Clinical Trial Results

NOVARTIS

Research Sponsor: Novartis

Location of Headquarters: Basel, Switzerland

Drug Studied: BVS857

Protocol #: CBVS857X2202

Full Trial Title: A two-part, placebo-controlled study to evaluate the safety, tolerability and preliminary efficacy of BVS857 in patients with spinal and bulbar muscular atrophy (SBMA)

Full Scientific Summary: www.novctrd.com

Trial Date: February 2014 to April 2016

Thank you!

Thank you for taking part in the clinical trial for the treatment BVS857. You helped researchers learn how BVS857 works in people with spinal and bulbar muscular atrophy, also called SBMA.

Novartis, the sponsor of this trial, 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 has happened since the trial ended?

This trial had 2 parts. Part A lasted about 16 weeks. Part B lasted about 24 weeks. The whole trial took about 2 years to complete.

The trial included 37 patients from 7 trial sites in Denmark, Germany, Italy, and the United States. 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 help patients with SBMA. Most patients with SBMA are men. Patients with SBMA have muscle cramps and weakness in their arms, legs, face, mouth, or throat. Over time, patients with SBMA can lose muscle. This loss can result in muscle weakness in their legs.

Patients with SBMA have low levels of a protein called IGF-1 in their bodies. The trial drug, BVS857, acts like IGF-1. Researchers compared BVS857 to a placebo in this trial. A placebo looks like medicine but does not have any real medicine in it. Using a placebo helps researchers better understand the actual effect of a trial drug.

In your trial, researchers wanted to know:

- What medical problems did patients have during the trial?
- Did patients who got BVS857 have more muscle in their thighs than patients who got the placebo?
- Did BVS857 help patients more than the placebo in other ways?
- How much BVS857 got into the blood?

To answer these questions, researchers asked for the help of men like you. The patients in this trial were 36 to 80 years old and had SBMA.

What kind of trial was this?

The first 2 patients in both Parts A and B got “open-label” treatment. This meant that the patients, trial doctors, trial staff, and sponsor staff knew that the patients were getting BVS857. The rest of the trial was “double-blind”. This means that none of the patients, trial doctors, trial staff, or sponsor staff knew if patients were getting BVS857 or the placebo.

Some trials are done this way because knowing what treatment each patient is getting can affect the results of the trial. Doing a trial this way helps make sure the results are looked at fairly.

When the trial ended, the research sponsor found out what all the patients got so they could create a report of the trial results.

What happened during the trial?

Before the trial started, the trial doctors did tests to check patients’ overall health. Trial doctors also checked patients’ SBMA symptoms and measured patients’ thigh muscles using a medical imaging test called magnetic resonance imaging, or MRI.

During Part A of the trial, treatment lasted 9 weeks. Patients were randomly put into 2 groups. Patients received trial treatment every other week for 9 weeks. The first dose was through a needle put into their vein, called an infusion. The rest of the doses were given through an injection under the skin.

- In Group 1, patients got different doses of BVS857 every other week.
- In Group 2, patients randomly got either BVS857 or the placebo at different doses every other week.

Patients from Part A could participate in Part B after a "washout period" that lasted at least 2 months. During this time, patients did not take any drugs. This helped get rid of any effects from previous treatments.

All of the patients had a final check-up 3 weeks after taking their last treatment dose.

During Part B of the trial, treatment lasted up to 12 weeks. Patients were randomly put into 2 groups.

All treatments were given through an IV needle:

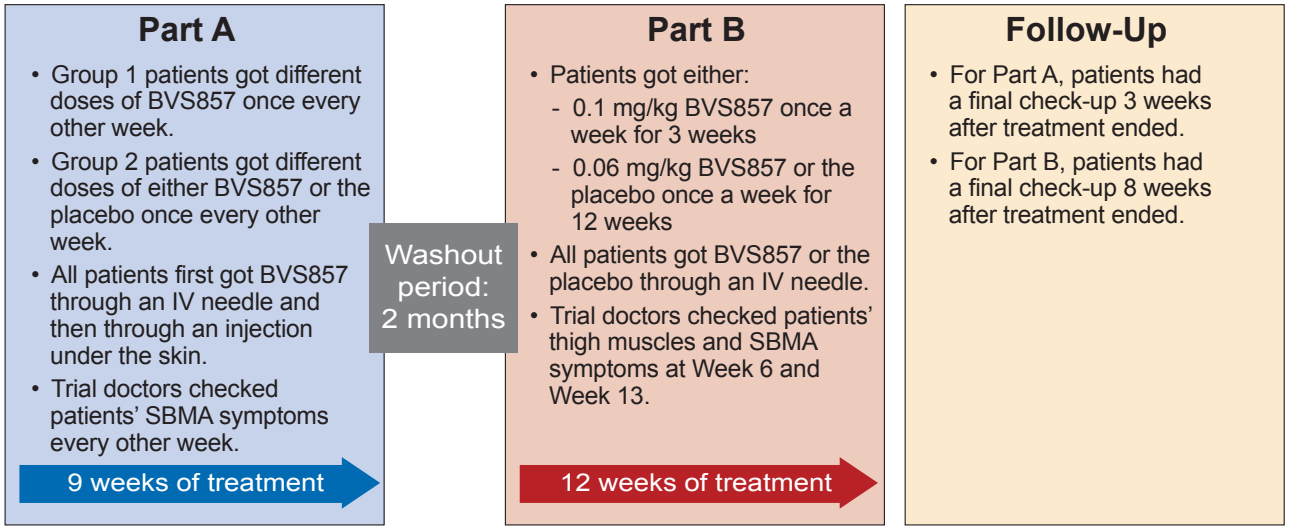
- 0.1 mg/kg BVS857 once a week for 3 weeks
- 0.06 mg/kg BVS857 or the placebo once a week for 12 weeks

On Days 36, 85, 106, and 134, the doctors also measured the size of patients' thigh muscles using an MRI and checked their SBMA symptoms.

All of the patients had a final check-up 8 weeks after taking their last treatment dose.

Throughout both parts of the trial, the doctors checked patients' overall health and took blood and urine samples. They also asked patients how they were feeling and if they were taking any new medicines.

The figure below shows how the trial was done:



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. You should not make changes to your treatment based on the results of a single trial without first talking to your doctor.

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 sign or symptom that may or may not be caused by the trial drug.

How many patients had adverse events during the trial?

Most patients in each treatment group had at least 1 adverse event:

- In Part A, all 8 patients (100.0%) had adverse events.
- In Part B, 26 of the 29 patients (89.7%) had adverse events.

The tables below and on the next page show how many patients had adverse events during Part A and Part B.

Adverse events in Part A of this trial

	BVS857 Group 1 (Out of 2 patients)	BVS857 Group 2 (Out of 4 patients)	Placebo (Out of 2 patients)	Total (Out of 8 patients)
How many patients had adverse events?	2 (100.0%)	4 (100.0%)	2 (100.0%)	8 (100.0)
How many patients had serious adverse events?	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
How many patients stopped taking the treatment because of adverse events?	2 (100.0%)	3 (75.0%)	0 (0.0%)	5 (62.5%)

Adverse events in Part B of this trial

	BVS857 0.1 mg/kg (Out of 2 patients)	BVS857 0.06 mg/kg (Out of 18 patients)	Placebo (Out of 9 patients)	Total (Out of 29 patients)
How many patients had adverse events?	1 (50.0%)	17 (94.4%)	8 (88.9%)	26 (89.7%)
How many patients had serious adverse events?	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
How many patients stopped taking the treatment because of adverse events?	0 (0.0%)	2 (11.1%)	0 (0.0%)	2 (6.9%)

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 had serious adverse events during this trial. No patients died during this trial.

What were the most common non-serious adverse events?

In Part A, the most common non-serious adverse event was redness where the injection was given. The table below shows the most common non-serious adverse events that happened to at least 2 patients out of all patients in Part A.

Most common non-serious adverse events in Part A of this trial

Non-serious adverse event	BVS857 Group 1 (Out of 2 patients)	BVS857 Group 2 (Out of 4 patients)	Placebo (Out of 2 patients)	Total (Out of 8 patients)
Redness where the injection was given	2 (100.0%)	3 (75.0%)	0 (0.0%)	5 (62.5%)
Common cold symptoms	0 (0.0%)	1 (25.0%)	2 (100.0%)	3 (37.5%)
Dizziness	0 (0.0%)	2 (50.0%)	0 (0.0%)	2 (25.0%)
Fall	1 (50.0%)	1 (25.0%)	0 (0.0%)	2 (25.0%)
An unexpected benefit of the treatment	2 (100.0%)	0 (0.0%)	0 (0.0%)	2 (25.0%)

In Part B, the most common non-serious adverse event was common cold symptoms. The table below shows the most common non-serious adverse events that happened to at least 3 patients out of all patients in Part B.

Most common non-serious adverse events in Part B of this trial

Non-serious adverse event	BVS857 0.1 mg/kg (Out of 2 patients)	BVS857 0.06 mg/kg (Out of 18 patients)	Placebo (Out of 9 patients)	Total (Out of 29 patients)
Common cold symptoms	0 (0.0%)	4 (22.2%)	1 (11.1%)	5 (17.2%)
Headache	0 (0.0%)	3 (16.7%)	1 (11.1%)	4 (13.8%)
Back pain	0 (0.0%)	1 (5.6%)	2 (22.2%)	3 (10.3%)

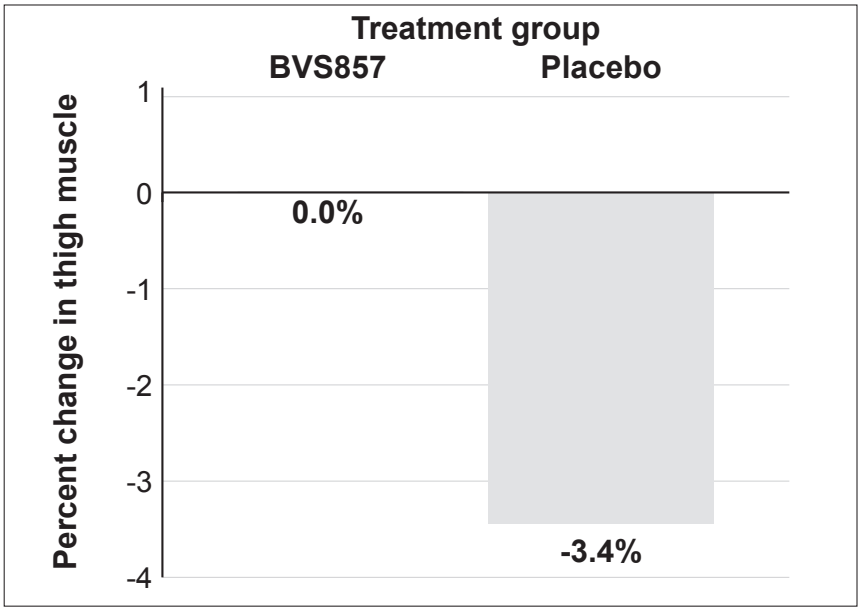
Did patients who got BVS857 have more muscle in their thighs than patients who got the placebo?
Yes. But researchers are not confident that BVS857 caused the difference between the 2 groups. After 12 weeks of treatment in Part B, patients who got BVS857 had no change in the amount of muscle in the thigh. But patients who got the placebo lost more thigh muscle over 12 weeks than what doctors expected for patients with SBMA.

Researchers measured the amount of muscle in patients' thighs before and after 12 weeks of treatment:

- Patients who got BVS857 had no change in the amount of thigh muscle after treatment.
- Patients who got the placebo lost 3.4% of their thigh muscle after treatment.

The chart below shows this change in the amount of thigh muscle after 12 weeks of treatment.

Percentage of change in the amount of thigh muscle after 12 weeks of treatment



Did BVS857 help patients more than the placebo in other ways?
No. Researchers found that patients who got BVS857 and patients who got the placebo had about the same:

- Muscle strength and function
- Lean body mass, or their total body weight without counting their fat

The difference between the groups was too small for researchers to know if one treatment was better than the other. The difference seen could have been due to chance.

How much BVS857 got into the blood?
Researchers also wanted to know how much BVS857 got into the blood after treatment. Overall, they learned that:

- When patients got BVS857 through an IV needle put into their vein, patients who got higher doses had higher amounts of BVS857 in their blood. BVS857 did not stay in the blood for as long as researchers expected.
- When patients got BVS857 through an injection under the skin, the amount of BVS857 in the blood was very different from one patient to another.

How has this trial helped patients and researchers?

Overall, this trial tested BVS857 in a small group of patients with SBMA.

These results should be looked at with caution, because the difference in results between treatment with BVS857 and the placebo resulted from the unexpected drop in the amount of thigh muscle in patients who got the placebo and not from a gain in thigh muscle in patients who got BVS857. No further trials are planned for BVS857.

Where can I learn more about this trial?

More information about the results and the full list of adverse events that happened 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 **CBVS857X2202** 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 # NCT02024932
- https://www.clinicaltrialsregister.eu/ctr-search - EU Clinical Trial # 2013-002608-15

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

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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