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/new-agents-in-hypertension-the-brightn-trial/14372/

Released: 11/23/2022
Valid until: 11/23/2023
Time needed to complete: 1h 08m

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

New Agents in Hypertension: The BrigHTN Trial

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. Vemulapalli:
Hi, my name is Dr. Sreekanth Vemulapalli. I'm an assistant professor at Duke University School of Medicine, and today I'm going to be talking to you about new agents, hypertension, or recap from AHA 2022 specifically about the BrigHTN Trial. So as background, 10% of patients with hypertension in the United States actually have resistant hypertension and treatment-resistant hypertension is defined as uncontrolled blood pressure on at least three drugs at maximally tolerated doses of different classes including a diuretic. Patients with treatment-resistant hypertension are at increased risk for cardiovascular and renal events. At present, Spironolactone is the currently guideline-suggested fourth agent to use in these patients. However, the efficacy of this agent can be limited by off-target effects, which can limit the dosing. Baxdrostat is an oral aldosterone synthase inhibitor that was trialed in the BrigHTN Trial.

So BrigHTN was a phase-two, dose-ranging trial, which had inclusion and exclusion criteria as follows. You had to be over at the age of 18 and be on stable doses of at least three antihypertensives, including a diuretic, and you needed to have a mean office blood pressure of greater than 130 over 80. Exclusions included mean office blood pressures of greater than 180 over 110, uncontrolled diabetes, or a GFR of less than 45 ml per 1.73 meters squared. And as you can see from the image on the right the study had a run-in phase. Ultimately 275 patients underwent randomization, and they were randomized either to placebo, 0.5 milligrams, one milligram, or two milligrams of Baxdrostat.

The endpoints for the study included a primary endpoint of change in mean seated blood pressure from baseline to 12 weeks in the Baxdrostat doses versus placebo. And there were pre-specified safety events including hyperkalemia, hyponatremia, and hypertension requiring intervention.

Here you can see the baseline characteristics and I'll just point out a few. You can see that the mean age was in the 60s. There were around 20% African American patients. Around 30% Hispanic or Latinx patients. The body mass index was around the low 30s and importantly 100% of the patients were on a diuretic, to begin with. And you can see most were also on ACE/ARB and calcium channel blockers with beta-blockers also used in some of these patients.

So, what were the findings? The primary endpoint here is shown in this graph. You can see the change in systolic blood pressure over that 12-week time period. In placebo, it was a reduction of about nine millimeters of mercury. And then in the two-milligram dose of Baxdrostat, it was a reduction of about 20 millimeters of mercury. And you can see the P value there of 0.001. Again, looking also at the one-milligram dose of Baxdrostat, that achieved about 17.5-millimeter reduction in systolic blood pressure. And then you can see in the panel on the right, the reduction in diastolic blood pressure. Again, placebo was around nine millimeters of mercury. The two-milligram dose of Baxdrostat was at 14 millimeters of mercury and the one-milligram dose at 11 millimeters of mercury. Neither of which reached statistical significance. How about the pharmacodynamic measures? These are important because other aldosterone synthase

inhibitors have had off-target effects in terms of affecting cortisol production and therefore have not been used for treating hypertension. So, if you look here, you can see the 24-hour urinary aldosterone, which was normalized for creatinine. This is on the panel on the left. You can see placebo there was no change. Whereas the two-milligram dose of Baxdrostat reduced substantially the urinary excretion of aldosterone. Essentially, the same finding in the serum aldosterone levels. You can see in the panel underneath that with a substantial reduction both in the Baxdrostat one and two-milligram doses. And then I'll direct your attention down to the bottom right panel where you can see the total serum cortisol dose. Again, not that different between placebo and the Baxdrostat dosing indicating that there wasn't a substantial impact of Baxdrostat on cortisol production.

How about adverse events? While the most commonly reported adverse events included UTI, headache, hyperkalemia, and fatigue, importantly 89% of these were judged to be not related to the study drug. You can see here in the table that I've reproduced there were a number of serious adverse events increasing in frequency with the Baxdrostat dose from 0.5 milligrams to two milligrams. But again, most of these were deemed as not related to the drug.

So, in conclusion, treatment-resistant hypertension is common and associated with adverse cardiovascular and renal events. Spironolactone is the currently suggested fourth-line therapy but is somewhat limited in its use and its dosing because of off-target effects. Baxdrostat lowered the mean office systolic blood pressure as compared to placebo in patients with resistant hypertension and there wasn't any substantial impact on cortisol levels. We will need phase three trials with longer follow-up and larger sample sizes to understand where this will fit in our armamentarium for the treatment of hypertension. And ideally, a direct comparison to Spironolactone as a fourth-line agent would be needed to understand whether this should be preferred over Spironolactone in clinical practice. Thank you all for your attention.

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. Thank you for listening.