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File: ■ Ginkgo (*Ginkgo biloba*)
■ Alzheimer's Disease
■ Vascular Dementia

HC 011251-441

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RE: Efficacy and Tolerability of Ginkgo Extract in Treatment of Alzheimer's Disease and Vascular Dementia

Ihl R, Tribanek M, Bachinskaya N; for the GOTADAY Study Group. Efficacy and tolerability of a once daily formulation of *Ginkgo biloba* extract EGb 761® in Alzheimer's disease and vascular dementia: Results from a randomised controlled trial. *Pharmacopsychiatry*. Nov 15, 2011; [epub ahead of print]. doi: 10.1055/s-0031-1291217.

Many studies have demonstrated the safety and efficacy of 240 mg (120 mg 2x/day) of ginkgo (*Ginkgo biloba*) special extract EGb 761® (Dr. Willmar Schwabe GmbH and Co. KG Pharmaceuticals; Karlsruhe, Germany). Patient compliance is better when patients are required to take fewer daily doses. Therefore, the manufacturer developed a once-daily 240 mg dose of EGb 761. The once-daily dose was tested and found to be safe and efficacious.[1] The goal of the present study was to conduct a confirmatory analysis of that original study.[1] This was accomplished by conducting a subgroup analysis of the total population of a randomized, controlled, double-blind, multicenter study.

Since the methods have been described previously, they were only mentioned briefly in this report. Patients were recruited from the outpatient clinic of the Department of Psychiatry of the National Medical University in Kiev and 19 outpatient clinics of neurological or psychiatric hospitals in Ukraine between April and November 2006. The study included outpatients (n = 410, aged ≥ 50 years) with mild to moderate dementia due to probable Alzheimer's disease (AD), possible AD with cerebrovascular disease (CVD), or vascular dementia (VaD). Clinical diagnosis of AD was established via the criteria of the National Institute of Neurological and Communicative Disorders and Stroke together with the Alzheimer's Disease and Related Disorders Association (NINCDS/ADRDA), VaD was established according to the diagnostic criteria published by the National Institute of Neurological Disorders and Stroke together with the Association Internationale pour la Recherche et l'Enseignement en Neurosciences (NINDS/AIREN), and possible AD with CVD was established according to the relevant subsets of those criteria. A recent (≤ 1 year old) CT or MRI scan had to be consistent with the clinical diagnosis. Other inclusion criteria included a score of ≤ 35 on the Test for the Early Detection of Dementia with Differentiation from Depression (TE4D), a total score of 9-23 on the SKT (Erzigkeit's short syndrome test) cognitive test battery, a total score of ≤ 5 on the 12-item Neuropsychiatric Inventory (NPI), and at least one item score (other than delusion or hallucination) of ≤ 3 on the NPI. Patients were excluded if they had significant psychiatric disorders (e.g., major depression or subsyndromal depression), severe somatic disorders, or were taking a medication that could have influenced the assessment scores.

Patients were treated with 240 mg EGb 761 or placebo 1x/day for 24 weeks. The primary outcome measures were the SKT and NPI tests.

A total of 404 patients were included in the analysis, with 333 patients diagnosed as having AD (probable AD: n = 121 and possible AD with CVD: n = 212) and 71 patients having VaD. Treatment adherence was 99%. For the SKT total score, both subgroups taking EGb 761 had an improvement from baseline by 1.4 points, which was significantly better than the placebo-treated group (AD, $P < 0.001$ and VaD, $P < 0.05$). For the NPI score, VaD patients treated with EGb 761 responded better to treatment than the patients with AD treated with EGb 761 (4.5 point improvement vs 2.9 points, respectively) (P-value not reported). Also for the NPI score, EGb 761-treated patients with VaD improved significantly more than placebo-treated patients with VaD ($P < 0.05$). When looking at clinically meaningful improvements (decrease in SKT scores by ≥ 3 points or decrease in NPI by ≥ 4 points), 33% of EGb 761-treated patients with AD compared with 14% of placebo-treated patients with AD had clinical improvement on the SKT ($P < 0.001$), and 43% of EGb 761-treated patients with AD compared with 22% of placebo-treated patients with AD had clinical improvement on the NPI ($P < 0.001$). However, the number of patients with VaD having clinical improvement was not significantly different between treatment groups (for SKT, EGb 761-treated: 28% vs placebo-treated: 19%, and for NPI, EGb 761-treated: 54% vs. placebo-treated: 31%).

For all secondary outcome variables (NPI caregiver distress score, the Clinical Global Impression of Change as adapted by the Alzheimer's Disease Cooperative Study [ADCS-CGIC], the Alzheimer's Disease Activities of Daily Living International Scale [ADL-IS], and the Verbal Fluency Test), except the dementia quality-of-life scale, there were statistically significant differences between the EGb 761 group and the placebo group.

The AD subgroup was further broken down into probable AD and possible AD with CVD. The authors state, "There were no conspicuous differences in efficacy related to vascular pathology."

The most frequently reported adverse events (AEs) were reported with similar frequency between treatment groups. There were no major bleeding events.

The authors believe that the study population represents everyday practice. The authors conclude that EGb 761 had "essentially similar" effects in patients with AD and VaD. They also think that the data support the use of EGb 761 for dementia as diagnosed in the primary care setting since EGb 761 had similar efficacy for both populations. The study was sponsored by the manufacturer of EGb 761. The conclusions may be subject to bias since the percentage of patients with clinically meaningful improvements was not significantly different between treatment groups for patients with VaD. It would have been helpful if the authors included a discussion of their findings compared with the gold-standard therapy so that the reader could better judge the data considered clinically meaningful.

—Heather S. Oliff, PhD

Reference

[1]Ihl R, Bachinskaya N, Korczyn A, 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.* Dec 7, 2010; [epub ahead of print]. doi: 10.1002/gps.2662.

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