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Time needed to complete: 1h 49m

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(866) 423-7849

Hot Topics from the New ERS/ESC PH Guidelines: Focus on Treatment

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Dr. Channick:
So hello, my name is Richard Channick. I'm at UCLA Medical Center. And today we're going to be talking about hot topics from the recent ERS/ESC guidelines. And we're going to focus on treatment aspects of the guidelines. Delighted to be joined by my colleague, Dr. Rajan Saggar from UCLA also. Welcome, Raj. And Dr. Ioana Preston from Tufts University. Welcome, Ioana.

So let's dig right into the algorithm. These guidelines have a treatment algorithm associated with them. And a lot of this algorithm reflects some of the concepts that we talk about all the time with risk assessment, initial combination therapy. So we're not going to go into all the every little detail of the algorithm. One of the things that really emerged that was, I would say, is definitely a hot topic is this concept of comorbidities. And maybe you can very briefly, Ioana, summarize what the algorithm said related to comorbidities, that was a big change, I think.

Dr. Preston:
Yes, Rich. Indeed, a big change. So the treatment algorithm divided clearly, patients into two buckets, patients with a typical PAH phenotype, and they were called PAH patients without comorbidities. And patients who have other conditions that do not cause PAH, but they're significant enough that they have to be taken into consideration. And those are called PAH with comorbidities. And it recommends for first bucket, the treatment algorithm for the typical PAH double combination therapy, triple combination when it's necessary, and whatnot. And then suggest for those patients with comorbidity, a much more cautious approach and not start dual, but monotherapy and then rethink.

Dr. Channick:
Yeah, and Raj, why do you think they made the change? And what's the rationale there?

Dr. Saggar:
Well, I think, you know, just going back to why we have group 1 and group 2 PAH to begin with, right, is the idea obviously, that you can have pulmonary hypertension from different, you know, from left heart disease, which can cause group 2 PH. But the concept was, for many years was that look, you know, we don't want to treat patients with these drugs who have left heart disease driving their PH, because we may make these patients worse. But what we've realized over time is that a lot of these patients present with - I mean, they're very heterogeneous, so you can have patients with left heart disease and mild, sort of pulmonary hypertension, and then the spectrum all the way to severe.

So this was first looked at in the AMBITION study, as we all know. And in the AMBITION study, where we now, you know, got the dual therapy, you know, upfront dual therapy, which is now standard of care, they had, as you all know, a group of patients in there sort of early on in this trial, which had three or more risk factors or comorbidities for left heart disease. And I think that study showed that, yeah, while the patients who had comorbidities didn't do as well as the patients without comorbidities, they still had a 30% reduction in clinical

failure, as opposed to the 50% reduction in clinical failure as compared to the pooled monotherapy. Yet, they also had more side effects with the medications, they were more likely to discontinue the medications, but they still benefited to some degree. And I think that theme has sort of gone through with several registry approaches to this.

So I think while things are muted with those patients, they still potentially, if they have a significant PH phenotype, perhaps deserve a little bit more of a spectrum approach, maybe not just monotherapy up front.

Dr. Channick:
Yeah, and I think - I mean, I think the message was that, you know, you consider monotherapy upfront, but obviously the still reassessing and maybe taking a stepwise approach rather than two drugs at once if they have this what they call left heart, or you know, cardiopulmonary phenotype they referred to. I mean, let's start talking about your practice, I mean, are there patients where you take that exact approach?

Dr. Preston:
As our population of PAH patients lives longer, and the age at diagnosis has moved compared to the 1980s, we do diagnose group 1 PAH patients that have several other comorbidities. But if you have a 50-year-old woman with group 1 PH idiopathic, who also has systemic hypertension that's well controlled, you know, with one anti-hypertensive, is that a patient with comorbidity? I think the guidelines, because if you read the footnotes - and that's the problem, that wasn't put in the main graph algorithm. If you read the footnotes, they want you to highlight those patients who have significant comorbidities and an atypical phenotype of PAH that need a little bit more cautious approach, not the typical PAH to with a comorbidity.

Dr. Channick:
Yeah, that's a really good point. Not all comorbidities are created equal.

Dr. Preston:
Exactly.

Dr. Channick:
You have to look at it with a little more nuance.

I want to change gears and the remaining minute or so that we have, you know, we talk all about the guidelines and treatments and all these things, these great things in PAH, but one of the overwhelming problems we really have, to be perfectly honest, is actually getting these therapies to all of our patients. And we have a very large, underserved population. We do, and I'm sure you do. And obviously, this isn't something we're going to solve right now. But, you know, how should we approach these patients to try to help them out?

Dr. Preston:
Yeah, it's a very good question. And it's an acute question. And it's not only in PAH, which is a rare disease, but it's more acute in PAH because it's a rare disease. So access to diagnosis to the right specialist, access to knowledge that there is such a thing, not only for patients who are underserved, but doctors who work in underserved areas who don't have the resources to look for rare conditions.

Dr. Channick:
And I think with the technology we have, we should be able to get at these patients.

Dr. Preston:
Close the gap.

Dr. Channick:
I mean, is that the future of technology?

Dr. Saggar:
I think obviously COVID has made televisits more mainstream, but the patients have to find us or we have to find the patients. So you're still stuck with the situation.

Dr. Preston:
Yeah. Yeah. So, you know, as we're talking, I'm thinking artificial intelligence tools that can pick modifications on a regular EKG or a chest x-ray to trigger the question for pulmonary vascular disease.

Dr. Channick:
Yeah, that's where it seems to be headed.

Dr. Preston:

That's going to be one way to go to pick those patients who don't have the support system in the community.

Dr. Channick:
Yeah. Well, thank you. That's all the time we have. Thanks. It's a great discussion. A lot more we could talk about. And thank you all for listening.

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