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).

OBJECTIVE

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

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).

DISCUSSIONS

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. The BI values above 3.0 can be considered as positive. n = 5 mice/group.

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

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

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.