Gene Abnormalities and ILD

Dr. Timothy Whelan: We're here in Nashville at the PFF Summit, and today there was a great session on the genetics of IPF. Dr. Danoff, what did you think about the session?

Dr. Sonye Danoff: I really enjoyed the session today. It's really amazing how much progress there's been. There were three really wonderful talks about disease related to the telomerase family. And these are the genes that are associated with maintaining the structural integrity of the caps of chromosomes, called telomeres.

The first talk was a wonderful abstract that received an award at the session, and was related to the characterization of patients in the Vanderbilt cohort who have mutations in three of the telomerase genes. What they found that I think was really interesting is that even within a family, the radiographic appearance and the clinical appearance of individuals who are affected with lung disease could be quite different. So some patients looked like they had hypersensitivity whereas another patient in the family might look like they had more classic idiopathic pulmonary fibrosis. They also found that they had a lot of unclassifiable CT scans.

The next talk really focused on telomere length, which can be used clinically now and may help us in thinking about whether we need to do biopsies in some of our patients, where we think they have familial pulmonary fibrosis related to a telomerase mutation, because those patients might be able to be tested with telomere length, and if they have extremely short telomeres, that might give us the confidence, even with a CT that isn't classic for UIP, that indeed they have this familial pulmonary fibrosis.

The last talk that we heard was one that was also very interesting, which was looking at not only inactivating mutations but possibly the presence of some activating mutations in telomerase. We still don't know what the significance of those changes will be, but I think that that's something that's going to create a lot of interest and provide potentially other new interesting therapies, looking forward to the future.

What were the things that you thought were interesting in the session?

Dr. Timothy Whelan: So, there were also two additional sessions that talked about some additional gene abnormalities, so newer gene abnormalities that are not directly telomerase associated. One was a centromere component, and all of these

genes appear to be regulating DNA repair. So the idea of cell aging being impacted and not being able to repair mechanisms relating to disease. I think these are very, very exciting new areas that, again, are potential targets for future therapy and also will help us better truly identify the differences between this heterogeneous population. So it's really amazing, all of the genetic work that's going on.

Another great thing about this session was that one of our industry partners presented their data from their cohort, and the gene work that they're doing, and with several thousand patients that they've identified that, not looking for specific point mutations, but looking for collective areas of abnormalities within known genes, actually is really associated with a much higher risk for IPF. Again, identifying a subset of patients more clearly since it is such a difficult diagnosis to make clinically.