Differences in MS disability with various Disease Modifying Therapies

Disability due to MS is an important measure of the disease, but it is also the most difficult to measure. It is the outcome of most importance to patients because disability is what most affects their day to day lives. Attack rates and MRI activity reflect episodes of inflammation, but attacks may be temporary, making disability the most important measure of the impact of MS on a person’s life. The FDA requires that a clinical measurement be used as the main outcome in studies of MS medications. Clinical measures may include attack rate or disability. Furthermore, the FDA requires that changes in these clinical outcomes be sufficient to make a difference in a person’s life. This requirement assures that trivial differences that are not noticeable or important to the patient are not used as the basis for approval of medications. There is only one measure of MS disability that has been validated sufficiently to meet these FDA requirements, the Expanded Disability Status Scale (EDSS).

It is tempting to compare disability outcomes between various studies of MS medications. However, such comparisons are not scientifically valid. The patients enrolled in different studies have differences that cannot be corrected for. One example is the difference in disease severity, with more recent studies enrolling patients that are earlier in the disease course and with fewer attacks per year. Patients come from different regions that have differences is the timing of diagnosis, different treatments and different genetic backgrounds. Many differences are due to factors that cannot even be identified. Because of the impossibility of identifying and correcting for the differences in these populations, scientists strongly discourage comparisons across different studies.

Nevertheless, comparisons have been made and are frequently discussed among those deciding on the use of DMTs. These comparisons are often driven by marketing of particular medications with data selected to favor that particular product. Such comparisons are strongly discouraged. Examples of differences in disability in large phase III studies include:

- Avonex: 37% (time to increased EDSS)
- Betaseron: 13% (time to increased EDSS)
- Copaxone: 28% (number worsening on EDSS)
- Gilenya: 30% (number worsening on EDSS)
- Mitozantrone: 14% (average change in EDSS value)
- Rebif: 44% (time to increased EDSS)
- Tysabri: 42% (risk of worsening on EDSS)

As you can see, the actual measure of disability between these various studies differed between studies, making comparisons difficult. Results from charts like the one above are misleading because different ways of calculating disability outcomes are used. A true comparison would require that similar outcome measures were available, which they are not. Note that Extavia was approved using data from the Betaseron study. The Avonex study used the time to increase in the EDSS as the primary endpoint, making this the most statistically powerful outcome measure for
that particular study. The Betaseron study used attack rate as the primary outcome, with changes in EDSS being less important secondary outcomes. The Betaseron study had an unusually low rate of EDSS change in the placebo, making it difficult for the medication to demonstrate a positive result for this particular outcome. The Copaxone, Rebif and mitoxantrone studies were designed to look at attack rate, with EDSS changes being secondary outcomes with less statistical power. The Tysabri study had two primary endpoints, attack rate at one year, and disability at two years.

Since we believe that disability cannot be scientifically compared between different studies, we strongly advise that patients make decisions on which DMT to use based on other factors. We believe that only head-to-head studies of medications can accurately predict which one is stronger. Information about head-to-head studies is available on our website.