GA Depot (long-acting IM injection of glatiramer acetate) Presents Improved Safety and Tolerability Features: Results from a Multinational, Double-Blind, Placebo-Controlled Phase III Study in Subjects with Relapsing Forms of Multiple Sclerosis

Aaron Miller[1] MD, Laura Popper[2] MD, Joseph Berger[4] MD, Amit Bar-Or[4] MD, Robert Zivadinov[5] MD, Alexey Boyko[6], MD, Hadar Kolb[3] MD, Nadav Bleich Kimelman[2], Shai Rubnov[2], 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]Tel Aviv Sourasky Medical Center (Tel Aviv, Israel), [4]University of Pennsylvania (Philadelphia, PA, USA), [5]Buffalo Neuroimaging Analysis Center, University at Buffalo, State University of New York, (Buffalo, NY, USA), [6]Pirogovs Russian National Research University and Federal Center of Brain Research and Neurotechnologies (Moscow, Russia)

BACKGROUND

Multiple sclerosis (MS) is a chronic disease requiring lifelong therapy. Glatiramer acetate (GA) long-acting injection (GA Depot) consists of extended-release microspheres containing GA, administered every 28 days. GA Depot significantly reduced the rate of MS relapses and the number of newly enhanced lesions in a double-blind, randomized, placebo-controlled phase III study in subjects with relapsing forms of Multiple Sclerosis.

OBJECTIVE

To assess the safety and tolerability of GA Depot compared with that of Copaxone® (GA solution administered daily or thrice weekly) by analyzing the injections site reactions (ISRs), serious adverse events (SAEs), and the immediate post-injection reactions (IPIR), one of Copaxone®'s noted side effects, defined as a constellation of symptoms that may occur immediately (within seconds to minutes) after the injection and include at least 2 of the following: flushing, chest pain, palpitations, tachycardia, anxiety, dyspnea, constriction of the throat, and urticaria.

DESIGN/METHODS

ISRs yearly event rate was calculated using the data collected during the 1st year placebo-controlled period of the phase III study and the data for the 2nd treatment year with GA Depot collected during the open label period of the study. Data were compared with the annualized rate of ISRs from Copaxone®'s published GLACIER study data (a 4-month open-label study with published ISR rates for once daily and thrice-weekly Copaxone® adjusted for one year). The percentage of subjects experiencing SAEs was compared to data published in the GALA study (one-year placebo-controlled phase III study with thrice weekly Copaxone®). IPIR percentage was compared to the data in the Copaxone® US label.

RESULTS

- ISR rate (calculated as the number of events/exposure in person-years) was significantly lower for GA Depot (2.43 in the 1st treatment year and 0.98 in the second year compared with once-daily subcutaneous GA (ISR rate of 70.4) or thrice weekly (ISR rate of 35.2), (Figure 1).
- In patients treated with GA Depot, the incidence of SAEs (after excluding COVID-19 infection) was 3.7% in the 1st year of treatment and 1.2% in the second, compared with 4.5% in patients treated with Copaxone® 40 mg thrice weekly (Figure 2).
- IPIR was significantly less frequent in patients treated with GA Depot compared to subjects treated with Copaxone® 20 mg daily or Copaxone® 40 mg thrice weekly (0.8% in the 1st treatment year and 0 in the second, 16%, and 2%, respectively) (Figure 3).

Figure 1: ISR rate with GA Depot and Copaxone®

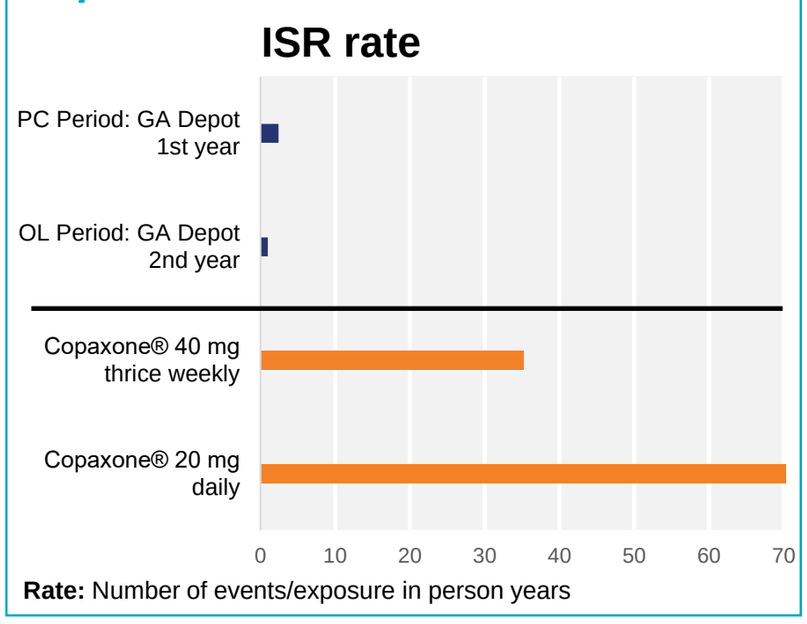


Figure 2: Incidence of SAEs with GA Depot and Copaxone®

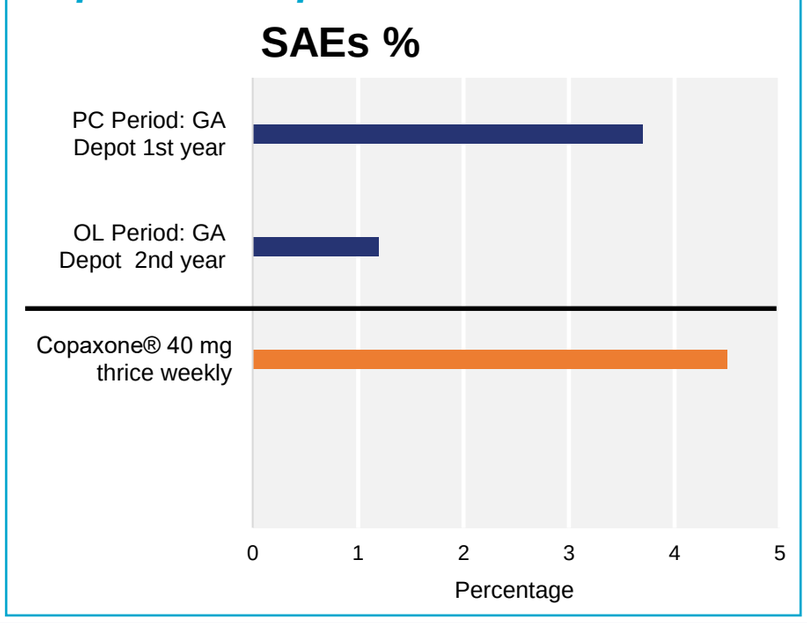
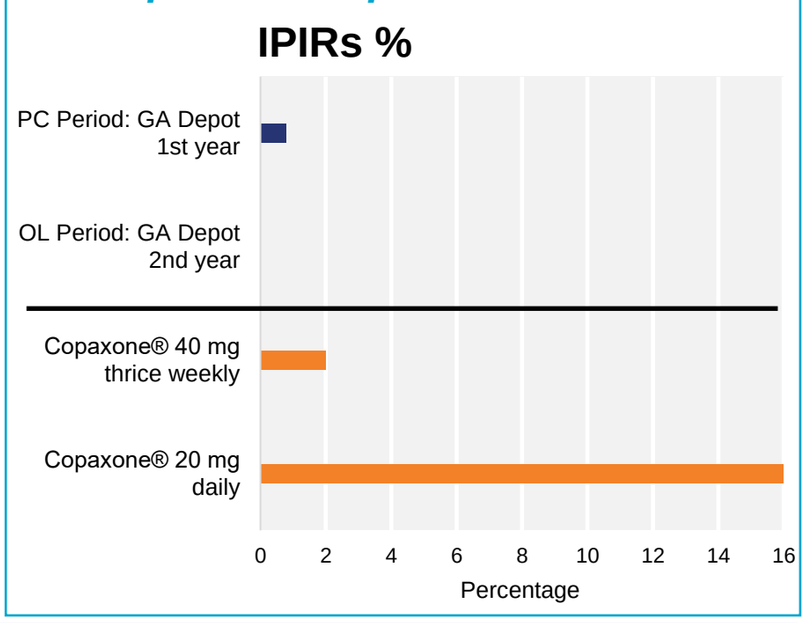


Figure 3: Incidence of IPIR with GA Depot and Copaxone®



CONCLUSIONS

Overall, GA Depot shows a favorable safety and tolerability profile compared to daily or thrice weekly use of GA formulation. These advantages are expected to increase patient adherence and improve patient's quality of life.

DISCLOSURES

Aaron Miller is the Coordinating PI of the study. Laura Popper, Nadav Bleich Kimelman, Shai Rubnov (co-inventor of GA Depot) and Uri Danon are employed by Mapi Pharma. Joseph Berger is the chairman of the Data Monitoring Committee of the study, Amit Bar-Or and Alexey Boyko are members of the steering committee of the study, Robert Zivadinov is head of the central MRI reading center of the study. Hadar Kolb acts as the Coordinating PI for phase II with GA Depot and is a consultant to Mapi Pharma. Ehud Marom is a co-inventor of GA Depot and founder and CEO of Mapi Pharma.