Glatiramer Acetate Long-Acting Injection (GA Depot) Effect in A Mouse Model of IBD

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Introduction and Objective

The pathogenesis of IBD is largely driven by dysregulated immune responses. Glatiramer Acetate (GA) which is a known immunomodulator has demonstrated significant therapeutic effects in mitigating DSS-induced colitis. GA Depot, a long-acting formulation of GA designed for parenteral administration every 28 day is available either as a lyophilized powder for reconstitution and intramuscular injection or as a ready-to-use medium chain triglyceride (MCT) suspension for subcutaneous self-injection. Two studies were conducted to assess the efficacy of a single administration of GA Depot in alleviating DSS-induced colitis symptoms in mice. The objective of the first study was to evaluate the effects of different doses and solvents of GA Depot on DSS-induced colitis. The second study aimed to compare the efficacy of GA Depot with that of infliximab (IFX), an established treatment for IBD.

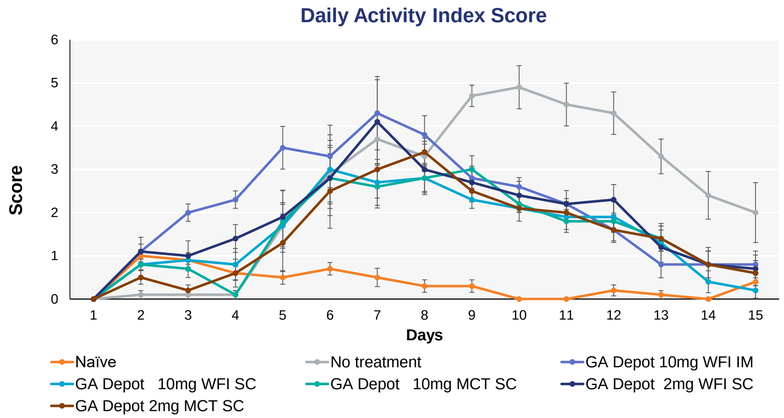
Design/Methods

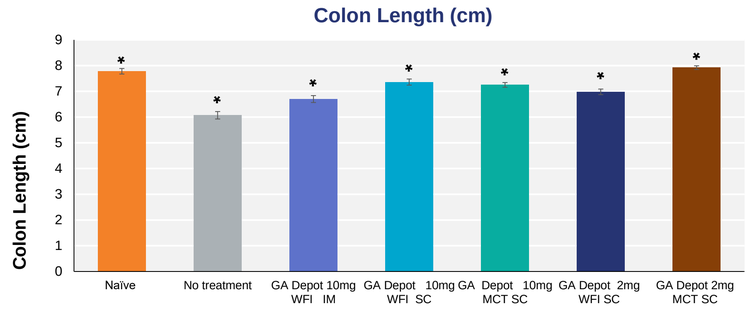
In the first study, seven groups (n=10 per group) were included: naïve controls, untreated controls and groups receiving GA Depot at 2 or 10 mg administered intramuscularly (IM) or subcutaneously (SC), with the formulation suspended in either water for injection (WFI) or medium chain triglyceride (MCT). The second study included naïve and untreated controls, GA Depot at 2 and 10 mg (suspended in MCT and administered SC), and Infliximab (IFX) administered intravenously (IV). All treatments were administered once on day 1 of the study.

Results

In both studies, all treatment groups demonstrated beneficial effects on DSS-induced colitis, including reductions in daily activity index (DAI), improved histopathological scores and less colon shortening compared to untreated controls. GA Depot, administered SC in MCT at doses of 2 or 10 mg, exhibited comparable efficacy to IFX in reducing DSS-induced colitis symptoms.

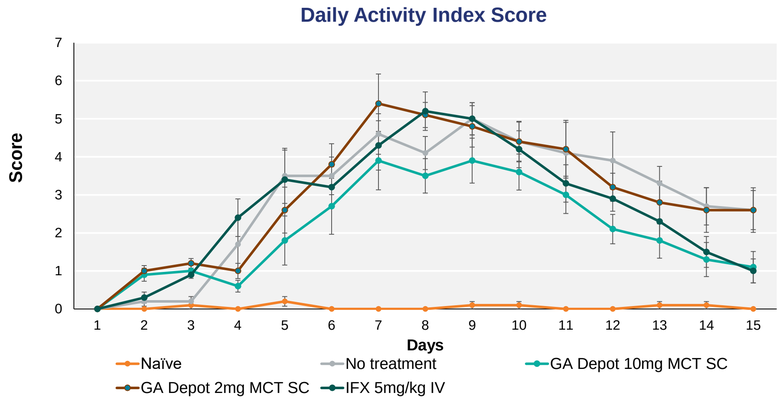
Figure 1: GA Depot Effect over DSS-Induced Colitis, Study 1

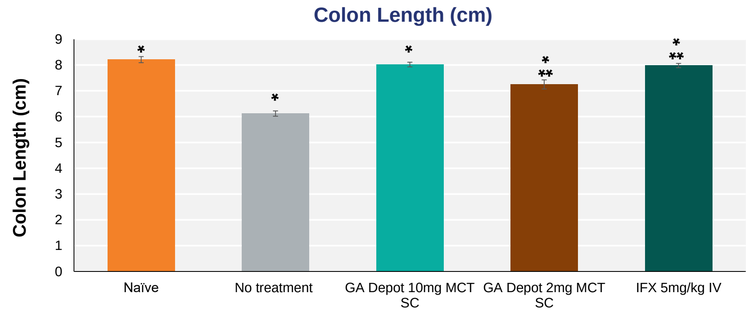




Daily activity index (calculated by grading of change in weight, intestinal bleeding and stool consistency) was lower in all treatment groups compared with the No Treatment control group. Colon length reduction was significantly lower in treated group compared with the untreated control (n=10/group, data presented as mean +/- SE, *p<0.05, ANOVA followed by T-test).

Figure 2: GA Depot Effect over DSS-Induced Colitis, Study 2





Daily activity index was lower in all treatment groups compared with the No Treatment control group. Colon length reduction was significantly lower in treated group compared with the untreated control. (n=10/group, data presented as mean +/- SE, *, **p<0.05, ANOVA followed by T-test).

Conclusions

The results indicate that GA Depot shows similar efficacy to Infliximab, a widely used treatment for Crohn's Disease and ulcerative colitis. These findings provide proof of concept for the potential future clinical use of GA Depot in these indications. Excellent safety profile is expected based on the clinical experience with GA Depot in Phase II and III studies.

Disclosures

Nadav Bleich Kimelman DMD PhD, Shai Rubnov PhD (co-inventor of GA Depot) and Uri Danon are employed by Mapi Pharma. Ehud Marom is a co-inventor of GA Depot, founder and CEO of Mapi Pharma.

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