Glatiramer Acetate Depot (Extended-Release) Phase II Study in Patients with Relapsing Remitting Multiple Sclerosis: Safety, Tolerability and Efficacy (NEDA) - Two Years Data

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BACKGROUND

Multiple sclerosis (MS) is a chronic disease, requiring lifelong therapy. While several disease-modifying treatments (DMTs) have been developed and approved, low treatment adherence, which leads to sub-optimal clinical outcomes, remains an unmet need. Glatiramer acetate (GA) long-acting injection (GA Depot) consists of extended-release microspheres containing GA, intended for administration once every 28 days. Results of a GA Depot phase II one-year core study in relapsing remitting MS (RRMS) patients suggest that GA Depot treatment was safe, tolerable and efficacious. Subjects who completed the core study were offered to continue to the study extension.

OBJECTIVE

Assess the safety, tolerability and efficacy of GA Depot in patients with RRMS by the proportion of patients with No Evidence of Disease Activity (NEDA-3, defined as: no relapses, no 12-week confirmed disability progression, no new T2 lesions and no gadolinium-enhancing lesions on MRI) after two years of treatment with GA Depot in a subgroup of 13 patients that completed the core study and continued to the study extension.

DESIGN/METHODS

Main eligibility criteria included: age 18-70 years, diagnosis of RRMS and treatment with Copaxone® for ≥12 months prior to study enrollment. Patients received GA Depot intramuscularly every 28 days, at doses of 80mg or 40mg in the core study (52 weeks) and 40mg in the study extension (additional 48 weeks, see figure 1).

Figure 1: study design

RESULTS

Related Adverse events (AEs) mainly included mild injection site reactions and no unexpected AEs were reported. Overall, the number of AEs was reduced during the second year (GEE model, P<0.001, Table 1). No immediate post-injection reactions, as reported with other GA preparations, were detected. Patients received all injections as per protocol. Mean EDSS score after two years showed no significant change compared to baseline (Figure 2). One patient had two relapses during the two-year study. No MRI activity was noted in any patient during that period. Two years NEDA-3 was achieved by 81.8% of the patients (Table 2).

Table 1: Two Years Adverse Events (mITT)

Severity	1st year				Extension			
	Not Related		Related		Not Related		Related	
	N	Rate*	N	Rate*	N	Rate*	N	Rate*
Mild	37	0.22	104	**0.62**	24	0.17	40	**0.28**
Moderate	21	0.12	8	**0.05**	10	0.07	5	**0.04**
Severe	0	0	0	**0**	0	0	1	**0.01**

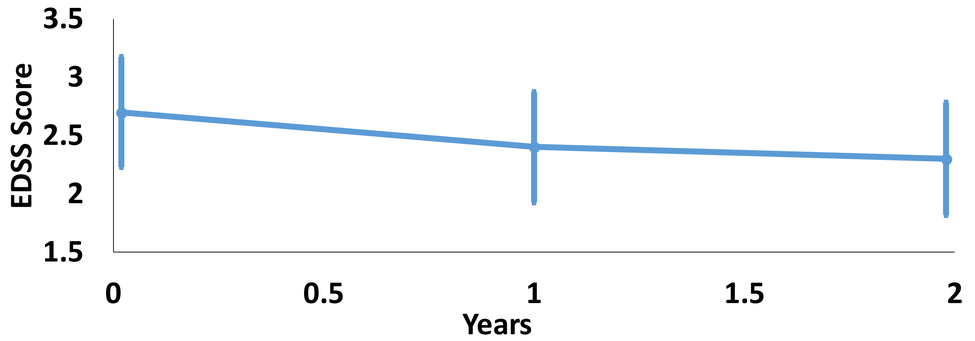
*Rate is number of Adverse Events adjusted to number of injections (169 for core study and 142 in the extension). A statistical significant reduction in AE number was noted in the extension period (GEE model, p < 0.0001).mITT: modified Intent To Treat population.

Table 2: Two Years NEDA-3

Two years' NEDA	Core study and extension: 40mg		Core study: 80mg, Extension: 40mg		All	
	N	%	N	%	N	%
PP*	7/7	100	2/4	50	9/11	81.8
mITT (LOCF)	8/8	100	2/5	40	10/13	76.9

PP: Per Protocol Population; 11 patients that completed the two years.
mITT: modified Intent To Treat population, 13 patients, Last Observation Carried Forward analysis.

Figure 2: Mean EDSS score from baseline until two years (mITT*)



Data presented as mean ± SE. n=13 for screening and 12 months, 11 for 24 months. Two patients had early termination. EDSS of these patients was 3.5 at screening and at early termination (no change).

* EDSS performed up to 4 weeks following planned time point was included in the analysis. mITT: modified Intent To Treat population.

CONCLUSIONS

Encouraging results of the GA Depot two-year data support the product's safety, tolerability, and efficacy in this study cohort. It further supports the assumption of GA Depot's potential to improve MS treatment by significantly reducing the frequency of injections, increasing adherence and providing a therapeutic benefit.

DISCLOSURES

Prof. Ariel Miller participated as the core-study Coordinating Principal Investigator and as a site Principal investigator (PI) in the study funded by Mapi Pharma. Dr. Shlomo Flechter participated as the extension-study Coordinating Principal Investigator and as a site Principal investigator (PI) in the study funded by Mapi Pharma. Dr. Ron Milo, Prof. Joab Chapman, Dr. Alla Shifrin, Prof. Ronit Gilad, Prof. Dimitrios Karussis and Dr. Arnon Karni participated as PIs in the study funded by Mapi Pharma. Dr. Chen Hoffmann participated as the central reading MRI facility in the study funded by Mapi Pharma. Laura Popper, Nadav Bleich Kimelman, Shai Rubnov (co-inventor of GA Depot) and Uri Danon are employed by Mapi Pharma. Ehud Marom is a co-inventor of GA Depot, and founder and CEO of Mapi Pharma. *Study Supported by: Mapi Pharma Ltd*