Epinephrine Administered via Sublingual Film (Anaphylm™), Manual Injection, or Auto-Injectors in Healthy Subjects: Pharmacodynamic Results

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INTRODUCTION

- Patient/caregiver-administered epinephrine is the first-line treatment for anaphylaxis.[1]
- Both rapid onset and durability of the pharmacodynamic effects of epinephrine are needed to stabilize patients experiencing the most severe symptoms of anaphylaxis so that they have adequate time to seek emergency medical care.[2]
- In the United States, >90% of the population can be reached by emergency services within 26 minutes of a 911 call for help.[3]
- Anaphylm (also known as DESF), a novel prodrug of epinephrine delivered via sublingual film, is being developed for the emergency treatment of Type 1 allergic reactions.
- Anaphylm is easily carried (eg, in a wallet, pocket, or small purse) and can be quickly administered by placing the film under the tongue and allowing it to dissolve in the saliva.
- The objective of this study was to compare epinephrine pharmacodynamics (PD) following administration via various methods.

METHODS

STUDY DESIGN

- This phase 1, randomized, single-center, open-label crossover study was performed in healthy adults aged 18 to 50 years.
- During the study, subjects received:
  - –Anaphylm 12 mg
  - –Epinephrine IM (manual injection) 0.3mg
  - –EpiPen® 0.3mg
  - –Auvi-Q® 0.3mg
- Subjects were assessed for changes over time in systolic (SBP) and diastolic (DBP) blood pressure and pulse rate (PR)

RESULTS

PHARMACODYNAMIC DATA

- For SBP (Figure 1) and DBP (Figure 2), the mean maximum effect (E_{max}) was highest and the median time to maximum effect (TE_{max}) occurred earliest with Anaphylm (Table 1).
- For PR (Figure 3), E_{max} was highest for Auvi-Q followed by Anaphylm, and TE_{max} was fastest for Anaphylm.
- Mean change from baseline in SBP and DBP remained ≥5 mmHg from 2 to 60 mins post-dose for Anaphylm, while it only achieved for SBP and sustained briefly for the other administration methods. This threshold was never reached for DBP.

RESULTS

Table 1: Pharmacodynamic Parameters

Dosage Form	n	SBP		DBP		PR	
		Mean E_{max}, mmHg	Median TE_{max}, min	Mean E_{max}, mmHg	Median TE_{max}, min	Mean E_{max}, beats/min	Median TE_{max}, min
Anaphylm	29	20.8	11	12.3	11	13.5	11
Epi IM	27	3	34	0.3	39	8.9	39
EpiPen	27	7.5	29	-7.1	29	11.8	19
Auvi-Q	29	7.4	29	-3.9	24	16.8	29

Figure 1: Mean Change from Baseline in Systolic Blood Pressure

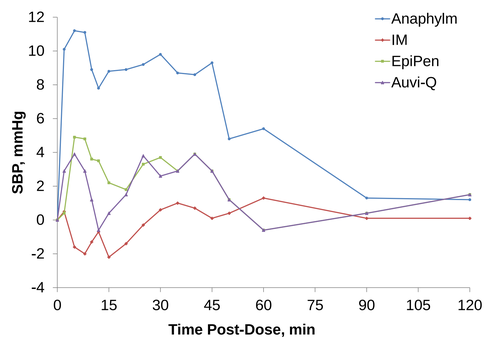


Figure 2: Mean Change from Baseline in Diastolic Blood Pressure

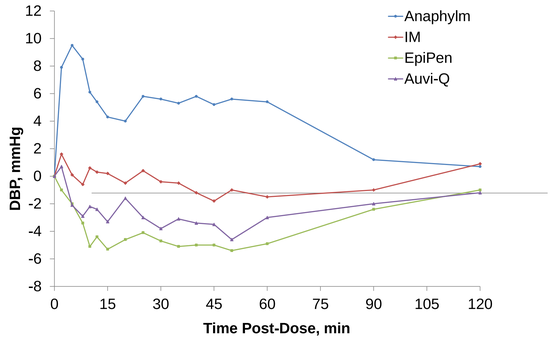
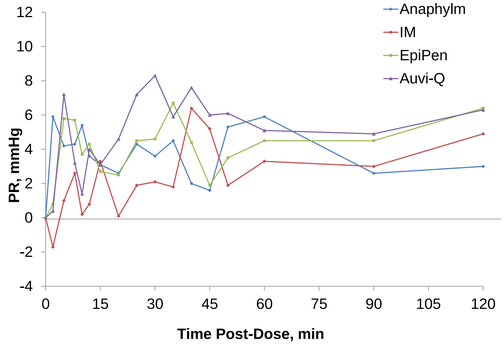


Figure 3: Mean Change from Baseline in Pulse Rate



SAFETY AND TOLERABILITY

- Most adverse events were consistent with known physiologic effects of epinephrine and were similar across treatments.
- There were no significant treatment-emergent adverse events (TEAEs) reported.
- In general, the reported TEAEs were mild, transient, and resolved with minimal intervention.

CONCLUSIONS

- **Changes in SBP, DBP, and PR are key indicators of clinical response to epinephrine in patients experiencing anaphylaxis.**
- **Anaphylm elicits a rapid, robust increase in SBP, DBP, and PR that persisted for up to 60 min post-dose, providing adequate time to seek emergency medical care.**
- **The data suggest sublingual administration of epinephrine may provide enhanced pharmacodynamic benefits to patients experiencing allergic reactions.**

REFERENCES

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DISCLOSURES

Drs. Golden, Bernstein, Lieberman are members of the advisory board and consultants to Aquestive Therapeutics. Dr. Freedman is an employee of Pharma Medica Research, Inc. Dr. Slatko, Ms. Berg, and Dr. Wargacki are employees of Aquestive Therapeutics.