Pharmacoepidemiology study to define the long-term safety profile of tenofovir disoproxil fumarate (Tenofovir DF, Viread®) and describe the management of Tenofovir DF-associated renal and bone toxicity in Chronic Hepatitis B (CHB)-infected adolescents aged 12 to <18 years in Europe (Viread HBV PASS)

First published: 28/04/2017

Last updated: 01/04/2024

Study Finalised

Administrative details

EU PAS number

EUPAS18825

Study ID

27926

DARWIN EU® study

No

Study countries

- [ ] Belgium
- [ ] Bulgaria
- [ ] France
- [ ] Greece
- [ ] Italy
- [ ] Romania
- [ ] Spain
- [ ] United Kingdom

Study description

GS-EU-174-1403: The study was a prospective cohort comprised of HBV infected adolescents who initiated Tenofovir DF therapy in clinics across Europe. The subjects were assigned to one of two monitoring groups using a validated computer-generated tool for randomization. Subjects were assigned to Group 1 or 2 upon enrollment into the study but prior to Baseline laboratory and DEXA imaging assessments.Group 1 received Tenofovir DF for the treatment of CHB infection, followed over 96 weeks using an enhanced monitoring protocol which included more frequent laboratory bone biomarker testing and lumbar spine and whole-body DEXA scans than specified for Group 2. With the exception of an enhanced monitoring protocol for bone and renal outcomes, subjects were managed according to local standards of care.Group 2 was the comparator group of subjects receiving Tenofovir DF for the treatment of CHB infection and with the exception of pre-specified bone monitoring, managed according to local standards of care. Group 2 received bone biomarker testing, lumbar spine and wholebody DEXA at Baseline, Weeks 48 and 96.Both groups were monitored for 96 weeks on Tenofovir DF during clinic visits for response to treatment, AEs, adherence to supplementary vitamins and

mineral intake assessments. Both groups were be required to have DEXA (whole body and spine) scans for BMD at Baseline (week 0) and prior to receipt of Tenofovir DF, and at the end of the study period (Week 96). Group 2 was a comparator cohort to Group 1 in evaluating the hypothesis of whether enhanced monitoring for renal and BMD changes and AEs provided a net benefit in preventing renal- or bone-related adverse outcomes to adolescents receiving Tenofovir DF therapy for HBV.

Study status

Finalised

Research institutions and networks

Institutions

Gilead Sciences

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Last updated: 12/02/2024

Institution | Pharmaceutical company

Multiple centres: 21 centres are involved in the study

Contact details

Study institution contact

Gilead Study Director GileadClinicalTrials@gilead.com

Study contact

GileadClinicalTrials@gilead.com

Primary lead investigator

Study Director Gilead

Primary lead investigator

Study timelines

Date when funding contract was signed

Planned: 05/01/2015

Actual: 05/01/2015

Study start date

Planned: 30/06/2015

Actual: 03/07/2015

Date of interim report, if expected

Actual: 23/01/2017

Date of final study report

Planned: 03/09/2019

Actual: 25/09/2018

Sources of funding

- Pharmaceutical company and other private sector

More details on funding

Gilead Sciences Europe Limited

Study protocol

protocol+GS-EU-174-1403-FINAL-COMPLETE Amendment 2.pdf (928.43 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

This is an interventional study involving two assigned monitoringgroups of chronic HBV infected adolescents who will receivetreatment with open-label, market-authorized Tenofovir DF andfollowed prospectively to a primary endpoint at 96 weeks.

Methodological aspects

Study type

Study type list

Study topic:

Disease /health condition

Human medicinal product

Study type:

Clinical trial

Main study objective:

To characterize the long term (i.e. 96 weeks of follow up) bone safety profile of open-label Tenofovir DF treatment in CHB-infected adolescents. This includes prospectively evaluating and comparing the bone mineral density (BMD) change between CHB- infected adolescents 12 to < 18 years of age treated with Tenofovir DF.

Study Design

Clinical trial regulatory scope

Post-authorisation interventional clinical trial

Clinical trial phase

Therapeutic use (Phase IV)

Clinical trial randomisation

Randomised clinical trial

Study drug and medical condition

Anatomical Therapeutic Chemical (ATC) code

(J05AF) Nucleoside and nucleotide reverse transcriptase inhibitors

Nucleoside and nucleotide reverse transcriptase inhibitors

Medical condition to be studied

Chronic hepatitis B

Population studied

Short description of the study population

Patients with following criteria were included:

1. Aged 12 to <16 years

2. Weight ≥ 35 kg

3. Documented chronic HBV infection (e.g. positive serum HBsAg ≥ 6 months)

4) Able to swallow oral tablets

5) Negative serum β-HCG pregnancy test (for females of childbearing potential)

6) Estimated glomerular filtration rate (creatinine clearance) ≥ 80 mL/min/1.73m2

7) Parent or legal guardian of potential study subjects able to provide written informed consent prior to any screening evaluations and willing to comply with study requirements or subject able to provide written assent as determined by IEC/local requirements and at the Investigator’s discretion.

Age groups

- Adolescents (12 to < 18 years)

Special population of interest

Hepatic impaired

Estimated number of subjects

30

Study design details

Outcomes

The identification of bone AEs occurring in subjects taking Tenofovir DF between Baseline and Week 96 of treatment including the identification of ≥ 4% reduction in BMD within subjects and between monitoring groups from Baseline. Documentation of renal or bone AEs and outcomes among subjects receiving Tenofovir DF, including time to medication withdrawal or discontinuation.Subjects' cumulative exposure time on Tenofovir DF at the time renal or bone AEs are detected up to and including Week 96 or to study discontinuation.

Data analysis plan

All individual subject data will be listed as measured. All statistical summaries and analyses will be performed using SAS® software or other standard software tools including the STATA software. An efficacy analysis will be conducted after the last assigned subject reaches Week 96. The analysis will evaluate the difference in the proportion of subjects (Group 1 and 2 data will be pooled, as subjects have exposure to a single mode of therapy) achieving a composite endpoint of HBV DNA □ 400 copies/mL and ALT normal at Week 96, using a two-sided Fisher exact test with a non-completer equals failure approach.

Documents

Study results

GS-EU-174-1403-CSR Synopsis_f-redact.pdf (296.29 KB)

Data management

ENCePP Seal

The use of the ENCePP Seal has been discontinued since February 2025. The ENCePP Seal fields are retained in the display mode for transparency but are no longer maintained.

Data sources

Data sources (types)

Other

Data sources (types), other

Prospective patient-based data collection

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

Unknown