A Multicenter, Randomized, Double-Blind, Double-Dummy, Phase 3 Study of the Safety and Efficacy of Ritonavir-Boosted Elvitegravir (EVG/r) Versus Raltegravir (RAL) Each Administered With a Background Regimen in HIV-1 Infected, Antiretroviral Treatment-Experienced Adults.

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Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Viral infectious disorders
Study type	Interventional

Summary

ID

NL-OMON33886

Source
ToetsingOnline

Brief title
nvt

Condition

- Viral infectious disorders

Synonym
AIDS

Research involving
Human

Sponsors and support

Primary sponsor: Gilead Sciences
Source(s) of monetary or material Support: Gilead

Intervention

Keyword: AIDS, antiretroviral therapy, HIV

Outcome measures

Primary outcome

The primary efficacy endpoint is the proportion of subjects

achieving and maintaining confirmed HIV-1 RNA < 50 copies/mL

through Week 48.

Secondary outcome

* The proportion of subjects achieving and maintaining

confirmed HIV-1 RNA < 400 copies/mL through Week 48

* The proportion of subjects with HIV-1 RNA < 50 copies/mL at

Week 48

* The time to pure virologic failure for HIV-1 RNA cutoff at 50 copies/mL up to

Week 48

* The time to pure virologic failure for HIV-1 RNA cutoff at 400 copies/mL up

to Week 48

* The proportion of subjects with HIV-1 RNA < 400 copies/mL

at Week 48

* The change from baseline in log10 HIV-1 RNA (copies/mL) at

Week 48

* The change from baseline in CD4+ cell count at Week 48

Study description

Background summary

Approximately 33.2 million people are infected with the human immunodeficiency virus
(HIV) worldwide. While combination antiretroviral therapy has been largely successful in reducing the morbidity and mortality associated with HIV disease, a significant proportion of subjects eventually experience loss of virologic, immunologic, or clinical benefit from their current regimens. Poor tolerability, toxicity or the development of resistance can limit options for treatment. Developing safe and effective therapies for treatment-experienced subjects to expand the
range of treatment options remains a priority.
Newer treatments targeting alternative steps in the viral replication cycle are needed to
expand the treatment options for all treatment-experienced patients. In all subjects, the ideal goal of therapy remains complete suppression of HIV ribonucleic acid (RNA).

Study objective

To assess non-inferiority of a regimen containing ritonavir-boosted elvitegravir versus
raltegravir, each administered with a background regimen in HIV-1 infected, antiretroviral treatment-experienced adult subjects as determined by the proportion of
subjects achieving and maintaining confirmed HIV-1 RNA < 50 copies/mL through Week 48

Study design

Eligible subjects will be randomized in a 1:1 ratio to one of the following two treatment arms:
Treatment Arm 1:
Ritonavir-boosted elvitegravir 150 mg QD (ritonavir-boosted elvitegravir85 mg QD for subjects taking atazanavir/r or lopinavir/r as part of their BR) +
raltegravir placebo BID + BR (N = 350)

Treatment Arm 2:
Raltegravir 400 mg BID + elvitegravir placebo QD + BR (N = 350)

After Week 48, subjects will continue to take their blinded study drug and attend visits every
8 weeks until treatment assignments have been unblinded, at which point they will be given
the option to participate in an open-label rollover study. Open-label raltegravir 400 mg will
not be provided to subjects in the open-label rollover study.
Viread(R) will be provided to subjects in the open-label rollover study if they received it as part of their BR.

Intervention

Elvitegravir 85 mg, 150 mg or matching placebo administered orally QD (with ritonavir-boosted PI) to be taken with food

Reference Therapy,
Raltegravir 400 mg tablets or matching placebo administered orally BID and to be taken according to the prescribing information.

Darunavir 800mg QD boosted with 100mg ritonavir QD is permitted if approved by applicable regulatory authorities.

Study burden and risks

For a list of possible AEs, see page 52 of the protocol.
The patient will have to visit the hospital more times than for standard treatment.

Contacts

Public
Gilead Sciences

333 Lakeside Drive
Foster City, CA 94404
Verenigde Staten
Scientific
Gilead Sciences

333 Lakeside Drive
Foster City, CA 94404
Verenigde Staten

Trial sites

Listed location countries

Netherlands

Eligibility criteria

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

Inclusion criteria

Subjects participating in Study GS-US-183-0144 who have either met all screening criteria or have enrolled are eligible to participate and continue with their regular visit schedule.
Subjects must consent to participate in Study GS-US-183-0145.;* Plasma HIV-1 RNA levels * 1,000 copies/mL at screening using the AmpliPrep/Taqman HIV-1 Test®
* Subjects must have documented resistance, as defined by current IAS-USA definitions, or at least six months experience prior to screening with two or more different classes of antiretroviral agents.
* Subjects must be eligible to receive one of the fully-active ritonavir-boosted-PIs, based on the results of screening phenotype analysis provided by Monogram Biosciences, and an allowed second agent. Fully-active PIs are defined as those with fold changes below the lower clinical or biological cutoff for each drug.
* Normal ECG (or if abnormal, determined by the investigator to be not clinically significant).
*Adequate renal function: Estimated glomerular filtration rate * 60 mL/min according to the Cockcroft-Gault formula
* Hepatic transaminases (AST and ALT) * 5 × upper limit of normal (ULN).
* Total bilirubin * 1.5 mg/dL, or normal direct bilirubin (subjects with documented Gilbert*s Syndrome or hyperbilirubinemia due to indinavir or atazanavir therapy may have total bilirubin up to 5 × ULN).
* Adequate hematologic function (absolute neutrophil count * 1,000/mm3; platelets * 50,000/mm3; hemoglobin * 8.5 g/dL).
* Serum amylase < 1.5 × ULN (subjects with serum amylase * 1.5 × ULN will remain eligible if serum lipase is * 1.5 × ULN).
* Negative serum pregnancy test (females of childbearing potential only).

* Males and females of childbearing potential must agree to utilize highly effective contraception methods from screening throughout the duration of study treatment and for 30 days following the last dose of study drugs.
* Female subjects who utilize hormonal contraceptive as one of their birth control methods must have used the same method for at least three months prior to study dosing.
* Female subjects who are postmenopausal for less than two years are required to have FSH > 40 mIU/mL. If the FSH is * 40 mIU/mL, the subject must agree to use highly effective method of birth control (as described above) to participate in the study.
* Male subjects who are sexually active must be willing to use effective barrier contraception (e.g., condom with spermicide) during heterosexual intercourse from screening through completion of the study and continue for at least 30 days from date of last dose of study drug.
* Age * 18 years.
* Life expectancy * 1 year.
* The ability to understand and sign a written informed consent form, which must be obtained prior to initiation of study procedures.

Exclusion criteria

* A new AIDS-defining condition diagnosed within the 30 days prior to screening
* Prior treatment with any HIV-1 integrase inhibitor
* Subjects experiencing ascites
* Subjects experiencing encephalopathy
* Females who are breastfeeding
* Positive serum pregnancy test at any time during the study (female of childbearing potential)
* Subjects receiving ongoing therapy with any medication listed below that is not to be taken with a component of the BR, including drugs not to be used with ritonavir (refer to prescribing information)
* Current alcohol or substance use judged by the investigator to potentially interfere with subject study compliance.
* A history of or ongoing mailgnancy other than cutaneous Kaposi's sarcoma (KS), basal cell carcinoma, or resected, non-invasive cutaneous squamous carcinoma. Subjects with biopsy-confirmed cutaneous KS are eligible, but must not have received any systemic therapy for KS within 30 days of Baseline and are not anticipated to require systemic therapy during the study.
* Active, serious infections (other than HIV-1 infection) requiring parenteral antibiotic or antifungal therapy within 30 days prior to Baseline.
* Participation in any other clinical trial (except for the Etravirine or Maraviroc expanded access
programs), without prior approval from the sponsor, is prohibited while participating in this trial.
* Any other clinical condition or prior therapy that, in the opinion of the investigator, would make the subject unsuitable for the study or unable to comply with the dosing

requirements.
* Known hypersensitivity to the study drugs, the metabolites or formulation excipients.

Study design

Design

Study phase:	3
Study type:	Interventional
Intervention model:	Parallel
Allocation:	Randomized controlled trial
Masking:	Double blinded (masking used)
Control:	Placebo
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	02-03-2009
Enrollment:	6
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	Isentress
Generic name:	Raltegravir
Product type:	Medicine
Brand name:	nvt
Generic name:	elvitegravir

Ethics review

Approved WMO

Date:	11-07-2008

Application type:	First submission
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	13-10-2008
Application type:	First submission
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	03-12-2008
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	19-01-2009
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	01-04-2009
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	07-05-2009
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	24-08-2009
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	25-08-2009
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)

Approved WMO Date:	14-09-2009
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	15-09-2009
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	04-11-2009
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	17-03-2010
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)

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
Other	000
EudraCT	EUCTR2007-004225-26-NL

Register	ID
CCMO	NL24022.078.08