Glatiramer Acetate Depot (extended-release) phase IIa study in patients with Primary Progressive Multiple Sclerosis: Safety and Efficacy 1 Year Interim snapshot analysis

Shlomo Flechter[1], Laura Popper[2], Nadav Bleich Kimelman[2], Shai Rubnov[2], Uri Danon[2], Ehud Marom[2], Ron Milo[3,4], Ronit Gilad[5], Boaz Weller[6], Adi Vaknin-Dembinsky[7], Mark Hellmann[8], Alla Shifrin[9], Arnon Karni[10,11].

[1]Sheba Medical Center, [2]Mapi Pharma Ltd., [3]Barzilai University Medical Center, [4]Ben-Gurion University of the Negev, [5]Kaplan Medical Center, [6]Bnai Zion Medical Center, [7]Hadassah Medical Center, [8]Rabin Medical Center, Beilinson Hospital, [9]Rambam Medical Center, [10]Tel Aviv Sourasky Medical Center, [11]Sackler faculty of Medicine, Tel Aviv University

BACKGROUND

PPMS is characterized by worsening neurologic function from the onset of symptoms, without early relapses or remissions. GA Depot consists of extended-release microspheres containing GA, administered intramuscularly (IM) once every 28 days at a 40mg dose. Results of a 5-year GA Depot phase IIa trial in relapsing remitting MS suggest that GA Depot is safe, tolerable and efficacious. It is hypothesized that the IM administration route together with the slow-release formulation may result in a noted effect on PPMS patients as well.

OBJECTIVES

To assess the safety and efficacy of Glatiramer Acetate (GA) Depot treatment (for up to 52 weeks) in primary progressive MS (PPMS) subjects treated with GA Depot.

DESIGN/METHODS

Main eligibility criteria included: age 18-65, PPMS diagnosis with rapid disease progression (rate of ≥ 1 point increase/year on EDSS score) in the year prior to screening and an EDSS score of 2.0 - 6.5 at baseline. Safety (n=15) was assessed by adverse events (AEs), hematology and chemistry tests. Efficacy (n=13) was assessed by EDSS, 9HPT, T25FW, and by MRI. This interim analysis includes data on all subjects who were enrolled and completed one year study or withdrawn before.

RESULTS

Eighty eight (88) percent of the AEs recorded in the study were mild. Main AEs included injection site reactions and asthenia. No unexpected AEs were reported, and two SAEs (one related and one not related to study drug) were reported. EDSS score remained stable for all patients and no 12 weeks confirmed disability progression (CDP) was detected. Mean 9HPT and T25FW remained stable. No Evidence of Progression (NEP) was observed in 69.2% of the patients. MRI volumetric analysis demonstrated the following: baseline to 1-year and 6 months to 1 year: (-0.89%) and (-0.34%) change in brain volume respectively; and: (-2.59%) and (-1.31%) change in cortical volume respectively.

Table 1: Adverse Events

Severity	Not related***			Related**			Unknown		
	N (events)	%	Rate*	N (events)	%	Rate*	N (events)	%	Rate*
Mild	20	26.7%	0.13	43	57.3%	0.28	3	4%	0.02
Moderate	1	1.3%	0.01	8	10.7%	0.05	0	0	0
Severe	0	0	0	0	0	0	0	0	0

*Rate is number of Adverse Events adjusted to number of injections (153 injections) **Related includes possibly related, probably related. ***Not related includes: Unlikely related and not related

Figure 1: Mean EDSS score per visit - mITT

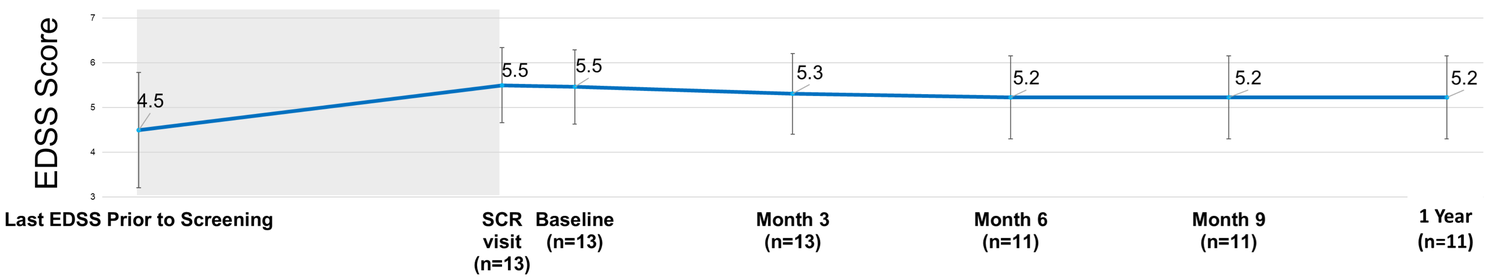

Figure 1:Data presented as mean ± SE. n=13. Mean EDSS score is presented prior to the study start, baseline and every 3 months thereafter. mITT: modified Intent To Treat population.

CONCLUSIONS

These 1-year interim snapshot data suggest that GA Depot is a safe and effective treatment for patients with PPMS, based on the low rate of AEs detected and the stable EDSS for both man and woman, no 12 weeks confirmed disability progression (CDP) that contributed to a high NEP (69.2%) disability measures observed. These results encourage us to test GA Depot in controlled global double blind phase III study.

DISCLOSURES

Prof. Arnon Karni participated as the PPMS study Coordinating PI and as a site PI in the PPMS study, both funded by Mapi Pharma. Dr. Shlomo Flechter, Dr. Ron Milo, Prof. Ronit Gilad, Prof. Boaz Weller, Prof. Adi Vaknin-Dembinsky, Dr. Mark Hellmann and Dr. Alla Shifrin, participated as a site PI in the PPMS study, funded by Mapi Pharma.
Dr. Laura Popper, Dr. Nadav Bleich Kimelman, Dr. Shai Rubnov (co-inventor of GA Depot) and Uri Danon are employed by Mapi Pharma. Ehud Marom is a co-inventor of GA Depot, founder, and the CEO of Mapi Pharma.