

Galantamine was effective in mild-to-moderate Alzheimer disease

Rockwood K, Fay S, Song X, et al. Attainment of treatment goals by people with Alzheimer's disease receiving galantamine: a randomized controlled trial. *CMAJ*. 2006;174:1099-105.

Clinical impact ratings: GIM/FP/GP ★★★★★☆☆ Geriatrics ★★★★★☆☆ Neurology ★★★★★☆☆

QUESTION

In patients with mild-to-moderate Alzheimer disease, does galantamine improve clinical outcomes?

METHODS

Design: Randomized placebo-controlled trial (Video-Imaging Synthesis of Treated Alzheimer's Disease [VISTA] trial).

Allocation: Concealed.*

Blinding: Blinded (clinicians, patients, outcome assessors, data analysts, [and data collectors]†).*

Follow-up period: 16 weeks.

Setting: 14 sites in Canada.

Patients: 130 patients 51 to 94 years of age (mean age 77 y, 63% women) with mild-to-moderate dementia (Mini-Mental State Examination score 10 to 25 and cognitive subscale of the Alzheimer Disease Assessment Scale [ADAS-cog] score ≥ 18). Exclusion criteria were residence in nursing homes, disabling communication difficulties, active medical issues or competing causes of dementia, receipt of antidementia medications within 30 days, hypersensitivity to cholinomimetic agents or bromide, or participation in other galantamine trials.

Intervention: Galantamine, 8 mg/d for 4 weeks, followed by 16 mg/d for 4 weeks, then 16 to 24 mg/d for 8 weeks (*n* = 64), or placebo (*n* = 66).

Outcomes: Extent of attainment of personal goals on the Goal Attainment Scaling (GAS) score (much worse, no change, much better) assessed by physicians and by patients and caregivers. Secondary outcomes included

mean change on the 11-item ADAS-cog (0 = no impairment to 70 = severe impairment), Clinician's Interview-based Impression of Change plus Care-giver Input (CIBIC-plus) (1 = very much improved to 7 = very much worse), Disability Assessment for Dementia (DAD) (higher scores = better performance), and Caregiving Burden Scale (CBS) scores (higher scores = higher burden); and adverse events.

Patient follow-up: 98% (intention-to-treat analysis).

MAIN RESULTS

Patients in the galantamine group had better goal attainment on clinician-based assessment of GAS scores than did those in the placebo group, but groups did not differ for GAS scores assessed by patients and caregivers (Table). Patients who received galanta-

mine also had better ADAS-cog and CIBIC-plus scores (Table). Groups did not differ for DAD and CBS scores (Table). More patients in the galantamine group had adverse events than did those in the placebo group (Table).

CONCLUSION

In patients with mild-to-moderate Alzheimer disease, galantamine improved clinical outcomes, but adverse effects were common.

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For correspondence: Dr. K. Rockwood, Dalhousie University, Halifax, Nova Scotia, Canada. E-mail kenneth.rockwood@dal.ca.

*See Glossary.

†Information provided by author.

Galantamine vs placebo for mild-to-moderate Alzheimer disease at 16 weeks†

Outcomes	Absolute difference	Standardized response means (SRM)	P value
Goal Attainment Scaling (GAS) score assessed by clinicians	4.0	0.41	0.02
GAS score assessed by patients and caregivers	1.9	0.20	0.27
Cognitive subscale of the Alzheimer Disease Assessment Scale score	—	-0.36 [§]	0.04
Clinician's Interview-based Impression of Change plus Care-giver Input score	—	-0.40 [§]	0.03
Disability Assessment for Dementia score	—	0.28	0.13
Caregiving Burden Scale score	—	-0.17 [§]	0.38

	Galantamine	Placebo	RRI (95% CI)	NNH (CI)
Adverse events	84%	62%	36% (10 to 72)	5 (3 to 15)

‡Abbreviations defined in Glossary; RRI, NNH, and CI calculated from data in article.

§A negative SRM was a positive treatment effect.

COMMENTARY

After several randomized trials of cholinesterase inhibitors for Alzheimer disease, controversy persists over the clinical meaningfulness of statistically significant but small treatment effects that have been found using such standardized psychometric scales as the ADAS-cog. With GAS, in the study by Rockwood and colleagues, the clinician identifies dementia-related problems that the patient or caregiver wishes to change (the goals), then sets outcome levels that reflect degrees of improvement and deterioration. Standardized scoring adjusts for the number as well as the importance of the goals, enabling GAS to be used as a research tool. That the clinician-based GAS, the ADAS-cog, and the CIBIC-plus all showed significant improvement in the galantamine group compared with the placebo group provides concurrent validity for using individualized, clinically meaningful GAS as an outcome measure, and confirms previous studies showing the short-term efficacy of galantamine in Alzheimer disease. Both galantamine and donepezil have been shown to reduce caregiver time spent helping with activities of daily living by > 50 min/d in moderate-to-severe Alzheimer disease

(1, 2), an amount most would consider to be clinically meaningful.

For the practicing physician, for whom research scales are impractical, dementia-related problems that the patient or caregiver recognizes and considers relevant may be a more sensitive way to assess response to pharmacologic treatment of dementia. A functional deficit that is a major concern for 1 family may not be important to another. With the GAS method, achievement of clinician and patient-caregiver goals may occur despite declines in more global scales (3).

*Calvin Hirsch, MD
UC Davis Medical Center
Sacramento, California, USA*

References

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