Clinical Study Results

This summary reports the results of only one study. Researchers must look at the results of many types of studies to understand if a study medication works, how it works, and if it is safe to prescribe to patients. The results of this study might be different than the results of other studies that the researchers review.

Sponsor: Pfizer Inc.

Medicine(s) Studied: Somatropin (PNU-180307)

Protocol Number: A6281323

Dates of Study: 09 February 2021 to 06 December 2022

Title of this Study: Use of Somatropin in Japanese Patients with Prader-Willi Syndrome (PWS)
[A Phase 3 Multicenter, Open Label, Multi Cohort Study to Evaluate the Efficacy and Safety of Somatropin in Japanese Participants With Prader-Willi Syndrome (PWS).]

Date(s) of this Report: 08 November 2023

– Thank You –

If you or your child participated in this study, Pfizer, the Sponsor, would like to thank you for your participation.

This summary will describe the study results. If you have any questions about the study or the results, please contact the doctor or staff at your study site.

Why was this study done?

What is Prader-Willi Syndrome (PWS)?

Prader-Willi (PRAH-dur VIL-e) syndrome is a rare genetic disorder. It is sometimes called PWS. A person with PWS may have different physical and mental problems. Often, they will be constantly hungry or never feel full after eating a meal. This can mean that they are overweight, which can cause other health problems like diabetes.

What is somatropin?

Growth hormone (GH) replacement therapy is often used to treat people with PWS. Somatropin is a type of GH replacement therapy. Somatropin (so-ma-tro-pin) is given every day or 6 times weekly by an injection under the skin.

In Japan it is prescribed to children with PWS who are shorter than normal for their age. It is not licensed for use in other people with PWS in Japan, for example, in children to improve their body composition or for adults.

What was the purpose of this study?

The purpose of this study was to learn about the effect of somatropin on the lean body mass of participants. Lean body mass is the weight of everything in a person's body apart from fat. This includes bone, muscle, all organs (e.g., heart, kidneys, lungs, liver, brain etc), blood and skin.

Researchers wanted to know:

- **How did the lean body mass of participants change after 12 months of somatropin treatment?**

What happened during the study?

How was the study done?

Researchers tested somatropin on study participants to find out how the participants' lean body mass changed with treatment. There were 3 different groups of participants treated in this study.

These groups were:

- Participants under 18 years of age who had not previously been treated with GH.
- Participants under 18 years of age who had previously been treated with GH.
- Participants 18 years of age or older who had not been treated with GH in the previous 12 months (in this document, participants in this group are referred to as adult participants).

Somatropin was given by a subcutaneous injection every day or 6 times weekly. Subcutaneous means the injection is given just under the skin. All participants were given somatropin. The dose or amount of somatropin given to each participant was different. This was because the dose depended on the weight of the participant, their age, or if they had previously been given GH. The dose could also be adjusted by the doctor based on the results of a blood test.

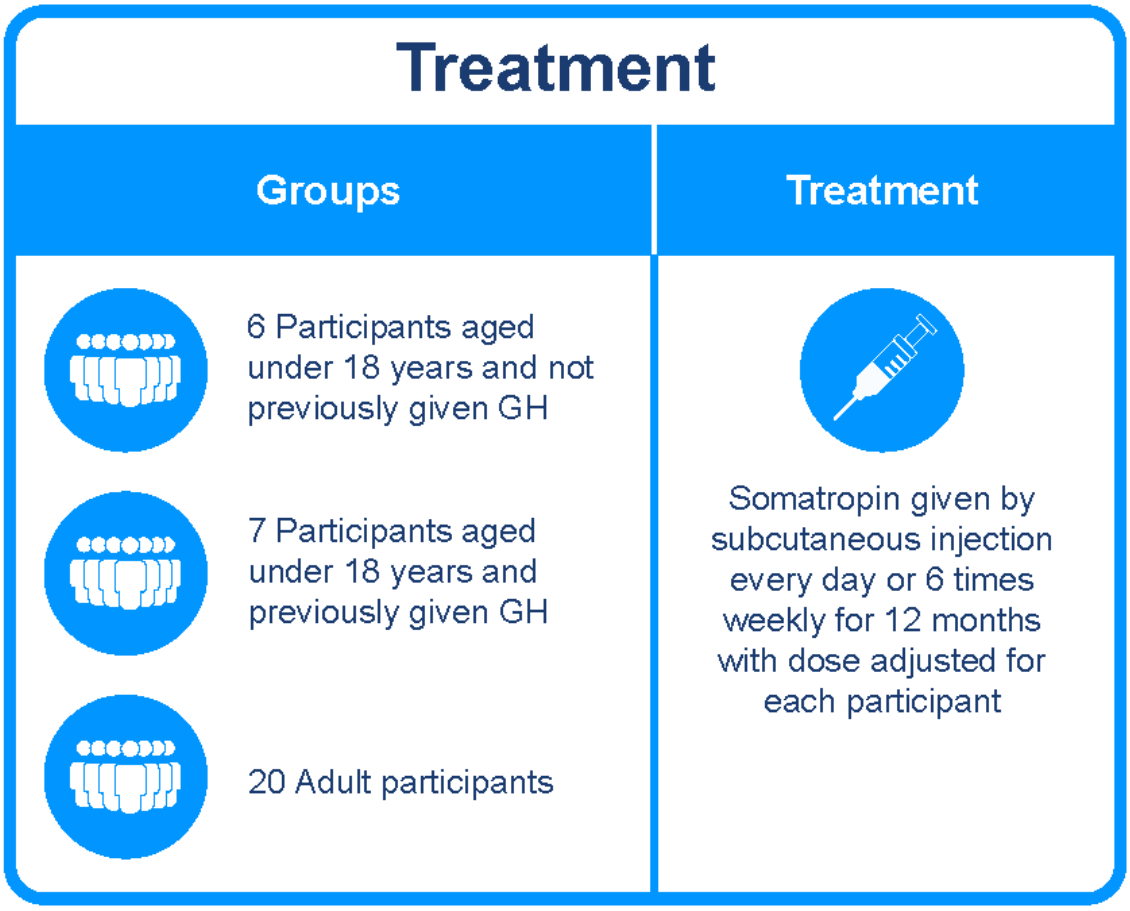
This was an open label study. Open label means that everyone knew what treatment the study participants were given.

Participants were treated in this study for up to 12 months. At the end of the study, participants could continue somatropin treatment in an extension

study. This extension study was for a further 36 months (3 years) or until somatropin was licensed in Japan.

The design of the study is shown in Figure 1.

Figure 1. What happened during the study?



Note: The adult participants were 18 years or older and had not been treated with GH in the previous 12 months.

At the end of the 12 month study, participants could continue somatropin in an extension study. This was for a further 36 months (3 years) or until somatropin was licensed in Japan.

Where did this study take place?

The Sponsor ran this study at 5 locations in Japan.

When did this study take place?

The main part of the study began 09 February 2021 and ended on 06 December 2022. The extension part of the study is ongoing.

Who participated in this study?

The study included participants with PWS who had either not previously been treated with GH or who had been previously treated with GH. Participants 18 years or older were not to have been treated with GH during the previous 12 months.

- A total of 7 men and 8 boys participated.
- A total of 13 women and 5 girls participated.
- All participants were between the ages of 4 and 26.5 years.

Participants were to be treated for 12 months in this study. Of the 33 participants who started the study, all finished 12 months of treatment. All 33 participants continued somatropin in the extension study.

How long did the study last?

Study participants were in the main study for up to 13 months. The extension study is ongoing.

When the main study ended in December 2022, the Sponsor began reviewing the information collected. The Sponsor then created a report of the results from the main study. This is a summary of that report.

What were the results of the study?

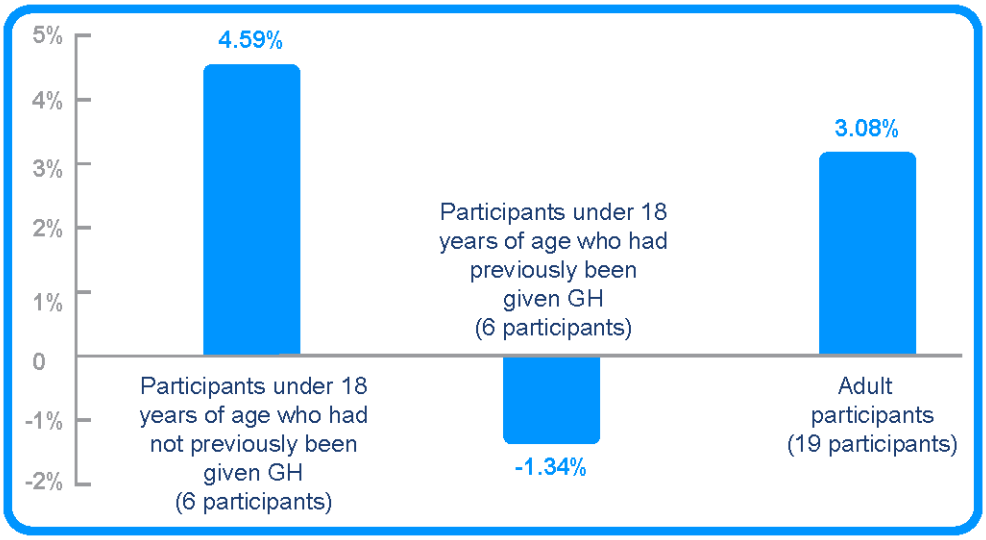
How did the lean body mass of participants in Japan change after 12 months of somatropin treatment?

The researchers measured each participant's lean body mass at the start of the study, during the study, and at the end of the study. They did this using special scales that estimated the amount of fat in a person's body using an imaging technique called dual-energy x-ray absorptiometry (DEXA). The researchers then calculated how the lean body mass of participants had changed after 12 months of treatment with somatropin.

Did the somatropin increase lean body mass after 12 months of treatment?

The difference in average lean body mass after 12 months of treatment with somatropin compared to the start of the study is shown in Figure 2. This difference is often described as the change from baseline.

Figure 2. Change from baseline in average lean body mass in participants after 12 months of treatment



Note: The adult participants were 18 years or older and had not been treated with GH in the previous 12 months.

There was an increase in lean body mass of 3.08% in adult participants after 12 months of treatment compared to the start of the study. For participants under 18 years who had not been treated with GH, this increase was 4.59%. For participants under 18 years who had been previously treated with GH, there was a slight decrease of 1.34%. The researchers were not concerned by this decrease and thought that body weight had remained clinically stable in this group.

This does not mean that everyone in this study had these results. This is a summary of just some of the main results of this study. Other studies may have different results.

What medical problems did participants have during the study?

The researchers recorded any medical problems the participants had during the study. Participants could have had medical problems for reasons not related to the study (for example, caused by an underlying disease or by chance). Or, medical problems could also have been caused by a study treatment or by another medicine the participant was taking. Sometimes the cause of a medical problem is unknown. By comparing medical problems across many treatment groups in many studies, doctors try to understand what effects a study medication might have on a participant.

There were 29 out of 33 (87.8%) participants in this study who had at least 1 medical problem. Most of the medical problems were mild or moderate in severity. The most common medical problems – those reported by more than 1 participant in any group – are described below.

Below are instructions on how to read Table 1.

Instructions for Understanding Table 1.

- The **1st** column of Table 1 lists medical problems that were commonly reported during the study. All medical problems reported by more than 1 participant in any group are listed.
- The **2nd** column tells how many of the 6 participants under 18 years who had not previously been treated with GH reported each medical problem. Next to this number is the percentage who reported the medical problem.
- The **3rd** column tells how many of the 7 participants under 18 years who had been previously treated with GH reported each medical problem. Next to this number is the percentage who reported the medical problem.
- The **4th** column tells how many of the 20 adult participants reported each medical problem. Next to this number is the percentage who reported the medical problem.
- Using these instructions, you can see that 1 out of the 6 (16.7%) participants under 18 years who had not previously been treated with GH had a fall. There was 1 out of the 7 (14.3%) participants under 18 years who had been previously treated with GH who reported a fall. A total of 3 out of the 20 (15.0%) adult participants had a fall.

Table 1. Commonly reported medical problems by study participants

Medical Problem	Participants under 18 years who had not previously been treated with GH (6 Participants)	Participants under 18 years who had been previously treated with GH (7 Participants)	Adult participants (20 Participants)
Fall	1 out of 6 participants (16.7%)	1 out of 7 participants (14.3%)	3 out of 20 participants (15.0%)
Bruise or bruising of the skin	1 out of 6 participants (16.7%)	1 out of 7 participants (14.3%)	2 out of 20 participants (10.0%)
Increased blood sugar (as estimated from glycosylated hemoglobin levels in blood)	1 out of 6 participants (16.7%)	0	3 out of 20 participants (15.0%)
Insulin-like growth factor increased in blood	1 out of 6 participants (16.7%)	0	2 out of 20 participants (10.0%)

Table 1. Commonly reported medical problems by study participants			
Medical Problem	**Participants under 18 years who had not previously been treated with GH (6 Participants)**	**Participants under 18 years who had been previously treated with GH (7 Participants)**	**Adult participants (20 Participants)**
Fever (high temperature)	0	1 out of 7 participants (14.3%)	3 out of 20 participants (15.0%)
Constipation	0	0	3 out of 20 participants (15.0%)
Nose, sinus, and throat infection	1 out of 6 participants (16.7%)	0	2 out of 20 participants (10.0%)
Common cold	1 out of 6 participants (16.7%)	1 out of 7 participants (14.3%)	0
Bite from an insect, spider or bug	0	1 out of 7 participants (14.3%)	1 out of 20 participants (5.0%)

Table 1. Commonly reported medical problems by study participants			
Medical Problem	**Participants under 18 years who had not previously been treated with GH (6 Participants)**	**Participants under 18 years who had been previously treated with GH (7 Participants)**	**Adult participants (20 Participants)**
Scratch on the skin	0	1 out of 7 participants (14.3%)	1 out of 20 participants (5.0%)
Increased blood triglycerides	1 out of 6 participants (16.7%)	0	1 out of 20 participants (5.0%)
Joint pain	0	0	2 out of 20 participants (10.0%)
Headache	2 out of 6 participants (33.3%)	0	0
Acne	0	0	2 out of 20 participants (10.0%)

Table 1. Commonly reported medical problems by study participants			
Medical Problem	**Participants under 18 years who had not previously been treated with GH (6 Participants)**	**Participants under 18 years who had been previously treated with GH (7 Participants)**	**Adult participants (20 Participants)**
Bleeding under the skin	2 out of 6 participants (33.3%)	0	0
High blood pressure	0	0	2 out of 20 participants (10.0%)

Note: The adult participants were 18 years or older and had not been treated with GH in the previous 12 months.

There were no participants who left the study permanently because of medical problems, but 1 adult participant (5.0%) permanently stopped somatropin because of a medical problem (sleep apnea). Sleep apnea is when the person experiences frequent interruptions of their breathing during sleep. The researchers did not think that the sleep apnea was related to somatropin.

The dose of the somatropin treatment was reduced or temporarily stopped because of medical problems in 10 out of the 33 (30.3%) participants overall including:

- Two (2) out of 6 (33.3%) participants under 18 years who had not previously been treated with GH.
- One (1) out of 7 (14.3%) participants under 18 years who had been previously treated with GH.
- Seven (7) out of 20 (35.0%) adult participants.

Did study participants have any serious medical problems?

A medical problem is considered “serious” when it is life-threatening, needs hospital care, or causes lasting problems.

There were 3 participants (9.1%, or 3 out of 33 participants) who had serious medical problems.

- 1 participant under 18 years who had been previously treated with GH had an ankle fracture.
- 1 adult participant had a fractured skull and bruising of the brain.
- 1 adult participant had high blood pressure.

None of the serious medical problems were thought related to somatropin.

No participants died during the study.

Where can I learn more about this study?

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

For more details on your study protocol, please visit:

www.pfizer.com/research/research_clinical_trials/trial_results	Use the protocol number A6281323

The full scientific report of this study is available online at:

www.clinicaltrials.gov	Use the study identifier NCT04697381

Please remember that researchers look at the results of many studies to find out which medicines can work and are safe for patients.

Again, if you or your child participated in this study, **thank you** for volunteering. We do research to try to find the best ways to help patients, and you helped us to do that!