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- Hi everyone. My name is Dr. Florian Rader. I am the co-director of the Hypertrophic Cardiomyopathy Centre here at Cedar-Sinai in Los Angeles, California. And I was one of the investigators for the MAVA-LTE trial that I'm going to present at the ACC this year.

Importance of this study

Yeah, I think the backdrop of this study is that since investigators started to unravel the disease of hypertrophic cardiomyopathy, now over more than 60 years ago, there really hasn't been any specifically designed treatment for this disorder. So mavacamten is probably one of the most promising candidates for this role. In addition, it's important to notice that many patients with obstructive hypertrophic cardiomyopathy have significant symptoms and these symptoms are only partially relieved right now with medications. And many of those have to go on to invasive procedures to relieve the obstruction.

Study design and patient cohort

So the MAVA-LTE study is a long term open label extension of the previous pivotal trial of mavacamten, the EXPLORER-HCM trial for patients with obstructive hypertrophic cardiomyopathy. Those patients who finished the EXPLORER-HCM trial were weaned off mavacemten, and then re-enrolled into the long-term extension study. This is a study we're looking at right now. So this is an ongoing dose-blinded but otherwise open label trial of all patients who previously participated in EXPLORER-HCM. So patients in the MAVA-LTE long-term extension trial will be enrolled or followed for up to 252 weeks. What we're looking at here at this interim analysis is interim outcomes of these patients at a medium follow-up duration of 63 weeks.

Key findings

Yeah, the key findings here are that very similarly to the results in the parent study, EXPLORER-HCM, we found significant reductions in left ventricular outflow tract gradients. So a relief of the obstructive portion of this disorder. We also saw an expected decrease in ejection fraction by about 7 to 9% during follow up. And this is expected because the mechanism of mavacamten does reduce the force of contraction and that's how the obstruction is being relieved. And importantly, I think we also saw that along with very dramatic reductions in NTproBNP levels, sort of a marker of heart failure, improvement status also improved or a functional class, New York Heart Association functional class improved significantly. So specifically there were at week 48, 67.5% who improved at least one New York Heart Association class of shortness of breath.

Considerations for use

So based on these results. So we already know from the EXPLORER-HCM trial that mavacamten is effective for relieving LVT gradients improving functional class and symptom status in patients with obstructive hypertrophic cardiomyopathy. Now we sort of also have learned that longer term extension of the use of this medication is just as effective. And importantly, we now have more follow up data. So we also learned more about the safety of this medication. Overall, the safety profile of this medication was very good. There were of course, a large amount of adverse events recorded during the study. That's how we learn about potential risks of new medications but overall there were no new safety signals in terms of new concerns that would make us require more intense surveillance of echo follow up or pharmacodynamic data that we already knew after EXPLORER-HCM.

Take-home messages

So I think the take-home messages are that mavacamten continues to be the most promising contender for a first specifically designed medication or drug therapy for obstructive hypertrophic cardiomyopathy. And it seems to be extremely effective when it comes to relief of the obstructive portion of hypertrophic cardiomyopathy. It seems to be extremely effective in reducing BMP levels, along with improvements in New York Heart Association Functional class status and another important take home message is that the medication seems to be safe and overall very well tolerated and reductions in injection fraction that only very rarely exceed the level of 50% are in almost all instances reversible. So this medication does seem to be very safe and very useful for clinical practice.

Further research required

I think regulators will continue to look at the outcomes and further interim analysis of this long term extension trial. Like I said, this trial will go on for a total of over 250 weeks. So as we go along, we might learn more about additional ways to manage these patients. We will learn more about the durability of the medication and we will also learn more about the long term safety of this medication and therefore the usefulness in clinical practice. It also will inform, I think the question of how frequently do we have to check echocardiograms for example, to make sure that ejection fraction stays in an optimal range. So I think this will be very important for treating physicians and practitioners but also for regulatory bodies.