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The BeyoND study: Design and patient baseline characteristics of a study evaluating the long-term safety of ND0612 for Parkinson's disease

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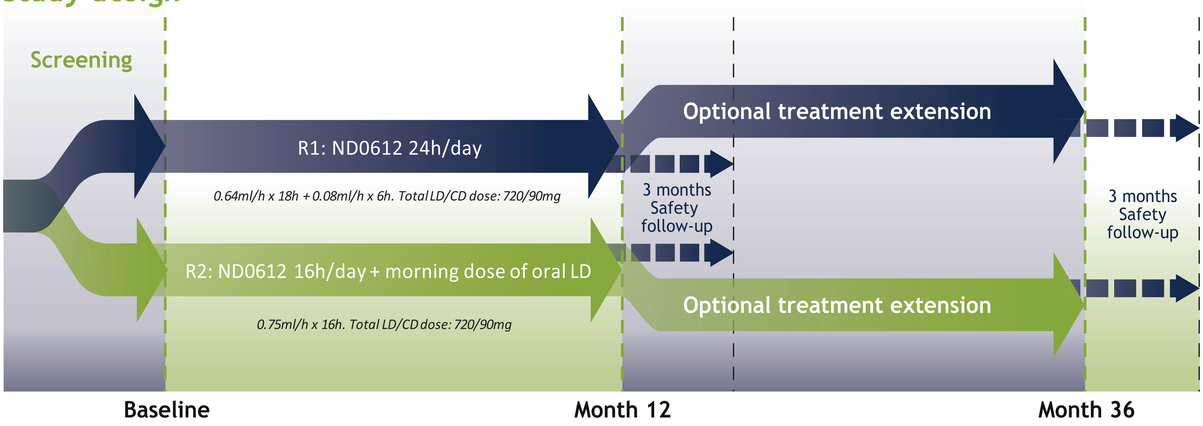
Introduction

- Continuous levodopa/carbidopa infusion is considered the optimal delivery route for treating patients with PD and advanced motor fluctuations because it avoids the peaks and troughs associated with oral dosing.[1, 2] However, current infusion systems must be surgically routed to the duodenum and are therefore associated with potentially serious complications.[3, 4]
- NeuroDerm has developed ND0612, a proprietary drug-device combination that continuously delivers liquid levodopa/carbidopa (60/7.5 mg/mL) by subcutaneous infusion through a non-surgical mini-pump system to reduce motor complications in fluctuating PD.
- Early Phase 2 trials have demonstrated that the low dose of ND0612 maintained steady, therapeutic levodopa plasma concentrations that were associated with reduced OFF time.[5, 6]
- The aim of this multi-center, international, open-label, Phase 2b safety study is to assess the long-term safety (systemic and local) and tolerability of continuous subcutaneous infusion of ND0612 by adverse events, vital signs, local tolerability.

Design

- BeyoND is an ongoing study of ND0612 for the management of motor fluctuations in PD. It is registered at Clinicaltrials.gov as NCT02726386.
- The study has 2 cohorts:
  1. Patients who recently (within 1 month of enrollment to BeyoND) completed the previous 006 study[6] (See poster P231 at this Congress).
  2. ND0612 naïve subjects and subjects who completed treatment in a ND0612 clinical study >1 month before screening.

Study design



Patients are assigned to open-label treatment with high dose ND0612 for either 24 hours or 16 hours + morning dose of oral LD, to a total LD/CD daily dose of 720/90mg. Adjunct oral PD medications can be taken as needed. Study treatment is administered by the patients and/or their study partners with clinic visits at Week 1, and Months 1, 2, 3, 4, 6, 9, and 12. After month 12, patients will be allowed to continue with study treatment for an extension period of 24 more months (Months 12-36) during which they return for clinic visits every 3 months.

Key inclusion/exclusion criteria

Key inclusion criteria	Key exclusion criteria
Male and female patients, aged 30 to 85 years	Previously unable to tolerate ND0612 and/or have experienced intolerable adverse drug reactions associated with its use, regardless of the dosing regimen administered
Modified Hoehn & Yahr score ≤3 during ON	**For patients new to ND0612 treatment:** • Atypical or secondary parkinsonism. • Acute psychosis or hallucinations in past 6 months • Any relevant medical, surgical, or psychiatric condition • Prior neurosurgical procedure for PD or LCIG treatment • Clinically significant ECG rhythm abnormalities
Taking ³4 levodopa doses/day (³3 doses/day of Rytary) and taking, or have attempted to take, at least 1 other PD treatment for at least 30 days in the previous year	
³2 hours of OFF time per day with predictable early morning OFF periods	

Baseline Characteristics

Characteristic	(N=209)
Percent male	66%
Age (years); mean ±SD	64. 1 ± 8.76
Duration of disease (years);	9.5 ± 4.9
Time with motor fluctuations (years); mean ±SD	5.23 ± 4.20
Duration of daily OFF time (hours); mean ±SD	5.47 ± 2.72
UPDRS motor score; mean ±SD	27.4± 12.5
MMSE score; mean ±SD	28.8 ± 1.2
Levodopa dose (mg); mean ±SD N (%) patients taking ≥900mg LD/day	1060 ± 665 109 (52.2%
Use of COMT inhibitor; N (%)	54 (25.8)

Conclusions

- Baseline characteristics are typical of patients with PD who suffer from motor fluctuations despite optimized oral treatment.
- This will be the first study to evaluate the long-term safety of high dose ND0612 in patients with PD experiencing motor fluctuations not adequately controlled with oral therapies.

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Disclosures

W. Poewe, F. Stocchi and A. Espay are investigators in the BeyonND study, and they or their institutions have received payment for participation. Clintrex LLC (K. Kieburtz and C. W. Olanow) provided consultancy for this study. S. Oren and R. Case are employed by NeuroDerm, and T. Rachmilewitz Minei was employed by NeuroDerm at the time of this study. No author has received financial remuneration for the preparation of this report. Assistance for this poster was provided by A. White and A. Patel (funded by NeuroDerm).