

SUPPLEMENTAL MATERIAL

Prevalence of Dyskinesia and OFF by 30-minute Intervals Through the Day and Assessment of Daily Episodes of Dyskinesia and OFF: Novel Analyses of Diary Data from Gocovri Pivotal Trials

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Part 1: Table 1. Diary population as derived from the mITT population

Diary Population	Gocovri (n = 100)	Placebo (n = 96)
Subjects with complete/evaluable diaries for both 24-hour periods at baseline and week 12	77 (77.0%)	85 (88.5%)
Subjects without complete/evaluable diaries for both 24-hour periods at either baseline or week 12	23 (23.0%)	11 (11.5%)
<i>Reason for exclusion</i>		
Incomplete at baseline but complete at week 12	2 (2.0%)	0
Complete at baseline and reached week 12, but with incomplete/not evaluable diary at week 12	3 (3.0%)	1 (1.0%)
Discontinued prior to week 12: Other: Suicide attempt during study	1 (1.0%)	0
Discontinued prior to week 12: Subject discontinued study drug and wished to withdraw	15 (15.0%)	5 (5.2%)
Discontinued prior to week 12: Subject lost to follow-up	1 (1.0%)	1 (1.0%)
Discontinued prior to week 12: Subject unwilling to proceed	1 (1.0%)	4 (4.2%)

Table 2. Mean changes (hours) across the entire day (24 hours) from baseline through week 12 in ON time with troublesome dyskinesia, OFF time, and ON time without troublesome dyskinesia

		Gocovri	Placebo
		(n = 77)	(n = 85)
<i>ON time with troublesome dyskinesia</i>			
Baseline	Mean (SD)	4.8 (2.58)	5.2 (2.77)
Week 12	Mean (SD)	1.5 (2.52)	3.1 (2.72)
Change from Baseline	LS Mean (SE)	-3.5 (0.30)	-2.0 (0.28)
	95% CI	-4.04, -2.87	-2.54, -1.43
Treatment Difference (Active-Placebo)	LS Mean (SE)	-1.5 (0.40)	
	95% CI	-2.27, -0.67	
	P-value	0.0004	
<i>OFF time</i>			
Baseline	Mean (SD)	3.1 (2.30)	2.6 (2.02)
Week 12	Mean (SD)	2.3 (2.12)	3.1 (2.55)
Change from Baseline	LS Mean (SE)	-0.7 (0.21)	0.4 (0.20)
	95% CI	-1.13, -0.28	0.04, 0.85
Treatment Difference (Active-Placebo)	LS Mean (SE)	-1.2 (0.29)	
	95% CI	-1.73, -0.57	
	P-value	0.0001	
<i>ON time without troublesome dyskinesia</i>			
Baseline	Mean (SD)	8.5 (3.31)	8.1 (3.06)
Week 12	Mean (SD)	12.2 (3.26)	9.5 (3.61)
Change from Baseline	LS Mean (SE)	3.9 (0.37)	1.4 (0.35)
	95% CI	3.22, 4.66	0.71, 2.08
Treatment Difference (Active-Placebo)	LS Mean (SE)	2.5 (0.50)	
	95% CI	1.56, 3.53	
	P-value	<0.0001	

Treatment difference were calculated using the Mixed-Effect Model Repeated Measure model.

Part 2: Instructions for patients' Parkinson's disease (PD) home diaries (as specified in each study's Statistical Analysis Plan).

Diary keeping:

Each subject will record data to score 5 different conditions in 30-minute intervals: ASLEEP, OFF, ON without dyskinesia, ON with non-troublesome dyskinesia, and ON with troublesome dyskinesia (Hauser, Friedlander, 2000). A set of 2 consecutive 24-hour PD home diaries (48 hours total) will be completed during screening and prior to each specified visit. The consecutive 24-hour diaries may be started 3 days before a visit, if the subject's schedule makes it difficult to complete a diary during the day before a visit. The schedule for diary completion should be determined in advance for each subject.

Criteria for evaluable diaries:

All 24-hour diaries will be reviewed for evaluability. If 4 or fewer 30-minute intervals are marked "Subject did not respond" or "missing" on the Electronic Case Report Form (eCRF), the 24-hour diary will be considered evaluable and will be included in the analysis. If more than four 30-minute intervals are marked "Subject did not respond" on the eCRF, the 24-hour diary will be considered unevaluable and will not be included in the analysis. The value for "missing intervals" of the evaluable diaries will be imputed from the prior and subsequent intervals as described below.

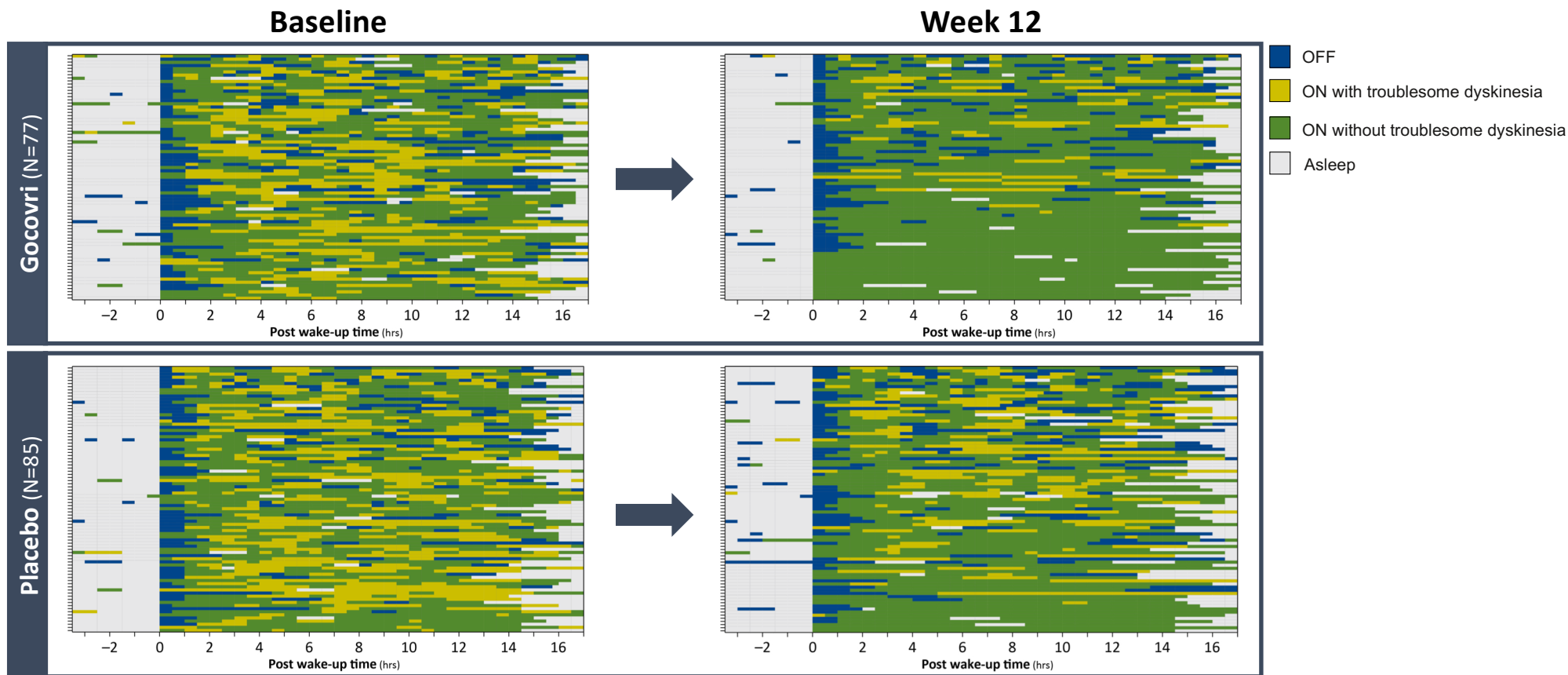
Imputation rules for missing data:

If 4 or fewer 30-minute intervals are not available or are missing, the value for a missing response interval will be imputed by assigning the 30 minutes of each missing interval, in equal portions of 15 minutes each, to the responses of the immediately preceding and subsequent completed (non-missing) intervals. If a missing response interval occurs at the beginning or end of a 48-hour diary reporting period such that it does not have both preceding and subsequent completed intervals, then the 30 minutes of the missing interval will be assigned to the closest completed (non-missing) interval. If both 24-hour diaries are evaluable for a study visit, data from both diaries may be used to impute missing interval values.

Part 3: PD home-diary time lines recorded at baseline and at 12 weeks by individual diary-population patients (N = 162)

Note: This analysis includes mITT population subjects who have evaluable diaries for both 24- hour periods at baseline and Week 12. The WAKE-UP time ($t = 0$) will be identified for each subject as the start of the first of 4 consecutive intervals that do not contain "ASLEEP," beginning at 3:00 AM (the 3:30 AM time interval) from the first 24-hour period.

Individual Patient Diary Plots (N=162)^a



^aPatients are organized in descending order of number of episodes reported at week 12 (with baseline reordered to match, so that patient order is the same at baseline and week 12)