**Statistical Analysis Plan**

**Study ID:** 205678

**Official Title of Study:** Reporting and Analysis Plan for A Phase II, Open Label, Randomized, Two-Arm Study to Investigate the Efficacy and Safety of Two Doses of the Antibody Drug Conjugate GSK2857916 in Participants with Multiple Myeloma Who Had 3 or More Prior Lines of Treatment, Are Refractory to Proteasome Inhibitor and an Immunomodulatory Agent and Have Failed an Anti-CD38 Antibody (DREAMM 2)

**NCTID:** NCT03525678

**Date of Document:** 06 Apr 2022

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|---|---|---|
| **Division** | : | Worldwide Development |
| **Information Type** | : | Reporting and Analysis Plan (RAP) |
| **Title** | : | Reporting and Analysis Plan for A Phase II, Open Label, Randomized, Two-Arm Study to Investigate the Efficacy and Safety of Two Doses of the Antibody Drug Conjugate GSK2857916 in Participants with Multiple Myeloma Who Had 3 or More Prior Lines of Treatment, Are Refractory to a Proteasome Inhibitor and an Immunomodulatory Agent and Have Failed an Anti-CD38 Antibody (DREAMM 2) |
| **Compound Number** | : | GSK2857916 |
| **Effective Date** | : | **06** Apr 2022 |

**Description:**

- The purpose of this RAP is to describe the planned analyses and outputs to be included in the Clinical Study Report for Protocol 205678/ Amendment 06 (TMF-13990464 ).
- This RAP is intended to describe the efficacy, safety, pharmacokinetic (PK), pharmacodynamic (PD), and patient reported outcome (PRO) analyses required for the study.
- This RAP will be provided to the study team members to convey the content of the Interim Analysis (IA) and Statistical Analysis Complete (SAC) deliverable.

**RAP Author(s):**

| Approver | Approval Method |
|---|---|
| PPD<br>Senior Statistician (Oncology, Clinical Statistics) | TMF |
| PPD<br>PPD (Clinical Pharmacology Modelling & Simulation) | E-mail |

**RAP Team Approvals:**

| Approver | Approval Method |
|---|---|
| PPD<br>PPD (Oncology, ES Clinical) | TMF/E-mail |
| PPD<br>PPD Clinical Scientist | TMF/E-mail |
| PPD<br>Safety Development Leader (Pharmacovigilance, Safety & Medical Governance) | E-mail |
| PPD<br>Programming Leader (Oncology, Clinical Programming) | TMF/E-mail |

**Clinical Statistics and Clinical Programming Line Approvals:**

| Approver | Approval Method |
|---|---|
| PPD<br>PPD (Oncology, Clinical Statistics) | TMF/E-mail |
| PPD<br>PPD (Oncology, Clinical Programming) | TMF/E-mail |

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# 1. INTRODUCTION

The purpose of this reporting and analysis plan (RAP) is to describe the analyses to be included in the Clinical Study Report for Protocol 205678:

| **Protocol Revision Chronology:** | | |
|---|---|---|
| 2017N330177_00 | 18-JAN-2018 | Original |
| 2017N330177_01 | 02-APR-2018 | Amendment 01<br>The protocol has been amended to address regulatory agency advice. The original single arm design with 1 dose level (3.4 mg/kg GSK2857916 Q3W) was amended to an open-label, randomized, 2-arm study with 2 dose levels by including the 2.5 mg/kg Q3W dose. In addition, a new exploratory cohort of 25 participants, who will receive a lyophilized configuration of GSK2857916, has been added to gain clinical experience with the lyophilized configuration. To accommodate these main changes, the overall sample size and related analytical methods have been changed. |
| 2017N330177_03 | 04-SEP-2018 | Amendment 02<br>Republishing of protocol amendment 2 2017N330177_02 (Dated: 30 Aug 2018), which was not distributed outside GSK.<br>The protocol has been amended to address feedback from regulatory agencies, EC/IRB, and investigators. The updates include the addition of Exclusion Criteria defining the use of high dose steroids, clarification of specific timeframe from last treatment required for systemic anti-myeloma therapy,and increase of QTcF criteria. Additional PK sampling timepoints were added to capture the Cmax of the free cytotoxic drug (cys-mcMMAF) and to better define the kinetics of cys-mcMMAF and the elimination phase of ADC and cys-mcMMAF. Soluble BCMA collection timepoints were also added to capture the effect of GSK2857916 administration on soluble BCMA concentrations over time as a marker of pharmacodynamic effect. The dose modifications guidelines for GSK2857916 related Corneal Events clarify dose adjustments for GSK Scale Grade 2 events. |
| 2017N330177_04 | 17-DEC-2018 | Amendment 03<br>The protocol has been amended to address over-enrolment in the frozen liquid solution portion of the study.<br>Due to the over-enrolment, the primary analysis will be based on all randomized participants (anticipated ~200) enrolled into the frozen liquid solution arms. In addition, a sensitivity analysis based on the first 130 participants will be performed to account for the original design. |

| Protocol Revision Chronology: | | |
|---|---|---|
| TMF-13990464 | 19-Nov-2021 | Amendment 06<br>The protocol has been amended to introduce the approved standard language for belantamab mafodotin studies implementing PACT |

## 1.1. RAP Amendments

Revision chronology:

| RAP Section | Amendment Details |
|---|---|
| **Reporting and Analysis Plan_Study205678_Final_V1 [02-MAY-2019]** | |
| **Reporting and Analysis Plan_Study205678_Amendment_Final_V1 [16-JUL-2019]** | |
| **Reporting and Analysis Plan_Study205678_Amendment2_Final_V1 [06 Apr 2022]** | |
| RAP Authors/Team Approval | • Update the approvers. |
| Section 2.1 Changes to the Protocol Defined Statistical Analysis Plan | • Updated protocol version and document number |
| Section 2.3 Study design | • Updated reference to IA section per PA06. |
| Section 3.1 Interim analyses | • Updated protocol version and document number |
| Section 3.1.2 Additional Comparative Futility Stopping Rule Based on Bayesian Approach | • Update protocol document number |
| Section 3.2 primary analysis | • Updated reference to end of study section per PA06. |
| Section 6.2 disposition of subjects | • Added analysis regarding visits and assessments Impacted by COVID-19 Pandemic will be presented |
| Section 6.5 Extent of exposure | • Added listing of all dose delays due to corneal events (GSK scale) and listing of dose delays and associated Eye Disorder Events (CTCAE)<br>• Added analysis for duration of exposure by response category,<br>• Added KM curve for time to treatment discontinuation by response category and for subject who received at least 3 cycle of the study treatment<br>• Added Swim-lane plot for duration of study treatment for responder based on IRC |
| Section 7.2.1.5 Progression Free survival Table 4 | • Updated Adequate baseline assessment definition for Serum FLC assay: Involved FLC level >=10 mg/dL (>=100 mg/L) based on PA06 |
| Section 7.2.1.7 Overall survival | • Updated reference to end of study section per PA06. |
| Section 7.2.2 Summary measure | • Added a KM curve for Duration of response by dose delay category , by response category per IRC. Added Hazard ratio estimate by Pike estimator.<br>• Added a summary for time to best response based on IRC<br>• Added KM curve for PFS and Overall survival by response category per IRC. |

| RAP Section | Amendment Details |
|---|---|
| **Reporting and Analysis Plan_Study205678_Final_V1 [02-MAY-2019]** | |
| **Reporting and Analysis Plan_Study205678_Amendment_Final_V1 [16-JUL-2019]** | |
| **Reporting and Analysis Plan_Study205678_Amendment2_Final_V1 [06 Apr 2022]** | |
| Section 8.2.3 Corneal events (GSK scale) | • Update protocol document number<br>• Added new summaries and characteristics tables for Blurred vision, Dry Eyes, Ocular symptoms, Visual acuity change , BCVA, Eye disorder under #10-72<br>• Added profile plot for patients with maximum toxicity grade<br>• Added Bar chart for toxicity grade by cycle<br>• Added plot for time to recovery post treatment discontinuation for corneal exam findings and for keratopathy<br>• Added plot for visual acuity and corneal findings grade for subject experiencing more than 1 corneal events for 2.5 mg/kg arm. |
| Section 8.5 Ocular findings from ophthalmic exam | • Updated reference to Schedule of activities section per PA06. |
| Section 15.7.2.1 Handling of Missing and Partial Dates | • Added study end date handling for subjects continuing to PACT as “For PACT subjects, subject’s last Visit date will be used as subject’s end of study date, wherever required” |
| Section 15.12.1 Abbreviations | • Added description for PACT |
| Section 15.13. List of data displays | • Added SAC [2] against displays to be produced for End of Study (EoS) SAC.<br>• Added Section for COVID19 displays<br>• Added F1.00010 F1.00011 F1.00013 T1.11140 F2.00402 T2.0061 F2.10010 T2.10010 F2.10020 T2.10040 T2.10041 T2.10050 F2.10080 F2.30305 F2.70033 L3.10010 L3.10011 F3.10031 T3.12030 T3.12461 T3.12471 T3.12472 T3.12473 T3.12480 T3.12490 T3.12731 T3.12735 T3.12737 T3.12738 T3.12751 T3.12753 T3.12761 T3.12763 T3.12770 T3.12771 T3.12772 T3.12773 T3.12774 T3.12781 T3.12791 T3.12793 T3.12801 T3.12811 T3.12821 T3.12823 T3.12831 T3.12841 T3.12851 T3.12852 T3.12861 T3.12871 T3.12873 T3.12881 T3.12891 T3.12921 T3.12931 T3.12941 T3.12951 T3.12961 T3.12971 T3.12981 T3.50013 T3.50020 T3.50021 T3.50022 F3.50030 F3.53010 F3.53020 T3.60100 T3.70010 T3.70012 T3.90010 T3.90020 T3.90040 T3.90050 L30.0191 L8.0102 L8.0103 T8.50070 T8.50080 F1.0082 L1.0082,<br>• Updated table number for 3.0250 to 3.2051 for Overview of Keratopathy Event (CTCAE) , 3.0252 for Overview of Dry Eye Event (CTCAE),3.253 for Overview of Blurred Vision Event (CTCAE)<br>• Updated table title for T3.1280 to Logistic Regression Analysis of Possible Risk Factors for Developing Corneal Events Grade >=2 (GSK Scale<br>• Corrected table number for Shift in Corneal Epithelium Findings from Baseline to Worst Post-Baseline to 3.0852 based on primary_01 RE<br>• Per team discussion, updated programming note for Table 3.0710 . Removed “In the current footnote, replace ‘<=25000 ng/mL’ with ‘<=500000 ng/mL’. Added “Replace ‘Negative, Conclusive’ and |

| RAP Section | Amendment Details |
|---|---|
| **Reporting and Analysis Plan_Study205678_Final_V1 [02-MAY-2019]** | |
| **Reporting and Analysis Plan_Study205678_Amendment_Final_V1 [16-JUL-2019]** | |
| **Reporting and Analysis Plan_Study205678_Amendment2_Final_V1 [06 Apr 2022]** | |
| | 'Negative, Inconclusive' rows with 'Negative' " . |
| RAP Authors/Team Approval | • Update the approvers required and method for approval per SOP_54838 (6.0). |
| Section 4 Analysis Population | • Clarified that same participant enrolled more than once will be counted only once based on the last randomization number |
| Section 5.1 Study Treatment Display Description | • Fixed the error in code labelling and made minor format changes. |
| Section 5.3.2. Examination of Subgroups | • Added a subgroup Baseline renal impairment status per eGFR (ml/min/1.73 $m^2$), which will be included in the existing forest plot for ORR.<br>• Change the wording "Caucasian' to 'White' to be consistent with CRF. |
| Section 6.3 Demographic and Baseline Characteristics | • Added 'number of prior lines of therapy' to the summary table of disease characteristics at screening. |
| Section 8.1 Adverse Event Analysis | • Fixed the typo 'dose delay' to 'permanent discontinuation of study treatment' for AE overview table. |
| Section 8.2 Adverse events of special interest | • Per team decision: replace the 'corneal event (CTCAE)' with 'eye disorder (CTCAE)'; remove the displays associated with corneal event (CTCAE); add Section 8.2.2 to specify displays associated with eye disorder (CTCAE). |
| Section 8.2.3 Corneal events (GSK scale) | • Added clarifying edits and fixed typos. |
| Section 8.5 Ocular findings from ophthalmic exam | • Per team decision: 1) added the shift table from baseline to worst post-baseline by eye (R/L) for Schirmer's Test and Tear Break-up Time; 2) remove the analyses related to refraction (spherical equivalent) due to data collected in text field.<br>• Added clarifying edits and fixed typos. |
| Section 15.6.2 | • Clarify the definition of 'Duration of Exposure'. |
| Section 15.6.4 | • Replace the 'corneal event (CTCAE)' with 'eye disorder (CTCAE)' |
| Section 15.8.2 | • Clarified that ECG displays will be based on central reading unless otherwise specified, |
| Section 15.13. Appendix 13: List of Data Displays | • Remove the displays associated with corneal event (CTCAE): T3.0190/3.0210/3.0211/3.0230/3.0240/3.0260<br>• Replace/add displays associated with eye disorder (CTCAE) as specified in Section 8.2.2: T3.0170-3.0174, T3.0180-3.0184, T3.0200-3.0204, T3.0250-3.0255, T3.0950-3.0954, 3.1320-3.1324, L1.0290/1.0300.<br>• For corneal event (GSK scale), add tables 3.0911/3.1330/3.1331; remove Table 3.0390/3.0400<br>• For visual acuity (GSK scale), add table 3.0912.<br>• For refraction (spherical equivalent), remove table 3.0750, and figures |

| RAP Section | Amendment Details |
|---|---|
| **Reporting and Analysis Plan_Study205678_Final_V1 [02-MAY-2019]** | |
| **Reporting and Analysis Plan_Study205678_Amendment_Final_V1 [16-JUL-2019]** | |
| **Reporting and Analysis Plan_Study205678_Amendment2_Final_V1 [06 Apr 2022]** | |
| | 3.0010/3.0011.<br>• Add shift table for Schirmer's Test and Tear Break-up Time as specified in Section 8.5: T3.1340/3.1350<br>• Updates the displays for QLQ-My20: T8.0080/8.0081)<br>• Made clarifying edits in title/footnote, update delivery priority, and fixed typos in various mock shells to incorporate comments/decision following dry run reviews. |
| Section 15.14. Appendix 14: Example of Mock Shells | • Add mock shell Safe_T4b, Safe_T9a, Safe_T21, and Safe_T22.<br>• Made clarifying edits in title/footnote, and fixed typos in various mock shells to incorporate comments from dry run reviews. |

# 2. SUMMARY OF KEY PROTOCOL INFORMATION

## 2.1. Changes to the Protocol Defined Statistical Analysis Plan

There were no changes or deviations to the originally planned statistical analysis specified in the protocol amendment 6 GSK Document Number TMF-13990464 (Dated: 19-Nov-2021).

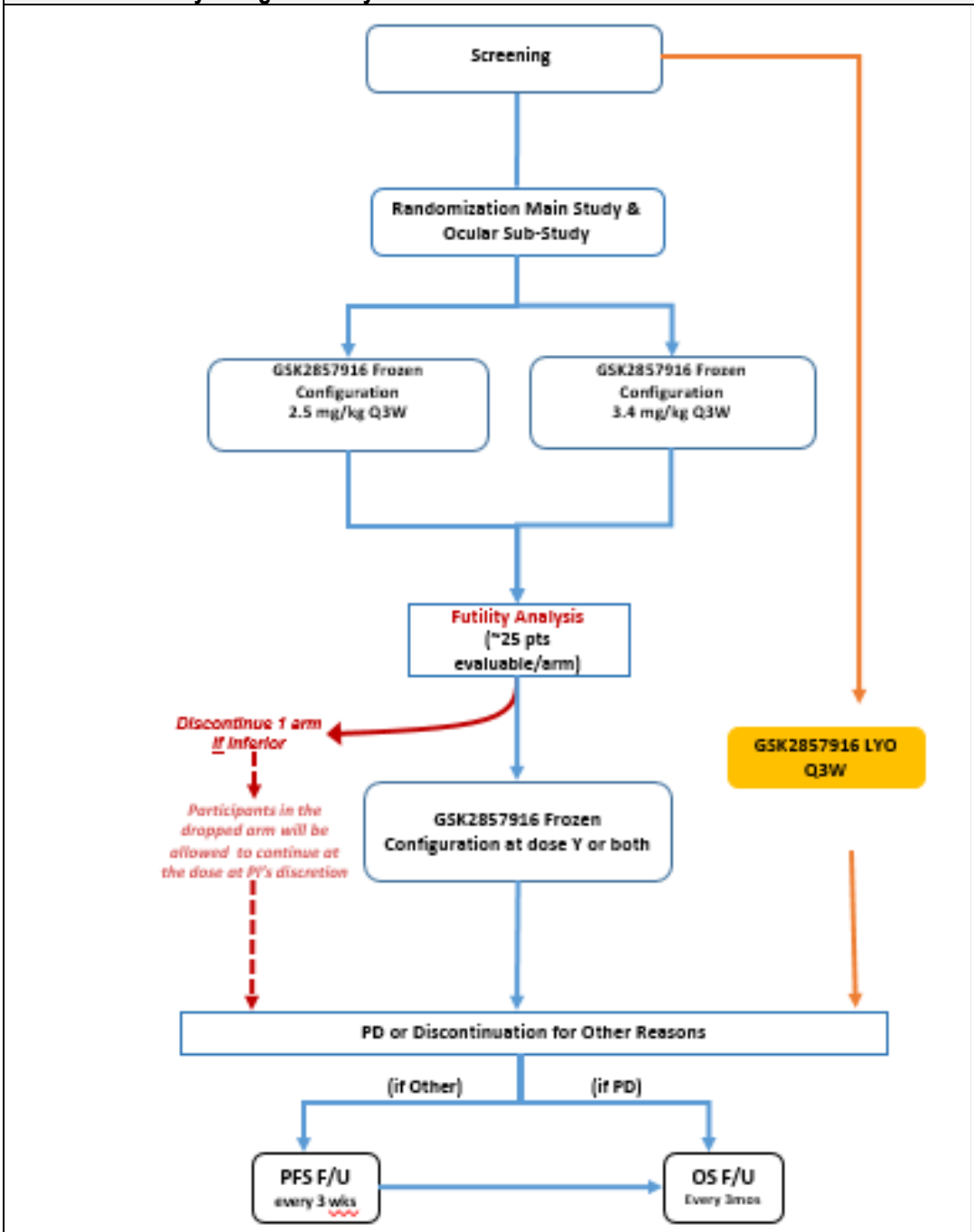
## 2.2. Study Objective(s) and Endpoint(s)

| Objectives | Endpoints |
|---|---|
| **Primary Objectives** | **Primary Endpoints** |
| • To evaluate the clinical efficacy of 2 doses of GSK2857916 in participants with relapsed/refractory multiple myeloma. | • ORR, defined as the percentage of participants with a confirmed partial response (PR) or better (i.e., PR, very good partial response [VGPR], complete response [CR] and stringent complete response [sCR]), according to the 2016 International Myeloma Working Group (IMWG) Response Criteria by Independent Review Committee (IRC). |
| **Secondary Objectives** | **Secondary Endpoints** |
| • To further evaluate the clinical measures of efficacy of GSK2857916 in participants with RRMM | • ORR, defined as the percentage of participants with a confirmed partial response (PR) or better, according to the 2016 International Myeloma Working Group (IMWG) Response Criteria by investigator assessment<br><br>• Clinical benefit rate (CBR), defined as the percentage of participants with a confirmed minimal response (MR) or better according to the 2016 International Myeloma Working Group (IMWG) Response Criteria<br><br>• Duration of response (DoR), defined as: the time from first documented evidence of PR or better until the earliest date of documented disease progression (PD) |

| Objectives | Endpoints |
|---|---|
| | per IMWG; or death due to PD occurs among participants who achieve an overall response, i.e., confirmed PR or better.<br><br>• Time to response, defined as the time between the date of randomization and the first documented evidence of response (PR or better).<br><br>• Progression-free survival, defined as the time from randomization until the earliest date of documented disease progression (PD) per IMWG, or death due to any cause.<br><br>• Time to progression, defined as the time from randomization until the earliest date of documented PD per IMWG, or death due to PD.<br><br>• Overall survival, defined as the time from randomization until death due to any cause. |
| • To evaluate the safety of GSK2857916 in participants with RRMM. | • The safety profile of GSK2857916 will be evaluated in participants with RRMM as assessed through: standard clinical and laboratory tests (haematology and chemistry, physical examination, vital sign measurements, and diagnostic tests) through the collection of adverse events (AEs) and serious adverse events (SAEs)<br>• AE of special interest<br>• ocular findings on ophthalmic exam |
| • To evaluate the pharmacokinetic profile of GSK2857916 | • Plasma concentrations of GSK2857916 (ADC, total mAb, and cys-mcMMAF)<br>• Derived pharmacokinetic parameter values (e.g., AUC, Cmax, tmax, t½), as data permit. |
| • To assess anti-drug antibodies (ADAs) against GSK2857916 | • Incidence and titers of ADAs against GSK2857916 |
| • Participant self-reported symptomatic adverse effects by evaluation of tolerability of GSK2857916 | • Symptomatic adverse effects and related impacts as measured by the PRO-CTCAE, NEI-VFQ-25 and OSDI |
| • To evaluate disease and treatment related symptoms and impact on function and health-related quality-of-life | • Health-related quality-of-life as measured by the EORTC QLQ-C30 and EORTC QLQ-MY20 |
| **Exploratory Objectives** | **Exploratory Endpoints** |
| • To explore the relationship between clinical response and other biologic characteristics including BCMA expression on tumor cells and sBCMA concentrations | • Determine BCMA expression levels and other markers on malignant cells, serum sBCMA levels, and evaluate the relationship of these factors to clinical response |
| • To investigate the relationship between genetic variants in the host and response to GSK2857916 | • Possible relationship between host genetic variation and response to GSK2857916 |
| • To evaluate disease and treatment | • Qualitative telephone interview(s) |

| Objectives | Endpoints |
|---|---|
| related symptoms and impact on function and health-related quality-of-life | |
| • To explore exposure-response relationships between GSK2857916 exposure and clinical endpoints | • Explore relationships between GSK2857916 exposure (e.g., dose, dose intensity, concentration, Cmax, or AUC) and clinical endpoints (e.g., response, corneal event), if data permit |
| • To assess Minimal Residual Disease (MRD) in participants who achieve ≥VGPR or better | • Minimal Residual Disease (MRD) negativity rate, defined as: the percentage of participants who are MRD negative by Next Generation Sequencing (NGS). |
| • To assess the safety, efficacy, immunogenicity, and pharmacokinetics of GSK2857916 in a lyophilized configuration (n = approximately 25 participants) | • AEs, clinical and laboratory assessments; Descriptive analyses of ORR, duration of response, time to response, time to progression, overall response; incidence and titers against GSK2857916; plasma concentrations of GSK2857916 (ADC, total mAb, and cys-mcMMAF) and derived pharmacokinetic parameters, if data permit |
| • **Ocular sub-study objective** | |
| • To evaluate the effect of topical corticosteroids on corneal findings in approximately 30 participants who will receive monocular topical corticosteroids for the first 4 cycles | • Description of differences in corneal findings in each eye based on ophthalmic examinations (participant-level). |
| • Abbreviations: IV = intravenous; Q3W: once every 3 weeks; RRMM = relapsed refractory multiple myeloma; BCMA = B-cell maturation antigen; MMAF = monomethyl auristatin-F; MRD = minimal residual disease; NGS = Next Generation Sequencing; ORR = overall response rate; CI = confidence interval; CR = complete response; VGPR = very good partial response; PR = partial response; PFS = progression free survival; AUC = area under the curve; Cmax = maximum observed concentration; tmax = time to maximum observed concentration; t½ = terminal phase half-life; PRO-CTCAE = Patient Reported Outcomes-Common Terminology Criteria for Adverse Events; NEI-VFQ-25 = National Eye Institute Visual Functioning Questionnaire 25; OSDI = Ocular Surface Disease Index; EORTC = European Organisation for Research and Treatment of Cancer; QLQ-C30 = Quality of Life Questionnaire 30-item Core module; FLC = free light chain; SCT = stem cell transplant; QLQ-MY20 = ; Quality of Life Questionnaire 20-item module for MM; QTcF = QT interval corrected by Fridericia's formula; HIV = human immune deficiency virus; RNA = ribose nucleic acid. | |

## 2.3. Study Design

| Overview of Study Design and Key Features | |
|---|---|
|  | |
| **Design Features** | • **GSK2857916 Frozen Configuration Cohorts**<br>○ Population: Subjects with relapsed/refractory MM (130 subjects (65/arm) as planned)<br>○ Objective: evaluate the efficacy and safety of 2 doses of GSK2857916 in participants with RRMM who have received at least 3 prior lines of anti-myeloma therapy, have failed an anti-CD38 antibody, and are refractory to PI and IMiDs. |

| Overview of Study Design and Key Features | |
|---|---|
| | • **Independent GSK2857916 Lyophilized Configuration Cohort**<br>○ Population: Subjects with relapsed/refractory MM (at least 25 subjects)<br>○ Objective: To assess the safety, efficacy, immunogenicity, and PK of GSK2857916 in a lyophilized configuration.<br>• **Ocular Sub-Study**<br>○ Population: Subjects with relapsed/refractory MM (up to 30 subjects (15 subjects each dose))<br>○ Objective: evaluate the effect of topical corticosteroids on corneal findings in subjects who will receive monocular topical corticosteroids for the first 4 cycles and sign an optional ICF. |
| **Dosing** | • **GSK2857916 Frozen Configuration Cohorts**<br>○ GSK2857916 will be administered at a calculated dose of 2.5 mg/kg or 3.4 mg/kg as an IV infusion over at least 30 minutes at the study sites.<br>○ **Independent GSK2857916 Lyophilized Configuration Cohort**<br>○ GSK2857916 will be administered at a calculated dose of 3.4 mg/kg as an IV infusion over at least 30 minutes at the selected study sites when the lyophilized configuration becomes available.<br>○ Lyophilized configuration cohort will be initiated at 2.5 mg/kg if the results of the IA indicate that 3.4 mg/kg should not be continued. . |
| **Time & Events** | • Refer to Appendix 2: Schedule of Activities |
| **Treatment Assignment** | • This is a two-arm, randomized, multi-center, open-label study for GSK2857916 frozen configuration cohort.<br>• For independent lyophilized cohort, there is only one dose group |
| **Interim Analysis** | **GSK2857916 Frozen Configuration Cohorts**<br>• One interim analysis (IA) is planned for the primary endpoint ORR after approximately 25 participants per arm are evaluable for response. Further details can be referred to in Section 3 of RAP and Section 4.1 of the protocol (Version: GSK Document Number TMF-13990464 ). |

## 2.4. Statistical Hypotheses / Statistical Analyses

Study 205678 is designed to provide evidence with respect to ORR to either support the null hypothesis, $H_0$: ORR $\leq$15%, or reject $H_0$ in favor of the alternative hypothesis, $H_1$: ORR$\geq$33%. The hypothesis testing will be performed within each arm separately. No hypothesis testing for comparing ORR between the two arms will be performed.

# 3. PLANNED ANALYSES

## 3.1. Interim Analyses

Details of the interim analysis can be referred to in Protocol Amendment 6 (GSK Document Number. TMF-13990464 ) and the IDMC charter. Details of the planned displays are provided in Appendix 13: List of Data Displays.

### 3.1.1. Futility Stopping Rule Based on Group Sequential Design

For each arm (2.5 mg/kg or 3.4 mg/kg), a single futility IA is planned for the primary endpoint ORR after approximately 25 participants (~38% information fraction) per arm are evaluable. A user-defined gamma spending function ($\gamma$=*1.1*) [Hwang, 1990] was used as a beta-spending function to determine the non-binding futility boundary (as implemented in East 6.4). With this β-spending function, the stopping boundary in IA is identified as 0.16 on the proportion scale (4 responders out of 25 participants), which is close to the historical control of 0.15. The spending function and associated boundary were chosen to ensure good operating characteristics, specifically, the type 1 error and power are well controlled.

A two-step approach is used to identify the futility stopping rule based on a group sequential design under the assumption of exact binomial distribution.

First, as described in Section 3.1.1.1, an initial design based on the assumption of normal approximation of binomial proportion was identified by East 6.4.

The interim futility and primary efficacy analysis boundaries were then converted to number of responders needed in 25 participants per arm who are evaluable at IA and the 65 participants per arm initially planned at the primary analysis.

With a total sample size of 100 participants per arm and an IA with approximately 25 participants per arm, the same futility boundary (≤ 4 responders out of 25 participants) will still apply with a user-defined gamma spending function ($\gamma$=*5.4*). For the primary analysis, the boundary for claiming efficacy is the minimum number of responders required for the lower bound of the two-sided 97.5% exact C.I. to exceed 15% (i.e. 24 responders for sample size of 100 per arm).

Statistical properties of the group sequential design with sample sizes of 65, and 100 per arm are summarized in Table 1.

**Table 1 Probabilities of Crossing Boundaries at the Interim or Primary ORR Analysis based on Group Sequential Design**

| Look | Sample Size (per arm) | Boundaries | Cumulative Boundary Crossing Probabilities | |
|---|---|---|---|---|
| | | # of Responders | Under $H_0$ | Under $H_1$ |
| Interim (futility) | 25 | ≤4 | 68.21% | 4.96% |
| Primary (Efficacy) | 65 | ≥17 | 1.23% | 88.00% |
| | 100 | ≥24 | 0.97% | 93.70% |

Note: The Cumulative Boundary Crossing Probabilities are calculated based on exact binomial distribution theoretically.

#### 3.1.1.1. Operating Characteristics of the Stopping Rules for Futility

The following assumptions were made in the estimation of the required sample size:

- Normal approximation of binomial proportion
- A response rate of ≥33% in the BCMA arm and ≤15% for the historical control
- A 1.25%, one-sided risk of erroneously claiming superiority of the BCMA arm, in the presence of no true underlying improvement
- A ~90% chance of rejecting the null hypothesis when the alternative hypothesis is true

An IA after approximately 38% of information is available (i.e., approximately after 25 participants out of originally planned 65 participants per arm are evaluable for IA), with a futility rule based on a gamma spending function.

The operating characteristics were refined using simulation to account for the within arm futility rule and the comparative futility rule. Based on the simulation results with the originally planned sample size of 65 participants per arm, there is 86.90% power to reject the null hypothesis within each arm with a 1-sided type I error of 1.23%.

Due to over enrolment, it is estimated that approximately 200 participants (~100 per arm) will be randomized to the frozen liquid solution. At the primary analysis, the null hypothesis will be rejected if the lower bound of 2-sided 97.5% exact C.I. exceeds the historical control rate of 15%.

With no change to the planned IA (i.e., approximately after 25 participants/arm are evaluable for IA, and same futility boundary), simulation results show that there is 92.38% power to reject the null hypothesis within each arm with a 1-sided type I error of 0.97% for 100 participants per arm as shown in Table 1.

### 3.1.2. Additional Comparative Futility Stopping Rule Based on Bayesian Approach

If both arms pass the futility boundaries based on group sequential design described above, posterior probability of observing a better RR in one arm relative to the other will be calculated. If such a probability is at least 97.5%, then the treatment arm with lower RR will be dropped due to lack of efficacy. This additional guidance was put in to allow for dropping an arm with substantially inferior response rates (e.g. absolute difference > 28%).

To calculate the posterior probability, a non-informative Beta prior (0.025,0.1) will be used for each arm. Details about calculating the posterior probabilities are provided in Appendix 12 of the protocol amendment 3 (GSK Document Number TMF-13990464 ).

Statistical properties for different scenarios based on both futility rules are summarized in Table 2.

**Table 2 Probabilities of Stopping for Futility at the Interim or Claiming Efficacy at the Primary ORR Analysis based on Both Futility Rules**

| Scenarios | Participants per arm | Response Rate | | Futility Stopping Boundary Crossing Probabilities at IA [1] | | Probabilities of Claiming Efficacy at Primary [1] | |
|---|---|---|---|---|---|---|---|
| | | Arm 1 [2] | Arm 2 [2] | Arm 1 [2] | Arm 2 [2] | Arm 1 [2] | Arm 2 [2] |
| **1** | 65 | 33% | 60% | 53.59% | 0.01% | 44.83% | 99.99% |
| **2** | 65 | 33% | 45% | 16.95% | 0.47% | 77.94% | 99.49% |
| **3** [3] | 65 | 33% | 33% | 6.33% | 6.33% | **86.90%** | 86.92% |
| **4** | 65 | 33% | 25% | 5.09% | 23.83% | 87.89% | 42.39% |
| **5** | 65 | 33% | 20% | 4.97% | 44.59% | 87.98% | 12.52% |
| **6** | 65 | 33% | 15% | 4.96% | 69.99% | 87.99% | 1.20% |
| **7** | 65 | 33% | 10% | 4.96% | 90.85% | 87.99% | 0.01% |
| **8** [4] | 65 | 15% | 15% | 68.22% | 68.22% | **1.23%** | 1.24% |
| **9** | 100 | 33% | 60% | 53.59% | 0.01% | 46.11% | 99.99% |
| **10** | 100 | 33% | 45% | 16.95% | 0.47% | 82.09% | 99.53% |
| **11** [3] | 100 | 33% | 33% | 6.33% | 6.33% | **92.38%** | 92.39% |
| **12** | 100 | 33% | 25% | 5.09% | 23.83% | 93.57% | 53.93% |
| **13** | 100 | 33% | 20% | 4.97% | 44.59% | 93.68% | 15.46% |
| **14** | 100 | 33% | 15% | 4.96% | 69.99% | 93.70% | 0.94% |
| **15** | 100 | 33% | 10% | 4.96% | 90.85% | 93.70% | 0.003% |
| **16** [4] | 100 | 15% | 15% | 68.22% | 68.22% | **0.97%** | 0.97% |

Note:

[1] The Boundary Crossing Probabilities are calculated based on 10,000,000 simulations using R program.

[2] Arm 1 and Arm 2 in the table just represent two different treatment arms and are not necessarily refers to 3.4 mg/kg and 2.5 mg/kg, respectively.

[3] The power is shown in Scenario 3, and 11 as **86.90%** and **92.38%** for sample size of 65, and 100 respectively.

[4] The type I error is shown in Scenario 8, and 16 as **1.23%,** and **0.97%** for sample size of 65, and 100 respectively.

## 3.2. Primary Analyses

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

1. The study reaches 6 months after the last participant in frozen liquid configuration is randomized in the study.
2. All required database cleaning activities have been completed and database release (DBR) and database freeze (DBF) have 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.

An updated analysis for OS will be performed at end of study as defined in Section 4.6 of protocol (Version: GSK Document Number TMF-13990464 ).

# 4. ANALYSIS POPULATIONS

| Population | | Definition / Criteria | Analyses Evaluated |
|---|---|---|---|
| **All Screened** | | • All participants who sign the ICF to participate in the study. | • Study Population |
| **Enrolled** | | • All participants who passed screening. Note screening failures (who never passed screening even if rescreened) and participants screened but never enrolled into the study (Reserve, Not Used) are excluded from the Enrolled population as they did not enter the study. Same participant enrolled more than once will be counted only once based on the last randomization number.<br>• This population will be based on the treatment the participant was randomized to. | • Study Population |
| **Frozen liquid configuration** | **Intent-to-Treat (ITT)** | • All randomized participants whether or not randomized treatment was administered.<br>• This population will be based on the treatment the participant was randomized to.<br>• Any participant who receives a treatment randomization number will be considered to have been randomized.<br>Same participant receiving multiple randomization numbers will be counted only once using the last randomization number. | • Study Population<br>• Efficacy<br>• EORTC QLQ-C30 and EORTC QLQ-MY20 |
| | **Efficacy** | • Efficacy population will consist of first 130 ITT participants whether or not randomized treatment was administered. This population will be based on the treatment to which the participant was randomized and will be used for sensitivity analysis of | • Selected efficacy |

| Population | | Definition / Criteria | Analyses Evaluated |
|---|---|---|---|
| | | primary and selected secondary efficacy endpoints. | |
| | **Evaluable** | • All participants who have at least two doses of study treatment and have completed at least one disease assessment after the second dose, or progressed or died or discontinued treatment due to other reasons. | • Futility analyses at IA |
| | **Safety** | • All randomized participants who received at least one dose of Frozen liquid study treatment.<br>• This population will be based on the treatment the subject actually received (first dose). | • Safety<br>• PRO-CTCAE, NEI-VFQ-25 and OSDI. |
| | **Ocular Sub-Study** | • All randomized participants to ocular sub-study who received at least one dose of study treatment.<br>• This population will be used to evaluate the effect of topical corticosteroids on corneal events/findings in approximately 30 participants who will receive monocular topical corticosteroids for the first 4 cycles | • Corneal events/findings |
| **Lyophilized configuration** | **Lyo** | • All randomized participants who receive at least 1 dose of lyophilized study treatment. | • All analysis other than PK |
| **Full Analysis** | | • All participants included in either ITT or Lyo population<br>• This population will be based on the treatment the participant was randomized to | • Study population<br>• Efficacy<br>• EORTC QLQ-C30 and EORTC QLQ-MY20 |
| **Full Safety** | | • All participants who receive at least 1 dose of study treatment (frozen liquid or lyophilized).<br>• This population will be based on the treatment the subject actually received (first dose). | • Safety<br>• PRO-CTCAE, NEI-VFQ-25 and OSDI. |
| **Full Pharmacokinetic (PK)** | | • All participants in the Full Safety population who had at least 1 non-missing PK assessment (Non-quantifiable [NQ] values will be considered as non-missing values). | • PK |

**Note:** Refer to Appendix 13: List of Data Displays which details the population used for each display being generated in the final version of the RAP.

## 4.1. Protocol Deviations

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

Protocol deviations will be tracked by the study team throughout the conduct of the study in accordance with the Protocol Deviation Management Plan [Version 4.0, dated 22Mar2022].

- Data will be reviewed prior to freezing the database to ensure all important deviations are captured and categorised on the protocol deviations dataset.
- This dataset will be the basis for the summaries and listings of protocol deviations.

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

# 5. CONSIDERATIONS FOR DATA ANALYSES AND DATA HANDLING CONVENTIONS

## 5.1. Study Treatment & Sub-group Display Descriptors

| Treatment Group Descriptions | | | |
|---|---|---|---|
| RandAll NG | | Data Displays for Reporting | |
| Code | Description | Description | Order in TLF |
| B | 2.5 mg/kg frozen liquid solution of GSK2857916 | 2.5 mg/kg | 1 |
| A | 3.4 mg/kg frozen liquid solution of GSK2857916 | 3.4 mg/kg | 2 |
| C | lyophilized configuration of GSK2857916 | 3.4 mg/kg Lyo, actual dose level subject to IA result | 3 |
| L | receive topical corticosteroids in left eye only | "3.4 mg/kg treated eye" for the treated eyes of participants in 3.4 mg/kg group (frozen liquid); | 4 |
| | | "3.4 mg/kg untreated eye" for the untreated eyes of participants in 3.4 mg/kg group (frozen liquid) | 5 |
| R | receive topical corticosteroids in right eye only | "2.5 mg/kg treated eye" for the treated eyes of participants in 2.5 mg/kg group (frozen liquid); | 6 |
| | | "2.5 mg/kg untreated eye" for the untreated eyes of participants in 2.5 mg/kg group (frozen liquid). | 7 |

## 5.2. Baseline Definitions

For all endpoints (except as noted in baseline definitions) the baseline value will be the latest pre-dose assessment with a non-missing value, including those from unscheduled visits. If time is not collected, Day 1 assessments are assumed to be taken prior to first dose and used as baseline. For subjects who did not receive study treatment during the study, baseline will be defined as the latest, non-missing collected value.

For laboratory data, baseline will be the latest non-missing pre-dose value from central lab. If no central lab value is available, the latest non-missing pre-dose value from local lab will be used.

For ECG analyses, subject level baseline is defined as the mean of triplicate baseline assessments.

Unless otherwise stated, if baseline data is missing, no derivation will be performed, and baseline will be set to missing.

## 5.3. Examination of Covariates, Other Strata and Subgroups

### 5.3.1. Covariates and Other Strata

The list of strata may be used in descriptive summaries and statistical analyses, some of which may also be used for subgroup analyses. Additional strata of clinical interest may also be considered.

| Category | Details |
|---|---|
| Number of prior lines of therapy | ≤4, >4 |
| Cytogenetic risk | high risk, Other (non-high risk - all others) |

**NOTES:** A subject is considered as high risk if the subject has any of the following cytogenetics: t(4;14), t(14;16), and 17p13del.

### 5.3.2. Examination of Subgroups

The list of subgroups may be used in descriptive summaries and statistical analyses. Additional subgroups of clinical interest may also be considered.

- If the percentage of subjects is small within a particular subgroup, then the subgroup categories may be refined prior to unblinding the trial.

| Subgroup | Categories |
|---|---|
| Age Group (at screening) | 18 to <65, 65 to < 75, ≥ 75 |
| Sex | Male, Female |
| Ethnic Background | White, Black, Other |
| ISS Staging at Screening | I, II, III, Other (Unknown or Missing) |
| Baseline renal impairment status per eGFR (ml/min/1.73 $m^2$) | Normal (≥ 90), Mild (≥ 60, < 90), Moderate (≥ 30, < 60), Severe (≥ 15, < 30) |
| Number of prior lines of therapy | <=4, >4 |
| Type of myeloma | IgG, Non-IgG |
| Cytogenetics Risk [1] | High, Other (non-high risk - all others) |
| Refractory to prior anti-cancer therapy | Any Proteasome Inhibitor (PI)<br>Bortezomib<br>Carfilzomib<br>Ixazomib<br>Any Immunomodulator (IMiD)<br>Thalidomide<br>Lenalidomide<br>Pomalidomide<br>Any Monoclonal Antibodies<br>Elotuzumab<br>Isatuximab<br>Daratumumab<br>Daratumumab alone [2] |

| Subgroup | Categories |
|---|---|
| | Daratumumab in combination [3]<br>PI+IMiD<br>Daratumumab+PI+IMiD<br>Penta-refractory [4] |

**NOTES:**

[1] A subject is considered as high risk if the subject has any of the following cytogenetics: t(4;14), t(14;16), and 17p13del.

[2] Defined as prior CTX regimen with Daratumumab as the only drug in the regimen.

[3] Defined as prior CTX regimen with Daratumumab and other drugs.

[4] Defined as refractory to: Bortezomib, AND Carfilzomib AND Lenalidomide AND Pomalidomide AND Daratumumab.

## 5.4. Other Considerations for Data Analyses and Data Handling Conventions

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

| Section | Component |
|---|---|
| Section 15.3 | Appendix 3: Assessment Windows |
| Section 15.4 | Appendix 4: Study Phases and Treatment Emergent Adverse Events |
| Section 15.5 | Appendix 5: Data Display Standards & Handling Conventions |
| Section 15.6 | Appendix 6: Derived and Transformed Data |
| Section 15.7 | Appendix 7: Reporting Standards for Missing Data |
| Section 15.8 | Appendix 8: Values of Potential Clinical Importance |

# 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 for frozen liquid cohort alone, and 'Full Analysis' population for frozen liquid cohort plus lyophilized cohort (side-by-side presentation). If needed, the study population analyses for lyophilized cohort alone will be based on the "Lyo" population.

Unless otherwise specified, no 'Total' column will be provided for study population outputs.

Study population analyses including analyses of subject's disposition, protocol deviations, demographic and baseline characteristics, prior and concomitant medications, subsequent anti-cancer therapy, and exposure and treatment compliance will be based on GSK Core Data Standards. Details of the planned displays are presented in Appendix 13: List of Data Displays.

## 6.2. Disposition of Subjects

A summary of the number of subjects in each of the analysis populations described in Section 4 will be provided (for primary analysis, Evaluable population will not be included). In addition, the number of subjects enrolled by centre will be summarized by dose level using the "Enrolled" population. A separate summary for exclusions from each study population will be displayed (for primary analysis, Evaluable population will not be included). A listing of subjects excluded from analysis populations will also be provided.

A summary of subject status and reason for study withdrawal will be provided. This display will show the number and percentage of subjects who withdrew from the study, including primary reasons for study withdrawal. Reasons for study withdrawal will be presented in the order they are displayed in the eCRF.

A summary of study treatment status will be provided. This display will show the number and percentage of subjects who are ongoing or discontinued study treatment and a summary of the primary reasons for discontinuation of study treatment. Reasons for study treatment discontinuation will be presented in the order they are displayed in the eCRF. A listing of study treatment discontinuation will be generated. The listing will include last dose date, and reasons for study treatment discontinuation.

A listing of subjects with visits and assessments Impacted by the COVID-19 Pandemic will be presented. A stacked bar chart depicting visits impacted by COVID-19 will be presented.

## 6.3. Demographic and Baseline Characteristics

The demographic characteristics (e.g., age, race, ethnicity, sex, baseline height, and baseline body weight and baseline BMI) will be summarized and listed. Age, height,

weight and BMI will be summarized using the mean, standard deviation, minimum, median, and maximum. The count and percentage will be computed for sex and ethnicity.

Race and racial combinations will be summarized and listed.

Disease history and characteristics (e.g. time since initial diagnosis in years, stage at initial diagnosis, date of initial diagnosis) at initial diagnosis and screening will be listed. Separate summaries of disease characteristics at initial diagnosis and screening will be provided. Disease characteristics at screening, including stage, type of multiple myeloma, number of prior lines, and types of therapy, myeloma light chain and myeloma immunoglobulin, extramedullary disease, lytic bone lesion, and genetic characteristics (including high cytogenetic risk) will be summarized and listed.

Medical conditions collected at screening will be listed and will be summarized by past and current and by cancer-related and non-cancer related categories.

Substance use, including smoking history and alcohol use will be summarized.

Prior anti-cancer therapy will be coded using GSK Drug coding dictionary, then summarized by type of therapy and listed. A listing of prior anti-cancer therapy will show the relationship between ATC Level 1, Ingredient, and verbatim text. A summary of the best response to the most recent prior anti-cancer therapy will be provided. A summary of the number of prior anti-cancer therapy regimens will also be produced.

Prior anti-cancer therapy for multiple myeloma subjects will also be summarized by type of therapy, and drug class. A summary of multiple myeloma subjects' refractory to prior anti-cancer therapy by drug class will be provided.

Anti-cancer radiotherapy will be listed. Prior cancer and non-cancer related surgeries will be summarized. Prior and on treatment cancer and non-cancer related surgeries will be listed.

## 6.4. Treatment Compliance

Summaries of study treatment exposure and dose modifications (e.g., number of dose reductions, number of dose delays) will further characterize compliance. These analyses are described in Section 6.5 'Extent of Exposure'.

## 6.5. Extent of Exposure

Extent of exposure to GSK2857916 will be summarized.

The number of cycles administered to study treatment will be summarised with mean, median, standard deviation, minimum, and maximum.

Dose delivered per cycle (mg/kg/cycle) will be summarized using mean, median, standard deviation, minimum, and maximum by cycle and overall. The dose intensity (mg/kg/3 weeks), which is calculated as the cumulative actual dose (mg/kg) divided by expected duration of exposure in 3 weeks (last infusion date – first infusion date +

21)/21), will also be summarized. A by subject summary listing of data on exposure to all study treatments will be produced.

Dose reductions will be summarised by number of reductions and reasons for reductions. Dose delays will be summarised by number of delays, reasons for the delays, and delay duration (days). The number and percentage of the delays for intervals of 1-21, 22-42 and >42 days will be computed. Primary reasons for dose reductions and dose delays will also be summarized by cycle. Listing of all dose delays due to corneal events (GSK scale) and listing of dose delays and associated Eye Disorder Events (CTCAE) will be produced.

Duration of delays is defined as period from the expected start date of dose to actual start date of current dose. Calculation: (actual start date of current dose - expected start date of dose). Expected start date of dose = actual start date of previous dose + 21.

The summaries of dose modifications will be provided. All the dose reductions, dose escalations, infusion interruptions, incomplete infusions and dose delays will be listed. A plot showing the number and percentage of subjects treated at different dose levels over time will be provided.

The duration of exposure to study treatment (from first day to last day of treatment) will be calculated and summarized using mean, median, standard deviation, minimum, and maximum. A horizontal bar graph of duration of treatment will be produced that displays duration of treatment in months for each subject. Summary of duration of exposure by response category based on IRC will be presented.

A Kaplan Meier curve for time to treatment discontinuation by Response Category Based on IRC, and a Kaplan Meier curve for time to treatment discontinuation for subjects who have received at least 3 cycles of the study treatment will be presented.

Swim-lane Plot of duration of study treatment for responder based on Independent Reviewer-Assessed Response will be produced.

## 6.6. Concomitant Medications

Concomitant medications will be coded using GSK Drug coding dictionary, summarized, and listed. The summary of concomitant medications will show the number and percentage of subjects taking concomitant medications by Ingredient. Multi-ingredient products will be summarized by their separate ingredients rather than as a combination of ingredients. Anatomical Therapeutic Chemical (ATC) classification Level 1 (Body System) information will be included in the dataset created but will not appear on the listing or summary.

In the summary of concomitant medications, each subject is counted once within each unique ingredient. For example, if a subject takes Amoxycillin on two separate occasions, the subject is counted only once under the ingredient “Amoxycillin”. In the summary of concomitant medications, the ingredients will be summarized by the base only, using CMBASECD and CMBASE. Note: In order to be considered a concomitant medication, the concomitant medication must have been taken at some point during the on-treatment window.

Prophylactic medication for infusion-related reactions and prophylactic topical eye medications will be summarized by drug class and drug name and listed separately. In addition, the percentage of duration of exposure (see Section 15.6.2 for definition) that was on prophylactic steroid eye drop use will also be summarized.

Blood products or blood supportive care products with onset date within the on-treatment window will be included in the summary tables. The frequency and percentage of subjects using blood products and blood supportive care products after the start of study medication will be provided. Supporting listings will also be provided.

## 6.7. Subsequent Anti-Cancer Therapies

The number and percentage of subjects that received chemotherapy, immunotherapy, hormonal therapy, biologic therapy, radioactive therapy, small molecule targeted therapy, as subsequent anti-cancer therapy will be summarized. Time from study treatment discontinuation to the first post study treatment anti-cancer therapy will also be included in this summary table, if available.

Follow-up anti-cancer therapy will be coded using GSK Drug coding dictionary, then summarized by ingredient. A listing of the type of follow-up anti-cancer therapy received (chemotherapy, immunotherapy, hormonal therapy, biologic therapy, radioactive therapy, and small molecule targeted therapy) for each subject will be provided.

# 7. EFFICACY ANALYSES

The efficacy analyses will be based on the 'Intent-to-Treat' or 'Efficacy' population for frozen liquid cohort alone, and 'Full Analysis' population for frozen liquid cohort plus lyophilized cohort (side-by-side presentation). If needed, the efficacy analyses for lyophilized cohort alone will be based on the 'Lyo' population.

Unless otherwise specified, no 'Total' column will be provided for efficacy outputs

## 7.1. Primary Efficacy Analyses

### 7.1.1. Overall Response Rate (ORR) based on IRC assessment

ORR, defined as the percentage of participants with a confirmed partial response (PR) or better (i.e., PR, very good partial response [VGPR], complete response [CR] and stringent complete response [sCR]), according to the 2016 International Myeloma Working Group (IMWG) Response Criteria [Kumar, 2016]. ORR based on Independent Review Committee (IRC) will be analyzed as the primary endpoint.

ORR at primary analysis will be analyzed based on the confirmed responses, which will be derived based on the algorithm specified in Table 3.

Only the assessments from the start of treatment up to the earlier of confirmed disease progression or the start of new anti-cancer therapy will be considered. Only new systemic anti-cancer drugs taken are considered as anti-cancer therapy (radiotherapy and surgeries are not considered as systemic anti-cancer therapy for the purpose of this analysis).

Subjects with only assessments of Not Evaluable or missing response will be treated as non-responders; i.e. they will be included in the denominator when calculating the percentage.

#### 7.1.1.1. Derivation of Confirmed Response

The derivation of confirmed response shall be based on the algorithm specified in Table 3. The date of the first of the two consecutive assessments will be used as the date of the confirmed response.

**Table 3 Response confirmation algorithm**

| # | Response at the First Time Point | Response at Subsequent Disease Assessment[1] | Confirmed Response at the First Time Point |
|---|---|---|---|
| 1 | sCR | sCR | sCR |
| 2 | sCR | CR | CR |
| 3 | CR | sCR/CR | |
| 4 | sCR/CR | VGPR | VGPR |
| 5 | VGPR | sCR/CR/VGPR | |
| 6 | sCR/CR/VGPR | PR | PR |
| 7 | PR | sCR/CR/VGPR/PR | |
| 8 | sCR/CR/VGPR/PR | MR | MR |
| 9 | MR | sCR/CR/VGPR/PR/MR | |

| # | Response at the First Time Point | Response at Subsequent Disease Assessment[1] | Confirmed Response at the First Time Point |
|---|---|---|---|
| 10 | sCR/CR/VGPR/PR/MR | SD | SD |
| 11 | sCR/CR/VGPR/PR/MR | PD (any reason)<br><br>OR<br>No subsequent disease assessment: **subject died or discontinued study or started new anti-cancer therapy** before further adequate disease assessment | NE |
| 12 | PD (due to reasons other than imaging, i.e., plasmacytoma or bone lesion) | PD (any reason) including PD after initiation of new anti-cancer therapy<br><br>OR<br>No subsequent disease assessment: subject **died due to PD** before further adequate disease assessment (including death due to PD after initiation of new anti-cancer therapy) | PD |
| 13 | PD (due to reasons other than imaging, i.e., plasmacytoma or bone lesion) | sCR/CR/VGPR/PR/MR/SD<br><br>OR<br>No subsequent disease assessment: subject died **due to reasons other than PD** before further adequate disease assessment<br><br>OR<br>No subsequent disease assessment: subject **discontinued study** before further adequate disease assessment | NE |
| 14 | sCR/CR/VGPR/PR/MR/PD (due to reasons other than imaging, i.e., plasmacytoma or bone lesion) | No subsequent disease assessment: subject has not died, discontinued from study or (except for PD) started new anti-cancer therapy; but as yet has no further adequate disease assessments | Unconfirmed sCR/CR/VGPR/PR/MR/PD.<br><br>Will be categorized as NE for final ORR analysis.<br><br>For ORR analysis in IA, the UC response (PR or better) will be counted as responder. |
| 15 | SD | Any<br><br>OR<br>No subsequent disease | SD |

| # | Response at the First Time Point | Response at Subsequent Disease Assessment[1] | Confirmed Response at the First Time Point |
|---|---|---|---|
| | | assessment | |
| 16 | PD due to imaging (plasmacytoma or bone lesion) | Any<br><br>OR<br>No subsequent disease assessment | PD |
| 17 | NE or missing | Any<br><br>OR<br>No subsequent disease assessment | NE |

1. Subsequent disease assessment is defined as the next adequate (not missing or NE) disease assessment following the first timepoint before (or on the same date of) start of new anti-cancer therapy except for confirmation of PD, for which PD or death due to PD after new anti-cancer therapy are considered for confirmation of PD. No minimal time interval is required for the subsequent disease assessment, but a different sample is required for confirmation.
2. SD does not need to be confirmed.
3. PD due to imaging (i.e., plasmacytoma or bone lesion) does not need to be confirmed.
4. Where criteria are not mutually exclusive, take the first that applies.

### 7.1.2. Summary Measure

The number and percentage of participants with best overall response (BOR) in the following response categories will be summarized by dose level: sCR, CR, VGPR, PR, overall response (sCR+CR+VGPR+PR), minimal response (MR), stable disease (SD), progressive disease (PD), and not evaluable (NE). The corresponding 2-sided 97.5% exact CI for ORR will also be provided. Participants with only unknown or missing responses will be treated as non-responders, i.e., these participants will be included in the denominator when calculating percentages of response. A list of IRC-assessed response at each visit will be listed.

For subgroup analysis, ORR will be presented using forest plot for the following categories: Age, Sex, Ethnic Background, ISS Staging at Screening, Number of prior lines of therapy, Type of myeloma, , Refractory to prior anti-cancer therapy, Cytogenetics Risk as defined in Section 5.3.2

A waterfall plot showing the maximum percent reduction from baseline in Serum M-protein, or Urine M-protein, or difference between two types Serum FLC [Kappa light chain (Kappa LC) and Lambda light chain (Lambda LC)] for each subject will be produced using by dose level. The plot will be color-coded for M-protein types and Serum FLC, etc. Indication of the best overall response will be provided below the plot. Only the assessments from the start of treatment up to the start of new anti-cancer therapy will be considered. Only new systemic anti-cancer drugs taken are considered as anti-cancer therapy (radiotherapy and surgeries are not considered as systemic anti-cancer therapy for the purpose of this analysis).

The maximum percent reduction will be plotted in the following hierarchical order:

[1] Plot Serum M-protein maximum percent reduction from baseline if data is available;

[2] If [1] is not feasible, plot Urine M-protein maximum percent reduction from baseline if data is available;

[3] If both [1] and [2] are not feasible, plot maximum percent reduction from baseline for difference between two types of Serum FLC if data is available;

**Difference between two types of Serum FLC**

The percent change from baseline for difference between two types of Serum FLC is defined as:

(post-baseline difference-baseline difference) / baseline difference *100%

To calculate the difference, the "involved" and "non-involved" light chains must be determined at first based on the ratio of non-missing values for Serum Kappa LC protein and Serum Lambda LC protein at baseline.

The detailed algorithm is provided as below:

- If the baseline ratio of (Kappa LC/Lambda LC)>1.65, then Kappa LC is defined as involved FLC, and Lambda LC is defined as non-involved FLC. Then
  - Difference between involved and uninvolved = Kappa LC-Lambda LC
- If the baseline ratio of (kappa/lambda) <0.26, then Lambda light chain is defined as involved FLC, and Kappa light chain is defined as non-involved FLC
  - Difference between involved and uninvolved = Lambda LC-Kappa LC
- If the baseline ratio of (Kappa LC/Lambda LC) ≤1.65 and ≥ 0.26, then "involved" and "non-involved" FLC can not be determined (ratio is normal), and maximum percent reduction from baseline for difference between two types of Serum FLC won't be available.

### 7.1.3. Population of Interest

ORR at primary analysis will be analyzed using both ITT and Efficacy population for frozen liquid cohort, and Lyo population for lyophilized cohort.

### 7.1.4. Statistical Analyses / Methods

Details of the planned displays are provided in Appendix 13: List of Data Displays and will be based on GSK data standards and statistical principles.

## 7.2. Secondary Efficacy Analyses

### 7.2.1. Endpoint / Variables

#### 7.2.1.1. ORR based on Investigator Assessment

ORR based on investigator-assessed response will be analysed as one of the secondary endpoints.

ORR at primary analysis will be analyzed based on the confirmed responses, which will be derived based on the algorithm specified in Table 3.

ORR at IA should also be analyzed based on confirmed responses if available. However, in case a participant has achieved a response of PR or better at data cut, which was not confirmed due to the time constraints (too short timeframe for the next assessment) but with a potential to be confirmed through subsequent assessments after interim, the participant will also be considered as a responder; if the participant dies or discontinues study or starts other anti-cancer therapy prior to confirming the response, the participant will not be considered as a responder at IA.

#### 7.2.1.2. Clinical Benefit Rate (CBR)

CBR is defined as the percentage of participants with a confirmed minimal response (MR) or better, according to the IMWG Response Criteria [Kumar, 2016]. CBR will be summarized in the same way as ORR. No hypothesis testing will be performed for CBR. At primary analysis, CBR based on both IRC and investigator assessment will be summarized. At interim analysis, only CBR based on investigator assessment will be summarized.

#### 7.2.1.3. Duration of Response (DoR)

DoR is defined as the time from first documented evidence of confirmed PR or better until the earliest date of confirmed disease progression (PD) per IMWG, or death due to PD among participants who achieve a response (i.e., confirmed PR or better). Responders without confirmed PD will be censored at the censoring time point for Time to Progression as specified in .Table 5 of Section 7.2.1.6.

DoR will be analysed at the time of final ORR analysis, also at study close out if applicable, based on responses assessed by both IRC and investigator.

#### 7.2.1.4. Time to Response (TTR)

TTR is defined as the time between the date of randomization and the first documented evidence of confirmed response (PR or better), among participants who achieve a response (i.e., confirmed PR or better).

TTR will be analysed at the time of final ORR analysis, based on responses assessed by both IRC and investigator.

#### 7.2.1.5. Progression Free Survival (PFS)

PFS is defined as the time from randomization until the earliest date of confirmed PD per IMWG, or death due to any cause.

PFS will be analysed at the time of final ORR analysis, also at study close out if applicable, based on responses assessed by both IRC and investigator.

A summary of the assignments for progression and censoring dates for PFS are specified in Table 4 below.

**Table 4 Assignments for Progression and Censoring Dates for PFS Analysis**

| Situation | Date of Event (Progression/Death) or Censoring | Outcome Event (Progression/Death) Or Censored |
|---|---|---|
| No *(or inadequate)* baseline tumor assessments [1] and the subject has not died (if the subject has died follow the rules for death indicated at the bottom of the table) | Randomization | Censored |
| No post-baseline assessments and the subject has not died (if the subject has died follow the rules for death indicated at the bottom of the table) | Randomization | Censored |
| Progression documented without extended loss-to-follow-up time | Date of assessment of progression [1] | Event |
| No progression *(or death)* | Date of last 'adequate' assessment of response [2] | Censored |
| New anticancer treatment started *(prior to documented disease progression or death)* [3]. | Date of last 'adequate' assessment of response [2] *(on or prior to starting anti-cancer therapy)* | Censored |
| Death without extended loss-to-follow-up time | Date of death | Event |
| Death or progression after an extended loss-to-follow-up time (two or more missed cycles + 7 day window) [4] | Date of last 'adequate' assessment of response [2] prior to PD/death *(prior to missed assessments)* | Censored |

| Situation | Date of Event (Progression/Death) or Censoring | Outcome Event (Progression/Death) Or Censored |
|---|---|---|
| Death or progression after an extended loss-to-follow-up time from randomization | Date of randomization | Censored |

[1] Adequate baseline assessment is defined as at baseline, a patient has at least one of the following measurements: a. Serum M-protein ≥0.5 g/dL (≥5 g/L) or b. Urine M-protein ≥200 mg/24h or c. Serum FLC assay: Involved FLC level ≥10 mg/dL (≥100 mg/L) and an abnormal serum free light chain ratio (<0.26 or >1.65)
[2] An adequate assessment is defined as an assessment where the IRC/Investigator determined response is sCR, CR, VGPR, PR, MR, or SD.
[3] If PD or death and New anti-cancer therapy occur on the same day assume the progression or death was documented first (e.g., outcome is progression or death and the date is the date of the assessment of progression or death). If anti-cancer therapy is started prior to any adequate assessments, censoring date should be the date of randomization.
[4] Refer to Section 15.5.4 "Extended Loss to Follow-up or Extended Time without an Adequate Assessment".

#### 7.2.1.6. Time to Progression (TTP)

TTP is defined as the time from randomization until the earliest date of confirmed PD per IMWG, or death due to PD.

TTP will be analysed at the time of final ORR analysis, also at study close out if applicable, based on responses assessed by both IRC and investigator.

A summary of the assignments for progression and censoring dates for TTP are specified in Table 5.

**Table 5 Assignments for Progression and Censoring Dates for TTP Analysis**

| Situation | Date of Event (Progression/Death) or Censoring | Outcome Event (progression/Death) Or Censored |
|---|---|---|
| No *(or inadequate)* baseline tumor assessments [1] and the subject has not died (if the subject has died follow the rules for death indicated at the bottom of the table) | Randomization | Censored |
| No post-baseline assessments and the subject has not died (if the subject has died follow the rules for death indicated at the bottom of the table) | Randomization | Censored |

| Situation | Date of Event (Progression/Death) or Censoring | Outcome Event (progression/Death) Or Censored |
|---|---|---|
| Progression documented at or between scheduled visits | Date of assessment of progression [1] | Event |
| No progression *(or death)* | Date of last 'adequate' assessment of response [2] | Censored |
| New anticancer treatment started *(prior to documented disease progression or death)* [3]. | Date of last 'adequate' assessment of response [2] *(on or prior to starting anti-cancer therapy)* | Censored |
| Death due to progression without extended loss-to-follow-up time | Date of death | Event |
| Death from causes other than progression without extended loss-to-follow-up time | Date of death | Censored |
| Death or progression after an extended loss-to-follow-up time (two or more missed cycles + 7 day window) [4] | Date of last 'adequate' assessment of response [2] prior to PD/death *(prior to missed assessments)* | Censored |
| Death or progression after an extended loss-to-follow-up time from randomization | Date of randomization | Censored |

Adequate baseline assessment is defined as at baseline, a patient has at least one of the following measurements: a. Serum M-protein ≥0.5 g/dL (≥5 g/L) or b. Urine M-protein ≥200 mg/24h or c. Serum FLC assay: Involved FLC level ≥5 mg/dL (≥50 mg/L) and an abnormal serum free light chain ratio (<0.26 or >1.65).

An adequate assessment is defined as an assessment where the IRC/Investigator determined response is sCR, CR, VGPR, PR, MR, or SD.

If PD or death and New anti-cancer therapy occur on the same day assume the progression or death was documented first (e.g., outcome is progression or death and the date is the date of the assessment of progression or death). If anti-cancer therapy is started prior to any adequate assessments, censoring date should be the date of randomization.

Refer to Section 15.5.4 "Extended Loss to Follow-up or Extended Time without an Adequate Assessment".

#### 7.2.1.7. Overall Survival (OS)

OS is defined as the time from randomization until death due to any cause. Participants who withdraw consent from the study or are lost to follow-up will be censored at the time of withdrawal or lost to follow-up. Participants who do not have a death record at the clinical cut-off date for the analysis will be censored at the last known alive date. The last contact date will be determined by the maximum collection/assessment date from among selected data domains within the clinical database.

An OS analysis will be performed at the time of the primary ORR analysis. An updated OS analysis will be performed at the end of study as defined in Section 4.6 of the protocol.

### 7.2.2. Summary Measure

- For ORR based on investigator-assessed responses, the number and percentage of participants with BOR in the following response categories will be summarized by dose level: sCR, CR, VGPR, PR, overall response (sCR+CR+VGPR+PR), minimal response (MR), stable disease (SD), progressive disease (PD), and not evaluable (NE). The corresponding 2-sided 97.5% exact CI for ORR will also be provided. Participants with unknown or missing responses will be treated as non-responders, i.e., these participants will be included in the denominator when calculating percentages of response. A list of investigator-assessed response at each visit will be listed. In addition, a summary table of IRC-assessed and investigator-assessed best response with confirmation will be provided to assess the concordance rate.

- For CBR, the number and percentage of participants with the BOR in the following response categories will be summarized by dose level: sCR, CR, VGPR, PR, MR, clinical benefit response (sCR+CR+VGPR+PR+MR), SD, PD, and NE. The corresponding exact 95% CI for CBR will also be provided. Participants with unknown or missing responses will be treated as non-responders, i.e., these participants will be included in the denominator when calculating percentages of response. Analysis of CBR will be based on both IRC and investigator assessed responses assessed by both IRC and investigator.

- DoR will be summarized using Kaplan-Meier method by dose level for participants with a confirmed PR or better. If there are a sufficient number of responders who subsequently progress or die due to PD, median DoR, first and third quartiles and 95% CI, will be estimated using the Brookmeyer-Crowley method [Brookmeyer, 1982]. A figure and listing of DoR time will also be provided. Analysis of DoR will be based on both IRC and investigator-assessed responses. A Kaplan Meier curve of Duration of Response by Dose Delay Category Based on Independent Reviewer - Assessed Response will be provided. A Kaplan Meier curve of Duration of Response by Response Category based on Independent Reviewer-Assessed Response will be provided. Hazard ratio estimated using the Pike estimator will be provided.

- TTR will be summarized descriptively if there are sufficient number of responses by dose level, using median(s) and quartiles for participants with a confirmed response of PR or better. Analysis of TTR will be based on both IRC and investigator-assessed

responses. Summary of Time to Best Response based on Independent Reviewer - Assessed Response will also be provided.

- PFS will be summarized using Kaplan-Meier method by dose level. If there is a sufficient number of progressions or deaths, median PFS, first and third quartiles, 6-month PFS rate, and 95% CIs will be estimated using the Brookmeyer-Crowley method [Brookmeyer, 1982]. A figure and listing of PFS time will also be provided. Analysis of PFS will be based on both IRC and investigator-assessed responses. Summary and Kaplan Meier curve by Response Category Based on Independent Reviewer-Assessed Response will be provided.

- TTP will be summarized using Kaplan-Meier method by dose level. If there is a sufficient number of progressions or death due to PD, median TTP, first and third quartiles and 95% CI, will be estimated using the Brookmeyer-Crowley method [Brookmeyer, 1982]. A figure and listing of TTP time will also be provided. Analysis of TTP will be based on both IRC and investigator-assessed responses.

- OS will be summarized using the Kaplan-Meier method by dose level. For each dose level, the Kaplan-Meier estimates for the median overall survival time, the first and third quartiles will be presented, along with 95% CIs if there are a sufficient number of deaths. A graph of survival curves and a listing of survival times will also be provided. In addition, pending on maturity of data, the survival probability at 6, 12 and 18 months with 95% CI will be estimated using Kaplan-Meier method. Summary and Kaplan Meier curve by Response Category Based on Independent Reviewer-Assessed Response will be provided.

### 7.2.3. Population of Interest

For frozen liquid cohort, CBR, TTR, and DoR will be analyzed using both ITT and Efficacy population, and other TTE endpoints will be analyzed using ITT population only.

For lyophilized cohort, all secondary efficacy endpoints will be analyzed using Lyo population.

### 7.2.4. Statistical Analyses / Methods

Details of the planned displays are provided in Appendix 13: List of Data Displays and will be based on GSK data standards and statistical principles.

Unless otherwise specified, endpoints / variables defined in Section 7.2.1 will be summarised using descriptive statistics, graphically presented (where appropriate) and listed.

## 7.3. Exploratory Efficacy Analyses

### 7.3.1. Endpoint / Variables

#### 7.3.1.1. Minimal Residual Disease (MRD) Negativity Rate

MRD negativity rate is defined a: the percentage of participants who are MRD negative by Next Generation Sequencing (NGS).

### 7.3.2. Summary Measure

#### 7.3.2.1. MRD Negativity Rate

For MRD negativity rate based on bone marrow testing using Next Generation Sequencing (molecular negativity), the number and percentage of participants who have achieved MRD negativity will be summarized by dose level. The corresponding exact 95% CI for MRD negativity rate will also be provided. If data permit, duration of MRD negativity will be analysed using Kaplan-Meier method in participants who have achieved MRD negativity. Information of MRD will be included in the listing of response. If data is available, imaging-based assessment of MRD (i.e. PET-CT) will also be included in the listing and related to NGS testing.

### 7.3.3. Population of Interest

The exploratory efficacy analyses will be based on the ITT population for frozen liquid cohort, and Lyo population for lyophilized cohort.

### 7.3.4. Statistical Analyses / Methods

Details of the planned displays will be provided in Appendix 13: List of Data Displays, based on GSK data standards, in the final version of the RAP.

# 8. SAFETY ANALYSES

The safety analyses will be based on the "Safety" population for frozen liquid cohort, and 'Full Analysis' population for frozen liquid cohort plus lyophilized cohort (side-by-side presentation). If needed, the safety analyses for lyophilized cohort alone will be based on the 'Lyo' population.

Unless otherwise specified, no 'Total' column will be provided for safety outputs, and the sorting will be based on descending order of incidence in 3.4 mg/kg arm. In case the 2.5 mg/kg becomes the selected dose post primary analysis, relevant outputs will be recreated with sorting based on descending order of incidence in 2.5 mg/kg arm

## 8.1. Adverse Events Analyses

Adverse events analyses including the analysis of adverse events (AEs), Serious AEs (SAEs) and other significant AEs will be based on GSK Core Data Standards.

An overview summary of AEs, including counts and percentages of subjects with any AE, AEs related to study treatment, Grade 3&4 AEs, Grade 3&4 AEs related to study treatment, AEs leading to permanent discontinuation of study treatment, AE leading to dose reductions, AEs leading to dose delays, AEs related to study treatment and leading to permanent discontinuation of study treatment, SAEs, SAEs related to study treatment, fatal SAEs, and fatal SAEs related to study treatment will be produced.

A summary of non-serious AEs that occurred in 5% of the subjects or above will be provided (no rounding for the percentage will be used in terms of 5% threshold, e.g., event with 4.9% incidence rate should not be included in this table). The summary will be displayed by SOC and PT.

The relationship between MedDRA SOC, PT, and Verbatim Text will be displayed.

Adverse events will be coded using the standard Medical Dictionary for Regulatory Affairs (MedDRA dictionary) and graded by the investigator according to the NCI-CTCAE, (version 4.03).

A summary of number and percentage of subjects with any adverse events by maximum grade will be produced. AEs will be sorted by Preferred term (PT) in descending order. The summary will use the following algorithms for counting the subject:

- **Preferred term row**: Subjects experiencing the same AE preferred term several times with different grades will only be counted once with the maximum grade.

- **Any event row**: Each subject with at least one adverse event will be counted only once at the maximum grade no matter how many events they have.

The frequency and percentage of AEs (all grades) will be summarized and displayed in two ways: 1) in descending order by PT only and 2) in descending order by SOC and PT. In the SOC row, the number of subjects with multiple events under the same SOC will be

counted once. In addition, a summary of cumulative incidence of AE by number of doses received at first occurrence will be provided.

A separate summary will be provided for study treatment-related AEs. A study treatment-related AE is defined as an AE for which the investigator classifies the relationship to study treatment as "Yes". A worst-case scenario approach will be taken to handle missing relatedness data, i.e. the summary table will include events with the relationship to study treatment as 'Yes' or missing. The summary table will be displayed in in two ways: 1) by maximum grade sorted by PT in descending order and 2) in descending order by SOC and PT.

In addition, AEs of maximum grade of 3 or higher will be summarized separately by PT.

All AEs will be listed. Additionally, a listing of subject IDs for each individual AE will be produced.

The details of the planned displays are provided in Appendix 13: List of Data Displays.

## 8.2. Adverse Events of Special Interest Analyses

Adverse events of special interest for GSK2857916 include eye disorder, thrombocytopenia, infusion related reactions, and neutropenia graded via CTCAE, and corneal event per GSK scale.

### 8.2.1. Thrombocytopenia, infusion related reactions, and neutropenia

For thrombocytopenia and infusion-related reactions (IRR), in addition to events identified and collected in eCRF, a comprehensive list of MedDRA terms based on clinical review will be used to identify each type of event. For neutropenia, event will be identified using a comprehensive list of MedDRA terms based on clinical review. Changes to the MedDRA dictionary could occur between the start of the study and the time of reporting and/or emerging data from on-going studies may highlight additional adverse events of interest, therefore the list of terms to be used for each event of interest and the specific events of interest will be based on the SRT agreements in place at the time of reporting.

Summaries of the number and percentage of subjects with these events will be provided for each type of events separately by preferred term and maximum grade. The time to onset and duration of first occurrence for each type of events will be summarized using summary statistics mean, standard deviation, median, minimum value, and maximum. The number and percentage of subjects who have time to onset of first occurrence (1-21, 22-42, 43-63, >63 days) will be reported. The number and percentage of subjects who have duration of first occurrence (1-21, 22-42, >42 days) will be reported.

The summary of event characteristics will also be provided, including number of subjects with any event, number of events, number of subjects with any event that is serious, number of subjects with any event that is related to study treatment, number of occurrences (One, Two, Three or more), maximum grade, outcomes and the action taken for the event. The percentage will be calculated in two ways, one with number of subjects

with event as the denominator and the other with total number of subjects as the denominator. The worst-case approach will be applied at subject level for the maximum grade, i.e. a subject will only be counted once as the worst case from all the events experienced by the subject. For action taken to an event, subject will be counted once under each action, e.g. if a subject has an event leading to both study treatment discontinuation and dose reduction, the subject will be counted once under both actions. For each of these events, a summary of cumulative incidence by number of doses received at first occurrence will be provided.

For thrombocytopenia, number and percentage of subjects with grade 3 or 4 platelet count decreased (based on lab data) and concomitant grade 2 or above bleeding event will be summarized. A bleeding event will be considered as concomitant only if the start date is within ± 3 days of the lab event.

For neutropenia, number and percentage of subjects with grade 3 or 4 neutrophil count decreased (based on lab data) and concomitant infection event will be summarized. An infection event will be considered as concomitant only if the start date is within ± 7 days of the lab event.

The details of the planned displays are provided in Appendix 13: List of Data Displays.

### 8.2.2. Eye disorder (CTCAE)

For AE in eye disorder SOC (CTCAE), an overview table and the listing will be provided.

In addition, for each of selected five types of event within eye disorder SOC (keratopathy, dry eye, blurred vision, photophobia, and eye pain), the following summary tables will be provided if the incidence rate ≥ 10%:is observed in 3.4mg/kg frozen liquid cohort

1. Event overview
2. Summary table by PT and Maximum Grade
3. Summary of event characteristics
4. Summary of time to onset, duration, and outcome

5. Summary of cumulative incidence by PT and number of doses received at first occurrence

6. Summary of percentage of time on study treatment with ongoing event

### 8.2.3. Corneal events (GSK scale)

Following discussions with regulatory agencies, GSK developed a grading scale to capture both corneal examination findings and visual acuity changes in participants treated with GSK2857916. This GSK scale differs from the CTCAE criteria for eye disorders which relies mainly on patient's symptoms and patient's ability to attend to 'activities of daily living' for grading of events. Details of derivation this GSK scale based on corneal findings and visual acuity Ophthalmic Exam (collected from Ocular

form) can be found in Appendix 9 Table 22 and Table 23 of study protocol (Version: GSK Document Number TMF-13990464 ).

In addition to the listing, the following outputs will be provided for corneal events graded using the GSK scale:

1. Overview for corneal event (GSK scale)
2. Summary of grade of GSK scale
    a. Summary of characteristics of corneal events (GSK scale) including the percentage of duration of exposure (see Section 15.6.2 for definition) with corneal events (GSK scale) of grade ≥ 2 and grade ≥ 3 respectively
    b. Summary of onset time and duration of the first occurrence of corneal event (GSK scale) of a) grade 2 or above; 2) grade 3 or above.
3. Summary of actions taken with study treatment (e.g. dose reduction/delay/permanent discontinuation)
4. Summary of time to re-initiation of study treatment post treatment delay due to corneal events (GSK scale)
5. Change in grade of corneal events (GSK scale) from EOT to last follow-up
6. Summary of worst post-baseline corneal events (GSK scale)
7. Summary of worst post-baseline corneal events (GSK scale) by best response (PR or better vs. otherwise)
8. Summary of resolution (improve to grade 1 or better) in corneal events (GSK scale) during Follow-up period (from EOT visit to last follow-up visit).
9. Logistic regression analysis will be performed to explore possible risk factors for developing corneal Events (GSK scale ≥ 2). In addition to dose arm (3.4 mg/kg vs 2.5 mg/kg), Sex (Male vs Female), Age Group (< 65 vs. ≥ 65 years), Race (White, Other), the following risk factors will also be considered:
    a. History of intraocular surgery: (Yes vs. No)
    b. Lens status (pseudophakia vs natural lens) at baseline
    c. Known history of dry eye per screening questionnaire (Presence vs. Absence)
    d. Presence of keratopathy at baseline exam (None vs. Mild vs. Moderate/Severe)

    Covariates will be selected using stepwise variable selection with entry and exit criteria of alpha=0.05.
10. Summary of Blurred Vision and Dry Eye Events versus GSK Scale.
11. Summary of Ocular Symptoms and Visual Acuity Change (GSK Scale) by Worst Grade of Keratopathy
12. Summary of Ocular Symptoms and Visual Acuity Change (GSK Scale) by Worst Grade of Corneal Events (GSK Scale)
13. Summary of Ocular Symptoms and Visual Acuity Change (>=2 lines in Better Eye) by Worst Grade of Corneal Exam Finding
14. Summary of Eye Disorder Events (CTCAE) Leading to Dose Delays by Preferred Term and Maximum Grade.
15. Summary of Subjects with Dose Delay due to Eye Disorder Events (CTCAE) at the Time of Data Cutoff

16. Summary of Vision Blurred, and Dry Eye by Preferred Term in Subjects with Keratopathy
17. Summary of Vision Blurred, and Dry Eye by Preferred Term and Maximum Grade in Subjects with Keratopathy
18. Summary of Ocular Symptoms (CTCAE) by Preferred Term and Maximum Grade in Subjects with Keratopathy
19. Summary of Ocular Symptoms (CTCAE) by Preferred Term and Maximum Grade
20. Summary of Blurred Vision and Dry Eye Events versus Keratopathy
21. Summary of Ocular Symptoms (CTCAE) versus Keratopathy
22. Summary of Duration of Keratopathy with Concurrent Blurred Vision or Dry Eye
23. Summary of Duration of Keratopathy with Concurrent Ocular Symptoms (CTCAE)
24. Summary of GSK scale Events Characteristics II
25. Summary of Corneal Exam Finding (GSK scale) Characteristics II
26. Summary of Visual Acuity Change (GSK scale) Characteristics II
27. Summary of Maximum Grade for Corneal Exam Finding (GSK scale)
28. Summary of Maximum Grade for Visual Change (GSK scale)
29. Summary of Worsening in Best Corrected Visual Acuity (BCVA) Score (logMAR Score) Characteristics II
30. Summary of Blurred Vision and Dry Eye Event Characteristics II in Subjects with Keratopathy
31. Summary of Ocular Symptoms (CTCAE) Event Characteristics II in Subjects with Keratopathy
32. Summary of Unilateral Worsening in Best Corrected Visual Acuity (BCVA) to 20/50 or Worse Characteristics II
33. Summary of Bilateral Worsening in Best Corrected Visual Acuity (BCVA) to 20/50 or Worse Characteristics II
34. Summary of Unilateral Worsening in Best Corrected Visual Acuity (BCVA) to 20/200 or Worse Characteristics II
35. Summary of Bilateral Worsening in Best Corrected Visual Acuity (BCVA) to 20/200 or Worse Characteristics II
36. Percentage of Subjects with Blurred Vision/Dry Eye Event Associated with Worsening in Best Corrected Visual Acuity (BCVA) to 20/50 or Worse
37. Percentage of Subjects with Ocular Symptoms (CTCAE) Associated with Worsening in Best Corrected Visual Acuity (BCVA) to 20/50 or Worse
38. Update of Resolution Status for Unresolved Corneal Exam Finding
39. Update of Resolution Status for Unresolved Corneal Exam Finding Patients with Interview Clinical data
40. Update of Resolution Status for Unresolved Worsening in Best Corrected Visual Acuity (BCVA) Score (logMAR Score)
41. Update of Resolution Status for Unresolved Blurred Vision and Dry Eye Events in Subjects with Keratopathy
42. Update of Resolution Status for Unresolved Ocular Symptoms (CTCAE) in Subjects with Keratopathy
43. Summary of Worst Post-baseline Change in Best Corrected Visual Acuity (BCVA)

44. Summary of Worsening in Best Corrected Visual Acuity (BCVA) Score (logMAR Score >=0.12) Characteristics II
45. Update of Resolution Status for Unresolved Worsening in Best Corrected Visual Acuity (BCVA) Score (logMAR Score >=0.12)
46. Summary of Vision Blurred by Preferred term and Best Response Based on Independent Review Committee
47. Summary of Dry Eye by Preferred term and Best Response Based on Independent Review Committee
48. Summary of Vision Blurred by Maximum Grade, and Best Response Based on Independent Review Committee
49. Summary of Dry Eye by Maximum Grade, and Best Response Based on Independent Review Committee
50. Summary of Best Corrected Visual Acuity (BCVA) Score (Snellen Score) at Baseline Compared to 20/50
51. Worsening in Best Corrected Visual Acuity (BCVA) Score (logMAR Score) Excluding Subjects with Follow-up Shorter Than 80 Days
52. Summary of worst-case post baseline shift from baseline by BCVA categories
53. Summary of Worst-case Post Baseline Change from Baseline in Best Corrected Visual Acuity (BCVA)Score (logMAR score)
54. Summary of Worst-case Post Baseline Change from Baseline in Best Corrected Visual Acuity (BCVA)Score (logMAR score) in Subjects with Worsening to 20/50 or Worse in the Better Eye
55. Summary of Worst-case Post Baseline Change from Baseline in Best Corrected Visual Acuity (BCVA)Score (logMAR score) in Subjects with Worsening to 20/50 or Worse in at Least One Eye but not the Better Eye
56. Summary of Characteristics II for Keratopathy
57. Summary of Dose Modifications for Subjects with Keratopathy
58. Summary of Maximum Grade for Corneal Events (GSK scale)
59. Summary of Time from Onset of Last Occurrence to Last Exam in Subjects Who Did Not Recover from Grade 2 or Higher Corneal Exam Finding (GSK Scale) When Follow Up Ended
60. Summary of Ocular Symptoms by Preferred Term and Maximum Grade in Subjects with Worst Grade of Corneal Exam Findings (GSK scale) =1
61. Summary of Duration of Exposure since Re-start after First Dose Delay Due to Eye Disorder Events (CTCAE)
62. Summary of Corneal Events (GSK Scale) Occurrences After Dose Reduction to 1.92 mg/kg
63. Summary of Characteristics II for the Event of Giving up Driving due to Eyesight
64. Summary of Characteristics II for the Event of Giving up Reading due to Eyesight
65. Listing of Resolution in Grade of Corneal Events (GSK Scale) for each Corneal Event in patients experiencing >1 event
66. Listing of BCVA for patients who gave up driving due to eyesight
67. Listing of BCVA for patients who experienced difficulty reading newspapers due to eyesight
68. Bar Chart of Grade of Corneal Exam Finding by Cycle

69. Plot of Time to Recovery Post Treatment Discontinuation for Corneal Exam Findings
70. Plot of Time to Recovery Post Treatment Discontinuation for Keratopathy
71. Profile plot of patients with maximum corneal toxicity grade will be provided.
72. Plot of Visual Acuity and Corneal Finding Grade for subjects experiencing >1 Corneal Event (GSK Scale) for 2.5 mg/kg arm will be produced.

Details of the planned displays are provided in Appendix 13: List of Data Display.

## 8.3. Deaths and Serious Adverse Events

All deaths will be summarised based on the number and percentage of subjects. This summary will classify subjects by time of death relative to the last dose of medication (>30 days or ≤30 days) and primary cause of death (disease under study, SAE possibly related to study treatment, or other). A supportive listing will be generated to provide subject-specific details on subjects who died.

All SAEs will be tabulated based on the number and percentage of subjects who experienced the event. Separate summaries will also be provided for study treatment-related SAEs. The summary tables will be displayed in descending order by PT. The summary of all SAEs will also be created by SOC and PT. In addition, a summary of cumulative incidence of SAE by number of doses received at first occurrence will be provided.

A study treatment-related SAE is defined as an SAE for which the investigator classifies the relationship to study treatment as "Yes". A worst-case scenario approach will be taken to handle missing data, i.e. the summary table will include events with the relationship to study treatment as 'Yes' or missing.

SAEs are included in the listing of all adverse events. Separate supportive listings with subject-level details will be generated for

- Fatal SAEs
- Non-Fatal SAEs.

## 8.4. Adverse Events Leading to Discontinuation and Dose Modification

The following categories of AEs will be summarized separately by PT and separate supportive listings will be generated with subject level details for those subjects:

- AEs Leading to Permanent Discontinuation of Study Treatment
- AEs Leading to Dose Interruptions or Delays
- AEs Leadings to Dose Reductions

## 8.5. Ocular findings from ophthalmic exam

As outlined in study protocol (Version: GSK Document Number TMF-13990464 ) Schedule of Activities (Table 1 of Section 1.2), ophthalmic exams are scheduled at

screening, during the study, and follow-up period for subjects in both general study and ocular sub-study. The ocular findings from ophthalmic exams will be analysed as described below.

1. For general study from baseline to last follow-up, the following analysis will be performed:

    a. Best corrected visual acuity (BCVA): BCVA (logMAR score) at baseline, EOT visit, and last follow-up visit as well as worst and most frequent category (definite worsen, possible worsen, and no change/improved) of change from baseline will be summarized by eye (R/L) and subject (worse eye and better eye). Number (%) of subjects with a decline in BCVA to 'light perception' (LP) or 'no light perception' (NLP) due to corneal finding anytime post-baseline will also be provided.
    b. Intraocular Pressure (IOP): summary table of 1) Number (%) of subjects with IOP ≥ 22mm Hg anytime post-baseline; 2) Number (%) of subjects who start treatment for IOP after 1$^{st}$ dose of study drug.
    c. Pupillary Exam: shift table (Normal to Abnormal) from baseline to worst post-baseline by subject (worse eye)
    d. Extraocular Muscle Movement: shift table (Full Intact: Yes to No) from baseline to worst post-baseline by eye (R/L) and subject (worse eye)
    e. External Exam: shift table (Ptosis: No to Yes) from baseline to worst post-baseline by eye (R/L) and subject (worse eye)
    f. Lids/Lashes/Lacrimal System: shift table (Blepharitis/MGD: No to Yes) from baseline to worst post-baseline by eye (R/L) and subject (worse eye)
    g. Conjunctival Exam:
        i. shift table (Chemosis: Absent to Present; Bulbar Conjunctiva White and Quiet: Yes to No; Palpebral Conjunctiva within normal limits: Yes to No) from baseline to worst post-baseline by eye (R/L) and subject (worse eye)
    h. Sclera: shift table (Scleritis: No to Yes) from baseline to worst post-baseline by eye (R/L) and subject (both eyes in same ocular exam)
    i. Corneal Exam:
        i. Corneal epithelium findings:
            1. Shift table from baseline to worst post-baseline by eye (R/L) and subject (worse eye) for Corneal epithelium (Normal to Abnormal), Corneal ulcer (No to Yes), Microcystic edema (No to Yes), Microcystic without edema (Yes/No), Subepithelial haze (No to Yes), Corneal neovascularization (No to Yes), Stroma (Normal to Abnormal), Active opacity (No to Yes), and Active edema (No to Yes).
            2. For punctate keratopathy, summary table of worst grade and most frequent grade across ocular exams by eye (R/L) and subject (worse eye)
        ii. Corneal endothelium findings:

1. Shift table from baseline to worst post-baseline by eye (R/L) and subject (worse eye) for Corneal endothelium (Normal to Abnormal)
2. Summary table by eye (R/L) and subject (either eye) for presence of Descemet's folds and Endothelial lesion at any post-baseline ocular exam.

j. Pachymetry: Summary table of number (%) of ≥ 5% increase from baseline at worst post-baseline by eye (R/L) and subject (either eye)

k. Schirmer's Test/ Tear Break-up Time:
   i. Summary table of change from baseline to worst post-baseline by eye (R/L).
   ii. Shift table from baseline to worst post-baseline by eye (R/L).The categories for Schirmer's Test are ≤ 5 mm, > 5 and ≤ 10 mm, and > 10 mm; the categories for Tear Break-up Time are: ≤ 5 sec, > 5 and ≤ 10 sec, and > 10 sec.

l. Slit Lamp Exam:
   i. Shift table from baseline to worst post-baseline by eye (R/L) and subject (worse eye) for Anterior Chamber: Deep/Quite (Yes to No); Iris: Flat, round and reactive (Yes to No); and Lens: Clear (Yes to No).
   ii. Summary tables of presence of iris findings ('Transillumination defect', 'Nodules', or 'Neovascularization') at any post-baseline ocular exam.
   iii. Shift table from baseline to worst post-baseline by eye (R/L) and subject (worse eye) for Pseudophakia (No to Yes), Nuclear sclerosis (No to Yes), Cortical cataract (No to Yes), and Posterior subcapsular cataract (No to Yes)
   iv. Summary table of number of subjects (%) underwent surgery due to cataract post-baseline.

m. FUNDUS Photograph: Shift table from baseline to worst post-baseline by eye (R/L) and subject (worse eye) for Vitreous normal in appearance (Yes to No), PVD (No to Yes), Vitreous cell (No to Yes), Vitreous haze (No to Yes), Optic nerve normal in appearance (Yes to No), and Retina normal in appearance (Yes to No).

2. General study from EOT visit to last follow-up visit: To assess the change in corneal findings after discontinuation of study treatment, among eyes and subjects (worse eye) with exam finding at EOT visit worse than baseline, the following analyses will be performed.

   a. Summary of change (worsening, no change, improvement) from EOT to last follow-up visit based on categories defined below by eye (R/L) and subject (worse eye)
   b. Summary of number (%) of eyes and subjects (worse eye) that resolve (improve to baseline level or better based on categories defined below), and descriptive summary of time from EOT visit to resolution among eyes and subjects (worse eye) that resolved

The parameters included in above analyses are:

1. BCVA change from baseline in log MAR scale (< 0.12, ≥ 0.12 to < 0.3, ≥ 0.3)
2. IOP (≥ 22mm Hg/<22mm Hg)
3. Corneal epithelium (Normal/Abnormal), Punctate Keratopathy (None/Mild /Moderate/Severe), Corneal ulcer (No/Yes), Microcystic edema (No/Yes), Microcystic without edema (No/Yes), Subepithelial haze (No to Yes), Corneal neovascularization (No to Yes), Stroma (Normal/Abnormal); Active opacity (No/Yes); Active edema (No/Yes)
4. Corneal endothelium (Normal/Abnormal), Descemet's folds (No/Yes; Peripheral/Central), Endothelial lesion (Peripheral/Central)
5. Pachymetry (increase from baseline < 5%, and ≥ 5%), Tear break up time (≤ 5 mm, > 5 and ≤ 10 mm, and > 10 mm), Schirmer's test (≤ 5 sec, > 5 and ≤ 10 sec, and > 10 sec)

3. Ocular sub-study (Cycle 1-4): To evaluate the effect of topical corticosteroids on corneal findings, pending on the availability of data, the following analyses will be performed in up to 30 participants who will receive monocular topical corticosteroids for the first 4 cycles:

   a. Summary of worst grade during Cycle 1-4 of corneal events (GSK scale) in eyes randomized to topical corticosteroids treatment and eyes not.
   b. BCVA at baseline, at worst during Cycle 1-4, and worst and most frequent category (definite worsen, possible worsen, and no change/improved) of change from baseline during Cycle 1-4 will be summarized in eyes randomized to topical corticosteroids treatment and eyes not. Eyes with a decline in BCVA to 'light perception' (LP) or 'no light perception' (NLP) due to corneal finding anytime post-baseline will also be summarized.
   c. Summary of onset time to first study treatment (BCMA)-related corneal finding (GSK scale) in eyes randomized to topical corticosteroids treatment and eyes not.
   d. Summary of onset time to initiation of topical corticosteroids treatment in eyes randomized to no such treatment.
   e. Shift in corneal findings (per ocular exam) from baseline to worst during Cycle 1- 4 in eyes randomized to topical corticosteroids treatment and eye not. Corneal findings include Corneal epithelium (Normal to Abnormal), Punctate Keratopathy (None/Mild to Moderate/Severe), Corneal ulcer (No to Yes), Microcystic edema (No to Yes), Microcystic without edema (Yes to No), Subepithelial haze (No to Yes), Corneal neovascularization (No to Yes), Stroma (Normal to Abnormal), Active opacity (No to Yes), and Active edema (No to Yes).

The details of the planned displays are provided in Appendix 13: List of Data Displays.

## 8.6. Pregnancies

While pregnancy itself is not considered to be an AE or SAE, any pregnancy complication or elective termination of a pregnancy for medical reasons will be recorded as an AE or SAE as described in the protocol. If subjects and subjects' partner become pregnant while on the study, the information will be included in the narratives and no separate table or listing will be produced.

## 8.7. Clinical Laboratory Analyses

Laboratory evaluations including the analyses of Chemistry laboratory tests, Haematology laboratory tests, Urinalysis, and liver function tests will be based on GSK Core Data Standards. The details of the planned displays are in Appendix 13: List of Data Displays. Summary of change from baseline by scheduled visits using mean, median, standard deviation, minimum and maximum will be provided.

Summaries of worst case grade increase from baseline grade will be provided for all the lab tests that are gradable by CTCAE v4.03. These summaries will display the number and percentage of subjects with a maximum post-baseline grade increasing from their baseline grade. Any increase in grade from baseline will be summarized along with any increase to a maximum grade of 3 and any increase to a maximum grade of 4. Missing baseline grade will be assumed as grade 0. For laboratory tests that are graded for both low and high values, summaries will be done separately and labelled by direction, e.g., sodium will be summarized as hyponatremia and hypernatremia.

For lab tests that are not gradable by CTCAE v4.03, summaries of worst case changes from baseline with respect to normal range will be generated. Decreases to low, changes to normal or no changes from baseline, and increases to high will be summarized for the worst case post-baseline. If a subject has a decrease to low and an increase to high during the same time interval, then the subject is counted in both the "Decrease to Low" categories and the "Increase to High" categories.

Separate summary tables for haematology, and chemistry laboratory tests will be produced. Liver function laboratory tests will be included with chemical chemistry.

For spot urine albumin/creatinine ratio (mg/g), a shift table from baseline to worst post-baseline will be provided.

A supporting listing of laboratory data for subjects with abnormalities of potential clinical concern will be provided. A separate listing of laboratory data with character values will also be provided.

Detailed derivation of baseline assessment is specified in Section 5.2

Unless otherwise specified, the denominator in percentage calculation at each scheduled visit will be based on the number of subjects with non-missing value at each particular visit.

### 8.7.1. Analyses of Liver Function Tests

Summaries of hepatobiliary laboratory events including possible Hy's law cases will be provided in addition to what has been described above.

A plot of maximum ALT vs. baseline ALT will be generated. Plots of maximum total bilirubin versus maximum ALT, maximum AST versus maximum LDH, maximum AST versus maximum Creatinine Kinase, and maximum LDH versus maximum Creatinine Kinase will be generated.

A Summary of Liver Monitoring/Stopping Event Reporting will be provided. The medical conditions data for subjects with liver stopping events will be listed. The substance use data for subjects with liver stopping events will be listed.

## 8.8. Other Safety Analyses

The analyses of non-laboratory safety test results including ECGs and vital signs will be based on GSK Core Data Standards, unless otherwise specified. The details of the planned displays are presented in Appendix 13: List of Data Displays.

Unless otherwise specified, the denominator in percentage calculation at each scheduled visit will be based on the number of subjects with non-missing value at each particular visit.

### 8.8.1. Performance Status

ECOG performance status will be summarized at baseline and each post-baseline scheduled visit. Summaries will use frequency and percentage of subjects at each planned assessment time. A summary of change from baseline by scheduled visits will be performed, as well as the worst case post-baseline and the best case post-baseline changes during the study (improved, no change, deteriorated).

A supporting listing will also be provided.

### 8.8.2. ECG

A summary of the number and percentage of subjects who had normal and abnormal (clinically significant and not clinically significant) ECG findings will be displayed by scheduled visits as well as for the worst case post-baseline.

The QTc values based on Fridericia formula will be rounded to the integer and the values will be categorized into the following CTCAE grade and ranges: Grade 0 (<450 msec), Grade 1 (450-480 msec), Grade 2 (481-500 msec), and Grade 3 (≥501 msec). Summaries of grade increase will be provided. These summaries will display the number and percentage of subjects with any grade increase, increase to grade 2 and increase to grade 3 in the worst case post-baseline only.

The changes in QTc values will be categorized into the clinical concern ranges which are specific to changes in QTc: 31-60 and >60 msec. A summary of change in QTc value will

display the number and percentage of subjects with a change within each range in the worst case post-baseline only. Subjects with missing baseline values will be excluded from this summary.

A listing of QTc values of potential clinical importance will be provided

The summaries and listing of QTc will use the collected values based on Fridericia formula.

A figure plotting the baseline QTc and the worst-case post-baseline values will be produced. The figure will have reference lines at 480 and 500 msec for both the ordinate and the abscissa axes. There will be diagonal reference lines at equality (i.e. a 45 degree line), at equality plus 30 msec, and at equality plus 60 msec.

### 8.8.3. LVEF

Absolute change from baseline in LVEF will be summarized in the worst case post-baseline only. Only the post-baseline assessments that used the same method (e.g. ECHO) as the baseline assessments will be used to derive the change from baseline. The change from baseline will be categorized as follows:

- No change or any increase
- Any decrease
- >0-<10 decrease
- 10-19 decrease
- >=20 decrease
- >=10 decrease and >= LLN
- >=10 decrease and < LLN
- >=20 decrease and >= LLN
- >=20 decrease and < LLN

### 8.8.4. Anti-Drug Antibody analyses

For each subject, the anti-GSK2857916 (drug) antibody results, titers, and neutralizing antibody assay results, and also ADC and total antibody concentration will be listed for each assessment time point. The frequency and percentage of subjects with positive and negative anti-drug antibody and neutralizing antibody assay results will be summarized for each assessment time and overall for each subject by dose cohort. The conclusive results will be based on the total antibody concentration.

# 9. PHARMACOKINETIC ANALYSES

The pharmacokinetic analyses will be based on the "Full Pharmacokinetic" population.

Concentration-time data collected in Cycles 1 and 3 under protocol amendment 2 were analysed using standard non-compartmental (NCA) methods at the time of primary analyses. Some parameters were determined for all participants and cycles. The concentration-time data may be combined with data from other studies and will be analysed in a population approach using nonlinear mixed effects modelling. Full details are presented in Appendix 13: List of Data Displays.

## 9.1. Drug Concentration Measures

Refer to Appendix 5: Data Display Standards & Handling Conventions (Section 15.5.3 Reporting Standards for Pharmacokinetic Parameters

### 9.1.1. Non-compartmental Analysis

- Pharmacokinetic parameters described in Table 6 below, were determined separately for each analyte, as data permitted.
- The pharmacokinetic parameters in Cycles 1 and 3 under protocol amendment 2 or later were calculated by standard non-compartmental analysis according to current working practices and using Phoenix WinNonlin, version 6.3 or later, as data permitted.
- The pharmacokinetic parameters C-EOI and Ctrough were determined directly from the concentration-time dataset for the other cycles under protocol amendment 2 and for participants enrolled prior to protocol amendment 2, as data permitted. Note: For the dosing occasions with only predose and end of infusion samples, the end of infusion concentration (C-EOI) was not identified as Cmax.
- All calculations of non-compartmental parameters were based on actual sampling times.

**Table 6 Derived Pharmacokinetic Parameters**

| Parameter | Parameter Description |
|---|---|
| AUC(0-t) | Area under the concentration-time curve from time zero to the time of the last quantifiable concentration (C(t)) will be calculated using the linear trapezoidal rule for each incremental trapezoid and the log trapezoidal rule for each decremental trapezoid |
| AUC(0-t') | Area under the concentration-time curve to a fixed time t' |
| AUC(0-τ) | Area under the concentration-time curve during the dosing interval |
| AUC(0-∞) | Area under the concentration-time curve extrapolated to infinity will be calculated as: **AUC = AUC(0-t) + C(t) / lambda_z** |
| %AUCex | The percentage of AUC (0-∞) obtained by extrapolation (%AUCex) will be calculated as: **[AUC(0-inf) – AUC(0-t)] / AUC(0-inf) x 100** |
| Cmax | Maximum observed concentration, determined directly from the concentration-time data for each cycle. Cmax will not be derived when only predose and EOI samples were collected. |
| tmax | Time to reach Cmax, determined directly from the concentration-time data for each cycle |
| Cτ, | Trough concentration prior to the next dose for each cycle |

| Parameter | Parameter Description |
|---|---|
| Ctrough | |
| C-EOI | Observed plasma concentration at the end of infusion |
| t½ | Apparent terminal half-life will be calculated as:<br>**t½ = ln(2) / lambda_z** |
| tlast | Time of last observed quantifiable concentration |
| CL | Clearance |
| Vss | Volume of distribution at steady state |
| λz, lambda_z | Terminal phase rate constant |

## 9.2. Population of Interest

The pharmacokinetic (PK) analyses will be based on the 'Full Pharmacokinetic' population as defined in Section 4, unless otherwise specified.

## 9.3. Statistical Analyses / Methods

Details of the planned displays are provided in Appendix 13: List of Data Display, based on GSK data standards and statistical principles. Unless otherwise specified, endpoints / variables defined in Section 9.1.1 will be summarised using descriptive statistics, graphically presented (where appropriate) and listed.

### 9.3.1. Statistical Methodology Specification

The following pharmacokinetic statistical analyses were performed when sufficient data were available.

#### 9.3.1.1. Assessment of Accumulation Ratio

To assess the extent of accumulation following GSK2857916 repeat dosing, the observed accumulation ratio (Ro) for GSK2857916, total antibody, and cys-mcMMAF were determined as ratio of AUC and Cmax at Cycle 3 to AUC and Cmax at Cycle 1, respectively, using the data collected under protocol amendment 2. The same AUC parameter [AUC(0-t') or AUC(0-τ)] were used on the two occasions for each analyte, but analytes may have used different AUC parameters depending upon the data.

Participants must have received the same dose without delay or change for Cycles 1, 2, and 3 to be included in this analysis (i.e., with dosing delays of ≤3 days).

Ro(AUC) = AUC C3 / AUC C1;
AUC is AUC(0-τ) or AUC(0-t')

Ro(Cmax) = Cmax C3 / Cmax C1
Accumulation ratios of AUC and Cmax were summarised using descriptive statistics by planned initial dose level, graphically presented (where appropriate) and listed.

An exploratory analysis was not performed considering the effect of dose delay or change on the ratio.

# 10. POPULATION PHARMACOKINETIC (POPPK) ANALYSES

Plasma GSK2857916 concentration-time data may be combined with data from other studies and will be analysed using a population pharmacokinetic approach. Details of the population PK analyses will be reported under a separate RAP, and the results of this analysis will be provided in a separate report.

# 11. PHARMACODYNAMIC AND BIOMARKER ANALYSES

If data permit, the relationship between clinical response and other biologic characteristics including BCMA expression on tumour cells and sBCMA concentrations may be explored. Details of these analyses will be specified within a separate biomarker RAP, and the results of these analysis will be provided in a separate report.

# 12. PHARMACOKINETIC / PHARMACODYNAMIC ANALYSES

## 12.1. Exposure-Response for Efficacy and Safety Endpoints

If deemed appropriate and if data permit, exposure-response relationships between GSK2857916 exposure (e.g., dose, dose intensity, concentration, Cmax, or AUC) and clinical activity and/or toxicity (e.g., response, corneal event, AESIs) may be explored using population methods. If data permit, the effects of covariates may be explored. Details of these analyses will be reported under a separate RAP, and the results of this analysis will be provided in a separate report.

## 12.2. Concentration-QTc Analyses

Concentration-QTc Analyses were performed at the time of the primary analyses. For each ECG assessment, the individual subject's QTcF change from baseline were calculated and were merged with time-matched PK concentration values for the timepoints at which they are available. QTcF change from baseline (y-axis) were plotted against the PK concentration data (x-axis) separately for each analyte (ADC, total mAb, and cys-mc-MMAF). Linear regression analyses were performed for each analyte-ΔQTcF plot.

# 13. HEALTH OUTCOMES ANALYSIS

The EORTC QLQ-C30 (version 3.0), EORTC QLQ-MY20, and the PRO-CTCAE are three oncology-specific Health-Related Quality-of-Life (HRQoL) assessments that will be analysed in this study.

In addition, the impact of potential corneal event on function and health-related quality-of-life will be assessed with the use of two visual function questionnaires, the NEI-VFQ-25 and Ocular Surface Disease Index (OSDI).

The analysis population for EORTC QLQ-C30 and EORTC QLQ-MY20 will follow the rule for efficacy analysis, while the analysis population for PRO-CTCAE, NEI-VFQ-25, and OSDI will follow the rule for safety analysis.

## 13.1. European Organization for Research and Treatment of Cancer Quality of Life Questionnaire 30-item Core module (EORTC QLQ-C30)

The EORTC QLQ-C30 is a 30-item questionnaire containing both single- and multi-item measures [Aaronson, 1993]. Details of deriving domain scores (9 scales and 6 single items) and summary score can be found in Section 15.11.1.

For summary score and each of domain scores, the following outputs will be provided:

- The descriptive summary of the actual value and change from baseline by visit.
- The number (%) of patients with improvement in score ≥ 10, and ≥ 5 points respectively by visit.

## 13.2. European Organization for Research and Treatment of Cancer Quality of Life Questionnaire 20-item Multiple Myeloma module (EORTC QLQ-MY20)

The EORTC QLQ-MY20 is a supplement to the QLQ-C30 instrument used in patients with multiple myeloma [Aaronson, 1993; Cocks, 2007]. The module comprises 20 questions that address four myeloma-specific HRQoL domains: Disease Symptoms, Side Effects of Treatment, Future Perspective, and Body Image. Three of the four QLQ-MY20 domains are multi-item scales: Disease Symptoms (includes bone aches or pain, back pain, hip pain, arm or shoulder pain, chest pain, and pain increasing with activity); Side Effects of Treatment (includes drowsiness, thirst, feeling ill, dry mouth, hair loss, upset by hair loss, tingling hands or feet, restlessness/agitation, acid indigestion/heartburn, and burning or sore eyes); and Future Perspective (includes worry about death and health in the future, and thinking about illness). The Body Image scale is a single-item scale that addresses physical attractiveness. Details of deriving domain scores can be found in Section 15.11.2.

For each of four domain scores, the following outputs will be provided:

- The descriptive summary of the actual value and change from baseline by visit
- Summary of the number (%) of patients with improvement in score ≥ 10, and ≥ 5 points respectively by visit.

## 13.3. Patient-Reported Outcome Version of the Common Term Criteria for Adverse Events (PRO-CTCAE)

The Patient-Reported Outcomes Version of the Common Terminology Criteria for Adverse Events (PRO-CTCAE) is a patient-reported outcome measure developed to evaluate symptomatic toxicity in patients on cancer clinical trials [Basch, 2014]. The PRO-CTCAE was designed to be used as a companion to the Common Terminology Criteria for Adverse Events (CTCAE), the standard lexicon for adverse event reporting in cancer trials. The PRO-CTCAE includes an item library of 124 items representing 78 symptomatic toxicities drawn from the CTCAE. PRO-CTCAE provides a systematic yet flexible tool for descriptive reporting of symptomatic treatment side effects in cancer clinical trials. The levels and related code values for PRO-CTCAE are shown below.

| | Levels and related code values | | | | |
|---|---|---|---|---|---|
| Response scale | 0 | 1 | 2 | 3 | 4 |
| Frequency | Never | Rarely | Occasionally | Frequently | Almost Constantly |
| Severity | None | Mild | Moderate | Severe | Very severe |
| Interference | Not at all | A little bit | Somewhat | Quite a bit | Very much |
| Present/Absence | No | Yes | | | |

For each selected item from the library: proportion of PRO-CTCAE scores for each item attribute (frequency, severity and/or interference) will be presented-with stacked bar charts by visit. Maximum PRO-CTCAE score at post-baseline for each item attribute will be summarized by counts and proportions. Proportion of patients with a maximum score of 3 or 4 for each item attribute (severe or very severe, frequently or almost constantly, quite a bit or very much) will also be reported. Proportions will be based on the number of patients with available data and subject with missing response will be excluded from analysis.

## 13.4. National Eye Institute Visual Function Questionnaire-25 (NEI-VFQ-25)

The NEI-VFQ-25 consists of a base set of 25 vision-targeted questions representing 11 vision-related constructs, plus an additional single-item general health rating question [Mangione, 2001]. The NEIVFQ-25 generates the following vision-targeted sub-scales: global vision rating, difficulty with near vision activities; difficulty with distance vision activities; limitations in social functioning due to vision; role limitations due to vision; dependency on others due to vision; mental health symptoms due to vision; driving difficulties; limitations with peripheral vision, limitations with color vision; and corneal

pain. Details of deriving domain scores and overall composite score can be found in Section 15.11.3.

For overall composite score and each of 11 sub-scale scores, the descriptive summary of the actual value and change from baseline by visit will be provided.

In addition, summary of worst change from baseline in overall composite score by worst grade of corneal event per GSK scale (0 vs 1-2, vs 3-4) will also be provided. The summary will be based on pooled data of frozen liquid cohort (2.5 and 3.4 mg/kg) and Lyo cohort (3.4 mg/kg).

## 13.5. Ocular Surface Disease Index

The Ocular Surface Disease Index (OSDI) is a 12-item questionnaire designed to assess both the frequency of dry eye symptoms and their impact on vision-related functioning [Schiffman, 2000].

For the OSDI, the total score will be calculated as well as scores for the three subscales (ocular symptom: item 1-3; visual related function: item 4-9; and environmental triggers: item 10-12).

The total OSDI score = ([sum of scores for all questions answered × 100]/[total number of questions answered ×4]). Subscale scores are computed similarly with only the questions from each subscale used to generate its own score. A score of 100 corresponds to complete disability (a response of “all of the time” to all questions answered), while a score of 0 corresponds to no disability (a response of “none of the time” to all questions answered). Therefore, decrease in score from baseline means improvement.

For total score and each of the three sub-scales, the descriptive summary of the actual value and change from baseline by time will be provided.

In addition, summary of worst change from baseline in total score by worst grade of corneal event per GSK scale (0 vs 1-2, vs 3-4) will also be provided. The summary will be based on pooled data of frozen liquid cohort (2.5 and 3.4 mg/kg) and Lyo cohort (3.4 mg/kg).

# 14. REFERENCES

Aaronson NK, Ahmedzai S, Bergman B, Bullinger M, Cull A, Duez NJ, et al. The European Organization for Research and Treatment of Cancer QLQ-C30: a quality-of-life instrument for use in international clinical trials in oncology. J Natl Cancer Institute. 1993 Mar 3;85(5):365-76.

Basch E, Reeve BB, Mitchell SA, Clauser SB, Minasian LM, Dueck AC, et al. Development of the National Cancer Institute's patient-reported outcomes version of the common terminology criteria for adverse events (PRO-CTCAE). J Natl Cancer Inst. 2014;106(9).

Brookmeyer R, Crowley J. A confidence interval for the median survival time. Biometrics. 1982 Mar 1:29-41.

Cocks K, Cohen D, Wisløff F, Sezer O, Lee S, Hippe E, et al. An international field study of the reliability and validity of a disease-specific questionnaire module (the QLQMY20) in assessing the quality of life of patients with multiple myeloma. European Journal of Cancer. 2007 Jul 31;43(11):1670-8.

Dmitrienko A, Wang MD. Bayesian predictive approach to interim monitoring in clinical trials. Statistics in Medicine. 2006 July 15;25(13):2178-2195.

Fayers et. al., The EORTC QLQ-C30 Scoring Manual (3rd Edition) 2001

GlaxoSmithKline Document Number TMF-13990464 Study ID205678.DREAMM-2: A Phase II, Open Label, Randomized, Two-Arm Study to Investigate the Efficacy and Safety of Two Doses of the Antibody Drug Conjugate GSK2857916 in Participants with Multiple Myeloma Who Had 3 or More Prior Lines of Treatment, Are Refractory to a Proteasome Inhibitor and an Immunomodulatory Agent and Have Failed an Anti-CD38 Antibody (DREAMM 2). Document Date 19-Nov-2021.

Hwang IK, Shih WJ, De Cani JS. Group sequential designs using a family of type I error probability spending functions. Stat Med. 1990;9(12):1439-45.

Kumar S, et al. International Myeloma Working Group consensus criteria for response and minimal residual disease assessment in multiple myeloma. The Lancet Oncology. 2016;17: e328-e346.

Mangione CM, Lee PP, Gutierrez PR, Spritzer K, Berry S, Hays RD, et al. Development of the 25-item National Eye Institute Visual Function Questionnaire. Arch Ophthalmol. 2001;119(7):1050-8.

Osoba D, Rodrigues G, Myles J, Zee B, Pater J. Interpreting the significance of changes in health-related quality-of-life scores. J Clin Oncol. 1998 Jan;16(1):139-44

Proskorovsky I., P. Lewis, C. D. Williams, K. Jordan, C. Kyriakou, J. Ishak, F. E. Davies. Mapping EORTC QLQ-C30 and QLQ-MY20 to EQ-5D in patients with multiple myeloma. Health Qual Life Outcomes. 2014 Mar 11; 12:35.

Rajkumar SV. Updated Diagnostic Criteria and Staging System for Multiple Myeloma. Am Soc Clin Oncol Educ Book. 2016;35:e418-23.

Schiffman RM, Christianson MD, Jacobsen G, Hirsch JD, Reis BL. Reliability and validity of the Ocular Surface Disease Index. Arch Ophthalmol. 2000;118(5):615-21.

# 15. APPENDICES

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

### 15.1.1. Exclusions from Per Protocol Population

No per protocol population was defined for the study.

## 15.2. Appendix 2: Schedule of Activities

### 15.2.1. Protocol Defined Schedule of Events

Refers to Section 1.2 of Protocol (Version: GSK Document Number TMF-13990464 ).

## 15.3. Appendix 3: Assessment Windows

### 15.3.1. Definitions of Assessment Windows for Analyses

Not applied to the study.

## 15.4. Appendix 4: Study Phases and Treatment Emergent Adverse Events

### 15.4.1. Study Phases

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

| Study Phase | Definition |
|---|---|
| Pre-Treatment | Date/time ≤ Study Treatment Start Date/time |
| On-Treatment | Study Treatment Start Date/time < Date/time |

For assessment or event on the first dosing day, whether it is Pre-Treatment or On-Treatment should be based on time if available. If time is not available, the first dosing day (Day 1) is considered Pre-Treatment for ECOG, ECG, vital signs, liver events, lab tests, cardiac scan, and other safety domains, and On-Treatment for adverse events and concomitant medications.

Concomitant Medication and Blood and Blood Supportive Care Product start and end dates will be assigned to study time periods in relation to first dose of study treatment as defined below. The start date references time flag variables and end date reference time flag variables will be added to the concomitant medications and blood and blood supportive products datasets, respectively.

- Start **relative to treatment:** Assign to 'BEFORE' if start date is prior to study treatment start date or if subject has not taken any study treatment or (start date is missing and end date is before study treatment start date). Else assign to 'DURING' if the start date falls into the on-treatment period as defined above or if subject is ongoing (not all study treatment discontinuation records completed) or start date is missing. Else assign to 'AFTER' if start date is after the on-treatment period.
- **End relative to** treatment: Assign to 'BEFORE' if end date is prior to study treatment start date or if subject has not taken any study treatment. Else assign to 'DURING' if start date falls into the on-treatment period or if subject is ongoing (not all study treatment discontinuation records completed) or (end date is missing and start relative to treatment not 'AFTER'). Else assign to 'AFTER' if start date is after the on-treatment period or (end date is missing and start relative to treatment='AFTER').

Only on-treatment blood and blood supportive care products that start after the start of study treatment are included in the Blood Products and Blood Supportive Care Product summaries. Therefore, for summary tables, include blood and blood supportive care product records where start relative to treatment in ('DURING') and end relative to treatment in ('DURING','AFTER'). All data will be reported in listings.

Concomitant medication starts relative to treatment and end relative to treatment flags are used to select data to include in the Concomitant Medication summaries as follows:

- Summary of Concomitant Medications: This summary will contain medications including those with start date prior to study treatment start date and continue (missing end date or end date after study treatment start date) on therapy. Note that any medications with start date and end date prior to study treatment start date will be excluded. In addition, any medication that was started during post-therapy will be excluded. Include concomitant medication records where start relative to treatment in ('BEFORE','DURING') and end relative to treatment in ('DURING','AFTER').
- Summary of Concomitant Medications with On-Therapy Onset: This summary will contain medications with start date after study treatment start date. In addition, any medication that was started during post-therapy (see above for definition of post-therapy) will be excluded. Include concomitant medication records where start relative to treatment in ('DURING') and end relative to treatment in ('DURING','AFTER').

## 15.4.2. Treatment Emergent Flag for Adverse Events

| Flag | Definition |
|---|---|
| Treatment Emergent | • Study Treatment Start Date ≤ AE Start Date<br>• AE Start Date is missing |

**NOTES:**

- If the study treatment stop date is missing, then the AE will be considered to be On-Treatment.
- Time of study treatment dosing and start/stop time of AEs should be considered, if collected.

# 15.5. Appendix 5: Data Display Standards & Handling Conventions

## 15.5.1. Reporting Process

| | |
|---|---|
| **Software** | |
| • The currently supported versions of SAS software will be used. | |
| **Reporting Area** | |
| HARP Server | : US1SALX00259 |
| HARP Compound | : arprod\gsk2859716\MID205678\ |
| **Analysis Datasets** | |
| • Analysis datasets will be created according to CDISC standards (SDTM IG Version 3.2 & ADaM IG Version 1.1. | |
| **Generation of RTF Files** | |
| RTF files will be generated for all tables. | |

## 15.5.2. Reporting Standards

| |
|---|
| **General** |
| • The current GSK Integrated Data Standards Library (IDSL) will be applied for reporting, unless otherwise stated (IDSL Standards Location: https://spope.gsk.com/sites/IDSLLibrary/SitePages/Home.aspx):<br>  • 4.03 to 4.23: General Principles<br>  • 5.01 to 5.08: Principles Related to Data Listings<br>  • 6.01 to 6.11: Principles Related to Summary Tables<br>  • 7.01 to 7.13: Principles Related to Graphics<br>• Do not include subject level listings in the main body of the GSK Clinical Study Report. All subject level listings should be located in the modular appendices as ICH or non-ICH listings |
| **Formats** |
| • GSK IDSL Statistical Principles (5.03 & 6.06.3) for decimal places (DP's) will be adopted for reporting of data based on the raw data collected, unless otherwise stated.<br>• Numeric data will be reported at the precision collected on the eCRF.<br>The reported precision from non eCRF sources will follow the IDSL statistical principles but may be adjusted to a clinically interpretable number of DP's. |
| **Planned and Actual Time** |
| • Reporting for tables, figures and formal statistical analyses:<br>  • Planned time relative to dosing will be used in figures, summaries, statistical analyses and calculation of any derived parameters, unless otherwise stated.<br>  • 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.<br>• Reporting for Data Listings:<br>  • Planned and actual time relative to study drug dosing will be shown in listings (Refer to IDSL Statistical Principle 5.05.1).<br>  • Unscheduled or unplanned readings will be presented within the subject's listings. |
| **Unscheduled Visits** |
| • Unscheduled visits will not be included in summary tables and/or figures.<br>  • For by planned time analysis, unscheduled visits will not be included;<br>  • For worst-case analysis, unscheduled visits will be included. |

| | |
|---|---|
| • All unscheduled visits will be included in listings. | |
| **Descriptive Summary Statistics** | |
| Continuous Data | Refer to IDSL Statistical Principle 6.06.1 |
| Categorical Data | N, n, frequency, % |
| **Graphical Displays** | |
| • Refer to IDSL Statistical Principals 7.01 to 7.13. | |

### 15.5.3. Reporting Standards for Pharmacokinetic

| | |
|---|---|
| **Pharmacokinetic Concentration Data** | |
| PC Windows Non-Linear (WNL) File | PC WNL file (CSV format) for the non-compartmental analysis by Clinical Pharmacology Modelling and Simulation function will be created according to SOP 00000314000: Non-Compartmental Analysis of Clinical Pharmacokinetic Data.<br>Note: Concentration values will be imputed as per GUI_51487 |
| Descriptive Summary Statistics, Graphical Displays and Listings | Refer to IDSL PK Display Standards.<br>Refer to IDSL Statistical Principle 6.06.1.<br>Note: Concentration values will be imputed as per GUI_51487 for descriptive summary statistics/analysis and summarized graphical displays only. |
| NONMEM/Pop PK File | See separate population PK/exposure-response analysis RAP |
| NONMEM/PK/PD File | See separate population PK/exposure-response analysis RAP |
| **Pharmacokinetic Parameter Derivation** | |
| PK Parameter to be Derived by Programmer | The following PK parameters will be derived by the Programmer:<br>• C-EOI and Ctrough for cycles with predose and EOI sampling only<br>• Accumulation ratios based on Cycle 1 and Cycle 3 AUC and Cmax values |
| **Pharmacokinetic Parameter Data** | |
| Is NQ impacted PK Parameters Rule Being Followed | Yes, refer to [Standards for Handling NQ Impacted PK Parameters]. |
| Descriptive Summary Statistics, Graphical Displays and Listings | Refer to IDSL PK Display Standards. |

### 15.5.4. Extended Loss to Follow-up or Extended Time without an Adequate Assessment

For subjects, if two or more scheduled disease assessments are missed and are then followed by an assessment of PD or death, PFS will be censored at the last adequate assessment prior to PD or death. When the scheduled disease assessment is every 3 weeks, a window of 49 days (6 weeks + 7 day window) will be used to determine whether there was an extended time without adequate assessment. That is, if the time difference between PD/death and last adequate assessment is more than 49 days, then PFS will be censored at the last adequate assessment prior to PD/death.

# 15.6. Appendix 6: Derived and Transformed Data

## 15.6.1. General

| Multiple Measurements at One Analysis 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.<br>• Participants having both High and Low values for Normal Ranges at any post-baseline visit for safety parameters will be counted in both the High and Low categories of "Any visit post-baseline" row of related summary tables. This will also be applicable to relevant Potential Clinical Importance summary tables. |
| **Study Day** |
| • Calculated as the number of days from First Dose Date:<br>  • Ref Date = Missing → Study Day = Missing<br>  • Ref Date < First Dose Date → Study Day = Ref Date – First Dose Date<br>  • Ref Data ≥ First Dose Date → Study Day = Ref Date – (First Dose Date) + 1 |

## 15.6.2. Study Population

| Extent of Exposure |
|---|
| • Number of days of exposure to study drug will be calculated based on the formula:<br>**Duration of Exposure in Days = min(Last infusionDate+20, Death date) – First infusion Date + 1**<br>• Participants who were randomized but did not report a treatment start date will be categorised as having zero days of exposure.<br>• The cumulative dose will be based on the formula:<br>**Cumulative Dose (mg/kg) = Sum of Dose at Each Cycle**<br>• Dose intensity will be calculated based on the formula:<br>• **Dose intensity (mg/kg/3 week) = Cumulative Dose/((last infusion date – first infusion date + 21)/21)** |

## 15.6.3. Efficacy

| Laboratory Parameters |
|---|
| **Serum M-protein, Urine M-protein, Serum FLC** |
| • 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.<br>  o Example 1: 2 Significant Digits = '< x 'becomes x – 0.01<br>  o Example 2: 1 Significant Digit = '> x' becomes x + 0.1<br>• Example 3: 0 Significant Digits = '< x' becomes x – 1 |

## 15.6.4. Safety

| Adverse Events |
| --- |
| **AE'S of Special Interest** |
| • Eye disorder (CTCAE)<br>• Thrombocytopenia<br>• Infusion-Related Reactions<br>• Neutropenia<br>• Corneal events (GSK scale): collected in Ocular form |

# 15.7. Appendix 7: Reporting Standards for Missing Data

## 15.7.1. Premature Withdrawals

| Element | Reporting Detail |
|---|---|
| General | • Subject study completion (i.e. as specified in the protocol) was defined as "A participant will be considered to have completed the study if he or she has received at least one dose of the study treatment and, has died or is still in follow-up when the study is closed, and has not withdrawn consent from study participation.".<br>• Withdrawn subjects will not be replaced in the study.<br>• All available data from participants who were withdrawn from the study will be listed and all available planned data will be included in summary tables and figures, unless otherwise specified.<br>• Withdrawal visits will be slotted as per Appendix 3: Assessment Windows or will be summarised as withdrawal visits. |

## 15.7.2. Handling of Missing Data

| Element | Reporting Detail |
|---|---|
| General | • Missing data occurs when any requested data is not provided, leading to blank fields on the collection instrument:<br>  ○ 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.<br>  ○ Answers such as "Not applicable" and "Not evaluable" are not considered to be missing data and should be displayed as such. |
| Outliers | • Any participants excluded from the summaries and/or statistical analyses will be documented along with the reason for exclusion in the clinical study report. |
| Responder Analysis | • For endpoints which determine the percentage of responders, subjects with unknown/not evaluable or missing best overall response will be assumed to be non-responders and will be included in the denominator when calculating the percentages. |
| Time to Event | • Because study treatment is dependent on the study endpoints (e.g., progression, i.e. not a fixed treatment duration), the length of treatment for each subject will depend on the efficacy and toxicity of the treatment, so the duration of treatment will vary across subjects. Similarly, the duration of follow up will also vary. All available time-to-event data will be analysed using suitable statistical methods; subjects with shorter treatment and follow-up due to the natural history of their disease or medical necessities of the treatment of their disease will not be considered to have missing time-to-event data. |

### 15.7.2.1. Handling of Missing and Partial Dates

| Element | Reporting Detail |
|---|---|
| General | • Partial dates will be displayed as captured in subject listing displays.<br>• Imputed partial dates will not be used to derive study day, duration (e.g. duration of adverse events), or elapsed time variables. In addition, imputed dates are not used for deriving the last contact date in the overall survival analysis dataset.<br>• Imputed dates will not be displayed in listings. However, where necessary, display macros may impute dates as temporary variables for the purpose of sorting data in listings only. In addition, partial dates may be imputed for 'slotting' data to study time periods or for specific analysis purposes as outlined below. |

| Element | Reporting Detail |
|---|---|
| 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.<br>○ Missing Start Day: First of the month will be used unless this is before the start date of study treatment; in this case the study treatment start date will be used and hence the event is considered On-treatment as per Appendix 4: Study Phases and Treatment Emergent Adverse Events.<br>○ Missing Stop Day: Last day of the month will be used.<br>• Completely missing start dates will remain missing, with no imputation applied. Consequently, time to onset and duration of such events will be missing.<br>• Completely or partially missing end dates will remain missing, with no imputation applied. Consequently, duration of such events will be missing. |
| Concomitant Medications/ Medical History | • Partial dates for any concomitant medications recorded in the CRF will be imputed using the following convention:<br>○ If the partial date is a start date, a '01' will be used for the day and 'Jan' will be used for the month<br>○ If the partial date is a stop date, a '28/29/30/31' will be used for the day (dependent on the month and year) and 'Dec' will be used for the month.<br>• The recorded partial date will be displayed in listings. |
| New Anti-Cancer Therapy/ Radiotherapy/ Surgical Procedures for Efficacy Evaluation (e.g., response rate, time to event) | • Start dates for follow-up anti-cancer therapy, radiotherapy (where applicable), and surgical procedures (where applicable) will be temporarily imputed in order to define event and censoring rules for progression-free survival, response rate, time to progression, duration of response or time to response (i.e. start date for new anti-cancer therapy). The imputed dates will not be stored on the anti-cancer therapy, radiotherapy, or surgical procedure datasets.<br>• If missing start day, month, and year, then no imputation for completely missing dates<br>• If missing start day and month, then no imputation should be done<br>• If missing start day, then do the following:<br>• If partial date falls in the same month as the last dose of study treatment, then assign to earlier of (date of last dose of study treatment+1, last day of month).<br>• If partial date falls in the same month as the subject's last assessment and the subject's last assessment is PD, then assign to earlier of (date of PD+1, last day of month).<br>• If both rules above apply, then assign to latest of the 2 dates<br>• Otherwise, impute missing day to the first of the month.<br>If missing end date, then no imputation should be done. |
| Covariates for efficacy analysis (Date of initial diagnosis/ Last recurrence/ Last progression) | • If both month and day are missing, first of January will be used<br>If only day is missing, first of the month will be used |
| Treatment end date | • If there is more than one study treatment, imputation of missing treatment end date will be applied to all applicable treatments following rules below and treatment end date is the latest treatment end date across all study treatments. In general, completely missing |

| Element | Reporting Detail |
|---|---|
| | end dates are not imputed, with the following exceptions for imputation of missing treatment end date at interim analyses.<br>• For imputation of missing exposure end date at an interim analysis when subjects are still on treatment, the following conventions will be applied:<br>  ○ If the missing end date is in the last exposure record, the earliest of: the date of the data cut-off, the date of withdrawal from the study, or the death date will be used<br>  ○ If the missing end date is not in the last exposure record, treatment start date for the record will be used<br>• The imputed treatment end date will be used to calculate cumulative dose and duration of treatment as specified in Section 15.6.2<br>If treatment end date is missing for a cycle, treatment start date for the cycle will be used. |
| PACT | • For PACT subjects, subject's last Visit date will be used as subject's end of study date, wherever required. |

## 15.8. Appendix 8: Values of Potential Clinical Importance

### 15.8.1. Laboratory Values

Reference ranges for all laboratory parameters collected throughout the study are provided by the laboratory. A laboratory value that is outside the reference range is considered either high abnormal (value above the upper limit of the reference range) or low abnormal (value below the lower limit of the reference range). Note: a high abnormal or low abnormal laboratory value is not necessarily of clinical concern. The laboratory reference ranges will be provided on the listings of laboratory data. Clinical laboratory test results outside of the reference range will be flagged in the listings.

To identify laboratory values of potential clinical importance, National Cancer Institute Common Terminology Criteria for Adverse Events (NCI-CTCAE v4.03) will be used to assign grades to the relevant laboratory parameters. NCI-CTCAE v4.03 can be found at http://ctep.cancer.gov/reporting/ctc.html.

For laboratory data which are not listed in the NCI CTCAE v4.03, a summary of values outside the normal range will be provided.

### 15.8.2. ECG Parameters and vital signs

For ECG and vital signs, outputs per the most updated IDSL standard up to the RAP effective date will be provided.

Unless otherwise specified, ECG displays will be based on central reading.

# 15.9. Appendix 9: Population Pharmacokinetic (PopPK) Analyses

## 15.9.1. Population Pharmacokinetic (PopPK) Dataset Specification

See separate population PK/exposure-response analysis RAP

## 15.9.2. Population Pharmacokinetic (PopPK) Methodology

See separate population PK/exposure-response analysis RAP

# 15.10. Appendix 10: Pharmacokinetic / Pharmacodynamic Analyses

## 15.10.1. Pharmacokinetic / Pharmacodynamic Dataset Specification

See separate population PK/exposure-response analysis RAP

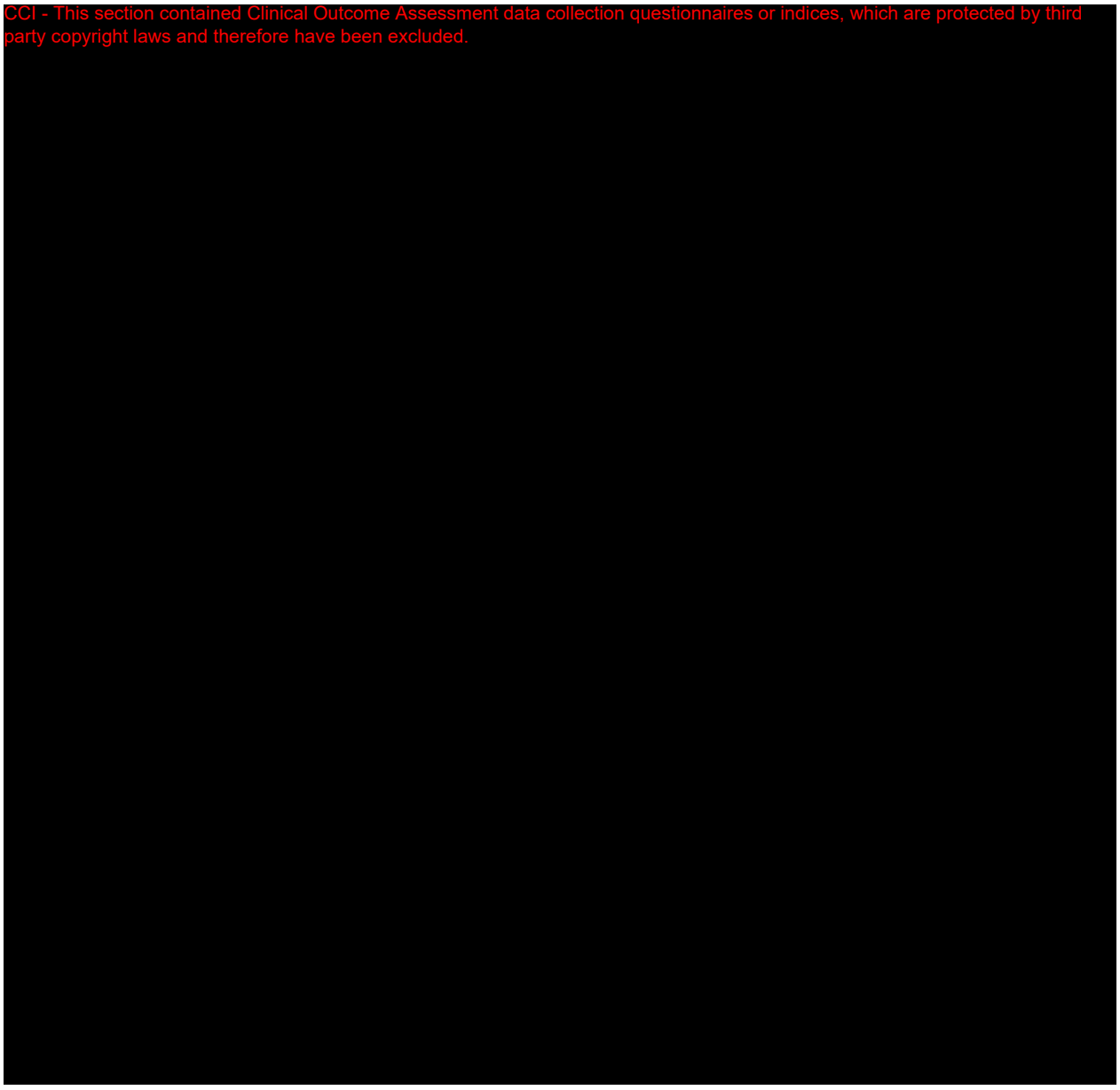
## 15.10.2. Pharmacokinetic / Pharmacodynamic Methodology

See separate population PK/exposure-response analysis RAP

## 15.11. Appendix 11: Health outcome Analyses

### 15.11.1. EORTC QLQ-C30

The EORTC QLQ-C30 is a 30-item questionnaire containing both single- and multi-item measures [Aaronson, 1993]. These include five functional scales (Physical, Role, Cognitive, Emotional, and Social Functioning), three symptom scales (Fatigue, Pain, and Nausea/Vomiting), a Global Health Status/QoL scale, and six single items (Constipation, Diarrhea, Insomnia, Dyspnea, Appetite Loss, and Financial Difficulties). The below image shows the details.



**Technical Summary**

In practical terms, if items $I_1, I_2, \ldots I_n$ are included in a scale, the procedure is as follows:

**Raw score**
Calculate the raw score
$RawScore = RS = (I_1 + I_2 + \ldots + I_n)/n$

**Linear transformation**
Apply the linear transformation to 0-100 to obtain the score $S$,

Functional scales: $S = \left\{1 - \frac{(RS-1)}{range}\right\} \times 100$

Symptom scales / items: $S = \{(RS-1)/range\} \times 100$

Global health status / QoL: $S = \{(RS-1)/range\} \times 100$

*Range* is the difference between the maximum possible value of *RS* and the minimum possible value. The QLQ-C30 has been designed so that all items in any scale take the same range of values. Therefore, the range of *RS* equals the range of the item values. Most items are scored 1 to 4, giving *range* = 3. The exceptions are the items contributing to the global health status / QoL, which are 7-point questions with *range* = 6, and the initial yes/no items on the earlier versions of the QLQ-C30 which have *range* = 1.

**Scoring of the QLQ-C30 Summary Score**

The EORTC QLQ-C30 Summary Score is calculated from the mean of 13 of the 15 QLQ-C30 scales (the Global Quality of Life scale and the Financial Impact scale are not included). Prior to calculating the mean, the symptom scales need to be reversed to obtain a uniform direction of all scales. The summary score should only be calculated if all of the required 13 scale scores are available.

QLQ-C30 Summary Score = [Physical Functioning+ Role Functioning+ Social Functioning+ Emotional Functioning+ Cognitive Functioning+ (100- Fatigue)+ (100-Pain)+ (100-Nausea_Vomiting)+ (100-Dyspnoea)+ (100-Sleeping Disturbances)+ (100-Appetite Loss)+ (100-Constipation)+ (100-Diarrhoea)]/13.

**Handling of missing items**

Single-item measures: if the item is missing, the score S will be set to missing.

Scales requiring multiple items: if at least half of the items from the scale are available, the score S will be calculated based on available items. If more than half of the items from the scale are missing, the score S will be set to missing (Fayers et. al., The EORTC QLQ-C30 Scoring Manual (3rd Edition) 2001).

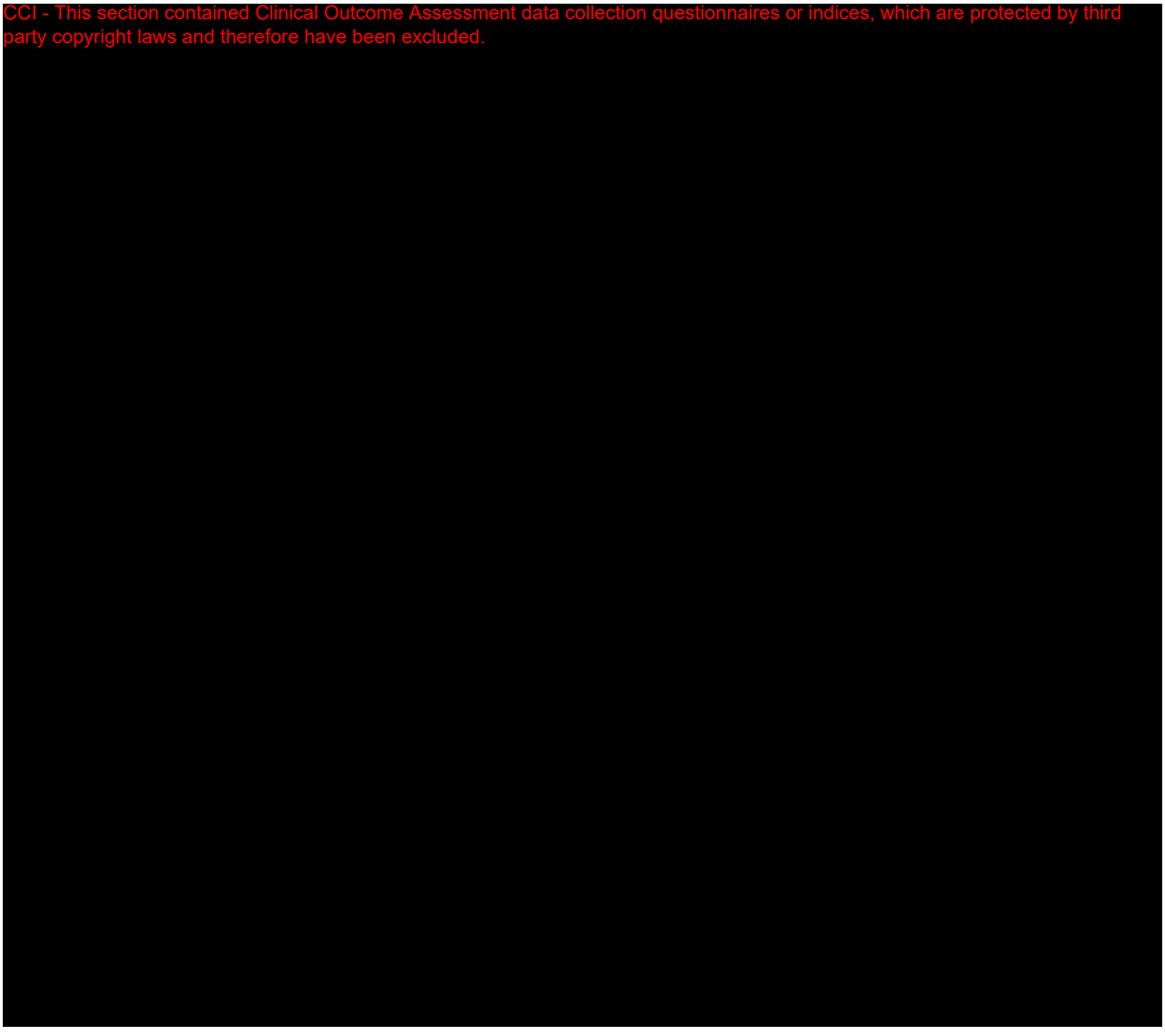
**Minimal Important Difference (MID):** In a sample of patients who received chemotherapy for either breast cancer or small-cell lung cancer (n=246, n=80

respectively), the mean change in EORTC QLQ-C30 score between baseline and follow-up was about 5 to 10 points on a 0-100 scale for patients who indicated “a little” change on the Subjective Significance Questionnaire (SSQ), either for better or for worse (Osoba, 1998).

### 15.11.2. EORTC QLQ-MY20

The EORTC QLQ-MY20 is a supplement to the QLQ-C30 instrument used in patients with multiple myeloma [Aaronson, 1993; Cocks, 2007]. The module comprises 20 questions that address four myeloma-specific HRQoL domains: Disease Symptoms, Side Effects of Treatment, Future Perspective, and Body Image. Three of the four QLQ-MY20 domains are multi-item scales: Disease Symptoms (includes bone aches or pain, back pain, hip pain, arm or shoulder pain, chest pain, and pain increasing with activity); Side Effects of Treatment (includes drowsiness, thirst, feeling ill, dry mouth, hair loss, upset by hair loss, tingling hands or feet, restlessness/agitation, acid indigestion/heartburn, and burning or sore eyes); and Future Perspective (includes worry about death and health in the future, and thinking about illness). The Body Image scale is a single-item scale that addresses physical attractiveness. (see below image for details).

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



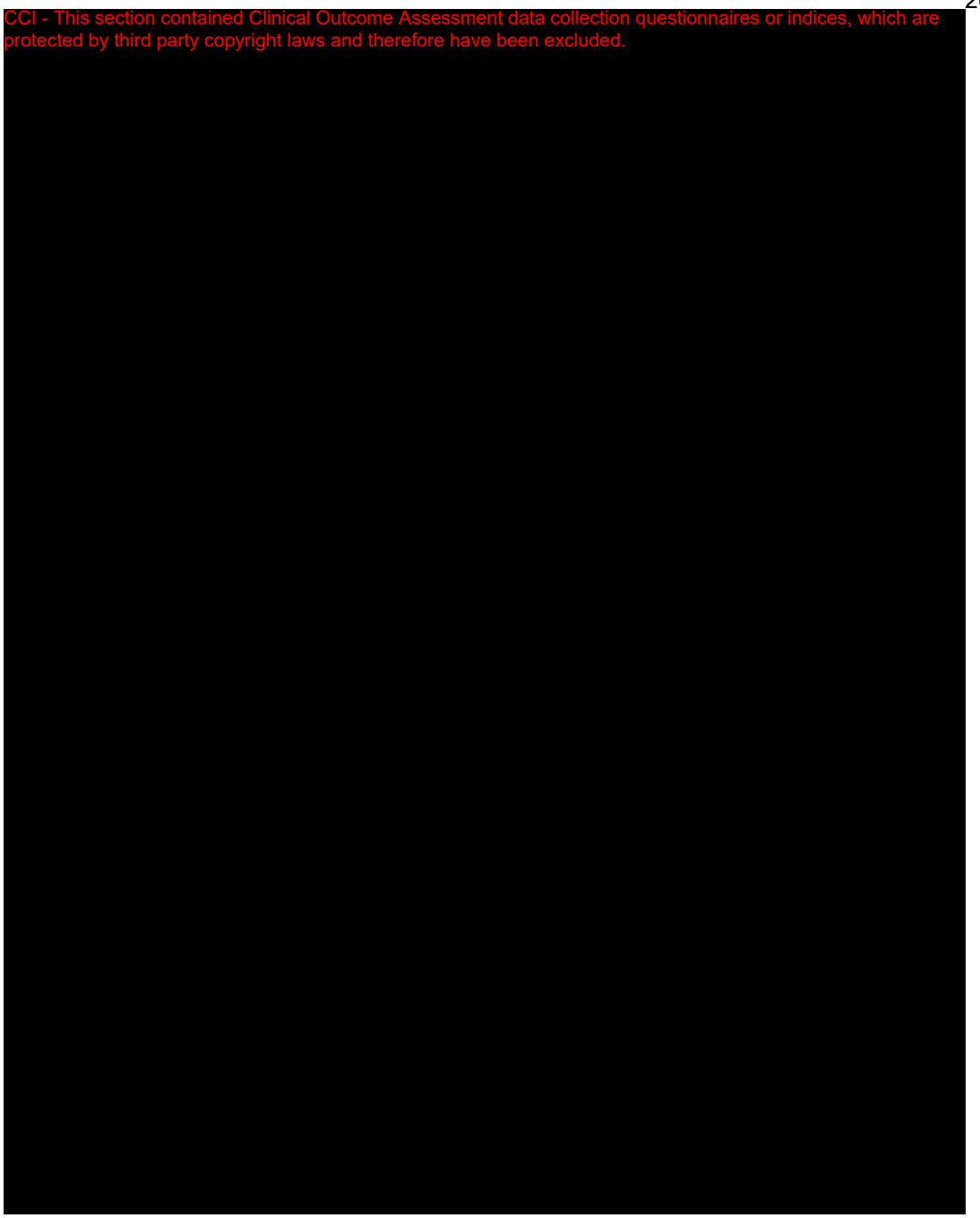
CCI - This section contained Clinical Outcome Assessment data collection questionnaires or indices, which are protected by third party copyright laws and therefore have been excluded.

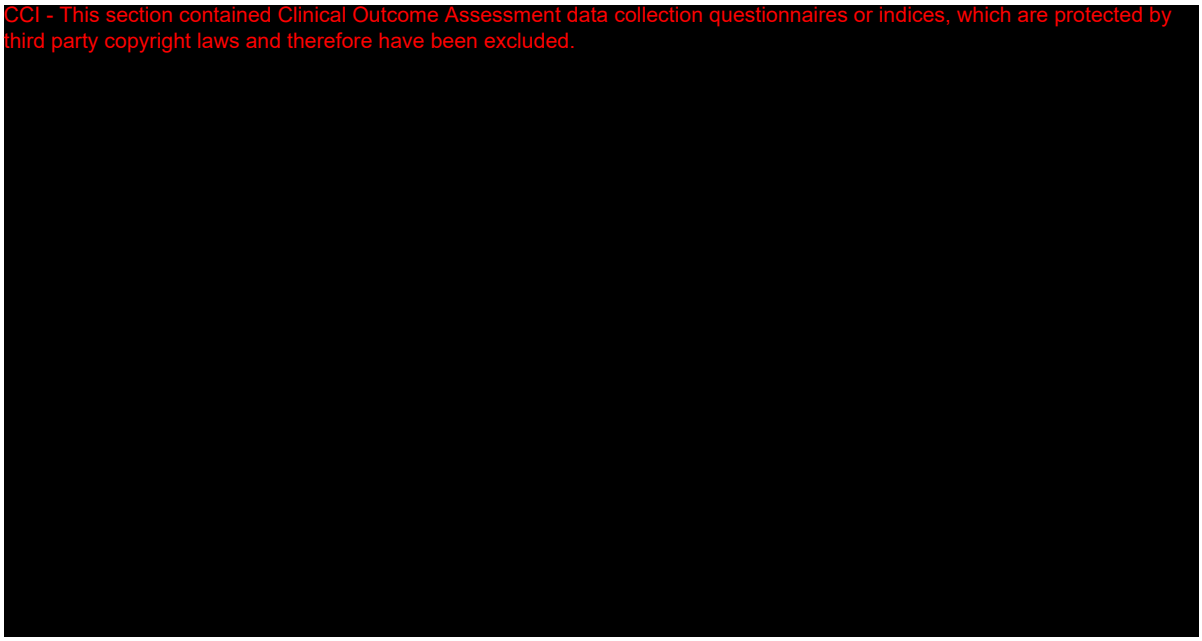
Missing items can be handled similarly to EORTC QLQ-C30 as described in Section 15.11.1.

### 15.11.3. NEI-VFQ-25

The NEI-VFQ-25 consists of a base set of 25 vision-targeted questions representing 11vision-related constructs, plus an additional single-item general health rating question [Mangione, 2001]. The NEIVFQ-25 generates the following 11 vision-targeted sub-scales: global vision rating, difficulty with near vision activities; difficulty with distance vision activities; limitations in social functioning due to vision; role limitations due to vision; dependency on others due to vision; mental health symptoms due to vision; driving difficulties; limitations with peripheral vision, limitations with color vision; and corneal pain.

The following two tables (from the NEI-VFQ-25 User Manuals) provide the details of converting the original response category to the recorded values, and items of which recorded values need to be averaged to generate the VFQ-25 sub-scales. Items that are left blank (missing data) are not taken into account when calculating the scale scores. Hence scores represent the average for all items in the sub-scale that the respondent answered. Sub-scales with at least one item answered can be used to generate a sub-scale score. To calculate an overall composite score for the VFQ-25, simply average the 11 vision-targeted sub-scale scores.


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


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

# 15.12. Appendix 12: Abbreviations & Trade Marks

## 15.12.1. Abbreviations

| Abbreviation | Description |
|---|---|
| A&R | Analysis and Reporting |
| ADA | Anti-Drug Antibodies |
| ADaM | Analysis Data Model |
| AE | Adverse Event |
| Ae(0-t) | Amount of drug excreted in urine from dosing to time t |
| AUC | Area under the concentration-time curve |
| BCVA | Best Corrected Visual Acuity |
| BOR | Best Overall Response |
| CBR | Clinical benefit rate |
| CDISC | Clinical Data Interchange Standards Consortium |
| CDISC | Clinical Data Interchange Standards Consortium |
| CI | Confidence Interval |
| CI | Confidence interval |
| CK-MB | Creatine kinase MB-isoenzyme |
| CL | Clearance |
| Cmax | Maximum observed plasma drug concentration |
| CPMS | Clinical Pharmacology Modelling & Simulation |
| CPMS | Clinical Pharmacology Modeling and Simulation |
| CR | Complete response |
| CR | Complete response |
| CRM | Continual Reassessment Method |
| CS | Clinical Statistics |
| CSR | Clinical Study Report |
| CTR | Clinical Trial Register |
| Ctrough | Concentration observed prior to the next dose |
| CVb / CVw | Coefficient of Variation (Between) / Coefficient of Variation (Within) |
| Cys-mcMMAF | Cysteine-maleimidocaproyl monomethyl auristatin F |
| DBF | Database Freeze |
| DBR | Database Release |
| DLT | Dose limiting toxicity |
| DOB | Date of Birth |
| DOR | Duration of response |
| DP | Decimal Places |
| ECOG | Eastern Cooperative Oncology Group |
| eCRF | Electronic Case Record Form |
| eDiary | Electronic Diary |
| EMA | European Medicines Agency |
| EOI | End of infusion |
| EORTC | European Organization for Research and Treatment of Cancer |
| EOT | Endo of treatment |
| FACTS | Fixed and adapted clinical trials simulator |

| Abbreviation | Description |
|---|---|
| FDA | Food and Drug Administration |
| FDAAA | Food and Drug Administration Clinical Results Disclosure Requirements |
| Fe(0-t) | Fraction of administered dose excreted in urine from dosing to time t |
| FLC | Free light chain |
| FTIH | First time in human |
| GSK | GlaxoSmithKline |
| IA | Interim Analysis |
| ICH | International Conference on Harmonization |
| IDMC | Independent Data Monitoring Committee |
| IDSL | Integrated Data Standards Library |
| IMMS | International Modules Management System |
| IMWG | International Myeloma Working Group |
| IOP | Intraocular Pressure |
| IP | Investigational Product |
| ITT | Intent-To-Treat |
| LDH | Lactate dehydrogenase |
| MM | Multiple Myeloma |
| MMAF | Monomethyl auristatin F |
| MMRM | Mixed Model Repeated Measures |
| MR | Minimal response |
| MRD | Minimal Residual Disease |
| MTD | Maximum Tolerated Dose |
| NCI-CTCAE | National Cancer Institute – Common Terminology Criteria for Adverse Events |
| N-CRM | A modification of the Continual Reassessment Method (CRM) proposed by Neuenschwander et al. |
| NEI-VFQ-25 | National Eye Institute Visual Functioning Questionnaire - 25 |
| NONMEM | Nonlinear mixed effects modelling |
| ORR | Overall response rate |
| OS | Overall survival |
| OSDI | Ocular Surface Disease Index |
| PACT | Post Analysis Continued Treatment |
| PCI | Potential Clinical Importance |
| PD | Pharmacodynamics |
| PD | Progressive disease |
| PDMP | 60 Plan |
| PET | Probability of early termination |
| PFS | Progression-free survival |
| PK | Pharmacokinetics |
| PopPK | Population PK |
| PP | Per Protocol |
| PR | Partial response |
| PRO-CTCAE | Patient-Reported Outcome Version of the Common Term Criteria for Adverse Events |

| Abbreviation | Description |
|---|---|
| QC | Quality Control |
| QLQ-C30 | Quality of Life Questionnaire 30-item Core module |
| QLQ-MY20 | Quality of Life Questionnaire 20-item Multiple Myeloma module |
| QoL | Quality of life |
| QTcB | Bazett's QT Interval Corrected for Heart Rate |
| QTcF | Fridericia's QT Interval Corrected for Heart Rate |
| RAMOS | Randomization & Medication Ordering System |
| RAP | Reporting & Analysis Plan |
| REML | Restricted maximum likelihood |
| Ro | Observed accumulation ratio |
| RP2 | Recommended Phase 2 |
| RRMM | Relapsed / refractory multiple myeloma |
| SAC | Statistical Analysis Complete |
| SAE | Serious adverse event |
| sBCMA | Soluble B-cell maturation antigen |
| sCR | Stringent complete response |
| SD | Stable disease |
| SDSP | Study Data Standardization Plan |
| SDTM | Study Data Tabulation Model |
| SOI | Start of infusion |
| SOP | Standard Operation Procedure |
| SPEP | Serum protein electrophoresis |
| SRT | Safety Review Team |
| t½ | Terminal phase half-life |
| TA | Therapeutic Area |
| TFL | Tables, Figures & Listings |
| tlast | Time of last quantifiable concentration |
| tmax | Time to maximum drug concentration |
| TTBR | Time to best response |
| TTP | Time to progression |
| TTR | Time to response |
| ULN | Upper limit of normal |
| UPEP | Urine protein electrophoresis |
| VGPR | Very good partial response |
| Vss | Volume of distribution at steady state |

### 15.12.2. Trademarks

| Trademarks of the GlaxoSmithKline Group of Companies |
|---|
| NONE |

| Trademarks not owned by the GlaxoSmithKline Group of Companies |
|---|
| East |
| NONMEM |
| SAS |
| WinNonlin |

# 15.13. Appendix 13: List of Data Displays

## 15.13.1. Data Display Numbering

The following numbering will be applied for RAP generated displays:

| Section | Tables | Figures |
|---|---|---|
| Study Population | 1.0010 to 1.xxxx | 1.0010 to 1.xxxx |
| Efficacy | 2.0010 to 2.xxxx | 2.0010 to 2.xxxx |
| Safety | 3.0010 to 3.xxxx | 3.0010 to 3.xxxx |
| Pharmacokinetic | 4.0010 to 4.xxxx | 4.0010 to 4.xxxx |
| Population Pharmacokinetic (PopPK) | 5.0010 to 5.xxxx | 5.0010 to 5.xxxx |
| Pharmacodynamic and / or Biomarker | 6.0010 to 6.xxxx | 6.0010 to 6.xxxx |
| Pharmacokinetic / Pharmacodynamic | 7.0010 to 7.xxxx | 7.0010 to 7.xxxx |
| Patient reported outcome | 8.0010 to 8.xxxx | 8.0010 to 8.xxxx |
| **Section** | **Listings** | |
| ICH Listings | 1.0010 to 1.xxxx | |
| Other Listings | 30.0010 to 30.xxxx | |

## 15.13.2. Mock Example Shell Referencing

Non IDSL specifications will be referenced as indicated and if required example mock-up displays provided in Appendix 14: Example Mock Shells for Data Displays.

| Section | Figure | Table | Listing |
|---|---|---|---|
| Study Population | POP_Fn | POP_Tn | POP_Ln |
| Efficacy | EFF_Fn | EFF_Tn | EFF_Ln |
| Safety | SAFE_Fn | SAFE_Tn | SAFE_Ln |
| Pharmacokinetic | PK_Fn | PK_Tn | PK_Ln |
| Population Pharmacokinetic (PopPK) | POPPK_Fn | POPPK_Tn | POPPK_Ln |
| Pharmacodynamic and / or Biomarker | PD_Fn | PD_Tn | PD_Ln |
| Pharmacokinetic / Pharmacodynamic | PKPD_Fn | PKPD_Tn | PK/PD_Ln |
| Patient reported outcome | PRO_Fn | PRO_Tn | PRO_Ln |

**NOTES:**

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

## 15.13.3. Deliverables

| Delivery [Priority] [1] | Description |
|---|---|
| IA [X] | Interim Analysis for IDMC |
| Headline [X] | Headline result for SAC |
| SAC [X] | Statistical Analysis Complete for [1] Primary Analysis and [2] End of Study analysis |

**NOTES:**

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

## 15.13.4. Study Population Tables

| Study Population Tables | | | | | |
|---|---|---|---|---|---|
| **No.** | **Population** | **IDSL / Example Shell** | **Title** | **Programming Notes** | **Deliverable [Priority]** |
| **Subject Disposition** | | | | | |
| 1.0010 | Full Analysis | ES8 | Summary of Subject Status and Reason for Study Withdrawal | ICH E3, FDAAA, EudraCT | IA [1], Headline, SAC [1],SAC [2] |
| 1.0020 | Full Analysis | SD4 | Summary of Treatment Status and Reasons for Discontinuation of Study Treatment | ICH E3 | IA [1], Headline, SAC [1] ,SAC [2] |
| 1.0030 | Screened | ES6 | Summary of Screening Status and Reasons for Screen Failure | Journal Requirements | SAC [1] |
| 1.0040 | Enrolled | NS1 | Summary of Number of Participants by Country and Site ID | EudraCT/Clinical Operations. | IA [1], SAC [1] |
| **Protocol Deviation** | | | | | |
| 1.0050 | Full Analysis | DV1 | Summary of Important Protocol Deviations | ICH E3 | SAC [1] ,SAC [2] |
| 1.0060 | Full Analysis | IE1 | Summary of Inclusion/Exclusion Criteria Deviations | | SAC [1] |
| **Population Analysed** | | | | | |
| 1.0070 | Enrolled | SP1 | Summary of Study Populations | IDSL. | Headline, SAC [1] |
| **Demographic and Baseline Characteristics** | | | | | |
| 1.0120 | Full Analysis | DM1 | Summary of Demographic Characteristics | ICH E3, FDAAA, EudraCT | IA [1], Headline, SAC [1] |
| 1.0121 | Evaluable | DM1 | Summary of Demographic Characteristics (Evaluable) | ICH E3, FDAAA, EudraCT | IA [1] |
| 1.0080 | Enrolled | DM11 | Summary of Age Ranges | EudraCT | SAC [1] |
| 1.0090 | Full Analysis | DM5 | Summary of Race and Racial Combinations | ICH E3, FDA, FDAAA, EudraCT | SAC [1] |

| Study Population Tables | | | | | |
|---|---|---|---|---|---|
| **No.** | **Population** | **IDSL / Example Shell** | **Title** | **Programming Notes** | **Deliverable [Priority]** |
| 1.0160 | Full Analysis | DC2 | Summary of Disease Characteristics at Screening | Include genetic characteristics | IA [1], Headline, SAC [1] |
| 1.0161 | Evaluable | DC2 | Summary of Disease Characteristics at Screening (Evaluable) | | IA [1] |
| 1.0100 | Full Analysis | DC1 | Summary of Disease Characteristics at Initial Diagnosis | | SAC [1] |
| **Prior and Concomitant Medications** | | | | | |
| 1.0110 | Full Analysis | MH1 | Summary of Current Medical Conditions | ICH E3 | SAC [1], ,SAC [2] |
| 1.0130 | Full Analysis | MH1 | Summary of Past Medical Conditions | ICH E3<br>Separate summaries for Current & Past conditions, if collected. | SAC [1] |
| 1.0210 | Full Safety | CM8 | Summary of Concomitant Medications | ICH E3 include 'medications taken on-treatment (including those started prior to treatment), and ''Medications that started on treatment' See Table 1.0210 produced by Veramed at IA) | IA [1], SAC [1] ,SAC [2] |
| 1.0140 | Full Safety | CM1 | Summary of Prophylactic Medication for Infusion-Related Reactions by Drug Class and Drug Name | Medication will be identified based on verbatim term, and the drug class will be based on the medication group in the excel file provided by Safety. | SAC [1] ,SAC [2] |
| 1.0150 | Full Safety | CM1 | Summary of Eye Medications by Drug Class and Drug Name | Medication will be identified based on verbatim term, and the drug class will be based on the medication group in the excel file provided by Safety. | SAC [1] |
| 1.0170 | Full Safety | Mock-up POP_T1 | Summary of Percentage of Duration of Exposure on Steroid Eye Drop Use | | SAC [1] |

| Study Population Tables | | | | | |
|---|---|---|---|---|---|
| **No.** | **Population** | **IDSL / Example Shell** | **Title** | **Programming Notes** | **Deliverable [Priority]** |
| **Prior and Follow-up Anti-Cancer Therapy** | | | | | |
| 1.0180 | Full Analysis | CM8 | Summary of Prior Dictionary Coded Anti-Cancer Therapy | | Headline, SAC [1] |
| 1.0190 | Full Analysis | programming note | Summary of Prior Anti-Cancer Therapy by Drug Class of Agents | See Table 1.0141 in BMA117159 (primary_01). | Headline, SAC [1] |
| 1.0200 | Full Analysis | programming note | Summary of Subjects Refractory to Prior Anti-Cancer Therapy by Drug Class of Agents | See Table 1.0151 in BMA117159 (primary_01). | Headline, SAC [1] |
| 1.0220 | Full Analysis | AC3 | Summary of Number of Prior Anti-Cancer Therapy Regimens | | IA [1], SAC [1] |
| 1.0230 | Full Analysis | AC4 | Summary of Best Response to Most Recent Prior Anti-Cancer Therapy | | SAC [1] |
| 1.0240 | Full Analysis | FAC1 | Summary of Follow-Up Anti-Cancer Therapy | | SAC [1] |
| **Prior Surgical Procedures** | | | | | |
| 1.0250 | Full Analysis | OSP2 | Summary of Prior Cancer and Non-Cancer Related Surgical Procedures | | SAC [1] |
| **Exposure and Treatment Compliance** | | | | | |
| 1.0300 | Full Safety | OEX5 | Summary of Exposure to GSK2857916 | ICH E3; by number of cycles, and included the summary of dose intensity (mg/kg per 3 weeks) | IA [1], Headline, SAC [1] ,SAC [2] |
| 1.0301 | Evaluable | OEX5 | Summary of Exposure to Study Treatment (Evaluable) | ICH E3; by number of cycles | IA [1] |
| 1.0260 | Full Safety | OEX1 | Summary of Duration of Exposure to GSK2857916 | Only include “Time on Study Treatment; Mean, median, SD, Min, Max of duration in weeks | Headline, SAC [1] ,SAC [2] |
| 1.0270 | Full Safety | OEX6 | Summary of Dose of GSK2857916 delivered by Cycle | | SAC [1] ,SAC [2] |

| Study Population Tables | | | | | |
|---|---|---|---|---|---|
| **No.** | **Population** | **IDSL / Example Shell** | **Title** | **Programming Notes** | **Deliverable [Priority]** |
| 1.0280 | Full Safety | ODMOD1 | Summary of Dose Reductions of GSK2857916 | | Headline, SAC [1] ,SAC [2] |
| 1.0290 | Full Safety | ODMOD3 | Summary of Dose Delays of GSK2857916 | | Headline, SAC [1] ,SAC [2] |
| 1.0310 | Full Safety | ODMOD5 | Summary of Primary Reason for Dose Reductions of GSK2857916 by Cycle | | SAC [1] ,SAC [2] |
| 1.0320 | Full Safety | ODMOD6 | Summary of Primary Reason for Dose Delays of GSK2857916 by Cycle | | SAC [1] ,SAC [2] |
| 1.11140 | Full Safety | OEX1 | Summary of Duration of Exposure to GSK2857916 by Response Category Based on Independent Reviewer-Assessed Response | | SAC [2] |
| **Duration of Follow-up** | | | | | |
| 1.0330 | Full Analysis | FAC2 | Summary of Duration of Follow-Up | | SAC [1] ,SAC [2] |
| **Blood and Blood Supportive Care Products** | | | | | |
| 1.0340 | Full Analysis | BP1A | Summary of Blood Products | | SAC [1] |
| 1.0350 | Full Analysis | BP1C | Summary of Blood Supportive Care Products | | SAC [1] |
| **Substance Use** | | | | | |
| 1.0360 | Full Analysis | SU1 | Summary of Substance Use | | SAC [1] |

## 15.13.5. Study Population Figures

| Study Population: Figures | | | | | |
|---|---|---|---|---|---|
| **No.** | **Population** | **IDSL / Example Shell** | **Title** | **Programming Notes** | **Deliverable [Priority]** |
| **Exposure** | | | | | |
| 1.0010 | Full Safety | programming note | Plot of Dose Reduction of GSK2857916 by Cycle | See Figure 11.0020 in BMA117159 (primary_01). | Headline, SAC [1] ,SAC [2] |
| 1.0020 | Full Safety | OEX12 | Plot of Duration of Study Treatment by Response | Split page by dose arm | SAC [1] ,SAC [2] |
| 1.00010 | Safety | Programming note | Graph of Kaplan Meier Curves of Time to Treatment Discontinuation by Response Category Based on Independent Reviewer-Assessed Response | Refer regqry_2020_10 | SAC [2] |
| 1.00011 | Safety | Programming note | Graph of Kaplan Meier Curves of Time to Treatment Discontinuation in Subjects Receiving at least 3 Cycles of GSK2857916 | Refer regqry_2020_10 | SAC [2] |
| 1.00013 | Safety | Programming note | Graph of Kaplan Meier Curves of Time to Treatment Discontinuation | Refer present_2020_04 | SAC [2] |
| **COVID-19** | | | | | |
| 1.0082 | Full Safety | PAN8 | Visits Impacted by COVID-19 Pandemic | | SAC [2] |

## 15.13.6. Efficacy Tables

| Efficacy: Tables | | | | | |
|---|---|---|---|---|---|
| **No.** | **Population** | **IDSL / Example Shell** | **Title** | **Programming Notes** | **Deliverable [Priority]** |
| **Response** | | | | | |
| 2.0010 | Full Analysis | RE1a | Summary of Independent Reviewer-Assessed Best Response with Confirmation | | Headline, SAC [1] ,SAC [2] |
| 2.0011 | Efficacy | RE1a | Summary of Independent Reviewer-Assessed Best Response with Confirmation | | Headline, SAC [1] ,SAC [2] |
| 2.0020 | Full Analysis | RE1a | Summary of Investigator-Assessed Best Response with Confirmation | | Headline, SAC [1] |
| 2.0021 | Efficacy | RE1a | Summary of Investigator-Assessed Best Response with Confirmation | | Headline, SAC [1] |
| 2.0030 | Evaluable | RE1a | Summary of Investigator-Assessed Best Response for Interim Futility Analyses | | IA [1] |
| 2.0040 | Full Analysis | Mock up EFF_T1 | Summary of MRD Negativity Rate by Best Response | MRD negativity will be based on test result with sensitivity of 10^5. | SAC [1] ,SAC [2] |
| 2.0050 | Full Analysis | RE3 | Summary of Independent Reviewer-Assessed and Investigator-Assessed Best Response with Confirmation | The response categories are: sCR, CR, VGPR, PR, MR, SD, PD, NE. One Table for 2.5mg, and one Table for 3.4mg | SAC [1] |
| **Time-to-Event** | | | | | |
| 2.0060 | Full Analysis | TTE1a | Summary of Duration of Response Based on Independent Reviewer-Assessed Response | | Headline, SAC [1],SAC [2] |
| 2.0061 | Efficacy | TTE1a | Summary of Duration of Response Based on Independent Reviewer-Assessed Response | | Headline, SAC [1],SAC [2] |

| Efficacy: Tables | | | | | |
|---|---|---|---|---|---|
| **No.** | **Population** | **IDSL / Example Shell** | **Title** | **Programming Notes** | **Deliverable [Priority]** |
| 2.0062 | Full Analysis | TTE1a | Summary of Duration of Response Based on Independent Reviewer - Assessed Response II | Include probability of Maintaining Response at different time points, and Hazard ratio estimated by Pike estimator. | SAC [2] |
| 2.0070 | Full Analysis | TTE1a | Summary of Duration of Response Based on Investigator-Assessed Response | | Headline, SAC [1] |
| 2.0071 | Efficacy | TTE1a | Summary of Duration of Response Based on Investigator-Assessed Response | | Headline, SAC [1] |
| 2.0080 | Full Analysis | TTE1a | Summary of Progression-Free Survival Based on Independent Reviewer-Assessed Response | Include the estimated PFS probability at Month 6. | Headline, SAC [1], SAC [2] |
| 2.0090 | Full Analysis | TTE1a | Summary of Progression-Free Survival Based on Investigator-Assessed Response | | Headline, SAC [1] |
| 2.0100 | Full Analysis | TTE1a | Summary of Time to Progression Based on Independent Reviewer-Assessed Response | | SAC [1], SAC [2] |
| 2.0110 | Full Analysis | TTE1a | Summary of Time to Progression Based on Investigator-Assessed Response | | SAC [1] |
| 2.0120 | Full Analysis | TTE1a | Summary of Time to Response Based on Independent Reviewer-Assessed Response | Among responders only | SAC [1], SAC [2] |
| 2.0121 | Efficacy | TTE1a | Summary of Time to Response Based on Independent Reviewer-Assessed Response | Among responders only | SAC [1], SAC [2] |
| 2.0130 | Full Analysis | TTE1a | Summary of Time to Response Based on Investigator-Assessed Response | Among responders only | SAC [1] |
| 2.0131 | Efficacy | TTE1a | Summary of Time to Response Based on Investigator-Assessed Response | Among responders only | SAC [1] |

| Efficacy: Tables | | | | | |
|---|---|---|---|---|---|
| **No.** | **Population** | **IDSL / Example Shell** | **Title** | **Programming Notes** | **Deliverable [Priority]** |
| 2.0140 | Full Analysis | Mock up EFF_T2 | Summary of Reasons for Censoring | | SAC [1] |
| 2.0150 | Full Analysis | TTE1a | Summary of Overall Survival | Include the estimated overall survival probability at Month 6 at primary analysis; add estimated overall survival probability at Month 12 at 90D Safety Update. | SAC [1], SAC [2] |
| 2.0160 | Full Analysis | TTE1a | Summary of Duration of MRD Negativity | MRD negativity will be based on test result with sensitivity of 10^5.Pending on amount of data available | SAC [1] |
| 2.0170 | Full Analysis | Programming note | Response, Adverse Events, and Dose Modifications by Dose Level | Use Table S4 in manuscript (https://ars.els-cdn.com/content/image/1-s2.0-S147020451830576X-mmc1.pdf) for BMA117159 as mock-up. | Headline, SAC [1] |
| 2.10010 | ITT | TTE1a | Summary of Time to Best Response Based on Independent Reviewer - Assessed Response | | SAC [2] |
| 2.10040 | ITT | TTE1a | Summary of Progression-Free Survival by Response Category Based on Independent Reviewer-Assessed Response | | SAC [2] |
| 2.10041 | FSAFL | TTE1a | Summary of Progression-Free Survival by Response Category Based on Independent Reviewer-Assessed Response | | SAC [2] |
| 2.10050 | ITT | TTE1a | Summary of Overall Survival by Response Category Based on Independent Reviewer-Assessed Response | | SAC [2] |

## 15.13.7. Efficacy Figures

| Efficacy: Figures | | | | | |
|---|---|---|---|---|---|
| **No.** | **Population** | **IDSL / Example Shell** | **Title** | **Programming Notes** | **Deliverable [Priority]** |
| **Response** | | | | | |
| 2.0010 | ITT | Programming note | Forest Plot - Overall Response Rate (ORR) Based on Independent Reviewer-Assessed Response | Similar to Figure 12.012 in BMA117159 (primary_01). See Section 5.3.2 for the subgroups to be included. | Headline, SAC [1], SAC [2] |
| 2.0020 | ITT | Programming note | Forest Plot - Overall Response Rate (ORR) Based on Investigator-Assessed Response | Similar to Figure 12.012 in BMA117159 (primary_01). See Section 5.3.2 for the subgroups to be included. | Headline, SAC [1] |
| 2.0030 | Full Analysis | RE8b | Percent Change at Maximum Reduction from Baseline in M-Protein (or FLC) Measurement | | Headline, SAC [1] |
| **Time-to-Event** | | | | | |
| 2.0040 | ITT | TTE10 | Graph of Kaplan Meier Curves of Duration of Response Based on Independent Reviewer-Assessed Response | | Headline, SAC [1], SAC [2] |
| 2.0041 | Efficacy | TTE10 | Graph of Kaplan Meier Curves of Duration of Response Based on Independent Reviewer-Assessed Response | | Headline, SAC [1], SAC [2] |
| 2.0050 | ITT | TTE10 | Graph of Kaplan Meier Curves of Duration of Response Based on Investigator-Assessed Response | | Headline, SAC [1] |
| 2.0051 | Efficacy | TTE10 | Graph of Kaplan Meier Curves of Duration of Response Based on Investigator-Assessed Response | | Headline, SAC [1] |
| 2.0060 | ITT | TTE10 | Graph of Kaplan Meier Curves of Progression-Free Survival Based on Independent Reviewer-Assessed Response | | Headline, SAC [1], SAC [2] |
| 2.0070 | ITT | TTE10 | Graph of Kaplan Meier Curves of Progression-Free Survival Based on Investigator-Assessed Response | | Headline, SAC [1] |
| 2.0080 | ITT | TTE10 | Graph of Kaplan Meier Curves of Time to Progression Based on Independent Reviewer-Assessed Response | | SAC [1], SAC [2] |

| Efficacy: Figures | | | | | |
|---|---|---|---|---|---|
| **No.** | **Population** | **IDSL / Example Shell** | **Title** | **Programming Notes** | **Deliverable [Priority]** |
| 2.0090 | ITT | TTE10 | Graph of Kaplan Meier Curves of Time to Progression Based on Investigator-Assessed Response | | SAC [1] |
| 2.0100 | ITT | TTE10 | Graph of Kaplan Meier Curves of Overall Survival | | SAC [1], SAC [2] |
| 2.00402 | ITT | Programming note | Graph of Kaplan Meier Curves of Duration of Response by Dose Delay Category Based on Independent Reviewer - Assessed Response | Refer regqry_2020_10 | SAC [2] |
| 2.10010 | ITT | Programming note | Graph of Kaplan Meier Curves of Progression-Free Survival by Response Category Based on Independent Reviewer-Assessed Response | Refer regqry_2020_10 | SAC [2] |
| 2.10020 | ITT | Programming note | Graph of Kaplan Meier Curves of Overall Survival by Response Category Based on Independent Reviewer-Assessed Response | Refer regqry_2020_10 | SAC [2] |
| 2.10080 | ITT | Programming note | Graph of Kaplan Meier Curves of Duration of Response by Response Category Based on Independent Reviewer-Assessed Response | Refer regqry_2020_10 | SAC [2] |
| 2.30305 | Full Safety | Programming note | Profile Plot of Patients with Corneal Events (GSK Scale) | Refer present_2020_04 | SAC [2] |
| 2.70033 | ITT | Programming note | Swim-lane Plot of Duration of Study Treatment for Responder Based on Independent Reviewer-Assessed Response | Refer regqry_2020_10 | SAC [2] |

## 15.13.8. Safety Tables

| Safety: Tables | | | | | |
|---|---|---|---|---|---|
| **No.** | **Population** | **IDSL / Example Shell** | **Title** | **Programming Notes** | **Deliverable [Priority]** |
| **Adverse Events (AEs)** | | | | | |
| 3.0010 | Full Safety | AE13 | Adverse Event Overview | Compared to what was delivered at IA, add two more categories: Grade 3&4 AEs, Grade 3&4 AEs related to study treatment, | IA [1], Headline, SAC [1] , SAC [2] |
| 3.0011 | Evaluable | AE13 | Adverse Event Overview (Evaluable) | | IA [1] |
| 3.0020 | Full Safety | AE1 | Summary of All Adverse Events by System Organ Class and Preferred Term | ICH E3<br>See version created at IA | IA [1], SAC [1] , SAC [2] |
| 3.0030 | Full Safety | AE3 | Summary of All Adverse Events by Preferred Term | | SAC [1] |
| 3.0040 | Full Safety | OAE07 | Summary of All Adverse Events by Preferred Term and Maximum Grade | | IA [1], Headline, SAC [1] , SAC [2] |
| 3.0041 | Evaluable | OAE07 | Summary of All Adverse Events by Preferred Term and Maximum Grade (Evaluable) | | IA [1] |
| 3.0050 | Full Safety | AE3 | Summary of Common (>=5%) Adverse Events by Preferred Term | ICH E3 | SAC [1] |
| 3.0060 | Full Safety | AE3 | Summary of Common (>=5%) Grade 2-4 Adverse Events by Preferred Term | ICH E3 | SAC [1] |
| 3.0070 | Full Safety | AE1 | Summary All Drug-Related Adverse Events by System Organ Class and Preferred Term | ICH E3 | SAC [1] |
| 3.0080 | Full Safety | OAE07 | Summary of All Drug-Related Adverse Events by Preferred Term and Maximum Grade | | SAC [1] |

| Safety: Tables | | | | | |
|---|---|---|---|---|---|
| **No.** | **Population** | **IDSL / Example Shell** | **Title** | **Programming Notes** | **Deliverable [Priority]** |
| 3.0090 | Full Safety | AE15 | Summary of Common (>=5%) Non-serious Adverse Events by System Organ Class and Preferred Term (Number of Participants and Occurrences) | FDAAA, EudraCT | SAC [1] |
| 3.0100 | Full Safety | AE3 | Summary of Common (>=5%) Drug-Related Grade 2-4 Adverse Events by Preferred Term | ICH E3 | SAC [1] , SAC [2] |
| 3.0110 | Full Safety | AE3 | Summary of Adverse Events of Maximum Grade 3 or Higher by Preferred Term | | Headline, SAC [1] , SAC [2] |
| 3.0560 | Full Safety | AE6 | Summary of Cumulative Incidence of Adverse Events by PT and Number of Doses Received at First Occurrence | Only PT term, no SOC needed. The number of doses received at first occurrence will be <= 1, <= 2, <= 4, <= 6, <= 8, <= 10, and Any | SAC [1] |
| 3.0570 | Full Safety | AE3 | Summary of Non-Serious Drug-related Adverse Events by Preferred Term | | SAC [1] |
| **Serious and Other Significant Adverse Events** | | | | | |
| 3.0120 | Full Safety | AE16 | Summary of Serious Adverse Events by System Organ Class and Preferred Term (Number of Participants and Occurrences) | FDAAA, EudraCT | IA [1], SAC [1] |
| 3.0580 | Full Safety | AE3 | Summary of Serious Adverse Events by Preferred Term | | Headline, SAC [1],SAC [2] |
| 3.0130 | Full Safety | AE3 | Summary of Adverse Events Leading to Permanent Discontinuation of Study Treatment by Preferred Term | | IA [1], Headline, SAC [1] , SAC [2] |
| 3.0140 | Full Safety | AE3 | Summary of All Serious Drug-Related Adverse Events by Preferred Term | | SAC [1] , SAC [2] |
| 3.0150 | Full Safety | AE3 | Summary of Adverse Events Leading to Dose Reduction by Preferred Term | | Headline, SAC [1] , SAC [2] |

| Safety: Tables | | | | | |
|---|---|---|---|---|---|
| **No.** | **Population** | **IDSL / Example Shell** | **Title** | **Programming Notes** | **Deliverable [Priority]** |
| 3.0160 | Full Safety | AE3 | Summary of Adverse Events Leading to Dose Delays by Preferred Term | | Headline, SAC [1] , SAC [2] |
| 3.0830 | Full Safety | AE6 | Summary of Cumulative Incidence of Serious Adverse Events by PT and Number of Doses Received at First Occurrence | Only PT term, no SOC needed. The number of doses received at first occurrence will be <= 1, <= 2, <= 4, <= 6, <= 8, <= 10, and Any | SAC [1] ,SAC [2] |
| **AEs of Special Interest** | | | | | |
| 3.0170 | Full Safety | OAE07 | Summary of Keratopathy Events (CTCAE) by Preferred Term and Maximum Grade | Table need to be created only if the observed incidence rate >= 10% in 3.4 mg/kg Frozen liquid cohort. | SAC [1] , SAC [2] |
| 3.0171 | Evaluable | OAE07 | Summary of Dry Eye Events (CTCAE) by Preferred Term and Maximum Grade (Evaluable) | Table need to be created only if the observed incidence rate >= 10% in 3.4 mg/kg Frozen liquid cohort. | SAC [1] , SAC [2] |
| 3.0172 | Full Safety | OAE07 | Summary of Blurred Vision Event (CTCAE) by Preferred Term and Maximum Grade | Table need to be created only if the observed incidence rate >= 10% in 3.4 mg/kg Frozen liquid cohort. | SAC [1] , SAC [2] |
| 3.0173 | Full Safety | OAE07 | Summary of Photophobia Event (CTCAE) by Preferred Term and Maximum Grade | Table need to be created only if the observed incidence rate >= 10% in 3.4 mg/kg Frozen liquid cohort. | SAC [1] |
| 3.0174 | Full Safety | OAE07 | Summary of Eye Pain Event (CTCAE) by Preferred Term and Maximum Grade | Table need to be created only if the observed incidence rate >= 10% in 3.4 mg/kg Frozen liquid cohort. | SAC [1] |
| 3.0180 | Full Safety | ESI1 | Summary of Characteristics of Keratopathy Events (CTCAE) | Table need to be created only if the observed incidence rate >= 10% in 3.4 mg/kg Frozen liquid cohort. Include summary of outcome of AE. | SAC [1] , SAC [2] |

| Safety: Tables | | | | | |
|---|---|---|---|---|---|
| **No.** | **Population** | **IDSL / Example Shell** | **Title** | **Programming Notes** | **Deliverable [Priority]** |
| 3.0181 | Full Safety | ESI1 | Summary of Characteristics of Dry Eye Events (CTCAE) | Table need to be created only if the observed incidence rate >= 10% in 3.4 mg/kg Frozen liquid cohort. Include summary of outcome of AE | SAC [1] , SAC [2] |
| 3.0182 | Full Safety | ESI1 | Summary of Characteristics of Blurred Vision Events (CTCAE) | Table need to be created only if the observed incidence rate >= 10% in 3.4 mg/kg Frozen liquid cohort. Include summary of outcome of AE | SAC [1] , SAC [2] |
| 3.0183 | Full Safety | ESI1 | Summary of Characteristics of Photophobia Events (CTCAE) | Table need to be created only if the observed incidence rate >= 10% in 3.4 mg/kg Frozen liquid cohort. Include summary of outcome of AE | SAC [1] |
| 3.0184 | Full Safety | ESI1 | Summary of Characteristics of Eye Pain Events (CTCAE) | Table need to be created only if the observed incidence rate >= 10% in 3.4 mg/kg Frozen liquid cohort. Include summary of outcome of AE | SAC [1] |
| 3.0200 | Full Safety | Mock-up SAFE_T21 | Summary of Keratopathy Events (CTCAE) Characteristics II | Table need to be created only if the observed incidence rate >= 10% in 3.4 mg/kg Frozen liquid cohort. | SAC [1] |
| 3.0201 | Full Safety | Mock-up SAFE_T21 | Summary of Dry Eye Events (CTCAE) Characteristics II | Table need to be created only if the observed incidence rate >= 10% in 3.4 mg/kg Frozen liquid cohort. | SAC [1] , SAC [2] |
| 3.0202 | Full Safety | Mock-up SAFE_T21 | Summary of Blurred Vision Events (CTCAE) Characteristics II | Table need to be created only if the observed incidence rate >= 10% in 3.4 mg/kg Frozen liquid cohort. | SAC [1], SAC [2] |
| 3.0203 | Full Safety | Mock-up SAFE_T21 | Summary of Photophobia Events (CTCAE) Characteristics II | Table need to be created only if the observed incidence rate >= 10% in 3.4 mg/kg Frozen liquid cohort. | SAC [1] |

| Safety: Tables | | | | | |
|---|---|---|---|---|---|
| **No.** | **Population** | **IDSL / Example Shell** | **Title** | **Programming Notes** | **Deliverable [Priority]** |
| 3.0204 | Full Safety | Mock-up SAFE_T21 | Summary of Eye Pain Events (CTCAE) Characteristics II | Table need to be created only if the observed incidence rate >= 10% in 3.4 mg/kg Frozen liquid cohort. | SAC [1] |
| 3.0250 | Full Safety | AE13 | Overview of Eye Disorder (CTCAE) | Same categories as AE overview | SAC [1] , SAC [2] |
| 3.0251 | Full Safety | AE13 | Overview of Keratopathy Event (CTCAE) | Table need to be created only if the observed incidence rate >= 10% in 3.4 mg/kg Frozen liquid cohort. Same categories as AE overview | SAC [1], , SAC [2] |
| 3.0252 | Full Safety | AE13 | Overview of Dry Eye Event (CTCAE) | Table need to be created only if the observed incidence rate >= 10% in 3.4 mg/kg Frozen liquid cohort. Same categories as AE overview | SAC [1], , SAC [2] |
| 3.0253 | Full Safety | AE13 | Overview of Blurred Vision Event (CTCAE) | Table need to be created only if the observed incidence rate >= 10% in 3.4 mg/kg Frozen liquid cohort. Same categories as AE overview | SAC [1] , SAC [2] |
| 3.0250 | Full Safety | AE13 | Overview of Photophobia Event (CTCAE) | Table need to be created only if the observed incidence rate >= 10% in 3.4 mg/kg Frozen liquid cohort. Same categories as AE overview | SAC [1] |
| 3.0250 | Full Safety | AE13 | Overview of Eye Pain Event (CTCAE) | Table need to be created only if the observed incidence rate >= 10% in 3.4 mg/kg Frozen liquid cohort. Same categories as AE overview | SAC [1] |
| 3.1320 | Full Safety | Mock-up SAFE_T22 | Summary of Percentage of Duration of Exposure with Keratopathy Events (CTCAE) | Table need to be created only if the observed incidence rate >= 10% in 3.4 mg/kg Frozen liquid cohort. | SAC [1], SAC [2] |

| Safety: Tables | | | | | |
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| **No.** | **Population** | **IDSL / Example Shell** | **Title** | **Programming Notes** | **Deliverable [Priority]** |
| 3.1321 | Full Safety | Mock-up SAFE_T22 | Summary of Percentage of Duration of Exposure with Dry Eye Events (CTCAE) | Table need to be created only if the observed incidence rate >= 10% in 3.4 mg/kg Frozen liquid cohort. | SAC [1], SAC [2] |
| 3.1322 | Full Safety | Mock-up SAFE_T22 | Summary of Percentage of Duration of Exposure with Blurred Vision Events (CTCAE) | Table need to be created only if the observed incidence rate >= 10% in 3.4 mg/kg Frozen liquid cohort. | SAC [1], SAC [2] |
| 3.1323 | Full Safety | Mock-up SAFE_T22 | Summary of Percentage of Duration of Exposure with Photophobia Events (CTCAE) | Table need to be created only if the observed incidence rate >= 10% in 3.4 mg/kg Frozen liquid cohort. | SAC [1] |
| 3.1324 | Full Safety | Mock-up SAFE_T22 | Summary of Percentage of Duration of Exposure with Eye Pain Events (CTCAE) | Table need to be created only if the observed incidence rate >= 10% in 3.4 mg/kg Frozen liquid cohort. | SAC [1] |
| 3.0270 | Full Safety | OAE07 | Summary of Thrombocytopenia by Preferred Term and Maximum Grade | | IA [1], SAC [1] , SAC [2] |
| 3.0271 | Evaluable | OAE07 | Summary of Thrombocytopenia by Preferred Term and Maximum Grade (Evaluable) | | IA [1] |
| 3.0280 | Full Safety | ESI1 | Summary of Characteristics of Thrombocytopenia | Include summary outcome of AE; | IA [1], SAC [1] , SAC [2] |
| 3.0290 | Full Safety | ESI2b | Summary of Onset and Duration of the First Occurrence of Thrombocytopenia | Algorithm of duration calculation need to be updated to follow what was done in T3.1171 in 117159 (Primary_02). | IA [1], SAC [1], SAC [2] |
| 3.0300 | Full Safety | OAE07 | Summary of Infusion-Related Reactions by Preferred Term and Maximum Grade | | IA [1], Headline, SAC [1] ], SAC [2] |
| 3.0301 | Evaluable | OAE07 | Summary of Infusion-Related Reactions by Preferred Term and Maximum Grade (Evaluable) | | IA [1] |

| Safety: Tables | | | | | |
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| **No.** | **Population** | **IDSL / Example Shell** | **Title** | **Programming Notes** | **Deliverable [Priority]** |
| 3.0320 | Full Safety | ESI1 | Summary of Characteristics of Infusion-Related Reactions | Include summary of outcome of AE; | IA [1], Headline, SAC [1] ], SAC [2] |
| 3.0330 | Full Safety | ESI2b | Summary of Onset and Duration of the First Occurrence of Infusion-Related Reactions | Algorithm of duration calculation need to be updated to follow what was done in T3.1171 in 117159 (Primary_02). | IA [1], Headline, SAC [1],SAC [2] |
| 3.0870 | Full Safety | OAE07 | Summary of Neutropenia by Preferred Term and Maximum Grade | | IA [1], SAC [1] ,SAC [2] |
| 3.0880 | Full Safety | ESI1 | Summary of Characteristics of Neutropenia | Include summary of outcome of AE; | IA [1], SAC [1] ,SAC [2] |
| 3.0890 | Full Safety | ESI2b | Summary of Onset and Duration of the First Occurrence of Neutropenia | Algorithm of duration calculation need to be updated to follow what was done in T3.1171 in 117159 (Primary_02). | IA [1], SAC [1] ,SAC [2] |
| 3.0900 | Full Safety | AE13 | Corneal Event (GSK Scale) Overview | including n (%) of subjects with any event IGSK scale), event related to study treatment, Grade 3&4 AEs, Grade 3&4 AEs related to study treatment, event leading to permanent discontinuation of study treatment, event leading to dose reductions, event leading to dose delays | Headline, SAC [1] ,SAC [2] |
| 3.0340 | Full Safety | Mock-up SAFE_T1 | Summary of Corneal Events (GSK Scale) by Grade and Visit | Add footnote that Visits 'Cycle 1-4 Day 1/Day 10' are from ocular sub-study subjects only. | SAC [1], SAC [2] |
| 3.0350 | Full Safety | ESI1 | Summary of Characteristics of Corneal Events (GSK Scale) | Include summary of outcome of AE; | Headline, SAC [1] , SAC [2] |

| Safety: Tables | | | | | |
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| **No.** | **Population** | **IDSL / Example Shell** | **Title** | **Programming Notes** | **Deliverable [Priority]** |
| 3.0360 | Full Safety | ESI2b | Summary of Onset and Duration of the First Occurrence of Corneal Events (GSK Scale) of Grade 3 or Above | Algorithm of duration calculation need to be updated to follow what was done in T3.1171 in 117159 (Primary_02). | SAC [1] , SAC [2] |
| 3.0910 | Full Safety | ESI2b | Summary of Onset and Duration of the First Occurrence of Corneal Events (GSK Scale) of Grade 2 or Above | Algorithm of duration calculation need to be updated to follow what was done in T3.1171 in 117159 (Primary_02). | Headline, SAC [1] ,SAC [2] |
| 3.0911 | Full Safety | Mock-up SAFE_T21 | Summary of Characteristics II of Corneal Events (GSK Scale) of Grade 2 or Above | | SAC [1] ,SAC [2] |
| 3.0912 | Full Safety | Mock-up SAFE_T21 | Summary of Characteristics II of Visual Acuity (GSK Scale) of Grade 2 or Above | | SAC [1] ,SAC [2] |
| 3.0370 | Full Safety | Mock-up SAFE_T2a | Summary of Corneal Events (GSK Scale) Leading to Action Taken with Study Treatment | | SAC [1] , SAC [2] |
| 3.0380 | Full Safety | Mock-up SAFE_T2 | Summary of Action Taken with Study Treatment for Corneal Events (GSK Scale) by Visit | No need to include EOT visit. Add footnote that Visits 'Cycle 1-4 Day 1/Day 10' are from ocular sub-study subjects only. | SAC [1] , SAC [2] |
| 3.0410 | Full Safety | Mock-up SAFE_T3 | Shift in Grade of Corneal Events (GSK Scale) from EOT to Last Follow-Up | | SAC [1] , SAC [2] |
| 3.0420 | Full Safety | Mock-up SAFE_T4a | Summary of resolution in Grade of Corneal Events (GSK Scale) from EOT to last Follow-Up. | | SAC [1] , SAC [2] |
| 3.0430 | Full Safety | Mock-up SAFE_T4b | Summary of Time to Re-initiation of Study Treatment Post Treatment Delay due to Corneal Events (GSK Scale) | | SAC [1] , SAC [2] |
| 3.0440 | Evaluable | Programming note | Summary of Worst Post-Baseline Corneal Findings (GSK Scale) Evaluable | This table was already produced by Veramed at IA | IA [1] |

| Safety: Tables | | | | | |
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| **No.** | **Population** | **IDSL / Example Shell** | **Title** | **Programming Notes** | **Deliverable [Priority]** |
| 3.0441 | Full Safety | Programming note | Summary of Worst Post-Baseline Corneal Events (GSK Scale) | Could also use T3.0440 produced by Veramed at IA as template. | SAC [1] |
| 3.0920 | Full Safety | Programming note | Summary of Worst Post-Baseline Corneal Events (GSK Scale) by Best Response Based on Independent Review Committee | Best Response categories: (PR/VGPR/CR/sCR vs. otherwise). Could also use T3.0440 produced by Veramed at IA as template. | SAC [1] ,SAC [2] |
| 3.1330 | Full Safety | Mock-up SAFE_T22 | Summary of Percentage of Duration of Exposure with Corneal Events (GSK scale) Grade >= 2 | | SAC [1], SAC [2] |
| 3.1331 | Full Safety | Mock-up SAFE_T22 | Summary of Percentage of Duration of Exposure with Corneal Events (GSK scale) Grade >= 3 | | SAC [1], SAC [2] |
| 3.0950 | Full Safety | AE6 | Summary of Cumulative Incidence of Keratopathy Event (CTCAE) by PT and Number of Doses Received at First Occurrence | Only PT term, no SOC needed. The number of doses received at first occurrence will be <= 1, <= 2, <= 4, <= 6, <= 8, <= 10, and Any | SAC [1] ,SAC [2] |
| 3.0951 | Full Safety | AE6 | Summary of Cumulative Incidence of Dry Eye Event (CTCAE) by PT and Number of Doses Received at First Occurrence | Only PT term, no SOC needed. The number of doses received at first occurrence will be <= 1, <= 2, <= 4, <= 6, <= 8, <= 10, and Any | SAC [1] ,SAC [2] |
| 3.0952 | Full Safety | AE6 | Summary of Cumulative Incidence of Blurred Vision Event (CTCAE) by PT and Number of Doses Received at First Occurrence | Only PT term, no SOC needed. The number of doses received at first occurrence will be <= 1, <= 2, <= 4, <= 6, <= 8, <= 10, and Any | SAC [1] ,SAC [2] |
| 3.0953 | Full Safety | AE6 | Summary of Cumulative Incidence of Photophobia Event (CTCAE) by PT and Number of Doses Received at First Occurrence | Only PT term, no SOC needed. The number of doses received at first occurrence will be <= 1, <= 2, <= 4, <= 6, <= 8, <= 10, and Any | SAC [1] |

| Safety: Tables | | | | | |
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| **No.** | **Population** | **IDSL / Example Shell** | **Title** | **Programming Notes** | **Deliverable [Priority]** |
| 3.0954 | Full Safety | AE6 | Summary of Cumulative Incidence of Eye Pain Event (CTCAE) by PT and Number of Doses Received at First Occurrence | Only PT term, no SOC needed. The number of doses received at first occurrence will be <= 1, <= 2, <= 4, <= 6, <= 8, <= 10, and Any | SAC [1] |
| 3.0960 | Full Safety | AE6 | Summary of Cumulative Incidence of Thrombocytopenia by PT and Number of Doses Received at First Occurrence | Only PT term, no SOC needed. The number of doses received at first occurrence will be <= 1, <= 2, <= 4, <= 6, <= 8, <= 10, and Any | SAC [1] ,SAC [2] |
| 3.0990 | Full Safety | AE6 | Summary of Cumulative Incidence of Neutropenia by PT and Number of Doses Received at First Occurrence | Only PT term, no SOC needed. The number of doses received at first occurrence will be <= 1, <= 2, <= 4, <= 6, <= 8, <= 10, and Any | SAC [1] ,SAC [2] |
| 3.1030 | Full Safety | AE6 | Summary of Cumulative Incidence of Infusion-Related Reactions by PT and Number of Doses Received at First Occurrence | Only PT term, no SOC needed. The number of doses received at first occurrence will be <= 1, <= 2, <= 4, <= 6, <= 8, <= 10, and Any | SAC [1], ,SAC [2] |
| 3.1210 | Full Safety | Mock-up SAFE_T1a | Summary of Cumulative Incidence of Corneal Events (GSK Scale) by Grade and Number of Doses Received at First Occurrence | | SAC [1] ,SAC [2] |
| 3.12030 | Full Safety | ESI2b | Summary of Blurred Vision and Dry Eye Events versus GSK Scale | | SAC [2] |
| 3.1280 | Safety | Mock-up SAFE_T5 | Logistic Regression Analysis of Possible Risk Factors for Developing Corneal Events Grade >=2 (GSK Scale) | See Section 8.2.2 Item 9 for details. | SAC [1], SAC [2] |
| 3.1290 | Full Safety | Mock-up SAFE_T11 | Summary of Thrombocytopenia and Bleeding Event | | SAC [1], SAC [2] |

| Safety: Tables | | | | | |
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| **No.** | **Population** | **IDSL / Example Shell** | **Title** | **Programming Notes** | **Deliverable [Priority]** |
| 3.12461 | Full Safety | OAE07 | Summary of Eye Disorder Events (CTCAE) with Dose Delays by Preferred Term and Maximum Grade | | SAC [2] |
| 3.12471 | Full Safety | Programming note | Summary of Ocular Symptoms and Visual Acuity Change (GSK Scale) by Worst Grade of Keratopathy | Refer regqry_2020_10 | SAC [2] |
| 3.12472 | Full Safety | Programming note | Summary of Ocular Symptoms and Visual Acuity Change (GSK Scale) by Worst Grade of Corneal Events (GSK Scale) | Refer regqry_2020_10 | SAC [2] |
| 3.12473 | Full Safety | Programming note | Summary of Ocular Symptoms and Visual Acuity Change (>=2 lines in Better Eye) by Worst Grade of Corneal Exam Finding | Refer regqry_2020_10 | SAC [2] |
| 3.12480 | Full Safety | OAE07 | Summary of Eye Disorder Events (CTCAE) Leading to Dose Delays by Preferred Term and Maximum Grade | Refer regqry_2020_04 | SAC [2] |
| 3.12490 | Full Safety | Programming note | Summary of Subjects with Dose Delay due to Eye Disorder Events (CTCAE) at the Time of Data Cutoff | Refer regqry_2020_04 | SAC [2] |
| 3.12731 | Full Safety | Programming note | Summary of Vision Blurred, and Dry Eye by Preferred Term in Subjects with Keratopathy | Refer regqry_2020_08 | SAC [2] |
| 3.12735 | Full Safety | Programming note | Summary of Vision Blurred, and Dry Eye by Preferred Term and Maximum Grade in Subjects with Keratopathy | Refer regqry_2020_08 | SAC [2] |
| 3.12737 | Full Safety | Programming note | Summary of Ocular Symptoms (CTCAE) by Preferred Term and Maximum Grade in Subjects with Keratopathy | Refer regqry_2020_10 | SAC [2] |

| Safety: Tables | | | | | |
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| **No.** | **Population** | **IDSL / Example Shell** | **Title** | **Programming Notes** | **Deliverable [Priority]** |
| 3.12738 | Full Safety | Programming note | Summary of Ocular Symptoms (CTCAE) by Preferred Term and Maximum Grade | Refer regqry_2020_08 | SAC [2] |
| 3.12751 | Full Safety | Programming note | Summary of Blurred Vision and Dry Eye Events versus Keratopathy | Refer regqry_2020_08 | SAC [2] |
| 3.12753 | Full Safety | Programming note | Summary of Ocular Symptoms (CTCAE) versus Keratopathy | Refer regqry_2020_08 | SAC [2] |
| 3.12761 | Full Safety | Programming note | Summary of Duration of Keratopathy with Concurrent Blurred Vision or Dry Eye | Refer regqry_2020_08 | SAC [2] |
| 3.12763 | Full Safety | Programming note | Summary of Duration of Keratopathy with Concurrent Ocular Symptoms (CTCAE) | Refer regqry_2020_08 | SAC [2] |
| 3.12770 | Full Safety | Programming note | Summary of GSK scale Events Characteristics II | Refer regqry_2020_10 | SAC [2] |
| 3.12771 | Full Safety | Programming note | Summary of Corneal Exam Finding (GSK scale) Characteristics II | Refer regqry_2020_10 | SAC [2] |
| 3.12772 | Full Safety | Programming note | Summary of Visual Acuity Change (GSK scale) Characteristics II | Refer regqry_2020_10 | SAC [2] |
| 3.12773 | Full Safety | Programming note | Summary of Maximum Grade for Corneal Exam Finding (GSK scale) | Refer regqry_2020_10 | SAC [2] |
| 3.12774 | Full Safety | Programming note | Summary of Maximum Grade for Visual Change (GSK scale) | Refer regqry_2020_10 | SAC [2] |

| Safety: Tables | | | | | |
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| **No.** | **Population** | **IDSL / Example Shell** | **Title** | **Programming Notes** | **Deliverable [Priority]** |
| 3.12781 | Full Safety | Programming note | Summary of Worsening in Best Corrected Visual Acuity (BCVA) Score (logMAR Score) Characteristics II | Refer regqry_2020_08 | SAC [2] |
| 3.12791 | Full Safety | Programming note | Summary of Blurred Vision and Dry Eye Event Characteristics II in Subjects with Keratopathy | Refer regqry_2020_10 | SAC [2] |
| 3.12793 | Full Safety | Programming note | Summary of Ocular Symptoms (CTCAE) Event Characteristics II in Subjects with Keratopathy | Refer regqry_2020_10 | SAC [2] |
| 3.12801 | Full Safety | Programming note | Summary of Unilateral Worsening in Best Corrected Visual Acuity (BCVA) to 20/50 or Worse Characteristics II | Refer regqry_2020_08 | SAC [2] |
| 3.12811 | Full Safety | Programming note | Summary of Bilateral Worsening in Best Corrected Visual Acuity (BCVA) to 20/50 or Worse Characteristics II | Refer regqry_2020_08 | SAC [2] |
| 3.12821 | Full Safety | Programming note | Percentage of Subjects with Blurred Vision/Dry Eye Event Associated with Worsening in Best Corrected Visual Acuity (BCVA) to 20/50 or Worse | Refer regqry_2020_08 | SAC [2] |
| 3.12823 | Full Safety | Programming note | Percentage of Subjects with Ocular Symptoms (CTCAE) Associated with Worsening in Best Corrected Visual Acuity (BCVA) to 20/50 or Worse | Refer regqry_2020_08 | SAC [2] |
| 3.12831 | Full Safety | Programming note | Summary of Unilateral Worsening in Best Corrected Visual Acuity (BCVA) to 20/200 or Worse Characteristics II | Refer regqry_2020_08 | SAC [2] |
| 3.12841 | Full Safety | Programming note | Summary of Bilateral Worsening in Best Corrected Visual Acuity (BCVA) to 20/200 or Worse Characteristics II | Refer regqry_2020_08 | SAC [2] |

| Safety: Tables | | | | | |
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| **No.** | **Population** | **IDSL / Example Shell** | **Title** | **Programming Notes** | **Deliverable [Priority]** |
| 3.12851 | Full Safety | Programming note | Update of Resolution Status for Unresolved Corneal Exam Finding | Refer regqry_2020_08 | SAC [2] |
| 3.12852 | Full Safety | Programming note | Update of Resolution Status for Unresolved Corneal Exam Finding Patients with Interview Clinical data | Refer present_2020_04 | SAC [2] |
| 3.12861 | Full Safety | Programming note | Update of Resolution Status for Unresolved Worsening in Best Corrected Visual Acuity (BCVA) Score (logMAR Score) | Refer regqry_2020_08 | SAC [2] |
| 3.12871 | Full Safety | Programming note | Update of Resolution Status for Unresolved Blurred Vision and Dry Eye Events in Subjects with Keratopathy | Refer regqry_2020_08 | SAC [2] |
| 3.12873 | Full Safety | Programming note | Update of Resolution Status for Unresolved Ocular Symptoms (CTCAE) in Subjects with Keratopathy | Refer regqry_2020_08 | SAC [2] |
| 3.12881 | Full Safety | Programming note | Summary of Worst Post-baseline Change in Best Corrected Visual Acuity (BCVA) | Refer regqry_2020_08 | SAC [2] |
| 3.12891 | Full Safety | Programming note | Summary of Worsening in Best Corrected Visual Acuity (BCVA) Score (logMAR Score >=0.12) Characteristics II | Refer regqry_2020_08 | SAC [2] |
| 3.12921 | Full Safety | Programming note | Update of Resolution Status for Unresolved Worsening in Best Corrected Visual Acuity (BCVA) Score (logMAR Score >=0.12) | Refer regqry_2020_08 | SAC [2] |
| 3.12931 | Full Safety | Programming note | Summary of Vision Blurred by Preferred term and Best Response Based on Independent Review Committee | Refer regqry_2020_08 | SAC [2] |

| Safety: Tables | | | | | |
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| **No.** | **Population** | **IDSL / Example Shell** | **Title** | **Programming Notes** | **Deliverable [Priority]** |
| 3.12941 | Full Safety | Programming note | Summary of Dry Eye by Preferred term and Best Response Based on Independent Review Committee | Refer regqry_2020_08 | SAC [2] |
| 3.12951 | Full Safety | Programming note | Summary of Vision Blurred by Maximum Grade, and Best Response Based on Independent Review Committee | Refer regqry_2020_08 | SAC [2] |
| 3.12961 | Full Safety | Programming note | Summary of Dry Eye by Maximum Grade, and Best Response Based on Independent Review Committee | Refer regqry_2020_08 | SAC [2] |
| 3.12971 | Full Safety | Programming note | Summary of Best Corrected Visual Acuity (BCVA) Score (Snellen Score) at Baseline Compared to 20/50 | Refer regqry_2020_08 | SAC [2] |
| 3.12981 | Full Safety | Programming note | Worsening in Best Corrected Visual Acuity (BCVA) Score (logMAR Score) Excluding Subjects with Follow-up Shorter Than 80 Days | Refer regqry_2020_08 | SAC [2] |
| 3.1300 | Full Safety | Mock-up SAFE_T11a | Summary of Neutropenia and Infection Event | | SAC [1],SAC [2] |
| 3.50013 | Full Safety | Programming note | Summary of Worst-case Post baseline shift from baseline by BCVA categories | Refer regqry_2021_01 | SAC [2] |
| 3.50020 | Full Safety | Programming note | Summary of Worst-case Post Baseline Change from Baseline in Best Corrected Visual Acuity (BCVA)Score (logMAR score) | Refer regqry_2020_10 | SAC [2] |
| 3.50021 | Full Safety | Programming note | Summary of Worst-case Post Baseline Change from Baseline in Best Corrected Visual Acuity (BCVA)Score (logMAR score) in Subjects with Worsening to 20/50 or Worse in the Better Eye | Refer regqry_2020_10 | SAC [2] |

| Safety: Tables | | | | | |
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| **No.** | **Population** | **IDSL / Example Shell** | **Title** | **Programming Notes** | **Deliverable [Priority]** |
| 3.50022 | Full Safety | Programming note | Summary of Worst-case Post Baseline Change from Baseline in Best Corrected Visual Acuity (BCVA)Score (logMAR score) in Subjects with Worsening to 20/50 or Worse in at Least One Eye but not the Better Eye | Refer regqry_2020_10 | SAC [2] |
| 8.50070 | Full Safety | Programming note | Summary of Characteristics II for the Event of Giving up Driving due to Eyesight | Refer regqry_2020_10 | SAC [2] |
| 8.50080 | Full Safety | Programming note | Summary of Characteristics II for the Event of Giving up Reading due to Eyesight | Refer regqry_2020_10 | SAC [2] |
| 3.60100 | Full Safety | Programming note | Summary of Characteristics II for Keratopathy | Refer regqry_2020_10 | SAC [2] |
| 3.70010 | Full Safety | Programming note | Summary of Dose Modifications for Subjects with Keratopathy | Refer regqry_2020_22 | SAC [2] |
| 3.70012 | Full Safety | Programming note | Summary of Maximum Grade for Corneal Events (GSK scale) | Refer regqry_2020_10 | SAC [2] |
| 3.90010 | Full Safety | Programming note | Summary of Time from Onset of Last Occurence to Last Exam in Subjects Who Did Not Recover from Grade 2 or Higher Corneal Exam Finding (GSK Scale) When Follow Up Ended | Refer regqry_2020_22 | SAC [2] |
| 3.90020 | Full Safety | Programming note | Summary of Ocular Symptoms by Preferred Term and Maximum Grade in Subjects with Worst Grade of Corneal Exam Findings (GSK scale) =1 | Refer regqry_2020_22 | SAC [2] |

| Safety: Tables | | | | | |
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| **No.** | **Population** | **IDSL / Example Shell** | **Title** | **Programming Notes** | **Deliverable [Priority]** |
| 3.90040 | Full Safety | Programming note | Summary of Duration of Exposure since Re-start after First Dose Delay Due to Eye Disorder Events (CTCAE) | Refer regqry_2020_22 | SAC [2] |
| 3.90050 | Full Safety | Programming note | Summary of Corneal Events (GSK Scale) Occurrences After Dose Reduction to 1.92 mg/kg | Refer regqry_2020_22 | SAC [2] |
| **Death** | | | | | |
| 3.0450 | Full Safety | DTH1a | Summary of Deaths | | IA [1], Headline, SAC [1] , SAC [2] |
| **Laboratory: Chemistry** | | | | | |
| 3.0460 | Full Safety | LB1 | Summary of Chemistry Changes from Baseline | ICH E3. Include the lab test 'Albumin Creatinine Ratio' | SAC [1] |
| 3.0470 | Full Safety | OLB11B | Summary of Worst Case Chemistry Changes from Baseline with Respect to the Normal Range | ICH E3 | SAC [1] |
| 3.0480 | Full Safety | OLB9B | Summary of Worst Case Chemistry Grade Changes from Baseline Grade | | IA [1], Headline, SAC [1] |
| 3.1220 | Full Safety | Programming note | Summary of Study Day and Number of Doses at the Onset of First Occurrence of AST Value >= 3 ULN | See similar post-hoc output in BMA117159 (primary_01) | SAC [1] |
| 3.1230 | Full Safety | Programming note | Summary of Study Day and Number of Doses at the Onset of First Occurrence of LDH Value >= 3 ULN | See similar post-hoc output in BMA117159 (primary_01) | SAC [1] |
| 3.1240 | Full Safety | Programming note | Summary of Study Day and Number of Doses at the Onset of First Occurrence of CPK Value >= 3 ULN | See similar post-hoc output in BMA117159 (primary_01) | SAC [1] |
| 3.1250 | Full Safety | Programming note | Summary of Duration from Onset of First Occurrence of AST Value >= 3 ULN to Grade 0 or 1 | See similar post-hoc output in BMA117159 (primary_01) | SAC [1] |

| Safety: Tables | | | | | |
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| **No.** | **Population** | **IDSL / Example Shell** | **Title** | **Programming Notes** | **Deliverable [Priority]** |
| 3.1260 | Full Safety | Programming note | Summary of Duration from Onset of First Occurrence of CPK Value >= 3 ULN to Grade 0 or 1 | See similar post-hoc output in BMA117159 (primary_01) | SAC [1] |
| 3.1270 | Full Safety | Programming note | Summary of Duration from Onset of First Occurrence of LDH Value >= 3 ULN to Grade 0 or 1 | See similar post-hoc output in BMA117159 (primary_01) | SAC [1] |
| 3.1310 | Full Safety | Mock-up Safe_T13 | Shift in Albumin Creatinine Ratio (mg/g) from Baseline to Worst Post-Baseline | | SAC [1] |
| **Laboratory: Haematology** | | | | | |
| 3.0490 | Full Safety | LB1 | Summary of Haematology Changes from Baseline | ICH E3 | SAC [1] |
| 3.0500 | Full Safety | OLB11B | Summary of Worst Case Haematology Changes from Baseline with Respect to the Normal Range | ICH E3 | SAC [1] |
| 3.0510 | Full Safety | OLB9B | Summary of Worst Case Hematology Grade Changes from Baseline Grade | | IA [1], Headline, SAC [1] |
| **Laboratory: Urinalysis** | | | | | |
| 3.0520 | Full Safety | LB1 | Summary of Urine Concentration Changes from Baseline | ICH E3 | SAC [1] |
| 3.0530 | Full Safety | UR1 | Summary of Worst Case Urinalysis Results (Discrete or Character Values) Post-Baseline Relative to Baseline | ICH E3 | SAC [1] |
| **Laboratory: Hepatobiliary (Liver)** | | | | | |
| 3.0540 | Full Safety | LIVER1 | Summary of Liver Monitoring/Stopping Event Reporting | IDSL | SAC [1] |
| 3.0550 | Full Safety | LIVER10 | Summary of Hepatobiliary Laboratory Abnormalities | IDSL | SAC [1] |
| **ECG** | | | | | |
| 3.0590 | Full Safety | EG1 | Summary of ECG Findings per Investigator Assessment | IDSL | SAC [1] |

| Safety: Tables | | | | | |
|---|---|---|---|---|---|
| **No.** | **Population** | **IDSL / Example Shell** | **Title** | **Programming Notes** | **Deliverable [Priority]** |
| 3.0600 | Full Safety | OECG1B | Summary of Worst-case Increases in Fridericia's QTc | Includes all ECG values (both baseline and post-baseline) regardless of whether they are calculated based on triplicate/duplicate/single measurement. | SAC [1] |
| 3.0610 | Full Safety | OECG2B | Summary of Worst-case Amount of Increase from Baseline Value in Fridericia's QTc | Includes all ECG values (both baseline and post-baseline) regardless of whether they are calculated based on triplicate/duplicate/single measurement. | SAC [1] |
| 3.0620 | Full Safety | EG2 | Summary of Change from Baseline in ECG Values by Visit | IDSL Includes all ECG values (both baseline and post-baseline) regardless of whether they are calculated based on triplicate/duplicate/single measurement. | SAC [1] |
| **Vital Signs** | | | | | |
| 3.0630 | Full Safety | VS1 | Summary of Change from Baseline in Vital Signs | ICH E3 | SAC [1] |
| 3.0640 | Full Safety | OVT1B | Summary of Worst Case Changes in Heart Rate from Baseline | | SAC [1] |
| 3.0650 | Full Safety | OVT2B | Summary of Worst Case Increases in Systolic Blood Pressure from Baseline | | SAC [1] |
| 3.0660 | Full Safety | OVT2B | Summary of Worst Case Increases in Diastolic Blood Pressure from Baseline | | SAC [1] |
| 3.0670 | Full Safety | OVT1B | Summary of Worst Case Changes in Temperature from Baseline | | SAC [1] |
| **ECOG Performance Status** | | | | | |
| 3.0680 | Full Safety | PS1A | Summary of ECOG Performance Status | | SAC [1] |
| 3.0690 | Full Safety | PS3A | Summary of Change in ECOG Performance Status from Baseline | | SAC [1] |
| **ECHO** | | | | | |
| 3.0700 | Full Safety | OLVEF1A | Summary of Worst Left Ventricular Ejection Fraction Change from Baseline | | SAC [1] |

| Safety: Tables | | | | | |
|---|---|---|---|---|---|
| **No.** | **Population** | **IDSL / Example Shell** | **Title** | **Programming Notes** | **Deliverable [Priority]** |
| **Anti-Drug Antibody** | | | | | |
| 3.0710 | Full Safety | Programming note | Summary of Human Anti-GSK2857916 Antibodies (ADA) Over Time | See Table 3.0841 from BMA117159 (primary_01) with following changes:<br>1.Under each visit, add another category:<br>'Neutralizing Antibody Results'<br>n<br>POSITIVE<br>NEGATIVE<br>2. Replace 'Negative, Conclusive' and 'Negative, Inconclusive' rows with 'Negative'<br>3. Add to note: Only samples with confirmed positive ADA results were tested in the Neutralizing Antibody Assay. | SAC [1],SAC [2] |

| Safety: Tables | | | | | |
|---|---|---|---|---|---|
| **No.** | **Population** | **IDSL / Example Shell** | **Title** | **Programming Notes** | **Deliverable [Priority]** |
| 3.0720 | Full Safety | Programming note | Summary of Human Anti-GSK2857916 Antibodies (ADA) | See Table 3.0851 from BMA117159 (primary_01) with following changes.<br>1. Under section for baseline ADA results, add following two categories:<br>. a "Number of subjects with confirmed positive ADA result that are positive for Neutralizing Antibodies"<br>b. "Number of subjects with confirmed positive ADA result that are negative for Neutralizing Antibodies"<br>2. Under section for post-baseline ADA results, add following two categories:<br>a "Number of subjects with at least one confirmed positive ADA result that are positive for Neutralizing Antibodies"<br>b. "Number of subjects with at least one confirmed positive ADA result that are negative for Neutralizing Antibodies"<br>3.In the table, replace two cases of '<=25000 ng/mL' with '<=500000 ng/mL'.<br>4. Add to note: Only samples with confirmed positive ADA results were tested in the Neutralizing Antibody Assay. | SAC [1],SAC [2] |

| Safety: Tables | | | | | |
|---|---|---|---|---|---|
| **No.** | **Population** | **IDSL / Example Shell** | **Title** | **Programming Notes** | **Deliverable [Priority]** |
| **Ocular findings for General study (Baseline to Last follow-up)** | | | | | |
| 3.0730 | Full Safety | Programming note | Summary of Best Corrected Visual Acuity Test (BCVA) Scores (logMAR score) | Use Table 3.0501 from BMA117159 (primary_01) study as template. Following "worst change from baseline', add summary for 'Most frequent change from baseline', and pick the worst category if there is tie. Under column 'Eye', in addition to Right/Left add 'Worse' (worse of two eye) and 'Better' (better of two eye). Definition of 3 categories of change are same as in BMA117159 (primary_01). | SAC [1] ,SAC [2] |
| 3.0732 | Full Safety | Programming note | Summary of Best Corrected Visual Acuity Test (BCVA) Scores (logMAR score) due to Corneal Finding (GSK Scale) | Use Table 3.0501 from BMA117159 (primary_01) study as template. Following "worst change from baseline', add summary for 'Most frequent change from baseline', and pick the worst category if there is tie. Under column 'Eye', in addition to Right/Left add 'Worse' (worse of two eye) and 'Better' (better of two eye). Definition of 3 categories of change are same as in BMA117159 (primary_01). Only include those visits with BCVA due to corneal finding flag='Y'. | SAC [1] ,SAC [2] |
| 3.0740 | Full Safety | Mock-up SAFE_T8 | Number (%) of Subjects with a Decline in Best Corrected Visual acuity (BCVA) to LP or NLP due to a Corneal Event Anytime Post-Baseline | Eye (R/L) and subject (either eye) | SAC [1] ,SAC [2] |
| 3.0760 | Full Safety | Mock-up SAFE_T8 | Number (%) of Subjects with Intraocular Pressure (IOP) >= 22mm Hg Anytime Post-Baseline | | SAC [1] |

| Safety: Tables | | | | | |
|---|---|---|---|---|---|
| **No.** | **Population** | **IDSL / Example Shell** | **Title** | **Programming Notes** | **Deliverable [Priority]** |
| 3.0770 | Full Safety | Mock-up SAFE_T8a | Number (%) of Subjects Who Start Treatment for Intraocular Pressure (IOP) after First dose of GSK2857916 | | SAC [1] |
| 3.0780 | Full Safety | Mock-up SAFE_T9 | Shift in Pupillary Exam Findings from Baseline to Worst Post-Baseline | By subject (worse eye). See Section 8.5 Ocular findings from ophthalmic exam for details. | SAC [1] |
| 3.0790 | Full Safety | Mock-up SAFE_T9 | Shift in Extraocular Muscle Movement from Baseline to Worst Post-Baseline | By eye (R/L) and subject (worse eye). See Section 8.5 Ocular findings from ophthalmic exam for details. | SAC [1] |
| 3.0800 | Full Safety | Mock-up SAFE_T9 | Shift in Ptosis from Baseline to Worst Post-Baseline | By eye (R/L) and subject (worse eye). See Section 8.5 Ocular findings from ophthalmic exam for details. | SAC [1] |
| 3.0810 | Full Safety | Mock-up SAFE_T9 | Shift in Blepharitis/MGD from Baseline to Worst Post-Baseline | By eye (R/L) and subject (worse eye). See Section 8.5 Ocular findings from ophthalmic exam for details. | SAC [1] |
| 3.0820 | Full Safety | Mock-up SAFE_T9 | Shift in Conjunctival Exam Findings from Baseline to Worst Post-Baseline | By eye (R/L) and subject (worse eye). Create shift table for each of 3 findings: Chemosis (Absent/Present); Bulbar Conjunctiva White and Quiet: (Yes/No); Palpebral Conjunctiva within normal limits (Yes/No);See Section 8.5 Ocular findings from ophthalmic exam for details. | SAC [1] |
| 3.0840 | Full Safety | Mock-up SAFE_T9 | Shift in Scleritis from Baseline to Worst Post-Baseline | By eye (R/L) and subject (both eyes in same ocular exam). See Section 8.5 Ocular findings from ophthalmic exam for details. | SAC [1] |
| 3.0852 | Full Safety | Mock-up SAFE_T9 | Shift in Corneal Epithelium Findings from Baseline to Worst Post-Baseline | By eye (R/L) and subject (worse eye). See Section 8.5 Ocular findings from ophthalmic exam for details. | SAC [1] ,SAC [2] |

| Safety: Tables | | | | | |
|---|---|---|---|---|---|
| **No.** | **Population** | **IDSL / Example Shell** | **Title** | **Programming Notes** | **Deliverable [Priority]** |
| 3.0851 | Full Safety | Mock-up SAFE_T9 | Shift in Corneal Epithelium Findings from Baseline to Worst Post-Baseline for Microcysts without Edema | | SAC [1],SAC [2] |
| 3.0850 | Full Safety | Mock-up SAFE_T9 | Shift in Corneal Epithelium Findings from Baseline to Worst Post-Baseline for Corneal Epithelium and Corneal Stroma | | SAC [1],SAC [2] |
| 3.0860 | Full Safety | Mock-up SAFE_T14 | Summary of Findings for Punctate Keratopathy | By eye (R/L) and subject (worse eye). See Section 8.5 Ocular findings from ophthalmic exam for details. | SAC [1],SAC [2] |
| 3.0930 | Full Safety | Mock-up SAFE_T9 | Shift in Corneal Endothelium Findings from Baseline to Worst Post-Baseline | By eye (R/L) and subject (worse eye). See Section 8.5 Ocular findings from ophthalmic exam for details. | SAC [1] |
| 3.0940 | Full Safety | Mock-up SAFE_T12 | Summary of Presence of Descemet's Folds/ Endothelial Lesion at Any Time Post-Baseline | By eye (R/L) and subject (either eye). See Section 8.5 Ocular findings from ophthalmic exam for details. | SAC [1] |
| 3.0970 | Safety | Mock-up SAFE_T10 | Summary for Change from Baseline in Pachymetry | See Section 8.5 Ocular findings from ophthalmic exam for details. Pachymetry: decrease in value means improvement; | SAC [1] |
| 3.0980 | Full Safety | Mock-up SAFE_T7 | Summary for Change from Baseline to Worst Post-Baseline in Schirmer's Test and Tear Break-up Time | See Section 8.5 Ocular findings from ophthalmic exam for details. Tear break-up time/Schirmer's test: increase in value means improvement., | SAC [1] ,SAC [2] |
| 3.1340 | Full Safety | Mock-up SAFE_T9a | Shift in Schirmer's Test from Baseline to Worst Post-Baseline | See Section 8.5 Ocular findings from ophthalmic exam for details | SAC [1] |
| 3.1350 | Full Safety | Mock-up SAFE_T9a | Shift in Tear Break-up Time from Baseline to Worst Post-Baseline | See Section 8.5 Ocular findings from ophthalmic exam for details | SAC [1] |
| 3.1000 | Full Safety | Mock-up SAFE_T9 | Shift in Slit Lamp Exam Findings from Baseline to Worst Post-Baseline | By eye (R/L) and subject (worse eye). See Section 8.5 Ocular findings from ophthalmic exam for details. | SAC [1] ,SAC [2] |

| Safety: Tables | | | | | |
|---|---|---|---|---|---|
| **No.** | **Population** | **IDSL / Example Shell** | **Title** | **Programming Notes** | **Deliverable [Priority]** |
| 3.1010 | Full Safety | Mock-up SAFE_T12 | Summary of Presence of Iris Findings at Any Time Post-Baseline | By eye (R/L) and subject (either eye). Summary tables for number (%) of eyes with 'Transillumination defect', 'Nodules', or 'Neovascularization' at any post-baseline ocular exam. See Section 8.5 Ocular findings from ophthalmic exam for details. | SAC [1] ,SAC [2] |
| 3.1020 | Full Safety | Mock-up SAFE_T9 | Shift in Pseudophakia and Cataracts from Baseline to Worst Post-Baseline | By eye (R/L) and subject (worse eye). See Section 8.5 Ocular findings from ophthalmic exam for details. | SAC [1] |
| 3.1040 | Full Safety | Mock-up SAFE_T8 | Number of Subjects (%) Underwent Surgery due to Cataract Post-Baseline | | SAC [1] |
| 3.1050 | Full Safety | Mock-up SAFE_T9 | Shift in Findings from FUNDUS Photograph from Baseline to Worst Post-Baseline | By eye (R/L) and subject (worse eye). See Section 8.5 Ocular findings from ophthalmic exam for details. | SAC [1] |
| **Ocular findings for General study from EOT to last follow-up visit** | | | | | |
| 3.1060 | Full Safety | Mock-up SAFE_T15 | Summary of Change (Worsening, No Change, Improvement) in Best Corrected Visual Acuity (BCVA) from EOT Visit to Last Follow-Up Visit | By eye (R/L) and subject (worse eye). | SAC [1] ,SAC [2] |
| 3.1070 | Full Safety | Mock-up SAFE_T15 | Summary of Change (Worsening, No Change, Improvement) in Intraocular Pressure (IOP) from EOT Visit to Last Follow-Up Visit | By eye (R/L) and subject (worse eye). For IOP, decrease in value means improvement. | SAC [1] |
| 3.1080 | Full Safety | Mock-up SAFE_T15 | Summary of Change (Worsening, No Change, Improvement) in Corneal Epithelium Findings from EOT Visit to Last Follow-Up Visit | By eye (R/L) and subject (worse eye). See Section 8.5 Ocular findings from ophthalmic exam for details | SAC [1] ,SAC [2] |
| 3.1090 | Full Safety | Mock-up SAFE_T15 | Summary of Change (Worsening, No Change, Improvement) in Corneal Endothelium Findings from EOT Visit to Last Follow-Up Visit | By eye (R/L) and subject (worse eye). See Section 8.5 Ocular findings from ophthalmic exam for details | SAC [1] ,SAC [2] |

| Safety: Tables | | | | | |
|---|---|---|---|---|---|
| **No.** | **Population** | **IDSL / Example Shell** | **Title** | **Programming Notes** | **Deliverable [Priority]** |
| 3.1100 | Full Safety | Mock-up SAFE_T15 | Summary of Change (Worsening, No Change, Improvement) in Pachymetry, Tear break up time, and Schirmer's test from EOT Visit to Last Follow-Up Visit | By eye (R/L) and subject (worse eye). Pachymetry: decrease in value means improvement; Tear break-up time/Schirmer's test: increase in value means improvement., | SAC [1] |
| 3.1110 | Full Safety | Mock-up SAFE_T4 | Summary of Resolution Time from EOT Visit in Best Corrected Visual Acuity (BCVA) | By eye (R/L) and subject (worse eye). | SAC [1] ,SAC [2] |
| 3.1120 | Full Safety | Mock-up SAFE_T4 | Summary of Resolution Time from EOT Visit in Intraocular Pressure (IOP) | By eye (R/L) and subject (worse eye). | SAC [1] |
| 3.1130 | Full Safety | Mock-up SAFE_T4 | Summary of Resolution Time from EOT Visit in Corneal Epithelium Findings | By eye (R/L) and subject (worse eye). See Section 8.5 Ocular findings from ophthalmic exam for details | SAC [1] ,SAC [2] |
| 3.1140 | Full Safety | Mock-up SAFE_T4 | Summary of Resolution Time from EOT Visit in Corneal Endothelium Findings | By eye (R/L) and subject (worse eye). See Section 8.5 Ocular findings from ophthalmic exam for details | SAC [1] ,SAC [2] |
| 3.1150 | Full Safety | Mock-up SAFE_T4 | Summary of Resolution Time from EOT Visit in Pachymetry, Tear break up time, and Schirmer's test | By eye (R/L) and subject (worse eye). | SAC [1] |
| **Ocular sub-study (Cycle 1- 4)** | | | | | |
| 3.1160 | Ocular Sub-Study | Mock-up SAFE_T16 | Summary of Worst Grade of Corneal Events (GSK Scale) during Cycle 1-4 by Randomized Topical Corticosteroids Treatment | | SAC [1] |
| 3.1170 | Ocular Sub-Study | Mock-up SAFE_T17 | Summary of Best Corrected Visual Acuity (BCVA) Scores (logMAR score) by Randomized Topical Corticosteroids Treatment | | SAC [1] |
| 3.1180 | Ocular Sub-Study | Mock-up SAFE_T18 | Summary of Onset Time to First Drug-Related Corneal Event (GSK Scale) by Randomized Topical Corticosteroids Treatment | | SAC [1] |

| Safety: Tables | | | | | |
|---|---|---|---|---|---|
| **No.** | **Population** | **IDSL / Example Shell** | **Title** | **Programming Notes** | **Deliverable [Priority]** |
| 3.1190 | Ocular Sub-Study | Mock-up SAFE_T19 | Summary of Onset Time to Initiation of Topical Corticosteroids Treatment in Eyes Not-Randomized to Topical Corticosteroids Treatment | | Headline, SAC [1] |
| 3.1200 | Ocular Sub-Study | Mock-up SAFE_T20 | Shift in Corneal findings (per Ocular Exam) from Baseline to Worst during Cycle 1-4 by Randomized Topical Corticosteroids Treatment | | SAC [1] |

## 15.13.9. Safety Figures

| Safety: Figures | | | | | |
|---|---|---|---|---|---|
| **No.** | **Population** | **IDSL / Example Shell** | **Title** | **Programming Notes** | **Deliverable [Priority]** |
| **Laboratory** | | | | | |
| 3.0020 | Full Safety | LIVER14 | Scatter Plot of Maximum vs. Baseline for ALT | IDSL | SAC [1] |
| 3.0040 | Full Safety | LIVER9 | Scatter Plot of Maximum Bilirubin versus Maximum ALT – eDISH Plot | IDSL | SAC [1] |
| 3.0050 | Full Safety | LIVER9 | Scatter Plot of Maximum AST vs Maximum LDH - eDISH Plot | IDSL | SAC [1] |
| 3.0060 | Full Safety | LIVER9 | Scatter Plot of Maximum AST vs Maximum Creatinine Kinase - eDISH Plot | IDSL | SAC [1] |
| 3.0070 | Full Safety | LIVER9 | Scatter Plot of Maximum LDH vs Maximum Creatinine Kinase - eDISH Plot | IDSL | SAC [1] |
| 3.0080 | Full Safety | LIVER9 | Scatter Plot of Maximum Albumin/Creatinine Ratio (> 2000 mg/g) vs. Concomitant Values of Serum Creatinine | Concomitant window = $\pm$ 7 days | SAC [1] |
| 3.0090 | Full Safety | EG8 | Box Plot of Values for Selected Lab Tests by Visit | Selected lab tests are: haemoglobin, platelets, neutrophils, serum creatinine, and albumin/creatinine ratio. | SAC [1] |
| **Profile Plot** | | | | | |
| 3.0030 | Evaluable | Programming note | Profile Plot for Subjects (Evaluable) | See Figure 3.0030 created at IA for 205678 | IA [1] |
| 3.0031 | Full Safety | Programming note | Profile Plot for Subjects | See Figure 12.0150 from BMA117159 (primary_01) | SAC [1] |

| Safety: Figures | | | | | |
|---|---|---|---|---|---|
| **No.** | **Population** | **IDSL / Example Shell** | **Title** | **Programming Notes** | **Deliverable [Priority]** |
| **ECG** | | | | | |
| 3.0100 | Full Safety | OECG4 | Fridericia's QTc Shifts from Baseline to Worst-case Post Baseline | | SAC [1] |

| Safety: Figures | | | | | |
|---|---|---|---|---|---|
| **No.** | **Population** | **IDSL / Example Shell** | **Title** | **Programming Notes** | **Deliverable [Priority]** |
| **Corneal events** | | | | | |
| 3.10031 | Full Safety | Programming note | Plot of Visual Acuity and Corneal Finding Grade for Subjects Experiencing >1 Corneal Event (GSK Scale), Initial Dose Level = 2.5 mg/kg | Refer present_2020_04 | SAC [2] |
| 3.53010 | Full Safety | Programming note | Plot of Time to Recovery Post Treatment Discontinuation for Corneal Exam Findings | Refer regqry_2020_10 | SAC [2] |
| 3.53020 | Full Safety | Programming note | Plot of Time to Recovery Post Treatment Discontinuation for Keratopathy | Refer regqry_2020_10 | SAC [2] |
| 3.50030 | Full Safety | Programming note | Bar Chart of Grade of Corneal Exam Finding by Cycle | Refer regqry_2020_10 | SAC [2] |

## 15.13.10. Pharmacokinetic Tables

| Pharmacokinetic: Tables | | | | | |
|---|---|---|---|---|---|
| **No.** | **Population** | **IDSL / Example Shell** | **Title** | **Programming Notes** | **Deliverable [Priority]** |
| **Concentration** | | | | | |
| 4.0010 | Full PK | PK01 | Summary of Plasma GSK2857916 (ADC) PK Concentration-Time Data | By dose level | SAC [1], SAC [2] |
| 4.0020 | Full PK | PK01 | Summary of Plasma GSK2857916 (Total Antibody) PK Concentration-Time Data | By dose level | SAC [1] ,SAC [2] |
| 4.0030 | Full PK | PK01 | Summary of Plasma cys-mcMMAF PK Concentration-Time Data | By dose level | SAC [1] ,SAC [2] |
| **PK Parameter** | | | | | |
| 4.0040 | Full PK | PK06 | Summary of Derived GSK2857916 (ADC) PK Parameters | PK06 with both transformed and untransformed values. | SAC [1] |
| 4.0041 | Full PK | PK13 | Listing of Derived GSK2857916 (ADC) PK Parameters (Untransformed) | | SAC [1] |
| 4.0050 | Full PK | PK06 | Summary of Derived GSK2857916 (Total Antibody) PK Parameters | PK06 with both transformed and untransformed values. | SAC [1] |
| 4.0051 | Full PK | PK13 | Listing of Derived GSK2857916 (Total Antibody) PK Parameters (Untransformed) | | SAC [1] |
| 4.0060 | Full PK | PK06 | Summary of Derived cys-mcMMAF PK Parameter | PK06 with both transformed and untransformed values. | SAC [1] |
| 4.0061 | Full PK | PK13 | Listing of Derived cys-mcMMAF PK Parameters (Untransformed) | | SAC [1] |
| **Accumulation Ratio** | | | | | |
| 4.0070 | Full PK | PK05 | Summary of Results of Accumulation Ratio Assessment for GSK2857916 (ADC) | Include Ro(AUC) and Ro(Cmax) with 95%CI in one table. | SAC [1] |

| Pharmacokinetic: Tables | | | | | |
|---|---|---|---|---|---|
| **No.** | **Population** | **IDSL / Example Shell** | **Title** | **Programming Notes** | **Deliverable [Priority]** |
| 4.0080 | Full PK | PK05 | Summary of Results of Accumulation Ratio Assessment for GSK2857916 (Total Antibody) | Include Ro(AUC) and Ro(Cmax) with 95%CI in one table. | SAC [1] |
| 4.0090 | Full PK | PK05 | Summary of Results of Accumulation Ratio Assessment for cys-mcMMAF | Include Ro(AUC) and Ro(Cmax) with 95%CI in one table. | SAC [1] |

## 15.13.11. Pharmacokinetic Figures

| Pharmacokinetic: Figures | | | | | |
|---|---|---|---|---|---|
| **No.** | **Population** | **IDSL / Example Shell** | **Title** | **Programming Notes** | **Deliverable [Priority]** |
| **Concentration** | | | | | |
| 4.0010 | Full PK | PK16 | Individual Plasma GSK2857916 (ADC) Concentration-Time Plots (Linear and Semi-Log) | | SAC [1], SAC [2] |
| 4.0020 | Full PK | PK16 | Individual Plasma GSK2857916 (Total Antibody) Concentration-Time Plots (Linear and Semi-Log) | | SAC [1] , SAC [2] |
| 4.0030 | Full PK | PK16 | Individual Plasma cys-mcMMAF Concentration-Time Plots (Linear and Semi-Log) | | SAC [1] , SAC [2] |
| 4.0040 | Full PK | PK17 | Mean Plasma GSK2857916 (ADC) Concentration-Time Plots (Linear and Semi-Log) | | SAC [1] , SAC [2] |
| 4.0050 | Full PK | PK17 | Mean Plasma GSK2857916 (Total Anti-body) Concentration-Time Plots (Linear and Semi-Log) | | SAC [1] , SAC [2] |
| 4.0060 | Full PK | PK17 | Mean Plasma GSK2857916 (ADC and Total Antibody) Concentration-Time Plots (Linear and Semi-Log) | See similar Figure 14.0190 from BMA117159 (primary_01) | SAC [1] , SAC [2] |
| 4.0070 | Full PK | PK17 | Mean Plasma GSK2857916 (cys-mcMMAF) Concentration-Time Plots (Linear and Semi-Log) | | SAC [1] , SAC [2] |
| 4.0080 | Full PK | PK18 | Median Plasma GSK2857916 (ADC) Concentration-Time Plots (Linear and Semi-Log) | | SAC [1] |
| 4.0090 | Full PK | PK18 | Median Plasma GSK2857916 (Total Anti-body) Concentration-Time Plots (Linear and Semi-Log) | | SAC [1] |
| 4.0100 | Full PK | PK18 | Median Plasma GSK2857916 (ADC and Total Antibody) Concentration-Time Plots (Linear and Semi-Log) | See similar Figure 14.0200 from BMA117159 (primary_01) | SAC [1] |

| Pharmacokinetic: Figures | | | | | |
|---|---|---|---|---|---|
| **No.** | **Population** | **IDSL / Example Shell** | **Title** | **Programming Notes** | **Deliverable [Priority]** |
| 4.0110 | Full PK | PK18 | Median Plasma GSK2857916 (cys-mcMMAF) Concentration-Time Plots (Linear and Semi-Log) | | SAC [1] |
| **Accumulation Ratio** | | | | | |
| 4.0120 | Full PK | PK28 | Plot of Individual (+Geometric Mean and 95%CI) of Accumulation Ratios for GSK2857916 Analytes (Linear and Semi-Log) | Plot accumulation ratios versus dose. Add a reference line at 1. Plot Ro(AUC)and Ro(Cmax) on different plots. Only include geometric mean and 95%CI. Plot analytes: ADC, total antibody, and cys-mcMMAF on the same plot. | SAC [1] |

## 15.13.12. Pharmacokinetic / Pharmacodynamic Figures

| Pharmacokinetic / Pharmacodynamic: Figures | | | | | |
|---|---|---|---|---|---|
| **No.** | **Population** | **IDSL / Example Shell** | **Title** | **Programming Notes** | **Deliverable [Priority]** |
| **[Insert Endpoint Category]** | | | | | |
| 7.0010 | Full PK | PK_F2 | Plot of Fridericia's QTc Change from Baseline versus PK Concentration for GSK2857916 (ADC) | Includes only ECG values (both baseline and post-baseline) calculated based on triplicate/duplicate measurement. | SAC [1] |
| 7.0020 | Full PK | PK_F2 | Plot of Fridericia's QTc Change from Baseline versus PK Concentration for GSK2857916 (Total Antibody) | Includes only ECG values (both baseline and post-baseline) calculated based on triplicate/duplicate measurement. | SAC [1] |
| 7.0030 | Full PK | PK_F2 | Plot of Fridericia's QTc Change from Baseline versus PK Concentration for cys-mcMMAF | Includes only ECG values (both baseline and post-baseline) calculated based on triplicate/duplicate measurement. | SAC [1] |

## 15.13.13. Health Outcomes Tables

| Health Outcomes: Tables | | | | | |
|---|---|---|---|---|---|
| **No.** | **Population** | **IDSL / Example Shell** | **Title** | **Programming Notes** | **Deliverable [Priority]** |
| **EORTC QLQ-C30** | | | | | |
| 8.0010 | Full Analysis | Mock-up PRO_T1 | Summary of Change in EORTC QLQ-C30 Summary Score from Baseline | Timepoints includes EOT visit | SAC [1], SAC [2] |
| 8.0020 | Full Analysis | Mock-up PRO_T1 | Summary of Change in EORTC QLQ-C30 Domain Scores from Baseline | Including score for 15 domains.<br>Timepoints includes EOT visit | SAC [1] ,SAC [2] |
| 8.0030 | Full Analysis | Mock-up PRO_T2 | Number (%) of Subjects with Improvement in EORTC QLQ-C30 Summary Score >= 10 by Visit | Timepoints includes EOT visit | SAC [1] |
| 8.0040 | Full Analysis | Mock-up PRO_T2 | Number (%) of Subjects with Improvement in EORTC QLQ-C30 Domain Score >= 10 by Visit | Including score for 15 domains.<br>Timepoints includes EOT visit | SAC [1] |
| 8.0050 | Full Analysis | Mock-up PRO_T2 | Number (%) of Subjects with Improvement in EORTC QLQ-C30 Summary Score >= 5 by Visit | Timepoints includes EOT visit | SAC [1] |
| 8.0060 | Full Analysis | Mock-up PRO_T2 | Number (%) of Subjects with Improvement in EORTC QLQ-C30 Domain Score >= 5 by Visit | Including score for 15 domains.<br>Timepoints includes EOT visit | SAC [1] |
| **EORTC QLQ-MY20** | | | | | |
| 8.0070 | Full Analysis | Mock-up PRO_T1 | Summary of Change in EORTC QLQ-MY20 Domain Scores from Baseline | Timepoints includes EOT visit.<br>Including score from 4 domains | SAC [1], SAC [2] |
| 8.0080 | Full Analysis | Mock-up PRO_T2 | Number (%) of Subjects with Improvement in EORTC QLQ-MY20 Domain Scores >= 10 by Visit | Pending on the availability of MID;<br>Timepoints includes EOT visit<br>Including score for 4 domains | SAC [1] |
| 8.0081 | Full Analysis | Mock-up PRO_T2 | Number (%) of Subjects with Improvement in EORTC QLQ-MY20 Domain Scores >= 5 by Visit | Pending on the availability of MID;<br>Timepoints includes EOT visit<br>Including score for 4 domains | SAC [1] |

| Health Outcomes: Tables | | | | | |
|---|---|---|---|---|---|
| **No.** | **Population** | **IDSL / Example Shell** | **Title** | **Programming Notes** | **Deliverable [Priority]** |
| **PRO-CTCAE** | | | | | |
| 8.0090 | Full Safety | Mock-up PRO_T3 | Summary of Maximum Post-Baseline PRO-CTCAE Score | For each selected item from PRO-CTCAE library: create summary table for maximum post-baseline PRO-CTCAE score for each of 3 attributes (frequency, severity and/or interference). | SAC [1], SAC [2] |
| **NEI-VFQ-25** | | | | | |
| 8.0100 | Full Safety | Mock-up PRO_T1 | Summary of Change in NEI-VFQ-25 Overall Composite Scores from Baseline | Timepoints includes EOT visit, last follow-up visit, and worst change from baseline. | SAC [1], SAC [2] |
| 8.0110 | Full Safety | Mock-up PRO_T1 | Summary of Change in NEI-VFQ-25 Subscale Scores from Baseline | 11 subscale score.<br>Timepoints includes EOT visit, last follow-up visit, and worst change from baseline. | SAC [1], SAC [2] |
| 8.0120 | Full Safety | Mock-up PRO_T4 | Summary of Worst Change from Baseline in NEI-VFQ-25 Overall Composite Score by Worst Grade of Corneal Event (GSK Scale) | | SAC [1] |
| **OSDI** | | | | | |
| 8.0130 | Full Safety | Mock-up PRO_T1 | Summary of Change in OSDI Total Scores from Baseline | Timepoints includes EOT visit, last follow-up visit, and worst change from baseline. | SAC [1], SAC [2] |
| 8.0140 | Full Safety | Mock-up PRO_T1 | Summary of Change in OSDI Subscale Scores from Baseline | Including 3 subscale scores.<br>Timepoints includes EOT visit, last follow-up visit, and worst change from baseline. | SAC [1] , SAC [2] |
| 8.0150 | Full Safety | Mock-up PRO_T4 | Summary of Worst Change from Baseline in OSDI Total Scores by Worst Grade of Corneal Event (GSK Scale) | | SAC [1] |

## 15.13.14. Health Outcomes Figures

| Health Outcomes: Figures | | | | | |
|---|---|---|---|---|---|
| **No.** | **Population** | **IDSL / Example Shell** | **Title** | **Programming Notes** | **Deliverable [Priority]** |
| **PRO-CTCAE** | | | | | |
| 8.0010 | Full Safety | Mock-up PRO_F1 | Stacked Bar Chart of PRO-CTCAE Score by Attributes and Visit | For each selected item from PRO-CTCAE library: create 3 sets of stacked bar charts (one for each of two dose arms) for PRO-CTCAE score for each of 3 attributes (frequency, severity and/or interference). | SAC [1], SAC [2] |

## 15.13.15. ICH Listings

| ICH: Listings | | | | | |
|---|---|---|---|---|---|
| **No.** | **Population** | **IDSL / Example Shell** | **Title** | **Programming Notes** | **Deliverable [Priority]** |
| **Subject Disposition** | | | | | |
| 1.0020 | Full Analysis | ES2 | Listing of Reasons for Study Withdrawal | ICH E3. | SAC [1], SAC [2] |
| 1.0030 | Full Analysis | SD2 | Listing of Reasons for Study Treatment Discontinuation | ICH E3 | SAC [1] , SAC [2] |
| 1.0040 | Full Analysis | CP_RA1 | Listing of Planned and Actual Treatments | IDSL | SAC [1] |
| **Protocol Deviations** | | | | | |
| 1.0050 | Full Analysis | DV2 | Listing of Important Protocol Deviations | ICH E3 | SAC [1] |
| 1.0060 | Full Analysis | IE3 | Listing of Participants with Inclusion/Exclusion Criteria Deviations | ICH E3 | SAC [1] |
| **Populations Analysed** | | | | | |
| 1.0070 | Enrolled | SP3a | Listing of Participants Excluded from Any Population | ICH E3 | SAC [1] |
| **Demographic and Baseline Characteristics** | | | | | |
| 1.0080 | Full Analysis | DM2 | Listing of Demographic Characteristics | ICH E3 | SAC [1] |
| **Prior and Concomitant Medications** | | | | | |
| 1.0100 | Full Safety | OCM1A | Listing of Concomitant Medications | IDSL | SAC [1] |
| **Exposure and Treatment Compliance** | | | | | |
| 1.0110 | Full Safety | OEX8A | Listing of Exposure Data | ICH E3 | SAC [1] , SAC [2] |
| **Adverse Events** | | | | | |
| 1.0170 | Full Safety | OAE04 | Listing of All Adverse Events | ICH E3 | SAC [1] |

| ICH: Listings | | | | | |
|---|---|---|---|---|---|
| **No.** | **Population** | **IDSL / Example Shell** | **Title** | **Programming Notes** | **Deliverable [Priority]** |
| 1.0180 | Full Safety | OAE03 | Listing of Subject Numbers for Individual Adverse Events | ICH E3 | SAC [1] |
| 1.0190 | Full Safety | AE2 | Listing of Relationship Between Adverse Event System Organ Classes, Preferred Terms, and Verbatim Text | IDSL | SAC [1] |
| **Serious and Other Significant Adverse Events** | | | | | |
| 1.0200 | Full Safety | OAE04 | Listing of Fatal Serious Adverse Events | ICH E3 | SAC [1], SAC [2] |
| 1.0210 | Full Safety | OAE04 | Listing of Non-Fatal Serious Adverse Events | ICH E3 | SAC [1], SAC [2] |
| 1.0220 | Full Safety | AE14 | Listing of Reasons for Considering as a Serious Adverse Event | ICH E3 | SAC [1] , SAC [2] |
| 1.0240 | Full Safety | OAE04 | Listing of Adverse Events Leading to Permanent Discontinuation of Study Treatment | | SAC [1] , SAC [2] |
| 1.0290 | Full Safety | OAE04 | Listing of Eye Disorder (CTCAE) | List AE under Eye Disorder SOC | SAC [1] , SAC [2] |
| 1.0300 | Ocular Sub-Study | OAE04 | Listing of Eye Disorder (CTCAE) in Ocular Sub-Study Subjects | List AE under Eye Disorder SOC | SAC [1] , SAC [2] |
| 1.0310 | Full Safety | OAE04 | Listing of Thrombocytopenia | | SAC [1] , SAC [2] |
| 1.0320 | Full Safety | OAE04 | Listing of Infusion Related Reactions | | SAC [1] , SAC [2] |
| 1.0380 | Full Safety | OAE04 | Listing of Neutropenia | | SAC [1] , SAC [2] |
| **Hepatobiliary (Liver)** | | | | | |
| 1.0330 | Full Safety | MH2 | Listing of Medical Conditions for Participants with Liver Stopping Events | IDSL | SAC [1] , SAC [2] |

| ICH: Listings | | | | | |
|---|---|---|---|---|---|
| **No.** | **Population** | **IDSL / Example Shell** | **Title** | **Programming Notes** | **Deliverable [Priority]** |
| 1.0340 | Full Safety | SU2 | Listing of Substance Use for Participants with Liver Stopping Events | IDSL | SAC [1] |
| **All Laboratory** | | | | | |
| 1.0350 | Full Safety | OLB7 | Listing of All Laboratory Data for Participants with Any Value of Potential Clinical Importance | ICH E3 | SAC [1] , SAC [2] |
| 1.0360 | Full Safety | OLB13 | Listing of Laboratory Data with Character Results | ICH E3 | SAC [1] |
| 1.0370 | Full Safety | UR2A | Listing of Urinalysis Data for Participants with Any Value of Potential Clinical Importance | ICH E3 | SAC [1] |
| **ECOG Performance Status** | | | | | |
| **Response** | | | | | |
| 1.0390 | Full Analysis | RE5 | Listing of Independent Review Committee-Assessed Responses | Also include information of MRD. | SAC [1] , SAC [2] |
| 1.0400 | Full Analysis | RE5 | Listing of Investigator-Assessed Responses | Also include information of MRD. | SAC [1] |
| 1.0410 | Full Analysis | TTE9 | Listing of Duration of Response based on Independent Review Committee-Assessed Responses | | SAC [1] , SAC [2] |
| 1.0420 | Full Analysis | TTE9 | Listing of Duration of Response based on Investigator-Assessed Responses | | SAC [1] |
| 1.0430 | Full Analysis | TTE9 | Listing of Progression-Free Survival based on Independent Review Committee-Assessed Responses | | SAC [1] , SAC [2] |
| 1.0440 | Full Analysis | TTE9 | Listing of Progression-Free Survival based on Investigator-Assessed Response | | SAC [1] |
| 1.0450 | Full Analysis | TTE9 | Listing of Time to Response based on Independent Review Committee-Assessed Responses | | SAC [1] , SAC [2] |
| 1.0460 | Full Analysis | TTE9 | Listing of Time to Response based on Investigator-Assessed Responses | | SAC [1] |

| ICH: Listings | | | | | |
|---|---|---|---|---|---|
| **No.** | **Population** | **IDSL / Example Shell** | **Title** | **Programming Notes** | **Deliverable [Priority]** |
| 1.0470 | Full Analysis | TTE9 | Listing of Time to Best Response based on Independent Review Committee-Assessed Responses | | SAC [1] , SAC [2] |
| 1.0480 | Full Analysis | TTE9 | Listing of Time to Best Response based on Investigator-Assessed Responses | | SAC [1] |
| 1.0490 | Full Analysis | TTE9 | Listing of Time to Progression based on Independent Review Committee-Assessed Responses | | SAC [1] , SAC [2] |
| 1.0500 | Full Analysis | TTE9 | Listing of Time to Progression based on Investigator-Assessed Responses | | SAC [1] |
| 1.0510 | Full Analysis | TTE9 | Listing of Overall Survival | | SAC [1] , SAC [2] |
| **Death** | | | | | |
| 1.0520 | Full Safety | DTH3 | Listing of Deaths | | SAC [1] |
| **Pharmacokinetics** | | | | | |
| 1.0530 | Full PK | PK07 | Listing of Plasma GSK2857916 (ADC) Pharmacokinetic Concentration-Time Data | | SAC [1] , SAC [2] |
| 1.0540 | Full PK | PK07 | Listing of Plasma GSK2857916 (Total Antibody) Pharmacokinetic Concentration-Time Data | | SAC [1] , SAC [2] |
| 1.0550 | Full PK | PK07 | Listing of Plasma cys-mcMMAF Pharmacokinetic Concentration-Time Data | | SAC [1] , SAC [2] |
| 1.0560 | Full PK | PK15 | Listing of GSK2857916 (ADC) AUC and Cmax Accumulation Ratio | | SAC [1] |
| 1.0570 | Full PK | PK15 | Listing of GSK2857916 (Total Antibody) AUC and Cmax Accumulation Ratio | | SAC [1] |
| 1.0580 | Full PK | PK15 | Listing of cys-mcMMAF AUC and Cmax Accumulation Ratio | | SAC [1] |

## 15.13.16. Non-ICH Listings

| Non-ICH: Listings | | | | | |
|---|---|---|---|---|---|
| **No.** | **Population** | **IDSL / Example Shell** | **Title** | **Programming Notes** | **Deliverable [Priority]** |
| **Response** | | | | | |
| 30.0010 | Full Analysis | RE12 | Listing of Investigator-Assessed Best Response for Interim Review by First Dose Date | | IA [1] |
| **Medical Conditions** | | | | | |
| **Concomitant Medications** | | | | | |
| 30.0020 | Full Safety | OCM1A | Listing of Prophylactic Medication for Infusion-Related Reactions | | SAC [1], SAC [2] |
| 30.0030 | Full Safety | OCM1A | Listing of Eye Medications | | SAC [1], SAC [2] |
| **Blood and Blood Supportive Care Products** | | | | | |
| 30.0040 | Full Analysis | BP4 | Listing of Blood Products | | SAC [1] |
| 30.0050 | Full Analysis | BP5 | Listing of Blood Supportive Care Products | | SAC [1] |
| **Substance Use** | | | | | |
| **Anti-Cancer Therapy, Radiotherapy and Surgical Procedures** | | | | | |
| 30.0060 | Full Analysis | AC6 | Listing of Prior Anti-Cancer Therapy | | SAC [1] |
| 30.0070 | Full Analysis | AC7 | Listing of Anti-Cancer Radiotherapy | | SAC [1] |
| 30.0080 | Full Analysis | OSP3 | Listing of Prior/On Treatment Cancer and Non-Cancer Related Surgical Procedures | | SAC [1] |
| 30.0090 | Full Analysis | FAC3 | Listing of Follow-Up Anti-Cancer Therapy | | SAC [1] |

| Non-ICH: Listings | | | | | |
|---|---|---|---|---|---|
| **No.** | **Population** | **IDSL / Example Shell** | **Title** | **Programming Notes** | **Deliverable [Priority]** |
| **Disease Characteristics** | | | | | |
| 30.0100 | Full Analysis | DC4 | Listing of Disease Characteristics at Screening | Include the genetic characteristics | SAC [1] |
| 30.0110 | Full Analysis | DC3 | Listing of Disease Characteristics at Initial Diagnosis | | SAC [1] |
| **Exposure** | | | | | |
| 30.0120 | Full Safety | OEX9 | Summary Listing of Overall Exposure and Dose Modifications | | SAC [1], SAC [2] |
| 3.10010 | Full Safety | Programming note | Listing of All Dose Delays due to Corneal Events (GSK scale) | See regqry_2020_02, 3.10010 | SAC [2] |
| 3.10011 | Full Safety | Programming note | Listing of Dose Delays and Associated Eye Disorder Events (CTCAE) | See regqry_2020_02 , 3.10011 | SAC [2] |
| **Laboratory** | | | | | |
| 30.0130 | Full Safety | OLB7 | Listing of Grade 3 and Grade 4 Laboratory Data | | SAC [1], SAC [2] |
| 30.0140 | Full Safety | LIVER13 | Listing of Subjects Meeting Hepatobiliary Laboratory Criteria Post-Baseline | | SAC [1] |
| 30.0150 | Full Safety | LIVER5 | Listing of Liver Monitoring/Stopping Event Reporting | | SAC [1] |
| **ECG** | | | | | |
| 30.0160 | Full Safety | OECG5A | Listing of Fridericia's QTc Values of Potential Clinical Importance | | SAC [1] |
| **Vital Signs** | | | | | |
| 30.0170 | Full Safety | OVT7A | Listing of Vital Sign Values of Potential Clinical Importance | | SAC [1] |

| Non-ICH: Listings | | | | | |
|---|---|---|---|---|---|
| **No.** | **Population** | **IDSL / Example Shell** | **Title** | **Programming Notes** | **Deliverable [Priority]** |
| **Anti-Drug Antibody** | | | | | |
| 30.0180 | Full Safety | Programming note | Listing of Human Anti-GSK2857916 Antibody Results | See Listing 30.0620 from BMA117159 (primary_01) with following change:<br>1. Add a new column 'Neutralizing Antibody Assay' between TITER and ADC Concentration. The result will be either 'POSITIVE' or 'NEGATIVE'.<br>2.Add a note: Neutralizing Antibody Assay was only applied to confirmed ADA positive samples. | SAC [1], SAC [2] |
| **Corneal Events (GSK Scale)** | | | | | |
| 30.0190 | Full Safety | Mock up SAFE_L2 | Listing of Corneal Events (GSK Scale) | List corneal findings by eye R/L and patient as well as action taken with study treatment. | SAC [1], SAC [2] |
| 30.0191 | Full Safety | Programming note | Listing of Resolution in Grade of Corneal Events (GSK Scale) for each Corneal Event in patients experiencing >1 event | See 30.0192 in present_2020_04 | SAC [2] |
| 30.0200 | Ocular Sub-Study | Mock up SAFE_L2 | Listing of Corneal Events (GSK Scale) in Ocular Sub-Study Subjects | List corneal findings by eye R/L and patient as well as action taken with study treatment.<br>When break down by treatment arm, also included the information on which eye is randomized to corticosteroids (e. g Eye randomized to topical corticosteroids treatment = L.) | SAC [1], SAC [2] |
| 8.0102 | Full Safety | Programming note | Listing of BCVA for patients who gave up driving due to eyesight | Refer present_2020_04 | SAC [2] |

| Non-ICH: Listings | | | | | |
|---|---|---|---|---|---|
| **No.** | **Population** | **IDSL / Example Shell** | **Title** | **Programming Notes** | **Deliverable [Priority]** |
| 8.0103 | Full Safety | Programming note | Listing of BCVA for patients who experienced difficulty reading newspapers due to eyesight | Refer present_2020_04 | SAC [2] |
| **Ocular Exam** | | | | | |
| 30.0210 | Full Safety | Programming note | Listing of Visual Acuity and Abnormal Corneal Exam Results | See Listing 30.0260 from BMA117159 (primary_01) | SAC [1] |
| 30.0220 | Full Safety | Programming note | Listing of Abnormal Conjunctival Exam Results | See Listing 30.0330 from BMA117159 (primary_01) | SAC [1] |
| 30.0230 | Full Safety | Programming note | Listing of Abnormal Slit Lamp Anterior Chamber, Slit Lamp Iris, and Slit Lamp Lens Exam Results | See Listing 30.0210 above | SAC [1] |
| 30.0240 | Full Safety | Programming note | Listing of Abnormal Dilated Fundoscopic Exam Results | See Listing 30.0210 above | SAC [1] |
| **Health Outcome** | | | | | |
| 30.0250 | Full Analysis | VS4 | Listing of EORTC QLQ-C30 Scores | use collected visit dates. List overall summary score and 14 domain scores | SAC [1] |
| 30.0260 | Full Analysis | VS4 | Listing of EORTC QLQ-MY20 Scores | use collected visit dates. List 4 domain scores | SAC [1] |
| 30.0270 | Full Safety | VS4 | Listing of PRO-CTCAE response | use collected visit dates. List response for Frequency, Severity, Interference, and Present/Absence. | SAC [1] |
| 30.0280 | Full Safety | VS4 | Listing of NEI-VFQ-25 Scores | use collected visit dates. List overall composite score and 11 sub-scores | SAC [1] |
| 30.0290 | Full Safety | VS4 | Listing of OSDI Scores | use collected visit dates. List total score and 3 sub-scores. | SAC [1] |

| Non-ICH: Listings | | | | | |
|---|---|---|---|---|---|
| **No.** | **Population** | **IDSL / Example Shell** | **Title** | **Programming Notes** | **Deliverable [Priority]** |
| **PK/PD** | | | | | |
| 30.0300 | Full PK | Programming Note | Listing of Fridericia's QTc Change from Baseline and GSK2857916 (ADC) Pharmacokinetic Concentration-Time Data | See Listing 30.0690 in BMA117159 (primary_01) | SAC [1] |
| 30.0310 | Full PK | Programming Note | Listing of Fridericia's QTc Change from Baseline and GSK2857916 (Total Antibody) Pharmacokinetic Concentration-Time Data | See Listing 30.0700 in BMA117159 (primary_01) | SAC [1] |
| 30.0320 | Full PK | Programming Note | Listing of Fridericia's QTc Change from Baseline and cys-mcMMAF Pharmacokinetic Concentration-Time Data | See Listing 30.0720 in BMA117159 ((primary_01) | SAC [1] |
| COVID 19 | | | | | |
| 1.0082 | Full Safety | PAN7 | Listing of All Subjects with Visits and Assessments Impacted by COVID-19 Pandemic | | SAC [2] |

## 15.14. Appendix 14: Example Mock Shells for Data Displays

Example POP_T1
Protocol: 205678 Page 1 of 1
Population: Safety (Data as of: 24APR2018)

Table X
Summary of Percentage of Duration of Exposure on Steroid Eye Drop

| | Treatment Group A (N=100) | Treatment Group B (N=100) |
|---|---|---|
| % of duration of exposure [1] that was on Prophylactic steroid eye drop | | |
| n | 100 | 100 |
| Mean | 20.5 | 15.1 |
| SD | 1.44 | 1.24 |
| Median | 18 | 14 |
| Min. | 3 | 1 |
| Max. | 40 | 30 |

Note:
1: Duration of Exposure in Days is calculated as minimum of (Treatment Stop Date+21, Death date) minus Treatment Start Date.

Example EFF_T1

Protocol: 205678 
Population: ITT

Table X.X
Summary of MRD Negativity Rate by Best Response

| | | Treatment Group A (N=xx) | Treatment Group B (N=xx) |
|---|---|---|---|
| Best response | | | |
| Stringent Complete Response (sCR) | n | xx | xx |
| | MRD Negativity Rate | xx (xx.x%) | xx (xx.x%) |
| | 95% Confidence Interval | (xx.x%, xx.x%) | (xx.x%, xx.x%) |
| Complete Response (CR) | n | xx | Xx |
| | MRD Negativity Rate | xx (xx.x%) | xx (xx.x%) |
| | 95% Confidence Interval | (xx.x%, xx.x%) | (xx.x%, xx.x%) |
| Very Good Partial Response (VGPR) | n | xx | xx |
| | MRD Negativity Rate | xx (xx.x%) | xx (xx.x%) |
| | 95% Confidence Interval | (xx.x%, xx.x%) | (xx.x%, xx.x%) |
| sCR/CR/VGPR | n | xx | xx |
| | MRD Negativity Rate | xx (xx.x%) | xx (xx.x%) |
| | 95% Confidence Interval | (xx.x%, xx.x%) | (xx.x%, xx.x%) |

Note: Minimal Residual Disease (MRD) negativity rate is defined as: the percentage of participants who are MRD negative by Next Generation Sequencing (NGS).

Example EFF_T2
Protocol: 205678
Population: Full Analysis



Table X.X
Summary of Reasons of Censoring

| Time to event endpoints | | Treatment Group A (N=xx) | Treatment Group B (N=xx) |
|---|---|---|---|
| Duration of response(DoR) | n | xx | xx |
| | Reason 1 | xx (xx.x%) | xx (xx.x%) |
| | Reason 2 | xx (xx.x%) | xx (xx.x%) |
| | Reason 3 | xx (xx.x%) | xx (xx.x%) |
| | …… | | |
| Progression free survival(PFS) | n | xx | xx |
| | Reason 1 | xx (xx.x%) | xx (xx.x%) |
| | Reason 2 | xx (xx.x%) | xx (xx.x%) |
| | Reason 3 | xx (xx.x%) | xx (xx.x%) |
| | …… | | |
| Time to progression(TTP) | n | xx | xx |
| | Reason 1 | xx (xx.x%) | xx (xx.x%) |
| | Reason 2 | xx (xx.x%) | xx (xx.x%) |
| | Reason 3 | xx (xx.x%) | xx (xx.x%) |
| | …… | | |
| Overall survival(OS) | n | xx | xx |
| | Reason 1 | xx (xx.x%) | xx (xx.x%) |
| | Reason 2 | xx (xx.x%) | xx (xx.x%) |
| | Reason 3 | xx (xx.x%) | xx (xx.x%) |
| | …… | | |

n is the number of subject who were censored, which will be used as denominator to calculate the percentage.

Example SAFE_T11
Protocol: 205678
Population: Full Safety



Table X.X
Summary of Thrombocytopenia and Bleeding Event

| | Treatment Group A (N=100) | Treatment Group B (N=100) | Treatment Group C (N=100) |
|---|---|---|---|
| Any Grade 3/4 Platelet Count Decreased | xx (xx.x%) | xx (xx.x%) | xx (xx.x%) |
| Any Grade 2 or Above Bleeding Event | xx (xx.x%) | xx (xx.x%) | xx (xx.x%) |
| Concomitant Platelet Count Decreased and Bleeding | xx (xx.x%) | xx (xx.x%) | xx (xx.x%) |
| | xx (xx.x%) | xx (xx.x%) | xx (xx.x%) |

Example SAFE_T11a
Protocol: 205678
Population: Full Safety



Table X.X
Summary of Neutropenia and Infection Event

| | Treatment Group A (N=100) | Treatment Group B (N=100) | Treatment Group C (N=100) |
|---|---|---|---|
| Any Grade 3/4 Neutrophil Count Decreased | xx (xx.x%) | xx (xx.x%) | xx (xx.x%) |
| Any Infection Event | xx (xx.x%) | xx (xx.x%) | xx (xx.x%) |
| Concomitant Neutrophil Count Decreased and Infection | xx (xx.x%) | xx (xx.x%) | xx (xx.x%) |
| | xx (xx.x%) | xx (xx.x%) | xx (xx.x%) |

Example SAFE_T1
Protocol: 205678
Population: Safety



Table X.X
Summary of Corneal Events (GSK Scale) by Grade and Visit

| | Treatment Group A (N=xx) | Treatment Group B (N=xx) |
|---|---|---|
| Baseline Visit | | |
| ANY EVENT | xx (xx%) | xx (xx%) |
| Grade 1 | xx (xx%) | xx (xx%) |
| Grade 2 | xx (xx%) | xx (xx%) |
| Grade 3 | xx (xx%) | xx (xx%) |
| Grade 4 | xx (xx%) | xx (xx%) |
| Week 4 visit | | |
| ANY EVENT | xx (xx%) | xx (xx%) |
| Grade 1 | xx (xx%) | xx (xx%) |
| Grade 2 | xx (xx%) | xx (xx%) |
| Grade 3 | xx (xx%) | xx (xx%) |
| Grade 4 | xx (xx%) | xx (xx%) |
| Week 7 visit | | |
| ANY EVENT | xx (xx%) | xx (xx%) |
| Grade 1 | xx (xx%) | xx (xx%) |
| Grade 2 | xx (xx%) | xx (xx%) |
| Grade 3 | xx (xx%) | xx (xx%) |
| Grade 4 | xx (xx%) | xx (xx%) |

Note: Visits ‘Cycle X Day 1/Day 10’ are from ocular sub-study subjects only. …….

Example SAFE_T1a
Protocol: 205678 
Population: Safety

Table X.X
Summary of Cumulative Incidence of Corneal Events (GSK Scale) by Grade and Number of Doses Received at First Occurrence

Treatment Group A (N=xx)

| | Number of Doses Received at First Occurrence | | | | | | |
|---|---|---|---|---|---|---|---|
| Grade (GSK Scale) | <= 1 | <= 2 | <= 4 | <= 6 | <= 8 | <= 10 | Any |
| ANY Grade | xx (xx%) | xx (xx%) | xx (xx%) | xx (xx%) | xx (xx%) | xx (xx%) | xx (xx%) |
| Grade 1 | xx (xx%) | xx (xx%) | xx (xx%) | xx (xx%) | xx (xx%) | xx (xx%) | xx (xx%) |
| Grade 2 | xx (xx%) | xx (xx%) | xx (xx%) | xx (xx%) | xx (xx%) | xx (xx%) | xx (xx%) |
| Grade 3 | xx (xx%) | xx (xx%) | xx (xx%) | xx (xx%) | xx (xx%) | xx (xx%) | xx (xx%) |
| Grade 4 | xx (xx%) | xx (xx%) | xx (xx%) | xx (xx%) | xx (xx%) | xx (xx%) | xx (xx%) |

Treatment Group B (N=xx)
……

Example SAFE_T2
Protocol: 205678 
Population: Safety

Table X.X
Summary of Action Taken with Study Treatment for Corneal Events (GSK Scale) by Visit

Treatment Group A (N=xx)

| Visit | n | Grade | Study treatment withdrawn | Dose reduction | Dose interrupted/ delayed |
|---|---|---|---|---|---|
| Week 4 | xx | All Grade | xx (xx%) | xx (xx%) | xx (xx%) |
| | | Grade 1 | xx (xx%) | xx (xx%) | xx (xx%) |
| | | Grade 2 | xx (xx%) | xx (xx%) | xx (xx%) |
| | | Grade 3 | xx (xx%) | xx (xx%) | xx (xx%) |
| | | Grade 4 | xx (xx%) | xx (xx%) | xx (xx%) |
| | xx | All Grade | xx (xx%) | xx (xx%) | xx (xx%) |
| | | Grade 1 | xx (xx%) | xx (xx%) | xx (xx%) |
| | | Grade 2 | xx (xx%) | xx (xx%) | xx (xx%) |
| | | Grade 3 | xx (xx%) | xx (xx%) | xx (xx%) |
| | | Grade 4 | xx (xx%) | xx (xx%) | xx (xx%) |
| Week 7 | | | | | |

……

Treatment Group B (N=xx)

……..
Note: n reflects the number of participants with available GSK scale data at a given visit.
Visits ‘Cycle 1-4 Day 1/10’ are from ocular sub-study subjects only.

Example SAFE_T2a
Protocol: 205678 
Population: Safety

Table X.X
Summary of Corneal Events (GSK Scale) Leading to Action Taken with Study Treatment

| Action Taken with Study treatment | Grade | Treatment Group A (N = xx) | Treatment Group B (N = xx) |
|---|---|---|---|
| Study treatment withdrawn | All Grades | xx (xx%) | xx (xx%) |
| | Grade 1 | xx (xx%) | xx (xx%) |
| | Grade 2 | xx (xx%) | xx (xx%) |
| | Grade 3 | xx (xx%) | xx (xx%) |
| | Grade 4 | xx (xx%) | xx (xx%) |
| Dose reduction | All Grades | xx (xx%) | xx (xx%) |
| | Grade 1 | xx (xx%) | xx (xx%) |
| | Grade 2 | xx (xx%) | xx (xx%) |
| | Grade 3 | xx (xx%) | xx (xx%) |
| | Grade 4 | xx (xx%) | xx (xx%) |
| Dose interrupted/ delayed | All Grades | xx (xx%) | xx (xx%) |
| | Grade 1 | xx (xx%) | xx (xx%) |
| | Grade 2 | xx (xx%) | xx (xx%) |
| | Grade 3 | xx (xx%) | xx (xx%) |
| | Grade 4 | xx (xx%) | xx (xx%) |

Note: If a given participant had multiple incidence of same action taken with study treatment, only the action with highest grade will be included in the summary.

Example SAFE_T3
Protocol: 205678 
Population: Safety (Data as of: 24APR2018)

Table X
Shift in Grade of Corneal Events from Baseline to Worst Post-Baseline up to EOT visit

| | Baseline | | Worst post-baseline value | | | | | |
|---|---|---|---|---|---|---|---|---|
| | | | Grade 0 | Grade 1 | Grade 2 | Grade 3 | Grade 4 | Missing |
| Treatment Group | | n (%) | n (%) | n (%) | n (%) | n (%) | n (%) | n (%) |
| Treatment Group A (N=xx) | Grade 0 | xx (xx.x) | xx (xx.x) | xx (xx.x) | xx (xx.x) | xx (xx.x) | xx (xx.x) | xx (xx.x) |
| | Grade 1 | xx (xx.x) | xx (xx.x) | xx (xx.x) | xx (xx.x) | xx (xx.x) | xx (xx.x) | xx (xx.x) |
| | Grade 2 | xx (xx.x) | xx (xx.x) | xx (xx.x) | xx (xx.x) | xx (xx.x) | xx (xx.x) | xx (xx.x) |
| | Grade 3 | xx (xx.x) | xx (xx.x) | xx (xx.x) | xx (xx.x) | xx (xx.x) | xx (xx.x) | xx (xx.x) |
| | Grade 4 | xx (xx.x) | xx (xx.x) | xx (xx.x) | xx (xx.x) | xx (xx.x) | xx (xx.x) | xx (xx.x) |
| | Missing | xx (xx.x) | xx (xx.x) | xx (xx.x) | xx (xx.x) | xx (xx.x) | xx (xx.x) | xx (xx.x) |
| | Total | xx (xx.x) | xx (xx.x) | xx (xx.x) | xx (xx.x) | xx (xx.x) | xx (xx.x) | xx (xx.x) |
| Treatment Group B (N=xx) | | | | | | | | |
| ..... | | | | | | | | |

- Baseline percentage is based on N. percentage for last post-Baseline value is based on Baseline n.

Example SAFE_T4
Protocol: 205678 
Population: Safety (Data as of: 24APR2018)

Table X
Summary of Resolution Time from EOT in Best Corrected Visual Acuity (BCVA)

Parameter = Best Corrected Visual Acuity (BCVA)

| | Treatment | Treatment |
|---|---|---|
| Right eye: n [1] | 100 | 100 |
| Number (%) of eyes that resolved [2] | 50 (50%) | 40 (40%) |
| Time from EOT Visit to resolution, days | | |
| Mean | 20.5 | 15.1 |
| SD | 1.44 | 1.24 |
| Median | 18 | 14 |
| Min. | 3 | 1 |
| Max. | 40 | 30 |
| Left eye: n [1] | 100 | 100 |
| Number (%) of eyes that resolved [2] | 50 (50%) | 40 (40%) |
| Time from EOT Visit to resolution, days | | |
| Mean | 20.5 | 15.1 |
| SD | 1.44 | 1.24 |
| Median | 18 | 14 |
| Min. | 3 | 1 |
| Max. | 40 | 30 |
| Subject (worse eye): n [1] | 100 | 100 |
| Number (%) of subjects that resolved [2] | 50 (50%) | 40 (40%) |
| Time from EOT Visit to resolution, days | | |
| Mean | 20.5 | 15.1 |
| SD | 1.44 | 1.24 |
| Median | 18 | 14 |
| Min. | 3 | 1 |
| Max. | 40 | 30 |

Note:
1: n is the number of eyes or subjects (worse eye) with exam result worse than baseline at EOT, which will be used as denominator to calculate the percentage.
2: Resolution is defined as improvement to baseline level or better.

Example SAFE_T4a

Protocol: 205678 
Population: Safety (Data as of: 24APR2018)

Table X
Summary of Resolution in Corneal Events (GSK Scale) during Follow-up Period

| | Treatment Group A (N=100) | Treatment Group B (N=100) |
|---|---|---|
| n [1] | 100 | 100 |
| Number (%) of Participants that Resolve[2] | 50 (50%) | 40 (40%) |
| Time from EOT Visit to resolution[3], days | | |
| Mean | 20.5 | 15.1 |
| SD | 1.44 | 1.24 |
| Median | 18 | 14 |
| Min. | 3 | 1 |
| Max. | 40 | 30 |

Note:
1: n reflects the number of participants who had corneal event (GSK Scale) with grade worse than baseline at EOT
2: Resolution is defined as improvement to grade 1 or better
3: Calculated as the date of resolution minus the (last dose date +20 days).

Example SAFE_T4b
Protocol: 205678 
Population: Safety (Data as of: 24APR2018)

Table X

Summary of Time to Re-initiation of Study Treatment Post First Treatment Delay due to Corneal Events (GSK scale)

| | Treatment Group A (N=100) | Treatment Group B (N=100) |
|---|---|---|
| Number (%) of subjects with treatment delay due to corneal event (GSK scale) | 43 | 33 |
| Re-initiation of study treatment | 22 (51%) | 19 (58%) |
| Time to re-initiation [1], days | | |
| Mean | 20.5 | 15.1 |
| SD | 1.44 | 1.24 |
| Median | 18 | 14 |
| Min. | 3 | 1 |
| Max. | 40 | 30 |

Note:
1: Time to re-initiation of study treatment is calculated as the date of first dose post treatment delay minus (the date of last dose prior to treatment delay +21).

Example SAFE_T5

Protocol: 205678 
Population: Safety (Data as of: 24APR2018)

Table x.xxxx

Logistic regression analysis of possible risk factors for developing Corneal Events (GSK Scale)

| Variable | OR | 95% CI | P-value |
|---|---|---|---|
| 3.4 mg/kg vs. 2.5 mg/kg | xx.x | (xx.x, xx.x) | 0.xxx* |
| Male vs. Female | xx.x | (xx.x, xx.x) | 0.xxx |
| >= 65 vs. < 65 | xx.x | (xx.x, xx.x) | 0.xxx |
| Race | xx.x | (xx.x, xx.x) | 0.xxx |
| | xx.x | (xx.x, xx.x) | 0.xxx |
| | xx.x | (xx.x, xx.x) | 0.xxx |
| | xx.x | (xx.x, xx.x) | 0.xxx |
| Moderate/Severe vs. None | xx.x | (xx.x, xx.x) | 0.xxx |

* p<0.05

Example SAFE_T6
Protocol: 205678
Population: Safety


(Data as of: 24APR2018)

Table x.xxxx

Summary of Change from Baseline in Refraction (Spherical Equivalent)

| Timepoints | Eye | | Refraction | Treatment Group A (N=xxx) | Treatment group B (N=xxx) |
|---|---|---|---|---|---|
| Baseline | Right | Actual | n | xxx | xxx |
| | | | Mean | x.x | x.x |
| | | | SD | x.xx | x.xx |
| | | | Median | x.x | x.x |
| | | | Min | x | x |
| | | | Max | xxx | xxx |
| | Left | Actual | n | xxx | xxx |
| | | | Mean | x.x | x.x |
| | | | SD | x.xx | x.xx |
| | | | Median | x.x | x.x |
| | | | Min | x | x |
| | | | Max | xxx | xxx |
| End of | Right | Change from Baseline | n | xxx | xxx |
| | | | Mean | x.x | x.x |
| | | | SD | x.xx | x.xx |
| | | | Median | x.x | x.x |
| | | | Min | x | x |
| | | | Max | xxx | xxx |
| | Left | Change from Baseline | n | xxx | xxx |
| | | | Mean | x.x | x.x |
| | | | SD | x.xx | x.xx |
| | | | Median | x.x | x.x |
| | | | Min | x | x |
| | | | Max | xxx | xxx |
| | Right | Absolute Change from | n | xxx | xxx |
| | | | Mean | x.x | x.x |
| | | | SD | x.xx | x.xx |
| | | | Median | x.x | x.x |
| | | | Min | x | x |
| | | | Max | xxx | xxx |
| | Right | Absolute Change from | n | xxx | xxx |
| | | | Mean | x.x | x.x |
| | | | SD | x.xx | x.xx |
| | | | Median | x.x | x.x |
| | | | Min | x | x |
| | | | Max | xxx | xxx |

Last follow-up
Largest absolute
Change from
baseline

Example SAFE_T7

Protocol: 205678 
Population: Safety (Data as of: 24APR2018)

Table x.xxxx

Summary for Change from Baseline to Worst Post-Baseline in Schirmer's Test and Tear Break-up Time

| Parameter | | Statistics | Treatment Group A (N=xxx) | Treatment Group B (N=xxx) |
|---|---|---|---|---|
| Schirmer's Test (unit = mm) | Right eye | n | xxx | xxx |
| | | Mean | x.x | x.x |
| | | SD | x.xx | x.xx |
| | | Median | x.x | x.x |
| | | Min | x | x |
| | | Max | xxx | xxx |
| | Left eye | n | xxx | xxx |
| | | Mean | x.x | x.x |
| | | SD | x.xx | x.xx |
| | | Median | x.x | x.x |
| | | Min | x | x |
| | | Max | xxx | xxx |
| Tear Break-up time (unit = sec) | Right eye | n | xxx | xxx |
| | | Mean | x.x | x.x |
| | | SD | x.xx | x.xx |
| | | Median | x.x | x.x |
| | | Min | x | x |
| | | Max | xxx | xxx |
| | Left eye | n | xxx | xxx |
| | | Mean | x.x | x.x |
| | | SD | x.xx | x.xx |
| | | Median | x.x | x.x |
| | | Min | x | x |
| | | Max | xxx | xxx |

Example SAFE_T8
Protocol: 205678
Population: Safety



Table x.xxxx
Summary of Intraocular Pressure (IOP) ≥ 22mm Hg Anytime Postbaseline

| | | Treatment Group A (N = 342) | Treatment Group B (N = 365) |
|---|---|---|---|
| Right eye | n | 342 | 364 |
| | IOP ≥ 22mm Hg Anytime Post-baseline | 1 (<1%) | 2 (<1%) |
| Left eye | N | 342 | 364 |
| | IOP ≥ 22mm Hg Anytime Post-baseline | 1 (<1%) | 2 (<1%) |
| Subject (either eye) | n | 342 | 364 |
| | IOP ≥ 22mm Hg Anytime Post-baseline | 1 (<1%) | 2 (<1%) |

Example SAFE_T8a
Protocol: 205678
Population: Safety



Table x.xxx
Summary of Subjects Who Start Treatment for Intraocular Pressure (IOP) after 1st Dose of Study Drug

| | Treatment Group A (N = 342) | Treatment Group B (N = 365) |
|---|---|---|
| Subjects (n/%)Started Treatment for IOP after 1st Dose of Study Drug | 1 (<1%) | 2 (<1%) |

Example SAFE_T9
Protocol: 205678 Page 1 of 1
Population: Safety (Data as of: 24APR2018)

Table X

Shift in Pupillary Exam Findings from Baseline to Worst Post-Baseline

Treatment Group A

| | Baseline | Worst Post-Baseline | | | |
|---|---|---|---|---|---|
| | | | Category1 | Category 2 | Missing |
| | | n (%) | n (%) | n (%) | n (%) |
| Right eye (N=xx) | Category 1 | xx (xx.x) | xx (xx.x) | xx (xx.x) | xx (xx.x) |
| | Category 2 | xx (xx.x) | xx (xx.x) | xx (xx.x) | xx (xx.x) |
| | Missing | xx (xx.x) | xx (xx.x) | xx (xx.x) | xx (xx.x) |
| Left eye (N=xx) | | | | | |
| Subject (Worse eye) (N = xx) | | | | | |
| Both eyes at same exam (N = xx) | | | | | |

- Baseline percentage is based on N. percentage for worst post-Baseline value is based on Baseline n.

Treatment Group B

……..

Programming note: 'Right eye' and 'Left eye' are always included. 'Worst eye' and 'Both eye' are optional based on the programming note.

Example SAFE_T9a
Protocol: 205678 Page 1 of 1
Population: Full Safety (Data as of: 24APR2018)

Table X
Shift in Schirmer's Test from Baseline to Worst Post-Baseline

Treatment Group A

| | Baseline | Worst Post-Baseline | | | | |
|---|---|---|---|---|---|---|
| | | | Category1 | Category 2 | Category 3 | Missing |
| | | n (%) | n (%) | n (%) | n (%) | n (%) |
| Right eye (N=xx) | Category 1 | xx (xx.x) | xx (xx.x) | xx (xx.x) | xx (xx.x) | xx (xx.x) |
| | Category 2 | xx (xx.x) | xx (xx.x) | xx (xx.x) | xx (xx.x) | xx (xx.x) |
| | Category 3 | xx (xx.x) | xx (xx.x) | xx (xx.x) | xx (xx.x) | xx (xx.x) |
| | Missing | xx (xx.x) | xx (xx.x) | xx (xx.x) | xx (xx.x) | xx (xx.x) |
| Left eye (N=xx) | Category 1 | xx (xx.x) | xx (xx.x) | xx (xx.x) | xx (xx.x) | xx (xx.x) |
| | Category 2 | xx (xx.x) | xx (xx.x) | xx (xx.x) | xx (xx.x) | xx (xx.x) |
| | Category 3 | xx (xx.x) | xx (xx.x) | xx (xx.x) | xx (xx.x) | xx (xx.x) |
| | Missing | xx (xx.x) | xx (xx.x) | xx (xx.x) | xx (xx.x) | xx (xx.x) |

Note: Baseline percentage is based on N. percentage for worst post-Baseline value is based on Baseline n.

Treatment Group B

……..

Example SAFE_T10
Protocol: 205678 Page 1 of 1
Population: Safety (Data as of: 24APR2018)

Table x.xxxx
Summary for Change from Baseline in Pachymetry

| | | Treatment Group A (N=100) | Treatment Group B (N=100) |
|---|---|---|---|
| Right eye | n[1] | 100 | 100 |
| | Number (%) of ≥ 5% increase from baseline at worst post-baseline | 50 (50%) | 70 (70%) |
| Left eye | n [1] | 100 | 100 |
| | Number (%) of ≥ 5% increase from baseline at worst post-baseline | 50 (50%) | 70 (70%) |
| Subject (either eye) | n | 100 | 100 |
| | Number (%) of ≥ 5% increase from baseline at worst post-baseline | 50 (50%) | 50 (50%) |

Note: n is the number of eyes/subjects with baseline and at least one post baseline value.

Example SAFE_T12
Protocol: 205678 Page 1 of 1
Population: Safety (Data as of: 24APR2018)

Table x.xxxx
Summary of Presence of Descemet's Folds/Endothelial Lesions at Any Time Post-baseline

| | Treatment Group A (N=100) | Treatment Group B (N=100) |
|---|---|---|

| | | | |
|---|---|---|---|
| Right eye | n | 60 | 54 |
| | Descemet's fold | 25 (42%) | 34 (63%) |
| | Endothelial lesions | 45 (75%) | 48 (89%) |
| Left eye | n | 56 | 61 |
| | Descemet's fold | 23 (41%) | 37 (61%) |
| | Endothelial lesions | 42 (75%) | 53 (87%) |
| Subject (either eye) | n | 56 | 61 |
| | Descemet's fold | 23 (41%) | 37 (61%) |
| | Endothelial lesions | 42 (75%) | 53 (87%) |
| Right eye | n | 60 | 54 |
| | Descemet's fold | 25 (42%) | 34 (63%) |
| | Endothelial lesions | 45 (75%) | 48 (89%) |

Example SAFE_T13
Protocol: 205678 
Population: Safety (Data as of: 24APR2018)

Table x.xxxx

Shift in Albumin Creatinine Ratio (mg/g) from Baseline to Worst Post-Baseline

| | Baseline | | Worst Post-Baseline | | |
|---|---|---|---|---|---|
| | | | < 500 | [500, 2000] | > 2000 |
| | | n (%) | n (%) | n (%) | n (%) |
| Treatment Group A (N=xx) | < 500 | xx (xx.x) | xx (xx.x) | xx (xx.x) | xx (xx.x) |
| | [500, 2000] | xx (xx.x) | xx (xx.x) | xx (xx.x) | xx (xx.x) |
| | > 2000 | xx (xx.x) | xx (xx.x) | xx (xx.x) | xx (xx.x) |
| Treatment Group B (N=xx) | | | | | |
| Treatment Group C (N=xx) | | | | | |

- Baseline percentage is based on N. percentage for worst post-Baseline value is based on Baseline n.

Example SAFE_T14
Protocol: 205678
Population: Safety


(Data as of: 24APR2018)

Table x.xxxx
Summary of Findings for Punctate Keratopathy

| | | Dose Arm A (N=100) | Dose Arm B (N=100) |
|---|---|---|---|
| Right eye | n | 100 | 100 |
| | Worst grade among exams | | |
| | Mild | 5 (5%) | 10 (10%) |
| | Moderate | 34 (34%) | 17 (17%) |
| | Severe | 46 (46%) | 23 (23%) |
| | | 15 (15%) | 50 (50%) |
| | Most frequent grade among exams | | |
| | None | 5 (5%) | 10 (10%) |
| | Mild | | |
| | Moderate | 5 (5%) | 10 (10%) |
| | Severe | 34 (34%) | 17 (17%) |
| | | 46 (46%) | 23 (23%) |
| Left eye | | | |
| …….. | | | |
| Subject (worse eye) | | | |
| …… | | | |

1: n reflects the number of eyes with Punctate keratopathy worse than baseline at any post-baseline ocular exam

Example SAFE_T15
Protocol: 205678 
Population: Safety

Table x.xxxx
Summary of Change (Worsening, No Change, Improvement) in Best Corrected Visual Acuity (BCVA) from EOT Visit to Last Follow-up Visit

| | Change Category | Treatment Group A (N = 342) | Treatment Group B (N = 365) |
|---|---|---|---|
| Right eye | n | 342 | 364 |
| | Worsening | 1 (<1%) | 2 (<1%) |
| | No Change | 330 (96%) | 359 (98%) |
| | Improvement | 11 (3%) | 4 (1%) |
| Left eye | n | 342 | 364 |
| | Worsening | 1 (<1%) | 2 (<1%) |
| | No Change | 330 (96%) | 359 (98%) |
| | Improvement | 11 (3%) | 4 (1%) |
| Subject (Worse eye) | n | 342 | 364 |
| | Worsening | 1 (<1%) | 2 (<1%) |
| | No Change | 330 (96%) | 359 (98%) |
| | Improvement | 11 (3%) | 4 (1%) |

n is the number of eyes or subjects (worse eye) with exam findings at EOT visit worse than baseline, which will be used as denominator to calculate the percentage.

Example SAFE_T16
Protocol: 205678 
Population: Safety

Table x.xxxx
Summary of Worst Grade of Corneal Events (GSK Scale) during Cycle 1-4 by Randomized Topical Corticosteroids Treatment

| | | Treatment Group A (N = xx) | | Treatment Group B (N = xx) | |
|---|---|---|---|---|---|
| Timepoint | | Eyes randomized to corticosteroids | Eye randomized to no corticosteroids | Eyes randomized to corticosteroids | Eyes not randomized to corticosteroids |
| Baseline | **n** | 100 | 100 | 100 | 100 |
| | Grade 0 | 70 (70%) | 70 (70%) | 70 (70%) | 70 (70%) |
| | Grade 1 | 20 (20%) | 20 (20%) | 20 (20%) | 20 (20%) |
| | Grade 2 | 10 (10%) | 10 (10%) | 10 (10%) | 10 (10%) |
| | Grade 3 | 0 | 0 | 0 | 0 |
| | Grade 4 | 0 | 0 | 0 | 0 |
| Worst during Cycle 1-4 | n | 100 | 100 | 100 | 100 |
| | Grade 0 | 70 (70%) | 70 (70%) | 70 (70%) | 70 (70%) |
| | Grade 1 | 20 (20%) | 20 (20%) | 20 (20%) | 20 (20%) |
| | Grade 2 | 10 (10%) | 10 (10%) | 10 (10%) | 10 (10%) |
| | Grade 3 | 0 | 0 | 0 | 0 |
| | Grade 4 | 0 | 0 | 0 | 0 |

Example SAFE_T17
Protocol: 205678 
Population: Safety

Table x.xxxx
Summary of Best Corrected Visual Acuity(BCVA) score (logMAR score) during Cycle 1-4 by Randomized Topical Corticosteroids Treatment

| | | Treatment Group A (N =xx) | | Treatment Group B (N =xx) | |
|---|---|---|---|---|---|
| Timepoint | BCVA Score | Eyes Randomized to | Eye not to | Eyes Randomized to | Eyes not to |
| Baseline | N | xxx | xxx | xxx | xxx |
| | Mean | x.x | x.x | x.x | x.x |
| | SD | x.xx | x.xx | x.xx | x.xx |
| | Median | x.x | x.x | x.x | x.x |
| | Min | x | x | x | x |
| | Max | xxx | xxx | xxx | xxx |
| Worst during Cycle 1-4 | n | xxx | xxx | xxx | xxx |
| | Mean | x.x | x.x | x.x | x.x |
| | SD | x.xx | x.xx | x.xx | x.xx |
| | Median | x.x | x.x | x.x | x.x |
| | Min | x | x | x | x |
| | Max | xxx | xxx | xxx | xxx |
| | n | xxx | xxx | xxx | xxx |
| Worst change from baseline during Cycle 1- | No change/improve | xx(x.x%) | xx(x.x%) | xx(x.x%) | xx(x.x%) |
| | Possible worsened | xx(x.x%) | xx(x.x%) | xx(x.x%) | xx(x.x%) |
| | Definite worsened | xx(x.x%) | xx(x.x%) | xx(x.x%) | xx(x.x%) |
| Most frequent change from baseline during cycle 1-4 | No change/improve | xx(x.x%) | xx(x.x%) | xx(x.x%) | xx(x.x%) |
| | Possible worsened | xx(x.x%) | xx(x.x%) | xx(x.x%) | xx(x.x%) |
| | Definite worsened | xx(x.x%) | xx(x.x%) | xx(x.x%) | xx(x.x%) |
| Worst during Cycle 1-4 | BCVA decline to light perception | xx(x.x%) | xx(x.x%) | xx(x.x%) | xx(x.x%) |
| | BCVA decline to no light perception | xx(x.x%) | xx(x.x%) | xx(x.x%) | xx(x.x%) |

Note: No change/improved vision is defined as a change from baseline <0.12; a possible worsened vision is defined as a change from baseline >=0.12 to <0.3; a definite worsened vision is defined as a change from baseline >=0.3 logMAR score.

Example SAFE_T18
Protocol: 205678 
Population: Safety (Data as of: 24APR2018)

Table x.xxxx
Summary of Onset Time to First Drug-Related Corneal Event (GSK Scale) by Randomized Topical Corticosteroids Treatment

| | **Treatment Group A (N=xx)** | | **Treatment Group B (N=xx)** | |
|---|---|---|---|---|
| | Eyes randomized to corticosteroids | Eyes randomized to no corticosteroids | Eyes randomized to corticosteroids | Eyes randomized to no corticosteroids |
| Number (%) of eyes experienced drug-related corneal event (GSK scale) | 5 (50%) | 4 (40%) | 4 (40%) | 5 (50%) |
| Time to initiation, days | | | | |
| n | 5 | 5 | 5 | 5 |
| 1-21 | 1 (20%) | 1 (20%) | 1 (20%) | 1 (20%) |
| 22-42 | 2 (40%) | 2 (40%) | 2 (40%) | 2 (40%) |
| 43-63 | 1 (20%) | 1 (20%) | 1 (20%) | 1 (20%) |
| > 63 | 1 (20%) | 1 (20%) | 1 (20%) | 1 (20%) |
| Mean | 20.5 | 15.1 | 15.1 | 20.5 |
| SD | 1.44 | 1.24 | 1.24 | 1.44 |
| Median | 18 | 14 | 14 | 18 |
| Min. | 3 | 1 | 1 | 3 |
| Max. | 40 | 30 | 30 | 40 |

Example SAFE_T19
Protocol: 205678 
Population: Ocular Sub-Study (Data as of: 24APR2018)

Table x.xxxx
Summary of Onset Time to Initiation of Topical Corticosteroids Treatment in Eyes Not Randomized to Topical Corticosteroids Treatment

| | Treatment Group A (N = xx) | Treatment Group B (N = xx) |
|---|---|---|
| Number (%) of eyes that initiated topical Corticosteroids Treatment | 5 (50%) | 4 (40%) |
| Time to initiation, days | | |
| n | 5 | 5 |
| 1-21 | 1 (20%) | 1 (20%) |
| 22-42 | 2 (40%) | 2 (40%) |
| 43-63 | 1 (20%) | 1 (20%) |
| > 63 | 1 (20%) | 1 (20%) |
| Mean | 20.5 | 15.1 |
| SD | 1.44 | 1.24 |
| Median | 18 | 14 |
| Min. | 3 | 1 |
| Max. | 40 | 30 |

Note:
1: N reflects the number of eyes randomized to no topical corticosteroids treatment for ocular sub-study.

Example SAFE_T20
Protocol: 205678 
Population: Safety (Data as of: 24APR2018)

Table x.xxxx
Shift in Corneal Events (per Ocular Exam) from Baseline to Worst During Cycle 1-4 by Randomized Topical Corticosteroids Treatment

| | | Treatment Group A (N = xx) | | Treatment Group B (N= xx) | |
|---|---|---|---|---|---|
| Exam | Shift from Baseline to Worst (Cycle 1-4) | Eyes randomized to corticosteroids | Eyes not randomized to corticosteroids | Eyes randomized to Corticosteroids | Eyes not randomized to corticosteroids |
| Corneal Epithelium | n | 100 | 100 | 100 | 100 |
| | Normal to Normal | 30 (30%) | 30 (30%) | 30 (30%) | 30 (30%) |
| | Normal to Abnormal | 50 (50%) | 50 (50%) | 50 (50%) | 50 (50%) |
| | Abnormal to Normal | 0 | 0 | 0 | 0 |
| | Abnormal to Abnormal | 20 (20%) | 20 (20%) | 20 (20%) | 20 (20%) |
| Punctate Keratopathy | n | 100 | 100 | 100 | 100 |
| | None/Mild to None/Mild | 30 (30%) | 30 (30%) | 30 (30%) | 30 (30%) |
| | None/Mild to Moderate/Severe | 50 (50%) | 50 (50%) | 50 (50%) | 50 (50%) |
| | Moderate/Severe to None/Mild | 0 | 0 | 0 | 0 |
| | Moderate/Severe to Moderate/Severe | 20 (20%) | 20 (20%) | 20 (20%) | 20 (20%) |
| Corneal Ulcer | n | 100 | 100 | 100 | 100 |
| | Normal to Normal | 30 (30%) | 30 (30%) | 30 (30%) | 30 (30%) |
| | Normal to Abnormal | 50 (50%) | 50 (50%) | 50 (50%) | 50 (50%) |
| | Abnormal to Normal | 0 | 0 | 0 | 0 |
| | Abnormal to Abnormal | 20 (20%) | 20 (20%) | 20 (20%) | 20 (20%) |
| Microcystic Edema | n | 100 | 100 | 100 | 100 |
| | No to No | 30 (30%) | 30 (30%) | 30 (30%) | 30 (30%) |
| | No to Yes | 50 (50%) | 50 (50%) | 50 (50%) | 50 (50%) |
| | Yes to No | 0 | 0 | 0 | 0 |
| | Yes to Yes | 20 (20%) | 20 (20%) | 20 (20%) | 20 (20%) |

| | | | | | |
|---|---|---|---|---|---|
| Microcystic | n | 100 | 100 | 100 | 100 |
| Without Edema | No to No | 30 (30%) | 30 (30%) | 30 (30%) | 30 (30%) |
| | No to Yes | 50 (50%) | 50 (50%) | 50 (50%) | 50 (50%) |
| | Yes to No | 0 | 0 | 0 | 0 |
| | Yes to Yes | 20 (20%) | 20 (20%) | 20 (20%) | 20 (20%) |
| Subepithelial | n | 100 | 100 | 100 | 100 |
| Haze | No to No | 30 (30%) | 30 (30%) | 30 (30%) | 30 (30%) |
| | No to Yes | 50 (50%) | 50 (50%) | 50 (50%) | 50 (50%) |
| | Yes to No | 0 | 0 | 0 | 0 |
| | Yes to Yes | 20 (20%) | 20 (20%) | 20 (20%) | 20 (20%) |
| Corneal | n | 100 | 100 | 100 | 100 |
| Neovascularization | No to No | 30 (30%) | 30 (30%) | 30 (30%) | 30 (30%) |
| | No to Yes | 50 (50%) | 50 (50%) | 50 (50%) | 50 (50%) |
| | Yes to No | 0 | 0 | 0 | 0 |
| | Yes to Yes | 20 (20%) | 20 (20%) | 20 (20%) | 20 (20%) |
| Stroma | n | 100 | 100 | 100 | 100 |
| | Normal to Normal | 30 (30%) | 30 (30%) | 30 (30%) | 30 (30%) |
| | Normal to Abnormal | 50 (50%) | 50 (50%) | 50 (50%) | 50 (50%) |
| | Abnormal to Normal | 0 | 0 | 0 | 0 |
| | Abnormal to Abnormal | 20 (20%) | 20 (20%) | 20 (20%) | 20 (20%) |
| Active Opacity | n | 100 | 100 | 100 | 100 |
| | No to No | 30 (30%) | 30 (30%) | 30 (30%) | 30 (30%) |
| | No to Yes | 50 (50%) | 50 (50%) | 50 (50%) | 50 (50%) |
| | Yes to No | 0 | 0 | 0 | 0 |
| | Yes to Yes | 20 (20%) | 20 (20%) | 20 (20%) | 20 (20%) |
| Active Edema | n | 100 | 100 | 100 | 100 |
| | No to No | 30 (30%) | 30 (30%) | 30 (30%) | 30 (30%) |
| | No to Yes | 50 (50%) | 50 (50%) | 50 (50%) | 50 (50%) |
| | Yes to No | 0 | 0 | 0 | 0 |
| | Yes to Yes | 20 (20%) | 20 (20%) | 20 (20%) | 20 (20%) |

Example SAFE_T21
Protocol: 205678
Population: Full Safety



Table x.xxxx
Summary of Blurred Vision (CTCAE) Characteristics II

| | 2.5 mg/kg (N= xx) | 3.4 mg/kg (N= xx) | 3.4 mg/kg (N= xx) |
|---|---|---|---|
| Time to onset of first occurrence, days | | | |
| n | xx | xx | xx |
| Mean | xx.x | xx.x | xx.x |
| SD | xx.xx | xx.xx | xx.xx |
| Median | xx.x | xx.x | xx.x |
| Min. | xx | xx | xx |
| Max. | xx | xx | xx |
| 1 - 21 | xx (xx.x%) | xx (xx.x%) | xx (xx.x%) |
| 22 - 42 | xx (xx.x%) | xx (xx.x%) | xx (xx.x%) |
| 43 - 63 | xx (xx.x%) | xx (xx.x%) | xx (xx.x%) |
| 64 - 105 | xx (xx.x%) | xx (xx.x%) | xx (xx.x%) |
| >105 | xx (xx.x%) | xx (xx.x%) | xx (xx.x%) |
| Outcome of first occurrence [1] (n=xx) | | | |
| Resolved | xx (xx.x%) | xx (xx.x%) | xx (xx.x%) |
| re-started with dose delay and reduction | xx (xx.x%) | xx (xx.x%) | xx (xx.x%) |
| re-started with dose delay but no reduction | xx (xx.x%) | xx (xx.x%) | xx (xx.x%) |
| re-started with dose reduction but no delay | xx (xx.x%) | xx (xx.x%) | xx (xx.x%) |
| re-started without dose delay or reduction | xx (xx.x%) | xx (xx.x%) | xx (xx.x%) |
| not re-started | xx (xx.x%) | xx (xx.x%) | xx (xx.x%) |
| Not resolved, re-started | xx (xx.x%) | xx (xx.x%) | xx (xx.x%) |

| | | | |
|---|---|---|---|
| with dose delay and reduction | xx (xx.x%) | xx (xx.x%) | xx (xx.x%) |
| with dose delay but no reduction | xx (xx.x%) | xx (xx.x%) | xx (xx.x%) |
| with dose reduction but no delay | xx (xx.x%) | xx (xx.x%) | xx (xx.x%) |
| without dose delay or reduction | xx (xx.x%) | xx (xx.x%) | xx (xx.x%) |
| Not resolved, not re-started | xx (xx.x%) | xx (xx.x%) | xx (xx.x%) |
| not discontinued | xx (xx.x%) | xx (xx.x%) | xx (xx.x%) |
| discontinued, follow up ongoing | xx (xx.x%) | xx (xx.x%) | xx (xx.x%) |
| discontinued, follow up ended | xx (xx.x%) | xx (xx.x%) | xx (xx.x%) |
| Duration of first occurrence [1] [2] | | | |
| n | xx | xx | xx |
| Mean | xx.x | xx.x | xx.x |
| SD | xx.xx | xx.xx | xx.xx |
| Median | xx.x | xx.x | xx.x |
| Min. | xx | xx | xx |
| Max. | xx | xx | xx |
| Number of occurrences (based on subjects with the event) | | | |
| One | xx (xx.x%) | xx (xx.x%) | xx (xx.x%) |
| Two | xx (xx.x%) | xx (xx.x%) | xx (xx.x%) |
| Three or more | xx (xx.x%) | xx (xx.x%) | xx (xx.x%) |
| Outcome post treatment exposure | xx | xx | xx |
| Number of of subjects with unresolved Event at the end of treatment exposure, or with event onset post treatment exposure. | | | |
| Resolved | xx (xx.x%) | xx (xx.x%) | xx (xx.x%) |
| Not resolved, follow up ongoing | xx (xx.x%) | xx (xx.x%) | xx (xx.x%) |

| | | | |
|---|---|---|---|
| Not resolved, follow up ended | xx (xx.x%) | xx (xx.x%) | xx (xx.x%) |
| Time to resolution post treatment exposure, days | | | |
| n | xx | xx | xx |
| Mean | xx.x | xx.x | xx.x |
| SD | xx.xx | xx.xx | xx.xx |
| Median | xx.x | xx.x | xx.x |
| Min. | xx | xx | xx |
| Max. | xx | xx | xx |

[1] The duration is defined as time from onset of any **blurred vision** event to the first time the subject is free of any such event. It requires at least one day gap between the resolution of all events from first occurrence to the onset of second occurrence.

[2] Imputed AE stop date was used in the calculation of duration if the outcome of the event was resolved/resolved with sequalae and AE stop date was partial with day missing. Imputed AE start date was used in the calculation if the start date was partial with day missing.

[3] The end of treatment exposure is defined as last infusion date +20 days.

Programming note:

a. The event term (e.g. blurred vision) in footnote 1 need to be updated to be consistent with the title. b. Time to resolution post treatment exposure is calculated as (AE end date – end of treatment exposure) if there is unresolved event at the end of treatment exposure, or (first time the subject is free of any such event – onset date) if there is no unresolved event at the end of treatment exposure but with event onset post treatment exposure.

Example SAFE_T22
Protocol: 205678 
Population: Full Safety

Table x.xxxx

Summary of Percentage of Duration of Exposure with Blurred Vision (CTCAE)

| | 2.5 mg/kg (N=97) | 3.4 mg/kg (N=96) | 3.4 mg/kg Lyo (N=25) |
|---|---|---|---|
| Percentage of Duration of Exposure | | | |
| n | 48 | 31 | 11 |
| Mean | 52.9 | 46.8 | 42.8 |
| SD | 24.31 | 28.00 | 24.27 |
| Median | 55.4 | 51.2 | 48.8 |
| Min. | 2 | 2 | 5 |
| Max. | 95 | 89 | 75 |
| Category of Percentage of Duration of Exposure | | | |
| n | 48 | 31 | 11 |
| >0 to <=20% | 6 (13%) | 8 (26%) | 3 (27%) |
| > 20% to <= 40% | 8 (17%) | 6 (19%) | 1 (9%) |
| > 40% to <= 60% | 13 (27%) | 4 (13%) | 3 (27%) |
| > 60% to <= 80% | 13 (27%) | 9 (29%) | 4 (36%) |
| > 80% to <= 100% | 8 (17%) | 4 (13%) | 0 |

Note: n denotes the number of subjects with corneal events (CTCAE) of maximum grade >= 2 during exposure of study treatment.

Example: PRO_T1
Protocol: 205678
Population: ITT


(Data as of: 30MAY2001)

Table x.xxxx

Summary of Change in [EORTC QLQ-C30/EORTC QLQ-MY20] [Summary Score/Domain Scores] from Baseline by Visit

[summary score/domain score names (Physical Functioning, Role Functioning, etc)]

| Timepoint | | | Treatment Group A (N=xxx) | Treatment Group B (N=xxx) |
|---|---|---|---|---|
| Baseline | Actual Score | n | xxx | xxx |
| | | Mean | x.x | x.x |
| | | SD | x.xx | x.xx |
| | | Median | x.x | x.x |
| | | Min | x | X |
| | | Max | xxx | xxx |
| Week 4 | Actual Score | n | xxx | xxx |
| | | Mean | x.x | x.x |
| | | SD | x.xx | x.xx |
| | | Median | x.x | x.x |
| | | Min | x | x |
| | | Max | xxx | xxx |
| | Change from Baseline | n | xxx | xxx |
| | | Mean | x.x | x.x |
| | | SD | x.xx | x.xx |
| | | Median | x.x | x.x |
| | | Min | x | x |
| | | Max | xxx | xxx |
| Week x | Actual Score | n | xxx | xxx |
| | | Mean | x.x | x.x |
| | | SD | x.xx | x.xx |
| | | Median | x.x | x.x |
| | | Min | x | x |
| | | Max | xxx | xxx |
| | Change from Baseline | n | xxx | xxx |
| | | Mean | x.x | x.x |
| | | SD | x.xx | x.xx |
| | | Median | x.x | x.x |
| | | Min | x | x |
| | | Max | xxx | xxx |

Example: PRO_T2
Protocol: 205678
Population: ITT


(Data as of: 30MAY2001)

Table x.xxxx

Number (%) of patient with improvement in EORTC QLQ-C30EORTC QLQ-MY20 summary score/domain scores ≥ 5/10/MID by visit

summary score/domain score names (Physical Functioning, Role Functioning, etc)

| Timepoint | | Treatment Group A (N=xxx) | Treatment Group B (N=xxx) |
|---|---|---|---|
| Week 4 | N | xxx | xxx |
| | summary score/domain scores ≥ 5/10/MID | xxx(xx%) | xxx(xx%) |
| Week x | n | xxx | xxx |
| | summary score/domain scores ≥ 5/10/MID | xxx(xx%) | xxx(xx%) |

Example: PRO_T3
Protocol: 205678
Population: Safety


(Data as of: 30MAY2001)

Table x.xxxx

Summary of maximum post-baseline PRO-CTCAE score

| | Treatment Group A (N=xxx) | | | Treatment Group B (N=xxx) | | |
|---|---|---|---|---|---|---|
| | Frequency | Severity | Interference | Frequency | Severity | Interference |
| Item x | n=xxx | n=xxx | n=xxx | n=xxx | n=xxx | n=xxx |
| Response | | | | | | |
| 0 | xx(xx%) | xx(xx%) | xx(xx%) | xx(xx%) | xx(xx%) | xx(xx%) |
| 1 | xx(xx%) | xx(xx%) | xx(xx%) | xx(xx%) | xx(xx%) | xx(xx%) |
| 2 | xx(xx%) | xx(xx%) | xx(xx%) | xx(xx%) | xx(xx%) | xx(xx%) |
| 3 | xx(xx%) | xx(xx%) | xx(xx%) | xx(xx%) | xx(xx%) | xx(xx%) |
| 4 | xx(xx%) | xx(xx%) | xx(xx%) | xx(xx%) | xx(xx%) | xx(xx%) |
| 3+4 | xx(xx%) | xx(xx%) | xx(xx%) | xx(xx%) | xx(xx%) | xx(xx%) |
| Any Scale >0 | xx(xx%) | xx(xx%) | xx(xx%) | xx(xx%) | xx(xx%) | xx(xx%) |
| Item y | n=xxx | n=xxx | n=xxx | n=xxx | n=xxx | n=xxx |
| Response Scale | | | | | | |
| 0 | xx(xx%) | xx(xx%) | xx(xx%) | xx(xx%) | xx(xx%) | xx(xx%) |
| 1 | xx(xx%) | xx(xx%) | xx(xx%) | xx(xx%) | xx(xx%) | xx(xx%) |
| 2 | xx(xx%) | xx(xx%) | xx(xx%) | xx(xx%) | xx(xx%) | xx(xx%) |
| 3 | xx(xx%) | xx(xx%) | xx(xx%) | xx(xx%) | xx(xx%) | xx(xx%) |
| 4 | xx(xx%) | xx(xx%) | xx(xx%) | xx(xx%) | xx(xx%) | xx(xx%) |
| 3+4 | xx(xx%) | xx(xx%) | xx(xx%) | xx(xx%) | xx(xx%) | xx(xx%) |
| Any Scale >0 | xx(xx%) | xx(xx%) | xx(xx%) | xx(xx%) | xx(xx%) | xx(xx%) |

Note: For frequency levels, response scale stands for: 0-Never, 1-Rarely, 2-Occasionally, 3-Frequently, 4-Almost Constantly;for severity levels, response scale stands for: 0-None, 1-Mild, 2-Moderate, 3-Severe, 4-Very severe; for interference levels, response scale stands for: 0-Not at all, 1-A little bit, 2-Somewhat, 3-Quite a bit, 4-Very much.

Note: n1-n3 are the number of participants with at least one post-baseline response scale of the three attributes for a given item, which are used as denominator for calculation of percentage.

Example: PRO_T4
Protocol: 205678
Population: ITT


(Data as of: 30MAY2001)

Table x.xxxx

Summary of Worst Change from Baseline in NEI-VFQ-25 Overall Composite Score by Worst Grade of Corneal Event (GSK Scale)

| | | | Frozen Liquid (2.5 + 3.4 mg/kg) + Lyo (3.4 mg/kg) | | |
|---|---|---|---|---|---|
| | | | Worst Grade = 0 | Worst Grade = 1,2 | Worst Grade = 3,4 |
| | | | (N=xxx) | (N=xxx) | (N=xxx) |
| Baseline | Actual Score | n | xx | xx | xx |
| | | Mean | x.x | x.x | x.x |
| | | SD | x.xx | x.xx | x.xx |
| | | Median | x.x | x.x | x.x |
| | | Min | x.x | x.x | x.x |
| | | Max | xx.x | xx.x | xx.x |
| Worst Post-baseline | Actual Score | n | xx | xx | xx |
| | | Mean | x.x | x.x | x.x |
| | | SD | x.xx | x.xx | x.xx |
| | | Median | x.x | x.x | x.x |
| | | Min | x.x | x.x | x.x |
| | | Max | xx.x | xx.x | xx.x |
| | Change from Baseline | n | xx | xx | xx |
| | | Mean | x.x | x.x | x.x |
| | | SD | x.xx | x.xx | x.xx |
| | | Median | x.x | x.x | x.x |
| | | Min | x.x | x.x | x.x |
| | | Max | xx.x | xx.x | xx.x |

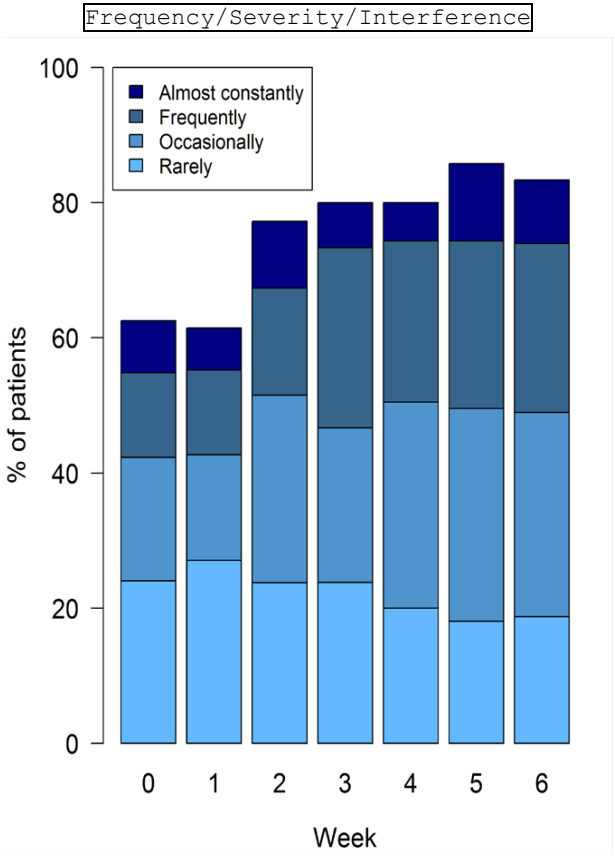
Example: PRO_F1
Protocol: 205678
Population: Safety


(Data as of: 30MAY2001)

Figure x.xxxx

Stacked Bar Chart of PRO-CTCAE Score by Attributes and Visit

Item X




Programming note: There is flexibility in choosing colour.

Example SAFE_L2
Protocol: 205678
Population: Safety


(Data as of: 24APR2018)

Listing X
Listing of Corneal Findings (GSK Scale)

Treatment Group A

| Centre Id/ Subj. | Age(y) / Sex/ Race | Eye | Grade/ Exam Finding(s) | Overall Grade of Corneal Examination Findings/Visual Acuity Grade/Overall Grade for GSK Scale for this eye | Date of Assessment /Visit | Time Since 1st Dose/ Last Dose | Action(s) Taken with study treatment/ Related |
|---|---|---|---|---|---|---|---|
| PPD | PPD | Left | Grade 2/ Moderate keratopathy, Grade 3/Diffuse Epithelial or stromal edema | Grade 3/ Not Applicable/ Grade 3 | PPD / Week 4 | 15 d/ 10 d | Dose reduced, Dose interrupted/delayed/ No |
| | | Right | Grade 3/ Diffuse microcysts | Grade 3/ Grade 1/ Grade 3 | PPD / Week 4 | 30 d/ 0 d | Dose interrupted/delayed/ Yes |
| | | Left | Grade 1/Mild superficial keratopathy | Grade 1/ Not Applicable/ Grade 1 | PPD / Week 7 | 32 d/ 0 d | Dose interrupted/delayed / No |
| | | Right | Grade 1/Mild superficial keratopathy | Grade 1/ Not Applicable/ Grade 1 | PPD / Week 7 | 32 d/ 0 d | Dose interrupted/delayed /No |

Treatment Group B
……..

Treatment Group C
……..