Treatment With Alemtuzumab Leads to Durable Benefits in Patients With Multiple Sclerosis

Written by Maria Vinall

Treatment with alemtuzumab is associated with durable improvements in magnetic resonance imaging (MRI) disease activity in patients with active relapsing-remitting multiple sclerosis, according to Douglas L. Arnold, MD, NeuroRX Research and Montreal Neurological Institute, McGill University, Montreal, Québec, Canada, who presented the 3-year results from An Extension Protocol for Multiple Sclerosis Patients Who Participated in Genzyme-Sponsored Studies of Alemtuzumab (ClinicalTrials.gov identifier: NCT00930553), an ongoing extension study of the Comparison of Alemtuzumab and Rebif® Efficacy in Multiple Sclerosis (CARE-MS) series of studies. The results showed that participants were free of gadolinium-enhancing, new or enlarging T_2, and new T lesions after 3 years of follow-up. Alemtuzumab also slowed the yearly rate of brain volume loss.

In 2 previous Phase 3 head-to-head trials with patients with active relapsing-remitting multiple sclerosis (CARE-MS I in treatment-naive patients and CARE-MS II in those who relapsed on prior therapy), 2 annual courses of alemtuzumab 12 mg proved superior to subcutaneous interferon-b1a (44 mg 3 times/wk) with respect to clinical efficacy and the reduction in MRI activity and brain volume loss over 2 years.

Patients treated with alemtuzumab in either of the CARE-MS studies continued uninterrupted follow-up in an extension study and were eligible for alemtuzumab retreatment (12 mg administered on 3 consecutive days ³12 months after their previous courses of therapy) on evidence of disease activity. MRI was performed at study entry and annually for each patient, and studies were centrally analyzed by experts masked to treatment group assignment. All patients underwent T_1-weighted pre- and post-Gd contrast, T_2-weighted and proton density precontrast, fluid-attenuated inversion recovery precontrast, and 3-dimensional gradient-echo postcontrast MRI sequences before the administration of methylprednisolone. Brain atrophy was measured by brain parenchymal fraction.

A total of 742 subjects entered the extension study (349 subjects from CARE-MS I and 393 from CARE-MS II). Durable effects on relapse rate and disability were reported at end of Year 1 of the extension study despite patients having been treated for only 2 years [Fox EJ et al. *Neurology* 2013].

The current report presents the results after 3 years of follow-up. In Year 3, 18% and 20% of the subjects in CARE-MS I and II, respectively, received retreatment with alemtuzumab; <3% of patients were treated with other disease-modifying therapies. The majority of alemtuzumab-treated patients were free of MRI activity (absence of both Gd-enhancing and new or enlarging T_2 hyperintense lesions) at both Year 2 and Year 3.

During the same period, alemtuzumab also slowed brain volume loss as measured by brain parenchymal fraction. The median yearly rate of brain atrophy decreased over time (Year 0 to 1, –0.59% and –0.48% for CARE-MS I and II, respectively; Year 1 to 2, –0.25% and –0.22%; Year 2 to 3, –0.19% and –0.10%).

These results support the efficacy of alemtuzumab for the treatment of relapsing-remitting multiple sclerosis in both treatment-naive and previously treated patients and provide evidence of durability of benefit.

Negative Florbetaben PET Scan Excludes the Presence of Amyloid Pathology

Written by Phil Vinall

There is a strong correlation between florbetaben (an F-labeled β-amyloid-targeted tracer) uptake and amyloid pathology, according to Marwan Sabbagh, MD, Banner Sun Health Research Institute, Sun City, Arizona, USA, who presented results of the Phase III Study of Florbetaben (BAY94-9172) PET Imaging for Detection/Exclusion of Cerebral β-Amyloid Compared to Histopathology trial (ClinicalTrials.gov identifier NCT01020838). These results support the use of florbetaben as a valuable diagnostic tool for the exclusion of Alzheimer's disease (AD) or differential diagnosis of dementia as the cause of cognitive decline.

Florbetaben has recently been approved as an adjunct to other diagnostic evaluations for positron emission tomographic (PET) imaging of the brain to estimate β-amyloid neuritic plaque density in adults with cognitive impairment who are being evaluated for AD and other causes of cognitive decline.

The aim of researchers in the present analysis was to assess the diagnostic efficacy of florbetaben and its negative predictive value in a large histopathology cohort of subjects who underwent antemortem florbetaben PET imaging. The analysis was based on data from the aforementioned large Phase 3 multicenter nonrandomized trial in 205 end-of-life subjects who underwent PET imaging 90 to 110 minutes after receiving an intravenous