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## How Will the Game Change with the Entry of New Agents/MOAs/Different Pharmacokinetics for Resistant Hypertension?

### Announcer:

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### Dr. Vemulapalli:

Hi, everybody, my name's Sreekanth Vemulapalli. I'm an Assistant Professor of Medicine in Cardiology at Duke Medical Center. And today, we have an expert panel to talk a little bit about the current and future state of resistant hypertension. And so, my esteemed panelists, I'll allow them to introduce themselves. Dr. Ferdinand, would you please introduce yourself?

### Dr. Ferdinand:

Hi, I'm Dr. Keith C. Ferdinand, I'm the Gerald S. Berenson Endowed Chair in Preventative Cardiology and Professor of Medicine at Tulane University here in New Orleans.

### Dr. Vemulapalli:

Great, thank you so much for being here, Dr. Ferdinand. Dr. Shah, would you introduce yourself, please?

### Dr. Shah:

Yeah, absolutely, thanks, Sreek. My name's Nishant Shah, I'm an Assistant Professor in Medicine and Cardiology at Duke University Medical Center. I'm a preventive cardiologist and work in the Cardiometabolic Prevention Clinic.

### Dr. Vemulapalli:

Thanks so much for being here today. So, I wanted to start the discussion off with you, Dr. Shah. So can you just tell me a little bit of how do you approach resistant hypertension? Meaning how do you actually make the determination that somebody has resistant hypertension?

### Dr. Shah:

Absolutely. Now, that's a really great question. And so, by definition, resistant hypertension is having a blood pressure over 130 over 80 on at least three different blood pressure agents, one of which being a diuretic. There's different forms of resistant hypertension as well. You could have blood pressure that's controlled, but you're requiring four different medications including a diuretic. And then also let's not forget about refractory hypertension, where you're on five different medications or more with or without controlled blood pressure, normally, uncontrolled, in this case. So, that's sort of how I identify. Now, how I necessarily see who has it and who doesn't, it depends on a lot of patient-specific factors. What medicines the patient has tried? Are they maximized on their current medications or not? Because being on maximal doses is part of those definitions for resistant hypertension. And what patient-specific issues are there in getting the medicines, for instance? And are there any side effects to the medicines as well? And so teasing that out is going to be very important to make sure you have a true resistant hypertension case. And, of course, we can't forget looking for causes of secondary hypertension as well because there may be another organic reason or even a medication interaction that is causing patients to have

high blood pressure. So, need to rule out all of those things first before we get to there.

**Dr. Vemulapalli:**

Thank you, Dr. Shah, I mean, you just went through several things in terms of thinking about primary and secondary causes, in terms of thinking about access to and "compliance" with medications. Dr. Ferdinand, how do you handle that in practice? That's a lot to go through with a patient. Do you have a multidisciplinary clinic? How do you approach that?

**Dr. Ferdinand:**

Oh, yes, certainly, I use advanced practice nurses, nurse practitioners, the patient, himself or herself, as part of that team. Especially if you look in the Southeastern part of the United States where both of us practice, you're going to have a high level of resistant hypertension related to, perhaps, more commonly seen in African Americans, patients with chronic kidney disease, obesity, salt sensitivity. Within the Jackson Heart Study, which is a cohort study similar to Framingham, but done in Jackson, Mississippi, in the self-identified African American population, only about 10% of them were taking the maximum medication. So, let's make sure patients are taking the medicines first. We know there are some novel tools that are being developed, both in terms of drugs and devices. And I think there will be a leap forward, but the first step is to make sure that the patient's adhering. One of the things that we do is text messaging. We just have a small study that might be approved for the American Heart Association in which we gave the persons valid devices using text messaging. We get the numbers and we text message back. So it's not doctors visits, it's not long phone calls, it's just keeping that person engaged. And without any changes in pharmacotherapy, after two months, systolic blood pressure dropped 10 millimeters of mercury. So clearly, patients are not taking the medicines as prescribed, but even if they do that, we're still going to have a significant number of patients who will benefit from advanced pharmacotherapy and devices.

**Dr. Vemulapalli:**

Perfect, thank you. I mean, we've just spent a few minutes talking about one of the major challenges which is how to engage with patients, how to make sure that we can sort of efficiently apply therapies. Dr. Shah, in terms of other patients you've seen with this, what are some of the other common difficulties that you run into in terms of managing patients with resistant hypertension once you've made that determination?

**Dr. Shah:**

Oh, absolutely. So, common things first is pill burden. We gotta make sure that patients are adherent to these medications, just like Dr. Ferdinand said, but patients all come with different social circumstances, different lifestyles, different pressures and stresses and anxieties. And sometimes, taking a lot of pills can be very difficult for them. I think patient education is very important, patient empowerment. Sometimes they don't understand why they are on so many different medications. And so, making sure, you know, engaging them through means like text messaging like Dr. Ferdinand was saying, or other sort of means through healthcare champions in a health system, or as someone in a community to help with education. All these things can certainly help, but usually it can be a barrier, too, if it's not well understood. And then side effects, the more drugs that you're on, the more side effects people have. And in the resistant hypertension patients, that's challenging because you're running out of different options to choose and maybe the option that they're having a side effect to really controlled their blood pressure well, but their quality of life is so diminished. And so, kind of juggling around different agents just to make sure they're tolerating them well is also a challenge when taking care of these patients. And I'll also add a plug for lifestyle modifications. That's the foundation, the cornerstone of management. So many cardiovascular risk factors and doing that in conjunction with the medications can be very hard with the patient. So just keeping them readily engaged is important but also a challenge.

**Dr. Vemulapalli:**

Dr. Ferdinand, Dr. Shah was just mentioning, it's difficult to sometimes employ lifestyle interventions, manage polypharmacy, deal with potential side effects, and really find the efficacious therapy regimen for a patient. So, I want to transition a little bit to some of the newer therapies that we think may be available here in the next year, including endothelial receptor antagonism, and potentially even renal denervation or other device-based therapies. So how do you think these may fit in given the challenges that we've just outlined?

**Dr. Ferdinand:**

Well, I'll give you the positive and the negative. The positive, if we do all the right things, lifestyle interventions, making sure they're on three or more medicines, one of which is the diuretic at maximally tolerated doses, eliminating secondary or identifiable causes of the hypertension. Let's say we do all those things, then I think having the endothelin receptor antagonists might be beneficial. This is actually something that may help Black patients because endothelin levels appear to be higher in that population, and renal denervation may help. Renal denervation will lower the pill burden, which makes it a little easier for patients to adhere. So that's the positive. Here's the negative. In the American healthcare system, those persons who don't have access, don't have adequate insurance, suboptimal insurance, don't have an identifiable source of primary care, they have shorter life spans, more heart failure, more heart attacks, more strokes. And this is something that won't be corrected simply by putting a new medicine out there or approving a device. If we don't have

access, that patients are not able to get that care, then we're going to see the same white-Black death gap, driven mainly by hypertension and cardiovascular disease, the same three times end-stage renal disease rates that we have seen for decades. And I can tell you, it would be very disappointing if these novel therapies, both from pharmacology and from device, are not applied equally to all patients, regardless of race, ethnicity, sex, gender, socioeconomic status, or geography. And we have not done that in the past.

**Dr. Vemulapalli:**

You bring up a really important point and one that I want to conclude with. So first off, I think we've hinted on this, which is that hypertension, and especially resistant hypertension, is sort of inequitably treated right now in the country. The second thing you bring up, which is that new therapies and new devices very, very often actually make inequities worse before they make them better. So how do we think about the fact that there are new therapies on the horizon, is there a system change? Is there a provider level change? Is it some other level policy change to make sure that these things can be used in a way that actually decreases inequities as opposed to increasing them? Dr. Shah, do you want to start first?

**Dr. Shah:**

Yeah, absolutely. I think it's multifactorial. I think that we need to engage all parties, from the patient, the provider, the health system, the community. That is the only way, I think, that we can improve equity and bridge these gaps. You know, I think you can have as many therapies out there as you want, but if they're not equally distributed, then I don't think it's going to matter. I think the health system can play certainly a big role in terms of providing assistance or partnering with pharmaceutical companies directly, potentially, to help improve access. So I think there's a lot that we can do on our end to help improve this.

**Dr. Vemulapalli:**

Dr. Ferdinand, your thoughts there?

**Dr. Ferdinand:**

I certainly agree. This was described by the Institute of Medicine in their landmark treatment, "Unequal Treatment" is the name of the publication, and it's the patients, we need to educate our patients, share decision-making, it's the health systems. Unfortunately, we, as doctors, are not running the healthcare system, business people are, but we need to work with them to make sure that if something's approved, that the various insurances, the Medicaid, Medicare, the government insurance, and the private insurances have it available for the patients. And then finally, the last part is we, as physicians and other clinicians, have bias. We don't treat people equally. We think we do, but when you look at healthcare registries even within large academic centers, some of the best places in the world, you look at how they treat patients, you see the gaps in terms of blood pressure control, attainment of A1C less than seven, high-intensity statin in patients with ASCVD. So those gaps are real and we cannot close our eyes to it. But I do think if we do all the right things, the new pharmacotherapy approaches and the devices may be a step forward.

**Dr. Vemulapalli:**

Thank you both for such a great discussion on this, and I think we've laid down the gauntlet here for how to improve care in resistant hypertension. Thanks, all.

**Announcer:**

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