1ST RESULTS FROM A PHASE 2B, OPEN-LABEL STUDY EVALUATING LONG-TERM SAFETY OF ND0612 IN PD PATIENTS WITH MOTOR COMPLICATIONS

W. Poewe (werner.poewe@i-med.ac.at), F. Stocchi, N. Giladi, L. Adar, S. Fuch-Orenbach, O. Rosenfeld, L. Salin, C.W. Olanow

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Background and objective

- ND0612 is an investigational subcutaneous (SC) delivery system providing minimally invasive, continuous infusion of liquid levodopa/carbidopa for patients with PD experiencing motor fluctuations
- Phase II clinical studies of ND0612 in PD patients with motor fluctuations have shown a clinically meaningful **reduction in OFF time** with an **increase in ON time** with no or mild dyskinesia[1,2]

Primary objective:

To assess the long-term safety (systemic and local) and tolerability of continuous SC infusion with ND0612

Two regimens were tested:

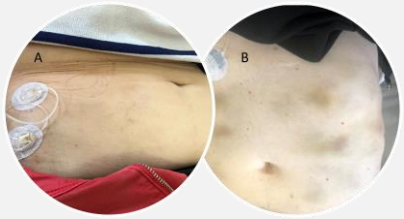
1. 24 hours 'round the clock' infusion
2. 16 hours 'waking day' infusion with a morning dose of oral levodopa

Both regimens provided a total LD/CD daily dose of 720/90mg

Baseline characteristics	24h/Day (N=90)	16h/Day (N=124)	Total (N=214)
Age (years)	64.2 ± 8.9	63.9 ± 8.9	64.0 ± 8.9
<65 years	47.8%	50.8%	49.5%
≥65 years	52.2%	49.2%	50.5%
Sex (Female/Male)	35.6% / 64.4%	32.3% / 67.7%	33.6% / 66.4%
Modified Hoehn & Yahr			
≤2	45.5%	45.9%	45.8%
2.5	18.9%	25.8%	22.9%
3	35.6%	28.2%	31.3%
Time since PD diagnosis (years)	10.6 ± 5.3	7.9 ± 3.8	9.0 ± 4.7
Time since fluctuations (years)	5.3 ± 4.3	5.2 ± 4.2	5.3 ± 4.2
Total daily levodopa dose (mg)	1090 ± 623	1004 ± 540	1040 ± 577
Concomitant medications			
Dopamine agonists	57.8%	46.8%	51.4%
MAO-B inhibitors	41.1%	35.5%	37.9%
COMT inhibitors	22.6%	26.7%	24.3%
Amantadine	27.8%	24.2%	25.7%

Adverse events	24h/Day (N=90)	16h/Day (N=124)	Total (N=214)
Any TEAE	78 (86.7%)	105 (84.7%)	183 (85.5%)
Drug-related TEAEs	65 (72.2%)	78 (62.9%)	143 (66.8%)
Infusion site TEAEs	55 (61.1%)	66 (53.2%)	121 (56.5%)
Serious TEAEs	17 (18.9%)	14 (11.3%)	31 (14.5%)
TEAEs leading to discontinuation	17 (18.9%)	20 (16.1%)	37 (17.3%)
Death	0	1 (0.8%)	1 (0.5%)

Infusion site TEAEs	24h/Day (N=90)	16h/Day (N=124)	Total (N=214)
Infusion site nodule	31 (34.4%)	35 (28.2%)	66 (30.8%)
Infusion site hematoma	24 (26.7%)	30 (24.2%)	54 (25.2%)
Infusion site infection	15 (16.7%)	11 (8.9%)	26 (12.1%)
Infusion site pain	13 (14.4%)	15 (12.1%)	28 (13.1%)
Infusion site erythema	9 (10.0%)	7 (5.6%)	16 (7.5%)
Infusion site edema	5 (5.6%)	5 (4.0%)	10 (4.7%)
Infusion site eschar	2 (2.2%)	15 (12.1%)	17 (7.9%)



Different patients' abdomens after 18 months of continuous infusion with ND0612

(A) Patient with a few nodules and hematomas

(B) Patient with more nodules and hematomas

- ✓ND0612 infusion was generally safe and well-tolerated
  - *Total exposure is >250 patient years*
  - *No unanticipated systemic TEAEs for levodopa/carbidopa*
  - *Mild to moderate infusion site reactions were common, and were typical for a continuous SC mode of drug administration*
- ✓Long-term data will continue to be collected in patients enrolled in the study extension, some of whom are now in their 5th year of treatment
- ✓A phase 3 double-blind, double-dummy pivotal efficacy trial (BouNDless) is underway to evaluate efficacy, safety and tolerability of ND0612 in a similar PD population

1. Giladi et al. 2015 Poster at MDS. 2. Olanow et al. 2021 Journal of Parkinson's Disease

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