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Conversations About PAH: Latest Developments and Key Insights for 2023 - Foundational Activity

Announcer:
Welcome to CME on ReachMD. This activity titled, Conversations About PAH: Latest Developments and Key Insights for 2023, Foundational Activity, is provided by AKH and supported by an independent medical education from Merck, Sharp and Dohme Corporation, a subsidiary of Merck and Company Incorporated. This replay of a live broadcast focuses on key insights about pulmonary arterial hypertension, PAH.

Now, here's your moderator, Dr. Jennifer Caudle.

Dr. Caudle:
I'm Dr. Jennifer Caudle and I'd like to welcome Dr. McLaughlin and Dr. Channick to the program. They're joining me to share a recent evidence that supports using novel agents for PAH. As part of the discussion they will also discuss how you can opt in optimize PAH treatment plans and integrate the latest guideline recommendations in your practice. So welcome to the program, Dr. McLaughlin and Dr. Channick.

Dr. McLaughlin:
Thank you, Dr. Caudle.

Dr. Channick:
Thanks.

Dr. Caudle:
Please note that our disclosures are available to you on the event page. You'll have the chance also to claim credit by completing an evaluation after participating in the course. To submit questions during the presentation, please type them into the chat control panel on the left side throughout the program. We'll try to answer as many questions as we can during the time allotted.

So let's begin. Dr. McLaughlin, how is PAH classified?

Dr. McLaughlin:
Great. Thank you so much, Dr. Caudle. If we can move to the next slide, it gives the current classification system for pulmonary hypertension or high blood pressure in the lungs. Group 1 is pulmonary arterial hypertension, what really - what we're really going to focus on for much of our time today. But that's a very rare disease. And we more commonly see other types of pulmonary hypertension. Group 2 pulmonary hypertension associated with left heart disease is actually the type of pulmonary hypertension that probably all of us see the most. Whether there's LV systolic dysfunction or diastolic dysfunction, or valvular heart disease, when the left heart filling pressures are elevated, they get transmitted to the lungs and can cause pulmonary hypertension. Group 3 pulmonary hypertension is also very common, and that's associated with lung disease or hypoxemia. So IPF, COPD, any sort of lung disease that causes hypoxemia, can cause a modest amount of pulmonary hypertension. Group 4 pulmonary hypertension is associated with pulmonary artery obstruction. So that's most commonly chronic thromboembolic pulmonary hypertension. So as we all know, PEs are common, and most of the time the PEs get resolved. But in a few percent of patients, you can have chronic scarring and narrowing of the pulmonary vasculature from pulmonary emboli that do not entirely resolve. And then Group 5 is pulmonary hypertension with unclear or

multifactorial mechanisms. And this is really a potpourri of disorders, glycogen storage disorders, sarcoidosis, some of the anemias, that can cause pulmonary hypertension via unclear or multifactorial mechanisms.

Dr. Caudle:
Thank you so much for that discussion.

Dr. Channick, we'll move to you. Now the ESC/ERS guidelines for the diagnosis and treatment of pulmonary hypertension were updated in 2022. What are the key messages in the 2022 update?

Dr. Channick:
Yeah, thanks. Thanks for the question. Actually, several things. I think is a sort of an important document, if we can go to the next slide. Maybe the most provocative and significant change, which is changing the definition shown on this slide. And as you can see, here, there's a number - a lot of numbers on here. But when we've defined pulmonary arterial hypertension, or pulmonary hypertension, for that matter, it's now recommended that a mean pressure over 20, or at least 20 millimeters of mercury, defines that condition. And that's based on pretty good data that our old number of 25 was probably too high.

You can see, in addition, there has been a really significant change with the European guidelines, which is just PVR cut off of 2 Wood units, where traditionally it's been 3 Wood units. And that's based on some data suggesting that patients who have a PVR even as low as, you know, 2 to 3 may have a higher mortality or worse outcomes. Now, there's some issues with that data. It's a lot of - there are a lot of reasons why these patients could have mild pulmonary hypertension, but it was felt that that was enough data to change this recommendation.

And then finally, the definition of exercise PH has kind of come back into the definition, where previously that was not. And now the European guidelines do list exercise pulmonary hypertension, and you can see there the definition of a pressure to flow slow or change in pressure to change in flow from rest to exercise being greater than 3, defining exercise-induced PH.

So those are some of the changes to the definition.

When we go to the next slide, we can see the - make some general points about the diagnostic approach. Now, you know, there's a lot involved with the diagnostic approach. But this slide from the guidelines, really, I think, outlines that early referral, you see in the bottom square to the expert center. And the so-called fast tracking of some patients who are really - have significant clinical suspicion for pulmonary hypertension, is really important.

Short of that though, there are some additional tests, of course, many of which we've always done to work up pulmonary hypertension. And that's kind of laid out a little bit more in the next slide, which talks about the various testing that's done from Echo, the routine pulmonary function and chest scanning, to ventilation perfusion scanning, which remains the test of choice for excluding chronic thromboemboli, the need for right heart catheterization, and then additional lab tests to try to confirm why a patient may have PAH. So a lot of this is familiar from previous algorithms. But some of those points about early referral to expert centers, and thinking about the common stuff is - continues to be in the guidelines.

And then finally, on the next slide, there's discussion. This just calls out that the VQ scan is really necessary for excluding that diagnosis of chronic thromboembolic disease.

And then on the next slide, it just refers to the details of right heart catheterization and some of the numbers and cut-offs that we look at.

Next slide. There is a comment about screening. And so, the guidelines do suggest that we screen certain high-risk populations like connective tissue disease, congenital heart disease, portal hypertension, for pulmonary hypertension. So that's really – it emphasizes this early diagnosis and even screening before symptoms in certain populations.

So that's sort of some of the highlights.

Dr. Caudle:
Excellent, thank you so much for that overview. You know, Dr. McLaughlin, why don't we go back to you? How is PAH differentiated from other types of pulmonary hypertension?

Dr. McLaughlin:
Yeah, it's a great question. I think we've talked a little bit about the classification and the diagnosis. But let's just take a step back and look at what happens pathophysiologically.

And if we could go to the next slide, we see on the left a normal pulmonary arterial that has a very thin intima media and adventitia. And of course, as we have naturally occurring compounds that help vasodilate and vasoconstrict, you know, there's an equilibrium. There's a balance in a normally functioning pulmonary arterial. And then what happens with pulmonary arterial hypertension is there is an

imbalance; there's more vasoconstriction and proliferation, as well as less relaxation. And there's also inflammation and cellular growth, such that you start to see intimal proliferation and smooth muscle cell hypertrophy and lack of apoptosis. So really just overgrowth of the pulmonary vasculature and narrowing of the lumen of those pulmonary arterioles. And then you have an increase in the pulmonary vascular resistance.

If you can advance the slide please. What happens once the pulmonary vascular resistance starts to go up is that very thin right ventricle, that right ventricle that's meant to pump against a very low pressure, low resistance circuit, starts to have to overwork and you get RVH, and you get pressure and volume overload of the right side. It increases the wall stress. Can even impact the interaction of the interventricular septum and the flow of the right and left ventricles. And then if you advance, really what happens is this can ultimately cause right ventricular failure. And this all contributes to the common symptoms that the patient has as well as the physical exam findings.

Dr. Caudle:
Thank you for that. For those of you who are just joining us, this is ReachMD. I'm your host, Dr. Jennifer Caudle, and joining me to talk about PAH are doctors McLaughlin and Channick. I'd like to encourage our viewers to submit questions for them as we go through the presentation.

So Dr. Channick, back to you. What are the current guideline recommendations for the management of PAH?

Dr. Channick:
Thank you. If we could have the slide. There's, you know, a lot, and Dr. McLaughlin and I have both been involved in this field for quite a long time and really have seen the development of all the therapies we now have. This is extremely exciting and more to come.

So currently we target three different pathways, as you can see on this slide, the prostacyclin pathway, the endothelin pathway, and the nitric oxide pathway. And these are targeted therapies that are aimed at either increasing or replacing prostacyclin, blocking the effects of endothelin, and augmenting, enhancing the effects of nitric oxide, and restoring that balance between the vasoconstrictive proliferative mediators in the vasodilating antiproliferative.

And that's really where we've been at with therapy. And you can see on the bottom, the various treatment options. So we have a number of prostacyclin pathway drugs that are either analogs of prostacyclin, or in the case of one drug, selexipag, actually binds and enhances the prosta - IP receptor, it's an agonist.

And then we have three endothelin receptor antagonists that bind either one or both of the endothelin receptors. And then in the nitric oxide pathway, we have drugs that either are PD5 inhibitors that, like sildenafil, tadalafil, and then drug - one drug riociguat, which stimulates guanylate cyclase. So directly increases cyclic GMP.

So all of these drugs are FDA approved and have been shown in pretty robust studies over time to be efficacious.

Dr. Caudle:
Excellent. And Dr. McLaughlin, what are some common adverse events of PAH-specific therapies?

Dr. McLaughlin:
Yeah, it's a great question. Because as we treat patients, our goal is to make them feel better, to improve the symptoms of the disease. But we have to balance that with the side effects of the drugs and that can be quite complex.

This slide summarizes some of the side effects from the medications that Dr. Channick reviewed. And I just want to reiterate, we are so grateful to have so many medications for pulmonary arterial hypertension, most of which have been approved just in the past 25 years or so.

So starting from the left, the endothelin receptor antagonists, these are oral agents that Dr. Channick has already reviewed. And they're generally pretty well tolerated, although sometimes we see anemia and so this needs to be monitored for with blood tests periodically, as well as elevated LFTs. They can cause some fluid retention and, of course, right heart failure and fluid retention is common in these patients, and so this needs to be monitored carefully as well. And these agents have embryofetal toxicity and so they should not be - or they should be used carefully, rather, in women of childbearing potential, and we need to get pregnancy tests on those patients as we administer those drugs.

The PDE5 inhibitors, again, are very potent vasodilators, and they can cause side effects such as nasal congestion, headaches, gastroesophageal reflux from relaxing smooth muscle as well.

The prostacyclin pathway agents as a class have a number of side effects that are associated with vasodilatation, such as flushing and headache. So more unusual side effects like jaw pain, the patients describe pain in their jaw like biting into the lemon, the very first bite of a meal, and then it goes away as they chew. It can have more chronic side effects like bone pain. But then we also have the side

effects associated with the route of administration. The most potent of the prostacyclins are delivered on a continuous I.V. or subq basis. And so, to be on a continuous I.V. infusion of this very potent medication, you need to have a chronic central venous catheter, and of course, you're then at risk for line infections and, in fact, rebound pulmonary hypertension if for some reason the line comes out. To obviate the need for continuous I.V. infusion, there's also a prostacyclin that's delivered on a subcutaneous continuous basis, much like insulin can be in some patients. But in about 85% of the patients there is pain or erythema at the site of the subcutaneous infusion. And we certainly have nurses that spend a lot of time on the phone with our patients helping to manage the site pain and the other side effects. And then there are inhaled prostacyclin pathway agents. And any inhaled drug can often cause a cough. So we see that sometimes.

And then there are the sGC stimulators. They also work on the nitric oxide pathways, and so have many of the same side effects as the PDE5 inhibitors do. They tend to have a little bit more of an impact on blood pressure and rarely can cause syncope, but also cause dyspepsia, headache, and lower extremity edema, and they also have embryo fetal toxicity, so monitoring of a patient with childbearing potential is important as well.

Dr. Caudle:
Thank you for that, and Dr. Channick, how has the treatment paradigm evolved in PAH?

Dr. Channick:
Yeah, it's actually evolved quite dramatically over the past several years. If we could have the slide up. Very simply, you know, when we started with the first drug approved, there wasn't a whole, you know, the strategy was to use that drug. And once we started getting all these drugs, then it became very important to understand how we use them together. And so, you know, initially as drugs came on board, we were talking about sequential therapy. So, you start with drug A, you assess the patient, then add the second drug, and in some cases, the third drug, as - if patients were not achieving what we wanted them to. And that, you know, may for some cases, still be the paradigm. But I think we've really evolved to this concept of upfront combination therapy. So we're starting, in most cases, two drugs upfront, and then maybe adding a third drug. There's also, as you'll see, some evidence for the efficacy of starting three drugs up front.

So this concept of upfront combination therapy really has taken hold and is really, you know, codified in a number of different guidelines or algorithms that, for most patients, we're starting two drugs up front. So that's, I think, a big evolution in how we've approached. It's really focusing on treatment strategy.

Dr. Caudle:
Excellent, and really quite interesting. You know, Dr. McLaughlin, taking that sort of a step further, what's the rule for triple therapy in treatment-naive patients?

Dr. McLaughlin:
Yeah, it's a great question. And I think there's a couple parts of this answer. One is that the sickest patients, the patients at very high risk, generally accept that they need triple therapy that includes a parenteral prostanoid. But for the rest of the patients, the question is, should a less invasive type of triple therapy be considered? And Rich referenced one of the trials back in the around 2015 time era that demonstrated upfront combination therapy with ERNA and PD5 is better than one or the other alone.

So then the next question is, well, are three drugs better than two? And so that led to the TRITON trial, which was a phase - actually phase 4 randomized, double-blind, placebo-controlled trial that looked at initial triple combination therapy with macitentan, tadalafil, and selexipag, which is a prostacyclin pathway agonist, versus initial double therapy with macitentan, tadalafil, and placebo in newly diagnosed treatment-naive patients. Now, this study really was kind of an exploratory study, really looking at pulmonary vascular resistance at week 26.

And on the next slide, you'll see that both groups, the triple therapy group and the double therapy group, had marked improvements in the pulmonary vascular resistance, greater than 50%, after 26 weeks of therapy. But there was no difference between the two groups. There were also marked improvements in the 6-minute hall walk, over 55 meters in both groups. And again, no difference between the groups. So really, both the double therapy and the triple therapy groups had substantial benefits over the 26 weeks. But there were no difference between the groups.

Now there was an exploratory analysis. And you know, just to be scientifically accurate, this needs to be interpreted with caution, because the primary endpoint was neutral. The trial did not meet the primary endpoint. And so anything else is really just hypothesis-generating rather than solid evidence. But in the exploratory analysis, there was a little signal for improved long-term outcomes in patients who receive triple combination therapy, versus patients who receive double combination therapy.

Dr. Caudle:
Excellent. And Dr. Channick, what are the treatment goals in PAH?

Dr. Channick:
Go to the slide. There's actually, again, a big evolution is in this area. And the whole concept that we have well-defined treatment goals,

I think, is a big development. This is sort of a busy slide. But, you know, I think this concept of really improving a patient to what we call low risk, and you can see in this pretty busy table, all the different parameters we may look at when we start treatment on a patient or treatment regimen, and then as we follow those patients. And getting a patient into that low risk or green area, I think is really critical for - not just for improving prognosis, but for actually improving how they feel. Because many of these parameters like functional capacity, walk distance, so really quality of life-type measures in terms of how a patient feels and functions. And so these are all parameters that we measure regularly. And whether it's subjective things like functional class all the way up to very detailed imaging of the right ventricle, these are things that have been laid out as important things to follow. And making changes in our therapy to meet those goals.

The other thing I want to point out is that we use what we call really four risk strata. Traditionally, in the past, it's been three. But it turns out that many patients on treatment still are in what we call intermediate risk. And because of that, it was sort of just separated into low, and high or intermediate in some analyses, that have shown to be pretty discriminating, and really helps us and helps make treatment decisions if a patient is, for instance, in low-intermediate versus high-intermediate, that may lead to very different changes in treatment.

Dr. Caudle:
Dr. McLaughlin, did you want to jump in with any comments?

Dr. McLaughlin:
Yeah. I mean, I think we've learned so much about risk stratification over the past decade or so. And I really love the refinements that have recently been made to the risk stratification methods to divide that intermediate-risk group up into low and high. And it's very easy to do. I really want to emphasize how important it is to do that every time you see a patient.

To do this, all you need are three measures which we generally get in clinic when we see patients. It's a functional class. So we talk to them, we assess their functional class. It's a hall walk. We generally do 6-minute hall walks. And then the biomarkers as well, the NT-proBNP or the BNP. And we actually now have a little smart phrase, we have a little flow sheet tool that we put that information in. And we actually generate that at the bottom of the note like what their score is and what category they fall into. And as Dr. Channick said, it really makes counseling the patient much, much more gratifying because you can give them a clear expectation of their risk, and talk about why they do or don't need other therapies. But on the other hand, it's just - it's one part, I think it's also important to consider the patient's comorbidities, their right ventricular function. There are other things that go into how we treat patients as well.

Dr. Caudle:
Excellent. Okay, and moving on. As a reminder, we do encourage you to submit questions for the faculty. So to submit questions during this presentation, please type them into the chat control panel on the left-hand side throughout the program. We certainly will try to answer as many of your questions as we can during our time allotted.

So moving forward. Dr. McLaughlin, what are some new and emerging therapeutic targets for PAH?

Dr. McLaughlin:
Well, Dr. Caudle, I have to say it's such an exciting time for research and pulmonary arterial hypertension. Rich, Dr. Channick, kind of outlined the three pathways that we've targeted for many years. But every time I explain that to an audience, I always say that's just the tip of the iceberg. We talk about those three pathways, because those are the ones we understand. And those are the ones that we can currently target with FDA approved therapies. But there's so much more to pulmonary arterial hypertension than just those three pathways.

And you can see on the slide, there are a number of pathways that are dysfunctional or dysregulatory in pulmonary arterial hypertension that we maybe don't understand or that we can't yet target. But it's an exciting time in research.

There are a number of trials going on with pathways that we currently know. But we're trying to make delivery or side effects a little bit easier for the patient. So other prostacyclin pathway agonists like, there's a trial going on, other types of inhaled treprostinil, that might make administration a little bit easier. But there are new pathways that are being studied. Many moons ago, we studied imatinib for pulmonary arterial hypertension. And the trial demonstrated efficacy, but it wasn't well tolerated in the oral formulation. So there are a couple of different formulations of inhaled imatinib, so that we can perhaps give lower doses directly to the lung and target the disease without causing side effects. So that's a really exciting potential. There are other kinase inhibitors, seralutinib, that are being studied. And then probably the most exciting thing right now is sotatercept.

Dr. Caudle:
And speaking of sotatercept, Dr. Channick, let's go back to you. Sotatercept is a promising new drug that is in a novel drug class for Group 1 PAH. How does this novel treatment pathways for PAH differ from current therapies?

Dr. Channick:
Yeah. No, I would certainly agree that this is a very exciting agent with pretty strong data that I'll discuss in a second. Very simply, it's a drug that say, what we call an activin, in works in the activin pathway. Activin is a molecule that is part of what we call the TGF-beta. And the bottom line is that that mediates a lot of growth and proliferation downstream. So this drug specifically eats up the activin, if you will,

and hopefully prevents it from doing or mediating those kind of downstream effects. And it turns out that that, in fact, is likely a benefit.

And so we have now, recently a phase 3 study called STELLAR, that was published in the *New England Journal of Medicine* just very recently, which looked at patients who are already on background therapy, stable, but still symptomatic, who were then randomized to sotatercept, which is a subcutaneous injection every 3 weeks, with the primary endpoint being improvement in the 6-minute walk test. And the results of that, if you can show in the next slide, was, you know, quite striking. So sotatercept, indeed, did improve 6-minute walk distance significantly, compared to placebo. And again, these are patients who, in many cases, have very long-standing pulmonary arterial hypertension, already maintained on, in some cases, very aggressive background therapy, including parenteral prostacyclin in about 40% of patients.

In addition, and this is very reassuring, there are a number of secondary endpoints that were also improved from, and you can see the list there from pulmonary vascular resistance, functional class, time to worsening, so delay in clinical worsening. A combined parameter of improvement, in fact, was also significant infected - affected the risk score, the French risk score. You can see that some of the quality of life measures as well, were improved. So very consistent data, both from the primary and secondary endpoints for this drug.

Dr. Caudle:
Very exciting, indeed. Dr. McLaughlin, what is the potential impact of these novel treatment pathways and new emerging therapeutic targets for PAH?

Dr. McLaughlin:
Yeah, it's a great question. You know, again, we're so thankful to have all the therapies that we have, and they have made a tremendous difference. But yet, we still lose far too many patients to this disease. You know, we still are having patients who don't respond, have poor quality of life, you know, higher mortality rates, despite these aggressive therapies. And so targeting new pathways, and potentially pathways that don't just relax the blood vessels, cause vasodilatation, but help rebalance the proliferation and the apoptosis, you know, really potentially causing reverse remodeling, may have the potential to really impact the course of the disease in many patients.

Dr. Caudle:
Excellent. Thank you both for this segment of the program. We are now moving into our Q&A section of the program. We have many questions that have come in from our audience, we thank you for that. So let's just jump right in and start with our first question. What is your - the question states: What is your recommendation for dealing with an overweight patient who has diabetes and PAH? Which - who would like to take that, Dr. Channick or Dr. McLaughlin?

Dr. McLaughlin:
You know, I can start with it and let Rich chime in. I think it goes back to making the correct diagnosis. I think Rich so eloquently went through the diagnostic algorithm. And we have to consider different types of pulmonary hypertension and different patients. And one type of patients that I feel like I see a lot these days are patients who perhaps they have high pulmonary pressures, but they have many risk factors for diastolic heart failure, and consequently, Group 2 pulmonary hypertension. So an obese patient with diabetes may have diastolic heart failure and may have pulmonary venous hypertension or Group 2 pulmonary hypertension. So I think it's really critical to go through that diagnostic algorithm and really determine the type of pulmonary hypertension that they have. And if indeed, it's Group 2, the treatment is very different. The treatment is sodium restriction, diuretics, management of risk factors, weight loss, perhaps SGLT2 inhibitors. So I think, to answer that question properly, we need a good diagnosis.

Dr. Channick:
I would certainly agree with that. And completely, as Val said, that's a very common scenario. One of the things though that’s come up is this concept of, you know, can a Group 1 patient have comorbidities? And that would include some things like diabetes, hypertension, obesity obviously being part of that. And this is where you have that kind of gray area or the overlap between, let's say, a patient who in fact does have PAH in our judgment, but also have some of these comorbidities like obesity. And that's where that the challenge comes in. And certainly, I wouldn't write the patients all off as having Group 2 PH. But even when we're making a diagnosis of PAH, we may need a little more caution in some of those patients. And this is actually a somewhat, sort of a hot button topic of, you know, do we treat those patients with comorbidities in Group 1 PAH differently? Like, more cautiously one drug, that kind of thing?

Dr. McLaughlin:
Yeah. And - but I think it also comes back to having the characteristics of the patients and having the hemodynamic. So the patient that Dr. Caudle described, the patient who has obesity and diabetes, you know, what does her Echo look like? Is her right ventricle normal in function? Or is it dysfunctional? When you cath her, is her PDR 3.2? Or is it 7? You know, so I think you need to answer that particular question, placing in context, the number and severity of the comorbidities, as well as the severity of the pulmonary vascular disease. So if she's in that former category, where her right ventricle is normal, and you cath her in her wedge is, you know, 14 because she's NPO, and the PVR is 3.5, you know, I would be more gingerly in that person. Whereas if she has right ventricular dysfunction and her PVR is 7, 8, you know, that, to me is a patient with PAH, and who just happens to have diabetes or obesity, which are common in our country, and I would treat that patient more aggressively.

Dr. Caudle:
Fair enough. Thank you both. And just moving forward. I would love if both of you could chime in on the answers to these questions, because you're so excellent in providing great insight.

So moving to the next question we've received this question asks: What is the role of multidisciplinary care teams in managing patients with PAH? And how can healthcare providers optimize collaboration to improve patient outcomes? Who would like to start with this?

Dr. Channick:
I'm happy to. I mean, there's a huge role for multidisciplinary teams, this is a, it takes a village type of situation to manage a pulmonary hypertension patient, not just the medical part of it, but all the other aspects of dealing with a chronic disease require, you know, from case managers, to our nursing people. You know, palliative care is plays a huge role now, in symptom management for our patients. You heard from Val about all the side effects of the drugs and then some of the difficulties. And then within the medical group, these patients have multi system disease. I mean, they have heart disease, lung disease, sometimes kidney disease, sometimes liver disease, so all of those specialists are involved in the care of our patients.

Dr. McLaughlin:
Yeah, I would echo that. And, you know, also, sometimes they need transplant, right? So then we're involving whole transplant teams, or, you know, we work with rheumatologists because we want them to screen patients and co-manage patients. So it really does take a village to care for these patients.

Dr. Caudle:
That's very helpful. You know, sort of kind of along those lines as it takes a village, you know, let's talk about helping your patients, you know, with adherence and making sure they're able to follow their care plans, what, you know, one to two pieces of advice do each of you have or things that you do to help your patients be adherent to their care plans, or help them stay on top of their care?

Dr. McLaughlin:
Sure, I think first of all, it starts with education. We need to educate them about the disease. We need to educate them about the serious nature of the disease, you know, in a way that they understand why it's so important to get - to be consistent with their care. We need to educate them about the medications and let them know what side effects to expect. But then to reassure them that we have teams to help manage them through the side effects. And this is where the multidisciplinary team comes into play. Because our nurses spend a great deal of time with these patients, helping them, you know, coach them through the medications, the side effects, and we often have our nurse practitioners do periodic video visits as they're starting the medication to just help them manage, titrate more appropriately for that patient. It's all highly individualized,

Dr. Channick:
Yeah, I would – you said it perfectly. I would add to your comment about the video visit, as, you know, obviously, this was something that we never did before the COVID pandemic, but it's actually, I think, really - is now a really valuable tool in maintaining compliance for patients. Because we can connect with these patients much more frequently to find out how they're doing when we start them on medication than previously. I mean a big, positive outcome.

Dr. Caudle:
Absolutely. No, I definitely think you're right. As a family doctor myself, you know, I've noticed that video visits can make things a little bit easier. So that's - your commentary from both of you about how you sort of navigate, this is really helpful.

We have another question about patients with comorbidities. I know you talked - both of you talked about this a little bit in our first question, but this question says, you know: What are some of the key challenges of treating PAH patients with comorbidities? And what's your advice for healthcare providers with this in dealing with these challenges?

Dr. Channick:
Yeah, I mean, I can take that. We talked about it a little bit. But I think, you know, in the – a bit of in the trenches, maybe where the question is coming from, because, you know, the patients that many people see in practice are not the 30-year-old, you know, thin patient with severe pulmonary arterial hypertension, what we used to have our primary, are now idiopathic PAH. But you see patients who have all these comorbidities, they may have some sleep apnea, they may have obesity, the diabetes, and in some cases, you know, they have pulmonary hypertension. And the question is, you know, really, what do you do with those patients? Can't necessarily send all of them to an expert center, they may not have access. So how do you work it up? And I think Val kind of said it nicely. It's really a systematic approach. So the first question is, you know, why do you think this patient has pulmonary hypertension? How severe is it? And what are the treatable comorbidities or conditions? So, for instance, if we see a patient with severe hypoventilation syndrome who's obese, treating that patient with CPAP or BiPAP, and diuretics may actually relieve or resolve the pulmonary hypertension. So you need to go through that stepwise approach. What you don't want to, what Val said, is throw them on PAH medicine without really understanding what's causing the problem.

Dr. McLaughlin:

Yeah, but if I could take it a step further, which I think maybe I interpreted the question as a little differently. So let's say you did that workup, you decide they have pulmonary hypertension that you're going to treat, be it, you know, a little more gingerly with one agent or two agents, what do you watch for? And I think that's a really important question, because there's lots of data to suggest that those sorts of patients with comorbidities have a blunted response, not that they won't have some response, but they have a blunted response. And they have more side effects. And so really engaging that nursing team and watching them for side effects, helping to manage the medication, often diuretics. Oftentimes, they have more lower extremity edema as we start these therapies, and we need to titrate diuretics a little bit more. I think those are things that you need to be cautious of if you're going to use PAH therapies in those patients, particularly with the cardiovascular comorbidities.

Rich, I would throw it back to you in patients with the pulmonary comorbidities, do you worry about things like VQ mismatch? Like, how do you monitor for that?

Dr. Channick:
Yeah, that's another great question. And I think, to be honest, it's probably a little bit overemphasized in our experience. And there's some data on this, that, you know, in the patients who may have some lung disease, and whether that's from COPD or even some pulmonary fibrosis, if they have significant pulmonary arterial hypertension, you know, we probably don't see significant worsening of oxygenation. The concept has been that, you know, you're dilating bad areas of the lung, and therefore worsening the VQ matching. That may happen occasionally, but in my experience, not very often. But still need caution, because, you know, you want to be sure that you're treating the right disease. Group 1 PH is one exception; there's one therapy, Treprostinil, which is approved for Group 3 PH.

Dr. Caudle:
Excellent. You know, I just wanted to say I appreciate both of your answers to that question. Taking the question and sort of dealing with it from two different angles, one from making sure that the diagnosis is correct, and that there's nothing underlying that we are missing or causing the PAH. The second is, what do we do when people are, you know, do have a true diagnosis of PAH and have comorbidity? So I appreciate that.

It looks like we just have a couple more questions. What are some important considerations when developing individualized treatment plans for patients with PAH? How can healthcare providers really work with their patients to tailor their care? You both did talk about, you know, that it takes a village, multidisciplinary care, is there anything else that you might add sort of in addition to that with individualized treatment plans?

Dr. McLaughlin:
Yeah, I think it's a great question. Because these patients, they're all highly individualized. And so, I think I would make a couple of points, and I'm sure Rich will have others. First is we need to talk about what the goals are. You know, what are the patient's goals? And try to have them set some goals. You know, maybe they come and they can't take care of their kids, or they can't go up a flight of stairs. Usually, their goal is to have an improvement in their shortness of breath and their ability to function, and trying to get an idea of what they want to do in their daily life, is an important goal.

I think we also have longer-term goals. Like we want to make them feel better, but we also want to have them live longer and not need hospitalizations or not get to transplant. So kind of balancing those short and intermediate/long-term goals is an important part of the conversation, especially as we talk to them about medications, which as we already discussed, all have side effects. Right?

So, trying to understand the goals and working together to get to both the short-and the long-term goals, I think is very, very important.

Dr. Channick:
Yeah, I would certainly agree with that wholeheartedly. I think that, you know, the other part of it is, you know, we talk about it, you know, with the patient, like it's really a journey. So you meet them and you start initial treatment, I can't tell them, you know, what their prognosis is. Our goal is to get them as good as possible and make changes along the way. So, you know, sometimes the patients, you know, rightfully so, have this come up with a lot of fear. And you have to relay that and say, 'No, this is a very treatable condition. What you're reading on the internet is likely outdated, inaccurate, and this is, you know, not universally fatal. You're not going to be dead in 3 years,' these kinds of things that the patients come and often that - giving them that reassurance is huge. And then just the concept of, you know, we make changes as we need to along the way. So taking the journey together.

Dr. Caudle:
I love that. That's excellent. I love the piece about the internet, because it can be very scary for patients for so many conditions. So absolutely right on about that.

And we, in our last 2 minutes of our Q&A, do either of you, or both of you, have any final comments or insights that you'd like to share with our audience before we close?

Dr. McLaughlin:
I mean, I think we covered a lot of great important things. If I could highlight a few things, one is to make the diagnosis correctly, right?

Like, you know, pulmonary hypertension is common. Pulmonary arterial hypertension is actually very, very rare. And the medications that we have for PAH might not be right for patients with other types of pulmonary hypertension. So I think really emphasizing the correct diagnosis is very, very important.

And then, I think Rich said it nicely, the treatment journey. We have so many therapies available. We need to discuss the patient's goals, start treatments, reassessed, risk assess, and then make the tweaks along the way. And the team is behind them, that good pulmonary hypertension centers have multidisciplinary teams that can provide a lot for the patient. And I think, really importantly, work with the local physicians, work with their local primary care provider who needs to stay in the loop. And so really having that good communication and providing a lot of care locally, but having the resource of the clinic, of the pulmonary hypertension clinic, is really a win-win for patients.

Dr. Caudle:
Excellent. Dr. Channick?

Dr. Channick:
Yeah, no, I think all those things are absolutely important. And I just want to emphasize, you know, the fact that there's more coming. And so, you know, as far as we've come in this disease and this condition and understanding it, and coming up with treatments, this is not stopping. And so, you know, we showed some of the data with sotatercept, and it's just a very exciting time. And we - I mean, I communicate that to my patients. I think they get that idea that this field is not stopping until, you know, hopefully, we're curing pulmonary hypertension sometime in the future.

Dr. Caudle:
Absolutely. And definitely an exciting time. So, thank you both. This was an excellent discussion. This was a great way to round our discussion on PAH as well. I'd like to thank my colleagues, Dr. Channick and Dr. McLaughlin, for helping us better understand this topic. It was really great speaking with you both today.

Dr. McLaughlin:
Great. And nice speaking with you as well.

Dr. Caudle:
And another presentation on this topic will take place on June 15th. We welcome you to register and join us again. To those listening to this course, please proceed to claim credit by completing the evaluation through ReachMD. Also through ReachMD, you can get a PDF of the slides, including explanations to the pre and post-test questions.

Announcer:
You've been listening to a replay of a live broadcast titled: Conversations about PAH: Latest Developments and Key Insights for 2023, Foundational Activity. This activity was provided by AKH, and supported by an independent medical education grant from Merck Sharp and Dohme Corporation, a subsidiary of Merck and Company Incorporated.

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