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Biomarkers of the Storm: Decoding IRI's Signature

Announcer:
Welcome to CME on ReachMD. This episode is part of our MinuteCE curriculum.

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Dr. Bhatt:
This is CME on ReachMD, and I'm Dr. Deepak Bhatt. Here with me today is Dr. Manesh Patel, a good friend and colleague, and we are going to talk about ischemia-reperfusion injury, sometimes abbreviated as IRI. It remains a significant challenge in patients with ST-segment elevation myocardial infarction who are undergoing percutaneous coronary intervention.

Manesh, what can you tell us about the latest therapeutic strategies to mitigate IRI and the role of biomarkers in guiding treatment decisions?

Dr. Patel:
Well, thanks, Deepak. As we've discussed, and as I think a lot of our clinicians and colleagues know, unfortunately, ischemia-reperfusion injury remains a challenge, something that I know we've studied with multiple therapies to try to improve.

Just to remind our audience, ischemia-reperfusion injury itself is the idea that while the myocardium is not getting blood flow, it's starting to go through a variety of adaptive mechanisms as it stops being able to produce ATP and starts to actually have myocyte cellular wall breakdown, and eventually it gets, as we've described, a hyperemic state once it gets reperfused. But there's these radical oxygen species, eventually inflammation, and neutrophil infiltration that leads to infarct size. And so that process where we try to open the artery faster, maybe one of the strongest things to reduce infarct size, is a key that we've all done. However, in this process, when we have ischemia-reperfusion injury, we have a variety of things happen. We have this, as I've highlighted, first we have inflammation, and we have actually this action where neutrophils are coming and we have cellular breakdown. So you can imagine some of the biomarkers in this biologic process I've talked about: proBNP to see what's the filling pressure, but also the size of the infarct and maybe even some of that damage; myeloperoxidase, another, like, direct measure of some of those reactive oxygen species; MMP matrix or metalloproteinases that, again, tell us about that process. Those are some of the biomarkers, along with infarct size and imaging or even LVF [left ventricular function] and, eventually, clinical outcomes that we care about.

Now, in our history, we've tried a lot of events and a lot of things to try to improve this. As you and I know, we've studied a lot of things in animals that look like they might be good. And then we've studied things in humans that have had some initial strategies that look good but haven't had future ones, things like in addition to opening the artery fast, adenosine and N-acetylcysteine, remote ischemic conditioning before reperfusion. And all of these are limited in some fashion, in that you want to hopefully help with this ischemia reperfusion by doing things at a specific timepoint, ideally before you open the artery and this damage occurs, and having enough of it around to reduce this sort of history of what we've seen as adverse events.

One of the exciting compounds that's coming along, a compound called FDY-5301, is aimed at this sort of, what I'll call, inflammatory

and, I'll call it, radical oxygen species of breakdown of those cellular therapies. The idea is that you would infuse this before opening the artery, open the artery, and reduce some of this storm that we've talked about.

And in some phase 2 data I know you know about and others have seen, is Iocyte AMI, a clinical trial in phase 2 that looked to do just that and study some of these biomarkers. And initial data there has shown some promising evidence that when you also look at the time of opening the artery, but also look at some of those biomarkers, like proBNP, myeloperoxidase, and MMP matrix, or the metalloproteinase 2, that we see some changes that would help us think that that biologic process of reducing some of that, I'll call it, radical oxygen injury to the heart is improving.

So that's some of the new stuff coming along with at least a review of some of the stuff we've tried in the past for ischemic-reperfusion injury.

Dr. Bhatt:
Yeah, no, that's a great summary. And we'll talk in another segment a bit more about FDY-5301, which is a sodium iodide formulation that's hopefully going to actually make an impact on ischemia-reperfusion injury. And you're right, there's already phase 2 data showing effects on markers of cardiac dysfunction, markers of inflammation, markers of myocardial remodeling, ie, proBNP, myeloperoxidase, MMP 2, or matrix metalloproteinase 2. So all of these changes in biomarkers will hopefully be associated with actual clinical benefit. In that phase 2 trial, there was also numerically lower rates of infarct size and better EFs [ejection fractions], so hopefully this will portend that there will be an effect on clinical events, but obviously a phase 3 trial is needed, and fortunately, there is such a trial ongoing with that compound. So I'd say stay tuned. Let's see if all this good science translates into clinical benefit.

Well, this has been a great micro discussion. Our time's up. Thanks for listening.

Announcer:
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