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Self-Administered Etripamil for Termination of Spontaneous Paroxysmal Supraventricular Tachycardia: Primary Analysis from the RAPID Study

Announcer:
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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 Me Ed On The Go session on a trial called RAPID, which studied the self-administered Etripamil for termination of spontaneous paroxysmal superventricular tachycardia, and the primary analysis from RAPID was presented at the meeting. You'll see that RAPID was actually funded by Milestone Pharmaceuticals and conducted by Medpace, but it's important to recognize that this study evaluated Etripamil, a new treatment for paroxysmal SVTs. It's a novel L-type calcium channel blocker, it's formulated for an intranasal spray with rapid onset, with a Tmax or action less than seven minutes, and it's short lasting, inactivated by blood esterases.

So it's ideal for the unmet need of self-administered therapy for people who have these PSVTs, and can effectively and rapidly terminate AV nodal-dependent PSVT. It's important to recognize from the Phase 3 NODE-301 Part 1 study results that this was a randomized, double-blind, placebo-controlled phase 3 study, and the primary endpoint was time to PSVT conversion to sinus rhythm. Now, this trial did not meet its primary endpoint for conversion of PSVT over five hours. And a post-hoc analysis showed us that, actually, a clinically meaningful treatment effect was occurring early on, consistent with the drug's pharmacology. And it was, of course, a safe and well tolerated self-administered therapy in the unsupervised setting.

So, it's worth recognizing that in 301, the efficacy time to conversion over 45 minutes, you can see that there was a rapid repeat dose escalation option, so you could take Etripamil at 70 milligrams and you could have another dose if you needed. And this was consistent with the PK you can see on the slide, and therefore the primary endpoint for rapid 301 node if you can see it, and it was done, it's post-hoc, but it shows that 54% versus 35% were there, and so that's how the primary endpoint for the RAPID trial was chosen. So this is the RAPID Phase III clinical study design, and it was to evaluate the efficacy and safety, again, of Etripamil, a nasal spray for patients experiencing PSVT. And the key inclusion criteria were, patients were 18 years old of course, and had a history of PSVT lasting more than 20 minutes, and they had to have a documented diagnosis of PSVT. Exclusion criteria included ventricular pre-excitation, second or third-degree AV block, and a history of significant hypotension or syncope.

A 70-milligram Etripamil repeat dose regimen test dose was given, and the test dose visit was done before patients were then randomized, and then they were randomized to placebo or Etripamil. And at home they would follow their usual care, and if they had a PSVT event, they would administer the double blinded study drug, and if the symptoms persisted more than 10 minutes they could dose again with the study drug. And then an independent committee reviewed the primary endpoints of PSVT, and there was power to identify the events.

As you look on the patient populations here, you can see that 706 patients received a test dose, 692 patients were randomized, and the efficacy populations, 184 people who actually took the therapy during a PSVT event. And you can see the blinded adjudication of the safety population, that 72% of 'em had PSVT, 9% had no ECG, and then 19% was not PSVT. The demographics and the patient population, here you can see, in general, these are people that are in middle age, 50-year-old individuals, you can see that there was a large proportion of women over 50%, and then the PSVT had been going on for some period of time, and you can see the medications that people had been on previously, like beta blockers and calcium channel blockers. Here you can see the primary endpoint conversion of the adjudicated PSVT-to-sinus rhythm. Their primary endpoint at 30 minutes showed 63% versus 31%, with a hazard ratio of not getting the therapy of 2.62, and this was statistically significant. And the 300 minute endpoint, even looking out several hours, again, 81% versus 69%, this was statistically significant also. In addition, the median time to conversion was importantly also much faster with Etripamil, 17 minutes, versus 52 minutes with placebo.

On this slide, you can see patient seeking medical intervention or going to the emergency department, both in the pooled group, or independent from NODE-301 and the rapid study together, so you can see across the two studies. And then the pooled study shows statistical significance, there's a trend towards needing less medical help, and then it's statistically significant when you pool the two studies. What about adverse events or other findings? Here you will see rapid safety direct ECG readings. And again, here you can see NSVT, PSVT, and atrial tachycardia, a variety of other findings, but pretty low rate of these findings in general. What about adverse events? It's reassuring that syncope, loss of consciousness pre-syncope and dizziness were really very rare in this study. There was more nasal congestion, nasal discomfort with the intranasal Etripamil, as you can imagine.

So I think this is a really important study, in that it highlights for us a new possible important therapy for our patients. The rapid study achieved primary efficacy endpoint of terminating PSVT with self-administered Etripamil using symptom-based optional repeat dosing. And the conversion to sinus rhythm happened in 64% at 30 minutes, and 73% at 60 minutes. The safety profile seems to be fairly tolerated. And the pooled analysis with node one shows less ED utilization. So there's ongoing analysis of the open label period of RAPID, and the Node-303 trial, which will provide more insights, but it's been interesting to see this field evolve and see that there we now have a new option for our patients who might have PSVT. Obviously, as these data come forward, we'll look forward to seeing if this can get to the market. Thank you for listening to me, this has been Manesh Patel talking about the rapid study from AHA.

Announcer:
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