

Transcript Details

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Anti-IgE Therapies and the Future of CSU Care

Announcer:

This is *On the Frontlines of Chronic Spontaneous Urticaria* on ReachMD. Here's your host, Dr. Gates Colbert.

Dr. Colbert:

Welcome to *On the Frontlines of Chronic Spontaneous Urticaria* on ReachMD. I'm Dr. Gates Colbert, and joining me to discuss the current and future role of anti-IgE therapies in the management of chronic spontaneous urticaria, or CSU for short, is Dr. Thomas Casale. He's a Professor of Medicine at the Morsani College of Medicine at the University of South Florida in Tampa.

Dr. Casale, thanks for being here today.

Dr. Casale:

Oh, thank you for the invitation.

Dr. Colbert:

Let's start with some context, Dr. Casale. Can you walk us through the current treatment landscape for CSU and where anti-IgE therapies fit into that?

Dr. Casale:

Sure. So, as you're aware, there's actually three different broad categories for urticaria. There's acute urticaria. So this is urticaria that you might get if you get stung by a bee or you eat something that you're allergic to. It comes on very quickly, and it disappears quickly.

Then there's chronic spontaneous urticaria, which occurs in about 0.5 to 1 percent of people. And this is a disease unto itself. And that's something that we often tell our patients, because number one, it can last for years. Number two, we almost never find a cause. And up until we had the approval of omalizumab for CSU back in 2013, it was one where we weren't very successful in treating it, because only about 45 to 50 percent of patients with chronic spontaneous urticaria respond to antihistamines.

The treatment algorithm is to start patients on licensed doses of non-sedating or second-generation antihistamines and to see how they do over a week or two. If they don't get better, we double that dose, and if they still don't get better, we go up to four times the licensed dose of one of these antihistamines.

Now, what we've learned is that about half of patients with CSU—even though they're on four times the licensed dose of antihistamines—still have a lot of symptoms. And these are the patients then would be considered for a biologic such as omalizumab or anti-IgE therapy.

Dr. Colbert:

So when you're deciding to initiate anti-IgE therapy, what clinical factors or patient characteristics tend to guide your decision making?

Dr. Casale:

I think the biggest thing is that a lot of people forget that CSU is a very debilitating condition and it produces a lot of impaired quality of life. You could imagine the anxiety and depression associated with the disease that can last for a long time. It could come on spontaneously at any point. So if you go to work, you go to a social event, or whatever, and all of the sudden you have hives all over your face or arms where other people could see it, it tends to be very debilitating for the patients.

And it's those patients that are suffering with chronic spontaneous urticaria—who can't sleep very well because of the itchiness and who

can't function as well because of the visible lesions on their body—that makes them curtail some of their activities, these are the ones that we would consider a biologic such as omalizumab for.

We do know that there's a couple of things that we ask patients and those are, are there things that seem to make their urticaria worse? Are there things that make their urticaria better? So we noted that, for example, if you take a hot bath or a hot shower or you exercise, anything that dilates cutaneous blood vessels is going to make urticaria worse.

So we consult patients about that. And then we talk to them about a drug like omalizumab. And basically, this is a treatment that, after about several weeks to months, a very high percentage of patients do well on. Not everybody, but it clearly works for a number of patients.

Dr. Colbert:

And with all of that being said, what impact have anti-IgE therapies had on the management of CSU, particularly in terms of disease control and patient expectations?

Dr. Casale:

You know, what I would consider under well control, an individual patient may or may not. So if I have a patient that has hives everywhere and I'm able to decrease their hives by 75 or 80 percent, I'm pretty happy. But the patient may not be. So it's one of those things that you have to use shared decision making and talk to them about.

So we want to counsel our patients and say, look, in some cases you may have a very rapid response, and in others you may not. The data would suggest that after six months, for example, about three quarters of patients have what we call well-controlled disease, and about half of patients have completely controlled disease. And those numbers, of course, over the first four weeks, are much lower. About a third of the patients have well-controlled disease, but only about, 10 to 15 percent have completely controlled disease.

So we have to tell our patients that this could be a process, and that you may not get immediate relief, but to hang in there and to keep taking the antihistamines. And we just keep assessing to make sure that they do have a good response.

Dr. Colbert:

For those just joining us, this is *On the Frontlines of Chronic Spontaneous Urticaria* on ReachMD. I'm Dr. Gates Colbert, and I'm speaking with Dr. Thomas Casale about the evolving role of anti-IgE therapies in chronic spontaneous urticaria.

So, Dr. Casale, we know that not all patients respond to current anti-IgE therapies. So what do we understand about the mechanism behind variable response?

Dr. Casale:

What we lack with CSU is really good biomarkers that are point of care. So if you have an individual patient in front of you, you could say, you have these characteristics; you may not respond as well, or you may respond slower.

And what we've noted is that, with omalizumab, if patients have very low IgE levels—very low being typically less than 30 international units per milliliter—or if they have a high BMI, they may not respond as rapidly as patients that have higher IgE levels and lower body weights. Because of that, many of the newer therapies that are being looked at—and two have recently been approved—now also look at these parameters.

So the two new therapies that were recently approved are dupilumab, which is an anti-IL-4 alpha monoclonal antibody that's now has 10 different indications including asthma, atopic dermatitis, nasal polyps, et cetera, and remibrutinib. Remibrutinib works by an entirely different mechanism. It's a BTK inhibitor. And BTK is important because when you trigger IgE on mast cells—which results in the mediator release of histamine and other things that give you the hives—before that happens, there are intermediate steps, and BTK is an important kinase involved in that. And if you block that, you could prevent that mast cell from degranulating and releasing the mediators.

So this BTK inhibitor that's approved, remibrutinib, is the first treatment we have that is an oral agent. You could take it orally twice a day, and it too has been shown to give good response. And it doesn't matter what the IgE levels or BMI is. And that's the same with dupilumab, which has a different mechanism of action. It, too, works regardless of the IgE levels or BMI.

So we look at all those factors and talk to our patients about what's best for them—what they would consider the most appropriate therapy that they're comfortable with, and then pick one of those if they are not responsive to second-generation or non-sedating antihistamines. I keep saying non-sedating because I want to make sure that people do not use drugs like diphenhydramine, because that impairs patients. So we always prefer second-generation or non-sedating antihistamines.

Dr. Colbert:

Now, looking ahead, how might next generation anti-IgE therapies or novel biologics expand treatment options for CSU?

Dr. Casale:

There's actually over 20 drugs in development that are targeting different mechanisms for chronic spontaneous urticaria. So we have a whole new next generation of anti-IgEs that are being looked at, and some of them are using what we call a mutation on the FC portion of the immunoglobulin, which basically makes that antibody last longer. So instead of having to dose somebody every two to four weeks, you might get away with dosing every two months to six months. Some of these have a higher affinity—that is, they bind to the IgE better. And some, actually, are able to take the IgE off the mast cell already.

But there are many other treatments that are being looked at, some of which are in late-stage development. We know that the mast cell is the critical cell involved in all types of urticaria, and there are what we call c-KIT inhibitors—c-KIT is a molecule that is critical for mast cell viability. So if you block that, mast cells die. Well, if you take out mast cells, then you're not going to have urticaria. And there are at least five or six new c-KIT inhibitor strategies that are being trialed to treat urticaria. And there are other BTK inhibitors out there. So there are many new things on the horizon for patients.

Dr. Colbert:

And, finally, Dr. Casale, as these therapies evolve, what practical considerations should clinicians keep in mind when integrating them into real-world practice?

Dr. Casale:

Unfortunately, all these biologics, whether it's for urticaria, asthma, rheumatoid arthritis, et cetera, are very expensive, and they could cost 30,000 to 60,000 dollars per year. And when you have a disease like chronic spontaneous urticaria that can last five or 10 years, in some cases, we have to consider that.

And the other thing that we've noted with drugs like omalizumab is they don't appear to be curative. So that cost issue could be extremely important, and we have to work with our patients to determine their insurance coverage and how we could help them navigate the system so that they get appropriate coverage and they don't have a huge out-of-pocket expense.

And once they start getting better, can we stop or at least decrease the antihistamines? Can we decrease the frequency of the biologics? There are some studies that suggest that with omalizumab, when patients are doing better, you might be able to spread out the dosing rather than every four weeks, maybe every six weeks. And all these things can make it easier for the patient and less expensive.

Dr. Colbert:

With those takeaways in mind, I want to thank my guest, Dr. Thomas Casale, for sharing his insights on how anti-IgE therapies fit into chronic spontaneous urticaria management. Dr. Casale, it was great having you on the program.

Dr. Casale:

Thank you.

Announcer:

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