Supplementary Material

List of Supplementary Material for the article

Disclaimer

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Supplementary eTable 1: SDS - Scores at baseline and last post-baseline assessment over 12 weeks of treatment (expressed as Mean ± SD)

	Agomelatine (N = 139)	Placebo (N = 131)	Escitalopram (N = 139)
Work			
Baseline	6.1 ± 2.0	6.5 ± 1.8	6.4 ± 1.8
Last value	2.7 ± 2.4	4.4 ± 2.8	2.8 ± 2.5
E (SE)	1.69 (0.35)		1.55 (0.35)
95% CI	[1.00 ; 2.38]		[0.87 ; 2.23]
P value [1]	<0.0001		<0.0001
Social life			
Baseline	6.5 ± 1.8	6.3 ± 2.1	6.6 ± 1.9
Last value	2.8 ± 2.4	4.4 ± 2.8	3.1 ± 2.6
E (SE)	1.55 (0.32)		1.28 (0.33)
95% CI	[0.92 ; 2.18]		[0.63 ; 1.92]
P value[1]	<0.0001		<0.001
Family life and home responsibilities			
Baseline	6.2 ± 1.9	6.1 ± 1.8	6.3 ± 1.7
Last value	2.9 ± 2.5	4.2 ± 2.7	2.9 ± 2.6
E (SE)	1.35 (0.32)		1.35 (0.32)
95% CI	[0.73 ; 1.98]		[0.70 ; 1.99]
P value[1]	<0.0001		<0.0001

[1] *Two sided Student's T-test for independent samples*
E (SE): Estimate (Standard Error) of the difference between treatment group means: Placebo minus Agomelatine or Escitalopram - 95% CI: Two-sided 95% Confidence Interval of the estimate - P value: p-value of treatment effect

Supplementary eTable 2: LSEQ in the FAS at last assessment over 12 weeks of treatment

		Agomelatine (N = 139)	Placebo (N = 131)	Escitalopram (N = 139)
Getting off to sleep score				
Last value	Mean ± SD	35.1 ± 15.9	41.8 ± 19.6	39.6 ± 20.0
	E (SE)		6.73 (2.17)	2.23 (2.41)
	95% CI		[2.45; 11.00]	[-2.52; 6.98]
	p-value [1]		0.002	0.357
Quality of sleep score				
Last value	Mean ± SD	30.7 ± 18.9	40.1 ± 23.6	37.5 ± 23.6
	E (SE)		9.40 (2.60)	2.66 (2.87)
	95% CI		[4.29; 14.51]	[-3.00; 8.32]
	p-value [1]		<0.001	0.355
Awakening score				
Last value	Mean ± SD	38.8 ± 19.7	43.7 ± 21.6	42.5 ± 21.5
	E (SE)		4.92 (2.52)	1.15 (2.62)
	95% CI		[-0.04; 9.88]	[-4.02; 6.31]
	p-value [1]		0.052	0.662
Integrity of behaviour score				
Last value	Mean ± SD	38.4 ± 20.3	43.5 ± 22.5	40.1 ± 22.2
	E (SE)		5.15 (2.61)	3.43 (2.72)
	95% CI		[0.02; 10.28]	[-1.92; 8.79]
	p-value [1]		0.049	0.208

[1] Two-sided Student's t-test

E (SE): Estimate (Standard Error) of the difference between treatment group means: Placebo minus Agomelatine or Escitalopram - 95% CI: Two-sided 95% Confidence Interval of the estimate - P value: p-value of treatment effect

Supplementary eTable 3: Most frequently reported emergent adverse events* during the double-blind treatment period (at least 2% of the patients in any group). – Safety set

Adverse events	Agomelatine (N = 139)	Placebo (N=131)	Escitalopram (N = 141)
All	47.5	44.3	48.2
Headache	7.2	7.6	12.8
Nasopharyngitis	4.3	5.3	5.7
Diarrhoea	4.3	1.5	6.4
Nausea	3.6	0.8	7.8
Dizziness	2.2	3.1	5.7
Somnolence	3.6	2.3	3.5
Insomnia	2.2	0.8	3.5
Hyperhidrosis	-	1.5	3.5
Dry mouth	1.4	2.3	0.7
Dyspepsia	2.2	1.5	0.7
Tension headache	-	3.1	1.4
Vision blurred	1.4	2.3	0.7
Anxiety	0.7	-	2.8
Abdominal pain	2.9	-	-
Bronchitis	2.2	0.8	-
Gamma-glutamyltransferase increased	2.2	-	0.7
Hypercholesterolemia	2.2	-	-
Neck pain	-	2.3	-

* expressed as percent of affected patients among exposed patients in the considered treatment group