



## Factors Associated with Disease Progression in the SENCIS Trial

In the present study on factors prognostic in the decline of the forced vital capacity, in patients with systemic sclerosis related ILD, the investigators of the study wanted to identify which factors would predict progression of ILD. And to do this, they examined the placebo arm from the census trial. So as some of you may recall, the census trial has been the largest study conducted today in the treatment of patients with systemic sclerosis related ILD or SSC ILD. And in the study, patients received nintedanib versus placebo. And this was done at multiple centers throughout the world and was comprised of over 500 patients. So in this study, patients were allowed to remain on background therapy when they started the study. And in fact, about half of patients who entered the study were on some background immunosuppressive therapy, the majority of which were taking mycophenolate. In the present analysis, the investigators wanted to understand which factors predicted that decline in the FVC. And they did this a few ways. They looked at the rate of decline of FVC, as well as the absolute and relative decrease in FVC over the course of the study.

What they found was very interesting. They found that patients who had a lower FVC at baseline, were more likely to have greater progression of their FVC over time. This was not statistically significant, but there was a trend for this association. Conversely, patients who have been taking mycophenolate at baseline, these patients appeared to have a more protective effect. So in other words, patients who are on mycophenolate had less of a decline of their FVC over the course of the study. And these results have important implications for our patients. So for example, if a patient comes in and they have a lower FVC at baseline, these are patients that probably will have more aggressive disease course and should be treated more aggressively upfront with therapy. In addition, the results of this study, again, demonstrate as we've seen in other studies that mycophenolate has a beneficial effect on modifying the course of disease in a patient with SSC ILD.

In this sub analysis of the census trial, the investigators wanted to understand whether the presence or absence of GERD or esophageal reflux disease, could affect the course of the FVC, in patients with systemic sclerosis related ILD. Theoretically, patients who have uncontrolled reflux disease may be at greater risk for progression of interstitial lung disease, but this has not been substantiated in many studies. And so this is an important study in helping to answer the question as to whether reflux disease participates in the progression of ILD in these patients. So in this study they identified patients who had reflux disease at baseline. And this was based on whether it was reported as a comorbidity both past or present on their case report format screening. And then if it hasn't been reported, they were considered to have no GERD. And so in the study, they looked at the course of the FVC between patients who had GERD at baseline, and those who did not, they also looked at the relative and absolute decline in FVC in these two groups.

They found that actually both groups were very similar. There was no significant difference in the course of the FVC or the change in the FVC between patients who had GERD at baseline and those who did not. But important thing to note about this study is that the diagnosis of GERD was just based on whether someone had completed it as a co-morbidity on the case report form. So it wasn't based on any kind of



objective measure of GERD. In addition, they didn't look at GERD severity. So there was no way to know whether a patient with more severe GERD, more reflux symptoms, would have greater progression of ILD compared to a patient with less severe GERD or mild GERD. So I think that's an important takeaway. Another limitation of the study is also that they only looked at it at one point in time and baseline.

It could have been that over the course of this study, someone could have developed GERD or started on therapy, but that wasn't captured and they maybe were not in the right group. But altogether, the results seem to suggest that if you look at whether or not patients had GERD at baseline or not, this didn't seem to have an impact on the course of their lung function in the course of the census trial. Based on this study, there aren't a lot of clinical takeaways, but I would say from my clinical experience in treating patients with systemic sclerosis, that the treatment of GERD is very important for these patients. Not only in terms of their risk of progression of lung disease, but also in terms of helping to improve their quality of life. And this is something that can have a major impact on how they feel. So even though this study doesn't specifically address quality of life, that would be another thing to consider in a study, looking at whether or not GERD presence or absence affects the course of lung disease, or even how a patient feels.