



ALSpire Study

Motivated to find ALS treatment options

ALSpire Study Brochure

Making Connections in ALS Research

Thank you for taking a moment to learn about the ALSpire Study, a clinical research study evaluating an investigational drug for people living with amyotrophic lateral sclerosis (ALS).

This study is enrolling adults living with ALS and adults who have ALS with a mutation (or change) in the *ATXN2* gene (also known as polyQ-ALS).

Researchers are looking to evaluate the safety and tolerability of the investigational drug BIIB105, in people with ALS and polyQ-ALS. The researchers will also look at what the body does to BIIB105, what BIIB105 does to the body, and if BIIB105 can slow the worsening of clinical function.

Potential study participants:

- Must be 18 years of age or older
- Must not have known mutations or a family history of mutations in the *SOD1* or *FUS* genes
- Must meet the study-specific criteria for diagnosis of ALS
- Must have a partner/caregiver who can attend the screening visit and provide information about the participant's health

Please speak with your doctor about what other eligibility criteria also apply.



Choosing to take part in a clinical research study is a big decision. It is important for you to understand what the clinical research study is about, the potential risks, and what your participation would involve before agreeing to take part.



About Clinical Research Studies

Clinical research studies are an important part of the development of medical treatments. They are conducted to determine the safety and effectiveness of an investigational drug.

Clinical research studies are subject to review and oversight by regulatory bodies in individual countries to ensure that they are being conducted correctly and that the rights of study participants are protected.

- Participation in a clinical research study is always voluntary.
- You may withdraw from the study at any time and for any reason.
- If you decide you do not want to participate, it will not affect your care now or in the future.

Even before a study starts, safety is our highest priority. Every study must be reviewed and monitored by either an Institutional Review Board (IRB) or an Independent Ethics Committee (IEC). These groups, made up of both scientists and nonscientists, review the study's plan to make sure that:

- The rights of participants and their study partners/ caregivers will be protected
- There are no unnecessary risks involved
- The study addresses important unanswered medical questions

Without people willing to volunteer for medical research and clinical research studies, it would be almost impossible to evaluate potential new treatments for medical conditions like ALS.

About Study Participation

The study is currently enrolling participants for the top dose cohorts (groups), Cohort D1 and Cohort D2. Cohorts D1 and D2 are studying the same dose of the investigational drug.

Participants with ALS will be enrolled into Cohort D1, and participants with polyQ-ALS will be enrolled in Cohort D2.

If you qualify and choose to participate, you will be randomly assigned (by chance) to receive either the investigational drug or placebo.

A placebo is a substance that looks like the investigational drug but contains no active drug.

This helps researchers make sure that any changes seen during the clinical research study are due to the investigational drug alone and not another reason. Study participants are assigned to their study treatment at random (by chance), and neither they nor the study team will be told which study treatment they have been given until after the study is finished.



Study participation consists of two parts:

PART 1

- Part 1 may last from 29 to 41 weeks, depending on whether the participant continues into Part 2.
- **In Cohort D1**, for every four participants, three will receive the investigational drug and one will receive placebo.
- **In Cohort D2**, for every three participants, two will receive the investigational drug and one will receive placebo.

PART 2

- Part 2 is also known as the open-label extension period, during which all participants will receive the investigational drug.
- Part 2 will last up to approximately 120 weeks, which includes a study treatment period of up to 104 weeks.

Eligible study participants will receive at no cost:

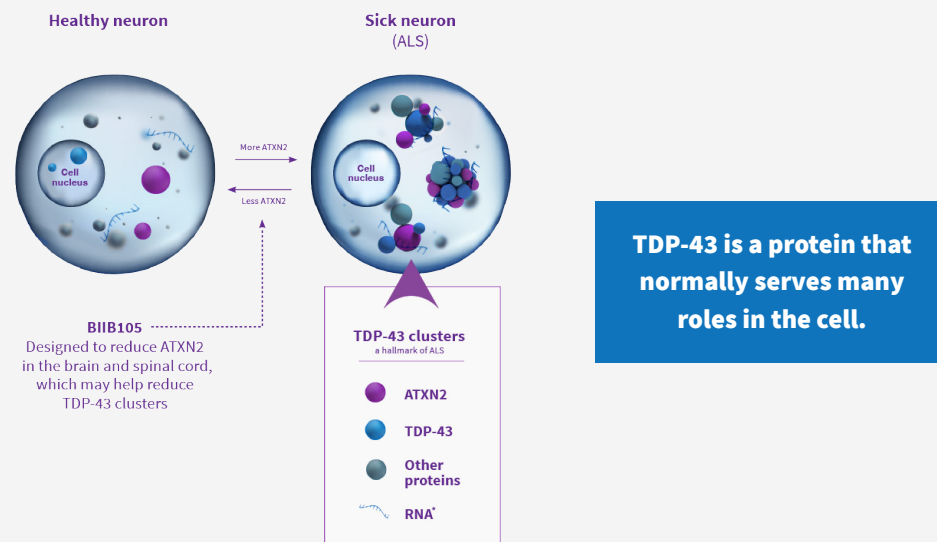
Investigational drug or placebo in Part 1 and the investigational drug in Part 2
Study-related health evaluations and monitoring
Appointments with the study doctor and site staff
Assistance with travel is also available

About the Science

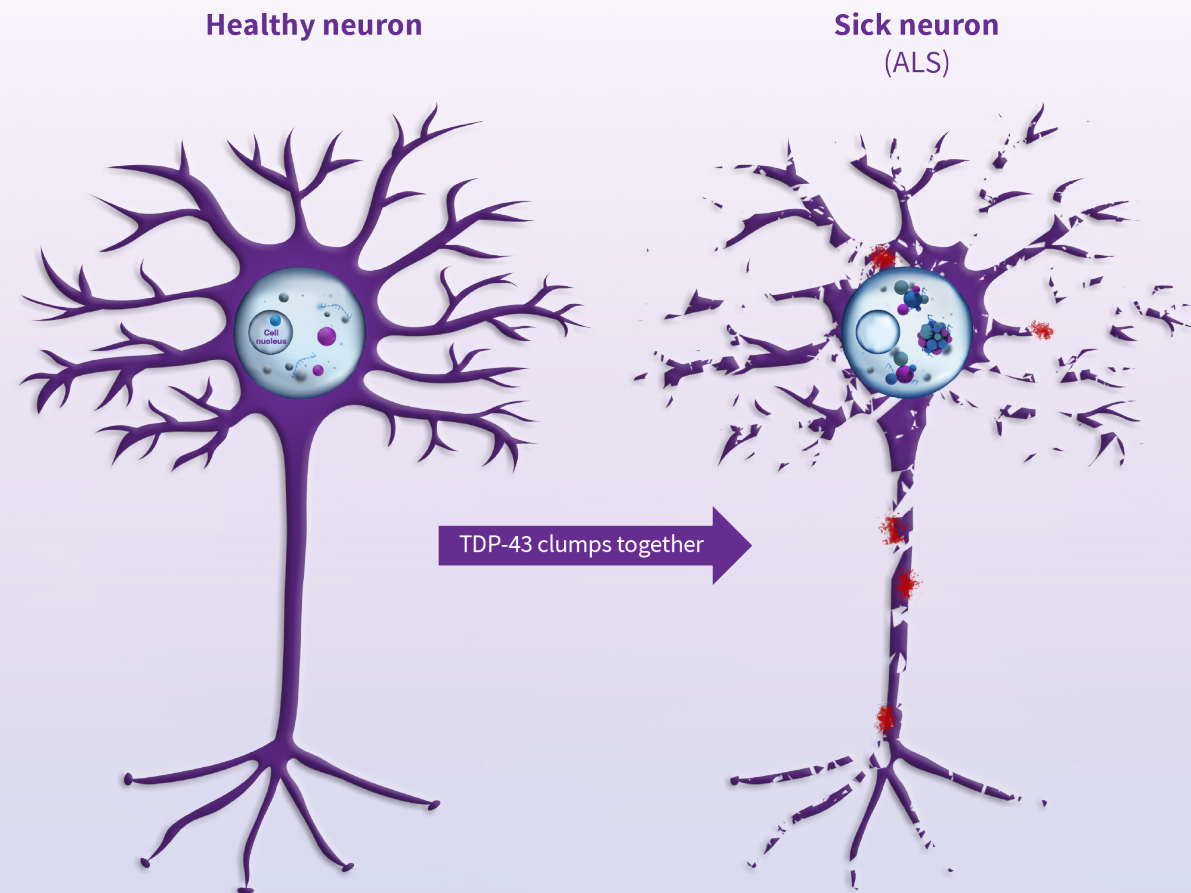
Research has shown that approximately 97% of people with ALS have toxic clusters of a protein called TDP-43 in their brain and spinal cord cells.* Scientists do not know exactly why TDP-43 proteins clump together, but these clusters are toxic and can lead to death of cells in the brain and spinal cord.

In addition, another protein called ataxin-2 (ATXN2) is thought to be involved in clumping TDP-43 proteins together, helping form these toxic TDP-43 clusters.

That is why the ALSpire Study is evaluating an investigational drug designed to reduce the level of ataxin-2 protein in the brain and spinal cord cells, which may help reduce toxic TDP-43 clusters.



*Ling SC, Polymenidou M, Cleveland DW. Converging mechanisms in ALS and FTD: disrupted RNA and protein homeostasis. *Neuron*. 2013;79(3):416-38



What questions are researchers looking to answer?

Researchers are looking to evaluate the safety and tolerability of the investigational drug, BIIB105, in people with ALS, with or without polyQ-ALS. The researchers will also look at what the body does to BIIB105, what BIIB105 does to the body, and if BIIB105 can slow the worsening of clinical function.

How Is the Investigational Drug Given

Lumbar Puncture

The investigational drug or placebo is given by intrathecal injection, which is also known as a lumbar puncture.

Three loading (initial) doses of the investigational drug or placebo will be given every two weeks, followed by maintenance doses given every four weeks thereafter.



During a lumbar puncture, a clinician inserts a thin needle through your lower back into the fluid-filled space below the end of your spinal cord.

X-rays may be used to help guide the clinician. Once the needle is inserted, approximately 10 mL (about two teaspoons) of cerebrospinal fluid (CSF) will be collected in two sample tubes.

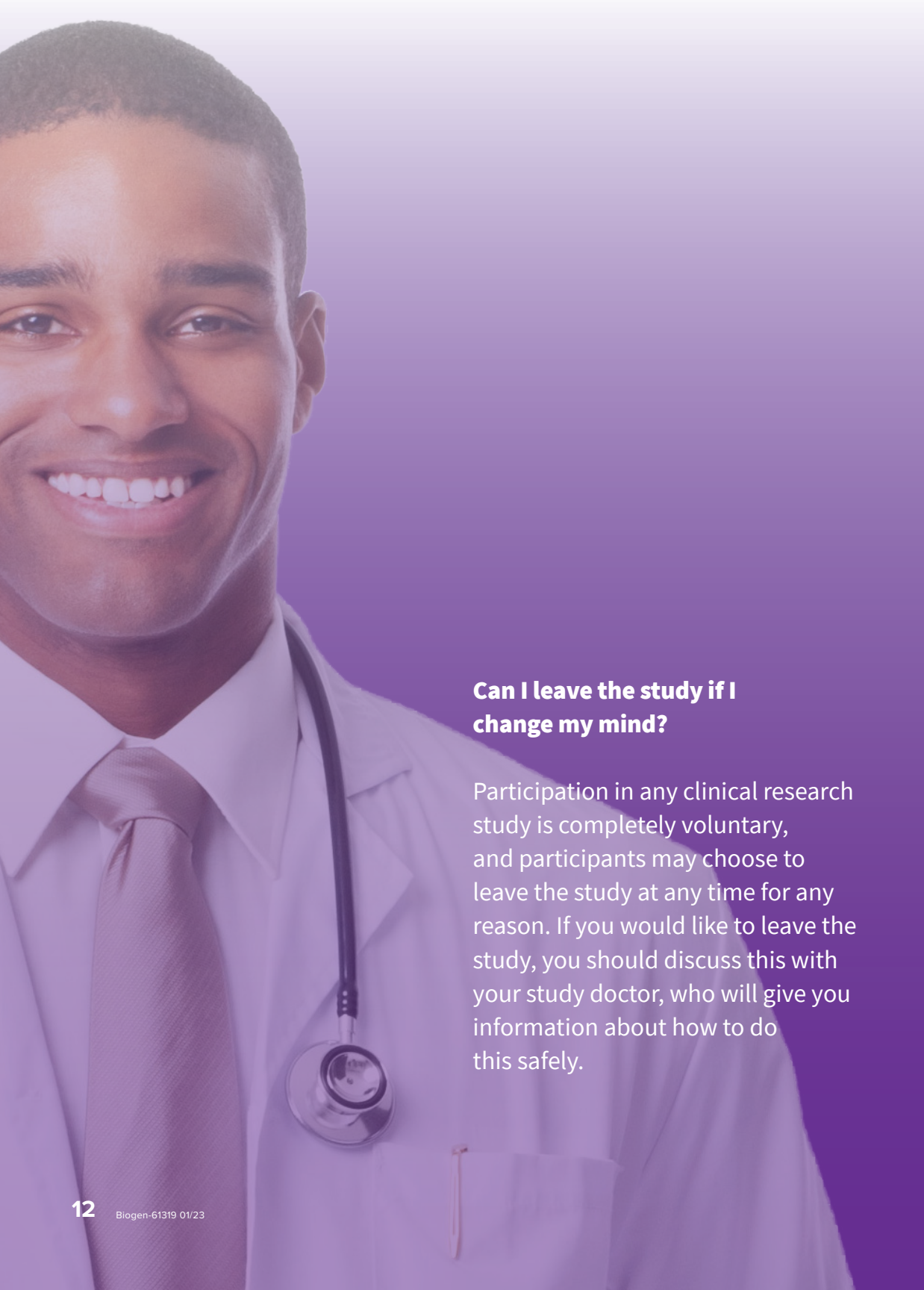
The study team will explain in detail the risks/complications associated with this procedure.

Side effects of the procedure may include headache and back discomfort or pain.

On the days when you are scheduled to receive the investigational medication or placebo, the clinician will inject it through the same needle used to collect the CSF. You have only one needle stick for both the CSF collection and injection.

Your study team will ask you to remain very still during the procedure. You may be asked to stay at the study site for up to six hours or more after the lumbar puncture to be monitored for your safety.

Ref: <https://www.mayoclinic.org/testsprocedures/lumbar-puncture/about/pac-20394631>



Can I leave the study if I change my mind?

Participation in any clinical research study is completely voluntary, and participants may choose to leave the study at any time for any reason. If you would like to leave the study, you should discuss this with your study doctor, who will give you information about how to do this safely.

All study participants will be monitored. Study assessments will vary from visit to visit but may include:

- Blood sample collection
- Urine sample collection
- Health questionnaires
- Vital sign measurements (measurements of your temperature, heart rate, breathing rate, blood pressure, and weight)
- Electrocardiogram (ECG; a test to check the electrical activity of the heart)
- Lumbar puncture
- Neurological exam
- Physical exam
- Clinical function assessments

Thank You

If you would like more information about taking part in this study, please contact the study team using the details below for an initial no-obligation consultation or visit our website at www.ALSpireStudy.com.

