) • FACS of peripheral lymphocytes: – B lymphocytes (CD19+, CD20+, CD20+/CD69+ activated, CD27hi/CD20- short-lived plasma, CD27+/CD20+ memory, CD27-/CD20+ naïve, CD138+/CD20- 138 plasma cells, CD138+/CD20+ plasmacytoid, CD19+/CD24b+/CD38b+/CD27-/IgD+/CD10+ transitional) – T cell subsets: CD3+/CD4+, CD3+/CD8+

2.2.2.2. Safety

Safety
• Adverse Events & Adverse Events of Special Interest (AESI) • Changes in Laboratory Parameters • Selected serious psychiatric events: Depression, suicide and self-injury • Suicidality Assessment: Columbia-Suicide Severity Rating Scale (C-SSRS) • Immunogenicity

2.3. Study Design

Overview of Study Design and Key Features	
	
Design Features	• Multi-center, multinational, randomized, parallel-group, double-blind study in subjects with WG or MPA following a standard induction regimen followed by a 6 month open-label extension (OLE) in Belgium only. • Subjects enrolled must have had an initial or relapsing episode of moderate to severely active WG or MPA that was treated with corticosteroids and either cyclophosphamide (CYC) or rituximab (RTX) in the 6 months leading up to randomization. Subjects who between 6 and 26 weeks of starting induction therapy, achieve a BVAS V3 score of 0 and are receiving ≤ 10 mg/day oral prednisone (or equivalent) on 2 consecutive visits at least 14 days apart may enroll. A minimum 6 week period should elapse between initiation of induction therapy and randomization. • Double-blind completion will be defined as 12 months having elapsed after the final subject is randomized (See Appendix 4).
Dosing	• All randomized subjects will be treated with oral azathioprine (AZA) at a target dose of 2 mg/kg/day. AZA may be initiated as soon as it is clinically indicated following administration of induction therapy. AZA should not be initiated any later than Day 0. • Eligible subjects will be randomized in a 1:1 ratio to also receive study agent (belimumab 10 mg/kg or placebo) administered intravenously over 1 hour. • Study agent will be administered at Day 0, 14, 28 and every 28 days thereafter until 12 months have elapsed following randomization of the last subject. • In the Belgium-only OLE, all subjects will receive belimumab 10 mg/kg every 28 days until Week 24, with a final evaluation at Week 28.
Treatment Assignment	• Approximately N=100 subjects will be randomly assigned to belimumab 10 mg/kg or placebo (1:1 ratio). • At randomization (Day 0), subjects will be stratified according to ANCA type (anti-PR3 vs. anti-MPO) [1], disease stage at induction (initial diagnosis vs. relapsing disease), and induction regimen (IV CYC vs. oral CYC vs. RTX). • During the open-label extension phase, subjects will be assigned to belimumab

Overview of Study Design and Key Features	
	10 mg/kg.
Interim Analysis	• No interim analysis is planned for this study.

[1] ANCA type historically assessed

2.4. Statistical Hypotheses

As the study is exploratory in nature, no formal hypothesis has been specified. However, the study will evaluate the superiority of belimumab versus placebo in the time to first relapse.

3. PLANNED ANALYSES

3.1. Interim Analyses

No interim analysis is planned for this study.

3.2. Primary and End of Study Analyses

The primary analyses will be performed at the end of the study, when the open-label phase is complete. The open-label phase data will be listed only together with the double-blind data.

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

1. Six months have elapsed after the last subject receives their first dose of belimumab open label.
2. All required database cleaning activities have been completed and final database release (DBR) and database freeze (DBF) has been declared by Data Management.
3. All criteria for unblinding the randomization codes have been met.
4. Randomization codes have been distributed according to RandAll NG procedures.

4. ANALYSIS POPULATIONS

Population	Definition / Criteria	Analyses Evaluated
Screened	• Comprise of all subjects who are screened in the study, irrespective of whether or not they receive study agent.	• Screening Failures
Randomized	• Comprise of all subjects who are randomized in the study, irrespective of whether or not they receive study agent.	• Study Population (listings)
Intent-To-Treat (ITT)	• Comprise of all randomized subjects who receive at least one dose of study agent (belimumab or placebo). • This population will be based on the treatment to which the subject was randomized.	• Study Population • Efficacy • Biomarkers • Safety
Per-Protocol (PP)	• Comprise of all randomized subjects who receive at least one dose of study agent and who do not incur any protocol deviations that could affect the primary efficacy endpoint. • Any subject excluded from the PP population will be excluded completely from the PP analysis. • Protocol deviations that would exclude subjects from the PP population are defined in Section 4.1 (Protocol Deviations). • A PP analysis of the primary and major secondary endpoints will be carried out if this population comprises between 50% and 95% of the ITT population.	• Efficacy
Pharmacokinetic (PK)	• Subjects in the 'ITT' population randomized to belimumab treatment for which a PK sample is obtained and analyzed.	• PK

NOTES :

- Refer to Appendix 12 which details population to be used for each display generated.

4.1. Protocol Deviations

- Please refer to the Protocol Deviation Management Plan (PDMP): Dated: 12/JAN/17 (Version 2) for full details.
- Important protocol deviations (including deviations related to study inclusion/exclusion criteria, conduct of the trial, patient management or patient assessment) will be summarized and listed.
- Important deviations which result in exclusion from the Per-Protocol population will also be summarized and listed. (Please refer to PDMP: Dated: 12/JAN/17 (Version 2)).
- Protocol deviations will be tracked by the study team throughout the conduct of the study in accordance with the Protocol Deviation Management Plan.

  - Data will be reviewed prior to unblinding and freezing the database to ensure all important deviations and deviations which may lead to exclusion from the analysis are captured and categorized on the protocol deviations dataset.
  - This dataset will be the basis for the summaries and listings of protocol deviations.
- A separate summary and listing of all inclusion/exclusion criteria deviations will also be provided. This summary will be based on data as recorded on the inclusion/exclusion page of the eCRF.

5. CONSIDERATIONS FOR DATA ANALYSES AND DATA HANDLING CONVENTIONS

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

Table 2 Overview of Appendices

Section	Component
10.1	Appendix 1 Time & Events
10.2	Appendix 2 Treatment States and Phases
10.3	Appendix 3 Data Display Standards & Handling Conventions
10.4	Appendix 4 Derived and Transformed Data
10.5	Appendix 5 Premature Withdrawals & Handling of Missing Data
10.6	Appendix 6 B Cell and T Cell Subsets
10.7	Appendix 7 BVAS Activity Assessment Form
10.8	Appendix 8 BVAS Item Scoring
10.9	Appendix 9 Vasculitis Damage Index (VDI)
10.10	Appendix 10 Laboratory Parameters & Adverse Events Grading

5.1. General Data Considerations

- This is a multi-center study and there are no planned adjustments for multiple centers or regions.

Unless otherwise stated, the following rules will apply:

- Data from the double-blind phase **only** will be displayed in tables and figures.
- Data collected in both the double-blind and open-label phases will be listed together and sorted by phase.
- Listings will be sorted by study phase and treatment group where applicable.
- Summaries and figures will present data by treatment group.
- The following statistics will be used to summarize the data:
  - **Continuous Variables:** n, mean, standard deviation (SD), median, minimum and maximum.
  - **Categorical Variables:** n, frequency counts and percentages.
- **Summaries by Visit:** Only scheduled visits at which parameters are collected as per the time and events table will be presented unless otherwise stated e.g. laboratory parameters. The "End of Double Blind" visit will not be presented in displays.
- Unscheduled visits will be included in the "Anytime post baseline" category for worst toxicity grading tables.

- Unscheduled visits will be listed.
- No imputation for missing values will be conducted.

5.2. Examination of Covariates, Subgroups & Other Strata

5.2.1. Examination of Strata and Covariates

Randomization (Day 0) included stratification according to the following variables:

- Anti-neutrophil Cytoplasmic Antibodies (ANCA) type (anti-PR3 vs. anti-MPO) historically assessed
- Disease stage at induction (initial diagnosis vs. relapsing disease)
- Induction regimen (IV cyclophosphamide vs. oral cyclophosphamide vs. rituximab)

  Note: The adjustment of induction regimen will be changed to rituximab vs. IV and/or oral cyclophosphamide if the number of events (relapse) is less than 5 in subjects using oral cyclophosphamide or IV cyclophosphamide.

Efficacy analyses will be adjusted based on the eCRF categorization.

If any factor does not converge it will be removed from the model.

5.2.2. Examination of Subgroups

- As a result of the significant reduction in sample size for this study from ~300 subjects to ~100 subjects (Protocol HGS1006-C1100 Amend 04 Summary of Modifications; GSK Document No.: 2013N167980_02), no subgroup analyses will be conducted but interactions with treatment group will be explored.
- Selected adverse event displays will be presented by the following subgroups:
  - Gender
  - Age (years): < 65 vs. ≥ 65
  - Induction Regimen: IV cyclophosphamide vs. oral cyclophosphamide vs. rituximab

- Selected efficacy summaries will be presented by the following subgroups as per the eCRF categorization:
  - Anti-neutrophil Cytoplasmic Antibodies (ANCA) type (anti-PR3 vs. anti-MPO)
  - Disease stage at induction (initial diagnosis vs. relapsing disease)
  - Induction regimen (IV cyclophosphamide vs. oral cyclophosphamide vs. rituximab)

- Selected displays will be presented by age subgroups ≥ 65 years and ≥ 75 years for inclusion in the Benlysta Elderly Analysis #3 report.

- Other subgroup analyses may be data-driven and conducted post-SAC, to further support evaluation of endpoints.

5.3. Rules for Relapse/Treatment Failure due to Receipt of Prohibited Medication

Subjects that are considered to be treatment failures by the treatment failure rules specified in the protocol and those specified by the study team will be adjudicated by representatives from safety, clinical and statistics at least once prior to DBR and once again after DBR and prior to DBF. Statistics and programming will program the agreed rules and output a spreadsheet to be completed by the committee. The adjudications will then be reflected back into the database.

5.3.1. Overview of Treatment Failure Rules as specified in the Protocol

All corticosteroids will be converted to a prednisone equivalent average daily dose (mg/day). The definition and derivation of this can be found in Appendix 4.

Concomitant medications will be coded using GSK Drug Dictionary Version 1.3 and those to be extracted as part of the treatment failure adjudication process will be identified as described in Appendix 4.

Subjects who start prohibited medication or therapies at ***any time*** during the double-blind phase will be considered as having relapsed as of the time of receipt of the prohibited medication and treatment with study agent will be discontinued. However, the subject will continue to be followed for survival through at least 12 months after randomization. The following medications and therapies are prohibited during the study:

- Other immunomodulatory investigational agents (biologic or non-biologic).
- Rituximab.
- Cyclophosphamide.
- Other immunosuppressive agents (e.g. cyclosporine) with the exception of methotrexate for AZA intolerance described in Section 5.5.3 of Protocol Amendment 04.
- Corticosteroids for vasculitis doses > 20 mg/day prednisone (or equivalent), or IV corticosteroid pulses at any dose.
  Note: Doses of prednisone up to a maximum of 20 mg/day (or equivalent) for vasculitis, for a maximum of 1 week, are only allowable within the first 2 months of the double-blind treatment period.
- Corticosteroids for reasons other than vasculitis: at an average daily dose of > 20 mg/day prednisone (or equivalent) for > 14 days where the average daily dose is calculated as the sum of the dose over 7 consecutive days divided by 7, or IV corticosteroid pulses > 125 mg prednisone (or equivalent).
  Note: Doses of prednisone (or equivalent) > 20mg/day for ≤ 14 days or IV corticosteroid pulses ≤ 125 mg prednisone (or equivalent) for reasons other than Vasculitis cannot be given more than once in any 365 day period (See also Protocol Amendment 04 Section 5.5.3).
- Plasmapharesis.

In addition to the above rules, subjects that receive more than 25mg of methotrexate in any 1 week period will be considered as potential treatment failures and will be adjudicated on a case-by-case basis.

5.3.2. Additional Detail for Treatment Failure Rules

- Treatment failures will be assessed from Day 0 until the last visit in the double-blind treatment period (see Appendix 4 for further detail).

- The time period of 14 days is defined as 14 consecutive days. Similarly, "1 week" is defined as 7 consecutive days.

- Average daily dose will be calculated for each study day, starting from Day 0 which is calculated as the average of the 7 days up to but not including Day 0. For all other study days, the average is calculated as the 7 days up to and including the study day of interest.

- When calculating the average daily dose of "corticosteroids for reasons other than vasculitis", corticosteroids for any indication will be included.

- The date at which a subject is considered to be a treatment failure will correspond to the date on which they meet the treatment failure rule. For example, a subject that receives a daily average dose of corticosteroid > 20mg/day for greater than 14 days is considered a treatment failure on the fifteenth day.

- For subjects that withdraw from the study, those that begin receiving escalated doses of corticosteroid prior to their last visit in the double-blind treatment period (see Appendix 4 for further detail) or who start a prohibited medication at the time of, or soon after, their last visit in the double-blind treatment period will also be considered as potential treatment failures. The Medical Monitor (MM) will assess subjects that withdraw from the study on a case-by-case basis and exert clinical judgment.

- The MM will manually review the concomitant medications record for investigational products on an ongoing basis. The MM will inform the Study Statistician via email if any cases are found and at the time of final adjudication will send a confirmation email of any cases found or no cases found. This email will be forwarded to the Group Mail Box.

- The MM will manually review the surgery dataset for cases of Plasmapharesis. Any cases found will be reported to the Study Statistician via email. At the time of final adjudication, the MM will send a confirmation email of any cases found or no cases found. This email will be forwarded to the Group Mail Box by the Study Statistician.

- Receipt of prohibited medication that is adjudicated as a treatment failure will be further evaluated for its relation to vasculitis (yes or no).

6. STUDY POPULATION ANALYSES

6.1. Overview of Planned Study Population Analyses

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

Table 3 provides an overview of the planned study population analyses, with full details of data displays being presented in Appendix 12.

Table 3 Overview of Planned Study Population Analyses

Endpoint / Parameter / Display Type	Data Displays Generated	
	Table	Listing
Subject Disposition		
Subject-Years on Study (Double-blind Phase)	Y	
Subject Disposition (Double-blind Phase)	Y(x3)[1]	Y
Subject Completion Status by Study Year (Double-blind Phase)	Y(x3)[1]	
Summary of Screen Failures (Screened Subjects Population)	Y	Y
Subjects by Country and Center (Randomized Subjects Population)	Y	
Reasons for Study Treatment Discontinuation		Y[2]
Reasons for Subject Study Withdrawal		Y[2]
Planned and Actual Treatments		Y
Protocol Deviations		
Inclusion/Exclusion Criteria Deviations (Double-blind Phase)	Y	Y[3]
Subjects with Important Protocol Deviations (Double-blind Phase)	Y	Y
Populations Analyzed		
Summary of Study Populations (Double-blind Phase)	Y	
Demographic and Baseline Characteristics		
Demographic Characteristics (Double-blind Phase)	Y(x3)[1]	Y
Baseline Disease Characteristics (Double-blind Phase)	Y(x3)[1]	
Randomized and Actual Strata (Double-blind Phase)		Y
Race and Racial Combinations (Double-blind Phase)	Y(x3)[1]	Y[4]
Other Baseline Characteristics		
Anti-Neutrophil Cytoplasmic Antibody at Baseline (Double-blind Phase)	Y	Y[2] [5] [6]
Complement (C3, C4) and BLyS Protein at Baseline (Double-blind Phase)	Y	Y[2] [5] [6]
Immunoglobulin (IgA, IgG, IgM) Levels at Baseline (Double-blind Phase)	Y	Y[2] [5] [6]
B Cells (FACS of peripheral lymphocytes) and T Cells at Baseline (Double-blind Phase)	Y	Y[2] [6]
Prior Medical Conditions and Concomitant Medications		
Prior Medical Conditions (Double-blind Phase)	Y	Y
Other Prior Medical Conditions (Double-blind Phase)		Y
Concomitant Medications (Double-blind Phase)	Y	Y[2]
Concomitant Procedures/Surgeries (Double-blind Phase)		Y[2]
Exposure and Treatment Compliance		
Duration of Exposure to Study Drug (Double-blind Phase)	Y(x3)[1]	Y[2]
Study Drug Administration		Y[2]
Time to Study Withdrawal (Double-blind Phase)	Y(x3)[1]	
Time to Withdrawal from Study Drug (Double-blind Phase)	Y	
Subjects switching from Azathioprine to Methotrexate (Double-blind Phase)		Y
Treatment Failures (Double-blind Phase)		Y

NOTES: Y = Yes display generated.
[1] Summary produced for all subjects and elderly subgroups (≥ 65 years and ≥ 75 years).
[2] Listing will display double-blind and open-label phase data.
[3] Listing also includes analysis population exclusions.
[4] Listing of race.
[5] Single listing of specific biomarker results to be generated.
[6] Listing will display all visits.

Time to study withdrawal and time to study treatment discontinuation will also be summarized with Kaplan-Meier curves.

6.1.1. Supplementary Information for Other Baseline Characteristics and Stratification Factors

A listing of randomized versus actual strata will be provided. Further detail regarding summary statistics to be produced is given in Table 4.

Table 4 Baseline Indicators and Stratification Factors

Baseline Indicator	Categories & Summaries at Baseline
Disease Classification	• Counts (%) of Granulomatosis with Polyangiitis (GPA) and microscopic Polyangiitis (MPA).
Anti-neutrophil Cytoplasmic Antibody	• Counts (%) of ANCA positive or ANCA negative as per immune-fluorescence assay (IFA). • Counts (%) of p-ANCA, c-ANCA or at-ANCA as per IFA. • Median, minimum and maximum summary of ANCA titer value as per IFA. • Counts (%) of ANCA type, anti-MPO or anti-PR3 (historically assessed).
	• Counts (%) of ANCA type, anti-MPO or anti-PR3 as evaluated by Q^2 Solutions.
Disease Duration	• Summary Statistics.
Previous Cyclophosphamide Use	• Counts (%) of yes or no. • Summary statistics of cumulative lifetime exposure in grams.
Vasculitis Damage Index	• Counts (%) of subjects with damage by organ domain.
Maintenance Therapy	• Counts (%) of Azathioprine and Methotrexate.
Average Daily Prednisone Dose	• Summary statistics of average daily prednisone-equivalent use.
Complement & BLyS Protein	**Complement** • Summary Statistics. • C3 count (%) of low (<90 mg/dL), normal and high (>180 mg/dL). • C4 count (%) of low (<10 mg/dL), normal and high (>40 mg/dL). **BLyS [ng/mL] Protein** • Summary statistics and count (%) of results below/above the limit of quantification [LOQ]).
Immunoglobulin (IgA, IgG, & IgM [g/L])	• Summary statistics. • Count (%) below the lower limit of normal (LLN) and above upper limit of normal (ULN).
B Cells and T Cells	• Summary statistics. • Only concentration and percentage will be presented.
Induction Regimen	• Counts (%) of IV Cyclophosphamide, oral Cyclophosphamide and Rituximab as per the eCRF categorization.
Current Disease Stage	• Counts (%) of initial and relapsing as per the eCRF categorization.

7. PRIMARY STATISTICAL ANALYSES

7.1. Efficacy Analyses

7.1.1. Overview of Planned Efficacy Analysis

The primary endpoint is time from Day 0 to the first relapse, defined as

- at least 1 major BVAS item (Appendix 8) OR
- a minimum total BVAS score of 6 (Appendix 8) OR
- receipt of prohibited medications (as defined in Section 5.3)

The primary efficacy analyses will be based on the Intent-to-Treat population. The primary efficacy analysis will be carried out on the double-blind data only.

A per-protocol analysis will be conducted if the PP population comprises between 50% and 95% of the ITT population.

Table 5 provides an overview of the planned efficacy analyses, with full details of data displays being presented in Appendix 12.

Table 5 Overview of Planned Efficacy Analyses

Endpoint	Absolute						
	Stats Analysis			Summary		Individual	
	T	F	L	T	F	F	L
Time from Day 0 to First Relapse	**Y(x7)**[1]			**Y(x6)**[1]	**Y**[1]		
Relapse				**Y**			**Y(x2)**

NOTES :

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

Time to relapse is defined as the number of days from Day 0 until the subject experiences a relapse (relapse date – Day 0 +1). Only post-baseline relapses will be considered in these analyses. Only relapses occurring up to and including the last visit date in the double-blind treatment period will be considered in these analyses (see Appendix 4 for further detail).

The following will apply to all statistical analyses of the primary endpoint, including sensitivity and exploratory analyses:

- A single summary table for each statistical analysis performed will be produced and will display model results for treatment group only unless otherwise specified. This table will not be produced for exploratory analyses of interaction terms.

- Other covariates included the model for the primary analysis of the ITT population only will be summarized in a separate table.

- Where interaction terms are explored, a single summary table will present p-values for interaction terms only.

A listing of relapse status at each visit for all subjects will be provided and will be sorted by relapse, center ID, subject ID and date of visit. For subjects that relapse, only visits up to and including the visit of relapse will be displayed.

A separate listing will be provided to detail the individual components of relapses due to BVAS. The disposition of subjects is defined as follows:

Subject Disposition	Event Met	Event Date
Subject Experiences Relapse [1]		
Subject experiences relapse as per BVAS assessment during the study	Yes	Date of BVAS assessment at which relapse is captured
Subject experiences relapse due to receipt of prohibited medication during the study	Yes	Date of receipt of prohibited medication
[1] If relapse as per BVAS and due to prohibited medication are observed at the same visit, the date of relapse will correspond to the earliest event date. If more than one condition for relapse is met on the same date, all reasons for relapse will be summarized and listed.		
Subject Does Not Experience Relapse		
Subject withdraws from the study	No	Censored at last available BVAS assessment (right censor)
Subject dies during the study	No	Censored at last available BVAS assessment (right censor)
Subject completes the study	No	Censored at last available BVAS assessment (right censor)

7.1.2. Planned Efficacy Statistical Analyses

Primary Statistical Analyses
Primary Endpoint
• Time from Day 0 to the first relapse, defined as – at least 1 major BVAS item (Appendix 8) OR – a minimum total BVAS score of 6 (Appendix 8) **OR** – receipt of prohibited medications (as defined in Section 5.3)
Model Specification
• Time to event endpoints will be statistically analyzed using a Cox Proportional Hazards (CPH) Model. • Terms fitted in the CPH model will be based on the eCRF categorization and will include: – Fixed categorical: ANCA type (anti-PR3 vs. anti-MPO), disease stage at induction (initial diagnosis vs. relapsing disease), and induction regimen (rituximab vs. IV cyclophosphamide vs. oral cyclophosphamide). *Note: The adjustment of induction regimen will be changed to rituximab vs. IV and/or oral cyclophosphamide if the number of events (relapse) is less than 5 in subjects using oral cyclophosphamide or IV cyclophosphamide.* • If a covariate in the model does not converge it will be removed (with the exception of induction regimen which should first be re-categorized as a binary variable). • If a subject withdraws or completes the study up to 12 months after the last subject is randomized without a relapse, time to first relapse will be censored at the time of the last available BVAS assessment. • Where ties are observed, these will be dealt with using the default method in the latest version of SAS (Breslow).
Model Checking & Diagnostics
• The assumption of proportional hazards between treatment groups will be assessed using appropriate methods.
Model Results Presentation
• The hazard ratio representing the estimated relative risk of relapse (belimumab – placebo) along with the 95% confidence interval and Wald chi-squared p-value will be presented. The same statistics will be presented in a separate table for other covariates from the CPH model. • For subjects who experience a relapse, the study day of the relapse will be summarized and the table will display the median, first and third quartiles and minimum and maximum if they are estimable. If they are non-estimable, the table will state this. • A Kaplan-Meier plot showing cumulative event rates for time to first relapse will be produced and Kaplan-Meier estimates will be given in a table. • For relapse due to BVAS a table summarizing organ domain involvement will be presented along with a listing of organ domain involvement and BVAS item. • A listing of reasons for treatment failure will be produced.

Sensitivity and Supportive Statistical Analyses
• Following review of the data, additional analyses may be conducted to further support the primary statistical analyses, if deemed appropriate.
• A sensitivity analysis adjusting for covariates based on the randomization strata to which a

Sensitivity and Supportive Statistical Analyses
subject was assigned at baseline will be presented. The hazard ratio representing the estimated relative risk of relapse (belimumab – placebo) along with the 95% confidence interval and Wald chi-squared p-value from the CPH model will be presented. This model will be fitted for the ITT population only. • Model estimates for covariates other than treatment group will not be provided.
• A sensitivity analysis including interaction terms between treatment group and each covariate will be included. Interactions will be fitted one at a time to the primary model (i.e. resulting in three independent models) and Wald Chi-Square p-values for interaction terms will be reported in a single table. These models will be fitted for the ITT population only. • Model estimates for covariates other than interactions will not be provided.
• A sensitivity analysis considering only vasculitis-related relapses may be performed if it is deemed appropriate. This will be assessed when treatment failures have been evaluated for their relation to vasculitis. If this analysis is carried out, subjects experiencing a relapse for reasons other than vasculitis will be censored at their previous BVAS assessment. Results will be displayed in the same way as for the primary efficacy analysis.Model estimates for covariates other than treatment group will not be provided. • Note: A vasculitis-related relapse is defined as a relapse occurring due to a minimum BVAS score of 6, any major BVAS item or receipt of a prohibited medication resulting in treatment failure that is adjudicated as vasculitis-related by representatives from Safety, Clinical and Statistics and Programming.
• A per-protocol (PP) analysis will be carried out on the primary efficacy endpoint if the PP population comprises of at least 50% and at most 95% of the intent-to-treat (ITT) population. The hazard ratio representing the estimated relative risk of relapse (belimumab – placebo) along with the 95% confidence interval and Wald chi-squared p-value from the CPH model will be presented. A Kaplan-Meier plot showing cumulative event rates for time to first relapse will be produced and Kaplan-Meier estimates will be given in a table. • Model estimates for covariates other than treatment group will not be provided.

8. SECONDARY STATISTICAL ANALYSES

8.1. Efficacy Analyses

The secondary efficacy analyses will be based on the Intent-to-Treat population.

8.1.1. Major Secondary Endpoint

Time from Day 0 to the first **major** relapse, defined as experiencing at least 1 major BVAS item (Appendix 8).

Due to a limited number of events occurring during the study, major relapses will be listed only.

Time to event is defined as the number of days from treatment start date (Day 0) until the subject meets an event (event date – treatment start date +1). Only post-baseline events will be considered. Only major relapses occurring up to and including the last visit date in the double-blind treatment period will be considered (see Appendix 4 for further detail).

8.1.2. Other Efficacy Endpoints

8.1.2.1. Overview of Planned Efficacy Analyses

All other efficacy endpoints will be summarized descriptively, in tabular format and where appropriate graphically. There are no planned formal statistical analyses.

Table 6 provides an overview of the planned efficacy summaries for other endpoints, with further details of data displays being presented in Appendix 12.

Table 6 Overview of Planned Efficacy Analyses for Other Endpoints

Endpoint	Absolute				Change from Baseline			
	Summary		Individual		Summary		Individual	
	T	F	F	L	T	F	F	L
Time to Event Endpoint								
Time from Day 0 to first minor or major relapse (defined as at least 1 minor BVAS item and/or using a dose of rescue medication [1]).	**Y**	**Y**						
Minor or Major BVAS item or Receipt of Rescue Medication				**Y**				
Continuous Endpoints [2]								
Birmingham Vasculitis Activity Score (BVAS)	**Y**				**Y**			**Y**
Vasculitis Damage Index (VDI)					**Y**			**Y**
Binary Endpoints								
Proportion of subjects with any increase in BVAS	**Y**	**Y**						
Proportion of subjects with any increase in VDI	**Y**	**Y**						
Proportion of subjects with any increase in BVAS organ domains	**Y**	**Y**						
Proportion of patients in remission (defined as BVAS=0 and corticosteroid dose ≤ 10 mg/ day)	**Y**	**Y**		**Y**				
Proportion of patients with no relapse	**Y**	**Y**						

NOTES:

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

[1] Rescue medication is defined as a prohibited medication resulting in treatment failure.

[2] BVAS: At double blind Week 48 of Year 1, double-blind Week 28 of Year 2 and by visit. VDI: At double blind Week 48 of Year 1, double-blind Week 24 of Year 2 and by visit.

8.1.2.2. Time to Event Endpoint

- Time to event is defined as the number of days from treatment start date (Day 0) until the subject meets an event (event date – treatment start date +1). Only post-baseline events will be considered. Only events occurring up to and including the last visit date in the double-blind treatment period will be considered (see Appendix 4 for further detail).

- For subjects who experience an event, the study day of the event will be summarized and the table will display the median, first and third quartiles and minimum and maximum where estimable. If they are non-estimable, this will be stated.

- A Kaplan-Meier plot showing cumulative event rates for time to first event by treatment group and table of Kaplan-Meier estimates will be produced.

- A listing of event status by treatment group and visit will be presented. Visits will be presented up to the first event only.

The disposition of subjects for the ***other secondary time to event endpoint*** is defined as follows:

Subject Disposition	Event Met	Event Date
Subject Experiences Minor or Major Relapse		
Subject experiences at least one minor relapse as per BVAS assessment during the study	Yes	Date of BVAS assessment at which minor relapse was captured
Subject receives a prohibited medication	Yes	Date of receipt of prohibited medication
Subject Does Not Experience Minor or Major Relapse		
Subject withdraws from the study	No	Censored at last available BVAS assessment (right censor)
Subject dies during the study	No	Censored at last available BVAS assessment (right censor)
Subject completes the study	No	Censored at last available BVAS assessment (right censor)

8.1.2.3. Continuous Endpoints

For continuous endpoints the following outputs will be produced:

- Table of summary statistics including n, mean, standard deviation, median, minimum and maximum by treatment group and visit for total score and observed change from baseline.
- For BVAS, a summary of organ system involvement by visit will be presented.
- Listing of VDI by treatment group, organ domain, item and visit.
- Listing of BVAS by treatment group, organ domain, item and visit.

8.1.2.4. Binary Endpoints

For binary endpoints the following outputs will be produced:

- Table of frequency counts and percentages by visit and treatment group
- Bar chart showing percentage (rather than proportion) of responders by treatment group and visit
- For the remission endpoint, a listing of remission status by treatment group and visit

Due to decreasing subject numbers figures will present data only to Year 2 Week 28 with the exception of VDI which will be displayed to Year 2 Week 24. Tables will summarize all visits at which the assessment of interest is scheduled.

The proportion of subjects with any increase in BVAS and the proportion of subjects with any increase in BVAS domains will be presented together in a single stacked bar chart and a single summary table.

Remission will be assessed on the date of visit only. If the BVAS assessment date is not equivalent to the visit date, remission will be assessed on the date of BVAS assessment provided it is no more than ±2 weeks from the visit date.

8.1.3. Biomarkers

8.1.3.1. Overview of Planned Biomarker Analyses

Biomarker efficacy analyses will be based on the Intent-to-Treat population. There are no planned formal statistical analyses.

Table 7 provides an overview of the planned biomarker analyses, with further details of data displays being presented in Appendix 12.

Table 7 Overview of Planned Biomarker Analyses

Parameter	Change from Baseline (Untransformed)			
	Summary		Individual	
	T	F	F	L
Anti-neutrophil cytoplasmic antibody (ANCA – p-ANCA, c-ANCA; anti-MPO, anti-PR3)	Y [1]			Y[2]
ANCA status over Time, compared to Baseline	Y			
Serum Complement (C3, C4)	Y[3]	Y[3]		Y[2]
Serum Immunoglobulin Isotypes (IgA, IgM, IgG)	Y[3]	Y[3]		Y[2]
C-reactive Protein (CRP)	Y[3]	Y[3]		Y[2]
Erythrocyte Sedimentation Rate (ESR)				Y[2]
Urinary Protein: Urinary Creatinine Ratio	Y[3]	Y[3]		Y[2]
Estimated Glomerular Filtration Rate (eGFR)	Y[3]	Y[3]		Y[2]
FACS of Peripheral Lymphocytes [4]	Y [1] [3]	Y [1] [3]		Y

NOTES:

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

[1] Display to be produced for all ITT subjects and elderly subgroups (≥ 65 years and ≥ 75 years)..
[2] Selected biomarker results combined into a single listing by treatment group and visit.
[3] Separate summaries of change from baseline and percentage change from baseline will be presented. Only change from baseline will be produced for elderly subgroups
[4] Includes: B lymphocytes (CD19+, CD20+, CD20+/CD69+ activated, CD27hi/CD20- short-lived plasma, CD27+/CD20+ memory, CD27-/CD20+ naïve, CD138+/CD20- 138 plasma cells, CD138+/CD20+ plasmacytoid, CD19+/CD24b+/CD38b+/CD27-/IgD+/CD10+ transitional), T cell subsets: CD3+/CD4+, CD3+/CD8+.

8.1.3.2. Absolute and Percent Change (Observed)

The absolute and percent change from baseline for complement levels (C3 and C4), immunoglobulins, C-reactive protein (CRP), estimated glomerular filtration rate (eGFR) and B cell and T cell subsets will be summarized by treatment group and visit. Other biomarkers will be listed by treatment group and visit. These summaries will be performed based on the observed data.

A line graph for the mean observed or percent change from baseline, along with 95% confidence intervals, in certain biomarkers will be presented by treatment group and visit up to Year 2 Week 28. Upon visual inspection of the data, if the distribution of any biomarker is considerably non-normal the median change will be displayed instead.

8.1.3.3. B and T cell Subsets

The observed change and percent change from baseline will be calculated for all B and T cell subset parameters. Events will not be displayed for any subsets. Percentage and concentration will not be displayed for rare B cell subsets; instead normalized count per millilitre (cells/mL) will be presented. The complete list of B and T cell subsets are given in Appendix 6.

Unit Conversion

All endpoints measured in GI/L should be converted to cells/cumm and presented as such using the following formula:

New Result = Old Result * 1000

Rare B Cell Subsets

Rare B cell subsets will then be converted to cells/ml using the following formula:

Normalized count/mL = [(rare cell event count) / (CD19+ event count)] * (CD19+ cells/cumm) * 1000

Endpoints to be normalized and values to be substituted into the formula are given in Table 8.

Table 8 Rare B cell subsets requiring normalization

PARAM type (rare cell event count)	CD19+ Event Count	CD19+ Counts[1]
CD20+ CD138+ Events (EVENTS)	CD19+ Events (EVENTS)[2]	CD19+ (cells/cumm)
CD20- CD138+ Events (EVENTS)	CD19+ Events (EVENTS) [2]	CD19+ (cells/cumm)
CD20+CD69+ Events (EVENTS)	CD19+ Events (EVENTS) [2]	CD19+ (cells/cumm)
CD27+b CD20- Events (EVENTS)	CD19+ Events (EVENTS) [2]	CD19+ (cells/cumm)
CD19+ CD24b+ CD38b+ CD27-IgD+ CD10 Events (EVENTS)	CD19+ Events (EVENTS) [3]	CD19+ (cells/cumm)

[1] Source data require conversion from GI/L to cells/mm^3.
[2] CD19+ Events based on the plasma panel assay, i.e. BIMETHCD = FLWPLSM.
[3] CD19+ Events based on the transitional panel assay, i.e. BIMETHCD = FLWTRANS.

The required parameters in the source data can be identified in Table 9.

Table 9 Source data from Q² Solutions required for Normalization of Rare B Cell Subsets

OU Name	Client RTC (BICATCD)	Client Analyte name	Biomarker test code (BITESTCD)	Biomarker testing method code (BIMETHCD)	Units of Measurement (BIORRESU)
TBNK	CD19[1]	CD19+	CONC	FLWTBNK	GI/L[1]
PLASMA	CD19	CD19+	EVENTS	FLWPLSM	EVENTS
PLASMA	CDX155	CD20+ CD69+	EVENTS	FLWPLSM	EVENTS
PLASMA	CDX143	CD20- CD138+	EVENTS	FLWPLSM	EVENTS
PLASMA	CDX145	CD20+ CD138+	EVENTS	FLWPLSM	EVENTS
PLASMA	CDX154	CD27+b CD20-	EVENTS	FLWPLSM	EVENTS
TRANS	CDX200	CD19+ CD24b+ CD38b+ CD27-IgD+ CD10	EVENTS	FLWTRANS	EVENTS

[1] Requires unit conversion to cell cells/cumm

B cells and T cells (percentage and concentration or normalized count/ml for rare B cell subsets) will be presented in the following order in all displays (BICATCD is given in parentheses for B cells, LBTESTCD is given for T cells as these are contained in the LAB dataset):

1. CD19+ (CD19)
2. CD27-/CD20+ naive (CDX136)
3. CD27+/CD20+ memory (CDX137)
4. CD19+/CD24b+/CD38b+/CD27-/IgD+/CD10+ transitional (CDX200)
5. CD20+/CD69+ activated (CDX141/CDX155)
6. CD20+ (CD20)
7. CD27hi/CD20- short-lived plasma (CDX154)
8. CD138+/CD20- 138 plasma cells (CDX143)
9. CD138+/CD20+ plasmacytoid (CDX145)
10. CD3+/CD4+ (LBTESTCD (CONC) = CD4+_BLC; LBTESTCD (%) = CD4+_BLQ)
11. CD3+/CD8+ (LBTESTCD (CONC) = CD8+_BLC; LBTESTCD (%) = CD8+_BLQ)

8.2. Safety Analyses

8.2.1. Overview of Planned Adverse Events Analyses

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

Table 10 provides an overview of the planned analyses, with further details of data displays being presented in Appendix 12.

Additional summaries, adjusting for subject years on study drug, may be performed if an imbalance in time on study drug is observed across treatment arms

Table 10 Overview of Planned Adverse Events Analyses

Endpoint	Absolute		
	Summary		Individual
	T	F	L
Pre-treatment Adverse Events by SOC & PT	**Y**		
AE Summary by Year Interval	**Y(x3)**[1]		
Cumulative AE Incidence Over Time		**Y**	
Survival Status at Week 52			**Y**
Relationship between SOC and Verbatim Text	**Y**		
Adverse Events by SOC			
AE by SOC & Year Interval	**Y**		
Serious AE by SOC & Year Interval	**Y**		
Severe AE by SOC & Year Interval	**Y**		
Study Drug Related AE by SOC & Year Interval	**Y**		
AE Leading to PD of Study Drug or WD from Study by SOC & Year Interval	**Y**		
Adverse Events Rates by SOC			
AE Rate by SOC & Year Interval	**Y**		
Serious AE Rate by SOC & Year Interval	**Y**		
Severe AE Rate by SOC & Year Interval	**Y**		
Study Drug Related AE Rate by SOC & Year Interval	**Y**		
AE Leading to PD of Study Drug or WD from Study Rate by SOC & Year Interval	**Y**		
Adverse Events by SOC & PT			
AE by SOC & PT & Year Interval	**Y(x3)**[1]		**Y(x3)**[1][2]
Serious AE by SOC & PT & Year Interval	**Y(x3)**[1]		**Y(x3)**[1][2]
Severe AE by SOC & PT & Year Interval	**Y**		
Serious or Severe AE Infections			**Y**[2]
Study Drug Related AE by SOC & PT & Year Interval	**Y(x3)**[1]		**Y**[2]
AE Leading to PD of Study Drug or WD from Study by SOC & PT & Year Interval	**Y(x3)**[1]		**Y(x3)**[1][3]
Deaths by SOC & PT & Year Interval	**Y(x3)**[1]		**Y**
Subject Numbers by Individual AE by SOC & PT			**Y**
Adverse Events Rates by SOC & PT			
AE Rate by SOC & PT & Year Interval	**Y**		

Endpoint	Absolute		
	Summary		Individual
	T	F	L
Adverse Events: Non-Serious, Serious & Fatal Serious by SOC & PT			
Common Non-Serious Adverse Events (>=5% incidence in any interval) by SOC and PT & Year Interval	**Y**		
Study Drug-Related Serious Adverse Events by SOC and PT & Year Interval	**Y**		
Fatal Serious Adverse Events by SOC and PT & Year Interval	**Y**		
Study Drug-Related Fatal Serious Adverse Events by SOC and PT & Year Interval	**Y**		
Non-Fatal Serious Adverse Events by SOC and PT & Year Interval	**Y**		**Y**[2]
Study Drug-Related Non-Fatal Serious Adverse Events by SOC and PT & Year Interval	**Y**		**Y**[2]
Adverse Events by SOC, PT and Gender			
AE by SOC, PT and Gender & Year Interval	**Y**		
Serious AE by SOC, PT and Gender & Year Interval	**Y**		
Adverse Events by SOC, PT and Age (< 65 and ≥ 65)			
AE by SOC, PT and Age Group (years) & Year Interval	**Y**		
Serious AE by SOC, PT and Age Group (years) & Year Interval	**Y**		
Adverse Events by SOC and PT and Induction Regimen			
AE by SOC, PT and Induction Regimen & Year Interval	**Y**		
Serious AE by SOC, PT and Induction Regimen & Year Interval	**Y**		
Adverse Events by PT			
AE by PT & Year Interval	**Y**		
Serious AE by PT & Year Interval	**Y**		
Severe AE by PT & Year Interval	**Y**		
Study Drug Related AE by PT & Year Interval	**Y**		
AE Leading to PD of Study Drug or WD from Study by PT & Year Interval	**Y**		
Deaths by Category and PT & Year Interval	**Y(x3)**[1]		
Adverse Events by Maximum Intensity			
AE by SOC & Maximum Intensity & Year Interval	**Y**		
AE by SOC, PT & Maximum Intensity & Year Interval	**Y**		
Adverse Events occurring Off-Treatment			
AE occurring Off-Treatment by SOC	**Y**		**Y**[4]

NOTES:

- BL = Baseline, PD = Permanent Discontinuation, PT = Preferred Term, SOC = System Organ Class, WD = Withdrawal, T = Table, F = Figures, L = Listings, Y = Yes display generated,
- Summary = Represents TFL related to any summaries (i.e. descriptive statistics) of the observed raw data.
- Individual = Represents FL related to any displays of individual subject observed raw data.
- Data in all displays will be presented by treatment group.

[1] Display to be produced for all ITT subjects and elderly subgroups (≥ 65 years and ≥ 75 years).
[2] Listing generated by Treatment Group, SOC, PT and Verbatim Term.
[3] Listing generated for AE results in study drug discontinuation
[4] AE occurring off-treatment will be included in overall AE listing

8.2.1.1. Adverse Events

- Treatment-emergent AEs are defined as adverse events that emerge on or after the first treatment dose, having been absent pre-treatment, or that worsen relative to the pre-treatment state.
- Only on-treatment adverse events will be summarized in tables and figures with the exception of summaries by year interval which will display events that occur during follow-up in the "Anytime Post Baseline" category. On-treatment events are defined as those occurring during the on-treatment study phase (see Appendix 2 for further detail). All treatment-emergent adverse events will be shown in listings.
- Adverse events will be coded to MedDRA dictionary version 19.1.
- Common AEs will be defined as ≥ 5% incidence in any treatment group.
- AEs with partial or missing start and/or stop dates will be assumed to be treatment-emergent unless there is evidence through comparison of partial dates to suggest otherwise.
- All treatment-emergent AEs will be listed for the double-blind phase and open-label phase together and sorted by study phase.
- Duration of AE (days) = Date of AE resolution – AE start date +1

8.2.1.2. Adverse Event Summaries

An overall summary of AEs will be presented showing the number (%) of subjects with at least one of the following:

- AE
- Study drug related AE
- SAE
- Severe AE
- SAE and/or severe AE
- AE resulting in study drug discontinuation and/or study withdrawal
- Death

The number (%) of subjects experiencing an AE by treatment group will be summarized for each of the AE categories in Table 11.

Table 11 Adverse Events Categories

AE's	Summary Category		
	By SOC	By SOC & PT	By PT
All	Y	Y	Y
Serious	Y	Y	Y
Severe	Y	Y	Y
Study Drug Related		Y	Y
Leading to permanent discontinuation of study drug and/or study withdrawal	Y	Y	Y
Deaths		Y	Y[1]

NOTES: Y = Yes display generated.
SOC = System Organ Class, PT = Preferred Term
[1] Deaths presented by Category and PT

Tabular summaries will be produced for each category of AE listed in Table 11, including:

- Number of subjects who reported at least one event.
- Percentage of subjects who reported at least one event (incidence).
- Number of adverse events.

The tables will be sorted by overall decreasing frequency of the SOC and then decreasing frequency of PT within the AE. Data in all tables will be presented by treatment group.

Summaries of AEs incidence, by SOC and severity will also be provided. For these displays, the number and percentage of subjects will be summarized as mild, moderate or severe based on the maximum severity observed across all PTs within the SOC for a given subject.

Total number of events will be calculated for the by SOC and by PT level tables and the AESI tables.

Adverse Event Rates

- An overall summary of AE event rates will be presented by SOC and PT. All other AE rate tables will display data by SOC only.
- A second summary will show the number of events reported and the event rate for the SOC level tables and the AESI tables.

The event rate of an AE will be calculated as the number of events per 100 subject years:

Event Rate = 100* Number of Events / Subject Years	
Overall Subject Years	$\frac{\sum_{\text{All Subjects in Population}} [(\text{Last Contact Date} - \text{1st Treatment Date} + 1)]}{365}$ NOTE: This will be the denominator for the "Any Time Post Baseline" column.
Subject Years in Year k	$\frac{\sum_{\text{All Subjects in Population}} (\text{End of Interval Day} - \text{Start of Interval Day} + 1)}{365}$

- Last contact date is the maximum of all assessment and event dates in the BEL115466 database excluding the "END OF DOUBLE BLIND", "LOGS" and "SURVIVAL" visits.
- AEs will be sorted by MedDRA SOCs, in descending order from the SOC with the highest overall 'Any Time Post Baseline' incidence/rate for any AE within the class, to the SOC with the lowest "Any Time Post Baseline" incidence/rate.
- Only SOCs with observed AE PTs will be presented. MedDRA PTs within SOC will be repeated using the same method.
- Tables which do not report the SOC will be sorted in descending order of incidence from the PT with the highest overall 'Any Time Post Baseline' incidence/rate group to the PT with the lowest 'Any Time Post Baseline' incidence/rate.
- If the overall 'Any Time Post Baseline' incidence/rate for any two or more adverse events is equal, the events will be presented in alphabetical order by SOC/PT as applicable.

A listing of which subjects reported each AE will also be produced. AEs will be grouped and sorted by SOC and PT. A figure of cumulative incidence of AEs by event type will be created for the ITT population.

8.2.2. Overview of Planned Adverse Event of Special Interest Analyses

Reporting of AESI will follow the principles outlined in the belimumab PSAP (Version 3, 14DEC2016), to ensure consistency across belimumab studies. Any specific BEL115466 modifications, additional AESI reporting or adjudication process requirements from the PSAP, are outlined below.

The following modifications from the PSAP (Section 14: AESI Definitions) will be applied for reporting the study:

- Preferred terms from MedDRA 19.1 will be used.

The following modifications from the PSAP (Section 15: GSK SRT Adjudication of AESI) will be applied for the study adjudication process:

- The milestone defined in the PSAP (i.e. before database release) for adjudications will be "database freeze".

Table 12 provides an overview of the planned Adverse Event analyses, with full details of data displays being presented in Appendix 12.

Table 12 Overview of Planned Adverse Events of Special Interest

Endpoint	Absolute	
	Summary	Individual
	T	L
Adverse Events of Special Interest (AESI)		
Overall AESI by Category & Year Interval	**Y(x3)**[1]	**Y** [2]
Malignant Neoplasm AESI by Category & PT & Year Interval	**Y**	
Infusion/Anaphylaxis/Hypersensitivity Reaction AESI by Category & PT & Year Interval	**Y**	
Serious Infusion/Anaphylaxis/Hypersensitivity Reaction AESI by Category & PT & Year Interval	**Y**	
Infection AESI by Category & PT & Year Interval	**Y**	
Serious Infection AESI by Category & PT & Year Interval	**Y**	
Severe Infection AESI by Category & PT & Year Interval	**Y**	
Serious/Severe Infection AESI by Category & PT & Year Interval	**Y**	
Infection AESI Leading to Discontinuation by Category & PT & Year Interval	**Y**	
Depression/Suicide/Self-injury AESI by Category & PT & Year Interval	**Y**	
Adverse Events of Special Interest (AESI) by Subgroups		
Overall AESI by Category and Induction Regimen & Year Interval	**Y**	
Malignant Neoplasm AESI by Category & PT & Induction Regimen & Year Interval	**Y**	
Infection AESI by Category & PT & Induction Regimen & Year Interval	**Y**	
Serious Infection AESI by Category & PT & Induction Regimen & Year Interval	**Y**	
Adverse Events of Special Interest (AESI) Rates		
Overall AESI Rate by Category & Year Interval	**Y**	
Malignant Neoplasm AESI Rate by Category & PT & Year Interval	**Y**	
Infusion/Anaphylaxis/Hypersensitivity Reaction AESI Rate by Category & PT & Year Interval	**Y**	
Serious Infusion/Anaphylaxis/Hypersensitivity Reaction AESI Rate by Category & PT & Year Interval	**Y**	
Infection AESI Rate by Category & PT & Year Interval	**Y**	
Serious Infection AESI Rate by Category & PT & Year Interval	**Y**	
Severe Infection AESI Rate by Category & PT & Year Interval	**Y**	
Serious/Severe Infection AESI Rate by Category & PT & Year Interval	**Y**	
Infection AESI Leading to Discontinuation Rate by Category & PT & Year Interval	**Y**	
Depression, Suicidality, and Self-injury AESI Rate by Category & PT & Year Interval	**Y**	

NOTES: T = Table, L = Listings, Y = Yes display generated.

- Summary = Represents TFL related to any summaries (i.e. descriptive statistics) of the observed raw data.
- Individual = Represents FL related to any displays of individual subject observed raw data.

[1] Display to be produced for all ITT subjects and elderly subgroups (≥ 65 years and ≥ 75 years
[2] Listing generated by Treatment Group, AESI Category, SOC, PT and Verbatim Term.

8.2.3. Adverse Events of Special Interest Summaries

An overall summary of AESI will be presented by treatment group and each specific category of AESI will be presented separately by PT.

An overall summary of AESI by treatment group and induction regimen will also be provided as well as each specific category by PT for malignant neoplasm AESI, infection AESI and serious infection AESI.

The number (%) of subjects with at least one occurrence and the number of events of the following AESI will be provided:

Malignant Neoplasms

- All Including non-melanoma skin cancer (NMSC)
- All Excluding NMSC
  - Solid Tumor
  - Hematologic
  - Skin (All)
    - NMSC
    - Excluding NMSC
  - Tumors of Unspecified Malignancy per GSK Adjudication

Post-Infusion Systemic Reactions

- Post-Infusion Systemic Reactions per Anaphylactic Reaction Customized MedDRA Query (CMQ) Narrow Search
- Post-Infusion Systemic Reactions per Anaphylactic Reaction CMQ Broad Search
- Post-Infusion Systemic Reactions per Anaphylactic Reaction CMQ Algorithmic Search
- Serious Anaphylaxis per Sampson Criteria
- Serious Acute Post-Infusion Systemic Reactions Hypersensitivity per GSK Adjudication
  - Serious Acute Post-Infusion Systemic Reactions Excluding Hypersensitivity per GSK Adjudication
  - Serious Acute Hypersensitivity Reactions per GSK Adjudication
- Serious Delayed Acute Post-Infusion Systemic Reactions per GSK adjudication
- Serious Delayed Non-Acute Post-Infusion Systemic Reactions per GSK adjudication

All Infections of Special Interest

- All Infections of Special Interest
  - Serious
  - All Opportunistic infections per GSK Adjudication.
    - Serious
  - Opportunistic Infections per GSK Adjudication Excluding Tuberculosis and Herpes Zoster
    - Serious
  - Active Tuberculosis
    - Serious
    - Non-opportunistic
      - Serious
    - Opportunistic
      - Serious
  - All Herpes Zoster
    - Serious
    - Non-opportunistic
      - Serious
    - Opportunistic
      - Serious
      - Recurrent
        - Serious
      - Disseminated
        - Serious
  - Sepsis
    - Serious

Depression/Suicide/Self-injury

- Depression/Suicide/Self-injury
  - Depression
    - Serious
  - Suicide/Self-injury
    - Serious
- Serious Suicide/Self-injury per GSK Adjudication
  - Suicidal Behavior per GSK Adjudication
    - Completed Suicide per GSK Adjudication
  - Suicidal Intent per GSK Adjudication
- Self-injurious Behavior without Suicidal Intent per GK Adjudication

Deaths

- Deaths

8.2.4. Overview of Planned Columbia-Suicide Severity Rating Scale (C-SSRS) Analyses

The safety analyses will be based on the Intent-to-Treat population, unless otherwise specified. These analyses will be performed for the double-blind phase only.

"Pre-treatment" is considered to be any time up to but not including Day 0.

Table 13 provides an overview of the planned C-SSRS analyses, with further details of data displays being presented in Appendix 12.

Table 13 Overview of Planned C-SSRS Analyses

Endpoint	Absolute		
	Summary		Individual
	T	F	L
C-SSRS Suicidal Ideation or Behavior during Treatment	**Y**		
Treatment Emergent C-SSRS Suicidal Ideation or Behavior Relative to Pre-Treatment	**Y**		
Shift of Changes in C-SSRS Categories from Pre-Treatment to On-Treatment	**Y**		
Possible Suicidality Related Questionnaire (PSRQ)			**Y**

NOTES:

- T = Table, F = Figures, L = Listings, Y = Yes display generated.
- Summary = Represents TFL related to any summaries (i.e. descriptive statistics) of the observed raw data.
- Individual = Represents FL related to any displays of individual subject observed raw data.
- Data in all displays will be presented by treatment group.
- Pre-treatment refers to any time up to Day 0.

8.2.4.1. C-SSRS Suicidal Ideation

Assessments are completed using the C-SSRS. If a "yes" response is given to any suicidal behavior or a "yes" response to suicidal ideation questions 3, 4 or 5 on the C-SSRS, the investigator will be prompted to complete the Possible Suicidality Related Questionnaire (PSRQ). A listing of the Possible Suicidality Related Questionnaire (PSRQ) will be presented.

Listings will be generated for the following:

- Suicidal ideation and behavior data for subjects who have any suicidal ideation or behavior recorded at any point on the study (including screening)
- Behavior details for subjects who have any suicidal behavior recorded at any point on the study (including screening)
- The most severe suicidal ideation details for subjects who have any suicidal ideation recorded at any point on the study (including screening).

8.2.4.2. C-SSRS Suicidal Ideation or Behavior during Treatment

The number (%) of subjects with each category of suicidal ideation or behavior during treatment (including Day 0 assessment onwards) will be presented, selecting the worst record a subject has for each category. The categories of suicidal ideation and behavior are presented in increasing order of severity from 1 to 10.

For the rows pertaining to *suicidal behavior*, the number of subjects who have the specified behavior at least once during treatment is presented.

For the rows pertaining to *suicidal ideation*, the number of subjects whose maximum ideation at any on-treatment assessment is the specified ideation is presented.

Within each category, subjects may have more than one type of suicidal ideation and behavior.

8.2.4.3. C-SSRS Suicidal Ideation or Behavior Relative to Pre-treatment

The number (%) of subjects with treatment-emergent suicidal ideation or behavior during treatment (including Day 0 assessment onwards) will be presented. A subject must have at least one pre-treatment assessment and at least one on-treatment assessment in order to be included in this display. A subject may have more than one treatment-emergent suicidal ideation and/or behavior.

8.2.4.4. C-SSRS Shift Changes in Categories from Pre-treatment to On-treatment

A summary of the shift from maximum pre-treatment C-SSRS category to maximum on-treatment (up to and including 4 weeks after the final treatment dose is administered) category will be produced. The pre-treatment period is based on the lifetime evaluation at screening.

A subject must have *at least one* pre-treatment assessment and *at least one* on-treatment assessment in order to be included in this display.

The table will display the number (%) of subjects within the specific shift categories: no suicidal ideation or behavior, suicidal ideation, and suicidal behavior.

8.2.5. Overview of Planned Laboratory & Immunogenicity Analyses

Table 14 provides an overview of the planned Laboratory, Immunogenicity, Immunoglobulins and Vital Signs analyses, with full details of data displays being presented in Appendix 12.

All laboratory parameters given in Appendix 6 of the protocol will be summarized with the exception of myelocytes, metamyelocytes and neutrophil bands in hematology displays. These parameters will be listed only.

Table 14 Overview of Planned Laboratory, Immunogenicity and Vital Signs

Endpoint	Absolute			Change from BL		
	Summary		Individual	Summary		Individual
	T	F	L	T	F	L
Laboratory Parameters (By Visit)						
Lab Parameters	Y (x5) [1][2]	Y (x5) [2]	Y (x6) [1]	Y (x6) [1][2][3]	Y (x5) [2][4]	
Worst Laboratory Toxicity Grade (By Year Interval)						
Worst Lab Toxicity Grade	Y (x6) [1][4]					
Lab Toxicity Grading Worsening by At Least 2 Grades from BL				Y (x6)[3]		
Grade 3 & 4 Lab Toxicity Results			Y (x6)[3]			
Laboratory Reference Range Shifts (By Visit)						
Lab Reference Shifts from BL				Y (x6)[3]		
Immunogenicity						
Immunogenicity Response by Visit	Y		Y			
Immunogenicity Response by Year	Y					
Vital Signs (By Visit)						
Vital Signs	Y		Y			

NOTES:

- BL = Baseline, T = Table, F = Figures, L = Listings, Y = Yes display generated, (xN) = Number of separate displays generated, LLN = Lower Limit of Normal.
- Summary = Represents TFL related to any summaries (i.e. descriptive statistics) of the observed raw data.
- Individual = Represents FL related to any displays of individual subject observed raw data.
- Data from the double-blind and open-label phases will be listed together.

[1] A combined display will be generated for absolute and change from baseline for each laboratory parameter. A combined display will also be generated for absolute and % change from baseline.

[2] Separate displays generated for [1] Hematology, [2] Liver Function, [3] Electrolytes, [4] Other Chemistries, [5] Immunoglobulins.

[3] Separate displays generated for [1] Hematology, [2] Liver Function, [3] Electrolytes, [4] Other Chemistries, [5] Urinalysis, [6] Immunoglobulins.

[4] Separate displays generated for [1] % Change from BL & [2] Change from BL.

8.2.5.1. Clinical Laboratory Evaluations

Continuous numeric values will be summarized using the mean, standard deviation, median, minimum and maximum.

Categorical results will be summarized using counts and percentages. Refer to Appendix 4 for handling of laboratory values that are above or below the lower limit of quantification.

Baseline is defined as described in Section 10.3.2 and a list of laboratory parameters collected and definition of the toxicity grades provided in Appendix 10.

Toxicities will be reported as derived by the central laboratory, as protocol toxicity grading was taken into account.

- For potassium, glucose, calcium, and sodium, toxicities are bi-directional (i.e. high and low directions) and both will be summarized by name of the toxicity.
- For example, calcium will have two toxicity sections, one for hypocalcaemia and one for hypercalcaemia, each with absolute values defining grades 1 to 4 (see Appendix 10 for further detail). Grade 0 will also be derived as any value less extreme than grade 1.

8.2.5.2. Laboratory Summaries by Study Year

Summary statistics (absolute and change from baseline) for each analyte will be displayed for each visit within continuation study year.

Line graphs will be produced for each analyte displaying the mean value by visit and treatment group and mean change from baseline value by visit and treatment group.

8.2.5.3. Worst laboratory toxicity grade post-baseline

Laboratory toxicity will be graded using Adverse Event Severity Grading Tables (Appendix 10) where defined.

The worst laboratory toxicity grade during treatment for each laboratory parameter within each laboratory category (hematology, chemistry, urinalysis, and immunoglobulins) will be presented. Only laboratory tests with toxicity grades will be presented.

8.2.5.4. Laboratory toxicity ≥ 2 grade shift post-baseline

Toxicity grade shifts from baseline of ≥ 2 grades will be summarized (i.e. baseline and post baseline data available) during treatment for each laboratory parameter within each laboratory category (hematology, chemistry, urinalysis, and immunoglobulins).

The summary will display the number (%) of subjects with at least one ≥ 2 grade shift as well as the specific shift categories: Grade 0 to 2, Grade 0 to 3, Grade 0 to 4, Grade 1 to 3, Grade 1 to 4, and Grade 2 to 4.

8.2.5.5. Laboratory reference range shifts from baseline by visit

For laboratory tests without toxicity grades, shifts relative to the normal range will be summarized for each analyte as shifts 'to low' and shifts 'to high.'

For the 'to low category' the percentage of subjects with at least one low post-baseline value relative to the baseline will be displayed using the categories: no shift to low and normal/high to low.

For the 'to high category' the percentage of subjects with at least one high post-baseline value relative to baseline will be displayed using the categories: no shift to high and normal/low to high.

A laboratory value that is above the testing laboratory's normal range will be considered a high abnormal laboratory value. A laboratory value that is below the testing laboratory's normal range will be considered a low abnormal value.

8.2.5.6. Immunoglobulin reference range shifts from baseline by visit

Reference range shifts will be summarized across all visits based on the baseline normal range category.

For subjects with immunoglobulin values below the LLN, the number (%) of subjects who 'remained low' or went 'to normal/high' post-baseline will be summarized.

For subjects with immunoglobulin values within the normal range or above the ULN, the number (%) of subjects who 'remained normal/high' or went 'to low' post-baseline will be summarized.

8.2.5.7. Immunoglobulin below LLN by visit

The number (%) of subjects with immunoglobulin values below the LLN at each visit will be presented for all subjects, and repeated for subjects based on their status at baseline.

8.2.5.8. Immunogenicity

Serum samples for anti-belimumab antibody measurements will be obtained from all randomized subjects before administration of study drug at the scheduled visits.

Two types of antibody assays will be performed:

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

in a titration assay step. The titer result is the inverse of the dilution at which the sample no longer tests positive in the screening assay.

- Neutralizing assay: Subjects who test positive for the binding assay are tested for the neutralizing assay, which produces a positive or negative result.

Immunogenicity response will be summarized for the binding antibody assay by treatment group and visit, as:

- *Negative*
- *Transient Positive* (i.e. single positive response that does not occur at the final assessment); or
- *Persistent Positive* (i.e. positive response that occurs at least 2 consecutive assessments or a single result at the final assessment)

Immunogenicity will also be summarized by study year, with the latest value in the year interval being reported if multiple occur during the period.

For the titer value, a table will be produced to include the number and proportion of subjects in each result category as follows:

- Positive (titer result ≤ Q1)
- Positive (titer result > Q1 - ≤ Q2)
- Positive (titer result > Q2 - ≤ Q3)
- Positive (titer result > Q3)

Where Q1 – Q3 represents quartiles of all titer values observed in the study.

The table will also summarize the highest binding assay confirmatory result obtained for each subject. If a subject has Negative and Positive results, they will be included in the Positive category. If a subject has titer results that fall into multiple titer result categories, they will be included in the highest category.

If a subject has a positive screening assessment but the confirmatory assessment is missing, the immunogenicity response will be considered as “Unknown”.

If titer value is missing, the immunogenicity response will still be assessed but that subject will not appear in the titer summary table.

8.3. Pharmacokinetic Analyses

The pharmacokinetic (PK) analyses will be based on the “Pharmacokinetic” population, unless otherwise specified.

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

9. REFERENCES

GlaxoSmithKline Document Number 2013N167980_02 Study ID BEL115466. A Multi-Center, Multinational, Randomized, Double-Blind, Study to Evaluate the Efficacy and Safety of Belimumab (HGS1006) in Combination with Azathioprine for the Maintenance of Remission in Wegener's Granulomatosis and Microscopic Polyangiitis. Effective Date 26-Feb-2015. Protocol Amendment 04, Effective Date 26-Feb-2015

GlaxoSmithKline Document Number 2015N245521_00 Study ID BEL115466. A Multi-Center, Multinational, Randomized, Double-Blind, Study to Evaluate the Efficacy and Safety of Belimumab (HGS1006) in Combination with Azathioprine for the Maintenance of Remission in Wegener's Granulomatosis and Microscopic Polyangiitis. Protocol Amendment 04, Local Amendment 01, Effective Date 06-Jul-2015.

GlaxoSmithKline Document Number 2013N167980_01 Study ID BEL115466. A Phase 3, Multi-Center, Multinational, Randomized, Double-Blind, Study to Evaluate the Efficacy and Safety of Belimumab (HGS1006) in Combination with Azathioprine for the Maintenance of Remission in Wegener's Granulomatosis and Microscopic Polyangiitis. Protocol Amendment 03 Summary of Modifications, Effective Date 04-Feb-2014.

Falk RJ, Gross WL, Guillevin L, Hoffman GS, Jayne DRW, Jennette JC, Kallenberg CGM, Luqmani R, Mahr AD, Matteson EL, Merkel PA, Specks U, Watts RA, for the American College of Rheumatology, the American Society of Nephrology, and the European League Against Rheumatism. Granulomatosis with polyangiitis (Wegener's): An alternative name for Wegener's granulomatosis. Arthritis Rheum 2011;63(4):863-864

10. APPENDICES

Section	Appendix
RAP Section 5 : General Considerations for Data Analyses & Data Handling Conventions	
Section 10.1	Appendix 1
Section 10.2	Appendix 2
Section 10.3	Appendix 3
Section 10.4	Appendix 4
Section 10.5	Appendix 5
Section 10.6	Appendix 6
Section 10.7	Appendix 7
Section 10.8	Appendix 8
Section 10.9	Appendix 9
Section 10.10	Appendix 10
Other RAP Appendices	
Section 10.11	Appendix 11
Section 10.12	Appendix 12
Section 10.13	Appendix 13

10.1. Appendix 1: Time & Events

10.1.1. Protocol Defined Time & Events

Table 15 Double-blind Treatment Phase Year One

Study Visit	Screening -60 days	Day 0	Week 2 ± 3 days	Week 4 ± 3 days	Week 8 ± 7 days	Week 12 ± 7 days	Week 16 ± 7 days	Week 20 ± 7 days	Week 24 ± 7 days	Week 28 ± 7 days	Week 32 ± 7 days	Week 36 ± 7 days	Week 40 ± 7 days	Week 44 ± 7 days	Week 48 ± 7 days	Exit[11]	8 Week Follow Up[13]	Un-scheduled
Written Informed Consent	X	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Demographics	X	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Medical History	X	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Eligibility Criteria	X	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Document Successful Induction Regimen	X	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Obtain Historical Biopsy Report (if available)	X	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Randomization	-	X	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Clinical Assessments																		
Complete Physical Exam[1]	X	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Symptom Driven Physical Exam	-	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	-	-
Weight	-	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	-	-
Vital Signs[15, 16]	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	-
12-lead ECG[16]	-	X	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
CSSRS	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	-	-
Record Concurrent Medications	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
Assess/Record Adverse Events[3]	X[2]	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X[12]	X	X
BVAS	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	-	-
VDI	X	X	-	-	-	X	-	-	X	-	-	X	-	-	X	X	-	-

Study Visit	Screening -60 days	Day 0	Week 2 ± 3 days	Week 4 ± 3 days	Week 8 ± 7 days	Week 12 ± 7 days	Week 16 ± 7 days	Week 20 ± 7 days	Week 24 ± 7 days	Week 28 ± 7 days	Week 32 ± 7 days	Week 36 ± 7 days	Week 40 ± 7 days	Week 44 ± 7 days	Week 48 ± 7 days	Exit[11]	8 Week Follow Up[13]	Un-scheduled
Laboratory Assessments																		
Serum Beta hCG	X	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
HIV, Hepatitis B, C[17]	X	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Hematology & Modified Chem-20 (non fasting)[4]	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X[14]
Coagulation – PT/aPTT and INR	X	X	-	-	X	-	-	-	X	-	-	-	-	-	X	X	-	-
Routine Urinalysis	X	-	-	-	-	X	-	-	X	-	-	X	-	-	X	-	-	-
Urine Pregnancy Test[5]	-	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	-	-
Urinary protein: urinary creatinine and creatinine clearance	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	-	X[14]
Pharmacokinetic Sampling (pre/post Belimumab dose)	-	X Pre	X Post (0-4 hrs)	-	X Pre	-	-	-	X Post (0-4 hrs)	-	-	-	-	-	X Pre	X	X	-
Pharmacogenetic Sampling[6]	-	X	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Immunogenicity (anti-belimumab antibodies)[7]	-	X	-	-	X	-	-	-	X	-	-	-	-	-	X	X	X	-
BLyS Protein	-	X	-	-	-	-	-	-	-	-	-	-	-	-	-			-
T cells/B cell subset	-	X	-	X	X	X	-	-	X	-	-	X	-	-	X	X	X	-
C3/C4 and ANCA	X	X	-	X	X	X	X	X	X	X	X	X	X	X	X	X	X	
Serum IgG	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	-
Serum IgA & IgM	X	X	-	-	-	X	-	-	X	-	-	X	-	-	X	X	X	
CRP & ESR	X	X	-	-	-	X	-	-	X	-	-	X	-	-	X	X	X	
Protocol Treatments																		
Study agent (Belimumab/Placebo)[8, 9]	-	X	X	X	X	X	X	X	X	X	X	X	X	X	X	-	-	-
AZA administration[10]	X	X	← Throughout the Study →													-	-	-

Footnotes on next page:

Table 15 **Footnotes:**

1. Complete physical examination, including height and weight.
2. Any SAEs occurring prior to the start of study agent administration and assessed as related to study participation (eg, protocol-mandated procedures, invasive tests) will be recorded on the SAE worksheet and reported as described in Section 7.2 of Protocol Amendment 04 from the time a subject consents to participate in the study.
3. All adverse events (AEs) and serious adverse events (SAEs) that are identified from the start of study agent administration (Day 0) through 8 weeks following administration of the last dose of study agent should be recorded on the Adverse Event Case Report Form (AE eCRF). SAEs that occur after the 8 week follow-up period that are assessed by the investigator as definitely, possibly or probably related to study agent must be reported to the Drug Safety designee on the SAE worksheet. (Post study SAEs will not be documented on the AE eCRF.)
4. Refer to Appendix 6 of Protocol Amendment 04 for laboratory assessments to be completed.
5. Results of urine pregnancy test at subsequent visits, if required, must be available prior to dosing. See Section 6.1 (Screening Procedures) of Protocol Amendment 04 for definition of those exempted from pregnancy testing.
6. In consenting subjects only (Appendix 9 of Protocol Amendment 04).
7. Immunogenicity samples are collected pre-dose at all time points. For any subject who had a positive antibody response at the 8-week follow-up visit (or last study visit at which immunogenicity was assessed if 8-week follow-up immunogenicity sample is not available), an attempt will be made to obtain a serum sample for anti-belimumab antibodies at least 6 months after the last dose of study agent or after completion and/or unblinding of the study, whichever is later.
8. Subjects who discontinue treatment with study agent (belimumab/placebo) will continue to be followed per this calendar schedule until relapse as defined in Section 8.5.1 of Protocol Amendment 04.
9. Subjects should remain under clinical supervision for 3 hours after completion of the first 2 study agent infusions. Should symptoms of acute hypersensitivity occur, an extended period of monitoring may be appropriate, based on clinical judgment.
10. Subjects naïve to azathioprine who develop Grade 3 or 4 leukopenia or thrombocytopenia, AST or ALT > 2 times ULN, or a severe gastrointestinal hypersensitivity reaction, characterized by severe nausea and vomiting, following initiation of azathioprine will be permitted to reduce the dose to no less than 1mg/kg/day. If the patient continues to experience the toxicities described above a switch to methotrexate at doses of up to 25 mg/week as an alternative to azathioprine will be permitted. For subjects previously identified as being intolerant to azathioprine, or for subjects identified as having undetectable or reduced activity of thiopurine methyltransferase (TPMT), it may be permissible for methotrexate to be used as an alternative to azathioprine for the maintenance of remission from the outset following discussion with the medical monitor.
11. Any visit in which the subject discontinues treatment becomes the Exit visit (ie, generally 4 weeks after the last dose of study agent). The Exit Visit should only be completed for subjects who discontinue the double blind treatment phase early or for subjects that have successfully completed the double-blind treatment phase and do not wish to participate in the open label extension phase. Subjects who discontinue treatment but have not relapsed will remain on the double blind study visit schedule. For subjects who complete the double blind phase and enter the open label phase, refer to Table 17 for visit details.
12. In subjects who discontinue study agent all AEs and SAEs will be reported on the AE eCRF through 8 weeks following administration of the last dose of study agent. After this time, all SAEs, regardless of relationship to study drug, will be collected until relapse or the study is analyzed for the primary endpoint, whichever occurs first.
13. The 8 week follow-up visit is to occur approximately 8 weeks after the last dose of study agent.
14. Hematology and Modified Chem 20, Urinary protein, urinary creatinine and creatinine clearance are not mandatory at Unscheduled Visits and should be obtained only when determined to be clinically indicated by the Principal Investigator.
15. Vital signs include temperature, sitting blood pressure (systolic and diastolic) and heart rate.
16. Complete prior to dosing.
17. HIV, Hepatitis B surface antigen, anti-HBc, anti-HBs and hepatitis C antibody (if hepatitis C antibody positive, HCV RNA-PCR assay will be performed on a subsequent blood sample to confirm the results).

Table 16 Double-blind Treatment Phase Additional Years

Study Visit	Week 4 ± 7 days	Week 8 ± 7 days	Week 12 ± 7 days	Week 16 ± 7 days	Week 20 ± 7 days	Week 24 ± 7 days	Week 28 ± 7 days	Week 32 ± 7 days	Week 36 ± 7 days	Week 40 ± 7 days	Week 44 ± 7 days	Week 48 ± 7 days	Exit[7]	8 Week Follow Up[9]	Un-scheduled
Clinical Assessments															
Symptom Driven Physical Exam	X	X	X	X	X	X	X	X	X	X	X	X	X	-	-
Weight	X	X	X	X	X	X	X	X	X	X	X	X	X	-	-
Vital Signs[11, 12]	X	X	X	X	X	X	X	X	X	X	X	X	X	X	-
C-SSRS	X	X	X	X	X	X	X	X	X	X	X	X	X	-	-
Record Concurrent Medications	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
Assess/Record Adverse Events[1]	X	X	X	X	X	X	X	X	X	X	X	X	X[8]	X	X
BVAS	X	X	X	X	X	X	X	X	X	X	X	X	X	-	-
VDI	-	-	X	-	-	X	-	-	X	-	-	X	X	-	-
Laboratory Assessments															
Hematology & Modified Chem-20 (non fasting)[2]	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X[10]
Coagulation – PT/aPTT and INR	-	-	-	-	-	X	-	-	-	-	-	X	X	-	-
Routine Urinalysis	-	-	X	-	-	X	-	-	X	-	-	X	-	-	-
Urine Pregnancy Test[3]	X	X	X	X	X	X	X	X	X	X	X	X	X	-	-
Urinary protein: urinary creatinine and creatinine clearance	X	X	X	X	X	X	X	X	X	X	X	X	X	-	X[10]
Pharmacokinetic Sampling (pre or post Belimumab dose)	-	-	-	-	-	X Pre	-	-	-	-	-	X Pre	X	X	-
Immunogenicity (anti- belimumab antibodies)[4]	-	-	-	-	-	X	-	-	-	-	-	X	X	X	-
T cells/B cells	X	-	-	-	-	X	-	-	-	-	-	X	X	X	-
C3/C4 and ANCA	X	X	X	X	X	X	X	X	X	X	X	X	X	X	-
Serum IgG	-	-	X	-	-	X	-	-	X	-	-	X	X	X	-
Serum IgA & IgM	-	-	X	-	-	X	-	-	-	-	-	-	X	X	-
CRP & ESR	-	-	X	-	-	X	-	-	-	-	-	-	X	X	-

Study Visit	Week 4 ± 7 days	Week 8 ± 7 days	Week 12 ± 7 days	Week 16 ± 7 days	Week 20 ± 7 days	Week 24 ± 7 days	Week 28 ± 7 days	Week 32 ± 7 days	Week 36 ± 7 days	Week 40 ± 7 days	Week 44 ± 7 days	Week 48 ± 7 days	Exit[7]	8 Week Follow Up[9]	Un-scheduled
Protocol Treatments															
Study Agent (Belimumab/Placebo)[5]	X	X	X	X	X	X	X	X	X	X	X	X	-	-	-
AZA administration[6]	X	← Throughout the Study →											-	-	-

Table 16 **Footnotes:**

1. All adverse events (AEs) and serious adverse events (SAEs) that are identified from the start of study agent administration (Day 0) through 8 weeks following administration of the last dose of study agent should be recorded on the Adverse Event Case Report Form (AE eCRF). SAEs that occur after the 8 week follow-up period that are assessed by the investigator as definitely, possibly or probably related to study agent must be reported to the Drug Safety designee on the SAE worksheet. (Post study SAEs will not be documented on the AE eCRF.)
2. Refer to Appendix 6 of Protocol Amendment 04 for laboratory assessments to be completed.
3. Results of urine pregnancy test at subsequent visits, if required, must be available prior to dosing. See Section 6.1 (Screening Procedures) of Protocol Amendment 04 for definition of those exempted from pregnancy testing.
4. Immunogenicity samples are collected pre-dose at all timepoints. For any subject who had a positive antibody response at the 8-week follow-up visit (or last study visit at which immunogenicity was assessed if 8-week follow-up immunogenicity sample is not available), an attempt will be made to obtain a serum sample for anti-belimumab antibodies at least 6 months after the last dose of study agent or after completion and/or unblinding of the study, whichever is later.
5. Subjects who discontinue treatment with study agent (belimumab/Placebo) will continue to be followed per this calendar schedule until relapse as defined in Section 8.5.1 of Protocol Amendment 04.
6. Subjects naïve to azathioprine who develop Grade 3 or 4 leukopenia or thrombocytopenia, AST or ALT > 2 times ULN, or a severe gastrointestinal hypersensitivity reaction, characterized by severe nausea and vomiting, following initiation of azathioprine will be permitted to reduce the dose to no less than 1mg/kg/day. If the patient continues to experience the toxicities described above a switch to methotrexate at doses of up to 25 mg/week as an alternative to azathioprine will be permitted.
7. Any visit in which the subject discontinues treatment becomes the Exit visit (ie, generally 1-4 weeks after the last dose of study agent). The Exit Visit should only be completed for subjects who discontinue the double blind treatment phase early or when subjects have successfully completed the double-blind treatment phase and do not wish to participate in the open label extension phase. For subjects who complete the double blind phase and enter the open label phase, refer to Table 17 for visit details.
8. In subjects who discontinue study agent all AEs and SAEs will be reported on the AE eCRF through 8 weeks following administration of the last dose of study agent. After this time, all SAEs, regardless of relationship to study drug, will be collected until relapse or the study is analyzed for the primary endpoint, whichever occurs first.
9. The 8 week follow-up visit is to occur approximately 8 weeks after the last dose of study agent.
10. Hematology, Modified Chem 20, Urinary protein/urinary creatinine and creatinine clearance are not mandatory at Unscheduled Visits and should be obtained only when determined to be clinically indicated by the Principal Investigator.
11. Vital signs include temperature, sitting blood pressure (systolic and diastolic) and heart rate.
12. Complete prior to dosing.

Table 17 Open Label Extension Phase

Study Visit	Day 0[7]	Week 4 ± 7 days	Week 8 ± 7 days	Week 12 ± 7 days	Week 16 ± 7 days	Week 20 ± 7 days	Week 24 ± 7 days	Week 28/ Exit[8]	8 Week Follow Up[9]	Un-scheduled
Clinical Assessments										
Symptom Driven Physical Exam	X	X	X	X	X	X	X	X	-	-
Weight	X	X	X	X	X	X	X	X	-	-
Vital Signs[11, 12]	X	X	X	X	X	X	X	X	X	-
Record Concurrent Medications	X	X	X	X	X	X	X	X	X	X
Assess/Record Adverse Events[1]	X	X	X	X	X	X	X	X	X	X
BVAS	X	-	-	-	-	-	X	X	-	-
VDI	X	-	-	-	-	-	X	X	-	-
Laboratory Assessments										
Labs: Hematology & Modified Chem-20 (non fasting)[2]	X	-	-	-	-	-	X	X	X	X[10]
Urine Pregnancy Test[3]	X	X	X	X	X	X	X	X	-	-
Urinary protein: urinary creatinine and creatinine clearance	X	-	-	-	-	-	X	X	-	X[10]
Immunogenicity (anti- belimumab antibodies)[4]	X	-	-	-	-	-	X	X	X	-
T cells/B cell subset	X	-	-	-	-	-	X	X	X	-
C3/C4 and ANCA	X	-	-	-	-	-	X	X	X	-
Serum IgG	-	-	X	-	-	-	X	X	-	-
Serum IgA & IgM	-	-	-	-	-	-	X	X	-	-
CRP & ESR	X	-	-	-	-	-	X	X	X	-
Protocol Treatments										
Study agent (belimumab)[5]	X	X	X	X	X	X	X	-	-	-
AZA administration[6]	X	← Throughout the Study →						X	-	-

Footnotes on next page:

Table 17 **Footnotes:**

1. All adverse events (AEs) and serious adverse events (SAEs) that are identified from the start of study agent administration (Day 0) through 8 weeks following administration of the last dose of study agent should be recorded on the Adverse Event Case Report Form (AE eCRF).
2. Refer to Appendix 6 of Protocol Amendment 04; Local Amendment 01 for Belgium for laboratory assessments to be completed.
3. Results of urine pregnancy test at subsequent visits, if required, must be available prior to dosing. See Section 6.1 (Screening Procedures) of Protocol Amendment 04; Local Amendment 01 for Belgium for definition of those exempted from pregnancy testing.
4. Immunogenicity samples are collected pre-dose at all timepoints. For any subject who had a positive antibody response at the 8-week follow-up visit (or last study visit at which immunogenicity was assessed if 8-week follow-up immunogenicity sample is not available), an attempt will be made to obtain a serum sample for anti-belimumab antibodies at least 6 months after the last dose of study agent or after completion and/or unblinding of the study, whichever is later.
5. Subjects should remain under clinical supervision for 3 hours after completion of the first 2 infusions. Should symptoms of acute hypersensitivity occur, an extended period of monitoring may be appropriate, based on clinical judgment.
6. AZA/MTX continued at the discretion of the investigator.
7. Day 0 is first visit in the extension phase of the trial and represents the first belimumab administration for placebo subjects.
8. Any visit in which the subject discontinues treatment becomes the Exit visit (ie generally 1-4 weeks after the last dose of study agent).
9. The 8 week follow-up visit is not required for subjects who participate in the separate continuation protocol.
10. Hematology, Modified Chem 20, Urinary protein/urinary creatinine and creatinine clearance are not mandatory at Unscheduled Visits and should be obtained only when determined to be clinically indicated by the Principal Investigator.
11. Vital signs include temperature, sitting blood pressure (systolic and diastolic) and heart rate.
12. Complete prior to dosing.

10.2. Appendix 2: Treatment States and Phases

10.2.1. Treatment Phases

Assessments and events will be classified according to the time of occurrence relative to the start date of study treatment (Day 0).

Treatment Phase	Definition
Pre-Treatment	Date < First Exposure Date
On-Treatment	Subjects not entering open-label phase: First Exposure Date ≤ Date ≤ Last Exposure Date + 4 Weeks
	Subjects entering open-label phase: First Exposure Date ≤ Date ≤ Open-Label Treatment Start Date
Post-Treatment	Subjects not entering open-label phase: Date > Last Exposure Date + 4 Weeks
Open-Label Treatment[1]	Open-Label Treatment Start Date < Date ≤ Open-Label Treatment Stop Date + 4 Weeks
Post-Open-Label Treatment[1]	Date > Open-Label Treatment Stop Date + 4 Weeks

[1] For subjects entering the Open-Label phase only.

10.2.2. Treatment States

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

10.2.2.1. Treatment States for Adverse Events

The following rules will be used for allocating AEs to study year:

- Each AE will be reported in the year it started.
- AEs continuing for more than one treatment year will only be reported in the year they first occurred.
- If distinct episodes (start and stop date) of an AE are reported in multiple years, the AE will be reported once in each study year in which the unique event began.
    - AEs with partial start and/stop dates will be assumed to have occurred on treatment unless there is evidence through comparison of partial dates to suggest otherwise.
    - Where possible the non-missing information will be used to assign the AE to a study year, if the non-missing information is insufficient to assign the AE to a study year then the AE will be assigned to the earliest plausible study year.
- If the AE onset date is missing assume the start date was in Year 0-1. The event will be reported in Year 1 and "Any Time Post Baseline."
- If the AE end date is missing assume the AE continued until the end of study. The AE will be reported in year of onset and "Any Time Post Baseline."
- AEs that begin and end on the first day of treatment will count in the Year 0-1 period and for "Any Time Post Baseline."

Table 18 Example of Assigning AEs to Study Years

Scenario	Pre-Treatment	Year 0-1	Year 1-2	Year 2-3	Year 3-4	Year 4-5	After End of Treatment
A	←			→			
B		←				→	
C		←					→
D	← →		← →				

NOTE: Arrow indicates the start and stop date of a single AE.

Scenario	Assignment of AE to Study Year					
	Any Time Post-Baseline	Year 0-1	Year 1-2	Year 2-3	Year 3-4	Year 4-5
A	No	No	No	No	No	No
B	**Yes**	**Yes**	No	No	No	No
C	**Yes**	**Yes**	No	No	No	No
D	Yes	No	**Yes**	No	No	No

10.3. Appendix 3: Data Display Standards & Handling Conventions

10.3.1. Study Treatment & Subgroup Display Descriptors

Treatment Group Descriptions			
RandAll NG		Data Displays for Reporting	
Code	Description	Description	Order [1]
1	Belimumab 10 mg/kg	Belimumab	2
0	Placebo	Placebo	1

NOTES:

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

For the open-label phase, descriptions for listings will be as follows:

- Placebo to Belimumab
- Belimumab to Belimumab

10.3.2. Baseline Definition & Derivations

10.3.2.1. Baseline Definitions

Day 0 is defined as date of first exposure.

For all endpoints the baseline value will be the latest pre-initial-dose assessment.

10.3.2.2. Derivations and Handling of Missing Baseline Data

Definition	Reporting Details
Change from Baseline	= Post-Dose Visit Value – Baseline
% Change from Baseline	= 100 x [(Post-Dose Visit Value – Baseline) / Baseline]
Maximum Change from Baseline	= Calculate the change from baseline at each given time point and determine the maximum change

NOTES :

- Unless otherwise specified, the baseline definitions specified in Section 10.3.2.1 Baseline Definitions will be used for derivations for endpoints / parameters and indicated on summaries and listings.
- Unless otherwise stated, if baseline data is missing no derivation will be performed and will be set to missing.
- The baseline definition will be footnoted on all change from baseline displays.

10.3.3. Reporting Process & Standards

Reporting Process	
Software	
• The currently supported version of SAS software will be used.	
Reporting Area	
HARP Server	: us1salx00259
HARP Area	: \arprod\gsk1550188\bel115466\final\
QC Spreadsheet	: \arwork\gsk1550188\bel115466\documents\QC_BEL115466.xlsm
Analysis Datasets	
• POP, DS, DSYEAR, TRT, AE, AEANAL, AEMQ, CONMEDS, CMANAL, DV, ELIG, MEDHIST, DEMO, RACE, EXPOSURE, VITALS, VSANAL, LAB, LABTOX, IMMUNO, IMMUNTOX, IMMUNOGLO, CSSRSV4, CSSRSSUM, SURVIVAL, PK, BVAS, TTE, VDI, BIOMARK, RELAPSE, REMISION, MEDDRA, PKCNC, TF1, TF2	
Generation of RTF Files	
• RTF files will be generated for all reporting efforts.	

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

Reporting Standards	
Unscheduled Visits	
• Unscheduled visits will not be included in summary tables with the exception of certain summaries by year interval in which unscheduled visits may appear in the "anytime post baseline" category where specified e.g. worst laboratory toxicity grades. • Unscheduled visits will not be included in figures. • All unscheduled visits will be included in listings.	
Descriptive Summary Statistics	
Continuous Data	Refer to IDSL Statistical Principle 6.06.1
Categorical Data	N, n, frequency, %
Reporting of Pharmacokinetic Concentration Data	
Descriptive Summary Statistics	Refer to IDSL Statistical Principle 6.06.1 Assign zero to NQ values (Refer to GUI_51487 for further details)
Graphical Displays	
• Refer to IDSL Statistical Principals 7.01 to 7.13.	

10.4. Appendix 4: Derived and Transformed Data

10.4.1. General

Date of Last Double-blind Treatment Period Visit
Efficacy endpoints will be assessed from Day 0 to the last double-blind treatment period visit. Last treatment period visit date in the double-blind phase will be defined in the following hierarchical order for all subjects: 1. Exit visit 2. Date of death 3. Last contact (this includes adverse events dates, concomitant medications dates, unscheduled visits and follow-up visit but does not include "END OF DOUBLE-BLIND" or "SURVIVAL" visits)
Multiple Measurements at One Time Point
• Mean of the measurements will be calculated and used in any derivation of summary statistics but if listed, all data will be presented. • If there are two values within a time window the value closest to the target day for that window will be used. If values are the same distance from the target then the mean will be taken. • Subjects having both High and Low values for Normal Ranges at any post-baseline visits for safety parameters will be counted in both the High and Low categories of "Any visit post-baseline" row of related summary tables.
Study Day

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

Study Completion
• Subjects that receive their final dose of IP at any time on or after 28 days prior to the published window (20MAY2016 – 17JUN2016) will automatically be eligible for study completion. • Any subject that is declared a completer on the end of double-blind form prior to this time point will be queried at the site-level. Based on the response, a study team decision will be made as to whether the completion flag should be amended. • A subject is therefore considered a completer if they are declared a completer on the end of double-blind form.

For subject completion status by year interval, overall status will be determined as follows:

- DSFAIL = "Y" → "Withdrawn"
- COMPL = "Y" → "Completed"

Where DSFAIL is the flag for premature study withdrawal and COMPL is the subject completion flag

A subject's status within a given year interval in the double-blind treatment period will be ascertained using the following conditions:

Condition	Subject Status
DSFAIL = "N" and COMPL = "N"	"ongoing"
DSFAIL = "N" and COMPL = "Y" and DBEXITDT > AENDT	"ongoing"
DSFAIL = "N" and COMPL = "Y" and ASTDT ≤ DBEXITDT ≤ AENDT	"completed"
DSFAIL = "Y" and COMPL = "N" and DBEXITDT ≤ ASTDT	"ongoing"
DSFAIL = "Y" and COMPL = "N" and ASTDT ≤ DBEXITDT ≤ AENDT	"withdrawn"

ASTDT is the start date of the year interval, AENDT is the end date of the year interval and DBEXITDT is the double-blind exit date.

Study Drug Completion

A subject's IP completion status within a given year interval in the double-blind treatment period will be ascertained using the following conditions:

Condition	Subject IP Completion Status
SDSTOPP = "N" and max(EXSTDT) > AENDT	"ongoing"
SDSTOPP = "N" and ASTDT ≤ max(EXSTDT) ≤ AENDT	"completed"
SDSTOPP = "Y" and max(EXSTDT) ≤ ASTDT	"ongoing"
SDSTOPP = "Y" and ASTDT ≤ max(EXSTDT) ≤ AENDT	"withdrawn"

ASTDT is the start date of the year interval, AENDT is the end date of the year interval and SDSTOPP is the flag for premature IP discontinuation.
EXSTDT is exposure start date.

The maximum exposure includes double-blind treatment exposure only.

10.4.2. Study Population

Demographics
Age

• Age will be calculated from birth date to Day 0.
• GSK standard IDSL algorithms will be used for calculating age where birth date will be imputed as follows:
  o Any subject with a missing day will have this imputed as day '15'.
  o Any subject with a missing date and month will have this imputed as '30th June'.
• Birth date will be presented in listings as 'YYYY'.

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

Extent of Exposure
Double-blind Phase
• Number of days of exposure to study drug will be calculated based on the formula: **Duration of Exposure in Days = (Last Exposure Date – First Exposure Date) + 28** • Subjects who were randomized but did not report a treatment start date will be categorized as having zero days of exposure.
Open-label Phase

Extent of Exposure
Subjects that received placebo during the double-blind phase • Number of days of exposure to study drug will be calculated based on the formula: **Duration of Exposure in Days = (Last Open-label Exposure Date – First Open-label Exposure Date) + 28** Subjects that received belimumab during the double-blind phase • Number of days of exposure to study drug will be calculated based on the formula: **Duration of Exposure in Days = (Last Open-label Exposure Date – First Double-blind Exposure Date) + 28** • If there are any treatment breaks during the study, exposure data will be adjusted accordingly.

Time to Withdrawal from Study Treatment
• Time to withdrawal from treatment will be calculated based on the formula: **Time to Withdrawal from IP in Days = (Last Exposure Date – First Exposure Date) + 1** • Subjects that complete the double-blind period (i.e. do not discontinue treatment prematurely) will be censored at the final dose of IP.
Time to Withdrawal from Study
• Subjects that withdraw from the study prematurely will be identified using DS.DSFAIL = "Y". • Time to withdrawal from the study will be calculated based on the formula: **Time to Study Withdrawal (Days) = (Exit Visit Date – Treatment Start Date) + 1** • Where exit visit is not available, the last visit in the double-blind treatment period will be used. • Subjects that complete the double-blind phase will be censored at their last visit in the double-blind treatment period. (See Appendix 4 for further detail).

10.4.3. Safety

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

Medications Categories and Prohibited Medication

- Concomitant medications are defined as medications that start on or before the first exposure date to study treatment, and end on or after the first exposure date to study treatment, or medications that start after the first exposure date to study treatment. Note that medications with partial or missing start and/or stop dates will be assumed to be concomitant unless there is evidence through comparison of partial dates to suggest otherwise.
- Concomitant medications will be reviewed and may be assigned to one of two categories (corticosteroids or immunosuppressants), based on their GSK Drug Dictionary Version 1.3 coded terms, for summarization throughout the course of the study and defined as:

Medication Category	Definition
Corticosteroids	ATC code starts with "H02" and route is considered to be systemic (intravenous, intramuscular, subcutaneous, intra-dermal, and oral routes, intra-arterial, intrapleural, intraperitoneal, parenteral, rectal, sublingual, transdermal).
Immunosuppressants	ATC code starts with "L04A", or the WHO Drug term contains CYCLOPHOSPHAMIDE or MERCATOPURINE or METHOTREXATE.

Average Daily Steroid Dose

- BEL115466 collects concomitant medications, including corticosteroids, throughout the study. Note that to determine average daily steroid dose and for the analysis of steroid use, all steroid dosages are converted to a prednisone equivalent dosage in milligrams.
- The average daily prednisone dose takes into account all steroids taken systemically for both **vasculitis and non-vasculitis reasons** except where specified in the treatment failure rules. At baseline, the average daily prednisone dose is the sum of all prednisone doses over 7 consecutive days up to, but not including Day 0, divided by 7.
- While on treatment, the average daily prednisone dose is the sum of all prednisone doses over 7 consecutive days up to and including the day of interest, divided by 7, unless otherwise specified.

Prednisone Equivalent Daily Dose Conversions

- Corticosteroids with CMTYPCD equal to 154 do not require conversion to prednisone equivalent as these are maintenance therapies which are required to be entered into the eCRF as prednisone equivalent.
- Reported dose for systemic steroid is converted to prednisone equivalent dose using conversion factor for each particular medication (refer to online calculator http://www.globalrph.com/corticocalc.htm).

DOSE2 (prednisone equivalent dose in mg) = DOSE (collected dose in mg) x Conversion Factor

DD (daily dose in mg/day) = DOSE2 (prednisone equivalent dose in mg) x Frequency Factor

Preferred Term	Conversion Factor for Prednisone-Equivalent Dose (mg)
BETAMETHASONE	8.33
BETAMETHASONE DIPROPIONATE	8.33
BETAMETHASONE SODIUM PHOSPHATE	8.33
BETAMETHASONE VAL	8.33
CELESTONA BIFAS	8.33
CORTISONE	0.2
CORTISONE ACETATE	0.2
DEFLAZACORT	5/6
DEPO-MEDROL MED LIDOKAIN	1.25
DEXAMETHASONE	6.67
DEXAMETHASONE SODIUM PHOSPHATE	6.67
FLUOCORTOLONE	3
HYDROCORTISONE	0.25
HYDROCORTISONE ACETATE	0.25
HYDROCORTISONE SODIUM SUCCINATE	0.25
MEPREDNISONE	1.25
METHYLPREDNISOLONE	1.25
METHYLPREDNISOLONE ACEP	1.25
METHYLPREDNISOLONE ACETATE	1.25
METHYLPREDNISOLONE SODIUM SUCCINATE	1.25
PARAMETHASONE	2.5
PREDNISOLONE	1
PREDNISOLONE SODIUM PHOSPHATE	1
PREDNISONE	1
PREDNISONE ACETATE	1
TRIAMCINOLONE	1.25
TRIAMCINOLONE ACETONIDE	1.25

10.4.4. Efficacy

Time to Event

- Time to event will be defined as:

Time to Event = Event Date – Treatment Start Date +1

BVAS

- BVAS is assessed at Day 0 and then at every visit during the double-blind treatment phase.
- Absolute change in BVAS at Visit X is interpreted as "observed" change and will be calculated based on the formula:

Absolute Change in BVAS at Visit X = BVAS at Visit X – BVAS at Day 0

- An increase in BVAS is defined as one or more points higher than that assessed at baseline.

Major Items

- Major BVAS items can be identified as follows:

Organ System	Description	Disease Code
Cutaneous	Gangrene (Extensive tissue necrosis)	2.5
Mucous membranes/Eyes	Sudden visual loss (Acute loss of vision	3.9
	Retinal changes (vascular/thrombosis/exudates/hemorrhage)	3.11
ENT	Sensorineural hearing loss	4.6
Chest	Massive haemoptysis/alveolar hemorrhage	5.7
	Respiratory failure	5.8
Cardiovascular	Ischemic cardiac pain	6.5
	Cardiomyopathy	6.6
	Congestive cardiac failure	6.7
Abdominal	Ischemic abdominal pain	7.4
Renal	Rise in creatinine > 30% or creatinine clearance fall > 25%	8.5
Nervous system	Cerebrovascular accident	9.6
	Spinal cord lesion	9.7
	Cranial nerve palsy	9.8
	Mononeuritis multiplex	9.10

- For the primary endpoint, where a subject attains a total score ≥ 6 **and** a major BVAS item at an assessment, both reasons for relapse should be presented in relevant displays. If a subject relapses due to receipt of prohibited medication on the same day as a BVAS relapse, both reasons for relapse will be given. If all three conditions are met, all three reasons for relapse will be displayed.
- Similarly, where the endpoint is any minor or major item, if a subject attains both categories at a single assessment, both reasons for relapse should be presented in relevant displays.

BVAS
Vasculitis-related Relapse
Vasculitis-related relapses include all relapses occurring as a result of a BVAS ≥ 6 or a major BVAS item or receipt of a prohibited medication resulting in treatment failure that has been adjudicated by clinical, safety and statistics representatives as being required for a vasculitis indication. Prohibited medications adjudicated as "vasculitis-related" are extracted from the TF2 dataset using the flag VASFL = "Y". Subjects adjudicated as treatment failures with VASFL = "N" will be censored at their most recent BVAS assessment, prior to the treatment failure date.

VDI
• VDI is assessed at Day 0 and then every 12 weeks during the double-blind treatment phase and should be presented as such. • Absolute change in VDI at Visit X is interpreted as "observed" change and will be calculated based on the formula: **Absolute Change in VDI at Visit X = VDI Score at Visit X – VDI Score at Day 0** • An increase in VDI is defined as one or more points higher than that assessed at Day 0.

Remission
• Remission is defined as a BVAS = 0 and corticosteroid dose ≤ 10 mg/day.

B Cell and T Cell Subsets
• All endpoints in units GI/L will be converted from GI/L to cells/cumm using the following conversion formula: New Result = Original Result * 1000 • Rare B cells will be normalized using the following formula: Normalized count/mL = [(rare cell event count) / (CD19+ event count)] * (CD19+ cells/mm^3 or uL) * 1000

10.5. Appendix 5: Premature Withdrawals & Handling of Missing Data

10.5.1. Premature Withdrawals

Element	Reporting Detail
General	• Subject study completion for the double-blind phase (i.e. as specified in the protocol) is defined as when 12 months have elapsed following randomization of the last subject with further details given in section 10.4.1. • Withdrawn subjects are not replaced in the study. • All available data from subjects who are withdrawn from the study will be listed and all available planned data will be included in summary tables and figures, unless otherwise specified.

10.5.2. Handling of Missing Data

Element	Reporting Detail

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

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

10.5.2.1. Handling of Missing Dates

Element	Reporting Detail
General	Partial dates will be displayed as captured in subject listing displays.
Concomitant Medications	• Where CMSTDT is completely missing but CMENDT is on or after Day 0, the CMSTDT will be imputed as TRTSDT. • Where CMSTDT is completely missing but CMONGOING = "Y", the CMSTDT will be imputed as TRTSDT and the medication will be considered as ongoing.

Adverse Events	• The eCRF allows for the possibility of partial dates (i.e., only month and year) to be recorded for AE start and end dates; that is, the day of the month may be missing. In such a case, the following conventions will be applied for calculating the time to onset and the duration of the event:
	  • Missing Start Day: First of the month will be used unless this is before the start date of study treatment; in this case the study treatment start date will be used and hence the event is considered On-treatment as per Appendix 2.
	  • Missing Stop Day: Last day of the month will be used, unless this is after the

Element	Reporting Detail
	stop date of study treatment; in this case the study treatment stop date will be used. • Completely missing start or end dates will remain missing, with no imputation applied. Consequently, time to onset and duration of such events will be missing.
Relapse	• If the date of relapse is completely missing, no imputation will be applied and subjects will be censored at the last available BVAS assessment.

10.5.2.2. Handling of Partial Dates

Element	Reporting Detail

Concomitant Medications	• For records where the year of the partial date is prior to or after the year of TRTSDT, impute with 01 for day and January for month, as needed, to assume that the duration of the concomitant medication was the longest possible duration.
	• For records where year matches the year of TRTSDT:
	  • If month is available & month is prior to or after the month of TRTSDT, set day to 01.
	  • If the month is the same as the month of TRTSDT, set the day to the same day as TRTSDT, to assume the AE started on treatment and with the longest possible duration.
	• If month is not available, set the entire date to TRTSDT.
	• End dates for concomitant medications will not be imputed, and the medication will be considered ongoing.

Adverse Events	• For partial or missing dates AE start dates, imputations will be performed conservatively to place the AE on or after TRTSDT (Treatment Start Date): unless there is evidence to the contrary:
	• For records where the year of the partial date is prior to or after the year of TRTSDT, impute with 01 for day and January for month, as needed, to assume that the duration of the AE was the longest possible duration.
	• For records where year matches the year of TRTSDT:
	  • If month is available & month is prior to or after the month of TRTSDT, set day to 01.
	  • If the month is the same as the month of TRTSDT, set the day to the same day as TRTSDT, to assume the AE started on treatment and with the longest possible duration.
	• If month is not available, set the entire date to TRTSDT, again to assume that the AE is treatment emergent and has the longest possible duration.

Relapse	• No imputation for partial dates will be performed. • Subjects will be censored at the last available BVAS assessment.

10.6. Appendix 6: B Cell and T Cell Subsets

BICATCD (B Cells)	LBTESTCD (T Cells)	Client Analyte name
CD19		Total CD19+ B-cells (CD19+)
CD20		Absolute B cell subsets CD20+
CDX136		CD20+/27– naïve
CDX137		CD20+/27+ memory
CDX141*/CDX155*[1]		CD20+/69+activated
CDX143*		CD138+/CD20- 138 plasma cells
CDX145*		CD138+/CD20+ plasmacytoid
CDX154*		CD27hi/CD20- short-lived plasma
CDX200*[2]		CD19+ CD24b+ CD38b+ CD27-IgD+ CD10
	Concentration: CD4+_BLC Percentage: CD4+_BLQ	CD3+/CD4+
	Concentration: CD8+_BLC Percentage: CD8+_BLQ	CD3+/CD8+

* Denotes rare B cell subset

[1] Concentration and percentage of CD20+/69+ correspond to BICATCD CDX141, whereas events correspond to CDX155.

[2] CD10+ transitional B cells are represented by CDX200 CD19+(CD24b+CDCD38b+CD27-IgD+CD10)

10.7. Appendix 7: BVAS Activity Assessment Form

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

10.8. Appendix 8: BVAS Item Scoring

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

10.9. Appendix 9: Vasculitis Damage Index (VDI)

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Final - 16 JUL 13

Protocol Identifier	Subject Identifier	Date of Assessment	Visit Description ✓*one:*		
BEL115466		Day Month Year	☐ Screening ☐ Day 0	☐ Year ____ ☐ Week 12 ☐ Week 24 ☐ Week 36 ☐ Week 48 ☐ Exit	☐ OL Day 0 ☐ OL Week 24 ☐ OL Week 28/Exit

VASCULITIS DAMAGE INDEX (VDI)

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

10.10. Appendix 10: Laboratory Parameters & Adverse Events Grading

10.10.1. Laboratory Parameters

Hematology

Total white blood cell count
Differential:
- Absolute Neutrophils
  - Segmented Neutrophils
  - Band Neutrophils
  - Myelocytes
  - Metamylocytes
  - Promyelocytes
- Lymphocytes
- Monocytes
- Eosinophils
- Basophils

Hemoglobin
Hematocrit
Red blood cell (RBC) count
Platelet count
Prothrombin time (PT)
Partial thromboplastin time (PTT)
INR
Serum Pregnancy

Urinalysis

Protein
Glucose
Ketones
Occult blood
Microscopic examination including:
- WBC per hpf
- RBC per hpf
- Casts (specified by type eg, RBC, WBC)

Spot Urine (protein : creatinine ratio)
Urine Pregnancy

Biological Markers

FACS of peripheral lymphocytes:
T cell subsets: CD3+/CD4+, CD3+/CD8+
B lymphocytes (CD19+, CD20+, CD20+/CD69+ activated, CD27hi/CD20- short-lived plasma, CD27+/CD20+ memory, CD27-/CD20+ naïve, CD138+/CD20- 138 plasma cells, CD138+/CD20+ plasmacytoid, CD27−/IgD+/CD10+ transitional)

BLyS protein
Serum complement (C3 and C4)
C-Reactive Protein (CRP)
Erythrocyte sedimentation rate (ESR)

Immunoglobulins

Serum immunoglobulin isotypes: IgG, IgM, IgA

PK and Immunogenicity

Autoantibodies

ANCA (anti-PR3; anti-MPO)

Modified Chem-20

Electrolytes:
- Sodium
- Potassium
- Magnesium
- Chloride
- Carbon dioxide
- Calcium adjusted for Albumin
- Inorganic Phosphate

Amend 01 22Jun12

Enzymes:
- SGOT (AST)
- SGPT (ALT)
- Alkaline Phosphatase
- Gamma glutamyl transferase (GGT)
- Lactate dehydrogenase (LDH)

Other:
- Creatinine
- Blood urea nitrogen (BUN)
- BUN/creatinine ratio
- Bilirubin, total
- Protein, total
- Albumin
- Uric acid
- Glucose
- HIV-1/2 antibody
- Hepatitis C antibody (± HCV RNA PCR for confirmation of positive antibody test)

Amend 02 25Apr13

- Hepatitis B surface antigen
- Hepatitis B surface and core antigen antibodies

Amend 02 25Apr13

- Estimated Creatinine Clearance/ GFR (Cockcroft-Gault)

Liver event follow-up assessments:

Amend 02 25Apr13

- Hepatitis A IgM antibody
- HBsAg and HB Core antibody (IgM)
- Hepatitis C RNA
- Cytomegalovirus IgM antibody
- Epstein-Barr viral capsid antigen IgM antibody
- Hepatitis E IgM antibody
- CPK
- Anti-smooth muscle antibody
- Type 1 anti-liver kidney microsomal antibodies

Amend 02 25Apr13

[1]Institution or country specific guidelines for blood sample volume limits must be followed in collection of the subsequent blood sample.

10.10.2. Adverse Events Grading

HEMATOLOGY	GRADE 1 MILD	GRADE 2 MODERATE	GRADE 3 SEVERE	GRADE 4 POTENTIALLY LIFE-THREATENING
Hemoglobin	> 9.5-11.0 g/dL	> 8.0-9.5 g/dL	6.5-8.0 g/dL	< 6.5 g/dL
Leukocytes	3000-3999/mm3	2000-2999/mm3	1000-1999/mm3	< 1000/mm3
Absolute Neutrophil Count	1500-1999/mm3	1000-1499/mm3	500-999/mm3	< 500/mm3
Platelets	75,000-99,999/mm3	50,000–74,999/mm3	25,000-49,999/mm3	< 25,000/mm3
Prothrombin Time (PT)	> 1.0-1.25 x ULN*	> 1.25-1.5 x ULN	> 1.5-3.0 x ULN	> 3.0 x ULN
Partial Thromboplastin Time (PTT)	> 1.0-1.66 x ULN	> 1.66-2.33 x ULN	> 2.33-3.0 x ULN	> 3.0 x ULN
Methemoglobin	5.0-10.0 %	10.1-15.0 %	15.1-20.0 %	> 20%

*ULN = Upper Limit of Normal.

Modified from DMID Adult Toxicity Tables, 2001

CARDIOVASCULAR	GRADE 1 MILD	GRADE 2 MODERATE	GRADE 3 SEVERE	GRADE 4 POTENTIALLY LIFE-THREATENING
Cardiac Arrhythmia	-	Asymptomatic/transient; dysrhythmia; no treatment req	Recurrent/persistent dysrhythmia. Symptomatic; treatment req	Unstable dysrhythmia hospitalization and treatment required
Hypotension	Transient orthostatic hypotension, no treatment	Symptoms correctable with oral fluid treatment	IV fluid req, no hospitalization req	Hospitalization req
Hypertension	Transient, increase > 20 mm/Hg; no treatment	Recurrent; chronic increase > 20 mm/Hg, treatment req	Acute treatment req; out patient hospitalization possible	Hospitalization req
Pericarditis	Minimal effusion	Mild/moderate asymptomatic effusion, no treatment	Symptomatic effusion, pain, ECG changes	Tamponade OR pericardiocentesis OR surgery req
Hemorrhage, Blood Loss	-	Mildly symptomatic; no treatment required	Gross blood loss OR 1-2 units transfused	Massive blood loss OR > 2 units transfused

Modified from DMID Adult Toxicity Tables, 2001

CHEMISTRIES	GRADE 1 MILD	GRADE 2 MODERATE	GRADE 3 SEVERE	GRADE 4 POTENTIALLY LIFE-THREATENING
Sodium				
Hyponatremia	130-135 meq/L	123-129 meq/L	116-122 meq/L	< 116 meq/L
Hypernatremia	146-150 meq/L	151-157 meq/L	158-165 meq/L	> 165 meq/L
Potassium				
Hypokalemia	3.0-3.4 meq/L	2.5-2.9 meq/L	2.0-2.4 meq/L	< 2.0 meq/L
Hyperkalemia	5.6-6.0 meq/L	6.1-6.5 meq/L	6.6-7.0 meq/L	> 7.0 meq/L
Phosphate				
Hypophosphatemia	2.0-2.4 mg/dL	1.5-1.9 mg/dL	1.0-1.4 mg/dL	< 1.0 mg/dL
Calcium- (Corrected For Albumin)				
Hypocalcemia	7.8-8.4 mg/dL	7.0-7.7 mg/dL	6.1-6.9 mg/dL	< 6.1 mg/dL
Hypercalcemia	10.6-11.5 mg/dL	11.6-12.5 mg/dL	12.6-13.5 mg/dL	> 13.5 mg/dL
Magnesium				
Hypomagnesemia	1.2-1.4 meq/L	0.9-1.1 meq/L	0.6-0.8 meq/L	< 0.6 meq/L
Albumin				
Hypoalbuminemia	3.00-3.49 g/dL	2.50-2.99 g/dL	2.00-2.49 g/dL	< 2.00 g/dL
Bilirubin (Total)				
Hyperbilirubinemia (Total)	> 1.0-1.5 x ULN	> 1.5-2.5 x ULN	> 2.5-5 x ULN	> 5 x ULN
Glucose				
Hypoglycemia	55-64 mg/dL	40-54 mg/dL	30-39 mg/dL	< 30 mg/dL
Hyperglycemia (nonfasting & no prior diabetes)	116-160 mg/dL	161-250 mg/dL	251-500 mg/dL	> 500 mg/dL
Triglycerides	151-399 mg/dL	400-750 mg/dL	751-1200 mg/dL	> 1200 mg/dL
Creatinine	> 1.0-1.5 x ULN	> 1.5-3.0 x ULN	> 3.0-6.0 x ULN	> 6.0 x ULN

(continued)

Modified from DMID Adult Toxicity Tables, 2001

CHEMISTRIES	GRADE 1 MILD	GRADE 2 MODERATE	GRADE 3 SEVERE	GRADE 4 POTENTIALLY LIFE-THREATENING
Uric Acid Hyperuricemia	7.5-10.0 mg/dL	10.1-12.0 mg/dL	12.1-15.0 mg/dL	> 15.0 mg/dL
Liver Transferases (AST, ALT, and GGT)	1.25-2.5 x ULN	> 2.5-5.0 x ULN	> 5.0-10.0 x ULN	> 10.0 x ULN
Alkaline Phosphatase	1.25-2.5 x ULN	> 2.5-5.0 x ULN	> 5.0-10.0 x ULN	> 10.0 x ULN
Pancreatic Enzymes				
Amylase	> 1.0-1.5 x ULN	> 1.5-2.0 x ULN	> 2.0-5.0 x ULN	> 5.0 x ULN
Pancreatic amylase	> 1.0-1.5 x ULN	> 1.5-2.0 x ULN	> 2.0-5.0 x ULN	> 5.0 x ULN
Lipase	> 1.0-1.5 x ULN	> 1.5-2.0 x ULN	> 2.0-5.0 x ULN	> 5.0 x ULN
*Hypoglobulinemia (IgG)**	550-700 mg/dL	400-549 mg/dL	250-399 mg/dL	< 250 mg/dL

*(Goldfarb et al, 2001; Yamani et al, 2001; Eibl and Rosen, 1995).

Modified from DMID Adult Toxicity Tables, 2001

GASTROINTESTINAL	GRADE 1 MILD	GRADE 2 MODERATE	GRADE 3 SEVERE	GRADE 4 POTENTIALLY LIFE-THREATENING
Nausea	Mild OR transient; reasonable intake maintained	Mod discomfort OR intake decreased for < 3 days	Severe discomfort OR minimal intake for ≥ 3 days	Hospitalization required
Vomiting	Mild OR transient; 2-3 episodes/day OR mild vomiting lasting < 1 week	Mod OR persistent; 4-5 episodes per day; OR vomiting lasting ≥ 1 week	Severe vomiting of all foods/fluids in 24 hours OR orthostatic hypotension OR IV treatment req	Hypotensive shock OR hospitalization required for IV treatment req
Diarrhea	Mild or transient; 3-4 loose stools per day OR mild diarrhea lasting < 1 week	Mod OR persistent; 5-7 loose stools per day or diarrhea lasting ≥ 1 week	Bloody diarrhea; OR orthostatic hypotension OR > 7 loose stools/day OR IV treatment req	Hypotensive shock OR hospitalization req
Oral Discomfort/Dysphagia	Mild discomfort, no difficulty swallowing	Difficulty swallowing but able to eat and drink	Unable to swallow solids	Unable to drink fluids; IV fluids req
Constipation	Mild	Moderate	Severe	Distention with vomiting

Modified from DMID Adult Toxicity Tables, 2001

RESPIRATORY	GRADE 1 MILD	GRADE 2 MODERATE	GRADE 3 SEVERE	GRADE 4 POTENTIALLY LIFE-THREATENING
Cough (for aerosol studies)	Transient; no treatment	Treatment associated cough; inhaled bronchodilator	Uncontrolled cough; systemic treatment req	-
Bronchospasm Acute	Transient; no treatment; FEV1 70% to < 80% (or peak flow)	treatment req; normalizes with bronchodilator; FEV1 50% to < 70% (or peak flow)	No Normalization with bronchodilator; FEV 25% to < 50% (or peak flow), retractions	Cyanosis; FEV1 < 25% (or peak flow) OR intubated
Dyspnea	Dyspnea on exertion	Dyspnea with normal activity	Dyspnea at rest	Dyspnea requiring O2 therapy

URINALYSIS	GRADE 1 MILD	GRADE 2 MODERATE	GRADE 3 SEVERE	GRADE 4 POTENTIALLY LIFE-THREATENING
Proteinuria: *Dipstick:* Protein	1 +	2-3 +	4 +	Nephrotic syndrome
Spot Urine: Protein:Creatinine Ratio mg/mg	0.2-1.0	> 1.0-2.0	> 2.0-3.5	> 3.5
24 hour Urine: Protein	200 mg - 1g loss/day	> 1-2 g loss/day	> 2-3.5 g loss/day	Nephrotic syndrome OR > 3.5 g loss/day
Hematuria	Microscopic only > 3 - < 10 RBC/hpf	Gross, No clots ≥ 10 RBC/hpf	Gross plus clots OR RBC casts	Obstructive OR transfusion required

RBC = red blood cell; hpf = high power field.

Modified from DMID Adult Toxicity Tables, 2001

MISCELLANEOUS	GRADE 1 MILD	GRADE 2 MODERATE	GRADE 3 SEVERE	GRADE 4 POTENTIALLY LIFE-THREATENING
Fever (oral > 12 hours)	37.7-38.5°C or 100.0-101.5°F	38.6-39.5°C OR 101.6-102.9°F	39.6-40.5°C OR 103-105°F	> 40.5°C OR > 105°F
Headache	Mild; No treatment req	Mod; or non-narcotic analgesia treatment	Severe; OR responds to initial narcotic treatment	Intractable; OR requiring repeated narcotic treatment
Allergic Reaction	Pruritus without rash	Localized urticaria	Generalized urticaria angioedema	Anaphylaxis
Cutaneous/Rash/ Dermatitis	Erythema, pruritus rash OR dry desquamation	Diffuse maculopapular OR dry desquamation	Vesiculation OR moist desquamation ulceration	ANY ONE: mucous membrane involvement, suspected Stevens-Johnson (TEN), erythema multiforme, necrosis req surgery, exfoliative dermatitis
Local Reaction (secondary to parenteral treatment- not vaccination or skin test)	Erythema	Induration < 10 mm OR inflammation OR phlebitis	Induration > 10 mm OR ulceration	Necrosis of skin
Fatigue	Normal activity Reduced < 25%	Normal activity Reduced 25-50%	Normal activity reduced > 50%; cannot work	Unable to care for self

Modified from DMID Adult Toxicity Tables, 2001

NEUROLOGIC	GRADE 1 MILD	GRADE 2 MODERATE	GRADE 3 SEVERE	GRADE 4 POTENTIALLY LIFE-THREATENING
Neuro-cerebellar	Slight incoordination OR dysdiadochokinesia	Intention tremor OR dysmetria OR slurred speech OR nystagmus	Ataxia requiring assistance to walk or arm incoordination interfering with ADLs	Unable to stand
Neuro-psych/ mood	-	None	Severe mood changes requires medical intervention	Acute psychosis requiring hospitalization
Paresthesia (burning, tingling, etc)	Mild discomfort; no treatment needed	Mod discomfort non-narcotic analgesia req	Severe discomfort; OR narcotic analgesia req with symptomatic improvement	Incapacitating; OR not responsive to narcotic analgesia
Neuro-motor	Mild weakness in muscle of feet but able to walk and/or mild increase or decrease in reflexes	Mod weakness in feet (unable to walk on heels and/or toes), mild weakness in hands, still able to do most hand tasks and/or loss of previously present reflex or development of hyperreflexia and/or unable to do deep knee bends due to weakness	Marked distal weakness (unable to dorsiflex toes or foot drop), and mod proximal weakness ie, in hands interfering with ADLs and/or requiring assistance to walk and/or unable to rise from chair unassisted	Confined to bed or wheelchair because of muscle weakness
Neuro-sensory	Mild impairment sensations, (ie, vibratory, pinprick, hot/cold in great toes) in focal area or symmetrical distribution	Mod impairment mod de-sensation, (ie, of vibratory, pinprick, hot/cold to ankles) and/or joint position or mild impairment that is not symmetrical.	Severe impairment (dec or loss of sensation to knees or wrists) or loss of sensation of at least mod degree in multiple different body areas (ie, upper and lower extremities)	Sensory loss involves limbs and trunk

Modified from DMID Adult Toxicity Tables, 2001

10.11. Appendix 11: Abbreviations & Trade Marks

10.11.1. Abbreviations

Abbreviation	Description
ADaM	Analysis Data Model
AE	Adverse Event
AESI	Adverse Events of Special Interest
AIC	Akaike's Information Criteria
A&R	Analysis and Reporting
ANCA	Anti-Neutrophil Cytoplasmic Antibody
Anti-MPO	Anti- myeloperoxidase
Anti-PR3	Anti-proteinase 3
at-ANCA	Atypical Antineutrophil Cytoplasmic Antibody
AZA	Azathioprine
BLyS	B lymphocyte Stimulator
BVAS	Birmingham Vasculitis Activity Score
C3	Complement Factor 3
C4	Complement Factor 4
c-ANCA	Cytoplasmic Antineutrophil Cytoplasmic Antibody
CDISC	Clinical Data Interchange Standards Consortium
CI	Confidence Interval
CPMS	Clinical Pharmacology Modelling & Simulation
CRP	C-Reactive Protein
CS	Clinical Statistics
CSR	Clinical Study Report
C-SSRS	Columbia-Suicide Severity Rating Scale
CTR	Clinical Trial Register
CV_b / CV_w	Coefficient of Variation (Between) / Coefficient of Variation (Within)
CYC	Cyclophosphamide
DOB	Date of Birth
DP	Decimal Places
ECL	Electrochemiluminescence
eCRF	Electronic Case Record Form
eGFR	Estimated Glomerular Filtration Rate
ESR	Erythrocyte Sedimentation Rate
FACS	Florescence activated cell sorting
GPA	Granulomatosis with Polyangiitis
GSK	GlaxoSmithKline
ICH	International Conference on Harmonisation
IDSL	Integrated Data Standards Library
IFA	Immune-fluorescence Assay
Ig	Immunoglobulin
IMMS	International Modules Management System
IP	Study agent

Abbreviation	Description
ITT	Intent-To-Treat
IV	Intravenous
LLN	lower limit of normal
LOC	Last Observation Carries Forward
LOQ	Limit of Quantification
OLE	Open-label Extension
MedDRA	Medical Dictionary for Regulatory Activities
MPA	Microscopic Polyangiitis
NMSC	Non-melanoma Skin Cancer
p-ANCA	Perinuclear Antineutrophil Cytoplasmic Antibody
PD	Pharmacodynamic
PDMP	Protocol Deviation Management Plan
PK	Pharmacokinetic
PP	Per-Protocol
PSRQ	Possible Suicidality Related Questionnaire
PT	Preferred Terms
QC	Quality Control
QTcF	Frederica's QT Interval Corrected for Heart Rate
QTcB	Bazett's QT Interval Corrected for Heart Rate
RAP	Reporting & Analysis Plan
RAMOS	Randomization & Medication Ordering System
RTX	Rituximab
SAC	Statistical Analysis Complete
SAE	Serious Adverse Event
SD	Standard Deviation
SDTM	Study Data Tabulation Model
SOC	System Organ Class
SOP	Standard Operation Procedure
TA	Therapeutic Area
TFL	Tables, Figures & Listings
VDI	Vasculitis Damage Index
ULN	Upper Limit of Normal
WG	Wegener's Granulomatosis

10.11.2. Trademarks

Trademarks of the GlaxoSmithKline Group of Companies
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Trademarks not owned by the GlaxoSmithKline Group of Companies
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10.12. Appendix 12: List of Data Displays

10.12.1. Data Display Numbering

The following numbering will be applied for RAP generated displays:

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

10.12.2. Mock Example Shell Referencing

Non IDSL specifications will be referenced as indicated and if required example mock-up displays provided in Appendix 13.

Section	Figure	Table	Listing
Study Population	POP_Fn	POP_Tn	POP_Ln
Efficacy	EFF_Fn	EFF_Tn	EFF_Ln
Safety	SAFE_Fn	SAFE_Tn	SAFE_Ln
Pharmacokinetic	PK_Fn	PK_Tn	PK_Ln
Biomarker	PD_Fn	PD_Tn	PD_Ln

NOTES:

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

10.12.3. Deliverable

Delivery	Description
H	Headline Results
SAC	Statistical Analysis Complete

10.12.4. Study Population Tables

Study Population Tables					
No.	**Population**	**Example Shell (IDSL)**	**Title**	**Programming Notes**	**Deliverable**
Subject Disposition					
1.1.	ITT	POP_T1	Summary of Subject-Years on Study (Double-blind Phase)	Study Specific	H, SAC
1.2.	ITT	ES1	Summary of Subject Disposition (Double-blind Phase)	ICH E3, GSK CTR, FDAAA, EudraCT	H, SAC
1.3.	Subgroup of ITT	ES1	Summary of Subject Disposition (Age ≥ 65 Yrs) (Double-blind Phase)	ICH E3, GSK CTR, FDAAA, EudraCT	SAC
1.4.	Subgroup of ITT	ES1	Summary of Subject Disposition (Age ≥ 75 Yrs) (Double-blind Phase)	ICH E3, GSK CTR, FDAAA, EudraCT	SAC
1.5.	ITT	POP_T2	Summary of Subject Completion Status by Study Year (Double-blind Phase)	Study Specific. Please include summary of study withdrawal on first page and summary of treatment withdrawal on second page.	SAC
1.6.	Subgroup of ITT	POP_T2	Summary of Subject Completion Status by Study Year (Age ≥ 65 Yrs) (Double-blind Phase)	Study Specific	SAC
1.7.	Subgroup of ITT	POP_T2	Summary of Subject Completion Status by Study Year (Age ≥ 75 Yrs) (Double-blind Phase)	Study Specific	SAC
1.8.	Screened	ES6	Summary of Screen Failures (Screened Subjects Population) (Double-blind Phase)	Journal Requirements	SAC
1.9.	Randomized	NS3	Summary of Subjects by Country and Center (Randomized Subjects Population) (Double-blind Phase)	EudraCT	SAC
Protocol Deviation					
1.10.	Randomized	DV1	Summary of Subjects with Important Protocol Deviations (Double-blind Phase)	ICH E3	SAC
1.11.	ITT	IE1	Summary of Inclusion/Exclusion Criteria Deviations (Double-blind Phase)		SAC

Study Population Tables					
No.	**Population**	**Example Shell (IDSL)**	**Title**	**Programming Notes**	**Deliverable**
Population Analyzed					
1.12.	Screened	SP1	Summary of Study Populations (Double-blind Phase)	IDSL	H, SAC
Demographic and Baseline Characteristics					
1.13.	ITT	DM1	Summary of Demographic Characteristics (Double-blind Phase)	ICH E3, GSK CTR, FDAAA, EudraCT Please give age categories as: <= 45, > 45 - < 65, >= 65 - < 75, >= 75	H, SAC
1.14.	Subgroup of ITT	DM1	Summary of Demographic Characteristics (Age ≥ 65 Yrs) (Double-blind Phase)	ICH E3, GSK CTR, FDAAA, EudraCT Please give age categories as: <= 45, > 45 - < 65, >= 65 - < 75, >= 75	SAC
1.15.	Subgroup of ITT	DM1	Summary of Demographic Characteristics (Age ≥ 75 Yrs) (Double-blind Phase)	ICH E3, GSK CTR, FDAAA, EudraCT Please give age categories as: <= 45, > 45 - < 65, >= 65 - < 75, >= 75	SAC
1.16.	ITT	POP_T3	Summary of Baseline Disease Characteristics (Double-blind Phase)		H, SAC
1.17.	Subgroup of ITT	POP_T3	Summary of Baseline Disease Characteristics (Age ≥ 65 Yrs) (Double-blind Phase)		SAC
1.18.	Subgroup of ITT	POP_T3	Summary of Baseline Disease Characteristics (Age ≥ 75 Yrs) (Double-blind Phase)		SAC
1.19.	ITT	DM5	Summary of Race and Racial Combinations (Double-blind Phase)	ICH E3, FDA, GSK CTR, FDAAA, EudraCT	SAC
1.20.	Subgroup of ITT	DM5	Summary of Race and Racial Combinations (Age ≥ 65 Yrs) (Double-blind Phase)	ICH E3, FDA, GSK CTR, FDAAA, EudraCT	SAC
1.21.	Subgroup of ITT	DM5	Summary of Race and Racial Combinations (Age ≥ 75 Yrs) (Double-blind Phase)	ICH E3, FDA, GSK CTR, FDAAA, EudraCT	SAC
Other Baseline Characteristics					

Study Population Tables					
No.	**Population**	**Example Shell (IDSL)**	**Title**	**Programming Notes**	**Deliverable**
1.22.	ITT	POP_T4	Summary of Anti-Neutrophil Cytoplasmic Antibody (ANCA) at Baseline (Double-blind Phase)		SAC
1.23.	ITT	POP_T5	Summary of Complement (C3, C4) and BLyS Protein at Baseline (Double-blind Phase)	Study Specific: Include C3, C4 and BLyS	SAC
1.24.	ITT	POP_T6	Summary of Immunoglobulins (IgA, IgG, IgM) Levels At Baseline (Double-blind Phase)	Study Specific	SAC
1.25.	ITT	POP_T7	Summary of B Cells (FACS of Peripheral Lymphocytes) at Baseline (Double-blind Phase)	Study Specific	SAC
Prior Medical Conditions and Concomitant Medications					
1.26.	ITT	POP_T8 (MH4)	Summary of Prior Medical Conditions (Double-blind Phase)	ICH E3	SAC
1.27.	ITT	CM1	Summary of Concomitant Medications (Double-blind Phase)	ICH E3	SAC
Exposure and Treatment Compliance					
1.28.	ITT	POP_T9	Summary of Duration of Exposure to Study Drug (Double-blind Phase)	ICH E3	SAC
1.29.	Subgroup of ITT	POP_T9	Summary of Duration of Exposure to Study Drug (Age ≥ 65 Yrs) (Double-blind Phase)	ICH E3	SAC
1.30.	Subgroup of ITT	POP_T9	Summary of Duration of Exposure to Study Drug (Age ≥ 75 Yrs) (Double-blind Phase)	ICH E3	SAC
1.31.	ITT	TTE7	Summary of Kaplan-Meier Estimates of Time to Study Withdrawal (Double-blind Phase)	Study withdrawals can be identified where DS.DSFAIL = "Y"	SAC
1.32.	Subgroup of ITT	TTE7	Summary of Kaplan-Meier Estimates of Time to Study Withdrawal (Age ≥ 65 Yrs) (Double-blind Phase)		SAC
1.33.	Subgroup of ITT	TTE7	Summary of Kaplan-Meier Estimates of Time to Study Withdrawal (Age ≥ 75 Yrs) (Double-blind Phase)		SAC

Study Population Tables					
No.	**Population**	**Example Shell (IDSL)**	**Title**	**Programming Notes**	**Deliverable**
1.34.	Subgroup of ITT	TTE7	Summary of Kaplan-Meier Estimates of Time to Study Treatment Withdrawal (Double-blind Phase)	Treatment withdrawals can be identified where SDSTOPP = "Y"	SAC

10.12.5. Efficacy Tables

Efficacy: Tables					
No.	**Population**	**IDSL / TST ID / Example Shell**	**Title**	**Programming Notes**	**Deliverable**
Primary Endpoint (Time from Day 0 to first relapse)					
2.1.	ITT	EFF_T1	Summary of Analysis of Time to Relapse (Double-blind Phase)	Event summary will be "BVAS Score ≥ 6", "Major BVAS Item" and "Prohibited Medication"	H, SAC
2.2.	Subgroup of ITT	EFF_T1	Summary of Analysis of Time to Relapse (Age ≥ 65 Yrs) (Double-blind Phase)	As above. No analysis is required, please do not include.	SAC
2.3.	Subgroup of ITT	EFF_T1	Summary of Analysis of Time to Relapse (Age ≥ 75 Yrs) (Double-blind Phase)	As above. No analysis is required, please do not include.	SAC
2.4.	PP	EFF_T1	Summary of Analysis of Time to Relapse (Per-Protocol Population) (Double-blind Phase)	As above. (Only produce if required).	SAC
2.5.	ITT	EFF_T1	Summary of Analysis of Time to Relapse: Sensitivity Analysis adjusting for Randomization Strata (Double-blind Phase)	The strata to which a subject was assigned can be found in the Randall dataset.	SAC
2.6.	ITT	EFF_T1	Summary of Analysis of Time to Relapse: Sensitivity Analysis of Vasculitis-Related Relapses (Double-blind Phase)	Only produce if required. Derived from TF adjudication.	SAC
2.7.	ITT	EFF_T2	Summary of Organ Domain Involvement for Subjects with Relapse due to BVAS (Double-blind Phase)		SAC
2.8.	ITT	TTE4	Summary of Analysis of Time to Relapse (Model Estimates for Other Covariates) (Double-blind Phase)	Include model estimates for covariates other than treatment group (i.e. ANCA type, induction regimen and disease stage).	SAC
2.9.	ITT	EFF_T3	Summary of Analysis of Time to Relapse: Exploratory Analysis adjusting for Interactions (Double-blind Phase)	Please add treatment:covariate interaction terms, Treatment:ANCA Type, Treatment:Induction Regimen, Treatment:Disease Stage, one at a time to the primary model.	SAC

Efficacy: Tables					
No.	**Population**	**IDSL / TST ID / Example Shell**	**Title**	**Programming Notes**	**Deliverable**
2.10.	ITT	TTE7	Summary of Kaplan-Meier Estimates of Time to Relapse (Double-blind Phase)		H, SAC
2.11.	PP	TTE7	Summary of Kaplan-Meier Estimates of Time to Relapse (Per-Protocol Population) (Double-blind Phase)		H, SAC
2.12.	ITT	TTE7	Summary of Kaplan-Meier Estimates of Time to Relapse: Sensitivity Analysis of Vasculitis-Related Relapses (Double-blind Phase)	Only produce if required. Derived from TF adjudication.	SAC
2.13.	Subgroup of ITT	TTE7	Summary of Kaplan-Meier Estimates of Time to Relapse by ANCA Type (anti-MPO vs. anti-PR3) (Double-blind Phase)		SAC
2.14.	Subgroup of ITT	TTE7	Summary of Kaplan-Meier Estimates of Time to Relapse by Induction Regimen (IV Cyclophosphamide vs. Oral Cyclophosphamide vs. Rituximab) (Double-blind Phase)		SAC
2.15.	Subgroup of ITT	TTE7	Summary of Kaplan-Meier Estimates of Time to Relapse by Disease Stage at Induction (Initial vs. Relapsing) (Double-blind Phase)		SAC
Time from Day 0 to first Minor or Major Relapse or Receipt of Rescue Medication					
2.16.	ITT	EFF_T1	Summary of Study Day of First Minor or Major Relapse or Receipt of Rescue Medication (Double-blind Phase)	No analysis for this endpoint so no HR to be produced. Events will be “Minor BVAS Item”, “Major BVAS Item” and “Recue Medication” with a footnote “Rescue medication is any prohibited medication as defined in the protocol”.	SAC
Birmingham Vasculitis Activity Score					
2.17.	ITT	EFF_T4	Summary of BVAS Organ System Involvement by Visit (Double-blind Phase)		H, SAC
2.18.	ITT	EFF_T5	Summary of BVAS Total Score (Observed and Change from Baseline) by Visit (Double-blind Phase)		H, SAC

Efficacy: Tables					
No.	**Population**	**IDSL / TST ID / Example Shell**	**Title**	**Programming Notes**	**Deliverable**
2.19.	ITT	EFF_T6	Summary of Proportion of Subjects with any increase from Baseline in BVAS Organ Domains by Visit (Double-blind Phase)	Use EFF_T6 and modify based on data. Include only organ domains where an increase is seen. Otherwise present only total BVAS. Include footnote "Note: Only organ domains for which the proportion of subjects with an increase in BVAS is greater than zero are displayed."	H, SAC
VDI					
2.20.	ITT	EFF_T5	Summary of VDI Total Score (Observed and Change from Baseline) by Visit (Double-blind Phase)		SAC
2.21.	ITT	EFF_T6	Summary of Proportion of Subjects with any increase from Baseline in VDI by Visit (Double-blind Phase)		SAC
Other					
2.22.	ITT	EFF_T6	Summary of Proportion of Subjects in Remission by Visit (Double-blind Phase)	Use EFF_T6 and modify based on data. Give definition of remission as footnote.	SAC
2.23.	ITT	EFF_T6	Summary of Proportion of Subjects with no Relapse from Baseline by Visit (Double-blind Phase)	Use EFF_T6 and modify based on data.	

10.12.6. Efficacy Figures

Efficacy: Figures					
No.	**Population**	**IDSL / TST ID / Example Shell**	**Title**	**Programming Notes**	**Deliverable**
Primary Endpoint					
2.1.	ITT	TTE10	Kaplan-Meier Plot of Time to Relapse (Double-blind Phase)	Please produce 1 – KM to indicate "Proportion with Relapse" on y axis	H, SAC
2.2.	PP	TTE10	Kaplan-Meier Plot of Time to Relapse (Per-Protocol Population) (Double-blind Phase)	Only generate if required. Please produce 1 – KM to indicate "Proportion with Relapse" on y axis	H, SAC
2.3.	ITT	TTE10	Kaplan-Meier Plot of Time to Relapse: Sensitivity Analysis of Vasculitis-Related Relapses (Double-blind Phase)	Only generate if required. Please produce 1 – KM to indicate "Proportion with Relapse" on y axis	SAC
2.4.	Subgroup of ITT	TTE10	Kaplan-Meier Plot of Time to Relapse by ANCA Type (anti-MPO vs. anti-PR3) (Double-blind Phase)	Please produce 1 – KM to indicate "Proportion with Relapse" on y axis	SAC
2.5.	Subgroup of ITT	TTE10	Kaplan-Meier Plot of Time to Relapse by Induction Regimen (IV Cyclophosphamide vs. Oral Cyclophosphamide vs. Rituximab) (Double-blind Phase)	Please produce 1 – KM to indicate "Proportion with Relapse" on y axis	SAC
2.6.	Subgroup of ITT	TTE10	Kaplan-Meier Plot of Time to Relapse by Disease Stage at Induction (Initial vs. Relapsing) (Double-blind Phase)	Please produce 1 – KM to indicate "Proportion with Relapse" on y axis	SAC
Time to First Minor or Major Relapse or Receipt of Rescue Medication					
2.7.	ITT	TTE10	Kaplan-Meier Plot of Time to First Minor or Major Relapse or Receipt of Rescue Medication (Double-blind Phase)	Please produce 1 – KM to indicate "Proportion with Minor or Major Relapse or Receipt of Rescue Medication" on y axis	SAC
Birmingham Vasculitis Activity Score					
2.8.	ITT	EFF_F1	Proportion of Subjects with any increase from Baseline in BVAS Organ Domains by Visit (Double-blind Phase)	Stacked bar chart. Only show visits up to Yr2 Wk28.	H, SAC
Vasculitis Damage Index					

Efficacy: Figures					
No.	**Population**	**IDSL / TST ID / Example Shell**	**Title**	**Programming Notes**	**Deliverable**
2.9.	ITT	EFF_F1	Proportion of Subjects with any increase from Baseline in VDI by Visit (Double-blind Phase)	Bar chart. Only show visits up to Yr2 Wk24	SAC
Other					
2.10.	ITT	EFF_F1	Proportion of Subjects in Remission by Visit (Double-blind Phase)	Bar chart. Add definition of remission to footnotes. Only show visits up to Yr2 Wk28	SAC
2.11.	ITT	EFF_F1	Proportion of Subjects with no Relapse by Visit (Double-blind Phase)	Bar char. Only show visits up to Yr2 Wk 28	SAC

10.12.7. Safety Tables

Safety: Tables					
No.	**Population**	**Example Shell (IDSL)**	**Title**	**Programming Notes**	**Deliverable**
Adverse Events					
3.1.	ITT	AE1	Pre-Treatment Adverse Events by SOC and PT (Double-blind Phase)		SAC
3.2.	ITT	SAFE_T1	Adverse Events Summary by Year Interval (Double-blind Phase)		H, SAC
3.3.	ITT	SAFE_T1	Adverse Events Summary by Year Interval (Age ≥ 65 Yrs) (Double-blind Phase)		SAC
3.4.	ITT	SAFE_T1	Adverse Events Summary by Year Interval (Age ≥ 75 Yrs) (Double-blind Phase)		SAC
Adverse Events by SOC					
3.5.	ITT	SAFE_T2	Adverse Events Summary by SOC and Year Interval (Double-blind Phase)		SAC
Adverse Events by SOC (Serious & Severe)					
3.6.	ITT	SAFE_T2	Serious Adverse Events by SOC and Year Interval (Double-blind Phase)		SAC
3.7.	ITT	SAFE_T2	Severe Adverse Events by SOC and Year Interval (Double-blind Phase)		SAC
Adverse Events by SOC (Drug-Related and Leading to Permanent Discontinuation or Withdrawal)					
3.8.	ITT	SAFE_T2	Study Drug-Related Adverse Events by SOC and Year Interval (Double-blind Phase)		SAC
3.9.	ITT	SAFE_T2	Adverse Events Leading to Permanent Discontinuation of Study Drug or Withdrawal from Study by SOC and Year Interval (Double-blind Phase)		H, SAC
Adverse Events occurring Off-Treatment					

Safety: Tables					
No.	**Population**	**Example Shell (IDSL)**	**Title**	**Programming Notes**	**Deliverable**
3.10.	ITT	SAFE_T3	Adverse Events occurring Off-Treatment by SOC (Double-blind Phase)	Off-treatment is defined as events occurring more than 28 days after final study drug exposure.	SAC
Adverse Events Rates by SOC (Serious and Severe)					
3.11.	ITT	SAFE_T4	Adverse Event Rate by SOC and Year Interval (Double-blind Phase)		SAC
3.12.	ITT	SAFE_T4	Serious Adverse Event Rate by SOC and Year Interval (Double-blind Phase)		SAC
3.13.	ITT	SAFE_T4	Severe Adverse Event Rate by SOC and Year Interval (Double-blind Phase)		SAC
3.14.	ITT	SAFE_T4	Study Drug-Related Adverse Event Rate by SOC and Year Interval (Double-blind Phase)		SAC
3.15.	ITT	SAFE_T4	Adverse Event Rate Leading to Permanent Discontinuation of Study Drug or Withdrawal from Study by SOC and Year Interval (Double-blind Phase)		SAC
Adverse Events by SOC and PT					
3.16.	ITT	SAFE_T5	Adverse Events by SOC and PT and Year Interval (Double-blind Phase)		H, SAC
3.17.	ITT	SAFE_T5	Adverse Events by SOC and PT and Year Interval (Age ≥ 65 Yrs) (Double-blind Phase)		SAC
3.18.	ITT	SAFE_T5	Adverse Events by SOC and PT and Year Interval (Age ≥ 75 Yrs) (Double-blind Phase)		SAC
Adverse Events by SOC and PT (Serious & Severe)					
3.19.	ITT	SAFE_T5	Serious Adverse Events by SOC and PT and Year Interval (Double-blind Phase)		H, SAC
3.20.	ITT	SAFE_T5	Serious Adverse Events by SOC and PT and Year Interval (Age ≥ 65 Yrs) (Double-blind Phase)		SAC

Safety: Tables					
No.	**Population**	**Example Shell (IDSL)**	**Title**	**Programming Notes**	**Deliverable**
3.21.	ITT	SAFE_T5	Serious Adverse Events by SOC and PT and Year Interval Age ≥ 75 Yrs) (Double-blind Phase)		SAC
3.22.	ITT	SAFE_T5	Severe Adverse Events by SOC and PT and Year Interval (Double-blind Phase)		SAC
Adverse Events by SOC and PT (Drug-Related and Leading to Permanent Discontinuation or Withdrawal)					
3.23.	ITT	SAFE_T5	Study Drug-Related Adverse Events by SOC and PT and Year Interval (Double-blind Phase)		H, SAC
3.24.	ITT	SAFE_T5	Study Drug-Related Adverse Events by SOC and PT and Year Interval (Age ≥ 65 Yrs) (Double-blind Phase)		SAC
3.25.	ITT	SAFE_T5	Study Drug-Related Adverse Events by SOC and PT and Year Interval (Age ≥ 75 Yrs) (Double-blind Phase)		SAC
3.26.	ITT	SAFE_T5	Adverse Events Leading to Permanent Discontinuation of Study Drug or Withdrawal from Study by SOC and PT and Year Interval (Double-blind Phase)		SAC
3.27.	ITT	SAFE_T5	Adverse Events Leading to Permanent Discontinuation of Study Drug or Withdrawal from Study by SOC and PT and Year Interval (Age ≥ 65 Yrs) (Double-blind Phase)		SAC
3.28.	ITT	SAFE_T5	Adverse Events Leading to Permanent Discontinuation of Study Drug or Withdrawal from Study by SOC and PT and Year Interval (Age ≥ 75 Yrs) (Double-blind Phase)		SAC
Adverse Events By SOC and PT (Death)					
3.29.	ITT	SAFE_T5	Deaths by SOC and PT and Year Interval (Double-blind Phase)		H, SAC
3.30.	ITT	SAFE_T5	Deaths by SOC and PT and Year Interval (Age ≥ 65 Yrs) (Double-blind Phase)		SAC
3.31.	ITT	SAFE_T5	Deaths by SOC and PT and Year Interval (Age ≥ 75 Yrs) (Double-blind Phase)		SAC
Adverse Events: Non-Serious, Serious & Fatal Serious by SOC and PT					

Safety: Tables					
No.	**Population**	**Example Shell (IDSL)**	**Title**	**Programming Notes**	**Deliverable**
3.32.	ITT	SAFE_T5	Common Non-Serious Adverse Events (>=5% incidence in any interval) by SOC and PT and Year Interval (Double-blind Phase)	The 'ANY EVENT' rows are based on the number of subjects that have non-serious adverse events that meet the threshold. Do not give 'ANY EVENT' for the individual SOC. Only display overall.	SAC
3.33.	ITT	SAFE_T5	Study Drug-Related Serious Adverse Events by SOC and PT and Year Interval (Double-blind Phase)		SAC
3.34.	ITT	SAFE_T5	Fatal Serious Adverse Events by SOC and PT and Year Interval (Double-blind Phase)		SAC
3.35.	ITT	SAFE_T5	Study Drug-Related Fatal Serious Adverse Events by SOC and PT and Year Interval (Double-blind Phase)		SAC
3.36.	ITT	SAFE_T5	Non-Fatal Serious Adverse Events by SOC and PT and Year Interval (Double-blind Phase)		SAC
3.37.	ITT	SAFE_T5	Study Drug-Related Non-Fatal Serious Adverse Events by SOC and PT and Year Interval (Double-blind Phase)		SAC
Adverse Event Rates by SOC and PT					
3.38.	ITT	SAFE_T4	Adverse Event Rate by SOC and PT and Year Interval (Double-blind Phase)	Include "Preferred Term" in column 1, similar to SAFE_T5.	SAC
Adverse Events by Subgroups					

Safety: Tables					
No.	**Population**	**Example Shell (IDSL)**	**Title**	**Programming Notes**	**Deliverable**
3.39.	ITT	SAFE_T5	Adverse Events by SOC and PT and Gender and Year Interval (Double-blind Phase)		SAC
3.40.	ITT	SAFE_T5	Serious Adverse Events by SOC and PT and Gender and Year Interval (Double-blind Phase)		SAC
3.41.	ITT	SAFE_T5	Adverse Events by SOC and PT and Age (<65 Yrs vs. ≥ 65 Yrs) and Year Interval (Double-blind Phase)		SAC
3.42.	ITT	SAFE_T5	Serious Adverse Events by SOC and PT and Age (<65 Yrs vs. ≥ 65 Yrs) and Year Interval (Double-blind Phase)		SAC
3.43.	ITT	SAFE_T5	Adverse Events by SOC and PT and Induction Regimen and Year Interval (Double-blind Phase)		SAC
3.44.	ITT	SAFE_T5	Serious Adverse Events by SOC and PT and Induction Regimen and Year Interval (Double-blind Phase)		SAC
Adverse Events by PT					
3.45.	ITT	SAFE_T5	Adverse Events by PT and Year Interval (Double-blind Phase)		SAC
Adverse Events by PT (Serious & Severe)					
3.46.	ITT	SAFE_T5	Serious Adverse Events by PT and Year Interval (Double-blind Phase)		SAC
3.47.	ITT	SAFE_T5	Severe Adverse Events by PT and Year Interval (Double-blind Phase)		SAC
Adverse Events By PT (Drug-Related and Leading to Permanent Discontinuation or Withdrawal)					
3.48.	ITT	SAFE_T5	Study Drug-Related Adverse Events by PT and Year Interval (Double-blind Phase)		SAC
3.49.	ITT	SAFE_T5	Adverse Events Leading to Permanent Discontinuation of Study Drug or Withdrawal from Study by PT and Year Interval (Double-blind Phase)		SAC
Adverse Events By PT (Death)					
3.50.	ITT	SAFE_T5	Deaths by Category, PT and Year Interval (Double-blind Phase)		SAC

Safety: Tables					
No.	**Population**	**Example Shell (IDSL)**	**Title**	**Programming Notes**	**Deliverable**
3.51.	ITT	SAFE_T5	Deaths by Category, PT and Year Interval (Age ≥ 65 Yrs) (Double-blind Phase)		SAC
3.52.	ITT	SAFE_T5	Deaths by Category, PT and Year Interval (Age ≥ 75 Yrs) (Double-blind Phase)		SAC
Adverse Events By Maximum Intensity					
3.53.	ITT	SAFE_T6	Adverse Events by SOC, Maximum Intensity and Year Interval (Double-blind Phase)		SAC
3.54.	ITT	SAFE_T7	Adverse Events by SOC, PT, Maximum Intensity and Year Interval (Double-blind Phase)		SAC
Adverse Events Relationship Between SOC and Verbatim Text					
3.55.	ITT	AE2	Relationship between System Organ Class and Verbatim Text (Double-blind Phase)		SAC
Adverse Events of Special Interest					
3.56.	ITT	SAFE_T8	Adverse Events of Special Interest by Category and Year Interval (Double-blind Phase)	See RAP for definitions of AEs of special interest.	H, SAC
3.57.	ITT	SAFE_T8	Adverse Events of Special Interest by Category and Year Interval (Age ≥ 65 Yrs) (Double-blind Phase)	See RAP for definitions of AEs of special interest.	SAC
3.58.	ITT	SAFE_T8	Adverse Events of Special Interest by Category and Year Interval (Age ≥ 75 Yrs) (Double-blind Phase)	See RAP for definitions of AEs of special interest.	SAC
3.59.	ITT	SAFE_T9	Malignant Neoplasm Adverse Events of Special Interest by Category, PT and Year Interval (Double-blind Phase)		SAC
3.60.	ITT	SAFE_T9	Infusion/Anaphylaxis/Hypersensitivity Reaction Adverse Events of Special Interest by Category, PT and Year Interval (Double-blind Phase)		SAC

Safety: Tables					
No.	**Population**	**Example Shell (IDSL)**	**Title**	**Programming Notes**	**Deliverable**
3.61.	ITT	SAFE_T9	Serious Infusion/Anaphylaxis/Hypersensitivity Reaction Adverse Events of Special Interest by Category, PT and Year Interval (Double-blind Phase)		SAC
3.62.	ITT	SAFE_T9	Infection Adverse Events of Special Interest by Category, PT and Year Interval (Double-blind Phase)		SAC
3.63.	ITT	SAFE_T9	Serious Infection Adverse Events of Special Interest by Category, PT and Year Interval (Double-blind Phase)		SAC
3.64.	ITT	SAFE_T9	Severe Infection Adverse Events of Special Interest by Category, PT and Year Interval (Double-blind Phase)		SAC
3.65.	ITT	SAFE_T9	Serious/Severe Infection Adverse Events of Special Interest by Category, PT and Year Interval (Double-blind Phase)		SAC
3.66.	ITT	SAFE_T9	Infection Adverse Events of Special Interest Leading to Discontinuation by Category, PT and Year Interval (Double-blind Phase)		SAC
3.67.	ITT	SAFE_T9	Depression/Suicide/Self-injury Adverse Events of Special Interest by Category, PT and Year Interval (Double-blind Phase)		SAC
Adverse Events of Special Interest by Subgroups					

Safety: Tables					
No.	**Population**	**Example Shell (IDSL)**	**Title**	**Programming Notes**	**Deliverable**
3.68.	ITT	SAFE_T8	Adverse Events of Special Interest by Category and Induction Regimen and Year Interval (Double-blind Phase)	See RAP for definitions of AEs of special interest.	SAC
3.69.	ITT	SAFE_T9	Malignant Neoplasm Adverse Events of Special Interest by Category, PT and Induction Regimen and Year Interval (Double-blind Phase)		SAC
3.70.	ITT	SAFE_T9	Infection Adverse Events of Special Interest by Category, PT and Induction Regimen and Year Interval (Double-blind Phase)		SAC
3.71.	ITT	SAFE_T9	Serious Infection Adverse Events of Special Interest by Category, PT and Induction Regimen and Year Interval (Double-blind Phase)		SAC
Adverse Events of Special Interest Rates					
3.72.	ITT	SAFE_T10	Adverse Events of Special Interest Rate by Category and Year Interval (Double-blind Phase)		SAC
3.73.	ITT	SAFE_T11	Malignant Neoplasm Adverse Events of Special Interest Rate by Category, PT and Year Interval (Double-blind Phase)		SAC
3.74.	ITT	SAFE_T11	Infusion/Anaphylaxis/Hypersensitivity Reaction Adverse Events of Special Interest Rate by Category, PT and Year Interval (Double-blind Phase)		SAC
3.75.	ITT	SAFE_T11	Serious Infusion/Anaphylaxis/Hypersensitivity Reaction Adverse Events of Special Interest Rate by Category, PT and Year Interval (Double-blind Phase)		SAC
3.76.	ITT	SAFE_T11	Infection Adverse Events of Special Interest Rate by Category, PT and Year Interval (Double-blind Phase)		SAC
3.77.	ITT	SAFE_T11	Serious Infection Adverse Events of Special Interest Rate by Category, PT and Year Interval (Double-blind Phase)		SAC
3.78.	ITT	SAFE_T11	Severe Infection Adverse Events of Special Interest Rate by Category, PT and Year Interval (Double-blind Phase)		SAC
3.79.	ITT	SAFE_T11	Serious/Severe Infection Adverse Events of Special Interest Rate by Category, PT and Year Interval (Double-blind Phase)		SAC

Safety: Tables					
No.	**Population**	**Example Shell (IDSL)**	**Title**	**Programming Notes**	**Deliverable**
3.80.	ITT	SAFE_T11	Infection Adverse Events of Special Interest Leading to Discontinuation Rate by Category, PT and Year Interval (Double-blind Phase)		SAC
3.81.	ITT	SAFE_T11	Depression, Suicidality, and Self-injury Adverse Events of Special Interest Rate by Category, PT and Year Interval (Double-blind Phase)		SAC
C-SSRS					
3.82.	ITT	CSSRS1	Subjects with C-SSRS Suicidal Ideation or Behavior during Treatment (Double-blind Phase)		SAC
3.83.	ITT	CSSRS2	Subjects with Treatment Emergent C-SSRS Suicidal Ideation or Behavior Relative to Pre-Treatment (Double-blind Phase)		SAC
3.84.	ITT	CSSRS3	Subjects with Shift of Changes in C-SSRS Categories from Pre-Treatment to On-Treatment (Double-blind Phase)		SAC
Laboratory					
3.85.	ITT	SAFE_T12	Laboratory Results (Observed and Change from Baseline) by Visit: Hematology (Double-blind Phase)		SAC
3.86.	ITT	SAFE_T12	Laboratory Results (Observed and Change from Baseline) by Visit: Liver Function (Double-blind Phase)		SAC
3.87.	ITT	SAFE_T12	Laboratory Results (Observed and Change from Baseline) by Visit: Electrolytes (Double-blind Phase)		SAC
3.88.	ITT	SAFE_T12	Laboratory Results (Observed and Change from Baseline) by Visit: Other Chemistries (Double-blind Phase)		SAC
3.89.	ITT	SAFE_T12	Laboratory Results (Observed and Change from Baseline) by Visit: Immunoglobulins (Double-blind Phase)		SAC
Worst Laboratory Toxicity Grade (By Year Interval)					
3.90.	ITT	SAFE_T13	Worst Laboratory Toxicity Grade by Year Interval: Hematology (Double-blind Phase)		SAC

Safety: Tables					
No.	**Population**	**Example Shell (IDSL)**	**Title**	**Programming Notes**	**Deliverable**
3.91.	ITT	SAFE_T13	Worst Laboratory Toxicity Grade by Year Interval: Liver Function (Double-blind Phase)		SAC
3.92.	ITT	SAFE_T13	Worst Laboratory Toxicity Grade by Year Interval: Electrolytes (Double-blind Phase)		SAC
3.93.	ITT	SAFE_T13	Worst Laboratory Toxicity Grade by Year Interval: Other Chemistries (Double-blind Phase)		SAC
3.94.	ITT	SAFE_T13	Worst Laboratory Toxicity Grade by Year Interval: Urinalysis (Double-blind Phase)		SAC
3.95.	ITT	SAFE_T13	Worst Laboratory Toxicity Grade by Year Interval: Immunoglobulins (Double-blind Phase)		SAC
3.96.	ITT	SAFE_T14	Laboratory Toxicity Grade Worsening of at Least 2 Grades from Baseline by Year Interval: Hematology (Double-blind Phase)		SAC
3.97.	ITT	SAFE_T14	Laboratory Toxicity Grade Worsening of at Least 2 Grades from Baseline by Year Interval: Liver Function (Double-blind Phase)		SAC
3.98.	ITT	SAFE_T14	Laboratory Toxicity Grade Worsening of at Least 2 Grades from Baseline by Year Interval: Electrolytes (Double-blind Phase)		SAC
3.99.	ITT	SAFE_T14	Laboratory Toxicity Grade Worsening of at Least 2 Grades from Baseline by Year Interval: Other Chemistries (Double-blind Phase)		SAC
3.100.	ITT	SAFE_T14	Laboratory Toxicity Grade Worsening of at Least 2 Grades from Baseline by Year Interval: Urinalysis (Double-blind Phase)		SAC
3.101.	ITT	SAFE_T14	Laboratory Toxicity Grade Worsening of at Least 2 Grades from Baseline by Year Interval: Immunoglobulins (Double-blind Phase)		SAC
Laboratory Reference Range Shifts (By Visit)					

Safety: Tables					
No.	**Population**	**Example Shell (IDSL)**	**Title**	**Programming Notes**	**Deliverable**
3.102.	ITT	SAFE_T15	Laboratory Reference Range Shifts from Baseline by Visit: Hematology (Double-blind Phase)		SAC
3.103.	ITT	SAFE_T15	Laboratory Reference Range Shifts from Baseline by Visit: Liver Function (Double-blind Phase)		SAC
3.104.	ITT	SAFE_T15	Laboratory Reference Range Shifts from Baseline by Visit: Electrolytes (Double-blind Phase)		SAC
3.105.	ITT	SAFE_T15	Laboratory Reference Range Shifts from Baseline by Visit: Other Chemistries (Double-blind Phase)		SAC
3.106.	ITT	SAFE_T15	Laboratory Reference Range Shifts from Baseline by Visit: Urinalysis (Double-blind Phase)		SAC
3.107.	ITT	SAFE_T15	Laboratory Reference Range Shifts from Baseline by Visit: Immunoglobulins (Double-blind Phase)		SAC
Immunogenicity					
3.108.	ITT	SAFE_T16	Immunogenic Response by Visit (Double-blind Phase)		SAC
3.109.	ITT	SAFE_T17	Immunogenic Response by Year Interval (Double-blind Phase)		SAC
3.110.	ITT	SAFE_T18	Immunogenic Summary (Double-blind Phase)		SAC
3.111.	ITT	SAFE_T18	Immunogenic Summary (Age ≥ 65 Yrs) (Double-blind Phase)		SAC
3.112.	ITT	SAFE_T18	Immunogenic Summary (Age ≥ 75 Yrs) (Double-blind Phase)		SAC
Vital Signs					
3.113.	ITT	SAFE_T19	Vital Signs by Visit (Double-blind Phase)		SAC

10.12.8. Safety Figures

Safety: Figures					
No.	**Population**	**Example Shell**	**Title**	**Programming Notes**	**Deliverable**
3.1.	ITT	TTE10	Kaplan-Meier Plot of Time to Study Withdrawal (Double-blind Phase)	Withdrawals can be identified where DS.DSFAIL = Y	SAC
3.2.	ITT	TTE10	Kaplan-Meier Plot of Time to Study Treatment Withdrawal (Double-blind Phase)	Treatment withdrawals can be identified where SDSTOPP = Y	SAC
3.3.	ITT	SAFE_F1	Cumulative AE Incidence Over Time (Double-blind Phase)	Order categories per order mock shell.	SAC
Laboratory					
3.4.	ITT	SAFE_F2	Laboratory Results by Visit: Hematology (Double-blind Phase)	Figures 3.5 to 3.13: Use figure format and if applicable, modify based on data. For "Change from Baseline" Figures: amend y-axis label to be "Change from Baseline".	SAC
3.5.	ITT	SAFE_F2	Laboratory Results by Visit: Liver Function (Double-blind Phase)		SAC
3.6.	ITT	SAFE_F2	Laboratory Results by Visit: Electrolytes (Double-blind Phase)		SAC
3.7.	ITT	SAFE_F2	Laboratory Results by Visit: Other Chemistries (Double-blind Phase)		SAC
3.8.	ITT	SAFE_F2	Laboratory Results by Visit: Immunoglobulins (Double-blind Phase)		SAC
3.9.	ITT	SAFE_F2	Laboratory Results Change from Baseline by Visit: Hematology (Double-blind Phase)		SAC
3.10.	ITT	SAFE_F2	Laboratory Results Change from Baseline by Visit: Liver Function (Double-blind Phase)		SAC
3.11.	ITT	SAFE_F2	Laboratory Results Change from Baseline by Visit: Electrolytes (Double-blind Phase)		SAC
3.12.	ITT	SAFE_F2	Laboratory Results Change from Baseline by Visit: Other Chemistries (Double-blind Phase)		SAC
3.13.	ITT	SAFE_F2	Immunoglobulin Levels Change from Baseline by Visit (Double-blind Phase)		SAC

10.12.9. Pharmacokinetic Tables

Pharmacokinetic : Tables					
No.	**Population**	**IDSL / TST ID / Example Shell**	**Title**	**Programming Notes**	**Deliverable**
4.1.	PK	PK_T1	Belimumab Concentrations (Observed) (Double-Blind Phase)		SAC

10.12.10. Pharmacokinetic Figures

Pharmacokinetic : Figures					
No.	**Population**	**IDSL / TST ID / Example Shell**	**Title**	**Programming Notes**	**Deliverable**
4.1.	PK	PK_F1	Median belimumab Concentrations (Observed) (Double-Blind Phase)		SAC
4.2.	PK	PK_F1	Mean belimumab Concentrations (Observed) (Double-Blind Phase)		SAC
4.3.	PK	PK_F1	Individual belimumab Concentrations (Observed) (Double-Blind Phase)		SAC

10.12.11. Pharmacokinetic Listings

Pharmacokinetic : Listings					
No.	**Population**	**IDSL / TST ID / Example Shell**	**Title**	**Programming Notes**	**Deliverable**
4.1.	PK	PK_L1	Serum belimumab PK Concentration-Time Data		SAC

10.12.12. Biomarker Tables

Biomarker : Tables					
No.	**Population**	**IDSL / TST ID / Example Shell**	**Title**	**Programming Notes**	**Deliverable**
5.1.	ITT	PD_T1	Summary of ANCA Status over Time (Double-blind Phase)		SAC
5.2.	Subgroup of ITT	PD_T1	Summary of ANCA Status over Time (Age ≥ 65 Yrs) (Double-blind Phase)		SAC
5.3.	Subgroup of ITT	PD_T1	Summary of ANCA Status over Time (Age ≥ 75 Yrs) (Double-blind Phase)		SAC
5.4.	ITT	PD_T2	Summary of ANCA Status Over Time, Compared to Baseline (Double-blind Phase)		SAC
5.5.	ITT	PD_T3	Complement Levels (Observed and Change from Baseline) by Visit (Double-blind Phase)		SAC
5.6.	ITT	PD_T3	Complement Levels (Observed and Percentage Change from Baseline) by Visit (Double-blind Phase)		SAC
5.7.	ITT	PD_T3	Immunoglobulin Levels (Observed and Change from Baseline) by Visit (Double-blind Phase)		SAC
5.8.	ITT	PD_T3	Immunoglobulin Levels (Observed and Percentage Change from Baseline) by Visit (Double-blind Phase)		SAC
5.9.	ITT	PD_T3	C-Reactive Protein (CRP) Levels (Observed and Change from Baseline) by Visit (Double-blind Phase)		SAC

Biomarker : Tables					
No.	**Population**	**IDSL / TST ID / Example Shell**	**Title**	**Programming Notes**	**Deliverable**
5.10.	ITT	PD_T3	C-Reactive Protein (CRP) Levels (Observed and Percentage Change from Baseline) by Visit (Double-blind Phase)		SAC
5.11.	ITT	PD_T3	Urinary Creatinine Ratio (Observed and Change from Baseline) by Visit (Double-blind Phase)		SAC
5.12.	ITT	PD_T3	Urinary Creatinine Ratio (Observed and Percentage Change from Baseline) by Visit (Double-blind Phase)		SAC
5.13.	ITT	PD_T3	Estimated Glomerular Filtration Rate (eGFR) (Observed and Change from Baseline) by Visit (Double-blind Phase)		SAC
5.14.	ITT	PD_T3	Estimated Glomerular Filtration Rate (eGFR) (Observed and Percentage Change from Baseline) by Visit (Double-blind Phase)		SAC
5.15.	ITT	PD_T3	B Cells (FACS of Peripheral Lymphocytes) (Observed and Change from Baseline) by Visit (Double-blind Phase)	Please include all B cell and T cell subsets. Concentration and percentage BIMETHCD only.	SAC
5.16.	Subgroup of ITT	PD_T3	B Cells (FACS of Peripheral Lymphocytes) (Observed and Change from Baseline) by Visit (Age ≥ 65 Yrs) (Double-blind Phase)		SAC
5.17.	Subgroup of ITT	PD_T3	B Cells (FACS of Peripheral Lymphocytes) (Observed and Change from Baseline) by Visit (Age ≥ 75 Yrs) (Double-blind Phase)		SAC
5.18.	ITT	PD_T3	B Cells (FACS of Peripheral Lymphocytes) (Observed and Percentage Change from Baseline) by Visit (Double-blind Phase)		SAC

10.12.13. Biomarker Figures

Biomarker: Figures					
No.	**Population**	**IDSL / TST ID / Example Shell**	**Title**	**Programming Notes**	**Deliverable**
5.1.	ITT	SAFE_F2	Complement Levels Change from Baseline by Visit (Double-blind Phase)	Display all visits to Year 2 Week 28. If distribution looks non-normal plot median change.	SAC
5.2.	ITT	SAFE_F2	Complement Levels Percentage Change from Baseline by Visit (Double-blind Phase)	Display all visits to Year 2 Week 28. If distribution looks non-normal plot median change.	SAC
5.3.	ITT	SAFE_F2	Immunoglobulin Levels Change from Baseline by Visit (Double-blind Phase)	Display all visits to Year 2 Week 28. If distribution looks non-normal plot median change.	SAC
5.4.	ITT	SAFE_F2	Immunoglobulin Levels Percentage Change from Baseline by Visit (Double-blind Phase)	Display all visits to Year 2 Week 28. If distribution looks non-normal plot median change.	SAC
5.5.	ITT	SAFE_F2	C-Reactive Protein (CRP) Levels Change from Baseline by Visit (Double-blind Phase)	Display all visits to Year 2 Week 28. If distribution looks non-normal plot median change.	SAC
5.6.	ITT	SAFE_F2	C-Reactive Protein (CRP) Levels Percentage Change from Baseline by Visit (Double-blind Phase)	Display all visits to Year 2 Week 28. If distribution looks non-normal plot median change.	SAC
5.7.	ITT	SAFE_F2	Urinary Creatinine Ratio Change from Baseline by Visit (Double-blind Phase)	Display all visits to Year 2 Week 28. If distribution looks non-normal plot median change.	SAC
5.8.	ITT	SAFE_F2	Estimated Glomerular Filtration Rate (eGFR) Change from Baseline by Visit (Double-blind Phase)	Display all visits to Year 2 Week 28. If distribution looks non-normal plot median change.	SAC
5.9.	ITT	SAFE_F2	Estimated Glomerular Filtration Rate (eGFR) Percentage Change from Baseline by Visit (Double-blind Phase)	Display all visits to Year 2 Week 28. If distribution looks non-normal plot median change.	SAC

Biomarker: Figures					
No.	**Population**	**IDSL / TST ID / Example Shell**	**Title**	**Programming Notes**	**Deliverable**
5.10.	ITT	SAFE_F2	B Cells (FACS of Peripheral Lymphocytes) Change from Baseline by Visit (Double-blind Phase)	Display all visits to Year 2 Week 28. If distribution looks non-normal plot median change. Please repeat for all B cell & T cell subsets	SAC
5.11.	Subgroup of ITT	SAFE_F2	B Cells (FACS of Peripheral Lymphocytes) Change from Baseline by Visit (Age ≥ 65 Yrs) (Double-blind Phase)		SAC
5.12.	Subgroup of ITT	SAFE_F2	B Cells (FACS of Peripheral Lymphocytes) Change from Baseline by Visit (Age ≥ 75 Yrs) (Double-blind Phase)		SAC
5.13.	ITT	SAFE_F2	B Cells (FACS of Peripheral Lymphocytes) Percentage Change from Baseline by Visit (Double-blind Phase)	Display all visits to Year 2 Week 28. If distribution looks non-normal plot median change. Please repeat for all B cell & T cell subsets	SAC

10.12.14. ICH Listings

ICH : Listings (Safety)					
No.	**Population**	**Example Shell**	**Title**	**Programming Notes**	**Deliverable**
Subject Disposition					
1.	Randomized	POP_L1	Listing of Subject Disposition (Double-blind Phase)		SAC
2.	Screened	ES7	Listing of Reasons for Screening Failure (Double-blind Phase)		SAC
3.	Randomized	ES2	Listing of Reasons for Subject Withdrawal (Double-blind and Open-label)		SAC
4.	Randomized	ES2	Listing of Reasons for Subject Study Treatment Withdrawal (Double-blind Phase)		SAC
5.	Randomized	POP_L2	Listing of Planned and Actual Treatment Arms (Double-blind Phase)		SAC
Inclusion / Exclusion Criteria					
6.	Randomized	IE3	Listing of Eligibility Criteria Not Met (Double-blind Phase)		SAC
Protocol Deviations					
7.	Randomized	DV2	Listing of Important Protocol Deviations		SAC
Baseline Demographic Characteristics					
8.	Randomized	DM2	Listing of Demographic Characteristics (Double-blind Phase)		SAC
9.	Randomized	COV2	Listing of Randomized and Actual Strata (Double-blind Phase)	Treatment group can go at top-left of table rather than being a column. Have Center ID / Subj. ID as one column to be consistent.	SAC
10.	Randomized	DM9	Listing of Race and Racial Combinations (Double-blind Phase)		SAC
Medical History					
11.	Randomized	MH2	Listing of Prior Medical Conditions (Double-blind Phase)	Please include footnote “Prior medical conditions as reported by Investigators.”	SAC

ICH : Listings (Safety)					
No.	**Population**	**Example Shell**	**Title**	**Programming Notes**	**Deliverable**
12.	Randomized	MH2	Listing of Other Prior Medical Conditions (Double-blind Phase)	Include all "other" medical conditions that could not be merged to MedDRA.	SAC
13.	Randomized	CM3	Listing of Concomitant Medications (Double-blind and Open-label)		SAC
14.	Randomized	POP_L3	Listing of Concomitant Procedures/Surgeries (Double-blind and Open-label)		SAC
Exposure and Treatment Compliance					
15.	Randomized	POP_L4	Listing of Study Drug Exposure (Double-blind and Open-label)		SAC
16.	Randomized	POP_L5	Listing of Study Drug Administration (Double-blind and Open-label)		SAC
17.	Randomized	POP_L6	Listing of Subjects switching from Azathioprine to Methotrexate		SAC
18.	Randomized	POP_L7	Listing of Treatment Failures (Double-blind Phase)		SAC
Adverse Events					
19.	Randomized	SAFE_L1	Listing of All Adverse Events (Double-blind and Open-label)		SAC
20.	Randomized	SAFE_L1	Listing of All Adverse Events (Age ≥ 65 Yrs) (Double-blind and Open-label)		SAC
21.	Randomized	SAFE_L1	Listing of All Adverse Events (Age ≥ 75 Yrs) (Double-blind and Open-label)		SAC
22.	Randomized	SAFE_L1	Listing of Serious Adverse Events (Double-blind and Open-label)		SAC
23.	Randomized	SAFE_L1	Listing of Serious Adverse Events (Age ≥ 65 Yrs) (Double-blind and Open-label)		SAC
24.	Randomized	SAFE_L1	Listing of Serious Adverse Events (Age ≥ 75 Yrs) (Double-blind and Open-label)		SAC
25.	Randomized	SAFE_L1	Listing of Serious or Severe Infections (Double-blind and Open-label)		SAC
26.	Randomized	SAFE_L1	Listing of Study Drug-Related Adverse Events (Double-blind and Open-label)		SAC

ICH : Listings (Safety)					
No.	**Population**	**Example Shell**	**Title**	**Programming Notes**	**Deliverable**
27.	Randomized	SAFE_L1	Listing of Non-Fatal Serious Adverse Events (Double-blind and Open-label)		SAC
28.	Randomized	SAFE_L1	Listing of Fatal Adverse Events (Double-blind and Open-label)		SAC
29.	Randomized	SAFE_L1	Listing of Adverse Events Resulting in Study Drug Discontinuation or Study Withdrawal (Double-blind and Open-label)		SAC
30.	Randomized	SAFE_L1	Listing of Adverse Events Resulting in Study Drug Discontinuation or Study Withdrawal (Age ≥ 65 Yrs) (Double-blind and Open-label)		SAC
31.	Randomized	SAFE_L1	Listing of Adverse Events Resulting in Study Drug Discontinuation or Study Withdrawal (Age ≥ 75 Yrs) (Double-blind and Open-label)		SAC
32.	Randomized	SAFE_L1	Listing of Deaths (Double-blind and Open-label)		SAC
33.	Randomized	SAFE_L2	Listing of Adverse Events of Special Interest (Double-blind and Open-label)		SAC
34.	Randomized	SAFE_L3	Listing of Subject Numbers for Individual Adverse Events (Double-blind and Open-label)		SAC
Laboratory					
35.	Randomized	SAFE_L4	Listing of Laboratory Results: Hematology (Double-blind and Open-label)		SAC
36.	Randomized	SAFE_L4	Listing of Laboratory Results: Liver Function (Double-blind and Open-label)		SAC
37.	Randomized	SAFE_L4	Listing of Laboratory Results: Electrolytes (Double-blind and Open-label)		SAC
38.	Randomized	SAFE_L4	Listing of Laboratory Results: Other Chemistries (Double-blind and Open-label)		SAC
39.	Randomized	SAFE_L4	Listing of Laboratory Results: Urinalysis (Double-blind and Open-label)		SAC

ICH : Listings (Safety)					
No.	**Population**	**Example Shell**	**Title**	**Programming Notes**	**Deliverable**
40.	Randomized	SAFE_L4	Listing of Laboratory Results: Immunoglobulins (Double-blind and Open-label)		SAC
41.	Randomized	SAFE_L5	Listing of Grade 3 or Grade 4 Laboratory Toxicity Results: Hematology (Double-blind and Open-label)		SAC
42.	Randomized	SAFE_L5	Listing of Grade 3 or Grade 4 Laboratory Toxicity Results: Liver Function (Double-blind and Open-label)		SAC
43.	Randomized	SAFE_L5	Listing of Grade 3 or Grade 4 Laboratory Toxicity Results: Electrolytes (Double-blind and Open-label)		SAC
44.	Randomized	SAFE_L5	Listing of Grade 3 or Grade 4 Laboratory Toxicity Results: Other Chemistries (Double-blind and Open-label)		SAC
45.	Randomized	SAFE_L5	Listing of Grade 3 or Grade 4 Laboratory Toxicity Results: Urinalysis (Double-blind and Open-label)		SAC
46.	Randomized	SAFE_L5	Listing of Grade 3 or Grade 4 Laboratory Toxicity Results: Immunoglobulins (Double-blind and Open-label)		SAC
Immunogenicity and Biomarkers					
47.	Randomized	SAFE_L6	Listing of Immunogenicity Results (Double-blind and Open-label)		SAC
48.	Randomized	SAFE_L7	Listing of Biomarker Results (Double-blind and Open-label)	Please list all biomarkers including eGFR.	SAC
49.	Randomized	SAFE_L7	Listing of B Cell (FACS of Peripheral Lymphocytes) Results (Double-blind and Open-label)	Please modify SAFE_L7 by giving B cell parameter rather than biomarker name	SAC
Vital Signs					
50.	Randomized	SAFE_L8	Listing of Vital Signs (Double-blind and Open-label)		SAC
C-SSRS					
51.	Randomized	CSSRS4	Listing of C-SSRS Suicidal Ideation and Behavior Data (Double-blind Phase)		SAC
52.	Randomized	CSSRS5	Listing of C-SSRS Suicidal Behavior Details (Double-blind Phase)		SAC

ICH : Listings (Safety)					
No.	**Population**	**Example Shell**	**Title**	**Programming Notes**	**Deliverable**
53.	Randomized	CSSRS6	Listing of Details of Most Severe C-SSRS Suicidal Ideation at Each C-SSRS Assessment (Double-blind Phase)		SAC
54.	Randomized	SAFE_L9	Listing of Possible Suicidality Related Questionnaire (Double-blind Phase)		SAC
55.	Randomized	SAFE_L10	Listing of Survival Status at Week 52 (Double-Blind Phase)		SAC

10.12.15. Non-ICH Listings

Non-ICH : Listings					
No.	**Population**	**IDSL / TST ID / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
Primary Endpoint					
56.	Randomized	EFF_L1	Listing of Relapses (Double-blind Phase)	Please sort by relapse then Center ID/Subj ID, then visit	SAC
57.	Randomized	EFF_L2	Listing of Domain and Item Scored for BVAS Relapses by Visit (Double-blind Phase)		SAC
Time to First Minor or Major Relapse or Receipt of Rescue Medication					
58.	Randomized	EFF_L1	Listing of Minor or Major Relapse or Receipt of Rescue Medication (Double-blind and Open-label)	Please change relapse column to "Event[1]" and add footnote "[1] Event defined as any minor or major BVAS item experienced or receipt of prohibited medication". Change "Relapse Date" to "Event Date"	SAC
Other Binary Endpoints					
59.	Randomized	EFF_L3	Listing of Remission Status by Visit (Double-blind and Open-label)		SAC
Vasculitis Damage Index					

Non-ICH : Listings					
No.	**Population**	**IDSL / TST ID / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
60.	Randomized	EFF_L4	Listing of Vasculitis Damage Index (VDI) by Organ Domain and Visit (Double-blind and Open-label)	Please sort by phase.	SAC
Birmingham Vasculitis Activity Score					
61.	Randomized	EFF_L5	Listing of Birmingham Vasculitis Activity Score (BVAS) by Organ Domain and Visit (Double-blind and Open-label)	Use EFF_F2 and modify based on data.	SAC
Other					
62.			Statistical Analysis of Time to First Relapse (SAS Output)	No example given, please provide SAS output for the primary.	SAC

10.13. Appendix 13: Example Mock Shells for Data Displays

Please refer to mock example document: RAP-BEL115466-Mock-Shells.doc