Reporting and Analysis Plan

Study ID: 213500

Official Title of Study: Reporting and Analysis Plan Amendment 1 for 213500:
A Phase IIIb, Randomized, Multicenter, Active-controlled, Parallel group, Non-inferiority, Open-label Study Evaluating the Efficacy, Safety, and Tolerability of Switching to Long-acting Cabotegravir Plus Long-acting Rilpivirine Administered Every Two Months from a Bictegravir/emtricitabine/tenofovir alafenamide Single Tablet Regimen in HIV-1 Infected Adults who are Virologically Suppressed.

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Title	:	Reporting and Analysis Plan Amendment 1 for 213500: A Phase IIIb, Randomized, Multicenter, Active-controlled, Parallel group, Non-inferiority, Open-label Study Evaluating the Efficacy, Safety, and Tolerability of Switching to Long-acting Cabotegravir Plus Long-acting Rilpivirine Administered Every Two Months from a Bictegravir/emtricitabine/tenofovir alafenamide Single Tablet Regimen in HIV-1 Infected Adults who are Virologically Suppressed
Compound Number	:	GSK1265744
Clinical Study Identifier	:	213500
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 213500.
- This RAP describes the statistical analyses required for the interim analysis when all participants have completed their Month 6 (OLI and BIK)/Month 5 (D2I) visit.
- The RAP also provides the content of the Primary Month 12 (OLI and BIK)/Month 11 (D2I) Statistical Analysis Complete (SAC) deliverable.
- The second amendment provides the content of the End of Study (EoS) reporting.

RAP Author(s):

Author	Date
Lead	Refer to Document Date
PPD Principal Statistician (HIV, Clinical Statistics)	

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

Approver
PPD
PPD (HIV, Clinical Statistics)

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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:		
2019N425725_00	27-MAY-2020	Original
2019N425725_01	30-JUN-2020	The primary reason for protocol amendment 01 is to add minor clarifications to address study completion, PK collection, and endpoint timings. Country-specific details were added to Appendix 10 to address UK MHRA requirements. The protocol short title was updated. Corrections to typographical errors in protocol text and title were made throughout.
TMF-12473407	08-SEP-2021	The primary reason for protocol amendment 02 is to address and clarify comments raised during the course of the study and to implement country specific changes following regulatory review.
TMF-14364917	10-FEB-2022	The primary reason for protocol amendment 03 is to address and clarify comments raised during the course of the study.

This first amendment includes amendments to the originally approved RAP effective 27Dec2021. The following changes were made prior to the M12 primary analysis:

Major (applicable to M12 only):

- Updated primary analysis population to mITT-E excluding subjects from site PPD
- Added modified CVF (mCVF) population excluding subjects from site PPD
- Updated that Per Protocol (PP) will be based on mITT-E
- Updated in Appendix 15 analysis population for the M12 analysis tables

Minor (typo corrections, clarifications, additional displays and format changes):

- Updated in Section 2.2 in consistency with updates in protocol amendment 3
- Updated in Appendix 2
- Updated in Section 8.4 that "Interactions between treatment and each of the covariates will not be assessed" For MMRM models.
- Updated the title for the listing "Listing of HIV-1 Associated Conditions " to "Listing of Stage 3 HIV-1 Associated Conditions".
- Updated the title for Safety Figure 3.2 "Plot of Incidence of Maintenance Phase Drug-Related Injection Site Reaction Adverse Events by Visit (Overall and Common)" by adding "Drug-Related" to the title for accuracy
- Updated the title for Safety Figure 3.3 "Plot of Incidence of Grade 3-5 Maintenance Phase Drug-Related Injection Site Reaction Adverse Events by Visit (Overall and Common)" by adding "Drug-Related" to the title for accuracy
- Updated the title for Safety Figure 3.9 "Plot of Incidence of Maintenance Phase Drug-Related Injection Site Reaction Adverse Events by Strata and Visit (Overall and Common) - CAB and/or RPV" by adding "Drug-Related" to the title for accuracy

- Clarified Safety Table 3.64 "Summary of Percent of Subjects with Metabolic Syndrome and Risk Factors" is for "Maintenance Phase"
- Removed the output "Proportion of Subjects with Plasma HIV-1 RNA <2 c/mL – Observed Case Analysis (Maintenance Phase)"
- Moved the listing of net assessment data into separate listings for CVF and non-CVF subjects due to space limit in the output files (2 extra listings added)
- Divided the figure "Patient Profile Plot of Clinical Diagnosis Factors for Patients with Metabolic Syndrome at Any Time Point" to separate figures for OLI, D2I and BIK due to space limit in the output files (2 extra figures added)
- Corrected a typo in Section 16.15.9 that the analysis population for Health Outcomes table 6.13 "Proportion of Subjects Scoring Each Option in the CCI Questionnaire at Month 13" is "Extension Switch" instead of ITT-E.
- Added in Section 16.15.9 "Statistical Analysis of HIVTSQs - Change from Maintenance Baseline (Day 1) in Total Treatment Satisfaction Score and individual items 5 (convenient), 6 (flexible) and 10 (continue) (Maintenance Phase) by Baseline Score Group" and "Summary of Shift in CCI [redacted]".
- Updated description in the CCI [redacted] questionnaire in Section 16.6.6 to align with eCRF wording.
- Corrected that the analysis population for listing "Listing of Plasma PK Concentrations at Withdrawal" will be ITT-E.
- Added in Section 16.15.12 "Listing of All Plasma PK Concentrations for CVF Subjects".
- Added clarification in Section 16.15.12 that the following two displays will not be produced if no subject becomes pregnant on Q2M: "Listing of Selected Laboratory Data for Subjects Who Became Pregnant During the Study", "Listing of Plasma PK Concentrations for Subjects Who Became Pregnant During the Study".
- Added clarification on data handling strategy for Q2M subjects who become pregnant on study in Section 16.13.

The second amendment includes amendments to the RAP amendment #1 effective 15-Jun-2022, the following changes were made:

Section 16.5 was updated to provide additional details of the planned analyses and data displays for 213500 EOS Final reporting.

2. SUMMARY OF KEY PROTOCOL INFORMATION

2.1. Changes to the Protocol Defined Statistical Analysis Plan

Due to critical audit findings at site PPD related to critical inclusion/exclusion criteria violations and major GCP non-compliance (reporting letter to FDA submitted), efficacy data from this site is deemed unreliable and as such the M12 primary analysis population will exclude all 11 randomized site participants (mITT-E). Efficacy analysis in the "mITT-E" population will be considered primary. Additional (sensitivity) efficacy analyses will be performed for the ITT-E population and this analysis will be considered secondary/supportive. Safety analyses will remain as planned and will include all randomized subjects who received at least one dose of study treatment (Safety). For virology tables (if applicable) and one efficacy table, the mCVF population will be summarized excluding any subject from the site. All listings and subject-level figures will be produced as planned, without exclusion of the site, where applicable. See Appendix 15. Note this update is made after the Month 6 but prior to the M12 analysis therefore such changes are only applicable to the M12 analysis.

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

Objectives	Estimands/Endpoints
Primary	
To demonstrate the non-inferior antiviral activity of CAB LA + RPV LA every two months compared to a BIK single tablet regimen administered once daily over 12 months in suppressed HIV-1 infected antiretroviral therapy (ART)-experienced participants	Proportion of participants with plasma HIV-RNA greater than or equal to 50 copies/mL as per Food and Drug Administration (FDA) Snapshot algorithm at Month 12 (OLI and BIK)/Month 11 (D2I) (Intent-to-Treat Exposed [ITT-E] population)
Secondary	
To demonstrate the antiviral and immunologic response with the use of CAB LA + RPV LA every 2 months compared to a BIK single tablet regimen administered once daily	Proportion of participants with plasma HIV-1 RNA <50 c/mL (c/mL) at Month 6 and Month 12 (OLI and BIK)/Month 5 and Month 11 (D2I) using the FDA Snapshot algorithm (Intent-to-Treat Exposed [ITT-E] population) Proportion of participants with protocol-defined confirmed virologic failure (CVF) through Month 6 and Month 12 (OLI and BIK)/Month 5 and Month 11 (D2I). Proportion of participants with HIV-RNA greater than or equal to 50 c/mL as per FDA Snapshot algorithm at Month 6, and Month 12 (OLI and BIK)/Month 5 and Month 11 (D2I) Absolute values and changes from Baseline in viral load and CD4+ cell count over time including Month 6 and Month 12 (OLI and BIK)/Month 5 and Month 11 (D2I)
To assess viral resistance in participants experiencing protocol-defined confirmed virologic failure	Incidence of treatment emergent genotypic and phenotypic resistance to CAB, RPV, BIC, FTC, and TAF through Month 6 and Month 12 (OLI and BIK)/Month 5 and Month 11 (D2I).
To evaluate renal (in urine and blood) and bone (in blood) biomarkers in participants treated with CAB LA + RPV LA compared to BIK	Change from Baseline (Day 1) in renal and bone biomarkers at Months 6 and 12 (OLI and BIK)/Month 5 and Month 11 (D2I).
To evaluate Metabolic Syndrome for participants treated with CAB + RPV and BIK	Change from Baseline in proportions of participants with Metabolic syndrome at Months 6 and 12 (OLI and BIK)/Month 5 and Month 11 (D2I)

Objectives	Estimands/Endpoints
To evaluate insulin resistance in participants treated with CAB LA + RPV LA compared to BIK	Change from Baseline (Day 1) in homeostasis model of assessment-insulin resistance (HOMA-IR) at Months 6 and 12 (OLI and BIK)/Month 5 and Month 11 (D2I).
To assess preference for CAB LA + RPV LA administered every 2 months compared to a BIK single tablet regimen administered once daily	Preference for CAB LA + RPV LA every 2 months compared to a BIK single tablet regimen will be assessed using a preference questionnaire at Month 12 (OLI)/Month 11 (D2I) (or Withdrawal).
To assess patient reported treatment satisfaction, and injection tolerability.	Change from baseline (Day 1) in total "treatment satisfaction" score, and individual item scores of the HIV Treatment Satisfaction Status Questionnaire (HIVTSQs) at Month 6 and Month 12 (OLI and BIK)/Month 5 and Month 11 (D2I), (or Withdrawal) Change in treatment satisfaction over time using the HIV Treatment Satisfaction Change Questionnaire HIVTSQc total score and individual item scores at Month 12 (OLI and BIK)/Month 11 (D2I) (or Withdrawal). Change from Month 2 in Dimension scores ("Acceptance of ISRs", "Bother of ISRs", "Leg movement", "Sleep") and individual item scores (assessing pain during injection, anxiety before and after injection, willingness to be injected in the future and overall satisfaction with mode of administration over time) will be assessed using the Perception of injection questionnaire (PIN) at Months 2, 6, and 12 (OLI)/Months 1, 5, 11 (D2I) (or Withdrawal)
Safety	
To evaluate the safety and tolerability of CAB LA + RPV LA every 2 months compared to a BIK single tablet regimen administered once daily	Incidence and severity of AEs and laboratory abnormalities over time including Month 6 and Month 12 (OLI and BIK)/Month 5 and Month 11 (D2I). Proportion of participants who discontinue treatment due to AEs over time including Month 6 and Month 12 (OLI and BIK)/Month 5 and Month 11 (D2I). Change from Baseline in laboratory parameters over time including Month 6 and Month 12 (OLI and BIK)/Month 5 and Month 11 (D2I).

Objectives	Estimands/Endpoints
CCI	[redacted]
[redacted]	
[redacted]	
[redacted]	
[redacted]	
[redacted]	
[redacted]	

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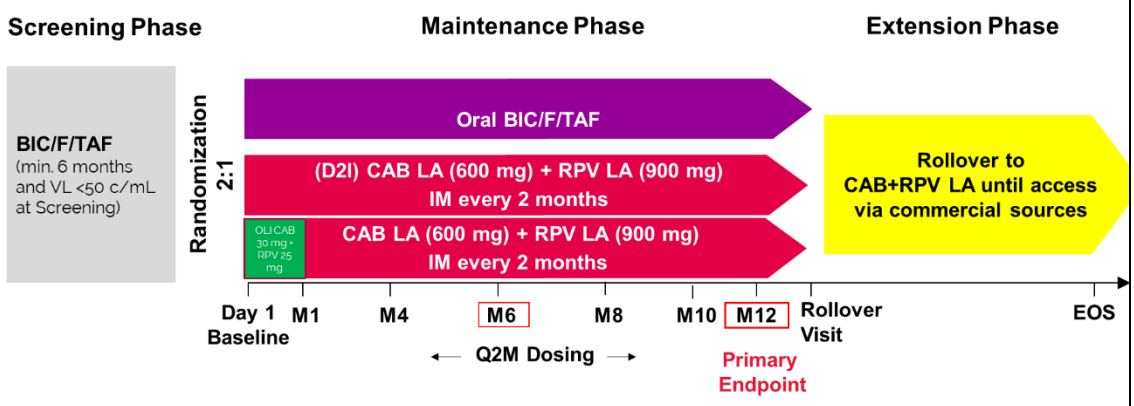
[redacted]

2.3. Study Design

Overview of Study Design and Key Features



Design Features	• The Solar Study (213500) is a Phase IIIb, randomized, open-label, active-controlled, multicenter, parallel-group, non-inferiority study designed to assess the antiviral activity and safety of a two-drug regimen of CAB LA + RPV LA administered every 2 months compared with maintenance of BIK. • The study comprises a Screening Phase (up to 35 days), a Maintenance Phase, and an Extension Phase. Any participant who receives at least one dose of CAB LA

Overview of Study Design and Key Features	
	and/or RPV LA and discontinues the CAB LA + RPV LA regimen for any reason will enter the Long-term Follow-up Phase on suppressive HAART for at least 52 weeks after the last dose of CAB LA and/or RPV LA.
Dosing	• Maintenance Phase: - CAB LA (600 mg) + RPV LA (900 mg) IM every 2 months - Oral BIK once daily • Extension Phase: - CAB LA (600 mg) + RPV LA (900 mg) IM every 2 months
Time & Events	• [Refer to Appendix 2]
Treatment Assignment	• Maintenance Phase: Approximately 654 subjects randomized 2:1 to CAB LA + RPV LA vs. Oral BIK. Subjects randomized to receive CAB LA + RPV LA may choose to begin oral therapy with CAB 30 mg + RPV 25 mg once daily (OLI) prior to administration of CAB LA + RPV LA, or transition directly to injections (D2I). • Extension Phase: if meeting eligibility requirements, subjects randomized to CAB LA + RPV LA will continue to have access to their randomized regimen; subjects randomized to BIK will have the option to either continue study participation by switching to CAB LA + RPV LA, or complete the study at Month 12. • GSK RandAll NG will be used to generate randomization schedules. • Stratified Randomization by participants' Baseline BMI (< 30 kg/m^2 , ≥ 30 kg/m^2) and Gender at Birth (female, male).
Interim Analysis	• An interim analysis will be conducted when all participants have completed their Month 6 (OLI and BIK)/Month 5 (D2I) visit. • The main analysis will be conducted to evaluate the primary objective of the protocol at Month 12(OLI and BIK)/Month 11(D2I). • Further data cuts and analyses may be conducted as necessary in order to support regulatory submissions and publications.

2.4. Statistical Hypotheses / Statistical Analyses

The study is to demonstrate the non-inferior antiviral activity of CAB LA + RPV LA (Q2M) every 2 months compared to a BIK single tablet regimen administered once daily over 12 months in suppressed HIV-1 infected antiretroviral therapy (ART)-experienced participants.

Non-inferiority will be concluded if the upper limit of a two-sided 95% confidence interval for the difference in proportion of participants with HIV-1 RNA ≥ 50 c/mL at Month 12 (OLI and BIK)/Month 11 (D2I) between the two treatment arms (Q2M - BIK) is less than 4%. Note that efficacy data for the primary endpoint from the OLI subjects at Month 12 and from the D2I subjects at Month 11 will be combined for the Q2M arm when assessing non-inferiority.

Let pc, pb be the proportion of participants with HIV-1 RNA ≥ 50 c/mL in the CAB LA+RPV LA (Q2M) and BIK arms respectively, then the primary statistical hypothesis can be written as follows:

H_0: pc - pb ≥ 4% vs. H_a: pc - pb < 4%

3. PLANNED ANALYSES

3.1. Interim Analyses

An interim analysis will be conducted when all participants have completed their Month 6 (OLI and BIK)/Month 5 (D2I) visit, focusing on the interim efficacy and key secondary efficacy endpoints, as well as key safety endpoints.

To minimise bias, the Month 6 interim results will not be shared with any participant and with most investigators. However, when a lead author(s) for a potential abstract presentation of the Month 6 interim results is (are) identified, that investigator(s) and the other co-authors on the abstract will have access to the interim results prior to its presentation. No other investigators will have knowledge of this data prior to the last participant completing their last visit for the primary Month 12 analysis. A Month 6 interim analysis abstract may be submitted to a conference for consideration only if the conference convenes after the Month 12 data collection has been completed.

Further data cuts and analyses may be conducted as necessary to support regulatory submissions, publications or for other purposes. Additionally, information collected on pregnant participants as collected in the eCRF may be reported descriptively or listed. The Month 12 analysis will be primary. No adjustment for multiplicity caused by repeated evaluation of the primary endpoint will be made as the Month 6 interim analyses will be secondary.

3.2. Final Analyses

The primary Month 12 analysis will be conducted to evaluate the primary objective of the protocol when all participants have completed their Month 12 (OLI and BIK)/Month 11 (D2I) visit. These analyses will be performed after the completion of the following sequential steps:

1. All participants have completed their Month 12 (OLI and BIK)/Month 11 (D2I) visit as defined in the protocol and had a re-test if necessary
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.
3. All criteria for unblinding the randomization codes have been met.
4. Randomization codes have been distributed according to RandAll NG procedures.

3.3. End of Study (EOS) Analyses

A final End-of-Study analysis will be conducted when all subjects have completed the study.

Details of which outputs will be produced at End of Study can be found in Section 16.5.

4. ANALYSIS POPULATIONS

Population	Definition / Criteria	Analyses Evaluated
Screened	• All participants who were screened for eligibility. • Subjects may be re-screened once and will be assigned a new subject number. • For disposition displays, except for the listing of subjects who were rescreened, only the latest re-screening data will be included.	• Study Population
Enrolled	• All participants who passed screening and entered the study. • Note screening failures (who never passed screening even if rescreened) and participants screened but never enrolled into the study are excluded from the Enrolled population as they did not enter the study.	• Study Population
Randomized	• All participants who were randomly assigned to treatment in the study. • This population will be based on the treatment the participant was randomized to.	• Study Population
Safety	• All randomized participants who received at least one dose of study treatment. • This population will be based on the actual treatment the participant received. • Note: participants who were not randomized but received at least one dose of study treatment will be listed separately.	• Safety • Virology (if applicable)
Intent-to-Treat Exposed (ITT-E)	• All randomized participants who receive at least one dose of IP during the Maintenance Phase of the study (on or after Day 1). • Participants will be analyzed according to the randomized treatment regardless of the actual treatment received.	• Study Population • Efficacy
Modified Intent-to-Treat (mITT-E)	• All ITT-E subjects excluding those from site PPD	• Study Population • Efficacy • Health Outcomes
Per-Protocol (PP)	• All participants in the mITT-E population except major protocol violators. • Protocol deviations that exclude subjects from the Per-Protocol population are defined in Section 4.1 (Protocol Deviations) and Appendix 1 (Protocol Deviation Management and Definition for Per-Protocol Population).	• Efficacy (Sensitivity Analysis)
Extension Switch (ES)	• All randomized subjects from BIK arm who receive at least one dose of CAB and/or RPV during the Extension Phase of the study. • Participants will be assessed according to actual treatment received during the Extension Phase.	• Safety and efficacy for BIK subjects switching to Extension Q2M if applicable

Population	Definition / Criteria	Analyses Evaluated
Pharmacokinetic (PK)	• All participants who receive CAB and / or RPV and undergo PK sampling during the study and provide evaluable CAB and / or RPV plasma concentration data with at least 1 non-missing PK assessment (Non-quantifiable [NQ] values will be considered as non-missing values). • Note: PK samples that may be affected by protocol deviations will be reviewed by the study team to determine whether or not the sample will be excluded.	• PK (Pregnant subjects on Q2M arm only for this RAP)
Confirmed Virologic Failure (CVF)	• All participants in the ITT-E population who met Confirmed Virologic Failure (CVF) • CVF during the Maintenance and/or Extension Phases is defined as: Rebound as indicated by two consecutive plasma HIV-1 RNA levels ≥200 c/mL (Day 1 values not applicable) after prior suppression to <200 c/mL	• Virology • Efficacy
Modified Confirmed Virologic Failure (mCVF)	• All participants in the mITT-E population who met Confirmed Virologic Failure (CVF) • Note this population is only applicable to summary tables	• Virology • Efficacy
Long-term Follow-up (LTFU)	• Discontinued subjects who have received at least one dose of CAB LA and/or RPV LA and have met any of the following criteria: - have at least one Long-term Follow-up phase clinic visit, - have filled out the LTFU phase conclusion form, - or have indicated the continuation to LTFU phase in the subject continuation form.	• Safety

Refer to Appendix 15: 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.

Important deviations which result in exclusion from the analysis population will also be summarised and listed. (Please refer to Appendix 1: Protocol Deviation Management and Definitions for Per Protocol Population)].

Protocol deviations will be tracked by the study team throughout the conduct of the study in accordance with the Protocol Deviation Management Plan.

- Data will be reviewed prior to unblinding and freezing the database to ensure all important deviations which may lead to exclusion from the analysis population(s) are captured and categorised on the protocol deviations dataset.
- This dataset will be the basis for the summaries and listings of protocol deviations.

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

5. CONSIDERATIONS FOR DATA ANALYSES AND DATA HANDLING CONVENTIONS

5.1. Study Treatment & Sub-group Display Descriptors

Treatment Group Descriptions			
RandAll NG Randomization System		Data Displays for Reporting	
Code	Description	Description	Order in TLF
A	CAB LA + RPV LA Q2M	Q2M	1
B	BIK QD	BIK	2

Note: Treatment comparisons will be displayed as follows using the descriptors as specified: Q2M vs. BIK (Q2M – BIK)

The following sub-display may be used as appropriate under the Q2M treatment group as noted in Appendix 15: List of Data Displays.

	Data Display for Reporting	Order for sub-display
For subjects randomized to Q2M during the Maintenance Phase	OLI	1
	D2I	2

In data displays of Extension Phase data for the Extension Switch population who switched from BIK, “Switch Q2M” will be used. In displays where sub study treatment will be displayed, descriptors are as shown below.

	Data Display for Reporting	Order for sub-display
Extension Phase data for the Extension Switch population (Switch Q2M)	Switch OLI	1
	Switch D2I	2

5.2. Baseline Definitions

For all endpoints (except as noted in baseline definitions) the baseline value will be the latest pre-dose assessment with a non-missing value, including those from unscheduled

visits. If time is not collected, Day 1 assessments are assumed to be taken prior to first dose and used as baseline.

Electrocardiograms (ECGs) are to be performed in triplicate prior to first dose on Day 1. The baseline value for an ECG parameter will be the mean of the last pre-treatment set of assessments from the same date.

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

5.3. Multicentre Studies

Data will be summarized for all centres combined. Country may be treated CCI [redacted] analyses of the primary efficacy endpoint (HIV-1 RNA ≥50 c/mL) as described in Section 7.1.5.1. and secondary efficacy endpoint (HIV-1 RNA <50 c/mL) as described in Section 7.2.5.1. CCI [redacted]

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 of clinical interest may also be considered for additional analyses on Health Outcomes and Biomarker analyses.

Category	Details
Strata	• For the proportion of participants with plasma HIV-RNA greater than or equal to 50 c/mL per FDA Snapshot algorithm at Month 12 (OLI and BIK)/Month 11 (D2I) (primary endpoint), a stratified analysis with Cochran-Mantel Haenszel (CMH) weights will be used to adjust the primary treatment comparison with the randomization strata corresponding to Gender at Birth (female, male) and Baseline BMI (<30 kg/m^2, ≥30 kg/m^2). • A similar approach will be used to adjust the analysis of the proportion of participants with HIV-1 RNA <50 c/mL (per the FDA's Snapshot algorithm) at Month 12(OLI and BIK)/Month 11 (D2I) • The analyses as described above will also be applied in the interim analysis for key efficacy endpoints at Month 6 (OLI and BIK)/Month 5 (D2I).
Covariates	See details in Section 5.4.2

5.4.2. Examination of Subgroups and Covariates

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

- If the percentage of participants is small within a particular subgroup, then the subgroup categories may be combined prior to unblinding the trial.
- If the category cannot be refined further, then descriptive rather than statistical comparisons may be performed for the particular subgroup.
- For subgroup analysis, per European Medicines Agency Guideline on the investigation of subgroups in confirmatory clinical trials (EMA, 2019), factors defining a subgroup population may be put in three categories:
    1. Factors with strong reason to expect an inconsistent response to treatment across the different levels of the factor to an extent that would make an overall assessment uninterpretable. In this case separate trials should usually be planned.
    2. Factors with reason to consider it prognostic for outcome, or at least some biological plausibility or external evidence such that an inconsistent response might be observed. In this study, stratified randomization strata, key demographic and baseline characteristic factors, will fall into this category. For these factors, subgroup analyses will be performed but likely underpowered so that a formal proof of efficacy will not be available individually in all subgroups. If consistent findings across multiple comparisons were observed, then these analyses would still be suggestive of a generalizable finding from the overall population.
    3. Factors with good argumentation why consistency of response to treatment is plausible or for which there is absence of pharmacological rationale and absence of clinical evidence from which to determine the plausibility of consistent drug effects. The impact of factor(s) falling into this category will be explored.

Subgroup Category	Subgroup and Subgroup Levels
EMA Subgroup Category 2:	
Randomization Strata	• Baseline BMI: <30 kg/m^2, ≥30 kg/m^2 • Gender at Birth: female, male For analysis purposes, randomization strata will be derived using eCRF data (which may differ from the strata captured in RAMOS NG). All statistical analyses will adjust for the above randomization strata, unless stated otherwise. Treatment-by-Strata interactions will be assessed as specified in the analysis sections.
Demographic and Baseline Characteristic Subgroups	• Age - Descriptive summaries: < 35, 35 - < 50, ≥ 50 - Statistical analyses: < 50, ≥ 50 - FDAAA: ≤18, 19 - 64, ≥ 65 - EMA: 18 - 64, 65 - 84, ≥ 85 • Race

Subgroup Category	Subgroup and Subgroup Levels
EMA Subgroup Category 2:	
	- White; Non-White - Black/ African American; Non- Black/ African American - White, Black/African American, Other For statistical modelling of biomarkers, use White, Black/African American vs. Other. For other statistical modelling, use White vs Non-White. • Country (not used for statistical modelling) - Canada - United Kingdom - Ireland - France - Germany - Spain - Italy - Switzerland - Austria - Netherlands - Belgium - Japan - Australia - United States • Region North America, Europe, Rest of World • Baseline CD4+ cell count (cells/mm^3) - <350, 350 to <500, ≥ 500 cells/mm^3 • Derived Maintenance Baseline (Day 1) Centres for Disease Control and Prevention (CDC) category: - Stage I, Stage II, Stage III • Baseline HIV-1 Subtype (if available at the time of the analysis) - A, A1, AE, AG, B, C, Other • INI Regimen prior to BIK - Raltegravir, Elvitegravir, Dolutegravir, none. • Duration of Prior ART (including BIK) use before study entry (<1 year, 1 - <2, 2 - <3 ,3-<4, >=4 years)

Subgroup Category	Subgroup and Subgroup Levels
EMA Subgroup Category 2:	
EMA Subgroup Category 3:	
ISR-related: Needle length	For the maximum toxicity grade of each preferred term of the common ISR (pain, induration, nodules and any other ISR with >=5% subjects in the Q2M treatment arm) during the maintenance phase: • Needle Length for Last CAB Injection prior to and including the onset date of the earliest corresponding CAB ISR with maximum toxicity grade during the Maintenance Phase: (<1.5, 1.5 to <2, ≥2 inch); • Needle Length for Last RPV Injection prior to and including the onset date of the earliest corresponding RPV ISR with maximum toxicity grade during the Maintenance Phase: (<1.5, 1.5 to <2, ≥2 inch); Note: If there is no ISR of interest reported during maintenance phase for a subject, the needle length of last injection during maintenance phase will be used in the summary.

5.5. Multiple Comparisons and Multiplicity

There are no planned adjustments for multiple comparisons or multiplicity.

5.5.1. Primary Analysis

The primary comparison of interest is the comparison between CAB LA + RPV LA (Q2M) and BIK for the primary endpoint in the mITT-E population at Month 12 (OLI and BIK)/Month 11 (D2I). The primary comparison will be made at a one-sided 2.5% level of significance. Treatment with CAB LA + RPV LA (Q2M) will be declared non-inferior to BIK if the upper bound of a two-sided 95% confidence interval for the difference (Q2M – BIK) in proportion of participants with HIV-1 RNA ≥ 50 c/mL is below 4%.

If the primary analysis demonstrates non-inferiority, then a superiority hypothesis will be tested at the two-sided 5% level of significance. Superiority favoring CAB LA + RPV LA (Q2M) will be declared if the upper limit of the confidence interval is below 0% for the mITT-E population analysis. If superiority is declared, the p-value for superiority will also be calculated.

No multiple comparison adjustment is necessary for testing non-inferiority followed by superiority (conditional on achieving significance in the non-inferiority test) since testing follows a pre-specified sequence of hypothesis such that if the first hypothesis tested is not significant, all subsequent tests will not be performed. This fixed sequence procedure controls the type I error rate at the nominal level.

Subjects who became pregnant during the study will be allowed to continue CAB LA + RPV LA (Q2M) treatment, while those who became pregnant on BIK will be withdrawn. To minimize bias, a "while on-treatment" strategy will be implemented. Viral load data collected after confirmed pregnancy will not be evaluated for summary tables and statistical analysis in the primary analysis (see Appendix 13: Data Handling for Pregnant Subjects).

5.5.2. Other Comparisons of Interest

The following sensitivity analysis will also be performed for consistency with the results from the primary analysis:

- Same analysis as described above with the PP population
- Same analysis as described above with the ITT-E population
- Same analysis as described above with all data as observed (not applicable if no subject on the Q2M arm becomes pregnant)

5.5.3. Secondary Comparisons

If the primary comparison of interest (Section 5.5.1) using the mITT-E population demonstrates non-inferiority of CAB LA + RPV LA (Q2M) compared to BIK at the primary analysis timepoint, then the following key secondary comparisons using the mITT-E population will be tested:

- Treatment comparisons between the two arms (Q2M – BIK) with respect to the proportion of participants with HIV-1 RNA < 50 copies/mL at Months 12 (OLI and BIK)/Month 11 (D2I) (defined by the US FDA snapshot algorithm), including the two-sided 95% confidence interval. If the lower limit of the confidence interval for the difference in response rates (Q2M-BIK) lies **above -12%** then non-inferiority can be concluded.
- Sensitivity analysis as described in Section 5.5.2 in the PP population and with all data observed will also be performed, for secondary comparisons. Additional comparisons of clinical interest between two treatment arms may also be performed as supportive analyses.
- In addition to the primary and the key secondary comparisons, the comparisons between two treatment arms for HIVTSQs (Treatment Satisfaction Status Score), HIVTSQc (Treatment Satisfaction Change score), the statistical test on change in PIN acceptance score within the Q2M arm over time using a two-sided 5% level of significance will also be performed as supportive analyses.

5.6. 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
16.3	Appendix 3: Assessment Windows
16.4	Appendix 4: Study Phases and Treatment State
16.5	Appendix 5: Data Display Standards & Handling Conventions
16.5	Appendix 6: Derived and Transformed Data
16.7	Appendix 7: Reporting Standards for Missing Data
16.8	Appendix 8: Values of Potential Clinical Importance
16.9	Appendix 9: Snapshot Algorithm Details
16.10	Appendix 10: Variables Defined for Time to Event Analysis
16.11	Appendix 11: Identification of Adverse Events of Special Interest (AESI)
16.12	Appendix 12: Identification of COVID-19 Adverse Events
16.13	Appendix 13: Data Handling for Pregnant Subjects

6. STUDY POPULATION ANALYSES

6.1. Overview of Planned Study Population Analyses

The study population analyses will be based on the Intent-to-Treat Exposed population, unless otherwise specified. Note in the Month 12 analysis, mITT-E will be used in summary tables.

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.

Table 1 provides an overview of the planned study population analyses, with full details of data displays presented in Appendix 15: List of Data Displays

Table 1 Overview of Planned Study Population Analyses

Display Type	Data Displays Generated	
	Table	Listing
Randomization		
Randomization [1]		Y[2]
Subject Disposition		
Study Populations [3]	Y	
Study Recruitment [3]	Y	
Reasons for Screening Failures [3]	Y	Y
Age categories	Y	
Subject Disposition	Y[4][5]	
Reasons for Withdrawal	Y[4][5]	Y
IP discontinuation	Y	Y
Important Protocol Deviations	Y	Y
Deviations leading to exclusion from PP	Y	Y
Inclusion and Exclusion Criteria Deviations	Y	Y
Demography and Baseline		
Demographics Characteristics [6]	Y	Y
Race & Racial Combinations [7]	Y	Y
Hepatitis Status at Entry	Y	
CDC Classification of HIV infection (2014) at Maintenance Baseline (Day 1)	Y	
Distribution of CD4+ Cell Counts at Screening and Maintenance Baseline (Day 1)	Y	
HIV Risk Factors	Y	
Medical Conditions, Concomitant Medications & Antiretroviral Therapy		
Medical Conditions (Current/Past) [8]	Y	
Medical Conditions: Sub-conditions (Current/Past) [9]	Y	
Concomitant Medications (non-ART)	Y[10]	
Prior Antiretroviral Therapy	Y	Y
Concomitant Antiretroviral Therapy during Maintenance Phase		Y
ART Medications Received during LTFU Phase		Y
Lipid Modifying Agents (Maintenance Baseline (Day 1) and During Maintenance Phase)	Y	
Substance use at Screening	Y	
Medical History of Seizure		Y
Other		
Study Treatment Accountability [11]		Y

NOTES:

- T = Tables, L = Listings, Y = Display Generated,

1. Based on Randomized population
2. One listing of participants randomized but not treated, and one listing of planned and actual treatment strata.
3. All Subjects screened population.
4. Participants who have not been recorded as either completing or withdrawing from the study will be categorized as "Ongoing at time of the analysis" for summary purposes.
5. Analysis of subject disposition may be performed for each study Phase separately if applicable, as well as for overall study conclusion.
6. Age and ethnicity collected at Screening; weight, height and BMI collected at Day 1,
7. The five high level FDA race categories and designated Asian subcategories will be summarised along with all combinations of high-level categories which exist in the data. The nine race categories collected will be summarised along with categories for mixed race. A by-subject listing of race will also be produced.
8. Medical conditions will be coded using the Medical Dictionary for Regulatory Activities (MedDRA).
9. Sub conditions include Cardiac, Gastrointestinal, Metabolism and Nutrition, Psychiatric, Renal and Urinary, and Nervous system Conditions.
10. Summarised by Ingredient combinations.
11. Dispensation information (dates and number of tablets dispensed and returned).

7. EFFICACY ANALYSES

7.1. Primary Efficacy Analyses

7.1.1. Endpoint / Variables

The primary objective of the study is to demonstrate the non-inferior antiviral activity of CAB LA + RPV LA every two months (Q2M) compared to a BIK single tablet regimen administered once daily over 12 months in suppressed HIV-1 infected antiretroviral therapy (ART)-experienced participants. The primary endpoint is proportion of participants with plasma HIV-RNA greater than or equal to 50 copies/mL as per Food and Drug Administration (FDA) Snapshot algorithm at Month 12 (OLI and BIK)/Month 11 (D2I).

7.1.2. Summary Measure

Difference between the two treatment groups (Q2M – BIK) in the proportion of participants with HIV-RNA ≥50 c/mL at Month 12 (OLI and BIK)/Month 11(D2I) (as defined by the US FDA snapshot algorithm) and its two-sided 95% confidence interval will be produced. Note for the Q2M arm, primary endpoint data from the Q2M OLI subjects at Month 12 and data from the Q2M D2I subject at Month 11 will be combined for demonstration of non-inferiority.

7.1.3. Population of Interest

The primary efficacy analyses will be based on the modified Intent-To-Treat Exposed (mITT-E) population, unless otherwise specified.

7.1.4. Strategy for Intercurrent (Post-Randomization) Events

As defined by the Snapshot algorithm, HIV-RNA ≥ 50 copies/mL is determined by the last available on-treatment HIV-1 RNA measurement within the analysis visit window of interest.

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 prior to the analysis window are classified as having HIV-RNA ≥ 50 copies/mL.

A "while on-treatment" strategy will be implemented when a Q2M subject becomes pregnant on study but is allowed to continue. Viral load data collected after confirmed pregnancy will not be evaluated for summary tables and statistical analysis in the primary analysis. Additional sensitivity analysis including all observed data may be performed to assess consistency. See Appendix 13: Data Handling for Pregnant Subjects for details.

7.1.5. Statistical Analyses / Methods

Details of the planned displays are provided in Appendix 15: 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.

7.1.5.1. Statistical Methodology Specification

Primary Statistical Analysis
Endpoint / Variables
• Proportion of participants with plasma HIV-RNA greater than or equal to 50 copies/mL at Month 12 (OLI and BIK)/Month 11 (D2I) per Snapshot algorithm for the mITT-E population.
Snapshot Dataset
• Virologic outcome ("HIV-RNA <50" or "≥50 c/mL") per Snapshot algorithm is determined by the last available on-treatment HIV-1 RNA measurement within the analysis visit window of interest (refer to analysis window defined in Section 16.3). In addition, participants who discontinue for reasons not related to adverse event with on-treatment HIV-1 RNA result at the time of discontinuation ≥50 c/mL or who change study treatment not permitted per protocol during Maintenance Phase before the analysis visit are classified as 'HIV-RNA ≥50 c/mL'. • Full details of the Snapshot algorithm are provided in Appendix 9: Snapshot Algorithm Details
Model Specification
• The primary efficacy endpoint will be analysed using a stratified analysis with Cochran-Mantel-Haenszel (CMH) weights, adjusting for the randomization strata BMI (<30, ≥30 kg/m^2) and Gender at Birth (female, male)

- The CMH estimate of the adjusted treatment difference will be calculated as a weighted average of strata-specific estimates of the treatment difference calculated within each stratum as follows:
    - Baseline BMI < 30 kg/m^2 and Male Gender at Birth
    - Baseline BMI < 30 kg/m^2 and Female Gender at Birth
    - Baseline BMI ≥ 30 kg/m^2 and Male Gender at Birth
    - Baseline BMI ≥ 30 kg/m^2 and Female Gender at Birth

- If n_k is the number of CAB LA + RPV LA (Q2M) treated participants, m_k is the number of BIK arm treated participants, and $N_k = n_k + m_k$ is the total number of participants in the k^{th} stratum, then the CMH estimate is given by

$$\hat{d}_{cmh} = \frac{\sum W_k \hat{d}_k}{\sum W_k}$$

where

$$W_k = \frac{n_k m_k}{N_k}$$

are CMH weights and $\hat{d}_k$ are estimates of the differences in proportions between the two treatment arms, p_{Q2M}-p_{BIK}, for the *k*th stratum.

- The corresponding two-sided 95% CI will be calculated as

$$\hat{d}_{cmh} \pm 1.96 \times \sqrt{\hat{\text{var}}(\hat{d}_{cmh})}$$

where the variance estimator [Sato, 1989] consistent in both sparse data and large strata is given below

$$\hat{\text{var}}\left(\hat{d}_{cmh}\right) = \frac{\hat{d}_{cmh}\left(\sum P_k\right) + \sum Q_k}{\left(\sum n_k m_k / N_k\right)^2} = \frac{\hat{d}_{cmh}\left(\sum P_k\right) + \sum Q_k}{\left(\sum W_k\right)^2}$$

where

$$P_k = \frac{n_k^2 y_k - m_k^2 x_k + n_k m_k (m_k - n_k)/2}{N_k^2}$$

$$Q_k = \frac{x_k (m_k - y_k)/N_k + y_k (n_k - x_k)/N_k}{2}$$

with x_k and y_k corresponding to the number of participants with Plasma HIV-1 ≥ 50 c/mL at Month 12 (OLI and BIK)/Month 11 (D2I) per FDA Snapshot for the Q2M and BIK arm, respectively, for the *kth* stratum.

Model Results Presentation

- Adjusted CMH estimate of the difference in the proportion of participants with "HIV-1 RNA ≥50" between each treatment group (Q2M – BIK) and corresponding 95% confidence interval.
- Non-inferiority will be concluded if the upper bound of the two-sided 95% confidence interval (CI) for the CMH adjusted difference in proportion of participants with 'HIV-1 RNA≥50' in the CAB LA + RPV LA (Q2M) group minus proportion of participants with 'HIV-1 RNA≥50' in the BIK group is less than 4%.
- If the analysis shows non-inferiority, then a superiority hypothesis will be tested at the two-sided 5% level of significance. Superiority favoring CAB LA + RPV LA (Q2M) will be declared if the upper limit of the confidence interval is below 0% for the mITT-E population analysis. If superiority is declared, the p-value for superiority will also be calculated.

Subgroup Analyses

- Treatment Heterogeneity across randomization strata:
  - The weighted least squares chi-squared statistic [Fleiss, 1981] will be used to test for one-way homogeneity across the levels of each categorical variable, with each categorical variable considered separately.
  - Following Lui and Kelly [Lui, 2000] ½ will be added to each cell in any strata for which the stratum-specific rate estimates of either p_{Q2M} or p_{BIK} are zero or one, and tests will be one-sided.
  - Any heterogeneity found to be statistically significant will be explored and if necessary, results will be reported for each level of the categorical variable. Investigation of heterogeneity will be confined to the primary endpoint. Tests of homogeneity will be assessed at the one-sided 10% level of significance.

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Sensitivity Analyses

- Per-Protocol population analysis:
  To assess the impact of important protocol deviations, statistical analysis will be repeated using the Per-Protocol population and compared for consistency with the results from the primary mITT-E population analysis.

- All Data as Observed:
  This analysis will include all observed data including those collected after confirmed pregnancy, in the mITT-E population.
- Efficacy Sensitivity:
  This analysis will be based on the ITT-E population at Month 12.

7.2. Secondary Efficacy Analyses

7.2.1. Endpoint / Variables

The key secondary efficacy endpoint is proportion of participants with plasma HIV-1 RNA <50 c/mL (c/mL) at Month 12 (OLI and BIK)/Month 11(D2I) using the FDA Snapshot algorithm.

Other secondary efficacy endpoints are listed below:

- Proportion of participants with plasma HIV-1 RNA <50 c/mL (c/mL) at Month 6 (OLI and BIK)/Month 5 (D2I).

- Proportion of participants with plasma HIV-1 RNA ≥50 c/mL (c/mL) at Month 6 (OLI and BIK)/Month 5(D2I)
- Proportion of participants with protocol-defined confirmed virologic failure (CVF) through Month 6 and Month 12 (OLI and BIK)/Month 5 and Month 11 (D2I).

- Changes from Baseline in viral load and CD4+ cell count over time including Month 6 and Month 12 (OLI and BIK)/Month 5 and Month 11 (D2I)

7.2.2. Summary Measure

Binary endpoints: difference in the proportion of participants with HIV-RNA ≥ 50 c/mL (or < 50 c/mL) as defined by the US FDA snapshot algorithm at specified time point between treatment groups (Q2M – BIK) will be produced.

Continuous endpoints (e.g. CD4+ cell count): descriptive summary statistics per GSK data standards will be produced.

7.2.3. Population of Interest

The secondary efficacy analyses will be based on the Intent-to-Treat Exposed (ITT-E) population, unless otherwise specified. Note in the Month 12 analysis, mITT-E will be used in summary tables.

7.2.4. Strategy for Intercurrent (Post-Randomization) Events

As defined by the snapshot algorithm, only participants with last available HIV-1 RNA measurement less than 50 c/mL while the participant is on treatment within the analysis visit window of interest are classified as HIV-1 RNA < 50 c/mL.

A "while on-treatment" strategy will be implemented as described in Section 7.1.4. Same approach will be applied to efficacy tables for protocol-defined confirmed virologic failure (CVF) and CD4+ cell count. Data after confirmed pregnancy will not be evaluated for the summary tables unless otherwise noted, but will be included in the listings if applicable.

7.2.5. Statistical Analyses / Methods

Details of the planned displays are provided in Appendix 15: List of Data Displays and will be based on GSK data standards and statistical principles.

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

7.2.5.1. Statistical Methodology Specification

Key Secondary Statistical Analysis
Endpoint / Variables
• Proportion of participants with plasma HIV-RNA < 50 copies/mL at Month 12(OLI and BIK)/Month11(D2I) per Snapshot algorithm for the mITT-E population. • Proportion of participants with plasma HIV-RNA < 50 copies/mL at Month 6(OLI and BIK)/Month 5(D2I) per Snapshot algorithm for the ITT-E population. • Proportion of participants with plasma HIV-RNA ≥50 copies/mL at Month 6(OLI and BIK)/Month 5(D2I) per Snapshot algorithm for the ITT-E population.
Snapshot Dataset
• Virologic outcome ("HIV-RNA <50" or "≥50 c/mL") per Snapshot algorithm is determined by the last available on-treatment HIV-1 RNA measurement within the analysis visit window of interest (please refer to analysis window defined in Section 16.3). In addition, participants who discontinue for reasons not related to adverse event with on-treatment HIV-1 RNA result at the time of discontinuation ≥50 c/mL or who change study treatment not permitted per protocol during Maintenance Phase before the analysis visit are classified as 'HIV-RNA ≥50 c/mL'. • Full details of the Snapshot algorithm are provided in Appendix 9: Snapshot Algorithm Details
Model Specification
• As specified in Section 7.1.5.1, with outcome being "HIV-1 RNA <50 c/mL" or "HIV-1 RNA ≥50 c/mL"
Model Results Presentation
• Adjusted CMH estimate of the difference in the proportion of participants with 'HIV-1 RNA <50' or with 'HIV-1 RNA ≥50' between two treatment groups (Q2M – BIK) and corresponding 95% confidence interval. • Non-inferiority will be concluded if the lower bound of the two-sided 95% confidence interval (CI) for the CMH adjusted difference (Q2M – BIK) in proportion of participants with 'HIV-1 RNA <50' is greater than -12% at Month 12 (OLI and BIK)/Month 11 (D2I).
Subgroup Analyses
• Treatment Heterogeneity across randomization strata at Month 12 (OLI and BIK)/Month 11 (D2I) As specified in Section 7.1.5.1, with outcome being "HIV-1 RNA <50 c/mL" or "HIV-1 ≥50 c/mL"

Sensitivity and Supportive Analyses

- Per-Protocol population analysis:
  To assess the impact of important protocol deviations, statistical analysis will be repeated using the Per-Protocol population and compared for consistency with the results from the primary ITT-E population analysis. Note for Month 12, PP population is based on the mITT-E population.
- All Data as Observed:
  This analysis will include all observed data including those collected after confirmed pregnancy, in the ITT-E population. Note for Month 12, this analysis will be based on the mITT-E population.
- Efficacy Sensitivity:
  This analysis will be based on the ITT-E population at Month 12.

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8. SAFETY ANALYSES

The safety analyses will be based on the Safety population, unless otherwise specified. A "while on-treatment" strategy which considers data collected after confirmed pregnancy non-evaluable in the Q2M arm will be implemented for selected analysis including clinical laboratory, biomarker, and metabolic analysis. See Appendix 13: Data Handling for Pregnant Subjects for details. Note for safety-related reporting including adverse events and ECG, all observed data will be included.

8.1. Adverse Events Analyses

Adverse events analyses including the analysis of adverse events (AEs), Serious (SAEs) and other significant AEs will be based on GSK Core Data Standards. Table 3 below provides an overview of the planned analyse with further details of data displays provided in Appendix 15: List of Data Displays.

Table 3 Overview of Adverse Events Analyses

Endpoint	Absolute				Change from Maintenance Baseline					Max Post Maintenance Baseline			
	Summary		Individual		Stats Analysis	Summary		Individual		Summary		Individual	
	T	F	F	L	T	T	F	F	L	T	F	F	L
Exposure													
Extent of Exposure[1]	Y			Y[2]									
Adherence to Dosing Schedule [1]	Y												
Dosing Errors and IP Device Malfunctions				Y									
Injection Needle													
Length and Gauge	Y												
Adverse Events[3]													
All AEs by SOC and PT	Y												
All AEs by SOC, PT and Toxicity	Y												
All Drug-Related AEs by SOC and PT	Y												
All Drug-Related AEs by SOC, PT and Toxicity	Y												
Common AEs by frequency [5]	Y	Y[6]											
Common Grade 2-5 AEs [5] by frequency	Y												

Endpoint	Absolute				Change from Maintenance Baseline					Max Post Maintenance Baseline			
	Summary		Individual		Stats Analysis	Summary		Individual		Summary		Individual	
	T	F	F	L	T	T	F	F	L	T	F	F	L
Drug-related Grade 2-5 AEs	Y												
All AEs				Y[4]									
Serious and other significant adverse events													
All SAEs by SOC and PT	Y												
Reason for Considering as a Serious Adverse Event (FDA)				Y									
All Drug-Related SAEs by SOC and PT	Y												
Fatal SAEs				Y									
Non-Fatal SAEs	Y			Y									
Drug-related non-fatal SAEs	Y												
AEs Leading to Withdrawal/Permanent Discontinuation of IP	Y			Y									
Common Non-serious AEs by SOC and PT	Y												
Subjects and Number of occurrences of SAEs, Fatal SAEs, and Drug-related SAEs	Y												
AESI													
Depression, Suicidal and Self-Injury AEs by Prior History	Y												
AESI by SOC and PT	Y												
Characteristics of AESI	Y												
Syncope and Presyncope AE	Y												
Suicidality assessment													
PSRAE				Y[7]									

Endpoint	Absolute				Change from Maintenance Baseline					Max Post Maintenance Baseline			
	Summary		Individual		Stats Analysis	Summary		Individual		Summary		Individual	
	T	F	F	L	T	T	F	F	L	T	F	F	L
Columbia suicidality (eC-SSRS)	Y												
Injection Site Reaction Adverse Events [12]													
ISR AEs (Event-Level) [17]	Y												
ISR AEs (Subject-Level) [18]	Y												
ISR AEs (Subject-Level) by Visit and Severity	Y	Y[19]											
Maximum ISR AE Grade by Needle Length [21]	Y												
Laboratory: Chemistry and Hematology													
Clinical Chemistry						Y				Y			
Lipids						Y							
NCEP shifts in lipids										Y[8]			
Hematology						Y				Y			
CCI													
Laboratory: Urinalysis (regardless of fasting status)													
Urine Dipstick	Y												
Urine Concentration						Y							
Proteinuria										Y[8]			
Laboratory: Hepatobiliary													
Liver Assessment				Y[14]									
Hepatobiliary Abnormality criteria	Y			Y									
Liver Chemistries				Y[11]							Y[9]		
Laboratory: Biomarkers													
Bone markers					Y	Y[10]							
Renal markers					Y	Y[10]							
CCI													
HOMA-IR, insulin and HbA1c					Y[16]	Y							
ECG													
ECG findings	Y			Y									

Endpoint	Absolute				Change from Maintenance Baseline					Max Post Maintenance Baseline			
	Summary		Individual		Stats Analysis	Summary		Individual		Summary		Individual	
	T	F	F	L	T	T	F	F	L	T	F	F	L
ECG values				Y[22]		Y							
QTC values by Category	Y					Y							
Other													
Vital Signs (BP, HR, temp)				Y		Y							
Weight, Height and BMI	Y			Y		Y							
Waist Circumference and Hip Circumference	Y			Y		Y							
CCI													
Tanita Scale Assessments (Body Fat Percentage, Bone Mineral Mass, Muscle Mass, Total Body Water Percentage)	Y			Y		Y							
Abacavir HSR				Y[13]									
Participants who became Pregnant				Y									
Patient Profiles				Y[20]									
Metabolic Syndrome	Y		Y	Y		Y							
CCI													

NOTES:

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

1. Refer to Section 16.6.2 and Section 16.6.4 for defining extent of exposure and adherence to dosing intervals.
2. Includes reason for any dose change/interruption.
3. For AEs reported more than once by a participant, the most severe intensity will be included. Separate summary tables including and excluding injection site adverse reactions.
4. Listing of all AEs including verbatim text and preferred term, and listing of subject numbers for individual AEs.
5. Common AEs are those with ≥5% incidence in Q2M or BIK summarised by frequency.
6. Plots of incidence rates and relative risk with 95% CI for Q2M vs.BIK.
7. Four PSRAE listings: Event and Description (Section 1 and Section 2), Possible Cause (Section 3), Section 4 and Section 5 - Section 8.

8. Shift table summarising Maintenance Baseline (Day 1) vs. maximum Maintenance Phase result.
9. Scatter plot of baseline vs. maximum post-baseline for ALT and BILT. Scatter plot of maximum ALT vs. maximum Bilirubin.
10. Bone markers: Bone-specific alkaline phosphatase, procollagen type 1 N-propeptide, type 1 collagen cross-linked C-telopeptide, osteocalcin, 25 hydroxy-Vitamin D. Renal markers: Cystatin C; Beta-2-Microglobulin; Retinol Binding Protein (RBP). CCI .
11. For subjects meeting hepatobiliary lab abnormality criteria.
12. Repeat for CAB/RPV, CAB, RPV respectively.
13. Separate listings for exposure to abacavir, history of drug allergies, family conditions, skin rash, symptoms, vital signs, individual symptoms and diagnostic category assignment. If no hypersensitivity to abacavir is observed, then only one blank listing will be provided for the exposure to abacavir.
14. Separate listings for event reporting, RUCAM score, biopsy, imaging, substance use and medical conditions.

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16. Statistical analysis will be performed for HOMA-IR.
17. Event-level summary: Percentages based on total number of ISR events including distribution of grade, duration, and event characteristics.
18. Subject-Level summary: Characteristics of ISR AE (Overall and by Common ISRs); Percentage based on number of participants; Includes distribution of grade and max grade, event characteristics, number of events per subject, rate of number of events per injection visit.
19. A corresponding plot for all grades and a separate plot for grade 3-5 events will be produced.
20. Patient profiles are not planned but can be produced post hoc, as necessary.
21. Please refer to Section 5.4 for derivation of needle length used in this summary.
22. For subjects with any value of potential clinical importance.

8.2. Adverse Events of Special Interest Analyses

Adverse events of special interest (AESI) are determined for CAB and/or RPV based on pre-clinical and clinical experience, along with information for the Integrase Inhibitor class of HIV medications and RPV safety profile. Table 4 shows the currently identified AESI, drug(s) of Interest and the reasons for inclusion. Changes to the MedDRA dictionary may occur between the start of the study and the time of reporting and/or emerging data from ongoing 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.

A summary by system organ class and preferred term will be provided for each of AESI. The characteristics of event occurrences during the maintenance phase will be summarized for AESIs. For Depression, anxiety and suicidal ideation/behaviour AESI, a summary by system organ class, maximum DAIDS toxicity grade and prior history of suicidal ideation will be provided.

The details of the current planned grouping, including Standardized MedDRA Query (SMQ) values (as applicable), and planned displays are provided in Appendix 11: Identification of Adverse Events of Special Interest (AESI) and Appendix 15: List of Data Displays.

Table 4 Adverse Events of Special Interest

Adverse Events of Special Interest	Drug(s) of Interest	Reason for Inclusion
Hepatic Safety Profile: Assessment of Risk of hepatoxicity	CAB+RPV	Clinical, Class, Regulatory Interest, More prevalent in HIV population
Hyperglycemia	CAB	Class, Regulatory Interest
Hypersensitivity Reactions (HSR)	CAB	Class, Regulatory Interest, Occurs in HIV population
Rash	RPV	Class, Regulatory Interest, Occurs in HIV population
Prolongation of the Corrected QT Interval of the ECG in Supratherapeutic Doses	RPV	Non-clinical, Clinical, Regulatory Interest
Suicidal Ideation/Behaviour	CAB+RPV	Clinical, Class, Regulatory Interest, More prevalent in HIV population
Depression	CAB+RPV	Clinical, Class, Regulatory Interest, More prevalent in HIV population
Bipolar Disorder	CAB+RPV	Clinical, Class, Regulatory Interest, More prevalent in HIV population
Psychosis	CAB+RPV	Clinical, Class, Regulatory Interest, More prevalent in HIV population
Mood Disorders	CAB+RPV	Clinical, Class, Regulatory Interest
Anxiety	CAB+RPV	Clinical, Class, Regulatory Interest
Sleep Disorders	CAB+RPV	Clinical, Class, Regulatory Interest, More prevalent in HIV population
Injection Site Reactions (ISR) from Study Drug Injections [1]	CAB+RPV	Clinical
Seizures and Seizure-like Events	CAB	Clinical, Regulatory Interest
Weight Gain	CAB	Clinical, Class
Rhabdomyolysis	CAB	Clinical, Class
Pancreatitis	CAB	Clinical, Therapeutic Area, More prevalent in HIV population

Adverse Events of Special Interest	Drug(s) of Interest	Reason for Inclusion
Impact on Creatinine	CAB+RPV	Regulatory Interest, Therapeutic Area, More prevalent in HIV population
Safety in Pregnancy	CAB	Regulatory Interest, Class
NOTE: [1] A separate analysis will be performed for ISRs from study drug injections as described in Section 8.2.1		

8.2.1. Analyses for Injection Site Reaction Adverse Events

Injection Site Reaction (ISR) adverse events of interest are those from study drug injections. For the summary of ISR 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), associated to CAB and/or RPV, or stratification by subgroup (such as needle length, refer to Section 5.4.2).

ISRs (based on investigator discretion) from study drug injections 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 the causal agent cannot be determined in cases where both drugs are given on one side or the ISR is reported non-specifically, then the attribution to a specific causal agent will remain unknown.

Common ISR adverse events during the Maintenance Phase are defined by MedDRA preferred terms including injection site pain, injection site induration, injection site nodules and preferred terms of any other ISR with ≥5% participants in the Q2M arm. The same set of common terms will be applied to 'overall' (CAB and/or RPV), CAB alone, RPV alone.

ISRs will be attributed to the needle length specifically based on the side of injection administration and the side of the reported ISR (as collected in the eCRF). If the needle length cannot be determined due to both drugs given on the same side with different needle lengths, then the attribution to a needle length will remain unknown.

8.3. Clinical Laboratory

Laboratory evaluations including the analyses of chemistry laboratory tests, hematology laboratory tests, urinalysis, and liver function tests will be based on GSK Core Data Standards.

For women who became pregnant on study, a data listing for selected parameters including the following will be provided. Additional parameters of interest may also be listed if applicable.

Clinical Chemistry: Creatinine, GFR, Glucose, HCG

Hematology: HbA1C, Hemoglobin, Hematocrit, Mean Corpuscular Volume, Platelets, Erythrocytes, Lymphocytes, Neutrophils, Basophils, Monocytes, Eosinophils

Immunology: CD4+ cell count, CD8+ cell count, CD4/CD8 cell count ratio, CD4/Lymphocytes, CD8/Lymphocytes

Urinalysis: Albumin/Creatinine, Glucose, Ketones, Occult Blood, Protein, Protein/Creatinine, Erythrocytes

8.4. Biomarker Analyses

Biomarker analysis (renal, bone, inflammation) will not be performed at the Month 6 interim analysis, and will only be performed when all expected data through Month 12 (OLI and BIK)/Month 11 (D2I) has been received from the laboratory. Statistical estimates for each planned visit will be provided in the Month 12 primary analysis using the MMRM model as describe in the below sections unless otherwise noted. The details of the planned displays are in Appendix 15: List of Data Displays.

8.4.1. Bone Biomarkers

Statistical Analyses
Endpoints
• Change from Maintenance Baseline (Day 1) in the following bone markers at Month 6 (OLI and BIK)/Month 5 (D2I) and at Month 12 (OLI and BIK)/Month 11 (D2I): ◦ Bone-specific alkaline phosphatase ◦ Procollagen type 1 N-propeptide ◦ Type 1 collagen cross-linked C-telopeptide ◦ Osteocalcin ◦ 25 hydroxy-Vitamin D
Covariates
• Baseline Value (continuous, log-transformed) • Gender at Birth (male, female) • Baseline BMI(<30 kg/m^2, >=30 kg/m^2) • Age (Continuous) • Race (White, Black/African American, Other) • Smoking Status (Never, Former, Current) • Vitamin D use (Yes vs no)

Data Handling

- OC (Observed Case) dataset will be used.

Model Specification

- Analysis values will be log-transformed (including the baseline value).
- The change in the log-transformed data from Maintenance baseline (i.e. log(value/ baseline value) or log(value) – log(baseline value)) for each bone marker will be analysed for the comparison between the two treatment arms.
- MMRM (Mix Model Repeated Measures) model with the observed margins (OM) option within PROC MIXED in SAS will be used including treatment group plus the above covariates, with visit as the repeated factor.
- The Kenward and Roger method for approximating the denominator degrees of freedom and correcting for bias in the estimated variance-covariance of the fixed effects will be used.
- No assumptions about the correlations between a subject's values will be made (the correlation matrix for within-subject errors will be unstructured). This will be estimated by treatment group by specifying "type=UN" and "group=treatment" options in the SAS MMRM models.
- In the event that this model fails to converge, alternative correlation structures may be considered such as CSH or CS. Akaike's Information Criteria (AIC) will be used to assist with the selection of covariance structure if needed.
- The repeated measures analysis will assume that the treatment difference can vary between visits (i.e. a treatment*visit interaction will be included in the model). Estimates and 95% confidence intervals will be produced for each visit.

Model Checking & Diagnostics

- Model assumptions will be applied, but appropriate adjustments maybe made based on the data.
- Distributional assumptions underlying the model used for analysis may be examined by obtaining a normal probability plot of the residuals and a plot of the residuals versus the fitted values (i.e. checking the normality assumption and constant variance assumption of the model respectively) to gain confidence that the model assumptions are reasonable.
- If there are any departures from the distributional assumptions, alternative models will be explored using appropriately transformed data.

Model Results Presentation

- For each treatment: Adjusted geometric means (for ratio to Maintenance BL) and 95% CI. Exponential transformation on the estimates from the MMRM model (based on the log-transformed data) will reflect the mean ratio of values post-baseline vs. Maintenance BL for each treatment arm. This ratio can then be translated into percent change from maintenance baseline (Day 1) (e.g. the ratio bb_{M12}/bb_{bl} = 1.3 can be translated into 30% increase from baseline).
- For treatment comparison: Adjusted geometric mean ratio between the two treatment groups (Q2M/BIK), 95% CI and *p*-value. This ratio can then be translated into percent comparisons in the ratio (value/baseline value) between Q2M vs. BIK (e.g. Q2M/BIK = 1.2 can be translated into 20% higher in the Q2M change from baseline ratio compared with BIK).

• Interactions between treatment and each of the covariates will not be assessed but may be explored post hoc.
Sensitivity Analyses
• Not applicable
Subgroup Analyses
• Not applicable

8.4.2. Renal Biomarkers

Statistical Analyses
Endpoints
• Change from Maintenance Baseline (Day 1) in the following renal markers at Month 6 (OLI and BIK)/Month 5 (D2I) and at Month 12 (OLI and BIK)/Month 11 (D2I): ◦ Cystatin C ◦ Retinol Binding Protein (RBP) ◦ Beta-2-Microglobulin (B2M)
Covariates
• Baseline Value (continuous) • Gender at Birth (male, female) • Baseline BMI(<30 kg/m2, >=30 kg/m2) • Age (continuous) • Race (White, Black/African American, Other) • Hypertension (Yes vs no) • Diabetes (Yes vs no) *Note:* *Hypertension is defined as having a medical history of hypertension or use of medication treating hypertension (current and past).* *Diabetes is defined as having a medical history of Diabetes or use of medication treating Diabetes (current and past) or fasting glucose at ≥ 126 mg/dL with HbA1c > 6.5% at Day 1.*
Data Handling
• OC (Observed Case) dataset will be used.
Model Specification
• Same as in Section 8.4.1
Model Checking & Diagnostics
• Same as in Section 8.4.1
Model Results Presentation
• Same as in Section 8.4.1
Sensitivity Analyses
• Not applicable
Subgroup Analyses
• Not applicable

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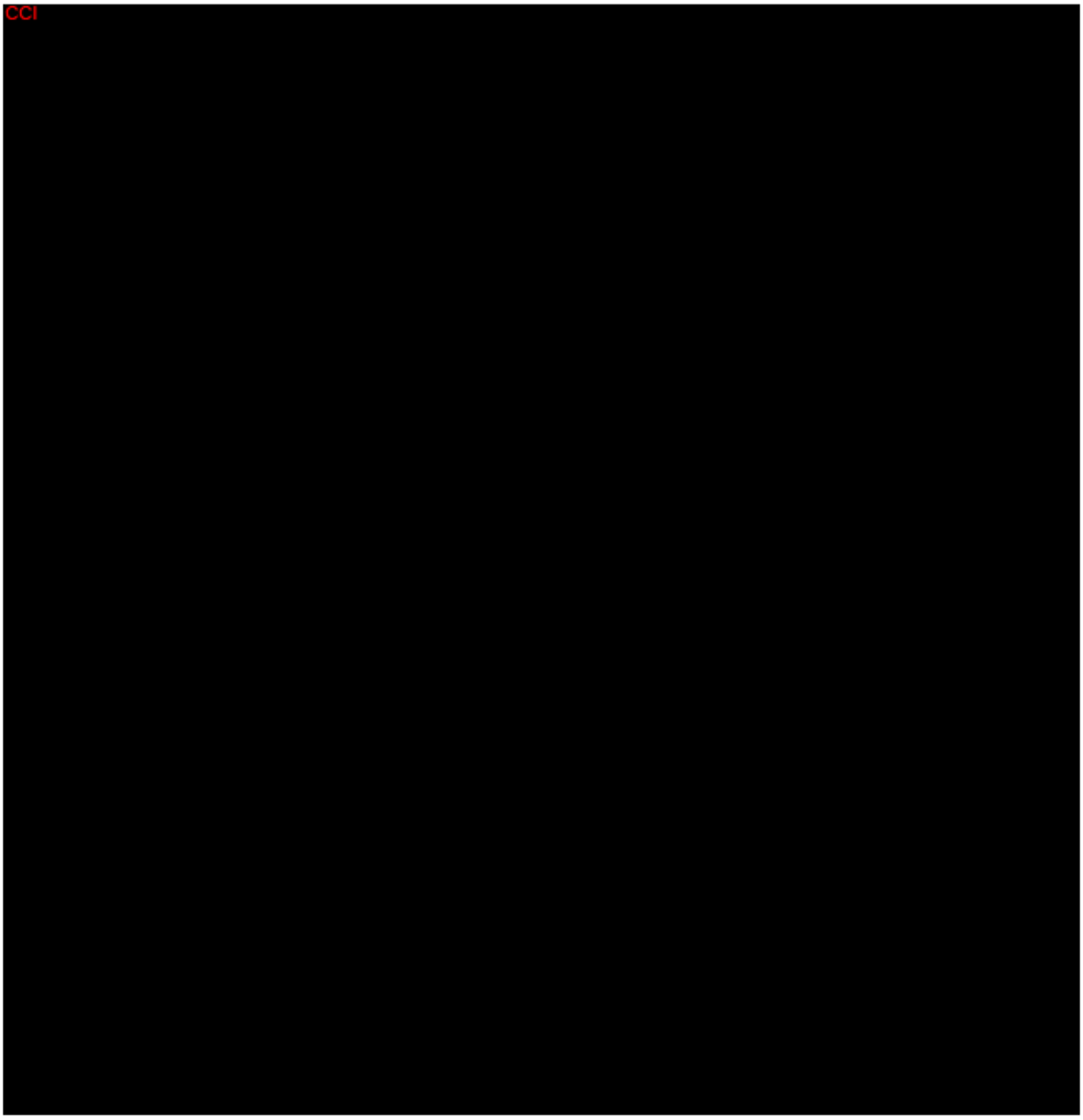

8.5. Other Safety Analyses

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 15: List of Data Displays.

8.5.1. ECG

ECG Values of Potential Clinical Interest are defined as a QTc of > 500 msec or increase from baseline in QTc ≥ 60 msec.

8.5.2. Metabolic Syndrome

Diagnosis of Metabolic Syndrome is defined as follows per joint interim statement of the International Diabetes Federation Task Force on Epidemiology and Prevention; National Heart, Lung, and Blood Institute; American Heart Association; World Heart Federation; International Atherosclerosis Society; and International Association for the Study of Obesity. Three abnormal findings out of the five risk factors would qualify a person for the metabolic syndrome(waist circumference, triglycerides, HDL, BP and fasting glucose) at each planned time point. See Section 16.6.4 for cutoff details. Percent of subjects diagnosed with metabolic syndrome will be produced. Patient profile as well as listing of clinical diagnosis factors over time may also be provided for those who are diagnosed with metabolic syndrome.

Statistical Analyses
Endpoints
• Proportion of subjects with metabolic syndrome at Month 6 (OLI and BIK)/Month 5 (D2I) and at Month 12 (OLI and BIK)/Month 11 (D2I)
Covariates
• Baseline CD4+ cell count (continuous) • Gender at Birth (male, female) • Baseline BMI(<30 kg/m^2, >=30 kg/m^2) • Age (35-<50, >=50, <35 years) • Race (White, Black/African American, Other) • Smoking Status (Never, Current, Former) • Hypertension (Yes vs no) • Baseline Triglyceride (High vs. Normal) • Baseline HDL (Low, High vs Normal) • Baseline HOMA-IR (2 to <3, 3 to <4, >=4 vs <2) Note: Hypertension is defined as having a medical history of hypertension or use of medication treating hypertension (current and past)
Data Handling
• OC (Observed Case) dataset will be used.
Model Specification
• A logistic regression model will be performed on the proportion of subjects with metabolic syndrome at Month 6(OLI and BIK)/5(D2I) and at Month 12(OLI and BIK)/11(D2I) adjusting for the covariates as above.
Model Checking & Diagnostics
• Upon delivery of data, an assessment regarding the amount of missing data will be made. If the amount of missing outcome data considered as a result of other impacts such as COVID-19 is substantial, the logistic regression analysis may not be performed. • If the percent of subjects are below 5% of the total number of subjects (observed data), or if complete or quasi-complete separation is observed in the data, then the analysis may not be performed.

Statistical Analyses
Model Results Presentation
• Odds ratios, confidence intervals and p-values will be presented for all covariates specified in the model.
Sensitivity Analyses
• Not applicable
Subgroup Analyses
• Not applicable

8.5.3. Anthropometric profile

Descriptive summaries will be provided for the following parameters to evaluate the metabolic profile of subjects:

- Weight, Height and BMI
- Waist circumference
- Hip circumference
- CCI [redacted]
- CCI [redacted]
- Tanita scale parameters (total body fat percent, total body water percent, muscle mass, and bone mineral mass)

Subjects with cosmetic procedures of the torso/thighs (exclude face/neck) including but not limited to liposuction/liposculpture/implants will be excluded from the above summary statistics at Month 12 (OLI and BIK)/Month 11 (D2I).

Data collected after initiation of lipid-modifying agents on treatment will be considered non-evaluable for anthropometric profile summaries (while on-treatment strategy).

8.5.4. HOMA-Insulin Resistance

HOMA-Insulin Resistance analysis will only be performed when all expected data through Month 12 (OLI and BIK)/Month 11 (D2I) has been received from the laboratory. Statistical estimates for each planned visit will be provided in the Month 12 primary analysis using the MMRM model as describe in the below sections unless otherwise noted. The details of the planned displays are in Appendix 15: List of Data Displays.

Statistical Analyses
Endpoints
• Change from baseline in HOMA-IR at Month 6 (OLI and BIK)/Month 5 (D2I) and at Month 12 (OLI and BIK)/Month 11 (D2I) *Note: the following subjects will be excluded from the statistical analysis:* ◦ *diabetic or have taken an anti-diabetic medication up to screening* ◦ *fasting glucose >126mg/dl and HbA1C >6.5% at Day 1* ◦ *have had a cosmetic procedure including liposuction/liposculpture of the thighs, buttocks, hips and/or abdomen*
Covariates

Statistical Analyses
• Baseline Value (continuous) • Gender at Birth (male, female) • Baseline BMI(<30 kg/m^2, >=30 kg/m^2) • Age (Continuous) • Race (White, Black/African American, Other) • Smoking Status (Never, Current, Former) • Hypertension (Yes vs no) Note: Hypertension is defined as having a medical history of hypertension or use of medication treating hypertension (current and past)
Data Handling
• OC (Observed Case) dataset will be used.
Model Specification
• Same as in Section 8.4.1
Model Checking & Diagnostics
• Same as in Section 8.4.1
Model Results Presentation
• Same as in Section 8.4.1
Sensitivity Analyses
• Logistic regression models will be performed on the proportion of subjects with HOMA-IR >=2, >=3 or >=4 at Month 12(OLI and BIK)/11(D2I) adjusting for the same covariates as specified in the MMRM analysis (without visit or interaction terms and without log transformation for the baseline value). Odds ratios, confidence intervals and p-values will be presented for all covariates specified in the model. • Upon delivery of data, an assessment regarding the amount of missing data will be made. If the amount of missing HOMA-IR outcome data considered as a result of other impacts such as COVID-19 is substantial, the logistic regression analysis may not be performed. • If the percent of subjects above any of the cutoffs are below 5% of the total number of subjects (observed data), or if complete or quasi-complete separation is observed in the data, then the analysis may not be performed.
Subgroup Analyses
• Not applicable

9. POPULATION PHARMACOKINETIC (POPPK) ANALYSES

Not applicable.

10. PHARMACOKINETIC ANALYSES

PK data collected for pregnant participants and at withdrawal visits for all subjects will be listed given data availability. Other PK samples are put to storage and there is no planned PK analysis at the time of the interim or the primary analysis. Future amendment will be made if pharmacokinetic data are to be explored further in the future.

11. PHARMACODYNAMIC (AND / OR BIOMARKER) ANALYSES

Not applicable.

12. PHARMACOKINETIC / PHARMACODYNAMIC ANALYSES

There is no plan for PK/PD analysis for the interim or the Month 12 primary analysis. Analysis details will be provided in future amendments if necessary.

13. HEALTH OUTCOMES ANALYSIS

13.1. Endpoint/Variables

- Absolute values and Change from baseline in total “treatment satisfaction” score, and individual item scores of the HIV Treatment Satisfaction Status Questionnaire (HIVTSQs) at Month 12 (OLI and BIK)/Month 11 (D2I), and at Month 6(OLI and BIK)/Month 5(D2I).

- Change in treatment satisfaction using the HIV Treatment Satisfaction Change (HIVTSQc) questionnaire at Month 12 (OLI and BIK)/Month 11 (D2I)(or withdrawal).

- Preference for CAB LA + RPV LA every 2 months compared to an oral BIK single tablet regimen as well as reasons for preference at Month 12 (OLI)/Month 11 (D2I).

- Change from Month 2(OLI)/Month 1(D2I) in Dimension scores (e.g., “Bother of ISRs”, “Leg movement”, “Sleep”, and “Acceptance of ISRs”) and in individual item

scores assessing pain during injection, anxiety before and after injection, willingness to be injected in the future and overall satisfaction with mode of administration over time using the Perception of injection questionnaire (PIN) at Month 12 (OLI and BIK)/Month 11 (D2I), and at Month 6(OLI and BIK)/Month 5(D2I).

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13.2. Summary Measure

Mean treatment difference (Q2M – BIK) in change from day 1 (baseline) at visits of interest for HIVTSQs and HIVTSQc.

Mean change at visits of interest for Change from Month 2(OLI)/Month 1 (D2I) in PIN Dimension and individual item scores.

13.3. Population of Interest

The primary health outcomes analyses will be based on the Intent-to-Treat Exposed population, unless otherwise specified. CCI CCI Note in the Month 12 analysis, mITT-E will be used in summary tables.

13.4. Strategy for Intercurrent (Post-Randomization) Events

If a participant discontinues treatment prior to the timepoint of interest such that there is no evaluable on-treatment assessment for the timepoint of interest, the data will not be computed or imputed. Assessment window slotting may be implemented for unscheduled and withdrawal visits per Section 16.3.4.

13.5. Statistical Analyses / Methods

Endpoints	Absolute							Change from Maintenance Baseline						
	Stats Analysis			Summary		Individual		Stats Analysis			Summary		Individual	
	T	F	L	T	F	F	L	T	F	L	T	F	F	L
Treatment Satisfaction Score (HIVTSQs) at Day 1, Month 6(OLI and BIK)/Month 5(D2I), Month 12 (OLI and BIK)/Month 11 (D2I)														
Individual Item Scores by visit				Y				Y[3]			Y			
Total Treatment Satisfaction Score				Y				Y			Y			
Treatment Satisfaction Score Change (HIVTSQc) at Day 1, Month 12 (OLI and BIK)/Month 11(D2I)														
Individual Item Scores				Y										
Treatment Satisfaction Score Change	Y			Y										
Treatment Preference for CAB LA + RPV LA every 2 months compared to an oral BIK single tablet regimen as well as reasons for preference														
Treatment: Every 2 Months vs Daily Oral BIK				Y										
Reasons for Preference				Y										
Perception of Injection (PIN) at Month 2(OLI and BIK)/Month 1(D2I), Month 6(OLI and BIK)/Month 5(D2I), Month 12 (OLI and BIK)/Month 11 (D2I) – Q2M only														
Individual Item Scores (Anxiety Before, Pain, Satisfaction, Anxiety After, Willingness)				Y							Y[2]			
Dimension scores (e.g., "Bother of ISRs", "Leg movement", "Sleep", and "Acceptance of ISRs")	Y[1]			Y							Y[2]			
Individual Questionnaire Scores (21 items)				Y										

CCI [redacted]

Endpoints	Absolute							Change from Maintenance Baseline						
	Stats Analysis			Summary		Individual		Stats Analysis			Summary		Individual	
	T	F	L	T	F	F	L	T	F	L	T	F	F	L
CCI														

NOTES:

Table 1 T = Table, F = Figure, L = Listings, Y = Display generated.

Table 2 Stats Analysis = Represents TFL related to any formal statistical analyses (i.e. modelling) conducted.

Table 3 Summary = Represents TFL related to any summaries (i.e. descriptive statistics) of the observed raw data.

Table 4 Individual = Represents FL related to any displays of individual participant observed raw data.

1. Statistical analysis (i.e. p-value) produced only for the acceptance score comparing to Month 2(OLI)/Month 1(D2I).
2. Change versus Month 2(OLI)/Month 1(D2I) for PIN.
3. Individual items 5 (convenient), 6 (flexible) and 10 (continue).

13.5.1. Statistical Methodology Specification

Details of the planned displays are provided in Appendix 15: List of Data Displays and will be based on GSK Data Standards and statistical principles.

Unless otherwise specified, endpoints/variables defined in Section 13.1 will be summarised using descriptive statistics and graphically presented (where appropriate). Observed data will be used for summaries and statistical analysis unless otherwise noted.

13.5.1.1. HIVTSQs

Statistical Analyses
HIVTSQS
Endpoints
Change from Maintenance Baseline (Day 1) at Month 6(OLI and BIK)/Month 5(D2I) and at Month 12 (OLI and BIK)/Month 11 (D2I) in: • HIVTSQs total treatment satisfaction score • Individual HIVTSQs items 5 (convenience), 6 (flexible), 10 (continue)
Covariates
Baseline score(continuous) Gender at Birth (male, female)

Statistical Analyses
Baseline BMI(<30 kg/m^2, >=30 kg/m^2) Age (<50, >=50 Years) Race (white, non-white)
Model Specification
• Month 6(OLI and BIK)/Month 5(D2I) Analysis: ANCOVA (analysis of covariance) model will be used for Maintenance Phase data including treatment group plus above covariates. • Month 12 (OLI and BIK)/Month 11 (D2I) Analysis: MMRM (Mixed Model Repeated Measures) will be used including treatment group plus above covariates. No assumptions will be made about the correlations between subject readings (i.e. the correlation matrix for within-subject errors is unstructured): • MMRM (Mix Model Repeated Measures) model with the observed margins (OM) option within PROC MIXED in SAS will be used including treatment group plus the above covariates, with visit as the repeated factor. • The Kenward and Roger method for approximating the denominator degrees of freedom and correcting for bias in the estimated variance-covariance of the fixed effects will be used. • No assumptions about the correlations between a subject's value will be made (the correlation matrix for within-subject errors will be unstructured). This will be estimated by treatment group by specifying "type=UN" and "group=treatment" options in the SAS MMRM models. • In the event that this model fails to converge, alternative correlation structures may be considered such as CSH or CS. Akaike's Information Criteria (AIC) will be used to assist with the selection of covariance structure if needed. • The repeated measures analysis will assume that the treatment difference can vary between visits (i.e. a treatment*visit interaction will be included in the model) . Estimates and 95% confidence intervals will be produced for each visit.
Dataset
• OC (Observed Case) dataset (with data slotting for the withdrawal/unscheduled visits) will be used. see Section 16.3.4 for details. No additional imputations will be used.
Model Results Presentation
• Adjusted means for each treatment group with 95% CI • Adjusted treatment difference (Q2M-BIK), 95% CI and the associated p-value for difference • Interaction between treatment and the baseline score

13.5.1.2. HIVTSQc

Statistical Analyses
HIVTSQc
Endpoint
• Treatment Satisfaction Score (Change) at Month 12 (OLI and BIK)/Month 11 (D2I)
Covariates
Gender at Birth (male, female) Baseline BMI(<30 kg/m², >=30 kg/m²) Age (<50, >=50 Years) Race (white, non-white)
Model Specification
• An analysis of variance (ANOVA) model will be used with above covariates • Adjusted point estimates will be derived as LSMEANS using the observed margins (OM) option within PROC MIXED in SAS. • Interactions between treatment and each of the covariates will not be assessed unless CCI [redacted] the primary endpoint highlights significant interactions. In this situation, the interaction(s) of interest may be assessed and, if necessary, results will be reported in the clinical study report. If interactions are found to be significant (p<0.10), results may be presented separately by subgroup.
Dataset
• OC (Observed Case) dataset (with data slotting for the withdrawal/unscheduled visits) will be used. see Section 16.3.4 for details. No additional imputations will be used.
Model Results Presentation
• Adjusted means for each treatment group with 95% CI • Adjusted treatment difference (Q2M-BIK), 95% CI and the associated p-value for difference

13.5.1.3. PIN

Statistical Analyses
PIN (Q2M arm only)
Endpoints
Change from Month 2(OLI)/Month 1(D2I) in the PIN acceptance score at: • Month 12(OLI)/Month 11(D2I) • Month 6(OLI)/Month 5(D2I)
Statistical Test
• The Wilcoxon Signed-Rank Test will be used to evaluable whether the change from Month 2/Month 1 to Month 6(OLI)/Month 5(D2I), and to Month 12(OLI)/Month 11(D2I), respectively, is statistically different from zero based on a two-sided significance level of 0.05. Separate tests will be performed for the change at each time point.

Statistical Analyses
Dataset
• OC (Observed Case) dataset (with data slotting for the withdrawal/unscheduled visits) will be used. see Section 16.3.4 for details. No additional imputations will be used.
Results Presentation
• Summary statistics at each analysis timepoint and p-value for each comparison.

14. VIROLOGY

Given data availability, the virology analyses will mainly use genotype and phenotype data based on plasma sample for CVF population, unless otherwise specified. Summary tables (if applicable) will be based on the mCVF population. Listings will include all CVFs in this study. Additional analyses for HIV-1 resistance may be carried out on peripheral blood mononuclear (PBMC) samples and/or on stored blood samples from relevant time points.

If pre-treatment genotypic/phenotypic results are available from both the central laboratory and Monogram Biosciences, then Monogram assays will take precedence.

Table 5 provides an overview of the planed analyses. Further details of the planned displays are provided in Appendix 15: List of Data Displays and will be based on GSK Data Standards and statistical principles.

Table 5 Overview of Planned Virology Analysis

Endpoint	Absolute			
	Summary		Individual	
	T	F	F	L
Genotypic resistance at time of CVF[1]				
Prevalence of Resistance Mutations	Y [2]			Y
Prevalence of Genotypic Susceptibility	Y			
Phenotypic resistance at time of CVF[1]				
Prevalence of Phenotype	Y [3]			Y
Fold Change to CAB, RPV and BIC	Y			Y[4]
IN, PR/RT Replication Capacity [5]				Y
Other				
Viral load, Genotypic and Phenotypic data for Participants with genotype and/or phenotype data for CVF and non-CVF participants				Y[4]
Net Assessment	Y			

NOTES:

- T = Table, F = Figure, L = Listing, Y = Yes display generated.

- Summary = Represents TFL related to any summaries (i.e. descriptive statistics) of the observed raw data.
- Individual = Represents FL related to any displays of individual participant observed raw data.
- If less than 5 CVFs are observed during the maintenance phase in the mITT-E population, summary tables may not be produced. All data will be provided in listings in this case.

1. CVF defined by two consecutive plasma HIV-1 RNA levels ≥200 c/mL after prior suppression to <200 c/mL. The first of these two consecutive visits is defined as 'suspected', and the 2nd is defined as "confirmed". Sample used for resistance testing is taken at the suspected visit, and only tested once virologic failure at a subsequent visit is confirmed. If the test fails with the sample at the suspected visit, it will be reported as 'no data'. CCI [redacted]
2. Number and percentage of participants with INI resistance mutations or major resistance mutations in the classes of NNRTI, NRTI, PI, respectively, as defined in Section 16.6.7.
3. Separate outputs by phenotypic susceptibility and by number of drugs to which participants are phenotypic resistant, partially sensitive or sensitive.
4. Fold change to CAB,RPV and BIC will be included in the listing for viral load, genotypic and phenotypic data for participants with genotype and/or phenotype data for CVF and non-CVF participants.
5. IN: integrase; PR: Protease; RT: reverse transcriptase

15. REFERENCES

Alberti KGMM et al. Harmonizing the metabolic syndrome: a joint interim statement of the International Diabetes Federation Task Force on Epidemiology and Prevention; National Heart, Lung, and Blood Institute; American Heart Association; World Heart Federation; International Atherosclerosis Society; and International Association for the Study of Obesity. Circulation. 2009;120:1640 –1645.

Chan, I. S. F. and Zhang, Z. (1999), "Test-Based Exact Confidence Intervals for the Difference of Two Binomial Proportions," Biometrics, 55, 1202–1209.

Chevat C, Viala-Danten M, Dias-Barbosa C, Nguyen VH. Development and psychometric validation of a self-administered questionnaire assessing the acceptance of influenza vaccination: the Vaccinees' Perception of Injection questionnaire. Health Qual Life Outcomes. 2008 mar 4; 7:21

D'Agostino RB, Vasan RS, Pencina MJ, et al. General Cardiovascular Risk Profile for Use in Primary Care (The Framingham Heart Study). Circulation 2008; 117: 743-753.

EMA/CHMP/539146/2013, Guideline on the investigation of subgroups in 4 confirmatory clinical trials, 31 January 2019

FDA Guidance for Industry: Human Immunodeficiency Virus-1 Infection: Developing Antiretroviral Drugs for Treatment, Nov 2015

Fleiss J.L. Statistical Methods for Rates and Proportions. 2nd ed. New York:John Wiley; 1981.

Grundy S.M., et al. Executive summary of the third report of the National Cholesterol Education Program (NCEP) Expert Panel on Detection, Evaluation and Treatment of High Blood Cholesterol in Adults (Adult Treatment Panel III). JAMA. 2001;285 (19):2486-2497.

HIVTSQ user guidelines, Health Psychology Research Unit, Royal Holloway, University of London, 2016

Holmes WC, HIV/AIDS-Targeted Quality of Life Instrument 1999.

Kalbfleisch J.D., Prentice R.L. *The Statistical Analysis of Failure Time Data.* 1st ed. New York: John Wiley & Sons; 1980.

Levey AI, Christopher HS, Hocine T, John HE, Harold IF, Tom G, et al. Estimating Glomerular Filtration Rate from Serum Creatinine and Cystatin C. N Engl J Med 2012, 367: 20-29.

Lui K.J., Kelly C. A Revisit on Tests for Homogeneity of the Risk Difference, Biometrics, 2000;56:309-315.

Mary E. Nilsson, Shailaja Suryawanshi, Cristiana Gassmann-Mayer, Sarah, Dubrava, Paul McSorley, and Kaihong Jiang. Columbia–Suicide Severity Rating Scale, Scoring and Data Analysis Guide, 2013

Nilsson ME, Suryawanshi S, Gassmann-Mayer C et al, Columbia–Suicide Severity Rating Scale, Scoring and Data Analysis Guide, 2013.

Posner K, Oquendo MA, Gould M, Stanley B, Davies M. Columbia Classification Algorithm of Suicide Assessment (C-CASA): classification of suicidal events in the FDA's pediatric suicidal risk analysis of antidepressants. *Am J Psychiatry*. 2007;164:1035–1043.

Ralph B. D'Agostino, Ramachandran S. Vasan, Michael J. Pencina, Philip A. Wolf, Mark Cobain, Joseph M. Massaro, William B. Kannel. 2008. General Cardiovascular Risk Profile for Use in Primary Care (The Framingham Heart Study). Circulation 2008; 117: 743-753.

Sato T. On the variance estimator for the Mantel-Haenszel risk difference. *Biometrics.* 1989;42:311-323.

Wensing AM et al, 2019 Update of the Drug Resistance Mutations in HIV-1, Volume 27 Issue 3 July/August 2019.

16. APPENDICES

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

16.1.1. Exclusions from Per Protocol Population

Important protocol deviations leading to exclusion from the Per Protocol population are those deviations which may

- directly impact the efficacy endpoint of HIV-1 RNA; or
- lead to permanent discontinuation of IP/withdrawal and hence indirectly impact the efficacy endpoint by causing data to be missing.

The following criteria define the protocol deviations which, if they occur prior to an analysis timepoint of interest (e.g. Month 12 or Month 6), will lead to exclusion of a participant from the Per-Protocol population for that analysis. Potential protocol deviations leading to exclusion from PP population will be reviewed by the study team to confirm that they meet these criteria. A final review will occur before the clinical database has been frozen for analysis.

A participant meeting any of the following criteria will be excluded from the Per Protocol population **based on case-by-case clinical determination**. Note exclusion category # 2 below will only be applied in the Month 12 analysis. Other categories will be applied in both Month 6 and Month 12 analysis.

Number	Exclusion Description
01	Participant deviates from inclusion or exclusion criteria that may significantly affect exposure, response to therapy or participant safety or that are fundamentally inconsistent with the intended study population, as recorded in the Protocol Deviation form in the eCRF based on study team review (where indicated in the PDMP as case-by-case determination).
02*	For Month 12 analysis only: Participant has non-compliance with IP (including IM dosing errors) or took/received incorrect IP (i.e., other than the one to which they were randomized) up to an analysis timepoint of interest, meeting the following conditions during the Maintenance Phase: 1. Two or more injection intervals affected by over dosage deviations, for example • Extra injection or excessive volume administered • Length of time between injections less than 21 days between the first and second injections (between M1 and M2 for OLI; between Day 1 and M1 for D2I), or less than 52 days for all subsequent dosing intervals, excluding split doses up to the analysis visit of interest (M12 for OLI /M11 for D2I) * 21 = 28 – 7; 52 = 28 + 31 – 7 (smallest possible dosing interval allowed – 7 days) 2. At least 10% of total time on-treatment with under dosing deviations in the Maintenance Phase up to the analysis visit of interest (i.e. Month 12 for OLI and BIK/Month11for D2I), where the % of non-compliance is calculated as: *(total number of non-compliant dosing days / total number of intended exposure days) * 100%*

Number	Exclusion Description
	Where : • *Total number of intended exposure days* = date of the last analysis timepoint snapshot viral load *(*up to Injection Study Day 372 for OLI subjects, up to Study Day 372 for D2I subjects and up to Study Day 378 for BIK subjects) – Start Date of Study Treatment + 1 • Total number of non-compliant dosing days up to the analysis timepoint visit (or date of IP discontinuation/ withdrawal, whichever is earlier), is derived as follows: **BIK Arm:** o Duration of interruptions in BIK arm for reasons other than treatment-related adverse events/laboratory abnormalities (based on Exposure eCRF forms) **Q2M Arm:** o Length of time (in days) in excess until next injection from date of dosage/administration deviation potentially resulting in under dosage. Examples include: - less than 3 ml administered - early stop of oral bridging prior to the next planned injection o Length of time (in days) in excess beyond 31 days between the first and second injections and beyond 69 days for all subsequent dosing intervals. * 69 = 31+ 31 + 7 (largest possible dosing interval allowed + 7 days) - For those with oral bridging (OB), length of time (in days) is calculated between the start of oral bridging and the *preceding* injection o Interrupted days in oral study treatment (oral lead-in or oral bridging) if the oral dose has been interrupted for 3 or more consecutive days and the primary interruption reason is not adverse event or laboratory abnormality (based on the eCRF Exposure forms). 3 days will be assumed if such interrupted days are not available in the database.
03	Prohibited medications: receiving ART medication other than that prescribed/allowed by the study (excluding permanent changes in ART regimen; such cases will be retained as 'HIV1-RNA ≥ 50 c/mL' in the per protocol snapshot analysis) or receiving prohibited concomitant medication that would impact exposure or response to therapy with duration and route of administration taken into consideration, as recorded in the Protocol Deviation form in the eCRF based on study team review (where indicated in the PDMP as case-by-case determination)
04	Permanent discontinuation of IP/withdrawal due to a reason of "Protocol Deviation" (as recorded in the eCRF Conclusion form).
05	Other important protocol deviations that exclude participant from Per Protocol population as recorded in the Protocol Deviation form in the eCRF based on study team review (where indicated in the PDMP as case-by-case determination).
* Note: Category 02 is only applicable to the Month 12 analysis.	

16.2. Appendix 2: Schedule of Activities

Time and Events Table for CAB LA + RPV LA Oral Lead In (OLI) Participants:

Procedure	Screening Visit [a]	Maintenance Phase							Extension Phase	Withdrawal Assessments[y]	Long-Term Follow-up [z]
		Day 1[b]	Month								
			1[c]	2	4	6	8	10	12	Q2M after Month 12		
Written Informed Consent	X											
Eligibility Verification (Inclusion/ Exclusion Criteria)	X	X[d]										
Randomization		X										
Demography	X											
Medical History[e]	X											
Cardiovascular risk assessment[e]	X	X							X		X	
Medication History/ Prior ART history	X											
Syphilis serology + reflex Rapid Plasma Reagin (RPR)	X	X										
Symptom Directed Physical Exam and Medical Assessment[f]	X	X	X	X	X	X	X	X	X	X	X	X
Weight, Height and BMI[g]		X		X	X	X			X		X	
Waist Circumference		X		X	X	X			X		X	
Hip Circumference		X		X	X	X			X		X	
Vital Signs (BP, HR, Temperature)[h]	X	X		X	X	X			X		X	
CCI												
12-lead ECG[i] (triplicate at Day 1 pre-dose)	X	X	X						X		X	
CDC HIV-1 stage[ff]	X	X										
HIV Associated Conditions		X	X	X	X	X	X	X	X	X	X	X
AEs, SAEs, Concomitant Medications	X[j]	X	X	X	X	X	X	X	X	X	X	X
ISR Assessment for IM injection			X	X	X	X	X	X	X	X	X	X

Procedure	Screening Visit [a]	Maintenance Phase								Extension Phase	Withdrawal Assessments[y]	Long-Term Follow-up [z]
		Day 1[b]	Month									
			1[c]	2	4	6	8	10	12	Q2M after Month 12		
Columbia Suicide Severity Rating Scale (eC-SSRS)[x]	X	X		X		X			X		X	
Clinical chemistry and Hematology	X	X	X	X	X	X	X	X	X	X	X	X
Pregnancy Testing[l]	S	U	U	U	U	U	U	U	U	U	S	U
HIV-1 RNA and sample for storage (S)[m]	X	X	X	X	X	X	X	X	X	X	X	X
HIV-1 RNA low copy sample		X							X			
CD4+ cell count	X	X	X	X	X	X	X	X	X	X	X	X
CD8+ cell count		X				X			X		X	
Urinalysis[n]		X	X			X			X		X	
Fasting Labs Glucose, Cholesterol (Total, HDL and LDL) and Triglycerides[o]		X				X			X		X[p]	
Hepatitis B (HBsAg), Anti-HBc, and Anti-HBsAG, Hepatitis C (anti-HCV Ab)	X											
PT/PTT/INR	X	X										
Whole Blood (Virology)		X				X			X		X	
[redacted]												
PBMCs [q]		X				X			X		X	
Insulin, HbA1c and renal, and bone biomarker analytes (blood urine)[r]		X				X			X		X[x]	
[redacted]												
Genetics sample [t]		X										
PK sampling [u] (S)=Storage only			S	S	S	S	S	S	S		X	S
Oral CAB and Oral RPV Dispensation [v]		X										

Procedure	Screening Visit [a]	Maintenance Phase							Extension Phase	Withdrawal Assessments[y]	Long-Term Follow-up [z]
		Day 1[b]	Month								
			1[c]	2	4	6	8	10	12	Q2M after Month 12		
IP accountability (Pill Counts)			X									
IM treatment administration [w]			X	X	X	X	X	X	X	X		
HIV TSQs[cc]		X				X			X		X[dd]	
HIV TSQc[cc]									X		X[dd]	
CCI												
Preference[cc]									X		X[dd]	
PIN[cc]				X		X			X		X[dd]	
CCI												
History of Cosmetic procedures[gg]									X		X	

Time and Events Table for CAB LA + RPV LA Direct to Injection (D2I) Participants:

Procedure	Screening Visit [a]	Maintenance Phase							Extension Phase	Withdrawal Assessments[y]	Long-Term Follow-up [z]
		Day 1[b]	Month								
			1[c]	3	5	7	9	11	Q2M after Month 11		
Written Informed Consent	X										
Eligibility Verification (Inclusion/ Exclusion Criteria)	X	X[d]									
Randomization		X									
Demography	X										
Medical History[e]	X										
Cardiovascular risk assessment[e]	X	X						X			
Medication History/ Prior ART history	X										
Syphilis serology + reflex Rapid Plasma Reagin (RPR)	X	X									
Symptom Directed Physical Exam and Medical Assessment[f]	X	X	X	X	X	X	X	X	X	X	X
Weight, Height and BMI[g]		X	X	X	X			X		X	
Waist Circumference		X	X	X	X			X		X	
Hip Circumference		X	X	X	X			X		X	
Vital Signs (BP, HR, Temperature)[h]	X	X	X	X	X			X		X	
[redacted]											
12-lead ECG[i] (triplicate at Day 1 pre-dose)	X	X						X		X	
CDC HIV-1 stage[ff]	X	X									
HIV Associated Conditions		X	X	X	X	X	X	X	X	X	X
AEs, SAEs, Concomitant Medications	X[j]	X	X	X	X	X	X	X	X	X	X
ISR Assessment for IM injection		X	X	X	X	X	X	X	X	X	X
Columbia Suicide Severity Rating Scale (eC-SSRS)[k]	X	X	X		X			X		X	

Procedure	Screening Visit [a]	Maintenance Phase							Extension Phase	Withdrawal Assessments[y]	Long-Term Follow-up [z]
		Day 1[b]	Month								
			1[c]	3	5	7	9	11	Q2M after Month 11		
Clinical chemistry and Hematology	X	X	X	X	X	X	X	X	X	X	X
Pregnancy Testing[l]	S	U	U	U	U	U	U	U	U	S	U
HIV-1 RNA and sample for storage (S)[m]	X	X	X	X	X	X	X	X	X	X	X
HIV-1 RNA low copy sample		X						X			
CD4+ cell count	X	X	X	X	X	X	X	X	X	X	X
CD8+ cell count		X			X			X		X	
Urinalysis[n]		X	X		X			X		X	
Fasting Labs: Glucose, Cholesterol (Total, HDL and LDL) and Triglycerides[o]		X			X			X		X[p]	
Hepatitis B (HBsAg), Anti-HBc, and Anti-HBsAG, Hepatitis C (anti-HCV Ab)	X										
PT/PTT/INR	X	X									
Whole Blood (Virology)		X			X			X		X	
CCI											
PBMCs [q]		X			X			X		X	
Insulin, HbA1c and renal, and bone biomarker analytes (blood urine)[r]		X			X			X		X[x]	
CCI											
Genetics sample [t]		X									
PK sampling [u] (S)=Storage only			S	S	S	S	S	S		X	S
IM treatment administration		X	X	X	X	X	X	X	X		
HIV TSQs[cc]		X			X			X		X[dd]	
HIV TSQc[cc]								X		X[dd]	
CCI											
Preference[cc]								X		X[dd]	

Procedure	Screening Visit [a]	Maintenance Phase						Extension Phase	Withdrawal Assessments[y]	Long-Term Follow-up [z]
		Day 1[b]	Month							
			1[c]	3	5	7	9	11	Q2M after Month 11	
PIN[cc]			X		X			X		X[dd]	
CCI											
History of Cosmetic procedures[gg]								X		X	

Time and Events Table for BIK Participants:

Procedure	Screening Visit [a]	Maintenance Phase							Withdrawal Assessments[y]
		Day 1[b]	Month						
			2	4	6	8	10	12[bb]	
Written Informed Consent	X								
Eligibility Verification (Inclusion/ Exclusion Criteria)	X	X[d]							
Randomization		X							
Demography	X								
Medical History[e]	X								
Cardiovascular risk assessment[e]	X	X						X	
Medication History/ Prior ART history	X								
Syphilis serology + reflex Rapid Plasma Reagin (RPR)	X	X							
Symptom Directed Physical Exam and Medical Assessment[f]	X	X	X	X	X	X	X	X	X
Weight, Height and BMI[g]		X	X	X	X			X	X
Waist Circumference		X	X	X	X			X	X
Hip Circumference		X	X	X	X			X	X
Vital Signs (BP, HR, Temperature)[h]	X	X	X	X	X			X	X
CCI									
12-lead ECG[i] (triplicate at Day 1 pre-dose)	X	X						X	X
CDC HIV-1 stage[ff]	X	X							
HIV Associated Conditions		X	X	X	X	X	X	X	X
AEs, SAEs, Concomitant Medications	X[j]	X	X	X	X	X	X	X	X
Columbia Suicide Severity Rating Scale (eC-SSRS) [k]	X	X	X		X			X	X
Clinical chemistry and Hematology	X	X	X	X	X	X	X	X	X
Pregnancy Testing[l]	S	U	U	U	U	U	U	U	S
HIV-1 RNA and sample for storage (S)[m]	X	X	X	X	X	X	X	X	X
HIV-1 RNA low copy sample		X						X	

Procedure	Screening Visit [a]	Maintenance Phase							Withdrawal Assessments[y]
		Day 1[b]	Month						
			2	4	6	8	10	12[bb]	
CD4+ cell count	X	X	X	X	X	X	X	X	X
CD8+ cell count		X			X			X	X
Urinalysis[n]		X			X			X	X
Fasting Labs Glucose, Cholesterol (Total, HDL and LDL) and Triglycerides[o]		X			X			X	X[p]
Hepatitis B (HBsAg), Anti-HBc, and Anti-HBsAG, Hepatitis C (anti-HCV Ab)	X								
PT/PTT/INR	X	X							
Whole Blood (Virology)		X			X			X	X
CCI									
PBMCs [q]		X			X			X	X
Insulin, HbA1c and renal, and bone biomarker analytes (blood urine)[r]		X			X			X	X[x]
CCI									
Genetics sample [t]		X							
BIK Dispensation		X	X	X	X	X	X	X[aa]	
IP accountability (Pill Counts)			X	X	X	X	X	X	
HIV TSQs[cc]		X			X			X	X[dd]
HIV TSQc[cc]								X	X[dd]
CCI									
CCI									
History of Cosmetic procedures[gg]								X	X

Time and Events Table for BIK to Oral Lead In – Extension Phase:

Procedure	Extension Phase				Withdrawal Assessments[y]	Long-Term Follow-up [z]
	Month					
	13	14	15	Q2M After Month 15		
Eligibility Verification (Inclusion/ Exclusion Criteria)	X[d]					
Symptom Directed Physical Exam and Medical Assessment[f]	X	X	X	X	X	X
Weight, Height and BMI[g]					X	
Waist Circumference					X	
Hip Circumference					X	
Vital Signs (BP, HR, Temperature)[h]					X	
12-lead ECG[i]					X	
HIV Associated Conditions	X	X	X	X	X	X
AEs, SAEs, Concomitant Medications	X	X	X	X	X	X
ISR Assessment for IM injection		X	X	X	X	X
Clinical chemistry and Hematology	X	X	X	X	X	X
Pregnancy Testing[l]	S	U	U	U	S	U
HIV-1 RNA and sample for storage (S)[m]	X	X	X	X	X	X
CD4+ cell count		X	X	X	X	X
CD8+ cell count					X	
Urinalysis[n]		X			X	
Fasting Labs Glucose, Cholesterol (Total, HDL and LDL) and Triglycerides[o]		X			X	
Whole Blood (Virology)					X	
[redacted]						
PBMCs [q]					X	

Procedure	Extension Phase				Withdrawal Assessments[y]	Long-Term Follow-up [z]
	Month					
	13	14	15	Q2M After Month 15		
PK sampling [u] (S)=Storage only		S	S		X	S
Oral CAB and Oral RPV Dispensation [v]	X					
IP accountability (Pill Counts)	X	X				
IM treatment administration [w]		X	X	X		
CCI	[redacted]					

Time and Events Table for BIK to Direct to Injection – Extension Phase:

Procedure	Extension Phase			Withdrawal Assessments[y]	Long-Term Follow-up [z]
	Month				
	13	14	Q2M After Month 14		
Eligibility Verification (Inclusion/ Exclusion Criteria)	X[d]				
Symptom Directed Physical Exam and Medical Assessment[f]	X	X	X	X	X
Weight, Height and BMI[g]				X	
Waist Circumference				X	
Hip Circumference				X	
Vital Signs (BP, HR, Temperature)[h]				X	
12-lead ECG[i]				X	
HIV Associated Conditions	X	X	X	X	X
AEs, SAEs, Concomitant Medications	X	X	X	X	X
ISR Assessment for IM injection	X	X	X	X	X
Clinical chemistry and Hematology	X	X	X	X	X
Pregnancy Testing[l]	S	U	U	S	U
HIV-1 RNA and sample for storage (S)[m]	X	X	X	X	X
CD4+ cell count		X	X	X	X
CD8+ cell count				X	
Urinalysis[n]		X		X	
Fasting Labs Glucose, Cholesterol (Total, HDL and LDL) and Triglycerides[o]		X		X	
Whole Blood (Virology)				X	
CCI					
PBMCs [q]				X	

Procedure	Extension Phase			Withdrawal Assessments[y]	Long-Term Follow-up [z]
	Month				
	13	14	Q2M After Month 14		
PK sampling [u] (S)=Storage only		S		X	S
IP accountability (Pill Counts)	X				
IM treatment administration [w]	X	X	X		
	CCI [redacted]				

Safety Follow Up Visit: Conduct approximately 4 weeks after the last dose of IP. Required only if the participant has ongoing AEs or lab abnormalities at the last on-study visit. This visit may be conducted by telephone.

Note: BP – Blood pressure, HR – Heart Rate, BMI – Body Mass Index, HDL – High Density Lipoprotein, LDL – Low Density Lipoprotein, PT - Prothrombin Time, PTT - Partial Thromboplastin Time, INR - International normalized ratio, PBMC – peripheral blood mononuclear cell, RNA – Ribonucleic acid, HbA1c = Glycated hemoglobin, HBsAg = hepatitis B surface antigen, HCV = hepatitis C virus, HIV-1 = human immunodeficiency virus type 1.

a. Complete all Screening assessments within 35 days. Participants may begin the Maintenance Phase as soon as all Screening assessments are complete. Participants may be rescreened once and will be assigned a new participant number.
b. For participants who elect to participate in the oral lead in period, oral CAB 30 mg + RPV 25 mg will be administered and the oral lead will start on Day 1. For participants who choose to go directly into injections, the first loading dose will be administered on Day 1. Visits for participants on the BIK arm are expected to occur every 56 days as projected according to the Day 1 visit. There is a ±3 day visit window, from the projected visit date (Maintenance Phase of the study).
c. For participants who elect to participate in the oral lead in period, the first loading dose will be administered and the oral lead in will end. For participants who choose to go directly into injections, the second loading dose will be administered.
d. Confirmation of eligibility to continue the Maintenance Phase, and eligibility to enter the Extension Phase.
e. Collect full routine medical history plus (report at Baseline visit): HIV risk factors (may be collected at a later study visit), cardiovascular risk factors (assessments include smoking status and history, family history of cardiac events), recent [≤6 months] illicit drug use, intravenous drug use, gastrointestinal disease, metabolic, psychiatric, renal, bone, and neurologic disorders. At Month 11 (D2I)/12 (OLI and BIK), assessments inclusive of smoking status, alcohol use and illicit drug use since the start of the study will be administered.
f. Physical exams should be conducted as part of normal routine clinical care. Medical assessments include any decisions the study staff must make for participants management and/or care of participant.
g. Height collected at Baseline Day 1 only. Recommended procedures to measure weight, waist and hip circumference can be found in protocol Section 10.10. Weight related measurements to be collected are weight, body fat %, total body water %, muscle mass, and bone mineral mass.
h. Measure vital signs after about 5 minutes of rest in a semi-supine position.

i. A 12-lead ECG will be performed after resting in a semi-supine position for at least 5 minutes. ECGs will be performed pre-dose. ECG pre-dose will be performed in triplicate at Day 1. A 2-hour post-dose ECG will also be performed at Day 1 (D2I), Month 1 (OLI) and Month 12 (OLI)/Month 11 (D2I) for participants receiving CAB LA + RPV LA with an allowable window of ± 30 minutes.
j. Only SAEs related to study participation or to a concomitantly administered ViiV/GSK product will be collected between obtaining informed consent and administration of study drug at Day 1.
k. On Day 1, the eC-SSRS is to be administered prior to randomization. The eC-SSRS will be completed at the beginning of the visit following administration of other PROs required prior to injections. The eC-SSRS is not required during the Withdrawal visit if withdrawal occurs during the Extension Phase.
l. Women of childbearing potential only. S=serum, U=urine. Pregnancy events will be captured starting at Day 1 following initial exposure to study drug. Serum pregnancy test can substitute for urine pregnancy test if locally required but must be appropriately timed to confirm pregnancy status prior to randomization and first IM administration. If the urine test is positive, perform a serum test and do not administer injection. The frequency of pregnancy tests should be performed according to local legal requirements.
m. Month 12 (OLI and BIK) and Month 11 (D2I) HIV-1 RNA retest (within 4 weeks) for results > 50 c/mL will be captured as unscheduled visit. Plasma for storage samples will be used for possible future analyses.
n. A morning specimen is preferred. To assess biomarkers: urine albumin/creatinine ratio; urine protein/creatinine ratio; urine phosphate; beta-2-microglobulin; and retinol binding protein.
o. An overnight fast is preferred; however, a minimum of a 6-hour fast is acceptable.
p. Only collect if the Withdrawal visit occurs at Month 6 or Month 12 (OLI and BIK); Month 5 or Month 11 (D2I).
q. Whole blood/PBMC collection samples may be used for virologic analyses. PBMCs will be collected at baseline Day 1, Month 6, Month 12, or Withdrawal if prior to Month 12 (OLI and BIK). PBMCs will be collected at baseline Day 1, Month 5, Month 11, or Withdrawal if prior to Month 11 (D2I)
r. Blood sample for insulin, HbA1c, and renal and bone biomarker assessments: **Renal:** CystatinC; Beta-2-Microglobulin; Retinol Binding Protein (RBP); **Bone:** bone specific alkaline phosphatase, procollagen type 1-N-propeptide, type 1 collagen cross-linked C-telopeptide, osteocalcin, 25 hydroxy-Vitamin D.
s. Blood sample fo[redacted]
t. Informed consent for genetic research must be obtained before sample collection. Sample may be collected at any visit after signing informed consent, but preferably at the Day 1 visit.
u. **One blood sample for CAB and RPV each to be collected at each PK timepoint**. At Month 1, for participants who elected to participate in the Oral Lead in, and Month 14 for participants who were randomized to BIK and switched to CAB LA + RPV LA in the Extension Phase and will participate in the Oral Lead in, Pre dose PK samples are to be collected: PRIOR to the final oral dose of CAB + RPV. **For pregnant participants** (on CAB+RPV arm): two blood samples for CAB and one RPV sample at each PK timepoint. Refer to protocol Section 10.6.6.3.
v. Participants who elected to participate in the Oral Lead in before switching to CAB LA + RPV LA injections, will take final dose of oral lead-in regimen in the clinic at the Month 1/Month 14 visit and begin injections.
w. 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. The first injection can be performed before central lab results become available and safety parameters are reviewed.
x. Collect sample for these assessments ONLY if the Withdrawal visit occurs at Months 6 and 12 (OLI and BIK); Month 5 and 11 (D2I).
y. Refer to Section 7.1 of the protocol for additional information on performing withdrawal assessments
z. Participants receiving one or more injections with CAB LA and/or RPV LA will be assessed with clinic visits at Months 3, 6, 9 and 12 during the Long-Term Follow-Up Phase
aa. BIK dispensation (1-month supply) for participants who plan on entering into the Extension Phase. Participants who do not enter the Extension Phase or do not wish to transition to the commercial supply will not receive 1-month supply at M12.

bb. Data from visit will be used to determine participant's eligibility to enter the Extension Phase of study. If participant elects to enter the Extension Phase, determine if the participant will elect to start injections immediately or start with oral lead in.

cc. All PROs are recommended to be administered before other assessments and injections take place at each designated visit.

dd. Only collected if Withdrawal visit occurs during the Maintenance Phase.

CCI [redacted]

ff. When assessing CDC stage at Screening/Baseline, consider only the latest available CD4 T-cell count, except when the participant had an active Stage 3 event 6 months prior to Screening.

gg. At Month 11 (D2I)/ Month 12 (OLI or BIK) or withdrawal, (depending which is sooner) participants will be asked if any cosmetic procedures were performed during the conduct of the study.

16.3. Appendix 3: Assessment Windows

16.3.1. Definitions of Assessment Windows for Analyses

Unless otherwise noted, laboratory data, vital signs, ECGs, Health Outcomes assessments, 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.

In most cases the window around an assessment will include all dates from the midpoints between the target day and that of the previous and the proceeding visits. The target Study Day or target Injection Study Day for is defined in Section 16.3.2.

For parameters which are not scheduled to be assessed at a particular visit, the all-inclusive assessment windows will still be used; however, data summaries will only report scheduled visits. Assessments at unscheduled visits will be included for "any time" and "on-treatment" time points and in data listings, as well any algorithms that make use of additional data (e.g., snapshot).

Maintenance phase assessments are assigned based on the Maintenance Phase Study Day, respectively. Extension phase assessments are assigned based on the Maintenance Phase Study day for subjects continuing CAB LA + RPV LA dosing (Q2M) into the Extension Phase, and based on the Extension Phase Study Day for subjects switching from the BIK arm to CAB LA + RPV LA dosing (Switch Q2M) for the Extension phase. Long-term Follow-up phase assessments are assigned based on the LTFU study day. See Section 16.6.1 for derivation of Maintenance, Extension and LTFU Study Day.

16.3.2. Definitions of Assessment Windows for Data Other than Health Outcomes

16.3.2.1. Assessment Windows for Screening, Maintenance and Extension Phase Data – Q2M OLI Subjects

All Parameters except for where noted[d]	Analysis Window	Target Study Day	Target Injection Study Day	Analysis Timepoint 1	Analysis Timepoint 2	Notes
	Study Day ≤ 1	Study day of the earliest record		Screening	Screening	Screening
	Last available recorded value up to and including the date of first Maintenance Phase dose of IP	1		Maintenance Baseline (Day 1)	Maintenance Baseline (Day 1)	Maintenance Baseline (Day 1)
Post-dose ECG	Value taken post-dose	1		Day 1 (Post Dose)	Day 1(Post Dose)	Day 1(Post Dose)
	Injection Study Day ≤ 15 and Study Day ≥2 For those with OLI only: 2<= Study Day<= Study Day of Last Oral Dose +1	31	1	Month 1	Month 1	Injection 1
Urinalysis	Injection Study Day ≤ 42 and Study Day ≥2 For those with OLI only: 2<= Study Day<= Study Day of Last Oral Dose +1					
Post-dose ECG	Value taken post-dose Month 1					
	16 ≤ Injection Study Day ≤ 60	61	31	Month 2	Month 2	Injection 2
	61 ≤ Injection Study Day ≤ 120	121	91	Month 4	Month 3/4	Injection 3
	121 ≤ Injection Study Day ≤ 180	181	151	Month 6	Month 5/6	Injection 4
Urinalysis[a], CD8, CD4/CD8 ratio, fasting glucose and lipids[b], weight, height, BMI, Waist and Hip Circumference, Vital Signs, CCI , Insulin, HbA1c, HOMA-IR,	121 ≤ Injection Study Day ≤ 192					

All Parameters except for where noted[d]	Analysis Window	Target Study Day	Target Injection Study Day	Analysis Timepoint 1	Analysis Timepoint 2	Notes
Renal, Bone and CCI [redacted] CCI [redacted]						
	181 ≤ Injection Study Day ≤ 240	241	211	Month 8	Month 7/8	Injection 5
	241 ≤ Injection Study Day ≤ 300	301	271	Month 10	Month 9/10	Injection 6
	301 ≤ Injection Study Day ≤ 360	361	331	Month 12	Month 11/12	Injection 7
Urinalysis[a], CD8, CD4/CD8 ratio, fasting glucose and lipids[b], weight, height, BMI, Waist and Hip Circumference, Vital Signs, CCI [redacted], Insulin, HbA1c, Renal, Bone and CCI [redacted][c]	301 ≤ Injection Study Day ≤ 372					
	361 ≤ Injection Study Day ≤ 420 For those who did not continue to Extension after completing Maintenance Phase: 361 ≤ Injection Study Day ≤ Injection Study Day of: max(Last Injection Date + 67, Date of Last Oral Dose + 1)	421	391	Month 14	Month 13/14	Injection 8
	(30*m - 59) ≤ Injection Study Day ≤ (30*m)	30*m + 1	30*m - 29	Month 16, 18, etc.	Month m-1/m	Injection (m/2+1)
If subject permanently discontinued study treatment:						
	Subject received at least 1 injection of IP: Date > min(LTFU ART start date, max(Last Injection Date + 67, Date of Last Oral Dose + 1)) **Subject received oral CAB/RPV only:** Date> (Date of Last oral CAB/RPV Dose +1)			Follow-up	Follow-up	Follow-up

NOTES:

- Analysis windows are applied after data has been assigned to the Maintenance Phase and Extension Phase as defined in Section 16.4.1
- Study day and injection study day is defined in Section 16.6.1
- Follow-up will be derived only for participants who permanently discontinued study treatment.
- Last oral dose may be CAB/RPV or SOC ART Oral Bridging where CAB/RPV is not available due to COVID-19 impact.
- Target Injection Study Day is only applicable to Q2M OLI subjects

[a] **Urinalysis:** All parameters provided by the central laboratory under the category of urinalysis.
[b] **Lipids**: Cholesterol, HDL Cholesterol Direct, LDL Cholesterol Calculation, LDL Cholesterol Direct, Total Cholesterol/HDL Cholesterol Ratio, Triglycerides
[c]**Bone Markers:** Bone-specific alkaline phosphatase, Procollagen type 1 N-propeptide, Type 1 collagen cross-linked C-telopeptide, Osteocalcin, 25 hydroxy-Vitamin D; **Renal Markers:** Cystatin C, Retinol Binding Protein, Beta-2-Microglobulin; [redacted].
[d] Analysis windows for parameters with sparse collection are noted.

16.3.2.2. Assessment Windows for Screening, Maintenance and Extension Phase Data – Q2M D2I Subjects

All Parameters except for where noted[c]	Analysis Window	Target Study Day	Analysis Timepoint 1	Analysis Timepoint 2	Notes
	Study Day ≤ 1	Study day of the earliest record	Screening	Screening	Screening
	Last available recorded value up to and including the date of first Maintenance Phase dose of IP	1	Maintenance Baseline (Day 1)	Maintenance Baseline (Day 1)	Injection 1
post-dose ECG	Value taken post-dose	1	Day 1 (Post Dose)	Day 1(Post Dose)	Injection 1
	2 ≤ Study Day ≤ 60	31	Month 1	Month 1	Injection 2
Urinalysis	2 ≤ Study Day ≤ 72				
	61 ≤ Study Day ≤ 120	91	Month 3	Month 3/4	Injection 3
	121 ≤ Study Day ≤ 180	151	Month 5	Month 5/6	Injection 4
Urinalysis[a], CD8, CD4/CD8 ratio, fasting glucose and lipids[b], weight, height, BMI, Waist and Hip Circumference, Vital Signs, CCI , Insulin, HbA1c, Renal, Bone and CCI	121 ≤ Study Day ≤ 192				
	181 ≤ Study Day ≤ 240	211	Month 7	Month 7/8	Injection 5
	241 ≤ Study Day ≤ 300	271	Month 9	Month 9/10	Injection 6
	301 ≤ Study Day ≤ 360	331	Month 11	Month 11/12	Injection 7
Urinalysis[a], CD8, CD4/CD8 ratio, fasting glucose and lipids[b], weight, height, BMI, Waist and Hip Circumference, Vital Signs, CCI Insulin, HbA1c, Renal, Bone and CCI	301 ≤ Study Day ≤ 372				

All Parameters except for where noted[c]	Analysis Window	Target Study Day	Analysis Timepoint 1	Analysis Timepoint 2	Notes
	361 ≤ Study Day ≤ 420 For those who did not continue to Extension after completing Maintenance Phase: 361 ≤ Study Day ≤ max(Last Injection Date + 67, Date of Last Oral Dose + 1))	391	Month 13	Month 13/14	Injection 8
	(30*m - 29) ≤ Study Day ≤ (30*m + 30)	30*m + 1	Month 15, 17, etc.	Month m/m+1	Injection ((m+3)/2)
If subject permanently discontinued study treatment:					
	Date > min(LTFU ART start date, max(Last Injection Date + 67, Date of Last Oral Dose + 1))		Follow-up	Follow-up	Follow-up

NOTES:

- Analysis windows are applied after data has been assigned to the Maintenance Phase and Extension Phase as defined in Section 16.4.1
- Study day is defined in Section 16.6.1
- Follow-up will be derived only for participants who permanently discontinued study treatment.
- Last oral dose may be CAB/RPV or SOC ART Oral Bridging where CAB/RPV is not available due to COVID-19 impact.

[a] **Urinalysis:** All parameters provided by the central laboratory under the category of urinalysis.
[b] **Lipids**: Cholesterol, HDL Cholesterol Direct, LDL Cholesterol Calculation, LDL Cholesterol Direct, Total Cholesterol/HDL Cholesterol Ratio, Triglycerides
[c]**Bone Markers:** Bone-specific alkaline phosphatase, Procollagen type 1 N-propeptide, Type 1 collagen cross-linked C-telopeptide, Osteocalcin, 25 hydroxy-Vitamin D; **Renal Markers:** Cystatin C, Retinol Binding Protein, Beta-2-Microglobulin; CCI [redacted]
[d] Analysis windows for parameters with sparse collection are noted.

16.3.2.3. Assessment Windows for Screening and Maintenance Phase Data –BIK

All Parameters except for where noted[d]	Analysis Window	Target Study Day	Analysis Timepoint 1	Analysis Timepoint 2	Notes
	Study Day ≤ 1	Study day of the earliest record	Screening	Screening	
	Last available recorded value up to and including the date of first Maintenance Phase dose of IP	1	Maintenance Baseline (Day 1)	Maintenance Baseline (Day 1)	
post-dose ECG	Value taken post-dose	1	Day 1 (Post Dose)	Day 1(Post Dose)	
	2 ≤ Study Day ≤ 84	57	Month 2	Month 2	
	85 ≤ Study Day ≤ 140	113	Month 4	Month 3/4	
	141 ≤ Study Day ≤ 196	169	Month 6	Month 5/6	
Urinalysis[a], CD8, CD4/CD8 ratio, fasting glucose and lipids[b], weight, height, BMI, Waist and Hip Circumference, Vital Signs, CCI , Insulin, HbA1c, Renal, Bone and CCI	141 ≤ Study Day ≤ 210				
	197 ≤ Study Day ≤ 252	225	Month 8	Month 7/8	
	253 ≤ Study Day ≤ 308	281	Month 10	Month 9/10	
	309 ≤ Study Day ≤ 350	337	Month 12	Month 11/12	
Urinalysis[a], CD8, CD4/CD8 ratio, fasting glucose and lipids[b], weight, height, BMI, Waist and Hip Circumference, Vital Signs, CCI , Insulin, HbA1c, Renal, Bone and CCI [c]	309 ≤ Study Day ≤ 378				
	351 ≤ Study Day ≤ Study Day of Last Maintenance BIK Dose +1	365	Month 13	Month 13/14	
If subject permanently discontinued study treatment:					
	Date> (Date of Last BIK Dose +1)		Follow-up	Follow-up	

NOTES:

- Analysis windows are applied after data has been assigned to the Maintenance Phase as defined in Section 16.4.1

- Note for the BIK arm, the "every two months" are implemented as "every 56 days", therefore the analysis windows are adjusted according to the actual visit schedules instead of nominal.
- Study day is defined in Section 16.6.1
- Follow-up will be derived only for participants who permanently discontinued study treatment.

[a] **Urinalysis:** All parameters provided by the central laboratory under the category of urinalysis.
[b] **Lipids**: Cholesterol, HDL Cholesterol Direct, LDL Cholesterol Calculation, LDL Cholesterol Direct, Total Cholesterol/HDL Cholesterol Ratio, Triglycerides
[c]**Bone Markers:** Bone-specific alkaline phosphatase, Procollagen type 1 N-propeptide, Type 1 collagen cross-linked C-telopeptide, Osteocalcin, 25 hydroxy-Vitamin D; **Renal Markers:** Cystatin C, Retinol Binding Protein, Beta-2-Microglobulin; CCI [redacted].
[d] Analysis windows for parameters with sparse collection are noted.

16.3.2.4. Assessment Windows for Extension Phase Data – BIK subjects Switching to CAB LA + RPV LA (Switch Q2M) and choose OLI (Switch OLI)

All Parameters except for where noted[c]	Analysis Window	Target Extension Study Day	Target Extension Injection Study Day	Analysis Timepoint 1	Analysis Timepoint 2	Notes
	Last available recorded value up to and including the date of first Extension Phase dose of CAB/RPV	1		Extension Baseline (Month 13)	Extension Baseline (Month 13)	
Urinalysis[a], fasting glucose and lipids[b]	Extension Injection Study Day ≤ 15 and Extension Study day ≥2 For those with Ext OLI only: 2<= Extension Study Day<= Extension Study Day of Last Extension Oral Dose +1	31	1	Month 14	Month 14	Extension Injection 1
	Extension Injection Study Day ≤ 42 and Extension Study day ≥2 For those with Ext OLI only: 2<= Extension Study Day<= Extension Study Day of Last Extension Oral Dose +1					
	16 ≤ Extension Injection Study Day ≤ 60	61	31	Month 15	Month 15	Extension Injection 2
	61 ≤ Extension Injection Study Day ≤ 120	121	91	Month 17	Month 16/17	Extension Injection 3
	121 ≤ Extension Injection Study Day ≤ 180	181	151	Month 19	Month 18/19	Extension Injection 4
	(30*(m-14) - 29) ≤ Extension Injection Study Day ≤ (30*(m -14)+ 30)	30*(m-13) + 1	30*(m-14) + 1	Month 21, 23, etc.	Month m-1/m	Extension Injection (m-11)/2
If subject permanently discontinued study treatment:						
	Subject received at least 1 injection of IP: Date > min(LTFU ART start date, max(Last Injection Date + 67, Date of Last Oral Dose + 1)) **Subject received oral CAB/RPV only:** Date> (Date of Last oral Dose +1)			Follow-up	Follow-up	

NOTES:

- Analysis windows are applied after data has been assigned to the Extension Phase as defined in Section 16.4.1
- Extension Study day and Extension Injection Study Day is defined in Section 16.6.1
- Follow-up will be derived only for participants who permanently discontinued study treatment.
- Last oral dose may be CAB/RPV or SOC ART Oral Bridging where CAB/RPV is not available due to COVID-19 impact.
- Target Extension Injection Study Day is only applicable to Switch Q2M subjects who choose OLI during the Extension Phase

[a] **Urinalysis:** All parameters provided by the central laboratory under the category of urinalysis.
[b] **Lipids**: Cholesterol, HDL Cholesterol Direct, LDL Cholesterol Calculation, LDL Cholesterol Direct, Total Cholesterol/HDL Cholesterol Ratio, Triglycerides
[c] Analysis windows for parameters with sparse collection are noted.

16.3.2.5. Assessment Windows for Extension Phase Data –BIK subjects Switching to CAB LA + RPV LA (Switch Q2M) and choose D2I (Switch D2I)

All Parameters except for where noted[c]	Analysis Window	Target Extension Study Day	Analysis Timepoint 1	Analysis Timepoint 2	Notes
	Last available recorded value up to and including the date of first Extension Phase dose of CAB/RPV	1	Extension Baseline (Month 13)	Extension Baseline (Month 13)	Extension Injection 1
Urinalysis[a], fasting glucose and lipids[b]	2 ≤ Study Day ≤ 60 2 ≤ Study Day ≤ 72	31	Month 14	Month 14	Extension Injection 2
	61 ≤ Study Day ≤ 120	91	Month 16	Month 16/17	Extension Injection 3
	121 ≤ Study Day ≤ 180	151	Month 18	Month 18/19	Extension Injection 4
	(30*(m-13) - 29) ≤ Study Day ≤ (30*(m -13)+ 30)	30*(m-13) + 1	Month 20, 22, etc.	Month m/m+1	Extension Injection (m-10)/2
If subject permanently discontinued study treatment:					
	Date > min(LTFU ART start date, max(Last Injection Date + 67, Date of Last Oral Dose + 1))		Follow-up	Follow-up	

NOTES:

- Analysis windows are applied after data has been assigned to the Extension Phase as defined in Section 16.4.1
- Extension Study day is defined in Section 16.6.1
- Follow-up will be derived only for participants who permanently discontinued study treatment.
- Last oral dose may be CAB/RPV or SOC ART Oral Bridging where CAB/RPV is not available due to COVID-19 impact.

[a] **Urinalysis:** All parameters provided by the central laboratory under the category of urinalysis.
[b] **Lipids**: Cholesterol, HDL Cholesterol Direct, LDL Cholesterol Calculation, LDL Cholesterol Direct, Total Cholesterol/HDL Cholesterol Ratio, Triglycerides
[c] Analysis windows for parameters with sparse collection are noted.

16.3.2.6. Assessment Windows for Summary of Snapshot Data - Data assigned to Maintenance Phase Only

Snapshot Analysis Windows (If no on-treatment viral load data in default window, use expanded window)		Analysis Timepoint 1	Analysis Timepoint 2
Default[a]	**Expanded +6 Week Upper Window**		
Last available recorded value up to and including the date of first Maintenance Phase dose of IP	Last available recorded value up to and including the date of first Maintenance Phase dose of IP	Maintenance Baseline (Day 1)	Maintenance Baseline (Day 1)
CAB LA + RPV LA (OLI)			
Injection Study Day ≤ 15 and Study Day ≥2 For those with OLI only: 2<= Study Day<= 45	Injection Study Day ≤ 42 and Study Day ≥2 For those with OLI only: 2<= Study Day<= Study Day of Last Oral Dose +1	Month 1	Month 1
16 ≤ Injection Study Day ≤ 60	16 ≤ Injection Study Day ≤ 72	Month 2	Month 2
61 ≤ Injection Study Day ≤ 120	61 ≤ Injection Study Day ≤ 132	Month 4	Month 3/4
109 ≤ Injection Study Day ≤ 192	109 ≤ Injection Study Day ≤ 192	Month 6	Month 5/6
181 ≤ Injection Study Day ≤ 240	181 ≤ Injection Study Day ≤ 252	Month 8	Month 7/8
241 ≤ Injection Study Day ≤ 300	241 ≤ Injection Study Day ≤ 312	Month 10	Month 9/10
289 ≤ Injection Study Day ≤ 372	289 ≤ Injection Study Day ≤ 372	Month 12	Month 11/12
CAB LA + RPV LA (D2I)			
2 ≤ Study Day ≤ 60	2 ≤ Study Day ≤ 72	Month 1	Month 1
61 ≤ Study Day ≤ 120	61 ≤ Study Day ≤ 132	Month 3	Month 3/4
109 ≤ Study Day ≤ 192	109 ≤ Study Day ≤ 192	Month 5	Month 5/6
181 ≤ Study Day ≤ 240	181 ≤ Study Day ≤ 252	Month 7	Month 7/8
241 ≤ Study Day ≤ 300	241 ≤ Study Day ≤ 312	Month 9	Month 9/10
289 ≤ Study Day ≤ 372	289 ≤ Study Day ≤ 372	Month 11	Month 11/12
BIK Arm			
2 ≤ Study Day ≤ 84	2 ≤ Study Day ≤ 98	Month 2	Month 2
85 ≤ Study Day ≤ 140	85 ≤ Study Day ≤ 154	Month 4	Month 3/4
127 ≤ Study Day ≤ 210	127 ≤ Study Day ≤ 210	Month 6	Month 5/6
197 ≤ Study Day ≤ 252	197 ≤ Study Day ≤ 266	Month 8	Month 7/8
253 ≤ Study Day ≤ 308	253 ≤ Study Day ≤ 322	Month 10	Month 9/10
295 ≤ Study Day ≤ 378	295 ≤ Study Day ≤ 378	Month 12	Month 11/12

NOTES:

- Apply Snapshot analysis windows only to viral load data that is on-treatment within the Maintenance Phase (See Section 16.4.2).

- An on-treatment viral load assessment may be assigned to more than one snapshot analysis window.
  a. ± 6 Week window is always used at key analysis timepoints (Month 5/6 and Month 11/12). For other analysis timepoints, if no viral load data in default window, expand upper bound to +6 weeks.

16.3.2.7. Assessment Windows for Summaries of Long-Term Follow Up Phase Data

Analysis Window	Analysis Timepoint	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

NOTES:

- Analysis windows are applied after data has been assigned to the LTFU Phase as defined in Section 16.4.1.
- Long-Term Follow-Up (LTFU) Study day is defined in Section 16.6.1
- An assessment may be slotted to both LTFU and Maintenance/Extension Phase

16.3.3. Assessment Window for Study Conclusion

The study conclusion and Phase conclusion records in disposition data will be slotted based on Section 16.3.1 for Maintenance and Extension Phase conclusion records. However, if the discontinuation date is post-treatment (based on Section 16.4.3), then the discontinuation will be slotted to the participant's last attained on-treatment analysis visit across all assessments (e.g. analysis visit corresponding to the last on-treatment lab assessment), rather than follow up.

16.3.4. Assessment Window for Health Outcome Data

16.3.4.1. HIVTSQs/HIVTSQc/PIN[redacted]

Assessments will be assigned to analysis visits as follows:

- Maintenance Baseline (Day 1) will be defined as last available recorded value up to and including the date of first Maintenance Phase dose of study treatment (expected to be collected at Day 1). Baseline is not applicable for PIN, HIVTSQc and other one-time questionnaires such as treatment preference.

- If the nominal visit identifier as captured in the source dataset corresponds to a scheduled collection per the Time and Events Schedule (see Section 16.2) and the assessment is collected in the Maintenance Phase (see Section 16.4.1.2), then the nominal visit identifier will be kept as the analysis visit (excluding Day 1 which will normally be assigned to Maintenance Baseline (Day 1).

- If the nominal visit identifier is unscheduled or withdrawal, then the following procedure will be used:
    a. Assign the assessment to a study Phase according to Section 16.4.1.2. Proceed to step b if the assessment is assigned to the Maintenance Phase.

b. Identify the 'last nominal visit' with the HO assessment performed prior to the unscheduled/withdrawal visit to be slotted.
c. Unscheduled/withdrawal visits will be slotted to the planned nominal visit subsequent to the 'last nominal visit'. If the 'last nominal visits' does not exist (e.g. no records originate from a planned nominal visit), then the unscheduled/withdrawal visit will be slotted to the first planned nominal visit after Day 1. If there is already an original (planned) value for the subsequent visit, then the original value will be selected instead of an "unscheduled" value.

Example 1, for HIVTSQs, for Q2M subjects with OLI, the planned nominal visits are Day 1, Month 6, and Month 12. If a participant has the 'last nominal visit' (with HIVTSQs assessment) at Month 6 prior to withdrawal at Month 8, the withdrawal assessment will be slotted to the subsequent planned nominal visit of Month 12.

Example 2, for HIVTSQs, for Q2M subjects with OLI if there is unscheduled visit between Month 6 and Month 12, this unscheduled visit will be slotted to Month 12. In this case, there are two assessments with analysis visit equal to Month 12 (i.e. the slotted value and the value at original nominal Month 12 visit). The original nominal value will be selected for summary per the rule below for multiple records—see Section 16.3.5.

Table 6 Planned Nominal Visit of Health Outcome Data

Questionnaire	Day 1	Month 1/2	Month 5/6	Month 11/12
PIN		x	x	x
HIVTSQs	x		x	x
HIVTSQc				x
CCI [redacted]				
NOTES: Day 1 visits are recorded as "Baseline" visits in the database.				

CCI [redacted]

16.3.4.3. Treatment Preference

The treatment preference questionnaire is taken at Month 11/12 and withdrawal. The nominal visit identifier will be kept as the analysis visit. Data will be reported separately for Month 11/12 and for withdrawal.

16.3.5. Multiple assessments within an Analysis Window

If after window assignment there are multiple valid assessments of a parameter within the same window, then the following hierarchy will be used to determine the value to be used for summary statistics of observed values:

For data other than health outcome:

- the assessment closest to the window target Study Day (or target Injection Study Day if injection study day is used for assessment window slotting);
- if there are multiple assessments equidistant from the target Study Day or target Injection Study Day, then the mean of these values will be used. For HIV-1 RNA, the geometric mean of the number of copies will be used as opposed to the arithmetic mean. For post-dose ECG, the assessment closest to two-hour post injection will be used.

Health outcome assessments:

- if there are multiple assessments assigned to the same analysis visit, the assessment from the original planned nominal visit will be used for summary statistics.
- if there are multiple assessments assigned to the same analysis visit and none originate from a planned nominal visit (e.g. two unscheduled/withdrawal nominal visits), then
    a. the assessment closest to the window target Study Day will be used;
    b. if there are multiple assessments equidistant from the target Study Day, then the earliest assessment will be used.

Assessments not chosen for use in summary statistics by this algorithm will still be included in the associated listings. Also, all applicable assessments, irrespective of proximity to the target study day, will be used when categorizing values across visits, such as ‘maximum grade’ or ‘at any time’, and for any algorithm that has specific rules for which observation to use (e.g., snapshot algorithm or CVF identification, where applicable).

16.4. Appendix 4: Study Phases and Treatment State

16.4.1. Study Phases

Assessments and events will be classified according to the time of occurrence relative to the Treatment Start Date defined in Section 16.6.1.

AEs will be assigned to study phases as defined in Section 16.4.1.1.

Laboratory data (efficacy, safety, and virology), HIV associated/ AIDS-defining conditions, health outcomes assessments, vital signs, and ECGs will be assigned to study phases as defined as in Section 16.4.1.2. For example, assessments/events occurring up to and including start of extension phase IP/LTFU ART will be assigned to the Maintenance Phase.

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

16.4.1.1. Study Phases for AEs

Study Phase	Date range
Screen	Date < Maintenance Treatment Start Date
Maintenance	**Q2M Arm (OLI and D2I):** ***For participants continuing into Extension Phase:*** **OLI:** Maintenance Treatment Start Date ≤ **Date** < Date of Nominal Month 14 Injection Visit **D2I:** Maintenance Treatment Start Date ≤ **Date** < Date of Nominal Month 13 Injection Visit ***For participants <u>not</u> continuing into Extension Phase:*** Maintenance Treatment Start Date ≤ **Date**< LTFU ART Start Date (if applicable) *Note:* *- For AEs leading to withdrawal and started on the same date as LTFU ART Start Date, Maintenance Phase, instead of Long-term Follow-up phase, will be assigned.* *- LTFU ART start date is not applicable for those who complete maintenance phase and transition to commercial supply.*
	BIK Arm: ***For participants continuing into Extension Phase:*** Maintenance Treatment Start Date ≤ **Date** < min (Start Date of Extension Phase CAB/RPV oral lead-in, Date of first Extension Phase CAB/RPV injection) ***For participants <u>not</u> continuing into Extension Phase:*** **Date** ≥Maintenance Treatment Start Date

Study Phase	Date range
Extension	***Participants continuing maintenance CAB LA + RPV LA into Extension Phase*** **OLI:** Date of Nominal Month 14 Injection Visit ≤ **Date** < LTFU ART Start Date (if applicable) **D2I:** Date of Nominal Month 13 Injection Visit ≤ **Date** < LTFU ART Start Date (if applicable) ***Participants Switching from Maintenance BIK Arm to CAB LA + RPV LA:*** min (Start Date of Extension Phase CAB/RPV oral lead-in, Date of first Extension Phase CAB/RPV injection) ≤ **Date** < LTFU ART Start Date (if applicable) *Note: LTFU ART start date is not applicable for those who transition to commercial supply.*

- **Date** = AE Start date
- **Maintenance Treatment Start Date:** refer to Treatment Start Date in Section 16.6.1

16.4.1.2. Study Phases for Lab assessments, ECG, Vital Signs, Health Outcomes, Protocol Deviations, and HIV associated/AIDS-defining conditions

Study Phase	Date range
Screen	Date ≤ Maintenance Treatment Start Date
Maintenance	**Q2M Arm:** ***For participants continuing into Extension Phase:*** **OLI:** Maintenance Treatment Start Date <**Date** ≤ Date of Nominal Month 14 Injection Visit **D2I:** Maintenance Treatment Start Date < **Date** ≤ Date of Nominal Month 13 Injection Visit ***For participants <u>not</u> continuing into Extension Phase:*** Maintenance Treatment Start Date < **Date** ≤ LTFU ART Start Date (if applicable) *Note: LTFU ART start date is not applicable for those who complete maintenance phase and transition to commercial supply.*

Study Phase	Date range
	BIK Arm: ***For participants continuing into Extension Phase:*** Maintenance Treatment Start Date < **Date** ≤ min (Start Date of Extension Phase CAB/RPV oral lead-in, Date of first Extension Phase CAB/RPV injection) ***For participants <u>not</u> continuing into Extension Phase:*** **Date** > Maintenance Treatment Start Date
Extension	***Participants continuing maintenance CAB LA + RPV LA into Extension Phase*** **OLI:** Date of Nominal Month 14 Injection Visit < **Date** ≤ LTFU ART Start Date (if applicable) **D2I:** Date of Nominal Month 13 Injection Visit < **Date** ≤ LTFU ART Start Date (if applicable) ***Participants Switching from Maintenance BIK arm to CAB LA + RPV LA:*** min (Start Date of Extension Phase CAB/RPV oral lead-in, Date of first Extension Phase CAB/RPV injection) < **Date** ≤ LTFU ART Start Date (if applicable) *Note: LTFU ART start date is not applicable for those who transition to commercial supply.*

- **Date** = start or assessment date
- **Maintenance Treatment Start Date:** refer to Treatment Start Date in Section 16.6.1

16.4.1.3. Long-Term Follow-Up Phase

Study Phase	Date range
Long-Term Follow-Up	**Date** > max (Last CAB/RPV Injection Date, Last Oral Bridging End Date)

- Date = Assessment/Start Date
- Only applicable to subjects who have received at least 1 injection
- LTFU phase is not applicable for those who transition to commercial supply.Last oral Bridging may be CAB/RPV or SOC ART Oral Bridging where CAB/RPV is not available due to COVID-19.

Note that the long-term follow-up Phase and Maintenance/Extension Phases are not necessarily mutually exclusive and are to be defined with separate Phase variables in the datasets.

16.4.1.4. Study Phases for Concomitant medication/ART

Study Phase	Date range
Prior	**Medication Taken** < Maintenance Treatment Start Date
Maintenance[a]	**Q2M Arm (OLI and D2I):** ***For participants continuing into Extension Phase:*** **OLI:** Maintenance Treatment Start Date ≤ **Medication Taken** < Date of Nominal Month 14 Injection Visit **D2I:** Maintenance Treatment Start Date ≤ **Medication Taken** < Date of Nominal Month 13 Injection Visit ***For participants <u>not</u> continuing into Extension Phase:*** Maintenance Treatment Start Date ≤ **Medication Taken** < LTFU ART Start Date (if applicable) *Note: LTFU ART start date is not applicable for those who transition to commercial supply.*
	BIK Arm: ***For participants continuing into Extension Phase:*** Maintenance Treatment Start Date ≤ **Medication Taken** < min (Start Date of Extension Phase CAB/RPV oral lead-in, Date of first Extension Phase CAB/RPV injection) ***For participants <u>not</u> continuing into Extension Phase:*** **Medication Taken** ≥Maintenance Treatment Start Date
Extension[b]	***Participants continuing maintenance CAB LA + RPV LA into Extension Phase*** **OLI:** Date of Nominal Month 14 Injection Visit ≤ **Medication Taken** < LTFU ART Start Date (if applicable) **D2I:** Date of Nominal Month 13 Injection Visit ≤ **Medication Taken** < LTFU ART Start Date (if applicable) ***Participants Switching from Maintenance BIK Arm to CAB LA + RPV LA:*** min (Start Date of Extension Phase CAB/RPV oral lead-in, Date of first Extension Phase CAB/RPV injection) ≤ **Medication Taken** < LTFU ART Start Date (if applicable) *Note: LTFU ART start date is not applicable for those who transition to commercial supply.*

Study Phase	Date range
Long-Term Follow-Up	***For participants who received at least one CAB and/or RPV Injection:*** **Medication Taken** ≥ LTFU ART Start Date *Note: LTFU phase is not applicable for those who transition to commercial supply.*

[a]: ART stopped on the start date of Maintenance Treatment will be considered a prior medication and will not be considered concomitant during the Maintenance 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 Maintenance phase.

[b]: ART stopped on the start date of Extension Phase IP will not be assigned to the Extension Phase.

If a partial date for medication/ART is recorded in the eCRF, the following convention will be used to assign the medication:

- if the partial date is a start date, a '01' will be used for missing days and 'Jan' will be used for missing months;
- if the partial date is a stop date, a '28/29/30/31' will be used for the missing day (dependent on the month and year) and 'Dec' will be used for the missing month; for medications recorded separately in the eCRF as prior ART, the earlier of this imputed date or the day before IP start will be used.

16.4.2. Study Periods

Certain displays will be produced for data collected during the oral-lead-in. These period variables are defined in the tables below and will be reflected in the datasets with separate variables.

16.4.2.1. Oral Lead-in Period for AE Data

Study Period	Date range
Maintenance Phase Oral Lead-in	**Q2M OLI subjects only:** ***For participants receiving at least one Injection:*** Maintenance Treatment Start Date ≤ **Date** < Date of First Maintenance Phase CAB/RPV Injection ***For participants withdrawing prior to first Injection:*** **Date** ≥ Maintenance Treatment Start Date 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 maintenance phase.
Extension Phase Oral Lead-in	**Switch Q2M OLI subjects only:** ***For participants receiving at least one Extension Phase Injection:*** Extension Oral CAB/RPV Start Date ≤ **Date** < Date of First Extension Phase CAB/RP injection ***For participants withdrawing prior to first Extension Phase Injection:*** **Date** ≥ Extension Phase Oral CAB/RPV Start Date

16.4.2.2. Oral Lead-in Period for Lab assessments

Study Period	Date range
Maintenance Phase Oral Lead-in	**Q2M OLI subjects only:** ***For participants receiving at least one Injection:*** Maintenance Treatment Start Date < **Date** ≤ Date of First Maintenance Phase CAB/RPV Injection ***For participants withdrawing prior to first Injection:*** **Date** > Maintenance Treatment Start Date 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 maintenance phase.

Extension Phase Oral Lead-in	**Switch Q2M OLI subjects only:** ***For participants receiving at least one Extension Phase Injection:*** Extension Oral CAB/RPV Start Date < **Date** ≤ Date of First Extension Phase CAB/RP injection ***For participants withdrawing prior to first Extension Phase Injection:*** **Date** > Extension Oral CAB/RPV Start Date

16.4.3. Treatment State

Within each treatment study phase (i.e. Maintenance, and Extension—based on assignment of study phase described in Section 16.4.1), only those assessments which occur within the ranges shown below will be considered 'on-treatment' for the given phase. Note "on-treatment" criteria will not be implemented for adverse event summaries.

Table 7 Treatment State within Study Phases

Study Phase[a]	Treatment State	Date Range
Screen	Pre-treatment	All assessments/events within Phase
Maintenance	On-treatment	Q2M Arm: **Date** ≤ max (Date of Last Injection Dose + 67, Date of Last Oral Dose + 1)
		BIK Arm: **Date** ≤ Maintenance ART Stop Date + 1
	Post-treatment	Q2M Arm: **Date** > max (Date of Last Injection Dose + 67, Date of Last Oral Dose + 1)
		BIK Arm: **Date** > Maintenance ART Stop Date + 1
Extension	On-treatment	**Date** ≤ max (Date of Last IP Injection Dose + 67, Date of Last Oral Dose + 1)
	Post-treatment	**Date** > max (Date of Last IP Injection Dose + 67, Date of Last Oral Dose + 1)
Long-Term Follow-up	On-treatment	**Date** ≤ min (LTFU ART start date, max (Date of Last IP Injection Date + 67, Date of Last Oral Dose + 1))
	Post-treatment	**Date** > min (LTFU ART start date, max (Date of Last IP Injection Date + 67, Date of Last Oral Dose + 1))

Note:
- Treatment State is determined after data has been assigned to the study Phases as defined in Section 16.4.1

- The upper bound with last IP injection / last oral dose /Maintenance ART Stop Date should only be applied to participants who permanently discontinue from study treatment
- Date = Assessment/Start Date.
- Last oral dose may be CAB/RPV or SOC ART Oral Bridging where CAB/RPV is not available due to COVID-19.

16.4.4. Combining Treatment Phases and States

On-treatment and Post-treatment assessments and events will be classified as occurring during the Maintenance Phase, Extension, or Long-term follow up Phase.

16.5. Appendix 5: Data Display Standards & Handling Conventions

16.5.1. Reporting Process

Software	
• The currently supported versions of SAS software or R/RStudio will be used. • The specific versions of SAS or R packages used to generate the analyses will be detailed in the ADRG.	
Reporting Area	
HARP Server	: us1salx00259
HARP Compound	: \ARPROD\GSK1265744\mid213500
Analysis Datasets	
• Analysis datasets will be created according to CDISC standards (SDTM IG Version 3.2 & ADaM IG Version 1.2). • For creation of ADaM datasets (ADCM/ADAE), the same version of dictionary datasets will be implemented for conversion from SI to SDTM.	
Generation of RTF Files	
• RTF files will be generated for reporting efforts described in the RAP.	

16.5.2. 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):
  • 4.03 to 4.23: General Principles
  • 5.01 to 5.08: Principles Related to Data Listings
  • 6.01 to 6.11: Principles Related to Summary Tables
  • 7.01 to 7.13: Principles Related to Graphics
• Do not include participant level listings in the main body of the GSK Clinical Study Report. All participant level listings should be located in the modular appendices as ICH or non-ICH listings

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. • Numeric data will be reported at the precision collected on the eCRF. • 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:
  ◦ Planned time relative to dosing will be used in figures, summaries, statistical analyses and calculation of any derived parameters, unless otherwise stated.
  ◦ The impact of any major deviation from the planned assessment times and/or scheduled visit days on the analyses and interpretation of the results will be assessed as appropriate.
• Reporting for Data Listings:

• If space permits, planned and actual time relative to study drug dosing will be shown in listings (Refer to GSK Standard Statistical Display Principle 5.05.1). • Unscheduled or unplanned readings will be presented within the participant's listings.	
Unscheduled Visits	
• Unscheduled visits will be slotted to analysis time points as per Section 16.3. • However, data summaries will only report visits that are planned assessment time points for each parameter (according to the Time and Events table). • Assessments at unscheduled visits will be included for 'any time On-treatment' time points and in data listings, as well any algorithms that make use of additional data (e.g., Snapshot and PDVF identification). • All unscheduled visits will be included in listings.	
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.	

16.6. Appendix 6: Derived and Transformed Data

16.6.1. General

Multiple Measurements at One Analysis Time Point

- If after window assignment there are multiple valid assessments of a parameter within the same window, then the following hierarchy will be used to determine the value to be used for summary statistics of observed values:
    - the assessment closest to the window target Study Day (or target Injection Study Day if injection study day is used for assessment window slotting);
    - if there are multiple assessments equidistant from the target Study Day or target Injection Study Day, then for continuous variables the mean of these values will be used and for categorical variables the worse assessment. For HIV-1 RNA, the geometric mean of the number of copies will be used as opposed to the arithmetic mean
- Assessments not chosen for use in summary statistics by this algorithm will still appear in the associated listings. Also, such valid assessments will be used when determining values of potential clinical concern for the 'any time ' time point, and for any algorithm that has specific rules for which observation to use (e.g., Snapshot).

Treatment Start Date

Treatment start date is defined as follows:

- Maintenance Phase
    - For participants randomized to Q2M: Date of first dose of CAB + RPV (oral or injection) entered in the IP exposure CRF form.
    - For participants randomized to BIK: BIK regimen start date entered in the Maintenance Phase IP exposure CRF

- Extension Phase
    - For participants continuing CAB LA + RPV LA (Q2M):
      - for Q2M OLI: Date of the nominal Month 14 injection date
      - for Q2M D2I: Date of the nominal Month 13 injection date
    - For participants switching from BIK to Q2M:
      Date of the nominal Month 13 Q2M injection date (BIK to D2I) or the oral CAB + RPV start date entered in the Extension Phase IP exposure CRF (BIK to OLI)

Study Day

The Study Day of an event (e.g., lab assessment, vital sign, ECG, start date of AE or HIV associated/AIDS-defining condition) will be derived as the number of days between the date of the event and the Maintenance Phase start date of study treatment as follows:

if date of event ≥ start date of study treatment, then

- Study Day = Date of Event – Start Date of Maintenance Phase IP + 1

if date of event < start date of study treatment, then

- Study Day = Date of Event – Start Date of Maintenance Phase IP

Note that the start date of study treatment on Maintenance Phase is considered to be on Study Day 1 and the day before this is Study Day -1; i.e., there is no Study Day 0.

Injection Study Day (Maintenance Phase) (Only applicable to Q2M OLI subjects)

The Injection Study Day of an event will be derived as the number of days between the date of the event and the date of first Maintenance Phase injection as follows:
if date of event ≥ first Maintenance Phase injection, then

- Injection Study Day = Date of Event – Date of First Maintenance Phase CAB/RPV Injection + 1

if date of event < first Maintenance Phase injection, then

- Injection Study Day = Date of Event – Date of First Maintenance Phase CAB/RPV Injection

Note that the date of first Maintenance Phase injection is considered to be on Injection Study Day 1 and the day before this is Injection Study Day -1; i.e., there is no Injection Study Day 0.

Extension Study Day

The Extension Phase Study Day of an event (e.g., lab assessment, vital sign, ECG, start date of AE or HIV associated/AIDS-defining condition) will be derived as the number of days between the date of the event and the initial start date of Extension Phase IP as follows:

if date of event ≥ start date of Extension Phase IP, then

- Extension Study Day = Date of Event – Start Date of Extension Phase IP + 1

if date of event < start date of Extension Phase IP, then

- Extension Study Day = Date of Event – Start Date of Extension Phase IP

Note that the start date of Extension Phase IP is considered to be on Extension Phase Study Day 1 and the day before this is Extension Phase Study Day -1; i.e., there is no Extension Phase Study Day 0.

Extension Injection Study Day (Only applicable to Extension Switch OLI subjects)

The Extension Phase Injection Study Day of an event (e.g., lab assessment, vital sign, ECG, start date of AE or HIV associated/AIDS-defining condition) will be derived as the number of days between the date of the event and the initial start date of Extension Phase injection as follows:

if date of event ≥ date of first Extension Phase injection, then

- Extension Injection Study Day = Date of Event – Date of First Extension Phase CAB/RPV Injection + 1

if date of event < date of first Extension Phase injection, then

- Extension Injection Study Day = Date of Event – Date of First Extension Phase CAB/RPV Injection

Note that the date of first Extension Phase Injection is considered to be on Extension Injection Study Day 1 and the day before this is Extension Injection Study Day -1; i.e., there is no Extension Phase Injection 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/AIDS-defining 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:

If the onset of event falls in Long-term Follow up Phase, then

- LTFU Study Day = Date of Event – End Date of IP

16.6.2. Study Population

Demographics and Baseline Characteristics

Age

- Age, in whole years, will be calculated with respect to the participant's Screening visit.
- GSK standard IDSL algorithms will be used for calculating age where birth date will be imputed as follows:
- Any participant with a missing date and month will have this imputed as '30th June'.
- Birth date will be presented in listings as 'YYYY'.
- Completely missing dates of birth will remain as missing, with no imputation applied. Consequently, the age of the participant will not be calculated and will remain missing.

Body Mass Index (BMI)

- BMI is calculated as Weight (kg) / Height $(m)^2$. Height is only collected at Baseline Day 1.

Hepatitis Status

- Hepatitis status at entry will be based on the assessments prior to/on the start of the study treatment.
- 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 test result below level of detection, however, 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 (i.e. "REACTIVE").
- Hepatitis C status will be determined using antibody (IgM or IgG) and/or hepatitis C virus (HCV) RNA assessments performed during screening or during the conduct of the study. 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. In the absence of an HBV RNA result, Hepatitis C antibody of "REACTIVE" or "BORDERLINE" will qualify as Hep C positive.

Framingham Risk Equation

- The predicted probability, $\hat{p}$, of having a cardiovascular disease (CVD) within the next 10-years according to the Framingham formula [D'Agostino, 2008] is

For females:

$$\hat{p}_F = 1 - S_0(t)^{\exp\{2.32888 \times \log(\text{age}) + 1.20904 \times \log(TC) - 0.70833 \times \log(HDL) + 2.76157 \times \log(SBPu) + 2.82263 \times \log(SBPt) + 0.52873 \times I_s + 0.69154 \times I_d - 26.1931\}},$$

For males:

$$\hat{p}_M = 1 - S_0(t)^{\exp\{3.06117 \times \log(\text{age}) + 1.12370 \times \log(TC) - 0.93263 \times \log(HDL) + 1.93303 \times \log(SBPu) + 1.99881 \times \log(SBPt) + 0.65451 \times I_s + 0.57367 \times I_d - 23.9802\}},$$

Demographics and Baseline Characteristics

Where

$$S_0(t) = \begin{cases} 0.95012, \text{females} \\ 0.88936, males \end{cases}$$

$$I_s = \begin{cases} 1, \text{current smoker} \\ 0, \quad otherwise \end{cases}$$

$$I_d = \begin{cases} 1, \quad \text{diabetic} \\ 0, \quad otherwise \end{cases}$$

TC = total serum cholesterol (mg/dL),
HDL = serum HDL cholesterol (mg/dL),
SBPu = systolic blood pressure (mmHg) if participant is not treated for high blood pressure
(note that if a participant is treated for high blood pressure then log(SBPu) = 0)
SBPt = systolic blood pressure (mmHg) if participant is treated for high blood pressure
(note that if a participant is not treated for high blood pressure then log(SBPt) = 0)

- A participant will be considered as treated for high blood pressure if during screening it has specified that is suffering from hypertension.A participant is classified as diabetic if current or past is indicated in the medical conditions eCRF for Type 1 or Type 2 diabetes mellitus, or if baseline (Day 1) fasting glucose ≥7.00 mmol/L (126 mg/dL) and HbA1C >6.5%.
- Smoking status is collected in the eCRF at Day 1. A current smoker is defined as currently smoking/using tobacco or has smoked/used tobacco within the previous 6 months; a former smoker is defined as previously smoked/used tobacco products and has not smoked/used tobacco products within the previous 6 months.
- This calculation will not be performed for participants who have indicated current or past myocardial infarction conditions on the eCRF. These participants will not be included in summary statistics of risk, but they will be counted in the highest category of risk in the summary by category.
- Framingham Risk will also be calculated at Month 6 and Month 12.
    - Baseline smoking status will be used for the Month 6 calculation. Smoking status collected at Month 12 will be used for the Month 12 calculation.
    - Diabetic status is defined as:
        1. Current or past is indicated in the medical conditions eCRF for Type 1 or Type 2 diabetes mellitus, or
        2. At any time prior to and including the analysis timepoint:
           2a. fasting glucose ≥7.00 mmol/L (126 mg/dL) and HbA1C >6.5%, or
           2b. an adverse event is collected as having “type 1 or type 2 diabetes mellitus”
    - “Treated for high blood pressure” at Month 6 and Month 12 is defined as
        1. hypertension at baseline or
        2. use of medication treating hypertension which started prior to and including the analysis time point

Lipid-modifying Agents

- The following ATC codes correspond to lipid-modifying agents:
    - ATC Level 2: C10
    - ATC Level 3: C10A, C10B (if Level 2 is not available)

Demographics and Baseline Characteristics

- ATC Level 4: C10AA, C10AB, C10AC, C10AD, C10AX, C10BA, C10BX (if level 2, 3 are not available)

- Participants are considered to have used a lipid-modifying agent at baseline if they are taking the medication at the time of their baseline fasting lipid testing date.
- Participants are also considered to have used a lipid-modifying agent at baseline if they stopped their lipid modifying medication within 12 weeks prior to their baseline fasting lipid testing date.

Treatment Compliance

- For defining protocol deviation (i.e. treatment non- compliance) leading to exclusion from the Per Protocol population, the total non-compliance days will be calculated (see details in Section 16.1). The percentage of the total number of non-compliant days to the Exposure ('overall exposure' for CAB+RPV treatment) will be used to define protocol deviation leading to exclusion from PP Population for the Month 12 analysis due to study treatment non-compliance (i.e. >10%).

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. For participants who choose oral lead-in (Q2M OLI), the first injection is planned at Month 1. For Q2M D2I participants, the first injection is planned at Day 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 2 ml of injection instead of 3 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.

The categories of Timeliness of Injections relative to date of Projected Dosing Visits for summary are listed below:

< -14 days
-14 to - 8 days
-7 to - 4 days
-3 to -2 days
-1 day
0 day
1 day
2 to 3 days
4 to 7 days
8 to 14 days
>14 days
Missed Injection without Oral Bridging
Missed Injection with Oral Bridging
Missed Injection with CAB+RPV Oral Bridging
Missed Injection with SOC Oral Bridging

16.6.3. Efficacy

HIV-1 RNA
CCI [redacted]
Target Detected / Target Non-Detected/ Super Low Viral Load Testing
• When a measurement of plasma HIV-1 RNA is below the limit of quantification (i.e. 40 c/mL) and is qualitatively observable that will be denoted as a "Target Detected" measure, while HIV-1 RNA below the limit of quantification that is not qualitatively observable that will be denoted as "Target Not Detected". Any measurements <40 c/mL characterised as "Target Not Detected" or "Target Detected" will be captured in the database. • SuperLow viral load will also be tested by BioMONTR Labs for viral loads below the limit of quantification at Day 1 and Month 11/12.
Confirmed Virologic Failure
• The definition of CVF is provided in the Protocol, Section 7.1.6 – Definition of Protocol-Defined Virologic Failure
Treatment (TRDF) and Efficacy Related (ERDF) Discontinuation = Failure
• The analysis of time to confirmed virologic failure (CVF) or discontinuation due to treatment related reasons (i.e., drug-related AE, intolerability of injections, protocol defined safety stopping criteria, or lack of efficacy) will censor participants who have not met CVF criteria and are ongoing in the study, or who have discontinued for reasons other than those related to treatment. This will be the Treatment Related Discontinuation = Failure (TRDF) data.

HIV-1 RNA

- Participants who have not met CVF criteria and are ongoing in the study, or who have discontinued for reasons other than lack of efficacy, will be censored in the analysis of the Efficacy Related Discontinuation = Failure (ERDF) data.
- Proportion of Participants without virologic (ERDF) or tolerability (TRDF) failure will be estimated using the Kaplan-Meier nonparametric method based on the time to ERDF or TRDF. The estimated proportion at time point of interest will be presented by treatment group, along with estimated difference in proportions between treatment groups and its associated two-sided 95% CI. The estimate of the standard error used to derive confidence intervals will be based on Greenwood's formula [Kalbfleisch,1980].
- See Appendix 10: Variables Defined for Time to Event Analysis for additional details.

CCI

[redacted]

Delay in IP Injection

IM dosing is expected to occur every 2 months starting from the third injection and onwards. The Delay in IP injection (days) will be calculated as:

For the second injection:

Delay in IP injection(days) = Injection date – date of preceding injection – 31

For other injections:

- *Delay in IP injection(days) = Injection date – date of preceding injection - 62*

Delay in IP injection will be grouped into: ≤1, 2-3, 4-7, >7 days.

- The proportion of participants with HIV-1 RNA≥50 c/mL at Month 12 will be summarized by last delay in IP Injection. The last delay in IP injection will be the delay in IP injection at Month 11(D2I) or Month 12(OLI), or the delay in last IP injection prior to Month 11/Month 12 if a participant does not receive their Month 11/12 injection (i.e. missing visit or withdrawal).
- Delays are defined as more than 31 or 62 days for the second and the subsequent injections, respectively.
- If there are subjects who did not receive any injection or received only one injection, then add the "No injection or only 1 injection" category.

16.6.4. 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 4.

Potential QTc Interval Prolonging Events of Interest

Potential QTc Interval Prolonging Events of Interest will be identified based on Standardised MedDRA Query (SMQ) for Torsade de pointes/QT prolongation, broad (MedDRA). The terms per this reference are listed below.

AE preferred term
Electrocardiogram QT interval abnormal
Electrocardiogram QT prolonged
Long QT syndrome
Long QT syndrome congenital
Torsade de pointes
Ventricular tachycardia
Cardiac arrest
Cardiac death
Cardiac fibrillation
Cardio-respiratory arrest
Electrocardiogram repolarisation abnormality
Electrocardiogram U wave inversion
Electrocardiogram U wave present
Electrocardiogram U-wave abnormality
Loss of consciousness
Sudden cardiac death
Sudden death
Syncope
Ventricular arrhythmia
Ventricular fibrillation
Ventricular flutter
Ventricular tachyarrhythmia

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

Estimate of Glomerular Filtration Rate (GFR) (Levey, 2012)

- Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI) equation [Levey, 2012]. be used by the central laboratory to provide an estimate of GFR, in mL/min per 1.73 m^2, as follows:

$$GFR = 141 \times \min\left(\frac{CRT_{mg/dL}}{\kappa}, 1\right)^{\alpha} \times \max\left(\frac{CRT_{mg/dL}}{\kappa}, 1\right)^{-1.209} \times 0.993^{Age} \times [1.018 \text{ if Female}] \times [1.159 \text{ if Black}]$$

Abbreviations / Units:

eGFR (estimated glomerular filtration rate) = mL/min/1.73 m^2

age = years at time of assessment

κ = 0.7 (if female) or 0.9 (if male)

α = -0.329 (if female) and -0.411 (if male)

min() = the minimum of CRT/κ or 1

max() = the maximum of CRT/κ or 1

CRTmg/dL = serum creatinine concentration in mg/dL. The serum creatinine concentration in mg/dL is obtained from GSK standard units of μmol/L as CRTmg/dL =0.0113x CRTμmol/L.

Lab Toxicities

- Toxicities will be based on the Division of AIDS (DAIDS) grading system, Version 2.1, March 2017, as specified in the protocol of Appendix 4. 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 summarising toxicity grades for such parameters, they will be categorised 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
Fasted glucose	Hypoglycemia	Hyperglycemia
Sodium	Hyponatremia	Hypernatremia
Potassium	Hypokalemia	Hyperkalemia

National Cholesterol Education Program (NCEP) Lipid Categories

- In addition to DAIDS toxicity grades (see protocol), lipid values will be categorized according to the 2001 NCEP Adult Lipid Guidelines [Grundy, 2001]

Parameter	Value Range (mmol/L)	Value Range (mg/dL)	Category
Triglycerides	<1.70	<150	Normal
	1.70 to <2.26	150 to <200	Borderline High
	2.26 to <5.65	200 to <500	High
	≥5.65	≥500	Very High
Total Cholesterol	<5.18	<200	Desirable
	5.18 to <6.21	200 to <240	Borderline High
	≥6.21	≥240	High
HDL Cholesterol	<1.04	<40	Low
	1.04 to <1.56	40 to <60	Normal
	≥1.56	≥60	High
LDL Cholesterol	<2.59	<100	Optimal
	2.59 to <3.37	100 to <130	Near/Above Optimal
	3.37 to <4.14	130 to <160	Borderline High
	4.14 to <4.92	160 to <190	High
	≥4.92	≥190	Very High

Total Cholesterol / HDL Cholesterol Ratio

- When both total cholesterol and HDL cholesterol results are available from the same date for a participant, then the ratio will be calculated by dividing the total cholesterol result by the HDL cholesterol result. The ratio can be classified as follows:

Parameter	Value Range
Total Cholesterol / HDL Ratio	< 3.5
	3.5 to < 4.4
	4.4 to < 5
	≥ 5

Percentage change for lipids

The percentage change from Baseline* is calculated as:

$$\% \text{ Change from BL} = \frac{\text{Value at Month X} - \text{BL value}}{\text{BL value}} \times 100\ \%$$

*Maintenance or Extension

Other Safety Endpoints

Extent of Exposure

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

Maintenance Phase: Q2M	
Exposure to CAB + RPV (oral lead-in) = * Q2M OLI subjects only	Oral lead-in CAB/RPV Stop Date – Oral lead-in CAB/RPV Start Date +1
Exposure to CAB LA + RPV LA =	Number of IP injections received during Maintenance Phase up to and include the Month 12 (OLI) or the Month 11 (D2I) injection
Overall Exposure to IP (Q2M OLI) =	min [Date of latest Maintenance Phase visit up to and including Month 14 (OLI), max (Date of last CAB LA + RPV LA injection +67, Date of last oral CAB/RPV dose)] – Oral lead-in CAB/RPV Start Date +1
Overall Exposure to IP (Q2M D2I) =	min [Date of latest Maintenance Phase visit up to and including Month 13(D2I), max (Date of last CAB LA + RPV LA injection +67, Date of last oral CAB/RPV dose)] – CAB LA + RPV LA Start Date +1
Overall Exposure to Study Treatment (OLI) =	min [Date of latest Maintenance Phase visit up to and including Month 14, max (Date of last CAB LA + RPV LA injection +67, Date of last oral CAB/RPV dose, Date of last oral SOC bridging)] – Oral lead-in CAB/RPV Start Date +1
Overall Exposure to Study Treatment (D2I) =	min [Date of latest Maintenance Phase visit up to and including Month 13, max (Date of last CAB LA + RPV LA injection +67, Date of last oral CAB/RPV dose, Date of last oral SOC bridging)] – CAB LA + RPV LA Start Date +1
Maintenance Phase: BIK arm	
Exposure = Min (Date of latest Maintenance Phase visit up to and including Month 13, Maintenance Phase Treatment Stop Date, Date of Maintenance Phase Discontinuation) – Maintenance Treatment Start Date + 1	
◦ Last oral dose may be CAB/RPV or SOC ART Oral Bridging where CAB/RPV is not available due to COVID-19 ◦ Last CAB LA + RPV LA injection / last oral dose is only applicable to participants who permanently discontinue from study	

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.,

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

QTc Values by Category

The following categories for QTc will be used:

- For absolute QTc values:

≤450
>450 to ≤480
>480 to ≤500
>500

- For change from baseline in QTc values:

≤30
>30 to ≤60
>60

Columbia Suicide Severity Rating Scale (C-SSRS) (Posner, 2007)

- Missing data will not have any imputation performed (Nilsson, 2013)

Homeostatic model assessment-Insulin Resistance (HOMA-IR)

- HOMA-IR = (fasting plasma insulin (mU/L) * fasting plasma glucose (mmol/L)) / 22.5.
- HOMA-IR categories will be categorised as follows for the shift table analysis:

1. <2
2. 2 to <3
3. 3 to <4
4. >=4

All HOMA-IR analyses will be based on fasting values and only patients with post-baseline values will be included in analyses (i.e. patients with missing post-baseline HOMA-IR will not be included in summary tables or figures).
The following subjects will be excluded from the HOMA-IR analysis:

- diabetic as captured on the medical history or have taken an anti-diabetic medication (ATC code "A10" (DRUGS USED IN DIABETES)) up to screening
- fasting glucose >126mg/dl and HbA1C >6.5% at Day 1
- have had a cosmetic procedure including liposuction/liposculpture of the thighs, buttocks, hips and/or abdomen

Metabolic Syndrome

- Diagnosis of Metabolic Syndrome is defined as follows per joint interim statement of the International Diabetes Federation Task Force on Epidemiology and Prevention; National Heart, Lung, and Blood Institute; American Heart Association; World Heart Federation; International Atherosclerosis Society; and International Association for the Study of Obesity.
- Three abnormal findings out of the following five qualifies a person for the metabolic syndrome:
    - Elevated waist circumference
      Males: ≥102 cm (≥40 in)
      Females: ≥88 cm (≥35 in)
    - Elevated triglycerides
      ≥150 mg/dL (1.7 mmol/L)
    - Reduced HDL-C
      Males: < 40 mg/dL (1.0 mmol/L)
      Females: < 50 mg/dL (1.3 mmol/L)
    - Elevated blood pressure (meeting either or both criteria)
      Systolic ≥130 and/or diastolic ≥ 85 mm Hg
    - Elevated fasting glucose
      ≥ 100 mg/dL

BMI (For Shift Table)
The following categories will be used for BMI shift tables: <Normal: <18.5 kg/m² Normal: 18.5 - <25 kg/m² Overweight: 25 - <30 kg/m² Obese: >= 30 kg/m²

16.6.5. Pharmacokinetic

N/A.

16.6.6. Health Outcomes

HIVTSQs

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

Treatment Satisfaction Score

- Total Treatment Satisfaction Score is computed with items 1-11. Items 1-11 are summed to produce a score with a possible range of 0 to 66.
- Item 12 will not be included in Total Treatment Satisfaction Score. Instead, it will be treated as a stand-alone item only.
- Higher scores represent greater treatment satisfaction as compared to the past few weeks.
- A maximum of 5 items can be missing, which can be imputed to reflect the mean of the completed item scores. If 6 or more items are missing, then the treatment satisfaction scale score should not be computed.

Individual Item Scores

- Items are rated as 6 CCI CCI
- Higher scores represent greater satisfaction with each aspect of treatment
- For individual item scores outputs, missing scores will not be computed (according to Page

7 of the [HIVTSQ User Guidelines, 2016]).

HIVTSQc

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

Treatment Satisfaction Score (Change)

- Total Treatment Satisfaction Score is computed with items 1-11. Items 1-11 are summed to produce a score with a possible range of -33 to 33
- Item 12 will be computed as an individual item only.
- The higher the score, the greater the improvement in satisfaction with treatment; the lower the score, the greater the deterioration in satisfaction with treatment. A score of 0 represents CCI
- A maximum of 5 items can be missing, the missing scores will be imputed with the mean of the completed item scores. If 6 or more items are missing, then the overall treatment satisfaction scale score should not be computed and will remain missing.

Individual Treatment Change Item Scores

- Items are rated as +3 CCI CCI to -3 CCI
- The higher the score, the greater the improvement in satisfaction with each aspect of treatment and the lower the score, the greater the deterioration in satisfaction with each aspect of treatment.

PIN

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

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[redacted]

Dimension Score (Chevat, 2008)

- Domains and Clusters
  - Bother from injection site reactions: items 3, 4, 5, 6, 7, 8
  - Leg movement: items 11, 12, 15, 16
  - Sleep: items 9, 10, 13, 14
  - Acceptability: items 17, 18
- 5 items not included in any of these domains and maintained as individual items (items 1, 2, 19, 20, 21) CCI [redacted]
- No overall score is calculated per the guidance
- The score of a domain is calculated as the mean of all items with the domain. Higher scores represent worse perception of injection.
- A maximum of <50% items can be missing within a domain, which can be imputed to reflect the mean of the completed item scores within the domain. Thus, if the number of missing items is ≥3 CCI [redacted] ≥2 CCI [redacted] ≥1 CCI [redacted], then the total score for the domain should not be computed.

Individual Item Scores

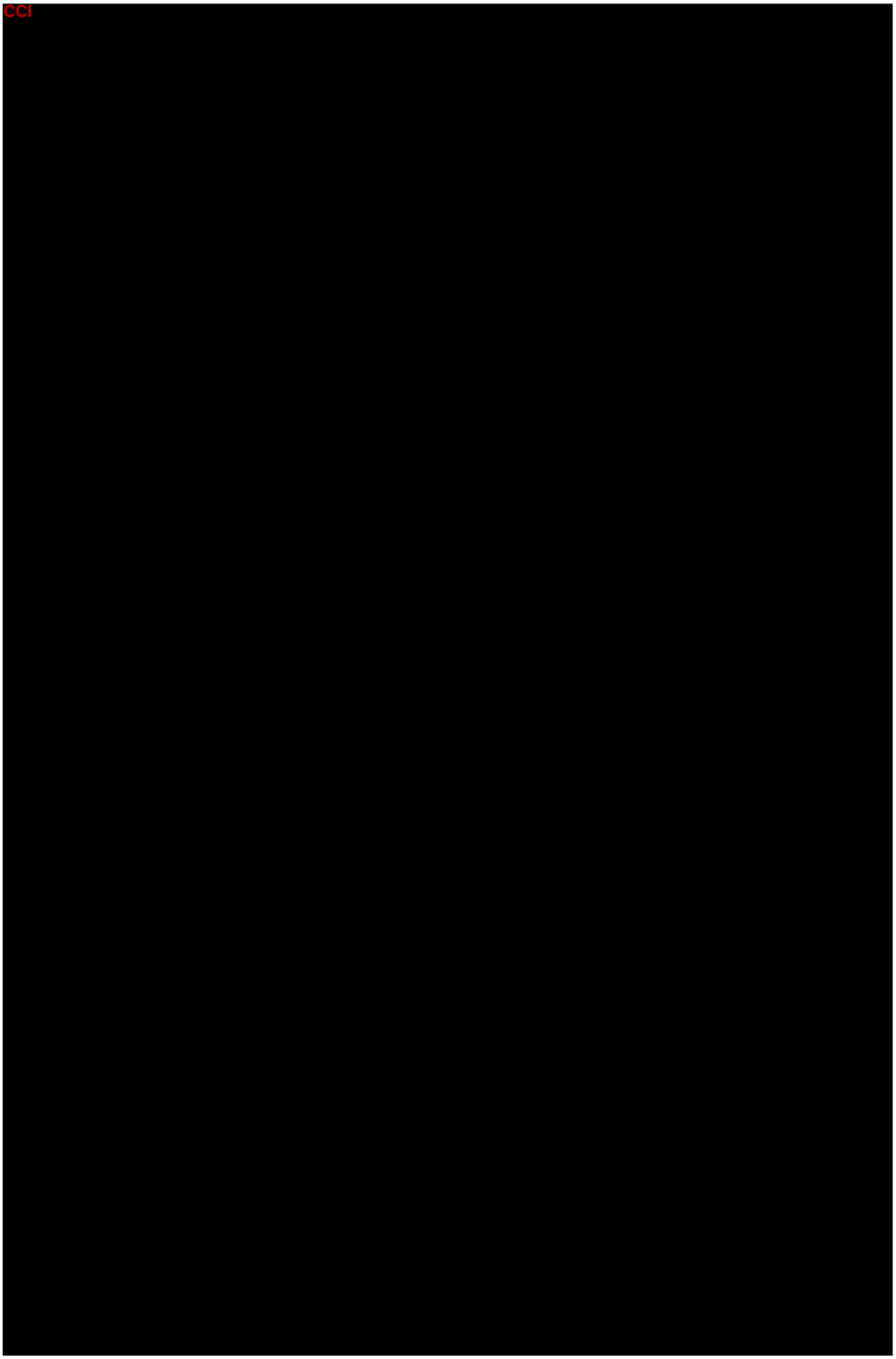
- Items are rated on a 5-point scale, ranging from 1 CCI [redacted] to 5 CCI [redacted]

- Lower scores represent worse perception of injection
- For individual item scores outputs, missing scores will not be computed.

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

CCI

CCI



CCI

[redacted]

16.6.7. Viral Genotype and Phenotype

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 BIC, RAL, EVG, CAB or DTG:

Amino Acids in HIV Integrase for Analysis	H51Y, **T66A/I/K**, **E92Q/V**/G, Q95K, T97A, **G118R**, **F121C/Y**, E138A/K/T, **G140**A/C/**R**/S, **Y143C/H/R/K/S/G/A**, **P145S**, **Q146P**, **S147G**, **Q148H/K/R/N**, **V151L**/A, S153F/Y, **N155H**/S/T, E157Q, G163R/K, S230R, D232N, R263K, L68V/I*, L74I/M*, E138D*, V151I*, G193E*

Notes:

- Draft listing; may be modified in case of additional substantive data availability.
- INI mutations listed taken from Stanford HIV Resistance Database (http://hivdb.stanford.edu/DR/cgi-bin/rules_scores_hivdb.cgi?class=INI cited 22Feb2021)
- INI substitutions listed above in bold had a score of =60.
  *Denotes additional INI mutations added as they were identified during in vitro passage of DTG or seen in a previous DTG study in INI-experienced subjects (ING112574).

- 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, I54M/L/V, Q58E, T74P, L76V, V82A/T/F/L/S, N83D, I84V, N88S,L90M

Note: List generated from IAS_USA Guideline, [Wensing. 2019]

- The pre-specified INI Mutations are identified as below:
  - Per the IAS-USA list of mutations (both minor and major) 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
  - 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
  - Mutations per FDA request for Study 201584: Q146L, T124A
- The NNRTI resistance associated mutations (RAMs) are identified per IAS-USA NNRTI mutations (IAS-USA 2019 resistance mutations update volume 27 issue 3, 2019):
  - V90I, A98G, L100I, K101E/H/P, K103N/S, V106A/I/M/T, V108I, E138A/G/K/Q/R, V179D/F/L/T, Y181C/I/V, Y188C/H/L, G190A/E/S, H221Y, P225H, F227C/L/R, M230I/L, L234I
- The RPV RAMs are identified per IAS-USA NNRTI mutations (IAS-USA 2019 resistance mutations update volume 27 issue 3, 2019):
  - L100I, K101E/P, E138A/G/K/Q/R, V179L, Y181C/I/V, Y188L, H221Y, F227C, M230I/L
- The NRTI major mutations associated with resistance to BIKTARVY (Emtricitabine and Tenofovir, IAS-USA 2019 resistance mutations update volume 27 issue 3, 2019):
  - K65R/E/N, K70E, M184V/I

Phenotype

Phenotypic Susceptibility

- Phenotypic susceptibility to all licensed antiretroviral drugs and CAB will be determined using PhenoSense HIV assays from Monogram Inc. and will be reported as fold change (FC) in IC50

relative to wild-type control virus NL4-3, i.e., FC of sample virus = IC50 of sample virus/IC50 of control virus.

- Since the maximum assay limit for FC for each ART varies from assay to assay, FC values that are greater than the maximum assay limit (e.g., '>100') will be interpreted as having a value equal to the smallest maximum assay limit for that ART in the study population for data analysis. Censored values will be presented 'as is' in the listings. Phenotypic susceptibilities will be categorised according to FC as shown in Table below (based on Monogram PhenoSense assay). Clinical cutoffs (where available) or biological cutoffs by PhenoSense will be used to define the phenotypic susceptibility of background treatment by Monogram. PHENOTYP dataset from Monogram contains the phenotypic susceptibility information derived from the cutoff listed below. Thus, phenotypic susceptibility (i.e. full sensitivity and partial sensitivity) will not be re-derived in our analysis.

- Replication capacity is generated as part of standard phenotypic assays

PhenoSense Algorithm

Drug	Abbreviation	Class	PhenoSense cutoff
Abacavir	ABC	NRTI	(4.5 – 6.5)[a]
Lamivudine	3TC	NRTI	3.5 [a]
Didanosine	ddI	NRTI	(1.3 – 2.2) [a]
Stavudine	d4T	NRTI	1.7 [a]
Zidovudine	AZT (ZDV)	NRTI	1.9
Emtricitabine	FTC	NRTI	3.5
Tenofovir	TDF	NRTI	(1.4 – 4) [a]
Delavirdine	DLV	NNRTI	6.2
Efavirenz	EFV	NNRTI	3
Nevirapine	NVP	NNRTI	4.5
Etravirine	ETR	NNRTI	(2.9-10) [a]
Rilpivirine	RPV	NNRTI	2.0
Doravirine	DOR	NNRTI	3.0
Fosamprenavir/r	FPV/r	PI	(4-11) [a]
Atazanavir	ATV	PI	2.2[a]
Atazanavir/r	ATV/r	PI	5.2[a]
Indinavir/r	IDV/r	PI	10 [a]
Lopinavir/r	LPV/r	PI	(9 – 55) [a]
Nelfinavir	NFV	PI	3.6
Saquinavir/r	SQV/r	PI	(2.3 – 12) [a]
Tipranavir/r	TPV/r	PI	(2 – 8) [a]
Darunavir/r	DRV/r	PI	(10 – 90) [a]
Ritonavir	RTV	PI	2.5
Enfuvirtide	T20	FI	6.48
Cabotegravir	CAB	INI	2.5
Raltegravir	RAL	INI	1.5
Elvitegravir	EVG	INI	2.5
Dolutegravir	DTG	INI	(4-13) [a]
Bictegravir	BIC	INI	(2.5- 10)

a. clinical cutoff (lower cutoff – higher cutoff).

- Phenotypic susceptibility to each drug in a subject's background regimen will be determined by applying drug-associated cutoffs as defined by the PhenoSense algorithm to the phenotypic fold resistance to that drug at a certain timepoint (e.g. Screening or Baseline).

Full Sensitivity

Fold Change	Interpretation
> clinical lower cutoff or biologic cutoff	resistance
≤ clinical lower cutoff or biologic cutoff	sensitive

Partial Sensitivity

Fold Change	Interpretation
> clinical higher cutoff	resistance
≤ clinical higher cutoff and > clinical lower cutoff	partially sensitive
≤ clinical lower cutoff	sensitive

Genotypic and Net Assessment Susceptibility

Genotypic and Net assessment susceptibility to all licensed antiretroviral drugs and CAB will be determined from Monogram Inc. Net assessment susceptibility will be reported with the categories of 'resistant', 'partially sensitive', and 'sensitive' as what will be performed for phenotypic susceptibility. Genotypic susceptibility will be reported with the categories of 'resistant', 'resistance possible' and 'sensitive'. Genotypic and Net assessment susceptibility will be assessed at time of CVF using plasma sample, Genotypic susceptibility may be assessed at baseline using PBMC.

16.7. Appendix 7: Reporting Standards for Missing Data

16.7.1. Premature Withdrawals

Element	Reporting Detail
General	• Participants are considered to have completed the study if they remain on therapy (i.e., have not permanently discontinued IP) and satisfy one of the following: - Randomly assigned to either treatment group, completed the randomized Maintenance Phase including Month 11/12 visits (with or without Month 11/12 study treatment) and did not enter the Extension Phase; - Randomly assigned to either treatment group, completed the randomized Maintenance Phase including Month 13, entered and completed the Extension Phase (defined as remaining on study until commercial supplies of the CAB LA + RPV LA Q8W regimen become locally available or development of CAB LA + RPV LA is terminated). Participants who withdraw from CAB LA + RPV LA and go into the Long-Term Follow Up Phase will be considered to have prematurely withdrawn from the study, even if they complete the 52-week follow-up Phase. In addition to the 52-week Follow-Up phase required for participants who receive one or more injections with CAB LA or RPV LA, an in-clinic Follow-Up visit will be conducted approximately 4 weeks after the last dose of study medication for participants who withdraw during the oral lead-in phase and who were randomized to BIK with ongoing AEs, serious adverse events (SAEs) and any laboratory abnormalities that are considered to be AEs or potentially harmful to the participant, at the last on-study visit. Assessments at the Follow-up visit should reflect any ongoing complaints (e.g., blood draws to follow a laboratory abnormality). Follow-Up visits are not required for successful completion of the study. • Withdrawn subjects were not replaced in the study. • 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. • Withdrawal visits will be slotted as per Appendix 3: Assessment Windows or will be summarised as withdrawal visits.

16.7.2. 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: • 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. • Answers such as “Not applicable” and “Not evaluable” are not considered to be missing data and should be displayed as such.

Element	Reporting Detail
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.

16.7.2.1. Handling of Missing and Partial Dates

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

Adverse Events	• The eCRF allows for the possibility of partial dates (i.e., only month and year) to be recorded for AE start and end dates; that is, the day of the month may be missing. In such a case, the following conventions will be applied for calculating the time to onset and the duration of the event:
	  ○ Missing Start Day: First of the month will be used unless this is before the start date of study treatment; in this case the study treatment start date will be used and hence the event is considered On-treatment as per Appendix 4: Study Phases and Treatment State.
	  ○ Missing Stop Day: Last day of the month will be used, unless this is after the last contact date; in this case the last contact date will be used.
	• Completely missing start or end dates will remain missing, with no imputation applied. Consequently, time to onset and duration of such events will be missing.

Concomitant Medications/Medical History	• Partial dates for any concomitant medications recorded in the CRF will be imputed using the following convention:
	  ○ If the partial date is a start date, a '01' will be used for the day and 'Jan' will be used for the month
	  ○ 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.
	  ○ For medications recorded in the eCRF as prior ART, the earlier of this imputed date or the day before Screening date will be used.
	• For medications with completely missing start date, they will be considered started prior to the maintenance phase treatment start date.
	• For medications with completely missing stop date, they will be considered ongoing unless recorded in eCRF as prior.
	• 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.
	• The recorded partial or missing date will be displayed in listings.

Health outcomes	• For the summary of individual item scores outputs, missing scores will not be computed.

16.7.2.2. Handling of Missing data for Statistical Analysis

Element	Reporting Detail
Snapshot	• In the Snapshot dataset, participants 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 RNA < 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'. See Appendix 9: Snapshot Algorithm Details.
Lipid Evaluable	• For subjects with lipid-modifying agent use, lipid assessments will be considered non-evaluable (equal to missing) after initiation without any imputation. • If participants take lipid modifying agents within 12 weeks prior to the start of the study treatment, all the post-baseline values will be non-evaluable. • The lipid evaluability rules will be used for the following displays: Summary of Fasting TC/HDL ratio Change from Baseline Summary of Fasting Lipids Percentage Changes from Baseline Summary of Chemistry Changes from Baseline • All other displays of lipids (i.e. toxicity tables and NCEP tables) will use observed fasting data, without considering lipid evaluability. • The same rule of "lipid evaluable" will be applied to anthropometric parameters as specified in Section 8.5.3: - Weight, Height and BMI - Waist circumferences - Hip circumference - CCI [redacted] - CCI [redacted] - Tanita scale parameters (total body fat percent, total body water percent, muscle mass, and bone mineral mass).

16.8. Appendix 8: Values of Potential Clinical Importance

Element	Reporting Detail
Laboratory Values and Adverse Events	• The DAIDS grading for severity of laboratory toxicities and clinical adverse events is included in the protocol. • The central laboratory will flag lab parameter toxicities directly in the provided datasets.
ECG values	• Defined as QTc > 500 msec or increase from baseline in QTc ≥ 60 msec

16.9. Appendix 9: Snapshot Algorithm Details

Detailed Algorithm Steps

- Consider an analysis visit window for Month X as defined in Section 16.3.1
- The HIV-1 RNA threshold of 50, 200 copies/mL will be analysed, respectively, 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 participant's 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 'Week 48' and HIV-1 RNA threshold of '50 c/mL' are used for the purpose of illustration. A participant's Snapshot response and reason at Week 48 are categorized as below.

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

    o  No Virologic Data at Week 48 Window
          Non-COVID-19 related
              Discontinued study due to AE or death
              Discontinued study for other reasons
              Not evaluated or discontinued due to confirmed pregnancy**
              On study but missing data in window
             COVID-19 related
              Discontinued study due to AE or death
              Discontinued study for other reason
              On study but missing data in window
```

- Note: since permanent changes in ART are not permitted in this protocol, all such participants who permanently change ART will be considered 'HIV-1 RNA ≥ 50 c/mL' if the change is made prior to an analysis timepoint. Participants with protocol permitted oral bridging treatment, CAB+RPV or SOC (during COVID-19 pandemic due to the unavailability of the CAB/RPV IM injections and oral CAB+RPV), or a temporary change in ART by mistake prior to an analysis timepoint (e.g. participant took the ART different from study treatment during oral lead-in by mistake for a short period of time and then went back to the study treatment) will not be considered 'HIV-1 RNA ≥ 50 c/mL' due to 'change in ART'.

- The steps in determining response and reasons are indicated in 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.

- ** This category is not needed if no subject on the Q2M arm becomes pregnant and continues in the study.

Detailed steps

Please note that the following scenarios will NOT be penalized per Snapshot algorithm (i.e. please exclude these scenarios from **Conditions** 1-4).

- Dose reduction, dropping a component, or change in formulation (e.g. 'Tivicay + Kivexa' to 'Triumeq' with the identical ingredients)
- Protocol permitted temporary oral bridging, or temporary change in ART by mistake

Condition ('Week 48' indicates Week 48 window)	**Response**	**Reasons**
1. If non-permitted change in background therapy prior to Week 48		
○ not due to COVID-19	HIV-1 RNA ≥ 50	Change in background therapy (non-COVID-19 related)
○ due to COVID-19	HIV-1 RNA ≥ 50	Change in background therapy (COVID-19 related)
2. If permitted change[a] in background therapy prior to Week 48 AND the latest on-treatment VL prior to/on the date of change is ≥ 50 c/mL (NA to this study)		
○ not due to COVID-19	HIV-1 RNA ≥ 50	Change in background therapy (non-COVID-19 related)

○ due to COVID-19	HIV-1 RNA ≥ 50	Change in background therapy (COVID-19 related)
3. If non-permitted change in background therapy during Week 48		
○ Last on-treatment VL during Week 48 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 Week 48 prior to/on the date of change < 50 c/mL	HIV-1 RNA < 50	
○ No VL during Week 48 prior to/on the date of change and the change in background therapy is not due to COVID-19	HIV-1 RNA ≥ 50	Change in background therapy (Non-COVID-19 related)
○ No VL during Week 48 prior to/on the date of change and the change in background therapy is due to COVID-19	HIV-1 RNA ≥ 50	Change in background therapy (COVID-19 related)
4. If permitted change[a] in background therapy during Week 48 AND the last on-treatment VL prior to/on the date of change is ≥ 50 c/mL (NA to this study)		
4.1 This last on-treatment VL occurs prior to Week 48		
• The change in background therapy is not due to COVID-19	HIV-1 RNA ≥ 50	Change in background therapy (non-COVID-19 related)
• The change in background therapy is due to COVID-19	HIV-1 RNA ≥ 50	Change in background therapy (COVID-19 related)
4.2 This last on-treatment VL occurs during Week 48 but prior to/on the date of change	HIV-1 RNA ≥ 50	Data in window not below 50
5. If none of the above conditions met		
5.1 On-treatment VL available during Week 48		
• Last on-treatment VL during Week 48 ≥ 50 c/mL	HIV-1 RNA ≥ 50	Data in window not below 50
• Last on-treatment VL during Week 48 < 50 c/mL	HIV-1 RNA < 50	
5.2 No on-treatment VL during Week 48		
5.2.1 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 th following date: **For Q2M arm:** Min[max(Date of last CAB/RPV LA Dose + 67, Date of last oral dose+1), withdrawal date] **For BIK arm:** Min (BIK Stop Date + 1, withdrawal date) Note: • Last oral dose: may be CAB/RPV or SOC ART Oral Bridging where CAB/RPV is not available due to COVID-19 impact. • Withdrawal Date: date the participant failed to complete per corresponding conclusion form		
5.2.1.1 If no on-treatment VL during Week 48 is not due to COVID-19		
• If no on-treatment VL is not due to confirmed pregnancy	No virologic data at Week 48 Window	On study but missing data in window (Non-COVID-19 related)
• If no on-treatment VL is due to confirmed pregnancy ("while on-treatment": data not evaluable)	No virologic data at Week 48 Window	Not evaluated or discontinued due to confirmed pregnancy(Non-COVID-19 related)
5.2.1.2 If no on-treatment VL during Week 48 is due to COVID-19	No virologic data at Week 48 Window	On study but missing data in window (COVID-19 related)
5.2.2 If participants withdraw before/during Week 48 due to		
5.2.2.1 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 Week 48 Window	Disc due to AE/death (Non-COVID-19 related)

5.2.2.2 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 Week 48 Window	Disc due to AE/death (COVID-19 related)
5.2.2.3 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 Conclusion Form)		
° Last on-treatment VL <50 c/mL OR no on-treatment VL available during study		
• Withdrew not due to pregnancy	No virologic Data at Week 48 Window	Disc for other reasons (Non-COVID-19 related)
• Withdrew due to pregnancy	No virologic Data at Week 48 Window	Not evaluated or discontinued due to confirmed pregnancy(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)
5.2.2.4 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 Week 48 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)

- 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-RNA = 580 copies/mL at Day 336, HIV-RNA below 50 copies/mL on Day 350. This should be categorized as HIV-RNA below 50 copies/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-RNA result, even if the HIV-RNA is below 50 copies/mL at the time of discontinuation.
- However, if a patient has an HIV-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:
  - HIV-RNA below 50 copies/mL at Day 336 and discontinues because of AE or even dies on Day 360 — this person is categorized as having HIV-RNA below 50 copies/mL.
  - HIV-RNA is 552 copies/mL on Day 336 and the patient discontinues on Day 360, the patient is categorized as having HIV-RNA greater than or equal to 50 copies/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-RNA greater than or equal to 50 row and not in the Discontinued for Other Reasons row.
- If a patient discontinues because of *subject withdrew consent* and his or her HIV-1 RNA result at the time of discontinuation was equal to or above 50 copies/mL, then he or she should be categorized as HIV-RNA greater than or equal to 50 and NOT as Discontinued for Other Reasons.
- If a patient discontinued because of *Lost to Follow-Up* and the last HIV-RNA result was 49 copies/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-RNA greater than or equal to 50 copies/mL row.

On study but missing data in window:

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

Not evaluated due to confirmed pregnancy:

Q2M subjects who became pregnant on study will be allowed to continue study treatment whereas BIK subjects will be withdrawn. HIV-1 RNA data will be treated as non-evaluable after confirmed pregnancy date as recorded on the eCRF, if a pregnant Q2M subject is allowed to continue.

16.10. Appendix 10: Variables Defined for Time to Event Analysis

Programming Instructions for the Kaplan-Meier analysis of treatment-related discontinuation equals failure (TRDF)		
Condition	**Censor Status**	**Event Description/AVAL**
1. Participant met CVF event criteria during the Maintenance Phase (based on derived CVF)	CNSR=0	EVNTDESC=CVF AVAL=Study Day of SVF* *immediately preceding CVF
2. Participant with Maintenance Phase withdrawal due to *'Lack of Efficacy', 'Treatment Related AE', 'Intolerability due to Injection',* or *'Protocol Defined Safety Stopping Criteria'* during Maintenance Phase Note: primary reason and/or standardized subreason for discontinuation based on Maintenance Conclusion form in the eCRF. 'Protocol Defined Safety Stopping Criteria' includes GSK defined liver chemistry stopping criteria, renal toxicity criteria and QTc withdrawal criteria. Treatment Related AE' is defined as participants who have primary reason for withdrawal =AE and who have at least one AE considered drug related and leading to withdrawal/permanent discontinuation of investigational product.	CNSR=0	EVNTDESC= terms in italic, respectively. For Q2M arm: AVAL= min [Study Day of Maintenance Phase Discontinuation, Study day of Starting LTFU HAART if applicable, max(Study Day of Last Maintenance Q2M IM Dose + 67, Study Day of Last Maintenance Oral Dose + 1)] For BIK arm: AVAL= min [Study Day of Maintenance Phase Discontinuation, Study Day of Maintenance IP Stop Date + 1] Note: • Last Q2M IM / last oral dose/ Maintenance IP Stop Date only applies to subjects who permanently discontinue from study treatment. • Date of Maintenance Phase discontinuation is from the Maintenance Phase Conclusion form in the eCRF.
If none of the above conditions met		
3. Participant with Maintenance Phase withdrawal due to other reasons	CNSR=1	EVNTDESC='Censored due to Study Discontinuation for Other Reasons' AVAL will be defined as the same as above 2
4. Participant who did not have premature withdrawal from the Maintenance Phase	CNSR=1	EVNTDESC='Censored due to data cutoff for analysis'

Programming Instructions for the Kaplan-Meier analysis of treatment-related discontinuation equals failure (TRDF)		
Condition	**Censor Status**	**Event Description/AVAL**
		AVAL = Study Day of last on-treatment date during the maintenance phase, which is defined as follows: For Q2M arm: min [Study Day of Month 13(D2I)/14(OLI) Visit, Study Day of Starting LTFU HAART, Study Day of Last Contact Date at time of analysis, max(Study Day of Last Maintenance Q2M IM Dose + 67, Study Day of Last Maintenance oral dose + 1)] For BIK arm: min [Study Day of Month 13 Visit, Day of Last Contact at time of analysis, Study Day of Maintenance IP stop Date + 1] Note: • Last Q2M IM / last oral dose/ Maintenance IP Stop Date only applies to subjects who permanently discontinue from study treatment

*Last oral dose may be CAB/RPV or SOC ART Oral Bridging where CAB/RPV is not available due to COVID-19 impact.

Note that last injection and last oral dose mentioned above are only applied to participants who permanently discontinued from the study treatment.

The similar approach will be used to derive for Kaplan-Meier analysis of efficacy-related discontinuation equals failure (ERDF), except that the reason of withdrawal in Condition 2 will be restricted to 'Lack of Efficacy'.

16.11. Appendix 11: Identification of Adverse Events of Special Interest (AESI)

The adverse events of special interest are identified based on MedDRA coded values and/or AE data available in the study database. The PT terms and codes below are from MedDRA 24.1. SMQs use narrow terms unless otherwise specified. 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. Additional events may be added based on the blinded review of AE data collected on study prior to the database freeze.

16.11.1. Hepatic Safety Profile

Hepatic failure, fibrosis and cirrhosis and other liver damage-related conditions (SMQ)

PT	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
Flood syndrome	10084797
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

PT	PT Code
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
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

PT	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
Hepatic cytolysis	10049199
Spontaneous bacterial peritonitis	10061135

Hepatitis, non-infectious (SMQ)

PT	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

PT	PT Code
Immune-mediated hepatitis	10078962
Ischaemic hepatitis	10023025
Lupus hepatitis	10067737
Non-alcoholic steatohepatitis	10053219
Radiation hepatitis	10051015
Steatohepatitis	10076331
Hepatic cytolysis	10049199

16.11.2. Hypersensitivity Reactions (HSR)

Drug reaction with eosinophilia and systemic symptoms syndrome (SMQ)

PT	PT Code
Drug reaction with eosinophilia and systemic symptoms	10073508
Pseudolymphoma	10037127
Granulomatous T-cell pseudolymphoma	10084214

PTs (select)

PT	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
Polymers allergy	10086347

16.11.3. Rash

Severe cutaneous adverse reactions (SMQ)

PT	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
Generalised bullous fixed drug eruption	10084905
Severe cutaneous adverse reaction	10085778

PTs (Select)

PT	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

PT	PT Code
Rash papular	10037876
Rash rubelliform	10057984
Rash scarlatiniform	10037890
Rash vesicular	10037898
Rash pruritic	10037884
Rash follicular	10037857
Rash pustular	10037888
Drug eruption	10013687

16.11.4. Prolongation of the Corrected QT Interval of the ECG in Supratherapeutic Doses

Torsade de pointes/QT prolongation (SMQ)

PT	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

PTs (Selective)

PT	PT Code
Electrocardiogram repolarisation abnormality	10052464

16.11.5. Suicidal Ideation/Behaviour

Suicide/self-injury (SMQ)

PT	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

PT	PT Code
Suicidal behaviour	10065604
Suicidal ideation	10042458
Suicide attempt	10042464
Suicide threat	10077417
Suspected suicide	10082458
Suspected suicide attempt	10081704

16.11.6. Depression

Depression (excl suicide and self injury) (SMQ)

PT	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
Depression rating scale score increased	10084390
Depressive symptom	10054089
Discouragement	10084257
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

16.11.7. Bipolar Disorder

HLGT Manic and Bipolar mood disorders and disturbances

PT	PT Code
Bipolar I disorder	10004939
Bipolar II disorder	10004940
Bipolar disorder	10057667
Cyclothymic disorder	10011724
Hypomania	10021030
Mania	10026749
Manic symptom	10084119

16.11.8. Psychosis

Psychosis and psychotic disorders (SMQ)

PT	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

PT	PT Code
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

PT	PT Code
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
Negative symptoms in schizophrenia	10084992
Pseudohallucination	10066297

16.11.9. Mood Disorders

HLGT Mood disorders and disturbances

PT	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
Discouragement	10084257
Dysphoria	10013954
Emotional disorder	10014551

PT	PT Code
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
Sibling rivalry disorder	10086385

16.11.10. Anxiety

HLGT Anxiety disorders and symptoms

PT	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

PT	PT Code
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 surgery	10084519
Fear of weight gain	10016280
Fear-related avoidance of activities	10080136
Generalised anxiety disorder	10018075
Glossophobia	10080077
Haemophobia	10073458

PT	PT Code
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

PT	PT Code
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
Aichmophobia	10085292
Olfactory reference syndrome	10085053
Frigophobia	10086104
Somniphobia	10085856

16.11.11. Sleep Disorders

HLGT Sleep Disorders and Disturbances

PT	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

PT	PT Code
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

PT	PT Code
Terminal insomnia	10068932
Upper airway resistance syndrome	10063968

HLGT Sleep disturbances (incl subtypes)

PT	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
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

PT	PT Code
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
Catathrenia	10085704

16.11.12. Injection Site Reactions (ISR)

ISR data available in the database, i.e. data collected from non-serious ISR AE eCRF form and collected serious adverse events with 'STUDY DRUG INJECTION SITE' included in the AE term.

16.11.13. Seizures and Seizure-like Events

Convulsions (SMQ)

PT	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

PT	PT Code
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
Faciobrachial dystonic seizure	10084187
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
Jeavons syndrome	10084303
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

PT	PT Code
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
Hemiconvulsion-hemiplegia-epilepsy syndrome	10085010
Juvenile absence epilepsy	10085031
Parietal lobe epilepsy	10085326
Epilepsy of infancy with migrating focal seizures	10086114
Photosensitive seizure	10086294
PURA syndrome	10085882
Epilepsia partialis continua	10015034

PTs (Selective)

PT	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

16.11.14. Weight Gain

HLT General nutritional disorders NEC (Selective)

PT	PT Code
Abdominal fat apron	10077983
Overweight	10033307
Abnormal weight gain	10000188
Central obesity	10065941
Obesity	10029883

PTs (Select) - Physical examination procedures and organ system status

PT	PT Code
Weight abnormal	10056814
Weight increased	10047899
Waist circumference increased	10064863
Body mass index abnormal	10074506
Body mass index increased	10005897

PTs (Select) - General Signs and Symptoms

PT	PT Code
Fat tissue increased	10016251
Sarcopenic obesity	10083992

16.11.15. Rhabdomyolysis

Rhabdomyolysis/myopathy (SMQ)

PT	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
Muscle infarction	10086278

PTs (Selective) - Muscle Disorders

PT	PT Code
Myalgia	10028411
Myositis	10028653

16.11.16. Pancreatitis

Acute pancreatitis (SMQ)

PT	PT Code
Cullen's sign	10059029
Grey Turner's sign	10075426
Haemorrhagic necrotic pancreatitis	10076058
Immune-mediated pancreatitis	10083072
Ischaemic pancreatitis	10066127
Oedematous pancreatitis	10052400
Pancreatic abscess	10048984
Pancreatic cyst drainage	10082531
Pancreatic haemorrhage	10033625
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
Subacute pancreatitis	10084554
Walled-off pancreatic necrosis	10085347

16.11.17. Impact on Creatinine

Acute renal failure (SMQ)

PT	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

PT	PT Code
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

PT	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

PT	PT Code
Scleroderma renal crisis	10062553
Traumatic anuria	10044501

16.11.18. Safety in Pregnancy

Use AE terms co-reported in pregnancy exposures to CAB and/or RPV.

16.12. Appendix 12: 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. PT terms and codes below are from MedDRA 24.1. 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. Additional events may be added based on the blinded review of AE data collected on study prior to the database freeze.

PT	PT Code
Asymptomatic COVID-19	10084459
COVID-19	10084268
COVID-19 pneumonia	10084380
Suspected COVID-19	10084451
SARS-CoV-2 carrier	10084461
SARS-CoV-2 test positive	10084271
Multisystem inflammatory syndrome	10086091
Multisystem inflammatory syndrome in adults	10085850
Multisystem inflammatory syndrome in children	10084767
SARS-CoV-2 viraemia	10084640
Post-acute COVID-19 syndrome	10085503
Coronavirus infection	10051905
Coronavirus test positive	10070255
Coronavirus pneumonia	10084381

16.13. Appendix 13: Data Handling for Pregnant Subjects

The SOLAR study allows pregnant subjects on the Q2M arm to continue CAB LA + RPV LA treatment, while those who became pregnant on the BIK arm will be withdrawn. To minimize bias, for summary tables, if Q2M subjects continue while being pregnant, data after date of confirmed pregnancy (as recorded in the eCRF EOS pregnancy form) will not be evaluable for pregnant Q2M subjects with documented evidence confirming pregnancy unless the confirmation occurs prior to or on the same day as termination of pregnancy (as recorded on the EOS pregnancy form and the AE form, respectively) within the same time period between two study visits. The above data handling strategy will not be implemented on the following:

- All adverse events
- ECG/QTc analysis
- Vital signs
- eC-SSRS
- CCI
- Health Outcomes
- Virology

Note all observed data collected for all pregnant subjects will be included in the listings.

For study outcomes based on the FDA snapshot algorithm, an additional sub-category will be added under "No Virologic Data": Not evaluated or discontinued due to confirmed pregnancy. Viral load after confirmed pregnancy of a Q2M subject will not be evaluated for snapshot outcomes (See Appendix 9: Snapshot Algorithm Details).

Sensitivity analysis including all data (all data as observed) will be provided for the following snapshot-based analysis is applicable:

- Summary of Study Outcomes (50 c/mL threshold)
- Summary of Analysis for Proportion of Subjects with Plasma HIV-1 RNA >=50 c/mL (or <50 c/ml)
- Proportion of Subjects with Plasma HIV-1 RNA >=50 c/mL (or <50 c/ml) by Visit

If no Q2M subject became pregnant on study, then the "while on-treatment" strategy will not be necessary and therefore no sensitivity analysis will be performed, and the additional sub-category mentioned above will not be needed.

16.14. Appendix 14: Abbreviations & Trade Marks

16.14.1. Abbreviations

Abbreviation	Description
3TC	Lamivudine, EPIVIR
ABC	Abacavir, ZIAGEN
ADaM	Analysis Data Model
AE	Adverse Event
AESI	Adverse Events of Special Interest
AIC	Akaike's Information Criteria
AIDS	Acquired immunodeficiency syndrome
ALT	Alanine aminotransferase
AST	Aspartate aminotransferase
A&R	Analysis and Reporting
BIK	Bictegravir/emtricitabine/tenofovir alafenamide Single Tablet Regimen
BMI	Body Mass Index
BP	Blood Pressure
CAB	Cabotegravir
CAB LA	Cabotegravir long-acting
CD4	Cluster of Differentiation 4
CD8	Cluster of Differentiation 8
CDC	Centers for Disease Control and Prevention
CDISC	Clinical Data Interchange Standards Consortium
CI	Confidence Interval
CKD-EPI	Chronic Kidney Disease Epidemiology Collaboration
CMH	Cochran-Mantel Haenszel
COVID-19	Coronavirus Disease 2019
CPMS	Clinical Pharmacology Modelling & Simulation
CS	Clinical Statistics
CSR	Clinical Study Report
C-SSRS	Columbia Suicide Severity Rating Scale
CTR	Clinical Trial Register
CVF	Confirmed Virologic Failure
mCVF	Modified Confirmed Virologic Failure
c/mL	Copies/milliliter
D2I	Direct to Inject
DAIDS	Division of Acquired Immunodeficiency Syndrome
DBF	Database Freeze
DBR	Database Release
DNA	Deoxyribonucleic acid
DOB	Date of Birth
DP	Decimal Places
ECG	Electrocardiogram
eCRF	Electronic Case Record Form

Abbreviation	Description
eGFR	Estimated Glomerular Filtration Rate
EMA	European Medicines Agency
ERDF	Efficacy Related Discontinuation Failure
FDA	Food and Drug Administration
FDAAA	Food and Drug Administration Clinical Results Disclosure Requirements
GSK	GSK
HAART	Highly active antiretroviral therapy
HBV	Hepatitis B virus
HbA1c	Glycated hemoglobin
HbsAg	Hepatitis B surface Antigen
HCV	Hepatitis C virus
HDL	High density lipoprotein
HIV	Human Immunodeficiency Virus
HIVTSQc	Change Version of HIV Treatment Satisfaction Questionnaire
IDMC	Independent Data Monitoring Committee
IDSL	Integrated Data Standards Library (GSK Standards Library)
IM	Intramuscular
IMMS	International Modules Management System
INI	Integrase Inhibitor
INR	International normalized ratio
INSTI	Integrase strand transfer inhibitor
IP	Investigational Product
ISR	Injection Site Reaction
ITT	Intent-To-Treat
ITT-E	Intent-To-Treat Exposed
mITT-E	Modified Intent-To-Treat Exposed
LA	Long Acting
LDL	Low density lipoprotein
LPV	Lopinavir
LPV/r	Lopinavir-ritonavir
LTFU	Long-Term Follow-Up
MMRM	Mixed Model Repeated Measures
NNRTI	Non-nucleoside Reverse Transcriptase Inhibitor
NRTI	Nucleoside Reverse Transcriptase Inhibitor
OLI	Oral Lead In
PBMC	Peripheral Blood Mononuclear Cell
PCI	Potential Clinical Importance
PD	Pharmacodynamic
PDMP	Protocol Deviation Management Plan
PI	Protease Inhibitor
PIN	Perception of Injection
PK	Pharmacokinetic

Abbreviation	Description
PopPK	Population PK
PP	Per Protocol
PRO	Protease
PTT	Partial Thromboplastin Time
PSRAE	Possible suicidality-related adverse event
Q2M	Every 2 Months
QC	Quality Control
QTcF	Frederica's QT Interval Corrected for Heart Rate
QTcB	Bazett's QT Interval Corrected for Heart Rate
RAL	Raltegravir
RAMOS	Randomization & Medication Ordering System
RAP	Reporting & Analysis Plan
RBP	Retinol Binding Protein
RNA	Ribonucleic acid
RPR	Rapid plasma reagin
RPV	Rilpivirine, Edurant
RPV LA	Rilpivirine long-acting
RT	Reverse transcriptase
RTV	Ritonavir
SAE	Serious Adverse Event
SAC	Statistical Analysis Complete
SDSP	Study Data Standardization Plan
SDTM	Study Data Tabulation Model
SMQ	Standardised MedDRA Query
SOC	System Organ Class or Standard of Care
SOP	Standard Operation Procedure
SRM	Study Reference Manual
TDF	Tenofovir disoproxil fumarate
TFL	Tables, Figures & Listings
TRDF	Treatment Related Discontinuation Failure
ULN	Upper limit of normal

16.14.2. Trademarks

Trademarks of the GSK Group of Companies
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16.15. Appendix 15: List of Data Displays

16.15.1. 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
Health Outcomes	6.1 to 6.n	6.1 to 6.n
Virology	7.01 to 7.n	7.01 to 7.n
Section	**Listings**	
ICH Listings	1 to x	
Other Listings	y to z	

* For the Month 12 analysis, only listings will be provided for the Pharmacokinetic section. The numbers for Table/Figures are reserved for future reports if applicable.

16.15.2. Mock Example Shell Referencing

Nonstandard specifications will be referenced as indicated and if required example mock-up displays will be provided in Appendix 16: Example Mock Shells for Data Displays or in a separate document:

Section	Description
HL	Headline
M6	Month 6 (OLI and BIK)/Month 5 (D2I)
M12	Month 12 (OLI and BIK)/Month 11 (D2I)

16.15.3. Deliverables

Delivery [Priority] [1,3]	Description
Month 6	Interim analysis when all participants have completed their Month 6 (OLI and BIK)/Month 5 (D2I) visit[2]
Month 12	Primary analysis when all participants have completed their Month 12 (OLI and BIK)/Month 11 (D2I) visit
EOS	Final End of Study analysis

NOTES:

1. Indicates priority (i.e. order) in which displays will be generated for the reporting effort
2. Will not be shared with any participant and with most investigators. See Section 3.1 for details.
3. The Month 6(OLI and BIK)/Month 5(D2I) and the Month 12(OLI and BIK)/Month 11(D2I) analyses may also be referred to as the “Month 6” and “Month 12” analysis, respectively.

16.15.4. Study Population Tables

Note analysis population below has been updated to reflect the M12 analysis plan. In the Month 6 analysis, ITT-E was used prior to this amendment.

Study Population Tables					
No.	**Population**	**GSK Standard / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
Subject Disposition					
1.1.	Screened	ES6	Summary of Screening Status and Reasons for Screen Failures		M6, M12
1.2.	Enrolled	NS1	Summary of Number of Subjects Enrolled by Country and Site ID	Only include "no treatment" if there is any enrolled but not randomized. Column Header style 2.	M6, M12
1.3.	mITT-E	Shell POP_T1	Summary of Subject Accountability: Study and Phase Conclusion Record	See 207966/primary_15/T1.3 Include the sections: "Outcome of Adverse Events Which Led to Study Withdrawal" (Fatal and Non-Fatal); "Type of Adverse Events Which Led to Study Withdrawal" (COVID-19 and Non-COVID-19)	HL, M6, M12, EOS
1.4.	mITT-E	Shell POP_T4	By Phase Summary of Subject Disposition	201584/primary_07/T1.14	M12, EOS
1.5.	mITT-E	HIV_ES1	Summary of Reasons for Withdrawals by Visit (Maintenance Phase)	201584/ primary_07/T1.9	M6, M12
1.6.	mITT-E	ES1	Summary of Study Drug Discontinuation	mid207966/primary_15/T1.10. Include the sections for fatal/non-fatal, COVID/Non-COVID	M6, M12, EOS

Study Population Tables					
No.	**Population**	**GSK Standard / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
Protocol Deviation					
1.7.	mITT-E	Shell POP_T2	Summary of Important Protocol Deviations	ICH E3	M6, M12, EOS
1.8.	mITT-E	IE1	Summary of Inclusion/Exclusion Criteria Deviations	Header Style 1	M6, M12
Population Analysed					
1.9.	Screened	Shell POP_T3	Summary of Study Populations		HL, M6, M12, EOS
1.10.	mITT-E	Shell POP_T2	Summary of Protocol Deviations Leading to Exclusion from the Per-Protocol Population - (Month X Analysis)	[X =12 or 6] Add footnote: Month 6 Analysis: Month 6 (OLI and BIK)/Month 5 (D2I) or Month 12 Analysis: Month 12 (OLI and BIK)/Month 11 (D2I)	M6, M12
Demographic and Baseline Characteristics					
1.11.	mITT-E	mid207966/primary_15/T1.16	Summary of Demographic Characteristics		HL, M6, M12
1.12.	Screened	mid207966/primary_15/T1.17	Summary of Age Ranges	Including a column for No treatment	M6, M12
1.13.	mITT-E	DM6	Summary of Race and Racial Combinations Details		M6, M12
1.14.	mITT-E	mid207966/primary_15/T1.20	Summary of Hepatitis Status at Entry		M6, M12
1.15.	mITT-E	CDC1	Summary of CDC Stages of HIV Infection at Maintenance Baseline		M6, M12

Study Population Tables					
No.	**Population**	**GSK Standard / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
1.16.	mITT-E	mid207966/primary_15/T1.23	Distribution of CD4+ Cell Count Results at Screening and Maintenance Baseline		M6, M12
1.17.	mITT-E	mid207966/primary_15/T1.25	Summary of HIV Risk Factors		M6, M12
Prior and Concomitant Medications					
1.18.	mITT-E	MH1	Summary of Current and Past Medical Conditions	Combine the current and past displays, by adding section headers: “Current”, “Past”	M6, M12
1.19.	mITT-E	MH4	Summary of Current and Past Cardiac, Gastrointestinal, Metabolism and Nutrition, Psychiatric, Renal and Urinary, Nervous System Conditions, and Hepatobiliary Disorders	Combine the two displays, by adding section headers: “Current”, “Past”	M6, M12
1.20.	mITT-E	CA3	Summary of Prior ART Medications		M6, M12
1.21.	mITT-E	CM8	Summary of Concomitant Non-ART Medication Ingredient Combinations - Maintenance Phase		M6, M12
1.22.	mITT-E	mid207966/primary_15/T1.33	Summary of Lipid Modifying Agent Use at Baseline and During Maintenance Phase	Combine the two displays, by adding a section header: “Maintenance Baseline”, “Started During Maintenance Phase”	M6, M12
1.23.	mITT-E	mid207966/primary_15/T1.35	Summary of Substance and Illicit Drug Use at Entry		M6, M12
COVID-19 Pandemic Impact					
1.24.	mITT-E	PAN4	Summary of Visits impacted by COVID-19 Pandemic		M6, M12, EOS

16.15.5. Efficacy Tables

Note: For subgroup analyses, include randomization strata, all demographic and baseline characteristic subgroups as mentioned in EMA Subgroup Category 2 in Section 5.4.2 if applicable, unless otherwise specified.

Note analysis population below has been updated to reflect the M12 analysis plan. In the Month 6 analysis, ITT-E and CVF were used prior to this amendment.

Efficacy: Tables					
No.	**Population**	**GSK Standard / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
Primary Efficacy Analyses					
2.1.	mITT-E	Shell EFF_T3	Summary of Analysis for Proportion of Subjects with Plasma HIV-1 RNA >=50 c/mL at Month 12 (OLI and BIK)/Month 11 (D2I) - Maintenance Phase - Snapshot Analysis - mITT-E	Q2M vs BIK. For Month 6/5 deliverable: replace “Month 12 (OLI and BIK) and Month 11 (D2I)” with “Month 6 (OLI and BIK) and Month 5 (D2I)”.	HL, M6, M12
2.2.	PP	Shell EFF_T3	Summary of Analysis for Proportion of Subjects with Plasma HIV-1 RNA >=50 c/mL at Month 12 (OLI and BIK)/Month 11 (D2I) - Maintenance Phase - Snapshot Analysis – Per Protocol	Q2M vs BIK. For Month 6/5 deliverable: replace “Month 12 (OLI and BIK) and Month 11 (D2I)” with “Month 6 (OLI and BIK) and Month 5 (D2I)”.	HL, M6, M12
2.3.	ITT-E	Shell EFF_T3	Summary of Analysis for Proportion of Subjects with Plasma HIV-1 RNA >=50 c/mL at Month 12 (OLI and BIK)/Month 11 (D2I) - Maintenance Phase - Snapshot Analysis – ITT-E (Efficacy Sensitivity)		M12

Efficacy: Tables					
No.	**Population**	**GSK Standard / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
2.4.	mITT-E	Shell EFF_T3	Summary of Analysis for Proportion of Subjects with Plasma HIV-1 RNA >=50 c/mL at Month 12 (OLI and BIK)/Month 11 (D2I) - Maintenance Phase - Snapshot Analysis - mITT-E (All Data as Observed)	Only required if there is any confirmed pregnancy on the Q2M arm.	M6, M12
2.5.	mITT-E	Shell EFF_T1	Summary of Study Outcomes (50 c/mL Threshold) at Month 12 (OLI and BIK)/Month 11 (D2I) - Maintenance Phase - Snapshot Analysis – Overall and by subgroup	For Month 6/5 deliverable: replace “Month 12 (OLI and BIK) and Month 11 (D2I)” with “Month 6 (OLI and BIK) and Month 5 (D2I)”. Add section header for “Overall” and “Subgroup:xx:xx”	HL (overall only), M6, M12
2.6.	ITT-E	Shell EFF_T1	Summary of Study Outcomes (50 c/mL Threshold) at Month 12 (OLI and BIK)/Month 11 (D2I) - Maintenance Phase - Snapshot Analysis – ITT-E (Efficacy Sensitivity)	Overall only	M12
2.7.	mITT-E	Shell EFF_T1	Summary of Study Outcomes (50 c/mL Threshold) at Month 12 (OLI and BIK)/Month 11 (D2I) - Maintenance Phase - Snapshot Analysis (All Data as Observed)	Only required if there is any confirmed pregnancy on the Q2M arm.	M6, M12
2.8.	mITT-E	SNAPSHOT3A	Treatment by Strata Tests of Homogeneity for Proportion of Subjects with Plasma HIV-1 RNA >=50 c/mL at Month 12 (OLI and BIK)/Month 11 (D2I) - Maintenance Phase - Snapshot Analysis	Q2M vs BIK. For Month 6/5 deliverable: replace “Month 12 (OLI and BIK) and Month 11 (D2I)” with “Month 6 (OLI and BIK) and Month 5 (D2I)”. For code refer to mid207966/primary_15/T2.10	M12

Efficacy: Tables					
No.	**Population**	**GSK Standard / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
2.9.	mITT-E	SNAPSHOT5	Summary of Analysis for Proportion of Subjects with Plasma HIV-1 RNA >=50 c/mL at Month 12 (OLI and BIK)/Month 11 (D2I) by Subgroup - Maintenance Phase - Snapshot Analysis	Q2M vs BIK. For Month 6/5 deliverable: replace "Month 12 (OLI and BIK) and Month 11 (D2I)" with "Month 6 (OLI and BIK) and Month 5 (D2I)". For code refer to mid207966/primary_15/T2.5	M12
Secondary Efficacy Analyses					
2.10.	mITT-E	Shell EFF_T3	Summary of Analysis for Proportion of Subjects with Plasma HIV-1 RNA < 50 c/mL at Month 12 (OLI and BIK)/Month 11 (D2I) - Maintenance Phase - Snapshot Analysis - mITT-E	Q2M vs BIK. For Month 6/5 deliverable: replace "Month 12 (OLI and BIK) and Month 11 (D2I)" with "Month 6 (OLI and BIK) and Month 5 (D2I)".	HL, M6, M12
2.11.	PP	Shell EFF_T3	Summary of Analysis for Proportion of Subjects with Plasma HIV-1 RNA < 50 c/mL at Month 12 (OLI and BIK)/Month 11 (D2I) - Maintenance Phase - Snapshot Analysis – Per Protocol	Q2M vs BIK. For Month 6/5 deliverable: replace "Month 12 (OLI and BIK) and Month 11 (D2I)" with "Month 6 (OLI and BIK) and Month 5 (D2I)".	HL, M6, M12
2.12.	ITT-E	Shell EFF_T3	Summary of Analysis for Proportion of Subjects with Plasma HIV-1 RNA < 50 c/mL at Month 12 (OLI and BIK)/Month 11 (D2I) - Maintenance Phase - Snapshot Analysis – ITT-E (Efficacy Sensitivity)		M12
2.13.	mITT-E	Shell EFF_T3	Summary of Analysis for Proportion of Subjects with Plasma HIV-1 RNA <50 c/mL at Month 12 (OLI and BIK)/Month 11 (D2I) - Maintenance Phase - Snapshot Analysis - mITT-E (All Data as Observed)	Only required if there is any confirmed pregnancy on the Q2M arm.	M6, M12

Efficacy: Tables					
No.	**Population**	**GSK Standard / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
2.14.	mITT-E	SNAPSHOT3A	Treatment by Strata Tests of Homogeneity for Proportion of Subjects with Plasma HIV-1 RNA < 50 c/mL at Month 12 (OLI and BIK)/Month 11 (D2I) - Maintenance Phase - Snapshot Analysis	Q2M vs BIK. For Month 6/5 deliverable: replace "Month 12 (OLI and BIK) and Month 11 (D2I)" with "Month 6 (OLI and BIK) and Month 5 (D2I)".	M12
2.15.	mITT-E	SNAPSHOT5	Summary of Analysis for Proportion of Subjects with Plasma HIV-1 RNA < 50 c/mL at Month 12 (OLI and BIK) and Month 11 (D2I) by Subgroup - Maintenance Phase - Snapshot Analysis	Q2M vs BIK. For Month 6/5 deliverable: replace "Month 12 (OLI and BIK) and Month 11 (D2I)" with "Month 6 (OLI and BIK) and Month 5 (D2I)".	M12
2.16.	mITT-E	SNAPSHOT4	Proportion of Subjects with Plasma HIV-1 RNA ≥50 c/mL by Visit (Maintenance Phase) – Snapshot Analysis	For code refer to mid207966/primary_15/T2.13	M6, M12
2.17.	mITT-E	SNAPSHOT4	Proportion of Subjects with Plasma HIV-1 RNA ≥50 c/mL by Visit	Only required if there is any confirmed pregnancy on the Q2M arm.	M6, M12, EOS
2.18.	mITT-E	SNAPSHOT6	Proportion of Subjects with Plasma HIV-1 RNA >=50 c/mL by Subgroup and Visit (Maintenance Phase) – Snapshot Analysis	For code refer to mid207966/primary_15/T2.14	M12
2.19.	mITT-E	SNAPSHOT4	Proportion of Subjects with Plasma HIV-1 RNA <50 c/mL by Visit (Maintenance Phase) – Snapshot Analysis		M6, M12

Efficacy: Tables					
No.	**Population**	**GSK Standard / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
2.20.	mITT-E	SNAPSHOT4	Proportion of Subjects with Plasma HIV-1 RNA <50 c/mL by Visit		M6, M12, EOS
2.21.	mITT-E	SNAPSHOT6	Proportion of Subjects with Plasma HIV-1 RNA <50 c/mL by Subgroup and Visit (Maintenance Phase) – Snapshot Analysis		M12
2.22.	mITT-E	SNAPSHOT4	Proportion of Subjects with Plasma HIV-1 RNA <200 c/mL by Visit (Maintenance Phase) – Snapshot Analysis		M6, M12
2.23.	mITT-E	SNAPSHOT4	Proportion of Subjects with Plasma HIV-1 RNA >=200 c/mL by Visit (Maintenance Phase) – Snapshot Analysis		M6, M12
2.24.	mITT-E	Shell EFF_T1	Summary of Study Outcomes (200 c/mL Threshold) at Month 12 (OLI and BIK)/Month 11 (D2I) (Maintenance Phase) – Snapshot Analysis	For Month 6/5 deliverable, replace “Month 12 (OLI and BIK) and Month 11 (D2I)” with “Month 6 (OLI and BIK) and Month 5 (D2I)” No subgroup needed	M6, M12
2.25.	mITT-E	mid207966/primary_15/2.19	Summary of Kaplan-Meier Estimates of Proportion of Subjects Without Confirmed Virologic Failure at Month 12 (OLI and BIK) /Month 11 (D2I) - Treatment Related Discontinuation = Failure	For Month 6/5 deliverable, replace “Month 12 (OLI and BIK) and Month 11 (D2I)” with “Month 6 (OLI and BIK) and Month 5 (D2I)”	M6, M12

Efficacy: Tables					
No.	**Population**	**GSK Standard / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
2.26.	mITT-E	mid207966/primary_15/T 2.20	Summary of Kaplan-Meier Estimates of Proportion of Subjects Without Confirmed Virologic Failure at Month 12 (OLI and BIK) /Month 11 (D2I) - Efficacy Related Discontinuation = Failure	For Month 6/5 deliverable, replace "Month 12 (OLI and BIK) and Month 11 (D2I)" with "Month 6 (OLI and BIK) and Month 5 (D2I)"	M6, M12
2.27.	mITT-E	mid207966/primary_15/T2.21	Proportion of Subjects with HIV-1 RNA >=50 c/mL at Month 12 (OLI and BIK)/Month 11 (D2I) (Snapshot) by Last Delay in IP Injection (Maintenance Phase)		M6, M12
2.28.	mITT-E	mid207966/primary_15/T2.38	Summary of Change from Maintenance Baseline (Day 1) in Plasma HIV-1 RNA (log10 c/mL) by Visit		M6, M12, EOS
2.29.	mITT-E	mid207966/primary_15/T2.23	Cumulative Proportion of Subjects Meeting Confirmed Virologic Failure Criteria by Visit During	Up to Month 13/14	HL, M6, M12, EOS
2.30.	mCVF	mid207966/primary_15/T2.25	By Phase Distribution of Quantitative Plasma HIV-1 RNA Results at Suspected and Confirmation of Confirmed Virologic Failure		M6, M12, EOS
2.31.	mITT-E	mid207966/primary_15/T2.28	Summary of Viral Load Category by Visit (Maintenance Phase)	Q2M and BIK only	M12

Efficacy: Tables					
No.	**Population**	**GSK Standard / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
2.32.	mITT-E	Shell EFF_T2	Summary of Change from Maintenance Baseline (Day 1) in CD4+ Cell Count (cells/mm^3) by Visit - Overall		M6, M12, EOS
2.33.	mITT-E	Shell EFF_T2	Summary of Change from Maintenance Baseline (Day 1) in CD8+ Cell Count (cells/mm^3) by Visit - Maintenance Phase	Baseline, M5/6, M11/12 No subgroup	M6, M12
2.34.	mITT-E	Shell EFF_T2	Summary of CD4+/CD8+ Cell Count Ratio by Visit – Maintenance Phase	Baseline, M5/6, M11/12 No subgroup	M6, M12
2.35.	mITT-E	CDC2	By Phase Summary of Stage-3 HIV-1 Associated Conditions	Add section header for "Including Recurrences" and "Excluding Recurrences"	M6, M12. EOS
CCI [redacted]					

16.15.6. Efficacy Figures

Note analysis population below has been updated to reflect the M12 analysis plan. In the Month 6 analysis, ITT-E was used prior to this amendment.

Efficacy: Figures					
No.	**Population**	**GSK Standard / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
Primary Efficacy Analyses					
1.	mITT-E	mid207966/primary_15/F2.1	Proportion (95% CI) of Subjects with HIV-1 RNA ≥50 c/mL by Visit (Maintenance Phase) – Snapshot Analysis		M6, M12
2.	mITT-E	mid207966/primary_15/F2.2	Unadjusted Treatment Difference in Proportion (95% CI) of Subjects with HIV-1 RNA ≥50 c/mL at Month 12 (OLI and BIK)/Month 11 (D2I) by Subgroup – Snapshot Analysis		M12
Secondary CCI [redacted] **Efficacy Analyses**					
3.	mITT-E	mid207966/primary_15/F2.3	Proportion (95% CI) of Subjects with HIV-1 RNA <50 c/mL by Visit (Maintenance Phase) – Snapshot Analysis		M6, M12
4.	mITT-E	mid207966/primary_15/F2.4	Unadjusted Treatment Difference in Proportion (95% CI) of Subjects with HIV-1 RNA <50 c/mL at Month 12 (OLI and BIK)/Month 11 (D2I) by Subgroup – Snapshot Analysis		M12
5.	CVF	mid207966/primary_15/F2.7	CCI [redacted] (log10 c/mL) Profiles by Visit for CVF Subjects		M6, M12, EOS

Efficacy: Figures					
No.	**Population**	**GSK Standard / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
6.	ITT-E	mid207966/primary_15/F2.8	Individual [CCI redacted] (log10 c/mL) Profiles by Visit for subjects Who are in the Category of 'HIV-1 RNA >=50 c/mL' at Month 12 (OLI and BIK)/Month 11 (D2I) per Snapshot Algorithm	For Month 6/5 deliverable, replace "Month 12 (OLI and BIK) and Month 11 (D2I)" with "Month 6 (OLI and BIK) and Month 5 (D2I)"	M6, M12

16.15.7. Safety Tables

Note: For the Month 6 analysis, remove "By Phase" in the title if applicable and add to the end "(Maintenance Phase)", unless otherwise noted.

Safety: Tables					
No.	**Population**	**GSK Standard/ Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
Exposure					
3.1.	Safety	Shell SAF_T2a and SAF_T2b	**By Phase** Summary of Extent of Exposure to Study Treatment including SOC Oral Bridging	ICH E3	M6, M12, EOS
3.2.	Safety	Shell SAF_T3	Summary of Needle Length and Gauge for CAB and RPV Injections (Maintenance Phase)		M6, M12
3.3.	Safety	mid207966/primary_15/T3.5	Summary of Adherence to CAB/RPV Injection Dosing Schedule (Maintenance Phase)		M6, M12

Safety: Tables					
No.	**Population**	**GSK Standard/ Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
Adverse Events					
3.4.	Safety	Shell SAF_T1a and SAF_T1b	**By Phase** Summary of All Adverse Events by System Organ Class and Preferred Term	ICH E3	M6, M12
3.5.	Safety	Shell SAF_T4a and Shell SAF_T4b	**By Phase** Summary of All Adverse Events by System Organ Class, Preferred Term and Maximum Toxicity	ICH E3 Include Unknown column if at last 1 AE exists with a missing/unknown toxicity grade mid207966/primary_15/T3.7	HL, M6, M12, EOS
3.6.	Safety	Shell SAF_T4a and Shell SAF_T4b	**By Phase** Summary of All Adverse Events Excluding Injection Site Reactions by System Organ Class, Preferred Term and Maximum Grade Toxicity		HL, M6, M12, EOS
3.7.	Safety	AE3	By Phase Summary of Common Adverse Events (>=5%) by Overall Frequency	ICH E3 mid207966/primary_15/T3.11	M6, M12, EOS
3.8.	Safety	AE3	By Phase Summary of Common Grade 2-5 Adverse Events (>=1%) by Overall Frequency	ICH E3 mid207966/primary_15/T3.12	M6, M12, EOS
3.9.	Safety	Shell SAF_T1a and SAF_T1b	**By Phase** Summary of All Drug-Related Adverse Events by System Organ Class and Preferred Term	ICH E3	M6, M12
3.10.	Safety	Shell SAF_T4a and Shell SAF_T4b	**By Phase** Summary of All Drug-Related Adverse Events by System Organ Class, Preferred Term and Maximum Toxicity	ICH E3	HL, M6, M12, EOS
3.11.	Safety	Shell SAF_T4a and Shell SAF_T4b	**By Phase** Summary of All Drug-Related Adverse Events Excluding Injection Site Reactions by System Organ Class, Preferred Term and Maximum Toxicity	ICH E3 For Month 6: remove “By Phase” and add “(Maintenance Phase)” to the end	HL, M6, M12, EOS

Safety: Tables					
No.	**Population**	**GSK Standard/ Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
3.12.	Safety	AE3	By Phase Summary of All Drug-Related Grade 2-5 Adverse Events by Overall Frequency	mid207966/primary_15/T3.17	M6, M12, EOS
Serious and Other Significant Adverse Events					
3.13.	Safety	Shell SAF_T1a and SAF_T1b	**By Phase** Summary of Serious Adverse Events by System Organ Class and Preferred Term	ICH E3	HL, M6, M12, EOS
3.14.	Safety	Shell SAF_T1a and SAF_T1b	**By Phase** Summary of Drug-Related Serious Adverse Events by System Organ Class and Preferred Term		M6, M12, EOS
3.15.	Safety	AE3	**By Phase** Summary of Non-Fatal Serious Adverse Events by Overall Frequency	mid207966/primary_15/T3.23	M6, M12
3.16.	Safety	AE3	**By Phase** Summary of Drug-Related Non-Fatal Serious Adverse Events by Overall Frequency	mid207966/primary_15/T3.24	M6, M12, EOS
3.17.	Safety	Shell SAF_T1a and SAF_T1b	**By Phase** Summary of Adverse Events Leading to Withdrawal/Permanent Discontinuation of Investigational Product by System Organ Class and Preferred Term		HL, M6, M12, EOS
3.18.	Safety	AE3	Summary of Common (>=5%) Non-Serious Adverse Events by System Organ Class and Preferred Term (Maintenance Phase)		M6, M12

Safety: Tables					
No.	**Population**	**GSK Standard/ Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
3.19.	Safety	AE15	Summary of Subjects and Number of Occurrences of Common (>=5%) Non-Serious Adverse Events by System Organ Class and Preferred Term (Maintenance Phase)	mid207966/primary_15/T3.28	M6, M12
3.20.	Safety	AE16	**By Phase** Summary of Subjects and Number of Occurrences of SAEs, Fatal SAEs, and Drug-related SAEs by System Organ Class and Preferred Term	mid207966/primary_15/T3.29	M6, M12, EOS
3.21.	Safety	Shell SAF_T5	Summary of Cumulative Adverse Events by Preferred Term and Visit (Maintenance Phase)	mid207966/primary_15/T3.30	M6, M12
Injection Site Reaction Adverse Events					
3.22.	Safety	207966/primary_15/T3.31	By Phase Event-level Summary of Injection Site Reaction Adverse Events by Preferred Term	Include Overall ISR as a Preferred Term D2I, OLI and Q2M	HL, M6, M12. EOS
3.23.	Safety	207966/primary_15/T3.33	Summary of Overall and Common Subject-level Characteristics of Injection Site Reaction Adverse Events by Preferred Term (Maintenance Phase)	Include Overall ISR as a Preferred Term D2I, OLI and Q2M Common ISR includes pain, induration, nodules and any other ISR with ≥5% subjects among randomized Q2M arm	M6, M12
3.24.	Safety	207966/primary_15/T3.36 and T3.40	Event-level Summary of Drug-Related Injection Site Reaction Adverse Events **by Investigational Product** and Preferred Term (Maintenance Phase)	Include Overall ISR as a Preferred Term D2I, OLI and Q2M Investigational Product: “CAB LA” or “RPV LA”, “CAB/RPV LA”	M6, M12

Safety: Tables					
No.	**Population**	**GSK Standard/ Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
3.25.	Safety	207966/primary_15/T3.37 and T3.41	Summary of Overall and Common Subject-level Characteristics of Drug-Related Injection Site Reaction Adverse Events **by Investigational Product** and Preferred Term (Maintenance Phase)	Include Overall ISR as a Preferred Term D2I, OLI and Q2M Investigational Product:"CAB LA" or "RPV LA", "CAB/RPV LA"	M6, M12
3.26.	Safety	207966/primary_15/T3.35	Summary of Overall and Common Injection Site Reaction Adverse Events by Preferred Term, Visit, and Maximum Severity (Maintenance Phase)	Include Overall ISR as a Preferred Term D2I, OLI and Q2M	M6, M12
3.27.	Safety	207966/primary_15/T3.38 and T3.42	Summary of Overall and Common Drug-Related Injection Site Reaction Adverse Events by **Investigational Product,** Preferred Term, Visit and Maximum Severity(Maintenance Phase)	Include Overall ISR as a Preferred Term D2I, OLI and Q2M Investigational Product: "CAB LA" or "RPV LA", "CAB/RPV LA"	M6, M12
3.28.	Safety	207966/primary_15/T3.39 and T3.43	Summary of Maximum Drug-Related Injection Site Reaction Adverse Event Grade **by Investigational Product,** Preferred Term and Needle Length (Maintenance Phase) - Common ISRs	Do not include Overall ISR as a Preferred Term D2I, OLI and Q2M Investigational Product: "CAB LA" or "RPV LA"	M6, M12
Laboratory: Chemistry and Hematology					
3.29.	Safety	Shell SAF_T6	Summary of Chemistry Changes from Baseline by Visit	ICH E3	M6, M12, EOS
3.30.	Safety	Shell SAF_T7	By Phase Summary of Maximum Emergent Chemistry Toxicities	207966/primary_15/T3.48	M6, M12, EOS
3.31.	Safety	Shell SAF_T6	Summary of Hematology Changes from Baseline by Visit	ICH E3	M6, M12, EOS

Safety: Tables					
No.	**Population**	**GSK Standard/ Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
3.32.	Safety	Shell SAF_T7	By Phase Summary of Maximum Emergent Hematology Toxicities	207966/primary_15/T3.50	M6, M12, EOS
Laboratory: Urinalysis					
3.33.	Safety	207966/primary_15/T3.39 and T3.52	Summary of Urinalysis Dipstick Results by Visit (Maintenance Phase)		M6, M12
3.34.	Safety	Shell SAF_T6	Summary of Urine Concentrations Changes from Baseline by Visit (Maintenance Phase)	207966/primary_15/ T3.53	M6, M12
3.35.	Safety	207966/primary_15/ T3.53	Summary of Changes in Proteinuria Baseline Laboratory Result to Maximum Post-Baseline Laboratory Result (Maintenance Phase)		M6, M12
Laboratory: Lipids					
3.36.	Safety	207966/primary_15/ T3.55	Summary of Changes from Maintenance Baseline (Day 1) NCEP Fasting Lipid Category to Maximum Maintenance Phase Category – Triglycerides		M6, M12
3.37.	Safety	207966/primary_15/ T3.56	Summary of Changes from Maintenance Baseline (Day 1) NCEP Fasting Lipid Category to Maximum Maintenance Phase Category – Total Cholesterol		M6, M12
3.38.	Safety	207966/primary_15/ T3.57	Summary of Changes from Maintenance Baseline (Day 1) NCEP Fasting Lipid Category to Minimum Maintenance Phase Category – HDL Cholesterol		M6, M12

Safety: Tables					
No.	**Population**	**GSK Standard/ Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
3.39.	Safety	207966/primary_15/ T3.58	Summary of Changes from Maintenance Baseline (Day 1) NCEP Fasting Lipid Category to Maximum Maintenance Phase Category – LDL Cholesterol		M6, M12
3.40.	Safety	207966/primary_15/ T3.59	Summary of Fasting Lipids Percentage Changes from Baseline by Visit (Lipid Evaluable) - Maintenance Phase		M6, M12
3.41.	Safety	207966/primary_15/ T3.60	Summary of Fasting TC/HDL Ratio Changes from Maintenance Baseline (Day 1) (Maintenance Phase) – Lipid Evaluable		M6, M12
Laboratory: Hepatobiliary (Liver)					
3.42.	Safety	LIVER1	By Phase Summary of Liver Monitoring/Stopping Event Reporting	GSK Statistical Display Standard 207966/primary_15/ T3.61	M6, M12, EOS
3.43.	Safety	207966/primary_15/ T3.62	By Phase Summary of Subjects Meeting Hepatobiliary Abnormality Criteria	GSK Statistical Display Standard Include 2 sections: OLI, Maintenance(See SAF_T7 for section headers)	M6, M12, EOS
Bone, Renal, Inflammation, Insulin Resistance Markers and [redacted]					
3.44.	Safety	SAF_T8	Summary of Changes from Maintenance Baseline (Day 1) - Bone, Renal, Inflammation and Insulin Resistance Markers (Maintenance Phase)	Ass section header: Bone Markers/Renal Markers/ [redacted] /Insulin Resistance Markers HOMA-IR for insulin resistance marker Q2M vs. BIK	M12
3.45.	Safety	SAF_T11	Summary of Shift in HOMA-Insulin Resistance Categories from Baseline by Visit (Maintenance Phase)		M12

Safety: Tables					
No.	**Population**	**GSK Standard/ Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
3.46.	Safety	SAF_T9	Statistical Analysis of Log-Transformed Ratio to Baseline in HOMA-Insulin Resistance - MMRM	201584 primary_16/T6.08	M12
3.47.	Safety	SAF_T10	Statistical Analysis of Proportion of Subjects with HOMA-IR ≥2, >=3 and >=4 at M12 (OLI and BIK) /M11(D2I) – Logistic Regression	See Section 8.5.4 for details. Note: Subjects with evidence of pre-study diabetes (via medical history or prior medications) are excluded.	M12
3.48.	Safety	SAF_T9	Statistical Analysis of Log-Transformed Ratio to Baseline in Bone Markers - MMRM	201584 primary_16/T6.08	M12
3.49.	Safety	SAF_T9	Statistical Analysis of Log-Transformed Ratio to Baseline in Renal Markers- MMRM	201584 primary_16/T6.08	M12
3.50.	Safety	SAF_T9	Statistical Analysis of Log-Transformed Ratio to Baseline in CCI [redacted] - MMRM	201584 primary_16/T6.08	M12
3.51.	Safety	SAF_T8	Summary of Change from Baseline in CCI [redacted] by Visit	Include baseline	M12
ECG					
3.52.	Safety	EG1	Summary of ECG Findings (Maintenance Phase)	207966/primary_15/T3.64	M12
3.53.	Safety	EG2	Summary of Change from Baseline in ECG Values by Visit (Maintenance Phase)		M12

Safety: Tables					
No.	**Population**	**GSK Standard/ Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
3.54.	Safety	EG10	Summary of QTc Values by Category (Maintenance Phase)	207966/primary_15/T3.66	M12
3.55.	Safety	EG10	Summary of Change from Baseline QTc Values by Category (Maintenance Phase)	207966/primary_15/T3.67	M12
Vital Signs and Anthropometric Profile					
3.56.	Safety	VS1	By Phase Summary of Change from Baseline in Vital Signs by Visit	Q2M and BIK only	M6, M12, EOS
3.57.	Safety	SAF_T12	Summary of Shift in BMI Categories from Baseline by Visit **(Overall and By Strata)** – Maintenance Phase	Q2M and BIK only 207966/primary_15/T3.70 Month 5/6 and Month 11/12 For month 6 remove " by visit" Only include Gender, as BMI is already one of the stratification factors (M12)	M6, M12
3.58.	Safety	SAF_T13	Summary of Change from Baseline in Weight and BMI by Gender, Baseline BMI, Race and by Visit (Maintenance Phase)	Q2M and BIK only 207966/primary_15/T3.71 Month 5/6 and Month 11/12 For month 6 remove " by visit". Do not need overall	M6, M12

Safety: Tables					
No.	**Population**	**GSK Standard/ Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
3.59.	Safety	SAF_T14	Summary of Percent Change from Baseline in Weight (Maintenance Phase)	Q2M and BIK only	M6. M12
3.60.	Safety	VS1	Summary of Anthropometric Parameters by Visit (Lipid Evaluable)	Q2M and BIK only. Include all planned visits Include: weight, height, BMI, waist and hip circumference, CCI [redacted] and Tanita scale measurements (total body Fat %, bone mass, musl mass, TBW%)	M6
3.61.	Safety	VS1	Summary of Anthropometric Parameters by Visit Excluding Subjects with Cosmetic procedures (Lipid Evaluable)	Q2M and BIK only add footnote: Cosmetic procedures include procedures of the torso/thighs (exclude face/neck) including but not limited to liposuction/liposculpture/implants.	M12
3.62.	Safety	VS1	Summary of Change from Baseline in Anthropometric Parameters by Visit (Lipid Evaluable)	Q2M and BIK only Same parameters as 3.60	M6

Safety: Tables					
No.	**Population**	**GSK Standard/ Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
3.63.	Safety	VS1	Summary of Change from Baseline in Anthropometric Parameters by Visit Excluding Subjects with Cosmetic Procedures (Lipid Evaluable)	Q2M and BIK only add footnote: Cosmetic procedures include procedures of the torso/thighs (exclude face/neck) including but not limited to liposuction/liposculpture/implants.	M12

Safety: Tables					
No.	**Population**	**GSK Standard/ Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
Metabolic Syndrome					
3.64.	Safety	SAF_T15	Summary of Percent of Subjects with Metabolic Syndrome and Risk Factors (Maintenance Phase)	Q2M and BIK only In addition to Metabolic syndrome, also include percentage for each of the 5 factors: Elevated waist circumference; Elevated triglycerides; Reduced HDL-C; Elevated blood pressure; Elevated fasting glucose	M6, M12
3.65.	Safety	SAF_T12	Summary of Shift in Metabolic Syndrome and Risk Factors at M12 (OLI and BIK) /M11(D2I) from Baseline	Update to M5/6 for M6 RE. Q2M and BIK only. Shift table from baseline to M5/6 or M11/12, Yes/No/Missing	M6, M12
3.66.	Safety	SAF_T10	Statistical Analysis of Proportion of Subjects with Metabolic Syndrome at M12 (OLI and BIK) /M11(D2I) – Logistic Regression		M6, M12

Safety: Tables					
No.	**Population**	**GSK Standard/ Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
Cardiovascular Risk and Substance Use					
3.67.	Safety	207966/primary_15/T1.22	Summary of Cardiovascular Risk Assessments by Visit (Maintenance Phase)	Add section header for each visit. For month 6, only calculate Framingham equation For month 12, also include smoking status Q2M vs. BIK	M6, M12
3.68.	Safety	SAF_T17	Summary of Substance and Illicit Drug Use (Maintenance Phase)	Q2M vs. BIK	M12
eC-SSRS					
3.69.	Safety	CSSRS1	By Phase Summary of Subjects with eC-SSRS Suicidal Ideation or Behaviour	207966/primary_15/T3.72 Q2M and BIK	M6, M12

Safety: Tables					
No.	**Population**	**GSK Standard/ Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
AEs of Special Interest (AESI)					
3.70.	Safety	207966/primary_15/T3.73	By Phase Summary of Depression, Anxiety and Suicidal Ideation/Behaviour Adverse Events by System Organ Class, Preferred Term, Maximum DAIDS Toxicity Grade, and Prior History (Depression, Anxiety or Suicidal Ideation) at Screening	3 Layers of section headers: Phase: Oral Lead-In Period(Maintenance)/Maintenance Treatment: Q2M, OLI(Q2M), D2I(Q2M), BIK Subjects has: yes/no prior history of depression, yes/or prior history of anxiety, yes/or prior history of suicidal ideation For Oral Lead-In period, only need to present the OLI(Q2M) groups	M6, M12, EOS
3.71.	Safety	SAF_T16a and SAF_T16b	**By Phase** Summary of Adverse Events of Special Interest by **AESI Category,** System Organ Class and Preferred Term (Number of Subjects and Occurrence)	207966/primary_15/T3.75	M6, M12, EOS
3.72.	Safety	207966/primary_15/T3.109	By Phase Summary of Characteristics of Adverse Events of Special Interest	Add footnote: AESIs with at least 1 event are included in the summary.	M6, M12, EOS
3.73.	Safety	207966/primary_15/T3.111 and T3.112	By Phase Summary of Syncope and Presyncope Adverse Events		M6, M12, EOS
COVID-19 Assessments					
3.74.	Safety	207966 primary 15/Table 3.113	Summary of COVID-19 Adverse Events by System Organ Class, Preferred Term and Maximum Toxicity (Maintenance Phase)	Q2M and BIK only	M6, M12

Safety: Tables					
No.	**Population**	**GSK Standard/ Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
3.75.	Safety	PAN1 / PAN1A	Summary of COVID-19 Assessments for Subjects with COVID-19 Adverse Events	Q2M and BIK only	M6, M12
3.76.	Safety	PAN3 / PAN3A	Summary of COVID-19 Symptoms for Subjects with COVID-19 Adverse Events	Q2M and BIK only	M6, M12
Additional Analysis					
3.77.	Safety	Shell SAF_T6	Summary of Absolute and Change from Baseline Values by Visit (Maintenance Phase) – Creatinine and GFR (Excluding Samples Impacted by Possible Faulty Reagents)	Q2M and BIK only. Note: Samples impacted by possible faulty reagents are those collected from Australia, Japan, USA and Canada between 21Dec 212020 and 30Mar2021, and those collected from all other European countries between 02Jan2021 to 28Feb2021.	M12
3.78.	Safety	Shell SAF_T7	Summary of Maximum Maintenance Phase Emergent Chemistry Toxicities – Creatinine and GFR (Excluding Samples Impacted by Possible Faulty Reagents)	Q2M and BIK only. Note: Samples impacted by possible faulty reagents are those collected from Australia, Japan, USA and Canada between 21Dec2020 and 30Mar2021, and those collected from all other European countries between 02Jan2021 to 28Feb2021.	M12
3.81.	Safety	Shell SAF_T6	Summary of Change from Baseline in Weight and BMI by Visit		M12, EOS

16.15.8. Safety Figures

Safety: Figures					
No.	**Population**	**GSK Standard / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
Adverse Events					
3.1.	Safety	AE10	Plot of Common Maintenance Phase Adverse Events and Relative Risk(Excluding ISRs) – Q2M vs. BIK	207966/primary_15/F3.1	M6, M12
3.2.	Safety	mid201584/primary_07/T3.14	Plot of Incidence of Maintenance Phase Drug-Related Injection Site Reaction Adverse Events by Visit (Overall and Common)	Q2M only. 3 Sections: CAB and or RPV CAB RPV	M6, M12
3.3.	Safety	201584/primary_07/F3.17	Plot of Incidence of Grade 3-5 Maintenance Phase Drug-Related Injection Site Reaction Adverse Events by Visit (Overall and Common)	Q2M only. 3 Sections: CAB and or RPV CAB RPV	M6, M12
Laboratory					
3.4.	Safety	LIVER14	Scatter Plot of Maximum vs. Baseline for ALT and BILT – Maintenance Phase	GSK Statistical Display Standard Q2M and BIK	M6, M12
3.5.	Safety	LIVER9	Scatter Plot of Maximum ALT vs. Maximum Total Bilirubin– Maintenance Phase	GSK Statistical Display Standard Q2M and BIK. Remove the reference lines where ULN = 1X (only keep the 2X for BILT and 3X for ALT).	M6, M12

Safety: Figures					
No.	**Population**	**GSK Standard / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
3.6.	Safety	mid207966/primary_15/F3.18	Bar Chart of Fasting Lipid NCEP Categories	Baseline, M5/6 and M11/12. Include all 4 parameters: Triglycerides, Total Cholesterol, LDL, HDL	M6, M12
3.7.	Safety	mid215307/iss_01/F3.5	Bar Chart of Total Cholesterol/HDL Ratio Categories	Q2M and BIK . Baseline, M5/6 and M11/12. Keep big N as denominator	M6, M12
3.8.	Safety	mid215307/iss_01/F3.6	Bar Chart of Fasting Blood Glucose	Q2M and BIK . Baseline, M5/6 and M11/12 Keep big N as denominator	M6, M12
3.9.	Safety	207966/primary_15/F3.21	Plot of Incidence of Maintenance Phase Drug-Related Injection Site Reaction Adverse Events by Strata and Visit (Overall and Common) - CAB and/or RPV	Q2M only. Color-code Severity grade within each bar	M6, M12
3.10.	Safety	SAF_F1	Line Plot of Mean Change from Baseline by Visit for Bone, Renal, Inflammation and Insulin Resistance Markers		M12
3.11.	Safety	SAF_F2	Patient Profile Plot of Clinical Diagnosis Factors for Patients with Metabolic Syndrome at Any Time Point (Treatment Q2M (OLI))	Five parameters for each patient, see Section 16.6.4 waist circumference, triglycerides, HDL, BP, fasting glucose. Note for M12 analysis, due to space limit, only those with metabolic syndrome at M11/12 will be plotted. Full plot including all subjects will be produced post hoc.	M6, M12

Safety: Figures					
No.	**Population**	**GSK Standard / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
3.12.	Safety	SAF_F2	Patient Profile Plot of Clinical Diagnosis Factors for Patients with Metabolic Syndrome at Any Time Point (Treatment Q2M (D2I))	Same as 3.11	M6, M12
3.13.	Safety	SAF_F2	Patient Profile Plot of Clinical Diagnosis Factors for Patients with Metabolic Syndrome at Any Time Point (Treatment BIK)	Same as 3.11	M6, M12

16.15.9. Health Outcome Tables

Note analysis population below has been updated to reflect the M12 analysis plan. In the Month 6 analysis, ITT-E as used instead of mITT-E prior to this amendment.

Health Outcome: Tables					
No.	**Population**	**GSK Standard / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
Perception of INjection Questionnaire (PIN)					
6.1.	mITT-E	201584/primary_07/T6.1	Proportion of Subjects with each individual Questionnaire item score in PIN by Visit (Maintenance Phase)	No BIK	M12
6.2.	mITT-E	201584/primary_07/T6.3	Summary and Statistical Analysis of PIN in Domain Scores (Bother of ISRs, Leg movement, Sleep, and Acceptance) and Individual Items Scores (Anxiety before, Pain, Satisfaction, Anxiety After, Willingness) by Visit (Maintenance Phase)	No BIK Wilcoxon Signed -rank test for analysis (acceptance score only)	M12
6.3.	mITT-E	201584/primary_07/T6.4	Summary of PIN Change from Month 2(OLI)/Month 1(D2I) in Domain Scores (Bother of ISRs, Leg movement, Sleep, and Acceptance) and Individual Items Scores (Anxiety before, Pain, Satisfaction, Anxiety After, Willingness) by Visit (Maintenance Phase)	No BIK	M12
Treatment Satisfaction (HIVTSQs)					
6.4.	mITT-E	201584/primary_07/T6.18	Proportion of Subjects with HIVTSQs – Treatment Satisfaction Individual Item Scores (Maintenance Phase)		M6, M12
6.5.	mITT-E	201584/primary_07/T6.18	Proportion of Subjects with HIVTSQs – Change from baseline in Treatment Satisfaction Individual Item Scores (Maintenance Phase)	Include all possible categories for CFB	M6, M12

Health Outcome: Tables					
No.	**Population**	**GSK Standard / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
6.6.	mITT-E	201584/primary_07/T6.21	Summary of HIVTSQs - Absolute and Change from baseline in Treatment Satisfaction Score by Visit (Maintenance Phase) - Total and Individual	Observed, use section headers "Absolute Value", "Change from Baseline"	M6, M12
6.7.	mITT-E	HO_T1	Statistical Analysis of HIVTSQs - Change from Maintenance Baseline (Day 1) in Total Treatment Satisfaction Score and individual items 5 (convenient), 6 (flexible) and 10 (continue) (Maintenance Phase)	ANCOVA for M6, MMRM for M12 201584/primary_07/T6.24 201584/primary_16/T6.08	M6, M12
6.8.	mITT-E	HO_T4	Statistical Analysis of HIVTSQs - Change from Maintenance Baseline (Day 1) in Total Treatment Satisfaction Score and individual items 5 (convenient), 6 (flexible) and 10 (continue) by Baseline Score Group (Maintenance Phase)	MMRM. See mock shell for details. 201584/primary_16/T6.09	M12
Treatment Satisfaction (HIVTSQc)					
6.9.	mITT-E	201584/primary_01/T6.25	Proportion of Subjects with HIV-Treatment Satisfaction Questionnaire Individual Item Score change (HIVTSQc) at Month 12(OLI and BIK)/Month 11(D2I) (Maintenance Phase)		M12
6.10.	mITT-E	201584/primary_01/T6.26	Summary of HIV-Treatment Satisfaction Questionnaire in Treatment Satisfaction Score Change (HIVTSQc) at Month 12(OLI and BIK)/Month 11(D2I) (Maintenance Phase) - Total and Individual		M12
6.11.	mITT-E	201584/primary_01/T6.27	Statistical Analysis of HIV-Treatment Satisfaction Questionnaire in Treatment Satisfaction Score Change (HIVTSQc) at Month 12 (OLI and BIK)/Month 11(D2I) (Maintenance Phase)		M12
CCI [redacted]					

Health Outcome: Tables					
No.	Population	GSK Standard / Example Shell	Title	Programming Notes	Deliverable [Priority]
CCI					

Health Outcome: Tables					
No.	**Population**	**GSK Standard / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
Treatment Preference for Q2M vs. BIK					
6.14.	mITT-E	HO_T2	Summary of Treatment Preference and Reason for Preference		M12
CCI [redacted]					

16.15.10. Virology Tables

Q2M vs. BIK only for virology tables in this section. Note no summary tables will be produced if less than 5 CVFs in total are observed (excluding subjects from site PPD). All planned listings will be produced regardless.

Note analysis population below has been updated to reflect the M12 analysis plan. No tables were produced at the M6 analysis (total number of CVFs <5).

Virology: Tables					
No.	**Population**	**GSK Standard / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
Genotypic					
7.1.	mCVF	207966/primary_15/T7.1	Summary of the Prevalence of Known INI Resistance Mutations at time of CVF (Maintenance Phase) – Plasma Sample		M6, M12
7.2.	mCVF	207966/primary_15/T7.2	Summary of the Prevalence of Major Resistance Mutations of NRTI, NNRTI and PI Class at time of CVF (Maintenance Phase) - Plasma Sample		M6, M12
7.3.	mCVF	207966/primary_15/T7.3	Summary of Genotypic Susceptibility at time of CVF (Maintenance Phase) - Plasma Sample		M6, M12
Phenotypic					
7.4.	mCVF	207966/primary_15/T7.4	Summary of Phenotype Susceptibility at Time of CVF (Maintenance Phase) - Plasma Sample		M6, M12

Virology: Tables					
No.	**Population**	**GSK Standard / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
7.5.	mCVF	207966/primary_15/T7.5	Summary of Phenotype: Number of Drugs to Which Subject is Phenotypic Resistant, Partially Sensitive or Sensitive at Time of CVF (Maintenance Phase) - Plasma Sample		M6, M12
7.6.	mCVF	207966/primary_15/T7.6	Summary of Fold Change to CAB, RPV and BIC at Time of CVF (Maintenance Phase) - Plasma Sample		M6, M12
Other					
7.7.	mCVF	207966/primary_15/T7.7	Summary of Net Assessment at Time of CVF (Maintenance Phase) - Plasma Sample		M6, M12

16.15.11. ICH Listings

ICH: Listings					
No.	**Population**	**GSK Standard / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
Study Population					
1.	Randomized	mid207966/primary_15/Listing 1	Listing of Subjects Randomized but Not Treated	ICH E3	M6, M12
2.	ITT-E	Shell POP_L1	Listing of Reasons for Study Withdrawal	ICH E3 Start from mid201584/primary_40 listing 40. Also see mock up.	HL, M6, M12, EOS
3.	ITT-E	ES2	Listing of Reasons for Study Drug Discontinuation	ICH E3	M6, M12, EOS
4.	ITT-E	DV2	Listing of Important Protocol Deviations	ICH E3 mid201584/primary_07 listing 6. Note: add if related to COVID-19 Column	M6, M12, EOS
5.	ITT-E	DV2	Listing of Protocol Deviations Leading to Exclusion from the Per-Protocol Population		HL, M6, M12
6.	ITT-E	IE3	Listing of Subjects with Inclusion/Exclusion Criteria Deviations	ICH E3	M6, M12, EOS
7.	ITT-E	DM2	Listing of Demographic Characteristics including Race	ICH E3 mid201584/primary_07 listing 9 and 10	M6, M12, EOS

ICH: Listings					
No.	**Population**	**GSK Standard / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
Efficacy					
8.	ITT-E	207966/primary_15/Listing 11	Listing of Study Outcome (50 c/mL Threshold) at Month 12(OLI and BIK)/Month 11(D2I) – Snapshot Analysis	For Month 6/5 deliverable, replace "Month 12 (OLI and BIK) and Month 11 (D2I)" with "Month 6 (OLI and BIK) and Month 5 (D2I)"	HL, M6, M12
9.	ITT-E	207966/primary_15/Listing 11	Listing of Study Outcome (50 c/mL Threshold) at Month 12(OLI and BIK)/Month 11(D2I) – Snapshot Analysis (All Data as Observed)	For Month 6/5 deliverable, replace "Month 12 (OLI and BIK) and Month 11 (D2I)" with "Month 6 (OLI and BIK) and Month 5 (D2I)"	M6, M12
10.	Randomized	Shell EFF_L1	Listing of All Plasma HIV-1 RNA Data		M6, M12, EOS
Safety: Exposure					
11.	Safety	207966 primary_02, L14 / EX3	Listing of Investigational Product Exposure Data	ICH E3	M6, M12
Safety: Adverse Events					
12.	Randomized	AE8	Listing of All Adverse Events	ICH E3	M6,M12, EOS
13.	Safety	AE7	Listing of Subject Numbers for Individual Adverse Events	ICH E3	M6,M12
Safety: Serious and Other Significant Adverse Events					
14.	Safety	AE8	Listing of Fatal Serious Adverse Events	ICH E3	M6,M12

ICH: Listings					
No.	**Population**	**GSK Standard / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
15.	Safety	AE8	Listing of Non-Fatal Serious Adverse Events	ICH E3	M6,M12
16.	Safety	AE14	Listing of Reasons for Considering as a Serious Adverse Event	ICH E3	M6,M12, EOS
17.	Safety	AE8	Listing of Adverse Events Leading to Withdrawal from Study/Permanent Discontinuation of Study Treatment	ICH E3	HL, M6,M12, EOS
18.	Safety	PSRAE1	Listing of Possible Suicidality-Related Adverse Event Data: Event and Description (Section 1-Section 2)		M6, M12
19.	Safety	PSRAE3	Listing of Possible Suicidality-Related Adverse Event Data: Possible Cause(s) (Section 3)		M6, M12
20.	Safety	PSRAE4	Listing of Possible Suicidality-Related Adverse Event Data (Section 4)		M6, M12
21.	Safety	PSRAE5	Listing of Possible Suicidality-Related Adverse Event Data (Section 5-Section 8)		M6, M12

16.15.12. Non-ICH Listings

Non-ICH: Listings					
No.	**Population**	**GSK Standard GSK Statistical Display Standard / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
Study Population					
22.	Screened	ES7	Listing of Reasons for Screen Failure	Journal Guidelines	M6, M12, EOS
23.	Randomized	TA1	Listing of Randomized and Actual Strata and Treatment Assignment	GSK Statistical Display Standard Add "Choice of OLI/D2I"	M6, M12, EOS
24.	ITT-E	CA3	Listing of Prior ART Medications		M6, M12
25.	ITT-E	mid207966/primary_15/listing37	Listing of Concomitant ART Medications during the Maintenance Phase		M6, M12, EOS
26.	ITT-E	CA3	Listing of ART Medications Received during LTFU Phase		M6, M12
27.	ITT-E	mid207966/primary_15/listing39	Listing of Investigational Product Accountability - Oral Regimens		M6, M12
28.	ITT-E	mid207966/primary_15/listing40	Listing of Medical History of Seizure		M6, M12
29.	ITT-E	PAN 7	Listing of All Subjects with Visits and Assessments Impacted by COVID-19 Pandemic		M6, M12
Efficacy					
30.	ITT-E	201584/primary_07/L54	Listing of Stage-3 HIV-1 Associated Conditions		M6, M12
31.	CVF	Shell EFF_L1	Listing of All Plasma HIV-1 RNA Data for Subjects with Confirmed Virologic Failure		HL, M6, M12
32.	ITT-E	Shell EFF_L1	Listing of HIV-1 RNA Data for Subjects Who Became Pregnant During the Study	Add: date of confirmed pregnancy. Only required if any subject becomes pregnant on Q2M.	M6, M12

Non-ICH: Listings					
No.	**Population**	**GSK Standard GSK Statistical Display Standard / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
Safety: Exposure					
33.	Safety	201584/primary_07/L72	Listing of Investigational Product Exposure Data during Oral Bridging		M6, M12
34.	Safety	201584/primary_07/L73	Listing of Dosing Errors and IP Device Malfunctions		M6, M12
Safety: Adverse Events					
35.	[Insert]	AE2	Listing of Relationship Between Adverse Event System Organ Classes, Preferred Terms, and Verbatim Text	GSK Statistical Display Standard	M6, M12
36.	Safety	AE8	Listing of Changes in Intensity/Grades of Injection Site Adverse Events	2011584/primary_07/Listing 22	M6, M12
37.	Safety	PAN12	Listing of COVID-19 Assessments and Symptom Assessments for Subjects with COVID-19 Adverse Events		M6, M12
38.	Safety	AE8	Listing of Grade 3 to 5 Adverse Events		M6, M12
Safety: All Laboratory					
39.	Safety	207966/primary_15/L59	Listing of Clinical Chemistry Data for Subjects with Any Grade 3 to 5 Lab Toxicity	Remove PCI flag. Treatment as section header. Only include the parameters with G3-5.	M6, M12, EOS
40.	Safety	207966/primary_15/L59	Listing of Selected Laboratory Data for Subjects Who Became Pregnant During the Study	Remove PCI flag. Treatment as section header. Selected parameters only. Do not produce if no subject became pregnant on Q2M.	M6, M12

Non-ICH: Listings					
No.	**Population**	**GSK Standard GSK Statistical Display Standard / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
Safety: Hepatobiliary (Liver)					
41.	Safety	MH2	Listing of Medical Conditions for Subjects with Liver Stopping Events	GSK Statistical Display Standard	M6, M12
42.	Safety	SU2	Listing of Substance Use for Subjects with Liver Stopping Events	GSK Statistical Display Standard	M6, M12
43.	Safety	201584/primary_07/L63	Listing of All Subjects Meeting Liver Stopping Criteria		M6, M12
44.	Safety	207966/primary_15/L52	Listing of Liver Monitoring/Stopping Event Reporting		M6, M12
45.	Safety	207966/primary_15/L53	Listing of Liver Event Information for RUCAM Score		M6, M12
46.	Safety	207966/primary_15/L54	Listing of Liver Biopsy Details		M6, M12
47.	Safety	207966/primary_15/L55	Listing of Liver Imaging Details		M6, M12
48.	Safety	207966/primary_15/L56	Listing of Subjects Meeting Hepatobiliary Lab Criteria		M6, M12
49.	Safety	207966/primary_15/L59	Listing of ALT, AST, Bilirubin (including Total and Direct Bilirubin), INR, and ALP for Subjects Meeting Hepatobiliary Lab Abnormality Criteria		HL, M6, M12
Safety: ECG					
50.	Safety	EG3	Listing of All ECG Values for Subjects with Any Value of Potential Clinical Importance	GSK Statistical Display Standard Check all 3: QTcB, QTcF, and Unspecified for PCI criteria	M6, M12
51.	Safety	EG5	Listing of Abnormal ECG Findings	GSK Statistical Display Standard	M6, M12
52.	Safety	207966/primary_15/L57	Listing of Potential QTc Interval Prolonging Events of Interest		M6, M12
53.	Safety	207966/primary_15/L58	Listing of ECG values for Subjects with Potential QTc Interval Prolonging Events of Interest		M6, M12

Non-ICH: Listings					
No.	**Population**	**GSK Standard GSK Statistical Display Standard / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
Safety: Vital Signs					
54.	Safety	VS4	Listing of All Vital Signs and Anthropometric Parameters	GSK Statistical Display Standard Include weight, height and BMI, waist and hip circumference, and Tanita scale measurements (body Fat, bone mass, musl mass, TBW)	M6, M12
55.	Safety	PREG1A	Listing of Subjects Who Became Pregnant During the Study	GSK Statistical Display Standard Required by GCSP Include Date of confirmed pregnancy	M6, M12
Safety: Metabolic Syndrome					
56.	Safety	SAF_L2	Listing of Clinical Diagnosis Factor Data by Visit for Subjects Diagnosed with Metabolic Syndrome (Maintenance Phase)		M6, M12
Safety: Abacavir Hypersensitivity					
57.	Safety	ABC_HSR _EXPO2	Listing of Abacavir Hypersensitivity Reaction Record - Exposure to Abacavir	Produce empty listing if no data to report	M6, M12
58.	Safety	ABC_HSR _DRUG2	Listing of Abacavir Hypersensitivity Reaction Record - Subject History of Drug Allergies	Do not produce if no data to report	M6, M12
59.	Safety	ABC_HSR COND2	Listing of Abacavir Hypersensitivity Reaction Record - Subject and Family Conditions	Do not produce if no data to report	M6, M12
60.	Safety	ABC_HSR _RASH2	Listing of Abacavir Hypersensitivity Reaction Record - Skin Rash Details	Do not produce if no data to report	M6, M12

Non-ICH: Listings					
No.	**Population**	**GSK Standard GSK Statistical Display Standard / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
61.	Safety	ABC_HSR _SYMP4	Listing of Abacavir Hypersensitivity Reaction Record - Symptoms	Do not produce if no data to report	M6, M12
62.	Safety	VS4	Listing of Abacavir Hypersensitivity Reaction Record - Vital Signs	Do not produce if no data to report	M6, M12
63.	Safety	ABC_HSR _SYMP6	Listing of Abacavir Hypersensitivity Reaction Record - Individual Symptoms and Diagnostic Category Assignments	Do not produce if no data to report	M6, M12
Virology					
64.	CVF	207966/primary_15/T7.8	Listing of Viral load, Genotypic, Phenotypic data for Subjects Who Met Confirmed Virologic Failure Criteria		HL, M6, M12, EOS
65.	Safety	207966/primary_15/T7.10	Listing of Viral load, Genotypic, Phenotypic data for Non-CVF Subjects with Genotypic and/or Phenotypic Data		M6, M12, EOS
66.	CVF	207966/primary_15/Listing 62	Listing of Replication Capacity in IN and PR/RT Region		M6, M12, EOS
67.	Safety	207966/primary_15/Listing 63	Listing of Resistance Associated Mutations (Pre-specified INSTI and IAS-USA NNRTI)		M6, M12, EOS
68.	CVF		Listing of Net Assessment data for Subjects Who Met Confirmed Virologic Failure Criteria		M6, M12, EOS
69.	Safety		Listing of Net Assessment data for Non-CVF Subjects with Genotypic and/or Phenotypic Data		M6, M12, EOS

Non-ICH: Listings					
No.	**Population**	**GSK Standard GSK Statistical Display Standard / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
PK					
70.	PK	207966/primary_15/L63	Listing of Plasma PK Concentrations for Subjects Who Became Pregnant During the Study	CAB and RPV With Section Headers. Do not produce if no subject became pregnant on Q2M and continued study	M12
71.	ITT-E	207966/primary_15/L63	Listing of Plasma PK Concentrations at Withdrawal		M12
72.	CVF	207966/primary_15/L63	Listing of All Plasma PK Concentrations for CVF Subjects		M12

16.16. Appendix 16: Example Mock Shells for Data Displays

Available upon request