**INTRODUCTION**

INS1009 is a lipid nanoparticle formulation of treprostinil prodrug C16TR (Bridgewater, NJ) used to expose rats to nebulized INS1009 aerosol.

**METHODS**

Male Sprague Dawley rats were placed in restraining tubes and exposed to nebulized drugs via the 12-port Jaeger-NYU Nose-Only Directed-Flow Inhalation Exposure System (CTI Technologies, Woodrow, NJ) (Figure 1). An air flow carrying nebulizer was provided to the system tower at a rate of 0.6 L/min. INS1009 was administered using Amouro® 3% (Aemco, Galway, Ireland) to deliver estimated pulmonary doses of 1 μg/kg, 3 μg/kg, 10 μg/kg, and 30 μg/kg. Rats received once-daily dosing for 1 day, 7 days, or 14 days, depending on the grouped protocol. A 6 mL volume of INS1009 at varying concentrations of C16TR (0.1, 0.3, 1, and 3 mM) was nebulized at a rate of approximately 0.2 mL/min. PK analysis: Blood samples were taken at selected times after nebulization over a 24-hour period to maintain bioactivity over 24 hours and is associated with a number of adverse events (AEs), the most prevalent of which is cough.

**RESULTS**

Figure 3. Blood plasma TRE in rats after dosing with nebulized INS1009 for 1, 7, or 14 days. The targeted pulmonary doses are shown. Values are the means ± standard deviation of 4 rats.

**CONCLUSIONS**

No difference was observed in the PK profiles between day 1 and day 14 of dosing with inhaled INS1009 for both TRE level in the plasma and C16TR concentration in the lungs.

**REFERENCE**

• Leifer F, et al, ATS Poster # P499 • Chapman RW, et al, ATS Poster # P500

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