Efficacy of Sublingual Apomorphine (APL-130277) for the Treatment of OFF Episodes in Patients with Parkinson’s Disease

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BACKGROUND
• Parkinson’s disease (PD) patients suffer from a variety of OFF episodes as the disease progresses.
• These consist of unpredictable wearing OFF, morning akinesia, delayed or No-ON periods.
• To date, OFF episodes have been managed using conventional dopamine replacement therapies, which have very limited efficacy and has significant limitations due to the generation-specific nature of treatment.
• More convenient, on-demand, medications for the management of OFF episodes are needed.
• APL-130277 is a “turning ON” medication.

OBJECTIVE
The primary objective of the study was to evaluate the efficacy, tolerability and safety of single treatments of APL-130277 in 19 PD patients with OFF episodes.

METHODS
• This was a Phase 2, open-label, single-arm study.
• Patients were instructed to take their last dose of levodopa no later than 10 pm the night prior and present to the clinic in the morning without taking their usual morning dose of levodopa and other medications.
• Patients were dosed with APL-130277 sublingually until they achieved a full ON state to the ON state, to a maximum dose of 30 mg pre-dose and at 15, 30, 45, 60 and 90 minutes after APL-130277 administration; those that were not fully ON at 90 minutes were dosed at 120 minutes.

RESULTS
• A total of 19 patients were dosed with APL-130277.

Table 1: Baseline demographics

<table>
<thead>
<tr>
<th>Variable</th>
<th>Total (n = 19)</th>
<th>Responders (n = 15)</th>
<th>Non-responders (n = 4)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>52</td>
<td>51</td>
<td>53</td>
</tr>
<tr>
<td>Sex (male/female)</td>
<td>Male: Female</td>
<td>10/9</td>
<td>9/6</td>
</tr>
<tr>
<td>Hoehn &amp; Yahr stage</td>
<td>I–III</td>
<td>I–III</td>
<td>I–III</td>
</tr>
</tbody>
</table>

• Of the 19 total patients dosed with APL-130277, 17 achieved a full ON response (84%).

Table 2: Mean change in MDS-UPDRS Part III following APL-130277 administration

<table>
<thead>
<tr>
<th>Time (min)</th>
<th>Responders (n = 15)</th>
<th>Non-responders (n = 4)</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>10</td>
<td>10</td>
</tr>
<tr>
<td>15</td>
<td>20</td>
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<tr>
<td>30</td>
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<tr>
<td>45</td>
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<tr>
<td>60</td>
<td>50</td>
<td>50</td>
</tr>
<tr>
<td>90</td>
<td>60</td>
<td>60</td>
</tr>
</tbody>
</table>

• Overall, APL-130277 was safe and well tolerated with no serious adverse events. All patients tolerated the treatment.

CONCLUSIONS
• Sublingual APL-130277 rapidly converted PD patients from the morning OFF state to the ON state.
• APL-130277 provided rapid, clinically meaningful improvement in motor function as assessed by MDS-UPDRS Part III scores.
• Duration of benefit was close to an hour or more with most patients having sustained benefit through 60 minutes after APL-130277 administration.
• Of 6 patients, 5 were full ON responders by 15 minutes, the other patient achieved full ON by 120 minutes.

REFERENCES