Glatiramer Acetate Depot (Extended-Release) Phase IIa One-Year Study in Patients with Relapsing-Remitting Multiple Sclerosis: Safety, Tolerability and Efficacy (NEDA) Analysis

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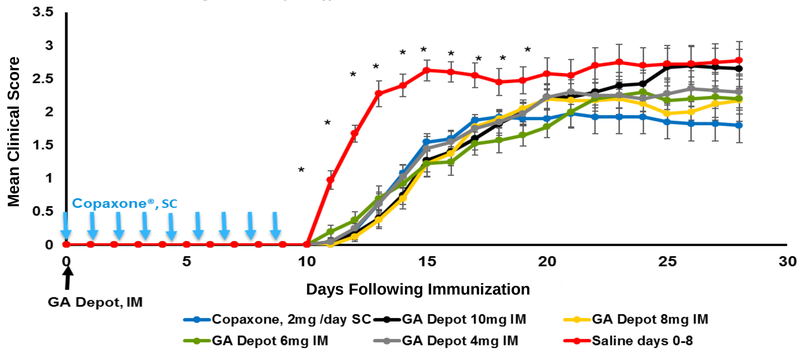
BACKGROUND

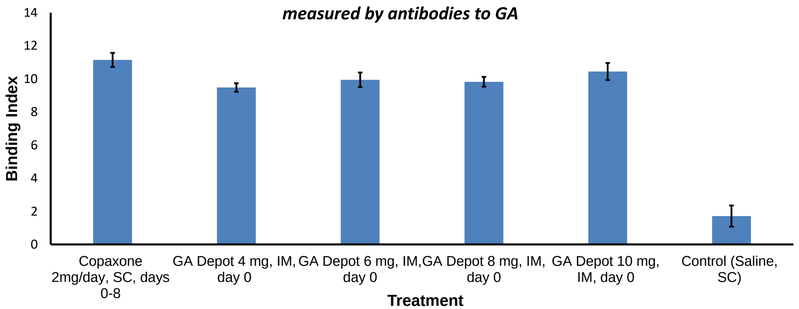
To date, Multiple Sclerosis (MS) cannot be cured and, as a chronic disease, MS requires lifelong therapy for which adherence is still a major challenge. While several disease-modifying treatments have been developed and approved for MS, still, unmet need remains to improve patient outcomes, by improving treatment efficacy, tolerability and adherence. Glatiramer acetate (GA) long-acting injection (GA Depot) consists of microspheres containing GA, which is released from its formulation continuously over 30 days. In vivo data generated in MOG-EAE mice model (*Myelin Oligodendrocyte Glycoprotein - Experimental Autoimmune Encephalomyelitis*), has shown that GA Depot is as effective as Copaxone® in ameliorating EAE symptoms (Fig 1). Immunological response induced by Copaxone® and GA Depot in escalating doses, was evaluated using serum samples isolated from mice in MOG-EAE model study at day 35. Level of antibodies to GA measured using ELISA assay were similar in all GA Depot treated groups and Copaxone® treated group suggesting similar immunological response to both drug treatments (Fig 2).

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



*n=20 / group, +/- standard error . *P<0.05 compared with untreated control, single factor ANOVA followed by one-tail two-sample T test assuming unequal variances. GA Depot given once, IM, at 4,6,8 or 10 mg dose was as efficacious as Copaxone®, given nine time SC, in ameliorating MOG-EAE symptoms in mice.*

Fig 2: Biomarker for GA Depot Activity – Immunological response in mice measured by antibodies to GA



Serum was isolated from mice in MOG-EAE study at day 35 following disease induction. Mice were treated with either GA Depot (at 4,6,8 or 10 mg) or Copaxone. Antibodies (Abs) quantity was evaluated using ELISA assay. Results are expressed as binding index (BI). The cut off value for BI is 2.0± 1.0. Values above 3.0 can be considered as positive. n = 5 mice / group.

OBJECTIVE

To assess the safety, tolerability and efficacy of GA Depot in relapsing-remitting multiple sclerosis (RRMS) patients.

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

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±8.3 years and mean EDSS score was 2.4±1.6, at baseline. Adverse events (AEs) mainly included mild injection site reactions (ISRs) and no unexpected AEs were reported. Statistically significant fewer ISRs were reported with the 40mg dose than with the 80mg dose. No immediate post-injection reactions, as recorded with GA (Copaxone®), were detected. Two relapses were recorded during treatment with Copaxone®, within 12 months prior to study enrollment; one relapse with no changes in EDSS score was recorded during the study. No changes in the mean EDSS score were recorded per protocol (PP) population (Fig 3). Above 92% of the PP population showed no changes (no new lesions nor newly enhancing lesions) in 12 months' MRI scans compared to baseline (Fig 4). **A composite outcome: No Evidence of Disease Activity (NEDA), defined as no relapses, no 12-week confirmed disability progression and no new lesions or no gadolinium-enhancing lesions, was achieved by 84.6% of the patients (PP population) in this GA Depot phase II one-year trial (Fig 5).**

Fig 3: Mean EDSS Score by Visit – All Subjects – PP population

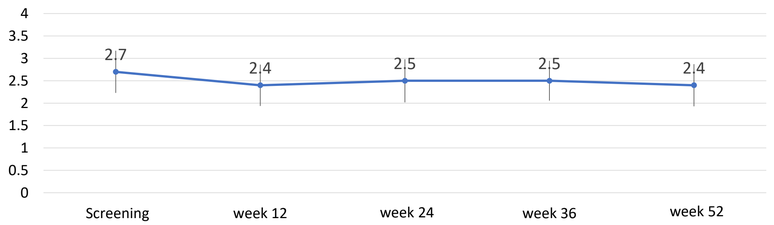


Fig 4: Percent of Subjects without MRI Changes from Baseline by Group - PP population

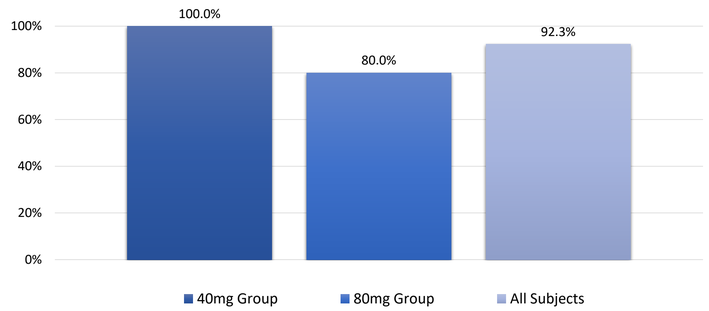
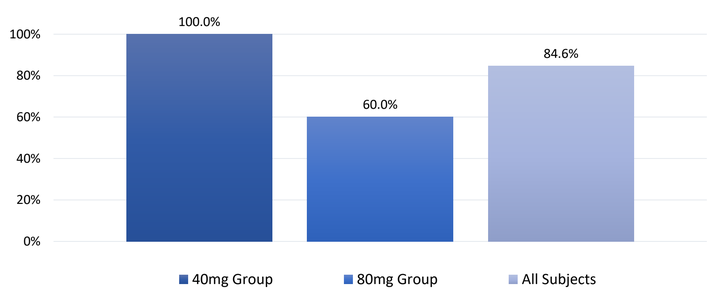


Fig 5: Percent of Subjects Achieving NEDA by Groups PP Population



CONCLUSIONS

The GA Depot small cohort one-year results support the assumption of its potential to improve MS treatment by significantly reducing number of injections, increasing adherence and providing a therapeutic benefit. GA Depot's safety, tolerability and encouraging efficacy data prompts the continuation to one phase III pivotal trial.

DISCLOSURES

Prof. Ariel Miller participated as 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 & Dr. Arnon Karni participated as PIs in the study. Dr. Chen Hoffmann participated as the central MRI reading facility. 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.

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