

Chronic Lymphocytic Leukemia (CLL): Advances in Research and Treatment
Health Radio
April 16, 2007
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Andrew Schorr:

Hello, and welcome to Patient Power live on Health Radio. I am Andrew Schorr, and now I am just past the date where I am now an 11-year leukemia survivor. Today you are going to meet the man who has really helped me through that. He has devoted his life to the kind of leukemia that I have, chronic lymphocytic leukemia, which I had never heard of 11 years ago, and helped not only to get me to health but also gave us the confidence to have a third child who is now 10 years old, little Eitan, who I got to school a little while ago, so I like to call him the miracle baby. The doctor you are going to meet in a minute is named Michael Keating, and I have often said, and I said it again to Eitan this morning, I said, you know maybe we should have named you "Michael."

How are you Michael? Michael Keating.

Dr. Keating:

Terrific, terrific Andrew.

Andrew Schorr:

Thank you for being with us. Well, Dr. Keating, folks, is a hematologist/oncologist. He has devoted his life to this particular illness, chronic lymphocytic leukemia, and I know we have some folks listening in today. And so, when I was diagnosed, and Dr. Keating I know you see thousands of patients, but for me it was, you know, a very big deal the day I saw you. I know you have people come from around the world like this. They see a local doctor wherever they may live who may have some familiarity with chronic lymphocytic leukemia but may have to treat many forms of cancer. This is not a particularly common one versus breast cancer, prostate lymphoma, and the blood cancers, so the advice I give everybody, and it's what I did and what people and one very famous lady, who unfortunately has passed on but I met her on the internet, "GrannyBarb" Lackritz, gave me. She said go to a CLL center, and she recommended that among the doctors I might consider is Dr. Keating at the University of Texas M.D. Anderson Cancer Center.

So, Dr. Keating, I saw you for the first time with my wife Esther like many people do. We were kind of terrified, and you gave Esther and you gave me a big hug, and you said. "You are going to live a long time." Here it is 11 years now still appearing to be, you know, no evidence of the leukemia, and on that day I just thought I would never see this day. So, I just want to publicly thank you again, and also as I mentioned we have Eitan, which we probably never would have had the confidence to have had we not seen somebody like you who is an expert in the condition and could bring in your years of experience.

We are making progress in chronic lymphocytic leukemia, don't you think? I mean, I am evidence of that.

Dr. Keating:

That is certainly true. Some time ago, there was a famous slide that was shown at all the lymphoma meetings from Stanford showing a lack of improvement in survival of patients with a low-grade lymphoma, and over the years we have built up our database so that we are able to demonstrate that in each 5-year period there has been a steady incremental increase in overall survival. Even in the most aggressive forms of CLL where patients need treatment because they have marrow failure, that is with Rai stage III and IV disease, we have increased that average survival from three and a half years to seven-plus years so that even in the most aggressive types there has been significant improvement, and each couple of years there is a significant new treatment that becomes available that is keeping patients that even have recurrence of their disease getting second and third remissions.

Andrew Schorr:

Well let's back up a little bit because, Dr. Keating, this program that I do every day on Health Radio is for a general audience. A lot of people are kind of clueless, as I was, about leukemia as a form of cancer and certainly chronic lymphocytic leukemia. Even though it is the most common adult-type, people do not understand that. So, I will give it a little perspective, and then I would love for you to join in, and that is, folks, we have talked about lots of illnesses. You know there are common conditions like migraine headache or vision problems, and among the cancers certainly there is breast cancer and prostate and colon and lung of course and others we have talked about on this program, but there are what we call hematologic malignancies, or leukemias, and those affect a smaller number of people. There are a lot of different subtypes, and chronic lymphocytic leukemia, which I was diagnosed with 11 years ago just through a routine blood test, was totally foreign to me, but Dr. Keating at M.D. Anderson, Michael Keating, is an expert in that, and he is part of a team of people who have really devoted themselves to it, and at M.D. Anderson, Dr. Keating, you really have the busiest leukemia clinic in the world, don't you?

Dr. Keating:

Far and away, but we used to be competitive with Memorial Sloan-Kettering. We had perhaps one-and-a-half times as many referrals as they do, but I think we are now up to four times more referrals than any other leukemia group in the United States and certainly in the world.

Andrew Schorr:

What I recommend to people is, you know, Dr. Keating is 2000 miles away from where I live in Seattle, but when you are diagnosed, particularly with something less common and certainly any leukemia is a less-common cancer and CLL for sure, and if you agree that medical progress is moving forward, and we have heard that from Dr. Keating a minute ago, then I think it really behooves you to have a consultation with what we call a subspecialist, and that is what Dr. Keating is in CLL. He's not just a hematologist, but he specializes in one particular disease and has devoted his life to it, and there is a whole research group that works with him and other peer physicians.

So, Dr. Keating, help us understand what chronic lymphocytic leukemia or CLL is, you know, versus other cancers. A lot of my audience is familiar with breast cancer, they feel a lump; or prostate cancer, there is a tumor there. But, in CLL, what is it?

Dr. Keating:

One of the things that's different about leukemia is the definition leukemia itself, and that comes from a term "white blood." It was found when patients would die 200-300 years ago that the blood when it clots normally is a dark, purplish-red color, but in some of the leukemias there were these streaks of white material, and they were collections of white cells.

In cancer generally, for example breast cancer, the cancer starts to multiply in the breast and then it spreads to lymph glands through the lymphatics and then into the bloodstream to other places. And what happens with the leukemia is the malignant cells are born in the bone marrow, and from the bone marrow they are liberated into the bloodstream, and then they can go to other places such as lymph glands around the body and the spleen, etc. In chronic lymphocytic leukemia, that is certainly what happens. The primary area of disease is the bone marrow where the leukemic cells are born, and they go round in the bloodstream so that the white cell count is increased, and a number of them will land and set up shop in lymph glands and the spleen and much less commonly in other organs.

So the expansion of the malignant cells is one feature, but one of the other features is that because it's a disease of the lymphocytes, which are the cells in the immune system, you get a lot of disturbance of the body's immunity so that some parts of the body's immune system do not work very well. So, most patients these days are diagnosed coincidentally where they have a blood count done for some other reason, and the white cell count is increased, but some people actually notice enlargement of the lymph glands and then they go and get checked or their bone marrow does not function normally, so that their production of red cells goes down, and they develop symptoms of fatigue due to anemia and really they just have repeated infections.

Andrew Schorr:

We are going to take a break, Dr. Keating, and be back and understand this more and how the progress that is being made in CLL has learnings for progress we are trying to make in cancer overall. We'll be back with more with Dr. Michael Keating who is world renowned in the treatment of chronic lymphocytic leukemia, the diagnosis I carry with me, and your questions and your calls on Patient Power. Stay with us.

Andrew Schorr:

Tomorrow evening on Patient Power, we are going to have a special edition. It coincidentally is with another expert from the University of Texas M.D. Anderson Cancer Center who is actually an expert in complimentary, alternative or integrative care for cancer patients, Dr. Lorenzo Cohen. So, that will be at 7:00 p.m. Central time right here, same place. You can also get it on mdanderson.org/patientpower . It will also be at 5:00 p.m. Pacific time where I am, or if you are in the New York area back east where they are having terrible weather, it will be at 8:00 p.m. That's tomorrow night.

Let's go back to Dr. Michael Keating who's also based in Houston at M.D. Anderson. He is a subspecialist in the condition that I have, chronic lymphocytic leukemia. So Dr. Keating, you

spoke to me about participating in research, and I did not have any treatment right away, but when it was time, I was in a clinical trial at M.D. Anderson, and that combined Rituxan, which I kind of call like a "cruise missile" for certain types of blood cancers, a targeted therapy with some earlier chemotherapies, and looking at whether the synergistic effect more effective, which it was, and I know you go around the world talking about this FCR combination, and that is what many people get now. Have the ideas from the benefits from that treatment transferred to beneficial knowledge about the ways to attack cancer or blood cancers more broadly than just CLL or the way we view subtypes of disease?

Dr. Keating:

They certainly have. You know one of the very important things about the management of cancer is one size does not fit all. Whereas in some patients, very simple treatment with one drug will be effective, in many circumstances we have to effectively combine different drugs which have limited effectiveness in their own right, but when they are combined effectively can dramatically change the way that patients respond. For example, there was a simple drug called chlorambucil or Leukeran that was used up until the mid 1980s and still used in some circumstances now that would give about a 3-5% complete remission rate in CLL, and it's moved along so that with the combination that you describe, the Rituxan or rituximab antibody with chemotherapy, more than 70% of patients are getting complete remissions, so that this principle now flowed through to a number of the acute leukemias, a number of lymphomas, multiple myelomas, solid tumors where combining different approaches to treatment is dramatically changing the outlook of patients with a variety of changes. My mentor, Dr. Freireich, used to say that leukemia was a window into cancer because it is very easy to evaluate the effects of treatment on cells in the bloodstream, whereas it is difficult to get pieces of colon cancer out, for example, so that we learn a lot of messages along the way that can be applied to a wide variety of different cancers.

Andrew Schorr:

Dr. Keating, so, would the therapy that I had, I viewed it as sort of a, you know, punch to the knees of the cancer cell and a punch to the stomach and a punch to the head to try to kill that cancer cells; my own cell gone haywire, if you will, inappropriate ineffective cells that could clog things up in the bone marrow as you described, and then have me not create the healthy cells I need. How are cancer cells so wily? You know, how do they escape the chemotherapies that we have had around for so long so that we can't kill every one, and then they just keep growing, and they don't die? They just seem to be really wily cells.

Dr. Keating:

They are very wily. The way that the early cancer cells get killed is that we give drugs which damage the DNA of the cancer cells, and normally there are repair enzymes in the body, but in the cancer cells, you have an excess of these repair enzymes so the damage that gets done by a particular drug will often be repaired by the natural enzymes because the malignant cells, all they worry about is staying alive. They don't have to do the functions that the normal cells do. For example, the liver cell has to metabolize different toxins in the body, but if you had a malignant liver cell, it doesn't care about the toxins. It just lets them go, and it is totally committed to staying alive so that it shifts a lot of its repertoire of body enzymes into repairing damage. Another way is that the cells have different enzyme systems that pump out poisons, and if we consider chemotherapy a poison to the cancer cell, these enzymes pump the drugs

out so that they can't have their desired effect. One of the problems we have with antibodies like Rituxan, for example, is that eventually the cells become resistant to it, and we are still trying to work out the mechanisms of resistance to antibodies. It's not very clear at the present time.

Andrew Schorr:

Dr. Keating, we have been getting some questions from some people living with CLL, as I am.

Dr. Keating:

Good.

Andrew Schorr:

Here is a question. So, there has been research into how can you have the body's own immune system, which failed and allowed the production of these malignant cells in the first place, how can you use that somehow to fight back? And so, we got a question via e-mail from Janet Vogel who writes, "Is M.D. Anderson sponsoring any immunotherapy or personalized vaccine trials for CLL people who have not yet required treatment?"

Dr. Keating:

The answer to that is yes, and I will try and explain to you why the immune system does not work very well in CLL and in other cancers as well to a degree. We think that the original cancer cell in CLL develops around about the time of birth, and during that time, the body is becoming used to a whole lot of new cells, and it becomes tolerant of the leukemic cells. There is just a very gradual buildup. So, it is like the leukemic cells are going through the immune system like a Stealth Bomber. They are either not sending a strong enough signal or the reception of these signals is weak. So, there are two ways that we can go about doing something about this, and one is to make the signal from the CLL cell stronger, and the second is to amplify the immune cells.

They way that we are doing it at M.D. Anderson is with a process that we call gene therapy that we have a way that we can incubate the leukemic cells with a killed virus, which carries a gene into the leukemic cell and then instead of the membrane being very dim, it becomes very, very bright, and as we give the cells back, the patient's CLL cells become their individual cell vaccine, and we can clearly demonstrate now that we can activate the immune system in response to this. So, that we have finished phase one of that approach of gene therapy, and within the next one-two months we will be activating phase two of that approach to treatment.

Now, the second way is a technology that was developed partly by a company called Xcyte.

Andrew Schorr:

Dr. Keating, I am just going to have you just hold this answer for a minute because we have to take a commercial break.

Dr. Keating:

Okay.

Andrew Schorr:

And we will understand this further, but I think that is exciting to me is research moves forward, and that is why I think when somebody is diagnosed with something serious like this, you want to investigate are there clinical trials that you might want to participate in. I did, and I think it made a big difference for me. We will be back with Dr. Michael Keating from the University of Texas M.D. Anderson Cancer Center, an expert in chronic lymphocytic leukemia, right after this and continue understanding the science and taking your calls. We will be right back.

Andrew Schorr:

Boy, am I glad I live in Seattle where the weather is pretty mild today. Back in Boston, where I was last weekend, did you see that Dr. Keating? People are trying to run the Boston Marathon. I haven't heard how it turned out, and I know my brother in New York is saying they're pumping his basement out of water, and boy, we flew out just in time.

Today we are talking to try and understand cancer a little better and cancer therapy, and we are using my condition and my doctor, Dr. Michael Keating who is a leukemia specialist at M.D. Anderson in Houston, to try to better understand that. So, Dr. Keating was explaining before the break about research that continues into trying to have the immune system be beefed up to basically fight the cancer that it missed the first time and also have ongoing surveillance for little signs that their cancer cells that are popping up or you are making ineffective cells that could otherwise be damaging.

Now, Dr. Keating, earlier we mentioned one particular monoclonal antibody therapy, Rituxan, which looks for certain characteristics cells, often cancer cells, B cells that I have, or others and say well, they are likely to be cancerous, let's destroy them. You have some toxicity with that. Certainly with chemotherapies more broadly, people have nausea and lose weight and lots of other things happen, and many women with breast cancer or other cancers think about toxic chemotherapies that kill the cancer cells, but they lose their hair or have fatigue, etc. So, the ideal would be to have your own immune system just do its job, and you were starting to speak before the break about other research and other approaches to try to restore the immune system and have it do that. Where are we with that research?

Dr. Keating:

I think we are well along. I think that there are different ways that we can take the immune cells out of the body and incubate them with some tiny beads, which have stimulating molecules on them. Overnight you can demonstrate an initial effect, but over about 7-10 days, you can expand up the number of these immune cells 100-fold to 1000-fold and then store them away so that when they are infused back to the patients, they actually help to rebuild the immune system so that, as I was mentioning before, you have to have a signal sent by the cancer cell and a reception by the immune cell so that we can teach the immune cells how to specifically kill the cancer cells of that particular patient. One of the encouraging things is that we know that if you have a transplant and give patients a new immune system, the immune system can kill off the leukemic cells or the cancer cells, and what we are trying to do now is to teach the patient's own immune cells to recognize the malignancy and get rid of it, and I think that this will be in place within the next two-three years.

Andrew Schorr:

Well, I sure hope so. You know, I can hear in the background, we've got a questioner. Roy? Are you joining us from Houston?

Roy:

Yes.

Andrew Schorr:

Roy, now, do you have CLL or you are curious it, or?

Roy:

Yes. I have had CLL for 11 years.

Andrew Schorr:

You and me both.

Roy:

I went to Dr. Keating in 2002.

Andrew Schorr:

Okay, and what's your question Roy, because we don't have a lot of time on here. What is your question?

Roy:

Right. My question is have they come up with anything to take the place of Campath? I've taken Campath four times, and I think I need something new.

Andrew Schorr:

Okay, well let's find out. And when you say "take the place" was is difficult for you or you just want to know what's next, or?

Roy:

No. Campath put me in the hospital two times.

Andrew Schorr:

So you want to know if there is something that would be easier but still be effective against your CLL. Well, take a listen Roy. So, Dr. Keating, Campath is a relatively new drug, but it is a very specific and powerful drug. Where are we with other lines of treatment, if you will, to try to help people like Roy?

Dr. Keating:

Well, Campath is a very powerful drug in that it's very good at getting rid of CLL cells from the blood, the bone marrow, and the spleen but not as good at getting rid of it from lymph glands so that there are a number of other approaches that are being taken. There is a drug called Revlimid, which is an oral drug which actually starves the cells to a degree of their nutrition and helps to expand up the immune system, and it certainly has activity in patients with CLL, so this is a new agent which has become available.

There is another antibody being explored called lumiliximab which instead of attacking the protein called CD20 on CLL cells, it attacks a protein called CD23.

There is a drug, which is being developed at Ohio State University, called flavopiridol, which is a very, very potent drug and along with that potency there are some challenges as to how to control the potency, and a lot of people are working very hard to try and understand how to integrate that into the whole process.

Many years ago, we just had one or two drugs that were available, and now we have a number of options, which is a luxury that we have, but it also challenges how to make it the best strategy for different people.

The other feature is that increasingly we are finding benefit from what are called the mini-transplants with CLL patients often doing very, very well with the transplants even up until their mid 70s whereas before with the full transplants, we could only have them undertaken in patients that were 50 to 55 years of age or younger than that. There are a number of other new drugs, which are being explored actively at the present time, and I think two to three of these will come into the marketplace in the next three to five years.

Andrew Schorr:

I am going to make just a couple of points before we go to the next break Dr. Keating, and I think Dr. Keating touched on it, so CLL unfortunately is for many people a long-term condition, so you really want to look at a strategy and have a, I believe certainly it's wise, Dr. Keating as my doctor, consult with someone who is as I like to say, "eats, drinks, and sleeps, thinks about, and has for decades, a condition like this," so that you can develop together a plan, and the plan might include current therapy, but it might include future therapies that are likely and how they could come in to play should you need them later on, so we will talk more about that, and that applies to any serious illness really. We will be back with more Patient Power discussion today about my illness, chronic lymphocytic leukemia, and Roy's from Houston, but lessons that we have for other illnesses that you might face too and a strategy to help you get well or be as well as you can. More Patient Power coming up right after this.

Andrew Schorr:

This is one of these days when I wish I had two hours for a topic. Today, we are visiting with my doctor, Dr. Michael Keating, who is a specialist in chronic lymphocytic leukemia at the M.D. Anderson Cancer Center in Houston. He is also world renowned, and so he spends a lot of time going around the world, and you hear his Australian accent, but he goes far and wide talking to doctors about the approaches in this illness, and so that leads me to a question Dr. Keating. So, somebody might see you or hear you today and talk about the different research going on, but they go back to their local oncologist, for example, and this could be the same in many illnesses of course, and there is a disconnect. The doctor is not familiar with that, doesn't have experience with it, doesn't want to execute it, it's not easy to do, and the patient feels kind of caught in the middle. How do you advise people?

Dr. Keating:

Well, I think the hardest part is that we will have an approach which will be developed and is important that we then try and coordinate that with the physician who is going to end up treating the patient, but sometimes that patient hasn't got a particular physician lined up in the first place or wants to change physicians or we don't establish adequate contact, or even after discussion, the doctor at home doesn't agree with the approach, and increasingly, people are practicing what's called evidence-based medicine, that is that you apply something which has been proven to be effective. To prove often takes about five, six, seven years after the idea has been put to the test, and you know research environments and clinical trials, you don't want to wait until you're absolutely sure before you move on to the next step.

So, what I recommend to patients is say if you're going to be recommended something by a physician, just say, "What's the evidence that this is likely to be beneficial in my particular case?" and that challenges the physician to say, "Well, in your particular case of CLL, you're different than the average, and therefore we want to do this, which has been shown in that particular clinical trial to be particularly effective for your sort of condition." Or if, for example, someone is being recommended to have a bone marrow transplant, they have to say, "Well, how many of these transplants have you done? Have you published your data? How many patients have done well? How many patients have not done well? And in my particular condition, what would you expect?" That is your right, and you know, for example, when we are buying an automobile, we know what the gas mileage is. We know what the acceleration is. We know what the brake systems are, etc. And we get all that information before we decide to buy it, so that it's also important to develop an intelligent relationship with all of your doctors and ask them the questions that are particularly bothering to you.

Andrew Schorr:

I just want to make another point. So, when I met with you 11 years ago, Dr. Keating, you told me in my particular situation I did not need treatment right away, and when I would need treatment that you'd probably have something in clinical trials that might be more effective than what you had in 1996, and that ended up being true, and the trial that I participated in with you was highly effective for me and now it's what is used with many people around the world, so we really have a partnership don't we? I mean, just patients diagnosed with a condition have the option of considering whether a clinical trial might be right for them. They can then partner with folks like you who are advancing research, but it also may give them the benefit of something that's very promising that could be potentially more effective than what otherwise they might have access to.

Dr. Keating:

Yeah, I think that this is very important in that CLL is a relatively uncommon condition, as you mentioned, and one of the important features that we have to take into consideration is what sort of clinical trials are ongoing and how many people have experience with it, and you will find that the studies that have been conducted at a national level with the Cancer and Leukemia Group B or the Eastern Cooperative Group are usually confirmatory of studies that are promising so that it depends on whether people want to be adventurous and be in the first wave of the clinical trials or whether you are a bit more conservative and want to play it safe with something that there's a lot more experience with, and it's very important, I think, that you end up feeling comfortable with the degree of risk and ask the questions, "How many patients like

this have been done, and why is this a good thing for me to do, and should I do it now or should I wait for a period of time?" And these are all important questions that we'd ask in any other transaction that we have.

Andrew Schorr:

Right. It's healthcare consumerism, but of course, your life may be on the line. These are important questions. Dr. Keating, we are going to take another break. When we come back, we will get some final comments from you. We have been visiting with Dr. Michael Keating who is a world renowned researcher and clinician in my illness, chronic lymphocytic leukemia, and he has also been my doctor, and I am very, very indebted to you Dr. Keating, and it helps me do this show every day because you help me get to this point. We will be back in just a minute with more on Patient Power. Stay with us.

Andrew Schorr:

Unfortunately, we are limited in time today. Dr. Keating, just a brief answer on something. Mary, who is a listener, wrote in and said, well you mentioned earlier in the program that some people might begin developing leukemia cells at birth. She worries, is CLL inherited? I understand to some degree it is in that it has been shown in families, but is that something any of us should worry about?

Dr. Keating:

I don't think people should worry unless there is a strong family history Andrew. For example, if two or three members of your immediate family, the parents or siblings that have CLL or a lymphoma, you may be concerned, but in actual fact, the vast majority of cases are not familial, and unless there is a strong family history, no one need be concerned. There are no specific tests that we can apply to family members to find out, although there is a very active research program ongoing at the present time to try and identify what genes may be involved with this.

Andrew Schorr:

Okay, just briefly Dr. Michael Keating. So, are you encouraged? It sounds like you are breaking CLL down, a blood cancer that you can observe in the bloodstream and really personalize medicine. Is this encouraging for cancer care in general?

Dr. Keating:

I think it's tremendously encouraging because all of the features that we dissect out with the leukemic cells are then applied to cancer cells generally and many of the very specific targeted treatments that have been developed can be explored in leukemia and then applied back to the management of other cancers. We recently had a birthday celebration for my mentor, Dr. Freireich, and a number of his alumni came back and demonstrated the tremendous advances that have been made in breast cancer with reduction in mortality rates there and multiple myeloma and all of the leukemias, and lung cancer is still tough, colon cancer is moving now.

Andrew Schorr:

But it's generally encouraging.

Dr. Keating:

Very encouraging.

Andrew Schorr:

Dr. Keating, we're going to have to go. I want to thank you for your time. I think for our listeners it's apparent when you can have somebody who has devoted their life and research to a specific illness and then get to talk to them and learn from them, it's really very enlightening. Dr. Keating, we wish you well. Keep me healthy for a long time, and we'll talk again soon. Thank you for being with us Dr. Keating from M.D. Anderson. Thank you.

Dr. Keating:

Okay. Thanks Andrew. Bye bye, and bye bye to the listeners.

Andrew Schorr:

Thank you, sir. Okay, we'll be back talking about complimentary, alternative, integrative medicine tomorrow night 7:00 p.m. Central on Patient Power. Remember, knowledge is the best medicine of all. Bye bye.

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