European Respiratory Society
Annual Congress 2013

Abstract Number: 2918

Publication Number: P4745

Abstract Group: 3.2. Airway Cell Biology and Immunopathology

Keyword 1: Anti-inflammatory **Keyword 2:** Biomarkers **Keyword 3:** Idiopathic pulmonary fibrosis

Title: PBI-compound, a novel first-in-class anti-inflammatory/fibrotic compound, reduces bleomycin-induced pulmonary fibrosis by inhibition of multiple pro-inflammatory/fibrotic key mediators

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Body: Background: We recently reported that PBI-Compound demonstrated anti-inflammatory and anti-fibrotic activities in acute and chronic kidney disease (5/6-nephrectomized rats, doxorubicin-induced nephrotoxicity, diabetes streptozotocin-induced, db/db mice) models. Aims: To investigate the effect of PBI-Compound on bleomycin-induced lung fibrosis at the pro-inflammatory/fibrotic biomarker mRNA expression level in lung tissue. Methods: C57BL/6 mice received bleomycin by intratracheal instillation on day 0. Mice were randomized according to their bleomycin-induced body weight loss, and then treated with an oral administration of PBI-Compound from day 7 to 21. Mice were euthanized on day 21 and inflammatory and fibrotic markers were quantified by quantitative Real-Time PCR. Results: Expression of collagen I and fibronectin mRNA (fibrotic markers) was increased by bleomycin. Treatment with PBI-Compound induced a significant reduction of these two fibrotic markers similar to the control level (sham). Furthermore, key inflammatory and profibrotic growth factors such as TGF-β, CTGF, IL-23p19 and IL-6 were significantly downregulated in PBI-Compound-treated mice. Conclusions: This data suggests that treatment with PBI-Compound may be beneficial in preventing the progression of lung injury as this reduces the accumulation of collagen and fibronectin, and downregulates the transcription of key pro-inflammatory/fibrotic growth factors which include TGF-β, CTGF, IL-23p19 and IL-6.