



ERS

EUROPEAN RESPIRATORY SOCIETY
INTERNATIONAL CONGRESS 2023
MILAN Italy, 9-13 September

Late Breaking Abstract - Claudin-1 is a potential airway-centric therapeutic target for pulmonary fibrosis

E. Cortesi (Leuven, Belgium), V. Anquetil (Allschwil, Switzerland), E. Polini (Allschwil, Switzerland), S. Blüme (Allschwil, Switzerland), H. El Saghire (Allschwil, Switzerland), L. Mailly (Strasbourg, France), T. Baumert (Strasbourg, France), A. Prasse (Hannover, Germany), A. Toso (Allschwil, Switzerland), M. Meyer (Allschwil, Switzerland), S. Toovey (Allschwil, Switzerland), L. Manenti (Allschwil, Switzerland), R. Iacone (Allschwil, Switzerland), F. Christ (Leuven, Belgium), B. Vanaudenaerde (Leuven, Belgium), M. Carlon (Leuven, Belgium), G. Teixeira (Allschwil, Switzerland), W. Wuyts (Leuven, Belgium)

Background and Aims: Claudin-1 (CLDN1), a transmembrane protein involved in epithelial tight junctions, can, in idiopathic pulmonary fibrosis (IPF), be exposed outside the tight junctions of proliferative airway epithelial cells. ALE.F02 is, a first-in-class monoclonal antibody (mAb) highly specific in targeting exposed CLDN1, currently in development for the treatment of liver and kidney fibrosis. By blocking CLDN1 on injured lung epithelial cells, ALE.F02 inhibits pro-fibrotic pathways and modulates extracellular matrix remodelling. This study investigated the functional role of CLDN1 as a therapeutic target for IPF.

Methods: CLDN1 expression in lung tissues from patients with different IPF stages was analyzed using immunohistochemistry. Using preclinical animal models of IPF and precision-cut lung slices (PCLS) generated from IPF lung explants, we investigated the individual and combined effects of ALE.F02 and Nintedanib or Pirfenidone on parameters related to the pathogenesis of IPF.

Results: In tissues of IPF patients, exposed CLDN1 increased during disease progression in the bronchiolar and the alveolar epithelia and around fibrotic areas. Preclinical studies in aged bleomycin mouse model showed that therapeutic treatment with anti-CLDN1 mAb reduced fibrosis and improved lung function. Treatment of IPF PCLS with ALE.F02 reduced fibrosis and disease biomarkers (MMP7, TIMP1, Col1a1, MCP-1).

Conclusion: Our results suggest a functional role for CLDN1 in the pathogenesis of IPF, providing preclinical proof-of-concept for ALE.F02 as a novel airway-centric therapeutic approach in patients with pulmonary fibrosis.
