Patient education: Chronic myeloid leukemia (CML) in adults (Beyond the Basics)

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CHRONIC MYELOID LEUKEMIA OVERVIEW — Chronic myeloid leukemia (also called CML or chronic myelogenous leukemia) is a chronic (long-term, slowly developing) leukemia. Leukemia is a type of cancer that affects the blood and bone marrow. Bone marrow is the spongy, red tissue that fills the large bones. All of the blood cells (red cells, white cells, platelets) are derived from stem cells in the bone marrow.

CML is not inherited. People with CML have acquired an abnormality that causes a section of one chromosome (a strand of genes) to break off and attach to another chromosome. This results in an abnormally short chromosome, known as the Philadelphia chromosome. This exchange of genetic information causes two genes, BCR and ABL, to fuse into one gene, called BCR-ABL.

The BCR-ABL gene causes bone marrow cells to produce an abnormal enzyme (the BCR-ABL tyrosine kinase); this enzyme stimulates CML white blood cells to grow out of control, resulting in elevations of the white blood cell count and an increase in the size of the spleen. These CML cells grow and survive better than normal blood cells. The overgrowth of these cells leads to an inadequate number of normal, healthy blood cells, including white blood cells, red blood cells, and platelets. This can result in:

- Neutropenia (low numbers of neutrophils) – Neutrophils are a type of white blood cells that help to fight infection. People with neutropenia are more likely to get infections.
- Anemia (low numbers of red blood cells) – Red blood cells carry oxygen to our tissues. People without enough red cells may be pale and are often tired and short of breath.
- Thrombocytopenia (low numbers of platelets) – Platelets help to prevent and stop bleeding. People with low platelets have bleeding and spontaneous bruising.

Some people have no symptoms when they are diagnosed with CML. Signs and symptoms tend to develop gradually and may include a sense of fullness in the upper left side of the stomach (due to an enlarged spleen), sweats at night, unexplained weight loss, and occasionally, the symptoms of neutropenia, anemia, and thrombocytopenia described above.

Eventually, the disease can transform into a more aggressive disease, called blast phase, which resembles acute leukemia. People with blast phase have an increased number of immature white blood cells (called blast cells) and more severe neutropenia, anemia, and thrombocytopenia.

More detailed information about CML, written for healthcare providers, is available by subscription. (See 'Professional level information' below.)

PHASES OF CHRONIC MYELOID LEUKEMIA — There are three phases of CML:

Chronic phase — In the chronic phase, there are less than 5 percent immature blast cells in the bone marrow. Approximately 85 percent of people are in the chronic phase when they are initially diagnosed. This phase generally lasts several years and is readily controlled with oral medications.

Accelerated phase — During the accelerated phase, maturation of white blood cells becomes progressively impaired, and there are between 10 and 19 percent blast cells in the blood or bone marrow. The number of abnormal cells in the body is more difficult to control with medications, likely because of new mutations that develop in the blast cells.

Blast phase — In the blast phase (also called blast crisis), there are more than 20 to 30 percent blast cells in the blood or bone marrow. Before recent advances in treatment, blast crisis typically occurred within four to five years after diagnosis and was often unresponsive to treatment. Progression to blast phase is now uncommon. However, when it occurs, it remains difficult to control.

CHRONIC MYELOID LEUKEMIA TREATMENT OPTIONS — Treatment decisions for people with CML are complex due to the variety of available options. Currently, the most frequently used treatment options include:

- Disease control with a group of medications called oral tyrosine kinase inhibitors (TKIs), such as imatinib (brand name: Gleevec), dasatinib (brand name: Sprycel), or nilotinib (brand name: Tasigna) (see 'Tyrosine kinase inhibitors (TKIs)' below)
- Potential cure with stem cell transplantation (also called bone marrow transplantation or hematopoietic cell transplantation), usually after the disease stops responding or relapses during treatment with a TKI (see 'Stem cell transplant' below)
- Treatment to reduce symptoms with chemotherapy (hydroxyurea, busulfan, omacetaxine, or interferon alpha with or without cytarabine) (see 'Interferon alpha' below)

The choice of therapy depends upon the phase of CML, the availability of a bone marrow donor, whether or not you are a candidate for stem cell transplantation, and your preference.

Goals of treatment — The primary goal of treatment is to reduce or eliminate the cells with the abnormal Philadelphia chromosome, which in turn markedly decreases the likelihood of worsening to blast phase. This is measured as the **cytogenetic response**. Such treatment, if effective, will also return the blood counts to normal. This is measured as the **hematologic response**.

While achieving a hematologic response will reduce the severity of symptoms associated with CML, progression to the accelerated or blast phase will continue unless a cytogenetic response is achieved. Achieving a hematologic response is important, but does not ensure that the disease is adequately controlled.

Another way to determine how well the disease is controlled is to perform sensitive molecular testing. Polymerase chain reaction (PCR) is an extremely sensitive blood test that can detect the BCR-ABL gene. The term "complete **molecular response**" has been used to describe cases in which there is no evidence of the BCR-ABL gene by PCR. However, different PCR tests have different abilities to detect low numbers of cells

(sensitivities). As such, many laboratories are now reporting molecular responses according to the sensitivity of the test used. The goal of stem cell transplantation is to achieve a molecular response. A molecular response can also be seen during longer term follow-up of people treated with TKIs. Chemotherapy rarely, if ever, produces such a response.

Initial management — Initial treatment with a TKI is well-tolerated and effective for at least 10 years in most people with chronic phase CML. (See 'Tyrosine kinase inhibitors (TKIs)' below.)

Successful stem cell transplantation can produce long-term suppression of CML with a very low chance of relapse because most people achieve a deep molecular response following transplant. However, transplantation has some potentially serious risks, including graft-versus-host disease and even death (see "Patient education: Hematopoietic cell transplantation (bone marrow transplantation) (Beyond the Basics)", section on 'Hematopoietic cell transplantation side effects'). While there have not been any randomized clinical trials directly comparing TKIs with stem cell transplantation in people newly diagnosed with chronic phase CML, most experts recommend initial treatment with a TKI, reserving transplantation for if/when the disease relapses.

Because relapses occur frequently in people with accelerated phase CML and in virtually all people with blast phase CML who are treated with a TKI, stem cell transplantation should be considered for these people when possible. Giving chemotherapy or a TKI prior to transplantation (to achieve chronic phase) is preferable to transplanting during the blast phase; the chance of a cure is greater when transplantation is done during the chronic phase.

TKI failure — People who cannot tolerate, fail to respond to, or stop responding to an initial TKI are faced with the decision of what treatment to try next. The options include:

- Control the disease with another TKI, and then proceed as soon as possible with stem cell transplant.
- Control the disease with another TKI with plans to proceed with transplant if the disease relapses a second time.

Relapses during treatment with a TKI are often due to the development of a new mutation in the BCR-ABL gene, which allows the disease to become resistant to treatment. Testing to determine whether additional mutations have developed in the BCR-ABL gene (called mutation analysis) can be performed. Some mutations (eg, T315I) will not respond to most commonly available TKIs (imatinib, dasatinib, or nilotinib); people with these mutations are generally encouraged to consider transplantation. (See 'Stem cell transplant' below.)

If transplantation is not an option, options include treatment with omacetaxine (brand name: Synribo), ponatinib (brand name: Iclusig), or enrollment on a clinical trial. Omacetaxine is a chemotherapy that can be given as an injection under the skin daily for two weeks and repeated every four weeks for a maximum of six cycles. Side effects include infection, diarrhea, nausea, fever, and fatigue. (See 'Ponatinib (brand name: Iclusig)' below and 'Clinical trials' below.)

A major cause of treatment "failure" is poor compliance with taking the medication, such as skipping doses or not taking the medication as directed. It is critical that you take your medications exactly as directed, and tell your doctor if you have missed any doses. Your doctor needs to be certain that you have been taking your TKI correctly before switching to a different treatment.

TYROSINE KINASE INHIBITORS (TKIs) — The Philadelphia chromosome, characteristic of CML, gives rise to the formation of a unique gene product, an abnormal enzyme called the BCR-ABL tyrosine kinase. Researchers directed their efforts at developing compounds that could selectively inhibit this abnormal enzyme, resulting in the development of a class of medications known as tyrosine kinase inhibitors (TKIs). TKIs slow or stop the

actions of BCR-ABL, which leads to the rapid death of cells containing the abnormal Philadelphia chromosome. Normal cells suffer fewer toxic effects from TKIs compared with traditional chemotherapy treatments.

Although they have not been proven to cure the disease, TKIs are able to achieve long-term control of CML in the majority of people; thus, they have become the initial treatment of choice for almost all people who are newly diagnosed with CML. All of the available TKIs are able to induce hematologic and cytogenetic responses in all stages of the disease [1-3]. As a result, a choice among these medications is usually based upon your medical history and the potential side effects of each medication (table 1). TKIs are relatively well tolerated, and you can return to your usual daily activities once you start treatment.

It is very important to take the recommended TKI dose on schedule and to avoid other medications or supplements that may impair efficacy. People who miss fewer doses are more likely to have better outcomes. Many prescription and non-prescription medications can interact with TKIs, potentially making the treatment less effective or dangerously increasing the amount of drug in the bloodstream. Two non-prescription medications that should be avoided are acetaminophen (brand name: Tylenol) and the herb St. John's wort (also called hypericum perforatum). Grapefruit juice should also be avoided.

Imatinib (brand name: Gleevec) — Imatinib mesylate is a TKI that can be used in people with all phases of CML. It is proven to have significant benefits. With imatinib, almost all people (>95 percent) will achieve a complete hematologic response, and a majority (76 percent) will have a complete cytogenetic response [1].

The relapse rate has been remarkably low in people followed for 10 or more years who achieved a complete cytogenetic response. At present, experts recommend continuing imatinib treatment indefinitely because the disease recurs, often within months, in the majority of people who stop taking it. Progression to blast crisis can occur despite imatinib treatment in people with accelerated phase disease and in those who acquire new genetic mutations. Testing for additional mutations should be performed at the time of progression.

The medication should be taken by mouth once daily, with a meal and a large glass of water.

It is extremely important to take every single scheduled dose of your imatinib. Skipping pills can seriously jeopardize your chances of having a good response. One study showed that you need to take over 90 percent of your pills to have a chance of a sustained complete response [4].

Side effects — Imatinib is generally very well tolerated; most side effects are mild to moderate and do not cause the person to stop taking it. Less than 5 percent of people will be unable to tolerate long-term treatment with imatinib. As with all of the TKIs, some side effects, perhaps most notably diarrhea and rash, often occur shortly after starting treatment and abate over time. Possible side effects include the following:

- Nausea and vomiting may occur, although this is not usually a problem when the drug is taken with meals.
- Diarrhea is usually mild to moderate, but can be severe.
- Muscle cramps are perhaps the most bothersome long-term symptom associated with imatinib, most commonly affecting the calves, feet, and hands. There is no definitive treatment, although some people benefit from treatment with calcium or magnesium supplements.
- Skin rash is uncommon. When it occurs, it is usually mild and often resolves with continued treatment.
- Breast enlargement (gynecomastia) may occur in a small number of men.
- Mild anemia, which manifests as fatigue or listlessness, is not uncommon in people who use imatinib for long periods.

- Some people note mild to moderate fatigue.

Pregnancy — Women and men who take imatinib usually have no increased difficulty achieving pregnancy. However, the risk of miscarriage and birth defects while taking imatinib is uncertain. Thus, men and women who take imatinib are strongly advised to use birth control during treatment.

Women who take imatinib and become pregnant are left with a difficult choice:

- Continuing imatinib, which may result in damage to the developing fetus.
- Stopping imatinib, which may allow CML to relapse in the mother. Many doctors recommend temporary treatment with interferon alpha in this situation. (See 'Interferon alpha' below.)

In one series of women exposed to imatinib during pregnancy, 50 percent delivered a healthy baby, 28 percent elected to have a termination (abortion), 14 percent had a miscarriage, and approximately 10 percent had a baby with a birth defect [5]. In addition, imatinib is passed into breast milk, and breastfeeding women are advised to avoid imatinib. If you become pregnant while taking imatinib (or any tyrosine kinase inhibitor), stop taking the drug immediately and contact your healthcare provider as soon as possible.

Dasatinib (brand name: Sprycel) — Dasatinib is a second generation TKI that may be recommended for treatment of CML after imatinib. It can also be used as initial treatment instead of imatinib. It is taken by mouth once or twice daily.

Side effects — People taking dasatinib may have low white blood cell and platelet counts. Too few white blood cells can increase the risk of infection and low platelet counts are associated with easy bruising and bleeding. Some have reported headaches.

Up to 35 percent of people who take dasatinib for advanced phase CML can develop a pleural effusion, a collection of fluid in space between the lining of the lung (the pleura) and the chest wall. In some cases, this complication requires a reduction in the dose of dasatinib, a temporary break in treatment, or a procedure to drain the fluid. Pleural effusions occur in approximately 10 percent of people treated with dasatinib in chronic phase and generally tend to be less severe than in people with advanced CML.

Rarely, people have developed pulmonary hypertension (high blood pressure in the blood vessels that carry blood to the lungs). Pulmonary hypertension causes you to have trouble breathing and to feel very tired.

An abnormal heart rhythm, known as QT prolongation, is a potential side effect of both dasatinib and nilotinib (see 'Nilotinib (brand name: Tasigna)' below). QT prolongation can potentially cause sudden cardiac death, although this complication is very rare. If you have an electrolyte imbalance (low blood level of potassium or magnesium) or an abnormal heart rhythm, or if you take medication to regulate your heart rhythm, talk to your doctor about the need for additional monitoring while taking dasatinib or nilotinib.

Women who are pregnant or breastfeeding should not use dasatinib due to the potential risk of harm to the infant; men and women are strongly encouraged to use a birth control method during treatment. If you become pregnant while taking dasatinib (or any tyrosine kinase inhibitor), stop taking the drug immediately and contact your healthcare provider as soon as possible.

Nilotinib (brand name: Tasigna) — Nilotinib is another second generation TKI that may be recommended for treatment of CML after imatinib. It can also be used as initial treatment instead of imatinib. It should be taken by mouth on an empty stomach (one hour before or two hours after eating) every 12 hours; taking the medication with food can lead to excessive amounts of the drug in the bloodstream and is not recommended.

Side effects — The most common side effects of nilotinib include rash, itching, nausea, and constipation. An abnormal heart rhythm, known as QT prolongation, is a potential side effect of both dasatinib and nilotinib (see above).

There is a higher rate of cardiovascular complications in people receiving nilotinib compared with those receiving imatinib, particularly in individuals with cardiovascular risk factors (high blood pressure, high blood cholesterol, diabetes, smokers). These complications include stroke, heart attacks, and symptoms related to decreased blood flow to the legs. The latter is called "peripheral arterial occlusive disease" and can cause leg pain that gets worse with activity. Muscle pain that gets worse with activity and improves with rest is called "claudication."

Women who are pregnant or breastfeeding should not use nilotinib; men and women are strongly encouraged to use birth control during treatment. If you become pregnant while taking nilotinib (or any tyrosine kinase inhibitor), stop taking the drug immediately and contact your healthcare provider as soon as possible.

Bosutinib (brand name: Bosulif) — Bosutinib is another TKI that may be recommended for treatment of CML after failure of another TKI. It should be taken daily by mouth with food. Major side effects include diarrhea, abnormalities in liver function tests, and nausea and vomiting. Some people have fluid retention. Fluid retention includes swelling in the legs (called edema) and fluid around the lungs (pleural effusion). Women who are pregnant or breastfeeding should not use bosutinib; men and women are strongly encouraged to use birth control during treatment. If you become pregnant while taking bosutinib (or any tyrosine kinase inhibitor), stop taking the drug immediately and contact your healthcare provider as soon as possible.

Ponatinib (brand name: Iclusig) — Ponatinib is another TKI that may be recommended for treatment of CML that has relapsed or is unresponsive to treatment with other TKIs. It is the only TKI that is active in CML with certain mutations (eg, T315I). Due to concerns regarding dangerous side effects, ponatinib is reserved for use in people who are not candidates for other TKIs. Potentially life-threatening side effects include cardiovascular problems (stroke, heart attack, peripheral artery disease), inflammation of the pancreas (pancreatitis), and liver failure. Women who are pregnant or breastfeeding should not use ponatinib; men and women are strongly encouraged to use birth control during treatment. If you become pregnant while taking ponatinib (or any tyrosine kinase inhibitor), stop taking the drug immediately and contact your healthcare provider as soon as possible.

STEM CELL TRANSPLANT — For a stem cell transplant (also referred to as hematopoietic cell transplant or bone marrow transplant), your diseased bone marrow cells are replaced with healthy ones from a donor. The donor's immune system, which is generated from the transplanted stem cells, recognize your cells, including the tumor cells, as foreign and rejects them. This beneficial reaction is called the **graft-versus-tumor** effect, while the harmful effect in which the donor immune cells attack other organs in the body, including the skin, liver, and gastrointestinal tract, is termed "graft-versus-host disease (GVHD)." GVHD can be a severe and sometimes fatal complication although medications are routinely given to prevent this problem. (See "Patient education: Hematopoietic cell transplantation (bone marrow transplantation) (Beyond the Basics)".)

Choice of donor — The donor is a person other than yourself; this is called an "allogeneic transplant." Allogeneic transplants can come from a relative (eg, sibling) or from an unrelated donor. Within a family, the best chance for a genetic match comes from siblings who have the same parents as you. Each sibling has a one in four chance of matching you. If you do not have a sibling who matches, an unrelated donor may be used. Related or unrelated donors who are fully matched are preferred. Under some circumstances, partially or half-matched ("haploidentical") donors, such as parents or children, can be used.

In CML, the chances of success with stem cell transplant are directly related to the phase of disease at the time of the transplant. In the past, transplantation of people in chronic phase within the first year resulted in the best outcomes. Several studies have suggested that treatment with a tyrosine kinase inhibitor (TKI) prior to transplantation does not reduce the chance that transplantation will be successful.

If a matched sibling donor can be found, 50 to 85 percent of people with CML transplanted in the first or second chronic phase of their disease achieve long-term remissions. Disease-free survival falls to 30 to 40 percent in people transplanted in the accelerated phase, and to 10 to 20 percent in people transplanted in blast phase.

Outcome — Your age has a major influence on the outcome after transplantation with cells from a sibling donor. For people under age 50 who undergo this procedure during the first year of diagnosis, 70 to 85 percent will be alive and free of disease five years later. However, people up to 70 years of age have successfully undergone transplantation with treatments that completely destroy the bone marrow (this is called myeloablative treatment). The development of "reduced intensity" regimens has permitted even older people to successfully undergo transplantation.

Relapse after transplant — Relapse or recurrence of CML may occur if cells containing the Philadelphia chromosome remain after the transplant procedure. However, finding residual disease with sensitive molecular tests (polymerase chain reaction) in the first six months following transplantation is **not** associated with eventual relapse because the anti-tumor effects of the graft may eventually destroy these cells (the graft-versus-tumor effect).

Relapse can be treated with a TKI or with infusions of leukocytes (white blood cells) from the original donor, with the hope of mounting a more effective graft-versus-tumor effect. Donor leukocyte infusions (DLIs) can be extremely effective, and remissions attained after DLI appear to be quite durable. However, graft-versus-host disease (when the donor's immune cells attack your healthy cells), and in some instances graft failure, may complicate DLI. (See "Patient education: Hematopoietic cell transplantation (bone marrow transplantation) (Beyond the Basics)", section on 'Graft-versus-host disease'.)

INTERFERON ALPHA — Interferon alpha (IFNa, brand name: Pegasys) was commonly used in the past for treatment of CML. In up to 90 percent of people, interferon can induce a hematologic response, improve symptoms, and reduce or eliminate enlargement of the spleen (splenomegaly). However, tyrosine kinase inhibitors (TKIs) are clearly superior to IFNa in studies comparing the two treatments.

As a result, interferon is considered to be a "palliative" treatment for CML, since it is not curative and only rarely results in a prolonged complete cytogenetic response. If you cannot tolerate TKIs, you might be offered IFNa with or without another chemotherapy medication, called cytarabine.

Side effects — Side effects are a major problem with IFNa, and include fever, chills, and flu-like symptoms. Typically, the drug is started at a relatively low dose three days per week and then slowly increased. IFNa must be injected, and many people prefer to take their injection at night along with acetaminophen (brand name: Tylenol) and an antihistamine such as diphenhydramine (brand name: Benadryl) to minimize the side effects.

CLINICAL TRIALS — Many people with CML will be asked about enrolling in a clinical (research) trial. A clinical trial is a carefully controlled way to study the effectiveness of new treatments or new combinations of known therapies. Ask your healthcare provider for more information, or read about clinical trials at:

- www.cancer.gov/clinicaltrials/
- http://clinicaltrials.gov/

Videos addressing common questions about clinical trials are available from the American Society of Clinical Oncology (http://www.cancer.net/pre-act).

WHERE TO GET MORE INFORMATION — Your healthcare provider is the best source of information for questions and concerns related to your medical problem.

This article will be updated as needed on our website (www.uptodate.com/patients). Related topics for patients, as well as selected articles written for healthcare professionals, are also available. Some of the most relevant are listed below.

Patient level information — UpToDate offers two types of patient education materials.

The Basics — The Basics patient education pieces answer the four or five key questions a patient might have about a given condition. These articles are best for patients who want a general overview and who prefer short, easy-to-read materials.

Patient education: Leukemia in adults (The Basics)
Patient education: Chronic myeloid leukemia (CML) (The Basics)
Patient education: Neutropenia and fever in people being treated for cancer (The Basics)

Beyond the Basics — Beyond the Basics patient education pieces are longer, more sophisticated, and more detailed. These articles are best for patients who want in-depth information and are comfortable with some medical jargon.

Patient education: Hematopoietic cell transplantation (bone marrow transplantation) (Beyond the Basics)

Professional level information — Professional level articles are designed to keep doctors and other health professionals up-to-date on the latest medical findings. These articles are thorough, long, and complex, and they contain multiple references to the research on which they are based. Professional level articles are best for people who are comfortable with a lot of medical terminology and who want to read the same materials their doctors are reading.

Cellular and molecular biology of chronic myeloid leukemia
Clinical manifestations and diagnosis of chronic myeloid leukemia
Clinical use of tyrosine kinase inhibitors for chronic myeloid leukemia
Genetic abnormalities in hematologic and lymphoid malignancies
Hematopoietic cell transplantation in chronic myeloid leukemia
Initial treatment of chronic myeloid leukemia in chronic phase
Interferon alfa for the treatment of chronic myeloid leukemia
Molecular genetics of chronic myeloid leukemia
Overview of the myeloproliferative neoplasms
Overview of the treatment of chronic myeloid leukemia
Treatment of chronic myeloid leukemia in accelerated phase
Treatment of chronic myeloid leukemia in blast crisis
Treatment of chronic myeloid leukemia in chronic phase after failure of initial therapy

The following organizations also provide reliable health information.

- National Library of Medicine

  (www.nlm.nih.gov/medlineplus/healthtopics.html)

- National Cancer Institute

  (www.cancer.gov)

- American Cancer Society

  (www.cancer.org)

- The Leukemia & Lymphoma Society

  (www.lls.org)

- National Marrow Donor Program

  (www.marrow.org)

- American Society of Clinical Oncology

  (www.cancer.net/cml)

- American Society of Hematology

  (http://www.hematology.org/Patients/)

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GRAPHICS

Comparison of tyrosine kinase inhibitors used for chronic myeloid leukemia

Generic name	United States brand name	How taken	Risks and side effects	Other
Imatinib	Gleevec	Daily (or twice daily) with food	▪ Low blood counts (increased infection) ▪ Swelling and fluid retention ▪ Diarrhea ▪ Rash ▪ Fatigue ▪ Muscle cramps ▪ Heart damage (uncommon) ▪ Liver damage (uncommon)	Most long-term safety data
Nilotinib	Tasigna	Twice daily without food	▪ Low blood counts (increased infection) ▪ Rash, itching ▪ Abnormal heart rhythm (called QT prolongation) ▪ Heart attack, stroke, and related events ▪ Electrolyte imbalance ▪ Liver damage ▪ Pancreatitis (inflammation of the pancreas that can cause stomach pain)	
Dasatinib	Sprycel	Daily with or without food	▪ Low blood counts (increased infection and fatigue) ▪ Pleural or pericardial effusions (fluid around the lung or heart) ▪ Pulmonary hypertension (high blood pressure in the blood vessels that carry blood to the lungs; uncommon) ▪ Abnormal heart rhythm (called QT prolongation) ▪ Easy bleeding and bruising ▪ Headache	
Bosutinib	Bosulif	Daily with food	▪ Low blood counts (increased infection and fatigue) ▪ Fever, fatigue, headache ▪ Swelling and fluid retention ▪ Diarrhea, nausea, vomiting ▪ Liver damage	
Ponatinib	Iclusig	Daily with or without food	▪ Low blood counts (increased infection and fatigue) ▪ Swelling and fluid retention ▪ Nausea, vomiting, diarrhea ▪ Heart failure ▪ High blood pressure ▪ Pancreatitis (inflammation of the pancreas that can cause stomach pain) ▪ Easy bleeding and bruising	Least long-term safety data; active in patients with BCR-ABL T315I mutation

			▪ Heart attack, stroke, and related events ▪ Liver toxicity	

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