UNITED STATES
SECURITIES AND EXCHANGE COMMISSION
Washington, DC 20549

FORM 8-K

CURRENT REPORT

PURSUANT TO SECTION 13 OR 15(d) OF THE
SECURITIES EXCHANGE ACT OF 1934

Date of Report (Date of earliest event reported): December 9, 2019

Aquestive Therapeutics, Inc.

(Exact name of Registrant as specified in its charter)

Delaware	**001-38599**	**82-3827296**
(State or Other Jurisdiction of Incorporation or Organization)	**(Commission File Number)**	**(I.R.S. Employer Identification No.)**

30 Technology Drive
Warren, NJ 07059
(908) 941-1900
(Address, Including Zip Code, and Telephone Number, Including Area Code, of Registrant's Principal Executive Offices)

Not Applicable
(Former name or former address, if changed since last report)

Check the appropriate box below if the Form 8-K filing is intended to simultaneously satisfy the filing obligation of the registrant under any of the following provisions:

☐ Written communications pursuant to Rule 425 under the Securities Act (17 CFR 230.425)

☐ Soliciting material pursuant to Rule 14a-12 under the Exchange Act (17 CFR 240.14a-12)

☐ Pre-commencement communications pursuant to Rule 14d-2(b) under the Exchange Act (17 CFR 240.14d-2(b))

☐ Pre-commencement communications pursuant to Rule 13e-4(c) under the Exchange Act (17 CFR 240.13e-4(c))

Securities registered pursuant to Section 12(b) of the Act:

Title of each class	Trading Symbol(s)	Name of each exchange on which registered
Common Stock, par value $0.001 per share	AQST	Nasdaq Global Market

Indicate by check mark whether the registrant is an emerging growth company as defined in Rule 405 of the Securities Act of 1933 (§ 230.405 of this chapter) or Rule 12b-2 of the Securities Exchange Act of 1934 (§ 240.12b-2 of this chapter).

Emerging growth company ☒

If an emerging growth company, indicate by check mark if the registrant has elected not to use the extended transition period for complying with any new or revised financial accounting standards provided pursuant to Section 13(a) of the Exchange Act. ☐

Item 7.01 Regulation FD Disclosure.

Aquestive Therapeutics, Inc. (the "Company") is furnishing the investor presentation attached as Exhibit 99.1 to this report for use at the Investor & Analyst Libervant™ (diazepam) Buccal Film Update Forum on Monday, December 9, 2019 at the American Epilepsy Society (AES) 2019 Annual Meeting. This investor presentation references the clinical data found in poster presentations conducted at that meeting which will be posted to the Company's website (under "Newsroom" and "Presentations") at the time of each presentation.

The Company also has been notified that a pre-IND meeting has been scheduled for February 4, 2020 with CDER of the US Food and Drug Administration to discuss AQST-108's clinical development strategy.

The information in this Item 7.01 (including Exhibit 99.1) is being furnished pursuant to Item 7.01 and shall not be deemed to be "filed" for purposes of Section 18 of the Securities Exchange Act of 1934, as amended (the "Exchange Act"), or otherwise subject to the liabilities of that section, nor shall it be deemed to be incorporated by reference in any filing under the Securities Act of 1933, as amended, or the Exchange Act, except as shall be expressly set forth by specific reference in any such filing.

Item 8.01 Other Events.

The Company was named as a defendant in a lawsuit filed by Neurelis, Inc. in the Superior Court of California on December 5, 2019. The complaint alleges, among other things, that the Company has made false and disparaging statements about Neurelis' product candidate, Valtoco, and engaged in other activities to delay potential FDA approval of Valtoco. The complaint seeks injunctive relief and unspecified monetary damages plus attorneys' fees. The Company believes these claims to be meritless and the Company intends to vigorously defend this lawsuit.

Item 9.01 Financial Statements and Exhibits

(d) Exhibits

Exhibit Number	Description
99.1	Investor presentation for use at the Investor & Analyst Libervant™ (diazepam) Buccal Film Update Forum on Monday, December 9, 2019 at the American Epilepsy Society (AES) 2019 Annual Meeting

SIGNATURE

Pursuant to the requirements of the Securities Exchange Act of 1934, as amended, the Registrant has duly caused this report to be signed on its behalf by the undersigned hereunto duly authorized.

Dated: December 9, 2019

Aquestive Therapeutics, Inc.

By: /s/ John T. Maxwell
Name: John T. Maxwell
Title: Chief Financial Officer

Exhibit 99.1


Aquestive
Investor and Analyst Update on LIBERVANT™
December 9, 2019
Advancing medicines.
Solving problems.
Improving lives.

Forward Looking Statement

Certain statements in this presentation and associated oral statements made by management may constitute "forward-looking statements" within the meaning of the Private Securities Litigation Reform Act of 1995. Words such as "believe," "anticipate," "plan," "expect," "estimate," "intend," "may," "will," or the negative of those terms, and similar expressions, are intended to identify forward-looking statements. These forward-looking statements may include, but are not limited to, statements about our growth and future financial and operating results and financial position, ability to advance Libervant to the market, regulatory approvals and pathways, clinical trial timing and plans, short-term and long-term liquidity and cash requirements, cash funding and cash burn, business strategies, market opportunities, and other statements that are not historical facts.

These forward-looking statements are based on our current expectations and beliefs and are subject to a number of risks and uncertainties that could cause actual results to differ materially from those described in the forward-looking statements. Such risks and uncertainties include, but are not limited to, risks associated with the Company's development work, including any delays or changes to the timing, cost and success of our product development activities and clinical trials; the risks of delays in FDA approval of our drug candidates or failure to receive approval; the risks inherent in commercializing a new product (including technology risks, financial risks, market risks and implementation risks and regulatory limitations); risk of development of our sales and marketing capabilities; risk of legal costs associated with and the outcome of our patent litigation challenging third party at risk generic sale of our proprietary products; risk of sufficient capital and cash resources, including access to available debt and equity financing and revenues from operations, to satisfy all of our short-term and longer term cash requirements and other cash needs, at the times and in the amounts needed; risk of failure to satisfy all financial and other debt covenants and of any default; risk related to government claims against Indivior for which we license, manufacture and sell Suboxone and which accounts for the substantial part of our current operating revenues; risks related to the outsourcing of certain sales, marketing and other operational and staff functions to third parties; risk of the rate and degree of market acceptance of our products and product candidates; the success of any competing products, including generics; risk of the size and growth of our product markets; risk of the effectiveness and safety of our products and product candidates; risk of compliance with all FDA and other governmental and customer requirements for our manufacturing facilities; risks associated with intellectual property rights and infringement claims relating to the Company's products; risk of unexpected patent developments; the impact of existing and future legislation and regulatory provisions on product exclusivity; legislation or regulatory action affecting pharmaceutical product pricing, reimbursement or access; claims and concerns that may arise regarding the safety or efficacy of the Company's products and product candidates; risk of loss of significant customers; risks related to legal proceedings, including patent infringement, investigative and antitrust litigation matters; changes in governmental laws and regulations; risk of product recalls and withdrawals; uncertainties related to general economic, political, business, industry, regulatory and market conditions and other unusual items; and other risks and uncertainties affecting the Company including those described in the "Risk Factors" section and in other sections included in the Company's Annual Report on Form 10-K filed with the SEC on March 14, 2019 and in our quarterly reports on Form 10-Q.

Given these uncertainties, you should not place undue reliance on these forward-looking statements, which speak only as of the date made. All subsequent forward-looking statements attributable to us or any person acting on our behalf are expressly qualified in their entirety by this cautionary statement. The Company assumes no obligation to update forward-looking statements or outlook or guidance after the date of this press release whether as a result of new information, future events or otherwise, except as may be required by applicable law.

This presentation shall not constitute an offer to sell or the solicitation of an offer to buy these securities, nor shall there be any sale of these securities in any state or jurisdiction in which such offer, solicitation or sale would be unlawful prior to registration or qualification under the securities laws of any such state or jurisdiction.

Welcome

- **Commercial-stage, specialty pharmaceutical company** with comprehensive capabilities to advance medicines from pipeline to market
- **Advancing a late-stage pipeline that** features promising treatments for patients and caregivers living with complex conditions, including hard to manage epilepsies and anaphylaxis
- **Completed rolling submission of New Drug Application (NDA)** to U.S. Food and Drug Administration (FDA) for Libervant™ (diazepam) Buccal Film for management of seizure clusters on November 27
- **Requested an accelerated review,** which is not guaranteed but, if granted, on track to potentially launch in early July*
- **If assigned a traditional review**, on track to potentially launch in early November*

*Subject to and assuming FDA approval obtained in this time period, which cannot be assured.

Aquestive

Aquestive®

Program Overview

Gary Slatko, MD
Chief Medical Officer

Advancing medicines.
Solving problems.
Improving lives.

Agenda

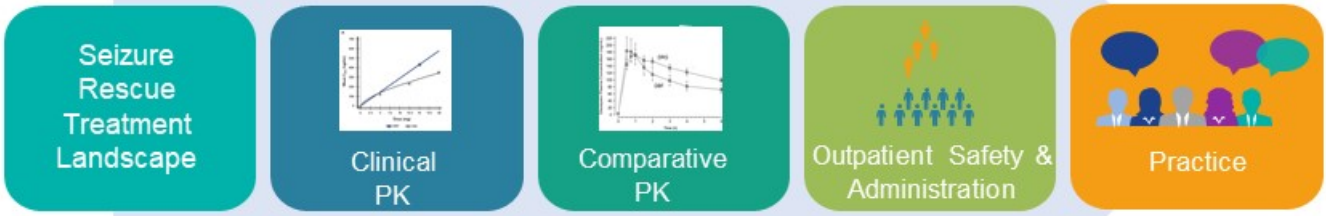
Topic	Time	Speaker
Opening Remarks	4:00 pm	Keith Kendall
Program Overview		Gary Slatko, MD
Treatment Landscape for Epilepsy Rescue: The Unmet Need	4:10 pm	Lawrence J. Hirsch, MD
LIBERVANT Clinical Development Program: Key Studies and Findings		
Early-Phase Program • Healthy Volunteer Studies With Diazepam Buccal Film (DBF) • Development of a Weight-Based Dosing Regimen • Pharmacokinetics of DBF in Adult Patients Dosed Under Interictal and Ictal/Periictal Conditions	4:25 pm	Allen H. Heller, MD, MPH
Demonstrating Comparability: Pharmacokinetics of Diazepam Buccal Film in Adult Patients With Epilepsy: Comparison With Diazepam Rectal Gel	4:40 pm	Michael A. Rogawski, MD, PhD
Outpatient Administration: Safety and Tolerability Associated With Chronic Intermittent Use of Diazepam Buccal Film in Pediatric, Adolescent, and Adult Patients With Epilepsy	4:55 pm	Syndi Seinfeld, DO, MS
Panel Discussion/Q&A	5:10 pm	Moderator: Dr. Slatko Panelists: Drs. Hirsch, Heller, Rogawski, Seinfeld
Closing Remarks	5:30 pm	Keith Kendall

LIBERVANT (diazepam buccal film; DBF) Development: Overview

- **Key challenges: comparability, safety, and usability**
- **Robust clinical development program**
  - Healthy volunteer studies
  - Patient studies
    - In-clinic single dose
    - Outpatient chronic, repeated use
- **Key findings**
  - Favorable pharmacology
  - Validated weight-based dosing regimen
  - Comparable diazepam exposure to reference listed drug
  - Expected diazepam safety profile without local safety issues
  - Readily administered by patients and caregivers
- **Clinical sections of NDA filed November 27, 2019**
  - Meets FDA timelines and expectations

FDA, US Food and Drug Administration; NDA, New Drug Application.

Today's Program



Dr. Hirsch
- How many patients
- Treatments available
- What patients need
- New options

Dr. Heller
- Healthy subject studies
- Dose proportionality
- Weight-based regimen
- Bioavailability
- Reliability of DBF

Dr. Rogawski
- Comparable PK
- Validation of regimen
- Time to effect
- Consistent, less variable
- High-fat meal findings

Dr. Seinfeld
- Outpatient intermittent use
- Low rate related TEAEs
- High success first try
- Patient self-administer 23%
- Local AEs rare
- No administration injuries

All
- Discussion
- Practice implications
- Questions

AE, adverse event; DBF, diazepam buccal film; PK, pharmacokinetics; TEAE, treatment-emergent adverse event.

Aquestive®

Treatment Landscape for Epilepsy Rescue: The Unmet Need

Lawrence J. Hirsch, MD
Professor of Neurology
Yale University
New Haven, Connecticut

Advancing medicines.
Solving problems.
Improving lives.

Definitions

- Clinically and in the literature, the most commonly used definitions for *cluster seizures* are:
  - 2-3 seizures occurring within 24 hours
  - 2 seizures occurring within 6 hours

- Statistical definitions (prevalence usually lower with these)
  - 3-4 times the patient's usual seizure rate
  - Differing from a Poisson distribution

- Virtually all humans and almost all rodents have nonrandomly distributed seizures; that is, everyone clusters to a degree

Prevalence of Cluster Seizures

(2-3 seizures within 6-24 hours; not necessarily distinguishable from habitual seizures)

Best estimate after a literature review and our prospective trial[1]

- Patients with refractory epilepsy (ongoing seizures at any rate)
  - 40% will have a cluster seizure in a given year
- 3.2 million patients with epilepsy in the United States
  - 13% (~425,000) will have a cluster seizure in a given year
  - Seizure cluster patients in 2 recent studies experienced an average of 10.7 and 12.7 cluster episodes per year[1,2]
- Main risk factors for having a cluster seizure
  - Frequent seizures
  - Prior cluster seizures or status epilepticus

1. Detyniecki K, et al. *Epilepsy Behav*. 2018;88:349-56.
2. Seinfeld S, et al. Poster presented at: Annual Meeting of the American Epilepsy Society; December 6-10, 2019; Baltimore, MD.

Aquestive

Consequences of Cluster Seizures, From a Review[1] of Retrospective Studies

- Higher risk of status epilepticus, emergency department (ED) visits, injury, loss of work/study, lower quality of life (QOL) for patient and caregiver, and possibly higher mortality if cluster seizures occur while on treatment[2]
- Postictal psychosis

1. Jafarpour S, et al. *Seizure*. 2019;68:9-15; 2. Sillanpää M, Schmidt D. *Brain*. 2008;131(pt 4):938-44;

Prospective Study of Rescue Medication Use for Cluster Seizures[1]

Rescue medication use

- Only 28% of patients with active epilepsy had a rescue medication prescribed
  - Including only 15% of those in the intermediate-risk group, even though 30% went on to have cluster seizures

- During the year-long study follow-up, only 11% of patients actually used a rescue medication. Of these:
  - 74% used oral lorazepam — Not a labeled indication
  - 14% used intranasal midazolam — Off label use of iv in a spray
  - 2% used rectal diazepam — Indicated for this use

- Rescue medications were used in 3% of 6-hour cluster cases

1. Detyniecki K, et al. *Epilepsy Behav*. 2018;88:349-56.

Aquestive

Why Are Rescue Medications So Underused?

- Per the literature
  - No seizure action plan in use
  - Poor physician–patient communication
  - Concerns about limited route(s) of administration
- For adults
  - Lack of an approved nonrectal option (until late 2019)
  - No one who can administer rescue medication

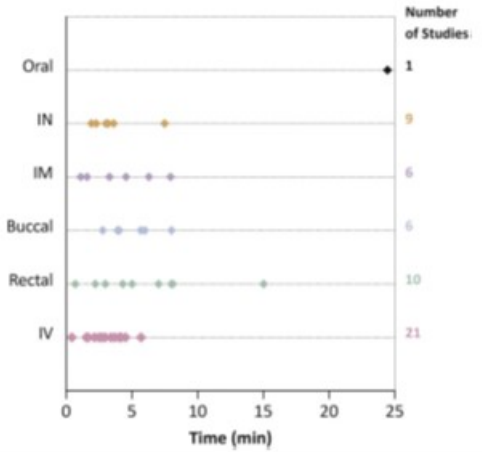
Rescue Therapies Currently Available in the United States

- Rectal diazepam (Diastat): only approved option until late 2019
- Oral lorazepam (Ativan); clonazepam, including clonazepam ODT (orally disintegrating tablets); similar medications (but slow onset)
- Nasal midazolam: approved and recently introduced
- Non-medicine
  - Vagus nerve stimulator magnet swipe
  - Deep brain stimulator (extra stimulation)

Systematic Review of Benzodiazepines for Seizure Emergencies[1]

- Broader inclusion, 75 studies
- Conclusions: for out-of-hospital use, buccal, IN, and IM are all comparable and better options than rectal or IV

Time to Seizure Cessation Following Drug Administration



IM, intramuscular; IN, intranasal; IV, intravenous.

1. Haut SR, et al. *Epilepsy Behav*. 2016;63:109-17.

Aquestive

Improving Treatments for Cluster Seizures

- Although benzodiazepines are considered the treatment of choice for terminating cluster seizures,[1,2] currently available drug formulations are suboptimal in terms of:
  - Onset of action
  - Dosing accuracy
  - Portability
  - Ease of administration
  - Route of administration[1,3,4]
- Ideal properties of a pharmacologic agent for treatment of cluster seizures[4]
  - Effective against a variety of seizure types
  - Quickly absorbed with rapid onset of action
  - Predictable and consistent interpatient bioavailability
  - Easily prepared and administered by anyone
  - Sustained duration of action
  - Minimal side effects

1. Penovich PE, et al. *Neurologist*. 2017;22:207-14; 2. Haut SR. *Curr Opin Neurol*. 2015;28:143-50; 3. Tatum WO. *Epilepsy Behav*. 2002;3:535-8; 4. Cereghino JJ. *Curr Treat Options Neurol*. 2007;9:249-55.

Aquestive

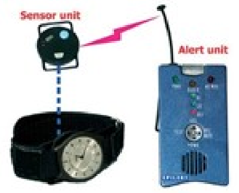
New Treatment Advances to the Rescue!

Company	UCB	Aquestive	Neurelis	Engage Ther.	Xeris Pharma	Epalex Corp.	Crossject
Product	Nayzilam	LIBERVANT	Valtoco (NRL-1)	STAP-001[1]	XeriJect Diazepam	EP-103	Zeneo Midazolam[2]
Generic	Midazolam	Diazepam	Diazepam	Alprazolam	Diazepam	Propofol	Midazolam
Administration	Intranasal	Buccc	Intranasal	Inhaled	Injection	Intranasal	Transdermal
Phase	Approved	Filed	Filed	Phase 2	Phase 1	Preclinical	Preclinical
Orphan Designation	October 2009	November 2016	November 2015	NA	May 2016	August 2016	February 2018
Patent Expiration	*Unknown*	2030+	January 2035	December 2022	December 2023	*Unknown*	*Unknown*

Sources: EvaluatePharma, accessed February 2019; BioMedTracker, accessed February 2019; US FDA, accessed February 2019.

Monitoring Devices: A Reasonable Precaution[1-6]

- Supervision leads to decreased risk of sudden unexpected death in epilepsy (SUDEP)[7]
- Devices can help with early intervention when a convulsive seizure occurs
- Having a caretaker present during or immediately after a seizure is an advantage
- Device technology is quickly evolving and will play a major role in the treatment of epilepsy



1. Ryvlin P, et al. *Epilepsia*. 2018;59(suppl 1):61-6. 2. Zhao X, Lhatoo SD. *Curr Neurol Neurosci Rep*. 2018;18(7):40; 3. Jory C, et al. *Seizure*. 2016;36:4-15;
4. van Andel J, et al. *Epilepsy Behav*. 2016;57(pt A):82-9; 5. Ulate-Campos A, et al. *Seizure*. 2016;40:88-101; 6. Van de Vel A, et al. *Seizure*. 2016;41:141-53;
7. Nashef L, et al. *Epilepsia*. 1997;38(11 suppl):S1-2.

Conclusions

- Cluster seizures are common, especially in patients with frequent seizures, and are potentially harmful
- Rescue medication is effective but greatly underused
- Treating early is beneficial
- Most patients should have a clear seizure action plan, preferably in writing and reviewed regularly
- Many better options for treating cluster seizures or prolonged seizures are just now becoming available
  - And not just rectal!
- Combining seizure alarms and rescue therapies can help prevent injuries, status epilepticus, ED visits, and possibly sudden death

Aquestive®

- Healthy Volunteer Studies With Diazepam Buccal Film (DBF)
- Development of a Weight-Based Dosing Regimen
- Pharmacokinetics of DBF in Adult Patients Dosed Under Interictal and Ictal/Periictal Conditions

Allen H. Heller, MD, MPH

Founder and CEO
Pharma Study Design, LLC

Clinical Professor of Preventive Medicine
Keck School of Medicine
University of Southern California
Los Angeles, California

Advancing medicines.
Solving problems.
Improving lives.

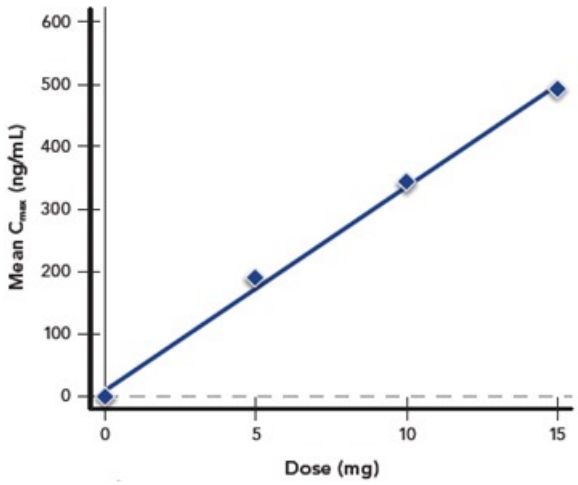
Healthy Volunteer Studies

Aquestive conducted a series of phase 1 studies using diazepam buccal film (DBF) and diazepam rectal gel (DRG) in healthy adults

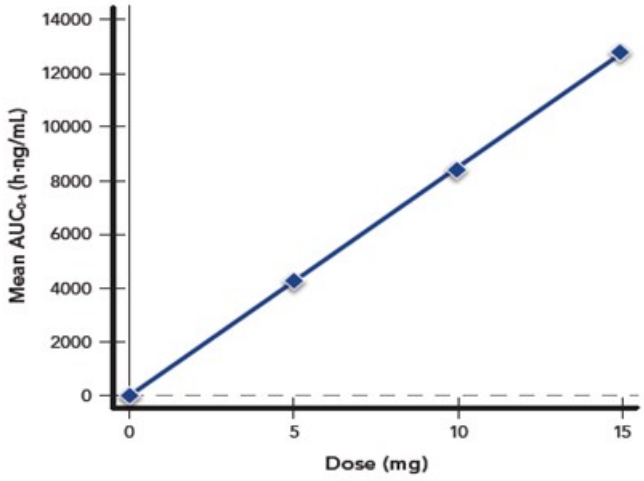
- DBF was **dose-proportional**—maximum plasma concentration (C_{max}) increased in proportion to the dose—whereas DRG was less than dose-proportional for C_{max}
- DBF showed **higher bioavailability** than DRG (more of the dose was absorbed)
- DBF (given its oral administration) showed a **food effect** (reduced C_{max} after a fatty meal) but no change in the amount absorbed
- DBF absorption was **more reliable** than DRG absorption

DBF Exhibits Dose-Proportional Pharmacokinetics in Healthy Adults

Mean C_{max} Values by Diazepam Dose



Mean AUC_{0-t} Values by Diazepam Dose



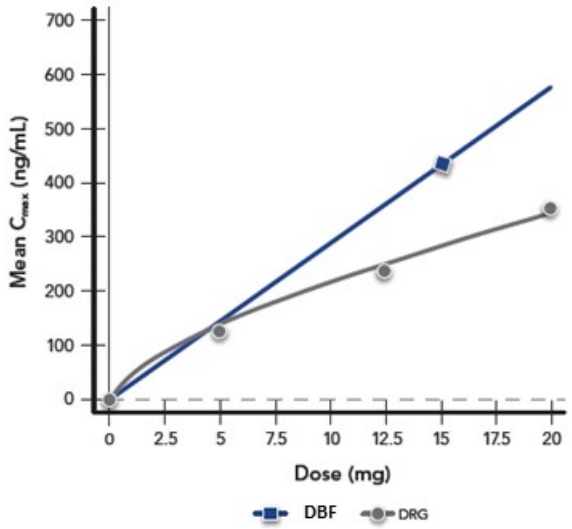
From Heller AH, et al. Presented at: Annual Meeting of the American Academy of Neurology; April 21-28, 2018; Los Angeles, CA; *Neurology*. 2018;90(15 suppl):P4.272.

AUC_{0-t}, area under the plasma concentration time curve from time zero until last measurable concentration; C_{max}, maximal plasma concentration; DBF, diazepam buccal film.

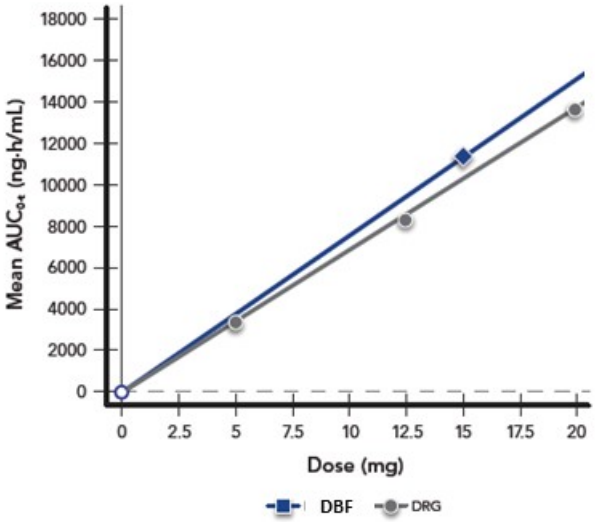
Aquestive

DRG Does Not Exhibit Dose-Proportional Pharmacokinetics

Mean C_{max} Values by Diazepam Dose



Mean $AUC_{0\text{-}t}$ Values by Diazepam Dose



From Heller AH, et al. Presented at: Annual Meeting of the American Academy of Neurology; April 21-28, 2018; Los Angeles, CA; *Neurology*. 2018;90(15 suppl):P4.273.

$AUC_{0\text{-}t}$, area under the plasma concentration time curve from time zero until last measurable concentration; C_{max}, maximal plasma concentration; DBF, diazepam buccal film; DRG, diazepam rectal gel.

Aquestive

Proposed Weight-Based Dosing Regimen for DBF

- The weight-based dosing regimen for DBF was modeled to account for differences betwee DBF and DRG (linear pharmacokinetics and food effect associated with oral dosing)
- The proposed dosing regimen for DBF is designed such that, after a moderate-fat meal, the C_{max} of diazepam from DBF is comparable to that from DRG

Weight Category (kg)	DBF (mg)	DRG (Diastat) (mg)
38-50	10.0	10.0
51-62	12.5	12.5
63-75	15.0	15.0
76-87	15.0	17.5
≥88	17.5	20.0

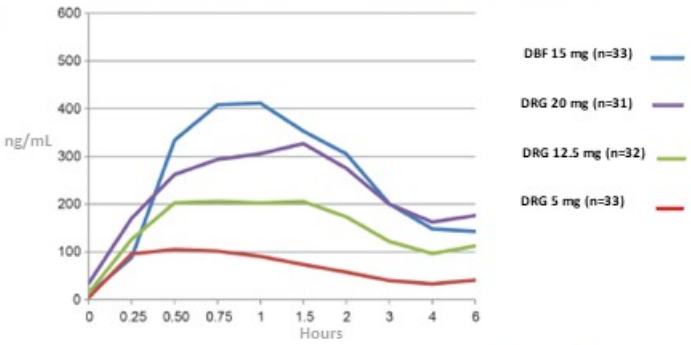
C_{max}, maximal plasma concentration; DBF, diazepam buccal film; DRG, diazepam rectal gel.

Aquestive

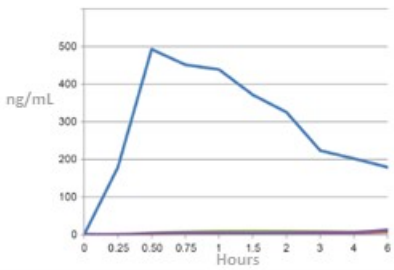
More Reliable Absorption With DBF Than With DRG

- DBF produces peak plasma levels similar to DRG using lower doses
- In a comparative PK study in healthy adults,[1] 3 subjects exhibited extremely low diazepam concentrations after one or more doses of DRG, whereas all subjects exhibited expected concentrations after DBF[2]

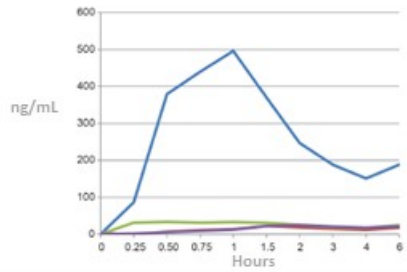
Mean Diazepam Plasma Concentration (All Subjects)



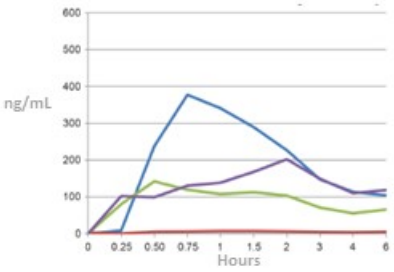
Subject 1



Subject 2



Subject 3



DBF, diazepam buccal film; DRG, diazepam rectal gel.

1. Heller AH, et al. Presented at: Annual Meeting of the American Academy of Neurology; April 21-28, 2018; Los Angeles, CA; *Neurology*. 2018;90(15 suppl):P4.273.
2. Heller AH, et al. Presented at: Annual Meeting of the American College of Clinical Pharmacology; September 15-17, 2019; Chicago, IL; *Clin Pharmacol Drug Dev*. 2019;8(S1):3.

Aquestive

Pharmacokinetics of DBF in Adult Patients Under Interictal and Ictal/Periictal Conditions in Epilepsy Monitoring Unit

- An in-clinic study of patients with epilepsy compared diazepam exposure after a fixed 12.5-mg dose of DBF under an interictal condition (not during seizure) and an ictal/periictal condition (during or shortly after seizure)[1]
- The 21 subjects who received both treatments, per protocol, had comparable diazepam exposure (C_{max}) and AUC_{0-4h} between the two conditions—indicating seizure activity did not affect diazepam exposure from DBF[1]
- A more recent study[2] used simulation to predict diazepam exposure based on the earlier study[1] if DBF were administered according to the proposed weight-based dosing regimen

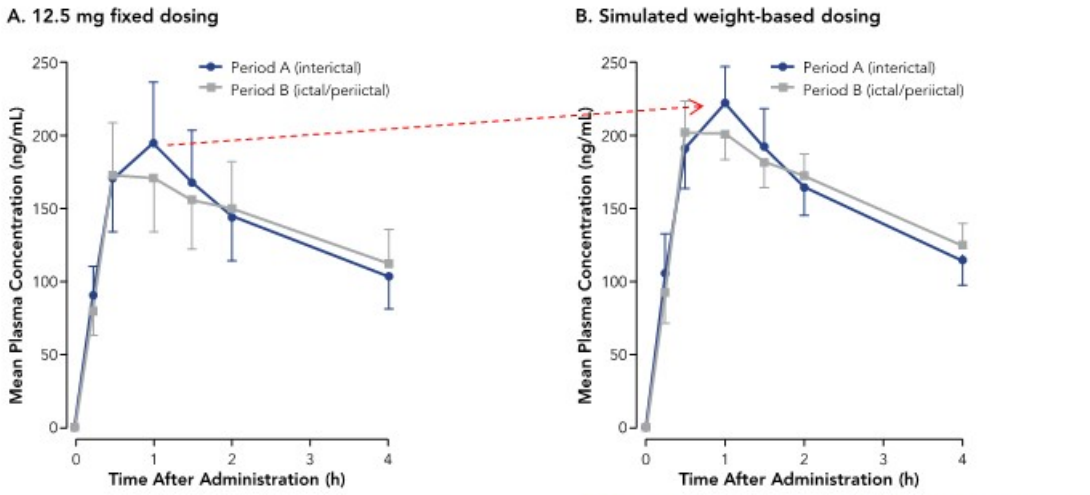
AUC_{0-4h}, area under the concentration curve assessed until 4 hours; C_{max}, maximal plasma concentration; DBF, diazepam buccal film.

1. Rogawski MA, et al. Presented at: Annual Meeting of the American Epilepsy Society; November 30-December 4, 2018; New Orleans, LA.
2. Heller AH, et al. Presented at: Annual Meeting of the American Epilepsy Society; December 6-10, 2019; Baltimore, MD.

Aquestive

Results

Mean Plasma Diazepam Concentration After Administration of DBF Under Interictal and Ictal/Periictal Conditions: Fixed Dose vs Weight-Based Dosing (Simulated)[1]



A. Mean plasma concentration after DBF at fixed dose of 12.5 mg

B. Mean plasma concentration predicted if DBF administered according to proposed weight-based dosing regimen

Predicted plasma concentrations based on data from 21 patients with valid profiles for both interictal and ictal/periictal conditions. Each time point is mean of concentration data from 16-21 patients. Error bars indicate standard error of mean.

DBF, diazepam buccal film.

1. Heller AH, et al. Presented at: Annual Meeting of the American Epilepsy Society; December 6-10, 2019; Baltimore, MD.

Aquestive

Conclusions: DBF Pharmacokinetics and Weight-Based Dosing Simulation

- DBF demonstrates a superior PK profile: linearity, bioavailability, reliability
- A weight-based dosing regimen was modeled from healthy volunteer studies adjusting for fed conditions; testing in adults with epilepsy confirmed that diazepam exposure is not affected by seizure activity
- The simulated weight-based dosing regimen (average dose, 14.9 mg/kg) predicts geometric mean C_{max} values greater than 200 ng/mL under both interictal and ictal/periictal conditions, well within the range generally considered therapeutic for diazepam antiepileptic activity
- The predicted geometric mean C_{max} values in this simulation are consistent with values found in a later single-dose PK study[1] in which patients were dosed using the DBF weight-based regimen that was simulated here

C_{max}, maximal plasma concentration; DBF, diazepam buccal film; PK, pharmacokinetics.

1. Rogawski MA, et al. Presented at: Annual Meeting of the American Epilepsy Society; December 6-10, 2019; Baltimore, MD.

Aquestive

PK of DBF in Adult Patients With Epilepsy: Comparison With DRG

Study Design and Patients

- Randomized, multicenter, single-dose, open-label, 2-treatment, 2-sequence crossover study (NCT03953820)
- Adult patients on a stable regimen of antiseizure drugs randomized to receive a single dose of DBF and a single dose of DRG in crossover fashion
- DRG: Dosed according to the FDA-approved weight-based regimen; DBF: dosed according to the weight-based regimen
- Treatments administered after a moderate-fat meal; 28-day washout. A subset of patients (n=10) was also administered DBF after an optional high-fat meal (exploratory analysis)

Weight-Based Dosing		
Weight (kg)	**DBF Dose**	**DRG Dose[1]**
38-50	10 mg	10 mg (2 mL)
51-62	12.5 mg	12.5 mg (2.5 mL)
63-75	15 mg	15 mg (3 mL)
76-87	15 mg	17.5 mg (3.5 mL)
≥88	17.5 mg	20 mg (4 mL)

Study Assessments

- Key PK parameters of interest included:
  - C_{max} (maximal plasma concentration)
  - T_{max} (time to C_{max})
  - AUC_{0-t} (area under concentration-time curve from time zero to last nonzero concentration)
  - AUC_{0-inf} (AUC from time zero extrapolated to infinity)
- Adverse events were monitored throughout the study

DBF, diazepam buccal film; DRG, diazepam rectal gel; FDA, US Food and Drug Administration; PK, pharmacokinetics.

1. Diastat C-IV (diazepam rectal gel) [package insert]. San Antonio, TX: DPT Laboratories; 2016.

Aquestive

Aquestive®

Pharmacokinetics of Diazepam Buccal Film in Adult Patients With Epilepsy: Comparison With Diazepam Rectal Gel

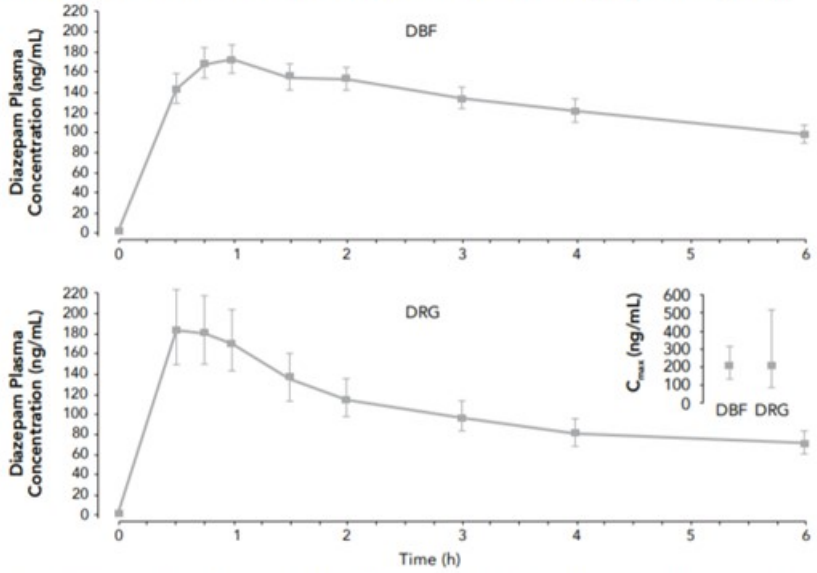
Michael A. Rogawski, MD, PhD
Professor of Neurology and Pharmacology
School of Medicine, University of California Davis
Davis, California

Advancing medicines.
Solving problems.
Improving lives.

Key Findings

- Geometric mean C_{max} values after DBF were comparable
- C_{max} values for DBF significantly less variable than *for* DRG (P<0.0001)

Figure 1. Geometric Mean (Geometric SE) Diazepam Plasma Concentrations Over Time Following Administration of DBF and DRG in the Overall Study Population (N=28)



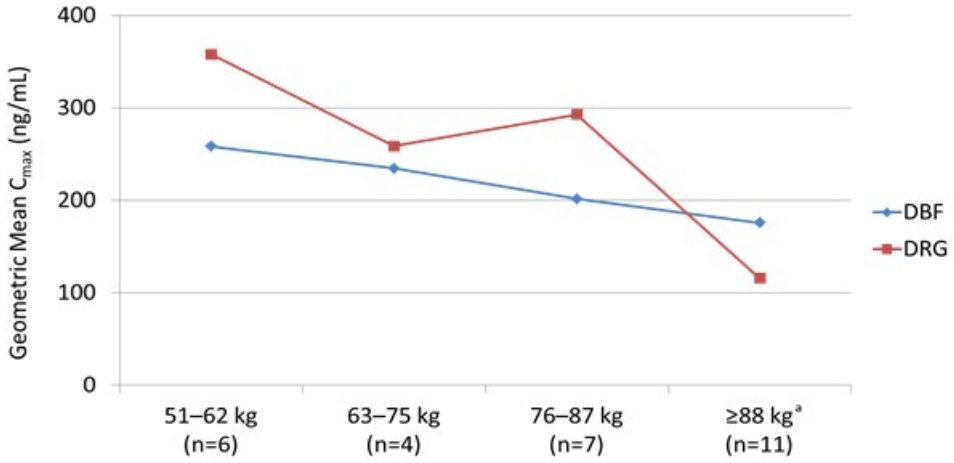
Values graphed are geometric mean (geometric SE) plasma concentrations. Inset shows geometric mean (geometric SD) C_{max} values.
C_{max}, maximum observed plasma drug concentration; DBF, diazepam buccal film; DRG, diazepam rectal gel; SD, standard deviation; SE, standard error.

Aquestive

Key Findings

- Geometric mean C_{max} values were less variable with DBF than with DRG across patient weight categories

Geometric Mean C_{max} Stratified by Weight Groups (N=28)



C_{max}, maximal plasma concentration; DBF, diazepam buccal film; DRG, diazepam rectal gel.
[a]Includes 4 patients with weight 112-124.5 kg.

Aquestive

Key Findings

PK Parameters After Administration of DBF and DRG (N=28)

Parameter	DBF	DRG	Ratio of Geometric Means, DBF/DRG (%)[a]	90% CI (%) for Ratio[b]
C_{max} (ng/mL), geometric mean	204.26	211.22	96.70	70.53, 132.58
AUC_{0-t} (ng•h/mL), geometric mean[c]	7290.40	5682.09	128.31	95.93, 171.61
AUC_{0-inf} (ng•h/mL), geometric mean[c]	8672.09	6880.96	126.03	103.67, 153.21
T_{max} (h), median	1.0	0.517[d]	NA	NA

[a]Calculated using least-square means according to formula $e^{(Difference)} \times 100$.
[b]90% geometric CI using ln-transformed data. [c]N=27. [d]$P<0.05$ vs DBF.

- AUC_{0-t} and AUC_{0-inf} values were higher for DBF than DRG
- The longer T_{max} for DBF vs DRG was reached earlier than the T_{max} of 1.5 hours reported in the DRG product labeling
- After moderate-fat meal, 3/28 subjects after DRG, but not after DBF, did not achieve plasma concentration ≥70 ng/mL
- For DBF after high-fat meal, geometric mean C_{max} (174 ng/mL) and DBF/DRG ratio (82.5%) reflect similar exposure level to DRG*

AUC_{0-t}, area under the plasma concentration time curve from time zero until last measurable concentration; AUC_{0-inf}, AUC from time zero extrapolated to infinity; C_{max}, maximal plasma concentration; CI, confidence interval; DBF, diazepam buccal film; DRG, diazepam rectal gel; PK, pharmacokinetics; SD, standard deviation; T_{max}, time to C_{max}.

Aquestive

Conclusions

- For patients with epilepsy after a moderate-fat meal, a single dose of DBF provides comparable overall exposure to diazepam to DRG with significantly less variability than DRG when each is administered according to its respective weight-based dosing regimen
  - These results confirm pharmacometric modeling and validate the proposed weight-based dosing regimen for DBF
- Unlike DRG, the geometric mean values for C_{max} after DBF was less variable and consistently ≥150 ng/mL for each of the weight categories; and there were no low responders to DBF after a moderate-fat meal
- The results support the use of DBF as an easily administered alternative to DRG for patients with epilepsy who experience seizure emergencies despite antiseizure medications

C_{max}, maximal plasma concentration; DBF, diazepam buccal film; DRG, diazepam rectal gel.

Aquestive

Aquestive®

Safety and Tolerability Associated With Chronic Intermittent Use of Diazepam Buccal Film in Pediatric, Adolescent, and Adult Patients With Epilepsy

Syndi Seinfeld, DO, MS
Director of Epilepsy
Joe DiMaggio Children's Hospital
Miami, Florida

Advancing medicines.
Solving problems.
Improving lives.

Introduction and Objective

- Cluster seizures and other bouts of more frequent or more severe seizures occur in many patients with epilepsy despite treatment with antiepileptic medications, and ca lead to injury, hospitalization, status epilepticus, and risk of death[1-3]
- Available treatment options for these episodes are suboptimal, particularly in terms of speed of onset of action and ease of administration[1,4,5]
- Currently, diazepam rectal gel and midazolam nasal spray are the only treatments approved by the FDA for patients with refractory epilepsy having bouts of increased seizure activity[6,7]
- **Objective:** The primary objective of this ongoing study (NCT03428360) is to assess the safety and tolerability of outpatient self- or caregiver-administered DBF in people with epilepsy
  - The usability of DBF is being assessed as a secondary objective

DBF, diazepam buccal film; FDA, US Food and Drug Administration.

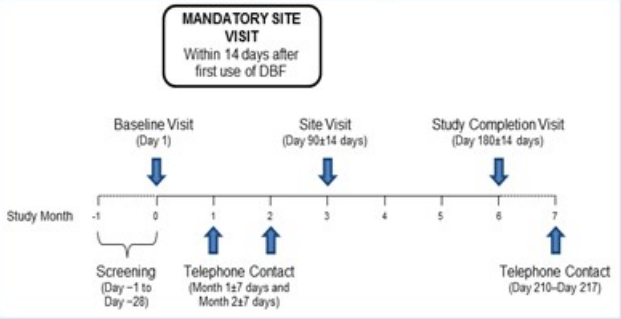
1. Penovich PE, et al. *Neurologist*. 2017;22:207-14; 2. Jafarpour S, et al. *Seizure*. 2019;68:9-15; 3. Sillanpää M, Schmidt D. *Brain*. 2008;131(pt 4):938-44; 4. Tatum IW. *Epilepsy Behav*. 2002;3:535-8; 5. Cereghino JJ. *Curr Treat Options Neurol*. 2007;9:249-55; 6. Diastat C-IV (diazepam rectal gel) [package insert]. San Antonio, TX: DPT Laboratories; 2016; 7. Nayzilam [package insert]. Smyrna, GA: UCB, Inc.; 2019.

Aquestive

Methods

Study Design and Patients

- Ongoing, phase 3, multicenter, open-label, long-term safety and tolerability study
  - Interim data from patients receiving ≥1 dose of DBF as of May 2019 are reported here



- Eligible patients include males and females between ages 2 and 65 years, inclusive, with established diagnosis of epilepsy who were deemed in need of benzodiazepine treatment for bouts of increased seizures at least once monthly on average

Administration and Dosing

- Study participants were instructed to administer DBF for treatment of seizure episodes occurring in their home environments in which a benzodiazepine would ordinarily be administered for seizure rescue
- DBF was dispensed at weight- and age-based doses ranging from 5 to 17.5 mg, which could be adjusted with aging or change in body weight during the study
- DBF could be administered for up to 5 seizure episodes per month; administration of a second dose was permitted within 4 to 12 hours after the first dose

Outcomes of Interest

- Adverse events
  - Occurring during study or up to 30 days after last study drug administration or until all drug-related toxicities are resolved, whichever is later
- DBF administration and usability
  - Assessed by patients and/or caregivers, recorded after each use of study drug , including successful placement/buccal insertion of DBF, oral cavity retention of DBF, and ability to open packaging and remove DBF

DBF, diazepam buccal film.

Aquestive

Results

- As of May 31, 2019, 72 patients had enrolled, used DBF at least once
- Mean (SD) duration on study at interim analysis cutoff date was 192.0 (97.0) days
- DBF dose administered
  - Mean (SD): 8.7 (10.1) mg
  - Median (range): 5 (1-49) mg

Characteristic	Adults (n=59)	Adolescents (n=7)	Pediatric (n=6)
Age, mean (SD), y	31.9 (10.5)	14.1 (1.5)	7.5 (2.7)
Female, n (%)	27 (45.8)	6 (85.7)	2 (33.3)
Race, n (%)			
White	45 (76.3)	4 (57.1)	4 (66.7)
Black	4 (6.8)	2 (28.6)	1 (16.7)
Other	10 (16.9)	1 (1.4)	1 (1.7)
Ethnicity, Hispanic or Latino, n (%)	12 (20.3)	2 (28.6)	3 (50.0)
BMI, mean (SD), kg/m²	26.0 (6.4)	22.1 (4.5)	16.1 (3.0)
Duration of epilepsy, mean (SD), y	20.2 (11.7)[a]	12.3 (4.2)[b]	6.6 (3.0)[c]

[a]n=44; [b]n=4; [c]n=5.

BMI, body mass index; DBF, diazepam buccal film; SD, standard deviation.

Aquestive

Results (cont'd)

Overall, 34 patients (47.2%) have reported 90 AEs

- 7 treatment-related AEs occurred in 5 (6.9%) patients; all were mild in severity and resolved
- 13 serious AEs were reported by 9 (12.5%) patients; none were considered treatment-related
- No patient discontinued study participation because of an AE
- Local buccal discomfort was reported by 1 adult and resolved within 1 day
- There were no reports of injury during buccal placement of DBF

AEs Reported in >2% of Overall Population

AE[a]	Overall Population (N=72)
Seizure	4 (5.6), 6
Pyrexia	4 (5.6), 4
Dizziness	3 (4.2), 3
Nausea	3 (4.2), 3
Somnolence	3 (4.2), 3
Weight decreased	3 (4.2), 3
Cough	2 (2.8), 2
Dehydration	2 (2.8), 2
Gastroenteritis viral	2 (2.8), 2
Lethargy	2 (2.8), 2
Vomiting	2 (2.8), 2
Weight increased	2 (2.8), 2

[a]All data reported as number (%) of patients, number of events.

Treatment-Related AEs

Treatment-Related AE[a,b]	Pediatric (n=6)	Adolescent (n=7)	Adult (n=59)	Total (N=72)
	Number (%) of Patients, Number of Events			
Somnolence	0	0	1 (1.7), 1	1 (1.4), 1
Lethargy	0	0	1 (1.7), 1	1 (1.4), 1
Altered consciousness	0	0	1 (1.7), 1	1 (1.4), 1
Mouth swelling	0	1 (14.3), 1	0	1 (1.4), 1
Oral discomfort	0	0	1 (1.7), 1	1 (1.4), 1
Gait disturbance	0	0	1 (1.7), 1	1 (1.4), 1
Skin sensitization	0	0	1 (1.7), 1	1 (1.4), 1

[a]Defined as AE categorized as having "possible" or "probable" relationship to study drug.
[b]All treatment-related AEs were mild in severity.

AE, adverse event; DBF, diazepam buccal film.

Medication Administration

- Of the 471 DBF exposures:
  - At least 107 (22.7%) were self-administered by the patient
  - The majority (308 or 65.4%) occurred within 5 minutes of a seizure
  - There were no administration-related injuries in this study or over the almost 1000 exposures in the DBF program
- 8 patients were exposed to a second DBF dose on 14 use occasions within the recommended 4-12 hours after the first DBF exposure
  - There were no instances of adverse events of interest

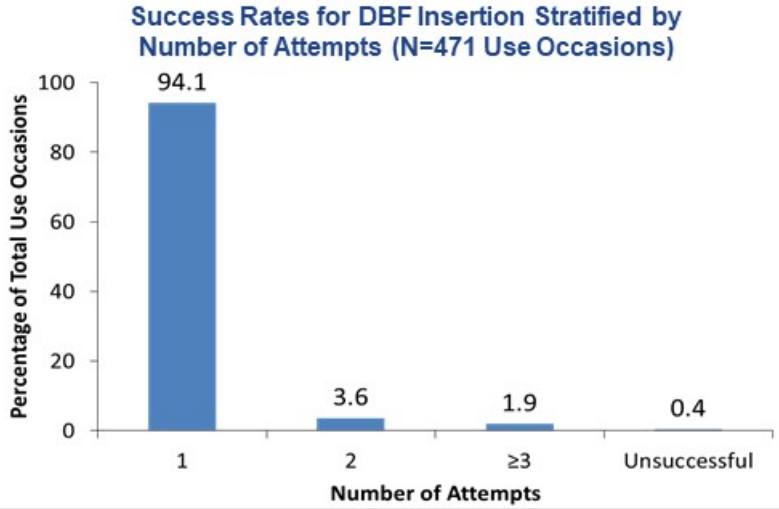
DBF, diazepam buccal film.

Aquestive

Results

DBF usability data were reported by 64 patients

- Mean (SD) administrations per patient: 7.4 (7.7)
- All patients had first-attempt success at DBF administration on at least one use occasion
- Almost all patients successfully administered DBF on first or second attempt (97.7%)



DBF, diazepam buccal film; SD, standard deviation.

Aquestive

Results (cont'd)

- There were no cases of unsuccessful placement owing to swallowing of DBF before it adhered to buccal mucosa (Table)
- Patients and caregivers reported no difficulty opening the packaging in the majority of use occasions
- Patients and caregivers reported no difficulty removing DBF from inner packaging in nearly all (96.6%) use occasions

Overview of Reported Reasons for Unsuccessful Placement of DBF

Reasons for Unsuccessful Insertion Attempts	Unsuccessful Attempts Based on 471 Use Occasions, n (%)[a]
Clenching jaw/won't open mouth	10 (2.1)
Excessive drooling	9 (1.9)
Spit out before DBF adhered to buccal mucosa	7 (1.5)
Clenching jaw/won't open mouth/excessive drooling	1 (0.2)
Other	8 (1.7)

[a]Respondents could choose more than 1 reason for unsuccessful insertion attempt; 35 reasons were given for 28 unsuccessful attempts.

DBF, diazepam buccal film.

Aquestive

Conclusions

- In this observational study of chronic intermittent administration and use, DBF was found to be safe and well tolerated by pediatric, adolescent, and adult patients with epilepsy experiencing seizure emergencies
- Treatment-related AEs, including somnolence, were relatively uncommon after DBF use, and all treatment-related AEs were mild in severity
- Patients were able to self-administer DBF; administration near time of seizure was common; there were no administration-related injuries, and local AEs were rare
- DBF ultimately was successfully placed on nearly all (99.6%) use occasions and readily used without difficulty when administered by patients and caregivers
- These results support the further development and use of DBF as an easily administered alternative to diazepam rectal gel for patients with epilepsy who experience cluster seizures and other bouts of more frequent or more severe seizures despite treatment with antiepileptic medications

AE, adverse event; DBF, diazepam buccal film.

Aquestive

Aquestive®

Panel Discussion/Q&A

Gary Slatko, MD
Lawrence J. Hirsch, MD
Allen H. Heller, MD, MPH
Michael A. Rogawski, MD, PhD
Syndi Seinfeld, DO, MS

Advancing medicines.
Solving problems.
Improving lives.

Discussion for Panel

- What would a medication like this—that's easy to carry and could be quickly administered—mean for patients with epilepsy and caregivers?
- How does this buccal formulation compare with nasal formulations?
  - Our data show a strong preference for oral formulations—what do your patients say?
- How could new seizure detection devices affect use of these rescue medications?

Aquestive®

Closing Remarks

Keith Kendall
President and Chief Executive Officer

Advancing medicines.
Solving problems.
Improving lives.