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

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## Precision Medicine in Obstructive HCM Care: The Promise of Cardiac Myosin Inhibitors

### Dr. Masri:

Hi, I'm Dr. Ahmad Masri, and I'm here today to discuss how cardiac myosin inhibitors are ushering in a new era in the care of patients with obstructive hypertrophic cardiomyopathy. As all of you are aware, we traditionally start treatment of symptomatic obstructive HCM with first-line therapy drugs like beta-blockers and calcium channel blockers, which traditionally lacked, really, evidence—robust evidence behind their use. However, the cardiac myosin inhibitors is a class of medications where we have mavacamten, which is an approved cardiac myosin inhibitor, and we have aficamten, which is an investigational cardiac myosin inhibitor, for the care of patients with obstructive HCM.

If patients have symptoms of obstructive HCM and they're using first-line therapy and they're still symptomatic, usually the guidelines recommend going ahead with one of a few options. One of the ones that is really well studied and has lots of clinical trials backing it up is cardiac myosin inhibitors. What they do, is that they reduce the amount of pathologic hypercontractility that we see in hypertrophic cardiomyopathy.

An interesting advancement in the field happened this year, which is the results of the MAPLE-HCM trial. The MAPLE-HCM trial showed that aficamten as a monotherapy—up-front and first-line monotherapy drug—as compared to metoprolol improved exercise capacity, improved symptoms, biomarkers, and a whole host of secondary endpoints. And that's important because after 60 years of the use of beta-blockers, this is the first relatively large, randomized clinical trial challenging the effect of metoprolol as a representative of all beta-blockers. And it's not just that aficamten was effective; it was that also metoprolol, again, as a representative beta-blocker, led to reduction in exercise capacity, so it was detrimental on peak VO<sub>2</sub>. It was detrimental on NT-proBNP, and it was detrimental on left atrial volume index. All of them are markers that are important in the care of patients with HCM.

And so there's a lot of science coming out on cardiac myosin inhibitors. And there are a lot of things that are happening. And again, some of them are already approved and you can use right now in patients with symptomatic obstructive HCM. And others, like aficamten, is being reviewed right now by regulatory agencies. But what's important, I think, with the amount of science and the amount of clinical trials that is going on, amount of activities that are happening, is to continue to focus on education, because that's how we can identify patients.

That's how we can identify them earlier and institute treatment to improve their lives, livelihood, and their ability to live a normal life.

And so, I'm Dr. Ahmed Masri, and thank you for watching.