CLINICAL TRIAL RESULTS

A Study to Learn About the Safety of BIIB113 and How Much of it Attaches to OGA Protein in Healthy Volunteers

Drug Studied: BIIB113
Protocol Number: 276HV101
Study Dates:
Start Date: February 14, 2022
Completion Date: July 10, 2023

Biogen

Thank you!

A clinical study participant belongs to the larger research community around the world. By participating in a study, they help researchers answer important health questions and learn about new medications.

In this study, researchers learned more about the **investigational drug BIIB113** and its safety **in healthy volunteers**. An investigational drug is one that has not yet been approved for use outside of clinical studies. This is also known as the **study drug**.

Biogen, the sponsor of this study, thanks those who participated and believes it is important to share the overall results of the study. If you have questions, please speak with the doctor or staff at the study research center.

Why was this study done?

Researchers are looking for a drug that may help people with **Alzheimer's Disease (AD)**.

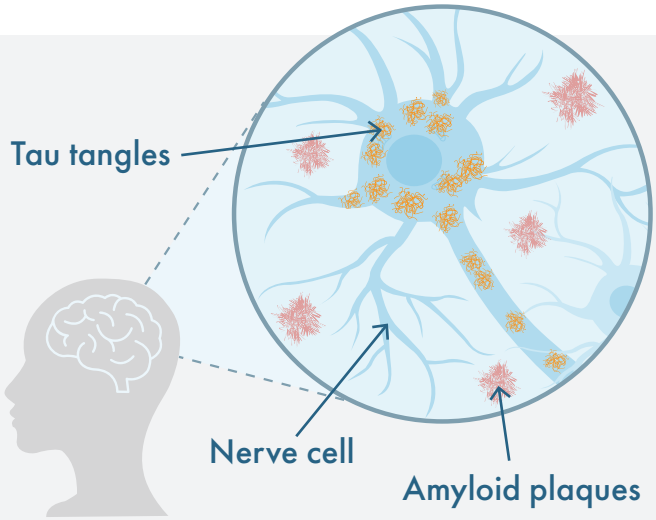
People with AD have memory loss and eventually lose their ability to think clearly and to carry on their daily activities. AD is a progressive illness, which means it slowly gets worse, and in some cases, can even lead to death.

People with AD have an abnormal build-up of proteins in the brain called **tau** and **amyloid**. These proteins normally support nerve connections in the brain. But when they build up, tau can form tangles, and amyloid protein can form plaques. **Tau tangles** are misfolded proteins that are found inside the nerve cells. **Amyloid plaques** are misfolded proteins in the spaces between nerve cells. Tau and amyloid protein build-ups are believed to affect the ability to think and function.

A drug called BIIB113 is being developed as a possible treatment for AD. BIIB113 attaches to a **protein called O-GlcNAcase (OGA)** and blocks its function. Researchers believe that reducing OGA activity can lower the build-up of tau protein in the brain.

Before researchers test a new drug in patients, they test the drug in healthy volunteers. In this study, researchers wanted to learn about the **safety of BIIB113**. They did this by giving different doses of BIIB113 or placebo to trial participants.

A **placebo** looks like a study drug but contains no real medicine. Using a placebo helps researchers learn about the effect of BIIB113.



Researchers also wanted to know how much BIIB113 attaches to OGA in the brain.

The main questions that the researchers wanted to answer were:

- How many participants had adverse events or serious adverse events during the study?
- Did the participants' health change after receiving BIIB113?
- What percentage of OGA in the brain was attached to BIIB113 after treatment?
- What possible adverse reactions did the participants have?

An **adverse event** is an unwanted health problem that may or may not be caused by the study drug or the placebo.

An **adverse reaction** is a medical problem the study doctors reported as possibly being caused by the study drug. This can happen during a clinical study or within a certain amount of time after the study has ended.

Who took part in the study?

The study included **72 participants**, which included 11 men and 61 women.

All participants were between **19 and 73 years old**.

The study took place at **2 research centers** in the United Kingdom and 1 in Sweden.

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

- Were between 18 and 75 years old
- Were considered healthy based on their medical history and a screening by the study doctors

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

- Had a history of long-lasting or frequent infections or allergic reactions
- Were taking certain supplements or medications that could interfere with the results of the study

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

What study drug did the participants receive?

Researchers studied the following drugs in this study:

BIIB113
various doses,
taken as capsules by mouth

Placebo
taken as capsules by mouth
to match BIIB113

What happened during the study?

How was the study done?

The study was split into 3 parts: **Part A**, **Part B**, and **Part C**.
All parts helped researchers learn about the safety of BIIB113.
Part C helped researchers learn about how BIIB113 attached to OGA.

This study was:

Phase 1	Blinded	Open label	Randomized
Researchers tested a new drug for the first time in humans. They wanted to find out if there were any adverse events during this study.	**Parts A** and **B** were blinded. This means that neither the researchers nor the participants knew if the participants received BIIB113 or placebo.	**Part C** was open label. This means that both the researchers and the participants knew that all participants received BIIB113 and the doses they were taking.	This means the researchers used a computer program to randomly choose the drug each participant took. This helped make sure the groups were chosen fairly.

A different set of participants joined each part of the study. **At the beginning of each part**, the participants had a **screening visit** to see if they were a good fit. Participants had a physical exam, and their medical history was checked.

The screening also included:


Neurological exam


Heart rhythm tests


Blood and urine tests

These tests were also done throughout the study.

Participants who joined **Part C** had a **magnetic resonance imaging (MRI) scan**, which is a type of brain imaging scan.

Part A

- A total of **35 participants** joined Part A.
- Participants were randomly assigned to receive a **single dose of BIIB113 or matching placebo**.

BIIB113 low dose	BIIB113 medium dose	BIIB113 higher dose	BIIB113 highest dose	Total placebo
6 participants	6 participants	6 participants	5 participants	12 participants

- Researchers tested doses in order from lowest to highest. They finished testing each group before starting the next one.
- Researchers decided whether to start the next group at a higher dose based on the safety results from the previous group.
- Participants took the doses after not eating anything for at least 8 hours. They also could not eat anything for at least 2 hours after the dose. This was called **fasting**.

> The participants who were assigned the **medium dose of BIIB113** or matching placebo were also given a **2nd dose** at least 2 weeks after the 1st dose.

- This 2nd dose was taken after eating a high-fat, high-calorie breakfast. Researchers wanted to see the differences between taking BIIB113 on an empty and full stomach.
- Participants taking 1 dose stayed in the study for up to 39 days.
- Participants taking 2 doses stayed in the study for at least 54 days.

Part B

- A total of **27 participants** joined Part B.
- Participants were randomly assigned to receive **multiple doses of BIIB113 or matching placebo**.

BIIB113 higher	BIIB113 highest dose	BIIB113 higher (elderly population)	Total placebo
6 participants	6 participants	6 participants	9 participants

- Participants took the doses once a day for 14 days.
- Participants took the doses while fasting.
- Researchers decided whether to start each group based on previous safety results.
- An extra group of participants who were between the ages of 65 and 75 took the higher dose of BIIB113 or matching placebo. This was done to see the effect of BIIB113 in an elderly population.
- Participants stayed in the study for up to 53 days.

Part C

- A total of **10 participants** joined Part C.
- Participants were randomly assigned to receive either a **single dose** or **multiple doses of BIIB113**. Placebo was not given.

BIIB113 medium dose (single dose)	BIIB113 low dose (single dose)	BIIB113 medium dose (multiple doses)
3 participants	4 participants	3 participants

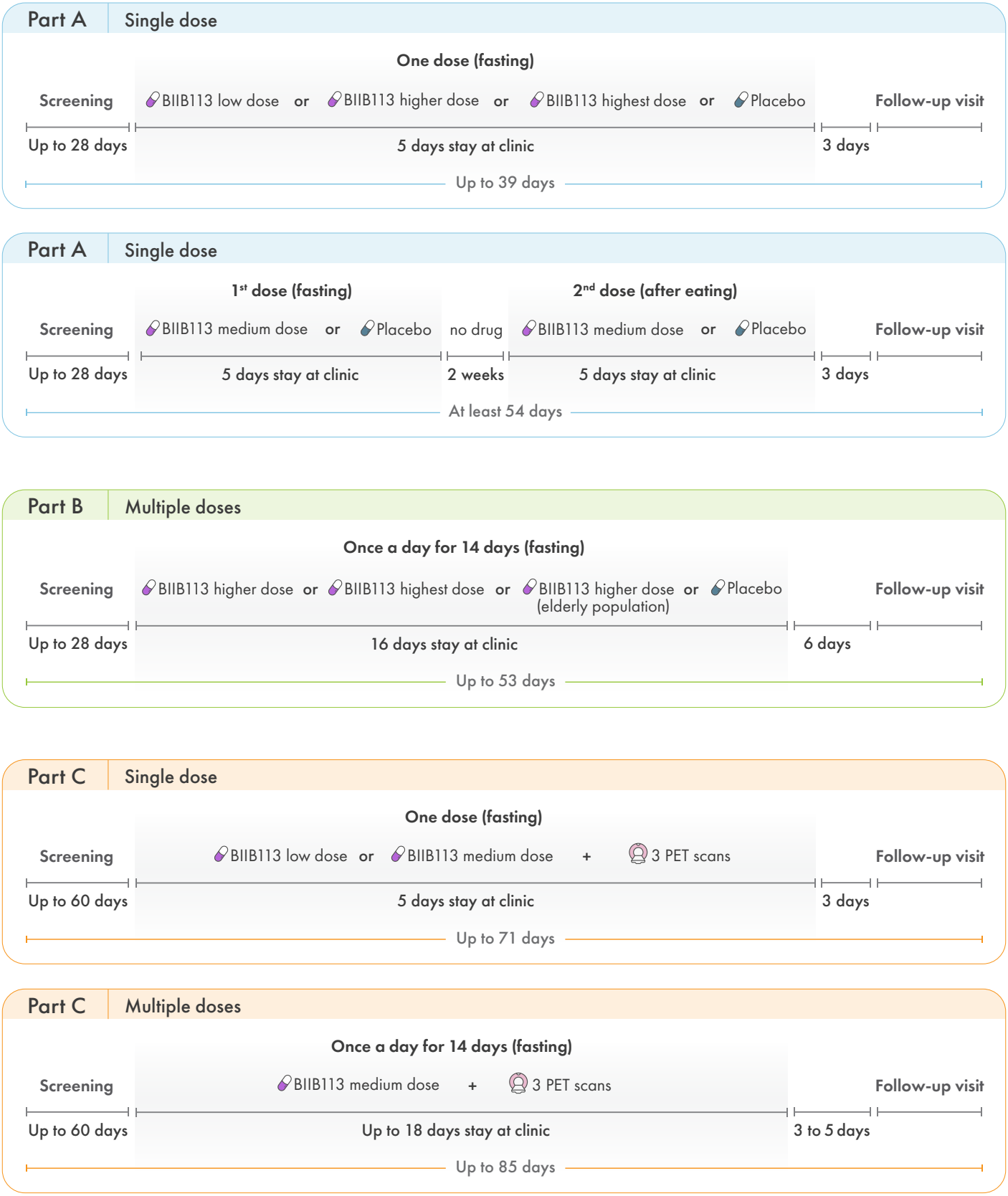
- Participants either took the doses once, or once a day for 14 days.
- Participants took the doses while fasting.
- Researchers performed 3 **positron emission tomography (PET)** scans on each participant. Before each PET scan, participants were injected with a tracer.

> A **PET scan** is a type of imaging test that uses a radioactive substance called a tracer to look for a target in the body. In this study, the target was OGA protein.

- Participants taking 1 dose stayed in the study for up to 71 days.
- Participants taking multiple doses stayed in the study for up to 85 days.

Participants in all parts of the study had a **follow-up visit for safety testing** after they left the study clinics.

The graphic below shows all possible timelines for participants joining the study.



What were the **study results?**

When the study ended, Biogen created a report of the results. This is a summary of that report. The summary results are presented for 72 participants who received BIIB113 or placebo. The individual results of each participant might be different and are not in this summary.

The results below are from this study only. Other studies may have different results. If you have questions, please ask your study doctor or study research center staff.

The following questions were the primary endpoints of the study. **Primary endpoints** are the main questions that researchers wanted to answer.

How many participants had adverse events or serious adverse events during the study?

This section is a summary of the adverse events the participants had during the study. An **adverse event** is an unwanted health problem that may or may not be caused by the study drugs. An adverse event is considered **serious** when it results in death, is life-threatening, causes lasting problems, or requires hospital care.

When new drugs are being studied, researchers keep track of all adverse events that participants have during the study. Not everyone experiences the same adverse events.

The table below shows how many participants had adverse events during this study. The number of participants is given in parenthesis.

Summary of adverse events

	Part A		Part B		Part C	
	Placebo 12 participants	**BIIB113** 23 participants	**Placebo** 9 participants	**BIIB113** 18 participants	**BIIB113 (single dose)** 7 participants	**BIIB113 (multiple dose)** 3 participants
How many participants had adverse events?	42% (5)	48% (11)	56% (5)	72% (13)	100% (7)	100% (3)
How many participants had serious adverse events?	0	0	0	0	0	0
How many participants stopped taking BIIB113 or placebo due to adverse events?	0	0	11% (1)	6% (1)	0	0

No participants had any serious adverse events during the study.

What were the most common adverse events?

The tables below show the most common adverse events that happened in the study.

Most common adverse events

	Part A		Part B	
	Placebo 12 participants	BIIB113 23 participants	Placebo 9 participants	BIIB113 18 participants
Headache	17% (2)	22% (5)	11% (1)	33% (6)
Dizziness	0	0	11% (1)	17% (3)
Shaking (tremor)	0	0	0	17% (3)

Most common adverse events

	Part C	
	BIIB113 (single dose) 7 participants	BIIB113 (multiple dose) 3 participants
Itchy, red, dry skin where medical device was used (medical device site eczema)	0	100% (3)
Pain in area where tube was inserted to check blood (catheter site pain)	29% (2)	0
Bruising (contusion)	29% (2)	0
Bruising after procedure (post procedural contusion)	29% (2)	0

Did the participants' health change after receiving BIIB113?

Researchers checked vital signs and performed medical tests to measure the overall state of the body.

- Vital signs include weight, temperature, blood pressure, heart rate, and breathing rate.
- Medical tests include blood tests, urine tests, and heart tests.

Researchers also used a questionnaire called the **Columbia-Suicide Severity Rating Scale (C-SSRS)** to see if participants had any suicidal thoughts or behavior.

Researchers compared the results of these tests before and after treatment. Then, they judged if there was a possible health issue or a need for closer attention from doctors.

Researchers did not find any concerning medical test results in any part of the study.

What percentage of OGA in the brain was attached to BIIB113 after treatment?

To answer this question, researchers performed **3 PET scans** on each participant in **Part C** of the study.

1st scan
Done before the first BIIB113 dose

2nd scan
Done 2 to 6 hours after the first BIIB113 dose

3rd scan
Done 1 to 3 days after the last BIIB113 dose

They could then compare the results at each timepoint to see how much OGA showed up on the scans.

Researchers concluded that:

- **A single medium dose** of BIIB113 stayed attached to **over 90% of OGA** up to 2 days after the dose.
- **Multiple low doses** of BIIB113 taken daily for 14 days stayed attached to **over 90% of OGA** up to 2 days after the final dose.

What possible **adverse reactions** happened during the study?

This section is a summary of the adverse reactions the participants had during the study. An **adverse reaction** is a medical problem that the study doctors reported as **related to the study drugs**. An adverse reaction is considered **serious** when it results in death, is life-threatening, causes lasting problems, or requires hospital care.

When new drugs are being studied, researchers keep track of all adverse reactions that participants have during the study. Not everyone experiences the same adverse reactions.

Study doctors decide if an adverse reaction is possibly related to the study drug. When they make this decision, the study doctors do not know if a participant is receiving BIIB113 or placebo. This is important so that study doctors are not influenced when making decisions about the study drug.

How many participants had adverse reactions during this study?

The table below shows how many participants had adverse reactions during this study. The number of participants is given in parenthesis.

Summary of adverse reactions

	Part A		Part B		Part C	
	Placebo 12 participants	**BIIB113** 23 participants	**Placebo** 9 participants	**BIIB113** 18 participants	**BIIB113 (single dose)** 7 participants	**BIIB113 (multiple dose)** 3 participants
How many participants had adverse reactions?	8% (1)	9% (2)	11% (1)	11% (2)	0	33% (1)
How many participants had serious adverse reactions?	0	0	0	0	0	0
How many participants stopped taking BIIB113 or placebo due to adverse reactions?	0	0	0	6% (1)	0	0

What serious adverse reactions happened during this study?

- None of the participants had serious adverse reactions during this study.
- None of the participants died during this study.

What adverse reactions happened during this study?

- A total of **5 adverse reactions** happened in **Part A**.
- A total of **3 adverse reactions** happened in **Part B**.
- Only **1 adverse reaction** happened in **Part C**.

The table below shows the adverse reactions that happened during this study.

Adverse reactions

	Part A		Part B		Part C	
	Placebo 12 participants	BIIB113 23 participants	Placebo 9 participants	BIIB113 18 participants	BIIB113 (single dose) 7 participants	BIIB113 (multiple dose) 3 participants
Headache	8% (1)	4% (1)	0	0	0	33% (1)
Soft stool (faeces soft)	0	4% (1)	0	0	0	0
Frequent bowel movements	0	4% (1)	0	0	0	0
Feeling tired (fatigue)	0	4% (1)	0	0	0	0
Dizziness	0	0	11% (1)	0	0	0
Shaking (tremor)	0	0	0	6% (1)	0	0
Nightmare	0	0	0	6% (1)	0	0

How has this study **helped** patients and researchers?

This study helped researchers learn more about the safety of BIIB113 and how well it attaches to its target, OGA, in the brain.

Overall, the researchers in this study found that:

- Both single and multiple doses of BIIB113 taken by mouth were **tolerated well by healthy participants**.
- **BIIB113 stayed attached to OGA in the brain** for up to 2 days, after taking either single or multiple doses.

It is important to know that the results in this summary are from this study only. Other studies may have different results. Future studies with BIIB113 are being planned.

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

You can find more information about the study online at the following websites:

ClinicalTrials.gov	https://clinicaltrials.gov/study/NCT05195008
UK Health Research Authority	https://www.hra.nhs.uk/planning-and-improving-research/application-summaries/research-summaries/276hv101-biib113-in-healthy-participants/

Official Study Title: A Phase 1 Randomized, Blinded, Placebo-Controlled, Single- and Multiple-Ascending Dose Study to Evaluate the Safety, Tolerability, and Pharmacokinetics, With an Open-Label Target Occupancy Study of BIIB113 in Healthy Participants

If you have **questions about BIIB113** or the results of this study, please speak with the doctor or staff at the study research center.

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.

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

Thank you!

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