INTRODUCTION

- Treprostinil inhalation therapy (Tyvaso®) is a candidate that is approved for the treatment of pulmonary arterial hypertension.
- Tyvaso® has been administered in several Phase 2 trials in PAH, but has not been tested in the United States.
- Prior studies of C16TR (Connexion Healthcare, Bridgewater, NJ) included a phase I clinical study showing that single dose C16TR for Inhalation resulted in low systemic exposure to treprostinil and was well tolerated at doses up to 340 µg.
- This study was designed to determine if the given dose of C16TR for Inhalation was safe and if the dose could be escalated, as planned, or if the dose escalation would need to be halted.

METHODS

Study Design

- This was a multicenter, double-blind, placebo-controlled, single ascending dose study, involving 3 cohorts randomized 3:1 in a double-blind, placebo-controlled fashion to receive a single dose of C16TR for Inhalation or placebo.
- Subjects in the subsequent 4 cohorts (Cohorts 2-5) were to be randomized 3:1 in a double-blinded fashion to receive a single dose of C16TR for Inhalation at 85 µg or placebo (phosphate-buffered saline).

Endpoints

- PK endpoints: The PK of treprostinil and C16TR after dosing with C16TR for Inhalation were assessed using plasma concentrations of treprostinil and C16TR. Among the PK parameters were area under the concentration-time curve from time zero to the last quantifiable time point (AUC0-t) and time to maximum plasma concentration (tmax).
- Safety endpoints: The safety of Tyvaso and C16TR for Inhalation was assessed on vital signs (blood pressure, heart rate), electrocardiograms, physical examination, and laboratory findings on electrocardiograms, and reporting of adverse events and serious adverse events.

Pharmacokinetic Analysis Methods

- Results of pharmacokinetic analysis were performed by RTI using Phoenix®/Winnonlin® Version 6.3 Platform (Certara LP, Princeton, NJ, USA).
- All subjects who received study drug or placebo were included in the PK analysis.

RESULTS

- Twenty-two subjects were enrolled in the study and received C16TR for Inhalation at doses of 85 µg, 170 µg, or 340 µg.

Objective

- Demographic and baseline characteristics of subjects are shown in Tables 1 and 2.

Safety Results of Part 2 of Study

- Mean treprostinil AUC0-t values were 0.614 ng*h/mL, 1.22 ng*h/mL, and 2.16 ng*h/mL for the 85 µg, 170 µg, and 340 µg doses, respectively.
- Volume of distribution (V) for treprostinil was approximately 45 L for the 170 µg and 340 µg, and 90 L for the 85 µg dose, respectively.

CONCLUSIONS

- The concentration-time profile of treprostinil after administration of C16TR for Inhalation demonstrated a dose-dependent trend.
- The concentration-time profile of treprostinil after administration of C16TR for Inhalation was dose proportional.
- The incidence of adverse events was similar across the 3 dose groups.
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- A dose-related trend was observed in the incidence of TEAEs with increasing dose levels of C16TR for Inhalation.
- The results of this study will be presented at this meeting.

DISCLOSURES

- The sponsor’s safety committee reviewed the safety data of each cohort after the entire cohort completed the study.
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Figure 1. Study design.

Figure 2. Trough plasma concentration-time profile of treprostinil after administration of C16TR for Inhalation.