Guide 2. Drug treatment for CLL

Generic name	Brand name (sold as)	Type of treatment
Alemtuzumab	Campath®	Targeted therapy
Bendamustine hydrochloride	Treanda®, Bendeka™	Chemotherapy
Chlorambucil	Leukeran®	Chemotherapy
Cyclophosphamide	–	Chemotherapy
Cytarabine	Cytosar-U®	Chemotherapy
Doxorubicin hydrochloride	–	Chemotherapy
Fludarabine phosphate	Fludara®	Chemotherapy
Ibrutinib	Imbruvica®	Targeted therapy
Idelalisib	Zydelig®	Targeted therapy
Lenalidomide	Revlimid®	Immunotherapy
Methylprednisolone; Methylprednisolone acetate; Methylprednisolone sodium succinate	A-Methapred, Depo-Medrol®, Medrol®, Solu-Medrol®	Steroid
Obinutuzumab	Gazyva™	Targeted therapy
Ofatumumab	Arzerra®	Targeted therapy
Oxaliplatin	Eloxatin®	Chemotherapy
Pentostatin	Nipent®	Chemotherapy
Prednisone	–	Steroid
Rituximab	Rituxan®	Targeted therapy
Venetoclax	Venclexta®	Targeted therapy
Vincristine sulfate	–	Chemotherapy

Steroids

Steroids are a type of drug that is often used to relieve inflammation. Steroids can also have anti-cancer effects. Methylprednisolone is a corticosteroid used to treat CLL. Read Part 4 for more information on when it's used.

Methylprednisolone is given in high doses along with rituximab. Rituximab is described in the *Targeted therapy* section in this chapter. Methylprednisolone can either be injected into your vein or swallowed in pill form. It is often taken for a few days during a 1-month cycle.

Prednisone is another steroid that is used to treat CLL. It is given along with some chemotherapy regimens. Prednisone is made in pill form and is taken once a day with food.

Most side effects of steroids fade away once the drugs are stopped. Common side effects include feeling hungry, trouble sleeping, slow wound healing, upset stomach, and swelling in the ankles, feet, and hands. Methylprednisolone with rituximab increases the likelihood of getting infections.

Immunomodulators

The immune system is your body's natural defense against illness. Immunomodulators are drugs that modify different parts of the immune system. Lenalidomide is an immunomodulator used to treat CLL.

Lenalidomide is made in pill form. It is given in cycles of treatment days followed by days of rest. A cycle may consist of 3 weeks of treatment and 1 week of rest. It may also be given for 4 straight weeks. Cycles may repeat until the cancer grows or side effects become severe.

Lenalidomide treats cancer in more than one way. As an immunomodulator, it boosts the immune system. It also helps stop cancer cells from increasing in number. Third, it also works like a type of targeted therapy called angiogenesis inhibitors. These drugs stop the growth of new blood vessels that would provide food (nutrients) to the cancer.

Common side effects include low blood counts, diarrhea, itching, rash, and fatigue. Serious but less common side effects include blood clots, bleeding disorders, loss of vision, and skin cancer. Ask your treatment team for a full list of side effects.

Targeted therapy

Targeted therapy is a class of drugs that stops the action of molecules that help cancer cells grow. It is less likely to harm normal cells than chemotherapy. There are multiple targeted therapies that are used to treat CLL. They include monoclonal antibodies and kinase inhibitors.

Monoclonal antibodies are man-made antibodies that attach to proteins on cancer cells. The monoclonal antibodies used to treat CLL attach to antigens. When antibodies are attached to antigens on a cell, the cell is marked to be destroyed by your immune system.

Kinases are molecules that move chemicals, called phosphates, from one molecule to another. Kinase inhibitors stop the phosphates from being moved. Kinase inhibitors often block growth signals within cancer cells. This reduces the number of new cancer cells being made.

Next, the targeted therapies for CLL are briefly described. Some side effects are listed. Ask your treatment team for a full list of common and rare side effects. In Part 4, information on who should receive these drugs is provided.

Alemtuzumab

Alemtuzumab is a monoclonal antibody that attaches to a molecule called CD52. CD52 is found on CLL cells, healthy B-cells and T-cells, as well as other cells. Alemtuzumab is used alone and sometimes with other medicines to treat CLL.

Alemtuzumab is a liquid that will be slowly injected into your vein. It may take up to two hours to get the full dose. Alemtuzuamb can also be given as an injection under the skin. Alemtuzumab is often given three times a week for 12 weeks.

Common side effects include an allergic reaction when receiving the medicine. Also, you may feel nausea, vomit, get diarrhea, and have trouble sleeping. Blood counts are often low when taking this medicine. Taking alemtuzumab will increase your chances of getting a cytomegalovirus or other infection.

Ibrutinib

Ibrutinib is a kinase inhibitor. It stops a kinase called BTK (**B**ruton's **t**yrosine **k**inase). This kinase is found inside of CLL cells and normal B-cells.

Ibrutinib is usually taken without other cancer medicines to treat CLL. It is made in pill form and taken once a day around the same time. Your doctor will tell you how many pills you need for your dose.

Common side effects of ibrutinib include diarrhea, tiredness, muscle and bone pain, bruising, nausea, upper respiratory tract infection, and rash. There may be a short-lived increase in lymphocytes when first taking ibrutinib. Serious but uncommon side effects include bleeding, severe infections, heart and kidney problems, and other cancers.

Idelalisib

Idelalisib is a kinase inhibitor. It stops a kinase called PI3K (**p**hospho**i**nositide **3**-**k**inase delta). This kinase is found inside of CLL cells and normal B-cells.

Idelalisib is used alone or sometimes with rituximab to treat CLL. It is made in pill form and is taken twice a day. Your doctor will tell you how many pills you need for your dose.

Common side effects of idelalisib include diarrhea, fever, fatigue, nausea, cough, lung infection, belly pain, chills, and rash. White blood counts are often low when taking this medicine. However, there may be a short-lived increase in lymphocytes when first taking idelalisib.

Serious but uncommon side effects include liver and lung problems, skin problems, severe diarrhea, and holes in your gut.

Venetoclax

Venetoclax is a small molecule inhibitor that targets the BCL-2 protein. This type of targeted therapy stops a function within the cell that helps it survive.

Venetoclax is used alone or sometimes with rituximab to treat CLL. It is recommended for CLL that responds to treatment but comes back (relapsed), or the first treatment doesn't work (refractory). It is made in pill form and is taken once a day.

Common side effects of venetoclax are low blood cells counts, diarrhea, nausea, upper respiratory tract infection, and tiredness. Venetoclax also increases your chances for tumor lysis syndrome. Ask your treatment team for a full list of side effects.

Obinutuzumab

Obinutuzumab attaches to a molecule on CLL cells called CD20. **See Figure 9.** It works by marking cells for destruction but it may directly kill the cells, too. It is used alone and sometimes with chemotherapy to treat CLL.

Obinutuzumab is a liquid that will be slowly injected into your vein. It takes a few hours to get the full dose. Obinutuzumab is given on some days during six 28-day treatment cycles.

You may have an allergic reaction while receiving obinutuzumab. Tumor lysis syndrome, infections, and hepatitis are more likely while taking obinutuzumab. Although not common, you may become confused, dizzy, and have difficulty walking, talking, or seeing.

Ofatumumab

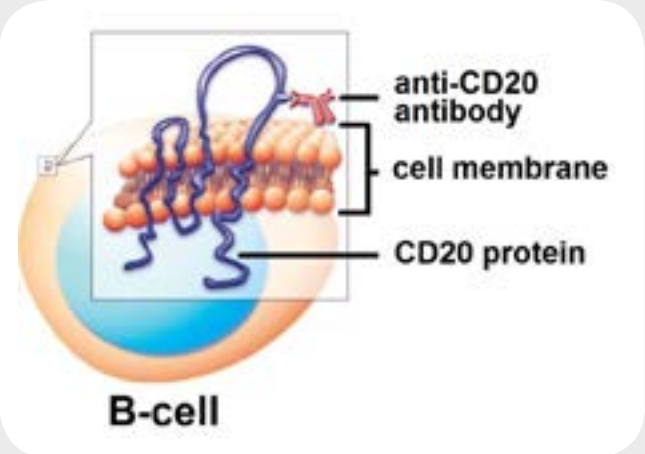
Ofatumumab is another monoclonal antibody that attaches to CD20. However, it attaches to a different part of CD20. It is used alone and sometimes with chemotherapy to treat CLL.

Ofatumumab is a liquid that will be slowly injected into your vein. It takes about 6 hours to receive the first dose. Other doses may be given in less time. Ofatumumab is often given once a week for 8 weeks. Then it's restarted after a 4- or 5-week break. After the break, ofatumumab is often received once a month for four months.

You may have an allergic reaction while receiving ofatumumab. Other common side effects include low blood cell counts, infections, diarrhea, nausea, fatigue, and rash. Hepatitis B can be reactivated while taking ofatumumab.

Figure 9
Anti-CD20 monoclonal antibody

Anti-CD20 monoclonal antibodies attach to CLL cells to mark them for destruction by your immune system.



Rituximab

Like obinutuzumab and ofatumumab, rituximab also attaches to CD20. It works by marking cells for destruction but it may directly kill the cells, too. It is sometimes used alone, with chemotherapy, or with another targeted therapy to treat CLL.

Rituximab is a liquid that will be slowly injected into your vein. It often takes a few hours to receive the full dose. How often you will receive rituximab depends on what other cancer medicines you are receiving.

You may have an allergic reaction while receiving rituximab. Other common side effects are chills, infections, body aches, tiredness, and low blood cell counts. Rituximab also increases your chances for tumor lysis syndrome, heart problems, and blockage and holes in your gut.

Stem cell transplant

Hematopoetic stem cells are cells that develop into mature blood cells. Stem cells and mature blood cells are made in bone marrow. The goal of a stem cell transplant is to cure cancer by replacing unhealthy blood stem cells with healthy ones that will attack cancer cells. This is done by suppressing the bone marrow and cancer with chemotherapy then transplanting healthy blood stem cells. The healthy blood stem cells will grow, form new marrow and blood cells, and attack remaining cancer cells. Using stem cells from a donor is called an allogeneic stem cell transplant. Besides a new immune system, another benefit of this transplant is the GVL (**g**raft-**v**ersus-**l**eukemia) effect. The GVL effect is an attack on cancer cells by the transplanted stem cells.

Allogeneic stem cell transplant is sometimes used to treat CLL. It is an option for some people after drug treatment has been received. The steps of treatment with allogeneic stem cell transplant are described next.

HLA typing

Special testing must be done to find the right donor for you. The donor and your tissue type must be a near-perfect match for this treatment to work. The test used to check tissue type is called HLA (**h**uman **l**eukocyte **a**ntigen) typing. A blood sample is needed to perform the test.

Conditioning chemotherapy

Before the transplant, you will receive chemotherapy. The chemotherapy will suppress your immune system, allowing the donor cells to grow. The high-dose chemotherapy also destroys normal cells in the bone marrow. This greatly weakens your immune system so that your body doesn't kill the transplanted stem cells. Not every person can tolerate the high-dose chemotherapy before the transplant. Side effects of chemotherapy are described earlier in this chapter.

Transplanting stem cells

After chemotherapy, you will receive the healthy stem cells through a transfusion. A transfusion is a slow injection of blood products through a central line into a large vein. A central line (or CVC, **c**entral **v**enous **c**atheter) is a thin tube. The tube will be inserted into your skin through one cut and into your vein through a second cut. Local anesthesia will be used. This process can take several hours to complete.

The transplanted stem cells will travel to your bone marrow and grow. New, healthy blood cells will form. This is called engraftment. It usually takes about 2 to 4 weeks.

Until then, you will have little or no immune defense. You may need to stay in a very clean room at the hospital. You may be given an antibiotic to prevent or treat infection. You may also be given a blood transfusion to prevent bleeding and to treat anemia. While waiting for the cells to engraft, you will likely feel tired and weak.