neffy, Epinephrine Nasal Spray, Demonstrates a Positive Efficacy and Safety Profile for the Treatment of Allergic Reactions in Pediatric Patients at Risk of Anaphylaxis: Phase 3 Study Results

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RATIONALE

Epinephrine is the first-line treatment for severe allergic reactions and anaphylaxis, and epinephrine auto-injectors (EAIs) are the most frequently used products for out-of-hospital treatment[1-3].

Despite epinephrine's well-established safety and efficacy profile, over 80% of at-risk patients report having failed to inject epinephrine, even when they knew they were having a severe allergic reaction[4-7].

neffy is an intranasal (IN) epinephrine spray that is a needle-free alternative epinephrine delivery device being developed 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.

The present study was conducted to assess the efficacy and safety of ***neffy*** (1.0 or 2.0 mg, based on weight) for the treatment of allergic symptoms (Grade 2 or higher) induced by an Oral Food Challenge (OFC). **Table 1**

METHODS

This was a Phase 3, single-period, single-dose open-label study in pediatric subjects (n = 15) who experienced allergic symptoms (Grade 2 or higher) induced by an OFC. Grading was determined by the Severity Classification of Organ Symptoms Induced by Anaphylaxis in the Anaphylaxis Guidelines of the Japanese Society of Allergology[8,9].

Table 1: Symptom Grading System from Anaphylaxis Guidelines[10]

	1 (Mild)	2 (Moderate)	3 (Severe)
Skin	Localized urticaria, exanthema, wheal, pruritus	Generalized urticaria, exanthema, wheal, pruritus	–
	Swollen eyelid or lip	Swollen face	–
Gastrointestinal tract	Pruritus of the throat or oral cavity	Throat pain	–
	Mild abdominal pain	Moderate abdominal pain	Cramps
	Nausea, emesis, diarrhea	Recurrent emesis, diarrhea	Continuous emesis, loss of bowel control
Respiratory tract	Intermittent cough, nasal congestion, sneezing, rhinorrhea	Repetitive cough	Persistent cough, hoarseness, "barking" cough
	–	Chest tightness, wheezing detectable via auscultation	Audible wheezing, dyspnea, cyanosis, saturation <92%, swallowing or speaking difficulties, throat tightness, respiratory arrest
Cardiovascular	–	Pale face, mild hypotension, tachycardia (increase >15 beats/min)	Hypotension, dysrhythmia, severe bradycardia, cardiac arrest
Neurological	Change in activity level, tiredness	Light-headedness, feeling of "pending doom," somnolence, headache	Confusion, loss of consciousness, incontinence

neffy was administered immediately following the observation of Grade 2 symptoms. Patients weighing 15 – 30 kg received ***neffy*** 1.0 mg and patients weighing ≥30 kg received ***neffy*** 2.0 mg. If symptoms remained unchanged or worsened patients were treated with IM epinephrine.

The study included 15 subjects between 6 and 17 years of age. Six subjects weighed between 15 and 30 kg and received neffy 1.0 mg and nine subjects weighed ≥30 kg and received ***neffy*** 2.0 mg.

EFFICACY RESULTS

OBSERVED ALLERGIC REACTIONS

A total of 18 Grade 2 reactions were observed following the OFC **(Table 2)**.

SUBJECTS REQUIRING A SECOND DOSE OF EPINEPHRINE

No patient needed a second dose of epinephrine within 15 minutes post-dose.

One patient developed a biphasic reaction 2 hours and 45 minutes following administration of ***neffy*** and was treated with epinephrine at the time of that reaction.

TIME TO SYMPTOM RESOLUTION

The time course for the resolution of all Grade 2 symptoms is presented by organ system **(Figure 1)**. With the exception of cardiovascular symptoms (n=1), mean symptom grades started decreasing within five minutes of ***neffy*** administration (the first assessment time point). Median times to resolution by organ system were; Respiratory symptoms – 15.5 (1 – 90) minutes, Gastrointestinal symptoms – 15. (10 -60) minutes, Skin/mucosal symptoms – 35 (10 -60) minutes, and Cardiovascular – 32 (--) minutes.

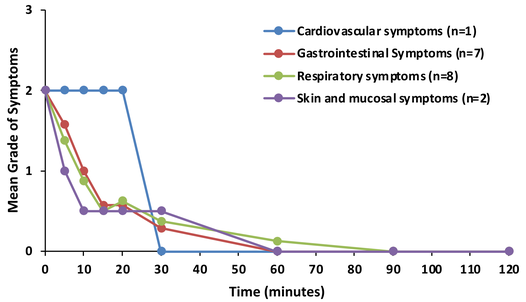
Of note, the grade for cardiovascular does not have Grade 1 **(Table 1),** and therefore**,** the next grade from Grade 2 (pale face, mild hypotension, tachycardia) was no symptom (grade 0).

The time course of total grade of each organ symptom is presented in **Figure 2**. For both dose groups, the mean total grade started decreasing within five minutes of *neffy* administration (the first assessment timepoint). Median time to resolution from Grade 2 to 0 was 16 (1-90) minutes.

Table 2: Observed Following Oral Food Challenge

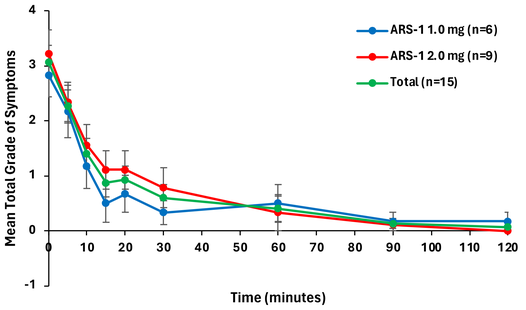
Organ System	neffy 1.0 mg (n = 6) n(%)	neffy 2.0 mg (n = 9) n(%)	Total (n = 15) n(%)
Cardiovascular	0 (0)	1 (8.3)	1 (5.6)
Gastrointestinal	3 (50.0)	4 (33.3)	7 (38.9)
Respiratory	3 (50.0)	5 (41.7)	8 (44.4)
Skin and Mucosal	0 (0)	2 (16.7)	2 (11.1)
Total	6	12	18

Figure 1: Time Course for the Resolution of Grade 2 Symptoms



Note: The grade for cardiovascular does not have Grade 1, therefore, the next grade from Grade 2 (pale face, mild hypotension, tachycardia) was no symptom (Grade 0).

Figure 2: Time Course for Total Grade of Organ Systems



TREATMENT EMERGENT ADVERSE EVENTS (TEAE)

Regardless of relationship to OFC, 10 subjects (66.7%) experienced at least one TEAE, with six subjects (40.0%) having a TEAE that was considered treatment related. Four subjects (26.7%) had a TEAE that was considered induced by the OFC, none of which was considered treatment related.

CONCLUSIONS

neffy appears to be a safe and effective needle-free option for the treatment of anaphylactic symptoms.

The results demonstrated that the efficacy observed following administration of ***neffy*** in the present study was comparable to what is typically observed for current epinephrine therapies, with most patients exhibiting marked symptom relief within five minutes of dosing.

The safety profile of ***neffy*** was also consistent with currently approved epinephrine injection therapies. Based on these results, patients and caregiver are likely to benefit from this easy-to-use and needle-free option for the emergency treatment of severe allergic reactions, including anaphylaxis.

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