Division	:	Worldwide Development
Information Type	:	Statistical and Analysis Plan (SAP)

Title	:	Statistical and Analysis Plan for Reporting and Analysis Plan for Phase I, Open-Label, Multi-Center Study to Evaluate Safety, Pharmacokinetics and Pharmacodynamics of GSK2798745 after 28 Day Repeat Oral Administration to Adults with Diabetic Macular Edema
Compound Number	:	GSK2798745
Clinical Study Identifier	:	212669
Effective Date	:	21 Jun 2022

Description:

The purpose of this SAP is to describe the planned analyses and output to be included in the Clinical Study Report for Protocol 212669.

This SAP will be provided to the study team members to convey the content of the final statistical analysis deliverable.

Details of mock shells for all endpoints are provided in accompanying Shell document and Appendix 11.

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TABLE OF CONTENTS

PAGE

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1. INTRODUCTION

The purpose of this statistical and analysis plan (SAP) is to describe the planned analyses and output to be included in the Clinical Study Report for Protocol 212669.

Protocol Revision Chronology:		
Original Document Number: 2019N404030_00	Dated: 19-Sep-2019	Version: Original
Original Document Number: 2019N404030_01	Dated: 11-May-2020	Version: Amendment 01
Original Document Number: 2019N404030_02	Dated: 28-Oct-2020	Version: Amendment 02
Original Document Number: TMF-11874499	Dated: 24-Mar-2021	Version: Amendment 03
Original Document Number: TMF-14073254	Dated: 11-NOV-2021	Version: Amendment 04
Original Document Number: TMF-14377129	Dated: 2-Feb-2022	Version: Amendment 05

It is noted that GSK terminated this study due to the futility analysis as described in Section 3.1 of this SAP. The SAP details the analysis that is planned based on the sponsor's decision to terminate the study.

2. SUMMARY OF KEY PROTOCOL INFORMATION

2.1. Changes to the Protocol Defined Statistical Analysis Plan

Table 1 Changes to Protocol Defined Analysis Plan

Protocol	Reporting & Analysis Plan	
Statistical Analysis Plan	**Statistical Analysis Plan**	**Rationale for Changes**
Section 9.4.1.2. Pharmacodynamics (PD) Analysis A Bayesian probability model will be used to analyse the mean change from baseline in OCT at Day 28.	Section 9.1.5. Statistical Methodology Specification The primary analysis is changed to a Bayesian Repeated Measure Analysis.	A repeated measures model will allow to model data collected at all visits in a single model and does not require an assumption that the SD is known.
Section 9.3 Populations for Analysis Modified Safety Population has been included in SAP.	Section 4 Analysis Populations The modified Safety Population includes "All subjects in the Safety population excluding subjects from Site number: PPD	Site number PPD was closed prematurely due to significant quality issues. Specifically, the following were observed: • Protocol non-compliance • ICF deficiencies • Investigational Product dosing concerns • Inadequate source documentation and multiple source documentation

Protocol	Reporting & Analysis Plan	
Statistical Analysis Plan	**Statistical Analysis Plan**	**Rationale for Changes**
		deficiencies / inconsistencies • Significant delay in the CRA's access to the Electronic Medical Records (EMR). Based on these findings, the site PPD data are considered in question and incomplete. The Analysis Population definitions and resultant Data Displays have been adjusted to address these considerations. All safety and relevant study population tables will be undertaken using the Modified Safety Set. Selected safety (Overall and Ocular AE and SAEs) will be repeated for the full safety population.
Appendix 10 and 11	Reductions in the number of tables, listings and figures	Due to study termination due to futility, the number of TFLs being presented has been reduced
Section 9	Bayesian repeated mixed model changed to Bayesian mixed model	Due to termination, analysis will now only consider the baseline and 28 Day visit. Day 14 no longer included in final model

2.2. Study Objective(s) Endpoint(s)

Objectives	Endpoints
Primary	**Primary**
• To characterize the safety and tolerability of GSK2798745 following 28 days of daily oral dose administration to adult subjects with confirmed Diabetic Macular Edema (DME).	• Safety parameters including: complete ophthalmic examination, visual acuity, physical examination findings, vital sign measurements, clinical lab tests, 12-lead ECG, clinical monitoring and observation and adverse event reporting.
• To evaluate the pharmacodynamics of 28 daily oral doses of GSK2798745 in the study eye of adult subjects with DME.	• Mean change from baseline in center subfield retinal thickness in the study eye as measured by SD-OCT.
Secondary	**Secondary**
• To evaluate the pharmacokinetics of 28 daily oral doses of GSK2798745 in adult subjects with DME.	• Plasma concentrations of GSK2798745, major metabolite M1, and derived PK parameters, as data permit.
Exploratory	**Exploratory**
CCI [redacted]	

2.3. Study Design

Overview of Study Design and Key Features

Design Features	• Study 212669 is a multi-center, open-label, single arm, 28-day treatment study. The study will be composed of 3 periods for all subjects (Screening, Treatment, and Follow-up). The screening period may occur across more than one visit. The treatment period is 28 days. The follow-up visit will be approximately 28 days after the final dose. • At least 20 participants will be screened and enrolled to ensure 20 evaluable participants can be achieved at the end of the 28-day treatment period. Subjects that are screened and meet eligibility criteria will be enrolled in the study. A maximum of 30 participants may be enrolled. A minimum of 5 enrolled participants will be consented to partake in the PK subset for intensive PK sampling on Day 7 and Day 28. • If subjects are prematurely discontinued from the study prior to completing the primary endpoint 28-day dosing period, additional replacement subjects may be enrolled at the discretion of the Sponsor in consultation with the Investigator. Replacement subjects may be enrolled until the protocol defined sample size is achieved.
Dosing	• Each subject enrolled will receive a single daily 3.2 mg oral dose of GSK2798745 for 28 days.
Time & Events	• Refer to Appendix 2: Schedule of Activities (SoA)
Treatment Assignment	• This is a single arm, open-label treatment study. Each subject enrolled will receive a single daily 3.2 mg oral dose of GSK2798745 for 28 days.
Interim Analysis	• As this is an open-label study, data will be reviewed on an ongoing basis and may be shared externally to support discussion with regulatory agencies. • After approximately 8 participants completed the Day 28 visit, OCT and CCI data will be analysed on an ongoing basis to assess futility and the study may be terminated early if the futility criteria are met. Additional endpoints may be reviewed as well if necessary. Full details will be provided in the interim analysis charter.

2.4. Statistical Hypotheses / Statistical Analyses

The first co-primary objective of this study is to estimate the treatment effect on mean change from baseline in center subfield retinal thickness in the study eye as measured by SD-OCT at 28 days.

To ensure high probability of accurate decision making around the change at Day 28 in SD-OCT, the decision criteria are defined as:

"Positive" if Prob [CFB in OCT @ 28days > 70 µm decrease|data] > 80% and
"Negative" if Prob [CFB in OCT @ 28days< 95 µm decrease|data] > 90%.

If neither Positive nor Negative criterion are meet, an evaluation of the CCI mean change from baseline will be performed. A positive outcome will be concluded if the mean change from baseline in CCI after completing 28 days of dosing is 3 letters or greater as reviewed in the context of all available PD data.

The second co-primary objective is to evaluate safety of and tolerability of the treatment following 28 days of daily oral dose administration to adult subjects with confirmed DME, hence no formal hypothesis will be tested.

The secondary objective is to evaluate the pharmacokinetics of 28 daily oral doses of GSK2798745 and related M1 metabolite in adult study subjects and derive corresponding PK parameters. Hence, no formal hypothesis will be tested.

CCI

3. PLANNED ANALYSES

3.1. Interim Analysis

After approximately 8 participants completed the Day 28 visit, OCT and [CCI] data will be analysed on an ongoing basis to assess futility and the study may be terminated early if the futility criteria are met. Additional endpoints may be reviewed as well if necessary. Full details will be provided in the interim analysis charter. The ongoing interim analyses will be the responsibility of GSK Biostatistics.

3.2. End of Treatment Period Analysis/Interim Analysis of 28 Day SD-OCT and [CCI]

A preliminary summary of 28-day SD-OCT and [CCI] based on uncleaned data will be performed after the completion of the following sequential steps:

1. A minimum of 20 subjects have completed the 28-day treatment period and provided evaluable assessments of SD-OCT and [CCI] at baseline and at Day 28.
2. The source data of SD-OCT from the Reading Center and eCRF data of [CCI] Demography, Exposure, Disposition and Protocol Deviation is received as SAS datasets. Data needs to be as clean as possible, since this analysis will be done before final data cleaning and database lock/freeze (DBL/DBF) of the study.

The end-of-treatment interim analysis will be the responsibility of IQVIA Statistics and Programming Functions.

3.3. Final Analyses

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

1. All enrolled subjects have completed the study.
2. All required database cleaning activities have been completed and final database lock (DBL) has been declared by Data Management.
3. The dry runs have been completed prior to the DBL for review by the study team.

These analyses will be the responsibility of IQVIA Statistics and Programming Functions.

4. ANALYSIS POPULATIONS

Population	Definition / Criteria	Analyses Evaluated
Screened	All subjects who were screened for eligibility	• Screen failures
Enrolled	All subjects who passed screening and are eligible for the study with intension to dose. Note screening failures (who never passed screening even if rescreened) and subjects screened but never enrolled into the study are excluded from the Enrolled population as they did not enter the study.	• Study populations
Safety	All enrolled subjects who received at least one dose of study treatment.	• Study Population • Selected Safety Tables • Population and Safety listings
Modified Safety	All subjects in the Safety population excluding subjects from Site number: PPD	• Selected Study Population • Safety Tables • Some selected listings repeated
Pharmacodynamic (PD)	All subjects in the modified Safety population who had at least 1 post-baseline non-missing PD assessment.	• Pharmacodynamics analysis
Pharmacokinetic (PK)	All participants in the modified Safety population for whom a pharmacokinetic sample was obtained and analysed.	• Pharmacokinetic analysis
Intensive Pharmacokinetic (PK)	All subjects in the modified Safety population who had intensive PK sampling on Day 7 and Day 28 per section 1.3.3 of the protocol.	• Intensive Pharmacokinetic analysis

Note: "Enrolled" means a participant's, or their legally acceptable representative's, agreement to participate in a clinical study following completion of the informed consent process. Potential participants who are screened for the purpose of determining eligibility for the study, but do not participate in the study, are not considered enrolled.

Refer to Appendix 10: List of Data Displays which details the population used for each display.

* This Site Number PPD had serious quality issues, multiple protocol violations and therefore not deemed reliable.

4.1. Protocol Deviations

A protocol deviation is any noncompliance with the clinical trial protocol or Good Clinical Practice (GCP). The noncompliance may be either on the part of the subject, the ,zrA , , , , Gi , , , , , , , ity criteria will be considered an enrolment deviation.

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.

Exclusion from the analysis sets due to a deviation will be determined programmatically using the criteria described in the table of Analysis populations above. These deviations will not be included in the SDTM dataset but will be programmed in the protocol deviation analysis (ADaM) dataset. This dataset will be the basis for the summaries and listings of protocol deviations.

Data will be reviewed after locking the database and subjects will be assigned to relevant Analysis populations. Suggested population assignments will be sent to GSK for approval before proceeding with the final analysis.

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	
Data Displays for Reporting	
Description	Order in TLF
GSK2798745 3.2 mg OD	1

5.2. Baseline Definitions

In general, baseline is defined as the last non-missing pre-dose assessment including scheduled and unscheduled visits, unless stated otherwise.

The following specific scenarios will be considered for baseline definition of all ophthalmic examinations including but not restricted to SD-OCT, [redacted]:

- If Day -1 value is not available and a value from any unscheduled visit within 72 hours prior to Day -1 or Day 1 pre-dose is available, then it will be considered as baseline.
- If multiple values are available, for example, on Day -1 as well as any unscheduled visit before Day 1 dosing, then latest assessment will be considered as baseline.

A missing baseline assessment will not be imputed.

5.3. Multicentre Studies

In this multicentre study, unless specified otherwise in specific displays, the data will be presented in an aggregated manner due to small sample size.

5.4. Study Eye and Fellow Eye

The central subfield data analysed and provided by a Central Reading Center will be used for the analyses. The CRF data will not be used for reporting. This data is captured as two records per subject per visit one for the right eye and another for the left eye indicated by the Laterality variable. The identification of the Study Eye will be made by the Randomized Laterality variable which specifies whether the study eye is the right or left eye.

5.5. 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
11.1	Appendix 1: Exclusions from Per Protocol Population
11.2	Appendix 2: Schedule of Activities
11.3	Appendix 3: Assessment Windows
11.4	Appendix 4: Study Phases and Treatment Emergent Adverse Events
11.5	Appendix 5: Data Display Standards & Handling Conventions
11.6	Appendix 6: Derived and Transformed Data
11.7	Appendix 7: Reporting Standards for Missing Data
11.8	Appendix 8: Values of Potential Clinical Importance
11.9	Appendix 9: Abbreviations & Trademarks
11.10	Appendix 10: List of Data Displays
11.11	Appendix 11: Example Mock Shells for Data Displays

6. STUDY POPULATION ANALYSES

6.1. Overview of Planned Study Population Analyses

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

Study population analyses including summaries of subject ,disposition, protocol deviations, demographic and baseline characteristics, prior and concomitant medications, exposure and treatment compliance.

Details of the planned displays or mock shells are presented in Appendix 11: Example Mock Shells for Data Displays and accompanying shells document.

7. SAFETY ANALYSES

The primary statistical analysis will be to evaluate the safety and tolerability of GSK2798745 following 28 days of daily oral administration to adult subjects with DME. Safety endpoints including adverse events, vital signs (heart rate and blood pressure), clinical laboratory tests,12-lead ECG and CSSRS will be descriptively summarised and listed.

All Safety and relevant study population tables will be presented using the modified Safety analysis population. Overall Adverse Events, Ocular Adverse Events and Serious Adverse Events will be repeated for the Safety Analysis population. Some population tables will be repeated for subjects who received treatment dosing from site# PPD (6 subjects).

All safety and relevant population listings will be presented using the Safety analysis population. Some safety and population listings will be repeated for the modified safety set as presented in the listing of outputs in Appendix 10: List of Data Displays, and accompanying shells document.

7.1. Adverse Events Analyses

All adverse events starting on or after the first dose of study treatment will be included in the summaries. Adverse events including Serious (SAEs) and events related to study treatment will be summarised descriptively using frequency and percentages overall and by treatment phases (i.e., pre-treatment and on-treatment as defined in Section 11.4.1). On-treatment adverse events include those that occurred in the follow-up phase.

Adverse events will be coded using the standard Medical Dictionary for Regulatory Affairs (MedDRA dictionary). A Standardised MedDRA Query (SMQ) will be used to identify all Ocular, Non-ocular, and COVID-19 AEs.

The incidence of AEs and SAEs (Fatal and Non-Fatal) of COVID-19, COVID-19 AEs leading to study drug discontinuation, COVID-19 AEs leading to study withdrawal, and COVID-19 AEs by severity, will be obtained from standard AE and SAE summaries, without separate outputs due to small sample size.

If >25% participants report ≥1 COVID-19 AE/ SAE, then summaries of onset and duration of the first occurrence of COVID-19 AEs/ SAEs, and of COVID-19 symptoms (from the COVID-19 eCRF page) will be produced, otherwise not.

AEs will be listed by subjects. The details of the planned displays are provided in Appendix 10: List of Data Displays, and accompanying shells document.

7.2. Adverse Events of Special Interest Analyses

There are no other Adverse Events of Special Interest defined in the protocol of this study.

7.3. Clinical Laboratory Analyses

Laboratory evaluations will be summarised descriptively and listed. The details of the planned displays are in Appendix 10: List of Data Displays, and accompanying shells document.

7.4. Other Safety Analyses

Other non-laboratory safety test results including CSSRS, ECGs and vital signs will be summarised descriptively and listed. The details of the planned displays are presented in Appendix 10: List of Data Displays, and accompanying shells document.

8. PHARMACOKINETIC ANALYSES

8.1. Pharmacokinetic Analyses

Intensive PK sampling in a subset (n 5) of subjects will be undertaken on Day 7 and Day 28 with all subjects providing a trough PK (C_{trough}) sample on these 2 days. The Day 7 PK data will be used to ascertain the systemic exposure of the parent drug at the 3.2mg OD is consistent with the predicted exposure (see Table 1 of Protocol).

The plasma concentrations of GSK2798745 and its major metabolite M1 obtained on day 7 and day 28 will be analysed using non-compartmental methods described below. At end of study, all plasma samples (intensive PK Day 7 and Day 28) and trough samples will be analysed using a non-linear mixed effects analysis and is described in the pharmaco-statistical Section 8.1.3. The Population PK analyses using AUC and C_{max} will be reported in a separate PK document, outside of the Clinical Study Report (CSR).

8.1.1. Pharmacokinetic Analysis For Intensive PK Sampling

Refer to Appendix 5: Data Display Standards & Handling Conventions Derived Pharmacokinetic Parameters.

All non-compartmental pharmacokinetic derivation for the subjects with intensive PK sampling will be conducted by GSK under auspices of Clinical Pharmacology Modelling & Simulation (CPMS). Pharmacokinetic parameters will be calculated by standard non-compartmental analysis according to current working practices and using the currently supported version of WinNonlin Professional. All calculations of non-compartmental parameters will be based on actual sampling times. Pharmacokinetic parameters listed will be determined from the concentration-time data, as data permits. Pharmacokinetic parameters for both parent drug and metabolite M1 will be undertaken.

From the plasma concentration-time data [intensive sampling group], the following pharmacokinetic parameters will be determined for each subject for parent (GSK2798745) and metabolite (M1), if data permits:

Parameter	Parameter Description
C_{max}	Maximum observed plasma concentration
C_{trough}	Trough concentration
t_{max}	Time to C_{max}
AUC_{0-T}	Area under the curve over the dosing interval

As the trial was terminated, only trough concentrations (C_{trough}) for pharmacokinetic analysis will be provided.

8.1.2. Population of Interest

The pharmacokinetic analyses (Non-Compartmental) will be based on the PK population, unless otherwise specified.

8.1.3. Statistical Analyses / Methods

Statistics and programming will prepare summaries of derived PK parameters provided by the CPMS team, if data permits.

PK concentration data will be $\log_e$-transformed and summarised using geometric mean, 95% CI for the geometric mean, SD of $\log_e$-transformed data, $\%CV_b$, and median, min, max of back-transformed data.

Details of the planned displays are provided in Appendix 10: List of Data Displays, and accompanying shells document.

The following PK modelling will be performed by GSK CPMS, if data permits.

8.1.3.1. Pharmaco-Statistical Methodology Specification

Endpoint / Variables
All GSK2798745 plasma concentrations at Day 7 and Day 28 including trough samples
Model Summary
Based on the historical population PK model for GSK2798745, a maximum *a posteriori* probability (MAP) Bayesian estimator based on the limited number of subjects and samples will be applied to derive population PK parameters and associated inter-subject variability taking into account demographic and physiological status of this population. These parameters will then be used in simulations to derive the C_{max} and AUC over dosing interval at steady state for each subject. Internal validation of the population PK model with this population will be undertaken using standard tools such as visual predictive checks and in accordance with the regulatory guidance https://www.fda.gov/media/128793/download . The PK metrics for GSK2798745 (C_{max}, C_{trough}, AUC over dosing interval) will be used to assess any relationship with relevant PD parameter.

9. PHARMACODYNAMIC ANALYSES

9.1. Primary Pharmacodynamic Analyses

The coprimary endpoint of change from baseline in SD-OCT will be analysed using a Bayesian Analysis model.

9.1.1. Endpoint / Variables

Change from baseline in center subfield retinal thickness and center point in the study eye as measured by SD-OCT at 28 days.

9.1.2. Summary Measure

Mean change from baseline in SD-OCT at day 28.

9.1.3. Population of Interest

The primary pharmacodynamics analyses will be based on the Pharmacodynamic population, unless otherwise specified.

9.1.4. Strategy for Intercurrent (Post-Randomization) Events

The intercurrent events identified are:

Permanent Discontinuation of the Study Treatment due to any reason
Lack of Compliance to Study Treatment

9.1.4.1. Permanent Discontinuation of the Study Treatment due to any reason

For the intercurrent event of treatment discontinuation prior to Day 28, a Principal Stratum Strategy will be used for the Primary Estimand, where we are interested to evaluate the treatment effect on subjects who did not permanently discontinue the treatment before 28 days to establish the proof of mechanism of the drug in this Phase 1b study.
Thus, this Principal Stratum of interest will only include subjects who completed the study treatment until Day 28 and provided evaluable data at baseline and on Day 28.

A supplementary analysis using a Hypothetical Strategy will be performed, where we are interested in a hypothetical situation that the treatment discontinuation would not occur. Data from all subjects whether completed treatment until Day 28 or not will be analysed using the same Bayesian Repeated Measures (BRM) analysis as done for the primary analysis.

9.1.4.2. Lack of Compliance to Study Treatment

For the intercurrent event of lack of treatment compliance, a Principal Stratum Strategy will be used, where we are interested in subjects who have a high compliance to treatment (defined as 92% of treatment compliance). This principal stratum will include subjects who complete Day 28 with 92% of treatment compliance.

For all other intercurrent events a Treatment Policy Strategy will be considered for the Study eye.

9.1.5. Statistical Analyses / Methods

Details of the planned displays are provided in Appendix 10: List of Data Displays, and accompanying shells document.

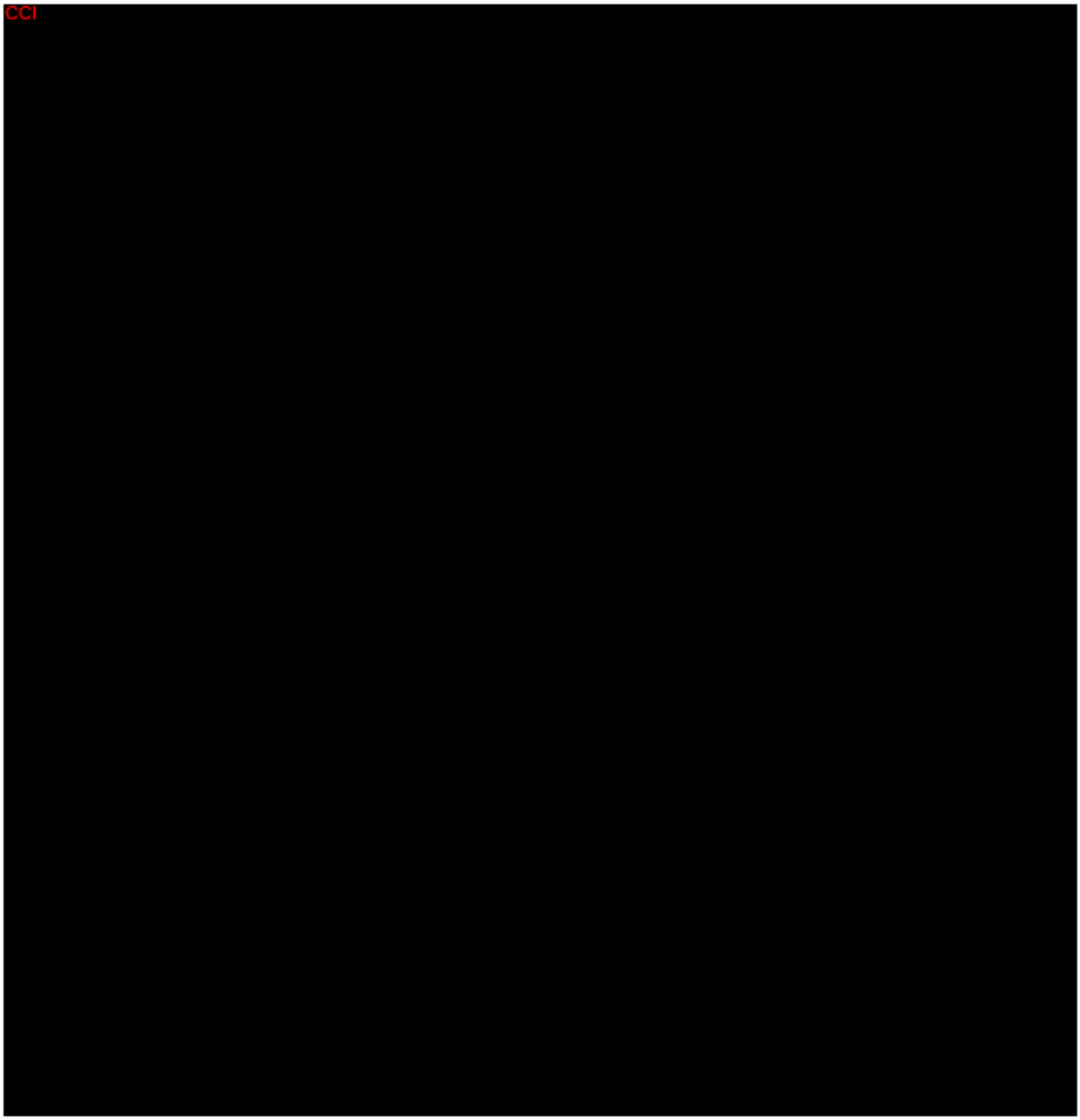
9.1.5.1. Statistical Methodology Specification

Endpoint / Variables
Change from baseline in subfield retinal thickness in the study eye as measured by SD-OCT at 28 days. Center Subfield retinal thickness is obtained from data provided by Merit CRO. The variables required from the external data (non-CRF collected data) are: Thickness Sector (thscr_c), laterality (lateral),). Laterality is to be matched with Study or Fellow Eye. Criteria of Center subfield thickness reliable (CTRSFTHR = 'Y). The values of THSCR_C must be multiplied by 1000 for reporting.
Bayesian Analysis Model Specification for the Primary Estimand using Principal Stratum Strategy (28 day Completers Analysis)
The mean change from baseline in OCT at Day 28 is assumed to have a t-distribution with (n-1) degrees of freedom. The variability will be calculated from the observed data. Evidence of an effect on 28-day OCT will be evaluated based on the posterior probabilities.
Model Checking & Diagnostics
Not applicable.
Model Results Presentation
Mean change from baseline, its 90% (equal-tailed) credible interval will be reported. The posterior probabilities that the CFB > 0 µm, CFB > 70 µm decrease and CFB < 95 µm decrease will be reported for Day 28 completers.

Additional analyses
• Exploratory Analyses: CCI [redacted]

9.2. Exploratory Pharmacodynamic Analyses

CCI [redacted]


CCI

10. REFERENCES

GlaxoSmithKline Document Number TMF-14377129 : Study Protocol Amendment 05 of 212669, Phase I, Open-Label, Multi-Center Study to Evaluate Safety, Pharmacokinetics and Pharmacodynamics of GSK2798745 after 28 Day Repeat Oral Administration to Adults with Diabetic Macular Edema .

11. APPENDICES

11.1. Appendix 1: Exclusions from Per Protocol Population

Per protocol population is not defined in this protocol. Important protocol deviations and exclusions from any other analysis population will be listed.

11.2. Appendix 2: Schedule of Activities

For a more detailed Schedule of Activities (SoA), please refer to the Section 1.3. Schedule of Activities of the protocol.

Procedure / Study Day:	Visit 1 Screening	Visit 2 Baseline	Treatment Period				Early Withdrawal (WD)	Follow-up Day 56 Week 8
			Day 1 Week 0	Visit 3 Day 7 Week 1	Visit 4 Day 14 Week 2	Visit 5 Day 28 Week 4		
Visit Window	-1 to -14	-3 to -1	1	6 8	13 16	27 30		54 - 58
Informed Consent	X							
Outpatient Visit	X	X		X	X	X	X	X
Demography	X							
Medical History (include substance usage & medication history)	X	X						
Complete Physical Examination	X						X	X
Brief Physical Exam		X			X	X		
12-Lead ECG	X	X		X[1]	X	X[1]	X	X
Fecal Occult Blood Test (FOBT)	X							
Columbia Suicidality Severity Rating Scale (CSSRS)	X			X	X	X	X	X
Vital Signs	X	X		X	X	X	X	X
Clinical Chemistry, Hematology & UA (including Cardiac Troponin, CPK)	X	X		X	X	X	X	X
HbA1c	X							
FSH / Estradiol	X							
Inclusion / Exclusion Criteria	X							
Dispense Study Medication		X						
Compliance Check for Study Medication				X	X	X	X	
First Day of Study Treatment			X					

Dosing in Clinic				X	X	X		
PK – Trough Sampling				X		X		
PK – Intensive Sampling				X		X		
Spectral Domain Optical Coherence Tomography (SD-OCT)	X	X			X	X	X	X
CCI								
General Ophthalmic Exam	X	X				X	X	X
CCI								
AE - SAE Assessment	X	X	X	X	X	X	X	X
Concomitant Medication	X	X	X	X	X	X	X	X

11.3. Appendix 3: Assessment Windows

11.3.1. Definitions of Assessment Windows for Analyses

There will not be multiple assessments for any of the endpoints and therefore assessment windows will not be used for reporting.
Unscheduled visits will be listed and included in the summary of worst case post-baseline assessments only.
Otherwise, only nominal time as per the protocol SoA will be used for all analysis.

11.4. Appendix 4: Study Phases and Treatment Emergent Adverse Events

11.4.1. Study Phases

Assessments and Adverse Events (AEs) will be classified according to the time of occurrence relative to taking the first dose of the study treatment.

Study Phase	Definition
Pre-Treatment	Date < Study Treatment Start Date
On-Treatment	Date ≥ Study Treatment Start Date (including follow-up period)

NOTE: Pre-treatment AEs will be listed only.

11.4.1.1. Study Phases for Concomitant Medication

Study Phase	Definition
Prior	If medication end date is not missing and is before study treatment start date.
Concomitant	Any medication or vaccine (including over-the-counter or prescription medicines, some vitamins, and/or herbal supplements), approved by the Investigator, in consultation with the GSK Medical Monitor, that the participant is receiving on or after the start of study treatment.

NOTE: Please refer to 12: Reporting Standards for Missing Data for handling of missing and partial dates for concomitant medication. Use the rules in this table if concomitant medication date is completely missing.

11.5. Appendix 5: Data Display Standards & Handling Conventions

11.5.1. Reporting Process

Software	
SAS 9.4 software will be used.	
Reporting Area	
SASAppU8_ADC Server	\\usadc-nas01a\cp_ops\BIOS\GlaxoSmithKline\GSK212669
Analysis Datasets	
Source dataset of SD-OCT from the Reading Center will be used for analysis 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 final analysis results	

11.5.2. Reporting Standards

General
Reporting will follow IQVIA SOP CS_WI_BS014 Revision 15 standards. Table specifications are created for each table output to describe the mapping of derived data to the tables. Specifications are considered optional for listings and figures – but the table specification template options (CS_TP_BS023 or CS_TP_BS024) will be used when creating specifications for listings and tables. Table, figures and listings displays will be used according to CS_TP_BS023 shell standards. Where displays are deemed similar to GSK Standards Library (IDSL) by STL, GSK displays will be used instead.
Formats
IQVIA SOP CS_WI_BS014 for decimal places (DP's) will be adopted for reporting of data based on the raw data collected, unless otherwise stated. Numeric data will be reported at the precision collected on the eCRF. The reported precision from non eCRF sources will follow the IQVIA SOP CS_TP_BS023 but may be adjusted to a clinically interpretable number of DP's.
Planned and Actual Time
Reporting for tables, figures and formal statistical analyses: Planned time relative to dosing will be used in figures, summaries, statistical analyses and calculation of any derived parameters, unless otherwise stated. The impact of any major deviation from the planned assessment times and/or scheduled visit days on the analyses and interpretation of the results will be assessed as appropriate. Reporting for Data Listings: Planned and actual time relative to study drug dosing will be shown in listings. 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. But will be included in the summary of worst-case post-baseline results. All unscheduled visits will be included in listings.

Descriptive Summary Statistics	
Continuous Data	N, n, mean, sd, median, min, max
Categorical Data	N, n, frequency, %
Graphical Displays	
Refer to IQVIA SOP CS_TP_BS023	

11.5.3. Reporting Standards for Pharmacokinetic

Reporting standards for PK data will be based on current CPMS NCA and POP PK guidance documents.

11.6. Appendix 6: Derived and Transformed Data

11.6.1. General

Multiple Measurements at One Analysis Time Point
• Not Applicable
Study Day

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

11.6.2. Study Population

Treatment Compliance
• Treatment compliance will be calculated based on the formula: **Treatment Compliance = Number of Actual Doses / (Planned Treatment Duration in Days * Frequency)** • Frequency is 2 for BID and 1 for daily. Treatment compliance could be greater than 100% if there are events of overdose. Cumulative compliance (since Day 1) at each visit will be calculated. • Planned Treatment Duration is defined as 28 days, with potential 8-week opt-in treatment period.
Extent of Exposure
• Number of days of exposure to study drug will be calculated based on the formula: **Duration of Exposure in Days = Treatment Stop Date – (Treatment Start Date) + 1** • Subjects who were randomized but did not report a treatment start date will be categorised as having zero days of exposure. • The cumulative dose will be based on the formula: **Cumulative Dose = Sum of (Number of Days x Total Daily Dose)** • If there are any treatment breaks during the study, exposure data will be adjusted accordingly.

11.6.3. Pharmacodynamic

SD-OCT
Change from baseline calculation
Change from Baseline = Post-Dose Visit Value – Baseline Value

CCI [redacted]

Other ophthalmology assessments will be summarised only descriptively using similar change from baseline assessments.

11.7. Appendix 7: Reporting Standards for Missing Data

11.7.1. Safety

ULN of Laboratory Results
Fold Upper Limit of Normal calculation
Fold ULN = Laboratory value / the Upper Limit of the Normal range.

LLN of Laboratory Results
Fold Lower Limit of Normal calculation
Fold LLN = Laboratory value / the Lower Limit of the Normal range.

11.7.2. Premature Withdrawals

Element	Reporting Detail
General	Subject's completion is defined as the completion of 28-day treatment period and provide an evaluable assessment of SD-OCT at 28 day Unscheduled assessments will only be included in listings

11.7.3. 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: o These data will be indicated by the use of a "blank" in subject listing displays. Unless all data for a specific visit are missing in which case the data is excluded from the table. o Answers such as "Not applicable" and "Not evaluable" are not considered to be missing data and should be displayed as such o In this analysis dataset, a missing assessment at any scheduled visit will be considered unevaluable, will not be imputed and will not be included in data analysis. Only observed (OC) cases will be included for all primary, secondary and exploratory endpoints.
Outliers	Any subjects excluded from the summaries and/or statistical analyses will be documented along with the reason for exclusion in the clinical study report.

11.7.3.1. Handling of Missing and Partial Dates

Element	Reporting Detail
General	Partial dates will be displayed as captured in subject listing displays. Where necessary, display macros may impute dates as temporary variables for sorting data in listings only.

11.8. Appendix 8: Values of Potential Clinical Importance

11.8.1. Laboratory Values

Haematology				
Laboratory Parameter	**Units**	**Category**	**Clinical Concern Range**	
			Low Flag (< x)	**High Flag (>x)**
Hematocrit	Ratio of 1	Male		0.54
		Female		0.54
		Δ from BL	↓0.075	
Hemoglobin	g/L	Male		180
		Female		180
		Δ from BL	↓25	
Lymphocytes	x109/ L		0.8	
Neutrophil Count	x109/ L		1.5	
Platelet Count	x109/ L		100	550
While Blood Cell Count (WBC)	x109/ L		3	20

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

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

11.8.2. Vital Signs

Vital Sign Parameter (Absolute)	Units	Clinical Concern Range	
		Lower	Upper
Systolic Blood Pressure	mmHg	90	180
Diastolic Blood Pressure	mmHg	40	120
Heart Rate	bpm	50	120

11.8.3. ECG

ECG Parameter	Units	Clinical Concern Range	
		Lower	Upper
Absolute			
Absolute QTc Interval	msec	> 450 [1]	
Absolute PR Interval	msec	< 110 [1]	> 220 [1]
Absolute QRS Interval	msec	< 75 [1]	> 110 [1]
Change from Baseline			
Increase from Baseline QTc	msec	> 60 [1]	

NOTES:

1. Represent standard ECG values of PCI for HV studies

11.8.4 Ophthalmic Examination Values of Potential Clinical Importance

Ophthalmic Parameter	Potential clinical concern
SD-OCT	If a patient has a central subfield change of >120 µm (this corresponds approximately with >15 letter change [Current Opinion in Ophthalmology 2010, 21:172–177]), as assessed by SD-OCT, then this assessment will be categorized as clinically significant.
CCI [redacted]	
IOP	If a patient has an IOP assessment which indicates hypo- or hypertonia as follows: Change from baseline of >= 5 mmHG IOP >= 25 mmHG IOP <8 mmHG Increase of >= 5mmHG from previous visit>= 5 mmHg difference between the two eyes at the same visit then this assessment will be categorized as clinically significant.
Pupil: pupillary defect	Any post-baseline finding of "Present" Afferent papillary defect (APD) in either eye if APD was not present in that eye at the baseline exam.
Motility	Post-baseline changes in eye motility in either eye if motility was normal in that eye at the baseline exam.

Ophthalmic Parameter	Potential clinical concern
Confrontation visual field	New post-baseline defects in the confrontation visual field.
Exam of upper and lower eyelids	Any serious change from baseline by clinical judgment of the investigator captured as an AE.
Meibomian gland dysfunction	Post-baseline 2-step worsening or 2+ worse per eye. PCIs include: 1) A subject that goes from absent to "obvious inspissation/mild injection, not trichiasis or lid thickening" or "inspissation, debris, obvious injection, lid thickening, may have trichiasis" 2) A subject that goes from "mild inspissation/debris without injection or thickening" to "inspissation, debris, obvious injection, lid thickening, may have trichiasis"
Conjunctival injection or chemosis	2-step worsening and 2+ or worse per eye change from baseline in dilation of conjunctival vessels, cilliary injection, subconjunctival hemorrhage, diffuse edema, subconj. fluid or prolapse of conj. over lower lid.
Tear Exam	Any serious change from baseline by clinical judgment of the investigator captured as an AE.
Cornea Epithelium	2+ worsening change from baseline for edema (i.e., a change from none to mild patchy microcystic changes), Any new opacity or whorl-like pattern
Corneal Stroma	Any serious change from baseline by clinical judgment of the investigator captured as an AE.
Corneal endothelium	Any serious change from baseline by clinical judgment of the investigator captured as an AE.
Anterior chamber cells	Post-baseline finding of Grade 2+ or worse per eye
Anterior chamber hypopyon	Any post-baseline finding of Present per eye
Anterior chamber flare	Any post-baseline finding of Grade 2+ or worse per eye
Lens Opacity	2+ or worse increase in any opacity as compared to baseline per eye (this can include cortical, nuclear, subcapsular). Any change to "cannot evaluate" will be flagged as PCI. The increase will be calculated by using the following codes: 1 - <1.0 = no Nuclear/Cortical/any subcapsular opacity, or less than Std. #1 2 - 1.0 = Nuclear/Cortical/any subcapsular opacity similar to Std. #1 3 - 1.5 = Nuclear/Cortical/any subcapsular opacity between Std. #1 and Std. #2 4 - 2.0 = Nuclear/Cortical/any subcapsular opacity similar to Std. #2 5 - 2.5 = Nuclear/Cortical/any subcapsular opacity between Std. #2 and Std. #3 6 - 3.0 = Nuclear/Cortical/any subcapsular opacity similar to Std. #3 7 - >3.0 = Nuclear/Cortical/any subcapsular opacity greater than Std. #3 8 - 8.0 = cannot evaluate
Iris	None
Vitreous	Any serious change from baseline by clinical judgement of the investigator captured as an AE.
Optic nerve head	Any serious change from baseline by clinical judgement of the investigator captured as an AE.
Posterior pole	Any serious change from baseline by clinical judgement of the investigator captured as an AE.

11.9. Appendix 9: Abbreviations & Trademarks

11.9.1. Abbreviations

Abbreviation	Description
AE	Adverse Event
ALT	Alanine aminotransferase (SGPT)
ANOVA	Analysis of Variance
AST	Aspartate aminotransferase (SGOT)
AUC	Area under concentration-time curve
AUC(0-τ)	Area under the concentration-time curve over the dosing interval
CCI [redacted]	
BMI	Body mass index
BP	Blood pressure
BPM	Beat Per Minute
BRM	Bayesian Repeated Measures
CI	Confidence Interval
CLr	Renal clearance
CL	Systemic clearance of parent drug
CL/F	Apparent clearance following oral dosing
C_{max}	Maximum observed concentration
CO2	Carbon Oioxide
CPK	Creatine phosphokinase
CPMS	Clinical Pharmacokinetics Modeling & Simulation
CPSR	Clinical Pharmacology Study Report
CPSSO	Clinical Pharmacology Science & Study Operations
eCRF	Electronic Case Report Form
CSME	Clinically Significant Macular Edema (CCI [redacted])
CSSRS	Suicidality Severity Rating Scale
C_{trough}	Pre-dose Trough Concentration measured at end of dosing interval
CV	Coefficient of variation
DA	Disc Area
DBP	Diastolic blood pressure
DM	Diabetes Mellitus
DME	Diabetic Macular Edema
DMPK	Drug Metabolism and Pharmacokinetics
DNA	Deoxyribonucleic acid
DR	Diabetic Retinopathy
ECG	Electrocardiogram
CCI [redacted]	
EVA	Electronic Visual Acuity
CCI [redacted]	
FDA	Food and Drug Administration
CCI [redacted]	
GLP	Good Laboratory Practice
GSK	GlaxoSmithKline

Abbreviation	Description
HbA1c	Glycated Hemoglobin
HBsAg	Hepatitis B surface antigen
h/hr	Hour(s)
HR	Heart rate
IB	Investigator's Brochure
ICH	International Conference on Harmonization of Technical Requirements for Registration of Pharmaceuticals for Human Use
IDSL	Integrated Data Standards Library
IND	Investigational New Drug
IP	Investigational Product
IRB	Institutional Review Board
IU	International Unit
IV	Intravenous
Kg	Kilogram
L	Liter
LDL	Low-density lipoprotein
LE	Left Eye
LFTs	Liver function tests
ln	Naperian (natural) logarithm
LLQ	Lower limit of quantification
Lp-PLA2	Lipoprotein associated phospholipase A2
µg	Microgram
µL	Microliter
MedDRA	Medical Dictionary for Regulatory Activities
Mg	Milligrams
mL	Milliliter
msec	Milliseconds
MMRM	Mixed Models Repeated Measures
NCA	Non-Compartmental Analysis
NQ	Non-quantifiable concentration measured as below LLQ
NVD	New Vessels on Disc
NVE	New Vessels – Elsewhere
SD-OCT	Optical coherence tomography
PA	Preliminary Analysis
PC	Phosphatidyl choline
PD	Pharmacodynamic
PDR	Proliferative Diabetic Retinopathy
PGx	Pharmacogenetics
pH	Power of Hydrogen
PK	Pharmacokinetic
PoC	Proof of Concept
Pop	Population
QC	Quality control
RAGE	Receptor for advanced glycation end products
RBC	Red blood cells

Abbreviation	Description
RE	Right Eye
RNA	Ribonucleic acid
SAC	Final Statistical Analysis Complete
SAE	Serious adverse event(s)
SAP	Statistical and Analysis Plan
SAS	Statistical Analysis Software
SD	Standard deviation
SD-OCT	Spectral domain optical coherence tomography
SGOT	Serum glutamic-oxaloacetic transaminase
SGPT	Serum glutamic pyruvic transaminase
SOP	Standard Operating Procedure
SPM	Study Procedures Manual
STL	Study Lead Statistician
$t_{1/2}$	Apparent Terminal Elimination Half-Life
t_{last}	Time of last observed quantifiable concentration
ULN	Upper limit of normal
UK	United Kingdom
US	United States
VEGF	Vascular Endothelial Growth Factor
WBC	White blood cells

11.9.2. Trademarks

Trademarks of the GlaxoSmithKline Group of Companies
NONE

Trademarks not owned by the GlaxoSmithKline Group of Companies
MONOLIX
NONMEM
RStudio
SAS
WinNonlin Professional

11.10. Appendix 10: List of Data Displays

Data displays include a combination of displays from standardized GSK IDSL library (with a corresponding reference number as GSK_XXX), IQVIA specific displays (referenced as IQVIA_Tx or IQVIA_Lx) and custom, non-standard displays.

A separate document provided the TFL templates is provided with this SAP. These templates describe the presentations for this study and therefore the format and content of the summary tables, figures, and listings to be provided by IQVIA Biostatistics.

11.10.1. Data Display Numbering

The following numbering will be applied for SAP generated displays:

Section	Tables	Figures
Study Population	1.1 to 1.8	None
Safety	3.1 to 3.22	None
Pharmacokinetic	4.1	None
Pharmacodynamic	6.1 to 6.7	6.1 to 6.3
Section	**Listings**	
ICH Listings	1 to 13	
Other Listings	14 to 34	

11.10.2. Mock Example Shell Referencing

Nonstandard specifications will be referenced as indicated and example mock-up displays provided in Appendix 11: Example Mock Shells for Data Displays, and accompanying shells document.

Section	Figure	Table	Listing
Study Population	POP_Fn	POP_Tn	POP_Ln
Safety	SAFE_Fn	SAFE_Tn	SAFE_Ln
Pharmacokinetic	PK_Fn	PK_Tn	PK_Ln
Pharmacodynamic	PD_Fn	PD_Tn	PD_Ln

NOTES:

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

11.10.3. Deliverables

This section includes deliverables of the IQVIA Statistics and Programming Functions.

Delivery	Description
PA	Preliminary Analysis (also referred to as the End of Treatment Analysis)
SAC	Final Statistical Analysis Complete

11.10.4. Study Population Tables

Study Population Tables						
No.	**Population**	**GSK Standard / Example Shell**	**Shell ID (Output ID)**	**Title**	**Programming Notes**	**Deliverable [Priority]**
Subject Disposition						
1.1.	Screened	GSK_ES6	GSK_ES6	Summary of Screening Status and Reasons for Screen Failure	ICH E3	SAC [1]
1.2.	Safety	GSK_ES1	GSK_ES1	Summary of Subject Disposition for the Subject Conclusion Record	ICH E3, Present the data by 2 groups mSafety, Site#PPD	SAC [1]
1.3.	Safety	GSK_SD1	GSK_SD1	Summary of Treatment Status and Reasons for Discontinuation of Study Treatment	ICH E3, Present the data by 2 groups mSafety, Site#PPD	SAC [1]
Protocol Deviation						

Study Population Tables						
No.	**Population**	**GSK Standard / Example Shell**	**Shell ID (Output ID)**	**Title**	**Programming Notes**	**Deliverable [Priority]**
1.4.	Enrolled	GSK_DV1	GSK_DV1	Summary of Important Protocol Deviations	ICH E3. Report only the protocol deviations which are defined as important. Present the data by 3 groups Enrolled, msafety and Site#PPD	SAC [1]
Population Analysed						
1.5.	Enrolled	GSK_SP1	GSK_SP1	Summary of Study Populations		SAC [1]
Demographic and Baseline Characteristics						
1.6.	Safety	GSK_DM1	GSK_DM1	Summary of Demographic Characteristics	ICH E3, FDAAA, EudraCT Present the data by 2 groups mSafety, Site#PPD	SAC [1]
1.7.	mSafety	POP_T1	POP_T1	Summary of Diabetes Type by Population	Type 1 and Type 2	SAC [1]
1.8.	mSafety	GSK_VS1	DIAB_T1	Summary of Diabetes Duration	In years	SAC [1]

11.10.5. Safety Tables

Safety: Tables						
No.	**Population**	**GSK Standard/ Example Shell**	**Shell ID (Output ID)**	**Title**	**Programming Notes**	**Deliverable [Priority]**
Adverse Events (AEs)						
3.1.	Safety	GSK_AE13	GSK_AE_SUM	Summary of Overall and Ocular Adverse Events	Please display study eye and fellow-eye separately as by groups.	SAC [1]
3.2.	mSafety	GSK_AE13	GSK_AE_SUM_mSAF	Summary of Overall and Ocular Adverse Events		SAC [1]
3.3.	mSafety	IQVIA_T2	AE007	Incidence of Ocular and Non-Ocular Adverse Events by System Organ Class and Preferred Term		SAC [1]
3.4	mSafety	IQVIA_T2	AE025	Incidence of Serious Ocular and Non-Ocular Adverse Events by System Organ Class and Preferred Term		SAC [1]
3.5	mSafety	IQVIA_T2	AE013	Incidence of Drug-Related Ocular and Non-Ocular Adverse Events by System Organ Class and Preferred Term		SAC [1]
3.6	mSafety	IQVIA_T2	AE014	Incidence of Serious Drug-Related Ocular and Non-Ocular Adverse Events by System Organ Class and Preferred Term		SAC [1]
3.7	mSafety	GSK_AE5A	AE019	Incidence of Ocular and Non-Ocular Adverse Events by System Organ Class and Preferred Term and Maximum Severity		SAC [1]

Safety: Tables						
No.	**Population**	**GSK Standard/ Example Shell**	**Shell ID (Output ID)**	**Title**	**Programming Notes**	**Deliverable [Priority]**
3.8	mSafety	GSK_AE15	AE030	Summary of On-Treatment Common (>=x%) Non-serious Adverse Events by System Organ Class and Preferred Term (Number of Subjects and Occurrences)		SAC [1]
COVID-19 related AEs						
3.9	mSafety	GSK_PAN1	GSK_PAN1	Summary of COVID-19 Assessments for Subjects with COVID-19 Adverse Events		SAC [1]
3.10	mSafety	GSK_PAN2	GSK_PAN2	Summary of COVID-19 Additional Assessments for Subjects with Suspected, Probable or Confirmed COVID-19 Case Diagnosis		SAC [1]
3.11	mSafety	IQVIA_PAN1	IQVIA_PAN1	Summary of time to onset and duration of first occurrence of COVID-19 Adverse Events	Optional, only if >25% participants reported ≥ 1 COVID-19 AE/SAE	SAC [1]
Laboratory: Chemistry including LFT						
3.12	mSafety	GSK_LB1	Chem001	Summary of Chemistry including Liver Function Test Changes from Baseline	Include LFT parameters	SAC [1]
3.13	mSafety	GSK_LB17	Chem002	Summary of Worst-Case Chemistry including Liver Function Test Results by PCI Criteria Post-Baseline Relative to Baseline	Include LFT parameters	SAC [1]

Safety: Tables						
No.	**Population**	**GSK Standard/ Example Shell**	**Shell ID (Output ID)**	**Title**	**Programming Notes**	**Deliverable [Priority]**
Laboratory: Hematology						
3.14	mSafety	GSK_LB1	Hem001	Summary of Hematology Changes from Baseline		SAC [1]
3.15	mSafety	GSK_LB17	Hem002	Summary of Worst-Case Hematology Results by PCI Criteria Post-Baseline Relative to Baseline		SAC [1]
Laboratory: Urinalysis						
3.16	mSafety	GSK_UR1	UR001	Summary of Worst Case Urinalysis Results Post-Baseline Relative to Baseline		SAC [1]
ECG						
3.17	mSafety	IQVIA_T10	EG001	Summary of ECG Values and Change from Baseline		SAC [1]
3.18	mSafety	IQVIA_T11	EG002	Summary of Shift from Baseline in ECG Findings		SAC [1]
Vital Signs						
3.19	mSafety	IQVIA_T10	VS001	Summary of Vital Signs Values and Change from Baseline Findings		SAC [1]
3.20	mSafety	IQVIA_T13	VS002	Summary of Subjects with Vital Sign Results outside PCI Ranges		SAC [1]

Safety: Tables						
No.	**Population**	**GSK Standard/ Example Shell**	**Shell ID (Output ID)**	**Title**	**Programming Notes**	**Deliverable [Priority]**
Columbia Suicidality Severity Rating Scale (CSSRS)						
3.21	mSafety	GSK_CSSRS1	CSSR01	Summary of Subjects with C-SSRS Suicidal Ideation or Behaviour during Treatment		SAC [1]
3.22	mSafety	GSK_CSSRS3	CSSR02	Shift Table of Changes in C-SSRS Categories from Pre-Treatment to On-Treatment		SAC [1]
3.23	mSafety	IQVIA_T13	EG003	Summary of Subjects with ECG Results outside PIC Ranges		SAC [1]

11.10.6. Safety Figures

Not planned due to small sample size.

11.10.7. Pharmacokinetic Tables

Pharmacokinetic: Tables						
No.	**Population**	**GSK Standard / Example Shell**	**Shell ID (Output ID)**	**Title**	**Programming Notes**	**Deliverable [Priority]**
GSK2798745 and M1 Metabolite						
4.1.	PK	GSK_PK01	PK001	Summary of GSK2798745 and M1 metabolite Pharmacokinetic Concentration-Time Data		SAC [1]

11.10.8. Pharmacodynamic Tables

Pharmacodynamic: Tables						
No.	**Population**	**GSK Standard/ Example Shell**	**Shell ID (Output ID)**	**Title**	**Programming Notes**	**Deliverable [Priority]**
SD-OCT						
6.1.	PD	PD_T1	PD001	Summary of Center Subfield Retinal Thickness in the Study and Fellow-Eye as Measured by SD-OCT, including change from baseline.	Present study eye and fellow eye as separate by groups	PA, SAC [1]
6.2.	PD	PD_T2	PD002	Bayesian Analysis of Change from Baseline in Center Subfield Retinal Thickness in the Study and Fellow Eye as Measured by SD-OCT at Day 28 (Day 28 Completers Analysis)	Includes only subjects who have completed Day 28	PA, SAC [1]
CCI [redacted]						

Pharmacodynamic: Tables						
No.	Population	GSK Standard/ Example Shell	Shell ID (Output ID)	Title	Programming Notes	Deliverable [Priority]
CCI [redacted]						

Pharmacodynamic: Tables						
No.	Population	GSK Standard/ Example Shell	Shell ID (Output ID)	Title	Programming Notes	Deliverable [Priority]
Other Exploratory Endpoints						
CCI [redacted]						

11.10.9. Pharmacodynamic Figures

Pharmacodynamic: Figures						
No.	**Population**	**GSK Standard/ Example Shell**	**Shell ID (Output ID)**	**Title**	**Programming Notes**	**Deliverable [Priority]**
SD-OCT						
6.1.	PD	SAFE_F2	PDFIG001	Individual Plot of Change from Baseline in Center Subfield Retinal Thickness in the Study Eye as Measured by SD-OCT	Mock shell provided is an example figure, not study specific X-axis is visit, Y-axis is change from baseline in center subfield retinal thickness. General comment: Format the intervals based on the interval of time.	PA, SAC [1]
CCI [redacted]						

Pharmacodynamic: Figures						
No.	**Population**	**GSK Standard/ Example Shell**	**Shell ID (Output ID)**	**Title**	**Programming Notes**	**Deliverable [Priority]**
SD-OCT & [redacted]						
6.3.	PD	SAFE_F2	PDFIG011	Correlation Plot of Change from Baseline in OCT versus [redacted] at Day 28.	Mock shell provided is an example figure, not study specific. X-axis is CFB of [redacted] at Day 28 , Y-axis is CFV of SDOCT at Day 28. Also present Pearson's Correlation coefficient (r).	SAC [1]

11.10.10. ICH Listings

ICH: Listings						
No.	**Population**	**GSK Standard / Example Shell**	**Shell ID (Output ID)**	**Title**	**Programming Notes**	**Deliverable [Priority]**
Subject Disposition						
1.	Screened	GSK_ES2	GSK_ES2	Listing of Reasons for Study Withdrawal	ICH E3	SAC [1]
2.	Safety	GSK_SD2	GSK_SD2	Listing of Reasons for Study Treatment Discontinuation	ICH E3	SAC [1]
Protocol Deviations						
3.	Enrolled	GSK_DV2	GSK_DV2	Listing of Important Protocol Deviations	ICH E3	SAC [1]
4.	Enrolled	GSK_IE3	GSK_IE3	Listing of Subjects with Inclusion/Exclusion Criteria Deviations	ICH E3	SAC [1]
Populations Analysed						
5.	Enrolled	GSK_SP3	GSK_SP3	Listing of Subjects Excluded from Any Population	ICH E3	SAC [1]
Demographic and Baseline Characteristics						
6.	Safety	GSK_DM2	DEMO	Listing of Demographic Characteristics	ICH E3	SAC [1]
7.	Safety	GSK_DM9	RACE	Listing of Race	ICH E3. Use Geographic ancestry data.	SAC [1]
Exposure and Treatment Compliance						

ICH: Listings						
No.	**Population**	**GSK Standard / Example Shell**	**Shell ID (Output ID)**	**Title**	**Programming Notes**	**Deliverable [Priority]**
8.	Safety	GSK_EX3	Exposure	Listing of Exposure	ICH E3	SAC [1]
9.1	Safety	GSK_COMP2a	Compliance	Listing of Compliance	ICH E3	SAC [1]
9.2	Safety	GSK_COMP2a	Noncompl_Reason	Listing of Reasons for Non-Compliance	ICH E3	SAC [1]
Adverse Events						
10.	Safety	GSK_AE8	AEList1	Listing of All Adverse Events	ICH E3;	PA, SAC [1]
11.	Safety	GSK_AE8	AEList3	Listing of Adverse Events Leading to Permanent Discontinuation of Study Treatment or Withdrawal from Study	ICH E3	SAC [1]
Serious Adverse Events						
12.	Safety	GSK_AE8	AEList5	Listing of Serious Adverse Events	ICH E3	SAC [1]
All Laboratory						
13.	Safety	IQVIA_L1 / GSK_LB5	LABList	Listing of All Laboratory Data for Subjects including Any Value of Potential Clinical Importance	ICH E3; include LFT and Urinalysis parameters	SAC [1]

11.10.11. Non-ICH Listings

Non-ICH: Listings						
No.	**Population**	**GSK Standard GSK Statistical Display Standard / Example Shell**	**Shell ID (Output ID)**	**Title**	**Programming Notes**	**Deliverable [Priority]**
Subject Disposition						
14	Screened	GSK_ES7	SCRFail	Listing of Reasons for Screen Failure	Journal Guidelines	SAC [1]
Prior and Concomitant Medications						
15	Safety	GSK_CM3	PM1	Listing of Diabetes Information	Listing-Other; Including Diabetes type, length of duration (in years)	SAC [1]
16	Safety	GSK_CM3	MH1	Listing of Medical History		SAC [1]
17	Safety	GSK_CM3	PM2	Listing of Prior Medication by Generic Term	For prior, including a column of relative time to first dosing day (Day 1) (in months, if month is missing, use December); DME medication[4] Listing-Other	SAC [1]
18	Safety	GSK_CM3	CM1	Listing of Concomitant Medication by Generic Term		SAC [1]
19	Safety	NA	LASERLIST	Listing of Laser History		SAC [1]
Adverse Events						
20	Safety	GSK_PAN7	COVList	Listing of All Subjects with Visits or Assessments		SAC [1]

Non-ICH: Listings						
No.	**Population**	**GSK Standard GSK Statistical Display Standard / Example Shell**	**Shell ID (Output ID)**	**Title**	**Programming Notes**	**Deliverable [Priority]**
				Impacted by COVID-19		
Hepatobiliary (Liver)						
21	Safety	IQVIA_L2	LFTList	Listing of Fold ULN for LFTs		SAC [1]
Ophthalmological Assessments						
22	PD	SAFE_T2	OPT001	Listing of General Ophthalmic Examinations Data including Abnormalities of Potential Clinical Importance	Include all subjects in the listing **excluding SD-OCT and** [redacted] and flag any values of potential clinical importance	SAC [1]
23	PD	SAFE_T3	OPT002	Listing of Absolute and Change from baseline in SD-OCT Numeric Endpoints for both eyes including Abnormalities of Potential Clinical Importance	Include all subjects in the listing and flag any values of potential clinical importance	SAC [1]
24	PD	SAFE_T4	OPT003	Listing of SD-OCT Non-numeric Endpoints for both eyes including	Include all subjects in the listing and flag any values of potential clinical importance	SAC [1]

Non-ICH: Listings						
No.	**Population**	**GSK Standard GSK Statistical Display Standard / Example Shell**	**Shell ID (Output ID)**	**Title**	**Programming Notes**	**Deliverable [Priority]**
				Abnormalities of Potential Clinical Importance		
25	PD	SAFE_T3	OPT004	Listing of Absolute and Change from Baseline in [redacted] Numeric Endpoints for Study and Fellow Eyes including Abnormalities of Potential Clinical Importance	Include all subjects in the listing and flag any values of potential clinical importance	SAC [1]
26	PD	SAFE_T4	OPT005	Listing of [redacted] Non-numeric Endpoints for both eyes included Abnormlities of Potential Clinical Importance	Include all subjects in the listing and flag any values of potential clinical importance	SAC [1]
27	PD	SAFE_T3	OPT006	Listing of Absolute and Change from baseline in [redacted] and [redacted] Endpoints for both eyes including Abnormalities of Potential Clinical Importance	Include all subjects in the listing and flag any values of potential clinical importance	SAC [1]

Non-ICH: Listings						
No.	**Population**	**GSK Standard GSK Statistical Display Standard / Example Shell**	**Shell ID (Output ID)**	**Title**	**Programming Notes**	**Deliverable [Priority]**
28	PD	SAFE_T4	OPT007	Listing of [redacted] and [redacted] Non-numeric Endpoints for both eyes including Abnormalities of Potential Clinical Importance		SAC [1]
ECG						
29	Safety	IQVIA_L3	ECGLIST01	Listing of Individual 12-lead ECG Results including Any Value of Potential Clinical Importance		SAC [1]
30	Safety	GSK_EG5	ECGLIST02	Listing of All ECG Findings for Subjects with an Abnormal Finding		
Vital Signs						
31	Safety	IQVIA_L5	VSLIST01	Listing of Individual Vital Signs Results including Any Value of Potential Clinical Importance		SAC [1]

Non-ICH: Listings						
No.	**Population**	**GSK Standard GSK Statistical Display Standard / Example Shell**	**Shell ID (Output ID)**	**Title**	**Programming Notes**	**Deliverable [Priority]**
Columbia Suicidality Severity Rating Scale (CSSRS)						
32	Safety	GSK_CSSRS4	CSSRLIST01	Listing of C-SSRS Suicidal Ideation and Behaviour Data		SAC [1]
PK Endpoints						
33	PK	GSK_PK07	PKLIST001	Listing of GSK279845 and M1 Metabolite Plasma Pharmacokinetic Concentration-Time Data [intensive & C_{trough} samples]		SAC [1]
34	PK	GSK_PK13	PKLIST002	Listing of Derived GSK279845 and M1 Metabolite Plasma Pharmacokinetic Paramaters [intensive & Ctrough samples]		SAC [1]

11.11. Appendix 11: Example Mock Shells for Data Displays

Please refer to the mock shells document.