

Supplementary

Supplementary Table 1. Comparison of sleep parameters in the pre-treatment attending to order sequence A/B vs. B/A for agomelatine or placebo obtained from ACM recordings.

Sleep parameters	Agomelatine – Pre-treatment				Placebo – Pre-treatment			
	A/B	B/A	p-value	Cohen's <i>d</i>	A/B	B/A	p-value	Cohen's <i>d</i>
Total Sleep Time (min)	459±202	420±84	0.473	0.25	551±76	535±136	0.628	0.15
Time in bed (min)	734±164	616±64	0.955	0.94	704±54	675±90	0.475	0.39
Sleep Onset Latency (min)	54±22	60±30	0.853	0.23	43±14	57±30	0.629	0.60
Number of awakenings	4±2	3±1	0.183	0.63	4±1	3±2	0.368	0.63
Wake After Sleep Onset (min)	148±129	94±13	0.824	0.59	91±8	90±50	1	0.03
Sleep Efficiency (%)	62	68	0.128	0.32	78	79	1	0.13

Data is expressed as mean ± standard deviation or as percentage. P values correspond to the comparison among individuals in sequence A/B vs B/A. Cohen's *d* refers to size effect. [A] Agomelatine, [B] Placebo, and [Min] minutes.

Supplementary Table 2. Comparison of sleep parameters in the post-treatment attending to order sequence A/B vs. B/A for agomelatine or placebo obtained from ACM recordings.

Sleep parameters	Agomelatine – Post-treatment				Placebo – Post-treatment			
	A/B	B/A	p-value	Cohen's <i>d</i>	A/B	B/A	p-value	Cohen's <i>d</i>
Total Sleep Time (min)	512±135	561±106	1	0.4	611±60	521±61	0.087	1.49
Time in bed (min)	696±140	732±84	0.639	0.31	761±66	694±79	0.639	0.92
Sleep Onset Latency (min)	61±17	43±25	0.104	0.84	51±22	55±27	0.806	0.16
Number of awakenings	4±2	5±3	0.804	0.39	4±1	3±2	0.452	0.63
Wake After Sleep Onset (min)	106±56	130±75	0.569	0.36	84±44	98±91	0.935	0.2
Sleep Efficiency (%)	73	77	0.626	0.35	80	76	0.512	0.41

Data is expressed as mean ± standard deviation or as percentage. P values correspond to the comparison among individuals in sequence A/B vs B/A. Cohen's *d* refers to size effect. [A] Agomelatine, [B] Placebo, and [Min] minutes.

Supplementary Table 3. Circadian sleep-wake rhythm indexes comparison for the motor activity rhythm in agomelatine and placebo treatments

Agomelatine					Placebo			
	Pre-treatment	Post-treatment	p-value	Cohen's <i>d</i>	Pre-treatment	Post-treatment	p-value	Cohen's <i>d</i>
IS	0.27±0.11	0.33±0.11	0.188	0.54	0.34±0.11	0.36±0.23	0.285	0.11
IV	1.05±0.22	1.09±0.12	0.500	0.23	0.94±0.34	0.98±0.11	0.285	0.16
RA	0.71±0.17	0.67±0.20	0.461	0.22	0.79±0.15	0.81±0.13	0.284	0.14
M10	18:16±5:53	14:45±1:57	0.024	0.80	14:43±1:36	15:26±2:08	0.180	0.38
VM10	27.54±16.43	31.44±11.28	0.216	0.28	29.21±14.98	26.78±11.11	0.285	0.18
L5	2:21±1:50	1:19±2:01	0.161	0.54	2:40±1:50	2:10±1:48	0.065	0.28
VL5	6.23±7.14	6.41±4.91	0.461	0.03	3.86±3.14	2.41±1.42	0.037	0.60
CFI	0.48±0.07	0.49±0.09	0.188	0.12	0.55±0.13	0.56±0.11	0.500	0.08

Non-parametric circadian rhythm analysis values expressed as mean ± SD. [IS] stands for inter-daily stability, [IV] for intraday variability, [RA] for relative amplitude, phase markers: [M5] and [M10], [L5] and [L10], indicate central values of consecutive 5- and 10- hour period of maximum and minimum values respectively, and [CFI] corresponds to the circadian function index. Statistically significant differences $p < 0.05$ are highlighted in bold. For all Cohen's *d* refers to size effect.

Supplementary Table 4. Circadian sleep-wake rhythm indexes comparison for the body position rhythm in agomelatine and placebo.

Agomelatine					Placebo			
	Pre-treatment	Post-treatment	p-value	Cohen's <i>d</i>	Pre-treatment	Post-treatment	p-value	Cohen's <i>d</i>
IS	0.36±0.17	0.48±0.15	0.213	0.75	0.42±0.20	0.57±0.21	0.039	0.73
IV	0.38±0.24	0.44±0.14	0.285	0.31	0.63±0.56	0.34±0.12	0.008	0.72
RA	0.42±0.18	0.44±0.17	0.252	0.11	0.52±0.08	0.58±0.13	0.078	0.55
M10	15:21±2:30	14:50±1:08	0.422	0.27	15:01±1:01	15:37±1:32	0.337	0.46
VM10	42.43±14.36	41.58±7.71	0.064	0.07	46.29±6.39	44.97±6.45	0.422	0.21
L5	23:26±4:38	1:57±2:13	0.074	0.69	2:54±2:18	2:21±2:31	0.200	0.23
VL5	19.02±13.00	16.54±6.79	0.180	0.24	15.05±4.39	12.17±4.74	0.156	0.63
CFI	0.53±0.11	0.57±0.11	0.180	0.36	0.59±0.08	0.66±0.09	0.031	0.822

Non-parametric circadian rhythm analysis values expressed as mean ± SD. [IS] stands for inter-daily stability, [IV] for intraday variability, [RA] for relative amplitude, phase markers: [M5] and [M10], [L5] and [L10], indicate central values of consecutive 5- and 10- hour period of maximum and minimum values respectively, and [CFI] corresponds to the circadian function index. Statistically significant differences $p < 0.05$ are highlighted in bold. For all Cohen's *d* refers to size effect.

Supplementary Table 5. Circadian sleep-wake rhythm indexes comparison for TAP rhythm in agomelatine and placebo treatments.

Agomelatine					Placebo			
	Pre-treatment	Post-treatment	p-value	Cohen's <i>d</i>	Pre-treatment	Post-treatment	p-value	Cohen's <i>d</i>
IS	0.49±0.24	0.55±0.13	0.406	0.32	0.55±0.1010	0.62±0.20	0.371	0.44
IV	0.48±0.32	0.47±0.11	0.289	0.04	0.52±0.26	0.39±0.19	0.231	0.57
RA	0.47±0.17	0.52±0.13	0.156	0.33	0.59±0.06	0.65±0.11	0.05	0.67
M10	15:46±2:17	14:51±1:26	0.242	0.31	15:11±1:14	15:06±2:03	0.10	0.05
VM10	0.60±0.18	0.56±0.06	0.125	0.30	0.56±0.09	0.56±0.09	0.473	0
L5	23:36±7:39	1:33±1:45	0.469	0.35	2:25±1:12	2:10±1:57	0.472	0.15
VL5	0.21±0.13	0.18±0.07	0.039	0.29	0.15±0.04	0.12±0.05	0.074	0.66
CFI	0.57±0.14	0.61±0.09	0.074	0.34	0.63±0.08	0.69±0.10	0.273	0.67

Non-parametric circadian rhythm analysis values expressed as mean ± SD. [IS] stands for inter-daily stability, [IV] for intraday variability, [RA] for relative amplitude, phase markers: [M5] and [M10], [L5] and [L10], indicate central values of consecutive 5- and 10- hour period of maximum and minimum values respectively, and [CFI] corresponds to the circadian function index. Statistically significant differences $p < 0.05$ are highlighted in bold. For all Cohen's *d* refers to size effect.

