At week 96, the median volume of new and newly enlarging T2 hyperintense lesions was significantly smaller in the DAC HYP group (17 mm^3) versus the IFN-β-1a group (248 mm^3; $P < .0001$). The change in volume of T2 hyperintense lesions from baseline with DAC HYP versus IFN-β-1a was –1.4% versus –0.3% ($P = .0188$) at week 24 and 0.2% versus 3.8% ($P < .0001$) at week 96. The change in volume of T1 hypointense lesions with DAC HYP versus IFN-β-1a was 2.7% versus 6.3% ($P = .0003$) at week 24 and 15.3% versus 25.2% ($P < .0001$) at week 96. Subgroup analysis by baseline disease characteristics showed that all subgroups benefited from DAC HYP versus IFN-β-1a treatment.

The percentage reduction in annualized brain volume change with DAC HYP versus IFN-b-1a was 0.67 versus 0.74 ($P = .03$) at week 24 and 0.52 versus 0.56 from week 24 to week 96, respectively ($P < .0001$).

DAC HYP significantly reduced the number of T2 hyperintense, GD+, and T1 hypointense lesions when compared with IFN-b-1a. These improvements were observed as early as week 24 and were sustained over 96 weeks. DAC HYP also reduced brain atrophy as compared with IFN-b-1a over 2 years of treatment. These results with the efficacy and safety results [Kappos L et al. ECTRIMS. 2014 (session FC1.1); Krzysztof S et al. ECTRIMS. 2014 (poster P094)] indicate that DAC HYP has the potential for greater efficacy and a positive benefit-risk profile in patients with RRMS as compared with IFN-β-1a.

ADVANCE Results: PEG-IFN-β-1a Decreases Disability in RRMS

Written by Brian Hoyle

Two-year data from the Efficacy and Safety Study of Peginterferon Beta-1a in Participants With Relapsing Multiple Sclerosis [ADVANCE; NCT00906399; Kieseier BC et al. ECTRIMS 2014 (poster P042)], a study of relapsing-remitting multiple sclerosis (RRMS) in more than 1500 patients, have confirmed the long-term capability of subcutaneously injected peginterferon beta-1a (PEG-IFN-β-1a) in lessening disability progression. The findings were presented by Bernd C. Kieseier, MD, Heinrich Heine University, Düsseldorf, Germany.

The 1-year data from the placebo-controlled ADVANCE study showed the efficacy of PEG-IFN-β-1a in reducing relapse and risk of disability progression [Calabresi PA et al. *Lancet Neurol.* 2014]. The present post hoc analysis assessed the effect of PEG-IFN-β-1a self-administered on a regular basis on the 2-year risk of disease progression in patients who had experienced a relapse in their MS.

In the first year of the study, patients (n = 1512) were randomized to subcutaneously self-injected PEG-IFN-β-1a 125 µg (n = 512) or placebo (n = 500) every 2 weeks or PEG-IFN-β-1a 125 µg every 4 weeks (n = 500). At 1 year, 1332 patients had completed the regimen (456 received placebo, and 876 received PEG-IFN-β-1a). These patients were re-randomized to self-inject the same dose of PEG-IFN-β-1a every 2 or 4 weeks. Thus, during year 2, each group contained 666 patients: 438 who continued to receive PEG-IFN-β-1a and 228 who newly received PEG-IFN-β-1a (delayed treatment). The baseline characteristics of the delayed arm (year 2) and the two arms from year 1 were comparable.

At 2 years, 143 patients had confirmed disability progression. The proportion of confirmed disability due to incomplete recovery from relapses among those who received PEG-IFN-β-1a every 2 weeks (10/512, 2.0%) was significantly lower than in the delayed-treatment group (30/500, 6.0%; $P = .0010$). The proportion of confirmed disability due to incomplete recovery from relapses among those who received PEG-IFN-β-1a every 4 weeks (27/500, 5.4%) was not significantly different from that of the delayed treatment group (30/500, 6.0%; $P = .6824$).

At year 2, 138 of 1332 patients had confirmed disability progression. The rate of disability progression due to incomplete recovery from relapses was significantly lower in patients treated with PEG-IFN-β-1a every 2 weeks for both years (8/438, 1.8%) compared with patients who received placebo in year 1 and who were now receiving PEG-IFN-β-1a every 4 weeks (16/228, 7.0%; $P = .0006$).

PEG-IFN-β-1a 125 µg administered every 2 weeks for 2 years lowered the risk of 24-week confirmed disability progression by 35% ($P < .05$) compared with patients in whom therapy was delayed until year 2. In patients who had a relapse, this PEG-IFN-β-1a dose schedule significantly reduced (by 49%) the proportion of patients experiencing a relapse compared with those in the delayed group. About half of patients with confirmed disease progression experienced a relapse, supporting the view that disease progression cannot be fully explained by accumulated relapse-related disability.

The data support the idea that PEG-IFN-β-1a delivered at the optimal dose and timing may reduce the risk of relapse and improve recovery from relapse, both of which act to prevent further disease progression.