An open-label randomised two-year trial comparing two first-line regimens in HIV-infected antiretroviral naïve subjects: darunavir/r + tenofovir/emtricitabine vs. darunavir/r + raltegravir

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Primary objective* To assess the non-inferiority of darunavir/r + raltegravir compared to darunavir/r + tenofovir/emtricitabine as first-line treatment strategies in HIV-1 infected, antiretroviral naïve adults over at least 96 weeks (i.e. to assess...

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

Summary

ID

NL-OMON36340

Source
ToetsingOnline

Brief title
NEAT001/ANRS 143

Condition

- Immunodeficiency syndromes
- Viral infectious disorders

Synonym
AIDS, HIV

Research involving
Human

Sponsors and support

Primary sponsor: Agence nationale de recherche sur le sida et les hépatites virales (ANRS), **Source(s) of monetary or material Support:** EU (FP6) en ANRS (Agence nationale de recherche sur le sida et les hépatites virales),Gilead Sciences,Janssen-Cilag,Merck

Intervention

Keyword: Darunavir, HIV, Raltegravir, Tenofovir emtricitabine

Outcome measures

Primary outcome

Time to virologic or clinical failure, as the first occurrence of any of the

following components:

* failure to achieve virologic response by W32 (defined as HIV-1 RNA * 50

copies/ml at W32, confirmed within 4 weeks)

* change of any component of the initial randomised regimen before W32 because

of documented insufficient virologic response, defined as HIV-1 RNA reduction <

1 log10 copies/ml by W18 or HIV-1 RNA * 400 copies/ml at W24 (confirmed within

4 weeks)

* HIV-1 RNA * 50 copies/ml (confirmed within 4 weeks) at any time after W32

* death due to any cause

* any new or recurrent AIDS defining event confirmed by the Endpoint Review

Committee

* any new serious non AIDS defining event confirmed by the Endpoint Review

Committee

Secondary outcome

* Time to loss of virologic response by W48 and W96 (TLOVR)

* Time to virologic failure (as defined in primary endpoint)*

* Time to clinical failure (as defined in primary endpoint)*

* Time to permanent discontinuation of any component of the initial randomised regimen for treatment-limiting adverse event, i.e. intolerance or toxicity

* Time to discontinuation of any component of the initial randomised regimen for any reason

* Change in absolute CD4 count and in percentage from baseline

* Adverse events: number, nature and time to occurrence of clinical and biological grade 3 and 4 events

* Genotypic resistance at virologic failure

* Change in quality of life scores from W00 to W96

Study description

Background summary

Antiretroviral treatment in HIV-infected patients requires long-term administration. Although the virologic efficacy of most antiretroviral regimens today is excellent, long-term toxicity of these treatments remains a major concern. Novel combinations of antiretroviral drugs may have the advantage of an excellent efficacy combined with little long-term toxicity and with convenient treatment modalities.
The triple therapy darunavir/r + tenofovir/emtricitabine is likely to become a relevant first-line treatment option in the years to come. One trial evaluating this regimen in antiretroviral naïve patients has demonstrated non-inferiority in comparison to lopinavir/r with a more favourable safety profile at 48 and 96 weeks. Significantly higher response rates were observed with darunavir/r in patients with HIV RNA > 5 log copies/ml.
The dual combination of boosted darunavir + raltegravir is an innovative treatment option that combines two potent new antiretroviral drugs, one of which belongs to a new drug class (integrase inhibitor). The expected efficacy profile of this combination is promising. Moreover, this combination might have

a better tolerance profile and has the advantage of sparing the NRTI class.
In the context of tenofovir/emtricitabine currently being a reference backbone in first-line antiretroviral regimens, we hypothesise that, in combination with darunavir/r, raltegravir may be an alternative option if its efficacy is non-inferior to tenofovir/emtricitabine.

Study objective

Primary objective
* To assess the non-inferiority of darunavir/r + raltegravir compared to darunavir/r + tenofovir/emtricitabine as first-line treatment strategies in HIV-1 infected, antiretroviral naïve adults over at least 96 weeks (i.e. to assess if the risk of clinical or virological failure with darunavir/r + raltegravir is at most 1.53 times the risk with darunavir/r + tenofovir/emtricitabine)

Secondary objectives
To compare the two different regimens in terms of:
* virologic response
* occurrence of disease progression
* occurrence of severe non AIDS defining events
* occurrence of death
* change in CD4 cell count
* occurrence of immune reconstitution syndrome
* genotypic resistance at virologic failure
* clinical and biological tolerance
* adherence
* quality of life

Study design

Patients are randomly allocated in a 1:1 ratio at trial entry to one of the first-line regimens of open-label treatment during at least 96 weeks with:

Group 1: darunavir/r + tenofovir/emtricitabine
darunavir 800 mg, i.e. 2 tablets of 400 mg (Prezista®) once daily (QD)
ritonavir 100 mg (Norvir®), 1 capsule or tablet once daily (QD)
tenofovir/emtricitabine 245/200 mg, fixed dose combination (Truvada®), 1 tablet once daily (QD)

Group 2: darunavir/r + raltegravir
darunavir 800 mg, i.e. 2 tablets of 400 mg (Prezista®) once daily (QD)
ritonavir 100 mg (Norvir®), 1 capsule or tablet once daily (QD)
raltegravir 400mg (Isentress®), 1 tablet twice daily (BID)

Intervention

Group 1: darunavir/r + tenofovir/emtricitabine
darunavir 800 mg, i.e. 2 tablets of 400 mg (Prezista®) once daily (QD)
ritonavir 100 mg (Norvir®), 1 capsule or tablet once daily (QD)
tenofovir/emtricitabine 245/200 mg, fixed dose combination (Truvada®), 1 tablet once daily (QD)

Group 2: darunavir/r + raltegravir
darunavir 800 mg, i.e. 2 tablets of 400 mg (Prezista®) once daily (QD)
ritonavir 100 mg (Norvir®), 1 capsule or tablet once daily (QD)
raltegravir 400mg (Isentress®), 1 tablet twice daily (BID)

Study burden and risks

The trail subject will undergo:
* physical examiniation,
* safety blood test for heamatology, chemistry and coagulation,
* bloodtest for genotype_ drug concentrations_ pharmacogenomic assessment
* ECG
* pregnancy test is applicable
* Urine test for safety assessment
* Hepatis test and test for HIV genotype
* hepatitis, HIV
* if patient participate in the substudy a DEXA scan will be done.
* completion of questionnaires.

Contacts

Public
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75013 Paris
FR
Scientific
Agence nationale de recherche sur le sida et les hépatites virales (ANRS),

101 rue de Tolbiac
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Trial sites

Listed location countries

Netherlands

Eligibility criteria

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

Inclusion criteria

Patient with confirmed HIV infection
Age >< = 18 years
Writtten informed consent
Male patient or non pregant, non lactating female
No previous treatment with any antiretroviral drugs while being seropositive. Having received ART while seronegative then HIV negative test should have been documented at least 3 months post-PEP or -Prep
HIV-1 RNA > 1000 copies/ml
Indication to start an antiretroviral treatment as long as subject has also a CD4 cell count <<=500/mm3 either at screening or another sample within 3 months of screening.
No major IAS-USA mutations on genotypic testing at screening visit or on any historical genotype, if available

Exclusion criteria

* Woman without effective contraception method (contraception during the trial must be mechanical + second method other than an oral contraceptive. Oral contraceptives are not to be used during the trial)
* Pregnant or breastfeeding woman
* Woman expecting to conceive during the study
* HIV-2 co-infection
* Creatinine clearance < 60 ml/min (Cockcroft & Gault equation), alkaline phosphatase, ASAT, or ALAT * 5 ULN
* Patient with significant impairment of hepatic function, defined as serum albumin < 2.8 mg/dl or INR > 1.7 or presence of ascites, in the absence of another explanation for the abnormal finding
* CD4 > 500/mm3, except in case of symptomatic HIV disease (defined
by conditions qualifiying for CDC category B or C)
* Any major IAS-USA mutation conferming resistance to one or more of reverse transcriptase or protease inhibitors on genotypic testing at screening or historical genotypic testing with no time limit

* Mycobacteriosis under treatment
* Malignancy requiring chemotherapy or radiotherapy
* Positive HBs Ag
* HCV infection for which specific treatment is ongoing or planned during the first year on trial treatment
* Known hypersensitivity to one of the trial drugs or its excipients
* Contraindicated concomitant treatment
* Anticipated non-compliance with the protocol
* Participation in another clinical trial with an on-going exclusion period at screening
* Subject under legal guardianship or incapacitation
* Subject, who in the opinion of the investigator, is unable to complete the study period

Study design

Design

Study phase:	3
Study type:	Interventional
Intervention model:	Parallel
Allocation:	Randomized controlled trial
Masking:	Open (masking not used)
Control:	Active
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	16-02-2011
Enrollment:	30
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	Isentress
Generic name:	Raltegravir
Registration:	Yes - NL intended use

Product type:	Medicine
Brand name:	Norvir
Generic name:	Ritonavir
Registration:	Yes - NL intended use
Product type:	Medicine
Brand name:	Prezista
Generic name:	Darunavir
Registration:	Yes - NL intended use
Product type:	Medicine
Brand name:	Truvada
Generic name:	Tenofovir/Emtricitabine
Registration:	Yes - NL intended use

Ethics review

Approved WMO Date:	25-06-2010
Application type:	First submission
Review commission:	METC Amsterdam UMC
Approved WMO Date:	28-03-2011
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	19-07-2011
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	17-04-2012
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	11-07-2013
Application type:	Amendment
Review commission:	METC Amsterdam UMC

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	EUCTR2009-015113-44-NL
ClinicalTrials.gov	NCT01066962
CCMO	NL32722.018.10