This document provides a short summary of this study for a general audience. You can find more information in the scientific summary of the study. A link to the summary is provided at the end of this document.

## Study names

Short Title: A study to assess how well tenofovir disoproxil fumarate works and how safe it is in patients with chronic hepatitis B who switched from entecavir.

Full Scientific Title: A multi-centre, one-arm prospective study to evaluate efficacy and safety of switching from entecavir to tenofovir disoproxil fumarate in Japanese chronic hepatitis B HBeAg-positive and HBV-DNA undetectable subjects.

Study Number: 205883

## Who sponsored this study?

GlaxoSmithKline (GSK)
GSK Clinical Support Help Desk
Website: clinicalsupporthd.gsk.com/contact.html
Email: GSKClinicalSupportHD@gsk.com

## General information about the clinical study

When and where was this study done?

The study started in October 2017 and ended in November 2019. All study sites were in Japan.

What was the main reason for this study?

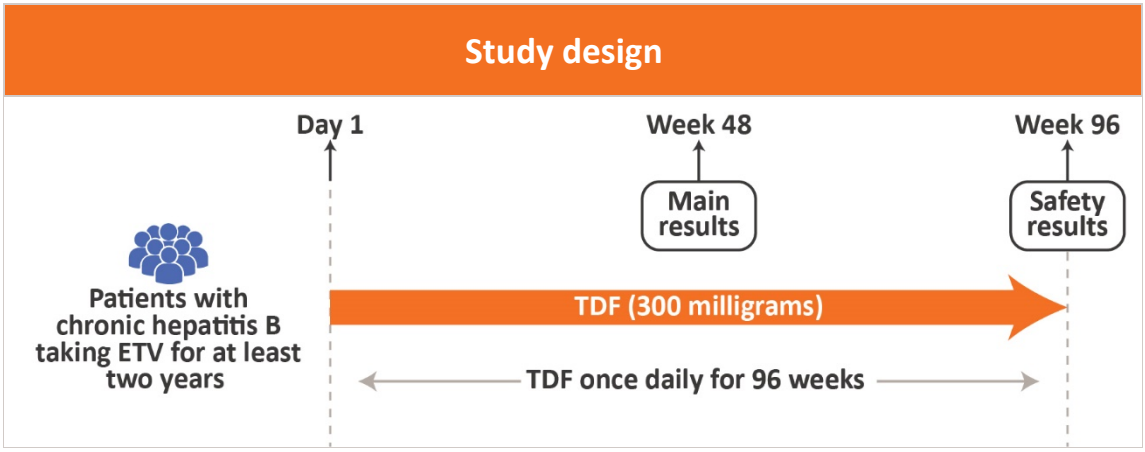
Chronic hepatitis B is a long-term infection of the liver caused by the hepatitis B virus (HBV). It can lead to serious liver diseases such as liver failure, cirrhosis, or liver cancer. Currently, there is no cure for chronic hepatitis B. The goal of any treatment for chronic hepatitis B is to manage the HBV infection by fighting the virus and slowing its ability to damage the liver.

The HBsAg and HBeAg proteins are found on the HBV virus. Doctors can monitor the amount of HBV in the body by measuring the levels of these proteins in blood.

Entecavir (ETV) and tenofovir disoproxil fumarate (TDF) are anti-viral medicines that are used to treat chronic hepatitis B. For this study, patients were considered to have responded to TDF if they achieved the required reduction in the blood HBsAg levels after switching from ETV to TDF. The researchers also studied the safety of TDF.

## Which medicine was studied?

As shown in the figure below, patients knew that they were taking TDF once daily for 96 weeks. This is called an open-label study.



## Which patients were included in this study?

Studies have a list of requirements for patients who can enrol (inclusion criteria) and those who can't (exclusion criteria). For this study, the main inclusion and exclusion criteria are listed below.

Men and women with chronic hepatitis B were included in the study if they:

- Were between 20 and 69 years old.
- Were taking ETV for at least two years before starting the study treatment and:
  - Their blood tested positive for the presence of HBeAg and HBsAg proteins at the start of the study.
  - Their blood tested negative for the presence of HBV DNA at the start of the study.

Men and women were excluded from the study if they had:

- Cancer or signs of disease in the liver.
- Infection with HIV or hepatitis C virus.
- Received hepatitis B vaccine or were treated with interferon (protein) within six months before starting the study.
- Received treatment with other anti-viral medicines, including TDF, adefovir, or tenofovir alafenamide fumarate, within two years before starting the study treatment.
- An organ or bone marrow transplant or planned to have one.
- Any other disease(s) or treatment(s) that the study doctor thought would affect the results of the study.

Overall, 75 patients received at least one dose of TDF. The study included 55 (73%) men and 20 (27%) women. The average age was 48 years. The youngest patient was 33 years old and the oldest patient was 69 years old.

For more detailed information about the patients included in this study, see the scientific results summary (a link to the summary is provided at the end of this document).

## What were the main results of the study?

Study doctors measured patients' HBsAg levels on Day 1 (baseline), Week 4, and every 12 weeks during the study.

The main focus of the study was to see the number of patients (percent) who responded to TDF at Week 48 compared to baseline. Results for 74 patients are shown in the table below.

| Number of patients (percent) who responded to TDF at Week 48 | |
|---|---|
| | **TDF**<br>**74 patients** |
| **Patients who achieved required reduction in blood HBsAg levels** | 3 (4%) |
| **Patients who did not achieve required reduction in blood HBsAg levels** | 71 (96%) |

At Week 48, only 4% of the patients responded to TDF and achieved the required reduction in the HBsAg levels.

More information about the study results is available in the scientific results summary (a link to the summary is provided at the end of this document).

## What were the side effects?

Unwanted medical events (adverse events) can happen to people when they receive a medicine. Study doctors record these events. A summary of these events can be found in the scientific results summary (a link to the summary is provided at the end of this document).

If the study doctor thinks that the event was caused by the study medicine, it is recorded as a possible side effect (adverse reaction).

In this summary, "side effects" refer to those events that the study doctor thinks may have been caused by TDF. The side effects in this summary may be different to those in the Informed Consent or other documents related to TDF.

No serious side effects were reported up to Week 96.

Non-serious side effects were reported by 18 patients (24%) up to Week 96. The only non-serious side effect reported by 2% or more of patients was increased levels of a protein (beta 2 microglobulin) in urine. This was reported by 15 patients (20%).

## How has this study helped patients and researchers?

The results of the study showed that most of the patients who switched from ETV to TDF did not have the required reduction in blood HBsAg levels. The side effects reported in the study were all non-serious.

## Are there plans for further studies?

Other studies on TDF in patients with chronic hepatitis B have been conducted and more are underway.

## Where can I find more information about this study?

Clinical studies have unique study numbers that are included in publications and other information about the study. The unique study number associated with this study is shown below with an internet link to the scientific summary and other information.

The scientific summary includes more details about the requirements for study enrolment, the study visit schedule, results from other endpoints, and more detailed information about adverse events.

| Organisation and website | Study Number |
|---|---|
| **United States National Institutes of Health (NIH) (www.clinicaltrials.gov)** | NCT03258710[1] |

Your doctor can help you understand more about this study and the results. Speak to your doctor about the treatment options available in your country. You should not

[1] https://clinicaltrials.gov/ct2/show/study/NCT03258710

make changes to your care based on the results of this or any single study. Keep taking your current treatment unless instructed by your doctor.

We would like to thank the patients who contributed to this study. The results of this study will help answer scientific questions about treating patients with chronic hepatitis B.

The content for this document was finalised by GSK on the 24th of June 2020. The information in this summary does not include additional information available after this date.