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The effects of galantamine treatment on caregiver time in Alzheimer's disease

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SUMMARY

Aim The aim of the study was to determine whether the clinical benefits of galantamine for patients with Alzheimer's disease lead to benefits for caregivers.

Methods Data were pooled from two concurrent, multi-centre, randomized, double-blind, placebo-controlled, 6-month trials. Time caregivers spent assisting with activities of daily living (ADL) and time patients could be left unsupervised each day were assessed using the Allocation of Caregiver Time Survey. In total, 825 patients with mild-to-moderate Alzheimer's disease were included.

Results At endpoint, caregivers of galantamine-treated patients were more likely to report reductions (41% *vs* 37%), maintenance (19% *vs* 14%) or smaller increases (26% *vs* 34% reporting an increase >30 minutes) in time assisting with ADL compared with the placebo group ($p = 0.026$; Wilcoxon rank-sum test). The mean daily time difference was 32 minutes ($p = 0.011$). Among patients with moderate Alzheimer's disease, caregivers of galantamine-treated patients were even more likely to report reductions (46% *vs* 37%), maintenance (15% *vs* 6%) or smaller increases (25% *vs* 42% for increases >30 min) *vs* placebo ($p = 0.004$), with a mean daily time saving of 53 minutes ($p = 0.021$). Caregivers of galantamine-treated patients were more likely to report increases (22% *vs* 18%), maintenance (45% *vs* 43%) or smaller reductions (30% *vs* 37% for reductions >30 minutes) in time the patient could be left unsupervised compared with placebo ($p = 0.027$). Mean daily time saving was 27 minutes. Among patients with moderate Alzheimer's disease, the treatment effect was greater ($p = 0.029$), with caregivers in the galantamine group reporting the change in time left unsupervised as 68 minutes longer each day than caregivers of patients receiving placebo.

Conclusion The clinical benefits of galantamine for patients with Alzheimer's disease are also associated with benefits to caregiving.

KEY WORDS — Alzheimer's disease; galantamine; caregiver time; informal care; activities of daily living; behavioural symptoms

INTRODUCTION

Alzheimer's disease (AD) is a progressive dementia characterized by loss of intellectual capacity, altered behaviour and the inability to care for oneself. In the early stages of the disease, patients may only require assistance with complex tasks such as organizing finances and legal matters (instrumental activities of daily living [ADL]). As the disease progresses, they require help with more basic ADL such as toileting, bathing and dressing (Reisberg, 1988). Patients with AD can also require a high degree of supervision to prevent wandering, falls and other accidents. Later stages of the disease are associated with motor impairment and behavioural symptoms including agitation, aggression and insomnia (Reisberg *et al*., 1987; Teri, 1997). Many patients in these later stages require constant (24-hour) care.

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For patients with mild-to-moderate AD, responsibility for providing care tends to fall upon family members, usually elderly spouses (Stone *et al*., 1987) or younger relatives with children of their own (Beach, 1997). The amount of time these individuals spend providing care is associated with increased stress, fatigue and reduced quality of life (Connell *et al*., 2001). Feelings of social isolation and disruption of relationships are also common (Clipp and Moore, 1995). Informal caregivers often spend a large proportion of each day caring for patients (Hu *et al*., 1986) and the support that they receive from formal care services can vary widely (Twigg, 1989). As patients deteriorate, caregiver time and the level of 'burden'—psychological, social and financial problems experienced by caregivers (Connell *et al*., 2001)—can be important factors in the decision, to admit a patient to long-term residential or nursing-home care (Whitehouse *et al*., 1998).

Reductions in caregiver time are, therefore, not only important to caregiving, but may also have a substantial impact on the wider costs associated with AD (Hux *et al*., 1998). Medications that can ease demands on caregiver time would be a welcome addition to the current treatment options for AD.

Galantamine, a cholinergic agent with a dual mode of action (Maelicke *et al*., 2001), has been shown to be significantly more effective than placebo for preserving cognitive function, daily functioning and behaviour in patients with AD disease (Raskind *et al*., 2000; Tariot *et al*., 2000; Wilcock *et al*., 2000). Therefore, galantamine would be expected to reduce the amount of time that caregivers spend assisting patients with ADL and providing supervision. Data regarding effects on caregivers are generally absent from most dementia studies and this area represents a significant gap in our knowledge about the clinical value of therapies for AD (Bayer, 1999). In this study, we examine whether the favourable effects of galantamine on cognition and other outcomes that have been reported in patients with mild-to-moderate AD translate into benefits to caregiving.

METHODS

Data

The amount of time caregivers spent assisting patients with mild-to-moderate AD with ADL, and the amount of time they reported that patients could be left unsupervised each day were collected as part of two similarly designed, randomized, double-blind, placebo-controlled trials. Patients included in the trials had a diagnosis of probable AD according to the criteria of the National Institute of Neurological and Communicative Disorders and Stroke, and the Alzheimer's Disease and Related Disorders Association (McKhann *et al*., 1984), mild-to-moderate dementia, as confirmed by a Mini-Mental State Examination (MMSE; Folstein *et al*., 1975) score of 11–24, and a score of $\geq$12 on the cognitive subscale of the Alzheimer's Disease Assessment Scale (ADAS-cog) (Rosen *et al*., 1984) at screening interview. All patients had a responsible caregiver. Full descriptions of the trial designs have been published previously (Raskind *et al*., 2000; Wilcock *et al*., 2000).

Outcome measures

Primary efficacy measures. The primary efficacy variables in these studies were the ADAS-cog, and the Clinician's Interview-Based Impression of Change plus Caregiver Input (CIBIC-plus) (Schneider *et al*., 1997). ADL were assessed using the Disability Assessment for Dementia (DAD) scale (Gelinas *et al*., 1999). The results have been reported previously (Raskind *et al*., 2000; Wilcock *et al*., 2000).

Allocation of Caregiver Time Survey. The Allocation of Caregiver Time Survey (ACTS) (Blesa, 2000) was used as an outcome measure in both trials. Data were collected using self-reports at baseline, Week 3, and at monthly intervals from Month 2 until Month 6. In both studies, the ACTS solicited information from the caregiver about the amount of time spent assisting the patient with six common activities (bathing, dressing, feeding, toileting, giving medication, housekeeping), with each of the two trials including one or two additional activities (answering questions, handling financial matters, providing transportation). An open-ended section was included in both trials where caregivers could include activities not covered by the main questions. The total time spent assisting the patient was calculated at each time-point by summation of the minutes reported for all available activities.

Measurement solely of time spent assisting with ADL does not fully reflect caregivers' commitment of time to the patient. Therefore, data on how long patients could be left unsupervised each day were also collected. This measure takes into account broader issues such as caregivers being there in case the patient needs them, or remaining with the patient to prevent accidents, falls or wandering. The questions asked were:

- 'Did the patient require round-the-clock supervision?'
- 'If no, how long could the patient be left alone on a typical (24 hours) day?'

'Round-the-clock' supervision was coded in the study as 24-hour care.

Statistical analyses

Information on patients treated with galantamine, 32 mg/day, galantamine, 24 mg/day, and placebo was collected during both trials. In the present analyses, however, we focus on comparisons of 24 mg/day with placebo to ensure consistency with the recommended dosing for galantamine (Janssen Pharmaceutica, 2001).

The analyses reported here are based on comparisons of change in caregiver time between baseline and 6 months (observed case [OC] analyses), as well as endpoint (the last observation under treatment) using intention to treat/last observation carried forward (LOCF) analyses.

Changes from baseline in the time spent assisting with ADL and the amount of time that the patient could be left unsupervised were analysed as categorical and continuous variables. Analyses were conducted for the total patient population and a *post hoc* analysis was carried out for mild and moderate patient subgroups. Mild and moderate AD were defined as MMSE >18 and ≤ 18, respectively, to ensure consistency with previously reported sub-group analyses of patients with AD (Wilcock *et al*., 2000; Getsios *et al*., 2001; Garfield *et al*., 2002).

Categorical analyses were employed to minimize the influence of skewness and outliers. Both measures of caregiver time were stratified into five categories representing change in time between baseline and endpoint:

- >30 minute reduction
- 1–30 minute reduction
- No change
- 1–30 minute increase
- >30 minute increase.

Depending on the measure of caregiver time, a positive response was considered to be either: (1) reduction in time spent assisting with ADL, or (2) increase in the time the patient could be left unsupervised.

The five category changes were analysed using the two-sided Wilcoxon rank-sum test. To take into account possible baseline effects, response rates were analysed using logistic regression and changes in the mean values were analysed using analyses of covariance.

All test results were interpreted as reaching statistical significance if they fell below the conventional 5% significance level.

RESULTS

The results of this study relate to 411 patients who received galantamine, 24 mg/day, and 414 who received placebo. The baseline characteristics of patients and their caregivers in the two treatment groups were similar (Table 1). For the mild and moderate subgroups, the baseline characteristics of patients and their caregivers were also similar between the two treatment groups.

Effects of galantamine on the time caregivers spent assisting patients with ADL

At endpoint, caregivers of patients treated with galantamine were more likely to report reductions (41% *vs* 37%), maintenance (19% *vs* 14%) or smaller increases (26% *vs* 34% reporting an increase of greater than 30 minutes) in the time they spent assisting with ADL compared with the placebo group ($p = 0.026$; Wilcoxon rank-sum test). OC analysis showed similar reported rates (Table 2). At endpoint, the reported change in time spent assisting with ADL was 32 minutes less each day for carers of galantamine-treated patients compared with carers of those receiving placebo ($p = 0.011$; LOCF analysis) (Figure 1).

For patients with moderate Alzheimer's disease (MMSE score ≤ 18), differences between treatment groups were more pronounced ($p = 0.004$; Wilcoxon rank-sum test) (Table 2). For example, 42% (66/156) of caregivers of moderate patients receiving placebo reported an increase of more than 30 minutes in time they spent assisting the patient with ADL compared with 25% (37/150) of caregivers of moderate patients treated with galantamine (Table 2). Results from OC analysis were consistent. Furthermore, the change in the amount of time caregivers reported assisting with ADL was 53 minutes lower for patients who received galantamine compared with those who received placebo ($p = 0.021$; LOCF analysis) (Figure 1).

Logistic regression analysis estimated that, if caregivers spent 3 or more hours per day assisting the patient with ADL at baseline, the caregivers of patients treated with galantamine were more likely

Table 1. Baseline characteristics of patients and caregivers

	Patients		Caregivers	
	Galantamine 24 mg/day ($n = 411$)	Placebo ($n = 414$)	Galantamine 24 mg/day ($n = 411$)	Placebo ($n = 414$)
Gender, *n* (%)*				
Male	149 (36)	157 (38)	179 (44)	148 (37)
Female	262 (64)	257 (62)	229 (56)	253 (63)
Age, mean ± SD (years)	73.8 ± 8.3	73.9 ± 8.2	63.8 ± 15.0	63.4 ± 13.9
Time since diagnosis of cognitive problems, mean ± SD (years)	3.7 ± 2.7	3.9 ± 2.8	—	—
Time since diagnosis of probable Alzheimer's disease, mean ± SD (years)	0.9 ± 1.3	0.9 ± 1.3	—	—
MMSE score, mean ± SD	19.5 ± 3.6	19.3 ± 3.7	—	—
Severity of Alzheimer's disease, *n* (%)			—	—
Mild	261 (64)	258 (62)		
Moderate	150 (36)	156 (38)		
Time spent providing care with ADL (hours), *n* (%)			—	—
0–1	176 (43)	168 (41)		
>1–4	149 (36)	157 (38)		
>4–10	61 (15)	71 (17)		
>10–16+	25 (6)	18 (4)		
Time patients can be left unsupervised (hours), *n* (%)†				
0–1	66 (16)	76 (19)		
>1–4	96 (24)	81 (20)		
>4–10	90 (22)	78 (19)		
>10–16+	150 (37)	171 (42)		
Resident with patient, *n* (%)*			299 (73)	294 (73)
Relationship to patient, *n* (%)‡				
Spouse/partner			254 (62)	253 (63)
Son/daughter			54 (13)	60 (15)
Other family member			82 (20)	67 (17)
Friend/neighbour			14 (3)	16 (4)
Other			3 (1)	4 (1)

*Missing data on three galantamine caregivers and 13 placebo caregivers.
†Galantamine: $n = 402$; placebo: $n = 406$.
‡Missing data on four galantamine caregivers and 14 placebo caregivers. Individuals with missing data were excluded from calculation of percentages.
ADL = activities of daily living; MMSE = Mini-Mental State Examination.

to report a reduction in the time spent caring compared with caregivers of patients treated with placebo (logistic regression: 0.0034 ± 0.006; $p < 0.0001$). This reported treatment response increased in relation to the reported time spent assisting with ADL at baseline (Figure 2). For example, caregivers spending 3 hours per day assisting with ADL at baseline were 1.39 times [95% Confidence Intervals (CI): 1.01, 1.91; LOCF analysis] more likely to report a reduction if the patient was treated with galantamine. For caregivers reporting 6 hours per day assisting with ADL at baseline, the estimated likelihood of a reported reduction was twice as high [odds ratio (OR): 2.00; 95% CI: 1.17, 3.42; LOCF analysis] if patients were treated with galantamine (Figure 2).

Effects of galantamine on the amount of time patients could be left unsupervised

At endpoint, caregivers of patients treated with galantamine reported more favourable changes in the amount of time that patients could be left unsupervised ($p = 0.027$; Wilcoxon rank-sum test) (Table 3). For example, 37% (149/406) of the caregivers of patients treated with placebo reported a reduction of more than half an hour compared with 30% (121/

Table 2. Categorical analysis of change from baseline to endpoint time spent by caregivers assisting with activities of daily living

	All patients, *n* (%)		Mild patients, *n* (%)		Moderate patients, *n* (%)	
	Galantamine 24 mg/day*	Placebo	Galantamine 24 mg/day†	Placebo	Galantamine 24 mg/day‡	Placebo
LOCF analyses						
>30 minute reduction	114 (28)	101 (24)	65 (25)	64 (25)	48 (32)	37 (24)
1–30 minute reduction	54 (13)	49 (12)	33 (13)	29 (11)	21 (14)	20 (13)
No change	77 (19)	58 (14)	54 (21)	49 (19)	23 (15)	9 (6)
1–30 minute increase	58 (14)	65 (16)	37 (14)	42 (16)	21 (14)	23 (15)
>30 minute increase	108 (26)	140 (34)	71 (27)	74 (29)	37 (25)	66 (42)
	Galantamine 24 mg/day†	Placebo	Galantamine 24 mg/day†	Placebo	Galantamine 24 mg/day**	Placebo
OC case analyses						
>30 minute reduction	85 (29)	85 (25)	49 (26)	57 (26)	35 (32)	28 (22)
1–30 minute reduction	39 (13)	46 (13)	24 (13)	27 (12)	15 (14)	19 (15)
No change	42 (14)	47 (14)	30 (16)	40 (18)	12 (11)	7 (6)
1–30 minute increase	45 (15)	56 (16)	28 (15)	35 (16)	17 (16)	21 (17)
>30 minute increase	86 (29)	111 (32)	57 (30)	60 (27)	29 (27)	51 (40)

*$p = 0.026$; †not significant; ‡$p = 0.004$; **$p = 0.023$ (All values *vs* placebo; Wilcoxon rank-sum test).

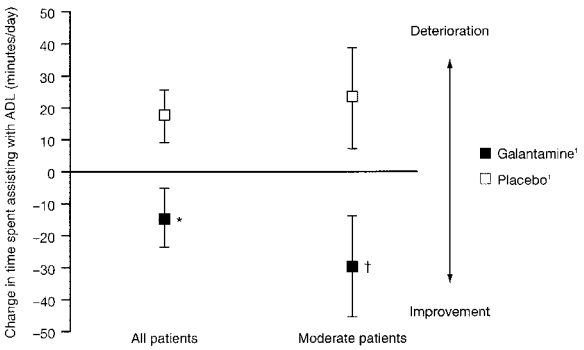

Figure 1. Caregiver time spent assisting with activities of daily living (ADL) (mean changes from baseline to endpoint)
[1]Least square means ± standard errors are presented, obtained by an ANCOVA model with baseline value as covariate.
*$p = 0.011$ *vs* placebo.
†$p = 0.021$ *vs* placebo.

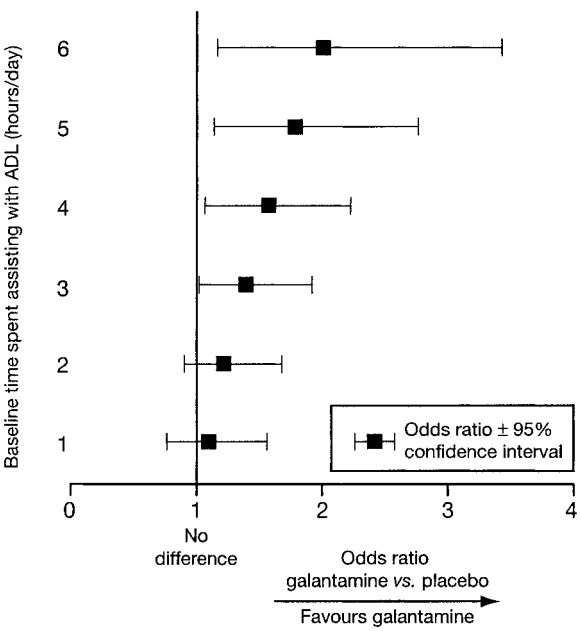

Figure 2. Odds ratios (LOCF analysis) for a positive response (reduction) in time spent assisting patients with activities of daily living (ADL)

402) of the caregivers of patients treated with galantamine. OC analysis showed broadly similar proportions of patients in the respective categories (Table 3). The mean time saving was 27 minutes (LOCF analysis; Figure 3).

Among patients with moderate Alzheimer's disease, the differences between treatment groups again favoured galantamine ($p = 0.029$; Wilcoxon rank-sum test). Results of the OC analysis were in broad agreement with the LOCF analysis (Table 3).

For moderate patients treated with placebo, the mean time that a patient could be left unsupervised declined significantly by 99 minutes at endpoint *vs* baseline ($p = 0.005$; LOCF analysis). By contrast, the decline in time that patients could be left unsupervised was less dramatic among patients treated with galantamine (32 minutes) and was not significantly different from baseline. The difference between the

Table 3. Categorical analysis of change from baseline to endpoint in time patients could be left unsupervised

	All patients, *n* (%)		Mild patients, *n* (%)		Moderate patients, *n* (%)	
	Galantamine 24 mg/day*	Placebo	Galantamine 24 mg/day†	Placebo	Galantamine 24 mg/day‡	Placebo
LOCF analyses						
>30 minute increase	82 (20)	70 (17)	50 (20)	45 (18)	32 (22)	25 (17)
1–30 minute increase	10 (2)	3 (1)	4 (2)	2 (1)	6 (4)	1 (1)
No change	182 (45)	176 (43)	120 (47)	118 (46)	62 (42)	58 (39)
1–30 minute reduction	7 (2)	8 (2)	4 (2)	2 (1)	3 (2)	6 (4)
>30 minute reduction	121 (30)	149 (37)	76 (30)	89 (35)	44 (30)	60 (40)
	Galantamine 24 mg/day**	Placebo	Galantamine 24 mg/day[a]	Placebo	Galantamine 24 mg/day†	Placebo
OC case analyses						
>30 minute increase	71 (24)	62 (18)	46 (25)	39 (18)	25 (23)	23 (19)
1–30 minute increase	8 (3)	2 (1)	3 (2)	2 (1)	5 (5)	0 (0)
No change	116 (40)	145 (42)	76 (41)	97 (44)	40 (37)	48 (39)
1–30 minute reduction	6 (2)	6 (2)	4 (2)	2 (1)	2 (2)	4 (3)
>30 minute reduction	92 (31)	130 (38)	56 (30)	81 (37)	35 (33)	49 (40)

*$p = 0.027$; †not significant; ‡$p = 0.029$; **$p = 0.022$; [a]$p = 0.075$ (All values *vs* placebo; Wilcoxon rank-sum test).

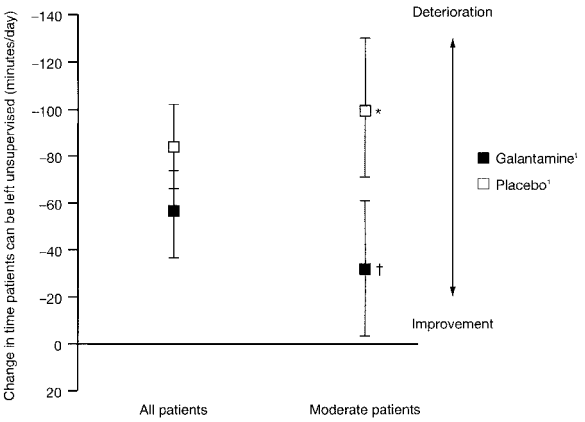

Figure 3. Amount of time that patients can be left unsupervised (mean changes from baseline to endpoint)
[1]Least square means ± standard errors are presented, obtained by an NACOVA model with baseline value as covariate.
*$p = 0.005$ *vs* baseline.
†$p = 0.092$ *vs* placebo.

groups was 68 minutes ($p = 0.092$; LOCF analysis) (Figure 3).

Logistic regression analyses estimated that, in overall terms, caregivers of patients treated with galantamine were approximately twice as likely to report an increase in the amount of time that patients could be left unsupervised compared with caregivers of patients treated with placebo (LOCF analysis—OR: 1.89; 95% CI: 1.13, 3.17; $p = 0.0152$; OC analysis—OR: 2.17; 95% CI: 1.23, 3.80; $p = 0.0071$).

Non-resident caregivers of patients treated with galantamine were more than three times more likely to report an increase in the amount of time that patients could be left unsupervised compared with caregivers of patients treated with placebo (LOCF analysis—OR: 3.15; 95% CI: 1.22, 8.12; $p = 0.177$; OC analysis—OR: 3.47; 95% CI: 1.23, 9.78; $p = 0.0184$). In comparison, reports by caregivers resident with patients showed no difference between the treatment groups in terms of the increase in time patients could be left unsupervised (LOCF analysis—OR: 1.14; 95% CI: 0.76, 1.70; $p = 0.5332$; OC analysis—OR: 1.35; 95% CI: 0.87, 2.10; $p = 0.1808$).

We also conducted exploratory analyses to examine the results for 32 mg galantamine. The results for changes in the time spent assisting with ADL were similar between 24 mg and 32 mg in comparison with placebo, with both active doses showing benefits *vs* placebo, especially for moderate patients. Unlike the results for the 24-mg group, there was no significant effect *vs* placebo in the time that patients could be left unsupervised.

DISCUSSION

Pooled analysis of data from two large clinical trials shows that treatment with galantamine not only benefits patients with mild-to-moderate AD, but also has a positive impact on the demands on their caregivers' time. Caregivers of patients treated with galantamine were more likely to report reductions, maintenance or smaller increases in the time they spent assisting with

ADL, compared with the placebo group. On average, caregivers of patients treated with galantamine could expect to spend about 3.5 hours less each week assisting with ADL compared with the caregivers of patients treated with placebo. Among patients with moderate Alzheimer's disease, the treatment effect was greater. For example, fewer caregivers of patients receiving galantamine reported an increase of more than 30 minutes: 25% *vs* 42% among moderate patients, and 26% *vs* 34% for mild and moderate patients combined. In moderate patients, the estimated time saving for caregivers of patients receiving galantamine compared with caregivers of patients receiving placebo would be more than 6 hours per week. Looking beyond helping with ADL, this study also demonstrates a positive response with galantamine in the amount of time that patients can be left unsupervised, although it should be noted that this measure is also likely to reflect caregivers' decisions as well as patients' abilities. Interestingly, the reported effect on the time patients could be left alone was pronounced among caregivers who were not resident with patients. For example, caregivers of patients treated with galantamine were approximately three times more likely to report an increase in the time the patient could be left unsupervised compared with caregivers who were resident with the patient.

A key strength of the study is that the data come from two randomized clinical trials, providing a large sample of more than 800 participants. The analysis focuses on treatment arms that reflect the clinically effective and approved dose. Thus, the previously demonstrated effectiveness is accompanied by effectiveness in reducing caregiver time. This suggests that the impact of galantamine in approved doses is beneficial across a broad range of domains.

One limitation of any study involving an assessment of caregiver time is the amount of inherent variability present in the parameter. Informal caregiver time is difficult to define and quantify, and published results show a wide range of values (McDaid, 2001). There are a number of possible reasons for this. For example, caregivers may find it difficult to accurately assess how much time is spent in caregiving, or they may overlook certain activities, such as cooking or shopping, that they do not consider to be part of 'caring' for the patient (McDaid, 2001). To increase the accuracy of assessments of caregiver time, a number of scales have been developed, including the ACTS, the Caregiver Activities Time Survey (Clipp and Moore, 1995), the Caregiver Activity Survey (Davis *et al*., 1997) and the Resource Utilisation in Dementia scale (Wimo *et al*., 1998). Although none of these scales has been fully validated, there are many similarities between the tests, and the scales behave as expected. For example, published data using the Caregiver Activities Time Survey, which is particularly similar to ACTS, showed a reduction in caregiver time compared with placebo when patients received an acetylcholinesterase inhibitor (Clipp and Moore, 1995).

Despite these limitations, the present study showed a statistically significant difference between the galantamine and placebo groups with regard to caregiver time. These findings are consistent with another trial, in which caregiver distress was significantly reduced when patients received galantamine rather than placebo (Tariot PN, Truyen L. Poster presented at the 10th Congress of the International Psychogeriatric Association, 2001). Although results from studies of other AD medications show some positive outcomes with respect to other aspects of caregiver burden, no significant benefit in actual time spent caregiving has been reported (Fillit *et al*., 2000; Shikiar *et al*., 2000).

The logistic regression indicates that the savings were related to the amount of time spent assisting at baseline level, suggesting that this measure of caregiver time is more sensitive to change in patients with greater impairment. Clinical trials of acetylcholinesterase inhibitors generally show a high placebo response for all parameters, including cognition assessed with validated scales such as ADAS-cog (Raskind *et al*., 2000; Wilcock *et al*., 2000). However, the treatment response for patients treated with galantamine was consistent for patients regardless of their baseline disease severity, while the response in the placebo group declined as baseline severity increased. The greater placebo response in patients with milder AD may represent the ability of such patients to respond to the greater interest being shown to them and their caregivers due to their participation in a clinical trial. The more pronounced treatment effect compared with placebo for patients with moderate AD is not surprising, as these patients are more likely to require assistance with ADL and to make significant demands on caregiver time. It is in these patients that time savings for caregivers are most meaningful and likely to make a true contribution to reducing the cost of care in this disease. One might project that this benefit would be observed in all patients as their need for assistance with ADL grows.

Approximately two-thirds of patients with moderate-to-severe dementia are cared for in the community (Melzer *et al*., 1997), reliant for care to a greater or lesser degree on informal caregivers. Studies in the

KEY POINTS

- Caregivers of galantamine-treated patients were more likely to report reductions, maintenance or smaller increases in time assisting with activities of daily living, compared with placebo.
- Caregivers of galantamine-treated patients were more likely to report increases, maintenance or smaller reductions in time the patient could be left unsupervised, compared with placebo.
- The effects of galantamine treatment were greater among patients with moderate Alzheimer's disease than among those with mild disease.
- The clinical benefits of galantamine for patients with Alzheimer's disease are also associated with benefits to caregivers.

US and UK show that when a monetary value is placed on informal care, it constitutes a significant proportion, if not the majority, of the overall costs of care (Stommel *et al*., 1994; Souetre *et al*., 1999; Moore *et al*., 2001). Moreover, a wider view of informal care shows that there are further hidden direct and indirect costs. For example, informal caregivers are at increased risk of psychological morbidity (Gonzalez-Salvador *et al*., 1999) and are likely to have increased utilization of healthcare resources and decreased productivity in the workplace (Seaward, 1999). In addition, among patients with caregivers, institutionalization is closely associated with caregiver exhaustion and patients' need for supervision (Hux *et al*., 1998). Including measures of outcome for caregivers in clinical trials is therefore important and likely to be of increasing relevance given the policy-driven moves to community-based care in the UK (Bowl, 1996) and other countries.

CONCLUSIONS

Cognitive, functional and behavioural decline are associated with caregiver burden (Teri, 1997). The positive effects of galantamine on these areas of patient functioning (Raskind *et al*., 2000; Tariot *et al*., 2000; Wilcock *et al*., 2000) are also associated with benefits to caregiving in terms of the time caregivers spend supervising patients and assisting with ADL.

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