A Phase 3, Open Label Study to Evaluate Switching from a TDF-Containing Combination Regimen to a TAF-Containing Combination Single Tablet Regimen (STR) in Virologically Suppressed, HIV 1 Positive Subjects

Published: 07-05-2013
Last updated: 24-04-2024

The primary objective of this study is:• To evaluate the non-inferiority of switching to a TAF Containing STR relative to maintaining TDF Containing Regimens in Virologically Suppressed HIV-1 positive subjects as determined by having HIV 1 RNA * 50...

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

Summary

ID

NL-OMON40276

Source
ToetsingOnline

Brief title
GS-US-292-0109

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: Farmaceutische industrie

Intervention

Keyword: antiretroviral (ARV), HIV-1, single tablet regimen (STR), Tenofovir alafenamide (TAF)

Outcome measures

Primary outcome

Criteria for Evaluation:

Safety:

- Adverse events and clinical laboratory tests, including DXA and selected bone and renal biomarkers to evaluate the safety and tolerability of the treatment regimens.

- The efavirenz-related symptom assessment to evaluate the efavirenz-related neuropsychiatric symptoms for subjects who took EFV/FTC/TDF as prior regimen.

Efficacy:

- The primary efficacy endpoint is the proportion of subjects that have HIV-1 RNA < 50 copies/mL at Week 48 as defined by the Food and Drug Administration (FDA) snapshot analysis.

- The secondary efficacy endpoints are:

• The proportion of subjects achieving virologic response at Weeks 48 (HIV-1

RNA <20 copies/mL, snapshot analysis)

• The proportion of subjects achieving virologic response at Weeks 96 (HIV-1

RNA < 50 copies/mL and <20 copies/mL, snapshot analysis)

• The change in CD4 cell count at Weeks 48 and 96

PK:

- The pharmacokinetics of TAF and tenofovir will be assessed. The

pharmacokinetics of other study drugs and their metabolites may be explored.

Health-related Questionnaires:

- Health related questionnaires will be administered including the Medical

Outcome Study Short Form-36 (SF-36) and the EQ 5D-3L health questionnaire. The

SF-36 and EQ-5D-3L questionnaires will be administered at Baseline, Week 24 and

every 24 weeks thereafter, and at the ESDD visit.

Secondary outcome

See primary parameters/ outcome

Study description

Background summary

The treatment of HIV infection requires the combination of several medications in order to decrease the amount of virus in the body, improve immune function and delay the progression of the disease. This has generally required patients to take a large number of pills each day, and many experience a loss of effectiveness of their current medication regimen over time or unacceptable side effects. Therefore, it is important to develop new drug regimens. In addition, the combination of drugs into a single tablet reduces the number of pills a patient has to take and makes it more convenient to stick to the

prescribed drug regimen.

The purpose of this study is to see if HIV-1 positive subjects currently taking an antiretroviral (ARV) regimen consisting of EVG/COBI/FTC/TDF (E/C/F/TDF) STR, EFV/FTC/TDF (Atripla®), cobicistat and atazanavir with FTC/TDF (Truvada®) or ritonavir and atazanavir with FTC/TDF (Truvada®) can safely switch to E/C/F/TAF STR without increasing the amount of HIV-1 in their blood. The safety and how well these drug combinations are tolerated will be determined based on physical exams, laboratory tests, bone scans and questions about any problems you might experience during the study.

Study objective

The primary objective of this study is:
• To evaluate the non-inferiority of switching to a TAF Containing STR relative to maintaining TDF Containing Regimens in Virologically Suppressed HIV-1 positive subjects as determined by having HIV 1 RNA * 50 copies/mL at Week 48 (FDA Snapshot Analysis).
The secondary objectives of this study are:
• To determine the safety of the two treatment arms as determined by the percent change from baseline in hip and spine bone mineral density at Week 48
• To determine the safety of the two treatment arms as determined by the change from baseline in serum creatinine at Week 48
• To evaluate the safety and tolerability of the two treatment arms through Week 48
• To evaluate the durability of the efficacy, safety and tolerability of the two treatment arms through Week 96

Study design

Een multi-centrum, gerandomiseerd, open label en actief gecontroleerd onderzoek.. Proefpersonen zullen gerandomiseerd worden in een verhouding 2:1 naar een van de twee behandelingsgroepen.

A randomized, multicentre open label active controlled study. Subjects will be randomized in a 2:1 ratio to one of the two treatment arms.

Intervention

Treatment group 1: Elvitegravir 150 mg/cobicistat 150 mg/emtricitabine 200 mg/tenofovir alafenamide 10 mg (E/C/F/TAF) STR administered orally QD
Treatment group 2: Current antiretroviral drug regimen consisting of E/C/F/TDF, EFV/FTC/TDF, ATV/r + FTC/TDF, or ATV/co + FTC/TDF administered orally QD

Study burden and risks

For a complete overview of all study procedures Please refer to the protocol and patientinformation leaflet. All risks are described in there.

Until November 2012, 112 HIV-positive subjects have been dosed with the E/C/F/TAF combination pill as part of a Phase 2 study to evaluate the drug*s safety and ability to suppress HIV viral load to undetectable levels (efficacy). After 6 months of therapy, 87% of subjects had undetectable viral loads (HIV-1 RNA < 50 copies/mL). Treatment was generally well tolerated as most AEs were mild and not associated with treatment discontinuation. No new or unexpected adverse events occurred. Subjects taking E/C/F/TAF had smaller changes in markers of kidney function and bone mineral density than subjects on a TDF-based regimen. The differences were statistically significant and may have important clinical relevance for individual patients. The frequency and type of adverse events and laboratory abnormalities was comparable to the TDF-based regimen.

In addition, more than 100 HIV-negative subjects have been dosed with the E/C/F/TAF combination pill as part of a Phase 1 study to evaluate the level of each drug in the blood (pharmacokinetics). No deaths or serious side effects occurred during the study. One subject discontinued from the study because of a nonserious adverse event of increased creatinine phosphokinase (CPK) levels in the blood that was assessed as related to study drug. The most frequently reported side effect was constipation. Other side effects included nausea, dizziness, headache, breast tenderness, and papular rash. No subject in any treatment arm developed any clinically significant abnormalities on ECG throughout the study.

Contacts

Public
Gilead Sciences

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Scientific
Gilead Sciences

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US

Trial sites

Listed location countries

Netherlands

Eligibility criteria

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

Inclusion criteria

• Currently receiving antiretroviral therapy consisting of E/C/F/TDF, EFV/FTC/TDF, ATV/r + FTC/TDF, or ATV/co + FTC/TDF for >=6 consecutive months preceding the final visit in their earlier study
• Completion of the Week 144 visit in studies GS-US-236-0102, GS US 236 0103, GS US 216 0114, or completion of the Week 96 visit in study GS-US-264-0110 (only subjects on an efavirenz-based regimen), or completion of studies GS-US-236-0104, GS US 216 0105.
• Plasma HIV 1 RNA concentrations at undetectable levels for at least 6 consecutive months prior to the screening visit and have HIV RNA <50 copies/mL at the screening visit
• Normal ECG (or if abnormal, determined by the Investigator to be not clinically significant)
• Estimated GFR >= 50 mL/min according to the Cockcroft Gault formula for creatinine clearance
• Hepatic transaminases (AST and ALT) <= 5 × upper limit of normal (ULN)
• Direct bilirubin <= 1.5 mg/dL x ULN
• 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)
• Females of childbearing potential must agree to utilize highly effective contraception methods or be non-heterosexually active or practice sexual abstinence from screening throughout the duration of study treatment and for 12 weeks following the last dose of study drug if receiving EFV/FTC/TDF regimen, and 30 days for those assigned to all other regimens.
* 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 have stopped menstruating for >= 12 months but do not have documentation of ovarian hormonal failure must have a serum follicle stimulating hormone (FSH) level at screening within the post-menopausal range based on the Central Laboratory reference range.
• Male subjects must agree to utilize a highly effective method of contraception during heterosexual intercourse or be non-heterosexually active, or practice sexual abstinence from

screening throughout the study period and for 12 weeks following discontinuation of investigational medicinal product if receiving EFV/FTC/TDF regimen, and 30 days for those assigned to all other regimens.
• Age >= 18 years

Exclusion criteria

• A new AIDS-defining condition diagnosed within the 30 days prior to screening
• Hepatitis B surface antigen (HBsAg) positive
• Hepatitis C antibody positive
• Subjects experiencing decompensated cirrhosis (e.g., ascites, encephalopathy, etc.)
• Females who are breastfeeding
• Positive serum pregnancy test
• Have an implanted defibrillator or pacemaker
• 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.
• 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.
• Participation in any other clinical trial (including observational trials) without prior approval from the sponsor is prohibited while participating in this trial.
• Subjects receiving ongoing therapy with any of the medications mentioned in the table in the protocol, including drugs not to be used with EVG, COBI, FTC, TDF, ATV, RTV, EFV and TAF (refer to the individual agents Prescribing Information); or subjects with any known allergies to the excipients of E/C/F/TDF STR, E/C/F/TAF STR, EFV/FTC/TDF, ATV, COBI, RTV, or FTC/TDF.

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):	14-10-2013
Enrollment:	7
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	Atripla
Generic name:	Efavirenz/ Emtricitabine/Tenofovir DF
Registration:	Yes - NL intended use
Product type:	Medicine
Brand name:	E/C/F/TAF
Generic name:	Elvitegravir/Cobicistat/Emtricitabine/Tenofovir Alafenamide (E/C/F/TAF) tablet
Product type:	Medicine
Brand name:	Reyataz
Generic name:	Atazanavir (ATV)
Registration:	Yes - NL intended use
Product type:	Medicine
Brand name:	Stribild
Generic name:	Elvitegravir/Cobicistat/Emtricitabine/Tenofovir DF (E/C/F/TDF) tablet
Product type:	Medicine
Brand name:	Truvada
Generic name:	Tenofovir DF/Emtricitabine
Registration:	Yes - NL intended use

Ethics review

Approved WMO Date:	07-05-2013
Application type:	First submission
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	20-09-2013
Application type:	First submission
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	22-11-2013
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	17-03-2014
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	01-04-2014
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	09-10-2014
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	18-11-2014
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO	

Date:	06-02-2015
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	16-03-2015
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	23-09-2016
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	17-10-2016
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	16-12-2016
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	23-01-2017
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	EUCTR2012-005114-20-NL
CCMO	NL43937.100.13

Study results

Results posted: 04-01-2021

First publication
18-11-2020