PLAIN LANGUAGE SUMMARY OF CLINICAL STUDY RESULTS

Study Sponsor: Gilead Sciences

Gilead Protocol Number: GS-US-320-0110

Dates of Trial: September 2013 to October 2022

Short Study Title: Study to Compare Tenofovir Alafenamide (TAF) Versus Tenofovir Disoproxil Fumarate (TDF) in Participants with Chronic Hepatitis B Infection Who are Positive for Hepatitis B e Antigen

Date of this Report: June 2023

The information in this summary does not include any information available after this date.

Thank you

Thank you to the participants who took part in the clinical study for **TAF**, also known as **Vemlidy**.

Gilead Sciences sponsored this study. We believe it is important to share the results with study participants and the general public.

If you participated in the study and have questions about the results, please speak with a doctor or staff member at the study site.

Always talk to a doctor or a health care provider before making any treatment changes.

This document is a short summary of this study written for a general audience. Links to scientific summaries of this study can be found at the end of this document.

What was the purpose of the study?

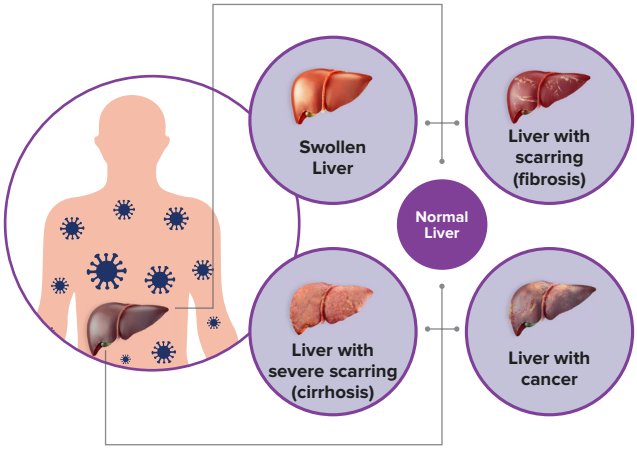
The purpose of this study was to learn how safe and how well treatment with experimental drug TAF works in comparison to standard treatment TDF in people with chronic (long-term) hepatitis B virus (HBV) infection who were positive for **hepatitis B e antigen (HBeAg)**.

Hepatitis B antigens are virus proteins present in the body, due to HBV infection. **HBeAg** is an antigen released by HBV. The test for HBeAg is important to assess the activity of the infection and guide the management and treatment decisions.

What is Chronic Hepatitis B?

Hepatitis B Hepatitis B is an infection of the liver. It is caused by a virus called HBV. About **296 million** people are living with hepatitis B in the world. It may spread from mother to child during birth or when people come in contact with the blood or other body fluids of someone who has hepatitis B. For some people, hepatitis B lasts for a short time.

Chronic hepatitis B (CHB): In some people, the hepatitis B infection persists for a long time, at least 6 months or longer and this is called chronic infection. Chronic hepatitis B infection is one of the leading causes of liver inflammation (liver with swelling or irritation), liver fibrosis (scarring of liver), liver cirrhosis (severe scarring of the liver), and liver cancer.



Common tests for checking CHB are:

- **Blood tests that look for specific proteins of virus in blood:** HBsAg and HBeAg are virus proteins that are used to detect hepatitis B infection. A person is likely to have CHB when they test positive for HBsAg 2 times at least 6 months apart.
- **HBV viral load test:** The test is based on the presence of **HBV DNA in the blood**. Viral load suggests the level of infection in the body.

DNA stands for deoxyribonucleic acid. It is an essential building block in all living organisms. **HBV DNA** is the DNA of the virus. HBV DNA plays a role in its growth and replication in the infected liver cells.

Current oral antiviral treatments for CHB interrupt replication of virus in the body. They are used in order to keep the levels of virus low in the body, but they do not always completely remove the virus or its particles from the body. Therefore, CHB currently requires lifelong treatment. There are known side effects of the current treatment options when taken for a long time. Side effects are seen more in people who already have other diseases, mainly related to kidneys or bones. Some of the current treatment options may also not work in people who received any other treatment for HBV in the past.

There is a need for new treatment options for CHB that work at least as good as current treatment options at a **lower dose** and **cause fewer side effects** when taken for a long time. Therefore, TAF was chosen to be studied for use in people with CHB.

Standard treatment, TDF was chosen to compare with TAF because it is an approved and common treatment used by doctors to treat people with CHB. Although highly effective, the daily use of TDF can sometimes cause kidney problems and weakening of the bones in some people (called reduced bone mineral density, or BMD). The researchers wanted to see if TAF is similarly effective to TDF and has fewer unwanted effects on the kidneys and bones.

The main questions the researchers wanted to answer in this study were:

- How many participants had viral load suppressed in their blood at Week 48?
- What side effects did participants have during the study, if any?

Who took part in the study?

- In total, **875 participants** living with CHB in **19** countries around the world took part in this study.
- 2 participants who left the study before taking treatment were not included in the study results.

This international study enrolled participants in multiple countries. A similar study was also done in subset of participants from China. This report includes results only for participants from countries other than China.

People took part in the study if they:

- Were 18 years of age or older
- Were positive for HBeAg and had HBV DNA of greater than 2x10^4 IU/mL at the start of the study
- Did not receive any previous treatment or had stopped any previous treatment for CHB at least 6 months before entering the study

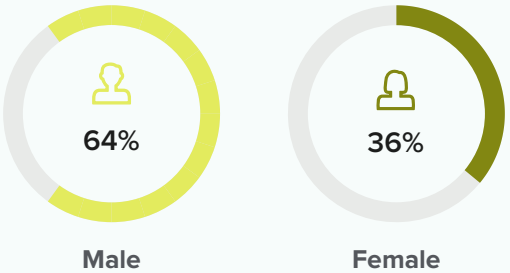
The study enrolled adult participants between the ages of **18 to 69 years**.

The graphic below shows how many study participants were from each country.

	Percentage of participants	Number of participants
South Korea	**20%**	173
Hong Kong	**14%**	121
India	**13%**	110
Canada	**9%**	83
Taiwan	**9%**	83
United States	**6%**	54
Russia	**6%**	49
Japan	**5%**	46
Romania	**4%**	33
Turkey	**3%**	26
Australia	**3%**	22
New Zealand	**2%**	17
Italy	**2%**	14
Poland	**1%**	12
Singapore	**1%**	9
United Kingdom	**under 1%**	8
Bulgaria	**under 1%**	6
France	**under 1%**	5
Spain	**under 1%**	4

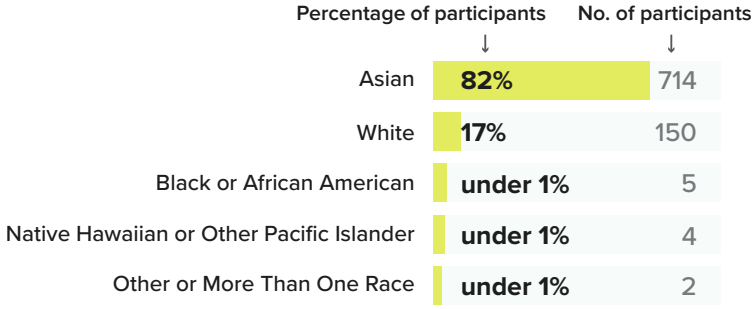
Sex of participants who took part are shown below.

Participant breakdown by sex

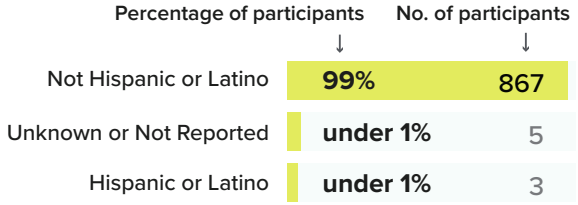


Race and ethnicity of participants who took part are shown below.

Participant breakdown by race



Participant breakdown by ethnicity



What happened during the study?

The study was done in **2 parts:**

Part 1 of the study was **Randomized** and **Blinded**.

Randomized: This means, researchers used a computer program to randomly choose the treatment each participant took. This helped make sure the treatments were chosen fairly.

Blinded: This means, none of the participants, doctors, or other study staff knew what treatment each participant took.

During this part of the study, participants had 2 out of 3 chances of receiving TAF and 1 out of 3 chances of receiving TDF. This means they were assigned in 2:1 ratio to receive the treatment as follows:

- **TAF Group:** Participants received a TAF tablet and a placebo tablet by mouth 1 time every day. The placebo tablet looked like TDF.
- **TDF Group:** Participants received a TDF tablet and a placebo tablet by mouth 1 time every day. The placebo tablet looked like TAF.

A **placebo** looks like a treatment but does not have any drug in it.

In this study, researchers used placebo tablets to help make sure that the participants did not know if they were taking TAF or TDF.

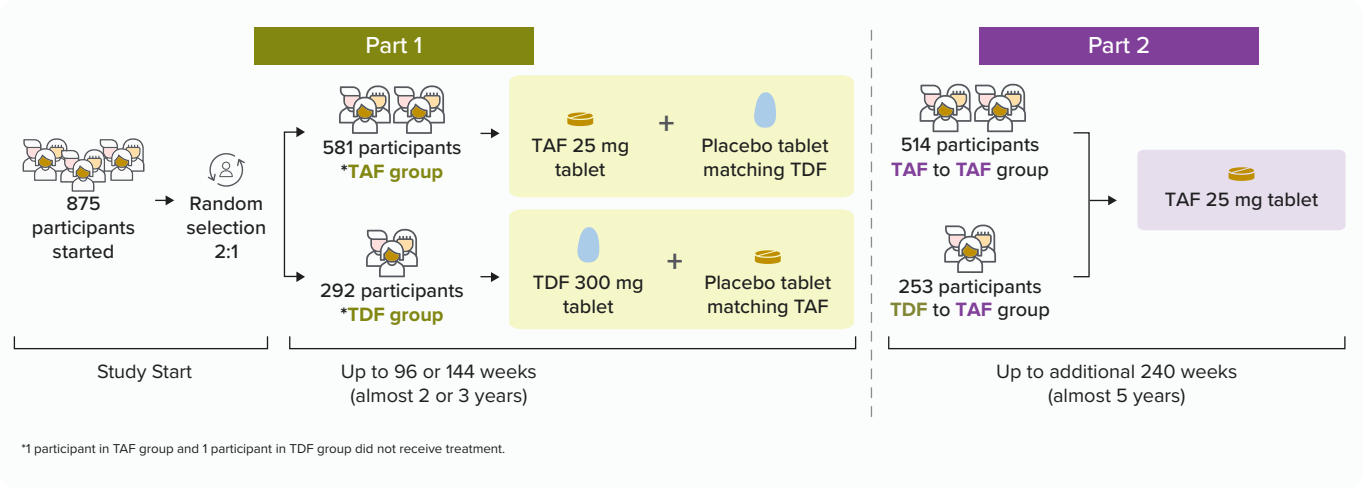
Part 2 of the study was **Open-label**.

Open-label: This means, the participants, doctors, and study staff knew what treatment each participant took.

During this part of the study, all study participants had an option to take TAF for an additional 240 weeks (almost 5 years) as follows:

- **TAF to TAF group:** Participants from TAF group continued to take TAF tablet.
- **TDF to TAF group:** Participants from TDF group switched to take TAF tablet.

Figure 1: The figure below shows what treatment participants took in each part:



At the start of the study, participants were to take treatment up to 96 weeks (almost 2 years) in Part 1. But it was later decided to extend Part 1 for up to 144 weeks (almost 3 years).

By the time this change was introduced, approximately half of the study participants completed Part 1 and moved to Part 2 of the study. The participants who joined late did not receive open-label TAF treatment at Week 96 and continued their Part 1 blinded treatment up to Week 144.

After the end of study treatment, most participants switched to commercially available anti-HBV treatments in their country. Some participants stopped treatment and were followed closely every 4 weeks, for up to 24 weeks (6 months). During these follow-up visits, study doctors checked participants' overall health and assessed if they had any medical events.

What were the results of the study?

This is a summary of the main results from this study. The individual results of each participant might be different and are not in this summary. Researchers wanted to find out if TAF worked as effectively as TDF in keeping participants' HBV infection under control after taking treatment for 48 weeks.

How many participants had viral load suppressed in their blood at Week 48?

HBV viral load is suppressed when participants have HBV DNA levels of less than 29 IU/mL in their blood. Researchers checked participants' HBV DNA levels at the start of the study and at Week 48. This would indicate whether the study participants with CHB infection were responding well to the treatment.

The table below shows the participants with HBV DNA viral suppression in their blood after taking TAF or TDF treatment at Week 48.

Participants Achieving Viral Load Suppression at Week 48	
TAF group (out of 581 participants)	**TDF group** (out of 292 participants)
Number of participants (%)	
371 (64%)	195 (67%)

Overall, no significant differences were noted between these 2 groups in percentage of participants with viral load suppression.

The researchers also checked if TAF has fewer unwanted effects on the kidneys and bones. A detailed presentation of the results for kidney and bone related parameters can be found on the websites listed at the end of this summary.

What side effects did participants have during the study?

For the purpose of this summary, "**side effects**" are defined as unwanted medical events that the study doctors thought might be related to the study treatment.

A side effect is considered "**serious**" if it:

- leads to death,
- is life-threatening,
- considered by the study doctor to be medically important,
- causes lasting problems, or
- requires inpatient hospital care.

The results from several studies are usually needed to help decide if a treatment actually causes a side effect.

Of the 873 participants who started in Part 1, 514 from TAF group and 253 from TDF group entered Part 2 of the study (as shown in Figure 1).

The table below shows how many participants had side effects during the study.

Overall side effects

	Part 1		Part 2	
	TAF group (out of 581 participants)	**TDF group** (out of 292 participants)	**TAF* to TAF group** (out of 514 participants)	**TDF* to TAF group** (out of 253 participants)
	Number of participants (%)			
How many participants had serious side effects?	0	0	4 (under 1%)	0
How many participants had any side effects?	94 (16%)	48 (16%)	28 (5%)	7 (3%)
How many participants stopped taking study treatment because of side effects?	4 (under 1%)	1 (under 1%)	4 (under 1%)	0

* Refers to data from the start of Part 2 up to the end of study treatment.

None of the participants **died** during this study.

The **serious side effects** that occurred during the study were increased level of liver protein in the blood (alanine aminotransferase increased), stroke, bone tissue death, and kidney tumor (1 participant each) in TAF to TAF group of the Part 2.

The table below shows the **top 5 most common side effects** that occurred during the study. There were other side effects, but those occurred in fewer participants. Some participants may have had more than 1 side effect.

The most common side effects were nausea and indigestion. These occurred in about as many participants taking TAF compared to participants taking TDF.

Most common non-serious side effects

	Part 1		Part 2	
	TAF group (out of 581 participants)	**TDF group** (out of 292 participants)	**TAF* to TAF group** (out of 514 participants)	**TDF* to TAF group** (out of 253 participants)
	Number of participants (%)			
Nausea	13 (2%)	9 (3%)	0	1 (under 1%)
Indigestion	6 (1%)	7 (2%)	0	1 (under 1%)
Tiredness (fatigue)	8 (1%)	5 (2%)	0	0
Headache	7 (1%)	5 (2%)	1 (under 1%)	2 (under 1%)
Diarrhea	4 (under 1%)	4 (1%)	2 (under 1%)	1 (under 1%)

* Refers to data from the start of Part 2 up to the end of study treatment.

How has this study helped researchers?

This study helped the researchers learn more about how well and safe the TAF and TDF treatments are in people living with CHB.

The results from several studies are needed to help decide which treatments work and are safe. This summary showed only the main results from this one study. Other studies may provide new information or different results. Always talk to a doctor or a healthcare provider before making any treatment changes.

The results of this study will be used in other studies to learn if TAF could help people who have CHB. Gilead Sciences have ongoing clinical studies with TAF.

Where can I learn more about this study?

You can find more information about this study on the websites listed below. If a full summary of the study results is available, it might be on these websites:

www.clinicaltrials.gov

Once you are on this website, type **NCT01940471** into the search box and click **Search**

www.clinicaltrialsregister.eu

Once you are on the website, click **Home and Search,** then type **2013-000636-10** into the search box and click **Search**

www.gileadclinicaltrials.com

Once you are on the website, type **GS-US-320-0110** into the search box and click **Search Now**

National Clinical Trials Number: NCT01940471
EU Clinical Trials Number: 2013-000636-10

Full Study Title: A Phase 3, Randomized, Double-Blind Study to Evaluate the Safety and Efficacy of Tenofovir Alafenamide (TAF) 25 mg QD versus Tenofovir Disoproxil Fumarate (TDF) 300 mg QD for the Treatment of HBeAg-Positive, Chronic Hepatitis B

For more information about clinical trials, **click here.**

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Thank you

Clinical study participants belong to a large community of people who take part in clinical research around the world. They help researchers answer important health questions and find medical treatments for patients.

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