Summary of Clinical Trial Results

A study to look at how well polatuzumab vedotin works in people with a type of lymphoma called 'diffuse large B-cell lymphoma' – and how safe it is

The full title of the study is: "A study comparing the efficacy and safety of polatuzumab vedotin with rituximab-cyclophosphamide, doxorubicin, and prednisone (R-CHP) versus rituximab-cyclophosphamide, doxorubicin, vincristine, and prednisone (R-CHOP) in participants with diffuse large B-cell lymphoma".

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.

This study started in November 2017 and this summary includes the complete results that were collected and analysed in June 2021. At the time of writing this summary, the study is still happening – this summary presents the complete results for one part of the study. The study will end in June 2026.

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

- DLBCL = diffuse large B-cell lymphoma
- R-CHOP = rituximab with cyclophosphamide, doxorubicin, vincristine and prednisone
- Pola-R-CHP = polatuzumab vedotin with rituximab, cyclophosphamide, doxorubicin and prednisone

Thank you to the people who took part in this study

The people who took part in the study have helped researchers to answer important questions about diffuse large B-cell lymphoma (known as 'DLBCL') and the medicine studied – 'polatuzumab vedotin'.

Key information about this study

- This study is being done to find out how well polatuzumab vedotin (the medicine being studied) works in people with previously untreated diffuse large B-cell lymphoma (known as 'DLBCL') and how safe it is.
- In this study, people were given either polatuzumab vedotin in combination with rituximab and chemotherapy (known as 'Pola-R-CHP'), or an existing combination of medicines, rituximab and chemotherapy (known as 'R-CHOP') – it was decided by chance which treatment combination each person was given.
- This study included 879 people in 22 countries.
- The main finding was that after 2 years, the proportion of people who had no worsening (growth or spread) of their DLBCL was 77% in those who received Pola-R-CHP and 70% in those who received R-CHOP.
- 34% of people taking Pola-R-CHP experienced a side effect (or more than one side effect) that was serious, compared with around 31% of people taking R-CHOP.
- At the time of writing this summary, the study is still happening. It will end in June 2026.

1. General information about this study

Why is this study being done?

Diffuse large B-cell lymphoma (known as 'DLBCL') is a type of blood cancer.

B-cells (also called lymphocytes) are a type of white blood cell that help fight infections. DLBCL develops when B-cells grow abnormally. It is called diffuse large B-cell lymphoma because when examined under a microscope, the abnormal cells are spread out (or 'diffuse') instead of grouped together, and are bigger than healthy cells.

When you have a lymphoma, the abnormal lymphocytes build up in pea-sized glands, called lymph nodes, or in other body organs and form a lump.

DLBCL is currently treated with a group of medicines that kill cancer cells – called 'R-CHOP'. This is a combination of a few medicines:

- **R – rituximab** (a medicine called a 'monoclonal antibody' used in cancer. Monoclonal antibodies are man-made proteins that stick to a protein called an 'antigen' on cancer cells to help the immune system to recognise the cancer)
- **C – cyclophosphamide** (a chemotherapy)
- **H – doxorubicin** (a chemotherapy)
- **O – vincristine** (a chemotherapy)
- **P – prednisone** (a steroid) or other steroid equivalents.

Around 6 out of every 10 people who have DLBCL will be cured (5 years remission) with R-CHOP treatment (Sehn LH & Salles G. N Engl J Med 2021;384:842–58). However, some people's DLBCL may continue to get worse after being given R-CHOP – meaning that the medicine has not worked. In those cases where R-CHOP does not work, doctors then give people a different type of treatment called a 'stem cell transplant'. This involves destroying any unhealthy blood cells and replacing them with healthy ones removed from the blood or

bone marrow. After these healthy stem cells are infused into a person's bloodstream, they travel to the bone marrow and begin the process of forming new, healthy blood cells.

However, not all people are well enough to be given a stem cell transplant, or this may not work to stop the cancer getting worse. Researchers are interested in looking at new medicines that might help improve outcomes in people with previously untreated DLBCL.

Polatuzumab vedotin is an 'antibody-drug conjugate' that is made up of a combination of a 'monoclonal antibody' that recognises cancer cells, and a 'chemotherapy' that kills the cancer cells when it reaches them, and stops them from multiplying.

This study is being done to find out how well polatuzumab vedotin works for people with DLBCL, and how safe it is, when given together with rituximab, chemotherapy (cyclophosphamide and doxorubicin) and a steroid (prednisone) – this combination of medicines is known as 'Pola-R-CHP'.

Polatuzumab vedotin is being evaluated as a replacement for vincristine in the R-CHOP regimen. Study participants will be given **either** R-CHOP **or** Pola-R-CHP.

What are the study medicines?

This study is looking at two combinations of medicines:

- **R-CHOP** – the standard-of-care treatment, consisting of rituximab in combination with cyclophosphamide, doxorubicin, vincristine and prednisone
- **Pola-R-CHP** – **polatuzumab vedotin** – the medicine that was studied, plus rituximab in combination with cyclophosphamide, doxorubicin and prednisone.

'R-CHOP' is an existing combination of medicines given to people with DLBCL and is usually given first before other treatments are tried:

- Rituximab is an anti-cancer medicine known as a monoclonal antibody
- Cyclophosphamide, doxorubicin and vincristine are anti-cancer medicines known as chemotherapy
- Prednisone is a steroid that reduces inflammation or swelling.

'Polatuzumab vedotin' is the medicine that was studied here:

- Polatuzumab vedotin is an anti-cancer medicine known as an antibody-drug conjugate. The monoclonal antibody part of the medicine attaches to a target on the surface of cancerous blood cells called B-cells. Once attached, the medicine releases the chemotherapy into the B-cells, causing them to die
- Polatuzumab vedotin is being evaluated as a replacement for vincristine in the R-CHOP regimen.

What do researchers want to find out?

- Researchers are doing this study to compare polatuzumab vedotin in combination with rituximab and chemotherapy (Pola-R-CHP) with R-CHOP, the standard-of-care, to see how well polatuzumab vedotin works (see section 4 "What were the results of the study?").

- They also want to find out how safe the combination of medicines is – by checking how many people have side effects and seeing how serious they are, when taking each of the combination of medicines during this study (see section 5 "What were the side effects?").

The main questions that researchers want to answer are:

1. How many people had no worsening (growth or spread) of their DLBCL after receiving Pola-R-CHP compared with people who received R-CHOP?
2. How safe are the combinations of drugs for the people in the study?

What kind of study is this?

This is a 'Phase 3' study. This means that Pola-R-CHP has been tested before in a smaller number of people with DLBCL, in a Phase 2 study.

In this study, a larger number of people with DLBCL were either given Pola-R-CHP or R-CHOP (the standard treatment for DLBCL) – this was to find out about the side effects of polatuzumab vedotin and to see how effective polatuzumab vedotin was at preventing the worsening (growth or spread) of DLBCL.

- The study is **randomised**. This means that it was decided at random by a computer programme which of the combinations of medicines people in the study would have. Randomly choosing which medicine people take makes it more likely that the types of people in both groups (for example, in terms of age, ethnicity) will be a similar mix. Apart from the medicines being tested in each group, all other aspects of care were the same between the groups.

- This is a **double-blind** study. This means that neither the people taking part in the study nor the study doctors know what study medicines people are taking.

- This is an **active and placebo controlled** study. This means that a medicine known to be effective is compared with the medicine being studied. There is also a placebo for the medicine not given (i.e. a placebo matching vincristine in the Pola-R-CHP group and a placebo matching polatuzumab vedotin in the R-CHOP group). A placebo contains no active ingredient and is used in order to 'blind' the study so neither you nor the study doctor will know which 'combination' you received. This is done so that you and your study doctor will not be influenced by expectations of the effects of either.

When and where is the study taking place?

This study started in November 2017 and this summary includes the complete results up until June 2021. At the time of writing this summary, further safety information is being collected. The study will end in June 2026.

The study is taking place at 243 study sites across 22 countries in Asia, Australasia, Europe, the Middle East, North America and South America.

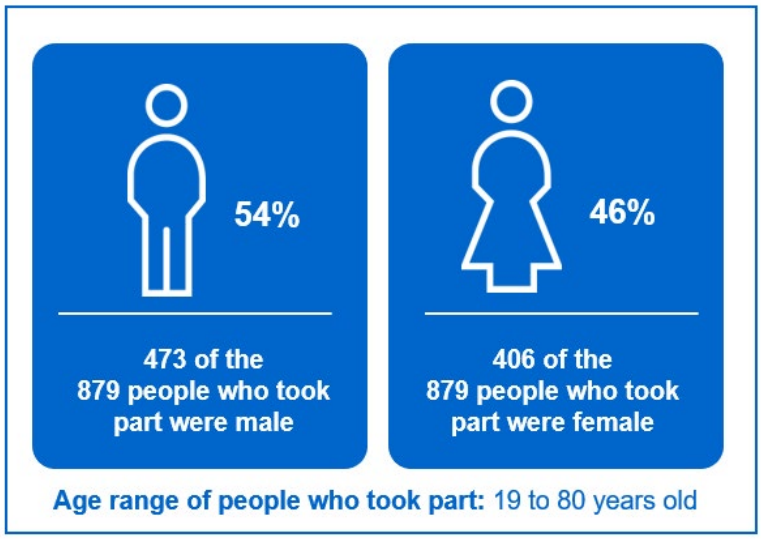
The following map shows the countries where this study is taking place.

- Australia
- Austria
- Belgium
- Brazil
- Canada
- China
- Czech Republic
- France
- Germany
- Italy
- Japan
- New Zealand
- Poland
- Republic of Korea
- Russia
- Spain
- Switzerland
- Taiwan
- Turkey
- Ukraine
- United Kingdom
- United States

2. Who is taking part in this study?

In total, **879 people with DLBCL** are taking part in this study.

More information about the people taking part is given below.



People could take part in the study if they:

- Were at least 18 years old, but not more than 80 years old
- Had CD20-positive DLBCL – CD20 is a marker or signal on the surface of B-cells that can be seen by researchers using a microscope
- Had not already received treatment for DLBCL
- Were at least capable of all selfcare, but may have been unable to carry out any work activities ('up and about' more than half of all waking hours).

People could **not** take part in the study if they:

- Had a history of indolent (very slow growing) lymphoma
- Had a history of severe allergic or anaphylactic reactions to any of the medicines within the R-CHOP combination
- Had cancer that had spread to the brain or spinal cord
- Were breastfeeding, pregnant or intending to get pregnant.

3. What happened during the study?

During the study, people were selected by chance to get one of two treatments. The treatments were selected at random by a computer and were given once every 3 weeks (a 'treatment cycle'). The treatments are described below.

Pola-R-CHP, consisting of:

- **Polatuzumab vedotin (the medicine being studied)**
- **Rituximab**
- **Cyclophosphamide**
- **Doxorubicin**
- **Prednisone** (or other steroid equivalents).

R-CHOP (the existing combination medicine), consisting of:

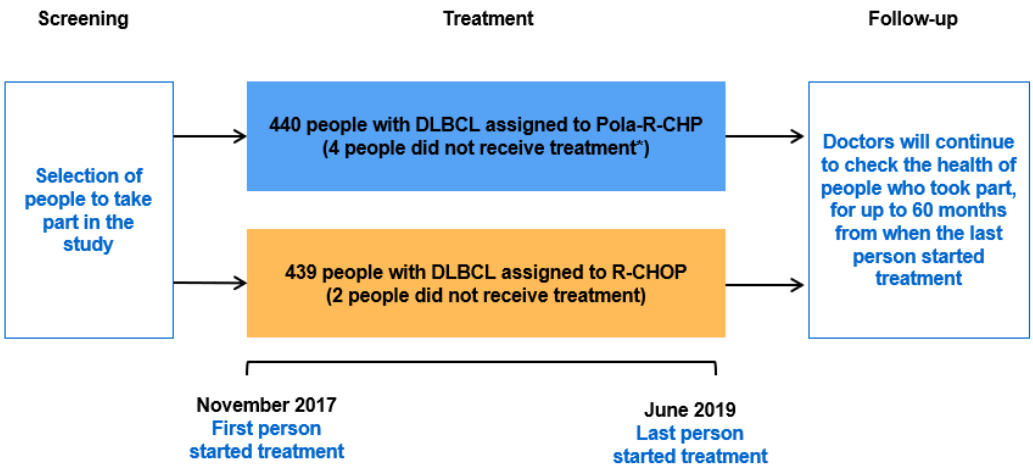
- **Rituximab**
- **Cyclophosphamide**
- **Doxorubicin**
- **Vincristine**
- **Prednisone** (or other steroid equivalents).

Polatuzumab vedotin, rituximab, cyclophosphamide, doxorubicin and vincristine were injected into a vein. Prednisone (or other steroid equivalents) was given as a tablet.

People had 6 treatment cycles with all the medicines, and then 2 treatment cycles of only rituximab (regardless of the combination of medicines that they received in the first 6 cycles).

This study is still happening. Everyone in the study has finished their treatment, but some people are undergoing tests to see if their cancer can still be detected. When the study ends, the people who took part will be asked to go back to their study centre to check their overall health.

Look below to see more information about what has happened in the study so far – and what the next steps are.



*One additional person did not receive polatuzumab vedotin, but did receive rituximab and prednisone, so they were included in the safety assessment for the R-CHOP group

4. What were the results of the study?

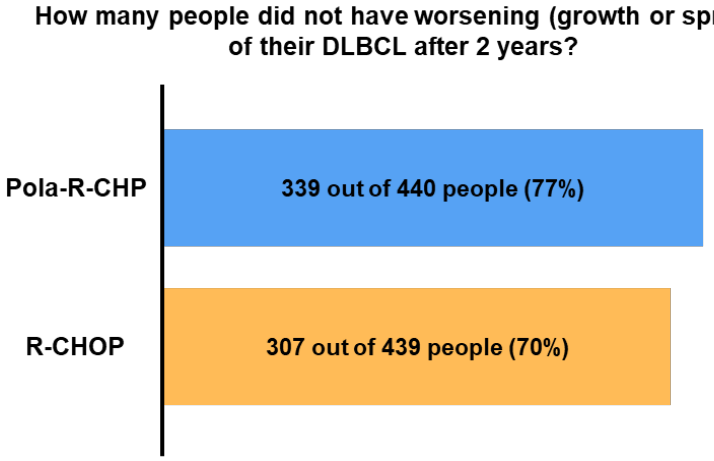
At the start of the study, researchers agreed on the questions that they wanted to answer, which are described below.

Question 1: How many people had no worsening (growth or spread) of their DLBCL after receiving Pola-R-CHP compared with people who received R-CHOP?

Researchers looked at how many people had no worsening (growth or spread) of their DLBCL, known as progression-free survival, after 2 years.

After following up for an average of almost 2.5 years, there was a 27% reduction in the risk for people who received Pola-R-CHP to have a worsening (growth or spread) of their DLBCL, to relapse or to die compared with people who were given R-CHOP.

After 2 years, the proportion of people who had no worsening (growth or spread) of their DLBCL was 77% (339 out of 440) in those who received Pola-R-CHP and 70% (307 out of 439) in those who received R-CHOP.



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 side effects?

Question 2: How safe are the combinations of drugs for the people in the study?

Serious side effects

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

During this study, around 3 in every 10 people (32%) had at least one serious side effect. Around 34% of people taking Pola-R-CHP had a serious side effect, compared with around 31% of people taking R-CHOP.

There were some people in the study who died due to side effects that may or may not have been related to one of the study medicines. Many of these were infections (pneumonia and sepsis):

- 13 out of 435 people (3%) in the Pola-R-CHP group
- 10 out of 438 people (2%) in the R-CHOP group.

During the study, some people stopped taking their medicine because of side effects:

- In the Pola-R-CHP group, 27 out of 435 people (6%) stopped taking their medicine
- In the R-CHOP group, 29 out of 438 people (7%) stopped taking their medicine.

Most common side effects

During this study, almost all of the participants had a side effect – 98% of people taking Pola-R-CHP and 98% of people taking R-CHOP.

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

The table includes all people who received any of the study medicines (known as the safety-evaluable population). This is slightly less than the total number of people who were randomised to treatment at the start of the study (6 people who were randomised to treatment did not actually receive study treatment, plus one person was assigned to Pola-R-CHP but only received rituximab with prednisone, and therefore was included in the R-CHOP assessment group).

Most common side effects reported in this study	**People taking Pola-R-CHP** (435 people total)	**People taking R-CHOP** (438 people total)
Peripheral neuropathy (all grades) *(a type of nerve damage causing pain and weakness)*	53% (230 out of 435)	54% (236 out of 438)
Nausea	42% (181 out of 435)	37% (161 out of 438)
Neutropenia *(low levels of a type of white blood cell called neutrophils)*	31% (134 out of 435)	33% (143 out of 438)
Diarrhoea	31% (134 out of 435)	20% (88 out of 438)
Anaemia	29% (125 out of 435)	26% (114 out of 438)
Constipation	29% (125 out of 435)	29% (127 out of 438)
Fatigue	26% (112 out of 435)	27% (116 out of 438)
Alopecia *(hair loss)*	24% (106 out of 435)	24% (105 out of 438)

Decreased appetite	16% (71 out of 435)	14% (62 out of 438)
Pyrexia *(abnormally high body temperature: fever)*	16% (68 out of 435)	13% (55 out of 438)

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 is this study helping research?

The information presented here is from a single study of 879 people with DLBCL. These results are helping researchers learn more about DLBCL and polatuzumab vedotin in combination with rituximab and chemotherapy (Pola-R-CHP).

So far, this study has shown that more people given Pola-R-CHP lived at least 2 years after they started taking the medicine, with no worsening (growth or spread) of their DLBCL, compared with those who were given the existing medicine, R-CHOP.
There were no new side effects for people who were given Pola-R-CHP compared with people given R-CHOP.

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?

Studies with polatuzumab vedotin in combination with rituximab and chemotherapy (Pola-R-CHP) are still happening, and further studies are 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/NCT03274492
- https://www.clinicaltrialsregister.eu/ctr-search/search?query=2017-002023-21
- https://forpatients.roche.com/en/trials/cancer/non-hodgkins-lymphoma/a-study-comparing-the-efficacy-and-safety-of-polatuzumab-vedotin.html

If you would like to find out more about the results of this study, the full title of the relevant scientific paper is: "Polatuzumab vedotin in previously untreated diffuse large B-cell lymphoma". The authors of the scientific paper are: Hervé Tilly, Franck Morschhauser,

Laurie H. Sehn, Jonathan W. Friedberg, Marek Trněný and others. The paper was published in the journal 'The New England Journal of Medicine' on 14 December 2021, and can be found here: DOI: 10.1056/NEJMoa2115304.

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-study-comparing-the-efficacy-and-safety-of-polatuzumab-vedotin.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 Switzerland; and Genentech, Inc., who have their headquarters in the United States. The study was conducted in collaboration with LYSA (Lymphoma Study Association) and LYSARC (Lymphoma Academic Research Organisation).

Full title of the study and other identifying information

The full title of this study is: "A study comparing the efficacy and safety of polatuzumab vedotin with rituximab-cyclophosphamide, doxorubicin, and prednisone (R-CHP) versus rituximab-cyclophosphamide, doxorubicin, vincristine, and prednisone (R-CHOP) in participants with diffuse large B-cell lymphoma".

The study is known as POLARIX.

- The protocol number for this study is: GO39942.
- The ClinicalTrials.gov identifier for this study is: NCT03274492.
- The EudraCT number for this study is: 2017-002023-21.