Glatiramer Acetate Depot (Extended-Release) Phase IIa Study in Patients with Relapsing Remitting Multiple Sclerosis: Safety, Tolerability and Efficacy (No Evidence of Disease Activity) Subpopulation Three-Years Analysis

S. Flechter[1] ,A. Miller[2,3], L. Popper[4], N. Bleich Kimelman[4], S. Rubnov[4], U. Danon[4], E. Marom[4], R. Milo[5,6], J. Chapman[7,8], A. Shifrin[9], R. Gilad[10], C. Hoffmann[11], D. Karussis[12], A. Karni[8,13]

[1] Multiple Sclerosis Clinical Research and Therapy Service, Department of Neurology, Shamir (Assaf Harofeh) Medical Center, Zerifin, [2]Rappaport Faculty of Medicine, Technion-Israel Institute of Technology, [3] Multiple Sclerosis & Brain Research Center, Carmel Medical Center, Haifa, [4] Mapi Pharma LTD., Ness Ziona, [5] Department of Neurology, Barzilai University Medical Center, Ashkelon, [6] Faculty of Health Sciences, Ben-Gurion University of the Negev, Beer Sheva, [7] Department of Neurology, Sheba Medical Center, Ramat Gan, [8] Sackler Faculty of Medicine, Tel Aviv University, Tel Aviv, [9] Department of Neurology, Rambam Medical Center, Haifa, [10] Department of Neurology, Kaplan Medical Center, Rehovot, [11] Diagnostic and Interventional Imaging, Sheba Medical Center, Ramat Gan, [12] Unit of Neuroimmunology-MS Center, Hadassah Medical Center, Ein Kerem, Jerusalem, [13] Neuroimmunology Clinic, Tel Aviv Sourasky Medical Center, Tel Aviv, Israel.

BACKGROUND

Multiple sclerosis (MS) is a chronic disease, requiring lifelong therapy. While several DMTs have been approved, improvement of treatment adherence remains an unmet need. Glatiramer acetate (GA) long-acting injection (GA Depot) consists of extended-release microspheres containing GA, administered intramuscularly once every 28 days. Results of GA Depot phase IIa one-year core study and two years extension period in relapsing remitting MS (RRMS) suggest that GA Depot is safe, tolerable and efficacious

OBJECTIVE

Assess the safety, tolerability and efficacy by NEDA, defined as: no relapses, no 12-week confirmed disability progression, no new T2 lesions and no gadolinium-enhancing lesions on MRI after three years of treatment with GA Depot in the subpopulation of 11 RRMS patients who completed the core study and continued through two years of the study extension

DESIGN/METHODS

Eligibility criteria included: age 18-70 years, diagnosis of RRMS and treatment with Copaxone® for ≥12 months prior to enrollment. Patients received GA Depot at doses of 80mg or 40mg in the core study and 40mg in the study extension. Patients who completed the core study (52 weeks) continued to two years of extension (up to week 148, see figure 1).

Figure 1: study design

RESULTS

Adverse events (AEs) mainly included mild injection site reactions. No unexpected AEs were reported. The number of AEs was significantly reduced during the second and third year (table 1). No systemic immediate post-injection reactions were detected. Patients received all injections as per protocol. Data analyzed by intention to treat population (mITT) (n=11): Mean EDSS score after three years showed no significant change compared to baseline (figure 2). One patient had 3 relapses during the three-year study. No MRI activity was noted during that period. Three years NEDA was achieved by 81.8% of the patients (mITT) or 90% of the per protocol population (table 2).

Table 1: Three Years Adverse Events (mITT)

Severity	Core				1st Extension year				2nd Extension year			
	Not Related		Related		Not Related		Related		Not Related		Related	
	N	Rate*	N	Rate*	N	Rate*	N	Rate*	N	Rate*	N	Rate*
Mild	27	**0.21**	71	**0.55**	22	**0.17**	25	**0.19**	20	**0.17**	13	**0.11**
Moderate	10	**0.08**	6	**0.05**	2	**0.02**	2	**0.02**	2	**0.02**	0	**0**

*Rate is number of Adverse Events adjusted to number of injections : 130 for core study, 130 for first extension year and 120 for the second extension year. A statistical significant reduction in AE number was noted in the extension period compared with the core study (GEE model, $p < 0.0001$).

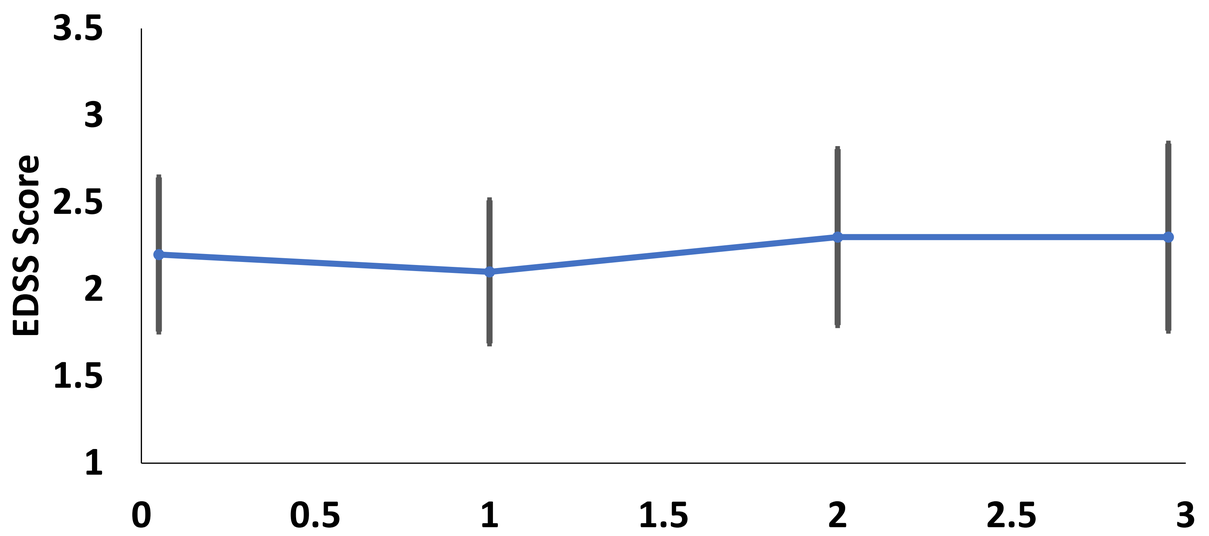
mITT: modified Intent To Treat population.

Table 2: Three Years NEDA-3

Three years' NEDA	Core study and extension: 40mg		Core study: 80mg, Extension: 40mg		All	
	N	%	N	%	N	%
PP*	7/7	100	2/3	66.7	9/10	90
mITT (LOCF) **	7/7	100	2/4	50	9/11	81.8

*PP: Per Protocol Population; 10 patients that completed the three years. **mITT: modified Intent To Treat population, 11 patients, Last Observation Carried Forward analysis.

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



Data presented as mean ± SE. n=10. 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 three-year study support its 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 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.

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