GA Depot (long-acting IM glatiramer acetate) and its impact on EDSS 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, Hadar Kolb[5] MD, Arnon Karni[5] 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]Tel Aviv Sourasky Medical Center (Tel Aviv, Israel)

Background

Multiple sclerosis (MS) is a chronic inflammatory, demyelinating disease characterized by neurological disability accumulation over time. The Expanded Disability Status Scale (EDSS) is widely used to assess disability worsening in both relapsing and progressive forms of MS. Glatiramer acetate (GA) Depot is a long-acting intramuscular (IM) formulation of GA administered once every 28 days.

Objective

To evaluate the impact of GA Depot on EDSS stability in patients with RMS and PPMS based on data from two clinical studies, including an analysis of early discontinued patients.

Design/Methods

EDSS assessments were collected from two prospective GA Depot clinical studies:

- An ongoing, up to three years, open-label, phase IIa study in PPMS patients (n=30).
- A one-year, double-blind, placebo-controlled, pivotal phase III study in RMS patients (n=1,016 of which n=508 in the active arm).

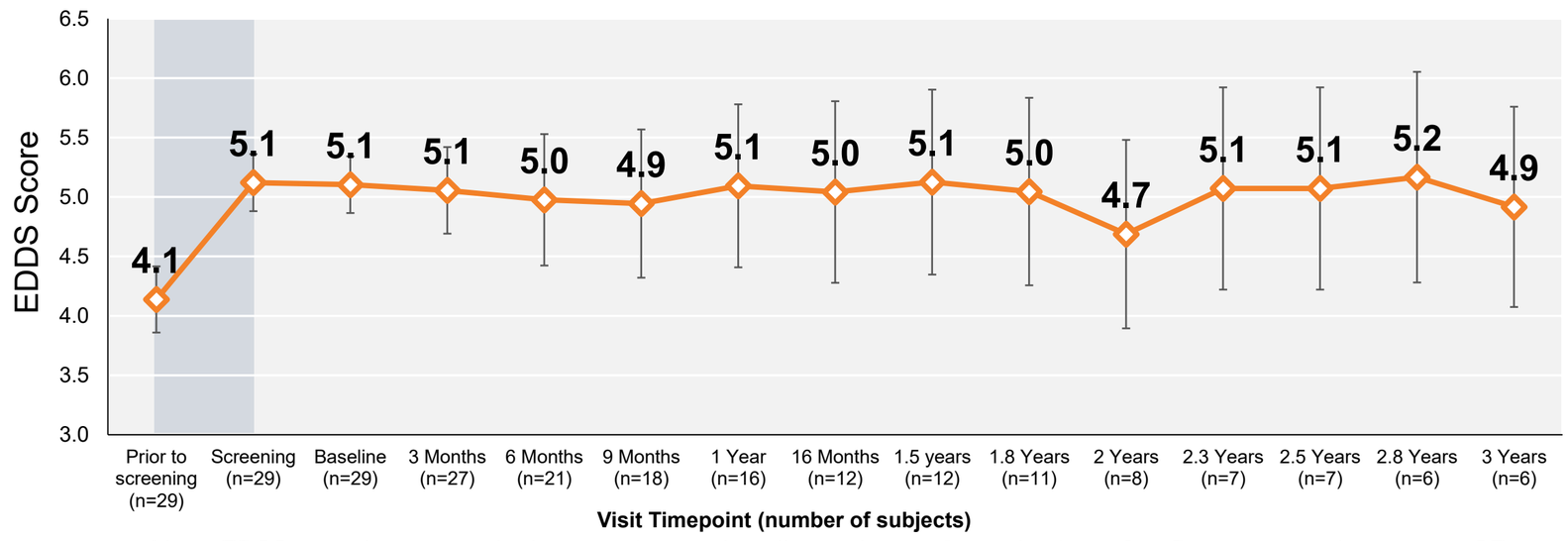
An additional post hoc analysis assessed EDSS changes in patients who discontinued early across both studies.

Results

In the phase II PPMS study, the mean EDSS at baseline was 5.1, remaining stable at week 148 (mean= 4.9), see Fig 1. In the phase III RMS study, the mean EDSS in the GA Depot group was 2.6 at baseline and 2.5 at the end of the one-year placebo-controlled period, see Fig 2. The Mixed Model Repeated Measures (MMRM) analysis of EDSS changes over time showed a small but statistically significant reduction in EDSS in the GA Depot group compared to placebo at Week 52 vs. baseline. A post hoc responder analysis indicated that 96.4% of GA Depot-treated patients had no EDSS increase at Week 52 versus 91.6% in the placebo group (p=0.0068), showing a higher proportion of stabilized patients with GA Depot.

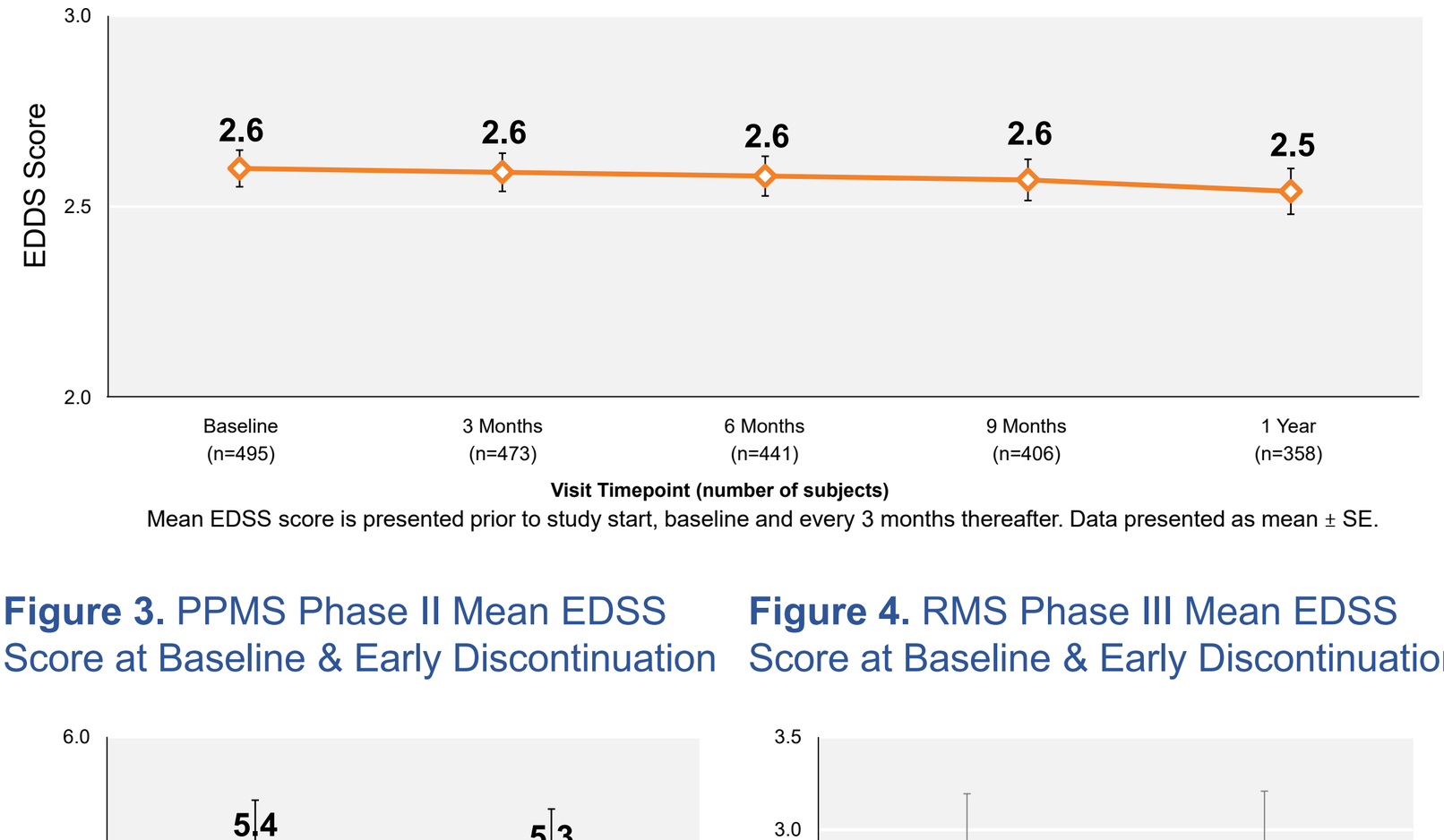
A subgroup analysis of early discontinued patients showed that EDSS remained unchanged from baseline to the last available assessment in both studies: In the PPMS study, early discontinued patients had a mean EDSS of 5.4 at baseline and 5.3 at their last assessment (Fig 3), while in the RMS study, early discontinued patients had a mean EDSS of 2.6 at both baseline and their last assessment (Fig 4).

Figure 1. PPMS Mean EDSS Score



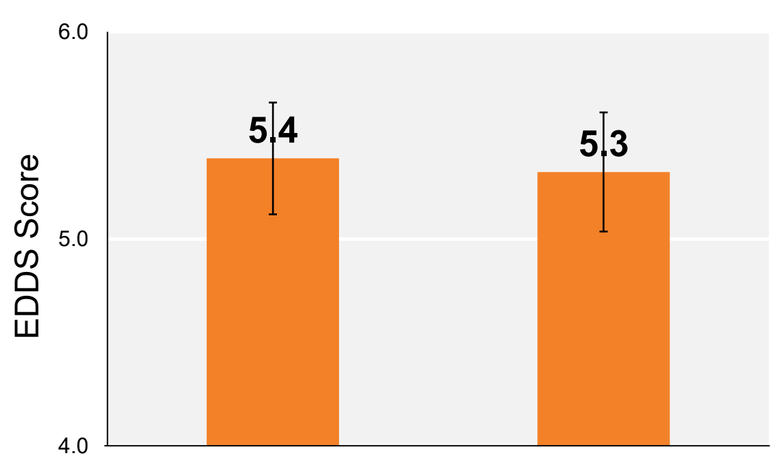
Mean EDSS score is presented prior to study start, baseline and every 3 months thereafter. Data presented as mean ± SE.

Figure 2. RMS Phase III Mean EDSS Score



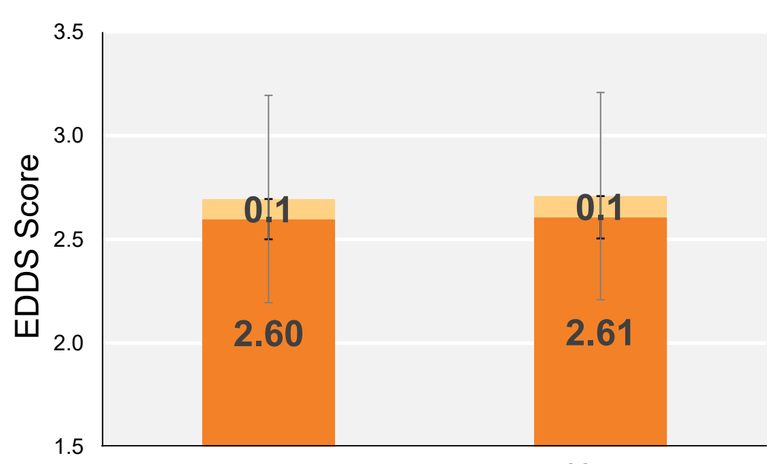
Mean EDSS score is presented prior to study start, baseline and every 3 months thereafter. Data presented as mean ± SE.

Figure 3. PPMS Phase II Mean EDSS Score at Baseline & Early Discontinuation



Data presented as mean ± SE

Figure 4. RMS Phase III Mean EDSS Score at Baseline & Early Discontinuation



Data presented as mean ± SE

Conclusions

GA Depot showed a stabilizing effect on EDSS in both RMS and PPMS patients, irrespective of baseline EDSS or early discontinuation. These findings suggest the potential of GA Depot in slowing disability progression, reinforcing its role in MS management.

Disclosures: Aaron Miller was the Coordinating PI of the RMS phase III study 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 was the Chairman of the Data Monitoring Committee of the RMS phase III study, Amit Bar-Or was a member of the steering committee of the RMS phase IIII study, Robert Zivadinov is head of the central MRI reading center of 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