Clinical Trial Results – Layperson Summary

A study to look at how safe different doses of the study medicine - DCDS0780A - were for patients with non-Hodgkin's Lymphoma that involved B cells

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 August 2015 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 one study may be different from other studies with the same medicine.

- You should not make 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 people who took part have helped researchers to gather important information about the study medicine and signs of whether it could be effective on blood cancers (non-Hodgkin's lymphoma with B cell involvement).

Key information about this study

- This study was done to find out what the safe dose was for a new medicine for patients with non-Hodgkin's lymphoma that involved B cells.
- Patients were treated with DCDS0780A – an experimental medicine.
- Different groups of patients got different doses of the medicine.
- Some patients got DCDS0780A combined with another medicine that was approved.
- This study included 60 patients in the United States of America.
- The main discovery was that this medicine caused a number of different side effects including effects on eyes and nerves. Some tumors shrank in some patients who received higher doses of this medicine.
- Patient disease did not get worse in half of the patients (median progression-free survival) for about 4 months when DCDS0780A was given alone, and for about 21 months when DCDS0780A was combined with an approved medicine.

1. General information about this study

Why was this study done?

Non-Hodgkin's lymphoma (NHL) is the most common blood cancer in adults. In 2010 there were about 94,000 new patients who got diagnosed with this disease in Europe, and about 66,000 in the United States.

Currently available medicines have brought improvements to the lives of many patients with NHL. However, not all patients benefit from available treatments. There is a need for new treatments that are safe and effective.

This study was done to test a new medicine in patients with NHL whose disease involved B cells. The new medicine, "DCDS0780A", was investigated alone and in combination with another medicine.

What was the study medicine?

DCDS0780A is a new medicine. It is a type of medicine known as an **antibody-drug conjugate** or **"ADC"**.

- Antibodies are proteins that only bind to one target.
- DCDS0780A is an ADC – it is a medicine linked to an antibody.
- The antibody allows DCDS0780A to bind to its target, a protein (**CD79b**) found on cancerous B cells.
- By binding to CD79b, the ADC is able to deliver the medicine directly to cancerous B cells.

Some patients got DCDS0780A and another medicine called "**rituximab**".

- Rituximab is not a new medicine. It is already in use by patients with certain types of diseases.
- Rituximab is an antibody. This type of medicine is known as a "**mab**".
- Rituximab binds to a protein (**CD20**) found on cancerous B cells.
- Rituximab causes cell death after binding to cancerous B cells.
- DCDS0780A + rituximab could become a potent treatment for patients with NHL that involves B cells.

What did researchers want to find out?

Researchers did this study to compare different doses of the new medicine, DCDS0780A. They also wanted to know if DCDS0780A was safe when used with and without rituximab.

The main questions that researchers wanted to answer were:

1. What dose of DCDS0780A could be considered safe for patients?
2. What was the largest dose of DCDS0780A that could be tolerated?
3. What dose of DCDS0780A do researchers recommend should be given to patients in future studies?
4. Was DCDS0780A safe when combined with rituximab?

Other questions that researchers wanted to answer included:

5. Does DCDS0780A cause any reactions in the immune system?
6. Does DCDS0780A (with and without rituximab) have any effect on cancer?

What kind of study was this?

This was a "**Phase 1/1b**" study, which means that this was one of the first studies for DCDS0780A to investigate this medicine in humans (Phase 1). In addition, this medicine was investigated in combination with other medicines (Phase 1b).

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

One part of the study (Phase 1) was called "**dose escalation**", which means that every new group of patients got a higher doses of the medicine. However, if a certain number of patients got certain side effects after getting 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 August 2015 and finished in July 2019. This summary was written after the study had ended.

The study took place in the United States of America.

2. Who took part in this study?

There were **60 patients** who took part in this study.

- The youngest patient was 32 years old while the oldest patient was 86 years old. Half of the patients were under 68 years old (median age).
- The majority of the patients (80%) were white.
- Just over half of the patients (53%) were men and less than half of the patients (47%) were women.
- Patients could take part in this study if their cancer came back (**relapsed disease**) or if no other medicine was effective (**refractory disease**).
- Patients with NHL were required to have a **B cell disease** confirmed by lab tests (histologically confirmed) in order to participate in the study.

Patients could take part in this study if:

- They were at least or over 18 years old.
- Doctors estimated their life span to be 3 months or more.
- They had NHL that had relapsed or was refractory, and involved B cells.
- They had tumor tissue samples (biopsy) available before starting the study.
- Their blood sugar level was under control.
- Patients with diabetes needed to be on the same medicine for at least 4 weeks before starting this study.
- Patients needed to make blood cells in their bodies without the use of medicine and without getting blood transfusion to correct their blood cell counts
- Patients needed to agree to use birth control methods while on the study.

Patient could not take part in the study if:

- They had received another type of cancer treatment within the last 2 weeks before the start of this study.
- They had received stem cell transplant from a donor at some time in the past.
- They underwent stem cell transplant using their own stem cells, within the last 3 months.
- They had B cell NHL disease (lymphoma) in their brain.
- They had a history of allergies or reactions to mab treatments.
- They had a major surgery within the last 4 weeks prior to this study.
- They have other health issues, such as another major disease or certain infections.
- Mothers who were nursing or who were pregnant were not allowed to take part in the study.

3. What happened during the study?

Patients joined the study at different times starting in August 2015.

Phase 1 study

- In Phase 1, patients received DCDS0780A by IV once every 3 weeks.
- One dose at a time was studied in one group of patients before the next group of patients got the next higher dose.
- Those patients who joined the study earlier got smaller doses of the medicine while patients who joined later received higher doses.
- Patients were allowed to get off the study at any time if they chose to do so, or if their doctors thought that that was the right decision.
- Patients were allowed to continue treatment once every 3 weeks for about one year. They could also increase the concentration of their dose that was given once every 3 weeks.
- Patients had to stop all treatments if their disease became worse.

Phase 1b study

- Patients received a combination treatment (DCDS0780A + rituximab) once every 3 weeks.
- Patients were allowed to get off the study at any time if they chose to do so, or if their doctors thought that that was the right decision.
- Patients were allowed to continue treatment for about a year. They had to stop all treatments if their disease became worse.

Study drug dose

All patients got their treatment once every 3 weeks, **intravenously** (through an IV tube).
Patients in Phase 1 were treated with a single medicine (DCDS0780A)
Patients in Phase 1b got a combination treatment (DCDS0780A + 375 mg/m^2 rituximab).

Phase 1 – dose of DCDS0780A	**Number of patients who got this dose**
0.3 mg/kg	3
0.6 mg/kg	3
1.2 mg/kg	5
2.4 mg/kg	10
3.6 mg/kg	17
4.8 mg/kg	13
Phase 1b – dose of DCDS0780A	**Number of patients who got this dose**
3.6 mg/kg	3
4.8 mg/kg	6

Phase 1 – some patients received up to 21 doses. Half of the patients received at least 4 doses (median number of doses).

Phase 1b – some patients received up to 13 doses. Half of the patients received at least 5 doses (median number of doses).

What was done on the study
Patients were seen by their doctors on a regular basis. The doctors collected samples from patients for lab analyses and also did tests and imaging. Doctors spoke with patients to find out how patients were reacting to the medicine.

Doctors took note of any side effects. If the side effects were minor, doctors gave out treatments for the side effects. Sometimes, the dose of the medicine was reduced to control side effects. Patients could also be taken off the medicine if their doctors thought it was the right decision.

4. What were the results of the study?

Question 1: What dose of DCDS0780A could be considered safe for patients?

Researchers looked at 6 different doses of DCDS0780A. There were side effects seen at all doses that were thought to be caused by the study medicine. Side effects seen at higher doses affecting the eye were difficult for patients. As a result, some patients had to come off the medicine. Others had to reduce the dose and it took time for their vision to return to normal.

Question 2: What was the largest dose of DCDS0780A that could be tolerated?

During dose escalation, the largest dose of DCDS0780A given to patients was 4.8 mg/kg, which was safe. Researchers did not go beyond this dose, so they did not find the dose that patients should not exceed.

Question 3: Based on the results of this study, what dose of DCDS0780A do researchers recommend should be given to patients in future studies?

Researchers recommended 3.6 mg/kg and 4.8 mg/kg as the doses to be tested further. These were then used in the Phase 1b section of the study.

Question 4: Was DCDS0780A safe when combined with rituximab?

Based on the results of this study, combining DCDS0780A with rituximab was safe.

Question 5: Does DCDS0780A cause any reactions in the immune system?

Researchers tested patients for "**anti-drug antibodies**" or **ADAs**. They took blood samples to test for ADAs that reacted against DCDS0780A.

Fifty-one patients were tested for ADA before receiving the first dose of the study medicine. Among the 51 patients, one patient (2%) tested positive for ADA.

Fifty-seven patients were tested for ADA after receiving treatment. Among the 57 patients, one patient (2%) tested positive for ADA.

ADA can cause a change in how quickly DCDS0780A is removed from the body. However, the effect of ADAs on DCDS0780A was not studied.

Question 6: Does DCDS0780A (with and without rituximab) have any effect on cancer?

The best response captured during the study was:

- **Complete response** (no detectable disease) in 17 patients (30%)
- **Partial response** (some change to disease) in 11 patients (19%)

Other patients had:

- **Stable disease**" (no change) in 6 patients (11%)
- **Progressive disease**" (became worse over time) in 23 patients (40%)

The disease did not get worse in half of the patients (median progression-free survival) for about 4 months in Phase 1, and for about 21 months in Phase 1b.

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.

Serious side effects

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

In this study there were 9 serious side effects thought to be related to the study medicine:

1. Pneumonia (2 patients reported pneumonia).
2. Kidney injury.
3. Labored breathing (acute respiratory distress syndrome).
4. Eye disease (corneal deposits).
5. Brain injury (hypoxic ischemic encephalopathy).
6. Buildup of a deposit in the lungs (lung infiltration).
7. Muscle weakness or numbness in the body (peripheral neuropathy).
8. Fever/chills, racing heartbeat, breathing fast (systemic inflammatory response syndrome).

Deaths

There were 4 patient deaths during the study, listed below. Two deaths (3 & 4) were thought to be caused by the study medicine.

1. Blood clot in the lung (pulmonary embolism).
2. Disease progression.
3. Hypoxic ischemic encephalopathy.
4. Pneumonia, caused study medicine.

Most common side effects

During this study, 54 patients (90%) reported at least one side effect that was not considered serious but was thought to be caused by the study medicine.

This summary lists the most common side effects seen in more than 10% of the patients:

Common side effects	What percentage of patients got this side effect
Blurred vision	21 patients (35%)
Eye condition (corneal deposits)	17 patients (28%)
Feeling tired (fatigue)	17 patients (28%)
Low white blood cell count (neutropenia)	16 patients (27%)
Feeling sick (nausea)	12 patients (20%)
Muscle weakness or numbness in the body (peripheral neuropathy)	12 patients (20%)
Diarrhea	11 patients (18%)
Discomfort involving touch, feel, or pain (sensory peripheral neuropathy)	8 patients (13%)
Not hungry (decreased appetite)	6 patients (10%)
Inflammation in the eye (keratitis)	6 patients (10%)

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 60 patients with NHL involving B cells. These results helped researchers find out how safe and effective DCDS0780A is for patients:

- The doses of this medicine that can be used safely.
- The effect of combining this medicine with another medicine.

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 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 with DCDS0780A.

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/NCT02453087

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: “Open-label, multicenter, Phase I/Ib dose escalation study evaluating the pharmacokinetics, safety, tolerability, and preliminary efficacy of DCDS0780A, alone or in combination with rituximab or obinutuzumab, in patients with relapsed/refractory B Cell non-Hodgkin’s lymphoma”.

- The protocol number for this study is: GO29687.
- The ClinicalTrials.gov identifier for this study is: NCT02453087