What's Next? Shaping the Future of Pulmonary Fibrosis Trials

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Clinical trials in IPF have historically been difficult to implement and it is only over the last 15 years that any of these have met with success. At this time, there are only two antifibrotic medications that have been approved and are variably available in different countries. More recently, the umbrella term of progressive pulmonary fibrosis (PPF) has been defined encompassing other fibrotic lung diseases that demonstrate progression of disease. How best to define progression is also somewhat controversial with a number of definitions employed but typically all require two of three domains to be met including increased breathlessness, worsening CT changes and/or physiologic evidence of progression. The primary endpoint that is most accepted for drug registrational purposes is the placebo-corrected change in forced vital capacity (FVC), typically at 52 weeks. There are many other endpoints that have been used mostly as secondary or exploratory. These include mortality, time to acute exacerbations of disease, time to respiratory hospitalization, change in the six minutes walk test and patient reported outcome questionnaires. Some of these have also been incorporated in composite endpoints. There have been numerous negative studies in IPF over the last decade with many lessons learnt from these in terms of future clinical trial design. It is only very recently that two new agents subjected to study in IPF have met with success, nerandomilast and inhaled Treprostinil. This lecture will explore the pros and cons of various endpoints, highlight the pitfalls in clinical trial design as well as provide suggestions for future clinical trials in IPF and PPF.