

Summary of Clinical Trial Results

A study to find if glofitamab or mosunetuzumab in combination with gemcitabine and oxaliplatin are safe and work for people with cancer of the lymph nodes (diffuse large B-cell lymphoma or high-grade B-cell lymphoma) that has come back or did not respond to prior treatment

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 June 2020 and finished in October 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

1. General information about this study
2. Who took part in this study?
3. What happened during the study?
4. What were the results of the study?
5. What were the side effects?
6. How has this study helped research?
7. Are there plans for other studies?
8. Where can I find more information?

Glossary

- Diffuse large B-cell lymphoma (DLBCL) = a fast-growing cancer of the lymph nodes.
- High-grade B-cell lymphoma (HGBCL) = a fast-growing cancer of the lymph nodes
- Relapsed or refractory = the cancer has come back after being treated or did not get better with the previous treatment

Thank you to the people who took part in this study

The people who took part have helped researchers to answer important questions about cancer of the lymph nodes – diffuse large B-cell lymphoma (DLBCL) or high-grade B-cell lymphoma (HGBCL) – and the medicines studied – glofitamab and mosunetuzumab.

1. General information about this study

Why was this study done?

Non-Hodgkin's lymphoma (NHL) is a cancer of the lymph nodes. In this type of cancer, white blood cells grow abnormally and form tumours throughout the body.

Most NHL cases affect B-cells, which are a type of white blood cell. There are different types of NHL. Diffuse large B-cell lymphoma is the most common type of NHL. High grade B-cell lymphoma is another type of NHL.

People with DLBCL or HGBCL may be given several different types of treatment, including:

- Chemotherapy – medicines that kill cancer cells in the body
- Immunotherapy – medicines that help the body's immune system to attack tumours
- Bone marrow transplant (also called stem cell transplant)– a procedure where healthy stem cells that produce blood are infused into the body to replace unhealthy or damaged bone marrow stem cells.

There is a need for new treatment options for people with DLBCL or HGBCL. The people in this study had previously been given medicine for DLBCL or HGBCL, but this medicine did not work (refractory lymphoma), or the cancer came back after treatment (relapsed lymphoma).

This study looked at whether a medicine called glofitamab or a medicine called mosunetuzumab in combination with chemotherapy called gemcitabine and oxaliplatin were safe and worked for people with relapsed or refractory DLBCL or HGBCL.

What were the study medicines?

Glofitamab and mosunetuzumab were the main medicines that were studied. The other medicines studied were obinutuzumab, tocilizumab, gemcitabine and oxaliplatin.

- **Glofitamab** is one of the main medicines that was studied here.
- You say this as 'glow – fit – ah – mab'.
- It is a new type of immunotherapy molecule called a bispecific antibody. Antibodies are a type of blood protein normally made by the immune system to help defend the body against infection and cancer. Glofitamab is called a bispecific antibody because it has two antibody arms. One arm attaches to the surface of a type of white blood cell called B cells, including the cancer cells that cause DLBCL or HGBCL. The other arm recognises another type of white blood cell called T cells. T cells are important for the body's immune system and can help destroy cancer cells.

- By binding to both B cells and T cells, the medicine acts like a bridge to bring the T cells near the cancerous B cells. This encourages the T cells to destroy the cancer cells
- **Mosunetuzumab** is one of the main medicines that was studied here.
- You say this as 'moe – sun – e – tooz – ue – mab'.
- It is a new type of immunotherapy molecule called a bispecific antibody. Antibodies are a type of blood protein normally made by the immune system to help defend the body against infection and cancer. Mosunetuzumab is called a bispecific antibody because it has two arms. One arm attaches to the surface of a type of white blood cell called B cells, including the cancer cells that cause DLBCL or HGBCL. The other arm recognises another type of white blood cell called T cells. T cells are important for the body's immune system and can help destroy cancer cells.
- By binding to both B cells and T cells, the medicine acts like a bridge to bring the T cells near the cancerous B cells. This encourages the T cells to destroy the cancer cells
- **Obinutuzumab** is a medicine that was studied here.
- You say this as 'oh – bin – oo – too – zoo – mab'.
- It is a type of immunotherapy called a monoclonal antibody. Obinutuzumab attaches to the surface of B cells. It was given to people before they received glofitamab to help prevent a possible side effect called cytokine release syndrome. Cytokine release syndrome can happen when the immune system reacts too strongly to drugs like glofitamab.
- **Tocilizumab** is a medicine that was studied here.
- You say this as 'toe – si – liz – oo – mab'
- It helps treat a possible side effect called cytokine release syndrome. Cytokine release syndrome can happen when the immune system reacts too strongly to drugs like glofitamab or mosunetuzumab.
- **Gemcitabine** is a medicine that was studied here.
- You say this as 'gem – sigh – ta – been'
- It is a chemotherapy medicine used to kill cancer cells.
- It is currently used to treat people with DLBCL or HGBCL.
- **Oxaliplatin** is a medicine that was studied here.
- You say this as 'ox – al – ee – pla – tin'
- It is a chemotherapy medicine used to kill cancer cells.
- It is currently used to treat people with DLBCL or HGBCL

What did researchers want to find out?

In this study people were selected to get 1 of 2 treatments. People in **Group A** were treated with glofitamab and chemotherapy (gemcitabine and oxaliplatin) and people in **Group B** were treated with mosunetuzumab and chemotherapy (gemcitabine and oxaliplatin).

- Researchers did this study

- to find out how safe glofitamab was in combination with chemotherapy by checking how many people had side effects and seeing how serious the side effects were (see section 5 “What were the side effects?”)
- to find out how safe mosunetuzumab was in combination with chemotherapy by checking how many people had side effects and seeing how serious the side effects were (see section 5 “What were the side effects?”).
- They also wanted to find out
 - how well glofitamab worked in combination with chemotherapy (see section 4 “What were the results of the study?”).
 - how well mosunetuzumab worked in combination with chemotherapy (see section 4 “What were the results of the study?”).

The main questions that researchers wanted to answer were:

1. What side effects did people with DLBCL or HGBCL have when treated with glofitamab and chemotherapy?
2. What side effects did people with DLBCL or HGBCL have when treated with mosunetuzumab and chemotherapy?

Other questions that researchers wanted to answer included:

3. How many people with DLBCL or HGBCL had smaller or no tumours after receiving treatment with glofitamab and chemotherapy?
4. How many people with DLBCL or HGBCL had smaller or no tumours after receiving treatment with mosunetuzumab and chemotherapy?

What kind of study was this?

This study was a ‘Phase 1b’ study, which means that this was one of the first studies for glofitamab and mosunetuzumab in combination with chemotherapy for people with DLBCL or HGBCL. In this study, people with DLBCL or HGBCL took glofitamab and chemotherapy or mosunetuzumab and chemotherapy to find out about the safety of glofitamab and mosunetuzumab and to see if glofitamab or mosunetuzumab worked with chemotherapy to treat DLBCL or HGBCL.

This was an ‘open label’ study. This means that both the people taking part in the study and the study doctors knew what study drugs people were taking.

When and where did the study take place?

The study started in June 2020 and finished in October 2021. This summary was written after the study had ended.

The study took place at 3 study centres across Australia.

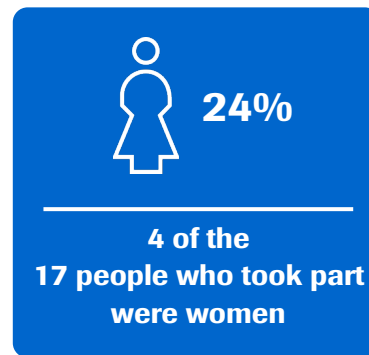
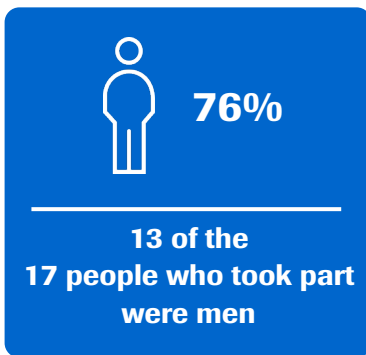
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2. Who took part in this study?

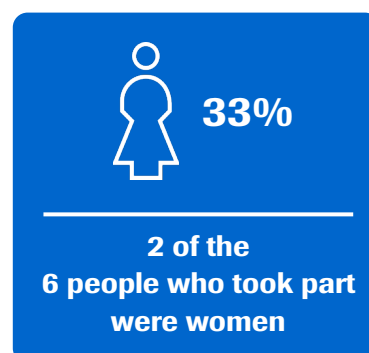
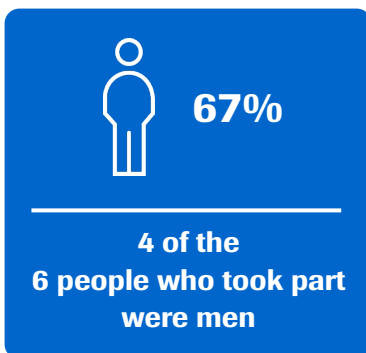
In this study, 23 people with DLBCL or HGBCL took part. There were two study groups, which are described in more detail in the next section. People in Group A took glofitamab and chemotherapy and people in Group B took mosunetuzumab and chemotherapy. There were 17 people in Group A, and 6 people in Group B.

Group A



Age range: 50 to 78 years old

Group B



Age range: 34 to 84 years old

People could take part in the study if:

- They had DLBCL or HGBCL.
- They previously had at least one treatment for DLBCL or HGBCL, but the treatment did not work, or the cancer came back.

- There was no other treatment that was expected to work.

People could not take part in the study if:

- Their doctor thought they should have a stem cell transplant to treat the disease.
- They had previously taken any medicines that work in a similar way to glofitamab or mosunetuzumab.
- They had previously taken glofitamab or mosunetuzumab.
- They had lymphoma that had spread to the brain or spinal cord.

3. What happened during the study?

During the study, people were selected to get 1 of 2 treatments.

The treatment groups were:

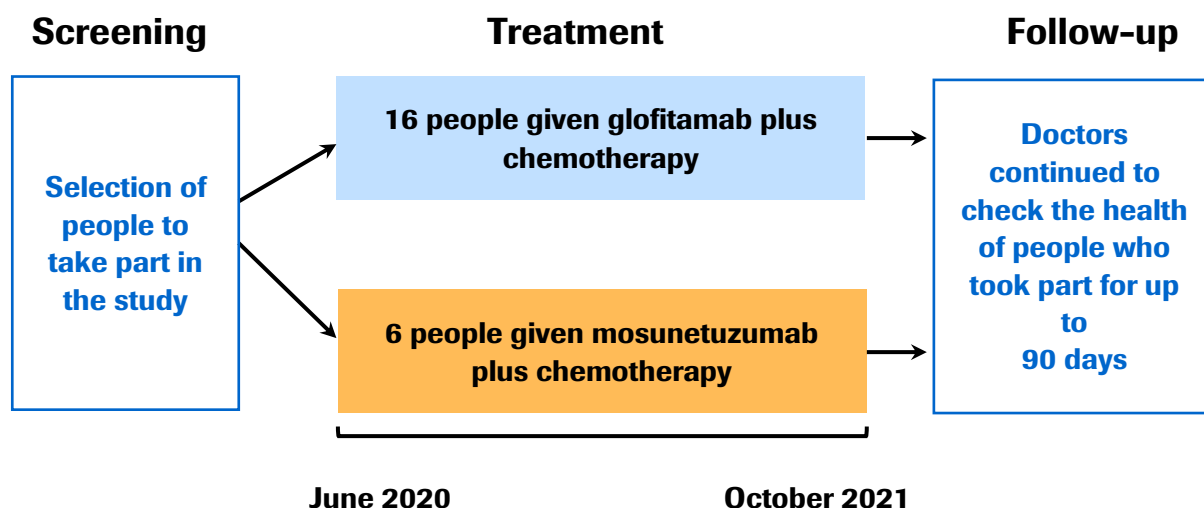
- **Group A** – people with DLBCL or HGBCL who were treated with glofitamab in combination with gemcitabine and oxaliplatin. People were given one dose of obinutuzumab before they received the first dose of glofitamab in combination with chemotherapy.
- **Group B** – people with DLBCL who were treated with mosunetuzumab in combination with gemcitabine and oxaliplatin.

The medicines in this study were given in “treatment cycles”.

- Each treatment cycle lasted 3 weeks.
- People in **Group A** received obinutuzumab on Day 1, gemcitabine and oxaliplatin on Day 2, and glofitamab on Day 8 and Day 15 of the first treatment cycle. From the second treatment cycle, people in Group A received glofitamab, gemcitabine and oxaliplatin on Day 1 of each treatment cycle. After 8 cycles of treatment, people received only glofitamab on Day 1 of each treatment cycle for 4 cycles. People stopped taking treatment after 12 treatment cycles.
- People in **Group B** received mosunetuzumab on Day 1, 8 and 15, and gemcitabine and oxaliplatin on Day 2 of the first treatment cycle. From the second treatment cycle, people in Group A received mosunetuzumab, gemcitabine and oxaliplatin on Day 1 of each treatment cycle. People stopped taking treatment after 8 treatment cycles.
- Tocilizumab was only given to people in Group A or Group B who experienced cytokine release syndrome and had symptoms that needed treatment. Cytokine release syndrome can happen when the immune system reacts too strongly when taking drugs like glofitamab or mosunetuzumab.

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 the treatment groups.



4. What were the results of the study?

Question 1: What side effects did people with DLBCL or HGBCL have when treated with glofitamab and chemotherapy?

Researchers asked people in Group A about any side effects that happened during the study. People in the study also had regular blood tests and measurements of their heart activity, body temperature, pulse rate and blood pressure.

These side effects may or may not be related to the treatment in the study. Some people had more than one side effect.

Side effects may be mild to very serious and can be different from person to person.

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

- 12 out of 16 people (75%) in Group A who received glofitamab had at least one **serious** side effect. The most common **serious** side effects and the number of people who had these serious side effects were:
 - 6 out of 16 people (38%) had fever
 - 3 out of 16 people (19%) had a severe illness in which the body is overwhelmed by infection (sepsis)
 - 2 out of 16 people (13%) had an aggressive immune response (cytokine release syndrome)
 - 2 out of 16 people (13%) had inflammation of the colon (colitis), and
 - 2 out of 16 people (13%) had a low number of a type of white blood cell (neutropenia).
- All patients (100%) in Group A had at least one side effect. The most common side effects – experienced by at least 1 in 10 (10%) of people – were:
 - 8 out of 16 people (50%) had an aggressive immune response (cytokine release syndrome)
 - 7 out of 16 people (44%) had diarrhoea

- 6 out of 16 people (38%) had nerve problems of burning, numbness and tingling
- 6 out of 16 people (38%) had fever
- 6 out of 16 people (38%) had low number of red blood cells (anaemia)
- 5 out of 16 people (31%) had low number of blood platelets (blood cell fragments that help to clot blood - thrombocytopenia)
- 5 out of 16 people (31%) had a low number of a type of white blood cells (neutropenia), and
- 5 out of 16 people (31%) had decreased blood level of magnesium.

Question 2: What side effects did people with DLBCL or HGBCL have when treated with mosunetuzumab and chemotherapy?

Researchers asked people in Group B about any side effects that happened during the study. People in the study also had regular blood tests and measurements of their heart activity, body temperature, pulse rate and blood pressure.

These side effects may or may not be related to the treatment in the study. Some people had more than one side effect.

Side effects may be mild to very serious and can be different from person to person. A side effect is considered 'serious' if it is life-threatening, needs hospital care, or causes lasting problems.

- 4 out of 6 people (67%) in Group B had at least one **serious** side effect. The serious side effects were:
 - 2 out of 6 people (33%) had a fall
 - 1 out of 6 people (17%) had life-threatening confusion
 - 1 out of 6 people (17%) had lack of energy
 - 1 out of 6 people (17%) had a urinary tract infection
 - 1 out of 6 people (17%) had diarrhoea
 - 1 out of 6 people (17%) had an aggressive immune response (cytokine release syndrome)
 - 1 out of 6 people (17%) had liver damage (cirrhosis), and
 - 1 out of 6 people (17%) had fever.
- All patients (100%) in Group B had at least one side effect. The most common side effects – experienced by at least 2 people – were:
 - 5 out of 6 people (83%) had diarrhoea
 - 4 out of 6 people (67%) had nausea
 - 4 out of 6 people (67%) had fatigue
 - 4 out of 6 people (67%) had a decreased blood level of magnesium
 - 4 out of 6 people (67%) had a decreased blood level of phosphate
 - 3 out of 6 people (50%) had constipation

- 3 out of 6 people (50%) had a fall
- 3 out of 6 people (50%) had a low number of red blood cells (anaemia)
- 3 out of 6 people (50%) had a urinary tract infection
- 3 out of 6 people (50%) had nerve problems of burning, numbness and tingling
- 2 out of 6 people (33%) had swelling especially of the ankles and feet
- 2 out of 6 people (33%) had bruising
- 2 out of 6 people (33%) had low blood potassium levels
- 2 out of 6 people (33%) had inflammation in a vein leading to a blood clot
- 2 out of 6 people (33%) had low blood platelet counts
- 2 out of 6 people (33%) had thrush, a fungal infection caused by Candida
- 2 out of 6 people (33%) had an increased blood level of liver enzymes (ALT/SGPT)
- 2 out of 6 people (33%) had an increased blood level of liver enzymes (AST/SGOT)

Question 3: How many people with DLBCL or HGBCL had smaller or no tumours after receiving treatment with glofitamab and chemotherapy?

Another piece of information that researchers collected was how many people in Group A had smaller or no tumours during the study – compared to the start of the study.

- 6 out of 17 people (35%) had smaller or no tumours.

Question 4: How many people with DLBCL or HGBCL had smaller or no tumours after receiving treatment with mosunetuzumab and chemotherapy?

Another piece of information that researchers collected was how many people in Group B had smaller or no tumours during the study – compared to the start of the study.

- 3 out of 6 people (50%) had smaller or no tumours.

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 from glofitamab and mosunetuzumab?

Side effects are medical problems (such as feeling tired or having an infection) that happen during the study.

- This section describes side effects that the study doctor believed were **related to treatment with glofitamab or mosunetuzumab**.
- 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.

4 out of 16 people (25%) given glofitamab and chemotherapy (Group A) had at least one serious side effect **from glofitamab**. One of the 17 patients in Group A did not receive glofitamab because they were not well enough.

2 out of 6 people (33%) given mosunetuzumab and chemotherapy (Group B) had at least one serious side effect **from mosunetuzumab**.

The most common serious side effects are shown in the following tables. Some people had more than one side effect – this means that they are included in more than one row in the table.

Group A

Serious side effects reported in this study (Group A) <u>from glofitamab</u>	People taking glofitamab and chemotherapy (16 people total)
Aggressive immune response (cytokine release syndrome)	13% (2 out of 16)
Fever	6% (1 out of 16)
Vomiting	6% (1 out of 16)

Group B

Serious side effects reported in this study (Group B) <u>from mosunetuzumab</u>	People taking mosunetuzumab and chemotherapy (6 people total)
Aggressive immune response (cytokine release syndrome)	17% (1 out of 6)
Life-threatening confusion	17% (1 out of 6)
Urinary tract infection	17% (1 out of 6)
Liver damage (cirrhosis)	17% (1 out of 6)

No people in the study died due to side effects that may have been related to one of the study medicines.

No people decided to stop taking their medicine because of side effects.

Most common side effects

During this study, 14 out of 16 people (88%) who received glofitamab had at least one side effect **from glofitamab**.

During this study, all 6 out of 6 people (100%) in Group B had at least one side effect **from mosunetuzumab**.

The most common side effects are shown in the following tables – these are the side effects experienced by at least 1 in 10 (10%) in Group A and at least 2 patients in Group B. Some people had more than one side effect – this means that they are included in more than one row in the tables.

Group A

Most common side effects reported in this study (Group A) <u>from glofitamab</u>	People taking glofitamab (16 people total)
Aggressive immune response (cytokine release syndrome)	50% (8 out of 16)
Fatigue	13% (2 out of 16)
Abnormal blood levels of liver enzymes and proteins	13% (2 out of 16)
Low levels of a type of white blood cells (neutropenia)	13% (2 out of 16)
Sudden reddening of the face and/or neck (flushing)	13% (2 out of 16)

Group B

Most common side effects reported in this study (Group B) from mosunetuzumab	People taking mosunetuzumab (6 people total)
Low number of red blood cells (anaemia)	50% (3 out of 6)
Urinary tract infection	50% (3 out of 6)
Decreased blood level of phosphate	50% (3 out of 6)
Nausea	33% (2 out of 6)
Increased blood level of liver enzymes (ALT/SGPT)	33% (2 out of 6)
Increased blood level of liver enzymes (AST/SGOT)	33% (2 out of 6)

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 23 people with DLBCL or HGBCL. These results helped researchers learn more about DLBCL and HGBCL and glofitamab and mosunetuzumab.

This study looked at whether it was safe to give people with DLBCL or HGBCL glofitamab and chemotherapy or mosunetuzumab and chemotherapy. It also looked at whether these medicines made the cancer smaller or go away altogether.

In Group A, the most common side effects from glofitamab were an aggressive immune response (cytokine release syndrome), fatigue, abnormal blood levels of liver enzymes and proteins, low levels of a type of white blood cell (neutrophils) and sudden reddening of the face and/or neck.

4 out of 16 people (25%) had at least one serious side effect from glofitamab. These included an aggressive immune response (cytokine release syndrome), fever and vomiting.

In Group B, the most common side effects from mosunetuzumab were a lack of enough red blood cells (anaemia), urinary tract infections, decreased blood level of phosphate, nausea and increased blood level of liver enzymes. 2 out of 6 people (33%) had at least one serious side effect from mosunetuzumab. These included an aggressive immune response (cytokine release syndrome), life-threatening confusion, urinary tract infection and liver damage.

People in this study did not have side effects that the researchers were not expecting them to have. These side effects were noted in other studies where the same medicines had been taken as a single medicine without chemotherapy.

It was difficult to determine how well glofitamab or mosunetuzumab worked in this study since only a small number of people were treated with these medicines.

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 glofitamab and mosunetuzumab 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/results/NCT04313608>
- <https://forpatients.roche.com/en/trials/cancer/non-hodgkins-lymphoma/a-study-evaluating-the-safety-and-efficacy-of-ro7082859-57995.htm>

Who can I contact if I have questions for 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-evaluating-the-safety-and-efficacy-of-ro7082859-57995.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 Evaluating the Safety and Efficacy of Glofitamab or Mosunetuzumab in Combination With Gemcitabine Plus Oxaliplatin in Participants With Relapsed or Refractory Diffuse Large B-Cell Lymphoma and High-Grade Large B-Cell Lymphoma”.

- The protocol number for this study is: G041943.
- The ClinicalTrials.gov identifier for this study is: NCT04313608.