Sublingual Epinephrine (Anaphylm™) Provides Consistent Pharmacokinetics in both Adult and Pediatric Subjects

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In both adult and pediatric subjects, Anaphylm (currently under review by the FDA) achieved a median Tmax of 12 and 10 min, and a narrow IQR at 5 and 12 min, respectively, suggesting early peak exposure with low interpatient variability. If approved, these data support the potential for clinical dependability.

INTRODUCTION

- Pediatric and adult risk for anaphylaxis is estimated at 1 to 761 cases per 100,000 person-years and 50 to112 per 100,000 person-years, respectively.[1,2]
- Epinephrine is the first-line treatment for anaphylaxis, typically administered via manual injection or auto-injector (e.g., EpiPen®, Auvi-Q®).[3]
- Rapid administration and drug exposure is critical, yet barriers to injection (i.e., poor carriage, needle phobia) put patients at risk.[1,3]
- Anaphylm (AQST-109) is a sublingual film containing a prodrug of epinephrine, designed as a needle-free, device-free, and portable alternative, with rapid absorption achieved via the sublingual mucosa.

OBJECTIVE

- To evaluate the pharmacokinetic (PK), pharmacodynamic (PD), and safety profile of Anaphylm in healthy high risk pediatric subjects (study AQ109302).
- To compare these data to a previously conducted study in adults (study AQ109301) that included comparison to intramuscular (IM) epinephrine.
- This comparison provides a bridge to adult study data where biocomparability to IM epinephrine products was conducted.

KEY TAKEAWAYS

Study Demographics:

A total of 32 pediatric participants were enrolled and completed the study.
A total of 64 adult participants were enrolled with 61 completing the study.

Pharmacokinetic Parameters:

These results suggest that in both pediatric and adult subjects that Anaphylm was well-tolerated with rapid absorption, achieving a T_{max} of 10 and 12 minutes, respectively.

Pharmacokinetic Curves:

Study data suggest PK comparability between pediatric and adult populations providing a bridge to IM epinephrine comparators included in the adult study.

Pharmacodynamic Comparison:

In the pediatric study, a transient increase in SBP, DBP and HR was observed, consistent with adult data and known pharmacological actions of epinephrine.

RESULTS

- Age range for enrolled pediatric subjects was 8 to 17, with the adult study enrolling participants between 19 and 55.
- Both study populations were majority male.
- Median BMI was lower in the pediatric study.

Table 1: Participant Demographics

Characteristic	Pediatric Overall (n=32)	Adult (n=64)
Median age yrs (range)	13.0 (8-17)	39.0 (19-55)
Male (%)	20 (62.5)	36 (56.3)
Median weight kg (range)	47.15 (30.2-73.8)	74.5 (52.2-100.5)
Median BMI kg/m^2 (range)	18.70 (14.7-24.6)	26.5 (19-30)

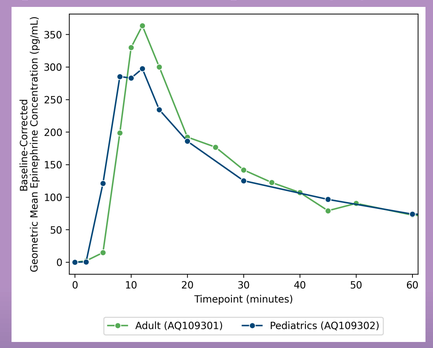
- Pediatric C_{max}, AUCs, and T_{max} were comparable to PK parameters observed in adults.
- AUC_{0-5} and T_{max} results provide additional data to suggest rapid plasma exposure after Anaphylm administration.

Table 2: PK Parameters (Geometric means unless indicated)

Parameter	Pediatric Overall (n=29)	Adult (n=61)
AUC_{0-5} (h*pg/mL)	3.8 (n=28)	1.6
AUC_{0-60} (h*pg/mL)	182.3	165.0
C_{max} (pg/mL)	568.6	470.2
Median T_{max} (min)	10.0	12.0

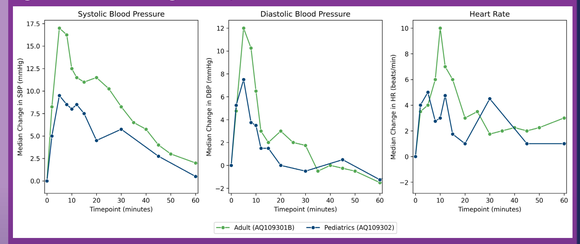
- A comparison of mean change in plasma epinephrine PK curves from AQ109302 and AQ109301 support comparability.

Figure 1: Geometric Mean Change in Plasma Epinephrine



- Comparison of pediatric and adult PD data with Anaphylm support comparability for SBP, DBP and HR.
- PD results suggest early effects of Anaphylm that coincide with the early reaction period.
- As observed with adults treated with Anaphylm, DBP increases in agreement with SBP, a finding not observed with IM epinephrine.

Figure 2: Median Change in SBP, DBP and HR



METHODS

Key Inclusion Criteria:

- **Pediatric - Non-smoking, ≥7 to 17 years, weighing ≥30 kg, with history of allergic reactions, an active epinephrine prescription, and at risk for a serious allergic event.**
- **Adult - Healthy, non-smoking, ≥18 years, BMI ≥18 and ≤30 kg/m2, weighing ≥45 kg if female or ≥50 if male.**

Study Design:

- **The pediatric study was a single arm, open-label phase 1 study conducted at seven sites in the USA and Canada. All participants received a single dose of Anaphylm 12 mg.**
- **The adult study was two-part, open-label phase 3 single center. Participants received Anaphylm and IM epinephrine products.**

During Study:

- **Blood samples were collected for PK analyses.**
- **Vital signs were measured for PD analyses.**
- **Assessments occurred at 30 and 15 minutes pre-dosing, and at 2, 5, 8, 10, 12, 15, 20, 30, 45, 60, 90, 120, 360 (adult) post-dosing.**
- **Vital sign measurements were recorded prior to blood sample collections.**

Safety Profile:

- **Adverse events (AE) were predominantly mild and resolved without intervention.**
- **No serious AEs were reported.**
- **Overall, the pediatric safety profile was consistent with findings in adults.**

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DISCLOSURES

Drs. Greenhawt and Golden are members of the advisory board and consultants to Aquestive Therapeutics, Inc. Dr. Anagnostou was a Principal Investigators for the AQ109302 study. Drs. Kraus and Confer are employees of Aquestive Therapeutic, Inc.

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