CLINICAL TRIAL RESULTS

A Study to Learn About the Safety and Effects of Tecfidera and Plegridy in Pediatric Participants With Relapsing-Remitting Multiple Sclerosis

Drugs Studied: Tecfidera (dimethyl fumarate, BG00012)
Plegridy (peginterferon beta-1a, BIIB017)
Protocol Number: 800MS301 (BLAST)
Study Dates:
Start Date: 16 April 2019
Completion Date: 21 July 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.

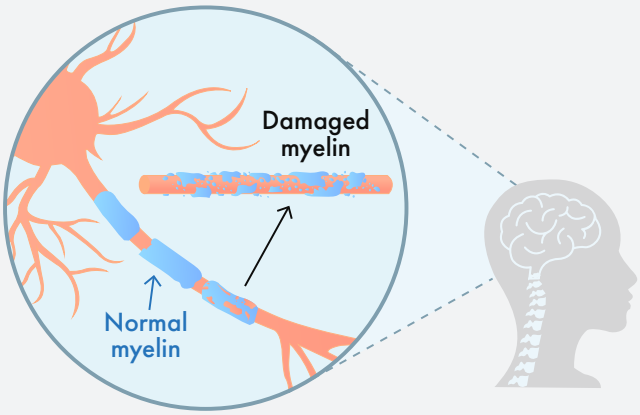
In this study, researchers learned more about the drugs Tecfidera and Plegridy in young patients with relapsing-remitting multiple sclerosis. Tecfidera and Plegridy are already approved for use in adults.

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 drugs that may help pediatric patients with certain types of **multiple sclerosis (MS)**.

In MS, the immune system attacks the nerves in the brain and spinal cord. This causes damage to the **myelin**, a protective covering on the nerves. 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, in rare cases, can lead to death.



Symptoms of MS include tiredness, numbness, tingling, and muscle weakness. Symptoms also include problems with vision, walking, thinking, and using the bathroom. In people with **relapsing-remitting MS**, also known as **RRMS**, these symptoms may last a few hours or days, then disappear only to come back again later. Relapses are when new symptoms start or there is a worsening of existing symptoms. When symptoms disappear, it is called **remitting**.

In people living with RRMS, disability can worsen over time with each relapse. A disability is when people find it difficult or impossible to do certain activities.

Currently, there are no drugs to cure RRMS or repair damaged nerves. However, several drugs have been shown to lower the number of relapses.

Current treatments for RRMS include drugs that try to prevent the immune system from attacking the nerves as often. The 2 drugs that researchers investigated in this study are **Tecfidera and Plegridy.** Tecfidera is also known as dimethyl fumarate or DMF. Plegridy is also known as peginterferon beta-1a. Both are approved to treat RRMS in adults.

However, there is a need to find new treatments for younger patients. As a result, researchers wanted to learn more about Tecfidera and Plegridy in participants with RRMS between the ages of 10 and 17.

The main questions that the researchers wanted to answer were:

- After starting study treatment, how much time did it take for the first MS relapse to occur?
- What possible adverse reactions did the participants have?

An **adverse reaction** is a medical problem the study doctors reported as possibly being caused by the study drugs. 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 11 participants, which included **3 boys** and **8 girls**.

All participants were between **13 and 17 years old**.

The study took place at **6 research centers** in Estonia, Jordan, Taiwan, Tunisia, and Turkey.

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

- Were between 10 and 17 years old
- Were diagnosed with RRMS
- Had relapses and/or areas of active inflammation in the brain before joining the study

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

- Had other forms of MS or conditions that looked like MS
- Had a relapse 1 month before taking the study drugs or had an ongoing relapse
- Were taking certain medications that could interfere with 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:

- **Tecfidera, 240 milligrams (mg)**, given twice daily as capsules taken by mouth.
- **Plegridy, 125 micrograms (µg)**, given once every 2 weeks as an injection under the skin.
- **Placebo**, given either as capsules taken by mouth or as injections under the skin.

A **placebo** looks like a study drug but contains no real medicine. The researchers used a placebo to better understand if differences between the groups were due to the study drugs.

What **happened** during the study?

How was the study done?

This study was:

Phase 3: This is usually the last phase of clinical studies before a new drug is submitted to government authorities for approval for use outside of clinical studies.

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

Randomized study: This study was randomized. This means the researchers used a computer program to randomly choose the drug each participant received. This helped make sure the groups were chosen fairly.

At the beginning of the study, all participants had a screening visit. This visit included a physical exam, heart tests, blood and urine tests, and other tests to check their RRMS symptoms. Participants or their caregivers also answered questions about their medical history.

After screening, a total of 11 participants were randomly put into 1 of 3 groups.

Participants in the **Tecfidera group**:

- Received 120 mg of Tecfidera twice a day for the first 7 days.
- Afterwards, they received 240 mg of Tecfidera twice a day for the rest of the treatment period.
- They also received a placebo injection under the skin once every 2 weeks that looked like Plegridy.

Participants in the **Plegridy group**:

- Received 63 µg of Plegridy on Day 1 of treatment.
- Then, they received 96 µg of Plegridy 2 weeks later.
- Afterwards, they received 125 µg of Plegridy every 2 weeks for the rest of the treatment period.
- They also received placebo capsules twice a day that looked like Tecfidera.

Participants in the **Placebo group**:

- Received placebo capsules twice a day that looked like Tecfidera.
- They also received a placebo injection under the skin once every 2 weeks that looked like Plegridy.

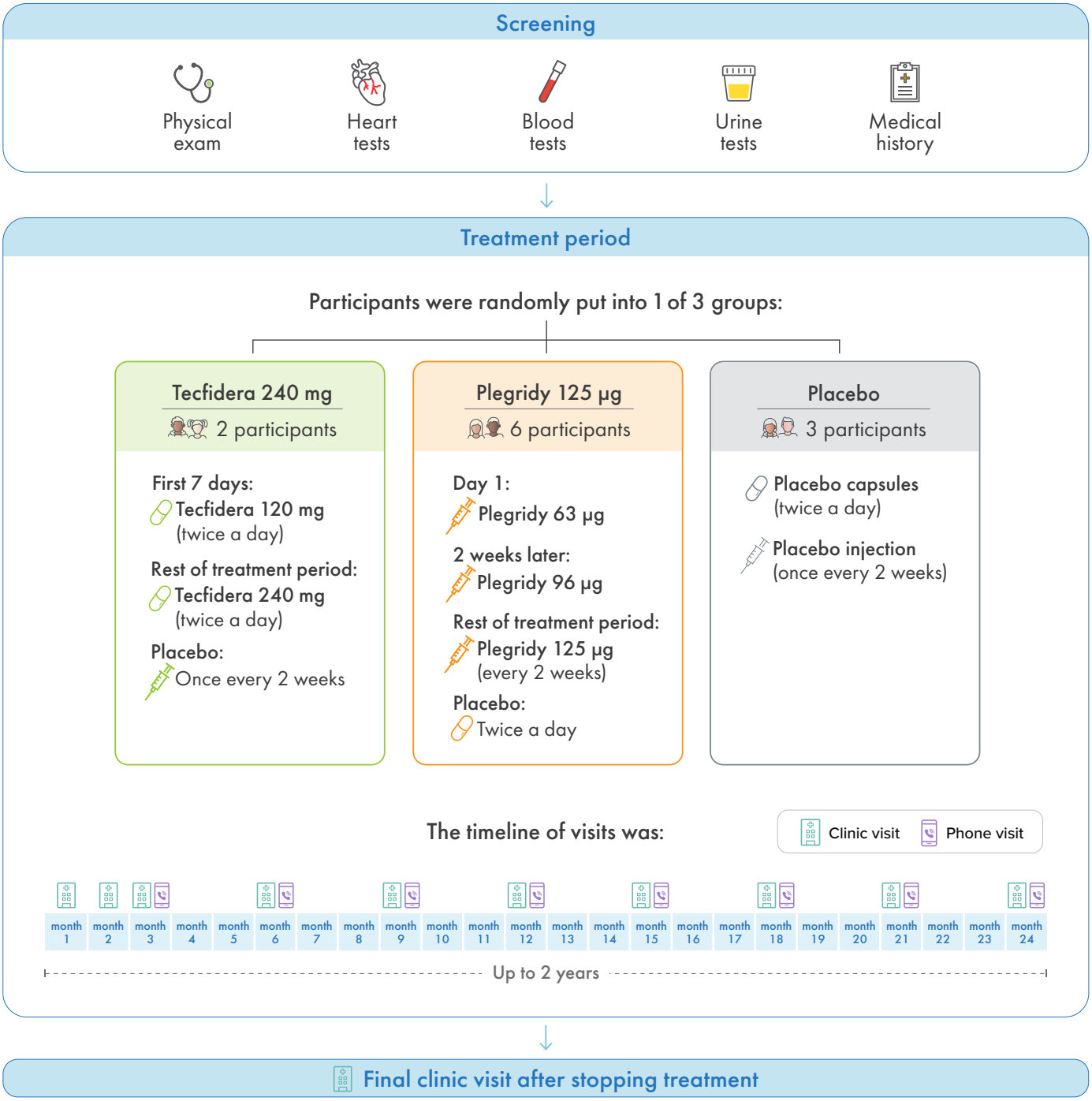
Participants were expected to continue taking the study drugs for up to about 2 years.

Participants visited the clinic regularly throughout the study. These visits took place once a month during the first 3 months of treatment. Afterwards, they visited the clinic once every 3 months. During these visits, participants took tests to assess their MS symptoms and their overall wellbeing. They also had additional physical exams and blood and urine tests. Participants had a final visit 1 month after stopping treatment.

Researchers also called participants on the phone once every 3 months to check on their health. During the clinic visits and phone calls, participants were checked for adverse events. Adverse events are medical problems that may or may not be caused by the study drugs.

If a participant had a relapse or their disease got worse, there were 2 options. Study doctors could change their treatment or remove them from the study.

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 of the results are presented for 11 participants who received Tecfidera, Plegridy, or the placebo. The individual results of each participant might be different and are not in this summary.

Researchers wanted to enroll over 200 participants. However, only 11 participants were able to join the study. As a result, the study was ended early.

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.

After starting study treatment, how much time did it take for the first MS relapse to occur?

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 recorded any relapses that participants had.

The study did not enroll enough participants. Because of this, researchers were not able to make any conclusions about how much time it may take for the first MS relapse to occur.

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

This section is a 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 related to the study drug. When they make this decision, the study doctors do not know whether a participant is receiving the study drugs or placebo. This is important so that study doctors are not influenced when making decisions about the study drugs.

It takes many studies to determine if adverse reactions are truly related to the study drugs or the placebo.

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

	Tecfidera (2 participants)	**Plegridy** (6 participants)	**Placebo** (3 participants)
How many participants had adverse reactions?	50% (1)	33% (2)	33% (1)

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

What common adverse reactions happened during this study?

A total of **36% of the participants** experienced an adverse reaction during the study. This was **4 out of the 11 participants.** One of the participants had more than 1 adverse reaction.

The table below shows the adverse reactions that happened.

List of adverse reactions

	Tecfidera (2 participants)	**Plegridy** (6 participants)	**Placebo** (3 participants)
Feeling cold	0	17% (1)	0
Bruising at the site of injection	0	17% (1)	0
Pink or red blotches at the site of injection	0	17% (1)	0
Disorder of the stomach and intestines	0	0	33% (1)
Pink or red blotches on the skin	50% (1)	0	0

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 Tecfidera and Plegridy in young people with RRMS.

There were not enough participants in this study for researchers to answer their main question. Overall, no new safety concerns were discovered in this study.

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 Tecfidera and Plegridy in pediatric participants are currently ongoing.

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

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

US Clinical Study Database	https://clinicaltrials.gov/ct2/show/NCT03870763
EU Clinical Trials Register	https://www.clinicaltrialsregister.eu/ctr-search/search?query=2018-000516-22

Official Study Title: A Randomized, Double-Blind, Double-Dummy, Placebo-Controlled, 3-Arm, Parallel-Group Study in Pediatric Subjects Aged 10 Through 17 Years to Evaluate the Efficacy and Safety of BG00012 and BIIB017 for the Treatment of Relapsing-Remitting Multiple Sclerosis

If you have questions about Tecfidera, Plegridy, 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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