included adverse events, serious adverse events, vital signs, and laboratory data.

The baseline mean IDS-C_{30} scores were 42.4 and 43.5 in the armodafinil and placebo groups, respectively. The respective reduction in the score at 8 weeks was −20.8 and −19.4; the difference was not statistically significant (p=0.272). At 8 weeks, there were no clinically significant differences compared with baseline in serum chemistries, lipid profiles, and urinalysis parameters. Mean weight at 8 weeks was reduced in the armodafinil group by 0.5 kg and was increased in the placebo group by 0.3 kg.

Armodafinil was well tolerated. Adverse events were similar in the two groups; most were mild or moderate, and no deaths occurred.

The finding of a benefit of armodafinil that was not statistically significant from placebo calls for more research to conclusively determine the clinical value of the drug for treatment of bipolar I depression.

Vilazodone Effective and Safe in Major Depressive Disorder

Written by Brian Hoyle

A multicenter, randomized, double-blind, placebo-controlled trial involving more than 1100 patients with major depressive disorder (MDD) has affirmed the efficacy and safety of vilazodone (VLZ) 40 mg/day and indicated the acceptability of a dose of 20 mg/day. The poster presenter was Carl Gommoll, MS, Forest Research Institute, Jersey City, New Jersey, USA [APA 2014 (poster NR6-103)].

VLZ is a selective serotonin (5-HT) reuptake inhibitor and partial agonist of the 5-HT_{1A} receptor. Two prior placebo-controlled Phase 3 trials reported the efficacy and safety of a 40-mg/day dose [Khan A et al. *J Clin Psychiatry* 2011; Rickels K et al. *J Clin Psychiatry* 2009]. Researchers of a 52-week open-label study reported the long-term safety and tolerability of the same dose [Robinson DS et al. *J Clin Psychopharmocol* 2011].

The current study [NCT01473381] was conducted to confirm the results using this now-approved dose, as well as to assess the effectiveness, safety, and tolerability of a lower dose of 20 mg/day. The study was placebo-controlled and incorporated citalopram (CIT) 40 mg/day as an active control for assay sensitivity. The study phases consisted of a 1- to 4-week drug-free screening period, 10-week double-blind treatment, and 1-week double-blind down-taper. The 1162 patients were randomly assigned 1:1:1:1 to receive placebo, VLZ 20 mg/day, VLZ 40 mg/day, or CIT 40 mg/day, respectively.

Included patients were aged 18 to 70 years, met *DSM-IV-TR* criteria for MDD and had ongoing major depressive episodes, had Montgomery-Asberg Depression Rating Scale (MADRS) total score ≥26 at screening and baseline, and were physically sound. Exclusion criteria included *DSM-IV-TR*-defined Axis I disorder other than MDD within the prior 6 months (excepting secondary diagnoses of comorbid generalized anxiety disorder, social anxiety, and/or specific phobia), defined suicide risk, absence of effect of ≥2 antidepressant drugs, and recent (within 2 weeks) use of psychoactive drugs or need for treatment with eszopiclone, zopiclone, or zaleplon.

The primary efficacy measure was MADRS total score. Secondary efficacy measures were Clinical Global Impressions-Severity (CGI-S) score and MADRS sustained response rate (≤12 for at least the last two clinic visits during the treatment period). CGI-Improvement and Hamilton Rating Scale for Anxiety (HAM-A) scores were also determined. Safety outcomes were adverse events, patient-monitored parameters, and ratings of suicidal ideation and sexual functioning.

The safety population comprised 281 placebo, 288 VLZ 20mg, 287 VLZ 40 mg, and 282 CIT patients. Patient demographics were generally similar between the groups. Approximately 70% of patients completed the study. The rate of discontinuation was significantly higher in the VLZ 40-mg/day group (34%) compared with the placebo (25%) group.

Compared with placebo, MADRS score improvement from baseline to Week 10 was significantly greater for VLZ 20 mg (least squares mean difference [LSMD], –2.57; adjusted p=0.0073) and VLZ 40 mg (LSMD, –2.82; adjusted p=0.0034) in the intent-to-treat population. CIT versus placebo had a similar pattern (LSMD, –2.74; p=0.0020), demonstrating assay sensitivity. In the same population, reductions in CGI-S scores were significantly greater than placebo for VLZ 20 mg (LSMD, –0.35; adjusted p=0.0073), VLZ 40 mg (LSMD,–0.33; adjusted p=0.0097), and CIT (LSMD, –0.35; p=0.0025). More patients met criteria for MADRS sustained response in the VLZ 20-mg (29.9%), VLZ 40-mg (33.5%), and CIT (31.1%) groups versus the placebo (26.3%) group; differences were not statistically significant.

All groups displayed similar adverse event (AE) profiles. Rates of treatment-emergent AEs (TEAEs) were similar for VLZ 20 mg (72.2%), VLZ 40 mg (77.4%), CIT (77.0%), and placebo (63.3%). TEAEs occurring in ≥5% of VLZ patients and twice placebo were diarrhea, nausea, vomiting, and insomnia. Majority of TEAEs were mild or moderate in severity. Serious AEs were reported in 2 placebo, 4 VLZ 20-mg, 4 VLZ 40-mg, and 6 CIT patients. One death occurred, in a patient receiving VLZ, which was not related to medication.

The data bolster support for the efficacy, safety, and tolerability of VLZ 40-mg/day and indicate the utility of the 20-mg/day dose.

Vortioxetine Improves Cognitive Function, Lessens Symptoms of Major Depression

Written by Brian Hoyle

A multinational, randomized, double-blind, placebo-controlled Efficacy Study of Vortioxetine on Cognitive Dysfunction in Adult Patients With Major Depressive Disorder (MDD) [FOCUS; NCT01422213] has demonstrated the drug's efficacy in improving cognitive function and lessening depression symptoms. The poster chronicling the study was presented by Roger S. McIntyre, MD, University Health Network, University of Toronto, Toronto, Ontario, Canada [APA 2014 (poster NR6-114)].

Vortioxetine is a novel multimodal antidepressant that functions as a human 5-HT_{3A} and 5-HT_{7} receptor antagonist, a 5-HT_{1B} receptor partial agonist, a 5-HT_{1A} receptor agonist, and an inhibitor of the serotonin transporter. It is thought to act directly on the serotonin receptor and on the inhibition of serotonin reuptake. Vortioxetine was approved in 2013 for the treatment of MDD by the US Food and Drug Administration.

The FOCUS study comprised secondary analyses of the effect on specified end points of acute treatment with vortioxetine doses of 10 mg/day (n=195) and 20 mg/day (n=207) versus placebo (n=196) for 598 adults with recurrent moderate-to-severe MDD. The patients were aged ≥18 years and ≤65 years, diagnosed with recurrent MDD according to *Diagnostic and Statistical Manual of Mental Disorders* (Fourth Edition, Text Revision; *DSM-IV-TR*) with a current depressive episode lasting 3 months or longer, and a Montgomery-Asberg Depression Rating Scale (MADRS) total score ≥26 at screening and baseline.

The primary outcome was the effect of cognitive assessments. Secondary outcomes were changes in depression symptom severity from baseline at Weeks 1, 4, and 8 in MADRS total score, MADRS response and remission, Clinical Global Impression-Severity of Illness (CGI-S), and the Clinical Global Impression-Improvement (CGI-I) scores.

The baseline characteristics of patients in the three study arms were similar. The mean baseline MADRS scores were indicative of moderate to severe depression in the patients (Table 1).

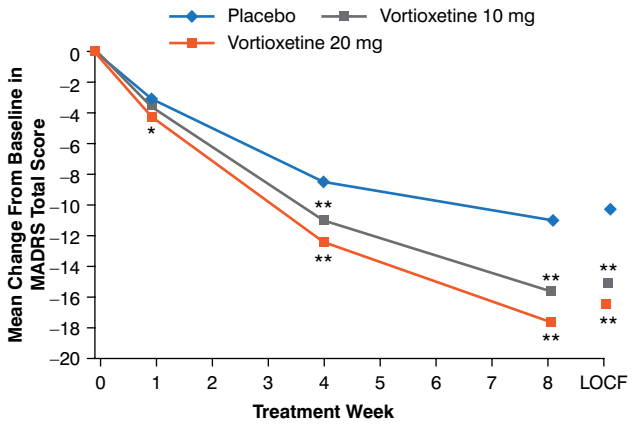
After 8 weeks, the mean MADRS decreased (improved) by 10.9, 15.6, and 17.6 points for the placebo, vortioxetine 10-mg, and vortioxetine 20-mg arms, respectively. The differences between the vortioxetine doses and placebo were significant (both p<0.001). The difference in the mean change from baseline to Week 8 in the MADRS total score was –4.7 and –6.7 for 10-mg/day and 20-mg/day vortioxetine, respectively (both p<0.001; Figure 1).

Table 1. Baseline Patient Characteristics

	Placebo (n=196)	Vortioxetine, 10 mg (n=195)	Vortioxetine, 20 mg (n=207)
Women, n (%)	129 (65.8)	134 (68.7)	133 (64.3)
Mean age, years (range)	45.6 (19 to 65)	45.4 (18 to 65)	46.1 (18 to 65)
Caucasian (%)	95.9	93.8	93.7
Median length of current major depressive episode, weeks	18	19	19
Previous major depressive episodes, mean number (range)	2.4 (1 to 11)	2.3 (1 to 11)	2.6 (1 to 13)
Assessment scores, mean	**n=194**	**n=193**	**n=204**
MADRS total score	31.3	31.6	31.7
CGI-S	4.55	4.60	4.62

CGI-S=Clinical Global Impression-Severity of Illness; MADRS=Montgomery-Asberg Depression Rating Scale.

Figure 1. Estimated MADRS Total Scores From Baseline to Week 8 and LOCF



*p<0.01, **p<0.001 vs placebo.
LOCF=last observation carried forward; MADRS=Montgomery-Asberg Depression Rating Scale.
Reproduced with permission from RS McIntyre, MD.