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Inhaled delivery of nezulcitinib with nasal high-flow oxygen in healthy participants

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Background

Oxygen delivery via high-flow nasal cannula (HFNC) is used in hospitalized patients with acute lung injury due to COVID-19 and may be coadministered with inhaled nezulcitinib in clinical trials.

Objective

Evaluate single inhaled doses of nezulcitinib in healthy participants to guide optimal administration with HFNC in future studies.

Methods

Phase 1, open-label, fixed-sequence, 4-period crossover study. Nezulcitinib was nebulized using Aerogen Solo; HFNC system included Precision Medical air-oxygen blender with Fisher & Paykel MR850 humidifier + MR290 humidifier chamber. Plasma pharmacokinetics and safety were assessed under the dose and administration conditions described in Table 1.

Results

Key nezulcitinib plasma pharmacokinetic parameters are reported in Table 1. A total of 3 mild treatment-emergent adverse events were reported by 2 participants; all were deemed not related to nezulcitinib.

Conclusions

Clinical dosing of nezulcitinib with HFNC oxygen should be via oral inhalation to achieve optimal delivery to the lungs.

Table 1. Nezulcitinib administration conditions and plasma pharmacokinetic data (mean ± SD).

Study Period (Subjects)	Conditions	C_{max} (ng/mL)	$AUC_{0\text{-}inf}$ (hr*ng/mL)
A (N=14)	3 mg nasal inhalation via HFNC circuit[a] (30 L/min)	1.7 ± 1.1	7.8 ± 6.9
B (N=14)	3 mg oral inhalation[b] with low-flow nasal cannula (6 L/min)	14.0 ± 7.2	54.0 ± 28.0
C (N=14)	3 mg oral inhalation[b] with HFNC (30 L/min)	14.2 ± 8.5	54.7 ± 35.4
D1 (N=7)	3 mg oral inhalation[b] with HFNC (50 L/min)	14.0 ± 7.7	52.3 ± 29.1
D2 (N=6)	9 mg oral inhalation[b] with HFNC (50 L/min)	43.7 ± 37.3	152.0 ± 117.3

[a]Aerogen Solo + T-adapter immediately prior to humidifier chamber

[b]Aerogen Solo + Ultra handheld device