Transcript Details

This is a transcript of a continuing medical education (CME) activity. Additional media formats for the activity and full activity details (including sponsor and supporter, disclosures, and instructions for claiming credit) are available by visiting:
https://reachmd.com/programs/cme/spanning-the-spectrum-of-vvc-diagnosing-and-managing-acute-and-recurrent-disease/14660/

Released: 12/12/2022
Valid until: 12/12/2023
Time needed to complete: 30 minutes

ReachMD
www.reachmd.com
info@reachmd.com
(866) 423-7849

Spanning the Spectrum of VVC: Diagnosing and Managing Acute and Recurrent Disease

Announcer:
Welcome to CME on ReachMD. This activity, entitled “Spanning the Spectrum of VVC: Diagnosing and Managing Acute and Recurrent Disease” was presented during Omnia Education's Women's Health 2022, Beyond the Annual Visit.

Prior to beginning the activity, please be sure to review the faculty and commercial support disclosure statements as well as the learning objectives.

Dr. Krychman:
Welcome, everybody to Omnia Education, Women's Health 2022 Beyond the Annual Visit. I'm Dr. Michael Krychman, and would like to welcome you to our talk today called Spanning the Spectrum of VVC, Diagnosing and Managing Acute and Recurrent Disease. I am a Clinical Health Professor of OB/GYN in the department of OB/GYN Division of GYN Oncology at the University of California, Irvine, located in Orange, California.

These are my disclosures. I'm the consultant and speaker for Scynexis.

Here are the learning objectives for today's educational activities. So after the activity, the participants should be able to be better able to diagnose the symptoms, exam findings, and discuss the diagnostic tests for VVC. They will be able to better define the criteria by which VVC infections are defined as either uncomplicated or complicated. And describe advantages limitations of the current therapeutic interventions for acute VVC, as well as describe the advantages, limitations of the current and emerging therapeutic interventions for recurrent VVC. At the end of the educational activity, we will have a brief question and answer period. So should you have any questions or concerns, please feel free to mark those down, and we will be certain to address them after the program.

Let's jump right in and talk about epidemiology and the prevalence of VVC and recurrent VVC. Well, you know, this is the bread and butter for women's healthcare providers, up to 75% of women, during their lifetime will experience an episode of VVC, and about 80% of those have multiple episodes. We know that about 35% have more than 5%, but more than 5 episodes, sorry, during their lifetime, and about 10% have recurrent VVC, which is defined as more than 4 episodes per year. And you'll see that in some references, they'll use 3 or 4 episodes. And again, it depends on the reference that you're using.

So as we've seen, the prevalence of VVC and recurrent VVC is not insignificant. And for me, I think this slide is quite important and really essential. And I think the concept that it's not just another yeast infection is quite important and really critical for both healthcare clinicians and patients as well. We know that VVC and recurrent VVC has far-reaching implications and has a direct impact on quality of life. And again, here you can see psychologically it may help - may affect mood, it may cause stress, depression, anxiety, it may impact confidence and self-esteem. We know women have a severe symptomatology, you know, of the burning and itching and pain that it will interrupt or impact sexual function in sexual satisfaction, as well as, you know, I have women that cannot participate in social events because of this constant irritation and burning in the vaginal and vulvar area. So it may even limit this physical activity or contact. We know that women are concerned, they're embarrassed, they don't want to talk about it, they minimize their symptoms as well. And again, I think this prevailing concept that it’s just another yeast infection really has to go by the wayside, because it is quite impactful for women. And for many years, we've only had very limited things in our war chest to help combat this.

So again, as we go through the presentation, I think it's quite important for everybody to remember that this is a very impactful, serious condition that can be pervasive and can really affect a woman's overall quality of life, her mood, her relationship as well.

There are certain challenges with VVC and recurrent VVC. You know, I think the issues are related to diagnosis and using the certain codes. It's underrecognized. And again, women themselves have trivialize the disease, the impact, as well as healthcare professionals. There are challenges from acute, recurrent, or persistent disease. And also, you know, we've seen that some women will actually even have this misperception that minimal symptoms are even acceptable, that there is something that they can have, you know, in terms of a little bit of burning and itching. And that's really normal. But again, we're seeing that that is changing with new data and new research in this.

Treatment has very much shortcomings. We've seen a lot of these issues, develop over COVID over the past several years. There's a lot of self-treatment, a lot of overuse, incorrect use, and not every burning and itch is a VVC. And again, this perception of discomfort of discussing symptoms. Women's healthcare professionals have been using telehealth, and we've been diagnosing over the phone. And again, this concept of see and treat, overtreating, misdiagnosis. And we know that normal discharge can really be abnormal, and abnormal discharge can appear normal. So really, this evaluation and assessment certainly is quite critical.

In management, we've been limited. You know, until recently, we had no approved treatments where we're currently be seen now we do have one FDA approved product. There were very few options all in the same class of medications. There was issues related to adverse effects, contraindications. And again, this off-label use of a lot of products that really had limited data or conflicting data as well. And as well, for outcomes, we've seen that there has been high recurrence and this concept of, you know, a variety of different opportunities for maintenance therapy until very recently, where we've had improved product for recurrent VVC. So the landscape certainly is changing, certainly has its challenges as well.

What have we been doing for diagnostic tests? Well, you know, when I was a resident, we used to do microscopy, those have a lot of limitations, 40 to 70%, sensitivity. Again, overdiagnosis, underdiagnosis. I work in an academic center, and very often they're not doing microscopy at all, and not learning how to do wet mount. So this concept of see and treat is, you know, very much persistent.

We've had issues related to cultures as well. and again, this is perceived as the gold standard. But again, there may be limitations related to time to get this back, prior authorization and may be limited by pretreatment as well.

And then there's certainly the advanced testing, which includes DNA probes and PCR. And again, this may give you results more immediately, but may have lower sensitivity, and again, cost, coverage and it may also miss certain species. And again, we are certainly seeing the nonalbicans candidiasis increasing for a variety of different reasons. And we certainly can talk about that shortly.

What are the risk factors? I mean, and you can see here that there's a multitude of risk factors listed on this slide. Very often they're linked to a change in the vaginal pH. we know that hormonal changes can certainly impact the vaginal biome. You know, diabetes, genetic predisposition, certainly we're at its infancy, learning that there may be a genetic predisposition for some women to develop a yeast infection. And again, hormonal changes, as well as immunocompromised conditions. I'm seeing very - a lot of women who have COVID candidiasis, which is really they recovered from COVID, they're on chronic steroids, they may have some immunosuppression. Their respiratory issues may not be problematic, but then again, their candidal symptoms may be more of a concern.

I think the important thing is to put this in context that at least more than 50% of women have no known risk factors. So, while we do have some risk factors, we really understand that there are many women that have no known risk factors. So, maintaining a high level of clinical suspicion is certainly very, very important, when you see a woman who comes into the clinic, comes into your center with complaints of vaginal discharge as well.

So, let's run through the pathophysiology and look at the concept of sporadic VVC versus recurrent VVC. And again, we talk about asymptomatic colonization of the vagina. And what I'm calling as pH disrupters, very common blood, semen, they may alter the vaginal pH, you may have an overgrowth, even medications. There's a whole multitude of medications that will upset the natural balance of the vaginal biome. We know that pre and postmenopausal women have different vaginal conditions that may actually be impactful for development of a yeast infection. Then you may get a sporadic VVC. It's a trigger-based overgrowth. Again, not belittling or minimizing the importance of a genetic predisposition, some women will be much more prone, others may not. And again, once you have that acute treatment, there's a whole variety of different treatments, whether they're oral, or topical, variety of different days, we have from 1 to 3 to 5 to 7 days, depending on clinician preference, depending on the treatment that they are chosen.

And then for some reason, no longer - there may not be triggers, maybe some genetic factors, there's recurrence. And again, this is kind of the lifecycle of what happens. There's a subset of women that are prone to recurrent VVC, and this is what they may experience, which may be quite impactful and quite problematic.

And then we talk about maintenance therapy. And again, I think if you look at what is going on in the community, there's a whole variety of things that are being done

currently right now, whether it is long-term fluconazole use, whether it is topical suppression use, whether it's probiotics or things like off-label boric acid. So, and again, the maintenance therapies are not 100%, and some of those patients will actually experience recurrence.

So again, this kind of the lifecycle of what has been transpiring with sporadic and recurrent VVC conditions. So, you know, what I tried to do here is kind of break it up into more of a, you know, bite-sized issue. When you talk about the frequency, it's really infrequent versus 3 or 4 episodes for recurrence. Triggers, you may have a known trigger, chronic antibiotics, intercourse, diabetes, estrogen. And in that respect, you may have avoidance of triggers may be quite helpful. So lifestyle impact may be really important as well.

For recurrent, you'll see there's very often no triggers or modifiable risk factors that can be impactful. And genetics may play more of a role than we actually had assumed. There's multiple treatments, short-term oral versus topical. And again, really about clinician expertise, what they choose, the medication of choice and the duration. These are really for sporadic. But again, for recurrent, we really didn't have anything until very recently. Now we have one FDA-approved treatment. There's long-term greater than 6 months of weekly oral fluconazole, which has kind of gained popularity from expert opinion.

The outcomes, really, we can see there's resolution for the sporadic. But for those that are on no maintenance therapy, there's really about 70% recurrence within 6 months. And if you have maintenance therapy, believe it or not, up to 50% recurrence after 12 months of stopping their maintenance therapy. So, we're really, you know, slightly impactful, not really making a huge dent, but again, really understanding that there's long-term issues really with quality of life, and impact in terms of symptomatology for those who are suffering from recurrent VVC.

So what about the treatments? We can see here azoles typically for the acute. These are all in the same class, as well as there's two orals, there's fluconazole and ibrexafungerp, which was recently approved in 2021. And again we'll talk about that in greater depth shortly.

For recurrent, we know that there's one recently approved just several months ago, oteseconazole. It was newly approved for recurrent VVC, and we'll jump into that in depth. And again, there's unapproved medications. We've been using oral fluconazole weekly, we've been using boric acid, probiotics. And as we talked about before really limited data as well. But again, we know from clinical experience that some of these things have been working quite well for our patients. Ibrexafungerp does have a PDUFA date in November of 2022. And we'll be looking to see whether or not this will be approved for recurrent VVC. And some of the compelling data will actually be presented shortly when we talk about ibrexafungerp as one of the newer medications, as well as oteseconazole newly approved. So very interesting time to be in healthcare, very interesting time to be in women's healthcare. And as well, very interesting time to be looking at VVC and recurrent VVC because the landscape is changing for the first time in many, many, many years.

What about uncomplicated versus complicated? And I think this is really important. Uncomplicated, you will have presence of all of the following. So infrequent or sporadic, it's usually candida albicans, mild to moderate symptoms, and you have a competent immune system. And very often, I, you know, in my experience, as I'm a tertiary referral, these uncomplicated ones very often are addressed by the patient themselves. They are going to their local community pharmacy, they're self-medicating, they're only coming to you when there's recurrent or persistent symptomatology, or when the symptoms are really more moderate to severe. So complicated ones really are really the bread and butter of what we're seeing in the office. And this may be recurrent, this may be people who have moderate to severe symptoms, or when we have complications, like uncontrolled diabetes, HIV, COVID, on steroids, or when we talk about the non-albicans candidiasis, like the glabrata, the Krusei. We're seeing more of those species when we're doing cultures. And again, I think that's a really important concept. And typically, if someone is suffering repetitively in my clinical experience, we're using 3, I don't wait for a 4th infection. I really start with maintenance therapy soon thereafter. So again, if it's uncomplicated versus complicated, I think it'll depend on how you evaluate looking at these criteria as well as choosing your therapeutics.

Uncomplicated, you can see here, topical 1 to 5 days or oral fluconazole. And again, I think it's really interesting, you know, I ask my residents, you know, what's the dose of fluconazole? They say, you know, 150 milligrams, take 1 now repeat in 72 hours, and dispense 3. And I said, 'No, it's one dose.' And these are for uncomplicated. So we're really knowing that sometimes there's some limitations from our current existing treatments.

When you have complicated, you're really extending that treatment, 5 to 7 days. You know, the CDC goes to 7 to 14, ACOG 10 to 14, or you're giving multiple doses, the fluconazole every 72 hours. And typically, we're seeing 2 to 3 doses, followed by maintenance, which would be weekly for 6 months. And again, really evaluating and looking at liver functions, and really monitoring those because chronic medications certainly have an impact, and we really need to monitor these women, as well.

So this is what we've been doing. And again, you know, for many years, all we had was azoles. And there certainly limitations, right, the non-albicans candidiasis. There's increased resistance, there is poorly response to the azoles. There's low tissue to plasma ratio, and they're less active in the lower pH. And my clinical experience, I have a lot of women who have underlying chronic conditions. They may have breast cancer, and they may not be on local estrogen, so they may have a tenuous vaginal pH, and these traditional azoles have not been working.

Also, again, we know that there are some issues with the local and systemic tolerability. Very often some of these topical medications may exacerbate burning and itching, as well as other concerns.

So, again, I think that there - the pervasive concept was, you know, we didn't really have much in our war chest to fight a VVC until very recently. And broad and frequent use of the azoles may have contributed to the increase in the non-albicans candidiasis and the fluconazole-resistant candidal species. Because all we did was if it didn't work, we gave more of the same and more of the same and more the same. And that is really challenging when you don't really have more in your war chest. And I'm excited to talk to you about some of the newer things.

So one of the newer medications, you know, oteseconazole is all first and only FDA approved medication for the treatment of recurrent VVC. It was recently approved April 26th of 2022. And here's the indication, to reduce the incidence of recurrent vulvovaginal candidiasis in women with a history of recurrent VVC, who are not of reproductive potential.

And again we're going to be giving a general overview of these medications. And I would encourage everybody to get a copy of the, you know, prescribing information, the product insert. The prescribing information is certainly available online for download. And it really is worth a good read to get a good download and get a better understanding. So, we're going to give you the you know, the overview, but again, I would encourage everybody to look at the PI as well.

So again, oteseconazole the indication to reduce the incidence of recurrent VVC in women with a history of recurrent VVC who are not of reproductive potential, contraindicated in females of reproductive potential, pregnant, or lactating, or are hypersensitivity to oteseconazole. It is a first in class. And it really is - works as the mechanism of action, it really - it inhibits the fungal CYP51 enzyme, which is, you know, involved in the cell membrane formation. This leads to potential fewer drug-drug interactions. And, you know, and it may inhibit certain enzymes that are listed here. The peak concentration 5 to 10 hours. And again you can take this medication with or without food. And again, half-life really is 138 days. And again, going on the basis of 5 times half-life, your drug exposure window is 690 days. And this is roughly, you know, a little bit less than 2 years. So, again, I think that's something to think about, and we'll certainly talk about it in a few slides as well.

Here's the high-level results. The FDA approved the product based on positive results from three phase 3 clinical trials, there were two global pivotal VIOLET trials and one U.S. focused ultraVIOLET study, 875 patients, 232 sites, 11 countries. And these are the high-level results from the global VIOLET and the U.S. ultraVIOLET. study. So, in the global VIOLET study, 93.3% and 96.1% of women with recurrent VVC who received oteseconazole did not have a recurrence for the 48-week maintenance period. So 48-week maintenance period compared to 57.2 and 60.6 of - percent of patients who receive placebo. Now, in the ultraVIOLET trial, this was a two-phase trial, we'll show you a little more of that in depth. About 90% of women with recurrent VVC, who received treatment, cleared the initial infection and did not have a recurrence for the 50 weeks maintenance period, compared to about 57% of those who receive fluconazole followed by placebo.

So we see here on this slide, this is oteseconazole, phase 3 trials for recurrent VVC. This was the VIOLET trial, which were the two global studies. And it was an open-label acute treatment for all patients, right, they received fluconazole 150 milligrams every 72 hours for 3 doses on day 1, 3, and 7. This was the open-label induction phase. And then 14 days later, if they had a VSS score of less than 3, they were randomized to 2 to 1 to either receive oteseconazole 150 milligrams daily for 7 days, then weekly for 11 days, or they had a matched placebo. And that was the maintenance phase.

Just a few words about the VSS score. So VSS score is the Vaginal Signs and Symptoms score. And that really is a composite score of signs and symptoms assessed by the patient, as well as the clinician. So again they were assessed, if they had their score less than 3, they were randomized to 2 to 1 to either receive oteseconazole or a matched placebo in the maintenance phase.

And we see here the results, 93.3% and 96.1% of women in the re - with a recurrent VVC who received oteseconazole, didn't have a recurrence for 48-week maintenance period compared to 57.2 and 60.6 of patients who received placebo. So again, interesting results from the global VIOLET two studies here.

Now this is the ultraVIOLET study, oteseconazole. It's the phase 3 trial for recurrent VVC. You had women who had a history of recurrent VVC of one episode, they came back in, they had symptoms and they received oteseconazole, and it's really 1,050 daily over

2 days, but the way it was broken up is 600 milligrams on day 1, and on day 2, 450 milligrams. And you see in the brackets here that it says 4 times 150 milligrams, well that's how the pills are supplied or 3 times 150 milligrams on day 2. In addition, versus the fluconazole group, they received 150 milligrams every 72 hours for 3 doses. This was the induction phase, so they either received oteseconazole or fluconazole. Again, returned 14 days thereafter with acute resolution. Those that weren't on oteseconazole received oteseconazole 150 milligrams weekly for 11 weeks, versus those that were on fluconazole received placebo. And that was in the maintenance phase.

So again, focus on the purple box on the slide, about 90% of women with recurrent VVC who received treatment cleared the initial yeast infection, didn't have a recurrence for 50-week maintenance period compared to 57.1% of those who receive fluconazole followed by placebo. And these results were statistically significant.

So again, what about the safety outcome? And again, I would encourage everybody to review the PI. The most frequent AE greater than 2% among treated in trials 1, 2, and 3, headache, including headache migraines, or sinus headache at 7.4%, nausea at 3.6%, and a very low discontinuation rate less than 1%, 0.2%. And you can see here.

I think an interesting point of discussion, and I think something that we need to kind of further evaluate and really assess, is the mean age for the patient population was 34 years with a range of 16 to 78, with 84% of the patients aged 18 to 44 years, and 16% of the patients aged 45 years and older. So females of reproductive potential were included in the clinical safety data. Remember, it's contraindicated in females of reproductive potential due to the risk of embryo fetal toxicity, and the potential drug exposure. And safety and efficacy is not established in premenarchal pediatric patients. And again, what the label reiterates is there are insufficient numbers of patients greater than 65 years of age or older to establish a specific response.

Let's shift gears and talk about ibrexafungerp. This was approved in June of 2021. It's the first and only oral non-azole fungicidal treatment for vaginal yeast infections. Now remember the other azoles are fungistatic. So this is fungicidal. The azoles previously discussed were fungistatic. So it again, I would encourage everybody to download the product label and review the details in depth because this is just a general high-level overview.

So what is the indication? It's indicated for the treatment of adult and post-menarchal pediatric females with VVC. They do have a PDUFA date for their data that was submitted for recurrent VVC, and I'll show you some of the data from the acute program that will help you convince that they are probably likely to get approval. And again, that's my opinion. I don't work for the FDA. But again very encouraging data. And we're all kind of sitting on pins and needles till November 30th of 2022. And the caveat is, if you are watching this video after November 30th of 2022, I would encourage you to look at some of the additional slides that we may have, because this may change as well.

What is it contraindicated? It's contraindicated in pregnancy use in specific populations who have a hypersensitivity to ibrexafungerp. And they have the caveat to prior to initiating treatment, you have to verify pregnancy status. And they're very clear on the wording, verify pregnancy status in females of reproductive potential and advise the patient to use effective contraception during treatment and for 4 days after the last dose. And 4 days after the last dose, if we skip down to the bottom of this slide that's related to the half-life of 20 hours.

And again, it's a first in class fungicidal triterpenoid. It's a glucan synthase inhibitor, also affecting the fungal cell wall. It's eliminated by the biliary excretion, and again can be taken with or without food, half-life of 20 hours as well. And that's why you have five half-lives, which is roughly 4 days after the last dose for contraception.

It had a phase 3 trial for acute VVC. So, there was two randomized placebo-controlled clinical trials, trial 1 and trial 2, identical design, conducted to evaluate the efficacy and safety of a single daily dose of 600 milligrams. Now again, 250 milligrams per dose and you had 1 dose, and then 12 hours thereafter, you had another dose. So, it's a 1-day treatment for acute VVC. So, you had symptomatic, then they were randomized either they received placebo. So, they received 300 milligrams PO BID for 1 day or matched placebo, and then looked at the endpoints.

And here is, I know this is a busy slide, but we'll go over it a little bit in detail. You have graph 1, 2, and 3.

Graph 1 really is the primary endpoint, which is the complete resolution of VVC signs and symptoms at day 10. And you can see in the light blue, you have 50% and 64% in trial 1 and trial 2, versus 28 and 45 in placebo. And remember, this was a VSS score of zero, so no symptoms at all.

Moving on to graph 2 in the middle. You will see this was mycological eradication, and those that received a negative culture at day 10. And again, light blue lines are your focus, 50 and 59, trial 1 and trial 2, verses 19 and 29, respectively.

The last graph, graph 3, is probably for me one of the more important slides. This is really discussing what I would say sustained

resolution at day 25. So again, sustained resolution of symptoms at day 25. You have trial 1, and trial 2, and ibrexafungerp 60% and 73%, versus 44, and 49, respectively. So, you can see here the concept that they were thinking. They have good sustained resolution at day 25. Perhaps this may be something we need to study for recurrent VVC that people can be dosed on, you know, what we're talking about, is a monthly basis. So we'll briefly talk about some of that as well.

Moving on to the safety data. And I think, again, if you look at the PI, which I would encourage everybody to do every drug certainly has positives and negatives, we can see here, predominantly GI issues with diarrhea, nausea, abdominal pain, and vomiting being the most significant. But again, if you look down into the fine print, only 0.4% discontinued treatment, one for vomiting and one for dizziness. So very well tolerated. But again, I think very important to mitigate these issues, is really to dose the medication with food. And that's what I've been advocating in my clinical experience is really to dose whatever medications you're giving, that may have an impact in AEs is really with food as well.

What about the status update? So, we talked about the PDUFA date November 30th, 2022. And just as a caveat, if it is approved, it will be the first and only approved therapy for both acute treatment and prevention of recurrent VVC.

We look at the CANDLE study. These were the data that was published, you can look at some of the research online. And again, efficacy and safety were demonstrated you know, defined as subject to having a test of cure evaluation, no mycological proven presumed or suspected recurrence of VVC up to week 24. It showed efficacy demonstrating, you know, no mycological proven recurrence. And again, there was no safety issues identified.

And you can see here from this the ITT population, this gives you more of it in graphic form. You can see the endpoints on your left-hand side, and ibrexafungerp versus placebo here. You know, clinical success, no recurrent mycologically proven presumed or suspected at 24 weeks, you have 64% versus 53.1% in placebo. And then you have no mycological proven recurrence, a tested cure at 24 weeks.You have almost 71% versus 58.5%. Clinically success at follow-up and this was at 36 weeks and you have almost 58% versus 46.2%, and no mycological proven recurrence at the follow-up at week 36. Again, 65.4% versus 53.8%. So again, this is kind of a snapshot peek view of some of the data that has been submitted.

So, you know, just to summarize, I think, you know, these are the key takeaways. You know, acute VVC is underrecognized both by patients and clinicians, it's frequently undermanaged, and it's really not a trivial disease. There are far-reaching implications. And, you know, I think it's really exciting that we have newer medications, newer classes, newer opportunities, new things in our war chest to help really combat a really prevalent common condition that is quite impactful for a lot of women. We need to have a better understanding of what we're seeing in the trenches in our offices and what's going on in the local drugstore as well. The uncomplicated versus complicated.

You know, we've only had one really class of drugs, we've really only really looked at, you know, the azoles, we've only had one opportunity for almost 30 years until very recently. And I think it's really important to recognize that even though we have new things, it doesn't mean that we have to throw out the old just because we have the new. I think we need to recognize that fluconazole, ibrexafungerp, oteseconazole, they all have unique qualities. And what I mean by unique qualities, I think as clinicians, we need to do a detailed analysis of half-life, concentration in vaginal tissue, increased potency against candida species, the non-albicans candidiasis, the potential for drug-drug interactions. More of our - more and more of our patients are taking multiple drugs. And what is going to happen with recurrence rates, and then choose appropriately. And again we also need to think about, you know, cost consideration coverage, a whole lot of other things that go into medical decision-making. But I think when you partner with your patient, you really can have some key successes. And having more in your war chest is always good to choose from.

I think the landscape is changing for treatment, it's dynamic, it's changing, we need to keep up with therapeutics. And, you know, and as we span the spectrum of VVC activity, clinical approaches will - and guidelines will continue to evolve, novel therapeutic options will be met, clinical needs will be met. But ultimately, we'll be providing, you know, the best possible care for our patients to minimize suffering, and really improve overall quality of life.

So with that, I'll conclude. I want to thank everybody for the opportunity to speak with you today. I look forward to some questions. And please feel free to address those. Thank you so much.

Announcer:
You have been listening to CME on ReachMD. This activity is provided by Omnia Education.

To receive your free CME credit, or to download this activity, go to ReachMD.com/Omnia. Thank you for listening.