Protocol Final
Study ID 224047

NON-INTERVENTIONAL STUDY PROTOCOL

Protocol Final
Study ID 224047

STUDY DETAILS

UNIQUE IDENTIFIER	224047
TITLE	CABFIDENCE: Global Real-World Evidence Cohort Study to evaluate Utilization, Clinical and Patient-Reported Outcomes among CAB+RPV LA users
STUDY ACCOUNTABLE PERSON	PPD
SCIENTIFIC LEAD	
CONTRIBUTING AUTHORS	
ASSET ID	GSK1265744, TMC278
GSK or ViiV ASSET	Cabotegravir + Rilpivirine LA
EFFECTIVE DATE	01 May 2025

INDICATION	HIV-1
DATA COLLECTION TYPE	PRIMARY AND SECONDARY
SAFETY OBJECTIVE	Yes
ASSET INVOLVEMENT	Yes
TSS/PASS ASSESSMENT PERFORMED	Yes
STUDY CLASSIFICATION	TSS, Voluntary PASS
EVALUATING A PRODUCT (TIER TYPE)	Tier 1
REGULATORY COMMITMENT	No

Protocol Final
Study ID 224047

TITLE PAGE

Study ID: 224047

Division: Global Medical

Information Type: Non-Interventional Study Protocol

Title:	CABFIDENCE: Global Real-World Evidence Cohort Study to evaluate Utilization, Clinical, and Patient-Reported Outcomes among CAB+RPV LA users
Effective Date:	01 May 2025

Author(s):

PPD (ViiV Healthcare)

PPD (ViiV Healthcare)

PPD (ViiV Healthcare)

PPD (ViiV Healthcare)

PPD (ViiV Healthcare)

PPD (ViiV Healthcare)

PPD (RTI Health Solutions)

PPD (RTI Health Solutions)

PPD (RTI Health Solutions)

PPD (RTI Health Solutions)

PPD (RTI Health Solutions)

PPD (RTI Health Solutions)

PPD (RTI Health Solutions)

PPD (RTI Health Solutions)

PPD (ViiV Healthcare)

PPD (ViiV Healthcare)

PPD (ViiV Healthcare)

Protocol Final
Study ID 224047

STUDY INFORMATION

Title	CABFIDENCE: Global Real-World Evidence Cohort Study to evaluate Utilization, Clinical and Patient-Reported Outcomes among CAB+RPV LA users
Protocol version identifier	V1
Date of last version of protocol	NA
EU PAS (ENCEPP) register number	
Active substance	Cabotegravir Rilpivirine
Medicinal product	VOCABRIA® 30 mg film-coated tablets Edurant® 25 mg film-coated tablets Cabenuva
Product reference	NDA 212887 VOCABRIA (cabotegravir) tablets NDA 202022 EDURANT (rilpivirine) tablets NDA 212888 CABENUVA (cabotegravir extended-release injectable suspension; rilpivirine extended-release injectable suspension), copackaged, for intramuscular use
Procedure number	NA
Marketing authorisation holder(s)	ViiV Healthcare
Joint PASS	No

Research question and objectives	Using global real-world clinical data, this study will describe utilization, clinical and patient-reported outcomes among people with HIV on CAB+RPV LA regimen
Country(-ies) of study	United States, United Kingdom, Italy, Portugal, France, Spain, Germany and Australia
Author	PPD, ViiV Healthcare PPD PPD ViiV Healthcare PPD

MARKETING AUTHORISATION HOLDER(S)

Marketing authorisation holder(s)	ViiV Healthcare
MAH contact person	PPD ViiV Healthcare PPD PPD, ViiV Healthcare PPD

TABLE OF CONTENTS

PAGE

LIST OF ABBREVIATIONS

ADR	adverse drug reaction
AE	adverse event
AEMPS	Agencia Española de Medicamentos y Productos Sanitarios
AIFA	Italian Medicines Agency
ANSM	Agence nationale de sécurité du médicament et des produits de santé
ART	antiretroviral therapy
ARV	antiretroviral
BfArM	Bundesinstitut für Arzneimittel und Medizinprodukte
BMI	body mass index
CAB	cabotegravir
CAB+RPV LA	cabotegravir + rilpivirine long-acting
CD4	cluster of differentiation 4
CNIL	Commission Nationale de l'Informatique et des Libertés
CPP	Comité de Protection des Personnes
CVF	confirmed virologic failure
EC	Ethics Committee
eCRF	electronic case report form
EDC	electronic data capture
EU	European Union
GPDP	Garante Per la Protezione dei Dati Personali
GPP	Good Pharmacoepidemiology Practices
HCRW	Health and Care Research Wales

HIV	human immunodeficiency virus
HRA	Health Research Authority
HREC	Health Research Ethics Committee
HSC	Health and Social Care
ICMJE	International Committee of Medical Journal Editors
ICSR	individual case safety reports
ID	identifier
INI	integrase inhibitor
INSTI	integrase strand transfer inhibitor
IRAS	Integrated Research Application System
IRB	institutional review board
ISPE	International Society for Pharmacoepidemiology
LA	long-acting
NHS	National Health Service
NNRTI	nonnucleoside reverse transcriptase inhibitor
NRSPCC	Research Scotland Permissions Coordinating Center
REC	Research Ethics Committee
SI RIPH 2G	Système d'Information des Recherches Impliquant la Personne Humaine
RPV	rilpivirine
RSO	Registro Studi Osservazionali
RTI-HS	RTI Health Solutions
SAE	serious adverse event
UK	United Kingdom

US	United States
VL	viral load
WHOQOL-HIV BREF	World Health Organization Quality of Life-Human Immunodeficiency Virus BREF

TRADEMARK INFORMATION

Trademarks of the GSK\ViiV group of companies
CABENUVA™
VOCABRIA™

Trademarks not owned by the GSK\ViiV group of companies

1. RESPONSIBLE PARTIES

MARKETING AUTHORISATION HOLDER

ViiV Healthcare Company

Sponsor Legal Registered Address:

ViiV Healthcare Company

410 Blackwell St.

Durham, NC 27701

Protocol Final
Study ID 224047

1.1. Sponsor Signatory

Title: CABFIDENCE: Global Real-World Evidence Cohort Study to evaluate Utilization, Clinical and Patient-Reported Outcomes among CAB+RPV LA users

Compound Number: GSK1265744, TMC278

PPD

11 April 2025

Gayathri Sridhar
Primary Author/NI Scientific Lead

Date (DD Month YYYY)

PPD

11 April 2025

Vani Vannappagari
Therapy Area Leader/+1 Manager

Date (DD Month YYYY)

PPD

Nassrin Payvandi
VP & Head, Safety & Pharmacovigilance

Date (DD Month YYYY)

PPD

29-Apr-2015

Jen Ulrich Stegman
Qualified Person for Pharmacovigilance /Delegate

Date (DD Month YYYY)

Note: Not applicable if an eSignature process is used to get the sponsor approval.

1.2 Investigator Protocol Agreement Page

- I confirm agreement to conduct the study in compliance with the protocol.
- I acknowledge that I am responsible for overall study conduct. I agree to personally conduct or supervise the described study.
- I agree to ensure that all associates, colleagues, and employees assisting in the conduct of the study are informed about their obligations. Mechanisms are in place to ensure that site staff receive the appropriate information throughout the study.

Investigator Name:

David Richardson

PPD

Investigator Signature

01 May 2025

Date (DD Month YYYY)

2. SYNOPSIS

Title CABFIDENCE: Global Real-World Evidence Cohort Study to evaluate Utilization, Clinical and Patient-Reported Outcomes among CAB+RPV LA users

Rationale and Background

Cabotegravir + rilpivirine long-acting (CAB+RPV LA) injectable is the first complete long-acting antiretroviral (ARV) regimen approved for treatment of human immunodeficiency virus type 1 (HIV-1) in the United States (US), Europe, and Australia. It is indicated for people with HIV (PWH) who are virologically suppressed (HIV-1 RNA viral load [VL] < 50 copies per mL) on a stable ARV regimen, with no history of treatment failure and no known or suspected resistance to CAB or RPV (in the US)/agents of the nonnucleoside reverse transcriptase inhibitor (NNRTI) and integrase inhibitors (INI) class (in Europe). While clinical studies have established the efficacy, safety, and tolerability of CAB+RPV LA, this study will assess the global utilization patterns, adherence, persistence, discontinuation, virologic effectiveness, and patient-reported outcomes of this regimen in a real-world clinical setting.

Research Question and Objective(s)

The overall objective of this global study is to describe characteristics, assess clinical outcomes, and patient-reported outcomes among people with HIV who receive CAB+RPV LA regimen.

Primary Objectives:

1. To describe baseline demographics, clinical characteristics and patterns of use among individuals receiving CAB+RPV LA
2. To assess the persistence, discontinuation, and adherence among individuals receiving CAB+RPV LA
3. To assess virologic effectiveness among individuals receiving CAB+RPV LA
4. To assess factors associated with confirmed virologic failure (CVF) among individuals receiving CAB+RPV LA regimen

Secondary Objectives:

1. Subgroup analyses by body mass index (BMI) (< 30 and ≥ 30 kg/m^2) at initiation, age at initiation (18-49, 50-64, ≥ 65 years), sex assigned at birth (female, male), race/ethnicity, country (if sample sizes allow), to assess characteristics, adherence, persistence, discontinuation and virologic effectiveness

2. To estimate the frequency of documented injection site reactions and hypersensitivity reactions among individuals receiving CAB+RPV LA injections

3. To describe HIV resistance and proviral DNA testing at the time of discontinuation/CVF, history of resistance and proviral DNA testing prior to discontinuation/CVF, and the ART regimen and virologic outcomes after discontinuation/CVF

4. To describe reasons for initiating CAB+RPV LA, health-related quality of life, treatment-related stigma, and benefits, and reasons for missed injections and discontinuation among new initiators of CAB+RPV LA

Study Design

This is a non-interventional prospective observational cohort study using data from individual medical records from participating clinical sites and participant-reported data from electronic questionnaires. The study population will include treatment-experienced virologically suppressed (VL < 50 copies/mL) individuals who are 18 years or older and received at least one every 2 month dosing CAB+RPV LA injection between January 2023 and March 2028. Participants will be followed from the date of their first CAB+RPV injection until switching to monthly dosing CAB+RPV LA dosing, death, loss to follow-up (12 months after last clinical contact), or study end (30 September 2028).

Population

The study population will consist of people living with HIV who are aged 18 years and older on CAB+RPV LA from participating clinical sites in US, United Kingdom (UK), Italy, Portugal, France, Spain, Germany and Australia. For the experienced participants, those who have discontinued the treatment for any reason will be included and individuals who are deceased or lost to follow up will not be included.

Inclusion Criteria:

- Diagnosed with HIV-1
- Aged ≥ 18 years at time of CAB+RPV LA injection
- Treatment experienced
- VL < 50 copies/mL at initiation
- Initiated every 2 month dosing CAB+RPV LA between 1 January 2023 and 31 March 2028
  - For new initiators, study enrollment should occur within 1 month after their initial CAB+RPV LA injection

Exclusion Criteria:

- Received CAB+RPV LA regimen as part of a randomized, controlled clinical trial
- Treatment naïve
- VL ≥ 50 copies/mL at initiation
- Individuals with prior virologic failure to agents of NNRTI or INSTI class (if data is available)

Variables

All users of CAB+RPV LA regimen treated as per indication for CAB and RPV LA formulations will be included in the study.

Outcomes:

- Persistence
- Discontinuation
- Adherence
- Virologic effectiveness
- Resistance
- ART regimen after discontinuation /CVF
- Health-related quality of life
- Treatment-related stigma, and benefits
- Reasons for initiating CAB+RPV LA
- Reasons for discontinuing CAB+RPV LA
- Reasons for missed injection(s)

Potential Confounders to be Evaluated:

- Baseline: age, sex, gender, race, ethnicity, region, marital status, risk of HIV transmission, payer type, cluster of differentiation 4 (CD4) cell count, VL, prior regimen, years since HIV diagnosis and antiretroviral therapy (ART) initiation, weight, BMI, co-infections, comorbidities, and concomitant medications

Data Sources

Data for this study will be obtained via the following sources:

- **Participant medical information via site-completed electronic case report form (eCRF):** The investigator or authorized medical staff will record clinical and treatment data from participants' medical records into an eCRF at enrollment, applicable follow-ups (i.e., month 12, month 24, month 36, and month 48, and month 60), and upon discontinuation of CAB+RPV LA, if applicable.

- **Participant surveys:** New initiators of CAB+RPV LA will be asked to complete an online survey at enrollment, at month 12, and if they discontinue CAB+RPV LA. Participants will be asked to complete the World Health Organization Quality of Life-HIV BREF (WHOQOL-HIV BREF) (O'Connell, 2012) and several bespoke questionnaires developed for this study. Appropriate agreements with the copyright owners will be in place for use in this study. It is estimated that the participant surveys will take approximately 20 minutes to complete.

Study Size

The study aims to enroll a total of 1,000 participants. Among the participants, it is estimated that 250 participants are already receiving CAB+RPV LA (experienced participants), and 750 participants will be newly initiating CAB+RPV LA (new initiators). A participant will be considered as a new initiator of CAB+RPV LA if study enrollment occured within 1 month after their initial CAB+RPV LA injection.

Data Analysis

Baseline characteristics and outcomes will be described using counts and relative frequencies for categorical variables. Continuous variables will be summarized using summary statistics (means, standard deviations, medians, minimums, maximums, and quartiles 1 and 3). For event outcomes assessed at any point during follow-up, incidence rates will be estimated using unadjusted Poisson regression, accounting for person-time since index (i.e., first CAB+RPV LA injection). Additional analytic approaches may also be considered (e.g., Kaplan-Meir estimator/curve). Analyses will be stratified by BMI (< 30 kg/m^2 vs. ≥ 30 kg/m^2), age (18-49, 50-64, ≥ 65 years), sex assigned at birth (female, male) and race and ethnicity, and country, if sample sizes allow, at initiation of CAB+RPV LA regimen. Factors associated with CVF will be assessed using a logistic regression model. Participant surveys will be summarized descriptively for item and summary score (where applicable). The WHOQOL-HIV BREF will be scored according to instrument scoring guidelines and derived scores will be summarized descriptively. All analyses will be performed on the observed data only and no missing values will be imputed.

Milestones

The study will start after the protocol is approved, for a total of 5 years of data collection from January 2023 to September 2028. The final study report will be completed by middle of 2029.

3. AMENDMENTS AND UPDATES

Amendment or update no	Date	Section of study protocol	Amendment or update	Reason

4. MILESTONES

Milestone	Planned date
Draft protocol	7 March 2025
Final protocol	25 April 2025
Registered with HMA-EMA catalogue	30 April 2025
Start of retrospective data collection	1 January 2023
Start of prospective data collection	16 June 2025
Baseline analysis tables (data from January 2023 to September 2025)	Draft – 31 December 2025 Final – 30 April 2026
12-month interim tables data from January 2023 to September 2026)	Draft – 31 December 2026 Final – 30 April 2027
24-month interim tables (data from January 2023 to September 2027)	Draft – 31 December 2027 Final – 30 April 2028
Last day of enrollment	31 March 2028
End of data collection	30 September 2028
Final report (Data from January 2023 to September 2028)	Draft – 31 January 2029 Final – 30 April 2029

5. RATIONALE AND BACKGROUND

Cabotegravir (CAB), an HIV-1 integrase strand transfer inhibitor (INSTI), in combination with rilpivirine (RPV), an HIV-1 NNRTI, is indicated as a complete regimen for the treatment of HIV-1 infection in adults who are virologically suppressed (HIV-1 RNA < 50 copies /mL) on a stable ART regimen without present or past evidence of viral resistance to, and no prior virological failure with CAB or RPV (in the US)/agents of the NNRTI and INI class (in Europe).

The novel long-acting ART delivered through intramuscular injection—CAB+RPV LA—has been shown to be non-inferior to daily oral therapy. Before starting the regimen, the healthcare provider should carefully select people with HIV who agree to the required injection schedule and counsel individuals about the importance of adherence to scheduled dosing visits to help maintain viral suppression and reduce the risk of viral rebound and potential development of resistance associated with missed doses. After discontinuation of CAB+RPV LA injection, it is essential to adopt an alternative, fully suppressive ARV regimen.

CAB in combination with RPV has a prolonged pharmacokinetic tail, which presents individuals with the opportunity to take their HIV treatment once monthly or once every 2 months instead of daily, potentially allowing for much improved adherence. While clinical studies have established the efficacy, safety, and tolerability of CAB+RPV LA, this study will assess global utilization patterns, adherence, persistence, discontinuation, effectiveness, and resistance among virologic failures with available resistance testing data, as well as patient-reported outcomes of this regimen in a real-world clinical setting.

6. RESEARCH QUESTION AND OBJECTIVE(S)

6.1. Primary Objective

The overall objective of this global study is to describe participant characteristics and assess clinical outcomes and patient-reported outcomes among people with HIV who receive CAB+RPV LA regimen.

1. To describe baseline demographics, clinical characteristics and patterns of use among individuals receiving CAB+RPV LA
   - Descriptive analysis of study population by baseline demographic and clinical characteristics
   - Monitor for use of optional oral lead-in

2. To assess the persistence, discontinuation, and adherence among individuals receiving CAB+RPV LA
   - Persistence: Proportion of participants still on CAB+RPV LA after 6, 12, 24, 36, 48, and 60 months of use and at study end
   - Proportion of individuals discontinuing the regimens of interest will be assessed

a. Reasons for discontinuation will be assessed

- Non-adherence to the dosing schedule will be assessed by:

a. Estimating the number of individuals who missed 1 or more consecutive injections without taking daily oral bridging therapy or any other oral ARV regimen while not on CAB+RPV LA and estimating the mean and median number of injections missed during a 12-month period
b. Estimating the number of individuals who received the injections more than 7 days later than their scheduled injection visit and median duration of delayed injections
c. Estimating the number of individuals who missed 1 or more consecutive injections without taking daily oral bridging therapy or those who received the injections more than 7 days later than their scheduled injection visit (combined group A or B) and describe individual characteristics for the individuals who are non-adherent.

3. To assess virologic effectiveness (i.e., proportion of individuals experiencing virologic suppression and CVF) among individuals receiving CAB+RPV LA regimen
   - Estimate the proportion of individuals with virologic failure during the first 6 months after initiation of CAB+RPV LA
   - Estimate the proportion of individuals with virologic failure, 6, 12, 24, 36, 48, and 60 months after initiation of CAB+RPV LA
   - Assessment of virologic suppression among individuals on CAB+RPV LA regimen at 6, 12, 24, 36, 48, and 60 months after initiation of the regimen

4. To assess factors associated with CVF among individuals receiving CAB+RPV LA regimen

6.2. Secondary Objectives

1. Subgroup analyses by BMI (< 30 and ≥ 30 kg/m^2) at initiation, age at initiation (18-49, 50-64, ≥ 65 years), sex assigned at birth (female, male), race and ethnicity, and country, if sample sizes allow, to assess characteristics, adherence, persistence, discontinuation, and virologic effectiveness

2. To estimate the frequency of documented injection site reactions and hypersensitivity reactions among individuals receiving CAB+RPV LA injections

3. To describe resistance and ART regimen among individuals after discontinuation/CVF of CAB+RPV LA, where VL data are available and resistance testing has been done as part of routine clinical practice

- Describe resistance (where this has been done as part of routine clinical practice) at the time of discontinuation/CVF and history of resistance and proviral DNA testing before discontinuation/CVF
- Describe the ART regimen and virologic outcomes after discontinuation/CVF of CAB+RPV LA
    - To describe the demographic and clinical characteristics of individuals who continue to stay on CAB+RPV LA as compared to those who switched regimens after discontinuation or CVF
    - To describe virologic response (suppression, non-response, confirmed virologic failure) to ART regimen after discontinuation/CVF of CAB+RPV LA

4. To describe reasons for initiating CAB+RPV LA, health-related quality of life, treatment-related stigma, benefits, and reasons for missed injections and discontinuation among new initiators of CAB+RPV LA

7. RESEARCH METHODS

7.1. Study Design

This is a non-interventional prospective observational cohort study using data from individual medical records, assessments from participating clinical sites, and participant-reported data from electronic questionnaires. Data will be collected from January 2023 to September 2028 to meet the study objectives. Participants will be followed from the date of their first CAB+RPV injection until switching to monthly CAB+RPV LA dosing, , death, loss to follow-up (12 months after last clinical contact), or study end (30 September 2028). Participants that discontinue CAB+RPV LA will continue to be followed to describe virologic response and treatment switching post-discontinuation. Experienced participants will be included in the study regardless of whether they are still on CAB+RPV at the time of the study start and will have all applicable data collected. Individuals who are deceased or lost to follow up will not be included.

For this non-interventional study, treatment and laboratory testing decisions will be made by the treating physician according to standard practice, taking into account the treatment history, individual characteristics, the approved prescribing information or summary of product characteristics for CAB+RPV LA formulation, contemporary regimen and local guideline or recommendations. Testing for resistance and subtype at discontinuation/virologic failure will be part of the standard of care at selected sites, and the study will include only the clinical sites that conduct resistance and subtype testing as standard of care. The study protocol will be implemented by RTI Health Solutions (RTI-HS).

7.2. Study Population and Setting

The study population includes treatment-experienced, virologically suppressed (VL < 50 copies/mL) individuals who are 18 years or older and received at least one every 2 month dosing CAB+RPV LA injection between January 2023 and March 2028 from participating clinical sites in the US, UK, Italy, Portugal, France, Spain, Germany and Australia. Enrollment will take place as part of a participant's standard of care visit at a participating site.

The sampling methodology will be designed with the goal of maximising the probability that each individual treated with CAB+RPV LA will have an equal opportunity to be selected. In some sites, it is likely that all treated individuals will be selected.

New initiators will be recruited and enrolled as they come in for a scheduled visit within 1 month of their first CAB+RPV LA injection.

Experienced participants will be recruited and enrolled as they come in for a scheduled visit, however if the volume of experienced users at a site is large, a customized, site-specific sampling approach may be devised to achieve an efficient method of obtaining a representative sample of experienced participants.

The study will aim to select a diverse group of medical practices to represent diversity in clinical practice settings and to support recruitment of a diverse sample of participants (e.g., prioritizing non-cisgender males, individuals aged 50 years or older, and individuals with BMI ≥30 kg/m^2).

Individuals who are viremic (VL ≥ 50 copies/mL) at initiation will not be included in this study. Individuals with VL results available around the time of initiation at VL < 50 copies/mL will be included in the study regardless of VL levels following enrollment. For the experienced participants, those who have discontinued the treatment for any reason will be included and individuals who are deceased or lost to follow up will not be included. Once enrolled, follow-up will continue from first injection until the earliest censoring event.

7.2.1 Inclusion criteria:

- Diagnosis of HIV-1
- Aged ≥ 18 years at time of CAB+RPV LA injection
- Treatment experienced
- VL < 50 copies/mL at initiation
- Initiated every 2 month dosing CAB+RPV LA between 1 January 2023 and 31 March 2028
  - For new initiators, study enrollment should occur within 1 month after their initial CAB+RPV LA injection

7.2.2 Exclusion Criteria

- Received CAB+RPV LA regimen as part of a randomized controlled clinical trial
- Treatment naïve
- VL ≥ 50 copies/mL at initiation
- Individuals with prior virologic failure to agents of NNRTI or INSTI class (if data is available)

7.3. Variables

7.3.1. Exposure Definitions

All users of CAB+RPV LA regimen treated per the approved prescribing information or summary of product characteristics for CAB+RPV LA will be included in the study.

7.3.2. Outcome Definitions

Endpoint	**Definition**
Primary	
Persistence	▪ Proportion of initiators still on CAB+RPV LA after 6, 12, 24, 36, 48 and 60 months of use and at study end
Discontinuation	▪ Proportion discontinuing after last injection: o Date of discontinuation will be the date of the last injection prior to: ▪ > 127 days after last injection with no injections and documentation of oral bridging ▪ Physician confirmed treatment switch from CAB+RPV LA to another ARV regimen ▪ Physician confirmed treatment stop of CAB+RPV LA Median time to discontinuation ▪ Proportion of individuals who discontinued and reinitiated the regimen within 6 months from discontinuation
Adherence	▪ Adherence to the dosing schedule will be assessed as the proportion of individuals who received their injections within the +/- 7-day dosing window relative to their target treatment date as detailed below (see table: Days After Last Injection) ▪ Non-adherence to the dosing schedule will be assessed as follows:

<table>
<tr><th>Endpoint</th><th>Definition</th></tr>
<tr><td></td><td>

Describe the proportion of individuals who received CAB+RPV LA more than 7 days later than their target treatment date

Mean/median (range) number and duration of delayed injections and number of individuals with 1, 2, 3 and ≥4 delayed injections

Describe the proportion of individuals who missed one consecutive injection with and without taking daily oral therapy or any other oral ARV regimen while not on CAB+RPV LA

Mean and median number of injections missed, length of delay during a 12-month period and number of individuals with 1, 2, 3 and ≥4 missed injections

<table>
<tr><td></td><td colspan="2">Days after last injection</td></tr>
<tr><td></td><td>Q2M 2nd initiation injection</td><td>Q2M continuation injection</td></tr>
<tr><td>On-time</td><td>23-37</td><td>53-67</td></tr>
<tr><td>Late</td><td>38-67</td><td>68-127</td></tr>
<tr><td>Delayed (Short delay)</td><td>38-67</td><td>68-97</td></tr>
<tr><td>Long delay (requiring re-initiation)</td><td>NA</td><td>98-127</td></tr>
<tr><td>Requiring re-initiation/ Discontinuation</td><td>>67</td><td>>127</td></tr>
</table>
</td></tr>
<tr><td>CVF</td><td>Proportion of individuals with:

▪ 2 consecutive HIV RNA VL ≥ 200 copies/mL prior to/by assessment timepoint
OR
▪ 1 HIV RNA VL level ≥ 200 copies/mL prior to/by assessment timepoint followed by core agent/regimen discontinuation within 4 months of HIV RNA VL level ≥ 200 copies/mL</td></tr>
<tr><td>Virologic suppression</td><td>▪ Proportion of individuals with VL measurement < 50 copies/mL during follow-up</td></tr>
</table>

Endpoint	Definition
Non-response	▪ Not achieving re-suppression after CVF - VL ≥50 copies/mL following CVF with no VL of <50 copies/mL during follow up
Secondary	
Injection site reactions	▪ Proportion of individuals with documented diagnostic code/diagnosis of injection site reaction or nodules attributed to administration of CAB+RPV LA ▪ Proportion of individuals Division of AIDS grading 1-4 to classify severity
Hypersensitivity reactions	▪ Proportion of individuals with documented diagnosis of Hypersensitivity, anaphylactic reaction, allergic reaction or drug allergy to CAB+RPV LA ▪ 2 or more events are reported from 2 or more of the following groups of signs/symptoms: o Rash, fever, gastrointestinal symptoms (nausea, vomiting, diarrhea, abdominal pain), constitutional symptoms (lethargy, fatigue, malaise, myalgia, arthralgia, general ill feeling) respiratory symptoms (dyspnea, sore throat, cough, chest x-ray changes, predominantly infiltrates, which can be localized) that are not excluded based on other causes of the hypersensitivity reaction-like events ▪ Cases where there is a negative rechallenge with CAB+RPV LA, Cases where symptoms resolved (or did not worsen/result in withdrawal from the study)
Emergent resistance	▪ Proportion of individuals with resistance and and proviral DNA testing at discontinuation/CVF. ▪ Proportion of individuals with history of resistance and proviral DNA testing prior to discontinuation/CVF. ▪ The proportion of individuals tested with any resistance mutation will be reported at discontinuation/CVF and history of prior to discontinuation/CVF, as will mutations associated with reduced susceptibility at the class-level and drug-level o All mutations will be reported; specific resistance mutations of interest to CAB+RPV LA can be highlighted and identified using the International Antiviral Society mutations list and Stanford HIV drug resistance database.
Patient-reported outcomes	

Endpoint	Definition
Reasons for initiating CAB+RPV LA	▪ Descriptive summary of bespoke questionnaire (2 items) completed at baseline
Baseline adherence	▪ Descriptive summary of bespoke questionnaire (4 items) completed at baseline
HIV health-related quality of life	▪ Descriptive summary of WHOQOL-HIV BREF (31 items) completed at baseline and month 12, if applicable
HIV treatment-related worries	▪ Descriptive summary of HIV Treatment-Related Worries (HRW; 3 items) completed at baseline and month 12, if applicable
HIV treatment-related stigma	▪ Descriptive summary of bespoke questionnaire (1 item) completed at baseline and month 12, if applicable
Treatment-related benefits	▪ Descriptive summary of bespoke questionnaire (7 items) completed at month 12, if applicable
Reasons for missed injection(s)	▪ Descriptive summary of bespoke questionnaire (4 items) completed at month 12, if applicable
Reasons for discontinuation	▪ Descriptive summary of bespoke questionnaire (3 items) completed at discontinuation
Social determinants of health (SDoH)	▪ Descriptive summary of bespoke questionnaire (7 items) completed at baseline and month 12, if applicable

ARV = antiretroviral; CAB = cabotegravir; CVF = confirmed virologic failure; HIV = human immunodeficiency virus; LA = long-acting; RPV = rilpivirine; VL = viral load; WHOQOL-HIV BREF = World Health Organization Quality of Life-Human Immunodeficiency Virus BREF.

7.3.3. Confounders and Effect Modifiers

Standard variables to be evaluated and included at the index date:

Demographic variables at index

- Age (years, also categorized as 18-49, 50-64, ≥ 65 years)
- Sex assigned at birth (female, male)
- Gender identity
- Race
- Ethnicity
- Marital status (single, married/domestic partner, widowed, separated/divorced, unknown)

- Geographic region
- Route of HIV infection (men who have sex with men, people who inject drugs, heterosexual, vertical, Other)
- Payer type (Medicaid, Medicare, commercial insurance, AIDS Drug Assistance Programs/Ryan White, cash)

Virologic variables at regimen initiation

- HIV VL at initiation of CAB+RPV LA regimen
  - Continuous (copies/mL)
  - Categorical:
    - < 50 copies/mL (or < limit of detection in clinics where limit of detection > 50 copies/mL)
    - ≥ 50 to < 200 copies/mL
    - ≥ 200 to < 1,000 copies/mL
    - ≥ 1,000 to < 10,000 copies/mL
    - ≥ 10,000 to < 100,000 copies/mL
    - ≥ 100,000 copies/mL
    - Missing

Immunologic variables at regimen initiation

- CD4 cell count at initiation of CAB+RPV LA regimen
  - Continuous (cells/µL)
  - Categorical:
    - > 500 cells/µL
    - > 350 to ≤ 500 cells/µL
    - > 200 to ≤ 350 cells/µL
    - > 50 to ≤ 200 cells/µL)
    - ≤ 50 cells/µL
    - Missing

Clinical variables at regimen initiation

- Number of years since HIV diagnosis
- Date of ART initiation
- HIV subtype where available
- History of previous use of integrase inhibitor-based or NNRTI-based regimen
- History of previous ARV exposure before CAB+RPV LA
  - Number of core agents experienced

  - Number of ARV classes experienced
  - Duration of last ARV regimen
  - Prior core agent class
- History of previous virologic failure
- History of previous HIV drug resistance and any historical HIV-1 subtype information, where available
- BMI, height, weight
- History of AIDS-defining events
- Co-infections
  - Hepatitis B co-infection including serology status
  - Hepatitis C co-infection
  - Syphilis infection (ever)
- Comorbidities
  - Autoimmune disease
  - Cardiovascular disease
  - Invasive cancer
  - Endocrine disorder
  - Mental health disorder
  - Liver disease
  - Bone disorder
  - Peripheral neuropathy
  - Renal disease
  - Hypertension
  - Substance abuse
  - Non-AIDS–defining malignancies (excluding hepatocellular carcinoma)
  - Any of the above
- Concomitant medications
  - Anticonvulsants
    - Carbamazepine
    - Oxcarbazepine
    - Phenobarbital
    - Phenytoin
  - Antimycobacterials
    - Rifampin

    - Rifapentine
    - Rifabutin
  - Glucocorticoids
    - Dexamethasone
  - Macrolide or ketolide antibiotics
    - Azithromycin
    - Clarithromycin
    - Erythromycin
- Narcotic analgesic
  - Methadone

7.4. Data Sources

- **Participant surveys:** New initiators of CAB+RPV LA will be asked to complete an online survey at enrollment, at month 12 (if applicable), and if they discontinue CAB+RPV LA. The online survey will include the WHOQOL-HIV BREF (O'Connell, 2012) and several bespoke questionnaires developed for this study. Appropriate agreements with the copyright owners will be in place for use in this study. It is estimated that the participant surveys will take approximately 20 minutes to complete.
- **Participant medical information via site-completed eCRF:** The investigator or authorized medical staff will record clinical and treatment data from participants' medical records into an eCRF at enrollment, applicable follow-ups (i.e., month 12, month 24, month 36, month 48, and month 60), end of study, and upon discontinuation of CAB+RPV LA, if applicable.

Participant surveys and medical record information will be linked by a common participant identifier (ID) code that will be retained by the site.

7.5. Study Size

The study will aim to enroll a total of 1,000 participants. Among them, it is estimated that 250 participants are already receiving CAB+RPV LA at the time of study start, and 750 participants will be newly initiating CAB+RPV LA.

There is no formal statistical hypothesis to be tested in these analyses. The study will be descriptive in nature and will focus on absolute effectiveness estimation. A precision calculation was performed using post-authorization safety study software version 14 using the exact Clopper-Pearson method based on the cumulative probabilities of the binomial distribution for 1 proportion.

In order to demonstrate the estimated precision for the total sample size and also among the groups of participants already receiving and newly initiating CAB+RPV LA, Table 1 presents the precision calculations for the width of 95% confidence intervals for a range of proportions and a combination of sample sizes. It is anticipated that data from 1,000 participants are thought adequate to provide reasonable precision around a point estimate

(here defined as a proportion) to meet the study objectives. With 1,000 participants, the 2-sided 95% confidence interval precision width for the estimation of virologic failure rate will range from 1.85% and 3.1% for a failure rate ranging from 2% to 6%.

Table 1. Exact Confidence Intervals for Various Combinations of Sample Size and Proportions

Confidence level	Sample size (N)	Proportion (P)	95% Lower limit	95% Upper limit	Actual width
0.95	250	0.0200	0.0065	0.0461	0.0395
	250	0.0300	0.0126	0.0595	0.0469
	250	0.0400	0.0193	0.0723	0.0530
	250	0.0500	0.0265	0.0848	0.0583
	250	0.0600	0.0340	0.0970	0.0631
	300	0.0200	0.0074	0.0430	0.0356
	300	0.0300	0.0138	0.0562	0.0424
	300	0.0400	0.0208	0.0688	0.0480
	300	0.0500	0.0283	0.0811	0.0529
	300	0.0600	0.0359	0.0932	0.0572
	750	0.0200	0.0112	0.0328	0.0215
	750	0.0300	0.0190	0.0449	0.0259
	750	0.0400	0.0271	0.0566	0.0295
	750	0.0500	0.0355	0.0681	0.0326
	750	0.0600	0.0441	0.0795	0.0354
	800	0.0200	0.0115	0.0323	0.0208
	800	0.0300	0.0193	0.0443	0.0250
	800	0.0400	0.0275	0.0560	0.0285
	800	0.0500	0.0360	0.0675	0.0315
	800	0.0600	0.0446	0.0788	0.0342
	850	0.0200	0.0117	0.0318	0.0201
	850	0.0300	0.0196	0.0438	0.0242
	850	0.0400	0.0279	0.0554	0.0276
	850	0.0500	0.0363	0.0669	0.0305
	850	0.0600	0.0450	0.0781	0.0331
	900	0.0200	0.0119	0.0314	0.0195
	900	0.0300	0.0199	0.0433	0.0235
	900	0.0400	0.0282	0.0549	0.0268
	900	0.0500	0.0367	0.0663	0.0296
	900	0.0600	0.0454	0.0776	0.0322
	950	0.0200	0.0121	0.0311	0.0190
	950	0.0300	0.0201	0.0429	0.0228
	950	0.0400	0.0285	0.0545	0.0260
	950	0.0500	0.0370	0.0658	0.0288
	950	0.0600	0.0458	0.0770	0.0313

Confidence level	Sample size (N)	Proportion (P)	95% Lower limit	95% Upper limit	Actual width
	1,000	0.0200	0.0123	0.0307	0.0185
	1,000	0.0300	0.0203	0.0426	0.0222
	1,000	0.0400	0.0287	0.0541	0.0253
	1,000	0.0500	0.0373	0.0654	0.0281
	1,000	0.0600	0.0461	0.0766	0.0305

7.6. Data Management

The Qualtrics electronic data capture (EDC) system will be used to capture data from eCRFs and participant surveys. The system will be programmed and tested by RTI-HS data management staff. Participants who consent and are formally enrolled in the study will be asked to complete their surveys on their own device via an electronic link provided by RTI-HS. If participants skip a question, they will be prompted to complete it. If they still wish to skip it, they will be able to continue to the next question. Investigators or authorized staff will enter clinical data from participants' medical records directly into the EDC system at the protocol specified timepoints. There is no plan to reconcile any discrepancies in data between individual responses to the survey and their medical record data.

Data will be linked by a common participant identification (ID) code (i.e., participant data are de-identified). Limited personal IDs (e.g., age but not names or email addresses) will be stored with the data.

All data management activities will be fully documented in a detailed data management plan. The plan will describe the EDC system used in the study, user acceptance testing of the system, data sources, data collection/entry methods, querying of missing or unclear data, data cleaning plans, data storage procedures during the study, data set creation, database lock, and data archival.

7.7. Data Analysis

7.7.1. Primary Analysis

7.7.1.1. Main analytical approach

Baseline characteristics and outcomes will be described using counts and relative frequencies for categorical variables and means, standard deviations, medians, minimums, maximums, and quartiles 1 and 3 for continuous variables. For event outcomes, incidence rates will be estimated using unadjusted Poisson regression, accounting for person-time since index (i.e., first CAB+RPV LA injection). Additional analytic approaches may also be considered for select time-to-event outcomes (e.g., time

to discontinuation) such as estimators that take into account right-censoring (e.g., Kaplan-Meier estimator).

Analyses will be stratified by BMI (< 30 kg/m^2 vs. ≥ 30 kg/m^2), age (18-49, 50-64, ≥ 65 years), sex (male, female), race/ethnicity (Non-Hispanic White, Non-Hispanic Black, Hispanic, other) and country at first CAB+RPV LA injections, as sample size allows, to assess characteristics, adherence, persistence, discontinuation, and virologic effectiveness. Other demographic and clinical variables may also be considered for stratification, if relevant.

Additionally, factors such as, age, sex assigned at birth, race, geographic region, BMI, IDU, CD4 count, and comorbidities associated with CVF will be explored using a logistic regression model.

7.7.1.2. Data handling conventions

Data handling conventions applicable to this study design as described in the Guidelines for Good Pharmacoepidemiology Practices (GPP) issued by the International Society for Pharmacoepidemiology (ISPE) will be followed to ensure ethical and scientific recording and reporting of non-interventional trials that involve data from human subjects. The following procedures will be undertaken:

- Automatic checks and prompts are built into the EDC program (e.g., checks for out-of-range numeric values). Each individual eCRF will be further evaluated for logical consistency between study variables, potential outliers, and missing information.
- Inconsistencies noted in the eCRF data will be queried with the site using data-clarification procedures. Sites will be queried for clarification via the EDC system if any such issues are identified. Database lock will be issued when all queries have been resolved.
- Participant medical chart data will be abstracted into the eCRF by qualified site staff, identified only by the unique subject identification number. Linkage between the identification number and the participant records will be recorded at a site-level only and will not be shared externally with RTI-HS or ViiV Healthcare. Data will be abstracted by site staff from participant medical records and entered into an eCRF hosted on the secure EDC system. The link between the subject identification code and the individual participant must be destroyed by the site at the end of the study.

7.7.1.3. Sensitivity analyses

No sensitivity analyses are planned.

7.7.2. Secondary Analysis/Exploratory Analysis

Individual surveys will be summarized descriptively for item and summary score (where applicable). The WHOQOL-HIV BREF will be scored according to instrument scoring guidelines. All analyses will be performed on the observed data only, and no missing values will be imputed.

7.8. Quality Control and Quality Assurance

This project will be conducted in accordance with all applicable regulatory requirements. The Office of Quality Assurance, an independent unit that reports to the vice president of RTI-HS, will oversee quality assurance for this study.

Standard operating procedures will be used to guide the conduct of the study. These procedures include rules for secure and confidential data storage, methods to maintain and archive project documents, quality control procedures for programming, standards for writing analysis plans, and requirements for senior scientific review.

All programming written by one study analyst will be independently reviewed by a different analyst, with oversight by a senior statistician.

All key study documents, such as the analysis plan, data collection forms, and study reports, will undergo quality control review, senior scientific review, and editorial review.

7.8.1. Site Training

Investigators and study coordinators will be trained via an initial web-based training session on the protocol, including adverse event (AE) reporting, study flow, EDC system, documentation, site responsibilities and expectations, and any applicable study processes. Any new information relevant to the performance of this study will be forwarded to the medical staff during the study.

No on-site monitoring visits will be performed for this study. Remote data monitoring will be conducted during the life of the study to ensure linkage and integrity between the eCRFs and the participant surveys and to identify missing or unclear data in the eCRFs and issue queries.

RTI-HS will closely monitor the participant recruitment and data collection on a regular basis. Specifically, RTI-HS will provide oversight of activities, including screening participants, recruiting and obtaining consent from participants, and completion of electronic surveys and eCRFs. RTI-HS will maintain regular communication with all sites and will assess progress and site performance and address any issues as they arise.

7.9. Limitations of the Research Methods

Limitations of this study are common to non-randomized non-interventional study. This is a study of routine clinical care and reflects treatment practice across multiple countries and diverse clinical sites. This will be a single treatment group analysis with no formal

statistical comparisons. While the study aims to include approximately 1,000 users of the CAB+RPV LA regimen, market uptake of the regimen and individuals' willingness to participate will dictate timelines for enrollment and data collection. The results from this study should be interpreted cautiously, with careful consideration given to the limitations of the observational study design.

7.9.1. Study Closure/Uninterpretability of Results

Not applicable; these are descriptive analyses of observational, real-world data.

7.10. Other Aspects

None

8. PROTECTION OF HUMAN SUBJECTS

8.1. Ethical Approval and Subject Consent

The study will be conducted in accordance with legal and regulatory requirements; with scientific purpose, value, and rigor; and will follow generally accepted research practices described in GPP issued by Public Policy Committee of the ISPE.

Ethics review requirements and processes for prospective studies vary among countries and are governed by local standards. This study will be conducted in accordance with such standards in each country.

RTI-HS, with assistance from local clinical research associates, will work in collaboration with the site Principal Investigators to submit the necessary ethics review applications in each country at both the site and the national or regional levels, where applicable. The following activities are anticipated in each country:

- US
  - Study documents will be submitted to an institutional review board (IRB) for review and approval
  - It is possible that some participating sites may require full review by their respective IRB
- UK
  - An application through the Integrated Research Application System (IRAS) will be used to submit the study for applicable Research Ethics Committee (REC) and Health Research Governance Authority (i.e., Health Research Authority [HRA] and Health and Care Research Wales [HCRW] for England and Wales, National Health Service [NHS] Research Scotland Permissions Coordinating Center [NRSPCC] for Scotland, Health and Social Care [HSC] for Northern Ireland) review and approval

- France
  - An application through the Système d'Information des Recherches Impliquant la Personne Humaine (SI RIPH 2G) will be used to submit the study for Comité de Protection des Personnes (CPP) review and approval
  - The study design is expected to be compliant with Reference Methodology MR003 (for research involving human subjects but not requiring informed consent—information letter and opt-out option to be collected instead), else a request for authorization will be sought from Commission Nationale de l'Informatique et des Libertés (CNIL [Data Protection Agency])
  - A notification to French Health Authority (Agence Nationale de sécurité des médicaments et des produits de santé [ANSM]) will be completed
- Germany
  - Mandatory national notification of all human subjects' studies are made to Germany's primary medical regulatory body, the Bundesinstitut far Arzneimittel und Medizinprodukte (BfArM [Federal Institute for Pharmaceuticals and Medical Products])
  - Ethics approval is required at only the designated lead site
  - Notification of lead site approval will be provided to other sites
  - Sites (other than the lead site) may require full review by their respective ethics review committee
- Italy
  - The study will be notified to AIFA and registered on the observational study registry (Registro Studi Osservazionali [RSO])
  - Ethics approval is required only at the designated lead site
  - Notification of lead site approval will be provided to other sites
  - Sites (other than the lead site) may require full review by their respective ethics review committee
  - Sponsor's Privacy Impact Assessment to be communicated to Italian Data Protection Agency (Garante Per la Protezione dei Dati Personali [GPDP])
- Spain
  - The study will be notified to AEMPS
  - Ethics approval is required only at the designated lead site
  - Notification of lead site approval will be provided to other sites
  - Sites (other than the lead site) may require full review by their respective ethics review committee
  - Submission to autonomous community ethics committee of each participating site may also be required

  - As of 2 January 2021, a new Royal Decree came into effect; study classification of such studies by the Spanish Agency of Medicines and Medical Devices (Agencia Española de Medicamentos y Productos Sanitarios [AEMPS]) is no longer needed

- Portugal
  - Ethics approval is conducted in each participating site
  - The study will be notified to Infarmed
- Australia
  - Review and approval is required from an accredited Health Research Ethics Committee (HREC). If sites are part of the national mutual acceptance scheme for multiple center research, then only 1 approval is needed, otherwise, approval from each site's HREC is required. In addition, for nonpublic sites, site specific authorization (Research Governance Office) is required
  - Notification to Health Authority is not required for studies with no investigational product

If necessary, other activities to obtain ethics clearance in each country will be performed upon request of local ethics authority/EC/IRB.

Informed consent will be obtained from individuals (or their legally acceptable representative) by site study staff before data collection. The person obtaining consent will be responsible for ensuring that each participant fully understands the nature, purpose, risks, and benefits associated with participation. Each participating individual will be provided with a copy of his or her signed informed consent form. The investigator, or a person designated by the investigator, will retain the original of each individual's signed consent form.

Individuals (or the individual's legally acceptable representative) may choose to withdraw consent at any time. At time of withdrawal, all data that have already been processed and analyzed will be kept to guarantee the integrity of the study. Once data has been processed and analyzed (i.e., at the point of data analysis), the information may continue to used.

8.2. Subject Confidentiality

ViiV and all investigators will ensure adherence to applicable data privacy protection regulation. The research team at RTI-HS and any approved vendors will have access to pseudonymized individual data. Sites will maintain a subject identification log with the names/initials/identifiers of individuals who consented to participate in the study and study subject ID. Sites will assign subject ID at time of individual enrollment. Subject identification logs will be maintained at the sites and will never be shared with the research team at RTI-HS, third parties, or ViiV. Additionally, the collected data (eCRF and individual questionnaires) will not contain any individual-identifying information to further protect confidentiality (for instance, age or year of birth will be collected in lieu of a full birth date). To comply with applicable data protection regulations, European Union

(EU) and UK personal data will be collected and stored in the EU or UK and only staff dedicated to this project and located in EU will have access to these. Pseudonymized data sets will be transferred to the US. Finally, only aggregated data in the form of analysis tables will be made available to ViiV. Thus, any reports generated will not contain any participant identifiers.

9. LEGAL BASIS FOR PROCESSING INDIVIDUAL HUMAN DATA

The authors confirm that study data is Individual Human Data not owned by ViiV, but that the proposed use of the Individual Human Data aligns with the 'purpose of use' outlined in the source contract and/or the terms and conditions of use of the data source and it will comply with any specified prohibitions of use.

10. MANAGEMENT AND REPORTING OF ADVERSE EVENTS/ADVERSE REACTIONS

This study has safety objectives. Safety collection and reporting will correspond to the following study types:

The participant surveys represent study type 1: Primary data collection studies with or without sites/investigators with safety objectives where there is consent and/or data collection direct from individuals. This part of the study is able to identify solicited events only.

Collection of Adverse Events/Reactions (Solicited Events)

Solicited Events are defined as adverse events related to the GSK/ViiV product under evaluation and identified for collection in the study database as per study objectives. A Safety Management Plan (SMP) will be developed as per VQD-WI-053775: Non-Interventional Study Safety Management Planning. The SMP will include more detailed definitions of AE types as well as details of the causality assessment. Reporting timelines and safety contact details will also be provided in accompanying SMP.

Solicited events must be collected in the study database and reported to GSK for entry into the GSK Safety database. All AEs/SAEs, pregnancies and incidents, systematically collected in the Participant Surveys, which will be based on closed ended questions[1] only, according to study objectives and considered causally related to the GSK/ViiV product being evaluated (ADRs) should be reported to the GSK Safety department (timing and contact information provided in the safety management plan). For primary data collection studies, where there is direct collection of data from individuals, these will be classified as solicited individual case safety reports (ICSRs). Valid ICSRs will be managed, classified, and submitted for onward reporting to regulators in line with the appropriate time frames as detailed in the Safety Management Plan. These will also be summarised in interim, if applicable, and final study reports.

[1] A closed ended question is where a respondent can only choose a pre-set response.

Reporting of Adverse Events/Reactions (Spontaneous Events)

Adverse events related to CAB+RPV LA cannot be reported due to interview/survey structure based on closed ended questions only. Study staff will be trained on how to report suspected adverse reactions if a individual should report them outside of the conduct of the study.

The site completed e-CRF represent study type 5: Secondary data collection studies including unstructured data with human review with safety objectives. These studies can identify solicited events in aggregate at study end but cannot identify spontaneous events.

Collection of adverse events/reactions (Solicited Events)

Solicited Events are defined as adverse events related to the GSK/ViiV product under evaluation and identified for collection as per study objectives.

The purpose of the study is to monitor exposure to CAB+RPV LA and to evaluate persistence, adherence, discontinuation and virologic effectiveness among PWH receiving CAB+RPV LA regimen. For CAB+RPV LA regimen, pre-defined safety events of interest persistence, adherence, discontinuation and virologic effectiveness, will be systematically recorded in aggregate. These will be summarised in final study reports. This study is based on secondary use of existing health data and as such Individual Case Safety Reporting (ICSRs) to regulatory agencies is not required.

Reporting of adverse events/reactions (Spontaneous Events)

This study is based on data previously collected for other purposes e.g., routine healthcare encounters. As such, there is no requirement for the collection and reporting of Individual Case Safety Reports (ICSRs). Although the study is based on human review of unstructured data, the nature of the secondary data protocol driven data collection and analysis does not allow for reporting of serious and non-serious AEs, pregnancy exposures, or incidents related to any GSK/ViiV product during the conduct of this research. In addition, the minimum criteria of identifiable patient, reporter, exposure and event, needed to report individual case safety reports may not be present in the information reviewed within the context of the study. The data also may lack an identifiable patient and reporter and may be insufficient to establish attribution between a potential safety event and an individual patient using a GSK/ViiV product.

11. PLANS FOR DISSEMINATING AND COMMUNICATING STUDY RESULTS

The target audience for these data includes healthcare providers, health plan population-based decision-makers, and regulatory and health authorities.

Abstracts will be prepared for both the interim and final analysis, with a manuscript developed from the final data set. All publications will comply with the *International Committee of Medical Journal Editors* (ICMJE) guidelines. A final full study report will be submitted to the Sponsor. Study results will be submitted to scientific conferences and for peer-reviewed journal publication.

12. REFERENCES

O'Connell, KA, Skevington, SM. An international quality of life instrument to assess wellbeing in adults who are HIV-positive: a short form of the WHOQOL-HIV (31 items). AIDS Behav. 2012;16:452-60. doi:10.1007/s10461-010-9863-0.