POSTER #P4.024

Phase 1 Evaluation of Anaphylm Sublingual Film: Pharmacokinetics, Pharmacodynamics, Safety, and Tolerability in Pediatric Patients at High Risk for Allergic Reactions

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As a needle-free, rapidly absorbed epinephrine formulation, Anaphylm represents a potential and novel alternative to current administration methods. Its Pharmacokinetic (PK) profile, combined with ease of use, may help address known challenges associated with epinephrine treatment, including delays in administration.

INTRODUCTION

- Pediatric risk for anaphylaxis is estimated at 1 to 761 per 100,000 person-years.[1]
- Epinephrine is the first-line treatment for anaphylaxis, typically administered via manual injection or auto-injector (e.g., EpiPen®, Auvi-Q®).[2]
- Rapid administration is critical, yet barriers to injection (i.e., poor carriage, needle phobia) put patients at risk.[1,2]
- Anaphylm (AQST-109) is a sublingual film containing a prodrug of epinephrine, designed as a needle-free, device-free, portable alternative for anaphylaxis treatment. Its novel delivery system enables rapid absorption via the sublingual mucosa.
- Anaphylm is compact, discreet, and easily carried (e.g., wallet, pocket, cell phone case), potentiating "always within reach" carriage.

OBJECTIVE

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

KEY TAKEAWAYS

Subject Demographics:

A total of 32 eligible participants were included and treated, all of whom completed the study.

Pharmacokinetics:

The results of this study suggest that in a pediatric population, Anaphylm was well-tolerated with rapid absorption, achieving T_{max} within 10 minutes of administration.

Pharmacokinetic Bridging to Adult:

These findings support PK comparability between pediatric and adult populations utilizing PK data from a phase 3 study of Anaphylm in healthy adult subjects.

Pharmacodynamics and Safety:

A transient increase in SBP, DBP and HR was observed with Anaphylm, consistent with adult data and known pharmacological actions of epinephrine.

RESULTS

- A sample size of 24 pediatric participants was calculated to provide an 80% probability of study success.
- Success was based on observed geometric mean estimates for three of four primary PK parameters (AUC0-10, AUC0-20, AUC0-30, and AUC0-45) reaching at least 80% of the geometric mean estimates for corresponding PK endpoints in adults.
- 32 healthy at-risk subjects were enrolled.

Table 1: Subject Demographics

Characteristic	7-11 Years (n=9)	12-17 Years (n=23)	Overall (n=32)
Median age yrs (range)	9.0 (8-11)	14.0 (12-17)	13.0 (8-17)
Male (%)	4 (44.4)	16 (69.6)	20 (62.5)
Median weight kg (range)	33.60 (30.2-42.3)	55.70 (34.4-73.8)	47.15 (30.2-73.8)
Median BMI kg/m^2 (range)	17.30 (15.3-21.7)	19.40 (14.7-24.6)	18.70 (14.7-24.6)

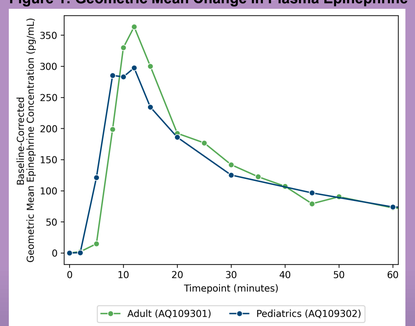
- Study data support agreement with results generated in adults (study AQ109301) where IM epinephrines (EpiPen, Auvi-Q, manual IM injection) were comparators.
- For reference, adult data after Anaphylm are AUCs (0-5 1.563, 0-60 165.0), Cmax (470.2), Tmax (12.0), and for EpiPen (0-5 5.237, 0-60 233.9, 469.2, 20.0), Auvi-Q (0-5 5.134, 0-60 269.0, 520.6, 30.0) and manual IM injection (0-5 1.026, 0-60 133.8, 308.2, 50.0).

Table 2: PK Parameters

Parameter	7-11 Years (n=8)	12-17 Years (n=21)	Overall (n=29)
AUC_{0-5} (h*pg/mL)	3.2 (131.0)	4.0 (170.7) (n=20)	3.8 (155.8) (n=28)
AUC_{0-60} (h*pg/mL)	174.6 (46.5)	185.4 (123.9)	182.3 (102.1)
Geometric Mean C_{max} (pg/mL)	449.1	622.1	568.6
Median T_{max} (min)	11.0	10.0	10.0

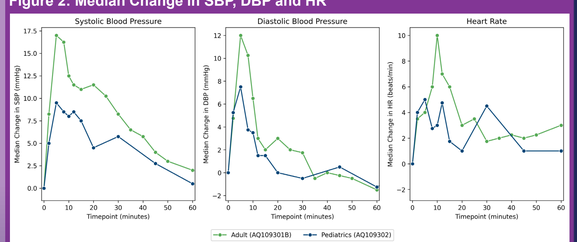
- Comparison of median plasma epinephrine form this study to the Anaphylm PK curve from AQ109301 supports comparability.

Figure 1: Geometric Mean Change in Plasma Epinephrine



- Comparison of pediatric and adult PD data with Anaphylm support comparability for SBP, DBP and HR.
- Peak SBP, DBP and HR were lower for pediatric subjects when compared to adults.
- PD results suggest early effects of Anaphylm that coincide with critical treatment period during of a reaction.
- As observed with adults when 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:
Healthy, non-smoking children, aged ≥7 to 17 years, weighing ≥30 kg, with a history of allergic reactions and an active epinephrine prescription, who were considered by the investigator to be at continued risk for serious allergic events were enrolled between December 2024 and March 2025.

Study Design:
This 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, administered sublingually while in an upright position. Participants were prohibited from eating 2 hours prior to dosing, with water permitted up to study procedures.

During the 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, and 120-minutes post-dosing.**
- **Vital sign measurements were recorded prior to blood sample collections.**

- **Adverse events (AE) in this study were predominantly mild and resolved without intervention.**
- **No serious AEs were reported.**
- **Most frequently reported AEs were administration site conditions.**
- **Overall, the safety profile was consistent with findings in healthy adults.**

REFERENCES

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2. Shaker MS, Wallace DV, Golden DBK, et al. J Allergy Clin Immunol. 2020;145(4):1082-1123.

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DISCLOSURES

Dr. Greenhawt is a member of the advisory board and consultant to Aquestive Therapeutics, Inc. Drs. Mack, Mustafa and Li were Principal Investigators at sites for the AQ109302 study. Drs. Kraus and Confer are employees of Aquestive Therapeutic, Inc.

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