Effect of a multi-layer, extended-release methylphenidate formulation (PRC-063) on sleep in adults with ADHD: A randomized, double-blind, forced-dose, placebo-controlled trial followed by a 6-month open-label extension

CNS Drugs

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SUPPLEMENTARY MATERIAL

Online Resource 1: Global PSQI score: double-blind treatment and open-label extension

	Double-blind treatment		Open-label extension
	PRC-063 (all doses) (N=297)	**Placebo (N=78)**	**PRC-063 (all doses) (N=184)**
Global PSQI change from baseline at the end of double-blind treatment			
LS mean	-0.7	-1.3	
LS mean difference vs. placebo	0.6		
95% CI difference vs. placebo	-0.1, 1.4		
P value [a]	0.0972		
Mean (SD) global PSQI			
End of double-blind treatment (N=181)			7.8 (3.55) [b]
Month 1 (N=175)			5.8 (3.11)
Month 2 (N=163)			5.4 (3.00)
Month 3 (N=147)			5.5 (3.23)
Month 4 (N=139)			5.4 (3.19)
Month 5 (N=133)			5.3 (3.40)
Month 6 (N=124)			5.4 (3.21)

CI confidence interval, *LS* least-squares, *PSQI* Pittsburgh Sleep Quality Index, *SD* standard deviation

[a] Change from baseline vs. placebo (analysis of covariance with baseline score as a covariate)

[b] Mean (SD) global PSQI score at the end of double-blind treatment for patients who entered the open-label extension study and had available data for analysis.

Online Resource 2: Shift table for good and poor sleepers: double-blind treatment and open-level extension

	Sleep status[a] at baseline[b]							
	Double-blind study					**Open-label extension**		
	PRC-063 (all doses) (N=297)		**Placebo (N=78)**			**PRC-063 (all doses) (N=184)**		
Sleep status at end of study, n (%)[a]	Good	Poor	Good	Poor	Missing	Good	Poor	Missing
Good	31 (11.2%)	39 (14.0%)	14 (19.4%)	14 (19.4%)		28 (22.8%)	42 (34.1%)	
Poor	26 (9.4%)	182 (65.5%)	2 (2.8%)	42 (58.3%)		7 (5.7%)	46 (37.4%)	
Missing	5	14	2	3	1[c]	12[d]	48[e]	1[f]

PSQI Pittsburgh Sleep Quality Index

[a] Global PSQI score >5 indicates poor sleep quality and a score ≤5 indicates good sleep quality

[b] Baseline for the double-blind study refers to start of study; baseline for the open-label extension study refers to end of the double-blind study

[c] One patient who received placebo in the double-blind study did not complete a baseline PSQI or end of study PSQI but did complete the study

[d] For patients with good sleep at baseline in the open-label extension study, 7 of the 12 patients with missing shift data (58.3%) had withdrawn from the open-label extension study

[e] For patients with poor sleep at baseline in the open-label extension study, 19 of the 48 patients with missing shift data (39.6%) had withdrawn from the open-label extension study

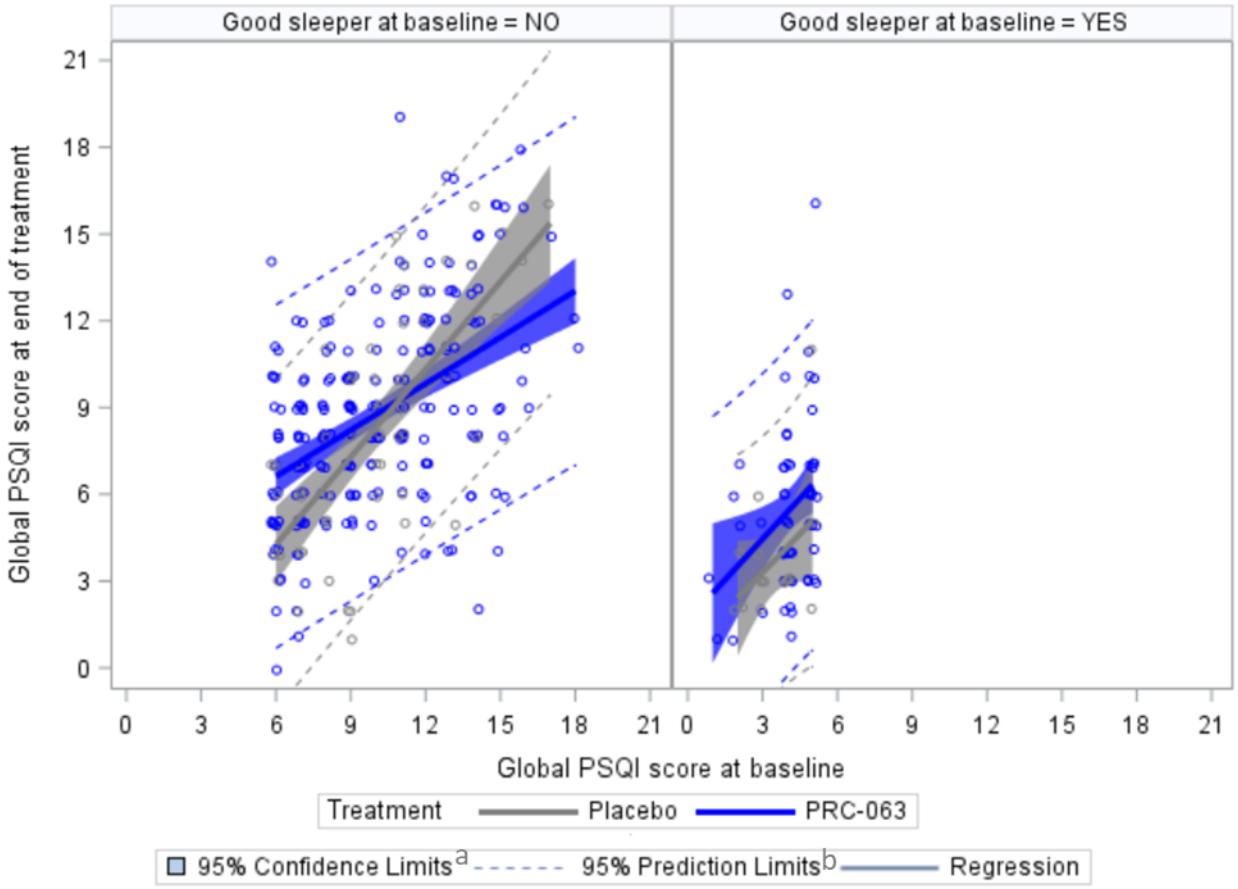
[f] One patient did not complete a baseline PSQI or end of study PSQI

Online Resource 3: Type 3 logistic regression analysis of effects of different variables as predictors of poor sleep (global PSQI score >5) at the end of double-blind treatment

Effect	DF	Wald chi-square	P value
Study treatment	4	6.87	0.1428
Sex	1	3.04	0.0814
Age	1	2.68	0.1017
Global PSQI score at baseline	1	57.60	<0.0001
Prior ADHD stimulant treatment	1	0.00	0.9442
BMI	1	0.15	0.7001
ADHD type	2	2.39	0.3032

ADHD attention deficit/hyperactivity disorder, *BMI* body mass index, *DF* degrees of freedom, *PSQI* Pittsburgh Sleep Quality Index

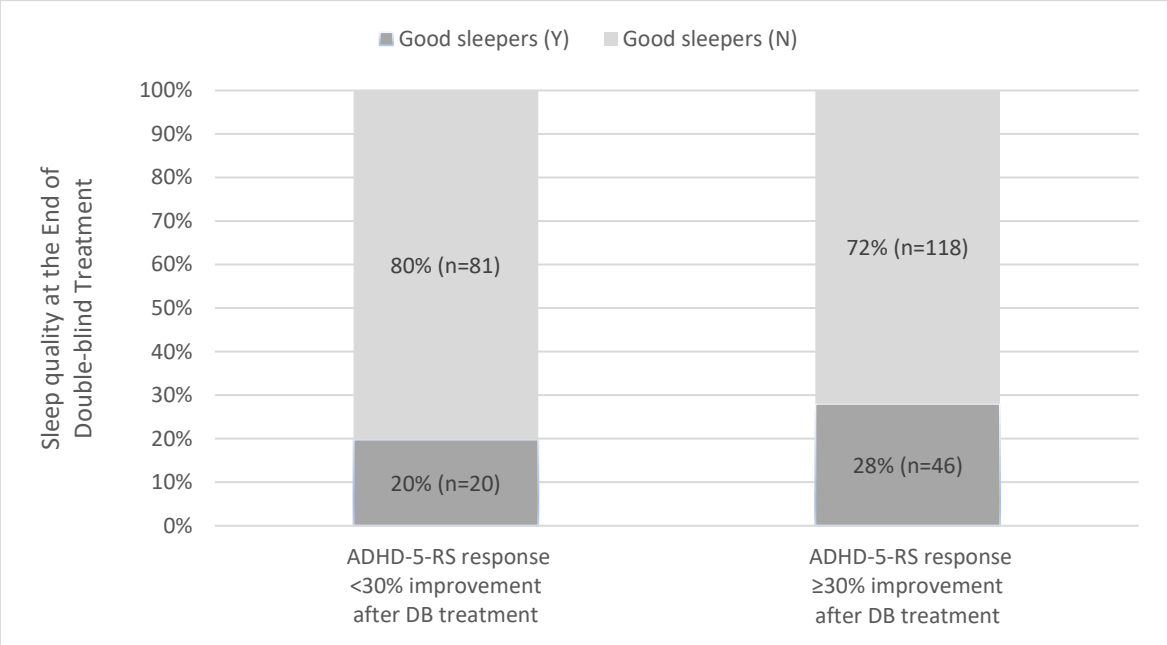
Online Resource 4: Scatter plot of individual global Pittsburgh Sleep Quality Index (PSQI) scores at baseline and end of double-blind treatment for patients treated with PRC-063 versus placebo. Left: "poor" sleepers at baseline. Right: "good" sleepers at baseline. Good sleep was defined as a global PSQI score of ≤5 and poor sleep as a global PSQI score of >5.



[a] 95% confidence limits are the shaded areas around the regression line representing the 95% upper and lower confidence intervals for the expected value of the dependent variable (mean) for each observation.

[b] 95% prediction limits are the dashed lines providing the 95% upper and lower confidence intervals for an individual predicted value.

Online Resource 5: Proportion of good sleepers at the end of double-blind treatment according to attention deficit/hyperactivity disorder (ADHD) symptom response for patients treated with PRC-063. ADHD responders were patients who showed a ≥30% improvement in ADHD-5-RS score between baseline and the end of double-blind treatment. Good sleep was defined as a global Pittsburgh Sleep Quality Index score of ≤5. *DB* double-blind, *N* no, *Y* yes.



Online Resource 6: Mean global Pittsburgh Sleep Quality Index (PSQI) scores for PRC-063-treated patients who were good sleepers at the end of double-blind treatment according to ADHD response. ADHD responders were patients who showed a ≥30% improvement in ADHD-5-RS score between baseline and the end of double-blind treatment. Good sleep was defined as a global PSQI score of ≤5 and poor sleep as a global PSQI score of >5. Solid red lines indicate mean values. *N* no, *Y* yes.