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

Title	:	Reporting and Analysis Plan for GLP116174: A long term, randomised, double-blind, placebo-controlled study to determine the effect of albiglutide, when added to standard blood glucose lowering therapies, on major cardiovascular events in patients with Type 2 diabetes mellitus. Harmony Outcomes Trial.
Compound Number	:	GSK716155
Effective Date	:	30-NOV-2017

Description :

The purpose of this RAP is to describe the planned analyses and output to be included in the Clinical Study Report (CSR) and study disclosure related reporting for Protocol GLP116174.

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1. REPORTING & ANALYSIS PLAN SYNPOSIS

Overview	Key Elements of the RAP
Purpose	• This RAP describes the planned analyses and outputs required for the final CSR and study disclosure related reporting for study GLP116174.
Protocol	• This RAP is based on protocol amendment 3 (Dated: 04-APR-2017) of study GLP116174 (GSK Document No. : 2014N193553_03) and the most recent version of the electronic Case Report Form (eCRF).
Primary Objective	• To assess the effect of albiglutide with respect to MACE (major adverse cardiovascular events) when added to glycaemic standard of care versus standard of care alone
Primary Endpoint	• Time to first occurrence of adjudicated MACE (cardiovascular death, myocardial infarction, or stroke) The primary analysis will be non-inferiority. If the pre-specified non-inferiority criterion is met then superiority testing will be performed.
Study Design	• Randomized, double blind, parallel-group, placebo-controlled, multicenter study • Approximately 9400 subjects with type 2 diabetes and a previous history of cardiovascular disease and who do not have optimal glycaemic control will be randomly allocated in a 1:1 ratio to receive either once weekly albiglutide or matching placebo subcutaneous injections. • All subjects will receive standard of care which can be adjusted by their usual care provider(s) during the study according to clinical need. • The study will continue until it is projected that at least 611 adjudicated MACE events will have occurred while requiring that the projected median duration of subject follow-up be at least 1.5 years. Assuming a true hazard ratio of 1.0, 611 events will be needed to have 90% power to rule out a non-inferiority margin of 1.3 for the hazard ratio with two-sided type I error of 0.05. • Once it is projected that the target number of MACE events will have been collected and that the projected median duration of subject follow-up is at least 1.5 years, a 3 month window will be defined for conducting the final face to face visit.
Planned Analyses	• It is planned that database freeze will occur after the specified number of first MACE events has occurred and that the projected median duration of subject follow-up is at least 1.5 years and subjects complete the final face to face visits. Planned analyses will be performed after database freeze. • An Independent Data and Monitoring Committee (IDMC) is chartered to ensure external objective medical and/or statistical review of safety and/or efficacy issues in order to protect the ethical and safety interests of subjects and to protect the scientific validity of the study. There are no plans to adjust the final alpha on account of safety reviews conducted by the IDMC. • No other interim analyses are planned for this study.

Overview	Key Elements of the RAP
Key Analysis Populations	• Intent-to-Treat (ITT) population will be comprised of all randomized subjects excluding subjects who did not provide consent, based on the treatment to which the subject was randomized, and will be used to evaluate efficacy and Value Evidence and Outcomes endpoints. • Safety population will be comprised of all randomized subjects who receive at least one dose of study treatment excluding subjects who did not provide consent, based on the treatment the subject actually received, and will be used to evaluate safety.
Hypotheses	This trial will examine the following primary question: • Whether albiglutide is non-inferior by a margin of 1.3 with respect to its effect on adjudicated MACE, when added to glycaemic standard of care, versus standard of care alone. Letting λ_1 = hazard ratio for time to first MACE for albiglutide vs placebo, then: Null hypothesis: $\log \lambda_1 \geq \log(1.3)$ Alternative hypothesis: $\log \lambda_1 < \log(1.3)$ • If non-inferiority is established, the effect on adjudicated MACE will be tested for superiority in a closed testing procedure. Letting λ_1 = hazard ratio for time to first MACE for albiglutide vs placebo, then: Null hypothesis: $\log \lambda_1 \geq \log(1.0)$ Alternative hypothesis: $\log \lambda_1 < \log(1.0)$
Primary Analysis	Analysis of time to first occurrence of MACE will be performed using Cox Proportional Hazards regression with treatment group as the only covariate. The hypothesis of non-inferiority of albiglutide relative to placebo will be tested. If non-inferiority is established, the hypothesis of superiority of albiglutide relative to placebo will be tested.

Secondary Analyses	Secondary endpoints:
	• Time to first occurrence of the following:
	  • MACE or urgent revascularization for unstable angina
	  • The individual components of the primary endpoint (cardiovascular death, myocardial infarction, stroke)
	  • Cardiovascular death or hospitalization due to heart failure
	• Time to initiation of insulin of more than 3 months duration for those subjects not treated with insulin at study start
	• Time to initiation of prandial insulin in those subjects on basal insulin at study start
	• Proportion of subjects achieving glycaemic control (HbA1c $\leq$ 7.0% at final assessment) with no severe hypoglycaemic incidents and weight gain <5% of body weight
	• The time to first occurrence of a clinically important microvascular event (see

Overview	Key Elements of the RAP
	Section 11.6.4) • Change in glycated haemoglobin (HbA1c) • Change in body weight • Patient reported outcomes from Treatment Related Impact Measure-Diabetes (TRIM-D)/EQ-5D • All cause mortality • Non-fatal serious adverse events (SAEs) • Adverse events (AEs) leading to discontinuation of investigational product (IP) • AEs of special interest • Change in estimated glomerular filtration rate (eGFR) calculated using the Modification of Diet in Renal Disease (MDRD) formula • Change in blood pressure (BP) and heart rate

2. SUMMARY OF KEY PROTOCOL INFORMATION

2.1. Changes to the Protocol Defined Statistical Analysis Plan

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

Table 1 Changes to Protocol Defined Analysis Plan

Protocol	Reporting & Analysis Plan	
Statistical Analysis Plan	**Statistical Analysis Plan**	**Rationale for Changes**
• Section 2 indicated that electronic health records (EHR) analyses would be undertaken after the main trial results are published.	• Indicates that EHR analyses will be done after the completion of the Clinical Study Report (Section 2.2).	• The RAP reflects the EHR workplan.
• The endpoint of time to initiation of prandial insulin for subjects on basal insulin at study start did not have a defined duration.	• Time to initiation of prandial insulin (for subjects on basal insulin at study start) requires a 3 month duration (Section 8.1.1).	• Consistency with time to initiation of insulin endpoint.
• Section 6.2.1.1 specified "Revascularization (other than urgent revascularization for unstable angina, a component of a secondary endpoint)" as an "Other CV" event.	• Specifies "Revascularization (other than revascularizations intended for CEC adjudication)" as an "Other CV" event (Section 9.2.1).	• More precise description of the events of interest.
• Section 6.2.3 specified "Injection Site Reactions" as an adverse event of special interest.	• Specifies "Investigational Product Injection Site Reactions" as an adverse event of special interest (Section 8.2.1).	• Clarification of protocol.
• Section 6.3.1 did not specify that questionnaires were to be collected only while subjects were on study treatment.	• Reflects that questionnaires are to be collected only while subjects are on study treatment (Section 8.3.1).	• Clarification of protocol.
• Section 8.3.1 described a Per-Protocol Population along with a corresponding Per-Protocol Analysis	• Includes a Per-Protocol Analysis that excludes data from the ITT population based on timing of specified noncompliance (see Section 11.1.2). No Per-Protocol population is defined.	• More complete utilization of subject data.
• Enrolled population was not defined in the protocol	• Includes an Enrolled population (Section 4).	• Recently implemented standards indicate this is required for specified disclosure summaries.
• Section 8.3.6.1 specified a recurrent events analysis in which the total number of all	• Specifies a recurrent events analysis in which the total number of all MACE, MI, or	• Recurrent event analysis is not needed for CV death since number of events is

Protocol	Reporting & Analysis Plan	
Statistical Analysis Plan	**Statistical Analysis Plan**	**Rationale for Changes**
MACE or any of its components would be analyzed.	stroke (but not CV death) events will be analyzed (Section 7.1.2).	either 0 or 1.
• Section 8.3.6.2 specified a recurrent events analysis for severe hypoglycaemic events using a Poisson regression model with treatment and visit as factors.	• Specifies a recurrent events analysis for severe hypoglycaemic events in a manner similar to that specified for MACE, MI and stroke (Section 8.2.2).	• Consistency in recurrent event analysis methodology.
• Section 8.3.6.5 specified analysis by an analysis of covariance (ANCOVA) model for change from baseline TRIM-D and EQ-5D.	• Specifies use of mixed model repeated measures (MMRM) instead of ANCOVA (Section 8.3.2).	• Consistency in repeated measures analysis methodology.

2.2. Study Objectives and Endpoints

Objectives	Endpoints
Primary Objective	**Primary Endpoint**
To assess the effect of albiglutide with respect to MACE when added to glycaemic standard of care versus standard of care alone	• Time to first occurrence of MACE (cardiovascular death, myocardial infarction, or stroke) The primary analysis will be non-inferiority. If the pre-specified non-inferiority criterion is met then superiority testing will be performed[1].
Secondary Objectives	**Secondary Endpoints**

To supplement the primary objective by further characterization of the effects of albiglutide on cardiovascular outcomes	• Time to first occurrence of the following:
	  • MACE or urgent revascularization for unstable angina
	  • The individual components of the primary endpoint (cardiovascular death, myocardial infarction, stroke)
	  • Cardiovascular death or hospitalization due to heart failure

To evaluate the effects of albiglutide on metabolic management of type 2 diabetes	• Time to initiation of insulin of more than 3 months duration for those subjects not treated with insulin at study start • Time to initiation of prandial insulin in those subjects on basal insulin at study start • The proportion of subjects achieving glycaemic control (HbA1c $\leq$ 7.0% at final assessment) with no severe hypoglycaemic incidents and weight gain <5% of body weight. • The time to first occurrence of a clinically important microvascular event (see Section 11.6.4) • Change in HbA1c • Change in body weight • Patient reported outcomes from TRIM-D/EQ5D

Objectives	Endpoints
To evaluate the safety of albiglutide	• All cause mortality • Non-fatal serious adverse events (SAEs) • Adverse events (AEs) leading to discontinuation of investigational product (IP) • AEs of special interest • Change in estimated glomerular filtration rate (eGFR) calculated using the Modification of Diet in Renal Disease (MDRD) formula • Change in blood pressure (BP) and heart rate
Exploratory Objectives	**Exploratory Endpoints**
To evaluate patient reported experience of diabetes treatment	• Patient reported outcomes from study-specific questionnaire
To evaluate (at a subset of sites) barriers to using the electronic health record (EHR) to facilitate trial enrolment and the quality of EHR data for use in populating baseline characteristics and identifying events of interest during trial follow-up[2]	• Workflow impact of an EHR-generated list of subjects to facilitate trial enrolment. • Concordance, sensitivity, specificity and accuracy of baseline characteristics extracted from the EHR compared with those reported on the electronic case report form (eCRF)[3] • Concordance, sensitivity, specificity and accuracy of EHR-identified events compared with study events.[3,4]

1. As part of a closed testing procedure and therefore no adjustment will be made to the significance level (see Section 11.11).
2. Details are provided in a separate EHR ancillary study protocol (see Section 11.7 of the main study protocol). Results from this exploratory investigation will be reported separately from the main clinical study report.
3. Comparison of EHR identified events with study events will be conducted in the same data subset.
4. Analyses to be undertaken after the completion of the Clinical Study Report.

2.3. Study Design

Overview of Study Design and Key Features	
Design Features	• Randomized, double blind, parallel-group, placebo-controlled, multicenter study.
Dosing and Treatment Assignment	• Approximately 9400 subjects with Type 2 diabetes and a previous history of cardiovascular disease and who do not have optimal glycaemic control will be randomly allocated in a 1:1 ratio to receive either once weekly albiglutide or matching placebo subcutaneous injections. • All subjects will receive standard of care which can be adjusted by their usual care provider(s) during the study according to clinical need. • Randomization schedule was generated by PPD. Centralized randomization via PPD Interactive Response Technology (IRT) system will be used for treatment allocation and assignment of Investigational Product (IP).
Planned Analysis	• The study will continue until it is projected that at least 611 adjudicated MACE events will have occurred while requiring that the projected median duration of subject follow-up be at least 1.5 years. Assuming a true hazard ratio of 1.0, 611 events will be needed to have 90% power to rule out a non-inferiority margin of 1.3 for the hazard ratio with two-sided type I error of 0.05. • The aggregate blinded event-rate data will be periodically reviewed by the Executive Committee and the sponsor. Should emerging data diverge significantly from protocol assumptions, the total sample size and/or follow up time may be adjusted, within the bounds of feasibility, to achieve the event target. • Once it is projected that the target number of MACE events will have been collected and that the projected median duration of subject follow-up is at least 1.5 years, a 3 month window will be defined for conducting the final face-to-face visit. • It is planned that database freeze will occur after the specified number of MACE events have occurred and that the projected median duration of subject follow-up is at least 1.5 years and subjects complete the final face-to-face visits. Planned analyses will be performed after database freeze. • An Independent Data Monitoring Committee (IDMC) will monitor progress of the study and ensure that it meets the highest standards of ethics and subject safety. There are no plans to adjust the final alpha on account of safety reviews conducted by the IDMC. • No other interim analyses are planned for this study
Adjudication Committees	• A Cardiovascular Endpoint Committee (CEC) and a Pancreatitis Adjudication Committee (PAC) blinded to treatment allocation will review and adjudicate events as described in the protocol. Events reviewed by the CEC include myocardial infarction, stroke, unstable angina requiring hospitalization, hospitalization for heart failure, sudden cardiac death, and transient ischemic attack (TIA). In addition, all clinical events submitted for adjudication and all other SAEs with a fatal outcome will be reviewed and adjudicated to classify the cause of death as cardiovascular, non-cardiovascular, or undetermined.

2.4. Statistical Hypotheses

This trial will examine the following primary question:

- Whether albiglutide is non-inferior by a margin of 1.3 with respect to its effect on adjudicated MACE, when added to glycaemic standard of care, versus standard of care alone. Letting λ_1 = hazard ratio for time to first MACE for albiglutide vs placebo, then:

  Null hypothesis: $\log \lambda_1 \geq \log(1.3)$
  Alternative hypothesis: $\log \lambda_1 < \log(1.3)$

- If non-inferiority is established, the effect on adjudicated MACE will be tested for superiority in a closed testing procedure. Letting λ_1 = hazard ratio for time to first MACE for albiglutide vs placebo, then:

  Null hypothesis: $\log \lambda_1 \geq \log(1.0)$
  Alternative hypothesis: $\log \lambda_1 < \log(1.0)$

3. PLANNED ANALYSES

This study is being conducted under the sponsorship of the GlaxoSmithKline (GSK) group of companies. Unless specified otherwise, the statistical analyses are being performed under contract with PPD, in collaboration with the GSK group of companies.

3.1. Interim Analyses

An Independent Data Monitoring Committee (IDMC) will monitor progress of the study and ensure that it meets the highest standards of ethics and subject safety. An independent statistical data analysis center (SDAC) will perform the unblinded analyses to support the IDMC reviews.

There is no planned, pre-defined test to determine whether the study should be stopped early for benefit or non-inferiority. However, in order for the IDMC to fulfil its ethical accountability to protect subjects it is not prevented or prohibited from considering stopping the trial in case of overwhelming evidence of MACE benefit.

All cardiovascular (CV) event data, together with other data, will be sent to the IDMC for review approximately every 6 months after the first subject has been randomized to receive treatment. This frequency may be adjusted, if deemed necessary by the IDMC, depending on factors such as the enrolment rates and the rate of safety events. There are no plans to stop the study early for a non-inferiority or benefit claim, however should the IDMC identify in the course of its scheduled reviews overwhelming evidence of MACE benefit (e.g., $p < 0.001$), with directionally consistent findings on all-cause mortality, the IDMC might consider recommending early stopping. This approach essentially preserves the final alpha for the end-of-study analysis at 5% and hence there are no plans to adjust

the final alpha on account of safety reviews conducted by the IDMC. The IDMC charter, reporting and procedures are outlined in separate documents.

No other interim analyses are planned for this study.

If the trial is stopped for reasons outlined above (e.g., for increased MACE risk or other safety concerns), point estimates, 95% confidence intervals, and p-values will be generated for the primary and key secondary endpoints. P-values will be compared against a nominal two-sided 0.05 level and will be provided for descriptive purposes only.

3.2. Final Analyses

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

1. It is projected that the target number of primary endpoint events (611) has been attained and the projected median duration of subject follow-up is at least 1.5 years, as defined in the protocol, and final face-to-face visits have occurred.
2. Completion of adjudication of CV and pancreatitis events.
3. All required database cleaning activities and study data tabulation model (SDTM) conversion have been completed. The final system independent (SI) database release, SDTM database release, source data lock (SDL) and database freeze have been declared by GSK Data Management.
4. All criteria for unblinding the randomization codes have been met.
5. Randomization codes have been distributed by PPD to GSK according to GSK and PPD procedures.

In addition, it is planned that Duke Clinical Research Institute (DCRI) will independently confirm the analyses included in the main journal manuscript following standard DCRI procedures.

4. ANALYSIS POPULATIONS

Population or Analysis	Definition / Criteria	Analyses Evaluated
Intent-To-Treat (ITT) Population	• Comprised of all randomized subjects excluding subjects who did not provide consent. • This population will be based on the treatment to which the subject was randomized. • Any subject who is assigned a treatment randomization number by the PPD IRT system	• Primary Endpoint and other Efficacy • Health Outcomes • Study Population (selected outputs)

Population or Analysis	Definition / Criteria	Analyses Evaluated
	will be considered to have been randomized. If there is documented evidence that a subject was randomized in error (not intended by Investigator), inclusion of the subject in the ITT population will be determined prior to unblinding.	
Safety Population	• Comprised of all randomized subjects who receive at least one dose of study treatment. Subjects who did not provide consent will be excluded. • This population will be based on the treatment the subject actually received. • If a placebo subject is dispensed and may have used incorrect container(s) and wrong treatment at more than one visit then the subject will be assigned to albiglutide.	• Safety • Study Population (selected outputs)
Per-Protocol (PP) Analysis	• Analysis includes all randomized subjects who provide consent and receive at least one dose of study treatment, excludes data prior to treatment start date and data after the date of last dose of study treatment + 56 days, and excludes data via censoring for subjects experiencing specified conditions. • Specified conditions that would result in exclusion (via censoring in the analysis) of subject data from the PP analysis are defined in Section 4.1 and Section 11.1. • The analysis will be based on the treatment to which the subject was randomized. Data for subjects assigned incorrect study drug will be censored as specified in Section 11.1.	• Primary Endpoint assessed using the Per-Protocol analysis
Non-insulin (NI) Population [1]	• Comprised of subjects in the 'Intent-To-Treat' population who are not on insulin at baseline. Subjects will be included in the NI population based on medication data recorded in the eCRF.	• Time to Insulin endpoint
Basal Insulin (BI) Population [1]	• Comprised of subjects in the 'Intent-To-Treat' population who are on basal insulin but not on other insulin at baseline (i.e., will not include a subject on a mixed insulin or on a prandial-only insulin). Subjects will be included in the BI population based on medication data recorded in the eCRF.	• Time to Prandial Insulin endpoint

Population or Analysis	Definition / Criteria	Analyses Evaluated

Enrolled Population	• Screening Failures (who never passed screening even if rescreened) who are not randomized are excluded from the Enrolled population. Subjects who did not provide consent will be excluded.
	• The following subjects are included in the Enrolled population:
	  ○ Randomized Subjects
	  ○ Subjects where no treatment was assigned (i.e. never randomized) even though they passed screening
		• Study Population (selected outputs including required disclosure summaries)

NOTES :

- Please refer to Section 11.15 which details the population to be used for each display being generated.

[1] NI and BI population definitions are provided in Section 11.13

4.1. Protocol Deviations

- Important protocol deviations (including deviations related to study inclusion/exclusion criteria, conduct of the trial, subject management or subject assessment) will be summarized and listed (refer to Section 11.1).
- Events which result in exclusion of data (via censoring in the analysis) in the Per-Protocol analysis will also be summarized and listed (refer to Section 11.1 Appendix 1).
- Protocol deviations will be tracked and reviewed by a subgroup of the study team throughout the conduct of the study in accordance with the Protocol Deviation Management Plan (PDMP).
  - Data will be reviewed prior to unblinding and freezing the database to ensure all important deviations and deviations which may lead to exclusion of data from the Per-Protocol analysis are captured and categorized on the protocol deviations dataset.
  - This dataset will be the basis for the summaries and listings of protocol deviations.
- A separate summary and listing of all inclusion/exclusion criteria deviations will also be provided. This summary will be based on data as recorded on the inclusion/exclusion page of the eCRF.

5. CONSIDERATIONS FOR DATA ANALYSES AND DATA HANDLING CONVENTIONS

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

Table 2 Overview of Relevant Appendices

Section	Component
11.1	Appendix 1: Protocol Deviation Management and Definitions for Per Protocol Analysis
11.2	Appendix 2: Time & Events
11.3	Appendix 3: Assessment Windows
11.4	Appendix 4: Treatment States and Phases
11.5	Appendix 5: Data Display Standards & Handling Conventions
11.6	Appendix 6: Derived and Transformed Data
11.7	Appendix 7: Premature Withdrawals & Handling of Missing Data
11.8	Appendix 8: Values of Potential Clinical Importance
11.9	Appendix 9: Multicenter Studies
11.10	Appendix 10: Examination of Covariates and Subgroups
11.11	Appendix 11: Multiple Comparisons & Multiplicity
11.12	Appendix 12: Model Checking and Diagnostics for Statistical Analyses
11.13	Appendix 13: Medication Groupings

6. STUDY POPULATION ANALYSES

6.1. Overview of Planned Analyses

The study population analyses will be based on the ITT population unless otherwise specified.

Table 3 provides an overview of the planned study population analyses, with full details of data displays being presented in Section 11.15.

Table 3 Overview of Planned Study Population Analyses

Display Type	Data Displays Generated		
	Table	Figure	Listing
Subject Disposition			
Study Populations [1]	Y		
Subjects Excluded from Populations [2]	Y (x2)		Y [3]
Reasons for Screen Failures [4]	Y		Y
Rescreened Subjects			Y
Subjects by Country and Site ID	Y		
Subjects by Region and Country	Y		
Subject Disposition	Y	Y	Y
Subject Disposition by Region and Country	Y		
Subject Survival Status	Y		
Subject Primary Endpoint Status	Y		
Study Treatment Discontinuation	Y	Y	Y
Study Treatment Discontinuation by Region and Country	Y		
Study Treatment Discontinuation Status by Study Completion Status	Y		
Subject Contact at Each Scheduled Visit	Y		
End of Study Contact	Y		
Subject Follow-up	Y	Y [5]	
Protocol Deviations			
Important Protocol Deviations	Y		Y
Events Leading to Exclusion of Data From Per-Protocol Analysis	Y		Y
Inclusion and Exclusion Criteria Deviations	Y		Y
Demography			
Demographics and Baseline Characteristics	Y (x2) [6]		Y [7]
Race and Racial Combinations	Y (x2) [6]		
Race and Racial Combinations Details	Y (x2) [6]		Y

Display Type	Data Displays Generated		
	Table	Figure	Listing
Subgroup Factors	Y (x2) [6]		
Medical Conditions (History)			
History of Prior glucagon-like peptide-1 (GLP-1) / dipeptidyl peptidase IV (DPP-IV) Use	Y		
Substance Use	Y		
Medical / Surgical Procedures	Y		
Medical Conditions	Y		
Medical Conditions: Coronary Artery Disease, Cerebrovascular Disease, or Peripheral Arterial Disease	Y		
Diabetic Eye Disease History	Y		
Nephropathy	Y		
Cancer History	Y		
Thyroid Cancer History	Y		
Family History of Cardiovascular Risk Factors	Y		
Medications			
Cardiovascular Medication Use Categories	Y (x2) [8]		Y
Anti-hyperglycaemic Medications	Y (x6) [9]		Y
Anti-hyperglycaemic Medication Categories	Y (x2) [10]		
Recorded Medications Other than Anti-hyperglycaemic [11]			Y
Relationship between ATC Level 1, Ingredient and Verbatim Text			Y
Exposure			
Study Treatment Exposure [12]	Y	Y (x2) [13]	Y
Planned and Actual Treatments			Y [14]
Dose Changes [12]	Y		
Treatment Compliance [12]	Y (x2) [15]		Y
Treatment Blind Broken			Y
Disclosure requirements			
EMA			
Subjects Enrolled by Country and Site ID [3]	Y		
Age Ranges [3]	Y		

NOTES :

- Y = Display Generated

[1] Include all populations.
[2] For all screened subjects and ITT population.
[3] Enrolled population.
[4] Include all screened subjects.
[5] CV and vital status.
[6] For the ITT population and the Safety population.
[7] Listing includes a subset of key assessments.

[8] For the ITT population and the Safety population: each showing by visit, any post-baseline, and study end.
[9] For the ITT population and the Safety population: baseline, any post-baseline, and study end.
[10] For the ITT population and the Safety population, each showing categories of medications for baseline, any post-baseline, and study end.
[11] See Section 6.2.3.
[12] Safety population.
[13] Duration of exposure including breaks, duration of exposure excluding breaks.
[14] ITT population; format outputs to facilitate distribution to centers.
[15] Treatment compliance including breaks, treatment compliance excluding breaks.

6.2. Supplementary Information for Study Population Tables and Listings

6.2.1. Disposition of Subjects

- Screened subjects who do not provide consent will be excluded from all summaries and listings.

- The Summary of Reasons for Screen Failures will exclude subjects who were rescreened, met eligibility criteria when rescreened and were randomized. For subjects who were rescreened and were not randomized, the summary will include the latest reason why the subject was not randomized.

- The Summary of Subject Contact at Each Scheduled Visit includes the number of subjects by visit type (in person with subject, telephone or video contact with subject, other contact with subject, contact with party other than subject, no contact).

- The Summary of End of Study Contacts includes the number and % of subjects by subject status during end of study window, type of end of study contact, and timing of end of study contact.

- There will be a Listing and a Summary of Inclusion and Exclusion Criteria Deviations for the ITT population.

6.2.2. Demographic and Baseline Characteristics

- The Summary of Demographics and Baseline Characteristics will be produced for both the ITT and Safety Populations and will include sex, age, age group (≤18, 19-64, ≥65 years), ethnicity (Hispanic or Latino, Not Hispanic or Latino), race detail, nephropathy, heart failure, duration of diabetes (years), height, weight, body mass index (BMI) (kg/m^2), BMI category (<25, ≥25 to <30, ≥30 to < 35, ≥35), baseline HbA1c (Central or local lab, Central lab, local lab), baseline HbA1c category (Central or local lab, Central lab, local lab) (≤6.5%, >6.5 - 7.0%, >7.0-8.0%, >8.0-9.0%, >9.0%), baseline eGFR (Central or local lab, Central lab, local lab), baseline eGFR category (Central or local lab, Central lab, local lab) (normal ≥ 90, mild ≥60 to <90, moderate ≥30 to < 60, and severe <30, and also <60 and <90), systolic blood pressure, and diastolic blood pressure. Summaries of eGFR will be based on

values computed using the protocol-specified formula based on the measured creatinine.

- Medical conditions will be summarized including cardiovascular disease risk categories (any, coronary artery disease, cerebrovascular disease, and peripheral arterial disease; also number of CV risk categories per subject).

6.2.3. Medications

- Details for all anti-hyperglycaemic medications and for all medications used within the 30 days prior to the onset and throughout the duration of an SAE, AE of special interest, or an AE leading to discontinuation of investigational product will be recorded in the eCRF. Medications used within the 30 days prior to the onset and throughout the duration of an SAE, AE of special interest, or an AE leading to discontinuation of investigational product will be included in listings but not summarized.

- Cardiovascular medications taken during the study will be recorded in the eCRF at each visit by class of agent. Use of cardiovascular medications by class of agent will be summarized for both the ITT and Safety Populations by visit, any post-baseline use, and use at latest visit, and will also be listed for the ITT population. It is possible that a cardiovascular medication may be recorded in more than one class of agent.

- Anti-hyperglycaemic medications will be summarized for both the ITT and the Safety Populations by Anatomical Therapeutic Chemical (ATC) level 1 (body system) and term for use at baseline, any post-baseline use, and use at latest visit, and will also be included in listings for the ITT population. In addition, a listing showing the relationship between ATC level 1, ingredient and verbatim text for these medications will be produced. Anti-hyperglycaemic medication use for both the ITT and Safety Populations at baseline, post-baseline, and latest visit will be summarized for the following categories of medications: none, insulin only, insulin alone or in combination with another anti-hyperglycaemic agent (AHA), insulin and 1 non-insulin AHA, insulin and 2 non-insulin AHAs, insulin and >2 non-insulin AHAs, no insulin and 1 non-insulin AHA, no insulin and 2 non-insulin AHAs, no insulin and >2 non-insulin AHAs, biguanide, sulfonylurea, non-sulfonylurea secretagogue, thiazolidinedione, alpha-glucosidase inhibitors, DPP-IV inhibitors, sodium-glucose co-transporter 2 (SGLT-2) inhibitor, GLP-1 analogues other than study drug, other anti-hyperglycaemic agent. These categories are shown in Section 11.13.

6.2.4. Exposure

- Extent of study treatment exposure will be summarized for the Safety population based on duration of exposure including breaks and duration of exposure excluding breaks, as continuous and categorical values for placebo and albiglutide (overall,

30mg, 50mg).

The frequency of subjects with dose escalations and with dose reductions will be summarized, along with the corresponding reasons. Number of dose escalations and dose reductions per subject will be summarized. Time to first dose escalation and time to first dose reduction will be summarized (continuous and categorical measure). In addition, the frequency of subjects by dose at latest dispensing (overall and by study treatment discontinuation status (yes, no)) will be summarized.

7. PRIMARY STATISTICAL ANALYSES

7.1. Primary Efficacy Analyses

7.1.1. Overview of Planned Primary Efficacy Analyses

The primary efficacy analyses will be based on the ITT population.

Table 4 provides an overview of the planned primary efficacy analysis, and Table 5 provides an overview of the planned sensitivity and supportive analyses of the primary endpoint; full details of data displays are presented in Section 11.15.

Table 4 Overview of Planned Primary Efficacy Analysis

Display Type	Absolute						
	Stats Analysis			Summary		Individual	
	T	F	L	T	F	F	L
Primary Analysis of Primary Endpoint							
Time to MACE [1]	Y (x2) [2]	Y (x2) [3]	Y	Y (x2) [4]			

NOTES :

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

[1] Time to first occurrence of adjudicated MACE (CV death, MI or stroke) during the CV Follow-up time period.
[2] Summary of results, raw SAS output.
[3] Kaplan-Meier and Cumulative Incidence plots.
[4] Incidence for all and components, incidence for first occurrence overall and by components.

Table 5 Overview of Planned Sensitivity and Supportive Analyses of the Primary Endpoint

Display Type	Absolute						
	Stats Analysis			Summary		Individual	
	T	F	L	T	F	F	L
Key Sensitivity Analyses							
On-treatment Period [1]	Y	Y		Y			
On-therapy Period [2]	Y	Y		Y			
Per-Protocol Analysis	Y	Y		Y			
Other Sensitivity Analyses							
Excluding unknown cause of death	Y	Y		Y			
Including additional data from publicly available sources in subjects withdrawing consent	Y	Y		Y			
Tipping Point Analysis		Y					

Display Type	Absolute						
	Stats Analysis			Summary		Individual	
	T	F	L	T	F	F	L
Forest Plot of primary and sensitivity analyses		Y					
Supportive Analyses and Summaries							
Subgroups [3]	Y	Y					
Recurrent events analyses	Y			Y (x3) [4]			
Censoring and follow-up time				Y			
Events By Time Periods [5]				Y			

NOTES :

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

[1] On-treatment = first dose of study treatment to last dose of study treatment
[2] On-therapy = first dose of study treatment to last dose of study treatment + 56 days
[3] Subgroups are specified in Section 11.10
[4] Number of Adjudicated MACE, MI, Stroke events
[5] Events during and after defined follow-up periods

7.1.2. Planned Primary Efficacy Statistical Analyses

Primary Statistical Analyses
Endpoint
• Time to MACE, defined as the time to first occurrence of CEC-adjudicated MACE (CV death, MI or stroke)
Model Specification
• The primary endpoint will be statistically analyzed using a Cox Proportional Hazards (PH) regression model with treatment group as the only covariate. The SAS PHREG procedure will be used to fit the Cox Proportional Hazards (PH) regression model.
Model Checking & Diagnostics
• Refer to Section 11.12.
Model Results Presentation
• Treatment effect will be estimated via the hazard ratio and associated two-sided 95% Wald confidence interval (CI). • The hypothesis of non-inferiority of albiglutide relative to placebo with a margin of 1.3 with respect to cardiovascular risk will be tested at the end of the study when approximately 611 first CEC-adjudicated MACE events have occurred and the projected median duration of subject follow-up is at least 1.5 years. The strength of evidence for non-inferiority will be determined by testing the hypothesis that the observed hazard ratio is significantly different from the null margin of 1.3 (a one-sided p <0.025 for such a test with result in appropriate direction being equivalent to the upper 95% confidence limit for the hazard ratio being less than 1.3) [FDA, 2008]. This test will be based on the Wald statistic. If non-inferiority is established, the hypothesis of superiority of albiglutide relative to placebo will be tested. • The product-limit estimates of the probabilities of first MACE over time will be computed and displayed as Kaplan-Meier (KM) curves by treatment group. Cumulative incidence functions will also be computed adjusting for the competing risk of non-CV death [Kalbfleisch, 2002]. • A summary of the number and percentage of subjects having first-occurrence MACE will be provided. The number and percentage of the types of events that make up the first occurrence of MACE will also be provided. • A summary of all MACE including the number and percentage of subjects and number of events (including first and subsequent MACE) by type of event will be provided. • The hazard ratio, two-sided 95% CI, p-value for the statistical non-inferiority test, and p-value for the superiority test will be presented. The number and percentage of subjects with a MACE event and the number censored, the MACE incidence rate per 100 person-years, and the absolute rate difference per 100 person-years and associated 95% CI will be displayed. • The hazard ratio, 95% CIs and non-inferiority and superiority p-values will be displayed on a forest plot together with sensitivity analysis results (On-treatment period, On-therapy period, Per-protocol Analysis, Excluding Unknown Cause of Death, Inclusion of Additional Data from Publicly-Available Sources).
Notes:
• The analysis will be based on events positively adjudicated by the CEC and will use the CEC adjudicated event onset dates. • First occurrence of adjudicated MACE for a subject is defined as the first adjudicated event, determined by the event date, that is indicated as CV death, MI or stroke. Further details

Primary Statistical Analyses
regarding definitions of events, time to event and time period are provided in Section 11.6.4. • Deaths for which the CEC is unable to establish cause (undetermined cause) will be analyzed as CV deaths except for Analysis Excluding Unknown Cause of Death. • For subjects who withdraw consent for all follow-up, events occurring up to the date of consent withdrawal will be included in the primary analysis of MACE (i.e. deaths and events collected via publicly available sources subsequent to withdrawal of consent will not be included in the primary analysis but rather in a sensitivity analysis of the primary endpoint). • Fatal events which are adjudicated to be due to a CV cause, may also have a corresponding CV event adjudicated to determine whether specific endpoint criteria were met (e.g. MI, stroke, heart failure (HF)). Therefore, there may be two adjudication reports for the same fatal CV event. Also, it is possible, for example, that an adjudicated CV death with cause = MI may not meet the adjudication criteria required for MI; and similarly for other fatal events.

Sensitivity and Supportive Statistical Analyses
• As sensitivity analyses, the primary analysis will be repeated based on the On-treatment period (first dose of study treatment to last dose of study treatment) and also based on the On-therapy period (first dose of study treatment to last dose of study treatment + 56 days) using the ITT population, censoring subjects not receiving study treatment at date of randomization. • A Per-Protocol sensitivity analysis of the primary endpoint will be conducted including all randomized subjects who provide consent and receive at least one dose of study treatment, excluding data after the date of last dose of study treatment + 56 days, and excluding data via censoring for subjects experiencing specified conditions (corresponding definitions are provided in Section 11.1). The Per-Protocol analysis can be viewed as an extension of the On-therapy analysis that in addition accounts for specified conditions. • Two additional analyses will be conducted in which the primary analysis will be repeated with modifications: one analysis will exclude deaths with unknown cause as events, and the other will include additional data obtained from publicly available sources for subjects who withdrew consent. • For within-group rates per 100 person-years, the 95% CI will be obtained using an exact Poisson method based on [Daly, 1992] following [Fleiss, 2003]. For the difference in rates between treatments, the 95% CI will be constructed with a Normal approximation using Wald's method [Liu, 2006]. • A tipping point analysis of the primary endpoint will be conducted to explore the sensitivity of the primary analysis results to potentially different event hazard rates in study non-completers as compared to completers. Assuming a proportional hazards relationship for MACE hazard rates in non-completers vs. completers, the hazard ratio between albiglutide and placebo arms can be expressed as a function of several parameters: probability of non-completion, treatment hazard ratio among completers, survival functions in completers (all estimated from the data), and hazard ratios for completers vs non-completers in each arm (c0 in the placebo arm and c1 in the albiglutide arm, both of which are varied across a range of values). Non-inferiority would not be met for values c0 and of c1 such that the upper limit of the 95% Wald confidence interval for hazard ratio exceeds 1.3. The results of this analysis will be displayed graphically as a grid of points corresponding to different combinations (c0, c1), where plotting symbols are used to indicate whether or not non-inferiority was met at each combination. • Recurrent event analyses of MACE, MI and Stroke will be conducted using the negative binomial regression model which is an extension of Poisson regression [Agresti, 2002]. In

Sensitivity and Supportive Statistical Analyses
particular, each subject is assumed to have events generated by a Poisson process with subject-specific rates which are distributed according to a gamma distribution. The negative binomial regression model is an event count based model that does not assume an equal mean and variance across subjects and allows for overdispersion in the data, which occurs when the variance is greater than the conditional mean. The MACE event rates will be analysed using a negative binomial generalized linear model with a log link function using SAS PROC GENMOD. The model will include a term for treatment group. The log of follow-up time will be used as an offset. The estimated mean rates will be presented by treatment group along with treatment ratios of albiglutide vs. placebo and associated p-values and 95% confidence limits. If difficulties are encountered in fitting the negative binomial model (e.g. lack of convergence), then use of alternative approaches such as Poisson regression will be considered. • For MACE, subgroup analyses will be performed for the subgroups of interest identified in Section 11.10 using a Cox PH model including treatment group, the subgroup of interest and the subgroup by treatment interaction. The hazard ratio and associated 95% confidence interval for the treatment effect for MACE will be provided for each subgroup level for which analysis is performed as well as p-value for subgroup by treatment interaction. The interaction will be assessed using a nominal alpha level of 0.10. A forest plot will graphically display the results of these analyses for the subgroup levels of interest. As the number of subgroup variables may be large, the probability of observing at least one nominally statistically significant result may be high; no formal conclusions will be drawn based on the results of these analyses. • In the event an investigator and/or any member of their staff is documented to have improper or poor study conduct (such as audit findings indicative of data irregularities), analyses may be performed as described next. All data will be included in the primary analyses. Separate summaries and analyses will be performed with the exclusion of all subjects at the noted site(s). At a minimum, the summaries and analyses excluding the noted site(s) will include the primary analysis of the primary endpoint.

8. SECONDARY STATISTICAL ANALYSES

8.1. Secondary Efficacy Analyses

8.1.1. Overview of Planned Secondary Efficacy Analyses

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

Table 6 provides an overview of the planned secondary efficacy analyses, with further details of data displays being presented in Section 11.15.

Table 6 Overview of Planned Secondary Efficacy Analyses

Endpoints	Absolute							Change from Baseline						
	Stats Analysis			Summary		Individual		Stats Analysis			Summary		Individual	
	T	F	L	T	F	F	L	T	F	L	T	F	F	L
CV Endpoints														
Secondary efficacy CV endpoints				Y (x2) [1]										
Time to MACE or Revascularization [2], Time to CV Death, Time to MI, Time to Stroke, Time to CV Death or HF hospitalization [3]	Y (x5)	Y (x7)	Y (x5)											
Supplemental Time to MI , Supplemental Time to Stroke	Y (x2)													
Percutaneous Intervention, Coronary Artery Bypass Graft, Catheterization				Y (x4) [4]										
Details for Adjudicated Events				Y (x3) [5]										
Events That Do Not Meet CV Endpoint or TIA Definition				Y (x2)										
Metabolic Endpoints														
Time to Insulin [6], Time to Prandial Insulin [7]	Y (x2)	Y (x2)	Y (x2)											
Proportion of subjects achieving composite metabolic endpoint [8]	Y		Y											
Proportion of subjects	Y													

Endpoints	Absolute							Change from Baseline						
	Stats Analysis			Summary		Individual		Stats Analysis			Summary		Individual	
	T	F	L	T	F	F	L	T	F	L	T	F	F	L
achieving composite metabolic endpoint [8] – On-treatment period														
Time to Microvascular event [9]	Y	Y	Y	Y (x2) [10]										
HbA1c– OC [11,12]				Y (x2) [13]	Y							Y		Y
HbA1c ≤7.0 %, Central Lab only				Y										
HbA1c– OC [11,12] – 8 monthly assessments only								Y (x2) [13]				Y (x2) [14]		
HbA1c – OC [11,12] – On-treatment period – 8 monthly assessments only								Y (x2) [13]				Y		
HbA1c– OC [11] – 8 monthly assessments only, Central lab only								Y (x2) [13]						
Body weight – OC [11]				Y	Y							Y		Y
Body weight - OC [11] - 8 monthly assessments only								Y				Y (x2) [14]		
Body weight – OC [11] – On-treatment period 8 monthly assessments only								Y				Y		

NOTES :

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

[1] Incidence of all in one summary, incidence of first occurrence of composite endpoints in one summary.
[2] Time to first occurrence of adjudicated MACE or urgent revascularization for unstable angina.
[3] Time to adjudicated CV death or hospitalization due to heart failure.
[4] Incidence of all in one summary, and also separate summary of details for each intervention.
[5] Death, MI, stroke.
[6] Time to initiation of insulin of more than 3 months duration for those subjects not treated with insulin at study start (NIN population).
[7] Time to initiation of prandial insulin of more than 3 months duration in those subjects on basal insulin at study start (BIN population).
[8] Proportion of subjects achieving glycaemic control (HbA1c $\leq$ 7.0% at final assessment) with no severe hypoglycaemic incidents and weight gain <5% of body weight.
[9] Time to first occurrence of a clinically important microvascular event (see Section 11.6.4).

[10] Incidence of all in one summary, incidence of first occurrence in one summary.
[11] OC = Observed Case (see Appendix 7).
[12] Including baseline local and Central lab data and post-baseline scheduled visit Central lab data.
[13] HbA1c to be summarized for units=% and also units=mmol/mol.
[14] Plots of raw means vs time and also adjusted means vs time.

8.1.2. Planned Secondary Efficacy Statistical Analyses

Statistical Analyses
Endpoints
• Time to MACE or Revascularization = Time to first occurrence of adjudicated MACE or urgent revascularization for unstable angina (UA) • Time to CV Death = Time to adjudicated CV Death • Time to MI = Time to first occurrence of adjudicated MI • Time to Stroke = Time to first occurrence of adjudicated Stroke • Time to CV Death or HF Hospitalization = Time to first occurrence of adjudicated CV Death or HF Hospitalization • Time to Insulin = Time to initiation of insulin of more than 3 months duration (NI population) • Time to Prandial Insulin = Time to initiation of prandial insulin of more than 3 months duration (BI population) • Proportion of subjects achieving composite metabolic endpoint (glycaemic control (HbA1c≤ 7.0% at final assessment) with no severe hypoglycaemic incidents and weight gain <5% from baseline) • Time to Microvascular Event = Time to first occurrence of a clinically important Microvascular Event (see Section 11.6.4) • Change from baseline in HbA1c • Change from baseline in body weight
Model Specification
• Analyses of time to event endpoints will be done in a similar manner as the primary endpoint: treatment group comparisons will be done using a Cox Proportional Hazards regression model. The analysis will compare time to event using a Wald test evaluated at the two-sided 5% significance level. The p-value, estimated hazard ratio and associated 95% Wald confidence interval will be obtained using a Cox PH model with treatment group as the only covariate. The SAS PHREG procedure will be used to fit the Cox PH regression model. • For time to first occurrence of adjudicated MI, events will include adjudicated MI or death with adjudicated cause = MI. In a similar manner, for time to first occurrence of adjudicated stroke, events will include adjudicated stroke or death with adjudicated cause = stroke. • Supplemental analysis of time to MI will be done including adjudicated MI events but excluding events which do not meet the adjudication criteria for MI but are classified by the CEC as deaths due to MI. This analysis will be done in a similar manner as the primary endpoint. Similarly, a supplemental analysis of time to stroke will be done including adjudicated stroke events but excluding events which do not meet the adjudication criteria for stroke but are classified by the CEC as deaths due to stroke. • For the composite metabolic endpoint, treatment group comparisons will be done with the nonparametric, covariance-adjusted, extended Mantel-Haenszel test using the SAS FREQ procedure. Covariates will include baseline HbA1c (<8.0% versus ≥ 8.0%) and prior diabetes

Statistical Analyses
therapy (diet and exercise alone versus all other therapies). As a sensitivity analysis, this will also be done for the On-treatment period excluding subjects who did not receive at least one dose of study treatment. • Summaries of HbA1c by visit will be provided by the following categories: ≤6.5%, >6.5 - 7.0%, >7.0-8.0%, >8.0-9.0%, >9.0%. • For change from baseline HbA1c and change from baseline body weight, treatment group comparisons will be done using a mixed model repeated measures (MMRM) analysis including Observed Case data from the Month 8 and Month 16 scheduled post-baseline assessments [Mallinckrodt, 2008]. PROC MIXED in SAS [Littell, 1996] will be used to fit the model, using the restricted maximum likelihood estimation method and the Kenward-Roger option to estimate denominator degrees of freedom and standard errors. An unstructured covariance structure will be used to model the within-subject errors, shared across treatments. If the analysis using an unstructured covariance structure does not converge, analyses using AR(1) or other covariance structures will be considered. Missing data will be assumed to be missing at random. Analyses will include the fixed, categorical effects of treatment, visit, and treatment-by-visit interaction, as well as the continuous, fixed covariates of baseline and baseline-by-visit interaction. Due to the event-driven nature of the study, beyond Month 16 only summary statistics will be provided. For these two endpoints the primary treatment comparison will be the contrast between treatments (Albiglutide - Placebo) at the Month 16 visit using the two-sided p-value from the corresponding t-test at α=0.05. As sensitivity analyses, these will also be done for the On-treatment period excluding subjects who did not receive at least one dose of study treatment.
Model Checking & Diagnostics
• Refer to Section 11.12.
Model Results Presentation
• For time to event endpoints, p-values and estimates of hazard ratios and 95% confidence intervals (CIs) will be presented, along with Kaplan-Meier (KM) curves by treatment group. For time to MI and time to stroke, cumulative incidence functions will also be computed adjusting for the competing risk of death. • For change from baseline endpoints, least square means, 95% CIs and nominal p-values will be presented, along with plots of least square means vs time by treatment group.

8.2. Secondary Safety Analyses

8.2.1. Overview of Planned Secondary Safety Analyses

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

Table 7 provides an overview of the planned secondary safety analyses, with further details of data displays being presented in Section 11.15.

Table 7 Overview of Planned Secondary Safety Analyses

Endpoints	Absolute				Change from Baseline			
	Summary		Individual		Summary		Individual	
	T	F	F	L	T	F	F	L
Adverse Events								
All cause mortality (time to death)	Y (x3)[1]	Y (x3)[1]		Y[1]				
AE Overview	Y (x2)							
Serious adverse events (SAE)	Y (x4) [2]							
Reason for Seriousness				Y				
All AEs planned to be collected	Y (x4) [2]							
Treatment related AEs planned to be collected	Y [3]							
AEs planned to be collected by subgroup	Y (x3) [4]							
AEs planned to be collected by maximum intensity	Y (x3) [5]							
Common (≥2%) AEs planned to be collected	Y (x2) [6]							
All reported AEs	Y (x2) [6]			Y				
Reported AEs for subjects with baseline eGFR <30				Y				
Fatal SAEs, Nonfatal SAEs	Y (x4) [7]			Y (x2)				
Treatment-related SAEs, Treatment-related fatal SAEs	Y (x2) [3]							
Common (≥2%) SAEs	Y (x2)[8]	Y						
SAEs by Subgroup	Y (x3) [4]							
AE leading to discontinuation of IP: Overall, serious	Y (x2)			Y [9]				
Non-serious AEs not AESIs nor led to				Y				

Endpoints	Absolute				Change from Baseline			
	Summary		Individual		Summary		Individual	
	T	F	F	L	T	F	F	L
discontinuation of IP								
Subject Numbers for Individual AEs				Y [10]				
Relationship between AE SOCs, PT and Verbatim Text				Y [10]				
AEs of special interest (AESIs): Overview	Y (x2) [11]	Y						
AEs of special interest: Development of thyroid cancer [12], Haematologic malignancy, Pancreatic cancer, Investigator-reported Pancreatitis [12], Investigational Product injection site reactions [12], Immunological reactions [12], Severe hypoglycaemic events [12], Hepatic events, Hepatic enzyme elevations (including GGT), Serious gastrointestinal (GI) events, Appendicitis, Atrial fibrillation/flutter [12], Pneumonia [12], Worsening renal function [12], Diabetic retinopathy [12]	Y (x69) [13]	Y (x2) [14]		Y (x10) [15]				
Immunogenicity data	Y (x2)			Y (x4)				
AEs of Special Interest: Adjudicated Pancreatitis	Y (x5) [16]			Y (x2)				
AEs of Special Interest: severe hypoglycaemic events by baseline HbA1c, eGFR, age, and sulfonylurea(SU) / insulin	Y (x8) [17]							
AEs of Special Interest: Recurrent event analysis of Severe Hypoglycaemic events	Y (x4) [18]							

Endpoints	Absolute				Change from Baseline			
	Summary		Individual		Summary		Individual	
	T	F	F	L	T	F	F	L
Malignant neoplasms	Y (x10) [19]			Y				
Other significant AEs				Y				
Liver monitoring/stopping events	Y [20]			Y (x5)				
Hepatobiliary Abnormalities	Y [3]			Y				
Liver Function Tests of Potential Clinical Concern	Y							
AEs of Special Interest Overview by Subgroup	Y (x3) [21]							
AEs of Special Interest by Subgroup (Age, Sex)	Y (x4)							
Other								
eGFR [22]	Y (x2) [23]	Y			Y (x3)	Y (x2) [24]		Y [22]
eGFR (Central Lab only) [25]					Y (x2)			
BP and heart rate	Y (x2) [26]	Y (x3)			Y (x3) [27]	Y (x3)		Y [28]

NOTES :

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

[1] ITT Population; for vital status follow-up, On-therapy, and On-treatment time periods.
[2] Frequency for On-therapy and Post-therapy combined, On-therapy, time periods (SOC and Preferred Terms, and also SOC, high level term (HLT) and Preferred Terms).
[3] Frequency for On-therapy time period.
[4] Subgroups are Age, Sex, eGFR; frequency overall and by system organ class (SOC) and HLT for the On-therapy time period.
[5] On-therapy and post-therapy combined, on-therapy, and on-therapy treatment-related.
[6] Frequency for On-therapy and Post-therapy combined, On-therapy time periods.
[7] For each type: Frequency for On-therapy and Post-therapy combined, On-therapy, time periods (SOC and Preferred Terms).
[8] Frequency for On-therapy and Post-therapy combined, On-therapy time periods (Preferred Terms).
[9] Includes any AE leading to discontinuation of IP.
[10] Includes all reported AEs/SAEs.
[11] On-therapy and Post-therapy combined, On-therapy time periods (eCRF event specific page or defined list of terms).
[12] Event-specific details recorded.
[13] Frequency overall and by SOC and Preferred Term, along with summary of characteristics, each done for On-therapy and Post-therapy combined, On-therapy time periods; also details for AESI with event-specific page for On-therapy time period.
[14] Kaplan-Meier plots for serious GI events and Investigational Product Injection Site reactions only, On-therapy time period.
[15] Listings of event-specific details will be provided for appropriate AESIs, along with AE listings for all AESIs.

[16] Frequency overall and by SOC and Preferred Term (PT), each done for On-therapy and Post-therapy combined, On-therapy time periods for events adjudicated as definite or possible; adjudication details done for On-therapy and Post-therapy combined, On-therapy time periods; summary of characteristics for On-therapy events adjudicated as definite or possible.
[17] Frequency for On-therapy and Post-therapy combined, On-therapy time periods for each of 4 subgroups.
[18] Analysis for On-therapy and On-treatment time periods, each overall and stratified by baseline SU/Insulin use.
[19] Frequency for On-therapy and Post-therapy combined, On-therapy time periods by SOC, HLT and PT; overall, by insulin use at baseline, by history of malignancy at baseline; also corresponding Mantel-Haenszel tests by insulin use at baseline, by history of malignancy at baseline.
[20] On-therapy and and Post-therapy combined time period.
[21] Subgroups are Age, Sex, eGFR for AESIs for which incidence is >=1.0% in either treatment group; frequency for the On-therapy time period.
[22] Computed using MDRD formula per protocol; including baseline local and Central lab creatinine data and post-baseline scheduled visit Central lab creatinine data.
[23] Raw, categories.
[24] Plots of raw means vs time and also adjusted means vs time.
[25] Computed using MDRD formula per protocol; including baseline and post-baseline scheduled visit Central lab creatinine data.
[26] Raw, potential clinical concern.
[27] Change from baseline, potential clinical concern, shift table.
[28] Listing includes value and change from baseline; for BP and heart rate only including subjects with values of potential clinical concern.

All serious adverse events, including deaths, will be recorded in the eCRF, as well as AEs leading to discontinuation of IP and AEs of special interest (AESI). MI, stroke, unstable angina requiring urgent revascularization, hospitalization for heart failure, TIA and sudden cardiac death will not be recorded as AEs or SAEs, but will instead be recorded on event-specific eCRF forms. For some AESIs (development of thyroid cancer, pancreatitis, investigational product injection site reactions, immunological reactions, severe hypoglycaemic events, atrial fibrillation/flutter, pneumonia, worsening renal function, diabetic retinopathy), additional event-specific details are also recorded in the eCRF; summaries of incidence will be provided based on these data. For the remaining AESIs, summaries of incidence will be based on defined lists of coded terms. Summaries of the AESI event-specific details will also be provided. For AESIs with incidence ≥1.0 % in either treatment group, summaries of incidence at the highest level will be provided by baseline eGFR (≥90, ≥60 to <90, <60 ml/min/1.73m^2), age (<65, ≥65 to <75, ≥75 years), and sex (female, male) subgroups. For severe hypoglycemic events, summaries of incidence will be provided by baseline HbA1c (<8.0%, ≥8.0% to <9.0%, ≥9.0%), baseline eGFR (≥ 90, ≥60 to <90, < 60 ml/min/1.73m^2) , age (<65, ≥65 to <75, ≥75 years), and baseline sulfonylurea/insulin use (yes, no) subgroups. Data related to liver monitoring/stopping event reporting are recorded in the eCRF. Additional detail regarding definitions used to identify the AESIs are provided in Section 11.6.3.

For subjects treated with albiglutide, the frequency of immunological reaction AESIs will be summarized for the On-therapy and Post-therapy combined time period by anti-albiglutide antibody status (positive, negative, unknown) and also by IgE antibody status (positive, negative, unknown).

Frequency of malignant neoplasms (non-serious AEs or SAEs) will be summarized overall, by insulin use at baseline (yes, no), and by history of malignancy at baseline (yes, no). See Section 11.6.3 regarding definitions to be used to identify malignant neoplasms.

8.2.2. Planned Secondary Safety Statistical Analyses

Statistical Analyses
Endpoints
• All cause mortality (time to death) • Non-fatal SAEs • AEs of special interest • eGFR (computed)
Model Specification
• For time to death, analysis will be done in a similar manner as the primary endpoint: treatment group comparisons for the ITT population will be done using the Wald test p-value from a Cox Proportional Hazards regression model with treatment group as the only covariate. For time to death, an estimate of the hazard ratio and 95% confidence interval will be presented, along with Kaplan-Meier (KM) curves by treatment group. Frequency of death will be summarized for the vital status follow-up, On-therapy, and On-treatment time periods. • For each common SAE (i.e., those Preferred Terms with frequency ≥2% in either treatment group) frequency of occurrence by Preferred Term will be summarized for the On-therapy and Post-therapy combined, and On-therapy time periods, and the relative risk and 95% confidence interval will be computed. The relative risk for an event will be defined as the ratio of the probability of a subject in the albiglutide treatment group having at least 1 event to the probability of a subject in the placebo treatment group having at least 1 event. PROC FREQ in SAS will be used to compute relative risk and the associated exact unconditional confidence interval. In addition, AE density and incidence rates per 100 person years (PY) by Preferred Term will be computed. A plot of relative risk and 95% CI will be produced for the most common SAEs for the On-therapy time period. • For each common (i.e., those Preferred Terms with frequency ≥2% in either treatment group) AE planned to be collected (SAEs, AEs leading to discontinuation of IP, and AESIs), frequency of occurrence by Preferred Term will be summarized for the On-therapy and Post-therapy combined, and On-therapy time periods. • For each AESI (including Investigator-reported pancreatitis and adjudicated pancreatitis) frequency of occurrence by SOC and Preferred Term will be summarized for the On-therapy and Post-therapy combined, and On-therapy time periods, and the relative risk and 95% confidence interval will be computed as previously described. In addition, AE density and incidence rates per 100 PY will be computed. Intensity, seriousness, relationship to IP, action taken, outcome, time relative to treatment start, time relative to treatment stop, and event duration will be summarized. A plot of relative risk and 95% CI will be produced for the AESI based on the On-therapy time period. Time to first AESI for the On-therapy time period will be summarized using KM curves by treatment group for serious GI events and Investigational Product Injection Site reactions. • For malignant neoplasms during the On-therapy and Post-therapy combined time periods, treatment group comparisons will be done with the nonparametric, extended Mantel-Haenszel test adjusting for baseline insulin use (yes, no) using the SAS FREQ procedure. As a sensitivity analysis, this will also be done for the On-therapy time period. These analyses will also be done adjusting for baseline history of malignancy (yes, no).

Statistical Analyses
• For severe hypoglycaemic events during the On-therapy time period an additional recurrent event analysis will be performed in a manner similar to that done for MACE (see Section 7.1.2). As a sensitivity analysis, this will also be done for the On-treatment time period. It is recognized that sulfonylurea /insulin use may increase risk of hypoglycaemic events; hence the recurrent events analysis will be also be done stratified by baseline sulfonylurea/insulin use (yes, no). • Summaries and analyses of eGFR will be based on values from scheduled visits computed using the protocol-specified formula based on the measured creatinine, including baseline local and Central lab creatinine data and post-baseline scheduled visit Central lab creatinine data. For change from baseline eGFR, treatment group comparisons will be done using a MMRM analysis as previously described using an On-treatment analysis. Due to the event-driven nature of the study, beyond Month 16 only summary statistics will be provided. In addition, eGFR will be categorically summarized by visit as Normal ≥ 90, Mild ≥60 to <90, Moderate ≥30 to < 60, and Severe <30. Shift tables of eGFR from baseline to post-baseline planned relative timepoints will be provided including a summary of the shifts to the most severe eGFR category determined post-baseline. Sensitivity analyses will be done using the protocol-specified equation and measured creatinine, including baseline and post-baseline scheduled visit Central lab creatinine data. These will include the MMRM analysis and the shift tables.
Model Results Presentation
• For time to event endpoints, p-values and estimates of hazard ratios and 95% confidence intervals (CIs) will be presented, along with Kaplan-Meier (KM) curves by treatment group. • For change from baseline endpoints, least square means, 95% CIs and nominal p-values will be presented, along with plots of least square means vs time by treatment group.

8.3. Secondary Value Evidence and Outcomes Analyses

8.3.1. Overview of Planned Secondary Value Evidence and Outcomes Analyses

The secondary Value Evidence and Outcomes analyses will be based on the ITT population.

Table 8 provides an overview of the planned secondary Value Evidence and Outcomes analyses, with further details of data displays being presented in Section 11.15. Although not specified in the protocol, it was subsequently clarified in the Study Reference Manual and the eCRF Completion Guidelines that questionnaires were not to be completed after subjects discontinued study treatment; hence such data should not be entered into the eCRF and will be programmatically excluded from all summaries and analyses (but included in listings with corresponding flag). For the TRIM-D and EQ-5D, if one or more questionnaire responses are missing at a timepoint for a subject, then the corresponding endpoint score will be missing.

Table 8 Overview of Planned Secondary Value Evidence and Outcomes Analyses

Endpoints	Absolute							Change from Baseline						
	Stats Analysis			Summary		Individual		Stats Analysis			Summary		Individual	
	T	F	L	T	F	F	L	T	F	L	T	F	F	L
Patient Reported Outcomes														
TRIM-D- OC					Y			Y	Y (x2) [1]	Y	Y (x6)			
EQ-5D - OC				Y (x6)	Y			Y	Y (x2) [1]	Y				
TRIM-D - LOCF				Y	Y									
EQ-5D - LOCF				Y	Y									

NOTES :

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

[1] Plots of raw means vs time and also adjusted means vs time.

8.3.2. Planned Secondary Value Evidence and Outcomes Statistical Analyses

Statistical Analyses
Endpoints
• Change from baseline in TRIM-D total score [1] • Change from baseline in EQ-5D Visual Analogue Scale (VAS) score
Model Specification
• For change from baseline TRIM-D total score and change from baseline EQ-5D VAS score, treatment group comparisons will be done using a MMRM analysis as previously described. Due to the event-driven nature of the study, beyond Month 16 only summary statistics will be provided. Summaries and analyses will exclude data assessed after subjects discontinue study drug. Summaries and analyses of change from baseline TRIM-D total score will exclude subjects not on diabetes medication at baseline.
Model Checking & Diagnostics
• Refer to Section 11.12.
Model Results Presentation
• For change from baseline endpoints, least square means, 95% CIs and nominal p-values will be presented, along with plots of least square means vs time by treatment group.

[1] Summaries and analyses of change from baseline TRIM-D total score will exclude subjects not on diabetes medication at baseline.

TRIM-D total score and change from baseline TRIM-D total score, along with score and change from baseline score for each of the five domains (Treatment Burden, Daily Life, Diabetes Management, Compliance, Psychological Health) will be summarized by visit. Summaries will exclude subjects not on diabetes medication at baseline.

EQ-5D responses for each of the five domains (Mobility, Self-Care, Usual Activities, Pain/Discomfort, Anxiety/Depression) will be summarized categorically by visit; EQ-5D VAS score and change from baseline VAS score will be summarized by visit.

9. OTHER STATISTICAL ANALYSES

9.1. Other Efficacy Analyses

9.1.1. Overview of Planned Other Efficacy Analyses

The other efficacy analyses will be based on the ITT population, unless otherwise specified.

Table 9 provides an overview of the planned other efficacy analyses, with further details of data displays being presented in Section 11.15.

Table 9 Overview of Planned Other Efficacy Analyses

Endpoints	Absolute							Change from Baseline						
	Stats Analysis			Summary		Individual		Stats Analysis			Summary		Individual	
	T	F	L	T	F	F	L	T	F	L	T	F	F	L
CV														
Time to Stroke or TIA [1]	Y	Y		Y										
Time to TIA [2]	Y	Y		Y										
Concordance Between Investigator-Reported and Adjudicated Events				Y (x6) [3]			Y							
Lipids (total cholesterol(TC), low density lipoprotein cholesterol (LDLc), high density lipoprotein cholesterol (HDLc), triglycerides (Tg), nonHDLc) [4]				Y (x2) [5]										

NOTES :

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

[1] Time to first occurrence of adjudicated stroke or TIA.
[2] Time to first occurrence of adjudicated TIA.
[3] Efficacy, MACE, Death, MI/UA, Stroke/TIA, Individual Endpoint Event.
[4] Assessed per routine clinical care.
[5] Standard and SI units.

For time to first adjudicated stroke or TIA and also for time to first adjudicated TIA, a Cox Proportional Hazards regression model with treatment group as the only covariate will be used; an estimate of the hazard ratio and 95% confidence interval will be presented, along with Kaplan-Meier (KM) curves by treatment group.

If significant drop-in of medications which have the potential to impact CV outcomes occurs, exploratory summaries and analyses may be considered.

9.2. Other Safety Analyses

9.2.1. Overview of Planned Other Safety Analyses

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

Table 10 provides an overview of the planned other safety analyses, with further details of data displays being presented in Section 11.15.

Table 10 Overview of Planned Other Safety Analyses

Endpoints	Absolute				Change from Baseline			
	Summary		Individual		Summary		Individual	
	T	F	F	L	T	F	F	L
CV								
Investigator-Reported Reason for Death	Y [1]			Y[1]				
Disclosure Requirements								
CTR								
SAEs by PT (descending frequency): Overall, fatal, drug-related, drug-related fatal [2]	Y (x4)							
Most Frequent 10 AEs [3]	Y							
FDAAA / EMA								
SAEs [4]	Y							
Common (≥5%) Non-serious AEs [5]	Y							
Other								
Aspartate aminotransferase (AST), alanine aminotransferase (ALT), alkaline phosphatase, bilirubin, creatinine, gamma glutamyl transferase (GGT)[6]	Y (x2) [7]	Y [8]	Y (x2) [9]	Y[10]	Y (x2)	Y [8]		
Creatinine [11]				Y	Y (x2) [12]			
Pregnancies				Y				
Requirement for Mexican MoH [13]				Y (x3)				
Other CV events: Arrhythmias [14],	Y (x2)[15]			Y (x6) [16]				

Endpoints	Absolute				Change from Baseline			
	Summary		Individual		Summary		Individual	
	T	F	F	L	T	F	F	L
Valvulopathy, Pulmonary Hypertension, Peripheral Arterial Thromboembolism, Deep Venous Thrombosis / Pulmonary Embolism, Revascularization (other than revascularizations intended for CEC adjudication)								
Subject Profiles				Y				
Creatinine Assay Issue Sensitivity Analyses								
Creatinine	Y				Y			
eGFR					Y (x2)			

NOTES :

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

[1] ITT population.
[2] Frequency overall and by Preferred Term for the On-therapy time period; required for disclosure.
[3] Most frequent 10 AEs in each treatment group; required for disclosure.
[4] Frequency overall and by SOC and Preferred Term for the On-therapy time period (Subjects with SAEs, SAEs, Drug-related SAEs, Fatal SAEs, Drug-related Fatal SAEs); required format for disclosure.
[5] Frequency overall and by SOC and Preferred Term for the On-therapy time period; required for disclosure, to be indicated as collected via "Non-systematic Assessment".
[6] Creatinine will include baseline local and Central lab data and post-baseline scheduled visit Central lab data.
[7] Raw, potential clinical concern.
[8] Box and whisker plot for creatinine and change from baseline creatinine.
[9] Evaluation of drug-induced serious hepatotoxicity (EDISH) plot of ALT vs total bilirubin (ULN = Upper Limit of Normal), maximum vs baseline for ALT (ULN).
[10] Subjects with abnormalities of potential clinical concern.
[11] Creatinine will include baseline and post-baseline scheduled visit Central lab.
[12] Potential clinical concern for shifts from baseline and for change from baseline by baseline eGFR.
[13] MoH = Ministry of Health.
[14] Excluding atrial fibrillation/flutter which is an AESI.
[15] Frequency for On-therapy and Post-therapy combined, On-therapy time periods.
[16] Subject profiles for each of the "Other CV events".

GSK has identified other CV events of special interest for studies. Such events (arrhythmias [other than atrial fibrillation/flutter which is an AESI], valvulopathy, pulmonary hypertension, peripheral arterial thromboembolism, deep venous thrombosis / pulmonary embolism, revascularization [other than revascularizations intended for CEC

adjudication]) that meet SAE criteria or are non-serious events that result in discontinuation of investigational product will have additional event-specific details recorded in the eCRF. Frequency of the other CV events of special interest will be summarized, and subject profiles will be provided. These events will be identified as described in Section 11.6.3.

Summaries of creatinine will include baseline local and Central lab data and post-baseline scheduled visit Central lab data. Summaries of creatinine by visit will include the frequency of subjects with post-baseline creatinine values of 1.5 times baseline and 2 times baseline, stratified by baseline eGFR category (Normal ≥ 90, Mild ≥60 to <90, Moderate ≥30 to < 60, and Severe <30 ml/min/1.73m^2). Box plots of creatinine and change from baseline creatinine will be provided. In addition, as a sensitivity analysis, a summary of shifts from baseline with respect to potential clinical concern will be done including baseline and post-baseline scheduled visit Central lab data.

During the study a creatinine assay quality issue was reported by the central lab which resulted in artificially high values. In addition to creatinine results, eGFR values may have been affected. The central lab indicated that this issue was restricted to samples assayed between 01Oct2016 and 13Jan2017 for sites in a subset of countries. It is anticipated that approximately 5%-20% of creatinine results that were assayed during this time period may be artificially high. Summaries will be provided to allow the potential impact of this issue to be evaluated. In particular, four summaries will be rerun excluding all data with sample dates in the time frame 26Sep2016-13Jan2017 (inclusive) for sites in the following countries: Argentina, Canada, Mexico, Peru, US. The specified time frame represents the earliest and latest dates of affected samples based on data provided by the central lab. The four summaries will include those for potential clinical concern for creatinine and change from baseline creatinine, along with the two MMRM analyses for change from baseline eGFR.

The Requirement for the Mexican Ministry of Health will be composed of the following:

- Listing of non-serious AEs for subjects at Mexican sites (this is expected to only include non-serious AESIs and non-serious AEs leading to discontinuation of IP)
- Listing of clinical events and SAEs for subjects at Mexican sites
- Listing of SAEs for subjects at non-Mexican sites

Subject profile listings will be generated for the following subjects in the Safety population: subjects with AESIs, subjects with AEs leading to discontinuation of IP, subjects withdrawn from study, and subjects who died. The listings will include demography, disposition, medical/surgical procedures, medical history, medication, all reported AEs and SAEs, CV event, death, lab, and vital signs data.

Narratives will be generated for subjects in the Safety population experiencing SAEs, pregnancies, non-serious AEs leading to permanent discontinuation of IP, non-SAE deaths (if any), and the following non-serious AEs that did not lead to permanent discontinuation of IP, but which are of potential clinical importance: severe hypoglycaemic episodes (not meeting the definition of Serious as these are in the set of SAEs listed above), and hepatic events recorded on the Liver Events eCRF that met the

monitoring or stopping criteria. It is planned that some of these narratives will originate from the GSK ARGUS system; the remainder may be developed programmatically but would be provided separately from the other RAP-specified outputs by a group other than PPD.

Treatment details for relevant subjects will be provided electronically as a comma-separated values (CSV) file; this is intended for GSK Global Clinical Safety and Pharmacovigilance (GCSP) use and is not for inclusion with other listings.

Albiglutide pen injection failures and user errors are collected outside of the eCRF. Detailed information on reported cases at clinical sites that are related to the pen injector and the use of the pen injector and pen needle over the entire duration of the study are collected on specially designed forms that were completed by study subjects and study site staff. The information on these forms has been entered onto spreadsheets outside of the INFORM database. Summaries of these data, linked as appropriate to information on AEs, may be generated but would be provided separately from the other RAP-specified outputs by a group other than PPD.

9.3. Other Value Evidence and Outcomes Analyses

9.3.1. Overview of Planned Other Value Evidence and Outcomes Analyses

The other Value Evidence and Outcomes analyses will be based on the ITT population.

Table 11 provides an overview of the planned other efficacy analyses, with further details of data displays being presented in Section 11.15. As noted in Section 8.3.1, although not specified in the protocol, it was subsequently clarified in the Study Reference Manual and the eCRF Completion Guidelines that questionnaires were not to be completed after subjects discontinued study treatment; hence such data will be programmatically excluded from all summaries (but included in listings with corresponding flag).

Table 11 Overview of Planned Other Value Evidence and Outcomes Analyses

Endpoints	Absolute							Change from Baseline						
	Stats Analysis			Summary		Individual		Stats Analysis			Summary		Individual	
	T	F	L	T	F	F	L	T	F	L	T	F	F	L
In-patient Healthcare Resource Utilization				Y										
Study-specific Questionnaire				Y							Y (x2) [1]			

NOTES :

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- Individual = Represents FL related to any displays of individual subject observed raw data.

[1] For Question 1 and Question 3.

In-patient healthcare resource utilization data (duration of stay) will be summarized overall and by level of care/ward.

Study-specific (Managing Diabetes) questionnaire data will be summarized categorically by question for the baseline and post-baseline assessments. For Question 1 and Question 3 the frequency of combinations of responses at baseline and post-baseline will be summarized. Summaries will exclude data assessed after subjects discontinue study treatment.

9.4. Electronic Health Record Ancillary Study

A separate RAP will be developed by Duke Clinical Research Institute (DCRI) for the Electronic Health Record Ancillary Study. Results from this exploratory investigation will be reported separately from and after the main clinical study report.

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11. APPENDICES

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

11.1.1. Important Protocol Deviations

Subject compliance to the protocol will be evaluated prior to unblinding the study (except for wrong study treatment administered, see Section 11.1.2) and subjects with important protocol deviations will be identified. Criteria for what constitutes an important protocol deviation are specified in the Protocol Deviation Management Plan (PDMP).

11.1.2. Exclusions from Per Protocol Analysis

The following criteria define the conditions which lead to exclusion of data from the PP analysis and are specified in the PDMP. These include protocol deviations which will be reviewed by a subgroup of the study team to assess and confirm whether they are likely to have sufficient impact to warrant the exclusion of subject data from the PP analysis. These reviews will occur before the database has been frozen for analysis. Assessment of whether a subject was dispensed the wrong study treatment (i.e. actual treatment differs from randomized treatment) will be confirmed after unblinding.

The PP analysis will be done using the Per-Protocol Analysis Time Period (see Section 11.6.4) and will include all randomized subjects who provide consent and receive at least one dose of study treatment, exclude data prior to treatment start date and data after the date of last dose of study treatment + 56 days, and exclude data via censoring for subjects experiencing the specified conditions.

Number	Data Exclusion Description	Data Excluded
01	Inclusion #1 – Did not have type 2 diabetes	Data on or after randomization (censored at day 1)
02	Exclusion #2 – Use of GLP-1 receptor agonist at Screening	Data on or after randomization (censored at day 1)
03	Non-study GLP-1 receptor agonist was taken	Data on or after first use of GLP-1 receptor agonist anytime after randomization
04	Incorrect study drug assignment of more than one container at a visit	Data on or after date that at least two containers with incorrect study drug are dispensed
05	Subject off study treatment for at least 56 consecutive days.	Data on or after the date off study treatment + 57 days

For criterion number 05, determination of whether subjects are off study treatment for at least 56 consecutive days will account for subjects who have gaps in study treatment as well as account for treatment stop date. For subjects with gaps who have multiple entries recorded in the Study Treatment Form eCRF, days off study treatment = (start date – previous stop date – 1). Exclude data on or after the earliest of the following:

- treatment stop date + 57 days
- IP stop date + 57 days, where IP stop date corresponds to the earliest such value for which days off study treatment is at least 56 days (if such cases of gaps in study treatment occurred).

For purposes of evaluating criterion 05 only, cases in which partial or missing stop dates are present will be handled as follows:

- Partial or missing last stop date will be imputed as specified for Treatment Stop Date in Section 11.6.1.
- Partial or missing stop dates other than last stop date will be handled as follows:
  - If imputing the earliest possible stop date consistent with the corresponding start date and subsequent start date results in days off study treatment < 56 days then do not exclude data. Otherwise handle as follows:
  - If only year is available, or if date is completely missing, then do not impute stop date and do not exclude data.
  - If month and year are available, but the day of month is missing, then determine the range of potential date values and use the middle of this range as the imputed stop date. The beginning of the potential range of date values is the maximum of the following two dates: start date + 1, the first of the month of the stop date of interest. The end of the potential range of date values is the last day of the month of the stop date of interest. If there is an even number of dates (n=2m) in the potential range of date values then use the date corresponding to the (m+1)th of the ordered dates.

For purposes of evaluating criterion 05 only, cases in which partial or missing start dates are present will be handled as follows:

- Partial or missing start dates will be handled as follows:
  - If imputing the latest possible start date consistent with the corresponding stop date and previous stop date results in days off study treatment < 56 days then do not exclude data.
  - If imputing the earliest possible start date consistent with the corresponding stop date and previous stop date results in days off study treatment ≥ 56 days then exclude data based on the earliest possible start date.
  - Otherwise handle as follows:
  - If only year is available, or if date is completely missing, then do not impute start date and do not exclude data.
  - If month and year are available, but the day of month is missing, then determine the range of potential date values and use the middle of this range as the imputed start date. The beginning of the potential range of date values is the first of the month of the start date of interest. The end of the potential range of date values is the minimum of the following two dates: stop date - 1, the last day of the month of the start date of interest. If there is an even number of dates (n=2m) in the potential range of date values then use the date corresponding to the (m+1)th of the ordered dates.

11.2. Appendix 2: Time & Events

The following two tables have been copied from the protocol.

11.2.1. Time and Events Table

Procedures[1,2]	Screening[3]	Randomization[3] /Baseline (can be same day as Screening Visit)	Study Drug Check Phone Call (4-6 wks post rand.)	Clinic Visit Month 4 ± 18 days then every 4 months ± 18 days throughout the study	Unscheduled dose adjustment visit (if warranted)	Final study clinic visit[4] (or early withdrawal)	Follow up Phone Call 5 ± 1 weeks after last IP dose
Written informed consent	X						
Review of Inc/excl criteria	X	X					
Demography & directed medical history	X						
Assessment of MACE and micro-vascular events				X		X	
HbA1c	X[5]			X		X	
Serum creatinine (eGFR)	X[5]			X (alternate visits) [2]		X	
Liver Function Tests (LFTs)[6]		X		X (alternate visits) [2]		X	
Record available information on most recent lipid assessment [7]		X		X (annually)		X	
Genetic sampling [8]		X					
Patient reported outcomes questionnaires [9]		X[10]		X (alternate visits) [2]		X	
Key concomitant non-diabetes medication		X		X		X	X
Diabetes medication		X		X		X	X
Study drug reminder			X	X	X		
Physical examination [11]		X		X (alternate visits) [2]		X	
SAEs, AEs of special interest, AEs leading to IP discontinuation		X	X	X	X	X	X
Pregnancy test [12]	X	X					
Study drug dispense/compliance [13]		X		X	X	X	

1. Subjects who discontinue investigational product should be handled as described in Protocol Section 4.4 and Section 4.5. and Table 2 .
2. Assessments at month 8, 16, 24 etc. will include patient reported outcomes questionnaires, serum creatinine (eGFR), LFTs and physical examination. Those at months 4, 12, 20 etc do not.
3. Screening and Randomization can occur at the same visit if all eligibility information is available. If Screening and Randomization occur at the same visit assessments should not be duplicated.
4. Once it is projected that the target number of MACE events will have been collected, a 3 month window will be defined for conducting the final, face to face visit.

5. HbA1c and creatinine assessed using local laboratories at Screening visit and measured no more than 6 months prior to randomization. If HbA1c or creatinine have not been assessed in the previous 6 months assessments to be performed via a central laboratory and results available prior to randomization. The investigator has the discretion to repeat screening HbA1c, and/or creatinine, based on clinical rationale even if previously available local results meet the eligibility criteria to allow the investigator to accommodate the possibility of change between screening and randomization.
6. Liver function tests: ALT, AST, alkaline phosphatase, bilirubin, GGT. Blood samples for LFTs at randomization must be collected prior to the first dose of investigational product.
7. Lipid values (TC, LDLc, HDLc, Tg) to be recorded as available from routine clinical care at baseline and annually thereafter. If results are unavailable, lipids tests are not to be performed for the study.
8. Informed consent for genetic research must be obtained before collecting a sample. This can be collected at any time after genetic consent has been obtained and randomization has occurred.
9. TRIM-D, EQ-5D and study specific questionnaire (details in Protocol Section 6.3).
10. TRIM-D is not required for subjects whose diabetes is treated by diet and exercise alone at Baseline.
11. See Protocol Section 6.2.7.
12. Only applies to women of child bearing potential. At screening perform urine pregnancy test. If positive, send serum sample to the central laboratory for confirmation. At Randomization perform a urine pregnancy test. If result is positive do not randomise the subject. If the urine pregnancy test is negative then the subject can be randomized. If Screening and Randomization are to take place at the same visit then follow the instructions for Screening. See Protocol Section 6.2.6.
13. Study drug dispensing not performed at final visit, compliance check not performed at Randomization.

11.2.2. Time and Events Table for Subjects Who Permanently Discontinue IP Prior to the End of the Study

Procedures	Clinic visit as soon after permanent discontinuation of IP as possible	Phone Call 5 ± 1 week after last IP dose	Continue contact schedule established at randomization 4 monthly ± 1 month. ***Telephone*** [1,2]	Continue contact schedule established at randomization 4 monthly ± 1 month. ***Clinic visit*** [1,3]	Final study clinic visit [4]
Assessment of MACE and micro-vascular events	**X**		**X**	**X**	**X**
HbA1c	**X**			**X**	**X**
Serum creatinine (eGFR)	**X**			**X**	**X**
Liver Function Tests (LFTs)[5]	**X**			**X**	**X**
Record available information on most recent lipid assessment[6]	**X**		**X (annually)**	**X (annually)**	**X**
Patient reported outcomes questionnaire[7]	**X**				
Key concomitant non-diabetes medication	**X**	**X**	**X**	**X**	**X**
Diabetes medication	**X**	**X**	**X**	**X**	**X**
Physical examination[8]	**X**			**X**	**X**
AEs leading to IP discontinuation	**X**				
SAEs, AEs of special interest,	**X**	**X**	**X**	**X**	**X**
Study drug compliance	**X**				

1. After subjects permanently discontinue IP, follow-up should continue on the 4-monthly schedule established at randomization.
2. Where a subject would have been scheduled to attend clinic at months 4, 12, 20, 28 etc after randomization, a telephone contact will be performed instead (with assessments as shown above).
3. Where a subject would have been scheduled to attend clinic at months 8, 16, 24, 32 etc after randomization, a clinic visit will be performed (with assessments as shown above).
   If a subject who has permanently discontinued IP is unable to attend clinic then they will be contacted by telephone instead and the telephone contact assessments will be performed.
4. Once it is projected that the target number of MACE events will have been collected, a 3 month window will be defined for conducting the final, face to face visit.
5. Liver function tests: ALT, AST, alkaline phosphatase, bilirubin, GGT.
6. Lipid values (TC, LDLc, HDLc, Tg) to be recorded as available from routine clinical care annually. If results are unavailable, lipids tests are not to be performed for the study.
7. TRIM-D, EQ-5D and study specific questionnaire (details in Protocol Section 6.3**)**.
8. See Protocol Section 6.2.7.

11.3. Appendix 3: Assessment Windows

11.3.1. Assessment Windows

Data will be analyzed based on the visit information recorded in the eCRF. Data for unscheduled visits (including AESI labs and vitals and also CV event vitals), final study clinic (i.e., End of Study) visits (those scheduled to occur within the 3 month window), follow-up phone calls (5 ± 1 weeks after last IP dose) and early withdrawal visits will be assigned to a scheduled visit if the visit date falls within the corresponding protocol-defined visit window (Section 11.2) as specified. For lab data other than lipids the assignment to post-baseline visits will only be done for Central lab data (local lab data will be excluded).

Scheduled Visit	Target Study Day of Visit	Slotting Intervals
Screening	Not applicable	Not applicable
Randomization/Baseline	1	Not applicable
Month X, X=4, 8, 12, 16, etc.	X calendar months after the randomization date. If there is no such date then target is the latest day of that month. For example, if randomization is 31 July then Month 4 target date is 30 November.	Target study day +/- 18 days (inclusive)

Lipid data from local labs are recorded in the Lipids Collection log eCRF. Baseline values will be determined as per Section 11.5.2. Post-baseline values will be assigned in the following manner:

Scheduled Visit	Target Study Day of Visit	Slotting Intervals
Month 12	Month 12 visit date	(treatment start date + 1) to Month 12 visit date (inclusive); if treatment start date is missing then use randomization date instead
Month 24.	Month 24 visit date	(Month 12 visit date + 1) to Month 24 visit date (inclusive)
Month 36, etc.	Analogous to Month 24	Analogous to Month 24

11.4. Appendix 4: Treatment States and Phases

11.4.1. Treatment States for MACE

Treatment State	Definition
Pre-treatment	Event Date < Study Treatment Start Date
On-treatment	If event date is on or after treatment start date & on or before treatment stop date. Study Treatment Start Date ≤ Event Date ≤ Study Treatment Stop Date
Post-treatment	If event date is after the treatment stop date Event Date > Study Treatment Stop Date
Pre-therapy	Event Date < Study Treatment Start Date
On-therapy (during treatment or up to 56 days post-treatment)	If event date is on or after treatment start date & within 56 days after treatment stop date. Study Treatment Start Date ≤ Event Date ≤ Study Treatment Stop Date+56 days
Post-therapy	If event date is after the treatment stop date+56 days. AE Start Date > Study Treatment Stop Date+56 days

11.4.2. Treatment States for AE data

Treatment State	Definition
Pre-therapy	AE Start Date < Study Treatment Start Date
On-therapy (during treatment or up to 56 days post-treatment)	If AE onset date is on or after treatment start date & within 56 days after treatment stop date. Study Treatment Start Date ≤ AE Start Date ≤ Study Treatment Stop Date+56 days
Post-therapy	If AE onset date is after the treatment stop date+56 days. AE Start Date > Study Treatment Stop Date+56 days

NOTES:

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

If only partial information is available for the onset date of an AE, or onset date is missing, then the AE will be included in the most conservative therapy period (On-therapy > Post-therapy > Pre-therapy) that is consistent with the therapy period definitions above and the available AE onset and resolution date information.

11.4.3. Treatment States for lab and vitals data

Treatment State	Definition
On-treatment	If assessment date is after treatment start date & on or before treatment stop date. Study Treatment Start Date < Assessment Date ≤ Study Treatment Stop Date

11.5. Appendix 5: Data Display Standards & Handling Conventions

11.5.1. Study Treatment & Sub-group Display Descriptors

Study Treatment Descriptions			
PPD IRT		Data Displays for Reporting	
Code	Description	Description	Order
1	Albiglutide	Albiglutide	2
2	Placebo	Placebo	1

11.5.2. Baseline and Screening Definition & Derivations

11.5.2.1. Baseline Definitions

The baseline value for an assessment is defined as the last non-missing value assessed on or before treatment start date. Generally the time of assessment is not collected; hence this definition assumes that assessments collected on the same day as treatment start were done prior to treatment start. For creatinine, eGFR and HbA1c, if both local and Central Lab results are available for a given date then the Central lab value will be used.

For medication use, baseline use is defined as recorded data for which the start date of the medication is on or before treatment start date and the end date is on or after the treatment start date or ongoing or missing.

For subjects not receiving any study treatment, who therefore have no study treatment start date, baseline values and baseline medication use will be determined based on date of randomization.

11.5.2.2. Derivations and Handling of Missing Baseline Data

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

NOTES :

- Unless otherwise specified, the baseline definitions specified in Section 11.5.2 will be used for derivations for endpoints / parameters and indicated on summaries and listings.
- Unless otherwise stated, if baseline data is missing no derivation will be performed and will be set to missing.

11.5.2.3. Screening Definitions

The screening value for an assessment is defined as the last non-missing value assessed on or before the screening visit date. For creatinine, eGFR and HbA1c, if both local and Central Lab results are available for a given date then the Central lab value will be used.

11.5.3. Reporting Process & Standards

General
Key efficacy tables will be generated according to current therapeutic area cardiovascular endpoint statistical display standards; otherwise, reporting will be done generally based on the current GSK Integrated Data Standards Library (IDSL) with some variations implemented so as to gain efficiencies from the use of standard PPD programming tools. All analyses will be conducted using SAS Version 9.2 or higher. In general, listings will be sorted by treatment group (arm), site ID, and unique subject ID. If no data are available for a table, listing, or figure then the text "No Data to Report" will be printed in the body of the display. All outputs will be provided by PPD as portable document format (PDF) files; also rich text format (RTF) files will be provided for tables and listings. SDTM version 3.1.3, Analysis Data Model (ADaM) version 2.1 and ADaM IG v1.0 will be used for datasets.

11.5.4. Laboratory Assessments

Censored Laboratory Assessments
Laboratory results that are beyond the limits of quantification will have the inequality sign dropped (<, ≤, >, ≥, 'less than', 'greater than', or text equivalents) and the quantification limit will be used as the numeric result for summarization.

11.5.5. Adverse Events Conventions

Adverse Events	
AE Onset Time Since First Dose (Days)	• If Treatment Start Date > AE Onset Date : **= AE Onset Date - Treatment Start Date** • If Treatment Start Date ≤ AE Onset Date : **= AE Onset Date – Treatment Start Date + 1** • Missing otherwise
AE Duration (Days)	• **AE Resolution Date – AE Onset Date + 1**
AE = Drug-related	• If relationship is marked 'YES' on eCRF OR value is missing.

11.5.6. Coding of Adverse Events and Medications

Medications
Medications collected on the concomitant medication eCRF screen will be coded using the GSK Drug coding dictionary and summarized by GSK-Drug Anatomical Therapeutic Chemical (ATC) classification level 1 (body system).
Adverse Events
Adverse events will be coded using the Medical Dictionary for Regulatory Activities (MedDRA).

11.6. Appendix 6: Derived and Transformed Data

11.6.1. General

Multiple Measurements at One Time Point

• If there are multiple valid records for an assessment within an assigned analysis visit (i.e., assigned by site and/or assigned by slotting), only one of these records will be used for summary statistics and analyses. The record to be used is determined using the following hierarchy (in decreasing order):
  ○ the record closest to the target visit day
  ○ the record with an original nominal visit that matches the analysis visit
  ○ the record earliest in time
  ○ if the above does not result in a unique record, then the maximum assessment value of the records identified will be used in the determination of summary statistics
• Regardless of the determination of the record to be used for summary statistics, if data are listed, all data will be presented.
• Subjects having both High and Low values for Normal Ranges at any post-baseline visits for safety parameters will be counted in both the High and Low categories of “Any visit post-baseline” row of related summary tables. This will also be applicable to relevant Potential Clinical Importance summary tables.

Randomization Date
• Date subject was randomized as recorded in the eCRF.
Treatment Start Date
• First IP start date
Study Completion/Withdrawal Date
• Date of subject completion or withdrawal is recorded in the eCRF and corresponds to the date of withdrawal for subjects withdrawing from study (date at which the investigator agreed, or determined, that the subject's participation in the study was over; typically, this will be last study visit date) or date of completion of study (last study visit date) for subjects who complete the study (per Section 11.7.1). Subjects who die while on study are considered to have completed the study and completion date is the date of death. For subjects lost to follow-up, the date of withdrawal corresponds to the last contact between the Investigator and the subject during the study period as defined in the protocol.

Treatment Stop Date

- Last IP stop date if complete date (day, month and year) is available
- If Last IP Stop date is completely missing and the subject has a non-missing treatment start date, then use the earliest of the following two items:
  - date of death,
  - latest of the following four items:
    - last visit date (exclude 5 week post-IP telephone call date),
    - last date of most recent IP injection from the Investigational Product injection site reaction eCRF,
    - last date of last study treatment dose from Liver pharmacokinetic (PK) eCRF,
    - earlier of (date of study completion/withdrawal, last IP start date (if not treatment start date) + 20 weeks).
- If Last IP stop date is partial (i.e., either only year, or month and year are nonmissing) then impute as the latest date on or before the earliest of the following two items:
  - date of death
  - latest of the following three items:
    - last visit date (exclude 5 week post-IP telephone call date)
    - last date of most recent IP injection from the Investigational Product injection site reaction eCRF,
    - last date of last study treatment dose from Liver PK eCRF

  that is consistent with the nonmissing date components.

Study Day

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

Treatment Day

- Calculated as the number of days from treatment start date:
  - Treatment Start Date = Missing → Treatment Day = Missing
  - Ref Date < Treatment Start Date → Treatment Day = Ref Date – Treatment Start Date
  - Ref Date≥ Treatment Start Date → Treatment Day = Ref Date – (Treatment Start Date) + 1

Last CV Assessment Date

- Last CV Assessment Date is the latest visit date on or before the date of the End of Study visit (clinic visit, telephone call, other contact, 3rd party contact) where all elements of the primary endpoint are captured (i.e., for which the Cardiac Ischemic Event event status and the Stroke/TIA event status are marked as “Yes” or “No”). For subjects who complete the study on treatment, the 5 week post IP telephone call will not be included. For subjects who have withdrawn consent for all follow-up, the Last CV Assessment Date is considered to be the date of withdrawal of consent or the Last CV Assessment, whichever occurs earlier.

Last Study Contact Date
• Last study contact date (clinic visit, telephone or video contact or other contact with the subject or contact with party other than the subject) is the date of last point of study follow-up at which vital status is known. For subjects who have withdrawn consent for all follow-up the last study contact date will include all follow-up where vital status has been established (e.g. via publicly available sources) after the date of withdrawal of consent.
Time Definitions (per GSK standard principles)
• 1 week = 7 days • 1 month = 30.4375 days • 1 year = 365.25 days

11.6.2. Study Population

Demographics and Baseline Data
Age
Only birth year is collected in the eCRF; birth day and month will be imputed as '30th June'. • Birth date will be presented in listings as year of birth, as 'YYYY'. • For randomized subjects, age, in whole years, will be calculated with respect to the date of randomization using the imputed date of birth. For subjects not randomized, age, in whole years, will be calculated with respect to the baseline visit date if visit done and date is available, and with respect to screening visit date otherwise.
Duration of Diabetes Disease History
• The duration of diabetes disease history is calculated as the years lapsed between screening visit date and type 2 diabetes diagnosis date. For partial missing diagnosis date, the missing month is imputed as January and the missing day is imputed as the first of the month to calculate duration.
Body Mass Index (BMI)
• Calculated as **Weight (kg) / [Height (m)]^2**

Race Groups
• Geographic ancestry data will be combined into categories as provided by the US Food and Drug Administration (FDA) and summarized as FDA race group: o American Indian or Alaskan Native o Asian (Asian-East Asian Heritage, Asian-Japanese Heritage, Asian-Central/South Asian Heritage, Asian-South East Asian Heritage, Asian-Mixed Race) o Black or African American o Native Hawaiian or Other Pacific Islander o White (White-Arabic/North African Heritage, White-White/Caucasian/European Heritage, White – Mixed Race) o Mixed Race (Multiple races are selected, but excludes Asian – Mixed Race and White – Mixed Race) Note: Asian – Mixed Race includes subjects who have more than one Asian category selected, but no other categories. White – Mixed Race includes subjects who have more than one White category selected, but no other categories.

Study Treatment Discontinuation, Study Withdrawal, and Follow-up Periods
Study Treatment Discontinuation
• Study Treatment Discontinuation Censored Time (days) = Censoring date – Treatment start date +1 where censoring date is determined as defined for Treatment Stop Date.
• Time to Study Treatment Discontinuation (days) = Treatment stop date – Treatment start date +1
• Study Treatment Person-Years = (Cumulative total of time to treatment discontinuation for subjects who discontinued study treatment + Cumulative total of treatment discontinuation censored time for subjects who did not discontinue study treatment) / 365.25
• Study Treatment Discontinuation Incidence Rate (per 100 person-years) = 100* Number of subjects who discontinued study treatment / study treatment person-years
Study Withdrawal
• Study Censored Time (days) = Study Completion date (per eCRF Conclusion form) – Randomization date +1
• Time to Study Withdrawal (days) = Study withdrawal date – Randomization date +1
• Study Person-Years = (Cumulative total time to study withdrawal for subjects withdrawing from the study + Cumulative total of study censored time for subjects who did not withdraw from study) / 365.25
• Study Withdrawal Incidence Rate (per 100 person-years) = (100 * Number of subjects who have withdrawn from study) / Study Person-Years
Completion Status
• Subjects completing study on IP: endpoints will be recorded in the eCRF up until date of final visit during 3 month window. • Subjects completing study off IP: endpoints will be recorded in the eCRF up until date of final subject contact during 3 month window. • Subjects lost to follow-up: efforts to locate and contact subject will continue up until study end. Endpoints will be recorded in the eCRF up until the date of final subject contact (could be after the 3 month window). If endpoint status during or after the 3 month window is obtained then the subject will have completed the study and no further data collection will occur. • Subjects who withdrew consent to contact: collection of information on endpoints will be sought from available sources up until study end. If endpoint status during or after the 3 month window is obtained then the subject will have completed the study and no further data collection will occur.
Possible Vital Status Follow-up Time
• Possible vital status follow-up time (days) is defined as the following: For subjects who died, use the date of death – randomization date +1 For subjects who did not die, and completed the study, use the Last Study Contact Date –

Study Treatment Discontinuation, Study Withdrawal, and Follow-up Periods

randomization date + 1
For subjects who did not die, and did not complete the study, use the date of the middle of the 3 month end of study window (i.e., window start date + floor ((window end date – window start date)/2) – randomization date + 1

- Total possible vital status follow-up time (person years) = Cumulative total of possible vital status follow-up time (days) for all subjects / 365.25

Possible CV Follow-up Time

- Possible CV follow-up time (days) is defined as the following:
  For subjects with a first MACE event, use the date of first MACE event – randomization date +1; otherwise use the following:
  For subjects who died, use the date of death – randomization date +1.
  For subjects who did not die, and who have an End of Study visit date is within the 3 month end of study window, use the End of Study visit date – randomization date + 1.
  For subjects who did not die, and whose last visit date is before the beginning of the 3 month end of study window, use the date of the middle of the 3 month end of study window (i.e., window start date + floor ((window end date – window start date)/2) – randomization date + 1).
- Total possible CV follow-up time (person years) = Cumulative total of possible CV follow-up time (days) for all subjects / 365.25

Follow-up Periods

The follow-up periods from the date of randomization associated with event driven analyses are described in the following table. Any endpoints that occurred before randomization are considered to be prior to the time period for follow-up of CV endpoints and will be excluded from all analyses.

Endpoint	Follow-up Period	Definition of Follow-Up Period (from date of randomization)
• Primary endpoint (CV death, MI, or Stroke) • Secondary CV Endpoints	CV Event Assessment [1]	Date of the 1st event or Latest of Last CV assessment date or death date in subjects who had not withdrawn consent' [2]
All-Cause Mortality	Vital Status Assessment	Date of death or Last study contact date [3]

[1] A sensitivity analysis will be performed to include post-WDC (withdrawal of consent) data (i.e., deaths and CV events if collected through publicly available sources for subjects who have withdrawn consent for all follow-up).
[2] Within the time period for follow-up of CV endpoints.
[3] Within the time period for follow-up of vital status.

Completeness of Follow-up

For disposition summaries, the completeness of follow-up will be ascertained for CV Event Assessment and Vital Status Assessment through to the End of Study. Definitions are as follows:

Study Treatment Discontinuation, Study Withdrawal, and Follow-up Periods

CV Event Assessment: A subject is considered to have complete CV event assessment through to study end if he/she underwent a clinical assessment for CV events at any time during or after the end of study window.

Primary Endpoint Assessment: A subject is considered to have complete primary endpoint assessment if the subject either had complete CV event assessment or experienced a component of the primary endpoint prior to the start of the end of study end visit window.

Vital Status Assessment: A subject is considered to have complete vital status assessment through to study end if he/she has been assessed for vital status at any time during or after the end of study window.

Subjects who have withdrawn consent for all follow-up prior to the start of the end of study visit window and are event free will be considered as having incomplete CV Event and incomplete Primary Endpoint Assessment at study end. However if they experienced a component of the primary endpoint prior to withdrawal of consent they will be considered complete for Primary Endpoint Assessment.

Extent of Exposure

The protocol specifies that subjects start at a dose of 30mg once weekly (albiglutide or albigultide matching placebo), and that dose increases to 50mg and subsequent dose decreases to 30mg are allowed as deemed appropriate by the Investigator.

Two measures of duration of exposure to study drug will be computed:

- Duration of Exposure Including Breaks = Treatment Stop Date – Treatment Start Date + 1

- Duration of Exposure Excluding Breaks, for which treatment breaks during the study based on eCRF data will be excluded from the overall exposure result. This will be computed as the sum of the durations of exposure determined by the individual entries in the Study Treatment Form.

Based on the eCRF completion guidelines, it is expected that individual entries will be recorded in the Study Treatment Form for breaks of 4 or more consecutive doses, or investigator directed temporary study treatment stoppages. In addition, entries are expected for dose escalations and dose reductions. Consecutive eCRF entries will not describe a break if the start date of the new dose is 10 or less days after the stop date of the previous dose (i.e., (start date – previous stop date) ≤ 10).

For albiglitude subjects only, the duration of exposure by dose level will be calculated based on the start and stop dates for each dose level separately.

Duration of exposure in weeks is computed as the corresponding duration of exposure in days divided by 7.

Total Study Treatment Exposure Including Breaks in Person-Years = Cumulative total of (Treatment

Study Treatment Discontinuation, Study Withdrawal, and Follow-up Periods

Stop Date – Start Date + 57) / 365.25

For albiglutide subjects only, Total Study Treatment Exposure Including Breaks in Person-Years will be computed by dose level; this will be done by adding 56 days to the duration of exposure for the latest dose level that was received by the subject.

Example:

Given the following exposure data for an albiglutide subject:

Dose	Start date	Stop date
30mg	SD1	ED1
30mg	SD2 = ED1 + 30	ED2
50mg	SD3 = ED2 + 7	ED3
30mg	SD4 = ED3 + 7	ED4

Duration of Exposure including breaks (weeks):
30mg = [(ED2 – SD1 + 1) + (ED4 – SD4 + 1)] / 7
50mg = [ED3 – SD3 + 1] / 7
Total = [ED4 – SD1 + 1] / 7

Total Study Treatment Exposure Including Breaks (PY):
30mg = [(ED2 – SD1 + 1) + (ED4 – SD4 + 1) + 56] / 365.25
50mg = [ED3 – SD3 + 1] / 365.25
Total = [ED4 – SD1 + 1 + 56] / 365.25

Duration of Exposure excluding breaks (weeks):
30mg = [(ED1 – SD1 + 1) + (ED2 – SD2 + 1) + (ED4 – SD4 + 1)] / 7
50mg = [ED3 – SD3 + 1] / 7
Total = [(ED1 – SD1 + 1) + (ED2 – SD2 + 1) + (ED3 – SD3 + 1) + (ED4 – SD4 + 1)] / 7

Time to first dose escalation and time to first dose reduction are based on start date of study treatment.

Study Treatment Compliance

Two types of study treatment compliance will be computed:

- % Treatment Compliance including breaks =

$$100 * \frac{\text{(Total \# pens dispensed – Total \# pens returned unused)}}{\text{(Expected \# pens used)}}$$

Study Treatment Discontinuation, Study Withdrawal, and Follow-up Periods

Expected # pens used = ceiling[Duration of Exposure Including Breaks / 7] where
ceiling [x] = smallest integer ≥ x

- % Treatment Compliance excluding breaks =

$$100 * \frac{\text{(Total \# pens dispensed – Total \# pens returned unused)}}{\text{(Sum of Expected \# pens used)}}$$

Expected # pens used = ceiling[(stop date – start date + 1) / 7] where
ceiling [x] = smallest integer ≥ x. This is computed for each set of start and stop dates recorded in the Study Treatment eCRF form, and then summed up to provide the denominator of the compliance computation.

Categories of treatment compliance will be created as follows: missing, <80%, >=80%.

If unused pens are missing/lost and no unused pens are returned, then the number of unused pens returned is expected to be recorded as blank (i.e., missing). If some unused pens are missing/lost but some are returned, then the actual number of unused pens returned is expected to be recorded.

Medication Use

Post-Baseline medications are those with end date on or after the treatment start date or ongoing or missing.

Latest visit medications are those being taken at the latest post-baseline visit (start date on or before latest visit date and end date on or after latest visit date or ongoing or missing).

11.6.3. Safety

Time to Death endpoint

- Time to Death is defined as follows:
  For subjects who died, time to death is the date of death - start date +1.
  For subjects who did not die, time to death (censored) is the censoring date – start date + 1.
  Occurrence and date of death will be determined based on data recorded in the CEC Death form; if adjudicated death date is missing then investigator-reported death date will be used.
  Start date and censoring date will be assigned based on the evaluation time period of interest as subsequently specified.

Evaluation Time Period for Vital Status

Time Period for Follow-up of Vital Status

The start date of the time period for capturing vital status is the date of randomization. The end of this time period is defined as follows:

- For all subjects known to have died, use the date of death
- Otherwise, use the Last Study Contact Date.

Any endpoints that occurred before the start of this time period are considered to be prior to the time

Time to Death endpoint
period for vital status, and any endpoints that occurred after the end of this time period are considered to be post the time period for vital status.
Time Period for On-treatment Deaths
The start date of the time period for capturing On-treatment deaths is the treatment start date for subjects who received study treatment, and the date of randomization otherwise. The end of this time period is defined as follows: • For subjects who did not receive study treatment, use the date of randomization • For all subjects known to have died, use the earliest of the following two dates: treatment stop date and date of death. • Otherwise, use the earliest of the following two dates: treatment stop date and Last Study Contact Date. If the censoring date as defined above for On-treatment deaths is after the censoring date as defined for the time period for follow-up of vital status, then use the censoring date as defined for the time period for follow-up of vital status. Any events that occurred before the start of this time period are considered to be prior to the time period for On-treatment deaths, and any events that occurred after the end of this time period are considered to be post the time period for On-treatment deaths.
Time Period for On-therapy Deaths
The start date of the time period for capturing On-therapy deaths is the treatment start date for subjects who received study treatment, and the date of randomization otherwise. The end of this time period is defined as follows: • For subjects who did not receive study treatment, use the date of randomization. • For all subjects known to have died, use the earliest of the following two dates: treatment stop date + 56 days and date of death. • Otherwise, use the earliest of the following two dates: treatment stop date + 56 days and Last Study Contact Date. If the censoring date as defined above for On-therapy deaths is after the censoring date as defined for the time period for follow-up of vital status, then use the censoring date as defined for the time period for follow-up of vital status. Any events that occurred before the start of this time period are considered to be prior to the time period for On-therapy deaths, and any events that occurred after the end of this time period are considered to be post the time period for On-therapy deaths.
• Endpoint person-years = (cumulative total time to death for subjects who died + cumulative total of censored time for subjects without the event) / 365.25 • Incidence rate (per 100 person-years) = (100 * number of subjects who died) / endpoint person-years • Endpoint absolute rate difference (per 100 person-years) = albiglutide incidence rate (per 100

Time to Death endpoint
person-years) – placebo incidence rate (per 100 person-years)

Adverse Events
General definitions
• Time to first AE is defined as follows: For subjects who had at least one AE of interest, time to first AE = onset date of first AE – treatment start date + 1. For subjects who did not have at least one AE of interest, time to first AE (censored) is the censoring date – treatment start date + 1. Censoring date will be assigned based on the evaluation time period of interest as subsequently specified. • AE incidence rate (per 100 person-years) = (100 * number of subjects with at least one AE) / first AE person-years • First AE person-years = (Cumulative total of time to first AE for subjects who have the AE + Cumulative total of censoring time for subjects without the AE) / 365.25 • AE density, also referred to as event density, will be calculated for specified AEs. AE density = number of events / AE density person-years and will be presented per 100 person-years. • AE density person-years = cumulative total of censoring time / 365.25, where censoring time is the censoring date – treatment start date + 1. Censoring date will be assigned based on the evaluation time period of interest as subsequently specified.
Time Period for On-treatment AEs
The time period for capturing On-treatment AEs begins at treatment start date. The end of this time period is the earliest of the following two dates: treatment stop date, latest of clinic visits, phone calls and other contact with subject. Any events that occurred before the start of this time period are considered to be prior to the time period for On-treatment AEs, and any events that occurred after the end of this time period are considered to be post the time period for On-treatment AEs.
Time Period for On-therapy AEs
The time period for capturing On-therapy AEs begins at treatment start date. The end of this time period is the earliest of the following two dates: treatment stop date + 56 days and latest of clinic visits, phone calls and other contact with subject. Any events that occurred before the start of this time period are considered to be prior to the time period for On-therapy AEs, and any events that occurred after the end of this time period are considered to be post the time period for On-therapy AEs.
Time Period for On-therapy and Post-therapy AEs
The time period for capturing On-therapy and Post-therapy AEs begins at treatment start date. The

end of this time period is the latest of the following: latest of clinic visits, phone calls and other contact with subject, latest non-missing AE start date, latest non-missing AE end date.

Any events that occurred before the start of this time period are considered to be prior to the time period for On-therapy and Post-therapy AEs, and any events that occurred after the end of this time period are considered to be post the time period for On-therapy and Post-therapy AEs.

AEs of Special Interest

Following are the protocol-specified AEs of special interest:

- Development of thyroid cancer
- Haematologic malignancy
- Pancreatic cancer
- Pancreatitis
- Investigational Product Injection site reactions
- Immunological reactions
- Severe hypoglycaemic events
- Hepatic events
- Hepatic enzyme elevations (including GGT)
- Serious GI events
- Appendicitis
- Atrial fibrillation/flutter
- Pneumonia
- Worsening renal function
- Diabetic retinopathy

For some of these AESIs (development of thyroid cancer, pancreatitis, investigational product injection site reactions, immunological reactions, severe hypoglycaemic events, atrial fibrillation/flutter, pneumonia, worsening renal function, diabetic retinopathy), event-specific details are recorded in the eCRF. Generally, the presence of these details will be used to identify these AESIs. However, for diabetic retinopathy, events will be identified if a diagnosis of diabetic retinopathy (background, pre-proliferative, or proliferative) for at least one eye is recorded on the Diabetic Eye Disease Event eCRF.

For the remaining AESIs (haematologic malignancy, pancreatic cancer, hepatic events, hepatic enzyme elevations (including GGT), serious GI events, appendicitis), these will be determined based on sets of coded terms as defined by safety review team (SRT) agreements. Per the protocol Section 6.2.3, severe hypoglycaemic events are defined as those episodes of hypoglycaemic symptoms for which the subject required assistance from another person and from which the subject recovered promptly after resuscitative actions and also including episodes of hypoglycaemic symptoms which are SAEs.

Pancreatitis events will be considered to be positively adjudicated if “Probability of Pancreatitis” = “Definite” or “Probability of Pancreatitis” = “Possible” as determined by the PAC.

Malignant Neoplasms

Malignant neoplasms are defined by SRT agreements.

Other CV Events

Following are the protocol-specified other CV events:

- Arrythymias
- Valvulopathy

- Pulmonary hypertension
- Peripheral Arterial Thromboembolism
- Deep Venous Thrombosis/Pulmonary Embolism
- Revascularization (other than revascularizations intended for CEC adjudication)

Arrhythmias will be determined based on data recorded in the Arrhythmia eCRF form excluding events that are indicated as having electrocardiogram (ECG) result of only "Atrial flutter" and/or "Atrial Fibrillation". Revascularization (other than revascularizations intended for CEC adjudication) will be determined based on data recorded in the percutaneous coronary intervention (PCI) eCRF form and the coronary artery bypass graft (CABG) eCRF form excluding events indicated as reason = "Acute coronary syndrome".

The remaining other CV events will be determined based on presence of data recorded in event-specific forms in the eCRF.

EGFR

eGFR will be computed based on measured creatinine and associated age using the formula specified in Section 6.2.6.1 in the protocol and reported in units of ml/min/1.73m^2. For this purpose associated age, in whole years, will be calculated with respect to the date of creatinine sample using the imputed date of birth (see Section 11.6.2).

nonHDLc

nonHDLc = TC - HDLc

If there are multiple values per date, compute nonHDLc as the maximum TC – maximum HDLc; if this results in a value < 0 then set to missing.

Albuminuria

History of albuminuria will be determined based on data recorded in the Nephropathy history eCRF (none, microalbuminuria, macroalbuminuria). Post-baseline albuminuria will be determined based on data recorded in the Renal Impairment eCRF (none, microalbuminuria, macroalbuminuria).

11.6.4. Efficacy

Time to Event endpoints

CV Events

- For all CV time to event endpoints (MACE, MACE or Urgent Revascularization for UA, CV Death, MI, Stroke, CV Death or HF Hospitalization), time to event is defined as follows:
  For subjects with one or more events, time to event is the date of first event - start date +1.
  For subjects with no event, time to event (censored) is the censoring date - start date +1.

Time to Event endpoints

CV Events

Start date and censoring date will be assigned based on the evaluation time period of interest as subsequently specified.

The definitions of MACE and other CV events are provided in Section 2 of the protocol. Following are more detailed descriptions of event determination.

- Adjudicated MACE events will be determined based on CEC-adjudicated cardiovascular death, myocardial infarction, or stroke. An adjudicated cardiovascular death event will be determined by a corresponding item being recorded in the CEC Death form and will include "Cause of Death" = "Cardiovascular" or "Cause of Death"="Undetermined Cause of Death"; date of event = date of death. An adjudicated myocardial infarction event will be determined by a corresponding item being recorded in the CEC MI/UA Requiring Hospitalization – Urgent Revascularization form in which "Did MI occur" = "Yes"; date of event = date of MI onset. An adjudicated stroke event will be determined by a corresponding item being recorded on the CEC Stroke/TIA form in which "Did stroke event occur" = "Yes"; date of event = date of stroke onset.

  For time to first occurrence of adjudicated MI, events will include adjudicated MI or death with adjudicated cause = MI. Thus, a fatal event which has adjudicated cause of death = MI but is not adjudicated as MI will be included as an event. A similar approach will be used for time to first occurrence of adjudicated stroke.

  Investigator-reported MACE events will be determined based on investigator-reported cardiovascular death, myocardial infarction, or stroke. A cardiovascular death event will be determined by a corresponding item being recorded in the Death eCRF form; these will include "Primary Cause of Death"="Cardiovascular" or "Primary Cause of Death"="Unknown", and date of event = date of death. A myocardial infarction event will be determined by a corresponding item being recorded in the Cardiac Ischaemic Event eCRF form in which "Final diagnosis"="MI", and date of event = date of onset of symptoms. A stroke event will be determined by one or more of the following items being recorded in the Stroke / TIA eCRF form: "Type of event"="Primary ischaemic stroke", "Type of event"="Primary intracranial hemorrhage", "Type of event"="Unknown type of stroke", and date of event = start date of neurological symptoms.

  Because of the way the eCRF is designed, a fatal MI is reported as both an MI and a death. Therefore, the MI event could have an event date that differs from the death date because the subject may have died as a result of the MI but not on the same day. For analysis of first occurrence of MACE, MI, or any other composite endpoint that includes both MI and death, the MI date will be used as the event date. For analysis of CV death only, CV death or hospitalization due to heart failure, and all-cause mortality only, the death date will be used. Similarly, fatal stroke events are reported as both a stroke and a death. For analysis of first occurrence of stroke, or any other composite endpoint that includes stroke and death, the stroke date will be used as the event date. For analysis of CV death only, CV death or hospitalization due to heart failure, and all-cause mortality only, the death date will be used.

  In the situation that there is a fatal MI (or fatal stroke) that does not have both an adjudicated MI (or stroke) endpoint and a death endpoint with adjudicated cause=MI (or stroke) reported, the

Time to Event endpoints
CV Events
date of the event that is reported and adjudicated as such will be used in the analysis of all relevant endpoints. In addition, situations may occur in which the MI (or stroke) occurs within an analysis period and the death occurs outside of the analysis period; in these situations the endpoint with the date in the analysis period will be used for all relevant endpoints. • Adjudicated urgent revascularization for unstable angina will be determined by a corresponding item being recorded on the CEC MI/UA Requiring Hospitalization – Urgent Revascularization form in which "Did UA Requiring Hospitalization occur" = "Yes" and "Did the subject have a coronary revascularization during this hospitalization?" = "Yes" and "Classification of Coronary Revascularization"="Non-Elective" (i.e., Urgent, Emergent or Salvage); date of event = date of coronary revascularization. Investigator-reported urgent revascularization for unstable angina will be determined by both of the following types of items being recorded in the eCRF: o "Final diagnosis" = "Unstable Angina" recorded in the Cardiac Ischemic Event eCRF form, o "Classification of Urgency" = "Urgent" or "Classification of Urgency" = "Unknown" recorded in the PCI eCRF form or the CABG eCRF form. Date of event = PCI date or CABG Procedure date, as applicable. To establish urgency the date of revascularization will be required to be no more than 7 days after the date of the UA. • Adjudicated HF hospitalization will be determined by a corresponding item being recorded on the CEC HF form in which "Did a hospitalization for heart failure occur?"="Yes"; date of event = date of hospitalization for heart failure. Investigator-reported HF hospitalization will be determined by "Was the subject hospitalized >= 24 hours?"="Yes" or "Was the subject hospitalized >= 24 hours?"="Unknown" and "Was the heart failure the primary reason for the hospitalization?" = "Yes" being recorded on the Heart Failure eCRF form. Date of event = date of event/episode recorded on the Heart Failure eCRF form. Because of the way the eCRF is designed, a fatal HF hospitalization is reported as both a HF hospitalization and a death. Therefore, the HF hospitalization event could have an event date that differs from the death date because the subject may have died as a result of the HF but not on the same day. In the situation that there is a fatal HF hospitalization that does not have both an adjudicated HF hospitalization endpoint and a death endpoint with adjudicated cause=HF or Cardiogenic Shock reported, the date of the event that is reported and adjudicated as such will be used in the analysis of CV death or hospitalization due to heart failure. • For all CV time to event endpoints, if multiple events occur on the same day and it is not clear which event first occurred, then the following order will be applied: MI Urgent revascularization

Time to Event endpoints
CV Events
Hospitalization for heart failure Stroke Death
• First event person-years = (cumulative total time to first event for subjects who have the event + cumulative total of censored time for subjects without the event) / 365.25 • First event incidence rate (per 100 person-years) = (100 * number of subjects with at least 1 event) / first event person-years • First event absolute rate difference (per 100 person-years) = albiglutide incidence rate (per 100 person-years) – placebo incidence rate (per 100 person-years)
Evaluation Time Periods for CV Endpoints
Time Period for Follow-up of CV Endpoints
• The start date of the time period for capturing CV endpoints is the date of randomization. The end of this time period is the later of the Last CV Assessment Date or the death date in subjects who had not withdrawn consent and had not reached the End of Study. Any events that occurred before the start of this time period are considered to be prior to the time period for follow-up of cardiovascular endpoints, and any events that occurred after the end of this time period are considered to be post the time period for follow-up of cardiovascular endpoints.
Time Period for On-treatment CV Endpoints
The start date of the time period for capturing On-treatment CV endpoints is the treatment start date for subjects who received study treatment, and the date of randomization otherwise. The end of this time period is defined as follows: • For subjects who did not receive study treatment, use the date of randomization • For subjects who did receive study treatment, use the earliest of the following: o treatment stop date o Last CV Assessment Date or the death date in subjects who had not withdrawn consent and had not reached the End of Study visit. If the censoring date as defined above for On-treatment CV endpoints is after the censoring date as defined for the primary analysis during the time period for follow-up of CV endpoints, then use the censoring date for the primary analysis time period. Any events that occurred before the start of this time period are considered to be prior to the time period for On-treatment CV endpoints, and any events that occurred after the end of this time period are considered to be post the time period for On-treatment CV endpoints.
Time Period for On-therapy CV Endpoints
The start date of the time period for capturing On-therapy CV endpoints is the treatment start date for subjects who received study treatment, and the date of randomization otherwise. The end of this time period is defined as follows: • For subjects who did not receive study treatment, use the date of randomization

Time to Event endpoints
CV Events
• For subjects who did receive study treatment, use the earliest of the following: o treatment stop date + 56 days o Last CV Assessment Date or the death date in subjects who had not withdrawn consent and had not reached the End of Study visit. If the censoring date as defined above for On-therapy CV endpoints is after the censoring date as defined for the primary analysis during the time period for follow-up of CV endpoints, then use the censoring date for the primary analysis time period. Any events that occurred before the start of this time period are considered to be prior to the time period for On-therapy CV endpoints, and any events that occurred after the end of this time period are considered to be post the time period for On-therapy CV endpoints.
Time Period for Per-Protocol Analysis CV Endpoints
This time period is intended to be used for the Per-Protocol Analysis to include all randomized subjects who provide consent and receive at least one dose of study treatment. The start date of the time period for capturing Per-Protocol Analysis CV endpoints is the treatment start date. The end of this time period is defined as follows: • Use the earliest of the following: o Earliest of censoring dates as defined in Section 11.1.2 o Last CV Assessment Date or the death date in subjects who had not withdrawn consent and had not reached the End of Study visit. If the censoring date as defined above for Per-Protocol Analysis CV endpoints is after the censoring date as defined for the primary analysis during the time period for follow-up of CV endpoints, then use the censoring date for the primary analysis time period. Any events that occurred before the start of this time period are considered to be prior to the time period for Per-Protocol Analysis CV endpoints, and any events that occurred after the end of this time period are considered to be post the time period for Per-protocol CV endpoints.

Time to Event endpoints

Metabolic Management Events

- Time to insulin and time to prandial insulin are defined as follows:
  For subjects with an event, time to event is the initiation date – treatment start date + 1.
  For subjects with no event, time to event (censored) is the censor date – treatment start date +1.

  For subjects not receiving any study treatment, who therefore have no treatment start date, time to event will be determined based on date of randomization.

  The censor date is the latest of clinic visits and phone calls.

  The definitions of these events are provided in Section 2 of the protocol. Following are more detailed descriptions of event determination:
  - An insulin event will require more than 3 months use of insulin for subjects in the NI population and will be determined based on data recorded in the Concomitant Medications eCRF form. Specifically this will require use of any type of insulin for a continuous duration of > 3 months (ie > 3*30.4375 days); this could involve multiple medication entries in the eCRF. In the determination of continuous duration of > 3 months, gaps in useage < 7 days will not be considered a break, but gaps in useage ≥ 7 days will be considered a break.
  - A prandial insulin event will require more than 3 months use of prandial insulin (i.e., either a prandial-only insulin or a mixed insulin) for subjects in the BI population and will be determined based on data recorded in the Concomitant Medications eCRF form. Specifically this will require use of prandial or mixed insulin for a continuous duration of > 3 months (ie > 3*30.4375 days); this could involve multiple medication entries in the eCRF. In the determination of continuous duration of > 3 months, gaps in useage < 7 days will not be considered a break, but gaps in useage ≥ 7 days will be considered a break. Insulin categories are shown in Section 11.13.
  - Initiation date is the date of the earliest medication use after treatment start date. Duration of use = latest stop date of medication – initiation date +1.
    If a medication stop date is missing, then the date of study completion will be used.

- Time to first occurrence of a clinically important microvascular event is defined as follows:
  For subjects with an event, time to event is the first event date – date of randomization +1.
  For subjects with no event, time to event (censored) is the censor date – date of randomization +1.

  The censor date is the latest of clinic visits and phone calls.

  The first event date is the date of first occurrence of a clinically important microvascular event. The definition of clinically important microvascular events is provided in Section 6.2.4 of the protocol. Based on this definition, such an event will be determined by one or more of the following items being recorded in the eCRF with a date on or after date of randomization:
  - Need for renal transplant or dialysis (Renal Impairment eCRF form, Event Treatment/Management: “Treatment required for the renal impairment” = “Renal transplantation”, “Haemodialysis”, or “Peritoneal dialysis”); event date is the corresponding treatment start date. Temporary renal replacement therapy will not

Time to Event endpoints
Metabolic Management Events
qualify as an event; such cases will be identified by recording as “Renal Replacement“ and also “Other, Specify“ with corresponding text description. o New diabetes-related blindness (Diabetic Eye Disease Event eCRF form, Visual Function, “Severity of Visual Impairment”= “Able to count fingers or worse (Blindness)” and also “Does the subject have visual impairment (after best possible correction with glasses)”=”Yes” and also “Is the visual impairment diabetes related”=”Yes”); event date is the date of diagnosis of new or worsening diabetic retinopathy/maculopathy. o Procedures (Diabetic Eye Disease Event eCRF form, Treatment: “Anti-VEGF Treatment=”Yes”, “Photocoagulation”=”Yes”, or “Vitrectomy” indicated in one or both eyes); event date is the corresponding date of treatment.

Composite Metabolic Endpoint
• The composite metabolic endpoint is defined in Section 2 of the protocol. Subjects will be defined as achieving the composite metabolic endpoint based on the following criteria: glycaemic control (HbA1c≤ 7.0% at final assessment) with no severe hypoglycaemic incidents and weight gain <5% from baseline • The final assessment is defined as the latest post-baseline assessment of both HbA1c and weight (on same date) in the corresponding time period (either overall or On-treatment). • Severe hypoglycaemic incidents will be determined by an event being recorded in the Severe Hypoglycaemic Event eCRF form with a start date that is post-baseline and is on or before the final assessment date defined above for the corresponding time period (either overall or On-treatment).

HbA1c
• For HbA1c measured in mmol/mol, values will be converted to % based on the following [Geistanger, 2008]: HbA1c (%) = [0.09148 * HbA1c (mmol/mol)] + 2.152 In a similar manner, for HbA1c measured in %, values will be converted to mmol/mol based on solving the above equation accordingly: HbA1c (mmol/mol) = [HbA1c (%) - 2.152] / 0.09148

Time to Event endpoints
TIA
• Time to first TIA and time to first Stroke or TIA are defined as follows: For subjects with an event, time to event is the date of first event – date of randomization +1. For subjects with no event, time to event (censored) is the Last CV Assessment Date – date of randomization +1.

Time to Event endpoints
TIA
• Definitions of adjudicated stroke and investigator-reported stroke have been previously provided. An adjudicated TIA event will be determined by a corresponding item being recorded on the CEC Stroke/TIA form in which "Did a TIA event occur" = "Yes"; date of event = date of TIA onset. An investigator-reported TIA event will be determined by the following item being recorded in the Stroke / TIA eCRF form: "Type of event"="Transient ischaemic attack (TIA)"; date of event = start date of neurological symptoms.
• First event person-years = (cumulative total time to first event for subjects who have the event + cumulative total of censored time for subjects without the event) / 365.25 • First event incidence rate (per 100 person-years) = (100 * number of subjects with at least 1 event) / first event person-years • First event absolute rate difference (per 100 person-years) = albiglutide incidence rate (per 100 person-years) – placebo incidence rate (per 100 person-years)
Evaluation Time Period for TIA Endpoints
• The evaluation time period for capturing TIA endpoints is the CV Follow-up time period (previously defined). Any events that occurred before the start of this time period are considered to be prior to the time period for follow-up of TIA endpoints, and any events that occurred after the end of this time period are considered to be post the time period for follow-up of TIA endpoints.

11.6.5. Value Evidence and Outcomes (VEO)

Questionnaires
• TRIM-D scoring will be done as specified in the TRIM-D Information Booklet [MAPI, 2013] with the exception that missing individual question responses will not be imputed. • EQ-5D scoring will be done as specified in the EQ-5D-5L User Guide [Oemar, 2013].

11.7. Appendix 7: Premature Withdrawals & Handling of Missing Data

11.7.1. Premature Withdrawals

Element	Reporting Detail
General	• Subject study completion (i.e. as specified in the protocol) was defined as completion of all periods of the study up to and including any follow-up period. Follow-up period here refers to continuing follow-up for CV events (i.e. not the 5 week follow-up visit post IP discontinuation). • Withdrawn subjects will not be replaced in the study. • All available data from subjects 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. • Per protocol, subjects may prematurely discontinue study drug but are encouraged to remain in the study.

11.7.2. 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 : 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 will be displayed as such.
Adverse Events	• Events with missing maximum intensity are considered “Severe” for summaries.
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.

11.7.2.1. Handling of Missing Dates

Element	Reporting Detail
General	Partial dates will be displayed as captured in subject listing displays.

11.7.2.2. Handling of Partial Dates

Element	Reporting Detail
Death	• The following rules for missing or partial death dates will be implemented as long as the imputed date is on or after the randomization date. If the imputed date is prior to the randomization date, then the date of randomization will be imputed for the death date.

Element	Reporting Detail
	○ The latest non-missing date of clinic visit or telephone or other contact with subject, endpoint date, AE or SAE date or date last known to be alive based on third party follow-up will be determined. If the year, month, and day of month of the death are missing then the death date will be imputed as the latest of the dates. ○ If only the day of the month of death is missing, then it will be imputed as the first day of the month (e.g., --FEB2016 would impute as 01FEB2016). However, if this imputed date results in a date that is prior to the latest non-missing date of clinic visit or telephone or other contact with subject, endpoint date, AE or SAE date or date last known to be alive based on third party follow-up then impute the missing day of death as equal to this date instead. For example: ▪ If –FEB2016 is given as the death date and there is a non-fatal MI on 08FEB1016, then the imputed date of death would be 08FEB2016 rather than 01FEB2016 such that the death is not before the non-fatal MI. ▪ If –MAR2016 is give as the death date and the latest date is a non-fatal MI on 08FEB2016 then the imputed date of death would be 01MAR2016. ○ If the month and day of the month of death are missing, then they will be imputed as 01JAN (e.g., -----2016 would impute as 01JAN2016). However, if this imputed date results in a date that is prior to the latest non-missing date of clinic visit or telephone or other contact with subject, endpoint date, AE or SAE date or date last known to be alive based on third part follow-up then impute the missing month and day of death as equal to this date instead. For example: ▪ If -----2016 is given as the death date and the latest date is a non-fatal MI on 08FEB2016 then the imputed date of death would be 08FEB2016 rather than 01JAN2016 such that the death is not before the non-fatal MI. ▪ If -----2017 is given as the death date and the latest date is a non-fatal MI on 08FEB2016 then the imputed date of death would be 01JAN2017. For deaths that occur after subjects have prematurely withdrawn from the study, missing or partial dates will be imputed as specified above except if the imputation places the death prior to or on the premature withdrawal date. In this case the death date will be imputed as the premature withdrawal date + 1 day. If the date of death provided by the Investigator is missing or partial, then it will be imputed by the date of death as determined by the CEC.
CV events	• If event dates are missing or partial and there is not sufficient information to classify the time period of the event, the event will be classified as occurring

Element	Reporting Detail
	On-treatment and post-randomization. The event will also be considered to have occurred during the follow-up for cardiovascular events as defined in Section 11.6.4. • The following rules for missing or partial event dates for events other than death will be implemented as long as the imputed date is on or after the randomization date. If the imputed date is prior to the randomization date, then the date of randomization will be imputed for the event date. o If only the day of the month is missing, impute the first day of the month (e.g., --FEB2016 would impute as 01FEB2016) o If the month and day of the month are missing, impute 01JAN (e.g., -----2016 would impute as 01JAN2016) o If the year, month, and day of month are missing, impute the randomization date If the CV event date provided by the Investigator is missing or partial, then it will be imputed by the corresponding date as determined by the CEC.
Microvascular Events	• Missing or partial event dates will be handled in a manner similar to that specified for CV Events.
Adverse Events	• Partial start dates will be imputed as the earliest possible date consistent with the partial date and assigned treatment state. Partial stop dates will be imputed as the latest possible date consistent with the partial date and assigned treatment state.
Medications	• Partial start dates of medications will be imputed as the earliest possible date consistent with the partial date. In the case of a completely missing start date, the start date will be assumed to be prior to date of the first administration of study drug. Partial stop dates of medications will be imputed as the latest possible date consistent with the partial date. In the case of completely missing stop date, the medication will be assumed to be ongoing.

11.7.2.3. Handling of Missing Data for Statistical Analysis

Element	Reporting Detail
Observed Case (OC)	• The Observed Case (OC) approach does not impute any missing data. This is the default approach used for most summaries and analyses.
Last Observation Carried Forward (LOCF)	• The Last Observation Carried Forward (LOCF) approach consists of imputing ("carrying forward") the last valid post-baseline observation to subsequent visits that have missing data; the baseline observation will not be carried forward for post-baseline visits. This approach will be used for Value Evidence and Outcomes endpoints as specified.

11.8. Appendix 8: Values of Potential Clinical Importance

11.8.1. Laboratory

Chemistry				
Laboratory Test	**Change from Baseline of Potential Clinical Concern**		**Potential Clinical Concern Value**	
	SI Units	**Conventional Units**	**SI Units**	**Conventional Units**
Alanine Transaminase (ALT)	None	None	>3 x ULN	>3 x ULN
Aspartate Aminotransferase (AST)	None	None	>3 x ULN	>3 x ULN
Alkaline Phosphatase	None	None	>3 x ULN	>3 x ULN
Total Bilirubin	None	None	>1.5 x ULN	>1.5 x ULN
Creatinine	> 2 x Baseline	> 2 x Baseline	>159 µmol/L	>1.80 mg/dL
Gamma Glutamyl Transferase	None	None	>3 x ULN	>3 x ULN

Liver Function Tests	
Laboratory Test	**Potential Clinical Concern Value**
ALT	≥ 2 x ULN ≥ 3 x ULN ≥ 5 x ULN ≥ 8 x ULN ≥ 10 x ULN ≥ 3 x ULN and Total Bilirubin ≥ 2 x ULN
AST	≥ 2 x ULN ≥ 3 x ULN ≥ 5 x ULN ≥ 8 x ULN ≥ 10 x ULN ≥ 3 x ULN and Total Bilirubin ≥ 2 x ULN
Total Bilirubin	≥ 1.5 x ULN ≥ 2 x ULN ≥ 3 x ULN ≥ 5 x ULN ≥ 8 x ULN ≥ 10 x ULN

11.8.2. Vital Signs

Parameter	Units	Change from Baseline of Potential Clinical Concern	Potential Clinical Concern Value
Systolic BP	mmHg	Decrease >30 mmHg Increase >30 mmHg	<100 mmHg >170 mmHg
Diastolic BP	mmHg	Decrease >20 mmHg Increase >20 mmHg	<50 mmHg >110 mmHg
Heart rate	bpm	Decrease >30 bpm Increase >30 bpm	<50 bpm > 120 bpm

11.9. Appendix 9: Multicenter Studies

11.9.1. Methods for Handling Centers

GLP116174 is a multi-center study. Listings and summaries by country or center will be in terms of the subject's assigned values at the point of database freeze. Summaries will be done using data from all centers combined unless otherwise indicated. Regions are defined as follows:

COUNTRY	REGION	REGIONCD
Canada United States	North America	1
Argentina Mexico Peru	Latin America	2
Hong Kong Korea, Republic of Philippines Taiwan Thailand	Asia Pacific	3
Bulgaria Czechia Hungary Poland Russian Federation Ukraine	Eastern Europe	4
Belgium Denmark France Germany Greece Italy Netherlands Norway South Africa Spain Sweden United Kingdom	Western Europe	5

11.10. Appendix 10: Examination of Covariates and Subgroups

11.10.1. Handling of Covariates, Subgroups & Other Strata

- The following is a non-exhaustive list of subgroups that 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.
- If the category cannot be refined further, then descriptive rather than statistical comparisons may be performed for the particular subgroup.
- Summaries and analyses of the primary endpoint will be done for the following subgroups using the ITT population (see Section 7.1). Subgroup analyses are intended to assess consistency with the overall results; they may have low power, especially if the subgroup is small or has a low number of events. Subgroup analyses will not be adjusted for multiplicity.

Subgroup	Categories
Sex	Male, Female
Race/Ethnicity	non-Hispanic White, non-Hispanic Black or African American, Hispanic, Asian, Other
Age	<65 years, ≥65 to <75 years, ≥75 years
Region	North America, Latin America, Asia Pacific, Eastern Europe, Western Europe
Coronary Artery Disease	yes, no (based on Medical History eCRF data: Coronary Artery Disease includes Myocardial Infarction, Coronary Artery Disease with >= 50% Stenosis, Coronary Artery Bypass Graft (CABG) and Percutaneous Coronary Intervention (PCI))
Cerebrovascular Disease	yes, no (based on Medical History eCRF data: Cerebrovascular disease includes Stroke, Carotid Arterial Disease with >= 50% Stenosis, and Carotid Vascular Procedure)
Peripheral Arterial Disease	yes, no (based on Medical History eCRF data)
Number of CV Risk Categories	One CV risk category (only Coronary Artery Disease, only Cerebrovascular Disease, or only Peripheral Arterial Disease), 2 or 3 CV risk categories (based on Medical History eCRF data).
Heart Failure History	yes, no
Smoking History	current, former, never
Baseline eGFR	<60, ≥60 to <90, ≥90 ml/min/1.73m^2
Baseline BMI	<30, ≥30 kg/m^2
Duration of Diabetes	<10, ≥10 to <20, ≥20 years
Baseline HbA1c	<8.0%, ≥8.0% to <9.0%, ≥9.0%
Baseline insulin	yes, no (based on Concomitant Medications eCRF data)

Baseline metformin	yes, no (based on Concomitant Medications eCRF data)
Prior DPP-IV	yes, no (based on History of Prior GLP-1 / DPP-IV Use eCRF data)
Baseline statin	yes, no (based on baseline CV medications eCRF data, recorded as “Statin Therapy”)
Baseline antiplatelet	yes, no (based on baseline CV medications eCRF data, recorded as “P2Y12 Inhibitors” or “Acetylsalicylic Acid (Aspirin)”

11.11. Appendix 11: Multiple Comparisons & Multiplicity

11.11.1. Handling of Multiple Comparisons & Multiplicity

If non-inferiority is established for the primary endpoint, the data will be used to test for evidence of superiority. This approach is a closed testing procedure, and therefore, no adjustment for multiplicity is required [Hung, 2009].

Secondary Endpoints and Subgroup Analysis

The following secondary endpoints will provide supportive evidence for cardiovascular safety and metabolic efficacy and will not use any multiplicity adjustment procedure. Results will be presented with confidence intervals and nominal p-values:

- Components of primary endpoint (CV death, MI, stroke)
- MACE + urgent revascularization for unstable angina
- Cardiovascular death or hospitalization for heart failure
- Time to initiation of insulin of more than 3 months duration for those subjects not treated with insulin at study start
- Time to initiation of prandial insulin in those subjects treated with basal insulin at study start
- The proportion of subjects achieving glycaemic control (HbA1c $\leq$ 7.0% at final assessment) with no severe hypoglycaemic incidents and weight gain <5% of body weight
- Mean HbA1c and change from baseline at scheduled visits
- Mean body weight and change from baseline at scheduled visits
- Mean eGFR and change from baseline at scheduled visits
- Composite Microvascular endpoint

To examine the degree of consistency of the overall treatment effect in terms of important prognostic factors, subgroup analyses of the primary outcomes will be performed based on pre-defined subgroups. These exploratory subgroup analyses will not be adjusted for multiple comparisons and will be interpreted only descriptively.

11.12. Appendix 12: Model Checking and Diagnostics for Statistical Analyses

11.12.1. Statistical Analysis Assumptions

Endpoint	• Time to first MACE
Analysis	• Cox PH regression model

- PROC PHREG in SAS will be used to fit the model.
- The log hazard ratio estimate obtained from the Cox PH model is a consistent (asymptotically unbiased) estimate.
- Graphical assessments of the proportional hazards assumption will be performed by plotting the log(-log) of the probability of survival versus time or logarithm of time for each treatment group. If the hazards are proportional, the difference in the plots of log(-log) of the probability of survival versus time is expected to be constant across time. In addition, plots of scaled Schoenfeld residuals will be generated to assess nonproportionality.
- Should there be evidence of a violation of the proportional hazards assumption, the following methods may be considered:
  - Use of a stratified Cox proportional hazards model (including prognostic factors in a STRATA statement in PROC PHREG, rather than in the MODEL statement).

11.13. Appendix 13: Medication Groupings

11.13.1. Medication Groupings

Grouping
Non-insulin (NI) Population: Subjects having no baseline use of “Insulin”
Basal Insulin (BI) Population: Subjects having baseline use of “Basal insulin” but not “Prandial insulin” or “Mixed insulin”
Anti-hyperglycaemic agents (composed of the following):
Insulin
Basal insulin
Prandial insulin
Mixed insulin
Biguanide
Metformin
Sulfonylurea
Non-sulfonylurea secretagogue
Thiazolidinedione
Alpha-glucosidase inhibitors
DPP-IV inhibitors
SGLT-2 inhibitor
GLP-1 analogues other than study drug
Other anti-hyperglycaemic agent.

11.14. Appendix 14: Abbreviations & Trade Marks

11.14.1. Abbreviations

Abbreviation	Description
ADaM	Analysis Data Model
AE	adverse event
AESI	adverse event of special interest
AHA	anti-hyperglycaemic agent
ALT	alanine aminotransferase (SGPT)
ANCOVA	analysis of covariance
AST	aspartate aminotransferase (SGOT)
ATC	Anatomical Therapeutic Chemical
BI	Basal Insulin
BMI	body mass index
BP	blood pressure
CABG	coronary artery bypass graft
CEC	Cardiovascular Endpoint Committee
CI	confidence interval
CSR	Clinical Study Report
CSV	comma-separated values
CV	cardiovascular
DCRI	Duke Clinical Research Institute
DPP-IV	dipeptidyl peptidase IV
ECG	electrocardiogram
eCRF	electronic Case Report Form
EDISH	evaluation of drug-induced serious hepatotoxicity
eGFR	estimated glomerular filtration rate
EHR	electronic health records
FDA	US Food and Drug Administration
GCSP	Global Clinical Safety and Pharmacovigilance
GGT	gamma glutamyl transferase
GI	gastrointestinal
GLP-1	glucagon-like peptide-1
GSK	GlaxoSmithKline
HbA1c	glycated haemoglobin
HDLc	high density lipoprotein cholesterol
HF	heart failure
HLT	high level term
ICH	International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use
IDMC	Independent Data Monitoring Committee
IDSL	Integrated Data Standards Library
IP	investigational product
IRT	Interactive Response Technology
ITT	Intent-to-treat

Abbreviation	Description
KM	Kaplan-Meier
LDLc	low density lipoprotein cholesterol
LFT	liver function test
LOCF	last observation carried forward
MACE	major adverse cardiovascular events
MDRD	Modification of Diet in Renal Disease
MedDRA	Medical Dictionary for Regulatory Activities
MI	myocardial infarction
MMRM	mixed model repeated measures
MOH	Ministry of Health
NI	Non-Insulin
OC	Observed Cases
PAC	Pancreatitis Adjudication Committee
PCI	percutaneous coronary intervention
PDF	portable document format
PDMP	Protocol Deviation Management Plan
PH	proportional hazards
PK	pharmacokinetic
PP	Per-Protocol
PPD	Pharmaceutical Product Development
PT	preferred term
PY	person years
RAP	Reporting and Analysis Plan
RTF	rich text format
SAE	serious adverse event
SDAC	Statistical Data Analysis Center
SDL	source data lock
SDTM	study data tabulation model
SGLT-2	sodium-glucose co-transporter 2
SI	system independent
SOC	system organ class
SU	sulfonylurea
TC	total cholesterol
Tg	triglycerides
TIA	transient ischemic attack
TRIM-D	Treatment Related Impact Measure - Diabetes
UA	unstable angina
ULN	upper limit of normal range
VAS	visual analog scale
VEO	Value Evidence and Outcomes

11.14.2. Trademarks

Trademarks of the GlaxoSmithKline Group of Companies
NONE

Trademarks not owned by the GlaxoSmithKline Group of Companies
EQ-5D
SAS
TRIM-D

11.15. Appendix 15: List of Data Displays

11.15.1. Data Display Numbering

The following numbering will be applied for RAP generated displays:

Section	Tables	Figures
Study Population	1.01 to 1.19; 1.21 to 1.54	1.01 to 1.05
Efficacy	2.01 to 2.70	2.01 to 2.32
Safety	3.001 to 3.179	3.01 to 3.20
VEO	4.01 to 4.20	4.01 to 4.08
Section	**Listings**	
ICH Listings	1 to 24	
Other Listings	25 to 82	

11.15.2. Study Population Tables

Table No.	Title	Population	Programming note
1.01	Summary of Study Populations	All Screened Subjects	
1.02	Summary of the Exclusions From the Intent to Treat Population	All Screened Subjects	
1.03	Summary of the Exclusions From the Safety, Non-Insulin, and Basal Insulin Populations	ITT	
1.04	Summary of Screening Status and Reasons for Screen Failures	All Screened Subjects	
1.05	Summary of Number of Subjects by Country and Site ID	ITT	
1.06	Summary of Number of Subjects by Region and Country	ITT	
1.07	Summary of Subject Disposition for the Subject Conclusion Record	ITT	
1.08	Summary of Subject Disposition for the Subject Conclusion Record by Region and Country	ITT	
1.09	Summary of Subject Survival Status	ITT	
1.10	Summary of Subject Primary Endpoint Status	ITT	
1.11	Summary of Study Treatment Discontinuation	ITT	
1.12	Summary of Study Treatment Discontinuation by Region and Country	ITT	
1.13	Summary of Study Treatment Discontinuation Status by Study Completion Status	ITT	
1.14	Summary of Subject Contact at Each Scheduled Visit	ITT	

Table No.	Title	Population	Programming note
1.15	Summary of End of Study Contact	ITT	
1.16	Summary of Subject Followup	ITT	
1.17	Summary of Important Protocol Deviations	ITT	
1.18	Summary of Events Leading to Exclusion of Data From Per-Protocol Analysis	ITT	
1.19	Summary of Inclusion and Exclusion Criteria Deviations	ITT	
1.21	Summary of Demographics and Baseline Characteristics	ITT	
1.22	Summary of Demographics and Baseline Characteristics (Safety Population)	Safety	
1.23	Summary of Race and Racial Combinations	ITT	
1.24	Summary of Race and Racial Combinations (Safety Population)	Safety	
1.25	Summary of Race and Racial Combinations Details	ITT	
1.26	Summary of Race and Racial Combinations Details (Safety Population)	Safety	
1.27	Summary of Subjects Randomized by Subgroups	ITT	Summarize by each defined subgroup factor
1.28	Summary of Subjects Randomized by Subgroups (Safety Population)	Safety	Include the following subgroups: age, race, sex, baseline HbA1c, baseline eGFR, baseline sulfonylurea/insulin use, insulin use at baseline, history of malignancy at baseline

Table No.	Title	Population	Programming note
1.29	Summary of History of Prior GLP-1 / DPP-IV Use	ITT	
1.30	Summary of Substance Use	ITT	
1.31	Summary of Medical/Surgical Procedures	ITT	
1.32	Summary of Medical Conditions	ITT	Erectile dysfunction should be summarized for males only.
1.33	Summary of Medical Conditions: Coronary Artery Disease, Cerebrovascular Disease, or Peripheral Arterial Disease	ITT	
1.34	Summary of Diabetic Eye Disease History	ITT	
1.35	Summary of Nephropathy	ITT	
1.36	Summary of Current and/or Past Cancer History	ITT	Summarize gender-specific cancers accordingly (e.g., prostate, etc.)
1.37	Summary of Current and/or Past Thyroid Cancer History	ITT	
1.38	Summary of Family History of Cardiovascular Risk Factors	ITT	
1.39	Summary of Cardiovascular Medication Use Categories	ITT	Summarise by visit, any post baseline visit, and Latest Visit
1.40	Summary of Cardiovascular Medication Use Categories (Safety Population)	Safety	Summarise by visit, any post baseline visit, and Latest Visit.
1.41	Summary of Anti-hyperglycaemic Medications: Baseline	ITT	
1.42	Summary of Anti-hyperglycaemic Medications: Baseline (Safety Population)	Safety	
1.43	Summary of Anti-hyperglycaemic Medications: Post-Baseline	ITT	
1.44	Summary of Anti-hyperglycaemic Medications: Post-Baseline	Safety	

Table No.	Title	Population	Programming note
	(Safety Population)		
1.45	Summary of Anti-hyperglycaemic Medications: Latest Visit	ITT	
1.46	Summary of Anti-hyperglycaemic Medications: Latest Visit (Safety Population)	Safety	
1.47	Summary of Anti-hyperglycaemic Medication Categories	ITT	Summarise for baseline, any post-baseline, and Latest Visit.
1.48	Summary of Anti-hyperglycaemic Medication Categories (Safety Population)	Safety	Summarise for baseline, any post-baseline, and Latest Visit.
1.49	Summary of Study Treatment Exposure	Safety	
1.50	Summary of Dose Changes	Safety	
1.51	Summary of Treatment Compliance Including Breaks	Safety	
1.52	Summary of Treatment Compliance Excluding Breaks	Safety	
1.53	Summary of Number of Subjects Enrolled by Country and Site ID	Enrolled	For FDAAA/EudraCT
1.54	Summary of Age Ranges	Enrolled	For FDAAA/EudraCT

11.15.3. Study Population Figures

Figure No.	Title	Population	Programming note
1.01	Kaplan-Meier Plot of Time to Premature Study Withdrawal	ITT	
1.02	Kaplan-Meier Plot of Time to Investigational Product	ITT	

Figure No.	Title	Population	Programming note
	Discontinuation		
1.03	Endpoint Follow-up	ITT	
1.04	Cumulative Distribution Plot of Duration of Exposure Including Breaks	Safety	Non-censored
1.05	Cumulative Distribution Plot of Duration of Exposure Excluding Breaks	Safety	Non-censored

11.15.4. Efficacy Tables

Table No.	Title	Population	Programming note
2.01	Summary of All Adjudicated MACE (CV Follow-up Time Period)	ITT	
2.02	Summary of First Occurrence of Adjudicated MACE (CV Follow-up Time Period)	ITT	
2.03	Summary of Analysis of Time to First Occurrence of Adjudicated MACE (CV Follow-up Time Period)	ITT	Primary analysis of primary endpoint Include HR, 95% CI, non-inferiority p-value, superiority p-value.
2.04	Summary of SAS Output for Analysis of Time to First Occurrence of Adjudicated MACE (CV Follow-up Time Period)	ITT	Primary analysis of primary endpoint
2.05	Summary of First Occurrence of Adjudicated MACE Censoring and Follow-up Time (CV Follow-up Time Period)	ITT	
2.06	Summary of All Adjudicated MACE During CV Follow-up, On-treatment and On-therapy Time Periods	ITT	

Table No.	Title	Population	Programming note
2.07	Summary of First Occurrence of Adjudicated MACE (CV On-treatment Time Period)	ITT	
2.08	Summary of Analysis of Time to First Occurrence of Adjudicated MACE (CV On-treatment Time Period)	ITT	Include HR, 95% CI, non-inferiority p-value, superiority p-value.
2.09	Summary of First Occurrence of Adjudicated MACE (CV On-therapy Time Period)	ITT	
2.10	Summary of Analysis of Time to First Occurrence of Adjudicated MACE (CV On-therapy Time Period)	ITT	Include HR, 95% CI, non-inferiority p-value, superiority p-value.
2.11	Summary of First Occurrence of Adjudicated MACE (Per-Protocol AnalysisPer-Protocol Analysis Time Period)	ITT	
2.12	Summary of Analysis of Time to First Occurrence of Adjudicated MACE (Per-Protocol Analysis, Per-Protocol Analysis Time Period)	ITT	Include HR, 95% CI, non-inferiority p-value, superiority p-value.
2.13	Summary of First Occurrence of Adjudicated MACE Excluding Unknown Cause of Death (CV Follow-up Time Period)	ITT	
2.14	Summary of Analysis of Time to First Occurrence of Adjudicated MACE Excluding Unknown Cause of Death (CV Follow-up Time Period)	ITT	Include HR, 95% CI, non-inferiority p-value, superiority p-value.
2.15	Summary of First Occurrence of Adjudicated MACE Including Additional Data From Publically Available Sources for Subjects who have Withdawn Consent for Follow-Up (Vital Status Time Period)	ITT	
2.16	Summary of Analysis of Time to First Occurrence of Adjudicated MACE Including Additional Data From Publically Available Sources for Subjects Who Have Withdawn Consent for Follow-Up(CV Follow-up Time Period)	ITT	Include HR, 95% CI, non-inferiority p-value, superiority p-value.

Table No.	Title	Population	Programming note
2.17	Summary of Subgroup Analysis of Time to First Occurrence of Adjudicated MACE (CV Follow-up Time Period)	ITT	See RAP Appendix 10 for subgroup specification.
2.18	Summary of Number of Adjudicated MACE Events (CV Follow-up Time Period)	ITT	
2.19	Summary of Number of Adjudicated MI Events (CV Follow-up Time Period)	ITT	
2.20	Summary of Number of Adjudicated Stroke Events (CV Follow-up Time Period)	ITT	
2.21	Summary of Adjudicated MACE, MI and Stroke Recurrent Event Analysis (CV Follow-up Time Period)	ITT	
2.22	Summary of Secondary Efficacy Cardiovascular Endpoints (CV Follow-up Time Period)	ITT	
2.23	Summary of First Occurrence of Secondary Composite Efficacy Cardiovascular Endpoints (CV Follow-up Time Period)	ITT	
2.24	Summary of Analysis of Time to First Occurrence of Adjudicated MACE or Revascularization for UA (CV Follow-up Time Period)	ITT	
2.25	Summary of Analysis of Time to First Occurrence of Adjudicated CV Death (CV Follow-up Time Period)	ITT	
2.26	Summary of Analysis of Time to First Occurrence of Adjudicated MI (CV Follow-up Time Period)	ITT	
2.27	Summary of Analysis of Time to First Occurrence of Adjudicated Stroke (CV Follow-up Time Period)	ITT	
2.28	Summary of Analysis of Time to First Occurrence of Adjudicated CV Death or Hospitalization for HF (CV Follow-up Time Period)	ITT	
2.29	Summary of Supplemental Analysis of Time to First Occurrence of MI (CV Follow-up Time Period)	ITT	Exclude events which do not meet the adjudication criteria for MI but are

Table No.	Title	Population	Programming note
			classified by the CEC as deaths due to MI.
2.30	Summary of Supplemental Analysis of Time to First Occurrence of Stroke (CV Follow-up Time Period)	ITT	Exclude events which do not meet the adjudication criteria for stroke but are classified by the CEC as deaths due to stroke.
2.31	Summary of Percutaneous Coronary Intervention (PCI), Coronary Artery Bypass Graft (CABG) and Catheterization Events (CV Follow-up Time Period)	ITT	
2.32	Summary of All Percutaneous Coronary Intervention (PCI) Event Details (CV Follow-up Time Period)	ITT	
2.33	Summary of All Coronary Artery Bypass Graft (CABG) Event Details (CV Follow-up Time Period)	ITT	
2.34	Summary of All Catheterization Event Details (CV Follow-up Time Period)	ITT	
2.35	Summary of Adjudicated Cause of Death (Vital Status Follow-up Time Period)	ITT	
2.36	Summary of All Adjudicated Myocardial Infarction Event Details (CV Follow-up Time Period)	ITT	
2.37	Summary of All Adjudicated Stroke Event Details (CV Follow-up Time Period)	ITT	
2.38	Summary of All Adjudicated Stroke or TIA Events (CV Follow-up Time Period)	ITT	
2.39	Summary of All Adjudicated TIA Events (CV Follow-up Time Period)	ITT	
2.40	Summary of Time to First Occurrence of Adjudicated Stroke or TIA (CV Follow-up Time Period)	ITT	No p-values

Table No.	Title	Population	Programming note
2.41	Summary of Time to First Occurrence of Adjudicated TIA (CV Follow-up Time Period)	ITT	No p-values
2.42	Summary of Concordance Between Investigator Reported and Adjudicated Efficacy Endpoints (CV Follow-up Time Period)	ITT	<by variable> = Total, Albi and Placebo
2.43	Summary of Concordance Between Investigator Reported and Adjudicated MACE (CV Follow-up Time Period)	ITT	
2.44	Summary of Concordance Between Investigator Reported and Adjudicated Death Events (Vital Status Follow-up Time Period)	ITT	
2.45	Summary of Concordance Between Investigator Reported and Adjudicated Myocardial Infarction and Unstable Angina Requiring Urgent Revascularization Events (CV Follow-up Time Period)	ITT	
2.46	Summary of Concordance Between Investigator Reported and Adjudicated Stroke and TIA (CV Follow-up Time Period)	ITT	
2.47	Summary of Concordance Between Investigator Reported and Adjudicated Individual Endpoint Events (CV Follow-up Time Period)	ITT	
2.48	Summary of Events Other than Deaths That Do Not Meet CV Endpoint or TIA Definition (CV Follow-up Time Period)	ITT	
2.49	Summary of Events That Do Not Meet CV Endpoint or TIA Definition by Investigator-reported Event Type (CV Follow-up Time Period)	ITT	
2.50	Summary of Analysis of Time to Initiation of Insulin of More Than 3 Months Duration For Subjects Not Treated With Insulin At Study Start	NI	Include HR, 95% CI, superiority p-value.
2.51	Summary of Analysis of Time to Initiation of Prandial Insulin of More Than 3 Months Duration For Subjects on Basal Insulin at Study Start	BI	Include HR, 95% CI, superiority p-value.
2.52	Summary of Mantel-Hasenszel Analysis of Composite Metabolic	ITT	p-value only at 8 monthly visits

Table No.	Title	Population	Programming note
	Endpoint Stratified by Baseline HbA1c and Prior Diabetes Therapy		(i.e. Month 8, 16, 24 ..) and Final Assessment
2.53	Summary of Mantel-Haenszel Analysis of Composite Metabolic Endpoint Stratified by Baseline HbA1c and Prior Diabetes Therapy (On-treatment Period)	ITT	p-value only at 8 monthly visits (i.e. Month 8, 16, 24 ..) and Final Assessment; excluding subjects who did not receive at least one dose of study treatment
2.54	Summary of All Clinically Important Microvascular Events	ITT	Components are defined in Section 11.6.4 in RAP
2.55	Summary of First Occurrence of Clinically Important Microvascular Events	ITT	Components are defined in Section 11.6.4 in RAP
2.56	Summary of Analysis of Time to First Occurrence of Clinically Important Microvascular Events	ITT	
2.57	Summary of HbA1c (%) (Baseline Data from Local or Central Laboratory and Post-Baseline Central Laboratory Data, Observed Cases)	ITT	Assessments are at Screening, Baseline and every 8 months.
2.58	Summary of HbA1c (mmol/mol) (Baseline Data from Local or Central Laboratory and Post-Baseline Central Laboratory Data, Observed Cases)	ITT	Assessments are at Screening, Baseline and every 8 months.
2.59	Summary of Subjects with HbA1c <= 7.0 % (Post-Baseline Central Laboratory Data, Observed Cases)	ITT	At 8 monthly visits (i.e. Month 8, 16, 24 ..) and Final Assessment
2.60	Summary of MMRM Analysis of HbA1c (%) Change From Baseline (Baseline Data from Local or Central Laboratory and Post-Baseline Central Laboratory Data, Observed Cases)	ITT	At Month 8, 16
2.61	Summary of MMRM Analysis of HbA1c (mmol/mol) Change From Baseline (Baseline Data from Local or Central Laboratory and	ITT	At Month 8, 16

Table No.	Title	Population	Programming note
	Post-Baseline Central Laboratory Data, Observed Cases)		
2.62	Summary of MMRM Analysis of HbA1c (%) Change From Baseline (Baseline Data from Local or Central Laboratory and Post-Baseline Central Laboratory Data, Observed Cases, On-treatment Time Period)	ITT	At Month 8, 16; excluding subjects who did not receive at least one dose of study treatment
2.63	Summary of MMRM Analysis of HbA1c (mmol/mol) Change From Baseline (Baseline Data from Local or Central Laboratory and Post-Baseline Central Laboratory Data, Observed Cases, On-treatment Time Period)	ITT	At Month 8, 16; excluding subjects who did not receive at least one dose of study treatment
2.64	Summary of MMRM Analysis of HbA1c (%) Change From Baseline (Central Laboratory Data Collected from Baseline, Observed Cases)	ITT	At Month 8, 16
2.65	Summary of MMRM Analysis of HbA1c (mmol/mol) Change From Baseline (Central Laboratory Data Collected from Baseline, Observed Cases)	ITT	At Month 8, 16
2.66	Summary of Weight (Observed Cases)	ITT	Assessments are at baseline and every 8 months
2.67	Summary of MMRM Analysis of Weight Change From Baseline (Observed Cases)	ITT	At Month 8, 16
2.68	Summary of MMRM Analysis of Weight Change From Baseline (Observed Cases, On-treatment Time period)	ITT	At Month 8, 16; excluding subjects who did not receive at least one dose of study treatment
2.69	Summary of Lipids (standard units)	ITT	TC, LDLc, HDLc, TG, non-HDLc
2.70	Summary of Lipids (SI units)	ITT	TC, LDLc, HDLc, TG, non-HDLc

11.15.5. Efficacy Figures

Figure No.	Title	Population	Programming note
2.01	Kaplan-Meier Plot of Time to First Occurrence of Adjudicated MACE (CV Follow-up Time Period)	ITT	
2.02	Kaplan-Meier Plot of Time to First Occurrence of Adjudicated MACE (CV On-treatment Time Period)	ITT	
2.03	Kaplan-Meier Plot of Time to First Occurrence of Adjudicated MACE (CV On-therapy Time Period)	ITT	
2.04	Kaplan-Meier Plot of Time to First Occurrence of Adjudicated MACE (Per-Protocol Analysis, CV Follow-up Time Period)	ITT	
2.05	Kaplan-Meier Plot of Time to First Occurrence of Adjudicated MACE Excluding Unknown Cause of Death (CV Follow-up Time Period)	ITT	
2.06	Kaplan-Meier Plot of Time to First Occurrence of Adjudicated MACE Including Additional Data from Publicly Available Sources in Subjects Withdrawing Consent (Vital Status Time Period)	ITT	
2.07	Cumulative Incidence Plot of Time to First Occurrence of Adjudicated MACE (CV Follow-up Time Period)	ITT	Adjust for the competing risk of non-CV death.
2.08	Time to First Occurrence of Adjudicated MACE Tipping Point Analysis	ITT	
2.09	Forest Plot of Hazard Ratios for Time to First Occurrence of Adjudicated MACE By Subgroups	ITT	
2.10	Forest Plot of Hazard Ratios for Time to First Occurrence of Adjudicated MACE (Primary Analysis and Sensitivity Analyses)	ITT	
2.11	Kaplan-Meier Plot of Time to First Occurrence of Adjudicated MACE or Revascularization	ITT	
2.12	Kaplan-Meier Plot of Time to Adjudicated CV Death	ITT	

Figure No.	Title	Population	Programming note
2.13	Kaplan-Meier Plot of Time to First Occurrence of Adjudicated MI	ITT	
2.14	Cumulative Incidence Plot of Time to First Occurrence of Adjudicated MI	ITT	Adjust for the competing risk of death.
2.15	Kaplan-Meier Plot of Time to First Occurrence of Adjudicated Stroke	ITT	
2.16	Cumulative Incidence Plot of Time to First Occurrence of Adjudicated Stroke	ITT	Adjust for the competing risk of death.
2.17	Kaplan-Meier Plot of Time to First Occurrence of Adjudicated CV Death or Hospitalization Due to Heart Failure	ITT	
2.18	Kaplan-Meier Plot of Time to Initiation of Insulin of More Than 3 Months Duration For Subjects Not Treated With Insulin At Study Start	NI	
2.19	Kaplan-Meier Plot of Time to Initiation of Prandial Insulin of More Than 3 Months Duration For Subjects on Basal Insulin at Study Start	BI	
2.20	Kaplan-Meier Plot of Time to First Occurrence of a Clinically Important Microvascular Event	ITT	
2.21	Line Graph of Mean (+/-SE) HbA1c (%) Over Time	ITT	
2.22	Line Graph of Mean (+/-SE) Change From Baseline HbA1c (%) Over Time	ITT	
2.23	Line Graph of Mean (+/-SE) Change From Baseline HbA1c (%) Over Time (8 monthly assessments only)	ITT	
2.24	Line Graph of Adjusted Mean (+/-SE) Change From Baseline HbA1c (%) Over Time (8 monthly assessments only)	ITT	Plot adjusted means.
2.25	Line Graph of Mean (+/-SE) Change From Baseline HbA1c (%) Over Time (On-treatment Period, 8 monthly assessments only)	ITT	

Figure No.	Title	Population	Programming note
2.26	Line Graph of Mean (+/-SE) Body Weight (kg) Over Time	ITT	
2.27	Line Graph of Mean (+/-SE) Change From Baseline Body Weight (kg) Over Time	ITT	
2.28	Line Graph of Mean (+/-SE) Change From Baseline Body Weight (kg) Over Time (8 monthly assessments only)	ITT	
2.29	Line Graph of Adjusted Mean (+/-SE) Change From Baseline Body Weight (kg) Over Time (8 monthly assessments only)	ITT	Plot adjusted means.
2.30	Line Graph of Mean (+/-SE) Change From Baseline Body Weight (kg) Over Time (On-treatment Period, 8 monthly assessments only)	ITT	
2.31	Kaplan-Meier Plot of Time to First Occurrence of Adjudicated Stroke or TIA	ITT	
2.32	Kaplan-Meier Plot of Time to First Occurrence of Adjudicated TIA	ITT	

11.15.6. Safety Tables

Table No.	Title	Population	Programming note
3.001	Summary of Analysis of Time to Death (Vital Status Follow-up Time Period)	ITT	
3.002	Summary of Analysis of Time to Death (On-therapy)	ITT	
3.003	Summary of Analysis of Time to Death (On-treatment)	ITT	
3.004	Summary of On-therapy and Post-therapy Investigator-reported Cause of Death	ITT	

Table No.	Title	Population	Programming note
3.005	Overview of On-therapy and Post-therapy SAEs, AESIs and AEs Leading to Permanent Discontinuation of Study Treatment	Safety	Any AE planned to be reported (all, related to IP, leading to d/c IP), Any AE planned to be reported by max. intensity, SAE, Fatal SAE, SAE leading to d/c IP etc.
3.006	Overview of On-therapy SAEs, AESIs and AEs Leading to Permanent Discontinuation of Study Treatment	Safety	Any AE planned to be reported (all, related to IP, leading to d/c IP), Any AE planned to be reported by max. intensity, SAE, Fatal SAE, SAE leading to d/c IP etc.
3.007	Summary of On-therapy and Post-therapy SAEs, AESIs and AEs Leading to Permanent Discontinuation of Study Treatment by SOC and PT	Safety	SOC and PT, #/% of subjects and # of events, event density
3.008	Summary of On-therapy SAEs, AESIs and AEs Leading to Permanent Discontinuation of Study Treatment by SOC and PT	Safety	SOC and PT, #/% of subjects and # of events, event density
3.009	Summary of On-therapy and Post-therapy SAEs, AESIs and AEs Leading to Permanent Discontinuation of Study Treatment and Any Other Non-serious AEs Recorded by the Investigator by SOC and PT	Safety	SOC and PT, #/% of subjects and # of events

Table No.	Title	Population	Programming note
3.010	Summary of On-therapy SAEs, AESIs and AEs Leading to Permanent Discontinuation of Study Treatment and Any Other Non-serious AEs Recorded by the Investigator by SOC and PT	Safety	SOC and PT, #/% of subjects and # of events
3.011	Summary of On-therapy Adverse Events Leading to Permanent Discontinuation of Study Treatment by SOC and PT	Safety	SOC and PT, #/% of subjects and # of events, event density
3.012	Summary of On-therapy and Post-therapy SAEs, AESIs and AEs Leading to Permanent Discontinuation of Study Treatment by Maximum Intensity, SOC and PT	Safety	Max intensity, SOC and PT, #/% of subjects
3.013	Summary of On-therapy SAEs, AESIs and AEs Leading to Permanent Discontinuation of Study Treatment by Maximum Intensity, SOC and PT	Safety	Max intensity, SOC and PT, #/% of subjects
3.014	Summary of On-therapy Treatment-related SAEs, AESIs and AEs Leading to Permanent Discontinuation of Study Treatment by SOC and PT	Safety	SOC and PT, #/% of subjects and # of events, event density
3.015	Summary of On-therapy Treatment-related SAEs, AESIs and AEs Leading to Permanent Discontinuation of Study Treatment by Maximum Intensity, SOC and PT	Safety	Max intensity, SOC and PT, #/% of subjects
3.016	Summary of Common (>=2%) On-therapy and Post-therapy SAEs, AESIs and AEs Leading to Permanent Discontinuation of Study Treatment by Overall Frequency	Safety	PT, #/% of subjects, and # of events, event density Include any AEs reported by >=2% of subjects (before rounding the percentage)in either treatment group.

Table No.	Title	Population	Programming note
3.017	Summary of Common (>=2%) On-therapy SAEs, AESIs and AEs Leading to Permanent Discontinuation of Study Treatment by Overall Frequency	Safety	PT, #/% of subjects, and # of events, event density Include any AEs reported by >=2% of subjects (before rounding the percentage) in either treatment group.
3.018	Summary of On-therapy and Post-therapy SAEs, AESIs and AEs Leading to Permanent Discontinuation of Study Treatment by SOC, HLT and PT	Safety	SOC, HLT and PT, #/% of subjects and # of events, event density
3.019	Summary of On-therapy SAEs, AESIs and AEs Leading to Permanent Discontinuation of Study Treatment by SOC, HLT and PT	Safety	SOC, HLT and PT, #/% of subjects and # of events, event density
3.020	Summary of On-therapy SAEs, AESIs and AEs Leading to Permanent Discontinuation of Study Treatment by Baseline eGFR, SOC and HLT	Safety	SOC and HLT, #/% of subjects and # of events, event density eGFR subgroups (<60, ≥60 to <90, ≥90 ml/min/1.73m2)
3.021	Summary of On-therapy SAEs, AESIs and AEs Leading to Permanent Discontinuation of Study Treatment by Sex, SOC and HLT	Safety	SOC and HLT, #/% of subjects and # of events, event density
3.022	Summary of On-therapy SAEs, AESIs and AEs Leading to Permanent Discontinuation of Study Treatment by Age, SOC and HLT	Safety	SOC and HLT, #/% of subjects and # of events, event density <65, ≥65 to <75, ≥75 years

Table No.	Title	Population	Programming note
3.023	Summary of On-therapy and Post-therapy Serious Adverse Events by SOC and PT	Safety	SOC and PT, #/% of subjects and # of events, event density
3.024	Summary of On-therapy Serious Adverse Events by SOC and PT	Safety	SOC and PT, #/% of subjects and # of events, event density
3.025	Summary of On-therapy and Post-therapy Serious Adverse Events by SOC, HLT and PT	Safety	SOC, HLT and PT, #/% of subjects and # of events, event density
3.026	Summary of On-therapy Serious Adverse Events by SOC, HLT and PT	Safety	SOC, HLT and PT, #/% of subjects and # of events, event density
3.027	Summary of On-therapy and Post-therapy Fatal Serious Adverse Events by SOC and PT	Safety	SOC and PT, #/% of subjects and # of events, event density
3.028	Summary of On-therapy Fatal Serious Adverse Events by SOC and PT	Safety	SOC and PT, #/% of subjects and # of events, event density
3.029	Summary of On-therapy and Post-therapy Non-fatal Serious Adverse Events by SOC and PT	Safety	SOC and PT, #/% of subjects and # of events, event density
3.030	Summary of On-therapy Non-fatal Serious Adverse Events by SOC and PT	Safety	SOC and PT, #/% of subjects and # of events, event density

Table No.	Title	Population	Programming note
3.031	Summary of On-therapy Treatment-related Serious Adverse Events by SOC and PT	Safety	SOC and PT, #/% of subjects and # of events, event density
3.032	Summary of On-therapy Treatment-related Fatal Serious Adverse Events by SOC and PT	Safety	SOC and PT, #/% of subjects and # of events, event density
3.033	Summary of Common (>=2%) On-therapy and Post-therapy Serious Adverse Events by Overall Frequency	Safety	PT, #/% of subjects, incidence rate (subjects/100PY) and # of events, event density, relative risk (95% CI) Include SAEs reported by >=2% of subjects (before rounding the percentage) in either treatment group.
3.034	Summary of Common (>=2%) On-therapy Serious Adverse Events by Overall Frequency	Safety	PT, #/% of subjects, incidence rate (subjects/100PY) and # of events, event density, relative risk (95% CI) Include SAEs reported by >=2% of subjects (before rounding the percentage) in either treatment group.

Table No.	Title	Population	Programming note
3.035	Summary of On-therapy SAEs by Baseline eGFR, SOC and HLT	Safety	SOC and HLT, #/% of subjects and # of events, event density eGFR subgroups (<60, ≥60 to <90, ≥90 ml/min/1.73m2)
3.036	Summary of On-therapy SAEs by Sex, SOC and HLT	Safety	SOC and HLT, #/% of subjects and # of events, event density
3.037	Summary of On-therapy SAEs by Age, SOC and HLT	Safety	SOC and HLT, #/% of subjects and # of events, event density <65, ≥65 to <75, ≥75 years
3.038	Summary of On-therapy Serious Adverse Events Leading to Permanent Discontinuation of Study Treatment by SOC and PT	Safety	SOC and PT, #/% of subjects and # of events, event density

Table No.	Title	Population	Programming note
3.039	Overview of On-therapy and Post-therapy Adverse Events of Special Interest	Safety	#/% of subjects, incidence rate (subjects/100PY) and # of events and event density (events/100PY): overall for each type of AESIs, relative risk (95% CI) - includes incidence based on CMQ/ SMQ for AESIs that do not have event-specific page, otherwise based on event-specific page only.
3.040	Overview of On-therapy Adverse Events of Special Interest	Safety	As per 8A, above.
3.041	Overview of On-therapy Adverse Events of Special Interest by Baseline eGFR (Incidence >=1% in Either Treatment Group)	Safety	As per 8A eGFR subgroups (<60, ≥60 to <90, ≥90 ml/min/1.73m2)
3.042	Overview of On-therapy Adverse Events of Special Interest by Sex (Incidence >=1% in Either Treatment Group)	Safety	As per 8A.
3.043	Overview of On-therapy Adverse Events of Special Interest by Age (Incidence >=1% in Either Treatment Group)	Safety	As per 8A. <65, ≥65 to <75, ≥75 years
3.044	Summary of On-therapy and Post-therapy AESIs by Age	Safety	SOC and PT, #/% of subjects and # of events, event density

Table No.	Title	Population	Programming note
3.045	Summary of On-therapy AESIs by Age	Safety	SOC and PT, #/% of subjects and # of events, event density
3.046	Summary of On-therapy and Post-therapy AESIs by Sex	Safety	SOC and PT, #/% of subjects and # of events, event density
3.047	Summary of On-therapy AESIs by Sex	Safety	SOC and PT, #/% of subjects and # of events, event density
3.048	Overview of On-therapy and Post-therapy AESIs: Thyroid Cancer Diagnosis	Safety	
3.049	Summary of On-therapy and Post-therapy AESIs: Thyroid Cancer Diagnosis, by SOC and PT	Safety	SOC and PT, #/% of subjects and # of events, event density
3.050	Overview of On-therapy AESIs: Thyroid Cancer Diagnosis	Safety	
3.051	Summary of Investigator-reported Characteristics of On-therapy AESIs of Thyroid Cancer Diagnosis	Safety	
3.052	Summary of On-therapy AESIs: Thyroid Cancer Diagnosis, by SOC and PT	Safety	SOC and PT, #/% of subjects and # of events, event density
3.053	Overview of On-therapy and Post-therapy AESIs: Haematologic Malignancy	Safety	

Table No.	Title	Population	Programming note
3.054	Summary of On-therapy and Post-therapy AESIs: Haematologic Malignancy, by SOC and PT	Safety	SOC and PT, #/% of subjects and # of events, event density
3.055	Overview of On-therapy AESIs: Haematologic Malignancy	Safety	
3.056	Summary of On-therapy AESIs: Haematologic Malignancy, by SOC and PT	Safety	SOC and PT, #/% of subjects and # of events, event density
3.057	Overview of On-therapy and Post-therapy AESIs: Pancreatitic Cancer	Safety	
3.058	Summary of On-therapy and Post-therapy AESIs: Pancreatitic Cancer, by SOC and PT	Safety	SOC and PT, #/% of subjects and # of events, event density
3.059	Overview of On-therapy AESIs: Pancreatitic Cancer	Safety	
3.060	Summary of On-therapy AESIs: Pancreatitic Cancer, by SOC and PT	Safety	SOC and PT, #/% of subjects and # of events, event density
3.061	Overview of On-therapy and Post-therapy AESIs: Investigator-reported Pancreatitis	Safety	
3.062	Summary of On-therapy and Post-therapy AESIs: Investigator-reported Pancreatitis, by SOC and PT	Safety	SOC and PT, #/% of subjects and # of events, event density
3.063	Overview of On-therapy AESIs: Investigator-reported Pancreatitis	Safety	
3.064	Summary of Investigator-reported Characteristics of On-therapy AESIs of Pancreatitis (All Pancreatitis Events Reported by Investigator)	Safety	

Table No.	Title	Population	Programming note
3.065	Summary of On-therapy AESIs: Investigator-reported Pancreatitis, by SOC and PT	Safety	SOC and PT, #/% of subjects and # of events, event density
3.066	Overview of On-therapy and Post-therapy AESIs: Investigational Product Injection Site Reactions	Safety	
3.067	Summary of On-therapy and Post-therapy AESIs: Investigational Product Injection Site Reactions, by SOC and PT	Safety	SOC and PT, #/% of subjects and # of events, event density
3.068	Overview of On-therapy AESIs: Investigational Product Injection Site Reactions	Safety	
3.069	Summary of Investigator-reported Characteristics of On-therapy AESIs of Investigational Product Injection Site Reactions	Safety	
3.070	Summary of On-therapy AESIs: Investigational Product Injection Site Reactions, by SOC and PT	Safety	SOC and PT, #/% of subjects and # of events, event density
3.071	Overview of On-therapy and Post-therapy AESIs: Hypersensitivity – Syndrome/Symptoms	Safety	
3.072	Summary of On-therapy and Post-therapy AESIs: Hypersensitivity – Syndrome/Symptoms, by SOC and PT	Safety	SOC and PT, #/% of subjects and # of events, event density
3.073	Overview of On-therapy AESIs: Hypersensitivity – Syndrome/Symptoms	Safety	
3.074	Summary of Investigator-reported Characteristics of On-therapy AESIs of Hypersensitivity – Syndrome/Symptoms	Safety	

Table No.	Title	Population	Programming note
3.075	Summary of On-therapy AESIs: Hypersensitivity – Syndrome/Symptoms, by SOC and PT	Safety	SOC and PT, #/% of subjects and # of events, event density
3.076	Overview of On-therapy and Post-therapy AESIs: Severe Hypoglycaemic Events	Safety	
3.077	Summary of On-therapy and Post-therapy AESIs: Severe Hypoglycaemic Events, by SOC and PT	Safety	SOC and PT, #/% of subjects and # of events, event density
3.078	Overview of On-therapy AESIs: Severe Hypoglycaemic Events	Safety	
3.079	Summary of Investigator-reported Characteristics of On-therapy AESIs of Severe Hypoglycaemic Events	Safety	
3.080	Summary of On-therapy AESIs: Severe Hypoglycaemic Events, by SOC and PT	Safety	SOC and PT, #/% of subjects and # of events, event density
3.081	Overview of On-therapy and Post-therapy AESIs: Hepatic Events	Safety	
3.082	Summary of On-therapy and Post-therapy AESIs: Hepatic Events, by SOC and PT	Safety	SOC and PT, #/% of subjects and # of events, event density
3.083	Overview of On-therapy AESIs: Hepatic Events	Safety	
3.084	Summary of On-therapy AESIs: Hepatic Events, by SOC and PT	Safety	SOC and PT, #/% of subjects and # of events, event density

Table No.	Title	Population	Programming note
3.085	Overview of On-therapy and Post-therapy AESIs: Hepatic Enzyme Elevations (including GGT)		
3.086	Summary of On-therapy and Post-therapy AESIs: Hepatic Enzyme Elevations (including GGT), by SOC and PT	Safety	SOC and PT, #/% of subjects and # of events, event density
3.087	Overview of On-therapy AESIs: Hepatic Enzyme Elevations (including GGT)	Safety	
3.088	Summary of On-therapy AESIs: Hepatic Enzyme Elevations (including GGT), by SOC and PT	Safety	SOC and PT, #/% of subjects and # of events, event density
3.089	Overview of On-therapy and Post-therapy AESIs: Serious GI Events	Safety	
3.090	Summary of On-therapy and Post-therapy AESIs: Serious GI Events, by SOC and PT	Safety	SOC and PT, #/% of subjects and # of events, event density
3.091	Overview of On-therapy AESIs: Serious GI Events	Safety	
3.092	Summary of On-therapy AESIs: Serious GI Events, by SOC and PT	Safety	SOC and PT, #/% of subjects and # of events, event density
3.093	Overview of On-therapy and Post-therapy AESIs: Appendicitis	Safety	
3.094	Summary of On-therapy and Post-therapy AESIs: Appendicitis, by SOC and PT	Safety	SOC and PT, #/% of subjects and # of events, event density
3.095	Overview of On-therapy AESIs: Appendicitis	Safety	

Table No.	Title	Population	Programming note
3.096	Summary of On-therapy AESIs: Appendicitis, by SOC and PT	Safety	SOC and PT, #/% of subjects and # of events, event density
3.097	Overview of On-therapy and Post-therapy AESIs: Atrial Fibrillation/Atrial Flutter	Safety	
3.098	Summary of On-therapy and Post-therapy AESIs: Atrial Fibrillation/Atrial Flutter, by SOC and PT	Safety	SOC and PT, #/% of subjects and # of events, event density
3.099	Overview of On-therapy AESIs: Atrial Fibrillation/Atrial Flutter	Safety	
3.100	Summary of Investigator-reported Characteristics of On-therapy AESIs of Atrial Fibrillation/Atrial Flutter	Safety	
3.101	Summary of On-therapy AESIs: Atrial Fibrillation/Atrial Flutter, by SOC and PT	Safety	SOC and PT, #/% of subjects and # of events, event density
3.102	Overview of On-therapy and Post-therapy AESIs: Pneumonia	Safety	
3.103	Summary of On-therapy and Post-therapy AESIs: Pneumonia, by SOC and PT	Safety	SOC and PT, #/% of subjects and # of events, event density
3.104	Overview of On-therapy AESIs: Pneumonia	Safety	
3.105	Summary of Investigator-reported Characteristics of On-therapy AESIs of Pneumonia	Safety	

Table No.	Title	Population	Programming note
3.106	Summary of On-therapy Adverse Events of Special Interest: Pneumonia, by SOC and PT	Safety	SOC and PT, #/% of subjects and # of events, event density
3.107	Overview of On-therapy and Post-therapy AESIs: Renal Impairment	Safety	
3.108	Summary of On-therapy and Post-therapy AESIs: Renal Impairment, by SOC and PT	Safety	SOC and PT, #/% of subjects and # of events, event density
3.109	Overview of On-therapy AESIs: Renal Impairment	Safety	
3.110	Summary of Investigator-reported Characteristics of On-therapy AESIs of Renal Impairment	Safety	
3.111	Summary of On-therapy AESIs: Renal Impairment, by SOC and PT	Safety	SOC and PT, #/% of subjects and # of events, event density
3.112	Overview of On-therapy and Post-therapy AESIs: Diabetic Retinopathy	Safety	
3.113	Summary of On-therapy and Post-therapy AESIs: Diabetic Retinopathy, by SOC and PT	Safety	SOC and PT, #/% of subjects and # of events, event density
3.114	Overview of On-therapy AESIs: Diabetic Retinopathy	Safety	
3.115	Summary of Investigator-reported Characteristics of On-therapy AESIs of Diabetic Retinopathy	Safety	
3.116	Summary of On-therapy AESIs: Diabetic Retinopathy, by SOC and PT	Safety	SOC and PT, #/% of subjects and # of events, event density

Table No.	Title	Population	Programming note
3.117	Summary of On-therapy and Post-therapy AESIs of Hypersensitivity – Syndrome/Symptoms, by Anti-albiglutide Antibody Status	Safety	SOC and PT, #/% of subjects and # of events
3.118	Summary of On-therapy and Post-therapy AESIs of Hypersensitivity – Syndrome/Symptoms, by Anti-albiglutide IgE Antibody Status	Safety	SOC and PT, #/% of subjects and # of events
3.119	Summary of Pancreatitis Adjudication Committee Results of On-therapy and Post-therapy AESIs of Pancreatitis	Safety	
3.120	Summary of On-therapy and Post-therapy AESIs: Pancreatitis Positively Adjudicated by the PAC, by SOC and PT	Safety	SOC and PT, #/% of subjects and # of events, event density
3.121	Summary of Pancreatitis Adjudication Committee Results of On-therapy AESIs of Pancreatitis	Safety	
3.122	Summary of On-therapy AESIs: Pancreatitis Positively Adjudicated by the PAC, by SOC and PT	Safety	SOC and PT, #/% of subjects and # of events, event density
3.123	Summary of Investigator-reported Characteristics of On-therapy AESIs of Pancreatitis Positively Adjudicated by the PAC	Safety	
3.124	Summary of On-therapy and Post-therapy Severe Hypoglycaemic Events by Baseline HbA1c, SOC and PT	Safety	SOC and PT, #/% of subjects and # of events, event density baseline HbA1c (<8.0%, ≥8.0% to <9.0%, ≥9.0%)

Table No.	Title	Population	Programming note
3.125	Summary of On-therapy Severe Hypoglycaemic Events by Baseline HbA1c, SOC and PT	Safety	SOC and PT, #/% of subjects and # of events, event density baseline HbA1c (<8.0%, ≥8.0% to <9.0%, ≥9.0%)
3.126	Summary of On-therapy and Post-therapy Severe Hypoglycaemic Events by Baseline eGFR, SOC and PT	Safety	SOC and PT, #/% of subjects and # of events, event density baseline eGFR (≥ 90, ≥60 to <90, < 60 ml/min/1.73m2)
3.127	Summary of On-therapy Severe Hypoglycaemic Events by Baseline eGFR, SOC and PT	Safety	SOC and PT, #/% of subjects and # of events, event density baseline eGFR (≥ 90, ≥60 to <90, < 60 ml/min/1.73m2)
3.128	Summary of On-therapy and Post-therapy Severe Hypoglycaemic Events by Age at Baseline, SOC and PT	Safety	SOC and PT, #/% of subjects and # of events, event density age (<65, ≥65 to <75, ≥75 years)

Table No.	Title	Population	Programming note
3.129	Summary of On-therapy Severe Hypoglycaemic Events by Age at Baseline, SOC and PT	Safety	SOC and PT, #/% of subjects and # of events, event density age (<65, ≥65 to <75, ≥75 years)
3.130	Summary of On-therapy and Post-therapy Severe Hypoglycaemic Events by Baseline Sulfonylurea/Insulin Use, SOC and PT	Safety	SOC and PT, #/% of subjects and # of events, event density Baseline sulfonylurea/insulin use = Yes or No
3.131	Summary of On-therapy Severe Hypoglycaemic Events by Baseline Sulfonylurea/Insulin Use, SOC and PT	Safety	SOC and PT, #/% of subjects and # of events, event density Baseline sulfonylurea/insulin use = Yes or No
3.132	Summary of Recurrent Event Analysis of On-therapy Severe Hypoglycaemic Events	Safety	
3.133	Summary of Recurrent Event Analysis of On-treatment Severe Hypoglycaemic Events	Safety	
3.134	Summary of Recurrent Event Analysis of On-therapy Severe Hypoglycaemic Events (Adjusting for Baseline Sulfonylurea/Insulin Use)	Safety	

Table No.	Title	Population	Programming note
3.135	Summary of Recurrent Event Analysis of On-treatment Severe Hypoglycaemic Events (Adjusting for Baseline Sulfonylurea/Insulin Use)	Safety	
3.136	Summary of On-therapy and Post-therapy Malignant Neoplasms by SOC, HLT and PT	Safety	SOC, HLT and PT, #/% of subjects and # of events, event density
3.137	Summary of On-therapy Malignant Neoplasms by SOC, HLT and PT	Safety	SOC, HLT and PT, #/% of subjects and # of events, event density
3.138	Summary of On-therapy and Post-therapy Malignant Neoplasms by Insulin Use at Baseline, SOC, HLT and PT	Safety	SOC, HLT and PT, #/% of subjects and # of events, event density
3.139	Summary of Mantel-Haenszel Analysis of On-therapy and Post-therapy Malignant Neoplasms, Stratified by Insulin Use at Baseline	Safety	
3.140	Summary of On-therapy Malignant Neoplasms by Insulin Use at Baseline, SOC, HLT and PT	Safety	SOC, HLT and PT, #/% of subjects and # of events, event density
3.141	Summary of Mantel-Haenszel Analysis of On-therapy Malignant Neoplasms, Stratified by Insulin Use at Baseline	Safety	
3.142	Summary of On-therapy and Post-therapy Malignant Neoplasms by History of Malignancy at Baseline, SOC, HLT and PT	Safety	SOC, HLT and PT, #/% of subjects and # of events, event density
3.143	Summary of Mantel-Haenszel Analysis of On-therapy and Post-therapy Malignant Neoplasms, Stratified by History of Malignancy at Baseline	Safety	

Table No.	Title	Population	Programming note
3.144	Summary of On-therapy Malignant Neoplasms by History of Malignancy at Baseline, SOC, HLT and PT	Safety	SOC, HLT and PT, #/% of subjects and # of events, event density
3.145	Summary of Mantel-Haenszel Analysis of On-therapy Malignant Neoplasms, Stratified by History of Malignancy at Baseline	Safety	
3.146	Summary of On-therapy and Post-therapy Liver Monitoring/Stopping Event Reporting	Safety	
3.147	Summary of On-therapy Hepatobiliary Laboratory Abnormalities	Safety	
3.175	Summary of Liver Function Tests of Potential Clinical Concern	Safety	
3.148	Summary of On-therapy and Post-therapy Other CV Events	Safety	Other CV event category, #/% of subjects and # of events, event density
3.149	Summary of On-therapy Other CV Events	Safety	Other CV event category, #/% of subjects and # of events, event density
3.150	Summary of Chemistry Values	Safety	
3.151	Summary of Change from Baseline Chemistry Values	Safety	
3.152	Summary of Chemistry Values of Potential Clinical Concern	Safety	
3.153	Summary of Change from Baseline Creatinine Values of Potential Clinical Concern by Baseline eGFR	Safety	baseline eGFR category (Normal ≥ 90, Mild ≥60 to <90, Moderate ≥30 to < 60, and Severe <30 ml/min/1.73m2)

Table No.	Title	Population	Programming note
3.154	Summary of Chemistry Shifts From Baseline with Respect to Potential Clinical Concern	Safety	
3.155	Summary of Change from Baseline Creatinine Values of Potential Clinical Concern (Central Laboratory Data) by Baseline eGFR	Safety	baseline eGFR category (Normal ≥ 90, Mild ≥60 to <90, Moderate ≥30 to < 60, and Severe <30 ml/min/1.73m2)
3.156	Summary of eGFR	Safety	Only use computed values
3.157	Summary of Change From Baseline in eGFR	Safety	Only use computed values
3.158	Summary of MMRM Analysis for On-treatment eGFR (ml/min/1.73m2) Change From Baseline (Baseline Data from Local or Central Laboratory, and Post-baseline Central Laboratory Data)	Safety	Only use computed values
3.159	Summary of MMRM Analysis for On-treatment eGFR (ml/min/1.73m2) Change From Baseline (Central Laboratory Data)	Safety	Only use computed values
3.160	Summary of eGFR Categories	Safety	Only use computed values
3.161	Summary of Shifts from Baseline in eGFR	Safety	Only use computed values
3.162	Summary of Shifts from Baseline in eGFR (Central Laboratory Data)	Safety	Only use computed values
3.163	Summary of Vital Signs	Safety	BP and Heart Rate
3.164	Summary of Change From Baseline Vital Signs	Safety	BP and Heart Rate
3.165	Summary of Vital Signs Outside Potential Clinical Concern Range	Safety	BP and Heart Rate

Table No.	Title	Population	Programming note
3.166	Summary of Vital Signs with a Change From Baseline of Potential Clinical Concern	Safety	BP and Heart Rate
3.167	Summary of Shifts from Baseline in Potential Clinical Concern Category for Vital Signs	Safety	BP and Heart Rate
3.168	Summary of On-therapy Serious Adverse Events By PT	Safety	CTR format
3.169	Summary of On-therapy Fatal Serious Adverse Events By PT	Safety	CTR format
3.170	Summary of Treatment-related On-therapy Serious Adverse Events By PT	Safety	CTR format
3.171	Summary of Treatment-related On-therapy Fatal Serious Adverse Events By PT	Safety	CTR format
3.172	Summary of On-therapy Most Frequent 10 Adverse Events by Overall Frequency	Safety	CTR format Non-systematic assessment of AEs Include most frequent 10 AEs in each treatment group
3.173	Summary of On-therapy Serious Adverse Events by SOC and PT	Safety	FDAAA/EudraCT format

Table No.	Title	Population	Programming note
3.174	Summary of Common (>=5%) On-therapy Non-serious AEs (AESIs, AEs Leading to Permanent Discontinuation of Study Treatment and Any Other Non-serious AEs Reported by the Investigator) by SOC and PT	Safety	FDAAA/EudraCT format Non-systematic assessment of AEs Include non-serious AEs reported by >=5% (before rounding the percentage) of subjects in either treatment group.
3.176	Summary of Creatinine Values of Potential Clinical Concern (Excluding Selected Data)	Safety	
3.177	Summary of Change from Baseline Creatinine Values of Potential Clinical Concern by Baseline eGFR (Excluding Selected Data)	Safety	baseline eGFR category (Normal ≥ 90, Mild ≥60 to <90, Moderate ≥30 to < 60, and Severe <30 ml/min/1.73m2)
3.178	Summary of MMRM Analysis for On-treatment eGFR (ml/min/1.73m2) Change From Baseline (Baseline Data from Local or Central Laboratory, and Post-baseline Central Laboratory Data) (Excluding Selected Data)	Safety	Only use computed values
3.179	Summary of MMRM Analysis for On-treatment eGFR (ml/min/1.73m2) Change From Baseline (Central Laboratory Data) (Excluding Selected Data)	Safety	Only use computed values

11.15.7. Safety Figures

Figure No.	Title	Population	Programming note
3.01	Kaplan-Meier Plot of Time to Death (Vital Status Follow-up Time Period)	ITT	
3.02	Kaplan-Meier Plot of Time to Death (On-therapy Time Period)	ITT	
3.03	Kaplan-Meier Plot of Time to Death (On-treatment Time Period)	ITT	
3.04	Common (>=2%) On-therapy Serious Adverse Events Sorted by Relative Risk	Safety	
3.05	On-therapy Adverse Events of Special Interest Sorted by Relative Risk	Safety	
3.06	Kaplan Meier Plot of Time to First Investigational Product Injection Site Reaction (On-therapy Time Period)	Safety	
3.07	Kaplan Meier Plot of Time to First Serious GI Event (On-therapy Time Period)	Safety	
3.08	Line Graph of Mean (+/-SE) eGFR (ml/min/1.73m^2) Over Time	Safety	
3.09	Line Graph of Mean (+/-SE) Change from Baseline eGFR (ml/min/1.73m^2) Over Time	Safety	
3.10	Line Graph of Adjusted Mean (+/-SE) Change from Baseline On-treatment eGFR (ml/min/1.73m^2) Over Time	Safety	Plot adjusted means.
3.11	Line Graph of Mean (+/-SE) SBP (mmHg) Over Time	Safety	
3.12	Line Graph of Mean (+/-SE) Change from Baseline SBP (mmHg) Over Time	Safety	
3.13	Line Graph of Mean (+/-SE) DBP (mmHg) Over Time	Safety	
3.14	Line Graph of Mean (+/-SE) Change from Baseline DBP (mmHg) Over Time	Safety	

Figure No.	Title	Population	Programming note
3.15	Line Graph of Mean (+/-SE) Heart Rate (bpm) Over Time	Safety	
3.16	Line Graph of Mean (+/-SE) Change from Baseline Heart Rate (bpm) Over Time	Safety	
3.17	Scatter Plot of Maximum vs. Baseline for ALT	Safety	
3.18	Scatter Plot of Maximum Total Bilirubin versus Maximum ALT - eDISH	Safety	
3.19	Box Plot of Creatinine (umol/l) Over Time	Safety	
3.20	Box Plot of Change from Baseline Creatinine (umol/l) Over Time	Safety	

11.15.8. VEO Tables

Table No.	Title	Population	Programming note
4.01	Summary of TRIM-D Total Score (Observed Cases)	ITT	Exclude subjects not on diabetes medication at baseline.
4.02	Summary of TRIM-D Total Score (LOCF)	ITT	Exclude subjects not on diabetes medication at baseline.
4.03	Summary of MMRM Analysis of TRIM-D Total Score Change From Baseline (Observed Cases)	ITT	Exclude subjects not on diabetes medication at baseline.
4.04	Summary of TRIM-D Treatment Burden Domain Score (Observed Cases)	ITT	Exclude subjects not on diabetes medication at baseline.
4.05	Summary of TRIM-D Daily Life Domain Score (Observed Cases)	ITT	Exclude subjects not on diabetes medication at baseline.
4.06	Summary of TRIM-D Diabetes Management Domain Score (Observed Cases)	ITT	Exclude subjects not on diabetes medication at baseline.

Table No.	Title	Population	Programming note
4.07	Summary of TRIM-D Compliance Domain Score (Observed Cases)	ITT	Exclude subjects not on diabetes medication at baseline.
4.08	Summary of TRIM-D Psychological Health Domain Score (Observed Cases)	ITT	Exclude subjects not on diabetes medication at baseline.
4.09	Summary of EQ-5D VAS Score (Observed Cases)	ITT	
4.10	Summary of EQ-5D VAS Score (LOCF)	ITT	
4.11	Summary of MMRM Analysis of EQ-5D VAS score Change From Baseline (Observed Cases)	ITT	
4.12	Summary of EQ-5D Mobility Domain (Observed Cases)	ITT	
4.13	Summary of EQ-5D Self-Care Domain (Observed Cases)	ITT	
4.14	Summary of EQ-5D Usual Activities Domain (Observed Cases)	ITT	
4.15	Summary of EQ-5D Pain/Discomfort Domain (Observed Cases)	ITT	
4.16	Summary of EQ-5D Anxiety/Depression Domain (Observed Cases)	ITT	
4.17	Summary of In-patient Healthcare Resource Utilization	ITT	
4.18	Summary of Managing Diabetes Questionnaire Data	ITT	
4.19	Summary of Managing Diabetes Questionnaire Data: Question 1	ITT	
4.20	Summary of Managing Diabetes Questionnaire Data: Question 3	ITT	

11.15.9. VEO Figures

Figure No.	Title	Population	Programming note
4.01	Line Graph of Mean (+/-SE) TRIM-D Total Score (Observed Cases)	ITT	
4.02	Line Graph of Mean (+/-SE) TRIM-D Total Score (LOCF)	ITT	
4.03	Line Graph of Mean (+/-SE) Change From Baseline TRIM-D Total Score (Observed Cases)	ITT	
4.04	Line Graph of Adjusted Mean (+/-SE) Change From Baseline TRIM-D Total Score (Observed Cases)	ITT	Plot adjusted means.
4.05	Line Graph of Mean (+/-SE) EQ-5D VAS (Observed Cases)	ITT	
4.06	Line Graph of Mean (+/-SE) EQ-5D VAS (LOCF)	ITT	
4.07	Line Graph of Mean (+/-SE) Change From Baseline EQ-5D VAS (Observed Cases)	ITT	
4.08	Line Graph of Adjusted Mean (+/-SE) Change From Baseline EQ-5D VAS (Observed Cases)	ITT	Plot adjusted means.

11.15.10. ICH Listings

Listing no.	Title	Population	Programming note
1	Listing of Reasons for Screen Failures	Screened Subjects	
2	Listing of Reasons for Study Withdrawal	ITT	
3	Listing of Subjects for Whom the Treatment Blind Was Broken	ITT	

Listing no.	Title	Population	Programming note
4	Listing of Planned and Actual Treatments	ITT	
5	Listing of Important Protocol Deviations	ITT	
6	Listing of Subjects with Inclusion/Exclusion Criteria Deviations	ITT	
7	Listing of Subjects Excluded from Any Population	Enrolled	
8	Listing of Demographic Characteristics	ITT	
9	Listing of Race	ITT	
10	Listing of Cardiovascular Medication Categories	ITT	
11	Listing of Anti-hyperglycaemic Medications	ITT	
12	Listing of Recorded Medications Other than Anti-hyperglycaemic Medications	ITT	
13	Listing of Exposure Data	Safety	
14	Listing of SAEs, AESIs, AEs Leading to Permanent Discontinuation of Study Treatment and Any Other Non-serious AEs Recorded by the Investigator	Safety	
15	Listing of Subject Numbers for Specified Adverse Events	Safety	
16	Listing of Relationship between System Organ Class, Preferred Term and Verbatim Text	Safety	
17	Listing of Fatal Serious Adverse Events	Safety	
18	Listing of Non-fatal Serious Adverse Events	Safety	

Listing no.	Title	Population	Programming note
19	Listing of Reasons for Considering as a Serious Adverse Event	Safety	
20	Listing of AEs Leading to Permanent Discontinuation of Study Treatment	Safety	
21	Listing of Medical Conditions for Subjects with Liver Stopping Events	Safety	
22	Listing of Substance Use for Subjects with Liver Stopping Events	Safety	
23	Listing of Laboratory Data for Subjects with Abnormalities of Potential Clinical Concern	Safety	AST, ALT, alkaline phosphatase, bilirubin, creatinine, GGT
24	Listing of Vital Signs for Subjects with Abnormalities of Potential Clinical Concern	Safety	

11.15.11. Non-ICH Listings

Listing no.	Title	Population	Programming note
25	Listing of Re-screened Subjects	ITT	
26	Listing of Reasons for Study Treatment Discontinuation	ITT	
27	Listing of Events Leading to Exclusion of Data From Per-protocol Analysis	ITT	
28	Relationship between ATC Level 1, Ingredient and Verbatim Text	ITT	
29	Listing of Compliance Data	Safety	
30	Listing of Time to First Adjudicated MACE (CV Follow-up Time Period)	ITT	

Listing no.	Title	Population	Programming note
31	Listing of Time to First Adjudicated MACE or urgent revascularization for unstable angina (CV Follow-up Time Period)	ITT	
32	Listing of Time to First Adjudicated CV Death (CV Follow-up Time Period)	ITT	
33	Listing of Time to First Adjudicated MI (CV Follow-up Time Period)	ITT	
34	Listing of Time to First Adjudicated Stroke (CV Follow-up Time Period)	ITT	
35	Listing of Time to First Adjudicated CV death or hospitalization due to heart failure (CV Follow-up Time Period)	ITT	
36	Listing of Time to Initiation of Insulin of More Than 3 Months Duration For Subjects Not Treated With Insulin At Study Start	NI	
37	Listing of Time to Initiation of Prandial Insulin of More Than 3 Months Duration For Subjects on Basal Insulin at Study Start	BI	
38	Listing of Composite Metabolic Endpoint	ITT	
39	Listing of Time to First Occurrence of a Clinically Important Microvascular Event	ITT	
40	Listing of HbA1c	ITT	Include value and change from baseline
41	Listing of Body Weight	ITT	Include value and change from baseline
42	Listing of Efficacy Endpoints	ITT	
43	Listing of Time to Death	ITT	
44	Listing of Non-serious AEs That Are Not AESIs Nor Led to Permanent Discontinuation of Study Treatment	Safety	

Listing no.	Title	Population	Programming note
45	Listing of SAEs, AESIs, AEs Leading to Permanent Discontinuation of Study Treatment and Any Other Non-serious AEs Recorded by the Investigator (Subjects with Baseline eGFR<30ml/min/1.73m2)	Safety	
46	Listing of Investigator-reported Characteristics of On-therapy AESIs of Thyroid Cancer Diagnosis	Safety	
47	Listing of Investigator-reported Characteristics of On-therapy AESIs of Pancreatitis	Safety	
48	Listing of Investigator-reported Characteristics of On-therapy AESIs of Investigational Product Injection Site Reaction	Safety	
49	Listing of Investigator-reported Characteristics of On-therapy AESIs of Hypersensitivity – Syndrome/Symptoms	Safety	
50	Listing of Investigator-reported Characteristics of On-therapy AESIs of Severe Hypoglycaemic Events	Safety	
51	Listing of Investigator-reported Characteristics of On-therapy AESIs of Atrial Fibrillation/Atrial Flutter	Safety	
52	Listing of Investigator-reported Characteristics of On-therapy AESIs of Pneumonia	Safety	
53	Listing of Investigator-reported Characteristics of On-therapy AESIs of Renal Impairment	Safety	
54	Listing of Investigator-reported Characteristics of On-therapy AESIs of Diabetic Eye Disease Event	Safety	
55	Listing of all AESIs	Safety	
56	Listing of Anti-Albiglutide Antibody Results	Safety	
57	Listing of Anti-GLP-1 Antibody Results for Anti-Albiglutide Antibody Positive Subjects	Safety	

Listing no.	Title	Population	Programming note
58	Listing of Anti-HSA Antibody Results for Anti-Albiglutide Antibody Positive Subjects	Safety	
59	Listing of Anti-Albiglutide IgE Antibody Results	Safety	
60	Listing of Investigator-reported Characteristics of On-therapy AESIs of Pancreatitis Positively Adjudicated by the PAC	Safety	
61	Listing of Events Adjudicated by the Pancreatitis Adjudication Committee	Safety	
62	Listing of Malignant Neoplasms	Safety	
63	Listing of Other Significant Adverse Events	Safety	
64	Listing of Liver Monitoring/Stopping Event Reporting	Safety	
65	Listing of Liver Biopsy Details	Safety	
66	Listing of Liver Imaging Details	Safety	
67	Listing of Subjects Meeting Hepatobiliary Laboratory Criteria Post-baseline	Safety	
68	Listing of eGFR	Safety	
69	Listing of Investigator-reported and Adjudicated Cause of Death	ITT	
70	Listing of Creatinine Assessed at Central Laboratory	Safety	
71	Listing of Subjects Who Became Pregnant During the Study	Safety	
72	Listing of Non-serious Adverse Events for Subjects at Mexican Sites	Safety	Expected to only include non-serious AESIs and non-serious AEs leading to discontinuation of IP
73	Listing of Clinical Events and Serious Adverse Events for Subjects	Safety	

Listing no.	Title	Population	Programming note
	at Mexican Sites		
74	Listing of Serious Adverse Events for Subjects at Non-Mexican Sites	Safety	
75	Subject Profile for Arrhythmias (other than Atrial Fibrillation/Flutter)	Safety	
76	Subject Profile for Valvulopathy	Safety	
77	Subject Profile for Pulmonary Hypertension	Safety	
78	Subject Profile for Peripheral Arterial Thromboembolism	Safety	
79	Subject Profile for Deep Vein Thrombosis/Pulmonary Embolism	Safety	
80	Subject Profile for CABG or PCI Revascularization (other than Urgent Revascularization for Unstable Angina)	Safety	
81	Listing of TRIM-D Total Score	ITT	Include value and change from baseline
82	Listing of EQ-5D VAS Score	ITT	Include value and change from baseline