AMASIA Study - Real World Insights on Siponimod Treated Patients with Secondary Progressive Multiple Sclerosis in Germany

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Conflict of interest

Disclosures

- **Olaf Hoffmann** served on scientific advisory boards, as consultant and received speaker honoraria from Bayer Healthcare, Biogen, Celgene, Janssen, Merck, Novartis, Roche, Sandoz, Sanofi, Teva; received financial support for research activities from Biogen, Novartis, and Sanofi.
- **Herbert Schreiber** received research grants and honoraria from Almirall, Bayer Healthcare, Biogen, Merck, Novartis, Roche, and Teva.
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- **Benedict Rauser** and **Caroline Baufeld** are employees of Novartis Pharma GmbH, Germany.
- **Tjalf Ziemssen** received speaking honoraria and financial support for research activities from Almirall, Biogen, Celgene, Novartis, Roche, Teva, and Sanofi.

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Introduction & Methods

Background

- 85% of Multiple Sclerosis (MS) patients are initially diagnosed with relapsing-remitting MS (RRMS).[1]
- 60% will convert to secondary progressive MS (SPMS) within 20 years due to evolvement of the disease over time.[2,3]
- Progressive motor dysfunction and cognitive decline are typical hallmarks of SPMS.[4-7]
- The EMA has approved Siponimod (Mayzent®), a selective sphingosine-1-phosphate receptor modulator, specifically for the treatment of active SPMS as evidenced by relapses or imaging features of inflammatory activity.
- Randomized controlled trials (RCTs) impose rigid inclusion criteria and assessment schedules for outcome parameters, whereas the general patient population seen in clinical routine is more variable. Thus, data from real world settings are mandatory to complement data obtained from RCTs.
- First real-world evidence on the long-term effectiveness and safety of Siponimod as well as the impact on quality of life and socioeconomic conditions is analyzed in the prospective non-interventional study AMASIA (Imp**A**ct of **M**ayzent® (Siponimod) on second**A**ry progressive multiple **S**clerosis patients in a long-term non-**I**nterventional study in Germ**A**ny).

Objective

- The non-interventional AMASIA study will provide real-world evidence on the long-term effectiveness and safety of siponimod as well as its impact on quality of life.

Study design

- Non-interventional (**Figure 1**)
- 1,500 Siponimod-treated SPMS patients
- 3 years in 250 centers across Germany
- Study visits every 6 months

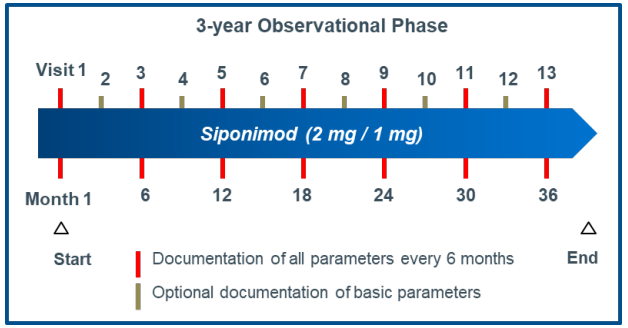

Figure 1: Study design.

Assessment

- Clinic: Laboratory, ophthalmic, and physical evaluation
- MS-activity: Magnetic Resonance Imaging (MRI), MS Activity Scale Score (MS-AS), Expanded Disability Status Scale (EDSS)
- Functional domains: Symbol Digit Modalities Test (SDMT), EDSS
- Patient's perspective: United Kingdom Neurological Disability Scale (UKNDS), Fatigue Scale For Motor And Cognitive Functions (FSMC), EuroQol-5D
- Physician's perspective: Clinical Global Impression CGI, progression questionnaire
- Socioeconomic factors: Multiple Sclerosis Health Resource Survey (MS-HRS)

1. Rio J, et el.; Curr Opin Neurol. 2011; 24(3), 230-237; 2. Tremlett H, et al. Mult Scler. 2008;14:314–24; 3. Scalfari A, et al. J Neurol Neurosurg Psychiatry. 2014;85:67–75; 4. Lublin FD, et al. Neurology. 2014;83(3):278-286; 5. Lublin FD, et al. Neurology. 996;46(4):907-911; 6. Lorscheider J, et al. Brain. 2016;139(Pt 9):2395-2405; 7. Brochet B, et al. Front Neurol. 2019;10:261.

Results – Baseline characteristics, treatment prior to study & disease history

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Variable	AMASIA	EXPAND active SPMS subgroup*
Number of patients, n	553	779
Age (years) (± SD)	54.5 (8.4)	47
Time since first MS diagnosis (years) (± SD)	17.2 (9.4)	13
EDSS (± SD)	5.2 (1.5)	6
SDMT (± SD)	39.2 (13.2)	38.3
Patients with relapse during past 24 months (%)	49.9	36
*Represents population of the EMA label		

Table 1: Baseline characteristics.

→ As of March 21st, 2022, 553 patients were enrolled in AMASIA and included in this interim analysis.

- Baseline data of AMASIA patients are depicted in **Table 1** and compared to the active SPMS subgroup population of the pivotal EXPAND RCT.
- The real-life population of AMASIA patients seem older with longer disease history when compared to the active subgroup of the pivotal trial EXPAND.
- Prior to Siponimod, more than half of the patients received baseline therapy or were untreated (**Figure 2**).

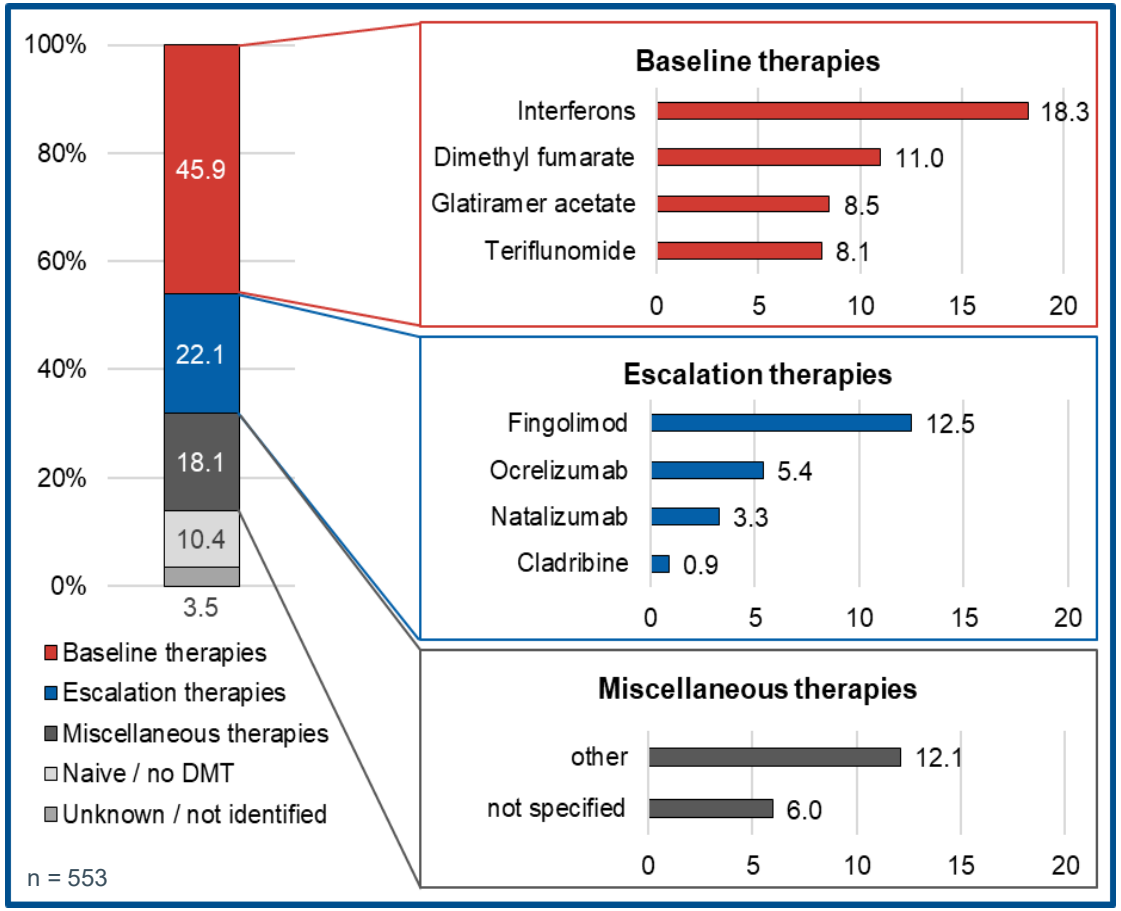

Figure 2: Last treatment before Siponimod (AMASIA).

Results – Treatment at start of study & disease history

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- Most patients began siponimod treatment within six months after having discontinued baseline or escalation therapies (**Figure 3**).

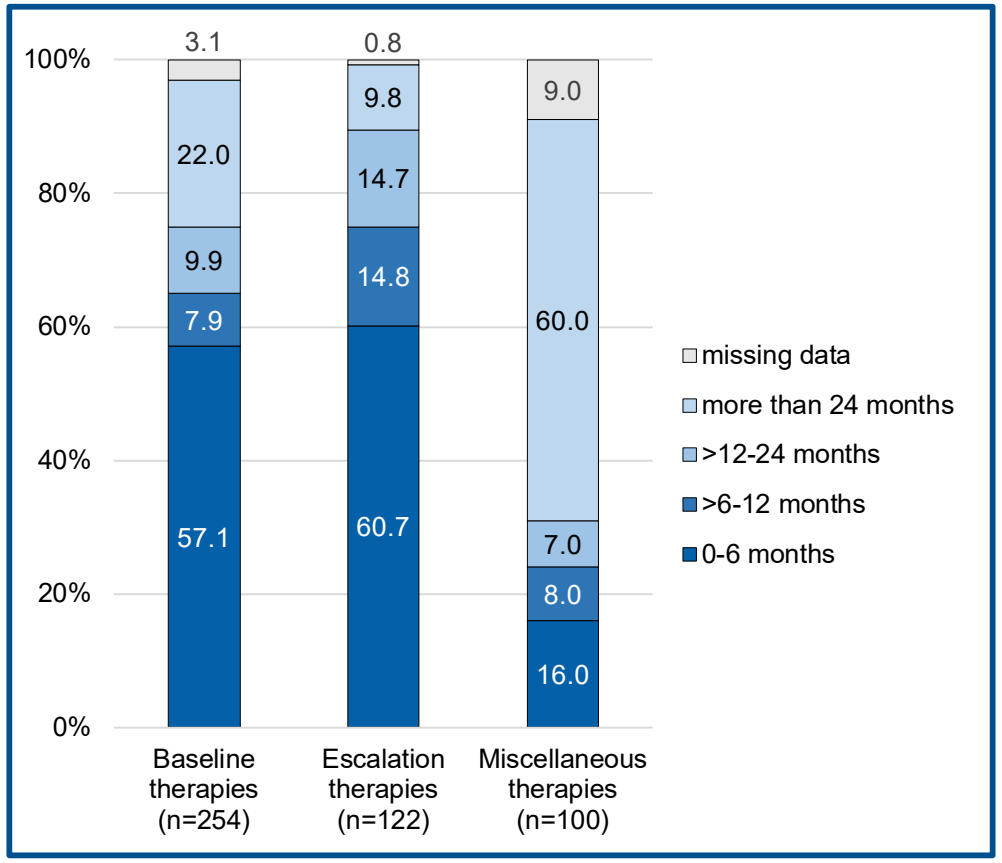

Figure 3: Time intervals between end of pretreatment and start of study.

- 80% of the patients are suffering from at least one concomitant disease, the most common diseases not related to MS are shown in Figure 4.

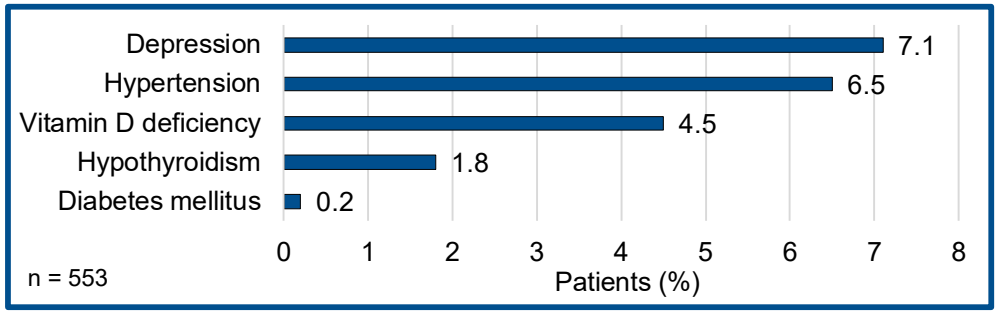

Figure 4: Most common concomitant diseases not related to MS.

- **Figure 5** illustrates which functional systems were affected in SPMS patients at baseline.

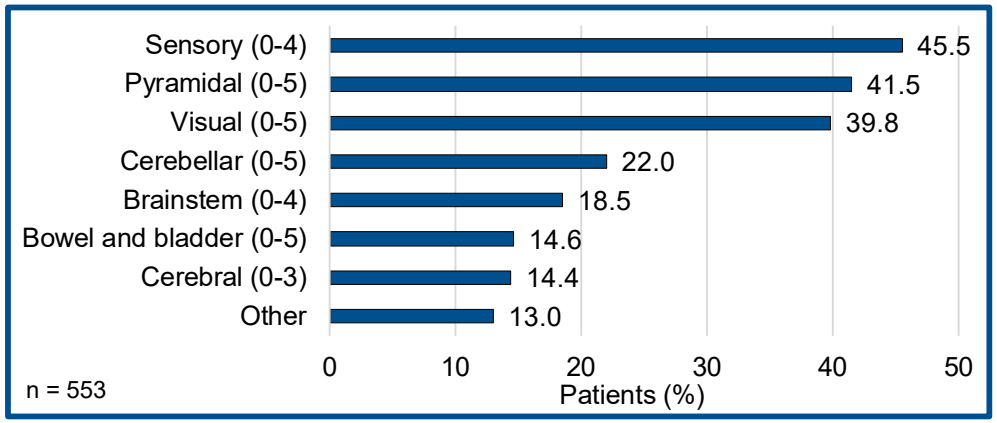

Figure 5: MS symptoms (in parentheses: scale used for different functional systems; 0=normal to x=strongly affected).

Results – SPMS genotype & medication at start of study, disability & cognition during study

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- The most frequent genotype in AMASIA is CYP2C9*1*1. The distribution of genotypes represents what is known from the literature[8] (**Figure 6**).

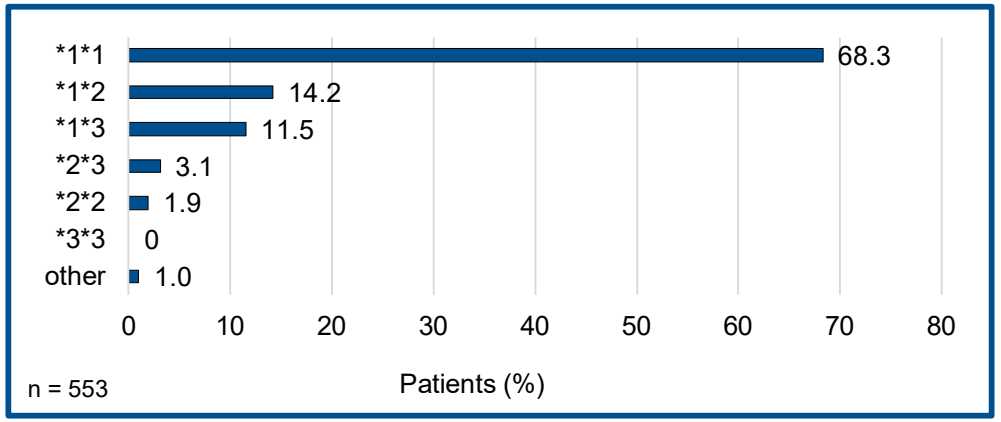

Figure 6: Distribution of CYP2C9 genotypes.

- Most patients (86.1%) receive 2 mg siponimod maintenance dose at study start (**Figure 7**).

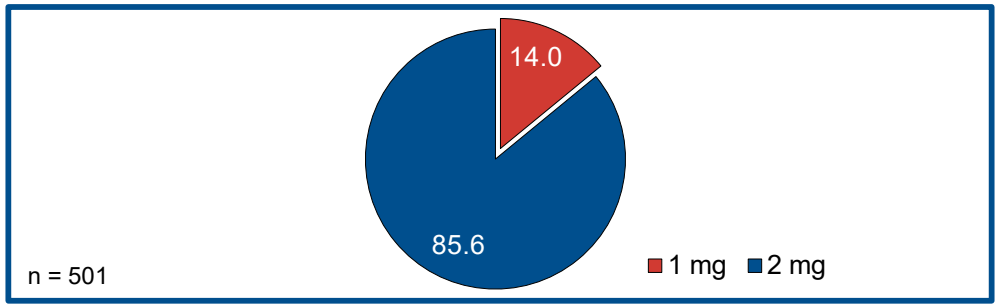

Figure 7: Siponimod maintenance dose at study start.

8. PharmGKB. CYP2C9 Diplotypentabelle. https://pharmgkb.org/page(cyp2c9RefMaterials. Retrieved December 2019.

- EDSS and SDMT remained stable during the first twelve months on siponimod (**Figure 8 and 9**).

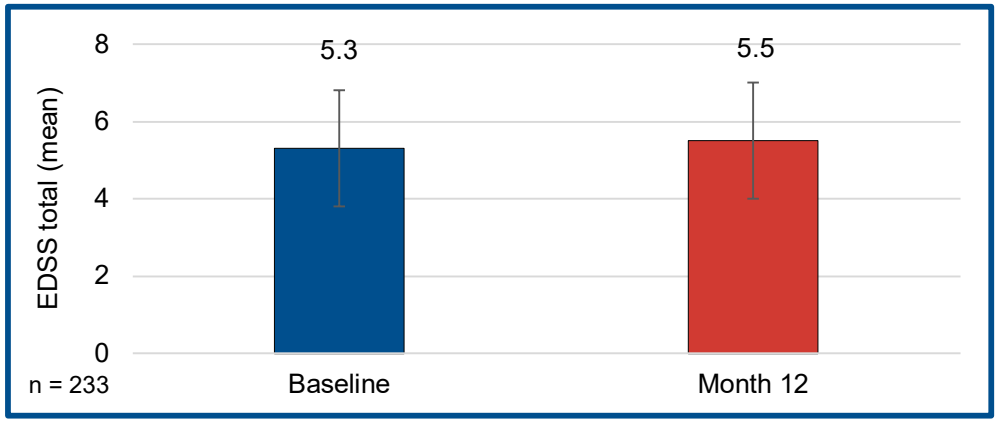

Figure 8: EDSS score.

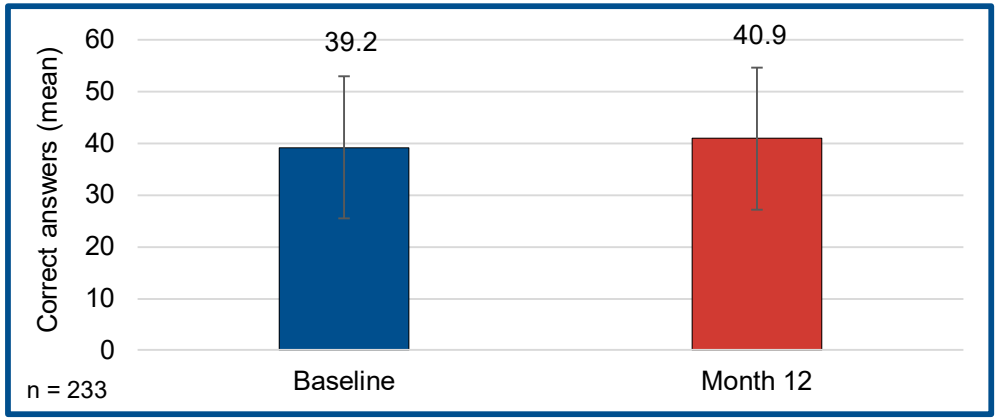

Figure 9: SDMT correct answers.

Results – Patient-reported outcomes, fatigue & motor function

- Satisfaction with treatment persisted after twelve months of treatment with siponimod (**Figure 10**) and EQ-5D remained overall stable (**Figure 11**).

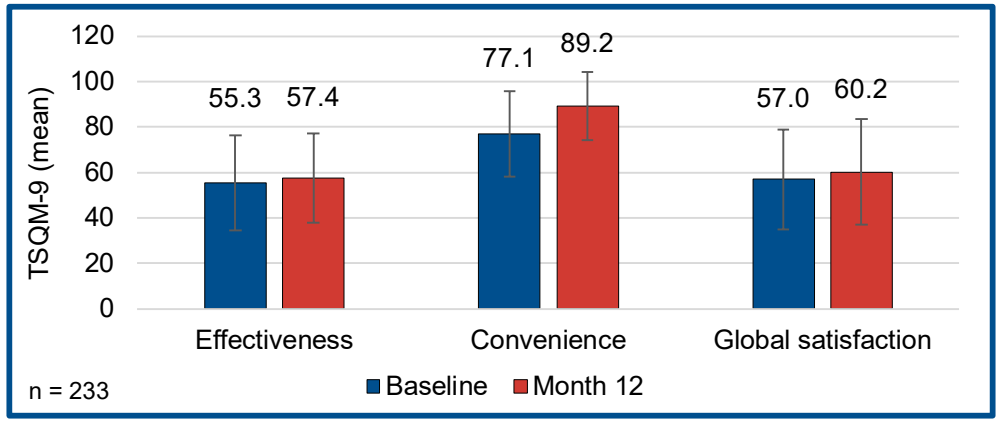

Figure 10: Treatment Satisfaction Questionnaire for Medication (TSQM-9; Follow-Up set).

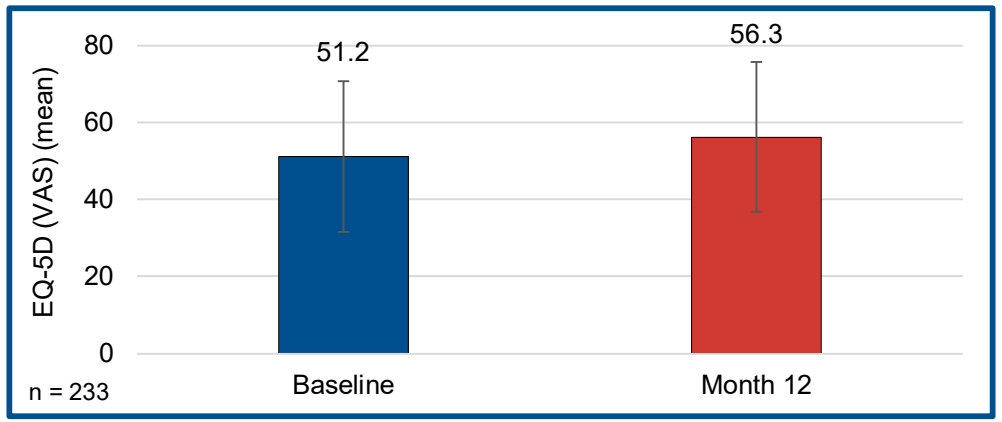

Figure 11: Visual analogous scale of EQ-5D.

- FSMC total score and results from nine-hole-peg test and 25-foot-walk test, respectively, remained stable across the first 12 months of treatment (**Figure 12 and 13**).

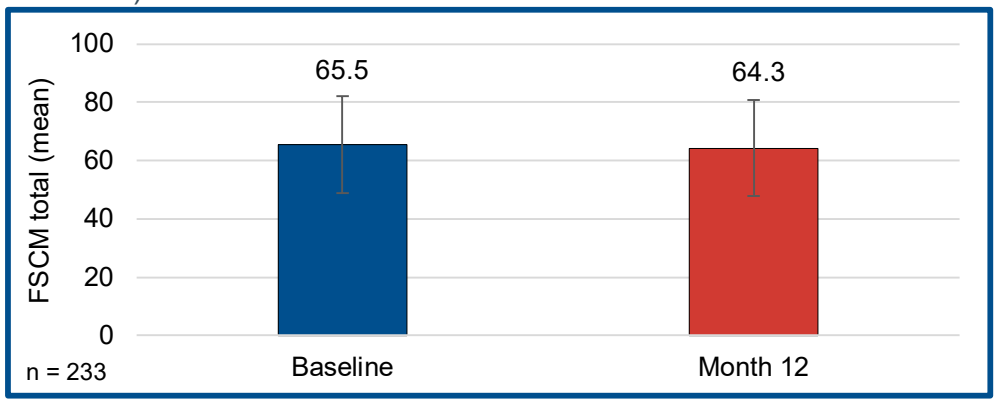

Figure 12: FSMC total score.

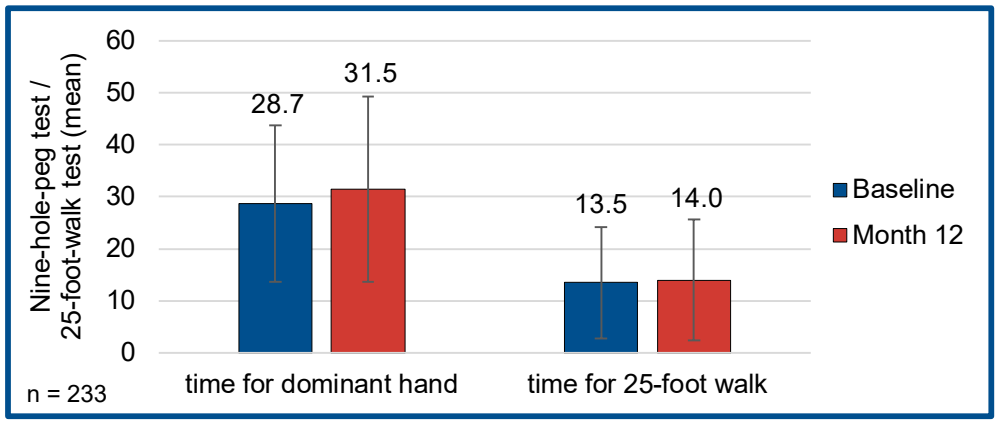

Figure 13: Results from nine-hole peg test and 25-foot walk test.

Conclusions

- Compared to the active SPMS subgroup in EXPAND, the real-world population of AMASIA seem to be older and exhibit a longer overall MS disease duration.
- EXPAND subgroup analyses demonstrate that younger patients with a recent diagnosis of SPMS particularly benefit from siponimod.
- Prior to Siponimod, more than half of the patients received baseline therapy or were untreated.
- Cognition and overall health status as reflected by EDSS, SDMT, FSMC, and EQ-5D remained stable during 12 months of siponimod therapy.
- Treatment satisfaction regarding “Global Satisfaction”, “Convenience”, and “Effectiveness” persisted and even improved after 12 months of siponimod therapy.

- **The present results provide insight into the siponimod patient profile in routine clinical practice.**
- **AMASIA enables a comparison of clinical trial data to the actual treatment context.**