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THE LONG-ACTING THERAPEUTICS PATENTS AND LICENCES DATABASE

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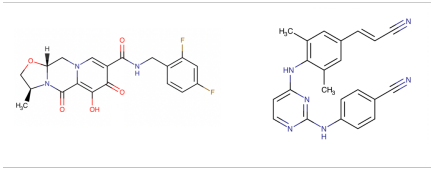


Cabotegravir and Rilpivirine

Developer(s)

ViiV Healthcare

Originator

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

Originator

https://www.janssen.com/

Belgium

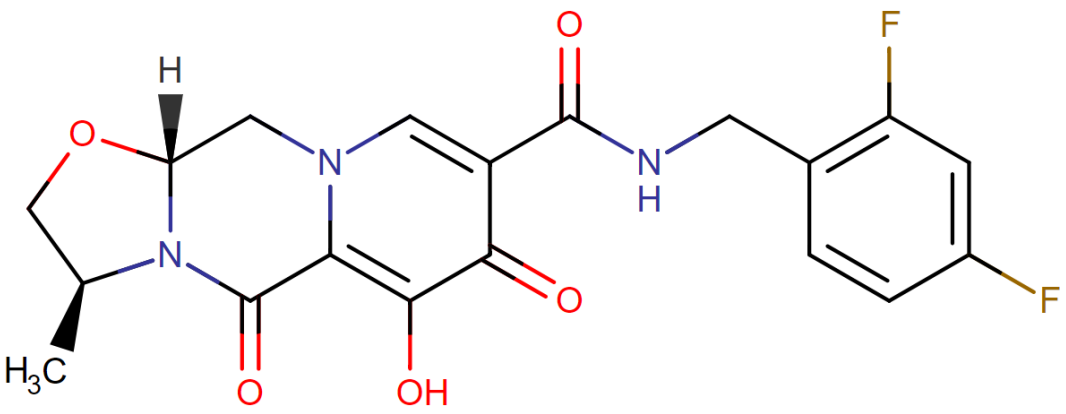
Janssen Pharmaceuticals is a subsidiary company of Johnson & Johnson headquartered in Beerse, Belgium. They manufacture and develop pharmaceutical products for use in areas such as, Immunology, Infectious Diseases & Vaccines, Pulmonary Hypertension, Cardiovascular & Metabolism, Oncology, and Neuroscience.

ViiV Healthcare(Vocabria) / Janssen-Cilag Ltd (Rekambys)

Originator

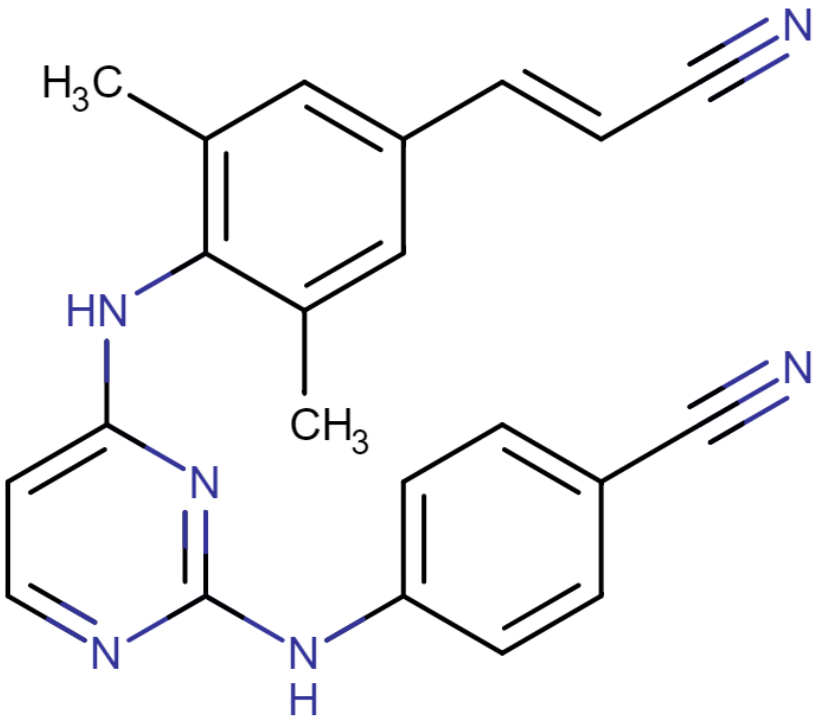
https://www.janssen.com/ https://viivhealthcare.com/

Drug structure



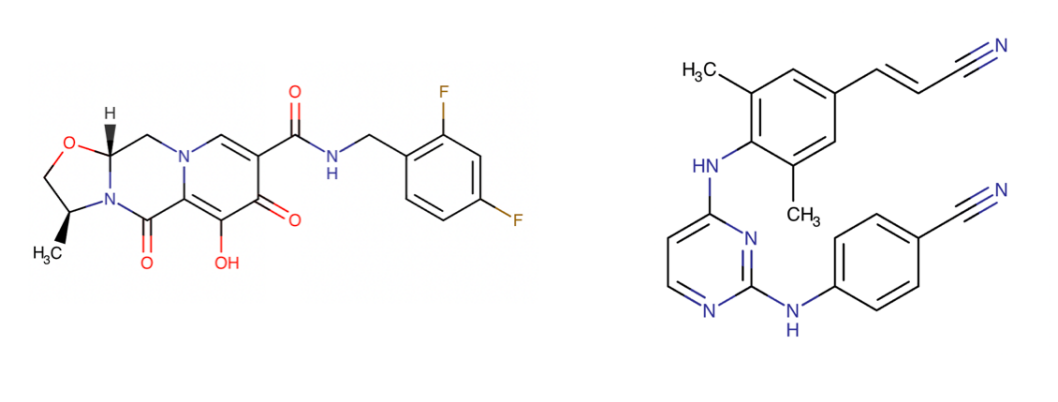
Cabotegravir Chemical Structure

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)

https://go.drugbank.com/drugs/DB11751
https://go.drugbank.com/drugs/DB08864

Generic name

Cabotegravir and Rilpivirine

Brand name

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

Compound type

Small molecule

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

Intervention 1

Drug: CAB LA intramuscular injection

Dosage: 600 mg

Intervention 2

Drug: RPV LA intramuscular injection

Dosage: 900 mg

Intervention 3

Drug: Oral RPV Tablet

Dosage: 25 mg

Intervention 4

Drug: Oral DTG Tablet

Dosage: 50 mg

Countries

United States of America

Canada

Sites / Institutions

Not provided

Trials dates

Anticipated Start Date

Not provided

Actual Start Date

2018-09-24

Anticipated Date of Last Follow-up

2024-05-13

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

Oral
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

Intervention 1
Drug: CAB LA intramuscular injection
Dosage: 400 mg (Maintenance Dose) and 600 mg (Loading Dose)

Intervention 2

Drug: RPV LA intramuscular injection

Dosage: 600 mg (Maintenance Dose) and 900 mg (Loading Dose)

Intervention 3

Drug: Oral CAB Tablet

Dosage: 30 mg

Intervention 4

Drug: Oral RPV Tablet

Dosage: 25 mg

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

2023-03-16

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

Inclusion Criteria: - Aged 18 years or older at the time of signing the informed consent. - HIV-1 infected and must be on an active highly active antiretroviral therapy (HAART) (2 or 3 drug) regimen for at least 6 months prior to Screening. - Be able to understand and comply with protocol requirements, instructions, and restrictions. - Understand the long-term commitment to the study and be likely to complete the study as planned. - Be considered appropriate candidates for participation in an investigative clinical trial with oral and intramuscularly injectable medications.

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

Oral
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

Completed

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

Intervention 1

Drug: RPV LA subcutaneous injection

Intervention 2

Drug: CAB LA injection

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

2024-06-24

Estimated Primary Completion Date

2024-05-23

Estimated Completion Date

2024-05-23

Actual Primary Completion Date

2024-05-23

Actual Completion Date

2024-05-23

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

Intervention 1

Drug: Cabotegravir Tablets (Oral Lead-in)

Dosage: 30 mg

Intervention 2

Drug: Rilpivirine Tablets (Oral Lead-in)

Dosage: 25 mg

Intervention 3

Drug: Cabotegravir Injectable Suspension

Dosage: 400 mg (Maintenance Dose) and 600 mg (Loading Dose) at 200 mg/mL

Intervention 4

Drug: Rilpivirine Injectable Suspension

Dosage: 600 mg (Maintenance Dose) and 900 mg (Loading Dose) at 300 mg/mL

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

2024-01-02

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

Inclusion Criteria: - Subjects who will be able to understand and comply with protocol requirements, instructions, and restrictions. - Understand the long term commitment to the study and be likely to complete the study as planned. - Be considered as an appropriate candidate for participation in an investigative clinical trial with oral and intramuscularly injectable medications (e.g., no active substance use disorder, acute major organ disease, or planned long-term work assignments out of the country, etc.). - Aged 18 years or older (or >=19 where required by local regulatory agencies), at the time of signing the informed consent.

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

Oral
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

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), 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
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

Intervention 1

Drug: Cabotegravir Tablets (Oral Lead-in)
Dosage: 30 mg

Intervention 2

Drug: Cabotegravir Injectable Suspension (CAB LA)

Dosage: 600 mg

Intervention 3

Drug: Rilpivirine Tablets (Oral Lead-in)

Dosage: 25 mg

Intervention 4

Drug: Rilpivirine Injectable Suspension (RPV LA)

Dosage: 900 mg

Intervention 5

Drug: BIKTARVY Tablets (BIK)

Dosage: 50 mg

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

2024-06-03

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

Inclusion Criteria: - Participants aged 18 years or older (or >=19 where required by local regulatory agencies), at the time of signing the informed consent. - A female participant is eligible to participate if she is not pregnant (as confirmed by a negative serum human chorionic gonadotropin (hCG) test at screen and a negative urine hCG test at Randomization). - Must be on the uninterrupted current regimen of BIK for at least 6 months prior to Screening with an undetectable HIV-1 viral load for at least 6 months prior to Screening. BIK must be the participant's first or second regimen. - Capable of giving signed informed consent, which includes compliance with the requirements and restrictions listed in the consent form and in this protocol.

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

Oral

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

Intervention 1

Drug: Cabotegravir (CAB) tablets (Oral Lead-in)

Dosage: 30 mg

Intervention 2

Drug: Rilpivirine (RPV) tablets (Oral Lead-in)

Dosage: 25 mg

Intervention 3

Drug: Cabotegravir - Injectable Suspension (CAB LA)

Dosage: 400 mg (Maintenance Dose) and 600 mg (Loading Dose) at 200 mg/mL

Intervention 4

Drug: Rilpivirine - Injectable Suspension (RPV LA)

Dosage: 600 mg (Maintenance Dose) and 900 mg (Loading Dose) at 300 mg/mL

Intervention 5

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

2024-02-13

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

Oral
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

Type of key results	Title	Website link
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

Intervention 1

Drug: Cabotegravir (CAB) tablets

Dosage: 30 mg

Intervention 2

Drug: Rilpivirine (RPV) tablets

Dosage: 25 mg

Intervention 3

Drug: Cabotegravir - Injectable Suspension (CAB LA)

Dosage: 400 mg and 600 mg (200 mg/mL)

Intervention 4

Drug: Rilpivirine - Injectable Suspension (RPV LA)

Dosage: 600 mg and 900 mg (300 mg/mL)

Intervention 5

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

Dosage: 600/50/300 mg

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

2024-02-14

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

Oral
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

Type of key results	Title	Website link
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

Intervention 1

Drug: Cabotegravir tablets (Oral Lead-in)

Dosage: 30 mg

Intervention 2

Drug: Rilpivirine tablets (Oral Lead-in)

Dosage: 25 mg

Intervention 3

Drug: CAB LA intramuscular (IM) injection

Dosage: 600 mg

Intervention 4

Drug: RPV LA intramuscular (IM) injection

Dosage: 900 mg

Intervention 5

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

2024-04-04

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

Oral

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

Active, not 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

Intervention 1

Drug: CAB LA injectable suspension

Dosage: 600mg as a 3mL IM injection

Intervention 2

Drug: RPV LA injectable suspension
Dosage: 900mg as a 3mL IM injection

Intervention 3
Drug: Oral TLD Tablet
Dosage: 245/300/50 mg

Intervention 4
Drug: Dolutegravir oral tablet with tenofovir alafenamide fumarate and lamivudine (l/TAF) oral in a fixed dose combination
Dosage: 50/25/300 mg

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
2024-04-26

Estimated Primary Completion Date
2025-03-01

Estimated Completion Date

2026-03-01

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

476

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

Intervention 1

Drug: Injectable Long-Acting Cabotegravir
Dosage: 600 mg

Intervention 2

Drug: Injectable Long-Acting Rilpivirine

Dosage: 900mg

Intervention 3

Drug: Antiretroviral (Oral antiretroviral therapy in the form of 2NRTIs + dolutegravir 50mg administered daily)

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

2023-10-19

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

Active, not 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

Intervention 1

Drug: Standard of Care (SOC) Oral ART
Dosage: SOC oral ART regimen must include at least 3 drugs with 2 or more drugs predicted to be fully active, including a boosted protease inhibitor (PI) and/or an

integrase strand transfer inhibitor (INSTI)

Intervention 2

Drug: Oral Rilpivirine tablets (Oral lead-in)

Dosage: 25 mg

Intervention 3

Drug: Oral Cabotegravir tablets (Oral lead-in)

Dosage: 30 mg

Intervention 4

Drug: Injectable RPV-LA

Dosage: 600 mg (Maintenance Dose) and 900 mg (Loading Dose) administered as an intramuscular injection in the gluteal muscle

Intervention 5

Drug: Injectable CAB-LA

Dosage: 400 mg (Maintenance Dose) and 600 mg (Loading Dose) administered as an intramuscular injection in the gluteal muscle

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

2024-08-15

Estimated Primary Completion Date

2024-09-30

Estimated Completion Date

2026-08-30

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

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

310

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

Oral

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

Intervention 1

Drug: CAB LA intramuscular injection
Dosage: 800 mg (Loading Dose delivered as two 400 mg IM injections) and 400 mg

(Maintenance dose) IM

Intervention 2

Drug: RPV LA intramuscular injection

Dosage: 600 mg (Maintenance Dose) and 900 mg (Loading Dose)

Intervention 3

Drug: Oral CAB Tablet

Dosage: 30 mg

Intervention 4

Drug: Oral RPV Tablet

Dosage: 25 mg

Intervention 5

Drug: ABC/3TC Oral tablets

Dosage: 600/300 mg

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

2024-06-11

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

Oral

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

Type of key results	Title	Website link
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

Intervention 1

Drug: Oral Cabotegravir Tablets (Oral Lead-in)

Dosage: 30 mg

Intervention 2

Drug: Oral Rilpivirine Tablets

Dosage: 25 mg (Oral Lead-in)

Intervention 3

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

Dosage: 600 mg (200 mg per mL)

Intervention 4

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

Dosage: 900 mg (300 mg per mL)

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

2023-11-03

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

Oral
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

Intervention 1

Drug: Oral GSK1265744 tablets (Oral Lead-in)

Dosage: 30 mg

Intervention 2

Drug: Injectable Intramuscular GSK1265744 LA

Dosage: 800 mg

Intervention 3

Drug: Injectable Subcutaneous GSK1265744 LA

Dosage: 200 mg

Intervention 4

Drug: Injectable Intramuscular TMC278 LA

Dosage: 1200 mg

Intervention 5

Drug: Injectable Intramuscular TMC278 LA

Dosage: 600 mg

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

2014-02-06

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

Inclusion Criteria: - AST, ALT, alkaline phosphatase and bilirubin greater than or equal to 1.5xULN (isolated bilirubin >1.5xULN is acceptable if bilirubin is fractionated and direct bilirubin <35%). - Healthy as determined by a responsible and experienced physician. - Male or female between 18 and 64 years of age inclusive, at the time of signing the informed consent. - Body weight greater than or equal to 50 kg for men and greater than or equal to 45 kg for women and body mass index (BMI) within the range 18.5-31.0 kg/m2 (inclusive). - All Study subjects should be counseled on the practice of safer sexual practices including the use of effective barrier methods (e.g.

male condom/spermicide).

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

Oral

Intramuscular

Use case

Unspecified

Key results

Not provided

CAPRI

Identifier

NCT05601128

Link

https://clinicaltrials.gov/study/NCT05601128

Phase

Phase III

Status

Active, not 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

Intervention 1

Drug: Oral Cabotegravir Tablets (Oral Lead-in)

Dosage: 30 mg

Intervention 2

Drug: Oral Rilpivirine tablets (Oral lead-in)

Dosage: 25 mg

Intervention 3

Drug: CAB LA intramuscular (IM) injection

Dosage: 400 mg (Maintenance Dose) and 600 mg (Loading Dose)

Intervention 4

Drug: RPV LA intramuscular (IM) injection

Dosage: 600 mg (Maintenance Dose) and 900 mg (Loading Dose)

Countries

United States of America

Sites / Institutions

Not provided

Trials dates

Anticipated Start Date

Not provided

Actual Start Date

2023-01-01

Anticipated Date of Last Follow-up

2024-03-22

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

Oral
Intramuscular

Use case

Treatment

Key results

Not provided

MOCHA

Identifier

NCT03497676

Link

https://clinicaltrials.gov/study/NCT03497676

Phase

Phase I/II

Status

Active, not 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

Intervention 1

Drug: Oral Cabotegravir (CAB) Tablets (Oral Lead-in)
Dosage: 30 mg

Intervention 2

Drug: Oral Rilpivirine (RPV) Tablets (Oral Lead-in)

Dosage: 25 mg

Intervention 3

Drug: Long-Acting Injectable Cabotegravir (CAB LA)

Dosage: 400 mg (Maintenance Dose) and 600 mg (Loading Dose)

Intervention 4

Drug: Long-Acting Injectable Rilpivirine (RPV LA)

Dosage: 600 mg (Maintenance Dose) and 900 mg (Loading Dose)

Intervention 5

Drug: Combination Antiretroviral Therapy (cART)

Countries

United States of America

Botswana

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

2024-04-22

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

168

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

Oral

Intramuscular

Use case

Treatment

Key results

Type of key results	Title	Website link
Article	Safety and pharmacokinetics of oral and long-acting injectable cabotegravir or long-acting injectable rilpivirine in virologically suppressed adolescents with HIV (IMPAACT 2017/MOCHA)	https://doi.org/10.1016/s2352-3018(23)00300-4
Article	Acceptability and tolerability of long-acting injectable cabotegravir or rilpivirine in the first cohort of virologically suppressed adolescents living with HIV (IMPAACT 2017/MOCHA):	https://doi.org/10.1016/s2352-3018(23)00301-6

VOLITION

Identifier

NCT05917509

Link

https://clinicaltrials.gov/study/NCT05917509

Phase

Phase III

Status

Active, not 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

Intervention 1

Drug: DTG/3TC

Intervention 2

Drug: Cabotegravir (CAB) LA

Intervention 3

Drug: Rilpivirine (RPV) LA

Countries

United States of America
Argentina
Canada
Chile
France
Germany
Italy
Puerto Rico
Spain

Sites / Institutions

Not provided

Trials dates

Anticipated Start Date

Not provided

Actual Start Date

2023-07-06

Anticipated Date of Last Follow-up

2024-06-10

Estimated Primary Completion Date

2025-08-21

Estimated Completion Date

2026-08-14

Actual Primary Completion Date

2026-01-30

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-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

171

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

ALADDIN

Identifier

NCT06468995

Link

https://clinicaltrials.gov/study/NCT06468995

Phase

Phase III

Status

Not yet recruiting

Sponsor

IRCCS San Raffaele

More details

This is a monocentric, prospective, double-arm, randomized, open-label, implementation-effectiveness hybrid type III study aimed at comparing hospital-based and home-based administration of CAB LA + RPV LA treatment for HIV-1-infected patients. Study participants receiving IM CAB + RPV will complete various questionnaires and scales, including FIM, AIM, IAM, EQ-5D-5L, HAT-QoL, and HIVTSQ, throughout the study. HCPs will also complete FIM, AIM, IAM, and a Likert scale.

Purpose

Antiviral Long Acting Drugs Landing in People Living With HIV

Interventions

Intervention 1

Surveys completion

Intervention 2

Home administration of Long-acting CAB+RPV Injectable Suspension

Dosage: CAB 600mg + RPV 900mg q2M IM administration and follow-up in hospital

Intervention 3

Hospital administration of Long-acting CAB+RPV Injectable Suspension

Dosage: CAB 600mg + RPV 900mg q2M IM administration and follow-up in hospital

Countries

Italy

Sites / Institutions

Not provided

Trials dates

Anticipated Start Date

2024-09-01

Actual Start Date

Not provided

Anticipated Date of Last Follow-up

2024-06-16

Estimated Primary Completion Date

2026-03-01

Estimated Completion Date

2026-11-01

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

Yes

Comments about the studied populations

Inclusion Criteria: - People living with HIV-1 infection that could, according to clinical practice, switch current ART to IM CAB + RPV; - Aged 18 years or older at the time of signing the informed consent. - People willing to switch to long-acting therapy - On a stable (≥6 months) antiretroviral regimen and virologically suppressed (HIV-1 RNA \<50 copies/ml): - Documented evidence of plasma HIV-1 RNA measurements \<50 c/mL in the 6 months prior to Screening. - Plasma HIV-1 RNA \<50 c/mL at Screening. - Ability to understand informed consent form and other relevant regulatory documents.

Health status

Negative to : HBV
Positive to : HIV

Study type

Interventional (clinical trial)

Enrollment

120

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

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

Compound patent families

Patent informations

Patent description	Representative patent	Categories	Patent holder	Licence with MPP	Patent source
Cabotegravir long-acting parenteral compositions Expiry date: 2031-09-15 The present invention relates to pharmaceutical compositions of cabotegravir useful in the treatment or prevention of Human Immunodeficiency Virus (HIV) infections.	WO2012037320	Composition	Glaxosmithkline Llc, Mundhra, Deepak B, Pan, Rennan, Viiv Healthcare Company	No	

Patent status

Patent status/countries	Low, Low- middle and upper-middle	High income
Granted	Brazil, China, Turkmenistan, Belarus, Tajikistan, Kazakhstan, Azerbaijan, Kyrgyzstan, Armenia, Moldova, Republic of, Türkiye, North Macedonia, Albania, Bosnia and Herzegovina, Montenegro, Serbia, Mexico, Ukraine, South Africa, India	Australia, Canada, Chile, Russian Federation, Belgium, Germany, France, Luxembourg, Netherlands, Switzerland, United Kingdom, Sweden, Italy, Austria, Liechtenstein, Greece, Spain, Denmark, Monaco, Portugal, Ireland, Finland, Cyprus, Bulgaria, Czechia, Estonia, Slovakia, Hungary, Poland, Iceland, Malta, Norway, San Marino, Croatia, Romania, Latvia, Lithuania, Slovenia, Israel, Japan, Korea, Republic of, Taiwan, Province of China, United States of America
Filed		
Not in force	World Intellectual Property Organization (WIPO)	World Intellectual Property Organization (WIPO), United States of America

Patent informations

Patent description	Representative patent	Categories	Patent holder	Licence with MPP	Patent source
Cabotegravir processes and intermediates Expiry date: 2031-03-22 Relates to the preparation of carbamoylpyridone derivatives and intermediates which are useful as HIV integrase inhibitors.	WO2011119566	Intermediate, Process	Glaxosmithkline Llc, Goodman, Steven N, Kowalski, Matthew, Mans, Douglas, Wang, Huan	No	

Patent status

Patent status/countries	Low, Low- middle and upper-middle	High income
Granted	China, Albania, Serbia, Bosnia and Herzegovina, Montenegro, Türkiye, North Macedonia, India	Liechtenstein, Italy, Norway, Malta, Denmark, Belgium, United Kingdom, Greece, Netherlands, Hungary, Croatia, Switzerland, Spain, San Marino, Slovenia, Austria, Romania, Iceland, Cyprus, Finland, France, Bulgaria, Slovakia, Poland, Latvia, Ireland, Estonia, Germany, Luxembourg, Portugal, Czechia, Lithuania, Monaco, Sweden, Japan, Korea, Republic of, United States of America
Filed		Singapore, Taiwan, Province of China
Not in force	World Intellectual Property Organization (WIPO)	World Intellectual Property Organization (WIPO)

Patent informations

Patent description	Representative patent	Categories	Patent holder	Licence with MPP	Patent source
Cabotegravir in combination with RPV Expiry date: 2031-01-24 A combination comprising cabotegraviror a pharmaceutically acceptable salt thereof, and one or more therapeutic agents selected from the group consisting of rilpivirine (TMC-278), or a pharmaceutically acceptable salt thereof, when administered simultaneously or sequentially.	CA3060290	Combination	Viiv Healthcare Company	No	

Patent status

Patent status/countries	Low, Low- middle and upper-middle	High income
Granted	Mexico	New Zealand, Korea, Republic of, Australia, Israel
Filed		Canada
Not in force	Türkiye, North Macedonia, Albania, Bosnia and Herzegovina, Montenegro, Serbia	Belgium, Germany, France, Luxembourg, Netherlands, Switzerland, United Kingdom, Sweden, Italy, Austria, Liechtenstein, Greece, Spain, Denmark, Monaco, Portugal, Ireland, Finland, Cyprus, Bulgaria, Czechia, Estonia, Slovakia, Hungary, Poland, Iceland, Malta, Norway, San Marino, Croatia, Romania, Latvia, Lithuania, Slovenia

Patent informations

Patent description	Representative patent	Categories	Patent holder	Licence with MPP	Patent source
Aqueous suspensions of rilpivirine micro- or nanoparticles Expiry date: 2027-06-22 This invention concerns pharmaceutical compositions for administration via intramuscular or subcutaneous injection, comprising micro- or nanoparticles of the NNRTI compound TMC278, suspended in an aqueous pharmaceutically acceptable carrier, and the use of such pharmaceutical compositions in the treatment and prophylaxis of HIV infection.	WO2007147882	Composition	Tibotec Pharmaceuticals Ltd	No	

Patent status

Patent status/countries	Low, Low- middle and upper-middle	High income
Granted	Brazil, China, Turkmenistan, Belarus, Tajikistan, Kazakhstan, Azerbaijan, Kyrgyzstan, Armenia, Moldova, Republic of, Türkiye, North Macedonia, Albania, Bosnia and Herzegovina, Serbia, Mexico, Ukraine, India, Benin, Cameroon, Burkina Faso, Chad, Guinea-Bissau, Mali, Senegal, Congo, Guinea, Gabon, Niger, Equatorial Guinea, Mauritania, Togo, Côte d'Ivoire, Central African Republic, Jordan, Philippines, Thailand	Canada, Australia, Chile, Cyprus, Denmark, Russian Federation, Belgium, Germany, France, Luxembourg, Netherlands, Switzerland, United Kingdom, Sweden, Italy, Austria, Liechtenstein, Greece, Spain, Monaco, Portugal, Ireland, Finland, Bulgaria, Czechia, Estonia, Slovakia, Hungary, Poland, Iceland, Malta, Croatia, Romania, Latvia, Lithuania, Slovenia, Israel, Japan, Korea, Republic of, New Zealand, Singapore, United States of America, Bahrain, Kuwait, Qatar, Saudi Arabia, Oman, United Arab Emirates
Filed	Egypt, Jordan, Pakistan, Venezuela (Bolivarian Republic of)	Cyprus, Denmark, Spain, Portugal, Finland, Poland, Croatia, Lithuania, Slovenia, Taiwan, Province of China, Uruguay, Brunei Darussalam, Macao, Hong Kong

Patent status/countries	Low, Low- middle and upper-middle	High income
Not in force	Botswana, Gambia (the), Ghana, Kenya, Lesotho, Malawi, Mozambique, Namibia, Sierra Leone, Sudan, Eswatini, Tanzania, United Republic of, Uganda, Zambia, Zimbabwe, Argentina, Peru, World Intellectual Property Organization (WIPO), Indonesia, South Africa, Viet Nam	United States of America, World Intellectual Property Organization (WIPO), Panama

Patent informations

Patent description	Representative patent	Categories	Patent holder	Licence with MPP	Patent source
Rilpivine parenteral formulation Expiry date: 2027-01-19 This invention relates to the use of a parenteral formulation comprising an anti-virally effective amount of TMC278 or a pharmaceutically acceptable acid-addition salt thereof, and a carrier, for the manufacture of a medicament for the treatment of a subject being infected with HIV, wherein the formulation is to be administered intermittently at a time interval of at least one week.	WO2007082922	Dose/Regimen, Use	Tibotec Pharmaceuticals Ltd	No	

Patent status

Patent status/countries	Low, Low- middle and upper-middle	High income
Granted	Turkmenistan, Belarus, Tajikistan, Kazakhstan, Azerbaijan, Kyrgyzstan, Armenia, Moldova, Republic of, Türkiye, North Macedonia, Albania, Bosnia and Herzegovina, Serbia, Montenegro, Malaysia, Ukraine, Philippines, Thailand, Benin, Cameroon, Burkina Faso, Chad, Guinea-Bissau, Mali, Senegal, Congo, Guinea, Gabon, Niger, Equatorial Guinea, Mauritania, Togo, Côte d'Ivoire, Central African Republic, Mexico, Nigeria, South Africa	Canada, Australia, Russian Federation, Belgium, Germany, France, Luxembourg, Netherlands, Switzerland, United Kingdom, Sweden, Italy, Austria, Liechtenstein, Greece, Spain, Denmark, Monaco, Portugal, Ireland, Finland, Bulgaria, Czechia, Estonia, Slovakia, Hungary, Poland, Iceland, Croatia, Romania, Latvia, Lithuania, Slovenia, Hong Kong, Israel, Japan, Korea, Republic of, New Zealand, Singapore, Taiwan, Province of China, United States of America, Malta
Filed	Egypt	Spain, Cyprus, Croatia, Hong Kong, Japan, Korea, Republic of, Singapore, United States of America

Patent status/countries	Low, Low- middle and upper-middle	High income
Not in force	Botswana, Gambia (the), Ghana, Kenya, Lesotho, Malawi, Mozambique, Namibia, Sierra Leone, Sudan, Eswatini, Tanzania, United Republic of, Uganda, Zambia, Zimbabwe, Argentina, Brazil, China, World Intellectual Property Organization (WIPO), India, Viet Nam, Indonesia	United States of America, World Intellectual Property Organization (WIPO), Chile

Patent informations

Patent description	Representative patent	Categories	Patent holder	Licence with MPP	Patent source
Dolutegravir and Cabotegravir compounds Expiry date: 2026-04-28 The present invention is to provide a novel compound (I), having the anti-virus activity, particularly the HIV integrase inhibitory activity, and a drug containing the same, particularly an anti-HIV drug, as well as a process and an intermediate thereof. Compound (I) wherein Z<1> is NR<4>; R<1> is hydrogen or lower alkyl; X is a single bond, a hetero atom group selected from O, S, SO, SO2 and NH, or lower alkylene or lower alkenylene in which the hetero atom group may intervene; R<2> is optionally substituted aryl; R<3> is hydrogen, a halogen, hydroxy, optionally substituted lower alkyl etc; and R<4> and Z<2> part taken together forms a ring, to form a polycyclic compound, including e.g., a tricyclic or tetracyclic compound.	WO2006116764	Compound	Glaxosmithkline Llc	No	

Patent status

Patent status/countries	Low, Low- middle and upper-middle	High income

Granted	Brazil, China, Morocco, Mexico, Philippines, Ukraine, Viet Nam, South Africa, Türkiye, Armenia, Azerbaijan, Belarus, Kyrgyzstan, Kazakhstan, Moldova, Republic of, Tajikistan, Turkmenistan, Nigeria, Colombia, Indonesia, Malaysia, Algeria	United States of America, Australia, Canada, Cyprus, Hong Kong, Israel, Japan, Korea, Republic of, Luxembourg, Norway, New Zealand, Taiwan, Province of China, Austria, Belgium, Bulgaria, Switzerland, Czechia, Germany, Denmark, Estonia, Spain, Finland, France, United Kingdom, Greece, Hungary, Ireland, Iceland, Italy, Liechtenstein, Lithuania, Latvia, Monaco, Netherlands, Poland, Portugal, Romania, Sweden, Slovenia, Slovakia, Russian Federation, Trinidad and Tobago, Singapore
Filed	Egypt	United States of America, Cyprus, Luxembourg, Norway, Finland, France, Hungary, Lithuania, Netherlands, Slovenia
Not in force	Türkiye, India, World Intellectual Property Organization (WIPO)	United States of America, Cyprus, Hong Kong, Israel, Japan, Luxembourg, Austria, Belgium, Bulgaria, Switzerland, Czechia, Germany, Denmark, Estonia, Spain, Finland, France, United Kingdom, Greece, Hungary, Ireland, Iceland, Italy, Liechtenstein, Lithuania, Latvia, Monaco, Netherlands, Poland, Portugal, Romania, Sweden, Slovenia, Slovakia, World Intellectual Property Organization (WIPO)

Patent informations

Patent description	Representative patent	Categories	Patent holder	Licence with MPP	Patent source
Rilpivirine compound and analogues and their use in HIV Expiry date: 2022-08-09 The present invention is concerned with pyrimidine derivatives having HIV (Human Immunodeficiency Virus) replication inhibiting properties. The invention further relates to methods for their preparation and pharmaceutical compositions comprising them. The invention also relates to the use of said compounds for the manufacture of a medicament for the prevention or the treatment of HIV infection.	WO03016306	Compound	Janssen Pharmaceutica N.V	No	

Patent status

Patent status/countries	Low, Low- middle and upper-middle	High income
Granted	Brazil, Ukraine, Kazakhstan, Albania	Australia, Germany, Hungary, Israel, Japan, Korea, Republic of, Luxembourg, Norway, Poland, Slovenia, Taiwan, Province of China, United States of America, Austria, Belgium, Bulgaria, Switzerland, Cyprus, Czechia, Denmark, Estonia, Spain, Finland, France, Greece, Ireland, Italy, Liechtenstein, Monaco, Netherlands, Portugal, Sweden, Slovakia, Russian Federation, Chile, Romania, Latvia, Lithuania, Singapore
Filed	Venezuela (Bolivarian Republic of)	Hungary, Slovenia, Cyprus, France, Lithuania

Patent status/countries	Low, Low- middle and upper-middle	High income
Not in force	Argentina, Brazil, China, Egypt, Mexico, South Africa, Botswana, Ghana, Gambia (the), Kenya, Lesotho, Malawi, Mozambique, Sudan, Sierra Leone, Eswatini, Tanzania, United Republic of, Uganda, Zambia, Zimbabwe, Türkiye, Armenia, Azerbaijan, Belarus, Kyrgyzstan, Moldova, Republic of, Tajikistan, Turkmenistan, Burkina Faso, Benin, Central African Republic, Congo, Côte d'Ivoire, Cameroon, Gabon, Guinea, Equatorial Guinea, Guinea-Bissau, Mali, Mauritania, Niger, Senegal, Chad, Togo, India, Malaysia, Philippines, Thailand, Viet Nam, Sri Lanka, World Intellectual Property Organization (WIPO), Albania, North Macedonia, Jordan, Lebanon, Pakistan, Indonesia	Canada, Germany, Hong Kong, Croatia, Japan, Luxembourg, Norway, New Zealand, Panama, Poland, Slovenia, Taiwan, Province of China, United States of America, Austria, Belgium, Bulgaria, Switzerland, Cyprus, Czechia, Denmark, Estonia, Spain, Finland, France, United Kingdom, Greece, Ireland, Italy, Liechtenstein, Monaco, Netherlands, Portugal, Sweden, Slovakia, World Intellectual Property Organization (WIPO), Romania, Latvia, Lithuania, Kuwait, United Arab Emirates, Bahrain, Saudi Arabia, Oman, Qatar, Macao, Trinidad and Tobago

Patent informations

Patent description	Representative patent	Categories	Patent holder	Licence with MPP	Patent source
Rilpivirine compound and analogues (Markush structure) Expiry date: 2021-02-26 Pyrimidine derivatives of formula (I) wherein Q1, Q2, G and R<1> are as defined within; and pharmaceutically acceptable salts and in vivo hydrolysable esters thereof are described. Processes for their manufacture, pharmaceutical compositions and their use as cyclin-dependent serine/threonine kinase (CDK) and focal adhesion kinase (FAK) inhibitors are also described.	WO0164656	Compound	Astrazeneca Ab, Astrazeneca Uk Limited	No	

Patent status

Patent status/countries	Low, Low- middle and upper-middle	High income
Granted		Austria, Belgium, Denmark, Finland, France, Greece, Ireland, Italy, Luxembourg, Netherlands, Sweden
Filed		Norway, Cyprus, France
Not in force	World Intellectual Property Organization (WIPO), Brazil, China, Mexico, South Africa, Türkiye, Albania, North Macedonia	Canada, United Kingdom, World Intellectual Property Organization (WIPO), Australia, Hong Kong, Israel, Japan, Korea, Republic of, Norway, New Zealand, United States of America, Switzerland, Cyprus, Germany, Spain, Liechtenstein, Monaco, Portugal, Romania, Latvia, Lithuania, Slovenia

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

Access principles

Collaborate for development

Consider on a case by case basis, collaborating on developing long acting products with potential significant public health impact, especially for low- and middle-income countries (LMICs), utilising the referred to long-acting technology

Not provided

Share technical information for match-making assessment

Provide necessary technical information to a potential partner, under confidentiality agreement, to enable preliminary assessment of whether specific medicines of public health importance in LMICs might be compatible with the referred to long-acting technology to achieve a public health benefit

Not provided

Work with MPP to expand access in LMICs

In the event that a product using the referred to long-acting technology is successfully developed, the technology IP holder(s) will work with the Medicines Patent Pool towards putting in place the most appropriate strategy for timely and affordable access in low and middle-income countries, including through licensing

Not provided

Comment & Information

Not provided