Clinical Trial Results

NOVARTIS

Research Sponsor:	Novartis
Location of Headquarters:	Basel, Switzerland
Drug Studied:	BAF312 (Siponimod)
Protocol #:	CBAF312X2205
Full Trial Title:	A multi-centre, double-blind, placebo-controlled, proof of concept study to evaluate the efficacy and tolerability of BAF312 in patients with polymyositis
Full Scientific Summary:	www.novctrd.com
Trial Date:	April 2013 to August 2016

Thank you!

Thank you for taking part in the clinical trial for the drug BAF312, also called siponimod. You helped researchers learn more about how BAF312 works in people with active polymyositis or PM.

Novartis, the sponsor of this trial, thanks you for your help and thinks it is important for you to know the results of your trial. An independent non-profit organization called CISCRP prepared this summary of the trial results for you. We hope it helps you understand your important role in medical research.

If you have questions about the results, please speak with the doctor, research nurse, or other team member at your trial site.

What's happened since the trial ended?

You were in this trial for up to 9 months, but the trial took more than 3 years to complete. This is because people started and stopped the trial at different times. The trial planned to include at least

45 patients from 20 sites in 8 countries: Belgium, Canada, Czech Republic, Hungary, Poland, Switzerland, Taiwan, and the United States. But, only 14 patients enrolled. Researchers ended the trial earlier than planned because they could not find enough patients with PM in time to join the trial. So, the researchers could not get clear results. When the trial ended, the sponsor reviewed the data and created a report of the results. This is a summary of that report.

Why was the research needed?

Researchers were looking for a better way to treat PM. People with PM have muscle weakness, tenderness, and pain. These symptoms are caused by white blood cells in the immune system called T-lymphocytes that inflame the muscle. This inflammation may damage the muscle. People with PM may also have higher levels of an enzyme in the blood called creatine kinase, or CK. The amount of CK in the blood can rise when tissues that use CK, like skeletal muscles, are damaged.

The trial drug BAF312 makes lymphocytes stay where they are created so that they cannot move to the muscle and cause inflammation. In this trial, researchers were trying to find out if BAF312 lowers CK levels and helps muscle strength in people with PM. Researchers compared BAF312 with a placebo. A placebo looks like a drug, but does not have any medicine in it. Using a placebo helps researchers better understand the actual effect of the trial drug.

In your trial, researchers wanted to know:

- Did BAF312 increase muscle strength more than the placebo?
- Did BAF312 lower CK levels in the blood more than the placebo?
- Did BAF312 help patients walk more than the placebo?
- How much BAF312 got into the blood?
- What medical problems did patients have during the trial?

To answer these questions, researchers asked for the help of men and women like you.

What kind of trial was this?

The patients in this trial were 24 to 68 years old and had active PM. This trial had 2 parts: Part 1 and Part 2.

Part 1 was "double-blind". This means that none of the patients, trial doctors, trial staff, or sponsor staff knew which patients took the trial drug or the placebo. Some trials are done this way because knowing what drug each patient is taking can affect the results of the trial. This way, it ensures that the results are looked at fairly. During Part 1, patients took either BAF312 or a placebo. When the sponsor ended the trial early, the sponsor found out which drug patients took in Part 1.

Part 2 was "open-label". This means that the patients, trial doctors, trial staff, and the sponsor knew what drug each patient took. During Part 2, all patients took BAF312. But the trial ended before any patients who took the placebo in Part 1 began taking 10 milligrams, or mg, of BAF312 in Part 2.

After the trial ended, the sponsor created a report of the trial results.

What happened during the trial?

Before the trial, trial doctors did a checkup of all patients to make sure they could join the trial. Trial doctors:

- Took blood and urine samples
- Checked the height, weight, blood pressure, and heart rate of each patient
- Checked the heart of each patient using an electrocardiogram, or ECG
- Checked lung function and did eye exams
- Asked patients about their symptoms

During the trial, Part 1 lasted 12 weeks:

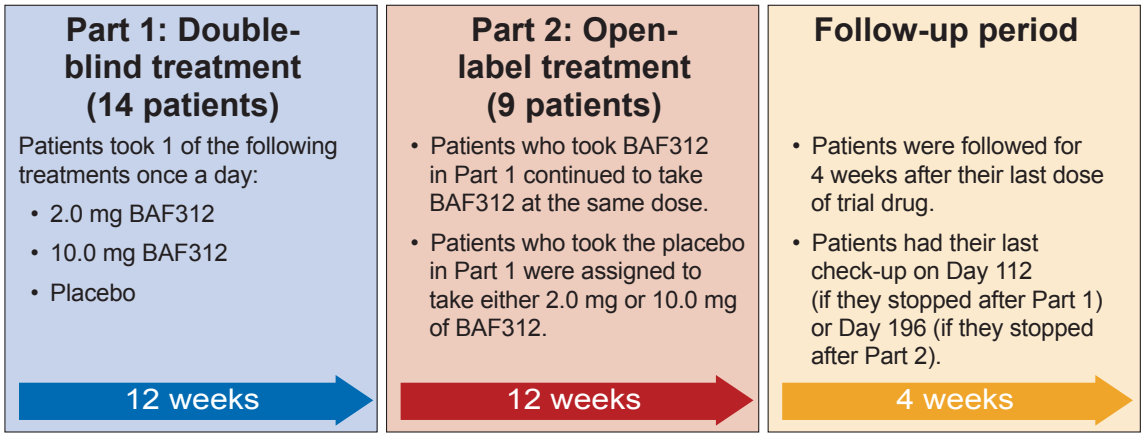
- Patients took either 2.0 mg or 10.0 mg of BAF312 or a placebo, once a day.
- The treatment was decided randomly using a computer program.
- Trial doctors checked lung function and did eye exams and a chest x-ray.

During the trial, Part 2 lasted 12 weeks:

- After finishing Part 1, patients could have continued into Part 2.
- Patients who took BAF312 in Part 1 continued to take BAF312 at the same dose.
- Patients who took the placebo in Part 1 were assigned to take either 2.0 mg or 10.0 mg of BAF312.
- The treatment given was decided randomly using a computer program.
- Trial doctors checked lung function and did eye exams.

The trial ended before any patients began taking 10.0 mg of BAF312 in Part 2.

The figure below shows how the trial was done.



For Parts 1 and 2, patients had a “titration” period of 10 days at the beginning of each part. Titration means that patients started with a low dose and increased the dose over 5-10 days of treatment to reach the full dose.

Throughout the trial, trial doctors measured the muscle strength of patients and checked how well each patient could walk. Trial doctors also took blood and urine samples and checked the height, weight, blood pressure, and heart rate of patients.

The follow-up period lasted 4 weeks:

- After finishing Part 1 or Part 2 treatment, trial doctors still checked how patients were feeling and if their symptoms were improving for 4 weeks after their last dose.
- Patients who stopped after Part 1 of the trial had their last check-up on Day 112.
- Patients who stopped after Part 2 of the trial had their last check-up on Day 196.

What were the results of the trial?

This is a summary of the overall results of your trial, not your individual results. The results presented here are for a single trial. Researchers look at the results of many trials to decide which drugs work best and are safest for patients. Other trials may provide new information or different results. You should not make changes to your medications or treatment plan based on the results of a single trial without first talking to your doctor.

Did BAF312 increase muscle strength more than the placebo?
After 12 weeks of treatment, an increase in muscle strength was seen in patients who took 10.0 mg of BAF312 compared to patients who took placebo. But, the number of patients in each treatment group was too small for researchers to be confident that BAF312 caused the difference in muscle strength. No difference in muscle strength was seen in patients who took 2.0 mg of BAF312.

To find out if BAF312 increased muscle strength more than the placebo, trial doctors used a test that looked at how well patients could use different muscles in their body. For example, patients were asked to sit in a chair and lift their arm. The trial doctor then pressed on the arm of the patients. The trial doctor told the patients to resist the doctor's pushing as best they could. Trial doctors gave each patient a score based on this test. The higher the score, the better the muscle strength.

At the end of Part 1 after 12 weeks of treatment, researchers found that:

- **Placebo:** Patients who took the placebo had a change of 9.1 points
- **2.0 mg BAF312:** Patients who took 2.0 mg of BAF312 had a change of 11.2 points
- **10.0 mg BAF312:** Patients who took 10.0 mg of BAF312 had a change of 39.0 points

The results seemed to show that, overall, patients who took 10 mg BAF312 had more muscle strength compared to patients who took the placebo. But, the number of patients in each treatment group was too small. So, the difference between the groups could be due to chance.

Did BAF312 lower CK levels in the blood more than the placebo?
Patients who took BAF312 did have lower CK levels in their blood compared to patients who took placebo. But, the number of patients in each treatment group was again too small for researchers to be confident that BAF312 lowered CK levels.

To find out if BAF312 treatment lowered CK levels, researchers took blood samples and measured CK levels in the blood. Lower CK levels meant less muscle damage. At the end of Part 1 after 12 weeks of treatment, researchers found that:

- **Placebo:** Patients who took the placebo had 0.5% less CK in the blood
- **2.0 mg BAF312:** Patients who took 2.0 mg of BAF312 had 19.7% less CK in the blood
- **10.0 mg BAF312:** Patients who took 10.0 mg of BAF312 had 55.6% less CK in the blood

The results seemed to show that, overall, patients who took BAF312 had lower CK levels in the blood compared to patients who took the placebo. But the number of patients in each treatment group was too small. So, the difference between the groups could be due to chance.

Did BAF312 help patients walk more than the placebo?
Patients who took BAF312 did walk more than patients who took the placebo. But, the number of patients in each treatment group was too small for researchers to be confident that BAF312 helped patients walk more.

To find out if BAF312 helped patients walk more than the placebo, trial doctors used a test that measured how far patients could walk without help in a 6-minute period. The longer the distance was, the better the muscle strength.

In Part 1, researchers found that:

- **Placebo:** Patients who took the placebo walked 6 meters less
- **2.0 mg BAF312:** Patients who took 2.0 mg of BAF312 walked 47 meters more
- **10.0 mg BAF312:** Patients who took 10.0 mg of BAF312 walked 23 meters more

In Part 2, researchers found that:

- **Placebo in Part 1 and 2.0 mg BAF312 in Part 2:** Patients who took the placebo in Part 1 and then 2.0 mg of BAF312 in Part 2 walked 4 meters more
- **2.0 mg BAF312 in both Part 1 and Part 2:** Patients who took 2.0 mg of BAF312 in both Part 1 and Part 2 walked 49 meters more

The trial was ended before any patients began taking 10.0 mg of BAF312 in Part 2.

The results showed that, overall, patients who took BAF312 walked more than patients who took the placebo. But, the number of patients in each treatment group was too small. So, the difference between the groups could be due to chance.

How much BAF312 got into the blood?
Researchers also wanted to know how much BAF312 got into the blood after treatment.

Overall, they learned that:

- On average, BAF312 reached expected levels in the blood after patients took 2.0 mg or 10.0 mg of BAF312.

What medical problems did patients have?

A lot of research is needed to know whether a drug causes a medical problem. So, when new drugs are being studied, researchers keep track of all medical problems that patients have. These medical problems are called “adverse events”. An adverse event is any unwanted sign or symptom that may or may not be caused by the trial drug.

How many patients had adverse events during the trial?
Some patients had adverse events during the trial and 2 patients left the trial because of adverse events.

The tables below and on the next page show how many patients had adverse events and serious adverse events during each part of the trial. The tables include all patients who took BAF312 and all patients who took the placebo.

Adverse events in Part 1

	Placebo (out of 5 patients)	2.0 mg BAF312 (out of 7 patients)	10.0 mg BAF312 (out of 2 patients)	Total (out of 14 patients)
How many patients had adverse events in Part 1?	4 (80.0%)	6 (85.7%)	2 (100.0%)	12 (85.7%)
How many patients had serious adverse events in Part 1?	0 (0.0%)	1 (14.3%)	0 (0.0%)	1 (7.1%)
How many patients left the trial because of adverse events in Part 1?	1 (20.0%)	1 (14.3%)	0 (0.0%)	2 (14.3%)

Adverse events in Part 2

	Placebo to 2.0 mg BAF312 (out of 3 patients)	2.0 mg BAF312 to 2.0 mg BAF312 (out of 6 patients)	Total (out of 9 patients)
How many patients had adverse events in Part 2?	2 (66.7%)	4 (66.7%)	6 (66.7%)
How many patients had serious adverse events in Part 2?	0 (0.0%)	0 (0.0%)	0 (0.0%)
How many patients left the trial because of adverse events in Part 2?	0 (0.0%)	0 (0.0%)	0 (0.0%)

Did any patients have serious adverse events?

An adverse event is considered “serious” when it is life-threatening, causes lasting problems, or leads to hospitalization. During a trial, all serious adverse events are reported and written down, whether or not they are caused by the trial drug.

No patients died during this trial. One patient who took 2.0 mg of BAF312 in Part 1 experienced the serious adverse events of severe kidney damage, lowered red blood cell count, and abnormal destruction of red blood cells. The trial doctors thought these serious adverse events could have been related to the trial treatment.

What were the most common adverse events?
Headache was the most common adverse event in this trial. The table below shows the common adverse events that happened in at least 2 patients during Part 1 of this trial.

Common adverse events in Part 1

Common adverse event	Placebo (out of 5 patients)	2.0 mg BAF312 (out of 7 patients)	10.0 mg BAF312 (out of 2 patients)	Total (out of 14 patients)
Headache	2 (40.0%)	2 (28.6%)	0 (0.0%)	4 (28.6%)
Dizziness	2 (40.0%)	0 (0.0%)	1 (50.0%)	3 (21.4%)
Upper abdominal pain	1 (20.0%)	1 (14.3%)	0 (0.0%)	2 (14.3%)
Nausea	1 (20.0%)	1 (14.3%)	0 (0.0%)	2 (14.3%)

During Part 2, the only common adverse event that happened in at least 2 patients was an infection of the nose, throat, and airways. This happened to 1 patient in the placebo-to-2.0 mg BAF312 group and 1 patient in the 2.0 mg BAF312-to-2.0 mg BAF312 group.

How has this trial helped patients and researchers?

The results presented here are for a single trial. This summary shows only the main results from this 1 small trial, which ended early. Overall, this trial tested BAF312 in a small group of patients with PM. Because the trial ended early, the number of patients in each treatment group was too small to reach any clear conclusion. So, any differences seen between the groups could be due to chance. This trial could not show that BAF312 helped with muscle strength. BAF312 will not be further tested for the treatment of PM. However, we thank the participants for their help in testing BAF312.

Even though BAF312 did not work for PM, the information we learned will help us treat other diseases. Researchers look at the results of many trials to decide which treatments work best and are safest. It takes volunteers in many trials all around the world to advance medical science.

Where can I learn more about this trial and future trials?

More information about the results and the full list of adverse events that occurred in this trial can be found in the scientific summary of the results available on the Novartis Clinical Trial Results website (www.novctrd.com). Once on the site, click **"Clinical trial results"** at the bottom of the page. After agreeing to enter the Novartis website, type **CBAF312X2205** into the keyword search box and click **"Search"**. If you have questions about the results, please speak with the trial doctor or staff at your trial site.

You can find more information about this trial on the websites listed below. If a full report of the trial results is available, it can also be found here:

- Clinical Trials.gov (https://clinicaltrials.gov/) National Clinical Trial # NCT01801917
- EU clinical register (https://www.clinicaltrialsregister.eu/) EU Clinical Trial # 2012-002859-42

Currently, there are no further studies planned for BAF312 in PM. If more clinical trials are planned, they will be listed on the above public websites or www.novartisclinicaltrials.com.
Search for **"BAF312"**.

Thank you

As a clinical trial patient, you belong to a large community of patients around the world. You helped researchers answer important health questions and test new medical treatments.

CISCRP

The Center for Information & Study on Clinical Research Participation (CISCRP) is a non-profit organization focused on educating and informing the public about clinical research participation. CISCRP is not involved in recruiting patients for clinical trials, nor is it involved in conducting clinical trials.

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