The Effect of Vortioxetine on Health-related Quality of Life in Patients With Major Depressive Disorder

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ABSTRACT

Purpose: Major depressive disorder (MDD) has detrimental effects on health-related quality of life (HRQoL). We describe the effect of vortioxetine on HRQoL in MDD patients by using patient-reported outcome instruments.

Methods: HRQoL was evaluated in 5 short-term (6–8 weeks), randomized studies of vortioxetine (5–20 mg/d; n = 2155) versus placebo (n = 1316) in adults with MDD by using the 36-item Short-Form Health Survey (SF-36), the Quality of Life Enjoyment and Satisfaction Questionnaire–Short Form, the EuroQol 5-Dimension Questionnaire (EQ-5D), and the 12-item Health Status Questionnaire in 1 study in elderly patients. Only patients receiving the approved doses of vortioxetine 5, 10, 15, or 20 mg/d were included in the analysis. A random effects meta-analysis was performed on the 4 adult MDD studies that used the SF-36. A within-studies mixed model for repeated measures analysis based on the full analysis set (FAS) was used unless otherwise specified. Standardized effect size (SES) was calculated to reflect clinical relevance, based on a Cohen's d of 0.2.

Findings: Vortioxetine produced significantly better results compared with placebo in the SF-36 mental component summary score (5 mg: 2.6, $P = 0.001$, SES of 0.22, n = 604; 10 mg: 4.8, $P < 0.001$, SES of 0.42, n = 328) and 4 domain scores (vitality, social functioning, role emotional, and mental health). Vortioxetine was also significantly better in the EuroQoL-5 Dimension Questionnaire Health State score (10 mg: 7.5, $P < 0.05$, SES of 0.33, n = 86) and Quality of Life Enjoyment and Satisfaction Questionnaire–Short Form total score (15 mg: 3.3, $P < 0.01$, SES of 0.38, n = 127; 20 mg: 4.5, $P < 0.0001$, SES of 0.52, n = 134) (FAS, last-observation-carried-forward). In the study of elderly patients, vortioxetine 5 mg (n = 136) improved 12-item Health Status Questionnaire scores significantly more than placebo (n = 148) for the domains of health perception (10.4, $P < 0.0001$, SES of 0.54), mental health (7.9, $P < 0.001$, SES of 0.44), and energy (6.4, $P < 0.05$, SES of 0.28) (FAS, mixed model for repeated measures).

Implications: Vortioxetine yielded significant, meaningful HRQoL improvements in 6 MDD studies of 6 to 8 weeks' duration. (*Clin Ther*. 2015;37:2309–2323) © 2015 The Authors. Published by Elsevier HS Journals, Inc.

Key words: antidepressant, health-related quality of life, major depressive disorder, patient-reported outcomes, vortioxetine.

INTRODUCTION

Major depressive disorder (MDD) is a debilitating medical condition that results in burdens on individuals, families, and society and is a significant cause of disability worldwide. MDD is characterized by the presence of ≥1 major depressive episode (MDE) with symptoms including depressed mood, loss of interest or pleasure, disturbed sleep, reduced appetite, low energy, feelings of guilt and/or low self-worth, and poor concentration. These problems can lead to substantial impairments in health-related quality of life (HRQoL) as well as in the ability to take care of everyday responsibilities.

Depression recurs in up to 80% of all patients with MDD who have achieved remission; it can become chronic (ie, lasting ≥2 years) in nearly 20% of

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patients.[1,2] The risk of relapse or recurrence, chronicity (as measured by the duration of episodes), and treatment resistance increases with each new MDE. Thus, treatment to full remission (often defined as a score ≤ 7 on the 17-item Hamilton Depression Scale or a 50%–80% reduction on this scale compared with the beginning of treatment) and continued treatment to prevent relapse or recurrence have high priority in the management of MDD.[3,4] Furthermore, depression may lead to suicide; the mortality rate due to suicide is ~10% to 15% among patients with MDD treated by psychiatrists.[5–7]

It is widely recognized that the mood symptoms of MDD are associated with impairment in perceived health; reductions in a patient's physical, psychological, and social functioning; and a range of HRQoL domains related to overall well-being.[8–14] Although a variety of antidepressants are available, only about one third of acutely treated patients achieve remission.[15] Moreover, even after undergoing multiple antidepressant therapies, >30% of patients remain symptomatic in the short term: 2 of 5 patients with clinical depression do not respond adequately to antidepressant treatment even after they have completed fourth-line therapy.[16] A recent study of remitted MDD patients suggests that physical and mental functioning remained lower in remitted patients compared with the general population, highlighting that antidepressant therapies do not always prevent residual symptoms.[17] The results of the STAR*D (Sequenced Treatment Alternatives to Relieve Depression) study suggest that greater depressive symptom severity is directly associated with poorer HRQoL, with significant impairments seen across psychological, physical, and social domains.[10,18] Therefore, the assessment of HRQoL, as part of the ongoing evaluation of depression treatment, is necessary for clinicians and patients.[14]

The assessment of HRQoL depends largely on the selection of the appropriate HRQoL tools.[19] Studies have demonstrated the relevance of traditional subjective assessment scales such as the 36-item Short-Form Health Survey (SF-36), the Quality of Life Enjoyment and Satisfaction Questionnaire (Q-LES-Q), the EuroQol 5-Dimension Questionnaire (EQ-5D), and the Health Status Questionnaire-12 (HSQ-12)[10,18,20,21] for the assessment of HRQoL in patients with MDD. The rest of the listed scales are generic but contain different domains capturing various aspects of the patient's functioning and HRQoL, as well as overall perceptions of quality of life (**Table I**). The utilization of the range of different HRQoL measures enables a comprehensive evaluation of aspects of HRQoL and functioning relevant to patients with depression.[22]

Vortioxetine (Lu AA21004) is an antidepressant with a multimodal mechanism of action[23] approved in Europe for the treatment of MDEs in adults and in the United States for the treatment of adults with MDD. The clinical development program for vortioxetine that supported the marketing authorization application for MDD or MDE in Europe entailed 13 short-term studies, 3 long-term extension studies, and 1 twelve-month relapse-prevention study; these studies included nearly 6000 patients with a total exposure of >2000 patient-years. As of January 2015, the total clinical development program for vortioxetine in these indications entailed 17 short-term studies, 5 long-term extension studies, and 1 twelve-month relapse-prevention study; this program included >9700 patients with a total exposure of >3450 patient-years.

The aim of the present analysis was to report the effect of vortioxetine on HRQoL in adult patients with MDD in randomized placebo-controlled studies, as evaluated by using various HRQoL instruments.

MATERIALS AND METHODS

Vortioxetine Registration Studies

The present across-study comparison of HRQoL included the 5 short-term (6–8 weeks) studies conducted in adults aged 18 to 75 years (NCT00672958, NCT00735709, NCT00635219, NCT00839423, and NCT01140906), and 1 dedicated study in elderly patients aged ≥65 years (NCT00811252) in which quality of life measures were included for evaluation.[24–29] The primary efficacy end point in the short-term trials was the change from baseline to week 6/8 on the Montgomery-Åsberg Depression Rating Scale or the 24-item Hamilton Depression Scale total score to evaluate the effect of vortioxetine on depressive symptoms. The primary statistical method applied used either a mixed model for repeated measures (MMRM) analysis using all available observed data or an analysis of covariance (ANCOVA) model using the last-observation-carried-forward (LOCF). Only patients who received the approved doses of