Clinical Trial Results

NOVARTIS

Research Sponsor:	Novartis
Location of Headquarters:	Basel, Switzerland
Drug Studied:	BAF312 (Siponimod)
Protocol #:	CBAF312X2206
Full Trial Title:	A double blind, randomized, placebo-controlled study to evaluate, safety, tolerability, efficacy and preliminary dose-response of BAF312 in patients with active dermatomyositis (DM)
Full Scientific Summary:	www.novctrd.com
Trial Date:	November 2013 to February 2016

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.

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 dermatomyositis or DM. This trial started in November 2013 and ended in February 2016.

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.

CISCRP
THE CENTER FOR INFORMATION & STUDY ON CLINICAL RESEARCH PARTICIPATION

What's happened since the trial ended?

You were in this trial for up to 48 weeks, but the trial took close to two and a half years to complete. The trial included 17 patients from 24 sites in Belgium, Canada, Czech Republic, Hungary, Japan, Poland, Taiwan, and the United States. Researchers ended the trial earlier than planned because the researchers could not get clear results. When the trial ended in February 2016, 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 DM. People with DM have weakness in their muscles, especially in the hips, thighs, upper arms, shoulder area, and neck. DM can also cause skin symptoms.

The cause of DM is unknown. DM shares many characteristics with autoimmune diseases in which the body mistakenly attacks itself. Researchers have found that in DM some white blood cells (called lymphocytes) build up around blood vessels in the muscles and skin. The build-up of lymphocytes causes inflammation. Inflammation caused by lymphocytes in the muscles and skin may damage those areas and cause your medical condition.

The trial drug BAF312 lowers the number of lymphocytes found in the blood stream. In this trial, researchers wanted to find out if BAF312 helps lower the number of lymphocytes in people with DM. Researchers also wanted to know if lowering the number of lymphocytes in the blood stream helps with muscle strength in people with DM. Researchers compared BAF312 with a placebo. A placebo looks like medicine but does not have any real medicine in it.

In your trial, researchers wanted to know:

- Does BAF312 help with muscle strength more than the placebo in patients with DM?
- Did BAF312 lower lymphocyte counts in the blood in patients with DM?
- What medical problems did patients with DM have during the trial?

To answer these questions, researchers asked for the help of men and women like you. The patients in this trial were 22 to 61 years old and had active DM.

What kind of trial was this?

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 what drug each patient took. Some trials are done this way because knowing what drug each patient is getting 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.

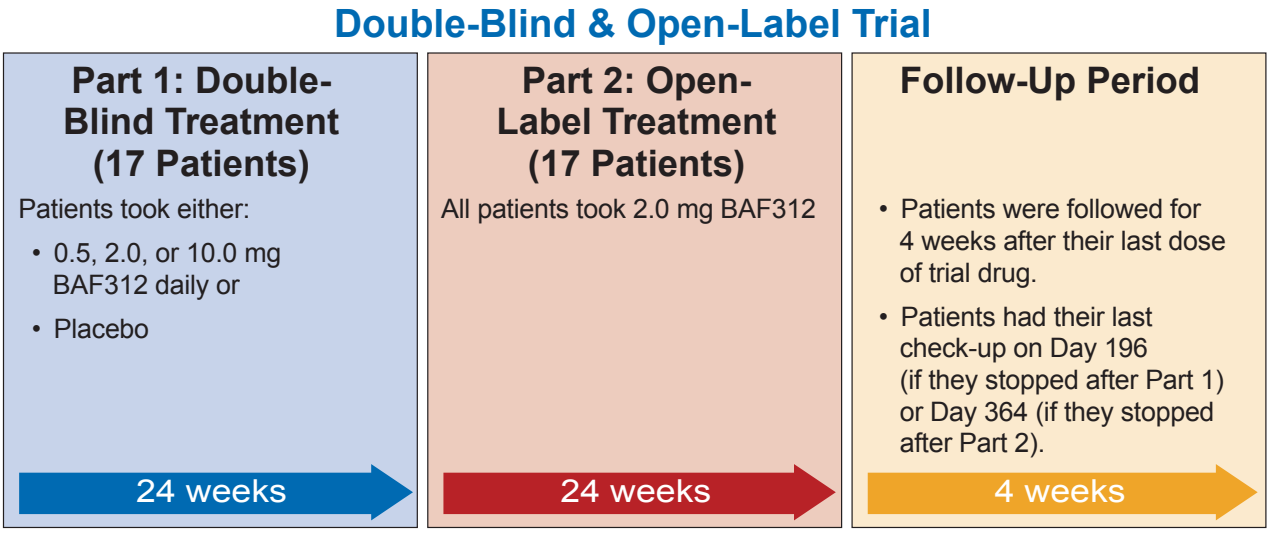
When the Sponsor ended the trial early, the Sponsor found out which drug patients took in Part 1.

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.

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

What happened during the trial?

The figure below shows how the trial was done.



Trial doctors did a full check-up of all patients to make sure they could join the trial. In Part 1, patients were randomly assigned, like flipping a coin, to take either BAF312 or the placebo. Patients gave blood and urine samples. Trial doctors checked the height, weight, blood pressure, and heart rate of the patients. Trial doctors also checked the heart health of patients using an electrocardiogram, or ECG, and asked patients about their symptoms.

Part 1 lasted 24 weeks:

- Patients took either 0.5 milligrams (mg), 2.0 mg, or 10.0 mg of BAF312 or a placebo once a day during Part 1 for 24 weeks.

Part 2 lasted 24 weeks:

- After finishing Part 1, patients could have continued into Part 2. All patients took 2.0 mg of BAF312 once a day during Part 2 for 24 more weeks.

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 their dose over time to reach the full dose after 10 days of treatment.

Throughout the trial, trial doctors measured the muscle strength of patients, took their blood and urine samples, and checked their height, weight, blood pressure, and heart rate.

The follow-up period lasted 4 weeks:

Patients had a final checkup if they stopped after Part 1 or Part 2. 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.

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 studies to decide which treatments work best and are safest for patients. Other trials may provide new information or different results. You should not make therapeutic changes to your treatment based on the results of a single trial without first talking to your doctor.

Did BAF312 help with muscle strength more than a placebo in patients with DM?

No. Overall, the difference between the treatments was not large enough to show that BAF312 helped with muscle strength compared to a placebo after 24 weeks of treatment.

To find out if BAF312 helped with 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 one arm. The trial doctor then pressed on that arm. 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 what they saw when testing muscle strength in patients. The higher the score, the better the muscle strength.

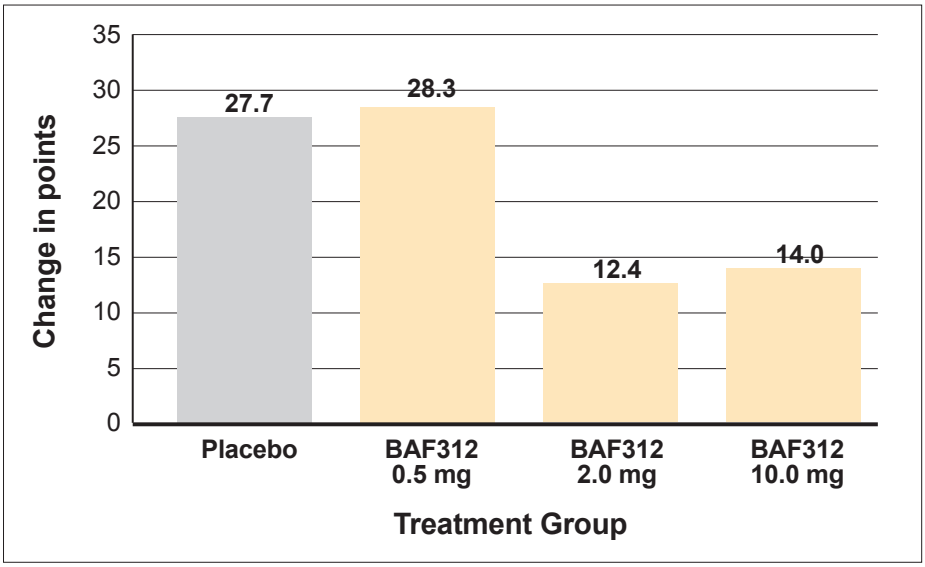
Researchers found that:

- **Placebo:** Patients who took the placebo had a change of 27.7 points after 24 weeks of treatment
- **BAF312 0.5 mg:** Patients who took 0.5 mg of BAF312 had a change of 28.3 points after 24 weeks of treatment
- **BAF312 2.0 mg:** Patients who took 2.0 mg of BAF312 had a change of 12.4 points after 24 weeks of treatment
- **BAF312 10.0 mg:** Patients who took 10.0 mg of BAF312 had a change of 14.0 points after 24 weeks of treatment.

The results showed that, overall, none of the BAF312 doses were better than the placebo at helping with muscle strength. The small difference seen between the placebo group and the BAF312 0.5 mg group is probably due to chance.

The figure below shows the results of the muscle strength test for all patients in the trial after 24 weeks of treatment.

Change in Muscle Strength Score After 24 Weeks of Treatment



Did BAF312 lower lymphocyte counts in the blood in patients with DM?

Yes. BAF312 did lower the number lymphocytes found in the blood stream. However, this change in lymphocyte count was not associated with a change in muscle strength.

What medical problems did patients with DM 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 sign or symptom that may or may not be caused by the trial drug.

How many patients had adverse events during the trial?

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 a placebo.

Adverse Events in Part 1

	Placebo (out of 5 patients)	BAF312 0.5 mg (out of 4 patients)	BAF312 2.0 mg (out of 4 patients)	BAF312 10.0 mg (out of 4 patients)	Total (out of 17 patients)
How many patients had adverse events in Part 1?	2 (40.0%)	1 (25.0%)	4 (100.0%)	4 (100.0%)	11 (64.7%)
How many patients had serious adverse events in Part 1?	1 (20.0%)	0 (0.0%)	0 (0.0%)	1 (25.0%)	2 (11.8%)
How many patients left the trial because of adverse events in Part 1?	1 (20.0%)	0 (0.0%)	1 (25.0%)	1 (25.0%)	3 (17.6%)

Adverse Events in Part 2

	Placebo to BAF312 2.0 mg (out of 5 patients)	BAF312 0.5 mg to 2.0 mg (out of 4 patients)	BAF312 2.0 mg to 2.0 mg (out of 4 patients)	BAF312 10.0 mg to 2.0 mg (out of 4 patients)	Total (out of 17 patients)
How many patients had adverse events in Part 2?	2 (40.0%)	1 (25.0%)	4 (100.0%)	2 (50.0%)	9 (52.9%)
How many patients had serious adverse events in Part 2?	0 (0.0%)	0 (0.0%)	1 (25.0%)	1 (25.0%)	2 (11.8%)
How many patients left the trial because of adverse events in Part 2?	0 (0.0%)	0 (0.0%)	1 (25.0%)	1 (25.0%)	2 (11.8%)

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.

No patients died during the trial. However, some patients had serious adverse events as shown in the tables below.

Out of 17 patients, 2 patients (11.8%) in Part 1 and 2 patients (11.8%) in Part 2 had serious adverse events. The tables below and on the next page show the serious adverse events that happened in this trial. Each serious adverse event happened in 1 patient each.

Serious Adverse Events in Part 1

Serious Adverse Event	Placebo (out of 5 patients)	BAF312 0.5 mg (out of 4 patients)	BAF312 2.0 mg (out of 4 patients)	BAF312 10.0 mg (out of 4 patients)	Total (out of 17 patients)
Dermatomyositis (inflammatory disease of patients in this trial)	1 (20.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (5.9%)
Pneumonia	1 (20.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (5.9%)
Pain due to a procedure	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (25.0%)	1 (5.9%)
Blood clot in the lungs	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (25.0%)	1 (5.9%)

Serious Adverse Events in Part 2

Serious Adverse Event	Placebo to BAF312 2.0 mg (out of 5 patients)	BAF312 0.5 mg to 2.0 mg (out of 4 patients)	BAF312 2.0 mg to 2.0 mg (out of 4 patients)	BAF312 10.0 mg to 2.0 mg (out of 4 patients)	Total (out of 17 patients)
Deep cuts	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (25.0%)	1 (5.9%)
Bleeding in the brain	0 (0.0%)	0 (0.0%)	1 (25.0%)	0 (0.0%)	1 (5.9%)
Dizziness	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (25.0%)	1 (5.9%)

What were the non-serious adverse events?

The tables below show the non-serious adverse events that happened in this trial.

Non-Serious Adverse Events in Part 1

Non-Serious Adverse Event	Placebo (out of 5 patients)	BAF312 0.5 mg (out of 4 patients)	BAF312 2.0 mg (out of 4 patients)	BAF312 10.0 mg (out of 4 patients)	Total (out of 17 patients)
Tiredness	0 (0.0%)	0 (0.0%)	1 (25.0%)	2 (50.0%)	3 (17.6%)
Headache	0 (0.0%)	0 (0.0%)	1 (25.0%)	2 (50.0%)	3 (17.6%)
Common cold	0 (0.0%)	0 (0.0%)	3 (75.0%)	0 (0.0%)	3 (17.6%)
Joint pain	0 (0.0%)	0 (0.0%)	1 (25.0%)	1 (25.0%)	2 (11.8%)
Weakness	0 (0.0%)	0 (0.0%)	0 (0.0%)	2 (50.0%)	2 (11.8%)
Diarrhea	0 (0.0%)	0 (0.0%)	1 (25.0%)	1 (25.0%)	2 (11.8%)
Muscle spasms	0 (0.0%)	1 (25.0%)	0 (0.0%)	1 (25.0%)	2 (11.8%)
Muscle weakness	0 (0.0%)	0 (0.0%)	2 (50.0%)	0 (0.0%)	2 (11.8%)

Non-Serious Adverse Events in Part 2

Non-Serious Adverse Event	Placebo to BAF312 2.0 mg (out of 5 patients)	BAF312 0.5 mg to 2.0 mg (out of 4 patients)	BAF312 2.0 mg to 2.0 mg (out of 4 patients)	BAF312 10.0 mg to 2.0 mg (out of 4 patients)	Total (out of 17 patients)
Headache	0 (0.0%)	0 (0.0%)	2 (50.0%)	1 (25.0%)	3 (17.6%)
Fainting	0 (0.0%)	0 (0.0%)	1 (25.0%)	1 (25.0%)	2 (11.8%)

What is important to know about these results?

Overall, this trial could not show that BAF312 helped with muscle strength. BAF312 will not be further tested for the treatment of DM. However, we thank the participants for their help in testing BAF312.

However, even though BAF312 did not work for DM, the information we learned could help us treat other diseases.

Where can I learn more about this trial?

Researchers look at the results of many trials to decide which treatments work best and are safest for patients. It takes volunteers in many trials all around the world to advance medical science.

More information about the results and adverse events 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 **CBAF312X2206** 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.

This trial was registered on the following websites:

- Clinical Trials.gov (https://clinicaltrials.gov/) - National Clinical Trial # NCT02029274
- EU clinical register (https://www.clinicaltrialsregister.eu) - EU Clinical Trial # 2013-001799-39

Thank you

It is said that the greatest gift is one which is given anonymously, giving when you do not know whether you will get direct personal benefit.

This is the gift that you have given by taking part in a clinical trial. It is a brave and selfless act, one that advances medical knowledge and benefits public health.

Thank you for the gift of your participation in clinical research.

CISCRP
THE CENTER FOR INFORMATION & STUDY ON CLINICAL RESEARCH PARTICIPATION

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 participants for clinical trials, nor is it involved in conducting clinical trials.

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