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TRANSFORM Trial: Overview and Potential Implications

Announcer:
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Dr. Taub:
This is CME on ReachMD, and I'm Dr. Pam Taub. And here with me are my colleagues, Dr. Deepak Bhatt and David Maron. And today we're going to be talking about how artificial intelligence [AI] has become increasingly incorporated into different aspects of medicine, including clinical trials.

Deepak and David are the leaders of a very innovative trial called the TRANSFORM trial that's looking at the application of artificial intelligence technology to interpretation of CT [computed tomography] coronary angiography and then using this data to guide clinical practice. And so let's talk about the potential implications of AI in clinical trials like TRANSFORM.

And let's start with you, Deepak, first.

Dr. Bhatt:
Absolutely. Well, TRANSFORM is a trial that's really intended to try and transform cardiovascular medicine, in particular cardiovascular prevention by using CT angiography and an AI-enabled algorithm to help determine risk much more precisely than we can now, and I'm talking about individual patient risk, and using that information to then tailor the intensity of medical therapy. So that's really the goal of TRANSFORM, to do what's been done in cancer care, where we stage atherosclerosis in a manner similar to how oncologists might stage cancer and then titrate the therapy based on the stage of atherosclerosis.

Dr. Taub:
I think what's really appealing about TRANSFORM is it's recruiting patients that have not had an event but are at risk for an event. So we're starting to call this group of patients high-risk primary prevention, because that's truly our goal is to prevent patients from having a heart attack or stroke.

So one aspect of TRANSFORM is there are personalized heart disease care strategies. David, could you elaborate on this?

Dr. Maron:
Sure. Thanks, Pam. So with the anatomic information that we get from the CCTA [coronary computed tomography angiography] AI-enabled output, we're able to tailor therapy, as Deepak said, according to the patient's own burden of atherosclerosis. And this is very different from the way we practice primary prevention, which is based on risk factors. As you know, people can have risk factors and have no atherosclerosis, and we see patients with atherosclerosis that have no obvious risk factors. And treating the atherosclerosis allows us to really adjust the appropriate intensity of therapy, as Deepak said, according to their level of risk.

Dr. Taub:
Great. Deepak, can you provide an overview of the trial design and specifically go over how we are using AI to analyze the CCTA

images and how we're generating personalized treatment plans?

Dr. Bhatt:
Yeah, absolutely. So TRANSFORM will randomize approximately 7,500 or so patients to 1 of 2 arms. One is standard therapy, although it's actually better, probably, than standard therapy; it's really guideline-concordant care for primary prevention-type patients, versus an approach that is informed by this AI-enabled CT angiography of the coronary arteries. And the idea is that all the patients get a CT angio at baseline. In the control arm, which is getting guideline-concordant care, the patient and physicians and everybody are blinded until the end of the study to what the CT angio shows.

In the investigational arm, however, the doctor, the patient, they know what the CT angio has found, so if there is atherosclerosis, that will hopefully then motivate them to treat it more aggressively than they would have otherwise without that knowledge. And using an AI-enabled algorithm we'll be able to say what stage of atherosclerosis they have. Stage 0, for example, would be no plaque. Stage 3 would be a lot of plaque. And looking at characteristics such as the amount of plaque, the distribution of plaque, whether there's ischemia in the vessel, the constituents of the plaque, lipid-rich plaque being particularly bad, using that information and pictures from millions of other CT angios, it's possible using machine learning techniques to then correlate images with risk. And that's based on images that have been obtained in the past but being applied to patients in the present.

And the interesting thing about this sort of algorithm is it can only get better and smarter as more data are inputted. So the idea is to use this knowledge to more precisely estimate a patient's risk and, importantly, then tailor to therapy. So here we're really trying to blast down the LDL cholesterol using things like bempedoic acid and using things like SGLT1/2 inhibitors, sotagliflozin specifically, using colchicine in patients with elevated hsCRP [high-sensitivity C-reactive protein].

So using therapies that are available and approved, but perhaps going beyond the specific trials that led to their approval, testing them in novel ways to reduce risk in a primary prevention setting but informed by this AI-enabled CT angiographic information.

Dr. Taub:
Okay, that's a great summary. And it's really amazing to me how much subclinical plaque patients can have. And so I think CT coronary angiography is really the most innovative way to characterize plaque and to really look for this hidden subclinical plaque that sometimes doesn't even show up on angiography.

So your thoughts about just CCTA and AI as the future of risk assessment?

Dr. Maron:
Pam, if I could mention one of the great features of the design of TRANSFORM is that after 2 years, a repeat CT angiogram will be performed in both arms, and that will give us an opportunity to monitor response to therapy and adjust therapy as needed, depending on what we see on the follow-up. And the AI will help us do a side-by-side comparison, looking for evidence of progression or a favorable response to therapy.

Dr. Taub:
Let's conclude with some takeaways. I think my key takeaway from this discussion is that there are a lot of patients that have subclinical atherosclerosis, and we need better modalities to detect that subclinical atherosclerosis.

Dr. Bhatt:
I guess my takeaway would be that people listening to this should stay tuned and see what TRANSFORM shows. Obviously, the results will be a few years away, but I think it will tell us whether we should keep doing what we're doing – which is use risk scores and sort of guesstimate what patients' risk might be and then figure out how to titrate their medical therapy, which is rather imprecise, I think, in many cases – or whether actually knowing that the patient has plaque and acting on it is the way to go. And I think whatever the trial shows, it'll be informative.

Dr. Maron:
I would say just we're applying universal principles, adjusting the intensity of therapy to the level of risk, but we've got some new tools to help us really target therapy even better.

Dr. Taub:
Well, this has been a great and lively discussion. Our time is up. Thanks for listening.

Announcer:
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