Effect of Switching Atripla to Eviplera on neurocognitive and emotional functioning

Published: 12-03-2015
Last updated: 16-04-2024

This study aims to investigate the effect of switching from Atripla® to Eviplera® on neurocognitive performances (neurocognitive testing) and imaging (functional MRI scanning) in virologically suppressed HIV-infected patients and stable on atripla.

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Immunodeficiency syndromes
Study type	Interventional

Summary

ID

NL-OMON45204

Source
ToetsingOnline

Brief title
ESCAPE

Condition

- Immunodeficiency syndromes
- Viral infectious disorders
- Cognitive and attention disorders and disturbances

Synonym
HIV-associated dementia, neurocognitive impairment

Research involving
Human

Sponsors and support

Primary sponsor: Universitair Medisch Centrum Utrecht

Source(s) of monetary or material Support: Farmaceutisch bedrijf,Gilead Sciences

Intervention

Keyword: eviplera, fMRI, HIV, neurocognition

Outcome measures

Primary outcome

Neurocognitive composite score on 12 weeks after switching from Atripla to Eviplera corrected for the baseline-level and compared to a controlgroup of patients on Atripla

Secondary outcome

1) neuronal activity measured by functional MRI on 12 weeks after switching from Eviplera to Atripla corrected for baseline-level and compared to a control group of patients on Atripla

2) correlation between changes in NP-score and fMRI-data after 12 weeks of Eviplera, measured with a reliability coefficient

3) change in SF-36 total score (health-related quality of life) after 12 weeks of Eviplera

4) change in HADS-score (emotional functioning) and USER-P-score (participation) after 12 weeks of Eviplera

5) correlation between drug levels and changes in neurocognitive performance measured by NP-testing and fMRI

6) the usefulness of PROMIS instruments in HIV research

7) the correlation between NFL plasma levels and NP-score

Study description

Background summary

Efavirenz, an antiretroviral drug used for the treatment of human immunodeficiency virus 1 (HIV-1) infections, is known for its neurological and psychiatric adverse events. Efavirenz is part of Atripla®, a single tablet regimen (STR), currently the most perscribed antiretroviral drug in the Netherlands. Recently, a new STR has become available, Eviplera® containing a successor of Efavirenz, named Rilpivirin. It has been shown in the phase-3 ECHO and Thrive studies that Atripla® as well as Eviplera® have excellent and comparable antiretroviral efficacy in naive HIV-infected patients. Furthermore, data from these studies have shown that Eviplera® was associated with fewer neurological and psychiatric adverse events than Atripla® over 48 weeks. However, this was only patient reported adverse events, not neuropsychological evaluation. Moreover, there might be a bias in these kind of switch studies due to the fact that those patients who switch will mostly regard their new combination better than the old one. Contrary, data on the long term impact of Efavirenz on neuropsychological performance and symptoms are conflicting. Finally, is there a large goup of patients stable on atripla without complaints. With newer drugs becoming available and efavirenz becoming generic, there is disscussion whether to switch those stable patients or to keep them on efavirenz. To gain more insight and guide this decision, this study will be performed.

Study objective

This study aims to investigate the effect of switching from Atripla® to Eviplera® on neurocognitive performances (neurocognitive testing) and imaging (functional MRI scanning) in virologically suppressed HIV-infected patients and stable on atripla.

Study design

Randomized Controlled Trial

Intervention

At start of the study patients will be randomly assigned to the intervention group or the control group. The intervention group will switch to open-label FTC/RPV/TDF STR (Eviplera®), the control group shall continue with Atripla®. At baseline and at week 12, a standard set of neuropsychological tests will be performed together with brain functional magnetic resonance imaging (fMRI) with the purpose to correlate neurocognitive improvement to functional imaging. Furthermore, drug levels of both drugs will be measured. Moreover, similar to

routine outpatients care, 2 and 4 weeks after switch, routine laboratory measurements and outpatients care will be provided to the intervention group.

Study burden and risks

Eviplera is a medicin proven to be safe, and registered for the treatment of HIV. Like Atripla, it is to be taken once daily. However, unlike Atripla, Eviplera has to be taken during the meal. This is a change in routine and thus requires an effort on the patient's side. Both the neuropsychological testing and the functional MRI-scan are safe procedures with a minimal risk of side effects. The few venapunctions pose a minimal burden and risk (haematoma's, local infection). Patients will have to come to the hospital for three visits, or five when they are in the intervention group. Two study-visits are of longer duration, approximately three hours (fMRI and neuropsychological testing).

Contacts

Public
Universitair Medisch Centrum Utrecht

Heidelberglaan 100
Utrecht 3584CX
NL
Scientific
Universitair Medisch Centrum Utrecht

Heidelberglaan 100
Utrecht 3584CX
NL

Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)

Elderly (65 years and older)

Inclusion criteria

- Male, between 25 and 50 years
- HIV-1 RNA < 50 copies/mL on last routine measurement during outpatient clinic
- on EFV/FTC/TDF STR (Atripla) continuously for *6 months preceding the screening visit
- Have a HIV genotype prior to starting cART with EFV/FTC/TDF STR with no known resistance to any of the study agents at any time in the past including, but not limited to RT mutations K65R, K101E/P, E138G/K/Q/R, Y181C/I/V, M184V/I and H221Y
- Negative TPHA or VDRL < 12 months prior to or at the screening visit
- no signs of an acute or chronic hepatitis C infection within the past 12 months before screening as defined in the Dutch guideline (Arends et al. Neth J Med 2011)
- No subjective neurocognitive complaints in the preceding 12 months
- willingness to take Eviplera together with food according to the manufacturer*s prescriptions.
- Estimated glomerular filtration rate *50 mL/min (Cockcroft-Gault formula) on last routine measurement during outpatient clinic
- able to understand and comply to study procedures and to provide written informed consent

Exclusion criteria

- Insufficient fluency in written and spoken Dutch
- Proven major depression through psychiatric consultation within the past year or on anti-depressant drugs (SSRI or TCA)
- Active or known from medical history past CNS opportunistic infections
- History of proven neurologic disease (e.g. multiple sclerosis, brain tumor, cerebrovasculair event, etc)
- Active psychiatric disorders classified according to the DSM V criteria
- History or evidence of alcohol or drug abuse defined according to DSM V criteria
- TSH not within normal reference values on last routine measurement during outpatient clinic
- Contraindications for undergoing an MRI; a pacemaker or metallic devices/foreign bodies in situ, proven claustrophobia.

Study design

Design

Study phase: 4

Study type:	Interventional
Intervention model:	Parallel
Allocation:	Randomized controlled trial
Masking:	Single blinded (masking used)
Control:	Active
Primary purpose:	Diagnostic

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	09-07-2015
Enrollment:	66
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	Atripla
Generic name:	efavirenz/emtricitabine/tenofovir
Registration:	Yes - NL intended use
Product type:	Medicine
Brand name:	Eviplera
Generic name:	emtricitabine/rilpivirin/tenofovir
Registration:	Yes - NL intended use

Ethics review

Approved WMO

Date:	12-03-2015
Application type:	First submission
Review commission:	METC Universitair Medisch Centrum Utrecht (Utrecht)

Approved WMO

Date:	15-06-2015
Application type:	First submission
Review commission:	METC Universitair Medisch Centrum Utrecht (Utrecht)

Approved WMO

Date:	29-07-2015
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Utrecht (Utrecht)
Approved WMO Date:	14-08-2015
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Utrecht (Utrecht)
Approved WMO Date:	02-12-2015
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Utrecht (Utrecht)
Approved WMO Date:	09-12-2015
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Utrecht (Utrecht)
Approved WMO Date:	08-06-2016
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Utrecht (Utrecht)
Approved WMO Date:	21-06-2016
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Utrecht (Utrecht)
Approved WMO Date:	27-06-2017
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Utrecht (Utrecht)

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	EUCTR2014-004297-42-NL
ClinicalTrials.gov	NCT02308332
CCMO	NL52694.041.15