Effect of Switching Atripla to Eviplera on neurocognitive and emotional functioning

Published: 26-01-2015
Last updated: 21-04-2024

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	Not approved
Status	Will not start
Health condition type	Immunodeficiency syndromes
Study type	Interventional

Summary

ID

NL-OMON40774

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

To evaluate the neurocognitive performance (NP composite score) after 12 weeks in stable HIV-infected patients switched from Atripla to Eviplera compared to a control group of patients on Atripla.

Secondary outcome

1) to assess the correlation between neurocognitive improvement (testing) and functional imaging (fMRI) after switching Atripla to Eviplera.

2) to evaluate correlation between neurocognitive performance and health related quality of life (SF-36 total score) after switching from Atripla to Eviplera.

3) to assess the emotional functioning (HADS total score) after switching Atripla to Eviplera.

4) to assess USER-P after switching Atripla to Eviplera.

5) to assess drug levels of Efavirenz and Rilpivirin in relation to changes in neurocognitive performance and fMRI in both patient groups.

6) to evaluate the usefulness of PROMIS instruments in HIV research.

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

Single Blind 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

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)
Elderly (65 years and older)

Inclusion criteria

- Male, between 30 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

- Non-native Dutch speakers
- 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 type:	Interventional
Intervention model:	Parallel
Allocation:	Randomized controlled trial
Masking:	Single blinded (masking used)
Control:	Active

Primary purpose:	Diagnostic

Recruitment

NL

Recruitment status:	Will not start
Enrollment:	60
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

Not approved

Date:	26-01-2015
Application type:	First submission
Review commission:	METC NedMec

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	NL50959.041.14

Study results

Date completed:	11-05-2017
Results posted:	28-12-2018
Actual enrolment:	58

First publication
28-12-2018