GA Depot (long-acting IM injection of glatiramer acetate) Impact on EDSS stability in Relapsing forms of Multiple Sclerosis (RMS) and Primary Progressive Multiple Sclerosis (PPMS)

Aaron Miller[1] MD, Laura Popper[2] MD, Joseph Berger[3] MD, Amit Bar-Or[3] MD, Robert Zivadinov[4] MD, Alexey Boyko[5], MD, Hadar Kolb[6] MD, Arnon Karni[6] MD, Ornit Almog[2], Nadav Bleich Kimelman[2] DMD PhD, Shai Rubnov[2] PhD, Uri Danon[2], Ehud Marom[2]

1 Icahn School of Medicine at Mount Sinai, Neurology (New York, NY, USA), 2 Mapi Pharma Ltd (Ness Ziona, Israel), 3 University of Pennsylvania (Philadelphia, PA, USA), 4 Buffalo Neuroimaging Analysis Center, University at Buffalo, State University of New York, (Buffalo, NY, USA), 5 Pirogovs Russian National Research University and Federal Center of Brain Research and Neurotechnologies (Moscow, Russia), 6 Tel Aviv Sourasky Medical Center (Tel Aviv, Israel)

Background

Multiple sclerosis (MS) is a chronic disease requiring lifelong therapy, where patients accumulate disability over time, as measured by the Expanded Disability Status Scale (EDSS). Glatiramer acetate (GA) Depot, a formulation of GA in extended-release microspheres, is administered intramuscularly once every 28 days.

Objective

To analyze the effect of GA Depot on disability accumulation using EDSS data from GA Depot clinical studies in RMS and PPMS patients.

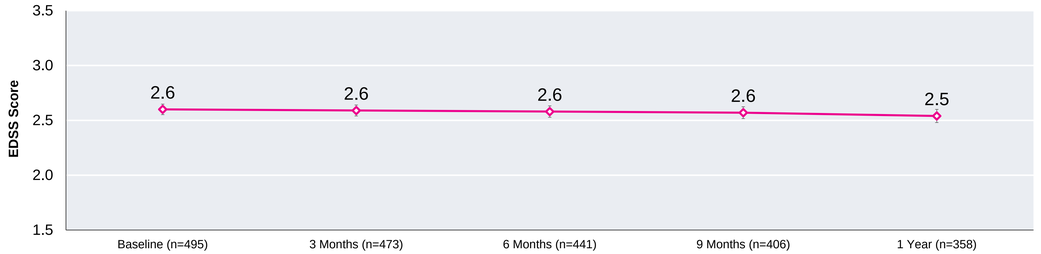
Design/Methods

EDSS data were collected from three GA Depot studies: i) a double-blind, placebo-controlled, phase III study with 508 RMS patients randomized to the active arm; ii) interim analysis of an ongoing, open-label, long-term phase IIa study in 13 RMS patients; and iii) interim analysis of an ongoing open-label phase IIa study in 30 PPMS patients.

Results

In the phase III RMS study, the mean EDSS score in the GA Depot group was 2.6 at baseline and 2.5 at week 52 (end of the placebo-controlled period) (Figure 1). Results of the mixed model repeated measures (MMRM) analysis showed a statistically significant small numerical reduction in mean EDSS at Week 52 for GA Depot over Placebo (LS means difference: -0.058; p=0.0191).
In a responder analysis, 96.4% of GA Depot-treated patients showed no increase in EDSS at Week 52 vs. 91.6% in the placebo group (p=0.0068).
In the long-term RRMS study, EDSS remained stable over six years, from 2.7 at baseline to 1.9 at the end (Figure 2). In the PPMS study, the mean EDSS score remained stable, with a baseline of 5.1 and 4.9 at year 3 (end of the study), (Figure 3).

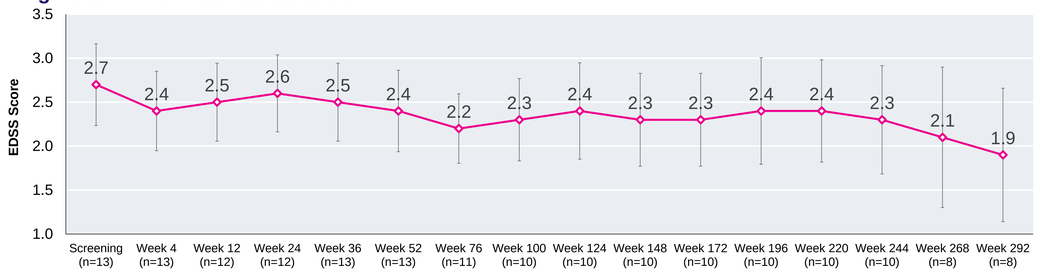
Figure 1. RMS Phase III Mean EDSS score



Visit Timepoint (number of subjects)

Mean EDSS score is presented at baseline and every 3 months thereafter. Data presented as mean ± SE

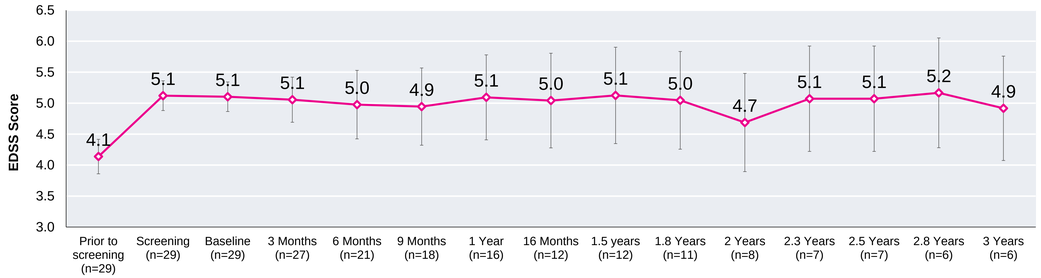
Figure 2. RRMS Mean EDSS score



Visit Timepoint (number of subjects)

Mean EDSS score is presented at baseline and every 3 months thereafter. Data presented as mean ± SE

Figure 3. PPMS Mean EDSS score



Visit Timepoint (number of subjects)

Mean EDSS score is presented at baseline and every 3 months thereafter. Data presented as mean ± SE

Conclusions

GA Depot appears to maintain a stabilizing effect on EDSS scores across three studies in RMS and PPMS patients. This effect was consistent regardless of baseline EDSS, supporting the role of GA Depot in preventing disability accumulation, a critical goal in MS treatment.

Disclosures: Aaron Miller is the Coordinating PI of the RMS phase III study. Laura Popper, Nadav Bleich Kimelman, Shai Rubnov (co-inventor of GA Depot) Ornit Almog and Uri Danon are employed by Mapi Pharma. Joseph Berger is the chairman of the Data Monitoring Committee of the RMS phase III study, Amit Bar-Or and Alexey Boyko are members of the steering committee of the RMS phase III study, Robert Zivadinov is Head of the central MRI reading center for the RMS phase III study and the PPMS phase II study. Hadar Kolb acts as the Coordinating PI for the RRMS phase II study with GA Depot and is a consultant to Mapi Pharma. Arnon Karni is the Coordinating PI of the PPMS phase II study. Ehud Marom is a co-inventor of GA Depot and founder and CEO of Mapi Pharma.

Studies Supported by: Mapi Pharma Ltd