PLAIN LANGUAGE SUMMARY OF CLINICAL STUDY RESULTS

Study Sponsor: Gilead Sciences

Gilead Study Number: GS-US-380-4458

Date of Study: May 2018 to March 2024

Short Study Title: A Study of Bictegravir/Emtricitabine/Tenofovir Alafenamide (B/F/TAF) versus Dolutegravir (DTG) + Emtricitabine/Tenofovir Disoproxil Fumarate (F/TDF) in People Living with HIV-1 and Hepatitis B Co-Infection Who Haven't Been Treated Before

Study Nickname: ALLIANCE

Date of this Plain Language Summary: October 2024

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 **B/F/TAF**, also known as **bictegravir/emtricitabine/tenofovir alafenamide**, or **GS-9883/F/TAF**, brand name: **Biktarvy**.

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 healthcare 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.

General information of the study

Human immunodeficiency virus (**HIV**) and hepatitis B are two different types of viral infections that affect the body in different ways.

What is HIV?

HIV is a virus that attacks the immune system (the body's defense system) and makes it more likely for people to get sick. HIV-1 is a type of HIV. There is no cure for HIV-1. Once people get it, they have it for life until the researchers find a cure for HIV-1. If HIV-1 is not treated, it can lead to acquired immunodeficiency syndrome (AIDS). If a person with AIDS is not treated, they may die. However, HIV-1 can be controlled with proper treatment.

What is hepatitis B?

Hepatitis B is an infection of the liver. It is caused by a virus called hepatitis B virus (HBV). 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. It can be short-term or long-term. The long-term hepatitis B may cause liver problems like liver fibrosis (scarring of the liver), liver cirrhosis (severe scarring of the liver), and liver cancer.

When someone has both HIV-1 and hepatitis B co-infection (both viral infections at the same time), their health is at a greater risk. It gets hard for the body to keep a check on HBV in the presence of HIV-1. This can damage the liver more quickly, making it more likely to develop liver problems. To stay healthy, people with HIV-1 and HBV co-infection need special care to protect their liver and immune system.

B/F/TAF is a pill (tablet) that combines three medicines—bictegravir (B), emtricitabine (F), and tenofovir alafenamide (TAF) into one single tablet. It is an approved medicine for the treatment of HIV-1.

There is another approved treatment regimen available for HIV-1 that includes dolutegravir (DTG) along with a combination of emtricitabine (F) and tenofovir disoproxil fumarate (TDF). In this study, the researchers compared investigational drug B/F/TAF with DTG + F/TDF in treating people living with HIV-1 and HBV co-infection.

This was a Phase 3 study. This means that researchers looked at how B/F/TAF worked in a large group of people living with HIV-1 and HBV co-infection.

What was the purpose of the study?

The purpose of this study was to test the effectiveness of B/F/TAF single tablet compared to DTG + F/TDF in participants living with HIV-1 and hepatitis B co-infection. This included participants who either did not take any treatment or took it for a very short time for HIV-1 and HBV co-infection.

Most HIV-1 and HBV treatments stop the viruses from making copies of themselves and thus stop them from infecting new cells. If an HIV-1 or HBV treatment works, the amount of the virus in a person's blood (**viral load**) drops to a very low level. When the viral load is suppressed, people can live long and healthy lives.

Viral load: It is the amount of virus in the blood, measured by viral **RNA** or **DNA** levels. It shows the level of viral infection in the body.
RNA stands for ribonucleic acid; **DNA** stands for deoxyribonucleic acid. They are the essential building blocks of all living organisms. The HIV-1 RNA and HBV DNA play a role in their growth and replication in the infected cells.

- **HIV-1 viral load is suppressed when HIV-1 RNA levels are below 50 copies per milliliter (mL) of blood.**
- **HBV viral load is suppressed when HBV DNA levels are below 29 international units (IU) per mL of blood.**

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

- How many participants have their **HIV-1 viral load suppressed** after 48 weeks of treatment, if any?
- How many participants have their **HBV viral load suppressed** after 48 weeks of treatment, if any?
- What side effects did participants have during the study, if any?

Who took part in the study?

- **244** participants living with HIV-1 who were co-infected with HBV in **12** countries around the world took part.
- **1** participant left the study before taking treatment.

People could take part in the study if they:

Were at least 18 years of age

Had confirmed HIV-1 and HBV infections

Did not take any prior treatment for HIV-1 or HBV (or took for few days, less than 10 days for HIV-1 or less than 3 months for HBV)

The participants enrolled in the study were between the ages of **19** to **66** years.

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

Thailand	94 **(39%)**	Japan	8 **(3%)**
China	56 **(23%)**	Spain	7 **(3%)**
Malaysia	37 **(15%)**	Hong Kong	5 **(2%)**
Taiwan	12 **(5%)**	United States	3 **(1%)**
Dominican Republic	10 **(4%)**	South Korea	2 **(less than 1%)**
Turkey	9 **(4%)**	Puerto Rico	1 **(less than 1%)**

Race of participants is shown below (Number (%) of participants).

Asian	215 **(88%)**	Black or African American	8 **(3%)**
White	19 **(8%)**	Other or more than one race	2 **(less than 1%)**

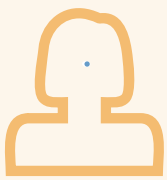
Ethnicity of participants is shown below (Number (%) of participants).

Not Hispanic Or Latino	227 **(93%)**	Hispanic Or Latino	17 **(7%)**

Participant breakdown by sex
Number (%) of participants

Male
233 **(95%)**

Female
11 **(5%)**



What happened during the study?

This study was done in **2 parts**: **Part 1** and **Part 2**.

Part 1

Part 1 of the study was **randomized** and **double-blind**.

Randomized: This means the researchers used a computer program to put participants into treatment groups by chance. This helped make sure the treatments were chosen fairly. In this study, participants had an equal chance of taking B/F/TAF or DTG + F/TDF. This is called 1:1 randomization.

Double-blind: This means none of the participants, doctors or other study staff, and the sponsor personnel directly involved in conducting the study knew what treatment each participant took. This was done to ensure the study results were not influenced in any way. To address any safety concerns, the safety measures were in place.

During this part of the study, the participants took the following treatment for 96 weeks (almost 2 years):

B/F/TAF group:	Participants took a B/F/TAF tablet and 2 **placebo** tablets once daily. One placebo tablet looked like DTG, while the other looked like F/TDF.
DTG + F/TDF group:	Participants took 1 tablet each of DTG, F/TDF, and placebo once daily. The placebo tablet looked like B/F/TAF.

Placebo: A placebo looks like a treatment but does not have active drug in it.

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

Part 2

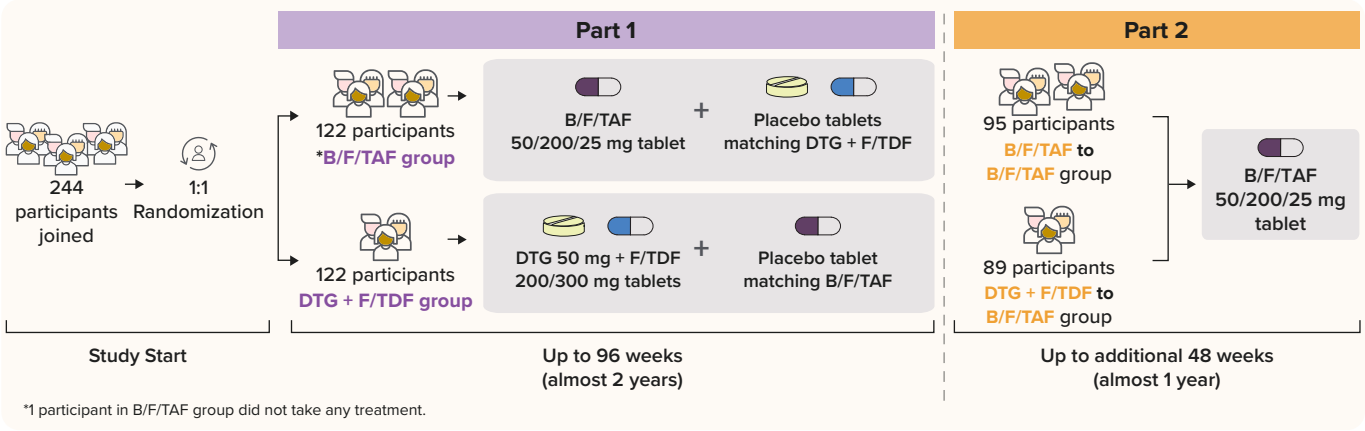
Part 2 of the study was **open-label**.

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 B/F/TAF for an additional 48 weeks (almost 1 year) or until it was accessible to participants through an access program or until the sponsor decided to stop the study in that country, whichever was earlier.

B/F/TAF to B/F/TAF group:	Participants from B/F/TAF group continued to take B/F/TAF tablet once daily.
DTG + F/TDF to B/F/TAF group:	Participants from DTG + F/TDF group switched to take B/F/TAF tablet once daily.

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



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. A detailed presentation of the results can be found on the websites listed at the end of this summary.

Of 244 participants, 1 participant left the study before taking any study treatment in the B/F/TAF group. In the same group, 2 participants did not have HIV-1 RNA and HBV DNA levels information after taking the treatment. So, the results in this section only include 241 participants. This includes 119 participants in B/F/TAF group and 122 participants in DTG + F/TDF group.

Researchers checked participants' HIV-1 RNA levels and HBV DNA levels at the start of the study and at Week 48. This would indicate whether the study participants were responding to the treatment.

How many participants have their HIV-1 viral load suppressed after 48 weeks of treatment, if any?

The table below shows the participants with HIV-1 RNA viral load suppression after taking B/F/TAF or DTG + F/TDF treatment at Week 48.

Participants Who Had HIV-1 Viral Load Suppression at Week 48	
B/F/TAF group (out of 119 participants)	**DTG + F/TDF group** (out of 122 participants)
Number of participants (%)	
113 (95%)	111 (91%)

Overall, both groups had similar number of participants with HIV-1 viral load suppression.

How many participants have their HBV viral load suppressed after 48 weeks of treatment, if any?

The table below shows the participants with HBV DNA viral load suppression after taking B/F/TAF or DTG + F/TDF treatment at Week 48.

Participants Who Had HBV Viral Load Suppression at Week 48	
B/F/TAF group (out of 119 participants)	**DTG + F/TDF group** (out of 122 participants)
Number of participants (%)	
75 (63%)	53 (43%)

Overall, greater number of participants who took B/F/TAF had HBV viral load suppression than the participants who took DTG + F/TDF.

What side effects did participants have during the study?

Unwanted medical events can happen to the study participants when they take study treatments. In this summary, **"side effects"** are defined as unwanted medical events that the study doctors thought might be caused by the study treatment.

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

A side effect is considered "serious" if it:

- results in death
- is life-threatening
- is considered by the study doctor to be medically important
- causes lasting problems
- requires hospital care
- causes a birth defect

Of 244 participants, 1 participant left the study before taking any study treatment in the B/F/TAF group. So, the results in this section only include 243 participants. This includes 121 participants in B/F/TAF group and 122 participants in DTG + F/TDF group.

Of the 243 participants who started in Part 1, 95 participants from B/F/TAF group and 89 participants from DTG + F/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		
	B/F/TAF (out of 121 participants)	**DTG + F/TDF** (out of 122 participants)	**B/F/TAF to B/F/TAF** (out of 95 participants)	**DTG + F/TDF to B/F/TAF** (out of 89 participants)	**Total** (out of 243 participants)
Overall side effects	Number of participants (%)				
Serious side effects	1 (less than 1%)	0	0	0	1 (less than 1%)
Side effects	37 (31%)	36 (30%)	12 (13%)	17 (19%)	80 (33%)

None of the participants died or left the study treatment due to any side effects.

What were the serious side effects?

1 out of 121 (less than 1%) participants in the B/F/TAF group in Part 1, had a serious side effect of inflammation of the outer layer of brain or spinal cord due to a bacterial infection (meningitis cryptococcal).
None of the participants in the DTG + F/TDF group had any serious side effects.

What were the non-serious side effects?

The table below shows the **top 10 most common non-serious side effects** that occurred during the study. These side effects were not serious in nature and did not meet the definition of 'serious side effects' mentioned in the section above in this summary.

Most Common Non-serious Side Effects

	Part 1		Part 2		
	B/F/TAF (out of 121 participants)	**DTG + F/TDF** (out of 122 participants)	**B/F/TAF to B/F/TAF** (out of 95 participants)	**DTG + F/TDF to B/F/TAF** (out of 89 participants)	**Total** (out of 243 participants)
Non-serious side effects	Number of participants (%)				
Weight increased	9 (7%)	9 (7%)	3 (3%)	4 (4%)	19 (8%)
Liver enzyme increased (Alanine aminotransferase increased)	3 (2%)	8 (7%)	1 (1%)	2 (2%)	13 (5%)
Abnormal weight gain	3 (2%)	3 (2%)	3 (3%)	4 (4%)	9 (4%)
Liver enzyme increased (Aspartate aminotransferase increased)	3 (2%)	4 (3%)	1 (1%)	0	7 (3%)
Protein in urine (Proteinuria)	3 (2%)	2 (2%)	0	2 (2%)	7 (3%)
Headache	4 (3%)	2 (2%)	0	0	6 (2%)
Feeling sick to the stomach (Nausea)	1 (less than 1%)	5 (4%)	0	0	6 (2%)
A sensation of spinning around and losing one's balance (Dizziness)	2 (2%	3 (2%)	0	0	5 (2%)
High level of cholesterol and/or fats in the blood (Dyslipidaemia)	3 (2%)	1 (less than 1%)	1 (1%)	1 (1%)	5 (2%)
High level of bad cholesterol in the blood (Low density lipoprotein increased)	1 (less than 1%)	2 (2%)	0	3 (3%)	5 (2%)

There were other non-serious side effects, but those occurred in fewer participants. Some participants may have had more than 1 non-serious side effect.

How has this study helped researchers?

The researchers learned more about the effectiveness and safety of B/F/TAF and how it worked in people living with HIV-1 and HBV co-infection. The results from several studies are needed to help decide which treatments work and are safe. This summary shows only the main results from this one study. Other studies may provide new information or different results.

Gilead Sciences has ongoing studies and plans to have further clinical studies with B/F/TAF.

Where can I learn more about this study?

You can find more information about this study on the websites listed below.

Organization (Website)	Study Identifier
European Medicines Agency (www.clinicaltrialsregister.eu)	EudraCT: 2018-000926-79
United States National Institutes of Health (NIH) (www.clinicaltrials.gov)	ClinicalTrials.gov ID: NCT03547908
www.gileadclinicaltrials.com	GS-US-380-4458

Please note that information on this/these websites may be presented in a different way from this summary.

Full Study Title: A Phase 3, Randomized, Double-Blind Study to Evaluate the Safety and Efficacy of Fixed Dose Combination of Bictegravir/Emtricitabine/Tenofovir Alafenamide Versus Dolutegravir + Emtricitabine/Tenofovir Disoproxil Fumarate in Treatment Naïve, HIV-1 and Hepatitis B Co-Infected Adults (Alliance)

To learn more about clinical trials in general,
please visit this page on www.clinicaltrials.gov website

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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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