Treating Chronic Myeloid Leukemia

General information

This section starts with general comments about types of treatments used for chronic myeloid leukemia (CML). This is followed by a discussion of treatment options based on the phase of CML.

Targeted therapy drugs are the main treatment for CML. Some patients might also need other treatments, such as:

- Interferon
- Chemotherapy
- Radiation therapy
- Surgery
- Stem cell transplant

For information on common treatment plans, see Treating Chronic Myeloid Leukemia by Phase.

Thinking about taking part in a clinical trial

Clinical trials are carefully controlled research studies that are done to get a closer look at promising new treatments or procedures. Clinical trials are one way to get state-of-the-art cancer treatment. In some cases they may be the only way to get access to newer treatments. They are also the best way for doctors to learn better methods to treat cancer. Still, they are not right for everyone.

If you would like to learn more about clinical trials that might be right for you, start by asking your doctor if your clinic or hospital conducts clinical trials. You can also call our clinical trials matching service at 1-800-303-5691 for a list of studies that meet your medical needs, or see the Clinical Trials section to learn more.
Considering complementary and alternative methods

You may hear about alternative or complementary methods that your doctor hasn’t mentioned to treat your cancer or relieve symptoms. These methods can include vitamins, herbs, and special diets, or other methods such as acupuncture or massage, to name a few.

Complementary methods refer to treatments that are used along with your regular medical care. Alternative treatments are used instead of a doctor’s medical treatment. Although some of these methods might be helpful in relieving symptoms or helping you feel better, many have not been proven to work. Some might even be dangerous.

Be sure to talk to your cancer care team about any method you are thinking about using. They can help you learn what is known (or not known) about the method, which can help you make an informed decision. See the Complementary and Alternative Medicine section to learn more.

Help getting through cancer treatment

Your cancer care team will be your first source of information and support, but there are other resources for help when you need it. Hospital- or clinic-based support services are an important part of your care. These might include nursing or social work services, financial aid, nutritional advice, rehab, or spiritual help.

The American Cancer Society also has programs and services – including rides to treatment, lodging, support groups, and more – to help you get through treatment. Call our National Cancer Information Center at 1-800-227-2345 and speak with one of our trained specialists on call 24 hours a day, every day.

The treatment information given here is not official policy of the American Cancer Society and is not intended as medical advice to replace the expertise and judgment of your cancer care team. It is intended to help you and your family make informed decisions, together with your doctor. Your doctor may have reasons for suggesting a treatment plan different from these general treatment options. Don’t hesitate to ask him or her questions about your treatment options.

Targeted Therapies for Chronic Myeloid Leukemia
Chronic myeloid leukemia (CML) cells contain an oncogene, \textit{BCR-ABL}, that isn't found in normal cells. This gene makes a protein, BCR-ABL, which causes CML cells to grow and reproduce out of control. BCR-ABL is a type of protein known as a \textit{tyrosine kinase}. Drugs known as \textit{tyrosine kinase inhibitors} (TKIs) that target BCR-ABL are the standard treatment for CML. These include:

- Imatinib (Gleevec)
- Dasatinib (Sprycel®)
- Nilotinib (Tasigna®)
- Bosutinib (Bosulif®)
- Ponatinib (Iclusig®)

All of these drugs can have serious or even deadly interactions with other drugs, over the counter supplements, and even certain foods (such as grapefruit and pomegranate). Be sure that your doctor always has an up-to-date list of any medicines you are taking, including over-the-counter medicines, vitamins, and herbal supplements. You also need to check with your doctor before starting any new medicine, to be sure it is safe.

It is also important to understand that all of the TKIs can harm the fetus if taken during pregnancy. These drugs seem to work best on CML that is still in the chronic phase, but they also can help patients with more advanced disease for some time.

**Imatinib**

Imatinib (Gleevec) was the first drug to specifically target the BCR-ABL tyrosine kinase protein, and it quickly became the standard treatment for CML patients. Because it was the first TKI, imatinib is known as a \textit{first generation} tyrosine kinase inhibitor.

Almost all CML patients respond to treatment with imatinib, and most of these responses seem to last for many years. This drug doesn't seem to make the leukemia go away and stay away, so patients need to take it indefinitely (or until it stops working). Imatinib is taken by mouth as a pill with food, usually once a day.

Common side effects can include diarrhea, nausea, muscle pain, and fatigue. These are generally mild. About 30\% of people taking the drug have itchy skin rashes. Most of these symptoms can be treated effectively, if needed.

Another common side effect is fluid buildup around the eyes, feet, or abdomen. In rare cases the fluid may collect in the lungs or around the heart, which can cause trouble breathing. Some studies have suggested that some of this fluid buildup may be caused by effects of the drug on the heart, though this is rare. It's not yet clear how serious this is or if it might go away if treatment is stopped. If you are taking this drug, tell your
doctor right away if you notice sudden weight gain or fluid buildup anywhere in the body or have trouble breathing.

Another possible side effect is a drop in a person's white blood cell and platelet counts. When this happens at the beginning of treatment, it might be because the blood-forming cells that are making these are part of the malignant process. If this is the case, normal blood-forming cells take over and the blood counts will begin to rise to normal over time.

Your doctor might tell you to stop taking the drug for a short period if your blood counts get too low. This can also happen later on in treatment. In the past, low red blood cell counts were treated with a red cell growth factor, such as erythropoietin (Procrit®) or darbepoietin (Aranesp®), but these drugs are used less often now. Instead, your doctor may lower the dose of imatinib to see if your blood counts improve.

In some patients, imatinib eventually seems to stop working. This is known as imatinib resistance. Resistance to imatinib seems to be caused by changes in the genes of the CML cells. Sometimes this resistance can be overcome by increasing the dose of imatinib, but some patients need to change to a different drug, such as one of the other TKIs described further on.

**Dasatinib**

Dasatinib (Sprycel) is another tyrosine kinase inhibitor that targets the BCR-ABL protein. Because it was developed after imatinib, it is called a second generation TKI. Like imatinib, this drug is a pill taken by mouth.

Dasatinib can be used as the first treatment for CML, but it can also be helpful for patients who can’t take imatinib because of side effects or because imatinib isn’t working.

When it was first approved, dasatinib was a pill taken twice a day, but more often now a larger dose is taken once a day.

The possible side effects of dasatinib seem to be similar to those of imatinib, including fluid buildup, lowered blood cell counts, nausea, diarrhea, and skin rashes. A serious side effect that can occur with this drug is fluid buildup around the lung (called a pleural effusion). This side effect is more common in patients taking this drug twice a day. The fluid can be drained off with a needle, but it can build up again, and may require the dose of dasatinib to be decreased.

**Nilotinib**
Nilotinib (Tasigna) is another second generation TKI that targets the BCR-ABL protein. Like dasatinib, this drug can be used as a first treatment for CML, as well as for use in people who can’t take imatinib or whose CML no longer responds to it.

Side effects of nilotinib seem to be mild, but can include fluid buildup, lowered blood cell counts, nausea, diarrhea, and some lab test abnormalities. It can cause high blood sugar and pancreatitis, although this is rare.

This drug can also affect the rhythm of the heart, causing a condition called prolonged QT syndrome. This usually doesn't cause any symptoms, but can be serious or even fatal. This is why patients should have an electrocardiogram (EKG) before starting nilotinib and then again while being treated. This heart rhythm problem can sometimes be caused by nilotinib interacting with other drugs or supplements, so it's especially important to be sure that your cancer doctor knows about any medicines you take, including over-the-counter medicines and supplements. You also need to check with your doctor before starting any new medicine, to be sure it is safe.

**Bosutinib**

Bosutinib (Bosulif®) is another TKI that targets the BCR-ABL protein. At this time, this drug is only approved by the US Food and Drug Administration to treat patients after they have been treated with another TKI.

Common side effects are usually mild and include diarrhea, nausea, vomiting, abdominal pain, rash, fever, fatigue, and low blood cell counts (including low platelet counts, low red blood cell counts, and low white blood cell counts). Less often, this drug can also cause problems with fluid retention, liver damage, and severe allergic reaction. Your doctor will check your blood test results regularly to watch for problems with your liver and low blood counts.

**Ponatinib**

Ponatinib (Iclusig®) is a new TKI targeting the BCR-ABL protein. Because of risks of some serious side effects, this drug is only used to treat patients with CML if all of the other TKIs don’t work or if their leukemia cells have a certain gene change called the T315I mutation. This mutation (gene change) occurs in the leukemia cells of some CML patients who are treated with a TKI, and it prevents other TKIs from working. Ponatinib is the first TKI to work against CML cells that have this mutation.

This drug is a pill taken once a day.
Most side effects are mild and can include abdominal (belly) pain, headache, rash or other skin problems, and fatigue.

High blood pressure is also fairly common, and it may need to be treated with a blood pressure drug.

There is also a risk of serious blood clots that can lead to heart attacks and strokes, or block arteries and veins in the arms and legs. Rarely, blood clots in patients taking this drug have cut off circulation, and lead to an arm or leg needing to be amputated (cut off). Surgery or some other procedure may be needed to treat these blood clots. The risk of serious blood clots is higher in older patients, those with certain risk factors, such as high blood pressure, high cholesterol, or diabetes, and those who have already had a heart attack, stroke, or poor circulation.

More rarely, this drug can also weaken the heart muscle, leading to a condition known as congestive heart failure. It can also cause liver problems, including liver failure, as well as pancreatitis (inflammation of the pancreas, which can lead to severe belly pain, nausea, and vomiting).

For general information about targeted therapy, see Targeted Therapy.

- References

See all references for Chronic Myeloid Leukemia

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Interferon Therapy for Chronic Myeloid Leukemia

Interferons are a family of substances naturally made by our immune system. Interferon-alpha is the type most often used in treating chronic myeloid leukemia (CML). This substance reduces the growth and division of leukemia cells. Interferon was once considered the best treatment for CML, but imatinib (Gleevec®) was shown to be better. Now, the tyrosine kinase inhibitors are the mainstay of treatment and interferon is rarely
used.

To treat CML, this drug is most often given as a daily injection under the skin. It may also be injected into a muscle or vein. To treat CML, interferon is given for several years.

Interferon can cause significant side effects. These include "flu-like" symptoms like muscle aches, bone pain, fever, headaches, fatigue, nausea, and vomiting. Patients taking this drug may have problems thinking and concentrating. Interferon can also lower blood cell counts. These effects continue as long as the drug is used, but can become easier to tolerate over time. They do improve after the drug is stopped. Still, some patients find it hard to deal with these side effects every day and may need to stop treatment because of them.

For more information about drugs that use the immune system, see Immunotherapy.

- References
  See all references for Chronic Myeloid Leukemia

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Chemotherapy for Chronic Myeloid Leukemia

Chemotherapy (chemo) is the use of anti-cancer drugs that are injected into a vein or taken by mouth. These drugs enter the bloodstream and reach all areas of the body, making this type of treatment useful for cancers such as leukemia that spread throughout the body. Any drug used to treat cancer (including tyrosine kinase inhibitors or TKIs) can be considered chemo, but here chemo is used to mean treatment with conventional cytotoxic drugs that mainly kill cells that are growing and dividing rapidly.

Chemo was once one of the main treatments for patients with chronic myeloid leukemia (CML), but it is used much less often now that TKIs like imatinib (Gleevec®) are
available. Now, chemo may be used to treat CML when the TKIs have stopped working. It is also used as part of the treatment during a stem cell transplant.

The chemo drug hydroxyurea (Hydrea®) is taken as a pill, and can help lower very high white blood cell counts and shrink an enlarged spleen. Other drugs sometimes used include cytarabine (Ara-C), busulfan, cyclophosphamide (Cytoxan®), and vincristine (Oncovin®).

Omacetaxine (Synribo®) is a chemo drug that was approved to treat CML that is resistant to some of the TKIs now in use. It can help some patients whose CML has developed the T315I mutation that keeps most TKIs from working (discussed in the section about targeted therapy).

**Side effects of chemotherapy**

Chemotherapy drugs work by attacking cells that are dividing quickly, which is why they work against cancer cells. But other cells in the body, such as those in the bone marrow, the lining of the mouth and intestines, and the hair follicles, also divide quickly. These cells are also likely to be affected by chemotherapy, which can lead to side effects.

Possible side effects depend on the type and dose of drugs given and the length of time they are taken. Some common side effects of chemotherapy include:

- Hair loss
- Mouth sores
- Loss of appetite
- Nausea and vomiting
- Low white blood cell counts (*leukopenia*), which increases the risk of serious infection
- Low blood platelet counts (*thrombocytopenia*), which can lead to easy bruising or bleeding
- Low red blood cell counts (*anemia*), which can lead to feeling tired and weak

Still, different drugs can have different side effects. For example, vincristine can cause nerve damage (*neuropathy*) leading to numbness, tingling, or even pain or weakness in the hands or feet. Lung damage from busulfan is rare, but can be severe. Before starting treatment, speak with your health care team about the drugs you will receive and their possible side effects. Most side effects last a short time and go away once treatment is finished, but some can be permanent.
While getting treatment, be sure to tell your cancer care team about any side effects you have because there may be ways to lessen them. For example, drugs can be given to prevent or reduce nausea and vomiting.

If your white blood cell count gets very low after treatment with chemo, drugs known as growth factors, G-CSF (Neupogen®) and GM-CSF (Leukine®), for example, may be given to increase the white blood cell counts and reduce the chance of infection.

For information on infections and how to avoid them, see Infections in People With Cancer.

If your platelet counts are low, you may be given drugs or platelet transfusions to help protect against bleeding. Likewise, if low red blood cell counts are causing problems (like shortness of breath and/or weakness), you may be treated with red blood cell transfusions.

More information about chemotherapy can be found in the chemotherapy section of our website.

- References
  See all references for Chronic Myeloid Leukemia

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Radiation Therapy for Chronic Myeloid Leukemia

Radiation therapy is treatment with high-energy rays or particles to destroy cancer cells. Radiation therapy is usually not part of the main treatment for patients with chronic myeloid leukemia (CML), but it is used in certain situations.

Patients may have symptoms if swollen internal organs (such as an enlarged spleen) press on other organs. For instance, pressure against the stomach may affect appetite. If these symptoms are not helped by chemotherapy, radiation therapy to shrink the
spleen may be an option.

Radiation therapy can also be useful in treating pain from bone damage caused by the growth of leukemia cells within the bone marrow.

Radiation therapy is sometimes given in low doses to the whole body, just before a stem cell transplant (see Stem Cell Transplant for Chronic Myeloid Leukemia).

The main short-term side effects of radiation therapy depend in part on what area of the body is treated.

- Fatigue (tiredness) is a common side effect (no matter what part of the body is treated)
- Skin changes can occur in the treated area which range from mild redness to blistering and peeling.
- If the radiation is aimed at the areas of the head or neck, the inside lining of your mouth and throat may become red and irritated - this is called mucositis.
- Radiation to the belly or pelvis can cause nausea and vomiting and/or diarrhea.
- If large parts of the body are treated with radiation, the bone marrow may be affected, leading to low blood counts.

More information on radiation therapy can be found in the radiation section of our website.

- References
  See all references for Chronic Myeloid Leukemia

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Surgery for Chronic Myeloid Leukemia

Leukemia cells spread widely throughout the bone marrow and other organs, so surgery cannot be used to cure this type of cancer. Surgery rarely has any role even in diagnosing chronic myeloid leukemia (CML), since a blood test or bone marrow aspirate and biopsy are usually all that is needed.
If leukemia spreads to the spleen, that organ can become large enough to compress nearby organs and cause symptoms. If chemotherapy or radiation does not help shrink the spleen, it may be removed with surgery. This operation, called a splenectomy, is meant to improve the symptoms of an enlarged spleen — it has no role in curing CML.

Splenectomy may also improve blood cell counts and lower the need for blood product transfusions. One of the spleen’s normal functions is to remove worn-out blood cells from the bloodstream. If leukemia or other diseases cause the spleen to become too large, it may become too active in removing blood cells, leading to a shortage of red blood cells or platelets. Taking out the spleen may improve red blood cell and platelet counts in some patients.

Most people have no problem living without a spleen. The risk for certain bacterial infections is increased, which is why doctors often recommend certain vaccines be given before the spleen is removed.

- References

See all references for Chronic Myeloid Leukemia

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**Stem Cell Transplant for Chronic Myeloid Leukemia**

The usual doses of chemotherapy drugs can cause serious side effects to quickly dividing tissues such as the bone marrow. Even though higher doses of these drugs might be better at killing leukemia cells, they are not given because the severe damage to bone marrow cells would cause lethal shortages of blood cells.

For a stem cell transplant (SCT), high doses of chemotherapy are given to kill the leukemia cells. Sometimes the whole body also is given a low dose of radiation. This treatment kills the leukemia cells, but also damages the normal bone marrow cells. Then after these treatments, the patient receives a transplant of blood-forming stem cells to restore the bone marrow.
Blood-forming stem cells used for a transplant are obtained either from the blood (called a peripheral blood stem cell transplant, or PBSCT) or from the bone marrow (called a bone marrow transplant, or BMT). Bone marrow transplant was more common in the past, but it has largely been replaced by PBSCT.

The 2 main types of stem cell transplants are allogeneic and autologous.

For an **autologous transplant**, the patient’s own stem cells are collected from the blood or bone marrow and then given back after treatment. The problem with that is that leukemia cells may be collected with the stem cells.

In an **allogeneic transplant**, the stem cells come from someone else (a donor). To lower the chance of complications, the donor needs to “match” the patient in terms of tissue type. Often, a close relative, such as a brother or sister is a good match. Less often, a matched unrelated donor may be found.

Because collecting the patient’s stem cells can also collect leukemia cells, allogeneic transplants are the main type of transplant used to treat patients with chronic myeloid leukemia (CML). Allogeneic stem cell transplant is the only known cure for CML. Still, this type of transplant can cause severe or even life-threatening complications and side effects, and it is often not be a good option in people who are older or have other health problems.

Before modern targeted therapy drugs like imatinib (Gleevec), SCT was commonly used to treat CML. The drugs that were available at that time did not work very well, and fewer than half of patients survived more than 5 years after diagnosis. Now, targeted drugs like imatinib are the standard treatment, and transplants are being used less often. Still, because allogeneic SCT offers the only proven chance to cure CML, doctors may still recommend a transplant for younger patients, particularly children. It is more likely to be considered for those with an available matched donor, like a well-matched brother or sister. Transplant may also be recommended if the CML is not responding well to the targeted drugs.

For more information on stem cell transplants, see [Stem Cell Transplant (Peripheral Blood, Bone Marrow, and Cord Blood Transplants)]

- References
  See all references for Chronic Myeloid Leukemia

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How Do You Know If Treatment for Chronic Myeloid Leukemia Is Working?

If you have chronic myeloid leukemia (CML) and are being treated with targeted drugs, your doctor will check your blood counts, examine you, and will order other tests like bone marrow biopsy and PCR (of blood and/or bone marrow). Doctors look for different kinds of responses to treatment:

**Hematologic response** is based on the complete blood count, and usually happens within the first 3 months of treatment.

- When blood cell counts return to normal, there are no immature cells seen in the blood, and the spleen has returned to normal size it is called a complete hematologic response (or CHR).
- A partial hematologic response means that there has been some improvement, but there are still signs or symptoms of CML. The white blood cell count is less than half of what it was before treatment, the platelet count is still high but is may be less than half what it was before treatment, and/or the spleen is still enlarged (but it has shrunk in size).

**Cytogenetic response** is based on testing of the bone marrow with either cytogenetics or FISH (these were discussed in How Is Chronic Myeloid Leukemia Diagnosed?). This takes longer to occur than the hematologic response.

- A complete cytogenetic response (CCyR) occurs when no cells with the Philadelphia chromosome can be found in the bone marrow.
- A partial cytogenetic response (PCyR) occurs when 1% to 34% of cells still have the Philadelphia chromosome.
- A major cytogenetic response (MCyR) includes both complete and partial responses, and means less than 35% of cells have the Philadelphia chromosome.
- A minor cytogenetic response occurs when 35% to 90% of cells still have the Philadelphia chromosome.

**Molecular response** is based on the results of the PCR test on either the blood or bone marrow.
• A complete molecular response (CMR) means that the PCR test does not find the BCR-ABL gene in the patient's blood.
• A major molecular response (MMR) means that the amount of BCR-ABL gene in the blood is 1/1000th (or less) of what is expected in someone with untreated CML.

References
See all references for Chronic Myeloid Leukemia

Treating Chronic Myeloid Leukemia by Phase

Treatment options for people with chronic myeloid leukemia (CML) depend on the phase of their disease (chronic, accelerated, or blast phase), their age, other prognostic factors, and the availability of a stem cell donor with matching tissue type.

Chronic phase

The standard treatment for chronic phase CML is a tyrosine kinase inhibitor (TKI) such as imatinib (Gleevec), nilotinib (Tasigna), or dasatinib (Sprycel). For imatinib, the usual starting dose is 400 mg per day. If the first drug stops working (or it never really worked well at all) the dose may be increased or the patient may be switched to one of the other TKIs (including bosutinib/Bosulif). Ponatinib (Iclusig) is an option after all of the other TKIs have been tried or if the leukemia cells later develop the T315I mutation.

Switching to another TKI is also an option if the patient can't take the first drug because of side effects.

Some people in chronic phase may be treated with an allogeneic stem cell transplant (SCT). This treatment was discussed in detail in "Stem cell transplant for chronic myeloid leukemia."

Monitoring treatment results
Monitoring the patient to see how they respond to treatment is very important. Blood counts are checked, and either the blood is checked with a polymerase chain reaction (PCR) test to measure the amount of the *BCR-ABL* gene or the bone marrow is checked to see if the Philadelphia chromosome is there. Blood counts may be checked more often, but testing for the *BCR-ABL* gene or the Philadelphia chromosome is usually done about 3 months after treatment with a TKI is started, and then every 3 to 6 months after that. If the results show that treatment is working well, the patient stays on their current drug. If the results show that treatment isn’t working well, a new drug or treatment may be needed.

If the CML is responding well to treatment, 3 months after starting treatment, the patient should have:

- A complete hematologic response (CHR), and
- Some type of cytogenetic response, and/or
- A reduction of the number of copies of *BCR-ABL* on the PCR test by 90% or more,

If treatment is working well, 18 months after starting treatment, the patient should have:

- A complete hematologic response (CHR), and
- A complete cytogenetic response (CCyR), and/or
- A major molecular response (MMR)

(For definitions of the different response types, see “How do you know if treatment for chronic myeloid leukemia is working?”)

**How often is treatment successful?**

Up to about 70% of people have a complete cytogenetic response (CCyR) within 1 year of starting imatinib, and the rate of CCyR is even higher with the other TKIs (nilotinib and dasatinib). After a year, even more patients will have had a CCyR. Many of these patients also have a complete molecular response (CMR). (For definitions of the different response types, see “How do you know if treatment for chronic myeloid leukemia is working?”)

But even patients in whom the *BCR-ABL* gene can no longer be found while on treatment with a TKI don’t seem to be cured, since *BCR-ABL* and CML cells come back in more than half of people who stop taking a TKI. For now, doctors recommend that people stay on TKIs indefinitely.

**If the first treatment doesn’t work**

If the leukemia doesn’t respond well to treatment, there are several options.
increasing the dose of the drug. This helps some people, although the higher dose often has worse side effects.

- Switching to another TKI, for example from imatinib to dasatinib, nilotinib, bosutinib, or ponatanib. The doctor may check the CML cells for genetic changes (mutations) to help decide what drug would be best.

- Interferon or chemotherapy (chemo) may be tried for those who can’t take these drugs or those for whom they are not working.

- Stem cell transplant may be an option, especially for younger people who have a donor with a matching tissue type.

**Treasuring CML after a stem cell transplant**

Some people who have a stem cell transplant may not get a complete response. If they do not have graft-versus-host disease (GVHD), doctors may try to get their new immune system to fight the leukemia. One way to do this is by slowly lowering the doses or stopping the immune suppressing drugs they are taking. This is done very carefully in order to have an anti-leukemia effect without getting too much GVHD. Patients are watched closely during this time. Another approach that helps some patients is an infusion of lymphocytes taken from the person who donated the stem cells for the transplant (called donor lymphocyte infusion). This can induce an immune reaction against the leukemia. Interferon may also be helpful.

In patients who do have GVHD after a stem cell transplant, boosting the immune system further is not likely to help. These patients are often treated with a TKI like imatinib.

**Accelerated phase**

When CML is in accelerated phase, leukemia cells begin to build up in the body more quickly, causing symptoms. The leukemia cells often acquire new gene mutations, which help them grow and might make treatments less effective.

The treatment options for accelerated phase CML depend on what treatments the patient has already had. In general, the options are similar to those for patients with chronic phase CML, but patients with accelerated phase CML are less likely to have a long-term response to any treatment.

If the patient hasn’t had any treatment, a TKI will be used. Imatinib (often at higher doses than used for chronic phase CML) is one option for most people. Most patients in this phase can respond to treatment with imatinib, but the responses do not seem to last as long as they do in patients in the chronic phase. Still, about half these patients are
still alive after 4 years. The newer drugs like dasatinib and nilotinib are often used in this phase, and other drugs are under study.

If the patient is already getting imatinib, the dose may be increased. Another option is to switch to one of the other TKIs (dasatinib, nilotinib, or bosutinib). Sometimes the CML cells are tested to see if they have genetic changes (mutations) that may mean that a certain TKI is more or less likely to work (see the section “CML with the T315I mutation”). In CML without that mutation, ponatanib is an option after all of the other TKIs have been tried.

Interferon is another option, but it is also much less effective in this phase than in the chronic phase. About 20% of patients have some response to chemo, but these responses are usually shorter than 6 months.

An allogeneic stem cell transplant may be the best option for most patients who are young enough to be eligible. About 20% to 40% of patients with accelerated phase CML are alive several years after a stem cell transplant. Most doctors prefer that the leukemia be controlled, preferably in remission, before beginning the transplant procedure. To achieve this, chemo will often be used.

In some cases, an autologous SCT may be an option to try to get the CML back into the chronic phase, but it's very unlikely to result in a cure.

**Blast phase**

In the blast phase of CML, the leukemia cells become more abnormal. The disease acts like an acute leukemia, with blood counts getting higher and symptoms appearing or becoming more severe.

For people with blast phase CML who haven't been treated before, high-dose imatinib may be helpful, although it works in a smaller number of people and for shorter lengths of time than when used earlier in the course of the disease. The newer agents, dasatinib and nilotinib, seem to be better in this phase, particularly if they hadn't been used earlier. Bosutinib is also an option for patients who had previously been taking another TKI. Ponatanib may be used, but only after all of the other TKIs have been tried. Patients who respond to these drugs may still want to consider having a stem cell transplant, if possible.

Most often, the leukemia cells in this phase act like cells of acute myeloid leukemia (AML), but they are often resistant to the chemo drugs normally used to treat AML. Standard chemo for AML (see Leukemia: Acute Myeloid (Myelogenous)) will bring about
a remission in about 1 out of 5 patients, but this is usually short-lived. If remission does occur, it may be a chance to consider some type of stem cell transplant.

A smaller number of patients have blast cells that act like cells of acute lymphoblastic leukemia (ALL). These cells are more sensitive to chemo drugs. Remissions can be induced in about half of these patients with drugs such as vincristine, prednisone, and doxorubicin, along with imatinib, if that hasn't been given yet. Like patients with ALL, these patients are at risk for having leukemia cells in the fluid that surrounds the brain and spinal cord, so they often get chemo (cytarabine or methotrexate) infused directly into that fluid (like during a spinal tap). Radiation therapy to the brain is another option but is used less often. For more information, see *Leukemia: Acute Lymphocytic*.

Allogeneic SCT is less successful for blast phase CML than for earlier phases, and the long-term survival rate is less than 10%. Still, it is the only known option that may cure the disease. It is more likely to be effective if the CML can be brought back to the chronic phase before the transplant.

Because most patients with blast phase CML can't be cured, *palliative treatment* (intended to relieve symptoms rather than cure the disease) is important. Radiation therapy can help shrink an enlarged spleen or reduce pain from areas of bone damaged by leukemia. *Chemo* (usually with drugs such as hydroxyurea) may relieve some symptoms for a time.

*Clinical trials* of new combinations of chemo, targeted agents, and biologic therapies are important options.

**CML with the T315I mutation**

As was mentioned in the section about *targeted therapy*, in some patients on TKI treatment, the cancer cells develop a gene change called the *T315I mutation* that keeps most of the TKIs from working. If your CML stops responding to treatment with a TKI, another one may be tried. Your doctor may also check to see if the cancer cells have developed the T315I mutation. If they have, you may be switched to ponatinib, which is the only TKI that works against CML with this mutation. If this doesn’t work or you can’t take it because of side effects, you may be started on chemotherapy (chemo). Omacetaxine (Synribo) is a newer chemo drug that has been shown to help sometimes in this situation, but other chemo drugs may help as well.

- **References**
  
  See all references for Chronic Myeloid Leukemia