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 Chinese patients with chronic hepatitis B who did not respond well to treatment with multiple nucleos(t)ide analogues.

Full Scientific Title: A multi-centre, single-arm, open-label study to evaluate the efficacy and safety of tenofovir disoproxil fumarate treatment in Chinese chronic hepatitis B subjects following failure of multiple nucleos(t)ide analogues.

Study Number: 201215

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 March 2015 and ended in August 2018. All study sites were in China.

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. Once infected, there is currently 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.

Nucleos(t)ide analogues (NAs) are a class of anti-viral medicines that are used to treat chronic hepatitis B. They work by controlling the amount of virus in the body. Doctors can monitor the amount of HBV in the body by measuring the HBV DNA levels in blood. Nucleos(t)ide analogues are considered not to be working well if a patient's HBV DNA level remains greater than 200 international units per millilitre (IU/mL).

Tenofovir disoproxil fumarate (TDF) is a type of NA. In this study, researchers wanted to see how well TDF works in Chinese patients with chronic hepatitis B who did not respond well to treatment with multiple NAs. They also studied the safety of TDF.

Which medicine was studied?

Patients took TDF (300 milligrams) tablet once daily for 144 weeks. The patients knew which treatment they received. 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 were included in the study if they:

- Were between 18 and 65 years old.
- Tested positive for HBV for more than six months.
- Had blood HBV DNA level greater than or equal to 200 IU/mL at the start of the study.
- Did not respond well to two or more different types of NAs, each taken for at least six months.

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

- Cancer or signs of disease in the liver.
- Decreased rate of removal of waste substance (creatinine) from blood by the kidney.
- Infection with human immunodeficiency virus (HIV) or any of the other hepatitis virus (A, C, D, or E).
- Higher than ten times the normal levels of a liver protein in the blood (alanine aminotransferase) before starting the study.
- Received treatment with TDF within six months before starting the study.

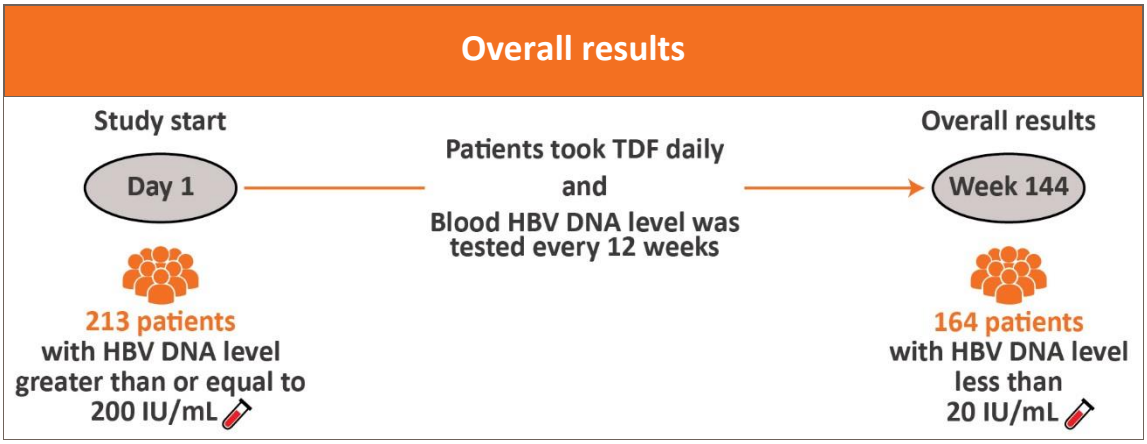
A total of 213 patients received at least one dose of TDF. The table below shows the gender and age of these patients.

Patients who received at least one dose of the study medicine	
	TDF **213 patients**
Gender - Number of patients (percent)	
Female	27 (13%)
Male	186 (87%)
Age - in years	
Range	21 to 66
Average	42

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 overall results of the study?

To determine how well TDF worked, study doctors measured the amount of HBV DNA in the blood. They collected blood samples and measured patients' HBV DNA levels on Day 1 and every 12 weeks during the study as shown in the figure below:



For this study, HBV DNA level less than 20 IU/mL indicated that the patient responded to TDF. The main focus of the study was to see the percentage of patients with blood HBV DNA level less than 20 IU/mL at Week 144.

At Week 144, 77% of the patients who had previously not responded to treatment with multiple NAs, responded to TDF.

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 all 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, they record this 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 the study medicine. The side effects in this summary may be different to those in the Informed Consent or other documents related to the study medicine.

No serious side effects were reported in this study.

The table below shows the number of patients (percent) with non-serious side effects that were reported by two percent or more patients in this study.

Number of patients (percent) with non-serious side effects that were reported by two percent or more patients	
	TDF **213 patients**
Higher than normal levels of a liver protein in the blood	6 (3%)
Lower than normal levels of phosphate in the blood	5 (2%)

How has this study helped patients and researchers?

This study showed that majority of the patients with chronic hepatitis B, who did not respond well to treatment with multiple NAs previously, responded to treatment with TDF. The side effects reported in this study were limited and 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	Website	Study Number
United States National Institutes of Health (NIH)	www.clinicaltrials.gov	NCT02195518[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 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 11th of November 2019. The information in this summary does not include additional information available after this date.

[1] https://clinicaltrials.gov/ct2/show/NCT02195518