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Generalizability of the VICTORIA Trial and the US FDA Label for Vericiguat to Patients Hospitalized for Heart Failure in the United States

Announcer:
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Dr. Butler:
Greetings. I'm Dr. Javed Butler, President of the Baylor Scott and White Research Institute and distinguished Professor of Medicine at the University of Mississippi in Jackson, Mississippi. I'm a heart failure cardiologist and a clinical trialist and I'm delighted to talk about this poster that we recently presented, related to the generalizability of the results of the VICTORIA trial in the patient population that we treat. So first, let me give you a little bit of a background of the trial that was done and why is this question of generalizability important in the first place? So, VICTORIA trial really focused on a specific high-risk population of patients with heart failure. The so-called worsening heart failure. And the way we define worsening heart failure is that there are biological characteristics of patients with heart failure that put them at high risk which is irrespective of where the patients are treated. So, if you're developing worsening signs and symptoms and you're failing on a standard medical therapy on which you were pretty stable then really doesn't matter whether you treated in the inpatient setting or in the outpatient setting you're nevertheless at a higher risk. So, the way worsening heart failure was defined was either hospitalizations for heart failure within the past six months or need for outpatient IV diuretics. So, this was a patient population that was studied in VICTORIA and with the use of vericiguat, there was a significant reduction in the risk of cardiovascular death or heart failure hospitalization.

Now, there is an interesting twist here that when you design clinical trials there are certain features of inclusion exclusion criteria that are, you know, defining the patient population. So, for instance, heart failure with reduced to preserve ejection fraction. So, in this particular trial, we included patients with ejection fraction less than 45%. Then there are certain criteria where which you are really not sure about the safety of the therapy. So, for in this trial, we included patients with eGFR down to 15 but we did not include patients in dialysis of those patients that had eGFR of less than 15. But then there are all of these other miscellaneous criteria which are primarily designed not because we don't think that the therapy will not work or there are any concerns, but those things are designed just so that we can have a trial that ends in a reasonable timeframe. You have a reasonable number of event rate and those characteristics usually do not enter, in terms of the FDA labeling per se. So, when the FDA labeling comes out, that may not be exactly the same as all the inclusion-exclusion criteria for the trial.

So, there's a general notion out there that the patients that are enrolled in the clinical trial are not representative of the real-life patients or of the patients that are eligible for the therapy after approval by the regulatory agencies. So, what we did in this study is not that the Victoria trial is positive and has been approved the indication by the FDA is for vericiguat to be used for reduction of cardiovascular death or heart failure hospitalization in patients with heart failure hospitalization or need for outpatient IV diuretics. So that's the indication. So, the one thing we wanted to look at, how many patients meet the criteria on the basis of the regulatory approval. But then

the second question was, well, what if you go line by line, every single inclusion-exclusion criteria, then how many patients will be eligible for the VICTORIA trial? So, to answer this question, we looked at the database from Get With The Guidelines from say 2014 to 2020, almost a quarter of million patients, about 240,000 patients with heart failure, rejection fraction less than 45% in over 500 hospitals all across US. and we looked at these data. So, the first thing that we learned from this study was what a high-risk group of patients these are.

We are talking about almost 30 plus percent mortality risk within one year of discharge in the Get With The Guideline registry for patients with EF less than 45%. You know, we all very appropriately are concerned about patients who come into the hospital with myocardial infarction, with a stroke. But the fact is that the prognosis after discharge from myocardial infarction or from stroke is actually better than with heart failure hospitalization. So about 30% risk of mortality, about 30% risk of readmissions for heart failure, about 60% risk for readmission for any cause within one year. So really high-risk population. And that underscores why we need to give the standard of care therapy to all of these patients because we really want to change the trajectory, the natural history of the disease process, as well as look for novel therapies and apply novel therapies as well. Now the second question, how many patients, how many of these patients will be eligible based on the FDA approval or the regulatory approval? Well, the answer is 9 out of 10. So, 9 out of the 10 patients will be eligible based on the FDA approval. Bigger reasons for not being eligible are need for dialysis eGFR less than 15.

But this again underscores the fact that the drug that is approved for the clinical trial that was done for this worsening heart failure population, that it's very common and these are the patients that we are seeing in the clinic all the time. This is not some niche or unusual population to which the therapy applies to as far as the FDA indication is concerned. But then if you go and you look at every single inclusion-exclusion criteria even those that were primarily put in just to get the calibrated risk so that you end the trial in a reasonable time fashion, but are not necessarily part of the FDA approval, then we are looking at almost 4 in 10 patients that will be eligible for enrollment in the VICTORIA trial. So about 40% eligible for enrollment in the Victoria Trial about 90% are eligible for therapy with very vericiguat based on the FDA label.

So, in short, we looked at about 240,000 patients across 500 hospitals, all across the US and what we found was that one, patients with EF less than 45% hospitalized in this Get With The Guideline registry, extraordinarily high risk, 30 plus percent mortality within one year, 30 plus percent risk for readmission for heart failure within one year. That vericiguat that in a clinical trial setting has been shown to reduce the risk of cardiovascular death, heart failure, hospitalization. That indication was eligible to 90% of the patients based on the FDA approval and 40% of the patient would meet all the criteria to be approved, to be enrolled in the VICTORIA trial. So, I hope that this information was helpful to you, and we should go back and treat our patients aggressively for all the therapies they deserve. Thank you.

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