EG05

Clinical Course of Relapsing-Remitting Multiple Sclerosis (RRMS) in Nonwhite MS Patients

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INTRODUCTION

- A growing body of literature suggests that there may be differences in multiple sclerosis (MS) baseline characteristics and disease severity between white patients, who represent the majority of clinical trial patients, and minority populations of African, Hispanic, and Asian descent.
- Some reports indicate suboptimal response to certain current MS disease-modifying treatments (DMTs) by patients of African descent[1]; other DMTs may demonstrate some efficacy in patients of African descent.[2]
- Most data are derived from registries or individual practices, but detailed clinical trial data are limited.
- The objectives of this analysis were to describe baseline characteristics and MS clinical course in white and nonwhite patients from 6 randomized placebo-controlled trials.

METHODS

- Patients randomized to placebo from 6 placebo-controlled studies (for 5 separate DMTs) in patients with relapsing-remitting MS (RRMS; Table 1) were grouped into 4 racial/ethnic groups: white, black, Asian, and Hispanic.
- Baseline characteristics and clinical/radiological outcomes were evaluated using white patients as the reference group. Magnetic resonance imaging (MRI) was performed in the trials.
- Hispanic status was only collected in AFFIRM (Natalizumab Safety and Efficacy in RRMS) but not the other 5 studies; hence, these patients (n=22) were not included in the baseline analysis.

Table 1. Placebo-controlled RRMS studies pooled for analysis

Study	Phase	Intervention	Duration	Sample size, n
ADVANCE	3	Peginterferon beta-1a	1 year	1512
AFFIRM	3	Natalizumab	2 year	942
CONFIRM	3	Dimethyl fumarate	2 year	1430
DEFINE	3	Dimethyl fumarate	2 year	1237
MSCRG	3	IM interferon beta-1a	2 year	172
SELECT	2b	Daclizumab high-yield process	1 year	621

ADVANCE = Efficacy and Safety Study of Peginterferon Beta-1a in Participants With Relapsing MS; CONFIRM = Comparator and an Oral Fumarate in RRMS; DEFINE = Determination of the Efficacy and Safety of Oral Fumarate in RRMS; IM = intramuscular; MSCRG = Multiple Sclerosis Collaborative Research Group; SELECT = Safety and Efficacy Study of Daclizumab High Yield Process (DAC HYP) to Treat RRMS.

RESULTS

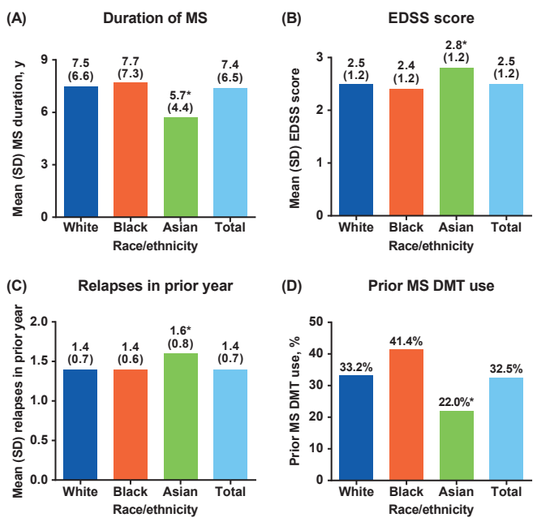
- In total, 1655 white, 29 black, and 141 Asian patients were included in the analysis (Table 2). Of all Asian patients, 95% (134) were from India.
- Baseline demographic and disease characteristics were similar between white and black patients (Table 2).
- Compared with white patients, Asian patients had a significantly lower mean age (34.3 vs. 37.2 years; Table 2), higher mean Expanded Disability Status Scale (EDSS) score (2.8 vs. 2.5), higher mean number of relapses in the prior year (1.6 vs. 1.4), shorter duration of MS since first MS symptom (5.7 vs. 7.5 years), and a lower proportion were previously treated with MS DMTs (22.0% vs. 33.2%; Figure 1).

Table 2. Baseline demographics

Characteristic	White n=1655	Black n=29	Asian n=141	Total N=1825
Mean (SD) age, y	37.2 (9.0)	36.8 (9.2)	34.3 (10.1)	36.9 (9.1)
Female, %	71.1	75.9	63.8	70.6
US patients, n (%)	240 (14.5)	24 (82.8)	2 (1.4)	266 (14.6)
Non-US patients, n (%)	1415 (85.5)	5 (17.2)	139 (98.6)	1559 (85.4)
Mean (SD) Gd+ lesion count	2.0 (4.7)	1.2 (1.4)	2.0 (4.2)	1.9 (4.7)
Mean (SD) T2 lesion count	47.8 (35.6)	29.0 (12.9)	45.3 (32.2)	47.5 (35.2)

Gd+ = gadolinium-enhancing.

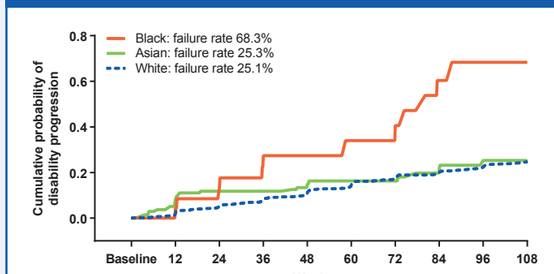
Figure 1. Baseline characteristics by race/ethnicity



*Indicates statistically significant difference compared with white patients.

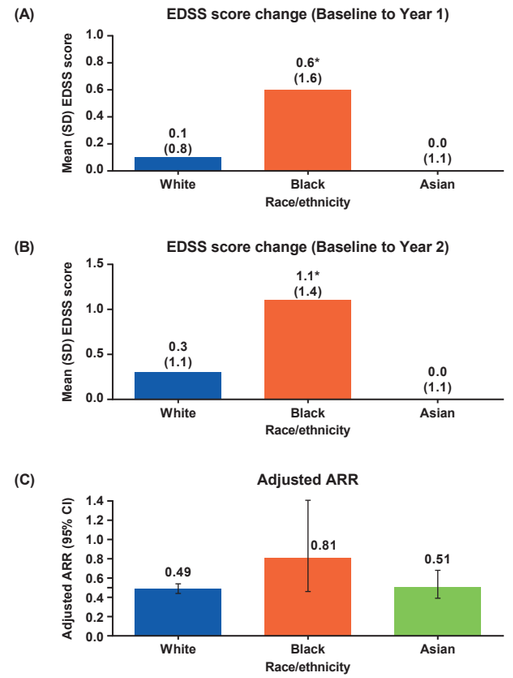
- Over the studies' duration, black patients had a higher risk of 12-week confirmed disability progression as assessed by EDSS score (hazard ratio [95% CI] vs. white patients, 3.6 [2.0–6.5]; *P*<.0001; Figure 2) and significantly greater mean increase in EDSS score vs. white patients from Baseline to Year 1 (0.6 vs. 0.1) and to Year 2 (1.1 vs. 0.3; Figure 3A, B).

Figure 2. Time to sustained (12-week) disability progression



The placebo group for all studies is shown.

Figure 3. Post-Baseline comparison of EDSS score and MRI results



ARR = annualized release rate. *Indicates statistically significant difference compared with white patients.

- No significant differences were observed in relapse endpoints between white and nonwhite patients (Figure 3C), except for a trend for a higher adjusted ARR in black vs. white patients (rate ratio, 1.65 [95% CI, 0.95–2.87]; *P*=.0749).

CONCLUSIONS

- In this analysis of placebo-treated patients from 6 MS clinical trials, several differences were noted between white and nonwhite patients.
- Over the course of the studies, baseline disease seemed to be more severe in the Asian population and disability outcomes were worse in black vs. white patients.
- The interpretation of results was methodologically limited by pooling across trials and low numbers of nonwhite patients.
- Data from Hispanic patients were limited (n=22) and only available from AFFIRM. Although these data were not included in the analysis presented here, a lower proportion of Hispanics had > 0 Gd+ lesion(s) and > 0 new or newly enlarging T2 lesion(s) at Year 1 compared with white patients, suggesting further research may reveal valuable insights.
- Leveraging observational data from registry or clinical databases on patients with diverse backgrounds is a valuable method to better understand the natural history of MS.
- These results also highlight the need to increase recruitment of nonwhite patients into MS clinical trials and large observational databases to gain a better understanding of MS disease activity and response to DMTs in these populations.
- In addition, as the data on minority populations are primarily retrospective, it will be important to verify these findings in prospective studies.

References

1. Cree BA, *et al. Arch Neurol*. 2005;62(11):1681-1683.
2. Cree BA, *et al. Arch Neurol*. 2011;68(4):464-468.

Disclosures

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