Supplementary material for:

Patterns of Daily Motor-Symptom Control with Carbidopa/Levodopa Enteral Suspension Versus Oral Carbidopa/Levodopa in Advanced Parkinson's Disease: Clinical Trial Post-hoc Analyses

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Supplementary Table S1. Baseline characteristics

	CLES		IR-CL	
	N = 33		N = 30	
Demographic Characteristics				
Age (years), mean (SD)	64.0	(9.7)	64.9	(6.6)
Age category, n (%)				
< 65 years	18	(54.5%)	13	(43.3%)
≥ 65 years	15	(45.5%)	17	(56.7%)
Male, n (%)	22	(66.7%)	21	(70.0%)
Race, n (%)				
White	32	(97.0%)	27	(90.0%)
Black, of African heritage or African American	0	(0.0%)	0	(0.0%)
American Indian or Alaska Native	1	(3.0%)	0	(0.0%)
Asian	0	(0.0%)	3	(10.0%)
Native Hawaiian or other Pacific Islander	0	(0.0%)	0	(0.0%)
Ethnicity, n (%)				
Hispanic or Latino	2	(6.1%)	1	(3.3%)
Not Hispanic or Latino	31	(93.9%)	29	(96.7%)
Country, n (%)				
Germany	6	(18.2%)	7	(23.3%)
New Zealand	1	(3.0%)	1	(3.3%)
United States	26	(78.8%)	22	(73.3%)
Clinical Characteristics				
Height (cm), mean (SD)	171.4	(9.3)	171.4	(10.4)
Weight (kg), mean (SD)	75.7	(17.2)	75.5	(19.8)
BMI (kg/m^2), mean (SD)	25.6	(4.6)	25.6	(5.5)
Disease-Related Characteristics				
Advanced PD-related medical history				
Duration of Parkinson's disease (years), mean (SD)	10.2	(4.9)	11.8	(5.7)
Diagnosis of bradykinesia, n (%)	33	(100.0%)	30	(100.0%)
Diagnosis of muscular rigidity, n (%)	33	(100.0%)	30	(100.0%)
Diagnosis of 4-6 Hz resting tremor, n (%)	26	(78.8%)	24	(80.0%)
Diagnosis of postural instability, n (%)	20	(60.6%)	20	(66.7%)
Baseline disease severity, mean (SD)				
CGI-S	4.2	(0.7)	4.6	(0.7)
Modified Hoehn and Yahr staging	2.3	(0.7)	2.6	(0.7)
Treatment Characteristics				
Antiparkinsonian medication use, n (%)	33	(100.0%)	30	(100.0%)
Dopamine agonists	20	(60.6%)	22	(73.3%)

COMT inhibitors	16	(48.5%)	14	(46.7%)
MAO-B inhibitors	14	(42.4%)	7	(23.3%)
Parkinson's disease treatment history, n (%)				
Taking only one PD medication	5	(15.2%)	2	(6.7%)
Taking two PD medications	10	(30.3%)	10	(33.3%)
Taking three PD medications	9	(27.3%)	10	(33.3%)
Taking > three PD medications	9	(27.3%)	8	(26.7%)
Baseline daily dose of levodopa (mg), mean (SD)	1027.3	(382.0)	1145.0	(481.4)

Abbreviations:

BMI: body mass index; CGI-S: Clinical global impression - severity; cm: centimeters; CLES: carbidopa/levodopa enteral suspension; COMT: catechol-O-methyl transferase; Hz: hertz; IR-CL: immediate-release carbidopa/levodopa; kg: kilograms; m: meters; MAO-B: monoamine oxidase B; PD: Parkinson's Disease; SD: standard deviation.

Notes:

[1] Pooled data from NCT00357994 and NCT00660387 (full analysis sample).

[2] From the full analysis sample, three patients (one from the CLES group and two from the IR-CL group) were removed due to missing data in week 12. In addition, three patients (two from the CLES group and one from the IR-CL group) were removed due to one or more invalid diary days on days that would be used in the calculation of health state-related outcomes.

Supplementary Table S2. Improvement in health states across the waking day between CLES and IR-CL and Change from baseline to week 12 in patients with occurrence of extreme fluctuations and number of transitions

	Treatment difference [CLES - IR-CL]			
Table S2a. Improvement in health states across the waking day between CLES and IR-CL	**LS Mean**	**95% CI**	**P-value[1]**	
Average duration (minutes), mean (SD)				
"Off" time [OFF]				
From wake-up time to 4 hours after wake-up time	-82	(-128, -35)	0.0008	*
From 4 hours after wake-up time to 8 hours after wake-up time	-37	(-70, -3)	0.0325	*
From 8 hours after wake-up time to 12 hours after wake-up time	-51	(-95, -6)	0.0272	*
From 12 hours after wake-up time to end of waking day	-25	(-79, 28)	0.3451	
"On" time without troublesome dyskinesia [ON-woTD]				
From wake-up time to 4 hours after wake-up time	44	(13, 74)	0.0058	*
From 4 hours after wake-up time to 8 hours after wake-up time	18	(-12, 48)	0.2362	
From 8 hours after wake-up time to 12 hours after wake-up time	35	(5, 66)	0.0240	*
From 12 hours after wake-up time to end of waking day	11	(-21, 43)	0.4840	

	Change from Baseline							
Table S2b. Change from baseline to week 12 in patients with occurrence of extreme fluctuations and number of transitions	**CLES**		**P-value**		**IR-CL**		**P-value**	
Analysis sample size	**N = 33**				**N = 30**			
Health state fluctuations[2]								
Patients with occurrence of extreme fluctuations in a day, N (%)	-6	(-18.2%)	0.0143	*	-4	(-13.3%)	0.2059	
Transitions between health states during the waking day[3]								
Number of health-state transitions, mean (SD)	-3.5	(3.2)	0.0000	*	-2.0	(3.3)	0.0044	*
Distribution of health-state transitions across patients, N (%)			<0.0001	*			0.0043	*
0 to 3 transitions	+13	(+39.4%)			+2	(+6.7%)		
> 3 and up to 6 transitions	+4	(+12.1%)			+4	(+13.3%)		
> 6 and up to 9 transitions	-10	(-30.3%)			+0	(+0.0%)		
> 9 and up to 12 transitions	-4	(-12.1%)			-3	(-10.0%)		
> 12 transitions	-3	(-9.1%)			-3	(-10.0%)		

Abbreviations:

CI: confidence interval; CLES: carbidopa/levodopa enteral suspension; IR-CL: immediate-release carbidopa/levodopa; SD: standard deviation.

Notes:

[1] The p-value for treatment difference was obtained from analysis of covariance (ANCOVA) models, including effects for treatment, country, and with the corresponding baseline value as a covariate. An asterisk "*" denotes a p-value < 0.05.

[2] Comparisons within the treatment groups between baseline and week 12 outcome levels were conducted using McNemar's tests. An asterisk "*" denotes a p-value < 0.05.

[3] Comparisons within the treatment groups between baseline and week 12 outcome levels were conducted using Wilcoxon signed-rank tests for continuous outcomes and multinomial logit models with cluster-robust standard errors clustered at the patient level and finite-sample adjustment for the distributions of the categorical outcomes. An asterisk "*" denotes a p-value < 0.05.

Supplementary Table S3. Average levodopa dose at week 12

	CLES N = 33		IR-CL N = 30		P-value
Average levodopa dose within 4 hours of waking (mg), mean (SD)	368.09	(140.46)	382.82	(182.55)	0.9713
Average levodopa dose during the waking day (mg), mean (SD)	1162.38	(420.60)	1413.99	(612.61)	0.1080
Received levodopa dose outside of the waking day, N (%)	8	(24.2%)	9	(30.0%)	0.6071
Average levodopa dose outside of the waking day (mg), mean (SD)	131.25	(59.39)	98.98	(46.45)	0.2447