DoRa studie

Gepubliceerd: 29-03-2018 Laatst bijgewerkt: 18-08-2022

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Ethische beoordeling	Niet van toepassing
Status	Anders
Type aandoening	-
Onderzoekstype	Observationeel onderzoek, zonder invasieve metingen

Samenvatting

ID

NL-OMON26416

Bron
Nationaal Trial Register

Verkorte titel
DoRa

Aandoening

PEP, HIV

Ondersteuning

Primaire sponsor: University Medical Centrum Utrecht
Overige ondersteuning: MSD

Onderzoeksproduct en/of interventie

Uitkomstmaten

Primaire uitkomstmaten

-Grade 2 to 4 neurocognitive adverse events (according to Division of AIDS (DAIDS) Table for Grading the Severity of Adult and Pediatric Adverse Events, version 2.0, published in November 2014)
-BSI questionnaire score
-SF-36 questionnaire score

-Insomnia severity questionnaire score

Toelichting onderzoek

Achtergrond van het onderzoek

Study will not start, because of withdraw sponsor.

Background of the study:

People who have been exposed to the risk of HIV transmission are offered the postexposure prophylaxis (PEP)
consisting of three antiretroviral drugs which are used during 28 days. This treatment should be started soon as
possible after an accident. Currently the guidelines recommend use of an integrase inhibitor (INSTI) dolutegravir (DTG)
or raltegravir (RAL) in combination with two nucleo(s)tide reverse transcription inhibitors (NRTIs). Both INSTI are
deemed to have a favorable side effects profile. All these antiretroviral drugs are registered and available in the
Netherlands for the treatment of HIV (Human immunodeficiency virus) infection. The guidelines of Dutch HIV
physicians association chose in 2014 for DTG as preferred INSTI component of the PEP due to better therapy
adherence because its once daily formulation. At that moment, RAL was only marketed for bid use. In 2017, the once
daily formulation of RAL has been approved as well.

In the registration studies and in the later meta-analyses no differences were found between the incidence of (serious)
side effects and discontinuation rates when DTG was compared to RAL for treatment of HIV infection. No study was
performed to compare these two INSTI in patients who use these medicines in the setting of the PEP, which brings an
acute emotional stress and requires start of treatment without delay. Generally, occurrence of side effects during the
PEP and early termination of this treatment are common, although most of the data are retrospective and regarded the
use of ‘older’ antiretroviral agents like zidovudine, complex treatment regimens with protease inhibitors and food
restrictions.

Recently, the data have emerged about the unexpectedly high incidence of neurocognitive and psychiatric side effects

and sleep disorders in the clinical cohorts of patients with HIV infection treated with DTG as a part of their antiretroviral
regimen. The proportion of patients who discontinued a DTG containing treatment varied considerably in different
analyses, from 3,8 to 10,8%. As the side effects were frequently seen in the first weeks after start of DTG, the question
arises if this agent is an appropriate option for the short PEP course in patients already exposed to an acute emotional
stress which may make them even more susceptible to neurocognitive or psychiatric adverse events. Although RAL
also was identified as a drug which can induce depression, the incidence of discontinuation due to neurocognitive
complaints was found to be lower than for DTG. As new RAL formulation now allows a construction of once-daily PEP
regimen, it is worthwhile to evaluate if there is any difference in the tolerability of RAL when compared to DTG in this
setting. To our best knowledge, no study was published by now which compared the tolerability of DTG and RAL as a
part of the PEP regimen.

Objective of the study:

Primary Objective:

To investigate whether significantly more patients on DTG will report at least one grade 2 to 4 side effect attributable to
the medication compared to patients on RAL, both used in combination with tenofovir disoproxil (TDF)/emtricitabine
(FTC) or TDF/lamivudine (3TC) as PEP, during the 28-days of treatment.

Secondary Objectives:

• Numerical frequency of any side effects in both groups

• Proportion of patients in both groups who switch or interrupt the initial PEP combination due to the side effects

• Impact of the PEP on the quality of life of the patients

• Proportion of patients with grade 3 or 4 laboratory abnormality in both groups

Study design:

Two-period, two-intervention cluster-randomized cross over trial, with two intervention periods of 6 months in every
participating center.

Every center will include patients during 12 months, which will be divided in two periods. Centers will include the
patients in two periods (cluster rotation) to either:

• Period 1 (month 1 through 6): DTG + TDF/FTC or 3TC

• Period 2 (month 7 through 12): RAL + TDF/FTC or 3TC

or

• Period 1 (month 1 through 6): RAL + TDF/FTC or 3TC

• Period 2 (month 7 through 12): DTG + TDF/FTC or 3TC

In period 1, centers will start with the treatment which is their standard of care at the moment of study initiation.
A switch between treatment strategies within 6 months in the same center is not allowed.

Dosages of the medication:

Dolutegravir 50 mg (= 1 tablet) qd

Raltegravir 1200 mg (= 2 tablets a 600 mg) qd

Tenofovir difumarate/emtricitabine 245/200 mg (= 1 tablet) qd

Tenofovir difumarate 245 mg (= 1 tablet) qd

Lamivudine 300 mg (= 1 tablet) qd

The choice of the NRTI backbone (co-formulated TDF/FTC versus TDF and 3TC given as separate tablets) will be at
discretion of the treating physician and will be the same during the two treatment periods for a participating center.
The whole regimen can be taken with or without a meal. All tablets should be taken at once, with an interval of
approximately 24 hours.

The duration of treatment is 28 days.

Study population:

Patients who start the PEP against HIV infection with DTG or RAL, both combined with TDF/FTC or TDF/3TC. Age 18
years or older.

Patients who present to the hospital (Emergency Department or Out-patient department of Infectious Diseases), fulfill
the inclusion and do not have any exclusion criteria, will be informed about the study and obtain the written study
information. During the first out-patient visit they will be asked if they want to participate in the study, additional
questions will be answered and if they chose to participate then informed consent will be signed. Patient will be asked
to consent that the clinical and laboratory information from the day of first presentation may be used for the study
purposes.

Primary study parameters/outcome of the study:

-Grade 2 to 4 neurocognitive adverse events (according to Division of AIDS (DAIDS) Table for Grading the Severity of
Adult and Pediatric Adverse Events, version 2.0, published in November 2014)

-BSI questionnaire score

-SF-36 questionnaire score

-Insomnia severity questionnaire score

Secundary study parameters/outcome of the study (if applicable):

-Grade 2 to 4 non-neurocognitive clinical adverse events

-Grade 3 to 4 laboratory adverse events

Both according to Division of AIDS (DAIDS) Table for Grading the Severity of Adult and Pediatric Adverse Events,
version 2.0, published in November 2014.

Nature and extent of the burden and risks associated with participation, benefit and group relatedness (if
applicable):

No risk or benefit for the participant. Less time is asked.

Doel van het onderzoek

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Onderzoeksopzet

all will be evaluate at the end of the study

Onderzoeksproduct en/of interventie

none

Contactpersonen

Publiek

-
B. Silvius
Utrecht
The Netherlands
-

Wetenschappelijk

-
B. Silvius
Utrecht
The Netherlands
-

Deelname eisen

Belangrijkste voorwaarden om deel te mogen nemen (Inclusiecriteria)

-Indication for start of postexposure prophylaxis with either DTG or RAL, next to two NRTI agents which will be prescribed by the attending physician at presentation

-No contra-indications against either DTG or RAL both with TDF / FTC or 3TC in the judgement of the prescribing physician

-Start of PEP ¡Ü 72 hours before the day of study inclusion
-18 years or older

-Able to understand the study information and sign an informed consent

-Willing and according to the investigator able to follow the study procedures

Belangrijkste redenen om niet deel te kunnen nemen (Exclusiecriteria)

-pregnancy

-lactation

-baseline laboratory results abnormalities which fall in Grade 3 and 4 according to the Division of AIDS (DAIDS) Table for Grading the Severity of Adult and Pediatric Adverse Events, version 2.0 November 2014

-not being able to adhere to study procedures according to the treating physician

-unable to fill of understand the study questionnaires (provided in Dutch or English)

-active hepatitis B

-eGFR<60 ml/min

-ALAT>5 times ULN

-positive HIV serology at baseline

Onderzoeksopzet

Opzet

Type: Observationeel onderzoek, zonder invasieve metingen

Onderzoeksmodel:	Cross-over
Toewijzing:	Niet-gerandomiseerd
Blindering:	Open / niet geblindeerd
Controle:	N.v.t. / onbekend

Deelname

Nederland

Status:	Anders
(Verwachte) startdatum:	01-05-2018
Aantal proefpersonen:	200
Type:	Onbekend

Voornemen beschikbaar stellen Individuele Patiënten Data (IPD)

Wordt de data na het onderzoek gedeeld: Nog niet bepaald

Ethische beoordeling

Niet van toepassing

Soort:	Niet van toepassing

Registraties

Opgevolgd door onderstaande (mogelijk meer actuele) registratie

Geen registraties gevonden.

Andere (mogelijk minder actuele) registraties in dit register

Geen registraties gevonden.

In overige registers

Register	ID
NTR-new	NL6926
NTR-old	NTR7122

Register	ID
Ander register	- : 2018-000974-31

Resultaten