Clinical Trial Results – Layperson Summary

A study of the safety of a new medicine (DCLL9718S) in patients with a type of blood cancer (acute myeloid leukemia)

See the end of the summary for the full title of the study.

About this summary

This is a summary of the results of a clinical trial; we will refer to the clinical trial as a "study" in this document.

This summary is written for:

- Members of the public.
- Patients who took part in the study, called "participants".

This summary is based on information known at the time of writing.

The study started in November 2017 and finished in July 2019. This summary was written after the study had ended.

No single study can tell us everything about the risks and benefits of a medicine. Many patients volunteer in several studies to help us find out everything we need to know.

The results from this study may be different from other studies with the same medicine.

- You should not make medical decisions based on this one summary.
- Always speak to your doctor before making any decisions about your treatment.

Contents of the summary

Thank you to the people who took part in this study

The patients who took part in this study have helped researchers to gather important information about the safety of the study medicine when given to patients for the treatment for leukemia (blood cancer).

Key information about this study

- This study was done to find out what the safe dose was for a new medicine (DCLL9718S).
- Eighteen patients were treated.
- Groups of patients received different doses of DCLL9718S.
- Researchers wanted to know what dose or how much study medicine was safe for patients to get.
- The main discovery was that it was not safe to go beyond 160 µg/kg.
- None of the patients' cancers had a response to the medicine in this study.
- Nine patients (50%) had a total of 37 side effects thought to be caused by the study medicine.
- The researchers decided to stop the study. DCLL9718S will not be developed as a treatment.

1. General information about this study

Why was this study done?

This study was done to test the safety of an experimental treatment in patients with acute myeloid leukemia (**AML**).

AML is an aggressive type of blood cancer.

Many patients respond to treatment for AML at first. However, the disease can come back (**relapse**). Also, the disease can stop responding to treatment (become **refractory**).

Patients with relapsed or refractory AML need new medicines.

Researchers wanted to test a new study medicine, DCLL9718S, in patients with relapsed or refractory AML.

Researchers wanted to find out what effects the study medicine had on patients – good, bad, or none. They wanted to know if it could be given to patients at a dose that was safe.

What was the study medicine?

- **DCLL9718S** is an "antibody-drug conjugate" or "ADC" – it is a medicine that is linked to an antibody.
- Antibodies are proteins that bind to a specific "molecule".
- CLL-1 is the "molecule" that the antibody in DCLL9718S binds to.
- **CLL-1** is a protein expressed on certain cancer cells (**AML blast cells**).
- DCLL9718S may be able kill cancer cells in patients with AML by binding to CLL-1.

What did researchers want to find out?

Researchers wanted to find out if DCLL9718S was safe for patients with AML.

The main question that researchers wanted to answer was:

1. What is the safe dose and can the side effects be tolerated when patients receive treatment with DCLL9718S?

Other questions that researchers wanted to answer included:

2. Is there any evidence that the study medicine had an effect on the disease in patients with AML?

What kind of study was this?

This was a "**Phase 1**" study, which means that this was one of the early studies in humans for DCLL9718S.

In addition, this was a "**first-in-human**" study, which means that this was the first time that the study medicine was given to humans.

This study was considered "**open label**" because doctors and patients knew which medicine the patients were getting, and which dose they were getting.

This was a "**dose escalation**" study, which means that new group of patients got higher doses of the medicine. However, if a certain number of patients got certain side effects after taking one dose of the medicine, then the next group would not get a higher dose of the medicine.

When and where did the study take place?

The study started in November 2017 and finished in July 2019. This summary was written after the study had ended.

The study took place in the United States (5 centers) and Canada (3 centers).

2. Who took part in this study?

There were **19 patients** who took part in this study. Among them, one patient did not get any medicine because the patient got an infection before starting treatment on this study.

Patients:

- The youngest patient was 19 years old while the oldest patient was 89 years old.
- Half of the patients were over 72 years old (median age).
- Sixteen patients (89%) were white.
- Over half of the patients (67%) were men and less than half of the patients (33%) were women.

Patients could take part in this study if:

- They were at least 18 years old.
- They had a life expectancy of at least 12 weeks.
- Their disease met one of the following conditions:
    - Became worse (disease progression).
    - Did not respond to treatment (at least one anti-leukemic therapy).
    - Patients who had another type of blood cancer that had changed and become AML.
- They had functioning liver, kidney, and blood system (other than having AML).
- Patients agreed to use birth control if necessary.

Patients could not take part in the study if:

- They had undergone an organ transplantation or stem cell transplantation.
- Their AML disease involved the brain.
- They had certain diseases or infections present at the time of the study.
- They had received certain types of treatments for AML at specific time points in relation to this study.
- They had plans to have a major surgery during this study.
- Mothers who were nursing or who were pregnant were not allowed to take part in the study.

3. What happened during the study?

In this study, patients joined a "dose escalation" group to receive the study medicine.

How was the treatment given

- Patients got the study medicine once every 3 weeks "intravenously" (by IV into their blood vein).
- Patients joined the study at different times. They joined different "study medicine dose groups" starting at the lowest dose.
- Only one dose level of the study medicine was studied at a time.
- Patients joined the next higher dose level group only if it was considered safe to do so.
- Those patients who joined the study early got lower doses of the study medicine while patients who joined later received higher doses.
- The table below shows the different doses tested and number of participants in each group:

Study medicine dose group	Number of patients in this group
10 µg/kg	4 patients
20 µg/kg	3 patients
40 µg/kg	6 patients
80 µg/kg	3 patients
160 µg/kg	3 patients

What was done on the study

Patients were seen by their doctors on a regular basis, who collected patient samples for lab analyses and also did tests. Doctors found out how patients were reacting to the medicine. They took note of and treated any side effects.

How much medicine did patients get

One patient who joined the 40 µg/kg dose group did not receive treatment because researchers discovered that the patient had an infection of the lung (pulmonary infection) before he/she started this study.

The other 18 patients got at least one dose of the study medicine.

What happened to patients on the study

The 18 patients stopped their treatment by the time the study was over. The reasons for stopping included disease became worse (14 patients, 78%), no effect on disease (2 patients, 11%), doctor's decision (1 patient 6%), and patient moved to hospice care (1 patient, 6%).

4. What were the results of the study?

Question 1: What is the safe dose and can the side effects be tolerated when patients receive treatment with DCLL9718S?

Half of the patients who received treatment (9 patients, 50%) experienced at least one side effect thought to be related to the study treatment.

Two out of 3 patients (67%) who received the highest dose (160 µg/kg) showed undesirable changes in the function of their livers. In one patient, this event was thought to be caused by DCLL9718S. In the other patient, the reason for this event was not clear.

Based on the side effects seen at 160 µk/kg, higher dose levels were not tested.

Question 2: Is there any evidence that the study medicine had an effect on the disease in patients with AML?

Researchers found that patient's cancers did not respond to the study medicine.

5. What were the side effects?

Side effects (also known as "adverse reactions") are unwanted medical problems (such as a headache) that happen during the study.

- No one in this study had all of the side effects.
- Some patients had a few of the side effects.

Most common side effects

Nine of the 18 patients (50%) who received at least one dose of the study treatment had a total of 37 side effects thought to be caused by the study medicine.

The most common side effects seen in 2 patients (11%) or more, and thought to be caused by the study medicine, are listed below:

Common side effects caused by the study medicine	Number of patients (and percentages) who got this side effect
Feeling sick to your stomach (nausea)	5 patients (28%)
Low calcium in the blood (hypocalcemia)	2 patients (11%)
Not feeling hungry (decreased appetite)	2 patients (11%)

Serious side effects

A side effect is considered "serious" if it is life-threatening, needs hospital care, or causes lasting problems.

All the serious side effects thought to be related to the study medicine are listed below:

Study medicine dose level	Serious side effects caused by the study medicine	Number of patients (and percentages) who got this side effect
10 µg/kg	None	-
20 µg/kg	None	-
40 µg/kg	Low platelets in the blood (thrombocytopenia)	3 patients (60%)
80 µg/kg	Fever and a low white blood cell (febrile neutropenia)	1 patient (33%)
160 µg/kg	None	-

Deaths
There were 15 patient (83%) deaths reported in this study. Five patients died after their disease become worse. While the study medicine once again had nothing to do with deaths of the other 10 patients, their individual reasons for death was not recorded.

Other side effects

You can find information about other side effects (not shown in the sections above) on the websites listed at the end of this summary – see section 8.

6. How has this study helped research?

The results presented here are from a single study of 19 patients with AML. Eighteen patients were treated with the study medicine, DCLL9718S.

These results helped researchers learn about the effects of DCLL9718S.

The results indicated that any benefit from this medicine was not worth the risk (side effects seen at the doses tested).

This study was stopped. This study medicine will not be developed for patients with AML.

No single study can tell us everything about the risks and benefits of a medicine. The results from this study may be different from other studies with the same medicine.

- This means that you should not make medical decisions based on this one summary.
- Always speak to your doctor before making any decisions about your treatment.

7. Are there plans for other studies?

At this time, there are no plans for other studies that investigate DCLL9718S in AML patients.

8. Where can I find more information?

You can find more information about this study on the website listed below:

- https://clinicaltrials.gov/ct2/show/NCT03298516

Who can I contact if I have questions about this study?

If you have any further questions after reading this summary:

- Visit the ForPatients platform and fill out the contact form https://forpatients.roche.com/en/About.html
- Or, contact a representative at your local Roche office.

If you took part in this study and have any questions about the results:

- Speak with the study doctor or staff at the study hospital or clinic.

If you have questions about your own treatment:

- Speak to the doctor in charge of your treatment.

Who organized and paid for this study?

This study was organized and paid for by Genentech, Inc., South San Francisco, CA, USA. Genentech is part of F. Hoffmann-La Roche Ltd., with headquarters in Basel, Switzerland.

Full title of the study and other identifying information

The full title of this study is, “An Open-Label, Phase I, Dose-Escalation Study Evaluating the Safety and Tolerability of DCLL9718S in patients with Relapsed or refractory Acute Myeloid Leukemia (AML) or DCLL9718S in combination with Azacitidine in patients with previously untreated AML Unsuitable for Intensive Induction Chemotherapy”.

- The protocol number for this study is GO39902.
- The ClinicalTrials.gov identifier for this study is NCT03298516.