Minimum MDS-UPDRS Part III Change Needed to Convert a Parkinson’s Disease Patient From the OFF to full ON State with Sublingual Apomorphine (APL-130277)

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BACKGROUND

Up to 2/3rds of Parkinson’s disease (PD) patients suffer from OFF episodes including:

- Wearing OFF
- Morning akinesia
- Delayed/no-ON and sudden OFF

OFF episodes in PD have a significant negative impact on quality of life of patients

APL-130277 is a soluble, sublingual film strip of apomorphine (Figure 1)

OBJECTIVE

To evaluate the minimum change on the MDS-UPDRS-Part III to convert a PD patient from OFF to full ON

METHODS

- Open-label, single-arm, Phase 2 study
- Patients took last dose of levodopa (LD) no later than 10 PM prior to presenting to clinic in a.m. without taking usual morning dose of LD and other PD meds
- Patients confirmed to be OFF were dosed with APL-130277 starting at 10 mg (Figure 2)
- APL-130277 was administered sublingually and allowed to dissolve over 2 minutes
- Patients could be dosed up to two times/day over 3 days
- Pre-treatment with trimethobenzamide (anti-emetic) was started 3 days prior to initiation of APL-130277 and was continued during its dosing
- MDS-UPDRS-Part III and assessment of OFF/ON were conducted pre-dose and at 15, 30, 45, 60 and 90 mins after APL-130277 administration

Patients

- Clinical diagnosis of PD (H&Y state 1-3 in ON state); no atypical/secondary forms
- >1 OFF episode/day and > 2 hours of daily OFF time
- Predictable OFF episodes upon awakening prior to receiving AM dose of LD
- May not have received any form of apomorphine within 30 days of dosing Day 1

Safety Assessments/Endpoints (Presented in 2.089)

Data Analyses: according to 3 datasets

- Modified Intention to Treat (mITT) – includes 19 patients dosed
- Responders – includes 15 patients who turned fully ON post APL-130277 treatment
- Per Protocol (PP) – includes 15 patients with no protocol dosing violations (excludes 3 patients who were improperly instructed to swallow the strip and 1 patient who was dosed in an OFF state following administration of their first dose of PD meds)

RESULTS

Table 1: Demographic and Baseline Characteristics

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>All Patients (N=19)</th>
<th>Responders (N=15)</th>
<th>Non-Responders (N=4)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>64.9 (56.0-73.7)</td>
<td>65.6 (56.0-73.0)</td>
<td>64.9 (53.3-75.5)</td>
</tr>
<tr>
<td>Gender (male)</td>
<td>8/19 (42%)</td>
<td>7/15 (47%)</td>
<td>1/4 (25%)</td>
</tr>
<tr>
<td>Daily levodopa dose (mg)</td>
<td>306 (200-450)</td>
<td>306 (200-450)</td>
<td>306 (200-450)</td>
</tr>
<tr>
<td>MDS-UPDRS Part III</td>
<td>29.0 (23-35)</td>
<td>29.0 (23-35)</td>
<td>50.0 (25-70)</td>
</tr>
<tr>
<td>ON duration (min)</td>
<td>25.0 (10-50)</td>
<td>25.0 (10-50)</td>
<td>25.0 (10-50)</td>
</tr>
</tbody>
</table>

CONCLUSIONS

An improvement of over 10 points or a 25% change in the MDS-UPDRS-Part III is needed to turn a PD patient from OFF to full ON

ACKNOWLEDGEMENTS

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