Clinical Trial Summary

A clinical trial to learn about the effects of the trial drug BYM338 in older adults with sarcopenia

Thank you!

Novartis, the sponsor of this clinical trial, thanks you and the other participants who helped make this clinical trial possible.

Trial overview

What was the purpose of this trial?

The clinical trial team wanted to learn more about the effects of a trial drug named BYM338, also called bimagrumab, on participants' strength and walking. The team also wanted to learn about any medical problems participants had during the trial.

All participants had sarcopenia, which is a greater than normal loss of muscle size and strength in older adults. It leads to less physical activity, greater risk of falling, and poor health.

Who was in this clinical trial?

- 217 men and women with sarcopenia began this clinical trial
- All participants were from 70 to 95 years old

What treatments were used in this trial?

In this trial, participants received BYM338 or a placebo through a vein, which is called an IV or intravenous infusion. A placebo looks like medicine but does not have any medicine in it.

This trial was designed to learn:

- The effects of BYM338 on participants' strength and walking
- Any changes in the distance and speed participants could walk after receiving BYM338
- Any changes in the amount of muscle participants had after receiving BYM338
- Any medical problems participants had during the trial.
  Keeping track of medical problems helped learn about the safety of BYM338.

What were the main results of this clinical trial?

The clinical trial team learned that BYM338 did not have a meaningful effect on participants' strength and walking in this clinical trial. Overall, the team found BYM338 to be safe in this clinical trial.

Trial number: CBYM338E2202

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Why was this research needed?

Researchers are looking for a better way to treat sarcopenia. Sarcopenia is a greater than normal loss of muscle size and strength in older adults that can make daily activities more difficult. For example, people with sarcopenia have trouble with activities like balancing, walking, and getting up from a chair. These difficulties can lower older adults' quality of life and lead to falls.

Currently, there are no medicines to treat sarcopenia. Exercise can help, but not everyone can do an exercise program. Researchers are looking for ways to treat sarcopenia beyond exercise.

The clinical trial team designed this clinical trial to learn if the drug BYM338, also called bimagrumab, had an effect on strength and walking in people with sarcopenia. Before a drug can be approved for patients to take, researchers do many clinical trials to find out how safe it is and how it works.

What was the purpose of the clinical trial?

In this clinical trial, the team wanted to learn about:

- The effects of BYM338 on participants' strength and walking
- Any changes in the distance and speed participants could walk after receiving BYM338
- Any changes in the amount of muscle participants had after receiving BYM338
- Any medical problems participants had during the trial

Who was in this clinical trial?

217 participants with sarcopenia, 91 men and 126 women, began this clinical trial. They were from 70 to 95 years old and 79-years-old on average.

Every participant in this clinical trial had:

- Sarcopenia based on a doctor's exam
- Trouble doing physical activities, such as walking, standing up from a chair, or climbing stairs

This clinical trial took place in 13 countries: Australia, Belgium, the Czech Republic, Denmark, France, Germany, Japan, the Republic of Korea, Russia, Spain, Switzerland, Taiwan, and the United States.

This trial began in December 2014 and ended in June 2018. Participants began this clinical trial on different dates. 29 participants did not complete this clinical trial.

For more information about who could and could not be in this clinical trial, visit novctrd.com. Use clinical trial number **CBYM338E2202** to find the scientific summary.

What type of clinical trial was this?

This clinical trial tested the safety of BYM338 and how well it worked in a group of participants with sarcopenia.

Trial staff used a computer program to randomly assign each participant to receive either BYM338 or a placebo. A **placebo** looks like medicine but does not have any medicine in it. A placebo is used to help better understand the actual effects of a trial drug.

Participants, trial staff, and sponsor staff did not know what treatment each participant received during the trial. Some clinical trials are done this way because knowing what treatment participants receive can influence the results. Not knowing what treatment participants receive helps make sure the results are looked at fairly.

What happened during this clinical trial?

Before treatment

Trial doctors first checked each participant's health to make sure they could be in this clinical trial. About 4 weeks before treatment, trial staff asked participants to start an exercise and nutrition program that included:

- Learning the proper way to perform exercises to improve muscle strength, balance, and flexibility
- Performing the exercises on their own 2-3 times a week
- Learning about and following a healthy meal plan that included the recommended amounts of protein and calories
- Taking vitamin D and a nutritional supplement daily

During treatment

Participants were assigned to 1 of 4 treatment groups:

- 70 mg (milligrams) of BYM338
- 210 mg of BYM338
- 700 mg of BYM338
- Placebo

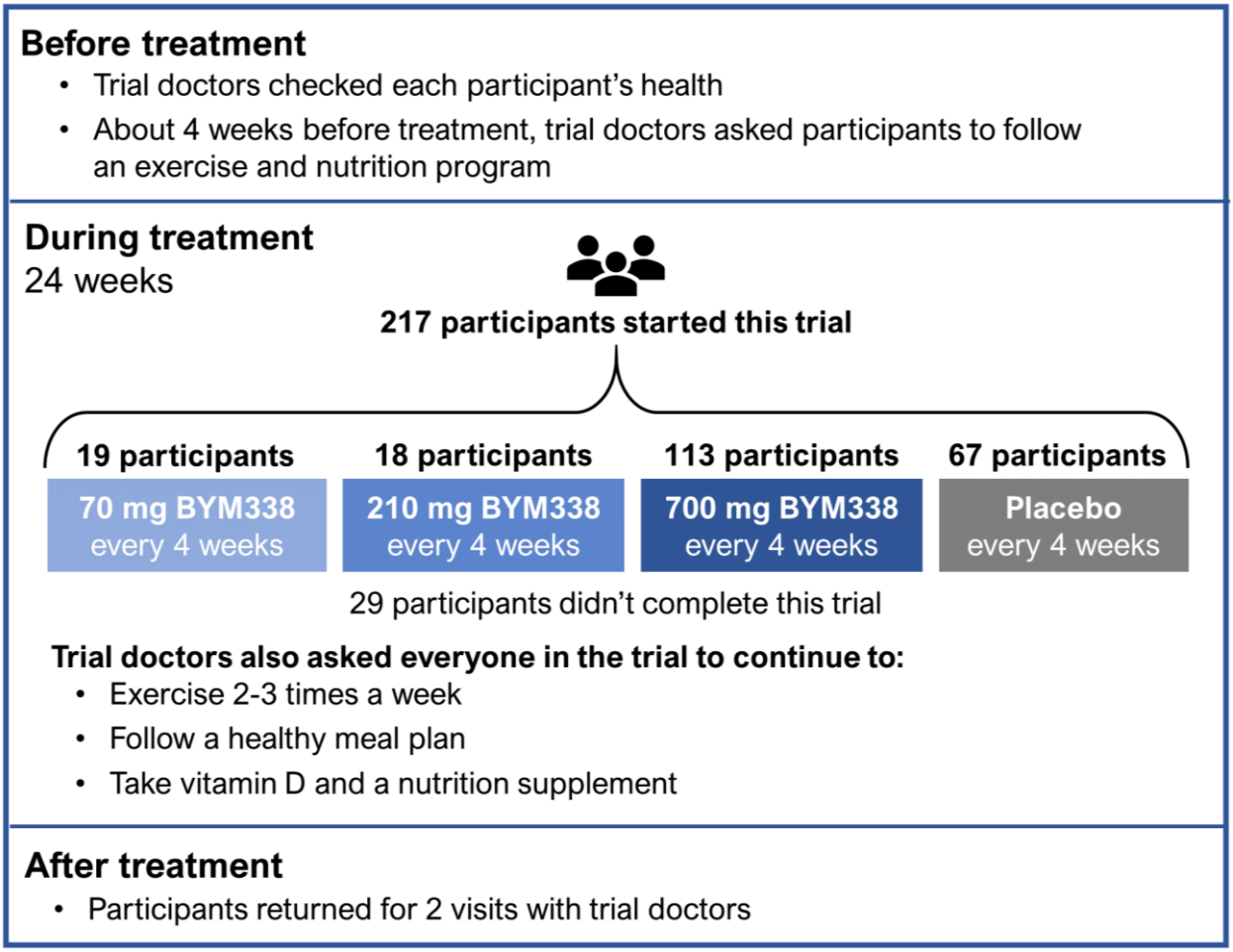
For 24 weeks, participants in each group received one dose of their assigned treatment every 4 weeks. Each participant received up to 6 doses of their assigned treatment. Trial staff gave participants BYM338 or the placebo through a vein, which is called an IV or intravenous infusion.

The trial staff asked every participant to continue the exercise and nutrition program throughout the trial.

After treatment

Participants returned for 2 visits with trial doctors after they received their last dose.

How this trial was designed:



What were the main results of this clinical trial?

This is a summary of the overall results of this clinical trial. Individual results from each participant may be different and are not included in this summary.

Researchers need many clinical trials to learn if a drug or other treatment is safe and works well. This is a summary of only one clinical trial. You should not use the results of this clinical trial to make decisions about your health care. Always talk to a doctor before making any changes to your health care.

The clinical trial team learned that BYM338 did not have a meaningful effect on participants' strength and walking beyond the exercise and nutrition program in this clinical trial.

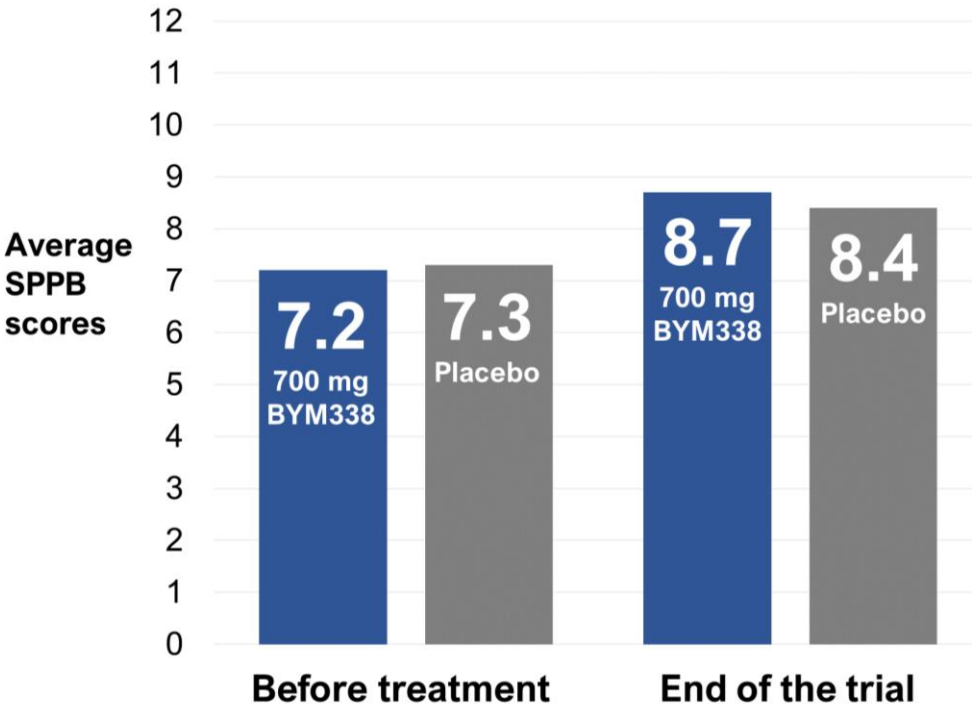
To check participants' strength and walking, trial staff used a test called the Short Physical Performance Battery, also called the SPPB. In the SPPB, a person is asked to do 6 activities to measure their balance, walking speed, and ability to stand up from a chair.

Each participant performed the SPPB test before they started treatment, during the trial, and again at the end of the trial. The clinical trial team compared the average change in SPPB scores for participants who received 70 mg, 210 mg, and 700 mg of BYM338 to those who received the placebo.

The team decided the changes in each group were not large enough to conclude that BYM338 had a meaningful effect on participants' strength and walking.

The following graph shows the results for participants who received 700 mg of BYM338 compared to the placebo. Those who received 70 mg and 210 mg had similar results to those who received 700 mg of BYM338.

Average SPPB scores for 700 mg of BYM338 and the placebo



What is the SPPB?

- A test to measure balance, walking speed, and the ability to stand up from a chair
- Scores range from 0 to 12
- Higher scores show a better ability to do these activities

What other key results were learned?

The exercise and nutrition program that participants followed in this clinical trial helped their strength and walking based on the average change in SPPB from before treatment to the end of the trial.

The clinical trial team also learned:

- **BYM338 didn't have an effect on how far participants could walk in 6 minutes**
  Participants were measured to see how far they could walk in 6 minutes before treatment, during the trial, and at the end of the trial. The clinical trial team compared this distance between the groups who received BYM338 and the placebo. They found the difference was not large enough to conclude that BYM338 had a meaningful effect.

- **BYM338 didn't have an effect on how fast participants could walk**
  Participants were measured to see how fast they walked for a certain distance before treatment, during the trial, and at the end of the trial. The clinical trial team compared walking speeds between the groups who received BYM338 and the placebo. They found the difference was not large enough to conclude that BYM338 had a meaningful effect.

- **Some participants who received BYM338 increased their amount of muscle**
  The amount of muscle a participant had was measured using a type of x-ray scan before treatment, during the trial, and at the end of the trial. The clinical trial team found that participants who received 210 mg and 700 mg of BYM338 increased the amount of muscle compared to those who received the placebo.

What medical problems happened during the trial?

Medical problems that happen during clinical trials are called “adverse events”. An **adverse event** is any unwanted sign or symptom that participants have during a trial. An adverse event is considered “**serious**” when it is life-threatening, causes lasting problems, or the participant needs hospital care.

Adverse events may or may not be caused by treatments in the trial.

Many trials are needed to know if a drug or treatment causes an adverse event. Trial doctors keep track of all adverse events that happen in trials, even if they do not think the adverse events might be related to the trial treatments.

Overall, the clinical trial team found BYM338 to be safe in this clinical trial.

During this clinical trial, 177 participants (82%) reported at least 1 adverse event. 6 participants left this clinical trial due to an adverse event.

Participants reporting adverse events

	BYM338 70 mg (out of 19 participants)	**BYM338** 210 mg (out of 18 participants)	**BYM338** 700 mg (out of 113 participants)	**Placebo** (out of 67 participants)
Participants who had adverse events	63% (12)	72% (13)	83% (94)	61% (41)
Participants who had serious adverse events	0% (0)	17% (3)	12% (14)	8% (5)
Participants who left this trial due to adverse events	5% (1)	0% (0)	4% (4)	2% (1)
Participants who died	0% (0)	0% (0)	2% (2)	0% (0)

How many participants reported serious adverse events?

2 participants died during this clinical trial. Both were in the group who received 700 mg of BYM338:

- Before the clinical trial, one participant had congestive heart failure, which is a buildup of fluid around the heart that prevents it from pumping blood well. The heart failure worsened during the trial, and the participant died from it.
- One participant died from a stroke caused by bleeding in the brain area

During this clinical trial, 22 participants reported at least 1 serious adverse event.

For more information about the serious adverse events reported in this clinical trial, visit novctrd.com. Use clinical trial number **CBYM338E2202** to find the scientific summary.

What adverse events did participants report?

Most participants reported medical problems or adverse events that were not serious. This section summarizes the most common adverse events participants had during this clinical trial.

This summary only includes adverse events reported:

- By more than 5% of the total number of participants in this clinical trial
- From the start of treatment to the end of the clinical trial

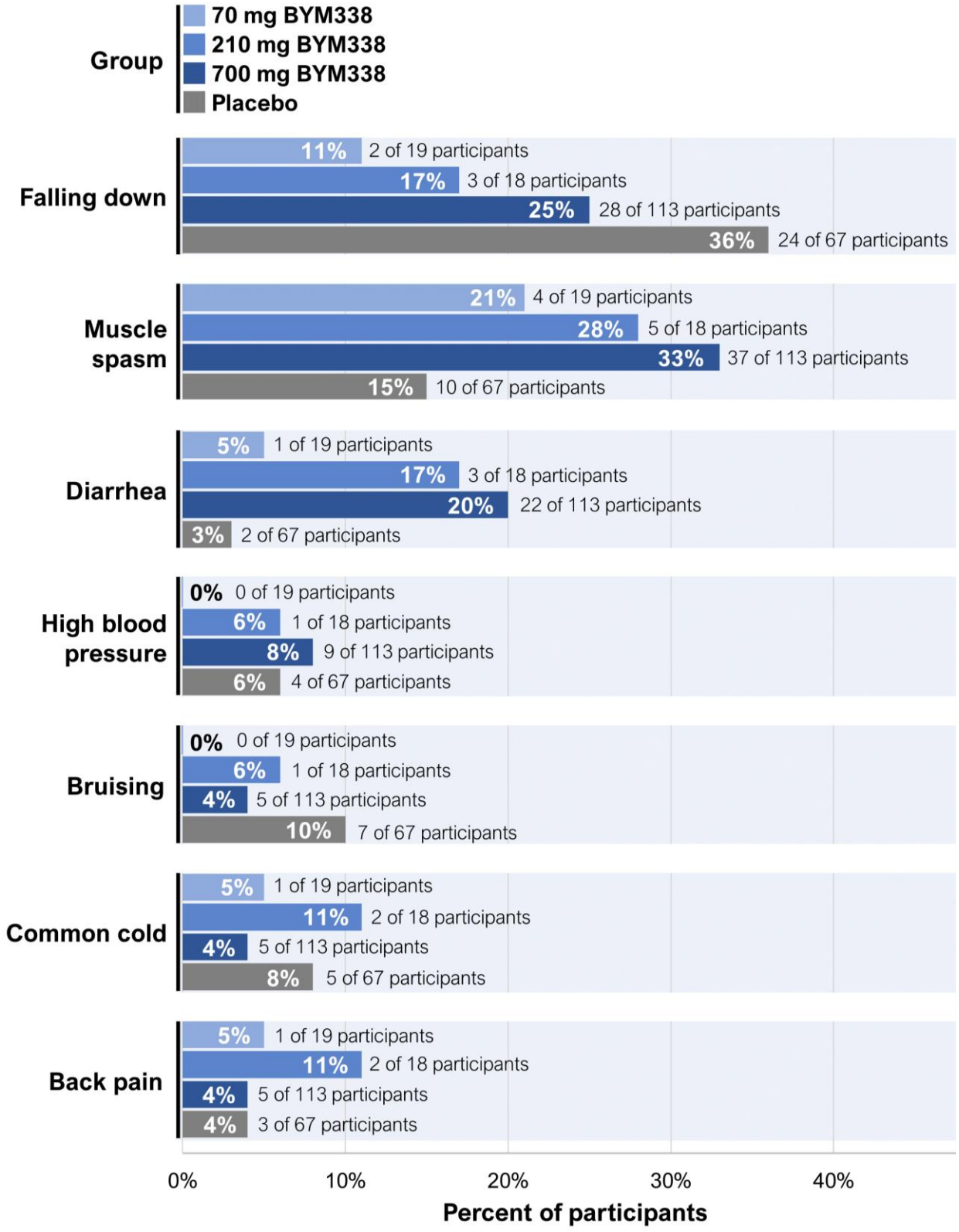
There were other adverse events, but these happened in fewer participants.

Below are the most common adverse events reported by participants:

- Falling down
- Muscle spasms
- Diarrhea
- High blood pressure, also called hypertension
- Bruising, also called contusion
- Common cold, also called an upper respiratory tract infection
- Back pain

For more information about the adverse events reported by participants in this clinical trial, visit novctrd.com. Use clinical trial number **CBYM338E2202** to find the scientific summary.

Participants reporting the most common adverse events



How has this clinical trial helped patients and researchers?

The results of this clinical trial helped the trial team understand the effects of BYM338 in people with sarcopenia. The clinical trial team learned that:

- BYM338 did not have a meaningful effect on participants' strength and walking in this clinical trial
- The exercise and nutrition program had a meaningful effect on participants' strength and walking in this clinical trial

These results are from one clinical trial. One clinical trial cannot give a complete picture of the benefits and risks of a trial drug. The results of many trials are needed to find out which treatments can be used for people with sarcopenia. This summary shows only the main results from this trial. Other clinical trials may provide new information or different results.

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

If you were in this clinical trial and have questions about the results, please speak with the doctor or staff where you took part in this clinical trial.

This is a summary of the results of one clinical trial.

You can find detailed results and more information about this clinical trial on the Novartis Clinical Trial Results website:

1. Visit novctrd.com
2. Click on **"Clinical trial results and trial summary for patients"** at the top right of the page
3. Read and scroll down, then click **"I accept"** to agree to use the Novartis website
4. Select **"Search by study number"** on the bottom left of the page
5. Type **"CBYM338E2202"** in the search box and click search

This clinical trial was registered on the following websites:

- ClinicalTrials.gov – https://clinicaltrials.gov
  To find this trial, type "**CBYM338E2202"** into the **Other terms** search box.
- European Union Clinical Trials Register – https://www.clinicaltrialsregister.eu/ctr-search
  To find this trial, type "**CBYM338E2202"** into the search box.

If more clinical trials are planned, they will appear on the public websites listed above or at www.novartisclinicaltrials.com. When there, search for "BYM338" or "Bimagrumab".

Full trial title:

A 28 week, randomized, double-blind, placebo-controlled, two-part, multi-center, parallel group dose range finding study to assess the effect of monthly doses of bimagrumab 70, 210, and 700 mg on skeletal muscle strength and function in older adults with sarcopenia (InvestiGAIT)

Thank you!

Novartis would like to thank all of the people who participated in this clinical trial. The participants made this clinical trial possible and helped researchers answer important health questions and learn about a possible medical treatment. Many volunteers and many clinical trials are needed to advance medical science.

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