

# Medical Update Memo

March 4, 2010

## Results of Phase II "CHOICE" Study Published, Showing that Daclizumab Reduced Disease Activity in Relapsing MS, and Revealing Novel Immune Mechanism

### Summary

230 people with relapsing MS taking interferon beta and having disease activity were administered one of two doses of daclizumab (Biogen Idec and Facet Biotech Corp.) or placebo - show that the higher dose reduced disease activity on MRI scans by 72% and the lower dose by 25%. Immune analyses show that this reduction was associated with a dramatic increase in CD56bright NK cells - an unexpected finding. Daclizumab is a laboratory-created monoclonal antibody that blocks the activity of interleukin-2 receptor-alpha, a key immune activator in MS. The drug is approved for use in organ transplant rejection.

The Lancet Neurology, Early Online Publication, 16 February 2010

### Details

The CHOICE study was a randomized double-blind, placebo-controlled study carried out at 51 centres in the USA, Canada, Germany, Italy, and Spain. Study participants with relapsing MS and who were taking interferon beta were selected for having active disease. Participants were randomised to one of the following study arms; 78 people received 1 mg daclizumab injection under the skin every 4 weeks, 75 received 2 mg every 2 weeks, and 77 received placebo, for 24 weeks and were observed for 48 weeks afterward. The primary endpoint was total number of new or enlarged gadolinium contrast-enhancing lesions (active areas of tissue damage) measured on brain MRI scans every 4 weeks between weeks 8 and 24. Other outcomes included clinical scales of disease severity such as the EDSS and MS Functional Composite. In addition, the effects of daclizumab on subsets of immune cells were analyzed.

After 24 weeks, compared to interferon and placebo, there was a 25% reduction in the number of new or enlarged areas of active damage on MRI in the 1-mg daclizumab group and a 72% reduction in the 2-mg group. No significant

improvement in clinical scales was seen in the daclizumab groups compared to the interferon/placebo group.

Daclizumab was not associated with significant changes in T cells or B cells - known players in the MS attack. However, the number of CD56bright natural killer cells was seven to eight times higher in both daclizumab groups than in the interferon beta/placebo group.

Severe adverse events occurred 20 of 165 (13%) patients in the daclizumab groups versus four of 77 (5%) in the interferon beta/placebo group, most frequently infections. All infections were treated successfully with standard therapies. Skin-related events, such as rash, occurred more frequently in the daclizumab groups than in the interferon/placebo group during weeks 25 to 44, but the difference declined in weeks 45 to 72. Two patients treated with daclizumab developed malignancies that appeared to be unrelated to study treatment.

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