Poster P376

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Longitudinal Observation of SPMS Patients Treated with Siponimod in Germany – Three Years Interims Data from Real World Study AMASIA

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KEY FINDINGS & CONCLUSIONS

1. The non-interventional AMASIA study provides real-world evidence on the use of siponimod in the treatment of active SPMS patients in Germany.
2. In this 3-year interim analysis, active SPMS patients treated with siponimod showed stabilized disease and overall health status as measured by the level of physical disability (EDSS, patient-reported UKNDS), cognitive performance (SDMT), and fatigue (FSMC).
3. Stabilization of these measures indicates a sustained effectiveness of siponimod over 3 years in preventing further disability progression.
4. Patient characteristics and disease burden at baseline highlight the difficulty and importance of an early SPMS diagnosis in the heterogenous real-world population, allowing timely initiation of effective treatment to maintain functional reserve and competencies in daily living.

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INTRODUCTION

- 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]
- In the EU, siponimod, a selective sphingosine-1-phosphate receptor modulator, is approved 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 heterogenous. Thus, data from real world settings are mandatory to complement data obtained from RCTs.

OBJECTIVE

- The non-interventional AMASIA study aims to investigate the long-term effectiveness and safety of siponimod for the treatment of patients suffering from active SPMS in a real-world setting and provides insight into the impact on disease progression and quality of life as well as clinical routines in Germany.

METHODS

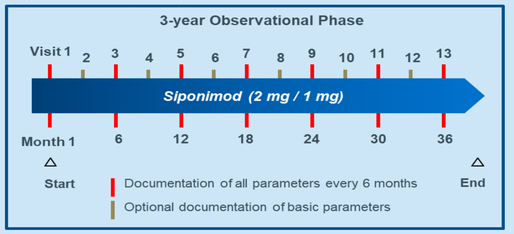
Study Design

- Multi-center non-interventional study in Germany, 670 siponimod-treated active SPMS patients are followed over 2-3 years
- Every 6 months, disability progression and changes in cognitive performance and fatigue are evaluated (**Figure 1**)

Assessments

- 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)
- Physician's perspective: Clinical Global Impression (CGI), progression questionnaire
- Socioeconomic factors: Multiple Sclerosis Health Resource Survey (MS-HRS)

Figure 1. Study design.



RESULTS

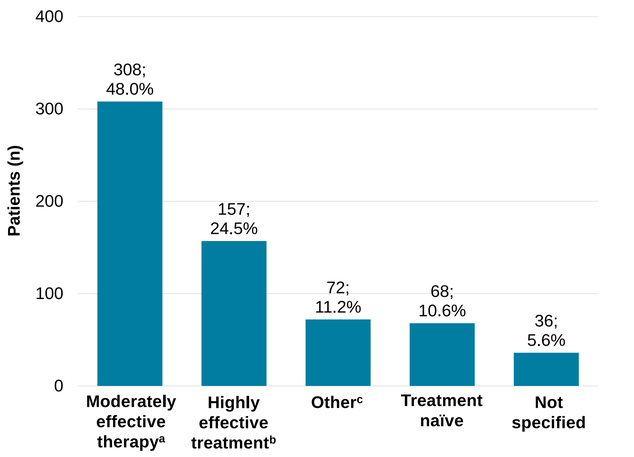
Study Population

- 641 patients were included in this analysis (cut-off date: 08-Dec-2023). Baseline characteristics are shown in **Table 1**.
- The majority of the study population is female (67.6%) with a mean (SD) age of 55 (8.4) years (**Table 1**).
- Before switching to siponimod, about half of all patients (48.0%) had received a moderately effective therapy and nearly one quarter of patients (24.5%) was treated with a highly effective therapy (**Figure 2**).
- About 11% of patients were treatment naïve at study start (**Figure 2**).

Table 1. Patient characteristics at baseline

Variable	AMASIA
Number of patients (n)	641
Age, n=641 (years) (mean ± SD)	54.8 ± 8.4
Gender, n=641 (female | male) (%)	67.6 | 32.4
Time since first MS diagnosis, n=573 (years) (mean± SD)	17.4 ± 9.4
EDSS, n=602 (score) (mean ± SD)	5.2 ± 1.5
SDMT, n=515 (score) (mean ± SD)	39.8 ± 13.1
Patients with relapse (past 24 months) (%)	45.2

Figure 2. Last therapy before siponimod treatment

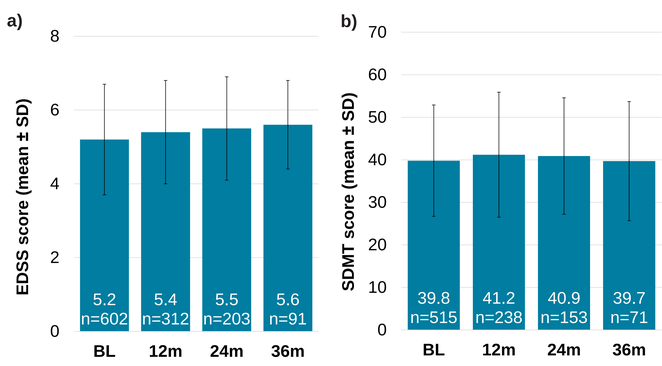


[a] Moderately effective treatment: interferons, dimethyl fumarate, teriflunomide, glatiramer acetate [b] Highly effective treatment: fingolimod, ocrelizumab, natalizumab, cladribine, alemtuzumab. [c] Other: mitoxantron, azathioprine, daclizumab, rituximab.

Disease Progression

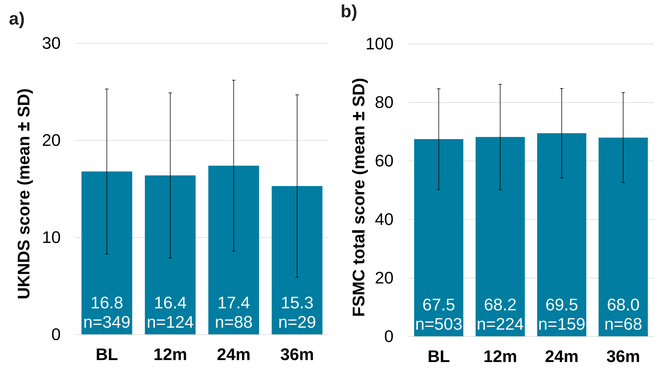
- Disease progression (EDSS, SDMT, UKNDS, FSMC) was monitored over 36 months.
- At baseline, AMASIA participants were already significantly impaired in the functional domains of disability and cognition as measured by EDSS (5.2 ± 1.5, **Figure 3. a**) and SDMT (39.8 ± 13.1, **Figure 3. b**).
- Mean EDSS and SDMT scores did not show clinically relevant changes from baseline (BL) until month 36, indicating a stable cognitive and general health status over 3 years of siponimod therapy.

Figure 3. a) EDSS score at baseline and after 12-, 24-, and 36 months b) SDMT score at baseline and after 12, 24, and 36 months



EDSS: Expanded Disability Status Scale; SDMT: Symbol Digit Modalities Test; BL: baseline; m: months; SD: standard deviation

Figure 4. a) UKNDS at baseline and after 12-, 24-, and 36 months b) FSMC at baseline and after 12, 24, and 36 months



UKNDS = United Kingdom Neurological Disability Scale; FSMC = Fatigue Scale For Motor And Cognitive Functions; BL: baseline; m: months; SD: standard deviation;

- Perception of disease burden was in accordance between physicians and patients as detected by UKNDS and FSMC.
- Disease burden at BL was reflected by UKNDS score of 16.8 ± 8.5 (**Figure 4. a**) and FSMC score of 67.5 ± 17.2 (**Figure 4. b**).
- UKNDS and FSMC data showed patient-reported stabilization of disease progression over 3 years on siponimod treatment.

Safety

- 642 patients were included in the safety set. 535 (83.3%) patients were affected by adverse events, 318 (49.5%) by serious adverse events. Three (0.5%) patients died (**Table 2**).

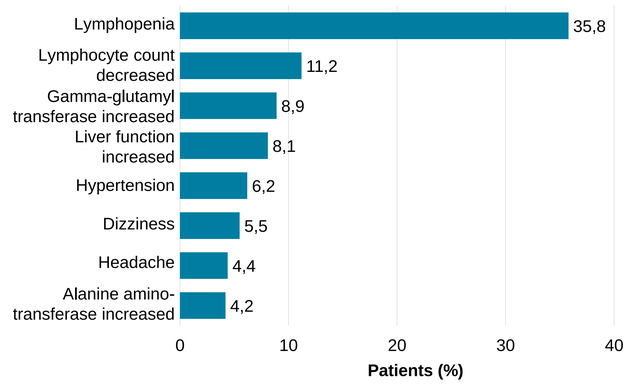
Table 2. Summary of adverse events (AEs), serious AEs and death

Number of patients with at least one event of the following types, n (%):	Total (N=642)
Adverse event (AE)	535 (83.3)
AE with suspected relationship to siponimod (ADR)	423 (65.9)
Serious adverse event (SAE)	318 (49.5)
Serious adverse event with suspected relationship to siponimod (SADR)	235 (36.6)
Death (i.e., outcome is fatal)[#]	3 (0.5)

#death were all classified as unrelated to siponimod.

- The most common adverse events with relationship to siponimod are shown in **Figure 5**.
- The top three common serious adverse events with relationship to siponimod are lymphopenia (22.7%), lymphocyte count decreased (4.8%) and leukopenia (3.3%).

Figure 5. Most frequent adverse events with suspected relationship to siponimod



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Disclosures

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