SUPPLEMENTARY TABLE S1. INCLUSION/EXCLUSION CRITERIA

Inclusion criteria

1. Be able to provide informed assent and their parent/guardian/LAR and caregiver had to provide written informed consent before the initiation of any study-specific procedures
2. Male or female outpatient (7–17 years, inclusive) at Screening (Visit 1)
3. Met DSM-IV-TR criteria for MDD, confirmed by K-SADS-PL, with a current depressive episode of ≥6 weeks duration at Screening (Visit 1)
4. Had a score of ≥40 on the CDRS-R at Screening (Visit 1) and Baseline (Visit 2)
5. Had a CGI-S score ≥4 at Screening (Visit 1) and Baseline (Visit 2)
6. Had a caregiver who was willing and able to be responsible for safety monitoring of the patient, provide information about the patient's condition, oversee the administration of IP, and accompany the patient to all study visits
7. Had normal physical examination findings, vital sign values, clinical laboratory test results, and ECG results, or abnormal results that were determined by the Investigator not to be clinically significant
8. Had a negative serum pregnancy test result if patient was female ≥9 years of age or had onset of menses

Exclusion criteria assessed at Screening (Visit 1)

Psychiatric criteria

1. Current (past 3 months) principal DSM-IV-TR-based diagnosis of an Axis I disorder other than MDD within 6 months before Screening (Visit 1) that was the primary focus of treatment
   Patients with comorbid diagnoses of learning disorders, attention deficit disorder (with or without hyperactivity), communication disorders, separation anxiety disorder, oppositional defiant disorder, and anxiety disorders were allowed to participate in the study as long as these conditions were not the primary focus of treatment and complied with concomitant medications/limitations in the Study Protocol
   Patients with conduct disorder were not allowed to participate
2. Prior diagnosis of mental retardation or amnesic or other cognitive disorders based on DSM-IV-TR criteria
3. Imminent risk of injuring self or others or causing damage to property as judged by the Investigator
4. Suicide risk, as determined by meeting any of the following criteria:
   Suicide attempt within the past year
   Significant risk judged by the Investigator based on the psychiatric interview or information collected in the C-SSRS

Treatment-related criteria

5. Requirement for concomitant treatment with any psychotropic drug or any drug with a psychotropic activity that does not comply with the concomitant medication limitations as listed in Appendix III of the protocol
6. Use of any psychoactive drug or psychoactive herbal remedy other than those allowed as listed in Appendix III of the protocol and Exclusion criterion #18 (including, but not limited to, St. John's wort, ginkgo biloba, kava kava, SAMe (*S*-adenosylmethionine), valerian root, DHEA (dehydroepiandrosterone), tyrosine, tryptophan, and 5-hydroxytryptophan), including antidepressants, anxiolytics, monoamine oxidase inhibitors, antipsychotics, or anticonvulsants/mood stabilizers (including, but not limited to, carbamazepine) within five half-lives before Baseline (Visit 2), or ever been treated with a depot antipsychotic
7. Patients who had initiated psychotherapy or behavior therapy within 3 months prior to the screening visit or who planned to initiate or change such therapies during the course of the study

Other medical criteria

8. A history of allergy, intolerance, or hypersensitivity to vilazodone, fluoxetine, or other drugs of the same class (the following text added for Canadian sites only during Protocol amendment #1) or known hypersensitivities to the IPs' nonmedicinal ingredients, including lactose and gelatin
9. Concurrent medical condition that might have interfered with the conduct of the study, confounded the interpretation of study results, or endangered the patient's well-being. This included a history or evidence (based on physical examination, laboratory results, or an ECG) of malignancy or any significant hematologic, endocrine, respiratory, renal, hepatic, gastrointestinal, or neurologic disease unless all of the following were true (discussion with the Study Physician was encouraged for these cases):
   The condition had been stable for >1 year (3 years for a malignancy other than excised basal cell carcinoma, for which 1 year of stability was required)
   The condition had been judged by the Investigator not to interfere with participation in the study
   The condition was fully documented in the patient's study records
10. Any cardiovascular disease or condition that was clinically significant, unstable, or decompensated. In addition, patients with any of the following conditions were excluded from participation in the study:
    Second-degree (if Mobitz II) or third-degree atrioventricular block
    PVC associated with clinical symptoms and/or any complex PVCs (i.e., PVCs that were frequent [>30/hour] or ≥2 beats if multifocal or showed bigeminy, trigeminy, quadrigeminy, couplets, triplets [salvos], or the R-on-T phenomenon)
    Atrial fibrillation or flutter that was symptomatic or associated with uncontrolled heart rate or hemodynamic instability, requiring anticoagulation, or was of recent (<12 months) or unknown onset
    Any systolic and/or diastolic blood pressure and/or manually measured pulse rate and/or QTc interval (Fridericia corrected) that was symptomatic or clinically significant as per the opinion of the Investigator
11. Hypo- or hyperthyroidism, unless stabilized on appropriate pharmacotherapy with no change in dosage for at least 3 months before Screening (Visit 1)
12. Any condition that would be expected to affect drug absorption (e.g., gastric bypass surgery)

(*continued*)

SUPPLEMENTARY TABLE S1. (CONTINUED)

13. History of seizure disorder (except simple childhood febrile seizures before age 5), unexplained syncope or blackout episodes, stroke, significant head injury, tumor of the central nervous system, or any other condition that predisposes the patient toward a risk for seizure
14. Liver enzyme test values (AST and/or ALT) >2.0 times the ULN
15. History of conditions that might have worsened with SSRIs (example, syndrome of inappropriate antidiuretic hormone secretion)
16. Any unapproved concomitant medication or herbal supplements excluded by the List of Concomitant Medications (Appendix III of the protocol) that could not have been discontinued or switched to an allowable alternative medication and stabilized for at least 2 weeks (unless otherwise specified in Appendix III of the protocol) preceding Baseline (Visit 2)
17. History of drug or alcohol abuse or dependence within the past year
18. Positive result from the UDS, if performed, for any prohibited substance, with the following exceptions:
    Positive UDS for amphetamines, barbiturates, benzodiazepines, or opiates could be allowed if the drug was used for a legitimate medical purpose, and its use, unless allowed as concomitant medication, could be discontinued (documented by a negative repeat test) before Baseline (Visit 2) (Exclusion criterion #6)
        Any use of benzodiazepines and opiates must have allowed for complete washout and extended past any withdrawal symptoms from discontinuing same
        Positive results for cannabinoids, cocaine, methadone, or phencyclidine were exclusionary with no exceptions
19. Pregnant, breastfeeding, and/or planning to become pregnant and/or breastfeed during
20. For females that were sexually active:
    Not practicing a reliable method of contraception that would have continued for the duration of the study and within 30 days following the end of study participation. Reliable contraception was defined as:
    Surgical sterilization (e.g., tubal ligation or hysterectomy)
    Oral contraceptives (consisting of an estrogen-progestin combination or progestin alone)
    Transdermally delivered contraceptives (e.g., Ortho Evra®) or depot injections (e.g., Depo-Provera®)
    Vaginal contraceptive ring (e.g., NuvaRing) or contraceptive implants (e.g., Implanon®, Norplant II/Jadelle®)

Note: Females using hormonal contraceptives must have been doing so for ≥1 month before Screening (Visit 1)

LAR, legally authorized representative; DSM-IV-TR, Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition, Text Revision (American Psychiatric Association 2000); MDD, major depressive disorder; K-SADS-PL, Kiddie Schedule for Affective Disorders and Schizophrenia–Present and Lifetime; C-SSRS, Columbia Suicide Severity Rating Scale; CDRS-R, Children's Depression Rating Scale-Revised; CGI-S, Clinical Global Impressions-Severity; ECG, electrocardiogram; PVC, premature ventricular contraction; QTc, QT interval corrected for heart rate; AST, aspartate aminotransferase; ALT, alanine aminotransferase; ULN, upper limit of normal; UDS, urine drug screen; SSRI, selective serotonin reuptake inhibitor; IP, investigational product.

Supplementary Reference

American Psychiatric Association: Diagnostic and Statistical Manual of Mental Disorders, 4th ed., Text Revision. Washington, DC: American Psychiatric Association; 2000.