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Newer antibodies against CD20

Newer antibodies against CD20 are beginning to offer alternatives to rituximab for some people with lymphoma.

On this page

We have separate information about the topics in **bold font**. Please get in touch if you'd like to request copies or if you would like further information about any aspect of lymphoma. Phone 0808 808 5555 or email **information@lymphoma-action.org.uk**.

Antibodies targeting CD20

All cells have different antigens (proteins) on their surface. CD20 is a protein on B cells (the white blood cells that are abnormal in **B-cell lymphomas**).

Antibodies bind (stick) to antigens on cells so your **immune system** can recognise and destroy the cell the antibody is attached to. Antibodies are produced naturally by your body to fight infection. **Antibody treatments** are made in a laboratory and are designed to bind a specific target on a cell.

Rituximab was the first antibody targeting CD20 to be approved to treat people with lymphoma. It allows your immune system to target cells it is bound to, including lymphoma cells. Your body can then get rid of the targeted cells. Rituximab is now used as part of treatment for many people with lymphoma.

There are newer antibodies that, like **rituximab**, target the CD20 antigen. Because CD20 is only on B cells, these are mainly used to treat **B-cell lymphomas**.

There are two newer antibodies targeting CD20 that are already approved for some people with lymphoma:

- **ofatumumab**
- **obinutuzumab**.

Ofatumumab (Arzerra®)

Ofatumumab is an antibody that binds to a slightly different part of CD20 to rituximab. It also binds to CD20 for longer than rituximab.

Who can have it?

At the time of writing, ofatumumab is only **approved in Europe** for **chronic lymphocytic leukaemia (CLL)**. It might be available for other types of lymphoma in **clinical trials**.

Ofatumumab can be used for:

- People with CLL who are having treatment for the first time and who can't have fludarabine (a **chemotherapy** drug often used as part of the first treatment for CLL). Ofatumumab is given with chlorambucil or bendamustine chemotherapy.
- People with CLL that has **relapsed** (come back). It is given with the chemotherapy drugs fludarabine and cyclophosphamide.
- People whose CLL did not respond ('refractory') to previous treatments with fludarabine and alemtuzumab (another **targeted drug**). Ofatumumab is given on its own in this case.

Is it available on the NHS in the UK?

You might be able to have ofatumumab **on the NHS** if you are having your first treatment for CLL and you can't have fludarabine or bendamustine, for example because you have other health conditions that mean it would be unsafe for you to have them.

You won't be able to have ofatumumab on the NHS if you have already had treatment for your CLL. It has been **assessed** for refractory CLL, but it is not funded for this use in the UK.

Benefits

For first-line treatment of CLL, ofatumumab was tested in a major clinical trial of 447 people who had not yet had treatment for their CLL but who couldn't have fludarabine. In the trial, some people were given chlorambucil chemotherapy alone and others were given chlorambucil with ofatumumab. The people who had ofatumumab and chlorambucil lived for nearly twice as long without their CLL getting worse than those who just had chlorambucil (22 months compared with 13 months).

Ofatumumab was tested in a clinical trial of 223 people who had previously had fludarabine or alemtuzumab and had not responded to treatment. Ofatumumab was not compared with another treatment in this trial. Half of the people who had ofatumumab responded to the treatment.

Ofatumumab has also been tested in clinical trials for people who have had other treatments but whose CLL gas come back. It may increase the time it takes for CLL to get worse in these people.

How is it given?

Ofatumumab is given intravenously (into a vein). It can take several hours to have a dose of ofatumumab.

For the first dose, you have only a small amount of ofatumumab. You start the treatment at a low rate of infusion (how quickly it is given into your vein) that is increased gradually. These precautions allow your medical team to see how the treatment affects you and manage any side effects. You also have other treatments like paracetamol, antihistamines (anti-allergy drugs) and **steroids** to help prevent side effects. If you do have problems, the infusion might be slowed down again, or stopped.

If you don't have troublesome side effects, you have your first full dose a week later.

If it is part of your first treatment for CLL, you then have ofatumumab monthly for up to 11 more doses.

Possible side effects

All medicines can cause **side effects** (unwanted effects of treatment). As ofatumumab is a new treatment, more information about possible side effects is still being gathered.

Ofatumumab can cause infusion-related side effects (effects that occur while the treatment is given or shortly afterwards), such as shivers, fevers, headache and other flu-like symptoms. Severe reactions can occur. They can make you feel very ill. If you have a severe reaction, you have treatment to manage the symptoms and ofatumumab might be stopped until you are better. These infusion reactions are more common with your first infusion, which is why the first dose is given slowly and at a low dose. The other medicines you have before and during your ofatumumab infusion help to reduce your risk of severe infusion reactions.

Other common side effects (effects that occur in more than 1 in every 10 people) include:

- increased risk of infection (including colds, sore throat and pneumonia)
- **neutropenia** (a drop in the number of neutrophils in your blood. Neutrophils are a type of white blood cell that fights infection – neutropenia can increase your risk of infection)
- **anaemia** (shortage of red blood cells)
- **nausea** (feeling sick) and diarrhoea (loose stools)
- fever (high temperature)
- rash
- difficulty breathing and cough
- fatigue (extreme tiredness).

Serious complications are not common but could include:

- tumour lysis syndrome (complications caused by the rapid breakdown of lymphoma cells)
- bowel obstruction (blockage)
- very rarely, progressive multifocal leukoencephalopathy (PML), which is a viral brain infection.

This is not a complete list of side effects that have been reported. Ask your **medical team** for the most up-to-date information about possible side effects. Ask all the questions you have. You also need to tell your medical team about any other conditions you have and any medicines, supplements or complementary therapies you are taking before you start any new treatment.

Are there any other precautions?

As ofatumumab reduces the number of B cells in your body, it can affect your response to **vaccinations.** You should not have any live vaccines (for example, the shingles vaccine) during your treatment and after treatment until the number of B cells in your blood has returned to normal. Talk to your doctor about the risks and benefits of any other vaccinations before you have them.

If you've ever had hepatitis B (an infection of your liver), you might need antiviral treatment to prevent the infection flaring up while you are having ofatumumab. If you have active hepatitis B, you won't be able to have ofatumumab until it is under control.

You need to be monitored closely if you have heart problems. You might need to have tests to see how well your heart is working before you start treatment.

People who are pregnant should not usually have ofatumumab during their pregnancy in case it could harm the unborn baby. You must use contraception to prevent pregnancy for at least 12 months after treatment and you must not breastfeed for the same period.

Obinutuzumab (Gazyvaro®)

Obinutuzumab is an antibody that has been modified to bind more tightly to CD20 than rituximab. It was previously known as GA101.

Who can have it?

At the time of writing, obinutuzumab is only **approved in Europe** for the following types of lymphoma. It might be available for other types of lymphoma in **clinical trials**.

Chronic lymphocytic leukaemia (CLL)

Obinutuzumab can be used:

- In combination with chlorambucil **chemotherapy** for people who need their first treatment for CLL and who can't have fludarabine (a type of chemotherapy often used as part of the first treatment for CLL).
- In combination with the targeted drug **venetoclax** for people with CLL who have not been treated before.

Follicular lymphoma

Obinutuzumab can be used for:

- People who need their first treatment for **advanced-stage** follicular lymphoma. It is given with **chemotherapy** and followed by **obinutuzumab maintenance**.
- People whose lymphoma was refractory (didn't respond) to treatment containing rituximab or whose lymphoma got worse during or within 6 months after treatment containing rituximab. It is given with bendamustine chemotherapy.

Is it available on the NHS?

Some people with CLL and follicular lymphoma might be able to have obinutuzumab as part of their treatment on the NHS.

CLL

You might be able to have obinutuzumab with chlorambucil on the NHS as a **first treatment for CLL** if you can't have fludarabine or bendamustine.

Follicular lymphoma

You can only have obinutuzumab on the NHS as part of your **first treatment for follicular lymphoma** if you have risk factors that mean your lymphoma is at moderate or high risk of getting worse soon after treatment. This is because evidence from clinical trials showed that people with these risk factors are more likely to benefit from having obinutuzumab instead of the usual treatment of rituximab with their chemotherapy. People in Scotland can't currently have obinutuzumab as part of their first treatment as it has not been recommended by the Scottish Medicines Consortium (SMC).

If you previously had rituximab as part of your treatment and your lymphoma did not respond or got worse within 6 months, obinutuzumab with bendamustine is available on the NHS.

Benefits

Clinical trials have shown that obinutuzumab could be more effective than rituximab for some people.

CLL

Clinical trials have been done in people with CLL who had other health conditions that meant they couldn't have fludarabine. The results showed that adding obinutuzumab to chlorambucil more than doubled the time people lived without their CLL getting worse compared with chlorambucil alone. Obinutuzumab with chlorambucil also significantly improved outcomes compared with rituximab with chlorambucil.

Follicular lymphoma

For people with untreated advanced-stage follicular lymphoma, obinutuzumab with chemotherapy slightly increases the time people live without their lymphoma getting worse compared with rituximab and chemotherapy. However, the new combination can cause more **side effects**. People with higher-risk untreated follicular lymphoma might particularly benefit from having obinutuzumab instead of rituximab.

Adding obinutuzumab to bendamustine chemotherapy for people with follicular lymphoma that has relapsed shortly after having rituximab or didn't respond to rituximab significantly improves outcomes. People having obinutuzumab with bendamustine live, on average, more than twice as long without their lymphoma getting worse than those who have bendamustine alone.

How is it given?

Obinutuzumab is given intravenously (into a vein). It takes several hours to have each dose.

CLL

For CLL, obinutuzumab is given slowly to begin with. You have a small amount of the drug at first and it is given at a slow infusion rate (how quickly it is given into your vein). You have the rest of the dose later the same day or the following day. The infusion rate may be increased gradually. You are closely monitored for side effects. If you do have problems, the infusion might be slowed down again, or stopped.

You have obinutuzumab twice more in the first month. You then have obinutuzumab once every 4 weeks. Each 4-week period is a cycle of treatment. You can have up to 6 cycles in total.

Follicular lymphoma

For follicular lymphoma, you have obinutuzumab once a week for 3 weeks. You then have obinutuzumab once every 3 or 4 weeks, depending on what chemotherapy you are having with it. You can have 6 to 8 cycles of obinutuzumab.

If you have follicular lymphoma and you responded to treatment with obinutuzumab, you might then have **maintenance therapy**. Maintenance therapy is given after initial treatment has put the lymphoma into **remission** (no evidence of lymphoma on scans). It aims to make your remission last longer. For maintenance, obinutuzumab is given every 2 months for up to 2 years.

Possible side effects

All medicines can cause **side effects** (unwanted effects of treatment). As obinutuzumab is a new treatment, more information about possible side effects is still being gathered.

Obinutuzumab can cause infusion-related side effects (effects that occur while the treatment is given or shortly afterwards), such as shivers, fevers, headache and other flu-like symptoms. Severe reactions can occur. They can make you feel very ill. If you have a severe reaction, you have treatment to manage the symptoms and ofatumumab might be stopped until you are better. Infusion reactions are more common with your first infusion, which is why the first dose is given slowly and at a low dose. You are given other medicines (for example, paracetamol and antihistamines) before and during the obinutuzumab infusion to reduce your risk of severe infusion reactions.

Other common side effects (effects that occur in more than 1 in every 10 people) of obinutuzumab include:

- increased risk of infection (for example colds, sore throats, pneumonia, urinary tract infections, cold sores)
- **neutropenia** (a drop in the number of neutrophils you have, a type of white blood cell) and leucopenia (low white blood cells of different types)
- increased risk of bruising and bleeding because of **thrombocytopenia** (low platelets)
- **anaemia** (low red blood cells)
- cough
- joint pain
- headache
- fever
- weakness
- difficulty sleeping
- **hair loss**
- itching
- **diarrhoea** or **constipation**.

Serious complications are not common but could include:

- tumour lysis syndrome (complications caused by the rapid breakdown of cancer cells)
- severe infections
- worsening of existing heart conditions
- very rarely, progressive multifocal leukoencephalopathy (PML), which is a viral brain infection.

This is not a complete list of side effects that have been reported. Ask your **medical team** for the most up-to-date information about possible side effects. Ask all the questions you have. You also need to tell your medical team about any other conditions you have and any medicines, supplements or complementary therapies you are taking before you start any new treatment.

Are there any other precautions?

As ofatumumab reduces the number of B cells in your body, it can affect your response to **vaccinations**. You should not have any live vaccines (for example, the shingles vaccine) during your treatment and after treatment until the number of B cells in your blood has returned to normal. Talk to your doctor about the risks and benefits of any other vaccinations before you have them.

If you've ever had hepatitis B (an infection of your liver), you might need antiviral treatment to prevent it flaring up while you are having ofatumumab. If you have active hepatitis B, you won't be able to have obinutuzumab until it is under control.

You need to be monitored closely if you have heart problems. You might need to have tests to see how well your heart is working before you start treatment.

People who are pregnant should not usually have obinutuzumab during their pregnancy in case it could harm the unborn baby. You should use contraception to prevent pregnancy for at least 18 months after treatment and you must not breastfeed for the same period.

References

The full list of references for this page is available on our website. Alternatively, email **publications@lymphoma-action.org.uk** or call 01296 619409 if you would like a copy.

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