CLINICAL TRIAL RESULTS

A Study to Learn More About the Safety of BIIB100 in Adults with Amyotrophic Lateral Sclerosis

- **Drug Studied:** BIIB100
- **Protocol #:** 261AS101
- **Study Dates:**
  - **Start:** 30 May 2019
  - **End:** 21 June 2021

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Thank you!

Thank you to the participants who took part in the study for **BIIB100**. All the participants helped researchers learn more about BIIB100 in people with **amyotrophic lateral sclerosis (ALS)**.

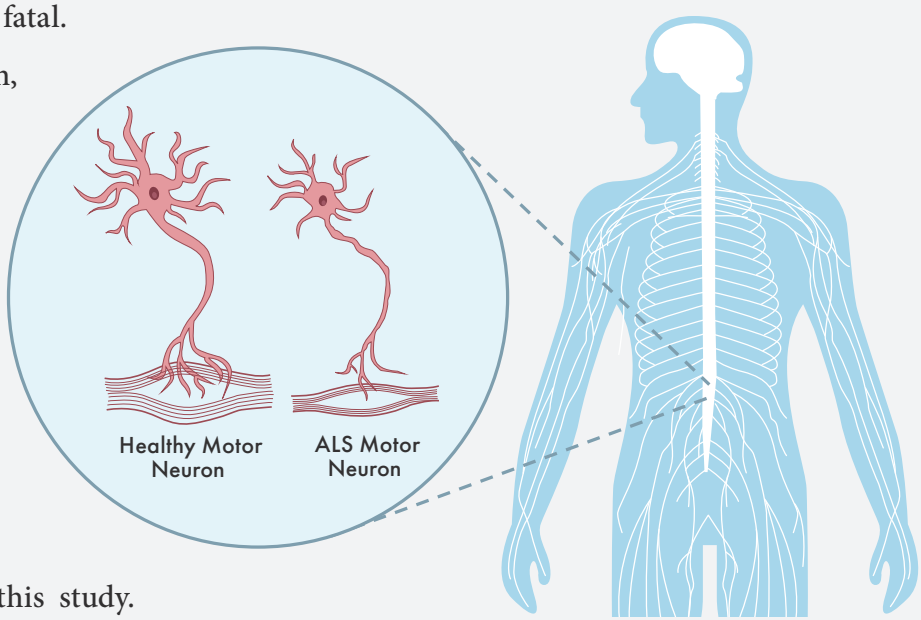
Biogen sponsored this study and reviewed the results when this study ended. Biogen thinks it is important to share the results with the participants and the public.

We hope this helps participants understand and feel proud of their important role in medical research. If you have questions, please speak with the doctor or staff at the study site.

Why was the study done?

Researchers are looking for a new drug to help people with ALS. ALS is a rare neurodegenerative disease, which is a condition that damages nerve cells and nerve connections. It affects the nerve cells in the brain and spinal cord that help control movement. These nerve cells are called motor neurons. ALS causes weakness in muscles that leads to difficulty walking, speaking, eating, and breathing, in addition to other problems. It is a progressive disease, which means that it gets worse with time and is eventually fatal.

The main cause of ALS is unknown, and researchers are looking for the mechanisms in the body that could be responsible. In certain cases of ALS, there may be issues with the transport of proteins and genetic material within the cell. XPO1 (also known as Exportin 1) is one of the transporter proteins. Researchers are trying to find new drugs that may regulate the function of XPO1, and in turn, help prevent ALS from getting worse.



BIIB100 was the study drug used in this study. Researchers believe that it has the potential to protect nerve cells by reducing the activity of XPO1. This study was done to learn more about the safety of BIIB100 in people with ALS.

The main questions that the researchers wanted to answer were:

- What medical problems happened during this study?
- How many participants had new medical problems or worsening medical problems after receiving a dose of BIIB100?

Who **took part** in the study?

The study included 49 participants at 9 research centers in the United States. The study included **29 (59%) men** and **20 (41%) women**. Participants were between **39 and 77 years old**, with an average age of 61.

29 (59%) men

20 (41%) women

Participants **were able to** take part in this study if they:

- Were 18 years of age or older
- Had ALS
- Had at least 65% of their original lung strength

Participants **were not able to** take part in this study if they:

- Were taking certain drugs
- Had certain medical conditions
- Had some ongoing or previous infections

For more information on who could take part in this study, please refer to the website listed on the last page of this summary.

What **happened** during the study?

How was the study done?

This was a **Phase 1, double-blind study**. In a Phase 1 study, researchers look to see how an experimental drug works in the human body, and they check for any side effects. Double-blind means the researchers, the investigators at the study center, and the participants do not know if they received BIIB100 or placebo. A placebo looks like the study drug but does not contain any active drug. Using a placebo helps researchers learn if the results of the study are due to the study drug or other factors. The researchers used a computer program to randomly choose if a participant received drug or placebo. Randomization helps to ensure that the groups will be similar and that any effects can be compared more fairly.

At the beginning of the study, all participants had an exam to make sure they could join the study. This included a physical exam and blood and urine tests. They also answered questions about their medical history. This part of the study lasted 4 weeks.

Researchers gave participants different doses of BIIB100 to learn more about its safety. At each dose level, at least 6 participants were given BIIB100, and 2 participants were given placebo.

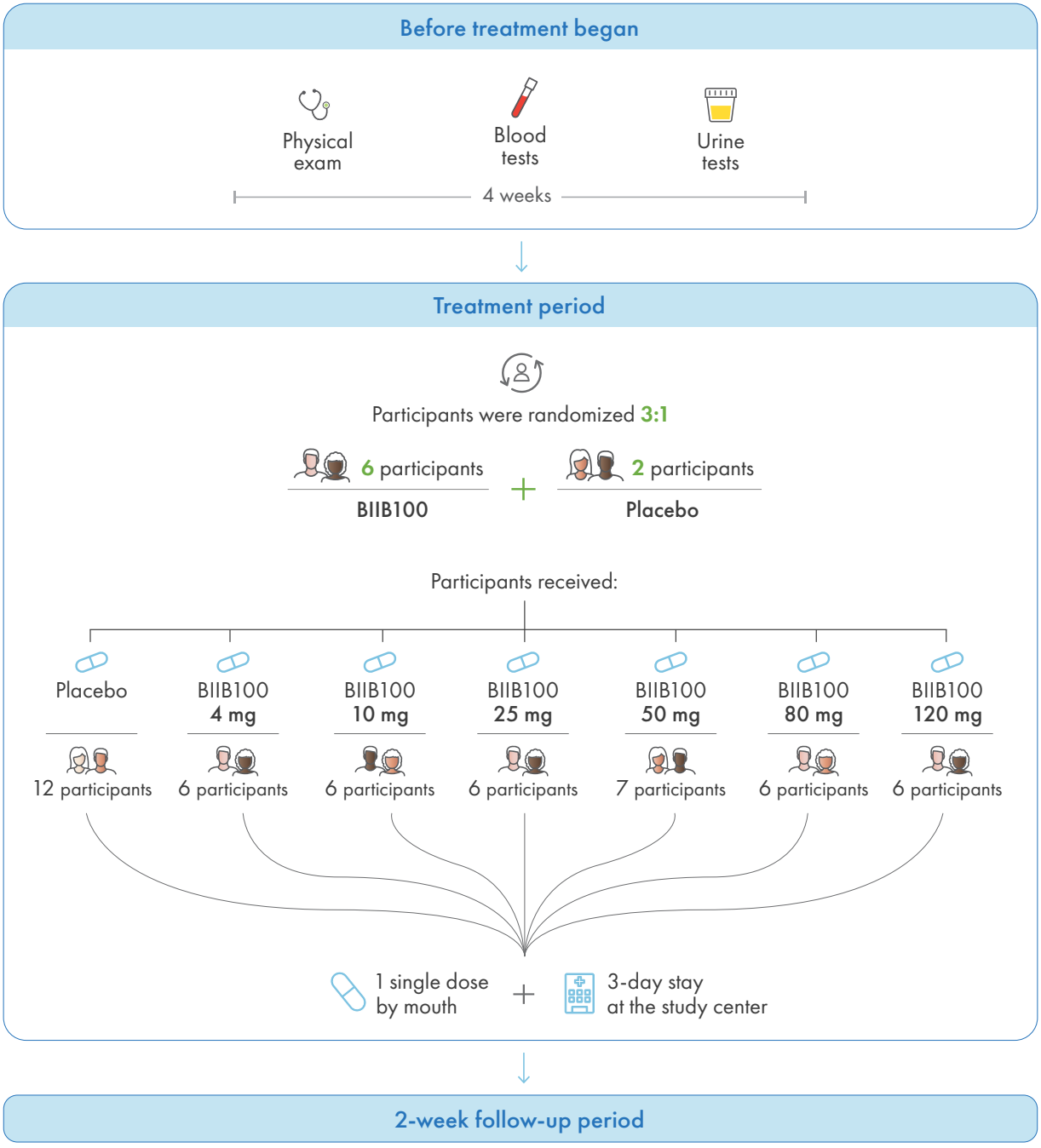
A **placebo** looks like the study drug but does not contain any active drug. Using a placebo helps researchers learn if the results of the study are due to the study drug or other factors.

The first group took the lowest dose of BIIB100. Researchers decided whether to move on to the next group at a higher dose based on the results from the first group. This continued for each of the following groups.

Participants took either BIIB100 or placebo as capsules or tablets by mouth only once. Then, they stayed at the study center for 3 days for monitoring. Researchers checked participants for any medical problems.

Participants visited the study center again a week after receiving the dose. Researchers called participants after 2 weeks to check to see if they had any new or worsening medical problems. Participants stayed in the study for a total of 6 weeks.

The graphic below shows the study design.



What were the study **results?**

When the study ended, the researchers evaluated the safety of BIIB100. This is a summary of that evaluation. The results below are from this study only. Other studies may have different results.

How many participants had new or worsening medical problems during the study?

This section is a summary of the medical problems the participants had during the study. A lot of research is needed to know whether a study drug causes a new or worsening medical problem, also called an **adverse event**. An adverse event can be serious or non-serious. An adverse event is considered serious when it results in death, is life-threatening, causes lasting problems, or requires hospital care. When experimental drugs are being studied, researchers keep track of all adverse events that participants have during a study. Not everyone experiences them, and they may or may not be caused by participating in the study.

Trained medical staff monitored participants after they took BIIB100 or placebo to see if they had any adverse events.

The results are shown below:

- **60% (22 out of 37)** of participants who received BIIB100 had **adverse events**.
- **50% (6 out of 12)** of participants who received placebo had **adverse events**.
- The majority of adverse events were **mild**.
- **None** of the participants in the study had **serious** adverse events after taking BIIB100 or placebo.
- **None** of the participants **left the study** due to adverse events.
- There were **no deaths** due to adverse events in the study.

How many participants had adverse events during this study?

The adverse events listed below are from this study only. The table below shows how many participants in each group had adverse events during this study.

Summary of participants who reported at least 1 adverse event								
	Placebo	**BIIB100**						
	12 participants	**4 mg** 6 participants	**10 mg** 6 participants	**25 mg** 6 participants	**50 mg** 7 participants	**80 mg** 6 participants	**120 mg** 6 participants	**Total** 37 participants
How many participants had adverse events?	50% (6)	100% (6)	67% (4)	50% (3)	43% (3)	50% (3)	50% (3)	60% (22)

What were the most frequent adverse events that happened during the study?

The table below shows the most common adverse events that happened in at least 5% of participants treated with any dose of BIIB100.

Most common adverse events								
	Placebo	**BIIB100**						
	12 participants	**4 mg** 6 participants	**10 mg** 6 participants	**25 mg** 6 participants	**50 mg** 7 participants	**80 mg** 6 participants	**120 mg** 6 participants	**Total** 37 participants
Headache	0	33% (2)	17% (1)	33% (2)	0	0	17% (1)	16% (6)
Fall	8% (1)	17% (1)	17% (1)	0	14% (1)	0	17% (1)	11% (4)
Nausea	8% (1)	17% (1)	0	0	0	33% (2)	17% (1)	11% (4)
Fatigue	8% (1)	0	0	17% (1)	0	17% (1)	17% (1)	8% (3)
Muscle cramps	0	0	0	0	0	17% (1)	33% (2)	8% (3)
Upper abdominal pain	0	17% (1)	17% (1)	0	0	0	0	5% (2)
Constipation	0	0	17% (1)	0	0	17% (1)	0	5% (2)
Diarrhea	0	17% (1)	0	0	0	17% (1)	0	5% (2)
Increase in digestive protein (lipase)	0	17% (1)	17% (1)	0	0	0	0	5% (2)

What serious adverse events happened during the study?

There were no serious adverse events that happened after taking BIIB100 or placebo.

What did we **learn** from this study?

The researchers found that no participants in this study had serious adverse events after taking BIIB100 or placebo. The majority of adverse events were mild. Overall, this was an important initial assessment of BIIB100.

It is important to know that the results in this summary are from this study only. Other studies may have different results.

Where can I **learn more** about the study?

You can find more information about the study online at www.clinicaltrials.gov. Once on the site, type **NCT03945279** into the search box and click **Search.**

If you have questions about BIIB100 or the results of this study, please speak with the doctor or staff at the study research center.

Official Study Title: A Phase 1, Double-Blind, Placebo-Controlled, Single-Ascending-Dose Study to Evaluate the Safety, Tolerability, Pharmacokinetics, and Pharmacodynamics of BIIB100 Administered Orally to Adult Participants With Amyotrophic Lateral Sclerosis

Biogen, the sponsor of this study, has its headquarters in Cambridge, Massachusetts (USA).

The results presented here are for a single study. You should not make changes to your therapy based on these results without first consulting your doctor.

US Clinical Study Database

- **https://www.clinicaltrials.gov/ct2/show/NCT03945279**
- www.clinicaltrials.gov
- Study #: NCT03945279

Thank you.

Biogen

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