Pharmacokinetics of Diazepam Buccal Film in Adult Patients with Epilepsy: Comparison of Bioavailability with Periictal and Interictal Administration

BACKGROUND

• Seizure clusters, also termed acute repetitive seizures, commonly occur in patients with drug-refractory epilepsy.
• Seizure clustering is associated with reduced quality of life, may be a risk factor for less satisfactory long-term outcomes for people with epilepsy, and may decrease to status epilepticus.
• Benzodiazepines such as diazepam are the mainstay of rescue therapy for seizure clusters.

Diazepam Buccal Film (DBF, formerly DBF-120) is a novel dosage form of diazepam under development as an alternative approach to the management of seizure clusters.

OBJECTIVES

• Compare the bioavailability of diazepam in adults with epilepsy following single doses of 12.5 mg DBF and 10 mg oral diazepam.

METHODS

STUDY SUBJECTS

• Adult men and women aged 17–65 years with a history of clusters (≥ 1 cluster/month) and with (a) ≥ 5 attacks in the last 30 days or (b) ≥ 5 days with ≥ 3 attacks in the last 30 days.

STUDY DESIGN

• Diazepam exposure following Treatment B was compared with that following Treatment A. Pharmacokinetic parameters within subject were evaluated by analysis of variance (ANOVA) with treatment as a fixed factor and subject as a random factor on the signed-rank test.

RESULTS

TABLE 1: SUMMARY OF DEMOGRAPHIC CHARACTERISTICS OF SUBJECTS

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Overall Mean (SD)</th>
<th>Treatment A</th>
<th>Treatment B</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>40.8 ± 11.0</td>
<td>39.8 ± 11.5</td>
<td>41.8 ± 11.5</td>
</tr>
<tr>
<td>Sex, n (%)</td>
<td>Male: 20 (57.1)</td>
<td>10/30</td>
<td>9/30</td>
</tr>
<tr>
<td>NIHSS</td>
<td>6.0 ± 9.1</td>
<td>6.0 ± 9.1</td>
<td>6.0 ± 9.1</td>
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</tbody>
</table>

• PK profiles valid for analysis until 4 hours after dosing for AUC, area under the plasma concentration-time curve; Cmax, maximum plasma drug concentration; CI, confidence interval; Tmax, time to reach maximum plasma concentration

COMPARISON OF PHARMACOKINETIC PARAMETERS FOLLOWING ADMINISTRATION IN THE INTERICTAL AND ICTAL/PERIICTAL STATE

• PK profiles valid for analysis until 2 hours after dosing in the interictal state and until 4 hours after dosing in the periictal state.

CONCLUSIONS

• DBF 12.5 mg is safe and well tolerated.

FUNDING AND DISCLOSURES

• Financial support for this study was provided by Aquestive Therapeutics. All authors contributed to the design of the poster and maintained control over the content. Michael A. Rogawski, Allen H. Heller and David J. Wyatt are employees of Aquestive Therapeutics.

REFERENCES