Inhaled Treprostinil in PH-ILD and PH-COPD: Lessons from the INCREASE and PERFECT Studies

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Pulmonary hypertension (PH) frequently complicates the course of patients with lung disease, including interstitial lung disease (ILD) and COPD. These forms of PH are categorized as group 3. It can be difficult to detect PH as it shared the common symptoms of shortness of breath (SOB); when the SOB is due to the underlying lung disease or supervening PH is uncertain. There are certain “clues” to the presence of occult PH in patients with lung disease including desaturation, supplemental oxygen needs, reduced six-minute walk distance, dyspnea that is out of proportion to the extent of the lung disease, a reduced diffusing capacity (<40% of predicted), and a large pulmonary artery segment on CT of the chest. The best screening tool is echocardiography, however this can be inaccurate in patients with lung disease and if there is strong suspicion of underlying PH, then it might be worthwhile proceeding with a definitive right heart catheterization no matter what the echo shows. An area of great interest is whether the PH associated with lung disease may be amenable to treatment with medications that are available for group 1 pulmonary arterial hypertension. This was the basis for the INCREASE and PERFECT trials, in which inhaled Treprostinil (iTre) was studied in patients with PH associated with ILD and COPD, respectively. The INCREASE study was positive with a 31-meter placebo-corrected improvement in the 6MWT at 16 weeks, with multiple secondary endpoints also being met, including time to clinical worsening. On the other hand, the PERFECT study of iTre in COPD was a negative study that was stopped early due to a suggestion of harm coupled with no efficacy signal. Why these two disparate results were obtained and the complexity of clinical trial design in the context of lung disease will be further explored in this lecture.