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Metabolic Impact of Darunavir monotherapy vs Atripla in HIV patients

Submission date
04/08/2010

Recruitment status
No longer recruiting

Registration date
12/11/2010

Overall study status
Completed

Last Edited
21/01/2019

Condition category
Infections and Infestations

[_] Prospectively registered
[_] Protocol
[_] Statistical analysis plan
[X] Results
[_] Individual participant data

Plain English summary of protocol

Background and study aims
The human immunodeficiency virus (HIV) is a type of virus known as a retrovirus. HIV attacks and weakens the immune system, making it more difficult for a sufferer to fight infections. It is a highly contagious disease, through bodily fluids such as blood, semen and vaginal fluids. There is currently no cure for HIV, but there are a range of drug treatments that can allow people who are HIV positive to lead a long and full life. Antiretroviral therapy (ART) is the standard treatment for HIV, where at least three different antiretroviral (ARV) drugs are given at the same time. This treatment is very effective at suppressing the virus and stopping the development of the disease. When a person has been on ART, the amount of HIV present in the blood (viral load) is reduced. After three to six months of treatment, the viral load should have fallen to undetectable levels (undetectable viral load). A commonly used ART is Atripla, which contains the three drugs efavirenz, emtricitabine, and tenofovir. Although this treatment can be very effective, it can cause long-term health problems, specifically problems with the bones and kidneys. A possible reason for this is the Atripla treatment could lead to reduced levels of different vitamins and minerals in the body, such as vitamin D and calcium, which can affect hormone levels. The aim of this study is to find out if treating HIV patients with the ARV's Darunavir/Ritonavir only (single-drug therapy) is less toxic for bones and kidneys than standard ART.

Who can participate?
HIV positive adults, currently taking Atripla, who have had an undetectable viral load in the last 6 months.

What does the study involve?
Participants are randomly allocated to one of two groups. Those in the first group continue their Aripla therapy, which involves taking the Atripla tablets (which contain efavirenz, emtricitabine, and tenofovir) daily for the 48 week study. Those in the second group stop taking their Aripla and take darunavir 800mg/ritonavir 100mg every day for 48 weeks. At the start of the study and then every month until 48 weeks, participants provide blood and urine samples in order to test kidney function and biomarkers (chemical indicators) of bone health.

What are the possible benefits and risks of participating?
Not provided at time of registration.

Where is the study run from?
St. Thomas’ Hosptial (UK)

When is the study starting and how long is it expected to run for?
October 2010 to October 2013

Who is funding the study?
Tibotec (Janssen-Cilag Ltd) (UK)

Who is the main contact?
Dr Julie Fox

Contact information

Type(s)
Scientific

Contact name
Dr Julie Fox

Contact details
Harrison Wing
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Additional identifiers

EudraCT/CTIS number

IRAS number

ClinicalTrials.gov number

Secondary identifying numbers
JF-001

Study information

Scientific Title
The metabolic impact of darunavir/ritonavir maintenance monotherapy after successful viral suppression with standard Atripla in HIV-1 infected patients: an unblinded, multicentre, randomised controlled trial

Acronym
MIDAs

Study objectives
This project aims to assess the potential long-term advantages of switching HIV patients from the standard therapy (Atripla) to a different regimen of treatment (darunavir 800 mg/ritonavir 100 mg) in terms of Vitamin D levels, calcium and phosphate homeostasis, renal (tubular) function, bone turnover and bone mineralisation and infection disease progression.

On 07/05/2014 the anticipated start date was changed from 01/03/2012 to 01/10/2014.

Ethics approval required
Old ethics approval format

Ethics approval(s)
Central London Research Ethics Committee 4, 04/08/2010

Study design
Multicentre open-label randomised controlled trial

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 contact details below to request a patient information sheet

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

Interventions
At baseline, patients will be randomised to receive either
1. Darunavir 800mg/ritonavir 100mg daily
2. Atripla® daily
Study medication/HIV regimen will be dispensed at each study visit.

All participants will have the opportunity to discuss continuing their study drug with their routine clinician at study end.

Intervention Type
Other

Phase
Phase IV

Primary outcome measure
Change in 25(OH)Vitamin D

Secondary outcome measures
1. Reduction in parathyroid hormone levels
2. Improvements in serum calcium, phosphate, alkaline phosphatase
3. Improvement in estimated glomerular filtration rate, albuminuria and proteinuria, tubular phosphate reabsorption and other markers of renal tubular dysfunction
4. Improvement in bone mineral density
5. Immune activation: change in immune activation (CD8+CD38+)
6. The proportion of participants without therapeutic failure (defined as two consecutive HIV-RNA values > 50 copies/ml)

Outcomes will be measured throughout the study period though lab analysis will be carried out at end of the study. Samples will be blood/urine samples and for substudy, genital secretions.

Overall study start date
01/10/2010

Completion date
01/10/2014

Eligibility

Key inclusion criteria
1. Between 18-65 Males and Females
2. Documented Positive HIV-antibody test and previous positive HIV-antibody test within three months of the start of the study
3. Plasma HIV RNA <50 copies/ml for at least six months on Atripla
4. Agree to NOT take vitamin D supplements for the duration of the study
5. Willing to use barrier contraception (condoms) for the duration of their participation in the study
6. Ability to give informed consent

Participant type(s)
Patient

Age group
Adult

Lower age limit
18 Years

Upper age limit
65 Years

Sex

Both

Target number of participants
70

Key exclusion criteria
1. Pregnancy or breast feeding
2. Patient unlikely to comply with protocol, and in particular adhere to therapeutic regimen
3. Patient likely to use narcotics during the study period
4. Hepatitis B co-infection (past or present)
5. Diabetes mellitus
6. Received vitamin D supplementation for more than one month within the previous 6 months
7. Current use or likely to require use of concomitant medication with known interactions with Darunavir or Ritonavir including rifampicin, amiodarone, flecainide, bupropion, clozapine, ergotamine, mexilitine, midazolam, pethidine, pimoziide, quinidine, sertindole, sildanefil, voriconazole, zolpidem, and St. Johns Wort would exclude a subject from the trial
8. Individuals experiencing side effects from their current regime will not be excluded from analysis

Date of first enrolment
01/10/2010

Date of final enrolment
01/10/2014

Locations

Countries of recruitment
England

United Kingdom

Study participating centre
St. Thomas' Hospital
Harrison Wing
2nd Floor Lambeth Wing
Westminster Bridge Road
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Sponsor information

Organisation
Guy's & St. Thomas' NHS Foundation Trust (UK)

Sponsor details
16th Floor, Tower Wing
Guy's Hospital
Great Maze Pond
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England
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Sponsor type
Hospital/treatment centre

ROR
https://ror.org/00j161312

Funder(s)

Funder type
Industry

Funder Name
Tibotec (Janssen-Cilag Ltd) (UK)

Results and Publications

Publication and dissemination plan
Not provided at time of registration

Intention to publish date

Individual participant data (IPD) sharing plan

IPD sharing plan summary
Not provided at time of registration

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Results article	results	02/01/2017	21/01/2019	Yes	No
Results article	results of switching from Atripla to darunavir/ritonavir Monotherapy on neurocognition, quality of life, and sleep,	01/12/2016	21/01/2019	Yes	No
Results article	results of the effects on vitamin D, bone and the kidney when switching from fixed-dose tenofovir disoproxil fumarate/emtricitabine/efavirenz to darunavir/ritonavir monotherapy,	01/01/2016	21/01/2019	Yes	No