# Leukemia - Chronic Myeloid - CML - Treatment Options [1]

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**ON THIS PAGE:** You will learn about the different ways doctors use to treat people with CML. To see other pages, use the menu on the side of your screen.

This section outlines treatments that are the standard of care (the best proven treatments available) for this specific type of cancer. When making treatment plan decisions, patients are also encouraged to consider clinical trials as an option. A clinical trial is a research study to test a new approach to treatment to prove it is safe, effective, and possibly better than the standard treatment. Clinical trials may test such approaches as a new drug, a new combination of standard treatments, or new doses of current therapies. Your doctor can help you review all treatment options. For more information, see the Clinical Trials [3] and Latest Research [4] sections.

### Treatment overview

In cancer care, different types of doctors often work together to create a patient?s overall treatment plan that combines different types of treatments. This is called a multidisciplinary team [5].

Descriptions of the most common treatment options for CML are listed below, followed by information on measuring treatment effectiveness and the common treatment recommendations outlined by the disease phase [6]. Treatments for CML have improved greatly in the last 12 years, completely changing how treatment is given and helping many patients live longer.

Treatment options and recommendations depend on several factors, including the phase of the disease, possible side effects, and the patient?s preferences and overall health. Your care plan may also include treatment for symptoms and side effects, an important part of cancer care. Take time to learn about all of your treatment options and be sure to ask questions about things that are unclear. Also, talk about the goals of each treatment with your doctor and what you can expect while receiving the treatment. It is also important to talk with your health care team about the costs of treatment, as many of the drugs discussed below need to be continued throughout a person?s life. Learn more about making treatment decisions [7].

**Targeted therapy**

Targeted therapy is a treatment that attacks the cancer?s specific genes, proteins, or the tissue environment that contributes to cancer growth and survival. This type of treatment blocks the growth and spread of cancer cells while limiting damage to healthy cells. For CML, targeted therapy is given by a medical oncologist, a doctor who specializes in treating cancer with medication, or a hematologist.

Recent studies show that not all cancers have the same targets. To find the most effective treatment, your doctor may run tests to identify the genes, proteins, and other factors involved in your leukemia. As a result, doctors can better match each patient with the most effective treatment whenever possible. In addition, many research studies are taking place now to find out more about specific molecular targets and new treatments directed at them. Learn more about targeted treatments [8].

For CML, the target is the unique protein called the BCR-ABL tyrosine kinase enzyme. There are five drugs currently used to target tyrosine kinase enzymes for CML, called tyrosine kinase inhibitors or TKIs: imatinib (Gleevec), dasatinib (Sprycel), nilotinib (Tasigna), bosutinib (Bosulif), and ponatinib (Iclusig). All five drugs can stop the BCR-ABL enzyme from working, which causes the CML cells to die quickly. These drugs are described in more detail below.

It is important to note that men and women taking TKIs should avoid fathering a child or becoming pregnant while taking the drugs because of risk to the developing child. To find the best treatment, patients should talk with their doctors about the risks and benefits of these drugs, including the possible side effects and how they can be managed. If a patient experiences too many side effects, another TKI can be used instead.

**Imatinib.** Imatinib was the first targeted therapy approved by the U.S Food and Drug Administration (FDA) for CML in 2001. It is taken as a pill once or twice a day and causes fewer side effects than the chemotherapy (see below) used to treat CML in the past. Nearly all patients with chronic phase CML have their blood counts return to normal and their spleen shrink after receiving this drug. Most importantly, 80% to 90% of patients newly diagnosed with chronic phase CML who receive imatinib no longer have detectable levels of cells with the Philadelphia chromosome. Imatinib may also be used to treat some adults with other types of cancer, such as acute lymphoblastic leukemia (ALL) [9] with the presence of the Philadelphia chromosome.

The risk of recurrence for patients whose CML completely responds to imatinib is very low, and patients with few numbers of cells with the Philadelphia chromosome remaining will stay in chronic phase longer by taking imatinib than they might have with previous treatments. Although it is too soon to know how long these responses will last or if patients will be cured with this medication alone, there are many patients who have been treated with imatinib since the first clinical trials in 1999 who still have no detectable cells with the Philadelphia chromosome.

The side effects of imatinib are mild but can include slight nausea, which is very uncommon when imatinib is taken with food, changes in blood counts, fluid retention, swelling around the eyes, fatigue, diarrhea, and muscle cramps.

**Dasatinib.** Dasatinib is approved by the FDA as an initial treatment for patients with newly-diagnosed chronic phase CML and when other drugs are not working. It is a pill that may be taken once or twice a day depending on the dose. The side effects include anemia, a low level of white blood cells called neutropenia, a low level of platelets called thrombocytopenia, and the build-up of fluid around the lungs or heart. The doctor will monitor a patient?s blood counts frequently after starting dasatinib and may adjust the dose or stop giving the drug temporarily if the patient?s blood counts drop too low. Dasatinib may also cause bleeding, fluid retention, diarrhea, rash, headache, fatigue, and nausea. Dasatinib requires stomach acid in order to be absorbed so patients should not take anti-acid medications.

**Nilotinib.** Nilotinib is also approved by the FDA as an initial treatment for patients with newly-diagnosed chronic phase CML and when other drugs are not working. It is a capsule that patients take by mouth twice a day on an empty stomach. Common side effects include low blood counts, rash, headache, nausea, diarrhea, and itching. Other possible but uncommon serious side effects include high blood sugar levels, fluid build up, and swelling of the pancreas or liver. The most serious side effect of nilotinib includes possibly life-threatening heart and blood vessel problems that can lead to an irregular heartbeat, stroke, and possible sudden death. However, this side effect is very rare. However, there can be interactions with other medications that may increase these risks, so be sure to talk with your doctor about all medications you are taking.

**Bosutinib.** In 2012, bosutinib was approved by the FDA to treat CML when one of the other TKIs was not effective or if a patient experienced too many side effects. The most common side effects include diarrhea, nausea and vomiting, low levels of blood cells, abdominal pain, fatigue, fever, allergic reactions, and liver problems.

**Ponatinib.** Ponatinib was also approved by the FDA in 2012 for patients when one of the other TKIs was not effective or if a patient experienced too many side effects. Ponatinib also targets CML cells that have a particular mutation, known as T315I, which makes these cells resistant to other currently approved TKIs. The most common side effects include high blood pressure, rash, abdominal pain, fatigue, headache, dry skin, constipation, fever, joint pain, and nausea. The FDA also warns that this drug may cause heart problems, severe narrowing of blood vessels, blood clots, stroke, or liver problems.

**Measuring treatment effectiveness.** Patients receiving a TKI should receive regular check-ups with the health care team to see how well the treatment is working. The response of CML includes:

- A complete hematologic response: the white blood cell and platelet counts have returned to normal, the spleen is of normal size and cannot be felt on physical examination, and there are no CML symptoms.
- A partial response: the blood counts are still abnormal, there may still be some blasts in the blood, and the spleen may still be enlarged, but the symptoms and blood test results have improved since treatment began. These responses are not stable, and there is a risk that the CML will worsen without more effective treatment. Sometimes this means continuing on the current TKI to see if the treatment helps further or it may mean changing to another TKI.

Other specific tests are used to find the number of cells that have the Philadelphia chromosome

or contain the *BCR-ABL* fusion gene. When CML is diagnosed, the Philadelphia chromosome is found in almost all of a person?s bone marrow and blood cells. Once a person?s CML shows a complete hematologic response, the doctor then looks for a cytogenetic response with tests such as FISH (see Diagnosis [10]).

- A complete cytogenetic response means that there are no cells with the Philadelphia chromosome found on the routine cytogenetic tests.
- A partial cytogenetic response means that between 1% and 35% of the cells still have the Philadelphia chromosome.
- A minor cytogenetic response means that more than 35% of the cells still have the Philadelphia chromosome.

A molecular response is when the PCR test is used to find the *BCR-ABL* fusion gene. A major molecular response means that a very small number of cells (more than 1,000 times fewer than when diagnosed) with the *BCR-ABL* fusion gene are found in the bone marrow or peripheral blood. A complete molecular response is when no cells with the *BCR-ABL* fusion gene are found in the bone marrow or peripheral blood.

An important goal of treatment is to achieve a complete cytogenetic response. This requires performing a bone marrow biopsy and is generally done three to six months after starting treatment when blood tests suggest that there are fewer leukemia cells. It is not clear whether any of these drugs can cure CML, and the disease may come back if treatment is stopped. If treatment with one of these drugs has worked, a patient no longer has evidence of cells with the Philadelphia chromosome and has normal levels of blood cells. This is called a complete cytogenetic remission. It is currently recommended that these drugs should be continued throughout the person?s life to prevent the CML from recurring.

**Monitoring.** More sensitive blood tests, such as PCR and rarely FISH (see Diagnosis [10]), are usually done every three months on a blood sample after a person has a cytogenetic response in the bone marrow cells. Patients who have no cells with the Philadelphia chromosome on regular cytogenetic tests often need to have PCR testing to find a molecular response. Patients who have a rapid decrease in the number of cells with the Philadelphia chromosome by three months after starting treatment may have the best long-term outcomes.

The most sensitive test to look for remaining CML is called a quantitative reverse transcriptase PCR (Q-RT-PCR) test. This test is recommended every three months on a blood sample. Generally, this test can find one CML cell remaining among 1 million normal blood cells, so, when this test is negative, it is very likely that the CML is nearly gone. On the other hand, if the results of this test begin to rise, then the current treatment is no longer working, and it may be time to switch medications before the disease recurs.

Sometimes, a TKI stops working and the CML develops resistance to it. Resistance can occur if patients do not take their medication regularly, as prescribed [11], so it is important for patients to take their medication as prescribed. Even if patients do take the medication correctly, CML may become resistant to a TKI, which is why it is important to receive regular monitoring with cytogenetic testing, FISH, or PCR to monitor how well the drug is continuing to work.

Both dasatinib and nilotinib have been shown to bring about a complete cytogenetic response

sooner and in more patients newly diagnosed with CML when compared with imatinib; however, imatinib has been used for longer. There is no difference in overall survival when using either imatinib or another one of these other drugs as initial treatment. Bosutinib and ponatinib are newer drugs but both have also produced complete cytogenetic responses in patients with CML. Because of possible severe side effects, caution and careful monitoring is needed if ponatinib is recommended after other drugs have stopped working. However, ponatinib is the only TKI that works for patients with the T315I mutation. If the medication you start with stops working, the dose may be increased or a different TKI may still be effective.

**Chemotherapy**

Chemotherapy is the use of drugs to destroy cancer cells, usually by stopping the cancer cells? ability to grow and divide. Chemotherapy is given by a medical oncologist or a hematologist.

Systemic chemotherapy is delivered through the bloodstream to reach cancer cells throughout the body. Common ways to give chemotherapy include an intravenous (IV) tube placed into a vein using a needle or in a pill or capsule that is swallowed (orally). Chemotherapy can also be given by an injection under the skin called a subcutaneous injection. A chemotherapy regimen (schedule) usually consists of a specific number of cycles given over a set period of time. A patient may receive one drug at a time or combinations of different drugs at the same time.

A drug called hydroxyurea (Hydrea, Droxia) is often given to lower the number of white blood cells until CML can be diagnosed with the tests described in the Diagnosis [10] section. Given in capsule form, this drug works well to return blood cells to normal levels within a few days or weeks and reduce the size of the spleen, but it does not reduce the percentage of cells with the Philadelphia chromosome and does not prevent blast crisis alone. Although hydroxyurea has few side effects, most patients newly diagnosed with chronic phase CML receive imatinib or another TKI (see above) as soon as possible. Side effects of chemotherapy depend on the specific drug and the dosage and usually go away when treatment is complete.

In 2012, the drug omacetaxine mepesuccinate (Synribo) was approved by the FDA for patients with chronic or accelerated phase CML that is not responding to one of the TKIs described above. Omacetaxine is given by injection under the skin daily for seven to 14 days. The most common side effects include thrombocytopenia, anemia, neutropenia, diarrhea, nausea, fatigue, weakness, skin irritation where the drug was given, fever, and infection.

Learn more about chemotherapy [12] and preparing for treatment [13]. The medications used to treat cancer are continually being evaluated. Talking with your doctor is often the best way to learn about the medications prescribed for you, their purpose, and their potential side effects or interactions with other medications. Learn more about your prescriptions by using searchable drug databases [14].

**Stem cell transplantation/bone marrow transplantation**

A stem cell transplant is a medical procedure in which bone marrow that contains leukemia is replaced by highly specialized cells, called hematopoietic stem cells, that develop into healthy bone marrow. Hematopoietic stem cells are blood-forming cells found both in the bloodstream and in the bone marrow. Today, this procedure is more commonly called a stem cell transplant,

rather than bone marrow transplant, because it is the stem cells in the blood that are typically being transplanted, not the actual bone marrow tissue.

Before recommending transplantation, doctors will talk with the patient about the risks of this treatment and consider several other factors, such as the type of leukemia, results of any previous treatment, and patient?s age and general health.

There are two types of stem cell transplantation depending on the source of the replacement blood stem cells: allogeneic (ALLO) and autologous (AUTO). ALLO uses donated stem cells, while AUTO uses the patient?s own stem cells. In both types, the goal is to destroy all of the cancer cells in the marrow, blood, and other parts of the body using high doses of chemotherapy and/or radiation therapy and then allow replacement blood stem cells to create healthy bone marrow. Only ALLO transplants are used to treat CML.

Learn more about stem cell and bone marrow transplantation [15].

**Immunotherapy**

Immunotherapy, also called biologic therapy, is designed to boost the body's natural defenses to fight the cancer. It uses materials made either by the body or in a laboratory to improve, target, or restore immune system function. Interferon (Roferon-A, Intron A, Alferon, Infergen) is a type of immunotherapy. It can reduce the number of white blood cells and sometimes decrease the number of cells that have the Philadelphia chromosome.

Interferon is given daily or weekly by an injection under the skin and sometimes causes flu-like side effects, such as fever, chills, fatigue, and loss of appetite. When given on an ongoing basis, it can also cause loss of energy and memory changes. Interferon therapy was the primary treatment for chronic phase CML before imatinib became available. However, interferon is no longer recommended as the first treatment for CML because research has shown that imatinib works better to treat CML and causes fewer side effects. Learn more about immunotherapy [16].

**Getting care for symptoms and side effects**

Leukemia and its treatment often cause side effects. In addition to treatment to slow, stop, or eliminate the disease, an important part of care is relieving a person?s symptoms and side effects. This approach is called palliative or supportive care, and it includes supporting the patient with his or her physical, emotional, and social needs.

Palliative care can help a person at any stage of illness. People often receive treatment for the leukemia and treatment to ease side effects at the same time. In fact, patients who receive both often have less severe symptoms, better quality of life, and report they are more satisfied with treatment.

Palliative treatments vary widely and often include medication, nutritional changes, relaxation techniques, and other therapies. You may also receive palliative treatments similar to those meant to eliminate the leukemia, such as chemotherapy, surgery, and radiation therapy. Talk with your doctor about the goals of each treatment in your treatment plan.

Before treatment begins, talk with your health care team about the possible side effects of your specific treatment plan and supportive care options. And during and after treatment, be sure to tell your doctor or another health care team member if you are experiencing a problem so it is addressed as quickly as possible. Learn more about palliative care [17].

## Treatment by phase

### Chronic phase

The immediate goals of treatment are to reduce any symptoms of CML. The longer-term goals are to decrease or get rid of the cells with the Philadelphia chromosome to slow down or prevent the disease from moving to blast crisis. Treatment will often first include one of the TKIs mentioned above. An ALLO stem cell transplantation would be considered afterwards only if the TKI treatment does not work.

### Accelerated phase

The same drugs used for chronic phase CML may also be used for accelerated phase CML. Although treatment with a TKI can work well for accelerated phase CML, it is less likely to work as well as it does for chronic phase CML. Dasatinib or nilotinib are more effective in providing longer remissions, but many patients have a recurrence within about two years. Therefore, an ALLO stem cell transplantation should be considered when possible. If an ALLO stem cell transplantation is not recommended or if a matched donor cannot be found, the treatment plan may include a different TKI or a clinical trial [3].

### Blastic phase

Treatment with a TKI only works well for a few months for patients in blast crisis, but it can help to control the CML while a stem cell/bone marrow transplant is being arranged. If the transplant can be done while imatinib or dasatinib is working, then the long-term results are better. Stem cell/bone marrow transplantation in the blast phase is less successful than in chronic phase, but this approach has worked well for some patients. Many people with CML in blastic phase receive imatinib or dasatinib plus chemotherapy similar to that used for patients with acute leukemia, such as acute myeloid leukemia (AML) [18] or acute lymphoblastic leukemia (ALL) [9]. The chance of remission from this approach is about 20% to 30%, although the leukemia recurs for most patients within weeks to a few months. Hydroxyurea (see Chemotherapy, above) is often given to patients because it can help control blood cell levels. If stem cell/bone marrow transplantation is not an option, the doctor may recommend a clinical trial [3].

### Refractory CML

If the leukemia does not respond to treatment, it is called refractory leukemia. Patients with this diagnosis are encouraged to talk with doctors who are experienced in treating this type of leukemia, because there can be different opinions about the best treatment plan. Learn more about seeking a second opinion [19] before starting treatment, so you are comfortable with the treatment plan chosen. This discussion may include clinical trials [3]. Supportive care will also be important to help relieve symptoms and side effects.

For most patients, a diagnosis of refractory leukemia is very stressful and, at times, difficult to bear. Patients and their families are encouraged to talk about the way they are feeling with doctors, nurses, social workers, or other members of the health care team. It may also be helpful to talk with other patients, including through a support group.

**Remission and the chance of recurrence**

It is not yet proven whether imatinib, dasatinib, or nilotinib, or the newer drugs bosutinib, ponatinib, or omacetaxine can cure CML. A remission is when leukemia cannot be detected in the body by cytogenetic testing and there are no symptoms. This may also be called ?no evidence of disease? or NED.

A remission can be temporary or permanent. This uncertainty leads to many survivors feeling worried or anxious that the leukemia will come back. While many remissions are permanent, it is important to talk with your doctor about the possibility of the disease returning. Understanding the risk of recurrence and the treatment options may help you feel more prepared if the leukemia does return. Learn more about coping with the fear of recurrence [20].

If the leukemia does return despite the original treatment, it is called recurrent leukemia. When this occurs, a cycle of testing will begin again to learn as much as possible about the recurrence, including whether the leukemia is in a different phase. After testing is finished, you and your doctor will talk about your treatment options. Often the treatment plan will include the therapies described above such as targeted therapy, chemotherapy, and immunotherapy, but they may be used in a different combination or given at a different dose. Your doctor may also suggest clinical trials that are studying new ways to treat this type of recurrent leukemia.

People with recurrent leukemia often experience emotions such as disbelief or fear. Patients are encouraged to talk with their health care team about these feelings and ask about support services to help them cope. Learn more about dealing with cancer recurrence [21].

**If treatment fails**

Recovery from leukemia is not always possible. If treatment is not successful, the disease may be called advanced or terminal leukemia.

This diagnosis is stressful, and this is difficult to discuss for many people. However, it is important to have open and honest conversations with your doctor and health care team to express your feelings, preferences, and concerns. The health care team is there to help, and many team members have special skills, experience, and knowledge to support patients and their families. Making sure a person is physically comfortable and free from pain is extremely important.

Patients who have advanced disease and who are expected to live less than six months may want to consider a type of palliative care called hospice care. Hospice care is designed to provide the best possible quality of life for people who are near the end of life. You and your family are encouraged to think about where you would be most comfortable: at home, in the hospital, or in a hospice environment. Nursing care and special equipment can make staying at home a workable alternative for many families. Learn more about advanced cancer care planning [22].

After the death of a loved one, many people need support to help them cope with the loss. Learn more about grief and loss [23].

*The next section helps explain clinical trials, which are research studies. Use the menu on the side of your screen to select About Clinical Trials, or you can select another section, to continue reading this guide.*

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**Links:**
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[2] http://www.cancer.net/about-us
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