European Respiratory Society
Annual Congress 2013

Abstract Number: 2037

Publication Number: P682

Abstract Group: 5.1. Airway Pharmacology and Treatment

Keyword 1: Idiopathic pulmonary fibrosis **Keyword 2:** Animal models **Keyword 3:** Treatments

Title: Nintedanib reduces bleomycin-induced lung inflammation and fibrosis in mice

Dr. Lutz 1200 Wollin stefan-lutz.wollin@boehringer-ingelheim.com [1], Dr. Isabelle 1201 Maillet maillet@cnrs-orleans.fr [2], Dr. Valérie 1202 Quesniaux quesniaux@cnrs-orleans.fr [2] and Prof. Bernhard 1203 Ryffel bryffel@cnrs-orleans.fr [2]. [1] Respiratory Diseases Research, Boehringer Ingelheim Pharma GmbH & Co. KG, Biberach, Germany, 88397 and [2] INEM - UMR7355 CNRS, Université D'Orléans, Orleans, France, 45071 .

Body: Introduction: In a Phase II clinical trial, 12 months' treatment with nintedanib (BIBF 1120) reduced the rate of decline in FVC in patients with idiopathic pulmonary fibrosis (IPF) by 68.4% versus placebo, which approached statistical significance. Aim: To explore its mode of action, nintedanib was tested in a preventive and therapeutic mouse model of lung inflammation and fibrosis. Methods: Lung fibrosis was induced in mice by a single intratracheal administration of bleomycin. Nintedanib was administered by gavage q.d. at 30 mg/kg or 60 mg/kg from day 0 to day 14 (preventive treatment) or from day 7 to 21 (therapeutic treatment). Results: After 14 days, bleomycin caused increased macrophages and lymphocytes in the BALF and elevated IL-1β, TIMP-1 and collagen levels in the lung. Histology revealed chronic inflammation and fibrosis. At day 21, the pathology was very similar to day 14, but histology revealed slightly increased inflammation and fibrosis and TIMP-1 levels were nearly doubled. Preventive nintedanib treatment significantly reduced lymphocytes but not macrophages. Furthermore, IL-1β, TIMP-1, and lung collagen were significantly reduced. Histological analysis showed significantly diminished lung inflammation and fibrosis. Therapeutic treatment at 60 mg/kg caused similar inhibitory effects compared to preventive treatment, but at 30 mg/kg the effect size was smaller. Conclusion: Nintedanib, when used as preventive or therapeutic treatment, effectively reduced lung inflammation and fibrosis in mice. The anti-inflammatory and anti-fibrotic features of nintedanib may impact the progressive course of fibrotic lung diseases like IPF.