CLINICAL TRIAL RESULTS

A Study to Learn About How BIIB091 is Processed by the Body in Healthy Volunteers

Drugs Studied: BIIB091
Protocol Number: 257HV105
Study Dates:
Start Date: 28 September 2020
Completion Date: 07 September 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.

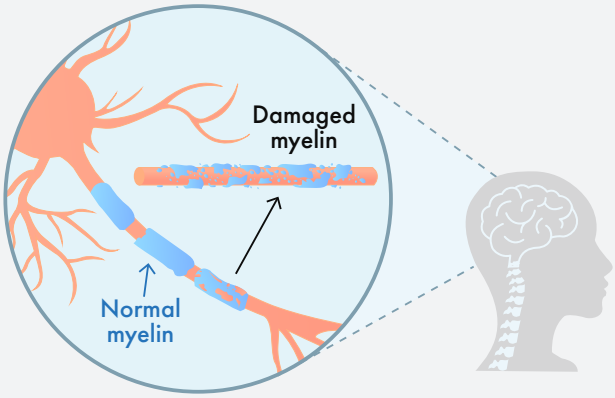
In this study, researchers learned more about a new investigational drug BIIB091 and how it is processed in the bodies of healthy volunteers.

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 drugs that could help treat patients with different forms of **multiple sclerosis (MS)**.

In MS, the immune system attacks the brain and spinal cord. This causes damage to the **myelin**, a protective covering on the nerves. Eventually the nerves are damaged as well. This makes it difficult for the brain to function and send messages throughout the body. MS is a progressive disease. This means that it slowly gets worse, and the body becomes more disabled over time.



Symptoms of MS include tiredness, numbness, tingling, and muscle weakness. Symptoms may also include problems with vision, walking, thinking, and using the bathroom.

Currently, there are no drugs to cure MS or repair damaged nerves. Existing treatments for MS include drugs that try to prevent the immune system from attacking the nerves as often.

An investigational drug called BIIB091 is being developed as a possible treatment for MS. Before researchers test a new drug in patients, they test the drug in healthy volunteers. In this study, researchers wanted to learn about how BIIB091 is processed by the human body. They wanted to test different forms and doses of BIIB091. They wanted to see what happened to BIIB091 in the blood after it was taken on an empty stomach compared to after eating a meal. They also wanted to see if other common drugs being taken at the same time would affect how BIIB091 was being processed. The study was split into multiple parts to answer these questions.

The main questions that the researchers wanted to answer were:

- **Part 1:** How were modified-release (MR) forms of BIIB091 processed by the body after a single dose?
- **Part 1B:** How were immediate-release (IR) forms of BIIB091 processed by the body after a single dose?
- **Part 2:** How was BIIB091 processed by the body when taken together with the CYP3A4 inhibitor itraconazole?
- **Part 2:** How was BIIB091 processed by the body when taken together with the proton pump inhibitor rabeprazole?
- **Part 3:** How was the IR form of BIIB091 processed by the body when taken twice a day for a week?
- What possible adverse reactions did the participants have during the study?

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 a total of **59 participants,** which included **36 men** and **23 women.**

36 (61%) men

23 (39%) women

All participants were between **20 and 55 years old.**

The study took place at 1 research center in the **United Kingdom.**

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

- Were between 18 and 55 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
- Were taking certain supplements, medications, or eating certain foods 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 drugs did the participants receive?

Researchers studied the following drugs in this study:

- **BIIB091,** various doses, taken as either tablets or capsules
- **Itraconazole, 200 milligrams (mg),** a CYP3A4 inhibitor, taken as capsules, once or twice a day
- **Rabeprazole, 20 mg,** a proton pump inhibitor, taken as tablets, once or twice a day

What happened during the study?

How was the study done?

This study was:

Phase 1: Researchers wanted to find out how BIIB091 is processed in the body. Researchers took blood samples from the participants before and after they took BIIB091. They wanted to see how the concentration of BIIB091 in the blood changed over time.

Open label: The study was open label. This means that both the researchers and the participants knew that all participants received BIIB091 and the doses they were taking.

Randomized study: Part 1B and Part 2 of the study were randomized. This means the researchers used a computer program to randomly choose the group each participant was in. This helped make sure the groups were chosen fairly. For both Part 1B and Part 2, participants were randomly chosen to take BIIB091 either on an empty stomach or after a meal.

A different set of participants joined each part of the study. **At the beginning** of each part, the participants had a **screening visit.** This visit included a physical exam, heart tests, and blood and urine tests. They also answered questions about their medical history.

In a previous study, researchers had given participants BIIB091 in a capsule with no other fillers or binders, which they call a **drug in capsule (DiC) formulation**. The results of that study showed that there was too much variation between participants in how much BIIB091 was found in the blood after taking it.

For Part 1 and Part 1B of this study, researchers wanted to find the ideal form and dose of BIIB091 to be used in the rest of the study. They were aiming for specific concentrations of BIIB091 in the blood based on earlier research. Concentration refers to the amount of a substance like BIIB091 that is in a certain volume of blood, such as nanograms per milliliter.

After a participant received a dose, researchers wanted the blood concentration of BIIB091 to be above a specific number right before the next dose. They also wanted the maximum concentration of BIIB091 to be below a certain number. Finally, they wanted the concentrations in the blood to be similar between the participants.

In Part 1, researchers tested modified-release tablets of BIIB091 which would slowly release BIIB091 over time. They gave different forms of these tablets to participants on an empty stomach.

Part 1 had **5 periods.** Each participant was treated with 4 forms of tablets and 1 DiC capsule. The DiC was used as a reference to compare the different forms of BIIB091. Each form was given only once per period. After each dose, participants waited at least 7 days before the next period. During this time, researchers performed tests to measure BIIB091 in the blood.

In Part 1B, researchers tested immediate-release tablets of BIIB091 which would release BIIB091 quickly after reaching the stomach. For this part, participants were split into 2 groups. Some participants took these tablets on an empty stomach while others took them after eating a meal. Both groups took the DiC on an empty stomach.

Part 1B had **4 periods.** Each participant was treated with immediate-release tablets at different doses and 1 DiC capsule. Just as in Part 1, different doses were given once per period with at least 7 days before the next period.

Once researchers found an ideal form and dose of BIIB091 to use, they moved on to Part 2.

In Part 2, researchers tested the chosen form of BIIB091. This part had **3 periods.** Period 1 tested BIIB091 alone. Period 2 tested BIIB091 with the CYP3A4 inhibitor. Period 3 tested BIIB091 with the proton pump inhibitor.

In **Period 1**, all participants took BIIB091 once after breakfast. Participants waited at least 7 days before Period 2.

In **Period 2**, all participants took the study drugs after breakfast.

- All participants took itraconazole 2 times on the 1st day.
- Then, they took itraconazole once a day for 3 days.
- On the 5th day, they took itraconazole once and BIIB091 once.
- On the 6th day, they took itraconazole once.
- Participants waited at least 10 days before Period 3.

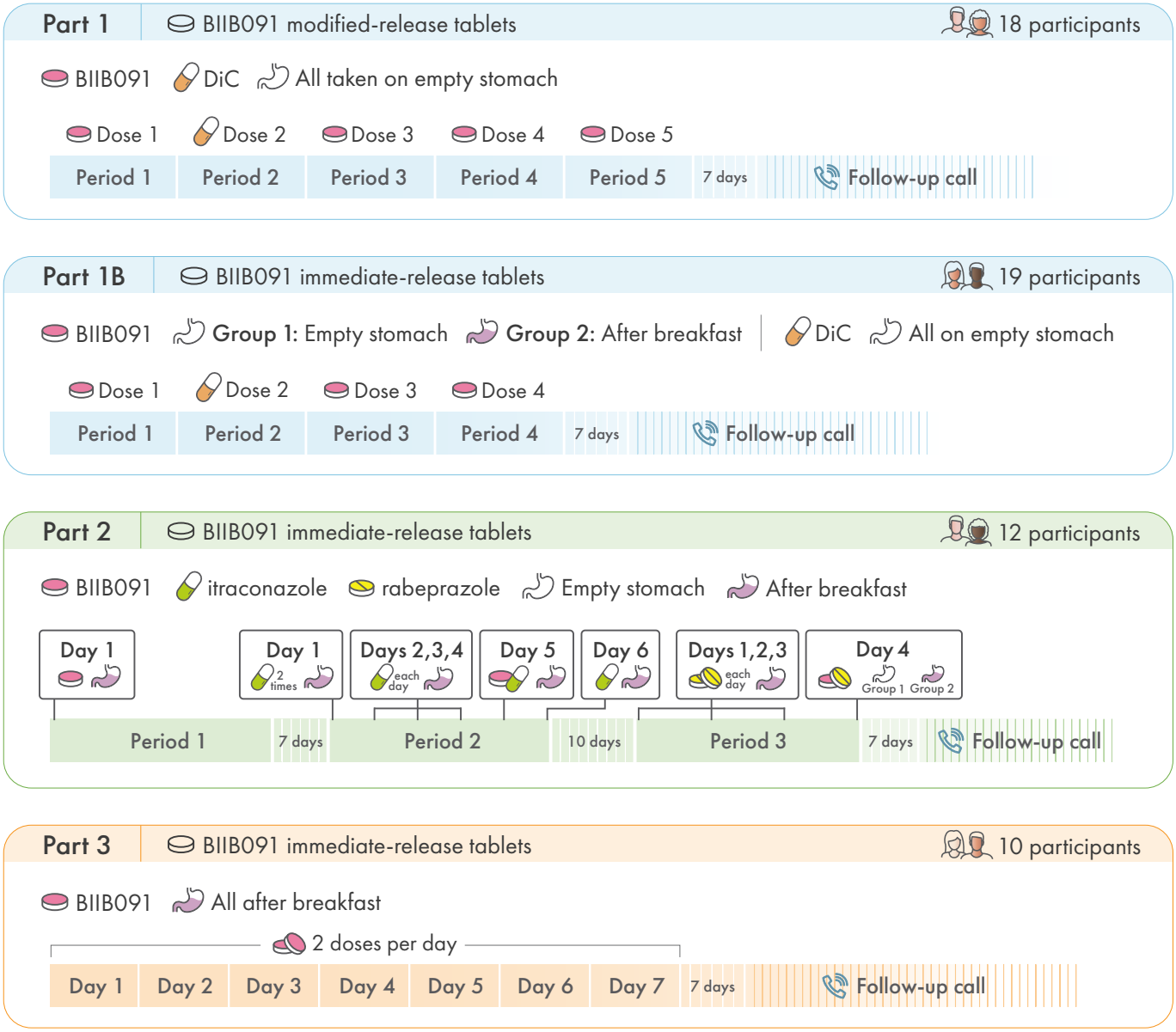
In **Period 3:**

- All participants took rabeprazole 2 times a day for 3 days. They all took it after breakfast.
- On the 4th day, they took rabeprazole once and BIIB091 once. Half of the participants took the study drugs on an empty stomach while the other half took them after breakfast.

In Part 3, researchers tested the chosen form of BIIB091, taken multiple days in a row. All participants took BIIB091 2 times a day for 7 days, after breakfast.

During each part of the study, participants stayed in the clinic while the tests were being done. For parts of the study that had multiple periods, participants stayed in the clinic for the testing and then went home until the next period began. After each part of the study, participants received a follow-up phone call about a week after their final doses to check on their wellbeing.

The graphic below shows how each part of 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 of the results are presented for 59 total participants who received BIIB091. 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.

Part 1: How were modified-release (MR) forms of BIIB091 processed by the body after a single dose?

None of the forms of BIIB091 tested during Part 1 had the results that researchers were looking for. The concentration of BIIB091 found in the blood after dosing was generally lower than expected. Also, differences between participants were higher than expected.

Part 1B: How were immediate-release (IR) forms of BIIB091 processed by the body after a single dose?

Overall, 2 of the doses tested during Part 1B did have the results researchers were looking for. One of the doses that met expectations was taken on an empty stomach while another was taken after breakfast. Differences in BIIB091 concentrations found between participants were acceptable and better than those found after taking the DiC capsule.

Researchers decided to use an IR form of BIIB091 for Parts 2 and 3.

Part 2: How was BIIB091 processed by the body when taken together with the CYP3A4 inhibitor itraconazole?

The highest concentration of BIIB091 found in the blood was about 2 times higher when taken with itraconazole. The total amount of BIIB091 present in the blood over time was about 3 to 4 times more when taken with itraconazole.

Differences in BIIB091 concentrations between participants were lower after taking itraconazole than when BIIB091 was taken alone.

A **CYP3A4 inhibitor** is a type of medicine that reduces the action of an enzyme called CYP3A4 in the body. CYP3A4 helps to break down foreign substances such as toxins and drugs so they can be removed from the body. BIIB091 is metabolized by the CYP3A4 enzyme. Taking a CYP3A4 inhibitor may cause drugs like BIIB091 to build up in the body more than usual which may cause unwanted medical problems.

Part 2: How was BIIB091 processed by the body when taken together with the proton pump inhibitor rabeprazole?

When BIIB091 was taken with rabeprazole on an empty stomach, the highest concentration of BIIB091 found in the blood was about 6 times lower than when BIIB091 was taken alone after a meal. Also, the total amount of BIIB091 that was present in the blood was about 3 times less than when BIIB091 was taken alone.

When BIIB091 was taken with rabeprazole after a meal, the highest concentration of BIIB091 found in the blood was about 2 to 3 times higher than when BIIB091 was taken with rabeprazole on an empty stomach. Also, the total amount of BIIB091 that was present in the blood was about 2 times more than when BIIB091 was taken with rabeprazole on an empty stomach.

A **proton pump inhibitor (PPI)** is a type of medicine that helps reduce stomach acid. It is often used to treat issues like heartburn, acid reflux, and stomach ulcers. Taking a PPI may affect how well another drug, such as BIIB091, is absorbed by the body.

Part 3: How was BIIB091 processed by the body when taken twice a day for a week?

Researchers found that BIIB091 built up in the blood at an expected rate after 7 days. Differences between participants were also acceptable.

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

This section is a summary of the adverse reactions that participants had 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.

It takes many studies to determine if adverse reactions are truly related to the study drug.

How many participants had adverse reactions during this study?

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

Summary of adverse reactions

	Part 1 (18 participants)	Part 1B (19 participants)	Part 2 (12 participants)	Part 3 (10 participants)	Total (59 participants)
How many participants had adverse reactions?	11% (2)	16% (3)	0	0	8% (5)

No participants in this study had serious adverse reactions.
No participants stopped taking BIIB091 or left the study due to adverse reactions.
No participants died during this study.

What common adverse reactions happened during this study?

A total of 8% of the participants experienced an adverse reaction during the study. This was 5 out of the 59 participants. Some participants had more than 1 adverse reaction.

In Part 1:

- 1 participant had itching, nausea, and headache.
- 1 participant had frequent urination.

In Part 1B:

- 1 participant had eyelid skin dryness and had rashes with both red bumps and discolored skin.
- 1 participant had dry skin.
- 1 participant had sleepiness.

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

This study helped researchers learn more about how a potential therapy for MS, BIIB091, was processed in the bodies of healthy volunteers.

Overall, researchers met their goals and found a form and dose of BIIB091 that would be appropriate to use for further studies. They also learned that the way BIIB091 is processed by the body is affected when taking either CYP3A4 inhibitors or proton pump inhibitors.

It is important to know that the results in this summary are from this study only. Other studies may have different results. Other studies investigating BIIB091 are currently ongoing and future studies are planned.

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

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

US Clinical Study Database	https://clinicaltrials.gov/ct2/show/NCT04564612

Official Study Title: An Open-Label, Pharmacokinetic Study to Evaluate the Pharmacokinetics and Relative Bioavailability of BIIB091 Formulations and to Assess the Impact of Food, a Proton Pump Inhibitor and CYP3A4 Inhibitor on BIIB091 Exposure using the Selected Formulation in Healthy Subjects

If you have questions about BIIB091 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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