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A study looking at using two drugs as dual anti-HIV therapy in people who have previously had brain injury caused by HIV

Submission date
01/03/2025

Recruitment status
Recruiting

Registration date
12/05/2025

Overall study status
Ongoing

Last Edited
09/09/2025

Condition category
Infections and Infestations

[X] Prospectively registered
[_] Protocol
[_] Statistical analysis plan
[_] Results
[_] Individual participant data
[X] Record updated in last year

Plain English summary of protocol

Background and study aims
People living with HIV can experience brain injury caused by the HIV virus multiplying uncontrolled in their brain (known as HIV-associated brain injury [HABI]). Modern anti-HIV therapy stops this happening, however, the brain injury that has been caused, often cannot be fully reversed. When a person has experienced a brain injury in the past, but the virus is no longer actively multiplying in the brain, it is known as legacy HABI. Anti-HIV therapy has traditionally consisted of three medications (triple therapy) taken in combination. Some of the newer anti-HIV medications are more potent and work better at controlling the HIV virus. Because of this, there are now two medication combinations (dual therapy) that are recommended. Taking two, rather than three, medications may cause fewer side effects. The aim of this study is to look at how effective and safe dual anti-HIV therapy is for people with HIV in whom the HIV virus has affected brain health previously. The dual anti-HIV therapy that is being used in this study is a combination of dolutegravir and lamivudine called Dovato.

Who can participate?
Patients aged 18 years and over who are living with HIV and, at some point, HIV will have affected the health of their brain, however, there will be no evidence that it is continuing to affect their brain health. Participants will be taking triple anti-HIV therapy and have never taken dual anti-HIV therapy.

What does the study involve?
Participants will be asked to attend at least 11 visits over roughly a 2-year period. Most will be at their routine clinic in the research department. They will complete some questionnaires and brain function (cognitive) tests and have some blood collected. In addition, they will have at least two lumbar punctures (also known as a spinal tap) performed. There will also be two scanning visits at a separate imaging facility where a brain (MRI) scan will be done.

What are the possible benefits and risks of participating?
The information gained from this study may be of benefit in the treatment of people with HIV in the future, especially people with HIV in whom HIV has previously affected brain health. There

are no direct benefits to patients for participating in this study.
Headache, which occurs in 10% (1 in 10 people) to 30% (3 in 10 people), is the most common complication following lumbar puncture. A spinal headache is a headache that is experienced when a person sits up or walks, but when they lie down it goes away. The headache typically starts several hours up to two days after the procedure and may be accompanied by nausea, vomiting and dizziness. Post-lumbar puncture headaches can last from a few hours to a week or more. To help relieve a headache, participants will be advised to lie down and drink extra fluids. If a spinal headache persists, and it is not relieved by bed rest, fluids, or pain relief medications, then participants will be advised to call their doctor.
In rare cases (less than 1% or 1 in 100 people) participants may need to have a further procedure known as a blood patch. This is where their own blood is injected back into the areas where the lumbar puncture was performed. This is done to prevent spinal fluid from leaking internally from the lumbar puncture entry site.
Some people feel back discomfort after a lumbar puncture. Participants may feel soreness at the site of the lumbar puncture.
As part of this study, participants will have blood taken. This procedure is uncomfortable but rarely results in any significant problems. Side effects that have been noted with taking blood include feeling light-headed or faint, fainting, formation of a blood clot, bruising and/or infection at the site of the needlestick.
Participants will change their anti-HIV therapy at the start and perhaps again at the end of the study. This is being done in a way that we would expect their anti-HIV therapy to continue to work effectively. Indeed, many studies have looked at switching anti-HIV therapy and shown this to be both safe and effective. Within the study participants will be monitored closely to check that their anti-HIV therapy continues to be effective. However, we cannot guarantee that switching their anti-HIV therapy will not pose any risks to participants. This study is specifically checking that dual antiretroviral therapy is safe in people in whom HIV has previously affected their brain health. We expect it to be safe, but we do not know for sure, hence why we are undertaking this study.
It is possible that if the anti-HIV drugs in this study are given to a pregnant woman it will harm the unborn child. Pregnant women must not therefore take part in this study, neither should women who plan to become pregnant during the study. If participants are female and able to get pregnant, they will need to have a negative pregnancy test before switching anti-HIV therapy. Women who suspect they might be pregnant will be asked to have pregnancy tests during the study. Women who could become pregnant must use a highly effective contraceptive during this study. Any participant who finds out that they have become pregnant while taking part in the study should immediately tell their research doctor.

Where is the study run from?
Imperial College London (UK)

When is the study starting and how long is it expected to run for?
February 2025 to March 2028

Who is funding the study?
ViiV Healthcare

Who is the main contact?
1. Dr Alan Winston, a.winston@imperial.ac.uk
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Contact information

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Scientific, Principal investigator

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Additional identifiers

Clinical Trials Information System (CTIS)
Nil known

Integrated Research Application System (IRAS)
1010067

ClinicalTrials.gov (NCT)
Nil known

Protocol serial number
22SM8070, CPMS 67374

Study information

Scientific Title

A study to assess dolutegravir and lamivudine as dual antiretroviral therapy in individuals with legacy HIV-associated brain injury

Acronym
Dual ART in Legacy HABI

Study objectives
People living with HIV can experience brain injury caused by the HIV virus multiplying, uncontrolled, in their brain (HIV-associated brain injury [HABI]). Modern anti-HIV therapy stops the virus from multiplying in the brain, however, the brain injury that has been caused, often cannot be fully reversed. In this case, it is known as legacy HABI.

Anti-HIV therapy has traditionally consisted of three medications taken in combination (triple anti-HIV therapy). Some of the newer anti-HIV medications are more potent and work better at controlling the HIV virus. Because of this, there are now two medication combinations (dual anti-HIV therapy) that are recommended. Taking two, rather than three, medications may cause fewer side effects.

Current medical guidance for people with legacy HABI recommends taking triple anti-HIV therapy. The aim of this study is to look at how effective and safe dual anti-HIV therapy is for people with legacy HABI.

Ethics approval required
Ethics approval required

Ethics approval(s)
approved 08/05/2025, London - Surrey Borders Research Ethics Committee (Equinox House, City Link, Nottingham, NG2 4LA, United Kingdom; +44 (0)207 104 8088, +44 (0)2071048117, +44 (0) 207 104 8131; surreyborders.rec@hra.nhs.uk), ref: 25/LO/0224

Study design
Non-randomized single-arm study

Primary study design
Interventional

Study type(s)
Safety, Efficacy

Health condition(s) or problem(s) studied
HIV infection

Interventions
This is a non-randomised, single-arm study. Dovato 50 mg/300 mg will be given to all participants who are enrolled into the study. Participants will take daily oral Dovato from baseline for the 2-year study duration.

Intervention Type
Drug

Phase
Phase IV

Drug/device/biological/vaccine name(s)
Dovato 50 mg/300 mg film-coated tablets (dolutegravir sodium, lamivudine)

Primary outcome(s)
Number of individuals with undetectable HIV RNA in the cerebrospinal fluid after study intervention

The primary endpoint is a composite endpoint based on:
1. Cerebrospinal fluid HIV RNA assessed at month 12
2. Cerebrospinal fluid HIV RNA assessed clinically at any time from baseline due to new onset of neurological symptoms which may be in keeping with cerebrospinal fluid escape

Measured either at 12 months or at an earlier timepoint if individuals have neurological symptomatology

Key secondary outcome(s))
1. Clinical parameters measured at baseline, 12 and 24 months, including:
1.1. Cognitive function measured using Montreal Cognitive Assessment (MoCA), Trail Making Test
1.2. Quality of life and wellbeing of people with HIV measured using HIV Positive Outcomes questionnaire
1.3. Depression measured using Patient Health Questionnaire (PHQ-9)
1.4. Anxiety measured using Generalized Anxiety Disorder 2 (GAD-2)
2. Plasma HIV RNA measured using local hospital laboratory HIV RNA assay at all study visits over 12 and 24 months
3. Cerebrospinal fluid parameters measured using local hospital laboratory protein, glucose, albumin, microscopy, HIV RNA CSF assays at baseline and 12 months
4. Cerebral MRI parameters measured at baseline and 12 months

Completion date
31/03/2028

Eligibility

Key inclusion criteria
1. HIV-1 positive
2. Age 18 years or over
3. Signed informed consent
4. Willing to switch therapy as per study protocol
5. Able to comply with the study protocol and tolerate the study regimen in the opinion of the investigator
6. On stable triple-drug antiretroviral therapy with no antiretroviral drug switches in the last 3 months and no prior use of dual antiretroviral therapy
7. Clinical diagnosis of legacy HABI with no evidence of active disease (as per protocol Section 4.2.2 Definition of legacy HABI)
8. Plasma HIV RNA <50 copies/mL at screening and on at least one other occasion over the last 12 months
9. Undetectable cerebrospinal fluid HIV RNA (<200 copies/mL) at screening

10. For patients assigned female at birth one of the following conditions must apply:
10.1. Non-childbearing potential defined as either post-menopausal (12 months of amenorrhea without an alternate medical cause), or physically incapable of becoming pregnant with documented tubal ligation, hysterectomy or bilateral oophorectomy
OR
10.2. Child-bearing potential with a negative pregnancy test at Baseline and agrees to use one of the following methods of contraception to avoid pregnancy:
10.2.1. Complete abstinence from penile-vaginal intercourse from at least 2 weeks prior to administration of study drug, throughout the study, and for at least 2 weeks after discontinuation of all study medications
10.2.2. Partner sterilisation, confirmed prior to the participant's entry into the study, provided that the sterilised partner is the sole partner for that participant
10.2.3. A contraceptive method that is highly effective (with an expected failure rate of <1% per year) (see protocol Section 6.3.1 Study sanctioned highly effective contraceptive methods, for a list of acceptable highly effective methods of contraception).

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Adult

Lower age limit
18 years

Sex
All

Key exclusion criteria
1. History of CSF HIV RNA escape (defined as a paired CSF HIV RNA greater than plasma HIV RNA)
2. History of plasma or cerebrospinal fluid HIV-drug resistance
3. Contraindication to dual antiretroviral therapy
4. Contraindication to lumbar puncture examination
5. Contraindication to MRI scan (claustrophobia, metal implants or other reasons)
6. ALT ≥5 times the upper limit of normal, OR ALT ≥3 times the upper limit of normal and bilirubin ≥1.5 times the upper limit of normal (with >35% direct bilirubin)
7. Creatinine clearance of <30 mL/min
8. Clinically significant abnormalities in screening laboratory results
9. Evidence of hepatitis B co-infection or, if at risk of hepatitis B, not hepatitis B immune
10. Chronic hepatitis C infection anticipated to require the introduction of new hepatitis C virus therapy (e.g. with oral direct-acting antivirals) prior to the primary endpoint of the study.
11. Current alcohol abuse or drug of abuse dependence
12. Severe mental health conditions that make patient unlikely to adhere to protocol
13. Active opportunistic infection or significant co-morbidities with a life expectancy of less than 2 years
14. Current disallowed concomitant medication as per SmPC
15. History or presence of allergy to the study drugs or their components
16. Pregnancy or breast/chestfeeding or patient envisages becoming pregnant during the study

Date of first enrolment
01/10/2025

Date of final enrolment
31/03/2026

Locations

Countries of recruitment
United Kingdom

England

Study participating centre
St Mary's Hospital
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Study participating centre
Royal Sussex County Hospital
Eastern Road
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Sponsor information

Organisation
Imperial College London

ROR
https://ror.org/041kmwe10

Funder(s)

Funder type
Industry

Funder Name
ViiV Healthcare

Alternative Name(s)
ViiV Healthcare Limited

Funding Body Type
Private sector organisation

Funding Body Subtype
For-profit companies (industry)

Location
United Kingdom

Results and Publications

Individual participant data (IPD) sharing plan
The data-sharing plans for the current study are unknown and will be made available at a later date

IPD sharing plan summary
Data sharing statement to be made available at a later date