

Ramelteon Improves Chronic Insomnia in Elderly

BY DAMIAN McNAMARA
Miami Bureau

BOCA RATON, FLA. — The newly approved drug ramelteon significantly reduced sleep latency and increased total sleep time in a phase III study of elderly patients with chronic insomnia. In addition, researchers reported no evidence of next-day residual cognitive, psychomotor, or memory effects.

"There was really no problem with next-day psychomotor impairment that you can see with gamma-aminobutyric acid (GABA)-ergic agents. This study was done in an elderly population, so that is particularly important," David Seiden, M.D., said in an interview at a poster presented at a meeting of the New Clinical Drug Evaluation Unit, sponsored by the National Institute of Mental Health. Use of sedative-hypnotic agents has been associated with increased risk of hip fractures from falls (*J. Am. Geriatr. Soc.* 1999;47:30-9).

Most agents approved by the Food and Drug Administration to treat insomnia work through the GABA-ergic system, including zolpidem (Ambien) or zaleplon (Sonata). But Dr. Seiden said ramelteon uses a novel approach and has a different mechanism of action through the melatonin system.

As a melatonin agonist, ramelteon has the ability to induce sleep and modulate

circadian rhythm by binding to the same receptors, M1 and M2, targeted by endogenous melatonin, said Dr. Seiden, medical director of the Broward Research Group and Sleep-Wake Disorders Center of South Florida in Pembroke Pines.

Dr. Seiden and his associates studied 100 elderly patients with chronic insomnia in a crossover design. The mean age was 71 years, and 37 participants were men. Each participant took either ramelteon 4 mg/night, ramelteon 8 mg/night, or

placebo for 5 weeks, followed by a 5- to 12-day washout period before switching. The drug was administered 30 minutes before the patient's usual bedtime.

The researchers used overnight polysomnography to assess efficacy. Patients also completed a postsleep questionnaire, Digital Symbol Substitution Test, and immediate and delayed memory recall tests.

"The major finding here is, there is an improvement in sleep latency," he said.

Participants taking 4-mg/night ramelteon fell asleep faster than those taking a placebo (29 minutes versus 38 minutes), according to polysomnography. Similar improvements occurred with the higher dose of ramelteon (31 minutes). These differences were statistically significant.

Patients' subjective assessments of sleep latency were significantly different between those taking the 4-mg/night dose of ramelteon and those taking placebo (48

Is Drink a Day Good for Women?

A drink a day appears to protect elderly women from cognitive decline, according to new data from the ongoing Nurses' Health Study.

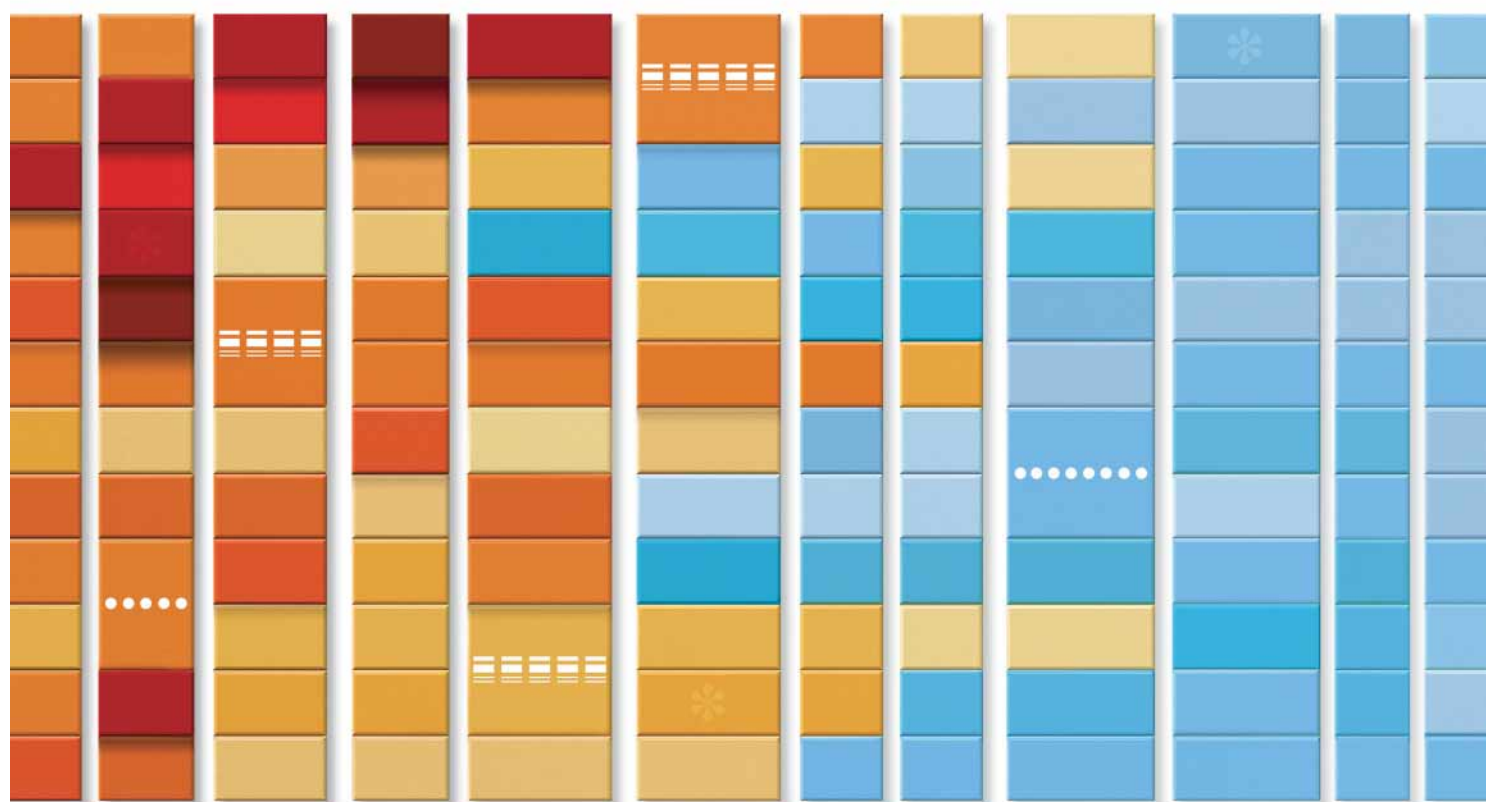
During a 2-year follow-up study, interviewers administered four cognitive tests to more than 11,000 women aged 70-81 years, said Meir Stampfer, M.D., of Brigham and Women's Hospital, Boston, and colleagues. They found that moderate drinkers (about one drink/day) had a 20% lower risk of cognitive decline than either nondrinkers or those who drank two or more drinks/day. Both wine and beer were associated with the protective effect (*N. Engl. J. Med.* 2005;3:245-53).

Moderate alcohol intake elevates the HDL level and reduces that of fibrinogen and other thrombotic factors. "Thus, moderate intake of alcohol may help preserve brain vasculature, may prevent subclinical strokes, and could thus result in better cognitive function," the authors said.

But more studies are needed before doctors advise elderly women to start hitting the bottle, Denis Evans, M.D., of Rush University, Chicago, said in an accompanying editorial: "Persons seeking to maximize cognition in old age must keep in mind both the uncertainty of the current results and the knowledge that alcohol consumption can be a double-edged sword, with the dangers of overindulgence being all too familiar."

—Michele G. Sullivan

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†Clinically significant weight gain was defined as an increase from baseline of B7%. Mean weight gain at study endpoint in 3-week trials was 2.3 lb in the Equetro™ group vs 0.1 lb in the placebo group ($P < 0.001$).

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min vs. 58 min). However, patients taking the 8-mg/night dose reported it took them 51 minutes to fall asleep, which was not statistically different from results seen with placebo.

"Another positive finding was improvement in total sleep time. It could be an effect of them falling asleep quicker," Dr. Seiden said. During the placebo phase, participants slept a mean of 350 total minutes, according to polysomnography. Total sleep time increased to 359 minutes at the 4-mg dose of ramelteon and 362 minutes at the 8-mg dose.

There were no consistent differences in wake time after sleep onset or number of

nighttime awakenings between the two treatment groups.

"This drug has a really well tolerated side effect profile," said Dr. Seiden, who has no financial affiliation with the company.

The most commonly reported adverse events were headache and nausea. Overall incidence of adverse events was similar between placebo (9%), ramelteon 4 mg (14%), and ramelteon 8 mg (7%) groups.

Dr. Seiden noted that the developer of ramelteon, Takeda Pharmaceuticals North America Inc., is currently looking at additional applications for the drug, including jet lag and shift work disorders. ■

Statins Don't Cut Dementia Risk

Statins do not appear to decrease the risk of Alzheimer's disease and other dementias, as several studies have suggested, reported Peter P. Zandi, Ph.D., of Johns Hopkins University, Baltimore, and his associates.

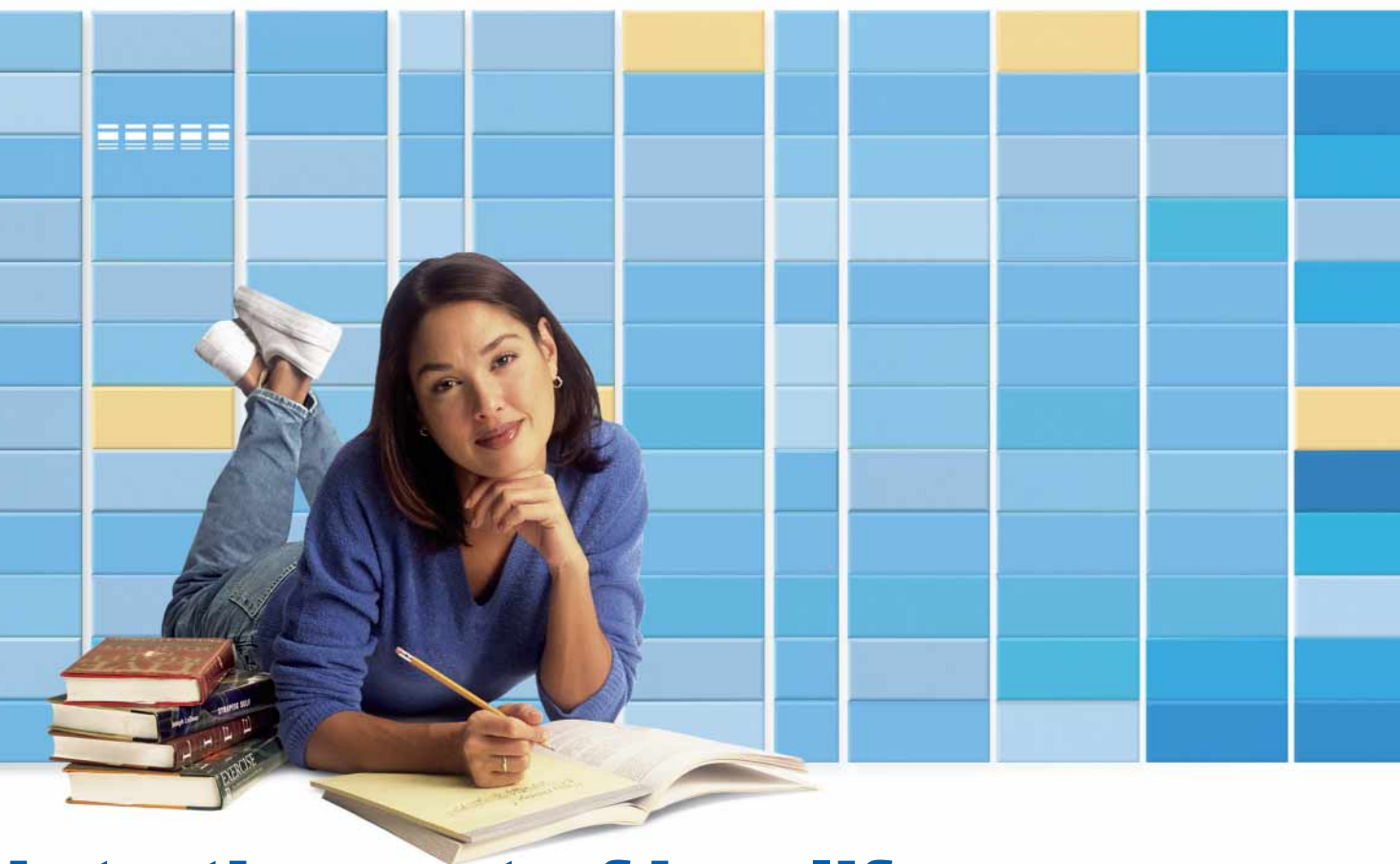
At least six observational studies have suggested an inverse association between statin use and dementia, but three randomized trials have found no such protective effect. To shed light on the issue, Dr. Zandi and his associates analyzed data from a study of nearly 5,000 elderly subjects living in Cache County, Utah.

Initial analyses of the investigators' data suggested that statin use lowered the risk of dementia. But that link disappeared in further analyses that adjusted for covariates, particularly subject age and sex.

The investigators concluded that the purported protective effect of statins that was found in cross-sectional studies is an artifact of the study design and simply is not borne out by further prospective analyses (*Arch. Gen. Psychiatry* 2005;62:217-24).

—Mary Ann Moon

with Bipolar I Disorder



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weight gain.^{†3}

drug should be considered if any evidence of significant bone marrow depression develops.

Carbamazepine should not be used in patients with a history of previous bone marrow depression, hypersensitivity to the drug, or known sensitivity to any of the tricyclic compounds.

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