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Serum Neurofilament Light Chain Levels and NEDA-3 Status With Ofatumumab Treatment in Diverse Racial/Ethnic Subgroups With Relapsing Multiple Sclerosis: 5-Year Results From ALITHIOS

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KEY FINDINGS & CONCLUSIONS

- The earlier and sustained benefit of OMB-OMB treatment on sNfL levels and achievement of NEDA-3 versus TER-OMB support the value of earlier initiation of high-efficacy therapy in pwRMS, irrespective of racial/ethnic background

- These results were consistent with those obtained for the overall population in the ALITHIOS extension study

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INTRODUCTION

- Serum neurofilament light chain (sNfL) is a biomarker of neuroaxonal injury; in relapsing multiple sclerosis (RMS), sNfL has been used to assess disease activity and response to treatment, and as a predictor of short- and long-term prognosis[1]
- Evidence indicates that achieving three-parameter no evidence of disease activity (NEDA-3) during the first 2 years of treatment confers a lower risk of long-term disability in RMS[2]
- In the phase 3 ASCLEPIOS I/II trials (NCT02792218/NCT02792231), ofatumumab (OMB) significantly reduced sNfL levels compared with teriflunomide (TER) in the first assessment at Month 3 and in all subsequent assessments over 2 years, and increased the likelihood of achieving NEDA-3 versus TER in people with RMS (pwRMS)[3]
- In the ALITHIOS open-label extension study (NCT03650114), early reduction of sNfL levels and higher odds of achieving NEDA-3 were noted in the OMB-OMB group compared with the TER-OMB group, supporting the value of earlier initiation of high-efficacy therapy compared with lower efficacy therapy[4]
  - However, the effect of long-term OMB treatment on sNfL levels and NEDA-3 in diverse racial/ethnic subgroups has not yet been investigated

OBJECTIVE

- To assess the long-term effect of OMB on sNfL levels and NEDA-3 in Asian, Black, Hispanic, Caucasian, and Other subgroups entering ALITHIOS

RESULTS

Baseline characteristics

- Of the 1882 participants randomized in the ASCLEPIOS I/II trials, 1367 (72.6%) participants entered the ALITHIOS extension study (Table 1) and received OMB for up to 5 years at the time of data cut-off (25-Sep-2022)

Table 1. Demographics and disease characteristics of participants

Characteristics[a]	OMB-OMB (N=946)		TER-OMB (N=936)	
	Baseline from core study (N=946)	Baseline from extension study (N=690)	Baseline from core study (N=936)	Baseline from extension study (N=677)
Age, years	38.4±9.0	38.1±8.7	38.0±9.2	40.1±9.2
Female, n (%)	637 (67.3)	483 (70.0)	636 (67.9)	456 (67.4)
Race, n (%)				
Asian	36 (3.8)	19 (2.8)	35 (3.7)	27 (4.0)
Black	26 (2.7)	12 (1.7)	38 (4.1)	19 (2.8)
Hispanic	76 (8.0)	63 (9.1)	69 (7.4)	42 (6.2)
Caucasian	766 (81.0)	568 (82.3)	772 (82.5)	574 (84.8)
Other[b]	42 (4.4)	28 (4.1)	22 (2.4)	15 (2.2)
MS duration since first symptom, years	8.3±7.1	9.9±6.7	8.2±7.3	9.9±7.1
Number of relapses in the year prior to screening	1.2±0.7	0.1±0.4	1.3±0.7	0.2±0.5
Time since onset of most recent relapse, months	7.5±13.0	30.6±15.3	7.8±13.8	24.6±13.9
EDSS score	2.9±1.4	2.8±1.5	2.9±1.4	2.8±1.5
Number of Gd+ T1 lesions	1.7±4.5	0.0±0.2	1.3±3.4	0.8±2.4
Participants free of Gd+ T1 lesions, n (%)	561 (59.3)	680 (98.6)	584 (62.4)	498 (73.6)
T2 lesion volume (cm³)[c]	13.7±13.8	—	12.5±13.8	—
Baseline sNfL (pg/mL), median	13.7±13.2	9.6±9.6[d]	12.5±9.9	12.8±11.1[d]

[a]Values are represented as mean±SD unless specified otherwise. [b]Racial subgroups described as "other" or "unknown" upon data collection. [c]Only baseline from core studies was used because baseline from extension study was not available for all patients. [d]Original values were used as assay-transformed values were not available for the extension study. EDSS, Expanded Disability Status Scale; Gd+, gadolinium-enhancing; MS, multiple sclerosis; OMB-OMB, continuous ofatumumab; SD, standard deviation; sNfL, serum neurofilament light chain; TER-OMB, switch from teriflunomide to ofatumumab.

Mean sNfL levels over time

- Lower mean sNfL levels versus baseline were recorded up to Year 5 in all racial/ethnic subgroups (Asian, Black, Hispanic, Caucasian, and Other) in the OMB-OMB group ([baseline/Year 5, pg/mL]: 13.1/8.5, 10.9/7.2, 12.0/8.1, 11.0/8.9, and 12.3/8.9, respectively) and in the TER-OMB group (10.8/7.4, 11.4/9.5, 10.0/8.5, 10.6/9.2, and 12.9/8.3, respectively)

- sNfL levels over time in the racial/ethnic subgroups were consistent with those of the overall population for the OMB-OMB and TER-OMB groups (Figure 1)

Figure 1. sNfL levels over time – Overall population and racial/ethnic subgroups

OMB-OMB, continuous ofatumumab; sNfL, serum neurofilament light chain; TER-OMB, switch from teriflunomide to ofatumumab.

NEDA-3 status

- Higher rates of NEDA-3 were achieved earlier across all racial/ethnic subgroups in the OMB-OMB versus TER-OMB groups (Figure 2)

  - At Year 2, approximately 80% of participants achieved NEDA-3 in the OMB-OMB group, except for the Black subgroup (73.7%)

  - NEDA-3 rates at Year 1/Year 5 in the OMB-OMB group were 48.3%/91.7%, 52.2%/85.7%, 50.0%/98.4%, 47.9%/93.3%, and 40.5%/89.3% in the Asian, Black, Hispanic, Caucasian, and Other subgroups, respectively

  - NEDA-3 rates at Year 1/Year 5 in the TER-OMB group were 32.4%/96.7%, 13.8%/78.9%, 30.0%/97.5%, 24.7%/90.2%, and 30.0%/100% in the Asian, Black, Hispanic, Caucasian, and Other subgroups, respectively

- NEDA-3 results for racial/ethnic subgroups were consistent with those of the overall population

METHODS

Participant population

- Data were analyzed up to 5 years in participants randomized to OMB in ASCLEPIOS I/II and continuing OMB in ALITHIOS (OMB-OMB) and those randomized to TER in ASCLEPIOS I/II and switching to OMB in ALITHIOS (TER-OMB)

Assessments

- Geometric means for sNfL levels and the proportion of participants achieving NEDA-3 over time were reported for the overall population and racial/ethnic subgroups (Asian, Black, Hispanic, Caucasian, and Other [racial subgroups described as "other" or "unknown" upon data collection)
  - Each patient was classified into one subgroup only

- sNfL levels were assessed using[5]:
  - Quanterix Simoa® NF-light™ Advantage Kit validated at Navigate BioPharma Services (Carlsbad, CA, USA) for the ASCLEPIOS I/II core period
  - Siemens Healthcare Laboratory (SHL) NfL laboratory developed test on Atellica® Immunoassay Analyzer, which is a part of the Atellica® Solution, validated at SHL (Berkeley, CA, USA), for the ALITHIOS extension period

- The sNfL values from the assay used in the core study were transformed to be comparable to the values from the assay used in the extension study[5]

- Due to small numbers in the racial/ethnic subgroups, except Caucasian, summary statistics were provided

Figure 2. NEDA-3 status by year – Overall population and racial/ethnic subgroups

NEDA, no evidence of disease activity; OMB-OMB, continuous ofatumumab; TER, teriflunomide; TER-OMB, switch from teriflunomide to ofatumumab; TER + OMB, patients with teriflunomide and ofatumumab.

Limitations

- The data presented for the racial/ethnic subgroups from ALITHIOS, except Caucasian, are based on small sample sizes

References
1. Consortium of Multiple Sclerosis Centers (CMSC) Consensus on Neurofilament Biomarkers in Multiple Sclerosis: CMSC best practices for the use of serum neurofilament (sNfL) in MS management. 2024. Accessed May 2024. <https://mscare.sharefile.com/share/view/s60a6a95b73684d83873c6d9cab9d66b8>. 2. Rotstein DL, et al. JAMA Neurol. 2015;72:152–158. 3. Hauser SL, et al. N Engl J Med. 2020;383:546–557. 4. Hauser SL, et al. Mult Scler. 2023;29:1452–1464. 5. Kuhle J, et al. Poster P1198. Presented at: ECTRIMS 2022.

Abbreviations
EDSS, Expanded Disability Status Scale; Gd+, gadolinium-enhancing; MS, multiple sclerosis; NEDA-3, three-parameter no evidence of disease activity; OMB, ofatumumab; OMB-OMB, continuous ofatumumab; pwRMS, people with relapsing multiple sclerosis; RMS, relapsing multiple sclerosis; SD, standard deviation; sNfL, serum neurofilament light chain; SHL, Siemens Healthcare Laboratory; TER, teriflunomide; TER-OMB, switch from teriflunomide to ofatumumab.