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Clinical Trial Summary

A study comparing the blood levels of both pegaspargase (S95014) formulations (liquid vs lyophilized) in the Treatment of Paediatric Patients with Acute Lymphoblastic Leukemia (ALL)

Full scientific title: A Multicenter, Phase II Randomized study, Open-label, with 2-arm Parallel Group, comparing the Pharmacokinetics of the Liquid and the Lyophilized Formulations of Pegaspargase (S95014) in Treatment of Paediatric Patients with Newly Diagnosed Acute Lymphoblastic Leukemia (ALL).

We thank all the participants and their families 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:
Phase 2

Version :
06/05/2023

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1 Why was this study done?

This study was done to compare 2 formulations of a drug called pegaspargase. One formulation was freeze-dried (or lyophilized, called here: LYO) and the other was a liquid formulation (called here: LIQ). This drug is approved in many countries for the treatment of Acute Lymphoblastic Leukemia (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 kind of leukemia is defined by the type of the immature blood cells that are involved.

The study drug is an "asparaginase" and is called pegaspargase. Asparaginases breakdown a substance in the blood called asparagine (one of the building blocks for proteins). The cancer cells in ALL need asparagine to survive. Pegaspargase has been modified to reduce the risk of allergy and to improve the ability to stay in the body.

This study was a phase 2 study.
The main aim was to compare the activity of the 2 formulations of pegaspargase by measuring the blood "plasma asparaginase activity".

2 When and where did this study take place?

When did the study take place?

- This study started in May 2021.
- It ended in May 2022.

Where did the study take place?

The study took place in Russia.

3 Who participated in the study?

Which participants were included in the study?

To take part, participants had to:

- Be diagnosed for the first time for ALL.
- Be between 1 and 18 years old.
- Be in good physical condition.

How many participants took part in the study?

89 children and adolescents took part in the study (42 girls and 47 boys).

How old were the participants?*

The average age of the participants was 6 years. The youngest participant was 1 year old and the oldest was 17 years old.
* who received the treatment

4 Which treatments did the participants receive?

Each participant received a single dose of pegaspargase (one of the 2 formulations; both have the product code S95014) by infusion into a vein. The infusion lasted about 1 hour.
The dose of pegaspargase was determined according to the body surface area (BSA). The BSA is calculated using the participant's height and weight. The dose was 2500 units per square meter of BSA.

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

5 How was the study carried out?

This kind of study is called a "randomized" study. This means that the participants were put by chance into one of 2 treatment groups: either the LYO group or the LIQ group.
There were 89 participants included in the study:

- 43 participants received the freeze-dried (LYO) formulation.
- 45 participants received the liquid (LIQ) formulation.
- 1 participant stopped the study before receiving the treatment.

The study is called an "open-label" study. This means that both the participants and the research doctors knew which treatment was taken by each participant.

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Patients with ALL are treated during 3 time-periods. This study, only focused on the first period of treatment. This period lasted 30 days. After that, eligible participants could join another study (CL2-95014-003) offering further treatment period with pegaspargase.

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.

	LYO group (out of 43 participants)	LIQ group (out of 45 participants)
Participants who had side effect(s)	38 (88%)	41 (91%)
Participants who had serious* side effect(s)	8 (19%)	4 (9%)
Participants who stopped the treatment because of side effect(s)	0 (0%)	0 (0%)

**See definition of serious side effects below*

What were the types of side effects?

The table below shows the most common side effects reported in the study (reported by at least 20% of participants in either group).

	LYO group (out of 43 participants)	LIQ group (out of 45 participants)
Decrease of a protein called fibrinogen (needed for blood clotting)	31 (72%)	31 (69%)
Decrease of a protein called Antithrombin III (needed to prevent blood clotting)	31 (72%)	28 (62%)
Decrease in of the number of white blood cells called lymphocytes	25 (58%)	18 (40%)
Decrease in the number of white blood cells	15 (35%)	13 (29%)
Lack of white blood cells	11 (26%)	5 (11%)
Increase in blood levels of bilirubin, indicating liver problems	11 (26%)	5 (11%)
Decrease in blood protein called protein S (needed to prevent blood clotting)	9 (21%)	6 (13%)
Lack of platelets, (needed for blood clotting)	5 (12%)	10 (22%)

= participants

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.

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The table below shows the most frequent serious side effects thought to be caused by pegaspargase that were reported in the study (reported in at least 2 participants in either group).

	LYO group (out of 43)	LIQ group (out of 45)
Decrease in the number of white blood cells	3 (7%)	1 (2%)
Decrease of a protein called Antithrombin III (needed to prevent blood clotting)	2 (5%)	1 (2%)
Decrease of a protein called fibrinogen (needed for blood clotting)	2 (5%)	1 (2%)
Type of sudden inflammation of the pancreas	2 (5%)	0 (0%)

No participant died during the study because of a side effect 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 aim of the study. Other results are available in other documents listed in section 10.

The main aim of the study was to compare the activity of the 2 formulations of pegaspargase. This was done by measuring "plasma asparaginase activity". The results showed that the activity (using several indicators) was the same with both formulations, LYO and LIQ.

8 How has this study helped research?

This study found that the 2 formulations of asparaginase (LYO and LIQ) have the same activity.

This is important because the LYO formulation has a much longer shelf-life. This means that it can be stored by hospitals for longer time

9 Are there plans for further studies?

No other studies with pegaspargase are planned so far. The previously mentioned study, CL2-95014-003, that enrolled participants from the current study has now finished. A separate report of this study will appear.

10 Further information

What are the identification numbers of the study?

- Protocol code: CL2-95014-002
- EudraCT number: 2020-004894-29
- US NCT number: 04954326

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/