Alzheimer's Talks Transcript

First-of-its-kind Alzheimer's Trial with Dr. Reisa Sperling

Friday, June 13, 2014

George Vradenburg: Welcome to Alzheimer's Talks and thank you to all for joining us this afternoon, at least this afternoon on the Eastern seaboard. This is our most popular call to date, we have over 1,100 people registered to participate on this call from 48 states, so we've got most of the states represented here today. And another more than 3,600 people have asked us to provide a summary and information about this call because they couldn't schedule this in their schedules. So this is an enormous expression of interest in clinical trials in Alzheimer's.

My name is George Vradenburg. I am the Co-founder and Chairman of USAgainstAlzheimer's, the convener as well of Leaders Engaged on Alzheimer's Disease and the Global CEO Initiative on Alzheimer's.

USAgainstAlzheimer's is an entrepreneurial and disruptive organization with a degree of passion and urgency that has demanded a solution to Alzheimer's by 2025. We're driven by the suffering of millions of families, the sense of almost a murderous indifference to this disease on the part of our elected officials, which I begin to believe is changing but nevertheless not at the pace and scale that we need it to change to reflect the scope and scale of the suffering of people globally and the cost of this disease to American families in their role as taxpayers or as family members. So we are pressing for greater urgency from government but also industry and the scientific community in the quest for an Alzheimer's cure. Accomplishing this through convenings, effective leadership, collaborative advocacy and strategic investments in new tools and technologies and approaches to this disease.

This call is made possible by the generous support of the Alzheimer's Drug Discovery Foundation. Thanks to their generous contribution we're able to bring this conversation to you today. It is through the efforts like the scientific work of Reisa Sperling, from whom you'll hear in just a second, and the investments of the Alzheimer's Drug Discovery Foundation that we're going to beat this disease hopefully before it gets to us but certainly before it gets to our children.

It's my pleasure to introduce you to Doctor Reisa Sperling. She's the Director of the Center for Alzheimer's Research and Treatment at Brigham and Women's Hospital and Massachusetts General Hospital and Professor of Neurology at Harvard Medical School. She's very involved with USAgainstAlzheimer's as a founding member of two of our four networks, WomenAgainstAlzheimer's and ResearchersAgainstAlzheimer's.

More importantly, she is the Principal Investigator of the Anti-Amyloid Treatment in Asymptomatic Alzheimer's (often referred to as the A4 study). This research has a potential to be a real game-changer as she is looking at a possible treatment for Alzheimer's before symptoms appear.

Reminder, if you have questions during the call please press star 3 on your phone. By pressing star 3 you'll be placed into the question queue, please have your question ready to share briefly with a member of our staff and we will try and get you live on the air as soon as possible when we open up for discussion.

Doctor Sperling participated in an Alzheimer's Talks in March 2013 and was very popular so I'm grateful that she agreed to return as our first repeat guest and her popularity has only increased. Doctor Sperling, thank you for being with us today and we look forward to your comments.

Dr. Reisa Sperling: Well, thank you so much George and thanks to everyone on the phone lines who are interested in this topic. I think it is a very exciting time and I hope a very fruitful trial that we are beginning.
So let me start by just telling you a little bit about the basic idea behind the A4 study and then I'll go into a bit more detail about the study design and in particular the participants whom we are seeking to join us in this fight against Alzheimer's disease and end up with how we can get you involved in this trial or other studies as might be appropriate.

So the A4 study is really based on the idea that there's increasing recognition that the brain changes of Alzheimer's disease begin many years, at least a decade, before the point that we get to what we call dementia or very significant memory and cognitive impairment due to Alzheimer's disease. And we've been able to detect evidence of Alzheimer's disease now in the living brain using PET scans, using spinal fluid, using MRIs, and other measures that allow us to peer into the brain and see the earliest changes of Alzheimer's disease. And as I said, it looks like these changes begin 10, maybe even 15 or 20 years before we get to the stage of Alzheimer's disease that causes so much suffering among patients and their families. For me, this is a glass half-full because it's an opportunity to try to intervene and change that curve and slow that disease process before it gets to the state of potentially irreversible brain damage.

So the idea of the A4 study is that we will identify individuals who have evidence of a specific pathology or brain change that we know is associated with Alzheimer's disease, and that is the buildup of amyloid plaques. I suspect many of you on the phone have heard about an amyloid or amyloid plaques but just to explain a little bit more. Amyloid is a protein that we all make in our brains normally but as we grow older, unfortunately we don't clear it as well from the brain and about a third of normal older individuals start to develop plaque buildup and again this occurs 10 or 15 years before we get to the stage of symptoms. We don't fully understand whether amyloid is the cause of Alzheimer's disease or whether it's just one of the contributing factors but it is the case that Alzheimer's disease patients with dementia always have amyloid plaques on their brains if we look after death. So we believe this is an important factor and again we believe this changes very early and that we have the opportunity to try to help the brain clear amyloid now through new medications.

The A4 study is therefore what we call a secondary prevention trial and what I mean by that in terms of prevention is that we are seeking individuals who have evidence of amyloid plaque buildup that we can see on a PET scan but who don't yet show the symptoms of Alzheimer's disease. Meaning they're clinically normal, they're able to live independently and go about their daily lives of being able to function pretty well. We will allow individuals who are little bit worried about their memory because we know some of these early memory concerns or what we sometimes refer to as subjective cognitive complaints, sometimes are an indicator of very, very early changes and actually increases the likelihood that a person who's still normal has amyloid plaque buildup that we can see on a PET scan.

This is a phase-3 FDA trial and for those of you who may not be familiar with that terminology, that means that this is the trial that if we succeed the FDA has told us that if the trial is positive they would consider provisionally approving this drug for individuals to use. That's very exciting because it really means I think our regulators are working with us in trying to develop novel trial design to really help us bend this curve.

Now because of that it's a very large trial. So we need over a thousand individuals in this trial. We are looking for people who are between the ages of 65 and 85 years of age and we believe we'll have to screen about 10,000 individuals to find the 1,000 who are the perfect fit for the study. In order to qualify for the study, again individuals must be 65 to 85 years of age, be clinically normal meaning they perform in a normal range on some screening memory test and if that's the case they go forward to get a PET scan and I can answer more questions about the PET scan later but this is a relatively simple imaging test which can now detect evidence of amyloid plaque build-up during life. And we will then look at these PET scans and also do some calculations so that we can find these individuals who have evidence of amyloid plaque buildup and would be the right candidates to come in to the A4 trial.

The trial itself is 3 years and 3 months, it's a long trial because we know that these very early changes in memory that are associated with amyloid plaques happen very slowly over time and therefore it's really important for us to follow people for a long period of time and to determine whether individuals who get the investigational treatment versus those who get the placebo, or the treatment that is not an active anti-amyloid treatment, whether they have a difference in the rate of memory loss that we think is due to Alzheimer's disease.

So the investigational treatment we chose for the first study for the A4 trial, is called Solanezumab. This is a medication that was tried in individuals who already had Alzheimer's disease/dementia in about 3,000 individuals. We looked very hard at multiple different medications over 18 months to try to make the best choice for the A4 study. And we decided on this drug, which is an antibody. And an antibody is a protein that your own body makes to try to help you clear foreign proteins or sometimes infections. And in this case, this is an antibody which was specifically made to try to help the brain remove an amyloid peptide so that they can't form more of these amyloid plaques and cause damage to nerve cells. The other reason we chose this particular antibody for the A4 study is that it has a good safety profile in that very large trial. The large trial in dementia did not show an overall benefit and it did show in the mildest subgroups some evidence of slowing of cognitive decline just in those individuals who only had very mild memory problems in dementia. And our hope was that if we went 10 years earlier, as we hope we will be in the A4 study, that we could really bend that curve and ultimately prevent memory loss due to Alzheimer's disease and prevent dementia.

A couple of other things about the A4 study, we are running the study at 60 sites in the US, Canada, and now in Australia. And in each of these sites there are personnel who are very expert about aging and memory and Alzheimer's disease who will evaluate individuals and again make sure that they are the right candidates to come in to the A4 study. We are very much seeking to get a diverse population in the A4 study. We're requiring that each site screen 1 out of every 5 individuals who will come from an under-represented minority. And this is really going to be challenging but we think critically important because we know that African-Americans and Latinos in our country are at a higher risk, almost double the risk, of developing Alzheimer's disease and dementia and yet we don't fully understand those factors. What is the difference in the biology, in genetics, or in other factors that might influence that increased risk. So that's something very important that we have the opportunity in the A4 study to be

able to understand whether there's a difference in ethnicity, in our likelihood of accumulation of amyloid plaque buildup or are there other factors that we might be able to intervene like lifestyle factors or other illnesses, hypertension, or diabetes that might also interact with Alzheimer's disease changes.

The study itself, as I mentioned, is 3 years and 3 months long. The study involves getting an infusion of the antibody or the placebo once a month. And when I first started to work on A4 and we decided on Solanezumab I thought, oh that's a big commitment once a month coming in to get an infusion, but it's only about 30 minutes every month and I started to realize that 30 minutes once a month in joining us in the fight against Alzheimer's disease and hopefully preventing memory loss due to Alzheimer's disease isn't really that much time. So we're greatly hoping that we will find individuals who really want to join us in this fight and we'll do everything possible to make it easy for individuals to come into the site get the testing and get the infusions without disrupting their life. We help with transportation and often try again to make it as easy as possible for scheduling.

Then there are some especially fun parts I think of the A4 study. So one of the things is we're trying to develop innovative ways or methods to be able to detect changes in memory that will make it even easier for us to do these trials in the future. So we have set of iPad tests, computerized tests that happen on the iPad, that people get to do as well as more traditional pencil and paper memory tests. And for those of you who might be wondering whether people between 65 and 85 will have any difficulty on the iPad, I can tell you that we piloted these tests on 50 individuals between the ages of 60 and 90 and amazingly every one of those 50 individuals could do that iPad test at the end of 30 minutes perfectly whereas somehow I am still struggling to make my iPad work. So I think this will actually be a fun part of a4 and help us again learn more about more innovative and more sensitive measures of memory.

There are also scans involved in the A4 study. As I mentioned we have the PET scan at the beginning, which will help us determine whether individuals have evidence of amyloid plaque buildup or not. And an important aspect of the A4 study is that we will tell individuals whether they have evidence of amyloid plaque buildup or we don't see that and that's an important part we refer to as disclosure and we do that in a very careful way where we ask people a lot of questions before they are scheduled to get their PET scan and then during the process itself because we want to study what individuals learn about their own amyloid status and what it means to them and if it changes their behaviors in terms of a more healthy lifestyle or their concerns about developing Alzheimer's disease.

So the A4 study has many different aspects in here that we hope will really help gain knowledge about Alzheimer's disease and of course most importantly we hope that it will demonstrate that intervening with the right drug at the right time of the disease can really bend that curve and help us prevent Alzheimer's disease, dementia.

So I think I might stop there George and see if people have questions that they want to ask, I saw a lot of good questions about eligibility and I'm happy to answer any questions that come up.

George Vradenburg: That's really been a terrific presentation and for all of those in this Alzheimer's world who've experienced it and who fear experiencing it I want to thank you for your dedication and commitment to this field. So I just wanted to say that at the outset.

I just want to remind people, we have a number of questions in the queue, but to remind those people who may have come on just a little late. If you do have a question during the call, please press star 3 on your phone. By pressing star 3 you'll be placed in a question queue. Please have your question ready to share briefly with a member of our staff and we'll get you on with Reisa Sperling as quickly as we can.
I think there are going to be a number of questions adjust on a question of how do I know whether or not I have a trial site near me, where can I find that out?

Dr. Reisa Sperling: Absolutely, so I should have mentioned that we have a website that's available it's a4study.org and on that website it shows you the map of all 61 sites in the US, Canada and Australia and it also has the name of the site, the city and state it's in, and the phone number of a coordinator or even easier has a click where you can just link and send an e-mail to the site personnel saying that you are interested.
And again, we're looking for individuals who are 65 to 85 who are interested in joining us in this fight. If you're younger than 65 or 85 there are other opportunities for people to participate, there's the Alzheimer's Prevention Registry and if you're an individual who's already suffering from Alzheimer's disease where you have mild cognitive impairment or have a loved one who has dementia there are many many trials available, trial match through the Alzheimer's Association, there's information at the National Institute on Aging.

But for A4 in particular it's a4study.org or you can call a number 844-A-4-STUDY (844-247-8839) if you'd like to talk to someone, that will be answered at the National Institute on Aging.

George Vradenburg: There are number of questions that came in before the call about exactly how Solanezumab works and where there many risks in participating in the study because of potential side effects from the use of that drug?

Reisa Sperling: Absolutely, so Solanezumab again is an antibody, which is a protein that can help the body clear out abnormal accumulation or substances that we don't want there and Solanezumab in particular is an antibody that binds to the amyloid peptide, the science jargon of that is 1-42 abeta. But it's the piece of amyloid that unfortunately starts to clump together in the brain that forms plaques and forms other smaller clumps that we think are toxic to nerve cells and by binding to that amyloid it allows the body to clear out amyloid more successfully, keep it out of the brain, and hopefully keep those plaques from forming.

In terms of side effects of course all medications can have side effects and one of the important things in this trial is there is a consent form that explains all of the potential side effects but also warns people that we will watch everyone in this trial like a hawk because we obviously want to keep people as safe and healthy as possible. We chose Solanezumab because it had the best safety profile of all of the antibodies that were being tested that we had look at so far. The biggest concern with some of the antibodies is causing brain swelling and we really did not see very much of that with Solanezumab we'll still be looking with MRI scans to make sure that we don't see evidence of this or other problems that could occur with an antibody treatment. But overall we felt that this was the safest antibody and the best one to take forward in the A4 study.

George Vradenburg: Paul Flicker from Florida has asked us to spell Solanezumab.

Dr. Reisa Sperling: Ah, oh dear. I might have to write it down to make sure I get it right. No, it's s-o-l-a-n-e-z-u-m-a-b.

And for those of you who are wondering how the drug companies ever come up with names like this. The -mab at the end stands for monoclonal antibody and then there's some group in Geneva or something that helps make a standardized format for naming all of these drugs but I'll be honest and say I refer to it by Sola that's a lot easier to pronounce and spell.

George Vradenburg: Great. You have... there's a question here from Lynn Walehousen. Lyn asked a question about transportation.

Dr. Reisa Sperling: So we are going to try very hard to make it easy for people to come to the site and this will be somewhat dependent on on which site you're adding what arrangements they have I can say for our own site in Boston at Brigham and Women's Hospital and Mass General we will pay for cabs if necessary, we will pay for gas, occasionally we've even paid for a driver if someone has difficulty getting cabs. So we really want to make it as easy as possible for people to come and obviously that it doesn't cost them money. We certainly reimbursed for parking if needed but again each site will try to work with the participants to make sure we cover the cost of transportation and make it easy for someone to come in.

George Vradenburg: Lynn, did that answer your question?

Question: Yes, it did. Thank you.

Dr. Reisa Sperling: Thanks for asking.

George Vradenburg: We have a question here from Elizabeth Trought from New Hampshire who asked a question which will trigger what things might exclude you from the trial or not. So Elizabeth?

Question: I'm wondering if we've been a part of the long term imaging study if that is an advantage or a disadvantage.

Dr. Reisa Sperling: It's neither an advantage nor disadvantage. Well I will say it's an advantage in that individuals who've been in our natural history imaging study have really contributed so much to allowing A4 to happen. It’s those studies that really taught us about the increased risks of amyloid buildup and have allowed A4 to be possible. We will allow individuals who are in those natural history studies if they want to, to come in and screen for the A4 study.

Again to participate in the A4 study itself, individuals must have evidence of amyloid buildup in their brains in a PET scan and obviously not everyone in our imaging studies will. But there's one other aspect that I didn't mention which is there will be an arm of the A4 study which we refer to as the LEARN study which stands for Longitudinal Evaluation of Amyloid Risk and Neurodegeneration and this will be for people who don't show evidence of amyloid plaque buildup. But these individuals still want to be in natural history studies and joining us in this will help us learn more about what the risk of amyloid buildup is at an individual level. So that will be somewhat like the imaging studies that you may have already been participating in.

Question: Thank you.

Dr. Reisa Sperling: Thank you.

George Vradenburg: We have a question here from Joyce Leftly from New Jersey. And she's got a question about the age limit.

Question: Ah, yes. Doctor Sperling, for people who maybe just a couple of months short of the 65 year age this year. Is there any possibility that the enrollment will continue into the early part of next year?

Dr. Reisa Sperling: Yes. Fortunately for those people not fortunately for me because I want to enrollment to go as fast as possible. But we believe that it will take about 18 months to complete our enrollment because again we're going to screen 10,000, probably do PET scans on 3,000 to find our 1,000 and that's going to take us 18 months. So if you are just shy of 65 I suspect we will still be enrolling probably through most of 2015.
Question: Wonderful, thank you.

Dr. Reisa Sperling: Thank you.

George Vradenburg: We have a number of questions that come in online as I gathered them but I'll ask one person to ask their question so that we get it answered for everybody. Connie Nolan from Kentucky. Connie, would you like to ask your question?

Question: Well, it revolves around the age limit. I'm only 62 but I'd really like to participate and I was wondering why there's the age limit?

Dr. Reisa Sperling: Yes, that's an excellent question and I'll explain why it is but also explain some plans for the future. So when we started to do our analyses for the A4 study we know that the risk of having evidence of amyloid plaque buildup increases very substantially with age and in fact the most efficient trial design would be to have people over the age of 70 because that's when the increase in amyloid plaque buildup is the highest. I felt strongly that we should at least go down to age 65 because I want to treat people as early as possible. But there's a huge decrease in a likelihood of being amyloid positive once you go below the age of 65. So between the ages of 60 and 65 it's only about 1 in 10 individuals has amyloid plaque buildup and therefore we'd have to do many, many more PET scans and the sad reality is I don't have enough funding to do that at this point. But in the future we hope that we'll be able to expand the age range of the next trials we do that are like the A4 study to be a little broader and go down perhaps to age 60 or someday I hope even to age 55 if we could more accurately predict individuals who are just in a very beginning of having amyloid plaque buildup. But right now we had to stop at age 65 because we know below that the chances of having amyloid buildup will go way way down which is a good thing for being 62 because by the time you're entering the age of increased risk above age 65 or 66, I hope we'll be getting answers that can help.

George Vradenburg: So Connie, good news for you. We have a question here from Laura Murphy about another question about inclusion and exclusion. Laura?

Question: Yes, I'm curious about whether having ApoE4 genotype will exclude me from the study.

Dr. Reisa Sperling: If it's okay with you I'm going to explain to others on the phone, who may not know all the facts about the Apolipoprotein E. So Apolipoprotein E we know is a genetic risk factor for Alzheimer's disease. It's not the same as having one of the autosomal dominant genes we call them more the deterministic genes but we know that it increases the risk later in life. Apolipoprotein E or

ApoE for short has three different alleles, we call them. The two alleles seem to be protective, the three is what most people have and has not increased or decreased risk, and the E4 increases risk. Each of us has two copies of ApoE one from our mom and one from our dad and in particular individuals who have two copies of ApoE4 have an increased risk of Alzheimer's disease or sometimes called the homozygote.

There is going to be a trial next year for ApoE4 carriers who are homozygote, have two copies, and that will be run at out of the Alzheimer's Prevention Initiative and I think will start sometime in the middle of 2015. We will absolutely in the meantime if an individual knows that he or she has an ApoE4 allele welcome them into A4 because we expect that we will have actually an over representation of individuals with a family history of Alzheimer's Disease and ApoE is part of that. So we would welcome you to come and screen for our study we won't require people to have an ApoE4 to come in because we know about 40% of Alzheimer's disease patients do not have ApoE4 as their genetic risk factor. So we want to be very broad in the A4 study to have people who both have that risk factor and who don't but we will be looking for people with evidence of amyloid plaque buildup. Did I answer your question?

Question: You did. Thanks for doing the study.

Dr. Reisa Sperling: Oh, thank you so much.

George Vradenburg: I must say, you are so clear in your answers that it is covering a lot of people's questions.

Marilee Hilgendorf of Clinton, Iowa has a question about inclusion criteria or exclusion criteria as well. Marilee?

Question: Oh, yes. I have been taking blood pressure medications since I was 35. I'm now 67. It's Avapro and I also take something for thyroid. Would I be excluded?

Dr. Reisa Sperling: That's a very important question. So we tried to for this A4 study make it as broad as possible to allow people to be on all of the common medications that people take for blood pressure or statins or diabetes or any of these drugs so all of them are allowed in A4.

The one set of drugs that we will not allow in the A4 study are people who are taking drugs for Alzheimer's disease or memory problems. So we will not allow people who are taking Aricept or Razadyne or Namenda/memantine but any other drugs pretty much that people are taking for blood pressure or other things would be allowable.

And I also want to mention that some of information about this and other exclusion or inclusion criteria are on the website as well. So the a4study.org has a little bit more information about that if I don't cover any of those inclusion questions.

Question: Thank you.

George Vradenburg: ... Trisha Prunty I want to bring you online to have this discussion about other studies that might be available. So Trisha would you ask your question.

Question: My mother started her Alzheimer's and my grandmother in their early 60s. My mother is now 74. My sister and I are now starting our 50s. We would like to be included but we don't know how to do

that with what study or where to look. This has definitely impacted our family and we want to be involved.

Dr. Reisa Sperling: Absolutely. So there are a couple of possibilities. And I agree with you. I'm in my 50s as well and I very much want us again to get eventually where we're doing trials in late midlife rather than in individuals who are already entering the stage of risk but for this study, again at age 50 it's very unlikely to have a lot of amyloid plaque buildup.

You may though in your family have some of these genetic influences that may increase the likelihood earlier and there are a couple of possibilities. So one is the Alzheimer's Prevention Registry which is absolutely collecting information from people of all ages and there will be future studies with genetic risk coming and if it's one of these rare genetic forms that might run in your family, the DIAN study, the Dominantly Inherited Alzheimer Network which you can also find online might be helpful as well. We hope as part of the A4 study that we're going to collect information on people who are interested across all ages again working with some these registries so that when we start trials even earlier, I hope maybe aged 55 or 60, we will be able to reach out to you for those studies.

Question: Thank you. Thank you for your work.

Dr. Reisa Sperling: Oh, thank you.

George Vradenburg: I have a short stroke question here but an important one from Lee Craine from Florida. Lee, you're live.

Question: Hi, I just had a question about the length of time required for a visit. I know you said 30 minutes for a PET scan but am I going to be there, do you think an hour or 2 hours?

Dr. Reisa Sperling: Very good question and I will tell you again, there's a little more information on the a4study.org website but we can also have the site detail out. So the 30 minutes really refer to the infusion for getting the study drug once a month. The PET scans actually take more like an hour, an hour and a half. Although part of that is that the dye that we use to see the amyloid gets given first and people have to wait a while before they go into the PET scan or for the imaging so that's why that takes a while. At the very first visit where people are going through all the memory tests and filling out questions about their family history and their medical history and questions, those are the visits that can take a long time. And so the first visit I would say is actually 2 or 3 hours depending on the site and how you're doing in terms of answering these questions. Over all I would say most visits are between 1 and 2 hours with the exception of the infusions which are quite short and that's the 30 minutes.

Question: Oh, good. All right thank you for clearing that up. I appreciate it and thank you so much for the study.

Dr. Reisa Sperling: Oh no, I really appreciate it. And again there is information as I said on the web a4study.org and also this is important for people to ask these questions the consent form that we've made for the study was very long I apologize it's many, many pages. But it has a lot of detail about how much time each of these procedures takes, which visits people need to come to and what order. So you can get that from the site ahead of time and get a chance to think about that, talk about it with your family.

One other important thing I didn't mention is that to be in A4 study, you must have a study partner and the study partner is someone who knows you, they don't have to live with you, but someone who has at least weekly contact with you by phone or e-mail or in person and about once a year, with your permission, we will ask that study partner about how you're doing as well. And this is really important because we need to get a second opinion about how things are going in terms of memory function and so it's important to realize that we do want somebody who's got a study partner who could help us in the fight as well.

George Vradenburg: We have one question that came in before the call that relates to your comment that those who are what we call worried well who have some selective concerns are permitted in the trial but not those who've been diagnosed with Alzheimer's. What about those who've been diagnosed with mild cognitive impairment?

Dr. Reisa Sperling: Yes, I'm very glad you're bringing up that point. So we absolutely are interested in having people who have memory concerns who are still performing normally so this subjective cognitive complaint. If somebody is really already experiencing memory trouble such as they have a diagnosis of mild cognitive impairment unfortunately, they would not be eligible for A4 because one of the A's in that A4 really stands for asymptomatic and at the stage of mild cognitive impairment, someone already has symptoms that can be recognized by a doctor. But there are many other studies that are ongoing at the stage of mild cognitive impairment. So it's little bit of a gray zone there will be people who have memory concerns, are worried about their memory but still performing pretty well, they absolutely will be eligible for A4 but individuals who really have mild cognitive impairment where a doctor is concerned about them as well or they may be on medication they would go to other trials in MCI or early Alzheimer's disease.

George Vradenburg: We have a question here that reflects a number about 3 or 4 other questions. This is from Dirk Walter and Dirk would you please ask your question which does reflect some interest on the part of other people.

Question: Yes, this is Dirk Walter and I've been as a participant in the research in the Phoenix /Scottsdale area with Mayo clinic and Banner

Dr. Reisa Sperling: Yes great.

Question: ... since sort of about 20 years ago and I've been through the various PET scans and so forth, the spinal fluid tap and so forth. Can they use that information as part of the registry or do we go through and just update it again.

Dr. Reisa Sperling: That's an excellent question. First of all, I want to thank you so much for participating in research because as I mentioned that kind of research is what enabled the A4 study to get started. So even if you've had a PET scan or spinal fluid before we will do another PET scan at the beginning of this study and that's important for two reasons. One, is that we're going to look at whether we can decrease the amount of amyloid plaque buildup with this antibody over 3 years and 3 months and therefore it's really important to have a good baseline scan to measure again that. And secondly, it's important because different scans and different types of fluid analysis all have different levels for what they would consider evidence of amyloid plaque buildup or being "amyloid positive" and for this study we want to be very certain that the people who come into the trial to get the antibody have clear evidence of amyloid plaque buildup. So we will do our own scan but that shouldn't interfere with all of the scans

you've had before. I think you would still eligible to come in and get screened and I think there are 2 sites in Phoenix. So look at the website and you can choose on a4study.org which of those sites that you might want to go to.

Question: Okay, thanks very much.

Dr. Reisa Sperling: Thank you.

George Vradenburg: Next question from Carmen Pastor in Arlington, Virginia.

Question: Yes, my name is Carmen Pastor. Can you hear me?

George Vradenburg: Yes.

Question: Hi, I run an organization called Fuerza Contra Alzheimer's or Force Against Alzheimer's. And I've been basically what we do is we create awareness of this horrendous disease within the Hispanic community. I have also been involved with the Alzheimer's Association because of my mother. My mother is in the latter stages of Alzheimer's for about 7 years now. She's been very sick in the past 4 weeks. As a matter of fact she's in been in bed for the past week and a half...

Dr. Reisa Sperling: Sorry.

Question: And my question is, do you have information in Spanish about this study because you know I've been giving workshops in the Arlington, Virginia area also I've been involved in New York specifically in the Bronx, in San Antonio, because the Hispanics you know that there are one and a half times more at risk to develop Alzheimer's. I would love for them to take advantage of this study.

Dr. Reisa Sperling: This is music to my ears because as I mentioned we are really trying to make as a critical part of A4 to have a very ethnically diverse group of participants and we very much especially want to reach out to the Hispanic and Latino community because your community has been under represented in almost all of Alzheimer's research and trials. So yes, there is information in Spanish and I will say we are working very hard and haven't fully finished this to be fair to make all of the testing materials translated into Spanish and validated. So that we're using the appropriate translations and I believe that will be finished by July.

Question: Okay wonderful..

Dr. Reisa Sperling: So at the end of this we can get your name or information and send it out

Question: Absolutely.

Dr. Reisa Sperling: We really need your help...

Question: Absolutely.

Dr. Reisa Sperling: I'm thrilled that you're interested...

Question: Oh, I would definitely. We're here to help it will be wonderful. I have a second question though. Can people with brain tumors, can they participate in this study?

Dr. Reisa Sperling: So it would depend on what kind of brain tumor it is. If it's really a tumor that is within the nerve cells themselves then unfortunately they probably would not be eligible because we wouldn't want to increase their safety risk in any way. If it's a benign tumor, you may have heard like a meningioma...

Question: Meningioma, yeah meningioma are mostly benign.

Dr. Reisa Sperling: Yeah, exactly. So most of meningiomas would be eligible but again it would be on a case by case basis but we're trying to make this as eligible as possible.

Question: Okay, wonderful but I'll be waiting then for... I would love to speak to you certainly more about this subject. Thank you so much.

Dr. Reisa Sperling: Terrific.

George Vradenburg: Thank you for your call. Next question from Patricia Teufel from Pennsylvania. Patricia, would you ask your question?

Question: Hi yes. Good day, thank you very much for the study. If you would be selected since the study runs for so long. Can you change locations where you can receive your infusion?

Dr. Reisa Sperling: Right, that's a very excellent question. So yes we're trying to make that possible. Certainly if you move to a new place you could change to a new location and we're working very hard. I'm in Boston so one of the first things I want to make sure is that we had an opportunity for what we call snowbirds, so people who go to Florida or to California in the winter that they could transfer. So it will be a little tricky but we're trying to make that possible and especially if we know ahead of time and we can make plans to easily transfer people we will do that.

Question: Excellent, thank you very much and thank you for helping us all out here.

Dr. Reisa Sperling: Thank you.

George Vradenburg: Our next question interesting question from Joan Englehautt from, I don't know where you from John, so your question please.

Question: Hi, if it's in the course of the study, the drug showed promise, would those on the placebo be given access to it? Thank you.

Dr. Reisa Sperling: Yeah, right. That's an excellent question. So yes, we very much hope that at the end of the study that we will be able to put everyone in the placebo group onto the active treatment as well, Solanezumab, and that will be particularly important if there's benefit because the FDA has allowed us to move forward with a single outcome of memory but we need long term follow up to show that we really are changing the course of this disease and having functional benefit. So we do anticipate that after the 3 year study we hope everyone will go on drug.

George Vradenburg: Another question here from, let's have Cassandra Brenton from Big Sandy, Texas – attracted in part Cassandra by your town.

Question: Yes, sir. I have a Hispanic background and my father died with Alzheimer's but I'm allergic to contrast dye. Is there any way I could participate in this study?

Dr. Reisa Sperling: Yes, you can because the contrast dye that you have is usually given with a CAT scan. And fortunately that's not at all the kind of dye that are used in PET scans. So they don't have any of the iodine which is what people are usually allergic to and the MRI scans do not have any contrast. So again each site will be different they'll screen you carefully but allergy to CT dyes are not a problem here.

Question: Wonderful okay thank you so much for your study.

Dr. Reisa Sperling: Oh, thank you.

And while we're waiting for the next question, I also just want to thank everyone on the phone for being so involved and active because one of the other things I really hope A4 will do is continue to really start a movement where we are talking about Alzheimer's disease in the same way that we cured cancer or at least have a successful treatment is when people stop being afraid to say the C word and made it part of a conversation and really joined the fight. And one of the great things about the A4 study is I believe now we can try to reach out to people at the point that they can speak for themselves and that they can really join us in this fight. A4 is really kind of a historical moment because it's bringing together governments and advocacy and pharmaceutical companies and academics and most importantly the public to really try to fight this disease in a very active way so if I forget at the end I just want to thank all of you on the phone for all the hard work you're doing and encourage you to locally and nationally to keep this conversation going.

George Vradenburg: So it's a mutual admiration society here.

Question from Mr. Smith, which is a very practical question.

Question: Yes. I'm aware that we will need a study partner and I have spoken a couple of people about potential being the study partner. How much time will be required of the study partner, I know it's annually but how much time will they need to spend?

Dr. Reisa Sperling: Right, that's a very good question. So we're obviously trying to make this at least burdensome as possible. The first visit, especially because we're hoping the study partners would come in with the person at the very first visit so they can understand everything that's involved in the study. So that one would be a couple of hours, but the study partner doesn't even have to stay the whole time. In the subsequent visits, once a year it's about an hour and in fact although this is not ideal but if needed we can do that visit over the phone so we've already have a few people where their study partner might be away or live in another state and we can do some of those questions by phone.

George Vradenburg: That's a really good question. Here's a technical question from Mary Madden. Mary would you ask your question please?

Question: Yes, hello Doctor Sperling

Dr. Reisa Sperling: Hello.

Question:... I will be, I am a participant, I have my first session at Yale in 4 weeks...

Dr. Reisa Sperling: Oh great

Question: ... so I'm really excited about that. You answered a lot of my questions actually. But as a chemistry teacher I'm interested in what will be the source of the Solanezumab for the infusion, like how will you get it?

Dr. Reisa Sperling: Very important question. So it's actually manufactured, so about 10 or 15 years ago chemistry professors like yourself figured out how you can take an antibody and fully make it what we call humanize so that there's no problems with reactions to it and mass produce it in a very careful and sterile way. It is I will say expensive to do that so far but we're able to make a whole lot of antibodies under very careful sterile conditions now and those will actually be shipped to each of the sites for the infusions. This has already been happening in some of the clinical trials that were done in dementia so those processes are well worked out.

And I'm not sure if everyone on the phone knows but we actually did our very first participant infusion in A4 this Monday. That was actually done down in Rhode Island and so we've got that process worked out well and it was a thrilling moment because this gentleman was so brave, brave enough to have his picture taken by Associated Press and it was in about 160 newspapers around the country and he said I want to join the fight here. He's got a brother with Alzheimer's disease and his mother died of Alzheimer's disease and he was willing to say I have amyloid plaque buildup and not only do I want to be in the A4 study, I want to get the word out, so it's really thrilling. But anyway in terms of getting the antibody produced and getting it to sites that's well worked out and I think that will be a terrific chance.

George Vradenburg: Just a couple of more quick questions and then we're going to have to close. But this has been a really quite extraordinary call. Ron Stallings, would you please ask your question.

Question: Yes. I was just wondering if there's going to be any more expansion of sites for the study? Where I'm located the closest place it's either Winston-Salem, North Carolina or Lexington, Kentucky?

Dr. Reisa Sperling: So Winston-Salem, I think actually we already do have a site pretty close. Again you can go on a4study.org to see the map and figure out which is the closest to you. It is possible that we will expand sites and in particular in the South, I would say you know we try to get as good geographic coverage as possible but I think there are part of the south that we don't have perfect coverage. But again we would do whatever possible to try to make you be able to get to sites and I do know that we've got a terrific site at Wake Forest, North Carolina, I don't know if that's even close enough to you, but there's a terrific investigative team there as well.

Question: Thank you very much.

George Vradenburg: We're going to just do two more questions here. Here's a practical question from Caroline Sinclair from Texas.

Question:... I'm just wondering if Doctor Sperling could describe what an infusion is?

Dr. Reisa Sperling: Absolutely. So an infusion means, I don't want to say a tiny needle, but I've had a few of these so I can say that. A needle goes into the vein, for those of you who are needle adverse as I am, it looks like a little what we call a butterfly so it's pretty much like getting your blood taken and the antibody comes through a tubing into fluid and goes into the veins. It actually can be done in about 10 minutes but we do it pretty slowly just to make sure that there are no problems and that's why it takes 30 minutes and then afterwards they put a little band aid on your vein and people can go about their business. This is done very commonly with giving IV medications if you've ever had an infusion for an antibiotic if you were in the hospital if you have to get fluid cause you were dehydrated. It's just like that.

Question: Thank you.

Dr. Reisa Sperling: Sure.

George Vradenburg: One last question and this actually reflects a few questions and this one is from Imogene Treichel in Minnesota. Imogene?

Question: I'm 85 years old. Is the cut off at the beginning of 84 or at the end of 85?

Dr. Reisa Sperling: We will take an 85 year old right now you can sign up and in fact Mayo Clinic in Minneapolis is already enrolling.

Question: I will enroll today.

Dr. Reisa Sperling: ... All right. We love it I've unfortunately had a couple of 87 year old who were already yelling at me, but hurry up and run over.

Question: I will. I'll get on the study site right now. Thank you very much.

Dr. Reisa Sperling: Oh, thank you so much.

George Vradenburg: I want to thank all of you on the phone. There are probably 30 questions that we're unable to get to and it does suggest Doctor Sperling I think we may want to have you back in the fall to give us an update just because there's so many questions and so much interest that it may be worthwhile in a couple of months as we take all the people on this phone call to come on board your trial, to renew and refresh people enthusiasm in a few months.

Dr. Reisa Sperling: That would be terrific, I would love to come back in the fall and again we'll be recruiting for the next year so we'll put updates on the website and I'm happy to come back anytime you'll have me.

George Vradenburg: Thank you. Thank you very much for joining us today, Doctor Sperling and for answering so many questions. We're all pretty excited about your study, your trial, and hope that it proves positive because Solanezumab which was being tested again by Lily and people with mild dementia and now being tested in earlier populations that we could get a demonstration that it could work before symptoms appear… in ways that would really extend the quality of life. It's an extraordinarily powerful concept and a very powerful trial.

Just as a reminder to everyone you can get more information on the website a4study.org. We'll be emailing everyone who signed up for the call today with that information.

For those of you on the phone who would like to be contacted by the A4 study, don't want to to go to the website for some reason, don't have access to the website for some reason, please press 1 now. We will share your contact information with the A4 study investigators who will contact you to answer any additional questions and see if you'd qualify to come in for a screening visit and where the trial site nearest you may be located. So just a reminder to press 1 now and we will reach back out to you.

We are also grateful to the Alzheimer's Drug Discovery Foundation for sponsoring this call so we could share this latest important and valuable Alzheimer's research information with you.

Thank you for participating today in about a week we'll have a copy of the recording and a transcript for you to share with your friends. That will be at the Alzheimer's talk website which is usagainstalzheimersnetwork.org.

I hope you'll be able to join us for the next call. The conversation will be on Tuesday, July 29 at 1:00 PM Eastern with Doctor Bruce Yankner he is a Professor at Harvard Medical School, a colleague of Reisa Sperling, who identified the protein called the REST protein which may protect against Alzheimer's. He will share with us with his exciting research and how this may help us get closer to a treatment or cure.

As always please stay on the line if you'd like to leave us a message with a question or comment. We are particularly interested in how you heard about this call and what you would like to discuss on future calls.

And if you'd like to be contacted by an A4 study personnel at a study site closest to you please press 1 now. Thank you very much for joining us today and one last thank you to Reisa Sperling for what you do and for your time today. We hope you all have a great afternoon.

Dr. Reisa Sperling: Bye-bye. Thank you.

George Vradenburg: Bye.