Scott C. Woller: Hello, everyone, and welcome to this American Heart Association sponsored podcast designed to educate on improving venous thromboembolism patient care and outcomes. This, in fact, is the fourth podcast in a series of five. Today, it's our delight to focus on recommended treatment duration of venous thromboembolism and bring in especially an important characteristic of treatment, and that is the patient care perspective.

My name is Scott Woller, I'm a professor of medicine here at Intermountain Health and a professor in the medical school at the University of Utah, and it's my delight to moderate this podcast today. In this podcast, it's our intention to firstly describe the appropriate duration of treatment and rationale for the extended treatment and secondary prevention of venous thromboembolism, especially weighing in the risks and benefits, and how we think about applying those to our individual patients. We hope likewise to help the learner be able to apply current evidence-based guidance when determining treatment duration for venous thromboembolism and, lastly, have the unique value of the importance of patient perspective in the treatment of venous thromboembolism.

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With that, let's go ahead and kick things off and meet our content experts today. Firstly, permit me to introduce Dr. Behnood Bikdeli. Dr. Bikdeli, would you take just a few moments and introduce yourself to the audience? Thank you.

Behnood Bikdeli: Thank you so much, Scott. Great to be here with you and Ann. I'm a cardiologist from Section of Vascular Medicine at Brigham & Women's Hospital, Harvard Medical School. I'm also affiliated with Yale Center for Outcomes Research and Evaluation, and I've been very much interested in venous and arterial thrombosis. I can't be more excited to join you and Ann for this podcast.

Scott C. Woller: We're delighted to have you here today. Thank you very much for your time and especially for your expertise. Dr. Ann Leonhardt-Caprio, welcome.

Ann Leonhardt-C...: Thank you, Scott. I too am thrilled to be here. I am the stroke program coordinator of the Comprehensive Stroke Center at the University of Rochester Medical Center and also an assistant professor of clinical nursing at the University of Rochester School of Nursing. The patient population I work with, stroke patients, does have a high risk of VTE, which is a personal interest of mine, as well, as you will hear towards the end of our session today. I am really honored to be part of this group to really try and spread the word and some more education about VTE management.

Scott C. Woller: Dr. Leonhardt-Caprio, we're so glad to have you join us, and we're so appreciative

for your expertise.

Oftentimes, venous thromboembolism is diagnosed in the emergency department or the inpatient setting, and a treatment regimen is initiated. Invariably, though, we end up on the order of weeks to months later trying to determine what the best therapy is for a given patient, how long it is that they should be treated, and patients are often confused surrounding how to best proceed once they are outside of that acute initial treatment period for venous thromboembolism. Ann, I'm wondering if you would be willing to take a few minutes and chat with us about how you think about a patient's presentation with blood clots and what, if any, particular characteristics of their presentation might affect your decision-making surrounding how long to treat those patients.

Ann Leonhardt-C...: Sure, Scott. I think that's a really important foundation to start this discussion with. As we start to consider the duration of treatment, weighing risks and benefits, what we really want to think about to start with is what caused this thrombosis, or what is the underlying mechanism? When we think about VTE, we think about them in terms of provoked or unprovoked. To start with a provoked DVT, really, you have a known event or a risk factor that could have led to the clot, things like surgery ... often, we think about joint replacement surgeries, hip or knee replacements, as being a high risk for VTE, or also other large surgeries, hospitalization, or any other kind of immobilization where someone is not up and getting around, they're not walking around, they can be at high risk of forming a thrombosis in the legs, trauma, and also the use of exogenous estrogen like birth control pills or hormone replacement therapy.

Alternatively, an unprovoked VTE is where there's no evident risk factor or identifiable provoking event that led to the VTE. In those circumstances, you will hear down the road that ... Behnood will talk about where we might want longer-term anticoagulation for someone who has an unprovoked DVT or VTE.

Scott C. Woller: That's super helpful. If I summarize correctly what you're describing, depending on how the patient presents, whether their venous thromboembolic event is provoked, especially by an easily identifiable major risk factor, or unprovoked, where it happens out of the blue or perhaps associated with persistent risk factor, those characteristics will all affect our decision-making surrounding how long we'll ultimately end up treating those patients.

Ann Leonhardt-C...: Absolutely. You have to think about why before you can think about how to treat.

Scott C. Woller: Thanks so much. It's often fun to jump into a clinical case and frame the thinking about these complex questions in the setting of a clinical scenario. Let me kick this one off, and Behnood, maybe I'll ask that you help us think through this together.

This case represents a 65-year-old man who experienced a deep-vein thrombosis about three weeks following hip replacement. He has a history of obesity, some hypertension. He was placed on a treatment with apixaban, 10 milligrams, twice

daily for the first seven days, followed by apixaban, 5 milligrams, twice daily thereafter. Now he's showing up in clinic to discuss optimal duration of anticoagulation at about the three-month mark. How do you think about the optimal duration of anticoagulation for this gentleman?

Behnood Bikdeli: Thank you, Scott. This is such an important question. I think in order to answer it most effectively, and we will try to do that, it's best to break it down really to a few different components, and we can go over them. I think the first message that I want to get out, which you very clearly shared, is for almost all of our patients with venous thrombosis, including this gentleman, it would be very reasonable to consider, at minimum, treatment for 12 weeks or three months. This is almost unanimous across the board for patients with pulmonary embolism and most patients with deep-vein thrombosis, barring any contraindications. I think that's one important component to consider.

About the question of duration of treatment, the way I want to think about it is to break it down to some components. First, as Ann very clearly taught us, about the different categories of patients. We can go over what the epidemiological studies show about the risk of recurrence events, which is something that encourages us to use the anticoagulants, versus the trade-off, which is the bleeding events on treatment. I think that's one area to talk about.

Second piece here becomes how the large randomized trials in this space were designed, and what did they actually show? I think that's the second component, which pivots us to the very important issue of practice guidelines, how they've summarized and synthesized this evidence, and what are their current recommendations? I'm sure you and Ann will discuss some other important elements about perspectives of patients and clinicians, as well.

Scott C. Woller: Behnood, that's such an eloquent way of breaking things down. Can you share with us how you approach applying the epidemiology surrounding risk for recurrence when thinking about a patient that presents with VTE?

Behnood Bikdeli: Of course. Thank you. I will borrow from Ann. I tend to think of patients as those with major provoking events, unprovoked events, and others. There are different categories in a lot of studies, but the one study that I want to quote is a systematic review and meta-analysis that was published now 13 years ago, but it's still valid today. They quoted the risk for people with provoked venous thrombosis events based off of whether or not they had surgery or medical illnesses, etc. ... minor variations, but as a rough estimate, close to four per every 100 person-years of these patients with non-surgical provoked venous thromboembolic events develop a recurrent event, so keep that in mind. Out of every 100 person years, close to four recurrent events. That's something to consider, and it's very different from those that Ann was referring to as unprovoked venous thrombosis, people who did not have clear identifiable risk factors. Then, the absolute risk is close to 10 per every 100 person-years of follow-up.

This risk is actually non-proportional. What do I mean by that? The risk is actually more frontloaded such that you get more of these events early on, and there might be fewer of them later on during the period of follow-up. Again, I think it's not a one-size-fits-all. A lot of other comorbid conditions and risk factors may play into it ... obesity, inflammatory bowel diseases, other risk factors. That's one side of it for recurrent events.

Scott C. Woller: That's incredibly helpful. When you and I have spoken in the past, you've so artfully described what we often think about as being the other side of the coin, the thrombosis risk on the one side, but then bleeding risk on the other. Are there any unique patient characteristics or considerations that you take into account when prescribing anticoagulation and thinking about duration of anticoagulation in respect to bleeding?

Behnood Bikdeli: Absolutely, and I think some of the issues that all of us as clinicians consider for risk of bleeding, including age, especially older age, comorbidities such as renal or kidney dysfunction ... Some of them are things that we can actually easily mitigate if we do a good enough job of talking to our patients and taking history. Many of them are not aware that NSAIDs do not go well with their anticoagulants. Some of them need it, but if it's not a necessary treatment, something to keep in mind. There are other factors to consider, as well ... baseline platelet counts, among others.

In one of the studies that was conducted for over 78,000 patients with venous thrombosis followed for 180 days, roughly three percent of them had a major bleeding event. These events accrue over time in a nuanced way. Some of them, like intracranial bleeds, they accrue fairly linearly and gradually over time. This is as opposed to, for example, gastrointestinal bleeds or hematomas, which are more often frontloaded and happen more so in the early period. I think we need to be cognizant of risk factors, we need to talk to our patients about them, and we need to educate them about the different things that could potentially mitigate it. I would love to hear what you and Ann think about this, as well.

Ann Leonhardt-C...: I appreciate that you brought up intracranial hemorrhage and the fact that this is a risk factor that many people fear. This is a patient population that I work with a lot. It's very important to be able to communicate with patients that that risk is spread over time, whereas in some other types of bleeding complications, you look more at risk that's frontloaded. As you're trying to determine the duration of treatment and you're weighing that risk-benefit of, for example, intracranial hemorrhage versus the risk of not treating the VTE, that really, your highest risk is from the VTE in the first time period, so looking at that three-month time period, as opposed to someone who's on anticoagulation long-term, which might increase their risk of ICH in the future. I think that's a really important conversation to have with patients whenever you're thinking about, for example, ICH risk, which is the one that scares everyone.

Scott C. Woller: That's incredibly helpful. Behnood, thank you so much for framing that in such a

concise fashion. If I were to summarize my takeaway from this section, it's that firstly, all patients with proximal deep-vein thrombosis or pulmonary embolism, there is a minimum 12 weeks of therapeutic anticoagulation, and then secondly, why it's important that we as physicians consider their risk of not only recurrent thromboembolism but also bleeding and the nuanced characteristics of how bleeding risk can present, either being frontloaded in certain bleeding characteristics, or perhaps, as in the setting of intracranial hemorrhage, more proportional over time.

Oftentimes, we try to glean information from the prospective randomized control trials to inform our clinical decision-making. We're fortunate, because there have been some really exceptional pivotal studies comparing the direct oral anticoagulants with conventional therapy, which historically, of course, was low-molecular-weight heparin, bridging to warfarin, and providing guidance, if you will, and information surrounding outcomes. If you layer on top of that our real-world evidence, now, with most of these medicines being on the market for at least approaching 10 years, we seem to have a good body of evidence surrounding the comparative safety and effectiveness of the direct oral anticoagulants with warfarin. Can you tell me a little bit about how you think about the way that these clinical trials have informed your decision-making in electing treatment for patients with venous thromboembolism, DOACs versus VKA?

Behnood Bikdeli: Of course. Thank you, Scott. I think you had an incredibly important prelude to this. I think it's not that we only have RCTs, or we only need routine practice evidence. The two of them complement each other. Of course, because we are looking at effectiveness and safety, randomized trials, by virtue of excluding some of the confounders, give us more high-quality evidence. For that reason, to me, it's very important that I want to share with my patients for a treatment decision what the randomized trial evidence base behind that might be. In that context, I think it's very helpful to know most of these randomized trials for extended duration treatment in patients with venous thromboembolism enrolled people who were treated at the very least for three months with anticoagulation, so the same thing that Ann, you, and I have discussed so far. Some of them actually went beyond and treated for a minimum of six months before enrolling these patients.

There were some of these trials ... The larger trial for apixaban was AMPLIFY-EXT that was published in the New England Journal 10 years ago. The other trial for rivaroxaban was EINSTEIN CHOICE, also published in the New England Journal six or seven years ago. The interesting part in both of these studies was that extended duration treatment with an anticoagulant [inaudible 00:17:39] was superior to control, which in the apixaban trial was placebo and in the rivaroxaban trial was low-dose aspirin. We can talk about aspirin itself in a few minutes, if there's time. To get back to my point, I think it's very important to consider that these trials included patients after an early period of treatment and showed benefit.

Last point that I want to make here is, again, going back to the description that Ann had for patient classification. Most patients in both of these trials combined were

those with unprovoked venous thromboembolic events. That's part of the reason we have more information in terms of how their outcomes changed with prolonged anticoagulation. Even though with the rivaroxaban trial, they also did include a fair number of people with provoked events and there was no statistical interaction, in terms of absolute numbers, the differences were smaller, and that's why there are some other ongoing randomized trials in this space.

Scott C. Woller: That's terrific. Being able to think about the limitations of the evidence that we have in the context of who is enrolled in prospective randomized control trials versus what is often characterized as real-world experience really helps me as a physician interpret the body of evidence that exists.

Ann, there are lots of different things that we try to keep in mind during the initial treatment of patients with venous thromboembolism involving the very beginning of their treatment through the time that we would consider them candidates to perhaps have their anticoagulation stopped. Can you talk us through how you think about orienting the patient to the treatment of venous thromboembolism?

Ann Leonhardt-C...: I think one of the first things that is important to orient the patient to is ... You've heard us say a lot today already, "Minimum of three months." I think the three-month or 12-week timeframe keeps coming up. That is something that it is important to bring home with patients. You really want to make sure that they understand that interruptions in anticoagulation during that first three months is really something that should be minimized. This is the highest risk of recurrent thrombosis, and there is a component that is important to educating patients, and we're actually going to talk about that in our next podcast, as well, but trying to ensure that they understand that there needs to be minimal interruption during that first three months ... As such, we want to recommend that any elective procedures should be delayed until three months after that VTE event. Anything that can wait should wait to minimize that interruption.

Also, I think that it's important to consider the unique dosing of the initiation phase with a loading dose of certain anticoagulants and the lead-in parenteral anticoagulants that are necessary for edoxaban and dabigatran prior to initiating this and making sure that patients understand that, as well.

Scott C. Woller: Ann, that's terrific. I especially appreciate the importance that you highlight on the initiation phase and what's often a higher dose of certain direct oral anticoagulants or the parenteral anticoagulant lead-in. That is so important in also minimizing any interruption of therapeutic anticoagulation during those first three months. Thank you so much.

I know, Behnood, that when extended duration anticoagulation is elected, there are options surrounding not only choice of medication but also dosing once a person has completed what we would characterize as the treatment phase and would now be entering the extended phase. Tell me a little bit about how you interpret the evidence that informs decision-making and, pragmatically, how you

tend to approach this decision-making.

Behnood Bikdeli: Such an important question, Scott. Thank you for that. I think again, going back to my [inaudible 00:22:09] about pursuing randomized trial evidence, apixaban, rivaroxaban, and dabigatran are the three DOACs that did have randomized trial evidence for extended-phase treatment, and for those, apixaban was studied in two different doses, two-and-a-half milligrams twice daily, five milligrams twice daily, and compared with placebo. To talk about apixaban, to make a very long story short, there was no added benefit from the higher dose. That's why many of the clinicians, when they want to switch to extended-phase treatment, they choose the dose of two-and-a-half milligrams twice daily with apixaban, and it does have a labeled indication with the FDA. As far as rivaroxaban is concerned, it was studied for the extended-phase treatment either as a 10-milligram daily or a 20-milligram daily, and the comparator here was aspirin.

Before I share the results of the trial, I want to take a step back and talk about aspirin itself. The reason aspirin was chosen as the control in the EINSTEIN CHOICE trial was that two prior randomized trials had actually suggested that aspirin in and of itself does confer some relative risk reduction for secondary venous thromboembolism prevention. That being said, in the EINSTEIN CHOICE trial, rivaroxaban beat aspirin to the extent that recurrent VTE events were lower than either of the rivaroxaban arms compared with aspirin, whereas rivaroxaban did not increase major bleeding. In conclusion from that trial, rivaroxaban was the winner, and the 20-milligram once-daily or 10-milligram once-daily dosing regimens were the ones that came out as potential options.

To be pragmatic in clinic, dabigatran has also been studied and does have a labeled indication for extended-duration treatment, but because of this accrued risk of bleeding over time that we were talking about, in my practice, I tend to choose either low-intensity apixaban or low-intensity rivaroxaban for that extended phase in most cases. I feel like I do want to give my patients some relative risk reduction against recurrent events if there is the indication, but I don't want to expose them to as much bleeding risk as the full-intensity treatment does. I would love to hear if you have different tips or thoughts for your practice, Scott.

Scott C. Woller: Thanks so much. I love the way that you frame the thinking about each of these medications, where the evidence lies, and again, as always, while considering that bleeding risk.

The one population where I'll tend to reach for aspirin are those patients that come to me and say, "Doc, I really appreciate that I have an increased risk for recurrent thrombosis, but I cannot afford or I have no interest in continuing an anticoagulant." In that setting, I'll say, "Okay, here's what we know. Aspirin, when compared to the direct oral anticoagulants for the secondary prevention of thrombosis in the extended phase, is not as good. However, it does appear to be better than nothing." Adopting the old something's better than nothing model, I will, in those patients, say, "If you're willing to take a baby aspirin a day, then that's

probably going to confer, when compared to placebo, about a 33 percent risk reduction in recurrent thrombosis."

For this astute audience, I'll highlight that both of those sentinel studies comparing aspirin for the protection of recurrent thromboembolism used the European dosing of 100 milligrams daily. Invariably, in the United States, of course, we have readily available the 81 milligrams daily. I tend to think of the two as being equivalent with respect to that risk reduction just from a pragmatic perspective.

Ann Leonhardt-C...: Scott, I just want to so thank you for bringing in the patient perspective to this. Whenever we are trying to determine treatment, listening to the patients and understanding what it is they are not only willing but also unfortunately sometimes able to do ... Cost is certainly a consideration, as well as willingness to take the risk of bleeding with long-term anticoagulation. The patient population that we see in our area that has a large portion of rural New York State ... Having someone who is a farmer who does a lot of work with heavy machinery who actually wants to weigh that risk-benefit of, "What if I had a serious injury in an area where I can't get to a hospital and I'm on a blood-thinning medication?" Those are things that I want to point out that we like to take into consideration, as well, whenever you're in that area where you're trying to make a decision of, "Is this absolutely long-term anticoagulation, or do we need to consider that patient perspective?"

Scott C. Woller: Ann, thank you for that. This is a perfect opportunity and just a lovely segue into my and our thanking you for being here today and providing for us why the perspective of the patient ... in addition to being a nurse practitioner and having expertise in this domain, why you shared with us that you personally have experience of venous thromboembolism. So often, we as physicians dial in the science and we dial in the treatment regimen, and arguably, we could do better in taking into account the patient's perspective. I'm wondering if you'd be willing to take a few minutes and just talk with us a little bit about your perspective experiencing venous thromboembolism as a patient.

Ann Leonhardt-C...: I would, and I will tell you that one of the things that we all tell each other in healthcare is that we are terrible patients. If we are good providers, we are probably terrible patients. A lot of the science that we know and a lot of the things that we think about can go out the window when we're taking care of ourselves.

In 2018, on a Friday afternoon, I noticed that I had this bizarre right-arm pain, and I hadn't been doing any upper-body exercises recently, it was positional ... Through Saturday, it got worse whenever I was doing housework, and by Sunday, I was unable to use my left arm without bursting into tears, because the pain with activity was so bad. I looked at my hand. My left hand was swollen to the point that I couldn't get my wedding ring off. When I say that we're not always the best patients ... My husband is a physician, and he's like, "I don't know."

Ultimately, we went to the emergency department, and that is where I was diagnosed with a left upper extremity DVT that stretched from my wrist into the

subclavian vein. I was prepared for them to start me on an anticoagulant and go home, at which point, I was told, "No, we're transferring you across the street to the academic medical center where you're going to have an emergency thrombectomy, as well as a venous catheter placement for continuous thrombolytic infusion, and you'll be admitted to the ICU," which was shocking, to say the least. Ultimately, I was diagnosed with thoracic outlet syndrome. I had two thrombectomies, and I had my first rib partially removed during that hospitalization and was started on anticoagulation with Xarelto.

Scott C. Woller: Ann, thanks for sharing that. Thanks for being so vulnerable to help us better understand the experience of a patient in this ... what had to have been an incredibly scary time, especially, perhaps, knowing all that you know. Circling back to, really, the heart of this podcast, how did you think about duration of anticoagulation? What personal factors in your presentation with thrombosis and lifestyle, perhaps, factors, in addition to anything that might have been done to mitigate your risk for recurrent thrombosis, ended up coming into play in your case?

Ann Leonhardt-C...: My DVT was considered to be provoked. I had two things, actually, at the time. I was on continuous oral contraceptive with estrogen, and when they did the angiogram, they were able to see that my rib was compressing my vein. I had thoracic outlet syndrome and was on an oral contraceptive. That was clearly thought to be provoked, although I am a healthcare provider, and we did every blood test to try and figure out, "Is there any increased tendency for clotting that might lead to longer-term anticoagulation?" All of that was negative.

I approached this in terms of thinking about, "Okay, I'm going to be on this for three months. Zip. I can do this for three months. I am a klutz. I am very active. I'm going to bruise a lot, but it's okay, and I'm going to get through it, and at the end of three months, I'll be able to stop."

Scott C. Woller: Ann, oftentimes, when I see patients in follow-up, they remark on how anxiety-inducing their diagnosis period and the treatment period has been and having uncertainty surrounding how things are going to play out. Can you share with us any insights regarding how you approached that anxiety associated with this diagnosis and treatment, and what, if any, resources you might have found that perhaps other patients and physicians might find as helpful?

Ann Leonhardt-C...: Sure. There was a lot of anxiety that went along with this, and I'll say that most of it was delayed. The 10 days I spent in the intensive care unit, I was cool as a cucumber, because it didn't ... First of all, I was in a place where I knew if anything bad happened, they could take care of it. Secondly, I don't think it had really sunk in yet that this isn't just a temporary thing, this is a big deal. When I got home, that's when the anxiety really kicked in, and I will tell you that I had the added bonus of having just had a rib removed, which can be pretty painful, and so every tweak or every funny sensation in my arm was an automatic thought, "Oh my God, is this clot regenerating? Is it coming back? What can I do here? Is it gone enough that I

can do my occupational therapy?"

Clearly, what I remember is about a month and a half or two months after being discharged from the hospital, I had a massage for the first time, and I'll admit, I had a little bit of a panic attack on the table as they approached my arm. All I could think was, "Oh my gosh, is it okay for them to touch this?"

Where I found support was through ... Actually, I had an outstanding vascular surgeon who was taking care of me, and he and his nurse practitioner that worked with him regularly were both willing to talk me through some of this. Also, while I didn't benefit from this, I've known some other patients that have truly benefited from some local support groups, as well.

Scott C. Woller: Ann, that concept of identifying and taking advantage of resources that are available, firstly, perhaps having a conversation with your physician and/or healthcare provider that has expertise in this domain, and then secondarily, by looking for support in other groups, is really key. Thanks for that.

Behnood Bikdeli: Ann, thank you so much for sharing this. Another element that I wanted to share ... Of course, in your case, you happened to be the expert who also unfortunately had the disease. My experience, and I'd love to hear what you and Scott think ... A lot of times, our patients would also find it beneficial when they get to learn more about their disease. Their anxiety is sometimes multifaceted, and some element of it comes from lack of sufficient knowledge of, "What is my disease? What am I going to expect [inaudible 00:35:25] over the next few days, weeks, and then months?" Sometimes, they have a better time approaching the condition when they have a better appreciation of what to expect. Of course, it's not 100 percent, but it's a starting point, and as you thoughtfully said, some of them find relief in talking to like-minded patients through support groups who've been through the real-world experience with their condition.

Scott C. Woller: Behnood, thank you so much. I'll just remark for our audience that the importance of this topic has not fallen on deaf ears. I know that there are efforts underway through the International Society of Thrombosis and Hemostasis, ISPH, to deliberately consider how we can better educate our physician and clinician colleagues to be able to provide an evidence-based approach of guidance, comfort, care, reassurance and education to our patients to better position them to weather the diagnosis and initial treatment of venous thromboembolism optimally, so thank you very much for highlighting the importance of that context in the treatment of the patient.

Ann Leonhardt-C...: I also think that when talking about the anxiety and the education, one of the things that was most helpful to me was knowing what the plan was. I think that as healthcare providers, we frequently think, "All right, this is the thing that I'm going to do if the ultrasound shows X, Y, or Z, if the angiogram shows that," but we don't always communicate to the patient, "Here is my plan going forward. These are the variables that might change that plan. I want you to be prepared for it." I think that

having known exactly what the plan was going to be from ... okay, day two, not day one, but day two through, actually, six months, because while I was anticoagulated for three months, we continued to follow [inaudible 00:37:32]

Scott C. Woller: Ann, that concept of assuring clear and continuous communication is so important. Thank you for that.

I know we're coming to the end of our time, but if you'll permit me one closing question, and that surrounds how we might think about proceeding if we elect cessation of anticoagulation and whether or not there may be certain circumstances when we decide, "Yes, we're going to stop anticoagulants," but in these circumstances, we might consider reintroduction or a more aggressive form of prophylaxis. Can you talk with me just simply how you think about that?

Behnood Bikdeli: That's a good question. You caught me off-guard, Scott. There are two scenarios that I can think about off the top of my head. First, I'm going to borrow from Ann. She was mentioning about the importance of continued anticoagulation for the first three months, and even if people have elective surgeries, to defer them. What if there is an urgent or emergent surgery? We're going to pause anticoagulation. Those would the kind of situations that I think, by default, we have to continue the anticoagulation as soon as it's safe for the patient again.

Separate from that, a second set of scenarios is if we've completed our routine period of anticoagulation and we don't find a compelling reason to continue at the time, but it's a dynamic conversation over time. What if that very patient gets exposed to high-risk provoking factors again? Be it medical hospitalization, major surgery, or even periods of prolonged immobility because of plaster immobilization or anything else, those would be the kind of scenarios that I tend to think reintroducing prophylactic anticoagulation might be reasonable in the right setting.

Scott C. Woller: Behnood, thank you very much for that additional nuanced guidance in how we approach these challenging situations when they arise. With that, I'd like to thank Dr. Ann Leonhardt-Caprio and Dr. Behnood Bikdeli for their time and expertise today. It's really been our delight to have this time with you and discuss recommended treatments for the duration of venous thromboembolism.

We hope that following this podcast, you now feel better-positioned to consider the appropriate treatment duration for patients that require anticoagulation in the setting of venous thromboembolism, we're hopeful that you can apply the evidence-based guidance that exists in your day-to-day practice, and we especially hope that you have a new and renewed value of the patients' perspective in the treatment of venous thromboembolism. Kindly look out for our subsequent podcast, and thank you very much for your time today.