# Memantine May Reduce Agitation in AD Patients

*Patients taking the drug showed improvements on the Neuropsychiatric Inventory agitation domain.*

BY DOUG BRUNK
*San Diego Bureau*

SAN DIEGO — Use of memantine in patients with moderate to severe Alzheimer's disease significantly reduced their behavioral disturbances and psychiatric symptoms, compared with placebo, Jeffrey L. Cummings, M.D., reported in a poster session at the annual meeting of the American Association for Geriatric Psychiatry.

"We think this represents an important, newly recognized benefit for the use of memantine in patients with Alzheimer's disease," Dr. Cummings, who is the director of the University of California, Los Angeles, Alzheimer's Disease Research Center, said in an interview with this newspaper.

"The question we posed was, does a drug like memantine, which is used for cognitive improvement, have any effect on agitation?" Dr. Cummings explained.

"What we saw was that in several analyses—whether we looked at week 12 or week 24, whether we looked at patients who were asymptomatic at baseline or symptomatic at baseline—memantine reduced agitation," Dr. Cummings added.

For the 24-week study, Dr. Cummings and his associates randomized 403 patients at 37 clinical centers who had moderate to severe Alzheimer's disease to receive either memantine 10 mg b.i.d. or placebo.

The memantine was titrated up weekly in 5-mg increments from a starting dose of 5 mg/day during week 1 to 20 mg/day at week 4.

All patients remained on donepezil throughout the study.

The study's investigators used the Neuropsychiatric Inventory to assess the patients' behavioral symptoms at baseline, week 12, and week 24.

Of the 403 community-dwelling patients, 202 received memantine and 201 received placebo.

The mean age of study participants was 76 years, and 65% were female. Most (91%) were white.

When compared with patients in the placebo group at 12 weeks, those patients who were in the memantine group had significant improvements on the Neuropsychiatric Inventory domains of agitation/aggression (–0.4 vs. 0.2), irritability/lability (–0.4 vs. 0.1), and appetite/eating change (–0.4 vs. 0.1), in which a negative value denotes improvement and a positive value signifies worsening of symptoms, Dr. Cummings said at the meeting.

**'The question we posed was, does a drug like memantine, which is used for cognitive improvement, have any effect on agitation?'**

Patients' improvements in all of these Neuropsychiatric Inventory domains remained statistically significant at 24 weeks.

"I was surprised by the magnitude and consistency of the effect," Dr. Cummings told this newspaper.

The study investigators also observed that, in patients who were asymptomatic at baseline, memantine treatment resulted in significantly less emergence of agitation/aggression and appetite/eating changes by week 24, compared with those patients who were taking a placebo.

According to Dr. Cummings, this is the first study to look at the effect of memantine on behavior in Alzheimer's disease.

Forest Laboratories Inc., the company that manufactures memantine, supported the study. ■

# Hallucinations May Predict Impairment in Alzheimer's

BY NORRA MACREADY
*Los Angeles Bureau*

LAS VEGAS — Hallucinations are a significant predictor of functional impairment in patients with Alzheimer's disease, Wing Yee Mok, M.D., said at the annual meeting of the American Geriatrics Society.

In a retrospective analysis of 100 patients at a mean age of 80 years and with a mean 3 years of education, the presence of hallucinations, as well as a low score on the Mini-Mental State Examination (MMSE), were independent predictors of problems in activities of daily living, said Dr. Mok, a resident in the department of medicine at Queen Mary Hospital in Hong Kong.

**Hallucinations were a significant independent predictor of impairment as measured by Lawton's Instrumental Activities of Daily Living.**

Cognitive impairment is known to affect functional capacity, but the impact of noncognitive symptoms, such as hallucinations, has not been studied as extensively, she said.

The patients were recruited from the memory clinic at Queen Mary Hospital. They underwent a series of tests to assess various aspects of their cognitive and functional abilities, including the MMSE, the Barthel Index of Activities of Daily Living (BADL), and Lawton's Instrumental Activities of Daily Living (IADL). They were also examined for noncognitive psychiatric symptoms, including hallucinations, delusions, anxiety, euphoria, and apathy.

The BADL measures the patient's ability to perform basic daily activities, such as bathing, eating, and grooming without assistance. Scores range from 0, suggesting complete incapacitation, to 20, complete independence. The patients in this study had a mean score of 18.4.

The IADL assesses the patient's ability to perform tasks that require some planning and abstraction, such as doing laundry, shopping for groceries, and managing money. Scores range from 0, suggesting inability to perform the task at all, to 8, meaning no help is needed with any of the activities. These patients had a mean score of 5.9.

The MMSE measures cognitive function by asking patients the date and place, having them name various objects, remember words, and subtract a series of numbers. Scores vary depending on the patient's age and level of education, but mean scores for unimpaired 80-year-olds range from 20, for those with up to a fourth-grade education, to 27, for those with a college degree. The mean MMSE score for these patients was 15.1.

In a multiple linear regression analysis, the presence of hallucinations was a significant independent predictor of impairment as measured by the IADL but not the BADL. A low score on the MMSE correlated strongly with low scores on the BADL and the IADL and was another independent predictor of poor functional status.

Screening for and managing hallucinations could improve functional status in this patient population, Dr. Mok said. ■

# *Medicare to Cover PET Scans in Cases Where Dementia Diagnosis Is Unclear*

BY KERRI WACHTER
*Senior Writer*

Medicare is extending coverage of PET scans to include patients who meet the criteria for both frontotemporal dementia and Alzheimer's disease but for whom the diagnosis remains unclear.

The Centers for Medicare and Medicaid Services concluded in September that $^{18}$fluorodeoxyglucose PET (FDG-PET) imaging can be useful in patients with a documented cognitive decline of at least 6 months and a recently established diagnosis of dementia.

To be eligible for the new coverage, these patients must meet criteria for both frontotemporal dementia (FTD) and Alzheimer's disease (AD), but have an unclear diagnosis even after extensive clinical evaluation and alternative imaging (MRI and CT).

The specific conditions required to receive PET scan coverage to distinguish FTD and AD include:

► The onset, clinical presentation, or course of impairment is atypical for AD, and FTD is suspected as an alternative neurodegenerative cause.

► The patient has had a comprehensive clinical evaluation—as defined by the American Academy of Neurology—encompassing a medical history from both the patient and a well-acquainted informant, a physical and mental status examination aided by cognitive scales or neuropsychological testing, laboratory tests, and structural imaging.

► The patient has been evaluated by a physician experienced in the diagnosis and assessment of dementia.

► The evaluation did not identify a likely, specific neurodegenerative disease that is causing the clinical symptoms.

It's estimated that 12%-16% of patients with degenerative dementia may have FTD, which is often misdiagnosed as AD.

FTD is characterized by the formation of microvacuoles, gliosis with or without inclusion bodies, and swollen neurons.

FDG-PET imaging can be particularly useful in distinguishing frontotemporal dementia from Alzheimer's disease.

FDG-PET imaging assesses brain activity, with regions of atrophy appearing inactive.

FTD leads to frontotemporally predominant atrophy, while AD pathology is typically more severe in posterior temporoparietal regions—patterns that are distinguishable in a PET scan.

"This is important because the treatments for Alzheimer's disease do not help patients with frontotemporal dementia," Gary W. Small, M.D., the director of the Center on Aging at the University of California, Los Angeles, said at a recent symposium on imaging sponsored by the Institute of Molecular Technologies.

Alzheimer's symptoms of memory and cognitive function impairment appear gradually.

Signs of frontotemporal dementia tend to appear as deficits in judgment and conduct, appearing early in disease development.

"There tends to be sort of a loosening of personality," Dr. Small said.

CMS also concluded that although there are not adequate data to support the use of PET imaging for the diagnosis of patients with mild cognitive impairment or early dementia, the technique shows promise. ■