Updates on Lymphoma
Webcast
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Introduction

Andrew Schorr:
Hello and thank you for joining us once again. Andrew Schorr broadcasting live from Seattle, and we're about to connect you with a leading M. D. Anderson lymphoma expert in Houston. We welcome your calls as we discuss the latest in lymphoma, update you from a big annual meeting they have every year discussing blood-related cancers and other blood-related illnesses. It's called the American Society of Hematology and, I don't know, 20-, 30,000 experts from around the country were there. M. D. Anderson was very well represented not just in attendance but their research being featured, and we'll discuss that in a minute.

Well, there aren't many experts who get to be on Patient Power twice in the space of about a year, but one is Felipe Samaniego. Dr. Samaniego is an associate professor of medicine at M. D. Anderson. He's a lymphoma specialist at the lymphoma and myeloma center. Dr. Samaniego, welcome back to Patient Power.

Dr. Samaniego:
Thank you for having me.

Andrew Schorr:
Well, it's a pleasure to have you once again. Well, what we're going to do is help people understand - whether they're new to lymphoma or not, what is it? What are we talking about? We talked about lymphomas because there are many, and some today happily are curable, and others increasingly are ones that we can make chronic where many people can go on about their business. Maybe they need to take medicine regularly or maybe they get a break and maybe hopefully the disease will stay at a low level, or maybe they'll need treatment again, but people are living with lymphoma, and people are being cured of some lymphomas as well. So, Dr. Samaniego, let's start with an overview for a moment. When you look at this time of where we are in the treatment of lymphomas, how hopeful can we be?

Dr. Samaniego:
I think the treatment for lymphoma has changed every year. The number of medications available for treatment of lymphoma have been many more than we had ten years ago. The concept of treating lymphoma has changed so that the medicines that worked many years ago may or may not be used now because we have new medications including antibodies that can give you equal remission but
will also give you less toxicity. And so there's a lot of optimism in the field in lymphoma and probably in many other cancer fields that you can probably do better now, and there's many medications that are coming on down the pipeline to make combination chemotherapy a new way of treating lymphomas and shifting from old-fashioned chemotherapy to monoclonal antibodies and other biological agents.

Andrew Schorr:
So it used to be that people would be treated for cancer, and the cancer might well be knocked back, kind of blown away for a while and hopefully the cancer would be cured, but there was always the risk that from those medicines you opened up a concern about later side effects of the treatment or even other cancers. So is that the idea, that we're trying to use targeted therapies that can help the immune system fight the cancer and go right after where the cancer is and also not cause that collateral damage, if you will?

Dr. Samaniego:
Yes. There's less toxicity with many regimens now. To give you an example, ten years we used to use CHOP, it's the acronym for the most common regimen for lymphoma, and those are medicines that can cause damage to DNA, to chromosomes, and can also lead to problems to the heart. We have changed some of the treatments to not be CHOP but to be other chemotherapy combinations. They use antibodies or eliminate some of those harmful drugs like Adriamycin and still be able to give you high clinical remissions but less toxicity. So CHOP may be replaced by new medications such as Revlimid and an antibody such as Rituxan. And those are either being tested on clinical trials or they are already standard of care, meaning the efficacy, how well it works, and the toxicity has been established so it has replaced the old-fashioned CHOP chemotherapy.

PCR Clinical Trial

Andrew Schorr:
All right. Let's talk about a specific study that you were involved in that made some news. The headline I'm looking at is "New Therapy Prevents Dangerous Side Effects For Lymphoma Patients." It was a combination of a drug called pentostatin, then cyclophosphamide and Rituxan, or rituximab, that you mentioned with the idea of particularly lowering the rate of a scary side effect, myelodysplastic syndrome. So tell us about this research that you personally presented at ASH.

Dr. Samaniego:
This is a clinical trial performed at M. D. Anderson. It's a trial to treat with a three-drug combination, as you mentioned, PCR, for patients with indolent lymphoma. And the goal of the study is to use an alternative regimen. Before this clinical trial we had another combination called FNDR, fludarabine, Novantrone, Decadron and Rituxan. The prior chemotherapy gave you very good remission rates, over 90 percent. However, it was a little bit toxic, meaning the chemotherapy combination, even though it gave you a high clinical remission, will
give you bone marrow problems, meaning the blood counts would not come up, the platelets may not come up, and sometimes you have to shorten the treatment plan. So that was the short-term toxicity.

The late-term toxicity is that if you use up the bone marrow sometimes you damage the bone marrow so much that you cause a second cancer coming directly from the treatment. That's MDS, myelodysplastic syndrome. And so we were seeing that side effect in about a year or two after giving FNDR chemo, and that's a problem. That means you now have to treat a second cancer. So the objective of the PCR, this program that we presented at ASH, at the ASH meeting, was to try to use something that appeared to be less toxic, and indeed we treated 80 patients with a regimen. We saw equal efficacy, meaning that you can induce a remission in over 90 percent of individuals, but we have not seen any MDS, and we also have not seen extensive bone marrow toxicity, meaning the counts do come up soon and very little bone marrow toxicity. So it may have an advantage over the FNDR or standard of care that we have for indolent lymphoma.

At M. D. Anderson the standard of care is still FNDR because the individuals who have been treated with the new combination regimen have been treated only for a short time. That means we don't know the long-term consequences of this new regimen, and the purpose of this study is to follow through and see if any MDS actually develops after a follow-up of about four to five years. So far we have not seen MDS, so we're optimistic, very optimistic.

**Categories of Lymphoma**

**Andrew Schorr:**
Let's back up for a minute and give people a little bit of sort of a lymphoma understanding. So we have different kinds of lymphoma. So there's B cell lymphoma and T-cell lymphoma, and I know there's diffuse and nondiffuse. So help us just understand it, to kind of put it in buckets, and then let's discuss what today seems curable and what we're hoping to keep chronic.

**Dr. Samaniego:**
As you mentioned the categories of lymphoma can be divided different ways. You describe the protein that are on the cell surface, the B versus the T group. I'll describe it in terms of aggressiveness.

**Andrew Schorr:**
Sure.

**Dr. Samaniego:**
There's the indolent lymphoma, slow-growing lymphomas. That's one category. And then there's intermediate grade lymphomas which also includes Bs and T cells. And then there's high grade. In the high grade and in the intermediate grade those lymphomas are considered curable and with the ability to maintain remissions in over 50 percent at five years.
The indolent lymphomas grow so slow that it's hard to get at every cell, and even though you can have a high remission rate the indolent lymphomas have a tendency to come back even many years after finishing therapy. So conceptually the indolent lymphomas we talk about them as giving you a long-term remission with the expectation that they may be back. It may take eight years or ten years, but they still keep coming back. Because they grow so slow, to get rid of every last tumor cell has been difficult with the treatment programs that we have.

So to go back now, the high-grade and intermediate-grade can be considered to be curable in a fraction of the lymphomas, and the indolent lymphomas we don't speak about cure. We speak about long-term remission, which can be very long indeed, and for all practical purposes it can be considered a cure, but we stay away from the word because we know it's going to come back but so many, many years down the line.

**Andrew Schorr:**
And when it does come back you may have to either repeat effective treatment or even something new at that time.

**Dr. Samaniego:**
For all the lymphomas, there's many combinations that are available. We have experience on what drugs work when a lymphoma comes back. A goal is to use a different combination regimen than the one used initially. For the indolent lymphomas we can go with repeated treatments for repeated relapses for four or five times, and there's been many ways you can use combinations and get effective treatment. So multiple relapses can be treated with effective regimen and give you remissions over and over again so you can do this over 10, 15 years. So we're very optimistic that the combinations that would be available in the future will be something new that can be offered to a patient because he'll be so far down the line.

**Andrew Schorr:**
I have a friend, Tim McLain, who I've done programs with. He lives here in Seattle, and he's had exactly that situation where he's been a lymphoma patient for many years, at least 15, maybe closer to 20, but 15 for sure, and he's needed treatment along the way. Sometimes the question of bone marrow transplant has come up. It's never gotten to that point. He's still working, playing golf, and leading a full life. He recognizes that he may need treatment along the way. Now, one thing that's happened to him, though, that I wonder if it has happened to others is sometimes he's had an indolent lymphoma but there have been other times when it's not been, and he's sort of ping-ponged a little back and forth. Is that typical? Can that happen to people?

**Dr. Samaniego:**
That is typical. There are some small risks that if you're treating indolent lymphoma and, in other words let the lymphoma be present without treatment
there's a small chance that the indolent lymphoma will transform to large cell, and that becomes a separate problem. The rates of transformation are low, those are around 20 percent over five years, but that's something that's monitored. But leaving lymphoma untreated sometimes can lead to a transformation to an intermediate-grade lymphoma.

Andrew Schorr:
Now, one other area I wanted you just to clarify for us because I can never keep it straight, there's Hodgkin's disease or Hodgkin's lymphoma and non-Hodgkin's. What's the difference?

Dr. Samaniego:
The difference, it's hard to describe. It's what the pathologists will tell you when they see the big lymph node that has lymphoma in it. It's the pattern that describes it as Hodgkin's disease versus non-Hodgkin's. The Hodgkin's lymphoma or Hodgkin's disease will have a particular cell type called LIs, basically two big cells next to each other that gives it the Hodgkin's disease lymphoma name. But not only is the appearance very distinct but the pattern of lymphoma puts it in a category all by itself. Hodgkin's disease is one of the first curable lymphomas, which now has a cure rate of 95 percent. Hodgkin's disease occurs usually in a young person. It's usually a college-age student with a neck or a chest mass, and they use ABVD chemotherapy, very distinct chemotherapy from the non-Hodgkin's lymphomas. So it's basically a constellation of features. One is the histology, the appearance, and the age group. It goes with a different presentation, and so it's really one of the first good examples of a curable cancer.

Andrew Schorr:
We're going to take a brief break and when we come back we're going to continue my conversation, very intimate here tonight, with Dr. Felipe Samaniego, lymphoma specialist at M. D. Anderson. We're going to update you on the latest research, and we're also going to help you with a way to process all that and say, does this relate to what I'm dealing with with lymphoma, what I'm concerned about for myself or a loved one? And then how do I get the best care? How do I make use of that, in your situation? Remember, the phone number to call if you have a question is 877-711-5611. 877-711-5611. Or send us an e-mail to patientpower@mdanderson.org. We will right back with much more of Patient Power.

Mantle Cell Lymphoma Study News

Andrew Schorr:
Thank you for joining us tonight for our update on lymphoma with a lymphoma specialist from M. D. Anderson Cancer Center, and that's Dr. Felipe Samaniego who has been on our program before about a year ago, so we're welcoming him back. And we're welcoming your questions if you have some. Some people have e-mailed them in. You can just e-mail them to patientpower@mdanderson.org. Remember, we do these programs on a variety of conditions every two weeks, so there's a vast
library in the Patient Power area of mdanderson.org. So it's just mdanderson.org/patientpower. We'll have a replay and then ultimately a transcript of tonight's program too.

Dr. Samaniego, I want to ask you about one other study that was presented by one of your colleagues from M. D. Anderson, and this one has a headline, "Intense Chemotherapy Wards Off Recurrence in Half of Mantle Cell Lymphoma Patients After Seven Years." And I know that in mantle cell lymphoma, which can be a very deadly type of non-Hodgkin's lymphoma, that often transplant is discussed with people, but the idea would be, and that has the mortality that goes with it too. So what about this research, about helping people with mantle cell lymphoma?

Dr. Samaniego:
Yes. Jorge Romaguera, my colleague at M. D. Anderson, has been working on refining the treatment for mantle cell lymphoma. Mantle cell lymphoma is a newcomer to the field. The entity was initially thought to be an indolent lymphoma, but once more technology was available to distinguish one lymphoma from another they found that this particular group has a distinct chromosomal breakage and really it's a lymphoma entity in itself. And it was moved from the indolent lymphomas over to the intermediate-grade lymphomas.

With that shift in the category, Dr. Romaguera was able to use a therapy specifically for mantle cell lymphoma, and with the older chemotherapy regimens he found that the lymphoma kept coming back. In other words, relapse was seen so common that when a person had lymphoma, mantle cell lymphoma come back they advise transplant. Instead of transplant Dr. Romaguera initiated a more intense chemotherapy, and that intense chemotherapy has matured to be actually two combinations, two chemotherapy combinations that are given alternatively.

I'll give you the acronym. It's R-hyperCVAD, and the second cycle is R-methotrexate/cytarabine. He found that if you combine these two in an alternative way, you treat six cycles and you shift the combination chemotherapy, you will get a high response rates and very few relapses. So Dr. Romaguera's presentation at ASH was the cumulative experience with this combination of drugs for mantle cell lymphoma at seven years. Across the United States this has been the best combination if you go by clinical remissions and if you go by long-lasting remissions.

Because the lymphoma kept coming back with other regimens he can justify that this regimen is needed, and indeed he has shown that the lymphoma stays away, but there is toxicity that comes along with this combination therapy. But I think when you look at mantle cell treated this way versus mantle cell treated with other chemotherapy regimens it seems to be the best as far as remissions and the level of toxicity. So that was the data presented at the ASH meeting.
Transplant

Andrew Schorr:
Dr. Samaniego, we've mentioned a couple of times just in passing here the word transplant, and that shows up for various cancers as an option. But increasingly there seem to be drug therapies that maybe can be used in place of it, and many people will respond. What's your feeling about transplant now, where its place is related to various lymphomas?

Dr. Samaniego:
We used to say that any time a lymphoma would come back the treatment plan would be chemotherapy to reduce the level of lymphoma followed immediately by a transplant if you were not over 60 years of age, meaning you were healthy enough to then tolerate additional chemo and get a transplant of either yourself or from another person. That used to be the rule. But because we are able to use more chemotherapy that doesn't damage bone marrow we have been able to give repeated chemotherapies and keep people alive without a transplant. So a lot of times where we used to advise transplant now we can say, well, maybe you don't need a transplant because there's more combinations of chemotherapies available that can be given over and over without using up all your bone marrow. So there is more flexibility as to when you do the transplant.

And so I think a lot of our experts in lymphoma treatment would say maybe the transplant cannot be recommended so soon after seeing somebody relapse but because there's options for more chemotherapy that maybe chemotherapy alone can take care of repeated relapses in the future.

T-Cell Lymphoma

Andrew Schorr:
We mentioned the different proteins a little while back, B cell and that's the majority of them, I believe, but also T-cell. And my lay understanding is that T-cell lymphoma can be more aggressive, and I had heard years ago that it had been more difficult to treat. But kind of roaming around the convention I saw that there were a lot of people developing or espousing newer T-cell lymphoma approaches. Is there any encouraging news there? Is that a new area of medicine as far as biologics and other approaches?

Dr. Samaniego:
T-cell lymphoma usually falls into the intermediate-grade category, and it's also a collection of different lymphomas that have categorized because they share the T-cell antigens. So by itself the T-cell lymphomas is really a mixture of different lymphomas. We're not good enough or we're not experts enough to distinguish a bad-acting T-cell versus a better-acting T-cell. So given that it's been very difficult to as a group say there's a superior treatment regimen for this category. We have
not done very well with T-cell lymphomas. I think most individuals that have this
diagnosis they see a remission duration of less than a half at five years, meaning
this is probably a category that has not done as well as the B cell category.

The advances in T-cell have been made when we--there is a monoclonal antibody
called Ontak, called Ontak, which has been effective for some T-cell lymphomas.
And that was probably the last big advancement, and we're using Ontak now for
T-cell lymphomas. Almost every patient that comes to M. D. Anderson and is
treated for T-cell lymphoma, almost everybody goes on a clinical protocol because
we don't have a real good standard of care. We use CHOP, C-H-O-P chemotherapy,
but that's not very good. So Barbara Pro, our expert in T-cell lymphomas at M. D.
Anderson almost on a regular bases puts everybody on a clinical trial in order to
find more effective regimens. So it's been a very difficult area to see any
advancements.

Andrew Schorr:
What we're going to do is we're going to take another short break, and when we
come back we're going to delve into what you just talked about for a minute but
across all lymphomas, and that is clinical trials. I was in a clinical trial for chronic
lymphocytic leukemia at M. D. Anderson, a phase 2 clinical trial, we're going to help
you understand what phase 1, phase 2, phase 3 is, and then now years later, eight
ears later, there were big European phase 3 trials. And guess what, the treatment
I received eight, eight and a half years ago at M. D. Anderson, a phase II trial,
worked for me, and now they say it works for most people, and it will be the
worldwide standard. So we're going to talk about clinical trials, the benefit for you
participating. We'll be right back with more Patient Power.

Clinical Trials

Andrew Schorr:
Welcome back. Dr. Samaniego, I have to share just a little story from ASH. So I
mentioned just before the break about my own chronic lymphocytic leukemia story.
So I had the opportunity to do a live webcast from ASH with someone you know,
Dr. Michael Keating, a chronic lymphocytic specialist known around the world but at
M. D. Anderson. And that's who I saw way back in 1996, and he's remained my
doctor throughout. So in 2000 he said, Andrew, you need treatment, and I would
recommend a trial of two chemotherapy drugs and one of the lymphoma drugs that
you mentioned, rituximab or Rituxan. So I was Patient No. 60 I think in a phase 2
clinical trial, and we're going to get you to explain the different phases for us.

Anyway, so here we are eight and a half years later, worked for me, had the
treatment, haven't needed any treatment since then, thank goodness, although I
recognize I could at some point, but anyway I'm not taking any medicine now. And
then there we are at ASH and there are two big phase 3 trials that come out,
hundreds and hundreds and hundreds of patients, biggest trials ever in CLL and it
says, guess what, that therapy that you all basically invented at M. D. Anderson
that I was fortunate enough to have, well, that works worldwide and I'm sure will
now fortunately be the standard of care. So I felt great. I said to Dr. Keating in
the webcast, I said, aren't you proud as a peacock, and he was very gracious and
he talked about the wonderful researchers worldwide and patients worldwide who
participated in research. So I'm happy that I was part of it and I'm really glad it
was validated.

So let's talk about clinical trials. So what's a phase 1 trial, what's phase 2, what's
phase 3, because that's the research that you are all presenting at something like
ASH, and unless there were people that participated we'd never know. So tell us
about clinical trials in your area.

Dr. Samaniego:
Clinical trials is a concentration in treating patients at M. D. Anderson. There's
different phases so that both doctors and patients can communicate effectively
about what trial they're talking about. The phases are to describe how much is
known about a particular drug in question. For example a phase 1 is the very first
trial in humans where the objective of the trial is to test to see if it's safe in
individuals. Usually patients when they go for a phase 1 really don't have any other
options, so it can be the remaining hope for somebody who has failed other
treatment regimens.

In the phase 2 there is some experience already known about the drug, and a
phase 2 can be one drug or several drugs, and the combination or single drug is
used in one particular cell type or one particular tumor type. So because we are
the department of lymphoma and myeloma, we basically focus mainly on
lymphoma or myeloma trials, and usually our trials are phase 2 so that we can do
some phase 1s which would be first ever in a human clinical trial.

The phase 3 trials are usually much bigger trials, and they're usually multi center,
multi cancer center trial participation. And the goal of a phase 3 trial is to establish
equal or superior activity in a particular cancer. So there you need many numbers
of individuals, usually in the hundreds, and the outcome is to test is this the same
or better than our standard of care, and there's usually two arms of the treatment.
You either go standard of care treatment or a combination that uses the
experimental or new drug in the combination of chemotherapy.

Andrew Schorr:
All right. Now, I mentioned I think what was implied in what I was saying was that
people should really consider this, and certainly M. D. Anderson is a research center
and often with earlier research, as you mentioned, phase 2 trials, that are going on
there and certainly very active in lymphoma. How many trials do you think you
have going on now, Dr. Samaniego, just in lymphoma?

Dr. Samaniego:
Just in lymphoma would be over 30 active clinical trials. By active I mean people
are enrolling and starting treatment. There are many trials that have been
completed, meaning everybody has enrolled but we follow the patients for five
years. But for active trials, active enrollment, there's over 30, and there's phase 1s, phase 2s. We occasionally participate in a phase 3, meaning we share the protocol with another medical center, but our focus is lymphoma and usually phase 2, some phase 1s.

And the categories can be medicines that have never been used in humans for the first time being used. To give you an example I run a clinical trial using an antibody to a marker on proteins, a marker on tumor cells called CD 74. Other experts in our department are leading other clinical trials using other strategies. So when you put all 18 or so lymphoma experts together we should be managing at least 30 or 40 active trials.

**Accurate Diagnosis: Subtypes of Lymphoma**

**Andrew Schorr:**
Well, now, let's talk to people about first of all getting an accurate diagnosis. With all these different types of lymphoma, and we were talking about mantle cell a little while ago, you said it really was only like separated out not that long ago as we have better testing, smarter, sharper pathologists, etc. So it would seem like wherever people are listening around the world when we talk about lymphoma first we have to say make sure you have an accurate diagnosis because I've heard you say during this hour that there are different therapies that line up with different subtypes of lymphoma.

**Dr. Samaniego:**
Yes. And when people first arrive here I think we go through very important confirmation steps of saying lymphoma is present, not present. If it is present there's a full set of tests to be done to see what stage, meaning how far it has spread. It's happened more than once that we see individuals who come with a lymphoma diagnosis but in reality it's not a cancer. It's an infection, and so we sometimes send home a patient who initially thought they had a cancer but indeed they had something else that's not cancer. So this process of confirming and going through every step of refining and testing and seeing if you have enough evidence for lymphoma, it's something that probably every individual ought to have as part of the evaluation of the diagnosis of cancer and the treatment of cancer. Because as a referral center our role has been largely to check on the work of evaluations performed at other centers, it's usually confirmation of the existing cancer and then designing or prescribing standard of care, or if there's no treatment for the patient to consider clinical trials.

**Andrew Schorr:**
I find myself saying this next comment all the time, but lymphoma is a fast-changing area, many of the lymphomas. And I'll tell you going to this big meeting, American Society of Hematology, thousands and thousands of doctors, researchers, a lot of work coming out of M. D. Anderson but coming out of centers around the world, and everybody talking about it. Then if you have one of these illnesses you want to get as close to the actionable items for your lymphoma as you
can for what comes out of that meeting. You don't want to find out six months later that you had therapy that was either outdated or proven not to be the most effective for what you've got. That's why I urge people to have a consultation at a major referral center such as M. D. Anderson. It can be a second opinion. It can be a third opinion. It can be where you choose to get your care.

And then the other thing that Dr. Samaniego was just saying that I echo all the time is, then when you discuss what your plan may be part of that may be to discuss does a clinical trial fit in as a treatment option. Knowing that it's still investigational, is that something that you should consider? That's what I chose, and it worked out for me, and I was happy to see that that's what they're saying around the world now is proving to be right. But you have to start with an accurate diagnosis as well.

**Options for the Future**

Well, Dr. Samaniego, let's take it further then. Someone gets a diagnosis. You discuss clinical trials. One of the things that people might wonder, if their disease is not curable but it may be something that will need treatment again, how do you have the best therapy to knock the cancer back now but not preclude your options in the future, in other words a road map? How do you discuss that with people today knowing that things are changing?

**Dr. Samaniego:**

Yes. I think for the indolent lymphomas the field may be changing quite a bit in how we prescribe treatment for the long run. You mentioned what do you do about lymphomas when they come back. What's the strategy for that? The older chemotherapy regimens, as I mentioned before, can be harsh, and sometimes it can give you toxicities that you don't want. So the new medications that are available, for example, antibodies, medications such as Revlimid, these are medications that have little toxicity and are able to give you a tumor regression and remission. Even though they are newer and less is known about long-term outcome those medications stand to probably take us further because we know they are relatively safe and we know that they have fewer effects on the bone marrow.

So our strategy for advising individuals who have, say, indolent lymphoma we would say start off with the medications that can bring down the level of lymphoma, perhaps give you clinical remission but avoid the toxicity of DNA-damaging agents such as cytoxan, Adriamycin. So that's been the strategy, and usually we offer those kinds of medications through a clinical trial. What my experience has been advising people to go on a clinical trial is that the notion is completely foreign to individuals, and really clinical trials should be seen as the best available therapy plus something else that may improve treatment. Usually it means good efficacy, but nowadays it usually means less toxicity. So a clinical trial will usually give you the best available therapy plus an additional component that may be the next standard of care, such as the example that you bring up about
yourself, meaning the FCR chemotherapy. Back then it was a clinical trial, but now it's a standard of care, and only through clinical trials can you test these kind of questions and offer the best therapy.

Andrew Schorr:
Right. Before these new studies came out in my leukemia I used to say, well, I participated in a clinical trial and I got what I hoped would be tomorrow's medicine today. Now that all these big studies have come out I'm saying I got today's therapy yesterday. Or eight years ago, more than yesterday, and it continues to work.

Just one other area that I wanted to ask you about before we take another break and that is we've talked previously about the idea of vaccine therapies in some lymphomas and the idea that your immune system a vaccine could be made, not to keep you from getting the flu but to retrain your immune system to recognize the lymphoma cells that it didn't kill the first time around and now with the disease knocked back that it could have the surveillance and kind of zap it so it never develops into a bigger deal. Where are we with that? I know that we've been waiting for big phase 3 results and they've been sort of mixed, so people wonder, well, whatever happened to the idea of vaccine therapy.

Dr. Samaniego:
Yes. For the future it has a lot of hope. There's a lot of hope that this will be a way of treating lymphoma because lymphoma is a cancer that responds to a strong immune system. We know from other medical conditions that if you improve the immune system sometimes you can get rid of certain cancers, and that's true for follicular lymphoma, a type of indolent lymphoma. And so some of the clinical trials to use tumor material as a vaccine have worked in the laboratory, and they're testing where that kind of benefit can be used in taking care of patients. There is some evidence that it works, but I think we still have some homework to do as to how to best apply this knowledge.

One example that has worked well is because several lymphomas have viruses in them, investigators have used the viruses that come from lymphomas as a vaccine to train the T-cells and immune cells from the body. If you can test this in a cell culture you can activate the immune cells to attack the virus and then put the cells back into the patient, a patient who has a lymphoma with a virus in the lymphoma. You can train the cells to attack the virus, and as they attack the virus it gets rid of the lymphoma. This principle has worked. It's very labor intensive and requires a lot of laboratory efforts to raise the immunity of the T-cells, but this is just to give you an example that immune therapy will work. We just haven't figured out where it could best work and finding all the details that can improve the immunity for most patients with lymphoma.

Andrew Schorr:
Well, for people listening, though, listen carefully because while it might not be ready for prime time now, should you need treatment down the road, several years
ago from now, this may be what we're talking about at Patient Power then. We'll be right back with more of our live webcast with Dr. Felipe Samaniego, associate professor of medicine and lymphoma specialist in the lymphoma and myeloma center at M. D. Anderson. We've got some e-mail questions for him. If you want to send one in, send it to patientpower@mdanderson.org, or give us a call, 877-711-5611. We will be right back with much more.

**Listener Questions**

**Andrew Schorr:**
As many people know, we do our programs with M. D. Anderson every two weeks. Our next program is going to be on January 6th, actually, a little after New Year's. And we're going to discuss advances in acute myeloid leukemia, AML, so that's January 6th. Join us for that.

We're going to continue our discussion about lymphoma with Dr. Felipe Samaniego, a lymphoma specialist and a two-time guest on Patient Power. We're delighted to have you back, Felipe. Here's a question for you. This one is from Juliet in Corsicana, Texas. She writes in, "My lymphoma has been in remission for about three years or so now, and I just had my first PET scan and a CT scan. I went to my doctor and he said I don't have to come back for a year. However," she's been looking at the PET scan results and she quotes it, "minimal increased activity as noted at the level of the pharynx." So now Juliet is worried. "Does that mean my lymphoma is starting to come back?"

Now, we don't know enough about Juliet, and we're not reading the whole report, but just generally, when somebody sees that, they say, oh, my god, here it comes again. Any comment on that?

**Dr. Samaniego:**
This is a very common question on the results of PET CT. I'm assuming you're talking about PET CT result. The PET CT is a very sensitive test that detects the collection of radioactive sugar that then shows up on an image. So it's a very sensitive test, and a lot of things will make tissues take in more sugar. So what you're looking at is an image that has a lot of activity in a certain area, and that's why they mentioned increased activity. There's more sugar collection.

There's many reasons for collection of sugar. Some of them could be that there's more metabolism for any reason. Let me give you an example. We had a student who was playing a video game underneath his gown while having a PET CT. Because he used so much of his muscle power the PET became positive in the muscles. So it collects sugar because he used that tissue. So a PET that has high activity in one area, all that means is that there is probably a reason that doesn't have to necessarily be lymphoma activity giving you the collection of sugar. It could be that there's an infection in the throat, for example. It could be a sub clinical infection, meaning there's no symptoms but somebody is recovering from an infection, and that could give you a localized area that's PET positive.
When a lymphoma doctor looks at a PET CT and looks for the return of lymphoma, we usually go and examine the areas where lymphoma typically returns. We look at the lymph nodes, and we look at the bone marrow. And if there's activity that correlates with the location of the lymph nodes then that's a hint that this could be lymphoma. Of course all this testing has to be confirmed by a biopsy to show that it's indeed lymphoma or another cause for the sugar collection. So that's one thing, look at the location and the activity.

The other part is to look at the intensity of the sugar collection. There's some numbers where tumors would produce. For example, the quantification of sugar can go from one to over 80 for a tumor that metabolizes a lot of sugar. Usually lymph nodes have a number of one, but if it's low level activity usually we're talking about very low numbers that can reflect an infection. A tumor that's growing very fast will give you a very high number. It could give you a 50 or higher. But a physician reviewing this will look at that, look at the intensity, will look at the location and based on those findings will say this is a high chance of being a lymphoma or not. By the description we have there's not a lot to say that this is caused by a lymphoma, both the location and the intensity.

Andrew Schorr:
Right. When I listen to you saying, I'm saying to Juliet, you know, don't lose sleep over this, and I think the bottom line is your doctor, and hopefully you have faith in your doctor, said come back in a year. And we can kind of worry about every little ripple in this, and certainly if you have a condition where it could come back you worry, and it's understandable.

Doris from Houston wrote in and she wants to know in what she called lymphoma specialist terms, and you qualify, certainly, Dr. Samaniego, how you do you define remission?

Dr. Samaniego:
For lymphoma remission, you start off with where the cancer was. In this case it's lymphoma. Usually we're talking about lymph node involvement or bone marrow involvement, and remission usually means that the size of the lymph nodes that were big have now come down to a size that is normal or near normal. So that's one.

The second part is if there was bone marrow involvement. There are repeated bone marrows done at the end of therapy to show whether or not the lymphoma has gone away with therapy. And so a remission usually requires having the sites that were big with lymphoma decrease to a size, and if we're talking about lymphomas in a lymph node that means usually coming down to a size of one centimeter.

Sometimes people can have very big tumor masses that were lymphoma. Occasionally see something that could be, say, 10 centimeters, and it's very hard
for the body to repair and heal and make that become one centimeter. So there we usually say that if you get 90 percent shrinkage of that original mass that would be a remission that will be obtained. You also want any other tests that were positive for lymphoma to turn negative at the end of therapy. So the example that you gave of a PET scan being positive in lymphoma would then have to be tested to see that it becomes negative. So in very general terms that's what you need to have to call it remission.

Andrew Schorr:
All right. Here's one other question we got in from Tina. Tina is worried about her family history. She says, "I'm 21 years old, and I'm worried about developing lymphoma. My mother died of Hodgkin's lymphoma at age 23, and my grandmother is a six-month survivor of non-Hodgkin's lymphoma. And what I want to know is should I take any precautions, are there any to take, because of family history. Do I have a high likelihood of developing it?"

Dr. Samaniego:
There is no evidence that having Hodgkin's or non-Hodgkin's lymphoma in the family means that you are at higher risk of lymphoma or related cancer. So there's really no known inherited conditions that give you lymphoma. So you can rest assured that there's no high risk for this type of cancer. It does exist for other cancers but not for lymphoma. Most of the causes for lymphoma are not known. Some of it may be related to virus infections, but there is no inherited predisposition to develop a lymphoma, so there's no special monitoring for this individual to follow.

Andrew Schorr:
Dr. Samaniego, as we come to near the end of our hour together I just want to recap some take-home messages for people. So you go to ASH. There are researchers, scientists, practicing physicians from around the world, number from M. D. Anderson, lots of research presented when it comes to lymphoma, and it seems to help you now with current therapies, refine them, combine them in less toxic ways, hopefully cure more of the lymphomas, some of which can be cured often. And it sounds like there is a lot in development. There are a lot of new drugs and you have you said 30 or so trials. I would say people could take away generally encouraging news. Wouldn't you agree?

Dr. Samaniego:
This is a very exciting time to be treating lymphomas and other cancers because the number of available therapies, potential therapies, it's a lot more than what we had ten years ago. So I think there's a lot of room for optimism in keeping people alive with lymphoma and other cancers.

Andrew Schorr:
And also not just keeping alive but it sounds like in many cases living well.
Dr. Samaniego:
Yes. I think the days of having to get chemotherapy and losing all your hair are probably behind us for many cancers including lymphoma, so nowadays it's taking medications and antibodies, and that may be enough to keep people healthy and without toxicity. So there's a lot of optimism.

Andrew Schorr:
Well, Felipe, I want to thank you for joining us. By the way, if anybody has seen my picture, no, I did not lose my hair because of cancer treatment. It was already, already gone, and I'm just keeping it short on an ongoing basis. Okay. Well, thank you so much, Dr. Felipe Samaniego, lymphoma specialist at M. D. Anderson for joining us. We wish you well and for you and your colleagues all the best with all your research.

And again for people consider a clinical trial as an option that you could discuss with an M. D. Anderson specialist or wherever you may be at a referral center and see if that's an option for you. Felipe, all the best. Thank you for joining us tonight.

I love doing these programs every two weeks with M. D. Anderson. I wish you a happy holiday season if you're listening to us live at the end of December and thanks to M. D. Anderson for helping make it possible. I'm Andrew Schorr. Remember, knowledge can be the best medicine of all. Good night.

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