CML AdvocatesNetwork

Treatment Recommendations for People Living with CML

A patient-friendly summary of the European LeukemiaNet recommendations (2013) for the management of Chronic Myeloid Leukemia

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Foreword by the Workgroup

Chronic Myeloid Leukemia (CML) is a chronic disease of the blood and bone marrow that results from a transformation of a stem cell. Stem cells are like seeds in the bone marrow that mature into any of the three major blood cells: white blood cells, red blood cells or platelets. CML stem cells are abnormal and result in overproduction of white blood cells that enter the bloodstream and circulate throughout the body. Usually, but not always, the spleen enlarges. Eventually, CML cells replace normal cells in the bone marrow and prevent production of normal blood cells. As the disease progresses, the number of healthy, normal white blood cells will decline. In addition, there may be an overproduction of immature leukemia cells known as blasts.

In CML cells, a part of one chromosome (number 9) is exchanged with a part of another chromosome (number 22), leading to the formation of the so-called Philadelphia chromosome. As a consequence of this, a gene called ABL that normally is found on chromosome 9 moves to join to the gene called BCR that is normally found on chromosome 22. The fusion of the BCR and ABL genes produces an abnormal gene with increased and not tightly controlled tyrosine kinase activity. This leads to an increase in the number of white blood cells and is thought to be the cause of CML. Treatment targeted to block the tyrosine kinase activity of BCR-ABL has revolutionized the treatment of CML in the past 15 years.

The European LeukemiaNet (ELN), a research network of excellence funded by the European Union, provided treatment recommendations in 2006, 2009 and again in 2013. These recommendations are based on a consensus of 32 CML experts from Europe, America and Asia-Pacific, based on the best scientific data available at the time of publication. They were developed for doctors to help CML patients like you to get the best standard of care and should be recognized as the standard of care by CML treating physicians.

The CML management recommendations may be difficult for patients to understand. We have developed this document in lay language to provide CML patients with a simplified summary of the information contained in the ELN Recommendations.

The 2013 update of the ELN Recommendations reflects that new drugs to treat CML had become available. Important endpoints for monitoring the effectiveness of therapy have been defined and the role of diagnostic tests to optimize follow-up have also been included. This document focuses only on the 2013 publication content and remains valid until the ELN provides a new and/or updated version of the CML Treatment Recommendations.

We hope this summary will be a helpful tool to discuss CML disease management and treatment choices with your doctor. Consider taking this document with you next time you visit your doctor.

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Currently available CML treatments

Chronic Myeloid Leukemia (CML) has evolved from a life-threatening disease to a well manageable disease for most patients. In patients that are well treated and respond well, CML is no longer the threat it once was. Since imatinib was first approved in 2001, doctors have made significant progress in the treatment of CML. Many patients not only survive long-term but also enjoy a good quality of life.

Consequently, the European LeukemiaNet (ELN) provided treatment recommendations in 2006, 2009 and again in 2013. Please note that individual patients may find that their own therapy differs from the recommendations given in this document. These differences may be based on their personal disease and health status. You can use this summary as a starting point for talking with your doctor. You can ask for an explanation if your doctor does not follow the ELN recommendations.

Treatments are prescribed in a certain order and are known as first line, second line and third line treatments. A patient will probably take a BCR-ABL inhibitor. BCR-ABL inhibitors are also called tyrosine kinase inhibitors or TKIs. These drugs work by blocking the activity of BCR-ABL, the gene that causes the CML. The drugs can reduce the disease to a minimum and restore health, but we cannot be sure whether they can cure CML.

In recent years, CML patients have benefited from better treatments including drugs like:

1. **Imatinib** (Glivec®)
2. **Dasatinib** (Sprycel®)
3. **Nilotinib** (Tasigna®)
4. **Bosutinib** (Bosulif®)
5. **Ponatinib** (Iclusig®)

The drugs available for treating CML are described below:

1. Imatinib and combinations

Imatinib is the first BCR-ABL tyrosine kinase inhibitor that has been used for the treatment of CML. It usually produces good treatment responses in most CML patients. Overall patient survival has been reported to be between 92% and 97% after 5 years. However, some patients might not respond at all or might not respond well enough to treatment. These patients are called resistant patients. Other patients might not tolerate the drug. Most of these resistant or intolerant patients are moved over to treatment with other tyrosine kinase inhibitors. Imatinib has also been used in combination with cytarabine and interferon alpha but these combinations did not achieve better survival than imatinib alone. Imatinib is generally used as first line therapy but in specific cases it can be used as second or even third line therapy. The classical dose is 400 mg daily but other doses have been used successfully.

2. Dasatinib or nilotinib

Your doctor could prescribe another BCR-ABL tyrosine kinase inhibitor — either dasatinib or nilotinib, often referred to as second generation tyrosine kinase inhibitors. Reasons for this could be: your current medical history, or your leukemia cells have changed. Leukemia cells may change biologically through mutation making them resistant to the current treatment. Some resistant cells may not respond well to dasatinib or to nilotinib or to both. Dasatinib and nilotinib can also be used as first line therapy instead of imatinib. Early results of clinical trials carried out in patients treated first line suggest that these drugs may achieve a faster and deeper response than imatinib. The drug of choice for your medical condition might be guided by the side effect profile of the drug or other drugs you are taking in parallel, by the presence of resistance due to specific mutations, and other medical conditions you might have. Dasatinib or nilotinib can be used as second line therapy in case of imatinib resistance or intolerance or immediately as first line therapy. In specific cases they can also be used as third line therapy.

3. Bosutinib

If you have been treated with one or more of the above BCR-ABL tyrosine kinase inhibitors and have not responded to, developed resistance to or did not tolerate your previous therapy, you might be given bosutinib (a second generation tyrosine kinase inhibitor). The BCR-ABL tyrosine kinase inhibitor bosutinib can be

prescribed as second line therapy for patients for whom imatinib, nilotinib and dasatinib are not considered appropriate treatment options.

4. **Ponatinib**

For some patients, the BCR-ABL tyrosine kinase inhibitor ponatinib (a second generation tyrosine kinase inhibitor) is another treatment option. You may receive ponatinib as second line therapy if you do not respond to first line therapy with imatinib, dasatinib or nilotinib. You may also be given ponatinib as third line therapy if you do not respond or become intolerant to two other tyrosine kinase inhibitors. Specifically the presence of a genetic mutation called T315I may cause resistance to all other drugs except ponatinib. However, if you have had heart diseases or any cardiovascular problems in the past, your doctor will carefully consider whether treatment with ponatinib is appropriate for you.

5. **Stem cell transplant**

If none of these drugs are working well, stem cell transplantation may be a treatment possibility for CML patients in the chronic phase who have shown resistance or intolerance to at least one second generation tyrosine kinase inhibitor. For CML patients in the accelerated phase, stem cell transplantation is an option when an optimal treatment response has not been achieved. Patients in the blastic phase should receive a stem cell transplant only if a second chronic phase can be established with intensive chemotherapy with or without a tyrosine kinase inhibitor.

Stem cell transplantation involves receiving healthy stem cells from a donor which is called allogeneic stem cell transplantation. The new stem cells can help your body make enough healthy red blood cells, white blood cells, and platelets. If the transplant is successful your disease can be cured. However, transplantation may also lead to serious health complications and even death. That's why in most cases, transplant is not the first option.

There is not enough data yet about the use of tyrosine kinase inhibitors before and/or after bone marrow transplantation in CML patients. However, specific safety issues have not been reported. Patients are given these drugs before and/or after bone marrow transplantation when the risk of relapse of the disease is considered high.

6. **Interferon alpha and combinations**

Before imatinib was introduced in the early 2000s, interferon alpha was the medical treatment of choice if stem cell transplant was not feasible. Interferon alpha causes cell death in CML cells. Administered as single therapy in high doses, good treatment responses can be achieved only in a small number of patients. In addition, side effects are common with the high doses required as a single therapy. Today, interferon alpha is tested in clinical trials in combination with BCR-ABL tyrosine kinase inhibitors, to try to induce additional immune effects against CML cells. Tyrosine kinase inhibitors should not be used in pregnancy as they may harm the unborn child. Therefore, interferon alpha might be useful to control the disease until delivery.

7. **Hydroxyurea**

Hydroxyurea is an oral chemotherapy that can be used for a short time before initiating a therapy with tyrosine kinase inhibitors, e.g. until the diagnosis of CML has been confirmed, or when blood counts are very high by the time of the diagnosis. It reduces the number of white blood cells.

Goals of CML treatment

People living with CML respond differently to treatment, but there are general goals that can be set and milestones that can show you and your doctor if your treatment is working. These may include:

- Returning blood counts to normal (hematologic response)
- Eliminating or reducing the number of leukemia cells, as determined by disappearance of the Philadelphia chromosome (complete cytogenetic response) and by the decrease of the level of BCR-ABL (various degrees of molecular response)

The following sections and tables are a summary of the latest treatment recommendations for the management of Chronic Myeloid Leukemia published by 32 CML experts connected through the European LeukemiaNet (ELN).

These are general recommendations. Your actual treatment goals may change over time based on the state of your CML at diagnosis, your age, the side effects you experience, your response to treatment, and your overall health. Throughout your treatment, your doctor will track your CML with blood and bone marrow tests. These tests will help your doctor assess if your treatment goals are being met. The tables below will help you make sense of your test results and your treatment choice.

Risk scores at the time of diagnosis

Several features such as your age, size of your spleen or specific blood cell counts can influence your response to treatment with tyrosine kinase inhibitors and the outcome of the treatment. These features must be assessed before you start any treatment and are called baseline prognostic factors. Their values are used to calculate your relative risk score which determines whether you are considered low or high risk after your CML diagnosis. Knowing the level of your risk helps you and your doctor to choose the right treatment for you.

Three prognostic systems are available to calculate your risk score: Sokal, Hasford and EUTOS. The three systems are considered to be of equal value.

There are other factors that, when present at the time of diagnosis, point to a less favorable prognosis. They include some additional specific chromosomal changes in cells with the Philadelphia chromosome, such as trisomy 8 and 19, and are called “major route” chromosomal changes.

Milestones in CML treatment

Response definitions

The word ‘response’ describes how your CML reacts to the treatment.

Optimal response
: means the treatment response is likely to allow a survival similar to that of the general population. There is no indication that a change in treatment is required.

Failure
: means that a certain treatment is not likely to work in the long run. Therefore, treatment should be changed. You and your doctor should discuss the options of switching treatment if possible.

Warnings
: are signs that your disease doesn’t respond to a certain treatment as desired. Your doctor may check you more frequently and may use these warning signs to decide if you require a change in treatment.

The goal of CML treatment is to achieve disease remission. For CML, remission is defined by:

- **Complete hematologic response (CHR)** — The blood cell count has returned to normal, and tests don’t show any immature white blood cells. Also, the spleen has returned to a normal size if it was enlarged.
- **Complete cytogenetic response (CCyR)** — No cells with the Philadelphia chromosome can be found with cytogenetic analysis of bone marrow cells.
- **Major molecular response (MMR)** — PCR (a blood test that allows to detect and count very small amounts of specific parts of a gene) can still detect BCR-ABL, but at a low level (BCR-ABL levels below 0.1%). Doctors consider this to be an excellent response.
- **Deep molecular response (MR4 or MR4.5)** — the PCR test can still detect CML, but at a very low level, close to the technical detection limit (BCR-ABL levels below 0.01% for MR4 and below 0.0032% for MR4.5).
- **Molecularly undetectable disease** — The PCR test can’t detect BCR-ABL in the blood or bone marrow. However, most people with CML might still have a tiny amount of the BCR-ABL gene which is technically undetectable.

Unlike other cancer patients, CML patients who are in remission are not cured, and current knowledge cannot recommend stopping treatment outside of controlled clinical studies except in individual patients with proper, high quality monitoring at monthly intervals. Even if tests can't find any trace of CML in your cells, the disease can still reappear and result in a relapse.

Your doctor will want you to have tests done at various times so that your body's response to the disease and treatment can be monitored. Table 1 outlines what your lab results will look like if you are in remission and how often you should be tested. Monitoring can be performed using a molecular or cytogenetic test or both.

Table 1.

	Remission	Testing
Hematologic Complete (CHR)	• Platelet count < 450,000/µL • White blood cells < 10,000/µL • Differential blood with no immature granulocytes and < 5% basophils • Non-palpable spleen	Blood test at diagnosis. Then every 15 days until complete hematologic response has been achieved and confirmed. Test at least every 3 months, or as required.
Cytogenetic None Minimal Minor Partial (PCyR) Complete (CCyR)*	 > 95% of cells with Philadelphia chromosome 66-95% of cells with Philadelphia chromosome 36-65% of cells with Philadelphia chromosome 1-35% of cells with Philadelphia chromosome No cells with Philadelphia chromosome (in at least 20 cells)	**Cytogenetic test** on bone marrow at diagnosis, 3, 6 and 12 months until complete cytogenetic response has been achieved and confirmed. After 12 months, if an MMR is achieved in molecular tests, cytogenetic testing on bone marrow is required only if standardized molecular testing is not available. In case of warning signs, repeat all cytogenetic and molecular tests as often as monthly. For treatment failure or progression to accelerated or blastic phase, cytogenetics of bone marrow cells, molecular testing (PCR), and mutational analysis should be performed.
Molecular Major (MMR) Deep molecular remission $MR^{4.0}$ $MR^{4.5}$ Undetectable	 ≤ 0.1% BCR-ABL on the international scale (IS) Either detectable disease with < 0.01% BCR-ABL (IS) or undetectable disease with > 10,000 ABL gene copies in the sample Either detectable disease with < 0.0032% BCR-ABL (IS) or undetectable disease with > 32,000 ABL gene copies in the sample The PCR test can't detect any of the BCR-ABL gene in the blood	**Molecular testing** (PCR): Every 3 months, until MMR (BCR-ABL ≤ 0.1%) has been achieved and confirmed. Then at least every 3-6 months.
Mutation analysis	No presence of mutations	**Mutational analysis** by Sanger sequencing (a specific technique to detect mutations) is recommended only in case of progression, failure and warning.

≤ means less than or equal to; > means more than

* This can also be measured by Fluorescence In Situ Hybridization (FISH) – another method to detect Philadelphia chromosome on blood cells.

Response levels and warnings in first line treatment

Are you in the chronic phase of CML and taking 400 mg per day of imatinib or 100 mg per day of dasatinib or nilotinib 300 mg twice daily as your first tyrosine kinase therapy after diagnosis? Read Table 2 to see the definitions of goals of treatment.

Table 2.

Time	Optimal response	Warnings	Failure
At diagnosis	(Does not apply at this stage)	High risk by Sokal/EUTOS/ Hasford score, or additional major chromosomal changes in cells with the Philadelphia chromosome*	(Does not apply at this stage)
At 3 months	BCR-ABL ≤ 10% in PCR test, and/or cells with the Philadelphia chromosome ≤ 35% in cytogenetic test	BCR-ABL > 10% in PCR test, and/or cells with the Philadelphia chromosome 36-95% in cytogenetic test	No complete hematologic response, and/or cells with the Philadelphia chromosome > 95% in cytogenetic test
At 6 months	BCR-ABL < 1% in PCR test, and/or no cells with the Philadelphia chromosome in cytogenetic test	BCR-ABL 1-10% in PCR test, and/or cells with the Philadelphia chromosome 1-35% in cytogenetic test	BCR-ABL > 10% in PCR test, and/or cells with the Philadelphia chromosome > 35% in cytogenetic test
At 12 months	BCR-ABL ≤ 0.1% in PCR test	BCR-ABL 0.1-1% in PCR test	BCR-ABL > 1% in PCR test, and/or at least 1 cell with the Philadelphia chromosome in cytogenetic test
Then, and at any time during treatment	BCR-ABL ≤ 0.1% in PCR test	Additional major chromosomal changes in cells that do not have the Philadelphia chromosome (e.g. abnormalities in chromosome 7 without presence of changes in chromosomes 9 and 22)	• Loss of complete hematologic response, complete cytogenetic response or MMR** • Mutations • Additional major chromosomal changes in cells with the Philadelphia chromosome

* Cells with the Philadelphia chromosome are also called Ph positive cells or Ph+ cells; cells without the Philadelphia chromosome are also called Ph negative cells or Ph- cells;

** Loss of MMR should be confirmed in two molecular tests one after another, with one having a BCR-ABL level ≥ 1%.

Response levels and warnings in second line treatment

Are you taking dasatinib, nilotinib, bosutinib or ponatinib as a therapy following treatment with another tyrosine kinase inhibitor? Read Table 3 to see definitions for goals of treatment. These definitions are mainly based on data reported for nilotinib and dasatinib, and until more data becomes available, provisionally serve also for bosutinib and ponatinib. These definitions cannot be used for treatment after failure of two other tyrosine kinase inhibitors!

Table 3.

Time	Optimal response	Warnings	Failure
At baseline (= right before starting second line therapy)	(Does not apply at this stage)	No or loss of complete hematologic response, or lack of complete cytogenetic response to 1st line tyrosine kinase inhibitors, or high risk by Sokal/EUTOS/Hasford score	(Does not apply at this stage)
At 3 months	BCR-ABL ≤ 10% in PCR test, and/or cells with the Philadelphia chromosome ≤ 65% in cytogenetic test	BCR-ABL > 10% in PCR test, and/or cells with the Philadelphia chromosome 66-95% in cytogenetic test	No complete hematologic response, or cells with the Philadelphia chromosome > 95% in cytogenetic test, or new mutations
At 6 months	BCR-ABL ≤ 10% in PCR test, and/or cells with the Philadelphia chromosome < 35% in cytogenetic test	Cells with the Philadelphia chromosome 35-65% in cytogenetic test	BCR-ABL > 10% in PCR test, and/or cells with the Philadelphia chromosome > 65% in cytogenetic test, and/or new mutations
At 12 months	BCR-ABL < 1% in PCR test, and/or no cells with the Philadelphia chromosome in cytogenetic test	BCR-ABL 1-10% in PCR test, and/or cells with the Philadelphia chromosome 1-35% in cytogenetic test	BCR-ABL > 10% in PCR test, and/or cells with the Philadelphia chromosome > 35% in cytogenetic test, and/or new mutations
Then, and at any time during treatment	BCR-ABL ≤ 0.1% in PCR test	Additional major chromosomal changes in cells that do not have the Philadelphia chromosome (e.g. abnormalities in chromosome 7), or BCR-ABL > 0.1% in PCR test	• Loss of complete hematologic response • loss of complete/partial cytogenetic response • new mutations • loss of MMR* • additional major chromosomal changes in cells with the Philadelphia chromosome

* Loss of MMR should be confirmed in two molecular tests one after another, with one having a BCR-ABL level ≥ 1%.

Choosing treatments in chronic phase

Are you in the chronic phase of your CML? Read Table 4 to learn options for first, second, and third line treatment including stem cell transplantation. Choice of drug depends upon the characteristics of the disease, your overall condition, the different typical side effects of each drug, and other factors.

Table 4.

Line of treatment	Which patients?	Which treatment?
1st line	All patients	Imatinib 400 mg once daily, nilotinib 300 mg twice daily or dasatinib 100 mg once daily. Determining the HLA type* of patients and siblings should be done only in case of warnings (high risk, additional major chromosome changes in cells with the Philadelphia chromosome).
2nd line (after imatinib, nilotinib or dasatinib)	Patients experiencing toxicity and intolerance	*In intolerant patients:* Switch to any of the other tyrosine kinase inhibitors approved for 1st line at the standard dose. *In resistant patients:* A higher dose (imatinib 400 mg twice daily, nilotinib 400 mg twice daily, dasatinib 70 mg twice daily or 140 mg once daily), taking into account potential mutations, side effects of previous treatments, and secondary diseases that may be of concern. A change of drug is preferred to an increase of imatinib dose.
2nd line (after imatinib)	Patients with treatment failure	Dasatinib, nilotinib, bosutinib (500 mg once daily) or ponatinib (45 mg once daily). Determine the HLA type of patients and siblings.
2nd line (after nilotinib)	Patients with treatment failure	Dasatinib, bosutinib or ponatinib. Determine the HLA type of patients and siblings. Consider stem cell transplant.
2nd line (after dasatinib)	Patients with treatment failure	Nilotinib, bosutinib or ponatinib. Determine the HLA type of patients and siblings. Consider stem cell transplant.
3rd line (after two tyrosine kinase inhibitors)	Patients who fail to respond and/or are intolerant to two tyrosine kinase inhibitors All eligible patients	Any of the remaining tyrosine kinase inhibitors. Stem cell transplant, if feasible, could be recommended.
Any line	Patients who carry the T315I mutation	Ponatinib. Determine the HLA type of patients and siblings. Consider stem cell transplant.

* Human leukocyte antigens (HLA) are specific markers found on most cells of your body. Your immune system uses these markers to know which cells belong in your body and which ones do not. HLA typing determines how closely the markers of the patient match the markers of the stem cell donor. The better the match, the less likely will the donated immune cells attack the patient's cells.

Choosing treatments in accelerated phase

If you are in either the accelerated or blastic phase of your disease, then read Table 5 to learn about treatment options.

Table 5.

Accelerated Phase and Blastic Phase	Which patients?	Which treatment?
Accelerated Phase and Blastic Phase, newly diagnosed	Patients who have never used a BCR-ABL inhibitor	• Imatinib 400 mg twice daily, dasatinib 70 mg twice daily or 140 mg once daily • Stem cell transplant for all blastic phase patients, and for accelerated phase patients who do not achieve optimal response • Chemotherapy may be necessary before stem cell transplant
Accelerated Phase and Blastic Phase, as a progression from Chronic Phase	Patients who have used a BCR-ABL inhibitor before and progressed	• Any of the tyrosine kinase inhibitors not used before progression (ponatinib in case of T315I mutation), with or without chemotherapy at the same time, followed by a stem cell transplant in all eligible patients • In case of uncontrolled, resistant blastic phase, allogeneic stem cell transplant is not recommended. For these patients, chemotherapy and/or palliative care might be more suitable.

Treatment discontinuation

ELN experts recommend that patients with CML who are responding optimally to treatment continue taking their standard recommended dose indefinitely. There have been clinical studies to stop imatinib in some patients who were in deep molecular response for at least two years. About 40% of them maintained the same degree of response. This is now called Treatment Free Remission. These patients were followed up for one to four years. Currently, however, not enough data is available to recommend that patients discontinue their treatment outside of well designed, controlled studies. Such studies are ongoing, and alternatives to discontinuation, like using imatinib on and off, are also being studied.

Stopping treatment may be considered in individual patients, also outside of clinical studies, if high quality and certified molecular monitoring can be assured at monthly intervals. This can be particularly important to women who plan to have children, because becoming pregnant is strongly discouraged during treatment with tyrosine kinase inhibitors.

Side effect patterns

Different drugs have different side effects. This is also true for the different tyrosine kinase inhibitors. Your doctor will consider this when choosing a drug to treat you, taking into account your specific CML as well as other health issues that are not related to your CML.

The side effects of tyrosine kinase inhibitors can be divided into three general classes:

1. The first includes major side effects that typically occur during the first phase of treatment. These side effects are manageable, but you may have to discontinue treatment or reduce your dose temporarily. About one in ten patients needs to discontinue treatment permanently.

2. The second class includes minor side effects that begin early during treatment and can persist becoming chronic. They are also manageable and tolerable but impair your quality of life. They keep patients from taking their drugs as prescribed and this is a major cause of treatment failure. Many of these side effects are common to all tyrosine kinase inhibitors, with some differences in how often they occur and how severe they are, so that some patients can benefit from changing the tyrosine kinase inhibitor.

3. The third class includes late complications (for example those not directly related to the drug effect) that, in the long run, can affect your heart and blood vessels, your respiratory system, organs like your liver or pancreas, your immune defense or your metabolism.

All tyrosine kinase inhibitors can affect the heart and should be used with great caution in patients with heart failure. You should therefore tell your doctor if you have previously had heart problems.

Nilotinib has been linked particularly with diseases of the arteries. Dasatinib has been associated particularly with complications of lung and pleura (a thin sheet of tissue that wraps around the outside of your lungs and lines the inside of your chest cavity). Little data was available on the side effects of bosutinib and ponatinib when the updated ELN Recommendations were issued in 2013; since then, some conclusive data have been published on the side effects and management of these drugs.

Late or long-term side effects and complications of second generation tyrosine kinase inhibitors are not yet fully understood. All patients should be continuously monitored.

Be an active patient

Some considerations and tips

These recommendations are not meant to replace medical advice, but are meant to provide you with a clearer understanding of CML treatment, tests, and results. In order to achieve the best results, you may want to be an active patient. Consider these tips:

1. **Find a doctor who knows a lot about your disease** and has treated many CML patients. This is especially important if your disease is advanced, if your test results are not clear or if you have had severe or unusual side effects from treatment. Experience counts.

2. **Be sure to talk with your doctor at any stage of your disease**, especially before stopping or changing your treatment. Keep asking until you get answers you understand.

3. **Know your treatment goals.** Consider to record your medication treatment history and your test results.

4. **Make sure your doctor keeps an eye on how well your treatment is working**. Don't miss your regular check-ups as CML is a life-threatening disease if not under control.

5. **Having side effects?** Write them down, and talk to your doctor about them at your next appointment. He or she may be able to help you manage them, but only if you tell about them.

6. **Ask your doctor whether clinical trials are an option for you.** In certain cases these might not only be of potential benefit to you, but also to future CML patients.

7. **Give your treatment time to work.** The choice to switch to a new treatment should be based on good data. If your test results are not clear, it may be wise to get tested again.

8. **Only drugs that are taken can actually work**. Make sure you take your treatment as prescribed. There is evidence that not following CML treatment as prescribed can threaten success of your CML treatment. Address your concerns to your doctor before you consider stopping or skipping your treatment.

9. **Get support and share experience**. Connect with other people who are living with the disease, and with support groups for CML patients – there are CML groups in more than 70 countries. You can visit the CML Advocates Network for a list of worldwide CML support groups here: http://www.cmladvocates.net/members

10. **Tell your family and friends how they can help.** Consider also to bring a family member or friend to the doctor’s appointment to help you listen and take notes. Remember—you don’t have to go through this alone.

Trying to find a CML support group?

Patient support groups can help you get in touch with other patients who have CML, learn more about your disease, identify helpful information, or find an experienced doctor for a second opinion. To find a group in your country, visit the CML Advocates Network group list here: http://www.cmladvocates.net/members

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