Siponimod Stabilises Physical Disability Scores in People Living With SPMS After 2 Years of Treatment: Analysis From the Novartis Global Managed Access Program

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Virginia de las Heras[1], Suzannah Ryan[1], Roxana Oana Istrate[1], Soudeh Ansari[1], Sophie Arnould[1], Daniela Piani-Meier[1]

[1]Novartis Pharma AG, Basel, Switzerland

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 versus 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 non-active SPMS[2]; however, most regions (including the European Union [EU]) 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 stabilise 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 siponimod Managed Access Program (MAP) was implemented to facilitate patient access to siponimod (under physician request) according to the local laws and regulations where marketing authorisation is pending and satisfactory alternative therapies are absent
- Though not the primary purpose of compassionate use programs, physicians could report back adverse events and effectiveness outcomes, which help ascertain whether patients are benefiting from the treatment

Objective

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

Methods

- The MAP started in March 2019 and is on-going 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 non-active) and an EDSS score of <7
  - From January 2021 onwards, access to the MAP required a diagnosis of SPMS with active disease (relapse or MRI in the prior 24 months) and an EDSS score of <7, in line with the approved EU/US label
- Treatment selection and patient monitoring were based on the physician's assessment
  - As this was 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 were not mandatory
- The global siponimod MAP cohort data were analysed using the internal Novartis database (GEMS) in which physician provided information and that was the data source
- Data collected at baseline, as reported by physicians include age, sex, country, relapses and MRI activity in the last 24 months (yes/no), and EDSS score
- Post-baseline data presented here, as reported by physicians, includes duration of exposure to siponimod treatment under the compassionate use program, reasons for closure of a re-supply 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 and with time as categorical factor
- Kaplan-Meier estimates were derived to provide estimates of 6-month CDP based on EDSS by time

Results

Patient demographics, baseline characteristics

- The MAP tool comprised of 632 patients; 60% were female and mean age was 52.4 (standard deviation [SD]: 8.7) years
- The median EDSS score at baseline was 5.5 (interquartile range [IQR]: 4.5–6.5), and around 51% of patients had a relapse in the last 2 years
- Of the 632 in the MAP cohort, MRI information at baseline was available for 324 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, mean (SD)	5.2 (1.27)
Median (Q1–Q3)	5.5 (4.5–6.5)
EDSS 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, n/N (%)	
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)
Non-active	87 (13.8)
Unknown	266 (42.1)

n=number with characteristic/N=number with available information.
EDSS, Expanded Disability Status Scale; MRI, magnetic resonance imaging; Q, quartile; SD, standard deviation

Data availability

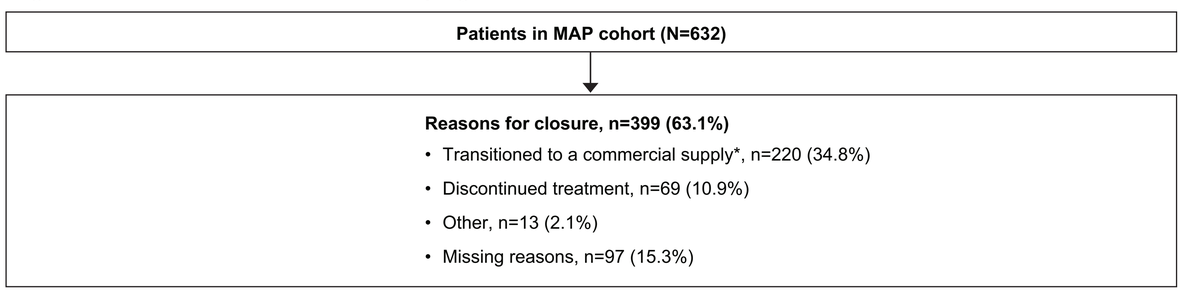
- Up to January 2021, 423 of 632 (66.9%) patients in the MAP made at least one request for re-supply of siponimod
- The mean (SD) follow-up time was 569 (212) days and the median (Q1–Q3) time between requests for re-supply was 132.4 (58.9–198.3) days

Post-baseline data assessment

Patient duration in the MAP

- Re-supply 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

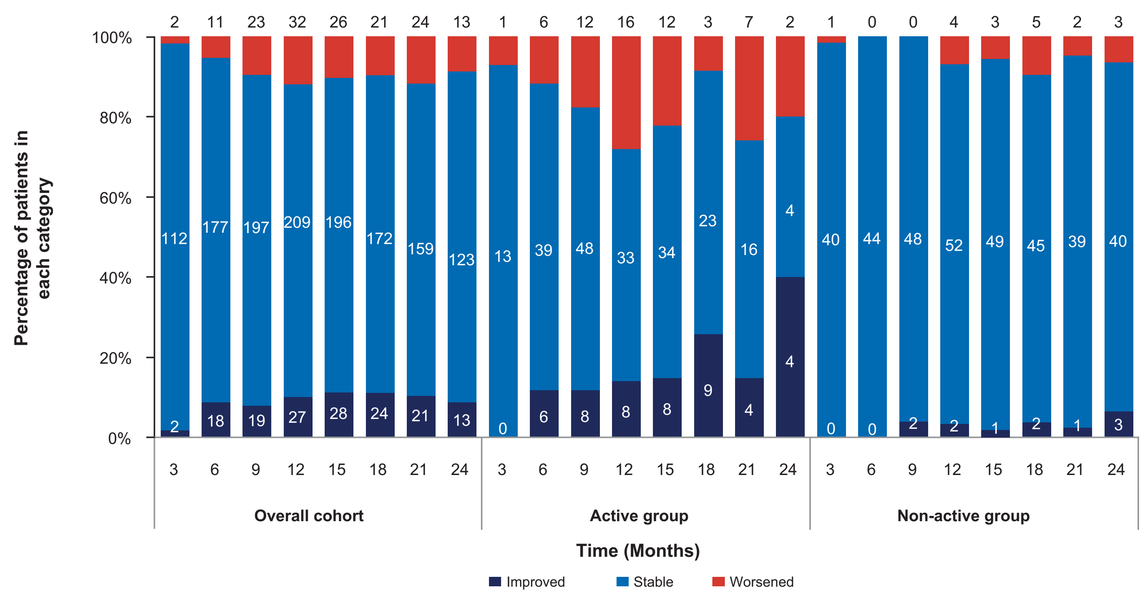


*The percentage for the 'Transition to a commercial supply' might be higher than calculated as a few countries encoded information under 'Other' or the rationale was missing.
MAP, Managed Access Program.

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 in the overall cohort was non-significantly 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 non-active subgroups were within 0.02 of a point
- As shown in **Figure 2**, where data were available, most patients maintained a stable EDSS over time regardless of disease status
  - In the overall cohort, 91% were either stable or improved at the end of 24 months (n=149)
  - Although EDSS data was available for a limited number of patients, notably those with active disease appeared to have more variability in their EDSS score, whereas those with non-active disease were more like to remain stable (**Figure 2**)

Figure 2. Change in EDSS status from baseline over time

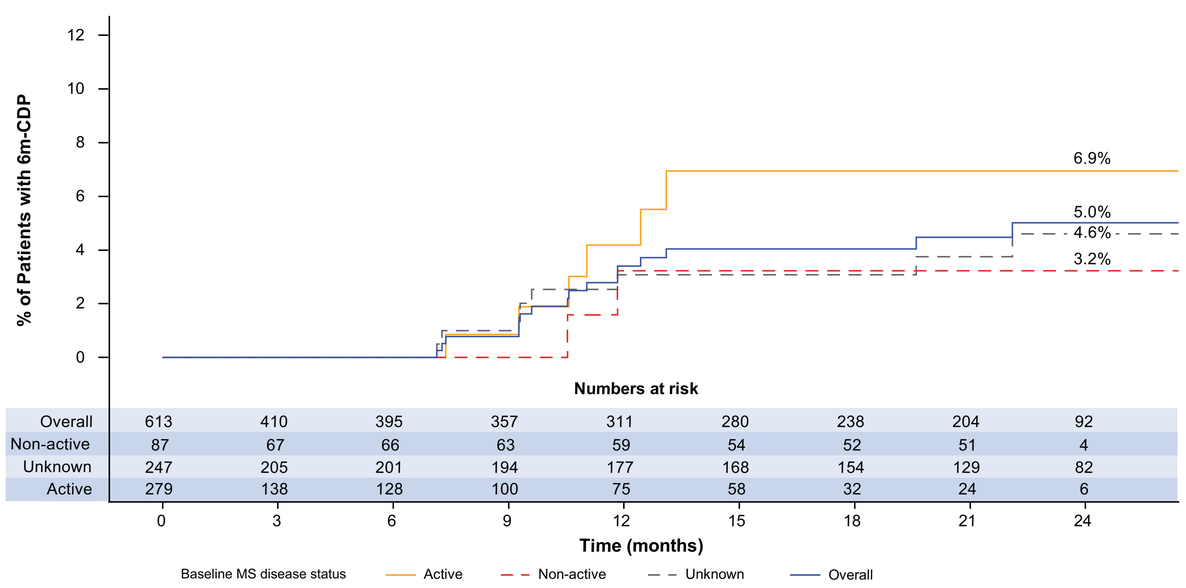


Definitions: Improved: decrease in EDSS compared to baseline; Stable: no change in EDSS compared to baseline; Worsened: increase in EDSS compared to baseline
Numbers of patients with data available for each category are given within the bars.
EDSS, Expanded Disability Status Scale; MS, multiple sclerosis.

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

Figure 3. Kaplan-Meier analysis of time to 6-month CDP* by MS disease status at baseline



6-month CDP as assessed in patients with at least two post-baseline EDSS assessment separated by >66 days.
6m-CDP, 6-month confirmed disability progression; MS, multiple sclerosis.

Annualised 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 for the active group (5/161), 0.009 for non-active (1/116) and 0.024 for the unknown group (9/381)

Conclusions

- The MAP comprised a heterogeneous cohort of 632 plwSPMS receiving siponimod in a real-world clinical setting and the majority of patients for whom data was collected (or available), including patients with non-active SPMS, had a stable EDSS score over 2 years
- A very-low ARR of 0.023 was observed in this real-world cohort of plwSPMS
- Some of the limitations in such settings included heterogeneity between countries in terms of clinical practice (e.g. frequency of re-supply request and EDSS assessments) and participants recruited
- 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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Disclosures

Virginia de las Heras, Suzannah Ryan, Roxana Oana Istrate, Soudeh Ansari, and **Sophie Arnould** are employees of Novartis. **Daniela Piani-Meier** was an employee of Novartis at the time of study conduct/abstract submission

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Presenter email address: virginia.delasheras@novartis.com

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