A Phase IIIb, open-label, hybrid type III trial evaluating implementation strategies for long-acting cabotegravir plus long-acting rilpivirine every two months in HIV-1 infected, virologically suppressed adults in select European healthcare settings.

Published: 07-07-2020
Last updated: 17-01-2025

The overall objective of the CAB LA + RPV LA clinical development programme is to develop a highly effective, well-tolerated, two-drug, long-acting injectable regimen which has the potential to offer improved treatment convenience, compliance and...

Ethical review	Approved WMO
Status	Completed
Health condition type	Viral infectious disorders
Study type	Interventional

Summary

ID

NL-OMON54940

Source
ToetsingOnline

Brief title
study 213199, CARISEL

Condition

- Viral infectious disorders

Synonym
HIV-1; HIV

Research involving
Human

Sponsors and support

Primary sponsor: ViiV Healthcare UK Limited
Source(s) of monetary or material Support: ViiV Healthcare UK Limited

Intervention

Keyword: Cabotegravir, HIV, implementation study, Rilpivirine

Outcome measures

Primary outcome

Study staff participants:

Change from baseline at Month 12 in Acceptability of Intervention Measure (AIM), Intervention Appropriateness Measure (IAM), and Feasibility of Intervention Measure (FIM)

Secondary outcome

Study participants

Length of patient study participant visit from arrival until departure from clinic assessed at Dose 1,Dose 2, Dose 4, and Dose 5.

Change in Acceptability of Intervention Measure (AIM) Score, Intervention Appropriateness Measure (IAM) Score, and Feasibility of Intervention Measure (FIM) Score over time. Assessed via questionnaires at Dose 7.

secundair -

Study staff participants

Total score of the Clinical Sustainability Assessment Tool (CSAT) at Month 12

Percentage of injections occurring within target window from the target date.

Proportion of participants with plasma HIV-1 RNA <50 c/mL over time

Incidence of treatment-emergent genotypic and phenotypic resistance to CAB and RPV in patient study participants with CVF (confirmed virologic failure)

Incidence and severity of AEs and SAEs over time and the proportion of participants who discontinue treatment due to AEs over time

Preference between CAB + RPV LA and daily oral ART medication (received prior to entering the study) at quantitatively assessed via preference questionnaire at Dose 7

Reported injection site reactions over time

Absolute values and changes in laboratory parameters over time

FRAME-IS outcome Months 2 - 12 (monthly)

Tertiar -

Change in treatment satisfaction over time from prior ART (assessed in Day 1 prior OLI initiation) using the HIV-Treatment Satisfaction Questionnaire (HIVTSQs) at Day 1, Dose 1, Dose 3, and Dose 7

Change in treatment satisfaction from prior daily oral ART medication using the HIV Treatment Satisfaction Questionnaire HIVTSQc at Dose 7

Proportion of participants who discontinue treatment due to AEs over time

Absolute values and changes in laboratory parameters over time

Study description

Background summary

The treatment of HIV-1 infection has advanced since the first oral antiretroviral agent (zidovudine, AZT) was approved for the treatment of HIV-1 infected individuals in 1987. Newer antiretrovirals are more potent, better tolerated and have enabled the formulation of multiple regimens that can provide viral suppression with a single tablet once daily. Moreover, clinic visits for laboratory monitoring have become less frequent; current standard of care for virally suppressed patients is a clinic visit with laboratory every 3-6 months. While there have been major advances in the field of HIV therapeutics, tolerability, long term safety concerns and adherence remain significant limitations to treatment success. Consistent lifetime daily adherence is difficult for many patients, reducing effectiveness of these treatments. Moreover, intermittent compliance can result in HIV drug resistance, with subsequent regimens being more complicated to construct.

Long acting injectable versions of drugs are being developed to enable therapy with infrequent dosing injection and represent an emerging paradigm for the treatment of HIV infection. CAB is a potent integrase inhibitor that possesses attributes that allow formulation and delivery as a long-acting product. RPV, also formulated as a LA product, is a diarylpyrimidine derivative and a potent non-nucleoside reverse transcriptase inhibitor (NNRTI) with in vitro activity against wild type HIV-1 and select NNRTI-resistant mutants. A two-drug regimen with CAB LA plus RPV LA (CAB LA + RPV LA) may offer many potential advantages over daily oral regimens including infrequent dosing that decreases the daily reminder to patients of their HIV status, decreased development of viral resistance due to intermittent compliance with oral agents and overall treatment satisfaction in virologically suppressed patients. Results to date have demonstrated the efficacy of a two-drug regimen of CAB LA + RPV LA as maintenance therapy with several on-going Phase 2 and 3 studies including LATTE-2, ATLAS, FLAIR, and ATLAS 2M.

Study objective

The overall objective of the CAB LA + RPV LA clinical development programme is to develop a highly effective, well-tolerated, two-drug, long-acting injectable regimen which has the potential to offer improved treatment convenience, compliance and improved quality of life for people living with HIV compared to current standard of care.

CAB LA + RPV LA represents a potential paradigm shift in the treatment of HIV with respect to the transition from daily oral antiretroviral therapy (ART) to long-acting injectable therapy. As such, it is important to understand how to optimise the implementation of CAB LA + RPV LA from the perspective of the patient as well as the healthcare provider, in order to mitigate any barriers to implementation in routine care.
Information from this study will be used to understand what level of clinic training and staff support is necessary for successful implementation of CAB LA + RPV LA. It will also be used to identify strategies to overcome any perceived barriers for the patients receiving the drug, as well as the healthcare providers and institutions administering the drug.

Study design

Patient:
For the patient this is a single-arm, open-label interventional study in respect to the drug regimen whereby all patients enrolled will receive the same intervention of the CAB LA + RPV LA regimen with a month oral lead in at Day 1 followed by CAB LA + RPV LA injections at Month 1, Month 2 and every 2 months thereafter. .

For Clinics:
For the implementation science aspect, this is a two-arm study where clinics will be randomized to either Enhanced or Standard Implementation Arms at the country level

Arm 1: The Enhanced Implementation Arm (arm-e) contains the Skilled Wrap-Around Team (SWAT) which is an interactive problem-solving meeting and an introduction to the principles of Continuous Quality Improvement (CQI) with follow-up CQI calls.

Arm 2: The Standard Implementation Arm (arm-s) will provide sites with the traditional standard practices for each country at the time of product availability provided by a medical science liaison or medical lead.

Both arms will have access to the toolkits aimed to support education and proper administration of CAB LA + RPV LA.

Intervention

Cabotegravir long-acting (CAB LA) and rilpivirine long-acting (RPV LA) is an investigational HIV-1 treatment regimen administered as two individual intramuscular injections, at the same time, once every two (2) months (following an oral lead-in period and initiation period).

Study burden and risks

Subject:
Burden:
Fill out questionnaires: 4x
Physical Examination: 6x
Interview by external party (if selected): 2x

Risks study procedures:
Blood samples can be painful and bruising may occur
Injection site reaction - the IP is given via IM injection. This can cause; pain or feeling uncomfortable, redness, swelling, itching, a bruise, lumps (hard swelling under the skin) or irritation at the puncture site.

Risk:
CAB LA
In more than 10% of the subjects: headache, fever and a reaction at the place where the injection was administered ('the puncture site')
In 1-10% of subjects: rashes, diarrhea or thin stools, nausea, vomiting, flatulence, abdominal pain, insomnia, nightmares, dizziness, anxiety, depressive feelings or thoughts, muscle pain, fatigue, feeling of weakness or discomfort
In 0.1-1% of subjects: drowsiness, dizziness or fainting during or after an injection, liver problems, transaminase increase (a protein in your blood), increase in weight
Allergic reactions to integrase inhibitors such as CAB have been reported. Symptoms included 'feeling sick', rash, fever, fatigue, swelling (sometimes of face or mouth with breathing problems), blisters, mouth ulcers, painful inflamed eyes, joint pain and muscle pain
Abnormal liver values
Seizures and convulsions (seizures)

RPV (LA)
In 1-10% of subjects: decreased appetite, sleep disorders, nausea, discomfort in the abdomen, dry mouth
In 0.1-1% of subjects: IRIS. IRIS is a condition in which some patients, especially those who have been HIV positive for a long time, can get inflammatory reactions. The symptoms are usually not specific. Symptoms include fever and worsening of the underlying disease. These inflammatory reactions are probably caused by the body's better resistance to inflammation. This is because the treatment reduces the amount of virus in the body.
Rashes.
Increased liver values.

Resistance to one or more drugs against HIV
Some patients with HIV infection have occasional depressive feelings or struggle with thoughts of self-harm or suicide

Site staff

Burden:
Fill out questionnaires: 3x
Interview by external party (about 4 people): 3x

Contacts

Public
ViiV Healthcare UK Limited

Great West Road 980
Brentford, Middlesex TW8 9GS
GB
Scientific
ViiV Healthcare UK Limited

Great West Road 980
Brentford, Middlesex TW8 9GS
GB

Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)
Elderly (65 years and older)

Inclusion criteria

1. 18 years or older
2. HIV-1 infected and must be suppressed on a guideline recommended active HAART regimen for at least 6 months prior to Screening.
3. Documented evidence of at least two plasma HIV-1 RNA measurements <50 c/mL in the 12 months prior to Screening: at least one < 6 months prior to Screening and one 6-12 months prior to screening;
4. Plasma HIV-1 RNA <50 c/mL at Screening

5. Women not pregnant, not lactating, or having a Non-reproductive potential or Postmenopausal

Exclusion criteria

1. Within 6 months prior to Screening, plasma HIV-1 RNA measurement >=50 c/mL;
2. During the previous 12 months, any confirmed HIV-1 RNA measurement >=200 c/mL
3. Women who are pregnant, breastfeeding, or plan to become pregnant or breastfeed during the study.
4. Any evidence of a current Center for Disease Control and Prevention (CDC) Stage 3 disease, except cutaneous Kaposi's sarcoma not requiring systemic therapy, and historical or current CD4+ counts <200 cells/mm3 are not exclusionary.
5. Any pre-existing physical or mental condition (including substance use disorder) which, may interfere with the participant's ability to comply with the dosing schedule and/or protocol evaluations or which may compromise the safety of the participant.
6. Participants with a high risk of seizures, including participants with an unstable or poorly controlled seizure disorder.
7. Participants who,pose a significant suicide risk.
8. The participant has a tattoo, gluteal implant/ enhancements or other dermatological condition overlying the gluteus region which may interfere with interpretation of injection site reactions
9. Evidence of Hepatitis B virus (HBV) infection
10. Participants who are anticipated to require HCV treatment within 12 months. Asymptomatic individuals with chronic hepatitis C virus (HCV) infection will not be excluded
11. Unstable liver disease
12. History of liver cirrhosis with or without hepatitis viral co-infection.
13. Ongoing or clinically relevant pancreatitis
14. Clinically significant cardiovascular disease
15. Ongoing malignancy other than cutaneous Kaposi's sarcoma, basal cell carcinoma, or resected, non-invasive cutaneous squamous cell carcinoma, or cervical intraepithelial neoplasia; other localized
16. Any condition which, may interfere with the absorption, distribution, metabolism or excretion of the study drugs or render the participant unable to receive study medication
17. History or presence of allergy or intolerance to the study drugs or their components or drugs of their class.

Study design

Design

Study phase:	3
Study type:	Interventional
Masking:	Open (masking not used)
Control:	Uncontrolled
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Completed
Start date (anticipated):	20-10-2020
Enrollment:	48
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	Cabotegravir longacting injections
Generic name:	Cabotegravir longacting injections
Product type:	Medicine
Brand name:	Cabotegravir Tablet
Generic name:	Cabotegravir Tablet
Product type:	Medicine
Brand name:	Edurant
Generic name:	Rilpivirine
Registration:	Yes - NL intended use
Product type:	Medicine
Brand name:	Rilpivirine longacting injections
Generic name:	Rilpivirine longacting injections

Ethics review

Approved WMO

Date:	07-07-2020
Application type:	First submission

Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	11-09-2020
Application type:	First submission
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	13-10-2020
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	19-10-2020
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	01-12-2020
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	07-12-2020
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	30-12-2020
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	08-01-2021
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO	

Date:	25-03-2021
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	02-04-2021
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	28-07-2021
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	11-08-2021
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	17-10-2021
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	27-10-2021
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	24-02-2022
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	02-03-2022
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United

(Nieuwegein)

Study registrations

Followed up by the following (possibly more current) registration

No registrations found.

Other (possibly less up-to-date) registrations in this register

No registrations found.

In other registers

Register	ID
EudraCT	EUCTR2020-000424-19-NL
CCMO	NL74423.100.20

Study results

Date completed: 14-09-2022

Results posted: 15-02-2023

First publication
23-11-2022