Adherence, HIV-1 Infection, Resistance, and Renal and Skeletal Adverse Event in Individuals Taking Emtricitabine/Tenofovir Disoproxil Fumarate (FTC/TDF, Truvada®) for HIV Pre-Exposure Prophylaxis (PrEP): A Pooled Observational Study

First published: 12/07/2018

Last updated: 23/04/2024

Study Finalised

Administrative details

EU PAS number

EUPAS24332

Study ID

41844

DARWIN EU® study

No

Study countries

- [ ] Austria
- [ ] Benin
- [ ] Brazil
- [ ] Canada
- [ ] Denmark
- [ ] Ecuador
- [ ] France
- [ ] Germany
- [ ] Ireland
- [ ] Italy
- [ ] Kenya
- [ ] Netherlands
- [ ] Peru
- [ ] South Africa
- [ ] Spain
- [ ] Thailand
- [ ] Uganda
- [ ] United Kingdom
- [ ] United States
- [ ] Zimbabwe

Study description

GS-US-276-0104:This is an observational study of HIV-1 negative individuals who participated in demonstration projects or clinical studies and took daily Truvada for PrEP. All individuals were enrolled and followed as described in the parent PrEP demonstration project or clinical study protocol until study completion, HIV-1 infection, discontinuation due to an adverse event, lost to follow-up, or administrative censoring. In the protocols of the parent PrEP observational or clinical studies, participants had follow-up visits on average

every 3 months for evaluation of adherence, HIV-1 status, renal and bone adverse events, and seroconversion. Adherence was determined by the specific FTC/TDF drug level measurement(s) outlined in the parent protocol. Gilead had collected data from 21 global PrEP demonstration projects and clinical studies for over 7,000 Truvada for PrEP users who had at least one measurement of adherence. Data from the different contributing studies were pooled for statistical analyses by Gilead.

Study status

Finalised

Research institutions and networks

Institutions

Gilead Sciences

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Institution | Pharmaceutical company

Multiple centres: 20 centres are involved in the study

Contact details

Study institution contact

Study Director Gilead ClinicalTrialDisclosure@gilead.com

Study contact

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Primary lead investigator

Study Director Gilead

Primary lead investigator

Study timelines

Date when funding contract was signed

Planned: 30/04/2013

Actual: 02/11/2012

Study start date

Planned: 01/01/2014

Actual: 07/10/2013

Date of final study report

Planned: 30/12/2021

Actual: 27/04/2021

Sources of funding

- Pharmaceutical company and other private sector

More details on funding

Gilead Sciences, Inc.

Study protocol

protocol GS-US-276-0104_f-redact.pdf(447.12 KB)

Regulatory

Was the study required by a regulatory body?

Yes

Is the study required by a Risk Management Plan (RMP)?

EU RMP category 3 (required)

Other study registration identification numbers and links

NCT01906255,,https://clinicaltrials.gov/ct2/show/NCT01906255?term=276-0104&rank=1

Methodological aspects

Study type

Study type list

Study topic:

Disease /health condition

Human medicinal product

Study type:

Non-interventional study

Scope of the study:

Assessment of risk minimisation measure implementation or effectiveness

Data collection methods:

Combined primary data collection and secondary use of data

Main study objective:

The study assessed level of adherence as measured by drug level and its relationship to renal and bone adverse events, risk of seroconversion, and resistance development in subjects taking Truvada for PrEP.

Study Design

Non-interventional study design

Case-control

Study drug and medical condition

Medical condition to be studied

Prophylaxis against HIV infection

Population studied

Short description of the study population

HIV-1 negative adults or adolescents (any sex/gender, including transgender) who had at least one measurement of adherence of TFV-DP in DBS or of TFV in plasma available while taking Truvada for PrEP.

Inclusion Criteria

To be eligible for study participation, an HIV-1 uninfected individual was required to satisfy the following criteria:

1. Participant in a Truvada PrEP observational or clinical study.
2. HIV-1 negative individual at the time of enrollment in a demonstration project or clinical study.
3. Participants with at least one measurement of TFV-DP in DBS or TFV in plasma.

Exclusion Criteria

This observational study collected HIV-1 infection and resistance information along with renal or skeletal adverse events without intervention. In the pooled analysis, only available TFV-DP or TFV measurements were analyzed. Individuals with no TFV-DP or TFV measurements within 48 weeks after PrEP initiation, with HIV-1 infection tested positive before PrEP initiation date or before the first adherence measurement, and with PrEP initiation date later than PrEP end date were excluded. Adherence measurements with laboratory test date prior to the Truvada for PrEP initiation date, and with extreme values of TFV-DP in DBS over 4,000 femtomole/punch (fmol/punch) were excluded, based on communication with from , whose laboratory conducted all the tests for adherence of the individual
studies.

Age groups

Adults (18 to < 46 years)

Adults (46 to < 65 years)

Adults (65 to < 75 years)

Adults (75 to < 85 years)

Adults (85 years and over)

Estimated number of subjects

7302

Study design details

Outcomes

The objectives of the study were to assess levels of adherence, evaluate the association between levels of adherence, and measure a gradient of adherence levels using available data on drug levels as the measure of adherence in participants taking Truvada for PrEP.

Data analysis plan

GS-US-276-0104 conducted an analysis of data from ongoing and planned demonstration projects (trials) including at least 7000 uninfected individuals taking Truvada® for a preexposure prophylaxis (PrEP) indication with the objective of examining the association between levels of adherence to the once-daily dosing regimen and risk of seroconversion, resistance development, and renal and skeletal adverse events. Levels of adherence measured a gradient of adherence levels rather than the simple dichotomy of ‘adherent’ versus ‘nonadherent’ using any available data on drug levels as the measure of adherence. Seroconversion was assessed every three months, and, upon each seroconversion, resistance testing was performed. Assessment for renal and skeletal adverse events was performed every three months, including

evaluation of available laboratory data. Analyses was performed by geographic region.

Documents

Study results

GS-US-276-0104-csr-final_f-redact.pdf(2.27 MB)

Data management

Data sources

Data sources (types)

Other

Data sources (types), other

Prospective patient-based data collection, Case-control surveillance database

Use of a Common Data Model (CDM)

CDM mapping

No

Data quality specifications

Check conformance

Unknown

Check completeness

Unknown

Check stability

Unknown

Check logical consistency

Unknown

Data characterisation

Data characterisation conducted

No