CLINICAL STUDY RESULTS SUMMARY

Study Sponsor: Gilead Sciences

Gilead Protocol Number: GS-US-493-5342

Dates of Trial: January 2019 to October 2021

Short Study Title: Study of Novel Hepatitis B Virus (HBV) Combination Therapies in Adults with Chronic Hepatitis B (CHB)

Thank you

Thank you to the participants who took part in the clinical study for **LDV/SOF, nivolumab, SLGN,** and **GS-4224.**

Gilead Sciences sponsored this study. We believe it is important to share the results with the 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 before making any treatment changes.

Date of this Report: September 2022

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

What is Chronic Hepatitis B?

Hepatitis B is a liver infection caused by a virus, called hepatitis B virus (HBV). There are about 250 to 350 million people living with hepatitis B in the world. Hepatitis B is most commonly spread from mother to child during birth, as well as through contact with blood or other body fluids of someone infected with hepatitis B. Most infected adults completely recover.

Chronic hepatitis B (CHB) is a liver disease, which is one of the leading causes of liver scarring, failure, and cancer. CHB requires lifelong treatment. Blood tests that look for specific pieces of virus called **hepatitis B surface antigen (HBsAg)** and **hepatitis B e antigen (HBeAg)** are used to diagnose hepatitis B and CHB. A patient is likely to have CHB when they test positive for HBsAg 2 times at least 6 months apart.

HBV viral load is based on the HBV **DNA in the blood.** It is said to be suppressed if participants had a HBV DNA level of less than 20 international units per milliliter (IU/mL). Current treatments for CHB keep the levels of virus in the body low but do not remove the virus and HBsAg from the body. Lowering HBsAg levels could allow some people with CHB to stop taking their medicines and live with HBV without fear of having problems or dying from this disease.

DNA, which stands for **deoxyribonucleic acid,** is an essential building block in all living organisms. DNA is housed inside all the cells of the body. It provides the information from which individual proteins are made. It also plays a role in the growth and replication of viruses in the human body.

LDV/SOF, nivolumab, SLGN and **GS-4224** were chosen to be studied in combination because of the need for new treatment options for CHB.

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

- How many participants had a desired level of decrease of HBsAg in their blood 8 weeks after stopping treatment?
- How many participants had unwanted medical events during the study?
- What side effects did participants have during the study, if any?

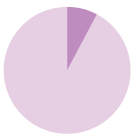
Who took part in the study?

In total, **51 participants** living with CHB in **Hong Kong** and **New Zealand** took part in this study.

People took part in the study if they:

- Were between the age of 18 to 65 years old
- Tested negative for HBeAg and had HBV DNA of less than 20 IU/mL at the start of the study
- Were taking certain available treatments for CHB for at least 6 months

Number of participants (%) **from each country**

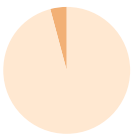


- New Zealand **47 (92%)**
- Hong Kong **4 (8%)**

Number of participants (%) **by sex**

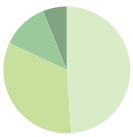
- Male **41 (80%)**
- Female **10 (20%)**

Number of participants (%) **by age**



- 18 to 64 years **49 (96%)**
- 65 years or older **2 (4%)**

Number of participants (%) **by race**



- Asian **25 (49%)**
- Native Hawaiian or Pacific Islander **17 (33%)**
- White **6 (12%)**
- Other **3 (6%)**

Number of participants (%) **by ethnicity**

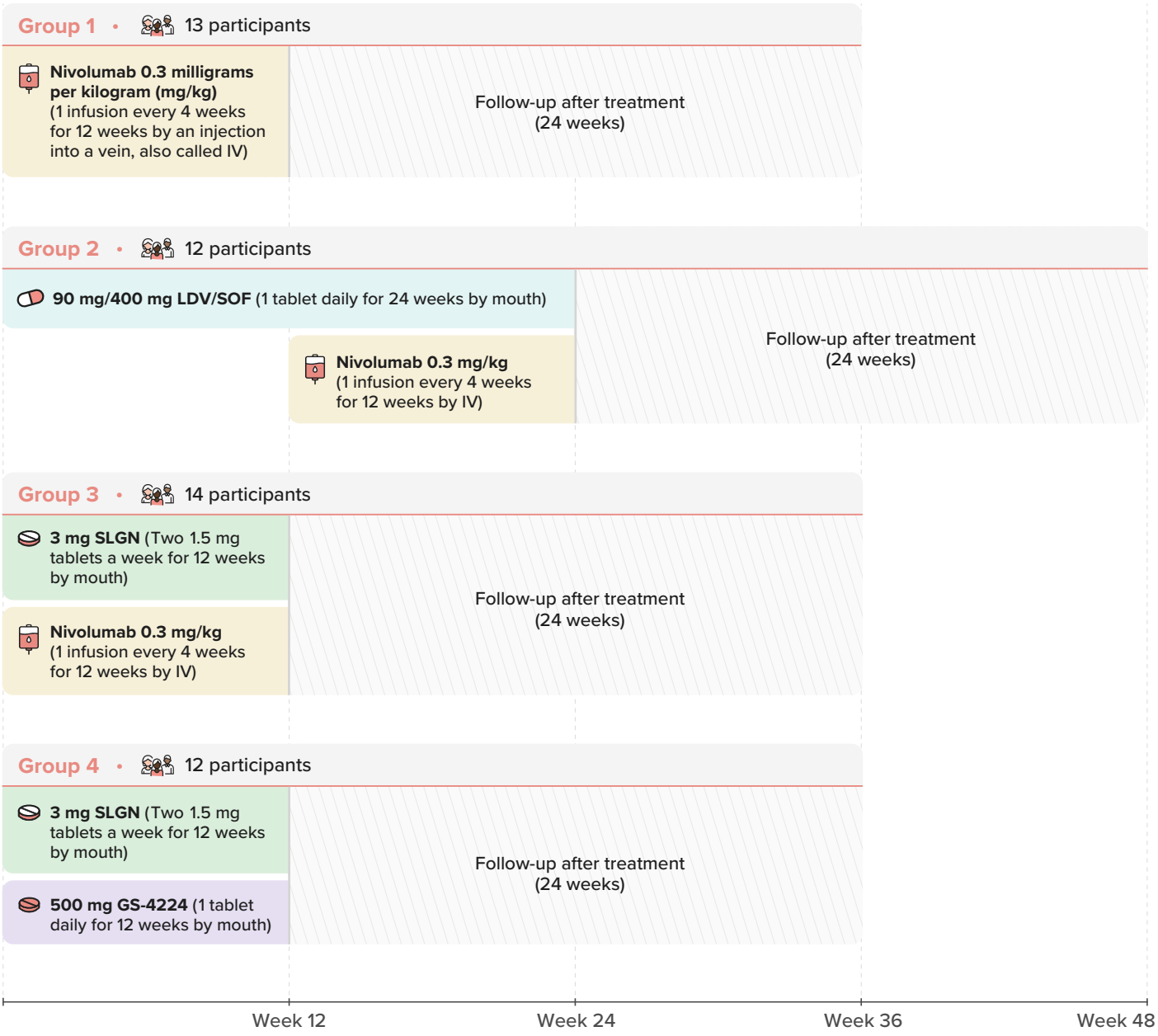
- Not Hispanic or Latino **49 (96%)**
- Hispanic or Latino **1 (2%)**
- Unknown **1 (2%)**

What happened during the study?

At the start of the study, the researchers checked to make sure each participant was a good fit for the study. They checked the participants' health and medical history.

In this study, participants were placed into one of 4 treatment groups. Each participant knew what treatments they were taking, and the doctors and study staff also knew.

The figure below shows how the study was done.



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.

How many participants had a desired level of decrease of HBsAg in their blood 8 weeks after stopping treatment?

Researchers wanted to see if there was a desired level of decrease of HBsAg because it would signal that the CHB infection was responding well to treatment.

Overall, there were no significant differences between the 4 groups in the number of participants who had a desired level of decrease of HBsAg.

The table below shows the number of participants with a desired level of decrease of HBsAg in their blood.

	Group 1 (out of 13 participants)	**Group 2** (out of 12 participants)	**Group 3** (out of 14 participants)	**Group 4** (out of 12 participants)
	Number of participants (%)			
Number of participants with a desired level of decrease of HBsAg	0	1 (9%)	1 (8%)	0

How many participants had unwanted medical events during the study?

The study doctors also kept track of any unwanted medical events that the participants had.

A medical event is any unwanted sign or symptom that participants have during a study. Study doctors keep track of all the unwanted medical events that happen in a study, even if they think they might not be caused by or related to the study treatment.

The table below shows the number of participants who had any unwanted medical events during the study:

	Group 1 (out of 13 participants)	**Group 2** (out of 12 participants)	**Group 3** (out of 14 participants)	**Group 4** (out of 12 participants)	**Total** (out of 51 participants)
	Number of participants (%)				
Number of participants with any unwanted medical events	12 (92%)	10 (83%)	13 (93%)	9 (75%)	44 (86%)

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 study treatment. A side effect is considered **serious** if it results in death, is life-threatening, or considered by the study doctor to be medically important. Side effects are also serious if they cause lasting problems or require hospital care.

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

Safety results for Group 2 have been separated into 2 parts. Part 1 was when participants were only taking **LDV/SOF** and Part 2 was when they were taking both **LDV/SOF** and **nivolumab.**

None of the participants had any serious side effects. No participants died from side effects. The table below shows how many participants had non-serious side effects during the study.

Overall side effects						
	Group 1 (out of 13 participants)	**Group 2 PART 1** (out of 12 participants)	**Group 2 PART 2** (out of 12 participants)	**Group 3** (out of 14 participants)	**Group 4** (out of 12 participants)	**Total** (out of 51 participants)
	Number of participants (%)					
How many participants had any side effects?	2 (15%)	3 (25%)	2 (17%)	10 (71%)	7 (58%)	24 (47%)
How many participants stopped taking study treatment because of side effects?	0	0	0	0	1 (8%)	1 (2%)

The table below shows the most common side effects that occurred in at least 2 participants in any group 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 feeling sick to the stomach, diarrhea, and vomiting.

Most common side effects						
	Group 1 (out of 13 participants)	**Group 2 PART 1** (out of 12 participants)	**Group 2 PART 2** (out of 12 participants)	**Group 3** (out of 14 participants)	**Group 4** (out of 12 participants)	**Total** (out of 51 participants)
	Number of participants (%)					
Feeling sick to the stomach (nausea)	1 (8%)	0	0	6 (43%)	3 (25%)	10 (20%)
Diarrhea	0	0	0	2 (14%)	5 (42%)	7 (14%)
Vomiting	0	0	0	5 (36%)	1 (8%)	6 (12%)
Belly discomfort	0	0	0	1 (7%)	4 (33%)	5 (10%)
Extreme tiredness (fatigue)	0	1 (8%)	0	2 (14%)	1 (8%)	4 (8%)
Headache	0	1 (8%)	1 (8%)	2 (14%)	0	4 (8%)
Feeling less hungry	0	0	0	0	2 (17%)	2 (4%)

How has this study helped researchers?

The researchers learned more about the safety of **LDV/SOF, nivolumab, SLGN,** and **GS-4224** and how well they work in people living with CHB.

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. Always talk to a doctor before making any treatment changes.

The results of this study may be used in other studies to help people who have CHB.

Gilead Sciences does not plan to have more clinical studies with **GS-4224** and **LDV/SOF**, but are planning studies with **nivolumab** and **SLGN**.

Where can I learn more about this study?

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

https://www.anzctr.org.au/

Once you are on the website, click on **Search Now** under **Searching for a trial?** and type **ACTRN12618001843246p** into the search box and click on search icon. Once the record appears, click on **View full record** or check the box **select for download**

www.gileadclinicaltrials.com

Once you are on the website, type **GS-US-493-5342** into the search box and click **Search Now**

Australian New Zealand Clinical Trials Registry (ANZCTR) Number: ACTRN12618001843246p

Full Study Title: A Phase 1b, Open-label, Proof of Concept Study to Evaluate the Safety and Efficacy of Novel Hepatitis B Virus (HBV) Combination Therapies in Chronic Hepatitis B (CHB) Subjects

For more information about clinical trials, click here.

Gilead Sciences sponsored this study and has its headquarters at 333 Lakeside Drive, Foster City, CA 94404, USA.

The email address for the Gilead Clinical Study Information Center is GileadClinicalTrials@gilead.com

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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