Q: My father and grandfather both died from ALS. I also have ALS but SOD1 did not show up in the DNA test. Why was this?

A: Only 10% of families with ALS carry the SOD1 gene mutation. There are several other genes that cause the familial form (FUS, C9orf72, TDP43, for example). These other gene mutations were only discovered recently so may not have been available for testing for your father or grandfather. One option is for you to get tested for these other genes. Your ALS physician could arrange that.

Q: How do I get invited to the meeting at the FDA with NEALS and ALSA? I am a PALS and live in the Washington DC area.

A: Once we know date of meeting, we will announce on our website and ask for volunteers. We will also be looking for participants for our third annual PALS Clinical Research Learning Institute, which meets in fall.

Q: We need to let patients have a much bigger say in the risk/benefit decision making process for treatments - do you see that happening soon?

A: Yes I do.

Q: I would like to participate in the Tiramisiv trial but have been told that I'd have to stop taking Dexpramipexole to participate in this study and possibly get a placebo - seems really unfair and it seems this could be a good way to test a cocktail - comment?

A: At moment, we don't know if dexpramipexole works in people with ALS. Dexpramipexole is considered experimental. The risks of combining with Tiramisiv are also unknown. The results will be available soon though for the dexpramipexole phase III study. If dexpramipexole is efficacious and becomes standard of care, people will be able to take it while participating in other studies (similar to what happens now with riluzole).

Q: I find that the neurologists and FDA are very willing to endorse EAP's for ALS but it seems that the companies just will not join in -- what are the biggest issues for the companies?

A: I have not worked at a company so may not be best person to answer this question. My thoughts are that there are a few factors that drive this. One is that they don't know if a drug works, and fastest way to determine that and get drug to market is through trials. The industry has a board and share holders that they are responsible to and they need to make business decisions that ensure safest and
fastest way to determine if their therapy works. This is through a well designed trial. There are some FDA guidelines on EAP too; in particular that if EAP would interfere with phase III trial and not allow determination of safety and efficacy of a drug, they would not allow. Discussion of EAP and how to move therapy development process much faster are topics we plan to discuss at a brainstorming session with FDA, industry, clinicians, researchers and PALS and their families.

Q: What can you share about Edaravone in Japan?

A: There is an ongoing phase III trial. I have not seen the results. We will try to learn if there is more information available.

Q: Given your experience with Dexprimipexazole and the associated study, have you heard anything anecdotally or not, regarding its potential for success trials?

A: I have not heard anything either way. The study is blinded, meaning the participants, doctors and company don't know who is on treatment and who is not.

Q: Can some of these drugs be useful to PLS?

A: I hope so. There is big need for research in PLS and related upper motor neuron disorders to better understand if the biology- the processes causing the disease are similar or not to ALS. If they are similar, then the drugs developed for ALS would be also useful in PLS. NEALS has formed a PLS network to develop treatments for people with ALS. We are applying now for our first trial and also for biomarker studies in PLS. WE hope to receive funding for these initiatives and really launch a therapeutic effort for PLS.

Q: There are any T-cell vaccination ongoing studies?

A: There are multiple efforts to develop and test therapies that target T Cells, though not a specific vaccine approach. These include fingolimod.

Q: Is IGF-1 research still ongoing?

A: There are ongoing investigations in the laboratory still on IGF-1, but no clinical trials at this point.

Q: Is the NurOwn trail ever going to be in EU?

A: I do not know the answer to this question, but we will ask Brainstorm.

Q: How important is riluzole in ALS if only it gives a very minimal of life extension?

A: It is the first crack at this illness. Hopefully other drugs in combination with riluzole will have larger effects.
Q: I watched a segment on AKG do you have any thoughts about using this?

A: There isn't a lot of data yet on AKG though I am encouraged that there are investigators who will start to test this in laboratory models and see if there is a rationale to develop this for ALS.

Q: Do you believe that the cure or treatment lies in stem cells or meds?

A: I believe we may need both; and that both approaches are important. The stem cell field is still very new; and a lot is unknown about which stem cells, how to deliver and use them as therapeutics. Knowledge on small molecules or other drugs is much greater and may be closer to having impact in ALS. It is great though that both approaches are taken in ALS.

Q: Are you aware of any encouraging Stem cell studies and what are the near term plans in this area?

A: Neuralstem and NurOWN are in people with ALS. There is also a group at Cedars Sinai, under Dr.Clive Svendsen who are working on another stem cell protocol for people with ALS. (http://www.alsconsortium.org/news_grant_stemcell.php)

Q: There is a fear about bio markers…if something is discovered to potentially lead to a devastating disease, will we be susceptible to creating "pre-existing" conditions for insurance companies…how can we fix this.

A: I think potential benefits outweigh risks, especially if eventually a therapy can prevent a disease from happening. I believe also that the new health care laws deal with this issue.

Q: We were in the Dexpramipexole study, and now are looking at other studies but the disease is now at the 3 yr point and when they list criteria, most are less then 2 yrs as a criteria, which is listed as advanced disease level. If you can still ride bikes and have good FSR, it seems like we rule out a lot of ALS folks by years

A: I agree. The inclusion criteria for studies are all different. They depend on the treatment and phase of therapy development. More often, therapies early in drug development have less restrictive inclusion criteria. We are learning more about what happens in the body in different stages of the illness and it may be that some therapies work best early, others later in course. It would be better to target inclusion criteria on the biochemistry that is happening in a person rather than years. To do that, we need better understanding of what is happening in body at each time point. There are several studies now that are asking people if blood and spinal fluid can be collected every few months- so that scientists can better understand what is happening at different stages.

Q: How can we the patient make a risk-taking decision, and actually get Trial drugs before FDA approvals? Is it possible for a patient to do an off study treatment with a liability waiver?

A: By participating in clinical trials, patients have access to experimental therapies prior to FDA approval. Often there is an open-access component to a clinical trial where participants in the study have access to the therapy until decision is made on FDA approval. Participating in ALS research is a way people can help field learn more about ALS and find new treatments. It is a partnership that is critical for rapid development of treatments for people with ALS. For some therapies, compassionate access is also an option. The decision on whether compassionate use is available depends on what is
already known about the therapy. A first step would be to discuss with your physician if they would ask for compassionate use. FDA and hospital ethics board approval is needed. In addition the manufacturer of therapy would need to agree. A physician would similarly need to be willing to file a compassionate use IND (investigational new drug application with FDA) and IRB (institutional review board) application.

Q: Could you elaborate on CY4026 trial?

A: The CY4026 trial (Tiramisiv) is a phase IIB trial which will enroll approximately 400 participants at centers in US, Canada and Europe. CY4026 is a troponin activator - this means that it helps muscles generate stronger contractions. In the study, participants will receive the study medication for approximately 12 weeks. As sites are activated (ready to enroll), they are listed on our website [www.alsconsortium.org](http://www.alsconsortium.org) and [www.clinicaltrials.gov](http://www.clinicaltrials.gov).

Q: Do they do genetic testing of trial subjects so that you can figure out if the patients who seem to have good results (or bad results) have a particular gene associated with ALS in common?

A: Often in clinical trials, DNA is collected with the participant’s permission for ALS research. This includes testing for known genes as well as for genetic changes (polymorphisms) that might be associated with response to treatment or prognosis.

Q: Is there any evolving consensus among the neurodegenerative research community about any breakthrough therapies or treatments?

A: Yes, absolutely. There are several themes that are emerging as important therapeutic targets; axonal transport, RNA metabolism, neuroinflammation, energy metabolism and toxicity from secreted proteins. These areas are important in ALS and also in other neurodegenerative disorders.

Q: Can you speak about the high fat diet?

A: We know from laboratory studies and epidemiology studies that higher BMI and cholesterol is associated with a slower course. In addition, a high fat, high calorie diet in an animal model of ALS has beneficial effects. There is an ongoing clinical study of a high fat/high calorie diet in people with ALS who have a feeding tube ([http://www.alsconsortium.org/trial.php?id=14](http://www.alsconsortium.org/trial.php?id=14)). We hope to have those results in a few months. It is believe to be important for people with ALS to maintain their weight. There are many ways to do this and it is important to dietary options discuss with your ALS team.