The effectiveness of glatiramer acetate in clinical practice: an observational study

Óscar Fernández-Fernández, Lucía García-Trujillo, Miguel Guerrero-Fernández, Antonio León, José C. López-Madrona, Ana Alonso, Rafael Bustamante, Victoria E. Fernández-Sánchez

Aim. To evaluate the clinical effectiveness and safety of glatiramer acetate for use in routine clinical practice.

Patients and methods. A retrospective, observational study was conducted on patients with multiple sclerosis who were treated with glatiramer acetate in clinical practice. The primary outcome was the clinical effectiveness of glatiramer acetate treatment.

Results. The study included a total of 104 patients (women, 59.6%; age at onset of glatiramer acetate treatment, 39.9 ± 10.9 years; prior treatment for multiple sclerosis, 30.8%). The patients had received glatiramer acetate treatment for an average of 3.6 ± 1.9 years. During the first year of glatiramer acetate treatment, the relapse rate decreased by 60%. At this time, the number of relapses had decreased for 47 patients (45.1%), 67 patients (68.4%) had not suffered a relapse and 78 patients (75.0%) showed no signs of progression. During the second year of glatiramer acetate treatment, the relapse rate decreased by 70%. At this time, the number of relapses had decreased for 43 patients (41.3%), 63 patients (75.9%) had not suffered a relapse and 59 patients (56.7%) showed no signs of progression. There were no reported relapses or progression in 56 patients (53.8%) and 41 patients (39.4%) during the first and second years of treatment, respectively. Discontinuation of glatiramer acetate was necessary in only three patients. The most common adverse effects included fatigue (28.9%) and spasticity (7.7%).

Conclusion. This evaluation of glatiramer acetate use in clinical practice supports the effectiveness and the safety profile observed in previously published clinical trial studies.

Key words. Effectiveness. Glatiramer acetate. Multiple sclerosis. Progression. Relapse. Safety. Treatment.

Institute of Clinical Neurosciences; Neurology Department (O. Fernández-Fernández, L. García-Trujillo, M. Guerrero-Fernández, A. León, J.C. López-Madrona, A. Alonso, R. Bustamante); Neurophysiology Department (V.E. Fernández-Sánchez); Hospital Regional Universitario Carlos Haya; Málaga, Spain.

Corresponding author:
Dr. Óscar Fernández Fernández. Institute of Clinical Neurosciences. Hospital Regional Universitario Carlos Haya. Avda. Carlos Haya, s/n. E-29010 Malaga.

Fax:
+34 951 030 157.

E-mail:
oscar.fernandez.sspa@juntadeandalucia.es

Funding:
Teva Innovative Spain has provided funding for this study.

Conflict of interest:
O.F.F. has received a honourarium as a consultant on the advisory committee, has acted as chairman or speaker at conferences and has also participated in clinical trials and other research projects sponsored by Biogen-Idec, Bayer-Schering, Merck-Serono, Teva and Novartis. The remaining authors declare no conflicts of interest.

Accepted:
09.11.11.

How to cite this article:
Fernández-Fernández O, García-Trujillo L, Guerrero-Fernández M, León A, López-Madrona JC, Alonso A, et al. The effectiveness of glatiramer acetate in clinical practice: an observational study. Rev Neurol 2012; 54: 1-9.

Versión española disponible en www.neurologia.com

Introduction

Multiple sclerosis is a chronic inflammatory and demyelinating disease of the central nervous system (CNS) characterised by focal lesions that are associated with the loss of myelin and axonal degeneration [1]. Multiple sclerosis is a major cause of disability in young adults, as this disease currently affects 656,000 individuals in Europe [2] and has a prevalence of 59 to 79 cases per 100,000 inhabitants in Spain [2-5].

Glatiramer acetate (Copaxone ®, Teva Pharmaceutical Industries) is a synthetic copolymer of amino acids and is analogous to myelin basic protein, whose mechanism of action, although not fully elucidated, is believed to modulate immune pathways involved in multiple sclerosis pathogenesis and to stimulate neurotrophin secretion in the CNS for neuronal repair [6-8]. Its effectiveness and safety have been previously demonstrated in clinical trials, which have shown that glatiramer acetate is effective in delaying disease conversion into the clinically definite form of multiple sclerosis [9]. Moreover, glatiramer acetate is also capable of reducing the relapse rate, activity and load, as measured by magnetic resonance imaging (MRI), and this treatment can slow the progression of the disease compared to a placebo for patients with relapsing-remitting multiple sclerosis (RRMS) [10,11]. In addition, direct comparison trials that have compared glatiramer acetate to interferon β have supported its effectiveness and safety in patients with RRMS, revealing both the absence of significant differences between the two treatments [12-14] and the cost-benefits of glatiramer acetate as a first-line drug treatment in Spain [15].

Although clinical trials provide compelling data for medical decision making, their translation to routine clinical practice is not always straightforward. Clinical trials are conducted in homogeneous populations whose variability has been reduced through the use of certain criteria and where patients are under strictly controlled conditions. For this reason, patient variability in multi-

ple sclerosis is not fully represented under such experimental conditions, and therefore, the effectiveness and safety profile of the results obtained from clinical trials do not necessarily represent the clinical scenario of the general population. To achieve clinical excellence, it is necessary to combine the results obtained from clinical trials with those from professional experience in daily clinical practice [16].

From this perspective, the objective of this study was to increase the currently available information regarding the clinical effectiveness and safety of glatiramer acetate administered under conditions encountered in daily clinical practice.

Patients and methods

Sample

This study included patients with multiple sclerosis diagnoses who were treated with glatiramer acetate (Copaxone®) at the Neurology Department at Hospital Regional Universitario Carlos Haya (Malaga, Spain). Glatiramer acetate is typically used for the treatment of patients who have experienced an initial, defined clinical episode and are at a high risk of developing clinically definite multiple sclerosis. This treatment is also used to reduce the frequency of relapses in ambulatory patients with RRMS. All patients provided informed consent for treatment with glatiramer acetate, which was obtained from commercial sources according to the technical specifications and clinical practice.

Study design

This study is a retrospective observational study on the effectiveness and safety of glatiramer acetate in patients treated at Hospital Regional Universitario Carlos Haya under clinical practice conditions. For this purpose, a specific database was created at the hospital containing information from the patient's medical records regarding their sex, date of birth, prior treatments for multiple sclerosis, duration of treatment with glatiramer acetate, expanded disability status scale scores (EDSS) (during the year prior to the onset of treatment with glatiramer acetate and in the following 2 years of treatment), number of relapses (during the year prior to the onset of treatment with glatiramer acetate and during the following 2 years of treatment), discontinuation of treatment with glatiramer acetate and adverse effects reported during treatment with glatiramer acetate.

The clinical measures of disease activity included the relapse rates and EDSS scores. Relapses were defined as the existence of current or recurrent neurological symptoms that lasted for more than 24 hours, were not associated with fever or infection and were accompanied by new objective neurological findings on physical examination. The EDSS scores were used to quantify the disability of the patients, and these ranged from 0 to 10, with greater scores representing increasing disability [17]. Progression was defined as a one-point increase in the EDSS score obtained at the onset of treatment with glatiramer acetate in patients with EDSS scores of ≤ 5.5 and as an increase of 0.5 points in patients with EDSS scores > 5.5.

The safety profile of glatiramer acetate was evaluated according to the existence of necessary treatment interruptions or adverse effects reported during the study period. An adverse effect was defined as any detrimental medical incident that occurred in a subject who had been administered a medication, regardless of whether there was a causal relationship associated with treatment. All adverse effects obtained from the medical records were included in the survey database, regardless of their intensity or causal relationship with glatiramer acetate treatment.

Statistical considerations

The primary efficacy outcome was the clinical effectiveness of treatment with glatiramer acetate under clinical practice conditions, which was based on the number of relapses and the EDSS scores. We performed a descriptive analysis for the relapses (annual relapse rate, patients with a reduced number of relapses and patients without relapse) and EDSS scores (EDSS scores, patients who did not progress and patients with improved EDSS scores). In addition, the relapse rate during the year prior to the onset of treatment with glatiramer acetate was compared with that during the first and second years of treatment using a Student's *t*-test. The changes in EDSS scores during the study period (the year prior to the onset of glatiramer acetate treatment, at the onset of treatment with glatiramer acetate and during the 2 years following treatment) were also evaluated using a Student's *t*-test.

The secondary effectiveness outcomes included the assessment of patient characteristics and clinical disease activity in patient subgroups without relapse, those without progression and those without relapse or progression during the first year of treatment with acetate glatiramer. The secondary effec-

tiveness outcomes were used to analyse clinical factors that could potentially be associated with treatment response, and patients with EDSS scores ≥ 4 at the onset of treatment with glatiramer acetate were used for the evaluation of clinical activity. A descriptive analysis on these secondary outcomes was also performed. Comparisons between patients without relapse, those without progression and those without relapse or progression were performed using the Chi-squared test or Student's *t*-test. To evaluate the clinical factors associated with the response, the characteristics of patients who did and did not progress after 1 year of treatment with glatiramer acetate were compared using the Chi-squared test. Changes in the number of relapses and EDSS scores in patients with an EDSS score ≥ 4 or ≤ 3 at the onset of treatment with glatiramer acetate were determined using Student's *t*-test.

The safety profile of glatiramer acetate administered under clinical practice conditions was also assessed according to the frequency of treatment discontinuation and the frequency of adverse effects reported during the study.

The assessment did not consider missing data, and the statistical analysis was performed using SPSS v. 11.0 at a significance level of 0.05.

Results

Characteristics of patients

The study included a total of 104 patients with the characteristics described in table I. Sixty-two patients (59.6%) were female, and the mean age of the patients was 43.8 ± 11.5 years (range: 21.2 to 71.7 years), as assessed on July 31, 2010. The mean age at the time of the first symptom of multiple sclerosis was 29.6 ± 9.4 years (range: 3.8 to 58.8 years), and the age at the onset of treatment with glatiramer acetate was 39.9 ± 10.9 years (range: 19.6 to 66.0 years). The mean EDSS score at the onset of treatment with glatiramer acetate was 1.7 ± 1.8 years (range: 0-7).

Thirty-two patients (30.8%) had received prior treatment for multiple sclerosis, including interferon β-1a, interferon β-1b, cyclophosphamide, mitoxantrone and azathioprine (Table I). Nine of these patients had received more than one type of prior treatment and began glatiramer acetate treatment due to adverse effects or the lack of previous treatment effectiveness at an average of 10.4 ± 8.1 years after the onset of multiple sclerosis. Patients were treated with glatiramer acetate for a mean duration of 3.6 ± 1.9 years (range: 0.7 to 8.6 years).

Table I. Demographic and clinical characteristics of patients (*n* = 104).

Age (years)	
As assessed on July 31, 2010	43.8 ± 11.5
At first symptom of multiple sclerosis	29.6 ± 9.4
At multiple sclerosis diagnosis	35.1 ± 11.1
At onset of GA treatment	39.9 ± 10.9
Sex	
Women	62 (59.6%)
Men	42 (40.4%)
Multiple sclerosis duration (years)	10.4 ± 8.1
Patients previously treated for multiple sclerosis	32 (30.8%)
Previous treatment for multiple sclerosis [a]	
Intramuscular interferon β-1a	15 (14.4%)
Subcutaneous interferon β-1a	13 (12.5%)
Mitoxantrone	7 (6.7%)
Interferon β-1b	5 (4.8%)
Azathioprine	2 (1.9%)
Cyclophosphamide	2 (1.9%)
Relapse rates during the year prior to the onset of GA treatment [b]	1.0 ± 0.9
EDSS score at the onset of GA treatment [c]	1.7 ± 1.8

GA: glatiramer acetate; EDSS: expanded disability status scale. [a] Multi-response variable; [b] Missing data, *n* = 9; [c] Missing data, *n* = 1.

Effectiveness

The relapse rate during the first year of treatment with glatiramer acetate was decreased by 60% compared to the year prior to the onset of treatment (1.0 ± 0.9 vs. 0.4 ± 0.7, $p < 0.001$) (Fig. 1a). In addition, the number of relapses decreased in 47 patients (45.1%), and 67 patients (64.4%) experienced no relapse during the first year of treatment (Fig. 1b). This decreased relapse rate was maintained and further improved during the second year of treatment, at which point the relapse rate was decreased by 70% compared to the year prior to the onset of treatment (1.0 ± 0.9 vs. 0.3 ± 0.6, $p < 0.001$), and 43 patients (41.3%) had reduced numbers of relapses. In addition, 63 patients (60.6%) reported

Figure 1. Clinical activity of multiple sclerosis according to relapses (a) and the percentage of patients without or with a decreasing number of relapses (b). [a] $p \leq 0.001$ vs. the year prior to treatment with glatiramer acetate (GA).

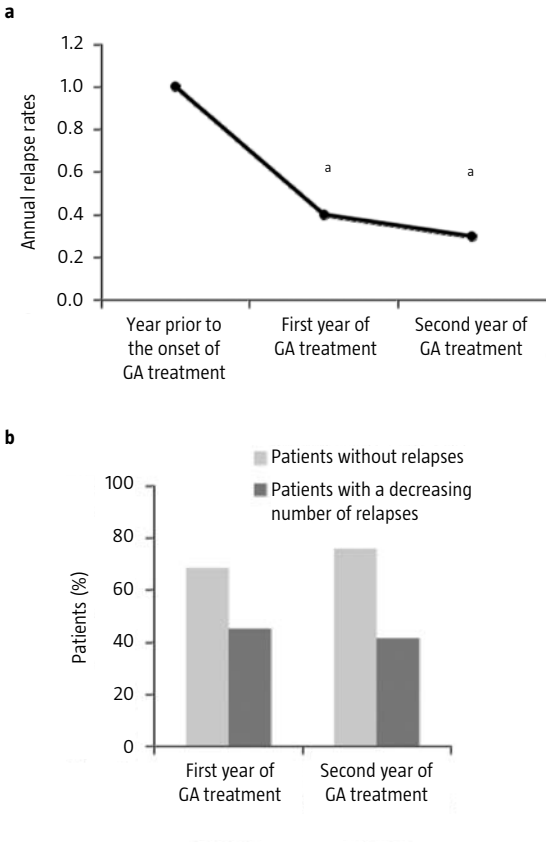
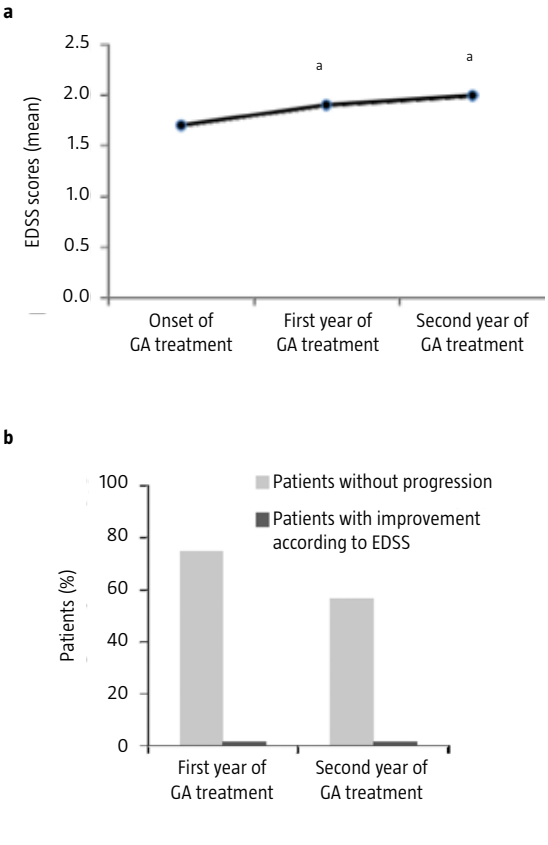


Figure 2. Progression of disability (a) and the percentage of patients without progression or improvement according to the scores on the expanded disability status scale (EDSS) (b). [a] $p \leq 0.001$ compared to the year prior to treatment with glatiramer acetate (GA).



that they had not suffered any relapses (Fig. 1b). Similarly, in a subgroup of 30 patients who had been previously treated with interferon, the switch to glatiramer acetate treatment reduced the relapse rate by 60% and 64% in the first (1.0 ± 0.9 vs. 0 4 ± 0.6, $p = 0.008$) and second (1.1 ± 1.0 vs. 0.4 ± 0.6, $p = 0.018$) years of treatment, respectively.

The analysis of patient disability showed a slight increase in the EDSS mean scores after the onset of treatment with glatiramer acetate in the first (1.7 ± 1.8 vs. 1.9 ± 1.9, $p = 0.001$) and second (1.6 ± 1.8 vs. 2.0 ± 1.9, $p < 0.001$) year of treatment (Fig. 2a). However, 78 patients (75.0%) did not show disease progression during the first year of treatment with glatiramer acetate, and two of the patients (1.9%) also showed improved EDSS scores. Similarly, 59 patients (56.7%) continued to show no progression in the second year of treatment, and the EDSS scores has also improved for two patients (1.9%) (Fig. 2b). Although there was a slight improvement in the average EDSS score for the subgroup of patients previously treated with interferon between the onset of treatment with glatiramer acetate and the first (2.1 ± 2.1 vs. 2.6 ± 2.4, $p = 0.025$) and second (1.9 ± 2.0 vs. 2.5 ± 2.4, $p = 0.012$) years of treatment, 17 patients (56.7%) and 9 patients (30 %) did not progress after one and two years of treatment, respectively.

There were no reported relapses or disease progression in 56 (53.8%) and 41 patients (39.4%) during the first and second years of treatment with glatiramer acetate, respectively. In addition, there were reports of improvements in the number of re-

Table II. Characteristics and clinical activity of those patients without relapse, those without progression and those without relapse or progression during the first year of treatment with glatiramer acetate.

		Without relapse (n = 67)	Without progression (n = 78)	Without relapse or progression (n = 56)	p
Patient characteristics	Sex				
	Women	38 (56.7%)	49 (62.8%)	33 (58.9%)	0.749
	Men	29 (43.3%)	29 (37.2%)	23 (41.1%)	
	Age (years)				
	As assessed on July 31, 2010	45.7 ± 11.4	43.5 ± 11.5	46.0 ± 11.4	0.367
	At presentation of MS	30.5 ± 9.9	29.6 ± 9.9	30.3 ± 10.1	0.849
	At onset of GA treatment	42.3 ± 11.1	39.9 ± 11.2	42.4 ± 11.2	0.32
	MS duration (years)	11.8 ± 8.5	10.3 ± 8.5	12.1 ± 8.9	0.416
Clinical activity	Relapse rate				
	Year prior to the onset of GA treatment	0.9 ± 0.9 [a]	1.0 ± 0.9	1.0 ± 0.9	0.761
	First year of GA treatment	0.0 ± 0.0	0.3 ± 0.6 [a]	0.0 ± 0.0	NA
	Second year of GA treatment	0.2 ± 0.4 [b]	0.3 ± 0.5 [e]	0.2 ± 0.5 [g]	0.405
	EDSS scores				
	Year prior to the onset of GA treatment	1.5 ± 2.0 [c]	1.5 ± 1.9 [f]	1.6 ± 2.0 [f]	0.951
	Onset of GA treatment	1.7 ± 1.9	1.7 ± 1.8	1.8 ± 2.0	0.945
	First year of GA treatment	1.8 ± 2.0 [d]	1.7 ± 1.8	1.7 ± 2.0	0.943
	Second year of GA treatment	1.9 ± 1.9 [b]	1.7 ± 1.8 [e]	1.7 ± 1.9 [g]	0.806

EDSS: expanded disability status scale; GA: glatiramer acetate; MS: multiple sclerosis; NA: not available. [a] Missing data, n = 1; [b] Missing data, n = 11; [c] Missing data, n = 4; [d] Missing data, n = 2; [e] Missing data, n = 13; [f] Missing data, n = 3; [g] Missing data, n = 8.

lapses and in patient EDSS scores during the first (1.0%) and second (1.0%) years of treatment.

The patient characteristics and clinical disease activity in the subgroups of patients without relapse, those without progression, and those without relapse or progression during the first year of treatment with glatiramer acetate are described in Table II. There were no significant differences observed in terms of the patient characteristics or the clinical activity between these patient groups.

The evaluation of the clinical factors associated with the response to treatment showed no significant differences between patients who progressed and those who did not after a year of treatment with glatiramer acetate in terms of gender –10 women (55.6%) vs. 49 males (62.8%), p = 0.599–, current age (as assessed on July 31, 2010; 43.1 ± 10.8 years vs. 43.5 ± 11.5 years, p = 0.887), age at the time of multiple sclerosis onset (29.6 ± 9.1 years vs. 29.6 ± 9.9 years, p = 0.999), age at the time of multiple sclerosis diagnosis (36.4 ± 11.2 years vs. 34.9 ± 11.5 years, p = 0.616), age at the onset of treatment with glatiramer acetate (39.5 ± 10.5 years vs. 39.9 ± 11.2 years, p = 0.901), disease duration (9.9 ± 6.4 years vs. 10.3 ± 8.5 years, p = 0.866), previous treatment with interferon –8 patients (44.4%) vs. 17 patients (21.8%), p = 0.072– or duration of treatment with glatiramer acetate (3.8 ± 2.2 years vs. 3.8 ± 1.8 years, p = 0.998). Similarly, no significant differences between patients who progressed and those who did not were observed in terms of the relapse rate in the year prior to the onset of glatiramer acetate

Table III. Adverse effects reported during the study (n = 104).

Fatigue	30 (28.9%)
Spasticity	8 (7.7%)
Depression	4 (3.9%)
Cognitive impairment	4 (3.9%)
Pain at the injection site	4 (3.9%)
Skin reaction	2 (1.9%)
Lipodystrophy	1 (1.0%)
Anxiety/palpitations	1 (1.0%)

treatment (1.0 ± 0.8 vs. 1.0 ± 0, 9, p = 0.916) or during the first (0.7 ± 0.8 vs. 0.3 ± 0.6, p = 0.056) or second (0.3 ± 0.8 vs. 0.3 ± 0, 5, p = 0.913) years of treatment. Although no significant differences in the EDSS scores were found between these groups during the year prior to the onset of treatment with glatiramer acetate (1.4 ± 1.6 vs. 1.5 ± 1.9, p = 0.869) or at the onset of treatment (1.3 ± 1.6 vs. 1.7 ± 1.8, p = 0.383), significantly higher EDSS scores were found in patients who experienced disease progression during the first year (2.7 ± 2.0 vs. 1.7 ± 1.8, p = 0.042) and second year (3.0 ± 2.1 vs. 1.7 ± 1.8, p = 0.015) of treatment.

In principle, only clinically diagnosed forms of RRMS were treated. It is possible, however, that some patients were also experiencing a secondary progressive form. Overall, clinically diagnosed and secondary progressive forms would all be considered recurrent forms, and there were only 14 patients with EDSS scores ≥ 4 at the onset of treatment with glatiramer acetate. The evaluation of clinical activity in these patients showed an absence of significant changes in the relapse rate between the year prior to and after the onset of treatment with glatiramer acetate (0.6 ± 0.7 vs. 0.2 ± 0.4, p = 0.055). Similarly, in this subgroup, there were no significant changes in the EDSS scores from the beginning of treatment with glatiramer acetate until the year following its onset (5.2 ± 1.0 vs. 5.4 ± 1.1, p = 0.189). By contrast, 81 patients with EDSS scores ≤ 3.5 at the time of onset of treatment with glatiramer acetate experienced a significantly lower relapse rate following treatment onset (1.1 ± 0.9 vs. 0.4 ± 0.7, p < 0.001), although their EDSS scores had increased slightly (1.0 ± 0.9 vs. 1.3 ± 1.2, p = 0.002).

Safety

It was necessary to suspend the glatiramer acetate treatment in only three patients (2.9%). The reasons for this discontinuation included a skin reaction in one patient (1.0%), elevated liver enzyme levels in one patient (1.0%) and pregnancy in another (1.0%).

The only adverse effects reported during the treatment with glatiramer acetate were fatigue, spasticity, depression, cognitive impairment, pain at the injection site, skin reaction, lipodystrophy and anxiety/palpitations (Table III).

Discussion

Herein, it has been shown that administration of glatiramer acetate under the conditions encountered during routine clinical practice reduces the relapse rate by 60-70% during the first 2 years of treatment, thus allowing between 68.4% and 75.9% of patients to be relapse-free and between 75% and 56.7% of patients to exhibit no disease progression. In addition, more than half of the patients showed no signs of relapse or progression during the first year of treatment, and over one-third of the patients displayed no recurrence or progression during the second year of treatment. These results are consistent with previous demonstrations of the effectiveness of glatiramer acetate during the first 2 years of treatment, and these previous clinical trials also showed significant relapse rate reductions between 59% and 82.6% following treatment [11-14]. In addition, 33.6% to 71.8% of these patients showed no relapse [11-14], and 78.4% to 91.3% of the patients showed no progression [11,13,14] during the first 2 years of treatment.

Although clinical trials provide reliable information regarding the treatment response, there are certain difficulties related to the extrapolation of these results to routine clinical practice. Indeed, the selection criteria used in these clinical trials involve the restriction of the study population to patients aged between 18 and either 45 [11], 55 [12,14] or 60 [13] years of age, those with EDSS scores between 0 and either 5 [11,14] or 5.5 [12,13] and those with at least 1 [12,14] or 2 [11] documented relapses within 6 months [12], 1 year [13,14] or 2 years [11] prior to participation in the study. In addition, the time since the emergence of the first relapse is often limited [11], such as in cases of neurological stability [11,13], where the patients received treatment prior to or concurrently with the current treatment [11-14]. In addition, the close monitoring of patients in

clinical trials may also influence the outcome. With more frequent monitoring, there are more possible times at which to detect relapses [16]. Although clinical trials represent a homogeneous and controlled scenario that hardly represents the variability observed among multiple sclerosis patients, our assessment of glatiramer acetate administration in a more heterogeneous patient population in clinical practice supports the results previously obtained under experimental conditions. In addition, although data from experimental studies are limited and it is often difficult to make comparisons, our results are consistent with those previously described regarding the reduction in relapse rates from 63.8% to 73.1% [17,18], the incidence of 58.2% to 67.4% of patients without relapse [18,19] and the lack of disease progression in 87.5% of the patients [19] during the first or second year of treatment with glatiramer acetate.

Moreover, an evaluation of the subgroup of patients who had been previously treated with interferon showed that switching from interferon to glatiramer acetate reduced the relapse rate by 60-64%, and more than half of these patients also showed no disease progression. These results coincide with the favourable clinical outcomes of previously reported observational studies in which interferon treatment was switched due to suboptimal responses or adverse effects [20-23]. Therefore, treatment with interferon not only does not adversely affect the effectiveness of subsequent treatment with glatiramer acetate but also may also benefit patients with unsatisfactory clinical outcomes and enable them to obtain significant improvement.

The absence of significant differences in the demographic or clinical characteristics of patients with relapses, of those with disease progression or those with relapses and disease progression does not indicate that patient characteristics can be used to predict the treatment response. Similarly, the evaluation of factors potentially associated with the response of patients who did or did not progress showed no significant differences in terms of gender, age, duration of illness, previous interferon treatment, duration of treatment with glatiramer acetate, annual relapse rate, EDSS score during the year prior to treatment with glatiramer acetate and EDSS scores at the onset of treatment. A significant increase was observed regarding the EDSS score during the first and second year of treatment for patients who showed disease progression, and this result likely reflects an underlying neurological deterioration of the scale. These results also support a lack of influence for most of the baseline patient characteristics regarding the effectiveness of glatiramer acetate, as described by a meta-analysis performed on placebo-controlled clinical trials [24]. Therefore, it is necessary to continue to investigate additional factors that may be associated with the response to glatiramer acetate treatment for clinical decision making.

For treatment decision making, an evaluation of the safety profile is absolutely necessary. The administration of glatiramer acetate under clinical practice conditions was well tolerated and demonstrated a safety profile equivalent to that described previously [25]. The reported frequencies of adverse effects were low, especially for skin reactions, which we interpreted to be due to the retrospective nature of the study. Medical records reported only serious reactions, and there was no evidence of mild to moderate skin reactions. Although the same was true of other adverse reactions, with the exception of skin reaction cases, we could not determine the existence of a causal relationship between these reactions and glatiramer acetate treatment. In addition, a very small proportion of patients discontinued treatment during the study period, which suggests that most patients tolerated the treatment and found it to be beneficial. In addition, the importance of patient care in a specialist unit was emphasised; the health professionals could adequately follow the patients with frequent and regular follow-ups and treat side effects, which increased the value of the continued treatment and provided on-going education and support.

The authors acknowledge that although observational studies provide valuable information regarding the administration of treatment under clinical practice conditions, these studies are not capable of providing conclusive data. Taken together, this acknowledgement combined with the constraints imposed by the retrospective nature of the study and the lack of a control group for comparison implies that our results need to be interpreted with caution. Although it is difficult to generalise the results of a population at a single centre, the patient characteristics in this study were similar to those previously described in a study conducted in Spain [26]. Furthermore, no information was available regarding the patients' MRI results. Although the clinical variables, such as relapses and disability, are essential for determining responses to treatment, MRI results provide additional data that support therapeutic decision making [15].

In conclusion, this study demonstrates that the administration of glatiramer acetate in clinical prac-

tice is beneficial in terms of the relapse rate and disease progression of patients, and these results coincide with those obtained in previous clinical trials. The safety profile of this treatment also coincided with that shown by previous studies (i.e., a low proportion of patients with adverse effects and treatment discontinuation). However, more studies are needed to confirm our results on the effects of glatiramer acetate under clinical practice conditions and to identify factors that may influence the response to treatment.

References

1. Trapp BD, Peterson J, Ransohoff RM, Rudick R, Mork S, Bo L. Axonal transection in the lesions of multiple sclerosis. N Engl J Med 1998; 338: 278-85.
2. Multiple Sclerosis International Federation. Atlas of multiple sclerosis database. URL: http://www.atlasofms.org. [04.07.2011].
3. Ares B, Prieto JM, Lema M, Dapena D, Arias M, Noya M. Prevalence of multiple sclerosis in Santiago de Compostela (Galicia, Spain). Mult Scler 2007; 13: 262-4.
4. Aladro Y, Alemany MJ, Pérez-Vieitez MC, Amela R, Conde R, Pino MP, et al. Prevalence and incidence of multiple sclerosis in Las Palmas, Canary Islands, Spain. Neuroepidemiology 2005; 24: 70-5.
5. Modrego PJ, Pina MA. Trends in prevalence and incidence of multiple sclerosis in Bajo Aragón, Spain. J Neurol Sci 2003; 216: 89-93.
6. Blanchette F, Neuhaus O. Glatiramer acetate: evidence for a dual mechanism of action. J Neurol 2008; 255 (Suppl 1): S26-36.
7. Arnon R, Aharoni R. Neurogenesis and neuroprotection in the CNS –fundamental elements in the effect of glatiramer acetate on treatment of autoimmune neurological disorders. Mol Neurobiol 2007; 36: 245-53.
8. Aharoni R, Kayhan B, Eilam R, Sela M, Arnon R. Glatiramer acetate-specific T cells in the brain express T helper 2/3 cytokines and brain-derived neurotrophic factor in situ. Proc Natl Acad Sci U S A 2003; 100: 14157-62.
9. Comi G, Martinelli V, Rodegher M, Moiola L, Bajenaru O, Carra A, et al. Effect of glatiramer acetate on conversion to clinically definite multiple sclerosis in patients with clinically isolated syndrome (PreCISe study): a randomised, double-blind, placebo-controlled trial. Lancet 2009; 374: 1503-11.
10. Comi G, Filippi M, Wolinsky JS. European/Canadian multicenter, double-blind, randomized, placebo-controlled study of the effects of glatiramer acetate on magnetic resonance imaging–measured disease activity and burden in patients with relapsing multiple sclerosis. European/Canadian Glatiramer Acetate Study Group. Ann Neurol 2001; 49: 290-7.
11. Johnson KP, Brooks BR, Cohen JA, Ford CC, Goldstein J, Lisak RP, et al. Copolymer 1 reduces relapse rate and improves disability in relapsing-remitting multiple sclerosis: results of a phase III multicenter, double-blind placebo-controlled trial. The Copolymer 1 Multiple Sclerosis Study Group. Neurology 1995; 45: 1268-76.
12. Cadavid D, Wolansky LJ, Skurnick J, Lincoln J, Cheriyan J, Szczepanowski K, et al. Efficacy of treatment of MS with IFNbeta-1b or glatiramer acetate by monthly brain MRI in the BECOME study. Neurology 2009; 72: 1976-83.
13. Mikol DD, Barkhof F, Chang P, Coyle PK, Jeffery DR, Schwid SR, et al. Comparison of subcutaneous interferon beta-1a with glatiramer acetate in patients with relapsing multiple sclerosis (the REbif vs Glatiramer Acetate in Relapsing MS Disease [REGARD] study): a multicentre, randomised, parallel, open-label trial. Lancet Neurol 2008; 7: 903-14.
14. O'Connor P, Filippi M, Arnason B, Comi G, Cook S, Goodin P, et al. 250 microg or 500 microg interferon beta-1b versus 20 mg glatiramer acetate in relapsing-remitting multiple sclerosis: a prospective, randomised, multicentre study. Lancet Neurol 2009; 8: 889-97.
15. Sánchez-De la Rosa R, Sabater E, Casado MA. Análisis del impacto presupuestario del tratamiento en primera línea de la esclerosis múltiple remitente recurrente en España. Rev Neurol 2011; 53: 129-38.
16. García-Merino MA, Fernández O, Montalban X, De Andrés C, Arbizu T. Documento de consenso de la Sociedad Española de Neurología sobre el uso de medicamentos en esclerosis múltiple: escalado terapéutico. Neurologia 2010; 25: 378-90.
17. Kurtzke JF. Rating neurologic impairment in multiple sclerosis: an expanded disability status scale (EDSS). Neurology 1983; 33: 1444-52.
18. Ziemssen T, Hoffman J, Apfel R, Kern S. Effects of glatiramer acetate on fatigue and days of absence from work in first-time treated relapsing-remitting multiple sclerosis. Health Qual Life Outcomes 2008; 6: 67.
19. Haas J, Firzlaff M. Twenty-four-month comparison of immunomodulatory treatments –a retrospective open label study in 308 RRMS patients treated with beta interferons or glatiramer acetate (Copaxone). Eur J Neurol 2005; 12: 425-31.
20. Carra A, Onaha P, Luetic G, Burgos M, Crespo E, Deri N, et al. Therapeutic outcome 3 years after switching of immunomodulatory therapies in patients with relapsing-remitting multiple sclerosis in Argentina. Eur J Neurol 2008; 15: 386-93.
21. Oreja-Guevara C, Bermejo PE, Miralles A, Gabaldón L, Aguilar MJ, Díez-Tejedor E. Glatiramer acetate in interferon beta non respondent relapsing-remitting multiple sclerosis. Neurologia 2009; 24: 435-8.
22. Caon C, Din M, Ching W, Tselis A, Lisak R, Khan O. Clinical course after change of immunomodulating therapy in relapsing-remitting multiple sclerosis. Eur J Neurol 2006; 13: 471-4.
23. Zwibel HL. Glatiramer acetate in treatment-naive and prior interferon-beta-1b-treated multiple sclerosis patients. Acta Neurol Scand 2006; 113: 378-86.
24. Martinelli BF, Rovaris M, Johnson KP, Miller A, Wollinsky JS, Ladkani D, et al. Effects of glatiramer acetate on relapse rate and accumulated disability in multiple sclerosis: meta-analysis of three double-blind, randomized, placebo-controlled clinical trials. Mult Scler 2003; 9: 349-55.
25. Carter NJ, Keating GM. Glatiramer acetate: a review of its use in relapsing-remitting multiple sclerosis and in delaying the onset of clinically definite multiple sclerosis. Drugs 2010; 70: 1545-77.
26. Fernández O, Fernández V, Arbizu T, Izquierdo G, Boscá I, Arroyo R, et al. Characteristics of multiple sclerosis at onset and delay of diagnosis and treatment in Spain (the Novo Study). J Neurol 2010; 257: 1500-7.

Efectividad del acetato de glatiramero en la práctica clínica: un estudio observacional

Objetivos. Evaluar la efectividad clínica y la seguridad del acetato de glatiramero en las condiciones de la práctica diaria.

Pacientes y métodos. Estudio retrospectivo, observacional, en pacientes con esclerosis múltiple tratados con acetato de glatiramero en las condiciones de la práctica clínica. El criterio principal de valoración fue la efectividad clínica del acetato de glatiramero.

Resultados. En el estudio se incluyeron un total de 104 pacientes (mujeres: 59,6%; edad de inicio del acetato de glatiramero: 39,9 ± 10,9 años; tratamiento anterior para la esclerosis múltiple: 30,8%). Los pacientes recibieron acetato de glatiramero durante 3,6 ± 1,9 años. Durante el primer año de tratamiento con el acetato de glatiramero, la tasa de recidiva se redujo un 60%, en 47 pacientes (45,1%) se redujo el número de recidivas, 67 pacientes (68,4%) no sufrieron recidiva y 78 pacientes (75%) no mostraron progresión. Durante el segundo año de tratamiento con acetato de glatiramero, la tasa de recidiva había disminuido un 70%, en 43 pacientes (41,3%) se redujo el número de recidivas, 63 pacientes (75,9%) no sufrieron recidiva y 59 pacientes (56,7%) no mostraron progresión. No se notificaron recidivas ni progresión en 56 (53,8%) y 41 pacientes (39,4%) durante el primer y segundo año de tratamiento, respectivamente. La suspensión del acetato de glatiramero sólo fue necesaria en tres pacientes. Los acontecimientos adversos más frecuentes fueron cansancio (28,9%) y espasticidad (7,7%).

Conclusión. La evaluación del acetato de glatiramero en las condiciones de la práctica clínica respalda el perfil de eficacia y seguridad observado en ensayos clínicos previamente publicados.

Palabras clave. Acetato de glatiramero. Efectividad. Esclerosis múltiple. Progresión. Recidiva. Seguridad. Tratamiento.