The Effect of Nintedanib in IPF Subgroups

The MBA trial is a large placebo-controlled randomized control trial showing that nintedanib, a drug approved for idiopathic pulmonary fibrosis at the dosage of 150 mg twice a day is also effective in reducing disease progression over 52 weeks in patients with non-idiopathic pulmonary fibrosis. In particularly these patients were progressive, so they did progress in terms of lung function, imaging, or symptoms and their fibrotics. In other words, they had a CT scan of the chest that's showing signs of fibrosis.

Now, this study has been very important and now nintedanib is approved by the FDA and by the EMA for the progressing fibrosing interstitial lung disease phenotype. The ups of that showed that there is no difference between different subgroups of interstitial lung disease in terms of efficacy of the drug. So, in other words, when you exclude from the analysis single group of entities like chronic pneumonitis or autoimmune interstitial lung disease or undifferentiated interstitial lung disease or nonspecific interstitial pneumonia, it doesn't matter which entities you are taking out.

The size of the effect of the drug on lung function is always the same. That means there is no one single entity driving the results of the trial, which is an indirect evidence that, basically, the mechanisms targeted by nintedanib are common across different types of interstitial lung disease which are progressive and fibrotic. So, the potential impact of the MBA trial in clinical practice is huge because we need to remember that, apart from IPF, there has been so far no drug approved for any other form of pulmonary fibrosis.

Everything we have been using so far in pneumonitis, sarcoid, nonspecific interstitial pneumonia, connective tissue disease is completely off label. I think these, for the first time, is providing physicians with a safe and effective treatment for patients with non-idiopathic pulmonary fibrosis; for patients which are progressive and fibrotic. I think it will constitute a starting point for an important change in the way we treat these patients because, for the first time, we have a drug which is safe and effective to treat these type of patients.

I think this abstract titled “The Effect Of Nintedanib In Patients With Limited and Extensive Systemic Sclerosis Associated Interstitial Lung Disease: Data From the Census Trial” is important in that it really breaks down the subsets of limited fibrosis versus more extensive fibrosis. Well, why does that matter? Well, prognostically, data has suggested that patients with more extensive disease may have a worse prognosis, so this particular abstract really asks, in patients with extensive disease or limited disease, does nintedanib have varying effects in that group and what does that treatment effect look like?

These patients were followed in the census trial. About 60% or so had extensive disease and they were followed for a period over 52 weeks. Interestingly enough, the effect of nintedanib versus placebo on the rate of decline of forced vital capacity was greater in subjects with more extensive disease on HRCT.

We didn't see that much of a difference when pulmonary function testing was different. Now, they defined extensive disease by fibrotic ILD on HRTC greater than 30% or a forced vital capacity of less than 70%. Essentially, the other was the milder or more limited disease.

In this study, they found that fewer treated patients with either limited or extensive disease had a forced vital capacity decline of greater than 10% or died over a 52-week period. So, what we're seeing is efficacy with nintedanib in this group of patients with both limited and extensive fibrotic disease due to systemic sclerosis. I think where this data will be most useful in clinical practice will be to reassure the physician that treating patients with extensive or more advanced fibrotic disease does have a significant impact in slowing disease progression in this population of more advanced fibrotic disease in patients with systemic sclerosis.

The next abstract we're going to review is entitled “Effects of Nintedanib in Subgroups Based on the Combined Pulmonary Fibrosis/Emphysema Index.” Now, to me, this is an interesting study because this is a group of patients we have very little treatment data on. Essentially, we know that the total lung capacity, forced vital capacity tends to be preserved in this population of patients in comparison to patients with IPF alone. This extract asks, how does nintedanib affect forced vital capacity decline in patients with combined pulmonary fibrosis and emphysema versus placebo when they're treated.

The group or subgroup of patients came from the Impulsive study because they were patients in the study that were allowed into the study with emphysema. All those who had emphysema, about 20% had greater than 10% emphysema, and about 80% or so had less than 10% emphysema. All those with greater than 10% emphysema, they typically had higher forced vital capacities than those with IPF alone, higher percent predicted forced vital capacities, lower DLCOs and more emphysema on imaging, not surprisingly.

If we look at the decline in forced vital capacity over one year, what do we see? Well, in the placebo group, we see in those patients with less than 10% emphysema a decline of about 234 ml over that year and, for those greater than 10% emphysema, we see a lower decline of 186 ml or so over that year that they were followed. In the treated nintedanib group, the decline is significantly less for both patients with less than 10% or greater than 10%, and the decline was really around same, 112 ml for less than 10% group and 117 ml for greater than 10% group.

In general, we can take away that nintedanib reduced the rate of annual decline of forced vital capacity in both patients who had combined pulmonary fibrosis/emphysema of less than 10% and of greater than 10%. The clinical management of patients with combined pulmonary fibrosis/emphysema has really been uncertain because these patients have not been a significant proportion of clinical trials in the past, and we really haven't had hard data to look at how therapies impact their disease progression and really to understand how their natural course of progression occurs or what it looks like in terms of forced vital capacity.

This particular abstract, I think, is important, not just in understanding better the natural history of disease progression and decline when we look at lung volumes, but also in giving us confidence that treating with nintedanib can be effective in this population of patients.