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Treatment Satisfaction With Siponimod in Patients With Advancing Relapsing Multiple Sclerosis: Interim Results of the EXCHANGE Study

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SUMMARY

1 Treatment satisfaction with siponimod is being assessed as a secondary objective in the phase 3b EXCHANGE study, which is evaluating the safety and tolerability of conversion to siponimod from other DMTs in patients with RMS

2 After switching to siponimod, patients reported numerical improvements in treatment satisfaction across the domains of Convenience, Global Satisfaction and Effectiveness; these improvements were generally maintained for the duration of the study

3 These findings may help to inform shared decision-making for treatment in patients with advancing RMS

INTRODUCTION

- Siponimod, an oral sphingosine-1-phosphate receptor type 1,5 ($S1P_{1,5}$) modulator, is approved in adults for the treatment of relapsing-remitting multiple sclerosis (MS) and active secondary progressive MS in the United States[1]
- EXCHANGE (NCT03623243)[2] is a prospective, 6-month, multicentre, open-label, single-arm, phase 3b study evaluating the safety and tolerability of switching to siponimod from previous disease-modifying therapy (DMT) in patients with advancing relapsing MS* (RMS) or a history of RMS†
- This analysis examined treatment satisfaction in patients switching to siponimod, a secondary objective of EXCHANGE
  - Treatment satisfaction is important to consider because it can impact treatment adherence in MS[3,4]

*As defined by principal investigator; †With or without progressive features

OBJECTIVE

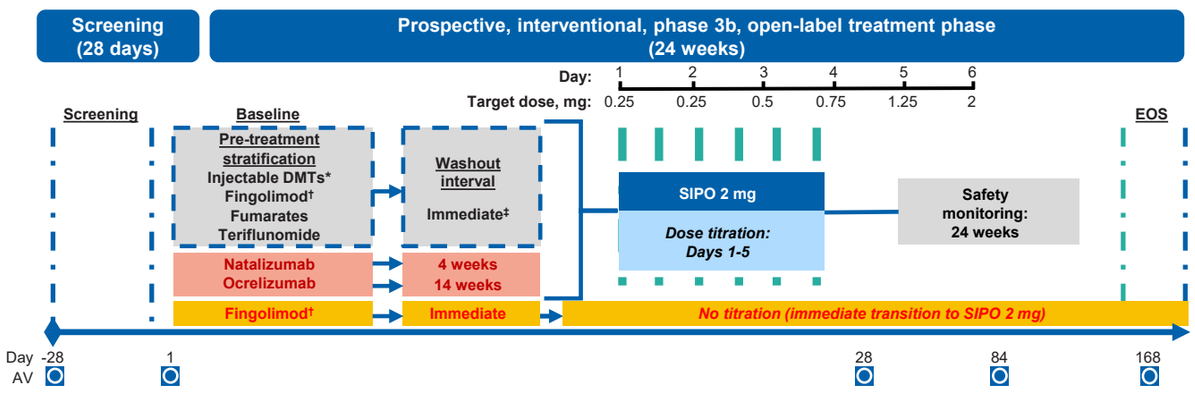
- To evaluate treatment satisfaction in patients with advancing RMS receiving siponimod in the EXCHANGE study

METHODS

PARTICIPANTS

- EXCHANGE enrolled patients aged 18-65 years with advancing forms of RMS, an Expanded Disability Status Scale score of 2.0-6.5 and who had received continuous treatment with oral/injectable/infusion DMTs for ≥3 months at the time of consent

Figure 1. EXCHANGE Study Design



AV, assessment visit; DMT, disease-modifying therapy; EOS, end of study; GA, glatiramer acetate; IFN, interferon; pegIFN, peginterferon; S1P, sphingosine-1-phosphate; SIPO, siponimod
*Injectable DMTs: IFN beta-1a, IFN beta-1b, GA, pegIFN beta-1a; †Patients previously treated with fingolimod were either converted immediately to maintenance dose of siponimod (2 mg) or underwent dose titration to enhance understanding of the role of titration when converting between S1P receptor modulators; ‡Defined as cessation of existing DMT and initiation of SIPO within 24 hours, followed by subsequent 5-day dose titration

STUDY DESIGN

- The EXCHANGE study design is shown in **Figure 1**
- Patients were switched to siponimod from a previous DMT, including fumarates, fingolimod, injectables (interferon [IFN] beta-1a, pegIFN beta-1a, IFN beta-1b or glatiramer acetate), natalizumab, ocrelizumab and teriflunomide
- Washout periods were applied per previous treatment received. For patients not immediately converted to the maintenance dose (2 mg), siponimod was titrated from 0.25 mg to 2 mg over 6 days

TSQM-9

- The Treatment Satisfaction Questionnaire for Medication (TSQM) is a validated tool that evaluates treatment satisfaction from the patient perspective[5]
  - The abbreviated 9-item TSQM (TSQM-9) evaluates the domains of Effectiveness, Convenience and Global Satisfaction[6]
  - Items have 5 (eg, extremely certain, very certain, somewhat certain, a little certain and not at all certain) or 7 response options (eg, extremely satisfied, very satisfied, satisfied, somewhat satisfied, dissatisfied, very dissatisfied and extremely dissatisfied)
  - Possible scores range from 0 to 100, with higher scores indicating greater treatment satisfaction
- The TSQM-9 was assessed at baseline, Day 28, Day 84 and Day 168 in the set of all patients who received ≥1 dose of study treatment
  - Change in TSQM-9 domain score from baseline to each post-baseline time point was evaluated using summary statistics (mean [standard deviation (SD)])
  - Individual TSQM-9 satisfaction categories were also assessed
- The TSQM-9 domain scores were computed using the following algorithms to standardize the score range between 0 and 100[7]:
  - Effectiveness: ([(Item 1 + Item 2 + Item 3) − 3] divided by 18) × 100
  - Convenience: ([(Item 4 + Item 5 + Item 6) − 3] divided by 18) × 100
  - Global Satisfaction: ([(Item 7 + Item 8 + Item 9R) – 3] divided by 12) × 100, where Item 9R = (Item 9 − 1) × (5/6)

RESULTS

PATIENTS

- A total of 163 patients with a mean (SD) age of 46.6 (10.3) years were enrolled in this interim analysis (**Table 1**)

Table 1. Patient Demographics and Baseline Characteristics

Characteristic	Siponimod (N=163)	
Age, years	46.6 (10.3)	
Female, n (%)	121 (74.2)	
Race, n (%)		
White	138 (84.7)	
Black or African American	23 (14.1)	
Asian	2 (1.2)	
Ethnicity, n (%)		
Hispanic or Latino	36 (22.1)	
Not Hispanic or Latino	126 (77.3)	
Not reported	1 (0.6)	
EDSS score	3.9 (1.5)	
Type of MS at study entry, n (%)		
Single demyelinating event	1 (0.6)	
PPMS	4 (2.5)	
SPMS	33 (20.2)	
RRMS	125 (76.7)	
Time since MS diagnosis, years	12.2 (8.7)	
Relapses in 12 months before screening, n (%)		
0	88 (54.0)	
1	57 (35.0)	
2	10 (6.1)	
≥3	8 (4.9)	
Previous MS treatments	**n (%)**	**Duration, month***
Previously treated patients	163 (100)	
Fingolimod	50 (30.7)	48.3 (31.0)
Glatiramer acetate	26 (16.0)	83.4 (68.7)
Dimethyl fumarate	34 (20.9)	34.9 (25.9)
Any IFN beta	19 (11.7)	82.7 (65.6)
Teriflunomide	28 (17.2)	29.6 (26.9)
Natalizumab	1 (0.6)	3.9 (NA)
Ocrelizumab	5 (3.1)	15.2 (12.7)

EDSS, Expanded Disability Status Scale; IFN, interferon; MS, multiple sclerosis; NA, not applicable; PPMS, primary progressive multiple sclerosis; RRMS, relapsing-remitting multiple sclerosis; SD, standard deviation; SPMS, secondary progressive multiple sclerosis
Values are shown as mean (SD) except where indicated
*Duration of previous MS treatments before switching to sipominod (months)

TSQM-9 SCORES

- The TSQM-9 was completed by 133, 111, 101 and 126 patients at baseline, Day 28, Day 84 and Day 168, respectively
- Mean (SD) TSQM-9 scores numerically increased at all visits vs baseline across all domains:
  - Effectiveness: 56.7 (19.9) at baseline, 68.3 (19.8) at Day 28, 64.6 (21.9) at Day 84 and 65.3 (23.9) at Day 168
  - Convenience: 69.9 (21.0) at baseline, 84.2 (15.3) at Day 28, 84.3 (15.0) at Day 84 and 83.7 (15.8) at Day 168
  - Global Satisfaction: 52.7 (23.7) at baseline, 65.6 (21.4) at Day 28, 65.0 (25.1) at Day 84 and 62.4 (30.5) at Day 168

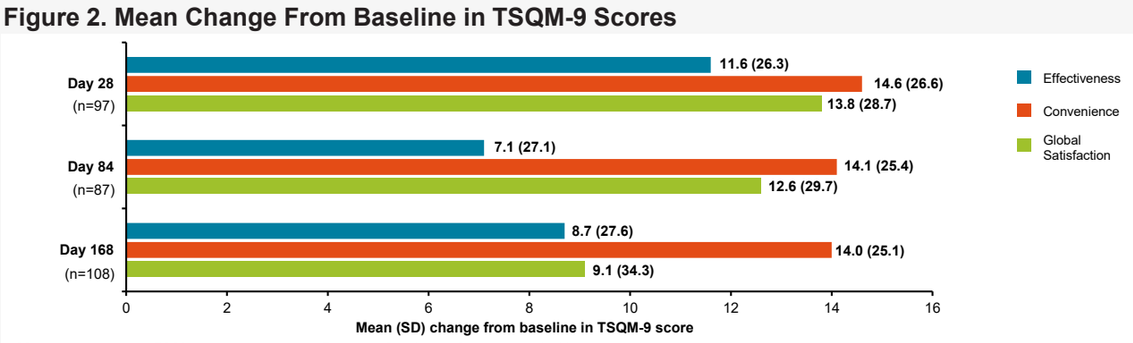
TSQM-9 SCORES: CHANGE FROM BASELINE

- The greatest improvements in mean TSQM-9 scores were observed from baseline to Day 28
- Increases in mean TSQM-9 scores from baseline were maintained from Days 28-168 in all cases (**Figure 2**)

TSQM-9 SCORES: INDIVIDUAL SATISFACTION CATEGORIES

- For all 3 questions (Q) in the Effectiveness domain (Q1-Q3), the proportion of patients reporting that they were very or extremely satisfied increased from baseline to Day 168 (16.5% and 42.9% for Q1, 13.5% and 33.3% for Q2 and 18.0% and 34.1% for Q3, respectively; **Figure 3**)
  - For Q1-Q3, the proportion of patients reporting that they were very or extremely dissatisfied was generally consistent at baseline (4.5-6.0%) and Day 168 (6.3-8.7%)
- For the Convenience domain questions (Q4-Q6), the proportion of patients reporting that their siponimod regimen was very or extremely easy to use (Q4, Q5) and very or extremely convenient (Q6) increased from baseline to Day 168 (41.4% and 72.2% for Q4, 37.6% and 71.4% for Q5 and 41.4% and 68.3% for Q6, respectively; **Figure 3**)
  - For Q4-Q6, ≤3% of patients reported that they found siponimod to be very or extremely difficult to use or very or extremely inconvenient at baseline and Day 168
- For the Global Satisfaction domain questions (Q7-Q9), the proportion of patients that reported they were very or extremely confident, very or extremely certain and overall very or extremely satisfied increased from baseline to Day 168 (33.8% and 59.5% for Q7, 33.8% and 58.7% for Q8 and 20.3% and 47.6% for Q9, respectively; **Figure 3**)
  - For Q7 and Q8, the proportion of patients reporting they were not at all confident or not at all certain increased by <7% from baseline to Day 168
  - For Q9, the proportion of patients reporting they were very or extremely dissatisfied was consistent at baseline (5.3%) and Day 168 (4.0%)

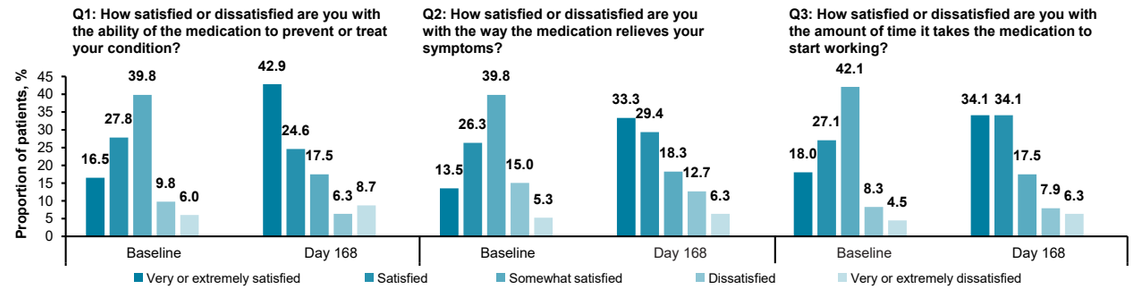
Figure 2. Mean Change From Baseline in TSQM-9 Scores



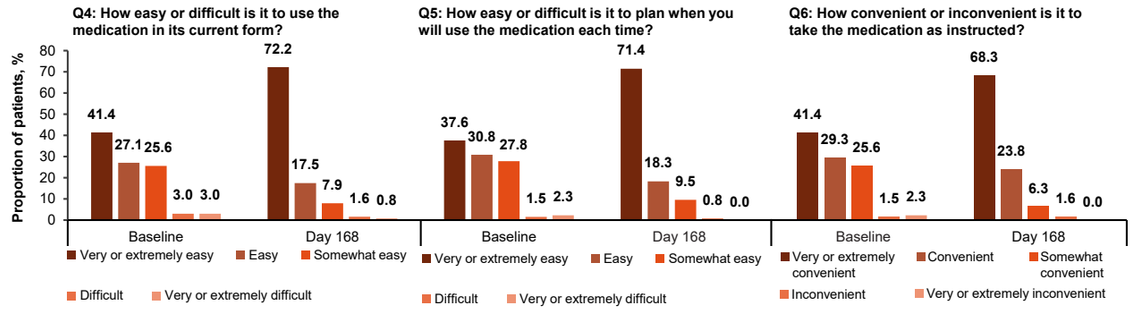
SD, standard deviation; TSQM-9, abbreviated 9-item Treatment Satisfaction Questionnaire for Medication
All analyses were based on observed data. No imputation was performed for missing data. Error bars not included due to high SD values. Patients must have had completed the TSQM-9 at baseline and at the study time point to be included

Figure 3. TSQM-9 Individual Satisfaction Categories at Baseline (n=133) and Day 168 (n=126)*

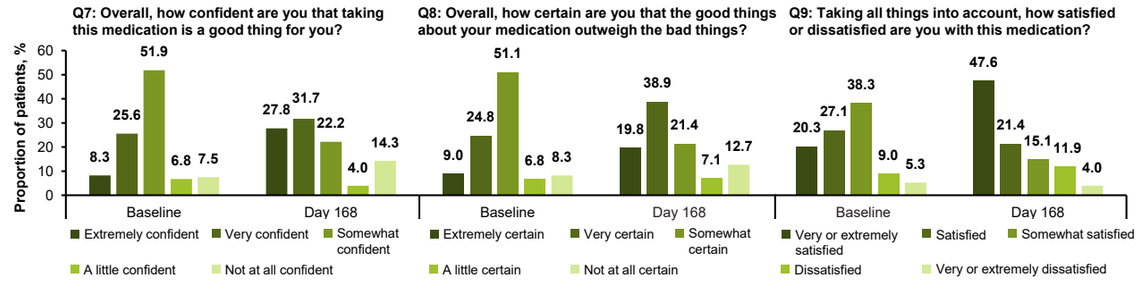
EFFECTIVENESS



CONVENIENCE



GLOBAL SATISFACTION



Q, Question; TSQM-9, abbreviated 9-item Treatment Satisfaction Questionnaire for Medication
All analyses were based on observed data. No imputation was performed for missing data. For some categories, individual "very" and "extremely" items have been combined
*25 patients had a TSQM-9 score at baseline but were missing a Day 168 score; 18 patients had a TSQM-9 score at Day 168 but were missing a baseline score

ABBREVIATIONS: AV, assessment visit; **DMT**, disease-modifying therapy; **EDSS**, Expanded Disability Status Scale; **EOS**, end of study; **GA**, glatiramer acetate; **IFN**, interferon; **MS**, multiple sclerosis; **NA**, not applicable; **pegIFN**, peginterferon; **PPMS**, primary progressive multiple sclerosis; **Q**, Question; **RMS**, relapsing multiple sclerosis; **RRMS**, relapsing-remitting multiple sclerosis; S1P, sphingosine-1-phosphate; **$S1P_{1,5}$**, sphingosine-1-phosphate receptor type 1,5; **SD**, standard deviation; **SIPO**, siponimod; **SPMS**, secondary progressive multiple sclerosis; **TSQM-9**, abbreviated 9-item Treatment Satisfaction Questionnaire for Medication.

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