Introduction

- Disease control is not sustained or is achieved in up to 20% of patients with asthma, despite the availability of standard-of-care therapies. Over the last 20 years, the use of oral corticosteroids has increased, but this is accompanied by increased adverse effects.
- While inhaled corticosteroids reduce persistent symptoms and exacerbations, they do not control these diseases. In asthma, sodium cromoglycate, inhaled long-acting β2 agonists, and mast cell stabilizers are being developed for immediate release.
- There are gaps in our understanding of disease mechanisms.

Objectives

- The objective of this study was to evaluate the pharmacodynamic and safety profile of AZD1402/PRS-060 in healthy volunteers.
- The primary objective was to determine target engagement in vitro.
- The secondary objective was to evaluate the safety profile in healthy volunteers.

Methods

- Study design: A phase 1 dose-escalation study. The study was designed as shown in Figure 2. Subjects received single doses of AZD1402/PRS-060, titrated from 0.25 mg to 400 mg.
- Subjects were randomly assigned to each cohort in a ratio of 1:1:1:1 for cohorts 4–7 and 1:1:1:1:1 for cohort 8.
- Subjects were assigned to one of ten cohorts according to a randomized code produced by blinded personnel.
- Blinding was maintained for all procedures involving patients and personnel.
- Safety review: A pharmacokinetic and safety review was performed between each cohort.
- Serum PK parameters: A pharmacokinetic and safety review occurred between cohorts.

Results

- Pharmacokinetic parameters: AZD1402/PRS-060 was well tolerated at the administered doses. Serum PK parameters are shown in Table 3.
- Pharmacodynamic results: AZD1402/PRS-060 inhibited IL-4 and IL-13 signaling.
- Tolerability: AZD1402/PRS-060 showed no unexpected adverse events.
- Serum PK parameters after AZD1402/PRS-060 oral inhalation/intravenous infusion at the delivered dose for cohorts 4–9 (PK population).

Conclusions

- AZD1402/PRS-060 was well tolerated at the administered doses. Serum PK parameters are shown in Table 3.
- Pharmacodynamic results: AZD1402/PRS-060 inhibited IL-4 and IL-13 signaling.
- Tolerability: AZD1402/PRS-060 showed no unexpected adverse events.

Reference