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Elevating the Standards of Care in Schizophrenia

### Announcer Introduction

You're listening to *NeuroFrontiers* on ReachMD, and this episode is supported by Sunovion Pharmaceuticals Inc. and Otsuka Pharmaceutical Co. Here's your host, Dr. Charles Turck.

#### Dr. Turck:

Welcome to *NeuroFrontiers* on ReachMD. I'm Dr. Charles Turck, and joining me to discuss the importance of elevating the standards of care for our patients with schizophrenia is Dr. Philip Harvey. Dr. Harvey is the Leonard M. Miller Professor of Psychiatry and Behavioral Sciences, Vice Chair for Research, and Director of the Division of Psychology at the University of Miami Miller School of Medicine. Dr. Harvey, thank you for being here today.

#### Dr. Harvey:

Oh, thanks for having me.

#### Dr. Turck:

Well to start us off, Dr. Harvey, would you give us a brief overview of our current therapeutic approaches to schizophrenia?

#### Dr. Harvey:

Well, the current therapies for schizophrenia are very good at reducing psychotic symptoms in most patients. The clozapine as a treatment alternative works with a lot of people who don't respond in terms of antipsychotic efficacy. But our treatments for schizophrenia on a pharmacological basis don't address two critical things: one of which is negative symptoms, the other of which is cognitive impairment. And both these things are targets for drug development that have been going on for a number of years.

#### Dr. Turck:

Now digging into that just a little bit more, if we were to zero in on the tolerability of the current treatment options, what are some of the most common adverse effects associated with them?

#### Dr. Harvey:

Well commonly, the challenge with current antipsychotic medications are either extrapyramidal side effects, which happens with drugs that blockade the dopamine receptor too aggressively, and also weight gain, which is a challenge with many of the current antipsychotic treatments where some people gain a considerable amount of weight with their treatments.

#### Dr. Turck:

And with regard to efficacy, do we face any challenges due to inadequate response to therapy?

#### Dr. Harvey:

Well, the vast majority of patients who take their medication or who are treated with long-acting injectable medications have a good response, maybe 60 to 70 percent. So the level of efficacy seen in adherent patients is probably as good as the treatment of most other medical conditions.

And as we said previously, the other challenge is in the other 30 percent of people who don't respond well. Probably a third of them respond well to clozapine, but clozapine is markedly underused. Clozapine also is the medication that has the most weight gain potential.

#### Dr. Turck:

And with all that in mind, what kind of burden do adverse events and suboptimal treatment responses represent to our patients?

**Dr. Harvey:**

Well once again, it's a little challenging because a lot of patients are nonadherent. They don't understand the reasons that they're being treated. So the burden comes from, in fact, relapse more commonly than side effects. People stop their medication, they routinely relapse, and wind up having to get treated either at an emergency room or in a hospital. And so consequently, the burden of the illness is the cyclical relapse and retreatment that we see in a lot of patients.

**Dr. Turck:**

For those just tuning in, you're listening to *NeuroFrontiers* on ReachMD. I'm Dr. Charles Turck, and I'm speaking with Dr. Philip Harvey about the efficacy and tolerability limitations of present schizophrenia treatment options.

So, Dr. Harvey, given the challenges related to current treatment approaches, are there any therapies on the horizon that might help address the unmet needs of our patients with schizophrenia?

**Dr. Harvey:**

Well, there are drugs in development for the treatment of both negative symptoms and cognitive impairments. Current antipsychotic treatments don't do much, if anything, for them. And so as a consequence, it's really important to develop other interventions. So there are drugs in development targeting negative symptoms and targeting cognitive impairments. It looks like there's not much crossover and that drugs that improve cognition don't necessarily improve negative symptoms and vice versa. So it may wind up that we have a multi-pronged therapeutic approach to the treatment of schizophrenia at the end of the day.

**Dr. Turck:**

And which of those treatments are you most excited about and why?

**Dr. Harvey:**

Well, they're different treatments with different targets. And so I think that what we need to focus on is that from the treatment of cognition side, the muscarinic agonist treatments are probably very good with high potential because we've known for a very long time that if you can stimulate that receptor, you can improve cognition.

Previous challenges with M1 agonists have included significant gastrointestinal side effects and lack of tolerability. So the recent advances in medicinal chemistry have actually allowed for an M1 agonist that is actually blockaded from having adverse events in the periphery.

The GlyT1 treatment direction is very focused on schizophrenia and the glutamatergic system. The results were good in the phase 2, and we'll have to see if it works out in phase 3.

**Dr. Turck:**

And before we close, Dr. Harvey, do you have any final thoughts you'd like to leave with our audience today?

**Dr. Harvey:**

Well, I think it's very important to consider the fact that antipsychotic medications that are currently available work fairly well. A lot of people have lack of adherence that leads to relapse. But that's not necessarily always because of side effects. But the most important thing to keep in mind about current treatments is they don't treat the major causes of disability in schizophrenia. There's been an effort for the last 20 years at least to identify treatments that work for that. We're closer in some ways than we had been at any point in the past. But none of these drugs are still approved by the FDA for either cognitive impairment or negative symptoms.

**Dr. Turck:**

Well as those final thoughts bring us to the end of today's program, I want to thank my guest, Dr. Philip Harvey, for joining me to take a look at some of the present challenges in treating schizophrenia and how emerging therapies might help address them. Dr. Harvey, it was great having you with us.

**Dr. Harvey:**

Thank you.

**Announcer Close:**

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