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 Studied:	Recifercept (PF-07256472)
Protocol Number:	C4181005
Dates of Study:	02 December 2020 to 27 March 2023
Title of this Study:	A Study to Learn About the Safety of Recifercept and How Well it Works in Children With Achondroplasia [A Phase 2 Multiple Dose, Randomized Study to Assess the Safety, Tolerability, Pharmacokinetics and Efficacy of Recifercept in Children With Achondroplasia]
Date of this Report:	30 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 or your child 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 achondroplasia?

Achondroplasia is a rare genetic disorder that causes problems with how children's bones and joints grow.

People with achondroplasia can have short arms and legs and other bone complications. Achondroplasia is the most common type of bone disorder seen in children.

What is recifercept?

Recifercept is an injectable medicine that was tested in this study for the treatment of achondroplasia. The use of recifercept in this study is investigational, which means it is not approved for the treatment of achondroplasia.

Recifercept is designed to help boost growth in children with achondroplasia.

What was the purpose of this study?

The purpose of this study was to learn if recifercept was safe and if it can help increase growth in children aged 3 months to less than 11 years old with achondroplasia.

Researchers wanted to know:

- **Did recifercept increase growth in participants?**
- **What medical problems did participants have during the study?**

What happened during the study?

How was the study done?

Researchers tested 3 dose levels of recifercept on a group of participants aged 3 months to less than 11 years old.

In this study, participants were split into 2 age groups:

- 3 months to 2 years old
- 2 years to less than 11 years old

Participants were assigned to receive 1 of the 3 doses by chance:

- Low dose: 1 mg/kg once a week
- Medium dose: 2 mg/kg two times a week
- High dose: 1.5 mg/kg once in a day

This was an open-label study. This means that the children or their parents/caregivers and the researchers knew the treatment being given.

Children in this study received at least 1 dose of recifercept as a subcutaneous (SC) injection given under the skin for 12 months. The dose of recifercept given was based on the child's weight.

Participants in the older age groups started with a low dose. If that dose did not cause medical problems, then younger age groups received higher dose until there were any medical problems.

Figure 1 below shows what happened during the study.

Screening	Treatment	Follow-up
 Children with achondroplasia aged 3 months to below 11 years old entered into the study. They were split into 2 age groups: • 3 months to 2 years old • 2 years to less than 11 years old	 Participants were assigned by chance to receive 1 of the 3 doses: • **Low dose:** 1 mg/kg once a week • **Medium dose:** 2 mg/kg 2 times a week • **High dose:** 1.5 mg/kg once in a day  Participants in the older age groups started with a low dose. If that dose did not cause medical problems, then younger age groups received higher dose until there were any medical problems.	 **28 to 35 days after the last dose** Study doctors or team called the participants' parents/caregivers to ask how the participants were feeling and medications they were taking.

Throughout the study, study doctors monitored the safety of participants.

Where did this study take place?

The study took place at 11 locations in 8 countries.

When did this study take place?

The study started on 02 December 2020 and ended on 27 March 2023.

Who participated in this study?

The study included children from 3 months to less than 11 years old with achondroplasia.

Overall, 58 participants started the study and 57 received at least 1 dose of recifercept during the treatment period. Of the 57 children:

- 33 were boys and 24 were girls.
- All were between the ages of 1 year and 10 years.

In total, 36 completed the treatment period. A total of 21 participants did not finish the treatment period.

- 1 participant left before the study was over by their parents'/caregivers' choice
- 20 participants did not finish the study as the Sponsor decided to stop the study.

How long did the study last?

Study participants were in the study for about 12 months. The entire study took about 27 months to complete.

The Sponsor decided to end the study earlier than planned in November 2022. This was because the results did not show the desired increase in growth compared to the those seen in children who had not received any treatment for achondroplasia from another study. The study did not end early due to any safety concerns with recifercept.

When the study ended in March 2023, the Sponsor began reviewing the information collected. The Sponsor then created a report of the results. This is a summary of that report.

What were the results of the study?

Did recifercept increase growth in participants?

Researchers measured how the children's height changed before and after receiving recifercept. This change in height is called growth. Researchers compared the change in height to children who had not received any treatment for achondroplasia from another study.

The study results did not show that the increase in growth in participants after receiving any of the recifercept doses (low dose, medium dose, and

high dose) was greater than the expected growth in children who had not received any treatment for achondroplasia from another study.

This does not mean that everyone in this study had these results but reflects average response. 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.

Of the 57 participants, 52 participants (91%) in this study had at least 1 medical problem.

- 17 out of 20 participants (85%) in the low dose recifercept group
- All 19 participants (100%) in the medium dose recifercept group
- 16 out of 18 participants (89%) in the high dose recifercept group

Injection site reactions were the most common medical problems of special interest. They were mild in severity.

No participant left the study because of a medical problem they had during the study.

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 3 or more participants in any group are listed.
- The **2nd** column tells how many of the 20 participants who were given the low dose of recifercept reported each medical problem. Next to this number is the percentage of the 20 participants who had the medical problem.
- The **3rd** column tells how many of the 19 participants who were given the medium dose of recifercept reported each medical problem. Next to this number is the percentage of the 19 participants who had the medical problem.
- The **4th** column tells how many of the 18 participants who were given the high dose of recifercept reported each medical problem. Next to this number is the percentage of the 18 participants who had the medical problem.
- Using these instructions, you can see that,
  - 3 out of the 20 participants (15%) taking the low dose recifercept reported having COVID-19.
  - 7 out of the 19 participants (37%) taking the medium dose recifercept reported having COVID-19.

- 4 out of the 18 participants (22%) taking the high dose recifercept reported having COVID-19.

The most common medical problems – those seen in 3 or more participants in any group – are described in Table 1 below.

Table 1. Commonly reported medical problems (reported by 3 or more participants in any group)

Medical Problem	Recifercept 1 mg/kg (20 Participants)	Recifercept 2 mg/kg (19 Participants)	Recifercept 1.5 mg/kg (18 Participants)
Joint pain	3 out of 20 participants (15%)	1 out of 19 participants (5%)	1 out of 18 participants (6%)
High phosphorus in blood	0 out of 20 participants (0%)	3 out of 19 participants (16%)	1 out of 18 participants (6%)
Cough	2 out of 20 participants (10%)	3 out of 19 participants (16%)	1 out of 18 participants (6%)
Ear infection	3 out of 20 participants (15%)	2 out of 19 participants (11%)	1 out of 18 participants (6%)
Ear pain	1 out of 20 participants (5%)	2 out of 19 participants (11%)	3 out of 18 participants (17%)
Collection of blood outside of blood vessels”	1 out of 20 participants (5%)	3 out of 19 participants (16%)	0 out of 18 participants (0%)

Table 1. Commonly reported medical problems (reported by 3 or more participants in any group)

Medical Problem	Recifercept 1 mg/kg (20 Participants)	Recifercept 2 mg/kg (19 Participants)	Recifercept 1.5 mg/kg (18 Participants)
Redness at injection site	4 out of 20 participants (20%)	5 out of 19 participants (26%)	4 out of 18 participants (22%)
Itching at injection site	3 out of 20 participants (15%)	3 out of 19 participants (16%)	2 out of 18 participants (11%)
Rash at injection site	4 out of 20 participants (20%)	4 out of 19 participants (21%)	2 out of 18 participants (11%)
Injection site reaction	0 out of 20 participants (0%)	3 out of 19 participants (16%)	1 out of 18 participants (6%)
Infection of nose and throat	5 out of 20 participants (25%)	5 out of 19 participants (26%)	2 out of 18 participants (11%)
Infection in middle ear	3 out of 20 participants (15%)	1 out of 19 participants (5%)	1 out of 18 participants (6%)
Pain in limbs or arms and legs	1 out of 20 participants (5%)	3 out of 19 participants (16%)	1 out of 18 participants (6%)
Fever	1 out of 20 participants (5%)	3 out of 19 participants (16%)	4 out of 18 participants (22%)
COVID-19	3 out of 20 participants (15%)	7 out of 19 participants (37%)	4 out of 18 participants (22%)

Table 1. Commonly reported medical problems (reported by 3 or more participants in any group)			
Medical Problem	**Recifercept 1 mg/kg (20 Participants)**	**Recifercept 2 mg/kg (19 Participants)**	**Recifercept 1.5 mg/kg (18 Participants)**
Irritation and swelling of the upper airways	3 out of 20 participants (15%)	3 out of 19 participants (16%)	1 out of 18 participants (6%)
Vomiting	3 out of 20 participants (15%)	2 out of 19 participants (11%)	1 out of 18 participants (6%)

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.

Out of 57 participants, 1 participant (5%) who received recifercept 1 mg/kg had a serious medical problem. This participant had a slow heartbeat which resolved while continuing recifercept. Researchers did not believe that this serious medical problem was related to the study medication.

No participant died during the study.

Where can I learn more about this study?

If you or your child 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 **C14181005**

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

www.clinicaltrials.gov	Use the study identifier **NCT04638153**
www.clinicaltrialsregister.eu	Use the study identifier **2020-001189-13**

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 and 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!