Transcript Details
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Clinical Perspective on New Therapies in Resistant Hypertension

Dr. Yancy:
Hi. This is Clyde Yancy, professor and chief of cardiology at Northwestern University Feinberg School of Medicine, and associate director of the Bluhm Cardiovascular Institute at Northwestern Medicine. I'm here at AHA 2025 Scientific Sessions and celebrating the release of so much spectacular information.

Interestingly, one of the big agenda items at this meeting has been this renewed interest in hypertension. Previously, I've talked about how we can focus not just on lowering blood pressure now, but changing the whole CKM space and the entire portfolio of conditions associated with dysregulated cardiometabolic scenarios, including high blood pressure, but including stroke, including heart disease, heart attacks, chronic renal disease, even preserving cognitive function. But how do we get there? What makes it so exciting?

The guidelines are important, and I would refer you to comments we and others have made about the new guidelines, but the new therapies are equally exciting, even more so. Think about therapies now that target aldosterone synthase. Why is that so important? We've learned that in people who have resistant hypertension or persistent hypertension despite being exposed to multiple therapies, there's a relative hyperaldosteronemia that is evident. So it's not just the prototypical primary hyperaldosteronemia or secondary hyperaldosteronemia, but in hypertensive patients, increased aldosterone seems to be driving the increase in blood pressure. So targeting aldosterone seems to be a good strategy.

Now that we can target the actual enzyme that generates aldosterone, we have a brand-new set of agents—2 in particular, baxdrostat and lorundrostat—target this aldosterone synthase and demonstrate the ability to profoundly change blood pressure. The clinical trials that have been done looked at patients either with uncontrolled hypertension or uncontrolled hypertension and already established chronic renal disease—a very important substrate. And some of the trials compared the new agents against placebo. In all scenarios, it was evident that these new agents that target aldosterone synthase are remarkably beneficial.

But there's one other caveat. Never before in treatment of blood pressure have we had a biological biomarker that we could survey and understand the effectiveness of these therapies. Now we can actually check aldosterone levels—they should be close to 0 with an aldosterone synthase inhibitor. This gives us a chance to work with patients and understand what are the barriers. Can we work together to achieve compliance? Once we have adherence to a multi-drug medical regimen, the ability to control high blood pressure and control outcomes is much better than it's ever been before.

But it's not just targeting aldosterone. Now we know that if we target the endothelin receptor, understanding the vasoconstrictor properties of endothelin, we might also achieve some benefit. Aprocitentan is a dual endothelin receptor antagonist. In the PRECISION trial, now published some 2 or 3 years ago, it was quite evident that this additional auxiliary approach on top of already-established antihypertensive therapy effectively lowered blood pressure.

So think about where we are. We have new guidelines. We have the opportunity to change not just blood pressure and the blood pressure-related illnesses, but renal disease and cognitive performance. And now we have an entire suite of new drugs and devices to really help us achieve ideal blood pressure control. If you remember nothing else, that ideal blood pressure control is less than 130/80. Get there as best you can, but know we have many more ways to get there than ever before.

Thanks for your attention.