Is Sertraline Treatment or Depression Remission in Depressed Alzheimer Patients Associated with Improved Caregiver Well Being? Depression in Alzheimer's Disease Study 2

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Objective: *We wanted to assess if sertraline treatment (versus placebo) or remission of depression at 12 weeks (versus nonremission) in Alzheimer patients is associated with improved caregiver well being.* **Methods:** *We conducted a randomized, double-blind, placebo-controlled clinical trial of the efficacy and safety of sertraline for the treatment of depression in individuals with Alzheimer disease in five clinical research sites across the United States. Participants were caregivers of patients enrolled in the Depression in Alzheimer's Disease Study 2 (N = 131). All caregivers received standardized psychosocial support throughout the study. Caregiver outcome measures included depression (Beck Depression Inventory), distress (Neuropsychiatric Inventory), burden (Zarit Burden Interview), and quality of life (Medical Outcomes Study Short Form Health Survey).* **Results:** *Fifty-nine percent of caregivers were spouses, 63.4% were women, and 64.1% were white. Caregivers of patients in both treatment groups had significant reductions in distress scores over the 24-week study period, but there was not a greater benefit for caregivers of patients taking sertraline. However,*

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caregivers of patients whose depression was in remission at week 12 had greater declines in distress scores over the 24 weeks than caregivers of patients whose depression did not remit by week 12. **Conclusion:** *Patient treatment with sertraline was not associated with significantly greater reductions in caregiver distress than placebo treatment. Distress but not level of depression or burden lessened for all caregivers regardless of remission status and even more so for those who cared for patients whose depression remitted. Results imply an interrelationship between caregiver distress and patient psychiatric outcomes.* (Am J Geriatr Psychiatry 2014; 22:14–24)

Key Words: Sertraline, depression, Alzheimer disease, caregivers, DIADS-2

INTRODUCTION

It has been estimated that over 5 million Americans have Alzheimer disease (AD).[1] Since people are living longer and the risk of AD increases exponentially with age, the number of AD cases is also expected to increase.[2] By 2050, the number of people with AD is projected to reach 16 million in the United States and 106 million worldwide.[3]

AD is characterized by gradual cognitive deterioration followed by functional decline, decreased quality of life, and loss of independence. Patients often need caregivers to assist them with day-to-day living activities. Accordingly, as the number of older adults with AD increases, so will the number of caregivers. The social, economic, and health effects of caring for adults with dementia have been well documented.[4–7]

Neuropsychiatric symptoms (NPS) such as depression are common in persons with AD.[8] Up to 90% develop at least one NPS over the course of the disease.[9,10] More specifically, 10%–24% of AD patients develop major depression, and an additional 40%–50% have milder depressive symptoms.[11–13] Depression of AD (dAD) has been associated with poorer patient quality of life,[8,14] more rapid cognitive decline,[8,15] poorer functioning,[8,16,17] earlier entry into nursing homes,[8,18] and relatively higher mortality.[8]

Depression in AD patients also has been associated with more caregiver stress,[19] depression,[8,20,21] burden,[8,21] and distress.[22] Thus, although dementia caregiving can be challenging already, there are additional negative effects on the caregiver if the patient is also depressed.[23] In previous studies, patient depression has been shown to be one of the "most consistent and powerful predictors of psychological morbidity"[22(p.248)] in caregivers, and 75%–100% of caregivers of depressed AD patients were found to be depressed also.[22,24]

Psychological interventions for patients to improve symptoms related to dAD have been developed as well as interventions for caregivers.[25,26] In particular, Teri and colleagues[27,28] developed behavioral treatment and caregiver training programs to address the needs of AD patients with depression that also have been related to positive, lasting effects in caregiver outcomes. Other researchers have found aerobic exercise to be related to a reduction in NPS in Alzheimer patients as well as attenuation of caregiver burden.[29]

Unlike nonpharmacologic interventions, fewer controlled trials that have been conducted for feasibility and effectiveness of pharmacologic interventions in dAD have included caregiver outcomes.[30] Because less is known about the effects of dAD pharmacologic treatments on caregivers, inclusion of mood and burden outcomes for caregivers was an important aspect of the Depression in Alzheimer's Disease Study 2 (DIADS-2) design[31] and is the primary focus of this report. Furthermore, the literature has less discussion of how improvements in patient symptoms relate to improvements in caregiver outcomes,[24,28–30] and more is needed to answer such questions.

Previous reports of results from DIADS-2, a randomized controlled trial of sertraline for dAD,[32–34] indicated no effect of sertraline on patient-centered outcomes. Nonetheless, we extended these