Welcome and Introductions

Stephanie Paul

[Slide 1] Greetings everyone, and thank you so much for joining us today. **[Slide 2]** This is Stephanie Paul, and I am the Vice President of Development and Marketing at the American Parkinson's Disease Association or APDA for short. I'm so pleased to welcome you to this telephone and Web education program for people with Parkinson's disease (PD), family members, and care partners. Healthcare providers will also find benefit from this program.

I'd like to thank Acorda Therapeutics and Lundbeck for generously funding this important program and to thank them for their continued appreciation for the need to provide educational programs like this one to people impacted by Parkinson's disease.

APDA was founded in 1961 with the dual purpose to ease the burden and find a cure for Parkinson's disease. Since then, APDA has raised and invested more than $87 million to fund research, patient services, and education and elevate public awareness. As the country's largest Parkinson's grassroots organization, APDA aims to ease the burden for the more than 1 million Americans with Parkinson's disease and their families through a nationwide network of chapters, information and referral centers, and support groups.

APDA pursues this effort to find the cure by funding Centers of Advanced Research and awarding grants to fund the most promising research towards discovering the causes and finding the cure for Parkinson's disease.

We also provide a number of educational programs and resources to the entire community, both healthcare providers and persons with Parkinson's disease and care partners, live, online, and in print. We invite you to visit our website at www.apdaparkinson.org to find the latest information on Parkinson's disease and its treatment as well as information on upcoming educational programs.

[Slide 3] Our presenters today are Dr. Marie Saint-Hilaire. She is an Associate Professor of Neurology, Medical Director of the Parkinson's Disease and Movement Disorder Program at the Boston University Medical Campus in Boston, Massachusetts. She is also an APDA Information and Referral (I&R) Center Medical Director and a member of the APDA Scientific Advisory Board. Our second speaker is nurse Ray James. He is a Clinical Research Coordinator at the Parkinson's Disease and Movement Disorder Center at Boston University Medical Campus in Boston, Massachusetts.

They will share an overview with us about the role of clinical trials, what is involved in participation, and how to find clinical trials. After the presentation, we will open the program up for questions from both telephone and Web participants. We encourage everyone on the line to complete the evaluation

after the program because your feedback is instrumental in helping us plan for future educational offerings, including teleconferences like this and other programs.

It is now my pleasure to introduce Dr. Marie Saint-Hilaire.

Presentation

Marie Saint-Hilaire, MD, FRCPC

[Slide 4] Thank you, Stephanie for inviting us to talk about this very important topic. If you listened to the previous webinar, you heard Dr. Standaert discuss all the treatments currently used in Parkinson's; and he also discussed the future treatments. And all of these treatments have been or are being validated through clinical trials, and we hope that this webinar will inform you better on how these trials are conducted.

[Slide 5] So, these are our disclosures, and the next slide **[Slide 6]** it's an overview of our talk today. I will start by talking about the role of clinical trials in Parkinson's and about the phases of clinical trials. Then Ray will explain all the aspects of clinical trials, such as the consent form, the inclusion and exclusion criteria, and finally how to find clinical trials in your area and how to get involved because, ultimately, we want people to be encouraged to participate more in clinical trials for Parkinson's.

[Slide 7] So, this is the timeline of approval of the major Parkinson's medications in the United States. As you can see, there have been much more medications that have been approved since the middle of the 1990s. So, PD treatment has evolved, and patients have overall been doing better. They are better cared for and have a much better quality of life than they had in the past, and we all have to thank all the people who participated in these trials, and they made all this possible.

[Slide 8] So, let's talk about what is a clinical trial. So, the World Health Organization has a definition, any research study that prospectively assigns human participants or groups of humans to one or more health-related interventions to evaluate the effects on health outcomes. So, in fewer words, we basically give a treatment to a group of people who have a condition and evaluate if this treatment works and if it is safe.

[Slide 9] Our other information we can get from clinical trials include how a medication works, how long it stays in the body for, what is the range of doses we can use, for what type of patient it works best. We can also find out if there are genetic influences and how the people will respond to the medication.

Finally, we want to know how these findings can be applied from the small group of patients on which the medication was studied to the general population of patients who have that disease.

[Slide 10] So, let's discuss the type of clinical studies. There are interventional studies and observational studies. So, clinical trials are interventional studies. So, participants receive a treatment, for example, a medication; and in many cases there's a group that receives a placebo or sugar pill to compare the treatment to. The researchers assess if the intervention, [and whether] the medication, the treatment is beneficial or not.

But, there are also observational studies, so these do not involve any treatment. The research is just following a population of patients, and they collect information on their health, and that can include taking samples of blood or urine, giving them questionnaires about diet or exercise. Sometimes the people are regularly examined throughout the study.

And these observational studies are also very important, and a great example of such a study is the Framingham Heart Study. Some of you might know about it. Researchers have been following this large group of people living in Framingham, which is a town in Massachusetts. They have been following them for many years, and they took all kind of data on their way of life, if they were smoking, if they had high blood pressure. And they did observe that smoking, high blood pressure; high cholesterol caused heart attacks and strokes. And then they applied these findings to make recommendations to improve the health of the whole population, the general population, and we all benefit from it. It really made an incredible difference in the public health to decrease the risk of strokes and heart attacks in the general population.

And I also want to stress that observational studies are done under strict guidelines, like the clinical studies, the clinical trials, because participants have to also sign a consent form like in the clinical trial; and these studies also have to be approved by institutional review boards or IRB, which are institutions, committees to approve trials that are done in that institution. And Ray will talk more in detail about what institutional review boards are.

[Slide 11] So, I want to show you some examples of interventional trials in Parkinson's. We, of course, think about medications, but interventions include surgeries and even nonmedical treatment. So, we test medications to treat symptoms, to slow down the progression of the disease. We test new ways to give old medications, such as testing the inhalable levodopa, which is an old medication but given in a new way, or we will test older medications for new indications. For example, the old blood pressure medication called isradipine is being tested to see if it slowed down progression in Parkinson's disease.

We are studying surgeries, and this is how deep brain stimulation was approved for Parkinson’s disease. And any new type of surgery, like cell transplant or gene transplant, they have to go through these rigorous trials before being approved. And let's not forget there are a lot of nonmedical interventions that are being studied, like if Tai Chi or intensive physical therapy will decrease falls, or if cognitive behavioral therapy will improve anxiety in Parkinson’s. And it's important to show the benefit of these nonmedical interventions because hopefully it will encourage the insurance companies to cover them for the patients when they need them.

[Slide 12] There are many observational studies in Parkinson's. The biggest one that many people know about is called the PPMI (Parkinson's Progression Markers Initiative) study. It's funded by the Michael J. Fox Foundation. It is to find a biomarker or test to diagnose Parkinson's, and the participants come to see us regularly and we examine them. We collect blood, urine, spinal fluid; and we also gather a lot of information on the natural progression of Parkinson's. For example, what is the risk of developing nonmotor symptoms, depression, or having compulsive behavior from the medications? And it is all useful information that will help us treat the people who have Parkinson's in general. There are studies of social self-management in Parkinson's. How does Parkinson's affect your social life? How decreased facial expression impacts your relations with others. So, these patients and their caregiver are followed for a few years, and we'll see the trajectory of their social activities.

There have been studies of exercise in Parkinson's. These are observational studies. This is how we discovered that even early on in the disease people who have Parkinson's disease don't exercise as much as they should.

[Slide 13] So, these are the phases of clinical research. There's the preclinical phase before it's tested in humans, and medications have to go through three phases before they can get approved by the FDA (Food and Drug Administration), Phase I, II, and III. And on average, it takes between 6 and 11 years from Phase I until the medication is approved by the FDA. So, I'll go through each phase of testing.

[Slide 14] So, the preclinical phase, it's before it's tested in humans. It can be tested in test tubes, in cells, in flies. Then it could go to mice, rats, and primates. It's to gather efficacy and toxicity and pharmacokinetic data to justify or not to continue testing that medication in humans. And only about 5 of 5,000 drug compounds continue on to human testing, and only 1 of these 5 has a chance to go to get approved by the FDA.

[Slide 15] So, Phase I trials are done on a small group of healthy volunteers. Sometimes they are done on patients also. It's to assess the dosing and the safety of the compound. So, this is the first stage of testing in human subjects, and these studies are usually conducted in very tightly controlled environments.

[Slide 16] So, Phase II studies are performed on larger groups, a few hundred volunteers with the disease. They assess dosing requirements and effect of the drugs. And when the development of a new drug fails, it usually occurs during Phase II, either because a drug doesn't seem to work as planned or they found that it has really unacceptable side effects.

[Slide 17] So, Phase III studies assess the effectiveness of the drug, and there are large scaled, randomized, controlled, multi-center trials; and Ray will also discuss that a little bit more in detail. But they're done on several hundred patients, and they are the definitive assessment of how effective a medication is.

So, these trials are the most expensive. They cost millions of dollars. They are time consuming; they're difficult to design and to run. And it is typically expected that there be at least two successful Phase III trials to obtain FDA approval. And about 50% of the drugs that are tested in Phase III either fail or are rejected by the FDA.

[Slide 18] And then there's Phase IV. So, Phase IV trials are done after the medication has been approved, so they are post-marketing surveillance trials after the drug has been on the market. So, it's to be sure that a drug is safe when it is used by thousands of people and that there's no rare or long-term side effects.

So, for example, there's a medication that was approved by the FDA called tolcapone or Tasmar®; and after it was on the market, it was found that it could cause, rarely, it was rare, but very significant liver damage. It even caused some deaths. So, the FDA jumped in and said, well, everybody who takes that medication has to have regular liver testing when they're on it to prevent any deaths from liver damage. So, this is an example of a postmarketing study.

There are also trials to expand the indication of a drug or an intervention. For example, there's a study to use deep brain stimulation in early Parkinson's rather than to wait later on until people have dyskinesias and fluctuations. Or a Phase IV trial might be to compare two approved treatments, such as a study comparing deep brain stimulation versus Duopa®, which is the duodenal form of levodopa. So, this type of comparison study would also be called a Phase IV trial, okay.

[Slide 19] So, who sponsors a study? So, everybody knows that pharmaceutical companies do sponsor studies, but there are also government agencies and some private foundations. So, the NIH or National Institutes of Health, for example, or the DoD, the Department of Defense, have funded Parkinson's studies. For example, the NIH is now funding the STEADY-PD study. It is a study of an old blood pressure pill called isradipine, to see if it's slowing down the Parkinson's disease. And this is the type of study that has to be funded by government because it cannot be funded by a pharmaceutical company because isradipine is a very old blood pressure medication. It's almost not used for blood pressure control. It's generic, and there is no money in it for a drug company to put money in it, to put millions of dollars for a trial.

The nonprofit foundations also fund trials. I talked about the Michael J. Fox Foundation, but I have to say that the APDA has funded many studies. For example, some of the trials showing how exercise is important in Parkinson's have been funded by the APDA.

And now I will have Ray explain the design of the studies and the regulations researchers have to follow to do studies and also how to find clinical trials.

Ray James, BS, RN

[Slide 20] Thank you very much, Dr. Saint-Hilaire. I'd like to thank the APDA for having this program today, and I'd like to also thank all of you who are listening to this webcast. I really think that this will help further your understanding of research and how it applies in Parkinson's.

[Slide 21] All right, so let's get started. I'd like to take you for a walk through a clinical drug trial and essentially highlight the important elements here, starting with study design, then moving on to responsibilities of the research team, oversight of trials, eligibility, the consent process, and also the schedule of activities.

[Slide 22] So, clinical study design, and just to build a little bit more on what Dr. Saint-Hilaire has already discussed, I'd like to lay out some important ways in which research is designed. It sounds like an abstract concept, but practically speaking, let's dive into what that means. And one way you can think about it is that it's a foundation on which you can use to help you to conduct a trial and help to answer a question about a particular therapy's effectiveness or even to understand the risks that may be involved in that particular therapy.

So, let's dive in here to an open-label study. If you were to participate in something called an open-label study, which means that everyone receives the drug or therapy. There's no question about that. It is open label. And this is often done in Phase I or Phase IV trials and can even be done at the level of a Phase III, just to think back on what Dr. Saint-Hilaire has already talked about.

There are also randomized, controlled trials, and these are important, and they involve randomness and they also involve using a control or a placebo. You can see from the picture in this slide, we have a person flipping a coin; and, essentially, that's how you would be assigned to a particular group if you're participating in this type of trial. So, you could be in the placebo group or you could be in the active drug or therapy group.

And these are very important because they help to reduce bias, and no one particular group of people is going to receive the intervention. In a single, blind, placebo-controlled trial, again, just to make sure you understand placebo that is actually a sugar pill or maybe an inactive therapy. This is when the subject does not know what group they're assigned, so there's some strength here in that there's some blinding that we're trying to eliminate some bias. But there is a bit of weakness because it may be that the researchers who are assessing you as the subject, they would know what therapy you're on; and so they would be subject to a little bit of bias there.

There's also the double-blind, placebo-controlled trials, and those are actually the gold standard in research today. They're one of the best ways to really help reduce bias when conducting research. And in these types of trials, the subjects and the researchers don’t know which group a subject is assigned to; and that's very important for helping to, again, eliminate bias in research.

[Slide 23] So, let's talk about the responsibilities of each study site. And before a study can even begin, study sites have to be selected, and this is done by various sponsors, often industry or may be done with a group that is running a trial supported by a government funder or someone in the private arena, and they select the best sites to conduct a study. Once a site is selected, there has to be a person who is put in charge. That person's called the principal investigator or the site PI.

So, in the process of selecting sites, you have to formulate a research team. That's going to be composed of the PI, and there may be a backup investigator. These are often physicians, nurse practitioners, or PAs even. And you have a subinvestigator who will assist in the trial as well. There is a study coordinator, and I happen to be one myself, and I tend to look at that role as being the glue in the research team, helping to connect all the parts together. There are also research assistants which are important for helping to add that tensile strength to that glue. They're very important in helping subjects make it to appointments or processing lab specimens and using study documents for the study. There's also a regulatory contact, someone who's going to be responsible for taking care of the licenses, the trainings, and making sure that information gets to sponsors and also to those institutional review boards, which I'm going to talk about a little bit later.

So, in this process we also have to train the study team and make sure that they're up to speed on all the different regulations and also how to conduct the study. There's something called good clinical practice. It's a guideline that's set down by the FDA, and this has come over many years of research; and essentially it's meant to protect research subjects so that certain clinical aspects are not ignored during a trial.

So, for example, if you were having a lab test done and you had a high blood sugar, you would want to make sure that you're notified about that. And so, it's good clinical practice that guides those researchers to tell you and discuss with you what that means, help to interpret that, and to refer you for appropriate care. So, these are important elements to a trial so that your clinical aspects are also taken care of as well, not just the research.

In order to do this, many sponsors put together what's called an investigator meeting; and this will involve the study teams that come from all across the United States, possibly other countries, and they go over research protocol. And research protocol is important to understand because it goes into the scientific background for a study, talks about how to conduct the trial, what are the eligibility criteria for a trial, how is safety being monitored by the research team. And a lot of this information has to be submitted to the institutional review board, so let's move on and talk about that.

[Slide 24] Now, obviously, the researchers are there. They're looking out for your well-being. But who's looking out over the researchers? Well that's where the ethics board or the institutional review board comes in. They're composed of physicians, nurses, scientists, and even people in your own community. They don't necessarily have to have a background in the study or the particular study medication or therapy, but they may pose some really important questions that might not otherwise be heard. And so, they are the ones who oversee the researchers.

There's also the Office of Human Research Protection. This is a government organization that's tied to the Department of Health & Human Services. They're there to protect your rights and well-being, and one way they do that is they oversee the IRBs. They make sure that the IRB is actually keeping up with the standards that are set down in research regulation and the laws and guidelines. They also help to develop educational programs, maintain regulatory oversight, provide advice on ethical and regulatory issues, and biomedical research.

There's also the Food and Drug Administration, which many may be familiar with. We usually refer to them as the FDA, and they provide a review of new drug applications. They also oversee research being done; and beyond the research, they also take a look at approved drugs and devices and make sure that they're safe. Sometimes you may see that down the road, after a drug or device has been approved, there are certain side effects; and that's because the FDA has to continually monitor for those types of things to make sure that what's out there is safe.

[Slide 25] So, how do you participate in a trial? Well the first thing is you need to look at a consent form, and you actually have to sign this. It is a document. Also, you're eligibility in the trial has to be determined. So, what does a consent form involve? Well, first of all, it involves the purpose of the study. Why are we doing this? What's the study drug or therapy? Also, what are the procedures that take place? Are there any payments, stipends? Oftentimes trials will provide reimbursement for travel. What are the risks? What are the benefits of a trial? It's important for consent forms to inform you of those things because it may steer what your decision finally is.

Also, your rights, those are disclosed. You're not ever stripped of your rights. You always have those as you participate in a trial. There's always the right to refuse or withdraw from a trial. And also the consent form describes confidentiality; something called HIPAA, which is the Health Information Portability & Accountability Act. It's kind of a mouthful there, but essentially whenever you go see your doctor, a hospital, or researchers, we're all bound by HIPAA; and it's a law set down- make sure that the people who are managing your information are keeping that confidential.

Also, there's something called the inclusion/exclusion criteria; and this is something that can be a big discouragement for folks who are looking to take part in trials because sometimes trials don't allow you to be taking any Parkinson's medications, and that can be a real frustration. Sometimes it's just one medicine that you happen to be on and suddenly you're not eligible for a trial. So, one thing I want to encourage you is not to get discouraged when something like that happens. There are many different trials out there, and maybe you just need to keep looking. So, I want to encourage you guys to do that.

[Slide 26] Researchers, as well as you as the subject, would be following a schedule of activities during a trial. First off, you have to start with a screening visit. Now the screening visit, obviously, the eligibility is reviewed; and we do many different lab tests. There's also verification of your condition, to make sure that you have the condition that's being studied; and there may be room for other conditions besides Parkinson's in studies such as in observational trials where they're comparing different conditions and also the natural progression history of the condition.

There's also a baseline visit, and at that time you would be randomized. Remember that word randomization. So, like the flip of a coin, you'd be assigned to a particular group, whether it's the active study drug or therapy or otherwise a placebo.

In interim visits, what happens there, the frequency of those things can actually vary depending on the complexity of the study. Sometimes there are only two or three visits. Other times there may be one every month. So, it's something to really consider as you approach the study, read through the consent form. You need to make sure that you can commit to that. And at those interim visits, it's important to show up for those because we need to monitor safety, the effectiveness of the particular therapy that's being studied as well.

And then there's a final visit, and at those times researchers want to ensure that the participant has gone through the trial safely, that they aren't experiencing any severe side effects. And if they are, they would have to be, those are reported to the sponsor and then ultimately to those government agencies. Also at final visits we want to get the impression from the study participant to see what their experience was like as they were able to undergo the therapy at hand.

[Slide 27] So, what happens after the trial? And there's usually a bittersweet end to participating in trials because you're happy that you were able to contribute and you got to experience the research process. But then a lot of people want to find out answers. They want to find out, okay, well what are the results and what group was I assigned to? Well, sometimes studies take a while to enroll. Sometimes they take two or three years to enroll. And so, if you were one of the first people to complete a trial, meaning you were one of the first ones to enroll, and they took two or three years, you have to wait for those other people to finish the trial before they'll release results; and sometimes that can be months to even years after those people finish. So, that can be a deep frustration, I think, for people it definitely requires some patience as you're going through this.

One thing that's interesting about trials is that in some cases, like with those double-blind, placebo-controlled trials, sometimes there's the option to actually enroll in an open-label trial. And that's one where you'll actually get the active study drug.

Participants are kept informed with webinars and letters from researchers, and that's one good thing to keep up with. As you go through a trial, look out for those things. And, yes, eventually you'll learn which treatment group you were assigned to, either the placebo or the active drug.

And, also, interestingly, the investigators and sponsors are responsible to publish results, whether they're positive or they're negative. And I'll talk a little bit about how that happens in another slide.

And once a research trial has been completed and all the people who have enrolled are done, experts have to review the data and have to analyze it, and they have to determine is it worth even submitting to the FDA. And if they think they have something valuable, that's approvable, they will submit that to the FDA for review by their committees.

[Slide 28] So, now that you have all this background information on clinical trials and what's involved, it would be good to find out how to determine whether a trial is right for you or where you can find information about trials. So, I do want to give you an overview here. And just before I do, I did want to highlight some interesting statistics and also kind of shed light on one of the major hurdles for clinical trials and something I came across in some readings.

So, 85% of trials actually face delays, that's pretty staggering; 30% never actually start because there's a lack of volunteers; and 10% of people with PD actually enroll in a trial, though 60% say that they're interested. So, there's, obviously, some barriers there. Maybe that has to do with eligibility criteria, but it also shows that we need people to keep knocking down the doors and keep seeking out studies and finding information that will help guide them to those research studies.

So, just to quickly highlight some of these important aspects of finding ongoing clinical trials, you definitely want to talk with your healthcare team. They're an important resource. They know you best. Sometimes the researchers are part of your healthcare team, but I do think that they help to give you a lot of options and think about a balanced approach to your decision.

There's also something called www.clinicaltrials.gov. This is a government-funded website, and any particular sponsor that is looking at testing a drug, a biologic or device, or has received government funding is required to submit their study to this website and have the information available to you. So, you can put in the information you're interested in, and you can get a lot of information about trials that may be available to you.

There's also a registry of completed trials there. This was enacted back in '08 and '09 because they want to make sure that researchers are still posting even negative results as well as positive results. The only issue with that database registry of trials is that they don't really give you an interpretation or conclusion. They just give you the results. Very interesting website would encourage you to check it out.

There's also something called Fox Trial Finder, and this is kind of like a matchmaking site for researchers and participants. It really helps for researchers to find eligible participants, and this is one way that people can do that. It was developed by the Michael J. Fox Foundation.

There's also a site called CenterWatch, and this is sponsored by a lot of other industry partners that put up information about trials and whether they're ongoing or they've completed enrollment, if there's any kind of stipends or funding available to you as you participate. That's a good website to check out. There's also the Parkinson's Study Group; and I mention them, they're a consortium of physicians and other healthcare providers from medical centers across North America. And they have expertise in clinical care as well as Parkinson's research. And they're really trying to move forward with a lot of interesting research studies and so novel therapies.

And, of course, there's the APDA Chapters and Information Referral Centers. I do encourage you guys to really make use of those resources that are right at your fingertips. Really valuable, they have a lot of great stuff available to help answer your questions.

And I mentioned here also the Parkinson's Advocates in Research or the PAIR program. That's actually put together by the Parkinson's Disease Foundation, and they help to train individuals with Parkinson's or those that have been impacted by Parkinson's in clinical research. And they helped them to be instrumental in guiding researchers at times with understanding more about the condition, to help them design studies at times, and also be a resource for those of you in the community.

And there's your local Parkinson's support group. I happen to be a leader myself, just north of Boston here, and I think it's really a great way to connect with others and discuss opinions, questions, and just to share your experiences. Often researchers will go to support groups and share information there too, so it's a really great way to stay educated and to stay up to date.

And with this next slide, I'd like to hand it over to Dr. Saint-Hilaire to provide us with some closing thoughts.

Marie Saint-Hilaire, MD, FRCPC

Thank you, Ray.

[Slide 29] I just wanted to show how subject participation has made a difference because this slide shows examples of how this has made a difference to develop things and studies.

So, people participating in studies have made available treatment, including levodopa, dopamine agonists, MAO inhibitors, COMT inhibitors, all these medications that have been approved is because people have participated in trials. It has improved the delivery methods of medications such as long-acting formulations of medication, patches, infusion pumps, inhalable medication.

Deep brain stimulation, it also has helped us understand better the role of genetics in Parkinson's, genetic forms of Parkinson's. It has shown us the importance of exercise in Parkinson's. It's not very long ago that people were just recommending physical therapy when patients had problems with their balance. Now we start right away people on an exercise program.

And, also, other clinical aspects that we learned from the studies such as a better knowledge of the nonmotor symptoms of Parkinson's, like constipation and low blood pressure and depression. This is all because people have participated in studies.

[Slide 30] And we hope we have shown to you how important clinical studies are and we hope that you will be more confident in participating in studies. If you're not interested in, for example, to

participate in clinical trials, you can still participate in observational studies if there is one in your area. You might be leery of trying a new medicine, but you'd say, "Well, I would do an exercise study. I would be interested in that." So, there are many possibilities, depending on which level of comfort you have with research.

And there are also PD studies that are looking for healthy controls, so even if you may not be a candidate for a study because of an exclusion/inclusion criteria, you can encourage your friends and families to participate in studies.

[Slide 31] And we just want to thank you for your time and attention, and we will be happy to take questions now. I think there are a lot that are waiting.

Question-and-Answer Session

Stephanie Paul

[Slide 32] Thank you so much, Dr. Saint-Hilaire and Mr. James for this very informative presentation today. It is now time for the Question-and-Answer Session.

Stephanie Paul

Thank you. We'll take our first question from the Web audience. This is a question for Dr. Saint-Hilaire. This is Mike calling from Wisconsin, and the question is, "How do I proceed if my physician does not think clinical trials are worthwhile, but I want to explore this as an option? Do I need to get his approval to participate?"

Marie Saint-Hilaire, MD, FRCPC

No, you don't need the approval of your physician to participate in a trial. So, if you go to Fox Trial Finder and you find there is a trial in your area for which you're a good candidate, you can check the site; and they might want copies of your charts, of your chart from your doctor, and you're allowed to get a copy of your chart to send them so they can look and see if you're a good candidate.

You know, by courtesy, you tell your physician I'm participating in that study; and sometimes we, the researcher, will send them a letter, "Your patient, so and so, is participating in this study"; and we give them information about the studies. So, you don't need to have the approval of your doctor.

Stephanie Paul

Okay, thank you, Dr. Saint-Hilaire.

I would like to take a question from the telephone audience please.

Operator

Thank you, our question comes from Erica, calling from New York. Please state your question.

Erica from New York

What question should an individual who'd like to participate ask their healthcare team before participating?

Marie Saint-Hilaire, MD, FRCPC

Ray, do you want to take that or I can take that.

Ray James, BS, RN

Yes, sure. Yes, hi, this is Ray. So, some questions you want to ask your healthcare team most importantly is whether or not you have any conditions or whether you're on any particular medications that might stop you actually from participating in that trial. It may not be in your best interest, so you want to ask them what their opinion is in terms of that – in terms of looking at your conditions, your medications. I think that's a really important component, and they understand how well you may be ambulating or how your activities of daily life are; so they may have a good opinion about whether or not a trial is appropriate.

You may want to present that healthcare team with the consent form and have them take a look at it and read at it and actually give you their opinion of the trial itself to see also if that trial is appropriate for you.

Marie Saint-Hilaire, MD, FRCPC

I can interject also sometimes patients bring me the consent form of a trial, and I can explain it to them. Even if it's a trial that we don't do, they want to participate in a trial somewhere else; and I can often have some of the knowledge of the trial, and I can explain to them what the trial is about. So, that can be helpful also.

Stephanie Paul

Let's take a question from the Web. This is, again, for Dr. Saint-Hilaire. We have Katherine from Virginia asking, "Most of the trials I have heard about for PD are focused on delivery methods for

administering carbidopa-levodopa without using the digestive system. The question is, are there trials going on now for drugs other than carbidopa-levodopa?"

Marie Saint-Hilaire, MD, FRCPC

There are. There are medications that are being tested, for example, I mentioned that there is isradipine which is a medication to slow down maybe the progression of Parkinson's. There is a trial that will start on inosine which is a supplement which increases uric acid that will maybe slow down the progression of the disease. So, there are trials of getting deep brain stimulation earlier, as I mentioned.

So, you know, there's some waxing and waning in trials. Sometimes a lot of the trials are for early Parkinson's. Sometimes there are more trials for late Parkinson's. So, that's why it's important to keep looking at your either Fox Trial Finder or your local APDA website to see what trials are being done in your area.

So, there might be more trials on medication to slow down the progression of the disease going on later on. We talk a lot about trials, about gene delivery of Parkinson's, but, it changes all the time so I think you keep looking at those sites to see what interests you. You have to keep looking.

Stephanie Paul

Okay, that's great advice, Dr. Saint-Hilaire. Let's take another question from our telephone audience please.

Operator

Our next question comes from Robert, calling from Florida. Please state your question.

Robert from Florida

Yes, my question is could you briefly describe what additional tests are being made for deep brain stimulation?

Marie Saint-Hilaire, MD, FRCPC

So, there are maybe studies on deep brain stimulation or the tests to get deep brain stimulation. I mean before people get deep brain stimulation, we test them, we do on/off testing, and psychological tests, and neuropsychological tests to be sure they're good candidates.

Now the studies that are being done involving deep brain stimulation, people are very interested to see if it should be used early in the disease, rather than wait later and see if the quality of life of people would be better if it's used early. And there's also studies to compare deep brain stimulation to Duopa, which is the duodenal infusion of levodopa, and see if there's any advantage to one compared to the other.

Stephanie Paul

Okay, let's take a question from the Web. This comes from Margaret in Tennessee, and I'll direct this question to Ray. If I'm doing well on the medication, can I continue when the trial program is over?

Ray James, BS, RN

That's a great question, and it's one of the difficulties of participating in a trial because you may find that you're actually [receiving] some benefit with that particular medication. And, essentially, what you would have to do is work with your healthcare provider, your physician to make sure that when you come off of that study medication, even though you're doing well, not all studies are geared to help you to continue on that study medication, between the time the study ends and when it finally gets approved. So, often you have to work closely with your healthcare provider, your neurologist or movement disorder specialist and make sure that the medication you're currently on can be accommodated to help your symptoms.

So, it is a frustration when there's a good medication out there and you can't continue it past the trial. But there are some studies that do have programs that allow people or set it up so that people can continue on the study medication, all the way until the time that the study intervention, the therapy is approved. So, there are trials like that, and it is worth asking your research team about that to find out more.

Stephanie Paul

Okay, great, thank you, Ray. Let's take another question from our telephone audience please.

Operator

Our next question comes from Gilbert, calling from Nevada. Please state your question.

Gilbert from Nevada

Yes, are there any studies being conducted that involve amino acids?

Marie Saint-Hilaire, MD, FRCPC

Any studies being done? Not that I know of, but I don't know all the studies on top of my head. Sometimes when I want to know which studies are being done, I go to www.clinicaltrials.gov myself.

I am not aware of any studies with amino acids. Inosine is a supplement, but it's not an amino acid. So, I am not aware, but you might want to go to the website just to be sure.

Stephanie Paul

Okay, so let's take another question from the Web. I'll direct this to Dr. Saint-Hilaire. This comes from Robert in New Jersey. "Is there a stage of the disease that is most desirable for clinical trials?"

Marie Saint-Hilaire, MD, FRCPC

Well, not necessarily because there are clinical trials for, in general, every stage of the disease. We do a lot of clinical trials on early Parkinson's, before people start medication, before the medication then might slow down the progression of the disease. There are a lot of trials for people who have more advanced disease, meaning people have fluctuations or dyskinesias to better control these. Maybe the people who are like the orphan of trials for medication are patients who are in the stable phase of their disease. They're taking medication, they're doing well, and they have no motor fluctuation. So, at this stage, there are not many trials that are geared toward that stage.

And as I mentioned before, sometimes we have a lot of trials for early disease but nothing for late disease; and sometimes we don't have any trial for late disease, but it really depends on the timing.

So, I would say every stage is important to study. And if you're in that stage where you're not a good candidate for a medication trial because you're stable and doing well, you might be a candidate for another type of trial, whether an exercise or physical therapy or an observational trial.

Stephanie Paul

Okay, let's take another question from our telephone audience please.

Operator

Our next question comes from Marie, calling from New Jersey. Please state your question.

Marie from New Jersey

My question is if you get the placebo, if you need to take Sinemet® (levodopa-carbidopa) and you're given the placebo, how do you function?

Ray James, BS, RN

I can mention one thing on that, Dr. Saint-Hilaire, and then I'll let you tag on, on that.

Marie Saint-Hilaire, MD, FRCPC

Go ahead.

Ray James, BS, RN

Yes, so this is Ray. That's a great question. A lot of times in clinical trials what happens is you continue on your current regimen of therapy without changing it. Oftentimes before you can get into a trial, it has to be stable for some weeks before you can enter a trial. So, very rarely will researchers actually have you come off of a medication that's effective for you. And often what they're doing is they're adding onto that medication or comparing your current medication with the active study drug. Dr. Saint-Hilaire, if you want to tag onto that too you can.

Marie Saint-Hilaire, MD, FRCPC

No, in general we want people to be stable to be in the study. We don't want to make them worse with the study, so I agree with Ray. We would continue the baseline medication, and add the study drug to see if they do better with the study drug.

Stephanie Paul

Okay, here's another question for Ray. This comes from Jeff in Texas. Are there clinical trials that look at the cognitive problems with Parkinson's disease?

Ray James, BS, RN

Yes, definitely. There's quite a number there that are looking into cognition. There are some drug studies that are looking on the effects of a particular drug on cognition. Definitely check out some of those websites that we had posted up there, even www.clinicaltrials.gov. Check out your APDA I&R

Center. The Trial Finder with Michael J. Fox; they'll really point you in a direction for trials that are looking at cognition.

And some of these trials do involve a medication, and sometimes they don't. Sometimes they're observational. They may just involve questionnaires. So, some of these can be relatively low impact and easy to participate in, but then there may be other trials that are more intensive; and they're definitely out there and really want to encourage you to get out there and look for those.

Stephanie Paul

So, a follow-up to that and this is actually a question that came from Beth in New Hampshire, and I think you mentioned this earlier, but can people who are well participate in clinical trials?

Ray James, BS, RN

Well, we're both really glad that that question is asked. We definitely need people who are considered well, people without a diagnosis of another condition because we do need controls for studies. We need to make comparisons between groups of people who don't have the condition versus those who do have the condition. You'll see that a lot in observational studies; and even as Dr. Saint-Hilaire had mentioned earlier on, you may see in Phase I trials we need healthy volunteers a lot of times. And so, that's another phase in research where individuals without a diagnosis of Parkinson's can really participate and make an impact.

Stephanie Paul

Terrific, thank you for that, I believe we have another phone question.

Operator

Thank you, our next question comes from Gilbert, calling from Nevada. Please state your question.

Gilbert from Nevada

Yes, what types of exercises are good?

Marie Saint-Hilaire, MD, FRCPC

Oh, okay, an important question, I've been talking about the importance of exercise and studies about physical therapy in Parkinson's since the beginning.

So, what is the best exercise for Parkinson's, I cannot tell you. There are guidelines of what are good exercises for Parkinson's. So, I will tell you what Terry Ellis, who is at Sargent College and has written the new book for the APDA, *Be Active*, recommends 150 minutes of aerobic exercise a week, so five times 30 minutes or three times 50 minutes. But it's 150 minutes of aerobic exercise. But which type of aerobic exercise, something that makes you a bit out of breath. So, it could be swimming, it could be bicycling, it could be walking at a brisk pace, right. And also she recommends some stretching exercise, some type of Tai Chi or Yoga, in addition to some strengthening exercise with weights.

So, basically, from what I understand, what she recommends is you exercise every day. You could do four days a week of aerobic exercise, two days of stretching exercise, and one day of weightlifting. Or you can do a little bit of each every day.

And what I would recommend is to call the APDA. They have a helpline for rehab. And what you can do is call that number. I'm sure the APDA will supply it to you, and you can speak to a physical therapist who will tell you exactly how you can combine these exercises. And they can also recommend a therapist in your area who has expertise in Parkinson's and can work with you to work on your exercise program.

Stephanie Paul

Okay, terrific. I think we have time for one more question. I will direct this to Dr. Saint-Hilaire. This comes from Lynn in Ohio. Why do so many of the clinical trials prefer not to include persons who have had successful long-term treatment with Sinemet and Mirapex® (pramipexole)?

Marie Saint-Hilaire, MD, FRCPC

So, well, it depends. If somebody is doing well on medication and don't have either major dyskinesias or on-off, then we assume these people are doing very well; and there might be more risk than benefit to put them on a new medication or to do surgery on them. On the other end, there might be other types of trials that person can participate in, like exercise trial or Tai Chi trial or some trials of cognition or social self-management.

So, yes, as I mentioned before, patients who are doing really well on their medication and are stable, this is probably the group of people in general that are the orphans of the trial world. There are not many trials for these people because if they're doing well, if it's not broken, why try to make it better? But, you know, Parkinson's evolves; and sometimes people are doing very well and then they can start having problems, like problems with their balance or problems with dyskinesias. And then at that point they might be good candidates for trials.

Ray James, BS, RN

And I did want to add on there too, Dr. Saint-Hilaire, just as well for this person and others that may be in that same kind of group is that we do have a burgeoning of genetic studies too in Parkinson's, which may be for someone who doesn't really need a different medication right now, but that might be of interest to them is the genetic studies in Parkinson's. And that's been a big area of big interest right now. So, I did want to add that in there too, something for both people with PD and also without.

Closing Remarks

Stephanie Paul

[Slide 33] Terrific, thank you, well, I want to thank everyone for participating in today's telephone and Web education program. I apologize that we weren't able to get to all of the wonderful questions. If you have additional questions, and would like to speak with someone from our Scientific and Medical Affairs Department, I encourage you to visit our website or to call 1-800-223-2732 and you can ask your questions there.

I would like to thank Acorda Therapeutics and Lundbeck for their generous support of today's webinar. I also want to thank our speakers for their presentation.

I want to emphasize to everyone on the phone that we really do appreciate your feedback and comments and want to make sure that you complete the program evaluation form that was in the confirmation email you received.

[Slide 34] We at the APDA are so proud to invest in patient services and education and to be a funding partner in most of the major Parkinson's disease-specific breakthroughs to get one step closer to discovering the causes and finding the cure.

To do all of this, we rely on the support of the entire Parkinson's disease community. If you are interested in supporting us, you can find out more information on our website at www.apdaparkinson.org.

So, again, thank you so much Dr. Saint-Hilaire and nurse Ray James and to all of you for joining us today. We agree that being informed about your disease and treatment options is the best way to empower yourself and take control of your care. Have a wonderful day everyone.