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Siponimod Stabilizes Physical Disability Scores in People Living With Secondary Progressive Multiple Sclerosis After 2 Years of Treatment: Analysis From the Novartis Global Managed Access Program

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SUMMARY

1 **Data from the ongoing, global Novartis Managed Access Program for siponimod were analyzed to describe demographics and clinical characteristics, and explore the EDSS score changes in a heterogeneous cohort of 632 patients living with SPMS receiving siponimod in a real-world clinical setting**

2 **The majority of patients for whom data were collected (or available), including patients with nonactive SPMS, had a stable EDSS score over 2 years and a very low annualized relapse rate of 0.023**

3 **While these analyses are limited due to the observational nature of the program and the lack of data on all patients, the findings support sustained effectiveness of siponimod in a broad SPMS population**

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INTRODUCTION

- Secondary progressive multiple sclerosis (SPMS) has very limited treatment options compared with relapsing-remitting multiple sclerosis (RRMS), with many disease-modifying treatments that are effective in RRMS proving ineffective in SPMS[1]
- In the phase 3 EXPAND trial, siponimod demonstrated significant reductions in the risk of confirmed disability progression (CDP) and confirmed worsening of cognitive processing speed vs placebo in people living with SPMS (PlwSPMS)[2]
- The EXPAND trial recruited a broad SPMS population, including both active (patients with relapses or magnetic resonance imaging [MRI] disease activity) and nonactive SPMS[2]; however, most regions (including the European Union) approved siponimod for the treatment of SPMS with active disease[3]
- Following the approval of siponimod, evidence from observational and real-world studies suggests that it may stabilize disease progression in PlwSPMS[4,5]; however, it is important to examine if these real-world effectiveness trends are borne out in different cohorts of PlwSPMS taking siponimod in routine clinical practice
- The ongoing global Novartis Managed Access Program (MAP) for siponimod was implemented to facilitate patient access to siponimod (under physician request) according to the local laws and regulations where marketing authorization is pending and satisfactory alternative therapies are absent
- Although not the primary purpose of compassionate use programs, physicians can report back adverse events and effectiveness outcomes, which helps ascertain whether patients are benefiting from the treatment

OBJECTIVE

- To describe demographics and clinical characteristics and explore Expanded Disability Status Scale (EDSS) score changes in PlwSPMS receiving siponimod as part of the global Novartis MAP for siponimod cohort (BAF2001M cohort)

METHODS

- The MAP started in March 2019 and is ongoing in countries where it is permitted and where siponimod is not already available
- From March 2019 to January 2021, PlwSPMS eligible to enter the MAP included adult patients with a diagnosis of SPMS (active and nonactive) and an EDSS score <7
  - From January 2021 onward, access to the MAP requires a diagnosis of SPMS with active disease (relapse or MRI in the previous 24 months) and an EDSS score <7, in line with the approved EU/US label
- Treatment selection and patient monitoring are based on the physician's assessment
  - Because this is not a clinical study and data gathering is not the core purpose, only minimal information about the patient and the disease is collected and regular visits or data entry/collection are not mandatory
- The global MAP for siponimod cohort data were analyzed using the internal Novartis database (GEMS), in which physicians provided information as the data source
- Data collected at baseline, as reported by physicians, include age, sex, country, relapses, MRI activity in the last 24 months (yes/no), and EDSS score
- Postbaseline data presented here, as reported by physicians, include duration of exposure to siponimod treatment under the compassionate use program, reasons for closure of a resupply request, EDSS score, and 6-month CDP

STATISTICAL METHODS

- Change from baseline in EDSS score was assessed using a mixed model for repeated measures adjusted for baseline EDSS score, with time as a categorical factor
- Kaplan-Meier estimates were derived to provide estimates of 6-month CDP based on EDSS score by time

RESULTS

PATIENT DEMOGRAPHICS AND BASELINE CHARACTERISTICS

- The MAP tool comprised 632 patients; 60% were female and mean (standard deviation [SD]) age was 52.4 (8.7) years (**Table 1**)
- The median (interquartile range) EDSS score at baseline was 5.5 (4.5-6.5), and around 51% of patients had a relapse in the last 2 years
- Of the 632 patients in the MAP cohort, MRI information at baseline was available for 324 patients, and of these, 154 (48%) showed activity as measured by new or active lesions on the MRI scan

Table 1. Baseline Demographics and Patient Characteristics

Variable	Total (N=632)
Age, years, mean (SD)	52.4 (8.74)
Range	24-76
Sex, n/N (%)	
Male	250/624 (40.1)
Female	374/624 (59.9)
EDSS score, mean (SD)	5.2 (1.27)
Median (Q1-Q3)	5.5 (4.5-6.5)
EDSS score category, n/N (%)	
<6.0	314/613 (51.2)
≥6.0	299/613 (48.8)
Relapse in last 24 months, n/N (%)	
No	192/390 (49.2)
Yes	198/390 (50.8)
MRI performed in last 24 months, n/N (%)	327 (51.7)
New or active lesions on MRI reported	
No	170/324 (52.5)
Yes	154/324 (47.5)
Country, n (%)	
Italy	399 (63.1)
Greece	135 (21.4)
Switzerland	37 (5.9)
Other	61 (9.7)
MS disease status, n (%)	
Active	279 (44.1)
Nonactive	87 (13.8)
Unknown	266 (42.1)

EDSS, Expanded Disability Status Scale; MRI, magnetic resonance imaging; MS, multiple sclerosis; n, number of patients with characteristic; N, number of patients with available information; Q, quartile; SD, standard deviation

DATA AVAILABILITY

- Up to January 2021, 423 of 632 (66.9%) patients in the MAP made ≥1 request for resupply of siponimod
- The mean (SD) follow-up time was 569 (212) days and the median (quartile [Q]1-Q3) time between requests for resupply was 132.4 (58.9-198.3) days

POSTBASELINE DATA ASSESSMENT

Patient Duration in the MAP

- Resupply was stopped for 399 of 632 (63.1%) patients, with the primary reason for discontinuation being transition to commercial supply (220; 34.8%), followed by patient withdrawal (69; 10.9%) (**Figure 1**)
  - The median (Q1-Q3) duration of treatment with siponimod within the MAP was 231 (220-721) days

Figure 1. Reasons for Closure of Treatment Program Access

MAP, Managed Access Program
*The percentage for the "Transition to a commercial supply" might be higher than calculated because a few countries encoded information under "Other" or the rationale was missing

CHANGE IN EDSS SCORE

- In patients where data were available, the mean EDSS score remained stable up to Month 24
  - The mean change in EDSS score in the overall cohort was nonsignificantly different from baseline and was -0.03 (95% confidence interval [CI]: -0.09, 0.03) at Month 6 and -0.02 (95% CI: -0.09, 0.05) at Month 24
  - In line with the overall cohort, changes in the mean EDSS score from baseline in the active and nonactive subgroups were within 0.02 of a point
- As shown in **Figure 2**, where data were available, most patients maintained a stable EDSS score over time, regardless of disease status
  - In the overall cohort, 91% of patients were either stable or improved at the end of 24 months (n=149)
  - Although EDSS data were available for a limited number of patients, notably, those with active disease appeared to have more variability in their EDSS score, whereas those with nonactive disease were more like to remain stable (**Figure 2**)

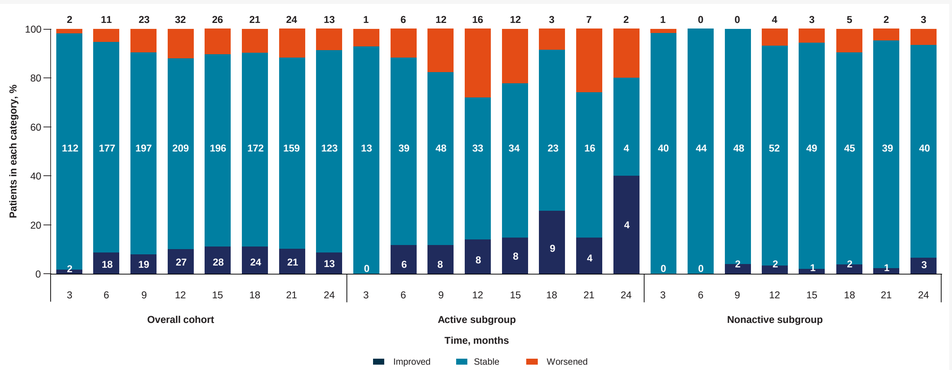
Time to 6-Month CDP in the MAP Cohort

- **Figure 3** shows that the rate of progression, as measured by time to 6-month CDP, was very low, regardless of disease status at baseline

Annualized Relapse Rate (ARR)

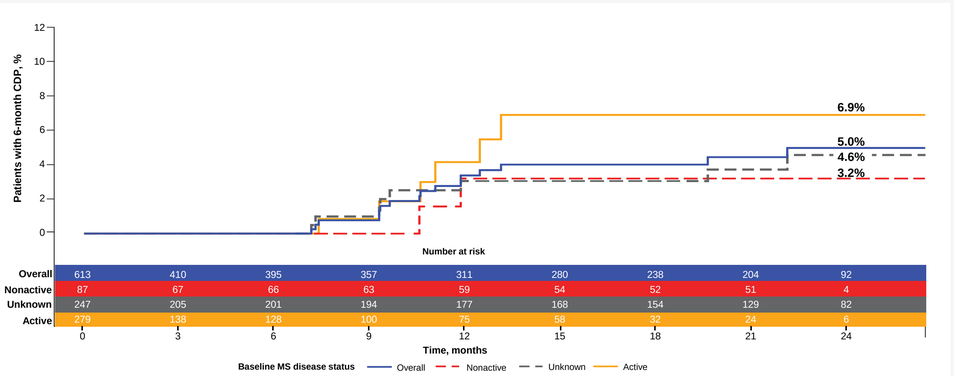
- In patients for whom data were available, the ARR (number of relapses/total number of follow-up years) was 0.023 (15/659) for the overall cohort, 0.031 (5/161) for the active subgroup, 0.009 (1/116) for the nonactive subgroup, and 0.024 (9/381) for the unknown subgroup

Figure 2. Change in EDSS Status From Baseline Over Time



EDSS, Expanded Disability Status Scale
Numbers of patients with data available for each category are given within the bars. Definitions: Improved: decrease in EDSS score compared with baseline; Stable: no change in EDSS score compared with baseline; Worsened: increase in EDSS score compared with baseline

Figure 3. Kaplan-Meier Analysis of Time to 6-Month CDP* by MS Disease Status at Baseline



6m-CDP, 6-month confirmed disability progression; EDSS, Expanded Disability Status Scale; MS, multiple sclerosis
*6-month CDP as assessed in patients with ≥2 postbaseline EDSS assessments separated by >66 days

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DISCLOSURES: Gina Mavrikis Cox, **Virginia de las Heras**, **Roxana Oana Istrate**, **Soudeh Ansari**, and **Sophie Arnould** are employees of Novartis. **Suzannah Ryan** and **Daniela Piani-Meier** were employees of Novartis at the time of study conduct/abstract submission