Glatiramer Acetate Depot (Extended-release) Phase IIa Study In Patients With Relapsing-Remitting Multiple Sclerosis: Six Months' Interim Analysis

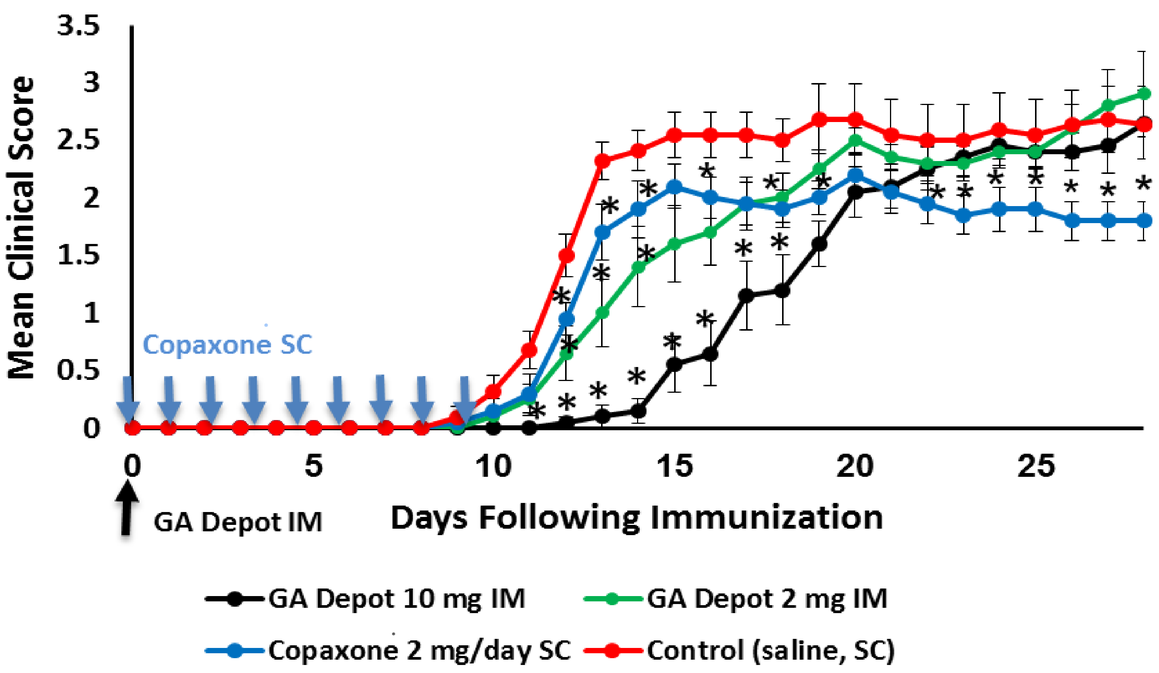
A. Miller[1,2], L. Popper[3], N. Bleich Kimelman[3], S. Rubnov[3], U. Danon[3], E. Marom[3], S. Flechter[4], R. Milo[5,6], J. Chapman[7,8], A. Shifrin[9], R. Gilad[10], C. Hoffmann[11], D. Karussis[12], A. Karni[8,13]

[1] Rappaport Faculty of Medicine, Technion-Israel Institute of Technology, [2] Multiple Sclerosis & Brain Research Center, Carmel Medical Center, Haifa, [3] Mapi Pharma LTD., Ness Ziona, [4] Multiple Sclerosis Clinical Research and Therapy Service, Department of Neurology, Assaf Harofeh Medical Center, Zerifin, [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

Relapsing-Remitting Multiple Sclerosis (RRMS) is the most common initial form of Multiple Sclerosis (MS). Glatiramer acetate (GA) long-acting injection (GA Depot) is a combination of extended-release microspheres containing GA for injection and diluent for parenteral use. GA is released from the depot formulation continuously over a 30 days' period. In vivo data in rodents showed that GA Depot is as effective as Copaxone® in ameliorating *Myelin Oligodendrocyte Glycoprotein - Experimental Autoimmune Encephalomyelitis* (MOG-EAE) symptoms (Fig 1).

Fig 1: GA Depot Effect on MOG-EAE in Mice



** P<0.05 compared with untreated control, single factor ANOVA followed by one-tail two-sample T test, assuming unequal variances, n=10 / group, +/- standard error. GA Depot at two dose level tested was as efficient as Copaxone® in ameliorating disease activity*

OBJECTIVE

To assess the safety, tolerability and efficacy of once-a-month long-acting IM injection of GA Depot in patients with RRMS.

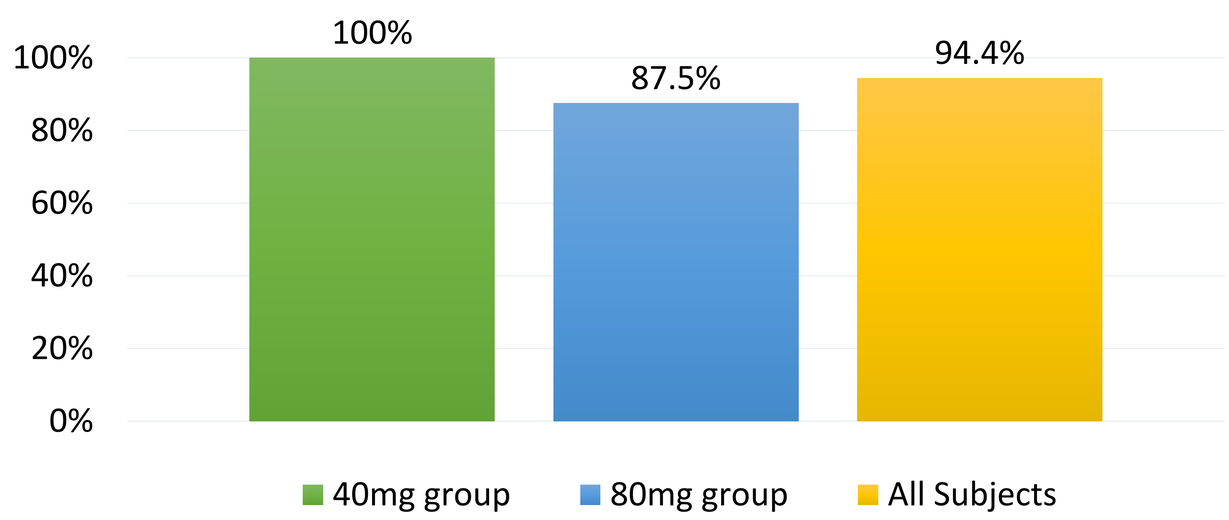
DESIGN/METHODS

Main eligibility criteria included age 18-70 years, RRMS diagnosis (McDonald criteria revision 2010) and treatment with Copaxone® for at least 12 months prior to study enrollment. Patients received GA Depot every 28 days (IM); either 80mg or 40mg, for up to 52 weeks.

RESULTS

Six months' data: Twenty-five RRMS patients were enrolled as follows: 80mg dose (n=12) and 40mg dose (n=13). Overall, 72% of study population were female, mean MS duration was 15.5 years and mean EDSS score was 2.4 at baseline. No unexpected safety issues were recorded with GA Depot. Adverse events (AEs) mainly included mild injection site reactions (ISRs). Statistically significantly fewer ISRs were reported with the 40mg dose than with the 80mg dose. No immediate post-injection reactions, as recorded with Copaxone®, were reported with GA Depot. AEs other than ISRs were mostly mild. Two relapses were recorded during treatment with Copaxone®, within 12 months prior to study enrollment. No relapses occurred during 6 months of treatment with GA Depot. No mean EDSS score changes were recorded. Ninety four percent of patients showed no changes (no new lesions nor newly enhancing lesions) in 6 months' MRI scans compared to baseline (Fig 2).

Fig. 2 Percent of Subjects without MRI Changes from Baseline



CONCLUSIONS

The encouraging results of the GA Depot six months' trial strengthen the original assumption that GA Depot has the potential to improve MS mode of treatment by significantly reducing the frequency of injections and providing a therapeutic benefit. GA Depot six months' efficacy, safety and tolerability data prompts the continuation to one phase III pivotal trial.

DISCLOSURES

Prof. Ariel Miller participated as the study Coordinating Principal Investigator and as a site Principal investigator (PI) in the study. Dr. Shlomo Flechter, 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. Dr. Chen Hoffmann participated as the central reading MRI facility in the study. Dr. Laura Popper, Dr. Nadav Bleich Kimelman, Dr. Shai Rubnov (co-inventor of GA Depot) and Uri Danon are employed by Mapi Pharma. Ehud Marom is a co-inventor of GA Depot, founder, and the CEO of Mapi Pharma.

Study Supported by: Mapi Pharma Ltd.