**Nintedanib, an Anti-Fibrotic Drug, Preserves Lung Alveolar and Vascular Growth and Prevents Pulmonary Hypertension in an Experimental Model Neonatal Lung Injury**

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**Background:**
Bronchopulmonary dysplasia (BPD), chronic lung dysfunction associated with prematurity, is characterized by poor alveolar and vascular growth, interstitial fibrosis, and pulmonary hypertension (PH). Recent work has shown that anti-fibrotic agents, including Nintedanib, can preserve lung function in adults with idiopathic pulmonary fibrosis. Whether Nintedanib treatment can prevent BPD and reduce PH is unknown.

**Objective:**
Determine if Nintedanib treatment will preserve lung alveolar and vascular growth, improve lung function, and prevent PH in a postnatal hyperoxia model of BPD in rats.

**Methods:**
Newborn rats were exposed to hyperoxia (90%) or room air (RA) and received daily treatment of Nintedanib or saline (control) by intraperitoneal injections (1 mg/kg) for 14 days. At day 14, a Flexivent system was used to measure total respiratory resistance and compliance. Lung tissue was evaluated for radial alveolar counts (RAC), mean linear intercept (MLI), and pulmonary vessel density (PVD). Right ventricular hypertrophy (RVH) was quantified using Fulton's index.

**Results:**
When compared with RA controls, hyperoxia exposure reduced RAC by 64%, PVD by 65%, increased MLI by 108% and RVH by 118% ($p<0.01$ for all). Hyperoxia increased resistance by 94% and reduced compliance by 75% ($p<0.01$ for all). Nintedanib restored RAC, MLI, RVH, and lung resistance to control values and improved PVD and lung compliance in the hyperoxia-exposed rats. Nintedanib treatment of control animals did not have adverse effects on lung structure or function.

**Conclusions:**
Nintedanib preserved lung alveolar and vascular growth, improved lung function and reduced RVH in the hyperoxia model of BPD in neonatal rats, without adverse effects in controls. We speculate that Nintedanib may provide a novel therapy for the prevention of BPD.