A study to look at how well polatuzumab vedotin plus bendamustine and rituximab works in Chinese people with a type of blood cancer called 'diffuse large B-cell 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:

- a general audience and
- people who took part in the study.

This summary is based on information known at the time of writing. The study started in July 2020 and finished in February 2022. 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

- DLBCL = diffuse large B-cell lymphoma (a type of blood cancer).
- BR = bendamustine with rituximab (a current treatment for DLBCL that has returned following successful treatment or has got worse during treatment).
- Pola+BR = polatuzumab vedotin in combination with bendamustine and rituximab (the combination being studied).

Thank you to the people who took part in this study

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

Key information about this study

- This study was done to look at a combination of medicines in Chinese people with a type of blood cancer known as diffuse large B-cell lymphoma (DLBCL). The study included only Chinese people as someone's ethnicity may affect their response to a medicine.
- In this study, people were given either polatuzumab vedotin in combination with bendamustine and rituximab (known as 'Pola+BR') or an existing combination of medicines, bendamustine and rituximab (known as 'BR'). It was decided at random which treatment combination each person was given.
- This study included 42 people from China.
- The main finding was that after finishing treatment, the number of people who had no evidence of cancer was:
    - 7 out of 28 people (25%) who were given Pola+BR
    - 2 out of 14 people (14%) who were given BR.
- Twelve out of 27 people (44%) taking Pola+BR had serious side effects, compared with 3 out of 14 people (21%) taking BR.

1. General information about this study

Why was this study done?

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

B-cells (also called lymphocytes) are a type of blood cell that help fight infections. DLBCL develops when B-cells grow abnormally. It is called diffuse large B-cell lymphoma because when scientists examine the cells under a microscope, they are spread out ('diffuse') and large, instead of grouped together and small, like healthy cells.

When you have a lymphoma, the abnormal cells build up in the lymph nodes or in other organs to form a lump (this is also known as a tumour).

DLBCL is currently treated with a group of medicines that kill cancer cells – called 'R-CHOP'. This is a combination of 5 medicines:

R – rituximab (a medicine called a 'monoclonal antibody' used in cancer. Monoclonal antibodies are man-made proteins that stick to a target 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 with R-CHOP treatment[1] (this is defined as 5 years with no active cancer). However, some people's DLBCL may initially improve after R-CHOP, but then their cancer may come back (this is known as 'relapsed DLBCL'). Additionally, some people's DLBCL may continue to get worse after being given R-CHOP – meaning that the medicine has not worked (this is known as 'refractory DLBCL').

People with relapsed or refractory DLBCL (known as R/R DLBCL) may be given another type of treatment called a 'stem cell transplant'. Stem cells are special cells produced by bone marrow (a spongy tissue found in the centre of some bones) that can turn into different types of blood cells. A stem cell transplant involves destroying all of a person's stem cells and replacing them with only healthy stem cells, usually extracted from their own 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.

Currently, there is no standard treatment offered to people with R/R DLBCL, but options include bendamustine and rituximab (known as BR) and other types of chemotherapy. Researchers are looking at new combinations of medicines to help improve outcomes in people with R/R DLBCL.

Polatuzumab vedotin is an 'antibody-drug conjugate' that is made up of a 'monoclonal antibody' that recognises cancer cells, and a 'chemotherapy' that kills the cancer cells when it reaches them. A study involving people from all over the world showed that a new combination of medicines (polatuzumab vedotin, bendamustine and rituximab) increased the number of people who had no evidence of cancer after treatment.[2] The present study was done to look at this combination of medicines specifically in Chinese people, as someone's ethnicity may affect their response to a medicine.

What are the study medicines?

This study looked at 2 combinations of medicines:
Bendamustine + rituximab (BR) – this is an existing treatment available for people with R/R DLBCL, it contains:

- **Bendamustine** (you say this as 'BEN-da-MUS-teen')
    - This is a type of anti-cancer medicine known as chemotherapy.
- **Rituximab** (you say this as 'rih-TUX-si-mab')
    - This is an anti-cancer medicine known as a monoclonal antibody.

Polatuzumab vedotin + bendamustine + rituximab (Pola+BR) is the combination of medicines that was studied here it contains:

- **Bendamustine** (you say this as 'BEN-da-MUS-teen')
    - This is a type of anti-cancer medicine known as chemotherapy.
- **Rituximab** (you say this as 'rih-TUX-si-mab')

    - This is an anti-cancer medicine known as a monoclonal antibody.
- **Polatuzumab vedotin** (you say this as 'poh-la-TOO-zoo-mab veh-DOH-tin')
    - This is an anti-cancer medicine known as an antibody-drug conjugate, which is a monoclonal antibody attached to a chemotherapy medicine
    - The monoclonal antibody part of the medicine attaches to a target on the surface of the abnormal blood cells called B-cells. Once attached, the medicine releases the chemotherapy into the B-cells, causing them to die.

The new combination of Pola+BR was being studied to treat people with R/R DLBCL to see if combining polatuzumab vedotin with BR combination may make the treatment more effective.

What did researchers want to find out?

- Researchers did this study to compare polatuzumab vedotin in combination with bendamustine and rituximab (Pola+BR) with an existing medicine bendamustine + rituximab (BR), to see how well the combination of medicines worked with the addition of polatuzumab vedotin (see section 4 "What were the results of the study?").
- They also wanted to find out how safe the combination of medicines was, by checking how many people had side effects and how serious the side effects were, when taking each of the combinations of medicines during this study (see section 5 "What were the side effects?").

The main question that researchers wanted to answer was:
How many people with R/R DLBCL had no evidence of cancer after receiving Pola+BR compared with people who received BR?

What kind of study was this?

This study was a 'Phase 3' study. This means that Pola+BR had been tested previously in people with R/R DLBCL before this study.

This study was smaller than most Phase 3 studies because it is a specific type of Phase 3 study called a 'bridging study'. This means that these treatments (Pola+BR and BR) have already been studied in a large number of people from across the world (in a global study). This bridging study evaluated these treatments in Chinese people only. As someone's ethnicity may affect their response to a medicine, this bridging study was done to confirm that the results from the global study applied to Chinese people.

- The study was **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 (for example, when considering age and gender) in both groups will be a similar mix. Apart from the exact medicines being tested in each group, all other aspects of care are the same between the groups.
- This is a **double-blind** study. This means that the people taking part in the study and the study doctors do not know what study medicines people are taking.

This is an **active- and placebo-controlled** study. Active-controlled means that a medicine known to be effective (in this study BR) is compared with the medicine being studied (in this study Pola+BR). There is also a placebo for the medicine not given (in this study people taking BR also took a placebo matching polatuzumab vedotin). This means every person in the study took 3 medicines:

- People taking Pola+BR took:
    - Polatuzumab vedotin
    - Bendamustine
    - Rituximab.
- People taking BR took:
    - A placebo that matched polatuzumab vedotin
    - Bendamustine
    - Rituximab.

Study doctors and participants did not know which medicine was polatuzumab vedotin and which was placebo. This was to ensure the study remained double-blind and to avoid study participants knowing which medicine they received, and study doctors knowing which medicines they were giving.

When and where did the study take place?

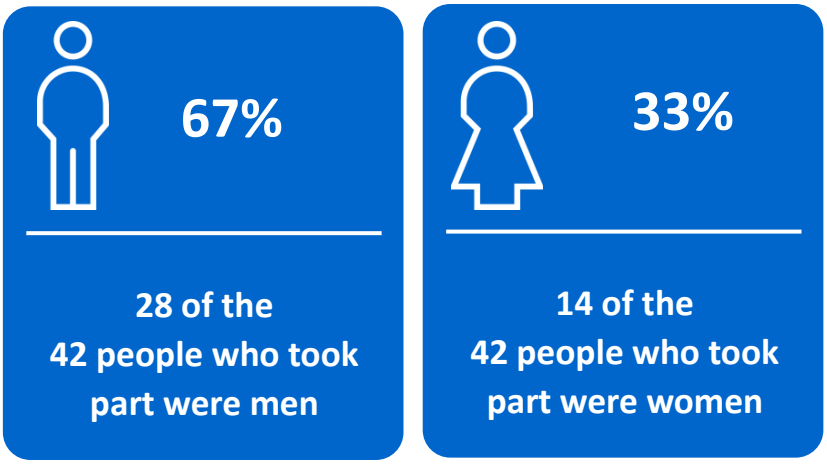
The study started in July 2020 and finished in February 2022. This summary was written after the study had ended.

The study took place at 8 study centres across mainland China.

2. Who took part in this study?

In total, 42 people with R/R DLBCL took part in this study.

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



Age range: 27 to 76 years old

People could take part in the study if they:

- Were 18 years old, or older.
- Had a confirmed diagnosis of R/R DLBCL and were not eligible for a stem cell transplant.
- Had at least one lesion (this means a group of cancer cells) that doctors could measure in scans.
- Were capable of all self-care, but may have been unable to carry out any work activities (this was defined as people being 'up and about' for more than half of all waking hours).
- Lived in mainland China.

People could not take part in the study if they:

- Had a severe allergic reaction to any of the medicines or medicine components within Pola+BR.
- Had a history of very slow growing lymphoma (known as indolent lymphoma).
- Had cancer within 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 at random by a computer to get 1 of 2 treatment combinations. The treatment groups were:

Pola+BR, consisting of**:**

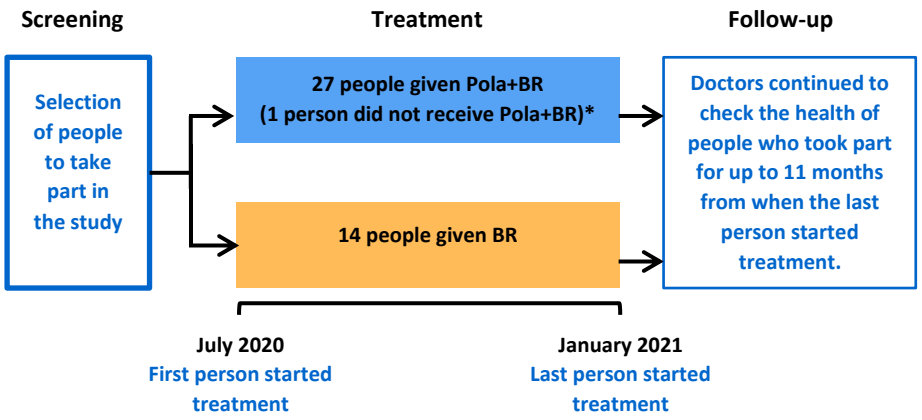
- Polatuzumab vedotin (the medicine being studied).
- Bendamustine.
- Rituximab.

BR (the existing combination medicine), consisting of:

- A placebo that matched polatuzumab vedotin.
- Bendamustine.
- Rituximab.

All medicines were injected into a vein. Treatments were given on set days for up to 6 cycles, a cycle was every 21 days.

People in the study took Pola+BR for an average of 3 months and BR for an average of 1 month. When the study finished, the people who took part were asked to go back to their study centre for more visits (follow-up) to check their overall health. Look below to see more information about what happened in the study. At this review of the study data (in July 2021), 15 out of 27 people (54%) in the Pola+BR group and 5 out of 14 people (36%) in the BR group were still having follow-up visits.



*One person left the study before receiving Pola+BR because after they joined the study they met one of the criteria participants were not allowed to have.

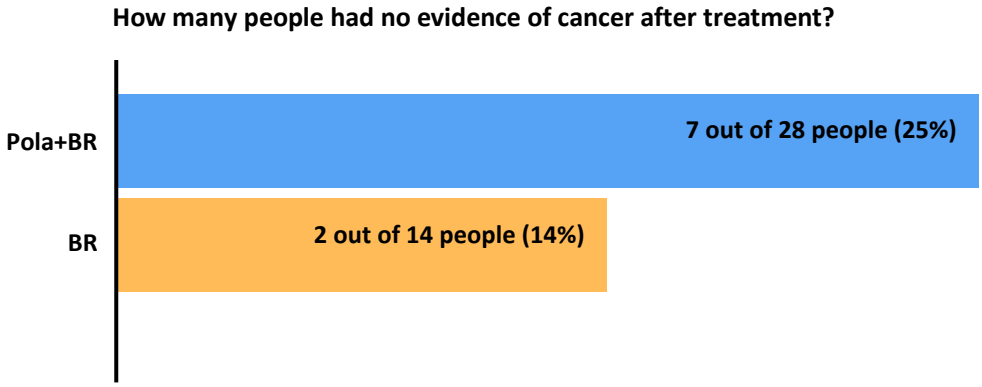
4. What were the results of the study?

At the start of the study, researchers agreed on the question that they wanted to answer.

Question: How many people with R/R DLBCL had no evidence of cancer after receiving Pola+BR compared with people who received BR?

Researchers looked at whether people's cancer was still visible using a positron emission tomography (PET) scan (a type of scan doctors use to see cancers) after finishing treatment.

- For people who received **Pola+BR: 7 out of 28 people (25%)** had no evidence of cancer after treatment.
- For people who received **BR: 2 out of 14 people (14%)** had no evidence of cancer after treatment.



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 "Where can I find more information").

5. What were the side effects?

Side 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 side effects.
- Side effects may be mild to very serious and can be different from person to person.
- It is important to be aware that the side effects reported here are from this single study. Therefore, the side effects shown here may be different from those seen in other studies, or those that appear on the medicine leaflets.
- Serious and common side effects are listed in the following sections.

Serious side effects

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

Many of the common serious side effects in this study were related to the patient's immune system. This is because several of the treatments given in this study work by targeting B cells, a type of white blood cell that makes up an important part of the immune system. Although the treatments are effective at killing the cancerous B cells, a large reduction in B cells can also make patients more prone to infections, which in some cases can be serious.

During this study, 15 out of 41 people (37%) had at least one serious side effect.

- 12 out of 27 people (44%) taking Pola+BR had a serious side effect.
- 3 out of 14 people (21%) taking BR had a serious side effect.

People taking Pola+BR took treatment for longer than people taking BR:

- People taking Pola+BR took treatment for an average of 6 treatment cycles.
- People taking BR took treatment for an average of 3 treatment cycles.

The small number of people taking each treatment combination, and the different number of treatment cycles may have had an effect on the number of people who had serious side effects.

The most common serious side effects are shown in the following table – these are the serious side effects that affected at least 1 in every 20 people (5%), in either treatment group. Some people had more than one side effect and are included in more than one row in the table.

Serious side effects reported in this study	People taking Pola+BR (27 people total)	People taking BR (14 people total)
Any serious side effect	**44%** (12 out of 27)	**21%** (3 out of 14)
Pneumonia (infection of one or both lungs)	**19%** (5 out of 27)	**0%** (0 out of 14)
Asthenia (feeling physically weak)	**0%** (0 out of 27)	**7%** (1 out of 14)
Gastrointestinal haemorrhage (heavy bleeding in the upper part of the digestive system)	**0%** (0 out of 27)	**7%** (1 out of 14)
Intervertebral disc protrusion (a back injury where a spinal disc bulges out of its normal position)	**0%** (0 out of 27)	**7%** (1 out of 14)

One of 14 people (7%) in the BR group died due to side effects that may have been related to one of the study medicines.

During the study, some people decided, or were advised by their doctors, to stop taking their medicine because of side effects:

- In the Pola+BR group, 3 out of 27 people (11%) stopped taking their medicine.
- In the BR group, 2 out of 14 people (14%) stopped taking their medicine.

Most common side effects

During this study, all participants (100%) across both treatment groups experienced at least one side effect.

The most common side effects are shown in the following table – these are the side effects that affected 2 or more of every 10 people (20%), in either treatment group. Some people had more than one side effect and are included in more than one row in the table.

Most common side effects reported in this study	People taking Pola+BR (27 people total)	People taking BR (14 people total)
A decrease in white blood cells (a type of blood cell which fights infections)	**67%** (18 out of 27)	**64%** (9 out of 14)
A decrease in neutrophil count (a specific type of white blood cell)	**63%** (17 out of 27)	**50%** (7 out of 14)
A decrease in platelets (a blood cell which helps with blood clotting)	**59%** (16 out of 27)	**43%** (6 out of 14)
A decrease in lymphocytes (a specific type of white blood cell)	**30%** (8 out of 27)	**71%** (10 out of 14)
An increase in alanine aminotransferase (a substance found in the liver)	**30%** (8 out of 27)	**7%** (1 out of 14)
An increase in aspartate aminotransferase (a substance found in the liver)	**22%** (6 out of 27)	**7%** (1 out of 14)
Fatigue (extreme tiredness)	**33%** (9 out of 27)	**36%** (5 out of 14)
Pyrexia (an increase in body temperature/fever)	**37%** (10 out of 27)	**7%** (1 out of 14)
Nausea (feeling sick)	**41%** (11 out of 27)	**29%** (4 out of 14)
Vomiting (being sick)	**37%** (10 out of 27)	**29%** (4 out of 14)
Diarrhoea (frequent bowel movements)	**22%** (6 out of 27)	**0%** (0 out of 14)
Hypokalaemia (an increase in the levels of potassium in the blood)	**37%** (10 out of 27)	**29%** (4 out of 14)
Decreased appetite	**22%** (6 out of 27)	**14%** (2 out of 14)
Anaemia (low levels of red blood cells or a protein called haemoglobin)	**52%** (14 out of 27)	**21%** (3 out of 14)
Pneumonia (infection of one or both lungs)	**22%** (6 out of 27)	**0%** (0 out of 14)

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 "Where can I find more information?".

6. How has this study helped research?

The information presented here is from a single study of 42 people with R/R DLBCL. These results helped researchers learn more about R/R DLBCL and Pola+BR.

This study has shown that more people given Pola+BR had no evidence of cancer after treatment, compared with people given BR.

All studies have limitations. The small number of people included in this study is a limitation and the fact that only Chinese people were included makes the results less relevant for other groups of people.

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?

Further studies with Pola+BR in other types of cancers 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/NCT04236141
- https://forpatients.roche.com/en/trials/cancer/non-hodgkins-lymphoma/a-study-to-evaluate-the-efficacy-and-safety-of-polatuzu-85981.html

You can find more information on the global study which looked at the same combination of medicines in people from across the world on the website listed below:

- https://clinicaltrials.gov/ct2/show/NCT02257567

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-to-evaluate-the-efficacy-and-safety-of-polatuzu-85981.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 study to evaluate the efficacy and safety of polatuzumab vedotin in combination with bendamustine and rituximab compared with bendamustine and rituximab alone in Chinese patients with relapsed or refractory diffuse large B-cell lymphoma (R/R DLBCL)".

The study is known as 'POLAROSE'.

- The protocol number for this study is: YO41543.
- The ClinicalTrials.gov identifier for this study is: NCT04236141.

References

1. Sehn LH and Salles G. Diffuse Large B-Cell Lymphoma. The New England Journal of Medicine 2021;384:842–858.
2. Sehn LH, et al. Polatuzumab Vedotin in Relapsed or Refractory Diffuse Large B-Cell Lymphoma. Journal of Clinical Oncology 2020;38:155–165.