Glatiramer Acetate Depot (extended-release) Phase IIa Study in Patients with Primary Progressive Multiple Sclerosis: Safety and Efficacy Snapshot

Shlomo Flechter[1] MD, Aaron Miller[2] MD, Laura Popper[3] MD, Ornit Almog[3], Nadav Bleich Kimelman[3] DMD PhD, *Shai Rubnov[3]* PhD, *Uri Danon[3], Ehud Marom[3], Ron Milo[4,5] MD, Anda Eilam[6]* MD, *Adi Vaknin-Dembinsky[7] MD, Mark Hellmann[8] MD, Alla Shifrin[9] MD, Arnon Karni[10,11] MD*

[1] Sheba Medical Center Israel, [2] Icahn School of Medicine at Mount Sinai, US [3] Mapi Pharma Ltd. Israel, [4] Barzilai University Medical Center, Israel, [5] Ben-Gurion University of the Negev, Israel, [6] Kaplan Medical Center, Israel, [7] Hadassah Medical Center, Israel [8] Rabin Medical Center, Belinson Hospital, Israel, [9] Rambam Medical Center, Israel, [10] Tel Aviv Sourasky Medical Center, Israel, [11] Faculty of Medicine, Tel Aviv University, Israel

Background

PPMS is characterized by a continuous decline in neurological function starting from the initial symptoms, without early relapses or remissions. GA Depot consists of extended-release microspheres containing GA, administered intramuscularly (IM) once every 28 days. Results from GA Depot phase III study in relapsing forms of MS showed that GA Depot 40 mg/monthly is effective, safe and tolerable. The IM administration route together with the slow-release formulation may result in a benefit for PPMS patients as well.

Objective

To assess two GA Depot doses' (40 mg or 25 mg) safety and efficacy in an ongoing three-year phase IIa study on primary progressive MS (PPMS) patients.

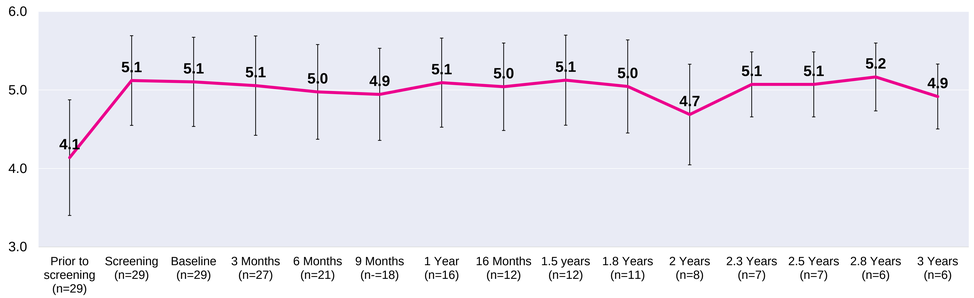
Design/Methods

The study enrolled 30 patients aged 18-65, diagnosed with PPMS, with documented disease worsening in the year before screening, in a rate of ≥ 1 point increase/year on EDSS score and baseline EDSS score of 2.0 - 6.5. Safety assessment includes the analysis of adverse events, hematology and chemistry blood tests. Efficacy assessments involve EDSS, Nine-Hole Peg Test (9HPT) and Timed 25-Foot Walk (T25FW) tests (change was defined as 12-week confirmed ≥ ±20%), as well as by MRI analysis.

Results

At baseline mean age was 50.3, even distribution between females and males, with a mean EDSS of 5.1. Overall, most adverse events (83.5%) were mild, with injection site reactions being the most common. No unexpected AEs were reported. Three SAEs were reported in the 40 mg dose, one of which was possibly related to study drug. A lower rate of AEs and ISRs was observed with GA Depot 25 mg compared to the 40 mg dose (Tables 3 & 4). EDSS scores remained stable with only one 12-week confirmed disability progression (CDP) (Figure 1). Notably, 72.4% of patients (68.4% in the 40 mg dose and 80% in the 25 mg dose) showed no evidence of progression (NEP), defined by the absence of 12-week CDP (96.6%), 12-week T25FW progression (79.3%) and 12-week 9HPT progression (93.1%) (Table 2). MRI analysis indicated low MRI activity.

Figure 1: Mean EDSS Score by visit – All subjects



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

Table 2: No Evidence of Progression

	GA Depot 40 mg	GA Depot 25 mg	All Subjects
No 12 weeks CDP	19/19 (100%)	9/10 (90%)	28/29 (96.6%)
No 12 weeks confirmed progression in T25FW of ≥20%	14/19 (73.7%)	9/10 (90%)	23/29 (79.3%)
No 12 weeks confirmed progression in 9HPT of ≥20%	17/19 (89.5%)	10/10 (100%)	27/29 (93.1%)
No Evidence of Progression (NEP)	**13/19 (68.4%)**	**8/10 (80%)**	**21/29 (72.4%)**

Table 3: Adverse Advents by Severity and Relatedness – GA Depot 40 mg

	Not related***			Related**			Unknown		
Severity	N (events)	%	Rate*	N (events)	%	Rate*	N (events)	%	Rate*
Mild	46	25.3	0.125	98	53.8	0.266	9	4.9	0.024
Moderate	7	3.8	0.019	15	8.2	0.041	0	0	0
Severe	1	0.5	0.003	6	3.3	0	0	0	0
Total			**0.147**			**0.323**			**0.024**

Table 4: Adverse Advents by Severity and Relatedness – GA Depot 25 mg

	Not related***			Related**		
Severity	N (events)	%	Rate*	N (events)	%	Rate*
Mild	17	56.7	0.136	7	23.3	0.056
Moderate	2	6.7	0.016	4	13.0	0.032
Severe	0	0	0	0	0	0
Total			**0.152**			**0.088**

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

Conclusions

These interim snapshot findings suggest GA Depot as a safe and effective treatment for PPMS patients with a remarkable 72.4% no evidence of progression (NEP), with stable EDSS, and high proportion of stable T25FW and 9HPT once treated with GA Depot. GA Depot 25 mg/month shows a favorable trend in efficacy with improved safety and tolerability. These results encourage further exploration during the ongoing study, emphasizing the potential of GA Depot to address the continuous neurological decline in PPMS.

Disclosures: Dr. Shlomo Flechter, Dr. Ron Milo, Dr. Anda Eilam, Prof. Adi Vaknin-Dambinsky, Dr. Mark Hellmann and Dr. Alla Shifrin, served as site Principal Investigators .Prof. Arnon Karni held a dual role as the study Coordinating PI and site PI. Prof. Aaron Miller serves as a consultant to Mapi Pharma and as the Coordinating PI for the Phase III trial of GA Depot in RMS. Dr. Laura Popper, Ornit Almog, Dr. Nadav Bleich Kimelman, Dr. Shai Rubnov (co-inventor of GA Depot) and Uri Danon are employed by Mapi Pharma. Ehud Marom, co-inventor of GA Depot, is the founder and CEO of Mapi Pharma

Study Supported by: Mapi Pharma Ltd