Baseline Disease Severity Not Predictive of Sublingual Apomorphine (APL-130277) Dose Needed to Convert a PD Patient from the OFF to ON State

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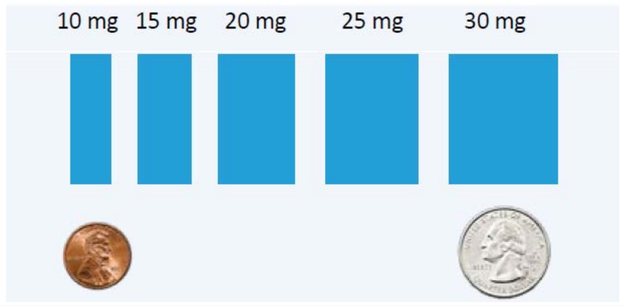
BACKGROUND

- 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 strip (APL-130277)



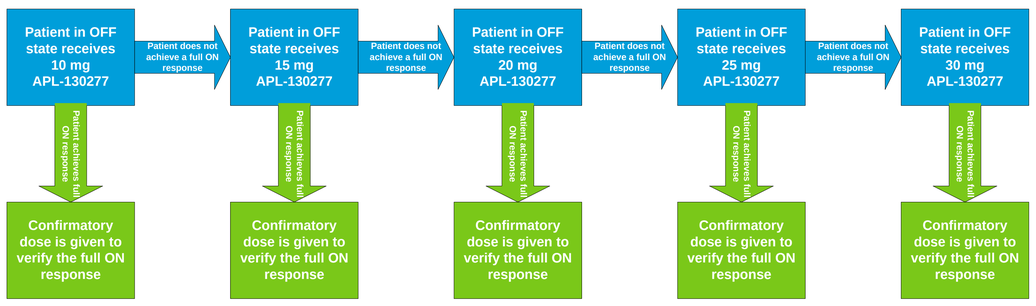
OBJECTIVE

Evaluate whether baseline PD disease severity predicted the effective dose of APL-130277

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 (Poster 2.086) & safety endpoints (Poster 2.089)

- 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
- Adverse events (AEs)
- ECG, vital signs (including orthostatic BP) and clinical lab values were evaluated

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)

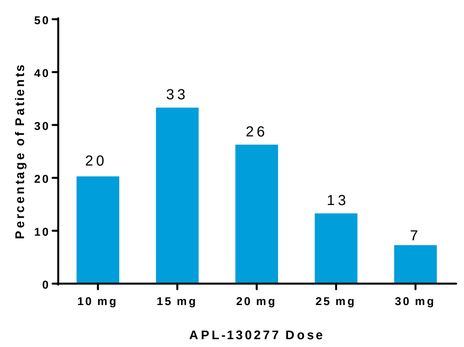
RESULTS

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)

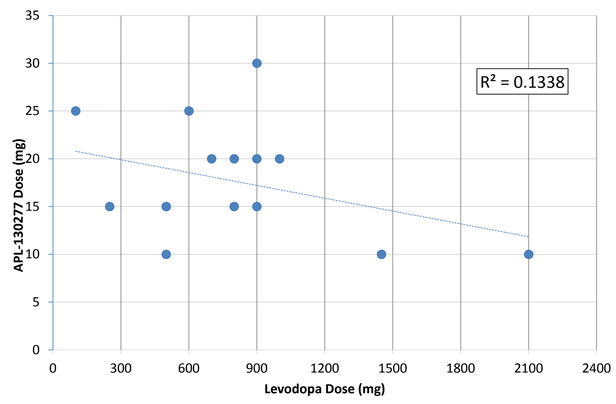
Figure 3: Dose Distribution at Full ON



APL-130277 Doses Converting Patients from OFF to a Full ON: All 5 Doses

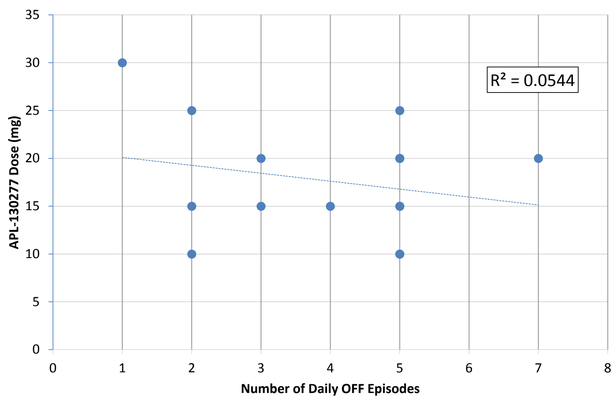
Mean Dose: 18.4 mg

Figure 4: Baseline Levodopa Dose vs. APL-130277 Dose at Full ON



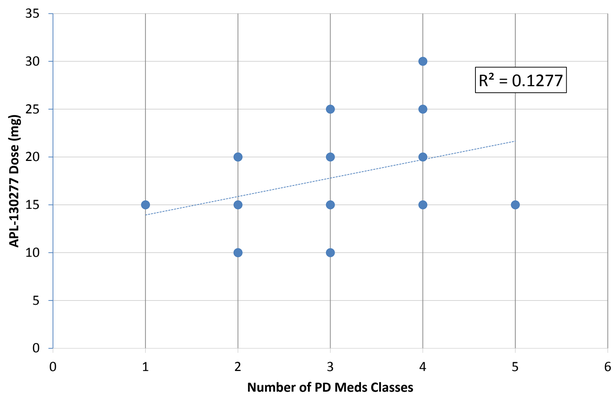
No correlation with baseline levodopa dose

Figure 5: Number of Daily OFF Episodes vs. APL-130277 Dose at Full ON



No correlation with # of daily OFF episodes

Figure 6: Number of PD Medications vs. APL-130277 Dose at Full ON



No correlation with # of daily PD medications

CONCLUSIONS

- APL-130277 rapidly converts PD patients from the OFF to the ON state.
- Baseline disease severity does not predict the effective dose needed to turn an OFF patient ON.
- PD patients should be titrated starting with the lowest possible dose.

ACKNOWELDGEMENTS

This study was supported by Cynapsus Therapeutics. Additionally, the Michael J. Fox Foundation provided a grant in support of the study. BD, TB, AG and AA are all employees of Cynapsus Therapeutics and hold stock or stock options. JD is a former employee of Cynapsus Therapeutics.

APL-130277 is currently an investigational product.

XXI World Congress on Parkinson's Disease and Related Disorders, 6-9 Dec 2015 ; Milan, Italy

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