

# Chronic Lymphocytic Leukemia (CLL): Targeted Therapy



## What is targeted therapy?

Targeted therapy is the use of medicines that take aim at parts of cancer cells that make them different from normal cells. This means they can damage cancer cells without affecting most normal, healthy cells. These medicines are different from standard chemotherapy (chemo) medicines. And they have different side effects.

When CLL needs to be treated, targeted therapy is often part of the first treatment used.

## Types of targeted therapy for CLL

### Monoclonal antibodies

This is a kind of targeted therapy that uses antibodies made in a lab. The antibodies are like those your immune system makes naturally. They attach to proteins on CLL cells and kill the cells or stop them from growing.

Monoclonal antibodies are often used alone, with other targeted therapy, or with chemo as part of the first treatment for CLL. They may also be used if other treatments don't work, or if the leukemia comes back after treatment. They might be the only treatment used for someone who's too sick to get chemo.

Monoclonal antibodies used to treat CLL include:

- Rituximab
- Ofatumumab
- Obinutuzumab
- Alemtuzumab

### BTK (Bruton tyrosine kinase) inhibitors

These medicines block BTK inside leukemia cells. BTK normally helps cancer cells grow and survive.

BTK inhibitors used to treat CLL include:

- Ibrutinib
- Acalabrutinib
- Zanubrutinib

### Venetoclax

This medicine is a BCL-2 inhibitor. It targets the BCL-2 protein in CLL cells that helps them live longer than they should. It's taken as a pill. It can be used alone or with a monoclonal antibody.

### PI3K inhibitors

PI3K is a protein that helps cells grow and survive. These medicines block this protein, which kills CLL cells and keeps them from growing. They may be used if other treatments stop working. They're taken every day as a pill.

- Idelalisib
- Duvelisib

## How targeted therapy is done

Monoclonal antibodies are given through a small, flexible tube that's put into a vein by IV (intravenously), often over several hours. They may be given in a healthcare provider's office, infusion clinic, or in the outpatient department of a hospital. These medicines sometimes cause allergic reactions while they're being given. This reaction may be serious in some people. Before treatment starts, you may be given medicine to help lower the chance of an allergic reaction. Treatments might be given anywhere from once a month to several times a week. Sometimes monoclonal antibodies are given along with chemo.

Kinase inhibitors are taken as pills or capsules each day. Even though they're taken as pills, these are strong medicines that can sometimes have serious side effects. It's very important to take these medicines exactly as your healthcare provider tells you.

Tell your healthcare provider about all other medicines you take. This includes over-the-counter and prescription medicines, and supplements such as herbs and vitamins. Also tell them if you use any form of marijuana or any illegal drugs. Some medicines and supplements can change the way targeted therapy medicines work.

During treatment, blood tests will be done regularly. These are needed to check for changes in your levels of white or red blood cells or platelets. Blood tests tend to be done more often at the very start of treatment.

## Possible side effects of monoclonal antibodies

The main side effects of monoclonal antibody therapy are headache, itching, fever, and chills during treatment. The fever may be high. It often goes down when the treatment is slowed or stopped. Some people have rashes. In rare cases, people may have more serious problems. These include trouble breathing, face and tongue swelling, feeling faint, and low blood pressure. These problems are most common with the first treatment. But because of these problems, medicines are given before each treatment to help prevent them.

You may also get an infection more easily. This is because these medicines can damage your immune system cells. This problem can sometimes be very serious with the medicine alemtuzumab. It can cause very low white blood cell counts. You may get antibiotics or antiviral medicines ahead of time to help reduce the risk of infection.

Other side effects include:

- Nausea
- Swelling
- Feeling very tired (fatigue)
- Headache
- Constipation or diarrhea
- Low blood cell counts, which can increase the risk of not only infection but also bleeding and bruising

Less common, but serious side effects can include:

- Allergic reactions
- The hepatitis virus becoming active again in the body. This is true only if it's already in your body from an old infection.

In rare cases, these medicines can cause tumor lysis syndrome. This can happen if you have very high white blood cell counts. Treatment kills the cancer cells so fast that the kidneys can't get rid of the waste products of

the dead cells fast enough. This can lead to serious health problems, including kidney failure. Extra IV fluids and certain medicines can be used to help keep this from happening.

## Possible side effects of BTK inhibitors, venetoclax, and PI3K inhibitors

These medicines all have the same kinds of side effects. They can include:

- Nausea
- Diarrhea
- Constipation
- Feeling very tired (fatigue)
- Rash
- Body aches
- Shortness of breath
- Low blood cell counts, which can increase the risk of infection, bleeding, and bruising

Less often, there can be more serious side effects, such as:

- Fluid buildup around the heart or lungs. This can cause trouble breathing.
- Serious infections
- Allergic reactions
- Liver damage
- Irregular heartbeat (atrial fibrillation)
- Lung inflammation (pneumonitis)
- Lung infection (pneumonia)
- Holes in the intestines

These medicines can also cause tumor lysis syndrome. This tends to happen if you have very high white blood cell counts. Treatment kills the cancer cells fast, and the waste products of the dead cells build up in the blood. The kidneys can't filter out the cell waste fast enough. This can lead to kidney failure and other serious problems. Extra IV fluids and certain medicines can be used to help keep this from happening.

## Working with your healthcare provider

It's important to know which medicines you're taking. Write down the names of your medicines. Ask your healthcare team how they work, and how and when you'll get them.

Talk with your healthcare providers about what side effects to watch out for, and when you should call your healthcare team. Know what number to call with problems or questions, even on evenings and weekends.

It may be helpful to keep a diary of your side effects. Write down any physical, thinking, and emotional changes. A written list will make it easier for you to remember your questions when you go to your appointments. It will also make it easier for you to work with your medical team to make a plan to manage your side effects.

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