Transcript Details
This is a transcript of an educational program. Details about the program and additional media formats for the program are accessible by visiting: https://reachmd.com/programs/on-the-frontlines-of-chronic-spontaneous-urticaria/ending-antihistamine-shuffle-csu/85415/

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

Ending the Antihistamine Shuffle in CSU

Announcer:
This is *On the Frontlines of Chronic Spontaneous Urticaria* on ReachMD. Here's your host, Dr. Charles Turck.

Dr. Turck:
You're listening to *On the Frontlines of Chronic Spontaneous Urticaria* on ReachMD, and I'm Dr. Charles Turck. Joining me to discuss treatment options for antihistamine-refractory chronic spontaneous urticaria, or CSU for short, is Dr. Michelle Tarbox. She's a board-certified dermatologist as well as Professor and Chair of the Department of Dermatology at Texas Tech University Health Sciences Center in Lubbock. She also spoke about CSU at the 2026 Fall Clinical Dermatology Conference. Dr. Tarbox, thanks for being here today.

Dr. Tarbox:
Thank you so much for having me on, Dr. Turck. I'm so excited to talk about one of my favorite nerdy topics, which is how we can help our patients with chronic spontaneous urticaria.

Dr. Turck:
So let's start with the basics, Dr. Tarbox. How do you determine that a patient with CSU is truly antihistamine refractory, and when do you start thinking about going beyond antihistamines?

Dr. Tarbox:
We have to use patient-reported outcome measures with CSU, because it is a condition that waxes and wanes. And in between periods of activity, there's actually no evidence of its presence in the skin. So you really do have to utilize some of the metrics that we have.

Now, fortunately, we have a very simple-to-use, very straightforward tool called the Urticaria Control Test, which we can use to help gain perspective on our patient's activity with their CSU and how good a job we're doing at managing it. It's a four-question questionnaire, and it basically is a report card for us as dermatologists or allergists who might be managing CSU about how well we're doing at controlling the disease state.

We want to make sure that they're taking the medication correctly. So they need to be second-generation H1 antihistamines that have been uptitrated either to patient tolerance or to four times daily dosing for at least two to four weeks. And that point is very important. With a lot of disease states, we have to give months to check for response, because there's permanence of the condition in the tissue. But with something that comes and goes within a day, we should be able to tell relatively quickly if our treatment is working or not.

So one of the key points I want to put forward is that we don't let patients languish for months on uptitrated antihistamines if they're just not working for that patient. So, if they've been on up to four times daily dosing of the H1 second-generation antihistamines for two to four weeks, or up to their level of tolerance of antihistamine for that period of time, and they're still not achieving control based off of the Urticaria Control Test—even though they're taking the medication daily and you've confirmed the diagnosis—then at that point, we would classify the patient as antihistamine refractory. And then all three agents that are FDA-approved would potentially be options to add to the patient's management to help control their symptoms.

Omalizumab is approved above age 12. Dupilumab has gotten approved down to age two. Remibrutinib is available for adults only. The omalizumab has the deepest evidence and longest safety record, but I'm very excited to have the options of dupilumab and remibrutinib as well, and they're all great options. But we do have to use those patient-reported outcome scores, because it's a condition that comes and goes, and often it's not there when we see them in clinic.

© 2026 ReachMD

Dr. Turck:
Are there any patient or disease characteristics that help you choose between the advanced therapeutic options?

Dr. Tarbox:
If the patient has a lot of IgE-mediated comorbidities, they have allergic asthma, they have food allergies that coexist with inducible or spontaneous urticaria, or if they have angioedema-predominant disease, which is rarely autoimmune, that's often going to respond better to omalizumab.

Now, who would be a poor choice for omalizumab? If patients have the type IIB autoimmune phenotype of CSU, where they might have other autoimmune conditions, they have low total IgE, and low eosinophils, this might be a patient that's not going to do as well on omalizumab, and they may do better with remibrutinib, dupilumab, or even cyclosporine. Remibrutinib and dupilumab work well regardless of baseline IgE, so if you have that data for the patient, that might guide your choice.

Now, if you've got a patient who's shot-phobic, we have an oral option, so long as the patient's an adult. The oral drug availability right now is remibrutinib. It's very quickly efficacious, which is nice. It has rapid relief, and onset of improvement is usually within about a one week. If they've had a prior omalizumab failure, there was a good phase 2b study with remibrutinib that showed benefit regardless of prior anti-IgE response. And if the patient has autoimmune or low-IgE disease, I would choose remibrutinib.

And then for dupilumab, you would choose this agent if they had coexisting type 2 diseases. Type 2 inflammation is an area of great interest of mine and something that we're really starting to explore in the world of dermatology and allergy. You get two birds with one stone. One drug treats two conditions. That's kind of fantastic.

Of course, if you have a younger child aged two to 10, dupilumab is your option. And if the patients have low IgE or they're omalizumab naive, that might be a great choice. For dupilumab, it's not quite as strong in omalizumab-failure patients as remibrutinib data shows, so that might not be your first choice in that scenario.

Dr. Turck:
For those just joining us, this is *On the Frontlines of Chronic Spontaneous Urticaria* on ReachMD. I'm Dr. Charles Turck, and I'm speaking with Dr. Michelle Tarbox about navigating advanced treatment options for CSU.

So, Dr. Tarbox, I'd like to dig into the clinical trial evidence just a little bit more, focusing first on remibrutinib. What do the pivotal trials tell us about how well it works and how safe it is, and what should clinicians keep in mind when using it?

Dr. Tarbox:
That's a great question, and the trials are really fun to talk about because they have a fun name. They're called REMIX-I and II, and I can't help myself. Whenever I hear or read the word, I think, "Remix!" I don't know why, that's how it comes into my brain. But it was a large trial. 925 adults were uncontrolled on standard-dose antihistamines, and they were randomized 2:1 to receive the 25-milligrams twice-daily remibrutinib or placebo.

And they had some pretty impressive findings. They saw significant improvement in their UAS7 by week one, and importantly, that improvement was sustained through week 52. For the UAS7 less than or equal to six, the REMIX-I and REMIX-II trials had patients between 46 and 49 percent achieving that metric. And for complete response, a UAS7 equal to zero, they were between around 28 percent to 31 percent.

Now, you asked about safety. In the pooled REMIX data, the overall adverse events matched placebo for things that are important for us to consider, like infection, cytopenia, and liver events. Those did not differ. Now, patients who had higher levels of liver dysfunction were not a part of the original trial, and you do need to be thoughtful when you're starting patients on remibrutinib if they have significant liver dysfunction.

There is one signal, and it's mucocutaneous bleeding: nine percent in the active arm of the trial, two percent in the placebo group, per the label. So it's about a seven percent difference between the patients who are on active drug and those on placebo. Most of the bleeding events were petechial or contusions. None of them were severe, and these occurred without changes in platelet counts or coagulation tests. The vast majority of these have been pinpoint petechial lesions that are seen potentially in places where patients are scratching, and they really don't seem to interfere significantly with the patient's activities or with their satisfaction on the drug. There was very good adherence long-term to the medication.

And then there are some practical points. So remibrutinib is designed to be swallowed whole. You're not supposed to crush or chew the tablet. If the patient does need to have surgery, you want to hold the medication three to seven days before and after surgery for invasive procedures. And the good thing about this medication is it is fast on and fast off.

© 2026 ReachMD

You do want to interrupt it if bleeding occurs and avoid those strong or moderate CYP3A4 inhibitors and inducers, also potentially avoiding things like PGP substrates, like digoxin. You would avoid live vaccines. And they did allow clopidogrel and aspirin in the trial, but they didn't study other anticoagulants. And of course, you would avoid it in hepatic impairment.

Dr. Turck:
And what about dupilumab? What does the evidence show, and what's important to remember about it?

Dr. Tarbox:
Dupilumab, of course, is a known entity for dermatologists. I don't think that there's a practicing dermatologist that's unfamiliar with this medication or with its long-term track record of safety.

The CUPID trials were the trials that got dupilumab approved for CSU. So the UAS7 difference was significant, and patients did achieve complete response with some significance as well. The signal, of course, is a little bit more gradual and gentle with dupilumab than it was seen to be with remibrutinib. Adverse safety events were very similar to placebo and consistent with dupilumab's known profile. So the standard counseling applies.

Interestingly, conjunctivitis was less common in patients with CSU on dupilumab than in those patients who have atopic dermatitis who are treated with dupilumab. And that might be more of a disease state-related adverse event.

The response is slower than remibrutinib, so you want to give it a little bit more time before you determine that it's not the right medication for the patient. I think that it's very helpful for us to have access to a therapeutic that, A, most of us are comfortable and familiar with, and that, B, most of us really know the ins and outs of. And of course, having access to a therapeutic for patients down to the age of two is also very important.

Dr. Turck:
Now, once a patient is on one of these therapies, how do you evaluate the response and what are your next steps for patients who are well-controlled versus those who aren't?

Dr. Tarbox:
This is another one of those moments that I have to stand on the hilltop and preach the gospel of patient-reported outcomes. With a disease state that waxes and wanes, often out of our perception, we need evidence to guide our treatment.

And so I usually will track the UCT at every visit. If the patient has angioedema, there's also a scale for that, the AAS7. And then the UAS7, which is the Urticaria Activity Score, ideally could be tracked. But if you are a busy practicing clinician, then you want to have an urticaria control test of 16, which is complete control. So there's four questions for the urticaria control test, and it's basically asking, how well is your urticaria under control? How much is it impacting your activities of daily living? A perfect score on each of those questions is four, which means you're doing a great job. You're a rock star dermatologist. And of course, if you remember rudiments three math, four times four is 16. So that's a perfect score. Anything lower than 12 indicates that there's not good control, and the patient might need to have consideration of changing the therapeutic.

I like to assess my patient's level of comfort with how we're going to treat their disease state. I like to determine if they are a person who is better living through chemistry, pedal to the metal, let's get this problem solved, or if they are a person who wants to maybe re-educate their immune system and give a little gentle restructuring to push the immune system a bit out of the abnormal response that it's developed with the chronic spontaneous urticaria.

You also want to look at the level of control. So if you have well-controlled or complete response, then you can start to gently taper antihistamines. And this is a point I really want to make. When you start these advanced therapeutics, you don't just stop the antihistamines. You have to dovetail these therapies over each other, because that is a way to engineer failure for your CSU patients. So when you start remibrutinib, dupilumab, or omalizumab, they need to stay on the dose of antihistamines they can tolerate. And then once the patient is well-controlled for a significant period of time—at least a month to two months—you can start to gently taper the antihistamines, usually by one tablet per week.

After about a year of complete control, you can then lengthen the interval of dosing for omalizumab or dupilumab. Retreatment with omalizumab does work if it has been tapered and the patient relapses with CSU. And if the patient breaks through when you're considering tapering or doing the interval extension for the injectable therapeutics, that resets the clock, and you have to remeasure. So if they're well controlled or complete response, you can start to taper the antihistamines. Then you can start to do interval extension for the dosing of the medications.

If they're partially controlled, then you want to optimize. So if your UCT is between 12 and 15, if you are using omalizumab, for example,

© 2026 ReachMD

you might increase the dose or increase the frequency of dosing. You might also consider, if you have a UCT less than 12, meaning you're losing control or it's not in good control, then you might want switch mechanism.

And of course, on all of the guidelines, after dupilumab, omalizumab, and remibrutinib, cyclosporine is still there. And I've been treating CSU for a long time because I am a dermatologist, but I'm married to an allergist in our system who has the same last name that I do. And all the CSU patients would get referred to me because urticaria is a skin disease. And so I've been using cyclosporine my entire career, and I am comfortable using it. It is not the easiest medication to use by a long shot, and I far prefer to use these advanced agents of remibrutinib, omalizumab, or dupilumab. But it's still accessible if patients are refractory to all of those other therapeutics or in the event that those other therapeutics are just not available for the patient.

You do want to reassess comorbidities for patients and revisit the diagnosis if it's just not responding to any of the available therapeutics.

Dr. Turck:
Now, as we wrap up, what are the key points you'd want clinicians to take away about caring for patients with antihistamine-refractory CSU?

Dr. Tarbox:
First, I want to thank everybody who's listening to this program for your interest in managing CSU. These patients really need us. Often, it takes them a very long time to get to a specialist who might be able to help them, and I'm so grateful for people taking the time to learn about what we can offer them besides putting them on the carousel of needless and futile antihistamine shuffling.

The key takeaways are, this is a disease state that fluctuates. It's a condition that comes and goes and does not leave a trace. So we do need to measure control with the Urticaria Control Test. It's very simple. The patient can do it right in your office. It takes minutes. And you want to shoot for a score that's at least greater than 12, which indicates good control. But a perfect score of 16 is ideal. Now, if the patient has a UCT less than 12, which is not good control of their chronic spontaneous urticaria, then you want to properly increase or titrate the antihistamines. And if they've still failed that and have refractory disease, that should prompt escalation, not repeated steroid courses or antihistamine shuffling. There is no magic combination of antihistamines that can cure antihistamine-refractory CSU. They need escalation to an agent that can actually help them.

And the good news is there are now three approved second-line mechanisms. Omalizumab is the reference standard. Remibrutinib matches its efficacy and has fast oral action. And dupilumab is a great option for patients who have type 2 comorbidities and, of course, also children down to the age of two.

The phenotype can help us guide our choice. If patients have IgE comorbidities, inducible urticaria, or angioedema-predominant disease, that may favor omalizumab. Low-IgE or autoimmune disease might favor remibrutinib, dupilumab, or cyclosporine. And atopic comorbidity would, of course, favor dupilumab. Remibrutinib also has achieved an indication for dermatographic urticaria. So if they have comorbid dermatographic urticaria, that would also be a great option to treat both of those troublesome symptoms.

And really, the nice thing about it is we have such great options for our patients. Remibrutinib does need some stewardship mindset. You have to counsel the patients about the bleeding, which is typically mild. You do want to hold the medication around procedures. CYP3A4 and anticoagulant screening should be done, so you'll need to know the medications your patient is taking, and you would avoid remibrutinib in hepatic disease.

The sequencing can matter as well. Dupilumab use after omalizumab may not be as successful, but there are some patients that will still respond even if they failed omalizumab. Every patient is different, and you do want to aim for complete control and then step down deliberately and thoughtfully. Most CSU will eventually remit over the next two to five years, so these patients aren't destined to be on these medications forever, and most patients don't want to take more medications than they need to. Long-term step-down data exists for omalizumab, but we expect it to be similar with dupilumab and remibrutinib as well, because the disease state is still the disease state.

We do want to make sure that we also share our information with each other as we learn more about this disease state, because we always learn new things about conditions when we have tools to treat them.

Dr. Turck:
With those valuable insights in mind, I want to thank my guest, Dr. Michelle Tarbox, for sharing her perspective on evaluating and optimizing advanced therapy for CSU. Dr. Tarbox, it was great having you on the program.

Dr. Tarbox:
Thank you so much for having me. I really enjoyed being a part of this.

© 2026 ReachMD

Announcer:
You've been listening to *On the Frontlines of Chronic Spontaneous Urticaria* on ReachMD. To access this and other episodes in our series, visit *On the Frontlines of Chronic Spontaneous Urticaria* on ReachMD.com, where you can Be Part of the Knowledge. Thanks for listening.

© 2026 ReachMD