ISRCTN08592155 https://doi.org/10.1186/ISRCTN08592155

Switching from efavirenz/tenofovir /emtricitabine (TDF/FTC/EFV) to abacavir /lamivudine/maraviroc (ABC/3TC/MVC) to assess antiretroviral activity in cerebrospinal fluid

Submission date	Recruitment status	[_] Prospectively registered
02/02/2011	No longer recruiting	[_] Protocol
Registration date	**Overall study status**	[_] Statistical analysis plan
18/04/2011	Completed	[X] Results
Last Edited	**Condition category**	[_] Individual participant data
21/01/2019	Infections and Infestations	

Plain English summary of protocol

Background and study aims
Despite a sharp decrease in human immunodeficiency virus (HIV)-associated dementia with the use of combined antiretroviral drugs, there is a high prevalence of mild or moderate neurocognitive disorders in patients receiving antiretroviral treatment. A low level viral activity may persist in the central nervous system even in those patients presenting undetectable viral load, leading to local inflammation, neuronal damage and neurocognitive impairment. The aim of this study is to find out whether switching from a first-line antiretroviral treatment to a combination with a higher penetration to the central nervous system could reduce inflammation and neurocognitive impairment

Who can participate?
HIV-positive adults aged over 18 on efavirenz/tenofovir/emtricitabine treatment for at least 24 weeks, undetectable HIV viral load in the last 24 weeks, and neurocognitive impairment.

What does the study involve?
Patients will be switched from emtricitabine/tenofovir/efavirenz once daily to lamivudine /abacavir once daily and maraviroc twice daily. A neuropsychological test will be performed at weeks 0 and 48, and a lumbar puncture at weeks 0 and 24. Every patient will continue with routine visits every 3 - 4 months.

What are the possible benefits and risks of participating?
The use of a combination treatment with better penetration into the brain could reduce neuronal damage and inflammation and improve neurocognitive impairment. Risks of taking part include the side effects associated with the new medications.

Where is the study run from?
Institute of Biomedical Investigations of Bellvitge (Spain).

When is the study starting and how long is it expected to run for?
The study ran from January 2011 to July 2013.

Who is funding the study?
ViiV Healthcare (UK).

Who is the main contact?
Dr Daniel Podzamczer

Contact information

Type(s)
Scientific

Contact name
Dr Daniel Podzamczer

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08907

Additional identifiers

EudraCT/CTIS number
2010-022202-41

IRAS number

ClinicalTrials.gov number

Secondary identifying numbers
2010-022202-41

Study information

Scientific Title
Switching from efavirenz/tenofovir/emtricitabine (TDF/FTC/EFV) to abacavir/lamivudine /maraviroc (ABC/3TC/MVC) to assess antiretroviral activity in cerebrospinal fluid: a prospective one-arm pilot study

Acronym
MRVstudy-10 (XUMAKER)

Study objectives

Change to a regimen with greater cerebrospinal fluid (CSF) penetration will be associated with a lower CSF viral load, a decrease in inflammatory markers and possibly with an improvement in neurocognitive tests.

On 19/06/2014 the following changes were made to the trial record:
1. The public title was changed from 'Switching from efavirenz/tenofovir/emtricitabine (TDF/FTC /EFV) to abacavir/lamivudine/nevirapine (ABC/3TC/NVP) to assess antiretroviral activity in cerebrospinal fluid' to 'Switching from efavirenz/tenofovir/emtricitabine (TDF/FTC/EFV) to abacavir/lamivudine/maraviroc (ABC/3TC/MVC) to assess antiretroviral activity in cerebrospinal fluid'
2. The scientific title was changed from 'Switching from efavirenz/tenofovir/emtricitabine (TDF /FTC/EFV) to abacavir/lamivudine/nevirapine (ABC/3TC/NVP) to assess antiretroviral activity in cerebrospinal fluid: a prospective one arm pilot study' to 'Switching from efavirenz/tenofovir /emtricitabine (TDF/FTC/EFV) to abacavir/lamivudine/maraviroc (ABC/3TC/MVC) to assess antiretroviral activity in cerebrospinal fluid: a prospective one-arm pilot study'
3. The anticipated end date was changed from 01/04/2012 to 01/07/2013

Ethics approval required
Old ethics approval format

Ethics approval(s)
University Hospital of Bellvitge, Barcleona [CEIC Hospital Universitari de Bellvitge, Barcelona] (Spain), 07/10/2010

Study design
Prospective one-arm pilot study

Primary study design
Interventional

Secondary study design
Non randomised controlled trial

Study setting(s)
Hospital

Study type(s)
Treatment

Participant information sheet
Not available in web format, please use the contact details below to request a patient information sheet

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

Interventions
Current interventions as of 19/06/2014:
1. This is a single-arm study. Patients presenting confirmed neurocognitive impairment, with documented CCR5+ viral tropism, will be switched from emtricitabine 200 mg/tenofovir 245 mg /efavirenz 600 mg once daily (OD) to lamivudine 300 mg/abacavir 600 mg OD and maraviroc 300

mg twice daily (BID)
2. A neuropsychological test will be performed at weeks 0 and 48, and a lumbar puncture at weeks 0 and 24
3. Every patient will continue with routine visits every 3 - 4 months

Previous interventions:
1. This is a single-arm study; all diagnosed of neuropsychological impairment, CCR5+ patients will be switched from emtricitabine 200 mg/tenofovir 245 mg/efavirenz 600 mg four times daily (QD) to lamivudine 300 mg/abacavir 600 mg QD and maraviroc 300 mg twice daily (BID).
2. A neuropsychological test will be performed at weeks 0, 24 and 48, and a lumbar puncture at weeks 0 and 48
3. Every patient will continue his/her routine control every 3 - 4 months

Intervention Type
Drug

Phase
Phase IV

Drug/device/biological/vaccine name(s)
Current drugs as of 19/06/2014: 1. Efavirenz/tenofovir/emtricitabine (TDF/FTC/EFV) 2. Abacavir /lamivudine/maraviroc (ABC/3TC/MVC) Previous drugs: 1. Efavirenz/tenofovir/emtricitabine (TDF /FTC/EFV) 2. Abacavir/lamivudine/nevirapine (ABC/3TC/NVP)

Primary outcome measure
Viral load (VL) less than 5 copies/ml in CSF, evaluated at week 48

Secondary outcome measures
Evaluated at week 48:
1. Viral load (VL) less than 50 copies/ml in CSF
2. Central nervous system (CNS) inflammatory markers change in CSF
3. Neurocognitive tests

Overall study start date
27/01/2011

Completion date
01/07/2013

Eligibility

Key inclusion criteria
1. Human immunodeficiency virus positive (HIV+)
2. Adults aged over 18 years
3. HLA-B*57:01:01 negative
4. On TDF/FTC/EFV treatment for at least 24 weeks and undetectable HIV viral load in the last 24 weeks
5. Neurocognitive impairment
6. CCR5+ (pro-viral deoxyribonucleic acid [DNA])
7. Signed informed consent

Participant type(s)
Patient

Age group
Adult

Lower age limit
18 Years

Sex
Both

Target number of participants
15

Key exclusion criteria
1. Alanine aminotransferase (ALT) greater than 5 fold upper normal limit
2. Renal impairment (creatinine clearance [Cl cr] less than 50 ml/min)
3. Haemoglobin less than 9 g/dl
4. Neutropenia (PMN) less than 1000/ml
5. Platelets less than 30,000/mm3
6. Opportunistic infection, cancer and /or any disease which could alter blood brain barrier permeability (meningitis, cancer, etc.)
7. Neuro-psychiatric disease (previous or current)
8. Illicit drugs use

Date of first enrolment
27/01/2011

Date of final enrolment
01/07/2013

Locations

Countries of recruitment
Spain

Study participating centre
c/Feixa Llarga s/n. L'Hospitalet
Barcelona
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Sponsor information

Organisation
Institute of Biomedical Investigations of Bellvitge [Institut d'Investigació Biomèdica de Bellvitge (IDIBELL)] (Spain)

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Sponsor type
Research organisation

Website
http://www.bellvitgehospital.cat/

ROR
https://ror.org/0008xqs48

Funder(s)

Funder type
Industry

Funder Name
ViiV Healthcare (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	01/07/2015	21/01/2019	Yes	No