Quality of life viral and Immunological dynamics in patients with effectively suppressed HIV who switch second or furtherline cART to a Once daily High genetic barrier Antiretroviral regimen of boosted darunavir and dolutegravir

Published: 26-04-2016
Last updated: 21-04-2024

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Ethical review	Approved WMO
Status	Will not start
Health condition type	Immunodeficiency syndromes
Study type	Observational invasive

Summary

ID

NL-OMON41798

Source
ToetsingOnline

Brief title
QIOHA

Condition

- Immunodeficiency syndromes
- Viral infectious disorders

Synonym
hiv

Research involving
Human

Sponsors and support

Primary sponsor: Onze Lieve Vrouwe Gasthuis
Source(s) of monetary or material Support: Subsidie is aangevraagd

Intervention

Keyword: HIV, quality of life, treatment simplification

Outcome measures

Primary outcome

Change in quality of life (QOL)

Secondary outcome

Investigation of the impact of switch to two high genetic barrier compounds on

(I) residual replication (presence of plasma and intracellular HIV-RNA) (II)

level of virus production from infected cells (reservoir; presence of HIV),

(III) number of HIV virological failures and resistance analysis and (IV)

Immunological markers (change in activation-, proliferation- and inflammation

markers).

Study description

Background summary

In the last two decades combination antiretroviral therapy (cART) has brought a substantial decrease in the death rate due to HIV-1 infection, changing it from a rapidly lethal disease into a chronic manageable condition. Unfortunately challenges remain. Due to a combination of adherence issues, whether or not related to toxicity, and the use of regimens with a low genetic barrier to development of antiviral resistance, viral rebound induced by drug resistant viruses is regularly observed. After each therapy failure, follow-up regimens tend to become more complex characterised by a higher pill burden, multiple

dosing and increased toxicity which are all at odds with long-term adherence and augment the burden of disease. The main focus of HIV treatment was to improve life expectancy, treat comorbidities and improve quality of life (QOL) through immune recovery by suppression of HIV, but in recent years the scope has broadened and other factors, such as long-term toxicity and intake schemes are becoming more prominent. Treatment simplification has been shown to be a major determinant for QOL and is expected to have positive effects on cART adherence and as such reduces the risk for drug resistance development and subsequent treatment failure. Combination of the newly licensed dolutegravir with the most active boosted protease inhibitor darunavir will make once daily therapy once again accessible for patients on second or further line therapy. This high genetic barrier combination is becoming common practice in the Netherlands. We aim to study quality of life and viral and immunological dynamics in these patients who change or have changed from suppressive second or further line therapy to dolutegravir and boosted darunavir.

Study objective

The primary objective is to investigate quality of life after switch to a combination therapy including boosted DRV and DTG. Secondary objectives are to investigate 1) the residual viral replication, 2) level of virus production from infected cells (reservoir), 3) number of HIV virological failures and 4) immunological markers. 5) Evaluating dolutegravir and darunavir drug levels (adherence). 6) Development of resistance mutations against dolutegravir or darunavir.

Study design

An observational cohort-study of 24 weeks in subjects on second or further line therapy with suppressed viremia that undergo or have undergone a treatment change (based on clinical reasons) towards a dual regimen with two high genetic barrier drugs. For the study, extra blood samples will be taken and digital quality of life questionnaires will be performed. After explicit consent also retrospective inclusion of patients meeting the inclusion criteria AND with blood stored at baseline, wk2 and/or wk4 and wk12 is also allowed (depending on timing of inclusion).

Study burden and risks

The study will follow the normal visits to the outpatient clinic after a therapy switch and therefore no extra visits are involved. An additional volume of blood will be taken at 5 time points during regular blood draws Normal clinical practice regarding clinical history taking, physical examination, viral load assessment, CD4 count measurements and safety controls in blood to monitor potential side-effects is followed. The additional burden lies in answering the quality of life questionnaires and the additional volume

of blood that is taken during routine visits for the virological and immunological analyses.

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

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

Inclusion criteria

- 18 years or older
- Switch on clinical grounds to dolutegravir/ darunavir/ritonavir
- Viral load <50cp/mL at least 2 consecutive measurements (at least 3 month in between) with cART currently in use.
- able to sign informed consent

Exclusion criteria

- Active opportunistic infections
- Hepatitis B coinfection AND treatment with drugs also used in HIV treatment (lamivudine, tenofovir)

Study design

Design

Study type: Observational invasive

Masking:	Open (masking not used)
Control:	Uncontrolled
Primary purpose:	Basic science

Recruitment

NL

Recruitment status:	Will not start
Enrollment:	100
Type:	Anticipated

Ethics review

Approved WMO

Date:	26-04-2016
Application type:	First submission
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)

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
CCMO	NL51134.100.14