

Families of Spinal Muscular Atrophy

Transcript of SMA Questions Chat, Thursday, May 12, 2005

This transcript has the proper question and answer put together for easier reading, and some of the questions and answers have been cleaned up, and some extra talk and some identifying information has been removed. Typos and errors may still exist although it has been reviewed by the doctors.

<i>administrator</i>	Hi everyone and welcome to the FSMA chat room. Today's chat subject is SMA Clinical Trials, and our guest experts are Dr. Sandra Reyna, Project Cure SMA Clinical Trials Manager, and Dr. Kathy Swoboda, Principal Investigator for Project Cure SMA. Welcome Dr Reyna! Welcome Dr Swoboda!
<i>rm</i>	Can a 6-year-old boy with Type II SMA (who is in the clinical trials) expect less favorable results from CARNI-VAL than a 3 or 4 year old with Type II?
<i>dr_swoboda</i>	A 6 year old won't necessarily do better than a 3 or 4 year old. Everyone responds differently. We are measuring benefit primarily with regard to a functional outcome scale rather than strength.
<i>rm</i>	What % of increase in strength can a Type II 6-year-old expect by participating in this trial?
<i>dr_swoboda</i>	We didn't measure strength directly, but looked at scores on a functional scale. There is a range of results, from no improvement in score to significant improvement, but we haven't quantified as a percentage.
<i>cm</i>	Why is the age cut off for group 3 age 3 instead of 2 years old like the other groups?
<i>dr_swoboda</i>	We cut off the second group at age 3 years, as we aren't sure whether kids younger than 3 can do all the items in the functional scale.
<i>mm</i>	Why are the trials restricted by age? I'm a 20 year old with Type II, and disappointed that recent trials exclude me.
<i>dr_swoboda</i>	We didn't want to have too broad an age range for the study as a starting point, because disease duration may impact how people might respond to the medication.
<i>mm</i>	I see. Thanks.
<i>rj</i>	I was under the impression that valproic acid depleted carnitine levels. How do the two combined work?
<i>dr_swoboda</i>	It is true that valproic acid depletes carnitine levels, so the purpose of giving the two together is to prevent the depletion of carnitine, thus allowing valproic acid to have a potentially positive effect, without it being balanced out by a negative effect from carnitine depletion.
<i>mk</i>	I was wondering how the drugs will be given to patients with SMA especially a 3 year old? Thank you.
<i>dr_swoboda</i>	The drug will be given by mouth, and we have picked the formulations specifically to work in that age range.
<i>jb</i>	I heard that anyone with spinal fusion expected in next six months

	will be excluded from participation. Does that include growth-rod extension? What is the rationale? Thanks.
<i>dr_swoboda</i>	Any spinal surgery expected within the next six months would preclude participation in the trial, as we expect that a major surgery could have implications regarding how the children are able to perform on the functional tests.
<i>jb</i>	Should I consider moving up a growth-rod surgery to June to be available for participation after July - or are you concerned about recovery periods?
<i>dr_swoboda</i>	Any child with a spinal rod is excluded from this trial.
<i>jb</i>	OK, I get it. Thanks.
<i>z</i>	How long is phase II of the study duration?
<i>dr_reyna</i>	The study duration for the SMA CARNI-VAL Trial is set for 2 years. To clarify, the study will last for a year and a year for results to be published. Our goal is to complete patient enrollment in the first 6 months of the study.
<i>rm</i>	In your experience, have 3 and 4 year old SMA participants had better results than older SMA children?
<i>dr_swoboda</i>	In our experience to date, it does seem that some of the younger children might be having a more obvious benefit. However, that may in part be related to developmental improvements and not all drug related. Even when there is a functional benefit, it is hard to know whether it is drug related or not, which is why we need to do the Carni-Val trial.
<i>rm</i>	Thank you.
<i>mk</i>	For SMA Sitters, will this drug get them to hopefully stand and take steps? Have any improved in this way? Thank you.
<i>dr_swoboda</i>	I don't know yet. I don't want to raise false expectations.
<i>mk</i>	OK, thanks.
<i>z</i>	Do contractures in the extremities affect the outcome of positive results?
<i>dr_swoboda</i>	Contractures in the extremities could limit some possible benefits, but there could still be other benefits we may be able to detect.
<i>jn</i>	Are there any plans to expand the trial locations in particular to countries outside of USA (Singapore, Australia, ...)?
<i>dr_reyna</i>	Our goal is to start with SMA CARNI-VAL Trial for now and soon initiate further studies at which time we may include other sites. Investigators in foreign countries are very interested in starting clinical trials for SMA patients.
<i>jn</i>	Thanks. Any investigators you know from Singapore?
<i>dr_reyna</i>	Not in Singapore but Taiwan and Hong Kong.
<i>cm</i>	In regards to weight gain, is it actual fat that is gained, or is it due to an increase in muscle mass?
<i>dr_swoboda</i>	In kids who show weight gain, it can be both in part, but in the children in whom we withdrew the medication due to excessive weight gain, it was largely due to increased fat mass.
<i>cm</i>	Thanks!
<i>rj</i>	Would giving carnitine alone be beneficial for a child with SMA 3 who is walking? Thanks.

<i>dr_swoboda</i>	Probably only if your child is carnitine deficient. This can be measured by a blood sample. In our natural history study, occasional children with type 1 and 2 were deficient, and one with type 3. It depends on a number of things, including how much meat an individual eats, which is where we receive most carnitine. Some formulas are also supplemented with carnitine.
<i>z</i>	Why does the study exclude people who use BiPAP more than 12 hours per day? Won't they also gain strength?
<i>dr_swoboda</i>	It is possible, but since these patients tend to be much weaker to start, it would likely be a more subtle improvement that we might not be able to easily detect using our functional scales.
<i>rh</i>	How frequently should carnitine levels be monitored to make sure that toxicity and loss in muscle are not affected?
<i>dr_swoboda</i>	It depends entirely on the specific situation, and whether or not that individual is taking carnitine, and in what dose.
<i>lw</i>	Have the results of Phase I of this study been published yet -- if so, where; if not, when? Thanks.
<i>dr_swoboda</i>	No, not as yet. We need to perform a complete analysis once all the patients have reached the point where they have received one year of drug. Hopefully, by the end of this year.
<i>jy</i>	I have seen a recent publication on valproic acid effects on ALS, with a possible neuroprotective effect considered. Is it also an effect that is considered for SMA or do we still think that there is a significant SMN2 expression increase?
<i>dr_swoboda</i>	It is difficult in a clinical trial with patients to determine how a given medication might be having an effect. We have been measuring SMN protein and mRNA levels from blood samples in the phase I study, but haven't analyzed those results as yet, and we will need to see if there is a correlation with the physical therapy testing.
<i>jb</i>	Is there another drug other than Valproic Acid that is going through trial?
<i>dr_swoboda</i>	There are certainly other drugs being considered for trials in the near future. There are two other trials currently in progress, one with hydroxyurea, and one with riluzole.
<i>z</i>	Can I ask any questions regarding CoenzymeQ10?
<i>dr_swoboda</i>	Go ahead, just not sure I can answer them.
<i>z</i>	Thanks. What dose can you give to an 8 year old and a 10 year old child? What have been the positive outcomes?
<i>dr_swoboda</i>	I have not performed a trial in SMA with CoQ 10, so I don't really know whether or not it could have a benefit.
<i>z</i>	Thank you.
<i>tf</i>	When one says functional benefit, does that just mean that SMA kids are better able to do things without necessarily an increase in physical strength?
<i>dr_swoboda</i>	A functional benefit usually occurs with an associated increase in strength. I just can't comment about strength in particular, because we didn't directly test it in the phase I. We will try to assess this in the CARNI-VAL trial in the children older than 5 years by using a

	hand held myometry device.
<i>lw</i>	Are there any restrictions/guidelines during the trial period regarding participants' diet or intake of supplements, vitamins, medications, etc., or just an attempt to maintain status quo?
<i>dr_swoboda</i>	There are no restrictions per se, except if your child is using substances that may interact with the study drug, or have been hypothesized in animal models or cell lines or other studies to have a beneficial effect in SMA.
<i>tf</i>	Is Project Cure SMA related to the NINDS translational research? I think NINDS possibly believes that researchers may discover some type of treatment within 5 years. Is that Project Cure's stance or belief?
<i>dr_swoboda</i>	Our work is indeed along the same lines as the NINDS translational project. I do believe that there is a good likelihood that an effective treatment will be uncovered in the next five years...however, whether that treatment will be applicable to most patients, and how effective a treatment it will be, is clearly unknown at this time.
<i>cm</i>	Do you consider the drug successful if you don't see an increase in strength, but don't see a decrease either?
<i>dr_swoboda</i>	We have determined in our natural history studies that patients in the age range which we are studying for the CARNI-VAL trial remain stable from a functional standpoint for at least six months using our outcome measures. Therefore, if no improvement in our outcome measure is detected, and that result occurred in everybody, that would indicate one of two things: 1) the drug is not effective, or 2) it is not very effective, and may lead to some benefit, but our outcome measures are too insensitive to detect the improvement. Under the best circumstances, we hope that all or most patients will improve in their scores, and that would clearly indicate a benefit. If some improve, some stay the same and some get worse, it could be difficult to interpret. However, even that doesn't mean the drug may not work in some patients.
<i>cm</i>	Thank you, Dr. Swoboda.
<i>z</i>	When you say increase in function, do you mean gain strength, such that a child can now hold and manipulate item that were to heavy to even hold before?
<i>dr_swoboda</i>	An example of improved function would be: a child couldn't roll over before, and now they can, or they couldn't lift up their head, and now they can, or they couldn't stand, and now they can. So, function and strength are clearly related in a very big way.
<i>lw</i>	Weight gain in my SMA 2 son has been a concern over this past year. Considering the possibility of additional weight gain during a Phase II study, would you say that we might be better off enrolling in one of the other upcoming drug trials, such as riluzole or hydroxyurea?
<i>dr_swoboda</i>	Every child responds differently to valproic acid, but careful attention to diet can help prevent additional weight gain, particularly since we are aware of the issue up front. We have a

	dietician who works closely with us to analyze dietary records and help provide guidelines for parents in this situation.
<i>ry</i>	What are the side effects?
<i>dr_swoboda</i>	See www.projectcureSMA.org for complete listing of side effects. Look in the FAQ (Frequently Asked Questions.)
<i>rh</i>	What tests will be used to measure "growth?" Will they be same as in phase one or will there be others in addition?
<i>dr_swoboda</i>	Growth will be measured using standard methods; we check weight, height, head circumference, abdominal circumference and chest circumference each visit.
<i>sm</i>	Do you know any investigators from Turkey?
<i>dr_swoboda</i>	I know of at least one investigator from Turkey, Dr. Haluk Toplaglu in Ankara. He is involved with the EuroSMART clinical trials group.
<i>sm</i>	Thank you Dr. Swoboda.
<i>administrator</i>	Our time is just about done. Thank you very much Dr Swoboda and Dr Reyna for coming and answering our questions!
<i>dr_reyna</i>	Dear All: Thank you for taking the time to talk to us.
<i>From many</i>	God bless and thank you, Drs. Swoboda and Reyna. Thank you doctors. Thank you very much. Thanks!!
<i>dr_swoboda</i>	I thank you all for your excellent and challenging questions!