# Reporting and Analysis Plan (RAP)

**Study ID:** 209493

**Official Title of Study:** Reporting and Analysis Plan for A qualitative hybrid III implementation study to identify and evaluate strategies for successful implementation of the cabotegravir + rilpivirine long-acting injectable regimen in the US

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

| | | |
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| **Title** | : | Reporting and Analysis Plan for A qualitative hybrid III implementation study to identify and evaluate strategies for successful implementation of the cabotegravir + rilpivirine long-acting injectable regimen in the US |
| **Compound Number** | : | GSK1265744 |
| **Clinical Study Identifier** | : | 209493 |
| **Effective Date** | : | Refer to Document Date |

**Description:**

- The purpose of this RAP is to describe the planned analyses and output to be included in the Clinical Study Report for Protocol 209493, specifically for clinical data. Any implementation science/health outcome analyses will be detailed in a separate Evidera SAP.
- This RAP will be provided to the study team members to convey the content pertaining to clinical data for the End of Study (EOS) analyses.

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# 1. INTRODUCTION

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

| **Revision Chronology:** | | |
|---|---|---|
| 2018N382441_00 | 02-JAN-2019 | Original |
| 2018N382441_01 | 02-APR-2019 | Amendment No. 1 |
| The reasons for this amendment include: addition of exclusion criterion regarding known major resistance mutations at Screening, clarification of timing for collection of visit length, removal of consent requirement for study staff, correction to allowable window around the Month 3 dosing visit, clarification of pregnancy testing requirements at Screening, clarification of wording to allow a single re-screen per subject, removal of color of vial stopper in product description to allow flexibility of packaging for cabotegravir and rilpivirine suspension, clarification of ECG collection during the study, clarification of wording to allow qualitative analyses to be performed by a CRO under GSK oversight. | | |
| 2018N382441_02 | 15-MAY-2020 | Amendment No.2 |
| The purpose of this amendment is to include an Appendix related to COVID-19 Pandemic and Clinical Trial Continuity. This appendix will replace the previous Appendix 11, and "Protocol Amendment History," will be included as Appendix 12. | | |
| 2018N382441_03 | 16-NOV-2020 | Amendment No. 3 |
| The primary purpose of this amendment is to allow participants who become pregnant while in the study to remain in the study and not be withdrawn as a result of the pregnancy. Allowing pregnant participants to continue in the study will negate any subsequent fetal exposures to new antiretrovirals agents that would occur if the pregnant participant was withdrawn from study and placed on an oral SOC regimen. An Appendix, "Information and Guidance for Managing Pregnant Participants" was inserted as Appendix 8 and all subsequent appendices were renumbered accordingly.<br>Minor additional edits were made which were previously addressed with a note to file (NTF), for clarity and/or correction. | | |

## 1.1. RAP Amendments

**Revision Chronology:**

| RAP Section | Amendment Details |
|---|---|
| **Reporting and Analysis Plan_Study209493_Final_V1 [29-OCT-2020]** | |
| **Reporting and Analysis Plan_Study209493_Amendment_1_Final_V1** | |
| Data Displays for End of Study Analysis | • Added the displays for summarizing and listing the data collected from the newly added eCRF form, Transition to CAB + RPV LA Marketed Product Status.<br>• Updated the standard shells for COVID-19 assessment and symptom displays per changes of the data collection.<br>• Updated the standard shell for the country level listing of COVID-19 pandemic measures to include the start and end dates of each wave of the pandemic.<br>• Added age group (18-24, 25-40, >40) and BMI group (<30, >=30) to the summary table of demographic characteristics.<br>• Added an efficacy table for summarizing the proportion of plasma HIV-1 RNA < 50 c/mL over time from the observed case analysis.<br>• Added a listing of COVID-19 vaccine.<br>• Updated the Extension phase visit slotting algorithm for HIV-1 RNA data . |
| General Updates | • Updated Schedule of Activities and other relevant sections per protocol amendment 03.<br>• Added additional minor clarifications and corrections to typographical errors/formatting to RAP text. |

# 2. SUMMARY OF KEY PROTOCOL INFORMATION

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

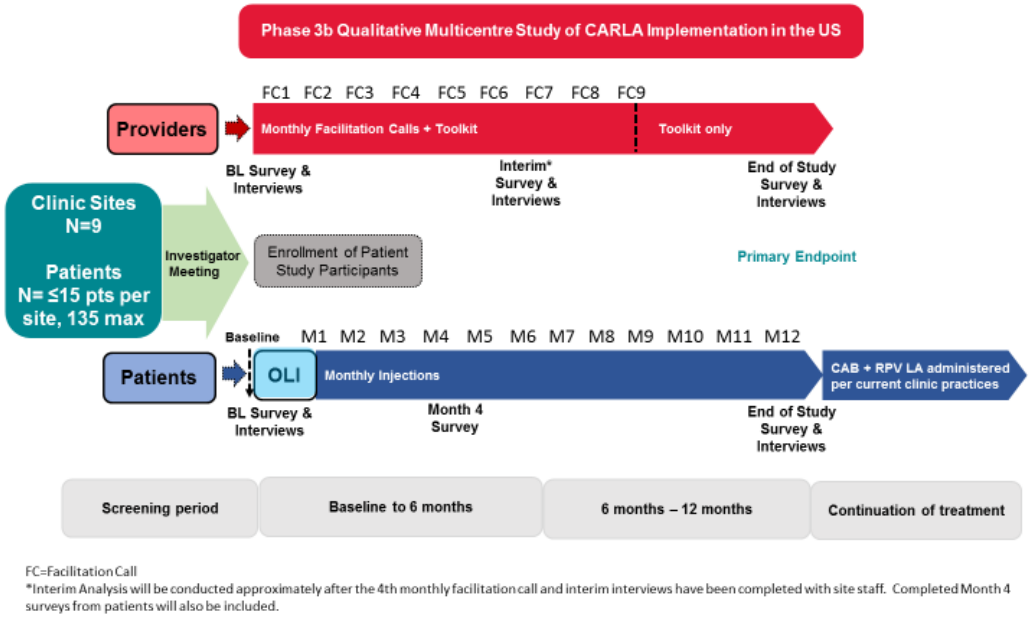
There were no changes or deviations to the originally planned statistical analysis specified in protocol amendment 03 [(Dated: 16/November/2020)].

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

| Objectives | Estimands / Endpoints |
|---|---|
| **Primary** | **Primary** |
| • To evaluate acceptability, appropriateness, and feasibility of delivering CAB+RPV LA | • Acceptability of Intervention Measure (AIM), Intervention Appropriateness Measure (IAM), and Feasibility of Intervention Measure (FIM). Assessed quantitatively by staff study participants at baseline- prior to any Month 1 visits, after at least 4 monthly facilitation calls and upon completion of all Month 12 visits at that site.<br>• Acceptability of Intervention Measure (AIM) and Intervention Appropriateness Measure (IAM). Assessed quantitatively by patient study participants at Month 1 prior to first injection, Month 4 and Month 12 |
| **Secondary** | **Secondary** |
| • To evaluate organizational facilitators and barriers | • Facilitators/Barriers: Semi-Structured Interview (SSI) conducted with staff study participants at baseline- prior to any Month 1 visits, after at least 4 monthly facilitation calls and upon completion of at least 50% of Month 12 visits at that site.<br>• Barriers, facilitators and best practice sharing amongst clinics assessed by short-term facilitation (coaching calls) for at least 6 months. These will be a combination of structured questions and open-ended questions.<br>• Use of support materials/toolkit assessed via Survey responses of staff study participants prior to any Month 1 visits, after at least 4 monthly facilitation calls and upon completion of all Month 12 visits at a site.<br>• Use of support materials/toolkit assessed via Survey responses of patient study participants via Survey responses at Month 1 and Month 4 and Month 12, as well as SSI responses prior to Month 1 and at Month 12. |
| • Patient Facilitators and Barriers | • Facilitators/Barriers: Semi-Structured Interviews (SSI) conducted with patient study participants prior to Month 1 and at Month 12. |

| Objectives | Estimands / Endpoints |
|---|---|
| • Implementation Fidelity | • Injections occurring within target window from the expected injection date<br>• Use of support materials/toolkit assessed through SSI of staff study participants at Day 1, after at least 4 monthly facilitation calls and upon completion of at least 50% of Month 12 visits at that site |
| • Implementation Sustainability | • Program Sustainability Assessment Tool (PSAT) assessed by staff study participants at Month 12 |
| • To measure patient satisfaction with process (timeliness of visits, length of visit, patient education) | • Patient Survey responses at Month 1, Month 4 and Month 12.<br>• Patient SSI responses prior to Month 1 and at Month 12<br>• Length of patient visit from arrival until departure from clinic at Month 1, Month 5 and Month 11 |
| • To evaluate the safety and efficacy measures of CAB LA + RPV LA | • Proportion of participants with plasma HIV-1 RNA <50 c/mL over time<br>• Proportion of participants with confirmed virologic failure (CVF) over time<br>• Incidence of treatment emergent genotypic and phenotypic resistance to CAB and RPV in patients with CVF<br>• Incidence and severity of AEs and laboratory abnormalities over time<br>• Proportion of participants who discontinue treatment due to AEs over time<br>• Reported injection site reactions over time<br>• Absolute values and changes in laboratory parameters over time |

## 2.3. Study Design

| **Overview of Study Design and Key Features** | |
|---|---|
|  | |
| N=115 patients; Open label with respect to treatment; patients randomized to CAB LA+RPV LA Interview: CAB LA + RPV LA Non-Interview | |
| **Design Features** | • A qualitative hybrid III implementation study to identify and evaluate strategies for successful implementation of the cabotegravir + rilpivirine long-acting injectable regimen in the US<br>• The CUSTOMIZE study comprises of screening phase (up to 21 days), Intervention Phase from Day 1 to Month 12, including Oral Lead-in, long term follow-up (LTFU) phase, and extension phase. During screening phase all clinical and laboratory assessments of eligibility must be performed and reviewed. Participants may be re-screened once |
| **Dosing** | • Intervention Phase is Open label with respect to treatment;<br>• Intervention Phase: randomized 1:3 to CAB LA+RPV LA Interview:CAB LA + RPV LA Non-Interview<br>• Randomized at Day 1 (1:3) to receive CAB LA + RPV LA Interview or CAB LA + RPV LA Non-interview respectively<br>• GSK Randall NG used to generate randomization schedule for interview group assignments |
| **Time & Events** | • Refer to Appendix 2: Schedule of Activities |
| **Treatment Assignment** | • CAB LA+RPV LA (N=115) |
| **Interim Analysis** | • Analysis at Month 4 to provide preliminary data to inform planning for the initial commercial availability of the CAB LA + RPV LA regimen<br>• Primary analysis will be conducted at Month 12 |

## 2.4. Statistical Hypotheses / Statistical Analyses

No formal hypothesis testing is planned.

# 3. PLANNED ANALYSES

This RAP describes standard analyses that will be applied to descriptively summarize clinical adverse events, laboratory evaluations, virologic parameters and other clinical safety and efficacy outcomes.

Details pertaining to reporting of survey/interview data and health outcomes/effectiveness analyses will be described in a separate analysis plan provided by Evidera or other CRO partner under GSK's oversight.

At least two analyses will be conducted to evaluate primary and secondary objectives of the protocol: an interim analysis at Month 4 and a primary analysis at Month 12.

A final end-of-study (EOS) analysis will be conducted when all subjects have completed the study.

## 3.1. Interim Analyses

One interim analysis at Month 4 was performed to provide preliminary data to inform planning for the initial commercial availability of the CAB + RPV LA regimen. No formal criteria for stopping or amending the study based on the interim analysis are envisioned. Analysis and reporting details can be found in the standalone Month 4 interim analysis RAP.

## 3.2. Final Analyses

The planned Month 12 primary analysis will be performed after the completion of the following sequential steps:

1. All participants have completed Month 12 of the study as defined in the protocol.
2. All required database cleaning activities have been completed and final database release (DBR), source data lock (SDL) and database freeze (DBF) have been declared by Data Management.

The planned EOS analysis will be conducted after the completion of the following sequential steps:

1. All participants have completed the study as defined in the protocol.
2. All required database cleaning activities have been completed and final database release (DBR), source data lock (SDL) and database freeze (DBF) have been declared by Data Management.

# 4. ANALYSIS POPULATIONS

| Population | Definition / Criteria | Analyses Evaluated |
|---|---|---|
| Screened | • All participants who were screened for eligibility | • Study Population |
| Enrolled | • All participants who passed screening and entered the study (i.e. were administered study treatment). | • Study Population |
| Safety | • All participants who received at least one dose of study treatment. | • Study Population, Safety, Efficacy, Virology, PK, Other Assessments |

Refer to Appendix 13: List of Data Displays which details the population used for each display.

## 4.1. Protocol Deviations

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

Protocol deviations will be tracked by the study team throughout the conduct of the study in accordance with the Protocol Deviation Management Plan [Version 4,12-May-2021].

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

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

Protocol deviations related to the implementation process, and not the clinical conduct of the study will be reported separately. The identification and categorization of PDs as important may be different for implementation PDs vs those associated with the clinical conduct of the study.

# 5. CONSIDERATIONS FOR DATA ANALYSES AND DATA HANDLING CONVENTIONS

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

| Treatment Group Descriptions | |
|---|---|
| **Data Displays for Reporting** | |
| **Description** | **Order in TLF** |
| CAB LA +RPV LA | 1 |

## 5.2. Baseline Definitions

For all endpoints the baseline value will be the latest pre-treatment (See Table 10) assessment with a non-missing value, including those from unscheduled visits. If time is not collected, assessments taken on the same date as treatment start date are assumed to be taken prior to first dose and used as baseline.

Electrocardiograms (ECGs) are to be performed in triplicate on Screening visit. The baseline value for an ECG parameter will be the mean of the last pre-treatment set of assessments from the same date so long as at least one of the triplicate assessments is available.

## 5.3. Multicentre Studies

In this multicentre global study, enrolment will be presented by investigator and Site type.

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

### 5.4.1. Covariates and Other Strata

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

| Category | Details |
|---|---|
| Covariates | Site Type |

### 5.4.2. Examination of Subgroups

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

- If the percentage of participants is small within a subgroup category, then the subgroup categories may be combined.

| Subgroup | Categories |
|---|---|
| Site Type | AIDS Healthcare Foundation, Federally Qualified Health Center, Health Maintenance Organization, Private Practice, University |

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

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

| Section | Component |
|---|---|
| 13.3 | Appendix 3: Assessment Windows |
| 13.4 | Appendix 4: Study Phases and Treatment Emergent Adverse Events |
| 13.5 | Appendix 5: Data Display Standards & Handling Conventions |
| 13.6 | Appendix 6: Derived and Transformed Data |
| 13.7 | Appendix 7: Reporting Standards for Missing Data |
| 13.8 | Appendix 8: Values of Potential Clinical Importance |

# 6. STUDY POPULATION ANALYSES

## 6.1. Overview of Planned Study Population Analyses

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

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

# 7. EFFICACY ANALYSES

Implementation Science/Health Outcomes endpoints will form the basis for the overall primary analysis of the study, and details of implementation science/health outcomes analyses are documented in a separate Evidera SAP. Clinical efficacy endpoints are evaluated as secondary objectives for this study.

## 7.1. Secondary Efficacy Analyses

### 7.1.1. Endpoint / Variables

- Proportion of participants with Plasma HIV-RNA < 50 copies/mL and plasma HIV-1 RNA ≥ 50 c/mL, respectively, over time using the FDA Snapshot Algorithm. See Section 13.9 for Snapshot Algorithm details.

Other secondary efficacy endpoints:

- Proportion of participants with confirmed virologic failure (CVF) over time
- Absolute values and changes from Baseline CD4+ cell count over time

### 7.1.2. Population of Interest

Secondary efficacy analyses will be based on the Safety population, unless otherwise specified.

### 7.1.3. Strategy for Intercurrent (Post-Randomization) Events

- Participants with last available HIV-1 RNA measurement less than 50 copies/mL while the participant is on treatment within the analysis visit window of interest are classified as HIV-1 RNA < 50 c/mL. Participants without evaluable HIV-RNA data for the visit of interest or who change treatment not permitted per protocol before the analysis window are considered non-responders.
- Participants with last available HIV-1 RNA measurement greater or equal to 50 copies/mL while the participant is on treatment within the analysis visit window of interest are classified as HIV-1 RNA ≥ 50 c/mL. Participants without evaluable HIV-RNA data for the visit of interest and who discontinue treatment for reasons not related to adverse event while having HIV-1 RNA ≥50 copies/mL at time of

discontinuation or who change study treatment not permitted per protocol before the analysis window are also classified as having HIV-RNA ≥50 copies/mL.

Missing viral load values for reasons related to COVID-19 issues (e.g. participant is unable to have viral load assessed due to barriers in attending the clinic during the pandemic or COVID-19 related adverse events leading to treatment discontinuation) will be imputed using an LOCF approach in which the last on-treatment viral load value will be carried forward and used in place of missing values.

### 7.1.4. Statistical Analyses / Methods

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

Unless otherwise specified, endpoints / variables defined in Section 7.1.1 will be summarised using descriptive statistics, graphically presented (where appropriate) and listed.

#### 7.1.4.1. Statistical Methodology Specification

| **Endpoint / Variables** |
|---|
| • Proportion of participants with plasma HIV-1 RNA < 50 c/mL over time using the FDA Snapshot algorithm (Safety population)<br>• Proportion of participants with plasma HIV-1 RNA ≥ 50 c/mL over time using the FDA Snapshot algorithm (Safety population) |
| **Results Presentation** |
| • The proportion of participants with HIV-1 RNA < 50 c/mL and HIV-1 RNA ≥ 50 c/mL, respectively, at each planned visit with corresponding 95% confidence intervals calculated using the Clopper-Pearson exact method.<br>• The proportion of participants in each Snapshot study outcome category and sub-category will be summarized at Month 12, in which default sub-categories have been expanded to present COVID-19 vs. non COVID-19 related impact (as described in Section 13.9). |

# 8. SAFETY ANALYSES

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

For the Month 12 and EOS analyses, safety displays will summarize data across the combined Intervention + Extension Phases, unless otherwise specified in the display title presented in Appendix 13: List of Data Displays.

## 8.1. Adverse Events Analyses

Adverse events analyses including the analysis of adverse events (AEs), Serious (SAEs), COVID-19 AEs, and other significant AEs will be based on GSK Core Data Standards. The details of the planned displays are provided in Appendix 13: List of Data Displays.

### 8.1.1. Injection Site Reaction Adverse Events

Injection Site Reaction (ISR) adverse events of interest are those from study drug injections.

For the summary of Injection Site Reaction Adverse Events by Visit and Maximum Severity (Overall and by Common ISRs), ISRs will be assigned based on onset date to the most recent planned IM injection visit prior or equal to the AE onset date.

Maximum grade at each visit will be derived as the maximum grade among ISRs assigned to the particular visit, with consideration for whether the summary applies to a particular preferred term (vs. across preferred terms), or drug-related associated to CAB and/or RPV.

Drug-related ISRs (based on investigator discretion) will be attributed to the causal agent (CAB vs. RPV) when this can be determined specifically based on the side of injection administration and the side of the reported ISR (as collected in the eCRF). If we are unable to determine the causal agent in those cases where both drugs are given on one side and the ISR is reported non-specifically, then the attribution to a specific causal agent will remain unknown.

Common study drug ISR adverse events are defined by MedDRA preferred terms including injection site pain, injection site induration, injection site nodules and preferred terms of any other ISR reported by ≥5% of participants overall.

## 8.2. Adverse Events of Special Interest Analyses

A comprehensive list of MedDRA terms based on clinical review will be used to identify Adverse Events of Special Interest (AESI). Changes to the MedDRA dictionary may occur between the start of the study and the time of reporting and/or emerging data from on-going studies may highlight additional adverse events of special interest, therefore the list of terms to be used for each event of interest and the specific events of interest will be based on the safety review team (SRT) agreements in place at the time of reporting. The details of the current planned grouping, including Standardized MedDRA Query (SMQ)

values (as applicable), and planned displays are provided in Appendix 10: AESI identification and Appendix 13: List of Data Displays.

## 8.3. Clinical Laboratory Analyses

Laboratory evaluations will be based on GSK Core Data Standards. The details of the planned displays are in Appendix 13: List of Data Displays.

## 8.4. Other Safety Analyses

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

# 9. PHARMACOKINETIC ANALYSES

## 9.1. Drug Concentration Measures

Available concentration-time data for CAB and RPV will be presented in listings as specified in Appendix 13: List of Data Displays and will be based on GSK Data Standards and statistical principles.

Refer Appendix 5: Data Display Standards & Handling Conventions (Section 13.5.3 Reporting Standards for Pharmacokinetic).

# 10. VIROLOGY

## 10.1. Genotypic and Phenotypic Data

Available genotypic and phenotypic data at all collection timepoints will be presented by subject (separately for CVF and Non-CVF subjects), as specified in Appendix 13: List of Data Displays.

# 11. OTHER ANALYSES

## 11.1. Study Visit Length

The details of the planned displays for study visit length data are in Appendix 13: List of Data Displays and will be based on GSK Data Standards and statistical principles.

## 12. REFERENCES

Wensing AM, et al. 2019 update of the drug resistance mutations in HIV-1. *Topics in antiviral medicine.* 2019;27:111-121.

# 13. APPENDICES

## 13.1. Appendix 1: Exclusions from Per Protocol Population

Instream and final analysis population reviews as per SOP 130050 are not planned for this study because it does not include a Per-Protocol population.

## 13.2. Appendix 2: Schedule of Activities

### 13.2.1. Protocol Defined Schedule of Events

#### 13.2.1.1. Schedule of Activities for Patient Study Participants (CAB LA + RPV LA Monthly Administration)

| Procedures | Screening[a] | Intervention Period | | | | | | | | | | | | WD[a] |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | Day 1 | Month 1 | Month 2 | Month 3 | Month 4 | Month 5 | Month 6 | Month 7 | Month 8 | Month 9 | Month 10[f] | Month 11[c] | Month 12[c] | |
| Written Informed Consent [b] | X | | | | | | | | | | | | | | |
| Demography | X | | | | | | | | | | | | | | |
| Eligibility Verification | X | | | | | | | | | | | | | | |
| Physical Exam | X | | | | | | | | | | | | | | |
| Medical History | X | | | | | | | | | | | | | | |
| Center for Disease Control and Prevention (CDC) Classification | X | | | | | | | | | | | | | | |
| Randomization for interviews | | X | | | | | | | | | | | | | |
| Rapid Plasma Reagin (RPR) | X | | | | | | | | | | | | | | |

| Procedures | Screening[a] | Intervention Period | | | | | | | | | | | | WD[a] |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | Day 1 | Month 1 | Month 2 | Month 3 | Month 4 | Month 5 | Month 6 | Month 7 | Month 8 | Month 9 | Month 10[b] | Month 11[c] | Month 12[c] | |
| Symptom Directed Physical Exam and Medical Assessment[d] | X | X | X | X | | X | | X | | X | | X | | X | X |
| Injection site reaction (ISR) assessment | | | X | X | X | X | X | X | X | X | X | X | X | X | X |
| Vital Signs (temperature, blood pressure [BP], heart rate [HR])[e] | X | X | X | X | | X | | X | | | X | | | X | X |
| Weight, Height & body mass index (BMI)[f] | X | X | X | | | | | X | | | | | | X | X |
| HIV Associated Conditions, AE and serious adverse event (SAE) Assessments& Con Meds | X | X | X | X | | X | | X | | X | | X | | X | X |
| 12-Lead ECG[g] | X | | | | | | | | | | | | | | X |

| Procedures | Screening[a] | Intervention Period | | | | | | | | | | | | WD[e] |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | Day 1 | Month 1 | Month 2 | Month 3 | Month 4 | Month 5 | Month 6 | Month 7 | Month 8 | Month 9 | Month 10[f] | Month 11[c] | Month 12[c] | |
| Clinical and Hematology | | | X | X | | X | | X | | | X | | | X | X |
| Pregnancy Testing (U)rine or (S)erum[h] | U | U | U | U | U | U | U | U | U | U | U | U | U | U | U |
| HIV-1 RNA | X | X | X | X | | X | | X | | X | | X | | X | X |
| Plasma sample for storage[i,j] | | X | X | X | | X | | X | | X | | X | | X | X |
| CD4+cell counts | X | X | X | X | | X | | X | | | X | | | X | X |
| Urinalysis | X | | | | | | | | | | | | | | X |
| Glucose | X | | | | | | | | | | | | | | |
| Prothrombin time (PT)/ partial thromboplastin time (PTT)/ international normalized ratio (INR) | X | | | | | | | | | | | | | | X |
| Oral study product dispensation | | X | | | | | | | | | | | | | |

| Procedures | Screening[a] | Intervention Period | | | | | | | | | | | | WD[o] |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | Day 1 | Month 1 | Month 2 | Month 3 | Month 4 | Month 5 | Month 6 | Month 7 | Month 8 | Month 9 | Month 10[f] | Month 11[c] | Month 12[c] | |
| LA study product administration[k] | | | X[n] | X | X | X | X | X | X | X | X | X | X | X | |
| Participant Visit Reminder Contact | X | X | X | X | X | X | X | X | X | X | X | X | X | X | |
| Participant Contact Detail Confirmation | X | X | X | X | X | X | X | X | X | X | X | X | X | X | |
| Record study visit length[l] | | | X | | | | X | | | | | | X | | |
| Patient Questionnaire | | | X | | | X | | | | | | | | X | |
| Selected Patient Interviews (SSI)[m] | | X | | | | | | | | | | | | X | |

See footnote "c" for continuation of visit schedule after Month 12, if required. Subjects will continue on study until the CAB + RPV LA regimen is either locally approved and commercially available, the participant no longer derives clinical benefit or meets a protocol-defined reason for discontinuation or until development is terminated.

a. A screening visit will be conducted within 21 days of Day 1. However, it is preferred for Day 1 to be conducted as soon as practical after all screening results are available.
b. After discussion of risk:benefit, a pregnancy specific ICF addendum must be signed by pregnant participants who wish to remain in the study
c. Continue this pattern for visits for the remainder of the study if needed, until commercial CAB + RPV LA is available. For example, Month 13 will be conducted as per Month 10, Month 14 will be conducted as per Month 11, Month 15 will be conducted as per Month 12, Month 16 will be conducted as per Month 10, and so on. The exception to this pattern is that no questionnaires, study visit length collection, or patient interviews will be conducted after the Month 12 visit.
d. Physical exams should be conducted as part of normal routine clinical care but data will not be collected in the electronic case report form (eCRF). Medical assessments include any decisions the study staff must make for participant management.
e. Measure vital signs after about 5 minutes of rest in a semi-supine position.

f. Height collected at Day 1 only.
g. At Screening, ECGs should be performed in triplicate at least 5 minutes apart and following 5 minutes of rest in a semi-supine position. ECG evaluations performed at subsequent visits should be obtained after dosing, preferably 2-4 hours post dosing. ECG at Withdrawal should be performed following 5 minutes of rest in a semi-supine position.
h. A (-) urine pregnancy test is required prior to any injection and as required by medical monitor after a treatment interruption. A (+) urine test should be confirmed with a stat serum test. A Serum pregnancy test should be performed at any time pregnancy is suspected by the Investigator and may be used in place of a urine test at the discretion of the investigator. Pregnant participants who remain in the study do not need pregnancy testing during the study, for the duration of their pregnancy. Pregnant participants remaining in the study have additional assessments required, as described in Appendix 8
i. Plasma for storage samples are collected for possible future analyses, back-up in cases of loss/damage in transit, geno/pheno analyses for virologic failures or PK in the event of maladministration or virologic failure.
j. Participants who get pregnant while in study will have additional PK samples for CAB and RPV obtained. See Appendix 8
k. Monthly injections are 1 x CAB LA 600 mg IM + 1 x RPV LA 900 mg IM at Month 1. Subsequent injections beginning at Month 2 are 1 x CAB LA 400 mg IM + 1 x RPV LA 600 mg IM. If possible, injections should be spaced approximately 2 cm from one another and from the site of any previous injection and/or any injection site reaction. Bring RPV LA to approximately room temperature prior to injecting. Time and location of injection (right or left) as well as needle length used will be collected in the eCRF. **IM dosing is expected to occur during the month in which the participant's projected visit falls (as according to the Day 1 visit). A dosing window of +0 / -7 days from date of projected visit is stipulated for IM dosing at Month 2 and Month 3. A (+ or -) 7 day window from date of projected visit is stipulated for IM dosing beginning at Month 4. All decisions regarding dose interruption/ resumption must be discussed with the medical monitor in advance.**
l. Length of study visit from arrival until departure from clinic will be evaluated. Time of arrival, time of appointment, and departure times will be recorded in the eCRF.
m. The first semi-structured interview will be scheduled between Day 1 and prior to Month 1 visit. The end of study SSI will be scheduled within approximately within approximately 4 weeks of their Month 12 study visit.
n. **Note:** Patient study participants with ≥ Grade 1 LFTs at screening and or day 1 must be discussed with the Medical Monitor prior to initiation of LA dosing; continuation in the study or progression onto LA dosing may require additional evaluations, including labs drawn after a period of oral dosing with CAB + RPV.
o. Follow Up Visit - Conduct ~4 weeks after the last dose of investigational product (IP) if not entering Long-Term Follow Up and only if the participant has ongoing AEs or lab abnormalities at the last on-study visit. May be conducted by telephone.

### 13.2.1.2. Schedule of Assessments Table for Staff Study Participants

| Procedures | Prior to Enrollment | Intervention Period (Month) | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | Day 1 | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 12 |
| Staff Study Participant Questionnaire | | X[a] | | | | X[b] | | | | | | X[b] |
| Staff Study Participant Interviews (SSI) | | X[a] | | | | X[b] | | | | | | X[b] |
| Staff Study Participant Monthly Facilitation Calls[c] | | X | X | X | X | X | X | X | X | X | X | |

a. Questionnaire and interview should be conducted prior to the first patient receiving their first CAB + RPV LA injection at that site.

b. Questionnaire and interview should be conducted within approximately 4 weeks of the targeted subject visit at each site for Month 4 and after at least 50% of patient study participant visits at Month 12.

c. Facilitation calls will continue during the enrollment period until the last enrolled subject achieves their Month 6 study visit.

### 13.2.1.3. Schedule of Activities Table for Patient Study Participants (Long Term Follow Up) [a]

| Procedures for Long-Term Follow Up[a] | Month 3 | Month 6 | Month 9 | Month 12 | WD | Notes |
|---|---|---|---|---|---|---|
| HIV Associated Conditions, AE and SAE Assessments, Con Meds | X | X | X | X | X | Every effort should be made to enter participants into the Long-Term Follow Up if they withdraw from or discontinue the study after receiving at least one dose of CAB LA and / or RPV LA.<br>a. The start of the 52-week follow-up period begins the day of the last CAB LA and/or RPV LA dose.<br>b. A PK sample for storage should be collected in the event of virologic failure during the LTFU phase<br>c. Participants who get pregnant while in study will have additional PK samples for CAB and RPV obtained, see Appendix 8<br>d. FRP only. U=urine; pregnant participants who remain in the study do not need pregnancy testing during the study, for the duration of their pregnancy<br>e. FRP should continue to receive counselling on the need to use adequate contraception for the entirety of the Long-Term Follow-Up Period.<br>f. Investigators must discuss choice of HAART regimen and timing of initiation with the medical monitor before initiating |
| HIV-1 RNA | X | X | X | X | X | |
| CD4+ cell counts | X | X | X | X | X | |
| Plasma for Storage | X | X | X | X | X | |
| PK Sample for Storage[b,c] | | | | | | |
| Clinical Chemistry and Hematology | X | X | X | X | X | |
| Pregnancy Testing[d] | U | U | U | U | U | |
| Urinalysis | | | | X | X | |
| PT/PTT/INR | | | | X | X | |
| Contraception Counselling[e] | X | X | X | X | X | |
| HAART Dispensation[f] | X | X | X | X | X | |

## 13.3. Appendix 3: Assessment Windows

### 13.3.1. Definitions of Assessment Windows for Analyses

Laboratory data, vital signs, ECGs, and genotypic/phenotypic data will be assigned to assessment windows according to actual dates rather than the nominal visit labels as recorded on the eCRF or in the laboratory database.

Prior to visit slotting, assessments are first assigned to a study phase (Screening, Intervention Phase, Extension, or Long Term Follow Up) as defined in Section 13.4.1.

According to the protocol, the nominal target study visit date will be based on the first injection, the Month 1 date. For instance, if Month 1 occurred on July 7th, all subsequent visits are expected to occur on the 7th of each month such that subsequent visits will be August 7th, September 7th, October 7th, etc. Since there are not >28 days in each month of the year, if the Month 1 injection occurred on the 29th, 30th, or 31st of the month, then the target study visit date for the remainder of the visits will be the 28th of the month.

The nominal target study visit day is derived as

- **M1 Target Day** = Date of Actual M1 Injection Visit Date – Date of First Oral lead-in Dose + 1, if subject receives M1 injection; else M1 Target Day = 30.
- **Mx Target Day** = Mx Nominal Target Study Visit Date – Date of First Oral lead-in Dose + 1, for x=2,3, …

Assessment windows will be derived based on the midpoint between two consecutive planned target study visit dates. For the Snapshot efficacy data, the same approach will be used, except for Month 12, which will use a ± 6-week window around the projected target study visit date at Month 12.

For parameters which are not scheduled to be assessed at visits, the all-inclusive assessment windows will still be used; however, data summaries will only report scheduled visits. Assessments at unscheduled visits will be included in summaries of worst-case values across visit (e.g. during the intervention phase) and in data listings, as well any algorithms that make use of additional data (e.g., Snapshot).

## Table 1 Assessment Windows for Screening, Intervention and Extension Phase Data (Excluding HIV-1 RNA and PK data)

| Target (Study Day) | Analysis Window | | Analysis Timepoint |
|---|---|---|---|
| | Beginning Timepoint | Ending Timepoint | |
| Day of earliest record | Assessment Study Day ≤1 | | Screening |
| For subjects discontinuing prior to receiving first injection: | | | |
| 30 | Assessment Study Day = 2 | Study Day of Last CAB/RPV Oral Dose+1 | Month 1 |
| | Assessment Study Day > (Study Day of Last CAB/RPV Oral Lead-in Dose +1) | | Follow-up |
| For subjects receiving first injection: | | | |
| Day of First Injection | Study Day = 2 | M1 target day + *floor* [(M2 target day – M1 target day)/2] | Month 1 |
| M2 Target Day | M1 target day + *floor* [(M2 target day – M1 target day)/2] + 1 | M2 target day + *floor* [(M4 target day – M2 target day)/2] | Month 2 |
| M4 Target Day | M2 target day + *floor* [(M4 target day – M2 target day)/2] + 1 | M4 target day + *floor* [(M6 target day – M4 target day)/2] | Month 4 |
| M6 Target Day | M4 target day + *floor* [(M6 target day – M4 target day)/2] + 1 | M6 target day + *floor* [(M9 target day – M6 target day)/2] | Month 6 |
| M9 Target Day | M6 target day + *floor* [(M9 target day – M6 target day)/2] + 1 | M9 target day + *floor* [(M12 target day – M9 target day)/2] | Month 9 |
| M12 Target Day | M9 target day + *floor* [(M12 target day – M9 target day)/2] + 1 | M12 target day + *floor* [(M15 target day – M12 target day)/2] | Month 12 |
| M15 Target Day | M12 target day + *floor* [(M15 target day – M12 target day)/2] + 1 | M15 target day + *floor* [(M18 target day – M15 target day)/2] | Month 15 |
| M18 Target Day | M15 target day + *floor* [(M18 target day – M15 target day)/2] + 1 | M18 target day + *floor* [(M21 target day – M18 target day)/2] | Month 18 |
| M***x*** Target Day | M***(x-3)*** target day - *floor* [(M***x*** target day – M(***x-3***) target day)/2] + 1 | M***x*** target day + *floor* [(M(***x+3***) target day – M***x*** target day)/2] | Month ***x*** For ***x*** = 21, 24, etc. |

| Target (Study Day) | Analysis Window | | Analysis Timepoint |
|---|---|---|---|
| | Beginning Timepoint | Ending Timepoint | |
| For subjects who permanently discontinue study treatment: | | | |
| | Assessment Study Day > Max (Study Day of Last Dose of Oral Study Treatment (CAB+RPV or SOC Bridging) + 1, Study Day of Last CAB + RPV Injection + 35) | | Follow-up |

**Table 2 Assessment Windows for Screening and Intervention Phase HIV-1 RNA Data**

| Target (Study Day) | Analysis Window | | Analysis Timepoint |
|---|---|---|---|
| | Beginning Timepoint | Ending Timepoint | |
| Day of earliest record | Assessment Study Day ≤1 | | Screening |
| | For subjects discontinuing prior to receiving first injection: | | |
| 28 | Assessment Study Day = 2 | Study Day of Last Oral Lead-in Dose +1 | Month 1 |
| | Assessment Study Day > (Study Day of Last CAB/RPV Oral Lead-in Dose +1) | | Follow-up |
| | For subjects receiving first injection: | | |
| Date of First Injection | Study Day = 2 | M1 target day + *floor* [(M2 target day – M1 target day)/2] | Month 1 |
| M2 Target Day | M1 target day + *floor* [(M2 target day – M1 target day)/2] +1 | M2 target day + *floor* [(M4 target day – M2 target day)/2] | Month 2 |
| M4 Target Day | M2 target day + *floor* [(M4 target day – M2 target day)/2] + 1 | M4 target day + *floor* [(M6 target day – M4 target day)/2] | Month 4 |
| M6 Target Day | M4 target day + *floor* [(M6 target day – M4 target day + 1 | M6 target day + *floor* [(M8 target day – M6 target day)/2] | Month 6 |
| M8 Target Day | M6 target day + *floor* [(M8 target day – M6 target day)/2] + 1 | M8 target day + *floor* [(M10 target day – M8 target day)/2] | Month 8 |
| M10 Target Day | M8 target day + *floor* [(M10 target day – M8 target day)/2] + 1 | M12 target day – 43 | Month 10 |
| M12 Target Day | M12 target day - 42 | M12 target day + 42 | Month 12 |
| M13 Target Day | Assessment Study Day > M12 target day + 42 | | Month 13 |

| Target (Study Day) | Analysis Window | | Analysis Timepoint |
|---|---|---|---|
| | Beginning Timepoint | Ending Timepoint | |
| For subjects who permanently discontinue study treatment during the Intervention Phase: | | | |
| | Assessment Study Day > Max (Study Day of Last Dose of Oral Study Treatment (CAB+RPV or SOC Bridging) +1, Study Day of Last CAB + RPV Injection + 35) | | Follow-up |

## Table 3 Assessment Windows for Extension Phase HIV-1 RNA Data

| Target (Study Day) | Analysis Window | | Analysis Timepoint |
|---|---|---|---|
| | Beginning Timepoint | Ending Timepoint | |
| M13 Target Day | Study Day of Nominal Month 13 Visit | M13 target day + *floor* [(M15 target day – M13 target day)/2] | Month 13 |
| M15 Target Day | M13 target day + *floor* [(M15 target day – M13 target day)/2] + 1 | M15 target day + *floor* [(M16 target day – M15 target day)/2] | Month 15 |
| M16 Target Day | M15 target day + *floor* [(M16 target day – M15 target day)/2] + 1 | M16 target day + *floor* [(M18 target day – M16 target day)/2] | Month 16 . |
| M18 Target Day | M16 target day + *floor* [(M18 target day – M16 target day)/2] + 1 | M18 target day + *floor* [(M19 target day – M18 target day)/2] | Month 18 |
| M***x*** Target Day | M(***x-1***) target day + *floor* [(M***x*** target day – M(***x-1***) target day)/2] + 1 | M***x*** target day + *floor* [(M(***x+2***) target day – M***x*** target day)/2] | Month ***x*** For ***x*** =19, 22, 25, 28 etc. |
| M***x*** Target Day | M(***x-2***) target day + *floor* [(M***x*** target day – M(***x-2***) target day)/2] + 1 | M***x*** target day + *floor* [(M(***x+1***) target day – M***x*** target day)/2] | Month ***x*** For ***x*** =21, 24, 27, 30 etc. |
| For subjects who permanently discontinue study treatment during the Extension Phase: | | | |
| | Assessment Study Day > Max (Study Day of Last Dose of Oral Study Treatment (CAB+RPV or SOC Bridging) +1, Study Day of Last CAB + RPV Injection + 35) | | Follow-up |

**Table 4 Assessment Windows for Study Visit Length Data (Intervention and Extension Phase)**

| Target (Study Day) | Analysis Window | | Analysis Timepoint |
|---|---|---|---|
| | Beginning Timepoint | Ending Timepoint | |
| Study Day of Actual M1 Injection | Study Day of Actual M1 Injection | | Month 1 |
| Study Day of Actual M5 Injection | Study Day of Actual M5 Injection | | Month 5 |
| Study Day of Actual M11 Injection | Study Day of Actual M11 Injection | | Month 11 |
| Study Day of Actual M14 Injection | Study Day of Actual M14 Injection | | Month 14 |
| Study Day of Actual M***x*** Injection | Study Day of Actual M***x*** Injection | | Month ***x*** For ***x***=17, 20, etc. |
| | If none of the above, then Analysis Timepoint = Other | | |

**Table 5 Assessment Windows for Summaries of Long-Term Follow-up Phase Data from Subjects who Received at Least One Injection of CAB+RPV and Permanently Discontinued from the Study**

| Day of Assessment | Assessment Window | Target LTFU Study Day of Window |
|---|---|---|
| 1 ≤ LTFU Study Day ≤ 135 | LTFU Month 3 | 90 |
| 136≤ LTFU Study Day ≤ 225 | LTFU Month 6 | 180 |
| 226 ≤ LTFU Study Day ≤ 315 | LTFU Month 9 | 270 |
| 316 ≤ LTFU Study Day ≤ 405 | LTFU Month 12 | 360 |
| (30*m-44) ≤ LTFU Study Day ≤ (30*m+45) | LTFU Month m M = 15, 18, 21 | 30*m |

- LTFU Study Day is defined in 13.6.1

### 13.3.2. Assessment Windows for PK Concentration Data

PK data will be presented in data listings according to planned nominal visits (i.e. as collected in the eCRF), without additional assignment to assessment windows.

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

### 13.4.1. Study Phases

AEs will be assigned to study phases as defined in Table 6. Laboratory data (efficacy, safety, and virology), HIV associated Conditions, health outcomes assessments, vital signs, and ECGs will be assigned to study phases as defined in Table 7.

Assessments/events are assigned to study phases sequentially, starting from the top of each table.

**Table 6 Study Phases for AEs**

| Study Phase | Definition |
|---|---|
| Screen | Date < Intervention Phase Treatment Start Date |
| Intervention | **For subjects continuing into the Extension Phase:**<br>Intervention Phase Treatment Start Date ≤ Date < Date of Nominal Month 13 Visit<br><br>**For subjects not continuing into the Extension Phase:**<br>Intervention Phase Treatment Start Date ≤ Date < LTFU ART Start Date [a]<br><br>For AEs leading to treatment withdrawal with start date equal to the LTFU ART Start Date, Intervention Phase instead of Long-term Follow-up Phase will be assigned. |
| Extension Phase | Date of Nominal Month 13 Visit ≤ Date < LTFU ART Start Date [a]<br><br>For AEs leading to treatment withdrawal with start date equal to the LTFU ART Start Date, Extension Phase instead of Long-Term Follow-up Phase will be assigned. |
| Long Term Follow-Up | **For subjects who receive at least one CAB/RPV injection and permanently discontinue study treatment:**<br>AE Start Date ≥ LTFU ART Start Date |
| AEs with completely missing start date:<br>• If AE end date is ≤ Intervention Phase Treatment Start Date, then assign to Screening Phase;<br>• Else if AE end date is completely missing or Intervention Phase Treatment Start Date < AE end date ≤ Date of Nominal Month 13 Visit, then assign to Intervention Phase;<br>• Else if AE end date > Date of Nominal Month 13 Visit, then assign to Extension Phase. | |

Date=AE Start Date

- [a] If participants have missing LFTU ART start date, only the lower bound will be considered in the derivation.

### Table 7 Study Phases for Laboratory, PK, ECG, Vital Signs, HIV-1 Associated Conditions, and Protocol Deviation Data

| Study Phase | Definition |
|---|---|
| Screen | Date ≤ Study Treatment Start Date |
| Intervention | **For subjects continuing into the Extension Phase:**<br>Intervention Phase Treatment Start Date < Date < Date of Nominal Month 13 Visit<br><br>**For subjects not continuing into the Extension Phase:**<br>Intervention Phase Treatment Start Date < Date ≤ LTFU ART Start Date [a] |
| Extension Phase | **For subjects continuing into Extension Phase:**<br>Date of Nominal Month 13 Visit ≤ Date ≤ LTFU ART Start Date [a] |
| Long Term Follow-Up | **For subjects who receive at least one CAB/RPV injection and permanently discontinue study treatment:**<br>Assessment Date > LTFU ART Start Date |

- Date = start or assessment date
- [a] If participants have missing LFTU ART start date, only the lower bound will be considered in the derivation.

Study phase of discontinuation will be determined according to Table 8.

### Table 8 Study Phases for Study Conclusion/IP Discontinuation

| Study Phase | Definition |
|---|---|
| Intervention Phase | For IP Discontinuation: Discontinuation Date is not missing, and no assessments collected at any extension phase nominal visits (e.g. Month 13, Month 15, Month 17 etc.).<br>For Study Conclusion: Discontinuation or Completion Date is not missing, and no assessments collected at any extension phase nominal visits (e.g. Month 13, Month 15, Month 17 etc.) and at any LTFU phase nominal visits (e.g. LTFU Month 3, LTFU Month 6, etc.) |
| Extension Phase | For IP Discontinuation: Discontinuation Date is not missing, and assessments collected at any extension phase nominal visits (e.g. Month 13, Month 15, Month 17 etc.).<br>For Study Conclusion: Discontinuation or Completion Date is not missing, and assessments collected at any extension phase nominal visits (e.g. Month 13, Month 15, Month 17 etc.) but no assessments collected at any LTFU phase nominal visits (e.g. LTFU Month 3, LTFU Month 6, etc.) |
| LTFU Phase | Not applicable for IP Discontinuation.<br>For Study Conclusion: Discontinuation or Completion Date is not missing, and assessments collected at any LTFU phase nominal visits or has taken any LTFU ART medications (e.g. LTFU Month 3, LTFU Month 6, etc.) |

- Discontinuation or Completion Date = date of failure to complete study/date of completing study/date of IP discontinuation

Medication use will be classified as prior and concomitant with study treatment according to Table 9, noting that a medication can be assigned as "taken" during more than one study phase.

### Table 9 Study Phases for Non-ART Medications/ART Medications

| | **Definition** |
|---|---|
| Prior | Medication Taken < Intervention Treatment Start Date |
| Concomitant during Intervention Phase | **For subjects continuing into Extension Phase:**<br>Intervention Treatment Start Date[a] ≤ Medication Taken < Date of Nominal Month 13 Visit<br><br>**For subjects not continuing into Extension Phase[b]:**<br>Intervention Treatment Start Date[a] ≤ Medication Taken < LTFU ART Start Date |
| Concomitant during Extension Phase | **For subjects continuing into Extension Phase[b]:**<br>Date of Nominal Month 13 Visit ≤ Medication Taken < LTFU ART Start Date |
| Received during Long-term Follow-up | **For subjects who received at least one CAB and/or RPV injection and have started LTFU ART:**<br>Medication Taken ≥ LTFU ART Start Date |

**NOTES:**

- Please refer to Appendix 7: Reporting Standards for Missing Data for handling of missing and partial dates for medications. Use the rules in this table if medication date is completely missing.

a. The ART medication stopped on start date of Intervention treatment will be considered a prior medication and will not be considered concomitant during the Intervention phase. If the stop date of ART medication is completely missing and this medication is recorded in eCRF as prior, it will be considered a prior medication and will not be considered concomitant during the intervention phase.

b. If subjects have missing LFTU ART start date, only the lower bound will be considered in the derivation.

### 13.4.2. Treatment State

Within each study phase (based on assignment of study phase described in Section 13.4.1), only those events/assessments which occur within the ranges shown in Table 10 will be considered 'on-treatment' for the given phase. No treatment states will be assigned to medications.

For adverse events, partial AE start date will use imputation as described in 13.7.2.1.

**Table 10 Treatment State within Study Phases**

| Study Phase | State | Definition |
|---|---|---|
| Screen | Pre-Treatment | All assessments/events within phase |
| Intervention/Extension | On-treatment | Date ≤ max (Date of Last CAB LA +RPV LA IM Dose + 35, Date of Last Dose of Oral Study Treatment (CAB+RPV or SOC Bridging) +1) |
| | Post-Treatment | Date > max (Date of Last CAB LA +RPV LA IM Dose + 35, Date of Last Dose of Oral Study Treatment (CAB+RPV or SOC Bridging) +1) |
| Long Term Follow-Up | Post-Treatment | All assessments/events within phase |

**NOTES:**

- Date = Assessment/Start Date

a. Treatment State is determined after data has been assigned to the study phases as defined in Section 13.4.1.

b. Last injection and/or last dose of oral study treatment (CAB+RPV or SOC bridging) are only applied to participants who permanently discontinued the study treatment. The assessments for participants who did not permanently discontinue the study treatment will be considered 'On-treatment'. For participants continuing into extension phase, all data assigned to intervention phase per Section 13.4.1 will be considered 'On-treatment'

### 13.4.3. Oral Lead-in Period

Certain displays will be produced for data collected or events occurring during the oral-lead-in period as defined in Table 11 and Table 12.

## Table 11 Oral Lead-in Period for AEs

| Study Period | Date Range |
|---|---|
| Oral Lead-in | **For participants receiving at least one Injection:**<br>Intervention Treatment Start Date ≤ Date [a] < Date of First IM Injection<br><br>**For participants withdrawing prior to first Injection:**<br>Date ≥ Intervention Treatment Start Date<br><br>Note that the oral lead-in period is only applicable to the participants who received at least one dose of study treatment during the oral lead-in period in the study. Oral lead-in period is within the intervention phase. |
| [a] AEs with completely missing start date which have been assigned to the Intervention Phase based on Table 6 will not be assigned to the Oral Lead-in Period. | |

**NOTES:**

- Date = AE Start date

## Table 12 Oral Lead-in Period for Laboratory Data

| Period | Date Range |
|---|---|
| Oral Lead-in | **For participants receiving at least one Injection:**<br>Intervention Treatment Start Date < Date ≤ Date of First IM Injection<br><br>**For participants withdrawing prior to first Injection:**<br>Date > Intervention Treatment Start Date<br><br>Note that the oral lead-in period is only applicable to the participants who received at least one dose of study treatment during the oral lead-in period in the study. Oral lead-in period is within the intervention phase. |

**NOTES:**

- Date = Date of assessment

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

### 13.5.1. Reporting Process

| **Software** | |
|---|---|
| • The currently supported versions of SAS software will be used. | |
| **Reporting Area** | |
| HARP Server | us1salx00259 |
| HARP Compound | \ARPROD\GSK1265744\mid209493\primary_01 |
| **Analysis Datasets** | |
| • Analysis datasets will be created according to CDISC standards (SDTM IG Version 3.2 & ADaM IG Version 1.1). | |
| **Generation of RTF Files** | |
| • RTF files will be generated for all reporting efforts described in the RAP. | |

### 13.5.2. Reporting Standards

| **General** |
|---|
| • The current GSK Statistical Display Standards in the GSK Standards Library (IDSL) will be applied for reporting, unless otherwise stated (Library Location: https://spope.gsk.com/sites/IDSLLibrary/SitePages/Home.aspx):<br>  • 4.03 to 4.23: General Principles<br>  • 5.01 to 5.08: Principles Related to Data Listings<br>  • 6.01 to 6.11: Principles Related to Summary Tables<br>  • 7.01 to 7.13: Principles Related to Graphics |
| **Formats** |
| • GSK Statistical Display Principles (5.03 & 6.06.3) for decimal places (DP's) will be adopted for reporting of data based on the raw data collected, unless otherwise stated.<br>• Numeric data will be reported at the precision collected on the eCRF.<br>• The reported precision from non eCRF sources will follow the GSK Standard Statistical Display Principles but may be adjusted to a clinically interpretable number of DP's. |
| **Planned and Actual Time** |
| • Reporting for tables, figures and formal statistical analyses:<br>  • Planned time relative to dosing will be used in figures, summaries, statistical analyses and calculation of any derived parameters, unless otherwise stated.<br>  • The impact of any major deviation from the planned assessment times and/or scheduled visit days on the analyses and interpretation of the results will be assessed as appropriate.<br>• Reporting for Data Listings:<br>  • Planned and actual time relative to study drug dosing will be shown in listings (Refer to GSK Standard Statistical Display Principle 5.05.1).<br>  • Unscheduled or unplanned readings will be presented within the participant's listings. |

| **Unscheduled Visits** | |
|---|---|
| • Unscheduled visits will be assigned to an analysis visit using the all-inclusive windows defined in Section 13.3.<br>• However, data summaries will only report visits that are planned assessment time points for each parameter (according to the Schedule of Activities in Section 13.2.1).<br>• Evaluable assessments at unscheduled visits will be used when categorizing values across visits, such as 'maximum grade during the intervention phase' or 'at any time post-baseline', and for any algorithm that has specific rules for which observation to use (e.g. snapshot algorithm, LOCF or CVF identification). | |
| **Descriptive Summary Statistics** | |
| Continuous Data | Refer to GSK Standard Statistical Display Principle 6.06.1 |
| Categorical Data | N, n, frequency, % |
| **Graphical Displays** | |
| • Refer to GSK Standard Statistical Display Principals 7.01 to 7.13. | |

### 13.5.3. Reporting Standards for Pharmacokinetic

| **Pharmacokinetic Concentration Data** | |
|---|---|
| Descriptive Summary Statistics, Graphical Displays and Listings | Refer to the GSK Standard PK Display Standard.<br>Refer to the GSK Standard Statistical Display Principle 6.06.1.<br>Note: Concentration values will be imputed as per GUI_51487 for descriptive summary statistics/analysis and summarized graphical displays only. |

## 13.6. Appendix 6: Derived and Transformed Data

### 13.6.1. General

| **Multiple Measurements at One Analysis Time Point** |
|---|
| • If there are two values within a time window (as per Section 13.3.1) the value closest to the target day for that window will be used. If values are the same distance from the target, then the mean (geometric mean for HIV-1 RNA, arithmetic mean for all other measurement) will be taken.<br>• Assessments not chosen for use in summary statistics by this algorithm will still appear in the associated listings.<br>• All applicable valid assessments, irrespective of proximity to the target study day, will be used when categorizing values across visits, such as 'maximum grade during the intervention phase' or 'at any time post-baseline', and for any algorithm that has specific rules for which observation to use (e.g. snapshot algorithm, LOCF or CVF identification).<br>• Participants having both High and Low values for Normal Ranges at any post-baseline visit for safety parameters will be counted in both the High and Low categories of "Any visit post-baseline" row of related summary tables. This will also be applicable to relevant Potential Clinical Importance summary tables. |
| **Treatment Start Date** |
| • Intervention Phase Treatment Start Date = Earliest date of CAB + RPV oral lead-in entered in the IP exposure eCRF form |
| **Nominal Month 13 Visit Date** |
| • For participants who received Month 13 injection, the nominal Month 13 visit date is defined by the Month 13 injection date.<br>• Otherwise, nominal Month 13 visit date is defined by the date of latest Month 13 assessment.<br>• For participants who continued into Extension Phase but missed the Month 13 visit, the nominal Month 13 visit date is defined by the last contact date prior to the date of the first nominal extension phase visit (e.g. Month 15, Month 17, etc.). |
| **Study Day** |
| • The Study Day of an event (e.g., lab assessment, vital sign, ECG, start date of AE or HIV associated condition) will be derived as the number of days between the date of the event and the Intervention Phase treatment start date as follows:<br>o If date of event ≥ start date of study treatment, then<br>▪ Study Day = Date of Event - Intervention Phase Treatment Start Date +1<br>o If date of event < start date of study treatment, then<br>▪ Study Day = Date of Event - Intervention Phase Treatment Start Date<br>• Note that the start date of intervention phase study treatment is on Study Day 1 and the day before this is Study Day -1; i.e., there is no Study Day 0. |
| **Long Term Follow-up Study Day** |
| • The Long-Term Follow Up (LTFU) Study Day of an event (e.g., lab assessment, start date of AE or HIV associated condition) will be derived as the number of days between the date of the event and the end of IP treatment [i.e. max(Last IM Injection Date, Last Oral Bridging End Date)] as follows:<br>o If the date of event falls in Long-term Follow up phase, then<br>▪ LTFU Study Day = Date of event - End date of IP + 1 |
| **Study Treatment** |
| • Refers to CAB+RPV oral lead-in, CAB + RPV oral bridging, SOC oral bridging, CAB LA + RPV LA |

### 13.6.2. Study Population

| **Demographics** |
|---|
| **Age** |
| • Age, in whole years, will be calculated with respect to the subject's Screening visit.<br>• GSK standard IDSL algorithms will be used for calculating age where birth date will be imputed as follows:<br>  • Any subject with a missing date and month will have this imputed as '30th June'.<br>• Birth date will be presented in listings as 'YYYY'.<br>• Completely missing dates of birth will remain as missing, with no imputation applied. Consequently, the age of the subject will not be calculated and will remain missing. |
| **Body Mass Index** |
| • Calculated as Weight (kg)/Height (m)$^2$ |
| **Hepatitis Status** |
| • Hepatitis C status will be determined using antibody and/or hepatitis C virus (HCV) RNA assessments performed during screening or during the conduct of the study.<br>• If both antibody and virus RNA assessments are available, then the latter will take precedence and positive/negative status will be based on whether HCV RNA is detectable (i.e., ≥ limit of quantification) or not.<br>• A participant will be considered positive for hepatitis B virus (HBV) if they have a positive surface antigen or detectable HBV DNA result. "HBV DNA DETECTED" in the lab comment takes precedence over HBV DNA test result for positive hepatitis B status; for example, if a participant has HBV DNA test result below level of detection and the lab comment shows that HBV DNA detected, this participant will be considered positive for hepatitis B. If HBV DNA result is available, it will be used to qualify hepatitis B status as positive or negative (positive if ≥ limit of quantification); otherwise Hepatitis B status will be determined using the surface antigen result.<br>• Hepatitis status at entry will be based on the assessments prior to/on the start of the study treatment. |
| **Adherence to CAB/RPV Injection Schedule** |
| • Timeliness of Injections relative to Date of Projected Dosing Visits are assessed by using "actual injection visit date - projected visit date from first injection". The injections of interest in adherence analysis are those after first injection at Month 1. (. Each injection visit is counted only once. Individual CAB and RPV injections administered at the same visit are not counted twice. "Extra" unscheduled injections are excluded from all derivations. For example, if during a scheduled visit a participant receives 1 ml of injection instead of 2 ml due to a dosing error, but this participant returns one week later for the remaining 1 ml injection, then the additional visit is excluded. If a participant receives an extra injection at an unscheduled visit by mistake, this visit will also be excluded.<br>• The categories of Timeliness of Injections relative to Date of Projected Dosing Visits are listed below:<br>  • < -14 days<br>  • -14 to - 8 days<br>  • -7 to 1 |

| **Demographics** |
|---|
| • 0<br>• 1 to 7 days<br>• 8 to 14 days<br>• >14 days<br>• Missed Injection without Oral Bridging (COVID-19 related)<br>• Missed Injection without Oral Bridging (Non COVID-19 related)<br>• Missed Injection with Oral Bridging (COVID-19 related)<br>• Missed Injection with Oral Bridging (non COVID-19 related)<br>• Injection visits are expected monthly from Month 2 until the nominal month of a participant's last injection visit during the phase(s) of interest. For example:<br>  • If a participant discontinues study treatment with last injection visit occurring at nominal visit Month 6 (without oral bridging), then injection visits are expected at Month 2, Month 3, Month 4, Month 5 and Month 6.<br>• Missed injections occurring during periods of on-going oral bridging (e.g. oral bridging is ongoing at the time of the data analysis cutoff or participant discontinues study treatment where last study treatment received is oral bridging) are not considered to be expected visits. |
| **Site Type** |
| • AIDS Healthcare Foundation (Site Id.= PPD )<br>• Federally Qualified Health Center (Site Id.= PPD )<br>• Health Maintenance Organization (Site Id.= PPD )<br>• Private Practice (Site Id.= PPD )<br>• University (Site Id.= PPD ) |

### 13.6.3. Efficacy

| **Efficacy** |
|---|
| **Snapshot** |
| • The Snapshot algorithm is intended to be primarily a virologic assessment of the endpoint, and as such follows a "virology first" hierarchy.<br>• 'HIV-1 RNA < 50 c/mL' or 'HIV-1 RNA ≥ 50 c/mL' within an analysis window (see Table 2 and Table 3) is typically determined by the last available HIV-1 RNA measurement in that window while the participant is On-treatment in the Intervention Phase (as assigned based on Section 13.3).<br>• When no HIV-1 RNA data is available within a window, a participant cannot be assigned to the category of 'HIV-1 RNA < 50 c/mL'. Depending on the reason for lack of data, the participant will be classified as 'HIV-1 RNA ≥ 50 c/mL' or reported as 'No Virologic Data at Week X'; in the latter case, the algorithm further classifies the nature of the missing data. Typically, a participant withdrawn (i) due to AE or, (ii) for another reason yet was suppressed at the time, will be counted as 'No Virologic Data at Week X'. Should a participant withdraw for reasons other than AE and was not suppressed at the time, they will be categorized as 'HIV-1 RNA ≥ 50 c/mL'. |

| **Efficacy** |
|---|
| • Full details of the algorithm, including the handling of special cases, are included in Appendix 9: Snapshot Algorithm Details. |
| **Plasma HIV-1 RNA** |
| • For summaries and analyses which use HIV-1 RNA level as a continuous measure, the logarithm to base 10 of the value will be used.<br>• HIV-1 RNA results may be provided as censored values, such as <40 or >9,999,999 c/mL. For the purposes of summary statistics, such values will be replaced by the next value beyond the limit of detection, e.g., 39 or 10,000,000 c/mL, respectively, for the given examples. Data listings will show the censored values as provided. |
| **Confirmed Virologic Failure (CVF)** |
| • For the purposes of clinical management in this study, CVF is defined as:<br>o Rebound as indicated by two consecutive plasma HIV-1 RNA levels ≥ 200 c/mL.<br>• The CVF definition is provided in the protocol Section 7.1.3<br>• Only plasma HIV-1 RNA values determined by the central laboratory will be used to assess virologic failure. |
| **CDC Classification for HIV-1 Infection (**2014**)** |
| • CDC HIV-1 Classification at Baseline is collected in eCRF and no derivation with be performed programmatically for analysis purposes. Please refer to study protocol for detail description of CDC HIV-1 Classification. |

### 13.6.4. Safety

| **Adverse Events** |
|---|
| **DAIDS Grading** |
| • Clinical adverse events will be graded based on the Division of AIDS Table for Grading the Severity of Adult and Pediatric Adverse Events Version 2.1, March 2017, as specified in the protocol Appendix 10.2.<br>• If a grade value is expected per DAIDS but is missing in the eCRF, then the missing grade will be given an ordinal grade value of -1 for determining the maximum grade within and across preferred terms. For example:<br>• if a participant has two separate instances of the same preferred term, one with grade 2 and one with missing grade, then the maximum grade for the preferred term will be set to grade 2.<br>• if a participant reports two different AE preferred terms overall, one with grade 1 and one with missing grade (where a DAIDS grade is expected), then the maximum grade across preferred terms (i.e. in the ANY EVENT row) will be set to grade 1.<br>• If a participant reports only one AE overall and this has a missing grade (where a DAIDS grade is expected), then this will be presented under a grade = missing category |
| **Days since First Dose (Days)** |
| • AE Start Date – Intervention Phase Treatment Start Date + 1 |

**Adverse Events**

**Days since Last Dose (Days)**

- AE Start Date – Date of Last Dose of Study Treatment (CAB+RPV, SOC bridging, CAB/RPV IM Injection) prior to/on the Start Date of AE + 1

**Days since Phase Start**

- For AEs in Intervention/Extension Phase:
  - AE Start Date - Intervention Treatment Start Date + 1
- For AEs in Long-term Follow-up Phase:
  - AE Start Date – Date of Last Dose of Study Treatment
  - Date of Last Dose of Study Treatment = max (Last IM Injection Date, Last Oral Bridging End Date [CAB+RPV, SOC ART]), only applicable to participants who permanently discontinued study treatment.

**Duration (Days)**

- AE Resolution Date – AE Start Date + 1

**Drug-related**

- If relationship is marked 'YES' on Inform/eCRF
- Injection site reactions will be considered as drug-related if the relationship to study drug value is missing in the eCRF.

**Laboratory Parameters**

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

**Lab Toxicities – DAIDS Grading**

- Toxicities will be based on the Division of AIDS (DAIDS) grading system, Version 2.1, March 2.17, as specified in the protocol of Appendix 10.2
- Toxicity grades provided by the central laboratory do not distinguish between abnormally high or low criteria, when both are relevant for a particular parameter.
- When summarizing toxicity grades for such parameters, they will be categorized as to whether they are above or below the midpoint of normal range.

| Parameter | Below Midpoint for those ≥Grade 1 | Above Midpoint for those ≥Grade 1 |
|---|---|---|
| Glucose | Hypoglycaemia | Hypoglycaemia |
| Sodium | Hyponatremia | Hyponatremia |
| Potassium | Hypokalaemia | Hypokalaemia |

**Other Safety Endpoints**

**Corrected QT (QTc)**

- When not entered directly in the eCRF, corrected QT intervals by Bazett's (QTcB) and Fridericia's (QTcF) formulas will be calculated, in msec, depending on the availability of other measurements.
- If RR interval (in msec) is provided, then missing QTcB and/or QTcF will be derived as

$$QTcB = \frac{QT}{\sqrt{RR/1000}} \qquad QTcF = \frac{QT}{\sqrt[3]{RR/1000}}$$

- where uncorrected QT interval is also measured in msec.
- If RR interval is not provided directly and one of QTcB or QTcF has been entered, then RR interval can be obtained from the above formulas and used to calculate the other correction method value; i.e.,

$$QTcB = \sqrt{\frac{QTcF^3}{QT}} \qquad QTcF = \sqrt[3]{QT \cdot QTcB^2}$$

**Extent of Exposure**

- Exposure to CAB+RPV (oral lead-in or oral bridging) and CAB LA+RPV LA will be calculated from the IP eCRF pages.

For Intervention Phase:

- **Exposure to CAB+RPV Oral Lead-in** = IP (oral lead-in) stop date - IP (oral lead-in) start date +1
- **Exposure to CAB LA + RPV LA** = Number of IP injection visits received during the Intervention Phase (up to but not including injections administered at Month 13)
- **Exposure to SOC oral bridging**: Duration of the SOC ART medication taken as oral bridging during the Intervention Phase. If the SOC oral bridging is taken in different periods during the Intervention Phase, the duration will be calculated by the sum of non-overlapped periods.
- **Exposure to CAB+RPV Oral Bridging (COVID-19 Related)**: Duration of the CAB+RPV taken as oral bridging for reasons related to COVID-19 during the Intervention Phase. If COVID-19 related CAB+RPV oral bridging is taken in different periods during the Intervention Phase, the duration will be calculated by the sum of the non-overlapped periods.
- **Exposure to CAB+RPV Oral Bridging (Non COVID-19 Related)**: Duration of the CAB+RPV taken as oral bridging for reasons not related to COVID-19 during the Intervention Phase. If non COVID-19 related CAB+RPV oral bridging is taken in different periods during the Intervention Phase, the duration will be calculated by the sum of the non-overlapped periods.
- **Overall Exposure to Study Treatment**: min [Date of Latest Intervention Phase Visit up to and including Month 13, max (Date of Last Injection + 35, Date of Last Dose of Oral CAB+RPV, Date of Last Dose of SOC Oral Bridging)] – min (Start Date for Oral lead-in CAB+RPV, Date of First CAB/RPV Injection) + 1
    - Note: Conditions in the above formula pertaining to Last Injection/Last Dose of Oral CAB+RPV/Last Dose of SOC Oral Bridging are only applicable to those who permanently discontinued study treatment.

**Other Safety Endpoints**

- **Overall Exposure to CAB + RPV** = Overall Exposure to Study Treatment – Exposure to SOC Oral Bridging

For Intervention + Extension Phase:

- **Exposure to CAB LA + RPV LA** = Number of IP injection visits received during Intervention Phase and Extension Phase
- Exposure to SOC or CAB+RPV Oral Bridging during the Intervention and Extension Phase will be calculated similarly to that during the Intervention Phase except that the exposure includes both Intervention and Extension Phase.
- **Overall Exposure to Study Treatment**: min [Date of Latest Intervention/Extension Phase Visit, max (Date of Last Injection + 35, Date of Last Dose of Oral CAB+RPV, Date of Last Dose of SOC Oral Bridging)] – min (Start Date for Oral lead-in CAB+RPV, Date of First Study Injection) + 1
    - Note: Conditions in the above formula pertaining to Last Injection/Last Dose of Oral CAB+RPV/Last Dose of SOC Oral Bridging are only applicable to those who permanently discontinued study treatment.
- **Overall Exposure to IP** = Overall Exposure to Study Treatment – Exposure to SOC Oral Bridging
- Duration of dosing in participant years will be calculated as the sum of participant duration of dosing in days (across all participants)/365.25

### 13.6.5. Virology

**Genotype**

**Amino Acid Changes**

- A mutation is considered present whenever the encoded amino acid residue differs from the amino acid that would have been encoded by the wild-type (e.g., HXB2, NL43) comparator gene; e.g., Q148K.
- If the encoded amino acid is seen as a mixture of wild-type and mutant amino acid, e.g., Q148Q/K, the mutated amino acid is considered present at the codon of interest.
- If the encoded amino acid is seen as a mixture of two or more amino acids, which may or may not include wild type, e.g., Q184K/H or Q184K/H/Q, etc., for the purposes of calculating the number of mutated amino acids, only one mutation is considered to be present at the codon of interest.

**Representation of Amino Acid Changes**

| Mutations | Amino Acid Change |
|---|---|
| T69S | Single mutation from amino acid 'T' (vendor reference) to 'S' (sample) at codon '69 |
| Q148H/K/R | Mixture of amino acid mutations ‘H’, ‘K’ and ‘R’ (sample) from amino acid ‘Q (vendor reference) at codon ‘148’ |
| _69_1T | First insertion of amino acid 'T' (sample) at codon '69' |
| _69_2S | Second insertion of amino acid 'S' (sample) at codon '69' |
| _69_3S/A | Third insertion of a mixture of amino acids 'S' and 'A' (sample) at codon '69' |

| **Genotype** | |
|---|---|
| L74L/- | Mixture of amino acid 'L' (sample) and a deletion at codon '74' |
| V75- | Single deletion of amino acid (sample) at codon '75' |

**Resistance Associated mutations**

Known INI mutations associated with the development of resistance to Integrase Strand Transfer Inhibitors:

| | |
|---|---|
| Amino Acids in HIV Integrase for Analysis | H51Y, **T66**A/**I**/K, L68V/I, L74I/M, **E92Q**/V/G, Q95K, T97A, **G118R**, **F121Y**, E138A/D/K/T, **G140**A/C/**R**/S, **Y143C**/**H**/**R**/K/S/G/A, P145S, Q146P, **S147G**, **Q148H/K/R**/N, V151/IL/A, S153F/Y, **N155H**/S/T, E157Q, G163R/K, G193E, S230R, **R263K** |

- Draft listing; may be modified in case of additional substantive data availability.
- Based on the IAS-USA list of mutations associated with resistance to Bictegravir, Cabotegravir, Dolutegravir, Elvitegravir, or Raltegravir (IAS-USA 2019 resistance mutations update volume 27 issue 3, 2019): T66A/I/K, L74M, E92Q/G, T97A, G118R, F121Y, E138A/K/T, G140A/C/R/S, Y143C/H/R, S147G, Q148H/K/R, S153F/Y, N155H, R263K) and observed mutations during in vitro passage of DTG or seen in a previous DTG study in INI-experienced subjects (study ING112574): H51Y, L74I, L68V/I, E92V, Q95K, E138D, Y143K/S/G/A, P145S, Q146P, V151I/L/A, N155S/T, E157Q, G163R/K, G193E, S230R.
- Major USA-IAS mutations associated with resistance to INSTI are bolded.

- Major resistance mutations to other classes (i.e., NRTI, NNRTI, PI) as defined by the International Antiviral Society-USA (IAS-USA). The most up to date IAS-USA guidelines available at the time of DBF will be used in the analysis [Wensing, 2019].

| **Class** | **Mutations** |
|---|---|
| NRTIs | M41L, A62V, K65R/E/N, D67N, 69 insert, K70E/R, L74V, V75I, F77L, Y115F, F116Y,<br>Q151M, M184V/I, L210W, T215Y/F, K219Q/E |
| NNRTIs | L100I, K101E/P, K103N/S, V106A/M, V108I, E138/A/G/K/Q/R, V179L, Y181C/I/V, Y188C/L/H, G190S/A, H221Y, P225H, F227C, M230I/L |
| PIs | D30N, V32I, M46I/L, I47A/V, G48V, I50V/L, I54V/M/L, Q58E, T74P, L76V, V82A/T/F/L/S, N83D, I84V, N88S, L90M |

- Draft listing; may be modified in case of additional substantive data availability.

### 13.6.6. Other Assessments

**Study Visit Length**

- Lead Time = Actual Start Time of Appointment – Arrival Time
- Process Time = Actual End Time of Appointment – Actual Start Time of Appointment
- Total Time = Actual End Time of Appointment – Arrival Time

## 13.7. Appendix 7: Reporting Standards for Missing Data

### 13.7.1. Premature Withdrawals

| Element | Reporting Detail |
|---|---|
| General | • Withdrawn participants were not replaced in the study.<br>• All available data from participants who were withdrawn from the study will be listed and all available planned data will be included in summary tables and figures, unless otherwise specified.<br>• Withdrawal visits will be slotted according to Appendix 3: Assessment Windows (excluding PK data) |

### 13.7.2. Handling of Missing Data

| Element | Reporting Detail |
|---|---|
| General | • Missing data occurs when any requested data is not provided, leading to blank fields on the collection instrument:<br>o These data will be indicated by the use of a "blank" in participant listing displays. Unless all data for a specific visit are missing in which case the data is excluded from the table.<br>o Answers such as "Not applicable" and "Not evaluable" are not considered to be missing data and should be displayed as such. |
| Outliers | • Any participants excluded from the summaries and/or statistical analyses will be documented along with the reason for exclusion in the clinical study report. |

#### 13.7.2.1. Handling of Missing and Partial Dates

| Element | Reporting Detail |
|---|---|
| General | • Partial dates will be displayed as captured in participant listing displays.<br>• Where necessary, display macros may impute dates as temporary variables for sorting data in listings only. In addition, partial dates may be imputed for 'slotting' data to study phases or for specific analysis purposes as outlined below. |
| Adverse Events | • Imputations in the adverse events dataset are used for slotting events to the appropriate study time periods and for sorting in data listings.<br>• Partial dates for AEs recorded in the CRF will be imputed using the following conventions:<br><br>Missing start day: • If study treatment start date is missing (i.e. participant did not start study treatment), then set start date = 1st of month.<br>• Else if study treatment start date is not missing:<br>o If month and year of start date = month and year of study treatment start date, then |

<table>
<tr><th>Element</th><th>Reporting Detail</th></tr>
<tr><td></td><td>
<table>
<tr><td></td><td>
<ul>
<li>If stop date contains a full date and stop date is earlier than study treatment start date, then set start date= 1st of month.</li>
<li>Else set start date = study treatment start date.</li>
</ul>
o Else
<ul>
<li>For Non-ISR AEs: set start date = 1st of month</li>
<li>For ISR AEs: if oral bridging taken during the month and year, set start date = min(last day of the month, day of AE stop date if available, day of study treatment discontinuation if occurring during the month and year); else set start date = 1st of month.</li>
</ul>
</td></tr>
<tr><td>Missing start day and month</td><td>
<ul>
<li>If study treatment start date is missing (i.e. participant did not start study treatment), then set start date = January 1.</li>
<li>Else if study treatment start date is not missing:
<ul>
<li>If year of start date = year of study treatment start date, then
<ul>
<li>If stop date contains a full date and stop date is earlier than study treatment start date, then set start date = January 1.</li>
<li>Else set start date = study treatment start date.</li>
</ul>
</li>
<li>Else set start date = January 1.</li>
</ul>
</li>
</ul>
</td></tr>
<tr><td>Missing stop day</td><td>Last day of the month will be used.</td></tr>
<tr><td>Missing stop day and month</td><td>No Imputation</td></tr>
<tr><td>Completely missing start/end date</td><td>No imputation</td></tr>
</table>
<ul>
<li>Completely missing start or end dates will remain missing, with no imputation applied.</li>
</ul>
</td></tr>
<tr><td>Non-ART Medications</td><td>
<ul>
<li>Partial dates for any concomitant medications recorded in the CRF will be imputed using the following convention:</li>
</ul>
<table>
<tr><td>Missing start day</td><td>
<ul>
<li>If study treatment start date is missing (i.e. participant did not start study treatment), then set start date = 1st of month.</li>
<li>Else if study treatment start date is not missing:
<ul>
<li>If month and year of start date = month and year of study treatment start date, then</li>
</ul>
</li>
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<table>
<tr><th>Element</th><th>Reporting Detail</th></tr>
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<tr><td></td><td>
<ul>
<li>If stop date contains a full date and stop date is earlier than study treatment start date, then set start date= 1st of month.</li>
<li>Else set start date = study treatment start date.</li>
</ul>
o Else set start date = 1st of month.
</td></tr>
<tr><td>Missing start day and month</td><td>
<ul>
<li>If study treatment start date is missing (i.e. participant did not start study treatment), then set start date = January 1.</li>
<li>Else if study treatment start date is not missing:
<ul>
<li>If year of start date = year of study treatment start date, then
<ul>
<li>If stop date contains a full date and stop date is earlier than study treatment start date, then set start date = January 1.</li>
<li>Else set start date = study treatment start date.</li>
</ul>
</li>
<li>Else set start date = January 1.</li>
</ul>
</li>
</ul>
</td></tr>
<tr><td>Missing end day</td><td>A '28/29/30/31' will be used for the day (dependent on the month and year)</td></tr>
<tr><td>Missing end day and month</td><td>A '31' will be used for the day and 'Dec' will be used for the month.</td></tr>
<tr><td>Completely missing start/end date</td><td>No imputation</td></tr>
</table>
<ul>
<li>The recorded partial date will be displayed in listings.</li>
</ul>
</td></tr>
<tr><td>ART Medications</td><td>
<ul>
<li>Partial dates recorded in the eCRF will be imputed using the following convention:
<ul>
<li>If the partial date is a start date, a '01' will be used for the day and 'Jan' will be used for the month.</li>
<li>If the partial date is a stop date, a '28/29/30/31' will be used for the day (dependent on the month and year) and 'Dec' will be used for the month. If medications recorded in the PRIOR ART form of the eCRF, then the earlier date of the imputed and the day prior to the Intervention phase treatment start date will be used, i.e. min (imputed stop date, Intervention phase treatment start date - 1).</li>
</ul>
</li>
<li>For medications with completely missing start date, they will be considered started prior to the Intervention phase treatment start date.</li>
<li>For medications with completely missing stop date, they will be considered ongoing unless recorded in the PRIOR ART form of the eCRF.</li>
<li>For ART booster medications, the start and stop dates are not recorded in the database (i.e. missing), the dates will be imputed to be the same as the dates of their parent medications.</li>
<li>The recorded partial or missing date will be displayed in listings.</li>
</ul>
</td></tr>
</table>

### 13.7.2.2. Handling of Missing Data for Statistical Analysis

| Element | Reporting Detail |
|---|---|
| Snapshot | • In the Snapshot dataset, subjects without HIV – 1 RNA data in the assessment window for the visit of interest (due to missing data or discontinuation of IP prior to the visit window) do not belong to 'HIV-1< 50 c/mL (or 200 c/mL) The nature of this missing data will be further classified in Snapshot summaries as either 'HIV-1 RNA≥50' or 'No Virologic Data at Week X';<br>• See Appendix 9: Snapshot Algorithm Details |
| LOCF (COVID-19 Related) | • Missing HIV-1 RNA values within an analysis visit for reasons related to COVID-19 will be imputed using the last on-treatment value from earlier analysis timepoints.<br>• This approach will be used in the primary snapshot analysis to address missing data due to COVID-19. |

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

ECG values of potential clinical importance are defined as QTc > 500 msec or increase from baseline in QTc ≥ 60 msec.

## 13.9. Appendix 9: Snapshot Algorithm Details

**Detailed Algorithm Steps**

- Consider an analysis visit window for Month X as defined in Table 2.
- The HIV-1 RNA threshold of 50 will be analysed, in this study
- The COVID-19 pandemic presents significant logistical challenges for many clinical sites around the world, with variable restrictions being placed on site resources and operations, and on an individual participants ability to attend clinic visits. The snapshot algorithm is modified to allow for the presentation of full scope of COVID-19 relatedness. The analysis window for 'Month 12' and HIV-1 RNA threshold of '50 c/mL' are used for the purpose of illustration. A participant's Snapshot response and reason at Month 12 are categorized as below.

```
o  HIV-1 RNA < 50 c/mL
o  HIV-1 RNA ≥ 50 c/mL
     Data in window not below 50
       Non-COVID-19 related
          Discontinued for lack of efficacy
          Discontinued for other reason while not
          below 50
       COVID-19 related
          Discontinued for lack of efficacy
          Discontinued for other reason while not
          below 50

o  No Virologic Data at Month 12 Window
       Non-COVID-19 related
          Discontinued study due to AE or death
          Discontinued study for other reasons
          On study but missing data in window
         COVID-19 related
          Discontinued study due to AE or death
          Discontinued study for other reasons
          On study but missing data in window
       Change in background therapy*
```

* Note: Use of CAB + RPV oral bridging and SOC oral bridging medication, where the latter is due to unavailability of CAB/RPV IM injections or oral CAB+RPV during the pandemic, will not be considered a "Change in background therapy" in the Snapshot algorithm. All other permanent changes in ART are not permitted in this protocol.

- The steps in determining response and reasons are indicated in the table below, in the order stated.

- Background therapy is not given to participants while on study. The "change in background therapy" in detailed steps below refers to the "change in ART" in this study.

**Detailed steps**

- Please note that the following scenarios will NOT be penalized in the Snapshot algorithm Oral bridging (CAB+RPV or SOC, where SOC oral bridging medication is permitted during COVID-19 pandemic due to the unavailability of the CAB/RPV IM injections and oral CAB+RPV)

| **Condition** ('Month 12' indicates Month 12 window) | **Response** | **Reasons** |
|---|---|---|
| 1. If non-permitted change in background therapy prior to Month 12 | HIV-1 RNA ≥ 50 | Change in background therapy |
| 2. If non-permitted change in background therapy during Month 12 | | |
| • Last on-treatment VL during Month 12 prior to/on the date of change ≥ 50 c/mL | HIV-1 RNA ≥ 50 | Data in window not below 50 |
| • Last on-treatment VL during Month 12 prior to/on the date of change < 50 c/mL | HIV-1 RNA < 50 | |
| • No VL during Month 12 prior to/on the date of change | HIV-1 RNA ≥ 50 | Change in background therapy |
| 3. If none of the above conditions met | | |
| 3.1. On-treatment VL available during Month 12 | | |
| • Last on-treatment VL during Month 12 ≥ 50 c/mL | HIV-1 RNA ≥ 50 | Data in window not below 50 |
| • Last on-treatment VL during Month 12 < 50 c/mL | HIV-1 RNA < 50 | |
| 3.2. No on-treatment VL during Month 12 | | |
| 3.2.1. If participants are still on study, i.e. a participant has not permanently discontinued the study treatment yet, or if a participant permanently discontinued the study treatment and the upper bound of analysis snapshot window is prior to the following date:<br>• Min[max(Date of last injection + 35, Date of Last Dose of Oral Study Treatment (CAB+RPV, SOC Bridging) + 1), LTFU ART Start Date] | | |

| | | |
|---|---|---|
| 3.2.1.1. If no on-treatment VL during Month 12 is not due to COVID-19 | No virologic data at Month 12 Window | On study but missing data in window (Non-COVID-19 related) |
| 3.2.1.2. If no on-treatment VL during Month 12 is due to COVID-19 | No virologic data at Month 12 Window | On study but missing data in window (COVID-19 related) |
| 3.2.2. If participants withdraw before/during Month 12 due to | | |
| 3.2.2.1. Non-COVID-19 related safety reasons (e.g. AE/death, liver chemistry stopping criteria, renal toxicity withdrawal criteria, QTc withdrawal criteria etc., as recorded in eCRF Conclusion form) | No virologic data at Month 12 Window | Disc due to AE/death (Non-COVID-19 related) |
| 3.2.2.2. COVID-19 related safety reasons (e.g. AE/death, liver chemistry stopping criteria, renal toxicity withdrawal criteria, QTc withdrawal criteria etc., as recorded in eCRF Conclusion form) | No virologic data at Month 12 Window | Disc due to AE/death (COVID-19 related) |
| 3.2.2.3. Non-safety and Non-COVID-19 related reasons (e.g. Lack of efficacy, protocol deviation, withdrew consent, loss to follow-up, study closed/terminated, investigator discretion etc., as recorded in eCRF Treatment Discontinuation Form) | | |
| ○ Last on-treatment VL <50 c/mL OR no on-treatment VL available during study | No virologic Data at Month 12 Window | Disc for other reasons (Non-COVID-19 related) |
| ○ Last on-treatment VL ≥ 50 c/mL AND withdrawal due to Lack of efficacy | HIV-1 RNA ≥ 50 | Disc. for lack of efficacy (Non-COVID-19 related) |
| ○ Last on-treatment VL ≥ 50 c/mL AND withdrawal due to all other non-safety related reasons | HIV-1 RNA ≥ 50 | Disc. for other reason while not below 50 (Non-COVID-19 related) |
| 3.2.2.4. Non-safety and COVID-19 related reasons (e.g. protocol deviation, withdrew consent, loss to follow-up, study | | |

| | | |
|---|---|---|
| closed/terminated, investigator discretion etc., as recorded in eCRF Conclusion Form) | | |
| ○ Last on-treatment VL <50 c/mL OR no on-treatment VL available during study | No virologic Data at Month 12 Window | Disc for other reasons (COVID-19 related) |
| ○ Last on-treatment VL ≥ 50 c/mL AND withdrawal due to Lack of efficacy | HIV-1 RNA ≥ 50 | Disc. for lack of efficacy (COVID-19 related) |
| ○ Last on-treatment VL ≥ 50 c/mL AND withdrawal due to all other non-safety related reasons | HIV-1 RNA ≥ 50 | Disc. for other reason while not below 50 (COVID-19 related) |

a. Excluding permitted change in background therapy where change or decision to change is made prior to/on the first on-treatment viral result

**Examples from FDA guidance**

Data in Window

Virologic outcome should be determined by the last available measurement while the patient is on treatment and continued on trial within the time window:

- HIV-1 RNA = 580 c/mL at Day 336, HIV-1 RNA below 50 c/mL on Day 350. This should be categorized as HIV-1 RNA below 50 c/mL.

No Data in Window

Discontinued study due to Adverse Event or Death:

- Any patient who discontinues because of an AE or death before the window should be classified as *Discontinued due to AE or Death* (as appropriate), regardless of the HIV-1 RNA result, even if the HIV-1 RNA is below 50 c/mL at the time of discontinuation.
- However, if a patient has an HIV-1 RNA value in the time window and also discontinues in the time window, the viral load data should be used to classify the patient's response. This is the Virology First hierarchy:
    a. HIV-1 RNA below 50 c/mL at Day 336 and discontinues because of AE or even dies on Day 360 — this person is categorized as having HIV-1 RNA below 50 c/mL.
    b. HIV-1 RNA is 552 c/mL on Day 336 and the patient discontinues on Day 360, the patient is categorized as having HIV-1 RNA ≥ 50 c/mL.

Discontinued for Other Reasons:

- Only patients who have achieved virologic suppression can be counted as *Discontinued for Other Reasons.*
- If a patient discontinues the study before the time window because of *lack of efficacy,* then the patient should be included in the HIV-1 RNA ≥ 50 row and not in the Discontinued for Other Reasons row.

| **Detailed Algorithm Steps** |
|---|
| • If a patient discontinues because *participant withdrew consent* and his or her HIV-1 RNA result at the time of discontinuation was equal to or above 50 c/mL, then he or she should be categorized as HIV-1 RNA ≥ 50 and NOT as Discontinued for Other Reasons.<br>• If a patient discontinued because of *Lost to Follow-Up* and the last HIV-1 RNA result was 49 c/mL, then the patient can be categorized as Discontinued for Other Reasons.<br>• If patients changed background treatment — *not permitted by protocol*— they should be considered an efficacy failure and captured in the HIV-1 RNA ≥ 50 c/mL row.<br>On study but missing data in window:<br>• If there are no data during Days 294 to 377, but there is an HIV-1 RNA below 50 c/mL on Day 380, this patient should be considered *On Study but Missing Data in Window.*<br>• If there are no data during Days 294 to 377, but there is an HIV-1 RNA equal to or above 50 c/mL on Day 280, this patient also should be classified as *On Study but Missing Data in Window.* |

## 13.10. Appendix 10: AESI identification

SMQ and PT codes based on MedDRA dictionary version 23.0 for the Month 12 analysis.

### 13.10.1. Hepatic Safety Profile

Medical concept of hepatic failure and hepatitis. Sub- SMQs (1) 'Hepatic failure, fibrosis and cirrhosis and other liver damage-related conditions' and (2) 'Hepatitis, non-infectious', both of parent SMQ 'Hepatic Disorders (SMQ code 20000005)'; only narrow terms selected from sub-SMQs. Some preferred terms, e.g. PT 'hepatitis fulminant' are duplicated.

| SMQ: 'Hepatic Disorders'; SMQ Code: 20000005<br>Sub-SMQ: 'Hepatic failure, fibrosis and cirrhosis and other liver damage-related conditions'<br>Category: A<br>Scope: Narrow | |
|---|---|
| Preferred Term | PT Code |
| Acquired hepatocerebral degeneration | 10080860 |
| Acute hepatic failure | 10000804 |
| Acute on chronic liver failure | 10077305 |
| Acute yellow liver atrophy | 10070815 |
| Ascites | 10003445 |
| Asterixis | 10003547 |
| Bacterascites | 10068547 |
| Biliary cirrhosis | 10004659 |
| Biliary fibrosis | 10004664 |
| Cardiohepatic syndrome | 10082480 |
| Cholestatic liver injury | 10067969 |
| Chronic hepatic failure | 10057573 |
| Coma hepatic | 10010075 |
| Cryptogenic cirrhosis | 10063075 |
| Diabetic hepatopathy | 10071265 |
| Drug-induced liver injury | 10072268 |
| Duodenal varices | 10051010 |

| SMQ: 'Hepatic Disorders'; SMQ Code: 20000005<br>Sub-SMQ: 'Hepatic failure, fibrosis and cirrhosis and other liver damage-related conditions'<br>Category: A<br>Scope: Narrow | |
|---|---|
| Preferred Term | PT Code |
| Gallbladder varices | 10072319 |
| Gastric variceal injection | 10076237 |
| Gastric variceal ligation | 10076238 |
| Gastric varices | 10051012 |
| Gastric varices haemorrhage | 10057572 |
| Gastrooesophageal variceal haemorrhage prophylaxis | 10066597 |
| Hepatectomy | 10061997 |
| Hepatic atrophy | 10019637 |
| Hepatic calcification | 10065274 |
| Hepatic cirrhosis | 10019641 |
| Hepatic encephalopathy | 10019660 |
| Hepatic encephalopathy prophylaxis | 10066599 |
| Hepatic failure | 10019663 |
| Hepatic fibrosis | 10019668 |
| Hepatic hydrothorax | 10067365 |
| Hepatic infiltration eosinophilic | 10064668 |
| Hepatic lesion | 10061998 |
| Hepatic necrosis | 10019692 |
| Hepatic steato-fibrosis | 10077215 |
| Hepatic steatosis | 10019708 |
| Hepatitis fulminant | 10019772 |
| Hepatobiliary disease | 10062000 |
| Hepatocellular foamy cell syndrome | 10053244 |
| Hepatocellular injury | 10019837 |
| Hepatopulmonary syndrome | 10052274 |

| SMQ: 'Hepatic Disorders'; SMQ Code: 20000005<br>Sub-SMQ: 'Hepatic failure, fibrosis and cirrhosis and other liver damage-related conditions'<br>Category: A<br>Scope: Narrow | |
|---|---|
| Preferred Term | PT Code |
| Hepatorenal failure | 10019845 |
| Hepatorenal syndrome | 10019846 |
| Hepatotoxicity | 10019851 |
| Immune-mediated cholangitis | 10083406 |
| Immune-mediated hepatic disorder | 10083521 |
| Intestinal varices | 10071502 |
| Intestinal varices haemorrhage | 10078058 |
| Liver dialysis | 10076640 |
| Liver disorder | 10024670 |
| Liver injury | 10067125 |
| Liver operation | 10062040 |
| Liver transplant | 10024714 |
| Lupoid hepatic cirrhosis | 10025129 |
| Minimal hepatic encephalopathy | 10076204 |
| Mixed liver injury | 10066758 |
| Nodular regenerative hyperplasia | 10051081 |
| Nonalcoholic fatty liver disease | 10082249 |
| Non-alcoholic steatohepatitis | 10053219 |
| Non-cirrhotic portal hypertension | 10077259 |
| Oedema due to hepatic disease | 10049631 |
| Oesophageal varices haemorrhage | 10030210 |
| Peripancreatic varices | 10073215 |
| Portal fibrosis | 10074726 |
| Portal hypertension | 10036200 |
| Portal hypertensive colopathy | 10079446 |

| SMQ: 'Hepatic Disorders'; SMQ Code: 20000005<br>Sub-SMQ: 'Hepatic failure, fibrosis and cirrhosis and other liver damage-related conditions'<br>Category: A<br>Scope: Narrow | |
|---|---|
| Preferred Term | PT Code |
| Portal hypertensive enteropathy | 10068923 |
| Portal hypertensive gastropathy | 10050897 |
| Portal vein cavernous transformation | 10073979 |
| Portal vein dilatation | 10073209 |
| Portopulmonary hypertension | 10067281 |
| Primary biliary cholangitis | 10080429 |
| Regenerative siderotic hepatic nodule | 10080679 |
| Renal and liver transplant | 10052279 |
| Retrograde portal vein flow | 10067338 |
| Reye's syndrome | 10039012 |
| Reynold's syndrome | 10070953 |
| Splenic varices | 10067823 |
| Splenic varices haemorrhage | 10068662 |
| Steatohepatitis | 10076331 |
| Subacute hepatic failure | 10056956 |
| Sugiura procedure | 10083010 |
| Varices oesophageal | 10056091 |
| Varicose veins of abdominal wall | 10072284 |
| White nipple sign | 10078438 |
| SMQ: 'Hepatic Disorders'; SMQ Code: 20000005<br>Sub-SMQ: 'Hepatitis, non-infectious'<br>Category: A<br>Scope: Narrow | |
| Preferred Term | PT Code |
| Acute graft versus host disease in liver | 10066263 |
| Allergic hepatitis | 10071198 |

| SMQ: 'Hepatic Disorders'; SMQ Code: 20000005<br>Sub-SMQ: 'Hepatic failure, fibrosis and cirrhosis and other liver damage-related conditions'<br>Category: A<br>Scope: Narrow | |
|---|---|
| Preferred Term | PT Code |
| Alloimmune hepatitis | 10080576 |
| Autoimmune hepatitis | 10003827 |
| Chronic graft versus host disease in liver | 10072160 |
| Chronic hepatitis | 10008909 |
| Graft versus host disease in liver | 10064676 |
| Hepatitis | 10019717 |
| Hepatitis acute | 10019727 |
| Hepatitis cholestatic | 10019754 |
| Hepatitis chronic active | 10019755 |
| Hepatitis chronic persistent | 10019759 |
| Hepatitis fulminant | 10019772 |
| Hepatitis toxic | 10019795 |
| Immune-mediated hepatitis | 10078962 |
| Ischaemic hepatitis | 10023025 |
| Lupus hepatitis | 10067737 |
| Non-alcoholic steatohepatitis | 10053219 |
| Radiation hepatitis | 10051015 |
| Steatohepatitis | 10076331 |

### 13.10.2. Hyperglycaemia

Medical concept of Hyperglycaemia/new onset diabetes mellitus - SMQs (1) 'Hyperglycaemia/new onset diabetes mellitus (SMQ) Narrow SMQ code 20000041.

| SMQ: 'Hyperglycaemia/new onset diabetes mellitus '; SMQ Code: 20000041<br>Sub-SMQ: 'Hepatic failure, fibrosis and cirrhosis and other liver damage-related<br>Category: A<br>Scope: Narrow | |
|---|---|
| Preferred Term | PT Code |
| Acquired lipoatrophic diabetes | 10073667 |
| Blood 1,5-anhydroglucitol decreased | 10065367 |
| Blood glucose increased | 10005557 |
| Diabetes complicating pregnancy | 10012596 |
| Diabetes mellitus | 10012601 |
| Diabetes mellitus inadequate control | 10012607 |
| Diabetes with hyperosmolarity | 10012631 |
| Diabetic arteritis | 10077357 |
| Diabetic coma | 10012650 |
| Diabetic coronary microangiopathy | 10080788 |
| Diabetic hepatopathy | 10071265 |
| Diabetic hyperglycaemic coma | 10012668 |
| Diabetic hyperosmolar coma | 10012669 |
| Diabetic ketoacidosis | 10012671 |
| Diabetic ketoacidotic hyperglycaemic coma | 10012672 |
| Diabetic ketosis | 10012673 |
| Diabetic metabolic decompensation | 10074309 |
| Diabetic wound | 10081558 |
| Euglycaemic diabetic ketoacidosis | 10080061 |
| Fructosamine increased | 10017395 |
| Fulminant type 1 diabetes mellitus | 10072628 |
| Gestational diabetes | 10018209 |

| SMQ: 'Hyperglycaemia/new onset diabetes mellitus '; SMQ Code: 20000041<br>Sub-SMQ: 'Hepatic failure, fibrosis and cirrhosis and other liver damage-related<br>Category: A<br>Scope: Narrow | |
|---|---|
| Preferred Term | PT Code |
| Glucose tolerance impaired | 10018429 |
| Glucose tolerance impaired in pregnancy | 10018430 |
| Glucose urine present | 10018478 |
| Glycated albumin increased | 10082836 |
| Glycosuria | 10018473 |
| Glycosuria during pregnancy | 10018475 |
| Glycosylated haemoglobin abnormal | 10018481 |
| Glycosylated haemoglobin increased | 10018484 |
| Hyperglycaemia | 10020635 |
| Hyperglycaemic hyperosmolar nonketotic syndrome | 10063554 |
| Hyperglycaemic seizure | 10071394 |
| Hyperglycaemic unconsciousness | 10071286 |
| Impaired fasting glucose | 10056997 |
| Insulin resistance | 10022489 |
| Insulin resistant diabetes | 10022491 |
| Insulin-requiring type 2 diabetes mellitus | 10053247 |
| Ketoacidosis | 10023379 |
| Ketonuria | 10023388 |
| Ketosis | 10023391 |
| Ketosis-prone diabetes mellitus | 10023392 |
| Latent autoimmune diabetes in adults | 10066389 |
| Monogenic diabetes | 10075980 |
| Neonatal diabetes mellitus | 10028933 |
| New onset diabetes after transplantation | 10082630 |
| Pancreatogenous diabetes | 10033660 |

| SMQ: 'Hyperglycaemia/new onset diabetes mellitus '; SMQ Code: 20000041<br>Sub-SMQ: 'Hepatic failure, fibrosis and cirrhosis and other liver damage-related<br>Category: A<br>Scope: Narrow | |
|---|---|
| Preferred Term | PT Code |
| Steroid diabetes | 10081755 |
| Type 1 diabetes mellitus | 10067584 |
| Type 2 diabetes mellitus | 10067585 |
| Type 3 diabetes mellitus | 10072659 |
| Urine ketone body present | 10057597 |

### 13.10.3. Hypersensitivity Reactions

Notes: Medical concept of hypersensitivity reactions/DRESS. Only narrow terms selected from Category A of SMQ 'Drug reaction with eosinophilia and systemic symptoms syndrome'. Algorithmic approach for this SMQ not used due to complexity in applying and poor specificity of remaining categories. Category A selected as PTs because more specific for concept (only narrow terms) and a pre-requisite for any combination in algorithmic search. Overlap of some preferred terms with SMQ 'Severe Cutaneous Adverse Reactions'. Plus additional preferred terms selected from HGLT 'Allergic conditions' under SOC 'Immune system disorders'.

| SMQ: Drug reaction with eosinophilia and systemic symptoms syndrome<br>SMQ Code: 20000225<br>Category: A<br>Scope: Narrow | |
|---|---|
| Preferred Term | PT Code |
| Drug reaction with eosinophilia and systemic symptoms | 10073508 |
| Pseudolymphoma | 10037127 |
| Additional preferred terms selected from HLGT 'Allergic conditions' under SOC 'Immune system disorders'; HLGT code 10001708 | |
| Preferred Term | PT Code |
| Drug hypersensitivity | 10013700 |
| Hypersensitivity | 10020751 |
| Type IV Hypersensitivity reaction | 10053613 |
| Eosinophillia | 10014950 |
| Eye swelling | 10015967 |

| SMQ: Drug reaction with eosinophilia and systemic symptoms syndrome<br>SMQ Code: 20000225<br>Category: A<br>Scope: Narrow | |
|---|---|
| Preferred Term | PT Code |
| Eyelid oedema | 10015993 |
| Lip swelling | 10024570 |
| Angioedema | 10002424 |
| Circumoral oedema | 10052250 |
| Face oedema | 10016029 |
| Idiopathic angioedema | 10073257 |
| Lip oedema | 10024558 |
| Mouth swelling | 10075203 |
| Oedema mouth | 10030110 |
| Periorbital oedema | 10034545 |
| Swelling face | 10042682 |
| Periorbital swelling | 10056647 |
| Swelling of eyelid | 10042690 |

### 13.10.4. Rash including severe cutaneous adverse reactions

Medical concept of rash including severe cutaneous adverse reactions. Only narrow terms from SMQ 'Severe cutaneous adverse reactions' selected. Plus several additional preferred terms selected from HLTs 'Rashes, eruptions and exanthems NEC', 'Pruritus NEC', 'Pustular conditions', 'Dermatitis ascribed to specific agent' all under SOC 'Skin and subcutaneous tissue disorders'.

| SMQ: Severe Cutaneous Adverse Reactions<br>SMQ Code: 20000020<br>Category: A<br>Scope: Narrow | |
|---|---|
| SMQ | PT Code |
| Acute generalised exanthematous pustulosis | 10048799 |
| Bullous haemorrhagic dermatosis | 10083809 |
| Cutaneous vasculitis | 10011686 |

| SMQ: Severe Cutaneous Adverse Reactions<br>SMQ Code: 20000020<br>Category: A<br>Scope: Narrow | |
|---|---|
| SMQ | PT Code |
| Dermatitis bullous | 10012441 |
| Dermatitis exfoliative | 10012455 |
| Dermatitis exfoliative generalised | 10012456 |
| Drug reaction with eosinophilia and systemic symptoms | 10073508 |
| Epidermal necrosis | 10059284 |
| Erythema multiforme | 10015218 |
| Erythrodermic atopic dermatitis | 10082985 |
| Exfoliative rash | 10064579 |
| Oculomucocutaneous syndrome | 10030081 |
| SJS-TEN overlap | 10083164 |
| Skin necrosis | 10040893 |
| Stevens-Johnson syndrome | 10042033 |
| Target skin lesion | 10081998 |
| Toxic epidermal necrolysis | 10044223 |
| Toxic skin eruption | 10057970 |
| Addition selected preferred terms from HLTs 'Rashes, eruptions and exanthems NEC', HLT Code 1005266; 'Pruritus NEC', HLT Code 10049293, 'Pustular conditions', HLT Code 10037573; 'Dermatitis ascribed to specific agent', HLT Code 10012437. | |
| Preferred Term | PT Code |
| Eyelid rash | 10074620 |
| Genital rash | 10018175 |
| Mucocutaneous rash | 10056671 |
| Nodular rash | 10075807 |
| Perineal rash | 10075364 |
| Rash | 10037844 |

| SMQ: Severe Cutaneous Adverse Reactions<br>SMQ Code: 20000020<br>Category: A<br>Scope: Narrow | |
|---|---|
| SMQ | PT Code |
| Rash erythematous | 10037855 |
| Rash generalised | 10037858 |
| Rash macular | 10037867 |
| Rash maculo-papular | 10037868 |
| Rash maculovesicular | 10050004 |
| Rash morbilliform | 10037870 |
| Rash papular | 10037876 |
| Rash rubelliform | 10057984 |
| Rash scarlatiniform | 10037890 |
| Rash vesicular | 10037898 |
| Rash pruritic | 10037884 |
| Rash follicular | 10037857 |
| Rash pustular | 10037888 |
| Drug eruption | 10013687 |

### 13.10.5. Prolongation of the Corrected QT Interval of the ECG in Supra Therapeutic Doses

Medical concept of QT prolongation and complications. Only narrow terms from SMQ 'Torsade de pointes/QT prolongation' selected plus one additional PT under HLT 'ECG investigations'.

| SMQ: Torsade de pointes/QT prolongation<br>SMQ Code: 20000001<br>Category: A<br>Scope: Narrow | |
|---|---|
| Preferred Term | PT Code |
| Electrocardiogram QT interval abnormal | 10063748 |
| Electrocardiogram QT prolonged | 10014387 |
| Long QT syndrome | 10024803 |
| Long QT syndrome congenital | 10057926 |
| Torsade de pointes | 10044066 |
| Ventricular tachycardia | 10047302 |
| Additional selected preferred terms from HLT 'ECG investigations', HLT Code 10053104. | |
| Preferred Term | PT Code |
| Electrocardiogram repolarisation abnormality | 10052464 |

### 13.10.6. Suicidal Ideation/Behaviour

Medical concept of suicidal ideation and behaviour. Sub-SMQ 'Suicide/self-injury' (SMQ) from parent SMQ of 'Depression and Suicide/Self Injury (SMQ Code 20000035)'. Only narrow terms from the sub-SMQ selected.

| SMQ: 'Depression and Suicide/Self Injury'<br>SMQ Code: 20000035<br>Sub-SMQ: 'Suicide/self-injury'<br>Category: A<br>Scope: Narrow | |
|---|---|
| Preferred Term | PT Code |
| Assisted suicide | 10079105 |
| Columbia suicide severity rating scale abnormal | 10075616 |
| Completed suicide | 10010144 |
| Depression suicidal | 10012397 |
| Intentional overdose | 10022523 |
| Intentional self-injury | 10022524 |
| Poisoning deliberate | 10036000 |
| Self-injurious ideation | 10051154 |
| Suicidal behaviour | 10065604 |
| Suicidal ideation | 10042458 |
| Suicide attempt | 10042464 |
| Suicide threat | 10077417 |
| Suspected suicide | 10082458 |
| Suspected suicide attempt | 10081704 |

### 13.10.7. Depression

Medical concept of Depression. Sub-SMQ 'Depression (excl suicide and self-injury)' (SMQ) from parent SMQ of 'Depression and Suicide/Self Injury'. Only narrow terms from the sub-SMQ selected.

| SMQ: ‘'Depression and Suicide/Self Injury'<br>SMQ Code: 20000035<br>Sub-SMQ: 'Depression (excl suicide and self-injury)'<br>Category: A<br>Scope: Narrow | |
|---|---|
| Preferred Term | PT Code |
| Activation syndrome | 10066817 |
| Adjustment disorder with depressed mood | 10001297 |
| Adjustment disorder with mixed anxiety and depressed mood | 10001299 |
| Agitated depression | 10001496 |
| Anhedonia | 10002511 |
| Antidepressant therapy | 10054976 |
| Childhood depression | 10068631 |
| Decreased interest | 10011971 |
| Depressed mood | 10012374 |
| Depression | 10012378 |
| Depression postoperative | 10012390 |
| Depressive symptom | 10054089 |
| Dysphoria | 10013954 |
| Electroconvulsive therapy | 10014404 |
| Feeling guilty | 10049708 |
| Feeling of despair | 10016344 |
| Feelings of worthlessness | 10016374 |
| Helplessness | 10077169 |
| Major depression | 10057840 |
| Menopausal depression | 10067371 |
| Mixed anxiety and depressive disorder | 10080836 |

| SMQ: ‘'Depression and Suicide/Self Injury'<br>SMQ Code: 20000035<br>Sub-SMQ: 'Depression (excl suicide and self-injury)'<br>Category: A<br>Scope: Narrow | |
|---|---|
| Preferred Term | PT Code |
| Perinatal depression | 10078366 |
| Persistent depressive disorder | 10077804 |
| Post stroke depression | 10070606 |
| Postictal depression | 10071324 |

### 13.10.8. Bipolar Disorder

Medical concept of bipolar disorder. All preferred terms from HLGT ‘Manic and Bipolar mood disorders and disturbances’ under SOC “Psychiatric disorders”; HLGT Code 10026753.

| Preferred Term | PT Code |
|---|---|
| Bipolar I disorder | 10004939 |
| Bipolar II disorder | 10004940 |
| Bipolar disorder | 10057667 |
| Cyclothymic disorder | 10011724 |
| Hypomania | 10021030 |
| Mania | 10026749 |

### 13.10.9. Psychosis

Medical concept of psychosis. Only narrow terms from SMQ 'Psychosis and psychotic disorders' selected.

| SMQ: 'Psychosis and psychotic disorders'<br>SMQ Code: 20000117<br>Category: A<br>Scope: Narrow | |
|---|---|
| Preferred Term | PT Code |
| Acute psychosis | 10001022 |
| Alcoholic psychosis | 10001632 |

| SMQ: 'Psychosis and psychotic disorders'<br>SMQ Code: 20000117<br>Category: A<br>Scope: Narrow | |
|---|---|
| Alice in wonderland syndrome | 10001666 |
| Brief psychotic disorder with marked stressors | 10048549 |
| Brief psychotic disorder without marked stressors | 10056395 |
| Brief psychotic disorder, with postpartum onset | 10006362 |
| Charles Bonnet syndrome | 10063354 |
| Childhood psychosis | 10061040 |
| Clang associations | 10009232 |
| Cotard's syndrome | 10059591 |
| Delusion | 10012239 |
| Delusion of grandeur | 10012241 |
| Delusion of parasitosis | 10012242 |
| Delusion of reference | 10012244 |
| Delusion of replacement | 10012245 |
| Delusion of theft | 10084030 |
| Delusional disorder, erotomanic type | 10012249 |
| Delusional disorder, grandiose type | 10012250 |
| Delusional disorder, jealous type | 10012251 |
| Delusional disorder, mixed type | 10012252 |
| Delusional disorder, persecutory type | 10053195 |
| Delusional disorder, somatic type | 10012254 |
| Delusional disorder, unspecified type | 10012255 |
| Delusional perception | 10012258 |
| Dementia of the Alzheimer's type, with delusions | 10012295 |
| Depressive delusion | 10063033 |
| Derailment | 10012411 |
| Epileptic psychosis | 10059232 |

| SMQ: 'Psychosis and psychotic disorders'<br>SMQ Code: 20000117<br>Category: A<br>Scope: Narrow | |
|---|---|
| Erotomanic delusion | 10015134 |
| Flight of ideas | 10016777 |
| Hallucination | 10019063 |
| Hallucination, auditory | 10019070 |
| Hallucination, gustatory | 10019071 |
| Hallucination, olfactory | 10019072 |
| Hallucination, synaesthetic | 10062824 |
| Hallucination, tactile | 10019074 |
| Hallucination, visual | 10019075 |
| Hallucinations, mixed | 10019079 |
| Hypnagogic hallucination | 10020927 |
| Hypnopompic hallucination | 10020928 |
| Hysterical psychosis | 10062645 |
| Ideas of reference | 10021212 |
| Illusion | 10021403 |
| Jealous delusion | 10023164 |
| Loose associations | 10024825 |
| Mixed delusion | 10076429 |
| Neologism | 10028916 |
| Neuroleptic-induced deficit syndrome | 10075295 |
| Paranoia | 10033864 |
| Paranoid personality disorder | 10033869 |
| Parkinson's disease psychosis | 10074835 |
| Paroxysmal perceptual alteration | 10063117 |
| Persecutory delusion | 10034702 |
| Postictal psychosis | 10070669 |

| SMQ: 'Psychosis and psychotic disorders'<br>SMQ Code: 20000117<br>Category: A<br>Scope: Narrow | |
|---|---|
| Post-injection delirium sedation syndrome | 10072851 |
| Posturing | 10036437 |
| Psychosis postoperative | 10065617 |
| Psychotic behaviour | 10037249 |
| Psychotic disorder | 10061920 |
| Psychotic disorder due to a general medical condition | 10061921 |
| Reactive psychosis | 10053632 |
| Rebound psychosis | 10074833 |
| Schizoaffective disorder | 10039621 |
| Schizoaffective disorder bipolar type | 10068889 |
| Schizoaffective disorder depressive type | 10068890 |
| Schizophrenia | 10039626 |
| Schizophreniform disorder | 10039647 |
| Schizotypal personality disorder | 10039651 |
| Senile psychosis | 10039987 |
| Shared psychotic disorder | 10040535 |
| Somatic delusion | 10041317 |
| Somatic hallucination | 10062684 |
| Substance-induced psychotic disorder | 10072388 |
| Tangentiality | 10043114 |
| Thought blocking | 10043495 |
| Thought broadcasting | 10052214 |
| Thought insertion | 10043496 |
| Thought withdrawal | 10043497 |
| Transient psychosis | 10056326 |
| Waxy flexibility | 10047853 |

### 13.10.10. Mood Disorders

Medical concept of mood disorders. All preferred terms from HLGT 'Mood disorders and disturbances NEC', under SOC 'Psychiatric disorders'; HLGT Code 10027946.

| Preferred Term | PT Code |
|---|---|
| Affect lability | 10054196 |
| Affective ambivalence | 10077173 |
| Affective disorder | 10001443 |
| Alexithymia | 10077719 |
| Anger | 10002368 |
| Apathy | 10002942 |
| Blunted affect | 10005885 |
| Boredom | 10048909 |
| Constricted affect | 10010778 |
| Crying | 10011469 |
| Diencephalic syndrome of infancy | 10012774 |
| Dysphoria | 10013954 |
| Emotional disorder | 10014551 |
| Emotional distress | 10049119 |
| Emotional poverty | 10014557 |
| Euphoric mood | 10015535 |
| Flat affect | 10016759 |
| Frustration tolerance decreased | 10077753 |
| Inappropriate affect | 10021588 |
| Irritability | 10022998 |
| Laziness | 10051602 |
| Lethargy | 10024264 |
| Listless | 10024642 |
| Moaning | 10027783 |
| Mood altered | 10027940 |

| Preferred Term | PT Code |
|---|---|
| Mood disorder due to a general medical condition | 10027944 |
| Mood swings | 10027951 |
| Morose | 10027977 |
| Neuroleptic-induced deficit syndrome | 10075295 |
| Premenstrual dysphoric disorder | 10051537 |
| Premenstrual syndrome | 10036618 |
| Screaming | 10039740 |
| Seasonal affective disorder | 10039775 |
| Steroid withdrawal syndrome | 10042028 |
| Substance-induced mood disorder | 10072387 |

### 13.10.11. Anxiety

Notes: Medical concept of anxiety disorders. All preferred terms from HLGT "Anxiety disorders and symptoms", under SOC "Psychiatric disorders"; HLGT Code 10002861.

| Preferred Terms | PT Code |
|---|---|
| Acrophobia | 10000605 |
| Activation syndrome | 10066817 |
| Acute stress disorder | 10001084 |
| Aerophobia | 10080300 |
| Agitation | 10001497 |
| Agitation postoperative | 10049989 |
| Agoraphobia | 10001502 |
| Akathisia | 10001540 |
| Algophobia | 10078056 |
| Animal phobia | 10002518 |
| Anniversary reaction | 10074066 |
| Anticipatory anxiety | 10002758 |
| Anxiety | 10002855 |

| Preferred Terms | PT Code |
|---|---|
| Anxiety disorder | 10057666 |
| Anxiety disorder due to a general medical condition | 10002859 |
| Arachnophobia | 10051408 |
| Astraphobia | 10078372 |
| Autophobia | 10071070 |
| Body dysmorphic disorder | 10052793 |
| Burnout syndrome | 10065369 |
| Catastrophic reaction | 10082329 |
| Cibophobia | 10082413 |
| Claustrophobia | 10009244 |
| Compulsions | 10010219 |
| Compulsive cheek biting | 10076510 |
| Compulsive handwashing | 10071263 |
| Compulsive hoarding | 10068007 |
| Compulsive lip biting | 10066241 |
| Compulsive shopping | 10067948 |
| Cryophobia | 10082662 |
| Dermatillomania | 10065701 |
| Dysmorphophobia | 10049096 |
| Emetophobia | 10070637 |
| Fear | 10016275 |
| Fear of animals | 10016276 |
| Fear of closed spaces | 10016277 |
| Fear of crowded places | 10050365 |
| Fear of death | 10066392 |
| Fear of disease | 10016278 |
| Fear of eating | 10050366 |
| Fear of falling | 10048744 |

| Preferred Terms | PT Code |
|---|---|
| Fear of injection | 10073753 |
| Fear of open spaces | 10016279 |
| Fear of pregnancy | 10067035 |
| Fear of weight gain | 10016280 |
| Fear-related avoidance of activities | 10080136 |
| Generalised anxiety disorder | 10018075 |
| Glossophobia | 10080077 |
| Haemophobia | 10073458 |
| Haphephobia | 10067580 |
| Herpetophobia | 10081809 |
| Hydrophobia | 10053317 |
| Hyperarousal | 10080831 |
| Immunisation anxiety related reaction | 10075205 |
| Kinesiophobia | 10078430 |
| Limited symptom panic attack | 10024511 |
| Mysophobia | 10078769 |
| Nail picking | 10066779 |
| Nervousness | 10029216 |
| Neurosis | 10029333 |
| Noctiphobia | 10057946 |
| Nocturnal fear | 10057948 |
| Nosocomephobia | 10083993 |
| Nosophobia | 10063546 |
| Obsessive need for symmetry | 10077179 |
| Obsessive rumination | 10056264 |
| Obsessive thoughts | 10029897 |
| Obsessive-compulsive disorder | 10029898 |
| Obsessive-compulsive symptom | 10077894 |

| Preferred Terms | PT Code |
|---|---|
| Ochlophobia | 10050095 |
| Osmophobia | 10060765 |
| Paediatric autoimmune neuropsychiatric disorders associated with streptococcal infection | 10072147 |
| Panic attack | 10033664 |
| Panic disorder | 10033666 |
| Panic reaction | 10033670 |
| Paruresis | 10069024 |
| Performance fear | 10034432 |
| Phagophobia | 10050096 |
| Pharmacophobia | 10069423 |
| Phobia | 10034912 |
| Phobia of driving | 10056676 |
| Phobia of exams | 10034913 |
| Phobic avoidance | 10034918 |
| Phonophobia | 10054956 |
| Photaugiaphobia | 10064420 |
| Postpartum anxiety | 10082233 |
| Postpartum neurosis | 10036419 |
| Postpartum stress disorder | 10056394 |
| Post-traumatic stress disorder | 10036316 |
| Procedural anxiety | 10075204 |
| Pseudoangina | 10056610 |
| Selective mutism | 10039917 |
| Separation anxiety disorder | 10040045 |
| Sitophobia | 10080170 |
| Social anxiety disorder | 10041242 |
| Social fear | 10041247 |

| Preferred Terms | PT Code |
|---|---|
| Stress | 10042209 |
| Tension | 10043268 |
| Terminal agitation | 10077416 |
| Thanatophobia | 10064723 |
| Thermophobia | 10075147 |
| Trichotemnomania | 10072752 |
| Trichotillomania | 10044629 |

### 13.10.12. Sleep Disorders

Medical concept of sleep disorders. All preferred terms from (1) HLGT 'Sleep Disorders and Disturbances', 'Psychiatric disorders' SOC plus (2) HLGT 'Sleep disturbances (incl subtypes)', 'Nervous system' SOC. Numerous duplicated preferred terms e.g. middle insomnia.

| HLGT Sleep Disorders and Disturbances, HLGT Code 10040991 | |
|---|---|
| Preferred Term | PT Code |
| Abnormal dreams | 10000125 |
| Abnormal sleep-related event | 10061613 |
| Advanced sleep phase | 10001423 |
| Behavioural induced insufficient sleep syndrome | 10081938 |
| Behavioural insomnia of childhood | 10072072 |
| Breathing-related sleep disorder | 10006344 |
| Cataplexy | 10007737 |
| Circadian rhythm sleep disorder | 10009191 |
| Confusional arousal | 10067494 |
| Delayed sleep phase | 10012209 |
| Dyssomnia | 10061827 |
| Exploding head syndrome | 10080684 |
| Hypersomnia | 10020765 |
| Hypersomnia related to another mental condition | 10020767 |

| HLGT Sleep Disorders and Disturbances, HLGT Code 10040991 | |
|---|---|
| Preferred Term | PT Code |
| Hypersomnia-bulimia syndrome | 10053712 |
| Hypnagogic hallucination | 10020927 |
| Hypnopompic hallucination | 10020928 |
| Hyposomnia | 10067530 |
| Initial insomnia | 10022035 |
| Insomnia | 10022437 |
| Insomnia related to another mental condition | 10022443 |
| Irregular sleep phase | 10022995 |
| Irregular sleep wake rhythm disorder | 10080301 |
| Loss of dreaming | 10065085 |
| Middle insomnia | 10027590 |
| Narcolepsy | 10028713 |
| Nightmare | 10029412 |
| Non-24-hour sleep-wake disorder | 10078086 |
| Parasomnia | 10061910 |
| Paradoxical insomnia | 10083337 |
| Periodic limb movement disorder | 10064600 |
| Pickwickian syndrome | 10035004 |
| Poor quality sleep | 10062519 |
| Rapid eye movement sleep behaviour disorder | 10077299 |
| Rapid eye movements sleep abnormal | 10037841 |
| Shift work disorder | 10078088 |
| Sleep apnoea syndrome | 10040979 |
| Sleep attacks | 10040981 |
| Sleep disorder | 10040984 |
| Sleep disorder due to a general medical condition | 10063910 |
| Sleep disorder due to general medical condition, hypersomnia type | 10040985 |

| HLGT Sleep Disorders and Disturbances, HLGT Code 10040991 | |
|---|---|
| Preferred Term | PT Code |
| Sleep disorder due to general medical condition, insomnia type | 10040986 |
| Sleep disorder due to general medical condition, mixed type | 10040987 |
| Sleep disorder due to general medical condition, parasomnia type | 10040988 |
| Sleep inertia | 10067493 |
| Sleep paralysis | 10041002 |
| Sleep sex | 10067492 |
| Sleep talking | 10041009 |
| Sleep terror | 10041010 |
| Sleep-related eating disorder | 10067315 |
| Somnambulism | 10041347 |
| Somnolence | 10041349 |
| Somnolence neonatal | 10041350 |
| Sopor | 10058709 |
| Stupor | 10042264 |
| Terminal insomnia | 10068932 |
| Upper airway resistance syndrome | 10063968 |
| HLGT Sleep disturbances (incl subtypes), HLGT code 10040998 | |
| Abnormal dreams | 10000125 |
| Abnormal sleep-related event | 10061613 |
| Advanced sleep phase | 10001423 |
| Behavioural induced insufficient sleep syndrome | 10081938 |
| Behavioural insomnia of childhood | 10072072 |
| Breathing-related sleep disorder | 10006344 |
| Cataplexy | 10007737 |
| Central-alveolar hypoventilation | 10007982 |
| Circadian rhythm sleep disorder | 10009191 |
| Confusional arousal | 10067494 |

| HLGT Sleep Disorders and Disturbances, HLGT Code 10040991 | |
|---|---|
| Preferred Term | PT Code |
| Delayed sleep phase | 10012209 |
| Dyssomnia | 10061827 |
| Fatal familial insomnia | 10072077 |
| Hypersomnia | 10020765 |
| Hyposomnia | 10067530 |
| Initial insomnia | 10022035 |
| Insomnia | 10022437 |
| Irregular sleep phase | 10022995 |
| Irregular sleep wake rhythm disorder | 10080301 |
| Loss of dreaming | 10065085 |
| Microsleep | 10076954 |
| Middle insomnia | 10027590 |
| Narcolepsy | 10028713 |
| Non-24-hour sleep-wake disorder | 10078086 |
| Periodic limb movement disorder | 10064600 |
| Pickwickian syndrome | 10035004 |
| Poor quality sleep | 10062519 |
| Rapid eye movement sleep behaviour disorder | 10077299 |
| Rapid eye movements sleep abnormal | 10037841 |
| Shift work disorder | 10078088 |
| Sleep apnoea syndrome | 10040979 |
| Sleep deficit | 10080881 |
| Sleep inertia | 10067493 |
| Sleep paralysis | 10041002 |
| Sleep sex | 10067492 |
| Sleep talking | 10041009 |
| Sleep terror | 10041010 |

| HLGT Sleep Disorders and Disturbances, HLGT Code 10040991 | |
|---|---|
| Preferred Term | PT Code |
| Sleep-related eating disorder | 10067315 |
| Somnambulism | 10041347 |
| Sudden onset of sleep | 10050014 |
| Terminal insomnia | 10068932 |
| Upper airway resistance syndrome | 10063968 |

### 13.10.13. Injection site Reactions

Use eCRF terms for ISR.

### 13.10.14. Seizures

Medical concept of seizures. Only narrow terms from SMQ 'Convulsions' selected plus selected PTs of possible seizure events from HLT 'Disturbances in consciousness NEC' under SOC 'Nervous systems disorders' and HLT 'Confusion and disorientation' under SOC 'Psychiatric disorders'.

| SMQ: ‘Convulsions’<br>SMQ Code: 20000079<br>Category: A<br>Scope: Narrow | |
|---|---|
| Preferred Term | PT Code |
| 1p36 deletion syndrome | 10082398 |
| 2-Hydroxyglutaric aciduria | 10078971 |
| Acquired epileptic aphasia | 10052075 |
| Acute encephalitis with refractory, repetitive partial seizures | 10076948 |
| Alcoholic seizure | 10056347 |
| Alpers disease | 10083857 |
| Aspartate-glutamate-transporter deficiency | 10079140 |
| Atonic seizures | 10003628 |
| Atypical benign partial epilepsy | 10056699 |
| Automatism epileptic | 10003831 |
| Autonomic seizure | 10049612 |

| SMQ: ‘Convulsions’<br>SMQ Code: 20000079<br>Category: A<br>Scope: Narrow | |
|---|---|
| Preferred Term | PT Code |
| Baltic myoclonic epilepsy | 10054895 |
| Benign familial neonatal convulsions | 10067866 |
| Benign rolandic epilepsy | 10070530 |
| Biotinidase deficiency | 10071434 |
| CEC syndrome | 10083749 |
| CDKL5 deficiency disorder | 10083005 |
| Change in seizure presentation | 10075606 |
| Clonic convulsion | 10053398 |
| Congenital bilateral perisylvian syndrome | 10082716 |
| Convulsion in childhood | 10052391 |
| Convulsions local | 10010920 |
| Convulsive threshold lowered | 10010927 |
| CSWS syndrome | 10078827 |
| Deja vu | 10012177 |
| Double cortex syndrome | 10073490 |
| Dreamy state | 10013634 |
| Drug withdrawal convulsions | 10013752 |
| Early infantile epileptic encephalopathy with burst-suppression | 10071545 |
| Eclampsia | 10014129 |
| Epilepsy | 10015037 |
| Epilepsy surgery | 10079824 |
| Epilepsy with myoclonic-atonic seizures | 10081179 |
| Epileptic aura | 10015049 |
| Epileptic psychosis | 10059232 |
| Febrile convulsion | 10016284 |

| SMQ: ‘Convulsions’<br>SMQ Code: 20000079<br>Category: A<br>Scope: Narrow | |
|---|---|
| Preferred Term | PT Code |
| Febrile infection-related epilepsy syndrome | 10079438 |
| Focal dyscognitive seizures | 10079424 |
| Frontal lobe epilepsy | 10049424 |
| Gelastic seizure | 10082918 |
| Generalised onset non-motor seizure | 10083376 |
| Generalised tonic-clonic seizure | 10018100 |
| Glucose transporter type 1 deficiency syndrome | 10078727 |
| GM2 gangliosidosis | 10083933 |
| Grey matter heterotopia | 10082084 |
| Hemimegalencephaly | 10078100 |
| Hyperglycaemic seizure | 10071394 |
| Hypocalcaemic seizure | 10072456 |
| Hypoglycaemic seizure | 10048803 |
| Hyponatraemic seizure | 10073183 |
| Idiopathic generalised epilepsy | 10071081 |
| Infantile spasms | 10021750 |
| Juvenile myoclonic epilepsy | 10071082 |
| Lafora's myoclonic epilepsy | 10054030 |
| Lennox-Gastaut syndrome | 10048816 |
| Migraine-triggered seizure | 10076676 |
| Molybdenum cofactor deficiency | 10069687 |
| Multiple subpial transection | 10079825 |
| Myoclonic epilepsy | 10054859 |
| Myoclonic epilepsy and ragged-red fibres | 10069825 |
| Neonatal epileptic seizure | 10082068 |

| SMQ: ‘Convulsions’<br>SMQ Code: 20000079<br>Category: A<br>Scope: Narrow | |
|---|---|
| Preferred Term | PT Code |
| Neonatal seizure | 10082067 |
| Partial seizures | 10061334 |
| Partial seizures with secondary generalisation | 10056209 |
| Petit mal epilepsy | 10034759 |
| Polymicrogyria | 10073489 |
| Post stroke epilepsy | 10076982 |
| Post stroke seizure | 10076981 |
| Postictal headache | 10052470 |
| Postictal paralysis | 10052469 |
| Postictal psychosis | 10070669 |
| Postictal state | 10048727 |
| Post-traumatic epilepsy | 10036312 |
| Schizencephaly | 10073487 |
| Seizure | 10039906 |
| Seizure anoxic | 10039907 |
| Seizure cluster | 10071350 |
| Seizure like phenomena | 10071048 |
| Severe myoclonic epilepsy of infancy | 10073677 |
| Simple partial seizures | 10040703 |
| Status epilepticus | 10041962 |
| Sudden unexplained death in epilepsy | 10063894 |
| Temporal lobe epilepsy | 10043209 |
| Tonic clonic movements | 10051171 |
| Tonic convulsion | 10043994 |
| Tonic posturing | 10075125 |

| SMQ: ‘Convulsions’<br>SMQ Code: 20000079<br>Category: A<br>Scope: Narrow | |
|---|---|
| Preferred Term | PT Code |
| Topectomy | 10073488 |
| Transient epileptic amnesia | 10081728 |
| Tuberous sclerosis complex | 10080584 |
| Uncinate fits | 10045476 |
| Additional selected preferred terms from HLT Disturbances in consciousness NEC, HLT code 10013509 and HLT Confusion and disorientation, HLT code 10010301. | |
| Preferred Term | PT Code |
| Confusional state | 10010305 |
| Loss of consciousness | 10024855 |
| Syncope | 10042772 |
| Sopor | 10058709 |
| Stupor | 10042264 |
| Altered state of consciousness | 10050093 |
| Depressed level of consciousness | 10012373 |
| Consciousness fluctuating | 10050093 |

### 13.10.15. Weight Gain

Medical concept of weight gain. Selected PTs from HLT 'General nutritional disorders NEC', under SOC 'Metabolism and nutrition disorders', and HLT 'Physical examination procedures and organ system status', under SOC 'Investigations' and HLT 'General signs and symptoms NEC', under SOC 'General disorders and administration site conditions'.

| PTs (Select) from HLT General nutritional disorders NEC, HLT code 10018067 | |
|---|---|
| Preferred Term | PT Code |
| Abdominal fat apron | 10077983 |
| Overweight | 10033307 |
| Abnormal weight gain | 10000188 |
| Central obesity | 10065941 |
| Obesity | 10029883 |
| Abdominal fat apron | 10077983 |
| Overweight | 10033307 |
| Abnormal weight gain | 10000188 |
| Central obesity | 10065941 |
| Obesity | 10029883 |
| PTs (Select) from HLT Physical examination procedures and organ system status, HLT Code 10071941 | |
| Preferred Term | PT Code |
| Weight abnormal | 10056814 |
| Weight increased | 10047899 |
| Waist circumference increased | 10064863 |
| Body mass index abnormal | 10074506 |
| Body mass index increased | 10005897 |
| PTs (Select) from HLT General signs and symptoms NEC, HLT Code 10018072 | |
| Preferred Term | PT Code |
| Fat tissue increased | 10016251 |
| Sarcopenic obesity | 10083992 |

### 13.10.16. Rhabdomyolysis

Medical concept of rhabdomyolysis. Only narrow terms only for SMQ 'Rhabdomyolysis/myopathy' plus 2 additional preferred terms selected from HGLT 'muscle disorders' under SOC 'Musculoskeletal and connective tissue disorders'.

| SMQ: 'Rhabdomyolysis/myopathy'<br>SMQ Code: 20000002<br>Category: A<br>Scope: Narrow | |
|---|---|
| Preferred Term | PT Code |
| Muscle necrosis | 10028320 |
| Myoglobin blood increased | 10028625 |
| Myoglobin blood present | 10059888 |
| Myoglobin urine present | 10028631 |
| Myoglobinaemia | 10058735 |
| Myoglobinuria | 10028629 |
| Myopathy | 10028641 |
| Myopathy toxic | 10028648 |
| Necrotising myositis | 10074769 |
| Rhabdomyolysis | 10039020 |
| Thyrotoxic myopathy | 10081524 |
| PTs (Select) from HGLT muscle disorders, HLGT Code 10028302 | |
| Preferred Term | PT Code |
| Myalgia | 10028411 |
| Myositis | 10028653 |

### 13.10.17. Pancreatitis

Medical concept of acute pancreatitis. Only narrow terms of SMQ 'Acute pancreatitis' selected. Algorithmic approach for this SMQ not used due to complexity in applying and poor specificity of remaining categories. Category A selected as PTs because more specific for concept (only narrow terms).

| SMQ: 'Acute pancreatitis'<br>SMQ Code: 20000022<br>Category: A<br>Scope: Narrow | |
|---|---|
| Preferred Term | PT Code |
| Cullen's sign | 10059029 |
| Grey Turner's sign | 10075426 |
| Haemorrhagic necrotic pancreatitis | 10076058 |
| Hereditary pancreatitis | 10056976 |
| Immune-mediated pancreatitis | 10083072 |
| Ischaemic pancreatitis | 10066127 |
| Oedematous pancreatitis | 10052400 |
| Pancreatic abscess | 10048984 |
| Pancreatic cyst drainage | 10082531 |
| Pancreatic haemorrhage | 10033625 |
| Pancreatic necrosis | 10058096 |
| Pancreatic phlegmon | 10056975 |
| Pancreatic pseudoaneurysm | 10081762 |
| Pancreatic pseudocyst | 10033635 |
| Pancreatic pseudocyst drainage | 10033636 |
| Pancreatic pseudocyst haemorrhage | 10083813 |
| Pancreatic pseudocyst rupture | 10083811 |
| Pancreatitis | 10033645 |
| Pancreatitis acute | 10033647 |
| Pancreatitis haemorrhagic | 10033650 |
| Pancreatitis necrotising | 10033654 |

| SMQ: 'Acute pancreatitis'<br>SMQ Code: 20000022<br>Category: A<br>Scope: Narrow | |
|---|---|
| Preferred Term | PT Code |
| Pancreatitis relapsing | 10033657 |
| Pancreatorenal syndrome | 10056277 |

### 13.10.18. Impact on Creatinine

Medical concept of worsening renal function/renal failure in the context of impact on creatinine. Only narrow terms from SMQ 'Acute renal failure' plus all PTs from HLT 'Renal failure and impairment', under SOC 'Renal and urinary disorders'. Numerous duplicated preferred terms e.g. renal failure

| SMQ: ‘Acute renal failure’<br>SMQ Code: 20000003<br>Category: A<br>Scope: Narrow | |
|---|---|
| Preferred Term | PT Code |
| Acute kidney injury | 10069339 |
| Acute phosphate nephropathy | 10069688 |
| Anuria | 10002847 |
| Azotaemia | 10003885 |
| Continuous haemodiafiltration | 10066338 |
| Dialysis | 10061105 |
| Foetal renal impairment | 10078987 |
| Haemodialysis | 10018875 |
| Haemofiltration | 10053090 |
| Neonatal anuria | 10049778 |
| Nephropathy toxic | 10029155 |
| Oliguria | 10030302 |
| Peritoneal dialysis | 10034660 |
| Prerenal failure | 10072370 |
| Renal failure | 10038435 |

| SMQ: ‘Acute renal failure’<br>SMQ Code: 20000003<br>Category: A<br>Scope: Narrow | |
|---|---|
| Preferred Term | PT Code |
| Renal failure neonatal | 10038447 |
| Renal impairment | 10062237 |
| Renal impairment neonatal | 10049776 |
| Subacute kidney injury | 10081980 |
| Renal Failure and Impairment HLT, HLT Code 10038443 | |
| Preferred Term | PT Code |
| Acute Kidney injury | 10069339 |
| Anuria | 10002847 |
| Atypical haemolytic uraemic syndrome | 10079840 |
| Cardiorenal syndrome | 10068230 |
| Chronic kidney disease | 10064848 |
| Crush syndrome | 10050702 |
| Diabetic end stage renal disease | 10012660 |
| End stage renal disease | 10077512 |
| Foetal renal impairment | 10078987 |
| Haemolytic uraemic syndrome | 10018932 |
| Hepatorenal failure | 10019845 |
| Hepatorenal syndrome | 10019846 |
| Nail-patella syndrome | 10063431 |
| Neonatal anuria | 10049778 |
| Oliguria | 10030302 |
| Pancreatorenal syndrome | 10056277 |
| Postoperative renal failure | 10056675 |
| Postrenal failure | 10059345 |
| Prerenal failure | 10072370 |

| SMQ: ‘Acute renal failure’<br>SMQ Code: 20000003<br>Category: A<br>Scope: Narrow | |
|---|---|
| Preferred Term | PT Code |
| Propofol infusion syndrome | 10063181 |
| Renal failure | 10038435 |
| Renal failure neonatal | 10038447 |
| Renal impairment | 10062237 |
| Renal impairment neonatal | 10049776 |
| Renal injury | 10061481 |
| Scleroderma renal crisis | 10062553 |
| Traumatic anuria | 10044501 |

### 13.10.19. Safety During Pregnancy

Use AE terms co-reported in pregnancy exposures to CAB.

## 13.11. Appendix 11: Identification of COVID-19 Adverse Events

COVID-19 adverse events are identified based on MedDRA coded values and/or AE referenced in the COVID-19 Coronavirus Infection assessment. The Lowest Level Terms (LLTs) and codes, Preferred Terms (PTs), High Level Terms (HLTs), High Level Group Terms (HLGTs), and System Organ Classes (SOCs), below are from MedDRA 23.0. In case there is a change to the version of MedDRA at time of reporting, the coded values based on the MedDRA version at the time of reporting will be used. The additional events may also be added based on the blinded review of AE data collected on study prior to the database freeze.

SOC: Infections and infestations

| LLT code | LLT | PT | HLT | HLGT |
|---|---|---|---|---|
| 10084459 | Asymptomatic COVID-19 | Asymptomatic COVID-19 | Coronavirus infections | Viral infectious disorders |
| 10084467 | Asymptomatic SARS-CoV-2 infection | Asymptomatic COVID-19 | Coronavirus infections | Viral infectious disorders |
| 10053983 | Corona virus infection | Coronavirus infection | Coronavirus infections | Viral infectious disorders |
| 10051905 | Coronavirus infection | Coronavirus infection | Coronavirus infections | Viral infectious disorders |
| 10084382 | Coronavirus disease 2019 | COVID-19 | Coronavirus infections | Viral infectious disorders |
| 10084268 | COVID-19 | COVID-19 | Coronavirus infections | Viral infectious disorders |
| 10084401 | COVID-19 respiratory infection | COVID-19 | Coronavirus infections | Viral infectious disorders |
| 10084270 | SARS-CoV-2 acute respiratory disease | COVID-19 | Coronavirus infections | Viral infectious disorders |
| 10084272 | SARS-CoV-2 infection | COVID-19 | Coronavirus infections | Viral infectious disorders |
| 10084381 | Coronavirus pneumonia | COVID-19 pneumonia | Coronavirus infections | Viral infectious disorders |
| 10084380 | COVID-19 pneumonia | COVID-19 pneumonia | Coronavirus infections | Viral infectious disorders |

| LLT code | LLT | PT | HLT | HLGT |
|---|---|---|---|---|
| 10084383 | Novel COVID-19-infected pneumonia | COVID-19 pneumonia | Coronavirus infections | Viral infectious disorders |
| 10084451 | Suspected COVID-19 | Suspected COVID-19 | Coronavirus infections | Viral infectious disorders |
| 10084452 | Suspected SARS-CoV-2 infection | Suspected COVID-19 | Coronavirus infections | Viral infectious disorders |
| 10084461 | SARS-CoV-2 carrier | SARS-CoV-2 carrier | Infectious disorders carrier | Ancillary infectious topics |

## 13.12. Appendix 12: Abbreviations & Trade Marks

### 13.12.1. Abbreviations

| Abbreviation | Description |
|---|---|
| ADaM | Analysis Data Model |
| AE | Adverse Event |
| AIC | Akaike's Information Criteria |
| A&R | Analysis and Reporting |
| CDISC | Clinical Data Interchange Standards Consortium |
| CI | Confidence Interval |
| CPMS | Clinical Pharmacology Modelling & Simulation |
| CS | Clinical Statistics |
| CSR | Clinical Study Report |
| CTR | Clinical Trial Register |
| $CV_b$ / $CV_w$ | Coefficient of Variation (Between) / Coefficient of Variation (Within) |
| DBF | Database Freeze |
| DBR | Database Release |
| DOB | Date of Birth |
| DP | Decimal Places |
| eCRF | Electronic Case Record Form |
| EEP | Efficacy Evaluable Population |
| EMA | European Medicines Agency |
| FDA | Food and Drug Administration |
| FDAAA | Food and Drug Administration Clinical Results Disclosure Requirements |
| GSK | GlaxoSmithKline |
| IA | Interim Analysis |
| ICH | International Conference on Harmonization |
| IDMC | Independent Data Monitoring Committee |
| IDSL | Integrated Data Standards Library |
| IMMS | International Modules Management System |
| IP | Investigational Product |
| ITT | Intent-To-Treat |
| MMRM | Mixed Model Repeated Measures |
| PBMC | Peripheral Blood Mononuclear Cells |
| PCI | Potential Clinical Importance |
| PD | Pharmacodynamic |
| PDMP | Protocol Deviation Management Plan |
| PK | Pharmacokinetic |
| PP | Per Protocol |
| PopPK | Population PK |
| QC | Quality Control |
| QTcF | Frederica's QT Interval Corrected for Heart Rate |
| QTcB | Bazett's QT Interval Corrected for Heart Rate |
| RAP | Reporting & Analysis Plan |
| RAMOS | Randomization & Medication Ordering System |
| SAC | Statistical Analysis Complete |

| Abbreviation | Description |
|---|---|
| SDSP | Study Data Standardization Plan |
| SDTM | Study Data Tabulation Model |
| SOP | Standard Operation Procedure |
| TA | Therapeutic Area |
| TFL | Tables, Figures & Listings |

### 13.12.2. Trademarks

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

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

## 13.13. Appendix 13: List of Data Displays

All data displays will use the term "subject" rather than "participant" in accordance with CDSIC and GSK Statistical Display Standards.

Where applicable, all summary displays will present data across both the Intervention and Extension phases unless explicitly stated otherwise in the display title.

### 13.13.1. Data Display Numbering

The following numbering will be applied for RAP generated displays:

| Section | Tables | Figures |
|---|---|---|
| Study Population | 1.1 to 1.n | 1.1 to 1.n |
| Efficacy | 2.1 to 2.n | 2.1 to 2.n |
| Safety | 3.1 to 3.n | 3.1 to 3.n |
| Pharmacokinetic | 4.1 to 4.n | 4.1 to 4.n |
| Virology | 5.1 to 5.n | 5.1 to 4.n |
| Other | 6.1 to 6.n | 6.1 to 6.n |
| **Section** | **Listings** | |
| ICH Listings | 1 to x | |
| Other Listings | y to z | |

### 13.13.2. Mock Example Shell Referencing

Nonstandard specifications will be referenced as indicated below (where a study specific mock shell is available) or the location of a similar display produced for a different study in the HARP reporting environment will be provided as reference. The example mock-up displays from other reporting efforts will be named in the format: Study Number/HARP Reporting Effort/Output Type (T/ F/L)/Display Number, where T stands for Table, F stands for Figure and L stands for Listing. For example, the Table 1.1 from primary_02 reporting effort for Study 201585 will be named by 201585/primary_02/T1.1. If required example mock-up displays provided in Appendix 14: Example Mock Shells for Data Displays.

| Section | Figure | Table | Listing |
|---|---|---|---|
| Study Population | POP_Fn | POP_Tn | POP_Ln |
| Efficacy | EFF_Fn | EFF_Tn | EFF_Ln |
| Safety | SAF_Fn | SAF_Tn | SAF_Ln |
| Pharmacokinetic | PK_Fn | PK_Tn | PK_Ln |
| Virology | VIR_Fn | VIR_Tn | VIR_Ln |
| Other | OTR_Tn | OTR_Fn | OTR_Ln |

### 13.13.3. Deliverables

| Delivery | Description |
|---|---|
| HL | Month 12 Headline |
| M12 | Month 12 Analysis |
| EOS | End of Study Analysis<br>Note that the TLFs with asterisk (i.e. EOS*) will only be produced when the underlying source data has been changed since Month 12 analysis. |

### 13.13.4. Study Population Tables

| Study Population Tables | | | | | |
|---|---|---|---|---|---|
| **No.** | **Population** | **GSK Standard / Example Shell** | **Title** | **Programming Notes** | **Deliverable** |
| **Subject Disposition** | | | | | |
| 1.1. | Safety | ES1 | Summary of Subject Disposition for the Subject Conclusion Record | ICH E3, FDAAA, EudraCT | HL, M12, EOS |
| 1.2. | Safety | SD1 | Summary of Treatment Status and Reasons for Discontinuation of Study Treatment | ICH E3 | M12, EOS |
| 1.3. | Safety | ES4 | Summary of Subject Disposition at Each Study Phase | ICH E3<br>Intervention/Extension phase: status and reason for withdrawal based on date and reason collected in the study treatment discontinuation form.<br>Long term Follow-up: completion/withdrawal based on data collected in the Study Conclusion form. | M12, EOS |
| 1.4. | Safety | ES5 | Summary of Reason for Withdrawal at Each Study Phase | FDAAA, EudraCT | HL, M12, EOS |
| 1.5. | Safety | ES11 | Summary of Outcome of Adverse Events Which Led to Study Withdrawal/Treatment Discontinuation at Each Study Phase | EudraCT | M12, EOS |
| 1.6. | Screened | ES6 | Summary of Screening Status and Reasons for Screen Failure | Journal Requirements | M12, EOS |

| Study Population Tables | | | | | |
|---|---|---|---|---|---|
| **No.** | **Population** | **GSK Standard / Example Shell** | **Title** | **Programming Notes** | **Deliverable** |
| 1.7. | Enrolled | NS1 | Summary of Number of Subjects by Country and Site ID | EudraCT/Clinical Operations | M12, EOS |
| 1.8. | Screened | NS1 | Summary of Number of Subjects by Site Type and Site ID | Replace Country with Site Type<br>Add column for Investigator Name | M12, EOS |
| **Protocol Deviation** | | | | | |
| 1.9. | Enrolled | DV1 | Summary of Important Protocol Deviations | ICH E3 | M12, EOS |
| 1.10. | Enrolled | DV1 | Summary of Important COVID-19 Related Protocol Deviations | Update the label for the first row to be “ANY IMPORTANT COVID-19 RELATED PROTOCOL DEVIATIONS” | M12, EOS |
| 1.11. | Enrolled | DV1 | Summary of Important Non-COVID-19 Protocol Deviations | Update the label for the first row to be “ANY IMPORTANT NON-COVID-19 RELATED PROTOCOL DEVIATIONS” | M12, EOS |
| 1.12. | Enrolled | DV1 | Summary of All COVID-19 Protocol Deviations by Site | Update the label for the first row to be “ANY COVID-19 RELATED PROTOCOL DEVIATIONS”.<br>Summary for each site and ‘Total’ across sites. | HL, M12, EOS |

| Study Population Tables | | | | | |
|---|---|---|---|---|---|
| **No.** | **Population** | **GSK Standard / Example Shell** | **Title** | **Programming Notes** | **Deliverable** |
| 1.13. | Enrolled | DV1 | Summary of All Implementation Protocol Deviations by Site | Update the label for the first row to be "ANY IMPLEMENTATION RELATED PROTOCOL DEVIATIONS"<br>Summary for each site and 'Total' across sites. | HL, M12, EOS |
| **Population Analysed** | | | | | |
| 1.14. | Screened | SP1 | Summary of Study Populations | GSK Statistical Display Standard | M12, EOS |
| 1.15. | Enrolled | SP2 | Summary of Exclusions from the Safety Population | GSK Statistical Display Standard | M12, EOS |
| **Demographic and Baseline Characteristics** | | | | | |
| 1.16. | Safety | DM1 | Summary of Demographic Characteristics | ICH E3, FDAAA, EudraCT. For EOS: add age group (18 - 24, 25 - 40, >40), BMI group (<30, >=30). | HL, M12, EOS |
| 1.17. | Enrolled | DM11 | Summary of Age Ranges | EudraCT | M12, EOS |
| 1.18. | Safety | DM6 | Summary of Race and Racial Combinations | ICH E3, FDA, FDAAA, EudraCT | M12, EOS |
| 1.19. | Safety | BASELINE2 | Distribution of CD4+ Cell Count Results at Screening and Baseline | | M12, EOS* |
| 1.20. | Safety | BASELINE3 | Summary of Hepatitis Status at Entry | | M12, EOS* |
| 1.21. | Safety | CDC1 | Summary of CDC Classification of HIV-1 Infection at Baseline | | M12, EOS* |

| Study Population Tables | | | | | |
|---|---|---|---|---|---|
| **No.** | **Population** | **GSK Standard / Example Shell** | **Title** | **Programming Notes** | **Deliverable** |
| **Prior and Concomitant Medications** | | | | | |
| 1.22. | Safety | MH1 | Summary of Past Medical Conditions | ICH E3 | M12, EOS* |
| 1.23. | Safety | MH4 | Summary of Past Cardiac, Gastrointestinal, Metabolism and Nutrition, Psychiatric, Renal and Urinary, Nervous System Conditions, and Hepatobiliary Disorders | ICH E3 | M12, EOS* |
| 1.24. | Safety | MH1 | Summary of Current Medical Conditions | ICH E3 | M12, EOS |
| 1.25. | Safety | MH4 | Summary of Current Cardiac, Gastrointestinal, Metabolism and Nutrition, Psychiatric, Renal and Urinary, Nervous System Conditions, and Hepatobiliary Disorders | ICH E3 | M12, EOS |
| 1.26. | Safety | CM9 | Summary of Concomitant Medications by Ingredient Combinations | ICH E3<br>See GSK Statistical Display Standard<br>Multi-ingredient medications will be labelled according to the sum of their ingredients, i.e., Generic Term. | M12, EOS |
| 1.27. | Safety | 207966/primary_15/T1.30 | Summary of Prior Antiretroviral Therapy Medications | Remove the footnote. Follow definitions in Section 13.4.1 to determine the prior ART medications. | M12, EOS* |

| Study Population Tables | | | | | |
|---|---|---|---|---|---|
| **No.** | **Population** | **GSK Standard / Example Shell** | **Title** | **Programming Notes** | **Deliverable** |
| 1.28. | Safety | 201585/primary_02/T1.30 | Summary of Antiretroviral Therapy Taken During Screening by Baseline Third Agent Class | Like Example shell but stratified by Baseline Third Agent Class (NNRTI, INI, PI); add 'Any' row under each class. | M12, EOS* |
| 1.29. | Safety | RF1 | Summary of HIV Risk Factors | | M12, EOS* |
| **Other** | | | | | |
| 1.30. | Safety | POP_T1 | Summary of Transition to CAB + RPV LA Marketed Product Status by Site Type and Site ID | | EOS |

### 13.13.5. Efficacy Tables

| Efficacy: Tables | | | | | |
|---|---|---|---|---|---|
| **No.** | **Population** | **GSK Standard/ Example Shell** | **Title** | **Programming Notes** | **Deliverable** |
| **Snapshot** | | | | | |
| 2.1. | Safety | EFF_T1<br>See Section 13.14 | Summary of Study Outcomes (50 c/mL cutoff) at Month 12 (Intervention Phase) – Modified Snapshot Analysis with COVID-19 related LOCF | Missing HIV-1 RNA due to COVID-19 are imputing using last post baseline value carried forward. | HL, M12 |
| 2.2. | Safety | EFF_T2<br>See Section 13.14 | Summary of Study Outcomes (50 c/mL cutoff) at Month 12 (Intervention Phase) –Snapshot Analysis | With expanded COVID-19 related/Non-related categories | HL, M12 |
| 2.3. | Safety | SNAPSHOT4 | Proportion of Subjects with Plasma HIV-1 RNA ≥ 50 c/mL Over Time (Intervention Phase) – Modified Snapshot Analysis with COVID-19 related LOCF | Missing HIV-1 RNA due to COVID-19 are imputing using last post baseline value carried forward.<br>Use Exact (Clopper-Pearson) method for 95% confidence Intervals. | M12 |

| Efficacy: Tables | | | | | |
|---|---|---|---|---|---|
| **No.** | **Population** | **GSK Standard/ Example Shell** | **Title** | **Programming Notes** | **Deliverable** |
| 2.4. | Safety | SNAPSHOT4 | Proportion of Subjects with Plasma HIV-1 RNA < 50 c/mL Over Time (Intervention Phase) – Modified Snapshot Analysis with COVID-19 related LOCF | Missing HIV-1 RNA due to COVID-19 are imputing using last post baseline value carried forward.<br>Use Exact (Clopper-Pearson) method for 95% confidence Intervals. | M12 |
| 2.5. | Safety | SNAPSHOT7 | Summary of Study Outcomes (50 c/mL cutoff) at Month 12 by Site Type (Intervention Phase) – Modified Snapshot Analysis with COVID-19 related LOCF | Missing HIV-1 RNA due to COVID-19 are imputing using last post baseline value carried forward. | M12 |
| **CVF** | | | | | |
| 2.6. | Safety | VF1 | Cumulative Proportion of Subjects Meeting Confirmed Virologic Failure Criteria Over Time (Intervention Phase) | | HL, M12 |
| 2.7. | Safety | 207966/primary_15/T2.23 | Cumulative Proportion of Subjects Meeting Confirmed Virologic Failure Criteria Over Time | | M12, EOS |
| **CD4** | | | | | |
| 2.8. | Safety | LB1 | Summary of CD4+ Cell Count (cells/mm^3) by Visit | | M12, EOS |
| 2.9. | Safety | LB1 | Summary of Change from Baseline in CD4+ Cell Count (cells/mm^3) by Visit | | M12, EOS |

| Efficacy: Tables | | | | | |
|---|---|---|---|---|---|
| **No.** | **Population** | **GSK Standard/ Example Shell** | **Title** | **Programming Notes** | **Deliverable** |
| **HIV Associated Conditions** | | | | | |
| 2.10. | Safety | CDC2 | Summary of Post-Baseline CDC Stage 3 HIV-1 Associated Conditions Including Recurrences | | M12, EOS |
| 2.11. | Safety | CDC2 | Summary of Post-Baseline CDC Stage 3 HIV-1 Associated Conditions Excluding Recurrences | | M12, EOS |
| **Plasma HIV-1 RNA** | | | | | |
| 2.12. | Safety | 209493/primary_01/T2.4 | Proportion of Subjects with Plasma HIV-1 RNA < 50 c/mL Over Time – Observed Case | | EOS |

### 13.13.6. Efficacy Figures

| Efficacy: Figures | | | | | |
|---|---|---|---|---|---|
| **No.** | **Population** | **GSK Standard / Example Shell** | **Title** | **Programming Notes** | **Deliverable** |
| 2.1. | Safety | SNAPSHOT8 | Percent (95% CI) of Subjects with Plasma HIV-1 RNA ≥ 50 copies/mL Over Time (Intervention Phase) – Modified Snapshot Analysis with COVID-19 related LOCF | Missing HIV-1 RNA due to COVID-19 are imputing using last post baseline value carried forward.<br><br>Use Exact (Clopper-Pearson) method for 95% confidence Intervals. | M12 |
| 2.2. | Safety | SNAPSHOT8 | Percent (95% CI) of Subjects with Plasma HIV-1 RNA < 50 copies/mL Over Time (Intervention Phase) – Modified Snapshot Analysis with COVID-19 related LOCF | Missing HIV-1 RNA due to COVID-19 are imputing using last post baseline value carried forward.<br><br>Use Exact (Clopper-Pearson) method for 95% confidence Intervals. | M12 |

| **Efficacy: Figures** | | | | | |
|---|---|---|---|---|---|
| **No.** | **Population** | **GSK Standard / Example Shell** | **Title** | **Programming Notes** | **Deliverable** |
| 2.3. | Safety | SNAPSHOT10 | Individual Plasma HIV-1 RNA for Subjects Snapshot Algorithm Plasma HIV-1 RNA >= 50 copies/mL at Month 12 – Modified Snapshot Analysis with COVID-19 related LOCF | The 1st vertical line indicates start of study treatment at Intervention Phase. The second vertical reference line indicates last IP on-treatment study day. i.e. min (last IP injection dose+35 days, LTFU HAART start date, date of last oral CAB+RPV+1). This vertical line is only for subjects who withdraw from Intervention Phase/Extension phase. | M12 |

| **Efficacy: Figures** | | | | | |
|---|---|---|---|---|---|
| **No.** | **Population** | **GSK Standard / Example Shell** | **Title** | **Programming Notes** | **Deliverable** |
| 2.4. | Safety | SNAPSHOT10 | Individual Plasma HIV-1 RNA for Subjects with Confirmed Virologic Failure | The 1st vertical line indicates start of study treatment at Intervention Phase. The second vertical reference line indicates last IP on-treatment study day. i.e. min (last IP injection dose+35 days, LTFU HAART start date, date of last oral CAB+RPV+1). This vertical line is only for subjects who withdraw from Intervention Phase/Extension phase. Include all plasma HIV-1 RNA data for a subject. | M12, EOS |

### 13.13.7. Safety Tables

Note: The summary table for individual AESI may be added or removed per final AESI list for the analysis.

| Safety: Tables | | | | | |
|---|---|---|---|---|---|
| **No.** | **Population** | **GSK Standard/ Example Shell** | **Title** | **Programming Notes** | **Deliverable** |
| **Exposure** | | | | | |
| 3.1. | Safety | 207966/primary_15/T3.1 | Summary of Exposure to Study Treatment (Intervention Phase) | | M12 |
| 3.2. | Safety | 207966/primary_15/T3.1 | Summary of Exposure to Study Treatment | | M12, EOS |
| 3.3. | Safety | SAF_T1 See Section 13.14 | Summary of Adherence to CAB LA + RPV LA Dosing Schedule by Visit, Site Type and COVID-19 Impact /Non-Impact (Intervention Phase) | COVID Impact refers to missed or out of window injections for COVID-19 related reasons (as captured as COVID-19 related protocol deviations) | HL, M12 |
| 3.4. | Safety | SAF_T2 See Section 13.14 | Summary of Adherence to CAB LA + RPV LA Dosing Schedule by Visit, Site ID and COVID-19 Impact /Non-Impact (Intervention Phase) | COVID Impact refers to missed or out of window injections for COVID-19 related reasons (as captured as COVID-19 related protocol deviations) | HL, M12 |

| Safety: Tables | | | | | |
|---|---|---|---|---|---|
| **No.** | **Population** | **GSK Standard/ Example Shell** | **Title** | **Programming Notes** | **Deliverable** |
| 3.5. | Safety | SAF_T1 See Section 13.14 | Summary of Adherence to CAB LA + RPV LA Dosing Schedule by Visit, Site Type and COVID-19 Impact /Non-Impact | COVID Impact refers to missed or out of window injections for COVID-19 related reasons (as captured as COVID-19 related protocol deviations) | EOS |
| 3.6. | Safety | SAF_T2 See Section 13.14 | Summary of Adherence to CAB LA + RPV LA Dosing Schedule by Visit, Site ID and COVID-19 Impact /Non-Impact | COVID Impact refers to missed or out of window injections for COVID-19 related reasons (as captured as COVID-19 related protocol deviations) | EOS |
| **Adverse Events (AEs)** | | | | | |
| 3.7. | Safety | AE3 | Summary of Adverse Events by Overall Frequency | ICH E3 | M12, EOS |
| 3.8. | Safety | AE5B | Summary of Adverse Events by System Organ Class and Maximum Grade | ICH E3 | HL, M12, EOS |
| 3.9. | Safety | AE5B | Summary of Adverse Events by System Organ Class and Maximum Grade — Excluding Study Drug Injection Site Reactions | | M12, EOS |
| 3.10. | Safety | AE5B | Summary of Adverse Events by System Organ Class and Maximum Grade (Oral Lead-in Period) | | M12 |
| 3.11. | Safety | AE3 | Summary of Common (>=5%) Adverse Events by Overall Frequency | ICH E3 | M12, EOS |

| Safety: Tables | | | | | |
|---|---|---|---|---|---|
| **No.** | **Population** | **GSK Standard/ Example Shell** | **Title** | **Programming Notes** | **Deliverable** |
| 3.12. | Safety | AE3 | Summary of Common (>=1%) Grade 2-5 Adverse Events by Overall Frequency | ICH E3 | M12, EOS |
| 3.13. | Safety | AE3 | Summary Drug-Related Adverse Events by Overall Frequency | ICH E3 | M12, EOS |
| 3.14. | Safety | AE5B | Summary of Drug-Related Adverse Events by System Organ Class and Maximum Grade | ICH E3 | HL, M12, EOS |
| 3.15. | Safety | AE5B | Summary of Drug-Related Adverse Events by System Organ Class and Maximum Grade — Excluding Study Drug Injection Site Reactions | | M12, EOS |
| 3.16. | Safety | AE15 | Summary of Common (>=5%) Non-serious Adverse Events by System Organ Class and Preferred Term (Number of Subjects and Occurrences) | FDAAA, EudraCT | M12, EOS |
| 3.17. | Safety | AE3 | Summary of Common (>=1%) Drug-Related Grade 2-5 Adverse Events by Overall Frequency | ICH E3 | M12, EOS |
| 3.18. | Safety | AE3 | Summary of Non-Serious Drug-Related Adverse Events by Overall Frequency | Plain Language Summary requirements. | M12, EOS |

| Safety: Tables | | | | | |
|---|---|---|---|---|---|
| **No.** | **Population** | **GSK Standard/ Example Shell** | **Title** | **Programming Notes** | **Deliverable** |
| **Serious and Other Significant Adverse Events** | | | | | |
| 3.19. | Safety | AE5B | Summary of Serious Adverse Events by System Organ Class and Maximum Grade | ICH E3 | HL, M12, EOS |
| 3.20. | Safety | AE16 | Summary of Serious Adverse Events by System Organ Class and Preferred Term (Number of Subjects and Occurrences) | FDAAA, EudraCT | M12, EOS |
| 3.21. | Safety | AE1 | Summary of Adverse Events Leading to Permanent Discontinuation of Study Treatment or Withdrawal from Study by System Organ Class and Preferred Term | GSK Statistical Display Standard | HL, M12, EOS |
| 3.22. | Safety | AE20 | Summary of Serious Fatal and Non-Fatal Drug-Related Adverse Events by Overall Frequency | Plain Language Summary requirements. | M12, EOS |
| **Injection Site Reaction Adverse Events** | | | | | |
| 3.23. | Safety | 201584/primary_7/T3.40 | Summary of Study Drug Injection Site Reaction Adverse Events (Event-level Summary) | | HL, M12, EOS |
| 3.24. | Safety | 201584/primary_7/T3.43 | Summary of Subject-level Characteristics of Study Drug Injection Site Reaction Adverse Events – Overall and Common | | HL, M12, EOS |
| 3.25. | Safety | 201584/primary_7/T3.46 | Summary of Study Drug Injection Site Reaction Adverse Events by Visit and Maximum Severity – Overall and Common | | HL, M12, EOS |

| Safety: Tables | | | | | |
|---|---|---|---|---|---|
| **No.** | **Population** | **GSK Standard/ Example Shell** | **Title** | **Programming Notes** | **Deliverable** |
| **Laboratory: Chemistry** | | | | | |
| 3.26. | Safety | LB1 | Summary of Chemistry Values | Includes pre-specified parameters repeated in conventional units.<br>Includes baseline values | M12, EOS |
| 3.27. | Safety | LB1 | Summary of Chemistry Changes from Baseline | ICH E3 | M12, EOS |
| 3.28. | Safety | LB16 | Summary of Chemistry Results by Maximum Grade Increase Post-Baseline Relative to Baseline | ICH E3 | HL, M12, EOS |
| 3.29. | Safety | LB16 | Summary of Chemistry Results by Maximum Grade Increase Post-Baseline Relative to Baseline (Oral Lead-in Period) | ICH E3 | M12 |
| **Laboratory: Hematology** | | | | | |
| 3.30. | Safety | LB1 | Summary of Hematology Values | Includes pre-specified parameters repeated in conventional units. | M12, EOS |
| 3.31. | Safety | LB1 | Summary of Hematology Changes from Baseline | Includes pre-specified parameters repeated in conventional units.<br>Includes baseline values | M12, EOS |
| 3.32. | Safety | LB16 | Summary of Hematology Results by Maximum Grade Increase Post-Baseline Relative to Baseline | ICH E3 | M12, EOS |

| Safety: Tables | | | | | |
|---|---|---|---|---|---|
| **No.** | **Population** | **GSK Standard/ Example Shell** | **Title** | **Programming Notes** | **Deliverable** |
| 3.33. | Safety | LB16 | Summary of Hematology Results by Maximum Grade Increase Post-Baseline Relative to Baseline (Oral Lead-in Period) | ICH E3 | M12 |
| **Laboratory: Hepatobiliary (Liver)** | | | | | |
| 3.34. | Safety | LIVER1 | Summary of Liver Monitoring/Stopping Event Reporting | GSK Statistical Display Standard | M12, EOS |
| 3.35. | Safety | LIVER10 | Summary of Hepatobiliary Laboratory Abnormalities | GSK Statistical Display Standard | HL, M12, EOS |
| 3.36. | Safety | LIVER11 | Summary of Liver Restart/Re-Challenges | GSK Statistical Display Standard | M12, EOS |
| **Vital Signs** | | | | | |
| 3.37. | Safety | VS1 | Summary of Change from Baseline in Vital Signs | ICH E3<br>Include Baseline values | M12, EOS |
| **Cardiovascular Risk Factors** | | | | | |
| 3.38. | Safety | FH1 | Summary of Family History of Cardiovascular Risk Factors | GSK Statistical Display Standard | M12, EOS |
| 3.39. | Safety | SU1 | Summary of Substance Use | GSK Statistical Display Standard | M12, EOS |

| Safety: Tables | | | | | |
|---|---|---|---|---|---|
| **No.** | **Population** | **GSK Standard/ Example Shell** | **Title** | **Programming Notes** | **Deliverable** |
| **COVID-19 Adverse Events** | | | | | |
| 3.40. | Safety | PAN1 | Summary of COVID-19 Assessments for Subjects with COVID-19 Adverse Events | GSK Statistical Display Standard, for EOS, use PAN1A shell and replace the first footnote with "[1] COVID-19 case diagnosis is based on WHO definition that was in effect at the time of diagnosis." | M12, EOS |
| 3.41. | Safety | PAN2 | Summary of COVID-19 Additional Assessments for Subjects with COVID-19 Adverse Events | GSK Statistical Display Standard, for EOS, use PAN2A. | M12, EOS |
| 3.42. | Safety | PAN3 | Summary of COVID-19 Symptoms for Subjects with COVID-19 Adverse Events | GSK Statistical Display Standard, for EOS, use PAN3A. | M12, EOS |
| **Adverse Events of Special Interest** | | | | | |
| 3.43. | Safety | 201584/primary_27/T3.140 | Summary of Depression, Anxiety and Suicidal or Suicidal Ideation/Behaviour Adverse Events by System Organ Class, Maximum DAIDS Toxicity Grade, and History of Depression, Anxiety or Suicidal Ideation/Behaviour at Screening | | M12, EOS |
| 3.44. | Safety | 201584/primary_07/T3.122 | Summary of Depression Adverse Events of Special Interest by System Organ Class and Preferred Term (Number of Subjects and Occurrences) | | M12, EOS |

| Safety: Tables | | | | | |
|---|---|---|---|---|---|
| **No.** | **Population** | **GSK Standard/ Example Shell** | **Title** | **Programming Notes** | **Deliverable** |
| 3.45. | Safety | 201584/primary_07/T3.125 | Summary of Anxiety Adverse Events of Special Interest by System Organ Class and Preferred Term (Number of Subjects and Occurrences) | | M12, EOS |
| 3.46. | Safety | 201584/primary_07/T3.128 | Summary of Suicidal Ideation/Behaviour Adverse Events of Special Interest by System Organ Class and Preferred Term (Number of Subjects and Occurrences) | | M12, EOS |
| 3.47. | Safety | 201584/primary_07/T3.134 | Summary of Seizures Adverse Events of Special Interest by System Organ Class and Preferred Term (Number of Subjects and Occurrences) | | M12, EOS |
| 3.48. | Safety | 201584/primary_07/T3.137 | Summary of Hepatic Safety Profile: Assessment of Risk of Hepatoxicity Adverse Events of Special Interest by System Organ Class and Preferred Term (Number of Subjects and Occurrences) | | M12, EOS |
| 3.49. | Safety | 201584/primary_07/T3.140 | Summary of Hypersensitivity Reactions (HSR) Adverse Events of Special Interest by System Organ Class and Preferred Term (Number of Subjects and Occurrences) | | M12, EOS |
| 3.50. | Safety | 201584/primary_07/T3.143 | Summary of Rash Adverse Events of Special Interest by System Organ Class and Preferred Term (Number of Subjects and Occurrences) | | M12, EOS |
| 3.51. | Safety | 201584/primary_07/T3.146 | Summary of Prolongation of the Corrected QT Interval of the ECG in Supratherapeutic Doses Adverse Events of Special Interest by System Organ Class and Preferred Term (Number of Subjects and Occurrences) | | M12, EOS |

| Safety: Tables | | | | | |
|---|---|---|---|---|---|
| **No.** | **Population** | **GSK Standard/ Example Shell** | **Title** | **Programming Notes** | **Deliverable** |
| 3.52. | Safety | 201584/primary_07/T3.149 | Summary of Bipolar Disorder Adverse Events of Special Interest by System Organ Class and Preferred Term (Number of Subjects and Occurrences) | | M12, EOS |
| 3.53. | Safety | 201584/primary_07/T3.152 | Summary of Psychosis Adverse Events of Special Interest by System Organ Class and Preferred Term (Number of Subjects and Occurrences) | | M12, EOS |
| 3.54. | Safety | 201584/primary_07/T3.155 | Summary of Mood Disorders Adverse Events of Special Interest by System Organ Class and Preferred Term (Number of Subjects and Occurrences) | | M12, EOS |
| 3.55. | Safety | 201584/primary_07/T3.158 | Summary of Sleep Disorders Adverse Events of Special Interest by System Organ Class and Preferred Term (Number of Subjects and Occurrences) | | M12, EOS |
| 3.56. | Safety | 201584/primary_07/T3.161 | Summary of Hyperglycaemia Adverse Events of Special Interest by System Organ Class and Preferred Term (Number of Subjects and Occurrences) | | M12, EOS |
| 3.57. | Safety | 201584/primary_07/T3.161 | Summary of Weight Gain Adverse Events of Special Interest by System Organ Class and Preferred Term (Number of Subjects and Occurrences) | | M12, EOS |
| 3.58. | Safety | 201584/primary_07/T3.164 | Summary of Rhabdomyolysis Adverse Events of Special Interest by System Organ Class and Preferred Term (Number of Subjects and Occurrences) | | M12, EOS |

| Safety: Tables | | | | | |
|---|---|---|---|---|---|
| **No.** | **Population** | **GSK Standard/ Example Shell** | **Title** | **Programming Notes** | **Deliverable** |
| 3.59. | Safety | 201584/primary_07/T3.167 | Summary of Pancreatitis Adverse Events of Special Interest by System Organ Class and Preferred Term (Number of Subjects and Occurrences) | | M12, EOS |
| 3.60. | Safety | 201584/primary_07/T3.170 | Summary of Impact on Creatinine Adverse Events of Special Interest by System Organ Class and Preferred Term (Number of Subjects and Occurrences) | | M12, EOS |
| 3.61. | Safety | 201584/primary_07/T3.173 | Summary of Safety in Pregnancy Adverse Events of Special Interest by System Organ Class and Preferred Term (Number of Subjects and Occurrences) | | M12, EOS |
| 3.62. | Safety | 207966/primary_15/T3.109 | Summary of Characteristics of Adverse Events of Special Interest | | M12, EOS |

### 13.13.8. Safety Figures

| Safety: Figures | | | | | |
|---|---|---|---|---|---|
| **No.** | **Population** | **GSK Standard / Example Shell** | **Title** | **Programming Notes** | **Deliverable** |
| **Adverse Events** | | | | | |
| 3.1. | Safety | 201584/primary_07/F3.14 | Plot of Incidence of Intervention Phase Study Drug Injection Site Reaction Adverse Events by Visit (Overall and Common) – CAB and/or RPV | For EOS, remove "Intervention Phase" from the title and include all ISRs from Intervention or Extension phase. | M12, EOS |
| 3.2. | Safety | 201584/primary_07/F3.17 | Plot of Incidence of Grade 3-5 Intervention Phase Study Drug Injection Site Reaction Adverse Events by Visit (Overall and Common) - CAB and/or RPV | For EOS, remove "Intervention Phase" from the title and include all Grade 3-5 ISRs from Intervention or Extension phase. | M12, EOS |
| **Laboratory** | | | | | |
| 3.3. | Safety | LIVER14 | Scatter Plot of Maximum vs. Baseline for ALT | GSK Statistical Display Standard | M12, EOS |
| 3.4. | Safety | LIVER9 | Scatter Plot of Maximum Total Bilirubin vs Maximum ALT – eDISH Plot | GSK Statistical Display Standard | M12, EOS |

### 13.13.9. Virology Tables

| No. | Population | GSK Standard / Example Shell | Title | Programming Notes | Deliverable |
|---|---|---|---|---|---|
| 4.1. | Safety | 201584/primary_17/T7.2 | Viral load, Genotypic and Phenotypic data for Subjects Who Met Confirmed Virologic Failure Criteria | | HL, M12, EOS |
| 4.2. | Safety | 201584/primary_17/T7.4 | Viral Load, Genotypic and Phenotypic Data for Non-CVF Subjects | Only include subjects with available genotypic or phenotypic data. | M12, EOS |

## 13.13.10. Other Tables

| Study Visit Length | | | | | |
|---|---|---|---|---|---|
| **No.** | **Population** | **GSK Standard / Example Shell** | **Title** | **Programming Notes** | **Deliverable** |
| 5.1. | Safety | OTR_T1 | Summary of Study Visit Length (minutes) by Visit and Site Type (Intervention Phase) | | HL, M12 |
| 5.2. | Safety | OTR_T1 | Summary of Study Visit Length (minutes) by Visit and Site (Intervention Phase) | | HL, M12 |

## 13.13.11. ICH Listings

| ICH: Listings | | | | | |
|---|---|---|---|---|---|
| **No.** | **Population** | **GSK Standard / Example Shell** | **Title** | **Programming Notes** | **Deliverable** |
| **Subject Disposition** | | | | | |
| 1. | Enrolled | ES2 | Listing of Reasons for Study Withdrawal | ICH E3<br>Add column for Phase | M12, EOS |
| 2. | Enrolled | SD2 | Listing of Reasons for Study Treatment Discontinuation | ICH E3<br>Add column for Phase | HL, M12, EOS |
| **Protocol Deviations** | | | | | |
| 3. | Enrolled | DV2 | Listing of Important Protocol Deviations | ICH E3<br>Add column for Phase<br>Add a column on the right for “COVID-19 Related”. The possible values in this column are Y and N, where Y indicates the deviation is COVID-19 related and N indicates the deviation is non-COVID-19 related. | M12, EOS |
| 4. | Enrolled | DV2 | Listing of Protocol Deviations Related to COVID-19 | FDA Request<br>Add column for Phase | HL, M12, EOS |
| 5. | Safety | IE3 | Listing of Subjects with Inclusion/Exclusion Criteria Deviations | ICH E3 | M12, EOS |
| **Populations Analysed** | | | | | |
| 6. | Enrolled | SP3 | Listing of Subjects Excluded from Safety Population | ICH E3 | M12 |

| ICH: Listings | | | | | |
|---|---|---|---|---|---|
| **No.** | **Population** | **GSK Standard / Example Shell** | **Title** | **Programming Notes** | **Deliverable** |
| **Demographic and Baseline Characteristics** | | | | | |
| 7. | Safety | DM2 | Listing of Demographic Characteristics | ICH E3 | M12, EOS |
| 8. | Safety | DM9 | Listing of Race | ICH E3 | M12, EOS |
| **Efficacy** | | | | | |
| 9. | Safety | SNAPSHOT11 | Listing of Qualitative and Quantitative Plasma HIV-1 RNA Data | | HL, M12, EOS |
| 10. | Safety | SNAPSHOT12 | Listing of Study Outcome (50 copies/mL cutoff) at Month 12 – Snapshot Analysis | Include both original and LOCF imputed outcomes | HL, M12 |
| 11. | Safety | VF4 | Listing of Plasma HIV-1 RNA and CD4+ Cell Count for subjects with Confirmed Virologic Failure | | M12 |
| **Exposure and Treatment Compliance** | | | | | |
| 12. | Safety | 207966/primary_15/L12 | Listing of Exposure Data | ICH E3<br>Remove Phase Day | M12, EOS |
| **Adverse Events** | | | | | |
| 13. | Safety | AE8 | Listing of All Adverse Events | ICH E3<br>Add Phase/Period, Side/Drug, see gsk1265744/mid207966/primary_15/L19 | HL, M12, EOS |
| 14. | Safety | AE8 | Listing of Grade 3-5 Adverse Events | Add Phase/Period, Side/Drug, see gsk1265744/mid207966/primary_15/L19 | M12 |
| 15. | Safety | AE7 | Listing of Subject Numbers for Individual Adverse Events | ICH E3 | M12, EOS |

| ICH: Listings | | | | | |
|---|---|---|---|---|---|
| **No.** | **Population** | **GSK Standard / Example Shell** | **Title** | **Programming Notes** | **Deliverable** |
| 16. | Safety | PSRAE1 | Listing of Possible Suicidality-Related Adverse Event Data: Event and Description (Section 1-Section 2) | Add Phase | M12 |
| 17. | Safety | PSRAE3 | Listing of Possible Suicidality-Related Adverse Event Data: Possible Cause(s) (Section 3) | Add Phase | M12 |
| 18. | Safety | PSRAE4 | Listing of Possible Suicidality-Related Adverse Event Data (Section 4) | Add Phase | M12 |
| 19. | Safety | PSRAE5 | Listing of Possible Suicidality-Related Adverse Event Data (Section 5-Section 8) | Add Phase | M12 |
| 20. | Safety | 201584/primary_07/L22 | Listing of Changes in Intensity/Grades of Study Drug Injection Site Adverse Events | Remove phase treatment | M12, EOS |
| 21. | Safety | AE8 | Listing of COVID-19 Adverse Events | Add Phase/Period, Side/Drug, see gsk1265744/mid207966/primary_15/L19 | HL, M12, EOS |
| 22. | Safety | PAN12 | Listing of COVID-19 Assessments and Symptom Assessments | | M12, EOS |
| 23. | Safety | PAN5 | Country Level Listing of Start Dates of COVID-19 Pandemic Measures | For EOS: change the title to be “Country Level Listing of Dates of Waves of COVID-19 Pandemic Measures” and use the PAN5A shell. | M12, EOS |
| **Serious and Other Significant Adverse Events** | | | | | |
| 24. | Safety | AE8 | Listing of Fatal Serious Adverse Events | ICH E3<br>Add Phase/Period, Side/Drug | M12, EOS |

| ICH: Listings | | | | | |
|---|---|---|---|---|---|
| **No.** | **Population** | **GSK Standard / Example Shell** | **Title** | **Programming Notes** | **Deliverable** |
| 25. | Safety | AE8 | Listing of Non-Fatal Serious Adverse Events | ICH E3<br>Add Phase/Period, Side/Drug | M12, EOS |
| 26. | Safety | AE14 | Listing of Reasons for Considering as a Serious Adverse Event | ICH E3 | M12, EOS |
| 27. | Safety | AE8 | Listing of Adverse Events Leading to Withdrawal from Study / Permanent Discontinuation of Study Treatment | ICH E3<br>Add Phase/Period, Side/Drug | M12, EOS |
| 28. | Safety | AE8 | Listing of All Adverse Events with Completely Missing Onset Date, Missing Relationship to Study Treatment, Severity and/or Grade | ICH E3<br>Add Phase/Period, Side/Drug, see gsk1265744/mid207966/primary_15/L19 | M12 |
| **Laboratory** | | | | | |
| 29. | Safety | UR2 | Listing of Urinalysis Data for Subjects with Any Value of Potential Clinical Importance | ICH E3<br>Include Grade<br>Note: Potential Clinical Importance is defined as:<br>1. Increase in Protein (dipstick) or Occult Blood (dipstick) post-baseline relative to baseline<br>2. Increase in any DAIDS graded values for Protein, Occult Blood or Glucose relative to baseline<br>3. If microscopy is performed. | M12, EOS |

### 13.13.12. Non-ICH Listings

| Non-ICH: Listings | | | | | |
|---|---|---|---|---|---|
| **No.** | **Population** | **GSK Standard GSK Statistical Display Standard / Example Shell** | **Title** | **Programming Notes** | **Deliverable** |
| **Subject Disposition** | | | | | |
| 30. | Screened | ES7 | Listing of Reasons for Screen Failure | Journal Guidelines | M12, EOS |
| 31. | Screened | ES9 | Listing of Subjects Who Were Rescreened | | M12, EOS |
| 32. | Safety | TA1 | Listing of Planned and Actual Treatments | GSK Statistical Display Standard | M12 |
| **Prior and Concomitant Medications** | | | | | |
| 33. | Safety | 207966/primary_15/Listing 36 | Listing of Prior ART Medications | Remove the column 'Phase during Which Concomitant' | M12, EOS* |
| 34. | Safety | 207966/primary_15/Listing 37 | Listing of Concomitant ART Medications | In case the same medication is concomitant during both intervention and extension phases, list each of them in two separate rows. Add a column "SOC Oral Bridging?" which has values of "Yes" and "No". | HL, M12, EOS |
| 35. | Safety | 207966/primary_15/Listing 38 | Listing of ART Medications Received during Long-term Follow-up Phase | Remove the column 'Phase during Which Concomitant' and "Start Date of the Long-term Follow-up ART/Study Day". | M12, EOS |

| Non-ICH: Listings | | | | | |
|---|---|---|---|---|---|
| **No.** | **Population** | **GSK Standard GSK Statistical Display Standard / Example Shell** | **Title** | **Programming Notes** | **Deliverable** |
| 51. | Safety | POP_L2 | Listing of COVID-19 Vaccine | | EOS |
| **Medical History** | | | | | |
| 36. | Safety | 201584/primary_01/L43 | Listing of Medical History of Seizure | | M12, EOS* |
| **Transition to CAB + RPV LA Marketed Product Status** | | | | | |
| 52. | Safety | POP_L1 | Listing of Transition to CAB + RPV LA Marketed Product Status | | EOS |
| **Efficacy** | | | | | |
| 37. | Safety | CDC4 | Listing of CDC Classification of HIV-1 Infection at Baseline | | M12, EOS* |
| 38. | Safety | CDC5 | Listing of CDC Stage 3 HIV-1 Associated Conditions | Add Phase | EOS |
| **Hepatobiliary (Liver)** | | | | | |
| 39. | Safety | LIVER5 | Listing of Liver Monitoring/Stopping Event Reporting | GSK Statistical Display Standard | M12, EOS |
| 40. | Safety | LIVER15 | Liver Stopping Event Profile | GSK Statistical Display Standard | M12 |
| 41. | Safety | LIVER13 | Listing of Subjects Meeting Hepatobiliary Laboratory Criteria Post-Baseline | GSK Statistical Display Standard | HL, M12, EOS |
| 42. | Safety | LB12 | Listing of ALT, AST, Bilirubin (including Total and Direct Bilirubin), INR, and ALP for Subjects Meeting Hepatobiliary Lab Abnormality Criteria | Add Phase | M12, EOS |

| Non-ICH: Listings | | | | | |
|---|---|---|---|---|---|
| **No.** | **Population** | **GSK Standard GSK Statistical Display Standard / Example Shell** | **Title** | **Programming Notes** | **Deliverable** |
| **ECG** | | | | | |
| 43. | Safety | EG3 | Listing of All ECG Values for Subjects with Any Value of Potential Clinical Importance | GSK Statistical Display Standard<br>By default, the definition of PCI is defined based on QTc value (e.g., QTcF Interval, Aggregate) where a subject has a QTc value >450 or a QTc increase of >30msec. | M12, EOS |
| 44. | Safety | EG5 | Listing of All ECG Findings for Subjects with an Abnormal ECG Finding | GSK Statistical Display Standard | M12, EOS |
| **Other** | | | | | |
| 45. | Safety | 207966/primary_15/L60 | Listing of Exposure Data for Subjects Receiving Oral Bridging | Add column to identify COVID relatedness. | HL, M12, EOS |
| 46. | Safety | 207966/primary_15/L61 | Listing of Dosing Errors and IP Device Malfunctions | Add Phase | M12, EOS |
| 47. | Safety | PREG1 | Listing of Subjects or Partners Who Became Pregnant During the Study | GSK Statistical Display Standard | M12, EOS |
| 48. | Safety | 201584/primary_17/L54 | Listing of Replication Capacity in IN and PR/RT Region | Add Phase | M12 |
| **PK Endpoints** | | | | | |
| 49. | Safety | PK07 | Listing of Plasma CAB Pharmacokinetic Concentration-Time Data | Add column ‘Reason for Collection” on the right. | M12, EOS |

| Non-ICH: Listings | | | | | |
|---|---|---|---|---|---|
| **No.** | **Population** | **GSK Standard GSK Statistical Display Standard / Example Shell** | **Title** | **Programming Notes** | **Deliverable** |
| 50. | Safety | PK07 | Listing of Plasma RPV Pharmacokinetic Concentration-Time Data | Add column 'Reason for Collection" on the right. | M12, EOS |

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

Data Display Specification will be made available on request

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

| | | |
|---|---|---|
| **Title** | : | Reporting and Analysis Plan for A qualitative hybrid III implementation study to identify and evaluate strategies for successful implementation of the cabotegravir + rilpivirine long-acting injectable regimen in the US |
| **Compound Number** | : | GSK1265744 |
| **Clinical Study Identifier** | : | 209493 |
| **Effective Date** | : | 29-OCT-2020 |

**Description:**

- The purpose of this RAP is to describe the planned analyses and output to be included in the Clinical Study Report for Protocol 209493, specifically for clinical data. Any implementation science/health outcome analyses will be detailed in a separate Evidera SAP.
- This RAP will be provided to the study team members to convey the content pertaining to clinical data for the Month 12 and End of Study (EOS) analyses.

**RAP Author(s):**

| Author | Date |
|---|---|
| **Lead** | 23-OCT-2020 |
| PPD<br>Manager, Statistics | |

**RAP Team Reviews:**

**RAP Team Review Confirmations**
**(Method: E-mail)**

| Reviewer | Date |
|---|---|
| PPD<br>PPD (Clinical Scientists, Early Development, ViiV Healthcare) | 27-OCT-2020 |
| PPD<br>PPD Innovation and & Implementation Science (US Health Outcomes, ViiV Healthcare) | 28-OCT-2020 |
| PPD<br>PPD (US Health Outcomes, ViiV Healthcare) | 27-OCT-2020 |
| PPD<br>Principal Programmer/Analyst (Dev Biostats Prog Dev) | 27-OCT-2020 |

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

**Clinical Statistics & Clinical Programming Line Approvals**
**(Method: Pharma TMF eSignature)**

| Approver | Date |
|---|---|
| PPD<br>Statistics Leader (Dev Biostats Stats Dev) | 29-OCT-2020 |
| PPD<br>Programming Leader (Dev Biostats Prog Dev) | 29-OCT-2020 |

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# 1. INTRODUCTION

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

| **Revision Chronology:** | | |
|---|---|---|
| 2018N382441_00 | 02-JAN-2019 | Original |
| 2018N382441_01 | 02-APR-2019 | Amendment No. 1 |
| The reasons for this amendment include: addition of exclusion criterion regarding known major resistance mutations at Screening, clarification of timing for collection of visit length, removal of consent requirement for study staff, correction to allowable window around the Month 3 dosing visit, clarification of pregnancy testing requirements at Screening, clarification of wording to allow a single re-screen per subject, removal of color of vial stopper in product description to allow flexibility of packaging for cabotegravir and rilpivirine suspension, clarification of ECG collection during the study, clarification of wording to allow qualitative analyses to be performed by a CRO under GSK oversight. | | |
| 2018N382441_02 | 15-MAY-2020 | Amendment No.2 |
| The purpose of this amendment is to include an Appendix related to COVID-19 Pandemic and Clinical Trial Continuity. This appendix will replace the previous Appendix 11, and "Protocol Amendment History," will be included as Appendix 12. | | |

# 2. SUMMARY OF KEY PROTOCOL INFORMATION

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

There were no changes or deviations to the originally planned statistical analysis specified in protocol amendment 02 [(Dated: 15/May/2020)].

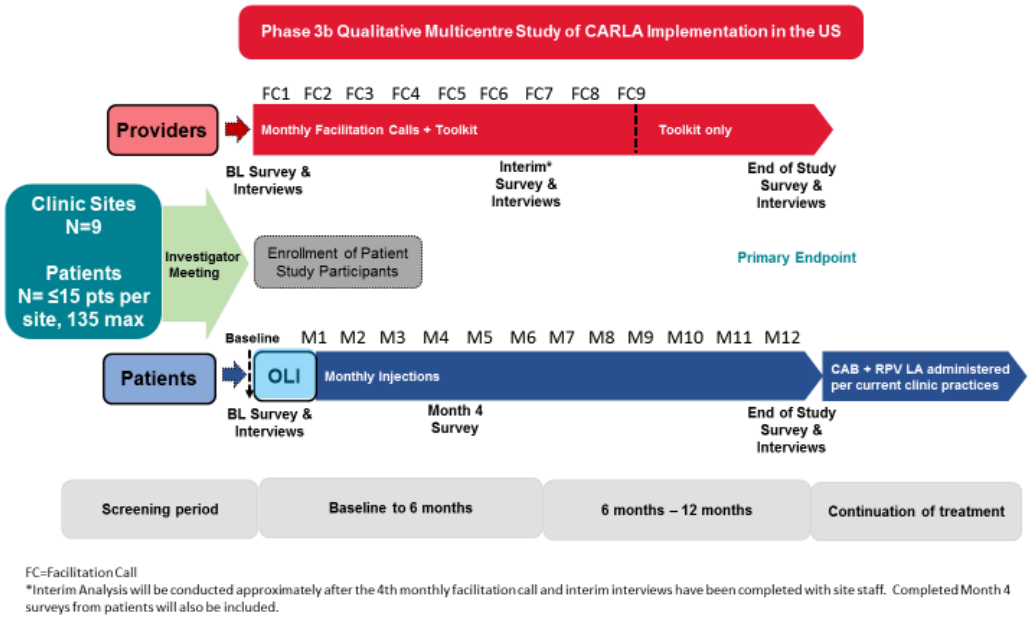
## 2.2. Study Objective(s) and Estimand(s) / Endpoint(s)

| **Objectives** | **Estimands / Endpoints** |
|---|---|
| **Primary** | **Primary** |
| • To evaluate acceptability, appropriateness, and feasibility of delivering CAB+RPV LA | • Acceptability of Intervention Measure (AIM), Intervention Appropriateness Measure (IAM), and Feasibility of Intervention Measure (FIM). Assessed quantitatively by staff study participants at baseline- prior to any Month 1 visits, after at least 4 monthly facilitation calls and upon completion of all Month 12 visits at that site.<br>• Acceptability of Intervention Measure (AIM) and Intervention Appropriateness Measure (IAM). Assessed quantitatively by patient study participants at Month 1 prior to first injection, Month 4 and Month 12 |
| **Secondary** | **Secondary** |
| • To evaluate organizational facilitators and barriers | • Facilitators/Barriers: Semi-Structured Interview (SSI) conducted with staff study participants at baseline- prior to any Month 1 visits, after at least 4 monthly facilitation |

| Objectives | Estimands / Endpoints |
|---|---|
| | calls and upon completion of at least 50% of Month 12 visits at that site.<br>• Barriers, facilitators and best practice sharing amongst clinics assessed by short-term facilitation (coaching calls) for at least 6 months. These will be a combination of structured questions and open-ended questions.<br>• Use of support materials/toolkit assessed via Survey responses of staff study participants prior to any Month 1 visits, after at least 4 monthly facilitation calls and upon completion of all Month 12 visits at a site.<br>• Use of support materials/toolkit assessed via Survey responses of patient study participants via Survey responses at Month 1 and Month 4 and Month 12, as well as SSI responses prior to Month 1 and at Month 12. |
| • Patient Facilitators and Barriers | • Facilitators/Barriers: Semi-Structured Interviews (SSI) conducted with patient study participants prior to Month 1 and at Month 12. |
| • Implementation Fidelity | • Injections occurring within target window from the expected injection date<br>• Use of support materials/toolkit assessed through SSI of staff study participants at Day 1, after at least 4 monthly facilitation calls and upon completion of at least 50% of Month 12 visits at that site |
| • Implementation Sustainability | • Program Sustainability Assessment Tool (PSAT) assessed by staff study participants at Month 12 |
| • To measure patient satisfaction with process (timeliness of visits, length of visit, patient education) | • Patient Survey responses at Month 1, Month 4 and Month 12.<br>• Patient SSI responses prior to Month 1 and at Month 12<br>• Length of patient visit from arrival until departure from clinic at Month 1, Month 5 and Month 11 |
| • To evaluate the antiviral and immunologic effects, safety and tolerability, and viral resistance of CAB LA + RPV LA for all patients | • Proportion of participants with plasma HIV-1 RNA <50 c/mL over time<br>• Proportion of participants with confirmed virologic failure (CVF) over time<br>• Incidence of treatment emergent genotypic and phenotypic resistance to CAB and RPV in patients with CVF<br>• Incidence and severity of AEs and laboratory abnormalities over time<br>• Proportion of participants who discontinue treatment due to AEs over time<br>• Reported injection site reactions over time<br>• Absolute values and changes in laboratory parameters over time |

## 2.3. Study Design

**Overview of Study Design and Key Features**




FC=Facilitation Call
*Interim Analysis will be conducted approximately after the 4th monthly facilitation call and interim interviews have been completed with site staff. Completed Month 4 surveys from patients will also be included.

N=115 patients; Open label with respect to treatment; patients randomized to CAB LA+RPV LA Interview: CAB LA + RPV LA Non-Interview

| | |
|---|---|
| **Design Features** | • A qualitative hybrid III implementation study to identify and evaluate strategies for successful implementation of the cabotegravir + rilpivirine long-acting injectable regimen in the US<br>• The CUSTOMIZE study comprises of screening phase (up to 21 days), Intervention Phase from Day 1 to Month 12, including Oral Lead-in, long term follow-up (LTFU) phase, and extension phase. During screening phase all clinical and laboratory assessments of eligibility must be performed and reviewed. Participants may be re-screened once |
| **Dosing** | • Intervention Phase is Open label with respect to treatment;<br>• Intervention Phase: randomized 1:3 to CAB LA+RPV LA Interview:CAB LA + RPV LA Non-Interview<br>• Randomized at Day 1 (1:3) to receive CAB LA + RPV LA Interview or CAB LA + RPV LA Non-interview respectively<br>• GSK Randall NG used to generate randomization schedule for interview group assignments |
| **Time & Events** | • Refer to Appendix 2: Schedule of Activities |
| **Treatment Assignment** | • CAB LA+RPV LA (N=115) |
| **Interim Analysis** | • Analysis at Month 4 to provide preliminary data to inform planning for the initial commercial availability of the CAB LA + RPV LA regimen<br>• Primary analysis will be conducted at Month 12 |

## 2.4. Statistical Hypotheses / Statistical Analyses

No formal hypothesis testing is planned.

# 3. PLANNED ANALYSES

This RAP describes standard analyses that will be applied to descriptively summarize clinical adverse events, laboratory evaluations, virologic parameters and other clinical safety and efficacy outcomes.

Details pertaining to reporting of survey/interview data and health outcomes/effectiveness analyses will be described in a separate analysis plan provided by Evidera or other CRO partner under GSK's oversight.

At least two analyses will be conducted to evaluate primary and secondary objectives of the protocol: an interim analysis at Month 4 and a primary analysis at Month 12.

A final end-of-study (EOS) analysis will be conducted when all subjects have completed the study.

## 3.1. Interim Analyses

One interim analysis at Month 4 was performed to provide preliminary data to inform planning for the initial commercial availability of the CAB + RPV LA regimen. No formal criteria for stopping or amending the study based on the interim analysis are envisioned. Analysis and reporting details can be found in the standalone Month 4 interim analysis RAP.

## 3.2. Final Analyses

The planned Month 12 primary analysis will be performed after the completion of the following sequential steps:

1. All participants have completed Month 12 of the study as defined in the protocol.
2. All required database cleaning activities have been completed and final database release (DBR), source data lock (SDL) and database freeze (DBF) have been declared by Data Management.

# 4. ANALYSIS POPULATIONS

| Population | Definition / Criteria | Analyses Evaluated |
|---|---|---|
| Screened | • All participants who were screened for eligibility | • Study Population |
| Enrolled | • All participants who passed screening and entered the study (i.e. were administered study treatment). | • Study Population |
| Safety | • All participants who received at least one dose of study treatment. | • Study Population, Safety, Efficacy, Virology, PK, Other Assessments |

Refer to Appendix 13: List of Data Displays which details the population used for each display.

## 4.1. Protocol Deviations

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

Protocol deviations will be tracked by the study team throughout the conduct of the study in accordance with the Protocol Deviation Management Plan [Version 1.0,17-Jun-2019].

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

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

Protocol deviations related to the implementation process, and not the clinical conduct of the study will be reported separately. The identification and categorization of PDs as important may be different for implementation PDs vs those associated with the clinical conduct of the study.

# 5. CONSIDERATIONS FOR DATA ANALYSES AND DATA HANDLING CONVENTIONS

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

| Treatment Group Descriptions | |
|---|---|
| **Data Displays for Reporting** | |
| **Description** | **Order in TLF** |
| CAB LA +RPV LA | 1 |

## 5.2. Baseline Definitions

For all endpoints the baseline value will be the latest pre-treatment (See Table 10) assessment with a non-missing value, including those from unscheduled visits. If time is not collected, Day 1 assessments are assumed to be taken prior to first dose and used as baseline.

Electrocardiograms (ECGs) are to be performed in triplicate on Screening visit. The baseline value for an ECG parameter will be the mean of the last pre-treatment set of assessments from the same date so long as at least one of the triplicate assessments is available.

## 5.3. Multicentre Studies

In this multicentre global study, enrolment will be presented by investigator and Site type.

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

### 5.4.1. Covariates and Other Strata

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

| Category | Details |
|---|---|
| Covariates | Site Type |

### 5.4.2. Examination of Subgroups

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

- If the percentage of participants is small within a subgroup category, then the subgroup categories may be combined.

| Subgroup | Categories |
|---|---|
| Site Type | AIDS Healthcare Foundation, Federally Qualified Health Center, Health Maintenance Organization, Private Practice, University |

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

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

| Section | Component |
|---|---|
| 13.3 | Appendix 3: Assessment Windows |
| 13.4 | Appendix 4: Study Phases and Treatment Emergent Adverse Events |
| 13.5 | Appendix 5: Data Display Standards & Handling Conventions |
| 13.6 | Appendix 6: Derived and Transformed Data |
| 13.7 | Appendix 7: Reporting Standards for Missing Data |
| 13.8 | Appendix 8: Values of Potential Clinical Importance |

# 6. STUDY POPULATION ANALYSES

## 6.1. Overview of Planned Study Population Analyses

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

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

# 7. EFFICACY ANALYSES

Implementation Science/Health Outcomes endpoints will form the basis for the overall primary analysis of the study, and details of implementation science/health outcomes analyses are documented in a separate Evidera SAP. Clinical efficacy endpoints are evaluated as secondary objectives for this study.

## 7.1. Secondary Efficacy Analyses

### 7.1.1. Endpoint / Variables

- Proportion of participants with Plasma HIV-RNA < 50 copies/mL and plasma HIV-1 RNA ≥ 50 c/mL, respectively, over time using the FDA Snapshot Algorithm. See Section 13.9 for Snapshot Algorithm details.

Other secondary efficacy endpoints:

- Proportion of participants with confirmed virologic failure (CVF) over time
- Absolute values and changes from Baseline CD4+ cell count over time

### 7.1.2. Population of Interest

Secondary efficacy analyses will be based on the Safety population, unless otherwise specified.

### 7.1.3. Strategy for Intercurrent (Post-Randomization) Events

- Participants with last available HIV-1 RNA measurement less than 50 copies/mL while the participant is on treatment within the analysis visit window of interest are classified as HIV-1 RNA < 50 c/mL. Participants without evaluable HIV-RNA data for the visit of interest or who change treatment not permitted per protocol before the analysis window are considered non-responders.
- Participants with last available HIV-1 RNA measurement greater or equal to 50 copies/mL while the participant is on treatment within the analysis visit window of interest are classified as HIV-1 RNA ≥ 50 c/mL. Participants without evaluable HIV-RNA data for the visit of interest and who discontinue treatment for reasons not related to adverse event while having HIV-1 RNA ≥50 copies/mL at time of

discontinuation or who change study treatment not permitted per protocol before the analysis window are also classified as having HIV-RNA ≥50 copies/mL.

Missing viral load values for reasons related to COVID-19 issues (e.g. participant is unable to have viral load assessed due to barriers in attending the clinic during the pandemic or COVID-19 related adverse events leading to treatment discontinuation) will be imputed using an LOCF approach in which the last on-treatment viral load value will be carried forward and used in place of missing values.

### 7.1.4. Statistical Analyses / Methods

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

Unless otherwise specified, endpoints / variables defined in Section 7.1.1 will be summarised using descriptive statistics, graphically presented (where appropriate) and listed.

#### 7.1.4.1. Statistical Methodology Specification

| **Endpoint / Variables** |
|---|
| • Proportion of participants with plasma HIV-1 RNA < 50 c/mL over time using the FDA Snapshot algorithm (Safety population)<br>• Proportion of participants with plasma HIV-1 RNA ≥ 50 c/mL over time using the FDA Snapshot algorithm (Safety population) |
| **Results Presentation** |
| • The proportion of participants with HIV-1 RNA < 50 c/mL and HIV-1 RNA ≥ 50 c/mL, respectively, at each planned visit with corresponding 95% confidence intervals calculated using the Clopper-Pearson exact method.<br>• The proportion of participants in each Snapshot study outcome category and sub-category will be summarized at Month 12, in which default sub-categories have been expanded to present COVID-19 vs. non COVID-19 related impact (as described in Section 13.9). |

## 8. SAFETY ANALYSES

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

For the Month 12 analysis, safety displays will summarize data across the combined Intervention + Extension Phases, unless otherwise specified in the display title presented in Appendix 13: List of Data Displays.

### 8.1. Adverse Events Analyses

Adverse events analyses including the analysis of adverse events (AEs), Serious (SAEs), COVID-19 AEs, and other significant AEs will be based on GSK Core Data Standards. The details of the planned displays are provided in Appendix 13: List of Data Displays.

### 8.1.1. Injection Site Reaction Adverse Events

Injection Site Reaction (ISR) adverse events of interest are those from study drug injections.

For the summary of Injection Site Reaction Adverse Events by Visit and Maximum Severity (Overall and by Common ISRs), ISRs will be assigned based on onset date to the most recent planned IM injection visit prior or equal to the AE onset date.

Maximum grade at each visit will be derived as the maximum grade among ISRs assigned to the particular visit, with consideration for whether the summary applies to a particular preferred term (vs. across preferred terms), or drug-related associated to CAB and/or RPV.

Drug-related ISRs (based on investigator discretion) will be attributed to the causal agent (CAB vs. RPV) when this can be determined specifically based on the side of injection administration and the side of the reported ISR (as collected in the eCRF). If we are unable to determine the causal agent in those cases where both drugs are given on one side and the ISR is reported non-specifically, then the attribution to a specific causal agent will remain unknown.

Common study drug ISR adverse events are defined by MedDRA preferred terms including injection site pain, injection site induration, injection site nodules and preferred terms of any other ISR reported by ≥5% of participants overall.

## 8.2. Adverse Events of Special Interest Analyses

A comprehensive list of MedDRA terms based on clinical review will be used to identify Adverse Events of Special Interest (AESI). Changes to the MedDRA dictionary may occur between the start of the study and the time of reporting and/or emerging data from on-going studies may highlight additional adverse events of special interest, therefore the list of terms to be used for each event of interest and the specific events of interest will be based on the safety review team (SRT) agreements in place at the time of reporting. The details of the current planned grouping, including Standardized MedDRA Query (SMQ) values (as applicable), and planned displays are provided in Appendix 10: AESI identification and Appendix 13: List of Data Displays.

## 8.3. Clinical Laboratory Analyses

Laboratory evaluations will be based on GSK Core Data Standards. The details of the planned displays are in Appendix 13: List of Data Displays.

## 8.4. Other Safety Analyses

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

# 9. PHARMACOKINETIC ANALYSES

## 9.1. Drug Concentration Measures

Available concentration-time data for CAB and RPV will be presented in listings as specified in Appendix 13: List of Data Displays and will be based on GSK Data Standards and statistical principles.

Refer Appendix 5: Data Display Standards & Handling Conventions (Section 13.5.3 Reporting Standards for Pharmacokinetic).

# 10. VIROLOGY

## 10.1. Genotypic and Phenotypic Data

Available genotypic and phenotypic data at all collection timepoints will be presented by subject (separately for CVF and Non-CVF subjects), as specified in Appendix 13: List of Data Displays.

# 11. OTHER ANALYSES

## 11.1. Study Visit Length

The details of the planned displays for study visit length data are in Appendix 13: List of Data Displays and will be based on GSK Data Standards and statistical principles.

# 12. REFERENCES

Wensing AM, et al. 2019 update of the drug resistance mutations in HIV-1. *Topics in antiviral medicine.* 2019;27:111-121.

# 13. APPENDICES

## 13.1. Appendix 1: Exclusions from Per Protocol Population

Instream and final analysis population reviews as per SOP 130050 are not planned for this study because it does not include a Per-Protocol population.

## 13.2. Appendix 2: Schedule of Activities

### 13.2.1. Protocol Defined Schedule of Events

#### 13.2.1.1. Schedule of Activities for Patient Study Participants (CAB LA + RPV LA Monthly Administration)

| Procedures | Screening[a] | Intervention Period | | | | | | | | | | | | WD[m] |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | Day 1 | Month 1 | Month 2 | Month 3 | Month 4 | Month 5 | Month 6 | Month 7 | Month 8 | Month 9 | Month 10[b] | Month 11[b] | Month 12[b] | |
| Written Informed Consent | X | | | | | | | | | | | | | | |
| Demography | X | | | | | | | | | | | | | | |
| Eligibility Verification | X | | | | | | | | | | | | | | |
| Physical Exam | X | | | | | | | | | | | | | | |
| Medical History | X | | | | | | | | | | | | | | |
| Center for Disease Control and Prevention (CDC) Classification | X | | | | | | | | | | | | | | |
| Randomization for interviews | | X | | | | | | | | | | | | | |
| Rapid Plasma Reagin (RPR) | X | | | | | | | | | | | | | | |

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| Procedures | Screening[a] | Intervention Period | | | | | | | | | | | | | WD[m] |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | Day 1 | Month 1 | Month 2 | Month 3 | Month 4 | Month 5 | Month 6 | Month 7 | Month 8 | Month 9 | Month 10[b] | Month 11[b] | Month 12[b] | |
| Symptom Directed Physical Exam and Medical Assessment[c] | X | X | X | X | | X | | X | | X | | X | | X | X |
| Injection site reaction (ISR) assessment | | | X | X | X | X | X | X | X | X | X | X | X | X | X |
| Vital Signs (temperature, blood pressure [BP], heart rate [HR])[d] | X | X | X | X | | X | | X | | | X | | | X | X |
| Weight, Height & body mass index (BMI)[e] | X | X | X | | | | | X | | | | | | X | X |
| HIV Associated Conditions, AE and serious adverse event (SAE) Assessments& Con Meds | X | X | X | X | | X | | X | | X | | X | | X | X |
| 12-Lead ECG[f] | X | | | | | | | | | | | | | | X |
| Clinical Chemistry and | X | X | X | X | | X | | X | | | X | | | X | X |

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| Procedures | Screening[a] | Intervention Period | | | | | | | | | | | | | WD[m] |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | Day 1 | Month 1 | Month 2 | Month 3 | Month 4 | Month 5 | Month 6 | Month 7 | Month 8 | Month 9 | Month 10[b] | Month 11[b] | Month 12[b] | |
| Hematology | | | | | | | | | | | | | | | |
| Pregnancy Testing (U)rine or (S)erum[g] | U | U | U | U | U | U | U | U | U | U | U | U | U | U | U |
| HIV-1 RNA | X | X | X | X | | X | | X | | X | | X | | X | X |
| Plasma sample for storage[h] | | X | X | X | | X | | X | | X | | X | | X | X |
| CD4+cell counts | X | X | X | X | | X | | X | | | X | | | X | X |
| Urinalysis | X | | | | | | | | | | | | | | X |
| Glucose | X | | | | | | | | | | | | | | |
| Prothrombin time (PT)/ partial thromboplastin time (PTT)/ international normalized ratio (INR) | X | | | | | | | | | | | | | | X |
| Oral study product dispensation | | X | | | | | | | | | | | | | |
| LA study product administration[i] | | | X[l] | X | X | X | X | X | X | X | X | X | X | X | |

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| Procedures | Screening[a] | Intervention Period | | | | | | | | | | | | WD[m] |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | Day 1 | Month 1 | Month 2 | Month 3 | Month 4 | Month 5 | Month 6 | Month 7 | Month 8 | Month 9 | Month 10[b] | Month 11[b] | Month 12[b] | |
| Participant Visit Reminder Contact | X | X | X | X | X | X | X | X | X | X | X | X | X | X | |
| Participant Contact Detail Confirmation | X | X | X | X | X | X | X | X | X | X | X | X | X | X | |
| Record study visit length[j] | | | X | | | | X | | | | | | X | | |
| Patient Questionnaire | | | X | | | X | | | | | | | | X | |
| Selected Patient Interviews (SSI)[k] | | X | | | | | | | | | | | | X | |

See footnote "b" for continuation of visit schedule after Month 12, if required. Subjects will continue on study until the CAB + RPV LA regimen is either locally approved and commercially available, the participant no longer derives clinical benefit or meets a protocol-defined reason for discontinuation or until development is terminated.

a. A screening visit will be conducted within 21 days of Day 1. However, it is preferred for Day 1 to be conducted as soon as practical after all screening results are available.
b. Continue this pattern for visits for the remainder of the study if needed, until commercial CAB + RPV LA is available. For example, Month 13 will be conducted as per Month 10, Month 14 will be conducted as per Month 11, Month 15 will be conducted as per Month 12, Month 16 will be conducted as per Month 10, and so on. The exception to this pattern is that no questionnaires, study visit length collection, or patient interviews will be conducted after the Month 12 visit.
c. Physical exams should be conducted as part of normal routine clinical care but data will not be collected in the electronic case report form (eCRF). Medical assessments include any decisions the study staff must make for participant management.
d. Measure vital signs after about 5 minutes of rest in a semi-supine position.
e. Height collected at Day 1 only.
f. At Screening, ECGs should be performed in triplicate at least 5 minutes apart and following 5 minutes of rest in a semi-supine position. ECG evaluations performed at subsequent visits should be obtained after dosing, preferably 2-4 hours post dosing. ECG at Withdrawal should be performed following 5 minutes of rest in a semi-supine position.

g. A (-) urine pregnancy test is required prior to any injection and as required by medical monitor after a treatment interruption. A (+) urine test should be confirmed with a stat serum test. If (+), participant will need to be withdrawn. A Serum pregnancy test should be performed at any time pregnancy is suspected by the Investigator and may be used in place of a urine test at the discretion of the investigator.
h. Plasma for storage samples are collected for possible future analyses, back-up in cases of loss/damage in transit, geno/pheno analyses for virologic failures or PK in the event of maladministration or virologic failure.
i. Monthly injections are 1 x CAB LA 600 mg IM + 1 x RPV LA 900 mg IM at Month 1. Subsequent injections beginning at Month 2 are 1 x CAB LA 400 mg IM + 1 x RPV LA 600 mg IM. If possible, injections should be spaced approximately 2 cm from one another and from the site of any previous injection and/or any injection site reaction. Bring RPV LA to approximately room temperature prior to injecting. Time and location of injection (right or left) as well as needle length used will be collected in the eCRF. **IM dosing is expected to occur during the month in which the participant's projected visit falls (as according to the Day 1 visit). A dosing window of +0 / -7 days from date of projected visit is stipulated for IM dosing at Month 2 and Month 3. A (+ or -) 7 day window from date of projected visit is stipulated for IM dosing beginning at Month 4. All decisions regarding dose interruption/ resumption must be discussed with the medical monitor in advance.**
j. Length of study visit from arrival until departure from clinic will be evaluated. Time of arrival, time of appointment, and departure times will be recorded in the eCRF.
k. The first semi-structured interview will be scheduled between Day 1 and prior to Month 1 visit. The end of study SSI will be scheduled within approximately 2 weeks following the Month 12 visit.
l. **Note:** Patient study participants with ≥ Grade 1 LFTs at screening and or day 1 must be discussed with the Medical Monitor prior to initiation of LA dosing; continuation in the study or progression onto LA dosing may require additional evaluations, including labs drawn after a period of oral dosing with CAB + RPV.
m. Follow Up Visit - Conduct ~4 weeks after the last dose of investigational product (IP) if not entering Long-Term Follow Up and only if the participant has ongoing AEs or lab abnormalities at the last on-study visit. May be conducted by telephone.

### 13.2.1.2. Schedule of Assessments Table for Staff Study Participants

| Procedures | Prior to Enrollment | Intervention Period (Month) | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | Day 1 | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 12 |
| Staff Study Participant Questionnaire | | X[a] | | | | X[b] | | | | | | X[b] |
| Staff Study Participant Interviews (SSI) | | X[a] | | | | X[b] | | | | | | X[b] |
| Staff Study Participant Monthly Facilitation Calls[c] | | X | X | X | X | X | X | X | X | X | X | |

a. Questionnaire and interview should be conducted prior to the first patient receiving their first CAB + RPV LA injection at that site.

b. Questionnaire and interview should be conducted within approximately 4 weeks of the targeted subject visit at each site for Month 4 and after at least 50% of patient study participant visits at Month 12.

c. Facilitation calls will continue during the enrollment period until the last enrolled subject achieves their Month 6 study visit.

### 13.2.1.3. Schedule of Activities Table for Patient Study Participants (Long Term Follow Up) [a]

| Procedures for Long-Term Follow Up[a] | Month 3 | Month 6 | Month 9 | Month 12 | WD | Notes |
|---|---|---|---|---|---|---|
| HIV Associated Conditions, AE and SAE Assessments, Con Meds | X | X | X | X | X | Every effort should be made to enter participants into the Long-Term Follow Up if they withdraw from or discontinue the study after receiving at least one dose of CAB LA and / or RPV LA.<br>a. The start of the 52-week follow-up period begins the day of the last CAB LA and/or RPV LA dose.<br>b. A PK sample for storage should be collected in the event of virologic failure during the LTFU phase<br>c. Women of childbearing potential only. U=urine<br>d. Women of childbearing potential should continue to receive counselling on the need to use adequate contraception for the entirety of the Long-Term Follow-Up Period.<br>e. Investigators must discuss choice of HAART regimen and timing of initiation with the medical monitor before initiating. |
| HIV-1 RNA | X | X | X | X | X | |
| CD4+ cell counts | X | X | X | X | X | |
| Plasma for Storage | X | X | X | X | X | |
| PK Sample for Storage[b] | | | | | | |
| Clinical Chemistry and Hematology | X | X | X | X | X | |
| Pregnancy Testing[c] | U | U | U | U | U | |
| Urinalysis | | | | X | X | |
| PT/PTT/INR | | | | X | X | |
| Contraception Counselling[d] | X | X | X | X | X | |
| HAART Dispensation[e] | X | X | X | X | X | |

## 13.3. Appendix 3: Assessment Windows

### 13.3.1. Definitions of Assessment Windows for Analyses

Laboratory data, vital signs, ECGs, and genotypic/phenotypic data will be assigned to assessment windows according to actual dates rather than the nominal visit labels as recorded on the eCRF or in the laboratory database.

Prior to visit slotting, assessments are first assigned to a study phase (Screening, Intervention Phase, Extension, or Long Term Follow Up) as defined in Section 13.4.1.

According to the protocol, the nominal target study visit date will be based on the first injection, the Month 1 date. For instance, if Month 1 occurred on July 7th, all subsequent visits are expected to occur on the 7th of each month such that subsequent visits will be August 7th, September 7th, October 7th, etc. Since there are not >28 days in each month of the year, if the Month 1 injection occurred on the 29th, 30th, or 31st of the month, then the target study visit date for the remainder of the visits will be the 28th of the month.

The nominal target study visit day is derived as

- **M1 Target Day** = Date of Actual M1 Injection Visit Date – Date of First Oral lead-in Dose + 1, if subject receives M1 injection; else M1 Target Day = 30.
- **Mx Target Day** = Mx Nominal Target Study Visit Date – Date of First Oral lead-in Dose + 1, for x=2,3, …

Assessment windows will be derived based on the midpoint between two consecutive planned target study visit dates. For the Snapshot efficacy data, the same approach will be used, except for Month 12, which will use a ± 6-week window around the projected target study visit date at Month 12.

For parameters which are not scheduled to be assessed at visits, the all-inclusive assessment windows will still be used; however, data summaries will only report scheduled visits. Assessments at unscheduled visits will be included in summaries of worst-case values across visit (e.g. during the intervention phase) and in data listings, as well any algorithms that make use of additional data (e.g., Snapshot).

**Table 1 Assessment Windows for Screening, Intervention and Extension Phase Data (Excluding HIV-1 RNA and PK data)**

| Target (Study Day) | Analysis Window | | Analysis Timepoint |
|---|---|---|---|
| | Beginning Timepoint | Ending Timepoint | |
| Day of earliest record | Assessment Study Day ≤1 | | Screening |
| For subjects discontinuing prior to receiving first injection: | | | |
| 30 | Assessment Study Day = 2 | Study Day of Last CAB/RPV Oral Dose+1 | Month 1 |
| | Assessment Study Day > (Study Day of Last CAB/RPV Oral Lead-in Dose +1) | | Follow-up |
| For subjects receiving first injection: | | | |
| Day of First Injection | Study Day = 2 | M1 target day + *floor* [(M2 target day – M1 target day)/2] | Month 1 |
| M2 Target Day | M1 target day + *floor* [(M2 target day – M1 target day)/2] + 1 | M2 target day + *floor* [(M4 target day – M2 target day)/2] | Month 2 |
| M4 Target Day | M2 target day + *floor* [(M4 target day – M2 target day)/2] + 1 | M4 target day + *floor* [(M6 target day – M4 target day)/2] | Month 4 |
| M6 Target Day | M4 target day + *floor* [(M6 target day – M4 target day)/2] + 1 | M6 target day + *floor* [(M9 target day – M6 target day)/2] | Month 6 |
| M9 Target Day | M6 target day + *floor* [(M9 target day – M6 target day)/2] + 1 | M9 target day + *floor* [(M12 target day – M9 target day)/2] | Month 9 |
| M12 Target Day | M9 target day + *floor* [(M12 target day – M9 target day)/2] + 1 | M12 target day + *floor* [(M15 target day – M12 target day)/2] | Month 12 |
| M15 Target Day | M12 target day + *floor* [(M15 target day – M12 target day)/2] + 1 | M15 target day + *floor* [(M18 target day – M15 target day)/2] | Month 15 |
| M18 Target Day | M15 target day + *floor* [(M18 target day – M15 target day)/2] + 1 | M18 target day + *floor* [(M21 target day – M18 target day)/2] | Month 18 |
| M***x*** Target Day | M(***x-3)*** target day - *floor* [(M***x*** target day – M(***x-3***) target day)/2] + 1 | M***x*** target day + *floor* [(M(***x+3***) target day – M***x*** target day)/2] | Month ***x*** For ***x*** = 21, 24, etc. |
| For subjects who permanently discontinue study treatment: | | | |
| | Assessment Study Day > Max (Study Day of Last Dose of Oral Study Treatment (CAB+RPV or SOC Bridging) + 1, Study Day of Last CAB + RPV Injection + 35) | | Follow-up |

**Table 2 Assessment Windows for Screening and Intervention Phase HIV-1 RNA Data**

| Target (Study Day) | Analysis Window | | Analysis Timepoint |
|---|---|---|---|
| | Beginning Timepoint | Ending Timepoint | |
| Day of earliest record | Assessment Study Day ≤1 | | Screening |
| | For subjects discontinuing prior to receiving first injection: | | |
| 28 | Assessment Study Day = 2 | Study Day of Last Oral Lead-in Dose +1 | Month 1 |
| | Assessment Study Day > (Study Day of Last CAB/RPV Oral Lead-in Dose +1) | | Follow-up |
| | For subjects receiving first injection: | | |
| Date of First Injection | Study Day = 2 | M1 target day + *floor* [(M2 target day – M1 target day)/2] | Month 1 |
| M2 Target Day | M1 target day + *floor* [(M2 target day – M1 target day)/2] +1 | M2 target day + *floor* [(M4 target day – M2 target day)/2] | Month 2 |
| M4 Target Day | M2 target day + *floor* [(M4 target day – M2 target day)/2] + 1 | M4 target day + *floor* [(M6 target day – M4 target day)/2] | Month 4 |
| M6 Target Day | M4 target day + *floor* [(M6 target day – M4 target day + 1 | M6 target day + *floor* [(M8 target day – M6 target day)/2] | Month 6 |
| M8 Target Day | M6 target day + *floor* [(M8 target day – M6 target day)/2] + 1 | M8 target day + *floor* [(M10 target day – M8 target day)/2] | Month 8 |
| M10 Target Day | M8 target day + *floor* [(M10 target day – M8 target day)/2] + 1 | M12 target day – 43 | Month 10 |
| M12 Target Day | M12 target day - 42 | M12 target day + 42 | Month 12 |
| M13 Target Day | Assessment Study Day > M12 target day + 42 | | Month 13 |
| For subjects who permanently discontinue study treatment during the Intervention Phase: | | | |
| | Assessment Study Day > Max (Study Day of Last Dose of Oral Study Treatment (CAB+RPV or SOC Bridging) +1, Study Day of Last CAB + RPV Injection + 35) | | Follow-up |

**Table 3 Assessment Windows for Extension Phase HIV-1 RNA Data**

| Target (Study Day) | Analysis Window | | Analysis Timepoint |
|---|---|---|---|
| | Beginning Timepoint | Ending Timepoint | |
| M13 Target Day | Study Day of Nominal Week 13 Visit | M13 target day - *floor* [(M15 target day – M13 target day)/2] | Month 13 |
| M15 Target Day | M13 target day - *floor* [(M15 target day – M13 target day)/2] + 1 | M15 target day + *floor* [(M17 target day – M15 target day)/2] | Month 15 |
| M***x*** Target Day | M(***x-2***) target day - *floor* [(M***x*** target day – M(***x-2***) target day)/2] + 1 | M***x*** target day + *floor* [(M(***x+2***) target day – M***x*** target day)/2] | Month ***x*** For ***x*** =17, 19 etc. |
| For subjects who permanently discontinue study treatment during the Extension Phase: | | | |
| | Assessment Study Day > Max (Study Day of Last Dose of Oral Study Treatment (CAB+RPV or SOC Bridging) +1, Study Day of Last CAB + RPV Injection + 35) | | Follow-up |

**Table 4 Assessment Windows for Study Visit Length Data (Intervention and Extension Phase)**

| Target (Study Day) | Analysis Window | | Analysis Timepoint |
|---|---|---|---|
| | Beginning Timepoint | Ending Timepoint | |
| Study Day of Actual M1 Injection | Study Day of Actual M1 Injection | | Month 1 |
| Study Day of Actual M5 Injection | Study Day of Actual M5 Injection | | Month 5 |
| Study Day of Actual M11 Injection | Study Day of Actual M11 Injection | | Month 11 |
| Study Day of Actual M14 Injection | Study Day of Actual M14 Injection | | Month 14 |
| Study Day of Actual M***x*** Injection | Study Day of Actual M***x*** Injection | | Month ***x*** For ***x***=17, 20, etc. |
| | If none of the above, then Analysis Timepoint = Other | | |

**Table 5 Assessment Windows for Summaries of Long-Term Follow-up Phase Data from Subjects who Received at Least One Injection of CAB+RPV and Permanently Discontinued from the Study**

| Day of Assessment | Assessment Window | Target LTFU Study Day of Window |
|---|---|---|
| 1 ≤ LTFU Study Day ≤ 135 | LTFU Month 3 | 90 |
| 136≤ LTFU Study Day ≤ 225 | LTFU Month 6 | 180 |
| 226 ≤ LTFU Study Day ≤ 315 | LTFU Month 9 | 270 |
| 316 ≤ LTFU Study Day ≤ 405 | LTFU Month 12 | 360 |
| (30*m-44) ≤ LTFU Study Day ≤ (30*m+45) | LTFU Month m<br>M = 15, 18, 21 | 30*m |

- LTFU Study Day is defined in 13.6.1

### 13.3.2. Assessment Windows for PK Concentration Data

PK data will be presented in data listings according to planned nominal visits (i.e. as collected in the eCRF), without additional assignment to assessment windows.

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

### 13.4.1. Study Phases

AEs will be assigned to study phases as defined in Table 6. Laboratory data (efficacy, safety, and virology), HIV associated Conditions, health outcomes assessments, vital signs, and ECGs will be assigned to study phases as defined in Table 7.

Assessments/events are assigned to study phases sequentially, starting from the top of each table.

**Table 6 Study Phases for AEs**

| Study Phase | Definition |
|---|---|
| Screen | Date < Intervention Phase Treatment Start Date |
| Intervention | **For subjects continuing into the Extension Phase:**<br>Intervention Phase Treatment Start Date ≤ Date < Date of Nominal Month 13 Visit<br><br>**For subjects not continuing into the Extension Phase:**<br>Intervention Phase Treatment Start Date ≤ Date < LTFU ART Start Date [a]<br><br>For AEs leading to treatment withdrawal with start date equal to the LTFU ART Start Date, Intervention Phase instead of Long-term Follow-up Phase will be assigned. |
| Extension Phase | Date of Nominal Month 13 Injection ≤ Date < LTFU ART Start Date [a]<br><br>For AEs leading to treatment withdrawal with start date equal to the LTFU ART Start Date, Extension Phase instead of Long-Term Follow-up Phase will be assigned. |
| Long Term Follow-Up | **For subjects who receive at least one CAB/RPV injection and permanently discontinue study treatment:**<br>AE Start Date ≥ LTFU ART Start Date |
| AEs with completely missing start date:<br>• If AE end date is ≤ Intervention Phase Treatment Start Date, then assign to Screening Phase;<br>• Else if AE end date is completely missing or Intervention Phase Treatment Start Date < AE end date ≤ Date of Nominal Month 13 Injection, then assign to Intervention Phase;<br>• Else if AE end date > Date of Nominal Month 13 Injection, then assign to Extension Phase. | |

Date=AE Start Date

- [a] If participants have missing LFTU ART start date, only the lower bound will be considered in the derivation.

**Table 7 Study Phases for Laboratory, PK, ECG, Vital Signs, HIV-1 Associated Conditions, and Protocol Deviation Data**

| Study Phase | Definition |
|---|---|
| Screen | Date ≤ Study Treatment Start Date |
| Intervention | **For subjects continuing into the Extension Phase:**<br>Intervention Phase Treatment Start Date < Date < Date of Nominal Month 13 Visit<br><br>**For subjects not continuing into the Extension Phase:**<br>Intervention Phase Treatment Start Date < Date ≤ LTFU ART Start Date [a] |
| Extension Phase | **For subjects continuing into Extension Phase:**<br>Date of Nominal Month 13 Visit ≤ Date ≤ LTFU ART Start Date [a] |
| Long Term Follow-Up | **For subjects who receive at least one CAB/RPV injection and permanently discontinue study treatment:**<br>Assessment Date > LTFU ART Start Date |

- Date = start or assessment date
- [a] If participants have missing LFTU ART start date, only the lower bound will be considered in the derivation.

Study phase of discontinuation will be determined according to Table 8.

**Table 8 Study Phases for Study Conclusion/IP Discontinuation**

| Study Phase | Definition |
|---|---|
| Intervention | Discontinuation Date is not missing, and no assessments collected at any extension phase nominal visits (i.e. Month 13, Month 15, Month 17 etc.). |
| Extension Phase | Discontinuation Date is not missing, and assessments collected at any extension phase nominal visits (i.e. Month 13, Month 15, Month 17 etc.). |

- Discontinuation Date = date of failure to complete study/date of IP discontinuation

Medication use will be classified as prior and concomitant with study treatment according to Table 9, noting that a medication can be assigned as "taken" during more than one study phase.

**Table 9 Study Phases for Non-ART Medications/ART Medications**

| | Definition |
|---|---|
| Prior | Medication Taken < Intervention Treatment Start Date |
| Concomitant during Intervention Phase | **For subjects continuing into Extension Phase:**<br>Intervention Treatment Start Date[a] ≤ Medication Taken < Date of Nominal Month 13 Visit<br><br>**For subjects not continuing into Extension Phase[b]:**<br>Intervention Treatment Start Date[a] ≤ Medication Taken < LTFU ART Start Date |
| Concomitant during Extension Phase | **For subjects continuing into Extension Phase[b]:**<br>Date of Nominal Month 13 Visit ≤ Medication Taken < LTFU ART Start Date |

| | Definition |
|---|---|
| Received during Long-term Follow-up | **For subjects who received at least one CAB and/or RPV injection and have started LTFU ART:**<br>Medication Taken ≥ LTFU ART Start Date |

**NOTES:**

- Please refer to Appendix 7: Reporting Standards for Missing Data for handling of missing and partial dates for medications. Use the rules in this table if medication date is completely missing.

a. The ART medication stopped on start date of Intervention treatment will be considered a prior medication and will not be considered concomitant during the Intervention phase. If the stop date of ART medication is completely missing and this medication is recorded in eCRF as prior, it will be considered a prior medication and will not be considered concomitant during the intervention phase.

b. If subjects have missing LFTU ART start date, only the lower bound will be considered in the derivation.

### 13.4.2. Treatment State

Within each study phase (based on assignment of study phase described in Section 13.4.1), only those events/assessments which occur within the ranges shown in Table 10 will be considered 'on-treatment' for the given phase. No treatment states will be assigned to medications.

For adverse events, partial AE start date will use imputation as described in 13.7.2.1.

**Table 10 Treatment State within Study Phases**

| Study Phase | State | Definition |
|---|---|---|
| Screen | Pre-Treatment | All assessments/events within phase |
| Intervention/Extension | On-treatment | Date ≤ max (Date of Last CAB LA +RPV LA IM Dose + 35, Date of Last Dose of Oral Study Treatment (CAB+RPV or SOC Bridging) +1) |
| | Post-Treatment | Date > max (Date of Last CAB LA +RPV LA IM Dose + 35, Date of Last Dose of Oral Study Treatment (CAB+RPV or SOC Bridging) +1) |
| Long Term Follow-Up | Post-Treatment | All assessments/events within phase |

**NOTES:**

- Date = Assessment/Start Date

a. Treatment State is determined after data has been assigned to the study phases as defined in Section 13.4.1.

b. Last injection and/or last dose of oral study treatment (CAB+RPV or SOC bridging) are only applied to participants who permanently discontinued the study treatment. The assessments for participants who did not permanently discontinue the study treatment will be considered 'On-treatment'. For participants continuing into extension phase, all data assigned to intervention phase per Section 13.4.1 will be considered 'On-treatment'

### 13.4.3. Oral Lead-in Period

Certain displays will be produced for data collected or events occurring during the oral-lead-in period as defined in Table 11 and Table 12.

### Table 11 Oral Lead-in Period for AEs

| Study Period | Date Range |
|---|---|
| Oral Lead-in | **For participants receiving at least one Injection:**<br>Intervention Treatment Start Date ≤ Date [a] < Date of First IM Injection<br><br>**For participants withdrawing prior to first Injection:**<br>Date ≥ Intervention Treatment Start Date<br><br>Note that the oral lead-in period is only applicable to the participants who received at least one dose of study treatment during the oral lead-in period in the study. Oral lead-in period is within the intervention phase. |
| [a] AEs with completely missing start date which have been assigned to the Intervention Phase based on Table 6 will not be assigned to the Oral Lead-in Period. | |

**NOTES:**

- Date = AE Start date

### Table 12 Oral Lead-in Period for Laboratory Data

| Period | Date Range |
|---|---|
| Oral Lead-in | **For participants receiving at least one Injection:**<br>Intervention Treatment Start Date < Date ≤ Date of First IM Injection<br><br>**For participants withdrawing prior to first Injection:**<br>Date > Intervention Treatment Start Date<br><br>Note that the oral lead-in period is only applicable to the participants who received at least one dose of study treatment during the oral lead-in period in the study. Oral lead-in period is within the intervention phase. |

**NOTES:**

- Date = Date of assessment

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

## 13.5.1. Reporting Process

| | |
|---|---|
| **Software** | |
| • The currently supported versions of SAS software will be used. | |
| **Reporting Area** | |
| HARP Server | us1salx00259 |
| HARP Compound | \ARPROD\GSK1265744\mid209493\primary_01 |
| **Analysis Datasets** | |
| • Analysis datasets will be created according to CDISC standards (SDTM IG Version 3.2 & ADaM IG Version 1.1). | |
| **Generation of RTF Files** | |
| • RTF files will be generated for all reporting efforts described in the RAP. | |

## 13.5.2. Reporting Standards

| |
|---|
| **General** |
| • The current GSK Statistical Display Standards in the GSK Standards Library (IDSL) will be applied for reporting, unless otherwise stated (Library Location: https://spope.gsk.com/sites/IDSLLibrary/SitePages/Home.aspx):<br>  • 4.03 to 4.23: General Principles<br>  • 5.01 to 5.08: Principles Related to Data Listings<br>  • 6.01 to 6.11: Principles Related to Summary Tables<br>  • 7.01 to 7.13: Principles Related to Graphics |
| **Formats** |
| • GSK Statistical Display Principles (5.03 & 6.06.3) for decimal places (DP's) will be adopted for reporting of data based on the raw data collected, unless otherwise stated.<br>• Numeric data will be reported at the precision collected on the eCRF.<br>• The reported precision from non eCRF sources will follow the GSK Standard Statistical Display Principles but may be adjusted to a clinically interpretable number of DP's. |
| **Planned and Actual Time** |
| • Reporting for tables, figures and formal statistical analyses:<br>  • Planned time relative to dosing will be used in figures, summaries, statistical analyses and calculation of any derived parameters, unless otherwise stated.<br>  • The impact of any major deviation from the planned assessment times and/or scheduled visit days on the analyses and interpretation of the results will be assessed as appropriate.<br>• Reporting for Data Listings:<br>  • Planned and actual time relative to study drug dosing will be shown in listings (Refer to GSK Standard Statistical Display Principle 5.05.1).<br>  • Unscheduled or unplanned readings will be presented within the participant's listings. |
| **Unscheduled Visits** |
| • Unscheduled visits will be assigned to an analysis visit using the all-inclusive windows defined in Section 13.3. |

| | |
|---|---|
| • However, data summaries will only report visits that are planned assessment time points for each parameter (according to the Schedule of Activities in Section 13.2.1).<br>• Evaluable assessments at unscheduled visits will be used when categorizing values across visits, such as 'maximum grade during the intervention phase' or 'at any time post-baseline', and for any algorithm that has specific rules for which observation to use (e.g. snapshot algorithm, LOCF or CVF identification). | |
| **Descriptive Summary Statistics** | |
| Continuous Data | Refer to GSK Standard Statistical Display Principle 6.06.1 |
| Categorical Data | N, n, frequency, % |
| **Graphical Displays** | |
| • Refer to GSK Standard Statistical Display Principals 7.01 to 7.13. | |

### 13.5.3. Reporting Standards for Pharmacokinetic

| **Pharmacokinetic Concentration Data** | |
|---|---|
| Descriptive Summary Statistics, Graphical Displays and Listings | Refer to the GSK Standard PK Display Standard.<br>Refer to the GSK Standard Statistical Display Principle 6.06.1.<br>Note: Concentration values will be imputed as per GUI_51487 for descriptive summary statistics/analysis and summarized graphical displays only. |

# 13.6. Appendix 6: Derived and Transformed Data

## 13.6.1. General

| **Multiple Measurements at One Analysis Time Point** |
|---|
| • If there are two values within a time window (as per Section 13.3.1) the value closest to the target day for that window will be used. If values are the same distance from the target, then the mean (geometric mean for HIV-1 RNA, arithmetic mean for all other measurement) will be taken.<br>• Assessments not chosen for use in summary statistics by this algorithm will still appear in the associated listings.<br>• All applicable valid assessments, irrespective of proximity to the target study day, will be used when categorizing values across visits, such as 'maximum grade during the intervention phase' or 'at any time post-baseline', and for any algorithm that has specific rules for which observation to use (e.g. snapshot algorithm, LOCF or CVF identification).<br>• Participants having both High and Low values for Normal Ranges at any post-baseline visit for safety parameters will be counted in both the High and Low categories of "Any visit post-baseline" row of related summary tables. This will also be applicable to relevant Potential Clinical Importance summary tables. |
| **Treatment Start Date** |
| • Intervention Phase Treatment Start Date = Earliest date of CAB + RPV oral lead-in entered in the IP exposure eCRF form |
| **Nominal Month 13 Visit Date** |
| • For participants who received Month 13 injection, the nominal Month 13 visit date is defined by the Month 13 injection date.<br>• Otherwise, nominal Month 13 visit date is defined by the date of latest Month 13 assessment.<br>• For participants who continued into Extension Phase but missed the Month 13 visit, the nominal Month 13 visit date is defined by the last contact date prior to the date of the first nominal extension phase visit (i.e. Month 15, Month 17, etc.). |
| **Study Day** |
| • The Study Day of an event (e.g., lab assessment, vital sign, ECG, start date of AE or HIV associated condition) will be derived as the number of days between the date of the event and the Intervention Phase treatment start date as follows:<br>  ○ If date of event ≥ start date of study treatment, then<br>  ▪ Study Day = Date of Event - Intervention Phase Treatment Start Date +1<br>  ○ If date of event < start date of study treatment, then<br>  ▪ Study Day = Date of Event - Intervention Phase Treatment Start Date<br>• Note that the start date of intervention phase study treatment is on Study Day 1 and the day before this is Study Day -1; i.e., there is no Study Day 0. |
| **Long Term Follow-up Study Day** |
| • The Long-Term Follow Up (LTFU) Study Day of an event (e.g., lab assessment, start date of AE or HIV associated condition) will be derived as the number of days between the date of the event and the end of IP treatment [i.e. max(Last IM Injection Date, Last Oral Bridging End Date)] as follows:<br>  ○ If the date of event falls in Long-term Follow up phase, then<br>  ▪ LTFU Study Day = Date of event - End date of IP + 1 |
| **Study Treatment** |
| • Refers to CAB+RPV oral lead-in, CAB + RPV oral bridging, SOC bridging, CAB LA + RPV LA |

## 13.6.2. Study Population

| **Demographics** |
|---|
| **Age** |
| • Age, in whole years, will be calculated with respect to the subject's Screening visit.<br>• GSK standard IDSL algorithms will be used for calculating age where birth date will be imputed as follows:<br>  • Any subject with a missing date and month will have this imputed as '30th June'.<br>• Birth date will be presented in listings as 'YYYY'.<br>• Completely missing dates of birth will remain as missing, with no imputation applied. Consequently, the age of the subject will not be calculated and will remain missing. |
| **Body Mass Index** |
| • Calculated as Weight (kg)/Height (m)$^2$ |
| **Hepatitis Status** |
| • Hepatitis C status will be determined using antibody and/or hepatitis C virus (HCV) RNA assessments performed during screening or during the conduct of the study.<br>• If both antibody and virus RNA assessments are available, then the latter will take precedence and positive/negative status will be based on whether HCV RNA is detectable (i.e., ≥ limit of quantification) or not.<br>• A participant will be considered positive for hepatitis B virus (HBV) if they have a positive surface antigen or detectable HBV DNA result. "HBV DNA DETECTED" in the lab comment takes precedence over HBV DNA test result for positive hepatitis B status; for example, if a participant has HBV DNA test result below level of detection and the lab comment shows that HBV DNA detected, this participant will be considered positive for hepatitis B. If HBV DNA result is available, it will be used to qualify hepatitis B status as positive or negative (positive if ≥ limit of quantification); otherwise Hepatitis B status will be determined using the surface antigen result.<br>• Hepatitis status at entry will be based on the assessments prior to/on the start of the study treatment. |
| **Adherence to CAB/RPV Injection Schedule** |
| • Timeliness of Injections relative to Date of Projected Dosing Visits are assessed by using "actual injection visit date - projected visit date from first injection". The injections of interest in adherence analysis are those after first injection at Month 1. (. Each injection visit is counted only once. Individual CAB and RPV injections administered at the same visit are not counted twice. "Extra" unscheduled injections are excluded from all derivations. For example, if during a scheduled visit a participant receives 1 ml of injection instead of 2 ml due to a dosing error, but this participant returns one week later for the remaining 1 ml injection, then the additional visit is excluded. If a participant receives an extra injection at an unscheduled visit by mistake, this visit will also be excluded.<br>• The categories of Timeliness of Injections relative to Date of Projected Dosing Visits are listed below:<br>  • < -14 days<br>  • -14 to - 8 days<br>  • -7 to 1<br>  • 0<br>  • 1 to 7 days<br>  • 8 to 14 days<br>  • >14 days<br>  • Missed Injection without Oral Bridging (COVID-19 related)<br>  • Missed Injection without Oral Bridging (Non COVID-19 related)<br>  • Missed Injection with Oral Bridging (COVID-19 related) |

- Missed Injection with Oral Bridging (non COVID-19 related)

- Injection visits are expected monthly from Month 2 until the nominal month of a participant's last injection visit during the phase(s) of interest. For example:
  - If a participant discontinues study treatment with last injection visit occurring at nominal visit Month 6 (without oral bridging), then injection visits are expected at Month 2, Month 3, Month 4, Month 5 and Month 6.
- Missed injections occurring during periods of on-going oral bridging (e.g. oral bridging is ongoing at the time of the data analysis cutoff or participant discontinues study treatment where last study treatment received is oral bridging) are not considered to be expected visits.

**Site Type**

- AIDS Healthcare Foundation (Site Id.= PPD )
- Federally Qualified Health Center (Site Id.= PPD )
- Health Maintenance Organization (Site Id.= PPD )
- Private Practice (Site Id.= PPD )
- University (Site Id.= PPD )

## 13.6.3. Efficacy

**Efficacy**

**Snapshot**

- The Snapshot algorithm is intended to be primarily a virologic assessment of the endpoint, and as such follows a "virology first" hierarchy.
- 'HIV-1 RNA < 50 c/mL' or 'HIV-1 RNA ≥ 50 c/mL' within an analysis window (see Table 2 and Table 3) is typically determined by the last available HIV-1 RNA measurement in that window while the participant is On-treatment in the Intervention Phase (as assigned based on Section 13.3).
- When no HIV-1 RNA data is available within a window, a participant cannot be assigned to the category of 'HIV-1 RNA < 50 c/mL'. Depending on the reason for lack of data, the participant will be classified as 'HIV-1 RNA ≥ 50 c/mL' or reported as 'No Virologic Data at Week X'; in the latter case, the algorithm further classifies the nature of the missing data. Typically, a participant withdrawn (i) due to AE or, (ii) for another reason yet was suppressed at the time, will be counted as 'No Virologic Data at Week X'. Should a participant withdraw for reasons other than AE and was not suppressed at the time, they will be categorized as 'HIV-1 RNA ≥ 50 c/mL'.
- Full details of the algorithm, including the handling of special cases, are included in Appendix 9: Snapshot Algorithm Details.

**Plasma HIV-1 RNA**

- For summaries and analyses which use HIV-1 RNA level as a continuous measure, the logarithm to base 10 of the value will be used.
- HIV-1 RNA results may be provided as censored values, such as <40 or >9,999,999 c/mL. For the purposes of summary statistics, such values will be replaced by the next value beyond the limit of detection, e.g., 39 or 10,000,000 c/mL, respectively, for the given examples. Data listings will show the censored values as provided.

**Confirmed Virologic Failure (CVF)**

- For the purposes of clinical management in this study, CVF is defined as:
  - Rebound as indicated by two consecutive plasma HIV-1 RNA levels ≥ 200 c/mL.
- The CVF definition is provided in the protocol Section 7.1.3

| **Efficacy** |
|---|
| • Only plasma HIV-1 RNA values determined by the central laboratory will be used to assess virologic failure. |
| **CDC Classification for HIV-1 Infection (2014)** |
| • CDC HIV-1 Classification at Baseline is collected in eCRF and no derivation with be performed programmatically for analysis purposes. Please refer to study protocol for detail description of CDC HIV-1 Classification. |

### 13.6.4. Safety

| **Adverse Events** |
|---|
| **DAIDS Grading** |
| • Clinical adverse events will be graded based on the Division of AIDS Table for Grading the Severity of Adult and Pediatric Adverse Events Version 2.1, March 2017, as specified in the protocol Appendix 10.2.<br>• If a grade value is expected per DAIDS but is missing in the eCRF, then the missing grade will be given an ordinal grade value of -1 for determining the maximum grade within and across preferred terms. For example:<br>  • if a participant has two separate instances of the same preferred term, one with grade 2 and one with missing grade, then the maximum grade for the preferred term will be set to grade 2.<br>  • if a participant reports two different AE preferred terms overall, one with grade 1 and one with missing grade (where a DAIDS grade is expected), then the maximum grade across preferred terms (i.e. in the ANY EVENT row) will be set to grade 1.<br>  • If a participant reports only one AE overall and this has a missing grade (where a DAIDS grade is expected), then this will be presented under a grade = missing category |
| **Days since First Dose (Days)** |
| • AE Start Date – Intervention Phase Treatment Start Date + 1 |
| **Days since Last Dose (Days)** |
| • AE Start Date – Date of Last Dose of Study Treatment (CAB+RPV, SOC bridging, CAB/RPV IM Injection) prior to/on the Start Date of AE + 1 |
| **Days since Phase Start** |
| • For AEs in Intervention/Extension Phase:<br>  ○ AE Start Date - Intervention Treatment Start Date + 1<br>• For AEs in Long-term Follow-up Phase:<br>  ○ AE Start Date – Date of Last Dose of Study Treatment<br>  ○ Date of Last Dose of Study Treatment = max (Last IM Injection Date, Last Oral Bridging End Date [CAB+RPV, SOC ART]), only applicable to participants who permanently discontinued study treatment. |
| **Duration (Days)** |
| • AE Resolution Date – AE Start Date + 1 |
| **Drug-related** |
| • If relationship is marked 'YES' on Inform/eCRF<br>• Injection site reactions will be considered as drug-related if the relationship to study drug value is missing in the eCRF. |

## Laboratory Parameters

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

## Lab Toxicities – DAIDS Grading

- Toxicities will be based on the Division of AIDS (DAIDS) grading system, Version 2.1, March 2.17, as specified in the protocol of Appendix 10.2
- Toxicity grades provided by the central laboratory do not distinguish between abnormally high or low criteria, when both are relevant for a particular parameter.
- When summarizing toxicity grades for such parameters, they will be categorized as to whether they are above or below the midpoint of normal range.

| Parameter | Below Midpoint for those ≥Grade 1 | Above Midpoint for those ≥Grade 1 |
|---|---|---|
| Glucose | Hypoglycaemia | Hypoglycaemia |
| Sodium | Hyponatremia | Hyponatremia |
| Potassium | Hypokalaemia | Hypokalaemia |

## Other Safety Endpoints

### Corrected QT (QTc)

- When not entered directly in the eCRF, corrected QT intervals by Bazett's (QTcB) and Fridericia's (QTcF) formulas will be calculated, in msec, depending on the availability of other measurements.
- If RR interval (in msec) is provided, then missing QTcB and/or QTcF will be derived as

$$\mathrm{QTcB} = \frac{\mathrm{QT}}{\sqrt{\mathrm{RR}/1000}} \qquad \mathrm{QTcF} = \frac{\mathrm{QT}}{\sqrt[3]{\mathrm{RR}/1000}}$$

- where uncorrected QT interval is also measured in msec.
- If RR interval is not provided directly and one of QTcB or QTcF has been entered, then RR interval can be obtained from the above formulas and used to calculate the other correction method value; i.e.,

$$\mathrm{QTcB} = \sqrt{\frac{\mathrm{QTcF}^{3}}{\mathrm{QT}}} \qquad \mathrm{QTcF} = \sqrt[3]{\mathrm{QT} \cdot \mathrm{QTcB}^{2}}$$

### Extent of Exposure

- Exposure to CAB+RPV (oral lead-in or oral bridging) and CAB LA+RPV LA will be calculated from the IP eCRF pages.

For Intervention Phase:

- **Exposure to CAB+RPV Oral Lead-in** = IP (oral lead-in) stop date - IP (oral lead-in) start date +1

**Other Safety Endpoints**

- **Exposure to CAB LA + RPV LA** = Number of IP injection visits received during the Intervention Phase (up to but not including injections administered at Month 13)
- **Exposure to SOC oral bridging**: Duration of the SOC ART medication taken as oral bridging during the Intervention Phase. If the SOC oral bridging is taken in different periods during the Intervention Phase, the duration will be calculated by the sum of non-overlapped periods.
- **Exposure to CAB+RPV Oral Bridging (COVID-19 Related)**: Duration of the CAB+RPV taken as oral bridging for reasons related to COVID-19 during the Intervention Phase. If COVID-19 related CAB+RPV oral bridging is taken in different periods during the Intervention Phase, the duration will be calculated by the sum of the non-overlapped periods.
- **Exposure to CAB+RPV Oral Bridging (Non COVID-19 Related)**: Duration of the CAB+RPV taken as oral bridging for reasons not related to COVID-19 during the Intervention Phase. If non COVID-19 related CAB+RPV oral bridging is taken in different periods during the Intervention Phase, the duration will be calculated by the sum of the non-overlapped periods.
- **Overall Exposure to Study Treatment**: min [Date of Latest Intervention Phase Visit up to and including Month 13, max (Date of Last Injection + 35, Date of Last Dose of Oral CAB+RPV, Date of Last Dose of SOC Oral Bridging)] – min (Start Date for Oral lead-in CAB+RPV, Date of First CAB/RPV Injection) + 1
    - Note: Conditions in the above formula pertaining to Last Injection/Last Dose of Oral CAB+RPV/Last Dose of SOC Oral Bridging are only applicable to those who permanently discontinued study treatment.
- **Overall Exposure to CAB + RPV** = Overall Exposure to Study Treatment – Exposure to SOC Oral Bridging

For Intervention ± Extension Phase:

- **Exposure to CAB LA + RPV LA** = Number of IP injection visits received during Intervention Phase and Extension Phase
- Exposure to SOC or CAB+RPV Oral Bridging during the Intervention and Extension Phase will be calculated similarly to that during the Intervention Phase except that the exposure includes both Intervention and Extension Phase.
- **Overall Exposure to Study Treatment**: min [Date of Latest Intervention/Extension Phase Visit, max (Date of Last Injection + 35, Date of Last Dose of Oral CAB+RPV, Date of Last Dose of SOC Oral Bridging)] – min (Start Date for Oral lead-in CAB+RPV, Date of First Study Injection) + 1
    - Note: Conditions in the above formula pertaining to Last Injection/Last Dose of Oral CAB+RPV/Last Dose of SOC Oral Bridging are only applicable to those who permanently discontinued study treatment.
- **Overall Exposure to IP** = Overall Exposure to Study Treatment – Exposure to SOC Oral Bridging
- Duration of dosing in participant years will be calculated as the sum of participant duration of dosing in days (across all participants)/365.25

## 13.6.5. Virology

**Genotype**

**Amino Acid Changes**

- A mutation is considered present whenever the encoded amino acid residue differs from the amino acid that would have been encoded by the wild-type (e.g., HXB2, NL43) comparator gene; e.g., Q148K.
- If the encoded amino acid is seen as a mixture of wild-type and mutant amino acid, e.g., Q148Q/K, the mutated amino acid is considered present at the codon of interest.

- If the encoded amino acid is seen as a mixture of two or more amino acids, which may or may not include wild type, e.g., Q184K/H or Q184K/H/Q, etc., for the purposes of calculating the number of mutated amino acids, only one mutation is considered to be present at the codon of interest.

**Representation of Amino Acid Changes**

| Mutations | Amino Acid Change |
|---|---|
| T69S | Single mutation from amino acid 'T' (vendor reference) to 'S' (sample) at codon '69 |
| Q148H/K/R | Mixture of amino acid mutations 'H', 'K' and 'R' (sample) from amino acid 'Q (vendor reference) at codon '148' |
| _69_1T | First insertion of amino acid 'T' (sample) at codon '69' |
| _69_2S | Second insertion of amino acid 'S' (sample) at codon '69' |
| _69_3S/A | Third insertion of a mixture of amino acids 'S' and 'A' (sample) at codon '69' |
| L74L/- | Mixture of amino acid 'L' (sample) and a deletion at codon '74' |
| V75- | Single deletion of amino acid (sample) at codon '75' |

**Resistance Associated mutations**

Known INI mutations associated with the development of resistance to Integrase Strand Transfer Inhibitors:

| | |
|---|---|
| Amino Acids in HIV Integrase for Analysis | H51Y, **T66**A/**I**/K, L68V/I, L74I/M, **E92Q**/V/G, Q95K, T97A, **G118R**, **F121Y**, E138A/D/K/T, **G140**A/C/**R**/S, **Y143C**/**H**/**R**/K/S/G/A, P145S, Q146P, **S147G**, **Q148H/K/R**/N, V151/IL/A, S153F/Y, **N155H**/S/T, E157Q, G163R/K, G193E, S230R, **R263K** |

- Draft listing; may be modified in case of additional substantive data availability.
- Based on the IAS-USA list of mutations associated with resistance to Bictegravir, Cabotegravir, Dolutegravir, Elvitegravir, or Raltegravir (IAS-USA 2019 resistance mutations update volume 27 issue 3, 2019): T66A/I/K, L74M, E92Q/G, T97A, G118R, F121Y, E138A/K/T, G140A/C/R/S, Y143C/H/R, S147G, Q148H/K/R, S153F/Y, N155H, R263K) and observed mutations during in vitro passage of DTG or seen in a previous DTG study in INI-experienced subjects (study ING112574): H51Y, L74I, L68V/I, E92V, Q95K, E138D, Y143K/S/G/A, P145S, Q146P, V151I/L/A, N155S/T, E157Q, G163R/K, G193E, S230R.
- Major USA-IAS mutations associated with resistance to INSTI are bolded.

- Major resistance mutations to other classes (i.e., NRTI, NNRTI, PI) as defined by the International Antiviral Society-USA (IAS-USA). The most up to date IAS-USA guidelines available at the time of DBF will be used in the analysis [Wensing, 2019].

| Class | Mutations |
|---|---|
| NRTIs | M41L, A62V, K65R/E/N, D67N, 69 insert, K70E/R, L74V, V75I, F77L, Y115F, F116Y, Q151M, M184V/I, L210W, T215Y/F, K219Q/E |
| NNRTIs | L100I, K101E/P, K103N/S, V106A/M, V108I, E138/A/G/K/Q/R, V179L, Y181C/I/V, Y188C/L/H, G190S/A, H221Y, P225H, F227C, M230I/L |
| PIs | D30N, V32I, M46I/L, I47A/V, G48V, I50V/L, I54V/M/L, Q58E, T74P, L76V, V82A/T/F/L/S, N83D, I84V, N88S, L90M |

- Draft listing; may be modified in case of additional substantive data availability.

### 13.6.6. Other Assessments

| **Study Visit Length** |
| --- |
| • Lead Time = Actual Start Time of Appointment – Arrival Time<br>• Process Time = Actual End Time of Appointment – Actual Start Time of Appointment<br>• Total Time = Actual End Time of Appointment – Arrival Time |

# 13.7. Appendix 7: Reporting Standards for Missing Data

## 13.7.1. Premature Withdrawals

| Element | Reporting Detail |
|---|---|
| General | • Withdrawn participants were not replaced in the study.<br>• All available data from participants who were withdrawn from the study will be listed and all available planned data will be included in summary tables and figures, unless otherwise specified.<br>• Withdrawal visits will be slotted according to Appendix 3: Assessment Windows (excluding PK data) |

## 13.7.2. Handling of Missing Data

| Element | Reporting Detail |
|---|---|
| General | • Missing data occurs when any requested data is not provided, leading to blank fields on the collection instrument:<br>  ○ These data will be indicated by the use of a "blank" in participant listing displays. Unless all data for a specific visit are missing in which case the data is excluded from the table.<br>  ○ Answers such as "Not applicable" and "Not evaluable" are not considered to be missing data and should be displayed as such. |
| Outliers | • Any participants excluded from the summaries and/or statistical analyses will be documented along with the reason for exclusion in the clinical study report. |

### 13.7.2.1. Handling of Missing and Partial Dates

| Element | Reporting Detail |
|---|---|
| General | • Partial dates will be displayed as captured in participant listing displays.<br>• Where necessary, display macros may impute dates as temporary variables for sorting data in listings only. In addition, partial dates may be imputed for 'slotting' data to study phases or for specific analysis purposes as outlined below.<br>• Imputed partial dates will not be used to derive study day, time to onset or duration (e.g., time to onset or duration of adverse events), or elapsed time variables (e.g., time since diagnosis). In addition, imputed dates are not used for deriving the last contact date in overall survival analysis dataset. |
| Adverse Events | • Imputations in the adverse events dataset are used for slotting events to the appropriate study time periods and for sorting in data listings.<br>• Partial dates for AEs recorded in the CRF will be imputed using the following conventions:<br><br>Missing start day: • If study treatment start date is missing (i.e. participant did not start study treatment), then set start date = 1st of month.<br>• Else if study treatment start date is not missing:<br>  ○ If month and year of start date = month and year of study treatment start date, then<br>  ▪ If stop date contains a full date and stop date is earlier than study treatment start date, then set start date= 1st of month.<br>  ▪ Else set start date = study treatment start date. |

<table>
<tr><th>Element</th><th>Reporting Detail</th></tr>
<tr><td></td><td>
<table>
<tr><td></td><td>• Else<br>○ For Non-ISR AEs: set start date = 1st of month<br>○ For ISR AEs: if oral bridging taken during the month and year, set start date = min(last day of the month, day of AE stop date if available, day of study treatment discontinuation if occurring during the month and year); else set start date = 1st of month.</td></tr>
<tr><td>Missing start day and month</td><td>• If study treatment start date is missing (i.e. participant did not start study treatment), then set start date = January 1.<br>• Else if study treatment start date is not missing:<br>○ If year of start date = year of study treatment start date, then<br>▪ If stop date contains a full date and stop date is earlier than study treatment start date, then set start date = January 1.<br>▪ Else set start date = study treatment start date.<br>○ Else set start date = January 1.</td></tr>
<tr><td>Missing stop day</td><td>Last day of the month will be used.</td></tr>
<tr><td>Missing stop day and month</td><td>No Imputation</td></tr>
<tr><td>Completely missing start/end date</td><td>No imputation</td></tr>
</table>
• Completely missing start or end dates will remain missing, with no imputation applied.
</td></tr>
<tr><td>Non-ART Medications</td><td>• Partial dates for any concomitant medications recorded in the CRF will be imputed using the following convention:
<table>
<tr><td>Missing start day</td><td>• If study treatment start date is missing (i.e. participant did not start study treatment), then set start date = 1st of month.<br>• Else if study treatment start date is not missing:<br>○ If month and year of start date = month and year of study treatment start date, then<br>▪ If stop date contains a full date and stop date is earlier than study treatment start date, then set start date= 1st of month.<br>▪ Else set start date = study treatment start date.<br>○ Else set start date = 1st of month.</td></tr>
<tr><td>Missing start day and month</td><td>• If study treatment start date is missing (i.e. participant did not start study treatment), then set start date = January 1.<br>• Else if study treatment start date is not missing:<br>○ If year of start date = year of study treatment start date, then<br>▪ If stop date contains a full date and stop date is earlier than study treatment start date, then set start date = January 1.<br>▪ Else set start date = study treatment start date.<br>• Else set start date = January 1.</td></tr>
<tr><td>Missing end day</td><td>A '28/29/30/31' will be used for the day (dependent on the month and year)</td></tr>
<tr><td>Missing end day and month</td><td>A '31' will be used for the day and 'Dec' will be used for the month.</td></tr>
<tr><td>Completely missing start/end date</td><td>No imputation</td></tr>
</table>
</td></tr>
</table>

| Element | Reporting Detail |
|---|---|
| | • The recorded partial date will be displayed in listings. |
| ART Medications | • Partial dates recorded in the eCRF will be imputed using the following convention:<br>  ○ If the partial date is a start date, a '01' will be used for the day and 'Jan' will be used for the month.<br>  ○ If the partial date is a stop date, a '28/29/30/31' will be used for the day (dependent on the month and year) and 'Dec' will be used for the month. If medications recorded in the PRIOR ART form of the eCRF, then the earlier date of the imputed and the day prior to the Intervention phase treatment start date will be used, i.e. min (imputed stop date, Intervention phase treatment start date - 1).<br>• For medications with completely missing start date, they will be considered started prior to the Intervention phase treatment start date.<br>• For medications with completely missing stop date, they will be considered ongoing unless recorded in the PRIOR ART form of the eCRF.<br>• For ART booster medications, the start and stop dates are not recorded in the database (i.e. missing), the dates will be imputed to be the same as the dates of their parent medications.<br>• The recorded partial or missing date will be displayed in listings. |

### 13.7.2.2. Handling of Missing Data for Statistical Analysis

| Element | Reporting Detail |
|---|---|
| Snapshot | • In the Snapshot dataset, subjects without HIV – 1 RNA data in the assessment window for the visit of interest (due to missing data or discontinuation of IP prior to the visit window) do not belong to 'HIV-1< 50 c/mL (or 200 c/mL) The nature of this missing data will be further classified in Snapshot summaries as either 'HIV-1 RNA≥50' or 'No Virologic Data at Week X';<br>• See Appendix 9: Snapshot Algorithm Details |
| LOCF (COVID-19 Related) | • Missing HIV-1 RNA values within an analysis visit for reasons related to COVID-19 will be imputed using the last on-treatment value from earlier analysis timepoints.<br>• This approach will be used in the primary snapshot analysis to address missing data due to COVID-19. |

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

ECG values of potential clinical importance are defined as QTc > 500 msec or increase from baseline in QTc ≥ 60 msec.

## 13.9. Appendix 9: Snapshot Algorithm Details

**Detailed Algorithm Steps**

- Consider an analysis visit window for Month X as defined in Table 2.
- The HIV-1 RNA threshold of 50 will be analysed, in this study
- The COVID-19 pandemic presents significant logistical challenges for many clinical sites around the world, with variable restrictions being placed on site resources and operations, and on an individual participants ability to attend clinic visits. The snapshot algorithm is modified to allow for the presentation of full scope of COVID-19 relatedness. The analysis window for 'Month 12' and HIV-1 RNA threshold of '50 c/mL' are used for the purpose of illustration. A participant's Snapshot response and reason at Month 12 are categorized as below.

```
o  HIV-1 RNA < 50 c/mL
o  HIV-1 RNA ≥ 50 c/mL
   Data in window not below 50
     Non-COVID-19 related
         Discontinued for lack of efficacy
         Discontinued for other reason while not below 50
     COVID-19 related
         Discontinued for lack of efficacy
         Discontinued for other reason while not below 50

o  No Virologic Data at Month 12 Window
     Non-COVID-19 related
         Discontinued study due to AE or death
         Discontinued study for other reasons
         On study but missing data in window
     COVID-19 related
         Discontinued study due to AE or death
         Discontinued study for other reasons
         On study but missing data in window
   Change in background therapy*
```

* Note: Use of CAB + RPV oral bridging and SOC oral bridging medication, where the latter is due to unavailability of CAB/RPV IM injections or oral CAB+RPV during the pandemic, will not be considered a "Change in background therapy" in the Snapshot algorithm. All other permanent changes in ART are not permitted in this protocol.

- The steps in determining response and reasons are indicated in the table below, in the order stated.
- Background therapy is not given to participants while on study. The "change in background therapy" in detailed steps below refers to the "change in ART" in this study.

| **Detailed steps**<br>• Please note that the following scenarios will NOT be penalized in the Snapshot algorithm Oral bridging (CAB+RPV or SOC, where SOC oral bridging medication is permitted during COVID-19 pandemic due to the unavailability of the CAB/RPV IM injections and oral CAB+RPV) | | |
|---|---|---|
| **Condition** ('Month 12' indicates Month 12 window) | **Response** | **Reasons** |

| | | |
|---|---|---|
| 1. If non-permitted change in background therapy prior to Month 12 | HIV-1 RNA ≥ 50 | Change in background therapy |
| 2. If non-permitted change in background therapy during Month 12 | | |
| • Last on-treatment VL during Month 12 prior to/on the date of change ≥ 50 c/mL | HIV-1 RNA ≥ 50 | Data in window not below 50 |
| • Last on-treatment VL during Month 12 prior to/on the date of change < 50 c/mL | HIV-1 RNA < 50 | |
| • No VL during Month 12 prior to/on the date of change | HIV-1 RNA ≥ 50 | Change in background therapy |
| 3. If none of the above conditions met | | |
| 3.1. On-treatment VL available during Month 12 | | |
| • Last on-treatment VL during Month 12 ≥ 50 c/mL | HIV-1 RNA ≥ 50 | Data in window not below 50 |
| • Last on-treatment VL during Month 12 < 50 c/mL | HIV-1 RNA < 50 | |
| 3.2. No on-treatment VL during Month 12 | | |
| 3.2.1. If participants are still on study, i.e. a participant has not permanently discontinued the study treatment yet, or if a participant permanently discontinued the study treatment and the upper bound of analysis snapshot window is prior to the following date:<br>• Min[max(Date of last injection + 35, Date of Last Dose of Oral Study Treatment (CAB+RPV, SOC Bridging) + 1), LTFU ART Start Date] | | |
| 3.2.1.1. If no on-treatment VL during Month 12 is not due to COVID-19 | No virologic data at Month 12 Window | On study but missing data in window (Non-COVID-19 related) |
| 3.2.1.2. If no on-treatment VL during Month 12 is due to COVID-19 | No virologic data at Month 12 Window | On study but missing data in window (COVID-19 related) |
| 3.2.2. If participants withdraw before/during Month 12 due to | | |
| 3.2.2.1. Non-COVID-19 related safety reasons (e.g. AE/death, liver chemistry stopping criteria, renal toxicity withdrawal criteria, QTc withdrawal criteria etc., as recorded in eCRF Conclusion form) | No virologic data at Month 12 Window | Disc due to AE/death (Non-COVID-19 related) |
| 3.2.2.2. COVID-19 related safety reasons (e.g. AE/death, liver chemistry stopping criteria, renal toxicity withdrawal criteria, QTc withdrawal | No virologic data at Month 12 Window | Disc due to AE/death (COVID-19 related) |

| | | |
|---|---|---|
| criteria etc., as recorded in eCRF Conclusion form) | | |
| 3.2.2.3. Non-safety and Non-COVID-19 related reasons (e.g. Lack of efficacy, protocol deviation, withdrew consent, loss to follow-up, study closed/terminated, investigator discretion etc., as recorded in eCRF Treatment Discontinuation Form) | | |
| ○ Last on-treatment VL <50 c/mL OR no on-treatment VL available during study | No virologic Data at Month 12 Window | Disc for other reasons (Non-COVID-19 related) |
| ○ Last on-treatment VL ≥ 50 c/mL AND withdrawal due to Lack of efficacy | HIV-1 RNA ≥ 50 | Disc. for lack of efficacy (Non-COVID-19 related) |
| ○ Last on-treatment VL ≥ 50 c/mL AND withdrawal due to all other non-safety related reasons | HIV-1 RNA ≥ 50 | Disc. for other reason while not below 50 (Non-COVID-19 related) |
| 3.2.2.4. Non-safety and COVID-19 related reasons (e.g. protocol deviation, withdrew consent, loss to follow-up, study closed/terminated, investigator discretion etc., as recorded in eCRF Conclusion Form) | | |
| ○ Last on-treatment VL <50 c/mL OR no on-treatment VL available during study | No virologic Data at Month 12 Window | Disc for other reasons (COVID-19 related) |
| ○ Last on-treatment VL ≥ 50 c/mL AND withdrawal due to Lack of efficacy | HIV-1 RNA ≥ 50 | Disc. for lack of efficacy (COVID-19 related) |
| ○ Last on-treatment VL ≥ 50 c/mL AND withdrawal due to all other non-safety related reasons | HIV-1 RNA ≥ 50 | Disc. for other reason while not below 50 (COVID-19 related) |

a. Excluding permitted change in background therapy where change or decision to change is made prior to/on the first on-treatment viral result

**Examples from FDA guidance**

Data in Window

Virologic outcome should be determined by the last available measurement while the patient is on treatment and continued on trial within the time window:

- HIV-1 RNA = 580 c/mL at Day 336, HIV-1 RNA below 50 c/mL on Day 350. This should be categorized as HIV-1 RNA below 50 c/mL.

No Data in Window

Discontinued study due to Adverse Event or Death:

- Any patient who discontinues because of an AE or death before the window should be classified as *Discontinued due to AE or Death* (as appropriate), regardless of the HIV-1 RNA result, even if the HIV-1 RNA is below 50 c/mL at the time of discontinuation.
- However, if a patient has an HIV-1 RNA value in the time window and also discontinues in the time window, the viral load data should be used to classify the patient's response. This is the Virology First hierarchy:
    a. HIV-1 RNA below 50 c/mL at Day 336 and discontinues because of AE or even dies on Day 360 — this person is categorized as having HIV-1 RNA below 50 c/mL.
    b. HIV-1 RNA is 552 c/mL on Day 336 and the patient discontinues on Day 360, the patient is categorized as having HIV-1 RNA ≥ 50 c/mL.

Discontinued for Other Reasons:

- Only patients who have achieved virologic suppression can be counted as *Discontinued for Other Reasons.*
- If a patient discontinues the study before the time window because of *lack of efficacy,* then the patient should be included in the HIV-1 RNA ≥ 50 row and not in the Discontinued for Other Reasons row.
- If a patient discontinues because *participant withdrew consent* and his or her HIV-1 RNA result at the time of discontinuation was equal to or above 50 c/mL, then he or she should be categorized as HIV-1 RNA ≥ 50 and NOT as Discontinued for Other Reasons.
- If a patient discontinued because of *Lost to Follow-Up* and the last HIV-1 RNA result was 49 c/mL, then the patient can be categorized as Discontinued for Other Reasons.
- If patients changed background treatment — *not permitted by protocol*— they should be considered an efficacy failure and captured in the HIV-1 RNA ≥ 50 c/mL row.

On study but missing data in window:

- If there are no data during Days 294 to 377, but there is an HIV-1 RNA below 50 c/mL on Day 380, this patient should be considered *On Study but Missing Data in Window.*
- If there are no data during Days 294 to 377, but there is an HIV-1 RNA equal to or above 50 c/mL on Day 280, this patient also should be classified as *On Study but Missing Data in Window.*

## 13.10. Appendix 10: AESI identification

SMQ and PT codes based on MedDRA dictionary version 23.0 for the Month 12 analysis.

### 13.10.1. Hepatic Safety Profile

Medical concept of hepatic failure and hepatitis. Sub- SMQs (1) 'Hepatic failure, fibrosis and cirrhosis and other liver damage-related conditions' and (2) 'Hepatitis, non-infectious', both of parent SMQ 'Hepatic Disorders (SMQ code 20000005)'; only narrow terms selected from sub-SMQs. Some preferred terms, e.g. PT 'hepatitis fulminant' are duplicated.

| SMQ: 'Hepatic Disorders'; SMQ Code: 20000005<br>Sub-SMQ: 'Hepatic failure, fibrosis and cirrhosis and other liver damage-related conditions'<br>Category: A<br>Scope: Narrow | |
|---|---|
| Preferred Term | PT Code |
| Acquired hepatocerebral degeneration | 10080860 |
| Acute hepatic failure | 10000804 |
| Acute on chronic liver failure | 10077305 |
| Acute yellow liver atrophy | 10070815 |
| Ascites | 10003445 |
| Asterixis | 10003547 |
| Bacterascites | 10068547 |
| Biliary cirrhosis | 10004659 |
| Biliary fibrosis | 10004664 |
| Cardiohepatic syndrome | 10082480 |
| Cholestatic liver injury | 10067969 |
| Chronic hepatic failure | 10057573 |
| Coma hepatic | 10010075 |
| Cryptogenic cirrhosis | 10063075 |
| Diabetic hepatopathy | 10071265 |
| Drug-induced liver injury | 10072268 |
| Duodenal varices | 10051010 |

| | |
|---|---|
| Gallbladder varices | 10072319 |
| Gastric variceal injection | 10076237 |
| Gastric variceal ligation | 10076238 |
| Gastric varices | 10051012 |
| Gastric varices haemorrhage | 10057572 |
| Gastrooesophageal variceal haemorrhage prophylaxis | 10066597 |
| Hepatectomy | 10061997 |
| Hepatic atrophy | 10019637 |
| Hepatic calcification | 10065274 |
| Hepatic cirrhosis | 10019641 |
| Hepatic encephalopathy | 10019660 |
| Hepatic encephalopathy prophylaxis | 10066599 |
| Hepatic failure | 10019663 |
| Hepatic fibrosis | 10019668 |
| Hepatic hydrothorax | 10067365 |
| Hepatic infiltration eosinophilic | 10064668 |
| Hepatic lesion | 10061998 |
| Hepatic necrosis | 10019692 |
| Hepatic steato-fibrosis | 10077215 |
| Hepatic steatosis | 10019708 |
| Hepatitis fulminant | 10019772 |
| Hepatobiliary disease | 10062000 |
| Hepatocellular foamy cell syndrome | 10053244 |
| Hepatocellular injury | 10019837 |
| Hepatopulmonary syndrome | 10052274 |
| Hepatorenal failure | 10019845 |
| Hepatorenal syndrome | 10019846 |
| Hepatotoxicity | 10019851 |
| Immune-mediated cholangitis | 10083406 |

| | |
|---|---|
| Immune-mediated hepatic disorder | 10083521 |
| Intestinal varices | 10071502 |
| Intestinal varices haemorrhage | 10078058 |
| Liver dialysis | 10076640 |
| Liver disorder | 10024670 |
| Liver injury | 10067125 |
| Liver operation | 10062040 |
| Liver transplant | 10024714 |
| Lupoid hepatic cirrhosis | 10025129 |
| Minimal hepatic encephalopathy | 10076204 |
| Mixed liver injury | 10066758 |
| Nodular regenerative hyperplasia | 10051081 |
| Nonalcoholic fatty liver disease | 10082249 |
| Non-alcoholic steatohepatitis | 10053219 |
| Non-cirrhotic portal hypertension | 10077259 |
| Oedema due to hepatic disease | 10049631 |
| Oesophageal varices haemorrhage | 10030210 |
| Peripancreatic varices | 10073215 |
| Portal fibrosis | 10074726 |
| Portal hypertension | 10036200 |
| Portal hypertensive colopathy | 10079446 |
| Portal hypertensive enteropathy | 10068923 |
| Portal hypertensive gastropathy | 10050897 |
| Portal vein cavernous transformation | 10073979 |
| Portal vein dilatation | 10073209 |
| Portopulmonary hypertension | 10067281 |
| Primary biliary cholangitis | 10080429 |
| Regenerative siderotic hepatic nodule | 10080679 |
| Renal and liver transplant | 10052279 |

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|---|---|
| Retrograde portal vein flow | 10067338 |
| Reye's syndrome | 10039012 |
| Reynold's syndrome | 10070953 |
| Splenic varices | 10067823 |
| Splenic varices haemorrhage | 10068662 |
| Steatohepatitis | 10076331 |
| Subacute hepatic failure | 10056956 |
| Sugiura procedure | 10083010 |
| Varices oesophageal | 10056091 |
| Varicose veins of abdominal wall | 10072284 |
| White nipple sign | 10078438 |
| SMQ: 'Hepatic Disorders'; SMQ Code: 20000005<br>Sub-SMQ: 'Hepatitis, non-infectious'<br>Category: A<br>Scope: Narrow | |
| Preferred Term | PT Code |
| Acute graft versus host disease in liver | 10066263 |
| Allergic hepatitis | 10071198 |
| Alloimmune hepatitis | 10080576 |
| Autoimmune hepatitis | 10003827 |
| Chronic graft versus host disease in liver | 10072160 |
| Chronic hepatitis | 10008909 |
| Graft versus host disease in liver | 10064676 |
| Hepatitis | 10019717 |
| Hepatitis acute | 10019727 |
| Hepatitis cholestatic | 10019754 |
| Hepatitis chronic active | 10019755 |
| Hepatitis chronic persistent | 10019759 |
| Hepatitis fulminant | 10019772 |
| Hepatitis toxic | 10019795 |

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|---|---|
| Immune-mediated hepatitis | 10078962 |
| Ischaemic hepatitis | 10023025 |
| Lupus hepatitis | 10067737 |
| Non-alcoholic steatohepatitis | 10053219 |
| Radiation hepatitis | 10051015 |
| Steatohepatitis | 10076331 |

### 13.10.2. Hyperglycaemia

Medical concept of Hyperglycaemia/new onset diabetes mellitus - SMQs (1) 'Hyperglycaemia/new onset diabetes mellitus (SMQ) Narrow SMQ code 20000041.

| SMQ: 'Hyperglycaemia/new onset diabetes mellitus '; SMQ Code: 20000041<br>Sub-SMQ: 'Hepatic failure, fibrosis and cirrhosis and other liver damage-related<br>Category: A<br>Scope: Narrow | |
|---|---|
| Preferred Term | PT Code |
| Acquired lipoatrophic diabetes | 10073667 |
| Blood 1,5-anhydroglucitol decreased | 10065367 |
| Blood glucose increased | 10005557 |
| Diabetes complicating pregnancy | 10012596 |
| Diabetes mellitus | 10012601 |
| Diabetes mellitus inadequate control | 10012607 |
| Diabetes with hyperosmolarity | 10012631 |
| Diabetic arteritis | 10077357 |
| Diabetic coma | 10012650 |
| Diabetic coronary microangiopathy | 10080788 |
| Diabetic hepatopathy | 10071265 |
| Diabetic hyperglycaemic coma | 10012668 |
| Diabetic hyperosmolar coma | 10012669 |
| Diabetic ketoacidosis | 10012671 |
| Diabetic ketoacidotic hyperglycaemic coma | 10012672 |
| Diabetic ketosis | 10012673 |

| | |
|---|---|
| Diabetic metabolic decompensation | 10074309 |
| Diabetic wound | 10081558 |
| Euglycaemic diabetic ketoacidosis | 10080061 |
| Fructosamine increased | 10017395 |
| Fulminant type 1 diabetes mellitus | 10072628 |
| Gestational diabetes | 10018209 |
| Glucose tolerance impaired | 10018429 |
| Glucose tolerance impaired in pregnancy | 10018430 |
| Glucose urine present | 10018478 |
| Glycated albumin increased | 10082836 |
| Glycosuria | 10018473 |
| Glycosuria during pregnancy | 10018475 |
| Glycosylated haemoglobin abnormal | 10018481 |
| Glycosylated haemoglobin increased | 10018484 |
| Hyperglycaemia | 10020635 |
| Hyperglycaemic hyperosmolar nonketotic syndrome | 10063554 |
| Hyperglycaemic seizure | 10071394 |
| Hyperglycaemic unconsciousness | 10071286 |
| Impaired fasting glucose | 10056997 |
| Insulin resistance | 10022489 |
| Insulin resistant diabetes | 10022491 |
| Insulin-requiring type 2 diabetes mellitus | 10053247 |
| Ketoacidosis | 10023379 |
| Ketonuria | 10023388 |
| Ketosis | 10023391 |
| Ketosis-prone diabetes mellitus | 10023392 |
| Latent autoimmune diabetes in adults | 10066389 |
| Monogenic diabetes | 10075980 |
| Neonatal diabetes mellitus | 10028933 |

| | |
|---|---|
| New onset diabetes after transplantation | 10082630 |
| Pancreatogenous diabetes | 10033660 |
| Steroid diabetes | 10081755 |
| Type 1 diabetes mellitus | 10067584 |
| Type 2 diabetes mellitus | 10067585 |
| Type 3 diabetes mellitus | 10072659 |
| Urine ketone body present | 10057597 |

### 13.10.3. Hypersensitivity Reactions

Notes: Medical concept of hypersensitivity reactions/DRESS. Only narrow terms selected from Category A of SMQ 'Drug reaction with eosinophilia and systemic symptoms syndrome'. Algorithmic approach for this SMQ not used due to complexity in applying and poor specificity of remaining categories. Category A selected as PTs because more specific for concept (only narrow terms) and a pre-requisite for any combination in algorithmic search. Overlap of some preferred terms with SMQ 'Severe Cutaneous Adverse Reactions'. Plus additional preferred terms selected from HGLT 'Allergic conditions' under SOC 'Immune system disorders'.

| SMQ: Drug reaction with eosinophilia and systemic symptoms syndrome<br>SMQ Code: 20000225<br>Category: A<br>Scope: Narrow | |
|---|---|
| Preferred Term | PT Code |
| Drug reaction with eosinophilia and systemic symptoms | 10073508 |
| Pseudolymphoma | 10037127 |
| Additional preferred terms selected from HLGT 'Allergic conditions' under SOC 'Immune system disorders'; HLGT code 10001708 | |
| Preferred Term | PT Code |
| Drug hypersensitivity | 10013700 |
| Hypersensitivity | 10020751 |
| Type IV Hypersensitivity reaction | 10053613 |
| Eosinophillia | 10014950 |
| Eye swelling | 10015967 |
| Eyelid oedema | 10015993 |

| | |
|---|---|
| Lip swelling | 10024570 |
| Angioedema | 10002424 |
| Circumoral oedema | 10052250 |
| Face oedema | 10016029 |
| Idiopathic angioedema | 10073257 |
| Lip oedema | 10024558 |
| Mouth swelling | 10075203 |
| Oedema mouth | 10030110 |
| Periorbital oedema | 10034545 |
| Swelling face | 10042682 |
| Periorbital swelling | 10056647 |
| Swelling of eyelid | 10042690 |

### 13.10.4. Rash including severe cutaneous adverse reactions

Medical concept of rash including severe cutaneous adverse reactions. Only narrow terms from SMQ 'Severe cutaneous adverse reactions' selected. Plus several additional preferred terms selected from HLTs 'Rashes, eruptions and exanthems NEC', 'Pruritus NEC', 'Pustular conditions', 'Dermatitis ascribed to specific agent' all under SOC 'Skin and subcutaneous tissue disorders'.

| SMQ: Severe Cutaneous Adverse Reactions<br>SMQ Code: 20000020<br>Category: A<br>Scope: Narrow | |
|---|---|
| SMQ | PT Code |
| Acute generalised exanthematous pustulosis | 10048799 |
| Bullous haemorrhagic dermatosis | 10083809 |
| Cutaneous vasculitis | 10011686 |
| Dermatitis bullous | 10012441 |
| Dermatitis exfoliative | 10012455 |
| Dermatitis exfoliative generalised | 10012456 |
| Drug reaction with eosinophilia and systemic symptoms | 10073508 |
| Epidermal necrosis | 10059284 |

| | |
|---|---|
| Erythema multiforme | 10015218 |
| Erythrodermic atopic dermatitis | 10082985 |
| Exfoliative rash | 10064579 |
| Oculomucocutaneous syndrome | 10030081 |
| SJS-TEN overlap | 10083164 |
| Skin necrosis | 10040893 |
| Stevens-Johnson syndrome | 10042033 |
| Target skin lesion | 10081998 |
| Toxic epidermal necrolysis | 10044223 |
| Toxic skin eruption | 10057970 |
| Addition selected preferred terms from HLTs 'Rashes, eruptions and exanthems NEC', HLT Code 1005266; 'Pruritus NEC', HLT Code 10049293, 'Pustular conditions', HLT Code 10037573; 'Dermatitis ascribed to specific agent', HLT Code 10012437. | |
| Preferred Term | PT Code |
| Eyelid rash | 10074620 |
| Genital rash | 10018175 |
| Mucocutaneous rash | 10056671 |
| Nodular rash | 10075807 |
| Perineal rash | 10075364 |
| Rash | 10037844 |
| Rash erythematous | 10037855 |
| Rash generalised | 10037858 |
| Rash macular | 10037867 |
| Rash maculo-papular | 10037868 |
| Rash maculovesicular | 10050004 |
| Rash morbilliform | 10037870 |
| Rash papular | 10037876 |
| Rash rubelliform | 10057984 |
| Rash scarlatiniform | 10037890 |

| | |
|---|---|
| Rash vesicular | 10037898 |
| Rash pruritic | 10037884 |
| Rash follicular | 10037857 |
| Rash pustular | 10037888 |
| Drug eruption | 10013687 |

### 13.10.5. Prolongation of the Corrected QT Interval of the ECG in Supra Therapeutic Doses

Medical concept of QT prolongation and complications. Only narrow terms from SMQ 'Torsade de pointes/QT prolongation' selected plus one additional PT under HLT 'ECG investigations'.

| SMQ: Torsade de pointes/QT prolongation<br>SMQ Code: 20000001<br>Category: A<br>Scope: Narrow | |
|---|---|
| Preferred Term | PT Code |
| Electrocardiogram QT interval abnormal | 10063748 |
| Electrocardiogram QT prolonged | 10014387 |
| Long QT syndrome | 10024803 |
| Long QT syndrome congenital | 10057926 |
| Torsade de pointes | 10044066 |
| Ventricular tachycardia | 10047302 |
| Additional selected preferred terms from HLT 'ECG investigations', HLT Code 10053104. | |
| Preferred Term | PT Code |
| Electrocardiogram repolarisation abnormality | 10052464 |

### 13.10.6. Suicidal Ideation/Behaviour

Medical concept of suicidal ideation and behaviour. Sub-SMQ 'Suicide/self-injury' (SMQ) from parent SMQ of 'Depression and Suicide/Self Injury (SMQ Code 20000035)'. Only narrow terms from the sub-SMQ selected.

| SMQ: 'Depression and Suicide/Self Injury'<br>SMQ Code: 20000035<br>Sub-SMQ: 'Suicide/self-injury' | |
|---|---|

| Category: A<br>Scope: Narrow | |
|---|---|
| Preferred Term | PT Code |
| Assisted suicide | 10079105 |
| Columbia suicide severity rating scale abnormal | 10075616 |
| Completed suicide | 10010144 |
| Depression suicidal | 10012397 |
| Intentional overdose | 10022523 |
| Intentional self-injury | 10022524 |
| Poisoning deliberate | 10036000 |
| Self-injurious ideation | 10051154 |
| Suicidal behaviour | 10065604 |
| Suicidal ideation | 10042458 |
| Suicide attempt | 10042464 |
| Suicide threat | 10077417 |
| Suspected suicide | 10082458 |
| Suspected suicide attempt | 10081704 |

### 13.10.7. Depression

Medical concept of Depression. Sub-SMQ 'Depression (excl suicide and self-injury)' (SMQ) from parent SMQ of 'Depression and Suicide/Self Injury'. Only narrow terms from the sub-SMQ selected.

| SMQ: ‘'Depression and Suicide/Self Injury'<br>SMQ Code: 20000035<br>Sub-SMQ: 'Depression (excl suicide and self-injury)'<br>Category: A<br>Scope: Narrow | |
|---|---|
| Preferred Term | PT Code |
| Activation syndrome | 10066817 |
| Adjustment disorder with depressed mood | 10001297 |
| Adjustment disorder with mixed anxiety and depressed mood | 10001299 |
| Agitated depression | 10001496 |

| | |
|---|---|
| Anhedonia | 10002511 |
| Antidepressant therapy | 10054976 |
| Childhood depression | 10068631 |
| Decreased interest | 10011971 |
| Depressed mood | 10012374 |
| Depression | 10012378 |
| Depression postoperative | 10012390 |
| Depressive symptom | 10054089 |
| Dysphoria | 10013954 |
| Electroconvulsive therapy | 10014404 |
| Feeling guilty | 10049708 |
| Feeling of despair | 10016344 |
| Feelings of worthlessness | 10016374 |
| Helplessness | 10077169 |
| Major depression | 10057840 |
| Menopausal depression | 10067371 |
| Mixed anxiety and depressive disorder | 10080836 |
| Perinatal depression | 10078366 |
| Persistent depressive disorder | 10077804 |
| Post stroke depression | 10070606 |
| Postictal depression | 10071324 |

### 13.10.8. Bipolar Disorder

Medical concept of bipolar disorder. All preferred terms from HLGT ‘Manic and Bipolar mood disorders and disturbances’ under SOC “Psychiatric disorders”; HLGT Code 10026753.

| Preferred Term | PT Code |
|---|---|
| Bipolar I disorder | 10004939 |
| Bipolar II disorder | 10004940 |
| Bipolar disorder | 10057667 |

| Preferred Term | PT Code |
|---|---|
| Cyclothymic disorder | 10011724 |
| Hypomania | 10021030 |
| Mania | 10026749 |

### 13.10.9. Psychosis

Medical concept of psychosis. Only narrow terms from SMQ 'Psychosis and psychotic disorders' selected.

| SMQ: 'Psychosis and psychotic disorders'<br>SMQ Code: 20000117<br>Category: A<br>Scope: Narrow | |
|---|---|
| Preferred Term | PT Code |
| Acute psychosis | 10001022 |
| Alcoholic psychosis | 10001632 |
| Alice in wonderland syndrome | 10001666 |
| Brief psychotic disorder with marked stressors | 10048549 |
| Brief psychotic disorder without marked stressors | 10056395 |
| Brief psychotic disorder, with postpartum onset | 10006362 |
| Charles Bonnet syndrome | 10063354 |
| Childhood psychosis | 10061040 |
| Clang associations | 10009232 |
| Cotard's syndrome | 10059591 |
| Delusion | 10012239 |
| Delusion of grandeur | 10012241 |
| Delusion of parasitosis | 10012242 |
| Delusion of reference | 10012244 |
| Delusion of replacement | 10012245 |
| Delusion of theft | 10084030 |
| Delusional disorder, erotomanic type | 10012249 |
| Delusional disorder, grandiose type | 10012250 |

| | |
|---|---|
| Delusional disorder, jealous type | 10012251 |
| Delusional disorder, mixed type | 10012252 |
| Delusional disorder, persecutory type | 10053195 |
| Delusional disorder, somatic type | 10012254 |
| Delusional disorder, unspecified type | 10012255 |
| Delusional perception | 10012258 |
| Dementia of the Alzheimer's type, with delusions | 10012295 |
| Depressive delusion | 10063033 |
| Derailment | 10012411 |
| Epileptic psychosis | 10059232 |
| Erotomanic delusion | 10015134 |
| Flight of ideas | 10016777 |
| Hallucination | 10019063 |
| Hallucination, auditory | 10019070 |
| Hallucination, gustatory | 10019071 |
| Hallucination, olfactory | 10019072 |
| Hallucination, synaesthetic | 10062824 |
| Hallucination, tactile | 10019074 |
| Hallucination, visual | 10019075 |
| Hallucinations, mixed | 10019079 |
| Hypnagogic hallucination | 10020927 |
| Hypnopompic hallucination | 10020928 |
| Hysterical psychosis | 10062645 |
| Ideas of reference | 10021212 |
| Illusion | 10021403 |
| Jealous delusion | 10023164 |
| Loose associations | 10024825 |
| Mixed delusion | 10076429 |
| Neologism | 10028916 |

| | |
|---|---|
| Neuroleptic-induced deficit syndrome | 10075295 |
| Paranoia | 10033864 |
| Paranoid personality disorder | 10033869 |
| Parkinson's disease psychosis | 10074835 |
| Paroxysmal perceptual alteration | 10063117 |
| Persecutory delusion | 10034702 |
| Postictal psychosis | 10070669 |
| Post-injection delirium sedation syndrome | 10072851 |
| Posturing | 10036437 |
| Psychosis postoperative | 10065617 |
| Psychotic behaviour | 10037249 |
| Psychotic disorder | 10061920 |
| Psychotic disorder due to a general medical condition | 10061921 |
| Reactive psychosis | 10053632 |
| Rebound psychosis | 10074833 |
| Schizoaffective disorder | 10039621 |
| Schizoaffective disorder bipolar type | 10068889 |
| Schizoaffective disorder depressive type | 10068890 |
| Schizophrenia | 10039626 |
| Schizophreniform disorder | 10039647 |
| Schizotypal personality disorder | 10039651 |
| Senile psychosis | 10039987 |
| Shared psychotic disorder | 10040535 |
| Somatic delusion | 10041317 |
| Somatic hallucination | 10062684 |
| Substance-induced psychotic disorder | 10072388 |
| Tangentiality | 10043114 |
| Thought blocking | 10043495 |
| Thought broadcasting | 10052214 |

| | |
|---|---|
| Thought insertion | 10043496 |
| Thought withdrawal | 10043497 |
| Transient psychosis | 10056326 |
| Waxy flexibility | 10047853 |

### 13.10.10. Mood Disorders

Medical concept of mood disorders. All preferred terms from HLGT 'Mood disorders and disturbances NEC', under SOC 'Psychiatric disorders'; HLGT Code 10027946.

| Preferred Term | PT Code |
|---|---|
| Affect lability | 10054196 |
| Affective ambivalence | 10077173 |
| Affective disorder | 10001443 |
| Alexithymia | 10077719 |
| Anger | 10002368 |
| Apathy | 10002942 |
| Blunted affect | 10005885 |
| Boredom | 10048909 |
| Constricted affect | 10010778 |
| Crying | 10011469 |
| Diencephalic syndrome of infancy | 10012774 |
| Dysphoria | 10013954 |
| Emotional disorder | 10014551 |
| Emotional distress | 10049119 |
| Emotional poverty | 10014557 |
| Euphoric mood | 10015535 |
| Flat affect | 10016759 |
| Frustration tolerance decreased | 10077753 |
| Inappropriate affect | 10021588 |
| Irritability | 10022998 |

| | |
|---|---|
| Laziness | 10051602 |
| Lethargy | 10024264 |
| Listless | 10024642 |
| Moaning | 10027783 |
| Mood altered | 10027940 |
| Mood disorder due to a general medical condition | 10027944 |
| Mood swings | 10027951 |
| Morose | 10027977 |
| Neuroleptic-induced deficit syndrome | 10075295 |
| Premenstrual dysphoric disorder | 10051537 |
| Premenstrual syndrome | 10036618 |
| Screaming | 10039740 |
| Seasonal affective disorder | 10039775 |
| Steroid withdrawal syndrome | 10042028 |
| Substance-induced mood disorder | 10072387 |

### 13.10.11. Anxiety

Notes: Medical concept of anxiety disorders. All preferred terms from HLGT “Anxiety disorders and symptoms”, under SOC “Psychiatric disorders”; HLGT Code 10002861.

| Preferred Terms | PT Code |
|---|---|
| Acrophobia | 10000605 |
| Activation syndrome | 10066817 |
| Acute stress disorder | 10001084 |
| Aerophobia | 10080300 |
| Agitation | 10001497 |
| Agitation postoperative | 10049989 |
| Agoraphobia | 10001502 |
| Akathisia | 10001540 |
| Algophobia | 10078056 |

| | |
|---|---|
| Animal phobia | 10002518 |
| Anniversary reaction | 10074066 |
| Anticipatory anxiety | 10002758 |
| Anxiety | 10002855 |
| Anxiety disorder | 10057666 |
| Anxiety disorder due to a general medical condition | 10002859 |
| Arachnophobia | 10051408 |
| Astraphobia | 10078372 |
| Autophobia | 10071070 |
| Body dysmorphic disorder | 10052793 |
| Burnout syndrome | 10065369 |
| Catastrophic reaction | 10082329 |
| Cibophobia | 10082413 |
| Claustrophobia | 10009244 |
| Compulsions | 10010219 |
| Compulsive cheek biting | 10076510 |
| Compulsive handwashing | 10071263 |
| Compulsive hoarding | 10068007 |
| Compulsive lip biting | 10066241 |
| Compulsive shopping | 10067948 |
| Cryophobia | 10082662 |
| Dermatillomania | 10065701 |
| Dysmorphophobia | 10049096 |
| Emetophobia | 10070637 |
| Fear | 10016275 |
| Fear of animals | 10016276 |
| Fear of closed spaces | 10016277 |
| Fear of crowded places | 10050365 |
| Fear of death | 10066392 |

| | |
|---|---|
| Fear of disease | 10016278 |
| Fear of eating | 10050366 |
| Fear of falling | 10048744 |
| Fear of injection | 10073753 |
| Fear of open spaces | 10016279 |
| Fear of pregnancy | 10067035 |
| Fear of weight gain | 10016280 |
| Fear-related avoidance of activities | 10080136 |
| Generalised anxiety disorder | 10018075 |
| Glossophobia | 10080077 |
| Haemophobia | 10073458 |
| Haphephobia | 10067580 |
| Herpetophobia | 10081809 |
| Hydrophobia | 10053317 |
| Hyperarousal | 10080831 |
| Immunisation anxiety related reaction | 10075205 |
| Kinesiophobia | 10078430 |
| Limited symptom panic attack | 10024511 |
| Mysophobia | 10078769 |
| Nail picking | 10066779 |
| Nervousness | 10029216 |
| Neurosis | 10029333 |
| Noctiphobia | 10057946 |
| Nocturnal fear | 10057948 |
| Nosocomephobia | 10083993 |
| Nosophobia | 10063546 |
| Obsessive need for symmetry | 10077179 |
| Obsessive rumination | 10056264 |
| Obsessive thoughts | 10029897 |

| | |
|---|---|
| Obsessive-compulsive disorder | 10029898 |
| Obsessive-compulsive symptom | 10077894 |
| Ochlophobia | 10050095 |
| Osmophobia | 10060765 |
| Paediatric autoimmune neuropsychiatric disorders associated with streptococcal infection | 10072147 |
| Panic attack | 10033664 |
| Panic disorder | 10033666 |
| Panic reaction | 10033670 |
| Paruresis | 10069024 |
| Performance fear | 10034432 |
| Phagophobia | 10050096 |
| Pharmacophobia | 10069423 |
| Phobia | 10034912 |
| Phobia of driving | 10056676 |
| Phobia of exams | 10034913 |
| Phobic avoidance | 10034918 |
| Phonophobia | 10054956 |
| Photaugiaphobia | 10064420 |
| Postpartum anxiety | 10082233 |
| Postpartum neurosis | 10036419 |
| Postpartum stress disorder | 10056394 |
| Post-traumatic stress disorder | 10036316 |
| Procedural anxiety | 10075204 |
| Pseudoangina | 10056610 |
| Selective mutism | 10039917 |
| Separation anxiety disorder | 10040045 |
| Sitophobia | 10080170 |
| Social anxiety disorder | 10041242 |

| | |
|---|---|
| Social fear | 10041247 |
| Stress | 10042209 |
| Tension | 10043268 |
| Terminal agitation | 10077416 |
| Thanatophobia | 10064723 |
| Thermophobia | 10075147 |
| Trichotemnomania | 10072752 |
| Trichotillomania | 10044629 |

### 13.10.12. Sleep Disorders

Medical concept of sleep disorders. All preferred terms from (1) HLGT 'Sleep Disorders and Disturbances', 'Psychiatric disorders' SOC plus (2) HLGT 'Sleep disturbances (incl subtypes)', 'Nervous system' SOC. Numerous duplicated preferred terms e.g. middle insomnia.

| HLGT Sleep Disorders and Disturbances, HLGT Code 10040991 | |
|---|---|
| Preferred Term | PT Code |
| Abnormal dreams | 10000125 |
| Abnormal sleep-related event | 10061613 |
| Advanced sleep phase | 10001423 |
| Behavioural induced insufficient sleep syndrome | 10081938 |
| Behavioural insomnia of childhood | 10072072 |
| Breathing-related sleep disorder | 10006344 |
| Cataplexy | 10007737 |
| Circadian rhythm sleep disorder | 10009191 |
| Confusional arousal | 10067494 |
| Delayed sleep phase | 10012209 |
| Dyssomnia | 10061827 |
| Exploding head syndrome | 10080684 |
| Hypersomnia | 10020765 |
| Hypersomnia related to another mental condition | 10020767 |

| | |
|---|---|
| Hypersomnia-bulimia syndrome | 10053712 |
| Hypnagogic hallucination | 10020927 |
| Hypnopompic hallucination | 10020928 |
| Hyposomnia | 10067530 |
| Initial insomnia | 10022035 |
| Insomnia | 10022437 |
| Insomnia related to another mental condition | 10022443 |
| Irregular sleep phase | 10022995 |
| Irregular sleep wake rhythm disorder | 10080301 |
| Loss of dreaming | 10065085 |
| Middle insomnia | 10027590 |
| Narcolepsy | 10028713 |
| Nightmare | 10029412 |
| Non-24-hour sleep-wake disorder | 10078086 |
| Parasomnia | 10061910 |
| Paradoxical insomnia | 10083337 |
| Periodic limb movement disorder | 10064600 |
| Pickwickian syndrome | 10035004 |
| Poor quality sleep | 10062519 |
| Rapid eye movement sleep behaviour disorder | 10077299 |
| Rapid eye movements sleep abnormal | 10037841 |
| Shift work disorder | 10078088 |
| Sleep apnoea syndrome | 10040979 |
| Sleep attacks | 10040981 |
| Sleep disorder | 10040984 |
| Sleep disorder due to a general medical condition | 10063910 |
| Sleep disorder due to general medical condition, hypersomnia type | 10040985 |
| Sleep disorder due to general medical condition, insomnia type | 10040986 |
| Sleep disorder due to general medical condition, mixed type | 10040987 |

| | |
|---|---|
| Sleep disorder due to general medical condition, parasomnia type | 10040988 |
| Sleep inertia | 10067493 |
| Sleep paralysis | 10041002 |
| Sleep sex | 10067492 |
| Sleep talking | 10041009 |
| Sleep terror | 10041010 |
| Sleep-related eating disorder | 10067315 |
| Somnambulism | 10041347 |
| Somnolence | 10041349 |
| Somnolence neonatal | 10041350 |
| Sopor | 10058709 |
| Stupor | 10042264 |
| Terminal insomnia | 10068932 |
| Upper airway resistance syndrome | 10063968 |
| HLGT Sleep disturbances (incl subtypes), HLGT code 10040998 | |
| Abnormal dreams | 10000125 |
| Abnormal sleep-related event | 10061613 |
| Advanced sleep phase | 10001423 |
| Behavioural induced insufficient sleep syndrome | 10081938 |
| Behavioural insomnia of childhood | 10072072 |
| Breathing-related sleep disorder | 10006344 |
| Cataplexy | 10007737 |
| Central-alveolar hypoventilation | 10007982 |
| Circadian rhythm sleep disorder | 10009191 |
| Confusional arousal | 10067494 |
| Delayed sleep phase | 10012209 |
| Dyssomnia | 10061827 |
| Fatal familial insomnia | 10072077 |
| Hypersomnia | 10020765 |

| | |
|---|---|
| Hyposomnia | 10067530 |
| Initial insomnia | 10022035 |
| Insomnia | 10022437 |
| Irregular sleep phase | 10022995 |
| Irregular sleep wake rhythm disorder | 10080301 |
| Loss of dreaming | 10065085 |
| Microsleep | 10076954 |
| Middle insomnia | 10027590 |
| Narcolepsy | 10028713 |
| Non-24-hour sleep-wake disorder | 10078086 |
| Periodic limb movement disorder | 10064600 |
| Pickwickian syndrome | 10035004 |
| Poor quality sleep | 10062519 |
| Rapid eye movement sleep behaviour disorder | 10077299 |
| Rapid eye movements sleep abnormal | 10037841 |
| Shift work disorder | 10078088 |
| Sleep apnoea syndrome | 10040979 |
| Sleep deficit | 10080881 |
| Sleep inertia | 10067493 |
| Sleep paralysis | 10041002 |
| Sleep sex | 10067492 |
| Sleep talking | 10041009 |
| Sleep terror | 10041010 |
| Sleep-related eating disorder | 10067315 |
| Somnambulism | 10041347 |
| Sudden onset of sleep | 10050014 |
| Terminal insomnia | 10068932 |
| Upper airway resistance syndrome | 10063968 |

### 13.10.13. Injection site Reactions

Use eCRF terms for ISR.

### 13.10.14. Seizures

Medical concept of seizures. Only narrow terms from SMQ 'Convulsions' selected plus selected PTs of possible seizure events from HLT 'Disturbances in consciousness NEC' under SOC 'Nervous systems disorders' and HLT 'Confusion and disorientation' under SOC 'Psychiatric disorders'.

| SMQ: ‘Convulsions’<br>SMQ Code: 20000079<br>Category: A<br>Scope: Narrow | |
|---|---|
| Preferred Term | PT Code |
| 1p36 deletion syndrome | 10082398 |
| 2-Hydroxyglutaric aciduria | 10078971 |
| Acquired epileptic aphasia | 10052075 |
| Acute encephalitis with refractory, repetitive partial seizures | 10076948 |
| Alcoholic seizure | 10056347 |
| Alpers disease | 10083857 |
| Aspartate-glutamate-transporter deficiency | 10079140 |
| Atonic seizures | 10003628 |
| Atypical benign partial epilepsy | 10056699 |
| Automatism epileptic | 10003831 |
| Autonomic seizure | 10049612 |
| Baltic myoclonic epilepsy | 10054895 |
| Benign familial neonatal convulsions | 10067866 |
| Benign rolandic epilepsy | 10070530 |
| Biotinidase deficiency | 10071434 |
| CEC syndrome | 10083749 |
| CDKL5 deficiency disorder | 10083005 |
| Change in seizure presentation | 10075606 |
| Clonic convulsion | 10053398 |

| | |
|---|---|
| Congenital bilateral perisylvian syndrome | 10082716 |
| Convulsion in childhood | 10052391 |
| Convulsions local | 10010920 |
| Convulsive threshold lowered | 10010927 |
| CSWS syndrome | 10078827 |
| Deja vu | 10012177 |
| Double cortex syndrome | 10073490 |
| Dreamy state | 10013634 |
| Drug withdrawal convulsions | 10013752 |
| Early infantile epileptic encephalopathy with burst-suppression | 10071545 |
| Eclampsia | 10014129 |
| Epilepsy | 10015037 |
| Epilepsy surgery | 10079824 |
| Epilepsy with myoclonic-atonic seizures | 10081179 |
| Epileptic aura | 10015049 |
| Epileptic psychosis | 10059232 |
| Febrile convulsion | 10016284 |
| Febrile infection-related epilepsy syndrome | 10079438 |
| Focal dyscognitive seizures | 10079424 |
| Frontal lobe epilepsy | 10049424 |
| Gelastic seizure | 10082918 |
| Generalised onset non-motor seizure | 10083376 |
| Generalised tonic-clonic seizure | 10018100 |
| Glucose transporter type 1 deficiency syndrome | 10078727 |
| GM2 gangliosidosis | 10083933 |
| Grey matter heterotopia | 10082084 |
| Hemimegalencephaly | 10078100 |
| Hyperglycaemic seizure | 10071394 |
| Hypocalcaemic seizure | 10072456 |

| | |
|---|---|
| Hypoglycaemic seizure | 10048803 |
| Hyponatraemic seizure | 10073183 |
| Idiopathic generalised epilepsy | 10071081 |
| Infantile spasms | 10021750 |
| Juvenile myoclonic epilepsy | 10071082 |
| Lafora's myoclonic epilepsy | 10054030 |
| Lennox-Gastaut syndrome | 10048816 |
| Migraine-triggered seizure | 10076676 |
| Molybdenum cofactor deficiency | 10069687 |
| Multiple subpial transection | 10079825 |
| Myoclonic epilepsy | 10054859 |
| Myoclonic epilepsy and ragged-red fibres | 10069825 |
| Neonatal epileptic seizure | 10082068 |
| Neonatal seizure | 10082067 |
| Partial seizures | 10061334 |
| Partial seizures with secondary generalisation | 10056209 |
| Petit mal epilepsy | 10034759 |
| Polymicrogyria | 10073489 |
| Post stroke epilepsy | 10076982 |
| Post stroke seizure | 10076981 |
| Postictal headache | 10052470 |
| Postictal paralysis | 10052469 |
| Postictal psychosis | 10070669 |
| Postictal state | 10048727 |
| Post-traumatic epilepsy | 10036312 |
| Schizencephaly | 10073487 |
| Seizure | 10039906 |
| Seizure anoxic | 10039907 |
| Seizure cluster | 10071350 |

| | |
|---|---|
| Seizure like phenomena | 10071048 |
| Severe myoclonic epilepsy of infancy | 10073677 |
| Simple partial seizures | 10040703 |
| Status epilepticus | 10041962 |
| Sudden unexplained death in epilepsy | 10063894 |
| Temporal lobe epilepsy | 10043209 |
| Tonic clonic movements | 10051171 |
| Tonic convulsion | 10043994 |
| Tonic posturing | 10075125 |
| Topectomy | 10073488 |
| Transient epileptic amnesia | 10081728 |
| Tuberous sclerosis complex | 10080584 |
| Uncinate fits | 10045476 |
| Additional selected preferred terms from HLT Disturbances in consciousness NEC, HLT code 10013509 and HLT Confusion and disorientation, HLT code 10010301. | |
| Preferred Term | PT Code |
| Confusional state | 10010305 |
| Loss of consciousness | 10024855 |
| Syncope | 10042772 |
| Sopor | 10058709 |
| Stupor | 10042264 |
| Altered state of consciousness | 10050093 |
| Depressed level of consciousness | 10012373 |
| Consciousness fluctuating | 10050093 |

### 13.10.15. Weight Gain

Medical concept of weight gain. Selected PTs from HLT 'General nutritional disorders NEC', under SOC 'Metabolism and nutrition disorders', and HLT 'Physical examination procedures and organ system status', under SOC 'Investigations' and HLT 'General signs and symptoms NEC', under SOC 'General disorders and administration site conditions'.

| PTs (Select) from HLT General nutritional disorders NEC, HLT code 10018067 | |
|---|---|
| Preferred Term | PT Code |
| Abdominal fat apron | 10077983 |
| Overweight | 10033307 |
| Abnormal weight gain | 10000188 |
| Central obesity | 10065941 |
| Obesity | 10029883 |
| Abdominal fat apron | 10077983 |
| Overweight | 10033307 |
| Abnormal weight gain | 10000188 |
| Central obesity | 10065941 |
| Obesity | 10029883 |
| PTs (Select) from HLT Physical examination procedures and organ system status, HLT Code 10071941 | |
| Preferred Term | PT Code |
| Weight abnormal | 10056814 |
| Weight increased | 10047899 |
| Waist circumference increased | 10064863 |
| Body mass index abnormal | 10074506 |
| Body mass index increased | 10005897 |
| PTs (Select) from HLT General signs and symptoms NEC, HLT Code 10018072 | |
| Preferred Term | PT Code |
| Fat tissue increased | 10016251 |
| Sarcopenic obesity | 10083992 |

### 13.10.16. Rhabdomyolysis

Medical concept of rhabdomyolysis. Only narrow terms only for SMQ 'Rhabdomyolysis/myopathy' plus 2 additional preferred terms selected from HGLT 'muscle disorders' under SOC 'Musculoskeletal and connective tissue disorders'.

| SMQ: 'Rhabdomyolysis/myopathy'<br>SMQ Code: 20000002<br>Category: A<br>Scope: Narrow | |
|---|---|
| Preferred Term | PT Code |
| Muscle necrosis | 10028320 |
| Myoglobin blood increased | 10028625 |
| Myoglobin blood present | 10059888 |
| Myoglobin urine present | 10028631 |
| Myoglobinaemia | 10058735 |
| Myoglobinuria | 10028629 |
| Myopathy | 10028641 |
| Myopathy toxic | 10028648 |
| Necrotising myositis | 10074769 |
| Rhabdomyolysis | 10039020 |
| Thyrotoxic myopathy | 10081524 |
| PTs (Select) from HGLT muscle disorders, HLGT Code 10028302 | |
| Preferred Term | PT Code |
| Myalgia | 10028411 |
| Myositis | 10028653 |

### 13.10.17. Pancreatitis

Medical concept of acute pancreatitis. Only narrow terms of SMQ 'Acute pancreatitis' selected. Algorithmic approach for this SMQ not used due to complexity in applying and poor specificity of remaining categories. Category A selected as PTs because more specific for concept (only narrow terms).

| SMQ: 'Acute pancreatitis'<br>SMQ Code: 20000022<br>Category: A | |
|---|---|

| Scope: Narrow | |
|---|---|
| Preferred Term | PT Code |
| Cullen's sign | 10059029 |
| Grey Turner's sign | 10075426 |
| Haemorrhagic necrotic pancreatitis | 10076058 |
| Hereditary pancreatitis | 10056976 |
| Immune-mediated pancreatitis | 10083072 |
| Ischaemic pancreatitis | 10066127 |
| Oedematous pancreatitis | 10052400 |
| Pancreatic abscess | 10048984 |
| Pancreatic cyst drainage | 10082531 |
| Pancreatic haemorrhage | 10033625 |
| Pancreatic necrosis | 10058096 |
| Pancreatic phlegmon | 10056975 |
| Pancreatic pseudoaneurysm | 10081762 |
| Pancreatic pseudocyst | 10033635 |
| Pancreatic pseudocyst drainage | 10033636 |
| Pancreatic pseudocyst haemorrhage | 10083813 |
| Pancreatic pseudocyst rupture | 10083811 |
| Pancreatitis | 10033645 |
| Pancreatitis acute | 10033647 |
| Pancreatitis haemorrhagic | 10033650 |
| Pancreatitis necrotising | 10033654 |
| Pancreatitis relapsing | 10033657 |
| Pancreatorenal syndrome | 10056277 |

### 13.10.18. Impact on Creatinine

Medical concept of worsening renal function/renal failure in the context of impact on creatinine. Only narrow terms from SMQ 'Acute renal failure' plus all PTs from HLT 'Renal failure and impairment', under SOC 'Renal and urinary disorders'. Numerous duplicated preferred terms e.g. renal failure

| SMQ: 'Acute renal failure'<br>SMQ Code: 20000003<br>Category: A<br>Scope: Narrow | |
|---|---|
| Preferred Term | PT Code |
| Acute kidney injury | 10069339 |
| Acute phosphate nephropathy | 10069688 |
| Anuria | 10002847 |
| Azotaemia | 10003885 |
| Continuous haemodiafiltration | 10066338 |
| Dialysis | 10061105 |
| Foetal renal impairment | 10078987 |
| Haemodialysis | 10018875 |
| Haemofiltration | 10053090 |
| Neonatal anuria | 10049778 |
| Nephropathy toxic | 10029155 |
| Oliguria | 10030302 |
| Peritoneal dialysis | 10034660 |
| Prerenal failure | 10072370 |
| Renal failure | 10038435 |
| Renal failure neonatal | 10038447 |
| Renal impairment | 10062237 |
| Renal impairment neonatal | 10049776 |
| Subacute kidney injury | 10081980 |
| Renal Failure and Impairment HLT, HLT Code 10038443 | |
| Preferred Term | PT Code |
| Acute Kidney injury | 10069339 |
| Anuria | 10002847 |
| Atypical haemolytic uraemic syndrome | 10079840 |
| Cardiorenal syndrome | 10068230 |

| | |
|---|---|
| Chronic kidney disease | 10064848 |
| Crush syndrome | 10050702 |
| Diabetic end stage renal disease | 10012660 |
| End stage renal disease | 10077512 |
| Foetal renal impairment | 10078987 |
| Haemolytic uraemic syndrome | 10018932 |
| Hepatorenal failure | 10019845 |
| Hepatorenal syndrome | 10019846 |
| Nail-patella syndrome | 10063431 |
| Neonatal anuria | 10049778 |
| Oliguria | 10030302 |
| Pancreatorenal syndrome | 10056277 |
| Postoperative renal failure | 10056675 |
| Postrenal failure | 10059345 |
| Prerenal failure | 10072370 |
| Propofol infusion syndrome | 10063181 |
| Renal failure | 10038435 |
| Renal failure neonatal | 10038447 |
| Renal impairment | 10062237 |
| Renal impairment neonatal | 10049776 |
| Renal injury | 10061481 |
| Scleroderma renal crisis | 10062553 |
| Traumatic anuria | 10044501 |

### 13.10.19. Safety During Pregnancy

Use AE terms co-reported in pregnancy exposures to CAB.

## 13.11. Appendix 11: Identification of COVID-19 Adverse Events

COVID-19 adverse events are identified based on MedDRA coded values and/or AE referenced in the COVID-19 Coronavirus Infection assessment. The Lowest Level Terms (LLTs) and codes, Preferred Terms (PTs), High Level Terms (HLTs), High Level Group Terms (HLGTs), and System Organ Classes (SOCs), below are from MedDRA 23.0. In case there is a change to the version of MedDRA at time of reporting, the coded values based on the MedDRA version at the time of reporting will be used. The additional events may also be added based on the blinded review of AE data collected on study prior to the database freeze.

SOC: Infections and infestations

| LLT code | LLT | PT | HLT | HLGT |
|---|---|---|---|---|
| 10084459 | Asymptomatic COVID-19 | Asymptomatic COVID-19 | Coronavirus infections | Viral infectious disorders |
| 10084467 | Asymptomatic SARS-CoV-2 infection | Asymptomatic COVID-19 | Coronavirus infections | Viral infectious disorders |
| 10053983 | Corona virus infection | Coronavirus infection | Coronavirus infections | Viral infectious disorders |
| 10051905 | Coronavirus infection | Coronavirus infection | Coronavirus infections | Viral infectious disorders |
| 10084382 | Coronavirus disease 2019 | COVID-19 | Coronavirus infections | Viral infectious disorders |
| 10084268 | COVID-19 | COVID-19 | Coronavirus infections | Viral infectious disorders |
| 10084401 | COVID-19 respiratory infection | COVID-19 | Coronavirus infections | Viral infectious disorders |
| 10084270 | SARS-CoV-2 acute respiratory disease | COVID-19 | Coronavirus infections | Viral infectious disorders |
| 10084272 | SARS-CoV-2 infection | COVID-19 | Coronavirus infections | Viral infectious disorders |
| 10084381 | Coronavirus pneumonia | COVID-19 pneumonia | Coronavirus infections | Viral infectious disorders |
| 10084380 | COVID-19 pneumonia | COVID-19 pneumonia | Coronavirus infections | Viral infectious disorders |
| 10084383 | Novel COVID-19-infected pneumonia | COVID-19 pneumonia | Coronavirus infections | Viral infectious disorders |
| 10084451 | Suspected COVID-19 | Suspected COVID-19 | Coronavirus infections | Viral infectious disorders |
| 10084452 | Suspected SARS-CoV-2 infection | Suspected COVID-19 | Coronavirus infections | Viral infectious disorders |
| 10084461 | SARS-CoV-2 carrier | SARS-CoV-2 carrier | Infectious disorders carrier | Ancillary infectious topics |

# 13.12. Appendix 12: Abbreviations & Trade Marks

## 13.12.1. Abbreviations

| Abbreviation | Description |
|---|---|
| ADaM | Analysis Data Model |
| AE | Adverse Event |
| AIC | Akaike's Information Criteria |
| A&R | Analysis and Reporting |
| CDISC | Clinical Data Interchange Standards Consortium |
| CI | Confidence Interval |
| CPMS | Clinical Pharmacology Modelling & Simulation |
| CS | Clinical Statistics |
| CSR | Clinical Study Report |
| CTR | Clinical Trial Register |
| $CV_b$ / $CV_w$ | Coefficient of Variation (Between) / Coefficient of Variation (Within) |
| DBF | Database Freeze |
| DBR | Database Release |
| DOB | Date of Birth |
| DP | Decimal Places |
| eCRF | Electronic Case Record Form |
| EEP | Efficacy Evaluable Population |
| EMA | European Medicines Agency |
| FDA | Food and Drug Administration |
| FDAAA | Food and Drug Administration Clinical Results Disclosure Requirements |
| GSK | GlaxoSmithKline |
| IA | Interim Analysis |
| ICH | International Conference on Harmonization |
| IDMC | Independent Data Monitoring Committee |
| IDSL | Integrated Data Standards Library |
| IMMS | International Modules Management System |
| IP | Investigational Product |
| ITT | Intent-To-Treat |
| MMRM | Mixed Model Repeated Measures |
| PBMC | Peripheral Blood Mononuclear Cells |
| PCI | Potential Clinical Importance |
| PD | Pharmacodynamic |
| PDMP | Protocol Deviation Management Plan |
| PK | Pharmacokinetic |
| PP | Per Protocol |
| PopPK | Population PK |
| QC | Quality Control |
| QTcF | Frederica's QT Interval Corrected for Heart Rate |
| QTcB | Bazett's QT Interval Corrected for Heart Rate |
| RAP | Reporting & Analysis Plan |
| RAMOS | Randomization & Medication Ordering System |

| Abbreviation | Description |
|---|---|
| SAC | Statistical Analysis Complete |
| SDSP | Study Data Standardization Plan |
| SDTM | Study Data Tabulation Model |
| SOP | Standard Operation Procedure |
| TA | Therapeutic Area |
| TFL | Tables, Figures & Listings |

### 13.12.2. Trademarks

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

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

## 13.13. Appendix 13: List of Data Displays

All data displays will use the term "subject" rather than "participant" in accordance with CDSIC and GSK Statistical Display Standards.

Where applicable, all summary displays will present data across both the Intervention and Extension phases unless explicitly stated otherwise in the display title.

### 13.13.1. Data Display Numbering

The following numbering will be applied for RAP generated displays:

| Section | Tables | Figures |
|---|---|---|
| Study Population | 1.1 to 1.n | 1.1 to 1.n |
| Efficacy | 2.1 to 2.n | 2.1 to 2.n |
| Safety | 3.1 to 3.n | 3.1 to 3.n |
| Pharmacokinetic | 4.1 to 4.n | 4.1 to 4.n |
| Virology | 5.1 to 5.n | 5.1 to 4.n |
| Other | 6.1 to 6.n | 6.1 to 6.n |
| **Section** | **Listings** | |
| ICH Listings | 1 to x | |
| Other Listings | y to z | |

### 13.13.2. Mock Example Shell Referencing

Nonstandard specifications will be referenced as indicated below (where a study specific mock shell is available) or the location of a similar display produced for a different study in the HARP reporting environment will be provided as reference. If required example mock-up displays provided in Appendix 14: Example Mock Shells for Data Displays.

| Section | Figure | Table | Listing |
|---|---|---|---|
| Study Population | POP_Fn | POP_Tn | POP_Ln |
| Efficacy | EFF_Fn | EFF_Tn | EFF_Ln |
| Safety | SAF_Fn | SAF_Tn | SAF_Ln |
| Pharmacokinetic | PK_Fn | PK_Tn | PK_Ln |
| Virology | VIR_Fn | VIR_Tn | VIR_Ln |
| Other | OTR_Tn | OTR_Fn | OTR_Ln |

### 13.13.3. Deliverables

| Delivery | Description |
|---|---|
| HL | Month 12 Headline |
| M12 | Month 12 Analysis |
| EOS | End of Study Analysis |

### 13.13.4. Study Population Tables

| Study Population Tables | | | | | |
|---|---|---|---|---|---|
| **No.** | **Population** | **GSK Standard / Example Shell** | **Title** | **Programming Notes** | **Deliverable** |
| **Subject Disposition** | | | | | |
| 1.1. | Safety | ES1 | Summary of Subject Disposition for the Subject Conclusion Record | ICH E3, FDAAA, EudraCT | HL, M12, EOS |
| 1.2. | Safety | SD1 | Summary of Treatment Status and Reasons for Discontinuation of Study Treatment | ICH E3 | M12, EOS |
| 1.3. | Safety | ES4 | Summary of Subject Disposition at Each Study Phase | ICH E3<br>Intervention/Extension phase: status and reason for withdrawal based on date and reason collected in the study treatment discontinuation form.<br>Long term Follow-up: completion/withdrawal based on data collected in the Study Conclusion form. | M12, EOS |
| 1.4. | Safety | ES5 | Summary of Reason for Withdrawal at Each Study Phase | FDAAA, EudraCT | HL, M12, EOS |
| 1.5. | Safety | ES11 | Summary of Outcome of Adverse Events Which Led to Study Withdrawal/Treatment Discontinuation at Each Study Phase | EudraCT | M12, EOS |
| 1.6. | Screened | ES6 | Summary of Screening Status and Reasons for Screen Failure | Journal Requirements | M12, EOS |
| 1.7. | Enrolled | NS1 | Summary of Number of Subjects by Country and Site ID | EudraCT/Clinical Operations | M12, EOS |
| 1.8. | Screened | NS1 | Summary of Number of Subjects by Site Type and Site ID | Replace Country with Site Type<br>Add column for Investigator Name | M12, EOS |
| **Protocol Deviation** | | | | | |
| 1.9. | Enrolled | DV1 | Summary of Important Protocol Deviations | ICH E3 | M12, EOS |

| Study Population Tables | | | | | |
|---|---|---|---|---|---|
| **No.** | **Population** | **GSK Standard / Example Shell** | **Title** | **Programming Notes** | **Deliverable** |
| 1.10. | Enrolled | DV1 | Summary of Important COVID-19 Related Protocol Deviations | Update the label for the first row to be "ANY IMPORTANT COVID-19 RELATED PROTOCOL DEVIATIONS" | M12, EOS |
| 1.11. | Enrolled | DV1 | Summary of Important Non-COVID-19 Protocol Deviations | Update the label for the first row to be "ANY IMPORTANT NON-COVID-19 RELATED PROTOCOL DEVIATIONS" | M12, EOS |
| 1.12. | Enrolled | DV1 | Summary of All COVID-19 Protocol Deviations by Site | Update the label for the first row to be "ANY COVID-19 RELATED PROTOCOL DEVIATIONS".<br>Summary for each site and 'Total' across sites. | HL, M12, EOS |
| 1.13. | Enrolled | DV1 | Summary of All Implementation Protocol Deviations by Site | Update the label for the first row to be "ANY IMPLEMENTATION RELATED PROTOCOL DEVIATIONS"<br>Summary for each site and 'Total' across sites. | HL, M12, EOS |
| **Population Analysed** | | | | | |
| 1.14. | Screened | SP1 | Summary of Study Populations | GSK Statistical Display Standard | M12, EOS |
| 1.15. | Enrolled | SP2 | Summary of Exclusions from the Safety Population | GSK Statistical Display Standard | M12, EOS |
| **Demographic and Baseline Characteristics** | | | | | |
| 1.16. | Safety | DM1 | Summary of Demographic Characteristics | ICH E3, FDAAA, EudraCT | HL, M12, EOS |
| 1.17. | Enrolled | DM11 | Summary of Age Ranges | EudraCT | M12, EOS |
| 1.18. | Safety | DM6 | Summary of Race and Racial Combinations | ICH E3, FDA, FDAAA, EudraCT | M12, EOS |
| 1.19. | Safety | BASELINE2 | Distribution of CD4+ Cell Count Results at Screening and Baseline | | M12, EOS |
| 1.20. | Safety | BASELINE3 | Summary of Hepatitis Status at Entry | | M12, EOS |

| Study Population Tables | | | | | |
|---|---|---|---|---|---|
| **No.** | **Population** | **GSK Standard / Example Shell** | **Title** | **Programming Notes** | **Deliverable** |
| 1.21. | Safety | CDC1 | Summary of CDC Classification of HIV-1 Infection at Baseline | | M12, EOS |
| **Prior and Concomitant Medications** | | | | | |
| 1.22. | Safety | MH1 | Summary of Past Medical Conditions | ICH E3 | M12, EOS |
| 1.23. | Safety | MH4 | Summary of Past Cardiac, Gastrointestinal, Metabolism and Nutrition, Psychiatric, Renal and Urinary, Nervous System Conditions, and Hepatobiliary Disorders | ICH E3 | M12, EOS |
| 1.24. | Safety | MH1 | Summary of Current Medical Conditions | ICH E3 | M12, EOS |
| 1.25. | Safety | MH4 | Summary of Current Cardiac, Gastrointestinal, Metabolism and Nutrition, Psychiatric, Renal and Urinary, Nervous System Conditions, and Hepatobiliary Disorders | ICH E3 | M12, EOS |
| 1.26. | Safety | CM9 | Summary of Concomitant Medications by Ingredient Combinations | ICH E3<br>See GSK Statistical Display Standard<br>Multi-ingredient medications will be labelled according to the sum of their ingredients, i.e., Generic Term. | M12, EOS |
| 1.27. | Safety | 207966/primary_15/T1.30 | Summary of Prior Antiretroviral Therapy Medications | Remove the footnote. Follow definitions in Section 13.4.1 to determine the prior ART medications. | M12, EOS |
| 1.28. | Safety | 201585/primary_02/T1.30 | Summary of Antiretroviral Therapy Taken During Screening by Baseline Third Agent Class | Like Example shell but stratified by Baseline Third Agent Class (NNRTI, INI, PI); add 'Any' row under each class. | M12, EOS |
| 1.29. | Safety | RF1 | Summary of HIV Risk Factors | | M12, EOS |

### 13.13.5. Efficacy Tables

| Efficacy: Tables | | | | | |
|---|---|---|---|---|---|
| **No.** | **Population** | **GSK Standard/ Example Shell** | **Title** | **Programming Notes** | **Deliverable** |
| **Snapshot** | | | | | |
| 2.1. | Safety | EFF_T1 See Section 13.14 | Summary of Study Outcomes (50 c/mL cutoff) at Month 12 (Intervention Phase) – Modified Snapshot Analysis with COVID-19 related LOCF | Missing HIV-1 RNA due to COVID-19 are imputing using last post baseline value carried forward. | HL, M12 |
| 2.2. | Safety | EFF_T2 See Section 13.14 | Summary of Study Outcomes (50 c/mL cutoff) at Month 12 (Intervention Phase) –Snapshot Analysis | With expanded COVID-19 related/Non-related categories | HL, M12 |
| 2.3. | Safety | SNAPSHOT4 | Proportion of Subjects with Plasma HIV-1 RNA ≥ 50 c/mL Over Time (Intervention Phase) – Modified Snapshot Analysis with COVID-19 related LOCF | Missing HIV-1 RNA due to COVID-19 are imputing using last post baseline value carried forward.<br>Use Exact (Clopper-Pearson) method for 95% confidence Intervals. | M12 |
| 2.4. | Safety | SNAPSHOT4 | Proportion of Subjects with Plasma HIV-1 RNA < 50 c/mL Over Time (Intervention Phase) – Modified Snapshot Analysis with COVID-19 related LOCF | Missing HIV-1 RNA due to COVID-19 are imputing using last post baseline value carried forward.<br>Use Exact (Clopper-Pearson) method for 95% confidence Intervals. | M12 |
| 2.5. | Safety | SNAPSHOT7 | Summary of Study Outcomes (50 c/mL cutoff) at Month 12 by Site Type (Intervention Phase) – Modified Snapshot Analysis with COVID-19 related LOCF | Missing HIV-1 RNA due to COVID-19 are imputing using last post baseline value carried forward. | M12 |
| **CVF** | | | | | |
| 2.6. | Safety | VF1 | Cumulative Proportion of Subjects Meeting Confirmed Virologic Failure Criteria Over Time (Intervention Phase) | | HL, M12 |

| Efficacy: Tables | | | | | |
|---|---|---|---|---|---|
| **No.** | **Population** | **GSK Standard/ Example Shell** | **Title** | **Programming Notes** | **Deliverable** |
| 2.7. | Safety | VF2 | Proportion of Subjects Meeting Confirmed Virologic Failure Criteria Over Time | | M12, EOS |
| **CD4** | | | | | |
| 2.8. | Safety | LB1 | Summary of CD4+ Cell Count (cells/mm^3) by Visit | | M12, EOS |
| 2.9. | Safety | LB1 | Summary of Change from Baseline in CD4+ Cell Count (cells/mm^3) by Visit | | M12, EOS |
| **HIV Associated Conditions** | | | | | |
| 2.10. | Safety | CDC2 | Summary of Post-Baseline CDC Stage 3 HIV-1 Associated Conditions Including Recurrences | | M12, EOS |
| 2.11. | Safety | CDC2 | Summary of Post-Baseline CDC Stage 3 HIV-1 Associated Conditions Excluding Recurrences | | M12, EOS |

## 13.13.6. Efficacy Figures

| Efficacy: Figures | | | | | |
|---|---|---|---|---|---|
| **No.** | **Population** | **GSK Standard / Example Shell** | **Title** | **Programming Notes** | **Deliverable** |
| 2.1. | Safety | SNAPSHOT8 | Percent (95% CI) of Subjects with Plasma HIV-1 RNA ≥ 50 copies/mL Over Time (Intervention Phase) – Modified Snapshot Analysis with COVID-19 related LOCF | Missing HIV-1 RNA due to COVID-19 are imputing using last post baseline value carried forward.<br><br>Use Exact (Clopper-Pearson) method for 95% confidence Intervals. | M12, EOS |

| Efficacy: Figures | | | | | |
|---|---|---|---|---|---|
| **No.** | **Population** | **GSK Standard / Example Shell** | **Title** | **Programming Notes** | **Deliverable** |
| 2.2. | Safety | SNAPSHOT8 | Percent (95% CI) of Subjects with Plasma HIV-1 RNA < 50 copies/mL Over Time (Intervention Phase) – Modified Snapshot Analysis with COVID-19 related LOCF | Missing HIV-1 RNA due to COVID-19 are imputing using last post baseline value carried forward.<br><br>Use Exact (Clopper-Pearson) method for 95% confidence Intervals. | M12, EOS |
| 2.3. | Safety | SNAPSHOT10 | Individual Plasma HIV-1 RNA for Subjects Snapshot Algorithm Plasma HIV-1 RNA >= 50 copies/mL at Month 12 – Modified Snapshot Analysis with COVID-19 related LOCF | The 1st vertical line indicates start of study treatment at Intervention Phase. The second vertical reference line indicates last IP on-treatment study day. i.e. min (last IP injection dose+35 days, LTFU HAART start date, date of last oral CAB+RPV+1). This vertical line is only for subjects who withdraw from Intervention Phase/Extension phase. | M12 |
| 2.4. | Safety | SNAPSHOT10 | Individual Plasma HIV-1 RNA for Subjects with Confirmed Virologic Failure | The 1st vertical line indicates start of study treatment at Intervention Phase. The second vertical reference line indicates last IP on-treatment study day. i.e. min (last IP injection dose+35 days, LTFU HAART start date, date of last oral CAB+RPV+1). This vertical line is only for subjects who withdraw from Intervention Phase/Extension phase. | M12, EOS |

## 13.13.7. Safety Tables

| Safety: Tables | | | | | |
|---|---|---|---|---|---|
| **No.** | **Population** | **GSK Standard/ Example Shell** | **Title** | **Programming Notes** | **Deliverable** |
| **Exposure** | | | | | |
| 3.1. | Safety | 207966/primary_15/T3.1 | Summary of Exposure to Study Treatment (Intervention Phase) | | M12 |
| 3.2. | Safety | 207966/primary_15/T3.1 | Summary of Exposure to Study Treatment | | M12, EOS |
| 3.3. | Safety | SAF_T1 See Section 13.14 | Summary of Adherence to CAB LA + RPV LA Dosing Schedule by Visit, Site Type and COVID-19 Impact /Non-Impact (Intervention Phase) | COVID Impact refers to missed or out of window injections for COVID-19 related reasons (as captured as COVID-19 related protocol deviations) | HL, M12 |
| 3.4. | Safety | SAF_T2 See Section 13.14 | Summary of Adherence to CAB LA + RPV LA Dosing Schedule by Visit, Site ID and COVID-19 Impact /Non-Impact (Intervention Phase) | COVID Impact refers to missed or out of window injections for COVID-19 related reasons (as captured as COVID-19 related protocol deviations) | HL, M12 |
| 3.5. | Safety | SAF_T1 See Section 13.14 | Summary of Adherence to CAB LA + RPV LA Dosing Schedule by Visit, Site Type and COVID-19 Impact /Non-Impact | COVID Impact refers to missed or out of window injections for COVID-19 related reasons (as captured as COVID-19 related protocol deviations) | EOS |
| 3.6. | Safety | SAF_T2 See Section 13.14 | Summary of Adherence to CAB LA + RPV LA Dosing Schedule by Visit, Site ID and COVID-19 Impact /Non-Impact | COVID Impact refers to missed or out of window injections for COVID-19 related reasons (as captured as COVID-19 related protocol deviations) | EOS |
| **Adverse Events (AEs)** | | | | | |
| 3.7. | Safety | AE3 | Summary of Adverse Events by Overall Frequency | ICH E3 | M12, EOS |
| 3.8. | Safety | AE5B | Summary of Adverse Events by System Organ Class and Maximum Grade | ICH E3 | HL, M12, EOS |

| Safety: Tables | | | | | |
|---|---|---|---|---|---|
| **No.** | **Population** | **GSK Standard/ Example Shell** | **Title** | **Programming Notes** | **Deliverable** |
| 3.9. | Safety | AE5B | Summary of Adverse Events by System Organ Class and Maximum Grade — Excluding Study Drug Injection Site Reactions | | M12, EOS |
| 3.10. | Safety | AE5B | Summary of Adverse Events by System Organ Class and Maximum Grade (Oral Lead-in Period) | | M12, EOS |
| 3.11. | Safety | AE3 | Summary of Common (>=5%) Adverse Events by Overall Frequency | ICH E3 | M12, EOS |
| 3.12. | Safety | AE3 | Summary of Common (>=1%) Grade 2-5 Adverse Events by Overall Frequency | ICH E3 | M12, EOS |
| 3.13. | Safety | AE3 | Summary Drug-Related Adverse Events by Overall Frequency | ICH E3 | M12, EOS |
| 3.14. | Safety | AE5B | Summary of Drug-Related Adverse Events by System Organ Class and Maximum Grade | ICH E3 | HL, M12, EOS |
| 3.15. | Safety | AE5B | Summary of Drug-Related Adverse Events by System Organ Class and Maximum Grade — Excluding Study Drug Injection Site Reactions | | M12, EOS |
| 3.16. | Safety | AE15 | Summary of Common (>=5%) Non-serious Adverse Events by System Organ Class and Preferred Term (Number of Subjects and Occurrences) | FDAAA, EudraCT | M12, EOS |
| 3.17. | Safety | AE3 | Summary of Common (>=1%) Drug-Related Grade 2-5 Adverse Events by Overall Frequency | ICH E3 | M12, EOS |
| 3.18. | Safety | AE3 | Summary of Non-Serious Drug-Related Adverse Events by Overall Frequency | Plain Language Summary requirements. | M12, EOS |

| Safety: Tables | | | | | |
|---|---|---|---|---|---|
| **No.** | **Population** | **GSK Standard/ Example Shell** | **Title** | **Programming Notes** | **Deliverable** |
| **Serious and Other Significant Adverse Events** | | | | | |
| 3.19. | Safety | AE5B | Summary of Serious Adverse Events by System Organ Class and Maximum Grade | ICH E3 | HL, M12, EOS |
| 3.20. | Safety | AE16 | Summary of Serious Adverse Events by System Organ Class and Preferred Term (Number of Subjects and Occurrences) | FDAAA, EudraCT | M12, EOS |
| 3.21. | Safety | AE1 | Summary of Adverse Events Leading to Permanent Discontinuation of Study Treatment or Withdrawal from Study by System Organ Class and Preferred Term | GSK Statistical Display Standard | HL, M12, EOS |
| 3.22. | Safety | AE20 | Summary of Serious Fatal and Non-Fatal Drug-Related Adverse Events by Overall Frequency | Plain Language Summary requirements. | M12, EOS |
| **Injection Site Reaction Adverse Events** | | | | | |
| 3.23. | Safety | 201584/primary_ 7/T3.40 | Summary of Study Drug Injection Site Reaction Adverse Events (Event-level Summary) | | HL, M12, EOS |
| 3.24. | Safety | 201584/primary_ 7/T3.43 | Summary of Subject-level Characteristics of Study Drug Injection Site Reaction Adverse Events – Overall and Common | | HL, M12, EOS |
| 3.25. | Safety | 201584/primary_ 7/T3.46 | Summary of Study Drug Injection Site Reaction Adverse Events by Visit and Maximum Severity – Overall and Common | | HL, M12, EOS |
| **Laboratory: Chemistry** | | | | | |
| 3.26. | Safety | LB1 | Summary of Chemistry Values | Includes pre-specified parameters repeated in conventional units.<br>Includes baseline values | M12, EOS |
| 3.27. | Safety | LB1 | Summary of Chemistry Changes from Baseline | ICH E3 | M12, EOS |
| 3.28. | Safety | LB16 | Summary of Chemistry Results by Maximum Grade Increase Post-Baseline Relative to Baseline | ICH E3 | HL, M12, EOS |

| Safety: Tables | | | | | |
|---|---|---|---|---|---|
| **No.** | **Population** | **GSK Standard/ Example Shell** | **Title** | **Programming Notes** | **Deliverable** |
| 3.29. | Safety | LB16 | Summary of Chemistry Results by Maximum Grade Increase Post-Baseline Relative to Baseline (Oral Lead-in Period) | ICH E3 | M12, EOS |
| **Laboratory: Hematology** | | | | | |
| 3.30. | Safety | LB1 | Summary of Hematology Values | Includes pre-specified parameters repeated in conventional units. | M12, EOS |
| 3.31. | Safety | LB1 | Summary of Hematology Changes from Baseline | Includes pre-specified parameters repeated in conventional units.<br>Includes baseline values | M12, EOS |
| 3.32. | Safety | LB16 | Summary of Hematology Results by Maximum Grade Increase Post-Baseline Relative to Baseline | ICH E3 | M12, EOS |
| 3.33. | Safety | LB16 | Summary of Hematology Results by Maximum Grade Increase Post-Baseline Relative to Baseline (Oral Lead-in Period) | ICH E3 | M12, EOS |
| **Laboratory: Hepatobiliary (Liver)** | | | | | |
| 3.34. | Safety | LIVER1 | Summary of Liver Monitoring/Stopping Event Reporting | GSK Statistical Display Standard | M12, EOS |
| 3.35. | Safety | LIVER10 | Summary of Hepatobiliary Laboratory Abnormalities | GSK Statistical Display Standard | HL, M12, EOS |
| 3.36. | Safety | LIVER11 | Summary of Liver Restart/Re-Challenges | GSK Statistical Display Standard | M12, EOS |
| **Vital Signs** | | | | | |
| 3.37. | Safety | VS1 | Summary of Change from Baseline in Vital Signs | ICH E3<br>Include Baseline values | M12, EOS |
| **Cardiovascular Risk Factors** | | | | | |
| 3.38. | Safety | FH1 | Summary of Family History of Cardiovascular Risk Factors | GSK Statistical Display Standard | M12, EOS |
| 3.39. | Safety | SU1 | Summary of Substance Use | GSK Statistical Display Standard | M12, EOS |

| Safety: Tables | | | | | |
|---|---|---|---|---|---|
| **No.** | **Population** | **GSK Standard/ Example Shell** | **Title** | **Programming Notes** | **Deliverable** |
| **COVID-19 Adverse Events** | | | | | |
| 3.40. | Safety | PAN1 | Summary of COVID-19 Assessments for Subjects with COVID-19 Adverse Events | GSK Statistical Display Standard | M12, EOS |
| 3.41. | Safety | PAN2 | Summary of COVID-19 Additional Assessments for Subjects with COVID-19 Adverse Events | GSK Statistical Display Standard | M12, EOS |
| 3.42. | Safety | PAN3 | Summary of COVID-19 Symptoms for Subjects with COVID-19 Adverse Events | GSK Statistical Display Standard | M12, EOS |
| **Adverse Events of Special Interest** | | | | | |
| 3.43. | Safety | 201584/primary_27/T3.140 | Summary of Depression, Anxiety and Suicidal or Suicidal Ideation/Behaviour Adverse Events by System Organ Class, Maximum DAIDS Toxicity Grade, and History of Depression, Anxiety or Suicidal Ideation/Behaviour at Screening | | M12, EOS |
| 3.44. | Safety | 201584/primary_07/T3.122 | Summary of Depression Adverse Events of Special Interest by System Organ Class and Preferred Term (Number of Subjects and Occurrences) | | M12, EOS |
| 3.45. | Safety | 201584/primary_07/T3.125 | Summary of Anxiety Adverse Events of Special Interest by System Organ Class and Preferred Term (Number of Subjects and Occurrences) | | M12, EOS |
| 3.46. | Safety | 201584/primary_07/T3.128 | Summary of Suicidal Ideation/Behaviour Adverse Events of Special Interest by System Organ Class and Preferred Term (Number of Subjects and Occurrences) | | M12, EOS |
| 3.47. | Safety | 201584/primary_07/T3.134 | Summary of Seizures Adverse Events of Special Interest by System Organ Class and Preferred Term (Number of Subjects and Occurrences) | | M12, EOS |

| Safety: Tables | | | | | |
|---|---|---|---|---|---|
| **No.** | **Population** | **GSK Standard/ Example Shell** | **Title** | **Programming Notes** | **Deliverable** |
| 3.48. | Safety | 201584/primary_ 07/T3.137 | Summary of Hepatic Safety Profile: Assessment of Risk of Hepatoxicity Adverse Events of Special Interest by System Organ Class and Preferred Term (Number of Subjects and Occurrences) | | M12, EOS |
| 3.49. | Safety | 201584/primary_ 07/T3.140 | Summary of Hypersensitivity Reactions (HSR) Adverse Events of Special Interest by System Organ Class and Preferred Term (Number of Subjects and Occurrences) | | M12, EOS |
| 3.50. | Safety | 201584/primary_ 07/T3.143 | Summary of Rash Adverse Events of Special Interest by System Organ Class and Preferred Term (Number of Subjects and Occurrences) | | M12, EOS |
| 3.51. | Safety | 201584/primary_ 07/T3.146 | Summary of Prolongation of the Corrected QT Interval of the ECG in Supratherapeutic Doses Adverse Events of Special Interest by System Organ Class and Preferred Term (Number of Subjects and Occurrences) | | M12, EOS |
| 3.52. | Safety | 201584/primary_ 07/T3.149 | Summary of Bipolar Disorder Adverse Events of Special Interest by System Organ Class and Preferred Term (Number of Subjects and Occurrences) | | M12, EOS |
| 3.53. | Safety | 201584/primary_ 07/T3.152 | Summary of Psychosis Adverse Events of Special Interest by System Organ Class and Preferred Term (Number of Subjects and Occurrences) | | M12, EOS |
| 3.54. | Safety | 201584/primary_ 07/T3.155 | Summary of Mood Disorders Adverse Events of Special Interest by System Organ Class and Preferred Term (Number of Subjects and Occurrences) | | M12, EOS |
| 3.55. | Safety | 201584/primary_ 07/T3.158 | Summary of Sleep Disorders Adverse Events of Special Interest by System Organ Class and Preferred Term (Number of Subjects and Occurrences) | | M12, EOS |

| Safety: Tables | | | | | |
|---|---|---|---|---|---|
| **No.** | **Population** | **GSK Standard/ Example Shell** | **Title** | **Programming Notes** | **Deliverable** |
| 3.56. | Safety | 201584/primary_ 07/T3.161 | Summary of Hyperglycaemia Adverse Events of Special Interest by System Organ Class and Preferred Term (Number of Subjects and Occurrences) | | M12, EOS |
| 3.57. | Safety | 201584/primary_ 07/T3.161 | Summary of Weight Gain Adverse Events of Special Interest by System Organ Class and Preferred Term (Number of Subjects and Occurrences) | | M12, EOS |
| 3.58. | Safety | 201584/primary_ 07/T3.164 | Summary of Rhabdomyolysis Adverse Events of Special Interest by System Organ Class and Preferred Term (Number of Subjects and Occurrences) | | M12, EOS |
| 3.59. | Safety | 201584/primary_ 07/T3.167 | Summary of Pancreatitis Adverse Events of Special Interest by System Organ Class and Preferred Term (Number of Subjects and Occurrences) | | M12, EOS |
| 3.60. | Safety | 201584/primary_ 07/T3.170 | Summary of Impact on Creatinine Adverse Events of Special Interest by System Organ Class and Preferred Term (Number of Subjects and Occurrences) | | M12, EOS |
| 3.61. | Safety | 201584/primary_ 07/T3.173 | Summary of Safety in Pregnancy Adverse Events of Special Interest by System Organ Class and Preferred Term (Number of Subjects and Occurrences) | | M12, EOS |
| 3.62. | Safety | 207966/primary_ 15/T3.109 | Summary of Characteristics of Adverse Events of Special Interest | | M12, EOS |

## 13.13.8. Safety Figures

| Safety: Figures | | | | | |
|---|---|---|---|---|---|
| **No.** | **Population** | **GSK Standard / Example Shell** | **Title** | **Programming Notes** | **Deliverable** |
| **Adverse Events** | | | | | |
| 3.1. | Safety | 201584/primary_07/F3.14 | Plot of Incidence of Intervention Phase Study Drug Injection Site Reaction Adverse Events by Visit (Overall and Common) – CAB and/or RPV | | M12, EOS |
| 3.2. | Safety | 201584/primary_07/F3.17 | Plot of Incidence of Grade 3-5 Intervention Phase Study Drug Injection Site Reaction Adverse Events by Visit (Overall and Common) - CAB and/or RPV | | M12, EOS |
| **Laboratory** | | | | | |
| 3.3. | Safety | LIVER14 | Scatter Plot of Maximum vs. Baseline for ALT | GSK Statistical Display Standard | M12, EOS |
| 3.4. | Safety | LIVER9 | Scatter Plot of Maximum Total Bilirubin vs Maximum ALT – eDISH Plot | GSK Statistical Display Standard | M12, EOS |

## 13.13.9. Virology Tables

| **No.** | **Population** | **GSK Standard / Example Shell** | **Title** | **Programming Notes** | **Deliverable** |
|---|---|---|---|---|---|
| 4.1. | Safety | 20184/primary_17/T7.2 | Viral load, Genotypic and Phenotypic data for Subjects Who Met Confirmed Virologic Failure Criteria | | HL, M12, EOS |
| 4.2. | Safety | 20184/primary_17/T7.4 | Viral Load, Genotypic and Phenotypic Data for Non-CVF Subjects | Only include subjects with available genotypic or phenotypic data. | M12, EOS |

## 13.13.10. Other Tables

| Study Visit Length | | | | | |
|---|---|---|---|---|---|
| **No.** | **Population** | **GSK Standard / Example Shell** | **Title** | **Programming Notes** | **Deliverable** |
| 5.1. | Safety | OTR_T1 | Summary of Study Visit Length (minutes) by Visit and Site Type (Intervention Phase) | | HL, M12, EOS |
| 5.2. | Safety | OTR_T1 | Summary of Study Visit Length (minutes) by Visit and Site (Intervention Phase) | | HL, M12, EOS |

## 13.13.11. ICH Listings

| ICH: Listings | | | | | |
|---|---|---|---|---|---|
| **No.** | **Population** | **GSK Standard / Example Shell** | **Title** | **Programming Notes** | **Deliverable** |
| **Subject Disposition** | | | | | |
| 1. | Enrolled | ES2 | Listing of Reasons for Study Withdrawal | ICH E3<br>Add column for Phase | M12, EOS |
| 2. | Enrolled | SD2 | Listing of Reasons for Study Treatment Discontinuation | ICH E3<br>Add column for Phase | HL, M12, EOS |
| **Protocol Deviations** | | | | | |
| 3. | Enrolled | DV2 | Listing of Important Protocol Deviations | ICH E3<br>Add column for Phase | M12, EOS |

| ICH: Listings | | | | | |
|---|---|---|---|---|---|
| **No.** | **Population** | **GSK Standard / Example Shell** | **Title** | **Programming Notes** | **Deliverable** |
| | | | | Add a column on the right for "COVID-19 Related". The possible values in this column are Y and N, where Y indicates the deviation is COVID-19 related and N indicates the deviation is non-COVID-19 related. | |
| 4. | Enrolled | DV2 | Listing of Protocol Deviations Related to COVID-19 | FDA Request<br>Add column for Phase | HL, M12, EOS |
| 5. | Safety | IE3 | Listing of Subjects with Inclusion/Exclusion Criteria Deviations | ICH E3 | M12, EOS |
| **Populations Analysed** | | | | | |
| 6. | Enrolled | SP3 | Listing of Subjects Excluded from Safety Population | ICH E3 | M12, EOS |
| **Demographic and Baseline Characteristics** | | | | | |
| 7. | Safety | DM2 | Listing of Demographic Characteristics | ICH E3 | M12, EOS |
| 8. | Safety | DM9 | Listing of Race | ICH E3 | M12, EOS |
| **Efficacy** | | | | | |
| 9. | Safety | SNAPSHOT11 | Listing of Qualitative and Quantitative Plasma HIV-1 RNA Data | | HL, M12, EOS |
| 10. | Safety | SNAPSHOT12 | Listing of Study Outcome (50 copies/mL cutoff) at Month 12 – Snapshot Analysis | Include both original and LOCF imputed outcomes | HL, M12, EOS |
| 11. | Safety | VF4 | Listing of Plasma HIV-1 RNA and CD4+ Cell Count for subjects with Confirmed Virologic Failure | | M12, EOS |
| **Exposure and Treatment Compliance** | | | | | |
| 12. | Safety | 207966/primary_15/L12 | Listing of Exposure Data | ICH E3<br>Remove Phase Day | M12, EOS |

| ICH: Listings | | | | | |
|---|---|---|---|---|---|
| **No.** | **Population** | **GSK Standard / Example Shell** | **Title** | **Programming Notes** | **Deliverable** |
| **Adverse Events** | | | | | |
| 13. | Safety | AE8 | Listing of All Adverse Events | ICH E3<br>Add Phase/Period, Side/Drug, see gsk1265744/mid207966/primary_15/L19 | HL, M12, EOS |
| 14. | Safety | AE8 | Listing of Grade 3-5 Adverse Events | Add Phase/Period, Side/Drug, see gsk1265744/mid207966/primary_15/L19 | M12, EOS |
| 15. | Safety | AE7 | Listing of Subject Numbers for Individual Adverse Events | ICH E3 | M12, EOS |
| 16. | Safety | PSRAE1 | Listing of Possible Suicidality-Related Adverse Event Data: Event and Description (Section 1-Section 2) | Add Phase | M12, EOS |
| 17. | Safety | PSRAE3 | Listing of Possible Suicidality-Related Adverse Event Data: Possible Cause(s) (Section 3) | Add Phase | M12, EOS |
| 18. | Safety | PSRAE4 | Listing of Possible Suicidality-Related Adverse Event Data (Section 4) | Add Phase | M12, EOS |
| 19. | Safety | PSRAE5 | Listing of Possible Suicidality-Related Adverse Event Data (Section 5-Section 8) | Add Phase | M12, EOS |
| 20. | Safety | 201584/primary_07/L22 | Listing of Changes in Intensity/Grades of Study Drug Injection Site Adverse Events | Remove phase treatment | M12, EOS |
| 21. | Safety | AE8 | Listing of COVID-19 Adverse Events | Add Phase/Period, Side/Drug, see gsk1265744/mid207966/primary_15/L19 | HL, M12, EOS |
| 22. | Safety | PAN12 | Listing of COVID-19 Assessments and Symptom Assessments | | M12, EOS |
| 23. | Safety | PAN5 | Country Level Listing of Start Dates of COVID-19 Pandemic Measures | | M12, EOS |
| **Serious and Other Significant Adverse Events** | | | | | |
| 24. | Safety | AE8 | Listing of Fatal Serious Adverse Events | ICH E3 | M12, EOS |

| ICH: Listings | | | | | |
|---|---|---|---|---|---|
| **No.** | **Population** | **GSK Standard / Example Shell** | **Title** | **Programming Notes** | **Deliverable** |
| | | | | Add Phase/Period, Side/Drug | |
| 25. | Safety | AE8 | Listing of Non-Fatal Serious Adverse Events | ICH E3<br>Add Phase/Period, Side/Drug | M12, EOS |
| 26. | Safety | AE14 | Listing of Reasons for Considering as a Serious Adverse Event | ICH E3 | M12, EOS |
| 27. | Safety | AE8 | Listing of Adverse Events Leading to Withdrawal from Study / Permanent Discontinuation of Study Treatment | ICH E3<br>Add Phase/Period, Side/Drug | M12, EOS |
| 28. | Safety | AE8 | Listing of All Adverse Events with Completely Missing Onset Date, Missing Relationship to Study Treatment, Severity and/or Grade | ICH E3<br>Add Phase/Period, Side/Drug, see gsk1265744/mid207966/primary_15/L19 | M12, EOS |
| **Laboratory** | | | | | |
| 29. | Safety | UR2 | Listing of Urinalysis Data for Subjects with Any Value of Potential Clinical Importance | ICH E3<br>Include Grade<br>Note: Potential Clinical Importance is defined as:<br>1. Increase in Protein (dipstick) or Occult Blood (dipstick) post-baseline relative to baseline<br>2. Increase in any DAIDS graded values for Protein, Occult Blood or Glucose relative to baseline<br>3. If microscopy is performed. | M12, EOS |

## 13.13.12. Non-ICH Listings

| Non-ICH: Listings | | | | | |
|---|---|---|---|---|---|
| **No.** | **Population** | **GSK Standard GSK Statistical Display Standard / Example Shell** | **Title** | **Programming Notes** | **Deliverable** |
| **Subject Disposition** | | | | | |
| 30. | Screened | ES7 | Listing of Reasons for Screen Failure | Journal Guidelines | M12, EOS |
| 31. | Screened | ES9 | Listing of Subjects Who Were Rescreened | | M12, EOS |
| 32. | Safety | TA1 | Listing of Planned and Actual Treatments | GSK Statistical Display Standard | M12, EOS |
| **Prior and Concomitant Medications** | | | | | |
| 33. | Safety | 207966/primary_15/Listing 36 | Listing of Prior ART Medications | Remove the column 'Phase during Which Concomitant' | M12, EOS |
| 34. | Safety | 207966/primary_15/Listing 37 | Listing of Concomitant ART Medications | In case the same medication is concomitant during both intervention and extension phases, list each of them in two separate rows. Add a column "SOC Oral Bridging?" which has values of "Yes" and "No". | HL, M12, EOS |
| 35. | Safety | 207966/primary_15/Listing 38 | Listing of ART Medications Received during Long-term Follow-up Phase | Remove the column 'Phase during Which Concomitant' and "Start Date of the Long-term Follow-up ART/Study Day". | M12, EOS |
| **Medical History** | | | | | |
| 36. | Safety | 201584/primary_01/L43 | Listing of Medical History of Seizure | | M12, EOS |
| **Efficacy** | | | | | |
| 37. | Safety | CDC4 | Listing of CDC Classification of HIV-1 Infection at Baseline | Add Phase | M12, EOS |

| Non-ICH: Listings | | | | | |
|---|---|---|---|---|---|
| **No.** | **Population** | **GSK Standard GSK Statistical Display Standard / Example Shell** | **Title** | **Programming Notes** | **Deliverable** |
| 38. | Safety | CDC5 | Listing of CDC Stage 3 HIV-1 Associated Conditions | Add Phase | |
| **Hepatobiliary (Liver)** | | | | | |
| 39. | Safety | LIVER5 | Listing of Liver Monitoring/Stopping Event Reporting | GSK Statistical Display Standard | M12, EOS |
| 40. | Safety | LIVER15 | Liver Stopping Event Profile | GSK Statistical Display Standard | M12, EOS |
| 41. | Safety | LIVER13 | Listing of Subjects Meeting Hepatobiliary Laboratory Criteria Post-Baseline | GSK Statistical Display Standard | HL, M12, EOS |
| 42. | Safety | LB12 | Listing of ALT, AST, Bilirubin (including Total and Direct Bilirubin), INR, and ALP for Subjects Meeting Hepatobiliary Lab Abnormality Criteria | Add Phase | M12, EOS |
| **ECG** | | | | | |
| 43. | Safety | EG3 | Listing of All ECG Values for Subjects with Any Value of Potential Clinical Importance | GSK Statistical Display Standard<br>By default, the definition of PCI is defined based on QTc value (e.g., QTcF Interval, Aggregate) where a subject has a QTc value >450 or a QTc increase of >30msec. | M12, EOS |
| 44. | Safety | EG5 | Listing of All ECG Findings for Subjects with an Abnormal ECG Finding | GSK Statistical Display Standard | M12, EOS |
| **Other** | | | | | |
| 45. | Safety | 207966/primary_15/L60 | Listing of Exposure Data for Subjects Receiving Oral Bridging | Add column to identify COVID relatedness. | HL, M12, EOS |
| 46. | Safety | 207966/primary_15/L61 | Listing of Dosing Errors and IP Device Malfunctions | Add Phase | M12, EOS |
| 47. | Safety | PREG1 | Listing of Subjects or Partners Who Became Pregnant During the Study | GSK Statistical Display Standard<br>Add Phase/Period | M12, EOS |

| Non-ICH: Listings | | | | | |
|---|---|---|---|---|---|
| **No.** | **Population** | **GSK Standard GSK Statistical Display Standard / Example Shell** | **Title** | **Programming Notes** | **Deliverable** |
| 48. | Safety | 201584/primary_17/L54 | Listing of Replication Capacity in IN and PR/RT Region | Add Phase | M12, EOS |
| **PK Endpoints** | | | | | |
| 49. | Safety | PK07 | Listing of Plasma CAB Pharmacokinetic Concentration-Time Data | | M12, EOS |
| 50. | Safety | PK07 | Listing of Plasma RPV Pharmacokinetic Concentration-Time Data | | M12, EOS |

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

Data Display Specification will be made available on request