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Beyond IGF-1R: IL-6R Inhibition and Future Sequencing

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Episode 8

Dr. Cockerham:
Hello, I'm Kimberly Cockerham. Joining me today is Dr. Prem Subramanian, who's a world expert in thyroid eye disease, and I'm happy to say has been a friend of mine for many decades since we were in training at Walter Reed many years ago.

In addition to IGF-1 blockage, IL-6 blockage is also a target for managing thyroid eye disease. What do you think about this blockage of IL-6? Do you think these targeted agents in development are going to be helpful and will work with the IGF-1 blockage or by themselves?

Dr. Subramanian:
Thanks, Kim. I think it's exciting and always important to consider new options. And while the IGF-1 receptor-targeting drugs have been really helpful, it never hurts to have other options.

And so if we look back again at the diagram of TED pathogenesis, you can see that IL-6 plays an important role in the development of the inflammatory cascade that is part of the fibroblast activation and leads to the changes within the orbit. And so because of that understanding of disease, there have been some retrospective studies that have been done looking at IL-6 receptor antagonism.

Tocilizumab, which is FDA approved for other indications, has been used in patients with TED, and in particular when we didn't have other drugs available in patients that failed corticosteroids, which were the mainstay of therapy. And what we found was that these patients would have a response to tocilizumab, that their inflammatory symptoms would go down. In some studies, their proptosis improved. This effect, not unlike in other treatment strategies, is better in patients who don't smoke, but still it seemed to be effective in reducing the things that bother our patients, their diplopia, their proptosis, and their inflammatory symptoms.

Now, IL-6 receptor antagonists have a different safety profile because they act through a different pathway, so we have to watch out for things like neutropenia, leukopenia, thrombocytopenia. It can result in opportunistic infections, although fortunately that seems to be less common, and it can lead to a transient hypertransaminasemia. So there you have to monitor liver enzymes.

Now, there's another IL-6 receptor antagonist that has been studied more recently, and that is satralizumab. Satralizumab, as you and I know as neuro-ophthalmologists, is FDA approved for the treatment of our patients with NMO spectrum disorder, and it has been studied in clinical trials now to see if it can help with the signs and symptoms of TED, both in patients with a shorter as well as a longer duration of disease symptoms and findings.

And so the SatraGO studies were recently reported out, and they demonstrated that there was a significantly better response of proptosis and diplopia in patients who were treated with satralizumab as opposed to placebo. And this drug also seemed to be quite well tolerated by patients. And I think that's one of the interesting aspects about this because the IGF-1 receptor antagonists have certain side effects associated with them that sometimes limit their use. And so we're always looking for agents that may just have a different profile in that regard.

And so because the SatraGO data showed that proptosis and diplopia seem to improve in both a shorter as well as a longer duration state, when you look at the adverse event profile, it is somewhat different. Like I talked about, we look at events like infections, serious infections. It's a subcutaneous drug, so there can be some injection-site reactions, but really the incidence of serious infections or other serious AEs was fortunately relatively low. So this is promising to potentially use this agent.

And what we don't know is, will we use this first? Will we use it second after some other agent? Will we use it in alternation? And that's something we as doctors need to figure out if and when these drugs become more widely available to us to treat our TED patients.

Dr. Cockerham:
So super exciting. I remember when multiple sclerosis had no treatments. Right now we have 20—more than 20. And I think that looking at these other pathways and how they can be useful for patients who are, for instance, have an inflammatory bowel disease, or diabetes, or have hearing loss.

So I agree with you. It's going to be really interesting to individualize treatment plans based on the patient's comorbidities and figure out just what's perfect for them.

But thanks so much. And we've come to the end. Audience, we appreciate all those who joined us today, and thank you for all being here, and we'll see you next time. Thanks so much.

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