

# Safety and Tolerability of Conversion to Siponimod in Patients with Advancing Relapsing Multiple Sclerosis: A Subgroup Analysis by Race and Ethnicity of EXCHANGE Interim Data

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## SUMMARY

**1** Minority groups are persistently underrepresented in clinical trials, resulting in limited data to inform clinical decision-making for these patients. EXCHANGE enrolled a higher proportion of minority groups vs other recent MS clinical trials

**2** Findings of this subgroup analysis by race/ethnicity provide some insights into treatment patterns and safety/tolerability in minority MS patient populations

**3** Siponimod safety/tolerability profile remained consistent with no new or unexpected safety findings identified through this analysis



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## BACKGROUND

- Siponimod (Mayzent®), an oral S1P receptor type 1, 5 modulator approved in the USA for adults with RMS (including CIS, RRMS, and active SPMS), reduces relapses and disability progression in patients with SPMS<sup>1-3</sup>
- EXCHANGE (NCT03623243) is a Phase 3b trial of safety and tolerability of immediate conversion to dose-titrated siponimod from other DMTs in patients with advancing RMS
- Minority groups are persistently underrepresented in clinical trials, resulting in limited data to inform clinical decision-making for these patients and presenting an urgent need for evidence-based clinical management<sup>4</sup>
- In four recent large-scale Phase 3 MS trials (OPERA, ORATORIO, RADIANCE, EXPAND), study populations included 0.5-5.3% Black and 0-6.5% Hispanic participants<sup>4</sup>
- The EXCHANGE study enrolled a diverse patient population and presents opportunity to assess MS treatment patterns and safety/tolerability in conversion to siponimod

## OBJECTIVE

- Report on a subgroup analysis of EXCHANGE interim data in patients with advancing RMS who identified as Hispanic/Latino or Black/African American

## RESULTS

### PATIENT DISPOSITION AND BASELINE CHARACTERISTICS

- Patient demographics and disposition are described in **Table 1**

**Table 1. Patient demographics and baseline characteristics**

Demographic, n (%) unless otherwise specified	Overall (N=163)	Black/African American (N=23)	Hispanic/Latino (N=36)
<b>Age, years, mean (SD)</b>	46.6 (10.3)	43.8 (8.6)	40.3 (11.3)
<b>Gender</b>			
Female	121 (74.2)	20 (87.0)	27 (75.0)
Male	42 (25.8)	3 (13.0)	9 (25.0)
<b>Race</b>			
White	138 (84.7)	-	-
Black or African American	23 (14.1)	23 (100.0)	-
Asian	2 (1.2)	-	-
<b>Ethnicity</b>			
Hispanic or Latino	36 (22.1)	-	36 (100.0)
Not Hispanic or Latino	126 (77.3)	-	-
Not Reported	1 (0.6)	-	-
<b>Type of MS at study entry</b>			
Single demyelinating event	1 (0.6)	-	1 (2.8)
PPMS	4 (2.5)	-	1 (2.8)
SPMS	33 (20.2)	3 (13.0)	3 (8.3)
RRMS	125 (76.7)	20 (87.0)	31 (86.1)
<b>Time since MS diagnosis, years, mean (SD)</b>	12.2 (8.7)	10.5 (7.1)	10.2 (7.7)
<b>Time since first MS symptom, years, mean (SD)</b>	14.4 (9.6)	12.3 (7.5)	13.0 (9.3)
<b>EDSS score, median</b>	3.5	3.5	3.0
<b>Relapses in 12 months before screening</b>			
0	88 (54.0)	8 (34.8)	15 (41.7)
1	57 (35.0)	7 (30.4)	17 (47.2)
2	10 (6.1)	5 (21.7)	2 (5.6)
3	6 (3.7)	1 (4.3)	2 (5.6)
≥4	2 (1.2)	2 (8.7)	-
<b>Relapses in 24 months before screening</b>			
0	86 (52.8)	10 (43.5)	10 (27.8)
1	39 (23.9)	5 (21.7)	13 (36.1)
2	24 (14.7)	4 (17.4)	8 (22.2)
3	7 (4.3)	2 (8.7)	3 (8.3)
≥4	7 (4.3)	2 (8.7)	2 (5.6)

- Of 163 patients in the overall EXCHANGE interim population (**Table 1**):
  - 126 (77.3%) identified as White, non-Hispanic/Latino
  - 23 (14.1%) identified as Black/African American
  - 36 (22.1%) identified as Hispanic/Latino
- The proportion of patients with no relapses in the year prior to screening were 54.0%, 34.8%, and 41.7% in the respective subgroups (**Table 1**)
- 77.8% of the Hispanic/Latino subgroup were on oral DMTs, vs 68.7% in the overall EXCHANGE interim population and 47.8% in the Black/African American subgroup (**Table 2**)
- 47.8% of the Black/African American subgroup were on injectable DMTs before switching to siponimod, vs 27.6% in the overall EXCHANGE interim population and 16.7% in the Hispanic/Latino subgroup (**Table 2**)

**Table 2. Prior MS DMTs before switching to siponimod**

Previous MS treatment, n (%)	Overall (N=163)	Black/African American (N=23)	Hispanic/Latino (N=36)
<b>Previously treated patients</b>	<b>163 (100)</b>	<b>23 (100)</b>	<b>36 (100)</b>
<b>Oral DMTs</b>			
Fingolimod	50 (30.7)	4 (17.4)	17 (47.2)
With dose titration	43 (26.4)	4 (17.4)	14 (38.9)
Without dose titration	7 (4.3)	-	3 (8.3)
Dimethyl fumarate	34 (20.9)	5 (21.7)	5 (13.9)
Teriflunomide	28 (17.2)	2 (8.7)	6 (16.7)
<b>Injectable DMTs</b>			
GA	26 (16.0)	5 (21.7)	5 (13.9)
Any IFNβ	19 (11.7)	6 (26.1)	1 (2.8)
<b>Infusion DMTs</b>			
Natalizumab	1(0.6)	1 (4.3)	-
Ocrelizumab	5 (3.1)	-	2 (5.6)

### EFFECT OF SIPONIMOD CONVERSION ON HEART RATE

- Mean heart rate at baseline and 6-hour post first dose in both patient subgroups were comparable to the findings observed in the overall EXCHANGE interim population
- There was no decrease in heart rate at 6 hours post first dose from baseline in the overall or any of the prior DMT groups in either patient subgroup

### SAFETY

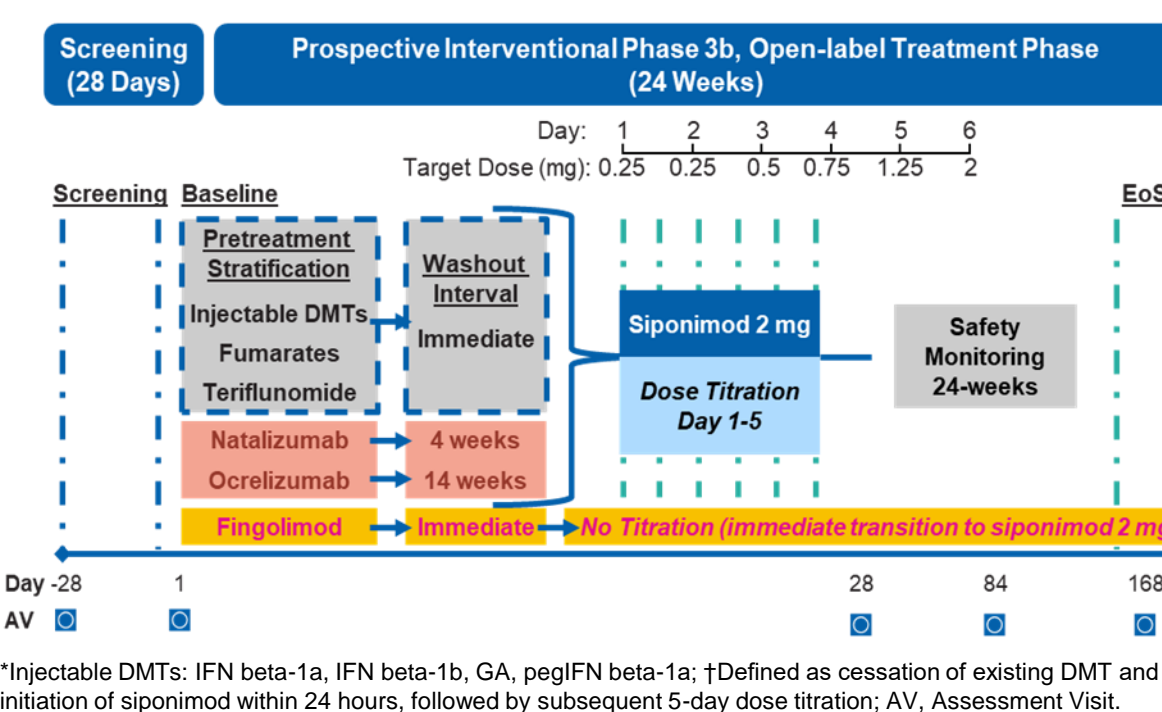
- Incidence of AEs are described in **Table 3**; safety profile was consistent with what has been previously reported<sup>5</sup> and no unexpected safety signals emerged
- The most common AE related to siponimod treatment by preferred term was headache in the overall population (n=13; 8.0%), 11 of whom were Hispanic/Latino

## METHODS

### STUDY DESIGN

- EXCHANGE is a 6-month, prospective, multicenter, open label, single arm trial (**Figure 1**) that has recently completed enrollment; the current analysis is representative of an interim dataset
- The trial included patients aged 18–65 years with advancing RMS, EDSS 2.0–6.5, and on continuous oral/injectable/infusion DMTs for ≥3 months at time of consent; primary endpoint was drug-related AE incidence
- Most patients initiating siponimod were titrated from 0.25 to 2 mg over 6 days
  - Patients transitioning from teriflunomide required 11-14 days' accelerated washout with cholestyramine or activated charcoal
  - Patients transitioning from natalizumab or ocrelizumab required ≥4- or ≥14-week washout period, respectively
  - Those converting from fingolimod immediately switched to siponimod 2 mg, with no dose-titration
- Subgroups were assessed according to patient-reported race/ethnicity

**Figure 1. EXCHANGE Study design**



- AEs that occurred in the Black or African American subgroup included: abscess limb, muscle spasms, MS relapse, peroneal nerve palsy, urinary incontinence – each n=1 (4.3%), 95% CI (0.2, 24.0)
- SAEs that occurred in the Black or African American subgroup included: asthenia, non-cardiac chest pain, cellulitis, hemiparesis, MS relapse, lymphoedema – each n=1 (4.3%)
- There were 4 patients who experienced AEs leading to permanent drug discontinuation in the Hispanic/Latino subgroup; the AEs were fatigue, oedema peripheral, pain in extremity, cognitive disorder, headache, MS relapse, tremor, insomnia – each n=1 (2.8%), except fatigue (n=2, 5.6%)

**Table 3. Incidence of adverse effects**

n (%) 95% CI	Overall (N=163)	Black/African American (N=23)	Hispanic/Latino (N=36)
<b>Summary of AEs, n (%)</b>			
Patients with ≥1 AE	115 (70.6)	18 (78.3)	26 (72.2)
Patients with ≥1 SAE	8 (4.9)	3 (13.0)	0
Patients with ≥1 AE leading to permanent drug discontinuation	11 (6.7)	0	4 (11.1)
<b>≥1 AE possibly related to siponimod treatment</b>	51 (31.3) (24.4, 39.1)	4 (17.4) (5.7, 39.5)	16 (44.4) (28.3, 61.7)
<b>Most common AEs related to siponimod by preferred term</b>			
Headache	13 (8.0) (4.5, 13.5)	0	11 (30.6) (16.9, 48.3)
Dizziness	7 (4.3) (1.9, 9.0)	0	3 (8.3) (2.2, 23.6)
Nausea	6 (3.7) (1.5, 8.2)	0	2 (5.6) (1.0, 20.0)
Bradycardia	5 (3.1) (1.1, 7.4)	0	0
Fatigue	5 (3.1) (1.1, 7.4)	0	1 (2.8) (0.1, 16.2)

Note: A patient with multiple AEs is counted only once in the "at least one AE" row

## CONCLUSIONS

- Representation of diverse patient populations in clinical trials is an important consideration; additional insights are needed on treatment patterns and safety/tolerability in minority patient populations in MS clinical trials
- Differences in baseline comorbidities and rates of AE reporting among patients and providers may provide limitations to interpretation of a differentiated profile
- Siponimod safety/tolerability profile remained consistent, with no new or unexpected safety findings identified through this analysis

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**ABBREVIATIONS:** AE, adverse event; bpm, beats per minute; CI, confidence interval; CIS, clinically isolated syndrome; DMT, disease modifying therapy; EDSS, Expanded Disability Status Scale; EoS, end of study; EoT, end of treatment; GA, glatiramer acetate; HCP, healthcare professional; IFN, interferon; MS, multiple sclerosis; N, number of patients; n, number of observations; PI, principal investigator; PPMS, primary progressive multiple sclerosis; RMS, relapsing multiple sclerosis; RRMS, relapsing-remitting multiple sclerosis; S1P, sphingosine 1-phosphate; SAE, serious adverse event; SD, standard deviation; SPMS, secondary progressive multiple sclerosis.

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