Clinical Trial Results

NOVARTIS

Research Sponsor:	Novartis
Location of Headquarters:	Basel, Switzerland
Treatment Studied:	HSC835
Protocol #:	CHSC835X2201
Full Trial Title:	A first-in-human, single-arm, single-center, open-label, proof-of-concept study to evaluate the safety and tolerability of infusing HSC835 (expanded umbilical cord blood hematopoietic stem cells) in patients with hematological malignancies
Full Scientific Summary:	www.novctrd.com
Trial Date:	January 2012 to October 2016

Thank you!

Thank you to the patients who took part in the clinical trial for a treatment called HSC835. The patients helped researchers learn how HSC835 works in people with blood cancer. This trial started in January 2012 and ended in October 2016.

Novartis, the sponsor of this trial, thanks the patients for their help and thinks it is important for them 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 patients have questions about the results, they should speak with the doctor, research nurse, or other team member at their trial site.

What's happened since the trial ended?

The patients were in this trial for about 1 year, but the trial took almost 5 years to complete. The trial included 27 patients from 1 trial site in 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 treat blood cancer. One common treatment for blood cancer is to give patients blood stem cell transplants. A blood stem cell can turn into all the common types of cells normally found in the blood. Sometimes the stem cells come from the bone marrow of a relative. In this case, a careful "match" is needed between the person donating stem cells and the person receiving the stem cells in order for the treatment to work. Finding this match is often very hard. Another possible source of stem cells is from umbilical cord blood. This is the blood left in the placenta after a baby is born. Using stem cells from umbilical cord blood does not require an exact match.

Usually, the patient gets a treatment called a "single-unit transplant" from 1 unit of umbilical cord blood, but the amount of stem cells from a single-unit transplant may not be enough to help treat a patient with blood cancer. So, sometimes the patient gets a "double-unit transplant" from 2 units of umbilical cord blood. Even with a double-unit transplant, the patient's body does not recover from the transplant quickly enough. So researchers are looking for new ways to help speed up the patient's recovery.

Researchers in this trial wanted to learn whether a treatment called HSC835 could increase the number of blood stem cells that came from the umbilical cord unit, to make the transplant process faster and safer. In this treatment, the cells in the umbilical cord blood are separated into 2 parts. One part is grown in the laboratory. HSC835 increases the number of blood stem cells. The rest of the cells are saved for later and are given as part of the treatment, too.

In this trial, researchers wanted to know:

- How many patients had medical problems in the first 48 hours after getting HSC835 that were caused by the treatment?
- How many patients had successful transplants?
- How many patients' stem cells successfully transplanted?
- How many patients died during the trial?
- How many patients had their blood cancer come back within 1 year of getting HSC835?
- How many patients survived their cancer for at least 1 year after getting HSC835?
- What medical problems did patients have during the trial?

To answer these questions, researchers asked for the help of people with blood cancer. The patients in this trial were men, women, and children who were 11 to 53 years old and had blood cancer.

What kind of trial was this?

This trial was "open-label". This means that the patients, trial doctors, trial staff, and the sponsor knew what each patient got. In this trial, all patients got HSC835.

What happened during the trial?

Before the trial started, trial doctors did a full checkup of all patients to make sure they could join the trial. Trial doctors did a physical exam, took blood and urine samples, did other tests, and checked patients' lung and heart health.

Trial doctors also asked questions about any medical problems and other drugs that the patients were taking. This trial had 2 stages. All patients went through both stages: Pre-transplant treatment and Transplant treatment.

The chart below shows how the trial was done.

Open-Label Trial

Stage 1: Pre-transplant treatment

All patients got:

- Chemotherapy for 3 days
- Rest 1 day
- Radiation therapy twice a day for 4 days
- Immune system-lowering medicine

8 days

Stage 2: Transplant treatment

All patients got HSC835 on Day 1.

HSC835 = cells grown in laboratory plus the cells that were saved for later.

There were 2 groups of patients. They received one of the following:

- **Group 1:** Double-unit transplant: Patients got both HSC835 and 1 unit of umbilical cord stem cells that was not grown in the laboratory
- **Group 2:** Single-unit transplant: Patients got HSC835

About 1 year

Stage 1 lasted 8 days. During this stage, each patient got high doses of chemotherapy and radiation therapy. These treatments helped their bodies get rid of cancer cells. In addition, each patient received medicines that would lower their immune system. These were started 3 days before the transplant and continued after the transplant. All of the treatments given in this stage were needed to make sure the immune system did not reject the transplanted stem cells.

- Patients got chemotherapy for the first 3 days, then had a day of rest.
- Patients then got radiation therapy twice a day for 4 days, with the last day being the day before getting HSC835.
- Patients got 2 immune system lowering medicines 3 days before the transplant and continued taking these after the transplant occurred.

Stage 2 lasted about 1 year. During this stage of the trial, patients got HSC835 on Day 1 through an infusion. A total of 27 patients received HSC835. The patients were split into 2 groups. Group 1 received HSC835 as part of a double-unit transplant and Group 2 received HSC835 as part of a single-unit transplant.

Group 1: A total of 18 patients got the double-unit transplant:

- Patients who got the double-unit transplant received the following infusions:
  - 1 unit of umbilical cord stem cells that was not grown in the laboratory
  - HSC835 (cells grown in the laboratory and the cells that were saved)
- A total of 15 adults and 3 children got the double-unit transplant.

Group 2: Next, researchers in the trial tried a single-unit transplant after they successfully tried the double-unit transplant. A total of 9 patients received a single-unit transplant:

- Patients who got the single-unit transplant received the following infusion:
  - HSC835 (cells grown in the laboratory and the cells that were saved)
- A total of 8 adults and 1 child got the single-unit transplant.

After the transplant, patients were checked on for 1 year to see how well they were handling the transplant and how they were feeling.

What were the results of the trial?

This is a summary of the overall results of this trial, not the patients' 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 changes to their treatment based on the results of a single trial without first talking to their doctor.

How many patients had medical problems in the first 48 hours after getting HSC835 that were caused by the treatment?

One of the main questions researchers asked in this trial was how well the patients handled the blood stem cell infusion. To answer this question, they looked at the number of patients who had medical problems or adverse events in the first 48 hours after getting HSC835. An adverse event is any unwanted sign or symptom that may or may not be caused by the trial drug.

Out of the 27 patients in the trial, 1 patient (3.7%) in the double-unit transplant group had 2 adverse events in the first 48 hours after getting HSC835 that trial doctors thought were caused by the treatment:

- Fever and a low number of white blood cells
- Low blood pressure

How many patients had successful transplants?

Researchers wanted to know how many patients had successful transplants. In this trial, a transplant was successful if blood cells called neutrophils grew back in the patients' bodies after treatment.

- All patients in the trial had successful transplants of HSC835.
- Both the single-unit and double-unit transplants with HSC835 were successful.

How many patients' stem cells successfully transplanted?

Researchers were also interested in how many patients had successful transplants in a 42-day period of time. In this trial, a transplant was successful if neutrophils grew in patients' blood after treatment. Researchers found that:

- All patients, whether they got the single-unit transplant or the double-unit transplant, had neutrophils grow from the transplanted blood stem cells and appear in their blood within 42 days of the transplant.

Researchers also looked at whether platelets grew in patients' blood after treatment. Platelets are tiny cells in the blood that help your blood clot. If you get a cut, some of your platelets stick together to plug the hole in the blood vessel wall caused by the cut. Researchers found that 74.1% of patients had platelets grow from the transplanted blood stem cells and appear in their blood within 6 months of getting HSC835. That was 20 out of 27 patients.

How many patients died during the trial because of the transplant?

Out of the 27 patients in the trial:

- 5 patients (18.5%) died within 100 days of getting the transplant.
- 8 patients (29.6%) died within 1 year of getting the transplant.

How many patients had their blood cancer come back within 1 year of getting HSC835?
Out of the 27 patients in the trial, 3 (11.1%) had their cancer come back within 1 year of getting HSC835:

- 2 of the 8 adults (25%) who got the single-unit transplant had their cancer come back within 1 year.
- 1 of the 3 children (33.0%) who got the double-unit transplant had their cancer come back within 1 year.

The 1 child who got the single-unit transplant and all 15 adults who got the double-unit transplant did not have their cancer come back within 1 year.

How many patients survived their cancer for at least 1 year after getting HSC835?
Out of the 27 patients in the trial, 16 (59.3%) survived their cancer for at least 1 year after getting HSC835.

Single-unit transplant:

- 5 of the 8 adults (62.5%) who got this survived their cancer for at least 1 year.
- The 1 child (100.0%) who got this survived their cancer for at least 1 year.

Double-unit transplant:

- 9 of the 15 adults (60.0%) who got this survived their cancer for at least 1 year.
- 1 of the 3 children (33.3%) who got this survived their cancer for at least 1 year.

What medical problems did patients have?

A lot of research is needed to know whether a treatment causes a medical problem. So, when new treatments 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 unwanted sign or symptom that may or may not be caused by the trial treatment.

How many patients had adverse events during the trial?
Overall, all 27 patients (100.0%) had adverse events during the trial. The table below shows how many patients in each group had adverse events during this trial.

Adverse events in this trial

	Single-unit transplant (Out of 9 patients)	Double-unit transplant (Out of 18 patients)	Total (Out of 27 patients)
How many patients had adverse events?	9 (100.0%)	18 (100.0%)	27 (100.0%)
How many patients had serious adverse events?	8 (88.9%)	17 (94.4%)	25 (92.6%)

Did any patients have serious adverse events?
Some patients also had serious adverse events. An adverse event is considered "serious" when it is life-threatening, causes lasting problems, or leads to hospitalization.

Out of the 27 patients, 11 patients (40.7%) died during this trial:

- 8 patients died because of serious medical problems related to the transplant.
- 3 patients died because their cancer came back.

Trial doctors did not think any of the deaths were related to HSC835 treatment.

In the first 48 hours after getting HSC835, there were 2 serious adverse events that happened in 1 patient who got the double-unit transplant:

- Fever and a low number of white blood cells
- Low blood pressure

Trial doctors thought that these 2 serious adverse events were related to HSC835 treatment.

From Day 3 after the transplant to the end of the trial, 24 of the 27 patients had serious adverse events. The table below shows the most common serious adverse events that happened to at least 15% of all patients from Day 3 to the end of the trial. Other serious adverse events happened in fewer total patients.

Most common serious adverse events from Day 3 to end of the trial

Serious adverse event	Single-unit transplant (Out of 9 patients)	Double-unit transplant (Out of 18 patients)	Total (Out of 27 patients)
Acute graft versus host disease (when the transplanted stem cells attack the body soon after the transplant)	5 (55.6%)	10 (55.6%)	15 (55.6%)
Bleeding in the lungs	2 (22.2%)	4 (22.2%)	6 (22.2%)
Sudden kidney failure	0 (0.0%)	5 (27.8%)	5 (18.5%)

What were the most common adverse events?

The most common adverse event that happened in the first 48 hours after getting HSC835 was high blood pressure. The table below shows the most common adverse events that happened to at least 15% of all patients in the first 48 hours after getting HSC835. Other adverse events happened in fewer total patients.

Most common adverse events in the first 48 hours after getting HSC835

Adverse event	Single-unit transplant (Out of 9 patients)	Double-unit transplant (Out of 18 patients)	Total (Out of 27 patients)
High blood pressure	6 (66.7%)	7 (38.9%)	13 (48.1%)
Decreased appetite	3 (33.3%)	6 (33.3%)	9 (33.3%)
Headache	4 (44.4%)	5 (27.8%)	9 (33.3%)
Fever and low number of white blood cells	1 (11.1%)	7 (38.9%)	8 (29.6%)
Nausea	2 (22.2%)	3 (16.7%)	5 (18.5%)

More adverse events happened from Day 3 to the end of the trial than in the first 48 hours after getting HSC835. The most common adverse event that happened from Day 3 to the end of the trial was painful sores in the mouth. The table below shows the adverse events that happened to at least 25% of all patients from Day 3 to the end of the trial. Other adverse events happened in fewer total patients.

Most common adverse events from Day 3 to end of the trial

Adverse event	Single-unit transplant (Out of 9 patients)	Double-unit transplant (Out of 18 patients)	Total (Out of 27 patients)
Painful sores in the mouth	8 (88.9%)	10 (55.6%)	18 (66.7%)
Acute graft versus host disease	5 (55.6%)	10 (55.6%)	15 (55.6%)
Fever and low white blood cell count	4 (44.4%)	10 (55.6%)	14 (51.9%)
Blood infection due to Staphylococcus aureus bacteria	4 (44.4%)	6 (33.3%)	10 (37.0%)
Infection due to BK virus	3 (33.3%)	6 (33.3%)	9 (33.3%)
Decreased appetite	2 (22.2%)	7 (38.9%)	9 (33.3%)
Too much fluid in the blood	3 (33.3%)	5 (27.8%)	8 (29.6%)
Blood infection due to cytomegalovirus	0 (0.0%)	7 (38.9%)	7 (25.9%)

For more information about the adverse events in this trial, please refer to the full scientific summary of the results available on the Novartis Clinical Trial Results website (www.novctrd.com).

Where can patients 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 **CHSC835X2201** 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 website:

- Clinical Trials.gov (https://clinicaltrials.gov/)- National Clinical Trial # NCT01474681

Thank you

Clinical trial patients belong to a large community of patients around the world. 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. CISCRP is not involved in recruiting patients for clinical trials, nor is it involved in conducting clinical trials.

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