Alzheimer's Talks Transcript
Women's Unique Risk for Alzheimer's
with Dr. Roberta Diaz Brinton

Thursday, February 12, 2015

Note: This transcript has been edited for content and clarity.

Jill Lesser: Welcome everyone to Alzheimer's Talks, a monthly teleconference series presented by USAgainstAlzheimer's where we bring you leaders working to stop Alzheimer's so that you can learn more about these efforts.

Thank you so much to everyone who has joined us today. My name is Jill Lesser and I'm a board member of USAgainstAlzheimer's and a Founder of the WomenAgainstAlzheimer's Network. We are an innovative, entrepreneurial organization that is dedicated to demanding a solution to this devastating disease. We are driven by the suffering of millions of families pressing for a greater urgency and collaboration from government, industry and the scientific community. We hope to accomplish this through effective leadership, collaborative advocacy and strategic investments. If you have not already done so, I hope you will join us. Together we will beat this disease. Please go to USAgainstAlzheimers.org to sign up. We know we can stop this by 2020 but we can't get there without all of the voices.

Today we have over 1,200 people registered for this call from all 50 states, D.C, Canada, the United Kingdom, and India and another 700 people who were unable to make the call but have signed up to get the recap materials afterwards. We are very excited about this interest.

If you have questions during the call, please press star 3 on your phone. When you press star 3 you'll be placed into a question queue and have your question ready to share briefly with a member of our staff and we'll try to get you live on the air as soon as possible. If you're listening online, you can type your questions in the box and we will get to as many questions as we can. We know there will probably be more questions than we can answer and we hope to communicate with you as we go forward.

So now it is my pleasure to introduce Dr. Howard Fillit, who is joining us today to introduce our guest speaker and is helping us put on this call today. Dr. Fillit is a geriatrician, neuroscientist and a leading expert in Alzheimer's disease research. He is the Founding Executive Director and Chief Science Officer of the Alzheimer's Drug Discovery Foundation. The ADDF's mission is to rapidly accelerate the discovery of drugs to prevent, treat and cure this horrible disease. They have assessed hundreds of suggested therapy ideas to prevent brain aging and dementia and recently built a web-based portal

CognitiveVitality.org to share evaluations of prevention strategies with the public. They have funded lots of key research efforts, including some of the work of our guest researcher. It is my pleasure to introduce Dr. Howard Fillit.

Dr. Howard Fillit: Thank you, Jill. It's a pleasure to be here today and I want to welcome all the listeners on the phone and thank you for your interest in Alzheimer's disease and trying to find a cure.

Today we have the privilege of hearing from Dr. Roberta Diaz Brinton. Dr. Brinton is the Vanderveen Chair in Therapeutic Discovery and Development and Professor of Pharmacology and Pharmaceutical Sciences, Biomedical Engineering and Neurology at the University of Southern California where she directs the Norris Foundation Laboratory for Neuroscience Research. Dr. Brinton has been working on a therapy for Alzheimer's disease called allopregnanolone for many years and is about to enter the clinic and she's going to tell us all about it. Doctor Brinton…

Dr. Roberta Diaz Brinton: Thank you Doctor Fillit, and I want to thank USAgainstAlzheimer's and the Alzheimer's Drug Discovery Foundation for the invitation to share our discoveries with you, and I want to thank all of you for joining us on this call and your interest in Alzheimer's disease. You are those who we devote our life to. We are in a time of great urgency and great promise and I want you to know that you are not alone, you are not forgotten, and that we will not forget you. You are our life's passion and purpose. There is reason to hope, reason to remain optimistic, and reason to fight on. We are making progress and together we will win this battle.

I will start first with sharing with you our research, our discoveries, and our efforts to develop therapeutics to prevent and delay and treat Alzheimer's disease. As many of you know already, the number of persons with Alzheimer's disease is increasing across the globe and women are disproportionately affected by the disease. Interestingly, men also have a risk of the disease and that really shows itself earlier in life, around 65-75, and at the same time women are beginning to increase in their risk as they age past 70.

Our discovery of allopregnanolone, which I will refer to as Allo, really came out of a serendipitous discovery in our laboratory in which we discovered that Allo generated new neurons, new nerve cells, in the brain and that discovery led the Alzheimer's Drug Discovery Foundation and Doctor Fillit to support this research that we developed over the past 10-20 years. That research has now led to funding by the National Institute on Aging for the development of that therapeutic and the clinical trial of that therapeutic.

So what did we discover? We discovered that Allo generates new nerve cells in the brain and that those new nerve cells can restore the memory function in the aging brain and not only was Allo able to restore memory function, it also reduced the pathology of the brain, that of Alzheimer's in the brain - which was actually a very exciting discovery for us. What's also interesting is that Allo is made by everyone, actually it's a natural molecule that's found in everyone, and it's made in especially high levels during pregnancy. That discovery, that knowledge, allowed us to begin our clinical trial treating individuals for 3 months as approved by the FDA. So this trial is now ongoing in Los Angeles through our National Institute on Aging funded Alzheimer's Disease Research Center at USC and I'm joined in that endeavor by my colleagues Dr. Lon Schneider and Dr. Helena Chui.

So to recap, we are developing the first ever regenerative therapeutic for Alzheimer's disease that we anticipate and are very hopeful will delay and prevent the development of Alzheimer's disease and is a strategy for the treatment of Alzheimer's disease. So we will keep you posted on updates on that trial.

Another topic that I wanted to discuss with you is why women's brains are more vulnerable? Why are they at greater risk for developing Alzheimer's disease? The first reason is that on average women live about 4-5 years longer than men. Age remains the greatest risk factor for Alzheimer's disease whether you're a female or a male and it's the question of how we age and how well the brain is aging and we know that the aging brain is a very dynamic brain. We typically think about aging as this linear decline in function but in truth the brain keeps working for you and the body keeps working for you and trying its best to sustain the ability of the brain to function and to function well. So we have really tried to understand how is it the brain is actually working for you and what is it that the brain is doing that both sustains the ability of the brain to remain healthy and to prevent Alzheimer's disease and what is happening in the case of individuals who are at greater risk for developing Alzheimer's disease? That risk actually is the flip side of keeping the brain healthy and keeping the brain healthy in many respects means keeping the brain's energy going. The brain is one of the most energy-demanding organs of the body, if not the most demanding.

So the ability of the brain to continue to generate the energy that it needs to sustain its function is critical. How do you do that? Well one of the ways that you can do that is literally what you feed the brain, and how you exercise the brain, and remembering that the brain is actually part of the body. So what you do to take care of the body will also take care of the brain. There are a number of interventions that have been studied around exercise, around diet, and many of that can be found on the Alzheimer's Drug Discovery Foundation website that was mentioned earlier. So for those of you who are working hard to prevent Alzheimer's disease, or suffering the early signs of the disease, or a loved one taking care of that person, the challenges obviously are many, but there are strategies, there are interventions that you can do now to promote the health of your brain.

One of them is again determining and making choices about what you feed the brain. There's a fair amount of information now, again that you can find on the Alzheimer's Drug Discovery Foundation page and on the National Institute on Aging website. Essentially lowering the amount of sugar that you ingest is key and the amount of exercise that you give your body is key. You have to remember that the body was evolved as a moving body, that sitting for long periods of time like we do frequently in our daily lives is actually not the way the body was designed, the body was designed to move and some of that movement can be walking and walking briskly, some of that movement can be exercising aerobically but the key message here is to move the body and to move it frequently throughout the day. The other is again coming back to what you eat and how well you maintain your diet and to reduce the amount of sugar that is consumed. Because the body likes to store sugar in the way of fat and that fat ultimately works against you. It worked for you if you were going to starve but it works against you if you continue to increase the amount of fat that is stored in the body. So understanding and being committed to what you feed yourself is actually feeding the brain as well.

So what can we do for you, and what can we gain from this partnership? Because while we develop therapeutics to prevent, delay, and cure the disease we are actually at that point where we need you to be part of this endeavor. Many of us have been conducting research now for several decades trying to

understand why the brain develops Alzheimer's disease and how can we intervene with therapeutics to prevent and delay and treat the disease and now is when we need you, we are ready. There are many therapeutics currently being tested in clinical trials and we also need to know about you and how you differ from other people with the disease or other people who are suffering the early stages and risk factors for the disease. Part of that is letting us know your data. What is it about you that makes you special? Some of that can be achieved by readily available wearable technologies that are now available for determining how much you moved and what you eat and when you're eating and when you're sleeping and those are available now globally to provide that kind of information to you which then can ultimately provide be provided to us. So that also comes back to giving researchers the opportunity to learn more from you by having access to your data, to the data / the information that you're collecting on you both personally as well as when you see your physician. So ask your physician if they are making your data available to people who are researching Alzheimer's disease and how that might help us in this struggle to cure the disease.

I think it's important for everyone to be aware of the changes that the brain undergoes during aging. It is important for you to be conscious of, those early points, because it is the early stage of disease development that is the critical point to intervene. Many of you have already experienced that, many of you have already seen the changes in your loved ones, and so the earlier we can intervene the better the chance of delaying or preventing the disease.

Lastly, I want to remind you that you are not alone, that you are not forgotten, and that we are here together and that we are ready with therapeutics to prevent and delay Alzheimer's disease and we need to test those therapeutics in partnership with you.

Dr. Howard Fillit: Thank you, Robbie. I wondered if you could talk about the possible cognitive changes that occur with menopause and your view about menopause as a risk factor in women for Alzheimer's disease?

Dr. Roberta Diaz Brinton: The menopausal transition in the female brain turns out to be an energy transition in the brain. It’s a transition that affects the ability of the brain to generate sufficient energy. Now that’s not true in all women but it is true in some women. Women can experience changes in cognitive function and neurological function during the perimenopause that include hot flashes, insomnia and difficulty in sleeping, difficulty in memory function and some women will experience depression. For some women they will experience these symptoms when they go through the menopausal transition and then once they transition through menopause those symptoms will disappear. For other women, however, those symptoms do not disappear and those symptoms remain throughout the postmenopausal years. Changes in memory function that really interfere with your ability to function well throughout the day and changes in the ability to sustain sleep during the night and others for those who experience depression, are symptoms that if they linger on after the menopause is reason for concern.

Dr. Howard Fillit: I understand that at a time in menopause, estrogen drops significantly in the blood and one of the causes of menopause is that women basically stop making estrogen. So what are the neurobiological effects do you think of that on the brain that are causing these clinical symptoms and what are the long term effects of that estrogen deprivation do you think on the brain?

Dr. Roberta Diaz Brinton: Estrogen regulates the ability of the brain to generate energy and that's actually probably one of its primary roles in the brain. Because of that, estrogen will also regulate and promote memory function. Estrogen if started at the right time can reverse menopausal associated depression the hot flashes that are apparent during the menopause and reverse some of the memory deficits that can be apparent in the menopause. The key message though is that the time of intervention is critical. Intervening early in this process of the menopause is critical. Once menopause has occurred the brain has changed. So if we are going to intervene with estrogen or hormone therapy there are two issues to be very conscious of: one is what is the time of the intervening? Intervening early is beneficial for many women, intervening after the menopause, after the brain has changed is not beneficial. So there's timing and there's also the case of what's actually in the hormone therapy? We know that there are molecules that can be in a hormone therapy that are not beneficial for the brain and that literature and those scientific studies are now well known in the field.

Dr. Howard Fillit: So should all women at the time of menopause go on estrogen replacement or hormone replacement therapy?

Dr. Roberta Diaz Brinton: There are some women who transition through the menopause and have no symptoms. Those women are not candidates for hormone therapy or estrogen therapy. Women who have had their ovaries removed before the menopause are good candidates for estrogen therapy. Women who are experiencing neurological symptoms like insomnia, like memory deficits, like hot flashes, like depression are very likely to be responsive to estrogen therapy.

Dr. Howard Fillit: And you've done some research with plant derived estrogens, these are compounds or molecules that kind of replace the estrogen but presumably don't have the side effects particularly some of the cancer side effects of estrogen on the breast and the uterus. Could you tell us something about the selective estrogen receptor modulators?

Dr. Roberta Diaz Brinton: Yes, thank you. We have developed a formulation, it's a natural molecule formulation, we term PhytoSERMs. We developed PhytoSERMs because we knew that women elect to not receive hormone therapy because of the potential risks but we knew that the brain would benefit from estrogen. So we developed a natural source formulation of natural molecules that will have the effect of estrogen in the brain but not in the breast and not in the uterus. Moreover, our goal is to have that available to women over the counter. There are many over the counter products that are available to women that either don't work or actually are harmful and our goal was to reach women as soon as possible with the best natural approach.

Dr. Howard Fillit: So when can we hope to go to a store and buy that?

Dr. Roberta Diaz Brinton: We just finished the clinical trial and we are analyzing that data now and if the data show that it was beneficial we anticipate within 6 months, 6 to 9 months to have that available.

Dr. Howard Fillit: So you're basically saying that gonadal hormones like estrogen are critically important for brain development, for brain function. What about men? What about testosterone in men does that play a role in brain development or in how men think or in old age when men get memory problems?

Dr. Roberta Diaz Brinton: This is an interesting question, there is some evidence to suggest that testosterone can be beneficial in men as estrogen has been beneficial in women. An interesting little

known scientific fact is that men convert testosterone to estrogen in their brain and I'm not suggesting that men take estrogen, I'm not suggesting that, but testosterone being converted in the brain to estrogen is probably one of its benefits. But like with estrogen, testosterone therapy is time-limited in men and it comes with risk factors. So it's an important area to pursue but it's also been relatively untested. What was interesting to us is that this molecule Allo that was supported by early funding by ADDF is actually very effective in both males and females. So we are testing this now in both men and women.

Dr. Howard Fillit: So just to say that a lot of men do develop low testosterone levels and it's important for a physician to evaluate men who have low libido and so on who might have low testosterone who could get testosterone replacement but most men shouldn't be taking testosterone therapy unless they have hypogonadism.

How is Allo related to estrogen and testosterone, is it a metabolite? You said we make it naturally, I wondered if it's in the pathway of this gonadal hormones and somehow.

Dr. Roberta Diaz Brinton: Right. Yes allopregnanolone is a metabolite, it's a daughter, if you will, of progesterone. In the pathway of steroid synthesis, progesterone is one of the early steroids from which allopregnanolone is derived.

Jill Lesser: Howard, I do want to remind everyone that if you want to call in a question, please just press star 3.

And then I want to ask a question, which is in reference to some of this therapy from a practical standpoint - obviously women are thinking about whether to engage in hormone therapy primarily as it relates to their menopausal symptoms and I wonder whether there is a consideration of thinking about guidelines for estrogen therapy or hormonal therapy really just for brain energy and brain function because I think there are many of us who do not get menopausal symptoms until well into menopause and may not actually seek out some of this replacement therapy until in your research from a brain standpoint it might not have as beneficial an effect as it would if it were started earlier in a pre-symptomatic way.

Dr. Roberta Diaz Brinton: I would say that estrogen therapy initiated when there are symptoms can be beneficial. It's when the women have been treated in their 60's and older that it is not beneficial, when they are started at that age. In women who are going through the perimenopause and in the early stage of menopause when they've stopped cycling that has been found to be a very effective time. But once women have been menopausal and they are post-menopausal 5, 10, 15 years that's just not the right time.

Jill Lesser: Right, but as a woman who's thinking about the risk of Alzheimer's versus the annoyance, if you will, of menopausal symptoms I think most of us are wondering whether to seek treatment for those symptoms when those symptoms are distressing but if we are generally thinking about our brain health should we be in our 40's when we know our hormone levels have decreased but our symptoms may not be debilitating begin to think about this therapy really not so much for the symptoms but for our brain health?

Dr. Roberta Diaz Brinton: I think Dr. Fillit and I both agree that would be a bit premature. What was interesting to me in our clinical trial is women know very clearly when they are not functioning well.

They are very conscious that the changes particularly in cognitive function are not annoyances they are in fact inferring with their capacity to be a professional to go through their daily lives. I think that's the time when women are most appropriate.

Dr. Howard Fillit: Well let me just say, the menopause is really characterized as you said by a loss of periodic cycling and I think we should be clear that just because someone's having psychological symptoms like depression or memory problems that's not an indication in a 45 year old woman to take estrogen, right? It has to be associated with menopausal symptoms such as an irregular cycling. I suppose one could go to one's gynecologist and get a better evaluation but we wouldn't want to have women who are pre-menopausal taking excess estrogen, or extra estrogen, I think that would be not a good thing, right?

Dr. Roberta Diaz Brinton: Yes, that's correct. There really has to be the transition into the perimenopause and menopause...

Dr. Howard Fillit: Which is characterized by changes in the menstrual cycle?

Dr. Roberta Diaz Brinton: Yes.

Dr. Howard Fillit: Okay.

Jill Lesser: We have several questions that have come in from our online queue, one of which may be on the minds of a number of women. It comes from a woman named Lois who's talking about having had uterine cancer and a hysterectomy and also a family history of Alzheimer's disease and I think is obviously concerned about how hormone therapy would impact a case like hers.

Dr. Howard Fillit: Right. Well I would just have to say that if someone has had a hysterectomy then that obviously eliminates the risk of uterine cancer but it doesn't eliminate an increased possible risk of breast cancer and I think in someone who has had cancer, as a clinician, I would be very reluctant to give someone estrogen for the purposes of brain health at this time. I think that the potential side effects or risks would outweigh the benefit at this point, we are just not clear about the long term benefits of estrogen on the prevention of Alzheimer's disease quite yet. Would you agree with that Robbie? I think it's not clear. And it goes to the question also which we haven't discussed, if a woman starts estrogen at the perimenopausal period for symptoms like hot flashes for example, how long should she stay on it right? That's another question.

Dr. Roberta Diaz Brinton: I think one of the reasons why maybe the science is not as clear as we would like is that for many women the use of hormone therapy is probably not required, that it's really a subset of women who clearly have symptoms, and particularly multiple symptoms, that are associated with an increased risk of Alzheimer's that if women have memory problems, they have insomnia, and they have depression. Those are all symptoms that we know are associated with risk of developing Alzheimer's disease that those women are probably the best candidates for estrogen therapy. Women who have very mild hot flashes are not probably going to have any benefit for estrogen therapy.

Jill Lesser: Okay, thank you very much.

So we have a question from Inez Schwartz in Washington, I hope I pronounced your name correctly, I'm going to bring Inez live and you can ask your question of Doctor Brinton.

Dr. Roberta Diaz Brinton: Hi Inez.

Question: Hello. My question is, in your research, were you dealing with the bioidentical hormone therapy or was this the normal chemical substitutes for hormones?

Dr. Roberta Diaz Brinton: Thank you, Inez, that's a terrific question. The answer is we have studied the effect of what is the endogenous estrogen, 17-beta estradiol, the one that all women make naturally. Through our research and that of many scientists, we have discovered estrogen actions in the brain and then we developed the formulation of natural molecules of plant based molecules that will have the same effect of the endogenous estrogen in the brain. Now what about the issue of bioidentical? My concern about bioidentical is really one of quality of product and the quantity, if you will. Oftentimes the idea that more is better is initiated in these bioidentical therapies and I will tell you that more is not better, that more actually can lead to the opposite effect than what we are actually hoping to achieve in the brain. So bioidenticals are an area of a disturbing lack of regulation and that's what concerns me, that you can't really be sure that you're getting the same quality and the same quantity every time. What also concerns me is the quality control for the synthesis of these molecules and what's actually in the product, that's a big concern. So does that answer your question Inez?

Question: It does. The bioidentical therapy that I am aware of is followed by testing just to verify that the correct dosages have been attained.

Dr. Roberta Diaz Brinton: That may be true, it's not uniform across the industry.

Jill Lesser: Okay, thank you so much.

We also have a question from Steven Hill from Delaware. I'm going to bring Steven live and go ahead and ask your question please.

Question: Hi. I wanted to know when we're referring to Alzheimer's and the diminishing cognition, are we also referring to dementia and the diminished cognition when you're talking about what you are pursuing as far as the trials with Allo because like someone with Alzheimer's may have dementia but someone with dementia may not have Alzheimer's and that's my concern. And the other part is the trials for the Allo, how far along with the Alzheimer's is too long in order to see some positive results from what you've seen from your trials using the Allo?

Dr. Roberta Diaz Brinton: So just to be clear we are currently conducting the trial. What we are targeting are individuals with mild cognitive impairment and early Alzheimer's disease because we think that has the best probability of the brain regenerating itself in those individuals. So those are the therapeutic targets that we are looking at, populations that we are looking at specifically with Allo. I think for later stage Alzheimer's disease there will likely be different approaches but at this point we are starting out in the early phases and then we will determine whether we can go into later stage.

Dr. Howard Fillit: Just a point of clarification, dementia has many different causes and it's a word we use to describe a patient who has cognitive impairment and various other disabilities related to their illness. They can have memory problems and language problems and problems in abstract thinking and so on and that's the word dementia that we used to describe those people. Alzheimer's disease is the most common cause of dementia and about 70% of people who have dementia have Alzheimer's disease in their brain but there are a number of other causes of dementia such as vascular disease, small strokes,

and some other more rare forms. So what Robbie is particularly interested in is dementia from the Alzheimer's type.

Jill Lesser: So we have a question from Susan Bolotin from online and she writes, the doctors have been discussing the benefits of estrogen therapy on both menopausal symptoms and brain health but I'm curious about progesterone. As a woman who has recently started menopause as well as bioidentical progesterone, I'm curious about the relationship between progesterone and brain health.

Dr. Roberta Diaz Brinton: I mentioned earlier, progesterone generates allopregnanolone. Part of what we don't yet know is how well progesterone given orally, or applied on the skin, can actually generate allopregnanolone. So the idea behind that particular therapy is that if you give progesterone, you will make estrogen eventually and part of that assumption is because progesterone is the early steroid from which testosterone and then estrogen is derived. So the idea is that if you give people progesterone that you will ultimately make estrogen, and that is actually not well substantiated in this population of people and part of it is that yes that might work in the brain but once you give that orally or on the skin does it still work that way? And I think the evidence is pretty clear that it's unlikely.

Dr. Howard Fillit: Right. So the progesterone is given to help the endometrium to shed, right it's under the influence of estrogen but in the brain we don't really know the effects. I think that by giving the progesterone we induce the cycling, isn't that how it works?

Dr. Roberta Diaz Brinton: By giving progesterone, again from a therapeutic perspective, in the brain there are cells that will convert progesterone ultimately to estrogen, not all cells, but again the idea that you can give progesterone as an alternative to estrogen just has not been well studied. It's based on some chemistry to be sure but the therapeutic benefit has not been well studied.

Dr. Howard Fillit: and the side effects are more…

Dr. Roberta Diaz Brinton: Yes. Interestingly breast cancer is actually more associated with the progesterone part of, or what's called the progestin, than it is with estrogen. There are some studies that show that there's no increased risk of breast cancer with estrogen. It's only when the estrogen has been combined with a progestin.

Jill Lesser: So we have been talking a lot about women, for obvious reasons. I wanted to ask a question from an online questioner Diane Severine who asked the following: My question has to do with my husband's already progressed Alzheimer's. When Allo is approved, do you expect it to be available right away for someone in the middle stages of Alzheimer's? My husband was diagnosed with early-onset almost 5 years ago.

Dr. Roberta Diaz Brinton: Once it is approved, it will be available to clinicians and we will have established whether this will be beneficial to people in the mid to late stages of the disease. We are obviously very hopeful that would be our goal. I couldn't say whether it's actually going to work out that way but again that's why we need people to participate in clinical trials, to be engaged in partnership with us as we move forward on therapeutic development.

Jill Lesser: I know there's information on the web but it might be helpful for you to just recap the ideal study participant that you're looking for, in terms of age in particular.

Dr. Roberta Diaz Brinton: We're enrolling individuals who are 55 years or older and who have been diagnosed with mild cognitive impairment and early Alzheimer's disease. It's a placebo-control trial in which we will be testing three doses of Allo and determining what dose is the best dose to move forward with in a larger trial. For this early trial we're limiting the participants to Los Angeles so that we can rapidly conduct the trial and move forward to the phase-two clinical trial, which will be countrywide to a certain extent.

I know that there was an individual who asked the question about bringing clinical trials to more rural zones in the United States and the reason why it's difficult to do clinical trials in rural regions is because we need a great number of people in trials and it's difficult to bring all of the necessary infrastructure, if you will, out to those rural zones but the National Institute on Aging has a distribution of Alzheimer's centers across the country and you can find the map of where those Alzheimer's research centers are on their website, and this particular person was in Georgia and there's an Alzheimer's center in Kentucky and in Florida. So there are places that are not exactly in Georgia, but they're close.

Jill Lesser: Okay, we have a somewhat related question, I think, from Sharon Hambro in New Jersey. Sharon we can bring you live and you can ask a question to Doctor Brinton.

Dr. Roberta Diaz Brinton: Hi Sharon.

Question: Can you hear me, okay?

Dr. Roberta Diaz Brinton: I can.

Question: Awesome. So my question pertains to clinical trials. First of all, I appreciate you having this conference. Second of all, I believe in my heart that the number of Alzheimer's patients is highly underestimated because I know people in my area alone, who haven't even seen physicians yet, who have Alzheimer's disease. Therefore I'm just wondering, we have so many people suffering, why are there not more clinical trials? People are desperate in all stages of this disease.

Dr. Roberta Diaz Brinton: Thank you Sharon for your heartfelt care for those individuals. There are 1,500 clinical trials that are ongoing or being conducted. One of the reasons that I am hopeful is that there are many different therapeutics that are now being tested. Our therapeutic approach for both Allopregnanolone and PhytoSERMs were really born 20 years ago, at least 20 years ago, and it takes that long to understand why the brain is developing Alzheimer's disease and then to translate those discoveries into therapeutics and it's now that 20 to 30 years of painstaking work is coming to fruition. I am very confident that there will be therapeutics to prevent, and delay, and treat Alzheimer's disease, they are in the pipeline, they are coming forward. Scientists and clinicians, we need you. We have been your silent partner for decades and as I tell the people who come into my clinical trials, I've been working for you for a quarter of a century and now we're ready for you. We are ready. There are many scientists like me who have been doing this work and bringing forward their discoveries into clinical trials. Now one of the important components of all of that is that what we now know is as you said, there are many people who are suffering silently and just as there are many people with Alzheimer's disease it turns out there are many ways to develop the disease that not one-size therapeutic will fit all. And that's what's so exciting about this time and this place is that there are many different therapeutics being developed and now we need to test them. It's one thing to test them in the lab and you know we have worked very hard to make certain that whatever we do in the lab is actually relevant to you and

now we need you. So thank you for being the advocate for those individuals with Alzheimer's who have yet to come to our attention and now we need you to be the advocate, to be the one that says there is hope, there are clinical trials and especially around these large urban centers, I know New Jersey is close to both Philadelphia and to New York. There are many clinical trials in those regions. Thank you.

Jill Lesser: Yes thank you so much Sharon for your question. For everyone on the phone, we will be providing some additional information on access to clinical trials so that you have that. Doctor Brinton has mentioned several great resources, which we will compile for you. And I just want to, at this moment, also reemphasize the importance of reaching into communities where it is sometimes difficult to acknowledge a disease like this where there are historic cultural stigmas, if you will, and we are working at USAgainstAlzheimer's very hard by putting together for example our African-American network and our network of Latinos specifically to address some of those cultural barriers to not only acknowledging Alzheimer's in their loved ones but also encouraging that they volunteer for the kinds of trials that Doctor Brinton is talking about and certainly that goes for the women's network, which I lead, which covers advocating on behalf of women from across a whole host of cultural and socio-economic backgrounds. So your question and the answer that Doctor Brinton gave is important on so many levels.

So we have time for one more question. I'd like to see if Cathy Pendergrass from California would like to ask her question and we'll bring you live right now.

Dr. Roberta Diaz Brinton: Hi Cathy.

Question: Oh hi. I'm a 68 year old woman and at 39 I had a hysterectomy and 2 years later I had my ovaries removed. At that time, I was placed on hormone replacement therapy and I was on that for like 2 years and then I stopped taking it because I didn't think I needed it and I still now have hot flashes at 68 and I have been diagnosed with early onset Alzheimer's and I was wondering if there's any correlation with all of this, and I do suffer from depression.

Dr. Roberta Diaz Brinton: Well I think you're making some very good associations there and yes there is a relationship, this is work that was done by Walter Rocca and colleagues from Mayo Clinic that show that women like you who had a hysterectomy and then the ovaries removed prior to natural menopause do have a risk and that the development of depression is also of concern. What I will say is that, I'm happy you're still having hot flashes.

Question: Oh really okay. I was wondering at 68 should I still have hot flashes?

Dr. Roberta Diaz Brinton: Because hot flashes tell us that the brain could be still responsive. Could be, I'm not saying is, but could still be responsive to intervention with estrogen. That's not typical, it's not what is in all of the scientific literature, but a woman who is still having hot flashes that is associated with a loss of estrogen may in fact be a candidate for estrogen therapy not of estrogen with progesterone, not hormone therapy but estrogen therapy. So you might want to talk to your doctor about that.

Question: Just estrogen.

Dr. Roberta Diaz Brinton: Yes.

Question: And since I have the onset of mild dementia or Alzheimer's, it would not hurt my brain?

Dr. Roberta Diaz Brinton: I think this is really where, talking to your physician and perhaps doing a short course of estrogen therapy and seeing how it worked for you and whether it had a beneficial effect may in fact be an avenue to pursue. That turned out to be an avenue that Doctor Howard Fillit pursued in his first clinical trial of estrogen and Alzheimer's disease. So there are some women, not many, but some women who remain responsive.

Question: Oh okay, and one other thing about sugar, do you mean sugar that you add or like fruit sugar? Will that sugar still hurt your brain?

Dr. Roberta Diaz Brinton: So I'm glad you asked that question. Essentially one of the real concerns that I have is the amount of invisible sugar that is in the diet and I think we really need to be very conscious about when we're eating something and when we're drinking something, how many grams of sugar are in that food or that beverage and the other is if you're going to eat fruit based sugar, actually have the fruit because the fruit actually helps with the metabolism of the glucose.

Question: Okay.

Dr. Roberta Diaz Brinton: Thank you.

Question: Thank you very much.

Jill Lesser: Thank you so much and I apologize for the background noise. We have unfortunately, because this has been such an informative conversation, come to the end of our hour. So I really want to thank Doctor Brinton. I want to thank Doctor Fillit for joining us today and for ADDF for making this call possible and for making so many critical investments in the drug development process.

I know there are lots of questions that we have not been able to get to today and I hope that in the follow-up to this call we'll be able to answer some of those. We do these calls regularly, on a monthly basis. Our next call will be Thursday, March 12th from 1:00 to 2:00 Eastern Time. We will focus on a clinical trial that is just beginning to study the effectiveness of coconut oil as a treatment for Alzheimer's, which is underway at the University of South Florida, Byrd Alzheimer's Institute.

To wrap up this call, once again thank you so much Doctor Brinton. I think all of us who tuned in today and certainly those of us who welcomed you as a founder of WomenAgainstAlzheimer's are really, really grateful for your passion and commitment to finding a cure for this disease and hope that your research garners conclusions and results that we all hope. So thank you very much.

Dr. Roberta Diaz Brinton: Well thank you so much. Thank you, and thanks to everyone for joining. Together we will win this battle. Thank you.

Jill Lesser: Thank you so much.