INTRODUCTION

Idiopathic pulmonary fibrosis (IPF) is considered the most common and severe form of pulmonary fibrosis, with a 5-year survival rate of only 20% reflecting the lack of effective therapies. The pathology of IPF is characterized by scar tissue formation (fibrosis) and excessive extracellular matrix deposition, resulting in the loss of lung function. Galectin-3 (Gal-3) is currently regarded as a potential inflammatory marker identified as a molecule that functions to drive the inflammatory response and oxidative stress.

OBJECTIVES

To evaluate the impact of Nintedanib on Gal-3 expression using both in-vitro and in-vivo models, in addition to IPF patient serum samples.

METHODS

Gal-3 levels were evaluated in IPF and control tissue samples, primary human lung fibroblasts (HLFs) following Nintedanib treatment (10-100nM, qPCR) and in a silica-induced-fibrosis mouse model with/without Nintedanib (0.021-0.21 mg/kg) by immunohistochemistry. Additionally, Gal-3 levels were analyzed in serum samples from 41 interstitial lung disease (ILD) patients with/without Nintedanib treatment by ELISA.

RESULTS

Nintedanib addition to HLFs resulted in significant elevations in Gal-3, pSTAT3, as well as IL-8 mRNA levels (p<0.05). Gal-3 expression was higher in IPF patient samples compared with non-IPF controls at the protein and mRNA levels (p<0.05). In the in-vivo mouse model, Gal-3 levels were increased following fibrosis induction and even further increased with the addition of Nintedanib, mostly in macrophages (p<0.05). Patients receiving Nintedanib presented with higher Gal-3 serum levels in comparison to those who did not (p<0.05).

CONCLUSIONS

Nintedanib elevates Gal-3 levels in both experimental models, along with patient samples. These findings highlight the possibility of using combined inhibition therapy for patients with IPF.