


ICLUSIG[®] (ponatinib) patient guide

A guide that helps you learn more about your disease and treatment with ICLUSIG

Please see Important Safety Information throughout and read the [Patient Medication Guide](#) in the accompanying full [Prescribing Information](#).


ICLUSIG[®]
(ponatinib) tablets
45 mg, 15 mg



Not an actual patient

Now that your doctor has brought ICLUSIG[®] (ponatinib) into the picture, here is a guide to help you:

- Understand your condition
- Know what you may experience with ICLUSIG
- Find additional support and resources

Whether you have **chronic myeloid leukemia (CML)** or **Philadelphia chromosome positive acute lymphoblastic leukemia (Ph+ ALL)** now is the time for a new plan.

See the full glossary on pages 32-33 for definitions of all the bold words in this guide that may be unfamiliar to you.

What is ICLUSIG?

ICLUSIG is a prescription medicine used to treat adults who have:

- chronic phase, accelerated phase, or blast phase chronic myeloid leukemia (CML) or Philadelphia chromosome positive acute lymphoblastic leukemia (Ph+ ALL) who cannot receive any other tyrosine kinase inhibitor (TKI) medicines
- a specific type of abnormal gene (T315I-positive) chronic phase, accelerated phase, or blast phase CML, or T315I-positive Ph+ ALL

ICLUSIG is not for use to treat people with newly diagnosed chronic phase CML.

It is not known if ICLUSIG is safe and effective in children less than 18 years of age.

Please see Important Safety Information throughout and read the [Patient Medication Guide](#) in the accompanying full [Prescribing Information](#).



What do I need to know about CML and Ph+ ALL, and ICLUSIG® (ponatinib)?

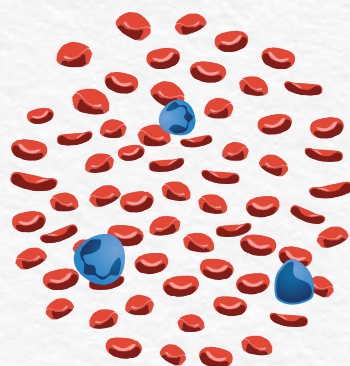
- What is CML and what are my treatment goals?
- What is Ph+ ALL and what are my treatment goals?
- Why start a new treatment?
- What is the most important information I should know about ICLUSIG (side effects)?
- What have studies of ICLUSIG in CML and Ph+ ALL shown?
- What should I know about taking ICLUSIG?

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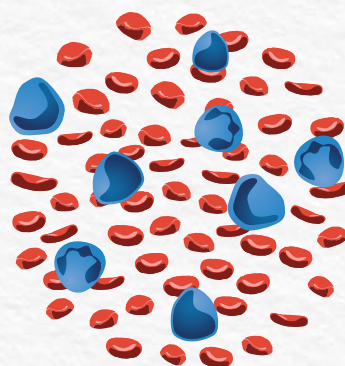
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What is CML?



Here is a brief overview of what **chronic myeloid leukemia (CML)** is and how it starts in the body.



Normal Blood



CML

-  **White blood cell** — Normal part of immune system that helps fight infection
-  **Red blood cell** — Carries oxygen around the body

CML starts when there is an abnormal change (or **mutation**) in a person's DNA. This mutation creates the "**Philadelphia**" or **Ph chromosome**. The Ph chromosome causes the body to make a protein called **BCR-ABL1**. This protein then causes the bone marrow to start making abnormal white blood cells. These are CML cells, and they crowd healthy white blood cells out of your bone marrow to cause leukemia.

CML has 3 phases: **chronic phase (CP)**, **accelerated phase (AP)**, and **blast phase (BP)**. Most people with CML are diagnosed in CP. An important goal of CP-CML treatment is to prevent progression to AP and BP.



Your healthcare provider is your primary source of information.
Always consult your healthcare provider if you have questions about your condition.

KEY TERMS

Accelerated phase CML (AP-CML): The second phase of CML progression, when the number of blast cells is increased.

BCR-ABL1: An abnormal protein that causes the creation of too many abnormal white blood cells (leukemia cells).

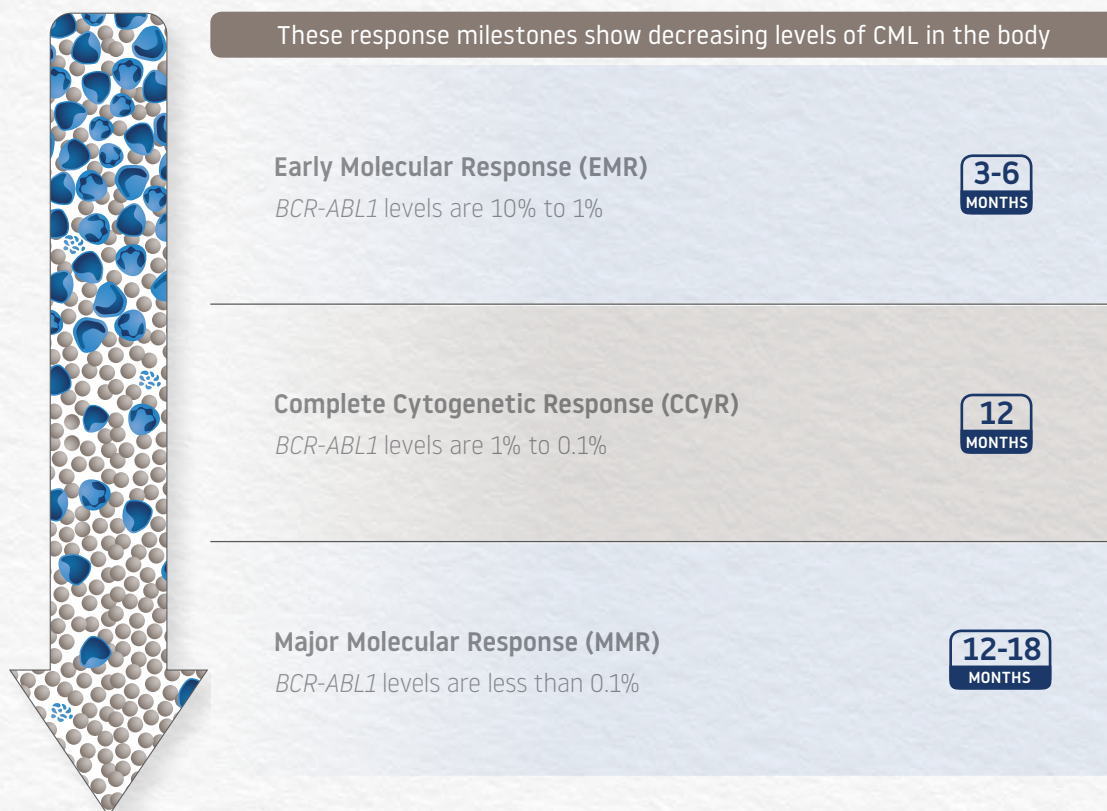
Blast phase CML (BP-CML): The third and final phase of CML progression, which has the highest number of blast cells in the blood and bone marrow.

Chronic phase CML (CP-CML): The first phase of CML, when there are more white blood cells than normal but may not cause symptoms.

Philadelphia (Ph) chromosome: An abnormal chromosome, which is associated with CML and Ph+ ALL.

What are my treatment goals?

Your healthcare provider will look for specific responses at different times in your treatment. These milestones may help your healthcare provider better understand if your treatment is working. Your healthcare provider will tell you which specific responses (often referred to as “milestones”) they are looking for and how you may be monitored while you are on treatment.



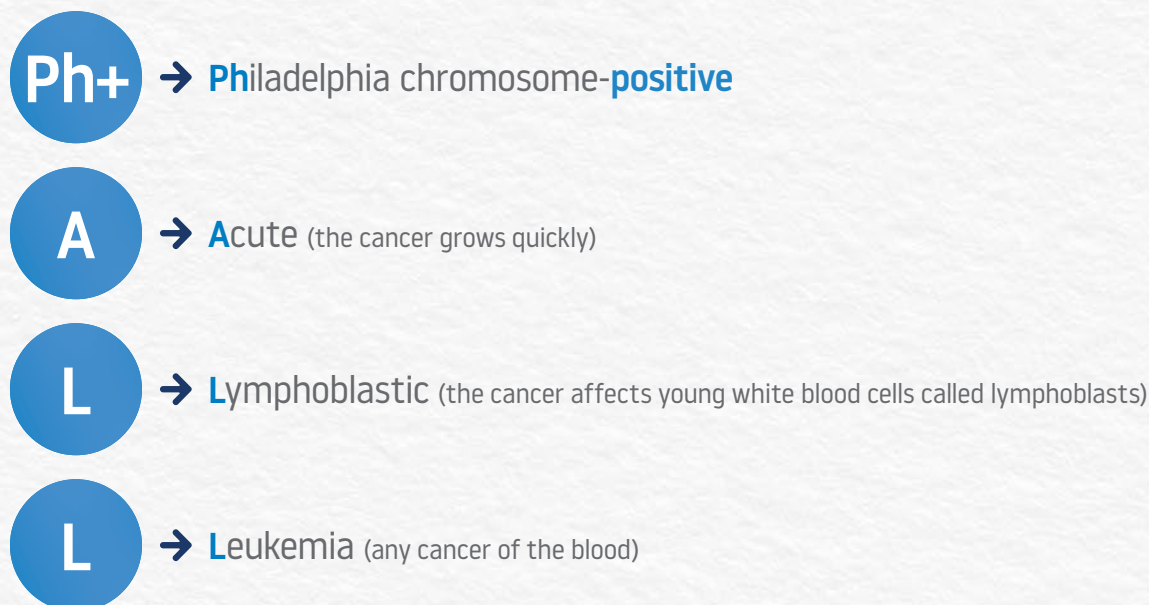
Other milestone terms you may hear about

- **Complete hematologic response (CHR):** Blood cell counts are normal, and no abnormal blood cells are detected.
- **Complete molecular response (CMR):** *BCR-ABL1* cannot be detected.
- **Major cytogenetic response (MCyR):** The number of blood cells with Ph chromosome has decreased by about one-third.

Please see Important Safety Information throughout and read the [Patient Medication Guide](#) in the accompanying full [Prescribing Information](#).

What is Ph+ ALL?

Let's review what Philadelphia chromosome positive acute lymphoblastic leukemia (Ph+ ALL) is and how it starts.



Ph+ ALL (or “Philadelphia-positive ALL”) is a fast-growing cancer of the blood that starts in young white blood cells (lymphoblasts or simply, **blast cells**). In people with Ph+ ALL, an abnormal change in a person’s **DNA (mutation)** creates the “**Philadelphia**” (or **Ph**) **chromosome**. The Ph chromosome causes the body to produce the **BCR-ABL1** protein. This protein causes the bone marrow to produce too many lymphoblasts, leading to leukemia.

KEY TERMS

BCR-ABL1: An abnormal protein that is made by the *BCR-ABL1* fusion gene and causes too many abnormal white blood cells (leukemia cells) to be made.

BCR-ABL1 mutations: Changes to the BCR-ABL1 protein that prevent certain tyrosine kinase inhibitors (TKIs) from working.

Blast cell: Abnormal, immature blood cell.

Chemotherapy: Medicines that kill fast-growing cells, including cancer cells and normal cells.

Clinical trial: Research on a test or treatment to assess its safety or how well it works.

Complete remission: When no leukemia cells are found in the blood or bone marrow and all signs and symptoms of the cancer are gone.

Corticosteroids: Medicines used to reduce redness, swelling, and pain, but also to kill leukemia cells; also called steroids.

DNA: The genetic information carried by cells.

MRD (or minimal residual disease): A very small number of cancer cells left in the body after treatment.

Mutation testing: Tests used to see if samples of deoxyribonucleic acid (DNA; the genetic information carried by cells) have changed (mutated).

Philadelphia (Ph) chromosome: An abnormal chromosome, which is associated with CML and Ph+ ALL.

Stem cell transplant: Treatment that replaces damaged or diseased cells in the bone marrow—soft tissue in the center of bones where blood cells are made—with healthy blood-forming cells called blood stem cells.

Tyrosine kinase inhibitor (TKI): A type of medicine that stops the growth of leukemic cells by blocking BCR-ABL1.

How is Ph+ ALL treated?

Treatment usually consists of **chemotherapy**, **corticosteroids**, and a **tyrosine kinase inhibitor (TKI)**. Many people with Ph+ ALL at some point may need a **stem cell transplant**. Your healthcare provider will find the treatment that is right for you.

What should I know about Ph+ ALL treatment goals, and how are they monitored?

If you have Ph+ ALL, your healthcare provider will track how your disease is responding to treatment on a schedule depending on the regimen she or he has you on, your age, and overall health.

- The goal of treatment is **complete remission**, which means that your blood counts are normal, your disease symptoms are gone, and your healthcare providers cannot see leukemia cells in a sample of your bone marrow using a microscope.
 - Even if you have complete remission, there may still be a small number of leukemia cells left behind called **minimal residual disease (MRD)** that can only be detected with sensitive tests.
- In addition to MRD testing, your healthcare provider may monitor the levels of BCR-ABL1 in your blood.
- If your Ph+ ALL does not go into complete remission after the first phase of treatment, your healthcare provider may order **mutation testing** because new **BCR-ABL1 mutations** can appear during treatment.
- If a new mutation is found, your doctor may consider a change in TKI therapy.



Always consult your healthcare provider if you need more information about Ph+ ALL treatment goals.

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Why is my healthcare provider changing therapy?

Some people will need to change their **tyrosine kinase inhibitor (TKI)** treatment over time. There are 2 main reasons why a person may need to change TKI therapy—resistance and intolerance. Resistance and intolerance can appear at any time.

Resistance: When a TKI does not work well for a person's particular type of CML or Ph+ ALL, or it stops working over time.

Intolerance: When a TKI causes side effects that result in a healthcare provider recommending a patient not continue taking it.

TKIs can stop the growth of leukemic cells by blocking the abnormal BCR-ABL1 protein. Many people with CML or Ph+ ALL respond well to the first TKI they try and may stay on that treatment for years.

Monitoring can help healthcare providers determine if you are resistant to other treatments

Regular monitoring can help your healthcare provider find early signs of resistance.

Your healthcare provider will use different tests to monitor your disease levels and check how your CML is responding to treatment.

Response monitoring tests

Molecular monitoring is sometimes called **QPCR**. It is a test that can measure small amounts of **BCR-ABL1** in the blood.

- Molecular monitoring is recommended every 3 to 6 months throughout treatment
- Many laboratories use an **International Scale** to make sure measurements are the same from lab to lab

Cytogenetic testing measures the number of cells in your bone marrow that contain the **Philadelphia chromosome**.

- Your healthcare provider may do this test before you start treatment
- This test may be repeated if your healthcare provider thinks you may be resistant to treatment

How do mutations affect treatment options?

Part of the difficulty of treating any type of cancer, including CML and Ph+ ALL, is that cancer cells can change (or mutate) over time. In CML and Ph+ ALL, mutations can appear in BCR-ABL1 during TKI treatment. This can cause you to stop responding to the TKI.

If you develop a new mutation while on a TKI, your healthcare provider may want to change your therapy to a different TKI that may work better against the new mutation.

T315I is a specific type of mutation that can occur in CML and Ph+ ALL. ICLUSIG® (ponatinib) is currently the only TKI that works in people with CML and Ph+ ALL who have the T315I mutation.



Please consult with your healthcare provider if you want to learn more about mutations, monitoring, and treatment.

KEY TERMS

BCR-ABL1: An abnormal protein that is made by the *BCR-ABL1* fusion gene and causes too many abnormal white blood cells (leukemia cells) to be made.

BCR-ABL1 mutations: Changes to the BCR-ABL1 protein that prevent certain TKIs from working.

International Scale (IS): A standardized scale for measuring and reporting *BCR-ABL1* levels.

Philadelphia (Ph) chromosome: An abnormal chromosome, which is associated with CML and Ph+ ALL.

QPCR: A very sensitive test that measures the number of cells in the blood or bone marrow that have *BCR-ABL1*.

T315I: A type of BCR-ABL1 mutation that causes cancer cells to not respond to certain TKIs.

Tyrosine kinase inhibitor (TKI): A type of medicine that stops the growth of leukemic cells by blocking BCR-ABL1.

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IMPORTANT SAFETY INFORMATION

What is the most important information I should know about ICLUSIG® (ponatinib)?

ICLUSIG can cause serious side effects, including:

Blood clots or blockage in your blood vessels (arteries and veins). Blood clots or blockage in your blood vessels may lead to heart attack, stroke, or death. A blood clot or blockage in your blood vessels can prevent proper blood flow to your heart, brain, bowels (intestines), legs, eyes, and other parts of your body. You may need emergency surgery or treatment in a hospital. Get medical help right away if you get any of the following symptoms:

- chest pain or pressure
- pain in your arms, legs, back, neck or jaw
- shortness of breath
- numbness or weakness on one side of your body
- leg swelling
- trouble talking
- headache
- dizziness
- severe stomach area pain
- decreased vision or loss of vision

Blood clots or blockage in your blood vessels can happen in people with or without risk factors for heart and blood vessel disease, including people 50 years of age or younger. The most common risk factors for these problems are a history of high blood pressure (hypertension), high levels of fat in the blood (hyperlipidemia), and heart disease. Blood clots or blockages in your blood vessels happen more often in people as they get older, and in people with a past history of decreased blood flow, high blood pressure, diabetes, or high levels of fats in the blood.

Heart problems. ICLUSIG can cause heart problems, including heart failure which can be serious and may lead to death. Heart failure means your heart does not pump blood well enough. ICLUSIG can also cause irregular slow or fast heartbeats and heart attack. Your healthcare provider will check you for heart problems during your treatment with ICLUSIG. Get medical help right away if you get any of the following symptoms: shortness of breath, chest pain, fast or irregular heartbeats, dizziness, or feel faint.

Liver problems. ICLUSIG can cause liver problems, including liver failure, which can be severe and may lead to death. Your healthcare provider will do blood tests before and during your treatment with ICLUSIG to check for liver problems. Get medical help right away if you get any of these symptoms of liver problems during treatment:

- yellowing of your skin or the white part of your eyes (jaundice)
- dark “tea-colored” urine
- sleepiness
- loss of appetite
- bleeding or bruising

See **“What are the possible side effects of ICLUSIG?”** on pages 20-21 for information about side effects.

Before you take ICLUSIG, tell your healthcare provider about all your medical conditions, including if you:

- have a history of blood clots in your blood vessels (arteries or veins)
- have heart problems, including heart failure, irregular heartbeats, and QT prolongation
- have diabetes
- have a history of high cholesterol
- have liver problems
- have had inflammation of your pancreas (pancreatitis)
- have high blood pressure
- are pregnant or plan to become pregnant. ICLUSIG can harm your unborn baby.
 - Your healthcare provider will do a pregnancy test before you start taking ICLUSIG.
 - You should not become pregnant during treatment with ICLUSIG.
- **For females who can become pregnant:**
 - Use an effective form of birth control during treatment and for **3 weeks** after your last dose of ICLUSIG.
 - Tell your healthcare provider right away if you become pregnant or think you might be pregnant during treatment with ICLUSIG.
 - ICLUSIG may affect your ability to have children. Tell your healthcare provider if this is a concern for you.
- are breastfeeding or plan to breastfeed. It is not known if ICLUSIG passes into your breast milk. **Do not** breastfeed during treatment and for **6 days** after your last dose of ICLUSIG.
- have bleeding problems
- plan to have any surgical procedures or have had a recent surgery
- are lactose (milk sugar) intolerant. ICLUSIG tablets contain lactose.
- drink grapefruit juice

Tell your healthcare provider about all the medicines you take, including prescription medicines and over-the-counter medicines, vitamins, and herbal supplements. ICLUSIG and other medicines may affect each other causing side effects.

Know the medicines you take. Keep a list of them to show your healthcare provider and pharmacist when you get a new medicine.

How should I take ICLUSIG?

- Take ICLUSIG exactly as your healthcare provider tells you to take it.
- Swallow ICLUSIG tablets whole. Do not crush or dissolve ICLUSIG tablets.
- You may take ICLUSIG with or without food.
- If you miss a dose of ICLUSIG, take your next dose at your regular time. Do not take 2 doses at the same time to make up for a missed dose.
- If you take too much ICLUSIG, call your healthcare provider or go to the nearest hospital emergency room right away.

**REMEMBER:**

- **Be sure to tell your healthcare provider about any side effects you have while taking ICLUSIG**
- **Your healthcare provider may change your dose, temporarily stop, or permanently stop treatment with ICLUSIG if you have certain side effects**

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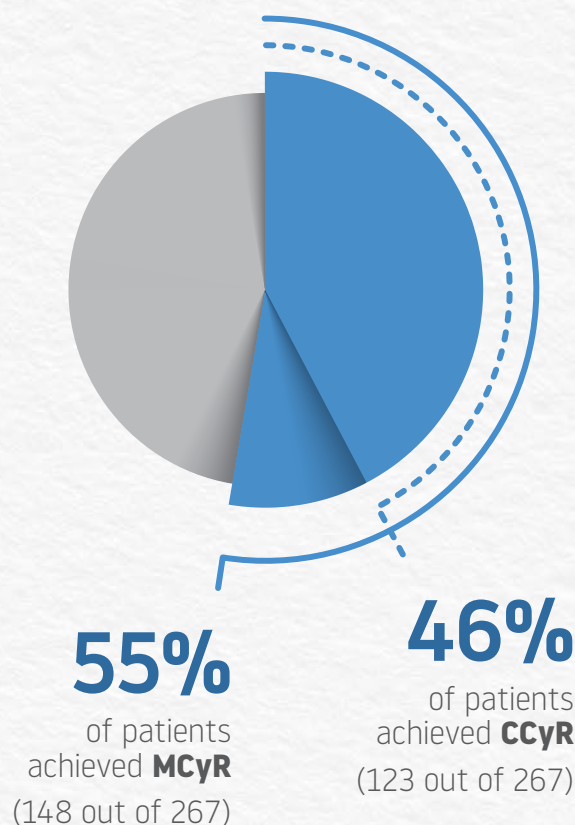
What has the study of ICLUSIG® (ponatinib) shown?

ICLUSIG was studied in a large clinical trial of more than 400 people who had been treated with at least 2 TKIs. It included people with CML and Ph+ ALL; most of them were people with CML.

The clinical trial included 267 people with CP-CML. The goal of this trial was for these patients to have a **major cytogenetic response (MCyR)** by 12 months, which includes patients having a **complete cytogenetic response (CCyR)** and patients having a **partial cytogenetic response (PCyR)**.

ICLUSIG was found to be effective in resistant or intolerant CP-CML

Response rates below should be balanced against side effects, and you should discuss this information with your healthcare provider.

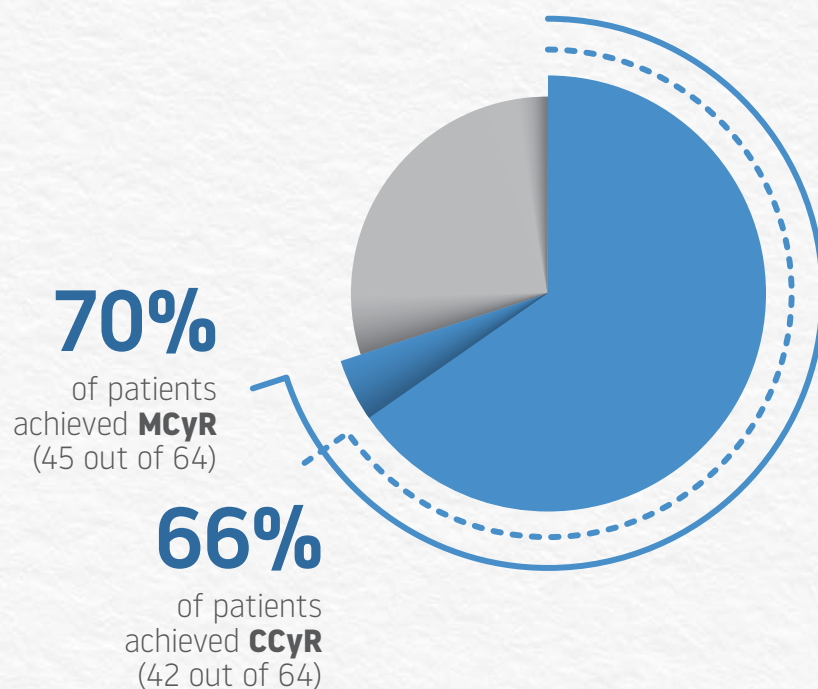


- Talk to your healthcare provider about these ICLUSIG results and others, including **major molecular response (MMR)**.
- Most people who had a response and stayed on treatment still had a response 4 years after starting ICLUSIG.



Talk to your healthcare provider about these ICLUSIG results.
Your personal experience may be different.

ICLUSIG® (ponatinib) is the only TKI indicated for people with the T315I mutation



- 64 people with CP-CML in the ICLUSIG trial had the **T315I** mutation. This has been linked to resistance to other **TKIs**.
- Many patients were able to achieve MCyR by 12 months with ICLUSIG.
- Responses lasted for at least 4 years in most patients who stayed on treatment.

KEY TERMS

Chronic phase CML (CP-CML): The first phase of CML, when there are more white blood cells than normal but may not cause symptoms.

Complete cytogenetic response (CCyR): Treatment response when no Ph chromosomes are seen in a bone marrow sample.

Intolerant: When treatment with a drug must be stopped because of side effects.

Major cytogenetic response (MCyR): Treatment response when about one-third (35% or less) of cells have the Ph chromosome.

Major molecular response (MMR): Treatment response when *BCR-ABL1* levels decrease to <0.1% by 18 months.

Partial cytogenetic response (PCyR): Treatment response when 1% to 35% of bone marrow cells still have the Ph chromosome.

Resistance (or resistant): When cancer cells do not respond to a treatment.

T315I: A type of *BCR-ABL1* mutation that causes cancer cells not to respond to certain TKIs.

Tyrosine kinase inhibitor (TKI): A type of medicine that stops the growth of leukemic cells by blocking *BCR-ABL1*.

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What has the study of ICLUSIG® (ponatinib) in Ph+ ALL shown?

The **clinical trial** included 32 people with **Ph+ ALL** who were resistant or having trouble taking other **TKI** treatments. The study also looked at the safety and effectiveness of ICLUSIG in Ph+ ALL.

The effects of ICLUSIG were evaluated based on the following types of responses:

Complete Hematologic Response (CHR)

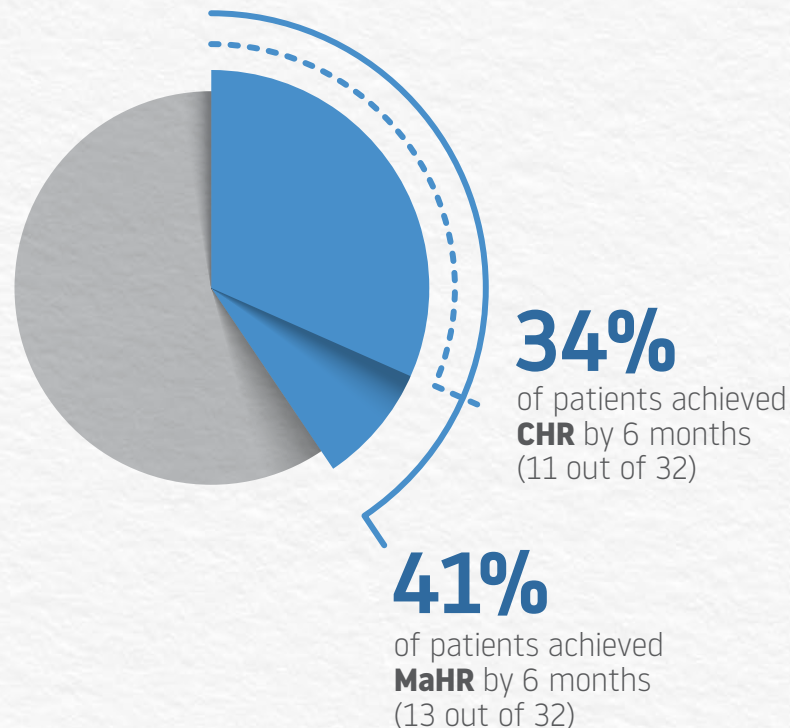
Your blood cell counts decrease to normal.
No young abnormal blood cells can be seen in your blood.

Major Hematologic Response (MaHR)

A combination of CHR and another type of hematologic response called no evidence of leukemia.

ICLUSIG was found to be effective in Ph+ ALL

Response rates below should be balanced against side effects, and you should discuss this information with your healthcare provider.



KEY TERMS

BCR-ABL1: An abnormal protein that is made by the *BCR-ABL1* fusion gene and causes too many abnormal white blood cells (leukemia cells) to be made.

Clinical trial: Research on a test or treatment to assess its safety or how well it works.

Ph+ ALL: Form of leukemia where the cells contain the abnormal Philadelphia chromosome.

Tyrosine kinase inhibitor (TKI): A type of medicine that stops the growth of leukemic cells by blocking BCR-ABL1.

IMPORTANT SAFETY INFORMATION (continued)

The most common side effects of ICLUSIG® (ponatinib) include:

- Stomach-area (abdomen) pain
- Skin rash
- Constipation
- Headache
- Dry skin
- Blood clots or blockage in blood vessels (arteries)
- Tiredness
- High blood pressure
- Fever
- Joint pain
- Nausea
- Diarrhea
- Increase in lipase levels (a blood test done to check your pancreas)
- Vomiting
- Muscle pain
- Pain in arms, hands, legs, and feet

Your healthcare provider may change your dose, temporarily stop, or permanently stop treatment with ICLUSIG if you have certain side effects.

Tell your healthcare provider if you have any side effect that bothers you or that does not go away.



Talk to your healthcare provider about these ICLUSIG results. Your personal experience may be different.

These are not all of the possible side effects of ICLUSIG. For more information, ask your healthcare provider or pharmacist.

Call your healthcare provider for medical advice about side effects. You may report side effects to the FDA at 1-800-FDA-1088.

Please see additional Important Safety Information throughout and read the [Patient Medication Guide](#) in the accompanying full [Prescribing Information](#).

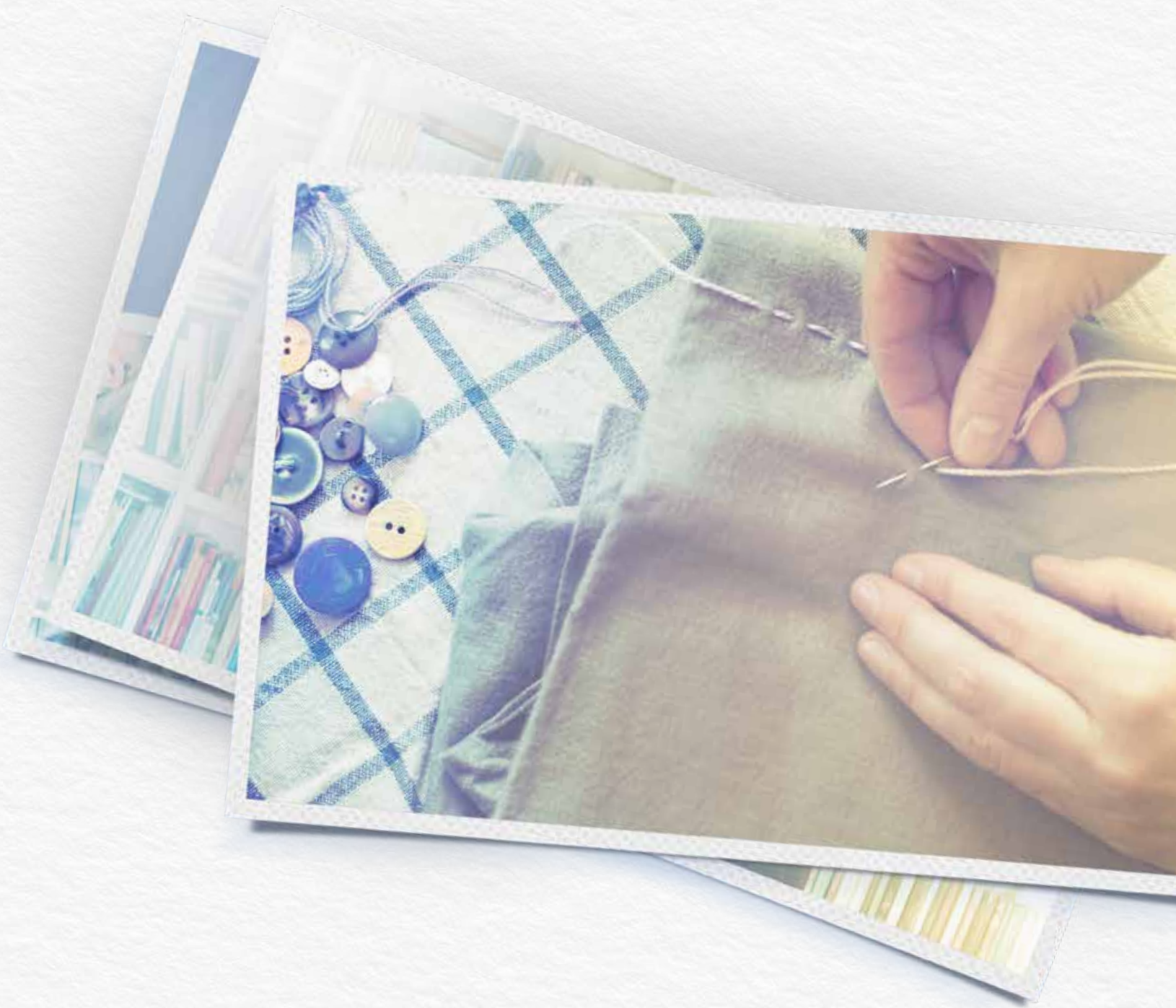
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What is the most important information I should know before taking ICLUSIG® (ponatinib)?

- What are the possible side effects of ICLUSIG?
- How do I work with my healthcare provider to help identify any side effects?

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IMPORTANT SAFETY INFORMATION (continued)

What are the possible side effects of ICLUSIG® (ponatinib)?

ICLUSIG may cause serious side effects, including:

See “What is the most important information I should know about ICLUSIG?”

- **High blood pressure.** Your blood pressure should be checked regularly and any high blood pressure should be treated while you are taking ICLUSIG. Tell your healthcare provider if you get confusion, headaches, dizziness, chest pain or shortness of breath.
- **Inflammation of the pancreas (pancreatitis).** Tell your healthcare provider if you get any of the following symptoms: sudden stomach-area pain or discomfort, nausea, and vomiting. Your healthcare provider should do blood tests to check for pancreatitis during treatment with ICLUSIG.
- **Neuropathy.** ICLUSIG may cause damage to the nerves in your arms, brain, hands, legs, or feet (neuropathy). Tell your healthcare provider if you get any of these symptoms during treatment with ICLUSIG:
 - muscle weakness, tingling, burning, pain, and loss of feeling in your hands and feet
 - double vision and other problems with eyesight, trouble moving the eye, drooping of part of the face, sagging or drooping eyelids, and change in taste
- **Effects on the eye.** Serious eye problems that can lead to blindness or blurred vision may happen with ICLUSIG. Tell your healthcare provider if you get any of the following symptoms: bleeding in the eye, perceived flashes of light, light sensitivity, floaters, dry inflamed, swollen, or itchy eyes, and eye pain. Your healthcare provider will monitor your vision before and during your treatment with ICLUSIG.
- **Severe bleeding.** ICLUSIG can cause bleeding which can be serious and may lead to death. Tell your healthcare provider if you get any signs of bleeding during treatment with ICLUSIG including:
 - vomiting blood or if your vomit looks like coffee-grounds
 - pink or brown urine
 - red or black (looks like tar) stools
 - coughing up blood or blood clots
 - unusual bleeding or bruising of your skin
 - menstrual bleeding that is heavier than normal
 - unusual vaginal bleeding
 - nose bleeds that happen often
 - drowsiness or difficulty being awakened
 - confusion
 - headache
 - change in speech
- **Fluid retention.** Your body may hold too much fluid (fluid retention). Tell your healthcare provider right away if you get any of these symptoms during treatment with ICLUSIG:
 - swelling of your hands, ankles, feet, face, or all over your body
 - weight gain
 - shortness of breath and cough

- **Irregular heartbeat.** ICLUSIG may cause an irregular heartbeat. Tell your healthcare provider right away if you experience loss of consciousness, fainting, dizziness, chest pain or palpitations.
- **Low blood cell counts.** ICLUSIG may cause low blood cell counts, which can be severe. Your healthcare provider will check your blood counts regularly during treatment with ICLUSIG. Tell your healthcare provider right away if you have a fever or any signs of an infection while taking ICLUSIG.
- **Tumor Lysis Syndrome (TLS).** TLS is caused by a fast breakdown of cancer cells. TLS can cause you to have:
 - kidney failure and the need for dialysis treatment
 - an abnormal heartbeat

Your healthcare provider may do blood tests to check for TLS.

- **Reversible Posterior Leukoencephalopathy Syndrome (RPLS – also known as Posterior Reversible Encephalopathy Syndrome - PRES).** ICLUSIG may trigger a condition called RPLS. Call your healthcare provider right away if you get headaches, seizures, confusion, changes in vision or problems thinking.
- **Possible wound healing problems.** If you need to have a surgical procedure, tell your healthcare provider that you are taking ICLUSIG. You should stop taking ICLUSIG at least 1 week before any planned surgery.
- **A tear in your stomach or intestinal wall (perforation).** Tell your healthcare provider right away if you get:
 - severe pain in your stomach-area (abdomen)
 - swelling of the abdomen
 - high fever

To report SUSPECTED ADVERSE REACTIONS, contact Takeda at 1-844-T-1POINT (1-844-817-6468) or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.



These are not all the possible side effects of ICLUSIG.
For more information, ask your healthcare team.

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How do I work with my healthcare provider to help identify any side effects?

By working with your healthcare provider, you can help identify signs and symptoms of side effects.

Starting a new treatment can be overwhelming. It can feel like there is a lot to learn. Take your time, read the medication guide, ask questions, and know that there are things you can do to help your healthcare provider manage the risks of treatment. Here are a few tips:

Look out for the signs and symptoms of ICLUSIG® (ponatinib) side effects.

Some people taking ICLUSIG have experienced side effects that are serious or even fatal.

It's important to know about the signs and symptoms of ICLUSIG side effects as some may need medical treatment, and your healthcare provider may need to adjust your treatment.

Tell your healthcare provider if you have any side effect that bothers you or that does not go away.

Take care of your cardiovascular health.

Cardiovascular side effects, including heart problems and blood clots can happen with ICLUSIG. High cholesterol, diabetes, and high blood pressure can increase these risks. A healthy diet, exercise, and stopping smoking may decrease the risk of cardiovascular side effects.

Talk to your healthcare provider if you are a woman who is pregnant, breastfeeding, or could become pregnant.

ICLUSIG can harm unborn children. You should not become pregnant if you are taking ICLUSIG. Use an effective form of birth control during treatment and for 3 weeks after your last dose.

Tell your healthcare provider right away if you become pregnant or think you might be pregnant during treatment with ICLUSIG.

ICLUSIG may affect your ability to have children. Tell your healthcare provider if this is a concern for you.

It is not known if ICLUSIG passes into your breast milk. Do not breastfeed while you are taking ICLUSIG and for 6 days after your last dose.

Try not to skip medications, tests, or medical appointments.

Your disease may get worse if you skip treatment. Talk to your team if you find it difficult to take your treatment as recommended.

Tell your healthcare provider about your other medical conditions.

Some medical conditions can increase your risk of experiencing side effects with ICLUSIG® (ponatinib). Before you take ICLUSIG, tell your healthcare provider about all of your medical conditions, including if you have:

- A history of blood clots in your blood vessels (arteries or veins)
- Heart problems, including heart failure, irregular heartbeats, and **QT prolongation**
- Diabetes
- A history of high cholesterol
- Liver problems
- Had inflammation of your pancreas (pancreatitis)
- High blood pressure
- Bleeding problems
- Plan to have any surgical procedures or have had a recent surgery
- Are lactose (milk sugar) intolerant. ICLUSIG tablets contain lactose.
- Drink grapefruit juice
- Are pregnant or plan to become pregnant. ICLUSIG can harm your unborn baby.
 - Your healthcare provider will do a pregnancy test before you start taking ICLUSIG.
 - You should not become pregnant during treatment with ICLUSIG.

You should also tell your healthcare provider if you are lactose intolerant (ICLUSIG tablets contain lactose) or if you are planning to have any surgical procedures or have had recent surgery.

Tell your medical team about all the medicines you take.

Some prescription medications, over-the-counter medicines, vitamins, and herbal supplements may affect each other causing side effects. Know the medicines you take. Keep a list of them to show your healthcare provider and pharmacist when you get a new medicine.

KEY TERM

QT prolongation: Electrical signals that help the heart pump are slowed, causing the heart to pump inefficiently.

Please see Important Safety Information throughout and read the [Patient Medication Guide](#) in the accompanying full [Prescribing Information](#).


ICLUSIG[®]
(ponatinib) tablets
45 mg, 15 mg



Getting started on ICLUSIG® (ponatinib)?

This section answers the following questions:

- How should I take ICLUSIG?
- How does dosing work?

Please see Important Safety Information throughout and read the [Patient Medication Guide](#) in the accompanying full [Prescribing Information](#).

**ICLUSIG**[®]
(ponatinib) tablets
45 mg, 15 mg

How should I take ICLUSIG® (ponatinib)?



- Take ICLUSIG exactly as your healthcare provider tells you to take it.
- Swallow ICLUSIG tablets whole. Do not crush or dissolve tablets.
- You may take ICLUSIG with or without food.
- If you miss a dose of ICLUSIG, take your next dose at your regular time. Do not take 2 doses at the same time to make up for a missed dose.
- If you take too much ICLUSIG, call your healthcare provider or go to the nearest hospital emergency room right away.
- Store ICLUSIG at room temperature between 68°F to 77°F (20°C to 25°C).
- Keep ICLUSIG and all medicines out of the reach of children.

Please talk with your healthcare provider if you have any questions about how to take ICLUSIG. Before taking ICLUSIG, tell your healthcare provider about any other medications you take, and any other illnesses you may have.

To report SUSPECTED ADVERSE REACTIONS, contact Takeda at 1-844-T-1POINT (1-844-817-6468) or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.

How does dosing work?

ICLUSIG is prescribed in multiple dose strengths to fit your individual treatment needs. The starting dose is usually 45 mg or 30 mg. Your healthcare provider will start you on the dose that is appropriate for you.

If you have a good response to ICLUSIG, your healthcare provider may decide to lower your dose. Your healthcare provider may also reduce your dose, stop it for a short time, or permanently stop treatment if you experience side effects. Tell your medical team if you have side effects, and ask your healthcare provider about your dose and how it may change over time.

45 mg

The recommended starting dose of ICLUSIG is 45 mg once daily. This dose comes in tablets stamped AP4.

30 mg

If you have liver problems, your healthcare provider may want you to start at 30 mg of ICLUSIG per day.

If you take medications that don't mix well with ICLUSIG your healthcare provider may have you start at 30 mg of ICLUSIG per day.

15 mg

If you experience some side effects, your healthcare provider may prescribe you a lower dose of ICLUSIG: either 30 mg or 15 mg per day.

Patients prescribed a lower dose will receive their ICLUSIG in 15 mg tablets stamped A5.

The optimal dose of ICLUSIG has not yet been identified.

Please see Important Safety Information throughout and read the [Patient Medication Guide](#) in the accompanying full [Prescribing Information](#).


ICLUSIG[®]
(ponatinib) tablets
45 mg, 15 mg





Takeda Oncology 1Point™ and other resources

In this section, you'll learn about:

- Takeda Oncology 1Point
- Additional support resources

RESOURCES

GLOSSARY



Support when you need it



Access Support

Takeda Oncology 1Point™ case managers are your connection to personalized support.



Financial Assistance

Takeda Oncology 1Point can help identify financial assistance programs that may be able to help you with the cost of treatment.



Helpful Resources

Takeda Oncology 1Point case managers can provide you with information about additional resources that may assist with the day-to-day support you might need.

Additional Resources

If you would like to connect with others who have been affected or learn more about your disease, the organizations listed below may be able to help.

Leukemia and Lymphoma Society

1-800-955-4572 (toll-free)
www.lls.org

National CML Society

1-877-431-2573
info@nationalcmlsociety.org
www.nationalcmlsociety.org/

American Heart Association

1-800-242-8721 (toll-free)
inquiries@heart.org
www.heart.org

National Heart, Lung, and Blood Institute

1-301-592-8573
nhlbiinfo@nhlbi.nih.gov
www.nhlbi.nih.gov

Smokefree60+

National Cancer Institute
1-877-448-7848
(1-877-44U-QUIT/toll-free)
cancergovstaff@mail.nih.gov
www.60plus.smokefree.gov

Cancer Care

800-813-HOPE (4673)
info@cancercares.org
www.cancercares.org

We hope you will use the resources above to find the people, tools, and education that will enable you to become an active participant in your care. Takeda Oncology is not affiliated with these organizations. By listing these resources, Takeda Oncology is not endorsing any particular service or group, and we are not responsible for the content of these sites or services. They are provided here for informational purposes and are not meant to replace your healthcare provider's medical advice.

If you have questions on any of the information provided in this treatment guide, please consult your healthcare provider.

Glossary

Accelerated phase CML (AP-CML): The second phase of CML progression, when number of blast cells is increased.

BCR-ABL1: An abnormal protein that is made by the *BCR-ABL1* fusion gene and causes too many abnormal white blood cells (leukemia cells) to be made.

BCR-ABL1 mutations: Changes to the BCR-ABL1 protein that prevent certain TKIs from working.

Blast cell: Abnormal, immature blood cell.

Blast phase CML (BP-CML): The third and final phase of CML progression, which has the highest number of blast cells in the blood and bone marrow and can be life-threatening.

Chemotherapy: Medicines that kill fast-growing cells, including cancer cells and normal cells.

Chronic myeloid leukemia (CML): Form of cancer of the blood-forming cells in the bone marrow that grows slowly and causes too many white blood cells to form.

Chronic phase CML (CP-CML): The first phase of CML, when there are more white blood cells than normal but may not cause symptoms.

Clinical trial: Research on a test or treatment to assess its safety or how well it works.

Complete cytogenetic response (CCyR): Treatment response when no Ph chromosomes are seen in a bone marrow sample.

Complete hematologic response (CHR): Treatment response when blood cell counts decrease to normal and no young abnormal blood cells are seen in the blood.

Complete molecular response (CMR): Treatment response when *BCR-ABL1* cannot be detected in the blood.

Complete remission: When no leukemia cells are found in the blood or bone marrow and all signs and symptoms of the cancer are gone.

Corticosteroids: Medicines used to reduce redness, swelling, and pain, but also to kill leukemia cells; also called steroids.

Cytogenetic testing: A test used to look for changes in chromosomes (the part of the cell that contains genetic information).

Deoxyribonucleic acid (DNA): The genetic information carried by cells.

Early molecular response (EMR): Treatment response when *BCR-ABL1* levels decrease to $\leq 10\%$ within 3 to 6 months of starting treatment.

International Scale (IS): A standardized scale for measuring and reporting results of a very sensitive test that measures the number of cells that have the *BCR-ABL1* gene.

Intolerance: When treatment with a drug must be stopped because of side effects.

Major cytogenetic response (MCyR): Treatment response when about one-third (35% or less) of cells have the Ph chromosome.

Major hematologic response (MaHR): Treatment response that is either a complete hematologic response or another type of hematologic response called no evidence of leukemia (NEL).

Major molecular response (MMR): Treatment response when *BCR-ABL1* levels decrease to <0.1% by 18 months.

Minimal residual disease (MRD): A very small amount of cancer cells left in the body after treatment.

Molecular monitoring: A very sensitive test that can measure very small amounts of *BCR-ABL1* in the blood; sometimes referred to as QPCR.

Mutation: Abnormal change.

Mutation testing: Tests used to see if samples of deoxyribonucleic acid (DNA; the genetic information carried by cells) have changed (mutated).

Partial cytogenetic response (PCyR): Treatment response when 1% to 35% of bone marrow cells still have the Ph chromosome.

Philadelphia chromosome positive acute lymphoblastic leukemia (Ph+ ALL): Form of leukemia where the cells contain the abnormal Philadelphia chromosome.

Philadelphia (Ph) chromosome: An abnormal chromosome that forms when pieces of chromosomes 9 and 22 switch places with each other. This forms a longer chromosome 9 and a shorter chromosome 22. The shorter chromosome 22 contains the *BCR-ABL1* gene and is known as the Philadelphia chromosome.

Quantitative reverse transcriptase polymerase chain reaction (QPCR): A very sensitive test that measures the number of cells in the blood or bone marrow that have *BCR-ABL1*.

QT prolongation: Electrical signals that help the heart pump are slowed, causing the heart to pump inefficiently.

Resistance (or resistant): When cancer cells do not respond to a treatment.

Stem cell transplant: Treatment that replaces damaged or diseased cells in the bone marrow—soft tissue in the center of bones where blood cells are made—with healthy blood-forming cells called blood stem cells.

T315I: A type of *BCR-ABL1* mutation that causes cancer cells to not respond to certain TKIs.

Tyrosine kinase inhibitor (TKI): A type of medicine that stops the growth of leukemic cells by blocking *BCR-ABL1*.

Takeda Oncology 1Point™ is a comprehensive support program committed to helping patients taking ICLUSIG® (ponatinib) navigate coverage requirements, identify available financial assistance,* and connect with helpful resources throughout their therapy.

Learn more at **ICLUSIG.com** or call Takeda at **1-844-T-1POINT (1-844-817-6468)**.

*Terms and Conditions apply.



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