The effect of subcutaneous foslevodopa/foscarbidopa on non-motor symptoms and non-motor fluctuations

Elisa Mantovani[1], Miriana Maria Bressan[1], Eleonora Bertoncello[1], Giorgio Lovato[1], Elisa Menini[1], Maria Conte[1], Ilaria Di Vico[1], Michele Tinazzi[1], Stefano Tamburin[1]

[1]Department of Neurosciences, Biomedicine and Movement Sciences, University of Verona, Italy

BACKGROUND AND AIMS

- Non-motor symptoms (NMS) and non-motor fluctuations (NMF) are common complications of Parkinson's disease (PD) and occur since early stages
- Their impact on patients' quality of life and disability increases in more advanced PD stages
- Subcutaneous foslevodopa/foscarbidopa has recently been introduced as an innovative treatment for motor fluctuations and troublesome dyskinesia in PD patients[1]
- **Aim:** to explore the effect of subcutaneous foslevodopa/foscarbidopa on NMS and NMF in PD patients

METHODS

- **Participants:** consecutive PD patients receiving subcutaneous foslevodopa/foscarbidopa at our Institution for inadequately controlled motor fluctuations
- **Procedures:** the Non-Motor Symptoms Scale (NMSS)[2] and the Non-Motor Fluctuation Assessment questionnaire (NoMoFa)[3] were administered at baseline and after 3, 6 and 12 months of therapy
- **Data analysis:** Normality was assessed using the Shapiro-Wilk test. Differences between assessment timepoints were analysed with the paired t-test (for normal distribution) or the Wilcoxon signed-rank test (for non-normal distribution). Statistical significance was set at $p < 0.05$ (two-tailed)

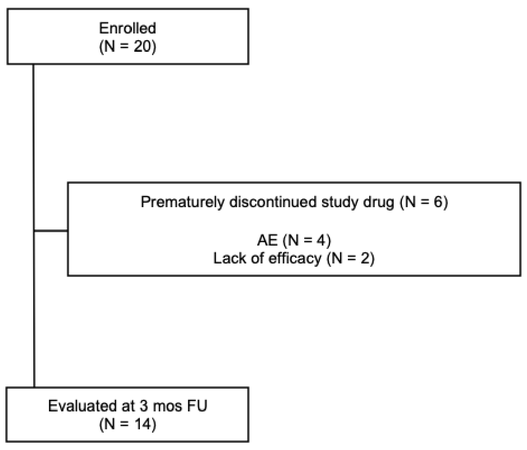

Figure 1. Patients' flow diagram. **Legend**. AE = adverse events; FU = follow-up; mos = months; N = number.

CONCLUSION

PD patients receiving subcutaneous foslevodopa/foscarbidopa may show improvements in NMS and NMF-related burden within a short time (3 months) after treatment initiation. Further data are needed to confirm these preliminary results.

RESULTS

- 20 patients were enrolled (Table 1) and a subset of 14 patients completed the baseline and 3-month follow-up assessments (Fig. 1)
- At baseline, all patients (100%) reported at least one NMS, with a mean total NMSS score of 71.0 (46.1)
- 16/20 patients (80%) reported at least one NMS in the OFF or ON state and were then considered as non-motor fluctuating, with a mean total NoMoFa score of 20.2 (16.0)
- The total NMSS score, cardiovascular and mixed subscores improved significantly at the 3-month follow-up (all $p < 0.05$) and a trend towards improvement was found for gastrointestinal and urinary subscores (all $p < 0.1$; Fig. 2)
- A trend towards improvement was also found for memory in the ON phase ($p = 0.087$), dysautonomia in the OFF condition ($p = 0.089$) and static score ($p = 0.087$; Table 2)

Table 1. Demographic and clinical variables of the overall sample at baseline

Variable[a]	Baseline (N = 20)
Demographic characteristics	
Gender (men/women), N (%)	9 (45%) / 11 (55%)
Age, y	69.9 ± 7.5
Education, y	10.2 ± 4.3
Clinical characteristics	
Age at PD onset, y	53.9 ± 7.1
PD duration, y	17.0 ± 6.1
H-Y	2.8 ± 1.1
UPDRS - III	48.5 ± 19.0
UPDRS - IV	9.4 ± 4.6
Daily "ON" time, hours	12.6 ± 3.9
Daily "OFF" time, hours	3.4 ± 2.5
Total LEDD, mg	1195.3 ± 468.3
MMSE, total score (raw)	26.4 ± 3.7
PDQ-8, summary index	14.2 ± 4.3

[a]Data reported as mean ± standard deviation unless otherwise stated

Legend. H-Y = Hoehn and Yahr stage; LEDD = Levodopa equivalent daily dose; mg = milligrams; MMSE = Mini Mental State Examination; N = number; y = years; PD = Parkinson's disease; PDQ-8 = 8-item Parkinson's Disease Questionnaire; UPDRS - III/IV = Movement Disorder Society-Unified Parkinson's Disease Rating Scale Part III/IV.

Figure 2. NMSS scores BL vs 3 mos FU

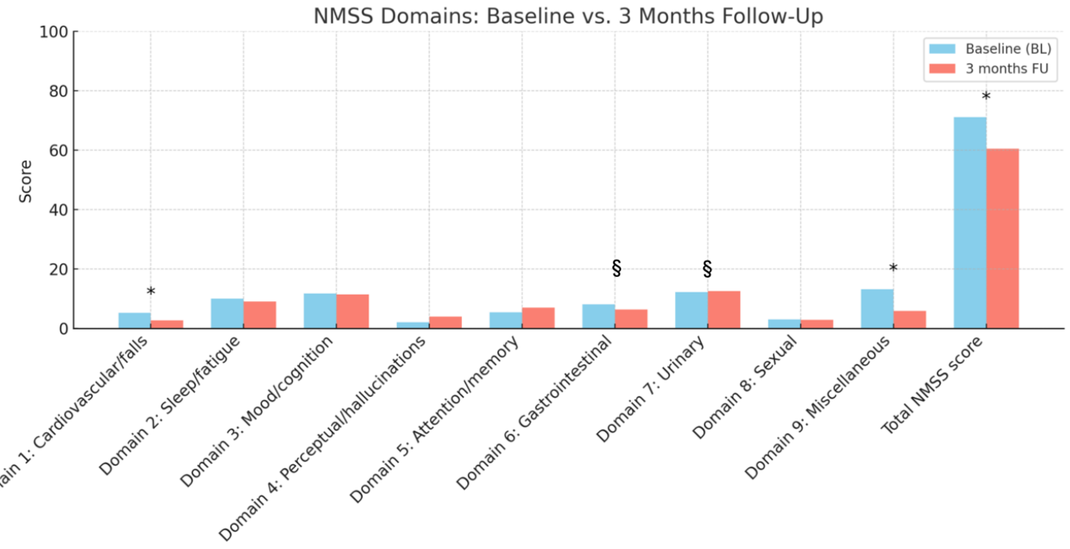

Table 2. Baseline and 3-month follow-up NoMoFa score and subscores, divided into the different non-motor symptoms domains.

NoMoFA domains	BL vs. 3 mos FU	Total symptoms[a]	NMF ON score[a]	NMF OFF score[a]	Total NMF score[a]	NMS (static) score[a]	NoMoFa score[a]
Attention (items 1-4)	**BL**	-	0.5 ± 1.5	0.8 ± 1.5	1.4 ± 2.2	1.4 ± 2.3	2.8 ± 3.3
	3 mos FU	-	0.9 ± 2.5	0.5 ± 1.1	1.5 ± 2.6	1.7 ± 2.5	3.1 ± 3.1
Language (item 5)	**BL**	-	0.1 ± 0.5	0.3 ± 0.8	0.4 ± 0.9	0.6 ± 0.8	1.0 ± 0.9
	3 mos FU	-	0 ± 0	0.6 ± 0.7	0.6 ± 0.7	0.2 ± 0.6	0.8 ± 0.8
Depression and Anxiety (items 6-10)	**BL**	-	0.4 ± 1.9	1.3 ± 3.0	1.8 ± 3.4	1.7 ± 2.6	3.4 ± 3.8
	3 mos FU	-	0 ± 0	1.2 ± 2.1	1.2 ± 2.1	1.4 ± 2.2	2.6 ± 2.6
Hallucinations/Perception (items 11, 23)	**BL**	-	0.3 ± 0.8	0 ± 0	0.3 ± 0.8	0.6 ± 1.0	0.9 ± 1.2
	3 mos FU	-	0.1 ± 0.3	0.5 ± 0.9	0.5 ± 0.9	0.7 ± 1.0	1.2 ± 1.4
Impulsiveness (items 12-14, 16)	**BL**	-	0.2 ± 0.5	0.3 ± 1.2	0.4 ± 1.5	0.9 ± 1.7	1.4 ± 2.0
	3 mos FU	-	0 ± 0	1.1 ± 2.5	1.1 ± 2.5	0.6 ± 0.9	1.7 ± 2.4
Memory (item 15)	**BL**	-	0.2 ± 0.7	0.1 ± 0.2	0.2 ± 0.7	0.7 ± 0.9	0.9 ± 0.9
	3 mos FU	-	***0 ± 0***[§]	0.5 ± 1.0	0.5 ± 1.0	0.6 ± 0.9	1.1 ± 1.1
Apathy (item 17)	**BL**	-	0.1 ± 0.5	0.1 ± 0.2	0.2 ± 0.5	0.2 ± 0.4	0.3 ± 0.6
	3 mos FU	-	0 ± 0	0.3 ± 0.6	0.3 ± 0.6	0.3 ± 0.6	0.6 ± 0.8
Sleep and fatigue (items 18, 19)	**BL**	-	0.3 ± 0.8	1.3 ± 1.8	1.6 ± 1.9	0.5 ± 0.9	2.1 ± 2.1
	3 mos FU	-	0 ± 0	1.1 ± 1.2	1.1 ± 1.2	0.9 ± 1.2	2.0 ± 1.1
Miscellaneous (items 20-22)	**BL**	-	0.7 ± 1.6	0.9 ± 1.4	1.5 ± 2.1	0.8 ± 1.3	2.3 ± 2.2
	3 mos FU	-	0 ± 0	1.1 ± 1.8	1.1 ± 1.8	1.1 ± 1.3	2.2 ± 1.6
Dysautonomia (items 24-27)	**BL**	-	0.3 ± 0.8	1.5 ± 2.3	1.8 ± 2.5	3.0 ± 2.7	4.8 ± 3.0
	3 mos FU	-	0.1 ± 0.3	***0.9 ± 1.4***[§]	1.0 ± 1.3	***2.7 ± 2.2***[§]	3.7 ± 2.0
Overall	**BL**	11 ± 7.0	3.2 ± 7.5	6.6 ± 9.3	9.8 ± 12.9	10.3 ± 9.2	20.2 ± 16.0
	3 mos FU	12.1 ± 5.9	1.1 ± 2.5	7.9 ± 10.7	9.0 ± 12.0	10.3 ± 8.7	19.3 ± 10.9

[a]Data reported as mean ± standard deviation unless otherwise stated.

Statistical difference between baseline and 3 mos FU value: * = $p < 0.05$; § = $p < 0.1$ (trend towards statistical significance).

Figure 2 and table 2 legend. BL = baseline; FU = follow-up; mos = months; NoMoFa = Non-Motor Fluctuation Assessment questionnaire; NMSS = Non-Motor Symptoms Scale.

REFERENCES

1. Soileau MJ, Aldred J, Budur K, et al. Safety and efficacy of continuous subcutaneous foslevodopa-foscarbidopa in patients with advanced Parkinson's disease: a randomised, double-blind, active-controlled, phase 3 trial. Lancet Neurol. 2023 Mar;22(3):e5. doi: 10.1016/S1474-4422(23)00048-0.
2. Cova I, Di Battista ME, Vanacore N, et al. Validation of the Italian version of the Non Motor Symptoms Scale for Parkinson's disease. Parkinsonism Relat Disord. 2017;34:38-42. doi: 10.1016/j.parkreldis.2016.10.020.
3. Balestrino R, Rinaldi D, Galli S, et al. Expanded and independent validation of the NoMoFA scale for Parkinson's disease: the Italian version. J Neurol. 2024;272(1):89. doi: 10.1007/s00415-024-12863-7.