Reaching LDL-c targets in patients at high CV risk: How well are we doing?

Dr. Brandt:

Hi. I'm Dr. Julia Brandt, and today I'm talking to you about reaching LDL cholesterol targets in patients at high cardiovascular risk and how well are we currently doing.

So to start with, there are several factors that contribute to whether we are successful in treating our patients and meeting LDL cholesterol treatment guidelines. However, that depends on the healthcare system we're working on. It depends on the patient in front of us. But it also depends on us, of course, as clinicians. How do we estimate a patient's cardiovascular risk and with what kind of intensity do we treat our patients? And this is what I want to start with.

So let's look at patients who are on lipid-lowering treatment. So this was the main inclusion criteria for the 2017-2018 DA VINCI registry. And what we can see, applying current guideline goals makes them appear pretty poor, with a 33% LDL cholesterol treatment goal attainment. So how are these patients treated? If we look on the right-hand side, we see that 80% of patients do receive statin monotherapy, and only 9% of patients did receive a combination with ezetimibe. Let's not talk about the 1% PCSK9 inhibitor combination.

So let's now look at populations that are at risk. So the SANTORINI study included patients at high and very high risk, independent of ACVD. And what they found, it's a bit more recent, but what they found is 21%, shown in the green bars, only achieved the current LDL cholesterol ESC-recommended treatment goal. And this is kind of the same for patients with ACVD. No ACVD, those in the very-high-risk category without ACVD are even doing a bit worse with 12% goal attainment. However, those who peak out a bit is the 32% patients on combination therapy who do achieve their goal.

So combination therapy was here a bit more common than in the DA VINCI study, with 24%, at least 16% on ezetimibe combination therapy. But if we look up in this figure, we see a striking number of 21% of patients on no lipid-lowering therapy.

So what else can we learn from the SANTORINI data? Just recently published was the 1-year follow-up data where the authors looked at whether patients had a change in their lipid-lowering treatment. And here, down below, you see at least 30% of patients, they did receive an escalation in lipid-lowering treatment, but in many more patients, about 70% of patients, this opportunity was missed, and they did receive no change in treatment.

Looking to our colleagues in the US, we see here data from the GOULD registry which were patients included from 2016 to '18, which all had an ACVD. And here, we can see the baseline and also the 2-year follow-up data. And we see at least a much more significant increase in uptake of LDL cholesterol treatment goal attainment on the left-hand side. What is very interesting is that those on a PCSK9 inhibitor therapy, even if it was a monotherapy, did much better in terms of treatment goal attainment.

So let's have a focus on some special populations next. First, we have patients with diabetes. And this here is data from the German Diabetes Registry. And don't be fooled by the bars on the left-hand side which show very good treatment goal attainment, because if you look in the table down below, you see that the orange bars for the patients with type 1 diabetes accounts only for 10% of the overall population. And even worse, for patients with type 2 diabetes, this is only 0.5% of the whole population. All the others are in the high- or

very-high-risk category, and here, treatment goal attainment is way below 25%. If we look at what are these patients treated with, or are they treated at all, we see only 1/2 of patients with type 2 diabetes are on a lipid-lowering therapy, and only 1/5 of patients with type 1 diabetes.

Moving on to the ultimate challenge, I call it, it's the patients with statin intolerance. So in this patient population, only 8% of patients overall achieved their recommended LDL cholesterol goal. Now, thinking about this classic statin intolerance, we could treat these patients with ezetimibe, and this is what has been shown in the study here. Let's simulate putting all these patients on ezetimibe treatment; we get 22% to goal. If we combine ezetimibe with bempedoic acid, then we may even get 1/2 of the patients to goal.

Therefore, to close, let's look at this simulation. This on the left-hand side is based on the DA VINCI data; right-hand side is based on the SANTORINI data. So if we take our ESC guidelines seriously and we apply the stepwise approach, then we see here on the left, optimizing statins, in blue, this only increased by 12% the goal attainment. Adding ezetimibe is really making a change with 40%. However, if we want to achieve the 93%, we need a PCSK9 inhibitor, which is shown in green. Moving on to the right, we are very lucky that we have now a third oral treatment available. And if we simulate within the SANTORINI cohort the addition of bempedoic acid, we see that we can move the bar from, at baseline, 36% attaining goal to 69% of patients attaining their LDL cholesterol goal.

So to conclude, there are persisting challenges. It's the low LDL cholesterol goal attainment. We have an underutilization of our intensive treatments. We have still at hand the problem with patients with statin intolerance, and there are many missed opportunities for up-titration in treatment. So what we should look for is an enhanced risk stratification. We should focus on the importance of our therapy, and we should raise awareness for the special populations, like patients with diabetes.