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THE LONG-ACTING THERAPEUTICS PATENTS AND LICENCES DATABASE

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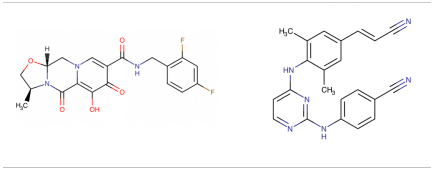


Cabotegravir and Rilpivirine

Originator/manufacturer

ViiV Healthcare
https://viivhealthcare.com/

United Kingdom

ViiV Healthcare is a pharmaceutical company that specializes in the development of therapies for HIV infection. The company is headquartered in Brentford in the United Kingdom and was initially formed in November 2009 as a part of a joint venture between GlaxoSmithKline and Pfizer.

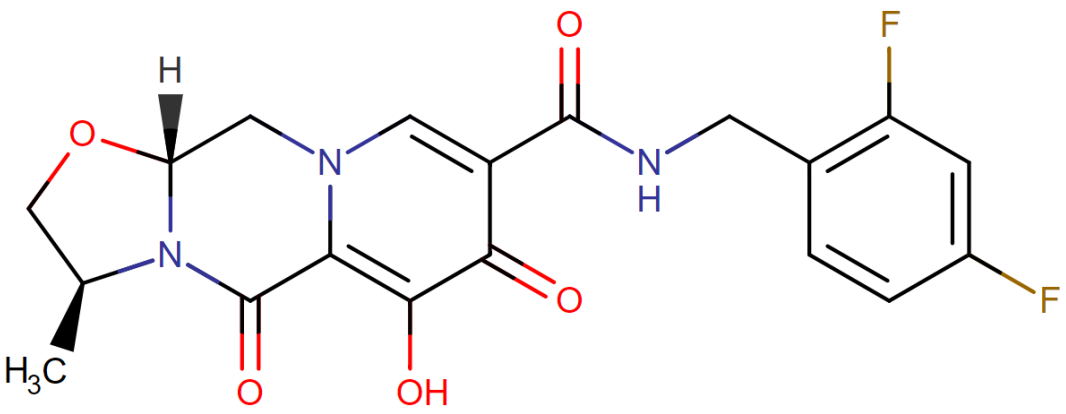
Janssen Pharmaceuticals
https://www.janssen.com/

Belgium

Janssen Pharmaceuticals is a subsidiary company of Johnson & Johnson headquartered in Beerse, Belgium. They manufacture and develop pharmaceutical products for use in areas such as, Immunology, Infectious Diseases & Vaccines, Pulmonary Hypertension, Cardiovascular & Metabolism, Oncology, and Neuroscience.

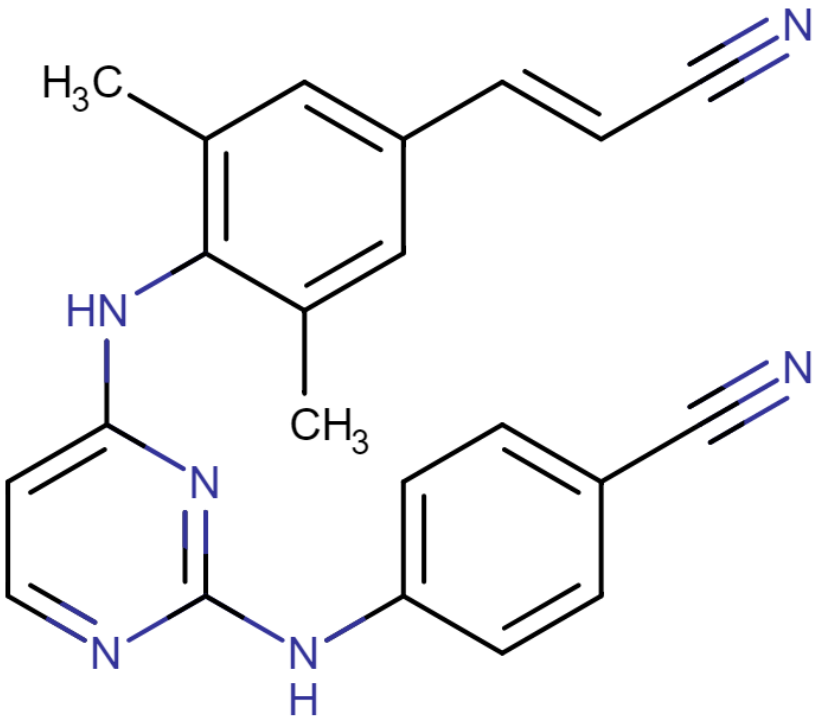
ViiV Healthcare(vocabria) / Janssen-Cilag Ltd (Rilprivine)

Drug structure



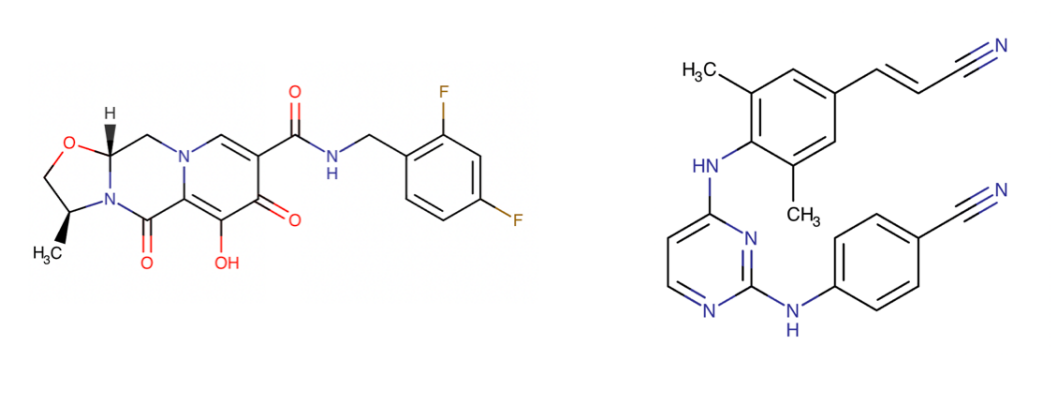
Cabotegravir Chemical Structure

Sourced from DrugBank



Rilpivirine Chemical Structure

Sourced from DrugBank



CAB/RPV Chemical Structures

Constituent Images Sourced from DrugBank

Drug information

Associated long-acting platforms

Aqueous drug particle suspension

Administration route

Oral, Subcutaneous, Intramuscular

Therapeutic area(s)

HIV

Use case(s)

Treatment

Use of drug

Ease of administration

Administered by a nurse
Administered by a specialty health worker
Self-administered

User acceptance

Not provided

Drug information

Drug's link(s)

Not provided

Generic name

Cabotegravir and Rilpivirine

Brand name

Cabenuva (Cabotegravir and Rilpivirine co-packaged medication) and Vocabria (Cabotegravir) co-administered with Rekambys (Rilpivirine).

Summary

Long-acting injectable Cabotegravir and Rilpivirine (CAB/RPV-LA) is a complete treatment regimen for HIV-1 infection consisting of two components: (1) Cabotegravir a HIV-1 integrase strand transfer inhibitor developed by ViiV Healthcare and (2) Rilpivirine a second-generation non-nucleoside reverse transcriptase inhibitor manufactured by Janssen. CAB/RPV-LA is designated for the treatment of HIV-1 infection in virologically suppressed (<50 copies/mL HIV-1 RNA) adults and adolescents aged twelve and over who weigh at least 77 pounds (35 kilograms) receiving a stable antiretroviral regimen with no history of treatment failure or resistance to either rilpivirine and/or cabotegravir.

Approval status

Cabotegravir and Rilpivirine extended-release injectable suspensions co-packaged as CABENUVA is approved by the USFDA, Health Canada, Australia, UAE and UK. Individually packaged extended-release Cabotegravir (VOCABRIA) and extended-release Rilpivirine (REKAMBYS) are approved in the Argentina, European Union, Botswana, Brazil, Canada, Chile, China, Hong Kong, Israel, Japan, Russia, Singapore, South Africa, South Korea, Taiwan, UAE, and UK for co-administration in the treatment

of HIV-1 infection. CAB- RPV LA injectables are awaiting approval in countries such as Colombia, Mexico and Thailand.

Regulatory authorities

CAB and RPV combination has received supplemental NDA approval with an Extended Label from the USFDA, inclusion in the Black Triangle Symbol Scheme by TGA Australia, and European Marketing Authorization by the EMA. This combination is specifically indicated for virologically suppressed adults with HIV-1 infection (HIV-1 RNA <50 copies per millilitre [c/ml]), weighing at least 35 kg. Eligible patients must have previously maintained stability on a treatment regimen without experiencing treatment failure or showing signs of resistance to Rilpivirine/Cabotegravir.

Delivery device(s)

No delivery device

Scale-up and manufacturing prospects

Scale-up prospects

Compounds are commercially manufactured.

Tentative equipment list for manufacturing

Conventional wet-bead milling apparatus (e.g. Netzsch ball mill), depyrogenated glass vials, high pressure homogenizer.

Manufacturing

Cabotegravir and Rilpivirine are formulated into a wet-mill suspension of approximately 200mg/ml and 300mg/ml respectively, due to their low aqueous solubility. This formulation results in the creation of nanocrystal drug particles which are amenable for intramuscular gluteal depot injection. The manufacturing process for RPV is considered to be non-standard due to the inclusion of an aseptic processing step. RPV is light-sensitive, and exposure to light can induce conversion into a Z-isomer form which can affect pharmacokinetic data and activity.

Specific analytical instrument required for characterization of formulation

PANalytical X’Pert PRO diffractometer equipped with a theta/theta coupled goniometer (or equivalent x-ray powder diffractor), Mettler TGA/DSC 1 instrument for thermal analysis, Laser diffractor (determine particle size), FT-IR UHPLC (chemical identification), UHPLC (chromatographic purity), paddle apparatus & UPLC/UV (determine in-vitro drug release for QC / dissolution testing).

Clinical trials

POLAR

Identifier

NCT03639311

Link

https://clinicaltrials.gov/study/NCT03639311

Phase

Phase II

Status

Completed

Sponsor

ViiV Healthcare

More details

Not provided

Purpose

Assess the antiviral activity and safety of CAB LA plus RPV LA, administered Q2M, in approximately 100 adult HIV-1 infected, antiretroviral therapy (ART) experienced participants.

Interventions

Drug: CAB LA

Drug: RPV LA

Drug: RPV

Drug: DTG

Countries

United States of America

Canada

Sites / Institutions

Not provided

Trials dates

Anticipated Start Date

Not provided

Actual Start Date

2018-08-20

Anticipated Date of Last Follow-up

Not provided

Estimated Primary Completion Date

Not provided

Estimated Completion Date

Not provided

Actual Primary Completion Date

2019-12-11

Actual Completion Date

2023-01-30

Studied populations

Age Cohort

- Adults
- Older Adults

Genders

- All

Accepts pregnant individuals

No

Accepts lactating individuals

No

Accepts healthy individuals

No

Comments about the studied populations

Participants will rollover from the NCT01641809 (LATTE) study, who have completed minimum duration of Week 312 and with demonstrated HIV-1 ribonucleic acid (RNA) suppression (less than [<]50 copies (c) per milliliter [mL]), while receiving a two-drug regimen consisting of once-daily oral CAB at 30 milligram (mg) plus RPV at 25 mg. The participants will be offered the option to switch to the LA, intramuscular injections of CAB LA plus RPV LA, Q2M or the oral fixed dose combination (FDC) of dolutegravir (DTG) plus RPV, for the continued maintenance of HIV-1 RNA suppression, known as the Maintenance Phase (From Day 1 to Commercial Approval).

Health status

Positive to : HIV
Negative to : HBV

Study type

Interventional (clinical trial)

Enrollment

97

Allocation

Non-randomized

Intervention model

Parallel Assignment

Intervention model description

This is an Intervention Model, with parallel assignment, where the primary purpose of the study is, treatment, with 2 arms and no masking.

Masking

Open label

Masking description

This is an open-label study, thus no masking.

Frequency of administration

Once every 8 weeks

Studied LA-formulation(s)

Injectable

Studied route(s) of administration

Intramuscular

Use case

Treatment

Key results

Type of key results	Title	Website link
Article	Long-acting cabotegravir and rilpivirine for HIV-1 suppression: switch to 2-monthly dosing after 5 years of daily oral therapy	https://doi.org/10.1097/qad.000000000

CUSTOMIZE

Identifier

NCT04001803

Link

https://clinicaltrials.gov/study/NCT04001803

Phase

Phase III

Status

Completed

Sponsor

ViiV Healthcare

More details

Not provided

Purpose

Identify and Evaluate Strategies for Successful Implementation of the Cabotegravir + Rilpivirine Long-acting Injectable Regimen in the US.

Interventions

Drug: CAB LA+RPV LA

Countries

United States of America

Sites / Institutions

Not provided

Trials dates

Anticipated Start Date

Not provided

Actual Start Date

2019-07-08

Anticipated Date of Last Follow-up

Not provided

Estimated Primary Completion Date

Not provided

Estimated Completion Date

Not provided

Actual Primary Completion Date

2020-10-05

Actual Completion Date

2022-03-18

Studied populations

Age Cohort

- Adults
- Older Adults

Genders

- All

Accepts pregnant individuals

No

Accepts lactating individuals

No

Accepts healthy individuals

No

Comments about the studied populations

Not provided

Health status

Positive to : HIV
Negative to : HBV

Study type

Interventional (clinical trial)

Enrollment

115

Allocation

Not provided

Intervention model

Single group assignment

Intervention model description

Not provided

Masking

Open label

Masking description

None (Open Label)

Frequency of administration

Monthly

Studied LA-formulation(s)

Injectable

Studied route(s) of administration

Intramuscular

Use case

Treatment

Key results

Type of key results	Title	Website link
Article	Perspectives of people living with HIV-1 on implementation of long-acting cabotegravir plus rilpivirine in US healthcare settings	https://doi.org/10.1002/jia2.26006
Article	Perspectives of healthcare providers on implementation of long-acting cabotegravir plus rilpivirine in US healthcare settings from a Hybrid III Implementation-effectiveness study (CUSTOMIZE)	https://doi.org/10.1002/jia2.26003

CR109089

Identifier

NCT05112939

Link

https://clinicaltrials.gov/study/NCT05112939

Phase

Phase I

Status

Active, not recruiting

Sponsor

Janssen Research & Development, LLC

More details

Not provided

Purpose

Characterize the single dose pharmacokinetics and evaluate the safety and tolerability of subcutaneous administration of RPV LA in combination with CAB LA in different conditions in healthy adults.

Interventions

Drug: RPV LA
Drug: CAB LA

Countries

United States of America

Netherlands

Sites / Institutions

Not provided

Trials dates

Anticipated Start Date

Not provided

Actual Start Date

2021-11-16

Anticipated Date of Last Follow-up

Not provided

Estimated Primary Completion Date

2024-05-23

Estimated Completion Date

2024-05-23

Actual Primary Completion Date

Not provided

Actual Completion Date

Not provided

Studied populations

Age Cohort

- Adults

Genders

- All

Accepts pregnant individuals

No

Accepts lactating individuals

Unspecified

Accepts healthy individuals

Yes

Comments about the studied populations

Participant must be healthy on the basis of physical examination, clinical laboratory tests, medical history, vital signs, and 12-lead electrocardiogram (ECG).

Health status

Not provided

Study type

Interventional (clinical trial)

Enrollment

126

Allocation

Randomized

Intervention model

Parallel Assignment

Intervention model description

Not provided

Masking

Single blind masking

Masking description

Single (Participant)

Frequency of administration

Other(s) : "Single dose. "

Studied LA-formulation(s)

Injectable

Studied route(s) of administration

Subcutaneous

Use case

Treatment

Key results

Not provided

ATLAS-2M

Identifier

NCT03299049

Link

https://clinicaltrials.gov/study/NCT03299049

Phase

Phase III

Status

Active, not recruiting

Sponsor

ViiV Healthcare

More details

Not provided

Purpose

Evaluating the Efficacy, Safety, and Tolerability of Long-acting Cabotegravir Plus Long-acting Rilpivirine in HIV-1-infected Adults Who Are Virologically Suppressed.

Interventions

Drug: Cabotegravir Tablets
Drug: Rilpivirine Tablets
Drug: Cabotegravir Injectable Suspension
Drug: Rilpivirine Injectable Suspension

Countries

United States of America
Argentina
Australia
Canada
France
Germany
Italy
Korea, Republic of
Mexico
Russian Federation
South Africa
Spain
Sweden

Sites / Institutions

Not provided

Trials dates

Anticipated Start Date

Not provided

Actual Start Date

2017-10-27

Anticipated Date of Last Follow-up

Not provided

Estimated Primary Completion Date

Not provided

Estimated Completion Date

2026-12-31

Actual Primary Completion Date

2019-06-06

Actual Completion Date

Not provided

Studied populations

Age Cohort

- Adults
- Older Adults

Genders

- All

Accepts pregnant individuals

No

Accepts lactating individuals

No

Accepts healthy individuals

No

Comments about the studied populations

Not provided

Health status

Positive to : HIV

Negative to : HBV

Study type

Interventional (clinical trial)

Enrollment

1049

Allocation

Randomized

Intervention model

Parallel Assignment

Intervention model description

Two groups of subjects will be randomized to receive CAB LA + RPV LA Q4W, or CAB LA + RPV LA Q8W regimen.

Masking

Open label

Masking description

This will be an open-label study and therefore no blinding is required.

Frequency of administration

Monthly
Once every 8 weeks

Studied LA-formulation(s)

Injectable

Studied route(s) of administration

Intramuscular

Use case

Treatment

Key results

Type of key results	Title	Website link
Article	Indirect comparison of 48-week efficacy and safety of long-acting cabotegravir and rilpivirine maintenance every 8 weeks with daily oral standard of care antiretroviral therapy in participants	https://doi.org/10.1186/s12879-022-07243-3
Article	Long-acting cabotegravir and rilpivirine dosed every 2 months in adults with HIV-1 infection (ATLAS-2M), 96-week results: a randomised, multicentre, open-label, phase 3b, non-inferiority study	https://doi.org/10.1016/s2352-3018(21)00185-5
Article	Week 96 extension results of a Phase 3 study evaluating long-acting cabotegravir with rilpivirine for HIV-1 treatment	https://doi.org/10.1097/qad.000000000
Article	Patient-Reported Outcomes Through 1 Year of an HIV-1 Clinical Trial Evaluating Long-Acting Cabotegravir and Rilpivirine Administered Every 4 or 8 Weeks (ATLAS-2M)	https://doi.org/10.1007/s40271-021-00524-0

Type of key results	Title	Website link
Article	Long-acting cabotegravir and rilpivirine dosed every 2 months in adults with HIV-1 infection (ATLAS-2M), 48-week results: a randomised, multicentre, open-label, phase 3b, non-inferiority study	https://doi.org/10.1016/s0140-6736(20)32666-0

SOLAR

Identifier

NCT04542070

Link

https://clinicaltrials.gov/study/NCT04542070

Phase

Phase III

Status

Completed

Sponsor

ViiV Healthcare

More details

Not provided

Purpose

Assess the antiviral activity and safety of a two-drug regimen of CAB LA + RPV LA compared with maintenance of BIK. BIKTARVY is a registered trademark of Gilead Sciences.

Interventions

Drug: Cabotegravir Tablets
Drug: Cabotegravir Injectable Suspension (CAB LA)
Drug: Rilpivirine Tablets
Drug: Rilpivirine Injectable Suspension (RPV LA)

Drug: BIKTARVY Tablets (BIK)

Countries

United States of America
Australia
Austria
Belgium
Canada
France
Germany
Ireland
Italy
Japan
Netherlands
Spain
Switzerland
United Kingdom

Sites / Institutions

Not provided

Trials dates

Anticipated Start Date

Not provided

Actual Start Date

2020-11-09

Anticipated Date of Last Follow-up

Not provided

Estimated Primary Completion Date

Not provided

Estimated Completion Date

Not provided

Actual Primary Completion Date

2022-07-13

Actual Completion Date

2023-04-17

Studied populations

Age Cohort

- Adults
- Older Adults

Genders

- All

Accepts pregnant individuals

No

Accepts lactating individuals

No

Accepts healthy individuals

No

Comments about the studied populations

Not provided

Health status

Positive to : HIV

Negative to : HBV

Study type

Interventional (clinical trial)

Enrollment

687

Allocation

Randomized

Intervention model

Parallel Assignment

Intervention model description

Not provided

Masking

Open label

Masking description

None (Open Label)

Frequency of administration

Once every 8 weeks

Studied LA-formulation(s)

Injectable

Studied route(s) of administration

Intramuscular

Use case

Treatment

Key results

Type of key results	Title	Website link
Article	Factors Associated with Health Care Providers' Preference for Forgoing an Oral Lead-In Phase When Initiating Long-Acting Injectable Cabotegravir and Rilpivirine in the SOLAR Clinical Trial	https://doi.org/10.1089/apc.2022.0168

ATLAS

Identifier

NCT02951052

Link

https://clinicaltrials.gov/study/NCT02951052

Phase

Phase III

Status

Active, not recruiting

Sponsor

ViiV Healthcare

More details

Not provided

Purpose

Establish if HIV-1 infected adult subjects with current viral suppression on a regimen with 2 NRTIs plus a third agent, remain suppressed upon switching to a 2 drug intramuscular regime of CAB/RPV-LA.

Interventions

Drug: Cabotegravir (CAB) tablets
Drug: Rilpivirine (RPV) tablets
Drug: Cabotegravir - Injectable Suspension (CAB LA)
Drug: Rilpivirine - Injectable Suspension (RPV LA)

Drug: 2 NRTIs plus an INI, NNRTI, or PI

Countries

United States of America
Argentina
Australia
Canada
France
Germany
Italy
Korea, Republic of
Mexico
Russian Federation
South Africa
Spain
Sweden

Sites / Institutions

Not provided

Trials dates

Anticipated Start Date

Not provided

Actual Start Date

2016-10-28

Anticipated Date of Last Follow-up

Not provided

Estimated Primary Completion Date

Not provided

Estimated Completion Date

2026-12-31

Actual Primary Completion Date

2018-05-29

Actual Completion Date

Not provided

Studied populations

Age Cohort

- Adults
- Older Adults

Genders

- All

Accepts pregnant individuals

No

Accepts lactating individuals

No

Accepts healthy individuals

No

Comments about the studied populations

Must be on uninterrupted current ARV regimen (either the initial or second ARV regimen) for at least 6 months prior to Screening. Any prior switch, defined as a change of a single drug or multiple drugs simultaneously, must have occurred due to tolerability/safety, access to medications, or convenience/simplification, and must NOT have been done for treatment failure (HIV-1 RNA ≥400 c/mL).

Health status

Positive to : HIV

Negative to : HBV

Study type

Interventional (clinical trial)

Enrollment

618

Allocation

Randomized

Intervention model

Parallel Assignment

Intervention model description

Not provided

Masking

Open label

Masking description

None (Open Label)

Frequency of administration

Monthly

Studied LA-formulation(s)

Injectable

Studied route(s) of administration

Intramuscular

Use case

Treatment

Key results

Type of key results	Title	Website link
Article	Week 96 extension results of a Phase 3 study evaluating long-acting cabotegravir with rilpivirine for HIV-1 treatment	https://doi.org/10.1097/qad.000000000
Article	Indirect comparison of 48-week efficacy and safety of long-acting cabotegravir and rilpivirine maintenance every 8 weeks with daily oral standard of care antiretroviral therapy in participants	https://doi.org/10.1186/s12879-022-07243-3
Article	Long-Acting Injectable Cabotegravir + Rilpivirine for HIV Maintenance Therapy: Week 48 Pooled Analysis of Phase 3 ATLAS and FLAIR Trials	https://doi.org/10.1097/qai.0000000000
Article	Long-Acting Cabotegravir and Rilpivirine for Maintenance of HIV-1 Suppression	https://doi.org/10.1056/nejmoa1904398

FLAIR

Identifier

NCT02938520

Link

https://clinicaltrials.gov/study/NCT02938520

Phase

Phase III

Status

Active, not recruiting

Sponsor

ViiV Healthcare

More details

Not provided

Purpose

Establish if HIV-1 infected adult participants whose virus is virologically suppressed on an INI STR will remain suppressed after switching to a two drug LA regimen of CAB and RPV.

Interventions

Drug: Cabotegravir (CAB) tablets
Drug: Rilpivirine (RPV) tablets
Drug: Cabotegravir - Injectable Suspension (CAB LA)
Drug: Rilpivirine - Injectable Suspension (RPV LA)

Drug: Oral ABC/DTG/3TC STR Tablet & Drug: Oral DTG Tablet

Countries

United States of America
Canada
France
Germany
Italy
Japan
Netherlands
Russian Federation
South Africa
Spain
United Kingdom

Sites / Institutions

Not provided

Trials dates

Anticipated Start Date

Not provided

Actual Start Date

2016-10-27

Anticipated Date of Last Follow-up

Not provided

Estimated Primary Completion Date

Not provided

Estimated Completion Date

2026-12-31

Actual Primary Completion Date

2018-08-30

Actual Completion Date

Not provided

Studied populations

Age Cohort

- Adults
- Older Adults

Genders

- All

Accepts pregnant individuals

No

Accepts lactating individuals

No

Accepts healthy individuals

No

Comments about the studied populations

Antiretroviral-naive (<=10 days of prior therapy with any antiretroviral agent following a diagnosis of HIV-1 infection). Any previous exposure to an HIV integrase inhibitor or non-nucleoside reverse transcriptase inhibitor will be exclusionary.

Health status

Negative to : HBV
Positive to : HIV

Study type

Interventional (clinical trial)

Enrollment

631

Allocation

Randomized

Intervention model

Parallel Assignment

Intervention model description

Not provided

Masking

Open label

Masking description

None (Open Label)

Frequency of administration

Monthly

Studied LA-formulation(s)

Injectable

Studied route(s) of administration

Intramuscular

Use case

Treatment

Key results

Type of key results	Title	Website link
Article	Long-Acting Cabotegravir and Rilpivirine after Oral Induction for HIV-1 Infection	https://doi.org/10.1056/nejmoa1909512
Article	Indirect comparison of 48-week efficacy and safety of long-acting cabotegravir and rilpivirine maintenance every 8 weeks with daily oral standard of care antiretroviral therapy in participants	https://doi.org/10.1186/s12879-022-07243-3
Article	Impact of Integrase Sequences from HIV-1 Subtypes A6/A1 on the In Vitro Potency of Cabotegravir or Rilpivirine	https://doi.org/10.1128/aac.01702-21
Article	Initiation of long-acting cabotegravir plus rilpivirine as direct-to-injection or with an oral lead-in in adults with HIV-1 infection	https://doi.org/10.1016/s2352-3018(21)00184-3
Article	Long-acting cabotegravir plus rilpivirine for treatment in adults with HIV-1 infection: 96-week results of the randomised, open-label, phase 3 FLAIR study	https://doi.org/10.1016/s2352-3018(20)30340-4
Article	Long-Acting Injectable Cabotegravir + Rilpivirine for HIV Maintenance Therapy: Week 48 Pooled Analysis of Phase 3 ATLAS and FLAIR Trials	https://doi.org/10.1097/qai.0000000000

CARISEL

Identifier

NCT04399551

Link

https://clinicaltrials.gov/study/NCT04399551

Phase

Phase III

Status

Completed

Sponsor

ViiV Healthcare

More details

Not provided

Purpose

Evaluating Implementation Strategies for Cabotegravir (CAB)+ Rilpivirine (RPV) Long-acting (LA) Injectables for Human Immunodeficiency Virus (HIV)-1 Treatment in European Countries

Interventions

Drug: Cabotegravir tablets (Oral lead-in)
Drug: Rilpivirine tablets (Oral lead-in)
Drug: CAB LA
Drug: RPV LA

Other: Continuous Quality Improvement (CQI) calls

Countries

Belgium

France

Germany

Netherlands

Spain

Sites / Institutions

Not provided

Trials dates

Anticipated Start Date

Not provided

Actual Start Date

2020-09-28

Anticipated Date of Last Follow-up

Not provided

Estimated Primary Completion Date

Not provided

Estimated Completion Date

Not provided

Actual Primary Completion Date

2022-03-07

Actual Completion Date

2023-03-13

Studied populations

Age Cohort

- Adults
- Older Adults

Genders

- All

Accepts pregnant individuals

No

Accepts lactating individuals

No

Accepts healthy individuals

No

Comments about the studied populations

HIV-1 infected and must be suppressed on a guideline recommended active Highly active antiretroviral therapy (HAART) regimen for at least 6 months prior to screening. Any prior switch, defined as a change of a single drug or multiple drugs simultaneously, must have occurred due to tolerability/safety, access to medications, or convenience/simplification, and must not have been done for virologic failure (on treatment HIV-1 RNA more than or equal to [>=]200 c/mL).

Health status

Positive to : HIV
Negative to : HBV, COVID 19

Study type

Interventional (clinical trial)

Enrollment

437

Allocation

Non-randomized

Intervention model

Parallel Assignment

Intervention model description

Not provided

Masking

Open label

Masking description

This is an open-label study hence no blinding is required.

Frequency of administration

Monthly
Once every 8 weeks

Studied LA-formulation(s)

Injectable

Studied route(s) of administration

Intramuscular

Use case

Treatment

Key results

Type of key results	Title	Website link
Abstract	Top Practices for Implementing Cabotegravir (CAB) and Rilpivirine (RPV) Long-Acting (LA) in European Clinics	https://www.bhiva.org/file/62a1ceca806

LATA

Identifier

NCT05154747

Link

https://clinicaltrials.gov/study/NCT05154747

Phase

Phase III

Status

Recruiting

Sponsor

University College, London

More details

Not provided

Purpose

Comparing the efficacy of long-acting injectable CAB+RPV administered every two months in comparison to daily oral HIV medications in young people.

Interventions

Drug: Cabotegravir, Rilpivirine Drug Combination
Drug: TLD

Countries

Kenya

South Africa

Uganda

Zimbabwe

Sites / Institutions

Not provided

Trials dates

Anticipated Start Date

Not provided

Actual Start Date

2023-06-22

Anticipated Date of Last Follow-up

Not provided

Estimated Primary Completion Date

2025-03-01

Estimated Completion Date

2025-03-01

Actual Primary Completion Date

Not provided

Actual Completion Date

Not provided

Studied populations

Age Cohort

- Children
- Adolescents
- Adults

Genders

- All

Accepts pregnant individuals

No

Accepts lactating individuals

No

Accepts healthy individuals

No

Comments about the studied populations

Study participants are individuals with HIV-1 infection aged 12-19 years in Sub-Saharan Africa. Participants with known HIV-2 infection are excluded.

Health status

Positive to : HIV
Negative to : HBV

Study type

Interventional (clinical trial)

Enrollment

460

Allocation

Randomized

Intervention model

Parallel Assignment

Intervention model description

Not provided

Masking

Open label

Masking description

None (Open Label)

Frequency of administration

Once every 8 weeks

Studied LA-formulation(s)

Injectable

Studied route(s) of administration

Intramuscular

Use case

Treatment

Key results

Not provided

IMPALA

Identifier

NCT05546242

Link

https://clinicaltrials.gov/study/NCT05546242

Phase

Phase III

Status

Recruiting

Sponsor

MRC/UVRI and LSHTM Uganda Research Unit

More details

Not provided

Purpose

Evaluating the Effectiveness of Switching to Two-monthly Long-acting Injectable CAB and RPV From First-line Oral Antiretroviral Therapy in HIV-1 Positive Virologically Suppressed Adults in SSA.

Interventions

Drug: Long-acting injectable Cabotegravir/Rilpivirine
Drug: Antiretroviral

Countries

Uganda

Kenya

South Africa

Sites / Institutions

Not provided

Trials dates

Anticipated Start Date

Not provided

Actual Start Date

2022-12-08

Anticipated Date of Last Follow-up

Not provided

Estimated Primary Completion Date

2024-11-01

Estimated Completion Date

2025-11-01

Actual Primary Completion Date

Not provided

Actual Completion Date

Not provided

Studied populations

Age Cohort

- Adults
- Older Adults

Genders

All

Accepts pregnant individuals

No

Accepts lactating individuals

No

Accepts healthy individuals

No

Comments about the studied populations

Participants must have a history of sub-optimal ART adherence or engagement in care based on one or more of the following criteria: 1. Documented detectable HIV-1 VL (>1000 c/mL) on all-oral ART (EFV/NVP or DTG-based) in the prior 2 years despite being ART-experienced for ≥3 months. 2. History of being lost to follow-up from care (>4 weeks elapsed since a missed scheduled clinic appointment or refill in the prior 2 years). 3. Failed to link to HIV care despite ≥3 months elapsed since HIV diagnosis.

Health status

Positive to : HIV
Negative to : HBV, TB

Study type

Interventional (clinical trial)

Enrollment

540

Allocation

Randomized

Intervention model

Parallel Assignment

Intervention model description

Parallel open-label phase 3b study. Participants will be randomised to continuing current therapy or switching to injectable therapy.

Masking

Open label

Masking description

None (Open Label)

Frequency of administration

Once every 8 weeks

Studied LA-formulation(s)

Injectable

Studied route(s) of administration

Intramuscular

Use case

Treatment

Key results

Not provided

LATITUDE

Identifier

NCT03635788

Link

https://clinicaltrials.gov/study/NCT03635788

Phase

Phase III

Status

Recruiting

Sponsor

National Institute of Allergy and Infectious Diseases (NIAID)

More details

Not provided

Purpose

Compare the efficacy, safety, and durability of two different strategies to treat participants with a history of sub-optimal adherence and control of their HIV infection.

Interventions

Drug: Standard of Care (SOC) Oral ART
Drug: Oral Rilpivirine tablets
Drug: Oral Cabotegravir tablets
Drug: Injectable RPV-LA
Drug: Injectable CAB-LA

Countries

United States of America
Puerto Rico

Sites / Institutions

Not provided

Trials dates

Anticipated Start Date

Not provided

Actual Start Date

2019-03-28

Anticipated Date of Last Follow-up

Not provided

Estimated Primary Completion Date

2025-06-30

Estimated Completion Date

2026-12-31

Actual Primary Completion Date

Not provided

Actual Completion Date

Not provided

Studied populations

Age Cohort

- Adults
- Older Adults

Genders

- All

Accepts pregnant individuals

No

Accepts lactating individuals

No

Accepts healthy individuals

No

Comments about the studied populations

Evidence of non-adherence to ART according to at least one of the following criteria: 1. Poor virologic response within 18 months prior to study entry (defined as less than 1 log10 decrease in HIV-1 RNA or HIV-1 RNA greater than 200 copies/mL at two time points at least 4 weeks apart) in individuals who have been prescribed ART for at least 6 consecutive months. 2. Lost to clinical follow-up within 18 months prior to study entry with ART non-adherence for greater than or equal to 6 consecutive months.

Health status

Positive to : HIV
Negative to : HBV

Study type

Interventional (clinical trial)

Enrollment

350

Allocation

Randomized

Intervention model

Parallel Assignment

Intervention model description

Not provided

Masking

Open label

Masking description

None (Open Label)

Frequency of administration

Monthly

Studied LA-formulation(s)

Injectable

Studied route(s) of administration

Intramuscular

Use case

Treatment

Key results

Not provided

LATTE-2

Identifier

NCT02120352

Link

https://clinicaltrials.gov/study/NCT02120352

Phase

Phase II

Status

Completed

Sponsor

ViiV Healthcare

More details

Not provided

Purpose

Evaluate the antiviral activity, tolerability, and safety of IM dosing regimens of GSK744 LA plus TMC278 LA, relative to GSK744 plus ABC/3TC given orally once daily, in ARV naïve HIV-1 patients.

Interventions

Drug: Oral GSK744 tablets
Drug: Injectable GSK744 LA
Drug: Injectable TMC278 LA
Drug: Oral ABC/3TC tablets

Drug: Oral RPV tablets

Countries

United States of America

Canada

France

Germany

Spain

Sites / Institutions

Not provided

Trials dates

Anticipated Start Date

Not provided

Actual Start Date

2014-04-28

Anticipated Date of Last Follow-up

Not provided

Estimated Primary Completion Date

Not provided

Estimated Completion Date

Not provided

Actual Primary Completion Date

2015-08-13

Actual Completion Date

2023-04-20

Studied populations

Age Cohort

- Adults
- Older Adults

Genders

- All

Accepts pregnant individuals

No

Accepts lactating individuals

No

Accepts healthy individuals

No

Comments about the studied populations

Participants must be ART-naïve defined as having no more than 10 days of prior therapy with any antiretroviral agent following a diagnosis of HIV-1 infection.

Health status

Positive to : HIV
Negative to : HBV

Study type

Interventional (clinical trial)

Enrollment

309

Allocation

Randomized

Intervention model

Parallel Assignment

Intervention model description

Not provided

Masking

Open label

Masking description

None (Open Label)

Frequency of administration

Monthly
Once every 8 weeks

Studied LA-formulation(s)

Injectable

Studied route(s) of administration

Intramuscular

Use case

Treatment

Key results

Type of key results	Title	Website link

Article	Experiences with long acting injectable ART: A qualitative study among PLHIV participating in a Phase II study of cabotegravir + rilpivirine (LATTE-2) in the United States and Spain.	https://doi.org/10.1371/journal.pone.019
Article	Efficacy, Safety, and Durability of Long-Acting Cabotegravir and Rilpivirine in Adults With Human Immunodeficiency Virus Type 1 Infection: 5-Year Results From the LATTE-2 Study.	https://doi.org/10.1093/ofid/ofab439
Article	Pharmacokinetics and antiviral activity of cabotegravir and rilpivirine in cerebrospinal fluid following long-acting injectable administration in HIV-infected adults.	https://doi.org/10.1093/jac/dkz504
Article	Patient-reported tolerability and acceptability of cabotegravir + rilpivirine long-acting injections for the treatment of HIV-1 infection: 96-week results from the randomized LATTE-2 study.	https://doi.org/10.1080/25787489.2019
Article	Long-acting intramuscular cabotegravir and rilpivirine in adults with HIV-1 infection (LATTE-2): 96-week results of a randomised, open-label, phase 2b, non-inferiority trial.	https://doi.org/10.1016/s0140-6736(17)31917-7

NCT04371380

Identifier

NCT04371380

Link

https://clinicaltrials.gov/study/NCT04371380

Phase

Phase I

Status

Completed

Sponsor

ViiV Healthcare

More details

Not provided

Purpose

Evaluate pharmacokinetics, tolerability, and safety of Cabotegravir long acting plus Rilpivirine long acting administered concomitantly as two separate IM injections in the Vastus Lateralis muscles.

Interventions

Drug: Oral Cabotegravir Tablets
Drug: Oral Rilpivirine Tablets
Drug: Cabotegravir extended release suspension for injection (long-acting)
Drug: Rilpivirine extended release suspension for injection (long-acting)

Countries

United States of America

Sites / Institutions

Not provided

Trials dates

Anticipated Start Date

Not provided

Actual Start Date

2020-09-16

Anticipated Date of Last Follow-up

Not provided

Estimated Primary Completion Date

Not provided

Estimated Completion Date

Not provided

Actual Primary Completion Date

2021-12-26

Actual Completion Date

2021-12-26

Studied populations

Age Cohort

- Adults

Genders

- All

Accepts pregnant individuals

No

Accepts lactating individuals

No

Accepts healthy individuals

Yes

Comments about the studied populations

Participants aged 18 to 50 who are overtly healthy as determined by medical evaluation including medical history, physical examination, laboratory tests, and cardiac monitoring.

Health status

Negative to : HIV, HCV, HBV, COVID 19

Study type

Interventional (clinical trial)

Enrollment

15

Allocation

Not provided

Intervention model

Single group assignment

Intervention model description

Eligible participants will receive orally, tablets of cabotegravir plus rilpivirine for 28 days. There will be 10 to 14 days wash out period followed by an IM injection of

cabotegravir long-acting plus rilpivirine long-acting.

Masking

Open label

Masking description

This is an open label study.

Frequency of administration

Other(s) : "Single dose of CAB LA plus RPV LA. "

Studied LA-formulation(s)

Injectable

Studied route(s) of administration

Intramuscular

Use case

Treatment

Key results

Type of key results	Title	Website link
Abstract	Pharmacokinetics and Tolerability of Cabotegravir and Rilpivirine Long-Acting Intramuscular Injections to the Vastus Lateralis (Lateral Thigh) Muscles of Healthy Adult Participants.	https://medinfo.gsk.com/5f95dbd7-245e-4e65-9f36-1a99e28e5bba/75cb786a-98e0-4615-8258-3cae0bdcfb29/75cb786a-98e0-4615-8258-3cae0bdcfb29_viewable_rendition__v.pd

LAI115428

Identifier

NCT01593046

Link

https://clinicaltrials.gov/study/NCT01593046

Phase

Phase I

Status

Completed

Sponsor

ViiV Healthcare

More details

Not provided

Purpose

Investigate the Safety, Tolerability and Pharmacokinetics of Repeat Dose Administration of Long-Acting GSK1265744 and Long-Acting TMC278 Intramuscular and Subcutaneous Injections.

Interventions

Drug: Oral GSK1265744 tablets
Drug: Injectable Intramuscular GSK1265744 LA
Drug: Injectable Subcutaneous GSK1265744 LA
Drug: Injectable Intramuscular TMC278 LA

Countries

United States of America

Sites / Institutions

Not provided

Trials dates

Anticipated Start Date

Not provided

Actual Start Date

2012-05-01

Anticipated Date of Last Follow-up

Not provided

Estimated Primary Completion Date

Not provided

Estimated Completion Date

Not provided

Actual Primary Completion Date

2013-11-01

Actual Completion Date

2013-11-01

Studied populations

Age Cohort

- Adults

Genders

- All

Accepts pregnant individuals

No

Accepts lactating individuals

Unspecified

Accepts healthy individuals

Yes

Comments about the studied populations

Not provided

Health status

Negative to : HIV, HCV, HBV

Considered at low risk of : HIV

Study type

Interventional (clinical trial)

Enrollment

43

Allocation

Randomized

Intervention model

Parallel Assignment

Intervention model description

Not provided

Masking

Open label

Masking description

None (Open Label)

Frequency of administration

Monthly

Studied LA-formulation(s)

Injectable

Studied route(s) of administration

Intramuscular

Use case

Unspecified

Key results

Not provided

CAPRI

Identifier

NCT05601128

Link

https://clinicaltrials.gov/study/NCT05601128

Phase

Phase III

Status

Recruiting

Sponsor

Allegheny Singer Research Institute

More details

Not provided

Purpose

Evaluate the efficacy and safety of CABENUVA (Long-acting Cabotegravir Plus Long-acting Rilpivirine) in patients with HIV infection and severe renal impairment.

Interventions

Drug: Injectable CAB LA + RPV LA

Countries

Not provided

Sites / Institutions

Not provided

Trials dates

Anticipated Start Date

Not provided

Actual Start Date

2023-01-01

Anticipated Date of Last Follow-up

Not provided

Estimated Primary Completion Date

2024-12-31

Estimated Completion Date

2025-12-31

Actual Primary Completion Date

Not provided

Actual Completion Date

Not provided

Studied populations

Age Cohort

- Adults
- Older Adults

Genders

- All

Accepts pregnant individuals

No

Accepts lactating individuals

No

Accepts healthy individuals

No

Comments about the studied populations

Participants are positive for HIV infection and severe renal impairment with or without hemodialysis.

Health status

Positive to : HIV
Negative to : HBV

Study type

Interventional (clinical trial)

Enrollment

12

Allocation

Not provided

Intervention model

Single group assignment

Intervention model description

Not provided

Masking

Open label

Masking description

None (Open Label)

Frequency of administration

Monthly

Once every 8 weeks

Studied LA-formulation(s)

Injectable

Studied route(s) of administration

Intramuscular

Use case

Treatment

Key results

Not provided

MOCHA

Identifier

NCT03497676

Link

https://clinicaltrials.gov/study/NCT03497676

Phase

Phase I/II

Status

Recruiting

Sponsor

National Institute of Allergy and Infectious Diseases (NIAID)

More details

Not provided

Purpose

Evaluate the safety, acceptability, tolerability, and pharmacokinetics of oral and long-acting injectable CAB and RPV in virologically suppressed HIV-infected children and adolescents.

Interventions

Drug: Oral Cabotegravir (CAB)
Drug: Oral Rilpivirine (RPV)
Drug: Long-Acting Injectable Cabotegravir (CAB LA)
Drug: Long-Acting Injectable Rilpivirine (RPV LA)

Drug: Combination Antiretroviral Therapy (cART)

Countries

United States of America
Botswana
Puerto Rico
South Africa
Thailand
Uganda

Sites / Institutions

Not provided

Trials dates

Anticipated Start Date

Not provided

Actual Start Date

2019-03-19

Anticipated Date of Last Follow-up

Not provided

Estimated Primary Completion Date

Not provided

Estimated Completion Date

2025-06-17

Actual Primary Completion Date

2023-02-18

Actual Completion Date

Not provided

Studied populations

Age Cohort

- Children
- Adolescents

Genders

- All

Accepts pregnant individuals

No

Accepts lactating individuals

No

Accepts healthy individuals

No

Comments about the studied populations

Not provided

Health status

Positive to : HIV
Negative to : HCV, HBV

Study type

Interventional (clinical trial)

Enrollment

155

Allocation

Non-randomized

Intervention model

Sequential assignment

Intervention model description

Not provided

Masking

Open label

Masking description

None (Open Label)

Frequency of administration

Monthly
Once every 8 weeks

Studied LA-formulation(s)

Injectable

Studied route(s) of administration

Intramuscular

Use case

Treatment

Key results

Not provided

VOLITION

Identifier

NCT05917509

Link

https://clinicaltrials.gov/study/NCT05917509

Phase

Phase III

Status

Recruiting

Sponsor

ViiV Healthcare

More details

Not provided

Purpose

Evaluate the efficacy, safety, implementation effectiveness, and patient-reported outcomes of once-daily oral DTG/3TC followed by an optional participant-determined switch to CAB/RPV-LA.

Interventions

Drug: DTG/3TC
Drug: Cabotegravir (CAB) LA
Drug: Rilpivirine (RPV) LA

Countries

United States of America

Sites / Institutions

Not provided

Trials dates

Anticipated Start Date

Not provided

Actual Start Date

2023-07-06

Anticipated Date of Last Follow-up

Not provided

Estimated Primary Completion Date

2025-09-29

Estimated Completion Date

2026-01-30

Actual Primary Completion Date

Not provided

Actual Completion Date

Not provided

Studied populations

Age Cohort

- Adults
- Older Adults

Genders

- All

Accepts pregnant individuals

No

Accepts lactating individuals

No

Accepts healthy individuals

No

Comments about the studied populations

Antiretroviral-naïve participants (defined as no prior therapy with any antiretroviral agent following a diagnosis of HIV-1 infection) prior to enrolment with plasma HIV-1 RNA ≥1,000 c/mL at screening. Participants enrolled in France must be affiliated to, or a beneficiary of, a social security category.

Health status

Positive to : HIV
Negative to : HBV, COVID 19

Study type

Interventional (clinical trial)

Enrollment

180

Allocation

Non-randomized

Intervention model

Parallel Assignment

Intervention model description

Not provided

Masking

Open label

Masking description

None (Open Label)

Frequency of administration

Once every 8 weeks

Studied LA-formulation(s)

Injectable

Studied route(s) of administration

Intramuscular

Use case

Treatment

Key results

Not provided

Excipients

Proprietary excipients used

No proprietary excipient used

Novel excipients or existing excipients at a concentration above Inactive Ingredients Database (IID) for the specified route of administration

The novel excipient poloxamer 338 (P338) is used in the final G001 Rilpivirine clinical formulation. Following both an in-vitro mammalian chromosome aberration and an Ames test, it was considered to be non-genotoxic with no evidence for mutagenicity. Further P338 fertility, genotoxicity and development studies have been conducted with no negative effects, in addition to a 6-week and 9- month minipig repeat-dose toxicity study. No adverse local or systemic toxicity was reported in the minipigs at 100mg/month (Margin of Exposure:19).

Residual solvents used

No residual solvent used

Patent info

There are either no relevant patents or these were not yet submitted to LAPaL

Supporting material

Publications

Bares SH, Scarsi KK. A new paradigm for antiretroviral delivery: long-acting cabotegravir and rilpivirine for the treatment and prevention of HIV. Curr Opin HIV AIDS. 2022 Jan 1;17(1):22-31. doi: https://doi.org/10.1097/COH.0000000000000708. PMID: 34871188; PMCID: PMC8694245.

Purpose of review

Cabotegravir (CAB) and rilpivirine (RPV) is the first long-acting injectable antiretroviral therapy (ART) option approved for virologically suppressed adults with HIV-1. In addition, long-acting CAB is a promising agent for HIV preexposure prophylaxis (PrEP). This review focuses on phase 3 clinical trial results and implementation considerations for these long-acting ART and PrEP strategies.

Recent findings

Long-acting CAB and RPV administered every 4 weeks demonstrated noninferiority to oral ART through week 96 in both the ATLAS and FLAIR studies, whereas ATLAS-2M found similar efficacy through 96 weeks when the long-acting injectable ART was administered every 8 weeks instead of every 4 weeks. For prevention, two phase 3 trials were stopped early due to fewer incident HIV infections in participants receiving long-acting CAB every 8 weeks compared with daily oral tenofovir disoproxil fumarate–emtricitabine for PrEP. The long-acting therapies were well tolerated across all clinical trials.

Summary

Clinical trial results support the use of long-acting CAB for HIV PrEP and long-acting

CAB and RPV as a switch strategy for adults with HIV-1 who are first virologically suppressed with oral ART. Implementation challenges persist, and data are urgently needed in populations who may benefit most from long-acting therapy, including adolescents, pregnant individuals, and those with barriers to medication adherence.

Additional documents

No documents were uploaded

Useful links

- FDA Approves Cabenuva and Vocabria for the Treatment of HIV-1 Infection
- CABENUVA FDA Highlights of Prescribing Information

Comment & Information

Not provided