## SPEAKER:

One of the biggest challenges that we face managing these patients is knowing who to treat and when to start treatment. As I said before, you want to make sure that you've done a very thorough job identifying the compelling evidence to begin treatment.

So on the one hand, if you believe that the bug is the culprit accounting for the radiographic findings and the symptoms, then of course, treatment is warranted in that patient. On the other hand, if we actually knew the natural history of these infections and we could predict that the disease would progress, then obviously, we could make an argument to initiate therapy earlier, because we're trying to prevent further complications, or maybe we'll have greater success because there's a lower burden of infection.

But unfortunately, we don't know the natural history of what will predicted to occur in those patients. I have patients that we have followed for over 10 years, and they have continued to grow the organism and yet have shown no change in their symptoms and no radiographic features to demonstrate progression. So it would be hard for me to argue that therapy in those patients would have been beneficial.

In our cystic fibrosis patients, we monitor them, we treat their bacterial infections. We treat with airway clearance and such. And we try to tease out when is the mycobacterium doing something different and causing a more rapid decline in lung function.

And in those cases, it's typically attributed to either a more steeper decline in lung function or more frequent exacerbations. Something has changed in their previous trajectory that now makes us suspicious that the microbe bacterium is playing a role in that.

But we don't have a good biomarker or other good test to tell us this is the patient who needs to be treated and who would benefit from treatment.

The general treatment of microbacterial lung disease involves multiple drugs over a long period of time. And so what we then have to do is balance what are the benefits of that approach to treatment, compared to the potential risks.

So for example, if you have a 65-year-old woman who is otherwise seemingly healthy, but has evidence of progression and is clearly symptomatic, that's different than, say, someone who is 89 years old, and is rather infirm, and suffering from symptoms. And you're trying to balance the decision about treatment.

Or perhaps there's other factors, like other medications that they're on. So if the patient has MAC and you want to use a rifampin-based program, if they're on thyroid medication or transplant medications, those potential drug interactions become rather important in terms of the decision making in those patients.

The key part is as you try to decipher who to treat, is to make sure that you're also tracking why you're choosing to treat them. Because that's what you're going to monitor in terms of assessing your response to therapy.