Clinical Study

Response to Interferon-Beta Treatment in Afro-Caribbeans with Multiple Sclerosis

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Received 24 November 2010; Revised 10 February 2011; Accepted 21 March 2011

Academic Editor: Francesca Bagnato

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Background. Multiple sclerosis (MS) patients of African ancestry have a more aggressive disease course than white patients and could be resistant to interferon-beta (IFN-beta). Methods. We studied the impact of IFN-beta in treatment-naive Afro-Caribbean (AC) with clinically definite MS using our European Database for Multiple Sclerosis (EDMUS) (2003–2010). Main outcome measures were annual relapse rate after 2 years of treatment, proportion of exacerbation-free subjects 48 weeks after initiating IFN-beta, and time to first relapse. Results. 76 AC-MS (59F/17M) were identified. Annual relapse rate of 1.29 decreased to 0.83 (−35.6%) after 2 years of treatment. The proportion of relapse-free patients at 48 weeks was 46.2%. Median time to first relapse was 52 weeks. Conclusion. IFN-beta is not strong enough to control AC-MS patients in many cases which is problematic in a population of worse MS prognosis.

1. Introduction

Subjects of African ancestry have a more aggressive course of multiple sclerosis (MS) than white patients [1–5]. In addition, they could be less responsive to interferon-beta (IFN-beta) than Caucasians [6]. We aimed to determine the effect of IFN-beta in a large sample of Afro-Caribbean (AC) MS patients.

2. Methods

All MS patient visits at the Fort de France Department of Neurology have been entered prospectively in the European Database for Multiple Sclerosis (EDMUS) since 2003. Data included sex, age at onset, date of IFN-beta initiation and discontinuation, type of IFN-beta, date and characteristics of relapses, and Expanded Disability Status Scale (EDSS) score. Patients are seen when IFN-beta is initiated, at months 1, 2, 3, and 6 and then twice a year, as requested by French Drug Agency. Data from patients with clinically definite MS [7] having received IFN-beta as first-line therapy and for any length of time were extracted from the Fort de France EDMUS database (August 31, 2010). Those with age between 18 and 55 years, EDSS of 0 to 5.5, and at least 2 relapses in the 2 previous years before IFN-beta-treatment initiation were eligible for the study. Data taken in consideration were age at onset, disease duration at the beginning of treatment, annualized relapse rate for the 2 years prior to IFN-beta therapy and for the first two years on IFN-beta therapy, and EDSS when treatment was initiated as well as at 2 years of treatment. Patients who remained free from relapses at 24 weeks, 48 weeks, and 104 weeks of IFN-beta therapy were identified. A Relapse was defined as the appearance of new neurological symptoms or worsening of pre-existing symptoms lasting at least 24 hours, preceded by 30 days of clinical stability, accompanied by objective change on examination (worsening of 0.5 point on the EDSS or 1.0 point on the motor, cerebellar, brainstem, or visual functional system scores) in the absence of fever (pseudorelapse). Relapses were treated with intravenous methylprednisolone. Subjects who did not confirm diagnosis of clinically definite MS and patient who fulfilled revised diagnostic criteria for neuromyelitis optica were excluded [8].

2.1. Statistical Analysis. Kaplan Meier curve was used to assess median time to first relapse and Log-rank test to evaluate the effect of categorical variables. The level of statistical significance was set at \( P < .05 \). Statistical analysis was conducted using StatView statistical version 5.0 software.
3. Results

We identified 76 AC-MS patients fulfilling inclusion criteria (Table 1): 59 females and 17 males (sex ratio F/M: 3.5). Of these, 50% received Betaseron (Shering AG, Berlin, Germany) 8 MIU every other day, 21.1% Rebif (Serono, Geneva, Switzerland) 44-µg three times weekly, and 28.9% Avonex (Biogen, Cambridge, Mass, USA) 30-µg each week. The mean age at onset of MS was 30.1 years, and the mean disease duration at initiation of INFB therapy was 4.7 years. Mean duration of treatment was 38.3 months (median: 34). In the two years preceding INFB therapy, mean number of relapses was 2.3 giving a mean annualized relapse rate of 1.29 that decreased to 0.83 (~35.6%) after 2 years of treatment. Mean EDSS at baseline was 2.52 (median: 2.5) and slightly increased to 2.66 at two years follow-up (P = .16).

Patients who remained free from relapses at 24 weeks, 48 weeks, and 104 weeks of INFB therapy were 66.6%, 46.2%, and 29.2%, respectively (7 relapse-free patients who received treatment for < 6 months were excluded because a period of < 6 months of therapy would be too short to evaluate a clinical treatment effect). The median time to first relapse was 12 months (95% Confidence Interval: 10.7–13.3 months). One variable trended to significance was identified to contribute to early failure of INFB therapy in AC-MS: men had a shorter time to first relapse than women (11 months versus 14 months; P = .08). Age at onset of MS, disease duration, EDSS at baseline, relapse rate before treatment, and type of INFB did not contribute.

4. Discussion

In our observational cohort of AC-MS subjects, mean disease duration, mean age at first symptom, and annualized mean number of relapses 2 years before INFB reproduce inclusion criteria of pivotal and head-to-head trials of INFB. INFB therapy reduced the relapse rate by 35.6% in this series. Mean duration of treatment was 38.3 months (median: 34). In the two years preceding INFB therapy, mean number of relapses was 2.3 giving a mean annualized relapse rate of 1.29 that decreased to 0.83 (~35.6%) after 2 years of treatment. Mean EDSS at baseline was 2.52 (median: 2.5) and slightly increased to 2.66 at two years follow-up (P = .16).

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Table 1: Demographic/clinical analysis of AC-MS, WA-MS, and AA-MS of EVIDENCE study.

| Clinical/demographic Information | AC-MS (EVIDENCE) \( n = 76 \) | WA-MS (EVIDENCE) \( n = 616 \) | AA-MS (EVIDENCE) \( n = 36 \) |
|---------------------------------|-------------------------------|-------------------------------|-------------------------------|
| Female, %                       | 77.6                          | 74.5                          | 86.1                          |
| Mean age at first symptom, years (range) | 30.1 (14–50) | 31.8 (18–55) | 32.1 (18–55) |
| Mean disease duration, years (median) | 4.7 (2)                   | 6.9                           | 5.6                           |
| Mean treatment duration, weeks   | 153.2                         | 62                            | 62                            |
| Mean EDSS at treatment (median)  | 2.52 (2.5)                    | 2.3                           | 2.8                           |
| Mean number of relapses in the 2 previous years (median) | 2.3 (2)                   | 2.6                           | 2.5                           |
| %, relapse free at 48 weeks      | 46.2                          | 57                            | 47                            |

References

[1] B. A. C. Cree, O. Khan, D. Bourdette et al., “Clinical characteristics of African Americans vs Caucasian Americans with multiple sclerosis,” Neurology, vol. 63, no. 11, pp. 2039–2045, 2004.
[2] B. Cree and E. Waubant, “Does race matter for multiple sclerosis?” *Neurology*, vol. 74, no. 7, pp. 532–533, 2010.
[3] B. A. Johnsson, J. Wang, E. M. Taylor et al., “Multiple sclerosis susceptibility alleles in African Americans,” *Genes & Immunity*, vol. 11, no. 4, pp. 343–350, 2010.
[4] I. Kister, E. Chamot, J. H. Bacon et al., “Rapid disease course in African Americans with multiple sclerosis,” *Neurology*, vol. 75, no. 3, pp. 217–223, 2010.
[5] M. Deboeverie, C. Lebrun, S. Jeannin et al., “More severe disability of North Africans vs Europeans with multiple sclerosis in France,” *Neurology*, vol. 68, no. 1, pp. 29–32, 2007.
[6] B. A. C. Cree, A. Al-Sabbagh, R. Bennett, and D. Goodin, “Response to interferon beta-1a treatment in African American multiple sclerosis patients,” *Archives of Neurology*, vol. 62, no. 11, pp. 1681–1683, 2005.
[7] C. M. Poser, D. W. Paty, and L. Scheinberg, “New diagnostic criteria for multiple sclerosis: guidelines for research protocols,” *Annals of Neurology*, vol. 13, no. 3, pp. 227–231, 1983.
[8] D. M. Wingerchuk, V. A. Lennon, S. J. Pittock, C. F. Lucchinetti, and B. G. Weinshenker, “Revised diagnostic criteria for neuromyelitis optica,” *Neurology*, vol. 66, no. 10, pp. 1485–1489, 2006.
[9] IFNB Multiple Sclerosis Study Group, “Interferon beta-1b is effective in relapsing-remitting multiple sclerosis. I. Clinical results of a multicenter, randomized, double-blind, placebo-controlled trial,” *Neurology*, vol. 43, no. 4, pp. 655–661, 1993.
[10] PRISMS Study Group, “Randomised double-blind placebo-controlled study of interferon beta-1a in relapsing remitting multiple sclerosis,” *The Lancet*, vol. 352, no. 9139, pp. 1498–1504, 1998.
[11] L. D. Jacobs, D. L. Cookfair, R. A. Rudick et al., “Intramuscular interferon beta-1a for disease progression in relapsing multiple sclerosis,” *Annals of Neurology*, vol. 39, no. 3, pp. 285–294, 1996.
[12] L. Durelli, E. Verdun, P. Barbero et al., “Every-other-day interferon beta-1b versus once-weekly interferon beta-1a for multiple sclerosis: results of a 2-year prospective randomised multicentre study (INCOMIN),” *The Lancet*, vol. 359, no. 9316, pp. 1453–1460, 2002.
[13] H. Panitch, D. S. Goodin, G. Francis et al., “Randomized, comparative study of interferon beta-1a treatment regimens in MS: the evidence trial,” *Neurology*, vol. 59, no. 10, pp. 1496–1506, 2002.
[14] E. Waubant, S. Vukusic, L. Gignoux et al., “Clinical characteristics of responders to interferon therapy for relapsing MS,” *Neurology*, vol. 61, no. 2, pp. 184–189, 2003.
[15] E. Byun, S. J. Caillier, X. Montalban et al., “Genome-wide pharmacogenomic analysis of the response to interferon beta therapy in multiple sclerosis,” *Archives of Neurology*, vol. 65, no. 3, pp. 337–344, 2008.