**Background**

- The intranasal route of drug administration may present challenges due to nasal anatomy and physiology, such as limited volume, residence time, and absorption.
- One such challenge is the possibility of variable absorption due to such conditions as colds and allergies.
- Per the literature, seasonal allergies and nasal congestion do not affect intranasal administration of agents such as tacrine and fentanyl.
  - However, for patients with epilepsy experiencing seizure clusters, it is important to determine whether this lack of impact also extends to the safety and effectiveness of intranasal therapies.
- Benzodiazepines are considered the mainstay of anticonvulsant therapy.
- Diazepam nasal spray (Valtoco®, NRL-1) is a unique intranasal formulation of diazepam formulated to bypass the nasal vestibule and achieve rapid absorption.
- Vitamin E is used to enhance the non-aqueous solubility of diazepam.
- Intravail A3 is a nonionic surfactant that is used as an absorption enhancer to overcome the increased transmucosal bioavailability of drugs.
- Patients may have limited absorption due to low water solubility.

**Methods**

- Enrolled patients were those with epilepsy who were expected to need benzodiazepine treatment for seizure control once every other month on average (ie, 6 times a year) despite a stable regimen of AEDs.
- Patients were randomized to 1 of 2 active treatment groups following a period of placebo washout.
- Investigators could adjust doses for efficacy/safety as needed during treatment.
- Safety was assessed in both groups based on safety measures included: treatment-emergent adverse events (TEAEs), physical/narrow electrocardiographic abnormalities, and alterations in awareness.

**Objective**

- In this interim analysis of the impact of a patient's history of seasonal allergies on the safety and doses needed per episode of diazepam nasal spray as rescue medication in patients with epilepsy who experience seizure clusters despite stable regimens of antiseizure drugs (ASDs).

**Results**

- The safety population of the interim analysis consisted of 132 patients aged 6 to 65 years (33.8% female, 82.6% white, mean age 25.7 ± 15.1 years).
- Allergic history was present in 27 patients (20.5%) aged 6 to 33 years of whom 17.0% were female and 70.4% white (Table 1).
- Seasonal allergies were the most common type of allergy (77.6%) in both subgroups (Table 1).
- Approximately half of the patients in both subgroups had a duration of exposure of at least 12 months (Table 2).

**Conclusions**

- In this interim analysis of long-term safety of diazepam nasal spray, the presence of seasonal allergies had no impact on the number of diazepam nasal spray doses needed for a seizure-cluster episode.
- In subgroups of patients with and without allergies, repeated dosing of diazepam nasal spray demonstrated a similar safety/tolerability profile.

### Table 2. Duration of Exposure and Seizure Episodes (N=132)

<table>
<thead>
<tr>
<th>Variable</th>
<th>Duration of exposure, n (%)</th>
<th>Seizure episodes requiring a second dose of diazepam nasal spray</th>
</tr>
</thead>
<tbody>
<tr>
<td>Male</td>
<td>10 (59.2)</td>
<td>4 (39.2)</td>
</tr>
<tr>
<td>Female</td>
<td>32 (60.8)</td>
<td>6 (54.5)</td>
</tr>
<tr>
<td>Total</td>
<td>42 (59.7)</td>
<td>10 (47.6)</td>
</tr>
</tbody>
</table>

### Table 3. Treatment- Emergent Adverse Events (TEAEs)

<table>
<thead>
<tr>
<th>Variable</th>
<th>Allergic History (N=132)</th>
<th>No Allergic History (N=105)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Vomitus</td>
<td>6 (4.6)</td>
<td>2 (1.9)</td>
</tr>
<tr>
<td>Nasal discomfort</td>
<td>7 (5.3)</td>
<td>7 (6.6)</td>
</tr>
<tr>
<td>Any TEAE</td>
<td>19 (70.4)</td>
<td>72 (68.6)</td>
</tr>
<tr>
<td>Respiratory allergy</td>
<td>1 (3.7)</td>
<td>NR</td>
</tr>
</tbody>
</table>

### References