CLINICAL TRIAL RESULTS

A Study that Learned if BIIB092 (Gosuranemab) Worked, and its Safety in Participants with Early Alzheimer's Disease

- **Drug Studied:** BIIB092 (gosuranemab)
- **Protocol #:** 251AD201
- **Study Dates:**
  Start: 03 May 2018
  End: 30 Aug 2021

Biogen

Thank you!

Thank you to the participants who took part in the study for **BIIB092**, also known as **gosuranemab**. All the participants helped the researchers learn more about using gosuranemab to potentially help people with decline in memory and thinking ability due to Alzheimer's disease.

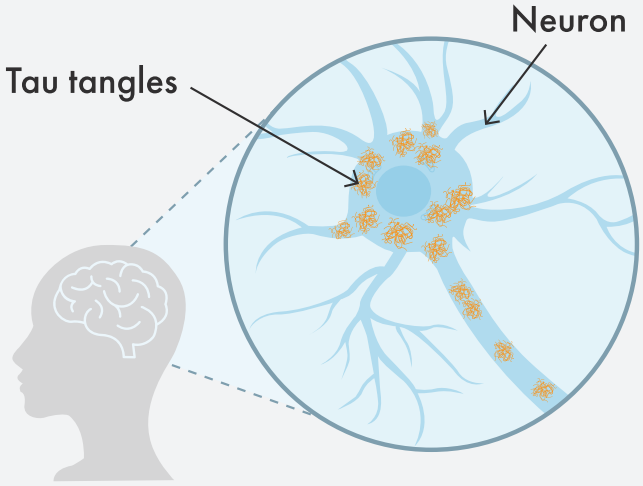
Biogen sponsored this Phase 2 study and reviewed the results when this study ended. Biogen thinks it is important to share the results with participants and the public.

We hope this helps participants understand and feel proud of their important role in medical research. If you have questions, please speak with the doctor or staff at the study site.

What was the **purpose** of this study?

Researchers are looking for different ways to treat patients with early **Alzheimer's disease.** People with Alzheimer's disease have memory loss and eventually lose their ability to think clearly and to carry on their daily activities. Alzheimer's disease is a **progressive illness**, which means it slowly gets worse, and in some cases, can even lead to death.

People with Alzheimer's disease have an abnormal build-up of certain proteins in the brain, including 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.** 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.



Most current treatments for Alzheimer's disease mainly help with symptoms. However, they do not stop the slow loss of mental ability. Recently, new treatments are being developed to change the abnormal tau protein and amyloid plaques that exist in the brains of Alzheimer's disease patients.

While progress is being made, much work remains to be done in Alzheimer's disease research. New treatments are needed, especially for people in the early stages of the disease, when symptoms may still be mild.

The study drug, **gosuranemab,** is a **monoclonal antibody.** Antibodies are proteins made by the body's immune system to fight diseases. Monoclonal antibodies are made in a laboratory. Gosuranemab works by attaching to pieces of tau protein in the cerebrospinal fluid, the fluid bathing the brain and spinal cord. Researchers think that this may help prevent build-up of tau tangles in different brain regions and, in turn, reduce decline in memory and thinking ability in people with early Alzheimer's disease.

The main question that the researchers wanted to answer was:

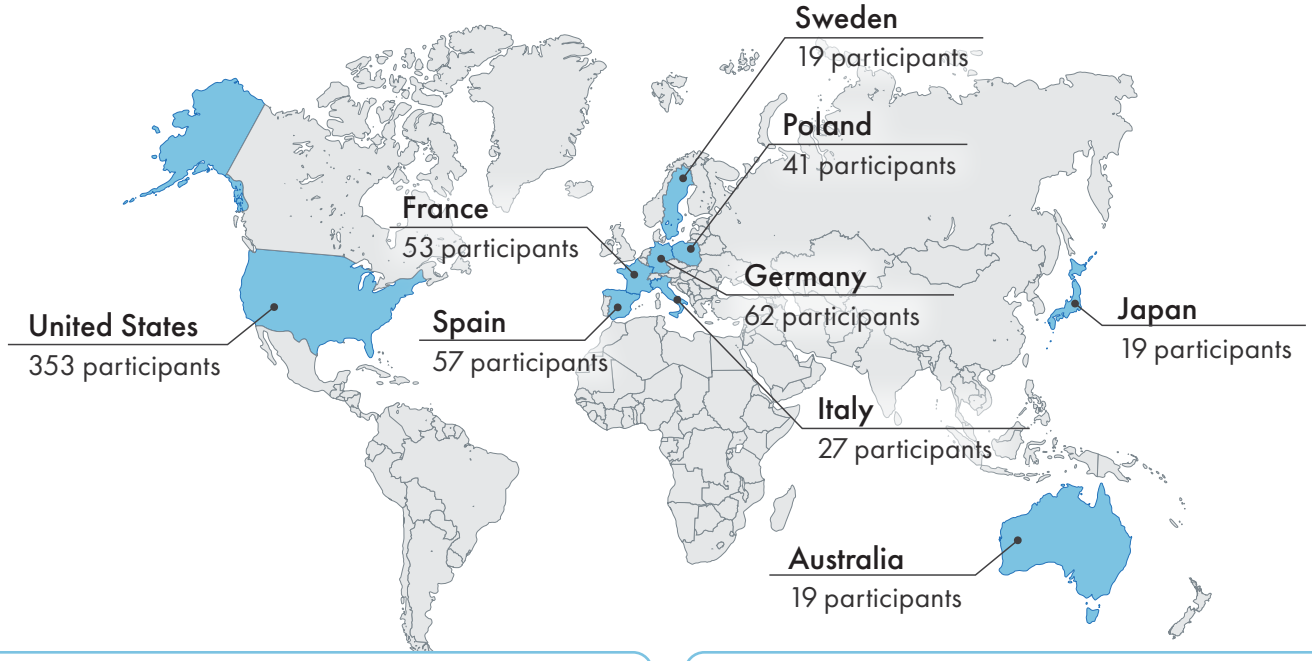
- What was the safety of gosuranemab?

Other questions were:

- How did gosuranemab affect the way that participants think and function over time?
- How else did gosuranemab affect the participants' daily life, including thinking and memory abilities?
- What percentage of study participants developed antibodies to gosuranemab?

Who **took part** in the study?

There were **654 participants** who were randomly assigned to treatment. This included 650 participants who received treatment. There were **104 research centers in 9 countries.** The study included male and female participants between the **ages of 50 and 80 years.** The map below shows how many participants who received treatment were in each country.



Participants **took part** in this study if they:

- Had a gradual change in memory ability over more than 6 months
- Had evidence of mild cognitive impairment
- Had 1 family member or friend that could help them take part in the study

Participants **did not take part** in this study if they:

- Had a different nerve or psychiatric condition that could interfere with taking part in the study
- Had a stroke in the past year

What **treatments** did the participants receive?

Researchers studied the following treatments:

- **Gosuranemab:** 125, 600, or 2000 milligrams (mg) every 4 weeks, or 375 mg every 12 weeks, given as an infusion, which is a slow injection into a vein
- **Placebo:** given as an infusion every 4 weeks

> A **placebo** looks like a study drug but contains no active ingredient or medicine in it. A placebo is used in some participants to compare to those who receive the study drug. This helps researchers learn about the side effects of a study drug and if it works in people with the disease.

What **happened** during the study?

The study started in **May 2018** and was **ended earlier than planned in August 2021**.

The study had 2 parts. However, Biogen decided to end the study early and discontinue clinical development of gosuranemab after data from Part 1 showed that it was not helping participants.

Part 1 of the study was a **double-blinded, placebo-controlled Phase 2 study.** Double-blinded means that the participants, study doctors, site staff, nurses and study sponsor did not know which treatment the participants received. A computer program randomly chose the treatment for each participant.

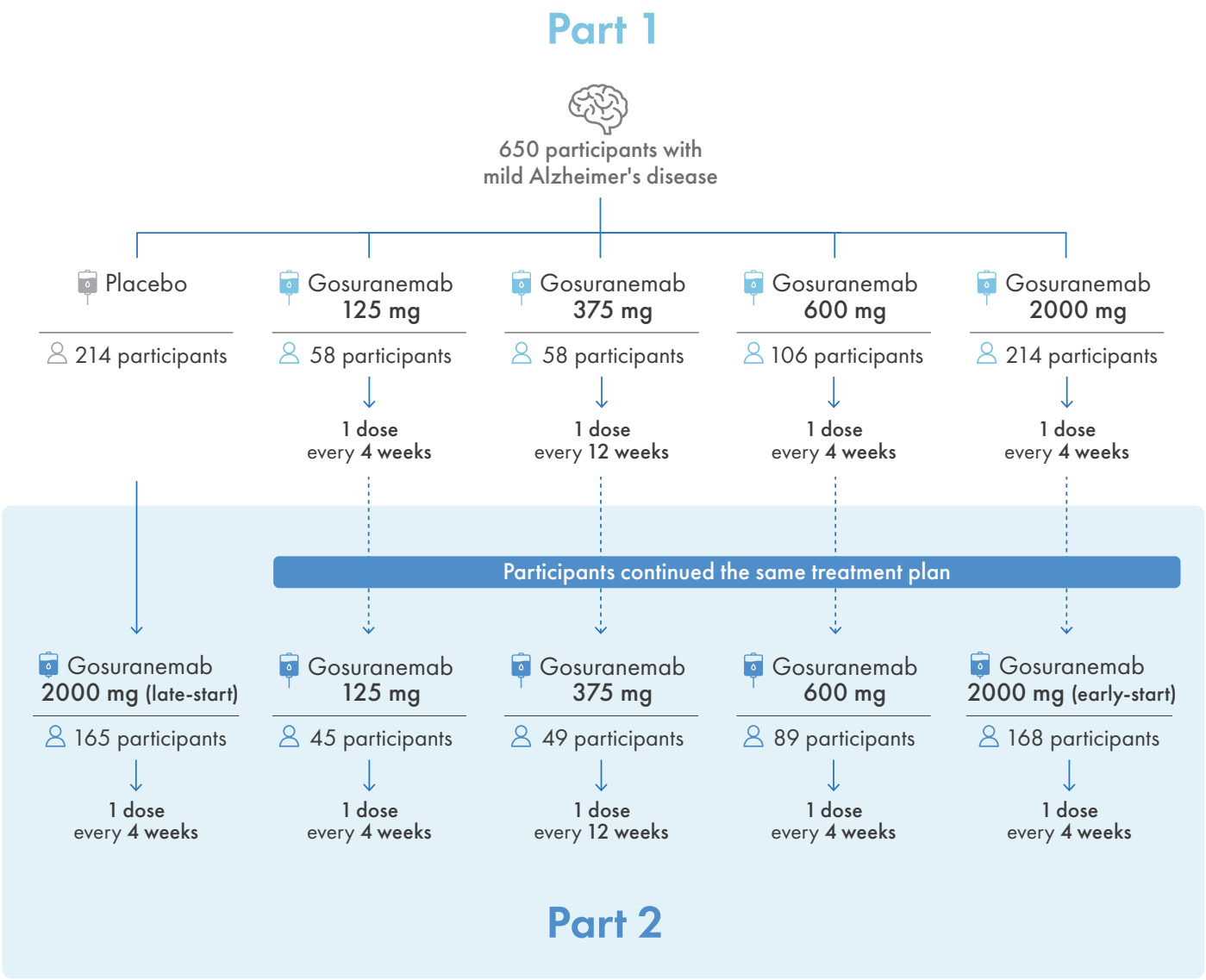
Part 2 of the study was a long-term extension period. Participants continued to receive gosuranemab. This part of the study was **dose-blinded.** This means that the participants, study doctors, site staff, nurses and study sponsor knew that all the participants received gosuranemab. However, except for Biogen, the study sponsor, they did not know which dose each participant received.

There were 650 people who participated in the study and received either gosuranemab or the placebo treatment in the placebo-controlled Phase 2 study. Participants had to have early Alzheimer's disease. Early Alzheimer's disease is mild loss of thinking ability (mild dementia). They answered questions about their medical history before the study began.

In Part 2, all participants stayed on the same dose of gosuranemab except the placebo group. Participants who received placebo in Part 1 of the study received 2000 mg of gosuranemab in Part 2.

Early-start participants received gosuranemab in the placebo-controlled and long-term extension periods. **Late-start** participants received placebo in the placebo-controlled period and gosuranemab in the long-term extension period.

The doses and number of participants for each group in **Part 1** and **Part 2** are shown below.



How was the study done?

During Part 1, participants received treatment for about 76 weeks. **In Part 2,** continuing participants could be treated for another 144 weeks before the study ended.

Participants had regular visits to the clinic. During these visits, researchers checked participants for possible medical problems. They did tests to be sure gosuranemab was safe for participants. Researchers also gathered information to help answer the key study questions.

What were the study **results?**

When the study ended, the sponsor reviewed the data and created a report of the results. This is a summary of that report. Below is an overall summary of the results and the key questions researchers asked during the study.

What medical problems happened during the study?

This section is a summary of the medical problems the participants had during the study. A medical problem occurring during the study is called an **adverse event.** A lot of research is needed to know whether it is the drug that causes an adverse event. An adverse event is considered **serious** when it results in death, is life-threatening, causes lasting problems, requires hospitalization, or is considered medically important. 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.

One goal of this study was to learn more about the potential adverse events due to gosuranemab. Information on adverse events was available for the participants who were assigned to a treatment and received at least 1 dose.

Did any adverse events happen during this study?

The table below shows a summary of adverse events from Part 1.

Summary of adverse events in Part 1					
	Placebo	**Gosuranemab**			
	(214 participants)	**125 mg** (58 participants)	**375 mg** (58 participants)	**600 mg** (106 participants)	**2000 mg** (214 participants)
How many participants had any adverse events?	181 (85%)	50 (86%)	48 (83%)	94 (89%)	189 (88%)
How many participants had serious adverse events?	26 (12%)	6 (10%)	6 (10%)	13 (12%)	25 (12%)
How many participants stopped treatment because of adverse events?	11 (5%)	4 (7%)	2 (3%)	0	8 (4%)
How many participants died due to adverse events?	1 (1%)	1 (2%)	0	0	1 (1%)

There were **3 deaths during Part 1** of this study. The serious adverse events that resulted in death were:

- **COVID-19 pneumonia in 1 (1%)** of the 214 participants who received placebo
- **Pancreatic cancer in 1 (2%)** of the 58 participants who received gosuranemab 125 mg
- **Bleeding in the space around the brain in 1 (1%)** of the 214 participants who received gosuranemab 2000 mg

Study doctors did not think any of these deaths were related to gosuranemab.

The table below shows a summary of adverse events from Part 2.

Summary of adverse events in Part 2					
	Gosuranemab				
	125 mg (45 participants)	**375 mg** (49 participants)	**600 mg** (89 participants)	**2000 mg (early-start)** (168 participants)	**2000 mg (late-start)** (165 participants)
How many participants had any adverse events?	31 (69%)	27 (55%)	52 (58%)	103 (61%)	99 (60%)
How many participants had serious adverse events?	5 (11%)	1 (2%)	9 (10%)	10 (6%)	13 (8%)
How many participants stopped treatment because of adverse events?	4 (9%)	0	0	0	1 (1%)
How many participants died due to adverse events?	2 (4%)	0	1 (1%)	1 (1%)	2 (1%)

There were **6 deaths during Part 2** of this study. The serious adverse events that resulted in death were:

- **Bleeding ulcer in the first part of the small intestine in 1 (1%)** of the 165 participants assigned to the gosuranemab 2000 mg (late-start) group. This participant completed Part 1 but died before receiving gosuranemab in Part 2.
- **Swelling of the lung tissue in 1 (2%)** and **heart attack in 1 (2%)** of the 45 participants who received gosuranemab 125 mg
- **Infection in parts of the body involved in breathing in 1 (1%)** of the 89 participants who received gosuranemab 600 mg
- **Respiratory failure in 1 (1%)** of the 168 participants who received gosuranemab 2000 mg (early-start)
- **COVID-19 pneumonia and respiratory failure in 1 (1%)** of the 165 participants who received gosuranemab 2000 mg (late-start)

Study doctors did not think any of these deaths were related to gosuranemab.

What common adverse events happened during the study?

The table below shows the most common adverse events that happened during Part 1 in at least 10% of participants.

Most common adverse events in Part 1					
	Placebo	**Gosuranemab**			
	(214 participants)	**125 mg** (58 participants)	**375 mg** (58 participants)	**600 mg** (106 participants)	**2000 mg** (214 participants)
Fall	23 (11%)	7 (12%)	11 (19%)	20 (19%)	30 (14%)
Diarrhea	12 (6%)	11 (19%)	3 (5%)	6 (6%)	11 (5%)
Nose and throat inflammation	22 (10%)	4 (7%)	6 (10%)	9 (9%)	24 (11%)
Joint pain	14 (7%)	6 (10%)	7 (12%)	9 (9%)	19 (9%)
Headache	20 (9%)	1 (2%)	6 (10%)	11 (10%)	22 (10%)
Constipation	8 (4%)	6 (10%)	1 (2%)	2 (2%)	6 (3%)

The table below shows the most common adverse events that happened in at least 5% of participants during Part 2.

Most common adverse events in Part 2					
	Gosuranemab				
	125 mg (45 participants)	**375 mg** (49 participants)	**600 mg** (89 participants)	**2000 mg (early-start)** (168 participants)	**2000 mg (late-start)** (165 participants)
Fall	5 (11%)	8 (16%)	6 (7%)	16 (10%)	18 (11%)
COVID-19	2 (4%)	1 (2%)	9 (10%)	2 (1%)	3 (2%)

What serious adverse events happened during the study?

The table below shows the serious adverse events that happened in at least 2 participants who received gosuranemab during Part 1.

Serious adverse events in Part 1					
	Placebo	**Gosuranemab**			
	(214 participants)	**125 mg** (58 participants)	**375 mg** (58 participants)	**600 mg** (106 participants)	**2000 mg** (214 participants)
Fall	2 (1%)	1 (2%)	1 (2%)	1 (1%)	1 (1%)
Dizziness	1 (1%)	1 (2%)	0	1 (1%)	2 (1%)
Coronary artery disease	0	0	0	2 (2%)	1 (1%)
Acute kidney injury	0	1 (2%)	0	0	1 (1%)
Hardened feces	0	1 (2%)	0	0	1 (1%)
Hernia in the lower belly	0	0	1 (2%)	1 (1%)	0
Arthritis of the bone	1 (1%)	0	0	2 (2%)	0
Collapsed lung	0	0	0	0	2 (1%)
Prostate cancer	0	1 (2%)	0	0	1 (1%)
Bleeding in the space around the brain	0	0	1 (2%)	0	1 (1%)
Problems due to lumbar puncture	0	0	0	1 (1%)	1 (1%)
Seizure	1 (1%)	0	0	1 (1%)	1 (1%)

The table below shows the serious adverse events that happened in at least 2 participants who received gosuranemab in Part 2.

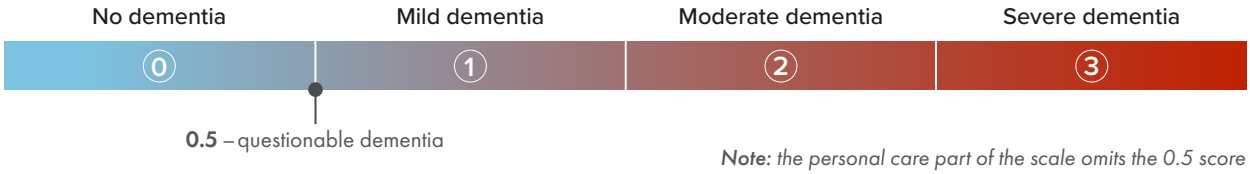
Serious adverse events in Part 2					
	Gosuranemab				
	125 mg (45 participants)	**375 mg** (49 participants)	**600 mg** (89 participants)	**2000 mg (early-start)** (168 participants)	**2000 mg (late-start)** (165 participants)
Fall	0	1 (2%)	0	3 (2%)	3 (2%)
Broken leg near the hip	0	1 (2%)	0	1 (1%)	0
COVID-19 pneumonia	0	0	1 (1%)	0	1 (1%)
Pneumonia	0	0	1 (1%)	1 (1%)	0

How did gosuranemab affect the way that participants think and function over time?

To answer this question, the researchers used a scale called the **Clinical Dementia Rating-Sum of Boxes,** also known as the **CDR-SB.** The CDR-SB is based on an interview with the participant and a family member or friend.

What do CDR-SB scores mean?

The CDR-SB uses a score between 0 and 3 to rate dementia, a serious Alzheimer's disease symptom. A score of 0 means that there are no signs of dementia. The other possible scores are:



Note: the personal care part of the scale omits the 0.5 score

The researchers asked questions about the participants' memory, problem-solving skills, social life, hobbies, and personal care.

The researchers used the CDR-SB to give the participants a score before receiving the study drug. The researchers also gave participants scores at Week 78 after starting their treatment during Part 1. A higher score on the CDR-SB meant that a participant's Alzheimer's disease symptoms were worse.

The table below shows the **average change in CDR-SB scores at Week 78 in Part 1.**

Change in CDR-SB scores at the end of Part 1				
	Placebo	**Gosuranemab**		
	(214 participants)	**125 mg and 375 mg** (116 participants)	**600 mg** (106 participants)	**2000 mg** (214 participants)
Change in CDR-SB score	1.9	2.2	2.2	1.9

The results for Part 1 showed that there was no difference in CDR-SB scores between the placebo group and the groups who received gosuranemab from the start of the study to Week 78.

How else did gosuranemab affect the participants' daily life, including thinking and memory abilities?

To answer this question, researchers used the following measurements before and after the participants received study drug during Part 1 to explore their daily life, including thinking and memory abilities:

- **Mini-Mental State Examination,** also known as the MMSE
- **Alzheimer's Disease Assessment Scale - Cognitive Subscale 13,** also known as the ADAS-Cog13
- **Alzheimer's Disease Cooperative Study - Activities of Daily Living - Mild Cognitive Impairment,** also known as the ADCS-ADL-MCI
- **Functional Activities Questionnaire,** also known as the FAQ

Overall, the researchers found that after 78 weeks of treatment during Part 1, gosuranemab did not improve participants' activities of daily living, health outcomes, or overall quality of life.

How many participants developed antibodies to gosuranemab before Week 90?

Results for this question were available for 596 participants. The results showed that **1 (1%) out of the 105 participants** in the gosuranemab 600 mg group developed antibodies to gosuranemab at any time before Week 90.

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

You can find more information about the study online at www.clinicaltrials.gov. Once on the site, type **NCT03352557** into the search box and click **Search.**

You can also find more information online at Clinical Trials Register. Once on the site, click **Home & Search,** then type **2017-002901-37** in the search box and click **Search.**

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

Official Study Title: Randomized, Double-Blind, Placebo-Controlled, Parallel-Group Study to Assess the Safety, Tolerability, and Efficacy of BIIB092 in Subjects with Mild Cognitive Impairment due to Alzheimer's Disease or with Mild Alzheimer's Disease

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

The results presented here are for a single study of an investigational drug. You should not make changes to your therapy based on these results without first consulting your doctor.

US Clinical Study Database

- **https://www.clinicaltrials.gov/ct2/show/NCT03352557**
- www.clinicaltrials.gov
- Study #: NCT03352557

EU Clinical Study Database

- **https://www.clinicaltrialsregister.eu/ctr-search/search?query=2017-002901-37**
- www.clinicaltrialsregister.eu
- Study #: 2017-002901-37

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Thank you.