間質性肺病的最新治療

ILD treatment – an update

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Idiopathic pulmonary fibrosis (IPF) is a chronic, progressive, irreversible, and usually fatal fibrotic disease of the lung. It typically affects elder patients beyond 60 years of age, and the disease nature course is not easy to predict due to disease heterogeneity. The most important known prognostic determinants for mortality are a decline in lung function, acute exacerbations (AE-IPF). AE-IPF, one of the significant risks of causing death, may attack IPF patients anytime, anywhere, regardless of disease stage or stability or not. Considering the poor prognosis of AE-IPF, the prevention of AE-IPF is more likely a better strategy on reducing the risk of mortality of IPF, as well as the preservation of lung function.

The prevalence and incidence of IPF are very different from countries. It might be due to the different situations in disease awareness and diagnosis rates in individual countries. Based on the current data we have, the worldwide prevalence of IPF is estimated from10 to 500 per 100 000 persons, and its incidence is about 3–93 per 100,000 persons per year. The average survival from the time of diagnosis is estimated as three to five years. Compared to the prevalence and incidence worldwide, the prevalence and incidence of Taiwan seem to be much lower than the average worldwide. So we assume IPF may be highly underestimated in Taiwan.

Despite extensive research over the past 25 years, No medication has been found to cure IPF, but two medications, nintedanib and pirfenidone, appear to slow disease progression. In addition, these agents appear to have a mortality benefit. Nintedanib, a receptor blocker for multiple tyrosine kinases that mediate elaboration of fibrogenic growth factors, appears to slow the rate of disease progression in IPF.

Nintedanib has been approved by the US-FDA,EMA and others countries, including Taiwan. In clinical trials, the main benefits of nintedanib are a reduction in the rate of decline in lung function and a longer time to first exacerbation. Patients receiving nintedanib therapy have better lung function stability, lung function improvement and low incidence of exacerbation. Its subgroup and post-hot analyses also show nintedanib has consistent efficacy and safety in broad-rage of IPF patients. Besides anti-fibrotic effect, nintedanib also showed anti-inflammatory and vascular remodeling effects in non-clinical models. To further explore nintedanib' impact on other ILD with high unmet needs such as SSc-ILD, PF-ILD, SENSCIS trial and INBUILD trial were designed to fulfill the objective. Both trials have been completed and published in NEJM 2019. The primary endpoint, slowing the decline of FVC, was met in both trials with significant difference. US-FDA has approved Nintedanib in the treatment of SSc-ILD. The indication of PF-ILD are in the process of application.

Another antifibrotics, Pirfenidone, is to inhibit transforming growth factor beta-stimulated

collagen synthesis, decrease the extracellular matrix, and block fibroblast proliferation in vitro. Pirfenidone is approved for marketing in a number of countries, including (among others) Germany, France, UK, Canada, Japan, and US. Pirfenidone has not been formally studied in patients with more advanced disease. In Pirfenidone major pivotal studies, Pirfenidone (2403 mg/day) has shown a significant effect in slowing the decline of FVC and progression-free, but no specific research in reduce of exacerbation, only some post-hoc analysis on hospitalization. Pirfenidone has not been formally studied in patients with more advanced disease.

As the natural course of IPF is quite heterogeneous and the response to the novel anti-fibrotic drugs have been reported to show great variability, it is needed to identify reliable predictive factors of indicating the risk of deterioration and the response to medical treatment, as well as side effects in a broad non-selected patient cohort. Therefore, a real-world data collection is necessary for further reference in clinical practice. NICEFIT (**N**on-**I**nterventional study **C**ollecting **E**xperiences **F**or **I**PF in **T**aiwan), a Taiwan real-world data collection for the treatment of IPF, is generated to fulfill the objective. In the one-year interim report, it indicated that the lung function of most enrolled patients with antifibrotics therapy (mainly received Nintedanib) are stable. Furthermore, around 50% of enrolled patients received antifibrotics have improvements in FVC. No unexpected adverse effect is observed for the anti-fibrotic drug. In my presentation today, I will demonstrate more details of the one year result of NICEFIT with my humble opinions, and brief the latest updates of the treatment of IPF.