A phase 3, randomized, double-blind study to evaluate the safety and efficacy of Elvitegravir/Emtricitabine/Tenofovir Disoproxil Fumarate/GS-9350 versus Ritonavir-Boosted Atazanavir plus Emitricitabine/Tenofovir Disoproxil Fumarate in HIV-1 infected, antiretroviral treatment-naive adults.

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The primary objective of this study is:To evaluate the efficacy of a regimen containing elvitegravir/emtricitabine/tenofovir disoproxil fumarate/GS 9350 versus ritonavir-boosted atazanavir plus emtricitabine/tenofovir disoproxil fumarate in HIV 1...

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

Summary

ID

NL-OMON39337

Source
ToetsingOnline

Brief title
GS-US-236-0103

Condition

- Viral infectious disorders

Synonym
Human Immunodeficiency Virus (HIV-1) Infections

Research involving
Human

Sponsors and support

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

Intervention

Keyword: Antiretroviral treatment naive, HIV-1

Outcome measures

Primary outcome

Safety: Adverse events and clinical laboratory tests to evaluate the safety and

tolerability of the treatment regimens.

Efficacy: The primary efficacy endpoint is the proportion of subjects that

achieve HIV 1 RNA < 50 copies/mL at Week 48 as defined by the Food and Drug

Administration (FDA) snapshot analysis

Secondary outcome

The proportion of subjects with HIV 1 RNA * 50 copies/mL at Week 96, 144 and

192 as defined by the FDA snapshot analysis

The change from baseline in CD4+ cell count at Weeks 48, 96, 144 and 192.

Study description

Background summary

Approximately 33.2 million people are infected with HIV worldwide.
Standard-care for the treatment of HIV involves the use of a combination of antiretroviral drugs to suppress viral replication and delay disease

progression. While combination ARV 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.
Newer active ARV therapy regimens that offer reduced toxicity are needed for treatment-naïve patients. In ongoing phase 2 and 3 clinical trials using elvitegravir (EVG), an experimental inhibitor of HIV integrase, in combination with other ARV drugs has been well tolerated and has not demonstrated an increased incidence of the side effects with current combination ARV therapy. The investigational pharmacoenhancer GS-9350 is devoid of anti-HIV activity, may have less adverse biochemical effects relative to ritonavir, and can be coformulated as a tablet with other ARV agents that require boosting. GS-9350 has been coformulated with EVG and the standard-of-care NRTI backbone FTC/TDF into a FDC tablet. This FDC regimen may be an attractive option for treatment-naïve patients with HIV-1 infection.

Study objective

The primary objective of this study is:
To evaluate the efficacy of a regimen containing elvitegravir/emtricitabine/tenofovir disoproxil fumarate/GS 9350 versus ritonavir-boosted atazanavir plus emtricitabine/tenofovir disoproxil fumarate in HIV 1 infected, antiretroviral treatment-naïve adult subjects as determined by the achievement of HIV 1 RNA < 50 copies/mL at Week 48
The secondary objectives of this study are:
To evaluate the efficacy, safety and tolerability of the two treatment regimens through 96 weeks of treatment
To evaluate the durability of the efficacy, safety and tolerability results of the two treatment regimens observed through 192 weeks of treatment

Study design

Randomized, double-blind, multicenter, active-controlled. Subjects will be randomized in a 1:1 ratio to one of the two treatment arms. Randomization will be stratified by HIV 1 RNA level (<= 100,000 copies/mL or >= 100,000 copies/mL) at screening.

Intervention

Treatment arm 1: EVG/FTC/TDF/GS-9350 active + ritonavir 100 mg placebo + atazanavir 300 mg placebo + Truvada® placebo.

Treatment arm 2: ritonavir 100 mg active + atazanavir 300 mg active +Truvada® active + EVG/FTC/TDF/GS-9350 placebo.

Study burden and risks

In case of an average of 2 visites after week 96:

7 x comlete physical exam
12 x physical exam as needed
4 x ECG
1 x length
19 x weight
8 x fasten glucose- and lipid panel

EVG; ELVITEGRAVIR SIDE EFFECTS
Mild headache, mild diarrhea, mild vomiting, mild fatigue, mild nausea, mild loss of appetite, dizziness, constipation, hypersensitivity, upper respiratory tract infection, hypertension, and difficulty sleeping. No additional side effects have been observed in clinical studies of EVG as an individual agent.

FTC; Emtriva® SIDE EFFECTS
(Emtricitabine)
Headache, diarrhea, nausea, rash, dizziness, changes in skin color, weakness, difficulty sleeping, abnormal dreams, pain, vomiting, stomach pain, problems with digestion, increased triglycerides (fatty acid), increased bilirubin in the blood, increased glucose in the blood, allergic reaction, hives, adverse effects on the function of the liver and pancreas, low white blood cell count, increased creatine kinase in the blood, actic acidosis, and liver problems with enlargement of the liver and fat in the liver, including fatal cases.

TDF; Viread® SIDE EFFECTS
(Tenofovir DF)
Diarrhea, nausea, vomiting, flatulence, dizziness, Immune Reconstitution Syndrome with symptoms of infections and inflammation, allergic reactions, weakness, abdominal pain, allergic reaction, pancreatitis, high levels of amylase in the blood, shortness of breath, rash, abnormalities of tests that measure hepatic function and hepatitis, lactic acidosis, liver problems with enlargement of the liver and fat in the liver, including fatal cases, kidney damage, and bone toxicity. Decreases in bone mineral density have been seen in humans. The risk of bone fractures associated with these types of changes is unknown.

GS-9350; SIDE EFFECTS
Upper extremity dyscoordination at the left side, difficulty concentrating, somnolence, headache, abnormal dreams, acute hepatitis with increase in liver enzyme levels, and mild decreases in estimated kidney function. No significant changes in serum immunoglobulins (antibodies), ECG, thyroid hormone levels or urine characteristics have been seen in clinical studies to date. In two ongoing studies mild decreases in estimated kidney function were observed. A follow-up study in healthy subjects showed that actual kidney function does not change. No additional side effects have been observed in clinical studies of

GS-9350 as an individual agent.

Suicidal ideation and suicide attempt in patients with a pre-existing history of depression or psychiatric illness has been identified as an uncommon adverse reaction to EVG/COBI/FTC/TDF (occurred in more than or equal to 0.1% and less than 1% of patients).

Contacts

Public
Gilead Sciences

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Scientific
Gilead Sciences

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

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

Inclusion criteria

Plasma HIV-1 RNA levels >= 5,000 copies/mL at screening
• No prior use of any approved or investigational antiretroviral drug for any length of time
• Screening genotype report provided by Gilead Sciences must show sensitivity to FTC, TDF and ATV

• Adequate renal function: Estimated glomerular filtration rate >= 70 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
• Adequate hematologic function (absolute neutrophil count >= 1,000/mm3; platelets >= 50,000/mm3; hemoglobin >= 8.5 g/dL)
• Serum amylase <= 5 × ULN (subjects with serum amylase > 5 × ULN will remain eligible if serum lipase is <= 5 × ULN)
• Age >= 18 years
• Life expectancy >= 1 year

Exclusion criteria

• A new AIDS-defining condition diagnosed within the 30 days prior to screening
• Subjects receiving drug treatment for Hepatitis C, or subjects who are anticipated to receive treatment for Hepatitis C during the course of the study.
• Subjects experiencing decompensated cirrhosis (e.g., ascites, encephalopathy, etc.)
• Have an implanted defibrillator or pacemaker
• Have an ECG PR interval >= 220 msec
• Current alcohol or substance use judged by the Investigator to potentially interfere with subject study compliance.
• A history of malignancy within the past 5 years (prior to screening) or ongoing malignancy other than cutaneous Kaposi's sarcoma (KS), basal cell carcinoma, or resected, non-invasive cutaneous squamous carcinoma. Subjects with cutaneous KS are eligible, but must not have received any systemic therapy for KS within 30 days of Baseline and must not be 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.
• Subjects receiving ongoing therapy with any of the medications as listed in the protocol v 15Mar2010 page 44.

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):	20-09-2010
Enrollment:	8
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	Atazanavir
Generic name:	-
Registration:	Yes - NL intended use
Product type:	Medicine
Brand name:	EVG/FTC/TDF/GS-9350 FDC Tablet
Generic name:	-
Product type:	Medicine
Brand name:	Ritonavir
Generic name:	-
Registration:	Yes - NL intended use
Product type:	Medicine
Brand name:	Tenofovir Disoproxil Fumaraat / Emtricitabine
Generic name:	-
Registration:	Yes - NL intended use

Ethics review

Approved WMO

Date:	13-04-2010
Application type:	First submission
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)

Approved WMO

Date:	11-06-2010
Application type:	First submission
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	27-07-2010
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	17-08-2010
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	13-09-2010
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	31-05-2011
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	12-07-2011
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	12-03-2012
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	07-06-2012
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United

	(Nieuwegein)
Approved WMO Date:	25-06-2012
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	21-09-2012
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	21-02-2013
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	05-03-2013
Application type:	Amendment
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
EudraCT	EUCTR2009--016758-4-NL

Register	ID
ClinicalTrials.gov	NCT01106586
CCMO	NL31159.100.10