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File: ■ Ginkgo (*Ginkgo biloba*)
■ EGb 761
■ Dementia

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RE: Once Daily Dosing of Ginkgo Extract Demonstrates Advantages in Dementia

Ihl R, Bachinskaya N, Korczyn AD, et al. Efficacy and safety of a once-daily formulation of *Ginkgo biloba* extract EGb 761 in dementia with neuropsychiatric features: a randomized controlled trial. *Int J Geriatr Psychiatry*. 2010; [epub ahead of print]. doi:10.1002/gps.2662.

Elderly patients with dementia have difficulty remembering to take their medicines. Once daily dosing improves treatment adherence. Ginkgo (*Ginkgo biloba*) is a popular treatment for memory loss; however, most ginkgo preparations require multiple daily dosing. The purpose of this randomized, double-blind, placebo-controlled study was to evaluate the safety and efficacy of a new once daily formulation of the ginkgo extract, EGb 761 (Dr. Willmar Schwabe; Karlsruhe, Germany). This once daily formulation consisted of a "dry extract from *Ginkgo biloba* leaves (drug-extract ratio 35-67:1), adjusted to 22.0-27.0% ginkgo flavonoids and 5.0-7.0% terpene lactones consisting of 2.8-3.4% ginkgolides A, B, C and 2.6-3.2% bilobalide, with a content of ginkgolic acids below 5 ppm."

Men and women (≥ 50 years old) with symptoms of dementia for ≥ 6 months, and diagnosis of probable Alzheimer's disease (AD), possible AD with cerebrovascular disease (CVD), or probable vascular dementia (VaD) participated in the study. Patients (n = 410) were enrolled from 20 outpatient clinics of psychiatric or neurological hospitals in the Ukraine. A CT or MRI scan ≤ 1-year-old had to be available that provided evidence consistent with the diagnosis and showed no evidence of other brain lesions that could account for the cognitive deficit. Patients also had to have a screening score of ≥ 35 on the Test for Early Detection of Dementia with Discrimination from Depression (TE4D), a score of 9 to 23 on the Syndrom Kurz Test (SKT) battery, a score < 6 on the clock-drawing tests (CDT), a score of ≥ 5 on the 12-item Neuropsychiatric Inventory (NPI), and a score < 20 on the 17-item Hamilton Rating Scale for Depression (HAMD). Patients with severe dementia were excluded. Treatment with other memory enhancing drugs/herbs was prohibited during the study and for ≥ 8 weeks prior to randomization. The primary efficacy measures were the SKT and NPI scores. The secondary efficacy measures were the Clinical Global Impression of Change (CGIC), the Alzheimer's Disease Activities of Daily Living International Scale (ADL-IS), the dementia quality of life proxy scale (DEMQOL), the Verbal Fluency Test, NPI caregiver distress score, and patient self-ratings of dizziness and tinnitus. Efficacy assessments were made at baseline, week 12, and week 24. Safety assessments were done at screening and week 24; adverse events (AEs) were recorded at baseline and weeks 6 and 18.

Most patients had concomitant medical conditions. The most frequently reported conditions were: nervous system disorders (EGb 761: 89%, placebo: 93%), vascular disorders (EGb 761: 92%, placebo: 90%), and cardiac disorders (EGb 761: 74%, placebo: 74%). The baseline HAMD scores were > 15 and < 20 (indicating moderate depression) in 23 patients (EGb 761: 10, placebo: 13). Concomitant prescription medications were used by 67% of the patients.

According to the SKT total score, a clinically significant improvement in cognition occurred in 32% of EGb 761-treated patients and in 15% of placebo-treated patients ($P < 0.001$). According to the NPI total score, significant improvements occurred in 45% of EGb 761-treated patients and 24% of placebo-treated patients ($P < 0.001$). All secondary efficacy measures for EGb 761 were statistically significant in superiority over placebo.

In each treatment group, 2 serious AEs (SAEs) were observed. An EGb 761-treated patient had an ischemic stroke following a history of hypertension and recurring ischemic attacks, and another had a stage IV lung cancer. A placebo-treated patient had an ischemic stroke, and a rapid deterioration of intellectual and motor function also occurred. Both groups' SAEs were considered by the investigators to be unrelated to the study medication. Patients in the placebo group had 7 times as many patients reporting tinnitus than the EGb 761 group. All other AEs occurred with no major differences between groups.

The authors conclude that the study successfully demonstrates the feasibility, safety, and efficacy of once daily administration of EGb 761 at doses of 240 mg for the treatment of dementia with neuropsychiatric features. EGb 761 treatment was significantly superior to placebo in improving patients' cognitive performance, neuropsychiatric symptoms, functional abilities, and overall condition. These improvements decreased the distress of the patients' caregivers. According to the authors, this was the first study to assess the effect of EGb 761 on quality of life for which there was a significant improvement ($P = 0.008$). The authors concede that overall the improvements were moderate. However, the improvements from EGb 761 were in the same range as that of cholinesterase inhibitors (anti-dementia drugs).

These findings are particularly interesting because the study included a heterogenous mixture of patients—a mixture similar to what would be seen by a physician. The study also included patients with clinically significant behavioral and psychological symptoms. Thus, EGb 761 was shown to be effective in a cohort that resembles the population that requires anti-dementia therapy. Nonetheless, it should be noted that the majority of the cohort had mild dementia. It is unknown how effective and safe this dosage would be for more severe forms of dementia.

—Heather S. Oliff, PhD

The American Botanical Council has chosen not to reprint the original article.