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Tailoring Treatment for Optimal Outcomes in Patients With AAV

Announcer:
Welcome to CME on ReachMD. This episode is part of our MinuteCE curriculum. Prior to beginning the activity, please be sure to review the faculty and commercial support disclosure statements as well as the learning objectives.

Dr. Hellmich:
This is CME on ReachMD, and I'm Dr. Bernhard Hellmich. Here with me today is Dr. Andreas Kronbichler.

Andreas, we've talked about induction and maintenance therapy previously, so let's switch to treatment of relapse. So what do you do with your patients who are experiencing a relapse, Andreas?

Dr. Kronbichler:
I think it became very clear, the recent years, that as soon as a patient experienced relapse, those patients do benefit from rituximab treatment and then from a prolonged likely maintenance phase of rituximab. Plus, what has been used in RITAZAREM is that most investigators opted out for a lower-dose glucocorticoid regimen.

So we have established relapse predictors, and that's PR3 ANCA positivity, higher percent in eGFR. So those patients with mild ANCA-GN ANCA positivity at the time of completion of induction therapy, and of course, previous relapses.

On the other hand side, we have treatment-related risk factors, and that is mainly associated with, let's say, milder forms of immunosuppression. If you compare methotrexate to cyclophosphamide, those on methotrexate do relapse more. It's also been proposed in different studies that those with IV cyclophosphamide do relapse more frequently than those receiving PO cyclophosphamide. But I think most of us not use per oral cyclophosphamide nowadays. And you know from several studies that rituximab, as a maintenance agent, is actually superior to azathioprine, although this has not been acknowledged in that clarity in the KDIGO guidelines.

I also wanted to flag the main result of RITAZAREM, which showed that if you use rituximab as a fixed regimen, you will see a significant reduction in disease relapses during the conduct of the trial, but once you stop your maintenance treatment, you see that the curves are running in parallel. And this is important to know that once you are stopping your treatment, independent of your treatment regimen, you need to expect disease relapses.

And as has already been outlined before, there are a couple of established biomarkers, which can be easily implemented in the clinical practice. One that has been shown from the Mayo Clinic is, if you have a patient with MPO ANCA vasculitis and you achieve MPO ANCA negativity independent of your treatment choice, you will have a very low relapse risk over the period of time the patients remain ANCA negative. Once the patients are turning ANCA positive again, the relapse risk actually mirrors the relapse risk of patients who always are MPO ANCA positive.

On the right side here, you can see the main results of the MAINTANCAVAS study, which has been conducted as a single-center study in the US. And they have investigated how we can use ANCA or B cell return as potential biomarker to predict relapse. And what they have found is that if you have a B cell return and you reinfuse rituximab, you can reduce the risk of relapse significantly.

Of course, you also need to acknowledge that there has been a disbalance in the infusion rate of rituximab because those in the B cell arm received 3.6 infusions versus 0.5 infusions in the ANCA arm. But clearly, if you want to re-dose rituximab and individualize your treatment, you need to go for a B cell-guided therapy.

And why do you want to reduce relapses? And when we speak about kidney relapses, we know that these patients have an almost 10-fold increased risk of end-stage kidney disease, and that is of course an outcome we want to prevent. But relapses also are leading to a higher cumulative dose of glucocorticoids, as has been shown by Bernhard's group recently but as has also been shown in the UK by Lauren Floyd, who also proposed that this is actually also increasing the glucocorticoid toxicity. So prevention of relapse is clearly something we want to achieve in clinical practice.

Dr. Hellmich:
Yeah. Thanks, Andreas. So it's clear there's much more room for research in this area. But unfortunately, our time is over again. Thanks, Andreas, and thanks to all of you for listening and bye-bye.

Announcer:
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