ORAL ANAPHYLM SYMPTOM INTERVENTION STUDY (OASIS)

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INTRODUCTION

- Epinephrine, administered intramuscularly via manual injection or auto-injector (e.g., EpiPen®, Auvi-Q®), is the standard treatment for anaphylaxis. However, needle-free alternatives may improve access and timely administration in emergency situations.
- Anaphylm (AQST-109, DESF) is a sublingual film containing a prodrug of epinephrine, designed for needle-free delivery and rapid absorption. Given that oral delivery of epinephrine is a novel route of administration, in combination with the known challenges of conducting traditional clinical efficacy trials in anaphylaxis, characterization of the absorption of Anaphylm under representative conditions of oral allergy symptoms was conducted.
- Oral physiological changes during anaphylaxis, such as swelling and altered saliva production, raise important considerations for drug absorption. Oral Allergy Syndrome (OAS), a Type 1 allergic reaction with shared immunological and clinical characteristics, offers a controlled model to study mucosal effects on absorption and symptom resolution. The Verbal Response Score (VRS) further supports this translational approach.

OBJECTIVES

- To compare the PK of baseline-corrected epinephrine following a single dose of Anaphylm in healthy adults with OAS after oral allergen challenge (OAC) to that of manual intramuscular (IM) epinephrine injection without OAC.
- To evaluate the translational relevance of OAS as a model for anaphylaxis treatment.

METHODS

KEY INCLUSION CRITERIA

- Healthy adult males and females aged 18 to 50 years with a body mass index (BMI) between 18 and 32 kg/m².
- Known history of Oral Allergy Syndrome (OAS) in response to exposure to any of the allergens.

METHODS

STUDY DESIGN

- This was a Phase 2, open-label, 2-part, 3-treatment randomized study comparing the pharmacokinetics (PK) and pharmacodynamics (PD) of Anaphylm to manual intramuscular (IM) injection in adult subjects with Oral Allergy Syndrome (OAS).
- Subjects received single and/or repeat doses of:
  - Anaphylm (sublingual): 12 mg
    - With and without OAC
  - Epinephrine (manual IM injection): 0.3 mg
- Allergen Challenge
  - Screening: Symptom resolution was assessed at baseline before allergen exposure.
  - OAC: The allergen challenge began ~20 minutes before Anaphylm administration. A known food allergen (e.g., apple, cherry, mango, melon, kiwi, celery, banana, or carrot) was applied to the upper and lower lips, gums, and tongue for up to 15 minutes or until symptoms developed.
  - Post-OAC: Symptom resolution was reassessed before and after Anaphylm administration to evaluate the impact of treatment on resolving PK/PD and allergic symptoms.

RESULTS

- The majority of subjects had symptoms of moderate severity after the OAC at screening (72.2%) (**Table 1**).

Table 1: Summary of Severity of OAC Symptoms at Screening

Severity	N (% of Subjects)
Mild	2 (5.6)
Moderate	26 (72.2)
Severe	8 (22.2)

CONCLUSIONS

- **Oral physiological changes did not alter the PK profile of Anaphylm, supporting its reliability under conditions that mimic real-world anaphylaxis.**
- **Anaphylm demonstrated a PK profile comparable to manual IM, with consistent partial AUC values across key time intervals and a faster median T_{max} of 12 minutes.**
- **The allergen challenge model provided a controlled and reproducible method for assessing drug absorption and symptom resolution in allergic reactions, demonstrating its potential utility in evaluating novel therapies**
- **Rapid symptom resolution with Anaphylm suggests its potential to address key treatment goals in anaphylaxis, including early intervention and symptom control.**
- **Anaphylm is a needle-free, orally-delivered, portable, and easy to administer potential alternative to traditional EAIs and manual IM for the treatment of anaphylaxis.**

RESULTS (cont'd)

PK DATA

- No PK differences were observed with single doses of Anaphylm, with and without OAC (**Table 2**).
- Partial AUC values for Anaphylm (with and without OAC) were greater than the values of manual IM across all timepoints between 10- and 60-minutes post-dose.
- Anaphylm achieved a comparable PK profile with a faster median T_{max} (12 minutes with OAC) compared to manual IM (50 minutes no OAC) (**Figure 1**).

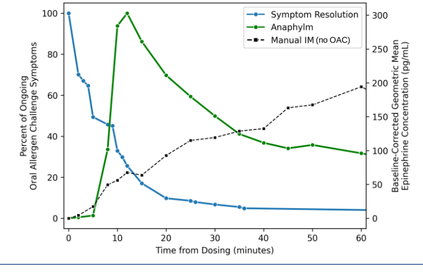
Table 2: Summary of Baseline-Corrected PK Parameters (Single Dose)

Treatment	N	C_{max} (pg/mL)	T_{max} (min)	$pAUC_{0\text{-}10min}$ (hr*pg/mL)	$pAUC_{0\text{-}60min}$ (hr*pg/mL)
Anaphylm (OAC)	24	404	12	14.5	160
Anaphylm (no OAC)	15	373	13	10.5	156
IM Epinephrine	24	261	50	6.16	123

SYMPTOM RESOLUTION TIMES

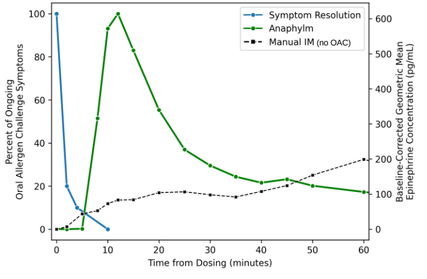
- After Anaphylm administration, median time to symptom resolution was 5.2 minutes (**Figure 1).**
- All symptoms of angioedema resolved by 10 minutes with median resolution time of 2 minutes (n=10 events) (**Figure 2**).

Figure 1: Median Time to Symptom Resolution (All Symptoms)



RESULTS (cont'd)

Figure 2: Median Time to Symptom Resolution (only Angioedema)



PD DATA

- Anaphylm with and without OAC showed similar PD profiles with rapid increases in SBP, DBP, and HR as compared with manual IM and are similar to what has been observed in in the Anaphylm clinical development program.
- Single doses of Anaphylm after OAC showed early peak effects and a sustained hemodynamic response in the first hour post-administration.

SAFETY AND TOLERABILITY

- Single doses of Anaphylm with and without OAC were safely administered and generally well tolerated in adult subjects with a history of OAS.
- There were no severe treatment-emergent adverse events (TEAEs) reported. All reported TEAEs were mild, transient, or resolved with minimal intervention.

REFERENCES

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

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DISCLOSURES

All authors are employees of Aquestive Therapeutic, Inc.