A Phase 3b, Randomized, Double-Blind Switch Study to Evaluate the Safety and Efficacy of Emtricitabine/Rilpivirine/Tenofovir Alafenamide (FTC/RPV/TAF) Fixed Dose Combination (FDC) in HIV-1 Positive Subjects who are Virologically Suppressed on Emtricitabine/Rilpivirine/Tenofovir Disoproxil Fumarate (FTC/RPV/TDF)

Published: 23-03-2015
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Main objective:To evaluate the non-inferiority of switching to the FTC/RPV/TAF FDC as compared to continuing FTC/RPV/TDF FDC in virologically suppressed HIV-1 infected subjects as determined by maintaining HIV-1 RNA < 50 copies/mL at Week 48 (FDA...

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

Summary

ID

NL-OMON42620

Source
ToetsingOnline

Brief title
Gilead GS-US-366-1216

Condition

- Immunodeficiency syndromes

Synonym
Human Immunodeficiency Virus (HIV-1) Infection

Research involving
Human

Sponsors and support

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

Intervention

Keyword: FTC/RPV/TAF, FTC/RPV/TDF, HIV-1 Positive Subjects

Outcome measures

Primary outcome

Safety:

Adverse events, clinical laboratory tests and DXA.

Efficacy:

The primary efficacy endpoint is the proportion of subjects with HIV-1 RNA < 50

copies/mL at Week 48 as defined by the Food and Drug Administration (FDA)

snapshot algorithm.

Pharmacokinetics: The pharmacokinetics of TAF and RPV will be explored. The PK

of

FTC and/or TFV may be explored.

Secondary outcome

The secondary efficacy endpoints are:

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

Study description

Background summary

As treatment guidelines recommend early treatment of HIV-1 infection, there is need for new regimens offering enhanced product safety and tolerability, effectiveness, and convenience for long-term treatment.

While TDF is an effective drug used broadly in the treatment of HIV-1 infection as a part of multiple combination regimens, including Complera/Eviplera, patients may benefit from anticipated improvements in the safety profile with the replacement of TDF with TAF. The development of FTC/RPV/TAF is expected to provide an additional option for HIV-1 infected patients: a TAF-containing, NNRTI-based FDC that can be administered as one tablet, once daily, with improved renal and bone safety.

This study will evaluate the safety, efficacy and tolerability of switching from Complera/Eviplera to FTC/RPV/TAF, thereby assessing the viability of FTC/RPV/TAF as a FDC option for HIV-infected patients.

Study objective

Main objective:
To evaluate the non-inferiority of switching to the FTC/RPV/TAF FDC as compared to continuing FTC/RPV/TDF FDC in virologically suppressed HIV-1 infected subjects as determined by maintaining HIV-1 RNA < 50 copies/mL at Week 48 (FDA Snapshot Algorithm).

Secondary objective:
To determine the safety of the two treatment arms as determined by the percent change from baseline in hip and spine bone mineral density as assessed by dual energy X-ray absorptiometry (DXA) at Week 48 in a subset of subjects.
To evaluate the safety and tolerability of the two treatment arms through Week 48.

Study design

Randomized, double-blind, multicenter study to evaluate the safety and efficacy of FTC/RPV/TAF FDC versus continuing FTC/RPV/TDF FDC in HIV-1 infected subjects

who are virologically suppressed (HIV-1 RNA < 50 copies/mL) on a stable regimen of
FTC/RPV/TDF FDC for >= 6 consecutive months prior to screening.

Subjects will be randomized in a 1:1 ratio to one of the following two treatment arms:

Treatment Arm 1: FDC of emtricitabine 200 mg/rilpivirine 25 mg tenofovir alafenamide 25 mg (FTC/RPV/TAF) QD + Placebo to match FDC of emtricitabine 200 mg/rilpivirine 25 mg /tenofovir disoproxil fumarate 300 mg (FTC/RPV/TDF) QD (n = 275)

Treatment Arm 2: FDC emtricitabine 200 mg/rilpivirine 25 mg/ tenofovir disoproxil fumarate 300 mg (FTC/RPV/TDF) QD + Placebo to match FDC of emtricitabine 200 mg/rilpivirine 25 mg/ tenofovir alafenamide 25 mg (FTC/RPV/TAF) QD (n = 275)
Subjects will be treated for at least 48 weeks. After the last subject completes the Week 48 visit and Gilead completes the Week 48 analysis, all subjects will attend the Unblinding Visit, at which point subjects will be given the option to receive FTC/RPV/TAF FDC in an open label extension phase for 48 weeks (except in UK) or until Gilead Sciences elects to terminate the study, whichever occurs first. Subjects who complete the study through Week 48 and do not wish to continue to participate in the open label extension will be required to
return to the clinic 30 days after the completion of the study drug for a 30-Day Follow-up Visit. After the Unblinding Visit, subjects in the UK will stop taking their study drug and complete a 30 day follow up visit.

Intervention

Test Product, Dose, and Mode of Administration:
Emtricitabine 200 mg/rilpivirine 25 mg/tenofovir alafenamide 25 mg (FTC/RPV/TAF) FDC administered orally QD with food

Reference Therapy, Dose, and Mode of Administration:
Emtricitabine 200 mg/rilpivirine 25 mg /tenofovir disoproxil fumarate 300 mg (FTC/RPV/TDF) FDC administered orally QD with food

Study burden and risks

For a complete overview of study procedures please refer to the protocol and patient information leaflet. All risks are described in there.

Laboratory analyses (hematology, chemistry, and urinalysis), HIV-1 RNA, CD4+ cell count, and complete or symptom directed physical examinations will be performed at the Screening, Baseline/Day 1, and all subsequent study visits.

Subjects will be treated for 48 weeks.

Subjects will return for study visits at Weeks 4, 8, 12, 24, 36 and 48.

Blood and urine for selected bone and renal safety evaluations will be collected at Baseline/Day 1, Weeks 24, 48, Unblinding and ESDD (if applicable).

Blood for pharmacokinetic analysis will be collected at Weeks 4, 8, 12 and 24.

A subset of subjects (approximately 300) who provide a separate informed consent, will participate in a DXA substudy. DXA scans will be performed prior to study drug administration at Baseline/Day 1, and then every 24 weeks throughout the study and at the

Early Study Drug Discontinuation Visit, if > 12 weeks since last scan. Scans will cover the spine and hip to measure changes in bone mineral density.

Subjects will be treated for at least 48 weeks. After the last subject completes the Week 48 visit and Gilead completes the Week 48 analysis, all subjects will attend the Unblinding Visit, at which point subjects will be given the option to receive FTC/RPV/TAF FDC in an open label extension phase for 48 weeks (except in UK) or until Gilead Sciences elects to terminate the study, whichever occurs first.

Subjects who complete the study through Week 48 and do not wish to continue to participate in the open label extension will be required to return to the clinic 30 days after the completion of the study drug for a 30-Day Follow-up Visit.

After the Unblinding Visit, subjects in the UK will stop taking their study drug and complete a 30 day follow up visit.

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

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

Inclusion criteria

Medically stable HIV-1 infected subjects who meet the following criteria:;• Currently receiving antiretroviral therapy consisting only of FTC/RPV/TDF FDC (Complera/Eviplera) continuously for 6 months preceding the Screening visit;• Documented plasma HIV-1 RNA levels < 50 copies/mL (or undetectable HIV-1 RNA level according to the local assay being used if the limit of detection is > 50 copies/mL) for >= 6 months preceding the Screening visit. After reaching HIV-1 RNA < 50 copies/mL, single values of HIV-1 RNA >= 50 copies/mL followed by resuppression are allowed;• HIV-1 RNA < 50 copies/mL at the Screening visit;• Adequate renal function defined as having an estimated glomerular filtration rate (eGFR) >= 50 mL/min as calculated by the Cockcroft-Gault formula;• Have no documented resistance to any of the study agents at any time in the past, including but not limited to the reverse transcriptase resistance mutations K65R, K70E, K101E/P, E138A/G/K/R/Q, V179L, Y181C/I/V, M184V/I, Y188L, H221Y, F227C, M230I/L, the combination of K103N+L100I, or 3 or more thymidine analog associated mutations (TAMs) that include M41L or L210W (TAMs are M41L, D67N, K70R, L210W, T215Y/F, K219Q/E/N/R)

Exclusion criteria

• Hepatitis B surface antigen (HBsAg) positive;• Hepatitis C antibody positive with detectable HCV RNA (subjects who have HCV antibody but no detectable HCV RNA are eligible to enroll);• Subjects receiving ongoing therapy with any of the specified medications in the protocol, including drugs not to be used with FTC, RPV and/or TAF (refer to the individual agents Prescribing Information);

or subjects with any known allergies to the excipients of FTC/RPV/TAF

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):	27-07-2015
Enrollment:	20
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	.
Generic name:	Emtricitabine/Rilpivirine/Tenofovir Alafenamide
Product type:	Medicine
Brand name:	Complera/Eviplera
Generic name:	emtricitabine/rilpivirine/tenofovir-disoproxilfumaraat
Registration:	Yes - NL intended use

Ethics review

Approved WMO

Date:	23-03-2015

Application type:	First submission
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	08-06-2015
Application type:	First submission
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	23-07-2015
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	21-08-2015
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	04-09-2015
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	24-11-2015
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	20-05-2016
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	22-07-2016
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)

Approved WMO Date:	03-07-2017
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	31-07-2017
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	EUCTR2014-004545-27-NL
ClinicalTrials.gov	NCT02345252
CCMO	NL52744.100.15

Study results

Results posted: 21-04-2020

First publication
30-07-2019