SUPPLEMENTAL INFORMATION

Therapeutic Potential of Vortioxetine for Anxious Depression: A Post Hoc Analysis of Data From a Clinical Trial Conducted in Japan

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S1 List of Independent Ethics Committees/Institutional Review Boards

ClinicalTrials.gov identifier for primary study: NCT02389816.

- Institutional Review Board of Medical Corporation Jisenkai Nankokokorono Clinic
- Suzuki Internal & Circulatory Medical Clinic Institutional Review Board
- Institutional Review Board of Medical Corporation Jisenkai Ichigaya-Himorogi Clinic
- Sugiura Clinic Institutional Review Board
- Shin-Nihonbashi Ishii Clinic Institutional Review Board
- Sakayori Clinic Institutional Review Board
- Review Board of Human Rights and Ethics for Clinical Studies Institutional Review Board
- Adachi Kyousai Hospital Institutional Review Board
- Japan Community Health-care Organization, Tokyo Shinjuku Medical Center Institutional Review Board
- Yamate Dermatological Clinic Institutional Review Board
- Clinical Research Hospital Tokyo Institutional Review Board
- Mizuo Clinic Institutional Review Board
- Yoyogi Mental Clinic Institutional Review Board
- Haradoi Hospital Institutional Review Board
- Goshogatani Home Clinic Institutional Review Board
- Yuge Neuropsychiatric Hospital Institutional Review Board
- Sapporo Psychotropic Institutional Review Board
- National Hospital Organization Kanazawa Medical Center Institutional Review Board
- Japan Conference of Clinical Research Institutional Review Board
- Nishi Hospital Institutional Review Board
- Hanna Hospital Institutional Review Board
- Imazato Gastrointestinal Hospital Institutional Review Board
- Institutional Review Board of Non-profit organization Tokyo Allergy and Respiratory Disease Research Institute
- Kyorin University Hospital Institutional Review Board
- Akasaka Clinic Institutional Review Board

S2 LS Mean Difference in MADRS Subscale Scores Versus Placebo, From Baseline to Week 8 (LOCF; Subgroup Analysis)

Subscale	**Anxious Depression**		**Non-Anxious Depression**	
	Vortioxetine 10 mg (n=94)	**Vortioxetine 20 mg (n=97)**	**Vortioxetine 10 mg (n=71)**	**Vortioxetine 20 mg (n=65)**
Apparent sadness	−0.36	−0.56	−0.31	−0.27
Reported sadness	−0.61	−0.74	−0.05	−0.12
Inner tension	−0.29	−0.51	−0.26	−0.30
Reduced sleep	−0.41	−0.39	−0.15	0.08
Reduced appetite	−0.56	−0.55	−0.06	0.18
Concentration difficulties	−0.20	−0.38	−0.29	−0.25
Lassitude	−0.21	−0.34	−0.10	−0.13
Inability to feel	−0.26	−0.42	−0.22	−0.13
Pessimistic thoughts	−0.45	−0.45	−0.11	−0.04
Suicidal thoughts	−0.16	−0.27	−0.01	0.03

Anxious depression was defined by a HAM-D anxiety/somatization factor score ≥7, whereas non-anxious depression was defined by a score <7. The HAM-D anxiety/somatization factor score is derived from the sum of the following subscales: Q10, Anxiety (psychic); Q11, Anxiety (somatic); Q12, Somatic Symptoms (G.I.); Q13, Somatic Symptoms (general); Q15, Hypochondriasis; and Q17, Insight. HAM-D, Hamilton Depression Rating Scale; LOCF, last observation carried forward; LS, least-squares; MADRS, Montgomery–Åsberg Depression Rating Scale.

S3 Changes in HAM-D17, DSST, SDS, and PDQ-5 From Baseline at Week 8 (LOCF; Subgroup Analysis)

Outcome Measure	Subgroup	Treatment	n	LS Mean Change	SE	LS Mean Difference From Placebo	95% CI
HAM-D17	Anxious depression	Placebo	85	−7.90	0.75	–	–
		Vortioxetine 10 mg	93	−10.29	0.72	−2.39	−4.44, −0.34
		Vortioxetine 20 mg	94	−11.19	0.72	−3.29	−5.33, −1.24
	Non-anxious depression	Placebo	68	−8.96	0.76	–	–
		Vortioxetine 10 mg	70	−10.06	0.75	−1.11	−3.22, 1.00
		Vortioxetine 20 mg	64	−8.71	0.79	0.25	−1.92, 2.41
DSST	Anxious depression	Placebo	91	3.33	0.87	–	–
		Vortioxetine 10 mg	94	4.72	0.86	1.38	−1.02, 3.78
		Vortioxetine 20 mg	97	5.32	0.84	1.99	−0.39, 4.37
	Non-anxious depression	Placebo	70	6.96	0.90	–	–
		Vortioxetine 10 mg	69	3.32	0.90	−3.64	−6.15, −1.13
		Vortioxetine 20 mg	65	4.06	0.93	−2.89	−5.44, −0.35

SDS	Anxious depression	Placebo	85	−2.68	0.62	–	–
		Vortioxetine 10 mg	93	−4.47	0.59	−1.79	−3.47, −0.10
		Vortioxetine 20 mg	94	−5.03	0.59	−2.35	−4.04, −0.67
	Non-anxious depression	Placebo	68	−3.05	0.64	–	–
		Vortioxetine 10 mg	70	−3.83	0.63	−0.77	−2.55, 1.00
		Vortioxetine 20 mg	64	−3.57	0.67	−0.51	−2.34, 1.32
PDQ-5	Anxious depression	Placebo	91	−1.43	0.32	–	–
		Vortioxetine 10 mg	94	−2.26	0.32	−0.83	−1.72, 0.07
		Vortioxetine 20 mg	97	−2.89	0.31	−1.45	−2.34, −0.57
	Non-anxious depression	Placebo	70	−1.38	0.34	–	–
		Vortioxetine 10 mg	71	−2.30	0.34	−0.92	−1.86, 0.02
		Vortioxetine 20 mg	65	−2.40	0.35	−1.02	−1.99, −0.05

Anxious depression was defined by a HAM-D anxiety/somatization factor score ≥7, whereas non-anxious depression was defined by a score <7. The HAM-D anxiety/somatization factor score is derived from the sum of the following subscales: Q10, Anxiety (psychic); Q11, Anxiety (somatic); Q12, Somatic Symptoms (G.I.); Q13, Somatic Symptoms (general); Q15, Hypochondriasis; and Q17, Insight. CI, confidence interval; DSST, Digit Symbol Substitution Test; HAM-D, Hamilton Depression Rating Scale; LOCF, last observation carried forward; LS, least-squares; PDQ-5, Perceived Deficit Questionnaire-5; SDS, Sheehan Disability Scale; SE, standard error.