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/nt-probnp-during-screening-in-the-study-of-vericiguat-in-participants-with-heart-failure-with-reduced-ejection-fraction-victoria-trial-insights-into-outcomes-and-vericiguat/15289/

Released: 03/27/2023
Valid until: 03/27/2024
Time needed to complete: 1h 18m

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

NT-proBNP During Screening in the Study of Vericiguat in Participants With Heart Failure With Reduced Ejection Fraction (VICTORIA) Trial: Insights Into Outcomes and Vericiguat

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. Westerhout:
I am Cynthia Westerhout, and I'm here to present today on behalf of my coauthors. We'll be speaking about NT-proBNP during screening in the VICTORIA trial insights into outcomes of vericiguat. My disclosures are listed here.

So today's aims are threefold. In this session, we will learn about the frequency and direction of NT-proBNP changes during the 30-day screening period in the VICTORIA trial, the associations of these changes with the primary composite endpoint of cardiovascular death and heart failure-related hospitalizations, and vericiguat's clinical benefit relative to these changes.

A little background about the VICTORIA trial. VICTORIA enrolled 5,050 patients with heart failure with a reduced ejection fraction of less than 45%, and they were randomized to either vericiguat or placebo in a 1:1 fashion. An important entry criteria was NT-proBNP greater than or equal to 1,000 picograms per milliliter for those with sinus rhythm, and greater than or equal to 1,600 picograms per milliliters for those with atrial fibrillation during a 30-day screening period.

A little background about these patients, the mean age was 67 years of age, and 24% of the population were females. There was a way to get into this trial; one of three ways, about two-thirds of these patients had had a heart failure-related hospitalization within 3 months, 17% of patients had a 3 to 6 – a hospitalization within 3 to 6 months, and I.V. diuretics incurred in the remaining a number of patients.

A little reminder about the primary results of VICTORIA. Remember, for the composite endpoint of cardiovascular death and heart failure-related hospitalization, there is a hazard ratio through the follow-up of 0.9, showing a significant benefit of vericiguat in the reduction of those primary endpoints.

As part of the prespecified second subgroup analyses, there was a look at the treatment effect according to quartiles of NT-proBNP that was taken at randomization. And what we observed here was that in this upper quartile for patients with NT-proBNP greater than 5,314, picograms per milliliter, there seemed to be a differential treatment effects with vericiguat. So our question here today is: Does what happens before randomization provide insights into these results?

This is a brief slide on methods. So of the 5,050 patients who were randomized, 3,821 patients had NT-proBNP at screening and we were able to look at the change between screening and randomization. For our purposes here, we classified change in a relative sense. So for those with a decreasing NT-proBNP of greater than 20%, you'll note the green font. For those with minimal change, either plus or minus within 20%, that was minimal change in blue. And in red, we're showing increased for greater than 20% increase.

So what we found overall was of the 3,800 patients, 1,600 were in a decreasing mode between screening and randomization. And that was - they were coming in about 12 days prior to randomization in a median way. Minimal change was in about 1,400 patients, and increase seen the in the group here was about 800 patients. So as I mentioned, we're interested in looking at how these changes pre-randomization may give us some insights into the treatment effects according to quartiles of NT-proBNP at randomization.

So I'm going to present to you, these are spaghetti plots that show you that the starting value or the screening value all the way to the randomization value of NT-proBNP according to quartiles of NT-proBNP at randomization. So what you see here on the left are two spaghetti plots. This is for the first quartile. So under 1,556 picograms per milliliter. We see a lot of patients certainly in that decreasing. You'll notice all the green that show up here. For the next quartile up, between 1,556 and 2,816 picograms per milliliter, we see kind of a more even distribution of decreasing, still predominant, no change, and some patients who are in the increasing trajectory. For the latter two quartiles, you'll see that they look quite different from the first two. As you move to higher levels of NT-proBNP at randomization, we're starting to see more patients who are actually in an increasing mode, and that's certainly true in the uppermost quartile.

In this slide, we're going to look at the associations of these changes in the screening period with the clinical outcomes. So this graph here looks at the changes in the NT-proBNP from screening to randomization in a continuous fashion. But we've kept the color coding the same. So you'll note the green, these folks are decreasing from screening to randomization, the blue are for people with a minimal change, and the red color is for those on increasing trajectory.

So what we see here is those who are on the decrease are experiencing a lower likelihood of these clinical events, the composite of cardiovascular death and heart failure hospitalization. Whereas for those who are in the increasing trajectory, their association is an increasing likelihood of the events. And just to bring you back to those categories, so we have started out with this provided the breakdown for the composite. So again, we're seeing higher rates or higher likelihood of these outcomes for the increasing and middle change compared to the decreasing group, similarly was shown when you break out the composites. So this is for cardiovascular death here in the middle. And at the bottom here is for heart failure, hospitalization, similar tract all the way along.

This slide here gets us to one of our primary objectives. This is a showing you a hazard plot that looks at three different endpoints cardiovascular death or heart failure hospitalization as a composite, cardiovascular death, and heart failure hospitalization. And what we're looking at here is the treatment effect for vericiguat versus placebo within these different endpoints. And we have broken it down into - this panel here is for patients who are in the first three quartiles of NT-proBNP at randomization, so those with less than 5,314 picograms per milliliter. And here, what we see is that there's no measurable treatment modification based on the screening change. So remember from increased minimal change or decrease, we're seeing that the benefit of vericiguat is consistent.

When we move to the group of patients who had NT-proBNP at randomization greater than 5,314 picograms per milliliter, we notice some different signals. Again, we're looking at the same endpoints, and we're looking at change in the same sort of way. And here what we're seeing is more heterogeneity in the treatment effect here. Now, while they don't reach statistical significance, we are thinking that this is a signal.

Let's look at the cardiovascular death and heart failure hospitalization first of all. We're noticing in patients who had a decreasing NT-proBNP from screening to randomization, we're seeing a point estimate benefit for vericiguat. Whereas the other change categories are not observing that. So that's an important finding and gives us some insight on what's going on to these patients at a very high NT-proBNP at randomization.

So in conclusion, and some implications, we noticed that changes in NT-proBNP were common during the screening period. Certainly, we saw more patients with decreasing values or in a minimal change setting. Certainly, more than those who are experiencing an increase. We also noticed that minimal change, and especially those with increasing NT-proBNP during screening, they had a greater risk of cardiovascular death and heart failure hospitalization. And in particular, for patients in the upper quartile of NT-proBNP at randomization, there appear to be a signal of benefit with vericiguat when NT-proBNP was decreasing. We believe that these findings are interesting in this type of high-risk heart failure patient population, underscoring the need to really take a look at how NT-proBNP is changing, particularly in a screening period as the trial is looking to enroll patients. And we think this would provide additional insights for those who are designing future trials.

Thank you for your participation today.

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.