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A Study of Recombinant Von Willebrand Factor in Children and Adults With Severe Von Willebrand Disease

THANK YOU!

Thank you to all participants and their caregivers who took part in this study.

Takeda sponsored this study and thinks it is important to share the results with the study participants and the public.

This summary reports the main results of this study.

Key points of the study:

Vonicog alfa (a recombinant von Willebrand factor) was being studied as a potential treatment for people with von Willebrand disease. This medicine works by replacing a missing protein called von Willebrand factor that helps blood clot in people with this condition. In this study, eligible participants from previous studies (071301 or 071102), or new participants who wanted to receive preventive treatment with vonicog alfa, took part. They either received preventive treatment or urgent treatment to control bleeding events. Researchers wanted to learn more about how well vonicog alfa worked in participants to stop bleeding events.

Overall, the study showed that vonicog alfa worked well to prevent and control bleeding events. The number of bleeding events remained low in participants during the study.

Why was this study done?

Von Willebrand disease (VWD) is a blood disorder usually passed on from parents to children. In people with VWD, the body has difficulty forming blood clots. Certain proteins in the blood help the blood to clot. Some of these proteins are the von Willebrand factor (VWF) and factor 8 (FVIII). These clotting factors bind together with platelets. Platelets are small particles in the blood that help with blood clotting, which can then seal a wound and stop further blood loss. People with VWD have low levels of these clotting factors or have a type of VWF that does not work well. Without enough VWF, it is difficult for the body to make blood clots which can lead to heavy bleeding.

VWD is of 3 types:

- **Type 1** – Most common type of VWD where people do not have enough VWF in their blood.
- **Type 2** – This type of VWD happens when the VWF in the body does not work well.
- **Type 3** – Rare type of VWD where people do not have VWF and very low levels of another protein that helps with blood clotting called FVIII.

Common symptoms of VWD may include heavy bleeding after surgery or dental procedures, nosebleeds, and easy bruising.

There are only a few medicines that help replace the missing proteins in the blood that form clots. Vonicog alfa is one such medicine that helps replace VWF. It is a recombinant VWF (rVWF). This means that it was made in the laboratory and works like the VWF produced by the body. Vonicog alfa has been approved to treat people with VWD to prevent and manage bleeding events. In this extension study, researchers wanted to learn more about the safety and how well it worked to prevent and control bleeding events in people who had VWD over a long period of time.

What were the main questions?

Researchers wanted to learn about how well vonicog alfa works to control the number of bleeding events in both adults and children during the first year of treatment. To do this, they asked the following question:

How often did participants have sudden bleeding events during the treatment?

Researchers recorded the number of sudden bleeding events in a year, also known as the annualized bleeding rate (ABR). They checked if preventive treatment with vonicog alfa helped control the number of bleeding events in a year.

Any medical problems that happened during the study were also recorded. Medical problems are any new or worsening problems that the participants had after they took the study medications. They may or may not be related to the study drug.

How was the study done?

What type of study was this?

Clinical studies are done as part of the development of a new treatment. The type of clinical study depends on the stage, or phase of development. These studies are called Phase 1 to Phase 4 studies.

- This was a Phase 3 study, which usually involves many people. This study helped researchers learn about the long-term safety of the treatment and how well it worked in participants with VWD.
- This was an open-label study. This means participants, doctors, and other study clinic staff knew which treatment each participant received.

What treatments were studied?

The participants received the following treatment:

Vonicog alfa, 40 to 60 international units per kilogram (IU/kg), given as a slow injection into the vein, also known as intravenous (IV) infusion, once or twice a week for preventive treatment, or when needed for urgent treatment. The dose could be increased, if needed, to a maximum of 80 IU/kg.

What happened during the study?

The study doctors checked that each participant met the study rules before they joined the study. Researchers wanted to learn how safe vonicog alfa was and how well it worked to prevent or stop bleeding events in participants with VWD.

Participants who had completed previous studies (071301 or 071102) or those who wanted to receive preventive treatment with vonicog alfa took part in this study.

Participants received the treatment in the following ways:

a) Vonicog alfa given on a regular schedule (once or twice a week) to prevent bleeding events from happening, also known as **prevention or prophylactic treatment**.

b) Vonicog alfa only given to control a sudden bleeding event when it happens, also known as **urgent or on-demand treatment**.

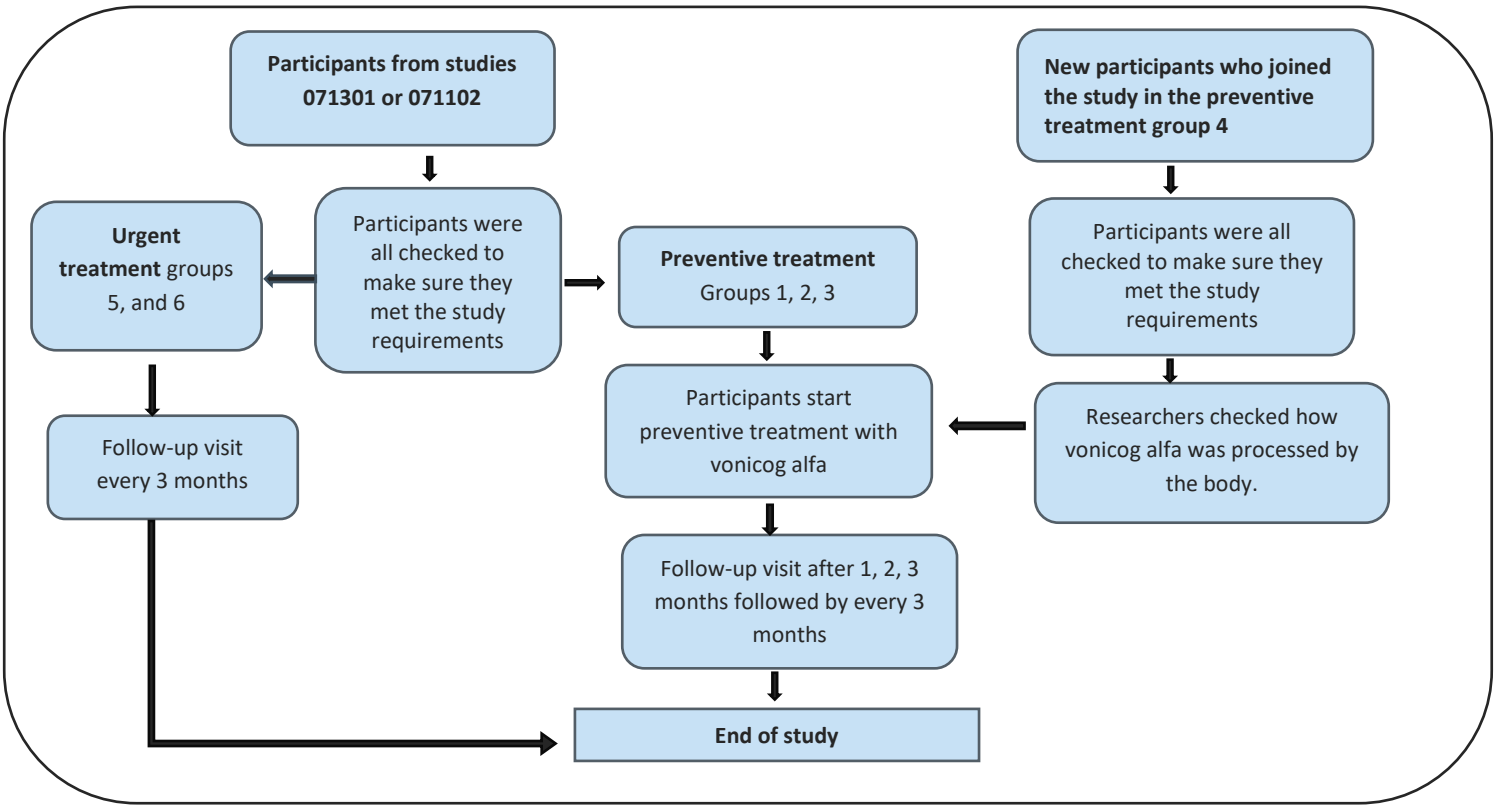
The study included 4 preventive and 2 urgent treatment groups, which included both adults and children. The participants in each group were as follows:

Preventive Treatment Groups:

- **Group 1**: Adults from the study 071301 who continued the treatment without any change in the dose.
- **Group 2**: Adults from the study 071301 who started this study with a smaller dose, because they did not have any severe bleeding events in the past 6 months.
- **Group 3**: Children from the study 071102 who switched from urgent to preventive treatment of vonicog alfa once or twice weekly.
- **Group 4**: New participants, both adults and children switching treatment from urgent treatment with any other VWF medicine to preventive treatment with vonicog alfa once every week.

Urgent Treatment Groups:

- **Group 5**: Children from the study 071102 who continued receiving urgent treatment
- **Group 6**: Adults from the study 071301 who switched back from preventive treatment in the previous study to urgent treatment in this study.



Who took part in the study?

Potential participants could take part if:

- They had completed previous studies 071301 or 071102 or
- They were new participants who had VWD, were at least 12 years old and had been receiving urgent treatment with a VWF medicine for at least a year.

Potential participants could not take part if:

- They had a blood clotting disorder other than VWD.
- They had a known allergy to vonicog alfa.

Out of 38 participants who joined the study, 35 were treated.

They were from 2 to 77 years old when they joined the study.

How many participants took part?	
38 participants joined the study 35 participants were treated	
Which treatment group were the participants in?	
17 participants were in the preventive treatment group All participants were treated	18 participants were in the urgent treatment group All participants were treated
10 men 7 women	8 men 10 women
12 to 77 years old	2 to 26 years old

Where was the study done?

This study took place in 23 study clinics in 8 countries worldwide.

When was the study done?

The study started in April 2019 and ended in January 2025. The study duration was 5 years and 9 months.

What were the study results?

This summary gives the main results of this single study. Other studies may give different results. Researchers look at the results of many studies to decide which medicines work best and are safest for patients. Always speak with your doctor before changing your treatment.

Researchers wanted to check how well vonicog alfa worked in controlling sudden bleeding events in participants with VWD. To do this, they answered the following question:

How often did participants have sudden bleeding events during the treatment?

Researchers recorded the annualized bleeding rate in participants to check if preventive treatment with vonicog alfa helped control the number of bleeding events in a year. Overall, the results showed that on average, the sudden ABR was 1.791. This meant that every participant had around 2 sudden bleeding events per year during the first 12 months of preventive treatment with vonicog alfa.

Were there any side effects?

In a clinical study, the study doctors record all medical problems the participants have during the study. They do this whether or not they think these problems were caused by the study treatment. These medical problems are called **adverse events**. If the study doctors think some of these medical problems might be caused by the study treatment, they are called **side effects**.

3 out of 38 participants left the study before receiving any study treatment.

So, the side effects shown here are from a total of 35 participants who received study treatment.

Possible side effects in this study may be different to the side effects shown on package leaflets of approved medicines. This summary shows the side effects as the medical problems that happened **during this study** that the doctors thought might be caused by the study treatment. Other studies of the same treatment may report different side effects. It takes the results of many studies to understand if medical problems may be caused by a treatment.

How many participants had side effects?

During this study, none of the participants had side effects.

None of the participants stopped study treatment early due to side effects.

How many participants had serious side effects?

Some side effects are called serious if they cause death, threaten life, cause ongoing health problems, or need a hospital stay or a longer stay in hospital.

None of the participants had any serious side effects in this study.

How has this study helped?

This study has helped researchers learn how well vonicog alfa worked to control the number of bleeding events in both adults and children during the first year of treatment. Overall, the study results showed that preventive treatment with vonicog alfa had meaningful benefits, and the number of bleeding events remained low in participants.

The results from several studies are needed to decide which treatments work best and are safest. This summary only shows the main results from this 1 study. Other studies may provide new information or give different results.

Further studies with vonicog alfa are ongoing.

More information about this study

The number of participants who took part in each country and region is shown here. This is out of a total of 35 participants who were treated in the study.

Country	Number of participants
Austria	1
France	3
Italy	3
Netherlands	1
Russia	2
Spain	3
Turkey	11
United States	11

Where can I learn more about this study?

Title of this study:	A Phase 3b, Prospective, Open-Label, Uncontrolled, Multicenter Study on Long-Term Safety and Efficacy of rVWF in Pediatric and Adult Subjects With Severe von Willebrand Disease (VWD)
Study number:	SHP677-304
Europe study number:	2018-003453-16
United States study number:	NCT03879135

More information about the study results is available here:

United States	www.clinicaltrials.gov Search this website using the study number NCT03879135
Europe	https://www.clinicaltrialsregister.eu/ctr-search/search Search this website using the study number 2018-003453-16
Takeda website	https://www.clinicaltrials.takeda.com/ Use the detailed search using the Study Identifier SHP677-304

Takeda and Baxalta, now a part of Takeda, sponsored this study.

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