

Introduction

- The aim of this study was to examine the efficacy of vortioxetine for depression in Alzheimer's disease (AD).
- Vortioxetine has a different mechanism of action from commonly prescribed TCAs, SSRIs, and SNRIs, so it may be considered a possible choice for treatment of depression in patients with AD.

Methods

A prospective, randomized, double-blind, placebo-controlled study included 100 depressed AD patients, who were assigned randomly to receive 12 weeks of daily treatment with vortioxetine or placebo.

Primarily, the change in depression symptoms were measured by the Cornell Scale for Depression in Dementia(CSDD) from baseline to 12 weeks. For further efficacy measuring, depressive symptoms (SGDS-K), the Korean version of the Mini-Mental State Examination (MMSE-K), cognitive function in several domains [the Seoul Verbal Learning Test (SVLT), the Digit Symbol Substitution Test (DSST), contrasting program, go-no-go, digit span, the verbal fluency, the Korean version of the Boston Naming Test (K-BNT), constructional praxis test, word list test, Basic Activities of Daily Living (BADL), Instrumental Activities of Daily Living (IADL)] were used. Safety and tolerability were also assessed. Intention-to-treat analysis using the hierarchical linear modeling was applied to confirm the efficacy of vortioxetine for patients with depression in AD. Independent t-test was also used to compare cognitive function scores between vortioxetine responders and non-responders.

Results

Figure 1. Flow of participants

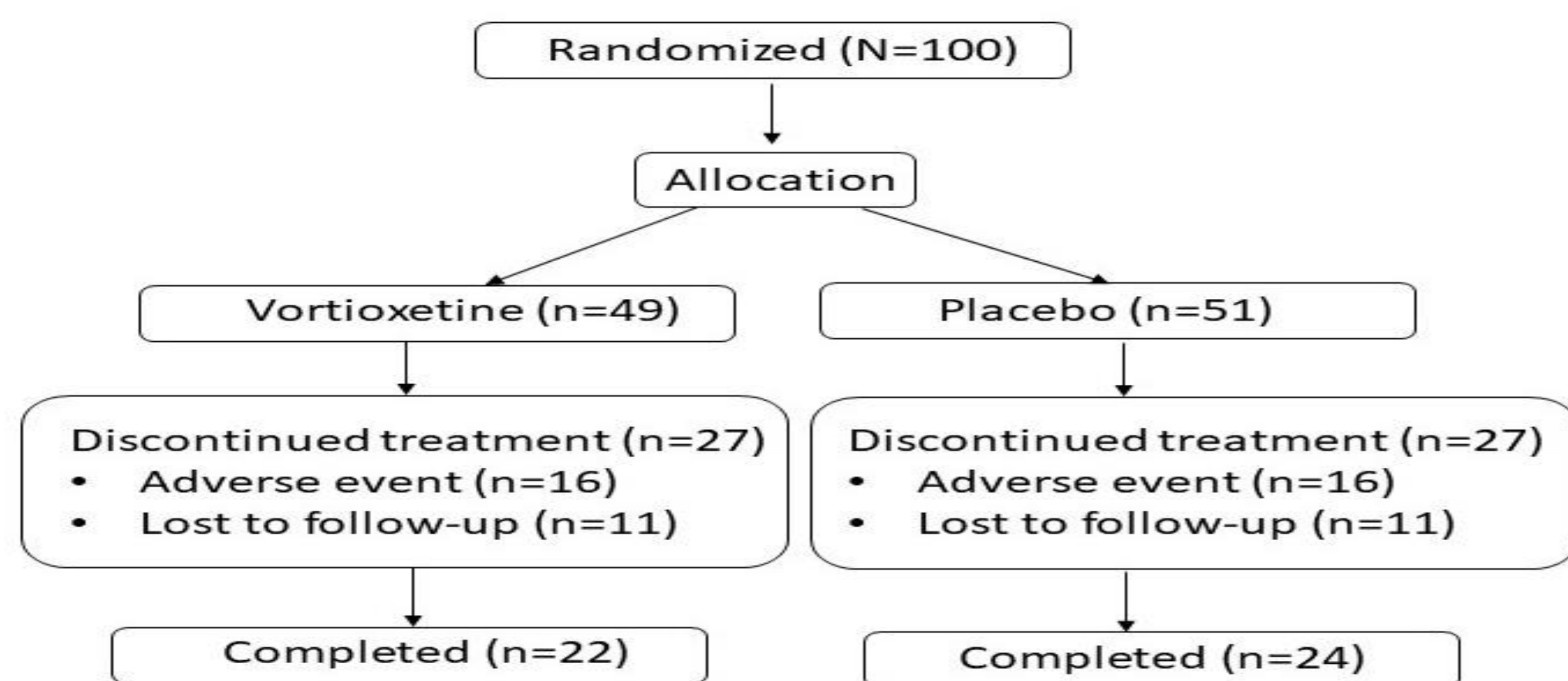


Table 1. Demographic characteristics and baseline scales of participants

	Vortioxetine group(N=49)	Placebo group(N=51)
Age, year	80.76±7.535	77.90± 6.900
Sex, female, N(%)	33(67.3)	41(80.4)
Education, year	3.34±4.70	3.33±4.08
CSDD	16.73±6.54	15.88±6.22
SGDS-K	9.81±3.45	10.17±5.18
Verbal fluency	5.47±2.95	5.43±3.03
K-BNT	4.89±2.72	5.30±2.87
MMSE-KC	13.64±4.80	14.19±4.39
Word list memory	7.36±4.19	6.29±3.12
Construction ability	5.50±2.35	5.79±2.38
Word list recall	1.39±1.81	0.90±0.98
Word list recognition	5.21±3.07	4.26±2.68
Construction recall	1.41±1.87	0.75±1.24
SBT-K	22.18±6.97	20.87±6.21

Table 1. (cont'd)

	Vortioxetine group(N=49)	Placebo group(N=51)
CDR	0.99±0.54	1.01±0.80
GDS	4.36±0.84	4.28±0.74
BADL	3.09±2.62	3.56±2.63
IADL	21.69±9.07	21.41±9.24
SVLT	6.02±4.13	6.80±3.60
Digit span-forward	3.77±1.48	3.91±0.94
Digit span-backward	1.16±1.21	1.57±1.19
Contrasting	11.51±6.83	10.33±6.74
Go No-go	8.68±5.94	8.28±5.44
SVLT-delayed recall	0.86±1.49	0.65±1.10
SVLT-immediate recall	6.17±2.92	6.50±3.33
DSST	5.11±9.69	2.79±4.28

Table 2. Treatment emergent adverse events reported

	Vortioxetine group(N=49)	Placebo group(N=51)
Vomiting	1(2.04)	2(3.92)
Nausea	4(8.16)	2(3.92)
Headache	1(2.04)	1(1.96)
Dizziness	1(2.04)	4(7.84)
Constipation	0(0.00)	1(1.96)
Diarrheas	3(6.12)	2(3.92)
Irritability	1(2.04)	0
Heartburn	2(4.08)	2(3.92)
General weakness	2(4.08)	0(0.00)
Paresthesia	1(2.04)	0
Belching	1(2.04)	1(1.96)

Note. Data are number (%) of patients.

Table 3. Change from baseline in all variances at week 12 for all efficacy endpoints

Variables	Level 1			Level 2				
	Value	t	pvalue	Estimate	Ubar	b	t	pvalue
Depressive symptoms								
SGDS	-0.59 ± 0.21	-2.88	0.01	-0.07	0.24	0.00	0.24	0.41
CSDD	-1.62 ± 0.33	-4.95	0.00	0.58	0.49	0.00	0.49	0.31
Cognitive function								
MMSE	0.59 ± 0.21	2.79	0.01	0.59	0.18	0.00	0.18	0.43
Word fluency	0.53 ± 0.14	3.76	0.00	-0.19	0.08	0.00	0.08	0.47
Naming	0.25 ± 0.08	3.02	0.00	-0.30	0.03	0.00	0.03	0.49
Construction	0.11 ± 0.10	1.14	0.26	-0.05	0.04	0.00	0.04	0.48
Word list memory	0.29 ± 0.14	2.10	0.05	0.46	0.07	0.00	0.07	0.47
Word list recognition	0.02 ± 0.14	0.15	0.88	0.53	0.07	0.00	0.07	0.47
Word list recall	0.13 ± 0.10	1.33	0.20	0.33	0.03	0.00	0.03	0.49
DS.F	0.07 ± 0.06	1.23	0.23	0.03	0.01	0.00	0.01	0.50
DS.B	0.14 ± 0.06	2.57	0.01	0.12	0.01	0.00	0.01	0.50
DSST	0.43 ± 0.28	1.52	0.13	1.00	0.31	0.00	0.31	0.38
Contrasting	0.62 ± 0.33	1.87	0.07	0.63	0.43	0.00	0.43	0.33
Go-no-go	0.56 ± 0.24	2.34	0.02	0.35	0.23	0.00	0.23	0.41
SVLT	0.44 ± 0.17	2.55	0.01	0.46	0.12	0.00	0.12	0.45
SVLT delay	0.05 ± 0.06	0.82	0.42	0.17	0.01	0.00	0.01	0.50
SVLT recognition	0.17 ± 0.16	1.05	0.30	0.05	0.10	0.00	0.10	0.46
ADL								
BADL	-0.17 ± 0.11	-1.60	0.12	0.09	0.04	0.00	0.04	0.48
IADL	-0.21 ± 0.42	-0.50	0.62	0.39	0.72	0.00	0.72	0.23

Values are presented as mean ± standard error.

Ubar, the mean of the variances; b, the within imputation variance; CSDD, the Cornell Scale for Depression in Dementia; SGDS, the Korean version of the short form of Geriatric Depression Scale; MMSE.KC, the Korean version of the Mini-Mental State Examination, BADL, Basic Activities of Daily Living; IADL, Instrumental Activities of Daily Living; SVLT, the Seoul Verbal Learning Test; DS.F, Digit Span Forward; DS.B, Digit Span Backward; DSST, the Digit Symbol Substitution Test.

Discussion / Conclusion

Our results suggest that vortioxetine may be might not be effective in reducing depressive symptoms or cognitive impairment in AD patients. However, general drug tolerance and patient safety were similar to those of placebo. Thus, additional studies are needed to replicate the effectiveness and tolerability of vortioxetine in AD patients with depression.