Response to Interferon Beta-1a Treatment in African American Multiple Sclerosis Patients

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Background: African Americans (AAs) with multiple sclerosis (MS) seem to have a more severe disease course than white Americans (WAs). To our knowledge, it is not known to what extent treatment with interferon beta-1a will effect the MS disease course within the AA population.

Objective: To compare the response to treatment with interferon beta-1a between AA and WA MS patients.

Design: This is an exploratory post hoc analysis of the Evidence of Interferon Dose-Response: European North American Comparative Efficacy (EVIDENCE) study.

Setting: The EVIDENCE study is a randomized controlled trial that compared the efficacy of once weekly, intramuscular, 30-µg interferon beta-1a treatment with thrice weekly, subcutaneous, 44-µg interferon beta-1a therapy in treatment-naive MS subjects.

Participants: Thirty-six AA subjects were compared with 616 WA subjects.

Main Outcome Measures: The number of MS exacerbations, the proportion of exacerbation-free subjects, and the number of new MS lesions present on brain magnetic resonance imaging were compared between AA and WA subjects at 24 and 48 weeks after initiating treatment with interferon beta-1a.

Results: The AA subjects experienced more exacerbations and were less likely to remain exacerbation free (statistical trends). The AA subjects developed more new MS lesions on T2-weighted brain magnetic resonance imaging at 48 weeks ($P = .04$).

Conclusions: Despite the small sample size, AA subjects appeared less responsive to treatment than WA subjects on outcome measures, reaching significance only for T2-weighted lesion count at 48 weeks. However, it is difficult to base these differences solely on response to treatment given the potential differing in MS disease course in AA patients.

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The disease course of multiple sclerosis (MS) for African American (AA) patients may be more severe than that of white Americans (WAs). Therefore, it is possible that disease-modifying drugs or the disease course, as studied in clinical trials, may be responsible for different effects in AA compared with WA MS subjects. To test this hypothesis, a post hoc analysis comparing AA with WA response to treatment with interferon beta-1a was investigated using the Evidence of Interferon Dose-Response: European North American Comparative Efficacy (EVIDENCE) data set. The EVIDENCE trial was a multicenter, randomized, assessor-blinded study comparing the efficacy of once weekly 30-µg interferon beta-1a (Avonex; Biogen Idec, Cambridge, Mass) with that of thrice weekly 44-µg interferon beta-1a (Rebif; Serono, Inc) on relapses and magnetic resonance imaging markers of disease activity during 48 weeks of therapy in previously untreated relapsing-remitting MS patients.

METHODS

The patients (616 WAs and 36 AAs) were randomized to receive either 30 µg once weekly (AA;21 patients) or 44 µg thrice weekly (AA;15 patients) of interferon beta-1a in the EVIDENCE trial. Twenty-five patients with a non-WA, a non-AA, or an unspecified ethnicity were excluded from this subgroup analysis. The response to treatment was compared using ethnicity as a predictor. Statistical analysis was performed using SAS statistical soft-
ware (SAS Institute Inc, Cary, NC) by Serono, Inc, biostatisticians. For baseline continuous variables, \( P \) values presented were calculated using the 2-sided Wilcoxon rank sum test. For baseline categorical variables, \( P \) values were calculated using the 2-sided Fisher exact test. An unadjusted comparison of mean values used the \( t \) test, and proportions were compared using the \( \chi^2 \) test. Multiple regression modeling was used to adjust for confounding by baseline covariates: treatment (30 \( \mu \)g once weekly or 44 \( \mu \)g thrice weekly of interferon beta-1a), baseline Expanded Disability Status Scale score, baseline attack rate, baseline magnetic resonance imaging findings, and sex. Covariates that did not contribute significantly to the model were dropped. Interactions between covariates were tested for, but none were identified.

**RESULTS**

The baseline characteristics of AA and WA subjects were similar: 13.9% of AA and 25.5% of WA subjects were men \((P = .16)\). The median age of onset was 32.1 years in AA subjects and 31.8 years in WA subjects \((P = .87)\). The median disease duration was 5.6 years in AA subjects and 6.9 years in WA subjects \((P = .14)\). The baseline median number of attacks in the 2 years before the study was 2.5 in AA subjects and 2.6 in WA subjects \((P = .95)\). The baseline median number of combined unique lesions (active T2- and T1-weighted gadolinium–diethylene triamine pentaacetic acid–enhancing lesions) was 2.3 in AA subjects and 2.6 in WA subjects \((P = .12)\). The baseline median Expanded Disability Status Scale score was 2.8 in AA subjects and 2.3 in WA subjects \((P = .06)\). The ratio of treatment with either once weekly or thrice weekly interferon beta-1a was 23:13 for AA subjects and 30:31 for WA subjects \((P = .12)\). In WA subjects, as in the entire EVIDENCE data set, there was a benefit of 3 times weekly subcutaneous interferon beta-1a compared with once-weekly intramuscular interferon beta-1a. Compared with WA subjects, AA subjects experienced more exacerbations (Figure 1) and were less likely to remain relapse free \((P = .07)\) and 48 weeks \((P = .24)\) of treatment with interferon beta-1a.

**Figure 1.** The African American (AA) subjects had more exacerbations than the white American (WA) subjects after 24 weeks \((P = .06)\) and 48 weeks \((P = .13)\) of treatment with interferon beta-1a.

**Figure 2.** The African American (AA) subjects were less likely than the white American (WA) subjects to remain relapse free after 24 weeks \((P = .07)\) and 48 weeks \((P = .24)\) of treatment with interferon beta-1a.

**Figure 3.** The African American (AA) subjects had more new lesions than the white American (WA) subjects at 24 weeks \((P = .15)\) and 48 weeks \((P = .04)\).
and treatment effect ($P = .10$). The AA subjects had 0.31 more relapses (log scale) than the WA subjects at 48 weeks, adjusting for baseline relapse count and treatment effect ($P = .21$). The AA subjects had 0.96 more new T2-weighted lesions at 48 weeks than the WA subjects, adjusting for baseline T2-weighted lesions and treatment effect ($P = .04$). The AA subjects had lesser odds (odds ratio, 0.51) of having no new T2-weighted lesions at 48 weeks compared with the WA subjects, adjusting for baseline T2-weighted lesions and treatment ($P = .09$). Similar results were found for the 24-week outcome measures.

**COMMENT**

Despite the small sample size, AA subjects appeared less responsive to treatment than WA subjects on outcome measures, reaching significance only for the T2-weighted lesion count at 48 weeks. However, it is difficult to base these differences solely on response to treatment given the potential differing in MS disease course in AA patients. Indeed, there are several lines of reasoning that suggest that these observations may be valid. This trial was not designed to detect differences in treatment response between ethnic groups and, consequently, was underpowered for this analysis. Nevertheless, these results are suggestive and are of considerable potential importance. Statistically significant differences may have been observed on additional outcomes if more AA subjects had been included in the EVIDENCE study. The AA MS subjects seemed less responsive (trends) to interferon beta-1a for all measures, a finding that would be unanticipated if these observations were spurious. Interestingly, a similar differential response to treatment with interferon alfa-2b in AA compared with WA subjects is observed for the treatment of hepatitis C. It is plausible that genetic variation between AA and WA subjects could result in a different biological response to interferon. Further studies on the interaction between ethnicity and response to interferon treatment and other disease-modifying drugs for MS are warranted.

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**REFERENCES**

