**BACKGROUND:**

Bleomycin-induced IPF in lean C57BL6/J mouse is a challenging animal model with several limitations for drug efficacy studies. Observational studies suggest a significant link between obesity and IPF in humans. Diet-induced obese (DIO) mice have higher levels of Angiotensin II, which is known to be pro-inflammatory and pro-fibrotic. Hence, the DIO mouse model has the potential to better respond to bleomycin challenge. We then evaluated the effects of bleomycin in DIO mice treated without or with the anti-fibrotic drug ALK5 inhibitor.

**METHODS:**

Before bleomycin administration, lungs of DIO mice have a pro-inflammatory and a pro-fibrotic profile compared to lean mice.

**RESULTS:**

- Bleomycin strongly raises Ashcroft scale and lung fibrosis in DIO mice. Both parameters are significantly improved by ALK5 inhibition.

- Biocellvia morphometric digital pathology confirms anti-fibrotic effects of ALK5 inhibition and its potential benefit on emphysema.

- PharmaNest quantitative digital pathology demonstrates that ALK5 inhibition markedly reduces fibrosis scores and complex collagen fibers.

**CONCLUSION**

- ALK5 inhibition significantly improves Ashcroft scale and lung fibrosis in bleomycin-induced IPF in DIO mice, as confirmed with AI-based digital pathology.

- Our data demonstrate that bleomycin-induced IPF in the DIO mouse represents a new translational model to evaluate drugs targeting IPF.