Clinical Trial Summary

A clinical study of SHP674 (Pegaspargase) in participants with newly diagnosed, untreated acute lymphoblastic leukaemia.

Full scientific title: A Phase 2 Clinical Study of SHP674 in patients with newly diagnosed, untreated acute lymphoblastic leukaemia.

We thank all the participants who took part in the study. Clinical study participants are very important for making progress in science, for the benefit of patients.
This document is a summary of the study. It is written for a general audience.

Researchers need many studies to decide which medicines work the best and are the safest for patients. For medical science to progress, many studies involving patients are running all around the world. This summary only shows the results from this one study. Other studies, evaluating the same drug, may find different results. You should not change your current treatment based on the results of this single study. If you have any questions about this study, please talk to your doctor.

Therapeutic area:
Oncology

Disease:
Acute lymphoblastic leukemia

Study phase:
CL1-95014-001

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Final version

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1 Why was this study done?

This study was done to support the approval of pegaspargase in Japan for paediatric population with acute lymphoblastic leukaemia (ALL). Pegaspargase has been already approved in many countries for ALL.

Leukemia is a cancer of the blood. When these cancers occur, abnormal white blood cells increase rapidly and uncontrollably. ALL is the most commonly diagnosed cancer in children. This type of leukemia is defined by the origin of the immature blood cells that are involved.

The study drug is an asparaginase called pegaspargase. Asparaginases breakdown a substance in the blood called asparagine. The cancer cells in ALL need asparagine to survive. An asparaginase is already in used in Japan for ALL. Pegaspargase has been modified to reduce the risk of allergy and to improve the ability to stay in the body. Thanks to that, fewer doses of pegaspargase are needed.

This study was a phase II study and combined 2 parts: part 1 and part 2.
The main aims were:

- For the part 1, to test the safety of one dose of pegaspargase in Japanese children and adolescents.
- For the part 2, to check the activity of the drug by measuring the “plasma asparaginase activity” in blood, 14 days after the first injection.

2 When and where did this study take place?

When did the study take place?

- This study started in October 2019.
- It ended in February 2022.

Where did the study take place?

The study took place in Japan.

3 Who participated in the study?

Which participants were included in the study?

To take part, participants had to:

- Be between 1 to 21 years old.
- Have good physical condition.
- Be newly diagnosed for ALL.
- Never be treated with anticancer drugs.

How many participants took part in the study?

28 children and adolescents took part in the study. 26 participants received the treatment (13 girls and 13 boys).

- 3 participants in Part 1 of the study.
- 23 participants in Part 2 of the study.

How old were the participants?

The average age of the participants was 5 years. The youngest participant was 1 year old and the oldest was 17 years old.

4 Which treatments did the participants receive?

The current name of the study drug in Japan is pegaspargase (product code SHP674 or S95014).

Each patient received the same treatment pegaspargase in solution by injection into a vein.

The dose of pegaspargase was determined according to the body surface area (BSA). The BSA is calculated using the participant’s height and weight:
- in case of BSA more than 0.6 square meter (m^2), the dose was of 2500 international units per m^2 of BSA.
- in case of BSA less than 0.6 m^2, the dose was 82.5 IU per kg.

In addition, all participants received other drugs routinely used to treat this cancer.

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5 How was the study carried out?

The study is called an "open-label" study. This means that both the participants and the research doctors knew which treatment was taken.
This is a "single arm" study. This means that all participants received the same treatment.

This study consisted of Part 1 and Part 2.
In Part 1, pegaspargase was administered to confirm if it can be administered safely in children and adolescents
In Part 2, patients received pegaspargase at the dose confirmed to be safe in Part 1. This part was done to check the activity of the drug.

Patients were divided into 3 groups (standard risk, medium risk, and high risk) according to medical criteria.

All patients took pegaspargase. The number of injections and the duration of treatment with pegaspargase was planned according to the risk group:
- For standard and medium risk groups: the patient had 3 infusions of pegaspargase over 10 months.
- For high-risk group: the patients had 8 infusions of pegaspargase over 11 months.

6 What were the side effects?

Side effects are unwanted medical events that the doctors think may be caused by the treatments in the study.

In this summary, we describe unwanted medical events thought to be caused by pegaspargase.
The results may be presented differently in other documents related to the study.

The table below shows the number of participants who had side effects in parts 1 and 2.

	Total (out of 26 participants)
Participants who had side effect(s)	26 (100 %)
Participants who had serious* side effect(s)	2 (7.7 %)
Participants who stopped the treatment because of side effect(s)	3 (11.5 %)

**See definition of serious side effects below*

What were the type of side effects?

The table below shows the most common side effects reported in the study (reported by at least 30 % of participants in parts 1 and 2).

	Total (out of 26 participants)
Decrease of a protein called fibrinogen (needed for blood clotting)	19 (73.1%)
Decrease of a protein called Antithrombin III (needed to prevent blood clotting)	15 (57.7%)
Decrease in the number of white blood cells	15 (57.7%)
Decrease in the number of platelets, cells that help the blood to clot	14 (53.8 %)
Decrease in the number of red blood cells	11 (42.3 %)
Fever with lack of white blood cells called neutrophils	11 (42.3 %)
Hair loss	10 (38.5%)
Low blood protein levels	10 (38.5%)
Vomiting	10 (38.5%)
Feeling sick	8 (30.8%)
High blood levels of triglycerides, a type of fat	8 (30.8%)

= participants

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What were the serious side effects?

A side effect is considered serious when:

- the participant needs to be hospitalised,
- it causes lasting damage or death,
- the participant's life is in danger or,
- it is medically important in the doctor's opinion.

In part 1 of the study, no participant had serious side effects (serious unwanted medical events thought to be caused by pegaspargase in the study).
In part 2 of the study, 2 participants (7.7%) had serious side effects. The serious side effects reported were vomiting and sudden inflammation of the pancreas.

In the study, no participant died because of an unwanted event thought to be caused by pegaspargase.

7 What were the study results?

The study was completed as planned.

This document presents only the results for the main aims of the study. Other results are available in other documents listed in section 10.

In part 1, the main aim was to test the safety of one infusion of pegaspargase.
No patient had an severe toxicity. This means that pegaspargase could be administered safely in part 2.

In part 2, the main goal of the study was to check the activity of the drug by measuring "plasma asparaginase activity" in the blood.
All participants had a good level of "plasma asparaginase activity" 14 days after the first injection. This means that the leukaemia cells in the blood were less able to survive.

8 How has this study helped research?

Findings from the study will be used to obtain an approval for using the treatment for paediatric population in Japan with acute lymphoblastic leukaemia.

9 Are there plans for further studies?

Another clinical study with pegaspargase is on-going in Russia in children and adolescents.

10 Further information

What are the identification numbers of the study?

- Protocol code: SHP674-201/CL1-95014-001
- EudraCT number: 2022-002190-28
- US NCT number: NCT04067518

Who did the study?

The company that organised and funded the research, called the "sponsor", is the Institut de Recherches Internationales Servier based in Suresnes, France.

How can you contact the sponsor?

Contact us on the Servier website
https://servier.com/en/

Where can you learn more about this study?

You can find more information about this study on these websites:

- https://clinicaltrials.servier.com
- https://www.clinicaltrialsregister.eu
- https://www.clinicaltrials.gov

In this document we translated medical terms into lay terms. You can find the corresponding medical terms in the Servier glossary at
https://clinicaltrials.servier.com/glossary/

You can find general information about clinical trials on https://clinicaltrials.servier.com/