Summary of Clinical Trial Results

A study of mosunetuzumab with chemotherapy alone or chemotherapy plus polatuzumab vedotin (Pola-CHP) compared with existing treatment (rituximab with Pola-CHP) – in people with B-cell non-Hodgkin lymphoma

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 (called a 'study' in this document) – written for:

- Members of the public and
- People who took part in the study.

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

The study started in March 2019 and finished in October 2023. This summary was written after the study had ended.

No single study can tell us everything about the risks and benefits of a medicine. It takes lots of people in many studies to find out everything we need to know. 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.

Contents of the summary

Glossary

- B-cell NHL = B-cell non-Hodgkin lymphoma

Thank you to the people who took part in this study

The people who took part have helped researchers to answer important questions about B-cell non-Hodgkin lymphoma (B-cell NHL) and the medicine studied – 'mosunetuzumab'.

Key information about this study

- This study was done to look at the safest doses of mosunetuzumab (the medicine being studied) to use and how well they worked compared with standard treatment for B-cell NHL.
- In this study, a group of people were given mosunetuzumab in combination with chemotherapy or with polatuzumab vedotin and chemotherapy (Pola-CHP). Then, another group of people were given mosunetuzumab in combination withPola-CHP, or an existing medicine (called 'rituximab' given with Pola-CHP) – it was decided by chance which treatment each person was given.
- This study included 117 people in 6 countries.
- The main findings were that:
    - No new safety issues were seen with mosunetuzumab combined with chemotherapy or Pola-CHP.
    - A similar number of people taking either mosunetuzumab or rituximab with Pola-CHP had no cancer detectable on tests or scans after treatment.
- Around 61% of people taking mosunetuzumab had a serious unwanted effect, compared with around 14% of people taking rituximab. These effects may or may not have been caused by the study medicine.

1. General information about this study

Why was this study done?

B-cell non-Hodgkin lymphoma (B-cell NHL) is a blood cancer that affects a type of immune cell called B cells. It starts in lymphoid tissues and can spread to other organs.

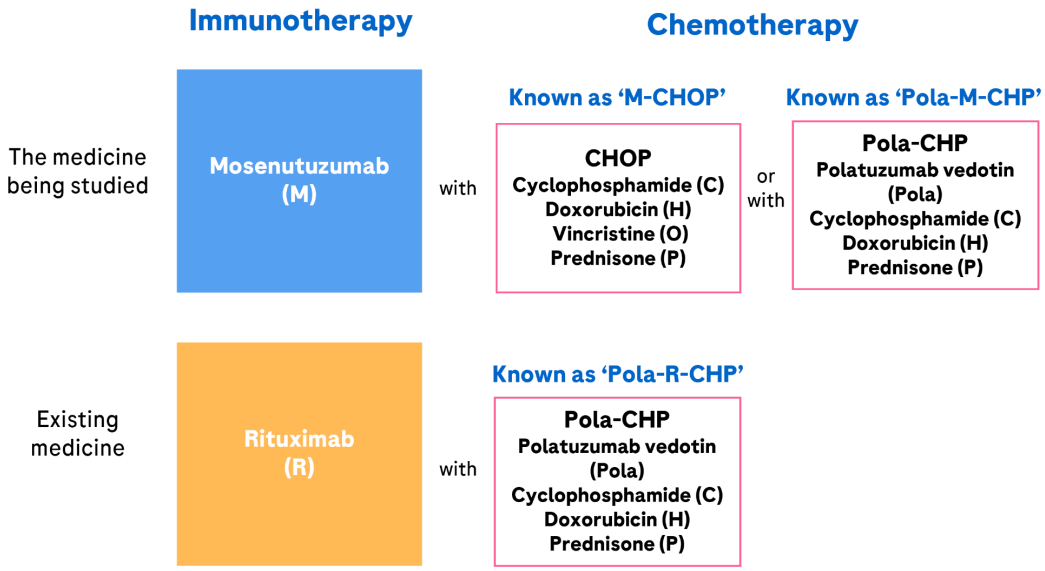
Diffuse large B-cell lymphoma (DLBCL) is a fast-growing type of B-cell NHL, and is the most common type of lymphoma.

The standard treatment for B-cell NHL, including DLBCL, is a combination of chemotherapy and immunotherapy. Immunotherapy is a medical treatment that helps the body fight off diseases.

For some people, their cancer does not respond to standard treatments or therapies (their disease is refractory) or their cancer returns (their disease relapses). This is known as 'relapsed or refractory', or 'R/R B-cell NHL'. Better drug combinations are needed to treat R/R B-cell NHL, and B-cell NHL when it is first diagnosed (known as 'first-line treatment').

What were the study medicines?

The study medicines



'Rituximab' is an existing medicine given in combination with chemotherapy to people with B-cell NHL.

- You say this as 'ri-TOOKS-im-mab'.
- Rituximab is an immunotherapy. It works by joining with a structure on B-cells called 'CD20'. This tags the cells for destruction by the body's natural defence (immune system).

'Mosunetuzumab' is the medicine that was studied here – it works in a different way to rituximab.

- You say this as 'mow-sun-eh-TOO-zoo-mab'.
- Mosunetuzumab is also an immunotherapy. It joins with CD20 on B-cells and cancer-killing cells of the immune system to bring them closer together.
- This may mean that mosunetuzumab could work better than rituximab against B-cell cancers.

'Tocilizumab' was also given in this study if people had an unwanted effect called 'cytokine release syndrome' after being given mosunetuzumab.

- You say this as 'tos-si-LI-zoo-mab'.
- Cytokine release syndrome can happen when the immune system reacts in an unusual way to an infection or cancer immunotherapy, like mosunetuzumab.

Standard chemotherapies for treating B-cell NHL were also given:

- Cyclophosphamide (C), doxorubicin (H), and prednisone (P) - together, these are known as 'CHP'.
- C, H, vincristine (O), and P - together, these are known as 'CHOP'.
- C, H and P given with polatuzumab vedotin - together these are known as 'Pola-CHP'.

In this study:

- CHOP or Pola-CHP were given in combination with mosunetuzumab ('M-CHOP' or 'Pola-M-CHP').
- Pola-CHP was given in combination with rituximab ('Pola-R-CHP').

The doses of chemotherapy that were given depended on a person's body weight.

What did researchers want to find out?

This study was in 2 parts:

- In Part 1, researchers wanted to find out the best dose of M-CHOP and Pola-M-CHP to use in Part 2. Researchers looked at how safe different doses of the medicines were – by checking how many people had unwanted effects and seeing how serious they were (see Section 4 'What were the results of the study?' and Section 5 'What were the unwanted effects?').
- In Part 2, researchers wanted to see whether Pola-M-CHP worked better than Pola-R-CHP at treating DLBCL (see Section 4 "What were the results of the study?").

The main questions that researchers wanted to answer were:

1. In Part 1, how many people had unwanted effects, and what were the best doses of M-CHOP and Pola-M-CHP to use?
2. In Part 2, how many people did not have cancer on tests or scans after treatment?

Other questions that researchers wanted to answer included:

3. How many people had a reduction of their cancer after treatment, and how long did this response last?
4. How long did people live without their cancer getting worse or needing a new cancer treatment?
5. How did the study medicine affect the immune system?

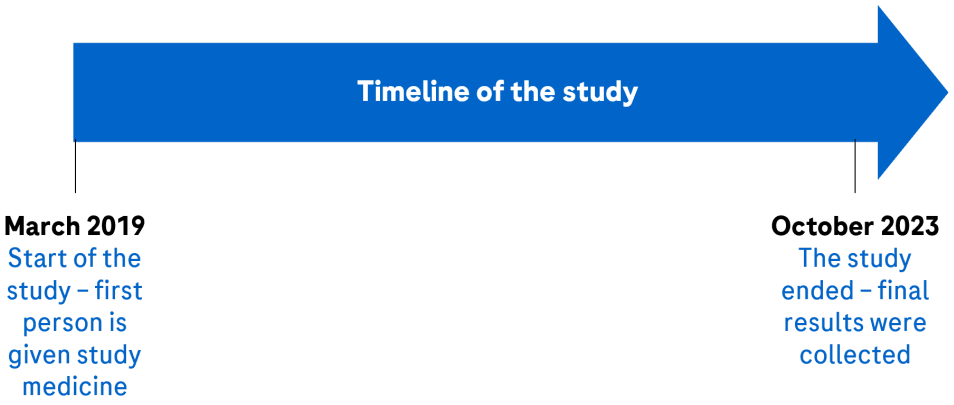
What kind of study was this?

This study was a 'Phase 1b/2' study. This means that mosunetuzumab had been tested in a number of people with B-cell NHL before this study. In this study, people with B-cell NHL either took mosunetuzumab combined with chemotherapy or Pola-CHP, or rituximab combined with Pola-CHP – this was to find out about the safety of mosunetuzumab treatment combinations, and if mosunetuzumab worked against B-cell NHL.

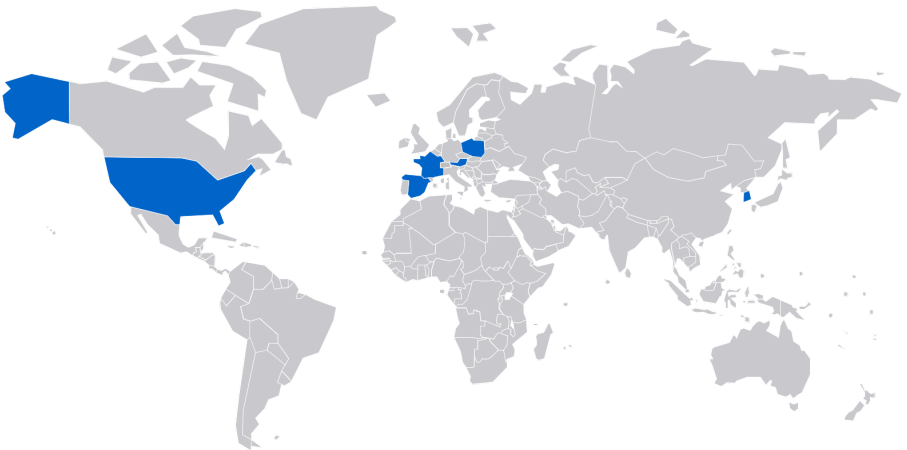
This was an open-label study. This means everyone involved, including the participant and the study doctor, know which study treatment the participant is given.

When and where did the study take place?

The study started in March 2019 and finished in October 2023. This summary was written after the study had ended.



The study took place at 33 study centres – across 6 countries in Asia, Europe and North America. The following map shows the countries where this study took place.

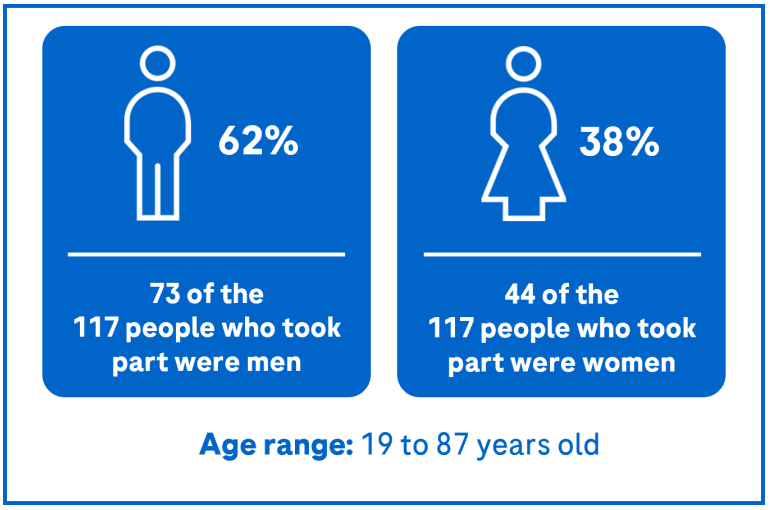


- Austria
- France
- Poland
- South Korea
- Spain
- United States of America

2. Who took part in this study?

In this study, 117 people with B-cell NHL took part.

More information on the people who took part is given below.



People could take part in the study if:

- They were at least 18 years old.
- For Part 1 - they had R/R B-cell NHL and been given at least 1 standard treatment for B-cell NHL.
- For Part 2 - they had DLBCL and had not been treated for it.

People could not take part in the study if:

- They had been given mosunetuzumab treatment before.
- They had other medical conditions, such as heart or lung disease.
- They were pregnant or breastfeeding.

3. What happened during the study?

The study medicines were given in 3-week treatment 'cycles'. A treatment cycle is the period of treatment and recovery time before the next set of treatment is given.

All study medicines were given as drips into the vein (infusion), except prednisone which was given as pills to be swallowed.

Part 1

Researchers looked at the best doses of M-CHOP or Pola-M-CHP to give, and the safest way to give it, starting with a lower dose and then progressively increasing the dosage over time (known as 'step-up dosing'), until the target dose was reached.

Participants were given:

- A low or high target dose of mosunetuzumab as part of M-CHOP.
- Pola-M-CHP.

Part 2

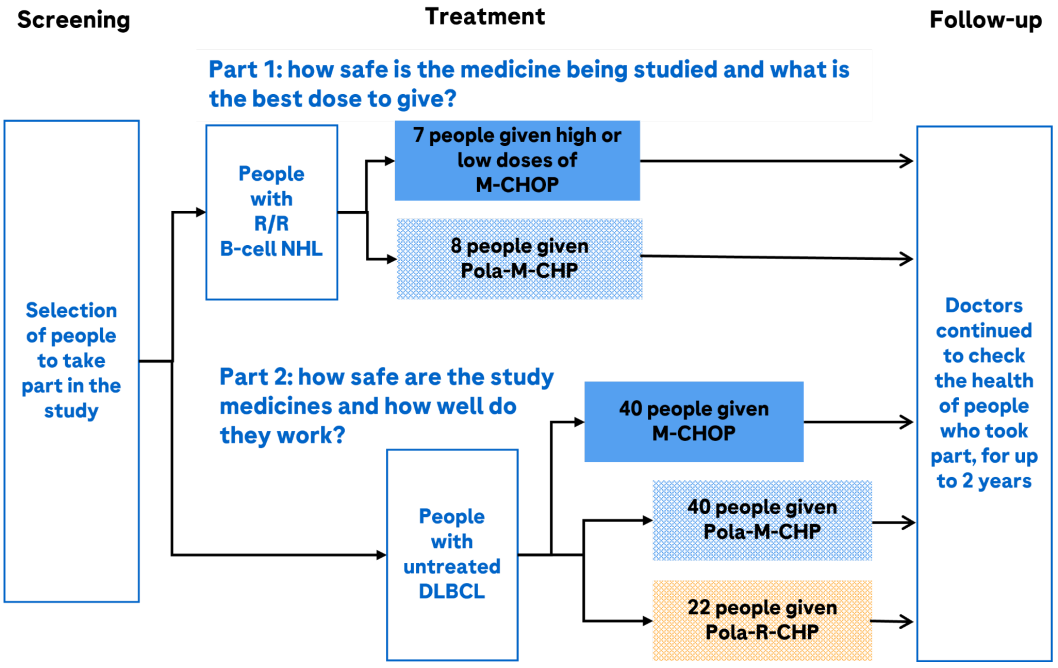
A group of people with DLBCL were given M-CHOP using the best dose of mosunetuzumab identified in Part 1. This was to check how safe M-CHOP was before people with DLBCL were given Pola-M-CHP.

Then, another group of people were selected by chance to get 1 of 2 treatments. This part of the study was 'randomised'. This means that it was decided by chance which of the medicines people in the study would have – like tossing a coin. Randomly choosing which medicine people take, makes it more likely that the types of people in both groups (for example, age, race) will be a similar mix. Apart from the exact medicines being tested in each group, all other aspects of care were the same between the groups. This part of the study looked at how well Pola-M-CHP worked versus existing treatment (Pola-R-CHP).

Participants were given:

- Pola-M-CHP (the medicine being studied).
- Pola-R-CHP (existing medicine).

People in the study took the treatments for up to 5 months. People in a mosunetuzumab treatment group who still had detectable cancer after this time could continue taking mosunetuzumab on its own for a further 8 months . When the study finished, the people who took part were asked to go back to their study centre for more visits – to check their overall health. Look below to see more information about what happened in the study.



4. What were the results of the study?

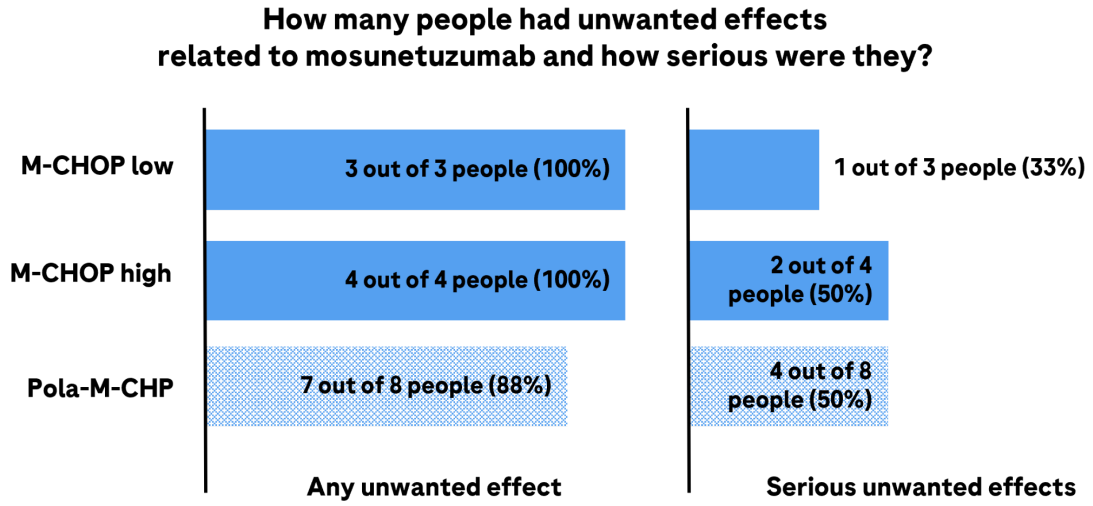
Question 1: In Part 1, how many people had unwanted effects, and what were the best doses of M-CHOP and Pola-M-CHP to use?

Unwanted effects are medical problems (such as feeling dizzy) that happen during the study.

- Not all of the people in this study had all of the unwanted effects.
- Unwanted effects may be mild to very serious and can be different from person to person.
- An unwanted effect is considered 'serious' if it is life-threatening, needs hospital care, or causes lasting problems.
- It is important to be aware that the unwanted effects reported here are from this single study. Therefore, the unwanted effects shown here may be different from those seen in other studies, or those that appear on the medicine leaflets.

In Part 1 of this study, groups of people with R/R B-cell NHL were given high or low target doses of mosunetuzumab as M-CHOP or Pola-M-CHP. The study doctors checked for unwanted effects to decide which dose to give in Part 2.

The number of people who had at least 1 serious unwanted effect, or who had at least 1 non-serious or serious unwanted effect (any unwanted effect) are shown in the image below.



The study doctors also checked to see how many people had unmanageable unwanted effects that prevented them from being given their intended dose.

- 1 person who was given the highest dose of mosunetuzumab had an unwanted effect that was thought to be related to mosunetuzumab. This meant they could not safely be given the dose of Pola-M-CHP again.
- This unwanted effect was changes in mental state due to disease, damage, or malfunction in the brain.

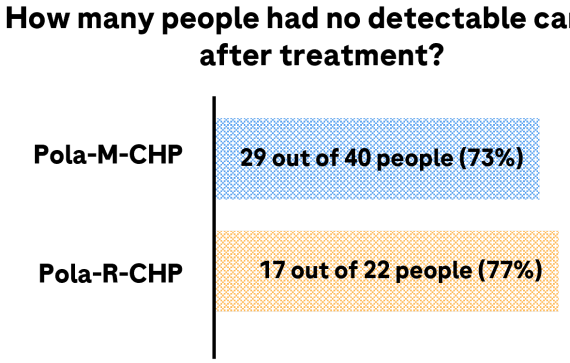
The highest target dose of mosunetuzumab tested was considered the recommended dose to use with CHOP or Pola-CHP. This dose was given in Part 2.

More information about unwanted effects in this study is shown in Section 5.

Question 2: In Part 2, how many people did not have cancer on tests or scans after treatment?

Another piece of information that researchers collected was the number of people who did not have DLBCL on tests or scans after treatment with Pola-M-CHP (the medicine being studied) or Pola-R-CHP (existing medicine) in Part 2.

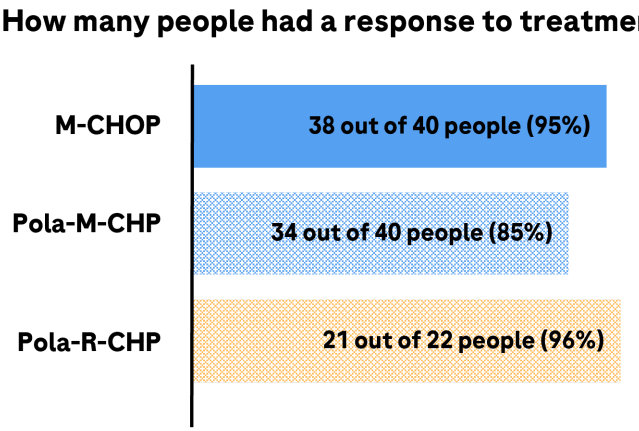
The results were similar in each treatment group.



Question 3: How many people had a reduction of their cancer after treatment, and how long did this response last?

Researchers also looked at the number of people with DLBCL that had shrunk after being given any of the study medicines in Part 2. This was looked at using different types of scans, and is known as 'best overall response'.

The results were similar between treatment groups.



They also looked at how long the response to treatment lasted, by looking at the amount of time it took for DLBCL to start getting worse, if this happened.

A small number of people had cancer that got worse after it had reduced. These were:

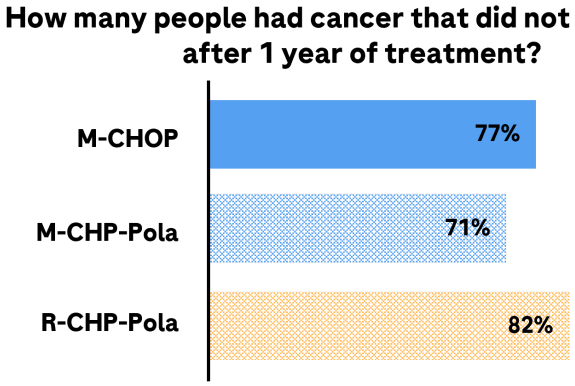
- 11 out of 40 people (29%) given M-CHOP.
- 9 out of 40 people (27%) given Pola-M-CHP.
- 4 out of 22 people (19%) given Pola-R-CHP.

This meant that the study doctors could not say how long a response to treatment lasted.

Question 4: How long did people live without their cancer getting worse or needing a new cancer treatment?

Researchers looked at the number of people in Part 2 with cancer that had not worsened or who needed a new treatment .

After 1 year of treatment, a similar amount of people in each group had cancer that had not worsened.



Researchers were not able to determine from this study how long people would live, on average, without their cancer getting worse or needing a new cancer treatment.

Question 5: How did the study medicine affect the immune system?

The immune system can react to some medicines to remove them from the body, which means the medicines do not work as well as expected. Researchers looked in the blood of people who had been given mosunetuzumab or polatuzumab vedotin for proteins called 'antibodies' that are made by the immune system.

- No one in the study had antibodies against mosunetuzumab.
- 1 in 50 people (2%) who were given polatuzumab vedotin had antibodies against polatuzumab vedotin.

This section only shows the key results from this study. You can find information about all other results on the websites at the end of this summary (see Section 8).

5. What were the unwanted effects?

Out of the 117 people in this study, 115 people were given the study medicines and are included in the safety analysis. Serious and common unwanted effects are listed in the following sections.

Serious unwanted effects

During this study, around 1 in every 2 people (52%) had at least one serious unwanted effect that may or may not have been caused by the study medicine. Around 61% of people taking mosunetuzumab had a serious unwanted effect, compared with around 14% of people taking rituximab.

The most common serious unwanted effects are shown in the following table – these were seen in 3 or more people across all treatment groups, and may or may not have been related to the study treatment. Some people had more than one unwanted effect – this means that they are included in more than one row in the table.

Serious unwanted effects reported in this study	**People taking mosunetuzumab (93 people total)**	**People taking rituximab (22 people total)**
A low level of a type of white blood cell that helps the body fight infections (neutrophils) in the blood, with fever	14% (13 out of 93)	5% (1 out of 22)
An over-reaction of the immune system to the immunotherapy (called 'cytokine release syndrome')	6% (6 out of 93)	0% (0 out of 22)
Low level of red blood cells	5% (5 out of 93)	0% (0 out of 22)
Loose, watery stools	4% (4 out of 93)	0% (0 out of 22)
Infection*	3% (3 out of 93)	5% (1 out of 22)
A low level of a type of white blood cell that helps the body fight infections (neutrophils) in the blood	4% (4 out of 93)	0% (0 out of 22)
Lung infection that can cause cough, fever, and difficulty breathing (pneumonia)	4% (4 out of 93)	0% (0 out of 22)

COVID-19	3% (3 out of 93)	0% (0 out of 22)
Death	3% (3 out of 93)	0% (0 out of 22)
An infection caused by a zoster virus that results in a painful rash with blisters (herpes zoster)	3% (3 out of 93)	0% (0 out of 22)
Not enough oxygen or too much carbon dioxide in a person's body	3% (3 out of 93)	0% (0 out of 22)

*Type of infection was not recorded.

There were some people in the study who died due to unwanted effects that may have been related to one of the study medicines. These were:

- 2 out of 47 people (4%) in an M-CHOP group.
- 1 out of 46 people (2%) in a Pola-M-CHP group.

During the study, some people decided to stop taking their medicine because of unwanted effects:

- In the M-CHOP group in Part 2, 3 out of 40 people (38%) stopped taking their medicine.
- In the Pola-M-CHP group in Part 2, 1 out of 40 people (8%) stopped taking their medicine.

Most common unwanted effects

During this study, almost everyone (112 out of 115 people [97%]) had an unwanted effect that was related to one of the study medicines. These were:

- Everyone (100%) taking mosunetuzumab.
- Around 86% of people taking rituximab.

The most common unwanted effects are shown in the following table – these are the 10 most common unwanted effects across all treatment groups. Some people had more than one unwanted effect – this means that they are included in more than one row in the table.

Most common unwanted effects reported in this study	People taking any study medicine (115 people total)
An over-reaction of the immune system to the immunotherapy (called 'cytokine release syndrome')	46% (53 out of 115)
Wanting to throw up	45% (52 out of 115)
A low level of a type of white blood cell that helps the body fight infections (neutrophils) in the blood	40% (46 out of 115)
Feeling tired or weak	38% (44 out of 115)
A low number of red blood cells	30% (34 out of 115)
Feeling less hungry than usual	27% (31 out of 115)
Hair loss	26% (30 out of 115)
Loose, watery stools	20% (23 out of 115)
Throwing up	20% (23 out of 115)
Damage to the nerves outside the brain and spinal cord	17% (20 out of 115)

Other unwanted effects

You can find information about other unwanted 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 information presented here is from a single study of 117 people with B-cell NHL. These results helped researchers learn more about B-cell NHL including DLBCL, and mosunetuzumab.

No single study can tell us everything about the risks and benefits of a medicine. It takes lots of people in many studies to find out everything we need to know. 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 the time of writing this summary, no more studies looking at mosunetuzumab as a first treatment for DLBCLare planned.

8. Where can I find more information?

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

- https://clinicaltrials.gov/ct2/show/results/NCT03677141
- https://www.clinicaltrialsregister.eu/ctr-search/trial/2018-001039-29/results
- https://forpatients.roche.com/en/trials/cancer/non-hodgkins-lymphoma/a-phase-ib-ii-study-investigating-the-safety--tolerabil-91932.html

If you would like to find out more about the results of Part 2 of this study, the full title of the relevant scientific paper is: 'Mosunetuzumab in combination with CHOP in previously untreated DLBCL: safety and efficacy results from a phase 2 study'. The authors of the scientific paper are: Adam J Olszewski, Tycel J Phillips, Marc S Hoffmann, Philippe Armand, Tae Min Kim and others. The paper is published in the journal 'Blood Advances', volume number 7, on pages 6055-6065.

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/trials/cancer/non-hodgkins-lymphoma/a-phase-ib-ii-study-investigating-the-safety--tolerabil-91932.html
- 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 organised and paid for this study?

This study was organised and paid for by F. Hoffmann-La Roche Ltd who have their headquarters in Basel, Switzerland.

Full title of the study and other identifying information

The full title of this study is: 'A Phase Ib/II, Open-Label, Multicenter, Randomized, Controlled Study Investigating the Safety, Tolerability, Pharmacokinetics, and Efficacy of Mosunetuzumab (BTCT4465A) in Combination With CHOP or CHP-Polatuzumab Vedotin in Patients With B-Cell Non-Hodgkin Lymphoma'.

The study is known as 'LUNSUMIO'.

- The protocol number for this study is: GO40515.
- The ClinicalTrials.gov identifier for this study is: NCT03677141.
- The EudraCT number for this study is: 2018-001039-29.