European Respiratory Society
Annual Congress 2013

Abstract Number: 3351

Publication Number: 186

Abstract Group: 5.1. Airway Pharmacology and Treatment

Keyword 1: COPD - management **Keyword 2:** Inflammation **Keyword 3:** Pharmacology

Title: A phase II, randomised, placebo controlled trial of 12 weeks treatment with an oral p38 inhibitor in patients with COPD on a background of ICS/LABA

Robert 20154 Fogel robert.fogel@pfizer.com MD [1], Kathleen 20155 Shields kathleen.shields@pfizer.com [1], Jared 20156 Christensen jared.christensen@pfizer.com [1], Jakob 20157 Ribbing jakob.ribbing@pfizer.com [1], Grant 20158 Langdon grant.langdon@pfizer.com [1], Christelle 20164 Perros-Huguet christelle_perros-huguet@pfizer.com [1] and Nicholas 20165 Clarke nick.clarke@pfizer.com [1]. [1] Inflammation and Remodelling, Pfizer Incorporated, Collegeville, PA, United States, 07059 .

Body: Despite the recognized role of pulmonary inflammation in the pathogenesis of the disease, anti-inflammatory drugs have demonstrated only limited efficacy in COPD. Inhibitors of the p38 MAP kinase may have an important role in treating inflammation in COPD. Here we extend previous findings (MacNee et. al. Eur Resp J 2010 36Suppl 54 718s) to report the effect of a novel oral p38 inhibitor (PH-797804) on top of a background of salmeterol/fluticasone. 377 subjects with moderate-severe COPD, currently on stable doses of ICS/LABA combination were randomized to receive either 6 mg of oral PH-797804 or placebo once daily orally for 12 weeks. Baseline trough FEV_1 was similar in both groups (0.50 -2.92L). Over the 12 week treatment period, trough FEV_1 demonstrated an improvement in PH-797804 treated subjects compared with placebo; at 12 weeks, statistically significant effects (mean ± SE) of 27 ± 18 mL was noted. The average difference from placebo over the 12 week treatment period was 31 mL. A statistically significant increase was observed on the Transitional Dyspnea Index at 12 weeks (0.57 ± 0.28 points). hs-C-reactive protein showed a decrease at week 2 that was consistent throughout the dosing period, indicating maintenance of the anti-inflammatory effect. PH-797804 was generally safe and well tolerated. The rate of discontinuations due to adverse events was somewhat higher in PH-797804 treated patients. Mild-moderate rash was observed in approximately 8% of PH-797804 treated patients. Our findings suggest that p38 inhibition could represent a potentially useful anti-inflammatory treatment for COPD.Study Sponsored by Pfizer.