Pre-clinical studies and evaluation of treatment need of glatiramer acetate depot

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Background: Glatiramer Acetate (GA) is the active pharmaceutical ingredient in Copaxone®, prescribed for treatment of relapsing remitting multiple sclerosis (RRMS). GA Depot is a long-acting formulation of GA intended for intramuscular (IM) injection once every 28 days. It is expected that GA Depot will significantly increase compliance of GA users and therefore will provide a therapeutic benefit.

Aims: (1) to compare monthly injected GA Depot activity to that of Copaxone®, (2) to assess the unmet need for such formulation among current Copaxone® users.

Methods: GA Depot was evaluated in vitro for GA release profile. In vivo, GA Depot’s effect on clinical manifestations of MOG-EAE was compared to that of Copaxone®. Additionally a questionnaire study was performed among RRMS patients treated with Copaxone® in order to assess the clinical need for GA Depot.

1. GA Depot releases GA for 28 days in a constant rate, in vitro

In order to analyze GA release profile from GA Depot, samples of GA Depot were suspended in PBS at 37°C and mixed continuously for over 30 days. Samples were retrieved periodically and analyzed for GA Content. Data demonstrate a steady and linear release of GA from the formulation over 30 days. By day 30, more than 90% of the GA is released from the formulation.

2. MAPI GA and GA Depot effect on MOG-EAE is similar to Copaxone®

Development of MOG-induced EAE in C57BL/6 mice was assessed by daily clinical scoring of the mice up to Day 28 post-inmunization. Study was designed to analyze the effect of GA Depot on EAE symptoms and to compare the activity of MAPI GA to commercial Copaxone®. MAPI GA activity in this model was highly similar to the effect of Copaxone® (figs. 2A & B). When GA Depot was tested, mean clinical score AUC (which denotes disease burden over time) was significantly reduced in all treatment groups compared with an untreated control (fig. 2C). When GA Depot 10 mg was used, the AUC was notably lower than the AUC of the commercial Copaxone® group and of the 2 mg GA Depot group (fig. 2B). A statistically significant reduction in mean disease score was observed from day 11 to 19 when the GA Depot 10 mg group was compared to the untreated control and from day 12 to 18 when GA Depot 2 mg was compared to the untreated control (fig. 2C).

3. There is an unmet need for GA Depot among Copaxone® users

In order to determine the need for GA Depot among current Copaxone® users, a questionnaire study (approved by Carmel MC IRB) was conducted. Questionnaires included 43 questions covering general demographics, general quality of life, compliance to Copaxone® treatment and the effect of dosing regimen on quality of life. Study population included Copaxone® treated RRMS patients (at least 1 year). Data show that while Copaxone® users are highly satisfied from the treatment, they are less satisfied from its dosing regimen (fig. 3A). Over 70% of subjects expressed: (1) increased satisfaction if frequency of injections would be reduced from once daily to once monthly, and (2) willingness to switch to IM GA Depot although it may cause increased injection site adverse events (fig. 3B).

Conclusions: in vitro and in vivo data suggests that GA Depot has a potential beneficial effect in RRMS. Moreover, there is a clear unmet need for such treatment among Copaxone® treated RRMS patients. An open-labelled phase IIa clinical study is being conducted in Israel to test the safety, tolerability and efficacy of GA Depot monthly injected.