CLINICAL TRIAL RESULTS

A Study to Evaluate the Safety and Efficacy of BIIB104 in Participants With Cognitive Impairment Associated With Schizophrenia (CIAS)

- **Drug Studied:** BIIB104
- **Protocol Number:** 263CS201 (TALLY)
- **Study Dates:**
  - **Start Date:** 04 December 2018
  - **Completion Date:** 07 April 2022

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Thank you!

A clinical study participant belongs to the larger clinical 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 BIIB104** and its safety in people with **cognitive impairment associated with schizophrenia (CIAS)**. 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 were looking for a drug that may help people with **cognitive impairment associated with schizophrenia (CIAS).**

Schizophrenia is a mental illness that has psychotic, negative, and cognitive symptoms.

Psychotic symptoms include seeing and feeling things that are not real, holding beliefs that are not true, and disorganized speech. **Negative symptoms** include difficulty showing emotions, low motivation and energy, and lack of social interest. **Cognitive symptoms** include problems with concentration, learning new things, and memory.

Although there are some drugs for schizophrenia, most of them focus on psychotic symptoms. Currently, there are no drugs for the cognitive symptoms of schizophrenia. For that reason, researchers wanted to see if a drug called BIIB104 can help cognitive ability in study participants with schizophrenia.

The main questions that the researchers wanted to answer were:

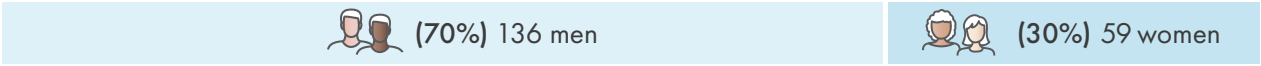
- Was there any change in a type of cognitive ability called **working memory** for participants after 12 weeks of treatment?
- What possible **adverse reactions** did the participants have?

Working memory is the ability to hold information in mind and use it to carry out mental tasks.

An **adverse reaction** is a medical problem the study doctors reported as possibly being caused by the study drug.

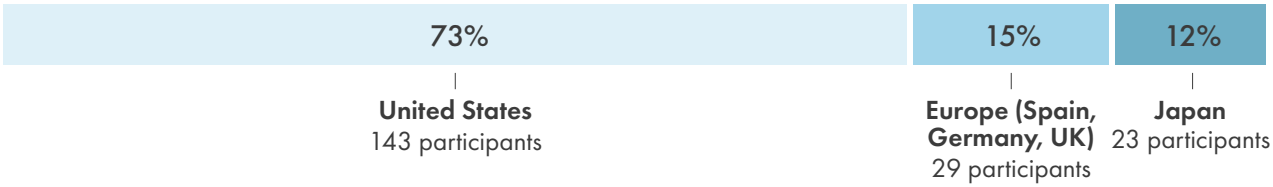
Who took part in the study?

The study included **195 participants**, which included **136 men** and **59 women**.



All participants were between **21 and 55 years old**.

A total of **52 research centers** around the world treated participants in the study.



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

- Were at least 18 years old
- Had confirmed schizophrenia for at least 2 years
- Had stable psychotic symptoms for at least 12 weeks
- Were taking stable treatment for psychotic symptoms for at least 8 weeks

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

- Were taking treatments that can affect cognitive ability
- Had any recent treatments for cognitive symptoms
- Were part of other ongoing studies
- Had other psychiatric conditions

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 drugs did the participants receive?

Researchers studied the following drugs:

- **BIIB104, 0.15 or 0.5 milligrams (mg)**, given twice daily as capsules taken by mouth
- **Placebo**, given twice daily as capsules taken by mouth

A **placebo** looks like a study drug but contains no real medicine. Using a placebo helps researchers learn the effect of BIIB104.

Participants needed to continue taking their normal drugs for schizophrenia during the study.

What **happened** during the study?

How was the study done?

This study was:

Phase 2: The researchers wanted to learn how well BIIB104 worked in a small number of participants with CIAS. They also wanted to find out if the participants had any adverse reactions.

Double blind: The study was double blinded. This means that neither the researchers nor the participants knew if the participants received BIIB104 or placebo.

Randomized study: This study was randomized. 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.

At the beginning of the study, all participants had a **screening** visit. This visit included tests of cognitive ability, a physical exam, heart tests, and laboratory tests. They also answered questions about their medical history.

Before receiving the study drug, participants received placebo for 1 week. This was to see if the participant could take the study drugs as scheduled. After this initial **placebo week**, participants received either BIIB104 or placebo for 12 weeks.

A total of 195 participants were randomly put into 1 of 3 study groups. They were:

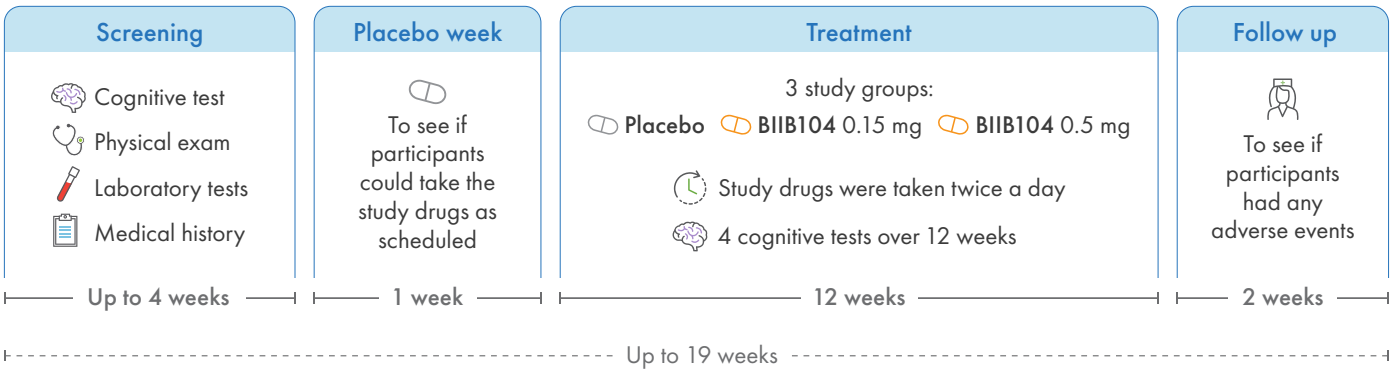
- BIIB104 0.15 mg
- BIIB104 0.5 mg
- Placebo

During both the initial **placebo week** and the **12-week treatment period**, participants took the study drugs 2 times a day.

Participants visited the clinic regularly throughout the study. Participants took tests of cognitive ability 4 times over the 12 weeks that they received BIIB104 or placebo.

Participants also had a **follow up** 2 weeks after their final dose of BIIB104 or placebo. During this follow up, participants were checked for adverse events. Adverse events are medical problems that may or may not be caused by the study drugs. Participants could be in the study for up to 19 weeks.

The graphic below shows how the study was done.



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 195 participants who received BIIB104 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.

Was there any change in a type of cognitive ability called working memory for participants after 12 weeks of treatment?

This was the primary endpoint of the study. A **primary endpoint** is the main question that researchers wanted to answer. To answer this question, researchers looked at the results of the **MATRICS Consensus Cognitive Battery (MCCB)** to see how working memory was affected.

The **MCCB tests 7 areas of cognitive ability** thought to be important in people with schizophrenia. One area is working memory. This is the ability to hold information in mind and use it to carry out mental tasks. Working memory is important for performing day-to-day activities.

The results showed no difference in MCCB test scores in either of the BIIB104 groups compared to the placebo group after 12 weeks.

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

This section is the summary of the adverse reactions that participants reported during the study.

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.

An **adverse reaction** is a medical problem that the study doctors reported as related to the study drug. An adverse reaction is considered serious when it results in death, is life-threatening, causes lasting problems, or requires hospital care.

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 the study drug or placebo. This is important so that study doctors are not influenced when making decisions about the study drug.

One goal of this study was to learn more about the possible adverse reactions of BIIB104. The adverse reactions listed below are those from this study only. Other studies may have different results.

How many participants had adverse reactions during this study?

The table below shows how many participants had adverse reactions during this study.

Summary of adverse reactions				
	Placebo (63 participants)	**BIIB104 0.15 mg** (66 participants)	**BIIB104 0.5 mg** (66 participants)	**BIIB104 Total** (132 participants)
How many participants had adverse reactions?	10% (6)	18% (12)	11% (7)	14% (19)
How many participants had serious adverse reactions?	0	2% (1)	0	1% (1)
How many participants stopped taking BIIB104 or placebo due to adverse reactions?	0	3% (2)	0	2% (2)

What serious adverse reactions happened during this study?

Only **1 out of 195 participants (less than 1%)** had a serious adverse reaction. This participant belonged to the BIIB104 0.15 mg group and experienced worsening of schizophrenia.

No participants died in this study.

What common adverse reactions happened during this study?

The most common adverse reactions that happened during this study were sleepiness, headache, and increased weight.

The table below shows the most common adverse reactions that happened in at least 2 participants.

Most common adverse reactions				
	Placebo (63 participants)	**BIIB104 0.15 mg** (66 participants)	**BIIB104 0.5 mg** (66 participants)	**BIIB104 Total** (132 participants)
Sleepiness	2% (1)	5% (3)	0	2% (3)
Headache	0	2% (1)	2% (1)	2% (2)
Sensations like tingling, numbness, or pins and needles	2% (1)	2% (1)	0	1% (1)
Increased weight	0	2% (1)	2% (1)	2% (2)
Vomiting	2% (1)	0	2% (1)	1% (1)

How did this study **help** patients and researchers?

Researchers look at the results of many studies to decide which treatments work best and are safest for patients. This study helped researchers learn more about the safety of BIIB104 and the potential to help people with CIAS.

Overall, the researchers in this study found that there was no difference in change in working memory between participants who took BIIB104 and those that took placebo. They also found that most adverse reactions were non-serious, and that they happened at a similar rate across the BIIB104 and placebo groups.

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 BIIB104 in people with schizophrenia are not currently planned.

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

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

US Clinical Study Database	https://clinicaltrials.gov/ct2/show/NCT03745820
EU Clinical Trials Register	www.clinicaltrialsregister.eu/ctr-search/search?query=2018-003825-27
JAPIC Clinical Trials Information	https://www.clinicaltrials.jp/cti-user/trial/ShowDirect.jsp?clinicalTrialId=34357

Official Study Title: A Phase 2, Randomized, Double-Blind, Multiple-Dose, Placebo-Controlled Study to Evaluate the Safety and Efficacy of BIIB104 in Subjects With Cognitive Impairment Associated With Schizophrenia (CIAS).

If you have questions about BIIB104 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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