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Proof**CONTROL ID:** 682412**PRESENTATION TYPE:** Oral**CATEGORY:** Asthma, Other Lower Airway Disorders**TITLE:** First clinical experience with FX125L, an anti-inflammatory oral small molecule with an entirely novel mechanism of action**AUTHORS (LAST NAME, FIRST NAME):** Wiesel, P.; Cooper, R.; Wang-Smith, L.; Reckless, J.; Champion, K. J.; Petrolese, V.; Grainger, D.**PRESENTER:** P Wiesel**ABSTRACT BODY:**

Abstract Body (Upper and Lowercase): Background: FX125L is the first molecule in the new class of Broad Spectrum Chemokine Inhibitors (BSCIs) to enter the clinic. BSCIs are anti-inflammatory small molecules with an entirely novel mechanism of action. Studies in animal models suggested that FX125L may have similar efficacy but better safety than corticosteroids and superior efficacy than montelukast. Unlike steroids, FX125L also inhibits neutrophil recruitment to lung. These findings suggest that FX125L may be useful for the treatment of asthma and COPD.

Objectives: The primary objective of the study was to characterize the safety, tolerability and pharmacokinetics (PK) of single ascending oral doses of FX125L in healthy subjects.

Methods: This was a randomised, double-blind, placebo-controlled study involving 66 subjects (mean age 26y, range 18-49y; 54% males; 90% White; demographics balanced across cohorts), in 8 dose cohorts (0.03mg to 3g of FX125L). Standard safety and PK assessments were included. Approval was obtained from the PRACS IRB and written informed consent obtained from all research subjects.

Results: FX125L was safe and well tolerated at all dose levels. No serious adverse events, subject withdrawal or dose-limiting toxicity were observed. A total of 16 subjects (10 on FX125L) reported 30 AEs (18 events on FX125L), most commonly Headache (9 occurrences; 4 subjects on FX125L and 2 on Placebo), then Dizziness (1 on FX125L and 1 on Placebo), and Nausea (1 on FX125L and on 1 Placebo). Of the 30 AEs, 27 were reported as mild and 3 as moderate in severity. All moderate AEs occurred in subjects on FX125L, including 1 occurrence of Syncope (which occurred pre-dose), 1 of Urinary tract infection and 1 of Vomiting. Of the 30 AEs, 21 were assessed by the Investigator as unrelated and 9 (Headaches, and Dizziness and Headache) as possibly related to FX125L. There were no clinically significant changes in any of the laboratory parameters, vital signs, ECGs or any physical abnormality. FX125L's PK were linear over the dose range studied; its absorption was rapid (tmax about 1h) and its elimination half-life was about 25h.

Conclusions: FX125L was shown to be safe and well tolerated at doses well above those expected to yield maximum anti-inflammatory efficacy, with pharmacokinetics consistent with once-daily oral dosing.

Educational Objectives: discuss the safety and PK profile of the novel anti-inflammatory compound FX125L in healthy subjects.

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