PLAIN LANGUAGE SUMMARY OF CLINICAL STUDY RESULTS

Study Sponsor: Gilead Sciences (MYR GmBH was initial sponsor, later acquired by Gilead)

Gilead Study Number: MYR301

Date of Study: April 2019 to August 2024

Short Study Title: Study of Bulevirtide in Adults With Chronic Hepatitis Delta

Date of this Plain Language Summary: November 2025

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

Thank you

Thank you to the participants who contributed to the clinical study of **bulevirtide**, also known as **GS-4438**, brand name: **Hepcludex** (in Europe)**, Myrcludex B** (in Russia).

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.

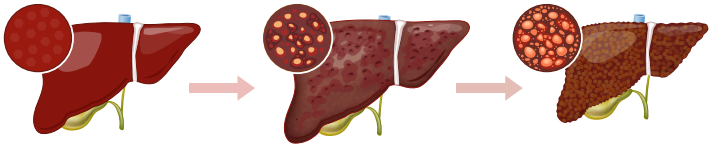
General information about the study

What is Chronic Hepatitis Delta?

Hepatitis delta, also known as **hepatitis D virus (HDV)** infection, is a liver disease. It is considered the most severe form of viral hepatitis. HDV needs support from another hepatitis virus to make copies of itself. Hence, it occurs in people who are already infected with **hepatitis B virus (HBV)**. HDV spreads through contact with the blood or other body fluids of an infected person.

For most people affected by HDV, the infection becomes chronic (a long-term illness). **Chronic HDV** infection may cause scarring of the liver, called liver fibrosis. Continuous liver damage worsens the scarring and leads to permanent liver damage, called liver cirrhosis. Chronic HDV infection also increases the risk of developing liver cancer.

The graphics below show healthy liver versus liver with chronic HDV infection and cirrhosis.



A common way to check for chronic HDV infection is through a blood test that looks for HDV RNA (ribonucleic acid)—the genetic material of the virus. Most treatments for HDV aim to lower the amount of HDV RNA in the body. The researchers also check levels of liver enzymes like—ALT (alanine aminotransferase) and AST (aspartate aminotransferase) through blood tests to assess the overall liver health. By lowering the virus level, the treatments help improve liver health and keep these liver enzyme levels within the normal range.

Bulevirtide 2 mg is an approved treatment for chronic HDV infection. This study looked at how bulevirtide worked and how safe it was over the long term, for people with chronic HDV infection.

This was a **Phase 3** clinical study, meaning it involved a larger group of people to test bulevirtide's effectiveness and safety.

What was the purpose of the study?

The purpose of the study was to find out how well different doses of bulevirtide worked in people with chronic HDV infection who received treatment for 48 weeks (almost 1 year), compared to those who did not receive the treatment during that time [called **Delayed Treatment (DT)** group].

Participants in the **DT** group did not receive bulevirtide for the first 48 weeks. This helped researchers compare results between those who started treatment right away and those who waited, to see how effective the treatment was.

The main question the researchers wanted to answer in this study was:

- How many participants had **combined response** after 48 weeks?

Combined response means they met 2 conditions at the same time:

- The amount of HDV RNA in their blood was either not detectable or had significantly dropped (a decrease of 2 $\log_{10}$ IU/ml in HDV RNA levels, which is a 99% decrease) from the start of the study.
- Their liver enzyme ALT levels—returned to normal.

Researchers also wanted to know the side effects that participants had during the study.

Who took part in the study?

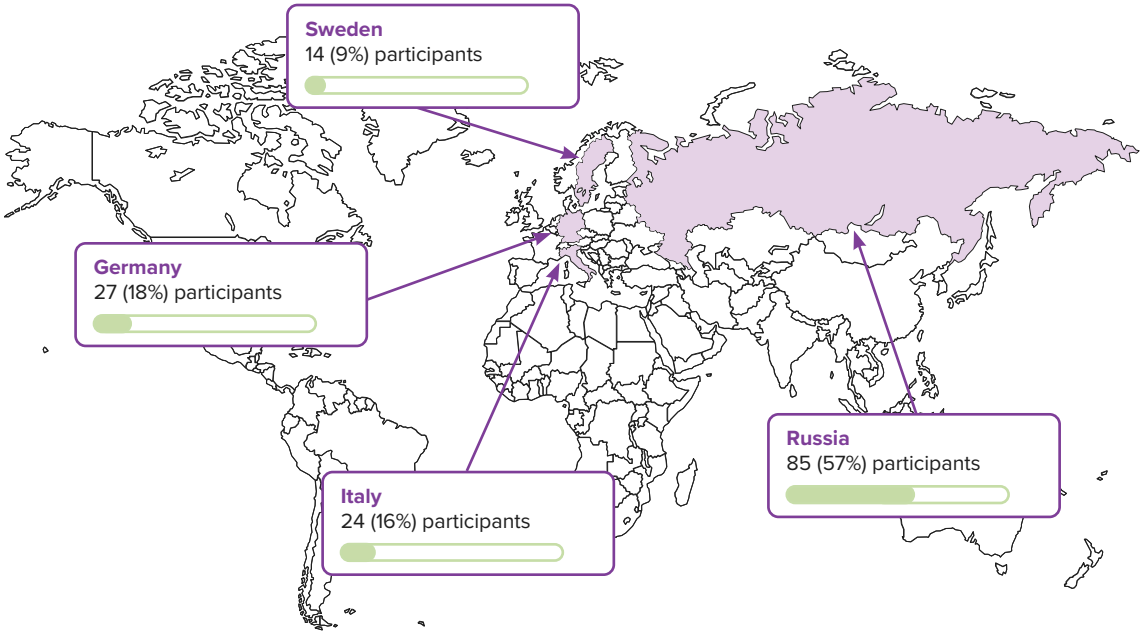
- **150** participants living with chronic HDV infection from **Germany**, **Italy**, **Russia**, and **Sweden** took part in this study.

People could take part in the study if they:

- Were at least 18 years of age
- Had confirmed chronic HDV infection
- Had a measurable amount of HDV RNA in their blood
- Had increased levels of ALT in their blood (more than 1 to less than 10 times of the upper limit of normal)

The study participants were between the ages of **19** and **62** years.

The participants from each country are shown below (Number (%) of participants).



The race of participants is shown below (Number (%) of participants).

White	124 **(83%)**
Asian	25 **(17%)**
Black or African American	1 **(below 1%)**

Sex of participants is shown below
Number (%) of participants

Male
86 **(57%)**

Female
64 **(43%)**

What happened during the study?

This was an **open-label**, **parallel group**, and **randomized** study.

Open-label means the participant or caregiver, the doctors, and the study staff knew which treatment each participant was receiving.

Parallel group means participants were assigned to different groups. All groups began with the assigned treatment upon joining the study: bulevirtide 2 mg, 10 mg, or delayed treatment with bulevirtide 10 mg.

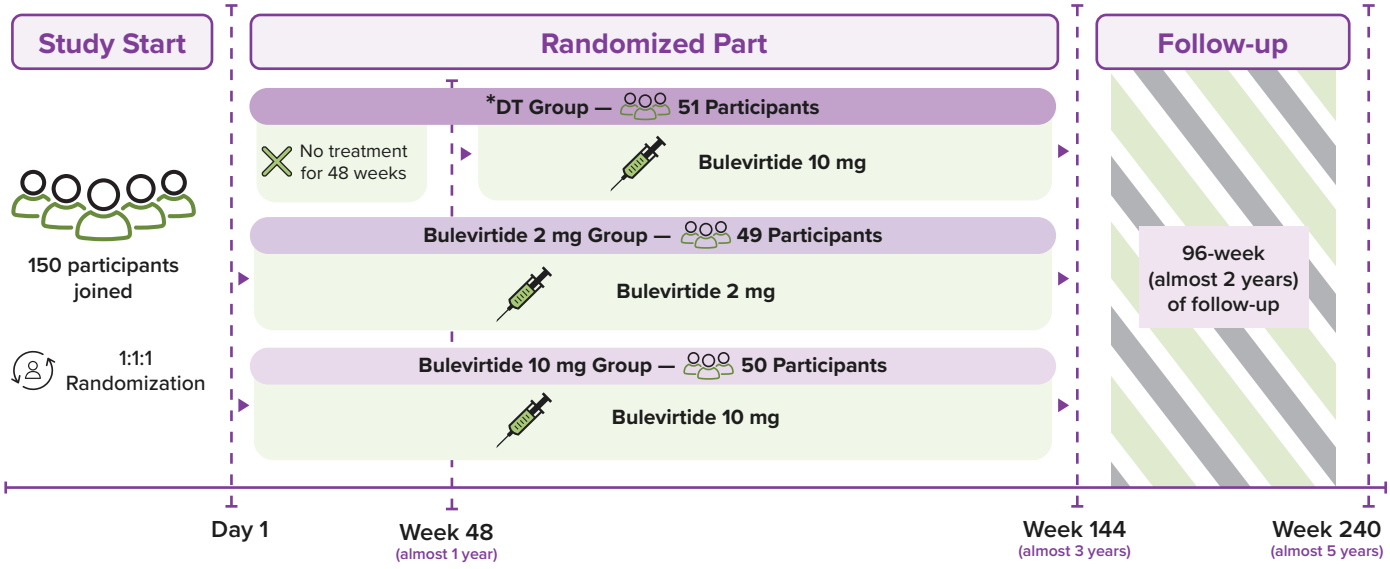
Randomized means the researchers used a computer program to assign participants to different treatment groups by chance. This helped make sure the treatments were compared fairly. In this study, each participant had an equal chance of getting placed in 1 of the 3 groups: bulevirtide 2 mg, bulevirtide 10 mg, or a delayed start with bulevirtide 10 mg. This is called 1:1:1 randomization.

Participants were placed in 1 of the 3 groups, mentioned below. Bulevirtide was given as a daily injection under the skin (subcutaneous, SC injection).

- ***DT Group (No treatment for 48 weeks »» Bulevirtide 10 mg; 51 participants):** Participants received no treatment for the first 48 weeks. After 48 weeks, they received bulevirtide 10 mg daily SC injection for 96 weeks (almost 2 years).
- **Bulevirtide 2 mg Group (49 participants):** Participants received immediate treatment with bulevirtide 2 mg daily SC injection for 144 weeks (almost 3 years).
- **Bulevirtide 10 mg Group (50 participants):** Participants received immediate treatment with bulevirtide 10 mg daily SC injection for 144 weeks (almost 3 years).

All groups underwent an additional 96-week follow-up, after treatment—from Week 144 to Week 240—bringing the total study duration to nearly 5 years from its start. During the follow-up period, the participants did not receive bulevirtide treatment.

The graphics below show the treatment plan.



*In DT group, 51 participants started, 50 continued with treatment at Week 48.

Participants visited the clinic during the treatment period and the follow-up visits. During these visits, the study doctors took samples to measure the amount of HDV RNA and ALT levels in participants' blood. Participants were also checked for any medical events and other health problems.

Out of 150 participants in the study, 149 received treatment and 138 stayed on the treatment till Week 144. By the end of the study at Week 240, 86 participants had completed all parts, including the follow-up after the treatment period. A total of 64 participants left the study early, mostly because they chose to stop participation, had medical problems, or their condition got worse.

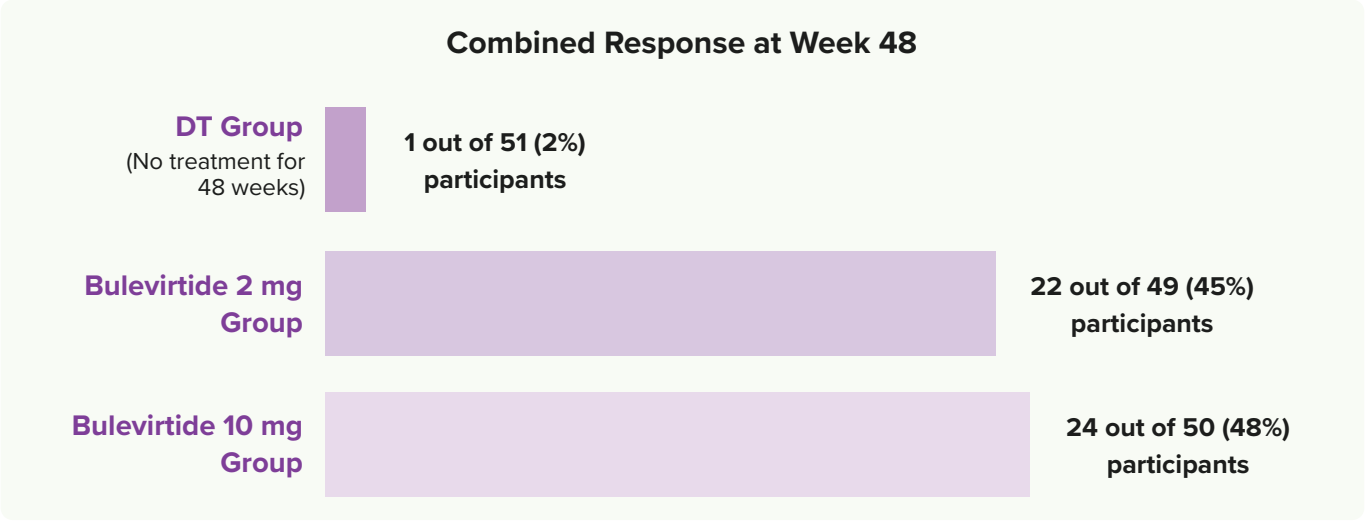
What were the results of the study?

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.

How many participants had combined response after 48 weeks?

Researchers compared the combined response in participants who received 2 mg and 10 mg doses of bulevirtide, with those in the DT group.

The chart below shows the number (%) of participants who had combined response at Week 48.



A higher percentage of participants achieved combined response in the bulevirtide groups: 45% in the 2 mg group and 48% in 10 mg group, compared to only 2% in the DT group.

What side effects did participants have during the study?

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

The results from several studies are usually needed to help decide if a study drug 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

The results below show the side effects that occurred from the start of treatment through Week 240, including both the treatment and follow-up periods.

- **Treatment Period (Start of treatment to Week 144)**

  Bulevirtide treatment for DT group started at Week 48. 1 participant in this group did not receive treatment. Results during bulevirtide treatment period were reported for 149 participants: 50 participants in DT group, 49 in Bulevirtide 2 mg group, and 50 in Bulevirtide 10 mg group.

- **Follow-up Period (Week 144 to Week 240)**

  Results during this period were reported for 142 participants: 49 in DT group, 46 in Bulevirtide 2 mg group, and 47 in Bulevirtide 10 mg group. These participants had at least one safety assessment after receiving their last dose of bulevirtide during the study treatment period.

The table below shows the side effects that occurred during the study.

Overall Side Effects

	Treatment Period (Start of Treatment to Week 144)			Follow-up Period (Week 144 to Week 240)			
	*DT Group No treatment for 48 Weeks »» Bulevirtide 10 mg (Out of 50 participants)	Bulevirtide 2 mg Group (Out of 49 participants)	Bulevirtide 10 mg Group (Out of 50 participants)	DT Group No treatment for 48 Weeks »» Bulevirtide 10 mg (Out of 49 participants)	Bulevirtide 2 mg Group (Out of 46 participants)	Bulevirtide 10 mg Group (Out of 47 participants)	Total (Out of 150 participants)
	Number (%) of participants						
How many participants had **any** side effects?	23 (46%)	27 (55%)	37 (74%)	3 (6%)	4 (9%)	6 (13%)	89 (59%)
How many participants had **any serious** side effects?	0	0	0	1 (2%)	0	1 (2%)	2 (1%)

*Side effects for DT Group are reported from Week 48 to Week 144.

- **No participant died due to any side effect.**
- **No participant stopped taking bulevirtide due to any side effect.**

What were the serious side effects?

No serious side effects were reported during the treatment period (start of treatment to Week 144). However, 2 serious side effects were reported during the follow-up period (Week 144 to Week 240), when participants were no longer receiving bulevirtide treatment:

- 1 participant from DT group had an abnormal liver function (hepatic function abnormal).
- 1 participant from Bulevirtide 10 mg group had liver enzyme increased (transaminases increased).

The study doctors thought these side effects might be signs that HDV, the original illness, had come back after stopping bulevirtide treatment.

What were the non-serious side effects?

The table below shows the most common non-serious side effects reported in **at least 5%** of total participants, 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.

Non-Serious Side Effects

	Treatment Period (Start of Treatment to Week 144)			Follow-up Period (Week 144 to Week 240)			
	*DT Group No treatment for 48 Weeks »» Bulevirtide 10 mg (Out of 50 participants)	Bulevirtide 2 mg Group (Out of 49 participants)	Bulevirtide 10 mg Group (Out of 50 participants)	DT Group No treatment for 48 Weeks »» Bulevirtide 10 mg (Out of 49 participants)	Bulevirtide 2 mg Group (Out of 46 participants)	Bulevirtide 10 mg Group (Out of 47 participants)	Total (Out of 150 participants)
	Number (%) of participants						
Itching (Pruritus)	0	5 (10%)	8 (16%)	0	0	0	13 (9%)
Vitamin D deficiency	2 (4%)	3 (6%)	7 (14%)	1 (2%)	0	0	13 (9%)
Headache	3 (6%)	3 (6%)	5 (10%)	0	0	1 (2%)	12 (8%)
Inflammation in or damage to the tissue surrounding where a drug was injected (Injection site reaction)	3 (6%)	3 (6%)	6 (12%)	0	0	0	12 (8%)
Extreme tiredness (Fatigue)	3 (6%)	3 (6%)	5 (10%)	0	0	0	11 (7%)
Abnormal redness at injection site (Injection site erythema)	2 (4%)	3 (6%)	5 (10%)	0	0	0	10 (7%)
Liver enzyme (ALT) increased	0	1 (2%)	2 (4%)	3 (6%)	2 (4%)	0	8 (5%)
Feeling sick to the stomach (Nausea)	1 (2%)	3 (6%)	4 (8%)	0	0	0	8 (5%)
A higher than normal level of eosinophils: a type of disease-fighting white blood cell (Eosinophilia)	0	4 (8%)	3 (6%)	0	0	0	7 (5%)

*Side effects for DT Group are reported from Week 48 to Week 144.

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 long-term safety and effectiveness of different doses of bulevirtide in participants with chronic HDV 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 clinical studies with bulevirtide.

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 Number: 2019-001213-17
United States National Institutes of Health (NIH) www.clinicaltrials.gov	ClinicalTrials.gov Number: NCT03852719
Gilead Website www.gileadclinicaltrials.com	MYR301

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

Full Study Title: A Multicenter, Open-label, Randomized Phase 3 Clinical Study to Assess Efficacy and Safety of Bulevirtide in Patients with Chronic Hepatitis Delta

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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