Glatiramer Acetate Depot (extended-release) Accumulated Safety Data in Relapsing Remitting Multiple Sclerosis & Primary Progressive Multiple Sclerosis phase IIa studies

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BACKGROUND

Multiple sclerosis (MS) is a chronic disease, requiring lifelong therapy. While several disease-modifying treatments have been approved, some may be associated with lasting effects on the immune system and/or serious adverse events. Glatiramer acetate (GA) Depot long-term safety data collected from a phase IIa study in relapsing remitting MS (RRMS) and initial descriptive safety data collected from a phase IIa study in primary progressive MS (PPMS) suggest that GA Depot is safe and tolerable.

OBJECTIVE

Assess GA Depot safety and tolerability in two phase IIa ongoing studies in MS.

DESIGN/METHODS

RRMS subjects treated with Copaxone® for ≥12 months prior to study entry and PPMS Copaxone® Naïve or long wash-out period subjects were enrolled in these two-independent, ongoing phase IIa studies and treated with GA Depot IM every 4 weeks.

RRMS study design

Core Study 1st year: GA Depot 80mg or 40mg IM
Once every 4 weeks

→ Study Extension period: On-going Study
All subjects were switched to GA Depot 40mg IM once every 4 weeks

PPMS study design

2 Years Study: On-going
GA Depot 40mg IM once every 4 weeks

Results

In both studies, most commonly reported related adverse events (AEs) were mild injection site reactions (ISRs). No unexpected AEs were recorded. No systemic immediate post-injection reactions labeled with GA (Copaxone®) were detected with GA Depot. RRMS subjects' safety data shows a statistically significant reduction in the AEs and ISRs during the 2nd year vs. the 1st year of treatment (p-value by GEE model <.0001). The related AEs were reduced by 59% and the ISRs by 66% in the 2nd year vs. the 1st year. Safety data collected from the PPMS study, suggest better safety and tolerability of GA Depot in the PPMS study cohort than in the RRMS study cohort.

Table 1: RRMS Study Two Years Subpopulation Adverse Events (mITT)

Severity	1st year				Extension			
	Not Related		Related		Not Related		Related	
	# Events	Rate*	# Events	Rate*	# Events	Rate*	# Events	Rate*
Mild	37	0.22	104	0.62	24	0.17	40	0.28
Moderate	21	0.12	8	0.05	10	0.07	5	0.04
Severe	0	0	0	0	0	0	1	0.01

*Rate is number of Adverse Events adjusted to number of injections (169 for 1st year and 142 in the 2nd year). A statistically significant reduction in AE number was noted in the extension period (GEE model, $p < 0.0001$). mITT: modified Intent To Treat population.

Table 2: RRMS Study Two Years Subpopulation ISRs (mITT)

Severity	1st Year		Extension	
	# Events	Rate*	# Events	Rate*
Mild	91	0.54	28	0.2
Moderate	6	0.04	4	0.03
Severe	0	0	1	0.01
All ISRs	*97*	*0.57*	*33*	*0.23*

*Rate is number of Adverse Events adjusted to number of injections (169 for 1st year and 142 in the 2nd year)

Table 3: PPMS snapshot Adverse Events

Severity	Not related		Related	
	# Events	Rate*	# Events	Rate*
Mild	4	0.061	23	0.348
Moderate	0	0	2	0.03

*Rate is number of Adverse Events adjusted to number of injections (66) in the study

CONCLUSIONS

GA Depot cumulative safety data, although in two small cohorts, suggest good safety and tolerability profile for GA Depot in GA Naïve subjects and in Copaxone® switchers. A statistically significant improvement with time is seen in GA Depot safety and tolerability profile. Phase IIa ongoing studies data support the assumption of GA Depot's potential to improve MS treatment by significantly reducing number of injections and improving safety and tolerability.

For GA Depot efficacy data see poster P1647

DISCLOSURES

Prof. Ariel Miller participated as the core-study Coordinating Principal Investigator and as a site Principal investigator (PI) in the study funded by Mapi Pharma. Dr. Shlomo Flechter participated as the extension-study Coordinating Principal Investigator and as a site Principal investigator (PI) in the RRMS study, and as a site PI in the PPMS study, both funded by Mapi Pharma. Dr. Ron Milo, Dr. Alla Shifrin, Prof. Dimitrios Karussis participated as PIs in the RRMS study funded by Mapi Pharma. Prof. Joab Chapman participated as a PI in the RRMS study, and as a member in the data safety monitoring board (DSMB) in the PPMS study, both studies funded by Mapi Pharma. Prof. Ronit Gilad participated as a site Pl in the PPMS and RRMS studies, both funded by Mapi Pharma. Dr. Arnon Karni participated as the PPMS study Coordinating PI and as a site Pl in the PPMS and RRMS studies, both funded by Mapi Pharma. Dr. Chen Hoffmann participated as the central reading MRI facility in the RRMS study funded by Mapi Pharma. Prof. Boaz Weller participated as a site Pl in the PPMS study funded by Mapi Pharma. Prof. Adi Vaknin-Dambinsky participated as a site Pl in the PPMS study funded by Mapi Pharma. Prof. Tamir Ben-Hur, Scientific Advisory Board member of 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.

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