

## **DIRECT COMPARATIVE DRUG STUDIES OF MS ARE AN IMPORTANT GUIDE TO MEDICAL PRACTICE - PRO**

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Neurologists practice under a moral obligation to do the best for their patients: first, to do no harm, and second, to offer their best care for diagnosis and management of neurologic issues.

Multiple Sclerosis (MS) is the major neurologic disease of young adults. In the last 15 years, with the advent of the disease modifying therapies (DMTs), MS has become a treatable condition. Increasing data indicates these therapies are changing the natural history of MS for the better.

At the current time there are six recognized and proven MS DMTs, encompassing four distinct classes of agents. Selecting the optimal DMT should take into account drug, disease, and patient factors. Perhaps the single most important drug-related factor is efficacy.

To compare efficacy between the MS DMTs requires large scale randomized, prospective, head to head trials. To date, four such studies have been reported (EVIDENCE, INCOMIN, REGARD, BEYOND). These direct comparative trials should guide medical practice.

EVIDENCE and INCOMIN, both previously published, compared low and high dose interferon Betas (IFN $\beta$ s). In both these studies, the efficacy of IFN $\beta$  was greater when given at higher dose several times a week vs low dose once a week.

REGARD and BEYOND, more recent studies, compared high dose IFN $\beta$ s with Glatiramer Acetate (GA). In both these studies, the onset of action and suppression of clinical disease attacks was similar between high dose IFN $\beta$  and GA. MRI activity suppression did show differences between the IFN $\beta$ s and GA.

All these direct comparison trials confirmed very good tolerability and safety profiles for the DMTs. REGARD and BEYOND had some additional surprising results. The DMTs worked better than expected on relapsing MS, with much lower relapse rates and relapse suppression than reported from the earlier pivotal trials. The explanation for this improved response likely reflects a somewhat different relapsing population who entered these trials, and that the DMTs work better when they are used in early and relatively intact MS patients.

These modern era (post Millennium) direct comparative drug studies have led to important changes in how we counsel MS patients and judge suboptimal responders/treatment failures. They provide additional support for early effective treatment. The most important results from these direct comparative trials will be reviewed, as well as how they should guide best medical practice.