

Transcript Details

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Assessing the Evidence for GLP-1 Receptor Agonists in Psoriatic Disease

Announcer:

This is *On the Frontlines of Psoriasis* on ReachMD. Here's your host, Dr. Mary Leuchars.

Dr. Leuchars:

This is *On the Frontlines of Psoriasis* on ReachMD. I'm Dr. Mary Leuchars, and joining me to discuss the potential impact of GLP-1 receptor agonists on psoriatic disease is Dr. Jeffrey Cohen. He's the Director of the Psoriasis Treatment Program and an Associate Professor of Dermatology and Biomedical Informatics and Data Science at Yale School of Medicine. Dr. Cohen, thanks so much for joining me today.

Dr. Cohen:

Thank you for having me. It's a pleasure to be here.

Dr. Leuchars:

So if we start with the big picture, Dr. Cohen, what do we currently know about the intersection between psoriatic disease and metabolic disease, and why is that important to think about when caring for these patients?

Dr. Cohen:

So there are a few things we know and that we've known for many years about psoriatic disease and metabolic disease that are important for all dermatologists to be aware of.

The first is that psoriasis and metabolic disease are very strongly linked together. There's lots of very strong epidemiologic data that helps us understand that individuals with psoriasis are at an increased risk for many metabolic disorders. And this includes things like obesity, hypertension, and diabetes, and it actually translates to outcomes. So we know that individuals with psoriasis are at an increased risk of a heart attack, stroke, and actually even cardiovascular death. And that is when you control for other factors that contribute to these outcomes. And so we are beginning to really see the picture, and we've seen over years the picture that psoriasis is not just a skin disease, but is actually a systemic inflammatory disease, and that this systemic inflammation has important implications for cardiometabolic outcomes and other metabolic diseases.

We also know that some of these metabolic diseases, like obesity and diabetes, are independent risk factors for the development of psoriasis and for psoriasis severity. So when we think about psoriasis and psoriatic disease, obviously we think about many different aspects of this. We think about the skin, we think about the joints, and we also think a lot about comorbidities. And these metabolic comorbidities are really front and center to a lot of what we should be thinking about.

And for many patients with psoriasis and psoriatic arthritis, their dermatologist or rheumatologist may be the doctor that they actually interface with the most. They might see a primary care physician once a year or they might not, but there's strong data to suggest that some of the interaction that they have with the medical system is strongest with people who are managing psoriatic disease as opposed to other aspects of their healthcare. And so that puts us in a very interesting position to be able to try to catch some of these metabolic comorbidities and direct people to appropriate care before they might otherwise get there.

For example, it's a really good idea—particularly for some of our more severe psoriasis patients and those who seem to have a metabolic disease phenotype like obesity—to check lipids or things like that, because we might actually catch something early, before it would have otherwise been identified, that can be intervened upon, maybe not by us, but maybe by a cardiologist or a primary care physician. That may provide an opportunity to prevent some of those outcomes that we just discussed from happening by treating

underlying metabolic disease.

Dr. Leuchars:

So where do the GLP-1 receptor agonists enter the conversation around caring for patients with psoriasis?

Dr. Cohen:

The GLP medications, as we all know, have really revolutionized the way we look at obesity and metabolic disease, and have had impacts broadly on many different areas of medicine. And it turns out psoriatic disease is no exception. There has been data coming from case reports and series showing that individuals who are given these GLP medications actually have superior psoriasis outcomes as compared to those who are not given these medications. And then, very excitingly, more recently, there were two randomized controlled trials that showed that GLP medications—specifically tirzepatide—in combination with biologics—specifically ixekizumab—improved outcomes in both psoriasis and psoriatic arthritis.

So to take a step back from that, what this study did was randomize individuals with psoriasis or psoriatic arthritis. There were two different studies—one called TOGETHER-PsO, the other called TOGETHER-PsA—and they randomized individuals to get either ixekizumab alone, which is an IL-17A inhibitor, or ixekizumab plus tirzepatide. And tirzepatide is one of the GLP medicines. And of course, they found that in both studies, individuals on the GLP medicines lost more weight than those who were not. That makes sense. But some of the most interesting information that we got there was that, actually, those individuals did better in terms of their PASI scores. Their psoriasis cleared more when they were on both the GLP and the psoriasis biologic. And in the case of psoriatic arthritis, their ACR scores were better, so they had better joint outcomes when they were on both the biologic and the GLP, as opposed to just the biologic alone.

And of course, we don't know exactly why or all the reasons why that has happened. But there are a few things that we do know. First, we know that the GLP medications have independent anti-inflammatory effects. So aside from any sort of weight loss that's going on, there are also inflammatory pathways that these GLP medications are impacting, and so they're reducing the burden of systemic inflammation in these individuals. And so that is improving psoriatic disease.

Second, there's good data to suggest that people who are heavier do not respond as well to the biologics for psoriasis. So that is to say that individuals who are heavier do not have as strong outcomes in terms of skin clearance. And actually, it's also been found that those individuals sometimes cycle through the medications more quickly. They stay on the medication for less time. And so, probably, some of the weight loss that is occurring from the GLP medication is allowing those patients to respond better to the biologic that they're getting for their psoriatic disease. And there may be more, and there likely is more in terms of reasons for what we observed and nuance there.

But these are some of the main hypotheses that we have right now and some of the, I think, important working thoughts about how GLPs and psoriasis biologics are interfacing.

Dr. Leuchars:

For those just joining us, this is *On the Frontlines of Psoriasis* on ReachMD. I'm Dr. Mary Leuchars, and I'm speaking with Dr. Jeffrey Cohen about our current understanding of GLP-1 receptor agonists in patients with psoriatic disease.

So, Dr. Cohen, given the evidence we have right now, how should clinicians consider the role of GLP-1 receptor agonists in caring for patients with psoriatic disease who also have obesity or metabolic disease?

Dr. Cohen:

There are a few different ways that someone who's caring for an individual with psoriatic disease who also has obesity or other metabolic disease to think about the GLP-1 medications. I think, at the very least, it is a helpful thing for us to be able to speak confidently with our patients about the existence of these medications and the opportunities that they present for the correct individual to have not only better outcomes in terms of their weight, cardiovascular disease, sleep apnea, other things that we know are helped by these GLP medications, but also to share with them the data that we have in the psoriatic disease space, because many people won't know that. And a lot of patients hear this and they actually become very interested, because they want to do everything they can to help improve their psoriasis or psoriatic arthritis.

It's also helpful to know people in the community who may be more readily prescribing these medications, because while some dermatologists do prescribe them and manage patients on these GLP medications, many do not, and that's okay. But it's good to have an action plan so that you can help a patient who wants to learn more, wants to consider doing it, or may want to go on one of these medications to connect with the appropriate individual who can help put them on the medication or talk more to them about whether they might be a good candidate for the medication.

And then I think the last thing that we should be thinking about with these medicines is, even if you're not prescribing it, suggesting, it or

talking about it, it's good to be aware of patients on these medicines because it may help you think about what you anticipate their outcome might be or help talk to them about, "Hey, it's a good thing you're on this medication because it turns out it's going to help your psoriasis too." Giving them some positive reinforcement, positive feedback, and reassurance is just going to help them maintain on the medication and have the best overall health outcome, regardless of whether you're actively managing that or not.

Dr. Leuchars:

Looking ahead, what evidence do we still need to determine whether the GLP-1 receptor agonists could play an even broader role in psoriatic disease?

Dr. Cohen:

I think this is really just the beginning, right now, of our journey with these GLP medications. We have some nice observational data. We have these clinical trials that we talked about. All of these pieces of evidence are pointing toward this being helpful and being something that we can use in addition to some of our other established psoriasis treatments.

But this is still early, and I think what we'll need is more trials looking at different combinations, longer trials, and longer-term outcome data, and looking to see, does using some of this medication prevent comorbidities from happening? In other words, does having someone on these medications, in addition to biologics, prevent psoriatic arthritis? It's an interesting question. There's lots to learn about all of the areas of impact here. I think that will come out over time as we have more experience with these medications and see how more patients do on them.

But for now, it's really exciting to see that evidence is pointing towards this being something that's really helpful in lots of different areas of medicine, including psoriasis, psoriatic disease, and also the comorbidities that we discussed in the beginning, that we know are very important for our psoriasis patients. So there's a lot of excitement around this. There's a lot of discussion around this, but certainly, there's more to learn over the years.

Dr. Leuchars:

They're great comments for us to think about as we come to the end of today's program. I want to thank my guest, Dr. Jeffrey Cohen, for joining me to explore what we currently know about GLP-1 receptor agonists and their use in patients with psoriatic disease. Dr. Cohen, thank you so much for joining us.

Dr. Cohen:

Thank you. It's been a real pleasure.

Announcer:

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