Clinical Trial Results Summary

NOVARTIS

The safety and effects of trial drug MCS110 for people with the joint disease PVNS, now called TGCT

Thank you!

Thank you to the participants who took part in the clinical trial for the drug **MCS110**. All of the participants helped the researchers learn more about the effects and safety of MCS110 for people with tenosynovial giant cell tumor, also called TGCT. Recently, PVNS (pigmented villonodular synovitis) and GCTTS (giant cell tumors of the tendon sheath) were grouped together as one disease called TGCT.

Novartis sponsored this trial and believes it is important to share what was learned from the results of this trial with the participants and the public. An independent organization prepared this summary of the trial results.

We hope this helps the participants understand their important role in medical research.

Trial information

Trial number: CMCS110X2201
Drug studied: MCS110
Sponsor: Novartis

You can find **more information** about this trial by going to the websites listed on **page 16** of this summary.

? If you participated in the trial and have **questions** about the results, please speak with the trial doctors or staff at your trial site.

This clinical trial at a glance

What was the purpose of this trial? Read more on **page 3**

This trial's purpose was to learn more about the trial drug MCS110, also known as lacnotuzumab. MCS110 is designed to treat a rare joint disease called PVNS, now called TGCT. In this disease, non-cancerous tumors grow in certain joints, which cause pain and can limit movement.

This trial was designed to answer these questions:

- Did MCS110 shrink the participants' tumors more than the placebo?
- Did higher doses of MCS110 shrink the participants' tumors more than the low dose?
- What medical problems did the participants have during the trial? Keeping track of medical problems helped to learn about the safety of MCS110.

Who was in this trial? Read more on **page 4**

- 36 male and female participants began this clinical trial
- Participants were 13 to 59 years old and had at least one TGCT tumor

What treatments did participants receive? Read more on **page 4**

Participants received at least one of these treatments:

- High dose of MCS110
- Medium dose of MCS110
- Low dose of MCS110
- Placebo – looks like the trial drug but has no trial drug in it. Using a placebo helps researchers better understand the actual effects of a trial drug.

Participants received treatments through a needle in a vein, which is called an intravenous infusion or IV infusion

What were the main results of this clinical trial? Read more on **page 6**

MCS110 shrank participants' tumors more than the placebo. Higher doses of MCS110 shrank participants' tumors more than the low dose of MCS110.

The clinical trial team found MCS110 to be generally safe during this trial. The most common medical problem participants had was puffy eyes.

What was the purpose of this clinical trial?

Researchers are looking for better ways to treat **TGCT,** which stands for tenosynovial giant cell tumor.
TGCT is a rare disease that causes non-cancerous tumors to grow in certain joints. These tumors usually do not spread to other parts of the body or become life-threatening. However, they can continue to grow, be painful, limit movement, and damage the bones around them.

Recently, PVNS and GCTTS were grouped together as types of one disease called **TGCT**:

- **PVNS**: Pigmented villonodular synovitis, which usually affects the knee and hip joints
- **GCTTS:** Giant cell tumors of the tendon sheath, which usually affects the joints in the fingers

Researchers aren't sure what causes TGCT, but they think the body's immune system may play a role. The immune system is made of cells and proteins that protect the body from disease and infection. One of these immune system proteins is called **M-CSF.** Its role is to attract certain immune system cells to the area of an infection to help stop it.

Researchers have found that people with TGCT have high levels of M-CSF in their joint with the tumor. M-CSF attracts immune system cells to these joints, which build up over time and may cause the tumor to grow.

The trial drug **MCS110**, also known as lacnotuzumab, is designed to block M-CSF. This may stop cells from building up and allow the body to break down the TGCT tumor over time. MCS110 is not yet approved for use. Before a drug can be approved for people to take, researchers do many clinical trials to find out how safe it is and if it works to treat the disease.

This trial was designed to answer these questions:

- Did MCS110 shrink the participants' tumors more than the placebo?
- Did higher doses of MCS110 shrink the participants' tumors more than the low dose?
- What medical problems did the participants have during the trial? Keeping track of the medical problems helped to learn about the safety of MCS110.

Who was in this trial?

36 participants began the trial – 14 males and 22 females. Participants were 13 to 59 years old. Their average age was 41.

This trial had 3 parts: Part A, Part B, and Part C. To be in any part of this trial, participants had to have at least one TGCT tumor that could be measured using an MRI, also called magnetic resonance imaging. An **MRI** uses magnets to create a detailed picture of the inside of the body.

Part A – to be in this part, participants**:**

- Had to be 18 years or older
- Had at least one PVNS-type tumor in their joint
- Had to have scheduled a surgery to remove their tumor after treatment

Part B – to be in this part, participants:

- Had to be 18 years or older
- Had either a PVNS- or GCTTS-type tumor in their joint

Part C – to be in this part, participants:

- Had to be 12 years or older
- Had either a PVNS- or GCTTS-type tumor in their joint

This clinical trial took place in Switzerland and the United States.

For more information about who could and could not be in this clinical trial, and the participants in this trial, visit novctrd.com. Use clinical trial number **CMCS110X2201** to find the scientific summary.

What treatments did participants receive?

A computer program was used to randomly assign each participant to at least one of these treatments:

- **High dose** of MCS110: 10 milligrams (mg) for every kilogram (kg) of their weight (mg/kg)
- **Medium dose** of MCS110: 5 mg/kg
- **Low dose** of MCS110: 3 mg/kg
- **Placebo:** looks like the trial drug but has no trial drug in it. Using a placebo helps researchers better understand the actual effects of a trial drug

Using a computer program to assign the treatments helped make sure the team compared the results as fairly as possible.

Participants received their assigned treatment through a needle in a vein, which is called an intravenous infusion or IV infusion.

During most of this trial, participants and trial staff did not know what treatment each participant received. Some 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.

After the first dose in Part B, all participants received the same treatment. Because of this, participants and the trial staff knew what treatment participants received at this point in Part B.

What happened during this trial?

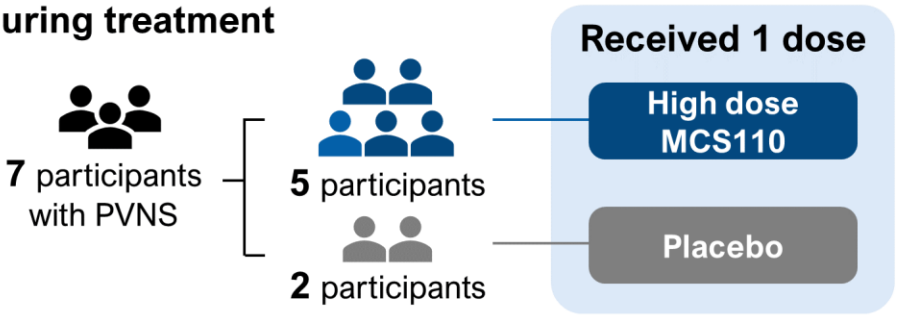
This trial began in April 2012 and ended in December 2018.

Part A: How this trial was done

Before treatment

- Participants had to have scheduled a surgery to remove their tumor after treatment
- Participants had an MRI to check the size of their tumor
- Trial doctors checked participants' health

During treatment



After treatment

- 4 weeks after their dose, participants had an MRI to check the size of their tumor
- About one week after the MRI, participants had surgery to remove their tumor

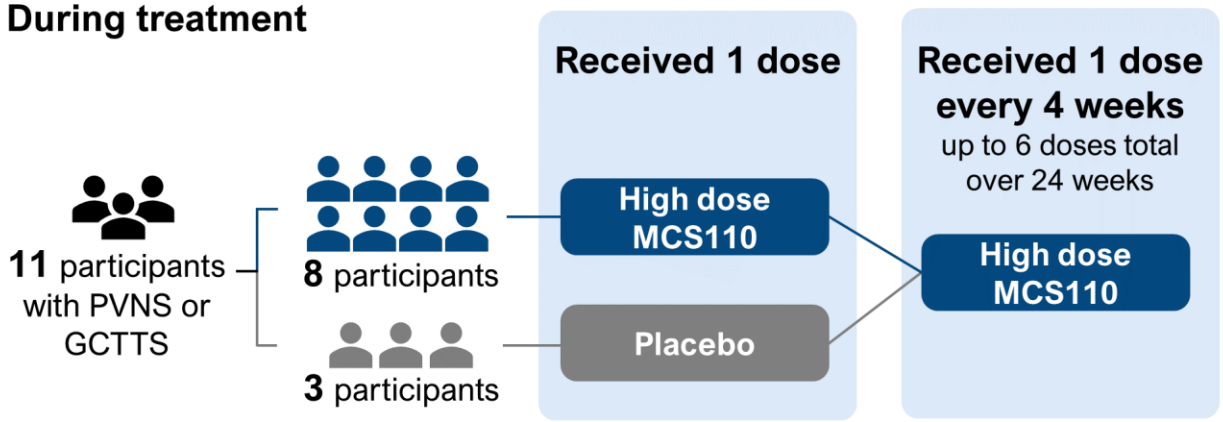
All participants in Part A completed the trial.

Part B: How this trial was done

Before treatment

- Participants had an MRI to check the size of their tumor
- Trial doctors checked participants' health

During treatment



- After every 4 weeks, participants had an MRI to check the size of their tumor

After treatment

- 8 weeks after their last treatment, participants had an MRI to check the size of their tumor
- About every 3 months for up to 2 years, participants returned to their trial site for trial doctors to check their health and tumor
- After 6 months, if a participant's tumor returned, they could receive MCS110 again

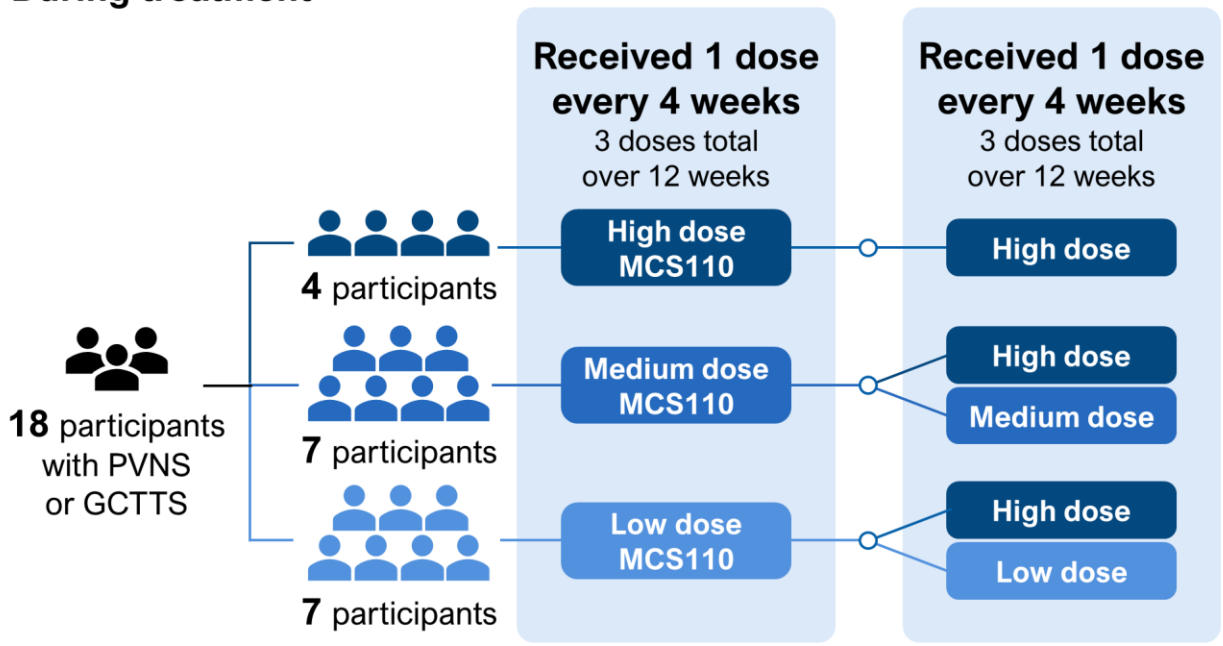
1 participant in Part B did not complete the trial.

Part C: How this trial was done

Before treatment

- Participants had imaging including an MRI to check the size of their tumor
- Trial doctors took samples of participants' tumors and fluid from their affected joint
- Trial doctors checked participants' health

During treatment



After a participant's 3rd dose, trial doctors checked their health. Imaging specialists used an MRI to check the size of their tumor. For those on the **Low** or **Medium** doses of MCS110:

- If their tumor shrank by about half or more, they stayed on the same dose
- Otherwise, trial doctors switched their treatment to the **High** dose of MCS110

After treatment

- Trial doctors took another sample of participants' tumors
- 8 weeks after treatment, participants had imaging including an MRI to check the size of their tumor
- About every 4 months for up to 2 years, participants returned to their trial site for trial doctors to check their health and tumors
- After 6 months, if a participant's tumor returned, they could receive MCS110 again

5 participants in Part C did not complete the trial.

What were the main results of this trial?

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

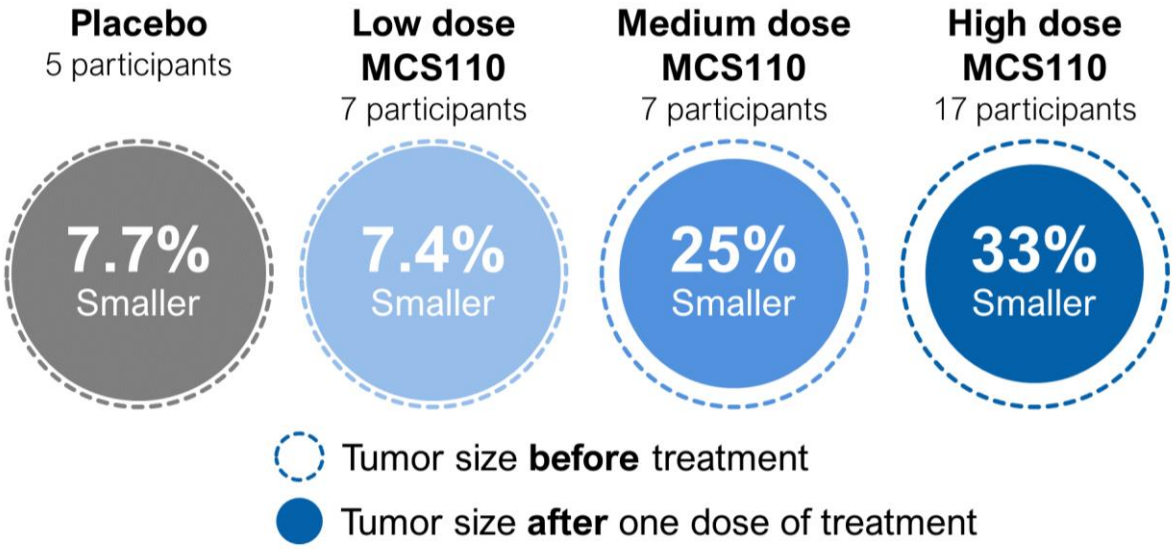
Researchers need many trials to learn if a drug or other treatment is safe and works well. Other trials may provide new information or different results. Always talk to a doctor before making any changes to your health care.

Did MCS110 shrink participants' tumors more than the placebo?

MCS110 shrank participants' tumors more than the placebo.

To find this out, the clinical trial team compared the average size of participants' tumors before treatment to their average size 4 weeks after receiving one dose of treatment. They did this for participants in all 3 parts of this trial. The team then looked at which treatment had more of an effect on tumor size. The chart below shows the change in tumor size for each treatment.

Average change in tumor size 4 weeks after one dose of treatment in all parts of this trial

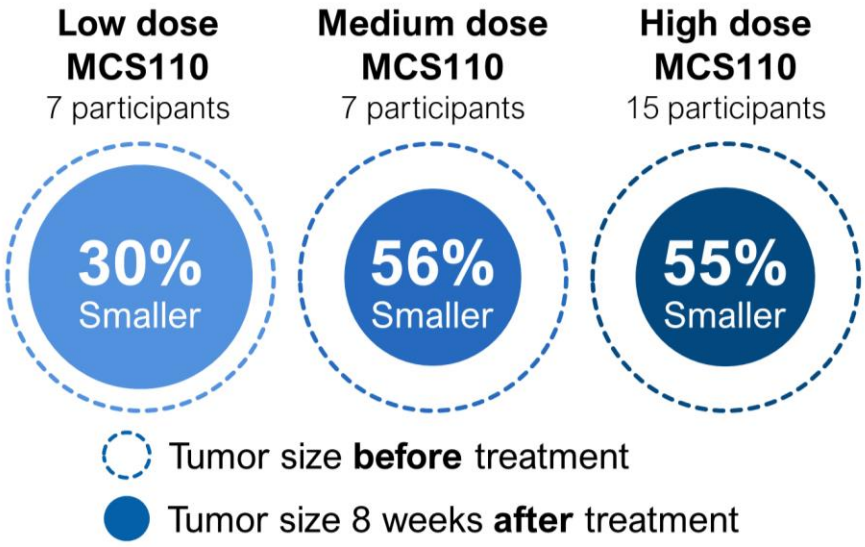


Did higher doses of MCS110 shrink participants' tumors more than the low dose?

The high and medium doses of MCS110 shrank participants' tumors more than the low dose of MCS110.

To find this out, the clinical trial team also compared the size of participants' tumors before treatment up to 8 weeks after their last treatment with MCS110 in Parts B and C. The team then compared the effect of each dose on participants' tumor size. The chart below shows the difference in participants' tumor size and the dose of MCS110 they were assigned at the start of treatment.

Average change in tumor size up to 8 weeks after several doses of treatment in Parts B and C



What medical problems did participants have during the trial?

Medical problems that happen during clinical trials are called **adverse events**. Trial doctors looked for any adverse events when they checked participants' health during the trial. Participants also reported adverse events.

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.

What is an adverse event?

- An **adverse event** is any unwanted sign or symptom that participants have during a trial
- It is considered **serious** when it is life-threatening, causes lasting problems, the participant needs hospital care, or results in death
- Adverse events **may or may not be caused** by treatments in the trial

The clinical trial team found MCS110 to be generally safe during this trial.

Part A: Adverse events

Participants who had:	High dose MCS110 out of 5 participants	Placebo out of 2 participants
Serious adverse events	0% (0 of 5)	50% (1 of 2)
Non-serious adverse events	60% (3 of 5)	50% (1 of 2)
Left this trial due to adverse events	0% (0 of 5)	0% (0 of 2)

Part B: Adverse events

Participants who had:	High dose MCS110 out of 11 participants	Placebo out of 3 participants
Serious adverse events	18% 2 of 11	0% 0 of 3
Non-serious adverse events	100% 11 of 11	100% 3 of 3
Left this trial due to adverse events	0% 0 of 11	0% 0 of 3

Part C: Adverse events

Participants who had:	Low dose MCS110 out of 7 participants	Medium dose MCS110 out of 7 participants	High dose MCS110 out of 12 participants
Serious adverse events	43% 3 of 7	14% 1 of 7	33% 4 of 12
Non-serious adverse events	100% 7 of 7	86% 6 of 7	92% 11 of 12
Left this trial due to adverse events	14% 1 of 7	0% 0 of 7	0% 0 of 12

What serious adverse events did participants have?

11 participants had serious adverse events during this trial. No participants died during this trial.

The following lists show the serious adverse events that happened during each part of this trial. Some of these adverse events are considered serious because a participant had them at the same time as other serious adverse events.

Part A: Serious adverse events

1 out of 7 participants who received **the placebo** had a serious adverse event:

- **New, severe pain in the upper-right belly due to gallbladder inflammation** (acute cholecystitis)

Part B: Serious adverse events

2 out of 11 participants who received the **High dose** of MCS110 had serious adverse events:

- **Lap band slipping** (device dislocation)
- **Feeling sick to the stomach** (nausea)
- **Throwing up** (vomiting)
- **Dehydration**
- **Swelling and pain in the voice box** (laryngitis)
- **Fever** (pyrexia)
- **Painful throat spasms** (esophageal spasm)
- **Abnormal heartbeat** (electrocardiogram ST segment depression)
- **Chest pain not related to the heart** (non-cardiac chest pain)
- **Shortness of breath** (dyspnea)
- **Slurred speech** (dysarthria)
- **Change in how they walked** (gait disturbance)
- **Feeling dizzy** (dizziness)
- **Viral infection**, like the common cold or flu
- **Stuffy nose** (nasal congestion)

Part C: Serious adverse events

8 out of 18 participants in Part C had serious adverse events.

4 participants who received the **High dose of MCS110** had serious adverse events:

- **Possible sign of muscle injury** (blood creatine phosphokinase increased)
- **Possible sign of liver injury** (alanine aminotransferase increased)
- **Possible sign of liver injury** (aspartate aminotransferase increased)
- **Meningitis infection** (meningoencephalitis viral)
- **Bacterial infection** (Streptococcal bacteremia)
- **Pain**

One participant who received the **Medium dose of MCS110** had serious adverse events:

- **Loss of facial movement** (facial paralysis)
- **Slurred speech** (dysarthria)

3 participants who received the **Low dose of MCS110** had a serious adverse event:

- **Problems from the IV infusion** (Infusion-related reaction) (in 2 participants)
- **Anemia** (Hemoglobin decreased)

What non-serious adverse events did participants have?

Some participants had adverse events that were not serious. This section reports the most common adverse events that **at least 35% of participants in a treatment group** had during each part of this trial.

Part A: Non-serious adverse events

	High dose MCS110 out of 5 participants	Placebo out of 2 participants
Headache	40% 2 of 5	0% 0 of 2
Possible sign of muscle damage Blood creatine phosphokinase increased	20% 1 of 5	50% 1 of 2
Feeling sick to the stomach Nausea	0% 0 of 5	50% 1 of 2

Part B: Non-serious adverse events

	High dose MCS 110 out of 11 participants	Placebo out of 3 participants
Feeling sick to the stomach Nausea	45% 5 of 11	0% 0 of 3
Common cold Nasopharyngitis	36% 4 of 11	0% 0 of 3
Diarrhea	36% 4 of 11	0% 0 of 3
Feeling tired Fatigue	36% 4 of 11	0% 0 of 3
Headache	36% 4 of 11	0% 0 of 3
Joint tumors Benign joint neoplasm	36% 4 of 11	0% 0 of 3
Puffy eyes Periorbital Edema	36% 4 of 11	0% 0 of 3
Rash	36% 4 of 11	0% 0 of 3
Possible sign of muscle damage Blood creatine phosphokinase increased	36% 4 of 11	0% 0 of 3

Part C: Non-serious adverse events

	Low dose MCS110 out of 7 participants	Medium dose MCS110 out of 7 participants	High dose MCS110 out of 12 participants
Puffy eyes Periorbital edema	71% 5 of 7	43% 3 of 7	33% 4 of 12
Feeling tired Fatigue	71% 5 of 7	29% 2 of 7	17% 2 of 12
Swelling in arms or legs Peripheral swelling	29% 2 of 7	43% 3 of 7	25% 3 of 12
Feeling sick to the stomach Nausea	29% 2 of 7	43% 3 of 7	8% 1 of 12
Joint tumors Benign joint neoplasm	0% 0 of 7	43% 3 of 7	17% 2 of 12

For more information about the adverse events, including those that happened to fewer participants in this trial, visit novctrd.com. Use clinical trial number **CMCS110X2201** to find the scientific summary.

What was learned from this trial?

This was the first trial to learn how well MCS110 works for people with TGCT. The clinical trial team concluded that MCS110 shrank participants' tumors more than the placebo. They also found that the medium and high doses of MCS110 shrank participants' tumors more than the low dose. The team concluded that MCS110 was generally safe for the participants in this trial.

The results presented here are for one clinical trial. One 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 TGCT. This summary shows only the main results from this trial. Other trials may provide new information or different results.

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

This is a summary of the results for one trial.

You can find detailed results and more information about this 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 information and the website
4. Select “Search by study number” on the bottom left of the page
5. Type **“CMCS110X2201”** in the search box and click search

If you would like to view the website in a language other than English, you can click the “Google Translate” button on the top right of the page.

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 clinical trial was registered on the following websites:

- ClinicalTrials.gov – https://clinicaltrials.gov/

  To find this trial, type **CMCS110X2201** in the **Other terms** search box
- European Union Clinical Trials Register – https://www.clinicaltrialsregister.eu/
  To find this trial, type **CMCS110X2201** in the search box

Full trial title:

A Phase II randomized, double-blind (Part A, B and C), placebo controlled (Part A and B only), study to assess safety, tolerability and efficacy of MCS110 on tumor size in patients with pigmented villonodular synovitis (PVNS)

If more clinical trials are planned, they will appear on the public websites listed on the previous page or at www.novartisclinicaltrials.com. When there, search for **MCS110** or **lacnotuzumab**.

Thank you!

Novartis would like to thank all of the people who participated in this clinical trial. The participants made this 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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