Model Based Meta-Analysis of Efficacy in Multiple Sclerosis for Disability Progression Incidence

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Objectives: Characterize the efficacy of different multiple sclerosis (MS) drugs in preventing disability progression as defined by the expanded disability status score (EDSS).

Methods: Publicly available information were used to create a database comprising summary level efficacy data for 27 drugs evaluated in 91 controlled trials in >41,000 MS subjects. A dataset that includes incidence of progression as defined by increase in EDSS score (31 trials, 13 drugs and 26,205 MS subjects) was used. Analysis was conducted using the generalized least squares method for nonlinear models (gnls) within the R nml package with the odds ratio of progression incidence estimated for the primary clinical trial endpoint. Variability was estimated using the large sample size approximation from a binomial likelihood distribution. Several covariates were tested for statistical significance within the model.

Results: The estimated odds ratios with 90% confidence intervals are presented in the Figure below. One treatment (dirucotide) was excluded due to the small number of total subjects (32) and large confidence intervals. Average age was the only statistically significant covariate at the p<0.01 level while the type of MS narrowly missed achieving statistical significance (p=0.026).

Conclusions: This meta-analysis suggests that most MS treatments have an estimated odds ratio of 0.6-0.8 for incidence of progression relative to placebo. For the approved MS treatments, when adjusting for average age of patients in each clinical trial, alemtuzumab was estimated as the most efficacious drug and interferon was estimated as the least effective. Patient age and type of MS are correlated however; age may have achieved statistical significance since it is a continuous variable while MS type is a discrete patient diagnosis.