Intramuscular Interferon Beta-1a Therapy Initiated During a First Demyelinating Event in Multiple Sclerosis (The CHAMPS trial)

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This was an important early paper in multiple sclerosis (MS) treatment, as the advent of interferon therapy for the treatment of MS was a massive advancement in the field, allowing physicians to help change the course of the disease for patients (hence the term "disease modifying therapy"). This study looked at the utility of early initiation of interferon-beta treatment in patients with MS.

Experimental Design and Statistics: This study was a randomized, double-blind, placebo-controlled clinical trial done across 50 centers, with the goal of determining if weekly IM injections of interferon beta-1a (Avonex) reduced the incidence of developing clinically definite MS in patients who presented with a first demyelinating clinical event, and lesions on brain MRI (including subclinical lesions). All enrolled patients (N=383) received initial treatment with IV solumedrol, specifically 1000mg for 3 days followed by a prednisone taper. Patients were then randomly assigned to two treatment groups: one received 30µg of weekly IM interferon beta-1a (N=193) and the other received a matching placebo (N=190). Both groups were similar at the start of the trial, including the type of initial demyelinating neurological event and the number of brain lesions on MRI. Treatment began after the course of IV solumedrol was completed and while patients were still receiving their oral prednisone taper. Patients in both treatment groups were examined by a treating and an examining neurologist (both unaware of treatment assignment) and all patients were followed for up to 3 years. The primary endpoint was the development of clinically definite MS[1]. Secondary endpoints included findings on follow up brain MRIs. All analyses were completed via the intention-to-treat principle. Some patients were lost to follow-up, while others stopped treatment early due to ASEs or for other reasons (see paper for details).

Results: This trial was terminated early as interferon beta-1a was deemed significantly better than treatment and the study authors could not ethically keep patients in their assigned groups. The cumulative probability of developing clinically definite MS was significantly lower in the interferon beta-1a group than in the placebo group (p=0.002, see Fig.1 for striking Kaplan-Meier curve). At 3 years, the cumulative probability of developing clinically definite MS was 35% in the interferon beta-1a group vs 50% in the placebo group. Further, on follow up brain MRIs, there were fewer new, fewer enhancing, and fewer enlarging lesions at 6, 12 and 18 months of follow up in the interferon beta-1a group vs. placebo. The most common adverse side effect of interferon beta-1a were flu-like symptoms (54% in the treatment group).

Conclusions: Overall, this study suggested that early administration of interferon beta-1a was superior to placebo in preventing or delaying a second attack of MS, and at reducing the subsequent lesion burden on brain MRIs. Though we no longer use interferon beta-1a as frequently today, due to the advent of newer, more effective disease modifying therapies for MS, this trial highlighted the importance of an early and accurate diagnosis of MS, early determination of an individual's risk/disease burden, and early initiation of treatment with a disease modifying therapy.

Summary Completed by Amy, Li Safadi, M.D.

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[1] Clinically definite MS: the development of either a new visual or neurologic event (new abnormality >48hrs in duration, clinically different from the patient's first event) OR progressive neurologic deterioration (increase of $\geq$1.5 points on the EDSS)