Efficacy of ND0612 for nocturnal parkinson symptoms and morning OFF: A blinded rater Phase 2 study

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Introduction

Nocturnal symptoms and early morning OFF (EMO) periods are significant contributors to poor quality of life in patients with Parkinson’s disease (PD) experiencing motor fluctuations.1,2 Patients suffer a variety of problems including difficulty turning in bed, restless legs and sleep fragmentation, as well as early morning akinesia, dystonia, and tremor.3

ND0612 is a drug-device combination that continuously delivers levodopa/ carbidopa (60/7.5 mg/ml) by subcutaneous infusion through a non-surgical mini-pump system to reduce motor complications in PD. Phase 1 & 2 trials have demonstrated that ND0612 maintained steady, therapeutic levodopa plasma concentrations that were associated with reduced OFF time.1

We have previously reported the primary efficacy results from this Phase 2 study (NCT02275253) which showed that continuous delivery of ND0612 reduced total daily OFF time. In this analysis of secondary outcomes, we focus on the benefits of treatment on nocturnal symptoms and EMO periods.

Methods

This was a 28-day randomised, parallel-group, open label, blinded-rater study.

Outcomes of interest include Change from baseline to endpoint in:

• Percentage of subjects with full ON at 8 & 9 AM (Key secondary endpoint)
• Night-time sleep quality, as assessed using PDSS-2
• Patient subjective assessment of sleep quality (5 point scale)
• Early morning (8 AM) UPDRS motor scores (post-hoc analysis).

Results

The proportion of subjects with full ON increased at 8AM and 9AM with 24 hour dosing (R1)

PDD-S scores significantly improved from baseline with 24-hour dosing (R1)

Early morning (8 AM) UPDRS motor scores significantly improved in both groups

Conclusions

24 hour, “round the clock” levodopa infusion with ND0612 significantly increased morning ON-time with a relevant improvement in motor status.

Sleep quality also improved, indicating that patients tolerated the pump overnight.

In this study, R2 (waking day dosing) was not optimised for night-time and early morning use because it provided a relatively low daily levodopa dose and daily treatment initiation was delayed until a nurse started the pump. A longer daytime regimen of 16 hours (LD/CD 720/90 mg) starting immediately upon waking is under evaluation (see poster 303 at this Congress for design and baseline characteristics of the Beyond study NCT02723886).

ND0612 may provide a novel non-surgical option for continuous 24 hour levodopa delivery in patients with PD experiencing motor fluctuations, in particular nocturnal symptoms and early morning OFF.

References


Disclosures

1. Study results were presented as a poster at the 22nd International Congress of Parkinson’s Disease and Movement Disorders, Hong Kong, October 5-9, 2018.

2. F. Stocchi and W. Poewe were investigators in the 006 study, and they or their institutions have received payment investigating the efficacy, safety and tolerability of 2 dosing regimens of ND0612. (Abstract). Mov Disord 2013;28(11 suppl 9):S740.

3. Ryan Case has received financial support from AbbVie, Pfizer, and Biogen for presentations at the 22nd International Congress of Parkinson’s Disease and Movement Disorders, Hong Kong, October 5-9, 2018.

4. F. Stocchi and W. Poewe are employees of NeuroDerm, and they or their institutions have received payment investigating the efficacy, safety and tolerability of 2 dosing regimens of ND0612. Mov Disord 2013;28:1151-60.