# A Single-Period, Single-Dose Study of the Pharmacokinetics of Epinephrine After Administration of Intranasal ARS-1 (*neffy*® Nasal Spray) to Pediatric Subjects with a History of Systemic Allergic Reactions

Poster Number: 8

HH Li[1], DM Fleischer[2], R Lockey[3], M Kaliner[4], R Lowenthal[5], S Tanimoto[5]

[1]Overland Park, KS, USA; [2]University of Colorado Denver School of Medicine, Aurora, CO, USA; [3]University of South Florida, Tampa, FL, USA; [4]Institute for Asthma & Allergy, Chevy Chase, MD, USA; [5]ARS Pharmaceuticals, San Diego, CA, USA

## RATIONALE

The current global prevalence of pediatric anaphylaxis is estimated to be as high as 1.8%[1], with food allergies being the most frequent trigger.[1] There has been a significant rise in the prevalence of food allergies over the past several decades[2] and approximately 40% of children with food allergies have experienced a severe allergic reaction such as anaphylaxis.[3]

Epinephrine is considered the first-line treatment for severe allergic reactions and anaphylaxis[4,5,6], and epinephrine auto-injectors (EAIs) are the most frequently used products for out-of-hospital treatment; however, they are considered inconvenient, cumbersome and painful to administer with up to 83% of patients/caregivers reporting failing or delaying use of EAIs, even during a severe allergic reaction.[7]

***neffy*** is an intranasal (IN) epinephrine spray and needle-free delivery device being developed as an alternative to EAIs for the emergency treatment of (Type I) allergic reactions, including anaphylaxis. ***neffy*** is expected to have significant clinical benefit by reducing apprehension and delay in dosing, reducing dosing errors, and making it easier to carry the product at all times.

A series of well-controlled clinical trials in adult subjects has demonstrated that neffy results in consistent pharmacokinetic (PK) and pharmacodynamic (PD) responses. The present study was conducted to evaluate the PK and PD of neffy in pediatric allergy subjects ranging from 4 to 17 years of age.

## METHODS

This was a Phase 1, single-dose, single-treatment study in pediatric allergy subjects. Each subject received one dose of ***neffy*** based on body weight:

- A single dose of ***neffy*** 0.65 mg (subjects between 15 kg and 30 kg)
- A single dose of ***neffy*** 1.0 mg (Subjects >30 kg) OR
- A single dose of ***neffy*** 2.0 mg (Subjects >30 kg)

## RESULTS

### PHARMACOKINETIC RESULTS (Figure 1 and Table 1)

- In pediatric subjects >30 kg, 1.0 mg and 2.0 mg doses of ***neffy*** resulted in mean $C_{max}$ values of 253 pg/mL and 540 pg/mL, respectively. The results are comparable to or slightly higher than the results observed in adult subjects (276 pg/mL and 485 pg/mL for 1.0 mg and 2.0 mg does, respectively).
- In pediatric subjects between 15 kg and 30 kg, ***neffy*** 0.65 mg resulted in a mean $C_{max}$ of 534 pg/mL.

### PHARMACODYNAMIC RESULTS (Table 2)

**Systolic Blood Pressure**

In pediatric subjects >30 kg, 1.0 mg and 2.0 mg doses of ***neffy*** resulted in a mean maximum response (SBP) $E_{max}$ of 8.23 mmHg and 11.9 mmHg, respectively. In pediatric subjects between 15 kg and 30 kg, ***neffy*** 0.65 mg resulted in a mean SBP $E_{max}$ of 12.25 mmHg.

**Diastolic Blood Pressure**

In pediatric subjects >30 kg, 1.0 mg and 2.0 mg doses of ***neffy*** resulted in a mean DBP $E_{max}$ of 4.92 mmHg and 7 mmHg, respectively. In pediatric subjects between 15 kg and 30 kg, ***neffy*** 0.65 mg resulted in a mean DBP $E_{max}$ of 10.6 mmHg.

**Heart Rate**

In pediatric subjects >30 kg, 1.0 mg and 2.0 mg doses of ***neffy*** resulted in a mean HR $E_{max}$ of 13.8 bpm and 15.4 bpm, respectively. In pediatric subjects between 15 kg and 30 kg, ***neffy*** 0.65 mg resulted in a mean HR $E_{max}$ of 17.7 bpm.

### SAFETY RESULTS

***neffy*** demonstrated a positive safety profile. There was one moderate TEAE (nasal discomfort following administration of ***neffy*** 2.0 mg in a subject > 30 kg). All other TEAEs were considered mild.

## CONCLUSION

In pediatric allergy subjects, both the 1.0 mg and 2.0 mg doses of ***neffy*** result in favorable pharmacokinetics that are comparable to what has been observed in adults.

# Administration of *neffy* to Pediatric Subjects >30 kg Resulted in:

- **Epinephrine Absorption (PK) that is Comparable to Adults.**
- **Epinephrine Levels that Appear to be Dose Proportional Between the 1.0 mg and 2.0 mg Doses.**

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**Figure 1: Change from Baseline - Mean Epinephrine Concentration versus Time Profiles**

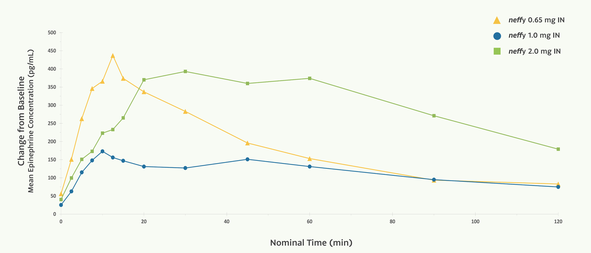


**Table 1: Summary Statistics of Epinephrine Pharmacokinetic Parameters**

| Treatment | N | $t_{max}$ (min) median (range) | $c_{max}$ (pg/mL) mean (%CV) | $AUC_{last}$ (min* pg/mL) mean (%CV) |
|---|---|---|---|---|
| 15 kg to 30 kg | | | | |
| *neffy* 0.65 mg IN | 11 | 12.5 (2.50 - 30.0) | 534 (58.7) | 21900 (49.7) |
| > 30 kg | | | | |
| *neffy* 1.0 mg IN | 25 | 20.0 (7.50 - 120) | 253 (66.2) | 14000 (53.0) |
| *neffy* 2.0 mg IN | 16 | 25.0 (2.50 - 120) | 540 (70.7) | 35500 (76.3) |

**Table 2: Maximum Pharmacodynamic Effect (Change from Baseline) and Time to Maximum Pharmacodynamic Effect**

| Treatment | N | Mean $E_{max}$ (CV) | | | Median $T_{Emax}$ (min) | | |
|---|---|---|---|---|---|---|---|
| | | SBP (mmHg) | DBP (mmHg) | HR (bpm) | SBP | DBP | HR |
| 15 kg to 30 kg | | | | | | | |
| *neffy* 0.65 mg IN | 11 | 12.25 (43.5) | 10.6 (80.3) | 17.7 (83.8) | 30.5 (10-120) | 25 (0-120) | 10.5 (0-91) |
| > 30 kg | | | | | | | |
| *neffy* 1.0 mg IN | 25 | 8.23 (85.3) | 4.92 (91.2) | 13.8 (72.4) | 20 (0-120) | 15.5 (0-122) | 18 (0-124) |
| *neffy* 2.0 mg IN | 16 | 11.9 (68.6) | 7 (76.0) | 15.4 (75.0) | 25 (0-90) | 17.5 (0-120) | 32.5 (0-90) |

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