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Ofatumumab Improves NEDA-3 Likelihood Compared With Teriflunomide in Black/African American Patients With Relapsing MS: Subgroup Analysis of the ASCLEPIOS Studies

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SUMMARY

1 **This post hoc analysis assessed the proportion of patients with RMS who achieved NEDA-3 in the Black/African American subgroup of 2 large, randomized, double-blind, phase 3 clinical trials of ofatumumab vs teriflunomide**

2 **39% of Black/African American patients undergoing ofatumumab treatment and 7% undergoing teriflunomide treatment achieved NEDA-3 during the full trial course, with ofatumumab providing an ~9-fold increase in the odds of achieving NEDA-3**

3 **83% of Black/African American patients undergoing ofatumumab treatment and 33% undergoing teriflunomide treatment achieved NEDA-3 when assessing Months 12 to 24, with ofatumumab providing an ~10-fold increase in the odds of achieving NEDA-3**

INTRODUCTION

- Black or African American people with multiple sclerosis (MS) often have earlier disease onset and a more severe disease course than White people[1-3]
  - Biological and genetic differences between Black/African American patients and other patients with MS have the potential to influence the efficacy of disease-modifying therapy[2,4]
- Ofatumumab, a fully human anti-CD20 monoclonal antibody, is approved by the US Food and Drug Administration for the treatment of adults with relapsing MS (RMS)
- ASCLEPIOS I and II were randomized, double-blind, phase 3 trials of subcutaneous ofatumumab vs oral teriflunomide in patients with RMS[5]
  - Previous analysis of ASCLEPIOS results in a Black/African American subgroup found that relapse rate reduction, pharmacokinetics/pharmacodynamics, and safety outcomes were similar to the overall trial population[6]

OBJECTIVES

- To report findings of a post hoc analysis from the phase 3 ASCLEPIOS I and II studies assessing achievement of 3-parameter no evidence of disease activity (NEDA-3) with ofatumumab vs teriflunomide in a subgroup of patients with RMS who identified as Black/African American and to compare findings with those of White patients

METHODS

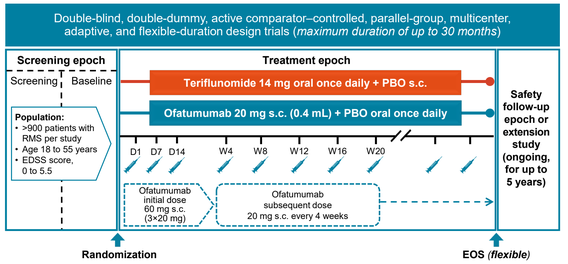
STUDY DESIGN

- This analysis pooled data from the ASCLEPIOS I and II studies (ClinicalTrials.gov identifiers, NCT02792218 and NCT02792231), which had identical study designs (**Figure 1**)
- Patients received injections of ofatumumab 20 mg or oral teriflunomide 14 mg for up to 30 months

ANALYSES

- NEDA-3 was analyzed via a logistic regression model in a modified full analysis set[7]
  - NEDA-3 was defined as no 6-month confirmed disability worsening (based on Expanded Disability Status Scale), no confirmed MS relapse, no new/enlarging T2 lesions, and no gadolinium-enhancing T1 lesions
- Race was self-reported by patients – categories included Black/African American (patients who selected “Black” as race) and “White” (patients who selected “Caucasian”)
- NEDA-3 outcomes were compared between treatment groups (within the Black/African American and White subgroups) via Fisher’s exact test
  - Hypothesis generation without adjustment for multiple comparison
- Rates of adverse events (AEs) were also reported

Figure 1. Study Design of ASCLEPIOS I and II



D, day; EDSS, Expanded Disability Status Scale; EOS, end of study; PBO, placebo; RMS, relapsing multiple sclerosis; s.c., subcutaneous; W, week

RESULTS

PATIENTS

- Of 1882 patients in the overall ASCLEPIOS population, 66 (3.5%) identified as Black/African American and 1658 (88.1%) as White
  - Black/African American patients were more likely to be female; otherwise, baseline characteristics were similar across subgroups (**Table 1**)

Table 1. Baseline Characteristics

Characteristic Shown as mean±SD or n (%)	Black/African American		White	
	Teriflunomide (n=38)	Ofatumumab (n=28)	Teriflunomide (n=829)	Ofatumumab (n=829)
Age, years	36.9±8.7	38.9±10.0	38.3±9.3	38.5±9.0
Female, n (%)	31 (81.6)	21 (75.0)	561 (67.7)	555 (67.0)
MS duration since diagnosis, years	5.33±5.29	5.47±6.33	5.57±6.18	5.76±6.36
Number of relapses in last 12 months	1.08±0.54	1.14±0.65	1.28±0.73	1.26±0.71
EDSS score, median (range)	2.75 (1.0-6.0)	2.75 (0.0-5.5)	2.50 (0.0-6.5)	3.00 (0.0-6.0)
T2 lesion volume, cm^3	13.80±13.02	16.93±13.95	12.32±13.85	13.29±13.71
Free of Gd+ T1 lesions, n (%)	22 (57.9)	15 (53.6)	519 (62.6)	498 (60.1)
Number of Gd+ T1 lesions	1.3±2.3	2.1±3.7	1.3±3.5	1.6±4.6

EDSS, Expanded Disability Status Scale; Gd+, gadolinium-enhancing; MS, multiple sclerosis; SD, standard deviation

ACHIEVEMENT OF NEDA-3

- In both the Black/African American and White subgroups, ofatumumab increased the odds of achieving NEDA-3 vs teriflunomide during Months 0 to 12 by ~6- and 3-fold (**Figure 2A**), Months 12 to 24 by ~10- and ~8-fold (**Figure 2B**), and Months 0 to 24 by ~9- and 3-fold (**Figure 2C**), respectively
  - In patients treated with ofatumumab, achievement of NEDA-3 was consistent between the Black/African American and White subgroups

SAFETY

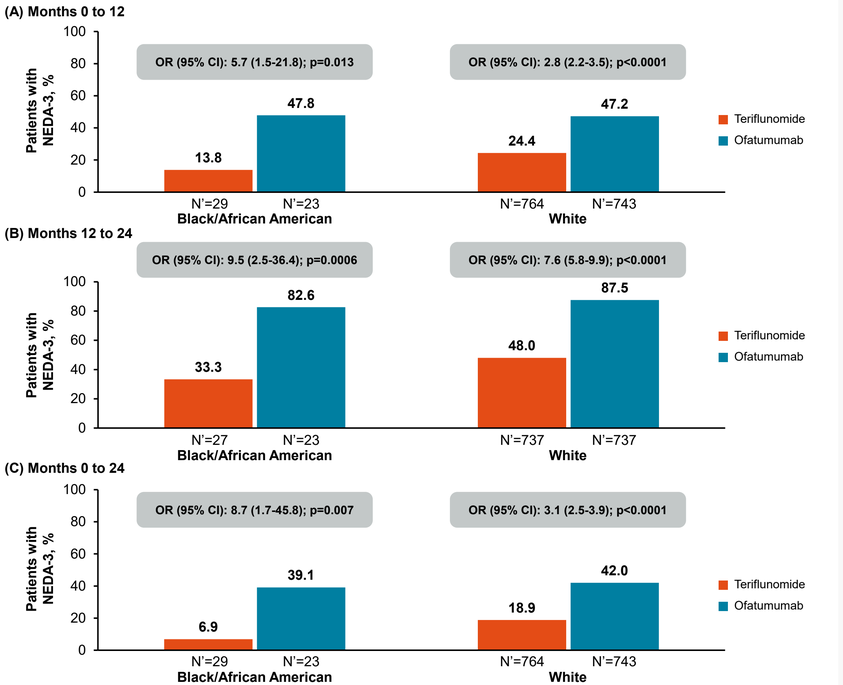
- Rates of AEs, serious AEs, and AEs resulting in discontinuation were balanced between ofatumumab and teriflunomide in each patient subgroup (**Table 2**)
  - There were no significant differences in types of reported AEs between subgroups
  - No specific serious AE occurred in >1 Black/African American patient

Table 2. Summary of AEs

Event, n (%)	Black/African American		White	
	Teriflunomide (n=38)	Ofatumumab (n=28)	Teriflunomide (n=829)	Ofatumumab (n=829)
Any AE	35 (92.1)	26 (92.9)	697 (84.1)	704 (84.9)
Any serious AE	3 (7.9)	3 (10.7)	67 (8.1)	78 (9.4)
Any AE resulting in discontinuation	2 (5.3)	0 (0)	44 (5.3)	52 (6.3)
Any serious infection	0 (0)	3 (10.7)	16 (1.9)	19 (2.3)

AE, adverse event

Figure 2. Achievement of NEDA-3



CI, confidence interval; mFAS, modified full analysis set; N’, patients available for analysis; NEDA-3, 3-parameter no evidence of disease activity; OR, odds ratio
The mFAS used for NEDA calculations consisted of all patients in the FAS, except those who discontinued from study drug prematurely for reasons other than ‘lack of efficacy’ or ‘death’ and had NEDA before early discontinuation. Patients who discontinued from study drug prematurely for reasons of ‘lack of efficacy’ or ‘death’ were considered as having evidence of disease activity in the analysis (even if no evidence of disease activity was reported)

ABBREVIATIONS: AE, adverse event; **CI**, confidence interval; **D**, day; **EDSS**, Expanded Disability Status Scale; **EOS**, end of study; **Gd+**, gadolinium-enhancing; **mFAS**, modified full analysis set; **MS**, multiple sclerosis; **N’**, patients available for analysis; **NEDA-3**, 3-parameter no evidence of disease activity; **OR**, odds ratio; **PBO**, placebo; **RMS**, relapsing multiple sclerosis; **s.c.**, subcutaneous; **SD**, standard deviation; **W**, week

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