Demographics and Baseline Disease Characteristics of Black and Hispanic Patients With Multiple Sclerosis in the CHIMES Trial

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**A F Okai** has received consulting fees from Alexion, Biogen, Bristol Myers Squibb, EMD, Serono, Greenwich Biosciences, Novartis, Roche, Genentech, Inc., Sanofi Genzyme and TG Therapeutics and serves on the speakers bureau for Alexion, Biogen, EMD Serono, F. Hoffmann-La Roche Ltd, Genentech, Inc., and Sanofi Genzyme.

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**A T Reder** has received consulting fees from Bayer, Biogen, F. Hoffmann-La Roche Ltd, Genentech, Inc., Merck Serono, Novartis and TG Therapeutics; is an editor for MedLink; and has received unrestricted grant support from Bayer, Biogen, F. Hoffmann-La Roche Ltd, Genentech, Inc., Mallinckrodt, Merck Serono and Novartis.

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Background

MS disease characteristics vary among racial and ethnic groups

• The demographics of multiple sclerosis (MS) in the United States are changing \(^1,2\)
  - Retrospective studies have shown incidence of MS in White people ranging from 6.9% to 9.3%, in Black people from 10.2% to 12.1% and in Hispanic people from 2.9% to 8.2% per 100,000 \(^3\)

• Black/African American (Black) and Hispanic/Latino (Hispanic) patients with MS have faster disease progression and greater eventual disability than White patients \(^4–7\)
  - Black and Hispanic patients are more likely to present with optic neuritis, transverse myelitis or cerebellar dysfunction \(^7–9\)
  - Black patients may have greater B-cell–mediated pathology, as evidenced by a higher immunoglobulin G index \(^10–13\)

• Differences in clinical characteristics in Black and Hispanic patients with MS may be the result of genetic, environmental, socioeconomic and/or cultural factors, \(^3\) any of which may lead to variation in disease severity \(^14\)

Background

Lack of diversity in clinical trials and barriers to Black and Hispanic participation

Despite differences in MS clinical characteristics, Black and Hispanic patients are vastly underrepresented in clinical trials

Race and ethnicity are underreported in MS clinical trial publications,\(^1\) but available data show underrepresentation of Black and Hispanic patients\(^a\)

- Black patients: 2.3–16.1%
- Hispanic patients: 7.0–7.5%

Barriers to healthcare and study participation are more common for Black and Hispanic patients\(^3^–^5\)

- Not invited to participate due to unconscious bias based on racial stereotypes and structural racism
- Lack of trial awareness and access due to location or insurance status
- Sociocultural factors, such as acculturation and perceptions
- Concern about risk to employment and legal status
- Socioeconomic status and education
- Financial and logistic burden on patients
- Mistrust of research, including concern about receiving poor-quality care or being taken advantage of
- Restrictive inclusion/exclusion criteria

\(^a\)Includes data from four published, multinational, randomized controlled trials that reported specifically on efficacy of MS disease-modifying treatments in Black or Hispanic patients.\(^2\)

The objective of the CHIMES trial is to investigate the efficacy and safety of ocrelizumab (OCR) in Black and Hispanic patients with relapsing MS (RMS).

The CHIMES trial (NCT04377555) is an open-label, single-arm, Phase IV clinical study.

OCR is a humanized monoclonal antibody that selectively targets CD20+ B cells and reduces the rates of disease activity and progression in patients with RMS or primary progressive MS.

Self-identified Black and Hispanic patients aged 18 to 65 years with RMS and an expanded disability status scale (EDSS) score of ≤5.5 were included.

Methods

CHIMES study design: timeline

**1st year: study**

<table>
<thead>
<tr>
<th>Screen</th>
<th>12 weeks</th>
<th>24 weeks</th>
<th>48 weeks</th>
<th>72 weeks</th>
<th>96 weeks</th>
</tr>
</thead>
<tbody>
<tr>
<td>-8 to 0 weeks</td>
<td>OCR 300mg</td>
<td>OCR 300mg</td>
<td>OCR 600mg</td>
<td>OCR 600mg</td>
<td>OCR 600mg</td>
</tr>
<tr>
<td>0 to 24 weeks</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>25 to 48 weeks</td>
<td></td>
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</tr>
<tr>
<td>49 to 72 weeks</td>
<td></td>
<td></td>
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<td></td>
<td></td>
</tr>
<tr>
<td>73 to 96 weeks</td>
<td></td>
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</tr>
</tbody>
</table>

**2nd year: extension**

- **OCR infusion**
- **History and physical examination**
- **Blood draw**
- **MRI**

**Primary endpoint:** disease activity, defined by the proportion of patients achieving no evidence of disease activity-3 (NEDA-3: clinical relapses, confirmed disability progression and MRI activity) at the end of Year 1.
Methods

CHIMES study design: addressing barriers to diversity in clinical trials

Identifying study centers that serve diverse communities

North America
  United States
  Puerto Rico

Africa
  Kenya

Addressing language and communication barriers

Addressing financial, time and logistic burdens on patients

Compensation for loss of earnings
  Ride Health patient transportation
  Childcare reimbursement
  Travel and meal reimbursement
  Flexibility in screening and visit schedule windows
## Results

### Demographic and baseline characteristics

BMI, body mass index.

a3 patients are of Hispanic ethnicity and identify their race as Black.


<table>
<thead>
<tr>
<th></th>
<th>Black patients n=113</th>
<th>Hispanic patients n=69</th>
<th>All patients N=182</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, mean (SD), years</td>
<td>36.3 (10.4)</td>
<td>34.2 (10.5)</td>
<td>35.5 (10.5)</td>
</tr>
<tr>
<td>Sex, n (%)</td>
<td>87 (77.0)</td>
<td>44 (63.8)</td>
<td>131 (72.0)</td>
</tr>
<tr>
<td>Ethnicity, n (%)</td>
<td>0</td>
<td>69 (100)</td>
<td>69 (37.9)</td>
</tr>
<tr>
<td>Hispanic</td>
<td>110 (97.3)</td>
<td>0</td>
<td>110 (60.4)</td>
</tr>
<tr>
<td>Not Hispanic</td>
<td>3 (2.7)</td>
<td>0</td>
<td>3 (1.6)</td>
</tr>
<tr>
<td>Race, n (%)</td>
<td>0</td>
<td>63 (91.3)</td>
<td>63 (34.6)</td>
</tr>
<tr>
<td>American Indian or Alaska Native</td>
<td>0</td>
<td>2 (2.9)</td>
<td>2 (1.1)</td>
</tr>
<tr>
<td>Blacka</td>
<td>113 (100)</td>
<td>3 (4.3)</td>
<td>116 (63.7)</td>
</tr>
<tr>
<td>White</td>
<td>0</td>
<td>63 (91.3)</td>
<td>63 (34.6)</td>
</tr>
<tr>
<td>Multiple</td>
<td>0</td>
<td>1 (1.4)</td>
<td>1 (0.5)</td>
</tr>
<tr>
<td>BMI, n</td>
<td>112</td>
<td>69</td>
<td>181</td>
</tr>
<tr>
<td>Mean (SD), kg/m²</td>
<td>31.64 (8.00)</td>
<td>29.86 (6.32)</td>
<td>30.96 (7.44)</td>
</tr>
</tbody>
</table>

Younger age and a higher BMI were observed in Black and Hispanic patients in the CHIMES trial when using the OPERA trial population¹ as a benchmark.
### Results

*Baseline MS disease history and previous DMT use*

<table>
<thead>
<tr>
<th></th>
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<th>Hispanic patients n=69</th>
<th>All patients N=182</th>
</tr>
</thead>
<tbody>
<tr>
<td>Time since symptom onset, mean (SD), years</td>
<td>5.15 (5.71)</td>
<td>4.60 (5.52)</td>
<td>4.94 (5.63)</td>
</tr>
<tr>
<td>Time since RMS diagnosis, mean (SD), years</td>
<td>2.87 (4.62)</td>
<td>2.91 (4.43)</td>
<td>2.89 (4.54)</td>
</tr>
<tr>
<td>Baseline EDSS (rounded), mean (SD)</td>
<td>2.51 (1.45)</td>
<td>2.01 (1.29)</td>
<td>2.32 (1.41)</td>
</tr>
<tr>
<td>No. of relapses in the past 24 months, mean (SD)</td>
<td>0.77 (0.58)</td>
<td>0.64 (0.51)</td>
<td>0.72 (0.56)</td>
</tr>
<tr>
<td>Patients taking previous DMT, n (%)</td>
<td>41 (36.3)</td>
<td>27 (39.1)</td>
<td>68 (37.4)</td>
</tr>
<tr>
<td>Duration between end of last DMT to initiation of OCR treatment, mean (SD), months</td>
<td>10.20 (17.96)</td>
<td>7.23 (11.03)</td>
<td>9.02 (15.55)</td>
</tr>
</tbody>
</table>

*Shorter duration of disease and time to diagnosis* were observed in Black and Hispanic patients in the CHIMES trial when using the OPERA trial population as a benchmark.

DMT, disease-modifying therapy; EDSS, expanded disability status scale; MS, multiple sclerosis; OCR, ocrelizumab; RMS, relapsing multiple sclerosis.

### Results

**Disease characteristics for brain MRI assessments at baseline**

<table>
<thead>
<tr>
<th></th>
<th>Black patients n=113</th>
<th>Hispanic patients n=69</th>
<th>All patients N=182</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>No. of T1 Gd-enhancing lesions</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>n</td>
<td>111</td>
<td>68</td>
<td>179</td>
</tr>
<tr>
<td>Mean (SD)</td>
<td>2.30 (5.05)</td>
<td>1.21 (2.47)</td>
<td>1.88 (4.29)</td>
</tr>
<tr>
<td><strong>No. of T2 lesions</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>n</td>
<td>113</td>
<td>68</td>
<td>181</td>
</tr>
<tr>
<td>Mean (SD)</td>
<td>49.75 (32.89)</td>
<td>48.44 (29.56)</td>
<td>49.26 (31.60)</td>
</tr>
<tr>
<td><strong>Volume of T2 lesions, cm³</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>n</td>
<td>113</td>
<td>68</td>
<td>181</td>
</tr>
<tr>
<td>Mean (SD)</td>
<td>21.36 (20.68)</td>
<td>14.87 (11.88)</td>
<td>18.92 (18.13)</td>
</tr>
<tr>
<td><strong>Normalized brain volume, cm³</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>n</td>
<td>112</td>
<td>68</td>
<td>180</td>
</tr>
<tr>
<td>Mean (SD)</td>
<td>1506.77 (94.23)</td>
<td>1533.69 (95.47)</td>
<td>1516.94 (95.34)</td>
</tr>
</tbody>
</table>

**Greater T2 burden** was observed in Black and Hispanic patients in the CHIMES trial when using the OPERA trial population\(^1\) as a benchmark.

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Gd, gadolinium.  
Conclusions

- Underrepresentation of Black and Hispanic patients in clinical trials limits the understanding of MS pathophysiology and treatment

- Data from the CHIMES trial, the first MS trial to focus on Black and Hispanic patients, indicate some differences in demographics and baseline disease characteristics between Black and/or Hispanic and White patients
  - Findings may improve the current understanding of MS disease biology, treatment response and clinical trial participation
Supplemental
In addition to addressing barriers, the CHIMES study will investigate a unique set of biomarkers, including B- and T-cell surface markers.

**Imaging**
- Volume/area change of whole brain, cervical spine and other structures/regions
- Change in T1 Gd-enhancing and T2 lesion counts, T1 nonenhancing lesion volumes, T2 lesion volumes, SEL count and volume

**Blood biomarkers**
- Peripheral blood T- and B-cell subpopulations
- Serum CXCL 13 levels
- Serum Ig levels (IgG, IgM, IgA)
- Serum NfL levels

**Genomics**
- HLA class II haplotypes, including DRB1*15:01
- Ancestral markers

CXCL 13, C-X-C motif chemokine ligand 13; Gd, gadolinium; HLA, human leukocyte antigen; Ig, immunoglobulin; NfL, neurofilament light chain; SEL, slowly expanding/evolving lesion.