WELCOME AND INTRODUCTION

Operator
Greetings, and welcome to the ***Clinical Trials or Standard Treatment? Understanding Options for Blood Cancers*** telephone and Web education program.

It is now my pleasure to introduce your moderator, Lizette Figueroa-Rivera, MA. Thank you, Ms. Figueroa-Rivera.

[Slide 1 – Welcome and Introductions]
Lizette Figueroa-Rivera, MA
Thank you and hello everyone. On behalf of The Leukemia & Lymphoma Society (LLS), a warm welcome to all of you. Special thanks to Dr. John P. Leonard for sharing his time and expertise with us today. We have over 2,500 people participating from across the United States and several countries around the world, including Albania, Algeria, Andorra, Barbados, Brazil, Canada, Colombia, Costa Rica, the Dominican Republic, Guatemala, Peru, Saudi Arabia, Singapore and the United Kingdom.

Before we begin, I'd like to introduce The Leukemia & Lymphoma Society's Executive Director of Policy Development and Regulatory Affairs, Bernadette O'Donoghue, who will share a few words. Bernadette, please go ahead.

Bernadette O'Donoghue
Thank you, Lizette. I would like to add my welcome to all who are on the line, and that includes patients, caregivers, healthcare professionals and anybody else who is attending this program today. For those of you who have worked with The Leukemia & Lymphoma Society in the past and those perhaps who have not, I think it's important to understand that we exist to find cures and ensure access to treatments for blood cancer patients.

Our overall vision is a world without cancer patients, and we have been involved in this business for over 60 years. To date, we have invested over one billion dollars in research to advance therapies to save lives. So, until there is a cure, we will continue to fund promising research from the bench to the bedside.

We're also of the opinion that it makes absolutely no sense for us to support and fund research and find cures for blood cancers unless patients actually have access to these innovative therapies. While we may be associated with research, what you may not know is that we also work very hard to ensure that blood cancer patients have access to the best available treatments today.

So, there's much more work to be done, and we invite all of you to join our Advocacy Network. The URL is www.LLS.org/raiseyourvoice if you want to sign up or for more information.

In addition, as today's program demonstrates, we are the leading source of free blood cancer information, education and support, and we assist patients in their communities, across the United States and Canada, through our 58 chapters. So, nothing more remains for me to do but to, again, welcome Dr. John Leonard. We're very fortunate and privileged to have him as a presenter with us

Bernadette O'Donoghue
today. Dr. Leonard is the Associate Dean for Clinical Research at the Weill Cornell Medical College in New York City. Dr. Leonard, on behalf of LLS, I would like to thank you for providing us today with this very important information on clinical trials and thank all of you again for your participation.

With that, I'll turn the program back to Lizette.

Lizette Figueroa-Rivera, MA
Thank you so much, Bernadette. We would also like to acknowledge and thank Genentech and Biogen Idec, Onyx Pharmaceuticals, an Amgen subsidiary, and Takeda Oncology for support of this program.

You should have received or downloaded program materials, including a biography for Dr. Leonard and slides for his presentation. Following the presentation, we will take questions from the audience.

[Slide 2 – John P. Leonard, MD]
Now, I am pleased to introduce Dr. John P. Leonard, Associate Dean for Clinical Research at Weill Cornell Medical College in New York, New York. On behalf of The Leukemia & Lymphoma Society, thank you for volunteering your time and expertise with us. Dr. Leonard, I'm now privileged to turn the program over to you.

PRESENTATION

John P. Leonard, MD
Well, thank you very much. It's a pleasure to be here today, and I'd like to thank all the audience members. I enjoy programs of this nature, and hopefully we can make this a useful and educational program for everyone. I would also like to thank The Leukemia & Lymphoma Society for their support of this program and for all that LLS does to support patients and research to cure these challenging diseases that many of us are facing. So, thank you for that, and I would encourage the audience to learn more about LLS and to do what they can to try to become more informed about the LLS's mission and what you can do to advance it.

So we'll now jump into our program, and the second part of the program will include questions from the audience. First, we have a presentation that will go through some of the aspects of deciding between clinical trials and standard therapy; for many patients, both are often part of their treatment program.

[Slide 3 – Disclosures]
So, I'd like to highlight some of my disclosures. I have provided some advice to companies on clinical trial design in various different situations in order to bring drugs forward to patients.

[Slide 4 – How a Drug is Developed for Blood Cancers]
John P. Leonard, MD
We're going to talk about a few different aspects of developing drugs for blood cancers and new therapies for blood cancers, as well as different types of clinical trials and clinical studies that are bringing these drugs and treatments forward to patients. There is a very extensive process that takes place as drugs and treatments are developed. Usually a new drug starts in the laboratory. There are investigators, researchers—largely in academic centers—who are researching the diseases and are trying to understand why cancers occur, what makes them resistant to treatment and different ways that we can go after these tumor cells using our understanding of novel pathways, and in the course of this are able to develop drugs or compounds that seem to have effects against tumor cells.

Once these compounds are characterized as potentially having an effect against the tumor cells, there is a very extensive process that goes on to turn a chemical into a drug. These involve turning it into the proper formulation that it can go into an intravenous solution or a pill, manufacturing aspects, understanding the dosing and the schedule of giving the drug. Then, this tends to move to animal studies where we get information on the side effects of new drugs, as well as the effectiveness of new drugs in certain model systems for representing the disease in question.

Then, typically drugs move through a variety of different phases in their development. These are different types of clinical trials, which we'll talk about in a few minutes, ranging from phase I, to phase II, to phase III and often phase IV. So, this process takes a very long time to happen, and I think it's very, very frustrating in some ways because it does take a long time to advance new drugs. But it's also reassuring that by the time a new drug gets to a patient and a patient is offered participation in a clinical trial, a lot of things have happened to study and characterize that drug. So as each step goes forward, we learn more about what to expect, and I think patients can have more and more confidence in what to expect out of a treatment regimen.

[Slide 5 – Blood Cancer Drug Development: Unique Challenges]
As you all know, there are many different types of blood cancers. It is sometimes challenging to develop new drugs because, in certain situations such as indolent lymphomas and CLL (chronic lymphocytic leukemia), the treatment approach may be to just observe the disease without any therapy if the patient is feeling well. Up into certain leukemias, lymphomas, and myelomas, we may do stem cell or bone marrow transplantation. So, there's a huge array of treatments that are out there as part of standard treatments. So, trying to make those better is quite difficult from the standpoint that you have lots of things to compare to, lots of things to try to improve. But, obviously, we do need new treatments to increase the cure rate of these disorders to make people live longer and give them better options when other treatments are not working as well as to develop therapies that have fewer side effects.

In blood cancers, we have to work together. Clinical trials often require the participation of many patients, and while certain studies are done at one center or just a few centers, many different studies are performed because they need larger numbers of patients to participate and there's interest in participation across the country or across the world.

The other thing that can be challenging is that many diseases have treatments that work reasonably well. They may not do everything we want to do. Often, they're less than what we want but, certainly, most blood cancers have at least some treatment that has some effectiveness, so we don't

John P. Leonard, MD
necessarily want to throw them out. We want to improve upon them one way or another, so we need to design our studies in a careful fashion.

It's also important to know that, obviously, this all takes a long time, requires lots of resources and is quite an expensive process. So, some of the funding for this comes from the National Institutes of Health and the National Cancer Institute. Some of this comes from foundations like LLS and others, but much of this comes from industry and pharmaceutical and biotechnology companies that are pursuing the development of new therapies. So, really, there are lots of different participants in this process.

[Slide 6 – Phase I Trials]
So, let's walk through the phases of clinical trials, starting with phase I. These are studies that involve a drug that has been developed, that's been characterized in animals, that has been formulated in a way that is predicted to be manageable and appropriate as far as being able to hit the target of the drug.

Phase I trials are usually relatively early in that patients are among the first humans to receive the drug, and I've been in situations where we've treated the first patient ever in the world to get a new drug. On the other hand, in certain phase I trials, there may be hundreds or thousands of patients who've already gotten the drug. Even though it's a phase I trial, it's being given in a new way or a different way or as a new combination; therefore, the dose in this particular situation is being changed. There's, obviously, a big difference between being the first person and the thousandth person to get a drug. So, if you're thinking about participating in a clinical trial, you have to get all the information you can to really understand where this fits in your situation and exactly what the details of the drug and the trial or the treatment regimen that are being explored are, because there can be a wide range.

The goal of a phase I trial is typically to define the proper dosing. We're looking primarily at side effects to make sure that the doses we're using are appropriate and not causing undue side effects. Typically, phase I trials are done in patients who've had many prior treatments. Often they're small, but it's very important to know that there can be combinations. So, there may be bigger studies. It also may be combinations of a new drug plus a standard regimen, and we participated in phase I trials where in that scenario these were newly diagnosed patients. They were getting the standard regimen plus a new drug at one of several different doses in order to understand that new drug in combination with a standard treatment. So, again, the devil's in the details.

By the time a drug gets to blood cancer patients, it's usually been studied in a number of humans, so we have more and more information about it.

One thing that's evolving in phase I trials is that the biggest dose may not be the best dose. Drugs can have a good effect, even if you're giving them at a relatively low dose. We are working very hard to develop new designs for phase I trials so we're not just giving as much as we possibly can without making somebody sick but, in fact, using the dose that is appropriate to have the biologic effect against the tumor rather than just avoiding toxicity.

[Slide 7 – Phase II Trials]
John P. Leonard, MD
Now we have phase II trials. Phase II trials, as the name implies, are typically the next step. These are very common in cancer, including blood cancers. These may look at a variety of different doses and schedules, but the typical scenario is that we have some information on the dose and schedule and now we want to say, "Well, how does this drug work? How well does this regimen work? Does it work in 30% of people…50% of people…90% of people? So typically we've found the dose in a phase I trial, and now we say, "Okay, we're ready to move forward. Let's let the rubber hit the road and see if this new regimen, whose dose we know, let's see how well it works in this disease, in this context."

So, these tend to be a little bit bigger studies. They often don't have comparison groups. Everyone is often treated the same way. Sometimes they can be randomized trials where it's two different doses because two different doses appear safe, but we're not sure which one is better. So, we would do a randomized trial where a patient would essentially go on the study and get one dose or the other dose. This allows us to, again, determine the efficacy of this regimen as well as getting extra data on toxicity.

Often, patients in these studies participate in what are called correlative studies, where they may get blood samples or tumor samples to really see that the drug is hitting the target and to see if there are subgroups of patients where this drug seems to work particularly well. So, that might be a component of some of these studies.

[Slide 8 – Phase III Trials]
Then, phase III trials are typically randomized trials, and the idea here is really to focus on measuring the effectiveness of a drug. The idea is along the lines of we have a standard regimen or a standard drug; we have a new regimen or a new drug. We need to determine which one is better. Is the new kid on the block better than the old kid on the block, and should everyone move to the new therapy or should we stick with the old therapy? So these tend to be larger studies. They tend to be randomized trials where patients tend to go on the study and either get the standard treatment or the new treatment, and we're making a comparison.

The primary goal of these studies is to determine, again, is the new regimen better than the old regimen? Now, it's very important to note that placebos are very, very rarely used in oncology. People need to know that. One of the most common misconceptions about clinical trials is placebos. It is very uncommon. I've participated in many, many clinical trials and it is by far the exception in cancer trials to have a placebo, because in most situations no treatment or a placebo treatment would not be appropriate. So, it is uncommon for there to be a placebo unless the treatment is no treatment, and that is uncommon, where we would not give any treatment for a cancer. So, typically, the randomized trials or phase III trials are standard treatment versus new treatment. Again, it's very important that you understand from your doctor and to go forward to know exactly what's going on in the individual clinical trial to make sure that people know what's happening there.

[Slide 9 – Lessons in Blood Cancers From Phase III Trials]
John P. Leonard, MD
So, I just want to give a couple of examples of phase III trials, because people might say, "Well, I don't want to go on a randomized trial. I don't want to go on a phase III trial. I want the standard treatment or the new treatment." There are lots of examples. Many of you who are dealing with non-Hodgkin lymphoma are familiar with the CHOP (cyclophosphamide, doxorubicin, vincristine and prednisone) regimen. Now R-CHOP (rituximab and CHOP) is a newer version of that. Back in the '70s and '80s, there were a number of different regimens: CHOP, MACOP-B (methotrexate, doxorubicin, cyclophosphamide, vincristine, prednisone, bleomycin, leucovorin), m-BACOD (bleomycin, doxorubicin, cyclophosphamide, vincristine, dexamethasone, methotrexate, leucovorin), ProMACE-CytaBOM (cyclophosphamide, doxorubicin, etoposide cytarabine, bleomycin, vincristine, methotrexate, prednisone)—you've probably not heard of those regimens. Everyone in the '70s and '80s thought, or many people thought, that they were better regimens. But when the phase III trial was done, CHOP remained the standard, and the other regimens were more toxic. So, without a randomized trial, one would never know what to move forward with.

ABVD (Adriamycin, bleomycin, vinblastine and dacarbazine) is the standard therapy for Hodgkin lymphoma, and that's been studied in randomized trials.

In aggressive lymphomas, we can cut back on therapy, give less chemotherapy, and sometimes substitute radiation. That was determined by randomized trials. So, just about every treatment for blood cancers that is a standard treatment was established as that standard treatment through randomized trials. So, it's important to keep in mind.

[Slide 10 – Lessons in Oncology From Phase III Trials]
On the flip side, some of you may remember if you go back probably 15 to 20 years or so, in patients with high-risk breast cancer or advanced breast cancer, there was a great feeling that high-dose chemotherapy and stem cell transplants in breast cancer was an essential thing to do. People thought it would be unethical to do a randomized trial where patients wouldn't get stem cell transplants for breast cancer—remembering what I'm referring to here is breast cancer. I know that stem cell transplants are done in lots of blood cancers in certain situations.

But in the '80s and '90s and even later, there was a lot of sentiment that that was the way to treat breast cancer; in fact, a randomized trial was finally done, several of them, that showed that this was not the way to go. So, you think you know the answer sometimes, and sometimes you're right and the new treatment is better; sometimes you're wrong, and the old treatment is better or just as good. So, that's why we need to do these randomized trials in some cases, and it's important to participate in them. If you're asked to participate in a randomized trial, it's because we truly don't know the answer. If I knew the answer, it wouldn't be right for me to encourage you to participate in a randomized trial. I'd treat you the way I knew the answer to be. If we don't really know the answer, but we're encouraged that a new approach might be better potentially, then that's when we want to do the randomized study.

[Slide 11 – R-CHOP for DLBCL]
John P. Leonard, MD
This is just one other example that some of you dealing with large cell lymphoma may be familiar with—that there have been randomized trials of R-CHOP versus CHOP, R being Rituxan® or rituximab, and those randomized trials show that adding rituximab improved outcomes for patients.

On the other hand, there were studies of maintenance rituximab in aggressive lymphoma, recognizing that maintenance may be done in other scenarios sometimes. In aggressive lymphoma, there appears to be no role for maintenance, again, also from randomized trials. So, again, these are very, very important studies. When your doctor tells you this is what we think you should do as far as treating your disease, it's largely because randomized trials have informed that. On the flip side, some of the patients that have been the first to benefit from new therapeutic advances are those who participated in randomized trials and, in some cases, received these new therapies before they were generally available. So, this can really, in some cases, benefit patients very well.

[Slide 12 – Recent US Phase III Trials in Lymphoma]
These are just a number of different recent US phase III trials in lymphoma. I'm not going to go through all of them but just to point out that there have been studies in Hodgkin lymphoma, aggressive lymphoma like large cell lymphoma and follicular lymphoma—again, randomized trials that have moved the field forward. Sometimes those studies have shown positive results, meaning a benefit to the new regimen, and sometimes negative results. Our hunches were proven to be wrong in some cases—that the new therapy wasn't necessarily better.

[Slide 13 – Phase IV Trials]
Now, what about phase IV trials? These are typically later trials, particularly after a drug has been approved. These are studies that are often expected by the FDA (Food and Drug Administration) to get some additional data on a new drug, perhaps to look at a new drug or a new regimen in different areas and a different way. These are kind of moving things forward but, in some cases, phase IV trials may be very helpful to patients and also move the field forward.

[Slide 14 – Correlative Laboratory Projects]
Now, there are various other types of clinical research, not so much clinical trials. You might be asked by your doctor or have the opportunity to participate in what are termed either clinical databases where someone says, "Would you allow us to collect your data so we can learn about you and add your information in a confidential way to that from other patients and learn more about the disease? Or, can we potentially take some of your blood or some of your tumor tissue from the blood or from your lymph nodes, for example, or your bone marrow, and use that in the laboratory to study the disease and ultimately develop new treatments?" So, these are very important projects that may be offered to patients, and one should think seriously about participating in them because this is another important way to advance the field and learn more about these diseases.

[Slide 15 – Who Conducts Clinical Trials?]
So, who conducts clinical trials? If you're across the country, across the world, many studies are led by the National Cancer Institute. There are a variety of cooperative groups. I happen to be very involved in the CALGB (Cancer and Leukemia Group B)/Alliance group. I chair the lymphoma group there. We collaborate with two other groups called SWOG (Southwest Oncology Group) and ECOG (Eastern Cooperative Oncology Group). These are acronyms for national clinical trials groups that

John P. Leonard, MD
work together to develop new therapies. These are often done by pharmaceutical companies as well, where they will organize groups of investigators, of physicians, and then individual academic centers, medical schools, hospitals, and sometimes community practices will often participate in clinical trials. So, there are lots of different opportunities. You don't necessarily have to go to a big city. You don't necessarily have to go to a big academic large hospital. But I would say that anyone in the field who I would consider a blood cancer expert, those are typically people who are doing trials. So if you're seeing a blood cancer expert, you should ask about clinical trials whenever you need treatment. If your doctor's not doing any clinical trials, you might want to think about having a participant in your care being somebody who is doing clinical trials because these tend to be people who are active in the field, thinking and interacting with various groups about new treatments.

[Slide 16 – Advantages to Research]
So, what are the advantages to participating? Why would you want to do this if you're a patient? Well, this may be a way to get new treatments. Perhaps you are not happy with the old treatments. We have lots of good treatments, but we want to make them better, and so this may be a way to potentially get something new, something different, potentially something improved. Often, you get cutting-edge care because you're dealing with experts in the disease. These are the people who are doing clinical trials and tend to be knowledgeable in clinical trials. We tend to be standardized in our staging and follow-up of patients, and so we tend to do things in a very organized fashion. You have a team approach. There are lots of different participants, lots of people looking after you, the expert behind this study, behind the clinical trial. It's been reviewed by many, many physicians and other professionals, and so they're involved in your treatment regimen, indirectly at least. So, you can feel assured that what you're getting is something that's been vetted by a lot of people, which may have a lot more oversight than what you're getting in standard care because that's largely your local team, your local doctor, nurse, etc. giving you that treatment.

This is something that could be helpful to society. But, obviously, you and most patients want to also help yourselves, and so it's important to recognize that there are opportunities to help yourself through clinical research and clinical trials but that it's important you understand the rationale, the goals. You should recognize that if you decide to change your mind, you're always welcome to do that. You also should know that you're entitled to know the results. So when the study is done, you can find out how everything went. As the study goes along and new information is learned, you should be updated.

[Slide 17 – Myths About Clinical Research]
There are myths about clinical research. I think we've touched on some of these. You can participate throughout the country. You don't necessarily have to be at a large academic center. Typically there are not placebos, as I mentioned earlier. Clinical research does not necessarily increase the cost of care. Most of the time it doesn't. Sometimes it can be cheaper because you're getting drugs supplied to you as part of the trial, but sometimes that's not the case. So, you really need to understand what will be the cost to you, and will it be more or less expensive and how much of an impact that will be for you.

It's also important to recognize that all treatments are not free, because as part of care, you will be responsible for the things that you would have been responsible for anyway as part of routine care for

John P. Leonard, MD
your condition. So, again, the issues of costs generally are not a big problem for people, but something you should understand and make sure you have your questions answered.

[Slide 18 – Cancer Clinical Trials]
So, it is very important that people consider participation in clinical trials. Only a small percentage of patients across the country participate in clinical trials, which is really, in my mind, a tragedy. I think that there are far too few patients participating. I think it's great that you're on this call learning more about it, and I hope that you will learn more about clinical trials and if you need a treatment, you will speak to your physician about this, and seek information. It may be that you become educated in this area and still decide not to do a clinical trial, which is fine. But at least you should be informed.

So, we need more patients to participate. Patients are missing out on benefits. The slow pace of participation results in a slow pace of progress and delays the development of new and better treatments, particularly for older patients. You can be an older patient and still participate. I've treated some patients in their '80s and '90s on clinical trials. So, that doesn't necessarily rule you out if you're older, again, assuming the trial is something that you're interested in and appropriate for you.

[Slide 19 – Why Don't Patients Enroll in Clinical Trials?]
Why do patients not enroll? Well, often they don't know about it. They're afraid of the nature of treatment. Perhaps they think, well, that's only for people who are late in the course of the disease, but, in fact, many of our trials are available and appropriate for people early in the course of the disease. Maybe patients are afraid. They have other medical problems. It seems complicated. The logistics may be a challenge, the distance, or it takes physicians' time. It takes some time to explain to patients and to run the clinical trial and have the support. So there are lots of reasons, and I think we need to continue to work hard to overcome these barriers.

[Slide 20 – Slow Accrual to Cancer Clinical Trials Causes Patients to Die Unnecessarily]
I'll give you one example of one national trial that was done several years ago that compared CHOP to R-CHOP. Again, I alluded to this a little bit earlier. This was a 600-patient trial. It took three years to have this study done. If we had gotten this done one year earlier, which basically would have meant across the country 100 more people participated per year, which is only about 1 to 2 more patients per center participating, what happened because of that was that basically about 4,000 patients died because that extra year that it took, that extra year with just a few more patients going on the study per year, took us a year longer to draw the conclusions from the study, a year longer to develop a new therapy, and about 4,000 patients in this particular example missed out on being cured because it took us an extra year to get the study done. So, this is a big issue. It's a big problem and all of us need to work together to try to solve it.

[Slide 21 – Is a Clinical Trial Right for You?]
So, is a clinical trial right for you? You need to ask your doctor about clinical trials. Perhaps they participate themselves. If not, they can send you to someone or refer you to references, to other centers and other places where you can get information. Most centers or most doctors who are experts in blood cancer are doing clinical trials or are very familiar with them. You can reach out to LLS and other organizations. There's information on the Internet. Sometimes companies, if they have an exciting new drug that you've heard about, may be able to direct you to information. I would recommend that for every situation you're in, you at least need to consider a clinical trial, whether

John P. Leonard, MD
you're just diagnosed, whether you've had the disease for a while, or whether you've been through lots of treatments and are running out of options. In all of those situations there are clinical trials that you should know about and at least consider as to whether or not that could potentially be the right thing for you.

So, with that I will stop and thank you all for your attention, and I look forward to the later part of our program when we'll talk a little bit more about some of these issues in detail. Thank you.

QUESTION-AND-ANSWER SESSION

[Slide 22 – Question & Answer Session]
Lizette Figueroa-Rivera, MA
Thank you, Dr. Leonard, for your very clear and informative presentation. It is time for the question-and-answer portion of our program.

We'll take the first question from our Web audience. Doctor, Jacqueline asks, "Once a trial is complete, how long does it take for the new treatments to become available to the public? Are the patients who participated in the trial able to stay on that treatment before the medication becomes available to the public?"

John P. Leonard, MD
Those are great questions. I'll answer the second one first. So, the question is you're on a clinical trial, you're getting a new drug, the trial ends, are you able to continue on the treatment? It's hard to generalize. I would say that, in most cases, if you're on the drug, there is a way to continue being on the drug if you're benefitting from it. It's not a guarantee, but in the vast majority of cases, it's in everybody's interest if the treatment is working well. Everybody involved wants you to stay on it because it's good for you and it's good for everyone who's trying to understand how well that drug works and for how long.

The availability of new treatments after a clinical trial really depends on the nature of the drug. So if it's a drug that's already available, let's say for one type of leukemia or lymphoma or myeloma, and now a trial comes along and says that it's now useful for the other or a newer type, a different type, then that drug may already be approved and available, and people can often use it relatively quickly. On the other hand, if it's a brand new drug that's not yet FDA approved, but a trial has shown that it has benefit, then that usually takes a little bit more time because the new drug has to be approved and made available. The review of that drug has to take place to be sure that it meets all the requirements to now be an approved drug.

Now, once we know that the trial was positive and it worked, the drug worked, then typically the process moves pretty quickly because, again, everyone's excited and recognizes that there's benefit. But it can take several months after the completion of a trial until that new treatment is available if, again, it's a new drug that hasn't been previously approved.

Lizette Figueroa-Rivera, MA
We'll take the next question from the telephone audience please.

Operator
Thank you. This question comes from Paul, calling from Ohio. Please state your question.

Paul, calling from Ohio
“Regardless of choice, either standard treatment or clinical trial, should a consent form list the specific drug that will be used or is a general term like chemotherapy enough by itself?”

John P. Leonard, MD
Consent forms are very complex documents for clinical trials and, in fact, there's a lot of research going on working to try to make them more clear and more transparent for people. Before a clinical trial is opened and activated, it is reviewed by many, many different groups—often the FDA, often different scientific review groups—and then each institution or collective institutions have what's called an Institutional Review Board, and that looks at the ethics of the clinical trial and makes sure that what's happening is appropriate and is a reasonable thing to do and that all of the ethical requirements to protect humans, and patients I should say, from anything that could go wrong, all the safeguards are in place and that it's an important way to go.

A part of that is the consent form or the consent process, and that is that it's very important if you're going to participate in a clinical trial that you understand what's in store. Often, that is much more complicated to go through than in standard treatment. In standard treatment your doctor can just have a brief conversation with you, maybe you meet with the nurse or the physician assistant, and you go ahead and get started. Some institutions or centers have written consent forms to get cancer treatment. But for a clinical trial, there's a more detailed document and a much more detailed discussion that says, "Here is your situation; here are the standard treatments; here's what we're proposing; this is why we're going to do it; these are the procedures, the techniques, the monitoring that's involved; these are all of the side effects that we know that can happen; these are the expectations of being on the study; these are the alternatives if you don't want to participate in the study."

So it depends on, in describing those alternatives and the other options, usually the consent form about what the treatment is going to be in that trial is very, very specific. So if it's a randomized trial and you may get treatment A or treatment B, there's a very detailed explanation of the specific drugs in treatment A, as well as the drugs in treatment B. That is something that is reviewed so that it's understandable to you and that it's honest to you and very clear so that you can get the full picture of what's involved in the study.

So, that is something that people should be very confident about. It's also very important that you shouldn't decide to participate in a clinical trial on a whim. You should make sure you have all your questions answered, that you have time to look at that consent form, that you have a meeting with people involved with the study where they go through it with you, answer your questions, and make things crystal clear.

Lizette Figueroa-Rivera, MA
The next question comes from the Web. Elizabeth asks, “Is there any easy location to see what clinical trials are available in my area of the country?”

John P. Leonard, MD
There are a number of different locations that you can go to. The big national area is called www.clinicaltrials.gov, and there was a link in one of my last slides. The Web address was there. That is not always the easiest system to explore because you have to enter your diagnosis and perhaps some details about your disease, and you might find a number of different sites that are a little hard to wade through, but that's a place where with some persistence, you can get information. It's a very, very comprehensive listing of clinical trials.

Again, you could contact the LLS and other organizations that can give you more information and steer you on the right track. The National Cancer Institute has other websites as well that you can get some information on, different pharmaceutical companies have information and another place would be some of the larger hospitals and academic medical centers. At Cornell we have a website that has our clinical trials listed. At many centers, the easiest thing to do is to just send an email or call one of the physicians or the study team, which you can typically find from a website, and have a conversation with someone. We do that all the time where we get on the phone and say, "What are you dealing with? What are you interested in? Okay, here are some of the studies we have at our center, as well as things that might be available in other locations." I would say that most centers have that, but talking through it and, again, the LLS also has resources to get you in the right direction and try to steer you into getting the best information possible as well.

Lizette Figueroa-Rivera, MA
Yes, Dr. Leonard, and also our Information Specialists at our Information Resource Center can conduct individual clinical trial searches for you, specifically for your particular type of blood cancer. You can contact them by calling 1-800-955-4572 or email them at infocenter@LLS.org. They're available from 9 AM to 9 PM Eastern Time for you.

We'll take the next question from the telephone audience please.

Operator
The next question comes from Deb, calling from New Mexico. Please state your question.

Deb, calling from New Mexico
“My question is I’ve had Revlimid® and now transferred to thalidomide, I now use dexamethasone. It has been dropped to half dose, just one day a week I take all of it. What is your theory on it? I read that sometimes it is administered throughout the 28-day cycle of thalidomide. Also, the side effects are different than Revlimid. However, they are difficult as well. What is your comment?”

John P. Leonard, MD
Well, I can't offer a specific comment on your individual situation or anyone else's without knowing all of the details. For many blood cancers, there are lots and lots of different treatments. There are a number of different dosing regimens that are used. Some of the important clinical trials that we've had have worked to be able to establish what is the best dose or perhaps one dosing regimen that's a little bit stronger, that might potentially be more effective, and yet balance out, but be more associated with side effects, could be compared to another one. So, that's an important aspect of clinical trials, of really giving us the information of can you adjust doses, what's the best way to adjust doses and combine different drugs?

John P. Leonard, MD
So, for your specific situation, I would speak with your doctor about that and see what the options are. My guess is your doctor would refer you to many of the clinical trials that are out there that have been published that give information about that situation and how to look at the pros and cons of doing things in one way versus another.

Lizette Figueroa-Rivera, MA
We'll take the next question from the Web audience. Dee asks, "If doctors are seeing success with a trial, can a patient in need enter into a trial that has already started?"

John P. Leonard, MD
So trials are typically open for a defined period of time, for defined numbers of patients, meaning when the trial is designed, one might estimate that one would need 20 patients or 200 patients or whatever the number is. Our biggest problem, as I said towards the end of the discussion, is since many patients don't participate, usually we're lagging behind and going slowly. So, we tend to have a fair number of opportunities, and things move a little slower than we would like because of the different barriers and challenges and lack of awareness and so on.

Most clinical trials are open for a period of time. There are some studies where a drug is very exciting and promising and many people want to participate because the early news is encouraging about a drug. So those studies may not be open for a long period of time, but in those cases that's usually because the drug is working very well and people are excited about it. Typically before long there are other opportunities to get access to a drug through companies and a variety of expanded access programs and other things that can make a drug available while we're waiting to see how the results of a trial come in.

Lizette Figueroa-Rivera, MA
Thank you, and we'll take the next question from the telephone audience please.

Operator
Thank you. William from Missouri, please state your question.

William, calling from Missouri
“Is MDS a part of a lot of studies?”

John P. Leonard, MD
MDS is an abbreviation for myelodysplastic syndromes. Myelodysplastic syndromes is a bone marrow disorder that is in the family of some types of leukemia. It's not necessarily a leukemia, but it's often treated by doctors and with some of the same drugs that are used in leukemia, although it's a very different entity.

Yes, there are a number of different clinical trials. There are certain drugs that have been approved for MDS, or myelodysplastic syndromes. There are drugs that have been approved. There are drugs that can benefit this group of patients; yes, there are a number of different clinical trials in that area, and I would encourage you to learn more about them if you're interested and are dealing with that situation.

Lizette Figueroa-Rivera, MA
Thank you, and the next question we'll take from the Web. Kathryn asks, “Would participation in a clinical trial ever make you ineligible to participate in a subsequent trial?”

John P. Leonard, MD
Clinical trials have eligibility criteria, and so, obviously, one would need to have the disease or the medical condition that is being studied. Some clinical trials are directed toward certain groups of patients for whatever reason. They may be restricted to newly diagnosed patients who've never had any treatment before. They may be restricted to patients who have had one or several prior treatments. They may be restricted to patients who have had or have not had a prior, a certain particular treatment. If the goal of the trial is to say, "Does this drug work in people who already had treatment A and it didn't work in them and now we want to know if treatment B works in this group of patients?" Then, you would have been required to have treatment A to go on the trial.

On the flipside, if the goal is to compare treatment A to treatment B and it's a randomized trial and you already had treatment A, you probably wouldn't or you might not want to go on that trial because part of going on that trial is to get something you already had. So, in that scenario, you might be excluded if you already had treatment A.

So, it depends on the goals of the trial, and sometimes trials are restricted by age, although usually not, or sometimes by certain other medical conditions. If a drug had heart side effects, it might be excluded for people who have had heart problems or kidney problems or there might be restrictions about blood counts or kidney function as an example because of the nature of how the drug works and its expected side effects, so it may be not appropriate for certain patients to participate.

In general, there are some eligibility criteria that may be somewhat restrictive or minimally restrictive on who can participate. It is pretty uncommon to be excluded from the trial on the basis of having had a previous treatment. But certain trials might be focused on newly diagnosed patients, and so if you had a treatment already, you wouldn't be newly diagnosed and, therefore, you couldn't go on the study. On the other hand, some might be restricted.

So, in general, getting a treatment does not preclude participation in the clinical trial, but there might be an occasional scenario where that affects things a little bit. But, in general, I would not avoid a treatment if you need it in the hopes of not wanting to interfere with future therapy on a clinical trial.

Lizette Figueroa-Rivera, MA
Thank you, and we'll take the next question from the telephone audience please.

Operator
Our next question comes from Ruth, calling from Pennsylvania. Please state your question.

Ruth, calling from Pennsylvania
“Yes, I'm very happy with my new medication for CLL, which is Imbruvica®, but I'm having some physical problems, just a few, and I wondered whether they were due to the drug or just for other reasons. Such physical problems as nausea, diarrhea and heartburn. Which of these symptoms are due to my medication and what other problems might I expect to encounter?”

John P. Leonard, MD
So, you mentioned one particular drug, ibrutinib, that's been approved for CLL recently. CLL is chronic lymphocytic leukemia. During the course of the clinical trials with that drug, as with any drug, the data were collected on what side effects those patients experienced. Those were reported and tallied up and partly are in the package insert for the drug that tell you a little bit about what percentage of patients have this side effect or that side effect and what side effects were most common.

So, all of what we learned or much of what we learned on drug side effects comes from clinical trials because that's a systematic way in which patients receive the drug. They're monitored very, very carefully to find out what side effects they've had; those side effects get attributed, meaning that the people involved say, "Well, yes, we think this is due to the drug or maybe it's due to something else or we're not sure." So that information is tallied up, and that's what gives you and your doctor information to say, "Look, when you get this drug, the typical side effects that were seen in those clinical trials include A, B, C, D; therefore, this is what may happen to you if you receive the drug or things we need to keep an eye out for."

You mentioned a number of different side effects. It's not possible for me to tell you which ones are from the drug that you're on versus potentially something else. But I think it is important to keep in mind that your doctor is your best source of information there, and presumably your doctor will look at the information that's been published and gathered from those clinical trials to say, "Yes, what you're experiencing is something that is expected or common or occasionally seen in people getting this drug or it's not and let's chase after it for another reason because it's not what was seen in those clinical studies."

So, that's how we answer these questions that we all have whenever we use a drug or take a new drug from information gathered in clinical trials. So they're, obviously, very important.

Lizette Figueroa-Rivera, MA
We have a question on the Web from Sam. Sam asks, "Are clinical trials available or recommended for patients in watch-and-wait for CLL?"

John P. Leonard, MD
There are a number of different blood cancers, including CLL and then follicular and other lymphomas, where at certain points in time a watch-and-wait or an observation approach without treatment might be an appropriate thing to do. So, the question is would you consider a clinical trial? There are certain clinical trials that might be appropriate for people that are in a watch-and-wait situation. By the fact that one is being watched and waited, meaning not needing any treatment, one might want to ask themselves, "Well, why would I want to go on a clinical trial? If I don't need any treatment, why would I get anything if I don't have to?" On the other hand, there are certain clinical trials that are focused on taking patients who are very early in the course of the disease, perhaps trying some gentle or newer or novel approaches to see if we can change the course of the disease by trying it early.

So, it’s not a typical thing but certainly something that, in some cases, would be a reasonable thing to do. There are a number of studies where one can give blood or participate in data analysis without

John P. Leonard, MD
getting any therapy that might be particularly also appropriate for people in a watch-and-wait situation.

Lizette Figueroa-Rivera, MA
Thank you, and we'll take the next question from the phone audience please.

Operator
Thank you. Our next question comes from Mike calling from Arkansas. Please state your question.

Mike, calling from Arkansas
"Well, it was reported on the news only two weeks ago that people with cancer no longer have to wait the lengthy time frame that the FDA takes to approve a drug."

John P. Leonard, MD
Well, there are a number of different initiatives going on to try to speed the way the drugs get approved and get studied and get approved by the FDA and brought to patients. Obviously, we would like to balance out the time it takes to understand the drug and its value and its side effects and the proper way to use it versus wanting to be faster to, obviously, help patients and get new drugs that can be beneficial to patients sooner.

So, that's an important balance. We want to take long enough to really do a good job and understand the drug and get it right but not so long that people are waiting around impatiently to get the drug when they need it. So, there are a number of different initiatives going on. Some of them are federal; some of them are in certain states. It's a complicated area that I don't have the time to go into. But certainly that is something that is very important work, and I know that we heard earlier about the Advocacy that LLS and other organizations do. I think there's a lot of work going on to try to make sure that this process goes well and goes as rapidly as possible to try to get new drugs to patients sooner. I would encourage you that probably the biggest delay in getting new drugs to patients sooner is the fact that not enough people are participating in clinical trials and that that's the roadblock—getting the information in the clinical trials. The sooner and the faster we get that information from people participating, the faster we'll be able to assess these new drugs and get them to the patients that need them.

CLOSING REMARKS

Lizette Figueroa-Rivera, MA
Thank you. The Leukemia & Lymphoma Society is working very hard with our Advocacy team to make sure that patients can get these new treatments as soon as possible.

Thank you all for your questions, and please help me thank Dr. Leonard for volunteering his time with us today. We hope this information will assist you and your families in your next steps.

[Slide 23 – The Leukemia & Lymphoma Society Offers]
The Leukemia & Lymphoma Society offers online chats for patients, as well as young adults and caregivers. These chats are moderated by oncology social workers and provide forums for patients

Lizette Figueroa-Rivera, MA
and caregivers to share experiences and support each other. For more information on how to participate, please go to www.LLS.org/chat.

If we were not able to get to your question today, please call The Leukemia & Lymphoma Society's Information Resource Center at 1-800-955-4572. Information Specialists are available to speak with you from 9 AM to 9 PM Eastern Time, or you can reach us by email at infocenter@LLS.org. We can provide information about treatment, including clinical trials, or answer other questions you may have about support, including questions about financial assistance for treatment.

Again, thank you, Dr. Leonard for sharing your knowledge with us today. To all of the patients, caregivers and professionals on the phone today and on the Web, on behalf of The Leukemia & Lymphoma Society, thank you for sharing your time with us today. Goodbye, and we wish you well.