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Subject: Caregiver Thought Leader Interview: Dr. Samuel Henderson

EDITOR'S PEN

Gary Barg, Editor-in-Chief

Caregiver Thought Leader Interview: Dr. Samuel Henderson

Vice President, Research and Development, Accera, Inc.

Dr. Henderson has more than 15 years of experience in neurodegenerative disease research. Dr. Henderson received his PhD in molecular genetics and cell biology from the University of Chicago.

Gary Barg: Why has it been so difficult to have successful clinical trial outcomes for Alzheimer's disease?

Dr. Samuel Henderson: That's a good question. It has been 12 years since any new compounds have been advanced for Alzheimer's disease. I think that reflects our fundamental misunderstanding of the disease. As you know, the primary hypothesis for Alzheimer's disease is what is called an amyloid cascade hypothesis. Unfortunately, all of the large phase, (what are called Phase Three efficacy trials), have failed. I think the field is really struggling now with what really does cause Alzheimer's disease and how we can tackle that best.

Gary Barg: So many times, people are held back from investigating clinical trials due to the myths, misunderstanding and misinformation surrounding participation. What would you say are the top five trial myths?

Dr. Samuel Henderson: The first one is that people believe that they do not need to come in and participate in the clinic because lots of other people will do

it. Clearly, that is not the case at all.

The second myth would be that people think the disease has advanced too far and nothing is going to work, so why bother? There are, in fact, trials running for all stages of the disease right now. There is hope for people with mild to moderate to severe Alzheimer's disease. That should not at all be a reason why you do not participate in a trial.

The third myth is that clinical trials are dangerous; you are going to be exposed to some dangerous compound that may have long-term effects on your wellbeing. While there are inherent risks in clinical trials because you are doing an investigation, all of these investigational new drugs have to go through a rigorous testing before they can enter the clinic. This is a big part of the job of the FDA. For any new investigational drug, you have to present the FDA with all of your safety data that you have accumulated over the years from animal, in-vitro, carcinogenicity, toxicology studies. Lots and lots of studies. It really is a pretty safe process to go into a clinical trial. You also get excellent medical care when you are in clinical trial because they do not require health insurance.

Myth number four, is that you will lose your primary care physician. This is not the case. Typically, you are going to that specific c

linical trial site just for that study. You also get the added benefit of usually working with a subject matter expert. In our case, with Alzheimer's disease, you are working with a physician who has dealt with Alzheimer's disease for 10 or 20 years. Almost every study will encourage you to keep seeing your normal primary care physician, get medical advice from him or her, and maintain your normal schedule with your doctor.

The Fifth Myth is that you might get a placebo. Once you complete what is called a double blind phase of the study, you can go into the open label phase where everybody gets the investigational drug. You get that for free for whatever period of time the sponsor decides that you will need it. In our case, you get it for six months, which is typical in the industry.

Gary Barg: You have a personal connection to this disease because your mother was living with Alzheimer's. Has that affected or influenced your work?

Dr. Samuel Henderson: Oh yeah, tremendously. That is what prompted me to work on Alzheimer's disease. It started at a Cracker Barrel Restaurant when we went to visit my mom for the holidays. She could not remember things. She would repeat questions. She forgot her purse. In a subsequent medical follow-up, she got the diagnosis of mild Alzheimer's disease. Previously I had been working on the genetics of aging. Once I saw this personal connection, I

became invested in trying to find new treatments and therapies for this disease. I shifted my research focus exclusively to Alzheimer's disease.

Gary Barg: In fact, can we talk about glucose hypermetabolism and ketosis, the clinical trial work you are involved with?

Dr. Samuel Henderson: After my mom's diagnosis, I began to pour over the literature. I came across a whole series of papers that demonstrated in the brains of an Alzheimer's patient, they begin to lose the ability to metabolize glucose. It is what you get when you eat any sort of carbohydrate. Your body will convert that to glucose, which turns out to be the primary fuel for your brain. Your brain runs almost exclusively on sugar all the time. Then with Alzheimer's disease they can see these patterns of declines in the ability of the brain's ability to utilize glucose. Back then, the primary thinking was that the brain is slowly disappearing therefore does not use glucose. I thought this was another way we can tackle the disease. That is where I came up with the hypothesis that if the brain of an Alzheimer's patient is having difficulty metabolizing glucose, is there a different fuel that we can give them that they can use in place of glucose? It turns out that that alternative fuel are what are called ketone bodies.

Ketone bodies are acids that your body produces when it is running low on glucose. For example, when you wake up in the morning, your body is starting to tap into your fat reserves to make ketone bodies because you have not eaten overnight and your blood glucose is a little low. Anyone who has ever done an Atkin's diet knows this very well because that is one of the signs that you are in what they call fat burning mode. In Atkin's diet, you eat very few carbohydrates, which really stimulates the production of ketone bodies.

Gary Barg: What have you learned?

Dr. Samuel Henderson: It turns out there are pretty easy ways to induce ketosis without having people fast or greatly restrict their carbohydrate and protein intake. You can do that by administration of specialized fats called medium chain triglycerides or MCTs. In the first study, we wanted to know if we induced a mild state of ketosis in someone with mild to moderate Alzheimer's disease, would this improve their cognitive performance. We published back in 2004 and were able to demonstrate the proof of concept. When we induced mild state of ketosis in these patients, we did improve their cognition very rapidly within 90 minutes of administration.

Gary Barg: What is the current process of the trial?

Dr. Samuel Henderson: Now, we are running our Nourish Alzheimer's disease trial, or Nourish AD. We have about 66 sites in the U.S. and are enrolling mild to moderate Alzheimer disease patients. These are patients who have some memory complains and even the moderate are pretty impaired in their memory and their activities of daily living.

Gary Barg: How do we find out more about the study?

Dr. Samuel Henderson: The easiest way is to go to our study website. That is www.ad-trial.com. There is also a phone number to call, 1-866-405-1998. They will refer you to someone who can help you find out information about the trial.

Gary Barg: What would the most important piece of advice you would like to share with Alzheimer's caregivers?

Dr. Samuel Henderson: My over-reaching message is that people need to get involved. The funding is low for Alzheimer's disease and clinical trials are having difficulty recruiting people. I know from personal experience, it is very difficult to be a caregiver for someone with Alzheimer's disease and that it takes a lot of time and effort. There is hope on the horizon, but we all need to pitch in together. Sign up for a clinical trial. It is going to help everybody in the long run for us to beat this disease.

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