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

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BACKGROUND

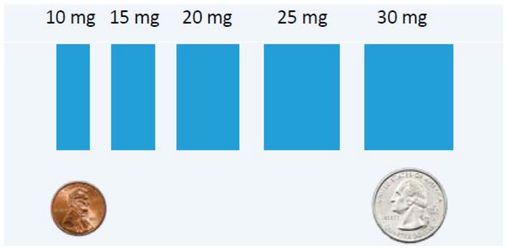
Up to 2/3rds of Parkinson's disease (PD) patients suffer from OFF episodes including:

- 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)



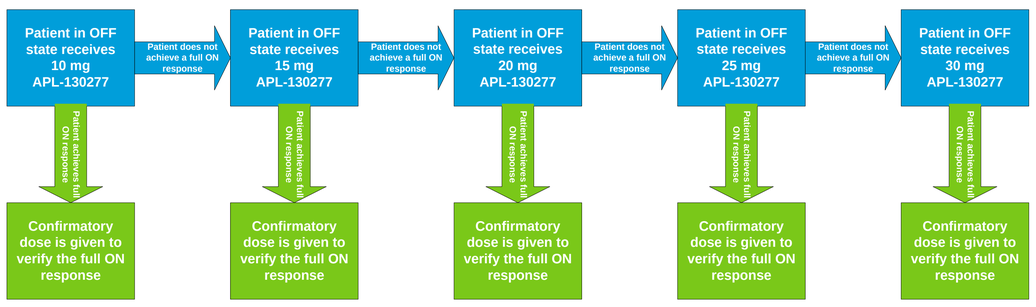
OBJECTIVE

To evaluate the efficacy of single treatments of APL-130277 in patients with PD and OFF episodes

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
- Patients who were OFF were dosed with APL-130277, starting at 10 mg (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 Endpoints

- Primary efficacy endpoint: % of patients turning fully ON as confirmed by the Investigator following an APL-130277 administration
- Secondary endpoints:
  - Change and % change in MDS-UPDRS Part III over time
  - % of patients fully ON at each time point
  - % of patients with a 5 and 10 point MDS-UPDRS Part III improvement following the first full ON dose for Responders or last dose for non-responders

Safety Assessments/Endpoints (Presented in Poster 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)

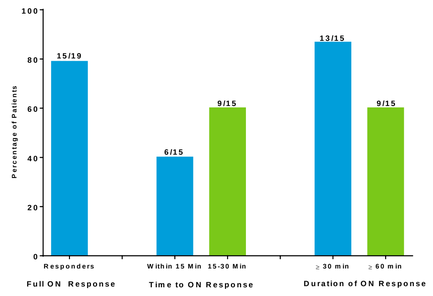
RESULTS

Table 1: Demographic and Baseline Characteristics

Characteristic	N=19 (dosed with APL-130277)
Age, years (range)	61.5 (48-79)
Male:Female	14 (73.7%) to 5 (26.3%)
Modified Hoehn & Yahr, mean (range)	2.2 (1-3)
# of daily OFF episodes, mean (range)	3.9 (1-7)
# of PD medication classes, mean (range)	3 (1-5)
Daily levodopa dose, mean (range)	776 mg (100-2100)
# of levodopa doses per day, mean (range)	5.4 (1-12)

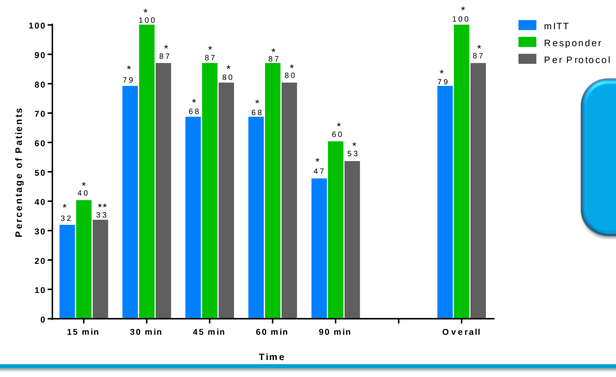
RESULTS (continued)

Figure 3: Responders, Time to Response and Duration of Response



Mean ON duration: 50 mins

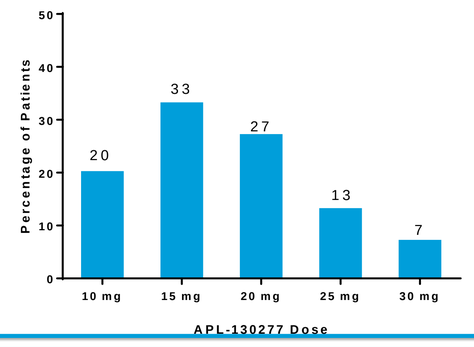
Figure 4: Percent of Patients Fully ON Overall and at Each Time-point



Patients who achieved full ON: 15/19 (79%)

*p ≤ 0.05
**p > 0.05

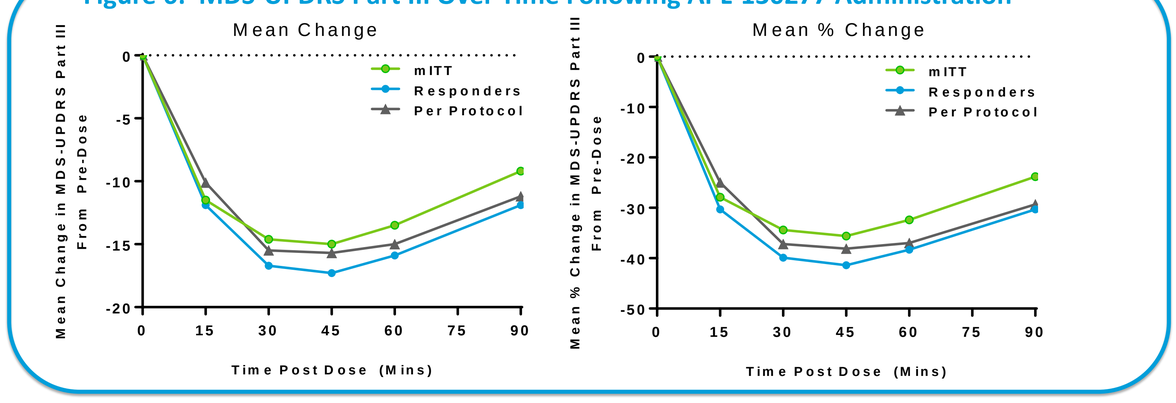
Figure 5: APL-130277 Dose Distribution at First Full ON (Responders)



Doses that converted patients from OFF to a full ON: All 5 Doses

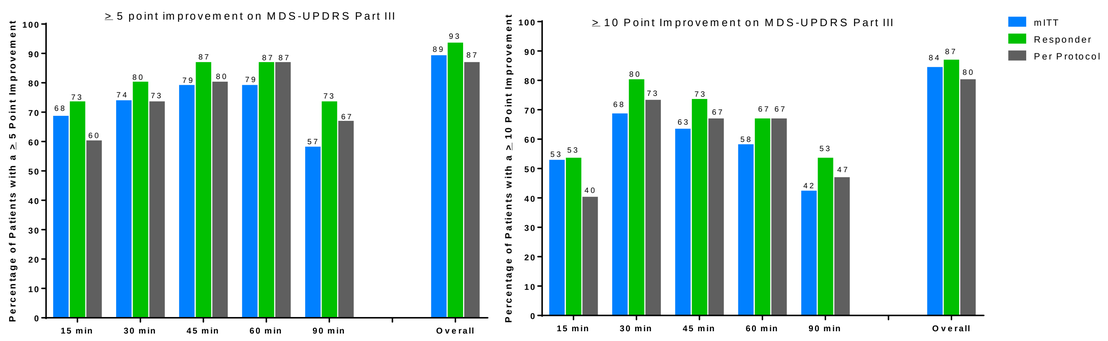
Mean Dose: 18.4 mg

Figure 6: MDS-UPDRS Part III Over Time Following APL-130277 Administration



- A statistically significant and clinically meaningful improvement in motor function was seen at all time-points as measured by MDS-UPDRS part III (Figure 6)

Figure 7: MDS-UPDRS Part III Improvement by Time-point



CONCLUSIONS

APL-130277:

- Rapidly converted PD patients' morning OFF to full ON
- Provided statistically significant and clinically meaningful improvement in motor function as assessed by MDS-UPDRS Part III scores

Average duration of benefit was nearly an hour

Most patients had a sustained benefit through 90 mins

Phase 3 studies have been initiated

ACKNOWELDGEMENTS

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