Clinical Trial Results

NOVARTIS

Research Sponsor: Novartis

Drug Studied: CSJ148

Protocol #: CCSJ148X2201

Thank you!

Thank you to the patients who took part in the clinical trial for the drug CSJ148. The patients helped researchers learn more about CSJ148 and how to treat human cytomegalovirus, also called HCMV. This trial helped researchers find out if CSJ148 prevents active HCMV infection and disease in patients getting stem cell transplants who already have HCMV.

Novartis sponsored this trial and believes it is important for the patients to know the results of this trial. An independent non-profit organization called CISCRP prepared this summary of the trial results for the patients. We hope it helps the patients understand their important role in medical research.

If the patients have questions about the results, they should speak with the doctor, research nurse, or other team members at their trial site.

What has happened since the trial ended?

The patients were in this trial for about 7 months. But, the trial took about a year and a half to complete. This is because the patients started and stopped the trial at different times. The trial started in June 2015 and ended in December 2016. The trial included 86 patients from 17 trial sites in 6 countries: Belgium, Germany, Republic of Korea, Singapore, Taiwan, and the United States.

After 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 are looking for a safer way to treat patients who are at risk of developing HCMV disease. HCMV disease includes a range of health problems caused by an active HCMV infection. Before a drug can be approved for patients to take, researchers do clinical trials to find out how well the drug works and how safe the drug is. This information is important to know before other trials can be done to find out if CSJ148 improves the health of patients who have HCMV or who are at risk of getting HCMV.

Infection with HCMV is common. HCMV usually does not cause problems. But, people with HCMV who have weak immune systems are at risk of developing HCMV disease. This includes patients who get stem cell transplants. Most patients who have HCMV can develop HCMV disease after stem cell transplants if no early treatment is given. The risk for HCMV disease is highest in the first 99 days after a transplant.

CSJ148 helps HCMV stop spreading. CSJ148 is made of 2 antibodies that block the virus from infecting cells. Antibodies are normally made by the immune system to fight infection. But, researchers can now use antibodies as medicines to treat a variety of conditions, including HCMV disease.

Other treatments are available to prevent and treat HCMV disease. But, these treatments may be toxic to patients who get stem cell transplants. Because the treatments could damage the bone marrow, doctors only give these treatments when there is no other choice. In this trial, the researchers compared CSJ148 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 effects of a trial treatment.

The main questions the researchers asked in the trial were:

- Did CSJ148 reduce the number of patients who needed early HCMV treatment?
- Did CSJ148 increase the amount of time until starting early HCMV treatment?
- Did CSJ148 reduce the number of times a patient needed early HCMV treatment?
- Did CSJ148 reduce the number of patients who got HCMV disease?
- How much CSJ148 got into the blood?
- What medical problems did patients have during the trial?

To answer these questions in this trial, researchers asked for the help of women and men who have HCMV. The patients in this trial were 22 to 76 years old and were scheduled to have a stem cell transplant. They also had an old HCMV infection that could be found in their blood but was not active before the transplant.

What kind of trial was this?

The first 6 patients in this trial got “open-label” CSJ148. This means that the sponsor staff, trial staff, and the patients knew the patients were getting CSJ148. This helped the sponsor staff decide how often the patients in the rest of the trial got treatment with CSJ148.

The rest of the trial included 80 patients and was a “double-blind” trial. This means that none of the patients, trial staff, or sponsor staff knew what treatment each patient got. Some trials are done this way because knowing what treatment the patients are getting can affect the results of the trial. A computer program was used to randomly assign the treatment each patient got. Doing a trial this way helps make sure the results are looked at fairly. When the trial ended, the sponsor staff found out which treatment patients got so they could create a report of the trial results.

What happened during the trial?

Before the trial treatment started, the trial doctors did tests to make sure patients could take part in the trial. The trial doctors:

- Measured HCMV levels in the blood
- Took blood and urine samples
- Checked the height, weight, blood pressure, and heart rate of each patient
- Checked the heart health of each patient using an electrocardiogram

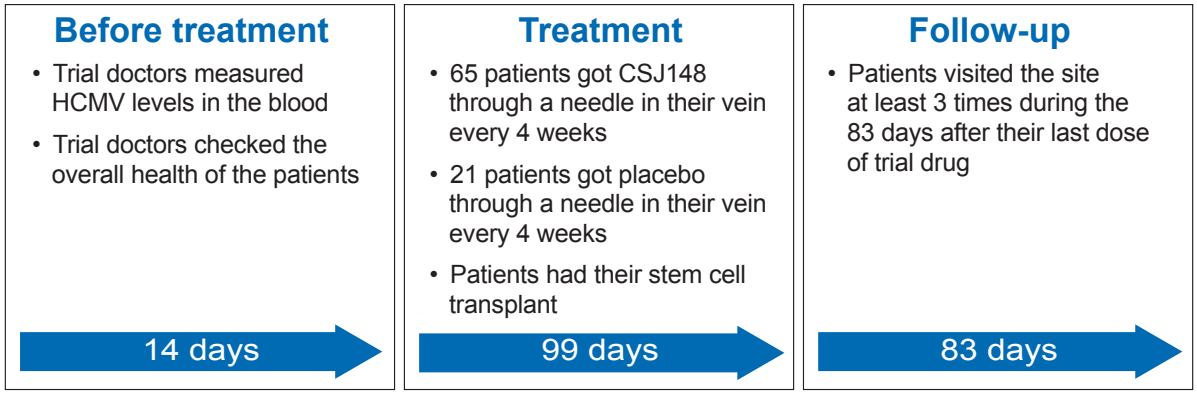
During the trial, all patients started treatment before they had their stem cell transplant. For every 3 patients who got the trial drug, 1 patient got the placebo.

- 65 patients got CSJ148 every 4 weeks.
- 21 patients got the placebo every 4 weeks.
- All patients got treatment through a needle put into a vein.

Throughout the trial, the trial staff:

- Checked the heart health and HCMV levels of patients before and after treatment
- Took blood and urine samples
- Asked questions about how patients felt and any other medicines they were taking

The chart below shows how the trial was done.



The follow-up period lasted 83 days. During this time, the patients visited their site at least 3 more times. The trial doctors checked HCMV levels. They also checked how patients were feeling and what medicines patients were taking.

What were the results of the trial?

This is a summary of the overall results of this trial, not individual results. The results presented here are for a single trial. Researchers look at the results of many trials to decide which treatments work best and are safest for patients. Other trials may provide new information or different results. Patients should not make medical decisions based on the results of a single trial without first talking to your doctor. Patients should always talk to a doctor before making any changes to medications or treatment plans.

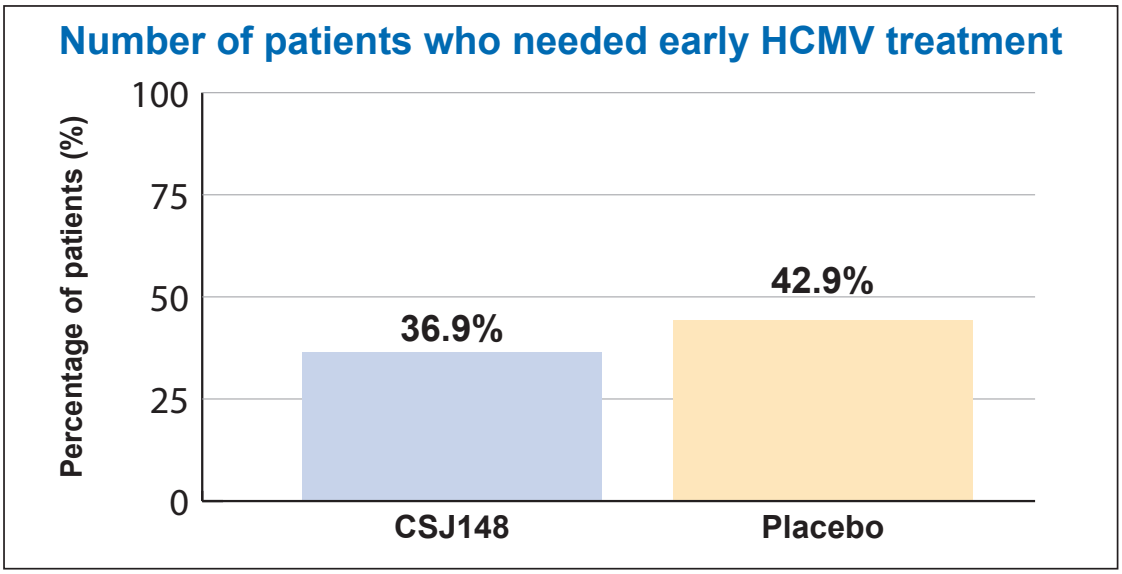
Did CSJ148 reduce the number of patients who needed early HCMV treatment?

Compared to getting the placebo, fewer patients who got CSJ148 needed early HCMV treatment. But, the difference between the treatment groups was too small for the researchers to know if CSJ148 changed how many patients needed early HCMV treatment. The difference could have been due to chance.

The researchers wanted to know if treatment with CSJ148 reduced the number of patients who needed early HCMV treatment. To answer this question, the researchers counted the number of patients in each treatment group who needed early HCMV treatment up to Day 99 after the stem cell transplant. The researchers found that:

- 36.9% of patients who got CSJ148 needed early treatment. This happened in 24 out of 65 patients.
- 42.9% of patients who got the placebo needed early treatment. This happened in 9 out of 21 patients.

The chart below shows how many patients needed early HCMV treatment in each treatment group up to Day 99 after the transplant.



Did CSJ148 increase the amount of time until starting early HCMV treatment?

Compared to getting the placebo, patients who got CSJ148 took more time on average before starting early HCMV treatment by Day 99. But, the difference between the treatment groups was too small for the researchers to know if CSJ148 changed the amount of time before patients started early HCMV treatment. The difference could have been due to chance. The researchers found that:

- Patients who got CSJ148 took an average of 62.0 days before starting early HCMV treatment.
- Patients who got the placebo took an average of 49.5 days before starting early HCMV treatment.

Did CSJ148 reduce the number of times a patient needed early HCMV treatment?

By Day 99, the difference between the treatment groups was too small for the researchers to know if CSJ148 reduced the number of times a patient needed early HCMV treatment. The difference could have been due to chance. The researchers found that:

- The average number of times patients who got CSJ148 needed early HCMV treatment was 2.1 times.
- The average number of times patients who got the placebo needed early HCMV treatment was 2.5 times.

Did CSJ148 reduce the number of patients who got HCMV disease?

No. CSJ148 did not reduce the number of patients who got HCMV disease. Overall, 8 patients developed HCMV disease:

- 10.8% of patients who got CSJ148 developed HCMV disease during or after the trial. This happened in 7 out of 65 patients.
- 4.8% of patients who got placebo developed HCMV disease during or after the trial. This happened in 1 out of 21 patients.

How much CSJ148 got into the blood?

To find out how much CSJ148 got into the blood after treatment, researchers took blood samples during the trial. Overall, they learned that the expected amount of CSJ148 was found in the blood in patients who got CSJ148.

What medical problems did patients have?

Medical problems that happen in clinical trials are called “adverse events”. An adverse event is any unwanted sign or symptom that patients have during a trial. An adverse event is considered “serious” when it is life-threatening, causes lasting problems, or the patients need hospital care. These problems may or may not be caused by the trial drug. A lot of research is needed to know whether a drug causes a medical problem. During a trial, all medical problems are reported and written down, whether or not they are caused by the trial drug. So, when new drugs are being studied, researchers keep track of all medical problems that patients have.

This section is a summary of the adverse events that happened during this trial.

How many patients had adverse events during the trial?

All patients had adverse events during the trial. This is normal for patients who get stem cell transplants. Two patients who got CSJ148 and 1 patient who got the placebo left the trial because of an adverse event.

The table below shows how many patients had adverse events during the trial.

Adverse events during this trial

	CSJ148 (out of 65 patients)	Placebo (out of 21 patients)	Total (out of 86 patients)
How many patients had adverse events?	65 (100.0%)	21 (100.0%)	86 (100.0%)
How many patients had serious adverse events?	46 (70.8%)	15 (71.4%)	61 (70.9%)
How many patients left the trial because of adverse events?	2 (3.1%)	1 (4.8%)	3 (3.5%)

Did any patients have serious adverse events?

A total of 25.6% patients died during or after the trial. This was 22 out of 86 patients.

- The causes of death were complications from the stem cell transplants.
- Most deaths occurred after the treatment period, or Day 99.

The trial doctors did not think any of the deaths were related to CSJ148 treatment.

The most common serious adverse event was severe graft versus host disease. This disease happens when the transplanted stem cells attack the body soon after the transplant. The trial doctors did not think this serious adverse event was related to the trial drugs. This is a common serious adverse event after a stem cell transplant.

The table on the next page shows the most common serious adverse events that happened in more than 5.0% of patients.

Most common serious adverse events in this trial			
Serious adverse event	**CSJ148 (out of 65 patients)**	**Placebo (out of 21 patients)**	**Total (out of 86 patients)**
Acute graft versus host disease (when the transplanted stem cells attack the body soon after transplant)	9 (13.8%)	2 (9.5%)	11 (12.8%)
Fever with low white blood cell count	8 (12.3%)	1 (4.8%)	9 (10.5%)
Pneumonia (lung infection)	5 (7.7%)	1 (4.8%)	6 (7.0%)
Organ damage caused by infection	4 (6.2%)	2 (9.5%)	6 (7.0%)
Recurring acute myeloid leukemia (a blood cancer)	4 (6.2%)	2 (9.5%)	6 (7.0%)
Sudden kidney failure	4 (6.2%)	1 (4.8%)	5 (5.8%)

What were the most common adverse events?

Nausea and diarrhea were the most common adverse events. The table below shows the most common adverse events that happened in 30.0% or more of patients.

Most common adverse events in this trial			
Adverse event	**CSJ148 (out of 65 patients)**	**Placebo (out of 21 patients)**	**Total (out of 86 patients)**
Nausea	46 (70.8%)	14 (66.7%)	60 (69.8%)
Diarrhea	44 (67.7%)	12 (57.1%)	56 (65.1%)
Vomiting	38 (58.5%)	14 (66.7%)	52 (60.5%)
Mouth sores	36 (55.4%)	15 (71.4%)	51 (59.3%)
Fever with normal blood cell count	38 (58.5%)	11 (52.4%)	49 (57.0%)
Fever with low white blood cell count	29 (44.6%)	11 (52.4%)	40 (46.5%)
Decreased appetite	27 (41.5%)	7 (33.3%)	34 (39.5%)
Cough	25 (38.5%)	9 (42.9%)	34 (39.5%)
Rash	24 (36.9%)	7 (33.3%)	31 (36.0%)
Headache	24 (36.9%)	6 (28.6%)	30 (34.9%)
High blood pressure	23 (35.4%)	5 (23.8%)	28 (32.6%)
Constipation	19 (29.2%)	8 (38.1%)	27 (31.4%)

For more information about the adverse events in this trial, please see the scientific summary that can be found on the websites noted at the end of the summary.

How has this trial helped patients and researchers?

The information described above helped researchers better understand if CSJ148 helps prevent HCMV disease in patients with the virus. The results presented here are for a single trial. Researchers look at the results of many trials to decide which treatments work best and are safest. This summary shows only the main results from this one trial. Other trials may provide new information or different results. It takes volunteers in many trials all around the world to advance medical science.

Where can I learn more about this trial?

More information about the results of this trial can be found in the scientific results summary 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 **"CCSJ148X2201"** 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.

- ClinicalTrials.gov (https://clinicaltrials.gov/) - National Clinical Trial # **NCT02268526**
- ClinicalTrialsRegister.eu (https://clinicaltrialsregister.eu/) - EudraCT # **2014-002150-39**

If more clinical trials are planned, they will be listed on the above public websites or

- www.novartisclinicaltrials.com. Search for **"CSJ148"**.

Short Trial Title: Efficacy and Safety Study of CSJ148 in Stem Cell Transplant Patients

Full Trial Title: A multi-center, randomized, double-blind, placebo controlled, study to evaluate the efficacy and safety of CSJ148 compared to placebo to prevent human cytomegalovirus (HCMV) replication in stem cell transplant patients

Thank you

Clinical trial patients belong to a large community of patients around the world. Clinical trial patients help 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.

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