LETTER TO THE EDITOR

Novel advances in chronic obstructive pulmonary disease treatment: Ensifentrine

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Madam, Chronic obstructive pulmonary disease (COPD) is a respiratory disorder involving chronic inflammation of the airways and excessive mucous production causing progressive, partially reversible airflow obstruction, and airway remodelling.[1] While a multitude of approved drugs- including short/long-acting muscarinic antagonists (SAMAs/LAMAs), short/long-acting β2-agonists (SABAs/LABAs) and inhaled corticosteroids (ICS)- and combination therapies exist; most patients remain significantly symptomatic on maximal doses and recurrent exacerbations pose a serious burden on their mental health and quality of life.[1]

Of these, ICS are associated with a heightened risk of pneumonia leading to hospitalisations while LABA and LAMA usage has been linked to heightened cardiovascular and urinary disease risks.[1] Thus, treatment which can provide consequential bronchodilation, relief of symptoms and limit the rates of exacerbations while also curbing the adverse effects seen with current treatments were needed. In this regard, a novel drug, Ensifentrine; a dual inhibitor of PDE3 and PDE4, has been approved by the US Food and Drug Administration (FDA) in June 2024 as inhaled suspension for maintenance treatment of COPD.[2]

Phosphodiesterases (PDEs) are a group of enzymes that are important regulators of cellular signal transduction. PDE3 mediates bronchial tone by regulating cAMP and cGMP levels in bronchial smooth muscle, therefore its inhibition leads to bronchodilation. PDE4 regulates cAMP and mediates stimulation and migration of inflammatory cells and thus its inhibition activates the cystic fibrosis transmembrane conductance regulator in bronchial epithelial cells causing increased ciliary beat frequency and mucus clearance.[1,3] Combined inhibition of PDE3 and PDE4 has displayed both additive as well as synergistic effects on suppression of the inflammatory response on bronchial smooth muscle contraction.[1]

In clinical trials, Ensifentrine demonstrated statistically significant and clinically meaningful improvements in COPD symptoms; most notably on breathlessness.[3,4] Statistically significant improvements in peak forced expiratory volume in 1 second (FEV1), as well as reductions in residual volume and exacerbation rates were also demonstrated after singular dosage with Ensifentrine- both on its own as well as in combination with existing therapy- as compared to placebo.[1,3,5]

Importantly, rates of adverse events (AEs) were comparable among Ensifentrine and placebo groups, with doses up to 6 mg BID found to be well tolerated.[1,3] Notably, nebulized Ensifentrine demonstrated a lack of the gastrointestinal side effects linked to oral forms of PDE4 inhibitors.[3] Thus, Ensifentrine with its promising improvements in symptoms and quality of life as well as similar safety profile as current therapy is a noteworthy step forward in maintenance therapy for COPD.

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