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The Future of TED

Announcer:
Welcome to CME on ReachMD. This episode is part of our MinuteCE curriculum.

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Dr. McGee:
It is an exciting time for thyroid eye disease treatment, with an abundance of clinical research happening. What are the therapies in the pipeline, and what does the future of TED look like?

This is CME on ReachMD, and I am Dr. Selina McGee. I'm privileged to have with me here today, joining me, Dr. Fatemeh Rajaii.

Dr. Rajaii, welcome.

Dr. Rajaii:
Thank you for having me. As a clinician and researcher in the field of thyroid eye disease, we're interested in finding new ways to address the underlying pathologies of thyroid eye disease. Teprotumumab and its success have established the IGF-1 receptor as an effective target, but we do wonder if it could be improved upon. There are numerous other IFG-1 receptor antagonists that are in investigation right now. These include VRDN-001 which is an infusion for active disease; VRDN-003, which has FcRn modifications to extend its half-life, and it's subcutaneously injected for chronic disease; lonigutamab, a higher potency IGF-1 receptor antibody that has subcutaneous delivery; and the makers of teprotumumab are also in early phases of developing a subcutaneous delivery molecule named AMG 732. And then finally, there's linsitinib which is a small molecule IGF-1 receptor inhibitor that is being investigated for oral therapy for active disease, which may be the most convenient of all these options for patients.

Dr. McGee:
Wow, lots to think about and very exciting. Are there any agents in development with targets other than IGF-1 receptors?

Dr. Rajaii:
That's a great question. So interleukin-6 and the neonatal Fc receptor, or FcRn, are other targets that are being investigated as possible treatments for thyroid eye disease. Interleukin-6 is a proinflammatory cytokine and it plays a role in inflammation, immune response, and other processes. And there are studies of off-label use of tocilizumab, which have shown favorable results. As a result, satralizumab, which is a subcutaneous IL-6 receptor antagonist, is being developed for thyroid eye disease, and TOUR006, which targets the IL-6 itself, is also being investigated for thyroid eye disease. Really an additional goal for therapy is greater convenience – subcutaneous administration versus IV administration – and trying to increase the dosing intervals. So satralizumab is the shortest of these, whereas TOUR006 dosing studies suggest that they may be able to dose it every 8 weeks, which would really increase the convenience for patients.

In terms of the FcRn, that's the neonatal fragment crystallizable region receptor antibody, and it works by prolonging the half-life of IgGs by rescuing them from degradation. Anti-FcRn antibodies increase Ig metabolism and therefore decrease their half-life by blocking that

interaction. So this could be useful for any autoantibody-mediated disease.

For thyroid eye disease, there's 2 molecules that are in development. Batoclimab is an anti-FcRn antibody and it's been studied in myasthenia gravis, which has shown efficacy in terms of decreasing antibody loads, but there have seen upper respiratory infections, elevated cholesterol and lipid levels, and are actually developing further molecules to try to reduce the elevated cholesterol complication. And then efgartigimod is another anti-FcRn molecule that's in development.

Dr. McGee:
I know most patients with active TED are working-age professionals with families. They're trying to do their everyday life, and there's a great, heavy burden on these patients, and any treatment that's convenient with a good efficacy and safety profile will certainly help our patients better manage their condition.

We're just about out of time today. Dr. Rajaii, any take home messages for our audience?

Dr. Rajaii:
Certainly. I think that the treatment landscape for TED is likely to change dramatically in the next few years, with many more targeted immunologics that are in trials, which will likely increase the available treatment options. Without head-to-head studies, it's going to take time to determine which treatments are really best for which patients, but you can look for more information about clinical trials on the Resources page of this activity.

Dr. McGee:
This has been CME on Reach MD. Thank you for being here to our audience and our listeners. Thank you, Fatemeh, for sharing your wealth of knowledge with us today. We really are all going to be better served, and our patients, with these developing therapies for TED.

Dr. Rajaii:
Thank you.

Announcer:
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