Clinical trial SUMMARY

Short study title

A study to evaluate the safety and efficacy of UCART19 in children with B cell lymphoblastic leukaemia that has relapsed or not responded to other treatments.

Full scientific title:

A phase 1, open label, non-comparative study to evaluate the safety and the ability of UCART19 to induce molecular remission in paediatric patients with relapsed /refractory B-cell acute lymphoblastic leukaemia.

Therapeutic area:
Oncology

Indication:
Paediatric acute lymphoblastic leukaemia

Study phase:
Phase 1

09 September 2021
Final version

In this summary:

CLINICAL TRIAL SUMMARY

A study to evaluate the safety and efficacy of UCART19 in children with B cell lymphoblastic leukaemia that has relapsed or not responded to other treatments.

We would like to thank all the patients who participated in the study. As clinical study participants, they help researchers to discover new medicines for the benefit of all 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 the patients. For medical science to progress, a lot of people in many studies are involved 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.

1 Why was this study done?

This study was done to test a new anticancer drug in children or young people with leukaemia.
The current name of the study drug is UCART19, also called "S68587".
UCART19 is made of specially modified human cells, designed to kill leukaemia cells.
It is a "cell-based gene therapy".
This study was called a "first-in-human study". It means that it was the first time UCART19 was given to human beings.

The main objective of this study was to look at the safety of UCART19.

2 When and where did this study take place?

When was it performed?

- This study started in June 2016.
- It ended in November 2020.

Where did the study take place?

The study took place in the following countries:

Country	Number of patients
United Kingdom	6 patients
United States	5 patients
France	2 patients

3 Who participated in the study?

Which patients were included in the study?

Patients in the study had to meet notably the following criteria:

- Be under the age of 18.
- Be diagnosed with a kind of blood cancer called CD19 positive B-acute lymphoblastic leukaemia.
- Have leukaemia that came back after standard treatment, or
- Have leukaemia that did not respond to the standard treatment
- For whom no treatment could be further used.

How many patients participated in the study?

13 patients took part in the study: 7 boys and 6 girls.

How old were the patients?

The average age of the patients was 7 years. The youngest patient was 10 months old and the oldest patient was 17 years old.

4 Which treatments did patients receive?

All patients received the same study drug, called UCART19.

Each patient received a single dose of UCART19 by intravenous (into a vein) infusion. The dose was given to patient according to his weight.

CLINICAL TRIAL SUMMARY

A study to evaluate the safety and efficacy of UCART19 in children with B cell lymphoblastic leukaemia that has relapsed or not responded to other treatments.

In the week preceding UCART19 infusion, patients had a treatment called lymphodepletion (LD). LD treatment aimed to eliminate the white blood cells called "lymphocytes" and prepare the blood to receive UCART19.

5 How was the study done?

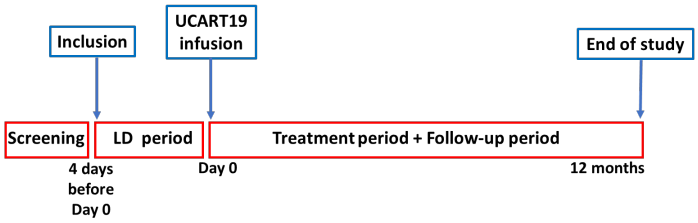
The study is called an "open-label" study. It means that patients and doctors knew which treatment was given to the patient.

Patients received UCART19 by infusion at hospital. They were then monitored at hospital for at least one month.

Patients then visited the doctors regularly. During these visits, the doctors collected information about the patients' health.

The mean duration of patient participation in the study was about 10 months.

Study design is presented in the picture below.



Once patients had completed the study, they were encouraged to be followed up for 15 years in a long-term follow-up study.

6 What were the side effects?

What about side effects?

Like all medicines, UCART19 can cause side effects although not everybody gets them.
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 related to:

- UCART19 alone or
- UCART19 + LD treatment.

The table below shows the number of patients who had side effects.

	Number of patients (out of 13 patients)
Patients who had side effect(s)	12 patients (92%)
Patients who had serious* side effect(s)	10 patients (77%)

**See definition below*

How many patients had serious side effects?

A side effect is considered "serious" when:

- The patient needs to be hospitalised.
- The patient's life is in danger.
- It causes permanent damage or death or,
- It may put the patient at risk and requires a medical intervention to prevent the situations listed above.

In this study, 10 patients out of 13 (77%) had serious side effects.
The serious side effects reported in at least 2 patients are described in the table below.

	Number of patients* (out of 13 patients)
Symptoms caused by the release of a large amount of chemicals from cells following the drug infusion (leading to fever, vomiting, shortness of breath, headache and/or low blood pressure etc.)	10 patients (77%)
Seeing, hearing or feeling things that are not there (hallucination)	2 patients (15%)

**One patient could have more than one serious side effects*

In the study, no patient died due to an unwanted event thought to be caused by UCART19.

CLINICAL TRIAL SUMMARY

A study to evaluate the safety and efficacy of UCART19 in children with B cell lymphoblastic leukaemia that has relapsed or not responded to other treatments.

What were the other side effects?

The table below shows the other side effects reported in the study. Only the most common (reported in at least 2 patients) are presented.

	Number of patients (out of 13 patients)
Low blood potassium level	3 patients (23%)
Increase in blood ferritin level, a protein that stores iron	3 patients (23%)
Confusion	2 patients (15%)
Headache	2 patients (15%)
Damages to the nervous system caused by toxic substances	2 patients (15%)

7 What were the study results?

The main objective of this study was to look at the safety of UCART19. Safety results are presented in section 6.

The company decided to stop the study. This was not due to safety reasons (see Section 9).

8 How has this study helped patients and researchers?

This study helped researchers in their understanding of UCART19 in leukaemia. By participating in this study, patients had close medical follow-up with experts in cancer.

9 Are there plans for further studies?

The company decided to stop the research on S68587 (a UCART19 Product) in this kind of cancer. Additional research with a similar drug is continuing for another kind of blood cancer called «non-Hodgkin lymphoma».

The company and its Partner are reviewing their development strategy for acute lymphoblastic leukaemia.

10 Further information

What is the identification number of the clinical study?

- Protocol Number: UCART19_02 (CL1-68587-001)
- EudraCT Number: 2015-004293-15

Who did the study?

The company organizing and funding the research, called “the sponsor”, is the Institut de Recherches Internationales Servier based in Suresnes, France.

This study used UCART19 which is an anti-CD-19 allogeneic CAR-T product developed based on an exclusive licence granted by Cellectis to Servier. UCART19 uses Cellectis’ technologies, including TALEN® gene-editing technologies.

How can you contact the sponsor?

Contact us on the Servier website (www.servier.com).

Where can you learn more about this study?

- The scientific summary is also available on the Servier Clinical Trial Data website. (https://clinicaltrials.servier.com/)
- In this document, we translated medical terms into lay terms. You can find the corresponding medical terms in the Servier glossary on the Servier Clinical Trial Data website.

In accordance with the recommendations of the Cancer Plan III (Measure 5.4), this document was submitted for review, and guidance to the Clinical Cancer Research Patients Committee of La Ligue Nationale contre le Cancer.