ReachMD
Be part of the knowledge.

TRANSCRIPT

Transcript Details

This is a transcript of a continuing medical education (CME) activity accessible on the ReachMD network. Additional media formats for the activity and full activity details (including sponsor and supporter, disclosures, and instructions for claiming credit) are available by visiting: https://reachmd.com/programs/cme/best-practices-treatment-tenosynovial-giant-cell-tumor-tgct/11706/

Released: 07/15/2020
Valid until: 07/15/2021
Time needed to complete: 15 minutes

ReachMD
www.reachmd.com
info@reachmd.com
(866) 423-7849

Best Practices in the Treatment of Tenosynovial Giant Cell Tumor (TGCT)

Announcer:
Welcome to CME on ReachMD. This activity, entitled “Best Practices in the Treatment of Tenosynovial Giant Cell Tumor (TGCT)” is provided by Prova Education and is supported by an independent educational grant from Daiichi Sankyo, Inc.

Prior to beginning the activity, please be sure to review the faculty and commercial support disclosure statements as well as the Learning Objectives.

Dr. Tap:
Welcome to the Clinical Countdown. I’m Dr. William Tap.

Dr. Healey:
And I’m Dr. John Healey.

Dr. Tap:
Thank you very much for joining us today. So, John, we’re here in the middle of a pandemic today – masks off but safe. I imagine –

Dr. Healey:
Just under 6 feet.

Dr. Tap:
Just under 6 feet, that’s right. I imagine millions are watching this because most people are used to remote video watching these days.

Dr. Healey:
We’re all accustomed to it.

Dr. Tap:
Does it make you nervous?

Dr. Healey:
I have ice water running in my veins and – which is quite good here in the heat of the summer.

Dr. Tap:
That's why today on Clinical Countdown, TGCT edition, we'll be taking a look at key factors at determining surgical and nonsurgical approaches to tenosynovial giant cell tumor, or TGCT, the update of clinical guidelines and what they mean for our patients, and also the management of adverse events. You ready, John?

Dr. Healey:
Absolutely, ready, rolling, and able.

Dr. Tap:
Let's get started.

Dr. Tap:
So, John, one of the most important things about our relationship along with the patient is we spend a lot of time trying to figure out how we should intervene and if we should intervene. And so much of that relies on the surgeon's expertise about when and if we may need to do an operation, what is our surgical window to potentially try medical management, what are the goals of therapy if we do that, and/or when do we watch a patient. So how do you approach a patient in clinic when you see them?

Dr. Healey:
Well, the first thing is to get the right diagnosis, and so, increasingly, we are able to do that now. Historically, it was more difficult, but now with a good quality MRI you can see something called a blooming artifact, which is related to the blood hemosiderin, the oxyhemoglobin that's in the tissues, and that is pretty much pathognomonic. So the need for biopsy is less frequent these days.

Dr. Tap:
Right.

Dr. Healey:
You then have to educate the patient about it and get an idea where they're headed in this process and how it's interfering with their life. Now, it also will differ significantly based on the joint, and the approach for the knee, which is the most common – 60% of the cases – is going to be different than for other large and certain small joints. So I weigh those issues carefully, and if the disability is sufficient, then I want to intervene. You ideally would like to prevent it from progressing to the point where you're going to get degenerative arthritis. Once that's set in motion, it's a one-way street.

Dr. Tap:
Yeah, it's interesting, too, because normally, you know, orthopedic colleagues – we're the gatekeeper of patients coming to the medical centers, but now with the advent of newer drugs, patients are coming to see us, too, and what's difficult for us is to say, "Oh, this patient has diffuse disease, so let's start medicine right off." It's really important that I refer the patient to you because of the expertise of the joint. Again, do we have a surgical window? Is there time to try a medicine, or do we need to act sooner?

Dr. Healey:
And if I can get a gross total excision of the tumor, then that may still be the right first move, and then we wait and see.

Dr. Tap:
Yeah.

Dr. Healey:
So use this selectively. It's not one-size-fits-all.

Dr. Tap:
That's exactly right, and that may allow patients to actually be pain-free, symptom-free and not need, you know, use of medications every day.

Dr. Healey:

Right.

Dr. Healey:
So – well, Bill, as you said, the standard treatment for a TGCT has been surgery –

Dr. Tap:
Yeah.

Dr. Healey:
- historically, but this paradigm is changing, and with the availability and success with a number of very exciting targeted agents, it's changing our whole thought pattern about this. And generally, because this disease is not emergent to intervene, we have the opportunity to communicate, and I would like to ask you, you know, how you view it at this stage.

Dr. Tap:
You know, the whole drug development strategy in this disease has taught us a lot about the disease, too, and allowed us to partner with patients and our colleagues in orthopedic oncology to really say, "How do we do this correctly and understand the disease?" So our understanding of the disease has grown exponentially in the last few years, and it was really the understanding that CSF1 plays a role in this tumor that gave us something to target. And as you know, we had weak CSF1 inhibitors such as imatinib mesylate and nilotinib, and these are drugs that we were able to use off-label, and they could actually help people. They don't always make the tumors melt away, but they can improve quality of life, and they definitely can help with symptoms. More recently, we've had fairly strong CSF1R inhibitors come out – strong and specific – and this has begun to revolutionize how we can treat these diseases medically. And one of the drugs that was recently FDA approved was pexidartinib, and as you know, it was based on a large, randomized, placebo-controlled phase 3 study, and what it shows was that patients who got pexidartinib had tremendous decrease in tumor mass – on average, about 36% resist response rates. So tumor shrinking greater than 30%, and that was at a finite period of 25 weeks, right? And that is really a dramatic response rate.

Dr. Healey:
That is huge, but I think it's even better than that because at as early as 15 days after the start, there were commonly significant improvements in the symptoms –

Dr. Tap:
Yeah.

Dr. Healey:
– that the patients had that they reported, and it took a while to get to the resist criteria. And then there are, you know, total line scores showing reduction of the disease, but the symptomatic improvement was often much faster.

Dr. Tap:
Yeah, exactly, and I – as you know, resist is a poor measurement, at least early on, with the unidimensional measurement of this tumor mass which can be pretty diffuse, and we did see, though, over time with continued use, response rates going as high as 56%. So it really opened up our ability to treat these patients. The caveat is that there was a rare cholestatic hepatotoxicity that we saw in patients, and, again, it was very rare, but it could be very dangerous. And that affected the label with a black box warning. And actually, before we prescribe the drug, we have to go through a risk and evaluation/mitigation strategy to understand, really, the side effects of the drug, but it also gives us pause to say, "Which is the right patient to try this drug on?" And so it did add a layer of complexity, but it brought pexidartinib into the type of drugs that we can use for patients. But thinking about when to use this drug or when we can just watch and wait and not necessarily use a medication, I think, is important considerations.

Dr. Healey:
How long do you think the response is sustained? What has been your impression?

Dr. Tap:

Yeah, what I found, which is really interesting, is as long as patients remain on the drug, and, again, the dose is of question – maybe not high doses of the drug – we seem to maintain responses, and it's actually very variable when you stop the drug. I have some patients where you can stop it and you'll maintain that response for years. In other patients, within, you know, three to six months, you'll begin to see some growth.

Dr. Healey:
So, so they might be able to have a holiday.

Dr. Tap:
Yeah. It's really important that part of the treatment is not only to preserve joint but also measure quality of life, right? And I think that's nice to have certain weapons now that we can do that, you know, against this disease. So, John, as you know, pexidartinib was FDA approved in the United States. It also allowed us to change the NCCN guidelines, making it available for patients, but it still calls in the different medical treatments that we can use for patients, which is wonderful. You know, we still have the use of other CSF1R inhibitors, and now even a lot of clinical trials – when you think of the different medical management, and I know, actually, you refer patients to us with having these discussions with your patients. What are some of the things that you discuss with them and your thoughts on the limitations of the therapy that we could offer?

Dr. Healey:
Well, I start at the beginning in helping them as best we can to understand that this is really targeted therapy with fairly limited off-target actions, and there are very few medicines that we use that are this specific, frankly, so –

Dr. Tap:
Yeah.

Dr. Healey:
– I'm very excited about it in that regard, and I try to share that excitement to the patients. So, yes, they may be frightened about certain things, and they came in not expecting the surgeon to be recommending drugs.

Dr. Tap:
Yeah.

Dr. Healey:
But I think it's important to set the stage and to show that we are on the same page about it.

Dr. Tap:
Yeah.

Dr. Healey:
Number two is it depends on what the joint is and what those symptoms happen to be for that joint.

Dr. Tap:
Yeah.

Dr. Healey:
And I'll give a couple of examples. You know, TGCT of the hip is particularly problematic. It's easy to get around the capsule of the hip, but the disease lurks centrally in the fovea, in the middle of the acetabulum and the ligamentum teres to the femoral head, and you cannot get there from here.

Dr. Tap:
Right.

Dr. Healey:

So it may be good in other ways, but I need you to be able to control that element of disease.

Dr. Tap:
Yeah, and I agree. And, you know, for us as we start to look for the longer term use of the drug, you know, the questions are do we start to see long-term toxicity? But it's interesting when patients first present. The ones that are candidates for the drugs are usually, you know, having significant side effects, right, of their disease, and we have to talk to them about this really rare but important cholestatic hepatotoxicity. But what we've found is that most of the time when that happens, it happens within the first three months, and so you watch a patient closely with almost weekly blood draws. And if they do well, what's interesting is their symptoms really start to improve on the drug. And then over time, you're trading kind of the side effects of the drug for what were once the symptoms of the disease, and oftentimes the use of the drug can become, you know, very difficult for patients. As you said, you know, they're healthy otherwise, and all of a sudden they're exchanging one for the other. So, you know, how can we begin to ameliorate them of the use of the drug as well?

Dr. Healey:
Yeah, precisely. And I have a large number of patients, and this often will affect young women, for example, who are in childbearing years.

Dr. Tap:
That's right.

Dr. Healey:
And so they want a treatment that's dependable, that has some time limitation on it so that then they can go ahead with their family planning issues, and I think this sort of accommodation, what I refer to as the sandwich effect or approach of drug-surgery-drug-done, that works well for such a population.

Dr. Tap:
Yeah, and as you know, there's even a next generation of drugs now coming into clinical trials that we hope, you know, may not have these side effects, the hepatotoxicity, right? And then would be easier to use in our patient population and maybe even bringing it earlier – smaller tumors, not as diffuse – you know, where we could think about some of these neoadjuvant/adjuvant approaches.

Dr. Healey:
Absolutely.

Dr. Tap:
I agree. So, now we're going to move on to the lightning round of the program where we're going to fire some questions at each other, and we'll see how we do. The first one is: what do you think about the recurrence rates of TGCT and, I'll say, diffuse TGCT after surgery?

Dr. Healey:
Sure. You're not going to give me the easy one on localized disease, which is almost always cured, but overall it's – I would say the number to have in your hip pocket is 50%. And so the data have shown that at three years it's 37%, five years 45%, 10 years 60%, and the longer you follow them, the higher it goes –

Dr. Tap:
Right.

Dr. Healey:
– and so that's why I started off saying it's not really the gold standard – maybe a bronze.

Dr. Healey:
You know, I'd ask you – when do you pull the plug on drug?

Dr. Tap:
Yeah, yeah, it's –

Dr. Healey:
You know, what is your threshold?

Dr. Tap:
It's a good question. I mean, I think as we spoke, you know, we're used to managing side effects of medications like this, but most of the time we're dealing with patients with cancer who the disease could be threatening their life. So, you know, you have a different risk-benefit profile in patients with TGCT. To me, you know, the idiosyncratic cholestatic hepatotoxicity is the biggest discussion. You know, once you get over that discussion and opt to use the drug, you have to have a very close monitoring program as actually prescribed by the label, and the reason is because not only is that idiosyncratic, but it's not necessarily – we cannot predict who and why will get it, and the labs that we look for are not predictive of it happening. They're causative after they begin to happen, but most of the side effects of this drug are easy, manageable.

Dr. Healey:
So, Bill, what's so good about the multidisciplinary approach afterward?

Dr. Tap:
Yeah, I think it's critical. We all bring a different expertise to the table. We all have different treatment options and a different understanding of what we're offering the patient, and I think by bringing that all together allows for a comprehensive approach of the best way to treat our patients. And it's not just surgical and medical oncologists, right, orthopedic oncologists. We have to think about having physical therapy; we have to think about potentially pain and palliative care specialists, maybe even rheumatologists – all the different members of our team that can better support the patient and improve their quality of life.

Dr. Tap:
Well, wonderful, and I think we're at the end of our time, so I wanted to thank Dr. Healey for joining us, and I wanted to thank you for the opportunity to talk to you a little bit about tenosynovial giant cell tumor and how the new treatments are helping us better understand the disease and better partner with our patients to help them. Thank you.

Announcer:
You have been listening to CME on ReachMD. This activity is provided by Prova Education and is supported by an independent educational grant from Daiichi Sankyo, Inc.

To receive your free CME credit, or to download this activity, go to ReachMD.com/Prova. Thank you for listening.