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# Inhaled NXP002 attenuates LPS-induced inflammatory and fibrotic mediator production in the rat lung

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## Introduction

Oral tranilast has been shown to attenuate fibrosis clinically but has limited use due to low bioavailability and systemic side effects. NXP002, a new salt form of tranilast, is a potential novel inhaled treatment for Idiopathic Pulmonary Fibrosis (IPF). These studies assess the distribution, tolerability and efficacy of NXP002 in the rat.

## Methods

NXP002 was administered by inhalation (Cirrus 2) to Sprague Dawley rats at target lung deposited doses of 0.1, 0.3 and 1 mg/rat. NXP002 (10 mg/kg) was also dosed orally. Inhaled Fluticasone propionate (FP, target 0.3 mg/rat) acted as a positive control. Animals were then challenged with aerosolized LPS (1 mg/mL).

Animals were culled 4 h post LPS challenge and blood samples taken. Bronchoalveolar Lavage (BAL) was obtained, centrifuged and the supernatant collected for bioanalysis, cell counting and mediator determination. NXP002 levels in plasma and lung homogenate were determined.

## Results

Inhaled NXP002 was well tolerated, with no inflammatory response observed. Dose-dependent increases of NXP002 in lung tissue and BAL were observed, equivalent to or higher than following oral administration despite lower plasma levels.

Inhaled NXP002 resulted in a dose-dependent decrease in LPS-induced BAL cell count, which was less than that seen following oral delivery. Despite this, inhaled delivery resulted in a greater reduction in LPS-induced BAL mediators, including MCP-1 and TGFß.

## Conclusions

This study demonstrates that inhaled NXP002 is well tolerated. Inhaled delivery has a superior effect on fibrosis related mediators whilst having a reduced systemic exposure than oral dosing.