The Effects of Sublingual Apomorphine (APL-130277) by Disease Characteristics on the Acute Management of OFF Episodes in Parkinson's Disease

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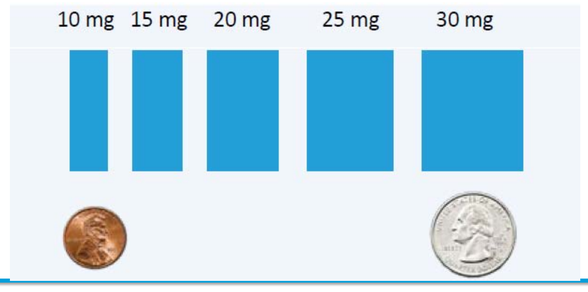
BACKGROUND

- 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)

Figure 1: Apomorphine Sublingual Thin Film Strip (APL-130277)



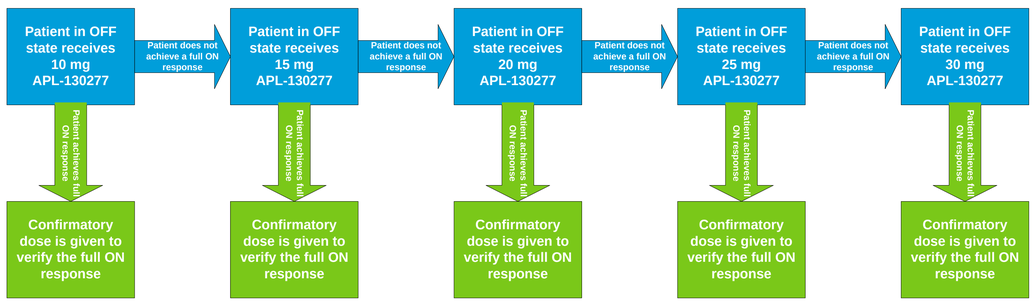
OBJECTIVE

To evaluate whether baseline disease characteristics affected the acute reversal of OFF episodes treated with APL-130277 in patients with PD

METHODS

- Open-label, single-arm, Phase 2 study
- Patients took their last dose of levodopa (LD) no later than 10 PM the night prior and presented to clinic in a.m. without taking usual morning dose of LD and other PD meds
- Starting at 10 mg, patients who were confirmed to be in the OFF state were dosed with APL-130277 (Figure 2)
- APL-130277 was administered sublingually and allowed to dissolve over 2 minutes

Figure 2: Study Design



- 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

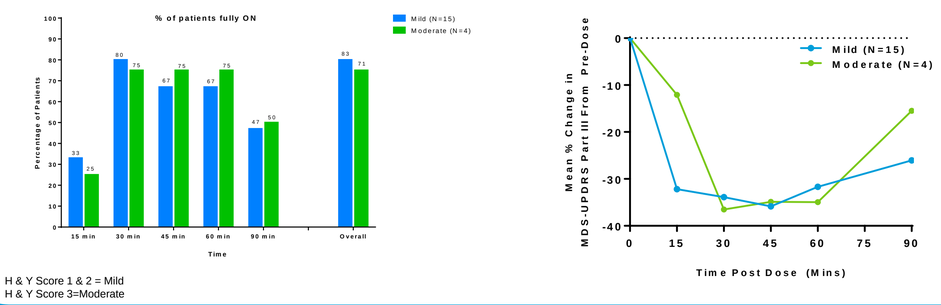
Efficacy and Safety Endpoints are presented in Poster 2.086 and P2.089, respectively

RESULTS

Table 1: Demographic and Baseline Characteristics

Subgroups		N (%)	Baseline UPDRS Score Mean (Range)
Hoehn and Yahr Score	Mild (1 or 2)	15 (79%)	45 (22-79)
	Moderate (3)	4 (21%)	33 (16-46)
Age	< 65 years	12 (63%)	46 (22-79)
	≥ 65 years	7 (37%)	37 (16-58)
Number of OFF Episodes	< 4	7 (37%)	34 (16-58)
	≥ 4	12 (63%)	48 (30-79)
Time Since OFF Onset	≤ 5 years	12 (63%)	45 (26-79)
	> 5 years	7 (37%)	38 (16-67)
Number of PD Med Classes	< 3	7 (37%)	43 (27-67)
	3	5 (26%)	46 (26-79)
	> 3	7 (37%)	40 (16-58)
Daily Levodopa Dose (mg)	≤ 600 mg	9 (47%)	42 (16-79)
	> 600 mg	10 (53%)	43 (22-67)

Figure 3: Hoehn and Yahr Score at Study Entry (mITT)



H & Y Score 1 & 2 = Mild
H & Y Score 3=Moderate

RESULTS (continued)

Figure 4: Average Number of OFF Episodes/day (mITT)

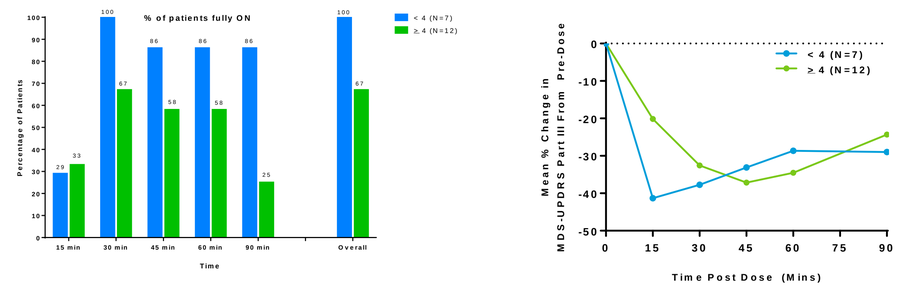


Figure 5: Age at Study Entry (mITT)

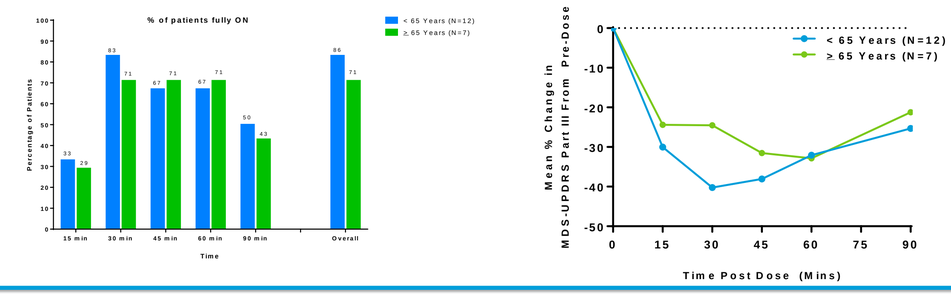


Figure 6: Total Levodopa Dose (mITT)

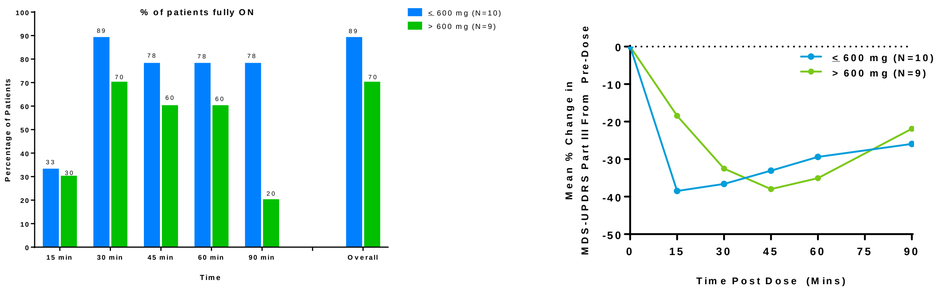
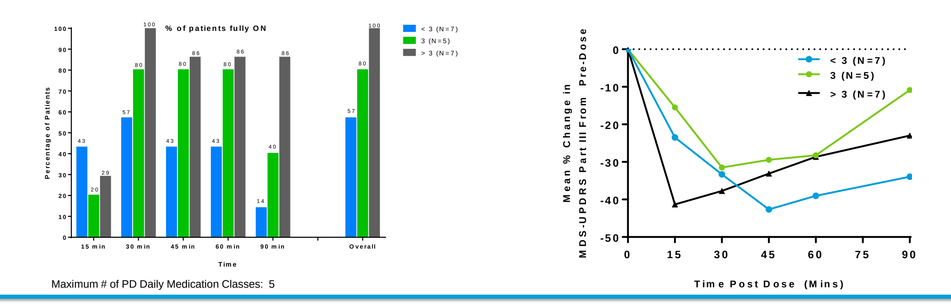
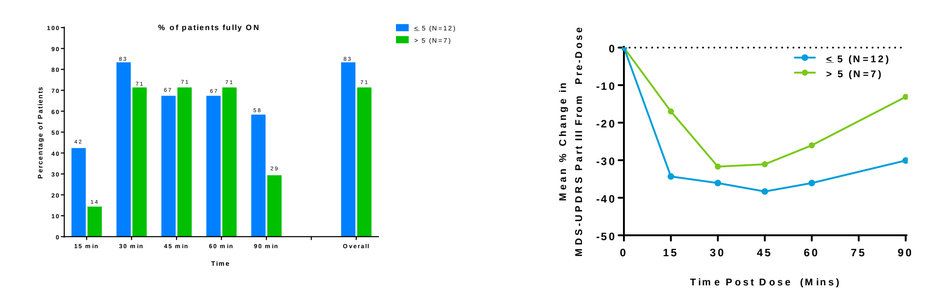


Figure 7: Number of PD Daily Medications Classes (mITT)



Maximum # of PD Daily Medication Classes: 5

Figure 8: Years of OFF Episodes (mITT)



CONCLUSIONS

- APL-130277 rapidly converts PD patients from OFF to the full ON state regardless of disease characteristics
- Phase 3 studies have been initiated

ACKNOWELDGEMENTS

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APL-130277 is currently an investigational product in some countries, including the United States.

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