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A study looking at the effects of switching anti-HIV therapy in people with HIV who have difficulty sleeping

Submission date
06/04/2020

Recruitment status
No longer recruiting

Registration date
23/04/2020

Overall study status
Completed

Last Edited
20/06/2023

Condition category
Infections and Infestations

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

Plain English summary of protocol

Current plain English summary as of 03/03/2022:
Background and study aims
Current anti-HIV therapy is very effective at controlling the HIV virus and keeping people well. But there is still much that isn't known about how taking the drugs affect some parts of the body, such as the nervous system. It also isn't known what effect different drugs might have on things like how well people sleep. Within one family of HIV drugs, called integrase inhibitors, it is thought that difficulty sleeping is higher when taking a drug called dolutegravir. The researchers of this study want to see if taking a different drug from within this family, called bictegravir, might cause less difficulties sleeping.

Who can participate?
HIV-positive people who are generally well but have difficulty sleeping (insomnia), 18 years old and above, who have been taking a drug called dolutegravir plus either one or two NRTIs.

What does the study involve?
Participants will be allocated by chance to either continue taking dolutegravir plus either one or two NRTIs or to switch to taking a drug called Biktarvry, which contains bictegravir. Participants will attend visits over about a 5-month period. There will be eight visits in total. Six visits will be at the routine clinic where blood and urine will be collected and several questionnaires completed. Two visits will be at a separate imaging centre where a brain scan will be performed.

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. There are no direct benefits for participating in this study. Having blood taken 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. It is possible that if the anti-retroviral drugs in this study are given to a pregnant woman it will harm the foetus. Pregnant women must not therefore take part in this study, neither should women who plan to become pregnant during the study. Women who are at risk of pregnancy will be asked to have pregnancy tests

during the study. Women who could become pregnant must use a highly effective contraceptive during this study. This also applies to men with heterosexual partners who could become pregnant. Any participant who finds out that they or their partner has become pregnant while taking part in the study must immediately notify the research doctor. Depending on which group participants are randomly allocated to they may change their anti-HIV therapy at the start and towards the end of the study. This is being done in a way that it is expected that the anti-HIV therapy will 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, the researchers cannot guarantee that switching anti-HIV therapy will not pose any risks to participants. Like all medicines, the medicines in this study can cause side effects, although not everybody gets them. The more serious or common side effects with a known or possible relationship to Biktarvy are listed below. The list does not include side effects seen with dolutegravir or NRTIs, as participants will already have been made aware of these when they started this medicine. During HIV therapy there may be an increase in weight and in levels of blood lipids and glucose. This is partly linked to restored health and lifestyle, and in the case of blood lipids sometimes to the HIV medicines themselves. Common side effects (may affect up to 1 in 10 people): depression, abnormal dreams, headache, dizziness, diarrhoea, nausea (feeling sick), fatigue (tiredness). Uncommon side effects (may affect up to 1 in 100 people): suicidal thoughts and attempt (particularly in patients who have had depression or mental health problems before). Rare side effects (may affect up to 1 in 1000 people): Stevens-Johnson syndrome (SJS). Side effects with an unknown frequency (frequency can't be estimated from the available data): bone problems.

Where is the study run from?
1. St Mary's Hospital (UK)
2. Royal Sussex County Hospital (UK)

When is the study starting and how long is it expected to run for?
November 2018 to May 2023

Who is funding the study?
Gilead Sciences (USA)

Who is the main contact?
Nicki Doyle
n.doyle@imperial.ac.uk

Previous plain English summary:
Background and study aims
Current anti-HIV therapy is very effective at controlling the HIV virus and keeping people well. But there is still much that isn't known about how taking the drugs affect some parts of the body, such as the nervous system. It also isn't known what effect different drugs might have on things like how well people sleep. Within one family of HIV drugs, called integrase inhibitors, it is thought that difficulty sleeping is higher when taking a drug called dolutegravir. The researchers of this study want to see if taking a different drug from within this family, called bictegravir, might cause less difficulties sleeping.

Who can participate?
HIV-positive people who are generally well but have difficulty sleeping (insomnia), 18 years old and above, who have been taking a drug called Triumeq (which contains dolutegravir)

What does the study involve?
Participants will be allocated by chance to either continue taking Triumeq or to switch to taking a drug called Biktarvry, which contains bictegravir. Participants will attend visits over about a 5-month period. There will be eight visits in total. Six visits will be at the routine clinic where blood and urine will be collected and several questionnaires completed. Two visits will be at a separate imaging centre where a brain scan will be performed.

What are the possible benefits and risks of participating?
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Where is the study run from?
1. St Mary’s Hospital (UK)
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When is the study starting and how long is it expected to run for?
November 2018 to May 2022

Who is funding the study?
Gilead Sciences (USA)

Who is the main contact?
Nicki Doyle
n.doyle@imperial.ac.uk

Contact information

Type(s)
Scientific

Contact name
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Additional identifiers

EudraCT/CTIS number
2019-004007-12

IRAS number
272955

ClinicalTrials.gov number
Nil known

Secondary identifying numbers
CPMS 44049, IRAS 272955

Study information

Scientific Title
Brain connectivity and patient-reported outcomes in people with HIV (PWH) with symptoms of insomnia switching integrase inhibitor-based ART: a randomised controlled study

Acronym
BIC CNS

Study objectives
In people with HIV with symptoms of insomnia, switching from a dolutegravir to bictegravir based antiretroviral therapy regimen will be associated with improvements in brain connectivity measured via functional MRI.

Ethics approval required
Old ethics approval format

Ethics approval(s)
Approved 20/05/2020, South Central - Oxford C Research Ethics Committee (Level 3, Block B, Whitefriars Building, Bristol Research Ethics Committee Centre, BS1 2NT, UK; +44 (0)207 104 8241 / 8041; oxfordc.rec@hra.nhs.uk), REC ref: 20/SC/0116

Study design
Randomized; Both; Design type: Treatment, Drug, Qualitative

Primary study design
Interventional

Secondary study design
Randomised controlled trial

Study setting(s)
Hospital

Study type(s)
Treatment

Participant information sheet
Not available in web format, please use the contact details to request a participant information sheet: Nicki Doyle n.doyle@imperial.ac.uk

Health condition(s) or problem(s) studied
Human immunodeficiency virus [HIV] disease

Interventions
Current intervention as of 03/03/2022:
46 people with HIV taking a drug called dolutegravir, plus one or two other drugs called NRTIs (nucleoside-reverse-transcriptase-inhibitors) for at least 4 months with an undetectable level of HIV virus will be enrolled. Brain function measures will be assessed via the following methods: i) Brain MR imaging, ii) patient reported outcomes (PRO).

At baseline (day 0), all participants will undergo assessment of these brain function measures. Participants will then be randomised on a 1:1 basis (50% chance of each group) to either:
1. Switch anti-retroviral therapy from dolutegravir plus either one or two NRTIs to another drug called Biktarvy™ (which contains drugs bictegravir, emtricitabine & tenofovir alafenamide)
2. Or, remain on dolutegravir plus either one or two NRTIs.

Randomisation will be stratified by recruiting site, sex at birth, age at screening, and participant's handedness and will be done on a 1:1 basis.

Biktarvy: 50 mg bictegravir/200 mg emtricitabine/25 mg tenofovir alafenamide - one tablet, orally, once daily.
Dolutegravir 50mg (as part of a regimen consisting of dolutegravir plus either one or two nucleoside-reverse-transcriptase-inhibitors [NRTIs]) - one tablet, orally, once daily.

Study visits will occur at day 30, day 60, day 120 and day 150. At the day 120 visit, assessment of MRI brain function measures and PRO will be repeated, and participants will resume/remain on their usual pre-study antiretroviral regimen (dolutegravir plus either one or two NRTIs). An end of study visit will be performed at day 150.

Participants will attend for 6 clinic visits in total at which they will have a physical examination, have blood collected for safety tests as well as an HIV viral load (the level of HIV virus in the blood) and a CD4 count (a measure of the immune system) at screening & baseline. Any female participants will also have urine collected for a pregnancy test. At the screening and day 120 visit they will complete a short questionnaire relating to their insomnia. At baseline and day 120 they will complete several questionnaires relating to sleep, side effects from anti-HIV medication, food cravings, and quality of life. At baseline and day 120 a research blood sample will be collected and stored for future, ethically approved, research in keeping with the results of this study.

In addition, participants will attend two imaging visits at a different location to have brain scans. They will be asked to complete various tasks whilst lying flat within the scanner.

Previous interventions as of 17/06/2021:
46 people with HIV taking a drug called Triumeq™ (which contains drugs called dolutegravir, abacavir & lamivudine) for at least 4 months with an undetectable level of HIV virus will be enrolled. Brain function measures will be assessed via the following methods: i) Brain MR imaging, ii) patient reported outcomes (PRO).

At baseline (day 0), all participants will undergo assessment of these brain function measures. Participants will then be randomised on a 1:1 basis (50% chance of each group) to A) switch anti-retroviral therapy from Triumeq™ to another drug called Biktarvy™ (which contains drugs bictegravir, emtricitabine & tenofovir alafenamide) or B) remain on Triumeq™.

Randomisation will be stratified by recruiting site, sex at birth, age at screening, and participant' s handedness and will be done on a 1:1 basis.

Biktarvy: 50 mg bictegravir/200 mg emtricitabine/25 mg tenofovir alafenamide - one tablet, orally, once daily.
Triumeq: 50 mg dolutegravir/600 mg abacavir/300 mg lamivudine - one tablet, orally, once daily.

Study visits will occur at day 30, day 60, day 120 and day 150. At the day 120 visit, assessment of MRI brain function measures and PRO will be repeated, and participants will resume/remain on their usual pre-study antiretroviral regimen (Triumeq™). An end of study visit will be performed at day 150.

Participants will attend for 6 clinic visits in total at which they will have a physical examination, have blood collected for safety tests as well as an HIV viral load (the level of HIV virus in the blood) and a CD4 count (a measure of the immune system) at screening & baseline. Any female participants will also have urine collected for a pregnancy test. At the screening and day 120 visit they will complete a short questionnaire relating to their insomnia. At baseline and day 120 they will complete several questionnaires relating to sleep, side effects from anti-HIV medication, food cravings, and quality of life. At baseline and day 120 a research blood sample will be collected to measure novel biomarkers of inflammation.

In addition, participants will attend two imaging visits at a different location to have brain scans. They will be asked to complete various tasks whilst lying flat within the scanner.

Previous interventions:
46 people with HIV taking a drug called Triumeq™ (which contains drugs called dolutegravir, abacavir & lamivudine) for at least 4 months with an undetectable level of HIV virus will be enrolled. Brain function measures will be assessed via the following methods: i) Brain MR imaging, ii) patient reported outcomes (PRO).

At baseline (day 0), all participants will undergo assessment of these brain function measures. Participants will then be randomised on a 1:1 basis (50% chance of each group) to A) switch anti-retroviral therapy from Triumeq™ to another drug called Biktarvy™ (which contains drugs bictegravir, emtricitabine & tenofovir alafenamide) or B) remain on Triumeq™.

Randomisation will not be stratified for any baseline characteristics and will be done on a 1:1 basis.

Biktarvy: 50 mg bictegravir/200 mg emtricitabine/25 mg tenofovir alafenamide - one tablet, orally, once daily.
Triumeq: 50 mg dolutegravir/600 mg abacavir/300 mg lamivudine - one tablet, orally, once daily.

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In addition, participants will attend two imaging visits at a different location to have brain scans. They will be asked to complete various tasks whilst lying flat within the scanner.

Intervention Type
Drug

Phase
Phase IV

Drug/device/biological/vaccine name(s)
Dolutegravir, abacavir, lamivudine, bictegravir, emtricitabine, tenofovir alafenamide

Primary outcome measure
1. Cerebral function parameters measured using MRI at baseline and day 120
2. Sleep, symptoms associated with antiretroviral therapy and health-related quality of life measured using validated patient-reported outcome questionnaires (HIV symptom index, Short form -36, Pittsburgh sleep quality index, Work productivity and activity impairment questionnaire, Epworth sleepiness scale, Fatigue severity scale of sleep disorders, Food cravings questionnaire – trait & state) measured at baseline and day 120

Secondary outcome measures
There are no secondary outcome measures

Overall study start date
23/11/2018

Completion date
11/05/2023

Eligibility

Key inclusion criteria
Current participant inclusion criteria as of 16/06/2022:
1. HIV-1 positive
2. Age ≥18 years
3. Plasma HIV RNA <50 copies/ml at screening and on at least one other occasion over the last 12 months
4. Acceptable medical history and laboratory parameters (haematology and chemistry) in the opinion of the investigator
5. On a stable antiretroviral regimen comprising of dolutegravir plus either one or two NRTIs once daily for >4 months
6. A total score of ≥8 on the Insomnia Severity Index
7. BMI ≥18

Previous participant inclusion criteria as of 03/03/2022:
1. HIV-1 positive
2. Age ≥18 years
3. Plasma HIV RNA <50 copies/ml at screening and on at least one other occasion over the last 12 months
4. Acceptable medical history and laboratory parameters (haematology and chemistry) in the opinion of the investigator
5. On a stable antiretroviral regimen comprising of dolutegravir plus either one or two NRTIs once daily for >4 months
6. A total score of ≥8 on the Insomnia Severity Index
7. BMI of 18-32, inclusive

Previous participant inclusion criteria as of 17/06/2021:
1. HIV-1 positive
2. Age ≥18 years
3. Plasma HIV RNA <50 copies/ml at screening and on at least one other occasion over the last 12 months
4. Acceptable medical history and laboratory parameters (haematology and chemistry) in the opinion of the investigator
5. On a stable antiretroviral regimen comprising of Triumeq™ once daily for >4 months
6. A total score of ≥8 on the Insomnia Severity Index
7. BMI of 18-32, inclusive

Previous participant inclusion criteria:
1. HIV-1 positive
2. Age > = 18 years

3. Plasma HIV RNA < 50 copies/mL at screening and on at least one other occasion over the last 3 months
4. Acceptable medical history and laboratory parameters (haematology and chemistry) in the opinion of the investigator
5. On a stable antiretroviral regimen comprising of Triumeq™ once daily for > 4 months
6. A total score of 8 or greater in the Insomnia Severity Index
7. BMI 18 - 32, inclusive

Participant type(s)
Patient

Age group
Adult

Lower age limit
18 Years

Sex
Both

Target number of participants
Planned Sample Size: 46; UK Sample Size: 46

Total final enrolment
19

Key exclusion criteria
1. Significant neurological disease
2. Current history of major depression or psychosis
3. Diagnosed sleep disorder (sleep apnoea, narcolepsy)
4. Current medication which is likely to interfere with sleep
5. Recent head injury (past 30 days)
6. Current alcohol abuse or drug of abuse dependence
7. Active opportunistic infection or significant co-morbidities
8. Pregnancy

Date of first enrolment
05/10/2021

Date of final enrolment
31/01/2023

Locations

Countries of recruitment
England

United Kingdom

Study participating centre
University Hospitals Sussex NHS Foundation Trust
Royal Sussex County Hospital
Eastern Road
Brighton
United Kingdom
BN2 5BE

Study participating centre
Imperial College Healthcare NHS Trust
St Mary's Hospital
Praed Street
London
United Kingdom
W2 1NY

Sponsor information

Organisation
University of Sussex

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c/o Dr Antony Walsh
Research and Enterprise Services
Falmer House
Brighton
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BN1 9QF
+44 (0)1273 872748
researchsponsorship@sussex.ac.uk

Sponsor type
University/education

Website
http://www.sussex.ac.uk/

ROR
https://ror.org/00ayhx656

Funder(s)

Funder type
Industry

Funder Name
Gilead Sciences; Grant Codes: IN-UK-380-5652

Alternative Name(s)
Gilead, Gilead Sciences, Inc.

Funding Body Type
Government organisation

Funding Body Subtype
For-profit companies (industry)

Location
United States of America

Results and Publications

Publication and dissemination plan
Planned publication in a high-impact peer-reviewed journal and presentation at relevant medical conferences within a year of the overall trial end date.

Intention to publish date
01/03/2024

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

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
HRA research summary			26/07/2023	No	No