

## SUPPLEMENTARY.

**Table S2. Main characteristics of the selected articles for the evaluation of the use of melatonergic antidepressants in comorbid depression and anxiety disorders**

Author, year	Sample characteristics	Affective disorder	Affective disorder assessment criteria	Details of medication treatment	Concomitant therapy	Duration of follow-up	Primary outcomes	Secondary outcomes	Adverse events	Number of dropouts
Petelin, Niinoya, et al., 2021	n=30, 30% men, mean age 40.27±16.2 years	F41.2	HAM-D HAM-A	Agomelatine (valdoxan) 25–50 mg	Not specified	84 days	↓HAM-D ↓HAM-A (p < 0.05)	↑SF12 (p < 0.05)	Agomelatine was shown to be well tolerated	4
Gushanskaya, Frolova, et al., 2015	n=42 patients, 35.7% men, mean age 45.6±6.8 years	F32.x, F43, F41.2, F33.x, F34, F31	HAM-D	Agomelatine (valdoxan) 25–50 mg	No data	42 days	↓HAM-D (p < 0.05)	↓CGI (p < 0.05)	Not specified	0
Butova, 2015	n=27, 25.9% men, mean age 48.56±9.10	F41.2	HAM-A HAM-D	Agomelatine (valdoxan) 25 mg	No data	90 days	↓HARS ↓HAM-D (p ≤ 0.001)	No data	No data	No data
Avedisova, Zakharova, et al., 2014	n=310, no data	F32.x, F33.x	HAM-D	Agomelatine (valdoxan) 25–50 mg	Diazepam — sibazon, relium (6.12%), phenazepam (3.06%), hydroxyzine — atarax (2.38%), medazepam — mezapam (2.04%), oxazepam — nozepam (0.34%).	8 weeks	↓HAM-D (p ≤ 0.001)	No data	Headache (1.94%), nausea (1.94%), dizziness (1.61%), daytime sleepiness (1.61%), less commonly heartburn, lethargy, neck muscle tension (0.32% each)	16
Pribytkov, Panova, et al., 2013	n=35, 25.7% men, mean age 38.7±13.1	F32.x, F33.x	MADRS	Agomelatine (valdoxan) 25–50 mg	No data	6 weeks	↓MADRS (p < 0.001)	↓CGI (p ≤ 0.001) ↓ISI (p ≤ 0.001)	Drowsiness (6.3%), nausea (6.3%), dizziness (3.1%)	No data
Avedisova, Zakharova, et al., 2013	n=310, 18.39% men, mean age 42.5±12.9	F32.x, F33.x	HAM-D	Agomelatine (valdoxan) 25–50 mg	Diazepam — sibazon, relium (6.12%), phenazepam (3.06%), hydroxyzine — atarax (2.38%), medazepam — mezapam (2.04%), oxazepam — nozepam (0.34%).	8 weeks	↓HAM-D (p ≤ 0.001)	↓LSEQ (p ≤ 0.001) ↓BSS (p = 0.023)	Headache (1.94%), nausea (1.94%), dizziness (1.61%), daytime sleepiness (1.61%), less commonly heartburn, lethargy, neck muscle tension (0.32% each)	16
Dubnitskaya, 2005	n=30, 37.5% men, mean age 39.8±2.5	F43	HAM-D	Fluvoxamine 100–300 mg	No data	8 weeks	↓HAM-D (p < 0.01)	↓CGI (p < 0.01)	Daytime sleepiness (20%), dyspeptic symptoms (16.7%), insomnia (3.3%)	0

Note: F41.2 — Mixed anxiety and depressive disorder; F32.x — depressive episode; F43 — adjustment disorder; F33.x — recurrent depressive disorder; F34 — cyclothymic disorder; F31 — bipolar affective disorder; HAM-D — Hamilton Depression Rating Scale; HAM-A — Hamilton Anxiety Rating Scale; MADRS — Montgomery-Åsberg Depression Rating Scale; SF12 — The Short Form (12) Health Survey; CGI — Clinical Global Impression Scale; ISI — Insomnia Severity Index; BSS — Beck Scale for Suicide Ideation; LSEQ — Leeds Sleep Evaluation Questionnaire; ↓ — decrease in indicators; ↑ — increase in indicators.