

CONFIDENCE IN EXISTING MS THERAPY VS. ENTHUSIASM FOR NEW ONES

P.K. Coyle

Department of Neurology, Stony Brook University, Stony Brook, New York, USA

The current recognized Multiple Sclerosis (MS) disease modifying therapies (DMTs) encompass the Interferon β s (IFN β s), Glatiramer Acetate (GA), Natalizumab, and Mitoxantrone. Mitoxantrone is a second line agent reserved for breakthrough activity not responsive to other treatments. Its adverse event profile (cardiomyopathy, treatment-related leukemia, limited lifetime duration of use) is well known. Natalizumab is associated with increased risk for Progressive Multifocal Leukoencephalopathy (PML). As of August 2008, there have been two cases in over 30,000 treated patients. The IFN β s and GA, considered first line agents, have well recognized and manageable adverse events. No surprising long term toxicity has emerged in patients on these DMTs over 10 to 15 years, while even early first attack relapsing MS patients tolerate these medications very well.

The most recent modern era (post Millennium) MS trials (AFFIRM, REGARD, BEYOND, CAMMS, BENEFIT, PRECISE, BECOME, FORTE) indicate that current DMTs work better and faster than predicted from the original pivotal trials. Clinical relapses are suppressed down to a level of one attack every 3 to 4 years, with accompanying strong disability and MRI disease activity suppression. The current DMTs are safe, well tolerated, have no surprising long term toxicity, and work even better than initially thought. They are also most effective when used in early and low EDSS MS.

The current DMTs all require parenteral administration. A number of novel oral agents, as well as monoclonal antibodies are in development. However, there are several concerns that raise a caution with regard to their use. First, their efficacy awaits validation in definitive Phase III trials. Second, novel mechanism of action drugs bring concerns about unexpected toxicity (recent reports with novel agents have included severe herpes infections, skin malignancy, idiopathic thrombocytopenic purpura, thyroid disease, and PML). Third, most novel drugs have been used in relatively small numbers of MS patients for relatively brief periods of time. Devastating adverse events are often not apparent until sufficient numbers and treatment duration are met.

In summary, the current MS DMTs, in light of recent trials, look even better with regard to efficacy and tolerability than originally thought. They will not be soon replaced. Pivotal supporting data for this statement will be reviewed.