Safety, Tolerability, and Pharmacokinetics of CHF10067 in Subjects With Idiopathic Pulmonary Fibrosis: A Phase Ib Study

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RATIONALE: Idiopathic pulmonary fibrosis (IPF) is a chronic, progressive lung disease with limited treatment options. This study (NCT05513950) aimed to assess the safety, tolerability, immunogenicity, and pharmacokinetics of CHF10067 (zampilimab) - an intravenous monoclonal antibody blocking transglutaminase-2 (TG2), enzyme involved in extracellular matrix deposition - in subjects with IPF. **METHODS:** This Phase Ib, multi-centre, multi-country, randomised, double-blind, placebo-controlled study involved 24 dosed subjects divided into three cohorts receiving single ascending doses of zampilimab (1000 mg, 2000 mg, and 3000 mg) or placebo (PBO, 3:1 ratio). Subjects were monitored for safety, tolerability, immunogenicity and pharmacokinetics (PK). TG2 was investigated in plasma as explorative objective of zampilimab target. Safety assessments included adverse events (AEs), clinical laboratory evaluations, vital signs, oxygen saturation, ECGs and pulmonary function. PK parameters such as area under the concentration-time curve (AUC_{0-t} and AUC_{inf}), maximum observed concentration (C_{max}), and terminal half-life ($t_{1/2}$) were evaluated. **RESULTS:** 24 subjects were treated with zampilimab or PBO, and all completed the study. Zampilimab was well tolerated at all dose levels, with no deaths or treatment-emergent adverse events (TEAEs) leading to discontinuation. One serious, non-treatment related TEAE of influenza was reported. The most common TEAEs after zampilimab administration were hypertension (16.7% [3] of subjects, 2 considered treatment-related, zero in PBO arm), headache, fatigue, and nasopharyngitis (each in 11.1% of subjects). One moderate, non-serious immediate hypersensitivity reaction was observed, which resolved completely without complications. PK analysis showed dose-proportional increases in C_{max} and more than dose-proportional increases in AUC_{0-t} and AUC_{inf}. The mean $t_{1/2}$ ranged from 11.7 to 19.1 days. One subject resulted positive for neutralizing anti-drug antibodies at the last timepoint (day 84), with no associated adverse events. No relevant differences in plasma TG2 levels were observed after zampilimab administration.

CONCLUSIONS: Zampilimab demonstrated a favorable safety and tolerability profile in subjects with IPF at all doses up to 3000 mg. These findings support further clinical development of zampilimab for the treatment of IPF.

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