Safety and Efficacy of Nabiximols in People With Multiple Sclerosis–Associated Spasticity: Post Hoc Analyses of a Controlled Enrichment Design Study

**SUMMARY**

**During Phase A:**
- The mean percent reduction from baseline in average 7-day spasticity Numeric Rating Scale (NRS) score was 44% for responders (n=266) vs 3% for nonresponders (n=306).
- The most frequently reported AE was dizziness, followed by fatigue, and dry mouth.
- The AE profile was generally similar between responders and nonresponders, except for increased incidence of dizziness in nonresponders.

**During Phase B:**
- Nabiximols was well tolerated.
- Nabiximols provided continued benefit relative to Phase A baseline for those randomized in Phase B to continue treatment with nabiximols.
- Those who were randomized to placebo in Phase B showed a variable loss of efficacy.

**INTRODUCTION**

- Nabiximols, an endocannabinoid system modulator, is a complex botanical mixture containing delta-9-tetrahydrocannabinol, cannabidiol, and other cannabinoid and noncannabinoid components.
- Efficacy of nabiximols in treating spasticity symptoms associated with MS has been demonstrated in multiple RCTs.1,10
- GWSP0604 used an enriched trial design: People with MS (PwMS) were treated with single-blind nabiximols in addition to SOC for 4 weeks and, those reporting at least 30% improvement in spasticity NRS score were randomized in Phase B (12 weeks); concomitant medications remained stable throughout both phases.
- Prior published analysis from study GWSP0604 reported results as change from Phase B baseline.
- The objectives of this post hoc analysis were as follows:
  - Assess adverse event profile during Phase A for Phase A responders vs Phase A nonresponders
  - Assess efficacy outcomes in Phase A and Phase B relative to Phase A baseline

**RESULTS**

**AEs Occurring in ≥5% of PwMS**

<table>
<thead>
<tr>
<th>Phase A Responders</th>
<th>Phase B Phase A Responders</th>
<th>Phase B Nonresponders</th>
</tr>
</thead>
<tbody>
<tr>
<td>SOC + Placebo</td>
<td>SOC + NBX (n=124)</td>
<td>SOC + Placebo (n=117)</td>
</tr>
<tr>
<td>Nabiximols</td>
<td>SOC + NBX (n=124)</td>
<td>SOC + Placebo (n=117)</td>
</tr>
<tr>
<td>Female sex (%)</td>
<td>54 (20)</td>
<td>57 (20)</td>
</tr>
<tr>
<td>Mean age (years)</td>
<td>47 (2)</td>
<td>47 (2)</td>
</tr>
<tr>
<td>Mean duration of MS years</td>
<td>11.8 (2)</td>
<td>11.8 (2)</td>
</tr>
<tr>
<td>Median spasticity NRS score</td>
<td>7 (2)</td>
<td>7 (2)</td>
</tr>
<tr>
<td>Median spasm frequency per day</td>
<td>1 (1)</td>
<td>1 (1)</td>
</tr>
<tr>
<td>Median SOSE score</td>
<td>5.9 (3)</td>
<td>5.9 (3)</td>
</tr>
<tr>
<td>Median duration of spasticity, p&lt;0.001</td>
<td>4.7 (2)</td>
<td>4.7 (2)</td>
</tr>
<tr>
<td>Median duration of spasm frequency, p&lt;0.001</td>
<td>4.7 (2)</td>
<td>4.7 (2)</td>
</tr>
</tbody>
</table>

**Spasticity NRS Score: Phase A Responders vs Nonresponders**

All patients on single-blind nabiximols (n=287). Responders vs Nonresponders.

**Caregiver Global Impression of Change (CGIC): Phase B**

- **Phase A responder** vs **Phase A nonresponder**:
  - 43% CFB

**Spasticity NRS Score and Spasm Frequency for Phase B Cohorts During Both Phases**

**METHODS**

- **Demographics, Baseline Characteristics, Previous Cannabis Use, and Dose of Study Drug**
- **RESULTS**
- **AEs Occurring in ≥5% of PwMS**
- **Spasticity NRS Score: Phase A Responders vs Nonresponders**
- **Caregiver Global Impression of Change (CGIC): Phase B**
- **Spasticity NRS Score and Spasm Frequency for Phase B Cohorts During Both Phases**
- **METHODS**

**Participants**
- Participants self-titrated during the first 14 days of Phase A, up-titrating through a predefined escalation scheme based on efficacy and tolerability to their individual optimal dose (maximum permitted dose: 12 sprays/day).
- Spasticity NRS minimally clinically important difference (MCID, 18%) and clinically important difference (CIDI, 30%) have been previously established in PwMS.14