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Title: PBI-compound, a novel first-in-class anti-fibrotic compound, reduces lung fibrosis in the bleomycin-induced lung fibrosis model: A comparative study with pirfenidone

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Body: Background: The pathobiological mechanisms underlying the development of idiopathic pulmonary fibrosis (IPF) are highly complex. Aims: To compare the effect of PBI-Compound, pirfenidone, and combination of both compounds on inflammatory/fibrotic mRNA expression of key mediators (inflammation/pro-fibrotic: TGF-β, CTGF, IL 6, IL23p19; fibrotic: collagen I, fibronectin; and remodeling: SPARC, MMP-2), and on histological lesions in the bleomycin-induced lung fibrosis model. Methods: Intratracheal instillation of bleomycin was administered on day 0. Mice were treated with PBI-Compound, or pirfenidone, or combination of both compounds starting on day 7 to 21. Results: Bleomycin induced a significant increase in mRNA expression of all key mediators in the lung. PBI-Compound and combination therapy significantly decreased TGF-β, CTGF, IL-6 and IL23p19 expression in lung, while pirfenidone had no effect on CTGF. All treatments induced a significant reduction of collagen I and fibronectin expression to the control level (no bleomycin). PBI-Compound and combination therapy induced a significant reduction of SPARC while pirfenidone demonstrated no effect. PBI-Compound and pirfenidone induced a weak inhibition of MMP-2 while the combination therapy induced a significant reduction. Based on Ashcroft's score, PBI-Compound and combination therapy demonstrated significant reduction of lung fibrosis while pirfenidone alone demonstrated weak but no significant activity at the histological level. Conclusions: PBI-Compound or combination therapy with pirfenidone may be an efficacious treatment in IPF.