Clinical Study Results

CSL Behring

Research Sponsor: CSL Behring GmbH
Treatment Studied: rIX-FP
Study Purpose: A study to learn about immune reactions to rIX-FP in participants with hemophilia B

Thank you

Thank you for taking part in the clinical study for rIX-FP, also called “Recombinant Coagulation Factor IX Albumin Fusion Protein”. You and all of the participants and caregivers helped researchers learn more about rIX-FP to help people with hemophilia B.

CSL Behring GmbH sponsored this study and thinks it is important to share the results of the study with you and the public. We hope it helps you understand and feel proud of your important role in medical research.

If you have questions about the results, please speak with the doctor or staff at your study site.

What is happening with the study now?

There were 2 main groups of participants who got study treatment in this study.

In **Part A**, the participants were in the study for about 4 years. Part A started in February 2014 and ended in June 2018. It included 83 participants in Australia, Austria, Bulgaria, Canada, Czech Republic, France, Germany, Israel, Italy, Japan, Malaysia, the Philippines, South Africa, Spain, and the United States.

In **Part B**, the participants were in the study for up to 3 years, but Part B took over 6 years to finish. Part B started in December 2014 and ended in June 2021. It included 12 participants in Australia, Austria, Germany, Italy, the Philippines, and the United States.

CSL Behring reviewed the data collected when the study ended and created reports of the results. This is a summary of the main results of those reports.

Why was the research needed?

Researchers are looking for a better way to treat people with severe hemophilia B. Before a treatment can be approved for patients to receive, researchers do clinical studies to find out how it works and how safe it is.

Hemophilia B is a bleeding disorder that happens mostly in males. Most cases are inherited, which means it is passed down to someone through their parents' genes. Hemophilia B may sometimes also be called "Christmas disease".

Normally, the body uses a protein called "Factor IX" to make blood clots. In people with hemophilia B, the body does not make enough Factor IX to help make blood clots. Without enough Factor IX, the blood cannot clot. This can lead to uncontrolled bleeding, including bleeding inside the body.

Treatments for hemophilia B work by replacing Factor IX. Normally, Factor IX replacements need to be given as regular injections, or through a needle into a vein, also known as an intravenous or "IV infusion". Getting regular injections or IV infusions can sometimes cause medical problems, such as infections.

The study treatment, rIX-FP, is a type of Factor IX replacement that has been combined with another protein called "albumin". Albumin is another protein that is found in the blood. Researchers think that giving Factor IX in this way may help it last longer in the body. This could mean that people with hemophilia B might need to have rIX-FP treatments less frequently than other types of Factor IX replacements.

The main questions the researchers wanted to answer in this study were:

- How many participants in **Part A** had immune reactions to rIX-FP?
- How many participants in **Part B** had immune reactions to rIX-FP?
- What were the levels of rIX-FP in the participants' blood in **Part B**?
- What medical problems did **any participants** have during the study?

What kind of study was this?

To answer the questions in this study, the researchers asked for the help of 2 groups of people with hemophilia B. This was an “open-label” study. This means the researchers and the participant knew what the participant was getting. All of the participants got rIX-FP through an IV infusion.

In **Part A**, the participants were males between 2 and 63 years old. The participants in Part A had either:

- been treated with rIX-FP in a previous study, or
- been treated with other Factor IX replacements but not rIX-FP, and had just had a major surgery

These participants got an IV infusion every 1 to 3 weeks. The dose of rIX-FP depended on the dose that the participants got in the previous study or their dose of other Factor IX replacements.

In **Part B**, the participants were males between 0 and 11 years old. They had never been treated with any Factor IX replacements before. These participants got an IV infusion every week. The dose of rIX-FP depended on what the researchers thought was best for each participant.

If any of the participants in Part A or Part B had bleeding episodes during the study, they could get extra doses of rIX-FP to stop the bleeding.

What happened during the study?

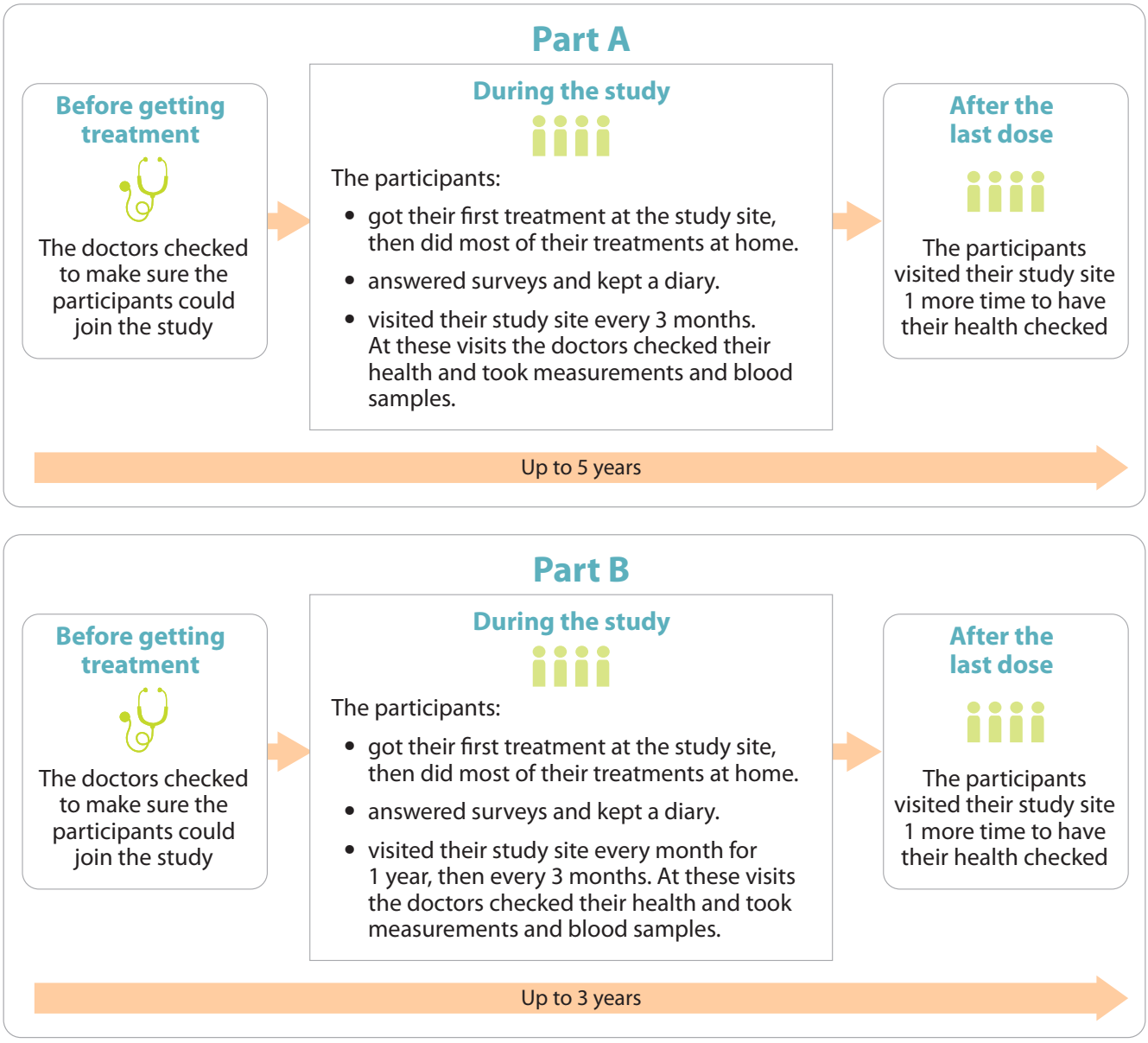
Before the participants got any study treatment, the doctors checked their overall health to make sure they could join the study. The doctors checked the participants’ blood pressure, measured their height and weight, and took blood samples. They also asked about the participants’ medical history. The participants or their caregivers answered surveys about their symptoms and kept a diary throughout the study.

During the study, the study staff gave the participants their first IV infusion at the study site. At this visit, they showed the participants how to give themselves their own infusion, or they showed a caregiver how to give the infusion. They also checked the participants’ health and took blood samples.

After this, the participants in **Part A** visited the study site every 3 months for as long as they were in the study. The participants in **Part B** visited the study site every month for the first year, then every 3 months for as long as they were in the study.

After the last dose of study treatment, the participants visited the study site 1 more time so that the doctors could check their health.

The chart below shows how the study was done.



What were the results of the study?

This is a summary of the main results from this study overall. The results each participant had might be different from the overall summary results. A full list of the questions the researchers wanted to answer can be found on the websites listed at the end of this summary. Once a full report of the study results is available, it may also be found on these websites.

It takes many studies to decide which treatments work best and are safest. Other studies may provide new information or different results.

How many participants in Part A had immune reactions to rIX-FP?

To answer this question, the researchers took blood samples throughout the study from the participants in Part A. The researchers looked for antibodies in the participants' blood.

Antibodies are a type of protein made by the body's immune system. Antibodies protect the body from anything that the immune system might recognize as dangerous, such as germs. Sometimes the immune system also recognizes drugs as dangerous and creates antibodies to target those drugs. Antibodies are unique to each germ, drug, or other danger that they target. Antibodies that target drugs are also known as "neutralizing inhibitors" and can work against drugs to lower their effectiveness.

The researchers counted how many participants in Part A had neutralizing inhibitors for rIX-FP in their blood.

Overall, the researchers found that **none** of the 83 participants in Part A had neutralizing inhibitors for rIX-FP in their blood.

How many participants in Part B had immune reactions to rIX-FP?

To answer this question, the researchers took blood samples throughout the study from the participants in Part B. The researchers counted how many participants in Part B had neutralizing inhibitors for rIX-FP in their blood.

Overall, the researchers found that **1 out of 12** participants in Part B had neutralizing inhibitors for rIX-FP in their blood. This was 8.3% of the participants in Part B.

What were the levels of rIX-FP in the participants' blood in Part B?

To answer this question, the researchers took blood samples from the participants before their first IV infusion and for several days after getting their first IV infusion. The researchers measured how much rIX-FP was in the participants' blood.

The researchers looked at the highest and lowest levels of rIX-FP in the participants' blood to decide how often to give the participants their IV infusions. Based on these results, the researchers decided that the participants should get their IV infusions every week for the rest of Part B.

What medical problems did any participants have during the study?

This section is a summary of the “adverse events” that happened during the study. An adverse event is any sign or symptom that participants have.

Adverse events may or may not be caused by the treatments in this study. A lot of research is needed to know whether a treatment causes an adverse event. Doctors keep track of all the adverse events that happen in studies, even if they do not think the adverse events might be related to the treatment.

An adverse event is considered “serious” when it is life-threatening, causes lasting problems, is medically significant, requires hospital care, or results in death.

How many participants had adverse events?

In **Part A**:

- There were **74 out of 83** participants who had adverse events during the study. This was 89.2% of participants.
- **None of the 83** participants stopped getting rIX-FP because of adverse events during the study.

In **Part B**:

- There were **11 out of 12** participants who had adverse events during the study. This was 91.7% of participants.
- There was **1 out of 12** participants who stopped getting rIX-FP. This was because they developed neutralizing inhibitors. This was 8.3% of participants.

How many participants had serious adverse events?

In **Part A**:

- There were **17 out of 83** participants who had serious adverse events during the study. This was 20.5% of participants. The researchers thought that 1 of these serious adverse events was related to rIX-FP. This serious adverse event was limited blood supply to the legs.
- There was **1 out of 83** participants who died due to serious adverse events during the study. This was 1.2% of participants. This serious adverse event was a motorcycle accident.

In **Part B**:

- There were **5 out of 12** participants who had serious adverse events during the study. This was 41.7% of participants. The researchers thought that 1 of these serious adverse events was related to rIX-FP. This serious adverse event was having high levels of neutralizing inhibitors for rIX-FP.
- **None of the 12** participants in Part B died due to serious adverse events during the study.

What adverse events did the participants have?

The table below shows the most common adverse events that happened during **Part A** in 10.0% or more of the participants. Some participants may have had more than 1 adverse event. There were other adverse events in Part A, but these happened in fewer participants.

Most common adverse events in Part A

Adverse event	**Part A** (out of 83 participants)
Joint pain	30.1% (25)
Common cold	18.1% (15)
Fever	18.1% (15)
Headache	13.3% (11)
Tooth decay	12.0% (10)
Stomach flu	12.0% (10)

The table below shows the most common adverse events that happened during **Part B** in 20.0% or more of the participants. Some participants may have had more than 1 adverse event. There were other adverse events in Part B, but these happened in fewer participants.

Most common adverse events in Part B

Adverse event	**Part B** (out of 12 participants)
Fever	50.0% (6)
Fall	33.3% (4)
Head injury	33.3% (4)
Common cold	25.0% (3)
Infection in the upper airways	25.0% (3)
Stomach flu	12.0% (10)

What serious adverse events did the participants have?

The table below shows the most common serious adverse events that happened during **Part A** in more than 1 participant. Some participants may have had more than 1 serious adverse event. There were other serious adverse events in Part A, but these happened in fewer participants.

Most common serious adverse events in Part A

Serious adverse event	**Part A** (out of 83 participants)
Head injury	3.6% (3)
Low levels of iron in the blood, also known as iron deficiency anemia	2.4% (2)
Bleeding inside a joint	2.4% (2)

The table below shows all the serious adverse events that happened during **Part B**.

All serious adverse events in Part B

Serious adverse event	**Part B** (out of 12 participants)
Head injury	8.3% (1)
High levels of neutralizing inhibitors for rIX-FP	8.3% (1)
Infection around the site of an inserted medical device	8.3% (1)
Influenza infection	8.3% (1)
Pneumonia infection	8.3% (1)

How has this study helped patients and researchers?

This study helped researchers learn more about immune reactions to rIX-FP in participants with hemophilia B.

Researchers look at the results of many studies to decide which treatments work best and are safest for patients. This summary shows only the main results from one study. Other studies may provide new information or different results. Always talk to a doctor before making any treatment changes.

Further clinical studies with rIX-FP are planned.

Where can I learn more about this study?

This summary can be viewed online at www.TrialSummaries.com.

You can find more information about this study by searching on the websites listed below. Once a full report of the study results is available, it may also be found there.

- www.clinicaltrials.gov Once you are on the website, type "**NCT02053792**" into the search box and click "**Search**".
- www.clinicaltrialsregister.eu Once you are on the website, click "**Home and Search**", then type "**2012-005489-37**" in the search box and click "**Search**".

Full study title: A Phase 3b Open-label, Multicenter, Safety and Efficacy Extension Study of a Recombinant Coagulation Factor IX Albumin Fusion Protein (rIX-FP) in Subjects with Hemophilia B

National Clinical Trials number: NCT02053792

EU Clinical Trials number: 2012-005489-37

CSL Behring GmbH protocol number: CSL654-3003

CSL Behring GmbH sponsored this study and has its headquarters at Emil-von-Behring-Strasse 76, 35041 Marburg, Germany

The phone number for the CSL Behring Information Center is 610-878-4000

The email address for CSL Behring Clinical Trial information is clinicaltrials@cslbehring.com.

Thank you

Clinical study participants belong to a large community of people who take part in clinical research around the world. They help researchers answer important health questions and find medical treatments for patients.

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 participants for clinical studies, nor is it involved in conducting clinical studies.

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