When Is It PF-ILD? Diagnosis, Monitoring, and Treatment of a Complex Disease

The symposium on progressive fibrosis and ILD is quite interesting. The concept of progressive fibro sing ILD is really relatively new, having emerged over the last several years. This really is a concept that goes in parallel with the existing paradigm of diagnosing the etiology of interstitial lung disease. So clearly the first and most important step in diagnosis of interstitial lung disease is trying to identify the cause and create a diagnosis. But once a diagnosis exists, say a connective tissue disease, ILD or hypersensitivity pneumonitis or any of a number of other diagnoses, the next step is then to think about the trajectory of disease. So the vast majority of say connective tissue disease, ILD will appropriately respond to immunosuppressive therapy in that the patient will either stabilize or improve. And for those patients, there really is a trajectory of resolution or improvement.

But unfortunately, even within that category of disease, there will be some patients who do not respond to standard of care therapy. And when that occurs, what can be ascertained is that there's progression in terms of CT scan, a drop in lung function and often patients and unfortunately, patients become more ill and have an increased risk of death. These are the patients that we consider to have progressive fibro sing interstitial lung disease. So regardless of what the primary diagnosis is, it's really the trajectory of disease, that patients who progress despite the use of appropriate therapy.

In those patients, there have recently been several clinical trials that have suggested there may be benefit to the use of an anti-fibrotic. And specifically there were the in-build trial, which looked at a broad variety of patients who have this progressive fibrosis and phenotype and looked at their response to the anti-fibrotic nintedanib. And just to give a top line summary of that study, what it showed was that in patients who have this progressive fibro sing phenotype, there is a reduction in the rate of loss of lung function of about 50% over the course of 52 weeks with the use of nintedanib in comparison to placebo on top of their standard of care therapy.

So what this suggests is that beyond the primary diagnosis of what is the etiology of disease, we now also need to really think about the trajectory of disease and consider the presence of antifibrotic as a potential therapeutic agent in that paradigm.

I think there's been a lot of controversy about what the clinical implications of this study is. I think it's really important to be very clear that this does not substitute for identifying the etiology of the interstitial lung disease. So any newly diagnosed patient with interstitial lung disease, the first and primary goal has to be, to identify the etiology, whether it be idiopathic pulmonary fibrosis, chronic hypersensitivity, pneumonitis, an environmental trigger, any of those things, connective tissue disease, and it should be treated initially with the therapeutic agents that are most appropriate to that diagnosis.

So for instance, for a patient with chronic, with hypersensitivity pneumonitis, they should have elimination of the antigen from their environment. The only place where this comes into play is for patients who having gone through this initial process of identification of the etiology and use of the appropriate initial therapy, that they still show progressive disease despite the appropriate use of

therapy. In those patients, then I think that there needs to be a shared decision making regarding whether an anti-fibrotic would be appropriate for those patients. And of course, again, this is a risk benefit ratio for every individual patient. The benefit of antifibrotic nintedanib in this context is to reduce the rate of loss of lung function. And the balance with that is that there are side effects, including diarrhea, which is a very common side effect with this medication. And so this is really a discussion that needs to be had with each individual patient and only in the context of having failed or progressed through standard of care therapy.