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KOL KNOCKOUT™: Oculoplastics Edition – Sculpting Sight For Patients With Thyroid Eye Disease - Round 1

Andrew Harrison:
Good evening and welcome to the KOL Knockout Oculoplastics Edition, Sculpting Sight for Patients with Thyroid Eye Disease. This is round one of three total rounds. This is one of our virtual rounds. We'll have another virtual round and then the last one will be live at the American Academy of Ophthalmology. This is an event provided by Evolve Medical Education.

I'm your host, Andy Harrison. I'm from the University of Minnesota where I direct the Oculoplastic service and co-direct our Center for Thyroid Eye Disease and I'm joined today by these three fighters.

In the red shorts we have Nicholas Mahoney, chief of Oculoplastics at the Wilmer Eye Institute, in the white in the center we have Amina Malik, associate professor of ophthalmology in the chief of Oculoplastics at Houston Methodist, and in the far right in the blue shorts we have Prem Subramanian who's joining us from the University of Colorado.

Here are our disclosures and the staff and planner disclosures from Evolve. None of the staff and planners have any financial relationships and they have full policies in place to identify and mitigate all financial relationships prior to this activity. I'd like to thank Amgen for supporting this event with an unrestricted educational grant.

The learning objectives tonight are first to conduct comprehensive clinical assessments, including the appropriate use of laboratory tests and radiologic imaging to recognize the heterogeneous presentation of thyroid eye disease and ascertain potential thyroid dysfunction, number two, to propose medically relevant treatment regimens together with customized surgical approaches to address the physical burden and reduced of life due to thyroid eye disease, and finally, to formulate effective co-management strategies with relevant healthcare professionals to optimize treatment outcomes and manage adverse events. All right, let's get ready to go. I want to just take the temperature of my fighters. How are you guys feeling, Prem?

Prem Subramanian:
I'm pumped up, Andy. I'm ready to go.

Andrew Harrison:
Amina?

Amina Malik:
Let's do this.

Andrew Harrison:
And in the bottom corner, Nick Mahoney.

Nicholas Mahoney:
I am so ready. Let's do it.

Andrew Harrison:

All right, everybody sounds like they're feeling good. Here's the first case. This is a 49-year-old gentleman that I saw. His history was that he had 3 months of red eyes that was treated by his local optometrist as dry eyes. He was waking with eye pain and they treated him with artificial tears initially. 1 month prior to coming in, he developed orbital pain and he was treated with some oral prednisone with minimal relief. 2 weeks prior to coming in, he developed binocular diplopia, and then the day prior to coming, his friend told him that his eyes looked different. And that's what kind of got him to our clinic.

His history is as follows. He was diagnosed with Graves in 2017. He underwent radioactive iodine treatment at that time. That was unsuccessful and he further underwent a thyroidectomy in 2019. His labs are shown and he was on currently on levothyroxine. He did have a smoking history of which he quit in 1998. Here's his eye exam drawn from the Epic in our medical record. You can see he has MRD1 readings of 6 millimeters in each eye with 2 millimeters of scleral show and about 1 millimeter of inferior scleral show. I'll show his pictures in a second. His exophthalmometry at 107 was 24 on the right, 26 in the left, he had edema, erythema, and some lagophthalmos, and his conjunctiva and sclera showed chemosis with minimal injection. Here's his Strab exam performed by the orthoptist and you can see he has some mildly reduced motility, especially in abduction and in supraduction. In primary he's ortho, at near he's got a small exophoria.

Here he is on first exam and this is, again, his first visit. This has been going on for about 3 months time at this point. Here's the up-the-nose view, which shows the kind of moderate proptosis, but I think what it shows more than that is the significant soft tissue swelling around the periorbital area.

This was our CAS score at the time, and again, each one of these is given one point for the clinical activity score. And you can see he has pain, pain with eye movement, eyelid swelling, erythema, conjunctival redness, and chemosis. So he has a CAS score of 6, which shows pretty active disease. The question to the group at this point is what would you do next? I'll start with Prem on this one.

Prem Subramanian:
Sure. So you have several treatment options listed here. Before I do any of that, I want to first see about maybe getting his chemical hypothyroidism under a little better control. His TSH was on the high side there and that could be stimulating this development of his newly active thyroid eye disease with all of the soft tissue manifestations that we're seeing. And so when I look at someone like this, you mentioned the CAS, but you also mentioned he has proptosis as well as diplopia. Going down the list with IV steroids, it will likely help with his pain when he was given a short course of oral steroids, he did okay, but it's probably not going to do anything for his proptosis and I'm not real sanguine it's going to help his diplopia, although maybe it'll stabilize it. Orbital radiation similarly might stabilize his strabismus, might decrease his soft tissue inflammation.

He's 49, he didn't tell us that he's diabetic, so he doesn't seem to have any significant contraindications to that. I wouldn't do surgery yet. He's in an acute changing phase. You detailed that in the history. And then as far as biologics, certainly teprotumumab is FDA approved for treating patients like this and with proptosis as being the primary outcome from the studies that were done, tocilizumab, rituximab off-label uses. I would probably start offer him teprotumumab because he has proptosis in addition to all of those soft tissue signs, because in the majority of patients it's going to be beneficial, but I would start with trying to get his thyroid function under better controls first.

Andrew Harrison:
Amina, any other ideas? What would you do with this guy?

Amina Malik:
I agree with what Prem said that in this situation I have a patient who's symptomatic from a thyroid eye disease, complaining of pain, he has double vision, he has the proptosis on exam, chemosis, edema. To me, those are all signs that he has active disease and he's clearly bothered by this where it's affecting his quality of life, presenting for treatment options. So I would offer the teprotumumab as a first line for similar reasons as Prem suggested and steroids can be helpful as decreasing some of the inflammation but not as effective with that significant proptosis we saw. Of course, I'd want to confirm that there were no issues with his medical history, diabetes or hearing issues prior to starting that therapy.

Andrew Harrison:
Nick?

Nicholas Mahoney:
Yeah, very comprehensive assessment by the panel. I think I would agree that an acute presentation, all that edema, steroids would be helpful, but teprotumumab in the long run is going to be the better option to reduce the proptosis. I do think that patients that I see that present with all that edema do respond really well and pretty quickly to teprotumumab. So I'd be excited that this guy came in at this time because you have that option for him.

Like Prem said, I think I'd also want to get his thyroid levels sort of managed a little bit. I probably would add to the mix a TSI just to sort of get a chemical sense of where his antibody productivity is. He's had a thyroidectomy and radioactive iodine so you're sort of inferring that there's not much thyroid activity going, so checking the antibody levels might have a role down the line if he ends up being difficult to manage. I think the only other thing maybe to talk about would be imaging for him, and I don't think I would image just at this point. But if we're talking about surgery down the line, I do like surgery to manage it, but I don't think there's a question of what the diagnosis is, so I don't think I'd image.

Andrew Harrison:
All right, nice. We did the same thing that you guys talked about. We talked about managing his thyroid dysfunction and decided to put him on teprotumumab. Basically, teprotumumab is a monoclonal antibody against insulin-like growth factor-1 receptor. It's been shown to decrease proptosis by 2 millimeters or more in patients with thyroid eye disease. It's given as an IV infusion every 3 weeks for eight full infusions. So 24 week total treatments. And that's what we did in this gentleman and I'll show you his results.

Here he is at baseline, here he is after four and after eight infusions. And at this point he was super happy with his result. Actually, what I didn't say at the beginning, this guy's a missionary and he was headed back to Africa once we were done treating him. So I didn't really have a chance to follow up at post infusion maybe a couple of months afterwards, but he was very happy at that time. Here's his up-the-nose view and you can see improvement in his proptosis of 3 millimeters in the right eye and 4 in the left and as CAS score came down to 0. So like you guys said, this is, as I say, a slam dunk, I think, for teprotumumab with an acute presentation with all the soft tissue swelling. They do incredibly well.

My question to you guys is what is the effect of teprotumumab on surgical management as far as how you choose what to do and when you choose what to do? Nick, I'll start with you.

Nicholas Mahoney:
Well, I think it's new enough that I'm not sure we're always right. I think a lot of what we're inferring here is based on maybe our own experience or talking to other people. In general, some people are going to relapse, some people are not going to have a response. This guy had a response. We're not 100% sure how durable that response will be because there is some regression of the proptosis reduction people get. So I probably am going to wait 6 months before I do anything. Assuming his thyroid levels are controlled and he looks just like this, I think we could start going down the surgical pathway at that time.

What's interesting is this guy hasn't followed the natural curvature of the typical patient in the textbook, which nobody does because he's not a 40-year-old woman, he's already a few years out from his initial diagnosis, his presentation was sort of divorced from his initial presentation of the Graves disease, and so I think you do have to wonder whether or not we're going to stimulate trouble with surgery in any patient like this and I don't think you get any additional protection with the teprotumumab. So I probably would manage him with local steroids at the time of surgery and maybe some perioperative steroids as well just because he had this sort of post original presentation flare of this disease and make sure his thyroid levels are really tightly controlled.

Andrew Harrison:
All right. Amina, what do you think? What's your waiting time after Tepro or during Tepro for surgical treatment?

Amina Malik:
Yeah, like Nick said, this is just such a young drug that we're all still sort of learning as we go. And for me, there's no set cutoff that I wait before operating. So if I see a patient after their last infusion, which typically I'll ask them to come in anywhere from 1 to 3 weeks after and I still see some residual proptosis, even though we know the drug can continue for 6 months, I will offer them a decompression. I have not seen a patient who's become enophthalmic from a decompression having operated 6 weeks after teprotumumab. But really it's a discussion with the patient of how symptomatic they are by any potential residual proptosis that they might be having, whether they'd want to consider surgery.

Other surgeries that we often do after teprotumumab would be sometimes blepharoplasties when the edema can stretch the skin or if they have residual fat prolapse. For those types of surgeries, I usually do like to wait at least 6 months to sort of see where they are, make sure they're not going to be having any flares or reactivation where the surgery wouldn't be appropriately timed. And then obviously we would want to see them euthyroid as well for at least 6 months.

Andrew Harrison:
Prem, what do you think

Prem Subramanian:
The points that Nick and Amina made about addressing what bothers the particular patient is really key. So I, like Amina, don't have a

problem with doing an orbital decompression relatively soon after teprotumumab treatment is finished if patient has residual proptosis that's still bothersome to them. The literature is showing now that if these patients are going to have regression of their treatment effect, it's maybe around 9 to 12 months out. And we don't know if operating would actually reduce that risk. Maybe, theoretically, by reducing tissue pressure within the orbital compartments. It's just an interesting idea. I do wait for strabismus or eyelid surgery on these individuals because I think I have seen some paradoxical worsening of strabismus in the period after teprotumumab because I think a fibrotic process can set in once the inflammatory aspect goes away with the Tepro treatment. So I do wait with strabismus for at least 6 and better 9 months after the drug is done.

Andrew Harrison:
All right, nice.

Andrew Harrison:
I think we all have similar ideas on what to do for this guy. But I agree. I think you need to wait on these guys a little bit.

Nicholas Mahoney:
Are you doing any perioperative steroids for strabismus surgery?

Prem Subramanian:
I'll do some periocular steroids, Nick. I don't give them systemic steroids, but in cases where I'm particularly concerned where they had a lot of inflammation initially, I will do a little bit of subtenon triamcinolone to try to get them through that early post-op period.

Andrew Harrison:
Is that what you're doing in decompression too? I've been adding some periocular at the end of my decompressions.

Prem Subramanian:
I have, yeah.

Nicholas Mahoney:
Yeah, I do IV forever and then oral after, but I started doing periocular. I actually read somebody else's op note, an established player in our field, not on the call currently, and I saw it in his op note like 5 years ago and I was like, "Well, that's a great idea."

Andrew Harrison:
That's so funny. I found it the same way.

Nicholas Mahoney:
Oh, really?

Andrew Harrison:
All right, let's move on to the next case. This is going to take us in a totally different direction. This is a 49-year-old woman who presented to an outside institution with left-sided proptosis, blurred vision, dryness and pressure. And you can see from her picture there the fairly significant proptosis on the left side. Here's her exam, her vision 20/15 in the right eye, 20/20 in the affected. Pressures mildly elevated. Her pupils are normal, Ishihara plates are intact. Confrontation visual fields are okay. She has some restriction to up gaze. Her Hertel, you can see the proptosis of the left eye. I don't believe those Hertel numbers, but that's what's written there. Her palpebral fissure you can see and her MRD is elevated on that side. What additional testing would you get on this patient? I'll start with Amina?

Amina Malik:
Great. With this, no previous medical history in unilateral proptosis definitely thyroid eye disease is going to be on the differential diagnosis, but she's someone where we would definitely want additional workups. So that would include imaging. And for me, I usually start with CT of the orbit without contrast to first, of course, rule out other etiologies for proptosis that could be present such as an orbital tumor, and then we also want to check for the classic signs of thyroid eye disease, looking for the enlargement of the extraocular muscles and increased orbital fat. And then for her thyroid workup I would get the thyroid levels as well as her antibodies. Can you go back one more time if you don't mind? Just wanted to check one other thing on her exam. Yeah, I mean she does have the lid retraction, the soft tissue. Many signs that are concerning for thyroid eye disease. But I would definitely want to start with some imaging and some labs.

Andrew Harrison:
All right, Prem.

Prem Subramanian:
I'm going to differ in terms of the imaging. So I absolutely agree that some further workup is needed and I would like to get an MRI of the

orbits instead of a CT in this patient. The reason is I often get CTs as my first line when thyroid eye disease is the highest thing on my list, and sure it's high, but I'd like to be able to see other things like the SOV to see if it is enlarged because carotid-cavernous fistula is on the differential and I don't want to give iodinated contrast to these patients and where I suspect they might have thyroid eye disease because that can lead to worsening of their disease.

So I get an MRI of the orbits, but that also is going to tell me if there's any abnormal enhancement and T2 or STIR hyperintensity in the muscles that can help to confirm a diagnosis and then, of course, look for alternative diagnoses as well. And beyond the imaging, as Amina said, getting the thyroid function test, getting TSI and TRAb in addition to help me to try to confirm a diagnosis of thyroid eye disease or to go in another direction. I would probably get a CBC and an ESR and a CRP as well. Just looking along the lines of inflammatory disease.

Andrew Harrison:
Nick, any additions there?

Nicholas Mahoney:
Well, I think there's a difference of opinion. So I guess I get to pick. Clinically, she does lean towards thyroid eye disease. She has a little lateral flare even on the right side. She has very enlarged retro orbicularis oculi fat that sort of roof or sub brow fat pad and thinning of the brows. That kind looks like the brows are full of plastic and the edema. So I think that thyroid it is high enough on the differential. You haven't told me anything that makes me think of a CC fistula other than it's unilateral. She has no whooshing, no corneal sensation, sixth nerve, Horner's syndrome, anything like that that all localized to the cavernous. So it doesn't look like episcleral flush.

I would agree that I like to look at the SOV and it's super cautious to not subject this patient's kidneys with an angiogram coming up, but I think I would just get a CT. I would probably get a wet CT rather than a dry CT. We have this argument at our institution that a dry CT is more than adequate for everything, but if you're worried about something acute, you can see the SOV on it, you can also see an abscess or something like that. But now that we've sort of talked it through and the CCF was discussed and I get my chance to pick when the dust is settled from two experts, I'm going to say a dry CT, TSI, I probably would not get ESR, CRP. I'd probably just get a CBC and kind of go from there. If we're going to go down the inflammatory workup pathway, we can do that after the imaging comes back.

Andrew Harrison:
All right. Again, this was done at an outside institution and you can see here she did get an MRI and this is the only two cuts. I'm not going to show the full thing, but you can see she has an enlarged lacrimal gland and her lateral rectus is quite big and it looks like her inferior rectus is lighting up a bit too.

They got TSH, which was a less than 0.01, and her T4 and T3 were within normal limits. This was, again, from the other group. They thought she had thyroid eye disease, but some things were just kind of weird. She had this large lateral rectus and lacrimal gland, no previous history of thyroid disease, although she is quite hyper at this point. Their plan at that point was to put her on an oral steroid taper and get TSI, TRAb and follow up in 2 months time.

She came back with worsening proptosis after the steroid taper. They decided to do an orbitotomy, actually, and they did a lacrimal gland and lateral rectus biopsy, and we can talk about that at some point as well. But I'll get to the point where she comes to our clinic. So that showed chronic inflammation, was negative for lymphoma or IgG4-related disease. And I'll say I've had cases before where there's been big inflamed muscles that I didn't think fit with thyroid that we did biopsy on, but this one was the lacrimal gland and the lateral rectus. Again, there are cases where the lateral rectus is kind of an innocent bystander to thyroid eye disease inflammation. So at this point she was diagnosed with orbital pseudotumor tumor and treated with oral prednisone.

Nicholas Mahoney:
Did you say her TSI?

Andrew Harrison:
She didn't have a TSI yet.

Prem Subramanian:
Still pending,

Andrew Harrison:
Still pending. So then she came up to Minneapolis and saw us at the university and this is how she looks after her oral steroids. So clearly the oral steroids weren't doing the trick. Here's her exam. Thankfully her vision's still good. She has normal pupils. Her confrontation visual fields intact. Her motility, you can see, especially in that left eye, is limited in multiple multiple gazes and she has an ET in primary and a hypo in primary as well with that left eye. You saw the exam, her Hertels at this point were 23 in the right. And 26 in

the left and you can see the swelling on both sides, significant periorbital and ocular swelling. We did get a CT scan. What do you guys think at this point? I'll start with Nick. We haven't started with you yet.

Nicholas Mahoney:
Yeah, sure. It certainly still could be Graves. I mean she has medial rectus and inferior rectus enlargement on this one for sure. The TSI, if this patient initially presented, would've been something to me that it's a very sensitive test for this. We've got a tendon-sparing muscle enlargement. Sometimes Graves does involve the lacrimal gland as far as the inflammatory and sometimes it involves all the muscles. We sort of dusted a little bit on CCF. It doesn't look like that. Even her SOV is visible here. It looks fine. She has sort of a non-neurologic motility disturbance at this point. So to me this is still concerning for Graves.

She got oral steroids, not IV steroids. I think these patients, if they have a hyperacute presentation and you're going to give steroids, I probably would've done IV with one of the various regimens like 500 weekly for 6 weeks and then taper to 250 for 6 weeks. But to me the TSI would be some sort of immunologic testing of a thyroid antibody disease. She's got a low TSH, I feel like we're headed down that path. So that's kind of where I'm at. Even if it's inflammatory, I'm probably still going to consider an IV course of steroids, but we can talk about other immunologic if the TSI is normal.

Andrew Harrison:
All right. Prem, what do you think?

Prem Subramanian:
No, I agree with Nick that the images here are potentially consistent with thyroid eye disease. The lack of any significant response to steroids, I don't know exactly what they gave her as a PO taper, but other types of orbital inflammation usually respond quite quickly to at least a reasonable dose of oral corticosteroid within a few days. And so the lack of response that thyroid eye disease when you treat with steroids often takes a little bit longer. And so I think that I too would like to see a TSI and a TRAb to see what they look like to help cement a diagnosis. But IV steroids in a pulsed fashion at this point would make sense. It might be diagnostically helpful.

The only thing that's just a little bit strange still from the face photo you showed us was that she has more puffiness and now she almost has ptosis on her right side and that suggestion of lateral flare that was there previously was gone. It could just be because she's so inflamed. But that does concern me just a little bit. I wouldn't jump straight to another biopsy, though, at this point.

Andrew Harrison:
Amina?

Amina Malik:
Yeah, I think they hit it. The fact that she didn't respond to the steroids, to me, and we know that that's often just a diagnostic indicator that it's orbital inflammation, it's pretty unusual that she progressed despite the oral steroids. I've definitely had patients who we know that lacrimal gland involvement can occur in thyroid eye disease. So I agree with what everyone has said. I would also consider IV steroids as the next step and having those antibodies to help diagnose. But I've also had patients who really don't have serological evidence of thyroid eye disease who just we know can still present, and we know that that set of patients exists where they don't show up on the lab work, but clinically they have thyroid eye disease and that means we still have to treat them.

Andrew Harrison:
All right. I think we talked about this, but I wanted to get to imaging in TED and when do you do it and what modalities you use. You guys talked about that, so let's go through it and the other testing. In this woman we got a TSI and it was elevated, 2.6. So do you guys use TSI and/or TRAb or both when you're looking at your thyroid patients and do you follow it? That's the question. I don't know what to do with that, but we do it right? We do do it. I don't know, Prem, we'll start with you again.

Prem Subramanian:
Sure. I definitely get them. There are two kinds of TSI, right? The one you have there is actually an indirect assay. The real TSI is a true bioassay and you get a percent of normal and that's a little more variable. This one is an immunofixation assay and it can be a little bit different in terms of the results you get, but when it's positive like this, it's usually pretty helpful. It just doesn't discriminate between blocking and stimulating antibodies. I tried for a while to follow TSI and TRAb levels and you've cited a reference. There are some studies that suggest that they do track with the progression of disease or quiescence of disease, but there are so many patients, I think, who don't follow that rule that I have found it not to be as helpful as I would like. I do it. I do it because I want to learn from it and see if it really is more helpful, but patients don't read the textbook, darn them.

Andrew Harrison:
Nick, do you get them?

Nicholas Mahoney:
I mean, absolutely get it if it hasn't been done when establishing care or if it's someone coming in for new diagnosis. I also, like Prem, did it for a while to track and I think it was better when you were getting percent activities. Now it's much more of a binary test, to me. It's either positive, which is very informative. I think it's very difficult to inform yourself by tracking it and it often actually confuses things. Because if it goes up and you're trying to get this patient in for surgery, you kind of don't know what to do with that information and sometimes patients see it in the chart now and they ask questions. I don't typically get anything beyond TSI unless I get a negative TSI and I've convinced myself that this is diagnostically wrong and then you need to get more testing and I get a TRAb or a TBII or something.

For imaging, we didn't talk about ultrasound. Our institution used to have expert ultrasonography, because to do ultrasound to measure the muscles, you need to sort of have a big data pool in your machine to standardize your probe for the measurements. We don't do it as much anymore, but for a while it was useful and I think it does have some utility out there in the world because you can get it in an ophthalmology center if your ultrasonographer is good.

Andrew Harrison:
Yeah. Amina, do you get the lab tests and do you follow them?

Amina Malik:
I do get them at baseline for just diagnostic aid, but I actually don't follow them. I treat the patient and what I see and their symptoms, and to me, rather than following that particular antibody, which as the other panelists have said, it can often be confusing and it not correlate with the clinical picture. So just at the onset.

Andrew Harrison:
You know what's interesting, I'd be interested to see what you guys, my endocrinologists tell me some patients at TSI never goes back to normal. If you watch, watch, watch, it never goes back to normal. That's one thing. The other thing was a paper that came out recently, and I can't quote it, but basically it showed that elevated TSI was a significant predictor of recurrence of disease after orbital decompression. So it kind of scares me when it's still elevated if I'm going to operate on them. So maybe it's better that you don't know, but I've definitely seen that. Where I've operated on patients and their disease got worse and then I get a TSI and it's sky-high. So I do kind of follow them because it scares me more than anything.

Nicholas Mahoney:
Well that's one other reasons I think local... Sorry, Prem, you can go.

Prem Subramanian:
Go ahead. No, please.

Nicholas Mahoney:
That's why I think it's a local inflammatory process that gets flared up. So that's one of the reasons why, if you're worried it's going to happen, adding more anti-inflammatory effect locally helps. But I also think everybody benefits from it and the potential risk is sort of nebulous. So I've gotten much more into the habit of expecting that you can flare the disease for these people without the lab marker telling you that.

Prem Subramanian:
Yeah, the TSI bioassay also is variable from time to time in lab to lab. And so that's another confounder in the whole mix of trying to follow this.

Andrew Harrison:
All right. So what would you do with this lady now? She comes in, she's fairly massively inflamed. Amina, what would you do with her?

Amina Malik:
I would probably, in her, start with the pulse IV steroids only because there's not this clear cut diagnosis of a thyroid disorder and see how she responds. But I would also discuss with her teprotumumab as a potential option just to see if she responds and see how she does. Radiation I wouldn't recommend at this stage because if she doesn't respond, sometimes after patients have had radiation, there can be more scarring intraoperatively and it can make the surgery more challenging if she does end up needing something like a decompression. We don't like to do surgery when she's hot and inflamed, which she clearly is in her image here. And then the other biologics we could talk about if she doesn't respond to the IV steroids.

Andrew Harrison:
Prem, what would you do?

Prem Subramanian:
For similar reasons. I think I would start with the IV steroids. It's an unknown question actually whether biologics, specifically teprotumumab, but the others they, by reducing inflammation, such as tocilizumab, rituximab could have a beneficial effect on whatever this process is, whether it's thyroid eye disease or some other kind of orbital inflammation because we still have a little diagnostic uncertainty. I start with the IV steroids because we have a lot of experience doing it over the years, we anticipate that there should be a good soft tissue response. I'd probably discuss teprotumumab, perhaps, as a follow on to the IV steroids if the other biochemical data and the overall clinical picture come together to make me more certain that she has thyroid eye disease to give what I hope is a better treatment that's going to chemically, medically reduce her proptosis as well as all of that inflammatory symptomatology and findings.

Andrew Harrison:
Nick?

Nicholas Mahoney:
Yeah, I think teprotumumab is tempting as a longer sort of view, but it would take enough time to get it onboard that she sort of has worsened. She's pretty acute looking now. She was acute looking when this started months ago. I would really want to just reverse course here, and while you're getting the teprotumumab paperwork through the ringer, I would probably start her on IV steroids and hope that she responds pretty quickly to keep moving.

Andrew Harrison:
We actually decided to try Tepro in her as a first-line agent. She had tried steroids. She wasn't a huge fan of steroids. I didn't say that in the outset. She didn't like the steroid effects and she got worse on them, albeit they were oral. So we treated her with Tepro and here she is. So that was at her presentation to outside institution, here she is when she came to see us, and here she was after I think her sixth treatment with teprotumumab. So we got lucky with getting it and her vision stayed fine, she did well, and she had a really dramatic response to the teprotumumab. She completed all eight infusions eventually. I think the pictures, the latest ones I had were after the sixth. But she had some cramping after, which is quite common as you guys know. And we can talk about side effects as well. But she was tolerating that well.

Nicholas Mahoney:
That's a pretty impressive before middle and after.

Andrew Harrison:
Yeah. I will say we got lucky with that one for sure.

Nicholas Mahoney:
How much steroids did she have? How much was the oral?

Andrew Harrison:
She came, I think she was on an oral prednisone taper of 1 mg for a kg tapering down 10 milligrams a week over 6 weeks or whatever.

Amina Malik:
Yeah, wow.

Andrew Harrison:
She had a solid dose and she was getting worse All right, audience, we're going to keep moving along. These are great discussions. Thank you guys. I'm learning a ton from this as well.

This is our third case. This is another 44-year-old male who came in complaining of dryness, grittiness, photophobia, pressure, pain, and diplopia, and side gazes especially upgaze. 8 months ago, started having eye pain and watering. 6 months ago, felt like his eyes didn't look normal. He does have a history of Graves disease. He's on methimazole and taking selenium from his outside provider. Here he is. You can see his vision's good. Pupils are normal, Ishihara plates are intact. His visual fields full. He has moderate exophthalmos with Hertel readings at 25 in the right and 23 in the left. You can see he's fairly restricted on upgaze. That's him looking up in the picture there. Our orthoptist graded it as -3 upgaze restriction, but you can see it's pretty significant there. There's his slit lamp exam, so some edema and erythema of the lids that you could see, moderate injection and chemosis, and the rest of his exam was normal. He had a CAS score of 7. So what would you do for this guy? We'll start with Nick. You get to start with this one. Trying to move it around.

Nicholas Mahoney:
Yeah, sure. So clearly all the cases are Graves. This is another pretty obvious one. Not only the known history, but he has that same that look with the roof hypertrophy, the flare, the caruncle being red. This guy, his CAS of 7 is not the same as our last patient's CAS of 6 in the way he looks. But he's endorsing progression, somewhat insidious pain. I think he hasn't reached the point of having anything

that's really compelling for you to push IV steroids. He has some double vision but he doesn't have an optic neuropathy or horrible edema, so this is another gentleman that I think you could discuss teprotumumab with. We probably need to get into the details of that, the workup of it, make sure he doesn't have diabetes and stuff just to have that on the table. But I would probably start there for him.

Andrew Harrison:
Amina, what do you think?

Amina Malik:
I would second that I would offer him teprotumumab. He has some proptosis, he has the restriction of gaze. He did have some redness and some edema on his exam that could potentially be helped with the teprotumumab. So that would be my first-line therapy as well at this stage.

Andrew Harrison:
Prem?

Prem Subramanian:
I think another advantage of teprotumumab in this patient, Nick pointed out the hypertrophied roof fat there and the Tepro really seems to have a benefit in reducing that in a way that IV steroids don't or even sometimes surgically it's kind of hard to do. So I think it's someone like this who his proptosis is not too severe in this sense that his eyes look different, maybe more from that periocular change. Again, if he doesn't have medical contraindications and he doesn't have preexisting hearing loss, he's 44, he's at lower risk for having any of those complications like sensorineural hearing loss just statistically, teprotumumab would be what I would offer him as long as we can get access to it.

Andrew Harrison:
All right. I live in Minnesota and they didn't let us give him teprotumumab. We have several of our insurance companies require what's called STEP therapy where they have to be treated with steroids first and fail that treatment before they can get the teprotumumab. So here he is. He came back 3 months later. We did the Kahaly protocol for steroids where they get 500 milligrams IV once a week for 6 weeks, followed by 250 milligrams IV a week for 6 weeks. After four infusions he became suicidal, and so we had to stop the steroids at that point. He's still quite inflamed. His Hertels are now 25 in each eye. It's hard for me, for somebody like this, to put them through an IV steroid protocol knowing that they're not going to do as well as they will with the teprotumumab. But that's the way our insurance companies around here work to some extent.

Amina Malik:
Do they mandate it with IV? Because I've had some insurance companies that say steroids, but then I'll just give them a little bit of oral and they'll turn around and say, "okay, Tepezza is approved," If they don't respond

Andrew Harrison:
Right. I know some insurance companies will say you can just give them steroid drops or any steroids. This company was very specific. You have to do the Kahaly protocol all the way through before we will approve them for teprotumumab.

Amina Malik:
Wow.

Prem Subramanian:
So did they at least let you say he failed after 3 months?

Amina Malik:
Yes.

Prem Subramanian:
Oh, okay. Good

Andrew Harrison:
At that point you could say he failed. So it's all how you'd spin it, I guess, to the patient. "If you don't like the steroids, you don't have to take them," Kind of deal. But yeah, unfortunately he did need to go through the IV steroids. I wanted to ask you guys about using steroids in thyroid eye disease. When you use them, which protocol, and what you've seen as the results using any of the ones that I have listed. Prem, do you want to start that one?

Prem Subramanian:
Sure. I'm the old guy like you Andy, and so I use steroids for a long time before we had alternatives and I would use it in patients who fit

that high CAS. I never offered it to patients with low CAS because CAS was really developed to predict who was going to respond to steroids and I would tell them that it was to reduce that inflammatory component of it. I stopped using oral steroids when Kahaly published the paper in 2007. And when I use steroids, I only use the pulsed IV and I use it typically at that mid-dose that we all tend to use of 500 a week for 6 weeks and then 250 a week for 6 weeks after that.

Periorbital steroids, I know that there are some of our colleagues, Roberto Ebner down in Argentina in particular, who really advocated for retrobulbar injection or orbital injection, peribulbar injection of things like triamcinolone. A lot of these patients, at least in my practice, they already have elevated intraocular pressure and I have a little concern with putting a big depot of steroids into their orbit in those circumstances. I know there are reports of it. It just hasn't been part of my practice. And as far as results that I've seen, again, over more than a decade of using an IV protocol, I would see improvement in the soft tissue signs. I can't say I ever was really impressed with any improvement in their diplopia, and certainly their proptosis didn't get better, and there was a high recurrence rate, a recrudescence of their inflammatory symptoms, and their proptosis might even progress after that. So before we had any good options, I still was not the greatest fan of corticosteroids in thyroid eye disease.

Andrew Harrison:
Amina, we'll go from the old guy to the young female.

Amina Malik:
All right. I use steroids for thyroid eye disease in patients who teprotumumab would be contraindicated, patients who might have severe hearing loss, or young females who are interested in getting pregnant in the next year or patients who have severe GI disease, inflammatory bowel disease can talk about IV steroids. Also use the IV just like the other gentlemen, won't comment on the old or young just gentleman, esteemed colleagues. The paper did show that the IV was superior world in terms of the both effectiveness as well as decrease in side effects. So patients tolerated it better. So I use the exact same protocol of 500 IV for 6 weeks and then 250 for 6 weeks. There are a few patients who huff and puff about coming to the medical center at Methodist where I work because that's where I offer the IV steroids, and so they ask to do oral and I will sometimes do that, but in my experience it tends to be a little less effective in terms of the results and those patients will often still need surgery.

And then for periorbital, I, like Prem, can have a lot of patients who might have elevated pressure and I do worry some about the side effects. It was interesting to hear you guys talk about doing the steroids during surgery the subtenon, Kenalog. That might be something I might add to my regimen, but for now I really don't offer any periorbital steroid injections. Some people have talked about steroid drops topically as well. That's not something I usually will prescribe for patients. Now, some patients who do have just some orbital pain and not too much soft tissue swelling or proptosis, I'll sometimes just give NSAID drops, ketorolac, a little bit and see how they do as well and can go from there.

Andrew Harrison:
Nick?

Nicholas Mahoney:
Yeah, I think we covered a lot there. Oral has a role for patients who are getting radioactive iodine. I think everybody knows that we just didn't really bring it up in there. I actually just used the original protocol of 0.4 rather than the reduced 0.2. And then for IV, my only addition there is I'd say I use it for patients with a new onset optic neuropathy, very severe debilitating strabismus, and extreme proptosis with the keratopathy. For the optic neuropathy patient, I actually begin the process of getting them in for an optic canal decompression at the time of steroids because I have found that when they're that acute and you give them the steroids and then they sort of taper off, they often have recurrence of the neuropathy. I do sometimes use teprotumumab there as well. But I sort of start building a case for surgery pretty early for those patients and I think of the steroids as a temporizing measure potentially also due to radiation in those cases too.

Andrew Harrison:
All right, so there's the Kahaly protocol. I actually put it in there. I think we all use that as our treatment. I'm going to go blast past radiation, no pun intended, just because I have one quick slide using orbital radiotherapy. There's been a lot of studies looking at this and there's some that show it's about 60% effective, especially in the active progressive disease. So I think correct patient selections is important. We still don't know how it works, which always kind of worries me and it seems to improve motility more than proptosis. We tend to avoid it in younger patients because it puts them at risk for a secondary malignancy in the radiated area, patients with retinopathy, severe hypertension, diabetes, those patients.

We talked about steroids in the Kahaly protocol is probably 50-80% effective in halting the disease, but the thing about steroids is that they don't reverse the disfigurement that you see in these patients. It really doesn't change the proptosis, at least that's what the studies

say. So radiation's about 60%. If you had steroids and radiation, maybe you can improve that.

In this we obviously couldn't do steroids in him. I'm just going to keep moving forward because I do want to get to the next case. We did put him on teprotumumab. He did well afterwards. He noticed that periorbital symptoms resolved after four infusions. His diplopia resolved. No pain with looking up. And I think we see this in a lot of the patients with one or two infusions, they'll start to get better. But there are some patients that don't start to get better until after the fourth infusion. So it's really variable and I wish we had a way of figuring out who's going to do better when.

He did have some side effects. He had diarrhea for a couple of days after the infusions. Again, muscle spasms are quite common, at least in our experience. About 30% of our patients will describe some kind of charlie horse or muscle spasm for the week following the infusion and then it gets better. And then dry skin afterwards. He didn't have any hearing changes. It's important to note if you are prescribing this medicine that on the label it says these patients need their hearing monitored before, during, and at the end of the treatment, and I think you need to make sure that you have your patients seen by ENT or audiology. We're lucky the audiologist is down the hall from us, so we just send him over there for testing.

Here he is after his fourth infusion, you can see he had a really nice result. Remember, his Hertels were at 25, now they're at 22. Here he is after all eight infusions. And then 1 year later he's still doing quite well. So this was another one that really had a nice response to teprotumumab.

All right, let's move on to case four.

Okay, this is a 56-year-old female. She has about a 10-year history of Graves disease, originally treated with radioactive iodine, and over the last 7 months she's noticed progressive redness, pain, tearing, and swelling in the right eye as well as some diplopia. She was diagnosed with allergies and dry eyes by her optometrist and then she saw an ophthalmologist who diagnosed her with orbital pseudotumor and treated her with 80 milligrams of prednisone. She comes in and here's her CT scan and her visual fields, her right eye on the right, left eye on the left as you look at the screen. So it's as she's looking at the screen. The CT is the opposite. I'll just describe here, you can see fullness in the orbital apex on the right side. So it looks like she's developing a compressive optic neuropathy in her right eye. I wanted to bring this up because I think Prem brought it up earlier, or Nick did, using steroids as a kind of bridge to optic neuropathy. Do you want to talk about how you would treat this woman first, Nick?

Nicholas Mahoney:
Yeah, sure. It does look like an optic neuropathy. I loved Kazim and Freitag and have that great paper about the inferior blob as the most common sign, but, whatever, you get what you get, this just looks like a Graves TON. Generally speaking, I would give this patient IV steroids because I think it's the quickest thing we can do for her. Before Tepro, I would then get her on for a posterior decompression. And in my practice we work with a very great sinus surgeon who can get the sort of annulus off of the optic canal and I do it endoscopically via them, and so I would actually line that up for this patient at the time of prescribing the steroids, hope that they have resolution but probably still proceed with surgery. A little bit debatable about whether that's necessary.

In the age of Tepro, I think you have this now additional thing where you can give them an IV steroid course to get things moving. It takes about 3 or 4 weeks for me to get somebody teprotumumab and I have given patients with a severe optic neuropathy teprotumumab and they have [inaudible 00:56:59], but I don't know that I can predict who that's going to be or get them the medicine quick enough for that to be my only option. I care so much about the quality of the vision. I think I know what works. I would probably stick with my plan and say IV steroids would certainly be the way I normally do this. I might bring up Tepro, but I don't think, at this point, I'm relying on it. But there definitely are case series showing that it's a useful tool for optic neuropathy and I'd like to see more of that evidence for me to commit to it for someone think as important as vision

Andrew Harrison:
Amina, what would you do?

Amina Malik:
Yes, generally if I have a patient with optic neuropathy from thyroid eye disease, I admit them for three days of IV steroids. And then yeah, before Tepro we would do the decompression within the next week with ENT. But in the age of teprotumumab, I have found, personally, very good results with using it in cases of optic neuropathy. At the last ASOPRS meeting, we had a poster presentation with myself and Roman Shindler where we had seven cases treated with teprotumumab for thyroid eye disease-related optic neuropathy. And none of those patients needed decompression and all responded and had preservation of their vision. So I think there is a role for this drug here.

Andrew Harrison:

Prem?

Prem Subramanian:
I agree. I had the opportunity pretty soon after teprotumumab came out to treat a patient who was a terrible surgical candidate and who developed a compressive optic neuropathy with teprotumumab and she did quite well. And so, subsequently, I don't know if it still exists, but at least in some places, there is a pathway for urgently obtaining the teprotumumab within 48 hours if you felt that your patient has a compressive optic neuropathy. I obviously discuss all the options with patients. They do tend to be older when they're getting the compressive optic neuropathy so they may be at higher risk for things like hearing loss, and so I will go through all of those options and risks and benefits with them. But I do consider the teprotumumab to be a viable option.

One of the things I've also learned wearing my neuro-ophthalmologist hat looking at the retinal nerve fiber layer and macular ganglion cell complex by OCT in these patients, I think we often, not always, but we may have a little more time to act than we thought we did in patients with compressive optic neuropathy. Again, this is not a sport for amateurs. The four of us here take care of a lot of these patients and there can be complex decision making, but there may be cases where you do have a little more time than you think to allow a drug like teprotumumab to be effective and potentially not have to go to the operating room.

Andrew Harrison:
All right. I do the same thing Nick does. I am an IV steroids, orbital decompression usually with ENT colleagues, but she had a great result. Thankfully the vision came back and she improved significantly. Here she is. So that was her right eye that was bad at first. Now she's coming back with worsening proptosis in the left eye. What would you do at this point? All right, we'll start with Amina.

Amina Malik:
So she has worsening proptosis in the left eye?

Andrew Harrison:
Yes.

Amina Malik:
Go back to the photo one more time. I just want to assess how much is soft tissue edema or any of the changes. And then do we know anything about her vision in the left eye.

Andrew Harrison:
At this point I believe it's okay.

Amina Malik:
It's okay.

Andrew Harrison:
Yeah.

Amina Malik:
So assuming she has a low CAS, since you already did the decompression on the right side and she responded well, was her CAS pretty low? Not a lot of inflammatory? No pain. With flash, but there's perhaps a little bit of soft tissue edema, but it looks not all that different from the right side.

Andrew Harrison:
She's kind of CAS 3/4 at this point.

Amina Malik:
Okay, so CAS 3/4, then she looks a little bit older. We could consider teprotumumab as a treatment option because of some of that CAS activity. If she had a lower CAS, I might say, let's just decompress the left side because you just did it on the right side and she responded well. But in a patient who does have inflammatory signs and symptoms, I usually would like to wait at least 3 to 6 months before doing surgeries because we don't want to operate when they're changing. And so assuming there was no optic neuropathy on that side, I think I would offer her teprotumumab on the left side. On the right side it sounds like that there was just a medial wall decompression done.

Andrew Harrison:
Correct.

Amina Malik:
So even if she did have some response on that side, I don't think, again, we were going to make her enophthalmic there.

Andrew Harrison:
Nick, what would you do?

Nicholas Mahoney:
Yeah, this is a great case, Andy. I think it really does bring up a lot of style that is a little different and I have a very similar sort of approach in both areas to both of the panelists. So when this patient comes, they're going to get IV steroids and they're going to get posterior decompression, and 5 years ago, I would've also radiated them, because this is, to me, the place where radiation works. Radiation doesn't have any role all by itself. The patient's not diabetic. They get their steroids, they get their surgery, and then they get radiation. Because I think that the disease is just long enough that you need to do all of that. Now they get Tepro in my hands, they'll get steroids, they'll get surgery and they'll get Tepro if they're a candidate.

My first case of teprotumumab infusion was January, March 2020. A patient with an optic neuropathy who we gave it to who was old, like Prem mentioned, and she was also the first case I reported of hearing loss because she had complete hearing loss and needed a cochlear implant. And so you get burned by seeing that, but the sort of socked in orbit of the old patient who comes in with the neuropathy, this is what they look like. They're dangerous patients even though they don't look so bad. So you've got to pay attention. And they're also the ones at risk for the hearing loss. So I would consider the Tepro, but I would do it with one foot out of the water just in case, and radiation would have some role in my hands if we're kind of worried about a hearing loss potential for her.

Andrew Harrison:
Prem?

Prem Subramanian:
He's calling 59 old. Them's fighting words, Mahoney. No, seriously. I guess we're all prisoners are our last case because, unlike Amina, I'm a little more concerned about inducing a teprotumumab enophthalmos. I've had two cases of very significant enophthalmos in patients who had exactly this picture of a previous orbital decompression for compressive optic neuropathy and then got treated with teprotumumab. Now that said, I would probably look at the extent of the decompression and if it really was a small posterior decompression, I'd be less concerned about that undesired effect afterwards. I would not take her to surgery right now because you're saying she has worsening proptosis, that means to me she's changing. And so I don't know what her end point is yet. So I think, again, yeah, Tepro is reasonable.

Andrew Harrison:
That's what we did. We did Tepro and she did relatively well. You can see she now has significant lid retraction, but her Hertels have improved significantly. She's 19 OU. She was 25 and 23 pre, and her CAS is 1. She does have lid retraction. She comes in 8 months later and she looks like this. CAS of 7. Now her Hertel, remember, she was 19 and 19, now she's 22 and 27. So she's had a recurrence of her active disease here at this point.

Nicholas Mahoney:
Should have irradiated her.

Prem Subramanian:
Should have irradiated her, right.

Amina Malik:
Yeah, radiation.

Andrew Harrison:
Should have irradiated her. We didn't, unfortunately. I'm going to move along again because this case keeps going, unfortunately. It's one of those. So we gave her steroids at this point and she developed an optic neuropathy in the left eye. And you can see she had a pretty good decompression on the right posteriorly, and now she's got a worsening of her left. You can see significant. So what would you do at this point? I think it's pretty obvious, right? We would all agree. I think we would do an orbital decompression on the left eye and thankfully she did well.

Nicholas Mahoney:
Yeah, I think I would also radiate her.

Andrew Harrison:
That's a good point, Nick. I don't know. Do you guys use radiation, Amina or Prem?

Prem Subramanian:

Rarely.

Amina Malik:
Rarely. I use it for patients who have recurrent disease flares and who have had optic neuropathy. I have a couple of patients just like this actually, Andy, who are really challenging, and I did radiate both of them.

Andrew Harrison:
I think this is the place where I would radiate them to or kind of thrown everything at them and they're still having issues.

Nicholas Mahoney:
You've also got to be mindful of her total steroid dose she's approaching, I think, the limits. So I would probably consider Rituxan. Personally, I know tocilizumab is something a lot of people, but rituximab has been successful for me in these kinds of steroid-resistant or ongoing cases in addition to radiation. But tough cases.

Andrew Harrison:
So there's two audience questions One is, if a patient already has hearing loss, is Tepro less of a risk? I think we would all say no, that's more of a risk and we would all be very, very careful in somebody who has preexisting hearing loss.

Prem Subramanian:
That seems to be the big factor, yeah.

Andrew Harrison:
That would steer me away from teprotumumab, actually.

Nicholas Mahoney:
Agree. Yeah.

Amina Malik:
Yeah.

Prem Subramanian:
I think that is a primary risk.

Andrew Harrison:
The other question is a good question. Say somebody comes in, mild disease, what do you offer as far as supportive care early on and they said cessation of smoking, et cetera. Obviously we all, I think, discuss cessation of smoking because we know smoking makes this disease worse. Do you guys add selenium and other anti-inflammatory, diet, things like that?

Nicholas Mahoney:
I do mention selenium and I tell them it's not really an issue in our soil and that we don't know what you get at GNC and to go eat some Brazil nuts. It gets a little bit of a laugh and builds rapport more than it actually helps their thyroid eye disease. Because most of them have heard about it, so if you don't say anything, you sound like a dope, right? Yeah, supportive care. One of these patients was on Lotemax. I give a lot of Restasis because I feel like a lot of these patients have some conj thickening or conj chalasis and it's pretty mild and they have dryness and it's probably a little bit of an anti-inflammatory effect without much risk. But if it's really mild disease, that's all I do.

Prem Subramanian:
I find fluorometholone drops also to be useful in that same kind of context, pretty low risk of increasing their IOP or other side effects.

Nicholas Mahoney:
They just have to be able to find it. I feel like it's harder and harder to find.

Prem Subramanian:
It is hard to find.

Andrew Harrison:
Amina, any?

Amina Malik:
Yeah, I usually discuss also the selenium and offer that to them. Sometimes these patients are desperate and even if it's not a selenium-deficient area, that placebo effect can sometimes help of doing something.

Andrew Harrison:
The other thing that I would add that I think Mike Kazim wrote it up using Glad Press'n Seal at night if they have significant lid retraction. Glad Press'n Seal is that thing you put on your food to keep it and it works better than Saran wrap. It kind of sticks. Because I find if you use tape, either they have a reaction to the tape or it falls off at night and then they get a corneal abrasion. But Glad Press'n Seal holds the eyes closed really nicely. That's my only other little trick.

Nicholas Mahoney:
Yeah, if they've got lagophthalmos and retraction that bad. I don't know, then I wouldn't say they're that mild of a disease. I think if they're at that level, sometimes I'll do Botox if their isolated sort of a thing is a dry eye and retraction. I'll give them some Botox to the levator to buy some time.

Amina Malik:
It was actually just a low-salt diet. Sometimes that can help with eyelid edema as well.

Andrew Harrison:
Yeah, no, that's a good point. All right. I'm not going to ask about Tepro failures and retreatment because I think that's going to open up a new can of worms. And we've reached the end of our time here, but it's been awesome. It's the kitchen sink thyroid eye disease case.

You guys hit it out of the park. That was fun. It is one of those diseases that it's so frustrating and so fun to deal with. Just kind of try to figure it out for these folks. I feel like I always say as an oculoplastic surgeon, people walk in and we diagnose them, operate, they leave, and we're done. But these are the patients that we're friends with for a long time. So it's been really rewarding.

Prem Subramanian:
Definitely.

Nicholas Mahoney:
It's become more rewarding with more options and potentially even more coming. So exciting stuff.

Andrew Harrison:
All right, we have a winner. I don't have an envelope. I feel like I need an envelope. I have the electronic envelope here.

Prem Subramanian:
Yeah, drum roll.

Andrew Harrison:
A drum roll please. And the winner tonight is Nicholas Mahoney.

Prem Subramanian:
All right.

Nicholas Mahoney:
Oh, wow.

Andrew Harrison:
Winner.

Prem Subramanian:
Yay, Nick.

Andrew Harrison:
Round one of the KOL Knockout.

Nicholas Mahoney:
Let the record show that I learned everything from Prem when he was my mentor for a couple of years.

Prem Subramanian:
Very kind of you.

Amina Malik:
Way to go.

Andrew Harrison:
I want to thank everybody. Thank you from all of us. It was a pleasure. I had a blast. I learned a ton and I look forward to round two and

Nick gets to move on to round three, the live one in Chicago.

Nicholas Mahoney:
Nice. Well, thanks for having us. This was really fun.

Prem Subramanian:
All right, Andy, thanks.

Andrew Harrison:
Thanks everybody.

Amina Malik:
Thanks, Andy.

Andrew Harrison:
Have a great night guys.