Background

- Motor complications: dyskinesia and OFF are associated with fluctuations in concentrations of dopamine, increased extracellular glutamate, and over-activation of the glutamatergic NMDA receptor.
- While NMDA receptor antagonism with amantadine IR has been used to treat dyskinesias, suboptimal efficacy, durability, and issues with tolerability at higher doses have limited its clinical utility.
- ADS-5102 (amantadine) extended-release capsule is a treatment for dyskinesia in patients with Parkinson’s disease (PD).

Study Design and Methods

- Two randomized, double-blind, placebo-controlled studies were conducted at 44 North American sites (EASE LID I and II) in the US and Western Europe (EASE LID II).
- PD patients with at least 1 hour of OFF time with troublesome dyskinesia and at mild to mild/mild functional impact were assigned to placebo or 274 mg ADS-5102 (340 mg amantadine HCl) taken once daily at bedtime.

Objective

- To evaluate the efficacy and safety of ADS-5102 compared with placebo in patients with levodopa-induced dyskinesia (LID).

Results

- Reduction in UDysRS was evident at the first post-baseline UDysRS assessment and maintained through Week 12.

Table 1. Baseline Demographics and PD Characteristics

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>EASE LID I</th>
<th>EASE LID II</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>N</td>
<td>50</td>
<td>50</td>
<td></td>
</tr>
<tr>
<td>Age, Mean (SD)</td>
<td>72 (7)</td>
<td>72 (7)</td>
<td></td>
</tr>
<tr>
<td>On-off time, Mean (SD)</td>
<td>12 (6)</td>
<td>12 (6)</td>
<td></td>
</tr>
<tr>
<td>UDysRS total score, Mean (SD)</td>
<td>40 (15)</td>
<td>40 (15)</td>
<td></td>
</tr>
</tbody>
</table>

Table 2. Percent Reduction in UDysRS Total Score from Baseline to Week 12

<table>
<thead>
<tr>
<th>Treatment</th>
<th>Baseline</th>
<th>Week 12</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>ADS-5102</td>
<td>40</td>
<td>25</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Placebo</td>
<td>40</td>
<td>25</td>
<td>&lt;0.0001</td>
</tr>
</tbody>
</table>

Conclusion

- ADS-5102 treatment resulted in a marked behavioral shift (improvement) in the cumulative response curve.

References

1. Carta, Brain, 2007
2. Carta, Movement Disorders, 2010
3. Goetz, Movement Disorders, 2012
5. Adams, JAMA Neurology, 2017
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