NDO in patients with MS over a long-term follow-up of up to 4 years.

In the 3-year extension study, 231 patients received ≥1 treatment of the same dose of onabotulinumtoxinA (200 U or 300 U) as that administered in the core trials; however, an amendment to the extension trial allowed a change in the treatment from 300 U to 200 U of onabotulinumtoxinA, if requested. Patients received treatment as needed over 4 years and the change in baseline UI episodes per day was evaluated, as were the incidence of adverse events (AEs) and the initiation of clean intermittent catheterization (CIC). At baseline, the mean number of UI episodes per day ranged from 4.6 to 4.8, and CIC was in use in 33% to 46% of patients.

Treatment with onabotulinumtoxinA resulted in a decrease in the number of UI episodes per day, and 45.2% to 61.9% of patients achieved complete continence at 6 weeks with the 200 U dose. The efficacy was similar in patients who switched from the 300 U to 200 U dose of onabotulinumtoxinA. The median duration of the anti-UI effect was 9.1 months for patients who received 200 U of onabotulinumtoxinA and 9.6 months for patients who received 300 U. After the first treatment cycle of onabotulinumtoxinA, de novo use of CIC was highest but declined after the second and third treatment cycles for both doses of the drug.

Common AEs included urinary tract infections and urinary retention. Retreatment with onabotulinumtoxinA did not increase the rate of AEs. Discontinuation of the study drug as a result of AEs or lack of efficacy occurred in 3% and 1.7% of patients, respectively.

In conclusion, Dr Aliotta stated that the results from this long-term extension trial indicate that the efficacy of onabotulinumtoxinA was maintained over 4 years, with no new safety signals.

Potential Genetic Locus Associated With MS Identified in African Americans

Written by Brian Hoyle

An analysis of genetic determinants of multiple sclerosis (MS) in African Americans has implicated the locus for non-sense-mediated mRNA decay factor 7 (*SMG7*), located on chromosome 1, as a potentially unique MS-associated site in this population. The results were reported by Noriko Isobe, MD, PhD, University of California at San Francisco, San Francisco, California, USA.

While the prevalence of MS in people of African origin was once thought to be relatively low, this may not be the case. In African Americans, not only is the prevalence of MS higher than anticipated, it appears to be on the rise [Langer-Gould A et al. *Neurology.* 2013; Wallin MT et al. *Brain.* 2012]. The MS that develops in African Americans has been described as more severe than that in Europeans [Cree BAC et al. *Neurology.* 2004], with *HLA-DRB1*15:01* and *HLA-DRB1*15:03* being especially associated with MS in African Americans [Isobe N et al. *Neurology.* 2013; Oksenberg et al. *Am J Hum Genet.* 2004].

The use of the ImmunoChip technology, in which different single nucleotide polymorphisms (SNPs) and small regions harboring genetic insertions or deletions are spaced out on a support that is used to probe entire genomes for the targets, has identified nearly 197 000 SNPs linked to a variety of diseases including type 1 diabetes, psoriasis, autoimmune thyroid disease, ankylosing spondylitis, ulcerative colitis, celiac disease, Crohn's disease, rheumatoid arthritis, MS, and others. Of these SNPs, 110 have been associated with MS in Europeans, with a further 48 identified as novel MS loci [IMSGC. *Nat Genet.* 2013].

The present study assessed whether the MS-associated loci identified in Europeans were also identified in African Americans, and if there were other, unique loci in this population. Chromosome samples from 843 African Americans with confirmed MS were examined along with samples from 1612 subjects without any symptoms of MS. Twenty one of 96 European MS loci were properly matched with the particular SNP, indicating the accuracy of the approach. A standard ImmunoChip analysis identified 110 MS-associated SNPs that were not present in Europeans. Of these, 8 were located in linkage disequilibrium regions ($r^2 > 0.5$) of the original MS-associated SNPs. Of the 8, 7 were determined to lie outside of known MS-associated SNPs ($P < .0001$). Finally, of the 7, *SMG7*, located on chromosome 1, was implicated as being associated with MS in African Americans.

The rs2702180 SNP involved with *SMG7* has been linked to the expression of *SMG7* in brain tissue and lymphoblastoid cells [Gibbs JR et al. *PLoS Genet.* 2010; Stranger BE et al. *Nat Genet.* 2007]. *SMG7* abuts *NCF2*, a gene that has been linked with systemic lupus erythematosus [Cunninghame Graham DS et al. *PLoS Genet.* 2011].

The researchers concluded that the *SMG7* locus located on chromosome 1 is a potential candidate site in African Americans with MS. Next, since the ImmunoChip focuses on SNPs and not functional variants, studies involving more samples and functional analyses are needed to conclusively assess this potential association.