

### 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/resistant-hypertension-key-takeaways/14371/>

Released: 11/23/2022

Valid until: 11/23/2023

Time needed to complete: 1h 08m

### ReachMD

[www.reachmd.com](http://www.reachmd.com)

[info@reachmd.com](mailto:info@reachmd.com)

(866) 423-7849

---

### Resistant Hypertension Key Takeaways

#### Announcer:

Welcome to CME on ReachMD. This episode is part of our MinuteCME curriculum.

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

#### Dr. Patel:

Hello, my name is Manesh Patel. I'm at the American Heart Association Scientific Sessions 2022, and thanks for joining us for this DukeHeart On The Go, MedEd ON THE GO session on resistant hypertension, things we're learning. I'm joined by a friend and colleague who's done a lot of this type of patient care and research with me in the past, Sreekanth Vemulapalli. Sreekanth, thanks for joining us.

#### Dr. Vemulapalli:

Yeah, thanks for having me, Manesh.

#### Dr. Patel:

Well, so I think a lot of people know blood pressure's important. And obviously, it's a significant and potentially, the most modifiable cardiovascular risk factor we have for our patients, that we can improve their outcomes. But what a lot of people have started to spend our time on over the last several years, is to understand what we'll call hard to treat, or resistant hypertension. And maybe the first thing for us to do is to define what resistant hypertension is.

#### Dr. Vemulapalli:

Great, thanks. So resistant hypertension is uncontrolled blood pressure after three medications of different classes, including a diuretic, at maximally tolerated doses. So that's really important. Usually, that's a calcium channel blocker, an ARB or an ACE, and then an appropriate diuretic, usually thiazide-type.

#### Dr. Patel:

So not controlled with three meds and at least having a diuretic in that regimen?

#### Dr. Vemulapalli:

Yep.

#### Dr. Patel:

And then I think, you know, at least the estimates we hear, is that it's something like 11 to 13 million people probably have resistant hypertension. Obviously, having resistant hypertension leads to adverse outcomes. So, we're really excited that the American Heart Association Scientific Sessions, they have a lot of science around blood pressure. And for the first time in a while, we're starting to see some drug therapy. There's been a lot of conversation about devices, which we'll come back to, but the first time in a while that we're going to see some drug therapy possibly. Maybe you can describe for us one of the studies. I think it's called Precision, that's a late-breaking clinical trial that was presented. What was the agent? And sort of tell us about that study.

**Dr. Vemulapalli:**

Yeah, so the agent is called apocritentan, and it's a dual endothelin antagonist. And so, for cardiologists, you may be familiar with endothelin antagonism in terms of pH, but here, it's being used for anti-hypertensive effect. And so, this was a placebo double-blind study of apocritentan. And the primary endpoint was change in ambulatory systolic blood pressure at trough at about four weeks. And so the main finding was there was a reduction of 3.8 millimeters of mercury against placebo. And actually, when we stopped the medicine, the blood pressure even went up an additional 5.8 points after that.

**Dr. Patel:**

Yeah, so really important design in a resistant hypertension population. Again, a blinded study. I think there are two doses, like a 12 1/2 or 25. But interestingly, they watched them while they took the medicine, and then when they came off and had this sort of washout period, they saw what happened with the blood pressure. And doing that, reasonably important in our patients who are in resistant hypertension. You know, people often say, "Oh what does four millimeters mean?" or "What does six millimeters mean?" But a 3.8 or to 4 millimeter drop and then an increased backup, you know, so it makes me think at least a significant reduction. And obviously, we've seen in the past and we've seen data that three, four, five, six millimeters from medications can make a difference. So that's really powerful. So maybe with that in context, we go to the the next study, at least talk about that and then we'll come back to sort of putting the findings in context. There was another study called BrigHTN. Again, pretty impressive that we're getting randomized studies and resistant hypertension patients with new agents. Tell us a little bit first about the agent. I think it was a phase two study. Tell us a little bit about the agent.

**Dr. Vemulapalli:**

Yeah, so it's called baxdrostat and this is a aldosterone synthase inhibitor. And as you mentioned, this was actually a phase two study, and really powerful results. Looked like an 11-millimeter mercury drop in ambulatory systolic blood pressure with this.

**Dr. Patel:**

Yeah, so importantly, I think they had, again, a few doses. Half a milligram, milligram, or two milligram and they had a randomized placebo control study. And I think importantly in this phase two study, the data monitoring committee, because of the level of blood pressure reduction in resistant hypertension. Recommended to stop the study. So of course, that's an important feature in that, it tells us a little bit about what we're going to learn about long term opportunities. What that therapy, but others, and again, I think even at some of those doses, getting something like 11 millimeters or 8 millimeters. and I think that again, that was a blood pressure in the office, a systolic blood pressure reduction. So meaningful differences, we often think about resistant hypertension with devices. So maybe we should just spend a moment on the SPYRAL on medication presentation that Dr. Kandzari did for the SPYRAL program. You know, I'll just start by saying that, it's been something that we should certainly welcome, and see that these investigators and the whole field has been lifted up by doing the SPYRAL program. And the resistant hypertension, at least device therapies, with now a few different devices. And what Dr. Kandzari showed us was that there's the full discussion of the patients. They had an 80 patient roll in. And then full extension of patients getting either sham or actual renal denervation with the SPYRAL catheter. Tell us a little bit about the patients that got in, will you?

**Dr. Vemulapalli:**

Yeah, I think this is important. The first two studies we mentioned were very well controlled in terms of being resistant hypertension patients. They were on specified drug regimens including diuretics. They weeded out pseudo-resistant patients. And then we talked about the results already. Here in SPYRAL, we had patients that were on anywhere from one to three medications with blood pressures then in the 150 to 160 range thereafter. So, it's not as clear of a resistant hypertension population.

**Dr. Patel:**

Yeah, so more of a blood pressure population, patients with one, two, or three, about a third in each group. So again, important, because I think coming out of HTN3, there was a lot of interest in proving that you could reduce and have an effect with the renal denervation, which we know we can. Cause, they did the off-med studies. And then on med, on some level of med to show, can you add incremental reduction? And in fact, in the 80 patients they'd had shown some data showing incremental reduction. But when they go to the full data set at six months, what they presented looked like there was no significant reduction in 24-hour ambulatory blood pressure. Office blood pressure about four to five millimeters, which was statistically significant. And I think Dr. Kandzari nicely showed us that there was some change after the extension and not showing much of a difference in the extension. Partly, potentially, as we were doing the study through Covid and other things, to get people to get an ambulatory blood pressure is complicated. Nevertheless, another piece of data that adds to our armamentarium, and we'll be seeing these things potentially come to the clinics.

**Dr. Vemulapalli:**

Absolutely, I mean I think what the providers are going to face basically, is when you get to that fourth line therapy, so you've done your

three medications, different classes, you're at maximum doses of a diuretic. Now, what do you do? The guidelines right now would say spironolactone, but we know spironolactone has off-target effects, there are side effects. So, we're going to have some other agents here, I think. Between apocintan and baxdrostat and then, now we have to throw the cath lab into the mix. So how do we decide between these things?

**Dr. Patel:**

Yeah, I think it's going to be importantly, hopefully some patient shared decision-making and also understanding what people can tolerate. I just, you know, end by saying that I think some of the important things, maybe not end, but say that the way I think about the decision-making is going to be a little bit about what they're on now, and what the additive opportunity is. And then also about adherence, ability to take a set of medicines, a procedure versus repeatedly adding a fourth medicine. And we haven't even talked about costs yet, and we don't know what the cost will be. So those are of course going to be important things to think about and you know, in the full presentations, and as people will go to it, as we follow these patients longer, there wasn't a tremendous number of side effects. I think in the baxdrostat there was a little bit of lower extremity edema that might have caused people to-

**Dr. Vemulapalli:**

That's right, so we know in that class of medications, fluid retention is an issue, and so how we'll use that in our heart failure patients will be remained to be seen.

**Dr. Patel:**

For sure. Well, I'll just end by saying thanks for joining. At the American Heart Association and at all of your practices, we've thought a lot about how do we manage blood pressure. In fact, Life's Essential 8 sort of recommendations has told us about those essential eight sort of behaviors and activities and certainly behaviors of lifestyle, of activity, not smoking, trying to maintain a healthy diet, try to make sure you have a healthy weight. Those are important things, and then the eighth one was sleep. Making sure people sleep. We know obstructive sleep apnea, abnormal sleep affects your blood pressure. And then, if you can manage the blood pressure you can really change people's outcomes. So thank you for joining us for this episode of MedEd ON THE GO, as we talked about resistant hypertension and some of the new data coming out at the American Heart Association Scientific sessions 2022.

**Announcer:**

You have been listening to CME on ReachMD. This activity is jointly provided by Global Learning Collaborative (GLC) and TotalCME, Inc. and is part of our MinuteCME curriculum.

To receive your free CME credit, or to download this activity, go to [ReachMD.com/CME](https://ReachMD.com/CME). Thank you for listening.