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

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Background

Multiple sclerosis is a chronic disease requiring lifelong therapy. During the disease course, patients accumulate disability, as measured by the Expanded Disability Status Scale (EDSS), which increases over time in RMS and PPMS patients. Glatiramer acetate (GA) Depot, consisting of extended-release microspheres containing GA, is administered intramuscularly once every 28 days.

Objective

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

Design/Methods

EDSS data was collected from the following 3 GA Depot prospective clinical studies:

i. Interim analysis of an ongoing, open-label, phase IIa study in 30 PPMS patients.
ii. Interim analysis of an ongoing, open-label, long-term phase IIa study in 13 RRMS patients.
iii. A double-blind, placebo-controlled, phase III study in which 508 RMS patients enrolled in the active arm.

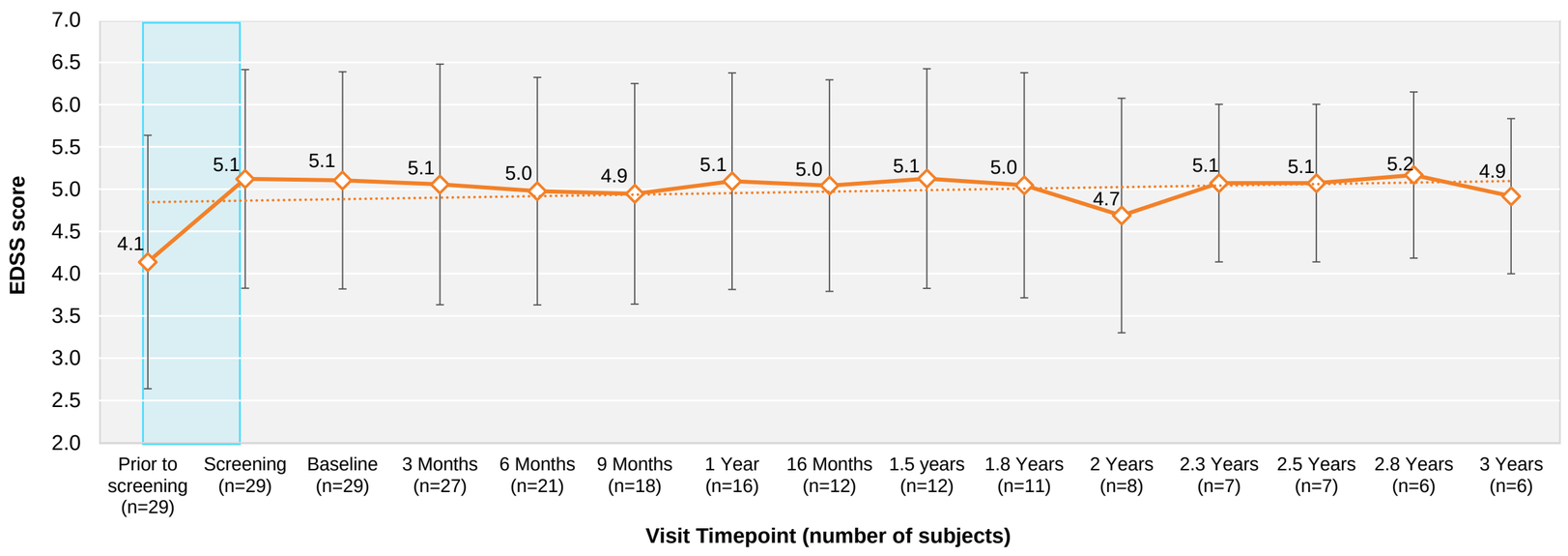
Results

The mean baseline EDSS score of patients in the PPMS study was 5.1 and remained stable up to week 148 (end of the study), Figure 1.

In a long-term open label study with RRMS patients, mean EDSS remained stable for six years, starting at a mean score of 2.7 and ending with a mean EDSS score of 1.9, Figure 2.

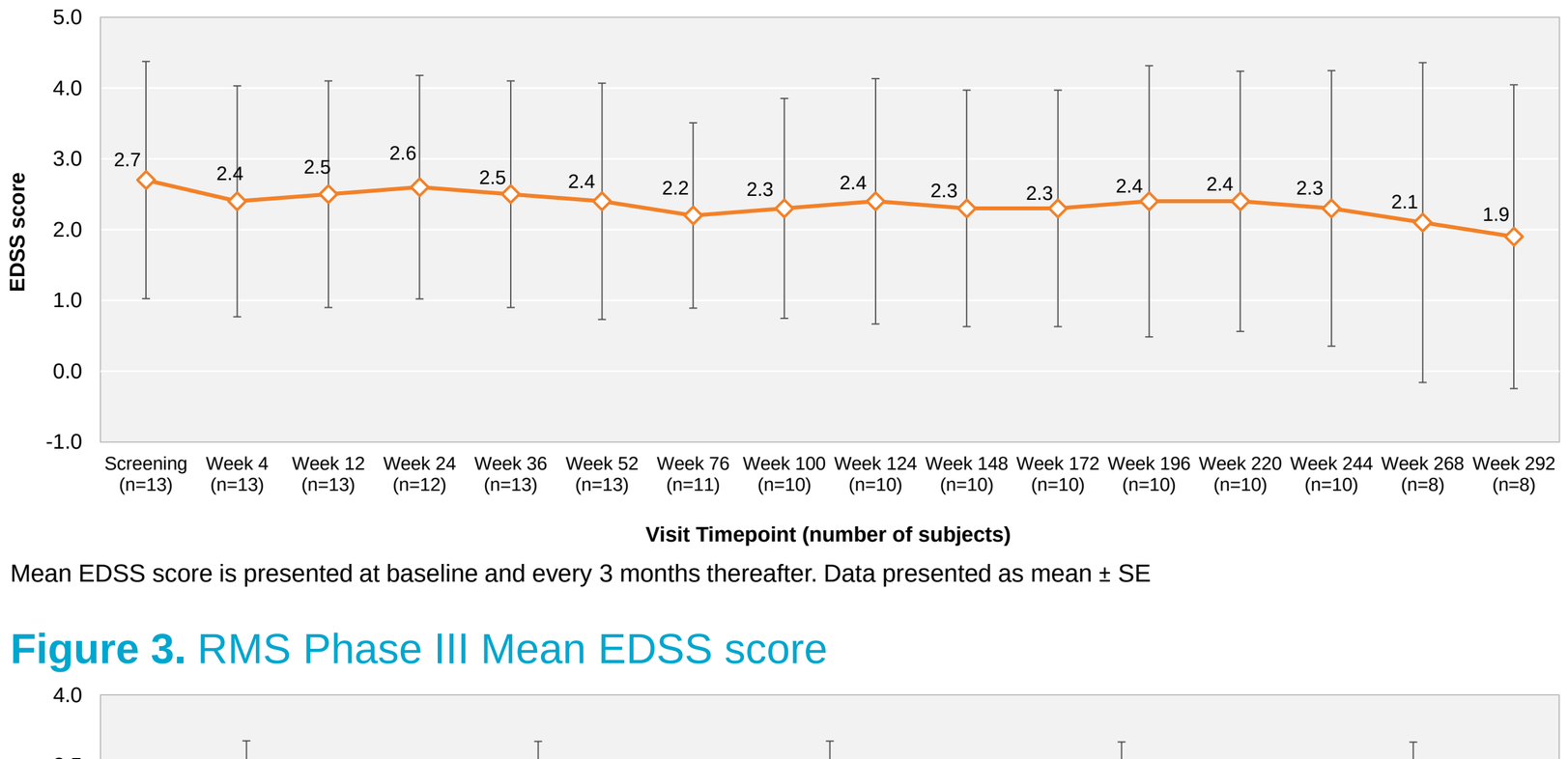
In a one year double-blind, placebo-controlled, phase III study in RMS patients, the mean EDSS score in the GA Depot group was 2.6 at baseline and 2.5 at the end of the PC period, Figure 3. A statistically significant, though small, reduction in mean EDSS score was seen in the GA Depot group vs. the placebo group at the end of one year. (LS means difference: -0.06, 95% CI: -0.11 to -0.01; p=0.0191). In a post hoc responder analysis, 96.4% of patient treated by GA Depot had no increase in the EDSS score from Baseline to Week 52 vs. 91.6% in the placebo group (p=0.0068), corresponding to a higher percentage of patients stabilizing in the GA Depot group.

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. RRMS Mean EDSS score



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

Figure 3. RMS Phase III Mean EDSS score

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

Conclusions

The presented analysis is keeping with a distinct stabilizing effect of GA Depot on EDSS scores observed in 3 different clinical studies with GA Depot in RRMS, RMS or PPMS patients, irrespective of the baseline EDSS score. This effect was consistent across studies and over a long-term follow-up. Preventing disability accumulation is the main goal of DMT use in MS and has a direct beneficial effect on patient's general health, well-being, and quality of life both in the short and long term.

Disclosures: Aaron Miller is 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 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 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.

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