CLINICAL TRIAL RESULTS

A Study to Learn About the Safety of BIIB094 in Adults With Parkinson's Disease

Study ID: 254PD101 (REASON)
Drug Studied: BIIB094
Study Dates:
Start Date: August 12 2019
Completion Date: August 12 2024

Biogen®

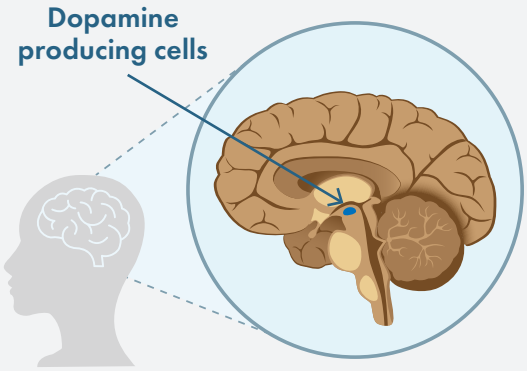
Thank you!

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 **BIIB094 and its safety in people with Parkinson's disease**. 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 **Parkinson's disease**, also known as **PD**.

PD is a brain disorder that can affect a person's ability to perform everyday activities. PD first develops when some of the brain cells that produce a natural chemical called dopamine stop working and die. Dopamine is a chemical messenger that carries signals or instructions from the brain to the rest of the body, telling it what to do. A lack of dopamine leads to problems with normal movement.

Common symptoms of PD include shaking or involuntary movement (tremors), slowness, stiffness, and problems with balance. PD also causes problems that are not related to movement. These may include sleep problems, depression, and constipation. PD is a progressive disease, which means that it slowly gets worse over time.

Current treatments for PD can help manage symptoms, but they do not treat the disease itself. When a protein called leucine-rich repeat kinase 2 (**LRRK2**) becomes too active, it can affect the brain cells involved in movement and other functions, which may lead to PD. The study drug, **BIIB094**, is designed to lower the activity of LRRK2, which may help delay the development of PD symptoms.

Some people with PD may have abnormal changes in the *LRRK2* gene that leads to the LRRK2 protein becoming too active. Others may have PD even without these abnormal *LRRK2* genes.

In this 2-part study, researchers wanted to learn more about the safety of BIIB094 in humans for the first time.

The main questions that the researchers wanted to answer were:

- How many participants had adverse events or serious adverse events during the study?
- 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. An **adverse reaction** is an adverse event that 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?

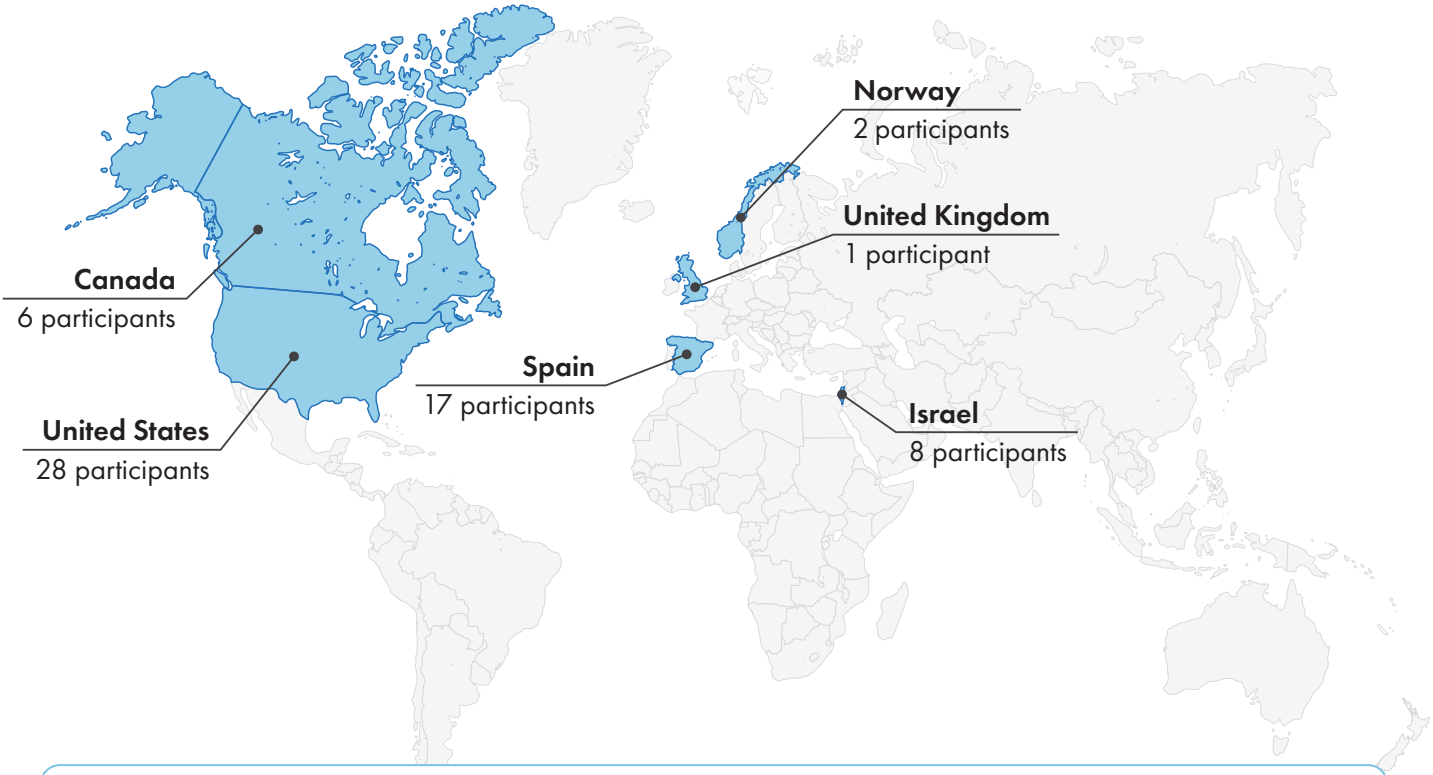
The study included a total of **62 participants**, which included 39 men and 23 women.

39 (63%) men

23 (37%) women

All participants were between **43 and 79 years old.**

The study took place at **15 research centers** in Canada, Israel, Norway, Spain, the United Kingdom, and the United States.



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

- Were between 35 and 80 years old
- Had been diagnosed with PD within 7 years of joining the study
- Had a combination of certain symptoms related to PD, including shaking, stiffness, and slowness of movement

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

- Had serious uncontrollable movement problems that could interfere with procedures in 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.**

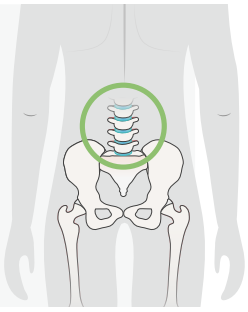
What **study drugs** did the participants receive?

Researchers studied the following drugs in this study:

- **BIIB094:** 10, 30, 40, 80, 120, or 150 milligrams (mg), given as an intrathecal (IT) injection
- **Placebo:** given as an IT injection to match BIIB094

A **placebo** looks like a study drug but contains no real medicine. Using a placebo helps researchers learn about the effect of BIIB094.

An **IT injection** is an injection into the fluid around the spinal cord in the lower back. This is done by a procedure called a lumbar puncture. Spinal fluid is a clear liquid that cushions and protects the brain and spinal cord.



What happened during the study?

How was the study done?

This study was:

Phase 1	Double blind	Randomized
Researchers tested a new drug for the first time in humans. They wanted to find out if there were any adverse events and adverse reactions during this study.	The study was double blinded. This means that neither the researchers nor the participants knew if the participants received BIIB094 or the placebo.	This means the researchers used a computer program to randomly choose the drug and dose each participant took. This helped make sure the groups were chosen fairly.

The study was split into 2 parts: **Part A** and **Part B**.

Participants could have joined either part of the study. Some participants who joined Part A continued into Part B.

Screening Period

- Participants were screened before they could join the study.
- For Part A, screening lasted 6 weeks and included 1 clinic visit.
- For Part B, screening up to 11 weeks and included 2 clinic visits.
- Participants who continued from Part A into Part B had their screening tests repeated before they received the dose in Part B.
- Participants had a physical exam, and their medical history was checked. The screening also included:

Neurological exam | Imaging scan of the brain | Test to check brain function | Blood and urine tests | Heart tests

Part A (single dose)

- A total of **40 participants** joined Part A.
- Participants were randomly assigned to receive a **single dose** of BIIB094 or the matching placebo.

BIIB094 10 mg	BIIB094 30 mg	BIIB094 40 mg	BIIB094 80 mg	BIIB094 120 mg	BIIB094 150 mg	Total placebo
3 participants	3 participants	7 participants	6 participants	6 participants	6 participants	9 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 earlier group.
- Participants stayed in the study clinic for 24 hours after receiving **1 dose** of BIIB094 or the placebo on Day 1.
- After the dose, participants stayed in the study for 12 weeks.
- Participants had to return to the clinic 3 more times, on Days 8, 29, and 57.
- They received 4 follow-up phone calls throughout Part A.

Part B (multiple doses)

- A total of **42 participants** joined Part B, including 20 participants from Part A.
- Participants joining from Part A had to wait at least 20 weeks after the dose in Part A before they could start Part B. This period helped researchers look out for any effects of the drug to make sure participants were safe to start the next part. This 20-week period also included the 12-week treatment period in Part A.
- All participants in Part B were randomly assigned to receive multiple doses of BIIB094 or the placebo.
- The 80 mg and 120 mg dose groups were also divided between participants who had an **abnormal *LRRK2* gene** or not.

BIIB094 40 mg	BIIB094 80 mg (normal *LRRK2*)	BIIB094 80 mg (abnormal *LRRK2*)	BIIB094 120 mg (normal *LRRK2*)	BIIB094 120 mg (abnormal *LRRK2*)	Total placebo
8 participants	6 participants	7 participants	6 participants	6 participants	9 participants

- Researchers decided whether to start each group based on earlier safety results.
- Participants received a total of **4 doses, once every 4 weeks**, on Days 1, 29, 57, and 85.
- Participants stayed in the study clinic for 24 hours after receiving the Day 1 dose.
- They stayed in the study clinic for 6 hours after receiving the next 3 doses. During this period, they were checked for any adverse events or reactions.
- Participants also had 7 more clinic visits, on Days 8, 36, 64, 92, 113, 169, and 253.
- They received 20 follow-up phone calls throughout Part B.

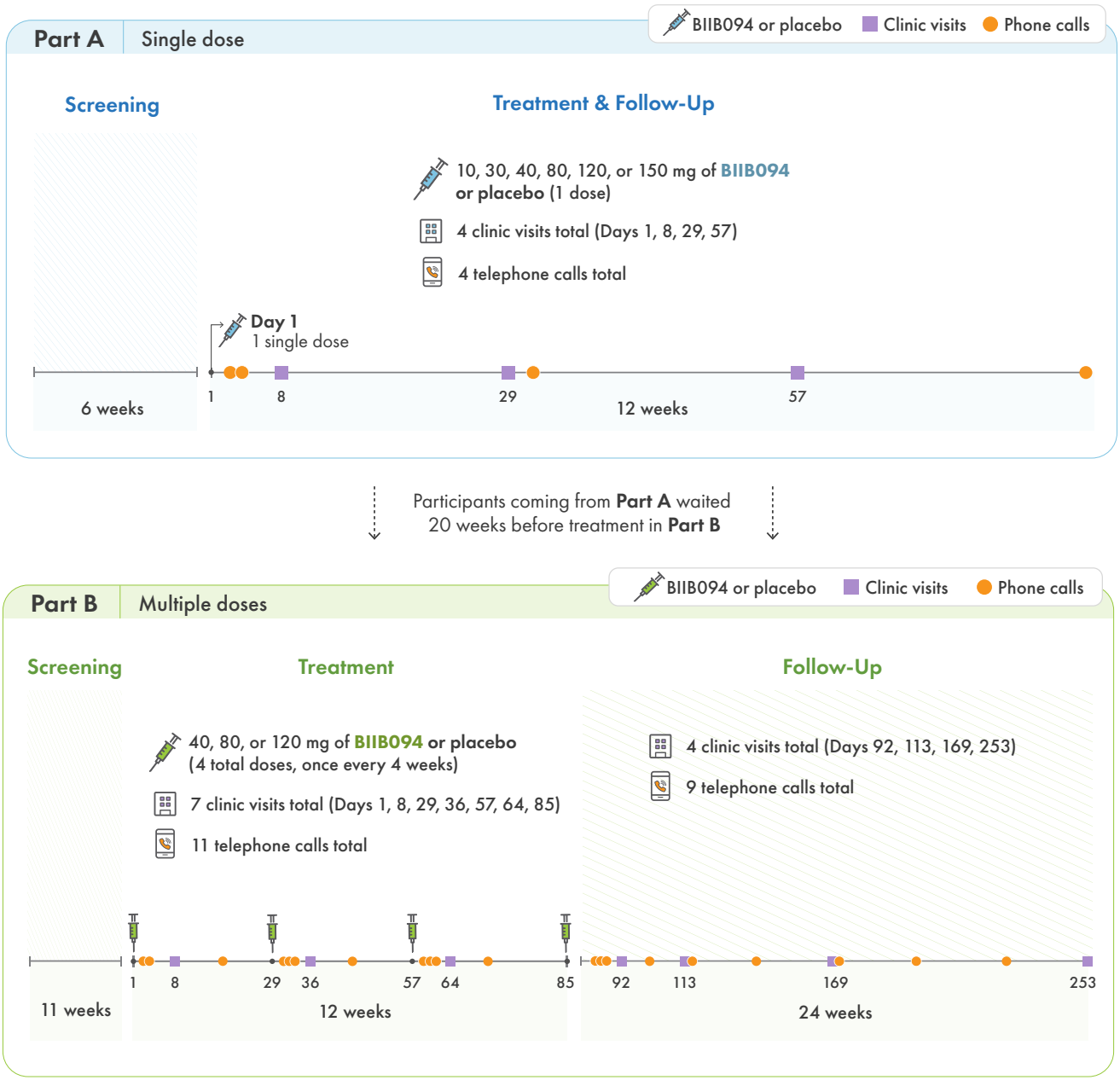
During both parts of the study, researchers continued to perform physical and neurological exams, as well as blood, urine, and heart tests regularly to check participants' health.

Participants also:

- Did tests related to their movement
- Answered questions about their quality of life
- Had spinal fluid collected

Participants in Part A stayed in the study for 18 weeks.
Participants in Part B stayed in the study for up to 47 weeks.
Participants who were in both parts stayed in the study for at least 62 weeks.

The graphic below shows the study's design.



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 62 participants who received BIIB094 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 question was the primary endpoint of the study. A primary endpoint is the main questions that researchers wanted to answer.

How many participants had adverse events or serious adverse events 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 in Part A.

Summary of adverse events in Part A

	Placebo	BIIB094					
	9 participants	10 mg 3 participants	30 mg 3 participants	40 mg 7 participants	80 mg 6 participants	120 mg 6 participants	150 mg 6 participants
How many participants had adverse events?	56% (5)	67% (2)	67% (2)	43% (3)	100% (6)	83% (5)	33% (2)
How many participants had serious adverse events?	0	0	0	0	0	0	0

- No participants had any serious adverse events during Part A.
- No participants left the study early during Part A.

The table below shows how many participants had adverse events in Part B.

Summary of adverse events in Part B

	Placebo	BIIB094				
	9 participants	40 mg 8 participants	80 mg (normal *LRRK2*) 6 participants	80 mg (abnormal *LRRK2*) 7 participants	120 mg (normal *LRRK2*) 6 participants	120 mg (abnormal *LRRK2*) 6 participants
How many participants had adverse events?	100% (9)	100% (8)	67% (4)	71% (5)	83% (5)	100% (6)
How many participants had serious adverse events?	0	0	33% (2)	14% (1)	0	0

3 participants had serious adverse events in Part B.

- 1 participant in the 80 mg (normal *LRRK2*) group had an irregular and fast heartbeat (atrial fibrillation).
- 1 participant in the 80 mg (abnormal *LRRK2*) group had a serious headache after the lumbar puncture (post lumbar puncture syndrome).
- 1 participant in the 80 mg (normal *LRRK2*) group had a growth inside the breasts (intraductal proliferative breast lesion). Doctors found that this growth had started before the participant began study treatment. The participant stopped treatment and left the study early.

What were the most common adverse events?

The table below shows the most common adverse events that happened in 2 or more participants in Part A. All other adverse events happened in 1 participant each and are not included in the table.

Most common adverse events in Part A

	Placebo	BIIB094					
	9 participants	10 mg 3 participants	30 mg 3 participants	40 mg 7 participants	80 mg 6 participants	120 mg 6 participants	150 mg 6 participants
Pain from the study procedures (procedural pain)	44% (4)	33% (1)	33% (1)	29% (2)	33% (2)	33% (2)	17% (1)
Headache after lumbar puncture (post lumbar puncture syndrome)	33% (3)	33% (1)	0	14% (1)	50% (3)	17% (1)	0
Headache	11% (1)	0	0	0	0	33% (2)	17% (1)

The table below shows the most common adverse events that happened in Part B. These events happened in at least 10% of all participants in Part B. There were other adverse events, but they did not happen as often and are not included in the table.

Most common adverse events in Part B

	Placebo	BIIB094				
	9 participants	40 mg 8 participants	80 mg (normal *LRRK2*) 6 participants	80 mg (abnormal *LRRK2*) 7 participants	120 mg (normal *LRRK2*) 6 participants	120 mg (abnormal *LRRK2*) 6 participants
Headache after lumbar puncture (post lumbar puncture syndrome)	67% (6)	63% (5)	33% (2)	43% (3)	67% (4)	33% (2)
Pain from the study procedures (procedural pain)	56% (5)	38% (3)	67% (4)	29% (2)	50% (3)	67% (4)
Headache	0	38% (3)	17% (1)	0	17% (1)	33% (2)
Fall	11% (1)	13% (1)	17% (1)	29% (2)	0	17% (1)

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 an adverse event that the study doctors reported as **possibly being caused by 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 event is possibly related to the study drug. When they make this decision, the study doctors do not know if a participant is receiving BIIB094 or placebo. This is important so that study doctors are not influenced when making decisions about the study drugs.

How many participants had adverse reactions during this study?

The table below shows how many participants had adverse reactions in Part A.

Summary of adverse reactions in Part A

	Placebo	BIIB094					
	9 participants	10 mg 3 participants	30 mg 3 participants	40 mg 7 participants	80 mg 6 participants	120 mg 6 participants	150 mg 6 participants
How many participants had adverse reactions?	0	0	0	0	17% (1)	0	17% (1)
How many participants had serious adverse reactions?	0	0	0	0	0	0	0

The table below shows how many participants had adverse reactions in Part B.

Summary of adverse reactions in Part B

	Placebo	BIIB094				
	9 participants	40 mg 8 participants	80 mg (normal *LRRK2*) 6 participants	80 mg (abnormal *LRRK2*) 7 participants	120 mg (normal *LRRK2*) 6 participants	120 mg (abnormal *LRRK2*) 6 participants
How many participants had adverse reactions?	11% (1)	13% (1)	17% (1)	0	0	33% (2)
How many participants had serious adverse reactions?	0	0	0	0	0	0

What serious adverse reactions happened during this study?

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

What adverse reactions happened during this study?

In Part A, there were 2 adverse reactions across 2 participants.

- 1 participant in the 80 mg group had a high number of white blood cells in the spinal fluid (pleocytosis).
- 1 participant in the 150 mg group had a headache.

In Part B, 5 participants had a total of 12 adverse reactions, with some participants having more than 1 adverse reaction. The table below shows the adverse reactions that happened in Part B.

Adverse reactions in Part B

	Placebo	BIIB094				
	9 participants	40 mg 8 participants	80 mg (normal *LRRK2*) 6 participants	80 mg (abnormal *LRRK2*) 7 participants	120 mg (normal *LRRK2*) 6 participants	120 mg (abnormal *LRRK2*) 6 participants
Headache	0	0	0	0	0	17% (1)
Tingling or a "pins and needles" feeling (paresthesia)	0	13% (1)	0	0	0	0
High number of white blood cells in the spinal fluid (pleocytosis)	0	0	0	0	0	17% (1)
Feeling before fainting (presyncope)	11% (1)	0	0	0	0	0
High levels of waste product in blood (blood creatinine increased)	0	0	17% (1)	0	0	0
Increased blood pressure	11% (1)	0	0	0	0	0
Increase in the number of white blood cells in the spinal fluid (CSF white blood cell count increased)	0	0	0	0	0	17% (1)
Reduced kidney function (glomerular filtration rate decreased)	0	0	17% (1)	0	0	0
Feeling tired (fatigue)	0	13% (1)	0	0	0	0
Headache after lumbar puncture (post lumbar puncture syndrome)	11% (1)	0	0	0	0	0
Muscle spasms	0	0	0	0	0	17% (1)
Stiff muscles and joints (musculoskeletal stiffness)	0	0	0	0	0	17% (1)

Pleocytosis and **CSF white blood cell count increased** mean similar things, but study doctors reported them using different medical terms.

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

This study helped researchers learn more about the safety of BIIB094 in humans for the first time and the potential to help people with Parkinson's disease (PD).

Overall, the researchers in this study found that:

- Participants had no major safety issues after receiving BIIB094 through a single dose 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. Studies with BIIB094 may be planned for the future.

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

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

ClinicalTrials.gov	https://www.clinicaltrials.gov/study/NCT03976349
UK Health Research Authority	https://www.hra.nhs.uk/planning-and-improving-research/application-summaries/research-summaries/254pd101-phase-1-study-biib094-administered-intrathecally-to-adults/

Official Study Title: A Phase 1 Single- and Multiple-Ascending-Dose Study to Assess the Safety, Tolerability, and Pharmacokinetics of BIIB094 Administered Intrathecally to Adults With Parkinson's Disease

If you have questions about **BIIB094** 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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