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Elevating Care for Patients With Severe Renal Disease in AAV

Announcer:
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Dr. Brix:
Hello, everyone. My name is Silke Brix, and this is a CME on ReachMD. Here with me today is Andreas Kronbichler.

Dr. Kronbichler:
So I would start with a patient case.

So what I wanted to do, because he had a biopsy lined up to start on a Sunday with a low-dose steroid regimen, so only 30 mg of steroids per day. We had to initiate IV glucocorticoids because this patient, after 3 days of low-dose steroid treatment, he had a dissection of his artery, arteria colica dextra. So IV steroids were started, then he received rituximab here, and you see that his inflammatory response actually was pretty good. So CRP was almost negative. But the creatinine didn't do what we wanted it to do, so he creeped it up with the creatinine, and you can see that here the creatinine up to 4 mg/dL, which is equivalent to roughly 340 µmol. So we had to initiate cyclophosphamide here. We gave him more rituximab and, in the end, we decided here, when the creatinine improved actually, to start avacopan.

And we have talked about that before. It's a novel drug which inhibits the C5a receptor 1. And why did we decide to do so? So what we've learned over the past years is that, clearly, kidney function recovery is a relevant endpoint. I will show you some data we have just been published in the *Kidney International*. We have investigated the whole PEXIVAS cohort and all the patients with ANCA-GN, and what we found here is that if you look at GFR recovery, there is a distinct pattern when it comes to PR3 ANCA positivity and MPO ANCA positivity.

So independent of treatment assignment, those with PR3 ANCA positivity have a higher likelihood to increase their GFR and also to have an improvement of at least 15 mL/min. So importantly, a patient with PR3 ANCA, like the patient I've showed you, has a good likelihood to improve kidney function.

I will show you some data of the ADVOCATE trial. So in total, 268 patients with kidney disease were included; 265 had a GFR at baseline at week 52, so were included here. And you can see at first sight that those in the avacopan arm had an increased improvement in GFR by 3.2 mL at Week 52 in all patients with a GFR below 60. But this even became more robust as soon as the GFR was lower. So if you look at the subset here with the GFR below 30, or the subset with the GFR below 20, these even got more striking.

So clearly what we've seen is that avacopan is the first agent which has a GFR-sparing effect, and so I think patients like ours here need to be started on avacopan as early as possible.

Why is it relevant? And this is data from the RADAR here to the left, which has been published recently. And you can see that even though patients with ANCA-GN here, on average, start with a GFR of 30, they will have an improvement in the first year. And then, importantly, this curve here for ANCA-GN in dark blue runs quite flat. So the GFR loss over time is not as bad as it is for other inflammatory kidney diseases. But nonetheless, if we gain more GFR here after initial diagnosis, I think also cardiovascular morbidity and mortality also improves in our patients' subset.

You see that especially those patients with kidney involvement have a lower survival probability as has been shown in the FAIRVASC cohort, where patients with 6.55 creatinine or 2.7 and 2.5 creatinine clearly had adverse overall survival over 10 years in comparison to those with a preserved kidney function. So clearly we are moving away from this classical BVAS renal items more so to a way where we actually look at improvement of kidney function, eGFR.

Dr. Brix:
I'd like to thank you all for your attention. I hope you found this useful and see you at the next CME. Goodbye.

Announcer:
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