A study to look at how effective and safe the drug combinations of obinutuzumab with polatuzumab vedotin and lenalidomide, or rituximab with polatuzumab vedotin and lenalidomide are in people with a type of cancer called 'lymphoma', whose previous treatment had not worked or stopped working

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.

The study started in March 2016 and finished in December 2021. 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

- NHL = a type of blood cancer of the lymph nodes called 'non-Hodgkin lymphoma'
- FL = follicular lymphoma (a type of NHL)
- DLBCL = diffuse large B-cell lymphoma (a type of NHL)
- G+Pola+Len = obinutuzumab, polatuzumab vedotin and lenalidomide
- R+Pola+Len = rituximab, polatuzumab vedotin and lenalidomide

Thank you to the people who took part in this study

The people who took part have helped researchers to answer important questions about two types of 'non-Hodgkin lymphoma' (NHL), called follicular lymphoma (FL) and diffuse large B-cell lymphoma (DLBCL), and the medicines studied – 'obinutuzumab', 'rituximab', 'polatuzumab vedotin', and 'lenalidomide'.

Key information about this study

- This study was done to find out how well two different combinations of medicines work, and how safe they are, in people with non-Hodgkin lymphoma (known as 'NHL'), whose previous treatment had not worked or had stopped working.
- In this study, people with follicular lymphoma (FL) were given obinutuzumab with polatuzumab vedotin and lenalidomide (known as 'G+Pola+Len'). People with diffuse large B-cell lymphoma (DLBCL) were given rituximab with polatuzumab vedotin and lenalidomide (known as 'R+Pola+Len').
- These medicines were looked at in people with FL and DLBCL separately, because these diseases behave differently.
- This study included 113 people in 3 countries.
- In people with FL, the main finding was that 61% had no signs of cancer after completing treatment with G+Pola+Len.
- In people with DLBCL, the main finding was that 31% had no signs of cancer after completing treatment with R+Pola+Len.
- There were no new side effects for people who were given either of the new medicine combinations, compared with what we already know from when the individual medicines are given on their own.
    - Overall, around 39% of people (22 out of 56 people) with FL taking G+Pola+Len had serious side effects that were related to study medicines.
    - Around 16% of people (9 out of 57 people) with DLBCL taking R+Pola+Len had serious side effects that were related to study medicines.

1. General information about this study

Why was this study done?

Follicular lymphoma (known as 'FL') and diffuse large B-cell lymphoma (known as 'DLBCL') are types of non-Hodgkin lymphoma (known as 'NHL').

In follicular lymphoma:
B cells (also called lymphocytes) are a type of white blood cell that help fight infections in the body. FL develops when B cells develop abnormally and build up to form a lump in pea-sized glands called lymph nodes, or in other body organs.

FL is currently treated with different combinations of medicines that kill cancer cells, including 'R-CHOP', 'BR' or 'R-CVP', which are described in more detail below:

R-CHOP:
- **R – rituximab** (this is a type of medicine called a 'monoclonal antibody', which is commonly used to treat cancer. Monoclonal antibodies are man-made proteins that stick to a protein called an 'antigen', found on cancer cells, to help the immune system recognise the cancer and fight it)
- **C – cyclophosphamide** (a type of chemotherapy)
- **H – doxorubicin** (a type of chemotherapy)
- **O – vincristine** (a type of chemotherapy)
- **P – prednisone** (a steroid), **or other types of steroids**

BR:
- **B – bendamustine** (a type of chemotherapy)
- **R – rituximab** (a monoclonal antibody)

R-CVP:
- **R – rituximab** (a monoclonal antibody)
- **C – cyclophosphamide** (a type of chemotherapy)
- **V – vincristine** (a type of chemotherapy)
- **P – prednisone** (a steroid)**, or other types of steroids**

In diffuse large B-cell lymphoma:
DLBCL also arises when B cells develop abnormally, but it progresses faster and is more common than FL. 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 smaller, like healthy cells. In the same way as FL, the abnormal cells build up in the lymph nodes or in other organs to form a lump.

DLBCL is currently treated with R-CHOP, a combination of medicines described above.

Almost 9 out of every 10 people who have FL will be cured (meaning they have been in remission with no evidence of lymphoma for at least 5 years after treatment).[1] More than 6 out of every 10 people who have DLBCL will be cured after treatment with R-CHOP.[2]

Although these medicines usually work at first, some people are not cured and their FL or DLBCL may return – this is called a 'relapse'. This means the medicine has stopped working. For other people with FL or DLBCL their medicine may not work at all, and their disease may continue to get worse over time – this is called 'refractory' disease.

This study was done to find out if a new combination of medicines could be effective and safe for people with FL or DLBCL whose previous treatment had not worked at all or had stopped working.

What were the study medicines?

This study looked at 2 new combinations of medicines:

- **People with FL were given G+Pola+Len:**
  - G = obinutuzumab
  - Pola = polatuzumab vedotin
  - Len = lenalidomide.

- **People with DLBCL were given R+Pola+Len:**
  - R = rituximab
  - Pola = polatuzumab vedotin
  - Len = lenalidomide.

Obinutuzumab (you say this as 'oh-bi-nuh-TOO-zoo-mab') and **rituximab** (you say this as 'rih-TUK-si-mab'):

- These are a type of medicine called monoclonal antibodies
- These are proteins that are made in a laboratory
- They are designed to target specific proteins (called antigens) that are found on cancerous B cells
- This 'flags' the cancer cells and triggers the body's immune system to attack the cells and destroy them.

Polatuzumab vedotin (you say this as 'poh-la-TOO-zoo-mab veh-DOH-tin'):

- This is a type of medicine called an 'antibody–drug conjugate'
- It is made of a combination of a monoclonal antibody that recognises cancer cells and attaches to them, and a 'chemotherapy' that enters these recognised cancer cells to stop them from multiplying and kill them
- The effects of this medicine can stop the cancer from growing or spreading.

Lenalidomide (you say this as 'len-ah-LID-oh-mide'):

- This is a type of medicine called an 'immunomodulator'
- It uses the body's immune system to prevent the growth and spread of cancer cells in a few different ways
- Scientists are still finding out how the medicine manages to stop the cancer from growing and spreading, but they do know that it can also directly attack cancer cells to destroy them.

What did researchers want to find out?

Researchers did this study to see:

- How well G+Pola+Len worked in people with FL (see section 4 'What were the results of the study?')
- How well R+Pola+Len worked in people with DLBCL (see section 4 'What were the results of the study?')
- They also wanted to find out how safe the combinations of medicines were, by checking how many people had side effects and how serious they were when taking each of the medicines during this study (see section 5 'What were the side effects?').

The main questions that researchers wanted to answer were:

1. How many people with FL whose previous treatment(s) had not worked or stopped working had smaller tumours or no tumours after taking G+Pola+Len?
2. How many people with DLBCL whose previous treatment(s) had not worked or stopped working had smaller tumours or no tumours after taking R+Pola+Len?

Other questions that researchers wanted to answer included:

3. How safe was the combination of G+Pola+Len for people with FL in the study?
4. How safe was the combination of R+Pola+Len for people with DLBCL in the study?

What kind of study was this?

This was a 'Phase 1b/2' study. This means that all the medicines used in the study (obinutuzumab, rituximab, polatuzumab vedotin, and lenalidomide) had been tested in a small number of people with FL or DLBCL before this study.

In this study, people with **FL** took **G+Pola+Len**, and people with **DLBCL** took **R+Pola+Len**. This was to find out if the two treatments worked in treating their cancer, and if they were safe to use.

The study was an 'open-label' study, which means the participants and doctors knew what treatments were being given.

The study was split into two parts:

- The first part was a **'dose-escalation'** phase. This is where people receive increasing doses of the medicine, to see how high the dose can get before the side effects get too strong. This phase shows scientists the best doses of the medicines to use – this is then called the 'recommended dose'
- The second part was a **'dose-expansion'** phase. This is where people receive the medicines at the recommended doses.

When and where did the study take place?

The study started in March 2016 and finished in December 2021. This summary was written after the study ended.

This study took place in 28 study sites across 3 countries – these were Spain (11 sites), the United Kingdom (9 sites) and the United States (8 sites).

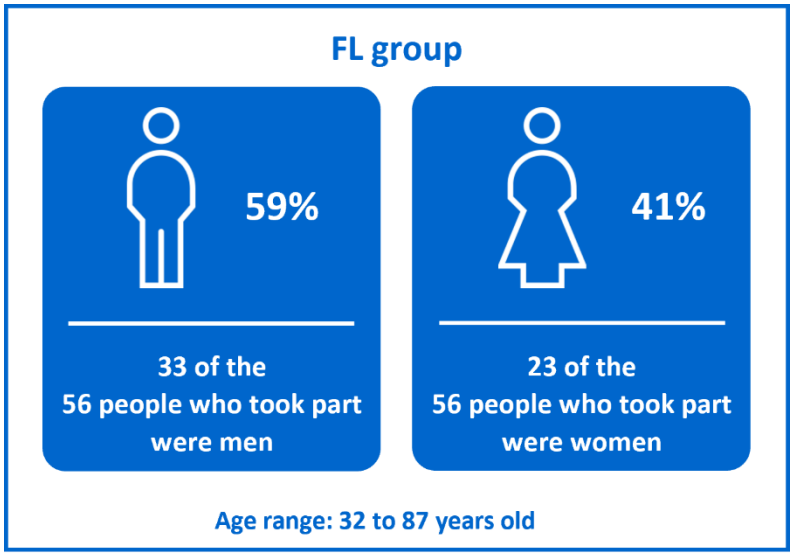
2. Who took part in this study?

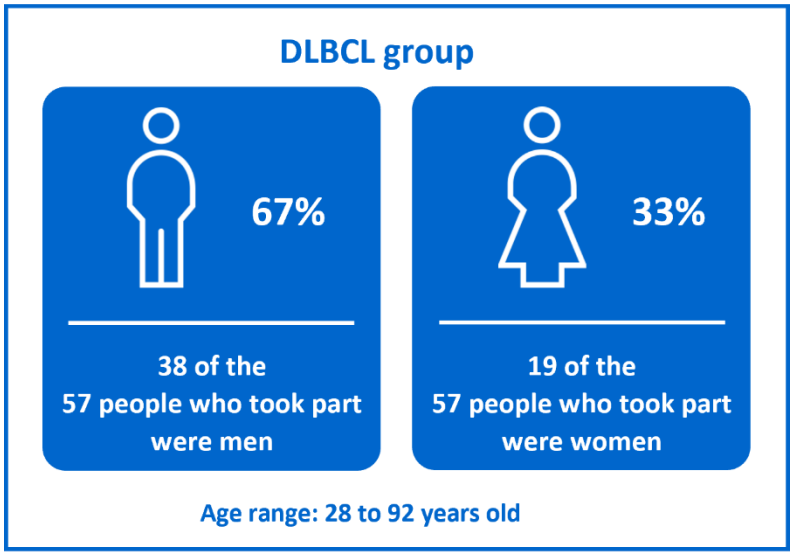
In this study, 113 people with NHL took part – this included:

- 56 people with FL
- 57 people with DLBCL

Most people with FL who took part in the study (57%; 32 people out of 56) were between 32 and 65 years of age, and most people who had DLBCL were older than 65 years old (67%; 38 people out of 57).

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





People with FL or DLBCL could take part in the study if they:

- Were at least 18 years old
- Had 'CD20-positive' FL or DLBCL – CD20 is a marker or signal on the surface of B cells that can be seen by scientists using a microscope
- Had lymphoma that was visible on a positron emission tomography scan, also known as a 'PET scan' (this is a type of scan doctors use to see cancers)
- Had at least one lesion (this means a group of cancer cells) that doctors could measure in scans
- Had previously received at least one treatment regimen that included chemotherapy and a monoclonal antibody (this is a type of medicine that helps the immune system to recognise and kill cancer cells) that targets cancer cells with the CD20 marker on them
- Had further cancer growth or spreading following previous treatment(s).

People could not take part in the study if they:

- Had Grade 3b FL (a severe form of FL)
- Previously had FL, which then further developed to become DLBCL
- Did not have the CD20 marker
- Had lymphoma that had spread to the central nervous system (this includes anywhere in the body's nerves, spine, or brain)
- Had received a type of treatment called stem cell transplant within 100 days of starting the study treatment. Stem cell transplants work by destroying unhealthy blood cells and replacing them with healthy blood cells that are taken from blood or bone marrow.

3. What happened during the study?

During the study, people received one of two treatment combinations depending on whether they had FL or DLBCL.

The treatment groups were:

- **G+Pola+Len for people with FL**
- **R+Pola+Len for people with DLBCL**

In both the dose-escalation and dose-expansion phases, people were given 'induction' treatment with G+Pola+Len (for people with FL) or R+Pola+Len (for people with DLBCL). The treatments were given for 6 'cycles' – each treatment cycle lasted 28 days before starting again. For those whose induction treatment worked, people with FL were given 'maintenance' treatment with G+Len for up to 2 years, and people with DLBCL were given 'consolidation' treatment with R+Len for up to 6 months.

The induction treatments were:

- **G – obinutuzumab (for people with FL)** – injected into a vein once a week for the first 3 weeks of the first treatment cycle, then once every cycle for the other 5 treatment cycles
- **R – rituximab (for people with DLBCL)** – injected into a vein once in every cycle
- **Pola – polatuzumab vedotin** – injected into a vein once in every cycle
- **Len – lenalidomide** – taken as a tablet every day for the first 3 weeks of each cycle

The maintenance treatments (for people with FL whose induction treatment worked) were:

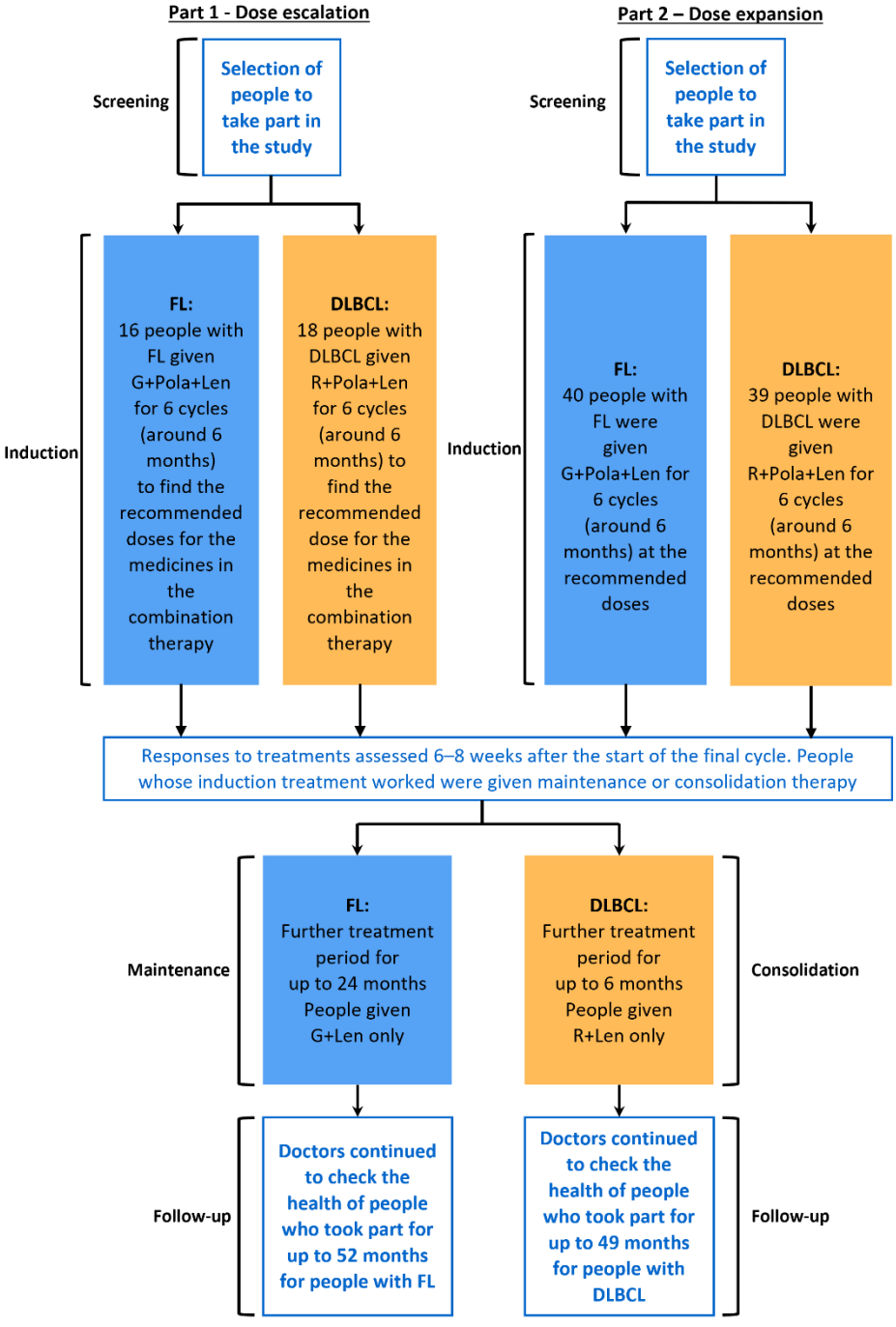
- **G – obinutuzumab** – injected into a vein once every other cycle for up to 2 years

- **Len – lenalidomide** – taken as a tablet every day for the first 3 weeks of each cycle for up to 1 year

The consolidation treatments (for people with DLBCL whose induction treatment worked) were:

- **R – rituximab** – injected into a vein once every other cycle for up to 6 months
- **Len – lenalidomide** – taken as a tablet every day for the first 3 weeks of each cycle for up to 6 months

People in the study took the treatments for 6–30 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.



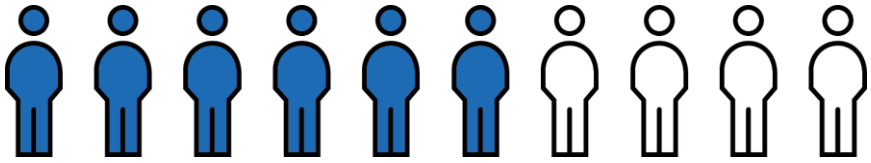
4. What were the results of the study?

The questions that researchers wanted to answer with this study are described below.

Question 1: How many people with FL whose previous treatment(s) had not worked, or stopped working, had smaller tumours or no tumours after taking G+Pola+Len?

Researchers looked at the proportion of people with FL who achieved a complete response after completing the G+Pola+Len regimen. A complete response means the person no longer has any signs of FL.

Of the people with FL who were given G+Pola+Len, 61% (28 people out of 46) had a complete response.

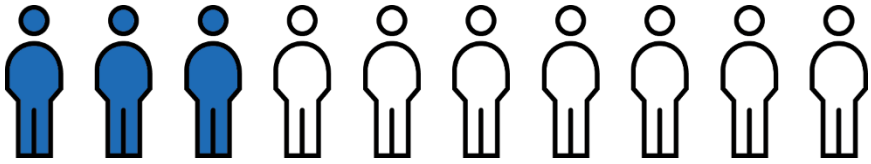


6 in every 10 people (61%) had a complete response, which means they showed no signs of cancer after induction treatment

Question 2: How many people with DLBCL whose previous treatment(s) had not worked, or stopped working, had smaller tumours or no tumours after taking R+Pola+Len?

Another piece of information that researchers collected was the proportion of people with DLBCL who achieved a complete response after completing treatment with R+Pola+Len.

Of the people with DLBCL who were given R+Pola+Len, 31% (15 people out of 49) had a complete response.



3 in every 10 people (31%) had a complete response, which means they showed no signs of cancer after induction 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).

5. What were the side effects?

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

- They are described in this summary because the study doctor believes the side effects were related to the treatments in 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.

Questions 3 and 4: How safe was the combination of G+Pola+Len for people with FL and the combination of R+Pola+Len for people with DLBCL in the study?

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 how the person's immune system responded to the medicines. This is because several of the treatments given in this study work by targeting a type of white blood cell called 'B cells' that are 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 people more prone to infections, which in some cases can be serious.

In people with FL receiving G+Pola+Len, 22 out of 56 people (39%) had at least one serious side effect that was related to treatment.

In people with DLBCL receiving R+Pola+Len, 9 out of 57 people (16%) had at least one serious side effect that was related to treatment.

The most common serious side effects are shown below – these are the most common serious side effects that were experienced by more than one person in each treatment group. Some people had more than one side effect – this means that they are included more than once.

In people with FL receiving G+Pola+Len:

- 4 out of 56 people (7.2%) had lower respiratory tract infections (an infection anywhere in the mouth, nose, throat, and lungs) or COVID-19 infection
- 2 out of 56 people (3.6%) had febrile neutropenia (abnormally high body temperature and low levels of a type of white blood cell called neutrophils)
- 2 out of 56 people (3.6%) had tumour lysis syndrome (where destroyed tumour cells release their contents into the blood)
- 2 out of 56 people (3.6%) had fever (abnormally high body temperature)
- 2 out of 56 people (3.6%) had infusion-related reactions (reactions to the way the medicines are infused into the blood).

In people with DLBCL receiving R+Pola+Len:

- 2 out of 57 people (3.5%) had neutropenic sepsis (a serious reaction to an infection and low levels of a type of white blood cell called neutrophils)
- 2 out of 57 people (3.5%) had tumour flare (increase in tumour size).

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

- 3 out of 56 people (5.4%) with FL receiving G+Pola+Len
- 5 out of 57 people (8.8%) with DLBCL receiving R+Pola+Len.

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

- In the FL group receiving G+Pola+Len:
    - 16 out of 56 people (29%) stopped taking obinutuzumab
    - 5 out of 56 people (9%) stopped taking polatuzumab vedotin
    - 15 out of 56 people (27%) stopped taking lenalidomide.

- In the DLBCL group receiving R+Pola+Len:
    - 6 out of 57 people (11%) stopped taking rituximab
    - 5 out of 57 people (9%) stopped taking polatuzumab vedotin
    - 6 out of 57 people (11%) stopped taking lenalidomide.

Most common side effects

During this study, in people with FL receiving G+Pola+Len, around 55 out of 56 people (98%) had at least one side effect that was related to treatment and was not considered serious.

In people with DLBCL receiving R+Pola+Len, 49 out of 57 people (86%) had at least one side effect that was related to treatment and was not considered serious.

The most common side effects are shown in the following table – these are side effects that occurred in at least 15% of people in each treatment group. Some people had more than one side effect – this means that they are included in more than one row in the table.

Most common side effects reported in this study	People with FL taking G+Pola+Len (56 people total)
Neutropenia (low levels of a type of white blood cell called neutrophils)	63% (35 out of 56)
Thrombocytopenia (low levels of a type of blood cell called platelets)	54% (30 out of 56)
Infusion-related reactions (reactions to the way the medicines are infused into the blood)	38% (21 out of 56)
Anaemia (low levels of red blood cells or a protein called haemoglobin)	36% (20 out of 56)
Diarrhoea (frequent bowel movements)	27% (15 out of 56)
Fatigue (extreme tiredness)	21% (12 out of 56)
Increased alanine aminotransferase (increased levels of a type of enzyme used to show how well the liver is functioning)	20% (11 out of 56)
Fever (abnormally high body temperature)	18% (10 out of 56)

Most common side effects reported in this study	People with DLBCL taking R+Pola+Len (57 people total)
Neutropenia (low levels of a type of white blood cell called neutrophils)	61% (35 out of 57)
Anaemia (low levels of red blood cells or a protein called haemoglobin)	19% (11 out of 57)
Thrombocytopenia (low levels of a type of blood cell called platelets)	18% (10 out of 57)
Diarrhoea (frequent bowel movements)	18% (10 out of 57)

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 information presented here is from a single study of 113 people with FL or DLBCL – two types of blood cancer. These results helped researchers learn more about FL and DLBCL and the two new combinations of medicines – G+Pola+Len and R+Pola+Len.

The results presented in this summary are specifically relevant to people with relapsed or refractory (R/R) FL or DLBCL (cancer that comes back after treatment or cancer that does not respond to treatment).

A key limitation of this study is that health outcomes for people with R/R FL or DLBCL receiving the new medicine combinations were not compared with people with R/R FL or DLBCL receiving the standard treatments currently prescribed. This means it is not as clear to scientists whether the new medicine combinations studied are better at treating cancer for people with R/R FL or DLBCL than current standard treatments.

This study has shown that the new medicine combinations, G+Pola+Len (for people with R/R FL) and R+Pola+Len (for people with R/R DLBCL) are effective and safe for use.

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 G+Pola+Len for R/R FL, or R+Pola+Len for R/R DLBCL 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/results/NCT02600897
- https://www.clinicaltrialsregister.eu/ctr-search/search?query=GO29834
- https://forpatients.roche.com/en/trials/cancer/non-hodgkins-lymphoma/a-study-of-obinutuzumab--polatuzumab-vedotin--and-lenalidomide-i.html

If you would like to find out more about the results of this study, the full title of a relevant scientific paper is: "Polatuzumab vedotin plus obinutuzumab and lenalidomide in patients with relapsed or refractory follicular lymphoma: a cohort of a multicentre, single-arm, phase 1b/2 study".

The authors of the scientific paper are: Catherine Diefenbach, Brad S Kahl, Andrew McMillan, Javier Briones, Lalita Banerjee, and others. The paper is published in the journal 'The Lancet Haematology', volume number 8 (2021), on pages e891–e901.

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-of-obinutuzumab--polatuzumab-vedotin--and-lenalidomide-i.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 of Obinutuzumab, Polatuzumab Vedotin, and Lenalidomide in Relapsed or Refractory Follicular Lymphoma (FL) and Rituximab in Combination With Polatuzumab Vedotin and Lenalidomide in Relapsed or Refractory Diffuse Large B-Cell Lymphoma (DLBCL)".

- The protocol number for this study is: GO29834.
- The ClinicalTrials.gov identifier for this study is: NCT02600897.
- The EudraCT number for this study is: 2015-001999-22.

References

1. Haematological Malignancy Research Network (HMRN)|Follicular lymphoma. Available at https://hmrn.org/statistics/survival (Accessed 17 November 2022).
2. Sehn LH and Salles G. Diffuse Large B-Cell Lymphoma. The New England Journal of Medicine 2021;384:842–858.