



*Hi, I am Bruce Barber and welcome to Yale Cancer Center Answers a weekly show focusing on the screening detection treatment and prevention of cancer. This week Dr. Ken Miller talks about leukemia. Dr. Miller is a medical oncologist. He is also the Director of the Connecticut Challenge Survivorship Clinic at Yale Cancer Center. Yale Cancer Center Answers is a great way to provide you with some of the most up to date information available on cancer care. If you have a specific question, please e-mail it to [canceranswers@yale.edu](mailto:canceranswers@yale.edu) or you can call 1888-234-4YCC. If you would like to hear past editions of Yale Cancer Center Answer,s or if you would like to learn more about a specific kind of cancer, all the shows are posted in audio and written formats on the Yale Cancer Center website at [www.yalecancercenter.org](http://www.yalecancercenter.org). As I just mentioned Dr. Miller is going to talk about leukemia this week with Dr. Peter Marks, keeping in mind there are four different kinds of leukemia and that every year over 30,000 people in the United States will develop leukemia. Dr. Marks is going to share the latest advances in treatment and research. Let's get right to it.*

Miller            The first thing I would like to do is talk about the word leukemia. There are many different kinds. Can you tell us in board terms about the different kinds?

Marks            Leukemias are all blood disorders that involve white blood cells. There are three major types of cells in the blood. There are red blood cells that carry oxygen, platelets that help in clotting and white blood cells that help the body fight infections. The white cells are further divided into two major types. The type of white blood cells that directly fight infections by engulfing invaders are called myeloid cells, and cells that help make antibodies and participate in immune reactions are called lymphoid cells. In general, when we talk about leukemias, we are talking about disorders of white blood cells, and in particular, disorders that either affect the myeloid cells or the lymphoid cells. Those are the major types of leukemia's, and then each of those is further subdivided into either acute or chronic. When it's all said and done we can speak of four major types of leukemias, acute myeloid leukemia; acute lymphoid leukemia; chronic myeloid leukemia and chronic lymphoid leukemia.

Miller            So there are four types. Can you tell us the two that are most different from each other?

Marks            Acute myeloid leukemia is one type where generally, especially in a younger individual, we would be very aggressive with treatment. Treatment would involve hospitalization for a month for chemotherapy followed by relatively intensive chemotherapy afterwards and then sometimes bone marrow transplantation or hematopoietic stem cell transplantation. That is one end of the spectrum. At the entire other end of the spectrum is chronic lymphoid leukemia which we can often detect at a time when it is asymptomatic and is likely to stay without any symptoms for years. Very often people are followed for long periods of time, 5,

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10 or 15 years, without ever needing treatment. We have on the one hand the disorder which needs very aggressive chemotherapy and another which sometimes, not all the times but sometimes, can be followed overtime before treatment is needed.

Miller It is a fascinating thing when you hear the word leukemia and on one end you have patients who are very sick and need to be treated and then you are saying there is another spectrum of the disease where you don't have to do anything.

Marks That's correct and it depends on what stage of chronic lymphoid leukemia a patient has, but in the early stages of the disorder people are often just followed. Sometimes it's a difficult concept to explain that it is perfectly fine to just follow people because there is no benefit that we know of at this time to treating someone who has a very early stage of chronic lymphoid leukemia. We make sure that nothing seems to be going wrong and make sure that nothing comes up that needs treatment. If things change overtime, we will intervene with treatment, and there are treatments available.

Miller Lets focus the discussion on the chronic leukemias, which I think you have started to tell us about. For example, a patient who has chronic lymphocytic leukemia, how would they know that they have a problem? How would that be discovered?

Marks Increasingly, chronic lymphoid leukemia is something that's picked up by a doctor in the doctor's office. For someone who goes for a yearly physical and is in their 60s, and their doctor happens to notice that their white blood cell count is slightly elevated and there are an increased number of lymphoid cells, the doctor might call for a complete blood count. If he notices that it's still elevated, that will trigger referral to a hematologist. The diagnosis is made by a blood sample and usually the person never realizes that there was anything wrong with them. That's one type of presentation. Other times people may present with symptoms such as swelling of lymph nodes, fevers, night sweats or weight loss. Very often today, I would say, the majority of patients who come into the office are patients who never knew that there was anything wrong with them, but their doctor noticed that their white blood cell count was somewhat elevated.

Miller If you saw a patient like that referred to you, what would the evaluation be?

Marks In general, we would start by looking at the white blood cell count to confirm the diagnosis and find out what type of leukemia it is. Usually we will then do a physical examination, complete history, laboratory studies and sometimes a bone marrow aspirate and biopsy depending on how high the white blood cell count is and the exact circumstances. Sometimes we'll also do CAT scans of the chest, abdomen and pelvis to make sure that there are no enlarged lymph nodes in those regions. That is the workup that we would tend to do and the tests that we decide

to do depend on the type of the patient that we are seeing; the degree of elevation in the white blood cell count that we see.

Miller You talked about a group of patients that you will watch and not offer any treatment for a number of years. What would be some of the triggers that would cause you to intervene and begin treatment?

Marks Well, one of the reasons we don't intervene is because there is no lymph node swelling or problems with blood counts. Some patients get very concerned about the fact that they have a white blood cell count that may be 50,000; 60,000; 70,000, but with chronic lymphoid leukemia, if they are otherwise well, we don't get very worried because that would just be treating a number which is not what's important; treating the person is what's important. But on the other hand, if somebody has enlarged lymph nodes, if their spleen is getting large and uncomfortable or if their blood counts are starting to suffer because of the leukemia, those would all be reasons to treat the leukemia. Sometimes, we also treat the leukemia if people are having immune side effects that are severe from the underlying leukemia. Often times, the same treatment that we give for those immune side effects also treats the leukemia, so it's a bit of a two way street.

Miller What would the treatment be?

Marks The treatment depends on the individual. In a younger individual, we tend to use a combination of drugs; chemotherapy medicines in conjunction with a type of monoclonal antibody that targets the cells involved in chronic lymphoid leukemia. In an older patient, we might use a single drug, perhaps that antibody or even sometimes an oral chemotherapy. It really is very individualized for the patient. In a younger patient, our goal is complete remission and to make the leukemia go away so we will use a combination of drugs. In an older patient, our goal is not to necessarily make it go away entirely but to control the symptoms such as the large lymph nodes, and to lower blood counts. In that case we would tend to use a gentler chemotherapy. Part of what motivates us here is that we don't generally cure chronic lymphoid leukemia with any of our standard chemotherapies. This is something that if we are going to try to cure we have to use hematopoietic stem cell transplantation; bone marrow transplant. In general, we move from one chemotherapy regimen to another trying to make this a chronic problem such as we see with people who have diabetes or other chronic disorders.

Miller There is a lot of talk in oncology now about targeted therapies and about antibodies. Are any of those used in chronic lymphocytic leukemia (CLL)?

Marks The antibody rituximab is directed against a molecule on the surface of the cell that's involved in CLL. When the antibody interacts with it, it leads to the death of those CLL cells. We consider it a targeted therapy. With that particular antibody,

one can't say it's just targeted to CLL though, because it is used in many other disorders and diseases today. It is even used in rheumatology for people with rheumatoid arthritis. It is used in many settings, but in the setting of chronic lymphoid leukemia, we consider it a targeted therapy.

Miller If you treat someone with this what would you expect to see?

Marks Very often we see that the lymphocyte count goes down very nicely. It is a nice therapy because aside from allergic reactions, which patients can experience with the normal drugs we use, patients have reasonably few side effects. No medicine is side effect free, but very often patients hardly know they have even received the drug. There is no hair loss and there is no nausea or vomiting that we associate with chemotherapy. That's why we treat older patients, even patients in their 80s, with this particular antibody because they tolerate it very well.

Miller It is a fascinating thing, this comparison between patients with acute leukemia who are so sick and patients with CLL where I sense a gentler approach.

Marks Correct.

Miller Can you tell us a little bit about hematopoietic stem cell transplant, or bone marrow transplant, which you talked about for younger patients. What is the concept there and how is that done?

Marks The idea of using hematopoietic stem cell transplantation is to try to cure the disease by wiping out all of the bad cells in the body and giving back fresh cells from a donor. Hopefully these cells will both reconstitute the blood formation for the recipient as well as have some effect against the underlying leukemia through an immune mechanism. In chronic lymphoid leukemia, success has not been quite as good as it has been in other forms of leukemia, so we don't rush to any type of hematopoietic stem cell transplantation in chronic lymphoid leukemia the same way we might in other types of leukemia such as acute myeloid leukemia.

Miller We would like to remind you to e-mail your questions to [canceranswers@yale.edu](mailto:canceranswers@yale.edu). We are going to take a short break for a medical minute. Please stay tuned to learn more information about the treatment of chronic leukemias with Dr. Peter Marks.

*The American Cancer Society estimates that in 2007 there will be over 62,000 new cases of melanoma in this country. Twenty-four hundred patients are diagnosed annually in Connecticut alone. While melanoma accounts for only about 4% of skin cancer cases, it causes the most skin cancer deaths. Early detection is the key. When detected early, melanoma is easily treated and highly curable. Each day, the patients are surviving melanoma due to increased access*

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*to advance therapies and specialized care. New treatments options and surgical techniques are giving melanoma survivors more help than they ever had before. Clinical trials are currently underway at Yale Cancer Center, Connecticut's federally designated comprehensive cancer center, to test innovative new treatments for melanoma. The patients enrolled in these trials to give an access to newly available medicines, which have not yet been approved by the Food and Drug Administration. This has been a medical minute brought to you as a public service by Yale Cancer Center. More information is available at [yalecancercenter.org](http://yalecancercenter.org)*

- Miller Welcome back to Yale Cancer Center Answers. This is Dr. Ken Miller. I am here with Dr. Peter Marks, the director of the leukemia program at the Yale Cancer Center. Peter, again, thanks for being with us.
- Marks You are welcome. Thank you.
- Miller I want to talk a little bit more about the other chronic leukemia which is called chronic myelogenous leukemia, but first, let me ask you, from what I have seen you have a very specific patient-centered focus on providing care. Can you tell us a little about your philosophy?
- Marks I find that no matter what type of leukemia somebody is diagnosed with it is generally a life-transforming event. It tends to affect not just the patient but also their families and friends. I take this to heart when I am treating new patients with leukemia. It is important to not only focus on the medical aspect of care but also the emotional and the social aspects of caring for patients. Helping them to understand the implications of the diagnosis and what their priorities are for the treatment of their leukemia is very important because for some older patients their priorities are to have a very high quality of life. They don't want to suffer in a hospital. They want to have as much time as possible with their loved ones; experiencing the joys of summertime or with their grandchildren. So for that, a very different approach might be taken than for a young person who has life that they have not experienced yet. We want to be very aggressive and try to cure leukemia, wipe it out entirely, so they can see their kids grow up and go through high school and go to college. It is very important to understand what the individual's goals are and to understand the context that the person is living in as we treat them.
- Miller Let me ask you a little bit more about this. It's a very important topic. Sometimes doctors, patients and other people think that these must be very difficult conversations to have regarding goals and where people are in terms of their wishes. When you have these conversations, do most people feel okay talking about these topics?

- Marks            There are exceptions, but in general I find that most people are willing to open up and talk if you are open and honest and give them the opportunity to raise their concerns. Actually, sometimes this is the first thing that is on their mind. For most patients it is less what chemotherapy they are going to receive and more about how it is going to affect their quality of life. Most patients welcome that openness and directness. Although it may not be something they will do immediately, they are very willing to talk about these things.
- Miller            A lot of care at the Yale Cancer Center is certainly individualized but it is also a team approach. Can you tell us a little bit about the team that would be involved in caring for someone with leukemia? How do you come up with the individualized treatment plan?
- Marks            Our care approach involves not just the doctors, but nurses who specialize in the care of patient's with cancer as well. We have social workers who are very experienced in the care of patients with cancer and some of whom are even sub-specialized in the care of patients who have bone marrow transplants and hematopoietic stem cell transplants. We have a variety of other people who are involved, care coordinators and people who are involved in studies, who all work together to help care for the patients. This is very important because, particularly in the inpatient setting, it is not just the doctor who is caring for the patient; it is the whole team of people that make sure the person's care is coordinated. They make sure it runs smoothly and that it is not just medically proper, but also socially proper in terms of giving the right psychosocial support. In the outpatient setting, it involves nurses who take care of patients who come in for outpatient therapies. They monitor them and help provide interactions with home care companies that sometimes give therapy. There is a lot of coordination that goes into the care and our goal is to make it look almost like ballet. It should look very easy from the patient's perspective; although it may not always be easy from our perspective and from the perspective of some of the nurses who are doing it. We would like the patient to see that it functions gracefully, like a ballet.
- Miller            That is a wonderful analogy; I am going to remember that one. Peter, as you know, my wife had acute leukemia about a year ago and thankfully is doing well. As you said, it is a life-changing event for everyone involved, and I wanted to thank you, and all the caregivers at the Cancer Center, for your sensitivity and understanding. What is cutting edge since my wife and others were treated in the last several decades? In the chronic leukemias, for example, what is on the cutting edge that you are excited about?
- Marks            In chronic myeloid leukemia there is tremendous excitement because this is a disorder that before 20-30 years, before the advent of bone marrow transplantation, was a routinely fatal disease three to four years after people came down with it. Then we had the era of bone marrow transplant, also known as

hematopoietic stem cell transplant, where many people were cured if they were young enough. Unfortunately, because chronic myeloid leukemia affects older people very commonly, many people were not candidates for bone marrow transplant. Today however, we are in a wonderful era because chronic myeloid leukemia is the leukemia for which there was one of the best examples of a targeted therapy that has been developed. It is a drug called imatinib known by the brand name of Gleevec. This drug specifically targets the protein that is abnormal in this leukemia that causes the leukemia. By doing so, it puts people into complete remission with minimal side effects. Unlike needing to have very high doses of chemotherapy that have to be given intravenously, these people take a pill once a day and in a month or two they go into remission. They hardly know they even had any problems. In fact, one of the oddest things is that we now have a problem with chronic myelogenous leukemia and making sure people are compliant with their medicine because they feel so good. It is quite remarkable.

Miller For a patient with chronic myelogenous leukemia, how would they know, or how would their doctor know, there is a problem? What would even bring it to their attention?

Marks Often times, chronic myeloid leukemia, just like chronic lymphoid leukemia, is detected in the doctor's office without a patient knowing. Although it is somewhat more common that patients will come in with symptoms. They might notice that they are having night sweats or fevers. Sometimes they will notice a kind of lump in their abdomen because their spleen has enlarged and they feel full early. Those are the types of vague constitutional symptoms that might make someone go to a doctor to get examined. The doctor will do a blood count and see a very high white blood cell count.

Miller What tests would they have?

Marks The standard workup today for chronic myeloid leukemia would be blood counts. We also do specialized tests because we know the one specific protein involved. We do a molecular diagnostic test which allows us to very precisely quantitate the abnormal protein and then we can follow that over the course of treatment to see how well they are doing. That allows us to intervene early if we feel like someone is not doing well enough. Because there are now other therapeutic alternatives besides Gleevec, there are second generations of those drugs that we can use if we need to. We will often do a bone marrow aspirate and biopsy so that we can make sure that we understand what is going on in the bone marrow and aside from that, there are really just other routine blood tests; blood chemistry tests and a physical examination.

Miller So if you make the diagnosis of CML, that patient would be put on Gleevec and hopefully have a very good response. For those patient who either then relapse or

progress on that medicine, what else is available?

Marks            There are two different paths that might be taken. In a young individual, one might take the path of going towards a bone marrow transplant. In an older individual, one would use one of the newer generations of inhibitors for this particular abnormality. The abnormality is called the PCRAble protein, and there are new generations of inhibitors of that protein that have become available. One of them is called dasatinib. Sprycel is the brand name, and sometimes we will switch to that drug which is now FDA approved. There is actually a third drug, which may be FDA approved shortly, called nilotinib, or Tassigna, and that drug would be there if they failed yet again. So there are quite a few therapeutic alternatives around. I should say that in a young patient with CML, someone who is in their 20s, we will sometimes consider bone marrow transplantation early on; that is particularly for someone who has a match that is related to them. There is some controversy there so it involves discussion with a hematologist, but in general, particularly for someone who is a little bit older, our approach would be to switch to one of the second agents if they had progression.

Miller            Peter, you are head of our Leukemia Program. What kind of research is going on at Yale for leukemia?

Marks            We have a number of protocols that are in the process of opening for the treatment of acute myeloid leukemia. For treating acute myeloid leukemia we're particularly interested in finding the best treatments for older patients and patients who have developed acute myeloid leukemia that first had a disorder called myelodysplastic syndrome. We have protocols that are about to open for treating those types of patients and we anticipate additional protocols over the next few months that will open in different areas of leukemia.

Miller            If someone wants to access that type of cutting edge care or information on clinical trials, how can they do that?

Marks            One of the places they could go is [www.yalecancercenter.org](http://www.yalecancercenter.org). Another place would be [www.clintrials.gov](http://www.clintrials.gov), which is an NIH sponsored, NCI site where they have many clinical trials across the country listed.

Miller            Going back to the issue that this is a disease with many aspects, both psychological and social, what type of support is available at Yale and in this area?

Marks            At Yale we have a variety of social workers and other people who assist in the care of patients. We have support groups that are run through the auspices of Yale and some of our social workers. The Leukemia and Lymphoma Society is a patient advocacy group that offers various types of things including meetings

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where they have an expert come and talk about a given disorder and answer questions for patients and their families. Those are the types of things available, and I cannot underestimate the importance of those patient advocacy groups. Some of them are very helpful in supporting various aspects of the care of patients, so we are very grateful for all of their help in caring for patients.

Miller Peter, again, thanks for being with us.

Marks Thank you very much for having me.

Miller This is Dr. Ken Miller and I want to thank you for listening. Join us next week when we will talk about major issues in cancer care. This is Dr. Ken Miller from the Yale Cancer Center wishing you a safe and healthy week.

*Thanks Dr. Miller and we would like to encourage you to go to [yalecancercenter.org](http://yalecancercenter.org) for more information about cancer and the resources available to you. You can also listen to past editions of Yale Cancer Center Answers in audio and written formats on the Yale Cancer Center website at [www.yalecancercenter.org](http://www.yalecancercenter.org). This has been Yale Cancer Center Answers on WNPR.*