

ELECTRONIC SUPPLEMENTARY MATERIAL

Appendix 1: Inclusion/exclusion criteria

Complete inclusion/exclusion criteria for this study consisted of the following:

Study participants were men and women of at least 50 years of age, with a diagnosis of probable AD based on criteria set forth by the National Institute of Neurological and Communicative Disorders and Stroke's Alzheimer's Disease and Related Disorders Association (NINCDS-ADRDA) [1] and the Diagnostic and Statistical Manual of Mental Disorders (DSM-IV-TR) [2]. In addition, the participants were required to have a Mini Mental State Examination Score (MMSE) [3] in the 3-14 range at screening and baseline, and results of a magnetic resonance imaging (MRI) or computed tomography (CT) scan, taken within the past 12 months, consistent with a diagnosis of probable AD. The Functional Assessment Staging Tool (FAST) was also administered at screening, to aid in assessing the severity of illness. At screening, all participants were required to be receiving ongoing cholinesterase inhibitor therapy, (stable dosage for at least 3 months), and to have normal (or abnormal but clinically non-significant, as judged by the site investigator) results on physical examination, laboratory evaluations, and electrocardiogram (ECG). Women were required to be post-menopausal for at least 2 years or surgically sterile. All individuals were required to have a reliable, knowledgeable caregiver to accompany them to all visits during the study. They were also required to be ambulatory (independently or aided) and have sufficient vision and hearing, with or without aids, to comply with testing procedures.

Individuals were excluded from the study if they had any of the following: clinically significant and active pulmonary, gastrointestinal, renal, hepatic, endocrine, or cardiovascular system

disease; neurologic disorder (e.g., stroke, Parkinson's disease, seizure disorder, or head injury with loss of consciousness) within the past 5 years; clinically significant B₁₂ or folate deficiency; any DSM-IV Axis I disorder other than AD (e.g., amnestic disorders, schizophrenia, bipolar disorder, current major depressive episode, psychosis, panic or post-traumatic stress disorder); CT or MRI compatible with hydrocephalus, stroke, space-occupying mass lesion, cerebral infection, or any other clinically significant disease involving the central nervous system; dementia complicated by other organic disease or predominant delusions; systolic blood pressure >180 or <90 mmHg, or diastolic blood pressure >105 or <50 mmHg at screening or baseline; treatment for an oncologic diagnosis within the previous 6 months; modified Hachinski Ischemic score >4 at screening; known or suspected history of alcoholism or drug abuse within 10 years of screening; memantine treatment within one month prior to screening; clinician's judgment of likely nursing home placement within 6 months; hypersensitivity to memantine, neramexane, rimantadine, or amantadine; cholinesterase inhibitor therapy that was likely to be interrupted or discontinued during course of the study, contraindication for cholinesterase inhibitor therapy, or therapy with multiple cholinesterase inhibitors; the inability to perform a minimum of one item on the Severe Impairment Battery (SIB) at baseline. Additional exclusion criteria included the unwillingness or inability of the patient or caregiver to fulfill the requirements of the study, any patient's condition deemed by the investigator to be unsuitable for the study, patient exposure to an investigational drug within 30 days (or 5 half-lives, whichever is longer) of screening, treatment with a depot neuroleptic within 6 months of screening, current or prior exposure to any unapproved concomitant medication that could not be discontinued or switched to an allowable alternative medication before baseline, and positive urine drug screen results for a prohibited drug.

References

1. McKhann. Clinical diagnosis of Alzheimer's disease: report of the NINCDS-ADRDA Work Group under the auspices of Department of Health and Human Services Task Force on Alzheimer's Disease. *Neurology*. 1984;34:939-44.
2. American Psychiatric Association Task Force on DSM-IV. *Diagnostic and Statistical Manual of Mental Disorders: DSM-IV-TR*. 4th ed. Washington, DC: American Psychiatric Association; 2000.
3. Folstein MF, Folstein SE, McHugh PR. "Mini-mental state". A practical method for grading the cognitive state of patients for the clinician. *J Psychiatr Res*. 1975 Nov;12(3):189-98.

Appendix 2: Co-investigators

The Memantine MEM-MD-50 Study Group consisted of the following members (affiliations reflect the time of study conclusion):

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