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.

• Two clinical paradigms: peak-dose OFF (PD-OFF) and early-morning OFF (E-M-OFF)

• PD-OFF may lead to significant disability, depression, and reduced quality of life.

• PD-OFF can be related to the frequency of ON time during daily activities or by i.v. infusions of levodopa, but despite these interventions, most PD patients suffer OFF episodes daily.

• The oral, subcutaneous, and intravenous routes of APL-130277 administration (Apokyn® or Rotofer®) are highly efficacious due to the optimization of dosage regimen in this Phase 2 study.

• This Phase 2 Study examined the effects of APL-130277 in PD patients with OFF episodes.

• This was a Phase 2, open-label, single-arm study of APL-130277 in 19 PD patients with OFF episodes.

• All patients were pretreated with trimethobenzamide for 3 days prior to initiation of treatments of APL-130277.

• If a patient achieved a full ON response, they received a subsequent confirmatory dose.

• More convenient, on-demand, medications for the management of OFF episodes are needed.

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.

RESULTS

• The study was a Phase 2, open-label, single-arm trial.

• Patients were instructed to take their normal morning dose of medication no less than 12 PM the night prior and to go to sleep during the morning OFF time.

• Patients were dosed with APL-130277 at 15, 30, 45, 60 and 90 minutes before their usual morning dose of PD medications.

• An approximately 30% or greater MDS-UPDRS Part III improvement was seen at all time-points with a maximum mean percent change at any time-point of -45.6 for ITT Responders.

• A large percentage of patients had an 8 to 10 point improvement in the MDS-UPDRS Part III score at each time-point.

• 100% of patients in the ITT had a 2 point or greater improvement at any time-point.

• 100% of patients in the ITT had a 10 point or greater improvement at any time-point.

• Patients who did not respond at their first dose were dosed with the next dose of APL-130277.

• Sublingual APL-130277 rapidly converted PD patients from the morning OFF state to the ON state.

• APL-130277 was generally well tolerated

• A range of doses were utilized but over half of patients responded to the two lowest doses.

• Duration of benefit was close to an hour on average with most patients having sustained benefit for at least an hour.

• There were no serious adverse events that were considered related to APL-130277.

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

• APL-130277 is a non-opioid pain reliever and is not intended for the treatment of PD OFF episodes.

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REFERENCES

CONCLUSIONS

• Sublingual APL-130277 rapidly converted PD patients from the morning OFF state to the ON state.

• APL-130277 produced rapid, clinically meaningful improvement in motor function as assessed by the MDS-UPDRS Part III score.

• APL-130277 is generally well tolerated

• Overall, APL-130277 was safe and well tolerated

• Full Safety Data is presented as a poster presentation at the 19th Movement Disorders, 2015;30:389-395.

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