

CURE Epilepsy Webinar
Cenobamate & Refractory Epilepsy: A New Treatment for Focal Seizures
(Transcript)

- Dr. Laura Lubbers: [00:01](#) Welcome everyone, to today's webinar. I am Laura Lubbers and I'm the Chief Scientific Officer for CURE Epilepsy. I want to thank you all for joining us today. Approximately 30% of people with epilepsy have seizures that are considered refractory. In other words, they become resistant to current treatment options. Therefore, it's critical that new and improved antiepileptic drugs continue to be developed.
- Dr. Laura Lubbers: [00:25](#) Today's webinar, entitled Cenobamate: A New Treatment Option for Partial Onset for Focal Seizures will spotlight one of the recently approved drugs for epilepsy. This webinar is supported in part by SK Life Science, and it's a part of CURE Epilepsy's 2021 Leaders in Research Webinar Series, where we highlight some of the critical research that's being done on epilepsy. As an additional resource, today's webinar, like all of our webinars, is being recorded for later viewing on the CURE Epilepsy website. You can now also download transcripts of all of our webinars for reading.
- Dr. Laura Lubbers: [01:04](#) For over 20 years, CURE Epilepsy has raised more than \$70 million to fund epilepsy research that supports our mission, which is to find a cure for epilepsy by promoting and funding patient-focused research. CURE Epilepsy provides grants that support novel research projects to advance the search for cures and more effective treatments.
- Dr. Laura Lubbers: [01:26](#) In 2020, we launched our CURE Epilepsy Catalyst Award to help accelerate the basic research we traditionally funded to the next stage of development and prepare potential new treatments for clinical trials.
- Dr. Laura Lubbers: [01:40](#) Today's webinar will provide an in-depth review of Cenobamate, also known as Xcopri, which is an FDA-approved drug made available to patients last year. It is approved for the treatment of partial onset seizures, also referred to as focal seizures. In this webinar, you'll learn what is known about Cenobamate, and how it reduces seizure activity, why it is a safe and effective treatment for partial onset seizure, and you'll also learn about the potential side effects that patients and caregivers should be aware of when considering this treatment option.
- Dr. Laura Lubbers: [02:15](#) Today's webinar is presented by Dr. Michael Sperling. Dr. Sperling is the Baldwin Keys Professor of Neurology and Vice Chairman of Clinical Affairs in the department of neurology at Thomas Jefferson University in Philadelphia, Pennsylvania. He's

also the director of the Jefferson Comprehensive Epilepsy Center and the Clinical Neurophysiology Lab at Thomas Jefferson University Hospital. His primary research interests include surgical treatment of epilepsy, mortality in epilepsy, epilepsy genetics, and clinical neurophysiology.

- Dr. Laura Lubbers: [02:50](#) Before Dr. Sperling begins, I'd like to encourage everyone to ask questions. You may submit your questions anytime during the presentation by typing them into the Q&A tab located at the bottom of your Zoom panel and then click send. I want to thank those who submitted questions in advance of today's webinar. We'll do our best to get through as many of those as we can.
- Dr. Laura Lubbers: [03:11](#) We do want this webinar to be as interactive and informative as possible. However, to respect everyone's privacy, we ask that you make your questions general and not specific to a loved one's epilepsy. With that, I'll turn it over to Dr. Sperling.
- Dr. Michael Sperling: [03:28](#) Thank you very much for the kind introduction. It's a pleasure to be able to speak today. I'm going to be speaking about Cenobamate, which is the brand name Xcopri. It's the newest drug out to treat focal epilepsy, or what used to be called localization-related epilepsy for focal or partial seizures. It's an interesting drug and I've got a lot of information to tell you, so let's move forward.
- Dr. Michael Sperling: [03:54](#) Now, I'm going to just start with a basic thing, because I'm not sure who's on this webinar and who's not. Just a simple definition and explain how drugs work. What is an epileptic seizure, and what is epilepsy?
- Dr. Michael Sperling: [04:07](#) A seizure is when too many brain cells fire at once, or neurons specifically, those specific type of brain cells. Too many fire at the same time, so you have excessive numbers of firing and excessive synchrony. This activity then can overshadow other brain functions and really override normal activity.
- Dr. Michael Sperling: [04:28](#) Then the expression of the seizure really depends upon how much of the rest of the brain it takes over. So, if it remains in a small area, you may just get a very minor or subtle seizure. For a focal seizure, for example, an aura where you get a funny feeling and nothing more. Whereas if it's in the motor area, maybe some jerking in the hand or the face or the foot, but nothing more.
- Dr. Michael Sperling: [04:47](#) When it starts taking over more and more neurons throughout the brain, you get more dramatic manifestations, so it can start

spreading to involve other areas. You can get movements of both sides when it spreads to both sides. Typically, you have some loss of awareness.

Dr. Michael Sperling: [05:03](#) And when it really is widespread, we get what's known as a focal to bilateral tonic-clonic seizure or secondarily generalized seizure (grand mal, the old terminology) where someone's unconscious and stiffened and shaking.

Dr. Michael Sperling: [05:15](#) So, how much does this make a difference? And then a seizure, lastly, is a discrete episode. There's a clear time when it starts and typically when it stops also, though continuous seizures or status epilepticus is a separate problem. Then epilepsy is simply the tendency to have seizures, or people have inherent tendency in the brain to have seizure from whatever cause.

Dr. Michael Sperling: [05:38](#) So, when we give drugs, we give drugs to prevent seizures. And what we want to do is block this excessive firing and this hyper-synchronous firing of neurons: too many firing to begin with, and then too many firing synchronously at once that can then override other activities. To block these seizures, we really look at multiple mechanisms. So, if you think about it at the level of neurons, brain cells talking to each other, you can do it by modifying the flow of certain anions and cations across the cell membrane. So, sodium, calcium and potassium, and then chloride is the fourth one are the major anions and cations that are balanced in between and out.

Dr. Michael Sperling: [06:18](#) When seizures occur and cells fire excessively, usually you've got an alteration in the firing of sodium and calcium in particular, and other anions and cations may be affected as well. If you can block that or slow it down, then you won't get as many cells firing much. There are receptors on the cells that react to transmitters, they're little chemical signals from one cell to the next that can modify this flow of these anions and also produce other activity inside the cell that makes a difference.

Dr. Michael Sperling: [06:49](#) You can modify these receptors on the cell surface, you can alter some of the internal processes. So for example, when one cell wants to send a message to another, it has to release a little packet of chemicals that diffuse across the gap between the two and cause the next cell to fire. One drug--originally Piracetam and then it has a couple of derivatives that have been used, levetiracetam or Brivaracetam--actually modify the outflow of chemicals from one cell to the other so it can modify the way cells trigger others to fire.

- Dr. Michael Sperling: [07:21](#) You can also alter the strength of connection. There are other mechanisms as well, but this is roughly how drugs are going to work. And we must confess that we don't fully understand how they work. We have an idea, but our ideas need to be improved. So, we prevent seizures from occurring and that's the purpose of giving medication. There have been many medications prescribed over the past 160 years. This is a graph borrowed from another person, references at the bottom of the slide, that shows that the first drugs that were developed were developed in the 1850s, they were bromides which basically a simple chemical.
- Dr. Michael Sperling: [07:59](#) And then it was over 60 years to 1912 until phenobarbital was invented. So, a long passage, then you can see paraldehyde shortly after that. And then the early, actually late 1930s and 1938 Phenytoin (brand name Dilantin) was developed, acetazolamide. And you can see the number of drugs develops. And then really after 1990, there's been an explosion with the number of drugs being approved and developed to treat epilepsy to try to prevent seizures.
- Dr. Michael Sperling: [08:28](#) However, there's a problem. While we have a lot of drugs, till now, by and large, one drug is about as good as the others. So this phenytoin that was first developed in 1938 and Carbamazepine for that matter in the 60s are as good, as effective as a lot of the drugs developed in the last decade or two. The efficacy is not really different. They work about as well.
- Dr. Michael Sperling: [08:53](#) Some drugs are better for some seizure types than others. So, for generalized seizures, for example, Divalproex, valproic also known as Depakote is the brand, is particularly potent and better than all of the others. For absence seizures Ethosuximide, which was developed in the 1950s is still the best drug. We need new drugs for that too.
- Dr. Michael Sperling: [09:11](#) So, there are some differences, but for focal seizures, the drugs are mostly the same. There are a few that are slightly different than the others. And the main difference we have is between side effects. Different ones have different side effects and they also affect the body differently. So, some drugs cause other drugs to be metabolized more or block the metabolism of other drugs and of other hormones in the body. Some drugs bind a lot to protein in the blood, others don't. So they can affect metabolism of hormones in your bodies and other chemicals differently and the side effects are different.

- Dr. Michael Sperling: [09:42](#) The efficacy till now has not been terribly different. And why do we need that? So, this is a graph that shows the effectiveness of drugs on blocking seizures, focal seizures in particular. So, if you look at number one, that bar, it shows that about half of the people who are prescribed a drug have it actually work and stop seizures completely.
- Dr. Michael Sperling: [10:07](#) Now, many of the remaining people may have the drug work somewhat. It may cut the number back a lot, it may make those seizures much milder, but they still might have some seizures. So, it would be nice if we had a drug that worked more than half the time. If you were going to get in your car to drive to work in the morning and you knew it would get you there half the time, you would very rapidly come up with a different mode of transportation.
- Dr. Michael Sperling: [10:32](#) For treating seizures, this is what we have, so we need better drugs. And you can see if the first drug doesn't work, so if a half of people who it didn't stop further seizures or you buy help in about a third of the remaining people. So an additional 12%, 13% of people will respond to drug number two, total. And if you think about it, 13%, maybe 14% out of the remaining 50 is maybe between a quarter and a half of the remaining people.
- Dr. Michael Sperling: [10:58](#) The third drug, you've got a little more benefit, but not very much. And you can see after that they hardly really do very well at all. That would be an added benefit from adding more drugs is not great. And that's why we think about brain surgery once two drugs have failed because once two drugs have failed the odds of the next drugs working and inducing permanent remission, meaning stopping seizures permanently, is very, very low and the risk of surgery then becomes less than the risk of taking pills.
- Dr. Michael Sperling: [11:24](#) It would be nice though, if we had additional medicine to use rather than that were more effective. And then this is a slide that just shows the effect of new drug development on seizure control. So, you can see that there are three lines that are superimposed, drugs developed in 1982 to '91, '92 to 2001, and those developed after 2001. And it looks, again, at the proportion of people who become seizure-free.
- Dr. Michael Sperling: [11:47](#) So, a probability of one looking at the Y axis on that curve would be a hundred percent of people seizure free. And this shows that when we put people up in the first 12 months, a little over half are seizure-free. And that's because some have had more than one drug at that point. But then as you follow along, it goes up and overall still, maybe about 70% are seizure-free in

this effect in the slide it shows. And you can see the response to drugs from the eighties, the nineties, or after that is about the same. So these new drugs are really not better by the evidence.

Dr. Michael Sperling: [12:26](#)

They're not as effective as they should be, and they need to be. Too many people have seizures despite appropriate treatment. So, we're giving the right drugs, they're just not responding the way they should. Seizures are breaking through. And we do have other methods, as I mentioned. We can do surgery, which works nicely in many people and stop seizures, neuro-stimulation like responsive neurostimulation, deep brain stimulation, or vagus nerve stimulation, which are palliative. They don't make seizures go away completely, but they can improve the situation for some people, for many people.

Dr. Michael Sperling: [12:54](#)

And then some people, selected people, usually kids, can be treated with diet, ketogenic diet, or modified Atkins. But we really need new drugs that are better to reduce the need for surgery in these other treatments. So, cenobamate was approved by the FDA in November, 2019, and was finally released in May, 2020.

Dr. Michael Sperling: [13:14](#)

And the first question you might ask me is, why did it take nearly six months to come out? And that's because once the FDA approves it, the company and the FDA still have to negotiate on the label of the drug, what the writing is that goes out to doctors and pharmacists and patients. It takes time. The company has no idea exactly when the drug is going to be improved and they have no assurance of when it's going to be approved. So they have to ramp up manufacturing so they can have a drug to do it.

Dr. Michael Sperling: [13:39](#)

And then what SK Life Science who makes this drug also did was they started working proactively in advance to start speaking with insurance companies so that when people like me wrote a prescription for people with epilepsy, the insurance companies would agree to pay for it because the drugs were, unfortunately, expensive and well beyond the means of the average person or even for a very well-to-do person they can be expensive. So, this is one of the things that has to be done. We have to make sure that they're paid for.

Dr. Michael Sperling: [14:10](#)

The drug has a similar structure to other drugs, Felbamate, which has been around since 1993. And then Carisbamate was in testing, fell out of testing and is now going back into testing again so it has a similar structure to those. And we know Felbamate as a potent drug, but it also is a drug that was a little scary and which is why it's hardly ever used. So we're hoping for

a similar chemical compound that will work well or even better than Felbamate, but not be quite as scary in terms of risk.

Dr. Michael Sperling: [14:37](#)

This drug has a mechanism of action that seems to be different than other drugs, we only partly understand it. It alters the flow of sodium into neurons, so it changes the flow of sodium by doing something technically called an activation of sodium channels. It reduces the activation of so the cells can't fire as readily. And also it modulates GABA-A receptors. And these are receptors that actually inhibit cell firing.

Dr. Michael Sperling: [14:59](#)

So, it blocks the excessive firing, and it actually helps in two ways, one by blocking sodium and also just by affecting GABA. So, it has two mechanisms that we're aware of. The drug looked very good. It's been subjected to two phase II trials. I'll give you the results of all the trials. This is one in which 222 patients were randomized in this study at 40 centers in the United States, India, Korea, and Poland.

Dr. Michael Sperling: [15:24](#)

And nobody asked me why those countries in particular. I can explain the U.S because we are a big country and drug companies can make a nice profit in the United States. I can explain Korea because SK Life Science is owned by Samsung, so the people who make my phone also make this drug, and my television for that matter. India, I don't understand, and Poland I don't understand. This is what they selected. There are many places.

Dr. Michael Sperling: [15:51](#)

And that's what's called a randomized controlled trial. So people were randomly, like the toss of a coin, assigned to either get drug or placebo. And you can see of 285 patients in the graph on the right who were assessed for the study, that 63 were excluded for various reasons. They didn't meet the formal criteria. 222 were randomized to about half getting drug and half getting placebo. And it's like a toss of a coin, so it's not going to be precisely be 111 each, was 113 and 109.

Dr. Michael Sperling: [16:18](#)

And then a couple of people drop out after that, for whatever reasons they decide they changed their mind they don't want to participate. Something comes up, they can. There's a four to eight week baseline, so you have to count seizures at that period of time and then people were treated for 12 weeks.

Dr. Michael Sperling: [16:31](#)

And you basically, in these trials, compare how often did seizures happen during the treatment phase with how often did they happen at baseline before the drug or placebo was administered? The average age of patients was 36 or 38 years old. They typically had seizures for about 20 years on average of

history. It was roughly equal male to female. And because of the place where the study was done, 57% to 58% were Caucasian or white, 41% to 43% were Asian and other races were minimally included and this is an artifact.

Dr. Michael Sperling: [17:03](#)

There's no reason to believe that a drug is less effective or more effective based upon ethnic background or race. There is reason to believe that the risk of an allergic reaction of some kind might be different. We know that some drugs like carbamazepine or oxcarbazepine are more likely to cause a serious allergic reaction and potentially life-threatening skin rash in people of East Asian and South Asian ancestry because of a certain genetic features there. So, it would be nice to have more information, which hopefully has been gathered.

Dr. Michael Sperling: [17:35](#)

And then how often were these people having seizures? You had to have, I believe, four seizures a month out in the trial. And the average was about seven and a half for people who were randomized to drug and five and a half per month who had placebo.

Dr. Michael Sperling: [17:48](#)

And what happened to the change in seizure frequency? And as you can see, I have the three seizure types on this curve. So, on the right, let's look at the right side where we'll do it right to left. The biggest, most severe seizure is the focal to bilateral tonic-clonic, that can also seizure for both [inaudible 00:18:04]. It was a 77% reduction in seizure frequencies and number of seizures were cut by three quarters of people who got drug.

Dr. Michael Sperling: [18:12](#)

And you'll see, there was a 33% reduction in people who got placebo, which is why we have to have placebo ones because people who get placebo still do better. Why? They're in a trial, maybe they're more reliable with their drugs. Maybe they're counting seizures more carefully once they start to take than before. I don't know, but there's a clear placebo response in it.

Dr. Michael Sperling: [18:32](#)

And actually the placebo response was pretty high in this trial. We would like to normally see a placebo response in the 10% to 15% range. This raises some questions in my mind as to who was included, frankly. But nonetheless, a statistically significant difference. If you look in the middle columns, focal impaired awareness, what we call complex partial or psychomotor seizures, placebo patients have their seizure frequency or the rate per month dropped by 21%, people treated dropped by 55%.

Dr. Michael Sperling: [19:01](#)

And then less severe seizures. So people who were awake and don't lose awareness but have some outward manifestation

that we can see with the movement of one side, or maybe freezing speech, smacking lips, whatever, 28% reduction in placebo arm and 76% in the treatment arm. So, statistically significant again, the drug worked.

Dr. Michael Sperling: [19:26](#)

What was most striking is shown in the bar on the right. Again, we're going right to left. For those of you who read Hebrew or Arabic, this is natural. The percentage of patients who became seizure-free for the 12 weeks, just for those 12 weeks, remember it's not long-term, it's the 12 week trial. But during that 12 weeks, you can see 8.8% of people given placebo had no seizures once the trial started.

Dr. Michael Sperling: [19:54](#)

28% of the people who got drug did. So, the absolute difference is 20% compared with the placebo arm. This is striking. This is striking. We've never seen something like this in trials before. This is the first trial that has shown such a striking effect with a high proportion of people stopping having seizures for that period of time. And we'll talk about longer time in a minute. So, don't write questions what about longer time that's coming up.

Dr. Michael Sperling: [20:17](#)

If you look in the middle, a greater than 90% reduction in seizures, you can see 8.8% versus 34%. So, if you think about it, the drug was started in the low dose and ramped up actually over the first four weeks before they had final dose. Some of the people who had seizures then stopped, but they might have had it in the first couple of weeks before they were in a therapeutic dose. They would have had a greater than 90% response. You can see it's still a big difference. And then at least a 75% response. Less striking, but nonetheless, statistically significant in improvement.

Dr. Michael Sperling: [20:50](#)

Now, what are the side effects that we saw in this trial? And remember that trials are not the real world. Most people don't qualify for trials. You'd have to have a certain number of seizures per month. You can't have any acute medical conditions. There are all sorts of things. They exclude people on certain kinds of drugs. It's very artificial. So, it really is a very small group of people. And that's why we need to do bigger trials afterwards that are open to more people to really know what happens.

Dr. Michael Sperling: [21:17](#)

If you have, for example, significant active liver problem, or a kidney problem, or a heart problem, or a severe depression now, the companies don't want you in trials. You're excluded because they don't want people dying in their trials or attempting suicide if they're depressed and their drug potentially tainted with that. In the real world though, I have to

treat people who have heart disease and depression and other things. And then I wind up not knowing what the effect is in these conditions. So, this is a problem with trials, just like small children are never included initially.

Dr. Michael Sperling: [21:45](#)

And even in this first trial, a few children were included. Because again, they don't want to potentially cause problems in kids. But then when we have to prescribe the drug, we often wonder, and then later studies can do it. So, the trial also is very artificial in that people are on their baseline drug or drugs, one or two or three drugs. And then this drug is added in.

Dr. Michael Sperling: [22:07](#)

And in the trial, you can't change the other medication at all. So, in the office, if you see me and I prescribe a new medicine for you, I will usually tell you if you become unsteady or feel tired, I want you to lower the dose of this other drug you're taking by X amount. And I tell you that when I started the new drug. I say, I don't even want you to call me. I want you to know in advance what our plan is. I should have a plan and you should know. And I want to empower you.

Dr. Michael Sperling: [22:33](#)

And those of you listening, when your doctor's starting a new medicine, they should also tell you what their idea is. What's their plan? If this happens and that happens, what is it? And that way, you know what to do. You know that the doctor has an idea, not call me and I'll decide. I should be able to decide when I start the drug what I'm going to do, and I should tell you so you know.

Dr. Michael Sperling: [22:52](#)

And that way, you don't have to worry. You feel it at 8:00 at night, you're going to call, will you get me? Will you get somebody else who knows what's going on? You know what to do. In a trial, we can't do that. If you have a problem, the drug still has to stay the same. So the incidence of side effects is utterly meaningless in this trials for that reason, because we don't have adjustments. And it's also utterly meaningless for a second reason.

Dr. Michael Sperling: [23:15](#)

And that is, if you say that you were tired once for three minutes and report that, I report somnolence or tiredness as a side effect, even though it was three minutes out of 12 weeks. The person who's groggy and can barely stay awake the whole time is also registered as somnolent.

Dr. Michael Sperling: [23:34](#)

So, there's no qualification of what it means by this. And this is another problem as well that we just, you have to take all of this with a side effect. What we know is that sleepiness was the most prominent, dizziness was most prominent. Is it from the

drug or is it just from being on too many medicines at once and it wouldn't have happened if we reduced it?

Dr. Michael Sperling: [23:55](#)

No, I can tell you, I have had a few patients who were very sleepy and I lowered the drug dose of their other medicines substantially and they were still sleepy. I'm convinced that cenobamate can cause tiredness in some people and it can cause dizziness and other things. And every other drug can as well.

Dr. Michael Sperling: [24:11](#)

But in terms of how common it is, we don't really know because of the artificial design of trial. What were the serious side effects seen in this trial? Two patients on cenobamate had what was considered serious. They had a rash, which they recover, though it was found in the urinary tract infection, which is probably completely unrelated. But if somebody has something in one arm of the trial, it's reported, if it turned out that 50 people had urinary tract infections on drug and none had it on placebo, we would say, "Aha, there's something wrong with his drug." It's associated with urinary tract.

Dr. Michael Sperling: [24:42](#)

But if you see it in both or just one patient it means nothing. And then it's interesting in the placebo there were four serious side effects. Two patients had status epilepticus or uncontrolled seizures had to be hospitalized. One doctor reporting convulsion as a side effect. I don't know why. And one person developed chest pain, maybe from the heart had a coronary angiogram, undoubtedly had nothing to do with anything. In fact, this patient was on placebo, could have had anything.

Dr. Michael Sperling: [25:07](#)

And then there was one moderate side effect of rash as well. So, what do we see here? We can see that on the right, any side effect, 76% of people on cenobamate, 63% on placebo. It's hard to say. But again, the most common somnolence, dizziness, headache was the same in both groups. Nausea was more common in cenobamate, fatigue more common. Nystagmus is jerky eye movements, it's not even a side effect. People typically don't notice it. Balance disorder, unsteadiness, more common. This urinary tract infection, I think has nothing to do with the drug it's just random bad luck, just like respiratory infections, random bad luck, is not significant. And tremors and shaking is probably not significant. And then constipation and diarrhea on drugs, so maybe. Any drug can produce either, maybe that's the real.

Dr. Michael Sperling: [26:04](#)

So, what are the conclusions? It was really remarkably effective for the percent reduction in seizures and the fact that the number of patients just stop having seizures in this trial that's

unusual. And in fact, it was so remarkably effective that when additional phase III studies needed to be done, the FDA said you don't have to do a study to show it's effective. You have two phase II, I just showed you one of them, both show remarkable effectiveness, but we're concerned about side effects.

Dr. Michael Sperling: [26:30](#)

And then to talk about now you need to do more safety studies to make sure this drug is safe. So, a significant proportion responded favorably, and it's a short term trial. It was only 12 weeks. We want to look at long-term data and I'll show you something which is not yet published, but there was a safety signal. So, overall, about 930 people in the early phases had some exposure to this drug, which could have been for a few days, or a few months, as you can see.

Dr. Michael Sperling: [26:57](#)

Three patients developed something called DRESS syndrome, Drug Reaction with Eosinophilia and Systemic Symptoms. So, it's a reaction to the drug. It's like an allergic reaction. Eosinophils are a type of white blood cell that you see in allergy and systemic symptoms. Typically, fever, rash is the drug reaction that we see. And often they can get inflammation in the liver and other parts of the body.

Dr. Michael Sperling: [27:22](#)

And of those three who had the DRESS reaction, one person died. Now, the one person who died was actually someone who was a healthy volunteer, who I can say, having seen the information, that I don't think was treated perhaps as ideally as it should have been. He had this reaction, he was treated at a drug trial site, not at an institution like you'd go to with your doctors where it's a doctor's office. They're people who set up private labs, where they put people on trials, they do trials and they have no great expertise in one disease. They have expertise to treat trials.

Dr. Michael Sperling: [28:06](#)

So, this person was at a trial center, had a reaction, was given a low dose steroid and sent home. Had that person seen, I think, any of your doctors or me, we would have admitted that patient to the hospital and give him much higher dose of [inaudible 00:28:19]. And we should wonder whether that person would have died or not. It's still possible, but I can tell you that I and my colleagues and your doctors too would have certainly treated this person differently and we wouldn't let them go home.

Dr. Michael Sperling: [28:32](#)

But nonetheless, it's scary. A DRESS typically developed two to eight weeks after starting treatment. We see this in a lot of drugs and other drugs that many people take with epilepsy, Lamotrigine, [inaudible 00:28:42] that causes it. Allopurinol,

which is used for gout. Minocycline which is used for acne. And there are other drugs that can cause this.

Dr. Michael Sperling: [28:50](#)

And there are other serious drug reactions that happen with drugs too, that we can see that I'll talk about. So, is this drug riskier than the other drugs? I don't think we have enough information to be certain, but the answer is probably not. In fact, Felbamate, its cousin, is probably riskier. And I talked about the inflammatory reaction and the fact that it is potentially fatal and was fatal in one case.

Dr. Michael Sperling: [29:14](#)

So, the phase III trial was just looking at safety. So, this was a little bit closer to the real world, but not fully close. You didn't have to have at least four seizures a month. You still nonetheless had to be healthy and no active significant medical conditions.

Dr. Michael Sperling: [29:31](#)

It's fine to have medical conditions. You can have high blood pressure or diabetes or whatever else under treatment, but it shouldn't be active and posing major problem. Patients who have had a history of drug allergy were excluded from this trial. So, we saw in the early signal from the first 930 people three severe allergic reactions. This trial was then done that if you had an allergic reaction ever in the past you weren't allowed.

Dr. Michael Sperling: [30:01](#)

So now that the drug's approved, if you come to me with a history of drug allergy, I know your risk of allergy is higher to a new drug, whatever drug I give you when you're allergic to one drug, but immediately this trial became less useful for clinical practice in the long run. Useful for the company and that less likely to have people with drug allergic reactions in this phase of trial and less likely to have serious reactions.

Dr. Michael Sperling: [30:24](#)

So, the drug would look a bit better. And from a safety point of view, since we know it has allergy, it makes sense for everybody's safety for the drug company to do this. They were being very responsible and making sure that people with the issue of drug allergy didn't get in to lower the risk of having a series of allergic reaction in the trial.

Dr. Michael Sperling: [30:44](#)

However, I, in the real world now, and you in the real world do have patients or do have drug allergies. And what do I do when you have that history? Is it safe for me to give you this drug or not? I don't really know the answer with certainty. I know that when people are allergic, they're more likely to have allergies to new drugs that they start. We have to be especially cautious and watch. We wind up prescribing it anyway.

- Dr. Michael Sperling: [31:06](#) We don't know how risky it is or isn't. And hopefully later trials will tell us. Now, in the initial phase II, the drug was started either 50 or 100 milligrams a day and increased every week. So you'd start at a 100 milligrams a day for at least half the people. And then week two, you would be on 200, week three maybe 300, week four 400. Or you start at 50, then went to a 100, 200 and up higher a notch.
- Dr. Michael Sperling: [31:31](#) Experts in immunology said that the way to prevent DRESS syndrome and other series of allergic reactions in drugs that are apt to produce this is start on a low dose and go up more slowly. The pharmacologist, the company and the doctors we can say hello and then the immunologist says, "We don't know, you just have to give it a try." They chose the arbitrary dose of 12 and a half milligrams, a quarter of the lowest dose that had been used before they had used 50.
- Dr. Michael Sperling: [31:59](#) So they try it. And we know that in 50 there were rashes. Let's go down to 12.5, just like lamotrigine, a typical therapeutic dose is a 100 or 200 or 300 or 500 milligrams a day. We start at 25. Let's start at the 12 and a half milligrams. Stay on that for two weeks. Then go up to 25, stay on that for two weeks, then go up to 50 and stay on that for two weeks and then go up to a hundred and stay on that for two weeks.
- Dr. Michael Sperling: [32:22](#) And what's the lowest effective dose? Probably around a hundred, although you might see some response even on lower doses. And really around a 100 to 150 is where the drug starts working well. So, you can see it takes three months to build up to what's a typical dose, 200 milligrams or 250, or pretty typical doses that people wind up taking on this drug. And it takes a few months to get to that.
- Dr. Michael Sperling: [32:45](#) But what happened by doing that is that nobody got the bad rash. So, we had 139 centers in 17 countries, North America. So, U.S, Mexico, a bunch of countries in Europe, Asia and Australia, 1,339 patients about equal males and females, 79% Caucasian, three and a half percent black, 5.5% Asian, quite different than the phase II trial I showed where 45% were Asian.
- Dr. Michael Sperling: [33:15](#) Average epilepsy duration is 23 years. Everybody had uncontrolled epilepsy, and most. 82% were taking two or three drugs when they enrolled in the trial and then cenobamate was added. And you can see that various people came out for reasons of one kind or another. But for whatever reason, 1,339, and then other people came out because it wasn't helping or they had problems. And long-term, 1078 stayed on the drug, which is pretty good.

- Dr. Michael Sperling: [33:48](#) And that's what you see on this slide. This is retention. So, zero to one, really a 100% as a fraction. And if you look at one year, you can see 0.79 or 79% of people were still on drugs. We go out to two years and about 75% are still on drug and this was stopped a little bit before two years, but in the two years I think that it's about 75%.
- Dr. Michael Sperling: [34:12](#) So, it's again remarkable. Why are people still on a drug? Generally because they like it. It's helping and they feel better or at least they feel better on this drug. So this, again, is very good. It's a higher retention rate than we normally see for people to stay on, if stay on it. And then what did we see for side effects? No DRESS syndrome at all. So, starting it this way, nobody had it.
- Dr. Michael Sperling: [34:34](#) 9 people out of 1,339. So, less than 1% developed a rash, non-life threatening, all rashes resolved and went away when the drug was stopped. We saw, again, the most common side effects, sleepiness, or somnolence, dizziness. And again, somewhat it could be developed somnolence. They then called, we lower the drug some, and then the somnolence goes away, but because they had it, it's still listed there.
- Dr. Michael Sperling: [34:59](#) So, it doesn't mean that 28% of people are somnolent on this drug. It means that 28% of people over the two years that they were in this trial, or more in some cases, reported some slowness at some point. And some people stayed up all night and they'd come in and say they were sleepy that day. And we still would report it because they were sleepy even though they stayed up all night and I would report it. This person was sleepy. And I don't think it's related to drug, but it's still reported.
- Dr. Michael Sperling: [35:26](#) Again, fatigue, you can see some headache. And again, it doesn't mean they had headaches all the time, it could have been once, it could have been a lot. You just don't know when you look at this. Again, the psychiatric side effects, which are a matter of concern: anxiety, irritability, insomnia, depression, about 2% confusional state. I don't know why that psychiatric, it's not necessarily 1.2%.
- Dr. Michael Sperling: [35:48](#) And again, this doesn't mean all the time. It could be once or part of the time and easily adjusted. Three patients had suicide attempts. It's a shame that that happened. I don't know that we can blame it on the drug. If you follow over a thousand people with epilepsy for a year, you're going to see, without any change in medications or thing, unfortunately, you'll see three suicide attempts usually as well.

Dr. Michael Sperling: [36:09](#) In fact, you may often see more than that. So, there's no obvious data saying that it has a significant cause of psychiatric symptoms. It looks quite benign in that regard. And then this is the efficacy in a long-term study. So, this is not yet published. I presented this information at the American Epilepsy Society Meeting, which was online in December and we're working on the paper. And Dr. William Rosenfeld, a colleague of mine who's in St. Louis really did the lion's share of the work with this and deserves this credit.

Dr. Michael Sperling: [36:39](#) I pushed heavily to have this done and Dr. Rosenfeld did the leg work and a lot of the brain work too on this. And what you can see for each seizure type, and again, we'll go right to left as we did before. So, out of the 1,339, we had 240 patients where we had good quality seizure data. So, in a lot of patients, a lot of the doctors didn't carefully track how often they were having seizures before or after. At a number of sites, including ours, was 10 sites, we had good data where we said we could confidently know what the effect was on seizures.

Dr. Michael Sperling: [37:13](#) And you see, for the full convulsive [inaudible 00:37:16] on the right, 28% of people became seizure-free and stopped having them. It's remarkable. A greater than 90% reduction in 48%. And then you can see 73% in 78%, 75% are 50% reduction. So, a great effect with 28% seizure-free. Focal impaired awareness or complex partial, 11% seizure-free, 31% had a more than 90% reduction and then less of a reduction, but still a good reduction and half to two-thirds are just three-quarters on this.

Dr. Michael Sperling: [37:45](#) And then the focal aware motor, that aura where you also have some movement or difficulty with speech or swallowing or something, 14.8, so about 15% seizure-free. And a substantial proportion of patients, 85%, had it reduced by half or more. So, this is long-term. Average follow-up was 30 months. So two and a half years average follow-up. Again, a striking thing that I can put somebody on this drug and have a one in four shot that that person's going to call me up and say, "My seizure stopped," for a year or two or three.

Dr. Michael Sperling: [38:18](#) Now, what will it mean over many years? I don't know. If we look at efficacy, any consecutive 12 months, 36% of people, the bar on the right, had at least one 12 month period over that period of time where they had no seizures at all. And you can see 44% at least a three months seizure-free period, 35% that went six months or more without seizures. So, again, a striking response with this drug.

- Dr. Michael Sperling: [38:48](#) So, rashes in general occurring 5% to 17% of drugs used to treat epilepsy. That's common. Some drugs are better than others. Levetiracetam, brand name Keppra is a very good one for that. Rashes are very rare. Other drugs lamotrigine, carbamazepine, oxcarbazepine, phenytoin and phenobarbital particularly commonly have rashes, maybe as many as 15% or 17%. And serious skin reactions like DRESS. Something called Stevens-Johnson syndrome, TEN, which is toxic epidermal necrolysis or Lyell's syndrome have been reported with all these drugs. I've seen it myself.
- Dr. Michael Sperling: [39:29](#) And there are at least eight other drugs, going through the literature carefully, which I did in preparation for this talk, that have also been reported to cause serious, potentially life-threatening drug reactions. So, cenobamate can do it too. Is it worse? We don't know yet. My suspicion is probably not, but I don't have the facts to back that up. I think the benefit makes it worthwhile giving it a try for that reason, because the chances of it helping are so great that the benefit and the risk that the risk I think is vastly outweighed by that. And for what it's worth, the way we presently dose it, nobody has had DRESS syndrome or these other serious syndromes.
- Dr. Michael Sperling: [40:08](#) Now, cenobamate can interact with other medications, especially phenytoin and pump the phenytoin level up a bit. And in one of the trials, the average level at the start of the trial was 11. And it went up to about 15 in the trial. In practice, in this long-term study where we can settle with drugs, we end up lowering other drugs a lot, but you may need to adjust it.
- Dr. Michael Sperling: [40:28](#) And other types of side effects are going to go with this drug as with others. And how much of this is related to taking multiple medicines? How much would happen if you only took cenobamate by itself? We don't fully know. So, I'll wrap up here. I ran a little over, I apologize, but we still have plenty of time for questions.
- Dr. Michael Sperling: [40:43](#) And it appears to be really a remarkable drug because of that ability to stop seizures completely on people that we haven't seen with others. Typically, I'll comment also in trials, things look better than they do once they get out widely. And there's a phenomenon that's been seen that drugs look great in early trials and the more you study them, the less impressive they look with time. This has remained impressive. We'll have to see how it works over the long run.
- Dr. Michael Sperling: [41:11](#) I might be showing you the best of all possible worlds, and maybe it'll settle out a bit lower, but it still looks great. It works

differently than other drugs probably because we see these people stop having seizures that we haven't seen in other trials to this extent. We know at least two points of attack blocking sodium channels and also enhancing a division with GABA receptors.

- Dr. Michael Sperling: [41:32](#) It significantly reducing seizure frequency even when seizures are not stopped. And it also appears to make seizures milder. So you saw that response to the convulsive seizures was really terrific. So, some of us people may have still had some seizures, but there were no longer having convulsive seizures, tonic-clonic seizures, anymore. Its side effect profile, in general, looks like other anti-seizure medicines and it seems to be well-tolerated.
- Dr. Michael Sperling: [41:54](#) The DRESS syndrome was in three of about a thousand people prescribed this drug and starting this as a 50 or a 100 and will increase the dose quickly and starting lower wasn't associated.
- Dr. Michael Sperling: [42:03](#) Probably I think if enough people get it, we will rarely see a serious drug reaction. Hopefully, the risk will be incredibly low. Well, under 1%, ideally a hundred point one percent. For the present study, we can say that it's going to be under 0.3% or less than three per thousand.
- Dr. Michael Sperling: [42:18](#) And then people who start this medicine, obviously you need to know in advance what to expect, and you should let your doctor know if there's a problem. So, I have a system set up at Jefferson, for example, in Philadelphia, where if somebody calls me at a reasonable time of day, not at 4:30 in the evening, I have a dermatologist who will see that person the same day. You call me at 4:00 in the afternoon and the dermatology office closes at 4:30, you might have to wait until the next morning. And I can look at your rash, but I'm not a dermatologist.
- Dr. Michael Sperling: [42:48](#) So, I think, it's good to have something like this set up or to have many people have their own dermatologists who can look at it. Many of my patients use their cellphones. They take a picture, they send me a message through their electronic medical record of it. I can then forward that to the dermatologist who can look at the photo. The dermatologist says that some of the photos are good enough that they can tell and some are not, it's hard for them to know.
- Dr. Michael Sperling: [43:11](#) But it's more the technical... The phones are generally good enough. It's did you have good lighting? Is more of the issue. So, we want to pay attention and let people know and, I think, be optimistic. And I will end here. Thank you very much.

- Dr. Laura Lubbers: [43:28](#) Terrific, Dr. Sperling. Thank you so much for that incredibly informative presentation. I know a lot of questions have already been addressed, but we will now start the Q and A session. So, if audience members have questions, please go ahead and submit them in the Q and A tab located at the bottom of the Zoom panel and click send.
- Dr. Laura Lubbers: [43:47](#) So, we will start digging into some of these questions. So, a couple of questions have come up regarding different types of epilepsy that cenobamate may be used to treat. For example, is this medication suitable for occipital lobe epilepsy?
- Dr. Michael Sperling: [44:07](#) It is approved and has been studied in all of the focal epilepsies. So, if you have occipital, or parietal, or frontal, or temporal, evidence exists that it works for focal epilepsy and occipital is a focal epilepsy. Is it good for generalized epilepsy, if you have Lennox-Gastaut syndrome, for example, or Dravet syndrome? Is it good if you have an idiopathic generalized epilepsy like juvenile myoclonic epilepsy or childhood absence epilepsy, or juvenile absence, or just generalized epilepsy with tonic-clonic seizures? It has not been studied in that. Studies need to be done.
- Dr. Laura Lubbers: [44:43](#) Okay. There was a similar question somebody is asking about frontal lobe epilepsy. So I [crosstalk 00:44:49].
- Dr. Michael Sperling: [44:49](#) Yeah, frontal lobe epilepsy is a focal epilepsy, absolutely appropriate.
- Dr. Laura Lubbers: [44:53](#) Okay. What other medications are good to be paired with cenobamate?
- Dr. Michael Sperling: [45:01](#) I am not a huge fan of pairing medicines. I do it more than I should, as do many doctors. But in the best of all possible worlds, you would be on only one drug because then you have less side effects. If you're going to pair it, however, drugs that work via a similar mechanism are probably not ideal because you're more likely to get side effects.
- Dr. Michael Sperling: [45:22](#) If you take a drug that's a sodium channel blocker already, and then a new drug is added, which also blocks sodium channels, you're more likely to have side effects. So you have to discuss with your doctors what's suitable for what you have. But drugs like lacosamide (brand name Vimpat), carbamazepine, which is Tegretol but basically Trileptal, and some others, like lamotrigine also (Lamictal brand name) are sodium channel blockers.

- Dr. Michael Sperling: [45:52](#) When you add cenobamate and you're more likely to get side effects. You can pair it, but I routinely have people start lowering their other drugs somewhat. Usually by, when they're going to start at 50 or 100 milligrams a day, depending on how much they're taking. Just start lowering the other drug to try to block side effects.
- Dr. Michael Sperling: [46:07](#) When you add cenobamate you're more likely to get side effects, but you can pair it. I routinely have people start lowering their other drugs somewhat--usually by 50 or 100 milligrams a day, depending on how much they're taking when they're starting--to try to block side effects. I tell them that if you start seeing side effects, you can start lowering it sooner. Drugs with a different mechanism of action--so levetiracetam (which is Keppra), brivaracetam (which is Briviact), perampanel (which is Fycompa)--they're probably going to be a bit less likely. There haven't been great studies on that.
- Dr. Michael Sperling: [46:29](#) Some analyses have been done looking at side effects and there have been some formal studies, but that's a general rule that one can follow. The details of the studies are almost irrelevant in some sense, because it's the dose that you're on that makes a difference more than anything.
- Dr. Laura Lubbers: [46:37](#) You've mentioned felbamate and that this is possibly viewed as a newer version of felbamate, but how does the effectiveness of cenobamate compare to felbamate?
- Dr. Michael Sperling: [46:54](#) Felbamate was studied in Lennox-Gastaut syndrome. There aren't formal studies in focal epilepsy so we can't really compare it quite as well. Now, many people, myself included, used it in focal epilepsy somewhat, but then felbamate was discovered to cause potentially fatal liver reactions and bone marrow reactions where people became profoundly anemic within a year of its appearance. So people use it very infrequently these days and mostly it's used in Lennox-Gastaut. So we don't have a good idea. We all thought that felbamate was a strikingly effective agent, however.
- Dr. Laura Lubbers: [47:31](#) Just to clarify, you mentioned the issues with Felbamate and liver toxicity. There is no worry about cenobamate in liver toxicity in this case?
- Dr. Michael Sperling: [47:43](#) You can do the numbers: 930 plus 1,339. We have over 2,200 people and there's been no significant abnormalities of liver reported with this. Does that mean that a less rare or less common reaction might not happen? It's possible. So, felbamate in the trials looked, say, for liver abnormalities also. It

wasn't until it started being prescribed that liver problems resulted.

Dr. Michael Sperling: [48:13](#) Keep in mind that when you start a new drug that just came out, we have reasonable evidence about it being effective. We have really modest evidence about safety. There's nothing gross and horrible, but if one person out of 5,000 has a serious liver reaction and a serious bone marrow reaction, you have to have 25,000 people get the drug before you can be reasonably confident that the rate is at least 1 in 5,000.

Dr. Michael Sperling: [48:38](#) If the rate's 1 in 50,000, a quarter of a million people have to have it. When drugs are approved after only 2,000 and 3,000 have had it, we know the risk is not large, it's going to be small, but it doesn't mean that there couldn't still be a 1 in a 1,000 or 1 in 5,000 or 1 in 10,000 reaction. Time will tell.

Dr. Michael Sperling: [49:00](#) We don't routinely order liver function tests when starting people on this drug. We just ask them how they feel and keep an eye on things. We don't order any blood tests with regularity because it's not that the blood tests really predict it. And if you have what's known as an idiosyncratic reaction, there's no evidence that monitoring in advance actually makes a difference. The body's exposed to it, something happens, and whether you take it for an extra one day or seven days probably doesn't make a difference. What's going to be is going to be at that point. And it's when people don't feel well that then we have to investigate more.

Dr. Laura Lubbers: [49:36](#) In terms of metabolic pathways, does cenobamate share a pathway with CBD? We know a lot of people are on CBD, whether it's the approved version, the FDA version, or medications or substances that are purchased at dispensaries. Is there any known interaction with CBD?

Dr. Michael Sperling: [50:01](#) A lot of people are taking it with CBD and products that contain CBD. Medical marijuana has many chemicals, one of which is presumably CBD. The enzymes in the liver that metabolize cenobamate also will metabolize CBD and other marijuana constituent chemicals. Does cenobamate alter the metabolism of CBD?

Dr. Michael Sperling: [50:29](#) Cenobamate does inhibit one of the enzymes within the liver that helps metabolize some compounds. It's a 2C-19 compound. There's a potential for an effect on that. How significant is it? We don't know, and there really haven't been great studies in people. In all those studies that were done, there's not a whole lot of measurement of CBD that we can know. This is one of the

things that needs to be studied. I'm sure there will be data that's out there.

- Dr. Michael Sperling: [50:56](#) In fact, I wouldn't be surprised that there's a paper or two published addressing this that I haven't noticed yet. In practice, we start a new drug, and if there are side effects that start to develop, it's common to start learning about other drugs and other medications. Again, for focal epilepsy, I would point out that there is no scientific evidence in humans that CBD has benefit. There's no data. People can try it. I have many patients who have given it a try, so give it a try see if it helps.
- Dr. Michael Sperling: [51:27](#) But there's actually no scientific data that it works. What the effect of CBD in people with focal epilepsy who have this drug is still needs further information and a large tail cross of people. Because they're not just on CBD, they're on usually one or two other drugs, or sometimes three other drugs. And it's the whole mixture of the gemisch that we need to understand that adding one more drug into the mix may not enlighten us as much as we'd like.
- Dr. Laura Lubbers: [51:59](#) Do you know if there are any studies on tuberous sclerosis and cenobamate, or if there's anything in the works?
- Dr. Michael Sperling: [52:06](#) Many seizures in tuberous sclerosis are focal. So I would expect that for focal seizures in tuberous sclerosis this will be beneficial. I don't think there are any formal randomized controlled trials like I showed you, but I'm certain that some people in tuberous sclerosis centers are starting to use this drug and tracking how their patients are doing. I would expect that we'll see some results relatively soon.
- Dr. Laura Lubbers: [52:32](#) Are there any reactions with warfarin (Coumadin)?
- Dr. Michael Sperling: [52:44](#) None that have been significant and been reported to date. I would still be cautious in the sense of checking the INR in people on warfarin when starting any new drug that can interact with liver enzymes because you can always be unpleasantly surprised. I would hope that most of the time we would be pleasantly surprised that it shouldn't make a difference with warfarin. But it's one of those things we want to keep an eye on.
- Dr. Laura Lubbers: [53:14](#) Do you have any recommendations for patient compliance in a digital world where there are virtual visits?
- Dr. Michael Sperling: [53:25](#) I'm not sure I understand the question. For digital compliance?

- Dr. Laura Lubbers: [53:32](#) For compliance, I think encouraging compliance.
- Dr. Michael Sperling: [53:34](#) For encouraging compliance, we talk to each other and we can talk to each other through computers or phones, which is how most of my patient visits are done during the pandemic. The vast majority are done that way. I think it's the same conversation we have. One of the things that we, as doctors, have to do is understand our patient's motivations.
- Dr. Michael Sperling: [53:58](#) In my experience, there are three main reasons people don't take their drugs. The most common is it bothers them. They have side effects from it so they'll skip a dose now and then because they don't feel well. If doctors don't ask about that, we don't know, and then we don't adjust. Or you don't tell me that you're skipping it every now and then because it bothers you because you don't want to disappoint me. You're not disappointing me. I want to know if you're having a problem; let me know and I'll adjust your doses. We want you to feel well. The idea is to take the pill, but otherwise not notice that it's there.
- Dr. Michael Sperling: [54:31](#) In my experience, I think a lot of it has to do with the drugs causing people not to feel well. They don't want to embarrass their doctors by making them feel bad that I gave them a drug that makes them feel bad. It's fine. I won't feel bad. I want you to feel well. Tell me. That's one reason.
- Dr. Michael Sperling: [54:45](#) The second reason, unfortunately, is affordability. We live in practically the only advanced country in the world--advanced economy, I should say-- advanced economy where healthcare and drugs aren't covered and drugs can be very expensive. Insurance companies have learned that your copay can be \$10 a month for the generic, and they can make it \$200 a month or a \$100 a month if you're on the brand.
- Dr. Michael Sperling: [55:12](#) If drugs are on brand, suddenly it's too expensive and people wind up skipping doses or taking less than they should. So, cost makes it different. Again, have a conversation with a doctor. If it's too expensive, you need to be on a different drug. Some of the companies have programs to provide drugs for free for people who have certain income qualifications who otherwise couldn't afford it.
- Dr. Michael Sperling: [55:37](#) We need our health system fixed where people with chronic conditions don't have to pay money to take drugs. Right now, I have patients who are on atorvastatin (Lipitor) for cholesterol lowering. If you're on a generic, there's no copay at all. If you

have epilepsy, you really shouldn't have a copay. There should be no barriers. So, that's the barrier.

Dr. Michael Sperling: [55:57](#) The third barrier--which I've been guilty of too--is that every once in a while, people forget, right? We all forget. We stay up late. We were out late in the pre-pandemic world more than now, but we're out late, we're doing something and we go to bed and we forget our medicine. We wake up in the morning, we're rushing, we're late for work. We have to go somewhere. We forget our medicine.

Dr. Michael Sperling: [56:17](#) That, you can try to do something about. I always encourage people to brush their teeth twice a day and keep your medicine with your toothbrush next to the toothbrush. It's there in the morning, it's there at night, if you're doing it once a day or twice a day. Set an alarm on your phone to ring. Set two alarms. One, if you're supposed to take your medicine at 10:00 at night, have it ring at 10:00 and then have it ring at five after 10:00 to nag you. You'll get in the habit and then you won't need the alarm anymore. It just becomes automatic.

Dr. Michael Sperling: [56:44](#) So there are a few techniques could be done. Most important, frankly, is to make sure that the drug doesn't bother you.

Dr. Laura Lubbers: [56:53](#) That's excellent advice. We have a tremendous number of questions that have come in more than we can possibly handle in this hour-long webinar. So, what I would like to do is ask Dr. Sperling if perhaps he could consider answering some questions. We'll also perhaps reach out to others who could also address, I'm looking at something like 50 questions in the queue.

Dr. Laura Lubbers: [57:20](#) This was clearly a very compelling and a very exciting opportunity for our community to learn about this new medication that is now available that looks very, very promising in the trials that have been performed so far and we'll certainly learn more as it gets into the epilepsy community as a treatment. Dr. Sperling, I want to thank you for your presentation. It was incredibly informative and your ability to answer such great questions.

Dr. Laura Lubbers: [57:53](#) I also want to thank SK Life Science for providing support for today's webinar, and of course, our audience for the incredible engagement that we have seen. So, if you have additional questions, please do forward them on, we will do our best to address them. If you would like to recommend any future webinar topics, we are always interested in hearing your thoughts on what you would like to learn.

Dr. Laura Lubbers: [58:18](#) If you also want to learn about more of CURE Epilepsy's research programs or their future webinars, please visit our website or our email address at research@cureepilepsy.org. Please also be sure to register for our next webinar on February 8th at 11:00 AM Central Time, which will recognize International Epilepsy Day.

Dr. Laura Lubbers: [58:40](#) The webinar is entitled International Disparities in Epilepsy Care: Social and Economic Effects of Epilepsy in Sub-Saharan Africa. And it will be presented by Dr. Gretchen Burbach while she is on her way to her research location in Zambia, East Africa. So, thank you again to all. See you at our next webinar.