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KOL KNOCKOUT™: Endocrinology Edition – Thyroid Titans Clash to Enhance Outcomes in Thyroid Eye Disease – Round 2

Announcer:
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Dr. Gupta:
Hi, everyone. Good evening. I'm Dr. Malini Gupta from Memphis, Tennessee, where I'm the director of G2Endo, a thyroid-focused group in Memphis, Tennessee. I will be your host this evening and I am happy to bring back Round 1 winner, Rokshana Thanadar from Chesapeake Virginia. We also have Melissa Young, from MidAtlantic Diabetes and Endocrinology Associates from New Jersey, and Kaniksha Desai, a Clinical Associate Professor of Endocrinology at Stanford University. Welcome.

Our faculty disclosures are as listed.

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There will be audience participations with some questions and voting. And you can click on the question mark icon to type a question for the panel. When it's time to vote, the poll will pop up, you enter your choice, and then click to submit.

These are some of our learning objectives.

And I think we're ready to begin. So, we're going to start with Case Number 1. Case Number 1 is a 74-year-old female who presented to clinic with jaundice and a marked elevation and liver functions, which were in the 400s. She had a weight loss of 30 pounds in 6 months, rapid heart rates, heat intolerance, hair loss, irritability. She had a history of osteoporosis treated with zoledronic acid annually. She had a fracture, and that fracture was in her wrist, and she had a fracture repaired. And she had a history of C-sections.

So, I'm going to start with some questions now. Kaniksha, I'm going to start with you. What comes to mind when you're seeing this photograph?

Dr. Desai:
So, the first thing, thank you for inviting me today. And I'm so excited to be joining everyone. As far as this patient, when you're looking at her, the most noticeable thing is probably her jaundice, which is the yellowing of her eyes. Other things that you might notice in this patient is that she has some eye state that you can clearly see. She also has some possible lid lag and some orbital swelling. She also has chemosis in her caruncle area, and a little bit of redness and swelling of the bottom of the eyelids as well. And it probably looks like the right eye might have a little bit of proptosis, hard to tell from a direct photo. And it looks like her pupil might be not centered on the right side, but it's a little bit challenging in this photo. So, that's what I would see when I looked at this photo.

Dr. Gupta:

That's great. Dr. Young, Melissa, what do you see when you're seeing some of the numbers? What are you thinking of when you're matching the numbers to this picture?

Dr. Garduno Young:
Well, the only number that we really had was transaminase if I remember correctly, right, 400? So, like was mentioned earlier, I think the most common thing is the jaundice, which may or may not be related to a thyroid disease. I just want to go back to the earlier question if you don't mind. I also think she you might have a disconjugate gaze. I think that the irises are not on the same horizontal plane; it's a little hard to tell sometimes in the picture, but it looks like there might be a slightly upward positioning of the left eye.

Dr. Gupta:
Okay, Rokshana, what are you seeing in this picture? And what would you want to order?

Dr. Thanadar:
So, I agree with, you know, my colleagues that there are very obvious things that can be seen here. Definitely the stare, definitely the yellowing of the eyes, and the redness around the eyes. She does have, it seems, some periorbital edema as well. And so, all of those things, you know, would lead to saying, well, could this be related to a thyroid issue? And so, you know, that would be the next workup I would say to do. I have to admit, I don't necessarily remember what the other numbers were there either. So, I don't know – as Dr. Young asked with respect to the numbers, but that would be the first place to say well, yeah. So, you know, we don't have any information about thyroid. And so, that would be kind of the first, I think the first step to do, obviously there with the other information. And thinking that if there's thyroid issue, then could this be related to thyroid eye disease? And there would be concerns of imaging and then thinking about referral to the appropriate people to be able to help treat.

Dr. Gupta:
Okay. Rokshana, what, in this history so far, would bring you to – if you weren't looking at the eyes, what would you – what key points in the history are leading you towards ordering thyroid tests?

Dr. Thanadar:
So, you know, the big one is the issue of the weight loss in such a short period of time. You know, it could be that she's been trying to lose weight. But many times, if you've asked further, they'll say, 'No, I haven't been trying to lose weight,' or, 'If I have been trying to lose weight, I certainly didn't expect I was going to lose this much weight in that short period of time.'

And then the other symptoms that kind of come with that, rapid heart rate, they may describe that they've got some palpitations or they're feeling the heart beat funny. And then just the temperature intolerance, feeling hot, the hair loss, and the irritability. Kind of also, just to expand on that, you know, are they things that bother them now, that didn't bother them before? Do they easily get annoyed with things? All of those things kind of lend towards saying, does she have excess thyroid hormone? I mean, I'm biased because I'm an endocrinologist. And so, I'm going to think that way. But those are the things that would, for someone who is just looking at this patient and say, maybe this is thyroid, let's check that out.

Dr. Gupta:
Dr. Desai, question for you. What do you think, just based on these, are your other differentials besides thyroid disease?

Dr. Desai:
So, she is an elderly woman, so she could actually have weight loss for many different reasons, cancer being one of them as well. Probably the most common cause in her age group. But her symptoms, as Dr. Thanadar had said, really lend itself well to the classic hyperthyroidism symptoms, because you wouldn't necessarily have those kinds of symptoms with other reasons. But as far as her eyes, there's also, you know, you can have orbital issues, orbital tumors as well and the differential diagnosis for her eye disease.

Dr. Gupta:
Okay. So, these are her labs. And I had ordered the following labs: CMP, CBC, TSH free T4, free T3, thyroid stimulating immunoglobulin, a TPO antibody, parathyroid, mag, phos, vitamin D, and an A1c. And so, the TSH was 0, had an elevation in free T3 and free T4. Calcium was markedly elevated. Vitamin D normal. Transaminase and bili were elevated. The WBC was low normal. Platelets also low. Parathyroid was elevated. Mag and phos were normal. A1c was normal. And she had a very high BUN to creatinine ratio. The heart rate was also intermittently elevated; sometimes into the low 100 range.

So, on these numbers, Dr. Young, can you tell us what you're thinking about some of the number interpretation?

Dr. Garduno Young:
So, I think she has more than one thing going on here. And I think, you know, as Rokshana mentioned, I think we'd focus on the endocrine part, the thyroid part, because that's why we're here tonight. But I think she has more than one disorder going on. She had

evidence of thyrotoxicosis hyperthyroidism, but her elevated calcium, which can sometimes occur if it's rapid bone turnover in hyperthyroidism, but it's paired with the PTH, which is not suppressed, so it looks like she also has primary hyperparathyroidism.

And I was concerned about the liver transaminases. So, if her heart rate is only intermittently elevated, I wouldn't expect the transaminase to be so high of passive congestion. And so, she may just have an intrinsic liver disorder as well. Especially since she has a low WBC and low platelets. I think she may have, you know, intrinsic liver disease, which is leading to – so, no mention yet a physical exam or anything other than the eyes. If she has splenomegaly, that could, you know, affect the blood cell counts, but I certainly think that she has more than just hyperthyroidism going on.

Dr. Gupta:
Dr. Thanadar, what do you think about the labs?

Dr. Thanadar:
Yeah, I agree with Dr. Young. You know, there was a very obvious thyrotoxicosis. I mean, her TSH is completely suppressed. And even though we don't necessarily have the numbers, with the free T4 and the free T3, it makes sense that both of those would be elevated. Free T4 gets converted into free T3 – I mean, T4 gets converted into T3, so the higher levels of that T4, you're automatically going to have some higher levels of the T3, and those are both sending signals to the pituitary. So, her numbers definitely do seem to reinforce the clinical suspicion that there's a thyrotoxicosis going on. And then the question is, what is the reasoning for it?

But again, as Dr. Young said, she does have elevations in other labs that don't necessarily fit the picture. And again, with that elevated calcium, your expectations would be a very low or suppressed PTH. And the question will be, well, what is causing her to have a PTH-mediated hypercalcemia? Or just fancy ways of saying that that PTH is seemingly causing her high levels, when it should be – that level should be down if it's responding to that calcium.

So, it does seem like there's a number of things going on. Of course, you know, the biggest thing you want to try to do is to keep it simple, try to find one thing that might explain all of these. And so, there would be maybe some further investigations to see, can we find one thing that ties all of this together?

Dr. Gupta:
Okay, great. I'm going to move on to what we're talking about today, her eyes. So, she did have, on the ophthalmic exam, increased proptosis and the dryness, icterus, the swelling of the upper eyelids, and that lagophthalmos or that lid lag. I do agree with you that there was a little bit of a deviation of one eye from the central point than the other eye, especially in the right eye.

And we're going to talk a little bit more about what I did. I went ahead and started the methimazole, despite the liver enzyme elevation, added some propranolol and increase the water intake. About a week after that, liver enzymes, I checked the liver enzymes, those are normal. Hypercalcemia actually was normal. And there was resolution of the low platelets. The parathyroid remained elevated. So, I do agree that she did have the two separate issues, the parathyroid and the thyroid, and we often do see them together.

I went ahead and referred her to oculoplastics for further testing. And they decided to go ahead and treat her with the teprotumumab which is a 24-week course. She got 8 infusions every 3 weeks. She had an unremarkable course. She had some nausea. The audiology testing before, during, and after treatment. And during the treatment, she still had some lagophthalmos, improvement in the proptosis, and improvement in lid swelling.

And now, Dr. Young, I'm going to ask you, if you were treating this patient, would you have waited to use the teprotumumab? Or would you have gone ahead with the teprotumumab?

Dr. Garduno Young:
I think given the severity of her eye disease, it was reasonable to evaluate her for treatment for teprotumumab, you know, having discussion with her about potential adverse effects. So, I think it was reasonable to start it at that point.

Dr. Gupta:
Okay, so I'm going to go ahead and move on to the next case. And this one is very interesting. She presented to me as a 74-year-old female who saw an endocrinologist 30 years ago. At that time, she was smoking one pack a day, she had lost 30 pounds, had a lot of anxiety, trouble sleeping, her bones hurt. And then she started to develop this periorbital swelling. And this is the picture that she gave to me from 30 years ago, which shows that periorbital swelling, the stare. And she was given iodine-131 for treatment, then placed on levothyroxine. So, as you can see, the eyes became worse.

Dr. Desai, what two things do you know had made this worse?

Dr. Desai:

Sure. So, for her, she was smoking one pack a day. I think that significantly made her eye disease worse. So, one of the first things I would have counseled on her is smoking cessation, not just for the cancer and all the other benefits it has, but specifically for her eyes. The second issue is that we gave her radioactive iodine treatment when she had what I presumed to be mild to moderate thyroid eye disease, and it can significantly make the eye disease worse in a considerable amount of patients, some of which who don't even have eye disease. But if you do have eye disease, it definitely has the potential of making it worse. I don't know if you said on here, but was she pretreated with steroids if you were going to give the radioactive iodine?

Dr. Gupta:
No, she was not.

Dr. Desai:
If you pretreat it. But probably those two were the worst factors that I would consider, the smoking treatment, disease a lot worse.

Dr. Gupta:
Dr. Thanadar, do you think that, you know, the steroids would have been helpful in her case?

Dr. Thanadar:
You know, it's a potential that it could have helped, but we know that it doesn't necessarily prevent the progression of eye disease, as the eye disease is there. I think as Dr. Desai said, there are a number of things that kind of led her down a path that potentially could have worsened it. And you know, the question is 30 years ago, what were the treatments that were available there? And really back then, probably the first line of treatment would have probably been some steroids, or just moving on to do treatment of what had looked like to be just the hyperthyroidism. And the thought process probably was that you treat the hyperthyroidism, you kind of stop everything. But we now know that thyroid eye disease and the hyperthyroidism that affects - that can be seen in Graves' disease, are separate parts of similar things. But they don't necessarily – fixing one doesn't necessarily fix the other. So, the common thought process was that treating the thyroid disease will then, in turn, keep her from having eye disease or stop the eye disease. But here, we can in some way see that there was elements that may have just continued on just because she did have some level of thyroid eye disease to begin with, and treatment of the thyroid issue itself wasn't going to be the only thing that was going to be able to help. Now, of course, we have more options to be able to help treat just thyroid eye disease and also treat their Graves' disease, but don't necessarily look to say that treating one is the cure-all for everything.

Dr. Gupta:
Dr. Young, when somebody is on levothyroxine after iodine-131 treatment, how often are you seeing patients having good resolution of their thyroid function? And do you, in your practice, see a lot of cases where the thyroid eye disease goes back and forth?

Dr. Garduno Young:
So, most of the patients who receive radioactive iodine and then become consequently hypothyroid and require levothyroxine therapy, most of them maintain normal thyroid function. You know, there are a few who get such a good dose of I-131 relatively low, who will have recurrence of their hyperthyroidism. And just like any other hypothyroid patients, there are some who will have some fluctuations in the dose that they're required of levothyroxine.

Also, it is still relatively rare for me to see patients have, sort of to develop thyroid eye disease after receiving I-131, or if they've received it in the past and they've been hypothyroid. I'm going to say that most of my patients who have thyroid eye disease have active hyperthyroidism still. I don't have anyone that I can think of off the top of my head who had received I-131 before the levothyroxine, and then later on had worsening of their eye disease. But maybe I and my patients are just lucky.

Dr. Gupta:
Okay, so 30 years later, she had called the office and got scheduled and came in. The thyroid function was going up and down. But then she was told recently to just completely stop the levothyroxine. And she still continues to smoke 15 cigarettes a day. Family history, her sister has hypothyroidism, mother had a goiter, brother had rheumatoid arthritis. And here's what she looks like now.

Dr. Young, can you describe some of the things that you're seeing in this photo?

Dr. Garduno Young:
So, she has periorbital edema and she has some degree of liver it looks like. It's hard to tell the degree of the proptosis because African Americans do have more prominent orbits than Caucasians and Asians. So, that would have to be measured with an exophthalmometer. It's hard to tell from the picture if she has some redness, especially there on the right eye, but it appears that she has a little bit of hyperemia of the conjunctiva.

Dr. Gupta:

Okay. Dr. Desai, what are you seeing in this photo?

Dr. Desai:
So, I agree with what Dr. Young had said as far as most of the eye findings. There might be borderline eye proptosis, it might be worth measuring with an exophthalmic measurement tool and seeing if she has true proptosis. And then she might have some mild chemosis; it's kind of really hard to tell on this photo.

I think the main question for her actually, is that does she have eyes symptoms that are actually bothering her? Does she have double vision? Does she have pain? Because she already had orbital decompression surgery, right? So, in theory, some of her symptoms should have improved with her surgery previously. So, where is she at right now as far as her quality of life, as well as one would be, kind of where I would go with this next too.

Dr. Gupta:
Dr. Thanadar, there's one thing that we haven't touched on in the eye exam that would give you a clue that this is more autoimmune than not. What can you see in the eyebrows?

Dr. Thanadar:
Well, and that may be difficult to say but she seems – now, her eyebrows do seem to be drawn on. And it may be that she's had that subtle loss of the eyebrows. It also may be that that is part and parcel of her beauty regimen, but it may have also become part of her beauty regimen because she's had that loss. And so that too, could be related to her thyroid disease.

Dr. Gupta:
So, these are some of the things that we saw on exam. There was swelling and redness of the upper and lower lids, dry eyes, there was redness of the inner caruncle. She had a grittiness of her eyes. The left eye hurt with movement looking left. The left eye felt bigger than the right eye, and she was having a lot of difficulty driving.

So, as Dr. Desai mentioned, there's was a significant quality of life issue. She avoids people. She works in the back of a bank. Her CAS score was calculated as a 7, and she did have significant changes in her quality of life. So, I think that we definitely need to figure out what can we do to help her out?

Dr. Young, do you think she's a good candidate for teprotumumab?

Dr. Garduno Young:
I think she's a good candidate. And I would have a conversation with her about the options. And one option would be intravenous corticosteroids. The other option would be teprotumumab. And then you would go over the, you know, risks and benefits of each and have her choose. But she would be a candidate for it.

Dr. Gupta:
Dr. Desai, at what point would you refer her to ophthalmology? What other tests would you order?

Dr. Desai:
So, actually, I would refer to ophthalmology now. I think it's worth getting a orbital MRI for her to see, post surgically how much swelling has, how that she has in those areas, because you can technically still have another surgery as well. So, I don't think that option is officially off the table. You could do the steroids, you can do the Tepezza, you could also do surgical management as well. So, I think it'd be worth seeing ophthalmology now to discuss all the treatment options.

Dr. Gupta:
Okay. Dr. Thanadar, are there any other tests that you would order before starting teprotumumab? Or any other referrals that you would make?

Dr. Thanadar:
Yeah. I mean, there are a lot of things, particularly if teprotumumab is a good option for her and it very well could be, we want to do some baseline testing of her thyroid function levels, of her glycemic control, audiology testing to make sure that there isn't any issues with hearing loss and having that baseline there. Because while it is a very good medication, just like almost every other medication, it has its risks and benefits, it has its side effects. And for the most part, many of the side effects are things that patients are willing to deal with to be able to have the improved outcomes they have in their vision, in the pain, in the quality of life. And even part of it is the cosmetic aspects to it, because that too lends to your quality of life. And we want to make sure that if there's anything that could be more serious that's happening, say, if there is issues with increased blood sugars, if there is a change in her hearing, that we are able to look at that and catch that earlier versus later. And having kind of all those baseline labs done prior would be an added benefit. But I agree, an early referral to ophthalmology, allowing for kind of that interdisciplinary kind of team to be able to be started, would be helpful earlier

as opposed to waiting further down the line to get them involved.

Dr. Gupta:
Okay. Those are some great answers. We're going to go ahead and vote on that case.

Dr. Desai:
And I think we said it before, but in case we didn't, we should also get antibodies.

Dr. Gupta:
I do agree. I tend to use a lot of Brazil nuts in practice now. As you know, the Brazil nuts have 90 micrograms of selenium in them. And selenium has been shown to help.

Dr. Desai:
So, two Brazil nuts a day?

Dr. Gupta:
Yeah. What do you guys use when somebody's allergic to nuts?

Dr. Desai:
You can order like selenium, actually like selenium tablets if you want it to, but –

Dr. Thanadar:
This is little trivia, what else would contain a lot of selenium? Yeah.

Dr. Gupta:
Alright, we're going to go on to our next case. This is Case Number 3, is an 18-year-old female who had an interesting course. She's had a lot of fatigue and she would complained about having a really rapid heart rate. She was always tired. Went to see her pediatrician, who referred her to cardiology for rapid heart rate. No labs were done in the pediatrician's office. Cardiology tested a TSH, and it was practically non-existent. Then she was referred over to endocrinology. So, ordered the antibodies, the thyroid stimulating immunoglobulin was 20 times the upper limit of normal. And she had a past medical history of a family history of celiac disease in a grandparent. She was on no medications. She did not smoke. Her grades had declined, but subtly over the past 2 years, she said she just couldn't concentrate and she was tired all the time. When I looked at the phone and interrogated the heart rate in the heart app, and found that the heart rate was 120 to 130 beats per minute over the past 2 years. She had no weight loss, but she had weight gain.

Dr. Thanadar:
Only an 18- or 19-year-old is going to be able to sustain a heart rate that fast for a couple years. The rest of us would have been just going ---

Dr. Gupta:
She had some increased pain in her left eye. So, here she is on presentation. Looking straight, looking to the left, and looking to the right.

Dr. Desai, what do you notice about her eyes?

Dr. Desai:
So, I think as far as her eyes are, she seems to have a little bit of a deviation in her right eye inwardly compared to her left eye. And then you can also sort of see it when she's looking to the left, you can see that there's an asymmetry there, which is a little bit better when she's looking to the right side. She doesn't look like she has that much proptosis as far as I can tell in these photos, and it doesn't look like she has, maybe some mild chemosis and maybe some mild, like super mild orbital edema underneath, as well as some mild lid swelling, especially – actually, it looks pretty bilateral. So, this would be very mild TED.

Dr. Gupta:
Dr. Thanadar, you do agree?

Dr. Thanadar:
I do. You can kind of see a little bit of swelling underneath. There seems to be kind of – her eyelashes look a little sparse, but I think it's just because there's more swelling kind of there. Again, there does seem to be some asymmetry to her gaze and more deviation of that right eye. It is kind of harder to see if there's any chemosis, but maybe in that middle picture it's little easier to see in that right eye. But yeah, I do agree with that this would be somewhat level of a mild, mild to maybe moderate eye disease.

Dr. Garduno Young:

I actually think the problem with the gaze is the left eye.

Dr. Desai:
The left eye? I know. I saw it afterwards, and I was like, oh, actually –

Dr. Gupta:
She had pain in the left. Okay, so I'm going to skip the voting part. Give me one second. I talked to you about the treatment. I started her on methimazole 20 mg twice a day. And I thought she had some left eye proptosis greater than the right eye. Sent her to oculoplastics. Did start on the short course of prednisone 10 mg over 5 days.

Dr. Young, do you use prednisone often when you're doing – before you send the patient to oculoplastics? Or do you let them initiate that?

Dr. Garduno Young:
We do let them initiate it. If I see – I have a very low threshold for referring patients to ophthalmology if I suspect they have thyroid eye disease, and I will usually defer to the eye specialist for the actual treatment.

Dr. Gupta:
Dr. Desai, what about you?

Dr. Desai:
I also agree with Dr. Young. Anybody who has thyroid disease, I like to involve the ophthalmologist earlier than later. I don't mind prescribing this steroid course, but if they need something else, something on top of that, I definitely would like a more multidisciplinary approach rather from the beginning. The other thing is that some of the ophthalmology referrals take a little while to get to the ophthalmologist, so you already have that built-in time that you can help treat them before they get to the ophthalmologist.

Dr. Gupta:
Dr. Thanadar, would you have done anything differently in this case?

Dr. Thanadar:
No, I agree, you know, getting ophthalmology and the oculoplastics involved earlier versus later in the process of treatment, I think would be helpful. Again, depending on what her feelings were and symptoms were, starting her on a course of prednisone for a short period of time has potential to have benefits and overall has relative low risk to her. So, if it has the potential to make some of that inflammation better and she feels better with that, I don't think that it would necessarily delay care or interfere with what the ophthalmologist would want to do afterwards.

Dr. Gupta:
Great. So, we're going to go to voting on this one. So, I definitely think that her case was pretty mild, but I like to get ophthalmology involved very early, as well. And I think a team approach to all of the thyroid eye disease cases is extremely valuable, both from their end and our end, in ophthalmology and endocrinology. I think both teams need to be seeing that patient as quickly as possible.

Dr. Thanadar:
I agree.

Dr. Gupta:
Alright. So, this next case, Case Number 4, is interesting. This is a 55-year-old, non-smoking female, who had a recent fall while going down the stairs. She had some vision problems looking up, looking down, to the sides, including double vision on both sides. No longer able to drive herself. Had a lot of heat intolerance and increased bowel movements. Her son was recently diagnosed with Graves'. And here's a picture of her looking up.

Dr. Young, what few things do you see with this picture?

Dr. Garduno Young:
It looks like he has some scleral edema in the upper lid, and some degree of proptosis. And it's kind of hard to tell from the picture, but it looks like she also has some chemosis bilaterally.

Dr. Gupta:
Dr. Desai, what do you see in this picture?

Dr. Desai:
Yes, I think she has a little bit of swelling on both her upper and lower eyelids. And then I think she has some chemosis, and then she

has inflammation in her caruncle area I think bilaterally. And there might – her eyes like deep, like they definitely have proptosis. I think picture is cut off over here, but it doesn't look very straight as far as her gaze is as well.

Dr. Gupta:
Dr. Thanadar, do you see anything that's worth commenting on in this picture?

Dr. Thanadar:
Yeah, I think again, it would be probably confirmed by a side view, but it does seem like she's probably got a significant amount of proptosis. And the description earlier too kind of lends towards that because she seems to be having limitations in eye movements, which would probably kind of balance that out as well. But no, I think Dr. Young and Dr. Desai pretty much caught all the things that I see as well.

Dr. Gupta:
Great. So, her labs in the in the office showed a TSH that was suppressed at 0.001. She had TPO antibodies, thyroid stimulating immunoglobulins, and anti-nuclear antibodies were all positive.

Dr. Young, what would be something that you would do next?

Dr. Garduno Young:
I'd like to get an MRI of her orbits to see, you know, how much of the soft tissue is involved. And like I said, I have a low threshold for referring, so I would probably refer her to ophthalmology.

Dr. Gupta:
Dr. Thanadar, what would you want to order?

Dr. Thanadar:
I agree. I think given the description of the impingements on her eye movements, there probably is going to be some significant findings on an orbital MRI. I think that information would be helpful for getting her further treatment. And then again, as we all seem to feel, getting ophthalmology and oculoplastics involved here, because even if treatment, medical treatment will help, she may also benefit from some surgical intervention as well, because there might be a significant extent that she's now kind of pushed beyond where it's not just medical treatment, but the surgical treatment may go hand in hand with her. So, I think getting them involved early is also going to be beneficial for her. And they would want to see the MRI of the orbit, so –

Dr. Gupta:
Dr. Desai, would you order anything? Or would you want to start her on anything right now?

Dr. Desai:
So, a couple of things. Compared to the last case that we had, I think that last case would have been a regular referral, this patient would have been more of an urgent referral, just because she already has some vision changes. So, I'd be significantly more concerned about that. I think we can get her started on treatment for her hyperthyroidism while we're waiting to get some of these, the orbital MRI done, and then send her over to oculoplastics. If you were considering Tepezza in this patient, then we would actually – I would get started on ordering her labs as far as her A1c, getting her audiology tests completed, and getting some of that pre-workup done as well, kind of – because I think this case is a lot more urgent as far as her eyesight is concerned. You know, we want to make sure she doesn't lose complete vision, that it doesn't get progressively worse. And she's already had a fall presumably from her poor eyesight.

Dr. Gupta:
Yes, definitely. Definitely. So, obviously Graves' disease was confirmed. I started her on the methimazole 20 twice a day and then titrated that. The ophthalmic exam, there was some lid swelling, chemosis, more proptosis in the left over the right, her eyes she was saying that they feel uneven, she had dry eyes, spontaneous eye pain on movement, and she had some restricted eye movements especially looking up and looking down. We gave her a CAS score of 6 to 7 and definitely asked for an urgent referral to oculoplastics. So, I think we're – these are some great things.

Dr. Young, when you are considering the teprotumumab for a patient like this, is there anything that you would also like to know, given the fact that she has family history of other autoimmune issues? What in her own history or her family history may you be looking for as well?

Dr. Garduno Young:
If you're considering Tepezza, then because that could increase their risk of hyperglycemia, I'd like to know if there is any family history of other autoimmune disorders, particularly type 1 diabetes. And since it has not been done in her case, I would make sure that, you know, step back until a hemoglobin A1c is done.

Dr. Gupta:
Okay, Dr. Thanadar, would you want to know about her GI history before starting teprotumumab?

Dr. Thanadar:
Well, yes, because there can be significant issues with GI symptoms. Kind of the common thing that can happen is the nausea but there can be also effects for aggravation or irritation of pre-existing bowel disease that can come with teprotumumab So, looking at that would be important as well.

Dr. Gupta:
Yeah, definitely. There can be an increased flare of Crohn's disease, especially using the teprotumumab. So, definitely agree with you.

Dr. Desai, is there anything else that you would like to add to this case on what you would want to do?

Dr. Desai:
I think we covered all the topics. I guess the question is this her diarrhea from her – I think you mentioned she had diarrhea, is that from her hyperthyroidism? Or would it be worth getting a colonoscopy in this patient prior to starting Tepezza, just to make sure that there's no IBD that could possibly be flared from her other, you know, she already has immune conditions, autoimmune conditions run in her family? It might be worth doing that but if you started the methimazole and the diarrhea went away, you wouldn't necessarily have to go down that route.

Dr. Gupta:
Good. Okay. So, let's go ahead and vote. I always thought that was an interesting one because she had so much of the quality of life issues, especially not being able to drive and not being able to see, so I think that, you know, having a good communication with your ophthalmologist and oculoplastics team is so important. And in this case really helped with being able to text somebody and getting them into clinic because it's so important.

I think we're still just a couple more seconds on voting before we move on to the next case.

Okay. I'm going to go on to Number 5. Now, this is a 34-year-old male who presented to his primary care physician with eye pain. He had some grittiness of the eyes, over time had watering eyes, the pain on movement, burning sensation, smokes two packs a day, had a family history of hypothyroidism, vitiligo, had headaches regularly, and he took a night job where he doesn't have to see many people.

So, Dr. Young, what is the significance to vitiligo in this history?

Dr. Garduno Young:
So, as you all know, vitiligo is another autoimmune disorder, as is the hypothyroidism, and so that family history makes him higher risk of developing an autoimmune disorder, such as Graves'.

Dr. Gupta:
Dr. Thanadar, what in his history would be an automatic flag for an increase in the risk of thyroid eye disease.

Dr. Thanadar:
Well, the big one is that he smokes two packs per day; that's a high one, but also the family history of hypothyroidism and vitiligo, those could both be two autoimmune conditions. And just because – so just hyperthyroidism isn't necessarily the only thing associated with thyroid eye disease. A number of people with thyroid eye disease are euthyroid or even about 10% are hypothyroid. So, the family history of hypothyroidism doesn't discount this to say, oh, this couldn't be thyroid eye disease because you can see thyroid eye disease in hypothyroidism. And so, I think those things would lend to still raise that red flag to say, could this be related to thyroid disease?

And then again, the other things that he's having, the grittiness in his eyes, that is part of it. The pain on movement, because that may say that things are progressing more and he's having more active disease. So, those things I think all do lend toward it. I think a lot of times people may discount saying that, 'Oh, well, he's hypothyroid or has family history of hypothyroidism, he can't have eye disease.' But, in fact, he can.

Dr. Gupta:
Great. Dr. Desai, what do you see in this photograph?

Dr. Desai:
Yeah, so, he actually has pretty active thyroid eye disease. So, he's got - I think he has bilateral proptosis, with his right being worse than his left. Again, you'd have to measure because as somebody had previously said, there is a slight difference in African Americans. He's got pretty bad chemosis. He's got inflammation of his caruncle. He's got orbital edema, eyelid swelling, definitely of the bottom

eyelid bilaterally and possibly of the top eyelid as well. And then he's got some eyelid retraction as well. And he's got a pretty classic stare for thyroid eye disease as well.

Dr. Gupta:

Okay. Dr. Thanadar, what else are you seeing in the picture?

Dr. Thanadar:
So again, I do see some wateriness in his eyes. The lids are retracted. There does seem to be maybe a little periorbital edema. But the stare is a very, by definition, very classic look, so – it's kind of hard not to see that.

Dr. Gupta:
Dr. Young, what about you? What are you noticing in the photograph?

Dr. Garduno Young:
In addition to what was already mentioned, I think he also has thinning of his eyebrows.

Dr. Gupta:
Yeah, I definitely agree. And so, he had noticed this grittiness in his eyes and, over time, it was getting much worse. I think that he definitely had – this was made worse with the smoking.

Dr. Thanadar, would you go ahead and – what kind of labs would you want on him?

Dr. Thanadar:
Well, you know, the primary labs of doing a TSH and free T4, doing antibodies would make sense. Doing just a baseline electrolyte panel, doing a BMP, getting some information, just what his baseline is. Particularly since there is that family history of at least what potentially is two autoimmune conditions, seeing what the antibodies would be helpful as well. That would be a start.

Dr. Gupta:
Okay, good. Dr. Young, would you get any further testing for anything with the heart or lungs? Or what would you want to see with that? Would you get a baseline EKG on him?

Dr. Garduno Young:
I think it would depend on the cardiac physical exam. I think that would determine whether or not an EKG would be necessary. In addition to the BMP, I would have to get comprehensive metabolic panel, including liver function tests. And if there's any thoughts of starting anti-thyroid drugs, I would also make sure that get a CBC to have a baseline of the various outcomes.

Dr. Gupta:
Okay, Dr. Desai, what else would you want to know about him?

Dr. Desai:
I actually wanted to add something else. I generally get a lot of baseline, like orbital MRIs for patients with type 2 diabetes, so I might consider getting that as well for him. And then as far as just asking, I mean, you asked most of the questions. The CAS score is probably pretty high because he's having this pain, and seeing what kind of impact does that have on his quality of life. It looks like he took a night job so he didn't have to see people and they don't notice his stare. So, it's probably impacting him in some way. That's not in a positive way, so –

Dr. Gupta:
Okay. So, Dr. Thanadar, let's say he had a lot of anxiety about seeing another provider and spending more time in the physician's office, what things would you tell him to help let him know that, hey, we're trying to help him, how do you get the anxiety level down in somebody who's already smoking two packs a day?

Dr. Thanadar:
Well, and you know, and again, it's important to have kind of a multidisciplinary team, have different people with different expertise that can be able to help him, be able to work on getting treatment, as well as kind of to help with some of the other things that go along with this. And, you know, I try to explain to them as well, that, you know, it's not always just about medications, or it's not always about having some sort of treatment or having some sort of procedure done. Many times, a lot of the things that we can help with are being able to work with some barriers or things that block them from having good quality of life. And that the quality of life is just as important as treating the symptoms of whatever issue that they're having, treating the symptoms of the eye disease, treating the symptoms of the Graves' disease, but being able to have more than one person to be able to answer questions and be able to be available for things that come up, only benefits him.

And it is - it can be difficult to be able to meet with different people. And you know, very interestingly enough, you know, the rise of telehealth and telemedicine has made that something that's a little easier to do because, again, we can have shared visits, or we can have – they don't necessarily have to go to a doctor, you know, they're not spending their whole day going from doctor office to doctor office to doctor office, they may be able to stay at home and may be able to talk with different people all within a smaller timeframe. That gives them the ability to have those connections and still be able to fit those things into their life. You know, somebody may not be able to take off from work to be able to go see all these doctors, but if they're able to do that more on a timeframe with telemedicine, that might be helpful.

But to reinforce that having just one person only gives them one perspective or only gives them the expertise in one area, but having more people who have expertise in different areas ends up giving them the best care that they possibly can have.

Dr. Gupta:
Dr. Young, so he had been started on the methimazole and had a rash immediately, what would you do next?

Dr. Garduno Young:
Well, if he developed a rash and looks like it's attributed to the methimazole, I would not advocate for I-131 treatment in this patient with him having obvious active thyroid eye disease. I would probably refer him to an endocrine surgeon for thyroidectomy.

Dr. Thanadar:
Well, it also depends on how bad is the rash? Is it a little rash? Is it an all-over-body rash? Can he take a little Benadryl and see if it will allow him to continue to take medicine. Obviously, if it's an all-over-body rash or something big, then that would be agreed, as would be something that would not be a treatment that he would do, and then definitive therapy with surgery would be more appropriate. But, you know, if he gets a little rash, maybe a little Benadryl when he takes the medicine with it, can help with that.

Dr. Desai:
You could also do PTU. There's cross-reactivity, but again, if the rash is not that bad, if it's like a rash, you might not want to do that, but you could also consider doing that, especially as a bridge to surgery if he's very hyperthyroid, you might consider doing that. It might benefit him from a thyroidectomy, because it does decrease the antibodies over time.

Dr. Gupta:
Okay. So, he's very skittish and doesn't want to have any surgeries done on his eye or his gland. What other options does he have at this point, as far as treatment? Would you use steroids in this case, Dr. Young?

Dr. Garduno Young:
So, I would – if he will not undergo surgery, then I think it makes sense, especially if the rash was relatively mild, to give him corticosteroids, as well as anti-thyroid drugs. I would say that if the rash was severe, then I think he just needs, you know, counseling, education, and really gear him towards surgery. But, you know, if it's relatively mild and he's dead set against surgery, then I think it's reasonable to kind of pre-treat him with corticosteroids, and that will help commence not just, you know, treating the thyroid dysfunction, but also will help with the inflammation of the thyroid eye disease.

Dr. Gupta:
Great. Dr. Thanadar, how would you get him to stop smoking?

Dr. Thanadar:
Well, you know, that one is a hard one, you know. But a lot of it does tend to be just repeated counseling, repeatedly saying that this will be important for smoking cessation. You know, patients do listen to their physicians, they do put a lot of store in what they say. And having that as a piece of information that is always a part of counseling, may be able to help get him in the mind frame to say, 'Yes, I can try.' And then it would be working on trying to get him to set a date to say when would he stop, so he kind of has a goal set to that. Kind of also to be able to get used to the idea of not smoking. Of course, there are medications there that can be able to help with the cravings, with the psychological addiction that comes with cigarettes, that too, can help. And then there are behavioral psychologists and psychiatrists that may be able to help with getting at that route, again, kind of the multidisciplinary aspect of having people who are experts in their field to be able to help with that. So, it's a little bit, I always kind of say, how do you eat an elephant? One bite at a time. So, each one of us takes a little bite, you know. As I see him in a visit, that it's part and parcel of discussions about having to find a timeline to say when can you stop, finding the ways that will help him think about stopping, being able to find other sources, either pharmacological or psychological, that may be, and/or psychological, that may help to give him the motivation to be able to then quit. But smoking is one of the hardest things to stop. And so, even if it's not a complete stoppage, maybe to get him to start to reduce on how much he smokes, that will maybe show him that he can do this, and then eventually may be able to get to the point where he stops completely.

Dr. Gupta:
So, one of the approaches that I use in my practice is I actually have them dump all of the weeks' worth of cigarettes into a bowl so they can see how much they're actually smoking, and then photograph that. And then have them write on each cigarette the date with a sharpie of when they can have that. So, a pack has about 20 cigarettes. So, if he's smoking 40 cigarettes, to go by down by 2 every week, so he would start off with 38 cigarettes a day and have those labeled. It's very time-consuming, but it makes him feel like he's getting somewhere and see how tedious it is, and he's not mindlessly smoking. He can't use another day's cigarettes. Then I have them just put them into a case where that is all they can get.

And also have them do some journaling, where they have to write down why did I need this cigarette, so that they are trying to understand the behavior. In a patient like this, you know, as we know, the smoking is going to make the thyroid eye disease worse and we're not going to get anywhere with treatment no matter how much money we're pouring into this without that smoking cessation. So, I feel like that's definitely an urgent, more urgent thing to help chip away with.

Dr. Thanadar:
Sometimes I'm saying how much it costs for them. To actually think about one pack of cigarettes costs like $10, and if you're smoking two packs a day, that's $20, multiply that by the week, multiply by the month, and then by the year. And well what could you have bought with that much money? And sometimes just putting that into perspective, they don't think about it that, 'Oh yeah, I'm spending $10 a day,' or 'I'm spending $20 a day, and how much does that truly add up to be?'

Dr. Gupta:
I totally agree.

Alright, so, let's go ahead and vote.

I think it's harder in hyperthyroidism when somebody has that level of anxiety and they are smoking, that anxiety is driving them to smoke, and that's making the eyes worse and becomes a terrible cycle to see.

Dr. Thanadar:
Well, and hopefully with – as the treatment of the hyperthyroidism helps some of that anxiety too, just the uncontrolled aspect of the Graves' probably is feeding into the anxiety and, as that gets better, hopefully then they are more receptive because now they're a little less anxious.

Dr. Gupta:
So, I'm going to tell you what I did. I went ahead and referred him to oculoplastics. There was consideration to refer him to a head and neck surgeon to remove the thyroid. And so, the primary care had already made that appointment, but we elected not to remove the thyroid in this case, to go ahead and start methimazole. He had the rash, it was mild, it went away after a week, did not use Benadryl, actually used Claritin or something that was similar to that, and worked to get some of that inflammation down, those hives down.

Okay, so we're going to move on to the next case. Case Number 6, this is a 61-year-old female who had a history of taking thyroid replacement for 20 years. She had decreased her dose multiple times. Her current TSH on no medications was 0.02. She did not smoke. And so, here she is.

Dr. Desai, what do you see in this photo?

Dr. Desai:
Okay, so this patient, she has chemosis bilaterally. She has lid retraction on the upper lids. She has orbital swelling and lid swelling on the bottom. She also has some caruncle inflammation. She might have some proptosis that's worse in her right eye than her left eye. But it's kind of a little difficult to tell. But, yeah, it looks like there's some proptosis in her right eye compared to her left eye. And her eyebrows look thin, since we're commenting on eyebrows.

Dr. Gupta:
Dr. Young, what do you see in this photo?

Dr. Garduno Young:
I agree with everything that Dr. Desai said. I'm trying to decide if she has limitations of lateral movement of her left eye. There is certainly a disconjugate gaze there, and I think it's her left eye that has the issue.

Dr. Gupta:
Okay. Dr. Thanadar, what do you see?

Dr. Thanadar:

So, it does seem maybe there is a little asymmetry in her eyes. And again, yes, there's definitely some periorbital edema, more so on the left – making sure I got the right eye – the left eye. And, yes, there is some thinning of her eyebrows, particularly on that right eye. Maybe some slight chemosis in her left eye. It's hard to tell in the right but there does seem to be maybe a little more proptosis in that right eye.

Dr. Gupta:
So, interestingly enough, when she had been seen by her optometrist, they never noticed that she had any difference in her vision or appearance. But I would definitely agree with you, all of you. The right eye had pain, watering, lid swelling especially in the morning. The left eye had occasional watering. The labs were positive TPO antibody, negative thyroid stimulating immunoglobulin.

Dr. Young, what else would you want to do?

Dr. Garduno Young:
Nobody had her TSH, correct? That was the presentation you just wet through, correct?

Dr. Gupta:
Yes. Yes. Would you get an MRI in her case?

Dr. Garduno Young:
I would, because, like I said, I think that there is some issue with range of motion of one of her eyes, and I think it's the left, so I would want to see, again, the extraocular musculature.

Dr. Gupta:
Dr. Thanadar, would you get an MRI?

Dr. Thanadar:
I may refer to ophthalmology first to see if they would feel MRI was necessarily needed for treatment with teprotumumab. I don't, you know, they may be able to say that she needs treatment without necessarily seeing imaging on that. I think that you could go either way. I mean, it depends also on who your ophthalmologists are; some ophthalmologists would like to be able to do their own imaging and some are happy to have it come to them.

Dr. Gupta:
Dr. Desai, would you do anything where the right eye has more pain than the left eye? What are you thinking in this?

Dr. Desai:
I just – significant, like unilateral disease of the right side – well, actually, she has bilateral disease, but the right side is worse than the left side, in symptoms and in signs, so I would get an MRI just to rule out any sort of tumor or something else that might be causing the disease. I mean, it's low on the differential, but you don't want to miss that since it's unilaterally worse on one side than the other.

And interestingly, if she didn't have a positive TSI, you could consider getting a TRAB antibody as well, just to add to that, but interestingly, she has TPO antibodies that are positive. But this goes with our theory that, you know, TED is a completely separate entity than Graves' disease, they're not one in the same.

Dr. Gupta:
I think this case is great for that. I agree that, you know, we have to make sure that people know that thyroid eye disease is a separate disease from Graves', disease, which Graves' disease and Hashimoto's are both autoimmune thyroid diseases, and they can occur on that spectrum.

A question from the audience, let me go into one of the questions. For patients with mild thyroid eye disease, how much can smoking cessation or reaching a euthyroid status modify the thyroid eye disease? Dr. Thanadar, do you want to tackle that one?

Dr. Thanadar:
Well, it probably does have some help and benefit in it. But is it the end all be all? No. You know, we can't tell the patients that if you stop smoking, or if we treat your Graves' disease, that your eye disease will also go away. We know that there may be some reduction, but there may be some things that are not going to respond to those changes. But just like, you know, being able to attack from different angles, every little bit is going to help. And so, while they may then still need treatment with teprotumumab, that it may allow for the medication to work a little better, because now you've reduced some of the other aggravating conditions. And so, we know that smoking definitely worsens things. So, can it help to roll back some of the issues? It can, but will it take it all away? No. So, it's going to be helpful, but it's not the end all be all treatment. If that was it, life would be a lot easier.

Dr. Gupta:
Dr. Young, what would you think about that?

Dr. Garduno Young:
So, decreasing the thyroid hormone levels thyrotoxic doesn't treat the thyroid eye disease per se, but it can at least improve to some extent the stare and the lid retraction. Conversely, if they get, you know, overtreated for their hyperthyroidism, it becomes hypothyroidism, and that can actually worsen the periorbital edema. So, we do want to keep them euthyroid. It doesn't prevent necessarily progression but it can - thyroid hormone abnormalities can worsen the symptoms. As far as the smoking cessation is concerned, there can be some improvement again in the progression of the disease, but continued smoking can also make the disease more refractory to treatment. So, it is very important for patients to stop smoking.

Dr. Gupta:
Dr. Desai, do you have anything that you'd like to add to that?

Dr. Desai:
I think both of them said it really well that, you know, the hyperthyroidism independently has some eye findings, which can improve with the treatment of the hyperthyroidism, and that can slightly improve the quality of life. I don't think it's going to make the proptosis any better, but some of the other things can be tackled with treating the thyroid disease. And then smoking cessation is absolutely essential, you know, it makes it refractory to certain treatments, and just in general, it can irritate the eyes as well.

Dr. Gupta:
Great, I think we can go ahead and vote on that case.

I think that, you know, as we're seeing more and more of these cases, I'm picking up on some subtle changes in the eyes. I think, I know in my practice, I am picking up a lot more thyroid eye disease just looking at the different components of the CAS score, and I'm definitely asking more questions with every autoimmune thyroid patient. So, we have picked up some thyroid eye disease on hypothyroid patients who were never hyperthyroid. And the other teams, oculoplastics or optometrists may not have picked that up, because in the past, they were thinking that Graves' disease – that this was a symptom of Graves' disease, and now we know that they're two separate diseases.

Dr. Desai:
It's probably significantly underdiagnosed, and I think it's important to take that time. And telemedicine, though it offers a lot of opportunities, it might make it slightly more challenging.

Dr. Gupta:
That's hard to see them on some of these pictures what – and you guys have done a great job of trying to figure out just on one picture, you have to really look at the eye in different dimensions to really see what's going on, and have them do multiple maneuvers to elicit some of the symptoms that they're having.

Dr. Thanadar:
I think just having the awareness to say I need to look for things. So, things like this, just looking at those pictures, in the first blush, when you see it, you probably would say, oh, maybe I see this or maybe I see that, but you don't look at - you don't see anything that unusual. But as we do these kinds of CMEs, as we look more into it, I think that as you see more of it, the more you pick up because now the more subtle things, as you said, will kind of come into more focus for you.

Dr. Gupta:
Yeah, I think so too. And this goes back to the telemedicine. I can't see vitiligo on telemedicine and that, for me, is a great clue when I even see one or two spots of it on the leg that, hey, this is an autoimmune case and we need to look more closely. This is not a toxic nodule, this is more likely to be an autoimmune thyroiditis, and that's a clue for me, which I don't think that telemedicine allows us to do easily.

So, in this case, I started her on 30 mg of methimazole in the morning and she did have 2 mm more of proptosis on the left eye which is the one that she was having more – it was bothering her, but the right eye had more watering. It did not have any redness that I noticed on the caruncle. There was no pain on movement. I did go ahead and send her to ophthalmology and had them take a look at her just to help with some of the dry eye more than anything.

So, I think we're ready with another question. This is a question for the audience: Patients with thyroid eye disease who are euthyroid and have no history of thyroid dysfunction, is it possible that they may never develop thyroid dysfunction? Or will they eventually develop it?

Okay, Dr. Desai, do you want to tackle that one?

Dr. Desai:
Yeah, so actually, thyroid eye disease can be the presentation prior to Graves', so a certain number of patients actually do present with their thyroid eye disease prior to presenting with Graves'. So, I would say at least in the first year or two, really watch that patient, make sure that they're not developing either hyper or hypothyroidism. But yes, technically, you can develop it later. But I think generally in the first year or two after is when most of the patients would develop it.

Dr. Gupta:
Dr. Young, do you have anything else that you'd like to add?

Dr. Garduno Young:
The question was, is it possible? I suppose it's possible that someone would have autoimmune eye disease and not necessarily develop thyroid dysfunction, but the large majority of patients will have some form of thyroid dysfunction at some point.

Dr. Gupta:
Dr. Thanadar, do you agree?

Dr. Thanadar:
Yeah, I mean, I agree overall, the large majority of people who have thyroid eye disease will probably have some thyroid dysfunction as well. But there is that small percentage of people who their manifestation of their antibodies is just the thyroid eye disease, and they don't actually have issues with either hyperthyroidism or hypothyroidism. And just because they have the antibodies, doesn't necessarily mean – that happens with many things – just because you have the antibodies, doesn't necessarily mean you'll develop a disease from it. So, potentially, the thyroid eye disease could be the initial presentation, and it could be the only presentation of their dysfunction.

Dr. Gupta:
Okay, great. I think we do have a winner. If we can go to the champion slide. And the audience has voted Dr. Desai is Round 2 winner of the KOL Endocrine Knockout.

Dr. Desai:
Thank you.

Dr. Gupta:
Congratulations.

Dr. Desai:
Thank you.

Dr. Gupta:
Thank you, guys, for being such great contestants in this round of KOL Knockout. Audience, you are going to receive an email shortly with more information on how you can complete a post-test and evaluation and submit it for credit for CME.

Announcer:
You've been listening to a replay of a live broadcast. This activity titled KOL Knockout: Endocrinology Edition – Thyroid Titans Clash to Enhance Outcomes in Thyroid Eye Disease – Round 2, is provided by Evolve Medical Education and is supported by an unrestricted educational grant from Horizon Therapeutics. To receive your free CME credit or to download this activity go to reachmd.com/CME. This is CME on ReachMD. Be part of the knowledge.